

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Petitioner
Symrise AG

v.

Patent Owner
Inolex Inc.

IPR2023-01439
U.S. Patent No. 10,882,803

DECLARATION OF DOUGLASS F. TABER

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I, Douglass F. Taber, declare as follows:

I. INTRODUCTION

1. I have been retained on behalf of Symrise AG and Symrise Inc. (collectively “Petitioner”) in connection with the above captioned *Inter Partes* Review (IPR) of U.S. Patent No. 10,882,803 (’803 Patent). I have been asked to study and provide my opinions as an independent expert witness regarding technology described in the ’803 Patent. I am being compensated at my usual and customary rate for my time. Such compensation, however, does not influence my opinion nor does the outcome of this proceeding impact my compensation.

II. QUALIFICATIONS

2. I have carried out research in organic chemistry and taught graduate and undergraduate classes on organic chemistry, including organic reaction mechanisms, throughout my 40-year career. I have published more than 200 research articles. In 2022, 74 of those articles were cited by other research groups, 34 of them more than once. I am the author of the weekly online scientific publication, *Organic Synthesis Highlights*, used by research groups all around the world.

3. I have conducted research and published scholarly papers on the preparation and reactions of alkenes, alcohols, epoxides, and esters. These have included the dehydration of alcohols to the corresponding alkenes with the control of regioselectivity. In fact, I published a new protocol for the conversion of a 1-

alkene to the corresponding 1-epoxide. Throughout my career I have routinely used the conversion of an epoxide to the corresponding 1,2-diol. I maintain a database of the most important organic chemical transformations, which currently contains more than 60,000 entries, any one of which I can access in minutes.

4. A copy of my *curriculum vitae* is attached as Appendix A. It includes a list of testimony I have provided in other legal proceedings, an outline of my research experience, and a list of my publications.

III. MATERIALS REVIEWED

5. In forming my opinions provided in this declaration, I have read and considered the following. I have also used my education, knowledge, and experience in organic synthesis and organic reaction mechanisms.

Document Reviewed	
Ex. 1001	U.S. Patent No. 10,882,803 (the “’803 Patent”) and the corresponding prosecution history of U.S. Application No. 16/262,898
Ex. 1003	U.S. Provisional Patent Application No. 16/262,898
Ex. 1004	File History of U.S. Patent No. 10,882,803
Ex. 1005	File History of U.S. Patent No. 10,995,048
Ex. 1006	File History of U.S. Patent No. 11,414,365
Ex. 1007	U.S. Patent Publication No. 2011/0196114A1 (“Le”)
Ex. 1008	U.S. Patent Publication. No. 2005/0065389A1 (“De Bruyn”)
Ex. 1009	U.S. Patent Publication. No. 2012/0238788 (“Wright ’788”)

Document Reviewed	
Ex. 1010	U.S. Patent No. 6,528,665 (“ Cheng ”)
Ex. 1011	PCT Written Opinion of the International Searching Authority, PCT/US2015/014943. Issued April 29, 2015
Ex. 1012	U.S. Patent No. 8,912,373 (“ Wright ’373 ”)
Ex. 1013	U.S. Patent No. 8,173,850 (“ Furuya ”)
Ex. 1020	U.S. Patent No. 10,894,750 (“ Vecchini ”)
Ex. 1021	U.S. Patent No. 9,908,837 (“ Colby ”)
Ex. 1022	U.S. Patent No. 8,765,430 (“ Parekh ”)
Ex. 1023	U.S. Patent No. 8,597,922 (“ Alibhai ”)
Ex. 1024	U.S. Patent No. 7,795,484 (“ Koivusalmi ”)
Ex. 1025	U.S. Patent No. 4,234,752 (“ Wu ”)
Ex. 1026	German Patent DE3915493 (“ Voeste ”) (translation)
Ex. 1027	N.P Makgoba <i>et al.</i> “ <i>Silication of -γ-alumina catalyst during the dehydration of linear primary alcohols,</i> ” Applied Catalysis A: General 297 (2006) 145-150 (“ Makgoba ”)
Ex. 1028	W.G. Appleby <i>et al.</i> “ <i>Vapor Phase Dehydration of 1-Heptanol over Activated Alumina,</i> ” J. AM. CHEM. SOC. 66: 1938-1939, 1944 (“ Appleby ”)
Ex. 1029	V. I. Komarewsky <i>et al.</i> “ <i>Catalytic Dehydration of 1-Hexanol and 1-Octanol,</i> ” J. AM. CHEM. SOC. 67: 557-558, 1945 (“ Komarewsky ”)
Ex. 1030	L. G. Wade, Jr. Organic Chemistry (8 th Ed. 2013) (“ Wade ”)
Ex. 1031	JAOCS Vol. 62, No. 2, 355-365 (1985) (“ Reck ”)
Ex. 1032	JAOCS Vol. 61, No. 2, 343-347 (1984) (“ Kreutzer ”)

