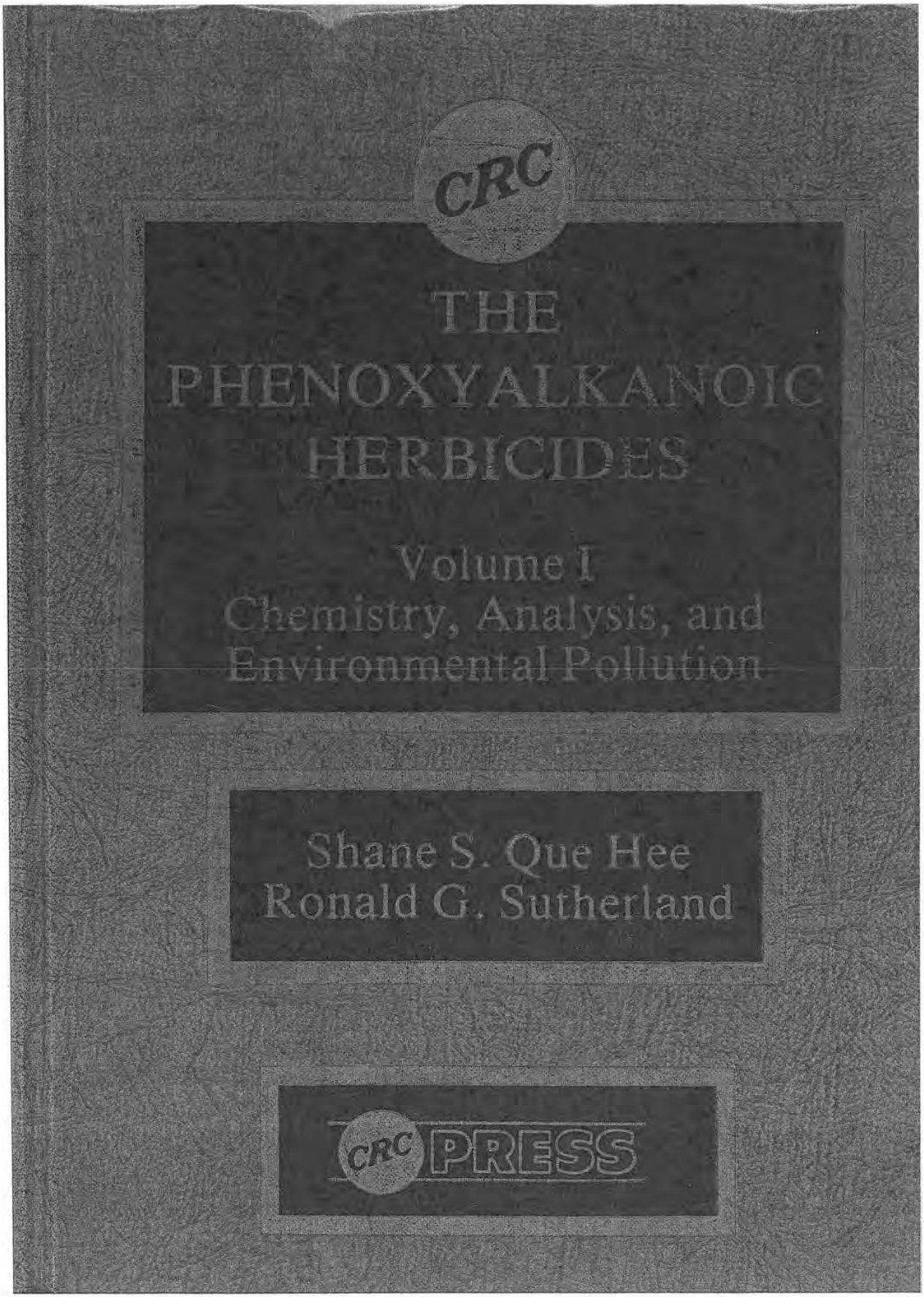


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THE PHENOMENAL KANOIC HERITAGE, Volume I

PRESS

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The Phenoxyalkanoic Herbicides

Volume I
Chemistry, Analysis, and Environmental Pollution

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FOREWORD

The present two-volume treatise on *The Phenoxyalkanoic Herbicides* by Drs. Shane S. Que Hee and Ronald G. Sutherland is a continuation of the Pesticide Series starting withe G. T. Brooks' *Chlorinated Insecticides* in 1974. Following the book on chlorinated insecticides, other specific topics having been covered include: *Organophosphorus Pesticides* by Eto; *Carbamate Pesticides* by Dorough and Kuhr; and *Controlled Release Pesticides Formulations* by Cardarelli.

It is especially pertinent at this time that Que Hee and Sutherland's book on phenoxyalkanoic herbicides be published. The recent action by the U.S. Environmental Protection Agency (February 28, 1979) to suspend most remaining uses for 2,4,5-T and Silvex has created a great interest to learn more about the chemistry, biology, and toxicology of these compounds as well as the chlorinated dioxin contaminants.

It is anticipated that subsequent volumes of the CRC Pesticide Series will cover other classes of herbicides, newer insecticides (e.g., synthetic pyrethroids), as well as pheromones and juvenile insect hormones. The editor welcomes suggestions of new topics and potential authors and encourages that interested readers correspond with him through the publisher.

Gunter Zweig, Ph. D.
Editor-in-Chief
CRC Series in Pesticide Chemistry

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THE EDITOR-IN-CHIEF

Gunter Zweig received his undergraduate and graduate training at the University of Maryland, where he was awarded the Ph. D. in biochemistry in 1952. Two years following his graduation, Dr. Zweig was affiliated with the late R. J. Block, pioneer in paper chromatography of amino acids. Zweig, Block, and Le Strange wrote one of the first books on paper chromatography which was published in 1952 by Academic Press and went into three editions. *Paper Chromatography* (1952) was also translated into Russian.

From 1953 till 1957, Dr. Zweig was research biochemist at the C. F. Kettering Foundation, Antioch College, Yellow Springs, Ohio, where he pursued research on the path of carbon and sulfur in plants, using the then newly developed techniques of autoradiography and paper chromatography. From 1957 till 1965, Dr. Zweig served as lecturer and chemist, University of California, Davis and worked on analytical methods for pesticide residues, mainly by chromatographic techniques. In 1965, Dr. Zweig became Director of Life Sciences, Syracuse University Research Corporation (research on environmental pollution), and in 1973 he became Chief, Environmental Fate Branch, Environmental Protection Agency in Washington, D.C. In 1980, he was appointed Senior Science Advisor in the same agency.

From 1953 till 1957, Dr. Zweig was research biochemist at the C. F. Kettering Foundation, Antioch College, Yellow Springs, Ohio, where he pursued research on the path of carbon and sulfur in plants, using the then newly developed techniques of autoradiography and paper chromatography. From 1957 till 1965, Dr. Zweig served as lecturer and chemist, University of California, Davis and worked on analytical methods for pesticide residues, mainly by chromatographic techniques. In 1965, Dr. Zweig became Director of Life Sciences, Syracuse University Research Corporation (research on environmental pollution), and in 1973 he became Chief, Environmental Fate Branch, Environmental Protection Agency in Washington, D.C.

During his government career, Dr. Zweig continued his scientific writing and editing. Among his works are (many in collaboration with Dr. Sherma) the now 11-volume series *Analytical Methods for Pesticides and Plant Growth Regulators* (published by Academic Press); the handbook series in chromatography for CRC Press, co-editor of *Journal of Toxicology and Environmental Health*; co-author of basic review on paper and thin-layer chromatography for *Analytical Chemistry* from 1968-1980; co-author of applied chromatography review on pesticide analysis for *Analytical Chemistry*, beginning in 1981.

Among the scientific honors awarded to Dr. Zweig during his distinguished career are the Wiley Award in 1977, Rothschild Fellowship to the Weizmann Institute in 1963/64; the Bronze Medal by the EPA in 1980.

Dr. Zweig has authored or co-authored over 75 scientific papers on diverse subjects in chromatography and biochemistry, besides being the holder of three U.S. patents.

At the present time (1980/81), Dr. Zweig is Visiting Scholar in the School of Public Health, University of California, Berkeley, where he is doing research on farmworker safety as related to pesticide exposure.

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PREFACE

This is the first of a two volume set detailing the properties, chemistry, analysis, environmental pollution, and biology of the herbicidal chlorinated phenoxyalkanoic acids and their compounds. It is strange that this is one of the first book of its kind for these compounds since they are the most widely used herbicides. Perhaps it is not too strange after all since *Chemical Abstracts*, *Biological Abstracts*, and *Index Medicus* list well over 50,000 entries, and the task of sifting and fusing this vast literature is (and was) gargantuan.

This first volume details the physical and chemical properties and environmental impact of the herbicidal chlorinated phenoxyalkanoic acids and related compounds, including contaminants. This book does not claim to be exhaustive in its coverage of the literature. We have elected to concentrate on the decade 1967 to 1980 inclusive, citing other important references when we deemed it necessary. We have endeavored to give overviews where possible, spiced with the appropriate detail. We have also tried to cite many foreign language sources in the hope of making the information accessible to scientists in all countries, and have cited the *Chemical Abstracts* reference for Eastern European, South American, and Asian sources.

There is a general paucity of information on the physical properties and chemistry of the phenoxys, and we have tended to go into more detail on these aspects than on other better known facets such as pollution and analysis. However, we have also presented methods for analysis in the hope this first volume can be used as a methods manual as well as a handbook for physical and chemical properties, and for pollution control. With regard to phenoxy residues, it is obviously futile to tabulate all of these since the list is literally endless. When necessary, we have referenced the reader for the appropriate sources. We have included sections on the fundamental principles of such properties as vapor pressure, droplet impingement and retentivity, adsorption etc. to make this a complete reference book.

We have also endeavored to suggest areas of profitable research potential.

The authors would like to thank Gail Gair for her excellent typing, as well as Mrs. Lois Carpenter for her typing contributions.

In addition, we would like to acknowledge the support of Dr. R. R. Suskind, Director, Institute of Environmental Health, Kettering Laboratory, University of Cincinnati, Ohio.

We wish to thank the Department of Biomedical Communications of the University of Cincinnati Medical Center for their expert artwork.

Shane S. Que Hee
Ronald G. Sutherland
January, 1981
Cincinnati, Ohio

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THE AUTHORS

Shane S. Que Hee, Ph.D., is Assistant Professor of Environmental Health at the University of Cincinnati Medical Center at Cincinnati, Ohio.

Dr. Que Hee received his training at the University of Queensland at St. Lucia, Australia receiving the B.Sc. degree in 1965 and the M.Sc. degree in 1971. He obtained his Ph.D. degree from the University of Saskatchewan at Saskatoon, Canada in 1976. He has been Assistant Professor at the University of Cincinnati since 1978.

Dr. Que Hee is a member of the American Association for the Advancement of Science, the American Association of University Professors, the American Chemical Society, and American Industrial Hygiene Association, the Weed Science Society of America, and the American College of Toxicology.

Dr. Que Hee is the author of more than 20 papers, mostly dealing with environmental pollution of the phenoxy herbicides and with bioluminescence. His current research interests are related to the environmental chemistry of pesticides and the detection and quantitation of chemicals in the workplace.

Ronald G. Sutherland, Ph.D., is Professor of Chemistry in the Department of Chemistry and Chemical Engineering at the University of Saskatchewan in Saskatoon.

Dr. Sutherland received his B.Sc. degree from Strathclyde University in 1959 and his Ph.D. from the University of St. Andrews in 1962. After postdoctoral experience at Columbia University and the California Institute of Technology, he joined the Chemistry Department of Queens College, the University of St. Andrews in Dundee (now the University of Dundee) in 1964. In 1967, he became associated with the University of Saskatchewan, and became Professor of Chemistry in 1974.

Dr. Sutherland is a member of the Chemical Society, the American Chemical Society, the Canadian Institute of Chemistry and a Fellow of the Royal Society of Chemistry.

Dr. Sutherland is the author of more than 80 papers. His major research interests are in organometallic chemistry, ultrasound, and in the chemistry and toxicology of herbicides.

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Chapter 1

PHYSICAL PROPERTIES OF HALOPHENOXYALKANOIC ACIDS

I. HISTORY

Nearly a century ago, Darwin speculated on the reasons why plants bend towards light while roots always grow downwards and concluded that some influence transmitted from the tips of roots or shoots was responsible. These "influences" are now known as growth hormones or auxins.[1]

These compounds promote growth by causing cells exposed to their influence to enlarge. Those obtained from pollen during fertilization are essential for the further development of the ovary. Indeed, fruits also require auxins to mature and to prevent them from falling from their twigs before they are ripe; pathological outgrowths, such as galls and various tumors, are characterized by high levels of hormones instead of the usual concentrations. Natural auxins were first isolated in 1934 by Kögl et al.[2] who later discovered heterauxin or auxin C, now known as indol-3-yl-acetic acid (IAA).

While research on growth hormones progressed slowly, the use of inorganics as herbicides flourished. Bonnet reported on the phytocidal effects of Bordeaux mixture and 6% copper sulfate against yellow charlock (*Sinapsis arvenis*) to the Agricultural Association at Rheims, France, December 12, 1896. Copper sulfate was the major herbicide from 1896 to 1911; sulfuric acid replaced it in importance from 1911 to 1933. Other inorganics used as herbicides were ferrous sulfate, copper nitrate, sodium nitrate, ammonium sulfate, calcium cyanamide, Kainit, sodium arsenite, sulfoarsenites, sulfoarsenates, sulfoxyarsenates, borax, boric acid, potassium perchlorate, sodium and potassium chlorate, ammonium thiocyanate, ammonium sulfamate, and cacodylic acid, the last one still being utilized. Long has written a comprehensive review on the use of inorganic herbicides before the 1930s.[4]

Although synergism seems to appear a modern concept, the phenomenon was first noted[5] in 1914 from a mixture of calcium cyanamide and Kainit. The use of organic compounds as weed-killers appears very natural today. The first organic herbicide, the sodium salt of 2-methyl-4,6-dinitrophenol (DNOC or Sinox), was first utilized in 1938 by Truffaut and Pastac,[6] who found it was readily absorbed by roots and acted foliarly as a contact herbicide. It is still used for preharvest desiccation of potatoes.

The separate but concurrent searches for plant hormones and better herbicides did not coalesce until the auxin properties of IAA were discovered in the mid-1930s, even though IAA had been synthesized by Fischer back in 1886.[7] Synthetic compounds related to IAA were applied to a wide range of plants by Zimmerman and Wilcoxon[8] in 1935, e.g., naphth-1-yl-acetic (NAA), naphth-2-yl-acetic, and naphth-2-yl-oxyacetic acids, but as rooting compounds rather than herbicides, and the crucial experiments concerning herbicidal activity towards dicotyledons were only done by Templeman et al.[9] and Nutman et al.[10] in Britain early in World War II. Subsequent tests showed that 2,4-dichlorophenoxy acetic acid (2,4-D) which had been synthesized by Pokorny[11] in 1941 on principles laid down by Holleman[12] in 1917 and 2-methyl-4-chlorophenoxy acetic acid (MCPA) were much better herbicides. The nitrophenols had the disadvantages of being too toxic, and because they did not penetrate the plant cuticle appreciably, acted primarily as contact herbicides. The work on IAA showed that the acetate side chain was essential for auxin behavior (indole itself was not an auxin), and once it had been shown that chlorinated phenoxy compounds could act as analogues for indolyl compounds, their lower toxicity and less polar nature led quickly to the suc-

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cessful demonstration of their herbicidal characteristics. During 1941 and 1942, these two British groups independently discovered and investigated the phytocidal effects of these plant-growth regulators. Nutman et al.,[10] based at the Rothamsted Experimental Station, found that 2-indol-yl-acetic acid and 1-naphthaleneacetic acid were phytotoxic at a dilution of one in ten million. The other group of workers, Slade et al.[9] at the Jealott's Hill Research Station, had been examining the effects of plant auxins since 1936. Their experiments in 1940 showed that 1-naphthylacetic acid at 25 lb/acre selectively killed charlock in an oat field,[13] while MCPA and 2,4-D were revealed to be selective killers of broad-leaved plants at extremely low doses (1 lb/acre). Both groups communicated their findings to the Secretary of the Agricultural Research Council of Great Britain in November 1942, but publication was not allowed until 1945.[9,10] Both teams then combined their efforts with those of G. E. Blackman, so that 1943 field trials fully vindicated the promise of MCPA and 2,4-D as selective herbicides.[9] Blackman,[36] in conjunction with a research team at the Imperial College of Science, London, found that many perennial weeds could also be controlled.

In 1942 in the U.S., Zimmerman and Hitchcock[15] reported that halogenated phenoxyacetic acids had marked physiological activity towards tomatoes, but it was not until 1944 that Hamner and Tukey[17] published a report on the selective herbicidal action of 2,4-D and 2,4,5-trichlorophenoxy acetic acid (2,4,5-T) on bindweed and on the superior effectiveness of 2,4,5-T as a brush-killer. The selectivity of 2,4-D on lawns was investigated by Marth and Mitchell.[14] Krause and Mitchell[16] also began experiments on 2,4-D and 2,4,5-T in 1943. Early in 1946, an exhaustive investigation of the herbicidal activities of 1100 synthetic growth-regulating compounds was entrusted to a team headed by Thomson et al.[57] at Camp Detrick, Md. In 1953, 2-(2,4,5-trichlorophenoxy) propionic acid (Silvex, fenoprop, or 2,4,5-TP) was shown[18] to be superior to 2,4,5-T for oak control in a Dow Chemical study. In 1956 (±)-2-(4-chloro-2-methylphenoxy) propionic acid (MCPP,Mecoprop) was reported[19] to be often herbicidal when other phenoxys were not. Whereas only 100,000 acres were treated with the phenoxys in the U.S. in 1946, several million were sprayed in 1947.[20] By 1949 about 10,000 tons of 2,4-D were manufactured.[3] Thus, the use of herbicides to kill unwanted weeds quickly accelerated in the 1950s.

Scientific research on herbicides until the 1960s largely concentrated on the phytocidal effects of the various halogenated phenoxyalkanoic compounds. It was found that inherently nonherbicidal analogues as gamma-(4-chloro-2-methylphenoxy) butyric acid (MCPB) and 2,4-dichlorophenoxyethylhydrogen sulfate (2,4-DES) were[21] converted by internal plant metabolism to the respective phenoxyacetic acids which then proceeded to show their herbicidal action. Powerful autoradiography techniques allowed labeled materials to be traced in the living plant,[22] so that translocation patterns in susceptible and resistant plants were thoroughly studied. However, analytical techniques at that time were not sensitive nor specific enough for precise separation, identification, or quantification of microquantities of plant residues and metabolites. Even today, the latter have not been fully characterized because of the analytical difficulties. In the 1950s, the available spectroscopic methods, UV visible and IR, were sensitive at best to the microgram level, and the means of separating complex mixtures were only then coming into common use. Gas liquid chromatography was introduced by James and Martin[23] in 1952, column chromatography by Martin and Synge[24] in 1941, thin layer chromatography by Stahl[25] in 1958, gel filtration chromatography by Porath and Flodin[26] in 1959. If the 1950s were the years of the development of chromatographic methods, then the 1960s were the time when researchers reaped the rewards of these new techniques, amidst a boom in the funding for scientific research. The 1960s also saw the advent of electron capture gas chromatography (EC/GC),[27] gas

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chromatography-mass spectometry (GC/MS),[28] high-speed liquid chromatography (HPLC),[29] and fluorescence detection,[30] as well as the appearance of halogen,[31] nitrogen,[32,33] phosphorus,[33] sulfur,[33] and flame photometric[34] detectors, all essentially refinements of the initiatives of the 1950s. The EC/GC technique, particularly, revolutionized the speed, sensitivity, and precision of the analysis of chlorinated and brominated compounds. Thus, much of the 1960s and early 1970s were devoted to the exploitation of these refined techniques.

With hindsight, one can now say that the 1950s and 1960s saw much data accumulated which was misleading, especially in the realms of residue analysis and in toxicity studies on nonplant targets. Thus, it has only been recently recognized that many quoted residue levels are minimal values because conjugates were not also quantitated. The presence of extremely potent contaminants such as the chlorinated *p*-dibenzodioxins[35] went unrecognized, as did certain synergistic and antagonistic effects. It is instructive to speculate why, for example, the dioxin situation remained undetected for so long, especially since the available analytical methods were sensitive enough to detect dioxins in large batches of 2,4,5-T. It was a mystery to researchers of that time that 2,4,5-T should be so much more toxic than 2,4-D and that this toxicity was often variable from one 2,4,5-T sample to another.[35] Further, classical thinking in analytical chemistry contributed to the confusion, since many analysts maintained that once an analysis accounted for all the active ingredients, then the system was as good as completely defined, a view in accordance with the law of diminishing returns. Thus, it was assumed that the effects of the major components, supposedly the most toxic, would "swamp" out those of the minor ones, and the toxicologist had to assume the "unknown" part of the mass balance contained compounds no more toxic than the active ingredients and that no synergism was occurring. The dioxin contaminants in 2,4,5-T have turned out to be some of the most teratogenic and acutely toxic agents known to man. These observations demonstrate the importance not only of specific methods of analysis for all constituents of commercial formulations, but also reveal that biological activity is not necessarily a dose-dependent phenomenon for materials which may contain varying traces of the formulating route from sample to sample, especially if different synthetic routes are used for commercial production and if quality control procedures differ.

The capability to detect trace amounts at the picogram level inevitably provided ammunition to fuel the public furor created by Rachel Carson in *Silent Spring*[37] and to verify the persistence of the insecticide, *p,p'*-DDT, all at the urging of a pollution-conscious society and government.

There is another trend which bears discussion. Science is becoming ever more compartmentalized and specialized. Thus, many biological workers cheerfully accept manufacturers' assurances of a stated purity of their starting chemicals, whether the compounds are formulated materials or reagent-grade chemicals, and often try to correlate toxic effects with the dose applied, and often the two do not agree in a reproducible way. On the other hand, many analytical chemists desire only to work in terms of well-defined systems and avoid experimentation concerning biological systems, whether from point of view of chemical analysis or defining biological effects of the chemicals they separate. The dioxin story has forcefully shown that biologists and chemists must collaborate to ensure that potential threats to the biosphere can be studied as efficiently as possible.

In spite of all that is known about the phenoxyalkanoic acids, the actual molecular processes responsible for their herbicidal action are still unknown despite over 40 years of research. The same statement can be made about the mode of action of the natural auxin, IAA. As analytical methods evolve to analyze large molecules in sensitive and specific ways, this major problem, too, may be solved.

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II. NOMENCLATURE AND TRADE NAMES

This section lists the more common phenoxyalkanoic acids and their commercial formulations and manufacturers. The following acronyms will be used:

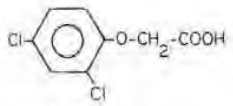
Registration of common names and nomenclature

ANSI	American National Standards Institute
BSI	British Standards Institution
IUPAC	International Union of Pure and Applied Chemistry
WSSA	Weed Science Society of America

Manufacturers and addresses

Ansul	The Ansul Company, 1 Stanton St., Marinette, Wis. 54143
Boots	The Boots Pure Drug Company, Station Street, Nottingham, England
Chipman	Chipman, Division of Rhodia, Inc., 120 Jersey Avenue, New Brunswick, N. J. 08903
CIBA-GEIGY	Research and Development Department, Agricultural Division, CIBA-GEIGY Corp., P.O. Box 11422, Greensboro, N.C. 27409
Diamond S.	Diamond Shamrock Corporation, Commercial Development Agricultural Chemicals Division, 1100 Superior Ave., Cleveland, Ohio 44114
DOW	The Dow Chemical Company, Midland, Mich. 48640
DuPont	E. I. duPont de Nemours and Company, Biochemicals Department, Wilmington, Del. 19898
Fisons	Fisons Pest Control, Ltd., Harston, Cambridge, England
I.C.I.	I.C.I. Plant Protection, Ltd., Fernhurst, Haslemere, Surrey, England
Kanesho	Kanesho Company, Ltd., Room 333, Marunouchi Building, Maunouchi, Chiyoda-ku, Tokyo, Japan
Mallinckrodt	Mallinckrodt Chemical Works, 360 North 2nd St., St. Louis, Mo. 63160
M&B	May and Baker, Ltd., Room 10, Dagenham, Essex 7XS, England
Merck	E. Merck, AG, 61 Darmstadt, Frankfurter Strasse 250, Germany
Nor-Am	Nor-Am Ag Products, 11710 Lake Avenue, Woodstock, Ill. 60098
Pepro	Pepro, B.P. 139, 69 Lyon, R.P. - France
Rhone-Poulenc	Rhone-Poulenc, Boite Postale N753.08, Paris - 8e - France
Stauffer	Stauffer Chemical Company, Agricultural Chemical Division, Westport, Conn. 06880
Transvaal	Transvaal Inc., P.O. Box 69, Marshall Road, Jacksonville, Ark. 72076
Union Carbide	Union Carbide Agricultural Product Company, Inc. South Charleston, W.Va.
Uniroyal	Uniroyal Chemical, Agricultural Chemical Division, Amity Road, Bethany, Conn. 06525
U.S. Borax	U.S. Borax Research Corporation, 3075 Wilshire Blvd., Los Angeles, Calif. 90010
Velsicol	Velsicol Chemical Corporation, 341 East Ohio Street, Chicago, Ill. 60611
Vineland	Vineland Chemical Company, West Wheat Road, Vineland, N.J. 08360

The information presented here comes from the *Herbicide Handbook of the Weed Science Society of America*, 4th edition, 1979; *Agricultural Chemicals: Book II — Herbicides*, 1975-1976 Revision, by W. T. Thomson, and the *Pesticide Manual*, 2nd edition, British Crop Protection Council, Boreley, Worcester, England, 1971.

	Common name (BSI:WSSA)	IUPAC name
	2,4-D (2,4-Dichlorophenoxy) acetic acid	(2,4-Dichlorophenoxy) ethanoic acid

$C_8H_6Cl_2O_3$

MW:221.0

Origin: Amchem, 1942 (U.S.)

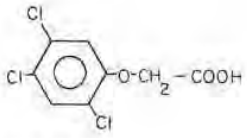
Bayer EX1026 (Part 1 of 2)

Amine salts	Manufacturer
1. Dimethyl (2,4-D amine)	
Chipman 2,4-D amine, No. 4	Chipman
DMA-4	DOW
Weed-Rhap A-4D	Transvaal
Weedar 64	Union Carbide
2. Dodecyl/tetradecyl (oil-soluble amine salt)	
Emulsamine E-3	Union Carbide
3. N-oleyl-1,3-propylenediamine (oil soluble salt)	
Dacamine (2,4,5-T/2,4-D)	Diamond S.
Esters	
1. Butoxyethanol ester (low volatile)	
Weedone 638 (2,4-D acid/ester)	Union Carbide
Weedone LV-4	Union Carbide
2. Butyl (high volatile)	
Chipman 128 (mixed butyl)	Chipman
3. Octyl (low volatile)	Chipman
Chipman 2,4-D Low Volatile Ester 4L	Chipman
Chipman 96	Chipman
Esteron® 99 Concentrate	DOW
Weed-Rhap LV 4D	Transvaal
Mixtures with other herbicides	
Aniten D (flurenol-*n*-butyl ester/2,4-D)	E. Merck (Celamerck)
Banvel D (dicamba/2,4-D)	Velsicol
DB Granular Mixture (borax/2,4-D)	U.S. Borax
Dacamine (2,4,5-T/2,4-D)	Diamond S.
Dinoxol (2,4,5-T/2,4-D)	Union Carbide
Envert 171 (2,4-DP/2,4-D esters)	Union Carbide
Fenac Plus ([2,3,6-trichlorophenyl]acetic acid/2,4-D)	Union Carbide
Iso-Cornox Plus (MCPP/2,4-D)	Boots
Knox Weed (EPTC/iso-octyl ester 2,4-D)	Stauffer
Lornox Plus (MCPP/2,4-D)	Boots
MAD (MSMA/2,4-D)	Diamond S
Mecopar (MCPP/2,4-D)	Nor Am
Reglone (diquat/2,4-D)	I.C.I.
Super Crab E. Rad 2 (AMA/2,4-D)	Vineland
Tordon 101 (picloram/2,4-D amine salt)	Dow
Trex-San (MCPP/dicamba/2,4-D)	Mallinckrodt
Vipar (diethanolamine salt MCPP/2,4-D)	Vineland
Weedmaster (dicamba/2,4-D)	Velsicol
Weedone 2,4-DP, Weedone 170 (2,4-DP/2,4-D esters)	Union Carbide

Other names

Amoxone, Aqua Kleen, Crotilin, Dacamine, DMA-4, Esteron, Formula 40, Hedonal, Krotiline, Phenox, Tributon, Verton, Weed-B-Gon, Weedar-64, Weedone

Common name (BSI, WSSA)	IUPAC name
2,4,5-T (2,4,5-Trichloro-phenoxy) acetic acid	(2,4,5-Trichlorophenoxy) ethanoic acid



$C_8H_5Cl_3O_3$

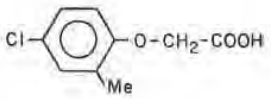
MW: 255.5

Origin:

Bayer EX1026 (Part 1 of 2)

	Manufacturer
Amine salts	
Amine 4T	Diamond S.
Brush - Rhap A-4T	Transvaal
Veon 245	Dow
Weedar® 2,4,5-T	Union Carbide
Esters	
Brush - Rhap LV-OXY-4T	Transvaal
Esteron® 245	Dow
LO-VOL 4T	Diamond S.
2,4,5-T Low Volatile Ester 6L	Chipman
Weedone® 2,4,5-T	Union Carbide
Mixtures with other herbicides	
Dinoxol (2,4-D/2,4,5-T)	Union Carbide
Semparol 1167 (Atrazine/MCPP/2,4,5-T)	CIBA-GEIGY
Tordon 155 (picloram/2,4,5-T esters)	Dow

Other names
Dacamine 4T, Envert-T, Phortox, Reddon, Tippon, Tributon, Trinoxol, Veon



Common name (BSI, WSSA)	IUPAC name
MCPA, MCP (2-Methyl-4-chlorophenoxy) acetic acid	(2-Methyl-4-chlorophenoxy) ethanoic acid

$C_9H_9ClO_3$

MW: 200·6

Origin: Plant Protection Ltd., England, 1945

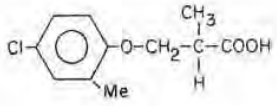
	Manufacturer
Amine salts	
Dow MCP Amine Weed Killer	Dow
Rhomene	Chipman
Esters	
Chiptox	Chipman
Rhonox	Chipman
Sodium salt	
Weedar Sodium MCPA	Union Carbide
Mixtures with other herbicides	
Aniten (fluorenol-*n*-butyl ester/MCPA)	E. Merck A. G.
Banlene Plus (Dicamba/mecoprop/MCPA)	Fisons
Bencornox (Dicamba/MCPA)	Boots
Brominal, Brominal Industrial, Brominal M (Canada) (bromoxynil/MCPA)	Union Carbide
Brominal Plus (bromoxynil/MCPA)	Union Carbide
Bronate (bromoxynil/MCPA)	Chipman
Buctril F (bromoxynil/MCPA)	Chipman
Cambilene (Dicamba/TBA/mecoprop/MCPA)	Fisons
Fisons 18-15 (TBA/MCPA)	Fisons
Legumex-DB (2,4-DB/MCPA)	Fisons
Ley-Cornox (Benazolin/2,4-DB/MCPA)	Boots
Ley-Cornox HN (benazolin/MCPB/MCPA)	Boots
Mondak (dicamba/MCPA)	Velsicol
New Legumex (MCPB/MCPA)	Fisons
Razol (dicamba/mecoprop/MCPA)	Fisons
Tri-Cornox (benazolin/dicamba/MCPA)	Boots
Tri-Cornox Special (benazolin/dicamba/2,4-DP/MCPA)	Boots

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Other names
Agritox, Bine-trol, Cornox-M, Dikotex, Kilsem, Krezone, Linormone, Mephanac, Metaxon, Methoxone, Raphone, Rhomene, Trasan, Zelan.

Common name
Mecoprop (WSSA)
MCPP, CMPP

IUPAC name
2-(2-Methyl-4-chlorophenoxy) propionic acid



$C_{10}H_{11}ClO_3$

MW:214.6

Origin: The Boots Company Ltd., 1957

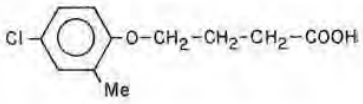
As sole active ingredient	Manufacturer
Iso-Cornox 64	Boots
Vipex	Vineland

Mixtures	
Banlene Plus (dicamba/MCPA/MCPP)	Fisons
Cambilene (dicamba/TBA/MCPP/MCPA)	Fisons
DM-68 (DNBP/MCPP)	Pepro
Iso-Cornox Plus (2,4-D/MCPP)	Boots
Lornox Plus (2,4-D/MCPP)	Boots
Lumetron 2412 (Gesaran/Simazine/MCPP)	CIBA-GEIGY
Mecopar (2,4-D/MCPP)	Nor Am
Razol (dicamba/MCPA/MCPP)	Fisons
Semparol 1167 (Atrazine/2,4,5-T/MCPP)	CIBA-GEIGY
Trex San (dicamba/2,4-D/MCPP)	Mallinckrodt
Vipar (diethanolamine salts (2,4-D/MCPP)	Vineland

Other names
CMPP, Kil-prop, Liranox, Mecoper, Mecopex, Mepro, Methoxone, Runcatex

Common name
MCPB (WSSA)

IUPAC name
4-(2-Methyl-4-chlorophenoxy) butyric acid



$C_{11}H_{13}ClO_3$

MW:228.5

Origin: May and Baker Co., England, 1955

As sole active ingredient	Manufacturer
Can-Trol	Chipman
Thistrol	Union Carbide

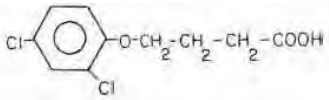
Mixtures	
Ebiden (dichlobenil/PCP-Na/MCPB)	Kanesho

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Legurame (carbetamide/MCPB)	Rhone Poulenc
Ley-Cornox HN (benazolin/MCPA/MCPB)	Boots
New Legumex (MCPA/MCPB)	Fisons

Other names
Bexane, Legumex, MCP-Butyric, Thitrol, Tritrol, Tropotox, Trotox

Common name	IUPAC name
2,4-DB (BSI, WSSA)	4-(2,4-Dichlorophenoxy) butyric acid



$C_{10}H_{10}Cl_2O_3$

MW:249.1

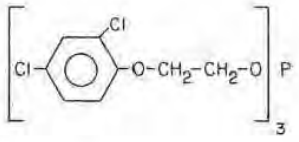
Origin: May and Baker, Inc., England, 1957

As sole active ingredient	Manufacturer
Butoxone Amine	Chipman
Butoxone Ester	Chipman
Butoxone SB	Chipman
Butyrac 118 (Amine Salt)	Union Carbide
Butyrac 175 (Amine Salt)	Union Carbide
Butyrac Ester	Union Carbide

Mixtures	
Legumex-DB (MCPA/2,4-DB)	Fisons
Ley Cornox (Benazolin/MCPA/2,4-DB)	Boots

Other names
2,4-D Butyric, Embutox

Common name	IUPAC name
2,4-DEP (WSSA)	Tris[2-(2,4-dichlorophenoxy) ethyl] phosphite



Tris form

$C_{24}H_{21}Cl_6O_6P$

MW:649.1

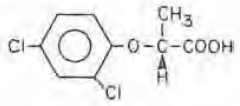
Origin: Uniroyal

As sole active ingredient	Manufacturer
Falone	Uniroyal
Falodin	Uniroyal

Mixtures	
(Dinoseb/2,4-DEP)	Uniroyal

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Common name	IUPAC name
Dichlorprop (WSSA), 2,4-DP	2-(2,4-Dichlorophenoxy) propionic acid



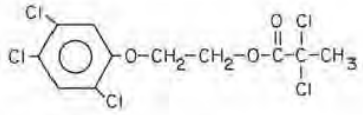
$C_9H_8Cl_2O_3$

MW: 235.1

Origin: Amchem, 1954 (now Union Carbide)

As sole active ingredient	Manufacturer
Nearly always coformulated	
Mixtures	
Envert 171 (2,4-D/2,4-DP esters)	Union Carbide
Tri-Cornox Special (benazolin/dicamba/MCPA/2,4-DP)	Boots
Weedone 2,4-DP (2,4-D/2,4-DP esters)	Union Carbide
Weedone 170 (2,4-D/2,4-DP esters)	Union Carbide

Common name	IUPAC name
Erbon (ANSI, WSSA)	2-(2,4,5-Trichlorophenoxy) ethyl-2,2-dichloropropionate



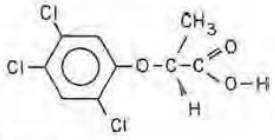
$C_{11}H_9Cl_5O_3$

MW: 366.5

Origin: Dow, 1956

As sole active ingredient	Manufacturer
Erbon 4	Dow
Erbon R	Dow
Other name	
Baron	

Common name	IUPAC name
Silvex (WSSA) fenoprop (BSI)	2-(2,4,5-Trichlorophenoxy) propionic acid



$C_9H_7Cl_3O_3$

MW: 269.5

Origin: Dow, 1952

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As sole active ingredient	Manufacturer
Kuron® (low-volatile esters)	Dow
Weedone® 2,4,5-TP (low-volatile esters)	Union Carbide

Other names
2,4,5-TP, Fenormone, Garlon, Kurosal, Propon

III. THE STRUCTURE OF HALOPHENOXYALKANOIC ACID COMPOUNDS

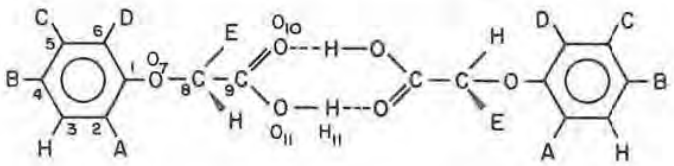
A. Free Acids

Recent years have seen the active interest of at least one X-ray crystallographic group in the structure of various phenoxyacetic acids.[39-42,44] The bond lengths and angles as well as the dimensions of the crystallographic unit cells are presented in Tables 1, 2, and 3, respectively. Noting that *o*-chlorophenoxyacetic acid (2-CPA) and 2,4,6-trichlorophenoxyacetic acid (2,4,6-T) are not auxins, the following conclusions can be made:

1. The free acids all form dimers held together by van der Waals' interactions by H-bonds of approximately the same length, approximately 268 pm, apart from the 2-CPA (approximately 245 pm).
2. There are few clear-cut differences in the bond lengths between corresponding atoms of nonherbicidal and herbicidal members (see Table 1). The average length for the C_5-C_6 bond in herbicidal members is approximately 160.1 pm, compared with 136.0 pm with that for nonauxins. However, the latter figure includes the very low 130.2-pm value for 2-CPA, and the length for 2,4,5-T and 2,4,6-T is the same. The bond lengths of C_6-H_6 do show variations in that the bond for Silvex (100 pm) and 2,5-D (97 pm) are much shorter than for 2,4-D and 2,4,6-T. There is one clear-cut difference. The C_8-C_9 bond length does appear to be shorter for nonauxins (<150 pm) than for auxins (151 to 152 pm).
3. The same nondiscriminating differences between herbicidal and nonherbicidal members can be discerned in the corresponding bond angles (see Table 2). The steric hindrance in 2,4,6-T is clearly evident, and the aromatic rings of 2,4,5-T and MCPA are much flatter than the others.
4. Consideration of the crystallographic systems for each does reveal some differences (see Table 3). All but the 4-CPA acid fall into the triclinic system, Space Group $P\bar{1}$, while 2-CPA acid belongs to the monoclinic system. The angle between the normals to the planes of the benzene ring and the carboxy groups varies widely. The angles for 2,4,6-T and 2,4,5-T are much lower than the rest. However, even though the dihedral angles of 2,4-D, 2,5-D, and Silvex are similar, that for 2,4,5-T is 4 to 15°; this means the 2,4,5-T dimer has all atoms, except the methylene group lying approximately in a plane — a behavior similar to that shown by most other substituted aromatic carboxylic acids. In addition, the benzene rings of 2,4-D, 2,5-D, and Silvex do not lie on top of one another.
5. The distance between the O^- of the carboxyl group and the fractional positive charge induced on a specific ring C is 420, 429, 417, and 428 pm for 2,4-D, 2,4,5-T, 2,5-D, and 2,4,6-T, respectively, compared to 412 pm for IAA.
6. For comparison with most other carboxylic acids:[46]

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Table 1
BOND LENGTHS IN pm BETWEEN THE DESIGNATED ATOMS FOR SOME PHENOXYALKANOIC ACIDS WHERE:



	A	B	C	D	E
2,4-D	Cl	Cl	H	H	H
2,4,5-T	Cl	Cl	Cl	H	H
2,5-D	Cl	H	Cl	H	H
Silvex	Cl	Cl	Cl	H	CH_3
2-CPA	Cl	H	H	H	H
2,4,6-T	Cl	Cl	H	Cl	H

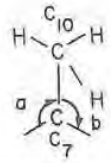
	Interatomic distances (pm)					
Bonds	2,4-D[28,39]	2,4,5-T[40]	2,5-D[41]	Silvex[42]	2-CPA[43]	2,4,6-T[44]
C_3–A	174.1	172.6	175.3	173.3	174.4	172.6
C_4–B	174.1	173.1	101.0	173.1	—	174.0
C_5–C	100.0	173.4	174.6	172.5	—	106.0
C_6–D	112.0	115.0	97.0	100.0	—	173.4
C_8–E	109.0	93.0	108.0	151.5	107.0	107.0
C_3–H_3	103.0	103.0	95.0	109.0	—	107.0
C_8–H_8	106.0	93.0	108.0	101.0	107.0	106.0
C_1–C_2	139.0	139.1	139.6	139.9	145.2	139.4
C_2–C_3	138.4	138.3	135.2	137.2	131.2	139.5
C_3–C_4	139.5	139.2	135.5	137.6	136.8	136.1
C_4–C_5	136.4	137.5	138.5	137.9	141.3	138.5
C_5–C_6	141.3	140.1	137.5	138.8	130.2	140.2
C_6–C_1	139.7	139.8	137.3	137.7	138.5	136.5
C_1–O_7	136.5	136.9	136.0	136.9	132.2	137.8
O_7–C_8	142.3	141.7	—	143.8	147.2	143.5
C_8–C_9	152.0	151.7	149.1	151.0	140.7	148.8
C_9–C_{10}	121.7	121.3	120.8	121.3	125.2	123.5
C_9–O_{11}	130.4	130.1	132.5	131.1	131.6	126.2
O_{11}–H_{11}	103.0	118.0	117.0	102.0	—	103.0
O_{11}–H_{11}–O_1	263.2	268.9	266.8	264.5	245.1	268.6
Average C–C ring Length	139.1	139.0	137.3	138.2	137.2	138.4
In E (Silvex)						
C_{Me}–H_1	—	—	—	86.0	—	—
C_{Me}–H_2	—	—	—	113.0	—	—
C_{Me}–H_3	—	—	—	99.0	—	—

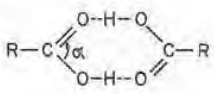
Bayer EX1026 (Part 1 of 2)

Table 2

BOND ANGLES IN DEGREES BETWEEN THE DESIGNATED ATOMS ABOVE TABLE 1 FOR PHENOXYALKANOIC ACIDS. THE DIHEDRAL L REFERS TO THE ANGLE BETWEEN THE NORMALS TO THE BENZENE RING AND THE CARBOXYL GROUP

	Bond angles (°)					
Angles	2,4-D[36,39]	2,4,5-T[44]	2,5-D[41]	Silvex[42]	2-CPA[43]	2,4,6-T[44]
$C_6-C_1-C_2$	119.1	119.8	117.1	118.8	121.0	—
$C_1-C_2-C_3$	122.2	121.1	121.9	120.0	122.6	—
$C_2-C_3-C_4$	117.3	119.5	121.7	119.8	113.1	—
$C_3-C_4-C_5$	122.7	119.5	117.0	120.9	126.2	—
$C_4-C_5-C_6$	119.1	121.9	122.4	120.0	119.9	—
$C_5-C_6-C_1$	119.6	118.1	119.9	118.8	116.7	—
$C_9-O_{11}-H_{11}$	111.5	114.8	—	111.9	—	115.9
$O_{10}-C_9-O_{11}$	123.1	124.4	123.8	124.1	125.3	126.2
$A-C_2-C_1$	118.9	119.9	117.1	119.5	122.2	139.4
$A-C_2-C_3$	118.8	119.1	121.0	119.7	115.2	139.5
$B-C_4-C_3$	117.6	119.0	—	118.7	—	136.1
$B-C_4-C_5$	119.6	121.6	—	121.5	—	138.5
$C-C_5-C_4$	—	121.4	118.8	120.9	—	—
$C-C_5-C_6$	—	116.6	118.7	118.8	—	—
$D-C_6-C_1$	—	—	—	—	—	136.5
$D-C_6-C_5$	—	—	—	—	—	140.2
$C_2-C_1-O_7$	116.2	116.1	117.8	119.7	116.9	137.8
$C_6-C_1-O_7$	124.7	124.0	125.1	125.5	122.1	136.5
$C_1-O_7-C_8$	118.8	117.0	118.9	118.3	115.5	137.8
$O_7-C_8-C_9$	111.1	106.7	111.9	110.4	107.0	107.0
$C_8-C_9-O_{10}$	123.2	122.9	124.1	123.9	121.4	115.9
$C_8-C_9-O_{11}$	112.2	112.7	112.0	111.9	113.2	126.2
In Silvex E						
a	—	—	—	105.0	—	—
b	—	—	—	109.4	—	—
Dihedral angle	85.23	4.15	81.2	77.8	6.6	32.03





α : 122°

R—C : 146 → 154 pm

C=O : 112 → 126 pm

C—O : 126 → 137 pm

O—H : 261 → 264 pm

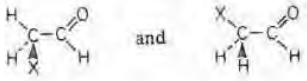
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Table 3
CRYSTALLOGRAPHIC CELL DIMENSIONS AND DENSITIES OF THE PHENOXYALKANOIC ACIDS

Cell dimensions	2,4-D[38]	2,4,5-T[40]	2,5-D[41]	Silvex[42]	2-CPA[43]	2,4,6-T[44]	4-CPA[56]
a (pm)	775.7	1089.5	891.7	1106	760.2	425.0	714
b (pm)	854.3	684.8	754.8	726.3	2216.4	862.8	744
c (pm)	912.2	683.8	751.5	725.5	532.8	1427.5	897
α (°)	103.54	81.33	111.72	101.2	—	97.58	88°26′
β (°)	89.39	78.90	77.41	104.5	114.3	73.24	120°40′
γ (°)	127.38	83.04	102.90	99.1	—	101.17	94°03′
D (g/cm^3)	1.597	—	—	1.66	1.523	1.73	1.498

In solution, dimers still predominate. The O–H group is usually *cis* and is more stable than the *trans* configuration by 2 kcal/mol. The barrier to rotation is approximately 11 kcal/mol. The C–C bond next to the C=O is shorter than expected, suggesting some sp^2 hybrid character. Its strength is about 55 kcal/mol. The sp^2 character in the C-C bond increases as the R group gets smaller. The bond length values for the herbicidal acids suggest less sp^2 character than for the nonherbicidal members.

There appear [47-49] to be equal amounts of

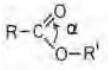


Thus, acids which are not sterically hindered should have an R group and the carbonyl O eclipsed. For sterically hindered acids, the H and the carbonyl O will be eclipsed instead.

The H bond energies appear to be independent of R group with energies around 6 to 7 kcal/mol.[49]

B. Esters

Unfortunately, there have been no crystallographic studies done on the crystalline esters, e.g., methyl esters of 2,4-D, 2,4,5-T, Silvex, etc.; however, the only real differences in bond lengths and angles should be in the ester group geometry. Thus, as above,[46]



C=O : 122 pm

C—O : 136 pm

α : 124°

The R group is *cis* (the internal rotation barrier for a methyl group is 1.2 kcal/mol). The dipole moment O to C is expected to range from 1.7 to 1.9 D. Theoretically, *cis* esters should be 1.53 D, and *trans* should be 3.53 D.[50] As the R group gets smaller, the C–O bond has more sp^2 character, e.g., when R = H, the C–O bond has 20% double bond character, but the C=O bond does not lengthen.[50,51] Resonance energies usually range from 13 to 18 kcal/mol, with no free rotation allowed around C–O.[52]

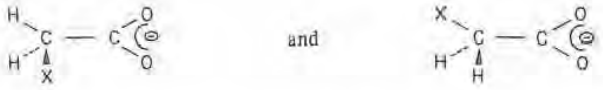
C. Salts

Again, no crystallographic studies have been done on the alkali or amine salts of the halogenated phenoxyalkanoic acids.

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1. Alkali Salts

It might be expected that the C–O bond lengths in the carboxylate anion should be equal, and that there should be free rotation of the αC to the carbonyl O. However, the latter is not generally observed,[53] so that there are equal amounts of



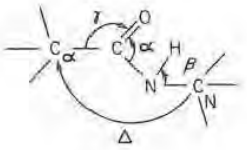
2. Amine Salts

Table 4 summarizes the kind of interatomic distances expected for various amine salts.[54] This data is expected to hold for the various amine salts formed by the halogenated phenoxyalkanoic acids.

D. Amides

Again, no structural data is available. However, only the amide link should be the major difference, with the geometry of the ring remaining constant and only the geometry around the αC to the carbonyl group being affected.

In general[55]



C_α—C	: 152 pm	α	= 134°
C=O	: 124 pm	β	= 115°
C—N	: 134 pm	γ	= 124°
N—H	: 45 pm	Δ	= 115°
N—C_N	: 144 pm		

Thus, C_O, C_N and N are coplanar, but the H on N is not. The C–N rotation is slow, E_a ~20 kcal/mol, and there is much double bond character in C–N. The H bonding distances are in Table 4.

IV. SELECTED PHYSICAL PROPERTIES

A. Melting Behavior

The mps and bps of some of the chlorinated phenoxyacetic acids, esters of 2,4-D, amine salts and amides of 2,4-D, esters and amine salts of 2,4,5-T, amides of amino acids of 2,4-D, are presented in Appendixes 1, 2, 3, 4, and 5, respectively. Appendix 6 lists the data for some miscellaneous compounds.

1. Free Acids (Appendix 1)

All the pure acids are white and odorless, and the mp rises (Appendix 1.1) with the degree of chlorination of the aromatic ring. The mps of 2,4-D and 2,4,5-T given by Pokorny in 1941 upon their first synthesis were recorded[11] as 138 and 153°C, but have been revised to 140.5 ± 0.5 and 157.5 ± 0.5, respectively.[58] There is even a report in the literature that a mp of 143.9 ± 1.0°C is attained when 2,4-D is recrystallized from a solution containing a detergent.[59] The generally quoted mp range is 1.0°C.[60] Synerholm and Zimmerman[61] obtained mps of 139.5 ± 0.5, 154.5 ± 0.5, and 177.5 ± 0.5 for 2,4-D, 2,4,5-T and Silvex, respectively.

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Table 4
SOME INTERATOMIC DISTANCES
EXPECTED FOR AMINE SALTS

A–H – – B	A–H type	A–B dist (pm)	Van der Waals' H–B distance (pm)
O–H – – N	All O–H	280 ± 9	305
+			
N–H – – O	Ammonium	288 ± 13	305
N–H – – O	Amide	293 ± 10	305
N–H – – O	Amine	304 ± 13	305
N–H – – H	All N–H	310 ± 13	330

Little work has been published on the differential thermal analysis (DTA) or differential scanning calorimetry (DSC) of the free acids. These techniques are used to assess the phase transition behaviour and thermal stability of compounds. As might be expected, 2,4-D and 2,4,5-T have received the most scrutiny. DTA of 4- to 100-mg samples using a dynamic argon furnace[62] atmosphere and heating at 10 ± 1°C/min elicited[63] endothermal peaks for 2,4-D at 160, 175, and 325°C, and for 2,4,5-T at 175 and 330°C. No CO or CO_2 evolution was observed, and it is strange that no fusion peaks were observed around the mps. Khattab and Haroun[64] reported on the DTA of 2,4,5-T, (2,4,5-trichlorophenoxy) ethanol, 2,4-D, and the 2,4-D methyl ester. Que Hee and Sutherland[65] obtained a heat of fusion (ΔH_f) of (5.60 ± 0.30) kcal/mol around the mp (see Appendix 1). Other available ΔH_f values[66] are also presented in Appendix 1. The mp depressions of MCPA, mecoprop, MCPB, and dichlorprop are [66] 0.066, 0.13, 0.085, and 0.13, respectively.

A polarizing microscope study[67] of the melting of 2,4,5-T, 2,5-D, 2,3,6-T, the sodium and potassium salts of 2,4,5-T, and 2,4,5-trichlorophenol showed that the purest 2,4,5-T melted around 157°C and that it exists in at least two forms, the stable Form I melting at 157°C and a metastable Form II which is formed around 60°C and transforms completely to Form I before melting. Very slow transformation occurs even at room temperature. Conoscopic observations on thin films revealed distorted interference figures, but both forms were biaxial negative. This birefringence behavior is compatible[68] with the X-ray diffraction study of 2,4,5-T which showed it to be of triclinic structure.[40] Presumably the X-ray diffraction study is detecting mostly Form I, but this should be verified. 2,3,6-T also recrystallizes from the melt to form high birefringent fibrous crystals,[67] but there is no evidence, however, for polymorphism. It forms a eutectic with Form I of 2,4,5-T which melts at 115°C. 2,5-D has at least two polymorphs, one melting at 142°C and another which recrystallizes from the melt in a form rather similar to the stable form of 2,4,5-T. However, this latter form melts at 134°C and in the presence of solvent vapors can be induced to transform to highly birefringent rods melting at 142°C. Very slow cooling of the melt also produces the stable form directly, and it forms an eutectic with 2,4,5-T melting at 123°C; 2,4,5 trichlorophenol/2,4,5-T forms a eutectic at 58°C. 2-CPA and 4-CPA also form a eutectic at 125.5°C of composition 44:56, respectively.[69]

2. Esters

The lower alkyl esters are low-melting solids, whereas the higher esters are liquids. The mps and bps increase with increasing ring chlorination (see Appendix 2, 3, and 6). The mp of the methyl ester of 2,4-D is[71] 43°C. DTA or DSC studies have been reported on the methyl ester of 2,4-D.[64]

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3. Salts

The mps for some amine salts of 2,4-D, of 2,4,5-T, and miscellaneous salts are presented in Appendixes 3, 4, and 6, respectively.

a. Alkali and Metal Salts

The sodium and potassium salts have high mps since they are ionic. The sodium salt of 2,4,5-T melts at 268°C with very little decomposition[67] and exists in at least two crystalline forms; it always recrystallizes from the melt into characteristic spherulites which are indefinitely stable at room temperature, but transform to the fibrous needles of the thermodynamically stable form when heated above 200°C. The potassium salt of 2,4,5-T, however, decomposes on heating above 300°C and is almost insoluble in molten 2,4,5-T, whereas the sodium salt is much more soluble. The potassium salt exhibits medium birefringence, but no similar studies have been reported for 2,4-D salts, even though the mp of the sodium salt is only 217°C. The 2,4-D potassium salt melts above 300°C. The mp behavior may seem anomalous, since the mp order is usually Li> Na>K>Rb>Cs, but the phenoxy acid salts appear to act like typical fatty acid salts, where potassium salts have higher mps and water solubilities than the corresponding sodium salts.[73]

DTA of various $(2,4,5\text{-T})_2 \cdot M \cdot nH_2O$ systems, where M = Cu, Zn,Cd, Co, Ni, and Mn and n = 2 or 4, and of $(2,4,5\text{-T})_3 \cdot Fe$ have been reported.[70] Most of these salts lost water of crystallization at ~40°C, and the thermal stability of the anhydrous salts ranged from 20°C for Cd to 130°C for the Zn salt. All salts formed stable oxides at high temperatures, excepting CdO, which was unstable.

b. Amine Salts

The phenoxyalkanoic acids are weak acids and the alkylamines are weak bases; their salts are weakly ionic and so have low mps (see Appendixes 3 and 4, respectively). Generally, the salt is converted to its corresponding amide between 150 to 200°C, but the latter's formation can be detected well beneath the mp of the salt.[65] The mp literature is difficult to evaluate, since the temperature used in salt synthesis is often not given; also, there are many stoichiometries that are possible other than 1:1 as well as polymorphic forms.

DSC of several 1:1 amine salts of 2,4-D was investigated by Que Hee and Sutherland.[65] The ΔH_f values for the dimethyl, methyl, *n*-butyl, *n*-dodecyl, and *n*-tetradecyl salts were 11.20, 6.53, 15.0, 31.2, and 39.2 kcal/mol, respectively. There is a linear relationship between ΔH_f and molecular weight obeying $\Delta H_f = 0.1445$ mol wt -27.4. At a heating rate of 10°C/min and for a nitrogen furnace atmosphere,[72] the methylamine salt showed endothermal transitions at 103 to 117, 139 to 157, and 165 to 182°C, after which decomposition set in. The dimethylamine salt had one peak from 64 to 74°C, a glass transition 134 to 136°C, and decomposed above 157°C. The *n*-butylamine salt had transitions from 98 to 111 and 162 to 195°C, with subsequent decomposition. The *n*-tetradecyl salt produced peaks between 57 to 64.5 and 163 to 202°C, with subsequent decomposition. The higher transitions correspond to the elimination of water in the formation of the corresponding amide, which is decomposed[65] beyond 200°C.

4. Amides

The melting points of various 2,4-D amides, 2,4-D amino acid amides, and miscellaneous amides are in Appendixes 3, 5, and 6, respectively. No DTA or DSC studies have been reported.

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5. Miscellaneous Compounds

The mp and bp data for these compounds are subdivided in Appendix 6 into

1. Free acids
2. Acid chlorides
3. Metal salts
4. Esters
5. Halogenated phenoxyalkanoxy esters
6. (N-chlorophenoxyalkanoic) amides
7. Amides
8. Other

The mps for the free acids decrease in the order $p > o > m$ except for fluoro compounds. The type of halogen does not affect the mp much in monosubstituted compounds, but the dibromo- and the diiodo- substituents do produce higher mps than chlorines in the 2,4-D analogues. A methyl group in the 2- or 4- positions usually lowers the mp, as does lengthening of the side chain, while increased chlorination raises mps and bps.

B. Solubility and Dissociation in Water

Since water is a polar hydrogen-bonding solvent, it might be expected that the esters, free acids, and salts will be soluble in this increasing order. However the solubilities of the amine salts decrease as the chain length in the alkylamine moiety increases (see Appendix 7) so that salts, such as the *n*-dodecyl- or the *n*-tetradecyl-, are as insoluble in water as the esters.

1. Free Acids

Appendix 1 contains data relating to some chlorinated phenoxyalkanoic acids at 25°C. In general, solubility decreases as the number of chlorines on the benzene ring increases for a given alkanoic acid and as the length of the side chain of a given halogenated phenoxy moiety increases. The solubility also increases as the temperature increases.

The net solubility of an acid is the sum of two effects: the proportion dissociated and the fraction solvated without ionization. A large literature exists reporting solubilities and pK_as of phenoxyacetic acids. However, there are many contradictory values. The figures in Appendix 1 are those which, in our opinion, are the most reliable.

The water solubility of 2,4-D as obtained from a number of sources is presented in Appendix 8. The contradictory nature of the literature is manifest, and in many cases, the temperature and analytical methods were not given in the original publications. Since Leopold et al.[74] compared the solubilities of a number of homologous acids under the same conditions and with the same analytical methods, their figures have been selected as being the best available. Thus, the solubility of 2,4-D is approximately 52.2 mg/100 mℓ or 522 ppm at 25°C, and a saturated solution is first produced at $2.36 \times 10^{-3} M$. The other literature sources chosen to provide data for the solubilities in Appendix 1 were the review by Bailey and White[233] and the *Weed Control Handbook*.[234]

The literature on pK_a values for 2,4-D is in a similar state (see Appendix 9). Although the temperature is generally cited, only two workers[76,77] give ionic strengths (I), and often the presence of dissolved carbon dioxide is ignored. In addition, since the solubility of 2,4-D is low and because the aqueous solution is a weak electrolyte, conductimetric methods that involve extrapolation of equivalent conductances to infinite dilution can be much in error, since steep increases in equivalent conductances occur at

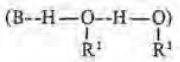
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high dilutions. Often mixed solvents were utilized (van Oberbeek et al.[75]). Phillips[76] showed that the pK_a of 2,4-D at I ~0.001 was 2.86 at 20°C, but was 4.10 in 1:1 ethanol/water (I ~ 0.005). The major criticism of the spectroscopic method of Phillips is that the molar absorptivity vs. wavelength curve has a very steep slope in the far UV region, even though the pK value cited is the average of pK_as done at four wavelengths. However, the discrepancy between the value of Nelson and Faust[77] and that of Phillips is not great. To check whether the solubility and pK_a data are compatible, the maximum possible pK_a value can be calculated from the solubility of 2,4-D (2.36×10^{-3} *M* at 25°C).[74] Since this represents the maximum (H^+), the lowest pK_a at 25°C should be around 2.63. The observed pK_a is 2.73 ($K_a = 1.86 \times 10^{-3}$), and this implies 79% of the acid is dissociated, and 21% is solvated without dissociation at saturation.

It is also interesting that the degree of chlorination of the ring does not affect the pK_a in a marked way, even though 4-CPA and 2-CPA have larger pK_as than 2,4-D, as does 2,4,5-T.[76] Even the pK_a of MCPA is not very different from that of 4-CPA, but MCPB, however, does have a much larger pK_a than MCPA.

Phillips' spectroscopic work is highly suggestive of the following relationships:[76]

1. The negative inductive effect of the phenoxy group (pK_a ~3.12) I = 0.001 responsible for the acid strengthening relative to acetic acid (pK_a ~3.74) is of the order of the iodo group and much greater than that of either the phenyl or hydroxyl groups.
2. Chloro substitution in the phenyl ring generally enhances acid strength; the magnitude depends on the number of chlorines, the distance of separation between the aromatic ring and the ionizing group, and solvent effects. In the phenoxyacetic acids, the effects of chloro substitution are swamped by solvent effects, e.g., pK_a values in water vs. those in 1:1 water to ethanol. The acid weakening effect of ethanol is due to the fact that open-chain H– bonded dimers are favored



in alcohol, whereas water allows other arrangements thus promoting greater dissociation. Also, ethanol can be regarded as preferring to solvate the undissociated molecule rather than the dissociated form.
3. The insertion of methylene groups between the phenoxy and ionizing group increases the pK_a as expected from inductive effects. Thus, β-(2,4-DP) is 1.5 pK units weaker than the corresponding acetic or α-substituted propionic acid. The insertion of another methylene group weakens it by a further 0.4 pK unit, so that the pK_a is the same as that for butyric acid, i.e., the phenoxy group does not affect the ionization at all and its effect is almost eliminated by the insertion of two methylene groups.
4. 2,6-Disubstituted derivatives, usually inactive as auxins, are much weaker acids than their parent acids, and this is attributable to steric hindrance which prevents the phenoxy group from interacting with the carboxyl group. Interestingly, although 2,6-dichloro and 2,4,6-trichlorophenoxyacetic acids are not auxins, 2-fluoro-4,6-dichloro- and 2,4-dichloro(6-fluoro)-phenoxyacetic acids are, and these also show greater acidity than their sterically hindered analogues.

2. Esters

These compounds are generally immiscible or insoluble in water, but gradual hydrolysis does occur (see Chapter 3).

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3. Salts

a. Metal Salts

The solubilities of some metal salts are given in Appendix 7. It is difficult to evaluate how valid these data are in light of those for the free acids. A careful study has been done of the solubility of magnesium and calcium salts of 2,4-D at various temperatures.[79] For the calcium salt, the solubility was 3.26 (4°C), 4.0 (25°C), and 5.21 (35°C) g/ℓ; for the magnesium salt, it was 8.4 (4°C), 11.1 (25°C), and 14.2 (35°C) g/ℓ.

b. Amine Salts (Appendix 7)

The same reservations expressed for the data of the free acids hold for the amine salts; the presence of salts of different stoichiometry may make these values very approximate. The solubility in water decreases as chain length increases, particularly beyond the butylamine salts. Ralston et al. have shown for a series of amine salts of many carboxylic acids that long chain salts had crystalloidal properties in dilute solutions and colloid and liquid crystalline properties in concentrated solutions.[81] This makes accurate solubilities of the longer chain salts extremely difficult to obtain. Addition of excess amine always increases the solubility[82,83] because of formation of n:1 amine salts where $n > 1$. Indeed, monomers and dimers predominated for primary, secondary, and tertiary ammonium salts, but monomer-trimers predominated for quarternary salts.[80,84]

The tremendous complexities in obtaining the phase diagrams of the amine salts obviously should be further investigated.

4. Amides

No data are available.

C. Solubility in Solvents Other than Water

Appendix 10 documents the solubilities of various free acids in some organic solvents. For a given solvent, the solubilities of MCPA, 2,4-D, and 2,4,5-T decrease in this order. However, the solubility of 2,4,5-T is greater than that of 2,4-D in benzene, toluene, and xylene. Interestingly, MCPA is also more soluble than Silvex or MCPB, whether the solvent is polar or not. This unusual behavior should be verified further. The best solvents are alcohols, acetone, dioxane, methyl butyl ketone, and lastly diethyl ether. Workers should be cautioned against using alcohols as solvents over long periods, since esterification slowly occurs,[85] even at refrigerator temperatures. The esters are soluble in most organic solvents, but particularly in benzene, hexane, and ethyl acetate. The amine salts are all soluble in alcohols, but become appreciably soluble in ether as the chain length increases. The amides are soluble in chloroform, ethyl acetate, and alcohols.

Early in the history of herbicide use, it was found that the more nonpolar the molecule, the faster it tended to penetrate the plant cuticle. However, the water solubility also decreased, and spraying became much more expensive if a paraffin oil had to be used as carrier. Ennis et al.,[86] as part of the Camp Detrick research, soon developed tributyl phosphate as a cosolvent for 2,4-D acid in petroleum oil solutions. Even such closely related compounds as triethyl and triolyl phosphate were unsatisfactory. At room temperature, tributyl phosphate dissolved 36% by weight of 2,4-D, and this solution could be diluted with petroleum oils without crystallization occurring. However, the tributyl phosphate itself had a marked contact burning effect on leaves. The solvent was also effective for 2,4,5-T, 4-CPA, MCPA, etc. The use of this solvent was soon superseded by the use of various surfactants to promote water solubility and rapid penetration, with little contact burning.

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D. Partition Behavior

Most clean-up procedures for pesticides involve liquid/liquid extraction and residues in water can often be separated and subsequently concentrated by this technique. The useful *p*-value concept, developed by Bowman and Beroza et al.[87,88] is simply "the fraction of the total solute that distributes itself in the nonpolar phase of an equivolume solvent pair, and is the partition coefficient defined on a fractional basis".

In two publications, Suffet[89,90] investigated the partitioning behavior of 2,4-D and 2,4,5-T acids and esters. All *p*-values were determined at 25°C, with an aqueous ionic strength of 0.02 or 0.2 *M* orthophosphate buffer relative to an immiscible organic solvent. Free acids were partitioned at pH 2, the pH being adjusted by the choice of phosphate salts in the buffer. Thus, for each extraction,

$$p = \frac{E}{\alpha(1 - E) + E} \tag{1}$$

where E is the total fraction of solute extracted into the solvent after one extraction; α is the volume of solvent (V_n)/volume of water (V_p) after the extraction.

For n successive extractions, the total fraction extracted out of the aqueous phase after n extractions (F_n) is

$$F_n = 1(E_1) + A(1 - E_1) + B(1 - E_1 - E_2) + \cdots \tag{2}$$

where A, B, --- are the fractional parts of the solute extracted in successive steps. If the solvent is "insoluble" in water, e.g., hexane, benzene, chloroform,

$$F_n = E_1 + E_1\{(1 - E_1) + (1 - E_1)^2 + \cdots (1 - E_1)^{n-1}\} \tag{3}$$

$$= 1 - (1 - E_1)^n \tag{4}$$

$$= 1 - \left(1 - \frac{\alpha p}{\alpha p - p + 1}\right)^n \tag{5}$$

After the second extraction step where the water is saturated with solvent and unsaturated solvent, the α_2 values for solvents that are somewhat more soluble in water, e.g., ethyl acetate and diethyl ether, are within experimental error of the theoretical α_2 value, and thus the latter can be used for all successive α_2 values after the first extraction step, i.e.,

$$F_n = E_1 + (1 - E_1)\{1 - (1 - A)^{n-1}\} \tag{6}$$

If α_2 is not constant, Equation 2 must be used. Ideally, the solute should have a *p* value of near 1, and the partitioning technique should utilize the smallest aqueous volume suitable, the minimum number of extraction steps, and the minimum volume of solvent. It was shown that *p* values >0.90 are necessary before >95% of a pesticide can be extracted from water in fewer than eight (and most usually in five) extractions. In addition, the classical separatory funnel technique utilizing solvent/aqueous solution ratios ≥0.1 was more efficient than vortex stirring and had smaller error. However, as the number of extractions increased, the errors became equal, so implying that the minimum number of extractions should be five. A pH study showed that an

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aqueous pH below the pK_a of of the free acid was necessary to extract the latter. Table 5 shows the experimental conditions and p values obtained for some chlorophenoxy alkanoic acids and esters. These p values agree with those calculated from other literature sources (see Reference 95). It can be seen that the more polar the herbicide the smaller is its p value and that different kinds of water make no significant difference to the observed p values. However, suspended particulates do affect recovery, but more so at pH 7 to 8 than at pH 2 (see Section IV.F). Water should be filtered before any solvent extraction is attempted.

The best solvents for extraction of the free acids are ethyl acetate and diethyl ether. Hexane is very poor. Diethyl ether and ethyl acetate are best for 2,4-D compounds, and benzene is optimal for 2,4,5-T. Benzene is a poor solvent for 2,4-D and MCPA. Thus, to separate a mixture of esters and free phenoxyacetic acids, one would use *n*-hexane to extract the esters, and then use ether or ethyl acetate to isolate the free acid. This procedure would not work for the propionic or butyric acids, although pH adjustment would most likely solve this problem. A two-step procedure with 200 and 50 mℓ of ethyl acetate was demonstrated to extract 99% of 2,4-D from 1 ℓ of aqueous solution adjusted before extraction to pH 2 with 0.2 *M* phosphate buffer.

Appendix 11 compares the literature of the recovery (F_a) of various herbicidal compounds from aqueous solution. Again, consistent recoveries of at least 99% are obtained with diethyl ether, confirming p-value predictions, even if the pH was adjusted by HCl or H_2SO_4 instead of phosphate buffer.

E. Vapor Pressures and Volatility

1. Introduction

A compound with a low vapor pressure (P) is often said to be "nonvolatile".

P is a thermodynamic property, and no time scale can be inferred, but volatilization is a kinetic process. Thus, although kinetic steady states are common, thermodynamic equilibrium is hardly ever attained. The atmosphere acts as an infinite reservoir, with the wind as a dispersing agent. The amount of material volatilized is then a function of wind speed, contact volume, exposed surface area, temperature, type of compound, and variety of flow, as well as vapor pressure. There are several distinct available approaches which are used to predict volatilization rates.

a. Ideal Gas Method

Since most phenoxy herbicides have a $P < 10^{-2}$ mmHg, the vapors can be described as ideal gases of volume, V, mass, m, and molecular weight, M, at a given temperature, T. Thus,

$$\rho_i = \frac{m_i}{v} = p_i \frac{M_i}{RT} \tag{7}$$

where ρ_i is the vapor density of component i, and p_i is its partial pressure; R is the gas constant in appropriate units.

When $p_i = P_i$, P_i is the maximum mass of the compound per unit volume able to be contained in the vapor phase at a given temperature under ideal conditions.

If the air is sampled at Z ℓ/min and if the vapor is sampled for t minutes, the mass of the compound i that can be collected from a saturated atmosphere is

$$\Sigma m_i = t\rho_i z = t P_i M_i \frac{Z}{RT} \tag{8}$$

where Σm_i is the total mass collected.

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Table 5
LIQUID-LIQUID EXTRACTION OF PHENOXYALKYL HERBICIDES FROM ORTHOPHOSPHATE BUFFER AT 25 ± 0.5[90]

Experimental conditions for the *p*-value determination of herbicides and herbicide esters[a]

Name	Chemical name	pk_a[b]	Experimental concentration (mg/ℓ)	Method of quantitation[c]
2,4-D	(2,4-Dichlorophenoxy)acetic acid	2.64—3.31	50.0	UV
2,4,5-T	(2,4,5-Trichlorophenoxy)acetic acid	2.88—3.46	38.6	UV
MCPA	(2-Methyl-4-chlorophenoxy)acetic acid	2.90—3.40	74.5	UV
2-CPA	2-Chlorophenoxyacetic acid	2.92—3.05	53.4	UV
4-CPA	4-Chlorophenoxyacetic acid	2.36—3.56	61.8	UV
MCPB	(2-Methyl-4-chlorophenoxy)butyric acid	4.80—6.21	23.8	UV, std additions
2,4-DB	4-(2,4-Dichlorophenoxy)butyric acid	4.58—5.90	16.6	UV, std additions
Isopropyl ester of 2,4-D	Isopropyl ester of (2,4-dichlorophenoxy)acetic acid		1.01	glc, internal std
n-Butyl ester of 2,4-D	*n*-Butyl ester of (2,4-dichlorophenoxy) acetic acid		0.94	glc, internal std
Isopropyl ester of 2,4,5-T	Isopropyl ester of (2,4,5-trichlorophenoxy)acetic acid		0.80	glc, internal std
n-Butyl ester of 2,4,5-T	*n*-Butyl ester of (2,4,5-trichlorophenoxy)acetic acid		0.97	glc, internal std

			p-Value (average of at least three determinations)					
Compound	pH	Ionic strength *M*	Ethyl acetate	Ether	Benzene	Chloroform	Carbon tetrachloride	Hexane
2,4-D	0—2	0.02—0.2	0.996	0.99+	0.915	0.95[e]	0.51[f]	<0.04[f]
2,4,5-T	0—2	0.02—0.2	0.99	0.99+	0.98	0.98[e]	0.81[f]	0.24[f]
MCPA	0—2	0.02—0.2	0.99+	0.99+	0.95	0.97[e]	0.69[f]	(0.16[f])
MCPB	2	0.02	0.99	0.99	0.98	0.99	0.96[e]	0.81[e]
2,4-DB	2	0.02	0.99	0.99	0.98	0.98	0.97[e]	0.81[e]

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Table 5 (continued)
LIQUID-LIQUID EXTRACTION OF PHENOXYALKYL HERBICIDES FROM ORTHOPHOSPHATE BUFFER AT 25 ± 0.5°[90]

Experimental conditions for the *p*-value determination of herbicides and herbicide esters[a]

Compound	pH	Ionic strength *M*	*p*-Value (average of at least three determinations)					
			Ethyl acetate	Ether	Benzene	Chloroform	Carbon tetrachloride	Hexane
2-CPA	2	0.2	0.99	0.99	(<0.50)	0.81[e]	(0.14)[f]	(<0.04)
4-CPA	2	0.2	0.99	0.99+	0.63	0.86[e]	(0.23)[f]	(<0.04)
Isopropyl ester of 2,4-D	2	0.2	0.97[e]	0.97[e]	0.99	—	—	0.99
n-Butyl ester of 2,4-D	2	0.2	0.96[e]	0.96[e]	0.96	—	—	0.96
Isopropyl ester of 2,4,5-T	2	0.2	0.96[e]	0.95	0.97	—	—	0.97
n-Butyl ester of 2,4,5-T	2	0.2	0.96[e]	0.96[e]	0.98	—	—	0.99

The Effect of Different Natural Waters on the *p*-Value Determination of 2,4-D from 0.2 *M*, pH 2 Orthophosphate Buffer at 25 ± 0.5°

Type of water	Benzene			Ethyl acetate		
	Average *p*-value	SD	Number of determinations	Average *p*-value	SD	Number of determinations
(Water to solvent ratio of 10:1)						
Distilled water	0.915	0.008	11	0.996	0.002	13

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Schuylkill River water	0.925	0.007	13	0.996	0.0005	11
River water (filtered)	0.911	0.007	2	0.997	0.0010	3
Wissahickon Creek water (high organic load)	0.920	—	1	0.998	—	1

Note: All values are the average of at least three determinations except those in parentheses, with a water:solvent ratio of 10:1.

[a] Amchem Products, Inc., analytical grade. All solids were recrystallized before use.
[b] After Nelson and Faust.[77]
[c] All compounds are soluble at these concentrations.
[d] All UV analyses on the water phase after solvent evaporation step.
[e] Water:solvent ratio changed to 5:1.
[f] Water:solvent ratio changed to 1:1.

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If the methyl ester of 2,4-D is collected for 8 hr with Z = 10 ℓ/min at 25°C and given P = 1.3×10^{-2} mmHg,[91] then $\varrho_i = 0.165$ mg/ℓ and $\Sigma m_i = 792$ g.

Usually, only a P at a reduced bp is known. However, the normal bp (T_b) can be estimated using the method of Hass and Newton.[93]

The calculation of a p at a given T then involves the use of the Clausius-Clapeyron Equation:

$$\log_{10} p_2 = \frac{\lambda_f (T_2 - T_1)}{4.576\, T_1 T_2} + \frac{\lambda_v (T_2 - T_1)}{4.576\, T_1 T_2} + \log_{10} p_1 \qquad (9)$$

where $\lambda_s = \lambda_f + \lambda_v$; λ_s, λ_f, and λ_v being the molar heats of sublimation, fusion, and vaporization, respectively.

This equation is valid only when these latent heats do not vary with temperature. Unfortunately, the reverse is often true.

Since $\lambda_f/T_m \sim 10$ cal/deg/mol (T_m being the normal mp) for most organic crystals and $\lambda_f/T_b \sim 21$ cal/deg/mol (Trouton's Rule),

$$\log_{10} p_2 = \frac{2.188}{4.576} \frac{T_m (T_2 - T_1)}{T_1 T_2} + \frac{4.585\, T_b (T_2 - T_1)}{T_1 T_2} + \log_{10} p_1 \qquad (10)$$

The methyl ester of 2,4-D has a melting point of 41.5°C and a bp (T_1) of 110°C at 10 mmHg (p_1).[92] To find p_2 at 25°C, the unspecified T_b must be estimated by the method of Hass and Newton.[93] The estimated T_b is 249°C. Thus, p_2 is $\sim 1.68 \times 10^{-1}$ mmHg, compared with the observed P of 1.3×10^{-2} mmHg.

The methyl ester often acts like a supercooled liquid at room temperature.[94] For liquids,

$$\log_{10} p_2 = \frac{4.585\, T_b (T_2 - T_1)}{T_1 T_2} + \log_{10} p_1 \qquad (11)$$

If $T_1 = T_b$ and $p_1 = 760$ mmHg,

$$\log p_2 = 4.585 \left(1 - \frac{T_b}{T_2}\right) + 2.8808 \qquad (12)$$

This p_2 is $\sim 2.76 \times 10^{-2}$ mmHg and is in better agreement with the observed value.

b. Kinetic Ideal Gas Approach[94-96]

Most kinetic processes follow a n-order disappearance law,

$$-\frac{dc}{dt} = k_n C^n \qquad (13)$$

where C is the concentration remaining at time t, n is the order of the process, and k_n is the appropriate rate constant.

If the air flow is kept constant,

$$-\frac{dm}{dt} = k_n m_r^n \qquad (14)$$

where m_r is the mass remaining at time t.

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For zero-order processes, typical of kinetic steady states,

$$X_v = 1 - X_t = \frac{k_0 t}{m_0} \tag{15}$$

where X_v and X_t are the fractions volatilized and still remaining, respectively, and m_o is the initial mass of substrate. Thus, a plot of X_v vs. t will be linear.

For first-order processes,

$$-\log X_t = \frac{k_1 t}{2.303} \tag{16}$$

Thus, a plot of $-\log X_t$ vs. t is linear.

For second-order processes,

$$\frac{Xv}{X_t m_0} = k_2 t \tag{17}$$

Thus, a graph of X_v/X_t vs. t is linear.

At low air-flow rates, the evaporative process appears to be pseudo first order,[94-96] although the initial portion of the curve obeys zero-order kinetics.[98,99] Assuming first-order kinetics,

$$-dm/dt|_o = k_1 m_o \tag{18}$$

Using the Ideal Gas Law (Equation 7),

$$\frac{dm}{V_o} = \frac{pM}{RT} \tag{19}$$

If $p = p_o$ near $t = o$ is a constant,

$$p_o = k_1 m_o \frac{RT}{M} \frac{1}{dV/dt|_o} = -\frac{dm/dt|_o}{dV/dt|_o} \frac{RT}{M} \tag{20}$$

where $dV/dt|_o$ is the flow rate.