Document Reviewed	
Ex. 1033	W. E. Schiegl and J. C. Vogel “ <i>Deuterium Content of Organic Matter,</i> ” EARTH AND PLANETARY SCIENCE LETTERS 7:303-313, 1970 (“ Schiegl ”)
Ex. 1034	Harmon Craig, “ <i>Standard for Reporting Concentrations of Deuterium and Oxygen-18 in Natural Waters,</i> ” SCIENCE 133: 1833-1834, 1961 (“ Craig ”)
Ex. 1035	WO 2001/044145 (“ Tiitta ”)
Ex. 1036	U.S. Patent No. 9,029,619 (“ Vermeiren ”)
Ex. 1037	WIPO Publication WO 2004/078336 (“ Ziehe ”)
Ex. 1038	Zhe Rui et al. “Discovery of a Family of Desaturase-Like Enzymes for 1-Alkene Biosynthesis” ACS Catalysis 2015 5 (12), 7091-7094 (“ Rui ”)
Ex. 1039	WO 2007/051284 (“ Gao ”)
Ex. 1040	U.S. Patent Publication. No. 2003/0065233 (“ Fuji ”)
Ex. 1041	Swern, <i>et al.</i> “ <i>Hydroxylation and Epoxidation of Some 1-Olefins with Pre-acids,</i> ” Eastern Regional Research Laboratory 68: 1504-1506, Aug., 1946 (“ Swern ”)
Ex. 1042	Sarma <i>et al.</i> “ <i>A rapid 1,2-dihydroxylation of alkenes using a lipase and hydrogen peroxide under microwave conditions,</i> ” Tetrahedron Letters 48 (2007) 6776–6778 (“ Sarma ”)
Ex. 1043	William E. Fristad and John R. Peterson “ <i>Iron(III) Catalyzed Persulfate Oxidation of Alkenes to Vicinal Diacetates,</i> ” Tetrahedron Lett. 24: 4547-4550, 1983 (“ Fristad ”)
Ex. 1044	Wolfgang A. Herrmann <i>et al.</i> “ <i>Methyltrioxoruthenium as Catalyst for Olefin Oxidation,</i> ” Angew. Chem. Int. Ed. 30:1638-1641, 1991 (“ Herrmann ”)

Document Reviewed	
Ex. 1045	Azhong Wang <i>et al.</i> “ <i>Palladium-Catalyzed Diacetoxylation of Alkenes with Molecular Oxygen as Sole Oxidant</i> ,” J. Am. Chem. Soc. 131: 3486, 2009 (“ Wang ”)
Ex. 1046	Isao Sakurada <i>et al.</i> “ <i>Dichlorotin oxide-catalyzed new direct functionalization of olefins: synthesis of trans β-azidohydrins and 1,2-diols</i> ,” Tetrahedron Lett. 41: 2415-2418, 2000 (“ Sakurada ”)
Ex. 1047	Chi-Ming Ho <i>et al.</i> “ <i>Ruthenium Nanoparticles Supported on Hydroxyapatite as an Efficient and Recyclable Catalyst for cis-Dihydroxylation and Oxidative Cleavage of Alkenes</i> ,” Angew. Chem. Int. Ed. 43:3303-3307, 2004 (“ Ho ”)
Ex. 1048	N. Miyaura and J. K. Kochi “ <i>Chromyl Complexes in the Direct Epoxidation of Alkenes</i> ,” J. Am. Chem. Soc. 105: 2368-2378, 1983 (“ Miyaura ”)
Ex. 1049	Waldemar Adam and Lluís Blancafort “ <i>Steric and Stereoelectronic Control of the Mode of Selectivity as a Function of Alkene Structure in the Reaction with Dimethyl α-Peroxy Lactone: Cycloadducts and Ene Products versus Epoxides</i> ,” J. Am. Chem. Soc. 118: 4778-4787, 1996 (“ Adam ”)
Ex. 1050	Williams <i>et al.</i> “ <i>Total Synthesis of (-)-Ratjadone</i> ,” Org. Lett. 3: 1383, 2001 (“ Williams ”)

IV. SUMMARY OF MY OPINIONS

6. I understand the following table summarizes the grounds of challenge (“Grounds”) raised in the Petition:

Ground	Invalidity Challenge	References	Challenged Claims
1	§ 103	Cheng in view of Le	1-7, 9-11, 24-26, 28 and 29
2	§ 103	Cheng in view of Wright ’788	1-7, 9-11, 24-26, 28 and 29

3	§ 103	Furuya in view of Le	1-7, 9-11, 24-26, 28, 29, 35 and 36
4	§ 103	Furuya in view of Wright '788	1-7, 9-11, 24-26, 28, 29, 35 and 36

7. After a review of the '803 Patent and the prior art, it is my opinion that the Challenged Claims are invalid under the proposed Grounds. My opinions, and the bases therefore, are detailed throughout this Declaration.

V. LEGAL PRINCIPLES

8. I am not an attorney and will not be offering legal conclusions. However, I have been informed of several principles concerning legal issues relevant to my analysis of the Challenges to the claims of the '803 Patent, and I relied on these principles to arrive at my conclusions.

9. I understand a claim is anticipated if all limitations are found in a single prior art reference, arranged as in the claim. The identical invention must be shown in as complete detail as is contained in the patent claim.

10. I understand a prior art reference can disclose an element not expressly identified in a reference if the element is “inherently present” in the reference. To be “inherent,” I understand the missing element must necessarily be present in the reference. An element is not “inherent” if the missing element is only probably present or if there is merely a possibility it is present.

11. I understand a claim is invalid as obvious under 35 U.S.C. § 103 if the differences between the subject matter sought to be patented and the prior art are such that the subject matter of the claim as a whole would have been obvious at the time of the patent's filing date to a Person of Ordinary Skill in The Art (POSITA). It is my understanding that the following factors are used to determine whether or not the claimed subject matter would have been obvious: (i) the scope and content of the prior art; (ii) the differences between the prior art and the claimed invention; (iii) the level of ordinary skill in the field of the invention; and (iv) any relevant objective considerations of non-obviousness.

12. I understand a party asserting obviousness based on a combination of prior art references must demonstrate that one of ordinary skill in the art would have been motivated to combine the teachings of those references to achieve the claimed invention with a reasonable expectation of success. It is my understanding that it is not sufficient to show that one of ordinary skill in the art *could* combine elements of multiple references. Instead, there must be a rational reason that would have prompted a POSITA to combine the elements in the way the claimed invention does; and the reason should be explained or articulated.

13. I understand a combination of references would not have been obvious if the alleged modification(s) to be made to the reference(s) are inconsistent with the stated goals of the reference(s). I understand a combination of references would not

have been obvious if the modification of the reference(s) to derive what is claimed would render the reference(s) unsatisfactory or inoperable for their intended purpose. I further understand the party asserting obviousness must explain why a POSITA would have selected components for combination in the manner claimed.

14. It is my further understanding that an invention would not have necessarily been obvious simply because all the elements of the invention may have been known separately in the prior art; there must be a reason to combine the separately known elements. Obviousness cannot be based on a hindsight combination of components selectively picked from the art using the claims as guide.

A. Level of Ordinary Skill in the Art

15. I understand that certain issues in an IPR, such as claim construction and whether a claim is invalid as obvious, are assessed from the view of a hypothetical person of ordinary skill in the relevant art at the time of the invention. I understand there are multiple factors relevant to determining the level of ordinary skill in the art, including: (1) the level of education and experience of persons working in the field at the time of the invention; (2) the sophistication of the technology; (3) the types of problems encountered in the field; and (4) the prior art solutions to those problems

16. In view of the above and based on my experience and knowledge, I believe a hypothetical Person of Ordinary Skill in The Art (POSITA) with regard to

the '803 patent is someone having a bachelor's degree and two years of experience or a master's degree in organic synthesis or chemical engineering, with education substituting for experience and vice versa.

B. Priority of '803 Patent

17. The '803 patent claims priority to a chain of applications originating with U.S. provisional application no. 62/623,985 filed on January 20, 2018. *See* '803 Patent.

C. Claim Construction

18. I understand that claim construction in an IPR proceeding is a legal question for the Patent Trial and Appeal Board (PTAB or Board) to decide. In general, I understand that claim terms are to be given their ordinary and customary meaning to a POSITA in the context of the patent at the time the patent was filed.

19. I also understand that in construing claim terms, the Board asks what the claim terms would mean to a person of ordinary skill in the relevant art in view of the plain claim language and the disclosures of the patent and prosecution history. I understand that the Board may also consider other external evidence, such as dictionaries, however the disclosures in the patent and prosecution history carry more weight than external evidence.

20. I have been informed by counsel for Petitioner that the proper construction for "about 5 to about 20 carbon atoms" ('803 Patent) is "4 to 21 carbon atoms." I have applied this construction in my analysis of the claims.

21. It is my opinion that these proposed constructions align with the plain meaning and context of the claim language, the specification, and the prosecution history.

VI. BACKGROUND

A. Summary of the Invalidity of the Inolex Patents

22. The '803 Patent claims various aspects of well-known processes for converting a bio-1-alcohol into a corresponding bio-1-alkene and then the bio-1-alkene into a bio-1,2-alkanediol. It is my opinion that before the Priority Date of the '803 Patent, a POSITA seeking a “green” or “natural” version of a bio-1-alkene to use as a starting material in a process of forming a bio-1,2-alkanediol would look to inter alia references like Le or Wright '788, which describe processes for making bio-1-alkenes from new carbon sources (from renewable or green carbon feedstock).

23. In addition to dehydration there were alternatives for producing bio-1-alkenes. For example it was known that naturally produced fatty acids can be converted to terminal olefins through oxidative decarboxylation. *See, e.g.*, Rui at 7091-7094. Rui taught a process for the biosynthesis of terminal olefins and establishes “a bioprocess to produce medium-chain 1-alkenes from renewable resources.” Rui at 7094.