For the case of the methyl ester of 2,4-D volatilized at $dV/dt|_o$ of 1 ℓ/min at 25°C, $-dm/dt|_o$ is approximately 165 μg/min, assuming enough ester is deposited to saturate the atmosphere. However, the usual field application rate (8 oz/acre = $\sim$5.6 $\mu g/cm^2$) is such that p_o is between 10^{-3} to 10^{-4} mmHg.[94,95] The minimum time for volatilization from 1 cm^2 of this uniformly covered acre is still of the order of several seconds, indicative of quick volatilization. However, there are many competing processes which are capable of lowering the p_o even further, e.g., adsorption to plant cuticles, soils, etc. Nevertheless, the above method only requires that the pseudo first-order rate constant be measured accurately at known m_o, T, M, and $dV/dt|_o$ and is thus a convenient and simple method to calculate vapor pressures.

This treatment looks at the volatility problem in terms of what is volatilized, rather than the surface layer responsible for the volatilization. It seems almost a truism to say that the greater the exposed surface area of the substrate, the more of the substance will be volatilized, even though the volatilization rate in grams per square centimeter

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per second will be the same. Yet, it has only been comparatively recently that the importance of the initial exposed surface area to applied mass ratio (Q_o) has been fully recognized and studied.[94-96]

$$\text{Since } \frac{dV_o}{dt} = A_o \frac{du}{dt} \tag{21}$$

where du/dt is the appropriate linear velocity, and A_o is the initial exposed surface area.

Then

$$p_o = \frac{RT}{M} \frac{k_1 m_o}{A_o\, du/dt|_o} = \frac{RT}{M} \frac{k_1}{Q_o} \frac{1}{du/dt|_o} = \frac{RT}{M} \frac{U}{du/dt|_o} \tag{22}$$

where

$$Q_o = \frac{A_o}{m_o}; U = \frac{-dm}{A_o\, dt} = \frac{k_1 m_o}{A_o} \tag{23}$$

A wind of 2 mi/hr (approximately 89 cm/sec) will cause the methyl ester of 2,4-D to have a maximum U of ~1.46 $\mu g/cm^2/sec$ at 25°C under saturating conditions, assuming no other competing processes.

c. Pressure Data using Gas Liquid Chromatography[100,101]

On a GC column, the net retention volume (V_N) of the compound of interest can be expressed by[102]

$$V_N = jK_d V_s = j F_c (t_r - t_{air}) = \frac{jC_S}{C_M} v_s = \frac{jn_s}{C_M} = j F_c \frac{z}{u} \tag{24}$$

where j is the pressure gradient correction of the GC column, K_d is the partition coefficient = C_S/C_M, where C_S is the concentration of solute in the stationary phase, and C_M is the concentration of solute in the mobile phase, V_s is the volume of the stationary liquid phase at T°C, F_c is the carrier gas flow rate, t_r is the time for the solute peak maximum to emerge after injection, t_{air} is the time for the air peak maximum to emerge after injection, n_s is the number of moles of solute in the stationary phase, z is the distance between the two peaks, and u is the recorder chart speed.

The relative retention is defined as[102]

$$\psi = \frac{V_{N_1}}{V_{N_2}} \tag{25}$$

where 1 and 2 are two different solutes. Under the conditions of internal standard quantitation, j, F_c, and u are constant,

$$\psi = \frac{V_{N_1}}{V_{N_2}} = \frac{z_1}{z_2} = \frac{n_{S_1}}{n_{S_2}} \frac{(C_M)_2}{(C_M)_1} \tag{26}$$

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Substituting the Ideal gas law at constant T and F_c,

$$\psi = \frac{z_1}{z_2} = \frac{n_{S_1}}{n_{S_2}} \frac{p_2}{p_1} \tag{27}$$

Since GC separation requires attainment of a kinetic steady state (and not necessarily thermodynamic equilibrium), these ps are generally partial pressures. Equilibrium can be demonstrated if ψ is invariant to F_c at a given T, since the equilibrium position is not dependent on flow rate.

If Raoult's law holds, i.e.,

$$p_i = x_i P_i \tag{28}$$

where X_i is the mole fraction of i in the stationary phase, P_i is the vapor pressure; if $n_{i\ TOT}$ is the total number of moles of all compounds dissolved in the stationary phase,

$$\psi = \frac{z_1}{z_2} = \frac{n_{S_1}}{n_{S_2}} \frac{p_2}{p_1} = \frac{n_{1\,TOT}}{n_{2\,TOT}} \frac{P_2}{P_1} \tag{29}$$

If $n_{S_1} \sim n_{S_2}$ or $n_{2\ TOT} = n_{1\ TOT}$

$$\psi = \frac{z_1}{z_2} \sim \frac{p_2}{p_1} \sim \frac{P_2}{P_1} \tag{30}$$

i.e., separation is effected only in terms of vapor pressures rather than both partitioning behavior and p.

The choice of reference compound is also important. Jensen and Schall[100] and Flint et al.[101] chose dibutyl phthalate as internal standard, but although this compound would certainly mimic the partitioning behavior of the unchlorinated phenoxyacetic acid esters, it might be expected that the partitioning coefficient for the chlorinated compounds in the usual nonpolar GC stationary phases might be higher than for the unsubstituted esters. The reference compound should be as soluble in the stationary phase as the solute.

Using the Clausius-Clapeyron Equation, it can be shown that p can be found from equations of form

$$\log_{10} p = A - \frac{B}{T} - \frac{C}{T_2} \tag{31}$$

where A, B, and C are constants.

It is assumed that the latent heat of vaporization is invariant over all of the temperature range studied. The experimental data is fitted by regression. Often C is set equal to zero.

d. The Molecular Distillation Approach

Langmuir[103] in 1913 derived an equation utilizing the kinetic theory of gases to quantitate the rate of volatilization per unit area (U) under the conditions of molecular distillation, i.e., evaporation into a vacuum:

$$U = P \left(\frac{M}{2\pi RT}\right)^{1/2} \text{(in cgs units)} \tag{32}$$

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For the methyl ester of 2,4-D at 25°C, P is $\sim 1.3 \times 10^{-2}$ mm Hg;[91] U is thus 672 μg/cm^2/sec under conditions of molecular distillation (compare to the answer given by the Kinetic Ideal Gas approach of Section IV.E.1.b).

The differentiated form of the Clausius-Clapeyron Equation for liquids can be written:

$$d\ln p/dt = \frac{\lambda_V}{RT^2} \tag{33}$$

In general,

$$\frac{d\lambda}{dt} = C_v - C_l \tag{34}$$

where C_v and C_l are the specific heats per mole of the vapor and liquid, respectively. Since most esters in the vapor phase are nonassociated, $C_v \sim 4.96$ cal/mol. However, carboxylic acids even in the vapor phase may be dimeric. C_l has to be evaluated directly.

Substituting in Equation 33 and integrating

$$\log_{10} p = A' - B'/T - C' \log_{10} T \tag{35}$$

compare Equation 31.

Since, from Equation 32,

$$\log_{10} U = \log_{10} p + \frac{1}{2} \log_{10} \frac{M}{2\pi R} - \frac{1}{2} \log_{10} T$$

then,

$$\log_{10} U = A'' - B'/T - C' \log_{10} T \tag{36}$$

where $$A'' = A' + \frac{1}{2} \log_{10} \frac{M}{2\pi R} \tag{37}$$

and $$C'' = C' + \frac{1}{2} \tag{38}$$

Again, A″, B′ and C″ can be found from regression analysis.

e. The Mass Transfer Approach from Thin Films[97]

The diffusion coefficient D is defined by Fick's First Law for an isothermal medium at rest by

$$U = -D \frac{d\rho i}{dx} \tag{39}$$

where U is the mass evaporated per unit area and unit time of component i, and i flows through a plane vertical to the direction χ, and ρ_i is the partial vapor density as defined in Equation 7.

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For an Ideal Gas (IG),

$$U_{IG} = \frac{-DM_i}{RT} \, dp_{i/dx} \tag{40}$$

If

$$U_K = K_M \, \Delta\rho_i \tag{41}$$

where K_M is the mass transfer coefficient, then,

$$U_{IG,K} = \frac{K_M M_i}{RT} \, \Delta p_i = K'_i \Delta p_i \tag{42}$$

where Δp_i is the difference in partial pressures of component i in the immediate vicinity of the surface and the bulk of the substrate. $K_i' = (K_M M_i)/RT$ is the mass transfer coefficient based on partial pressures. In terms of the kinetic treatment in Section IV.E.1.c, $K_m = du/dt$.

If mole fractions are utilized,

$$U_x = K_x \, \Delta X_i \tag{43}$$

where ΔX_i is the mole fraction gradient.
The quantity

$$\frac{U_x}{U_{IG}} = \frac{K_M \Delta x}{D} = Sh = \text{the Sherwood number} \tag{44}$$

For convective mass transfer,

$$U_C = u_c \Delta\rho_i \tag{45}$$

where u_c is the velocity of the convection, the quantity

$$\frac{U_x}{U_C} = \frac{K_M}{u_c} = St_M = \text{the Stanton number} \tag{46}$$

Also,

$$\frac{u_c}{D} = \frac{Sh}{St_M R_e} = Sc = \text{the Schmidt number} \tag{47}$$

where R_e is the Reynold's Number.

For an Ideal Gas, Sc ~1.

Another important parameter is the mass transfer factor (j_M)

$$j_M = St_M \, Sc^{\frac{2}{3}} = \frac{Sh}{R_e \, Sc^{1/3}} \tag{48}$$

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f. Volatilization from Droplets

Above a certain critical radius (usually >1 μm diameter), if vaporization is into an infinite reservoir,

$$K_D = \frac{D}{r_i}, \text{ or } Sh = \frac{2K_D r_i}{D} = 2 \quad (49)$$

In practice, Sh >2, since the vapor density will not be uniform. Free convection may also occur around the sphere.

For turbulent or laminar flow, i.e.,

$$0 < R_e < 1000, Sh = 2.0 + 0.6 R_e^{0.5} Sc^{1/3} \quad (50)$$

The mass transfer coefficient is inversely proportional to the square root of the contact time which is inversely proportional to the velocity u and hence to R_e.

For the case of a droplet or a thin circular film on a target, the geometry of the droplet or film can be regarded as a circular cylinder. In this case, for laminar flow (i.e., $R_e < 0.2$),

$$Sh = Const\ (R_e Sc)^{0.5} \quad (51)$$

For turbulent flow ($1 < R_e < 4000$) and for air, $S_c = 0.71$,

$$Sh = 0.43 + 0.48 R_e^{0.5} \quad (52)$$

R_e is best estimated by the diameter of the circular film or the cumulative diameters of all the droplets. Few of these constants have been determined for the phenoxy herbicides, but D for the methyl ester of 2,4-D at approximately 20°C was measured to be 3.9×10^{-11} cm²/sec.[108]

The nature of the liquid/air interface is the single most important quantity in controlling evaporation to the moving air stream above the interface, and the mass transfer approach concentrates on this interface in contrast to the methods utilizing the Ideal Gas and Clausius-Clapeyron Equations. At the boundary surface, surface tension increases on increasing mass transfer, and this leads to unstable laminations of the liquid. The state with the minimum surface work (Aδ) is thermodynamically stable. A is minimal for a sphere, but Aδ can also be reduced by decreasing δ. If the surface is enriched by a component increasing δ, the layers adjoining the surface are rapidly drawn into the core of the liquid through the resulting instability and replaced by fresh liquid with a lower δ. This explains why mass transfer occurs more rapidly in the direction in which δ is increased. Surfactants often form a rigid film on the surface which not only allows fewer molecules to penetrate to beyond the interface, but also reduces the surface turbulence and hence mass transfer. Probably the latter action is the chief reason for the lower volatility. In the case of the droplets on leaves, the pesticide may adsorb to the leaf, or it may also be subjected to oxygen bubbles released via transpiration; in addition, the presence of wind, microbial or chemical decomposition, etc. make the estimation of volatilization in the field a very uncertain science.

Droplets below 10 nm in diameter cannot be described in the usual way by the Clausius-Clapeyron Equation. Instead, the vapor pressure is greater than predicted for a film. This is called the Kelvin Effect[104] and is embodied by:

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$$\ln \frac{P_d}{P_p} = \frac{2\,M\delta}{RTdr} \qquad (53)$$

where P_d is the vapor pressure of the droplet, P_p is the vapor pressure from a plane surface, r is the droplet radius, δ is the surface tension, and d is the fluid density.

2. Data for Chlorinated Phenoxyalkanoic Acid Herbicides

a. Acids

Very little work has been done on the volatility or vapor pressures of the free acids, mainly because they are hardly ever used in spraying. However, it has been found that 2,4-D has a P of 1.05×10^{-7} mmHg at 25°C and boils at 160°C at 0.4 mmHg.[105]

b. Esters

It is instructive to compare the calculated values of P at 25°C for various esters calculated from the equations of Jensen and Schall[100] and those of Flint et al.,[101] who both utilized the same GC technique (see Chapter 1, Section IV. E.1.c) to find Ps of 2,4-D esters at high temperatures, as well as the same internal reference (see Appendix 12). It can be seen that the values for the 2-ethylhexyl, 2-octyl, and the 2-propyl esters of 2,4-D differ by more than an order of magnitude, with Jensen and Schall's values being higher. Some of the assumptions may be responsible for the contradictions (see Chapter 1, Section E.1.c). Consideration of the data of Jensen and Schall[100] leads to the conclusion that, as expected, the corresponding esters of 2,4,5-T have smaller Ps than those of 2,4-D, and branched isomers of the same acid have a higher vapor pressure than the normal esters. The relevant calculated values are also compared with Ps found experimentally (see Appendix 13). The latter show that there are still many contradictions. It can be concluded, however, that the calculated values of Flint et al.[101] are too low. The values for the 2,4-D *n*-butyl ester at 25°C range from 10^{-5} to 4.0×10^{-3} mmHg, with the correct value probably between 3.90×10^{-4} and 3.90×10^{-3} mmHg. The P of the methyl ester of 2,4-D at 25°C varies from 3.3×10^{-4} to 1.27×10^{-2} mmHg. The correct value is probably between 2×10^{-3} to 1.3×10^{-2} mmHg. The values for the i-propyl ester also range from 4×10^{-5} to 1.05×10^{-2} mmHg at 25°C, with the true value probably between 1.2×10^{-3} to 10^{-2} mmHg.

In general, the transpiration technique[91] produces higher P values than the other methods, although the method used by Que Hee et al.[94-96] and by Grover[98,99] does not, since the contact volume was always less than the nominal volume of air flowing over the surface deposit. Appendix 13 also presents the available ΔH_v data. As expected the values for the liquid esters are lower than ΔH_f for solid 2,4-D (see Appendix 1). The various equations developed through Section E.1 can then be utilized to find U values. Clearly, reliable P values have to be known before this is possible.

The volatility of the esters has also been measured directly on a number of surfaces. Pyrex is less adsorptive than is the cuticle of a plant, so that volatilization from glass surfaces should be a good model system for the worst field conditions at comparable temperature, surface/mass ratios (Q) and flow rates. A major difficulty with many of these kinetic studies is that the crucial parameters were not often specified. Thus, Que Hee and Sutherland[94,95] showed that only under the same conditions of Q_a, flow rate, and temperature did the volatilities of the 2,4-D esters follow the vapor pressures, i.e., as chain length decreased so does volatility. Grover,[98] using technical grade butyl esters of 2,4-D in a transpiration method, found that 238 ng/cm²/hr of butyl esters volatilized at 14 ℓ/hr at 30°C, whereas 447 ng/cm²/hr was the rate at 57.6 ℓ/hr. Que Hee and Sutherland found an evaporation rate of 4.45 μg/cm²/hr at 38°C for *n*-butyl ester at 56.4-ℓ/hr flow rate and a Q_a of 3.28 cm²/g. If it is remembered that each 10°C rise

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in temperature usually doubles the evaporation rate, then Grover's figures extrapolated to around 40°C yield a rate of around 1.0 $\mu g/cm^2/hr$ at 38°C for 57.6 ℓ/hr. Given the errors involved, the agreement is sufficient. Grover also found[99] that at 28.8 ℓ/hr flow rate at 30°C, the relative volatilities of technical grade 2-propyl, butyl, propylene glycol butyl ether and 2-octyl esters of 2,4-D to be 56 or 25,38, 4, and 1, respectively. Accordingly to Flint et al.,[101] the relative vapor pressure ratios are 27, unknown, 1.46, and 1, respectively at 25°C. According to the data of Jensen and Schall,[100] the ratios are 58.6, 16 to 23, unknown, and 1 at 25°C, in better agreement. Both Grover and Que Hee and Sutherland utilized almost the same transpiration technique, but whereas the former used a treatment based on the Clausius-Clapeyron Equation to interpret the data, the latter utilized the kinetic treatment outlined in Section E.1.b. The treatment based on the Clausius-Clapeyron Equation assumes the latent heat of vaporization λ_v is constant with T. The kinetic treatment has no such drawback.

It has been generally accepted that esters with $P>10^{-4}$ mmHg should be classed as "high volatile", and those with $P<5 \times 10^{-5}$ mmHg are "low volatile". Assuming that the data of Jensen and Schall are valid, the critical chain length for the "high volatile" designation is different for 2,4-D and 2,4,5-T, being $\leqslant C_6$ for 2,4-D esters, but being $\leqslant C_4$ for 2,4,5-T. MCPA esters would be expected to be more volatile than the corresponding 2,4-D esters. The order of volatility of the various esters has been studied by many other workers using both physical[106-108] and bioassay methods.[111-130] For example, the relative volatility of the *n*-butyl, 2-ethylhexyl, and 2(2-ethoxyethoxy) propyl esters of 2,4-D deposited on nickel planchettes with $Q_o \sim 10^6$ cm^2/g^{-1} was found [106] to be 50:3:1, 80%, 90%, and 90% volatilizing in 30 min, 10, and 24 hr, with $t_{1/2}$ values of 10.5 min, 2.5, and 9 hr, respectively. Thus, the designations "high" and "low" volatile are meaningless as absolute indicators. Que Hee and Sutherland[94] also showed the *n*-octyl ester of 2,4-D, supposedly "low volatile", at a Q_o value of 10^7 cm^2/g was just as "volatile" (on a percent basis) as the methyl ester at $Q_o \sim 3.28 \times 10^3$ cm^2/g at the same conditions of temperature and flow rate. Volatilities should always be expressed in units of mass per time per area. These values also depend on the type of adsorptive forces between the deposit and the surface it is situated on. Thus, the effective partial pressure may be lower or higher than expected compared with glass surfaces for deposits on plants,[95,96] in water,[109] and from soils.[110,125] Pollution from these surfaces will be discussed more fully in a later section.

The data from the extensive bioassay literature[111-130] tend to support the volatility rankings above. The difficulty of using sensitive plants is that the herbicidal response may be produced by other auxinic herbicides, e.g., picloram. In spite of this nonspecificity, much valuable information has been obtained. Thus, utilizing plant epinasty and a scale of 0 to 10 to assess the effects after 2,4-D exposure for 24 hr, the following volatility ranking[113] was obtained: Weedone 128 (i-propyl ester), 10; Weedone LV_4 (butoxyethyl ester),8; Weedone 638 (emulsifiable acid),7; and Emulsamine E-3 (oil-soluble dodecyl/tetradecyl amine),0 (6 hr). In addition it was suggested that water as carrier enhanced volatility probably via codistillation.[128] Hitchcock et al.[116] showed that tomato plants at room temperature could detect the vapor of the isopropyl ester of 2,4-D at concentrations of 1% of 0.1 mℓ, 10% of 0.01 mℓ, and 48% of 0.001 mℓ aqueous droplets after 4 hr. The isoctyl ester was not effective at any of the above concentrations, but its presence was detected after a day. Thus, the vapor of volatile compounds was also herbicidal. The epinastic effect was shown to be greater with longer treatment time, concentration in vapor form and temperature; glass was far more effective than filter paper as a volatilizing surface. It was also shown that the 2,4-D esters were more volatile than the corresponding esters of 2,4,5-T, the isoctyl, butoxyethyl, ethoxyethoxy propyl, and the propylene glycol butyl ether esters were "low volatile", and that the amine salts evoked no response at all. Amine salts, amides

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as well as the free acid, did not affect bean and tomato plants, and volatilities of many esters were reduced compared with the pure compounds when they were dissolved in diesel, corn, or cottonseed oil.[117] The latter effect is explainable by consideration of Raoult's Law which predicts a partial pressure above a homogeneous solution of constituents. Not only plants are affected by herbicides in the vapor phase. The germination of air-dried seeds was inhibited by "volatile" esters of 2,4-D and 2,4,5-T (C_1 to C_3 esters inhibiting more than C_4 to C_5 esters), when exposed to vapors for 30 to 60 days.[118] It was found that the vapor did not permeate the seed coats, but entered during inbibition of water early in the germination process. Cotton plants were also sensitive, as well as bean and tomato.[120] The designation "high volatile" and "low volatile" was first formulated by Baskin and Walker[119,122] and Zimmerman et al.,[116,123] using the tomato stem curvature test. It was shown that the C_1 to C_5 esters of 2,4-D were highly volatile and that with $>C_5$, the esters of 2,4-D and 2,4,5-T were "low volatile". The amine, alkanolamine, and alkali salts of 2,4-D and 2,4,5-T were also in the latter category. These results have also been confirmed in field trials.[114,115,126,129]

An interesting but unconfirmed report intimated that at temperatures near 38°C, plants become less sensitive to ester vapors than at room temperatures.[130] Many reviews in the field of general pesticide volatilization have considered the volatilities of the herbicidal phenoxy esters.[131-133]

c. Amine Salts

As expected of ionic or semi-ionic compounds, the amine salts are much less volatile than the nonpolar esters.[94-96, 98-99, 111-113, 115-118, 120-123, 128-133]

Que Hee and Sutherland[94] showed that the vapor pressures of the dimethyl, methyl, *n*-butyl, *n*-dodecyl, and *n*-tetradecyl amine salts of 2,4-D were 8, 9, 6, 3, and 2×10^{-10} mm Hg at Q_e values of 5×10^7 cm²/g at 38°C. These values are much lower than any of the calculated vapor pressures of the esters (see Appendix 12) and imply that very little vapor hazard is associated with their use. However, it has been reported[128] that the amine salts can cause severe epinasty when heated to 53°C.

Esters can often be more effective than amine salts in certain situations; the alkanolamine and alkylamine salts were developed, to combine the desirable characteristics of both. Their volatility is low.[123] The volatility of the herbicidal amides has not been assessed, but it should be lower than that of the corresponding ester, but much higher than for the corresponding salt (e.g., the methyl ester of acetic acid boils at 57°C (760 mmHg), whereas the *n*-methyl amide boils at 205°C (760 mmHg)).[58] In fact, the methyl and *n*-butyl amides of 2,4-D can be quantitated by a GC method, whereas the salts cannot.[134]

F. Adsorption

1. Introduction

Adsorption is a universal process whereby molecules show affinity for other molecules by preferential physical contact of their spheres of influence. If the interaction is reversible and no chemical reaction is involved, the adsorption is called "physical"; if a chemical reaction occurs, the process is called chemisorption and is not reversible except for certain cases. The importance of adsorption in herbicidal action is that it controls how and at what rate herbicides can enter a plant, since this rate must be proportional to the area of leaf covered. The interaction of the herbicide with the plant cuticle is essentially adsorptive, and although other mechanisms may be important, direct contact has been demonstrated to be more efficient than vapor-phase administration. Furthermore, the degree of adsorption can modify the volatility of herbicides.[110,125,135,136] It is also responsible for preemergence action of herbicides in soils[137] and for, of course, many deleterious effects to crops. The topic has not attracted much

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detailed attention in the field of herbicide studies, but its importance is undoubted. This section is concerned with adsorption in various model systems. Soil adsorption will be considered in detail in Chapter 5.

There are several types of adsorption isotherm:

1. Freundlich isotherm (physical adsorption)

$$\frac{M_A}{M_O} = K_F C^n \tag{54}$$

where M_A is the mass adsorbed, M_o is the mass of adsorbate, C is the equilibrium concentration of the solute being adsorbed, K_F and n are constants, n being near one for dilute solutions of nonpolar substrates, and K_F measures the extent of binding. This isotherm adequately describes adsorption on soils.

2. Langmuir isotherm (for chemisorption and monolayers)

$$\frac{M_A}{M_O} = \frac{abc}{1 + aC} \tag{55}$$

where a and b are constants, b being the capacity of the adsorbant. This isotherm best explains the data for adsorption onto charcoal.

3. BET isotherm (for multilayers)

$$\frac{C}{(C_O - C)\,M_A} = \frac{(K_M - 1)C}{bK_M\ C_O} + \frac{1}{bk_m MW} \tag{56}$$

where C_0 is the maximum amount of available chemical, and K_M is related to the molar heat of adsorption (Q) for a monolayer and of crystallization Q_L by

$$K_M = \frac{(Q - Q_L)}{RT} \tag{57}$$

Adsorption of chlorinated pesticides has been related to the partition coefficient between water and cyclohexane,[138] the parachor,[139] Hammett Functions,[140] pH,[141] and to the amount of organic matter.[142] Thus, for nonionic compounds, there is an inverse relation between their water solubility and the extent and strength of binding.[74] Decreasing temperature usually increases adsorption.[144] The heat of adsorption is generally <10 kcal/mol for physical adsorption, but higher for chemisorption.[143] In the multilayer case, the heat of adsorption approximates the heat of solution, and this is so for adsorption of 2,4-D onto charcoal (approximately 4 kcal/mol),[145] although this has been disputed.[166] Most adsorptive processes involving pesticides in soils are usually 70 to 80% complete within a few hours, but may take weeks for complete adsorption. The usual first-order kinetic treatment applicable to many physical processes does not usually suffice for pesticide-soil adsorption, since the latter is a diffusion controlled process rather than one dominated by one rate-determining step. Adsorption of vapors can be described by the above equations with C being replaced by P, the equilibrium pressure. The Freundlich isotherm is rarely applicable in vapor phase adsorption.

2. The Halophenoxyalkanoic Acids

2,4-D free acid obeys a Freundlich isotherm[147] when it is adsorbed onto illite, mont-

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morillonite, silica gel, sand, humic acid, or alumina (see Table 6). Thus, a plot of log M_A/M_0 vs. log C is linear, with slope n and intercept log K_F. It was found that the heat of adsorption varied exponentially with the amount adsorbed,[148] with sand and silica gel always giving higher values. This is probably caused by H bonding.[149]

Adsorption of 2,4-D on soils has been interpreted in terms of Eley's kinetic theory,[149] as well as that of Fava and Eyring.[150]

Several 2,4-D systems have been interpreted by the approach of Lindstrom et al.[151] who have shown that:

$$\frac{d\phi}{dt} = k_A(1-\phi)\left(1-\frac{\phi}{2}\right)e^{-b\phi} + k_D\left[\left(1-\frac{\phi}{2}\right)e^{b(2-\phi)} - \frac{\phi^2}{2}e^{b\phi}\right] \tag{58}$$

where k_A and k_D are the rate constants for adsorption and desorption, ϕ is the fraction of adsorbed chemical at time t, and b is a constant and usually, $k_A > k_D$. Table 7 also presents activation and free energy data, as well as values for the entropy of activation. A major criticism of this method is that pseudo first-order kinetics are not usually obeyed for soil systems, and so the kinetics must be studied for each system. Furthermore, most of the above systems are clays that adsorb very little phenoxyacetic acid (<1%).[152] The clay fraction is associated with organic matter in nature, and the latter should cause a considerable modification of adsorptive behavior. Khan[153] studied the adsorption of 2,4-D from aqueous solution onto a fulvic acid/montmorillonite clay complex (62:38). Fulvic acid is a natural soil constituent and can account for up to 75% of the organic matter. A Freundlich isotherm type of adsorption was observed[159] (see Table 6), and the slope n increased with increasing temperature; in contrast, log K_F values indicated that the adsorption capacity on the acid-clay complex for 2,4-D was smaller than that on humic acid,[148,164] but greater than the values reported for montmorillonite alone.[148] In addition, 2,4-D covered only a small proportion of the complex (6.5 and 5.2 μmol of 2,4-D per gram of organo clay complex were adsorbed at 5 and 25°C, respectively) in marked contrast to the large values obtained by Miller and Faust[154] (50% coverage per gram of complex, especially at low pH). The latter phenomenon appeared to be because of the presence of dimethylbenzyloctadecylammonium chloride and other free amines. The "isosteric" heat of adsorption of 2,4-D for the fulvic acid/clay complex was approximately 1.2 to −0.3 kcal/mol, compared with values of −2.0 to +2.0 kcal/mol for humic acid.[148] Humic acid also strongly adsorbed 2,4,5-T from solution,[155] and humic acid particles in river water have been implicated as the major downstream carrier of chlorinated hydrocarbons and polychlorinated biphenyls.[156,157] Also, the greater the organic content of the soil, the more 2,4,5-T is adsorbed.[158] Leaching is the common name for desorption from soils. As Table 7 shows, desorption usually requires more energy than adsorption. In addition, acid and salt forms of sepiolite and vermiculite were examined for their C^{14}-2,4-D leaching characteristics by Lopez-Gonzalez and Gonzalez-Gomez.[160] Sepiolite allowed greater movement and this appeared to be dependent on the number of exchange positions per unit surface area of the clays.

Ion-exchange capacity plays an important role in adsorption to many soil types, especially clays; thus, 2,4-D anions were found to be exchanged on such highly alkaline anion exchangers as Dowex 1X2 and Wofatit SBK.[161] Weaver[162,163] studied the degree of adsorption of 2,4-D, and its NH^+_4, Cu^{2+}, and Ca^{2+} salts as well as that of 2,4,5-T. Amberlite I R-100 H and Zeo Karb H adsorbed much of the herbicides, but Decalso and Zeo-Dur were not effective. Amberlite IR-4B and De-Acidite retained less Cu^{2+} salt of 2,4-D than the other 2,4-D compounds. Amberlite IR-100H was especially effective at pH <3.3. Much of the bound 2,4-D was not susceptible to leaching. These results indicated that adsorption may be important in acidic soils.

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Table 6
FREUNDLICH CONSTANTS K_F AND n FOR ADSORPTION OF 2,4-D FREE ACID ON SURFACES

Surface	pH	Temperature (°C)	Slope (n)	Intercept ($\log_{10} K_F$)
Alumina[147]	6—7	0	0.97	−0.06
		25	1.01	−0.08
Humic acid[147]	6—7	0	0.86	0.931
		25	2.01	1.9
Illite[147]	6—7	0	0.658	1.11
		25	0.719	1.02
Montmorillonite[147]	6—7	0	0.925	−0.63
		25	1.004	−0.186
Sand[147]	6—7	0	0.671	−0.984
		25	0.827	1.45
Silica gel[147]	6—7	0	0.90	0.58
		25	0.95	0.11
Fulvic acid/ montmorillonite[153] (62:38)	3—5	5	0.76	0.815
		25	0.83	0.716

Table 7
ADSORPTION PARAMETERS FOR VARIOUS SYSTEMS CONTAINING 2,4-D UTILIZING $d\phi/dt = k_A[(1-\phi)(1-\phi/2)e^{-b\phi}] + k_D[(1-\phi/2)e^{b(2-\phi)} - \phi^2/2\, e^{b\phi}]$ AND GIVING VALUES OF ΔE_a (ACTIVATION ENERGY IN kcal/mol), ΔS_a ENTROPY OF ACTIVATION (IN esu UNITS), AND ΔG_a (FREE ENERGY OF ACTIVATION IN KCAL/MOL); A IS THE SURFACE AREA IN CM^2/G

	System	T(K)	ΔE_a	k_A/sec	ΔH_a	ΔS_a	ΔG_a	b	Concentration (ppm)
Adsorption	Silica gel[147]	273/298	6.0	0.15	5.4	−44	18.4	2.2	10
	Illite[147]	273/98	3.3	0.011	2.7	−57	20	3.5	10
	Illite[152] ($A = 1.8 \times 10^6$)	298	3.5	—	4.1	76.2	1.9	—	1.27
	Kaolinite[152]	298	3.2	—	3.8	−75.5	1.5	—	1.27
	Montmorillonite[152]	298	5.5	—	6.1	70.5	4.0	—	1.27
Desorption	Illite[147]	273/298	5.6	1.1×10^{-5}	5.0	−68	25	3.5	10
	Silica gel[147]	273/298	7.0	1.2×10^{-5}	6.4	−61	23	4.2	10

2,4-D was shown to adsorb reversibly onto goethite[165] from aqueous suspensions, but at low concentrations, the anions were bound, so that the carboxylate groups were weakly bound to positive sites with the hydrophobic aromatic ends directed towards the solution; at high concentrations, the anion orientation was reversed, with the aromatic ring binding via π-π interaction, with the first adsorbed layer and the surface reverting to its hydrophilic nature. Concentration effects like these have rarely been intensively studied, especially on often undefined soil samples.

Adsorption on activated charcoal is important; it is a major method to remove organics and many inorganics from potable waters[169] and is also extensively used in air-sampling techniques in industrial hygiene.[170] Many publications have dealt with the adsorption of 2,4-D onto charcoal from aqueous solution;[143,145,166-168] it was found that the process had an activation energy of approximately 10 kcal/mol,[166] although a value of ~2.74 kcal/mol was obtained by Weber;[145] the adsorption process obeyed a Langmuir isotherm,[145,167] and the sorption was pH-dependent, with maximum adsorption

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being at a pH = pK_a (see Table 8) for all the chlorinated herbicides studied,[167,168] although different results were obtained in buffered solutions;[143] the molar adsorptive capacity for 2,4-D on 1 g of charcoal is approximately 2.2×10^{-4} mol at pH 7 and 26°C;[167] the effective diffusivity is between 2 to 9 cm/sec at 25°C with equilibrium occurring in 2 weeks to 5 months,[166] the rates depending on the concentration of the solution used;[145] the heat of adsorption of 2,4-D is −4.16 kcal/mol at 25°C.[145] That activated charcoal may be very effective at removing low concentrations of 2,4-D compounds from water is thus evident. Charcoal has been extensively used to remove volatile components from air samples,[170] but few applications regarding the phenoxys have been reported,[171] although silica gel samplers have been utilized[172,173] (see Chapter 5).

G. Miscellaneous Properties

Kulawik[173] studied the dielectric potentials (ε) and surface tensions (δ) of a number of 2,4-D derivatives in 0.1 *M* KCl at 25°C. Both properties were invariant with pH for 0.0024 *M* solutions of free acid from pH 3 to 12, the maximum potential (+335 mV) and maximum change in surface tension (66.5 dyne/cm) being at pH 1.4. Both potential and surface tension increased with increasing concentration at constant pH and temperature. Triethanolamine solutions showed invariant potential and surface properties in the pH range 2 to 6, but increased pH >7 to attain maximum ε (−105 mV) and δ (~70.6 dyne/cm) at pH 10. The triethanolamine 2,4-D salt (0.0725 *M*) showed an inverse relationship between ε and the pH, the maximum ε of +180 mV occurring at pH 5.4. The δ showed a minimum at pH 6.75. The δ and ε of solutions of the ethyl ester of 2,4-D showed no dependence on pH or concentration in the pH range 1.8 to 7.0. The maximum ε was +180 mV, and the maximum change in δ was 66.0 dyne/cm for a 0.0725 *M* solution (although it might be expected that the ester might form a thin layer across the surface of the solution). MCPA derivatives were also studied,[174] and it was found that the acid increased the ε of water, while its ethyl ester and 2,5-D reduced it. All three markedly reduced the δ of water. Surface tensions of the amine salt and the sodium salts of 2,4-D measured at 10 to 25°C by Yudina et al.[175] The surface tension decreased linearly with increasing temperature, and a 10°C temperature increase decreased it 0.98-fold.

The densities, relative and absolute viscosities, surface tension, and refractive indexes were measured for aqueous solutions of the sodium salt[176] of 2,4-D. Freezing point depressions were (molar concentration/degree depression) 0.005, 0.019°C; 0.010, 0.036°C; 0.025, 0.093°C; 0.050, 0.187°C. The refractive indexes at various temperatures of the saturated solutions were 1.3393 (0°C), 1.3410 (30°C), and 1.3426 (45°C). Solubilities (grams per liter) in water were 27.51 (0°C); 50.63 (30°C), and 74.9 (45°C). All the densities, refractive indexes, and viscosity values were nearly linear functions of concentrations at all temperatures studied, while conductances showed greater deviations from linearity, especially at the higher temperatures. Surface tension showed a nearly linear relation at 30°C, but not at 0° or 45°C. The ionic conductance vs. temperature plot of the 2,4-D anion was almost linear, with a limiting value estimated to be 24.1 mho^2cm^2 at 25°C. This value was 74.2 mho^2cm^2 for sodium 2,4-D.

Dielectric constants and refractive index data in dioxan at 25°C were determined for a number of phenoxyacetic acids by Colinese et al.,[177] who then calculated polarization and dipole moment data (see Appendix 1). The dipole moments of *para* substituted phenoxyacetic acids were also calculated from

$$\mu^2_{Cal} = 2.34^2 + \mu^2_{\phi - x} + 2(2.34)(\mu_{\phi - x} \cos 74°30') \quad (59)$$

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Table 8
ADSORPTION OF 10^{-4} *M* PHENOXYACETIC ACIDS[167] ON 10-MG ACTIVATED CARBON AT pH3 AND 25°C AT VARIOUS pHs UTILIZING LANGMUIR ISOTHERM DATA $m/m_o = abC/(1 + ac)^a$, WHERE C = μmol/ℓ μmol/g

	pH = 3				pH = 7				pH = 11			
Acid	Adsorbed (%)	a (ℓ μmol)	b (μmol)	m/m_o (μmol/g)	Adsorbed (%)	a (ℓ μmol)	b (μmol)	m/m_o (μmol/g)	Adsorbed (%)	a ($\ell\mu$mol)	b (μmol)	m/m_o (μmol/g)
Phenoxy acetic	44.0	0.423	446	436	8.0	0.229	105	86	4.0	0.209	64	43
4-CPA	55.0	0.362	575	560	17.7	0.101	198	180	9.8	0.115	145	133
2,4-D	60.1	0.279	629	607	18.8	0.112	223	205	14.3	0.070	154	135
2,4,6-T	65.3	0.672	676	666	21.8	0.095	239	216	12.5	0.073	144	127

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where 2.34 is μ for phenoxyacetic acid, 74° 30' is the angle the oxyacetic moiety makes with the 0–C ring bond in phenoxyacetic acid, and $\mu_{e\text{-}x}$ is the dipole moment for the parent monosubstituted benzenes.

The tabulated values were obtained after interaction moments along the O–C (ring) ions (μ_{int}) were found. Thus,

$$\mu^2 = 2.34^2 + (\mu_{\phi - x} + \mu_{int})^2 + 2(2.34)(\mu_{\phi - x} + \mu_{int}) \cos 74° 30' \quad (60)$$

In calculating μ_{int} and μ_{cal} for 2,4-D, allowance was made for free rotation of the ortho C-Cl dipole about the O–C (ring) bond (see Appendix 14), although this will become more restricted as the acid becomes sterically hindered.

The friction coefficients of 2,4-D were determined by Anopa et al.[178]

V. SPECTROSCOPIC PROPERTIES

A. UV Spectra

1. Free Acids

As might be expected for aromatic compounds, the phenoxy acids absorb in three distinct regions of the UV visible:[145,179-181,184] the aromatic $\pi^* \leftarrow \pi$ region, 250 to 300 nm; the $\sigma^* \leftarrow \sigma$ region, 210 to 190 nm; and an intermediate region, 250 to 215 nm; this latter peak is not present in 2,4,5-T. The weak C=O $\pi^* \leftarrow n$ transition is not distinguishable on the long wavelength side of the $\pi^* \leftarrow \pi$ transition. Unfortunately, λ_{max} for these acids are not sufficiently separated to analyze mixtures by UV means, although there is one report of this being achieved.[188] Thus, the λ_{max}/molar extinction coefficient in 1/mol/cm for 2,4-D, 2,4,5-T, and Silvex at the $\pi^* \leftarrow \pi$ transition are [145] 284 (1900), 289 (2500), and 289 (2500), respectively, in water, implying that chlorination increases ε_m and moves λ_{max} to longer wavelengths, but substitution at the methylene C causes no effect. Gordon[181] obtained ε_M values of 1981 at 284 nm and of 2509 at 289 nm for 2,4-D and 2,4,5-T, respectively, in a complex solvent phase (*n*-hexane saturated with formic acid/glacial acetic acid/methanol (0.4:1.6:18 mℓ)). As the carboxyl group became ionized, it was noted by Phillips[179] that the λ_{max} shifted towards the visible region. The presence of the phenolic atom was also crucial, since longer chain acids did not show these effects. Furthermore the acids with chlorines at both *ortho* positions show bathochromic shifts for their λ_{max} and possess much lower ε_M than other unhindered acids (see Appendix 15). This steric hindrance causes inhibition of free rotation about the phenolic oxygen[182,183] and reduces possible interaction with the carboxyl group, as well as conjugation between the phenolic 0 and the aromatic ring. Bandurski[184] reported no change in the UV spectrum of 2,4-D between a pH of 2.2 to 8.0 in water, although the pK_a was around 2.73;[77] the λ_{max} at 283.5 nm and the reported ε_M of 2.0×10^3 corresponds to the ionized species which should predominate in this pH region. However, in ether, the λ_{max} was 284.5. It was also shown that Beer's Law held between 6 to 250 ppm.

2. Esters

There are almost no differences in the UV spectra of the esters of the same acids in methanol as chain length increases, the λ_{max} and ε_M being determined almost solely by the substitution of the aromatic nucleus.[188] Three λ_{max}/molar extinction coefficients are shown by 2,4-D esters: 230 nm (10^4), 285 ($10^{3.4}$), and 293 ($10^{3.3}$). MCPA esters

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have absorptions at 230 (10^4), 280 ($10^{3.3}$), and 287 ($10^{3.2}$), but with no maximum at 230 nm. Thus, a bathochromic shift is observed in λ_{max} as chlorination increases; if the *ortho* chlorine is replaced by a methyl group, a hypsochromic shift occurs. Bathochromic shifts would also be expected for the corresponding propionic and butyric acid esters as with the free acids.

3. Salts

The UV spectra of the anions[179] have already been discussed above (see Appendix 15), and the λ_{max} of an aqueous solution of the 2,4-D sodium salt has been reported to be 283.5 nm in another investigation.[186]

The UV spectra of the amine salts are similar to the esters, being determined by the aromatic nucleus. However, as the alkylamine chain length increases, the λ_{max} do show bathochromic shifts[187] (see Appendix 16). The λ_{max} of the triethanolamine salt of 2,4-D was 283.5 nm,[186] and Beer's Law was obeyed from 2 to 50 μg/mℓ.

4. Amides

No data are available, although it would be expected that the aromatic nucleus would dominate as in the esters and salts.

B. IR Spectra

1. Free Acids

Appendix 17 presents the various major absorbing bands of several phenoxyalkanoic acids. The spectra using acetone solvent[189] show shorter wave lengths and some different absorption intensities compared with those done in a KCl pellet. As expected, the IR spectra show H-bonded −COOH bonds from 3 to 4 μm, as well as from 6 to 8 μm, making these regions unsuitable for analysis. No one wavelength is specific for each acid, so it is judicious to choose at least two for analysis. The IR spectra of various phenoxys are presented in Appendix 17.[180]

There are many reports on the IR of the phenoxyacetic acids.[189-196] Oki et al.[194-196] studied the OH and C=O stretches in nonsubstituted acids. Electron-donating groups on the ring increased the intensity of the 3390 to 3490 cm^{-1} *trans*–OH peak (compare to 3550 to 3500 cm^{-1} for *cis*) and the carbonyl peak at 1790 cm^{-1} *(trans)* relative to 1760 cm^{-1} (*cis*), thus enhancing the *trans* form, whereas electron withdrawing substituents favored the *cis* form. However, if intramolecular H-bonded dimers are present, the configuration must necessarily be *cis*. Bands at 935, 1435, and 1735 cm^{-1} have been assigned to the dimer.[202] In fact, the 1735-cm^{-1} band is quite strong for 2,4-D[72,180] (see Appendix 17). Aryl ethers show absorptions[202] in the 1270 to 1230-cm^{-1} region.

Oki also showed that α-propionic and α,α-butyric acids obeyed the above *cis/trans* behavior, with the *cis* form predominating. Sjoborg[193] gave the following λ_{max} for the respective phenoxyacetic acids: 2-methyl (13 to 22 μm), MCPA (12 to 38 μm), and 4,6-dichloro-2-methyl (13.05 μm). Blinn et al.[197-199] have reviewed the topic.

2. Esters

With the disappearance of the acidic H, the spectra show sharp C=O and aromatic stretches with no H-bonded peaks. Appendix 18 shows the IR spectra of the methyl and other esters of miscellaneous acids. The KCl disc spectra of the methyl esters[185] contain OH stretch peaks which could be caused by water or by acid impurity. The other major feature is the general simplification of the spectra compared with those of the corresponding acid. Since the esters have *cis* geometry, the C=O stretch peak at 1700 cm^{-1} is very much enhanced. It will be noted in Appendix 18 that the 12.56- and 13.72-μm wavelengths are used to quantitate the same ester of 2,4-D and 2,4,5-T, respectively, even though MCPA also absorbs strongly at 12.56 μm, but very weakly at

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13.72 μm. Nevertheless, 2,4-D and 2,4,5-T have a much more intense absorption at 11.45 μm than has MCPA, so these three can be differentiated. Clearly, the use of a number of wavelengths is desirable.

3. Salts

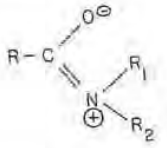
The IR spectra of the carboxylate salts show extensive COO^- broad bands at 4 to 2.75 μm and 5.8 to 9.0 μm. The sodium salt of 2,4-D has[72] the COO^- symmetric vibration[202] at 6.21 μm (1610 cm^{-1}), rather than the C=O vibration at 5.90 μm (1700 cm^{-1}) of the free acid. New bands also appear at 9.65 μm (1030 cm^{-1}) and at 7.50 μm (1330 cm^{-1}). Clearly, the spectrum of 2,4-D free acid itself seems to be a composite of the undissociated and dissociated forms along with dimers, with the former being very predominant.

For the amine salts, in addition to the carboxylate spectrum, there is also superimposed the spectrum of the amine, complicated by extensive H-bonded amine bands (2.9 to 4.2 to 5.8 μm and 5.9 to 9.0 μm) which make quantitative analysis in these regions almost impossible. Bands at 6.40 to 6.55, 7.75, and at 6.00 μm have been interpreted to imply the existence of $R-C(=O)-O^{\ominus}$, $R-C(=N)-O^{\ominus}$, and of an imino ether, respectively.[191,200] The presence of peaks around 4.2 to 4.8 μm may imply[72] $-C=N^+-H$. In fact, the lower salts show two frequencies at ~6.20 μm (1635 cm^{-1}) and 6.40 μm (1590 cm^{-1}), the shorter wavelength one migrating to 6.08 μm (1650 cm^{-1}) beyond the *n*-butylamine salt.[72]

4. Amides

Very little data are available.

Bands between 6 to 8 μm have been attributed to the structure



which contributes 15% to the resonance hybrid.[201] As might be expected, the amides show[72] simplified spectra compared with the corresponding amine salts, with strong bands at 2.90 μm (3440 cm^{-1}), N–H str; 5 to 90 μm (1695 cm^{-1}) – C=O; 6.50 μm (1550 cm^{-1}), Amide II; 8.0 μm (1250 cm^{-1}), and 8.3 μm (1300 cm^{-1}), Amide III.

C. ^{13}C and Proton NMR

Free 2,4-D in CD_3OD shows[72] no free H downfield of the aromatic absorptions, but shows an exchange peak with CD_3OD at 5.13 ppm relative to TMS. The CH_2 group absorbs at 4.72 ppm, H-3 at 7.35, H-5 at 7.12, and H-6 at 6.90 ppm. When these resonances are compared with those[203] of the sodium salt in D_2O (see Appendix 19), the CH_2 frequency has migrated downfield (~0.19 ppm), while those for the ring protons H-3 and H-5 have migrated in the reverse direction ~0.15 ppm; the H-6 absorption is hardly affected. Addition of $Eu(FOD)_3$ shift reagent shifts the aromatic absorptions upfield by 1 ppm without resolving the spectrum. It also shifts the exchange peak upfield without affecting the CH_2 absorption.[72] Both proton ^1H and ^{13}C spectra of various phenoxyacetic sodium salts in D_2O have been presented conveniently in one publication by Junghans and Sprinz[203] (see Appendix 19). It was found that, with a correlation coefficient of 0.99,

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$$\delta_{C^{13}} = a\delta_H + b \qquad (61)$$

where δ is the chemical shift with respect to TMS in ppm, a = 27.2, and b = 69.5 ppm.

The chlorine quadrupole resonance frequencies in 2,4-D solid were found at 34.62 and 35.64 at 30.5°C.[204] Another study[205] showed that the angle between Cl–C *para* and the Cl–C *ortho* vectors is <120°, implying some distortion, and that the partial double bond characters were 0.026 and 0.044, respectively. It is of interest that the NMR spectrum of 2,4-dichlorophenol, often present in 2,4-D samples, has also been obtained.[206]

The NMR frequencies of the methyl esters of some phenoxyacetic acids are given[185] in Appendix 20. The ring proton absorptions of H-3 and H-5 in a given series are hardly affected by lengthening the alkanoic side chain, but the resonance of H-6 is susceptible. The substitution of a methyl group at the α-C causes enhanced deshielding of the ester methyl protons. H^1-NMR of a series of *n*-butyl esters showed[207] that the chemical shifts of the lowest field proton (H-3) followed 2,4,6-T< 2,6-D < 2,4,5-T< 2,4-D. This was attributed to electron density in the 6 position as well as localization of positive charge on the sterically hindered C-atoms.

The NMR aromatic resonances of the 2,4-D amine salts in CD_3OD are almost the same as for the corresponding acid,[72] except that the methylene group and the H-6 ring absorptions are more shielded by about 0.10 ppm. In the corresponding amides ($CDCl_3$), only the H-6 absorption becomes more shielded, shifting upfield by 0.06 ppm. These changes imply that the side chain interacts in some way with the H-6 position. In fact, as the amide chain length becomes longer, the H-6 absorption migrates to still higher fields, e.g., ~6.20 ppm for the *n*-dodecylamide of 2,4-D (compare to 6.60 ppm for the salt). For the *n*-butylamine salt, H-6 begins at 6.86 ppm and ends up at 6.80 ppm for the amide.

NMR of herbicides has been reviewed by Haque and Biros.[208] Unfortunately, the sensitivity of H^1-NMR is only in the mg range. However, ^{13}C-NMR offers real advantages to the pesticide chemist, since it can detect microgram quantities with ease and may be sensitive to the ng level, utilizing the resources of Fourier Transform. The chemical shifts of the carbon atoms are typical of those expected (see Appendix 19).

D. Mass Spectrometry

Mass spectrometry,[208,209] especially coupled with on-line separative techniques, is probably the most versatile of all the spectroscopies for the phenoxyalkanoic acids: the chlorinated isotope distributions impart characteristic heights to chlorine containing peaks, the close proximity of the carboxyl group to the phenoxy ring allows the molecular ions to be intense providing the compound is volatile enough and the spectra are comparatively simple and yet characteristic. In addition, picogram sensitivity can be attained using the specific ion-monitoring mode. Even nonvolatile compounds can be induced to give mass spectra, either by field desorption or by chemical ionization modes.

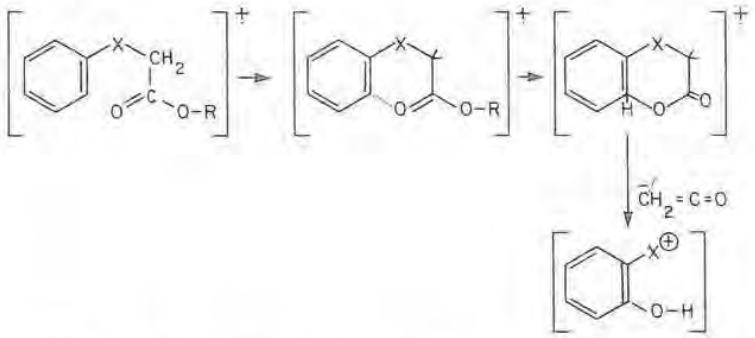
1. Free Acids

Electron impact spectra and some fragmentation patterns of the various herbicidal acids[210,223] are presented in Appendix 21.

In general, large $P-CH_2COOH$, $P-CH_2COO$ (with H transfer), P–COOH, and P–Cl peaks are shown. If the parent ion P has a phenolic $O-C^+H_2$ group, formaldehyde is easily lost, as is carbon monoxide if a phenolic O is present. HCl loss is also facile after initial fragmentation. No deuterium labeling studies have yet been reported, so that the fragmentation mechanisms have not been explicitly verified.

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Many studies have been carried out on related phenylpropionic acid and phenetole systems.[211-215] Thus, for phenylpropionic acid (ester),[211]



where X = CH_2 and R = alkyl or H. This production of ketene by a Retro Diels Alder process is enhanced by presence of an *ortho* chlorine relative to a *para*,[212] but phenetoles do not show this effect,[213] and this pathway would not be expected for phenoxyacetic acids (esters). It has been suggested[212] this behavior is because of the highest occupied molecular orbital (HOMO) of phenylacetates, a σ orbital situated mostly (47%) on the carbonyl O, i.e., the charge is mostly localized on the carboxyl group. In contrast, the HOMO for phenetole is a π orbital, with its largest contribution from the ether O p_z orbital (34%), even though this is antibonding with respect to ring carbon. Benoit[214] also concluded that ketene loss was unlikely if the positive charge was localized on the aromatic ring. It is interesting to note the ionization (IP) and appearance (AP) potentials of various substituted phenetoles for the transition M-ethylene relative to phenetole itself,[213] given the theoretical values 8.05 and 10.10 eV, respectively, 2-Cl, 8.12 and 10.19, 4-Cl, 7.87 and 10.62; 2,4-diCl, 8.05 and 10.62, and 2,6-diCl, 8.46 and 10.01, i.e., substitution does not change IP and AP very much. It is also instructive to note the IP and AP values for the M-Cl transition of *meta* substituted chlorobenzenes:[216] *m*-CH_3, 8.93 and 11.32 eV; *m*-Cl, 9.46 and 13.29 eV; *p*-Cl, 9.27 and 13.24 eV, respectively. It is implied therefore that production of phenol-type peaks is favored above dechlorination, as observed in the spectra of the halogenated phenoxyalkanoic acids.

Figure 1 shows the complete expected fragmentation pattern for 2,4-D acid.[72] There are metastables at 119.36 and 121.5 (220 → 162 and 222 → 164 transitions). The charge appears to reside on both aromatic ring and the carboxyl group, with the former predominating in the fragmentation. Thus, there are two possible m/e 75, 74, and 73 ions. A subtle pathway is 185 → 149, since the m/e 149 is partially hidden under the isotope ratios of peak m/e 145 which contains two chlorines.

As the chain length increases, the molecular ion decreases in intensity,[210] and scission α to the phenoxy O becomes more important with the charge retained by the aliphatic fragment (see Appendix 21). 2,4,5-T shows the same type of fragmentation as 2,4-D.[210,217]MCPA (see Appendix 21 F) has a large molecular ion and easily loses the alkyl part of the ether link, since the daughter ions can be stabilized by both quinoid and tropylium type structures. Indeed, a tropylium ion has been explicitly postulated for m/e 125.[210] Whereas 2,4-D and 2,4,5-T show M-35 peaks, MCPA does not, indicating that the *ortho* chlorine is lost preferentially in 2,4-D and 2,4,5-T (see Appendix 21 B, D). As in 2,4-D and 2,4,5-T, there is also a large phenolic rearrangement peak, probably via a five-membered transition state which does not involve the aromatic ring. MCPP and MCPB show no M-35 peaks, but show large m/e 142 peaks. However,

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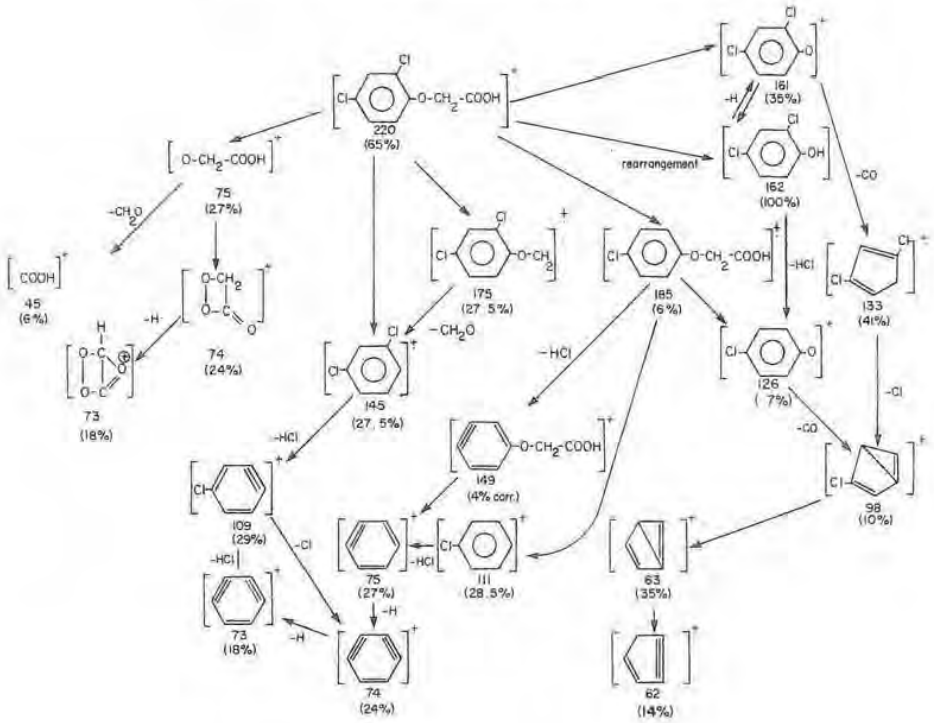


FIGURE 1. Mass spectral fragmentation scheme for 2,4-D.

whereas MCPB produces a large 83, MCPP cannot produce this particular peak. Characteristic peaks for MCPP are the hydroxytropylium ion m/e 107 (although MCPA does possess this peak) and the base peak m/e 142.

The purity of each compound can be ascertained by use of low electron volt mass spectrometry. Usually the molecular ion only is seen near the ionization potential. If the appearance potential is close to the ionization potential, other peaks may be seen, e.g., m/e 162 (164, 166) for 2,4-D [m/e 220 (222, 224)].

Negative ion mass spectrometry is also beginning to develop. Intense (M-1) peaks are obtained, and although it is less sensitive at present than the positive mode, recent advances in instrumentation have greatly improved the situation. Figure I in Appendix 21 shows the negative ion MS of 2,4,5-T.[218] There is a general lack of rearrangement ions, and (M-1)-Cl, m/e 195 (3 Cl), 182, 176 (1 Cl), 161 (2 Cl), and 79 (1 Cl) dominate.

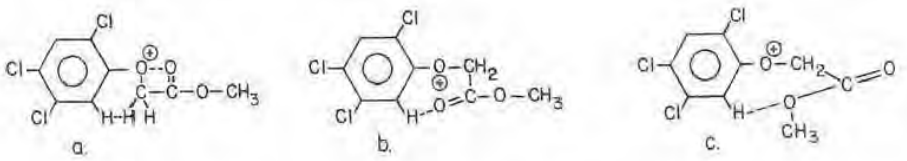
2. Esters

Appendix 22 shows the mass spectra of the methyl esters of various acids.[185,219]

Four mass spectra[72,185,219-220] of the methyl ester of 2,4-D are also presented, since it is evident that while the actual peaks are the same, the peak heights certainly vary from instrument to instrument, a problem when the specific ion monitoring mode is to be used.

In general, as the chain length increases, the molecular ion of the methyl ester decreases, and this implies some interaction of the side chain with the phenoxy ring in the short chain derivatives:

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Ion a is favored, since interaction of the α-methylene with the open ortho position of the ring, as well as sharing of the positive charge by the carboxyl and phenoxy O, in addition to the acquisition of partial tropylium character, are encouraged; furthermore, this can also account for the large P − 59, P − 73, 59, and 73 peaks. Ions b and c do not explain the observed fragmentation patterns and infer that a M-31 peak should be expected. This is only observed in MCPB, and methanol is eliminated for MCPA.[185] MCPP shows neither loss. Appendix 22 also contains the mass spectra of the methyl esters of 2,3-D and 3,4-D.[219] It is evident that 3,4-D has no M-Cl peak, but the peaks at m/e 234 and 175 are enhanced. Probably steric factors are responsible. It may also be possible that the $\cdot C(=O)-O-CH_3$ group is activated to leave, since the steric effect of the 2 Cl has been removed, and the parent ion is thus more stabilized.

Most of the herbicidal methyl esters thus show M−Cl, M−CH_2COOCH_3, M−$COOCH_3$, and M−OCH_2COOH_3 peaks. Phenoxy cations tend to lose C=O, and anisolic $-O-CH^+_2$ ions lose formaldehyde. For the 2,4-D methyl ester, m/e 162 is small. Metastables for the methyl ester of 2,4-D[72] are found at 171.1 (236 → 201), 169.8 (234 → 199), 130.9 (234 → 175), 83.9 (147 → 111), 81.9 (145 → 109), 85.8 (149 → 113), 123.5 (175 → 147), and 82.7 (145 → 110). The methyl ester of phenoxyacetic acid shows metastables at 68.9 (166 → 107), 55.5 (107 → 77), 58.5 (107 → 79), and 33.8 (77 → 51). The 2-CPA methyl ester shows metastables at 99.5 (200 → 141), 101.2 (202 → 143), 136.1 (200 → 165), 90.8 (141 → 113), 50.7 (111 → 75), 52.5 (113 → 77), and 51.6 (112 → 76). The 4-CPA methyl ester shows the same metastables as 2-CPA. Thus, transitions involving Cl, C=O, HCl, $C(=O)-O-CH_3$, and CH_2O loss have characteristic metastables.

The fragmentation of methyl esters is atypical, since all esters $>C_3$ show the ubiquitous McLafferty Rearrangement involving a γ -H in a six-membered transition state to produce the ion of the free acid, and hence the latter's characteristic spectrum. The mass spectra of the *n*-butyl esters of 2,4-D, 2,3-D, and 3,4-D are also presented[219] in Appendix 22 in addition to the MS of the butoxyethanol, isooctyl, and propylene glycol butyl ether esters of 2,4-D. Increasing ester chain length does decrease the intensity of the parent ion, but not as severely as would a corresponding lengthening of the side chain of the acid part, thus illustrating the crucial importance of the distance between the phenoxy ring and the carbonyl group. For the *n*-butyl esters, only 2,3-D and 2,4-D show a peak at m/e 185. Since the 220 peak for 3,4-D is much enhanced, the parent ion has been stabilized again as for the methyl esters. Only the 2,3-D *n*-butyl ester shows a M−Cl peak; m/e 199 and 185 have been used for specific ion monitoring purposes for the methyl and *n*-butyl esters of 2,4-D, respectively.

It might be expected that the *n*-butyl ester of 2,4-D would have metastables at 119.3 and 121.5 as for 2,4-D free acid. In addition, there are metastables at 123.9 (276 → 185), 125.8 (278 → 187), 81.9 (145 → 109), and 83.7 (147 → 111). There is a negligible (M-35) peak, but 2,3-D has a moderately high dechlorination peak (see Appendix 22); 3,4-D butyl ester also has a negligible M-35 peak. The absence of the M-35 peak is also characteristic for the longer chain esters (see Appendix 22). The molecular ions are still intense, however. For the *n*-octyl ester, metastables can be found at 119.3, 121.1, 145.7 (332 → 220), and 147.5 (334 → 222).

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3. Salts

a. Alkali Salts

In general, the alkali salts are not volatile enough for electron impact conditions to elicit mass spectra from them. However, field desorption mass spectrometry (FDMS) has been utilized to obtain characteristic mass spectra of the sodium salts of 2,4-D, MCPA, and their mixture.[221] Only 100 ng was necessary for analysis, and the sample did not have to be evaporated, only desorbed from 10-μm diameter tungsten needles. No parent ions are shown, but intense cluster ions $(M_A + Na)^+$ and $(2M_A + Na)^+$ (see Appendix 23) characterize the compounds. Strong $(Na\ ^{35}Cl + Na)^+$ and $(CH_3COONa + Na)^+$ at m/e 80.948 and 104.993, plus the appropriate isotope peaks, are also observed. Other peaks for MCPA are m/e 142.018 ($C_7H_7O^{35}Cl$), 200 (free acid), and 211 (dechlorinated disodium salt cation). The FDMS of the sodium salt of 2,4-D is similar to that for the salt of MCPA. 2,4-Dichlorophenol (m/e 162), dechlorination peaks (m/e 197,231), and the characteristic cluster ions $(M_A + Na)^+$ and $(2M_A + Na)^+$ are strongly present (see Appendix 23). The parent molecule is cationized by the monochlorophenoxyacetic acid sodium cluster (m/e 231) to generate the group of peaks at m/e 473 ff. The ion at m/e 323 to 325 is novel, being generated by cationization of the parent molecule by an inorganic cluster ion of disodium chloride $(Na_2Cl)^+$. The FDMS of the mixture shows essentially all the peaks of both components, thus showing good potential for mixture analysis. The major disadvantages of the technique are the tedious procedures required for desorption and for recording the ions on photographic plate. However, the method certainly is sensitive, produces spectra of nonvolatile compounds, and clearly will become important in the near future in the elucidation of high molecular weight metabolites of pesticides.

b. Amine Salts

Amine salts produce characteristic electron impact spectra that comprise the superposition of both acid and amine moieties. No parent ion peak is observed for the salt, but the ratio of the acid and amine parents is predictive of the stoichiometry of the salt[65] under conditions of low electron voltage; this relationship is not necessarily observed at 70 eV. These spectra also show the same metastables which characterize both acid and amine moieties.

4. Amides

Appendix 24 shows the mass spectra[72] for various amides of 2,4-D. In general, the parent ions are weak, P-35 peaks large (with (M-35) m*), and the aliphatic peaks below m/e 100 greatly enhanced, with the aromatic peaks greatly decreased. The P-35 ion would be the best choice for specific ion monitoring purposes.

Feung et al.[222] have systematically obtained the mass spectra of 20 amino acid conjugates of 2,4-D (see Appendix 25). All conjugates except for histidine exhibited molecular ions (M^+) and characteristic fragmentation patterns. Prominent ions arising from the 2,4-D portion of the molecule are m/e 220, 219, 184, 175, 162, 145, 133, 109, 98, 74, and 63 and the appropriate isotopic ions (see Appendix 25). The upper region of the spectra > m/e 223 is characteristic of the specific conjugate. The major peaks seen in this region are M−Cl, M−COOH, M−H_2O, and M−side chain fragmentation (see Appendix 25). The parent ion is larger than for the straight chain amides, since the presence of the α-carboxy group allows charge localization over the amino acid moiety. The M−Cl peak is still much larger than the molecular ion peak. The spectra for Val and Tryp contain too many 100% peaks for them to be considered correct.

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E. Fluorescence and Phosphorescence

Chlorobenzenes are nonfluorescent;[224] 2,4-dichloroanisole is quite fluorescent,[187] but phenoxyacetic acid does not fluoresce very strongly.[187] Thus, although the phenoxy O promotes fluorescence, the presence of the carboxylic acid group decreases its likelihood (by about 100 times). This is one reason why fluorescence is not used as a quantitative tool for these compounds. Also the fluorescence emission is wavelength and concentration dependent.[187]

Both fluorescence and phosphorescence spectra are broad, but the phosphorescence emission has been used for quantitative purposes.[226,227]

1. Free Acids

The λ_{max} fluorescence of 2,4-D/alcohol solutions at 25°C is wavelength and concentration dependent. Thus, excitation wavelengths of 250 to 300 nm elicit an λ_{max} of 345 to 360 nm from solutions of 2,4-D/*n*-butanol below 4 mg/mℓ, while at higher concentrations, 310 to 360 nm excitation evoke λ_{max} of 405 and 430 nm (uncorrected) which, upon correction for lamp wavelength variation, monochromator blaze, and photomultiplier sensitivity, become one maximum at 425 nm. This implies that the photophysical events in dilute and concentrated solutions differ. Above 4 mg/mℓ, the fluorescent response at 425 nm was proportional to concentration using 310 to 360 nm excitation, and this behavior was also observed for methanol and *n*-octanol. As the chain length of the alcohol increased, so did the intensity of fluorescence, consistent with a $\pi^* \leftarrow n$ state being the highest occupied molecular orbital (HOMO). It will be recalled that the HOMO for phenetoles is[212] a π orbital which has its largest contribution from the ether O p_x orbital, whereas in phenylacetates, the HOMO is a σ orbital situated mostly on the carbonyl group. Also, the further the carbonyl group is away from the phenoxy O, the more like phenetole will the molecule act. Thus, in the acetic acid compounds, the rival σ and π orbitals should be very close and will probably interact, leading to the prediction that the phenoxypropionic and butyric acids will be much more fluorescent than the acetic acid compounds.

The phosphorescence from clear alcohol glasses at liquid nitrogen temperatures also show concentration dependence. Beyond 30 mg/mℓ for 2,4-D/*n*-butanol glass, the emission at 510 nm (uncorrected) evoked by 340-nm excitation was constant; between 6 to 30 mg/mℓ, the emission decreased linearly with concentration due to self-absorption; below 6 mg/ℓ, the emission increased. The λ_{max} excitation (340 nm) was constant for methanol, *n*-butanol, and *n*-octanol glass matrices above 0.4 mg/mℓ and was independent of phosphorescence wavelength. The phosphorescence intensity increased as alcohol chain length increased for glasses of equal concentration. The λ_{max} phosphorescence for *n*-butanol and *n*-octanol solutions were around 510 nm (uncorrected) and were between 475 to 490 nm (uncorrected) for methanol.

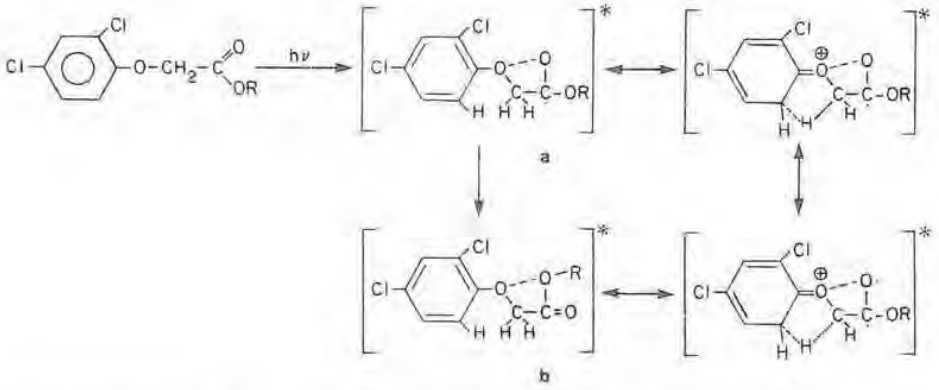
The corrected excitation, fluorescence, and phosphorescence spectra for 2,4-D/alcohol solutions above 4 mg/mℓ show fluorescence λ_{max} excitation at room temperature between 370 to 380 nm, as well as another one between 290 to 310 nm. Only the latter λ_{max} is observed in phosphorescence excitation and in the fluorescence of dilute solutions <4 mg/mℓ. If the corrected phosphorescence λ_{max} is 450 nm (63.5 kcal/mol) and the λ_{max} of fluorescence of dilute solutions is between 345 to 360 nm (82.9 to 79.4 kcal/mol), the S_1-T_1 gap for dilute solutions is large, namely, 16 to 19 kcal/mol. However, for 2,4-D/alcohol solutions >4 mg/mℓ, the λ_{max} fluorescence is 425 nm (67.3 kcal/mol), and the S_1-T_1 gap is only 4 to 5 kcal/mol, and large overlaps between fluorescence and phosphorescence curves should be seen, and this is observed. The fluorescent species in the concentrated solutions has been postulated to be[187] the excited dimer (excimer) or some kind of exciplex.

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The phosphorescence of various phenoxy acids in ethanol glasses at −196°C has been reported[226,227] for concentrations ranging from 30 p*M* to 10 m*M* (approximately 2 mg/mℓ). These data are all compared in Appendix 26. Most of the data are uncorrected, but it can be seen that λ_{max} excitation shift to the red as the degree of chlorination increases. Whereas 2-CPA has a λ_{max} phosphorescence at 518 nm (55.2 kcal/mol) with 4-CPA at 396 nm (72.2 kcal/mol), 2,4-D, 2,4,5-T, and 2,4,5-TP emit in the range 467 to 495 nm (61.2 to 57.8 kcal/mol). These latter values lie midway between the λ_{max} of 2-CPA and 4-CPA. It is interesting to note that the fluorescence λ_{max} for 4-chloro and 2,4,5-trichlorophenols lie generally further to the red than those of the corresponding phenoxyacetic acid.

2. Esters

The fluorescence and phosphorescence of various esters of the phenoxy compounds have been documented in a recent doctoral thesis.[187] The relevant λ_{max} excitation and emission are tabulated in Appendix 27. Relative to 2,4-dichloroanisole, it is again evident that the carbonyl group decreases the intensity of fluorescence and phosphorescence apart for the phosphorescence of the sterically hindered *n*-butyl ester of 2,4,6-T. The fluorescence of 2,4-dichloroanisole, the *n*-butyl esters of phenoxyacetic acid, 2-CPA, 2,4-D, 2,4,5-T, and MCPA are all wavelength dependent, with uncorrected λ_{max} ~350 nm and λ_{max} excitation ~315 nm and 350 nm. In contrast, the λ_{max} fluorescence and excitation of the sterically hindered ester of 2,4,6-T and the ester of the fully conjugated TBA are 350, 255 and 305, and 460 and 325 nm, respectively. This implies that some kind of interaction is occurring between the phenoxy ring and the carbonyl group, probably involving the open *ortho* H. Energy could flow in either direction. Since $\pi^* \leftarrow n$ transitions are weak, fluorescence and phosphorescence from the π^* state should also be weak.



Species a and b can be regarded as quasi dioxetane-type molecules. It is worthwhile to point out how similar these molecules are to indoleacetic acid and how energy transfer to or from the phenoxy group can be mediated by allowing the phenoxy O have charge transfer character, a well - documented property.

Most of the above *n*-butyl esters showed λ_{max} phosphorescence around 510 to 550 nm, with λ_{max} excitation being remarkably constant in the range 305 to 320 nm. The ester of 2,4,6-T also shows an λ_{max} at 250 nm. As chlorination increases, the λ_{max} phosphorescence tended to shift slightly to the blue. The ester of TBA was much more phosphorescent than the 2,4-dichloroanisole. The spectra imply that the excitation and fluorescence follow the Franck Condon principle, since both λ_{max} are very close. The

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overlap between the phosphorescence and fluorescence curves is small, indicative of large S_1-T_1 energy gaps (similar for dilute acid/alcohol solutions). The long wavelength excitation λ_{max} observed in concentrated solutions of the free acids is not seen in the esters. Thus, assuming λ_{max} fluorescence of 330 to 370 nm (86.6 to 77.3 kcal/mol) for the chlorinated unhindered phenoxyacetic esters and assuming 530 nm (54 kcal/mol) is the mean phosphorescence λ_{max}, the S_1-T_1 energy gap is ~23 to 33 kcal/mol, again similar to the S_1-T_1 gaps in dilute solutions of free acid/alcohol.

3. Salts

The fluorescence and phosphorescence of the amine salts of 2,4-D have been explored[187] (see Appendix 28). The λ_{max} of fluorescence for methanol solutions of ~0.1 *M* amine salts is ~420 to 440 nm (approximately 66 kcal/mol) for excitation wavelengths 300 to 340 nm, with the λ_{max} being dependent on excitation wavelengths longer than 340 nm. This is similar to the λ_{max} fluorescence of concentrated acid/alcohol solutions. As chain length increases λ_{max} fluorescence tended to shift to the blue and to become more intense. All phosphorescence λ_{max} lay at 540 nm (approximately 50 kcal/mol) for excitation from 200 to 300 nm. Beyond 300 nm, the phosphorescence λ_{max} was wavelength dependent. All excitation λ_{max} for phosphorescence and fluorescence occurred between 290 and 300 nm. The dimethylamine salt in water, however, showed a phosphorescence excitation λ_{max} at 330 nm. All amine salts also had another phosphorescence excitation λ_{max} at 275 nm. The latter is clearly caused by the π^*, π transition of the aromatic ring. The spectra are similar to those of the free acid, showing large overlap and small S_1-T_1 energy gaps (12 to 16 kcal/mol), and in addition, there is almost complete overlap of long wave excitation and fluorescence spectra. It is known the salts are 1:1 and are of structure $RCOO^- {}^+NH_3\text{-}R'$. This might imply the dimeric species in concentrated acid solutions is $RCOO^{\ominus}\text{-}H\text{-}{}^{\oplus}\underset{\underset{H}{|}}{O}OC\text{—}R'$.

F. Miscellaneous

Laser Raman spectroscopy at 632.8 nm of the sodium and potassium salts of 2,4-D has been studied by Reeves et al.,[228] who could detect as little as 500 ppm. Strong bands are observed at 343, 412, 840, and 1588 cm^{-1} for the potassium salt in water; the strong bands seen for this salt in powder form are 193, 355, 415, 654, 856, and 1588 cm^{-1}; thus, the two spectra are very different. The spectra of the sodium and potassium salts in a particular phase are nearly identical. The C-Cl stretch is responsible for either the 722 or 654 cm^{-1} bands. The bands at 840 and 857 cm^{-1} are because of the C-H out-of-plane bend. The 1411- and 1446-cm^{-1} bands may be due to the C=C ring stretches, and the one at 1588 cm^{-1} is probably the doubly degenerate C=C quadrant stretch. The latter could also be the H-bonded C=O stretch.

Diffuse reflectance spectroscopy of neodymium (3+) - 2,4-D, which is amorphous to X-ray studies as well as being "insoluble" in organic or inorganic solvents, shows spectra typical of strong covalent bonding.[229] This technique seems to be ideal to find electronic states in refractory or amorphous compounds.

X-ray fluorescence of 2,4-D residues has also been reported,[230] as have optical rotary dispersion studies on some of the optically active herbicidal acids.[231] No electron spin resonance data have been reported, although data for the cupric phenoxyacetate complex have been published.[232]

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Appendix 1
SOME PHYSICAL CONSTANTS FOR VARIOUS CHLORINATED PHENOXYALKANOIC ACIDS

Acid	MW	mp	sg[6] (25°C)	SOL	pK_a	$P'_{2\infty}$	ΔH_f	D[1]	S/M[9]
Phenoxyacetic	152.2	99.0[1,7]	—	—	3.12[14]	111.6	—	2.34	—
2-CPA	186.6	148.5[7]	—	6.85[8]	2.92[2]	—	—	—	—
3-CPA	186.6	110.0[13]	—	12.7[9]	2.97[14]	—	—	3.27	—
4-CPA	186.6	160.0[12]	—	5.13[8]	2.95[2]	218.9	—	3.27	51.2
2,3-D	221.0	—	—	1.55[8]	—	—	—	—	—
2,4-D	221.0	140.5[6,7]	1.565	2.36[8]	2.73[2]	227.4	5.60[4]	3.33	56.1
2,5-D	221.0	142.0[11,13]	—	2.42[8]	2.94[14]	—	—	—	—
2,6-D	221.0	—	—	7.05[8]	3.30[14]	—	—	—	—
3,4-D	221.0	141.0[13]	—	2.07[8]	2.92[14]	—	—	—	55.4
3,5-D	221.0	117.8[5]	—	4.35[8]	—	—	—	—	—
2,3,4-T	255.5	155,0[13]	—	0.808[8]	2.60[14]	—	—	—	—
2,3,5-T	255.5	—	—	1.00[8]	—	—	—	—	—
2,3,6-T	255.5	145.0[11]	—	2.40[8]	—	—	—	—	—
2,4,5-T	255.5	157.5[7]	1.80	1.05[8]	2.88[2]	—	—	—	60.5
2,4,6-T	255.5	190.0[13]	—	0.97[8]	—	121.2	—	2.43	—
3,4,5-T	255.5	—	—	1.15[8]	—	—	—	—	—
2,3,4,6-Tet	290.0	—	—	0.39[8]	—	—	—	—	—
2,3,4,5,6-P	324.5	—	—	0.18[8]	—	—	—	—	—
MCPA	200.6	119.5[3,7]	1.56	8.00[9]	3.05[2]	—	7.50[3]		56.4
MCPB	228.7	100.3[3,6]	—	0.193[9]	4.80[2]	—	8.20[3]		65.8
2,4,-DB	249.1	121.0[6]	—	0.33[9]	5.95[9]	—	—		65.4
Mecoprop	214.6	94.5[6,13]	—	4.15[9]	3.75[9]	—	6.90[3]		55.2
Dichlorprop	235.1	118.0[6]	1.64	1.49[10] (20°C)	3.00[9]	—	8.20[3]		54.6
Silvex	269.5	181.0[6]	—	0.52[9]	4.41[9]	—	—		59.1
2,4,5-TB	283.6	114.5[9]	—	0.155[9]	4.78[9]	—	—		69.7

Note: MW = molecular weight; mp = melting point (°C); sg = specific gravity; SOL = solubility in water at 25°C in molarity units × 10^{-3}; $P_{2\infty}$ = polarizibility; $pK_a = -\log_{10}(K_a)$; H_f = latent heat of fusion in kcal/mol; D = dipole moment (debye); S/M = surface area/molecule (A^2).