24. A further example is that Gao teaches it was well-known that primary ethers can be cracked to form olefins in the presence of a gamma-alumina catalyst. *See, e.g.*, Gao. Gao further discusses that while it was known to dehydrate alcohols

in the presence of gamma alumina, the literature was less clear about the efficacy of using ethers as starting materials. Gao discloses a process to convert ethers into 1-alkenes that is both efficient and with limited byproducts. Gao at 1-2. Gao further details that the market prefers alpha-olefins to internal or branched olefins so the process disclosed focuses on the preferential production of alpha-olefins. Gao at 3. Gao also teaches that it is preferable to use commercially available catalysts, and since gamma-alumina catalysts are commercially available and efficiently produce 1-alkenes, they are the preferred choice. Gao does not specify which catalyst to use because individual considerations will need to be made based on the cost of the commercially available catalyst and the design of the reactor. Gao at 3. Using the process of Gao, 1-octene was produced at a selectivity of greater than 95%.

25. A still further example is the use of bio-ethanol as a starting material to create bio-ethylene, which is used in an oligomerization reaction to create alpha-olefins. *See, e.g.,* Vermeirin. Vermeirin discloses that the ethanol from a “biological origin” is dehydrated to ethylene which is oligomerized into alpha-olefins having from 4 to 20 carbon atoms. Vermeirin at 19:65-20:8. In one example, the bio-ethylene is trimerized into a bio-1-hexene. Vermeirin at 20:58-67. Vermeirin also discusses that there are multiple known methods for producing the alpha-olefins, including at least a Ziegler process or a catalytic process. Vermeirin at 16:31-39.

26. Finally, as set out in the Le and Wright '788, discussed below, renewable or green carbon feedstock is routinely processed into bio-1-alcohols having a carbon chain length of five or more carbon atoms. *See also* Koivusalmi at 7:60-8:16 (describing bio-feedstocks). These bio-alcohols are converted into corresponding bio-1-alkenes having the same number of carbon atoms via dehydration. A POSITA would understand that the reactions set out in Le and Wright '788 are highly regioselective, generating greater than 95% bio-1-alkene and less than about 5% of impurities. The relevant source and outputs of the methods described in Le and Wright '788 are illustrated below:

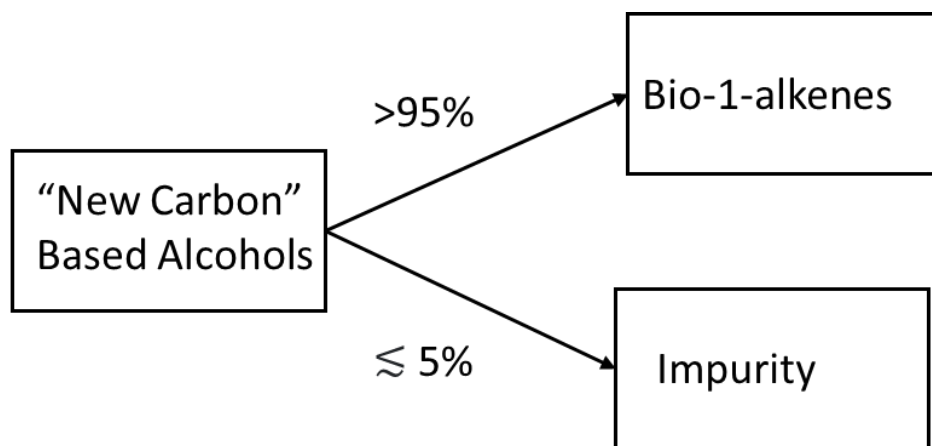


Illustration of Le and Wright '788 teaching

27. When using the Le or Wright '788 bio-1-alkene as the starting material, the result of Cheng or Furuya's process would be a plant-derived bio-1,2-alkanediol with reduced odor. Moreover, since the starting material from Le or Wright '788 is highly selective, it contains more than 95% bio-1-alkene, the resulting material

would likewise contain more than 95% bio-1,2-alkanediol and less than 5% impurity. A POSITA would understand that the conversion of the bio-1-alkene to the corresponding bio-1,2-alkanediol occurs at near unity yield, and therefore the proportion of alkene in the starting materials controls the resulting proportion of diol in the conversion of alkene to diol. This process of Cheng or Furuya is illustrated below:

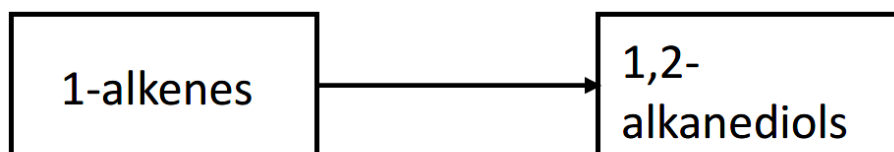


Illustration of Cheng or Furuya teachings

28. When all of these teachings are viewed together, it is my opinion that the art teaches the elements of the claims of the '803 Patent. A POSITA understands that Cheng or Furuya teach a process starting with 1-alkenes to make 1,2-alkanediols with reduced odor. A POSITA looking to improve marketing and environmental impact while reducing reliance on oil, would look to Le or Wright '788, which teach a process to make 1-alkenes from plant-derived sources.