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Appendix 2
MELTING AND BOILING POINTS OF SOME ESTERS OF 2,4-D

Ester	Ester mp (°C)	Ester bp (°C, mmHg)
Allyl		134.3 ± 0.2(2)[19]
i-Amyl		164(2)[19]
		137 ± 1(1)[19]
Benzyl	45.5 ± 0.5[1]	204 (1)
β-Bromoethyl	33.9 ± 0.3[19]	167 ± 1 (2)[19]
n-Butoxyethyl		159 ± 3 (1/1.5)[2]
		187 ± 3 (5.5/7)[2]
n-Butyl	9.0[5]	154 (2)[3]
		162 (2)[4]
n-Butyl		146.5 (1)[5,19]
i-Butyl	17.0[5]	133.5 ± 0.5 (1)[5,21]
γ-Chloro-but-β-enyl	33.5 ± 0.5[6]	187 ± 1(760)[6]
γ-Chlorocrotyl	198 ± 2[7]	
β-Chloroethyl	36.5[8]	183 (3)[8], 157.5(1.5)[10]
p-Chlorophenyl	185.0 ± 0.5[9]	
n-Decyl	43.0[5]	
2,3-Dichloropropyl		183.0 ± 1.5(2)[19]
2,4-Dichlorophenoxyethyl	33.5 ± 0.5[5]	187 ± 1 (1)[5]
2,4-Dichlorophenyl	112.0 ± 0.5[9]	
2,5-Dichloro-5-methoxybenzyl	92.0 ± 1.0[10]	
3,3-Difluoroallyl		156(760)[11]
Di-n-hexyl ketoxime	63.3 ± 0.2[12]	
Dimethylketoxime	78.5 ± 0.5[12]	
α-Ethoxy-β,β,β-trichloroethyl		194.5 ± 1.5 (1)[13]
		194.0 (1)[14]
Ethyl	15.3 ± 0.1[5]	149 (1)[3,5]
(Ethyl-4-carboxy-2-chlorobutoxy)methyl	53.5 ± 0.5[15]	
Ethyl glycollate	34[16]	
2-Ethyl hexyl		173.5 ± 0.5 (0.5)[19]
Dehydro furfuryl		197.5 ± 0.5 (2)[3]
Glycollic acid	116[16]	
n-Heptyl	15[5]	160(2)[3]
β-Hydroxy ethyl		177.5 ± 1.5 (1.5)[19]
2-(Methoxy-3,6-dichlorosalicylic) methyl	92 ± 1[10]	
Methyl	43.0[5]	119 (1)[3,5]
(Methyl reserpate)	204 ± 1[23]	
Mucochloric	121.5 ± 0.5[17]	
p-Nitrophenyl	152.0[18]	
n-Nonyl		173.5 ± 0.5 (0.5)[3]
n-Octyl		173.5 ± 0.5 (1)[19]
i-Octyl	12.0[5]	173.5 ± 0.5(1)[5]
(pentachlorophenyl)	195.5 ± 0.5[25]	
i-Pentyl		137.0 ± 1.0 (1)[5]
Phenyl	104.5 ± 0.5[20]	
α-Propoxy-β,β,β-trichloroethyl	51.5 ± 0.5[13]	
	51.2[14]	
α-i-Propoxy-β,β,β-trichloroethyl	51.0 ± 1.0[13]	
	50.2[14]	
n-Propyl		155 (10)[3]
i-Propyl	(1) 5—10[21]	140 (1)[3]
	(1) 22.5 ± 2.5[21]	130 (1)[21]
	24.0[3]	183[5]
		139.5 ± 0.5 (1)[19]
(p-(i-Propyl)phenyl)	103[18]	
(Salicylic)	193[22]	
(2,3,6-Trichlorobenzyl)	124.5[24]	

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Appendix 3
MELTING POINTS OF THE ALKYLAMINE SALTS AND AMIDES OF 2,4-D

Amine salt	Salt mp (°C)	Amide mp (°C)
Allyl-	106.5 ± 0.5[7, 12]	
Ammonium	180 ± 1[7, 12]	155[1]
Benzyl-	138.5 ± 0.5[7, 12]	
bis(2-Chloroethyl)-		136.5 ± 0.5[2]
n-Butyl-	98.0 ± 0.5[5]	
	94.0 ± 1.0[7, 12]	
Cyclohexyl-	148.5 ± 0.5[7]	
Di-*n*-butyl-	108.0 ± 1.0[7, 12]	
Diethanol-	146 ± 1[7]	94.0 ± 1.5[2]
	94.3 ± 0.2[12]	
Diethyl-	106.5 ± 1.5[4]	
	130 ± 1[12]	
Dimethyl-	86 ± 1[3, 4, 7, 12]	
n-Dodecyl-	75.5 ± 0.5[6]	
	61.0 ± 1.0[5]	
Ethanol-	146 ± 1[12]	
Ethyl-	130 ± 1[4]	108.3 ± 2[1]
N-ethyllactamide-	109.0 ± 0.5[9]	
Glycollic-		121[9]
Hydrazine-	171.0 ± 0.5[10]	
Hydroxyethyl-ethylene diamine-	135.3 ± 0.3[5]	
Lauryl-	88.5 ± 0.5[11]	
Methyl-	158.0 ± 1.0[7, 12]	(1) 100.3 ± 0.2[1]
	157.5 ± 0.5[4] (also 105 ± 5)	108.0 ± 0.5[1]
	140.0 ± 1.0[6]	
Morpholine-	136.3 ± 0.3[7, 12]	
Myristyl-	73.0 ± 1.0[11]	
n-Octadecyl-	77.5 ± 0.5[6]	
N-phenyl		109.5 ± 0.5[1]
Phenyl glycollo-		96[9]
1-Phenyl piperazine-	171.0 ± 0.5[13]	
Piperidine-	131.5 ± 0.5[7, 13]	
i-Propyl-		125.3 ± 0.2[1]
n-Propyl triphenyl-	111.5 ± 0.5[15]	
2,4,6-*tris*-(i-propylamino)-*s*-triazine	146[14]	
n-Tetradecyl-	57.0 ± 0.5[5]	
Tri-*n*-butyl	30[7]	
Triethanol-	143 ± 1[7]	
Triethyl-	Liquid	
2,4,6-*tris*-(iso(propylamino)-*s*-triazine		146

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Appendix 4
MELTING POINTS AND BOILING POINTS OF SOME SALTS AND ESTERS OF 2,4,5-T

Salt	Salt mp
Diethanolamine	158 ± 1[1]
Ethanolamine	180 ± 1[1]
Potassium	>300[2]
Sodium	268[2]
Triethanolamine	114 ± 1[2]
Triethylamine	105 ± 1[1]

Ester	Ester mp (°C)	Ester bp °C (mmHg)
n-Butyl	29[3]	
Butoxyethanoxypropanyl	0.0 ± 2.5	20 (10^{-3})[3]
2,4-Dinitro-6-phenyl	100 ± 1[4]	
Ethyl	66.8 ± 0.7[1]	
n-Hexyl	26[1]	
Methoxyethyl		147.5 ± 2.5 (1)[1]
Methoxy isopropyl		150 ± 2(1)[1]
n-Nonyl	43[1]	
n-Octyl		188 ± 1 (0.3)[1]
Pentachlorophenoxy	269.0 ± 0.5[1]	
n-Pentyl	15[1]	
Phenoxy	116.5 ± 0.5[1]	
i-Propyl	46[1,3]	
Miscellaneous		
2,4,5-T acetyl chloride	51.3 ± 1.0[5]	129 ± 1(2)[5]

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Appendix 5
MELTING POINTS OF THE AMIDES OF THE AMINO ACIDS OF 2,4-D

Acid	Amino acid	Amide[1]	Amide[2]
2,4-D	D-Ala		204.2 ± 0.5
	L-Ala	198.2 ± 1.0	
	DL-Ala	213.5 ± 0.5	
	β-Ala		173.4 ± 0.6
	D-Asp	201.3 ± 0.5	183.8 ± 0.5
	L-Asp	202.2 ± 0.4	186.9 ± 0.5
	DL-Asp	217.3 ± 0.2	180.8 ± 0.6
	D-Glu		184.5 ± 0.5
	L-Glu	178.7 ± 0.5	
	DL-Glu	192.0 ± 0.5	
	Gly	234.5 ± 0.5	
	Glycylglycine		184.5 ± 0.5
	DL-His	129.2 ± 0.5	
	D-i-Leu		144.5 ± 0.6
	L-i-Leu		143.6 ± 0.3
	DL-i-Leu	142.7 ± 0.7	
	D-Leu		156.2 ± 0.5
	DL-Leu	137.5 ± 0.5	
	β-Lys	86.5 ± 0.5	
	DL-Lys	175.6 ± 0.5	
	D-Met	130.8 ± 1.0	
	L-Met	134.3 ± 0.5	
	DL-Met	144.5 ± 0.6	
	L-Phe	178.7 ± 0.5	
2,4,D	D-Ser	172.3 ± 0.5	
	L-Ser	181.5 ± 1.5	
	D-Thr	131.5 ± 0.5	
	L-Thr	131.8 ± 0.8	
	D-Tryp	152.8 ± 0.6	177.7 ± 0.5
	L-Tryp		152.8 ± 0.6
	DL-Try	120.7 ± 1.0	
	D-Val		164.5 ± 0.3
	L-Val		164.5 ± 0.3
	N,N′-bis-Cys-S-S		218.5 ± 1.5
	bis-Cys-S-S		215.5 ± 1.5

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Appendix 6
MELTING AND BOILING POINTS FOR MISCELLANEOUS PHENOXYALKANOIC COMPOUNDS

Free acids

Phenoxyacetic	mp
-(2-acetyl-4-chloro)	175 ± 1[1]
-(2-bromo)	144.3 ± 0.2[2]
-(3-bromo)	108.7 ± 0.2[2]
-(4-bromo)	161.6 ± 0.2[2]
-(2-bromo-4-chloro)	139.7 ± 0.7[1]
-(2-bromo-4-methyl)	145[4]
-(4-bromo-2-methyl)	118[4], 123 ± 1[1]
-(6-bromo-2,4-dimethyl)	152[4]
-(2-carboxy)	187.5 ± 0.5[4]
-(2-carboxymethyl-4-chloro)	168.7 ± 0.8[1]
-(bis-2-chloro)	142[4]
-(2-chloro-4-bromo)	145.5 ± 1.0[1]
-(2-chloro-3,5-dimethyl)	141 ± 1[4]
-(2-chloro-4-iodo)	139.5 ± 1.5[1]
-(2-chloro-4-methyl)	138.5 ± 0.5[4]
-(4-chloro-2-chloromethyl)	128 ± 1[1]
-(4-chloro-2-cyanomethyl)	157.5 ± 1.5[1]
-(4-chloro-2-cyclohexyl)	169 ± 1.5[1]
-(4-chloro-3,5-dimethyl)	151[4]
-(4-chloro-2-ethyl)	110.5 ± 1.5[1]
-(4-chloro-2-iodo)	138 ± 2[4]
-(4-chloro-3-methyl)	177.5 ± 0.5[4]
-(4-chloro-3-nitro)	138.3 ± 0.2[2]
-(4-chloro-2-*n*-propyl)	116.5 ± 1.5[1]
-(4-chloro-5-methyl-2-i- propyl)	138[4]
-(2,4-dibromo)	152.7 ± 0.8[1]
-(2,6-dibromo-4-methyl)	200[4]
-(2,4-di-*t*-butyl-5-methyl)	153[4]
-(2,4-dichloro-5-methyl)	143[10]

Phenoxyacetic	mp
-(2,4-dichloro-3,5-dimethyl)	146.5 ± 0.5[4]
-(2,4-diiodo)	166 ± 1[1]
-(2,6-dimethyl)	128.5 ± 0.2[2]
-(3,5-dimethyl)	110.5 ± 1.5[1]
-(2-fluoro)	139.3 ± 0.2[2]
-(3-fluoro)	111.5 ± 0.2[2]
-(4-fluoro)	104.4 ± 0.2[2]
-(4-fluoro-2-methyl)	147.5 ± 0.5[1]
-(2-iodo)	135.8 ± 0.2[2]
-(3-iodo)	115.5 ± 0.5[2]
-(4-iodo)	159.7 ± 0.3[3]
-(2-methyl)	157.1 ± 0.3[3]
-(3-methyl)	103.3 ± 0.3[3]
-(4-methyl)	138.5 ± 0.3[2]
-(2-nitro)	158.4 ± 0.2[2]
-(3-nitro)	156.6 ± 0.2[2]
-(4-nitro)	187.4 ± 0.2[2]
-(4-phenyl)	189.5 ± 0.5[4]
-(2,3,5-trimethyl)	125[4]
-(2,4,5-trimethyl)	129[4]
-(3,4,5-trimethyl)	149[4]

α-Phenoxypropionic Acids	
-(2-chloro)	114.5 ± 0.5[4]
-(3-chloro)	113.5 ± 0.5[4]
-(2-chloro-4-methyl)	117[4]
-(3-chloro-2-methyl)	131.5 ± 0.5[1]
-(4-chloro-2-methyl)	92.5 ± 0.5[4]
-(4-chloro-3-methyl)	90.5 ± 0.5[4]

α-Phenoxypropionic	mp
-(4-chloro-2,3,-dimethyl)	137 ± 0.5[1]
-(4-chloro-3,5-dimethyl)	137.5 ± 0.5[4]
-(2,4-dichloro)	117.5 ± 0.5[4]
-(2,4-dichloro-3,5-dimethyl)	148.5 ± 0.5[4]
-(2-methyl)	93.5 ± 0.5[4]
-(3-methyl)	101 ± 1[4]
-(4-methyl)	101.5 ± 0.5[4]
-β-(2-naphthoxy)	140.5 ± 0.5[5]
-(2,4,5-trichloro)	177.5 ± 0.5[4]
-(2,4,6-trichloro)	115.5 ± 0.5[4]
-(3,4,5-trimethyl)	115.5 ± 0.5[4]

α-Phenoxybutyric Acids	
-(3-chloro)	74.3 ± 0.2[4]
-(2-methyl)	50[4]
-(3-methyl)	73[4]
-(4-methyl)	62.5 ± 0.5[4]
-(2,4,5-trichloro)	114.5 ± 0.5[1]
-(2,4,5-trimethyl)	71 ± 1[4]
-(3,4,5-trimethyl)	86.5 ± 0.5[4]

(ω-2,4-Dichlorophenoxy)alkanoic Acids	
Alkanoic acid	
-butyric	117[5]
-caproic	92[5]
-caprylic	109.5 ± 1.5[5]
-enanthic	67[5]
-propionic	93[5]

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Appendix 6 (Continued)
MELTING AND BOILING POINTS FOR MISCELLANEOUS PHENOXYALKANOIC COMPOUNDS

(ω-2,4-Dichlorophenoxy)alkanoic Acids	mp
-valeric	65[5]
Other acids	
γ-(2-Chlorophenoxy) butyric	112.5 ± 0.5[5]
γ-(2-Naphthoxy) butyric	120[5]
β-(2-Naphthoxy) propionic	140.5 ± 0.5[5]
γ-(2,4,5-Trichlorophenoxy) butyric	112.5 ± 0.5[5]
γ-(2,4,6-Trichlorophenoxy) butyric	119.5 ± 0.5[5]

Acid chlorides	mp (°C)	bp °C (mmHg)
4-CPA	23.0 ± 1.0[6]	92.0 (1.0)[6]
2,4-D	51.3 ± 1.0[6]	103.5 ± 1.5 (0.3)[6] 121.5 ± 1.5 (3)[15] 133.5 ± 0.5 (4)[15]
2,4-DB	19.5 ± 2.5[6]	138 ± 2 (0.2)[6]
Dichlorprop	Liquid 5°C[6]	76 (0.1)[6]
MCPA	29.3 ± 0.7[7]	70 (7×10^{-3})[7]
MCPB	71.0 ± 2.0[8]	118.5 ± 3.5 (0.2)[6]
Silvex	Liquid 5°C[6]	114 ± 3(0.3)[6]
2,4,5-T	51.3 ± 1.0[6]	129 ± 1[6]

Metal salts	
2,4-D	
-ethyl sulfonate sodium (sesone)	>270[9]
-2-phenoxy sodium	97 ± 1[9]
-potassium	>300[10]
-sodium	217 ± 1[10]

Halogenated phenoxyalkanoxy esters Stem compound	(2,4-dichlorophenoxyacetoxy) substituent	mp (°C)	bp °C (mmHg)
5-Acetyl quinoline	δ-( )	156.5 ± 0.5[11]	
2-Butyne	1,4-*bis*( )	110.5 ± 0.5[16]	
N-Phenyl-i-propanoic	2-( )	59 ± 2[12]	
4-Phospha-3,5,8-trioxabicyclo [2,2,2]-octane-4-sulfide	1-( )methyl	186 ± 1[14]	
2,2,4-Trimethyl-1-i-butyroxy-pentane	3-( )	78.5 ± 2.5[13]	188.5 ± 6.5[13]

(N-Chlorophenoxyalkanoic) amides Amide	4-CPA	2,4-D	2,4,5-T	MCPA	Dichlorprop
Amino benzoic[6]	238 ± 1	273.5 ± 1.5	312.5 ± 2.5	261.5 ± 1.5	208.5 ± 0.5
p-Amino[6] salicyclic acid	226 ± 1	257 ± 1	282.5 ± 1.5	225 ± 2	218 ± 3
p-Toluene[6] sulfonamide	170 ± 1	170.5 ± 0.5	178 ± 1	205 ± 1	124 ± 1

Amides
[mp 2,4-dichlorophenoxyalkanoic acid amide[5] (°C)]

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-tributyl tin	81 ± 1[11]	
-triphenyl tin	169 ± 1[11]	
Esters		
4-CPA		
-allyl		123 ± 1(2)[1]
-(2-bromoethyl)	40 ± 0.4[1]	183 ± 1(4.5)[1]
-(2-chloroethyl)	42 ± 0.5[1]	156.5 ± 0.5 (2.5)[1]
-(crotyl)		144.5 ± 0.5(2)[1]
-(2,3-dichloropropyl)		170 ± 1(2)[1]
-(2,4-dinitro-6-phenyl)	91.0 ± 0.5[7]	
-(2-hydroxyethyl)	29.5 ± 0.4[1]	164.5 ± 1.5 (1.5)[1]
MCPA		
-(2-bromoethyl)		154 ± 1(1)[1]
-(2,4-dinitro-6-phenyl)	106 ± 1[7]	
-(ethyl)		116 ± 1(1)[1]
-(2-nitro-2-methylpropyl)	60.1 ± 0.5[1]	
-(*n*-propyl)		110.5 ± 0.5 (0.5)[1]
-(i-propyl)		100 ± 1(1)[1]
-(2,2,2-trichloroethyl		179.5 ± 0.5(1)[1]
Mecoprop		
-DL-propionic acid *n*-butyl		197.5 ± 7.5 (0.2)[6]
-DL-propionic acid methyl		180.0 ± 10 (0.2)[6]
Silvex		
-DL-propionic acid *n*-butyl		190 ± 3 (0.2)[6]
-DL-propionic acid methyl		180 ± 10 (0.2)[6]
2,4-Dibromophenoxyacetic acid		
-(2-bromoethyl)	57 ± 1[1]	
-(2-chloroethyl)		183 ± 1(0.5)[1]
-(2,3-dichloropropyl)		192.5 ± 2.5 (0.5)[1]

Acetic	Propionic	Butyric	Valeric	Caproic	Enanthic	Caprylic
152	104	104	97	89	73	83.5 ± 0.5

Other	
bis(2,4-Dichlorobenzyl) disulfide	mp 70 ± 1[1]
bis(2,4-Dichlorobenzyl)sulfide	b_2 198.3 ± 0.7[1]
S-(2,4-Dichlorobenzyl)thioisourea HCl	mp 224.5 ± 2.5[1]
tris-[2,(2,4-Dichlorophenoxy)ethyl] phosphite [2,4-DEP; Falone; Falodin]	$b_{0.1}$ >200°C[18]
(3,5-Dichloro-2-pyridoxy)acetic acid (Dowco 233)	mp
Ethyl-2,4-dichlorophenyl carbonate	b_1 98.5 ± 0.5[1]
2-Hydroxy-ethyl-2,4-dichlorophenyl ether	b_1 98.5 ± 0.5/mp 57.5 ± 0.5[1]
Sodium 2,4-dichlorophenoxyethyl sulfate (2,4-DES; disul-Na; Sesone; Crag Herbicide)	mp >270[8]
2(2,4,5-trichlorophenoxy)ethyl-2,2-dichloropropionate (Erbon, Baron)	mp 49.5 ± 0.5; $b_{0.5}$ 162.5 ± 1.5[18]

bp (mmHg) or mp in °C

Stem compound	4-Cl phenoxy	2,4-DiCl phenoxy	4-Cl-2-Me-phenoxy	2,4,5-trichloro phenoxy
d-( ) Butyronitrile[1]	44.5 ± 0.1	47 ± 1; 137.0 ± 0.5(1)		
2,3-epoxy-propane[1]	94 ± 1(1)	108 ± 1(1)	104 ± 1(1)	
Fumaric acid[1]		235.5± 0.5(d)	225 ± 2	

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Appendix 6 (Continued)
MELTING AND BOILING POINTS FOR MISCELLANEOUS PHENOXYALKANOIC COMPOUNDS

Stem compound	4-Cl phenoxy	2,4-DiCl phenoxy	4-Cl-2 mephenoxy	Stem compound	4-Cl phenoxy	2,4-DiCl phenoxy	4-Cl-2 mephenoxy	2,4,5-trichloro phenoxy
2-Heptanoic acid[1]	79.7 ± 0.3	100.3 ± 0.3	72.8 ± 0.3	N-(m-Trifluoro-methylphenyl)-α-( )acetamide[1]	94.5 ± 0.5	148.9 ± 0.3	138.5 ± 0.5	192.0 ± 0.5
N-2-Hydroxy-ethyl-α-( ) aceta-mide[1]	94.8 ± 0.3	121.7 ± 0.3	98.5 ± 0.5					

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Appendix 7
SOLUBILITIES OF SALTS OF VARIOUS PHENOXY ACIDS IN WATER

	Solubility in g/100 *ml* (°C)				
Amine salt	2,4-D	Dichlorprop	MCPA	Mecoprop	2,4,5,-T
Allyl	1.2 (31.5)[5]				
Ammonium	3.0 (20)[1]		32 (20)[3]		
Benzyl	1.6 (31.5)[5]				
n-Butyl	1.8 (30.5)[5]				
Cyclohexyl	2.0[6] (31.0)[6]				
Diallyl	71.0(32)[2]				
Di-*n*-butyl	1.2 (31.5)[5]				
Diethanol	480(30)[5]	74 (20)[6]	58 (20)[5]	58 (20)[7]	>50 (20)[5]
Diethyl	>50 (20)[5]		58 (20)[5]		23.4 (20)[5]
Dimethyl	∞ (20)[5]				
n-Dodecyl	0.01 (25)[8]				
Ethanol	>50 (20)[5]				54.8 (20)[5]
Hydroxy ethylene-diamine	9.0 (31)[6]				
Methyl	450 (20)[5]				
Morpholine	220 (30)[5]				
2,2'2-Nitriloethanol	82[1] (32)				
n-Octadecyl	0.003 (25)[8]				
Piperidine	230 (31)[5]				
Tri-*n*-butyl	1.8 (31)[6]				
Triethanol	440 (32)[5]		28 (20)[6]		
Triethyl	340 (20)[5]				
					400 (20)[5]
Trimethyl					330 (20)[5]
Metal					
Calcium	0.40 (25)[3]		0.55 (20)[5]		
Magnesium	1.11 (25)[3]		7.6 (20)[5]	4.5 (20)[5]	
Potassium	7.0 (20)[5]	90 (20)[6]	48 (20)[5]	90.0 (20)[7]	
Sodium	4.5 (25)[4]	66 (20)[6]	27.0 (25)[1]	25.0 (0)[7]	3.5 (20)[5]

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Appendix 8
SOLUBILITIES FOR 2,4-D IN WATER

Analytical method	Solubility in water	Solubility in water (mg/100 mℓ)	Temperature (°C)	Ref.
U	"Insoluble"	?	?	1,2
A	$2.36 \times 10^{-3} M$	52.2	25	3
U	$2.5 \times 10^{-3} M$	55	?	4
U	40 mg/100 mℓ	40	?	5
U	5 mg/100 mℓ	5	?	6
U	53 mg/100 mℓ	53	17	7
U	400 ppm	40	?	8
U	725 ppm	72.5	25	8
U	900 ppm	90.0	?	8
U	550 ppm	55.0	?	9
U	50 mg/100 mℓ	50	?	10
U	620 ppm	62.0	?	11
U	90 mg/100 mℓ	90.0	25	12
U	620 ppm	62.0	25	13
U	54 mg/100 mℓ	54	20	14
U	89 mg/100 mℓ	89	25	15
U	"Very slightly"	?	?	16
U	"Very slightly"	?	?	17

Note: U = unknown method; A = excess compound shaken for 2 days and the solution diluted one tenth before the UV absorbance was read at 280 nm.

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Appendix 9
COMPARISON OF pK_a VALUES FOR 2,4-D

Analytical method	Thermodynamic convention	Temperature (°C)	Ionic strength (I)	pK_a	Ref
Potentiometric (CO_2 free)	$[OH^-]\rightarrow 0$	25.0 ± 0.1	0.05	2.73	1
Potentiometric mixed solvent	$[OH^-]\rightarrow 0$	25	?	2.81	2
Potentiometric	Conc.	25	?	2.96	3
Conductometric	?	25	?	2.64	4
Conductometric	Infinite dilution	25	?	2.90	5
Conductometric salt solution	Infinite dilution	25	?	2.92	6
Literature	?	25	?	3.28	7
Literature	?	25	?	3.31	8
Literature	?	25	?	2.63	9
				2.80	9
				3.31	9
Spectroscopic (λ = 239 nm)	Beer's Law	20	0.001	2.86	10
Emf theoretical	?	?	?	2.98	11
Literature	?	?	?	2.64	12

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Appendix 10
SOLUBILITIES OF CHLORINATED PHENOXYALKANOIC ACIDS IN SOME ORGANIC SOLVENTS AT 25°C UNLESS OTHERWISE INDICATED

Solvent	2,4-D	2,4-DB	Dichlorprop[1] (28°C)	MCPA[1]	MCPB[2]	Mecoprop	Silvex[1]	2,4,5-T
Acetone	85.0	10.0[5]	59.5		20		16.6 ± 1.4	
Benzene	1.07(28)		8.5			0.472[4]	1.03 ± 0.56	
Carbon Disulfide	0.5 (29)			i				
Carbon Tetrachloride	0.1						0.095	
Diesel oil	0.10		0.21					
(+ kerosene)	0.35							
Dioxane	78.5(31)							
50% Ethanol	10.3							
95% Ethanol	130			153	15			54.8[3]
Ethyl ether	27.0			77			9.76	23.4[3]
n-Heptane	0.115[5]			0.5			0.086	0.039[6]

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Appendix 10 (Continued)
SOLUBILITIES OF CHLORINATED PHENOXYALKANOIC ACIDS IN SOME ORGANIC SOLVENTS AT 25°C UNLESS OTHERWISE INDICATED

Solvent	2,4-D	2,4-DB	Dichlorprop[1] (28°C)	MCPA[1]	MCPB[2]	Mecoprop	Silvex[1]	2,4,5-T
Methanol							12.0 ± 1.5	49.60[6]
Methyl-i-butyl ketone	31.3							
i-Propanol	31.6 (31)		51.0					
Toluene	0.067		6.9	6.2				0.73[3]
Xylene	0.58		5.1	4.9				0.61[3]

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Appendix 11
THEORETICAL CALCULATION OF F_n (RECOVERY) FROM *p*-VALUE DATA VS. EXPERIMENTAL RECOVERY DATA FROM THE LITERATURE[5]

	F_n calculated from *p*-value		F_n recovery observed from literature			
Solvent	*p*-Value[a]	F_n calculated	Observed F_n recovery	pH	Water to solvent ratio	Ref.
2,4-D						
Chloroform	0.95	0.99+	0.92—0.94	<2	25:3 × 10	1
Ethyl ether	0.99+	0.99	1.00 ± 0.042—0.057		100:100	2
Ethyl ether	0.99+	0.99	0.82—0.99	2.0	800:150,2 × 50	3
Benzene	0.915	0.80	0.799 ± 0.0386	≈2	1000:100, 2 × 50	4
MCPA						
Chloroform	0.97	0.99+	0.92 ± 0.05	<2	25:3 × 10	1
Ethyl ether	0.99	0.99	1.00	b	100:100	2
Benzene	0.95	0.91	0.489	≈2	1000:100, 2 × 50	4
2,4,5-T						
Chloroform	0.98	0.99+	0.93 ± 0.045	<2	25:3 × 10	1
Ethyl ether	0.99+	0.99	0.90		100:100	2
Ethyl ether	0.99+	0.99+	0.86—1.10	2.0	800:150, 2 × 50	3
Benzene	0.98	0.99	0.957 ± 0.0603	32.0	1000:100, 2 × 50	4
MCPB						
Ethyl ether	0.99	0.99	1.00	—[b]	100:100	2
2,4-DB						
Ethyl ether	0.99	0.99	0.95	—[b]	100:100	2
n-Butyl ester of 2,4-D						
Benzene	0.96	0.94	0.92	≈2	1000:100, 2 × 50	4
Isopropyl ester of 2,4-D						
Benzene	0.99	0.90+	0.93	≈2	1000:100, 2 × 50	4

[a] 2 mℓ of H_2SO_4.
[b] Conc.

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Appendix 11 (Continued)
THEORETICAL CALCULATION OF F_n (RECOVERY) FROM *p*-VALUE DATA VS. EXPERIMENTAL RECOVERY DATA FROM THE LITERATURE[5]

1. Erne, K., *Acta Chem. Scand.*, 17, 1663, 1963.
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Appendix 12
TABULATION OF CALCULATED VALUES OF THE PARTIAL PRESSURE (p) AT THE ABSOLUTE TEMPERATURE T FITTED TO THE EQUATION $LOG_{10}P = A - B/T - C/UCT$,[2] AS USED BY FLINT ET AL.[1] AND JENSEN AND SCHALL[2] FOR ESTERS OF 2,4,-D AND 2,4,5-T

	2,4-D				2,4,5-T				
Ester	A	B	C	P (mmHg, 25°C)	A	B	C	P (mmHg, 25°C)	Ref.
Butoxyethanol (60%)	6.22	830	8.0×10^5	2.67×10^{-6}					1
(40%)	7.08	1650	6.2×10^5	3.64×10^{-6}					1
1-Butyl	8.975	3690	0	3.91×10^{-4}	9.679	4160	0	5.2×10^{-5}	2
2-Butyl	8.875	3611	0	5.72×10^{-4}					2
Ethyl	8.764	3463	0	1.39×10^{-3}	8.858	3590	0	6.47×10^{-4}	2
2-Ethylhexyl	9.548	4180	0	3.32×10^{-5}	9.755	4374	0	1.19×10^{-5}	2
2-Ethylhexyl	6.76	1360	7.1×10^5	1.59×10^{-6}					1
1-Heptyl	9.743	4275	0	2.50×10^{-5}	9.836	4404	0	1.14×10^{-5}	2
4-Heptyl	9.321	3966	0	1.03×10^{-4}					2
1-Hexyl	9.307	3987	0	8.47×10^{-5}	9.631	4236	0	2.6×10^{-5}	2
2-Hexyl	8.975	3760	0	2.28×10^{-4}					2
Methyl	8.681	3375	0	2.27×10^{-3}	8.724	3496	0	9.83×10^{-4}	2
1-Octyl	9.786	4354	0	1.50×10^{-5}	10.01	4554	0	5.35×10^{-6}	2
2-Octyl	9.548	4220	0	2.44×10^{-5}					2
2-Octyl(70%)	6.96	1550	6.7×10^5	1.64×10^{-6}					1
2-Octyl(40%)	7.22	1840	5.8×10^5	3.27×10^{-6}					1
1-Pentyl	8.965	3720	0	3.03×10^{-4}	9.406	4060	0	6.55×10^{-5}	2
2-Pentyl	9.125	3798	0	2.40×10^{-4}					2
1-Propyl	8.931	3608	0	6.66×10^{-4}	9.202	3841	0	2.05×10^{-4}	2
2-Propyl	8.67	3431	0	1.43×10^{-3}					2
2-Propyl	5.48	180	8.2×10^5	4.39×10^{-5}					1
Propylene glycol Butyl ether (90%)	6.94	1360	7.1×10^5	2.40×10^{-6}					2
Propylene glycol Butyl ether (10%)	8.37	2920	3.8×10^5	1.96×10^{-6}					

1. Flint, G. W., Alexander, J. J., and Funderburk, O. P., *Weed Sci.*, 16, 541, 1968.
2. Jensen, D. J. and Schall, E. D., *J. Agric. Food Chem.*, 14, 123, 1966.

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Appendix 13
EXPERIMENTAL VALUES OBTAINED FOR VAPOR PRESSURES (P) AND HEAT OF VAPORIZATION (ΔH_v IN KCAL/MOL) AT STATED TEMPERATURES (T) FOR SOME ESTERS OF 2,4-D AND MCPA

Acid	Ester	T (°C)	P (mm Hg)	ΔH_v (kcal/mol)	Method	Ref.
2,4-D	Butoxyethyl	25	4.50×10^{-6}			1
		25	1.70×10^{-3}	8.40	?	2
	1-butyl	16	3.42×10^{-6}		DTA	3
		25.4	9.55×10^{-6}		DTA	3
		34.6	2.01×10^{-5}		DTA	3
		44	5.84×10^{-5}		DTA	3
		25	3.90×10^{-3}	2.05	?	2
		38	$\geq 1 \times 10^{-4}$		Transpiration	4
		25	3.91×10^{-4}		Q_v = 3280 cm^2/g calculated	5
	Ethyl	25	8.6×10^{-4}		Knudson	6
		25	1.15×10^{-2}		Transpiration	7
		25	1.39×10^{-3}		Calculated	5
	1-heptyl	25	1.35×10^{-3}		Transpiration	7
		25	2.50×10^{-5}		Calculated	5
	Methyl	17.6	1.07×10^{-4}		DTA	3
		25	3.29×10^{-4}		DTA	3
		34.6	1.28×10^{-3}		DTA	3
		20	$\geq 1.10 \times 10^{-4}$		Transpiration; Q_v = 3280	4
		38	$\geq 2 \times 10^{-3}$		Transpiration; Q_v = 3280	4
		25	1.55×10^{-3}		Knudson	6
		25	1.27×10^{-2}		Transpiration	7
		25	2.27×10^{-3}		Calculated	5
	1-Octyl	38	$\geq 2.7 \times 10^{-5}$		Transpiration; Q_v = 3280	4
		25	1.50×10^{-5}		Calculated	5
	2-Propyl	25	1.05×10^{-2}	2.39	?	2
		25	1.20×10^{-3}		Knudson	6
		25	1.05×10^{-2}		Transpiration	7
		25	1.43×10^{-3}		Calculated	5
		25	4.39×10^{-5}		Calculated	8
		187	17.0		GC	5
		187	16.7		GC	8
		187	16.3		GC	9
MCPA	2-Butoxyethyl	25	4.8×10^{-3}	7.40	?	2
	2-Propyl	25	2.16×10^{-2}	3.51	?	2

Note: DTA = differential thermal analysis; GC = gas liquid chromatography; Q_v = surface area/mass ratio in cm^2/g.

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3. Van Valkenburg, J. W., *Adv. Chem. Ser.*, 86, 39, 1969.
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Appendix 14
VALUES OF $\alpha(d\varepsilon/dc)_{c=o}$, $\nu\,(dn^2/dc)_{c=o}$, P_∞ (POLARIZATION AT INFINITE DILUTION), μ_D(DIPOLE MOMENT) AND μ_{int} (INTERACTION OF $O-CH_2-COOH$ GROUP WITH THE O–Cl RING BOND) FOR VARIOUS PHENOXYACETIC ACIDS IN DIOXAN AT 25°C, UTILIZING DIELECTRIC CONSTANT (ε) AND REFRACTIVE INDEX (n) VALUES FOR SOLUTIONS OF KNOWN CONCENTRATIONS

Acid	$10^3\alpha$	$10^2\nu$	P_∞	μ_D	μ_{int}
PA	4867	37	111.6	2.34	0
4-CPA	7598	42	218.9	3.27	0.18
4-BrPA	5665	33	201.4	3.14	0.02
2,4-D	6646	35	227.4	3.33	0.64
2,4,6-T	3183	33	121.2	2.43	0.29
2,4,6-TriBr PA	2968	27	166.7	2.86	1.15
2,4,6-TriMe PA	4355	30	128.7	2.51	−1.69
4-Tolyl PA	4842	29	123.6	2.46	−1.19

Note: μ are in debye, and PA = phenoxyacetic acid.

From Colinese, D. C., Hall, J., and Ibbitson, D. A., *J. Chem. Soc.*, 1962, 983. With permission.

Appendix 15
MOLAR EXTINCTION COEFFICIENTS (ε×l/MOL/CM) AT VARIOUS WAVELENGTHS (λ) (IN NM) FOR THE UNDISSOCIATED AND DISSOCIATED PHENOXYALKANOIC ACIDS IN 0.01 *M* PHOSPHATE BUFFER (IONIC FORM) AND IN 0.1 *M* HCl (UNDISSOCIATED FORM)

Position of Cl substitution	Undissociated molecule				Anion			
	λ_1	ε_1	λ_2	ε_2	λ_{max}	ε_1	λ_2	ε_2
None	268.0	1300	274.5	1070	269.5	1420	275.5	1160
2	272.0	1600	279.0	1420	273.5	1840	280.5	1620
3	272.0	1520	279.5	1370	273.5	1630	280.5	1460
4	278.0	1290	284.0	1030	279.0	1350	285.5	1090
2,4	282.0	1820	289.0	1570	283.5	2070	290.5	1840
2,5	278.5	2080	286.0	1930	279.5	2350	287.0	2190
2,6	275.0	290	276.5	250	271.0	370	278.0	340
3,4	281.5	1550	289.0	1400	282.5	1690	289.5	1520
2,3,4	284.5	1530	292.5	1570	285.5	1720	293.5	1780
2,3,6	276.0	320	284.5	270	276.5	390	285.0	340
2,4,5	287.5	2260	295.0	2120	288.5	2600	296.5	2450
2,4,6	278.5	660	286.5	660	279.5	700	287.0	710

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Appendix 15 (Continued)
MOLAR EXTINCTION COEFFICIENTS ($\varepsilon \times 1/MOL/CM$) AT VARIOUS WAVELENGTHS (λ) (IN NM) FOR THE UNDISSOCIATED AND DISSOCIATED PHENOXYALKANOIC ACIDS IN 0.01 *M* PHOSPHATE BUFFER (IONIC FORM) AND IN 0.1 *M* HCl (UNDISSOCIATED FORM)

Position of Cl substitution	Undissociated molecule				Anion			
	λ_1	ε_1	λ_2	ε_2	λ_{max}	ε_1	λ_2	ε_2
Acid								
2,4-D	282.0	1820			283.5	2070		
α-(2,4-dichorophenoxy) propionic	282.5	1690	283.5	1730	284	1960		
β-(2,4-dichlorophenoxy) propionic	283	1790			283.5	1880		
γ-(2,4-dichlorophenoxy) butyric	283.5	1680						

From Phillips, J. N., *Aust. J. Chem.*, 12, 199, 1959. With permission.

Appendix 16
UV SPECTRA OF AMINE SALTS AND FREE 2,4-D IN METHANOL

Wave length (nm)	Absorbance value					
	Methyl ($8.4 \times 10^{-5} M$)	Dimethyl ($8.3 \times 10^{-5} M$)	*n*-Butyl ($7.5 \times 10^{-5} M$)	*n*-Dodecyl ($7.3 \times 10^{-5} M$)	*n*-Tetradecyl ($8.4 \times 10^{-5} M$)	Free acid ($2.2 \times 10^{-5} M$)
360	0	0.001	0.002	0.001	0	0.002
320	0.001	0.005	0.01	0.01	0.001	0.015
300	0.0055	0.035	0.06	0.06	0.055	0.025
290	0.013	0.085	0.14	0.1	0.13	0.095
280	0.014	0.080	0.12	0.09	0.14	0.11
260	0.09	0.021	0.035	0.02	0.09	0.055
250	0.065	0.020	0.030	0.015	0.065	0.045
240	0.18	0.17	0.322	0.22	0.18	0.21
230	0.32	0.36	0.61	0.45	0.32	0.36
220	0.26	0.30	0.53	0.37	0.26	0.33
210	0.85	0.92	>1	1	0.85	0.94
200	0.13	0.13	0.48	0.35	0.13	0.10

From Que Hee, S. S., Ph.D. thesis, University of Saskatchewan, Saskatoon, 1975; as cited in *Diss. Abstr. Int. B*, 38, 1216, 1977.

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Appendix 17
IR SPECTRAL DATA FOR VARIOUS PHENOXYACETIC ACIDS

Analysis of 2,4-Dichlorophenoxyacetic Acid
Part 1[1]

Component							
No.	Name	Formula	Range %	Accuracy %	λ or ν B.L. Pts.	Slit (mm) Δλ or Δν	Concn. (mg/mℓ) Length (mm)
1	2,4-Dichloro-phenoxy-acetic acid	$C_8H_6Cl_2O_3$	50—100	±1.0	13.85μ	1.000 0.174μ	100 0.1
2	2,6-Dichloro-phenoxy-acetic acid	$C_8H_6Cl_2O_3$	0—20	±0.5	13.58μ	0.800 0.140μ	100 0.1
3	2,4,6-Trich-loro-phenoxy-acetic acid	$C_8H_5Cl_3O_3$	0—20	±0.5	13.00μ	0.800 0.139μ	100 0.1
4	Di-(2,4-di-chlo-rophenoxy-acetic acid	$C_{14}H_8Cl_4O_4$	0—20	±0.5	9.39μ	0.450 0.094μ	100 0.1

Instrument: Perkin-Elmer Model 12, NaCl prism
Sample phase: Solution in acetone
Cell windows: NaCl
Absorbance measurement: Base line_____ Point X
Calculation: Inverse matrix X Successive approx._____Graphical_____

Relative Absorbance[a] - Analytical Matrix:

Component/λ	13.85	13.58	13.00	9.39
1	0.426	0.148	0.149	0.235
2	0.084	0.254	0.212	0.213
3	0.168	0.122	0.888	0.215
4	0.165	0.145	0.208	1.240

Material purity: Reference compounds 99 + % pure

[a] Relative absorbances are given as the slope of the Beer's Law concentration curves used expressed in terms of absorbance per 100% of constituent.

Appendix 17
IR SPECTRAL DATA FOR VARIOUS PHENOXYACETIC ACIDS

Part 2[2]

Component							
No.	Name	Formula	Range %	Accuracy %	λ or ν B.L. Pts.	Slit (mm) Δλ or Δν	Concn. mg/pellet mg pellet
1	Phenoxyacetic acid	$C_8H_8O_3$	10—100	±1.5	14.50	1.8 0.159	1.0 300
2	*o*-Chlorophenoxyacetic acid	$C_8H_7O_3Cl$	10—100	±1.5	13.94	1.8 0.156	1.0 300
			20—100	±1.5	9.62	0.4 0.044	1.0 300
3	*m*-Chlorophenoxyacetic acid	$C_8H_7O_3Cl$	10—100	±1.0	11.30	0.5 0.049	1.0 300

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Part 2[2]

Appendix 17 (Continued)
IR SPECTRAL DATA FOR VARIOUS PHENOXYACETIC ACIDS

Analysis of 2,4-Dichlorophenoxyacetic Acid
Part 2[2]

Component								
No.	Name	Formula	Range %	Accuracy %	λ or ν B.L. Pts.	Slit (mm) Δλ or Δν	Concn. (mg/mℓ) Length (mm)
4	*p*-Chlorophenoxyacetic acid	$C_8H_7O_3Cl$	15—100	±1.5	9.93	0.4 0.043	1.0 300
5	2,3-Dichlorophenoxyacetic acid	$C_8H_6O_3Cl_2$	20—100	±2.0	11.15	0.5 0.049	1.0 300
6	2,4-Dichlorophenoxyacetic acid	$C_8H_6O_3Cl_2$	15—100	±2.0	14.33	1.8 0.157	1.0 300
7	2,5-Dichlorophenoxyacetic acid	$C_8H_6O_3Cl_2$	10—100	±1.5	12.41	1.1 0.098	1.0 300
			20—100	±1.0	11.45	0.6 0.057	10 300
8	2,6-Dichlorophenoxyacetic acid	$C_8H_6O_3Cl_2$	10—100	±2.0	13.55	1.4 0.123	1.0 300
9	3,4-Dichlorophenoxyacetic acid	$C_8H_6O_3Cl_2$	20—100	±2.0	14.67	2.0 0.178	1.0 300
			20—100	±1.5	12.58	1.1 0.098	1.0 300
10	3,5-Dichlorophenoxyacetic acid	$C_8H_6O_3Cl_2$	10—100	±1.5	11.99	0.8 0.073	1.0 300
11	2,4,6-Trichlorophenoxyacetic acid	$C_8H_5O_3Cl_3$	20—100	±2.0	12.49	1.1 0.098	1.0 300
			5—100	±1.0	9.58	0.4 0.044	1.0 300
12	2,3,4-Trichlorophenoxyacetic acid	$C_8H_5O_3Cl_3$	10—100	±1.0	12.78	1.1 0.098	1.0 300
13	2,3,5-Trichlorophenoxyacetic acid	$C_8H_5O_3Cl_3$	20—95	±2.0	14.20	1.8 0.159	1.0 300
14	2,3,6-Trichlorophenoxyacetic acid	$C_8H_5O_3Cl_3$	50—90	±2.5	13.40	1.4 0.123	1.0 300
15	2,4,5-Trichlorophenoxyacetic acid	$C_8H_5O_3Cl_3$	20—90	±2.0	14.70	2.0 0.178	1.0 300
			10—95	±1.5	13.05	1.2 0.106	1.0 300
16	3,4,5-Trichlorophenoxyacetic acid	$C_8H_5O_3Cl_3$	5—100	±1.5	10.50	0.5 0.050	1.0 300

Instrument: Perkin-Elmer Model 112, NaCl prism
Sample phase: Sample in KBr pellet
Cell windows: KBr
Absorbance measurement:[a] Base line ____ Point X
Calculation: Inverse matrix X Successive approx ____ Graphical ____

Bayer EX1026 (Part 1 of 2)

Appendix 17 (Continued)
IR SPECTRAL DATA FOR VARIOUS PHENOXYACETIC ACIDS

Relative Absorbance[b] Analytical Matrix:

Component/λ	14.50	13.94	9.62	11.30	9.93	11.15	14.33	12.41	11.45	13.55	14.67	12.58	11.99	12.49	9.58	12.78	14.20	13.40	14.70	13.05	10.50
1	0.506	0.073	0.156	0.174	0.138	0.132	0.334	0.116	0.116	0.183	0.298	0.090	0.317	0.009	0.168	0.066	0.122	0.386	0.298	0.199	0.227
2	0.054	0.405	0.385	0.218	0.107	0.217	0.078	0.088	0.126	0.093	0.043	0.076	0.144	0.077	0.190	0.057	0.147	0.166	0.049	0.121	0.300
3	0.048	0.197	0.102	0.629	0.082	0.141	0.055	0.049	0.170	0.045	0.233	0.047	0.083	0.049	0.112	0.048	0.067	0.057	0.240	0.424	0.185
4	0.154	0.116	0.181	0.124	0.254	0.161	0.202	0.170	0.113	0.048	0.119	0.168	0.186	0.150	0.189	0.109	0.311	0.062	0.122	0.084	0.193
5	0.135	0.180	0.221	0.196	0.137	0.540	0.209	0.107	0.154	0.104	0.105	0.102	0.112	0.103	0.224	0.108	0.256	0.093	0.112	0.444	0.158
6	0.122	0.167	0.087	0.133	0.060	0.238	0.303	0.077	0.324	0.041	0.049	0.439	0.106	0.112	0.103	0.070	0.168	0.041	0.058	0.044	0.106
7	0.171	0.102	0.150	0.154	0.108	0.305	0.120	0.417	0.500	0.060	0.081	0.148	0.160	0.275	0.168	0.095	0.216	0.061	0.090	0.076	0.096
8	0.164	0.144	0.189	0.208	0.078	0.194	0.074	0.121	0.165	0.265	0.119	0.169	0.090	0.129	0.275	0.476	0.042	0.069	0.112	0.286	0.092
9	0.113	0.199	0.197	0.236	0.197	0.307	0.102	0.140	0.176	0.159	0.293	0.312	0.151	0.190	0.205	0.123	0.087	0.081	0.252	0.092	0.207
10	0.095	0.049	0.094	0.168	0.073	0.296	0.090	0.246	0.107	0.026	0.050	0.128	0.440	0.197	0.096	0.068	0.091	0.037	0.049	0.045	0.074
11	0.023	0.021	0.492	0.130	0.103	0.206	0.009	0.225	0.279	0.029	0.039	0.158	0.064	0.270	0.531	0.070	0.010	0.036	0.044	0.434	0.075
12	0.050	0.102	0.117	0.111	0.108	0.156	0.075	0.113	0.091	0.059	0.044	0.112	0.071	0.190	0.120	0.495	0.061	0.046	0.038	0.081	0.152
13	0.083	0.074	0.103	0.146	0.074	0.116	0.163	0.081	0.176	0.041	0.035	0.071	0.355	0.072	0.121	0.061	0.228	0.040	0.056	0.049	0.180
14	0.103	0.033	0.165	0.138	0.083	0.176	0.070	0.262	0.108	0.049	0.078	0.189	0.052	0.298	0.217	0.089	0.028	0.097	0.073	0.053	0.061
15	0.059	0.064	0.174	0.311	0.138	0.224	0.050	0.096	0.423	0.109	0.282	0.083	0.115	0.091	0.182	0.072	0.044	0.140	0.267	0.510	0.123
16	0.108	0.400	0.145	0.134	0.096	0.254	0.090	0.164	0.100	0.039	0.083	0.104	0.144	0.129	0.125	0.084	0.113	0.053	0.080	0.065	0.419

Material Purity: Reference compounds 98 + % pure

Note: Pellets were prepared by grinding a 3% mixture of sample in KBr for 3 minutes using a Perkin-Elmer vibrator and Harshaw 200- to 325-mesh KBr. A portion was then diluted with additional KBr to obtain the desired total weight and concentration. This mixture was then vibrated for 3 minutes and the pellet pressed at 18,000 pounds for 5 minutes in a 13-mm die.

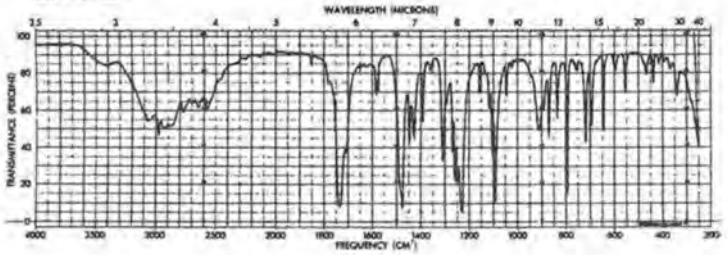
[a] The KBr pellets were rotated to six different positions and an absorbance reading was obtained at each position. The absorbance values are the averages of the six readings minus the KBr pellet background. A 300-mg KBr blank is prepared and absorbances determined at each wave length. The absorbances shown represent absorbances due only to the sample.

[b] Relative absorbances are given as the slope of the Beer's Law concentration curves used expressed in terms of absorbance per 100% of constituent.

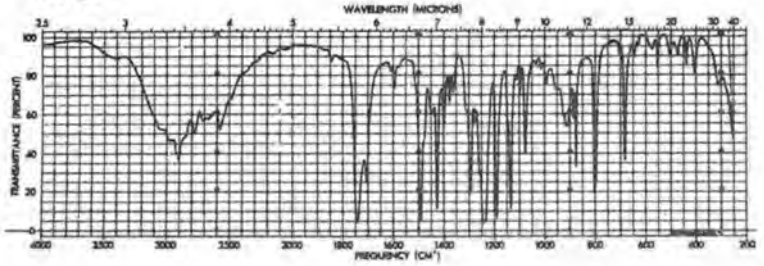
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Part 3[3]

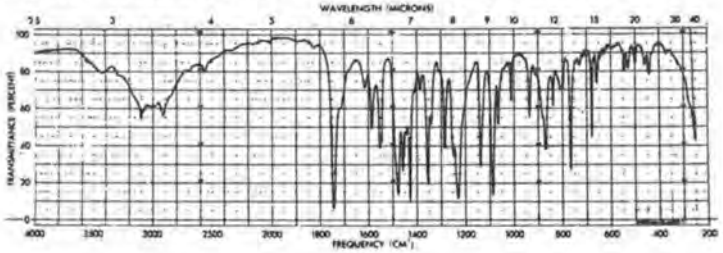
2, 4-D



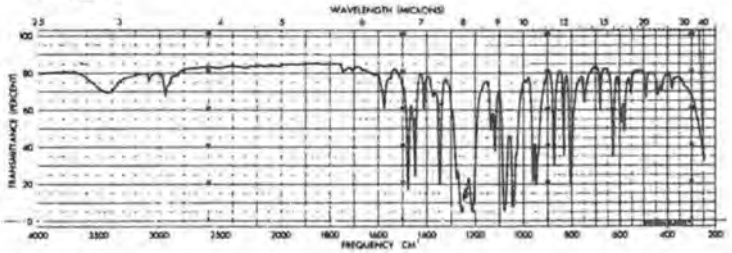
MCP



2,4,5 - TRICHLOROPHENOXYACETIC ACID



SES-T



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2. Reprinted with permission from Witmer, F. J., Thomas, D. N., and Vernetti, J. B., *Anal. Chem.*, 32, 887, 1960. Copyright by the American Chemical Society.
3. Gore, R. C., Hannah, R. W., Pattacini, S. C., and Porro, T. J., *J. Assoc. Offic. Anal. Chem.*, 54, 1040, 1971. With permission.

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Appendix 18
SPECTRA OF ESTERS OF SOME PHENOXYALKANOIC ACIDS

Analysis of Butoxy Ethoxy Propyl Esters of 2,4-Dichlorophenoxyacetic Acid and 2,4,5-Trichlorophenoxyacetic Acid Mixtures[1]

Component							
No.	Name	Formula	Range %	Accuracy %	λ or ν B.L. Pts.	Slit (mm) Δλ or Δν	Concn. (mg/mℓ) Length (mm)
1	2,4-Dichlorophenoxyacetic acid butoxy ethoxy propyl ester	$C_{17}H_{24}O_6Cl_2$	0—100	±1.0	12.55	0.400 0.039μ	100 0.10
2	2,4,5-Trichlorophenoxyacetic acid butoxy ethoxy propyl ester	$C_{17}H_{23}O_6Cl_3$	0—100	±1.0	13.67	0.400 0.038μ	100 0.10

Instrument: Perkin-Elmer Model 112, NaCl prism
Sample Phase: Solution in carbon disulfide
Cell Windows: NaCl

Absorbance Measurement: Point X
Calculation: Inverse matrix X

Relative absorbances[a]-Analytical Matrix:

Component/λ	12.55	13.67
1	0.450	0.147
2	0.041	0.360

Material Purity: Reference compounds 99 + % pure

Analysis of 2,4-Dichlorophenoxyacetic Acid Isopropyl Ester and 2,4-Dichlorophenoxyacetic Acid Butyl Ester Mixtures[2]

Component							
No.	Name	Formula	Range %	Accuracy %	λ or γ B.L. Pts.	Slit (mm) Δλ or Δυ	Concn. (mg/mℓ) Length (mm)
1	2,4-Dichlorophenoxyacetic acid iso-propyl ester	$C_{11}H_{12}O_3Cl_2$	0—100	±1.0	9.06	0.20 0.025μ	30 0.545
2	2,4-Dichlorophenoxyacetic acid butyl ester	$C_{12}H_{14}O_3Cl_2$	0—100	±1.0	12.54	0.50 0.047μ	30 0.545

Instrument: Perkin-Elmer Model 112, NaCl prism
Sample Phase: Solution in carbon disulfide
Cell Windows: NaCl

Absorbance Measurement: Point X
Calculation: Inverse matrix X

Relative Absorbances[a]-Analytical Matrix:

Component/λ	9.06	12.54
1	1.814	0.682
2	0.709	0.677

Material Purity: Reference compounds 99 + % pure

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Analysis of Iso-octyl Esters of 2,4-Dichlorophenoxyacetic Acid and 2,4,5-Trichlorophenoxyacetic Acid Mixtures[3]

Component			Range %	Accuracy %	λ or ν B.L. Pts.	Slit (mm) Δλ or Δν	Concn. (mg/mℓ) Length (mm)
No.	Name	Formula					
1	2,4-Dichloro-phenoxyacetic acid iso-octyl ester	$C_{16}H_{22}O_3Cl_2$	0—100	±1.0	12.56	0.500 0.047μ	25.0 0.545
2	2,4,5-Trichloro-phenoxyacetic acid iso-octyl ester	$C_{16}H_{21}O_3Cl_3$	0—100	±1.0	13.72	0.500 0.047μ	24.0 0.545

Instrument: Perkin-Elmer Model 112, NaCl prism
Sample Phase: Solution in carbon disulfide
Cell Windows: NaCl
Absorbance Measurement: Point X
Calculation: Inverse matrix X

Relative Absorbances[a]-Analytical Matrix:

Component/λ	12.56	13.72
1	0.268	0.61
2	0.020	0.173

Material Purity: Reference compounds 99 + % pure

Analysis of 2,4,5-Trichlorophenoxyacetic Acid Isopropyl Ester and 2,4,5-Trichlorophenoxyacetic Acid Butyl Ester Mixtures[4]

Component			Range %	Accuracy %	λ	Slit (mm) Δλ	Concn. (mg/mℓ) Length (mm)
No.	Name	Formula					
1	2,4,5-Trichloro-phenoxyacetic acid iso-propyl ester	$C_{11}H_{11}O_3Cl_3$	0—100	±1.0	9.02	0.30 0.025	50 0.10
2	2,4,5-Trichloro-phenoxyacetic acid n-butyl ester	$C_{12}H_{13}O_3Cl_3$	0—100	±1.0	8.78	0.30 0.026	50 0.10

Instrument: Perkin-Elmer Model 112, NaCl prism
Sample Phase: Solution in carbon disulfide
Cell Windows: NaCl
Absorbance Measurement: Point X
Calculation: Inverse matrix X

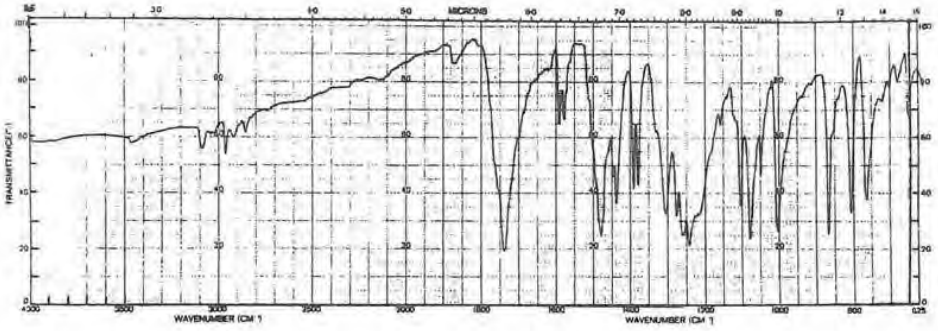
Relative Absorbances[a]-Analytical Matrix:

Component/λ	9.02	8.78
1	0.585	0.342
2	0.102	0.347

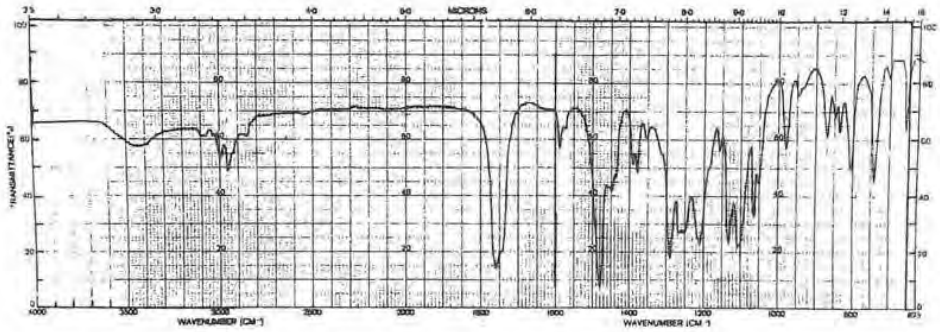
Material Purity: Reference compounds 99 + % pure

[a] Relative absorbances are given as the slope of the Beer's Law concentration curves used expressed in terms of absorbance per 100% of constituent.

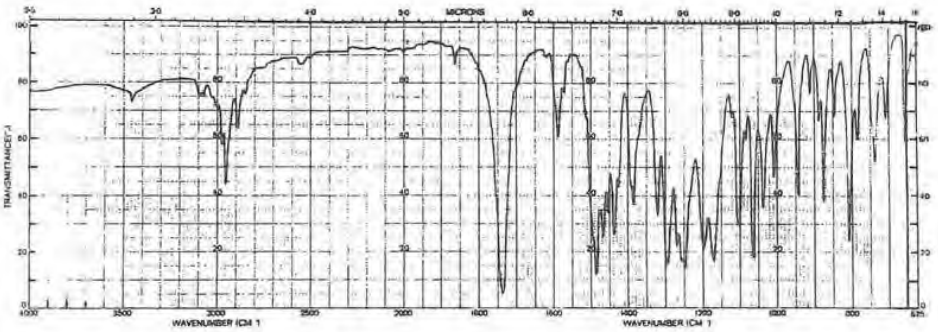
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IR spectrum of 2,4-D methyl ester.[5]

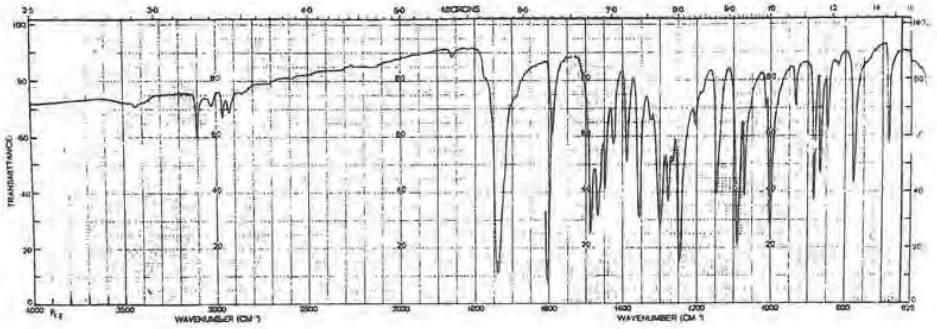


IR spectrum of 2,4-DP methyl ester.[5]

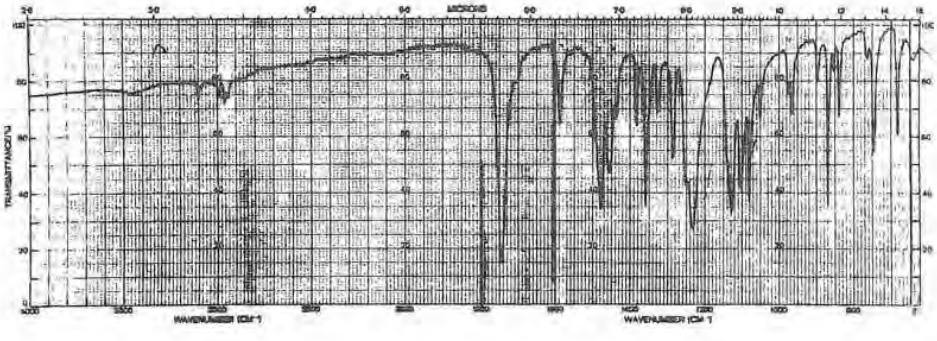


IR spectrum of 2,4-DB methyl ester.[5]

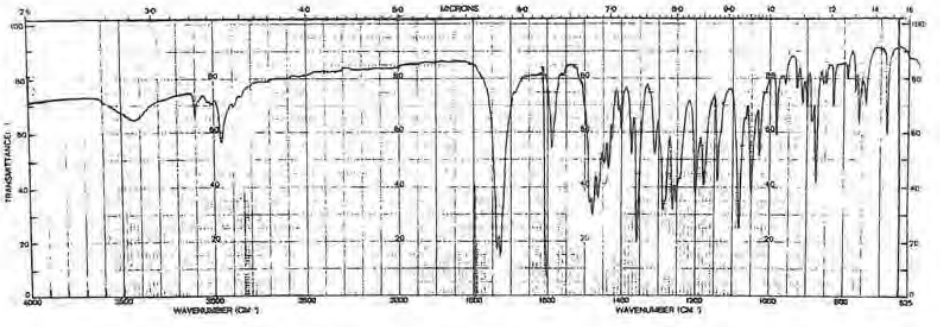
Bayer EX1026 (Part 1 of 2)



IR spectrum of 2,4,5-T methyl ester.[5]

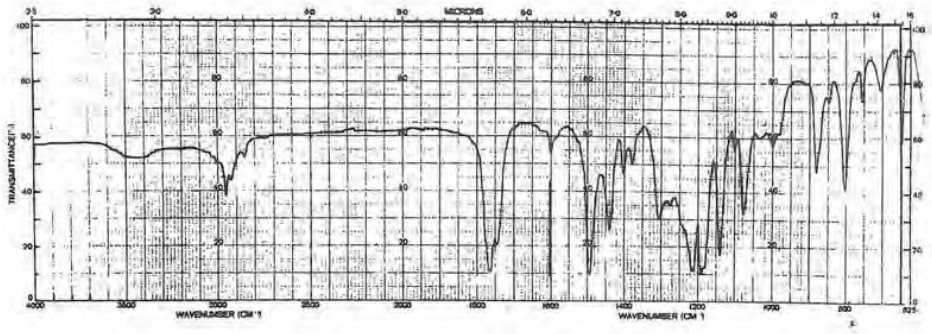


IR spectrum of 2,4,5-TP methyl ester.[5]



IR spectrum of 2,4,5-TB methyl ester.[5]

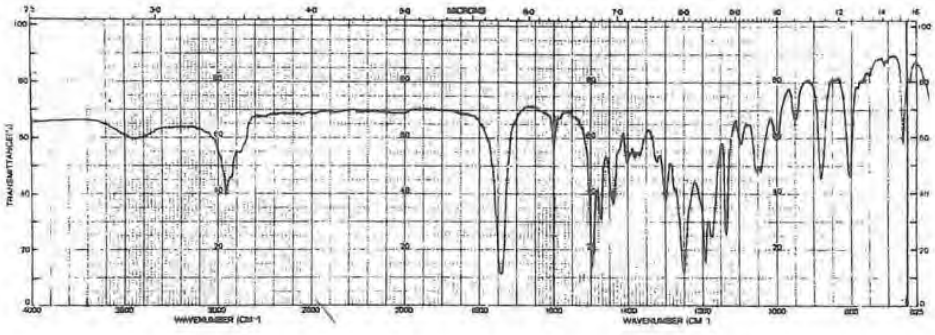
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IR spectrum of MCPA methyl ester.[5]



IR spectrum of MCPP methyl ester.[5]



IR spectrum of MCPB methyl ester.[5]

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Appendix 19
^{13}C and ^{1}H NMR DATA FOR VARIOUS PHENOXYACETIC SODIUM SALTS in D_2O

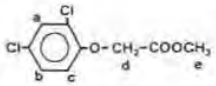
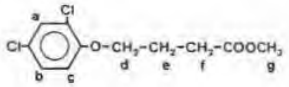
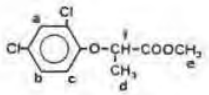
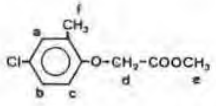
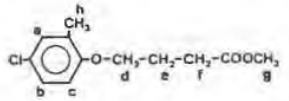
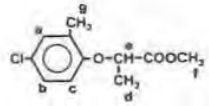
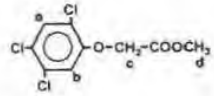
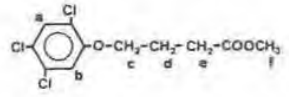
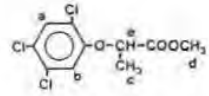
	Proton δ (ppm)						
	H-2	H-3	H-4	H-5	H-6	CH_2	J (H_2)
2-CPA		7.45	7.00	7.29	6.93	4.55	J(3,5) = 2.0; J(5,6) = 7.1, J(3,4) = 8.9; J(4,5) = 8.1; J(4,6) = 1.7
4-CPA	6.9	7.32	—	7.32	6.90	4.46	J(3,5) = 3.1; J(5,6) = 9.1; J(2,6) = 2.5,
2,4-D	—	7.49	—	7.27	6.86	4.53	J(3,5) = 2.7; J(5,6) = 9.0
2,4,5-T (DMSO-d)	—	7.92	—	—	7.66	5.15	
MCPA	—	7.24	—	7.19	6.73	4.47	J(3,5) = 2.5; J(5,6) = 8.1

	^{13}C δ (ppm)								
	COO^-	C_1	C_2	C_3	C_4	C_5	C_6	CH_2	Free valence Index $F_3 + F_6$
2-CPA	170.4	155.3	112.4	134.0	123.5	129.8	114.9	66.9	0.818
4-CPA	173.4	155.2	117.3	129.8	124.5	129.8	117.3	69.0	0.822
2,4-D	172.5	154.5	123.0	130.0	125.0	128.4	118.1	69.8	0.827
2,4,5-T	169.8	153.6	122.3	131.4	124.1	131.4	116.7	67.0	0.833
MCPA	173.3	157.1	126.7	129.9	124.4	129.2	114.2	69.4	0.829
2,4,6-T	169.8	150.3	129.9	130.3	129.9	130.3	129.9	70.5	0.742

From Junghans, J. and Sprinz, H., *Z. Chem.* 15(4),153, 1975. With permission.

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Appendix 20
PMR DATA FOR THE METHYL ESTERS OF CHLOROPHENOXY ACID HERBICIDES

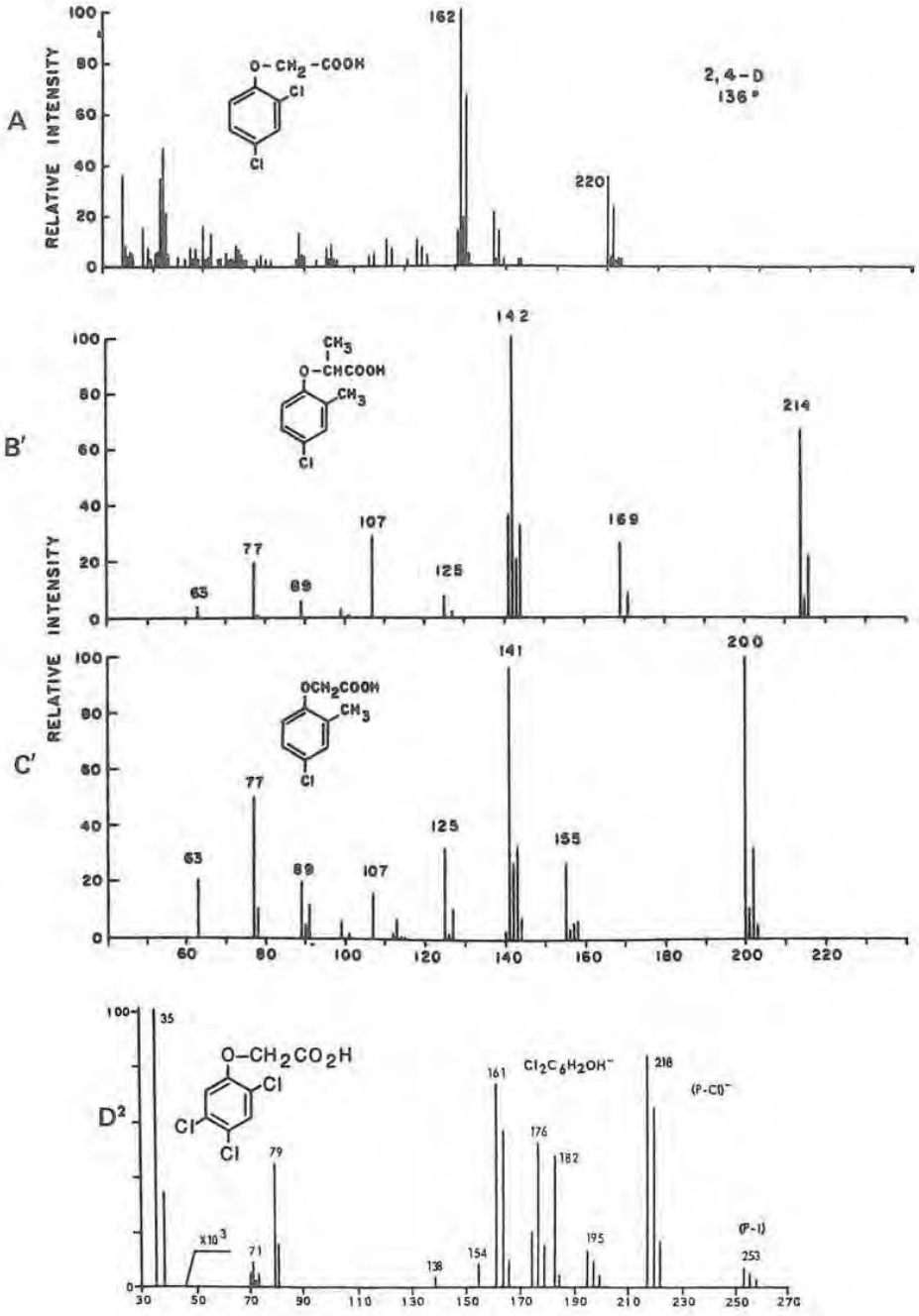
Compound	Proton	Shift in ppm (pattern)[a]
	a	7.34 (d)
	b	7.10 (q)
	c	6.73 (d)
	d	4.61 (s)
	e	3.74 (s)
	a	7.32 (d)
	b	7.15 (q)
	c	6.79 (d)
	d	4.05 (d)
	e	2.19 (m)
	f	2.57 (t)
	g	3.68 (s)
	a	7.32 (d)
	b	7.07 (q)
	c	6.70 (d)
	d	1.62 (d)
	e	3.68 (s)
	f	4.64 (q)
	a	7.03 (s)
	b	6.96 (q)
	c	6.49 (d)
	d	4.50 (s)
	e	3.69 (s)
	f	2.20 (s)
	a	7.01 (s)
	b	6.97 (q)
	c	6.60 (d)
	d	3.92 (t)
	e	2.10 (m)
	f	2.45 (t)
	g	3.63 (s)
	h	2.48 (s)
	a	7.05 (s)
	b	6.97 (q)
	c	6.49 (d)
	d	1.58 (d)
	e	4.64 (q)
	f	3.67 (s)
	g	2.21 (s)
	a	7.43 (s)
	b	6.89 (s)
	c	4.63 (s)
	d	3.77 (s)
	a	7.38 (s)
	b	6.93 (s)
	c	4.04 (t)
	d	2.16 (m)
	e	2.50 (t)
	f	3.65 (s)
	a	7.42 (s)
	b	6.88 (s)
	c	1.64 (d)
	d	4.66 (q)
	e	3.73 (s)

[a] s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet.

From Van Peteghem, C. H. and Heyndrickx, A. M., *J. Assoc. Offic. Anal. Chem.*, 58, 1001, 1975. With permission.

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Appendix 21
ELECTRON IMPACT MASS SPECTRA (70 eV) OF (A) 2,4-D, (B) 2,4-DB, and (C) MCPA, (D) NEGATIVE ION MASS SPECTRUM OF 2,4,5-T

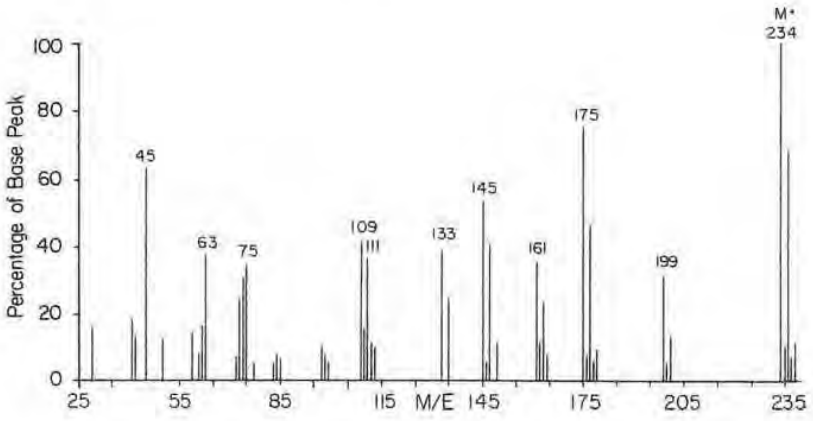


1. From Jorg, J., Houriet, R., and Spiteller, G., *Monatsh. Chem.*, 97, 1064, 1966. With permission.
2. From Rankin, P. C., *J. Assoc. Offic. Anal. Chem.*, 54, 1340, 1971. With permission.

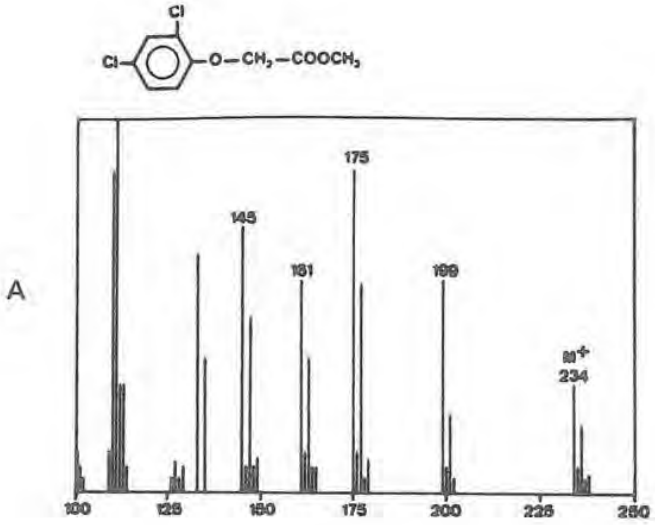
Bayer EX1026 (Part 1 of 2)

Appendix 22

ELECTRON IMPACT (70 eV) MASS SPECTRA OF THE METHYL ESTER OF 2,4-D (A, B(a), C(a), D); B(b) CD_3-METHYL ESTER OF 2,4-D; C(b) 2,3-D, C(c) 3,4-D; (E) METHYL ESTERS OF 2,4-DP; (F) 2,4-DB; (G) 2,4,5-T; (H) 2,4,5-TP; (I) 2,4,5-TB; (J)MCPA; (K) MCPP; and (L) MCPB; (M) *n*-BUTYL ESTERS OF 2,4-D, 2,3-D, and 3,4-D; (N) THE BUTOXYETHANOL, ISOOCTYL, AND PROPYLENE GLYCOL BUTYL ETHER ESTER OF 2,4-D; AND (O) THE ETHYL ESTER OF 2,4-D.

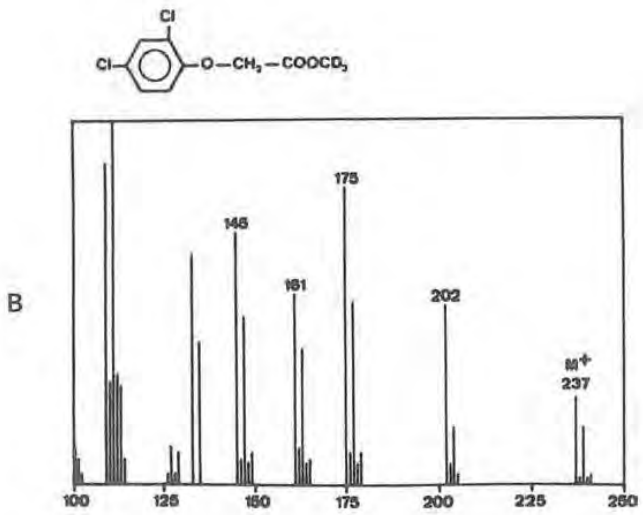


A[1]

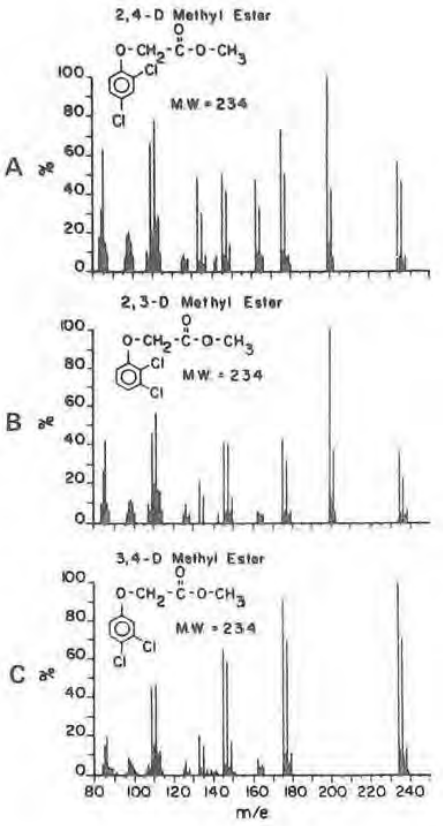


B(I)[2]

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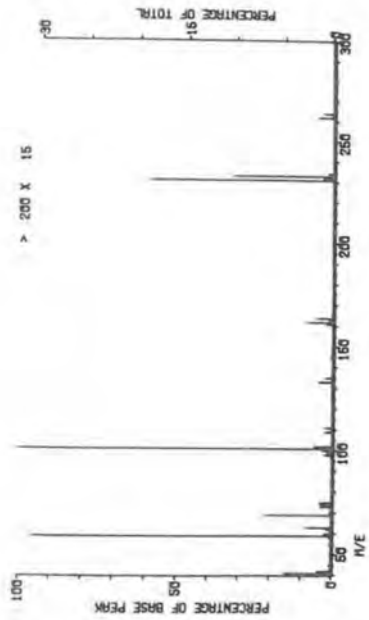


B(II)[2]

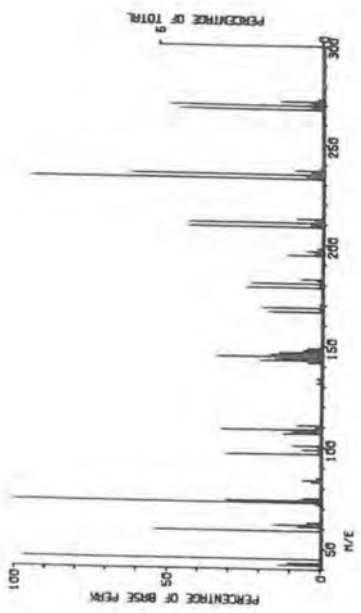


C[3]

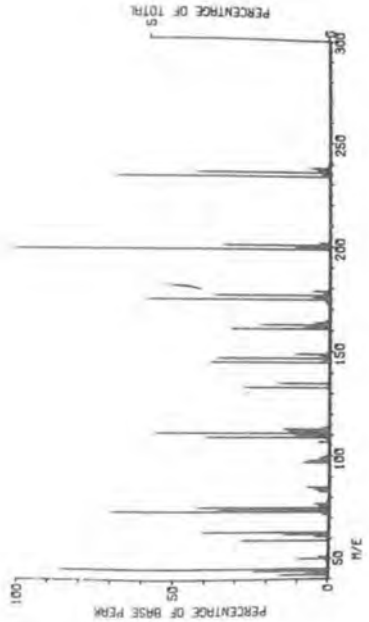
Bayer EX1026 (Part 1 of 2)



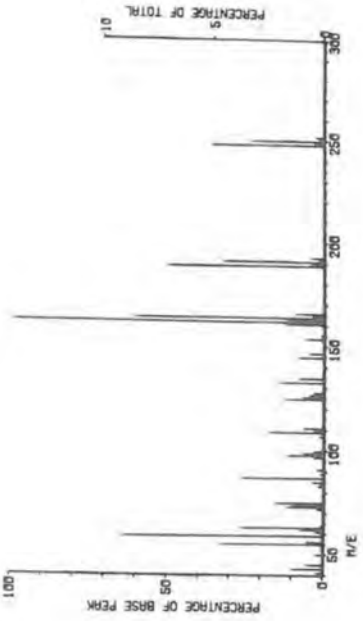
F'



G'

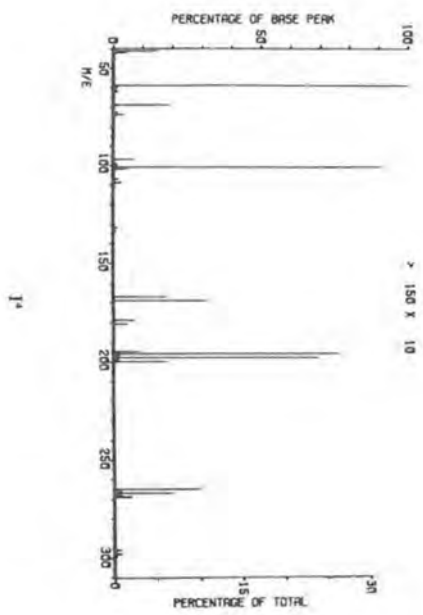


D'

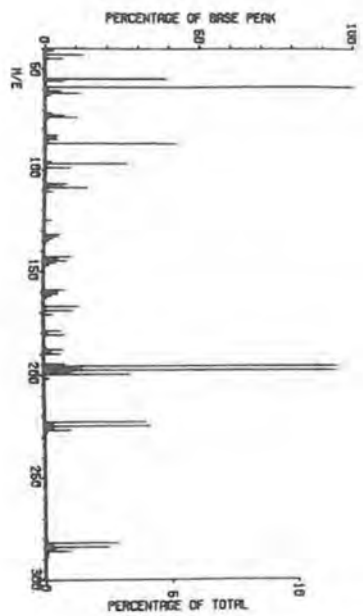


E'

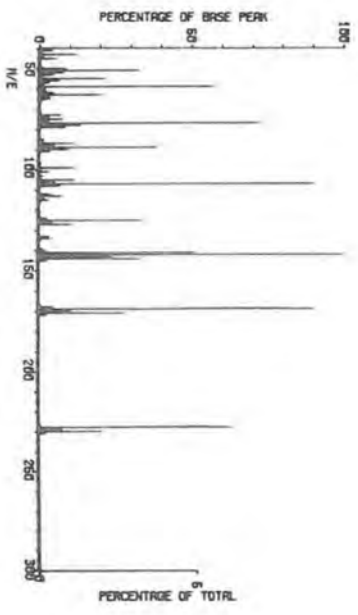
Bayer EX1026 (Part 1 of 2)



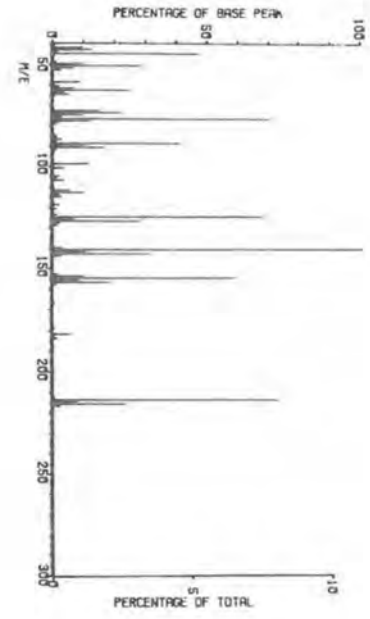
I+



H+

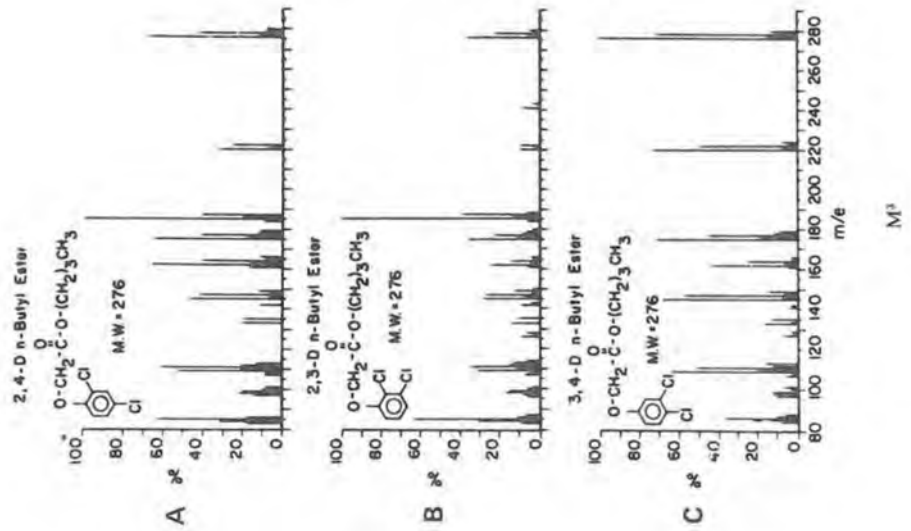


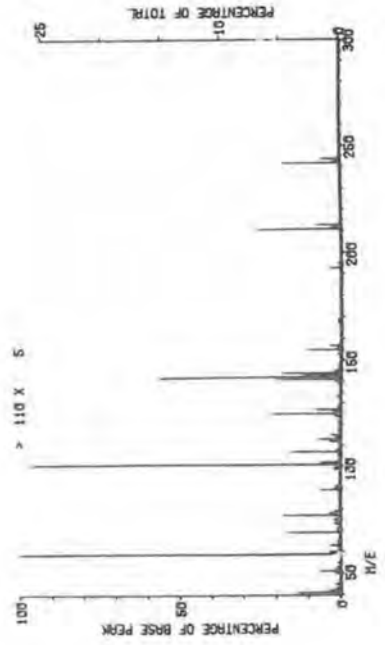
K+



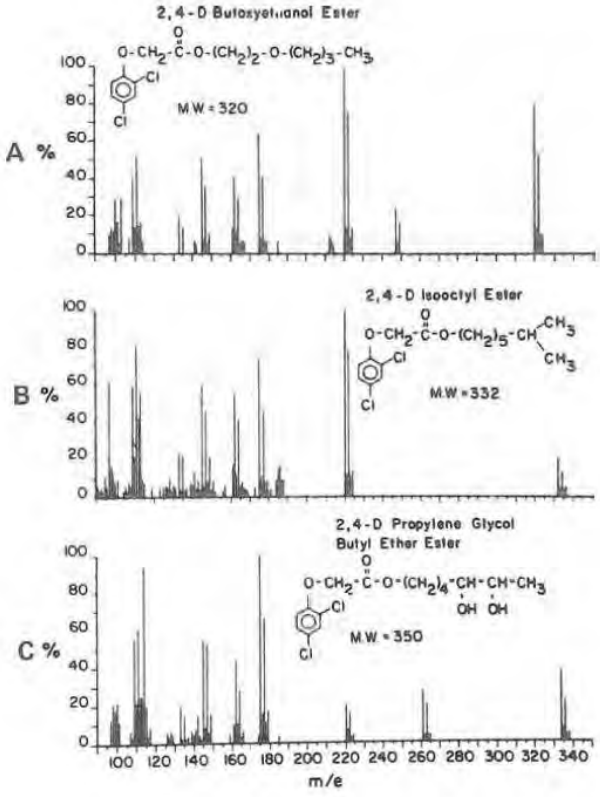
J+

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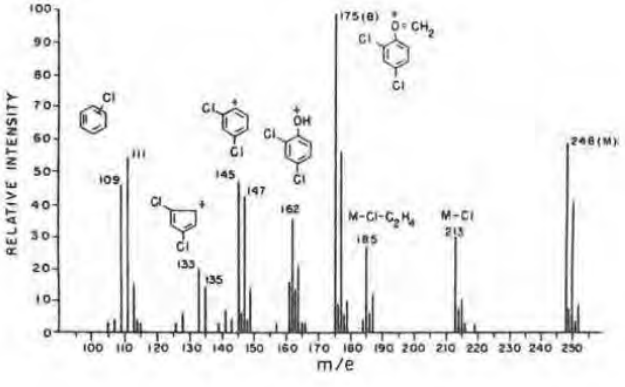




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N[3]



O[3]

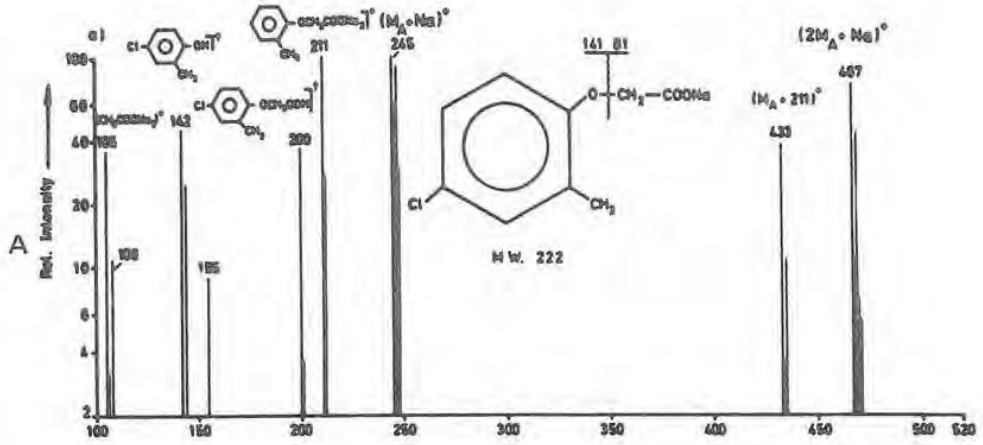
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1. Que Hee, S. S. and Sutherland, R. G., unpublished results.
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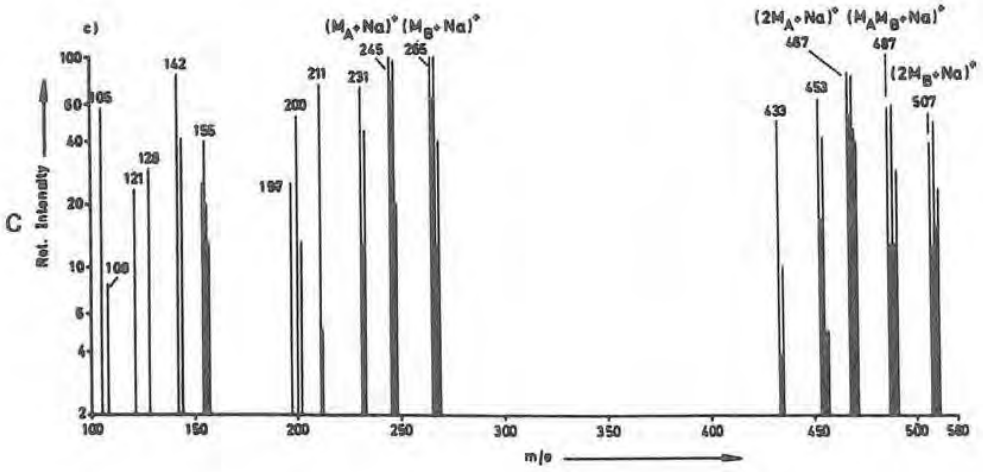
Bayer EX1026 (Part 1 of 2)

Appendix 23

(A) FDMS OF MCPA (2-METHYL-4-CHLOROPHENOXYACETIC ACID SODIUM SALT), SOLVENE WATER, BAT 15 TO 18 mA; (B) FDMS OF 2,4-D(2,4-DICHLOROPHENOXYACETIC ACID SODIUM SALT), SOLVENT WATER, BAT 20 TO 23 mA; (C) FDMS OF BI-HEDONAL (50% 2,4-DICHLOROPHENOXYACETIC ACID SODIUM SALT AND 50% 2-METHYL-4-CHLOROPHENOXYACETIC ACID SODIUM SALT), SOLVENT WATER; THE BEST TOTAL EMISSION WAS OBSERVED BETWEEN 15 AND 25 mA.



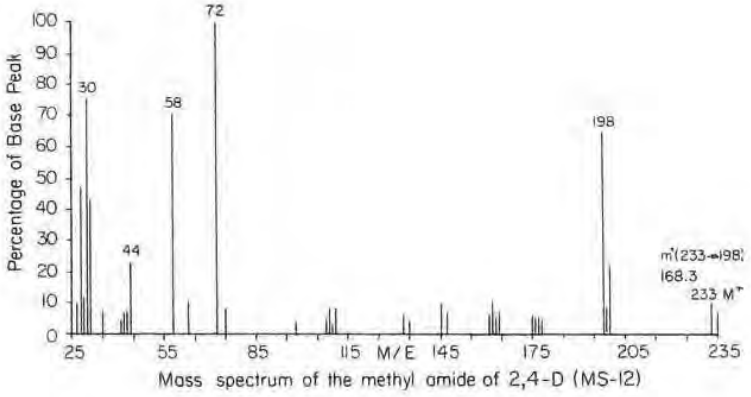
Bayer EX1026 (Part 1 of 2)



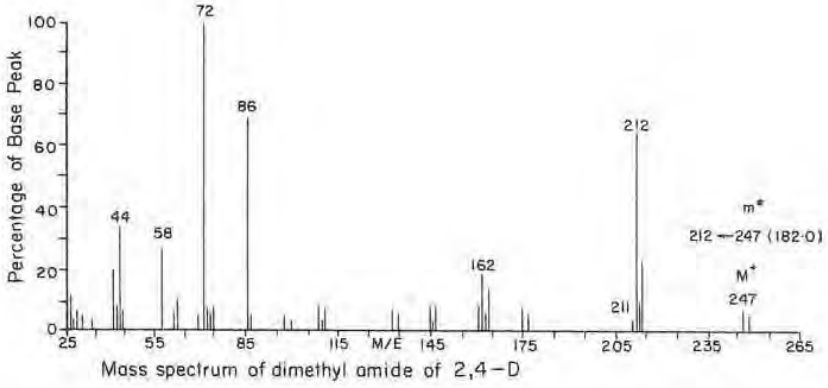
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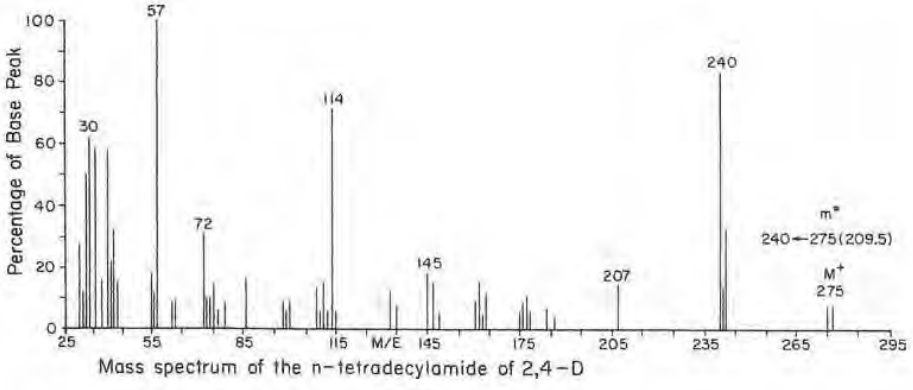
Appendix 24
MASS SPECTRA OF SOME *n*-ALKYLAMIDES OF 2,4-D (MS-12 INSTRUMENT, INLET 80°C, 70eV)



Mass spectrum of the methyl amide of 2,4-D (MS-12)

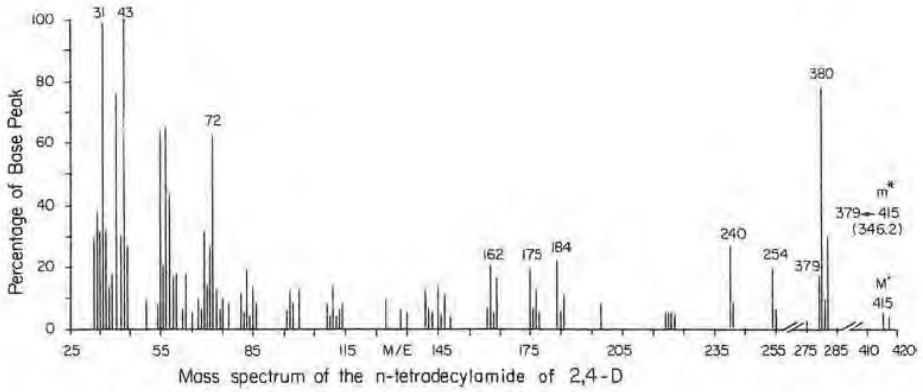


Mass spectrum of dimethyl amide of 2,4-D



Mass spectrum of the n-tetradecylamide of 2,4-D

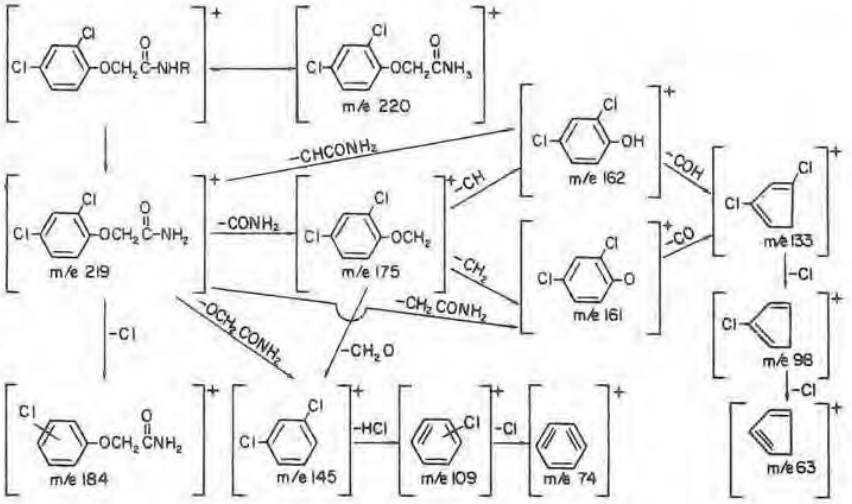
Bayer EX1026 (Part 1 of 2)



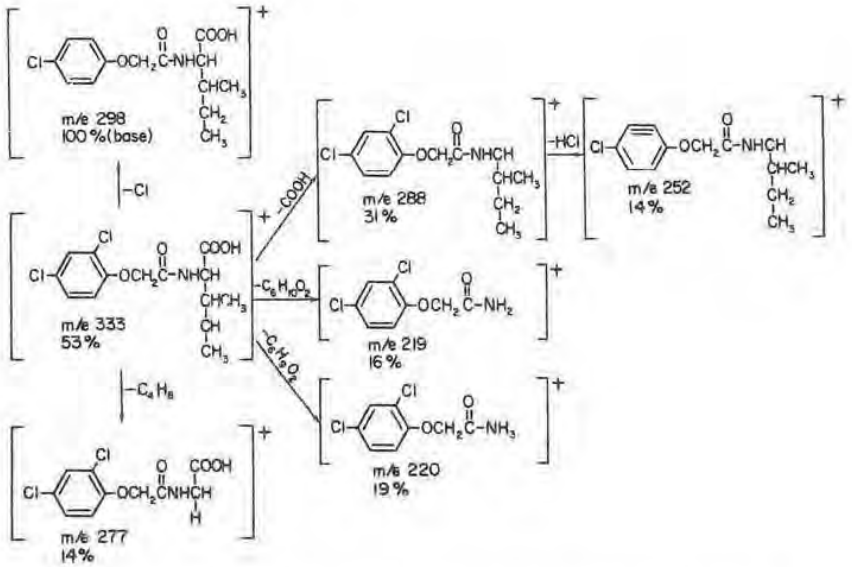
Mass spectrum of the n-tetradecylamide of 2,4-D

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Appendix 25
MASS SPECTRA OF AMINO ACID AMIDES OF 2,4-D



Prominent mass spectral ions arising from the fragmentation of the 2,4-D portion of the molecule of amino acid conjugates of 2,4-D



Prominent mass spectral ion arising from fragmentation of 2,4-D-He (m/e>219)

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Appendix 25 (continued)
MASS SPECTRA OF AMINO ACID AMIDES OF 2,4-D

Relative intensity of ions

m/e	Gly	Ala	Ser	Pro	Val	Thr	Cys	Leu	Ile	Hyp	Asp	Lys	Glu	Met	His	Phe	Arg	Tyr	Trp	Cys
41			18	27	39	22		4	57	4	9	47	92	28	6	8	14			89
42	30	35	42	15	61	44	22	3	20	12	12	40	99	19	7	14	11	17	21	98
43	14	37	18	39	100	100	20	4	31	100	49	100	74	25	100	9	29	26	20	75
44	8	100	20	9		57	18		17	7		39	44	22	6		24		35	71
45					46		20		18			77	29	19	14					59
46												18								
47							20							19						
50																		7		
51												17				11		11	20	
52																			6	
53																			7	
54			27																	96
55				18	100				29			47					15	5		
56	21	59		16	54		28		17		9	41		37				7		57
57		25			44				47	3		21								
58	20					71	31			76	10	26			40	9	9			73
59					50		64			3		30			17					75
60	16											47								
61															100					71
62											7							8		73
63	20	21	26	29	61	26	51	3	20	2	29	15	83	28	11	18	38	25	35	98
64															7					
65												23				28		9		
66												23								
67																				
68				16									68				9			
69					33	19			49			21						5		
70		36		74	85	24					8	19	23				40			
72	9	48	15		98							16								
73	9	17	13	16	33	10	22	4			22		30		6		9			84

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Appendix 25 (continued)
MASS SPECTRA OF AMINO ACID AMIDES OF 2,4-D

Relative intensity of ions

m/e	Gly	Ala	Ser	Pro	Val	Thr	Cys	Leu	Ile	Hyp	Asp	Lys	Glu	Met	His	Phe	Arg	Tyr	Trp	Cys
74	38	13	17	16	74	16	36	13	33		7		26	32	8	12			25	93
75	15	19	19	21	61	11	28				9		33	46		11			29	86
76							18													
77												55				20			100	
79												17				10				
80																				
82			19									24	47							68
83				38								55								
84					83			7			12	63	100				15			89
85													72							
86		23						13	22		7	30								
87							24				6							7		
88	33	37				6	45	8												
89																		5		
90																		6		
91																100				
92																20				
94																				
97						10						67								52
98	10	6	16	18	100	26	37	5	29	2	27	29	51	37	7	3	31	7	15	96
99	6	3	7	9	78	7	24	2	10	1	11	15	22	5	3	2	14	5	7	96
100	4	3	31	7	78	7	19	1	8	1	10	20	22	25	3	1	11	3	5	91
101																			16	
102		12											24						40	
103																14			81	
105																12				
107												27						100		
108												16						35		
109	17	16	22	24	65	10	21	6	14	1	12		32	15	5	13	5	18	21	91
110													26					8		43

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111	20	19	29	27	78	11	25	9	22	2	17	20	42	21	6	19	9	26	28	96
112				32				4		2								9		
113					39							15						9		
114				24	65			6			11									
116	23				100	9	21	10	29					46					29	80
117																			38	
120							16									16				
123																		6		
126								4			21		21				12			50
127								6			6	19	7				4			
128			20					61		2	19	29	16				4		30	61
129								5											58	
130		23						33											100	
131																			100	
132																16				
133	12	10	19	27	59	7	16	17	94	2	12		24	4	7	9	5	15	16	82
134	2	1	2	2	6	1	5	2	16		2		5	1	1	1	1	7	3	9
135	8	7	12	19	41	5	11	11	65	1	8		15	2	5	6	5	10	12	52
136																		6		
139								6												
140								4												
141	14							6									12			
143																			34	
144								6				43							25	
145	21	21	31	29	85	12	33	64	22	2	17	9	35	23	7	21	5	33	36	96
146	4	4	6	5	13	2	7	10	4	1	2	3	9	6	1	7	1	6	10	21
147	18	16	26	24	70	10	26	49	20	1	14	5	29	20	5	28	4	29	27	93
148							28									28		10		41
149																8		8		
153																	12			
154								4												
155				25													28			
156											10								24	
158					24			9											19	
161	8	11	18	34	30	7	25	18	10	2	15		19		10	11		8	21	77
162	52	27	100	100	80	42	100	100	88	9	100	26	100	100	36	15	100	23	40	100
163	9	10	18	29	17	7	21	17	12	2	20	4	23	12	9	7	9	12	7	82
164	33	18	72	74	52	29	71	67	47	6	95	17	94	66	25	9	71	100	27	98

Bayer EX1026 (Part 1 of 2)

Appendix 25 (continued)
MASS SPECTRA OF AMINO ACID AMIDES OF 2,4-D

Relative intensity of ions

m/e	Gly	Ala	Ser	Pro	Val	Thr	Cys	Leu	Ile	Hyp	Asp	Lys	Glu	Met	His	Phe	Arg	Tyr	Trp	Cys
165				15				6										24		
166								11									10			41
170												29	100							
172								30												
173								4												
175	21	27	39	43	65	14	72	67	43	2	25	6	40	30	10	31	4	36	26	98
176	9	10	7	7	13	3	13	23	8	1	4	3	9	10	1	4	1	4	5	36
177	13	18	25	29	46	9	47	61	29	2	17	4	26	19	7	21	3	24	17	89
183	4																			
184	1		10	5	48		50	41	57	2	5				17	59	4	10		64
185	2		3	1	7		10	6	10	1	2				4	9	1	2		9
186			4	2	17		19	13	20	1	2				6	25	1	4		18
187																			100	
188																			46	
196	12																			
197	2																			
198	6																			
203																		13		
204																		5		
205																		4		
208																				18
210		6	10				6	7			22		12							27
211		1	1				1	1			3		2							5
212		2	3				2	2			7		4							9
216																		3		
219	1			59	7				16							31		6		
220		2	18	9	6	4	47	9	19	4	25	3	12	5	17	5	3	9		64
221			4	39	5	1	12	3	13	1	3	2	2	1	2	20	1	5		14
222		1	12			4	33	6	12	2	17	2	10	4	11		2	6		41

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THE MASS SPECTRA OF AMINO ACID CONJUGATES OF 2,4-D>m/e 222

Gly		Ala		Ser		Pro		Val		Asp		Lys		Glu		Met		His	
m/e	%	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%
224	25	256	59	254	60	243	6	238	13	254	4	262	19	258	8	277	68	282	2
225	6	257	9	255	8			239	2	256	2	263	5	259	2	278	9	284	1
226	10	258	20	256	19	245	4	240	4	282	24	280	22	260	6	279	46	357(P)	1
232	22	291(P)	9	272	32	271	7	274	28	283	4	281	5	268	6	290	22		
233	6			273	6			275	6	284	8	295	17	270	4	291	6		
234	15	293	4	274	12	273	4	276	19	300	37	296	5	297	30	292	15		
242	100			289	13	281	89	284	70	301	6	297	6	298	4	304	32		
243	14			290	3	282	16	286	13	302	13	314	2	299	9	305	12		
244	36			291	9	283	40	287	25	318	16	330	9	304	4	306	26		
277(P)	9			307(P)	3	317(P)	8	319(P)	6	319	2	331	5	305	1	351(P)	5		
278	2					318	5	320	2	320	12	332	7	306	2	352	2		
279	7			309	2	319	7	321	5	335(P)	1	348(P)	3	314	100	353	4		
										337	1	350	2	315	22				
														316	44				
														331	7				
														332	2				
														333	5				
														349(P)	7				
														350	2				
														359	4				

Thr		Cys		Leu		Ile		Hyp		Phe		Arg		Tyr		Trp		Cys	
m/e	%	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%
224	7	270	49	232	11	252	14	298	3	286	1	281	9	281	2	360	21	242	71
226	2	271	8	234	7	253	3	300	1	322	2	282	2	283	1	361	22	243	11
242	15	272	18	246	5	254	6	333(P)	1	323	1	283	3	337	6	362	21	244	27
243	3	288	29	248	3	277	14	335	1	324	2	316	9	338	2	363	14	254	86
244	5	289	8	252	7	278	2			332	6	317	3	339	4	406(P)	2	255	16

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259	4	290	10	254	3	279	9	333	2	318	7	365	1	256	30
261	3	323(P)	18	259	4	288	31	334	2	376(P)	3	367	1	270	46
268	16	324	7	260	5	290	19	367(P)	2	377	2	383(P)	5	271	11
269	3	325	15	272	6	298	100	368	1	378	2	384	2	272	25
270	6			274	4	299	18	369	1			385	3	277	7
277	4			277	32	300	33							278	4
279	3			278	4	333(P)	53							279	5
286	2			279	22	334	18							289	32

Appendix Table (continued)
THE MASS SPECTRA OF AMINO ACID CONJUGATES OF 2,4-D>m/e 222

Thr		Cys		Leu		Ile		Hyp		Phe		Arg		Tyr		Trp		Cys	
m/e	%	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%	m/e	%
321(P)	1			288	36	335	35											290	14
				289	5													291	18
				290	25													323	6
				298	100													324	1
				299	23													325	2
				300	43													442(P)	1
				333(P)	5													444	1
				334	3														
				335	4														

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Appendix 26
PHOSPHORESCENCE λ_{max} EXCITATION, EMISSION, LIFETIME, AND DETECTION LIMITS FOR VARIOUS PHENOXY ACIDS IN ETHANOLIC GLASSES (METHANOL FOR REFERENCE 3)

Acid	λ_{max} Excitation (nm)	λ_{max} Emission (nm)	Lifetime (sec)	Detection limit ($\mu g/m\ell$)	Corrected spectra
2-CPA[1]	280	518	0.7	2×10^{-7}	–
4-CPA[1]	283	396	<0.5	4×10^{-9}	–
2,4-D[1]	289	490	<0.5	2×10^{-9}	–
2,4-D[2]	290	495	<0.2	4.4×10^{-9}	–
2,4-D[3]	290,340	490	—	—	–
	290	450→510 (?)	—	—	+
2,4,5-T[1]	294	473	1.1	5×10^{-10}	–
2,4,5-T[2]	300	480	<0.2	5×10^{-10}	–
2,4,5-TP[1]	294	467	<0.5	3×10^{-9}	–
4-Chlorophenol[1]	290	505	<0.2	2.3×10^{-8}	–
2,4,5-Trichlorophenol[1]	280,305	485	<0.2	3.0×10^{-9}	–

Note: All measurements in Reference 3 were performed on an Aminco-Bowman spectrofluorimeter using $\sim 10^{-2} - 10^{-3}$ *M* solutions at liquid nitrogen temperatures.

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Appendix 27
FLUORESCENCE AND PHOSPHORESCENCE λ_{max} FOR 0.096 *M N*-BUTYL ESTERS OF VARIOUS PHENOXY ACIDS IN *N*-HEXANE SOLVENT AT 25 AND −196°C, RESPECTIVELY

n-Butyl ester of acid	λ_{max} Fluorescence (nm)	λ_{max} Excitation (nm)	λ_{max} Phosphorescence (nm)	λ_{max} Excitation (nm)
CAA	350	285	490(200 → 330)	285(390 → 640)
PA	w/l dep(290 → 390)	300(290 → 340)	460(200 → 320)	305(390 → 640)
2-CPA	350(290 → 300)	295(300 → 330)	540(200 → 300)	315(390 → 640)
4-CPA	330(290 → 310)	300(310 → 360)	530(225 → 320)	310(390 → 550)
	375(320 → 350)			
2,4-D	w/l dep(300 → 410)	315(330 → 440)	510(200 → 330)	305(355 → 640)
2,4-D (in *n*-BuOH	w/l dep(300 → 410)	315(320 → 440)	550(200 → 360)	320(390 → 640)
2,4,5-T	w/l dep(300 → 360)	325(320 → 440)	540(200 → 350)	315(355 → 640)
2,4,6-T	350(260 → 330)	255(330 → 430)	520(200 → 330)	250(415 → 545)
		305(330 → 430)		315(355 → 640)
MCPA	w/l dep(280 → 340)	315(340 → 440)	510(200 → 360)	315(355 → 640)
TBA	460(280 → 380)	325(360 → 500)	455(200 → 360)	315(355 → 550)
2,4-Dichloroanisole	370(290 → 340)	345(380 → 440)	550(200 → 250)	325(550 → 630)

Note: The bracketed figures are the appropriate excitation or emission wavelengths over which λ_{max} is constant (CAA = chloroacetic acid; PA = phenoxyacetic acid; TBA = 2,4,6-trichlorobenzoic acid; w/l dep = wavelength dependent).

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Appendix 28
FLUORESCENCE AND PHOSPHORESCENCE λ_{max} FOR 0.10 *M* AMINE SALTS OF 2,4-D DISSOLVED IN METHANOL AT 25 AND −196°C, RESPECTIVELY

	Fluorescence		Phosphorescence	
Amine salt	λ_{max} Fluorescence (nm)	λ_{max} Excitation (nm)	λ_{max} Phosphorescence (nm)	λ_{max} Excitation (nm)
DMA	420(300 → 360)	320(360 → 540)	540(200 → 350)	310(375 → 550)
DMA (in H_2O)	425(300 → 340)	320(380 → 540)	535(200 → 350)	330(400 → 575)
MA	435(300 → 340)	320(380 → 570)	540(200 → 350)	300(375 → 550)
BAM	440(300 → 320)	315(370 → 510)	540(225 → 400)	305(400 → 575)
DDAM	425(300 → 340)	310(420 → 540)	535(200 → 340)	310(400 → 575)
TDAM	420(300 → 340)	320(400 → 450)	540(225 → 375)	310(400 → 575)

Note: The figures in parentheses are the appropriate excitation or emission wavelengths over which λ_{max} is constant (DMA = dimethyl amine; MA = methylamine; BAM = *n*-butylamine; DDAM = *n*-dodecylamine; TDAM = *n*-tetradecylamine).

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Chapter 2

SYNTHESIS

I. FREE ACIDS

The syntheses of 2,4-D and 2,4,5-T were first accomplished by Pokorny[1] of the C. B. Dolge Company, Westport, Conn. in 1941, who utilized procedures initially devised by Holleman[2] in 1917.

First Synthesis of 2,4-D and 2,4,5-T

Equimolar quantities of 2,4-dichlorophenol (30.7 mmole) and 2,4,5-trichlorophenol (25.5 mmole) were mixed separately with monochloracetic acid (39.2 and 32.4 mmole, respectively) and heated with a "slight excess" of sodium hydroxide (67.5 and 55.0 mmole, respectively) together with 0.833 and 1.666 mole of water, respectively, and the solution evaporated almost to dryness. The residues were dissolved in 100 and 200 mℓ respectively of hot water the solutions cooled to room temperature and acidified with hydrochloric acid. A heavy oil separated which soon crystallized. The mixtures were extracted with ether and the ether extracts washed with water and evaporated to dryness on a water bath. The yields of 2,4-D and 2,4,5-T were 87 and 85% respectively, with respective melting points of 138 and 153°C after benzene recrystallization. Both were white odorless crystals, almost insoluble in water.

Analysis 2,4-D:	Calcd = Cl, 32.08; neutr. equiv. 221.0
	Found = Cl, 32.10; neutr. equiv. 221
Analysis 2,4,5-T:	Calcd = Cl, 41.63; neutr. equiv. 255.5
	Found = Cl, 41.57; neutr. equiv. 256

The 2,4,5-T evidently contained more phenolic and other impurities than did 2,4-D. The reaction was thought to proceed by the following route:

$$R{-}OH + NaOH \xrightarrow{aq} R{-}O{-}Na + H_2O \quad (1)$$

$$Cl{-}CH_2{-}COOH + NaOH \xrightarrow{aq} Cl{-}CH_2{-}COONa + H_2O \quad (2)$$

$$R{-}O{-}Na + Cl{-}CH_2{-}COONa \xrightarrow{\Delta} R{-}O{-}CH_2{-}COONa + NaCl \quad (3)$$

$$R{-}O{-}CH_2{-}COONa + HCl \longrightarrow R{-}O{-}CH_2{-}COOH + NaCl \quad (4)$$

where R = substituted phenyl.

It is obvious that Pokorny had a 17% excess over twofold of base with respect to the phenol rather than the sum of the monochloroacetic acid plus phenol. It is equally obvious that the residues dissolved with 100 and 200 mℓ of hot water for 2,4-D and 2,4,5-T, respectively, were the sodium salts of the acids.

If the above scheme is correct and all the steps are of almost equal rate, the rate expression should be

$$d[ROCH_2COOH]/_{dt} = -d[ROH]/_{dt} = k'[ROH](ClCH_2COOH][NaOH]^2 \quad (5)$$

where k′ is a kinetic rate constant.

If Equation 3 is the rate limiting step, then

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$$d[ROCH_2COOH]/_{dt} = -d[ROH]/_{dt} = k[ROH][ClCH_2COOH] \quad (6)$$

and this was actually found by Kolte and Chandalia,[3] who also demonstrated:

1. The phenolic odor of the final product was because of chlorophenol impurities which could be eliminated by treatment with $KMnO_4$ solution or by extraction with carbon tetrachloride.
2. More than the stoichiometric amount of added base resulted in appreciable diminution of yields caused by Reaction 7[3,4]

$$ClCH_2COONa + NaOH \longrightarrow HO\,CH_2—COONa + NaCl \quad (7)$$

When 1.25 mole/ℓ of sodium phenoxide and sodium chloroacetate at 60°C were reacted in aqueous solution for 2.5 hr, with excess base amounts of 0, 25, 50, 75, and 100%, the 2,4-D yields were 72.5, 53.2, 43.0, 26.1, and 16.4%, respectively. If fewer than 2 mol were used, no reaction occurred. The hydrolysis of the monochloroacetate to glycolic acid (Equation 8) has been studied also in the temperature range 25 to 45°C.[5,6]

$$ClCH_2COON_a + H_2O \rightleftharpoons HOCH_2COOH + NaCl \quad (8)$$

Thus, it was suggested,

$$-d[ClCH_2COONa]/_{dt} = k_1[ClCH_2COONa] + k_2[ClCH_2COONa]^2 \quad (9)$$

Under the conditions of the condensation reaction (80, 90, and 100°C), k_1 values were 7.15×10^{-6}, 12.8×10^{-6}, and 18.6×10^{-6} sec^{-1}, respectively, and k_2 values were 3.01×10^{-5}, 5.89×10^{-5}, and 7.95×10^{-5} mol/ℓ/sec, respectively. Thus, as long as excess base is not present, Reactions 8 and 7 are negligible.

3. Addition of salt (NaCl) increased the rate of reaction, but markedly decreased the 2,4-D yield. Thus, when 1 mol/ℓ of sodium phenoxide and 0.5 mol/1 of sodium chloroacetate were reacted for 3.5 hr at 80°C in aqueous solution together with 0.0, 5, and 10 m*M* salt, 2,4-D yields of 93.6, 53.1, and 36.6%, respectively, were obtained. The authors of some patents had previously suggested that the addition of salt enhanced yields.[7]
4. The rate constants for Reaction 3 at 60, 70, 80, 90, and 100°C were 0.316, 0.567, 0.901, 1.57, and 2.86×10^{-4} mol/ℓ/sec, respectively, and the activation energy was calculated to be 13.6 kcal/mol, but it was assumed the second-order rate constants acted like first-order rate constants, and this is incorrect.
5. The optimum yield of 2,4-D of 98.4% was obtained under the following conditions: alkali, stoichiometric amount; concentration of sodium 2,4-dichlorophenolate 2 *M*; concentration of sodium monochloroacetate, 1 *M*; temperature 100°C; reaction time 1.5 hr, using homogeneous conditions of reaction and no evaporation of water.

Many researchers have used essentially the same type of reaction conditions,[7-30] but eliminate the evaporation step and allow the reaction to proceed for 3 to 6 hr at 100°C before cooling, acidification, ether extraction, and recrystallization. The synthetic route is often used in industry.

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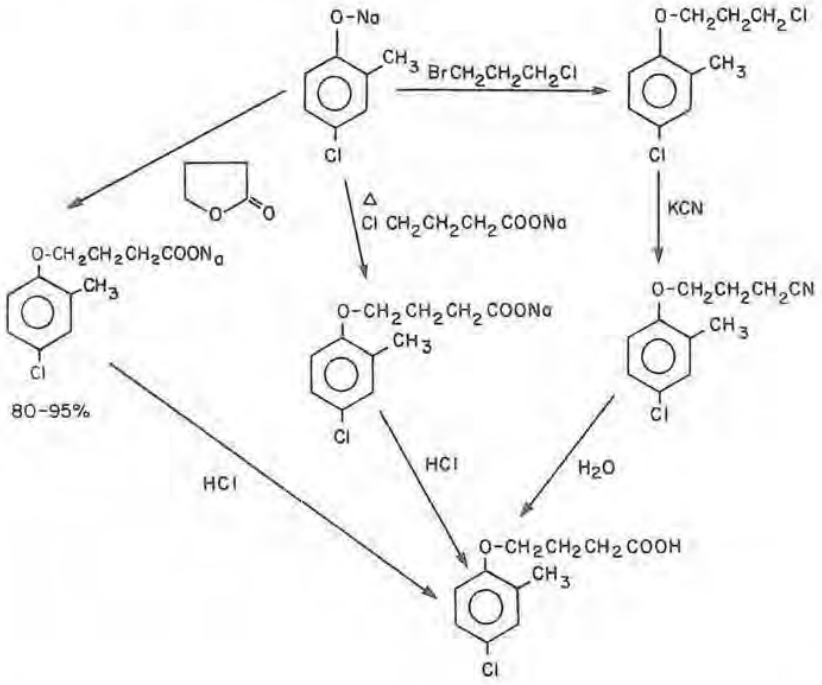
Eckstein et al.[7] found that the optimum temperature for 2,4-D synthesis was 105 to 107°C, and the reaction was complete within 30 to 60 min. Furthermore, Simonov[23] found the condensation Reaction 3 was overall second order and that the condensation of substituted phenolates with sodium monochloroacetic acid is much affected by the presence and type of *ortho* substituents. Hammett correlations were also found, and the isokinetic temperature was 163°C. However, the nonadditivity of electronic effects of the substituents on the ring implies that steric and polar interactions of the ortho substituents with the reaction center are important.

The 4-chloro-2-methylphenol used in the manufacture of MCPA is obtained by chlorination of 2-cresol with chlorine, alkali hypochlorites, or sulfuryl chloride. The latter affords the purest phenol. If chlorination is carried out, the reaction products are 60 to 70% 4-chloro-2-methylphenol, with traces of 6-chloro-2-methylphenol, and 4,6-dichlorophenol as impurities. The sodium phenolates are then reacted by the Pokorny procedure.[43]

2,4-Dichlorophenol produced by chlorination also contains much 2,6-dichlorophenol. However, 98% 2,4-dichlorophenol can be obtained when the chlorination is carried out in liquid sulfur dioxide below the boiling point of the latter; 2,6 and 2,4,6-chlorinated phenols are not produced.

The herbicidal propionic or butyric acids are also synthesized readily by this route[43] (see Appendix 1).

MCPB, 2,4,6-TB, and 2,4-DB can all be made using several closely related routes.[43] The major acylating agent is the butyrolactone.



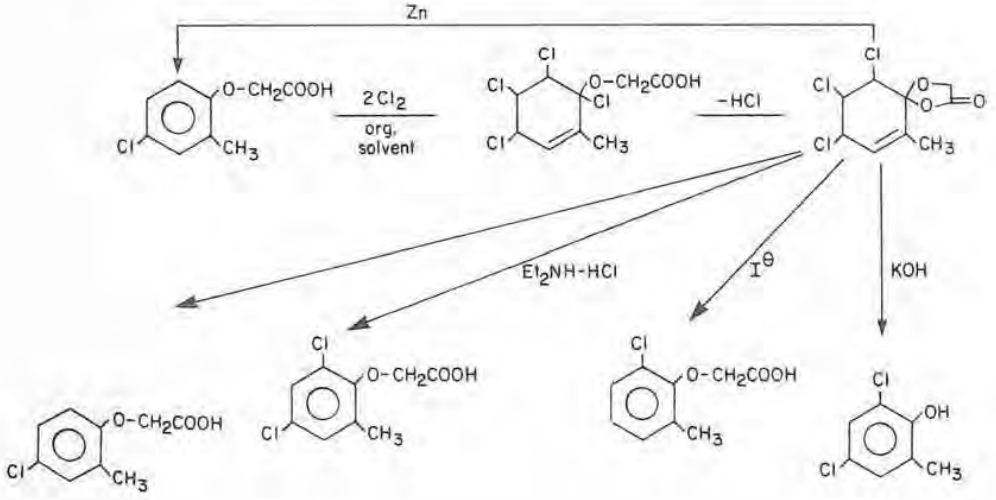
A laboratory variation of the original Pokorny synthetic route involves the formation of the phenolate and then its reaction with a halogenated ester to produce the phenoxy ester which is subsequently saponified and then acidified.[31-42] Thus, Synerholm and Zimmerman reacted[31] 0.156 mol of sodium in 100 mℓ of absolute ethanol

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with 0.153 mol 2,4-dichlorophenol and added 0.155 mole of ethylbromoacetate at reflux. The resultant ester was formed within half an hour, and the latter was saponified with sodium hydroxide, neutralized (HCl), and the acid recrystallized from C_6H_6/petroleum ether. The mp reported was 139 to 140°C, and the yield was 95%. Thus, this method produced 2,4-D in higher purity and yield than did Pokorny's original synthesis. The bromo ester was used, since the Br is a better leaving group than chlorine, the C-Br bond being weaker than the C-Cl bond. Excess HCl on prolonged reflux can cause some reformation of the phenol.[43]

Another important synthetic route is the chlorination of phenoxyacetic acid.[43-48] Chlorine, sodium hypochlorite, sodium chlorate with HCl, sulfuryl chloride, and chloramines can be used as chlorinating agents in aqueous or organic solvents or in a melt. The product has high 2,4-dichlorophenol content and is of lower quality than the Pokorny product, since 4-CPA, 2-CPA, 2,4,6-T, and 2,4,6-trichlorophenol are invariably present. Generally, the chlorination is carried out at 40 to 50°C, and the condensation takes approximately 1.5 hr for completion. Sometimes salts,[46] esters,[47] and phenoxyethanol[48] are used as the unchlorinated substrate. The phenoxyacetic acid substrate is obtained in 80 to 90% yield by the reaction of sodium phenolate with sodium monochloroacetate, analogous to the Pokorny synthesis (see Appendix 1).

Chlorination of 2-methylphenoxyacetic acid with chlorine or a hypochlorite in dry organic solvents occurs mostly at the 4 position in the benzene ring.[43] Small amounts of 6-chloro-2-methylphenoxyacetic acid, the ester acetal of 4,5,6-trichloro-2-methylcyclohexen-2-1 (mp 137°C), and glycolic acid are also produced.

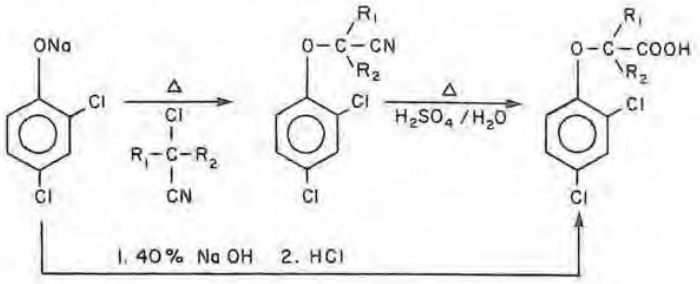


(10)

MCPB is also easily obtained by this method, and both organic and aqueous solvents can be used.[49]

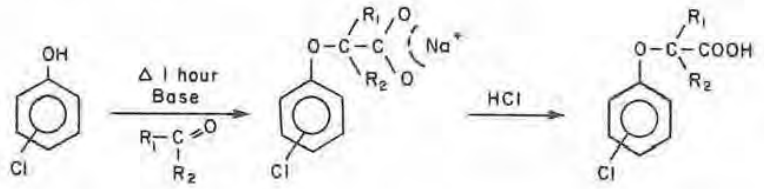
Other laboratory methods involve the oxidation of the corresponding nitrile,[34,50-52]

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(11)

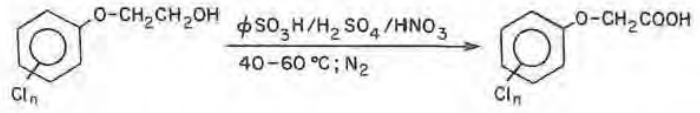
the reaction of a chlorophenol with a base and a ketone,[53,54]



(12)

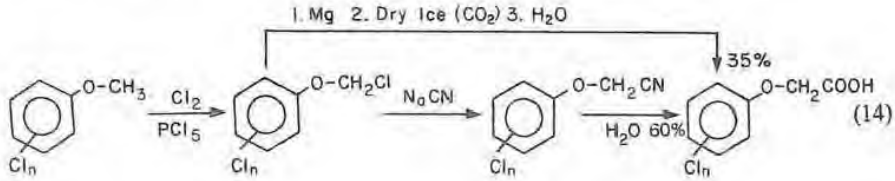
and the reduction of different chlorocyclohexanes under pressure at 200°C in alkali to produce various chlorophenols and subsequent condensation with monochloroacetic acetate in the same alkaline solutions.[18,55] This product is usually contaminated with the acids which correspond to the phenols present in the original phenol mixture.

Another route involves the reaction of 2,4-dichloroanisole with oxalyl chloride and dibenzyl peroxide to produce first the acid chloride which, on alkaline hydrolysis and finally acidification, produces 2,4-D.[56] The chlorinated phenoxyethanols have also been oxidized to phenoxyacetic acids by phenylsulfonic and sulfuric acids.[48,57,58] The yields are generally low, but are improved by a platinum catalyst.[43,58,60]

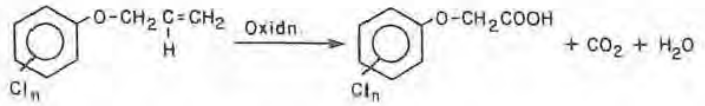


(13)

Other routes used are



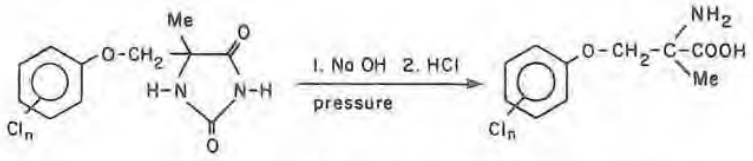
(14)



(15)

α-Amino acids can be synthesized by the following route:[61]

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(16)

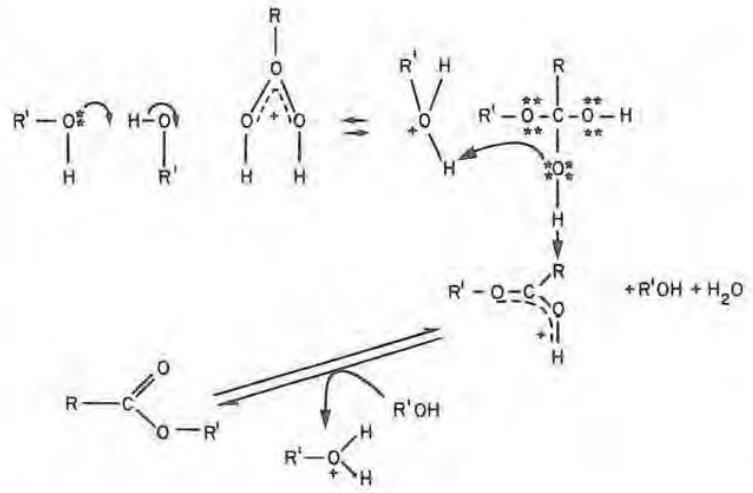
Optically active acids are usually obtained as racemic mixtures by any of the above preparations. (+)−Mecoprop was resolved by use of (+)-$PhCHMeNH_2$ and (+)-2,4-$Cl_2C_6H_3 \cdot O \cdot CHEt \cdot CO_2H$ and (+)-2,4-DP with strychnine. The (−) compounds were resolved with (−)-$PhCHMeNH_2$. All the (+) compounds (which are the most active auxins) were of the D-series.[62] (+)-α-2,4-DP was also obtained by the use of (+)(+) amphetamide, and the (−) acid with (−)(−) amphetamide.[63] (±)-Strychnine can also be utilized[64] to resolve (±)-2-(2-) and 2-(3-) chlorophenoxypropionic acid. Thus, the strychnine salt was dissolved in $EtOH/H_2O$. After 20 hr, the salt was filtered off, recrystallized (× 3), decomposed with Na_2CO_3, strychnine extracted, the residue acidified, and the (−)-acid extracted with Et_2O and recrystallized twice from cyclohexane. The mother liquor was extracted with CCl_4(× 2) and the (+)-acid recrystallized twice from cyclohexane and then from formic acid. The (+) forms of both acids were both D.

II. ESTERS

A. Esterification of Free Acids

Many reviews on esterification, its mechanism, and the role of conditions on yields of esters have appeared. It is not proposed to consider the voluminous literature in its entirety, but only as it applies to the acids presently under consideration.[65,66]

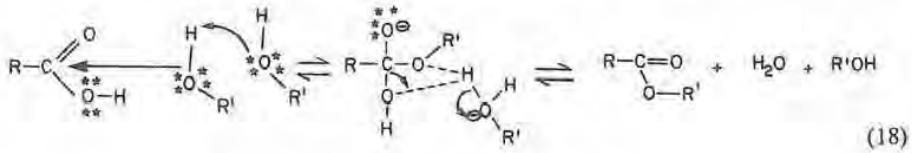
The most familiar route is acid catalyzed esterification ($A_{AC}2$ mechanism) which proceeds via a tetrahedral intermediate to produce a protonated ester which quickly loses its excess proton. Thus, *t*-butanol cannot be used for esterification under these conditions:



(17)

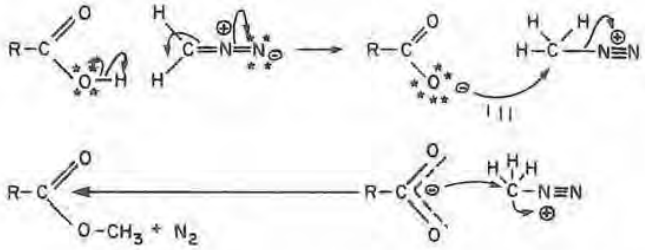
The esterification in neutral solution occurs via a tetrahedral intermediate also.

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(18)

Esterification by diazoalkylation is also commonly done.



(19)

On the other hand, the acid anion cannot be esterified readily in alcohol solutions, but can be made to esterify in alkyl halides or dialkyl sulfates.[65]

One comparative study of some methods of esterification for 2,4-D was published in 1974 by Horner et al.[67] Diazomethylation, alcohol/acid catalysis, BF_3/alcohol reaction, and silylation were considered (see Table 1). BF_3/alcohol was the preferred technique, giving the best product yields (+95%) and cleanest chromatogram. The latter feature occurs because the contaminant phenols are not also alkylated, unlike in diazoalkylation (yield +95%). In addition, silylation was inefficient (approximately 70%), and the silyl esters produced were sensitive to the presence of water. Acid/alcohol mixtures produced only approximately 52% yield. Other authors have used BCl_3/alcohol mixtures, and some have used chlorinated alcohols to improve electron capture GC sensitivity.[68]

Similar results were obtained for Fenac and picloram.[69] A kinetic study of the system 2,4-D/95% ethanol/H_2SO_4 in 1970[70] showed that equilibrium was attained at 78°C after 3 hr with an ester yield of 85%. The ratio of the hydrolysis to the esterification constant was 0.8, with the latter constant having a value of 625 $\ell mol^{-1}\ hr^{-1}$; i.e., esterification was a second-order process. The rate law was

$$dx/dt = k_E[(a - x)(b - x) - (k_h/k_E) \cdot x \cdot (C + x)]$$

where

$$k_h/k_E = \frac{(a - x)(b - x)}{x(C + x)} \qquad (20)$$

with x = ester concentration, a = acid concentration, b = alcohol concentration, and C = water concentration.

Most other reports give equilibrium values of 52 to 66%[67,71,72] (see Appendix 2), but quantitative production of the esters can be accomplished by azeotropic distillation[73-81] of water or by continuous removal of water,[82-84] e.g., by a Dean Stark trap, etc. BF_3 or BCl_3/alcohol reagents have been extensively used for esterification. Storrs and Burchfield[72] found that BF_3/methanol was not a good esterifying agent; however, Goerlitz and Lamar[85] using 2,4-D, 2,4,5-T, and Silvex, Horner et al.[67] using 2,4-D, Gutenmann and Lisk[86-87] using 2,4-D, 2,4-DB, and Silvex, and Woodham[68,88] found yields of esters to be greater than 92% with boron trihalide/alcohol. MCPA and MCPB have also been analyzed with this reagent.[87,89]

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Table 1
COMPARISON OF DIFFERENT ESTERIFICATION PROCEDURES

Method	Number of resolvable impurities (EC glc)	glc Purity[a] (%)	Yield ± SD (%)
2,4-D/MeOH/H_2SO_4	7	73	52 ± 5.5
2,4-D/MeOH/HCl	0	100	50 ± 4.2
2,4-D/CH_2N_2 unrefluxed	10	77	74 ± 6
2,4-D/CH_2N_2 refluxed	8	88	87 ± 5
2,4-D/MeOH/BF_3	0	100	96 ± 1.5
2,4-D/*n*-BuOH/BF_3	0	100	98 ± 4
2,4-D/*n*-OctOH/BF_3	0	100	99 ± 4
2,4-D/TriMe silyl chloride (pyridine)	0	100	71 ± 2

[a] $\frac{\text{Ester peak area (\%)}}{\text{Total peak area neglecting solvent}}$, glc = Gas liquid chromatography.

Procedure of Esterification Using BF_3/Alcohol

Boron trifluoride or trichloride gas is bubbled into the alcohol at 0°C until a concentration of 0.20 g BF_3(or BCl_3)/mℓ alcohol is attained. Use only pyrex or teflon tubing. Store the reagents at 0°C. Dissolve 2,4-D (1.7 g in alcohol (3 mℓ); add the BF_3(BCl_3)/alcohol reagent (3 mℓ), and reflux the solution for 10 min. After reaction, remove excess alcohol under vacuum at room temperature; add water (20 mℓ), and shake vigorously for 5 min before allowing the layers to separate. Extract with ether (3 × 10 mℓ), combine all extracts, and evaporate the excess ether under pressure to the desired volume. Hexane can also be used instead of ether.

Diazoalkylation has been used even more extensively than the BF_3/alcohol method. Since diazoalkanes can alkylate sterically hindered acids[94,95] (for which BF_3/alcohol produces poor yields) and phenols,[96-98] it is a much more reactive alkylating reagent. It does produce more noisy GC chromatograms than desirable for environmental studies.[67,109] Diazomethylation of 2,4-D has been shown to be at least 87% efficient;[67,85,90-93] 2,4,5-T, Silvex, MCPA, and 2,4-DB also allow quantitative reaction.[85,99-102] Diazoethane[103] and diazobutane[104] have also been utilized.

Procedure for Diazoalkylation

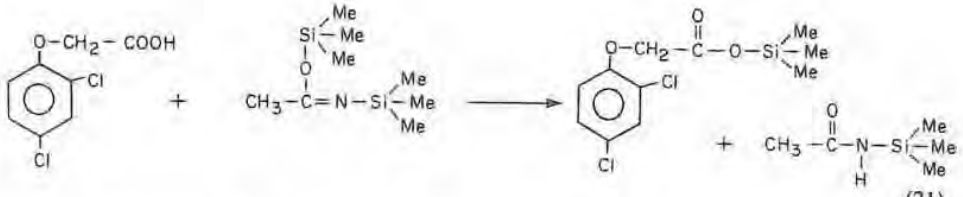
Diazomethane being very reactive and potentially explosive requires special precautions for its synthesis[105,106] and the article in *Organic Synthesis* should be consulted for the safety precautions.[105] It is prepared in an apparatus which has no ground glass joints and is usually obtained as an ethereal solution.

Dissolve 1.7 g of 2,4-D in dry methanol (4 mℓ); add 4 mℓ of the diazomethane/ether reagent, and reflux for 15 min. The color of the solution should be yellowish. Remove the excess ether under pressure (the solution should become colorless) and dilute to volume with the appropriate solvent, usually a nonpolar solvent such as *n*-hexane, ethyl acetate, etc.

Silylation of the phenoxy acids has also been studied.[67,107,108,115,116] Trimethylsilyl esters of 2,4-D, 2,4,5-T, and dicamba require different ratios of reagent/solvent for optimal yields.[107] A *N,O-bis*-(trimethylsilyl)acetamide (BSA)/dimethylformamide (DMF) ratio of 1:10 was required for 2,4-D and 2,4,5-T, but a ratio of 1:50 was necessary for dicamba. The reagents and esters were very susceptible to traces of moisture. However, Garbrecht did claim quantitative yields for 2,4-D, MCPP, dicamba (not esterified by BF_3/alcohol), MCPA, 2,4,5-TP, 2,4,5-T, and 2,4-DB using a 1:1 BSA/DMF reagent. These esters were stable for 12 hrs, but the reaction was very moisture sensitive. Garbrecht claimed pyridine-based silylating reagents did not form silyl esters,

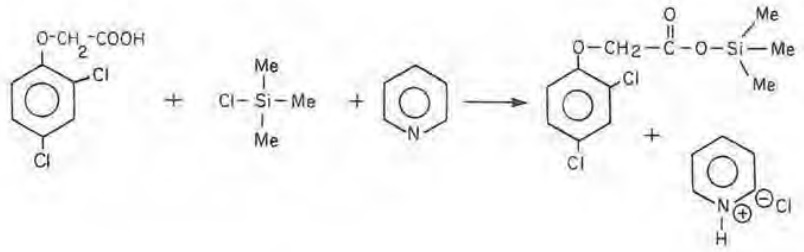
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but Horner et al. obtained[67] the trimethyl silyl ester in approximately 71% yield using a trimethylsilyl chloride/pyridine ratio of 1:3. However, the ester was only stable for 2 hr. When DMF was used as solvent for the same silylating agent, the ester was stable for only 1 hr. Halogenated phenols can also be silylated.[117,118] For the BSA reaction,



(21)

For the trimethyl silyl chloride reaction,



(22)

The fact that silylation products allow a linear GC response with respect to concentration[115] does not necessarily prove that the yield was quantitative.

Transesterification which proceeds by the same mechanism as esterification[65,66] has also been utilized for the quantitation of various phenoxy acids.[72,110,111] BF_3/alcohol and HCl/alcohol will produce esters with the same yield as for the free acid. Studies have been conducted on 2,4-D,[72,110,111] 2,4,5-T,[72,110,111] 2,4,5-TP,[110] MCPA,[110] 2,4-DB,[110] and Silvex.[111] Transesterification of the methyl ester of 2,4,5-T to its sucrose ester in DMF/K_2CO_3 was shown[134] to be zero order and to occur in two stages, the first being the elimination of methanol. In general, the yields for H^+/alcohol are not quantitative, since it is an equilibrium process. The inadvertant formation of esters during the extraction of tissues by alcoholic solvents can lead to losses of residues, particularly if the clean-up is designed for the acid.

Dimethyl sulfate in methanol when reacted with 2,4-D and 2,4,5-T produced[92] yields of approximately 88 and 80%, respectively. Similar results were found for 2-, 3-, and 4-CPA. The optimum reaction yield occurs with 5% reagent at 55 to 60°C. Although dimethyl sulfate is very toxic, it is inexpensive, readily available, is not explosive, has a long shelf life, and produces quantitative yields within 5 min.

Another alkylating agent of interest involves the pyrolysis of tetraalkyl ammonium salts which was first reported as far back as 1936.[112] Henkel used the pyrolysis of these salts to determine MCPA, MCPP, 2,4-D, 2,4,5-T, and 2-(2,4,5-T P) residues in soil extracts,[113] and Hyman[114] has used the technique for MCPA formulations. The temperature of the pyrolysis must be lower than 270°C; above this, chlorophenols and chlorocresols are produced. MCPA produces[113] a yield of 85% of ethyl ester using the tetraethyl salt, but the other acids give yields of 24 to 50%.

Several excellent reviews of the esterification techniques in herbicide analysis exist.[72,119-121]

There is extensive industrial literature on esterification[83,122-130] and transesterifica-

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tion[131-134] as a means of producing chlorinated phenoxyacetic acids. Most industrial processes utilize acid catalyzed esterification with azeotropic distillation of water.

B. Production of Esters by Routes Other than Direct Esterification

The production of esters by the reaction of a haloacetate with a phenolate has been partially dealt with earlier[24,31-33] in the synthesis of free acids after alkaline hydrolysis of the esters and then acidification of the liberated salts. Yields are generally >85%.

The general reaction,

$$R{-}O{-}M + R' - X \rightleftharpoons R{-}O{-}R' + MX \qquad (23)$$

where R is a substituted phenol[24,31-42,135-141] or phenoxyaryl moiety, R' is an alkyl group, X is a halogen (usually Br or Cl), and M is an alkali metal or base, has been much used industrially. When R is a substituted phenoxyacyl moiety,[124,142-154] the process generally requires a catalyst, e.g., *p*-toluene sulfonic acid, pentavalent As, or bases, and azeotropic distillation to obtain quantitative yields. The reaction is completely analogous to the esterification reaction considered in the previous section.

Another often-used route is the following.[30,147,165-170]

$$R{-}COOH \xrightarrow[\text{or } SOX_2]{POX_3} RCOX \xrightarrow[NaX]{R'ONa} R\,COOR' \qquad (24)$$

where R is a halophenoxy acyl moiety, X is a halogen, and R' is an alkyl group.

Usually, production of the acyl chloride RCOX is quantitative, but the yields of ester can vary anywhere between 50 to 100%, but mostly between 70 to 80%. The syntheses of O-phenoxyacetylketoximines[167,169] and oligonucleotide derivatives,[159] phenyl and thiophenyl esters,[156] by this method are noteworthy.

Another less-used route is to produce the esters by simultaneous chlorination and alcoholysis of either unchlorinated phenolates[47] or acid salts.[49,171,172]

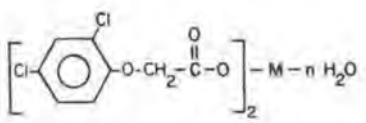
The references in Appendix 2, Chapter 1, also contain the synthetic method for the specific ester in many cases.

III. SALTS

A. Metal Salts and Organometallic Compounds

The syntheses of the alkali metal salts have already been treated indirectly in the preceding sections.[1,3-46,53-56]

Octahedral complexes with partial tetragonal distortion are formed[173] by Cu^{2+} and 2-, 3-, and 4-CPA anions in aqueous solutions. The complexes are generally $Cu(L)_2 \cdot 2H_2O$ where L is the halophenoxyacetate anion, but $Cu(L_2) \cdot 4H_2O$ and $(L{-}ClC_6H_4OCH_2CO_2)Cu$ are formed for the *ortho* compound. The structural assignment was derived from electronic and EPR spectra and the magnetic moments of the complexes. Ristici[174] showed that transition metal complexes with 2,4-D could be prepared from the sodium salt. These compounds were of the form:



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with M and n being, respectively, Cu, 4; Zn, 4; Cd, 2; Co, 6; Ni, 6; Mn, 2; and Fe, O. Thermogravimetric and activation energy of dehydration data were given also. Thus, the *ortho* chlorine in 2,4-D largely determines the geometry of the salts, since 2-CPA, but not the 3- or 4-, salts have the same structural formulae as the 2,4-D salts. Complex Ni salts of 2,4-D were also studied by Fisel and Giurgiu.[175]

2,4-D was found to form Th and Zr salts which precipitated out quantitatively at pH 2.5 to 3.5.[176] The reaction with thorium can be used as a specific quantitative test for that metal,[177-181] since the salt is soluble in aqueous ammonium carbonate solution (λ_{max} = 230 nm). However, iron, Ce (IV), and Zr interfere. The sensitivity is ~2 ppm. Hydrolysis slowly occurs and is complete after 3 days; the salt is unstable beyond 40°C. Faust and Aly prepared[182] the Mg and Ca salts of 2,4-D; the Nd^{3+}-2,4-D salt was made and studied by diffuse reflectance. Mercury salts were prepared[187] by reacting the sodium salt of 2,4-D with organomercury acetate. The stability constants of a number of 2,4-D metal salts were determined after their preparation.[184]

Interesting organometallic compounds include 1,3-bis(2,4-dichlorophenoxyacetoxy methyl) disiloxane produced[185] by refluxing 2,4-D,Et_3N, xylene, and $(ClCH_2Si)\cdot Me_2O$ for 18 hr. Triphenyl and tributyl-tin 2,4-D compounds were made by Eckstein and Ejmocki.[186]

B. Amine Salts

There is an enormous patent literature concerning these compounds. In general, stoichiometric quantities of amine and acid are reacted together in a compatible solvent and the salt precipitated.[188-220]

Procedure to Synthesize Amine Salts (Applicable for butyl to *n*-tetradecyl)[188]

Dissolve the calculated amounts of amine in benzene-acetone. Add the amine solution to the solid acid at 0°C. Shake the solutions until all the acid dissolves. Remove the solvent under pressure at room temperature. Recrystallize the salts from 1:1:1 ether-acetone-hexane until the melting points are constant. Note: Do not use alcohols as solvents, since a small (approximately 3 to 5%) amount of esterification results. Also, do not heat to reflux temperatures, since a small quantity of the corresponding amides may form.

If the two compounds are refluxed in a high-boiling solvent, contamination by the amide may become appreciable. This problem has been discussed in an earlier section concerning the melting point of the salts.

Skellysolve B, ethyl acetate, benzene, and toluene have been used in the syntheses of the *n*-dodecyl, octadecyl-, didodecyl, dioctadecyl-, and (octadecyl- and dioctadecyl) amine salts of 2,4-D, respectively.[189] The lower amine salts being water soluble can be prepared directly in aqueous solution. Often the sodium salt in alcohol is refluxed with the alkylamine or the alkylamine chloride, the solution cooled, filtered, and the solvent evaporated.[214] A variant of this method involves the prior reaction of the alkyl bromide with silver carbonate, the filtering of the solution (AgBr), the addition of acid, and the subsequent removal of the solvent.[215]

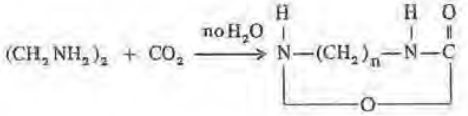
Other amine type salt compounds have also been made with cysteine[216] (using the methyl ester of 2,4-D as the substrate), N-methyl piperazine or N-phenyl piperazine,[217] theophylline or caffeine,[218] and ethanolamine salts.[219]

An interesting early paper on amine salt synthesis detailed how atmospheric CO_2 could interfere with amine salt formation.[220]

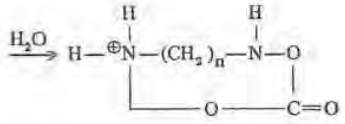
$$RNH_2 + CO_2 \xrightarrow{no\ H_2O} R{-}N{-}COO^{\ominus}\ H_3^{\oplus}N - R \qquad (25)$$

$$HO{-}(CH_2)_n{-}NH_2 + CO_2 \xrightarrow{no\ H_2O} HO{-}(CH_2)_n{-}\underset{\underset{H}{|}}{N}{-}COO^{\ominus}\ {}^{\oplus}NH_3{-}(CH_2)_n{-}OH \qquad (26)$$

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(27)

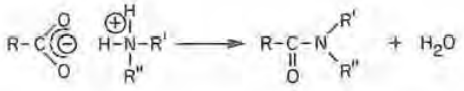


(28)

i.e., in aqueous solutions, carbonates may also be formed as well as the salt; for secondary amines, Equation 27 is favored; tertiary amines do not react with CO_2. Above 50°C, the CO_2 salts and carbonates dissociate back to the amine and CO_2.

IV. AMIDES

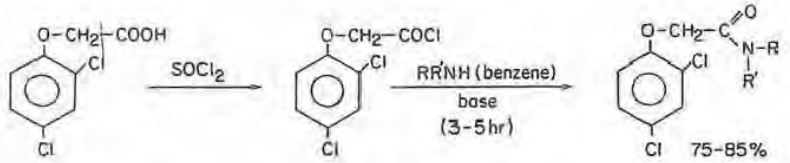
Heating an alkyl amine salt beyond 150°C and preferably at 190°C causes the corresponding amide to form by dehydration.[188,189] Tertiary amine-containing salts cannot form amides by this route. At 160°C, the yields of amides were 75 ± 3, 77 ± 4, 40 ± 2, and 46 ± 3%, together with dichlorophenol in 2% yield from the methyl, *n*-butyl, *n*-dodecyl, and dimethyl amine salts of 2,4-D, respectively, whereas at 190°C, the yields were 77 ± 4, 82 ± 4, 80 ± 3, and 82 ± 4%, respectively, in addition to 5% dichlorophenol. Amide was detectable by mass spectroscopy at 80 to 90°C. The activation energy was estimated to be 35 to 45 kcal/mol. The amides are not stable beyond 250°C.[222]



(29)

where R′ and R″ are H or alkyl.

Other workers have used Schotten-Baumann techniques[223,224] for synthesis.



(30)

where NaOH or pyridine can be the base.

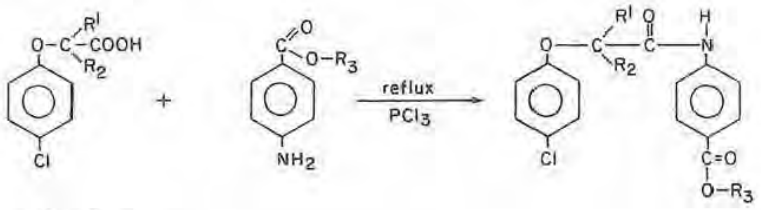
Especially noteworthy in this regard is the facile synthesis of many amino acid amides of 2,4-D and 2,4,5-T.[224-227,234] See Chapter 1, Appendix 5 for the melting points of these compounds.

Other methods involve the condensation of phenoxyacetic ester with an amine;[234,235,238] the condensation of a phenolate with an α-chloroamide[236] (71% yield); the treatment of acyl(aryloxyacetyl) isocyanates with aryl (alkyl) hydrazines;[237] and the reaction of an imine with the phenoxyacetyl chloride.[239] The latter reaction yields aryl-

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oxyacetylcyanamines as products. A similar synthesis allows the production of chloral 2,4-dichlorophenoxyacetylhydrazone[240] on admixture of the acid hydrazine and chloral hydrate.

Another interesting method is the condensation of a phenoxyacetic acid with an aniline in PCl_3 in a modified Schotten-Baumann reaction to produce the anilide (amide) in 72% yield.[241]



(31)

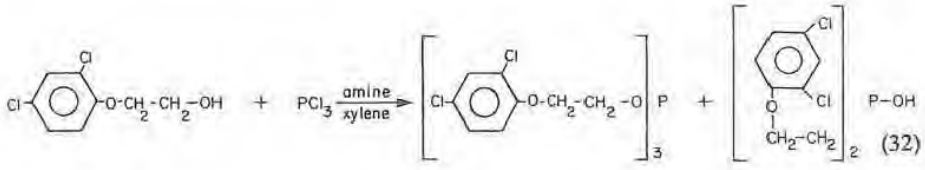
$R^1 = R^2 = H$

$R_3 = CH_2\,CH_2\,NEt_2$

V. MISCELLANEOUS COMPOUNDS

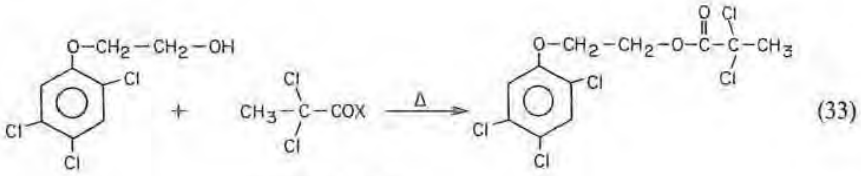
Halophenoxyalkyl esters of other acids are commercially less important herbicides, e.g. Erbon (Baron), DES (Sesone), DEP.

DEP is usually made by adding PCl_3 to 2,4-dichloroethylethanol in the presence of an amine in a kerosene or aromatic naphtha-type solvent;[242]



(32)

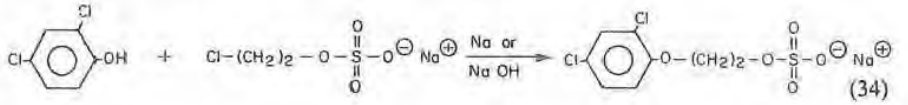
Erbon is prepared by the esterification of dalapon (2,2-dichloropropionic) acid with 2-(2,4,5-trichlorophenoxy) ethanol by the various procedures considered above to synthesize esters.[243,244]



(33)

X = −OH, −Cl, −OR

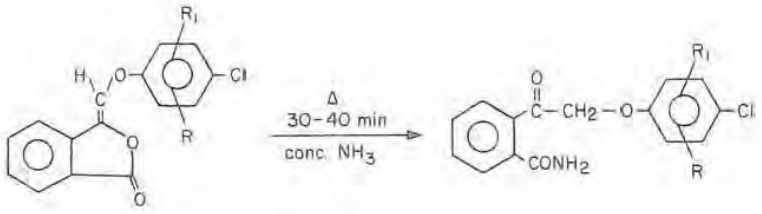
Sesone (DES) is no longer commercially important in Western countries, but it is still used in Eastern nations.[245]



(34)

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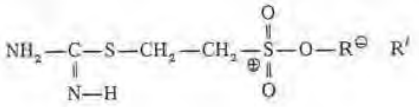
Other interesting derivatives have also been prepared:[246]



(35)

R = H, Cl; R_1 = H; 2–Cl; 2–, 3–Me

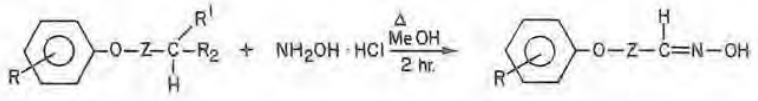
Aryl β-isothiuronium ethane sulfonate ester salts have been prepared.[247] Thus, in



(36)

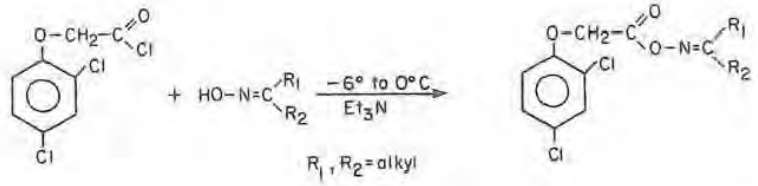
For R′ = 2,4-D, when R = 4-Cl phenyl, and 2,4-dichlorophenyl, the mps were 134.5 and 136.7°C, respectively. For R = 2,4-dichlorophenyl and R′ = HCl, the mp was 58 ± 1°C.