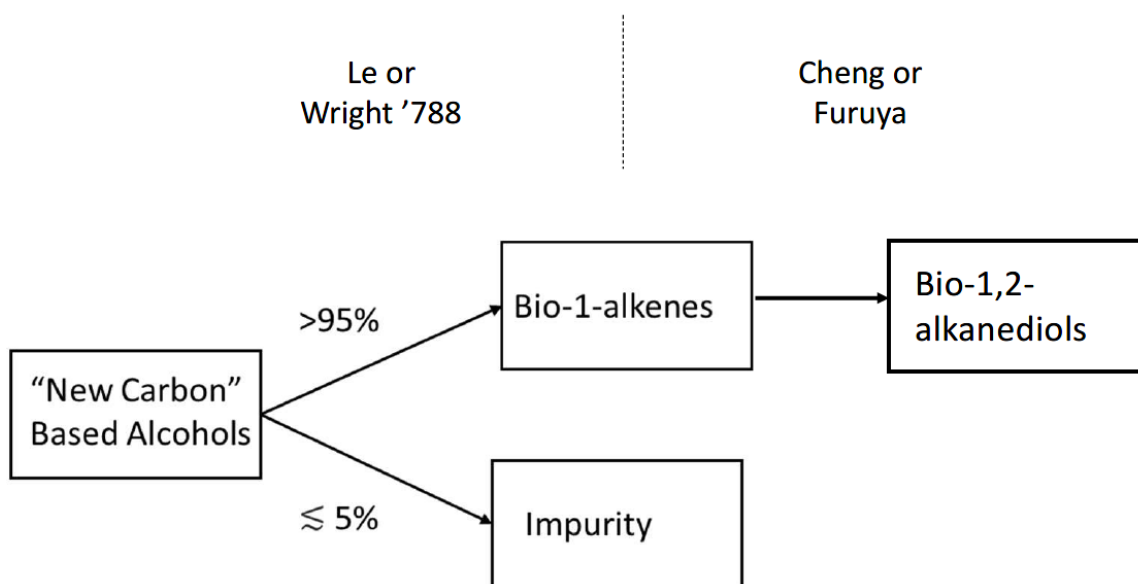


Illustration of combined teachings

29. As of the priority date of the '803 patent, in my opinion, all of the chemicals and reactions claimed in the '803 patent were well known for decades prior to the filing date of the '803 patent, and the '803 patent does not provide any explanation of how their proposed reactions differ from those identified in any general organic chemistry textbook.

B. New Carbon Compounds and Fossil Carbon Compounds Have the Same Properties and Chemical Reactivity

30. Compounds formed from new carbon compounds will have the same properties and chemical reactivity as the corresponding compounds formed from fossil carbon compounds. The difference between new carbon and fossil carbon is the age of the carbon compounds. Fossil carbon includes old carbon compounds found in petroleum and coal which formed millions of years ago, largely during the

Mesozoic era. The carbon compounds in petroleum and coal are therefore millions of years old. Compounds derived from modern-day plant and animal origins, however, contain new carbon compounds. Modern-day plants absorb carbon dioxide from the earth's current atmosphere. Plants absorb the carbon dioxide and convert it into new organic compounds via photosynthesis. Because these new organic compounds are formed from modern-day carbon dioxide, they contain new carbon atoms. Animals eat plants and therefore animals also provide a source of "new carbon" compounds.

31. Two differences between new carbon compounds and fossil carbon compounds are the percentage of carbon-14 (^{14}C) and the percentage of deuterium present in the compounds. Fossil carbon compounds contain less ^{14}C than new carbon compounds. Over long periods of time ^{14}C decays into nitrogen (^{14}N). Fossil carbon compounds are millions of years old and therefore some of the original ^{14}C has decayed into ^{14}N . The proportion of ^{14}C even in new carbon compounds is less than 1%. The small differences in ^{14}C substitution will not influence the chemical reactions discussed in this declaration or the physical properties of the products of those reactions. In other words, the age of the carbon compounds does not alter the chemical reactivity of the compounds or physical properties of the compounds. This would have been known and well-understood by a POSITA at the time of the invention.

32. The other difference between new carbon compounds and fossil carbon compounds is the deuterium substitution. One measure of deuterium concentration availability is the concentration of deuterium in the ocean, which is one part in 6400 compared to normal hydrogen. The deuterium (heavy hydrogen) content of new carbon compounds can differ from this measure by parts-per-million, as can the deuterium (heavy hydrogen) content of carbon compounds derived from petroleum or coal. A POSITA would understand that parts-per-million differences in deuterium substitution, already only one part in 6400, would also have no impact on the chemical reactions described in this declaration. The small differences in deuterium substitution will also not influence the physical properties of the products of those reactions. Again, the age of the carbon compounds does not alter the chemical reactivity of the compounds or physical properties of the compounds.

33. A POSITA would understand that the choice of new carbon versus fossil carbon starting materials might be driven by many considerations, *e.g.*, marketing, cost, availability, but would not be based on any fundamental differences in the chemistry. *See, e.g.*, Reck at 357; Kreutzer at 344. Further to this point, it is my opinion that a POSITA would understand that the origins of the carbon and hydrogen in a chemical compound, while having some marketing impact on the final product, does not alter the operation of the reaction when dehydrating a 1-alcohol to

a 1-alkene or converting the 1-alkene to a 1,2-diol. While the content of the starting materials (*e.g.*, unwanted impurities, etc.) and reaction conditions (*e.g.*, temperature, catalysts, etc.) can impact the outcome of a reaction, minor differences in the stable isotope composition of the starting materials will not impact the reaction. Indeed, if the starting materials were 100% new carbon, 100% fossil carbon, or a mixture of the two, when used in a reaction, it would have no significant effect on the outcome.