The aldoximes have also been synthesized.[247]



R = 2,4-diCl, 2,4,5-tri Cl, 2-Me-4-Cl, etc; R′=R_2=OMe; Z=CH_2 (37)

Another related synthetic route is the reaction of the acid chloride/hydroxylamines to produce herbicidal imino esters.[167]



R_1, R_2 = alkyl

(38)

Halophenoxyacetyl esters of various compounds have also been prepared, e.g., (1-[2,4-dichlorophenoxy] acetoxy methyl)-4-phospha-3,5,8-trioxiobicyclo [2,2,2] octane-4-sulfide,[248] the bis(2,4-dichlorophenoxyacetic ester) of 1,4-bis(1-hydroxycyclohexyl)-1,3-butadiyne, the bis(2,4-dichlorophenoxyacetic ester) of 3,8-dimethyl-deca-4,6-diyne-3,8-diol,[249] and also the 21-(2,4-dichlorophenoxyacetate of *l*-dehydrocortisone.[250]

Most of the above derivatives are herbicidal.

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VI. IMPURITIES IN REACTION PRODUCTS

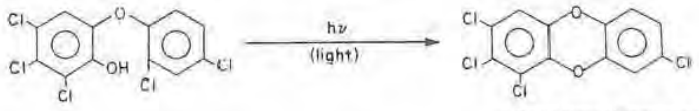
A given herbicidal product often contains traces of impurities characteristic of the synthetic route used.

Thus, for the Pokorny method, it is common to detect chlorophenols, chloroacetates, and base in the final acid product.[43]

Studies of the chlorination of phenol revealed not only the presence of chlorophenols, but also chlorinated 2-hydroxydiphenyl ethers (predioxins), chlorinated 4-hydroxydiphenyl ethers (isopredioxins), chlorinated dihydroxybiphenyls, chlorinated diphenyl ethers, and chlorinated dibenzofurans.[251] Chlorinated diphenyl ethers have been found in technical 2,4-D, e.g., bis-2,4-dichlorophenoxymethane, 2,2′,4,6′-tetrachlorodiphenoxymethane, and bis-2,4-dichlorophenoxymethane, the last three not being teratogenic to mammals.[252]

Similar impurities have been detected in 2,4,6-trichlorophenol, and these on heating or on exposure to UV light can form teratogenic dioxins.[253]

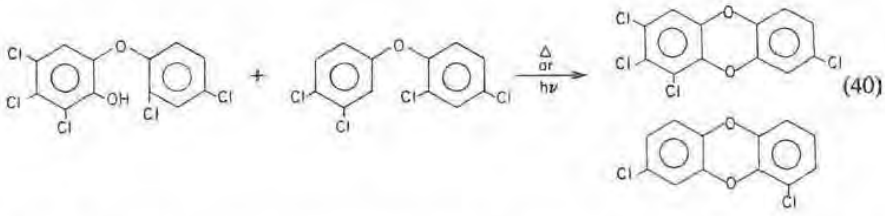
Thus,



(39)

+ 2-trichlorodibenzo-p-dioxins
+ one dichlorodibenzo-p-dioxin
+ one dichlorodibenzofuran

and



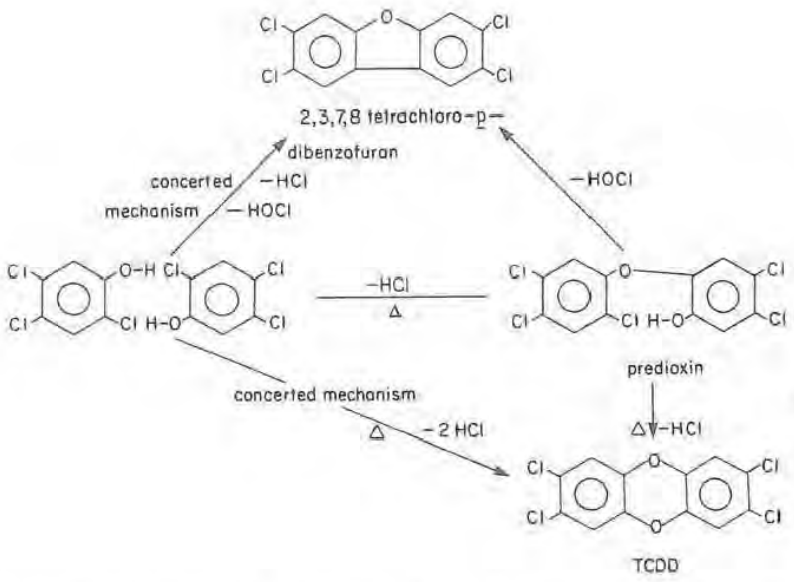
(40)

In the chlorination of 2-methyl-phenol by SO_2Cl_2 in the presence of $AlCl_3/Ph_2S$, 94% yield of the para derivative is obtained; there is also production of 6-chloro-2-methyl phenol (5%) and (4,6-dichloro-2-methyl) phenol (0.5%). The reaction transition state involves formation of Ph_2SCl_2 and $Ph_2S^+ ClAlCl_4^-$, the latter being the chlorinating agent.[254] The chlorination of 2-cresol with other agents usually produces only 65 to 70% of the desired product which is eventually fractionally distilled.

Although 2,4-dichlorophenol can be prepared from the high-pressure hydrolysis of the trichlorobenzene fraction from the synthesis of hexachlorobenzene, the yield is generally only ~20%.[18,43]

The major industrial route for production of 2,4,5-trichlorophenol begins with 1,2,4,5-tetrachlorobenzene which is hydrolyzed in basic media under pressure. The extremely teratogenic substance, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) is formed during this process along with tri-,[256] tetra-,[256] and pentachlorodioxins.[256,258]

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(41)

Discussion of the biological effects of the dioxins will be deferred until Volume II. Polychlorinated dibenzofurans may also be produced and may comprise up to 1% of technical chlorinated phenoxyacetic acid. Their level exceeds those of the dioxins, and values up to 100 to 1000 ppm have been reported.[251,259] These compounds may be almost as toxic as the dioxins. Agent Orange, one of the major defoliants used in the Vietnam War, has been shown to contain both dioxins and chlorinated dibenzofurans.[258]

Nucleophilic attack on the tetrachlorobenzene or an intermediate benzene by a hydroxyl ion yields the phenol, but an attack by the more powerful nucleophile, the 2,4,5-trichlorophenolate ion, yields a Cl_6-polychlorinated diphenyl ether, which on cyclization, can yield a Cl_6-polychlorinated dibenzofuran.[260] The ethers and the furans form at the beginning of the reaction before most of the tetrachlorobenzene reacts, whereas the dioxins are produced near the end of the reaction.[256,261] The reaction usually is operated at approximately 180°C and under 50 atmospheres pressure if the solvent is methanol. TCDD results mostly at temperatures from 230 to 260°C.[262] In many factories, ethylene glycol is used as solvent to avoid the high pressure, but this requires special precautions, since ethylene glycol polymerizes exothermically under basic conditions above 180°C, and TCDD is formed eventually.[262] Ethylene glycol adducts have also been found in technical trichlorophenol.[255,257] The Seveso explosion occurred at the point that the ethylene glycol had been distilled off with the alkaline solution at 170°C. Milnes[262] also attributed the accident at Bolsover, U.K. to the same set of exothermic reactions at this point. After some of the solvent has been distilled off, the reaction mixture is acidified and the phenols freed from TCDD by distillation with the result that TCDD is concentrated in the residues. Accidental poisoning using this concentrate occurred in horse areas in Missouri, U.S. in 1971.[263] The potential dioxins of MCPA and 2,4-D (e.g., the 2,6-dichlorodibenzo-*p*-dioxin), although present in some commercial preparations,[265,266] are much less toxic than TCDD,[264] chlorines in at least three of 2,3,7, and 8 positions being necessary for the highest teratogenicity to mammals. Dioxins and other polynuclear aromatics have been removed from the phenoxyalkanoic acids by various means, e.g., charcoal adsorption[267] and by liquid/liquid extraction.[268]

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Que Hee and Sutherland found that even "reagent-grade" 2- and 4-chlorophenoxyacetic acids contained from 1 to 5% 2,4-D as well as chlorophenols.[188] Ehrmantraut found 2,6-D to be a common impurity of 2,4-D.[279] A number of publications have dealt with the problem of removing phenolic impurities from the technical herbicidal acids.[270-273]

In addition to the type of acid, chlorophenols, and their by-products being present in technical ester products, most commercial alcohols contain many alcohols, so that butyl ester formulations contain *n*-, iso-, and *sec*-butyl esters of the various acids present and sometimes even higher or lower esters.[268] Often the crude esters are colored, but they can be bleached with 0.1 to 0.5% Cl_2 gas over the surface of the agitated ester.[274]

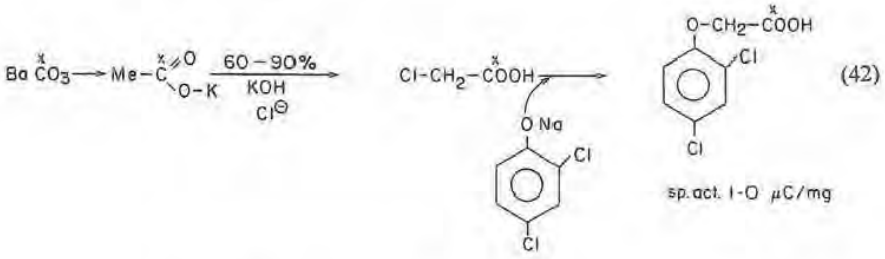
Phenolic impurities can be removed from the alkali salts by treatment with boiling chlorexperchlorethylene. The sodium salt of 2,4-D product then contains only 0.19% 2,4-dichlorophenol.[16] Another method involves treatment with HCl at 100°C.[278] A review also exists.[276]

Amine salts with heavy metal-containing adjuvants may become discolored and can be purified by reduction (e.g., with sodium dithionite), complexation of metals with EDTA, then treatment with Zn, and finally nitrilotriacetic acid.[277] Precipitation problems in some amine salts seem to be caused by impurities in the technical acids.[278] Generally, different amine salts are also present in formulations.

VII. RADIOLABELED MATERIALS

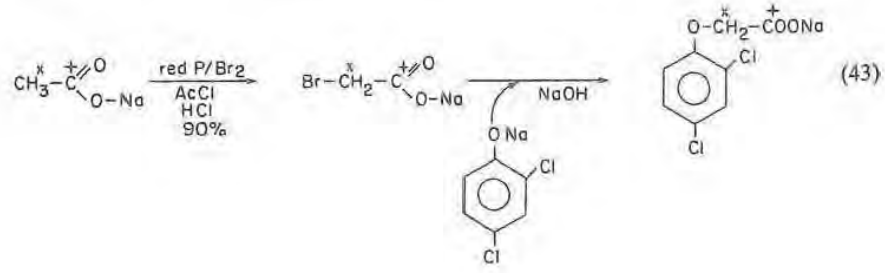
The synthesis of labeled phenoxyacetic acids was first reported in 1949[280-283] under the impetus of providing tagged material to investigate their distribution in living plants via the autoradiographic technique.

One method for C^{14} labeling was[280]



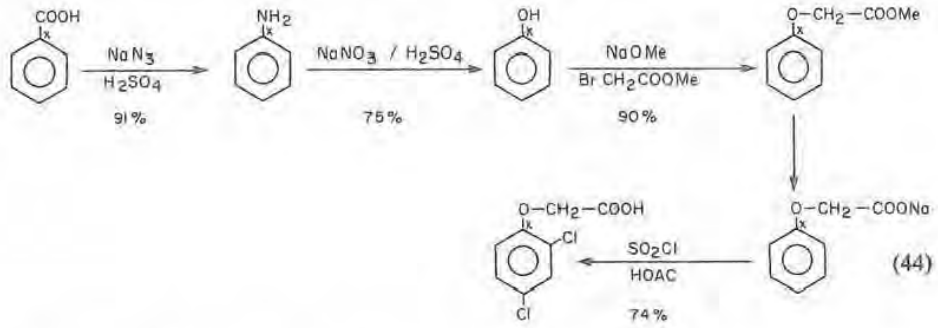
(42)

Fields et al. used the following routes:[281]



(43)

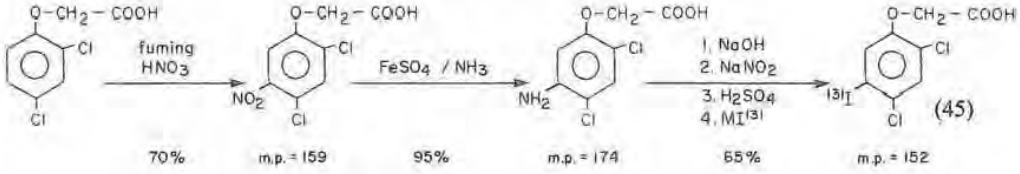
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(44)

Uniformly ring-labeled benzoic acid could be the starting point as well.

^{131}I-Labeled phenoxyacetic acids have also been made:[280,282,283]



(45)

Tritiated 2,4-D has also been prepared by exchange of the carboxyl H with the labile T in isopropanol.[284]

VIII. INDUSTRIAL MANUFACTURE AND USES

Many authors have elaborated on the industrial manufacturing of the herbicidal halophenoxyalkanoic acids.[285-290] Probably the most detailed are the books by Sittig[289] and the manual compiled under the auspices of the U.S. Environmental Protection Agency (EPA).[290] The relevant sections from Sittig's book are here reproduced with our grateful thanks (see Appendix 1).

The acids, esters, salts, or amides cannot be used directly without additives, since herbicides must be dispersed to be effective. The cheapest carrier is water, but the acids, esters, and most long-chain salts are not soluble in water. The water-soluble amine salts and alkali salts can be used directly, but they are not as effective as the other compounds, can be washed off the plant, and leached from soils after rain, as well as being precipitated in hard water.[43,189,190] Since the cheapest way to broadcast chemicals directly is to spray them in water from a nozzle, the specific gravity of the solution needs to be adjusted so that droplets of the correct diameter (>80 μm) impact on the target, and to allow as little spray or vapor drift as possible.[269] This is usually accomplished by using a fuel oil or kerosene component for the esters and an aromatic naphtha or kerosene for the free acids and long-chain amine salts; these gravity modifiers are called "the inert ingredients". The latter name can be quite misleading, as some "inert" ingredients have been shown to have auxin activity[291] and may also promote translocation and penetration of the herbicide.[292-295]

However, since the inert/active ingredient combination is water insoluble, a surfactant is required for use in water carriers. Surfactants can also be phytoactive and can modify the action of the herbicide.[296-298]

Sometimes, further adjuvants are added to optimize the desired properties of the emulsion concentrate. Thus, tributyl phosphate and ethylene glycol are often added

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to enhance water solubility and to stop freezing[299,300] (see Chapter 1, Section IV.B.2). Many reviewers have discussed the components of agricultural emulsion concentrates.[286,301-303,313,314]

For example,[190] for some long-chain amine salt formulations, xylene, fuel oils, kerosene, light summer oils, or heavy aromatic naphthas are used as the "inert ingredients", the surfactants can be alkyl aryl sulfonates, Agrimul 70A (a polyoxyethylene ether of alkylated phenol sold by Nopco Chemical Company), the Atlox® series of emulsifiers produced by the Atlas Chemical Company, e.g. Atlox G-1255 (polyoxyethylene sorbiol tall oil condensate) and Atlox 3300 (an alkyl sulfonate, reputedly), Atlox 3387 and 3396 (blends of nonionic and anionic surfactants), Atlas G-1086 (polyoxyethylene sorbitol hexyloleate) and G-8916-P (polyoxyethylene sorbitan ester of mixed fatty and resin acids), Ethomeen® T-12 and S-15 (supposedly ethylene oxide fatty amine condensates (Armour Chemical Company), and Toximul 102 (a blend of nonionic and anionic surfactants, Ninol Labs, Inc.).

Some short chain amine salt formulations contain 3,9-diethyltridecanol-6-sodium sulfate[304] or sulfonates[298] as surfactants and methyl cellulose as dispersing agent;[304] other amine salts are often used as cosurfactants,[308-311] along with cyclohexanone, xylene, and sorpol additives;[305] dimethylsulfoxide and EDTA have also been utilized.[191,306,307]

Ester formulations[305,312-314] usually contain a neutral or anionic surfactant or a blend (1 to 5%), along with the diesel or fuel oil inert components (5 to 10%). The alkyl or amine aryl sulfonates are probably the most popular surfactants along with the polyoxyethylene glycols (e.g., Tween 20 and Vonisol 100).

A convenient source of the chemical constituents used in pesticide surfactants is McCutcheon's detergents and emulsifiers.[315] The exact composition of the surfactant blend is considered a trade secret, so that complete analysis of formulations is made very difficult. Convenient U.S. suppliers of emulsifiers include GAF Corporation, Atlas Chemical Industries, Witco Chemical Corporation, Retzluff Chemical Company, Rohm and Haas Company, Amchem, Dupont, etc.

Invert emulsions, especially of the esters, are often used in agriculture. Such emulsions show non-Newtonian behavior, as a result of the inverted micellar liquid-crystalline structure; thus, the emulsions become quite viscous. Usually, 2 to 9% of emulsifier to <30% active ingredient is used so that water content is <70%.[313-317]

Granular solid formulations[313,318-320] have become popular especially for preemergence control. The herbicide is adsorbed on or impregnated into an inert carrier, e.g., clays, and these solid dry particles are then spread mechanically on or incorporated into the soil, where the active herbicide is released on hydrolysis. They are quite often used for aquatic weed control. For example, the 2,4-D Na salt 4.44, kaolin 0.15, Syntapon L surfactant 0.25, Versal scarlet dye 0.014, EtOH 0.001, and SiO_2 0.15 kg were homogenized in one powdered, dustless formulation.[319] Another granular formulation contained polystyrene 40, polyvinyl alcohol 60, and glycerine 15 to make 3-μm diameter pellets that were then impregnated with 20% sodium 2,4-D.[320] The major use of Sesone (2,4-DES-sodium) has been in this form, for, although Sesone solution itself is not herbicidal, the microorganisms in the soil appear to produce 2,4-D or 2-(2,4-dichlorophenoxy)ethanol so that deep roots are affected, while surface-growing plants, e.g., strawberries and nursery plantings of ornamentals, are left unscathed.[321]

The natural extension of the granular pesticides are the controlled-release pesticides[322-330] which have been developed to provide slow release of the herbicide to overcome the vapor drift problem and to enable the applied dose of active ingredient to be much lowered to prevent pollution and food chain concentration. Most of these formulations incorporate the active ingredient as a pendent side chain on a polymer. Esters of lignin and cellulose,[322,325] ethylene glycol copolymers[323,324] (often together

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with sodium pentachlorophenolate, copper 8-hydroxyquinoline and benzetorium chloride),[324] vinyl acetate polymers,[329] styrene,[330] polylactic acid,[326] or acrylate copolymers[328] have been utilized. Only ~50% of the 2,4-D is generally released in half a year. Herbicidal greases utilizing uni- and bivalent metal salts of 2,4-D, 2,4,5-T, and other phenoxys have also been used.[331]

The chlorinated phenoxyalkanoic compounds are best known as herbicides or defoliants in agriculture and for military purposes,[332] but there are other uses. For example, 2,4-D has been used as a photosensitizer for leuco bases of triphenylmethane in photographic development[333] and as a froth flotation collector.[334] The major nonherbicidal use of the phenoxy acids has been as a fire retardant for polyester fibers.[335-338] Certain tributyl tin salts have been applied in paint as bacteriocides and fungicides.[339] The papaverine salt of 4-CPA and the diisopropyl ammonium salt have been utilized as antihypotensives.[340] Chlorinated phenoxy derivatives have also been used as juvenile hormones.[341] The biological effects of various phenoxy compounds will be considered in detail in Volume II.

IX. GOVERNMENT REGULATIONS

In the U.S., the EPA is charged with the registration of pesticides and the establishment of a tolerance (legal residues of the parent compound and metabolites) in "raw agricultural crops". The legislation is known as FIFRA (Federal Insecticide, Fungicide, Rodenticide Act as amended[365] in 1978) and is meant to protect the general public from unreasonable hazard to man and the environment. The manufacturer or formulator is obligated to submit to the EPA data on efficacy, composition of matter, animal and wildlife toxicity (acute and chronic), environmental fate and mobility, and any other pertinent studies which might indicate a possible hazard to man and wildlife. The Administrator of EPA can authorize the suspension of a pesticide if it is shown that the chemical, even though it may be registered, has been demonstrated by new studies to cause an imminent hazard. An example of such an action was the suspension of 2,4,5-T and Silvex for all uses, except in rice paddies and for brush control, on February 28, 1979. At the time of this writing (Spring, 1981), there is a cancellation hearing to decide the fate of these two compounds as herbicides for use in the U.S. The Food and Drug Administration (FDA) monitors the food supply and confiscates raw agricultural crops that have residues of pesticides above tolerances. The National Institute of Occupational Safety and Health (NIOSH) is charged to ascertain if occupational exposures to pesticides meet the set time-weighted average (TWA) values; the Occupational Safety and Health Administration (OSHA) is empowered to regulate compliance. NIOSH operates under the aegis of the Department of Health and Human Services, and OSHA is under the Department of Labor.

In Great Britain, where specific regulations on the contamination of foodstuffs by pesticide residues are limited to two (for arsenic, ≥1 ppm, 1959, and for lead, ≥2 ppm, 1961), there is a voluntary scheme for the notification of new pesticides.[351] However, no new pesticide is put on the market unless it is safe and nonhazardous, to users, consumers, or wildlife. Largely as a result of deaths associated with the use of dinitrocresol, this voluntary notification scheme has been in operation since 1952. The Minister of Agriculture receives all toxicological data in confidence, and an advisory committee recommends to the Minister whether approval should be granted. The proposals become public only after agreement with the notifier. All particulars are then published in a dossier called "Chemical Compounds Used in Agriculture and Food Storage in Great Britain-User and Consumer Safety-Advice of Government Departments". If a compound suspected of being hazardous is marketed without notification, the Minister

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is empowered to ask the manufacturer to submit evidence of safety. If the substance is considered dangerously toxic, it can be classed as a scheduled poison under the Pharmacy and Poisons Act of 1933 and then becomes subject to Poisons Rules. It may also be subject to regulations prescribed under the Agriculture (Poisonous Substances) Act of 1952 which requires safety precautions. There is also a code of conduct for aerial spraying.

In Austria, the application of pesticides is regulated by federal law on plant protection (Pflanzenschutzgesetz). Pesticides are permitted to enter trade only by special permit of the Federal Ministry for Agriculture and Forestry, and this is granted only for products approved by the Federal Institute for Plant Protection in Vienna. Tolerances are based on those current in the U.S.[352] Similar types of approval systems also exist in Finland,[355] where pesticide regulation comes under the Poison Act (309/1969) and the Pesticide Act (327/1969); in Norway[358] (under the Act of Plant Protection Chemicals of 1963, pesticides must be registered every 5 years); in Egypt[359] reregistration every 5 years is also required.

In Sweden,[354] pesticide use and licensing is controlled by the National Poisons and Pesticides Board. In 1971, it banned all use of 2,4,5-T, but sanctioned foliage spraying in 1972 and only allowed the aerial spraying ban to be lifted in late 1975.

Canada[368] controls pesticides under the terms of the Food and Drug Act by the Canada Department of Agriculture and the Provincial Departments of Agriculture. The Canada Department of the Environment is empowered to monitor pesticides.

In New Zealand,[356] there are several legislative acts controlling pesticides, and their licensing largely involves nongovernment boards. The Agricultural Chemicals Board which registers and controls the use of pesticides used in plant protection reports to the Minister of Agriculture and Fisheries. The spraying of phenoxy herbicides is restricted within prescribed distances of vineyards.

In Argentina,[357] under Decree 3489 of March 24, 1958, any agricultural remedy must be classified according to its degree of toxicity, and Provision 174 of August 25, 1966 cites the rat acute oral LD_{50} (mg/kg) as the chief criterion. Thus, technical advisors of each firm have to file these data along with their registration or reregistration.

In Japan[353,367] there is no law concerned specifically with tolerance for pesticides, but these are controlled via a Food Sanitation Law which prohibits use and sale of hazardous foods and food additives. The tolerances are based on the lethal dose. There is no legislation against halophenoxyalkanoic acids, but a near relative, sodium pentachlorophenol, is classed as a "powerful agent".

The Eastern Bloc countries[360-362] also have a system of controls. The regulations pertaining to pesticide application are worked out by the Ministers of Agriculture in cooperation with the corresponding research institutes and are submitted to the Ministry of Public Works or similar bodies for implementation and control. LD_{50}, neurobehavioral responses, metabolite toxicity, the presence of cumulative effects, acute, subacute and chronic tests, teratology, mutagenicity, and analytical procedures are all researched before use.

Articles on government regulations in Portugal,[363] South Africa,[364] and Italy[366] can also be consulted.

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Appendix 1
COMMERCIAL MANUFACTURE OF VARIOUS HERBICIDAL PHENOXYALKANOIC ACIDS

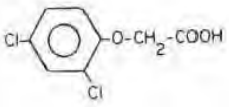
(M. Sittig, *Pesticides Process Encyclopedia*, Noyes Data Corp., Park Ridge, N.J., 1977.)

2,4-D

Function: Systemic herbicide[1,2,4]

Chemical Name: 2,4-Dichlorophenoxyacetic acid

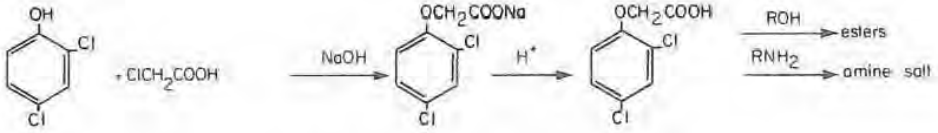
Formula:



Trade Names: Chloroxone®, Weedar®, Weedone®, Salvo®

Manufacture[3]

2,4-D is made by the following reactions and as shown in the flow diagram in Figure 1.



An improved process for 2,4-D manufacture is claimed by Manske.[5] His process is based on the discovery that phenol gives a better yield of phenoxyacetic acid than 2,4-dichlorophenol gives of 2,4-dichlorophenoxyacetic acid when they are reacted under comparable conditions with sodium hydroxide, and chloroacetic acid. For example, the yield of phenoxyacetic acid from sodium hydroxide, phenol, and chloroacetic acid under favorable conditions reached 94%.

Under similar conditions which were most favorable, the yield of 2,4-dichlorophenoxyacetic acid from 2,4-dichlorophenol, sodium hydroxide and chloroacetic acid was seldom more than 84%. Furthermore, the purity of the phenoxyacetic acid was slightly higher than that of the 2,4-dichlorophenoxyacetic acid.

The following is a specific example of the conduct of Manske's process. Phenoxyacetic acid having a melting point of 99°C was employed. Three hundred and four parts by weight of this material were heated to about 110°C in a vessel which itself was resistant to the corrosive action of chlorine and hydrogen chloride. A stream of chlorine was introduced into the molten phenoxyacetic acid. As chlorination proceeded, the 4-chlorophenoxyacetic acid which was formed tended to crystallize from the reaction mixture. The temperature was gradually raised to maintain the latter in solution so that by the time 2 atoms of chlorine had been introduced for every molecule of phenoxyacetic acid originally present, the temperature was approximately 150°C.

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PRODUCTION AND WASTE SCHEMATIC FOR 2,4-D (DOW CHEMICAL)

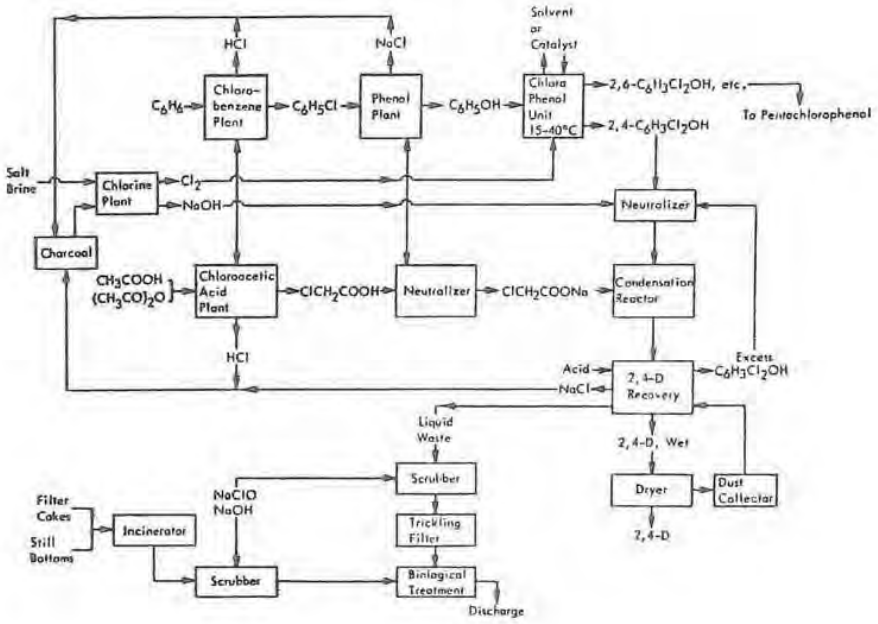


FIGURE 1. Production and waste schematic for 2,4-D (Dow Chemical).

The dissolved chlorine and hydrogen chloride were then removed by a stream of air and the liquid product was withdrawn and allowed to solidify by cooling to a pale yellow crystalline mass. The yield of crude 2,4-dichlorophenoxyacetic acid thus obtained was 442 parts by weight, that is 100%. It melted indefinitely at around 130°C. It was virtually free of chlorinated phenols. When it was recrystallized from benzene it melted at 137° to 138°C and the yield of once recrystallized product was about 375 parts by weight or 85% of theory. If desired, the 15% of impure 2,4-dichlorophenoxyacetic acid remaining in the mother liquor from the benzene recrystallization can be worked up to give more pure 2,4-dichlorophenoxyacetic acid.

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3. Midwest Research Institute, *The Pollution Potential in Pesticide Manufacturing*, Environmental Protection Agency, Washington, D.C., 1972.
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5. Manske, R. H. F., U.S. Patent 2,471,575, 1949; assigned to United States Rubber Company.

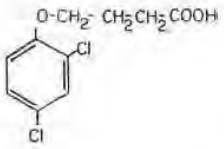
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2,4-DB

Function: Herbicide[1,2,4]

Chemical Name: 4-(2,4-Dichlorophenoxy)butanoic acid

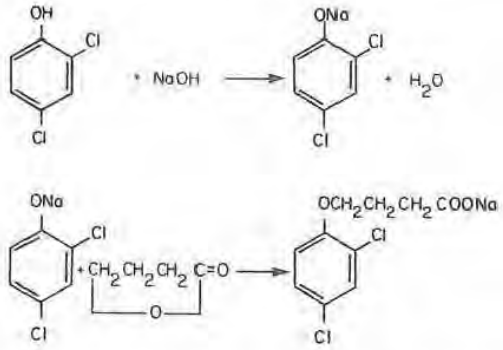
Formula:



Trade Names: MB2878 (May and Baker, Ltd.), Embutox (May and Baker, Ltd.), Butyrac®, Butoxone SB®

Manufacture[3]

The feed materials for 2,4-DB manufacture are 2,4-dichlorophenol and butyrolactone which react according to the following equations:



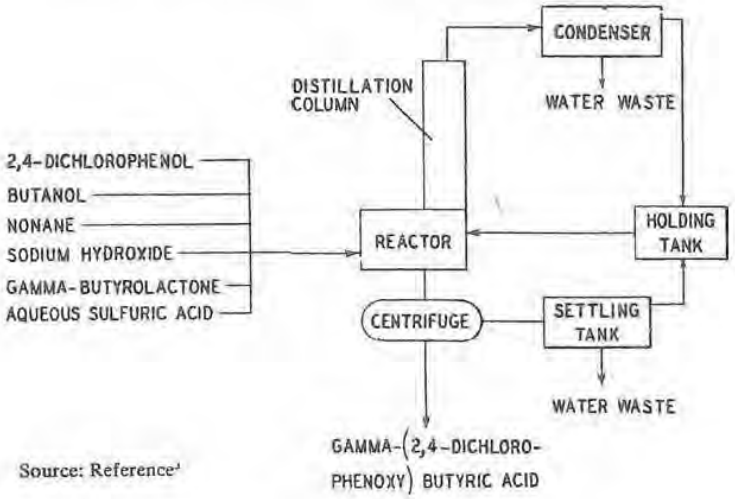
From 0.5 to 2.0 mols of sodium hydroxide per mol of phenol is the preferred feed ratio for the first reaction. In the second step, the lactone should be present in a mol ratio of from 0.5:1 to 2:1 based on the phenol. The conversion of phenol to alkali phenolate is carried out at a temperature of 50° to 200°C. The reaction of the phenolate with butyrolactone is carried out at 135° to 210°C and preferably at 160° to 165°C. The reaction of phenol with alkali is carried out at atmospheric pressure, as is the subsequent reaction of the phenolate with butyrolactone.

Reaction periods of from 0.5 to 24.0 hours may be used in the conversion of the phenol to the alkali phenolate. One hour was the period used in one typical example. The reaction of alkali phenoxide with butyrolactone may be conducted over a period of 1 to 24 hours. A more typical period is from 1 to 6 hours.

The conversion of phenol to phenoxide is preferably conducted in the presence of from 1.0 to 9.0 parts by weight, based on the phenol, of a solvent comprising an alcohol and a hydrocarbon. Suitable alcohols may contain 1 to 10 carbon atoms but butanol is the preferred alcohol; when it is used, higher product yields are obtained.

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PROCESS FLOW SCHEME FOR 2,4-DB MANUFACTURE



Source: Reference[1]

FIGURE 2. Process flow scheme for 2,4-DB manufacture.

Suitable hydrocarbons may contain from 5 to 14 carbon atoms and should preferably form a constant boiling mixture with the alcohol employed. A particularly desirable hydrocarbon solvent is commercial nonane (a C_7 to C_{10} fraction). Volume ratios of alcohol to hydrocarbon in the solvent mixture may vary from 1:2 to 1:1.

The second step is conducted in essentially the same liquid medium except that water formed in the first step should preferably be removed by distillation prior to the second step. No catalyst is employed in the conversion of phenol to alkali phenoxide, or in the subsequent reaction of the phenoxide with butyrolactone. An agitated reactor having a means for heating and cooling the reaction mixture and fitted with a distillation column is well suited to the conduct of both steps of this reaction. The scheme of operations is shown in Figure 2.

The initial alkoxide product from the first reaction step is not separated but is used directly in the second step reaction with butyrolactone. The alkali metal salt of the phenoxyalkanoic acid produced in the second step is neutralized with a mineral acid such as sulfuric, hydrochloric or phosphoric acid.

The final product can be recovered by centrifugation, filtration or other means for liquid-solid separation. The effluent from the solids-liquid separation may be introduced to a setting tank or other quiescent zone where two layers, a water layer and an organic layer separate out. The water layer, containing water-soluble salts such as Na_2SO_4 and the like formed by the reaction, is drawn off and discarded. The organic layer, containing substantially all of the unreacted phenol and lactone in addition to the alcohol hydrocarbon solvent, is recycled to the reactor.

If it is desired, traces of unreacted phenol remaining in the product may be removed by any of several well-known means such as by steam distillation or by solvent extraction with suitable solvents, such as petroleum, ether, hexane, heptane, or nonane. The final product may then be dried under reduced pressure. It can be further purified by slurrying in petroleum ether, diethyl ether, nonane, or other hydrocarbon solvent, centrifuging or filtering the resulting slurry, and drying the precipitate thus produced. Such purification is generally not necessary, however, since the product is substantially free of impurities.

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REFERENCES

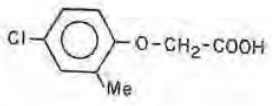
1. Martin, H. and Worthing, C. R., *Pesticide Manual*, 4th ed., British Crop Protection Council, 1974, 151. Photocopies available from Mr. A. W. Billitt, Clack's Farm, Blieley, Ombersley, Droitwich, Worcester, England.
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4. Wain, R. L., U.S. Patent 2,863,754, 1958; assigned to National Research Development Corp.

MCPA

Function: Herbicide[1,2]

Chemical Name: 4-Chloro-2-methylphenoxyacetic acid

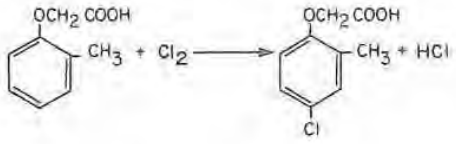
Formula:



Trade Names: Agroxone® (Plant Protection, Ltd.), Agritox® (May and Baker, Ltd.), Cornox M® (The Boots Co., Ltd.), Mephanac®, Methoxone®, Weedar®

Manufacture

The feed materials for MCPA manufacture may be methylphenoxyacetic acid (cresoxyacetic acid) and chlorine.[13] They react according to the equation:



The chlorination reaction may be carried out at temperatures ranging from 60° to 100°C. The reaction is exothermic and only when the chlorine concentration is low or when the reaction nears completion is it necessary to apply external heat. Atmospheric pressure is used and a typical reaction time is one hour. This reaction is carried out in the liquid phase in the presence of 1,2-dichloropropane as the solvent. The advantages obtained from such operation are substantial. Not only is any problem of equipment corrosion eliminated, but also the recovery of solvent is readily accomplished. Moreover, the 1,2-dichloropropane exhibits a singular combination of desirable properties not shared by other chlorinated aliphatic compounds. More particularly, 1,2-dichloropropane has a relatively low toxicity, which obviously is advantageous. In addition, it is not appreciably lost during the chlorination reaction, yet following the chlorination reaction it is readily removed from the reaction product.

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This process may be carried out in the absence of any catalyst or inhibitor, but the use of a small amount of iodine or ferric chloride may be desirable. Generally, iodine is the preferred solvent chlorination inhibitor because it is readily removed following the reaction. Also, it is easily inactivated with sodium thiosulfate in those cases where the filtrate is to be stored or where the solvent is to be distilled.

A chlorinator equipped with cooling means and a reflux condenser may be used for the conduct of this process. When the reaction is completed, the reaction mixture is cooled and the product precipitates out. It is recovered on a filter and washed with cold solvent and dried. Yields of 75 to 80% are obtained.

Alternatively, o-cresol may be chlorinated and the p-chlorocresol reacted with chloracetic acid to give MCPA.

REFERENCES

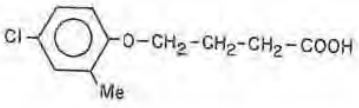
1. Martin, H. and Worthing, C. R., *Pesticide Manual*, 4th ed., British Crop Protection Council, 1974, 325. Photocopies available from Mr. A. W. Billitt, Clack's Farm, Blieley, Ombersley, Droitwich, Worcester, England.
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MCPB

Function: Herbicide[1-3]

Chemical Name: 4-(4-Chloro-2-methylphenoxy)butanoic acid

Formula:



Trade Names: MB 3046 (May and Baker, Ltd.), Tropotox® (May and Baker, Ltd.), Cantrol®, Thitrol®

Manufacture

MCPB can be made by the reaction of butyrolactone with sodium 4-chloro-o-cresylate. An alternative route is as follows:[4] 50 mℓ of absolute alcohol were placed in a 250 mℓ flask fitted with reflux condenser and calcium chloride guard tube and 1.2 grams sodium was added. When the reaction ceased, 7.1 grams of 2-methyl-4-chlorophenol, was added followed by 5.2 grams of γ-chlorobutyronitrile. After refluxing for 4 hours, 50 mℓ of 2 *N* sodium hydroxide solution were added and the mixture refluxed for 6 hours. The alcohol was then removed by distillation and the cold diluted solution was filtered into excess 4 *N* hydrochloric acid.

The buff colored precipitate (7.7 grams) was filtered, washed with water, dissolved in ether and the solution extracted three times with 5% sodium bicarbonate solution. The bulked aqueous layers were wormed to remove traces of ether, cooled and acidi-

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fied (Congo). The precipitate was filtered and dried. The dry product was crude γ-(2-methyl-4-chlorophenoxy)butyric acid in the form of a white powder, melting point 99° to 101°C. After recrystallization from petroleum ether, 4.5 grams of colorless needles (MP 100° to 101°C) were obtained.

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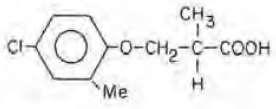
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MECOPROP

Function: Herbicide[1-4]

Chemical Name: 2-(4-Chloro-2-methylphenoxy)propanoic acid

Formula:



Trade Names: RD4593 (Boots Co., Ltd.), Iso-Cornox® (Boots Co., Ltd.), Mecopar®, Mecopex®, Mecoturf®, ViPex®, Compitox®, Clovotox®, Herrifex DS®

Manufacture

Mecoprop may be made by the condensation of 2-chloropropionic acid with 4-chloro-o-cresol.

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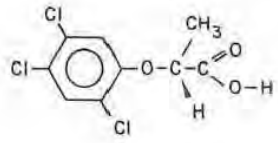
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SILVEX (U.S.A.)
FENOPROP (U.K.)
2,4,5-TP (France and U.S.S.R.)

Function: Herbicide[1-3]

Chemical Name: 2-(2,4,5-Trichlorophenoxy) propionic acid

Formula:



Trade Names: Kuron®(ester) (Dow), Kurosal® (K salt) (Dow), Aqua-Vex® (K salt), O-X-D®

Manufacture

Silvex may be made by the reaction of 2,4,5-trichlorophenol with sodium α-chloropropionate.

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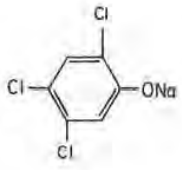
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SODIUM 2,4,5-TRICHLOROPHENATE

Function: Fungicide

Chemical Name: Sodium 2,4,5-trichlorophenate

Formula:



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Trade Names: Dowicide B®, Dowicide 25®

Manufacture[1]

The process comprises adding 2,4,5-trichlorophenol to an aqueous solution or suspension of an alkali metal hydroxide, maintaining the mixture at the proper reaction temperature for a suitable period of time, and cooling the reaction product whereby hydrated crystals of the phenolates are obtained.

In carrying out the foregoing method for the preparation of the various alkali metal trichlorophenolates, the compounds are obtained directly by crystalization in a hydrated form, generally the pentahydrate. However, upon exposure to the air at ordinary room temperatures the pentahydrate compounds lose about 4 molecules of water of crystallization. The resultant monohydrate may then be readily dehydrated to the anhydrous compounds, such as by heating them to a temperature between 40° and 60°C at atmospheric pressure, or by drying in vacuo over sulfuric acid or calcium chloride at room temperature.

The compounds are white, crystalline substances which do not melt, but decompose at varying temperatures upon heating; e.g., the sodium salt decomposes at 280°C. The compounds are partially decomposed in aqueous solution by carbon dioxide with the formation of the metal carbonates and trichlorophenol. The alkali metal phenolates are soluble in water, alcohol and acetone.

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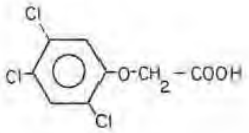
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2,4,5-T

Function: Herbicide[1,2]

Chemical Name: 2,4,5-Trichlorophenoxyacetic acid

Formula:



Trade Names: Weedone® 2,4,5-T (Amchem Products), Esteron®, Reddox®, Trinoxo®

Manufacture

The product 2,4,5-T is made by the reaction of 2,4,5-trichlorophenol with monochloroacetic acid according to the reaction:

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PROCESS FLOW DIAGRAM FOR THE MANUFACTURE OF 2,4,5-TRICHLOROPHENOXYACETIC ACID

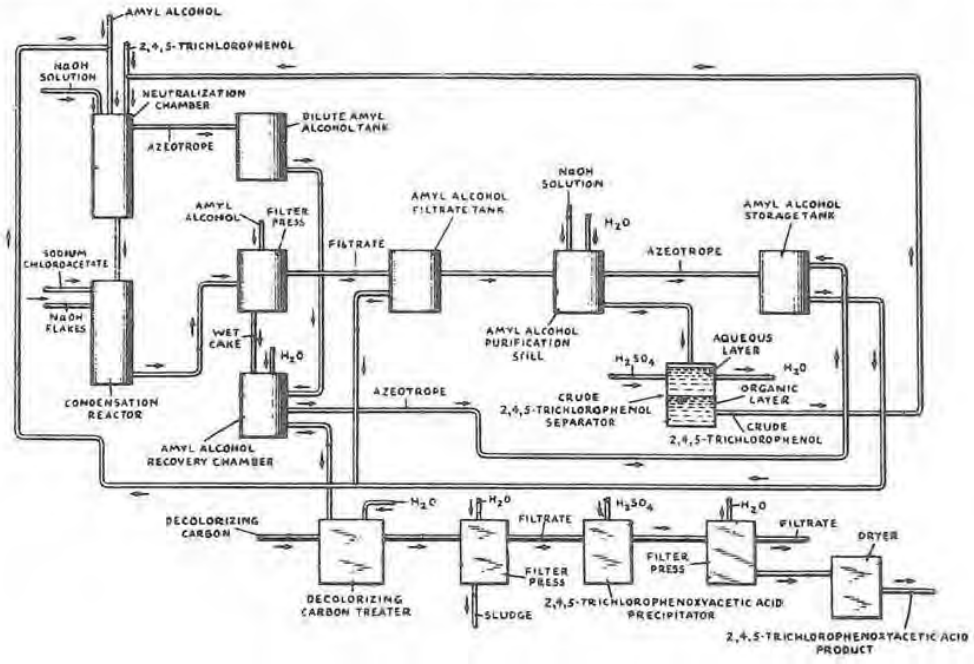
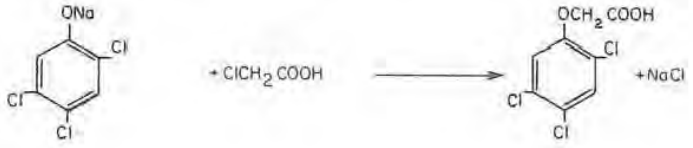


FIGURE 3. Process flow diagram for the manufacture of 2,4,5-trichlorophenoxyacetic acid.



The manufacture of 2,4,5-T is carried out at a temperature from 100° to 180°C depending on the reaction medium used and the pressure employed. It is preferred to use as high a temperature as possible in order to effect rapid reaction.

This reaction is carried out at essentially atmospheric pressure. Reaction periods of from 1.5 to 3.0 hours may be used in 2,4,5-T manufacture.

The reaction is preferably carried out in the presence of an inert organic liquid boiling above 100°C such as amyl alcohol. Lower boiling liquid media require pressure operation in order to attain economically desirable reaction temperatures and reaction rates.

The overall 2,4,5-T manufacturing process is shown in Figure 3.[4]

A production and waste schematic for 2,4,5-T manufacture is shown in Figure 4.[3]

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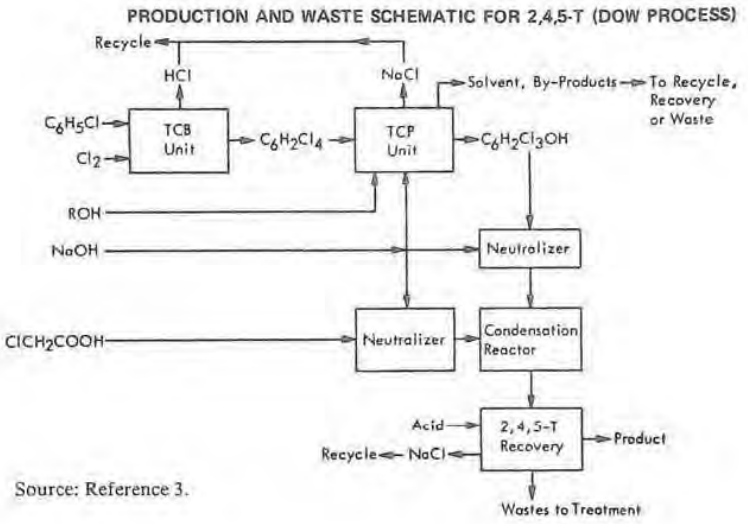


FIGURE 4. Production and waste schematic for 2,4,5-T (Dow Process).

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Appendix 2
YIELDS OF ESTERS PRODUCED IN 2,4-D/ALCOHOL/ACID SYSTEMS

Method	Conditions	Yield %	Ester	Ref.
2,4-D/alcohol	$EtOH/H_2SO_4$ (78°C; 3 hr), dipropylene glycol/*p*-toluene sulfonic acid/benzene	85 94	Ethyl dipropylene glycol	1
	Benzene/*p*-toluene sulfonic acid/xylene (120 to 300°C)	96	Phenyl	3
	2,4-D Na salt/*n*-BuOH/dichloroethane	97—98	*n*-Butyl	4
	$NaCl/H_2SO_4$, used benenesulfonic acid and $NaHSO_4$ catalysts	100		
	AcOn-Bu/*p*-toluene sulfonic acid/$MgSO_4/Na_2SO_4$ (reflux)	98.6	*n*-Butyl	5
	Mucochloric acid/toluene (15—25 hr)	75.3	Mucochloryl	6
	v-Chlorocrotyl alcohol/dichloroethane/*p*-toluene sulfonic acid (4—4 ½ hr)	84.1	v-Chlorocrotyl	7
	n-BuOH/C_6H_6/H_2SO_4 (69°C for 4 hr)	95	*n*-Butyl	8
	β-Dimethylaminoethanol/xylene	71.5	β-Dimethyl aminoethyl	9
	$EtOH/H_2SO_4$ also studied MCPA and phenoxy-acetic acid	66	Ethyl	10
	$MeOH/HC10_4$	78	Methyl	11
	MeOH/HCl or H_2SO_4	52	Methyl	12

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Chapter 3

CHEMISTRY

I. REACTIONS OF THE FREE ACIDS

A. Introduction

These acids contain both a carboxylic acid and a substituted aromatic ether moiety. Since there is a common α-C in the acetic acids, the latter are more reactive at this center than the longer-chain acids. As outlined in Chapter 1, progressive chlorination of the aromatic ring causes increasing acidity in the parent phenols which in the acids induces destabilization of the ether-o-methylene bond, especially when an *ortho* chlorine atom is present. The presence of a hydrogen on the common α-C, however, is essential for auxinic activity, even in the 4-chloro and unsubstituted phenoxyacetic acids, and this must be in the d configuration. Thus, the chlorinated 2-phenoxy-2-methylpropionic acids are antiauxins. Reactions at the α-C are therefore of considerable interest.

B. Thermodynamics

Van Klevelen and Chermin[1] considered the free energy of formation (ΔG_f) to be the sum of the free energies of the constituent functional groups in the molecule and that each contribution was a linear function of the temperature T. If we compare Equations 1 and 2,

$$\Delta G_{f\ group} = A + \frac{BT}{100} \tag{1}$$

$$\Delta G_f = \Delta H_f - T\Delta S_f \tag{2}$$

where ΔH_f and ΔS_f are the enthalpy and entropy of formation, respectively, then A and B/100 are analogous to ΔH_f and ΔS_f, respectively. For 2,4-D (see Table 1), the calculated ΔG_f is[2] −114.1 kcal/mol.

Water in equilibrium with the atmosphere has a dissolved oxygen content at pH 7 and 25°C corresponding to a partial pressure of 0.21 atmosphere, inducing a redox potential E_h of ∼800 mV and a pE of ∼13.75. Thermodynamically then, all organics ought to be decomposed to CO_2, HCO_3^-, and CO_3^{2-}, but as degradation is generally under kinetic control, various oxidation products of the original molecules will be actually present. Some $\Delta G°$ values for various model reactions with 2,4-D are in Table 2. Dissolved O_2 and alkaline permanganate give the most negative $-\Delta G°$ values. In reality, however, the sodium salt and the esters are resistant to oxidation by chlorine, chlorine dioxide, and potassium permanganate from pH 3 to 10 for contact times of 24 hr at 25°C.[2,3] At 100°C, oxidation by potassium permanganate was complete after 1 hr at pH 2.0 and was 23% complete after 1 hr at pH 3.1. No oxidation even at this temperature occurred at pH 5.0 and 7.4.

C. Typical Carboxylic Acid-Type Reactions

1. Salt Formation

$$RCOOH + M^{n+} \xrightarrow{MeOH/H_2O} (RCOO)_n - M + H^+ \tag{3}$$

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Table 1
CALCULATION OF FREE ENERGY OF FORMATION OF 2,4-DICHLOROPHENOXYACETIC ACID[2]

Groups present	A	B
$-\overset{O}{\overset{\|}{C}}-OH$	−94.755	+2.764
$-CH_2-$	− 5.283	+2.443
$-O-$	−49.178	+1.783
3 	3(+5.100)	3(+0.994)
3 	3(+3.100)	3(+0.610)
2 $-Cl$	2(−11.702)	2(−0.225)
1,2,4-Branching	+ 0.297	−0.070

$$\Delta G^{\circ}_{f_{2,4\text{-D}}} = \sum \text{Contributions of Composing Groups} + RT \ln \sigma$$

$$= \sum \left(A + \frac{B}{100} T \right)_{\text{group}} + RT \ln \sigma$$

At $T = 293$ K., $\sigma = 1$

$$\Delta G^{\circ}_{f_{2,4\text{-D}}} = -114.127 \text{ kCal Mol}^{-1}$$

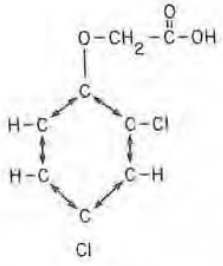


Table 2
REACTION MODELS FOR CHEMICAL OXIDATION OF 2,4-D[2]

Redox reaction model	ΔG° Reaction k/cal
$2C_8H_6O_3Cl_2 + 15O_2 = 16CO_2 + 4H^+ + 4Cl^- + 4H_2O$	−1600.78
$C_8H_6O_3Cl_2 + 15Cl_2 + 13H_2O = 8CO_2 + 32H^+ + 32Cl^-$	−915.33
$C_8H_6O_3Cl_2 + 11ClO^- + 10OH^- = 4C_2O_4^{-2} + 13Cl^- + 8H_2O$	− 910.69
$C_8H_6O_3Cl_2 + 6MnO_4^- + 16H^+ = 8CO_2 + 11H_2O + 6Mn^{2+} + 2Cl^-$	− 992.64
$3C_8H_6O_3Cl_2 + 22MnO_4^- + 8OH^- = 12C_2O_4^{2-} + 6Cl^- + 13H_2O + 22\,MnO_2$	−2504.38
$C_8H_6O_3Cl_2 + 6ClO_2 + H_2O = 8CO_2 + 8Cl^- + 8H^+$	− 936.66

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This reaction has been considered in Chapter 2, Section III.

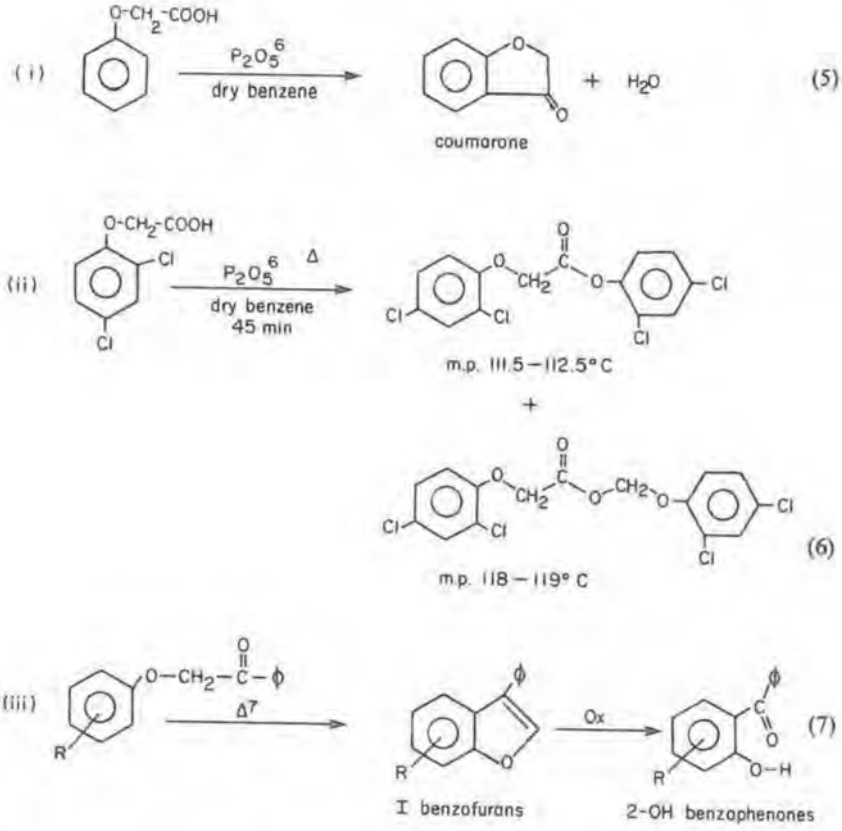
2. Condensation Reactions with Unlike Molecules

$$RCOOH + XZ \rightleftharpoons R - \overset{O}{\overset{\|}{C}} - Z + XOH \qquad (4)$$

Esterification (X = SH or OH; Z = alkyl, aryl) has been discussed in Chapter 2, Section II as have amidation (X = N–H; Z = $-C\begin{matrix}R_1\\R_2\end{matrix}$), where R_1 and R_2 are alkyl and/or aryl, (see Chapter 2, Section IV); acid halide formation (X = Br_2, Cl_2; Z = SO,PO (Chapter 2, Section II.B); ester hydrazone production (X = O–H, Z = $-N=C\begin{matrix}R_1\\R_2\end{matrix}$ Chapter 2, Section II.B); organo metallic production (e.g., X = $-CH_2-Si-(OMe)_2$; Z = Cl, Chapter 2, Section III.A). Additional condensation reactions are mixed anhydride production[4] (X = Cl; Z = $-O-\overset{O}{\overset{\|}{C}}-R_1$) and epoxide formation[5] (X = Cl; Z = $-CH_2-\underset{O}{\overset{H}{C}}-CH_2$).

3. Influence of Ring Substitution on Self-Condensation

Although many reactions of the chlorinated phenoxyalkanoic acids yield the same type of product, there are important differences. For example,

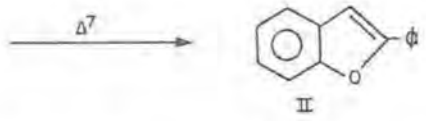


(5)

(6)

(7)

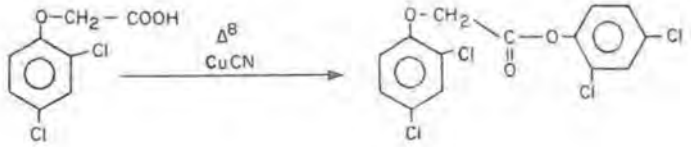
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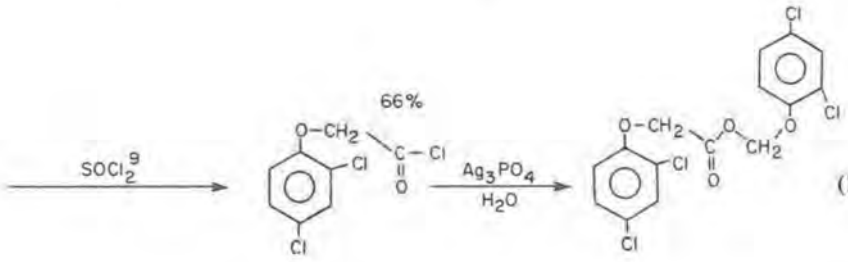
(8)

where R = 2-Cl, 2,3-diCl, 2,4-diCl produce I; R = 3-Cl, 4-Cl, 3,4-diCl produce ii; R = 2,5-diCl, 3,5-diCl produce I and II;[7] and R = H, alkyl produce the monosubstituted phenol, aldehyde, and carboxylic acid.[12]

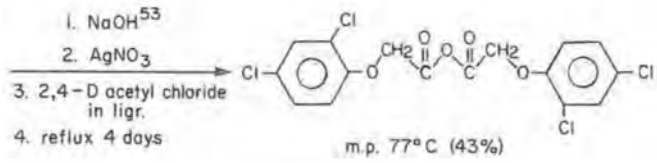
There is specific reagent control over the self-condensation product. Thus,



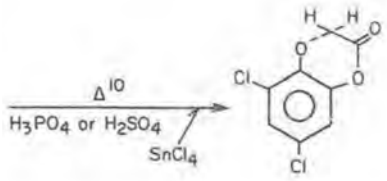
(9)



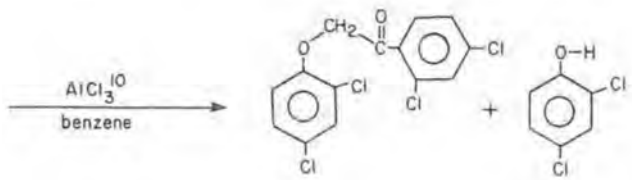
(10)



(11)

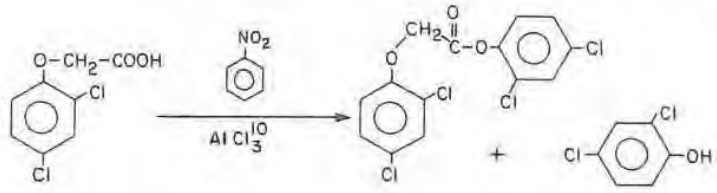


(12)

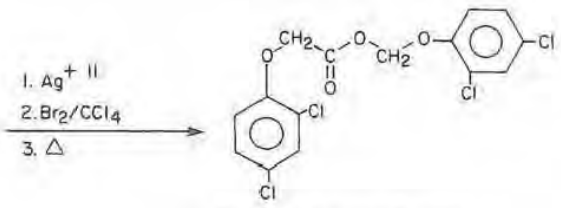


(13)

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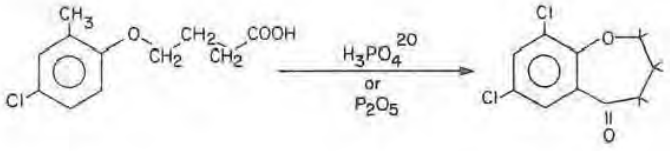


(14)

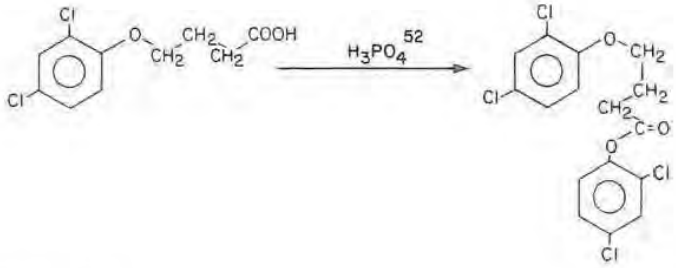


(15)

Birnbaum Simonini Reaction



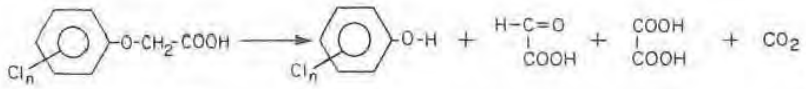
(16)



(17)

4. Ether Link Cleavage

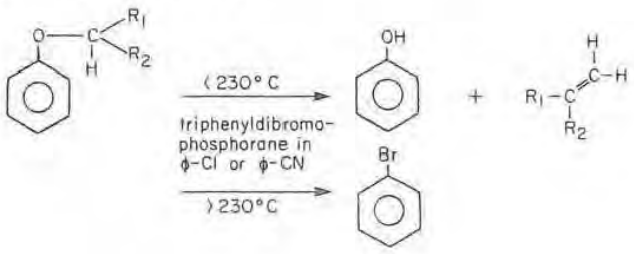
A variety of agents will cleave the ether link:



(18)

These include HCl/pyridine,[13] UV light under basic conditions,[14,15] chromotropic acid,[16] H_3PO_4/KI or P/acetic anhydride,[7] and $POCl_3$/pyridine.[18]

For higher phenoxyalkanoic acids,[19]



(19)

(20)

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Table 3
SECOND-ORDER HYDROLYSIS CONSTANTS FOR VARIOUS SUBSTITUTED PHENOXYACETIC ACIDS IN THE PRESENCE OF HCl/PYRIDINE[21] AT 100 AND 115°C

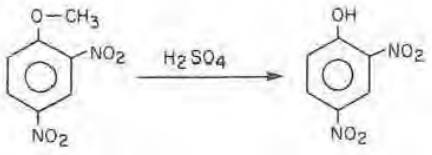
Substituent	10^6k (100°C) (1/sec)	10^6k (115°C) (1/sec)
H	2.23	10.9
2-F	2.23	9.14
4-F	2.36	10.9
2,4-DiF	2.42	10.1
2.Cl	2.01	8.90
4-Cl	1.74	7.61
2,4-DiCl	1.61	6.68

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Only the HCl/pyridine cleavage reaction has been subjected to kinetic scrutiny.[21] Here (see Table 3), the type of ring substitution does not affect rates very much, and in addition, the same hydrolysis rates at 115°C were obtained also for hydrolysis of chloro- and bromo-anisole with aqueous HCl at 120°C in acetic acid.[22] Furthermore, ether cleavage has been observed in HCl, HBr, or HI on prolonged reflux.[20] In fact, the HI reaction is rapid, and that with HCl is much slower.

A cleavage effect of H_2SO_4 has not been reported, but it should be noted that:

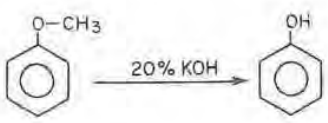
$$k = 32.1 \times 10^{-3} \quad 1/\text{min}\ (85°C)$$
$$k = 38.7 \times 10^{-3} \quad 1/\text{min}\ (25\text{-}6°C) \qquad (21)$$



Via $R{-}O{-}\phi + H_2SO_4 \rightleftharpoons RHSO_4 + \phi - OH$ directly, or by an A_1 mechanism ($\Delta S^* \pm \sim O \pm 0.10$ cal/deg).[23]

Ether cleavage in >80% H_2SO_4 and $HClO_4$ is possible also by the A_2 mechanism ($\Delta S^* \sim -15$ to -30 cal/deg) and is first order with respect to the ether.[23]

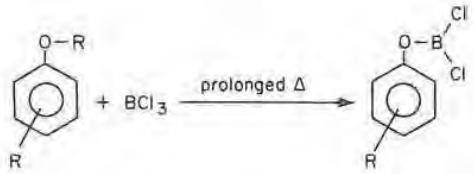
Base catalyzed ether cleavage is difficult to achieve, e.g.,



(22)

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Phenol (15%) was produced after 15 hr at 180 to 200°C, and 0.7% was produced after 7 hr at room temperature. In spite of this, the presence of electron-withdrawing groups, e.g., NO_2, halogens, on the ring enhances reactivity.[23,24] An interesting cleavage agent is BCl_3.[25]

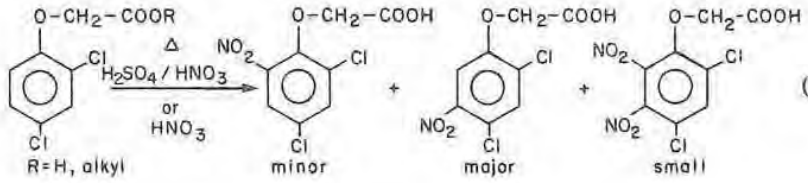


(23)

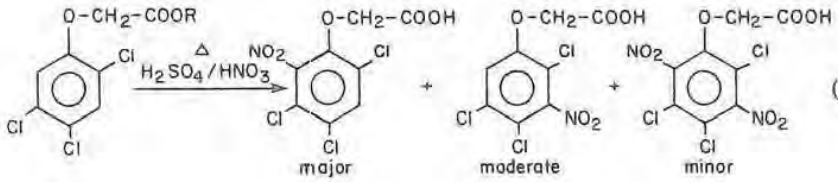
Since alcohol/BCl_3 solution is a well-known reagent for esterification (see Chapter 2, Section II.A), then longer reaction times than recommended should be avoided, since they may induce cleavage. The effects of other ether bond cleavage agents as *n*-butyl lithium,[26] $LiAlH_4$,[27] and alkali metals[28] or alkali metal/ammonia solutions[29] have not been reported for the halogenated phenoxyalkanoic acids, but enzymic cleavage at this bond has also been reported.[67]

5. Substitution at the Aromatic Ring

Nitration products depend on the acid involved:[30]

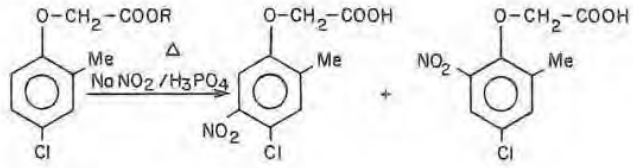


(24)



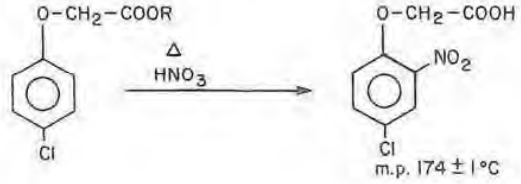
(25)

and[31]



(26)

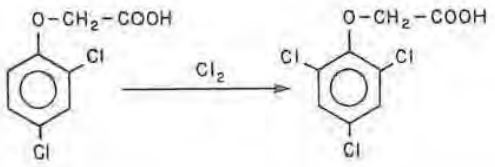
and[184]



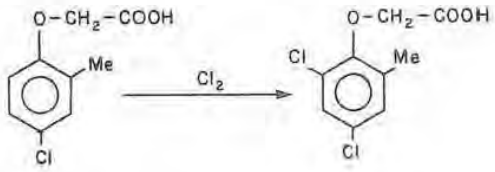
(27)

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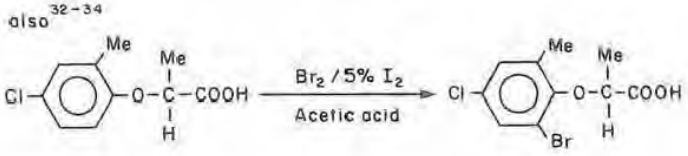
Halogenation is also facile.[20]



(28)



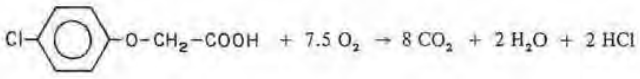
(29)



(30)

6. Side Chain Oxidation

Oxidation by chlorine, chlorine dioxide, and potassium permanganate are quite ineffective.[2] Hemmett and Faust decided that dissolved oxygen in water eventually would completely oxidize 4-CPA via zero-order kinetics.[35]

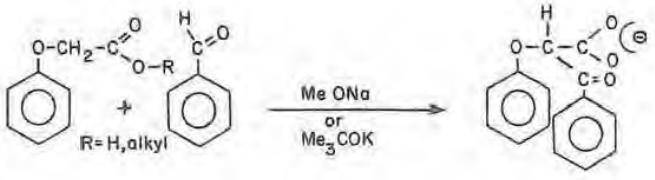


(31)

2,4-D has been oxidized to the methyl ether and phenol via a peroxide intermediate by H_2O_2[36]; degradation was slower with the more halogenated derivatives. In the additional presence of Fe(II), halogenated phenoxyacetic acids produced CO_2, CH_2O, phenols, and 1,2-diphenoxyethanes;[54] a 15-fold excess of ozone also degrades 60% of 2,4-D at a concentration of 20 mg/mℓ.[37]

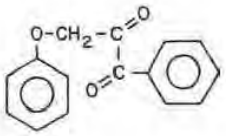
7. Reactions at the α-Carbon

Most of these reactions occur in alkaline solution via a carbanion intermediate. Thus,[38]



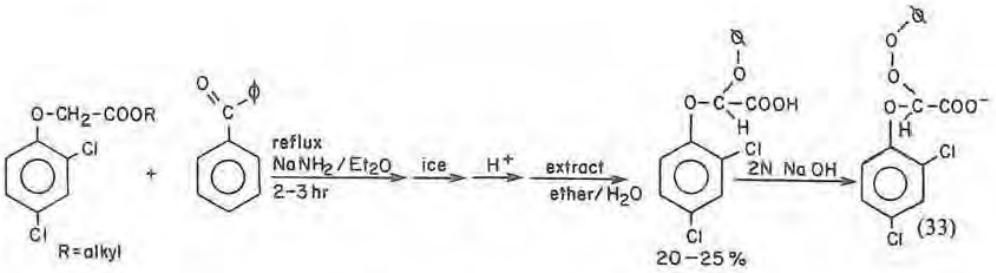
(32)

with Me_3COK



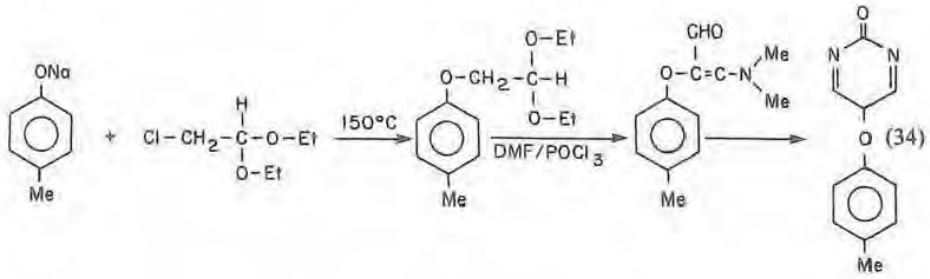
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Also,



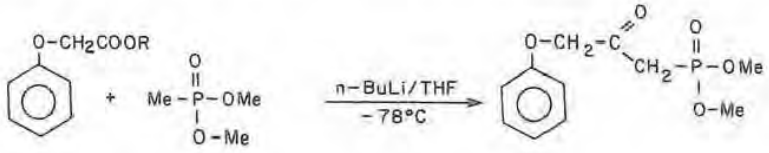
(33)

An extremely interesting reaction involves an acid acetal,[40]



(34)

A similar reaction type involves the α-C of a phosphate ester.[41]



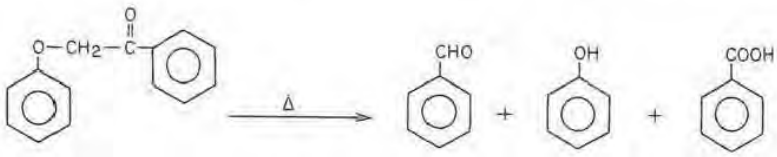
(35)

R = H, alkyl.

8. Pyrolysis

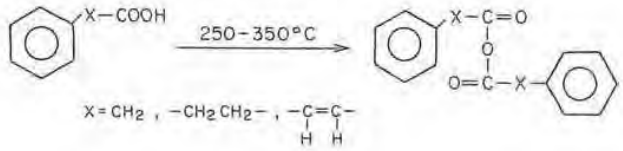
It is interesting to note the pyrolysis products of compounds similar to the halogenated phenoxyalkanoic acids.

Thus, for aryloxyacetophenones,[42]



(36)

For cinnamic, β-phenoxypropionic, and phenylacetic acid,[43]

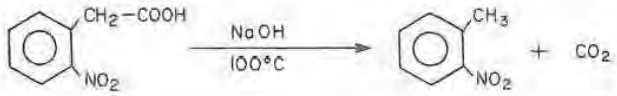


(37)

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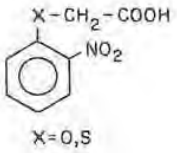
Beyond 350°C, most carboxylic acids decarboxylate with oxidation products having fewer than the original number of carbons,[44] i.e., $RCOOH \xrightarrow{>350°C} RH + CO_2 +$ oxidation products.

The 2-nitrophenylacetic acid decarboxylates in the presence of alkali at 100°C.[45]



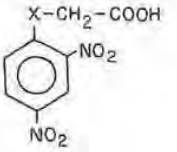
(38)

The 2- and 2,4-dinitrophenoxy or thioxy acetic acids also decompose.[46]



2H-1,4-benzoxazin-3 (4H)-one	(25%)	(39)
2-OH formanilide	(20%)	
Bibenzoxazole	(5%)	
Benzoxazolone	(5%)	
2-Nitrophenol	(3%)	

with X = S, get S analogues.



4-Nitro phenoxyacetic acid	(22%)	
2-Methyl-5-nitro-benzoxazole	(12%)	
Acetaldehyde	(5%)	
5-Nitro benzoxalone	(3%)	(40)

with X = S, get S analogues.

The reaction is postulated to involve intranuclear attack.

One of the early reports on 2,4,5-T pyrolysis alleged it was degraded at high temperatures, but the products were not investigated.[47] With the furor over the presence of dioxins in 2,4,5-T, the pyrolysis of the latter was studied by a number of groups with conflicting conclusions. Free 2,4,5-T, its sodium salt, and its butyl ester were shown by Buu Hoi et al.[48] to produce approximately 5% TCDD near 500 to 600°C, but this work has been questioned, since the mass spectrum reported for TCDD was not consistent with other mass spectra of TCDD. Langer et al. reported that in controlled heating experiments, only 0.13% of 2,4,5-T as the potassium salt was converted to TCDD upon heating to 400°C for up to 43 hr.[49] Stehl and Lamparski[50] combusted sodium 2,4,5-T, 2,4,5-T, and *n*-butyl 2,4,5-T impregnated on filter paper at 600 to 800°C and found dioxin levels to be only ~1 to 5×10^{-5}% (by weight). In addition, these same levels were found also for combusted phenols and phenolates. However, the latter study did not take into account the amount of 2,4,5-T or TCDD volatilized after spraying onto grass, and in these particular experiments, they should have compared the TCDD recovered with the amount of 2,4,5-T recovered before combustion. Nevertheless, the in vitro tests do indicate that TCDD production from 2,4,5-T is minor indeed. Furthermore, the 2-butoxyethanol ester of 2,4,5-T also formed <0.005% of dioxins of polychlorinated dibenzofurans.[51] The incineration of pesticides as a whole has been investigated,[55] and in general, sodium biphenyl is the best combustion promoter.

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The most widely used way of disposing of pesticides is to bury them in a sandy soil at a depth of 18 in. in a private disposal site or in a sanitary landfill type of dump, potentially hazardous procedures. Incineration poses some problems. Open-air incineration is impractical, since most of the pesticide is lost by sublimation rather than by oxidation. A differential thermal analysis study of the iso-octyl ester of 2,4-D for both standards and commercial formulations revealed[56] common endothermal peaks at 300 to 310 and 154 and 165°C. Common exothermic peaks were seen at 541 to 550°C. For 2,4,5-T free acid, the standard showed endothermal peaks at 168, 309, and 504°C, but the commercial formulation showed just one peak at 687°C. However, exothermic peaks were noted for the latter at 307, 380, 496, and 683°C, compared with 596 and 675°C for the pure acid. It was concluded that temperatures of ~1000°C were in general necessary to degrade 99% or more of most pesticides. When 50 to 100 mg of 2,4-D isooctyl ester and 2,4,5-T free acid were burned at 900°C for 15 min in a resistance-type furnace in a stream of pure oxygen, 96.0 and 99.5% of the respective compounds were degraded to CO_2 and H_2O. The above 2,4-D and 2,4,5-T formulations were also subjected to muffle furnace combustion, and all were quantitatively degraded above 600°C. Pure 2,4,5-T samples heated in a muffle furnace for 30 min decomposed 27.4, 63.6, 99.7, and 99.6% at temperatures of 200, 250, 300, 400, and 500°C, respectively. Hydrogen peroxide, nitric acid, sulfuric acid, sodium hydroxide, and ammonium hydroxide were ineffective in degrading the molecules completely.

In the light of the foregoing, it can be understood why a permit was issued by the Environmental Protection Agency (EPA) of the U.S. in 1977 to allow sea incineration of 800,000 tons of Agent Orange.[57] Analyses of these mixtures have been published.[58,59] Dioxins are totally destroyed above 800°C, forming HCl, H_2O, and CO_2.[59] Another mode of disposal involves exhaustive chlorination in a nickel bomb at 500°C at 90 bars pressure.[61] The observed products were

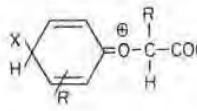
$$\text{"Agent Orange"} + 6.413\ Cl_2 \rightarrow 4.916\ CCl_4 + 1.682\ HCl + 0.758\ COCl_2 + 0.056\ CO_2 \qquad (41)$$

Reaction startup is difficult as is maintenance of the reaction temperature. The Diamond Shamrock Company used a similar process at 600 to 850°C/13.5 to 27 bar in a quartz-lined nickel-clad carbon steel reactor. Diluent CCl_4 improved the performance of the latter.

9. Photodecomposition

The usual electronic transitions[62] for aliphatic acids are at 210 nm ($\pi^* \leftarrow n$) and 160 nm ($\pi^* \leftarrow \pi$); for aromatic acids in nonpolar solvents, they are 280 nm ($\phi, \pi^* \leftarrow \pi$;), 230 ($\pi^* \leftarrow n$), and 200 ($\pi^* \leftarrow \pi$). Alcohols usually red shift these values.

The excited states have been described by the so-called molecules in molecules approach of the separation of the molecule into electron donors and acceptors.[63] In this model, it is assumed there is configurational interaction between the ground (G), locally excited −C=O (LE) and charge transfer (CT) configurations, thus assigning different populations of the electrons in the three bonding and antibonding orbitals of the −O−H and −C=O groups for each of these states. Solvent effects have also been considered in the model.[64] Even for benzoic acids, the lowest transition is of charge transfer type.[65] In analogy to the phenylpropionic and cinnamic acids,[66] the resonance form



(X = halogen, alkyl; R = H, alkyl, halogen)

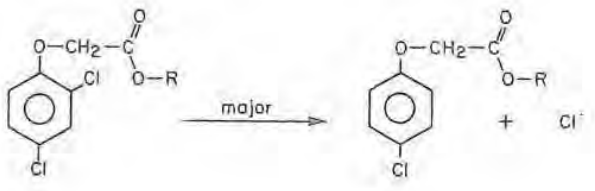
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implies much charge transfer character in the ground state. In *ortho*-substituted phenetoles,[68] the highest occupied molecular orbital (HOMO) of the ground state is a π orbital, with the largest contribution being from the ether oxygen p_x orbital (34%), but being antibonding with respect to ring carbon. The second highest HOMO is a σ orbital, with 30% of the electron density on oxygen. As discussed in Chapter 1, Section V.D.1 and E.1, the carboxyl group appears to perturb this energy arrangement both in the +1 ion (mass spectrometry) and in the excited state. Another way of looking at the situation is via the "β phenyl effect" on the carboxyl group by the benzene ring[69,70] which appears to retard the photodecomposition rate. Fluorescence data[71] indicates that since 2,4-dichloroanisole is much more fluorescent than 2,4-D or 2,4,5-T, the carboxyl group must be responsible for the drastic decrease. These physical processes for 2,4-D are concentration dependent, since in dilute acid primary or secondary alcohol solutions $<2 \times 10^{-5}$M, the λ_{max} fluorescence is ~350 nm, coinciding with that for 2,4-dichloroanisole. However, beyond this critical concentration, the λ_{max} fluorescence is wavelength dependent, centering around 425 nm for excitation wavelengths >300 nm. This has been assigned to the fluorescence of the excimer or an exciplex. The phosphorescence λ_{max} ~500 nm can be compared with the 550-nm emission from 2,4-dichloroanisole. Thus, the monomer has a S_1 level of 81.5 kcal/mol; and the excimer has a S_1 of 69.0 kcal/mol; the T_1 level of both appears to be around 57 kcal/mol.

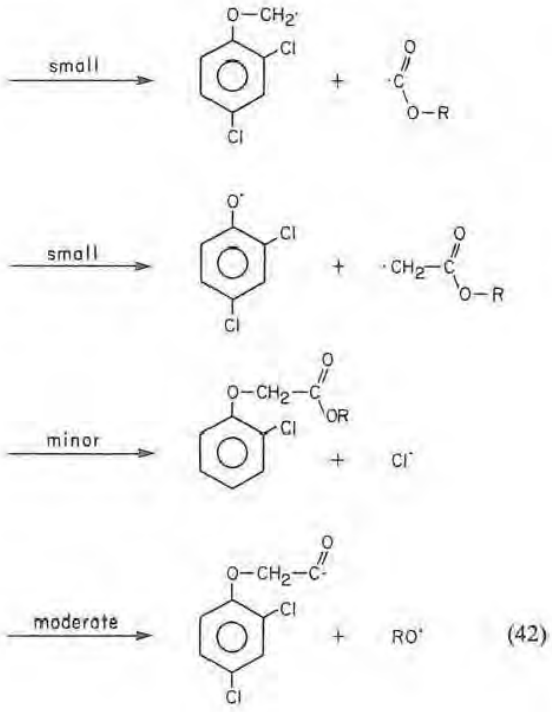
Above concentrations of 2×10^{-5} *M* 2,4-D in primary or secondary alcohols at wavelengths >300 nm, but < 420 nm, esterification occurs, increasing directly with concentration at 27°C. Below 2×10^{-5} *M*, negligible esterification is observed. Since negligible esterification occurs in *t*-butanol independent of concentration, the esterification has the usual $A_{AC}2$ steric requirements. Ethylene glycol on irradiation produces only monoesters in moderate yield (~50%). All kinetics were first order. Experiments with quenchers and consideration of the physical photoprocesses above imply the type of singlet state is important.

At or below 300 nm at 27°C, reductive dechlorination (see Tables 4 and 5) occurs preferentially in all alcohols and in saturated benzene solutions. For the latter, phenylation also occurs at the *ortho* position, and in primary and secondary alcohols esters are also present as photolysis products, depending on the concentration. Only small amounts (<5%) of chlorophenols are produced, and there is no humic acid polymer. Thus, in 30 mℓ of *t*-butanol, 2 g of 2,4-D produced 4-CPA (20%), 2,4-dichloroanisole (2%), and 4-chlorophenol (3%) after irradiation at 254 nm and 27°C for 12 hr, but produced no esters, apart from that present in the dark control. Irradiation of saturated benzene solutions under the same conditions for 24 hr produced phenoxyacetic acid (1%), 4-CPA (9%),2-chlorophenoxyacetic acid (1%), 2,4-dichloroanisole (9%), 2,4-dichlorophenol (3%), 2-phenyl-4-chlorophenol (3%), 2-phenyl-4-chlorophenoxyacetic acid (13%), unchanged 2,4-D (57%), and a polymer, probably from benzene. The dechlorination has been proposed to proceed by the singlet state.[71-74] It might be noted that adsorption in the solid phase will red shift the UV spectrum, thus making photodecomposition more likely. This has been observed in TLC work[75] and in paper chromatography.[76]

The primary processes ≤300 nm are



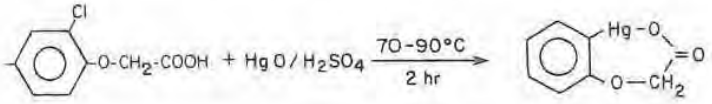
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(42)

10. Miscellaneous Reactions

A unique reaction occurs between 2-CPA and HgO/H_2SO_4.[77]



(43)

2,4-D was shown to have one active hydrogen by exchange with tritiated isopropanol.[78]

Chlorinated phenoxyacetohydrazides have been utilized in the synthesis of five-membered heterocycles.[79]

Chlorinated phenoxyacetic acid anhydrides substituted with an anilido group at the α-methylene carbon are good synthons in heterocycle syntheses because of their facility to form chlorinated phenols[80] via opening of the anhydride ring.

2,4-D in ether was acetylated easily with ketene.[81] Mixed anhydrides and simple anhydrides can be produced.

Polymerization of vinyl esters of 2,4-D can be promoted by mercuric acetate.[82,83]

$$\underset{0.09}{\text{2,4-D}} + \underset{0.0012}{\text{Hg(OAC)}_2} + \underset{0.72}{\text{vinyl acetate}} \xrightarrow[3\text{ hr}]{\text{reflux}} \underset{0.04\text{ m}\ell\ H_2SO_4}{\text{solid ester}} \rightarrow \text{polymer} \qquad (44)$$

Although no reactions with 2,4-D deuterated at the methylene position have been reported, the exchange constants for deuterated and undeuterated phenoxyacetic acid have.[84]

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Table 4
YIELDS OF PHOTOPRODUCTS FROM IRRADIATIONS OF 2,4-D/ALCOHOL MIXTURES AT VARIOUS WAVELENGTHS, INITIAL MASSES, AND ALCOHOLS (30 mℓ)[71]

Alcohol (hours irradiated)	Weight 2,4-D(g)	Wavelength (nm)	Yields of photoproducts (%)					
			Esters of corresponding alcohol				Free 2,4-D	2,4-DiCl phenol
			POA	2-CPA	4-CPA	2,4-D		
MeOH (35)	2	—	—	—	—	20	—	0.2
MeOH (35)	2	254	0.2	0.2	17	75	3	0.2
MeOH(35)	2	300	—	0.2	15	70	2	0.2
MeOH (35)	2	350	—	—	—	98	—	0.2
MeOH (100)	19.5×10^{-3}	350	—	—	—	60	40	0.2
MeOH (100)	3.5×10^{-3}	350	—	—	—	54	46	0.2
MeOH (35)	2	420	—	—	—	20	80	0.2
n-BuOH (35)	2	—	—	—	—	2	99	0.1
n-BuOH (35)	2	254	1	3	22	71	3	0.1
n-BuOH (35)	2	300	—	2	20	68	3	0.1
n-BuOH (35)	2	350	—	—	0.5	45	54	0.1
n-BuOH (100)	19.6×10^{-3}	350	—	—	—	10	90	0.1
n-BuOH (100)	3.6×10^{-3}	350	—	—	—	2	98	0.1
i-BuOH (13)	2	254	7	5	18	70	—	2.5
i-BuOH (13)	2	254	—	—	—	3	67	5.0
n-OctOH (35)	2	254	3	5	25	60	3	0.5
Ethylene glycol(12)	2	254	—	—	10	45	42	0.1

Table 5
THE RATE PARAMETERS k′ FOR DEGRADATION OF 2 G OF VARIOUS 2,4-D ESTERS IN 30 mℓ OF DIFFERENT SOLVENTS AT VARYING IRRADIATION WAVELENGTHS AT 27°C UTILIZING QUARTZ REACTOR[71]

2,4-D ester	Wavelength (nm)	Solvent	k′ (hr^{-1}) degradation $\times 10^{-3}$	Mean initial rate (mg/hr/mℓ)
Methyl	300	Methanol	(4.91 ± 0.51)	0.327
	254	Methanol	(13.8 ± 2.3)	0.920
n-Butyl	254	*n*-Butanol	(23.0 ± 2.5)	1.53
	300	Methanol	(ii) 62 ± 7 (3 → 15 hr)	4.13
			(ii)37 ± 4 (15 → 30 hr)	7.27
	350	Methanol	13.4 ± 0.1	0.893
i-Butyl	254	*i*-Butanol	27.6 ± 2.2	1.84
n-Octyl	254	*n*-Octanol	55.3 ± 5.8	3.68

II. REACTIONS OF THE ESTERS

A. Introduction

The ester link confers enhanced solubility to halophenoxyalkanoic compounds in nonpolar organic solvents and decreased water solubility. This is important in synthetic work, with many reactions proceeding quickly which would not occur or be too slow if the acid form were used.

B. Hydrolysis

It is only recently that reliable information has become available.

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Shcherbakov and Polubovarinova[85] showed that the 2,4-D butyl ester disappeared after 9 to 10 days in water. Although biological concentration was shown to be a factor, no other factors were investigated. Struif et al.[86] showed esters of 2,4-D and 2,4,5-T hydrolyzed under conditions of natural pH, temperature, or in buffer conditions. Basic hydrolysis was faster than acidic and depended on the pK_a of the acid and any steric hindrance. At pH 7, t ½ of ~5 to 30 days at 20°C; at 0°C, t ½ of ~30 to 180 days. It was also shown that 2,4-D or 2,4,5-T adsorbed strongly mainly via their C side chains to flocculated humic acid at low and neutral pH and that the hydrolysis of esters was accelerated by this phenomenon. Kenaga[87] also observed hydrolysis in natural waters under acidic conditions for esters of 2,4-D, 2,4,5-T, and Silvex. Zepp et al.[88-90] have thoroughly investigated the hydrolysis and subdivided it into acidic, neutral, and alkaline components. Neutral hydrolysis was found to be unimportant relative to acid or alkaline conditions. The processes were second order; the hydrolysis rates and enthalpies and entropies of activation are in Table 6. As found by Struif, basic hydrolysis was much faster than acidic (at least five orders of magnitude), the alkali salt being the product of the former, with the free acid being that of the latter. In buffer soluions (often the case for natural waters), the hydrolysis became pseudo first order.

Thus, for the latter case, neglecting neutral hydrolysis,

$$t^{1/2} = \frac{0.693}{k_{acid}[H^+] + k_{basic}[OH^-]} \tag{45}$$

and since $k_{basic} << k_{acid}$

$$t^{1/2} = \frac{0.693}{k_{basic}[OH^-]} \tag{46}$$

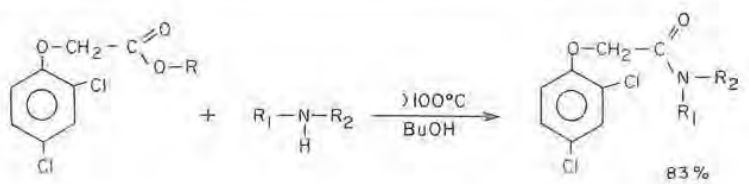
for the pH 5 to 9 range.

The half-lives of various esters are in Table 7. Apart from the methyl ester, all the hydrocarbon esters show much slower hydrolysis than the alkyl ether esters. It should be evident that the solubility of esters in water depends markedly on pH. At concentrations beyond 300 ppm at pH 7, emulsions tend to form. The "solubility" in basic solution would be completely overshadowed by the hydrolysis reaction. Even acidic solutions show moderate hydrolysis. The pH of the distilled water used by Zepp et al.[88-90] was not stated, however, it is well known that deionized or distilled water tends to be acidic because of CO_2 absorption. Nevertheless, the solubilities obtained for the methyl, 1-butyl, 1-octyl, and 2-butoxyethyl esters at 25°C in distilled water were 113, 1.0, 7.0×10^{-2} and 12 mg/ℓ respectively. The very high values for the methyl ester may contain a sizeable hydrolysis component (at pH 6, the half-life is 44 days at 28°C).

C. Condensation Reactions

Some of these reactions have already been mentioned in the corresponding sections for the free acids.

The esters can condense with amines or amino alcohols to produce amides.[91]



(47)

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Table 6
KINETIC DATA FOR ACID AND BASE HYDROLYSIS OF METHYL AND *n*-BUTOXYETHYL ESTERS OF 2,4-D[88]

2,4-D esters	Temperature (°C)	k_{ac}[a] ($M^{-1}sec^{-1}$)	k_b[a] ($M^{-1}sec^{-1}$)	$\Delta H^{\ddagger}$ (kcal/mol)	$\Delta S^{\ddagger}$ (eu)
BEE[b]	28		$(3.02 \pm 0.23) \times 10^{1}$	20.1 ± 1.4	14.8 ± 4.2
	47		$(2.35 \pm 0.13) \times 10^{2}$		
	67	$(6.59 \pm 0.13) \times 10^{-4}$		17.6 ± 0.9	-21.29 ± 2.9
	87	$(2.96 \pm 0.18) \times 10^{-3}$			
	28	$(2.0 \pm 0.5) \times 10^{-5}$[c]			
ME[d]	28		$(1.73 \pm 0.23) \times 10^{1}$		

[a] Determined from pseudo-first-order rate constants
[b] Butoxyethyl
[c] Extrapolated value
[d] Methyl.

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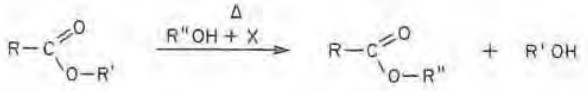
Table 7
KINETIC DATA FOR HYDROLYSIS OF 2,4-D ESTERS IN WATER AT 28°C[88]

Ester	k_b ($l\ mol^{-1}$) (sec^{-1})	$t_{1/2}$ pH 9 (hr)	$t_{1/2}$ pH 6 (days)
Methyl[a]	17.3	1.1	44
2-Propyl[b]	1.1	17	710
1-Butyl[b]	3.7	5.2	220
1-Octyl[b]	3.7	5.2	220
2-Octyl[b]	0.52	37	1500
2-Butoxyethyl[a]	30.2	0.6	26
2-Butoxy-methylethyl[b]	4.3	4.4	180

[a] Calculated from data in Table 6.
[b] Calculated assuming structure-reactivity relationship for 2,4-D esters is same for acetic acid esters.

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Esters can be transesterified (see Chapter 2, Section I.A).[92,93]



(48)

X = O or such catalysts as BF_3, *p*-toluenesulfonic acid.

D. Pyrolysis

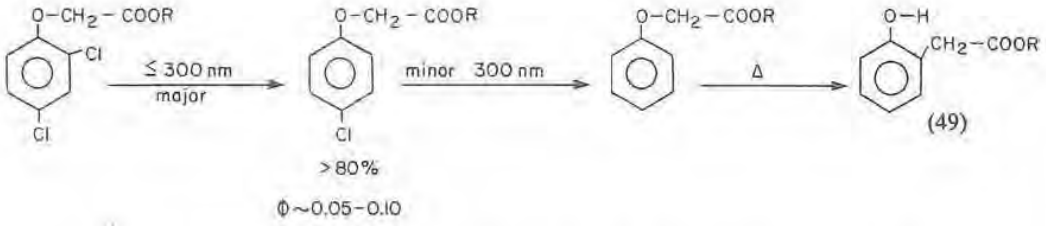
It is to be expected that the esters should be degraded at the same temperatures as the free acid (see Section I.C.8), and this topic has been already covered. It was demonstrated by IR that gas liquid chromatography at 210°C did not degrade the mole-

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cule.[94] In addition, Beckman and Bevenue[95] showed recovery of the 2,4-D methyl ester was 100% when the gas liquid chromatographic system was all glass (including injector block).

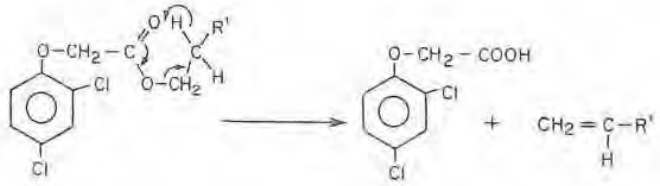
E. Photodecomposition

It has been shown by three groups of workers that reductive dechlorination at the *ortho* position of 2,4-D is the major event occurring in organic solvents,[71,88-90,96,97,98] in aqueous emulsion,[88-90] or in aqueous emulsions of liquid formulations.[98] The *p*-chlorophenoxyacetate is much more stable than 2,4-D, and only small further decomposition occurs to evolve the phenoxyacetate which eventually forms a photo-Fries product.[96-97] Reductive dechlorination at the *para* position is minor (approximately 3 to 5%).



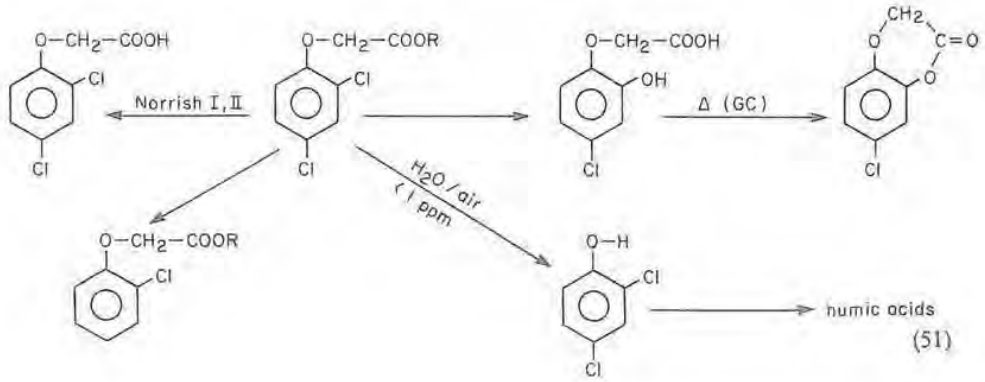
(49)

Que Hee[71] also showed that 5 to 10% of the ester in *n*-hexane re-formed the free acid by a Norrish Type II process in esters having a δ hydrogen.



(50)

In contrast, transesterification occurred in alcoholic solutions (30 mℓ) if the concentration was high (~2g/ester/alcohol), but this was never quantitative. Similarly, low (<1 ppm) concentrations of esters in aerated aqueous solutions caused formation of 2,4-dichlorophenol, dechlorination at the *ortho* position being followed by hydroxylation and resultant production presumably of humic acid, as occurs in alkaline solution.[99]

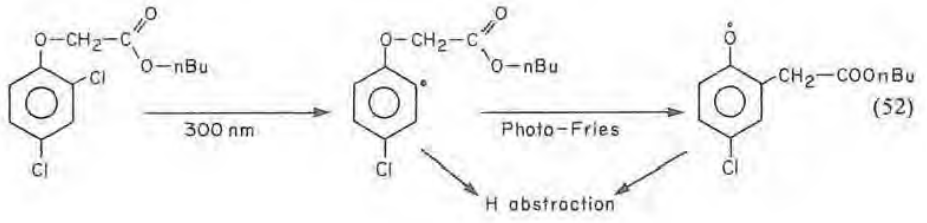


(51)

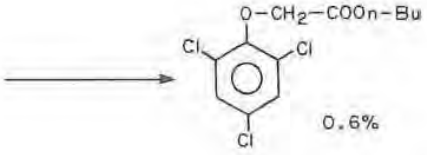
Bayer EX1026 (Part 1 of 2)

In 1964, Aly and Faust[100,101] reported that several 2,4-D esters yielded 2,4-dichlorophenol as product in irradiated aqueous solutions and that decomposition was much faster at pH 9 than at pH 4 or 7. At least in the pH 9 case, it is fairly certain the 2,4-dichlorophenol was produced via the alkali salt of 2,4-D. The photoreactions of sorbed esters on bentonite and on the other surfaces were also studied. An early report by Payne and Fults[102] did not contain the nature of any specific degradation products, but it was observed that light 340 to 389 nm activated the butyl ester towards the pea test of Went.

Obviously, the types of products evolved are wavelength, concentration, and solvent dependent. In this regard, irradiation at 300 nm of the pure butyl ester of 2,4-D yields[103] the expected reductive dechlorination products, as well as an unexpected photo-Fries product probably caused by the formation of a tight radical cage in the viscous ester solution.

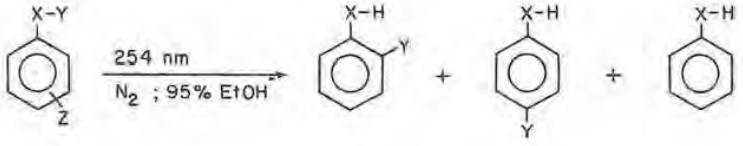


(52)



(53)

Pinhey et al.,[104-107] in a series of papers, investigated the photo-Fries behavior of phenoxy acids and esters in alcohols at 254 nm. Thus, it was shown



X = O; Z = H, 2- or 4-halogen;

Y = $-\underset{H}{N}-CH_3$, ϕ, $-\overset{O}{\overset{\|}{C}}-O-R'$, $-CH_2-R'$, $-\underset{R}{\overset{R}{\overset{|}{\overset{|}{C}}}}-COOR$, $-\underset{H}{\overset{R}{\overset{|}{\overset{|}{C}}}}=CH_2$, $-\overset{O}{\overset{\|}{C}}-R$;

(54)

and also for X = NH, Z = H, Y = $-\overset{O}{\overset{\|}{C}}-R$, $-\overset{O}{\overset{\|}{C}}-O-R$; R, R_1 and R_2 denote alkyl or H; R' denotes an alkyl, phenyl, or alkyl group.

If the two ortho positions were blocked, no *ortho* and very small amounts of *para* formed, but the H abstraction product yield was unaffected. The *ortho* rearrangement was found to be completely intramolecular, and the *para* was found to be 50%. The para isomer decreased in yield as the side chain became longer. Reductive dechlorina-

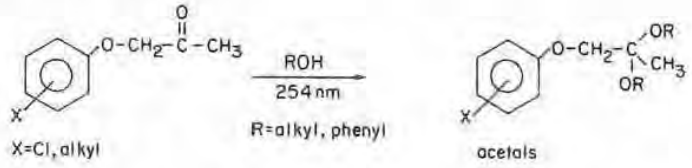
Bayer EX1026 (Part 1 of 2)

tion predominated for monohalophenoxyacetates.[106] In contrast, for halogenated *meta*-substituted phenols irradiated under the same conditions,[107] alkoxylation predominated over reduction if the halogen was chlorine. However, with bromine and iodine substituents, reduction still dominated. Chlorinated anisoles also give reduction products, but 2,4-D itself produced a complex mixture.[104]

Although Pinhey et al.,[104-107] Binkley and Oakes,[96,97] and Que Hee and Sutherland[71,98,103] did not observe the monohalogenated photo-Fries product in alcohol or hexane solution, other workers have certainly noted its formation in irradiation of *p*-chloroaryloxy 1,3,5-triazines,[108] and even in *ortho*-halogen substituted phenyl esters.[109]

In water around pH 7, the 2-butoxyethyl and methyl esters show[88-90] disappearance quantum yields ~0.031 to 0.056, with higher yields in *n*-hexane or *n*-hexadecane (~0.13 to 0.17). Acetone inhibited decomposition, thus indicating that singlet states were involved in the degradation, and this is also supported by work with various quenchers and with different solvents.[71] The fluorescence λ_{max} for both 0.0906 *M* 2,4-dichloroanisole and 2,4-D *n*-butyl ester in *n*-hexane are around 370 nm, although the anisole is over 200 times more fluorescent. In addition, the λ_{max} of the emission is wavelength dependent. The λ_{max} phosphorescence for 2,4-D butyl ester and the anisole are 510 nm and ~550 nm, respectively, and are thus comparable. Thus, the ester link causes a slight drop in the S_1 energy levels of 2,4-D (dilute solutions), but there is hardly any change in the T_1 energy level. Again this suggests that the singlet state is involved in dechlorination.

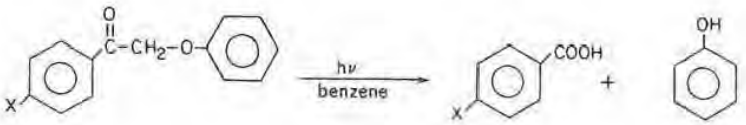
An interesting paper by Hill and Dirania has documented how phenoxyacetones can be photoacetylated by 254 nm light.[110]



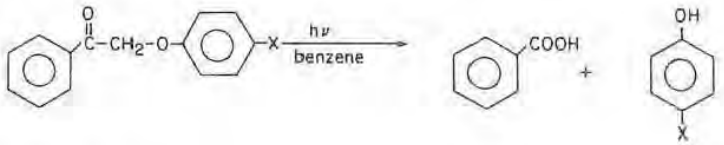
(55)

This is very similar to the transesterification of 2,4-D esters and esterification in concentrated alcoholic solutions of free 2,4-D observed by Que Hee.[71]

Phenoxymethylenephenones, in contrast, evolved phenols on irradiation in benzene[111]



(56)



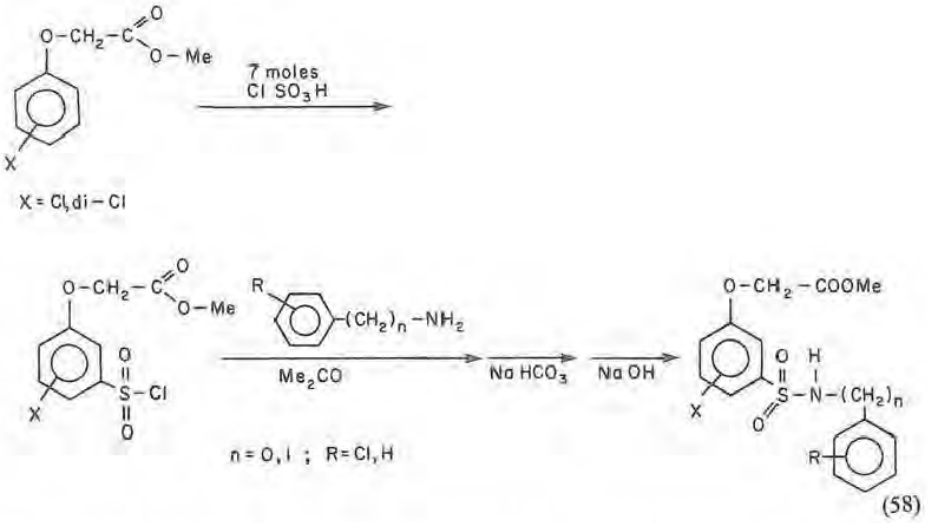
(57)

F. Miscellaneous Reactions

2,4-D esters can be substituted at the α-carbon by an aromatic aldehyde to produce the Claisen product in sodium methoxide and also the Stobbe product in potassium *t*-butoxide.[38]

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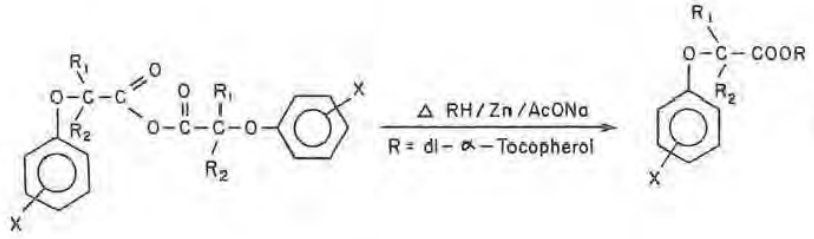
Chlorosulfonation[112-114] has been studied by Botez et al. in chlorosulfonic acid to produce the 3-substituted sulfonyl chloride that on condensation with an amine can produce sulfonamides.



(58)

The order of decreasing activation energy was[114] X = 2-Cl > 3-Cl > 4-Cl > 2,4-diCl > 2,5-diCl. When the ethyl ester of 2,4-D is chlorinated at 195 to 210°C, the esters of 2,4-dichloro, phenoxychloro, and dichloro-acetic acids and 2,4-dichlorophenylchloromethyl ether are obtained. In the presence of a catalyst, the 2,4,5-derivative is formed.[20]

Anhydrides of chlorinated phenoxyalkanoic acids have been acetylated with α-tocopherol.[115]



(59)

III. REACTIONS OF THE SALTS

A. Introduction

The alkali and short chain amine salts are soluble in water and other polar solvents. The alkali salts produce alkaline aqueous solutions when pure. The greater polarity tends to favor ionic type mechanisms rather than the usual type of mechanisms operative for the free acids and esters in nonpolar and moderately polar solvents.

B. Metal Salts

1. General Types of Reactions

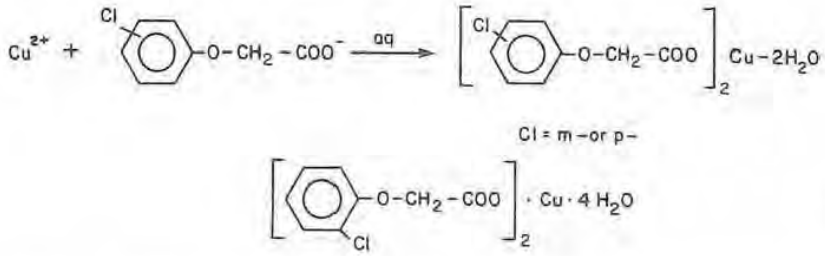
Some reactions have been considered in previous sections. Transition metal salts facilitate ligand substitution reactions.[116]

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$$Cu(O_2CCH_2OR)_2 \cdot H_2O + \text{bipyridine} \rightarrow \underset{\text{square pyrimidal}}{Cu(O_2CCH_2OR)_2Py_2} \cdot H_2O \quad (60)$$

$$+ \text{2-methylpyridine} \rightarrow \underset{\text{binuclear bridge}}{Cu(O_2CCH_2OR)_2L} \quad (61)$$

Also,[117]

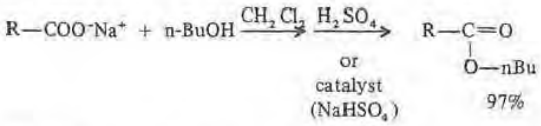


Cl = m-or p-

(62)

octahedral with partial tetragonal distortion.

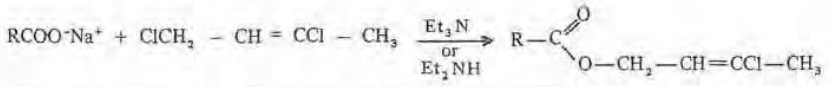
Other metal salts tend to participate in condensation reactions. For example, in esterification[118] by elimination of water,



(63)

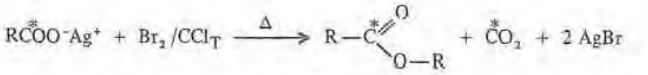
(R = 2,4-dichlorophenoxy methylene)

in esterification by elimination of alkali halide:[119]



(64)

in self-condensation (Birnbaum-Simonini reaction):[11]



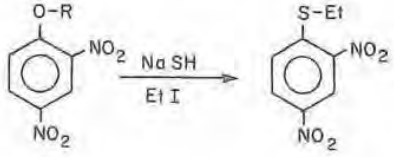
(65)

$C^* = {}^{14}C$; R = 2,4-dichlorophenoxymethylene

in the synthesis of organometallics.[154]

The pyrolysis reactions of the salts were considered in Section I.C.8.[45,48-50, 55]

Another interesting reaction of ethers in general which may be expected for the halogenated phenoxy compounds includes:[120]



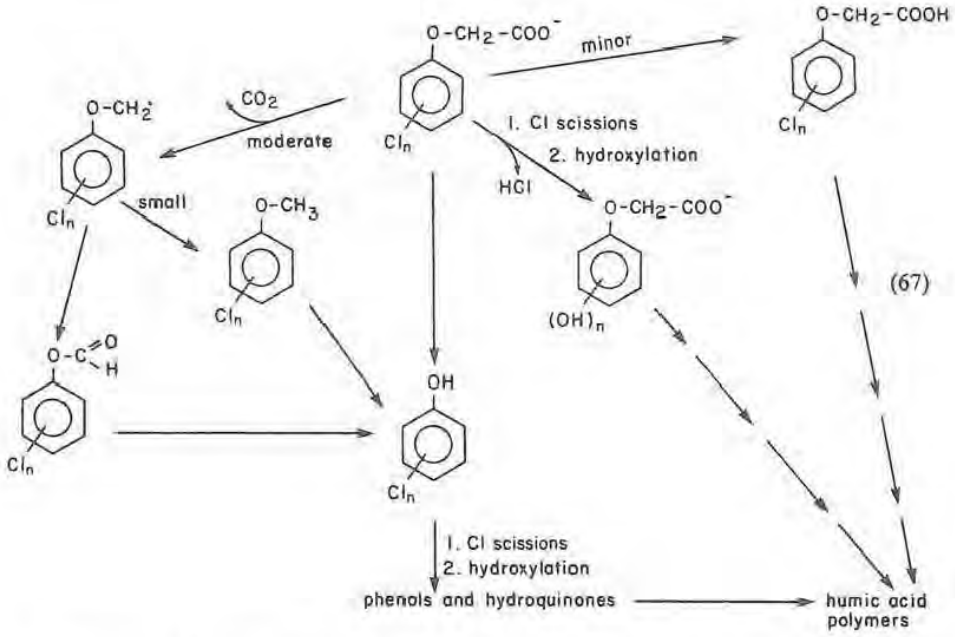
(66)

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2. Photodecomposition

Most published data on the photodecomposition of halophenoxy acids relates to events in aqueous alkaline solutions, but it has not been realized that the actual species being irradiated in these systems is the anion rather than the free acid and that polar mechanisms, including heteronuclear cleavage patterns, are likely to predominate, rather than the homonuclear type primary processes observed in organic solutions of the free acids or esters.

Crosby et al.[99,121-123] have made a systematic study of tbe photodecomposition of the sodium bicarbonate solutions of the halophenoxy alkanoic acids using artificial UV (254 to 450 mm) and sunlight. It was found that ring-Cl cleavage was followed by both reduction and hydroxylation, with the latter predominating. Free acid was also produced as well as phenols. In fact, ether link cleavage for 2,4,5-T[122] was three times faster than dechlorination. Humic acid polymers were also produced, depending on the pH, and their production was also enhanced by sodium bisulfite. The final pH of the aqueous solution ($\sim 2 \times 10^{-3}$ *M*) was around 3.5, indicative of the presence of hydrochloric acid. The chlorinated anisole was also detected in some of the irradiations, indicating that decarboxylation may also occur. The phenoxy formate was also formed; decomposition was always faster in basic solution.



The quantum yield (ϕ) for 2,4-D in basic solution was $\sim$0.044,[123] and the production of 2,4-dichlorophenol catalyzes further decomposition of the salt via peroxide production. With regard to the latter, it is well known that the phenoxide anion is oxidized extremely quickly, showing second-order kinetics ($k \sim 6.6 \times 10^8$ 1/mol/sec at 25°C), and this is an order of magnitude greater than reaction, e.g., hydroxylation, at the aromatic ring.[125] The ϕ for 2,4-dichlorophenol production was 0.012. Ring opening reactions were also implicated in the degradation.

No photo-Fries products, biphenyls, dioxins, glycolic, succinic, or oxalic acids were produced. However, at high concentrations of 4-CPA,[121] hydroxylated biphenyls were

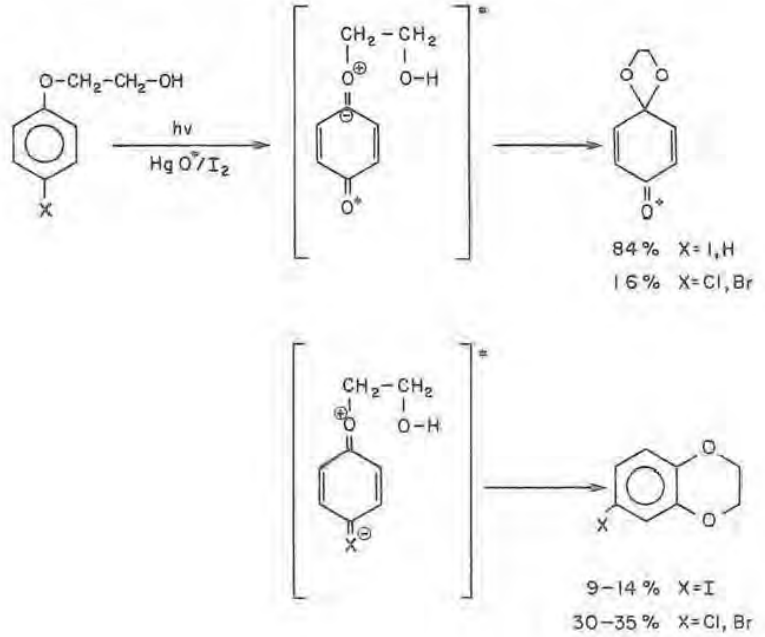
Bayer EX1026 (Part 1 of 2)

observed, thus implying concentration and hence cage effects are important. MCPA[123] > 2,4-D[99] > 4-CPA[121] > 2,4,5-T[122] in decomposition rate. Triplet sensitizers, e.g., acetone and riboflavin, enhanced the decomposition. These studies have been reported in many reviews.[126-129] Crosby's group also published similar results for other related alkaline aqueous systems, such as chlorinated phenylacetic acids,[130] naphthaleneacetic acids,[131] monuron[132] (little dechlorination), and propanil.[133] In fact, it was demonstrated that attack occurs at the bond α to the aromatic ring at the side chain, except if this bond is stabilized as a result of the extension of the conjugated structure of the benzene ring. Also, attack at a benzylic $-CH_2-$ group is preferred over that at a $-O-$ or $-N-$.

Aly and Faust[100,101] postulated that 2,4-dichlorophenol was the major photoproduct, although their colorimetric method of quantitation was not specific for this phenol. 2,4-Dichlorophenol was also detected by other workers at high concentrations of salt[134] and in dilute solution in the presence of riboflavine,[135-137] as postulated by Aly and Faust.[100,101]

Payne and Fults in their early 1947 study did not identify any products.[102] Baur et al. observed decomposition of the potassium salt of 2,4,5-T at 350 nm, with an apparent $\phi \sim 1$ in concentrated solution.[147]

Sensitization of photodecomposition[138-140] has been adjudged to be more important than the direct route because of the availability of humic acids, quinones, metal ions, and anionic sensitizers in natural waters. Thus, the uranyl ion was found to be three times more effective than riboflavin in the presence of Fe III when 2,4-D in heterogeneous alcoholic alkaline solutions was irradiated.[140] In the case of unsubstituted phenoxy or phenthioxyacetic acids, if benzophenone is used as a sensitizer, O_2 retarded the decomposition, but when quinones were utilized, O_2 did not.[139] The sensitized decomposition of 2,4-D on silica gel chromatoplates by anthroquinone has been noted.[75] Another similar type of reaction is important for photosensitization in halophenoxy ethanols by HgO/I_2 to give heterocyclic type compounds.[141]



(68)

Bayer EX1026 (Part 1 of 2)

The corresponding products for the phenoxyacetic acid compounds have not been reported.

Since chlorophenols and phenols are important photolysis products, it is of interest to examine their photochemical behavior.

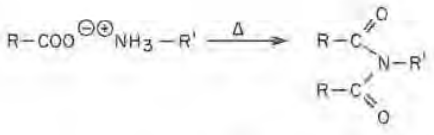
In phenolate solutions, an electron detaching state has been noted at 330 nm.[142] The conversion of 4,5,6-trichloro-2-(2,4-dichlorophenoxy) phenol, an impurity in 2,4,6-trichlorophenol, to one tetra-, two tri-, one di-chlorodibenzo-*p*- dioxins, and one dichlorodibenzofuran has been observed.[143] Solvated electron production has also been detected[144] in aqueous solution at pH 12, even for halogenated phenols, and it has been postulated the electrons are released from a charge transfer transition state which has oriented solvent molecules around the O. At pH 7, the production of solvated electrons appears biphotonic, but monophotonic for the phenolate. The phenoxy radical is thought to be produced at the same time as the solvated electron. 2,4-Dichlorophenol has been subjected to irradiation >290 nm in the solid and gas phases as well as solution.[145] In the solid phase, reductive dechlorination and progressive chlorination of the phenol was observed. The production of dioxins and furans via the 1,2-ketocarbene[150] from the higher chlorinated phenols is thus a distinct possibility. In solution, reductive dechlorination, self-condensation hydroquinone production, and hydroxylative dechlorination were observed. In the gas phase, reductive dechlorination alone occurred and was small. Thus, the type of phase may also determine the nature of the photolysis product. It is interesting that Que Hee et al. observed some internal chlorination of pure 2,4-D *n*-butyl ester liquid at 300 nm,[103] implying that thin film photochemistry may be rather different from that of homogeneous, nonviscous solutions. 3,4-Dichlorophenol produced hydroxy and chlorinated biphenyls in solutions irradiated below 290 nm.[145] Sensitization by eosin causes the irradiated alkyl- and halophenols to produce *p*-benzosemiquinones, detected by e.s.r.[146] Peroxide formation has also been reported.[125] Benzoquinone radicals can also be produced chemically.[147] The rate constants of phenoxy radical recombination are affected by the presence of metal ions, e.g., Cu^{+}, Cu^{2+}, Fe^{2+}, and Mn^{2+}, since the latter form stable complexes with the phenoxy radical.[148]

Gamma radiation of chlorophenols causes dechlorination and ring opening with production of oxalic acid.[149]

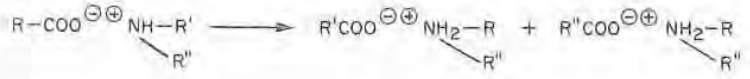
C. Amine Salts

1. General Types of Reactions

Pyrolysis to form amides has already been dealt with in Chapter 2, Section IV. The intermediate imides have been isolated in some cases,[151] and transacylation may also occur on pyrolysis.[152]



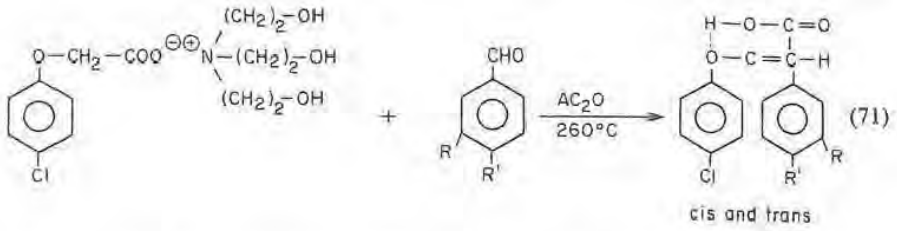
(69)



(70)

Under certain conditions, condensation may involve the α-C.[153]

Bayer EX1026 (Part 1 of 2)



Pyridine salts, usually 1:2 (pyridine/acid), may reform the free acid in alcohol.[155]

2. Photodecomposition

The short chain amine salts of 2,4-D in aqueous or organic solvents are dechlorinated by 300-nm radiation at the *ortho* chlorine position; solvent attack follows, together with reduction in both solvents. Methoxylation in methanol and phenylation in benzene also occurred. However, no 2,4-dichlorophenol above the level of the dark controls was detected in aqueous or methanolic solutions. Only 8 to 10% photodecomposition occurred at 300 nm and 27°C after 40 hr, but the same extent of degradation was attained in 2 to 5 hr at 254 nm. No esterification or amide formation was observed in methanol solutions of long or short chain amine salts. In benzene, small amounts (<5%) of 2,4-dichlorophenol were produced. Ether cleavage was thought to be followed by phenylation, or by a photo-Fries reaction to produce 2-phenyl-4-chlorophenol. Trace amounts of amides (<1%) appeared after 40 hr of irradiation of long chain salts $\geq C_4$ at 300 nm. Small amounts (<1%) of a compound m/e 218 (2Cl) formed for all salts after 40 hr, but was not identified. No free acids were detected.

The λ_{max} fluorescence for all 0.1 *M* salts is at 440 nm, similar to that observed for concentrated solutions of 2,4-D acid/alcohol. The λ_{max} excitation for all salts was ~300 nm, as for the esters and dilute solutions of the 2,4-D acid. The λ_{max} phosphorescence for all the salts lay ~540 nm. Thus, there is a small singlet/triplet gap of a 12 kcal/mol, and this is further supported by a large fluorescence/phosphorescence spectral overlap. As noted before, dechlorination has been postulated to be largely from the singlet state.[73] However, the proximity of the triplet level allows possible easy intersystem crossing. Since the triplet state is easily quenched by oxygen,[129] less dechlorination from this state should be observed, and this may account for the lower photolysis rates observed for the salts relative to the esters and free acids.

IV. REACTIONS OF THE AMIDES

A. General Reactions

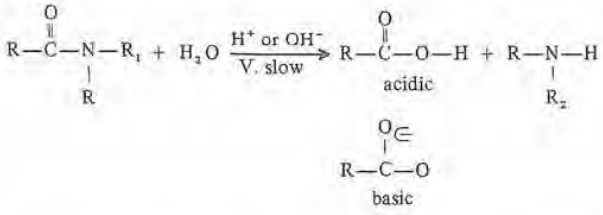
Specific reactions for the amides of the chlorophenoxy acids are difficult to find in the literature — hence the summary below. The secondary amides are rather like the corresponding esters, except that they show more marked amphoteric properties than esters and are less reactive.

Since amides are weak bases, they protonate only at very low pHs; they complex with phenols, amines, chloroform, cyclohexane, alcohols, BF_3 (via O), and octahedral metal ions.[152]

Acidic and basic hydrolysis of the amides have been reviewed recently.[152,156] Generally, nucleophilic attack by an O or N occurs first at the O (SN_1 process) to obtain the kinetic product which subsequently rearranges to the N-substituted thermodynamically stable product (SN_2 process). For acid conditions, O-substitution predominates, except at high temperatures, while N-substitution is the major event under basic conditions.

Bayer EX1026 (Part 1 of 2)

Basic hydrolysis is most facile at low temperatures. Acid hydrolysis requires temperatures >100°C to produce the acid and amine for short chain amides and requires an amide and alcohol for long chain amides.[157] Thus,

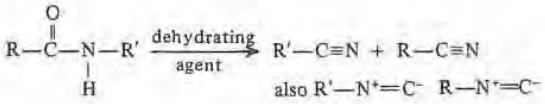


(72)

Alcoholysis also occurs to produce >60% O-alkylation[158] and also liberation of the original amine.

In the presence of other carboxylic acids, transacylation may occur;[159] for amines transamination may also be appreciable;[159] aldehydes in neutral or basic solution at 100 to 150°C will N-substitute.[152]

In concentrated acids or bases or in the presence of $POCl_3$, PCl_5, P_2O_5, $SOCl_2$, silanes, or sulfonylchlorides, exhaustive dehydration of secondary amides produce the various possible nitriles (thermodynamic) and isonitriles (kinetic).[152]

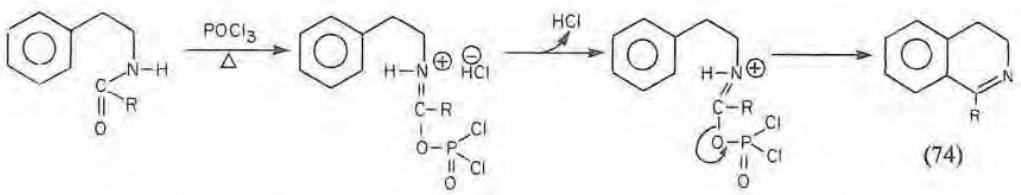


(73)

Primary amides on pyrolysis above 250°C produce nitriles,[160-162] probably via a isoimide.[163] Carboxylic acids can also be formed. The pyrolysis products of secondary amides above 250°C are usually olefines, lower amides, and small amounts of nitriles.[164]

Amides undergo N-alkylation via the Chapman Rearrangement[165,166] and O-alkylation by reaction with dimethyl sulfate (20 to 60°C) to form methyl esters and a tertiary amine and also with excess diazoalkanes to produce 96% yield of the alkyl ester of the parent acid of the amide.[152]

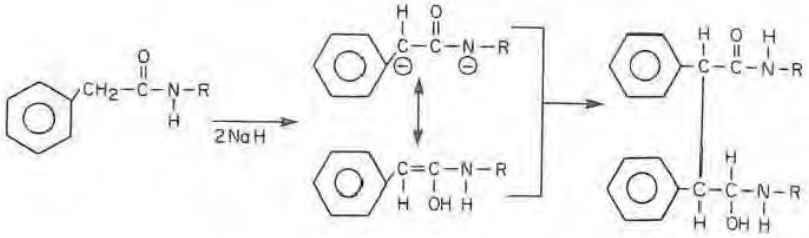
Cyclization can also occur under the right conditions, e.g., the Bischler-Napielski Reaction.[152]



(74)

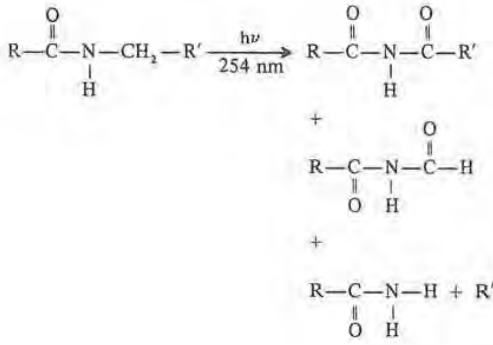
Reaction at the α-C to the carbonyl has been demonstrated when a carbanion can be formed.

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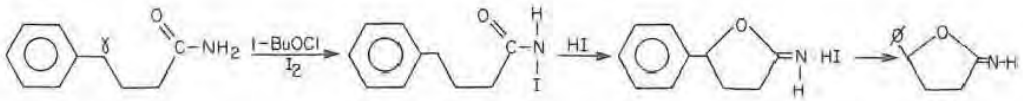
(75)

The photochemistry of the amides involves peroxy radical via removal of α_N hydrogen atoms and subsequent oxidation.[152]



(76)

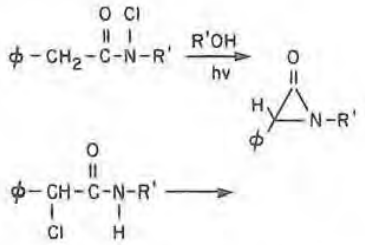
Gamma cyclization often occurs photochemically if a free radical initiator, e.g., I_2, is present.[152]



50%

(77)

However, photochemical events for some amides related to 2,4-D or 4-CPA are quite distinctive.[167]



(78)

Halogenation at the amide N can occur if the halogen (not F) is in the ionic form.[152] The halogen can also migrate from the amide N to a phenyl ring if the latter is close.[152]

B. Specific Reactions

Reductions occur with $LiAlH_4$.[168]

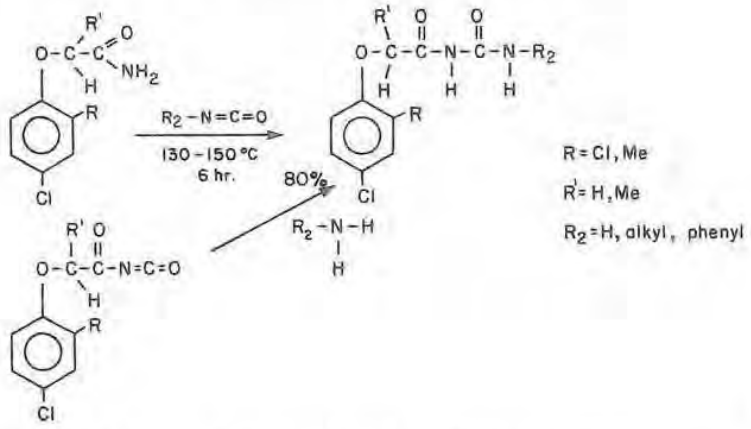
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R_1 and R_2 can be (halophenoxyalkyl)

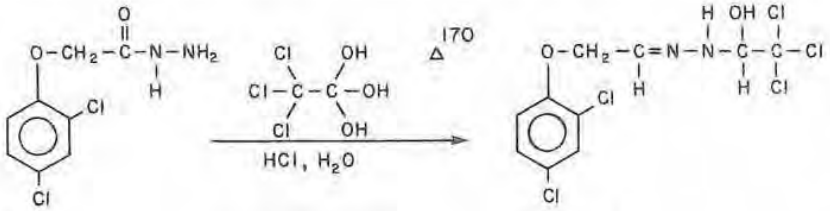
R_3 = alkyl (79)

Reactions with isocyanates and oxalylchloride have been noted.[169]

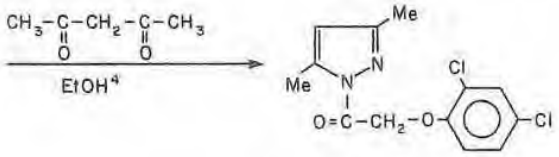


(80)

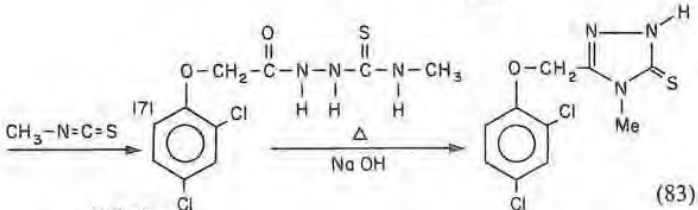
Reactions with hydrazide derivatives have been of some interest.



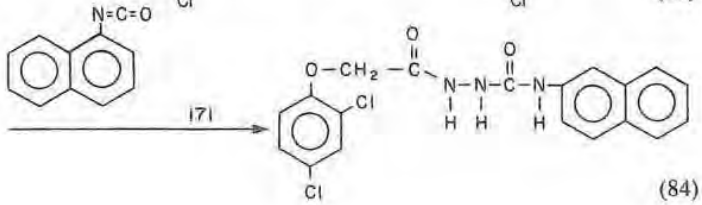
(81)



(82)



(83)



(84)

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Table 8
RATES OF HYDROLYSIS OF 2,4-DICHLOROPHENOXYACETAMIDES, DETERMINED IN 0.22*N*-POTASSIUM HYDROXIDE IN ALCOHOL CONTAINING 10% v/v OF WATER[183]

$Cl_2CH_3-O-CH_1-CO\cdot NRR'$

Compound number	R	R′	Temperature (°C)	$10^3 k$ (min^{-1})	$t_{1/2}$ (50°) (min)
1	H	H	40	7.8±0.83	90±9.4[b]
1	H	H	50	14±1.9	50±6.8
2	H	Me	50	2.1±0.10	330±14
3	H	Et	50	0.98±0.085	710±52
4	H	Pr	50	0.12±0.0050	5800±170
5	H	CH_2CH_2OH	50	3.1±0.11	220±7.9
6	H	Ph	50	2.7±0.14	260±10
7	H	C_6H_4Mep	50	2.1±0.14	330±22
8	H	$C_6H_4\cdot NO_2p$	50	—[a]	<20
9	H	$C_6H_4\cdot NO_2m$	50	9.7±0.69	72±5.1
10	H	$C_6H_4\cdot NH_2p$	50	2.8±0.21	250±19
11	H	$C_6H_4\cdot NH_2m$	50	3.8±0.42	185±20
12	H	C_6H_4Clp	50	3.6±0.12	190±6.5
13	H	$C_6H_1Cl_2$-3,4	50	6.7±0.65	100±10
14	Me	Me	50	14±1.5	50±5.5
15	CH_2CH_2OH	CH_2CH_2OH	50	—[a]	<20
16	Me	Ph	50	5.2±0.30	130±7.7
17	Pb	Ph	40	~20	~30[b]

[a] Reaction was too rapid to be followed by method employed.
[b] $t_{1/2}$ values at 40°C.

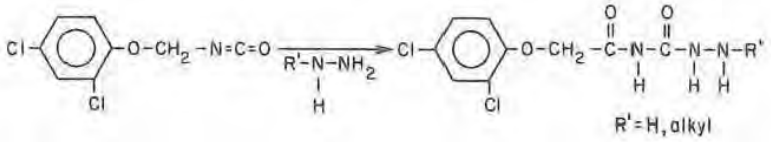
From Johnstone, A. M., *J. Chem. Soc.*, 1961, 2335.

Hydrolysis of 2,4-D amides in 0.22*N*-KOH/alcoholic aqueous solutions was studied by Johnstone (see Table 8),[183] and in excess alkali pseudo first-order kinetics were obeyed. The type of N-substituents did not markedly affect hydrolysis rates, even though disubstituted amides hydrolyzed faster than did monosubstituted ones.

IV. MISCELLANEOUS REACTIONS

2,4-D acetyl chloride is often used in the synthesis of amides (see Chapter 2, Section IV) esters[172-175] (including Sesone),[173] complex metal salts,[176] and amides.[4]

2,4-Dichloromethylene isocyanate has been used to react with hydrazines.[177]



(85)

A urea-polymeric formulation of 2,4-D was destroyed by UV radiation at 350 nm, whereas conventional formulations were resistant. Rylex H or Uvinol D-50 inhibited the degradation. The polymer formulation was resistant to pyrolysis, whereas conventional ones were destroyed. Both were quite volatile.[178] It also must be remembered that photochemical events are often affected by other formulation components such

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as the "inert" components.[179] Some chlorinated phenoxy amides have been used as sensitizers in photography,[180] and amine salts have been incorporated as a fire retardant.[181] 2-Chloro-4-azido-phenoxyacetic acid has been used to identify receptor molecules and sites by photoaffinity in plant cells.[182]

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Chapter 4

ANALYSIS

I. INTRODUCTION

The analysis of compounds can be considered under several divisions: extraction, cleanup, chromatography, detection, and quantitation; all or only the last two may be required, and combined chromatography-detection-quantitation is usually the method of choice in the final step of an analysis. Clean-up is generally necessary, since the herbicide or its metabolites comprise only a minute part of the sample, and there are many potential interferences. Concentration of the herbicidal compounds is often desirable; confirmation of the identity of the chromatographed material is essential, especially for samples with unknown past histories.

Many reviews and books have described the chromatographic methods used for pesticides,[1-26] including the halogenated phenoxyalkanoic acids, and thus we shall not attempt to be exhaustive here.

II. CHROMATOGRAPHY-DETECTION-QUANTITATION

A. Gas Liquid Chromatography (GC)

1. General

Gas liquid chromatography (GC) was first applied to pesticide analysis by Coulson et al.[27] in 1959 and Zweig and Archer[28] in 1960, who measured and separated milligram amounts utilizing a kathorometer detector. Coulson and Cavanagh also introduced[29] a combustion-coulometric titration technique for chlorinated pesticides in 1960, while Lovelock and Lipsky that same year unveiled the electron capture detector.[30] Even then GC-ED was capable of detecting nanogram quantities of chlorinated compounds, but can now detect picogram levels. It has completely revolutionized pesticide analysis. The most useful account of GC methodology is by Zweig and Sherma especially Volume 6.[1]

The free phenoxy acids and salts are too polar and nonvolatile to chromatograph directly, but the esters and lower amides can be gas chromatographed easily. Appendix 1 gives a short list of some representative GC columns and temperatures used for the phenoxy esters. In general, the injector temperature is 30 to 50°C higher than that of the column, and thermal conductivity (TCD) and electron capture detectors (ECD) are also usually maintained at least 50°C above column temperature. Silicone liquid phases, such as SE-30 and DC-200, have been most commonly used for general gas chromatography, but OV silicones cause low bleed even at 350°C, in contrast to the other two which bleed badly above 250°C. Since the esters and amides of the phenoxys tend to be thermally unstable above 250°C, the choice of liquid phase is not really crucial. However, OV phases should be utilized for GC/MS confirmation. The packing is usually diatomaceous earth, 80/100 or 100/120 mesh silanized and acid washed, e.g., Chromosorb W (DMCS/AW) which has been shown to give the most reproducible results. The column is usually constructed of borosilicate Pyrex, 1 to 1.8 m in length, with internal diameters 1 to 6 mm, and in contrast to copper columns, allows 100% recovery of injected esters[31] using on-column injection. With modern quality support materials, a loading of 2 to 5% of stationary phase is adequate, contrasting markedly with the heavy loadings utilized early in the GC era (see Appendix 1). Dimethylphthalate has been used as internal standard for TCD and FID.[32] Internal standard quantitation is more difficult for ECD, since quantitation is also a function of the

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number and type of halogen. Esters of 2-chloro-4-bromo-phenoxyacetic acid[33] have been used for 2,4-D, and esters of 2-chloro-4,5-dibromophenoxyacetic acid would be probably suitable for 2,4,5-T. The flame ionization detector is usually sensitive to microgram amounts, but it may respond to a few hundred nanograms under ideal conditions, but has not been often used in herbicide residue analysis, since it is a nonspecific detector, but has been used for formulations.

The theory of the electron capture detector has been described by Gudzinowicz,[34] and the importance of operating parameters has also been reviewed.[35-37] Two radioactive ionizing sources have been used — tritium foil and ^{63}Ni detector for 2,4-D esters; the latter was far superior, since it remained linear over four decades of sensitivity and agreed with levels obtained by specific ion monitoring mass spectroscopy, while the former was linear only over two decades and always gave higher levels than both the ^{63}Ni detector and GC/MS/specific ion monitoring (see Table 1). In addition, the ^{63}Ni detector can operate well above 225°C, the highest temperature usually used for the tritium detector, and can thus be decontaminated more easily. The sensitivity to ^{63}Ni ECD is approximately 50 pg, for the 2,4-D *n*-butyl ester[38] and 5 to 10 pg for 2,4-DP methyl ester.[39] The major advantage of ECD is its specific sensitivity to electron capturing groups, e.g., halogens, nitro groups, and nitriles, but an apparently "clean" ECD chromatogram may not reflect the true composition of the sample being studied. For best results, it is wise to clean up samples before quantitation. The contributions of electron capture-sensitive components in reagent-grade sulfuric acid, sodium hydroxide, ammonium hydroxide, sodium carbonate, and sodium bicarbonate to analysis of the chlorophenoxy acids have been discussed.[40] If low-picogram ECD sensitivity is desired, then derivatization is necessary. A 10% BCl_3/2-chloroethanol reagent was used by Woodham et al.[41] to produce the 2-chloroethyl esters of 2,4-D and 2,4,5-T (sensitivity ~1 pg) in approximately 30 min. These esters can be also produced by reaction of the acid with dicyclohexyldicarbodiimide in 2-chloroethanol, and in addition, dicamba (2-methoxy-3,6-dichlorobenzoic acid) which is unaffected by BCl_3 alcohol is also esterified.[42] Use of 20% (v/v) 2,2,2-trichloroethanol in trifluoroacetic anhydride in H_2SO_4 evoked 2,2,2-trichloroethyl esters of 2,4-D and MCPA which could be detected at the 0.06- to 0.10-ppb level (i.e., ~60 to 100 fg/$\mu\ell$).[43] The most useful EC-sensitive derivatives are the pentafluorobenzyl esters. Chau et al.[44-46] reported the preparation and GC properties of the esters for MCPA, 2,4-D, MCPB, 2,4,5-T, 2,4-DB, and 2,4-DP, and many were also characterized by De Beer et al.[47,48] by their mass, IR, NMR, and UV spectra[46] (see Appendix 2). Since sensitivity is approximately 100 fg/$\mu\ell$ and their lower volatility allows better separation of many related halogenated phenoxyalkanoic acid esters, their preparation is presented here.

Preparation of Pentafluorobenzyl Esters for 2,4-D, 2,4-DB, 2,4-DP, MCPA, MCPB, MCPP, 2,4,5-TB, and 2,4,5-TP[47,48]

Heat the free acid from evaporated extracts together with 1 mℓ 1% perfluorobenzylbromide solution (caution: lachrymator) in acetone and a few grains of anhydrous potassium carbonate at 60°C for 1 hr. Evaporate the solvent by a nitrogen stream, dissolve the residue in 0.5 mℓ isooctane and transfer quantitatively to a glass mini column (7 mm) containing 5 g Kieselgel 40 (70/230 mesh ASTM, Merck) that has been prewashed with hexane. Elute with 15 mℓ benzene in hexane and discard the wash. Elute with further 8 mℓ 75% benzene in hexane. Concentrate to 2 to 3 $\mu\ell$ and inject into the GC. The stoichiometry of the reaction is 1:1. For larger amounts of esters for standards comparison, reflux a 0.002 equimolar mixture of the acid pentafluorobenzylbromide with 60 mg anhydrous potassium carbonate in 60 mℓ acetone for 2 hr. Evaporate solvent. Dissolve the residue in 50 mℓ ether and wash twice with 20 mℓ water. Dry the ether layer over anhydrous Na_2SO_4 and evaporate to dryness under nitrogen. Recrystallize the residue from hot hexane.

The GC column should be a 1.83 m × 6.3 mm O.D. 2-mm ID pyrex column packed with 3.5% OV-101 and 5.5% OV-210 on 80/100 mesh Chromosorb W (DMCS/AW). The nitrogen carrier gas flow rate was 50 to 55 mℓ/min. Temperatures utilized were

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Table 1
ECD AND GC/MS-SID
COMPARISON STUDY[38] FOR 2,4-D
BUTYL ESTER[a]

Sample number	^{3}H ECD ($\mu g/M^3$)	^{63}Ni ECD ($\mu g/M^3$)	GC/MS-SID ($\mu g/M^3$)[b]
1	0.11	0.00	0.00
2	0.91	0.16	0.17
3	0.70	0.29	0.32
4	0.69	0.08	0.09
5	0.11	0.10	0.10
6	2.30	0.18	0.18
7	0.12	0.04	0.06
8	2.60	1.01	1.04
9	0.10	0.08	0.09
10	2.10	0.30	0.31
11	2.60	0.29	0.30
12	6.10	0.71	0.74
13	4.90	0.57	0.55
14	10.00	1.32	1.36
15	3.40	1.45	1.48
16	2.20	1.14	1.00
17	16.00	1.82	1.72
18	0.71	0.66	0.69
19	0.48	0.27	0.33
20	2.50	0.28	0.20
21	5.90	1.29	1.27
22	0.00	0.00	0.00
23	0.14	0.13	0.14
24	26.00	2.55	2.52
25	34.00	2.48	2.20
26	10.00	1.36	1.32
27	0.00	0.00	0.00
28	1.40	0.44	0.43
29	5.90	1.66	1.48
30	0.26	0.15	0.17
31	0.61	0.59	0.63
32	3.90	1.53	1.40
33	0.12	0.10	0.11
34	0.97	0.17	0.15
35	0.31	0.20	0.15

[a] The quantitative data are the averages of two injections per sample, where the two separate values agreed within ± 5%.
[b] SID m/e = 185.0.

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injection port, 250°C; column, 200°C; ^{63}Ni detector, 280°C, using 30 to 40 mℓ/min purge. Unfortunately, the 2,4-D and Silvex esters are superimposed, but were resolved using 3% OV-225 on 80/100 mesh Chromosorb Q (HP) packing; however, then MCPA and 2,4-DP are superimposed.

Another detector still used is the microcoulometric detector[10] which can be specific

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for N-, halogen-, or S-containing compounds. For halogenated compounds, the GC effluent is reductively pyrolyzed to produce HCl which is absorbed by an electrolyte, and the resulting ionic imbalance is measured by how much current is required to reestablish the steady state. The sensitivity is at the 50-pg level. It is still used for some determinations, e.g., 2,4,5-T in animal tissues[49] and in milk.[50] Many applications of the microcoulometer are cited by Lisk in Volume 5, page 362, of Reference 1, and by Marquardt et al. in Volume 4, page 108, of the same treatise.

Other GC detectors which have been used are the microwave emission detector (for MCPA silyl derivatives, sensitivity ~60 ng)[51] and the alkali flame detector (for 2,4-dichlorophenol diethyl phosphate from ether link cleavage of 2,4-D, sensitivity ~20 pg).[52] Surprisingly, specific derivatives which are sensitive to such other detectors as alkali flame ionization, electrolytic conductivity, and flame photometric detection have not been extensively investigated.

Work by Larose and Chau[53] showed that the logarithm of the retention time of phenoxy esters was a linear function of the number of carbon atoms in the esterifying alcohol of a homologous series. The phenoxy acids 2,4-D, 2,4,5-T, Silvex, 2,4-DB, and 2,4,6-T and alcohols, methyl-, ethyl-, *n*- and i-propyl, *n*-, i-, and *t*-butyl, and 2-chloroethyl were used; also, the volatility of the ester increased with isomer branching.

Table 2 shows relative retention and relative response data with respect to aldrin for some 2,4-D and 2,4,5-T esters on eight standard GC columns using ^{3}H-ECD.[54] It can be seen that OV-1 and D-200 are similar, as are OV-1/QF-1, SE-30/QF-1, and DC-200/QF-1. The DEGS column is atypical. The best column probably was OV-17/QF-1, but QF-1 is best replaced by its more thermally stable equivalent OV-210. More retention time data are available in Reference 56.

2. Confirmatory Methods

The retention time on a GC (or LC) column for a given compound is characteristic of that compound, but it is not unique, especially when environmental samples are being analyzed. GC or LC analysis will definitely tell only if a compound is not present in the detection range of the detector; if there is a peak at a particular retention time, the amount corresponding to the compound is the maximum possible for the suspected compound, enabling the analyst to know if negligible levels are likely, or if further confirmation is necessary. A multicolumn analysis improves the probability of identification, but is not foolproof; e.g., Que Hee et al.[55] showed that only 63% of two-column "identifications" of the *n*-butyl ester of 2,4-D could be confirmed on chemical derivatization, while 57% of the individual 2,4-D compounds were not detected by this two-column technique. This emphasizes that tentative identification can only be as exhaustive as the set of standards utilized and that even then, the analyst has a 30 to 40% chance of error. The difficulty of confirmation can be approached in several ways: by chemical derivatization, so that the sensitivity of specific detectors can be utilized or by spectroscopic methods.

As has been already shown in Chapter 3, free acids, esters, amides, and amine salts are easily hydrolyzed in basic solution without ether cleavage to form alkali salts which can be cleaned up at this point by organic solvent extractions, thus leaving only acid salts and phenolates. Upon acidification and extraction of the free acid and phenols, the acid can be esterified and then chromatographed.[55,57] All phenoxyalkanoic compounds are thus quantitated.[55,57] While this procedure is time consuming, picogram sensitivity is attainable. Two good reviews are available.[5,26]

Perhaps the most specific and sensitive method involves specific ion (SI) monitoring mass spectroscopy. Farwell et al.[38] have attained femtogram sensitivities using this technique. Briefly, instead of scanning an entire mass range, the SI mode monitors one or more characteristic ions of a specified m/e, thereby greatly increasing sensitiv-

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Table 2
RELATIVE RETENTION TIMES (RRT) AND RELATIVE PEAK HEIGHT (RPH) VALUES OF SOME ESTERS OF 2,4-D and 2,4,5-T ON SPECIFIC COLUMNS USING ALDRIN REFERENCE (RRT = 1, RPH = 1)

Columns	10% DC-200 200°C 100mℓ/min		3% OV-1 180°C; 70 mℓ/min		5% QF-1 180°C; 45 mℓ/min		3% DEGS 195°C; 70 mℓ/min		2% OV-1/3% QF-1 190°C; 60 mℓ/min		4%SE-30/6% QF-1 200°C; 70 mℓ/min		5%DC-200/7.5% QF-1 190°C; 100 mℓ/min		15%OV-17/1.95% QF-1 200°C; 60 mℓ/min	
esters	RRT	RPH	RRT	RPH	RRT	RPH	RRT	RPH	RRT	RPH	RRT	RPH	RRT	RPH	RRT	RPH
2,4-D i-propyl	0.41	0.090	0.40	0.110	0.93	0.120	0.96	0.100	0.59	0.079	0.56	0.081	0.54	0.089	0.54	0.061
2,4-D-*n*-butyl	0.60	0.045	0.06	0.057	1.29	0.037	1.33	0.031	0.87	0.034	0.79	0.037	0.80	0.040	0.79	0.049
2,4,5-T i-propyl	0.67	0.530	0.67	0.490	1.30	0.320	1.41	0.230	0.89	0.400	0.84	0.360	0.85	0.400	0.84	0.330
2,4-D-butoxy-ethanol	1.44	0.021	1.59	0.026	2.91	0.018	3.60	0.015	1.97	0.018	1.75	0.016	1.89	0.066	1.92	0.023
2,4-D-PBG ether ester	1.47	0.034	1.61	0.036	2.78	0.028	2.61	0.028	1.94	0.030	1.75	0.027	1.89	0.029	4.70	0.034
2,4-D-i-octyl	1.94	0.010	2.20	0.009	3.61	0.011	2.89	0.008	2.53	0.011	2.24	0.010	2.45	0.009	2.30	0.013
2,4,5-T-butoxy-ethanol	2.30	0.076	2.61	0.057	4.33	0.052	5.70	0.022	3.04	0.027	2.69	0.060	2.99	0.059	3.04	0.065
2,4,5-T i-octyl	3.05	0.032	3.56	0.025	5.21	0.013	0.80	0.031	3.89	0.030	3.37	0.028	3.92	0.025	3.50	0.033

Note: The packings were contained in 1.83-m long, 6.30-mm OD, 4.00-mm ID Pyrex columns; a ^{3}H-ECD parallel plate detector was used.[54]

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ity. Single-ion detection is more sensitive but less specific than multiple-ion detection. The electron impact mass spectra of representative 2,4-D esters have been given in Chapter 1, Appendix 11; m/e 175, 162, and 111 are large ions in all the spectra of the esters. However m/e 199 is specific for the methyl esters of 2,4-D and 2,3-D, while the m/e 185 is selective for the ethyl, *n*-pentyl, and *n*-butyl esters. GC/MS-SID was linear from 10 pg to 100 ng; nonlinearity below 10 pg could be a function of losses at the GC/MS interface or on the GC column. This technique will allow quantitation and identification of the esters at the picogram level.

De Beer et al.[48] have also used GC/MS-SID to quantitate the pentafluorobenzyl esters of the phenoxy alkanoic acids (compare with Appendix 1). Unlike the alkyl esters, there are no (e.g., as for the 2,4,5-TB-PFB ester) or very small molecular ions, and PFB-ester presence is characterized by a very strong pentafluorobenzylium ion (m/e 181). Whereas losses in the PFB esters depend on the type of acid, e.g., MCPP methyl ester loses CH_2=CH−COOR (where R = $-CH_2-C_6F_5$), and MCPB loses $-CH_2CH_2CH_2COOR$ and CH_2=CH−CH_2−COOR to produce m/e 141 and 142 not observed with the MCPA-PEB ester. All acetic acid derivatives show losses of −COOR, $-CH_2COOR$, and $-OCH_2COOR$. The same is true, but less marked, for the butyric and propionic derivatives. The only similarity within a group of compounds with identically substituted aromatic nuclei is the presence of the m/e 133 ion in the spectra of the dichloro derivatives. For 2,4-D-PFB, m/e 145, 175, and 400 were selected for specific ion monitoring. GC/MS has been reviewed recently.[10,17]

Other spectroscopic techniques in general do not have the nanogram to picogram sensitivity required for confirmation purposes at the residue level. Although Fourier transform IR and ^{13}C-NMR are capable of sensitivity approaching the nanogram level, they are still at an early stage of development and cannot compete as yet with MS/SID. One advantage both of these techniques possess is that the compounds to be analyzed do not have to be volatile; IR, UV, and NMR spectra for the PFB-esters of the acids are in Appendix 1, and those for the alkyl esters are in Chapter 1, Appendix 11. The microcoulometer which can provide the chlorine content of an eluting compound can also be used for confirmation purposes. Other important developments in GC analysis will probably involve Grob-type capillary columns, and publications regarding the halophenoxy acids are beginning to appear.[58]

B. Thin Layer Chromatography (TLC)

The stationary phase is a thin layer of an adsorbent, such as alumina or Kieselguhr, on a Pyrex or plastic plate, and the material to be separated is applied as a small spot near one end of the plate, and the components are resolved by differential partitioning between the solvent and solid phase. It is faster, more versatile, and achieves better resolution than paper chromatography. Detailed reviews are available.[59,60,77] The separated compounds are generally not colored, and these have to be visualized, e.g., by UV light or by a sprayed reagent, and quantitation can be done by reflectance densitometry,[61] fluorimetry,[62] scraping off the spots and eluting the compounds which are then quantitated,[48,63] or by labeled materials. Appendix 3 presents some representative TLC systems.

In addition, Van Peteghem and Heyndrickx[64] have separated the methyl esters of 2,4-D, 2,4-DB, 2,4-DP, MCPA, MCPB, MCPP, 2,4,5-T, Silvex, and 2,4,5-TB on Kieselgel G plates using two solvent systems and silver nitrate/UV light as the visualizing agent. In addition, they also nitrated the acids and detected the nitro group in the separated compounds. Sakagami has also utilized polyamide layers to separate nine phenoxy acids.[65]

The most recent advance is the availability of extremely sensitive visualizing agents. Thus, Meinard[66] used 4 g of chromotropic acid (1,8-dihydroxynaphthalene-3,6-disul-

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fonate) in 56 g of sulfuric acid in 40 g of water as a spray to detect 50 ng of 2,4-D or MCPA and 100 ng of 2,4,5-T. An even more sensitive reagent has been recently utilized by Duenges,[67] who synthesized the 4-bromomethyl-7-methoxy-coumarin (Mmc) ester of 2,4-D; its fluorescence allowed detection of 200 pg. A spray solution of 0.05% fisetin in isopropanol causes the phenoxys to fluoresce yellow with a sensitivity of 100 ng;[68] this reagent can be used for carbamates, phosphates, triazines, and sulfoxides, as well as chlorinated compounds. A survey of reagents and instrumental techniques to detect electron donor-acceptor complexes of pesticides at the microgram level is also available.[69]

TLC has been used for study of phenoxys in formulations,[70-71] milk, meat and tissues,[72] bees,[73], water,[74-76] soil,[78] and urine.[48]

C. Paper Chromatography

This has been largely superseded by TLC, since MCPB and 2,4-DB or MCPA and 2,4,5-T are difficult to resolve. Many of the solvent systems and visualization agents employed in TLC were adapted from paper chromatography. The work[79-83] of Mitchell placed research in paper chromatography of pesticides on a sound footing, and Appendix 4 summarizes the major solvent systems and visualizing agents utilized. Another visualizing agent that has been used is methyl yellow.[84] Paper chromatography gives good results only if extraneous material is kept to a minimum. Numerous solvent systems have been utilized for the phenoxys[85-87] (see Appendix 4). TLC and paper chromatography for the phenoxys have been compared.[87,88] The effects of substituent groupings on the paper chromatographic behavior of the various phenoxyacetic acids were investigated by Bark and Graham[89,90] utilizing *n*-BuOH/H_2O and *n*-BuOH saturated with 1.5 *N* NH_3/H_2O. It was found that chlorine-containing acids adsorbed via the phenoxy group and the chlorine, except for acids with chlorines at the 2 and 6 positions of the ring which adsorbed through the phenoxy group alone. It was further noted that the greater the H bonding of the solvent, the greater was the adsorption and the smaller were the R_f values.

D. Column Chromatography

This technique is frequently used in the cleanup of the large quantities of material, and specific procedures will be given later. Here, we shall concentrate our attention on applications where it is used as the final step before quantitation.

High performance liquid chromatography (HPLC) now appears much more inviting than it did a few years ago. The stationary phases are more efficient, and detectors sensitive to the picogram level are now available.[104] Comparatively little HPLC work has been reported for the phenoxys, and these involved UV detection.[91-92] A recent method[91] involves the separation of 2-, 4-, 2,4-, and 2,4,5- chlorinated phenoxyacetic acids on a reversed-phase 45 × 0.236 cm XAD-2 column, pore size 45 to 65 μm of weight, 710 mg, at a flow rate of 0.5 mℓ/min using buffers (phosphate below pH5, carbonate above pH 8.5) in 50% ethanol. 2- and 4-CPA can be separated from their phenols using 0.1 *M* NaOH in 20% ethanol pumped into 20 mℓ of 0.1 *M* $NaHCO_3$ in 20% ethanol at 0.5 mℓ/min; 2,4-D and 2,4,5-T can be separated from their phenols by 0.1 *N* $NaHCO_3$ in 20% acetonitrile at 0.6 mℓ/min, although the separation of 2,4-D and 2,4,5-T is not good. At a fixed amount of ethanol, lowering the pH increases the resolution, as does decreasing the ethanol content at pH 9.4. Thus, 0.1 *M* $NaHCO_3$ in 10% ethanol at 0.5 mℓ/min separates the free acids. Addition of salt also increases resolution. Another method[92] uses separation on Partisil® 5 using 92.5:7.5 *n*-hexane/acetic acid, but prior cleanup must be done. Recoveries were ∿76% for 2,4,5-T and 94% for 2,4-DB.