34. The term “bio” is often used in the art to describe compounds derived from new carbon (“bio-compounds”), *i.e.*, compounds derived from current plant or animal origins. Bio-compounds are considered renewable and therefore more environmentally sustainable. The POSITA would know that bio-compounds have been available long before the Priority Date of the '803 Patent. For example, new carbon compounds were investigated as starting materials in the 1940's because the United States government limited access to petroleum products due to the outbreak of World War II.

35. Bio-alcohols are a particularly important class of bio-compounds. Bio-alcohols are used widely for many reasons, for example, as fuel, in polymerization reactions, in cosmetics and other consumer products, *etc.* A POSITA would have known before the Priority Date of the '803 Patent that bio-alcohols were available and could be easily obtained or prepared by a variety of well-known methods. For example, bio-alcohols were prepared by reduction of fatty acids and esters present

in vegetable oils and animal fats, or by fermentation with yeast or bacteria. *See, e.g.,* Le, Vecchini, Gao, and Koivusalmi. Furthermore, bio-1-alkenes were prepared by oligomerization of bio-ethylene. Vermeiren at 1:33-46.

36. The starting alcohol in the '803 Patent is referred to as a "bio-1-alcohol". '803 Patent at 14:23-32. A POSITA would understand that a bio-1-alcohol is a 1-alcohol derived from modern-day vegetable or animal origins rather than from petroleum or coal. The use of bio-alcohols as starting materials for commercial chemical production was known before the Priority Date of the '803 Patent. Colby at 2:6-8, 9:41-53, 10:61-11:8 and 12:64-13:14.

37. For example, it was well-known to use biomass as a starting material to derive end-products via fermentation. Parekh at Abstract, 16:53-21:18. Parekh explains, "demand for renewable fuels and chemical[s] is growing significantly and is required to reduce reliance on petroleum-based products...." Parekh at 1:14-16; Alibhai at 1:31-4:44. Parekh describes a process for using biomass feedstock, a catalyst, and fermentation to create end products including bio-1-alkenes, bio-1-alcohols, and bio-diols, amongst many other more complicated end products. Parekh at 16:53-21:18; Alibhai at 7:49-51. A POSITA would understand that these bio-compounds were well-known and the processes for creating them were also well-known before

to the Priority Date of the '803 Patent. *See, e.g.*, Reck at 355-365; Kreutzer at 343-347.

38. A POSITA also would have known that bio-1-alcohols can be formed via numerous different chemical pathways, including hydrogenation [Makgoba at 3.3], from fatty acids, cracking ethers, or other product's waste material, amongst others. *See, e.g.*, Koivusalmi at 3:48-57. Notwithstanding the multiple known pathways for creating bio-1-alcohols, bio-1-alcohols were commercially available and readily obtainable before the Priority Date of the '803 Patent. *See, e.g.*, Koivusalmi at 3:58-4:29.

C. First Reaction Described by the '803 Patent: dehydration of 1-alcohol

39. As of the Priority Date of the '803 Patent, in my opinion, all of the chemical products and reactions claimed in the '803 Patent were well known, and had been well known for decades. For example, the chemical reactions described in the '803 Patent are taught in entry-level organic chemistry textbooks. The '803 Patent does not explain or identify how or why its chemical products and reactions differ from those known in the art.

40. Initially, the '803 Patent describes making a 1-alkene by dehydrating a bio-1-alcohol. The dehydration reaction takes place by heating the alcohol in a reactor with a catalyst to form the corresponding bio-1-alkene. I understand that according to the '803 Patent, "bio"-compounds such as bio-

alcohols and bio-alkenes are compounds derived from new carbon sources such as plants and animals. The '803 Patent explains, that “[t]rue natural products (bio-compounds) are formed using biomass (*e.g.*, material stored from carbon cycle processes in living plants and roots, etc. or released through animal respiration or through decomposition). '803 Patent at 3:41-44. The '803 Patent specifically states that bio-compounds “are intended to include materials derived from the carbon of plant sources/biomass, that exist recently and are also sustainable, and are not derived from fossil fuels.” '803 Patent at 3:47-50. As discussed above, the use of new carbon has no effect on the proposed chemical reactions or products of the '803 Patent or the prior art discussed below.

41. The dehydration of the 1-alcohol (also known as a primary alcohol) to the 1-alkene (also known as a terminal alkene or alpha olefin) is “one of the oldest catalytic reactions....” *See, e.g.*, Koivusalmi at 4:20-22; *see also* Tiitta at 3:9-18; Ziehe at 1:9-19. This straightforward reaction appears in entry-level organic chemistry textbooks, and has been a part of the scientific literature for decades. Wade at 312-314; Komarewsky at 557-558.