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A HPLC method is now[93,94] the official method for 2,4-D (and will be extended probably to the other acids) in the official methods of the Association of Official Analytical Chemists, replacing the total chlorine and titrative procedures formerly used.[95] All esters, amine salts, and acids are converted to the potassium salts which are protonated and then chromatographed on a reversed-phase column and detected at 280 nm.

Official Method for 2,4-D[93,94]

Eluant — Mix millipored (0.4 μm) acetonitrile and deionized water in a ratio of 1:4 and standard NaOH, so that the final molarity of the NaOH is 0.3 *M*. Add phosphoric acid to adjust the pH to 2.95. Replace the eluant after approximately 200 injections per liter.

Saponification-internal standard solution — Add 4 g of *p*-bromophenol to KOH in 2:1 isopropanol/H_2O, so that the final concentration of the KOH is 0.2 *M*.

2,4-D standard solution — Weigh accurately 300 mg 2,4-D (99%+) previously dried 15 min at 100°C into a 1- or 2-oz glass vial with a polyethylene-lined screwcap. Pipette in 25 mℓ of the saponification-internal standard solution; shake or stir (teflon-bar) 15 min.

Sample preparation — Accurately weigh approximately 300 mg of the sample into the same type of 1 or 2-oz vial as above. Adjust the isopropanol/H_2O ratio to dissolve the sample after the 15-min shaking or stirring time, e.g., 1:1 for amine salt formulations.

Liquid chromatograph conditions — 5000 psi pressure gauge; line filter in eluant reservoir; 10-mV full-scale deflection strip chart recorder. Chart speed, 0.2 cm/min; eluant flow rate, 0.9 to 3.0 mℓ/min; detector sensitivity, 0.64 A unit full scale at 280 nm; temperature, ambient; injection valve volume, 10 $\mu\ell$.

Liquid chromatographic column — Number 316 stainless steel, 250 × 4.6 ID mm Partisil® 10-μm ODS column with 50 × 4.6 10 mm Co: Pell ODS pellicular guard column (Numbers 6526-124 and 6561-404, respectively, Whatman Inc.). Regenerate, if necessary, by pumping acetonitrile through the column until the baseline is stable. If peaks "tail", repack the first 5 mm of the guard and main columns with Co: Pell ODS.

This procedure has been tested on a collaborative basis by nine laboratories using various formulations of 2,4-D.[96]

Since Kirkland described the first high-performance columns,[97,98] the major problem in LC work has been detector sensitivity, since column technology is now adequate.[99] Use of the fluorescence detector has enabled femtogram quantities to be detected in susceptible compounds.[99] No chlorophenoxys have been quantitated in this way, but the 4-bromomethyl-7-methoxy-coumarin (Mmc) esters should be suitable, especially as their reaction with 2,4-D is quantitative. These esters have been detected at the 200-pg level on TLC plates.[67] The inexpensive and simple electrochemical detector (LCEC) probably is the most promising.[100,101] The halophenoxys need to be derivatized, since they are relatively stable to oxidation or reduction, although the latter is easier. The acids can easily be derivatized to an alkyl amide (probably best by Schotten-Baumann techniques, see Chapter 2) or hydrolyzed to a phenol which will be susceptible to LCEC detection. LC/MS is now also a possibility,[102-107] and Finnegan Instruments has now produced the first commercial LC/MS interface (1978).[107] As in GC, the identities of suspected compounds need to be confirmed, especially if legal action is contemplated, and MS is by far the most sensitive accessible spectroscopic technique. Other means of detection, e.g., polarography, microcalorimetry, refractometry, and flame ionization are generally not sensitive enough for residue work. LC/IR or LC/^{13}C-NMR are possibilities which may bear development.

E. Colorimetry

Spectrophotometry has been previously considered in Chapter 1. In general, the acids cannot be distinguished. There is only microgram sensitivity, and they all absorb near the same wavelengths, <290 nm. UV detection is subject to many interferences. Nevertheless, it is still useful as a general detection technique, as long as suspected

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compounds are chromatographed and confirmed, e.g., the official method of the Association of Official Analytical Chemists utilizes it, as have many others.[108-114]

Colorimetry involves the synthesis of colored derivatives which can then be detected at a specific λ_{max}. These methods can be made specific and extremely sensitive (to parts per billion levels), but unfortunately there are no specific color tests for the phenoxys as a class. Appendix 5 presents a short summary of work which utilizes this method of detection. The earliest methods used chromotropic acid (1,8-dihydroxynaphthalene-3,6-disulfonic aicd) in concentrated sulfuric acid for the phenoxyacetic acids and the method depends on the evolution of formaldehyde from only the phenoxyacetic acids to produce the characteristic wine-colored product.[115,116] Thus, any compounds which evolve formaldehyde will interfere, and the propionic and butyric acids do not react. Aly and Faust showed that the related J acid (6-amino-1-naphthol-3-sulfonic acid) and phenyl-J acid (6-anilino-1-naphthol-3-sulfonic acid) gave similar reactions with 1.5 and 2.5 times the sensitivity of chromotropic acid, respectively. Again, the butyric and propionic acids do not react. A method applicable to all the phenoxy acids was devised by Marquardt and Luce[118,119] in which the ether linkage is cleaved by pyridine hydrochloride and the released phenol is determined colorimetrically after reaction with 4-aminoantipyrine and potassium ferricyanide. Unfortunately, the reaction occurs only at 200°C, and phenolic impurities will interfere. The sensitivity was ∿50 ng, similar to that for chromotropic acid. Esters have been detected by their hydroxamate - Fe III complexes,[120] but the sensitivity is low. Amine salts have been quantitated by reaction with butyl rhodamine or $FeCl_3$/HCl.[121]

The phenoxyacetic acids also interfere in the estimation of monochloroacetic acid by the thioindigo method.[122]

F. Other Detection and Separation Methods

The fluorescence and phosphorescence of the phenoxys has already been considered in Chapter 1, and reference has been made to the fluorescence capabilities of the 4-bromomethyl-7-methoxy-coumarin esters.[67] Guilbault and Sardar[123] showed that 2,4-D could be measured by lipase inhibition, using a fluorescence measurement of 4-methylumbelliferone produced by the action of porcine lipase on the corresponding nonfluorescent heptanoate. The sensitivity is in the parts per billion range. Organophosphorus compounds interfere. This fluorescent method was first used on TLC plate visualization by Abbott et al.[88]

An ion-selective electrode for 2,4-D was recently constructed by embedding tetrazolium salts in a liquid membrane, using nitrobenzene solvent.[124] The response is a constant in the pH range 6 to 10, and in the presence of other nonchlorinated acid anions present in tenfold excess. However, other chlorinated aromatic acids do interfere. The sensitivity is $\sim 10^{-4}$ *M* and is suitable for formulation analysis.

Isotope dilution analysis has been used[125] for 2,4-D, 2,4,5-T, 2-CPA, 4-CPA, 2,6-D, 2,4,6-T, 2,5-D, 2,3,6-T, 2,3,4,6-tetra P, MCPA, and homolog analysis in formulations and was precise to ±2% at the milligram level. Unfortunately, ^{36}Cl used in the procedure is expensive. Gutnick and Zweig[120] labeled 2,4-D, 2,4,5-T, and 4-CPA by reacting them with ^{14}C-diazomethane. The elution of the radioactivity on a GC column was almost quantitative (approximately 95%) and proved to be more sensitive (∿500 ng) than hydroxamate - Fe III colorimetry or thermal conductivity GC or GC-microcoulometry. Lopez-Gonzalez and Gonzalez Gomez[126] also utilized ^{14}C-labeled 2,4-D for quantitation purposes.

Other newer detection systems utilized for the phenoxy acids include Laser Raman spectroscopy[127] which is at present sensitive to 500 ppm, X-ray fluorescence[128] (sensitive to 1.12 kg/ha of area), and could be utilized to analyze eluants of the alkali salts from LC columns; plasma chromatography[129] which though sensitive to picogram lev-

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els is not very good for identification; polarography of nitrated 2,4-D[130] which has also been reviewed by Milicevic et al.[131] and further investigated by Hance[132] and refractive index detection[133] which is very insensitive.

Gel electrophoresis at pH 3.7[134] of the 2,4-D anion and paper electrophoresis (pH 5.6, 300 V)[87,135] have also been utilized, with the visualization agents common with TLC and paper chromatography. These methods are reputed to be more sensitive than paper chromatography or TLC, and resolution is better.

Titrative methods have been long used[111,136-147] for formulation analysis. The method is not very specific, since all the phenoxys are quantitated, and unless curves are actually plotted, the chlorophenols could also be included. The chlorophenols can be removed by extracting the aqueous acidified solution with *n*-hexane or petroleum ether.[111] The phenoxy acids can then be extracted by ether and, after evaporation of the solvent, titrated or backtitrated.

Plant bioassay techniques have been much used for analytical research,[148-163] e.g., cucumber root[149] (sensitive to 5 ppb), *Sorghum vulgare* root elongation,[150-152] oat (*Sativa*) root elongation,[153] *Chlorella pyrenoidosa*,[156] *Lemna minor*,[158,159] cotton (*Gossypium hirsutum* var *Acala*-(sensitive to 50 ng of 2,4-D via formation of cup or strap-shaped leaves),[148] the *Avena* curvature and straight-growth tests, and the pea stem curvature test.[160] Though excellent as qualitative, sensitive tests, the bioassays are much more variable and more prone to interfering variables, chemical and physical, than are the well-controlled instrumental methods. They are useful as preliminary tests for pollution.

Formulation analysis of the phenoxys has been alluded to in passing above. The residue analyst usually prefers great sensitivity at the sacrifice of accuracy, but the formulation analyst works in reverse. Titration methods,[111,136-147,221] GC methods,[111,136,137,164-166,221] LC,[93,94,96] spectrophotometry (see Chapter 1), TLC,[70-71] colorimetry[167,168] (by production of azo dyes or hydrazones), and total chlorine by the Parr Bomb technique[169] have been used. The LC and GC methods are the most specific, but the representativeness of the samples taken is the major problem. The internal standard utilized must not react with any component of the formulation. Analytical techniques for Agent Orange have also been published.[170,171]

III. EXTRACTION AND CLEANUP

The extraction of a herbicide residue is generally the initial step of an analysis. Many techniques have been used, e.g., shaking with solvents, blending, steam distillation, chemical reactions, ultrasonication etc., the type of extraction being dependent on whether free acids, esters, amine salts, alkali salts, or conjugates with proteins, sugars, lipids, etc. are present. Often the residue is extracted along with many other compounds. In general, maceration of the material with a solvent is more efficient than tumbling or Soxhlet extraction.[172] The macerated material can be further treated by ultrasonication or Soxhlet extraction.

For vegetable matter, many solvents have been used, including ether, acetone, isopropyl alcohol, water, and acidified water,[173-177] as well as mixed systems, e.g., benzene-alcohol,[172] methyl ethyl ketone-ether,[178] isopropyl alcohol-hexane,[179] water-isopropyl alcohol,[166] acidified ethanol-petroleum ether-ether,[172] chloroform-ether-acetic acid,[180] 10% alcoholic sulfuric acid-sodium chloride-water-ether-petroleum ether,[181] isopropanol-acetone,[182] and water-acetonitrile.[183] Protein-bound phenoxyacetic acids have been hydrolyzed enzymatically[181] by pepsin for milk samples[172] (compare with papain for animal studies).[184] Deproteination by phosphotungstic or phosphomolybdic acids[172,185] has also been employed. The major problem in analysis for residues in

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plants and animal tissues is that the phenoxy acid is nearly always present in conjugated form, such as a sugar glycoside or as an amino acid conjugate in plants. Thus, Allebone[186] macerated plant tissue in warm 2% acidic ethanol to obtain the free acid, esters, and some complexes in the filtrate. The plant residue insoluble in methanol was hydrolyzed in 25% NaOH for 30 min. Both fractions were cleaned up before EC/GC. Methods of analyzing plant metabolites were also the subject of a Ph.D. dissertation.[187] Chow et al.[188] showed that after 2 weeks, 40 and 100% of the residues of ^{14}C-2,4,5-T and MCPA, respectively, in wheat were in conjugated form. The surface residues were removed by a 1% $NaHCO_3$ rinse. The plants were macerated in 50% ethanol, and after clean-up and subsequent hydrolysis with H_2SO_4, extracted with ether to obtain the residues originally present as ester conjugates. Totals were also verified by alkaline hydrolysis of the macerate by 0.6 *M* NaOH and then cleanup. A two- to sevenfold increase in 2,4-D residues in potato tubers was reported when an acid hydrolysis step was inserted into the isolation scheme.[189] Acidic methanol extraction of wheat and barley before cleanup and GC/EC allowed 65 to 93% recoveries.[190] Improved recoveries (94 to 100% for 2,4,5-T and 72 to 96% for 2,4-D) were attained by Munro[191] by use of two extractions with two different buffers for tomato extracts before Kontes sweep distillation of the methyl esters and GC/EC. Although they are suitable for defining the amount of phenoxy residues, none of the above methods are suitable for elucidating the structure of plant metabolites or even answering such a simple question as is the acid free or conjugated in plants? Acid/alcohol extraction of macerates is very likely to produce esters by either esterification of free acid or by transesterification (see Chapter 2). Use of concentrated acids may hydrolyze some conjugates to the free acid, and reaction with concentrated base, in general more efficient than acid hydrolysis (see Chapter 3), produces the phenoxy salts. Hydrolysis should be done with KOH rather than NaOH, since the potassium salts of the phenoxy acids are more soluble (see Chapter 1). Feung and Hamilton et al.[192,193] have approached this problem by freezing plant callus tissue and blending in the presence of 95% ethanol, rinsing the homogenate on a Buchner with 80% ethanol, with subsequent cleanup by liquid/liquid extraction before TLC and column chromatography. The low-temperature isolation ensures minimal interference, and the advantages of TLC and column chromatography relative to GC are utilized, i.e., the compounds do not need to be derivatized into the volatile compounds necessary for GC analysis.

Extraction of the phenoxys from soils is dependent on soil type, the presence of microorganisms, etc. Early methods[3] made no provision for rupturing cells and liberating bound residues, and even today, each soil has to be considered individually.[194] An ultrasonic technique[195] gives the same amount of extraction in 30 sec as an 8-hr Soxhlet. Soil residues have also been extracted by 1:1:1 18 *N* H_2SO_4/ethanol/H_2O and 1:1 NaOH/$CHCl_3$,[196] 0.5% NaOH,[197] ether/H^+[41,88] (80 to 100% recovery), acidic acetone[190] (65 to 93% recoveries), alkaline hydrolysis,[198] 1:1 hexane/acetone and 2:1 hexane/diethyl ether,[199] acidified $CHCl_3$,[39] 0.05 *N* aq KCl/NaOH and $CHCl_3$.[74]

Many organic extraction procedures have been utilized for aqueous samples. The *p*-value concept considered in Chapter 1 is extremely useful here. Usually organic solvent extraction is followed by alkaline hydrolysis, acidification, and derivatization. Some representative liquid extraction procedures have used the following solvent systems: benzene,[200] toluene/pH 3.6 buffer,[201] ether-petroleum ether/H^+,[202] $CHCl_3$/H^+,[39,203] alkaline hydrolysis, acidification then chloroform extraction,[204] ether/NaCl/HCl,[206] 1:3 ether/$CHCl_3$ in acidified water[58,205] (100% recovery), ether/H^+,[76,111,196] methylene dichloride/H^+,[46,207] ethyl acetate/H^+,[44] and *n*-hexane/H^+ for esters,[57] with the resulting aqueous phase containing free acid and salts subjected to alkaline hydrolysis, reacidification with the free acids extracted in ether, and then derivatized for GC/EC. The

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organic extracts containing the herbicidal esters have been cleaned up by such column materials as alumina[202,213] (sometimes, difficulty is experienced in the desorption); florisil[198] (magnesium silicate) using acetonitrile/petroleum[202] or 5 and 20% diethyl ether/hexane;[198] and by silica gel (eluted by 90% methanol/10% acetic acid).[205] Direct ion exchange of the salts in water has also been tried. Amberlite XAD-4 (eluted by benzene),[43] AV 17 X8 anion exchange (sorption increased with phenoxyacetate <4-CPA < 2,4-D < 2,4,5-T anions, elution control using (m)ethanol), Amberlite XAD-2 at pH 2 (elution by acetone),[209] AN-2F anion exchange (elute by 1 *N* NaCl),[210] miscellaneous basic anion exchangers,[211] Dowex-1, Dowex-2, and 2 to 10% DVB (eluted with NaCl, Na_2SO_4).[212] Renberg[199] has published a column chromatographic method which is suitable for analysis of phenoxy residues in organic tissues, soil and water. For water samples, a 10 × 1 cm ID column filled with Sephadex QAE A-25 anion exchanger was utilized. The compounds are eluted with acidified methanol, and the acids are then extracted with benzene for EC/GC. This anion exchanger has high capacity (0.1 mg/mℓ at I = 0.1 *M*), and with appropriate prior cleanup, this final separation can be used in any analysis. Thus, soils are first extracted in 0.2 *M* NaOH, and organic tissues are homogenized in 1:2 hexane/acetone (v/v) before adding 1 *M* HCl and recovering the residues in 2:1 hexane/diethyl ether. Upon alkaline hydrolysis, the samples are ready for chromatography. This method has been used also by Tuinstra et al.[92], and Yip[214] considers it good enough to become a standard method. Counter current extraction has also been used for aqueous media and for animal tissues.[215-216] Reverse osmosis has also been employed[21,217] (only 65% retention). Problems with inorganic ions can be avoided by a prior extraction with methyl cellosolve.[123]

Urine and blood have been analyzed by techniques similar to those used for water analysis. Thus, benzene/H^+ has been utilized for urine,[48,228] and methods used for clofibrate (ethyl α,α-methyl-4-chloro phenoxy propionate) in plasma (benzene/H^+ extraction)[218-228] are also applicable for the phenoxys. 2,4-D has also been extracted from biological tissues with NaCl, using $ZnSO_4$ and alkali to clarify the solution which on acidification can be extracted with chloroform.[87] Methanol[222] and ammonium or sodium chloride[135] have also been used. 2,4-D contained in algal culture media was extracted with ether/H^+.[109] Residues in milk and forage were extracted with ether/H^+ before florisil cleanup and microcoulometric GC.[181] Autoradiography has also been used to show the distribution of phenoxys in plants.[223-226]

A. Specific Methods

The final steps in phenoxy quantitation, i.e., LC/UV detection (see Chapter 4, Section II.D), or derivatization-EC/GC (see Chapter 4, Section II.A.1) have already been given. We shall first describe two general cleanup procedures — one liquid/liquid extraction, together with an alternative EC/GC quantitation, and the other an ion-exchange method, and we shall then consider specific extraction or isolation procedures, favoring those citing recoveries. Obviously in some cases, methods will have to be adapted for specific needs.

1. Liquid/Liquid Cleanup

This method is a variant of those of Que Hee et al.[55,57,136] and Mierzwa and Witek.[43]

Initial sample — A homogeneous solution, organic or aqueous, containing free acids, esters, salts, amides of the phenoxy acids.

Method — Add an equal volume of 10 mℓ 10% NaOH or a volume of alkali so that pH >13. If an organic phase is present, evaporate the organic solvent under vacuum in the presence of the alkali. If the phase is already strongly alkaline (ph>13), no additional base is required. Reflux the aqueous alkaline solution for 20 min. Cool and extract with equal volumes of hexane or ether (× 3). This extraction removes all neutral

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compounds and any dioxins. Acidify the caustic solution with HCl (pH2 — pHydrion paper). Extract with equal volumes of benzene or ether (× 3). The method to here is approximately 91% efficient.

Derivatization — Add 1 mℓ of 2,2,2-trichloroethanol to the combined organic extract and evaporate off the solvent under vacuum. Add 1 mℓ 0.4 mℓ/mℓ freshly made up 2,2,2-trichloroethanol in trifluoroacetic anhydride and 5 μℓ of concentrated sulfuric acid, shake, and then reflux for 15 min. Cool to dispose of excess alcohol. Reduce the volume to approximately 0.1 mℓ by a nitrogen stream at room temperature, then add 2 mℓ of redistilled isooctane and 6mℓ of 0.5 *M* potassium hydroxide solution. Extract immediately. Separate the layers. Make to a known volume with isooctane. Inject 2 μℓ into an EC/GC or GC/MS. The esterification is ∼100% efficient.[43] If the EC/GC baseline is still excessively noisy, make a 4-cm bed of silica gel in a 10 × 1 cm ID pyrex column by filling with silica gel (70 to 230 mesh) in acetone. Superimpose a 1-cm layer of anhydrous sodium sulfate above the adsorbent. Wash the column with 10 mℓ of acetone and 5 mℓ of isooctane. Place a 1-mℓ volume of the isooctane extract on the column and allow the isooctane level to drop until the liquid level is almost at the top of the sodium sulfate layer. Wash the column then with 25 mℓ of isooctane. Elute the esters with 15 mℓ of benzene. The benzene eluant can be concentrated by a stream of nitrogen.

EC/GC of the 2,2,2-trichloroethyl esters — The pyrex column, 2 m × 3 mm ID is packed with 1:1 10% DC 200/15% QF-1 on 80/100 mesh Chromosorb W (AW-DMCS). The injector, column, and ^{63}Ni electron capture detector temperatures are 220, 195, and 220°C, respectively. The flow rate of nitrogen carrier is 80 mℓ/min. For ECD, a pulsating voltage of 50 V, 0.5 to 100 μsec is utilized.

Preparation of standards — Reflux 0.05 *M* phenoxy acid, 0.15 *M* ethanol in 40 mℓ of benzene together with 0.5% v/v concentrated sulfuric acid, so that product water is removed by a Dean Stark trap. Continue the reaction until no more water is evolved. Cool. Neutralize with $NaHCO_3$ (no bubbling), wash with water, dry over anhydrous sodium sulfate, and concentrate the solution to approximately 10 mℓ. Inject an aliquot into a thermal conductivity GC with the above GC column and at the above conditions and collect the pure esters in a preweighed capillary tube. Identify via spectroscopic means and make up the desired concentrations in isooctane. Preparative GC as detailed by Mierzwa and Witek[43] can also be carried out.

Comments — If the esterification reaction solution darkens, the sample requires more rigorous cleanup before esterification. This can be accomplished by acidifying to pH2 with H_2SO_4 instead of HCl and then passing the solution through a 6-cm Amberlite XAD-4 bed (0.3 to 0.7 mm) in a pyrex column (10 × 1 cm) at 15 mℓ/min. Dry the sorbent in a stream of nitrogen at room temperature. Elute the phenoxy acids by 40 mℓ benzene at approximately 5 mℓ/min. Evaporate the benzene ≤40°C under vacuum and remove the residue with at least three 2-mℓ portions of acetone. Evaporate the acetone washings to dryness at room temperature (N_2). Esterify the residue as above or as desired. The recovery for this step is 92%.[43]

Clearly if one wants maximum GC/EC sensitivity, either the above method or the pentafluorobenzyl ester derivatization method can be used. The latter can be utilized simply by evaporating the final benzene, ether, or acetone extract obtained at the end of the cleanup procedure to dryness and proceeding with the method outlined in Section II.A.1. These methods have not been compared, but the chloroalkyl esters do give diagnostic molecular ions in their mass spectra whereas the pentafluorobenzyl esters do not.

The technique using 2,2,2-trichloroethyl esters via EC/GC is 100 times more sensitive than the 2-chloroethyl esters which allow at least an order of magnitude greater sensitivity than the alkyl esters. If less sensitivity is desired, *n*-butylation as set out in Chapter 2, Section II.A.1 is adequate (97% efficiency).

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2. Ion Exchange Cleanup

This is based on a method first developed by Renberg.[199]

Initial sample — Salts of the phenoxy acids, either naturally in samples or by result of hydrolysis of esters, amides, and acids in 0.1 *M* NaOH.

Ion exchanger — Mix together equal volumes of 0.2 *M* HCl and 0.2 *M* KCl. Let the Sephadex® QAE A-25 anion exchanger swell in distilled water for 2 hr before use. Transfer a 3-mℓ bed volume of exchanger into a centrifuge tube (approximately 3 mℓ per 3-mℓ sample). Centrifuge. Discard the water. Add 3 mℓ of the basic extract (0.2 *M* NaOH) and 3 mℓ benzene. Shake for 5 min. Centrifuge and discard the liquid phase. Add three 3 mℓ of distilled water. Shake the tube for 30 sec. Centrifuge. Discard the water. Add 3 mℓ of benzene (with internal standard) and 3 mℓ of 1:1 0.2 *M* HCl/KCl. Shake for 5 min and transfer the benzene phase into a graduated test tube. Evaporate the benzene. Derivatize as desired. The recovery of 2,4-D was >97%, using fortified samples.

3. Extraction from Formulations

Tbe liquid chromatography method of the Official Analytical Chemists given in Chapter IV, Section II.D can be used.

Shake all formulations well before sampling.

Ester formulations can be analyzed[136] by first saturating a 10-mℓ aqueous emulsion containing 0.10 mℓ of the ester formulation (acid equivalent ~0.8 g/mℓ) with sodium chloride and extracting with equal volumes of acetonitrile (× 5). This enables separation of the esters from the surfactants often found in ester formulations. The efficiency of extraction is 99%. Add 10 mℓ of 10% NaOH and evaporate off the acetonitrile and continue with either of the cleanups above. For FID/GC - EC/GC, 20% BF_3/*n*-butanol (see Chapter 2, Section II.A) can be used as the esterifying agent, since extreme sensitivity is not required.

Amine salt solutions can be treated directly by the method in Section III.A.1. If LC is contemplated, the organic solvent extraction of the hydrolyzed alkaline solution as in this method is recommended before continuing with the rest of the Official Method. This separates out the free amines.

4. Plants

a. Surface Residues

Use 1% sodium bicarbonate solution for free acids and short chain amine salts.[188] The rest of the method in Section II.H.1 from the extraction of the alkaline solution onwards should be carried out. The long chain amine salts[227] and the esters can be washed off with neutral histological xylene, and the method of Section II.H.1 applied. The ion-exchange method is greatly improved if the organic solvent extraction after alkaline hydrolysis is done prior to addition of resin.

b. Whole Plants[188]

Macerate 25 g of plant tissue (plant, cut peel, callus, fruit flesh, and vegetable flesh) in a food blender with 125 mℓ of water. Transfer to a 400-mℓ beaker. Add 25 mℓ of 0.6 *M* sodium hydroxide. If plant juice or liquid is the starting fluid just add the alkaline solution. Reflux or heat on a steam bath for 2 hr. Filter and wash the filter cake with 100 mℓ of water. Combine the filtrates. Suspend the filter cake in 100 mℓ of 2 *M* HCl. Reflux or heat on a steam bath for 2 hr. Extract with equal volumes of ether (× 3). Combine these with the filtrate. Continue with the method in Section III.A.1. The above acid hydrolysis is done in case there are conjugates resistant to alkaline hydrolysis. The recovery of the above using only the alkaline hydrolysis was greater than 89 to 92% with ^{14}C-labeled material.

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Should the final organic extract in the methods in Sections III.A.1 and 2 still contain colored plant pigments, extract with pH 6.2 phosphate buffer (4 × 50 mℓ) to remove moderately strong acids.[186] Acidify the aqueous phase to pH 1 (HCl) and extract with ether (4 × 50 mℓ). Evaporate off the ether and derivatize as desired. Recoveries are still 80 to 96%.

Should a separation of conjugates and 2,4-D low molecular weight compounds be required, do the following:[186] macerate 20 g of plant material in MeOH/concentrated HCl (100:2 mℓ) three times in a Waring blender for 4 min, filtering between each extraction. Wash the residue with water until the washings are nonacidic (pH paper). The solid residue is an off-white powder. Reflux with 20 mℓ 25% sodium hydroxide for 30 min, filter, and acidify the brownish solution with HCl. This fraction contains 2,4-D from conjugated residues. Combine the original methanolic/HCl extracts and concentrate to ~20 mℓ under reduced pressure. Reflux with 25% sodium hydroxide (20 mℓ) for 30 min to hydrolyze 2,4-D low molecular weight compounds, e.g., esters, amides etc. Acidify with HCl. Extract both HCl solutions with ether, benzene, or chloroform, as required for the particular further cleanup or derivatization. Recoveries are 80 to 96%. Both HCl fractions can be combined if the total 2,4-D is desired.

If the GC or LC chromatogram is still noisy, Allebone and Hamilton[186] recommend silica gel TLC (0.25-mm layer), elution with benzene, benzene evaporation, addition of 3 mℓ of chloroform, placing the solution into a Hirsch tube with Adams' catalyst (Pd/PdO_2, 10 mℓ), and bubbling hydrogen in so as to agitate the catalyst over a period of 12 hr. Vent the hydrogenation products which are the saturated analogues of unsaturated plant pigments. The sensitivity is raised to 40 ppb with 80 to 96% recovery, and GC/EC chromatograms are much cleaner.

c. Metabolites in Plants

The stringent initial analysis conditions necessary in general for residue determination are inappropriate for metabolite identification. Clearly, the problem of degradation whenever tissues are macerated, blended, or reacted upon is difficult to assess. Radiolabeled ^{14}C compounds are best used to locate the most important fractions on separation; otherwise the analysis will become interminable. The following method has been developed by Hamilton et al.[193] and Feung et al.[192,229,230] to analyze for various metabolites.

Use ^{14}C-labeled 2,4-D (2.44 to 21.1 mCi/mmol) at the 1,2, or ring positions, depending on the study desired.

For leaf experiments, apply 10 μℓ of an ethanolic solution of 2,4-D containing 0.5% Tween-20 on the midvein of each primary leaf. Confine each treated area with vasoline and discard prior to processing of the leaf. Stems can be injected at the primary leaf axis by use of small glass capillary tubes (10 μℓ of ^{14}C-2,4-D in 95% ethanol 0.075 μCi per plant; 2,44 mCi/mmol), but only at those capillaries at which uptake of water is observed. Excised roots have first to be surface sterilized with 5% hydrogen peroxide and then shaken with ^{14}C-2,4-D for 6 to 8 hr. The roots must be washed copiously with distilled water prior to extraction. Callus tissue (10 g) in autoclaved nutrient medium should have 1 μCi of ^{14}C-2,4-D (2.44 mCi/m*M*) added via a few microliters of 95% ethanol and incubated for 2 days at room temperature. Filter under suction and rinse copiously with cold distilled water. Keep all washings. Store all weighed tissues in plastic bags at −20°C.

The following procedure can be used for all tissues. Grind the frozen tissues in a Waring Blendor® with 95% ethanol (the low temperature also ensures negligible transesterification, as well as minimizing metabolite degradation), filter with suction, and wash the residue with 80% ethanol until it becomes off-white/greyish. Store the residue at −20°C. Concentrate the ethanol-soluble fraction in vacuo, adjust the pH to 3

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(H_3PO_4), and extract with equal volumes of diethyl ether (× 4). Store the aqueous phase at −20°C. The ether phase contains mostly aglycones of the hydroxylated metabolites. Extract into equal volumes of 5% sodium bicarbonate (× 4). Store the spent ether phase at −20°C. Acidify the bicarbonate solution to pH 3 (H_3PO_4) and reextract into equal volumes of ether (× 3). Store the spent acidified bicarbonate solution at −20°C. Concentrate the combined ether extracts. Perform TLC on Adsorbosil-2 silica gel plates (0.25 mm) developed with anhydrous diethyl ether/petroleum ether (37 to 46.2°C)/formic acid (50:50:2,A), benzene/dioxane/acetic acid (90:25:4,B), isopropyl alcohol/NH_3/water (8:1:1,C). Paper chromatography is performed with ethanol/NH_3/H_2O (80:4:16,D), *n*-butanol/ethanol/3NNH_3 (4:1:5,E) on Whatman Number 1. Locate the spots by radiochromatogram scanning or autoradiography. Synthesize the hydroxylated metabolites as given in Hamilton et al.[193] and run the metabolites and standards on Silica Gel G TLC plates (0.25 mm) (which should be activated by prior heating for 2 hr at 140°C), using solvent A. Resolve by ascending paper chromatography (Whatman 3MM) using solvents C and D. Visualize by spraying with freshly made diazotized sulfanilic acid in 1 *N* HCl; then spray with 10% sodium carbonate. The spots can also be eluted (50% ethanol) and identified by mass spectroscopy after concentration.

Take the aqueous phase from the first ether extraction and extract with equal volumes of 1-butanol (× 4). Store the aqueous solution at −20°C. Concentrate the 1-butanol extracts to dryness under vacuo ≤40°C and dissolve the residue in 5 mℓ of distilled deionized water. Place the concentrate on a Biogel P-2 column bed 1.5 × 25 cm, eluting with 10 mℓ water. Incubate 25 mℓ of the aqueous eluate at pH 6.7 (H_3PO_4) with 0.7 mg/mℓ of emulsin (β-glucosidase) for 5 hr at 37°C. Acidify the pH3 (H_3PO_4) and extract with equal volumes of diethyl ether (× 4). Store the aqueous layer at −25°C. Concentrate the ether extracts down to approximately 6 mℓ. Resolve the components of the ether extract by using six TLC and one paper chromatographic solvent systems (see Table 3) and the relevant purified synthesized standards (Feung et al.[230] and Wood and Fontaine[231]) and their R_f values (see Table 3). The metabolites are detected by autoradiography and the standards by the diazotized sulfanilic acid spray. The spots can also be eluted with 50% ethanol, concentrated, and taken up with 95% ethanol for mass spectral analysis (see Chapter 1, Appendix 25). The TLC adsorbent was Supelcosil 12A (0.25 mm) with a zinc phosphor. Descending paper chromatography on Whatman Number 1 was also employed (see Table 3).

Probably, the amino acid conjugates could be detected at great sensitivity with LCEC or by LC/MS, and possibly this is likely where the future analytical advances will be made. All the stored fractions which contain comparatively little of the radioactivity can be subjected to TLC, paper chromatography, or HPLC. The task of elucidating the identification of these fractions (approximately 20 to 25% of total activity) has not yet been attempted.

The type of ^{14}C-2,4-D mass balance (approximately 70%) obtained for stem injected bean plants is found in Figure 1.[193] The amino acid conjugates in the *l*-butanol extract comprised ∼7 to 13% of the total extracted radioactivity, the latter being half that stem injected. The first ether extract contains mostly 2,4-D and aglycones (mostly 4-hydroxy-2,5-D), but the content is time dependent (see Figure 2). In contrast, nearly 70 to 76% of the incubated label in soybean callus tissue solution is contained after 48 hr in the first ether extract (see Figure 3), 50% of the applied 2,4-D being present as a 2,4-D-glutamate conjugate. This topic will be discussed in greater detail in Volume II.

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Table 3
R_f VALUES OF AMINO ACID CONJUGATES OF 2,4-D[230]

2,4-D Conjugate	Solvent system[a] TLC I	II	III	IV	V	VI	% VII
Gly	0.00	0.27	0.00	0.17	0.00	0.80	0.68
Ala	0.35	0.33	0.48	0.20	0.54	0.77	0.74
Ser	0.14	0.17	0.12	0.11	0.35	0.73	0.65
Pro	0.29	0.33	0.20	0.22	0.45	0.68	0.73
Val	0.36	0.39	0.52	0.27	0.50	0.74	0.79
Thr	0.19	0.25	0.17	0.13	0.35	0.69	0.69
Cys	0.34	0.08	0.42	0.07	0.36	0.76	0.59
Leu	0.40	0.42	0.56	0.29	0.58	0.75	0.82
Ile	0.42	0.43	0.56	0.27	0.58	0.74	0.82
Hyp	0.06	0.16	0.05	0.10	0.33	0.65	0.64
Asp	0.17	0.01	0.26	0.03	0.31	0.71	0.36
Lys	0.00	0.04	0.00	0.01	0.05	0.20	0.65
Glu	0.13	0.02	0.21	0.03	0.30	0.71	0.43
Met	0.37	0.43	0.47	0.28	0.51	0.74	0.74
His	0.00	0.15	0.00	0.08	0.03	0.20	0.61
Phe	0.33	0.37	0.49	0.25	0.49	0.74	0.80
Arg	0.00	0.07	0.00	0.03	0.01	0.23	0.76
Tyr	0.20	0.24	0.27	0.15	0.38	0.74	0.75
Trp	0.27	0.28	0.32	0.18	0.42	0.80	0.80
Cys	0.17	0.10	0.45	0.07	0.37	0.82	0.60
2,4 D	0.45	0.28	0.70	0.22	0.56	0.80	0.75

[a] I. benzene-dioxane-formic acid (90:25:2, v/v/v); II. chloroform-methanol-concentrated ammonium hydroxide (70:35:2, v/v/v); III. diethyl ether-petroleum ether (60-70)-formic acid (70:30:2, v/v/v); IV. benzene-triethylamine-methanol-concentrated ammonium hydroxide (85:15:20:2, by volume); V. benzene-methanol-cyclohexane-formic acid (80:10:20:2, by volume); VI. 1-butanol-acetic acid-water (90:20:10, v/v/v); and VII. 1-butanol-95% ethanol-3 *N* ammonium hydroxide (4:1:5, v/v/v).

5. Foods

a. Citrus Fruit

Erickson and Hield[175] first gave the basic method to extract phenoxy residues from citrus fruit. The following is a modification of this method.

Grind 100 to 250 g of chopped fruit in a Waring Blendor® with 100 to 250 mℓ of acetone. Transfer to a liter flask and reflux for 10 min. Cool and filter under suction. Regrind the pulp in fresh acetone as before. Combine the acetone extracts and cleanup as per the method in Section III.A.1 and derivatize. This gives 2,4-D originally in the form of free acid and esters, etc., but not as large conjugates.

Add 100 mℓ 10% NaOH to the extracted pulp (pectic substances) and reflux for 1 hr. Continue the cleanup procedure in the method in Section III.A.1 and derivatize. This gives the 2,4-D in conjugate form.

Originally, Erickson and Hield differentiated between esters and free acid, and although the recovery of fortified isopropyl ester of 2,4-D was ~96%, this was really the inappropriate fortification substance, since 2,4-D often exists as conjugates larger than alkyl esters. Fortification should be with radiolabeled 2,4-D as it was sprayed in

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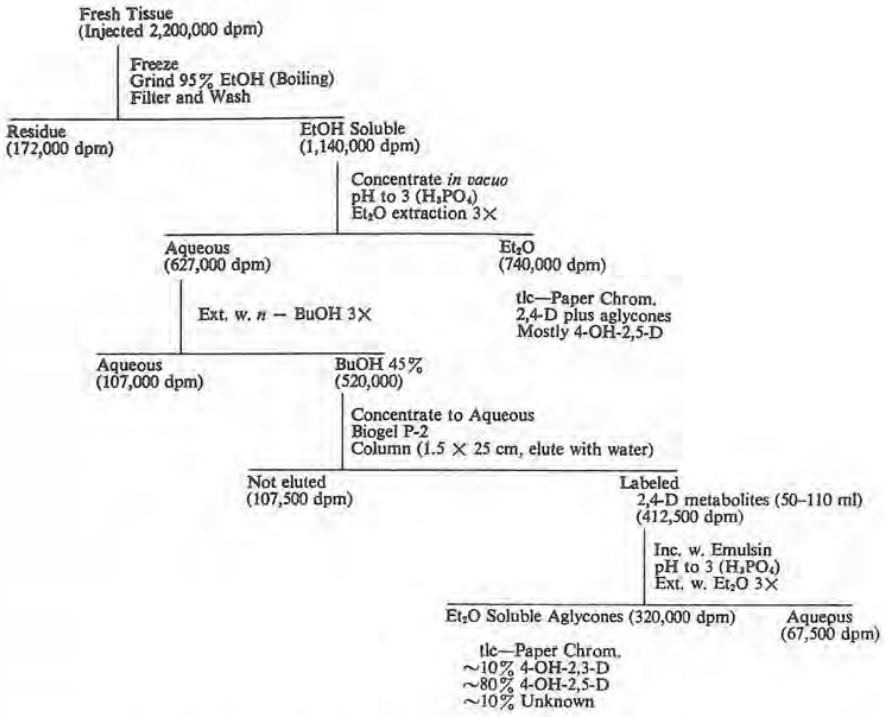


FIGURE 1. Flow diagram for the standard extraction procedure and radioactivity found in various fractions from 48-hr, 2,4-D-1-^{14}C stem-injected bean plants. (Reprinted with permission from Hamilton, R. H., Hurter, J., Hall, J. K., and Ercegovich, C. D., *J. Agric. Food Chem.*, 19, 480, 1971. Copyright by the American Chemical Society.)

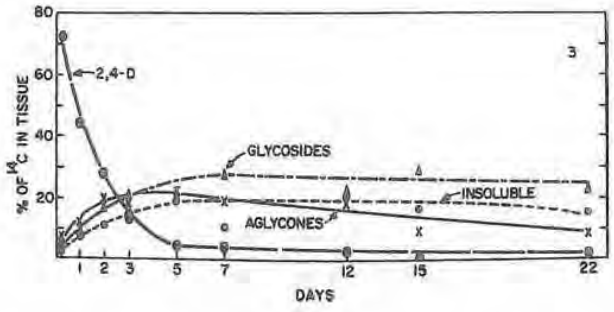


FIGURE 2. Changes in the percent of total ^{14}C found in various substances or fractions following stem injection of 14-day-old bean plants with 2,4-D-1-^{14}C. A total of 15 plants were extracted and fractionated as indicated above in Figure 1 after each time interval. (Reprinted with permission from Hamilton, R. H., Hurter, J., Hall, J. K., and Ercegovich, C. D., *J. Agric. Food Chem.*, 19, 480, 1971. Copyright by the American Chemical Society.)

the same form and allowed to metabolize, according to the methods by Hamilton et al.[193,229] for plants and callus tissues.

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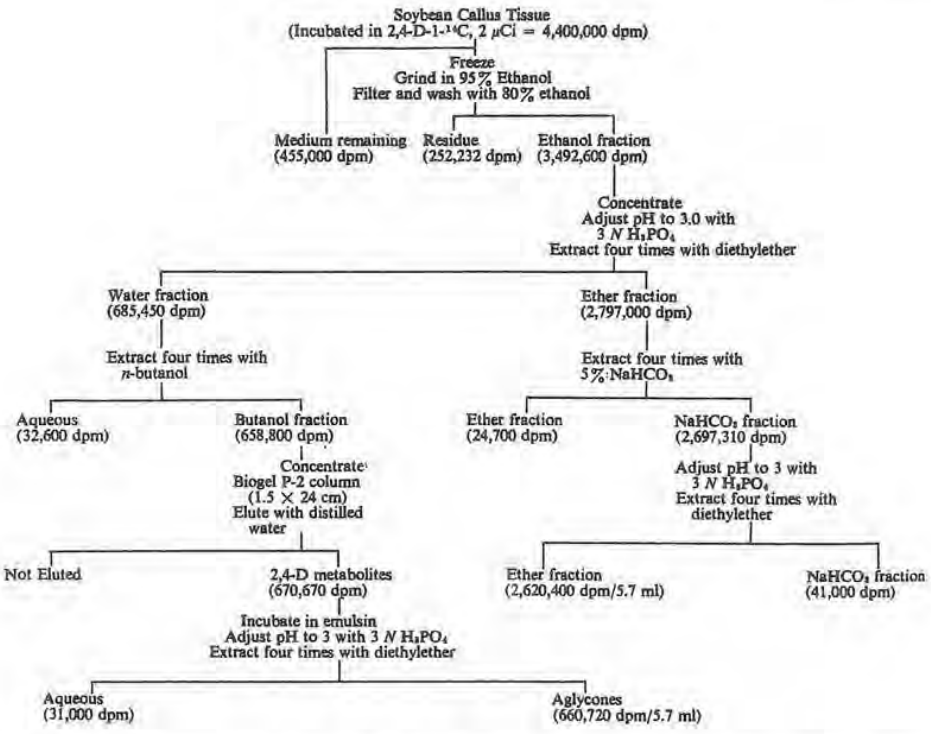


FIGURE 3. The extraction procedure and radioactivity in various fractions from soybean cotyledon callus after a 48-hr incubation in 2,4-D-1-¹⁴C. (Reprinted with permission from Feung, C. S., Hamilton, R. H. and Witham, F. H., *J. Agric. Food Chem.*, 19, 475, 1971. Copyright by the American Chemical Society.)

b. Milk

This extraction method was utilized by Storrs and Burchfield.[232] Hydrolyze 350 mℓ of frozen-then-thawed milk with 4.5 mℓ of HCl and 2 g pepsin. Swirl until all pepsin is dissolved. Cover the flask mouth with Saran wrap and shake slowly for 15 hr at 40°C. Then add 50 g anhydrous sodium sulfate. Boil for 2 min and cool. Extract with diethyl ether in a liquid/liquid extractor for 20 hr. Dry the ether extract over 10 to 15 g magnesium sulfate (first washed with an ether solution of *p*-toluene sulfonic acid, then washed with dry ether until neutral and dried before use). Filter (Whatman Number 2), wash the residue copiously, and evaporate in a stream of nitrogen ≤65°C. Extract the residue with 4 × 25 mℓ *n*-hexane, then 4 × 25 mℓ acetonitrile, and combine both extracts and shake. Discard the upper hexane phase containing lipids. Wash the acetonitrile solution with *n*-hexane (4 × 50 mℓ) discarding the upper layers. Continue then with the method in Section III.A.1.

Internal standards, e.g., 4-chloro- and 2-chloro-4-bromo-phenoxyacetic acids, must be used, since there is no cited recovery, and sometimes putrified milk contains substances that bind 2,4-D and any added internal standards.

A second, more-modern, method is based on one by LeRoy Bjerke et al.[50]

Separate the cream from the milk on a De Laval Model 100 electric farm separator adjusted to give medium heavy cream. Freeze the samples until analysis.

Rethaw and add 1 mℓ concentrated phosphoric (for MCPA) or sulfuric acid (for 2,4-D, 2,4,5-T) acid to 10 g of milk and reflux for 30 min and cool. Add 4 g of NaCl and 15 mℓ diethyl ether. Shake the capped sample for 5 min and centrifuge. Transfer

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the ether phase to a 1-g Woelm acidic alumina bed activity Grade I, in a 17 cm × 10 mm ID lipid chromatographic tube equipped with a coarse sintered glass disc. Collect the ether effluent. Extract the milk with 10 mℓ ether (× 4) and each time transfer the ether to the column and collect. Finally wash the column with 10 mℓ of diethyl ether. Apply the method in Section III.A.1 to the aqueous extracted residue to determine 2,4-D conjugates, ensuring excess alkali is present initially.

Add 5 mℓ 1 *N* NaOH to the combined column effluent, shake, and evaporate the ether. Reflux for 20 min and extract with ether (3 × 10 mℓ). Add 1 mℓ concentrated H_3PO_4, 4 g of NaCl, and 10 mℓ of benzene to the alkaline phase. Shake 3 min and centrifuge. Inject 2 μℓ of the benzene phase into the GC column of the method in Section III.A.1 at column temperature 150°C to determine the chlorophenols. Elute the alumina column with 20 mℓ of 0.25% $NaHCO_3$. Acidify with 0.5 mℓ of concentrated H_3PO_4 and add 4 g of NaCl. Extract with ether (5 × 10 mℓ). Add 1 mℓ of the appropriate alcohol, evaporate the ether, and derivatize as desired. Recoveries of fortified samples of 2,4-D, 2,4-dichlorophenol, 2,4,5-T, 2,4,5-trichlorophenol, Silvex, MCPA, 2-methyl-4-chlorophenol were 93, 88, 90, 88, 91, 89, and 79%, respectively.

For cream, dilute the 10-g samples with 5 mℓ of water before beginning the procedure.

This second method is faster and more convenient than the first, but the fortification procedure is based again on the assumption that no 2,4-D conjugates are present. Thus, a comparison of the two methods should be done on the same milk or the alkaline hydrolysis of the aqueous phase of the first acidified hydrolysate evaluated.

c. Flour

This method is based on one by Zero.[233]

Extract 2 g of flour suspended in acidified water (pH 2) with diethyl ether (5 × 10 mℓ). Subject the combined ether extracts to the method in Section III.A.1. Add excess 10% NaOH to the aqueous phase until the pH >13. Continue with the method in Section III.A.1.

6. Soil

This method has been used by Renberg.[199]

Shake the sample with 0.2 *M* NaOH (4 mℓ/g soil) for 30 min and centrifuge. Remove the basic solution. Repeat this procedure two more times. Combine the basic supernatants and proceed as per the methods in Sections II.A.1 and 2. Recoveries are ~74 to 84% using only the alkaline extraction. To ensure complete characterization, add 4 mℓ of water per 1 g of soil, add H_2SO_4 until pH <2, and 20 mℓ diethyl ether per 1 g of soil. Rotate the mixture on a concentric rotator for 4 hr and filter through a layer of sodium sulfate/Celite. Wash the residue well with ether. Continue as with the method in Section III.A.1 or add the first alkaline hydrolysates above to the ether, so as to combine all the extracted alkaline 2,4-D and continue as in the method in Section III.A.1. Woodham,[41] using only the acidic hydrolysis step, reported 84 to 103% efficiencies. The combined hydrolyses may produce more accuracy.

The extractions above are time consuming. It has been reported that ultrasonication for approximately 1 min is as efficient or even more so[195] than the standard methods of extraction and is recommended if an ultrasonicator is available.

It should be noted that Smith and Fitzpatrick,[74] who utilized 250 mℓ of 10% aqueous KCl 0.05 *N* with respect to NaOH obtained satisfactory results only for soils with organic contents ≤5%.

7. Organic Tissues

There are two major techniques, one proposed by Renberg[199] and the other by Clark et al.[234]

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a. In General

Renberg's method is simple, but not very quantitative (70 to 82% at 1 to 3 ppm). Homogenize 5 g of tissue in (5 mℓ of hexane + 10 mℓ of acetone), e.g., with an insertable homogenizer in a dropping funnel with a glass filter disc. Drop the liquid into 1 *M* HCl (5 mℓ) (use N_2 pressure if necessary) in a separatory funnel. Homogenize again with 10 mℓ of hexane + 5 mℓ of diethyl ether. Transfer the upper phase to the separatory funnel, shake, and transfer the upper phase to a centrifuge tube. Reextract the aqueous phase with 2 mℓ/2 mℓ of diethyl ether/hexane (× 2). Combine the extracts in the centrifuge tube. Add sodium sulfate (100 to 300 mg) and centrifuge. Transfer the supernatant to a weighed flask, rinse the sodium sulfate with diethyl ether (3 × 2 mℓ), combine the washings and supernatant, evaporate the solvent, and calculate the fat content. Dissolve the residue in benzene (1 mℓ/25 mg fat). Take 3 mℓ of this and add 3 mℓ of 0.1 *M* sodium hydroxide solution. Shake for 5 min and remove the benzene phase. The methods in Sections III.A.1 and 2 can now be utilized.

b. Muscle, Liver, and Kidney

This is based on the method of Clark et al.,[234] who achieved 88 to 93% recoveries for 2,4-D, 2,4,5-T, and Silvex.

Freeze-dry the thawed samples, then homogenize with hot ethanol, and reflux for 1 hr. Filter out the solids and chill the ethanol filtrate in an ice bath. Filter the precipitated fat from the chilled solution. Wash with chilled ethanol. Evaporate the alcohol filtrate. Digest the rest of the solid residue for 2 hr with papain at pH 5.0 and 55°C. Extract with equal volumes of ether (× 3). Continue as per the method in Section III.A.1. The method in Section III.A.2 can be utilized if 3 mℓ of 0.1 *M* NaOH is added with evaporation of the ether layer to 3 mℓ.

c. Fat Samples

Dissolve sample in hot ethanol; reflux for 1 hr, and chill as in the above section. Add 2 mℓ 0.1 *N* NaOH. Extract with diethyl ether (3 × 3 mℓ). Continue as in the method in Section III.A.1.

d. Urine

This method is based on one by Shafik et al.[228]

Add concentrated HCl in a volume equal to one fifth of the urine. Reflux for 1 hr. Add 2 mℓ 0.1 *N* NaOH. Extract with diethyl ether (3 × 3 mℓ). Continue as in the method in Section II.H.1.

e. Plasma

This is based on the method for the drug Clofibrate.[218-220]

Add enough HCl to the sample for pH ≤2. Extract with equal volumes of ether (× 3). Continue as in the method in Section III.A.1. To measure the 2,4-D in complex form, add aqueous NaOH to the aqueous layer and continue as in the method in Section III.A.1.

f. Metabolites

This is a general method recommended by McLeod and Wales.[235]

Reflux 5 g of tissue for 1 hr with 19 mℓ of acetone and 1 mℓ of benzene and separate the supernatant from particulates by filtration through a medium-porosity fritted glass funnel via negative pressure. Re-extract the particulate matter again with fresh 10 mℓ (19:1) acetone/benzene. Combine the filtrates and concentrate to 25 mℓ. Use the low-temperature bath apparatus as laid out by McLeod and Wales.[235] Further characteri-

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zation of the actual metabolites has not been accomplished. There is much room for further separation technology.

8. Water

Filter out any particulate matter.

Take a 1-ℓ or smaller volume sample. Saturate with sodium chloride. Adjust the pH to <2 with HCl. Extract with acetonitrile (5 × 500 mℓ). This extracts any esters and acids and avoids surfactant problems. Continue as in the method in Section III.A.1.

Adjust the saline solution to >pH 13 and extract with diethyl ether (3 × 500 mℓ). This extracts any free bases. Reacidify to <pH 2 with HCl and extract with acetonitrile (5 × 500 mℓ). Continue as in the method in Section III.A.1. Extraction is approximately 99% efficient for both methods.

Alternatively, transfer the swollen ion-exchange resin utilized by Renberg[199] (see the method in Section III.A.1) to create a 3 to 4-mℓ bed in a 10 × 1 cm ID pyrex column. Let the exchanger settle and connect the upper end of the column to the water sample (via Pyrex or Teflon® tubing). Faster flow rates are obtained by connecting the lower end of the column to a water pump. The usual flow is ~0.7 mℓ/min. Elute the column with 10 mℓ of acidified methanol (1 g of H_2SO_4/ 50 mℓ methanol). Add an equal volume of diethyl ether and four parts of 1 *M* HCl. Shake and centrifuge. Transfer the ether phase; add 1 mℓ of the appropriate alcohol, evaporate off the ether, and derivatize.

Probably the Renberg method is the most convenient.

9. Air Samples

For ester vapors, silica gel is an adequate adsorbent.[55]

Treat 60/70-mesh silica gel by Soxhlet extraction for 2 days using methanol. Dry the gel at 200°C for 2 days. Then 5 g of the gel packed into teflon or polyethylene air samplers described by Grover et al.[23] and shielded from moisture by wrapping in aluminum foil. Sampling can be done at 10 ℓ/min. The samplers are suitable for daily collection. If outside air sampling is contemplated, the sampler has to be shielded from rain and birds.

Desorption can be effected by washing the silica gel sample on a Buchner filter with boiling methanol (7 × 15 mℓ) under suction. This desorption procedure was 96 ±1% efficient (20 → 80 ng of vaporized *n*-butyl ester of 2,4-D).[55] Add 10 mℓ of 2 *M* NaOH and continue with the method in Section III.A.1. If no GC/MS is available, transesterify the final esters for confirmation purposes. The method is also suitable for industrial workplace sampling using 20/40-mesh silica gel in the usual personal sampling mode at flow rates of 1 to 2 ℓ/min.

If aerosol and vapor components need to be quantitated, the combined midget impactor/impinger system of Adams and Bamesberger[237] and Farwell et al.[238] should be used. The first stage of the system consists of a rotating disc impactor to collect particles ≥3 μm in diameter followed by a midget impinger utilizing a threaded-seal glass cup and filled with a two-phase collection solution of 1:1 *n*-decane/5% aqueous $NaHCO_3$. Individual esters in the *n*-decane can be directly chromatographed by GC/MS. The alkaline solution can be treated as in Section III.A.1 and the salt and free acid forms quantitated.

Samples must be stored in refrigerators in glass or Teflon® containers. The stability of 2,4-D salts and esters samples on various container materials has been discussed by De Mint and Frank.[239]

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Appendix 1
GAS LIQUID CHROMATOGRAPHIC COLUMNS AND TEMPERATURES USED TO SEPARATE ESTERS AND AMIDES OF HALOPHENOXYALKANOIC ACIDS. INJECTOR AND DETECTOR TEMPERATURES ARE IN GENERAL APPROXIMATELY 50°C ABOVE OVEN TEMPERATURE, EXCEPT FOR THE FLAME IONIZATION DETECTOR (ECD = ELECTRON CAPTURE DETECTOR; FID = FLAME IONIZATION DETECTOR; TCD = THERMAL CONDUCTIVITY DETECTOR; MCD = MICROCOULOMETRIC DETECTOR; GC/MS = GAS CHROMATOGRAPHY, MASS SPECTROMETRY)

Columns and conditions	Acid	Detector	Ref.
1 and 10% Polyamide 103a, 1,2,5, and 10% SE-30 on 50/100, 60/80, 80/100 mesh Chromosorb W (DMCS/AW), 1.83-m pyrex, copper, or stainless steel, 3-mm ID, 190 to 210°C; 5% ethyl acetate extract of Dow Corning High Vacuum Grease on 80/100 mesh Chromosorb W (DMCS/AW), 1.83-m pyrex, 4.7-mm ID, 192°C	2,4-D	ECD FID TCD GC/MS	1
4% SE-30/, 6% SP-2401 on 100/120 Supelcon (DMCS/AW), or 5% DC-200 on 80/90 mesh Anakrom ABS; 11.9-m pyrex, 3.20-mm ID, 190 to 210°C; 1.5% SP-2250/1.95% SP-2401 on 100/120 Supelcon (DMCS/AW); 5% Dexsil 300 on 60/80 Chromosorb W (DMCS/AW/HMDS); 5% Durapak Carbowax 400 on 100/120 Porasil F-Low K; 3% OV-1 on 80/100 mesh Supelcoport; 5% DC 510 on 80/90 Anakrom ABS; Bondapak C_{18}/Porasil C, 120/150 on 0.91-m stainless steel, 1.6-mm ID, 190 to 210°C.	2,4-D	ECD GC/MS	2
20% Dow Corning Silicone grease on Chromosorb, aluminum column, 225°C	2,4-D	MCD	3
30% Apiezon L on 48/60 Celite 545; 1-m stainless steel, 4-mm ID, 190°C	2,4-D	MCD	4
20% silicone on 30/60 Chromosorb P (AW), 1.83-m aluminum, 6.30-mm OD, 180°C	2,4-D 2,4,5-T	MCD	5
20% Dow Corning silicone grease purified by precipitation with ethanol from ethyl acetate solution on GC-22 firebrick (AW), 1.83-m aluminum, 6.30-mm OD, 250°C	2,4-D	MCD	6
5% Dow -11 on 60/80 Chromosorb W, 1.52-m pyrex, 3.2-mm ID, 180°C; 5% QF-1 on 60/80 Chromosorb W(HMDS), 1.52-m pyrex, 3.2-mm ID, 180°C	2,4-D 2,4,5-T	ECD	7
20% Dow-11 on 30/60 mesh Chromosorb P; 1.83-m copper, 6.30-mm OD, 210°C	2,4-D 2,4,5-T 4-CPA	TCD	8
5% FS-1265, SE-30, Polyethyleneglycoladipate, Dow silicone grease on 48/60 Celite 545, 1-m stainless steel, 4-mm ID, 190°C	2,4-D MCPA	TCD	9
15% QF-1/10% DC-200 on 80/100 Gas Chrom Q, 1.83-m pyrex, 4-mm ID or 1.83-m aluminum, 4.5-mm ID, 200 to 210°C	2,4-D 2,4,5-Y	ECD MCD	10
1.25% Versamid 906 on 70/80 Chromosorb G (DMCS/AW), 1.70-m copper, 4.5-mm ID, temperature program	2,4-D MCPA 2,4,5-T	FID	11
5% DC-200 on Chromosorb P, 1.83-m aluminum, 4.5-mm ID, 200°C	2,4-D	MCD	12
3% OV-17 on 80/100 mesh Gas Chrom Q, 1.83-m pyrex, 4-mm ID, 198°C	2,4-D 2,4,5-T	ECD MCD	13
10% SE-30 on 80/100 Diatoport S, 1.83-m stainless steel, 3.2-mm OD, 170°C	2,4-D 2,4,5-T	ECD	14

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Appendix 1 (continued)

GAS LIQUID CHROMATOGRAPHIC COLUMNS AND TEMPERATURES USED TO SEPARATE ESTERS AND AMIDES OF HALOPHENOXYALKANOIC ACIDS. INJECTOR AND DETECTOR TEMPERATURES ARE IN GENERAL APPROXIMATELY 50°C ABOVE OVEN TEMPERATURE, EXCEPT FOR THE FLAME IONIZATION DETECTOR (ECD = ELECTRON CAPTURE DETECTOR; FID = FLAME IONIZATION DETECTOR; TCD = THERMAL CONDUCTIVITY DETECTOR; MCD = MICROCOULOMETRIC DETECTOR; GC/MS = GAS CHROMATOGRAPHY, MASS SPECTROMETRY)

Columns and conditions	Acid	Detector	Ref.
5% DC-200 on Chromosorb P, 1.83-m aluminum, 4.5-mm ID, 200°C	2,4-D	MCD	12
3% OV-17 on 80/100 mesh Gas Chrom Q, 1.83-m pyrex, 4-mm ID, 198°C	2,4-D 2,4,5-T	ECD MCD	13
10% SE-30 on 80/100 Diatoport S, 1.83-m stainless steel, 3.2-mm OD, 170°C	2,4-D 2,4,5-T	ECD	14
5% DC-200 on 80/100 Chromosorb W(HP), 1.83-m pyrex, 1-mm ID, 190°C	2,4-D 2,4,5-TP	ECD	15
10% DC-200 on 100/120 Gas Chrom Q, 1.83-m pyrex, 190°C; 11% OV-17 or QF-1 on 80/100 Gas Chrom Q, 1.83-m pyrex, 205°C	2,4-D	ECD	16
3% SE-30 on 80/100 Chromosorb W (HP), 1.83-m pyrex, 230°C	2,4-D 2,4,5-T	ECD	17
6% DC-200 on 80/100 Gas Chrom Q, 1.85-m pyrex, 6.0 mm ID, 210°C; 4% LAC-446/0.55% H_3PO_4 on 80/100 Chromosorb W(HP), 1.85-m pyrex, 3.0-mm ID, 180 to 190°C	MCPA 2,4-D 2,4,5-T Silvex	MCD ECD	18
4% SE-30/6% QF-1 on 80/100 Chromosorb W(HP), 1.83-m pyrex, 6.30-mm ID, 175°C	2,4-D 2,4,5-T 2,4,5-TP	ECD	19
11% (OV17/QF-1) on 80/100 Gas Chrom Q or Chromosorb W, 1.52-m pyrex, 6.30-mm ID, 219 C; 3% Carbowax 20-M on 80/100 Gas Chrom Q or on Chromosorb W, 1.52-m pyrex, 6.30-mm ID, 230°C	2,4-D 2,4,5-T	ECD	20
8% QF-1 or 1% SF-96 or 67:33 8% (QF-1/4% SF-96) on 100/120 Chromosorb W(DMCS/AW), 1.60-m pyrex, 1.80-mm 160°C	2,4-D 2,4,5-T	ECD	21
3% OV-17 on 80/100 Gas Chrom Z, 2.74-m pyrex, 0.4-mm 200°C	2,4-D	ECD	22
1.5% OV-17/1.95% QF-1 on 80/100 Supelcoport, 1.83-m pyrex, 3-mm ID, 190°C	2,4-D 2,4,5-T Silvex	ECD	23
5% SE-30 on Chromaton N(DMCS/AW), 1.83-m pyrex, 3-mm ID, 186°C	2,4-DP	ECD	24
FFAP capillary, 30-m pyrex, 0.35-mm ID, 35 to 190°C	2,4-D MCPA, 2,4,5-T	FID	25

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Appendix 2
SPECTRA OF THE PENTAFLUOROBENZYL ESTERS OF NINE PHENOXYALKANOIC ACIDS

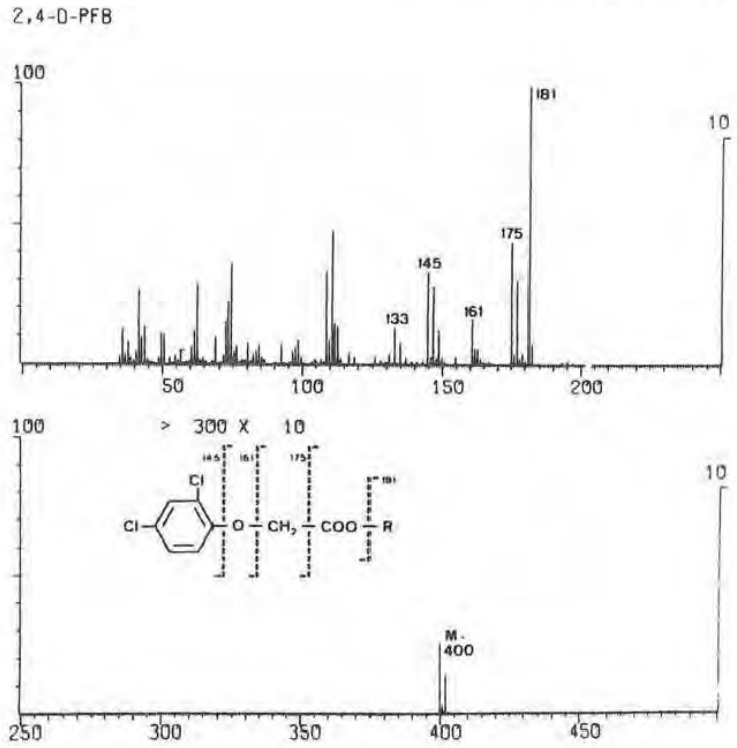


FIGURE 1. Mass spectrum of 2,4-D-PFB ester.

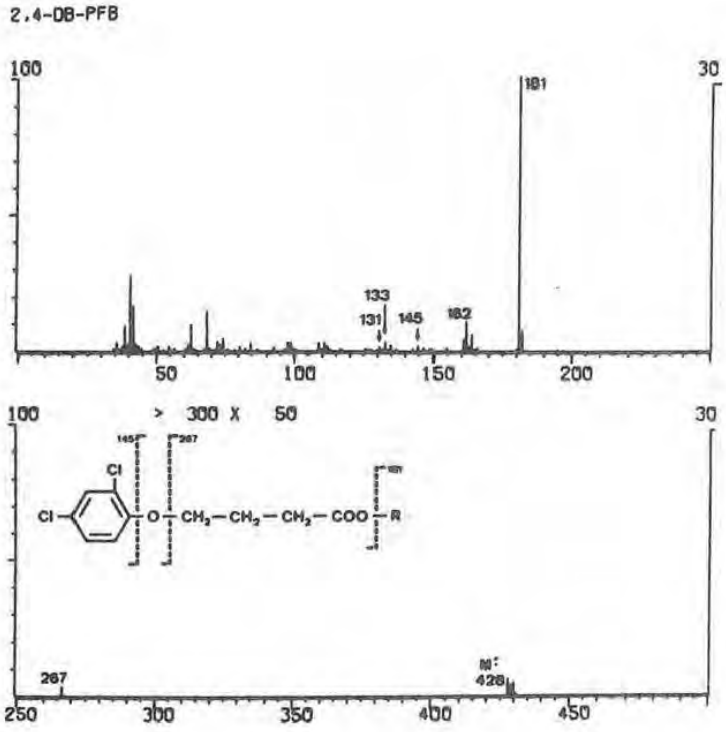


FIGURE 2. Mass spectrum of 2,4-DB-PFB ester.

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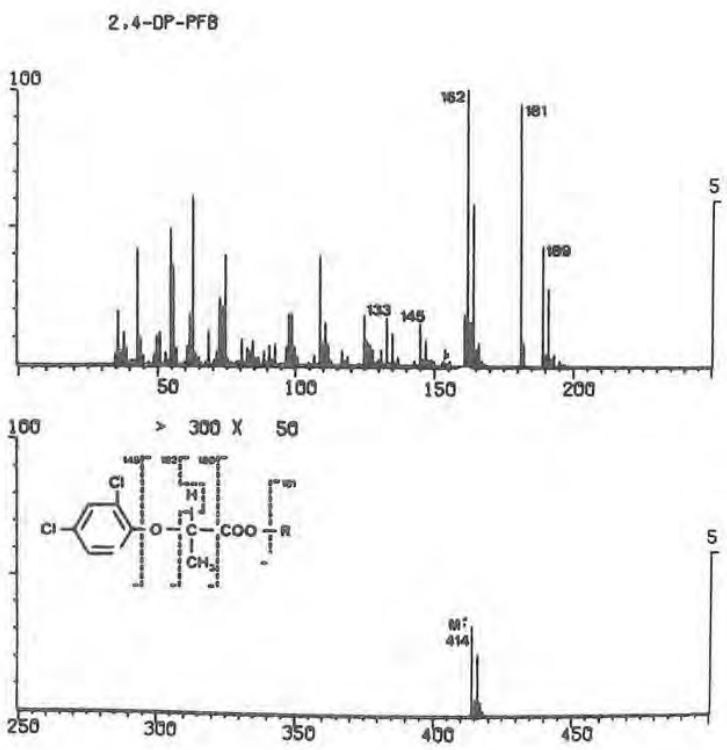


FIGURE 3. Mass spectrum of 2,4-DP-PFB ester.

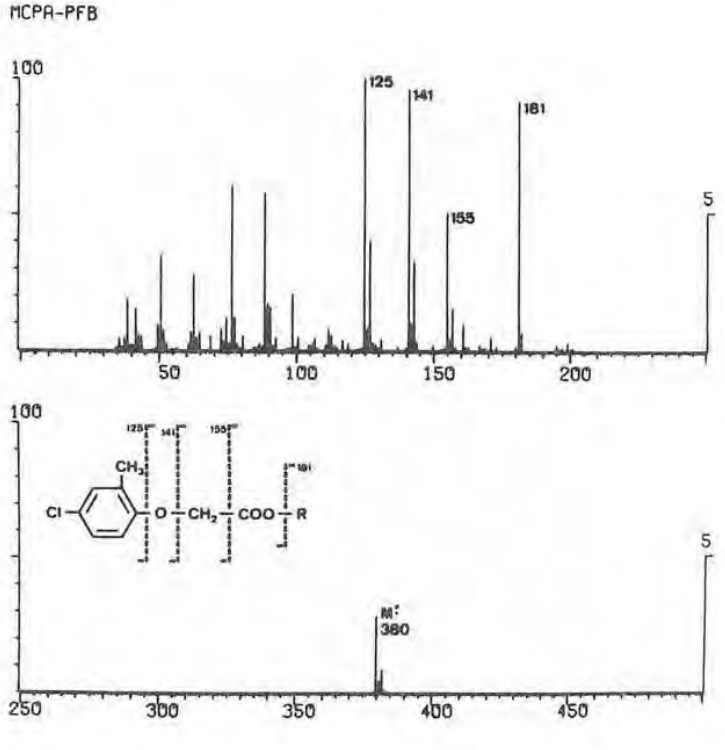


FIGURE 4. Mass spectrum of MCPA-PFB ester.

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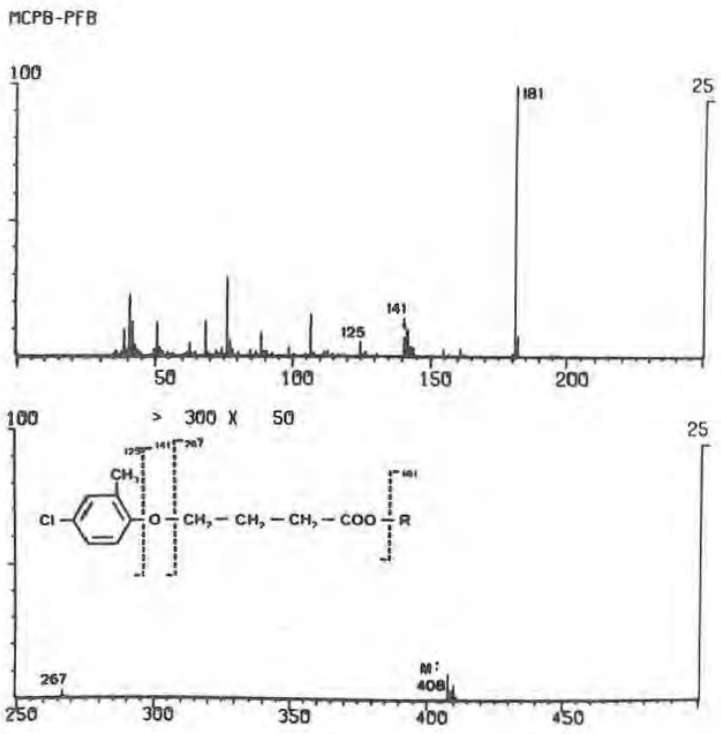


FIGURE 5. Mass spectrum of MCPB-PFB ester.

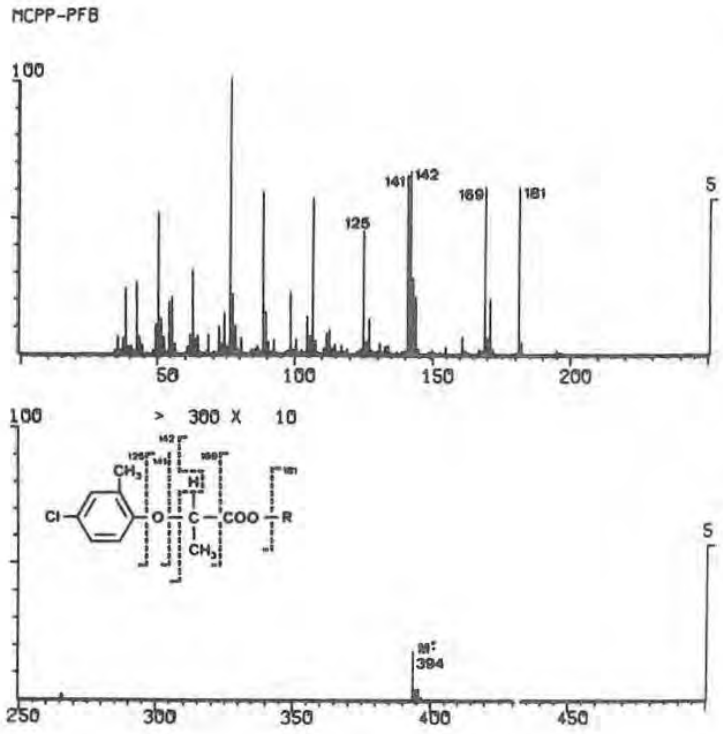


FIGURE 6. Mass spectrum of MCPP-PFB ester.

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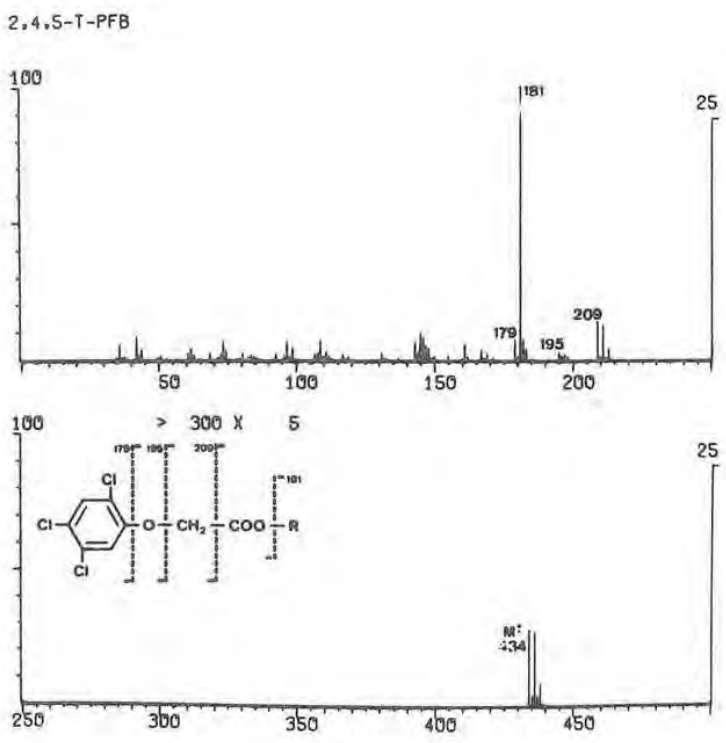


FIGURE 7. Mass spectrum of 2,4,5-T-PFB ester.

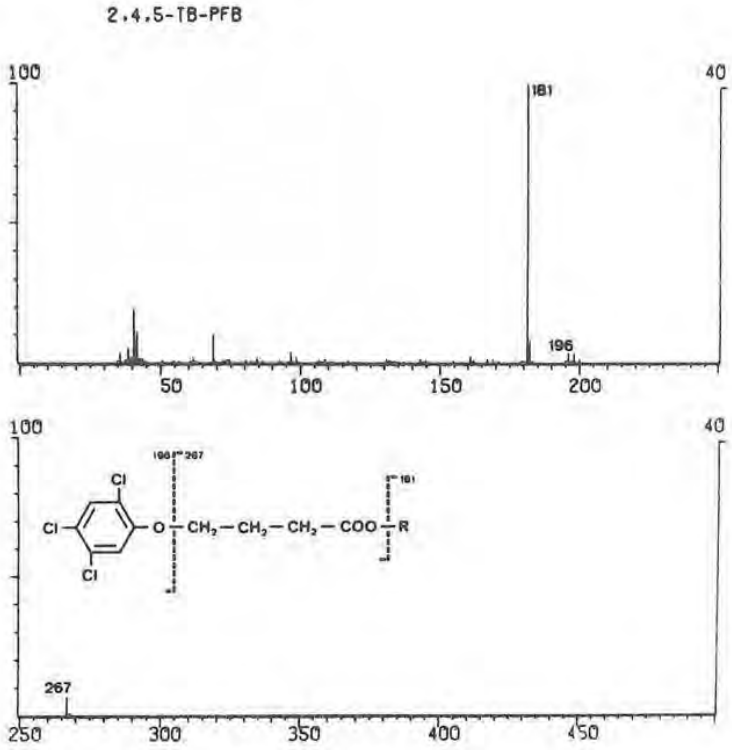


FIGURE 8. Mass spectrum of 2,4,5-TB-PFB ester.

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Table 1
ABSORPTION MAXIMA AND MOLAR EXTINCTION COEFFICIENTS OF 9 PENTAFLUOROBENZYL ESTER DERIVATIVES

Compound	$\lambda_{max.}$	log ϵ
2,4-D-PFB	270, 285, 293	3.2
2,4-DB-PFB	270, 287, 295	3.3
2,4-DP-PFB	270, 286, 294	3.2
MCPA-PFB	272, 281, 289	3.2
MCPB-PFB	272, 282, 290	3.3
MCPP-PFB	272, 282, 290	3.2
2,4,5-T-PFB	270, 291, 299	3.3
2,4,5-TB-PFB	269, 292, 300	3.4
2,4,5-TP-PFB	269, 291, 299	3.3

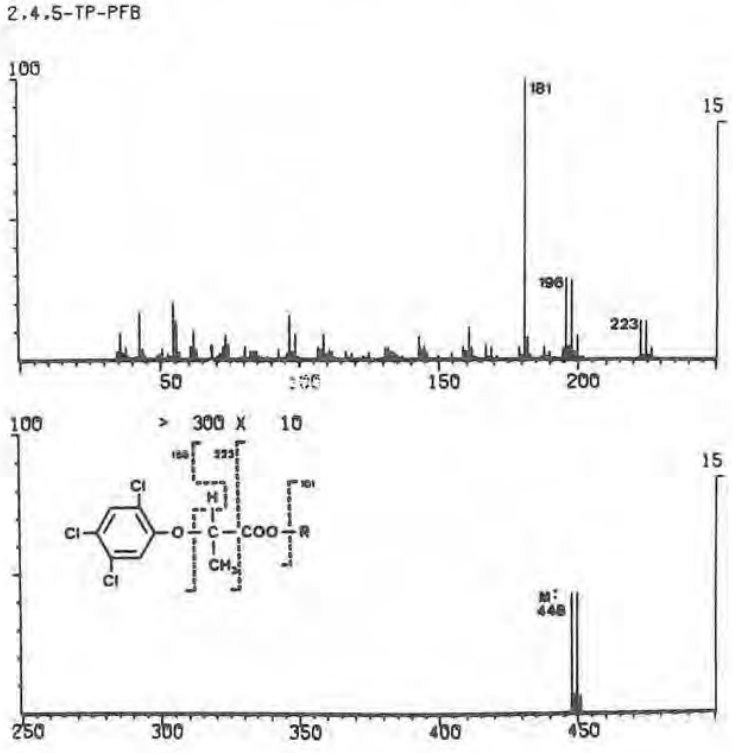


FIGURE 9. Mass spectrum of 2,4,5-TP-PFB ester.

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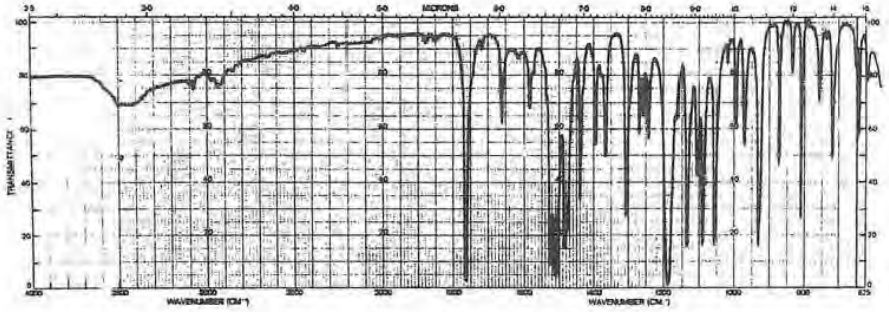


FIGURE 10. IR spectrum of 2,4-D-PFB ester.

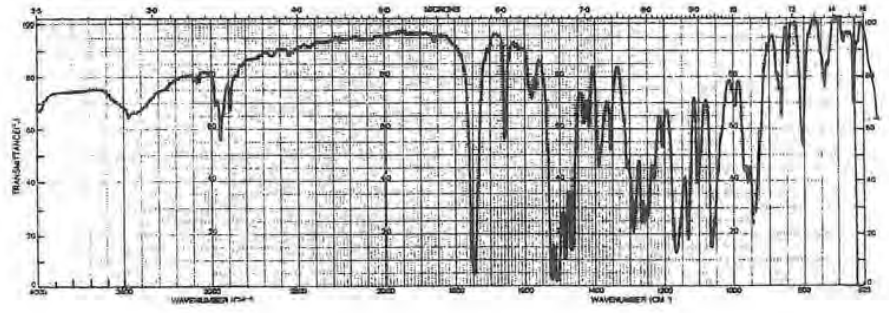


FIGURE 11. IR spectrum of 2,4-DB-PFB ester.

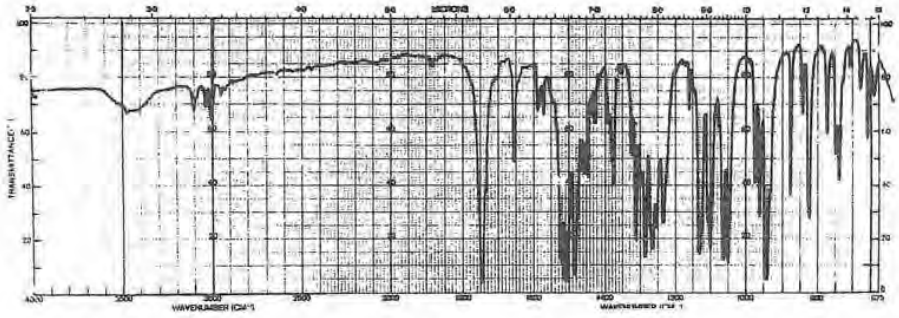


FIGURE 12. IR spectrum of 2,4-DP-PFB ester.

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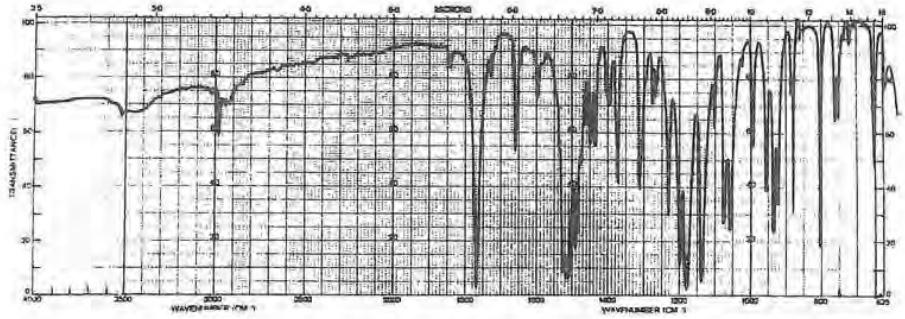


FIGURE 13. IR spectrum of MCPA-PFB ester.

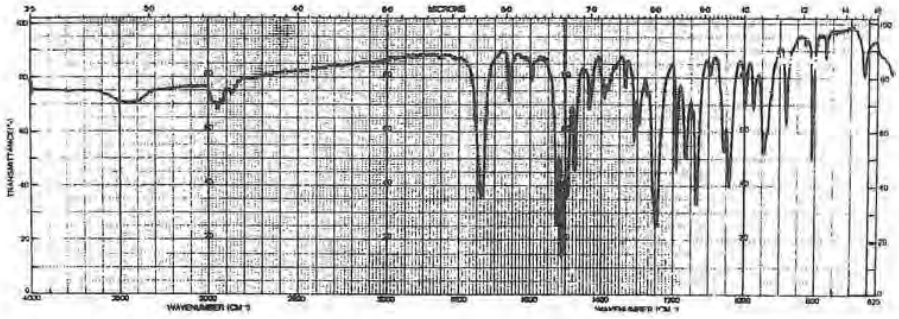


FIGURE 14. IR spectrum of MCPB-PFB ester.

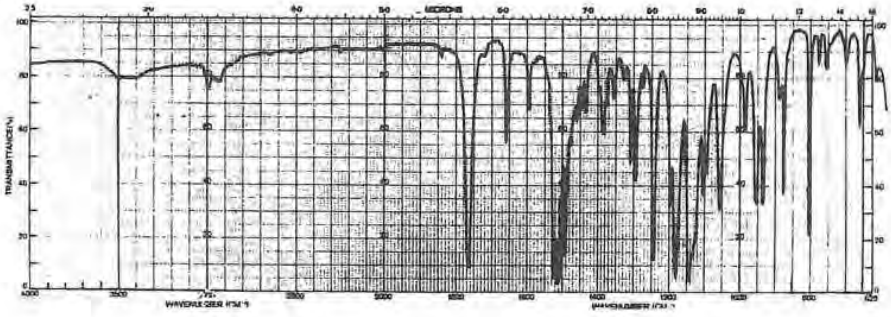


FIGURE 15. IR spectrum of MCPP-PFB ester.

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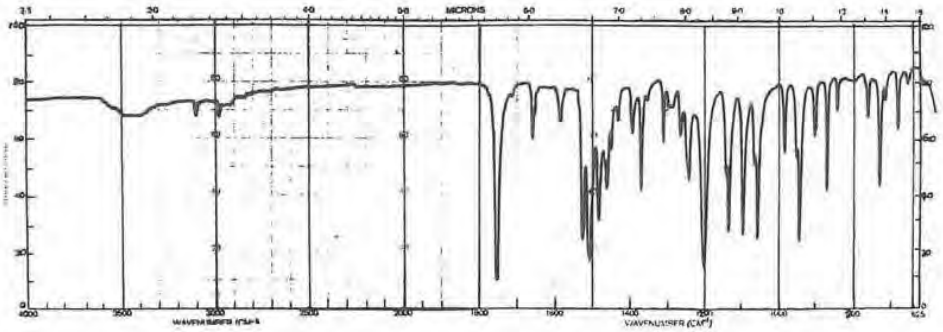


FIGURE 16. IR spectrum of 2,4,5-T-PFB ester.

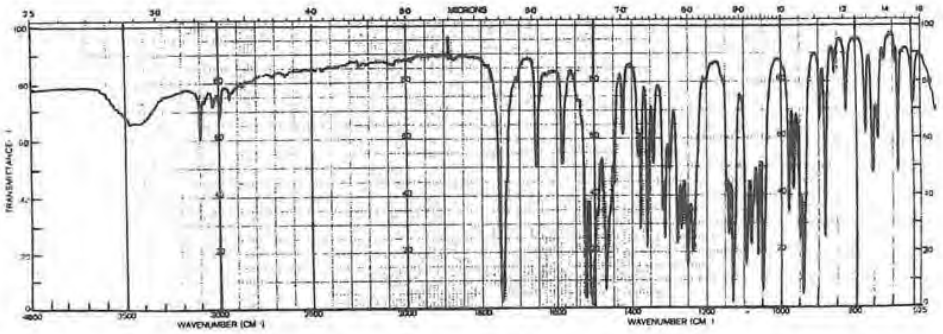


FIGURE 17. IR spectrum of 2,4,5-TB-PFB ester.

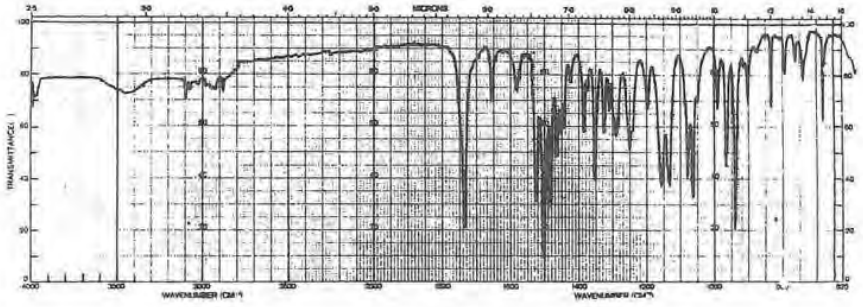
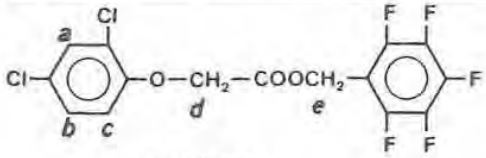
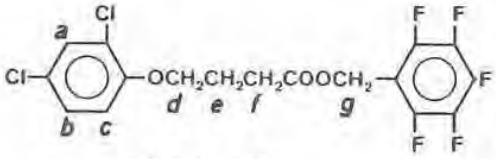
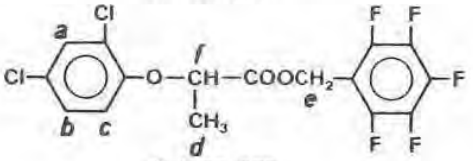
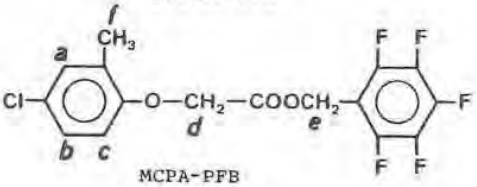
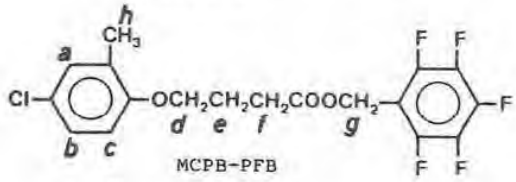
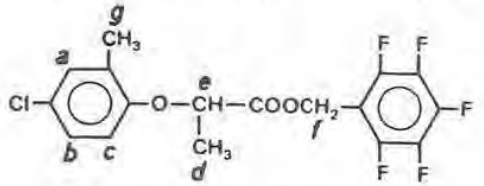


FIGURE 18. IR spectrum of 2,4,5-TP-PFB ester.

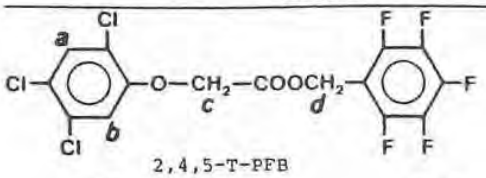
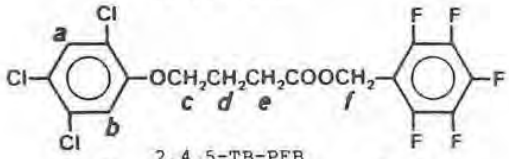
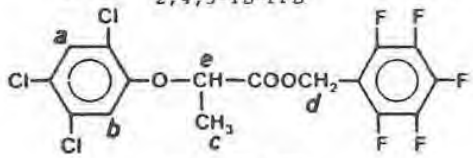
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Table 2
PMR DATA FOR THE PFB ESTERS OF CHLOROPHENOXY ACID HERBICIDES

Compound	Proton	Shift in ppm (pattern)[a]
 2,4-D-PFB	a	7.35 (d)
	b	7.13 (q)
	c	6.74 (d)
	d	4.70 (s)
	e	5.31 (s)
 2,4-DB-PFB	a	7.32 (d)
	b	7.17 (q)
	c	6.80 (d)
	d	4.05 (t)
	e	2.21 (m)
	f	2.62 (t)
	g	5.21 (s)
 2,4-DP-PFB	a	7.32 (d)
	b	7.08 (q)
	c	6.71 (d)
	d	1.66 (d)
	e	5.24 (s)
	f	4.74 (q)
 MCPA-PFB	a	7.09 (d)
	b	7.02 (q)
	c	6.55 (d)
	d	4.61 (s)
	e	5.27 (s)
	f	2.22 (s)
 MCPB-PFB	a	7.02 (d)
	b	7.01 (q)
	c	6.61 (d)
	d	3.93 (t)
	e	2.10 (m)
	f	2.57 (t)
	g	5.17 (s)
	h	2.13 (s)
 MCPP-PFB	a	7.05 (d)
	b	6.98 (q)
	c	6.51 (d)
	d	1.61 (d)
	e	4.72 (q)
	f	5.23 (s)
	g	2.20 (s)

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Table 2 (continued)
PMR DATA FOR THE PFB ESTERS OF CHLOROPHENOXY ACID HERBICIDES

Compound	Proton	Shift in ppm (pattern)[a]
 2,4,5-T-PFB	a	7.47 (s)
	b	6.90 (s)
	c	4.72 (s)
	d	5.84 (s)
 2,4,5-TB-PFB	a	7.37 (s)
	b	6.93 (s)
	c	4.02 (t)
	d	2.19 (m)
	e	2.58 (t)
	f	5.20 (s)
 2,4,5-TP-PFB	a	7.40 (s)
	b	6.82 (s)
	c	1.68 (d)
	d	5.28 (s)
	e	4.73 (q)

[a] s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet.

From De Beer, J. O., Van Peteghem, C. H., and Heyndrickx, A. M., *J. Assoc. Offic. Anal. Chem.*, 61, 1140, 1978. With permission.

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Appendix 3
THIN LAYER CHROMATOGRAPHIC SYSTEMS AND DATA FOR THE PHENOXYALKANOIC HERBICIDES AT 25°C UNDER SATURATED TANK CONDITIONS

Stationary phase	Solvent	Spotting solvent	Visualizing agent	Compounds(R_f values)	Ref.
Alumina	Acetonitile-saturated *n*-hexane	2,2,4-Dimethylpentane	$AgNO_3$/2-phenoxyethanol/UV	Methyl esters: 2,4-D(0.20); 2,4,5-T (0.23); 2,4-DB (0.30); MCPA (0.30); 2,4,5-TP (0.41)	1
Silica gel (activated for 15 min at 100°C)	(1) Develop 3.5 in. with 10:1 cyclohexane/acetic acid; (2) Remove and dry for 5 min; (3) Develop in same direction with 3:1 benzene/petroleum ether	Ethanol	$AgNO_3$/2-phenoxyethanol/UV	Free acids: 2,4-D (0.28); 2,4,5-T (0.33); MCPA (0.44); 2,4,5-TP (0.59); 2,4-DB (0.68)	2
Silica gel G/Kieselguhr G (60:40), other adsorbents also used with same solvent system	Cyclohexane, benzene/glac. acetic acid; liquid paraffin (20:3:2:1)	Ether	$AgNO_3$/2-phenoxyethanol/UV	2,4-D (0.21); 2,4,5-T (0.25); MCPA (0.32); 2,4-DB (0.52); MCPB (0.61)	3
Silica gel	(1) *n*-Hexane/benzene/glac. acetic acid/nitromethane (10:2:3:2:2) or (2) Cyclohexane/benzene/glac. acetic acid (10:2:3 or 12:2:3)	Chloroform	$KMnO_4$ or $AgNO_3$	Free 2,4-D	4

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Silica gel/Kieselguhr G (2:3)	Two dimensional, (1) hexane/EtOAc/HCOOH (80:20:0.4); (11)$CHCl_3$/*n*-hexane/glac. acetic acid (66:33:1)	Chloroform	Chromotropic acid	Free MCPA, MCPB, 2,4-D, 2,4,5-T (sens. 50 ng)	5
Silufol UV 254	Benzene/acetone 80:20	Alcohol	Rhodamine B in EtOH; bromocresol green in ethanolic NaOH; Bromocresol green/bromophenol blue in EtOH + $KMnO_4$ + Na_2CO_3	2,4-DP, MCPB, MCPP, MCPA, 2,4-D, 2,4-DB (sens. 600 ng)	6
Kieselgel G	Shell Sol A/glac. acetic acid (2.4:1)	Methanol	Blankophor DCB	2,4-D (0.10)	7
Silica gel G	Two dimensional, (1) glac. acetic acid/benzene/*n*-hexane (10:15:75); (2) Remove HOAc by evaporation; (3) Pet. ether 8P 80—100°C	Glac. acetic acid/benzene/*n*-hexane	0.5% diphenylamine in EtOH then UV	2,4-D, 2,4-DB, 2,4,5-T, MCPA, MCPP; 2,4-DB, and MCPP are unresolved	8
Florisil (0.25 mm)	Toluene	Acetone	$AgNO_3$/ethanol, then UV	Esters: 2,4,5-T *n*-butyl (0-57); 2,4,5-T i-butyl (0.52); 2,4,5-T i-propyl (0.53); 2,4,5-T *n*-propyl (0.49); 2,4,5-T ethyl (0.43); 2,4-D *sec*-butyl (0.51); 2,4-D i-butyl (0.43); 2,4-D *n*-butyl (0.47); 2,4-	9

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Appendix 3 (continued)

THIN LAYER CHROMATOGRAPHIC SYSTEMS AND DATA FOR THE PHENOXYALKANOIC HERBICIDES AT 25°C UNDER SATURATED TANK CONDITIONS

Stationary phase	Solvent	Spotting solvent	Visualizing agent	Compounds(R_f values)	Ref.
				D i-propyl (0.46); 2,4-D methyl (0.43); 2,4-D ethyl (0.43); 2,4-D methyl (0.32); 2,4,5-T butoxy-ethyl (0.26); 2,4-dichlorophenol (0.37); 2,4-D butoxyethyl (0.14); 2,4-dichlorophenoxyethanol (0.08)	
(a)Silica gel/Kieselguhr 2:3	*n*-Hexane/ethyl acetate/formic acid (80:20:0.4)	Acetone	(1)Ethanolic $AgNO_3$, then UV; (2) β-Methyl umbelliferone, then UV	Free acids: MCPA (0.57); MCPP (0.70); MCPB (0.62); 2,4-D (0.45); 2,4-DP (0.64); 2,4-DB (0.52); 2,4,5-T (0.57); 2,4,5-TP (0.70)	10
(b)Silica gel/Kieselguhr 2:3	*n*-Hexane/ethyl acetate/formic acid(150:15:0:2)	Acetone	As above	Free acids: MCPA (0.29); MCPP (0.46); MCPB (0.36); 2,4-D (0.16); 2,4-DP (0.35); 2,4-DB (0.27); 2,4,5-T (0.24); 2,4,5-TP (0.48)	
250 μm silica gel with fluorescent reagent	Two way (1) $CHCl_3$/glac. acetic acid (90:10); dry at 10°C for 3 min; (2) Benzene/hexane/acetone (50:100:20); (3) Dry at 110°C for 20 min	Ether	0.04% bromocresol green in EtOH plus NaOH until blue	2,4-D and 2,4,5-T do not resolve; MCPB, 2,4-DB, MCPP, 2,4-DP, MCPA do	11
Various (see compounds column)	Cyclohexane/benzene/glac. acetic acid/liq-	Ether	$AgNO_3$/2-phenoxy ethanol	See below	12

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	uid paraffin (20:3:2:1)				
Silufol	Hexane/MeOH/NH_3 (10:4:0:3)	Ether	UV light	2,4-D; (sens. 200 ng)	13
Silica gel KSK-2.5	(1) Acetone/NH_3 (8:1); (2) Hexane/acetone (9:1)	Ether or chloroform	?	2,4-D (0.50 to 0.62) 2,4-D *n*-Bu ester (0.70 to 0.72); 2,4,5-T *n*-Bu ester (0.35 to 0.38)	14
Silica gel/diatomaceous earth (4:6)	Pet ether/AcOH/paraffin (10:1:2)	Ether	$AgNO_3$/alk-formalin	2,4-DP; MCPA; MCPP (sens. 3$\mu g/l$)	15
Silica gel G	Two step: cyclohexane/diisopropyl ether (5:1)	Ether	Antimony chlorides; silver nitrate HNO_3; Rhodamine B	Six esters of MCPA and MCPP	16
Polyamide	Benzene/acetic acid (9:1) or CH_2Cl_2/AcOH (39:1)	Benzene	$AgNO_3$/UV	Nine phenoxy acids	17
Alumina	MeOH/NH_3 (25:1)	$CHCl_3$	Rhodamine C or bromocresol purple or $AgNO_3/NH_3$/UV	2,4-D	18
Silica gel	Pet. ether/Et_2O/HCOOH (50:50:2)	Ether	^{14}C	MCPA, 2,4,5-T (radioactive)	19

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Acid	R, Value on Percent of Kieselguhr G							
	0%	10%	30%	40%	50%	60%	70%	80%
MCPB	0.18	0.32	0.52	0.61	0.67	0.75	0.84	0.90
2,4-DB	0.17	0.26	0.44	0.52	0.60	0.66	0.76	0.86
MCPA	0.14	0.17	0.26	0.32	0.37	0.45	0.62	0.82
2,4,5-T	0.13	0.15	0.20	0.25	0.31	0.37	0.50	0.80
2,4-D	0.12	0.14	0.18	0.21	0.26	0.32	0.50	0.80
Dalapon	0.10	0.12	0.17	0.20	0.25	0.30	0.47	0.76

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Appendix 4
SYSTEMS UTILIZED FOR PAPER CHROMATOGRAPHY OF PHENOXY ACIDS[a]

Stationary phase	Solvents	Visualizing agent	Compounds (R_f values)	Ref.
?	Imm: 10% (v/v) 2-phenoxyethanol in Et_2O; Mob:2,2,4-trimethylpentane	$AgNO_3$/2-phenoxyethanol/UV	MCPA (0.88); 2,4,5-T (0.88); 2,4,5-TP (0.89); 2,4-D (0.91)	1
Whatman #1	AQ Imm:10% mineral oil/Et_2O Mob: 50% acetonitrile/H_2O	$AgNO_3$/2-phenoxyethanol/UV	Me ester 2,4,5-TP (0.31); 2,4-DB (0.34); i-propyl ester 2,4,5-T (0.48); MCPA (0.50); 2,4-D (0.64)	2
	Non-AQ Imm: 35% DMF/Et_2O Mob: 2,2,4-trimethylpentane	$AgNO_3$/2-phenoxyethanol/UV	2,4-D (0.39); i-propyl ester 2,4,5-T (0.50); MCPA (0.58); 2,4-DB (0.73); Me ester 2,4,5-TP (0.82)	
Whatman #1B (100% acetylated)	Imm: 2% (v/v) mineral oil/Et_2O Mob: 70% (v/v) acetone	$FeCl_3$/salicylsulfonic acid/Br_2	2,4-D; MCPA; Sesone; 2,4,5-T	3
Whatman #1	Imm: 5% (v/v) soybean oil/Et_2O Mob: H_2O/NH_3/t-BuOH/2 butanone (20:1:9:70)	$AgNO_3$/2-phenoxyethanol/UV	2,4-D; 2,4,5-T (sens. 1 μg)	4

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Appendix 4 (continued)
SYSTEMS UTILIZED FOR PAPER CHROMATOGRAPHY OF PHENOXY ACIDS[a]

Stationary phase	Solvents	Visualizing agent	Compounds (R_f values)	Ref.
Whatman #1	Mob: *sec*-butanol/5 *M* NH_3/H_2O (25:5:20)	4-Me-umbelliferone; $AgNO_3$/2-phenoxyethanol/UV	2,4-D (0.63); MCPA (0.62); 2,4,5-T (0.69); chloroacetic acid (0.38); phenoxyacetic acid (0.51); dalapon (0.52); 2,4-dichlorophenol (0.97); 4-chlorophenol (0.98); 2-methylphenol (0.99) (sens. ~500 ng; recoveries ~93%)	5
?	Mob: isoamyl alcohol/NH_3/H_2O (30:15:5)	Heat 130°C for 30 min; 0.03% anthrazo base in CH_3COCH_3	2,4-D	6
?	Mob: EtOH/NH_3/H_2O (30:15:5)	Rhodamine C or bromocresol purple or $AgNO_3/NH_3$/UV	2,4-D	7

[a] Imm = immobile phase; Mob = mobile phase.

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Appendix 5
COLORIMETRIC METHODS USED IN THE DETERMINATION OF THE PHENOXYALKANOIC ACIDS

Reagents	Sensitivity	Wavelength (nm)	Ref.
2,4-D + chromotropic acid + $H_2SO_4 \xrightarrow[2\ min]{150^\circ C}$	50 ng	565	1
2,4-D + chromotropic acid + $H_2SO_4 \xrightarrow{150^\circ C}$	50 ng	565	2
Na 2,4-D + chromotropic acid + H_2SO_4	50 ng	565	3
2,4-D + HCl + pyridine $\xrightarrow[60\ min]{210^\circ C}$ $H^+ \xrightarrow[distil]{steam}$	50 ng		4
Colorimetric agent: 1.0% 4-aminoantipyrine + pH 9.1 buffer + 2.0% potassium ferricyanide or use pH 7.8 buffer + 0.3% 4-aminoantipyrine + 1% potassium ferricyanide		515 505	
2,4-D, MCPA, 2,4,5-T + 0.40% w/v chromotropic acid in H_2SO_4 $\xrightarrow[25\ min]{150^\circ C}$ $\epsilon_{2,4\text{-D}} = 13{,}300$; $\epsilon_{MCPA} = 12{,}700$; $\epsilon_{2,4,5\text{-T}} = 13{,}100$	50 ng	580	5
2,4-D + chromotropic acid + H_2SO_4	50 ng	565	6
2,4-Dichlorophenol (from 2,4-D) + pH 7.6 to 8.2 buffer (Na_2HPO_4/citric acid) 2% 4-aminoantipyrine + 8% $K_3Fe(CN)_6$ → 15 min	50 ng	530	7
2,4-D, 2,4,5-T, 4-CPA methyl esters + alcoholic hydroxylamine hydrochloride + aq KOH until pH >10 $\xrightarrow[1\ min]{boil}$ → 1 *N* HCl until pH <1 $\xrightarrow[0^\circ C]{cool}$ 1% aq $FeCl_3$ (color stable only for 4 min)	20 μg	500	8
2,4-D, 2-CPA, 4-CPA, 2,4,5-T, MCPA + 0.3% (w/v)J acid in H_2SO_4 $\xrightarrow[2\ min]{165^\circ C}$ $\xrightarrow{20\%\ acetic\ acid}$	~35 ng	580	9

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Appendix 5
COLORIMETRIC METHODS USED IN THE DETERMINATION OF THE PHENOXYALKANOIC ACIDS

Reagents	Sensitivity	Wavelength (nm)	Ref.
Acids above + 0.31(w/v)phenyl J acid in H_2SO_4 $\xrightarrow[5\ min]{165^\circ C}$ H_2O $\longrightarrow$	~20 ng	635	
2,4-D $\xrightarrow[or\ (P/AC_2O)\ \Delta\ 200^\circ C]{H_3PO_4/KI}$ 2,4-Dichlorophenol $\longrightarrow$ 4-aminoantipyrine		515	10
2,4-D amine salt + butyl rhodamine, 2,4-D amine salt + $FeCl_3/HCl$			11
2,4-D, 2,4,5-T, MCPA + chromotropic acid + H_2SO_4 $\xrightarrow[25\ min]{150^\circ C}$	50 ng	580	12
2,4-D + chromotropic acid + H_2SO_4 $\xrightarrow[5\ min]{150^\circ C}$	50 ng	580	13
2,4-D-Bu ester + hydroxylamine hydrochloride + $FeCl_3$			
Phenol + >10-fold 4-aminoantipyrine/oxidant (1:1) at pH 7.5 to 9.5; colored species extracted by $CHCl_3$		515	14
Phenol + fluoro-2,4-dinitrobenzene $\xrightarrow[Et_3N]{DMF}$		540	15
Chlorophenols (from 2,4-D/pyridine-HCl) + aminoantipyrine + $K_3Fe(CN)_6$	50 ng	510	16
2,4-D + chromotropic acid + H_2SO_4 $\rightarrow$		580	17
2,4-D, MCPA + pyridine hydrochloride $\xrightarrow{\Delta}$ phenols, 3-methyl-2-benzothiazolinone, hydrazone hydrochloride	50 $\mu g/\ell$	550	18

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Chapter 5

ENVIRONMENTAL POLLUTION: PHYSICOCHEMICAL FACTORS

I. INTRODUCTION

Proper application and formulation design are necessary to achieve minimal pollution of the environment by applied pesticides. This is especially true for the phenoxy herbicides because of their universal use. The chemical and physical attributes of the phenoxys explored in Chapters 1 to 4 show that they can be rather reactive under the correct conditions. Chemicals can be quickly transported in the atmosphere in vapor, droplet, or dust form; they can be localized in the tissues of plants and animals, on the top layers of soil, and on dust or mud particles; they can be leached by rain; they can be degraded by heat, sunlight, water, microorganisms, or propitious encounters with chemicals in their microenvironments. There has been an unfortunate tendency by researchers to regard the action of free acids, the corresponding anions, and esters as interchangeable. Chapters 1 to 3 show that the anions are readily water soluble, amenable to ion exchange processes in soils and waters, are readily leached, and are not volatile. The free acids and esters, in general not very soluble (<0.1%) in water but very soluble in organic solvents, are adsorbed very quickly by organic matter, penetrate rapidly into plants, and are quite volatile compared with the salts. The free acids being more polar undergo the above processes more slowly than their esters. We have also seen (see Chapter 3) how photochemical events are also very dependent on whether a reducing (organic) or oxidative (aqueous) microenvironment is present. In aqueous solution of the free acid at equilibrium, it is expected that at pH values above the pK_a, i.e., ~3 (see Chapter 1), the concentration of the anion should dominate over the free acid, and the anion is expected to comprise 99.99% of the solution for a 10^{-3} *M* phenoxy acid initial concentration at a pH of ~7.0. In fact, below a pH of 3, adsorption onto the organic components of soils[1-3] is much enhanced (also see Chapter 1). For the esters at the usual application rates, alkaline hydrolysis is fast (see Chapter 4), so that for waters with pH values >7, the anion is the major species present, whether ester, salt, or free acid is applied. However, neutral hydrolysis (pH 6 to 7) and acid hydrolysis (pH 3 to 6) of esters are relatively slow, with the latter being much faster than the former (see Chapter 3). Thus, waters containing esters may show an age dependence, and chemical equilibrium may be attained after several months. The ultimate degradation or transfer process preferred depends markedly on the chemical species involved as well as the particular physical, chemical, and biological nature of the microenvironment. The chemical and physical properties of the phenoxys set up the potential field for their persistence and stability. It must be remembered that the environment consists of a series of heterogeneous interfaces rather than the homogeneous solutions utilized in test tube chemistry. Hence, reactive species can exist side by side in the soil or in plants, since they are selectively adsorbed (whether it be by a matrix or by an enzyme system). Since the reactants do not meet, they do not react. Mass transfer also shows a dependence on the material actually available for transfer (see Chapter 1), rather than on the amount of herbicide applied. Since ester vapors in the atmosphere are essentially single molecules surrounded by sunlight and oxygen, photooxidation is probably the ultimate fate here. The excess of sucrose in the phloem stream of plants combined with the reactivity of acids and esters towards alcohols would tend to suggest that the phenoxys here might be in the form of sucrose esters.

Chapters 2 and 4 also underline the fundamental importance of specific and sensitive

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methods of analysis, especially for formulations, since environmentally produced degradation products must be clearly differentiated from impurities in the original formulations (a topic dealt with in Chapter 2) to establish if an environmental degradation cycle is actually occurring. An area which has received comparatively little study is the stability of the phenoxys on storage, although most manufacturers ought to be well acquainted with such data. The ease of esterification and transesterification (see Chapter 2) implies that phenoxy esters of such alcohols as ethylene glycol and butoxyethanol will form in the presence of excess alcohol, and in fact, this has been observed for the latter.[4] The effects of container material, temperature, herbicide concentration, surface area, light, etc. on 2,4-D formulations have been discussed by De Mint and Frank.[5] The quality and concentration of formulations and reagent chemicals must be checked before use, since interpretation of results rests on the assumptions made. All too often workers in the field have accepted label contents without question or have utilized nonspecific analytical techniques. It came as a complete surprise to many specialists when toxic dioxins were found in 2,4,5-T and Silvex formulations (see Chapter 2). Recently, 2,4,5-T was found[6] to be responsible for the phytotoxic effects caused by some formulations of the acaracide tetradifon and was actually present to the extent of 4% (by weight). From the above considerations, it has been recognized that some form of pollution is inevitable, no matter the care exercised, and it is equally evident that the chemical and physical properties of compounds, although of fundamental importance, cannot alone define the seriousness of the potential pollution of the environment by pesticides and their degradation products. The four relevant criteria are toxicity, persistence, bioaccumulation, and stability. These may be effected by nonbiological and biological factors, but often, as in the case of soils,[7,8] the products are identical. This should not be too surprising, since the essential reactants — oxygen, water, nucleophilic reactive sites — are the same. The competitive nature of all the biological and nonbiological processes has not been investigated in an overall way by any one worker, and this is understandable in light of the complexities involved. It can be stated that transport of pesticides by atmospheric processes is much faster than transport by water or by biological systems. The phenoxys tend to be localized at soil and water surfaces and on particles; they are much diluted in the atmosphere and also in the anionic form in natural waters. Thermal degradation is negligible, but photochemical alteration may be facile, depending on the conditions. Biological concentration is of concern for some pesticides, but not for the phenoxys.[9,10] The establishment of the Codex Alimentarius Commission to formulate international tolerances of pesticide residues and other Food and Agriculture Organization/World Health Organization (FAO/WHO) expert groups is a welcome indication of international cooperation in the setting of common tolerances for pesticide residues, and such bodies are necessary to prevent world-wide ecological disasters.

This chapter concentrates on the nonbiological aspects of pollution, an artificial division, but a necessary one in view of the huge literature involved. Volume II of this book will consider in detail the biological ramifications from the use of the phenoxy herbicides.

II. POLLUTION FROM APPLICATION TO PLANT TARGETS

Herbicides are usually applied as an aqueous or paraffin spray, either from a boom spray or from aircraft. A spectrum of droplet sizes is produced, and the smallest droplets <100 μm are very prone to "drift" out of the application area ("spray drift"). Once the droplets have impacted, vapor drift may also occur. It was quickly found that 2,4-D sprayed in dust form from aircraft was unsuitable (>70% drift), and such

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applications have been banned in the U.S. since 1948. Granular formulations utilize bigger particles than dusts and so drift less. A typical 10% 2,4-D granular formulation is prepared by adding together 20.5% by weight of 2,4-D aqueous solution (50% acid equivalent) plus 79.5% by weight of 25/50-mesh LVM Attaclay (Attapulgite).[11] The granular formulations are applied usually at a rate of 1 lb/acre and generally for preemergence control, since granules do not adhere[12] well to plant surfaces and fall naturally to the soil. Liquid spraying accounts for nearly 85% of herbicide application, and we shall concentrate our attention on this.

A. Formulation Spraying

The size of particles in the droplet spectrum produced by spray nozzles depends[38] on the surface tension σ (an increase increases the amount deposited; σ varies usually from 40 (oils) to 72 dyne cm^{-1} for water),[13] viscosity (an increase leads to enlargement of droplets; varies from 1.0 (water) to 10 cP, but the effect is small compared to the effect of the type of nozzle), density (d) (the velocity of the droplet is increased by decreasing density; d = 0.8 g/mℓ for oil to 1.2 g/mℓ for technical materials, the type of nozzle,[15,16,38,39] and by temperature.

Small droplets tend to drift, and 40% of the output of a typical spray nozzle was lost when the nozzle was 36 ft from the ground.[14] Adjuvants are often added to increase the droplet diameter. When a hollow, cone nozzle was used to spray an aqueous 2,4-D solution, 8% of the droplets were <100 μm in diameter. With a water adjuvant, only 0.1% were below 100 μm.[17] Table 1 shows the dispersibility and terminal velocities of water droplets of various diameters. In addition, surfactants form layers inhibiting evaporation of water.[19] Thus, for a while, it was thought that foam applications inhibited spray drift through the surface layer resistance to evaporation. However, it was found that vapor drift was unchanged[37] and that the effect was caused by the coarse spray nozzles which produced large-diameter foam droplets.[20] Since plants, e.g., grapes, are sensitive[21,46] to 100 pg of 2,4-D, not much of an applied pesticide need drift to cause off-target damage to crops. As might be expected, most of the legal suits[22] involving drift have arisen from damage observed within 20 mi[46] of applications, although drift to 50 mi has been reported.[36] Drift out to 200[23-25] and 1500 ft[26-28] has been evaluated. Yates and Akesson[29-30] have shown that when the target crop is sprayed in a wind at 5.1 mi/hr from a height of 32 ft with a temperature gradient of ∿5°C, 70% of the spray was found within 82 ft of the target, and 7 to 8% was found between 82 to 160 ft and 160 to 2640 ft; 15% was lost via spray drift.[29] Only 3 to 5% drifted from nozzles 18 in. above the crop.[30,37] If concentrates are sprayed from planes, recoveries of 18 to 62% can be obtained,[32] whereas aqueous emulsions give 46 to 96% recovery.[32,40] These figures are independent of the vapor pressure of the herbicide[18] and also indicate that herbicides should be released from planes within 10 ft of the target. An interesting set of workshops sponsored by the Associate Committee on Agricultural and Forestry Aviation of the National Research Council of Canada has examined the mechanics of aerial spraying and vapor drift.[33-35] It was asserted that droplets initially of 100-μm diameter can lose nearly all their water mass in a few seconds under typical sunny prairie conditions and can drift several hundred meters before reaching ground.[37] In some forestry operations, there are occasions when 10 to 100% drift occurs, e.g., high winds or aircraft is too high.[41,42] Although there is no doubt that the smallest droplets cause the greatest pollution, there is some evidence that small droplets <100 μm on plants are more biologically effective than larger diameter ones,[43,44] assuming the compounds are not volatile.[45] Naturally, these small droplets when first produced at the spray nozzle must originally have been >100 μm in diameter, otherwise they would not have deposited. The theoretical aspects of volatilization from

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Table 1
DISPERSIBILITY OF WATER DROPLETS (SPECIFIC GRAVITY = 1.0) IN A 5 MI/HR WIND WHILE FALLING 20 FT IN NONTURBULENT FLOW CONDITIONS AND TERMINAL VELOCITIES IN NO WIND[6]

Drop diameter (μm)	Distance carried (ft)	Terminal velocity, no wind (20°C; 760 mm Hg; 50% RH) (ft/sec)
1000	11	13.2
500	22	6.8
100	172	0.89
50	587	0.25
10	3mi	0.01

droplets have been treated briefly in Chapter 1. Innumerable field trials have verified the above features for the phenoxy acids.[30,46-50] In-flight evaporation of droplets has also been reviewed.[33,64]

B. Leaf Retentivity

On impaction, an aqueous droplet first spreads as a thin film, then recoils to form a roughly conical shape whose top may detach, then continues spreading and retraction oscillations until equilibrium, where the droplet has the form of a spherical cap. This process is complete in <0.05 sec.[51] Oil droplets, on the other hand, tend to remain as films on leaves rather than as spherical caps. The larger the droplet, the more likely is the spherical cap likely to detach. If the surface is sprayed with droplets of diameter d just before impact and 100% deposition is achieved with a uniform cover at an application rate V (volume per unit area), then the droplet density or number of droplets per unit area (n_a) is

$$n_a = \frac{6V}{\pi d^3} \tag{1}$$

If each droplet impacts to cause the same covered circular area of diameter D, the area covered by one droplet is

$$A = \frac{\pi D^2}{4} \tag{2}$$

The coverage (total wetted area per unit area applied) is

$$n_a A = \frac{6V}{\pi d^3} \frac{\pi D^2}{4}$$

$$= \frac{3}{2} \frac{VD^2}{d^3} = \frac{3}{2} \frac{VF^2}{d} \tag{3}$$

where F = D/d. Coverage values are generally around 0.1 per unit area applied.

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Another important parameter is the spread factor (F), defined as the ratio of diameter wetted to diameter of the droplet just before impact. This spread factor is not a constant and varies from material to material and with impact velocity which for a given spray nozzle under constant operating conditions for a given solution is determined by the distance away of the target from the nozzle.[52-54] The spread factor can also be expressed in terms of the contact angle (θ) of the droplet at rest, the latter being determined by species, leaf position, age of leaf, environment, hairiness of leaves, and the surface roughness of the leaf.[55-57] In fact, leaf surfaces are so irreproducible that artificial surfaces are commonly used to study retention characteristics.[58-61]

The spread factor for a droplet with a spherical cap on a horizontal surface is

$$F = \left[\frac{4 \sin^{-3}\theta}{(1 - \cos\theta)^2 (2 + \cos\theta)}\right]^{\frac{1}{3}} \tag{4}$$

Retention is related to coverage, but in retention the surface actually wetted is the focus. In pollution, the area exposed to environmental factors is most important.

In terms of contact angle, it has been shown[62] that the area covered by one drop on a horizontal surface is

$$A = \left(\frac{4}{3}\right)^{\frac{2}{3}} \pi r^2 [1 - \cos\theta + \frac{1}{3}(\cos^3\theta - 1)]^{\frac{-2}{3}} \tag{5}$$

where r is the radius of the drop before impact.

Another way of looking at the situation is via the energetics involved. A free droplet just before impact has a surface energy (E_f) of[62]

$$E_f = 4\pi r^2 \sigma_L \tag{6}$$

where σ_L is the surface tension of the solution. For the surface energy (E_s) over the horizontal drop per leaf interface,[62]

$$E_s = \pi r^2 \sigma_L \left(\frac{4}{3}\right)^{\frac{2}{3}} [2(1 - \cos\theta) - \sin^2\theta \cos\theta][1 - \cos\theta + \frac{1}{3}(\cos^3\theta - 1)]^{\frac{-2}{3}} \tag{7}$$

If E_o is the energy of a plane surface of the solution, the minimum energy barrier between attached and free drops relative to a plane film (HLB) is[62]

$$(E_s - E_f)/E_o = \text{HLB} \tag{8}$$

For a droplet of diameter 100 μm, HLB = 0.014 for a θ of 179° required for reflection. Usually, $\theta \sim 110°$ and adherence occurs. For 200 and 400-μm diameter droplets, the reflection θ is 105 (HLB = 0.20) and 0°, respectively, and use of a surfactant which raises the HLB but lowers θ drastically is mandatory for good adherence. This retention is increased by reducing the surface tension, e.g., at σ <45 dyne/cm; high retentions are expected for droplets <150 μm impacting at their terminal velocity.[63]

For a 200-μm diameter droplet containing a surfactant so that σ_L = 35 dyne/cm and θ = 60°, A is 156,000 μm^2, increased 3.5 times over the situation where no surfactant is used. The area exposed to environmental influences is thus much higher also (at

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least two times greater than the area available for herbicidal action, assuming a spherical cap). To gain an idea how θ and 2r(D) control coverage, it has been shown[65] that for droplets with D = 250 μm, θ = 90°; D = 250 μm, θ = 35°; and D = 175 μm, θ = 35°, the coverage is 0.95, 2.50, and 5.00% of the surface. In practice of course, droplet spectra are not monodisperse, and by agreement the median diameter (50% mark) is used in the above equations. The above equations can be used safely in low- and medium-volume spraying, but in high-volume spraying, excess spray liquid may eventually drip off the leaf. The critical roll-off size is dependent not only on the intrinsic retentivity of the leaf, but also on the angle the leaf makes to the ground. This shows up by the fact that there are advancing and receding contact angles, θ_A and θ_R, respectively, to be considered as well as α, the slope of the leaf. The amount of retention, R, has been defined as the ratio of the volume of an incipiently rolling globule (Vα) to its base area.[55,65,66] Thus,

$$R = k \left[\frac{\pi\sigma(\cos\theta_R - \cos\theta_A)}{6F^3 dg \sin\alpha}\right]^{1/2} \qquad (9)$$

where d is the density of the liquid, g is the constant of gravitational acceleration in c.g.s. units, k is a constant and F is usually calculated from

$$\left(\frac{4}{F^3}\right)^{\frac{1}{2}} \approx (\theta_A + \theta_R)/2$$

The retention factor f is defined as

$$f = (\theta_A + \theta_R)/2\,[\sigma(\cos\theta_R - \cos\theta_A)/d]^{\frac{1}{2}} \qquad (10)$$

Retention (R) vs. f appears to be linear for most plants at a given leaf slope and age of leaf.

Thus, the early observations of Blackman et al.[67] can be explained, i.e., reduction in surface tension reduced retention for leaves which were easily wetted and increased retention for those which were not.

In some cases, the surfactant may be retained even better than the pesticide. However, this is only important in run-off conditions.[68]

To complicate things further, leaf inclination depends also on the age of a leaf. Small, immature leaves also have higher retentivity than more aged leaves in high-volume spraying. As might be expected, R increases as inclination is reduced, and below wind velocities <3 m/sec and droplet diameters >150 μm, R is hardly affected. Thus, R vs. log (volume median diameter) between 60 to 400 μm is linear at α = 30°, as is the relationship between R and log (critical volume for runoff).

Empirically, the constant k appears to be a measure of globule size distribution (since droplet coalescence must also be considered) and surface cover at incipient run-off, and is a function of droplet size and impact velocity.[66] Generally, k varies from 0.25 to 0.31 for diameters 520 to 120 μm.

Naturally, the chemical composition of the leaf surface determines the values θ and F. The chemistry of leaf surfaces will be considered in more detail in Volume II, since this relates to penetration into the leaf.

C. Vapor Drift

Once the droplets have impacted onto the leaf (or soil), the compounds can still

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escape in the vapor form. The amounts which do so are a net result of the amount tied up by surface adsorption (in soil, leaf, or other surfaces), and the amount lost by such other processes as leaf penetration and leaching.

In general, the water carrier evaporates first, followed by the "inert components", until finally the surface deposit consists in general of the surfactant or adjuvant and the active components in a very concentrated form. Good systemic herbicide design involves selection of the components so that the herbicide penetrates before the evaporation and/or crystallization of the pesticide.[69-71] However, as the pesticide gets more concentrated, increased penetration may occur,[72] but not for water-soluble salts;[73] the latter will be subject to negligible vapor drift[74-76] and may be easily washed off by rain, etc. Alternatively, organic-based carriers, e.g., diesel or paraffin oils, can allow the pesticide to penetrate very speedily,[77] thus making external pollution negligible. This effect was also observed for 2,4-D esters by Marth and Mitchell.[92]

The presence of a surfactant may increase or decrease the volatility of a pesticide. Enhancement is expected if the surfactant excludes the pesticide from its binding or adsorption sites.

That volatility on plant surfaces was also affected by penetration was shown by Que Hee and Sutherland.[45] It was demonstrated that 15 to 70% of the applied dose may penetrate into a leaf within 10 hr; 2,4-D butyl esters in droplets of mean diameter 55 μm volatilized much faster at 39°C than they penetrated. After 10 hr, approximately 70% had vaporized and approximately 8% was still on the outside of the leaf, with 20% inside. Droplets of mean diameter 255 μm allowed approximately 38% to vaporize in 10 hr, 4% was still on the outside of the leaf, and approximately 58% was inside. The volatility observed for the larger-diameter droplets was ascribed to the percentage of droplets below 250 μm in diameter. Thus, it was shown that the type of compound as well as droplet size must be considered in addition to such competing processes as penetration.

Pesticides in thin layers or in small droplets volatilize faster than pesticides in thick layers or large droplets.[74-78] The influences of the exposed surface area to mass applied ratio (Q_a), vapor pressure, air speed, temperature, etc. have already been considered (see Chapter 1). If the layer of air next to the impacted droplet is stagnant, the pesticide can escape only by diffusion (in general $\sim 3 \times 10^{-4}$ g cm^{-2} sec^{-1} at 25°C from a glass surface). For molecular distillation (evaporation into a vacuum), the rate is $\sim$0.25 g cm^{-2} sec^{-1}, or $\sim$1000 times faster. The maximum rate in the field may be between these two extremes and depends on environmental conditions, if laminar or turbulent flow prevails, and whether the vapor pressure of the compound is high enough. Sometimes "wick" effects or codistillation with water may occur.[78]

The air transport of pesticides has been a controversial subject. Thus, pesticides have been detected at the polar ice caps.[79,80]

Vapor of 2,4-D butyl esters from field spraying operations has been detected at 3000 ft in an aircraft.[81,109] One of the very first quantitative evidences of the dispersion of pesticides, other than from the direct consequence of air spraying, was reported by Cohen et al. in 1964.[82] An experimental agricultural plot at Coshocton, Ohio was hand sprayed with 4 lb/acre of atrazine and 2 lb/acre of Esteron 99 (a polypropylene glycol butyl ether ester of 2,4-D). Analysis of rainwater collected in a storm 3 weeks later revealed the presence of 2,4-D and atrazine which had been applied a mile away. It was thought that the vapors or spray drift were adsorbed by dust particles in the atmosphere, and these had been redeposited by rainfall on land areas remote from the site of the original deposition of the pesticides. 2,4,5-T has also been identified in rainwater samples.[83] Dust particles can be moved huge distances, even over continents[84] and oceans, e.g., nuclear explosion dusts. Thus, dust from an area in New

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Mexico and Texas on January 25, 1965 was collected in Cincinnati, Ohio on January 26, 1965 during a fortuitous gentle rain there. Various pesticides were found, including 2,4,5-T at 0.04 ppm. Thus, direct mass transfer by atmospheric processes has been shown to be important.

Vernetti and Freed[88] in 1962 were the first workers to describe an air sampling method designed specifically for 2,4-D detection. Both vapor and aerosol forms of 2,4-D were detected by Bamesberger and Adams[85] in Washington State. Ambient air was sampled at two field sites for 100 days. In this first report, aerosol and vapor forms were not distinguished. In later reports, both forms were quantitated[86,87] simultaneously by the impactor/two-phase midget impinger system referred to in Chapter 4. Air samples (24-hr)[86] collected near Pullman and Kennewick Highlands, Wash., between April 16 and August 6, 1964 contained detectable phenoxy herbicides on more than 75% of the 113 sampling days. For the isopropyl and butyl esters of 2,4-D, three to five times more compound was collected from the vapor than from the aerosol phase. Usually, the total 2,4-D content (up to ~5 $\mu g/m^3$) far outweighed the levels of the individual isopropyl and butyl esters (up to 1.30 $\mu g/m^3$) in the vapor phase, thus illustrating that quantitation of the total amount of herbicide is necessary to gain a realistic idea of pollution. The reasons for this have been discussed in Chapter 3. No vapor component was detected for the isooctyl ester of 2,4-D. Up to 0.78 $\mu g/m^3$ 2,4,5-T was also detected. All esters were found in the aerosol fraction. The ratio of aerosol to vapor-phase components depended on the proximity of spraying operations, dust conditions, on temperature, and on the frequency of rain; the problem of overlapping GC peaks was also encountered in this study. The volatile methyl and isopropyl esters of 2,4-D were soon banned in the U.S. as a result of this data. It is interesting that concern about aerosol phase pollution of phenoxy compounds which began in the U.S. after 1963 was reported in 1960 by Csanyi,[89] who collected sodium 2,4-D dust from approximately 100 ℓ of air on filter paper and analyzed the residue by a colorimetric method. Sodium salts and butyl esters of 2,4-D in air were also detected in 1967 by Gavrilova.[90] The ammonium salt of 2,4-D was also collected on perchlorovinyl filters and analyzed colorimetrically in 1969 by Lazareva.[91] Amine salts were also trapped in perchlorovinyl filters and analyzed colorimetrically in 1965 by Lazareva and Gavrilova[93] and Gavrilova.[94]

Interest in vapor drift of the phenoxys in the U.S. and Canada in the 1970s has in the main been in the hands of separate groups based in Washington State in the U.S. and in Saskatchewan, Canada.

Farwell et al.[95-98] reported on levels obtained in the 1973-1974 time period in south central Washington State, using the same sampling apparatus as Bamesberger and Adams[86] and utilizing GC/MS quantitation.[96] High-volatile (HV) esters were predominant in the vapor phase as expected: 76% of the detected mass was HV esters; low-volatile esters (LV) comprised 20%, and "nonvolatile" (NV) 2,4-D (amine salts, etc.) accounted for 4%. In May, 1973, the average total 2,4-D concentration was 0.21 to 0.38 $\mu g/m^3$; in June, 1973, ~0.24 $\mu g/m^3$ (44% HV; 46% LV; 10% NV). The *n*-butyl ester was predominant in the HV fraction. The major LV esters detected were the butoxyethyl and the PGBE esters, mostly >60% as aerosol. The highest average daily level recorded was 0.80 $\mu g/m^3$. In 1974, the average 2,4-D concentrations in April and May were 0.84 and 0.83 $\mu g/m^3$, respectively, with 66% being HV, 21% being LV, and 12% being NV approximately for both months. In June the average 2,4-D dropped to 0.52 $\mu g/m^3$, 92% of this being HV. Again the *n*-butyl ester was the dominant HV ester, and the preponderant LV esters were the butoxyethyl and PGBE esters, most being found in the vapor phase. The maximum 2,4-D level recorded was 1.71 $\mu g/m^3$. See Table 2 for more detail. In addition, crop injury appeared to correlate with the maxi-

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Table 2
CONCENTRATIONS OF 2,4-D COMPOUNDS FOUND IN THE AIR OF SOUTH CENTRAL WASHINGTON STATE IN 1973 TO 1974[95]

I. Average 2,4-D concentration ($\mu g/m^3$) by volatility type, May 1973.

Sampler location	High volatile	Low volatile	Nonvolatile	Total 2,4-D
Prosser	0.23	0.07	0.01	0.31
Kennewick	0.23	0.06	0.02	0.31
Benton City	0.23	0.09	0.02	0.34
Snake River	0.32	0.05	0.01	0.38
Sunnyside	0.24	0.08	0.01	0.33
Plymouth	0.18	0.02	0.01	0.21
Mabton	0.20	0.07	0.01	0.28
7-Station average	0.23	0.06	0.01	0.31

II. Average 2,4-D concentration ($\mu g/m^3$) by volatility type, June 1 to 18, 1973.

Sampler location	High volatile	Low volatile	Nonvolatile	Total 2,4-D
Prosser	0.10	0.18	0.02	0.30
Kennewick	0.07	0.06	0.02	0.15
Benton City	0.11	0.19	0.02	0.32
Snake River	0.10	0.08	0.02	0.20
Sunnyside	0.15	0.14	0.01	0.30
Plymouth	0.13	0.08	0.02	0.23
Mabton	0.06	0.07	0.03	0.16
Hanford	0.03	0.01	0.06	0.10
8-Station average	0.09	0.10	0.02	0.22

III. Average 2,4-D concentration ($\mu g/m^3$) by volatility type, April 1974.

Sampler location	High volatile	Low volatile	Nonvolatile	Total 2,4-D
Prosser	0.24	0.12	0.10	0.46
Kennewick	0.90	0.11	0.12	1.13
Benton City	0.51	0.15	0.15	0.81
Snake River	0.22	0.25	0.13	0.60
Burbank	0.35	0.09	0.12	0.56
Mabton	0.93	0.35	0.13	1.41
Mercer	0.74	0.13	0.13	1.00
Travis	0.54	0.13	0.11	0.78
8-Station average	0.55	0.17	0.12	0.84

mum 2,4-D concentrations in the air, although evident phytotoxic effects occurred from 1 to several days after the concentration front passed. A meteorological analysis[95,99] showed that the maximum levels occurred in weak frontal systems which acted

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Table 2 (continued)
CONCENTRATIONS OF 2,4-D COMPOUNDS FOUND IN THE AIR OF SOUTH CENTRAL WASHINGTON STATE IN 1973 TO 1974[95]

IV. Average 2,4-D concentration (μg/m³) by volatility type, May 1974.

Sampler location	High volatile	Low volatile	Nonvolatile	Total 2,4-D
Prosser	0.85	0.24	0.12	1.21
Kennewick	0.65	0.35	0.08	1.08
Benton City	0.62	0.29	0.09	1.00
Snake River	0.48	0.16	0.08	0.72
Burbank	0.63	0.14	0.12	0.89
Mabton	0.44	0.07	0.10	0.61
Mercer	0.29	0.16	0.06	0.51
Travis	0.50	0.04	0.09	0.63
8-Station average	0.56	0.18	0.09	0.83

V. Average 2,4-D concentration (μg/m³) by volatility type, June 1 to 17, 1974.

Sampler location	High volatile	Low volatile	Nonvolatile	Total 2,4-D
Prosser	0.85	0.03	0.03	0.91
Kennewick	0.69	0.01	0.02	0.72
Benton City	0.60	0.03	0.01	0.64
Snake River	0.20	0.01	0.01	0.22
Burbank	0.53	0.01	0.02	0.56
Mabton	0.24	0.06	0.00	0.30
Mercer	0.31	0.00	0.03	0.34
Travis	0.43	0.02	0.03	0.48
8-Station average	0.48	0.02	0.02	0.52

From Farwell, S. O., Robinson, G., Powell, W. J., and Adams, D. F., *J. Air Pollut. Control Assoc.*, 26, 224, 1976. With permission.

as a transport mechanism and as a stabilizing influence so limiting dilution. Low 2,4-D concentrations seemed to be correlated with wind directions opposite to that observed for the high levels. Another study by Farwell et al.[100] appeared in 1977 on the efficiency of XAD-2 resins on collecting 2,4-D esters from air.

Que Hee et al.,[101] using silica gel samplers, measured 2,4-D levels from central Saskatchewan from May to July, 1972 at stations near Rosetown, Melfort, and Saskatoon. The sampling procedure has been presented in Chapter 4 and the levels were obtained using a two-column GC technique and a confirmatory alkaline hydrolysis, cleanup, and esterification to give total 2,4-D levels. GC/MS was also used when possible. 2,4-D was detected in 65 of 480 samples using cleanup, and only 28% of these contained butyl or octyl esters. By direct GC without cleanup, 45 appeared to contain butyl or octyl esters, but only 63% were confirmed by the esterification procedure. At the Saskatoon station, 90% of the samples suspected of containing butyl or octyl esters

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were confirmed. Of samples cleaned up and esterified, only 40% contained butyl or octyl esters. The mean daily levels of total 2,4-D compounds for 33 days up to June 28, apart from a period June 4 to June 9, was 0.60 $\mu g/m^3$. However, in the interval June 3 to June 10, a mean value of 175 $\mu g/m^3$/day was observed, with negligible butyl or octyl esters. The maximum levels occurred on June 6 to June 8 (455, 208, 355 $\mu g/m^3$/day, respectively). At the Rosetown station, of the eight samples suspected of containing 2,4-D butyl or octyl esters, none were confirmed. Only one sample yielded 2,4-D using the cleanup procedure (0.080 $\mu g/m^3$). At the Naicam station, only 70% of the 24 samples suspected of containing butyl or octyl esters were confirmed. Of the 35 samples with 2,4-D as found by cleanup, only 50% contained butyl or octyl esters. The mean daily level for 47 days up to July 14 was 0.142 $\mu g/m^3$, the highest level being observed on June 2 (0.688 $\mu g/m^3$). It is manifestly evident that GC/MS is required for confirmation of individual esters, as shown by Farwell et al.[95,96] and that the total 2,4-D must be quantitated to obtain realistic levels, since quantitation via direct GC analysis is only as exhaustive as the set of standards employed.

Grover et al.[50,102-105] have also reported on 2,4-D concentrations in Saskatchewan air from eight sites. Less than 5% of *n*-butyl ester of 2,4-D was lost in the form of spray drift, and over 30% of the applied herbicide was lost in the vapor form after 1 hr in a field trial.[50,102] Air sampling by this group had been initiated in the years 1966 to 1968 and begun again in 1970 to 1975.[103] Up to 50% of all daily samples collected during the spraying season (May to July) at any of the locations at Aberdeen, Indian Head, Naicam, North Battleford, Regina, Rosetown, Saskatoon, Swift Current, and Yorkton contained 2,4-D. During the early sampling years, the esters were collected by bubbling air through toluene contained in midget impingers. Sampling in the later years utilized silica gel solid adsorbent in polyethylene samplers incorporating critical orifices. The levels quoted for the early years must be regarded as tentative in view of the fact that identification was based on retention times alone. Table 3 shows the levels of individual esters tentatively quantitated from the various sites. The mean concentrations ranged from 0.01 to 1.22 $\mu g/m^3$, 0.01 to 13.50 $\mu g/m^3$, and 0.05 to 0.59 $\mu g/m^3$ for the isopropyl, *n*-butyl, and isooctyl esters, respectively. The only station at which a total 2,4-D analysis was attempted was for Regina, 1973 to 1975. Of the 37 samples obtained at Regina in 1973, total acid values were approximately the same as the level of *n*-butyl ester in 20 samples. In three, the total acid concentration was 2 to 10 times the value of the butyl ester. In a further six samples (referring to their published table), the tentative identification was not confirmed. Most of the high concentrations were collected during rainfall periods. This was thought to indicate a general "wash-out", but it also indicates that the majority of the drift was occurring at heights well above the two meters used for sampling stations. The butyl esters again comprised the bulk of the HV esters. In any given year at any of the sampling sites, 30% of the samples contained less than 0.01 $\mu g/m^3$/day; 40% of the samples had 0.01 to 0.099 $\mu g/m^3$. Only 10% of the levels exceeded 1 $\mu g/m^3$. No particulate 2,4-D was detected in contrast to the results of Farwell et al.[95-98] Concentrations in the exhaust system of a 2,4-D formulating plant in Regina, Saskatchewan were 1.4 to 28 $\mu g/m^3$/day over a 2-week sampling period. Unfortunately no total 2,4-D estimate was made, since formulations seldom have just one ester present (see Chapter 2). Butyl esters were detectable, even when no 2,4-D was being formulated. It was also shown in another publication[105] that the *n*-butyl ester of 2,4-D could be collected by silica gel solid adsorbent and desorbed with ~100% efficiency for air concentrations 0.01 to 10 $\mu g/m^3$ independent of relative humidity.

2,4-D was tentatively identified[106] in urban Salt Lake City air in 1967 to 1968 at a concentration of 0.004 $\mu g/m^3$/day in just one sample. The analytical technique was

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Table 3
LEVELS OF 2,4-D RESIDUES FOUND IN AIR AT VARIOUS LOCATIONS IN SASKATCHEWAN, CANADA[103]

Location	Year	Number of samples	Concentration ranges for various esters and total 2,4-D			
			Iso-propyl (μg/m³)	Mixed butyl (μg/m³)	Iso-octyl (μg/m³)	Total 2,4-D (μg/m³)
Aberdeen	1970	46	—	0.32—1.55(11)	—(0)	—
Indian Head	1972—1973	102	—	0.06—1.90(49)	—(0)	—
Naicam	1971—1973	153	—	0.05—0.25(36)	—(0)	—
North Battleford	1973	52	—	0.05—0.29(27)	0.05—0.13(5)	—
Regina	1966—1972	181	0.01—1.22(6)*	0.01—4.24(72)	0.09—0.59(7)	—
Regina	1973—1975	129	—	—	—	0.01—23.14(57)
Rosetown	1971—1973	158	—	0.02—0.72(29)	0.05—0.08(5)	—
Saskatoon	1971—1973	167	—	0.01—0.41(38)	0.33—0.40(5)	—
Saskatoon	1974—1975	100	—	—	—	—(0)
Swift Current	1972—1973	95	—	0.06—13.50(47)	—(0)	—
Yorkton	1973	52	—	0.05—0.11(21)	—(0)	—

* Figures in parentheses indicate the number of samples in which 2,4-D was found.

From Grover, R., Kerr, L. A., Wallace, K., Yoshida, K., and Maybank, J., *J. Environ. Sci Health*, B11, 331, 1976, by courtesy of Marcel Dekker, Inc.

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far from clear, and so the identification is uncertain. 2,4-D was also tentatively identified[107] in the same year at Jordan, N.Y. (0.00115 $\mu g/m^3$/day) and Rome, N.Y. (0.00154 $\mu g/m^3$/day).

The levels established by the American Conference of Government Industrial Hygienists[108] for 2,4-D vapor in any form in 1971 for workplace air was 10 mg/m^3/8-hr day. This standard still is in force.[110] In addition, the tentative short-term exposure limit — the maximum concentration that workers can be exposed up to 15 min without harm — has been set at 20 mg/m^3/15 min. The same threshold limit values have been set for 2,4,5-T compounds. The presence of degradation products of the phenoxys in the atmosphere has not yet been conclusively proven. Que Hee and Sutherland[165] have demonstrated that very volatile compounds are produced on photolysis of 2,4-D *n*-butyl ester vapor at 300 nm, with reductive dechlorination at the *ortho* position predominating. The main photolysis products are phytotoxic in addition to being much more volatile. Cl was also demonstrated to be evolved, and this has been implicated recently in ozone depletion. It might be added that brominated or iodinated pesticides would degrade much faster since their halogen-C bond is weaker. Also, Br may be as potent as Cl in reacting with ozone. Another cause for concern is the possible role of evolved HCl from the photolysis being important in acid rains.

III. SOIL POLLUTION

A. Introduction

Soils are generally composed of silicaceous and other minerals providing large surface areas ideal for adsorption and also containing a comparatively minor organic component (<10%) which for organic herbicides often determines the adsorption and persistence characteristics, as well as providing localized sites for microbial degradation of the pesticide. Water is also present in varying amounts and may make the soils colloidal or clathrate-like, with pHs varying from 3 to 10.5 and, in addition, may stimulate microbial degradation of the herbicide. The major clay minerals (usually >90% of any soil) can be obtained in pure, crystalline form.[111] The organic fraction can be separated as well.[112,113] Many workers have used autoclaving[114-116] or chemical sterilization, e.g., by sodium azide[117] to try to differentiate between the biological and nonbiological influences in pesticide degradation in the soil. Unfortunately these two treatments can change soil chemistry so much that the experimental results may bear little relation to actual chemical events in real soils.[118] However, autoclaved soils appear to show[119] degradation rates of 2,4-D and MCPA which are half to one fifth those found in unsterilized soil, so implying that the bulk of phenoxy degradation in soils should be biologically based. However, for reasons given above, such an interpretation is too simplistic.

In general, the organic component of the soil provides a reducing medium, especially under anaerobic conditions, although this depends on pH and the presence of water. Although often regarded as "inert", the organic fraction has been demonstrated to have reactive free radicals.[1] The phenoxys can be dealkylated and converted by Fenton's reagent in vitro to the same products elicited in microbial metabolism.[120] In addition the soil contains[1] many enzymes not associated with living organisms which are adsorbed and stabilized on buffered particulate matter which can even survive high-energy gamma ray irradiation sufficient to kill living microorganisms. These adsorbed enzymes came from living or dead organisms, root exudates, and soil animals.[121] However, in spite of their proximity to each other, the adsorbed herbicide and enzyme must come in direct contact to cause degradation. Thus, except under certain conditions

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(e.g., conditions where there is an excess of a C or N source and the herbicide can be cometabolized), the substrate and the reactants are unavailable to each other.

The bulk of the soil is inorganic, principally complex aluminosilicates of colloidal particle size.[122] The clays bear negative charges which make them cation exchangers, and with their large surface areas, adsorption is very likely. Chemically speaking, they tend to be inert, but the carbonates and sulfides, when associated with Fe, Mn, Co, and other transition metals, can constitute reactive sites which may catalyze or take part in oxidations or reductions, e.g., the dehydrochlorination of *p,p'*-DDT and its relatives is catalyzed by such metal salts.[123] The metal ions can be present naturallly or supplied by fertilizer or sludge applications. In general the greater the water content, the more likely hydroxylation and oxidation will occur. In addition, amine salt formation can be catalyzed by naturally occurring ammonia, ethanolamine, glucosamine, purines/pyrimidines, or peptides/amino acids. Furthermore, for the phenoxys for soils where pH >7, hydrolysis and anion formation of esters are favored.[124,125] In contrast, between pHs 3 to 7, very little hydrolysis occurs, although at <pH 3, adsorption is predominant for the phenoxys.[2]

Photochemical reactions, as expected, occur mostly at soil surfaces, although UV radiation has been shown to penetrate soil for as much as 12 mm.[126] Photosensitization may also be important.[127] Unfortunately no thorough studies with the phenoxys have been done.

B. Adsorption onto Soils

Adsorption of the phenoxys onto the individual model components of soils has been discussed in Chapter 1. In general, the process on these and natural soils is described by a Freundlich isotherm, although in some cases pseudo first-order kinetics may be shown.

The difficulty of most of the research in this field has been its artificial nature. Thus, Hamaker et al.[3] showed that 2,4-D and 2,4,5-T anions were adsorbed more extensively as the organic content of the soil increased and as the pH decreased. It was also possible to elicit much adsorption on soils of low organic content, but with high Fe, Al, or Cu concentrations at low pHs. However only soils of high organic content showed a progressive saturation phenomenon, equilibrium sometimes taking months. These experiments do not approximate field conditions because of the slurry technique used. The results could pertain to hydrosols. At first sight, it might appear that these results might also be applicable for leaching behavior for freshly applied herbicide. It must be remembered that early part of the adsorption process is exponential, even though freshly applied herbicide would be more leachable.[129] The very water-soluble triisopropanolamine salt of 2,4-D was applied[130] to a thin coarse podzol in a Great Lakes forest clearing as a Tordon 101 (picloram/2,4-D) formulation and only <0.1% was leached during seven run-off events over a year, even though one occurred within 24 hr after spraying. Naturally, as expected, soils which adsorb more strongly will leach least.[3]

Most soils are dry or of low water content when pesticides are applied. Surprisingly few experiments with the phenoxys have been done on such soils. It was demonstrated that free 2,4-D and its dimethyl amine salt did not adsorb[131] well onto dry Saskatchewan prairie soils, but did so avidly in peat. Jyothi[132] investigated the movement of ^{14}C-2,4-D through columns containing glass beads (100 to 200 μm), Lakeland fine sand, Fellowship subsoil, and Everglades mucky peat under constant flow conditions. Easy movement occurred on all, but the peat column. Irreversible adsorption occurred on organic soils, but not on mineral soils. Kuo,[133] who studied ^{14}C-2,4-D movement on 43 soils, showed that <pH 7, adsorption was much enhanced in Minam, Woodcock, and Kinney soils and was also enhanced by increasing organic content and the extrac-

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tible Al present. At pHs >7, leaching was relatively easy. In another study[134] which examined the mobility of 2,4-D on 48 soils, the herbicide adsorbed to all to the extent of ~12.4%. When 2,4-D was applied to clayey soils, the downward movement was directly proportional to soil moisture.[135] All of these properties suggest that the anion is the major mobile species. Another related study utilizing soil thin layer chromatography (TLC) suggested[136] that mobility of 2,4-D was insensitive to the presence of coarse or medium-sized sand particles, soil layer thickness, temperature, sample size (0.3 to 50 μg), but was markedly dependent on pH, water flux, organic, and clay content. Tween 20 surfactant enhanced the mobility. Methyl esters were less mobile, but were also very volatile. Chlorinated dibenzo-*p*-dioxins were immobile. In addition, when 2,4-D in aqueous solution was percolated[137] through Lakeland fine sand at 2.08 or 4.10 cm/hr, the herbicide was eventually held at about the same depth in this soil regardless of irrigation rate. There is some confusion as to what actually happens when the phenoxy esters are applied to soils. Smith showed[138] that esters of 2,4,5-T, 2,4-DB, and 2,4-DP hydrolyzed to the free acid in four Saskatchewan soils if soil moisture was greater than the wilting point. Little hydrolysis occurred on air dried soils. In addition, hydrolysis was slower as the ester chain length increased. The same results were obtained for 2,4-D esters[124] in three other Saskatchewan soils. However, Wilson[140] using ^{14}C-carboxyl 2,4-D, found that the isooctyl ester of 2,4-D was converted 90% to the anion form in 96 hr and not the free acid. No data on soil pH are provided, however. In addition adsorption of the ester and the dimethylamine salt was greater near the soil surface than at lower depths. Furthermore, as the top surface dried, 2,4-D was moved up from beneath by capillary water action. Both ester and amine applications showed the same behavior, again suggestive of a common species.

It might be noted that the soil moisture content determines soil pH, the drier the given soil the less the pH.[139,142,152] The exact role of soil clays is still not resolved. Although adsorption of 2,4-D onto soil clays is well documented,[141-146] as well as onto the other soil constituents,[147,148] especially under acidic conditions,[148-150] organic matter content is held to be the greatest determinant of adsorption.[3,128] However, as the complexity or length of chain of 2,4-D compounds increased, more clay was required to obtain equivalent adsorption of 2,4-D.[148] In addition, the amount of kaolinite clay was shown[151] to have no influence on the bioactivity of 2,4-D, but increasing montmorillonite content moderately reduced the activity of 2,4-D. These results are probably caused by the greater surface area of the latter. Experiments with 2,4,5-T indicate that the organic fraction determines its adsorption.[204]

The major difficulty is the number of uncontrolled variables, especially the interdependency of pH, water content, surface area, and type of soil and pesticide. The nature of the exchangeable cation on the soil colloid influences,[152-154] the adsorption of organic molecules, and the pH at the colloid surface may be three to four pH units lower than in the soil solution.[153] In an effort to investigate which components of the soil were affected by 2,4-D, IR analysis of air-dry soils by Harter and Ahlrichs[149] was used, and this was suggestive of protonation occurring at a soil solution pH which was two to three units higher than the pK_a of 2,4-D. Adsorption then occurred on the colloid via charge transfer[155] or a direct interaction complex as observed for EPTC.[156] The pH of a soil is a reflection of its buffering capacity, and it has been suggested that a more reliable soil property in predicting adsorption and desorption may be titratible acidity.[157] According to some workers, the adsorptive capacity of soils for neutral pesticides is determined by an "active" organic fraction which, in its adsorptive characteristics, is essentially the same regardless of the origin of the soil.[158,159] However, increases in the soil moisture content increase adsorption of nonionic pesticides,[160,161] so that such generalizations are difficult to evaluate. Sullivan and Felbeck,[162] using IR

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techniques, concluded that the carboxyl and phenolic hydroxyl groups of humic acids were mainly involved in the adsorption of atrazine, a molecule with a pK_a similar to the phenoxyalkanoic acids with C_1 side chains. It is characteristic of the field that apparent correlations are easy to draw, and Adams[157] in his review has highlighted the pitfalls of statistical correlations. Nevertheless, Upchurch and Mason[128] in 1962 derived an equation for the GR_{50} of 2,4-D and Sesone to cotton in parts per million water.

$$GR_{50} = b_0 + b_1(\text{cation exchange capacity}) + b_2(\text{exchangeable Ca}) + b_3(\%\ \text{organic matter}) \quad (11)$$

where b_0 is the y intercept: b_1, b_2, and b_3 are the respective partial regression coefficients. For 2,4-D, $b_0 = -0.24$, $b_1 = -0.13$, $b_2 = 0.67$, and $b_3 = 0.61$, with a coefficient of multiple determination (R) of 1.00. For Sesone, $b_0 = 0.80$, $b_1 = 0.00$, $b_2 = 0.29$, $b_3 = 1.13$, with $R = 1.00$ It must be remembered that arbitrary properties such as cation exchange capacity are functions of organic matter, clay content, pH, and moisture content. Thus, for 2,4,5-T, 2,4-D, and MCPA, it was demonstrated[145,163] that below pH 3 to 4, protonated 2,4-D can be adsorbed on montmorillonite, but is negatively adsorbed on montmorillonite and illite as the anion at pH 6 to 7. In soils, the more chlorinated the phenoxy acid, the greater the adsorption[164] and the less the mobility, and 2,4,5-T is thus less mobile than 2,4-D or MCPA.[163]

The subject of adsorption of pesticides to soils has been the subject of many reviews.[112,117,122,153,157,163,166-176]

C. Movement Within Soils

Lateral movement of pesticides across soil surfaces is enhanced by steep topography, low soil permeability, and intense and/or prolonged rain. Little runoff occurs in general with 2,4-D or its amine salts, but more is observed[177] for the esters. In general, runoff behavior is the inverse of adsorption. Thus, 2,4-D can be desorbed from mineral soils, but not from those containing much organic matter.[136,178-180] The same factors as cited above for adsorption, work in reverse for leaching out. Leaching into soils is also influenced by moisture level and by the evapotranspiration rate.[181] Percolating water appears to be the principal means of movement of relatively nonvolatile compounds, and diffusion for these compounds in soil-water is important only for transport over very small distances. This certainly holds for the 2,4-D anion, and a mathematical treatment was presented by Lindstrom et al.[182] for its diffusion in water-saturated soils. The diffusion coefficient for the anion in nine soils was generally found to be inversely related to soil texture (0.06 to 1.0×10^{-6} cm^2/sec). The vertical movements of herbicides in soils can be likened to column chromatography, where ion-exchange, partitioning, solubility, and adsorption are in fine, instantaneous balance to produce concentration "fronts". Factors causing spreading or concentration of these fronts are also the same as in chromatographic processes.[183] Aldrich[169] observed that the sodium and triethanolamine salts of 2,4-D leached faster than the butyl ester from montmorillonite; the two salts leached equally quickly. Stein et al.[185] found the leachability order of different formulations of 2,4-D to be acetanilide < acetamide < *n*-butyl ester < triethanolamine salt. The relative persistence of 2,4-D[186,187] and MCPA[188] on soil colloids was found early in the history of the phenoxys. The shape of 2,4-D anion elution profiles from soil columns was studied by Elrick and MacLean[189] and appeared to fit pulse feed with constant inflow rate profiles.[190] Temperature effects can also be important. Hernandez and Warren[116] found that 2,4-D applied

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to the soil was still toxic to cabbage seeds 8 weeks after application when the soil temperature was 4.4°C, compared with only 4 weeks at 15°C. The major reason for this was probably enhanced microbial degradation at higher temperatures, but this was not unequivocally proved, especially since adsorption increases with decreasing temperature. The complex equilibria and steady states are all temperature dependent. Haque and Freed,[191] in a recent review, have assigned a leaching index of 1 to 2,4-D, 2,4,5-T, and MCPA free acids on loam soils at 25°C, i.e., the approximate number of centimeters moved through the soil profile with an annual rainfall of 150 cm is <10.

Upward movement of herbicide occurs when the surface dries or if rapid evaporation occurs there. This has been called the "wick" effect. Thus, the herbicide can be concentrated at the soil surface, where it can be photolyzed, transported by wind either on dust or in vapor form, or leached downwards again.

Volatilization of pesticides from soils was thought to be minor, even as recently as 1974.[191] The review by Spencer et al.[192] showed that volatilization by such chemicals as DDT, dieldrin, lindane, and trifluralin could be a major dissipation route under the right conditions, e.g., for nonpolar molecules on moist soils in which there is an upward water flow to carry the pesticide to the soil surface, where the pesticide and water then evaporate independently of each other. No "codistillation" effect appears to occur, however.[192,193] In the early years, residues could be demonstrated to be reduced with time but, apart from using expensive labeled compounds and uncertain bioassay techniques, the vapor could not be measured directly, since analytical methods were not specific or sensitive enough. This situation was remedied in the 1960s.[85]

Increasing the porosity and looseness of soils enables convective air currents to circulate, whereas if the soil is well packed, conductive transfer alone is the only important vapor-producing mechanism. Thus, when soils are freshly disked, pesticides near the top layers often slowly diffuse out to the atmosphere as the loosely packed top layer dries. Several "DDT compounds" were detected in this way.[194] There has only been one reported study[195] where actual volatilization rates were measured over the entire growing season from soil-incorporated pesticides conducted under normal farming conditions; 2.8% of dieldrin and 3.9% of heptachlor were lost during a season begun by disking the insecticides (both applied at 5.6 kg/ha) immediately after application to a depth of 7.6 cm followed by planting of corn. Volatilization from surface applications at the same rates without disking was much higher (3%/hr). This is conclusive and unassailable evidence that the vaporization of "nonvolatile" insecticides can be a major loss pathway under normal management practices. As might be expected, soils showing high organic content do not release pesticides as avidly as mineral soils, and moist soils allow more volatilization than dry soils.[192] It is important to realize that all these processes are essentially under kinetic rather than thermodynamic control. Wind continuously removes the vapor, but stagnant conditions do not drive the complex kinetic steady states in the direction of pesticide release from the soil. Models applicable for soil volatilization have been formulated by Letey et al.,[196] Leistra,[190] Spencer and Cliath,[197] Hamaker,[198] Hartley,[78] and Ehlers et al.[199] Degradation products of pesticides are also produced in soils, and many are more volatile than their parent molecules.[194] This aspect needs much more research.

The many field experiments which produced evidence of vapor drift of the phenoxy compounds have been described in Chapter 1 and earlier in this chapter in Section II.C. Soil temperatures in general are 30 to 40°F higher than the prevailing air temperature on typical summer days, even down to 1.5 cm beneath the surface, and this was cited by McLane[200] as another important variable ensuring fast volatilization. Naturally, this temperature differential will vary according to soil type and vegetation.[48,201-203]

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