42. The conversion of 1-octanol (a 1-alcohol or primary alcohol having a carbon chain length of 8) to 1-octene (a 1-alkene or terminal alkene having a carbon chain length of 8) is shown below:

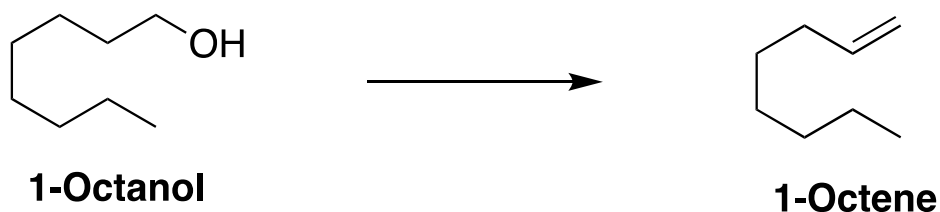


Figure 2: Conversion of 1-octanol to 1-octene

43. Acid-catalyzed dehydration of the 1-alcohol occurs when an acid donates a proton to the OH-group of the alcohol. This leads to the protonated alcohol as illustrated below. As the protonated alcohol leaves as water (H_2O) the proton on the adjacent carbon is also lost, resulting in the alkene. Wade at 312-314. This conversion is represented by the reaction equation below:

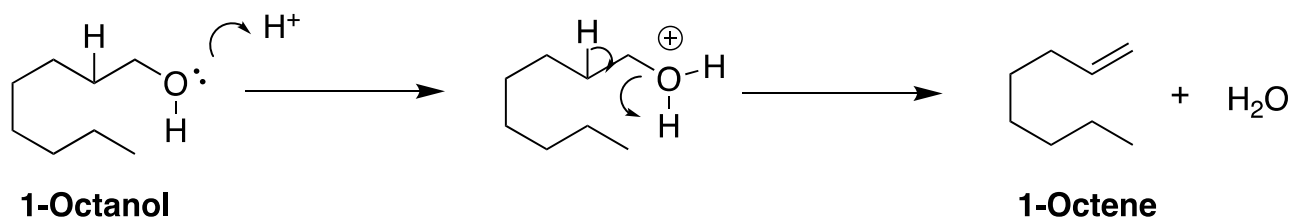


Figure 3: Dehydration of 1-octanol to 1-octene under acid catalysis

44. It is well-known that the intermediate compound (the protonated alcohol) can undergo additional reactions based on the reaction conditions. Colby at 8:17-29. Specifically, the intermediate protonated alcohol can react with another molecule of the primary alcohol starting material. This reaction will result in the formation of the protonated ether, which is also referred to in the art as a “protonated dimer”. The protonated ether (or protonated dimer),

however, is typically not problematic because under conditions for the acid-catalyzed dehydration, the protonated ether (or protonated dimer) can convert to the desired 1-alkene and the 1-alcohol, as shown below. The 1-alcohol can then be converted to the desired 1-alkene.

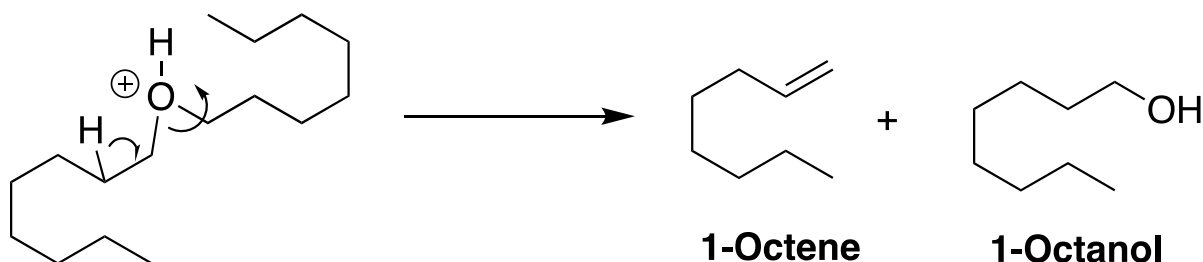


Figure 4: Reaction between primary and protonated alcohol

45. Isomerization of alkenes is a well-known concept in organic chemistry, taught in entry-level organic chemistry classes. Isomerization outcomes are predictable and were known prior to the Priority Date of the '803 Patent. *See* Fuji at [0002]-[0003] (referencing increased selectivity based on amount of base components used and/or lower reaction temperature), [0034] (altering conversion ratio to optimize selectivity). An example of isomerization can be shown with the primary alkene (1-octene) depicted in the dehydration reaction discussed above. The primary alkene (1-octene) can isomerize in the presence of an acid to form a 2-alkene (2-octene), as shown below. The isomerization will proceed by protonation of the 1-alkene to give

the intermediate carbocation. The 2-alkene is then formed by loss of a proton from the adjacent carbon. The isomerization reaction of the primary alkene to form the 2-alkene will deplete the yield of the 1-alkene product from the dehydration reaction described above. Therefore, a POSITA would seek to minimize isomerization in the manufacture of 1-alkenes.

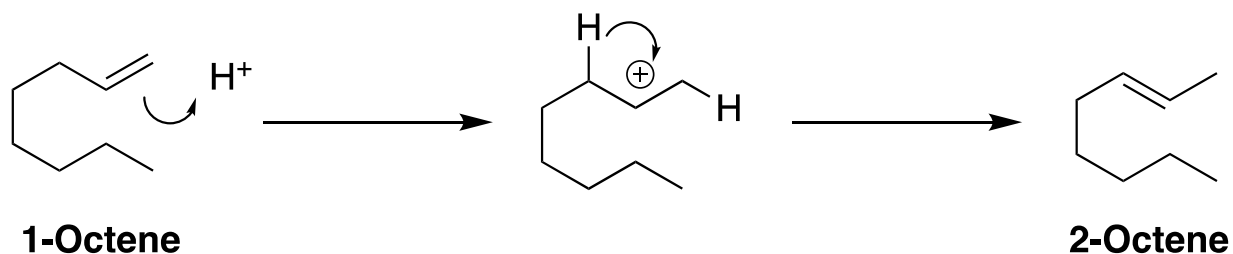


Figure 5: Isomerization from 1-alkene to 2-alkene

46. It was known before the Priority Date of the '803 Patent that to obtain high yields of 1-alkenes, and avoid isomerization reactions, the 1-alkenes should be removed from the acid-catalyzed dehydration reaction as quickly as possible. This process was known and extensively practiced prior to the filing date of the '803 Patent. Komarewsky at 557-558.

47. The dehydration reaction discussed above has been known for decades and has been and is practiced on metric ton scale. *See, e.g.,* Fuji at [0039]. The reactions have been optimized for various starting and ending conditions to prioritize production of 1-alkenes. For example, dehydration reactions are often carried out continuously, especially on an industrial scale.

The desired 1-alkenes are continuously removed so they cannot undergo isomerization, and the unreacted starting 1-alcohols and other byproducts are recycled back into the dehydration reaction. *See, e.g.,* Fuji at [0037].

48. The process of removing 1-alkenes to prevent isomerization has been known since at least 1945, as evidenced by Komarewsky. Komarewsky dehydrated 1-octanol to form 1-octene by flow over a hot alumina catalyst. Komarewsky at 557-558. Komarewsky reported “a small amount (of the order of 2%) impurity in the product.” Komarewsky at 558. Komarewsky indicates the small amount of impurity includes “*trans*-octenes” (2-, 3-, or 4-). Komarewsky at 558. Komarewsky shows similar results with 1-hexanol and Appleby shows similar results with 1-heptanol. Appleby at 1938-1939. It was also known that a catalyst with excess acidic sites could be altered to control (limit) formation of such impurities. Wu at 2:24-36.

49. A POSITA, based on the general understanding of dehydration reactions discussed above, as evidenced by Komarewsky, Appleby, Ziehe, Fuji, and Wu, would understand that isomerization is slower than dehydration resulting in only “about 2%” of the 1-alkenes being isomerized.

50. A POSITA would seek to optimize the conversion of 1-alcohol to 1-alkene, for example, by adjusting reaction temperatures, modifying catalysts, changing flow rates, *etc.* This is illustrated by Wright '788. Wright

'788 explains, "[a] purge gas is used to control dwell time in the reactor chamber and the temperature is modified to optimize bio-1-alkene production for a particular bioalcohol feedstock." Wright '788 at [0030]; *see also* Fuji at [0032]. Extensive literature relating to the optimization of such parameters was available to a POSITA before the Priority Date of the '803 Patent. *See, e.g.,* Voeste at 2-3; Fuji at [0002]-[0003] and [0026]-[0040].

51. Before the Priority Date of the '803 Patent, a POSITA would understand that varying one parameter of a reaction design might influence another parameter. For example, optimizing for yield might require more energy consumption (*e.g.,* higher temperatures). On the other hand, optimizing for energy consumption (*e.g.,* using lower temperatures) might produce a less pure final product. A POSITA would appreciate how multiple variables can be adjusted to achieve a desired outcome.

52. A POSITA optimizes reaction conditions to achieve a desired outcome (or "sufficient" outcome). For example, a desired outcome might be obtaining a product with 90% yield and 95% purity. To reach this desired outcome, the POSITA would vary reaction conditions until the POSITA reached or exceeded the desired outcome. There are multiple ways to achieve a desired outcome. In other words, there is not just one "optimal" set of conditions. In most cases, as in dehydration reactions, there are multiple ways

variables can be optimized to achieve a desired outcome. The figure below illustrates this point for just two reaction variables—temperature and flow rate. Dehydration reactions typically proceed more quickly at higher temperatures. Flow rate determines how long reactants are available to react with one another. Therefore, a high temperature combined with a high flow rate could lead to the desired outcome. Alternatively, a lower temperature combined with a slower flow rate could also lead to the desired outcome. This concept applies to a multitude of other reaction conditions including, for example, types of catalysts and methods for preparing the catalysts, including treating the catalyst with a base or a silanizing agent. Thus, a POSITA understands there is not only one single unique combination of optimized parameters required to successfully achieve a desired outcome.

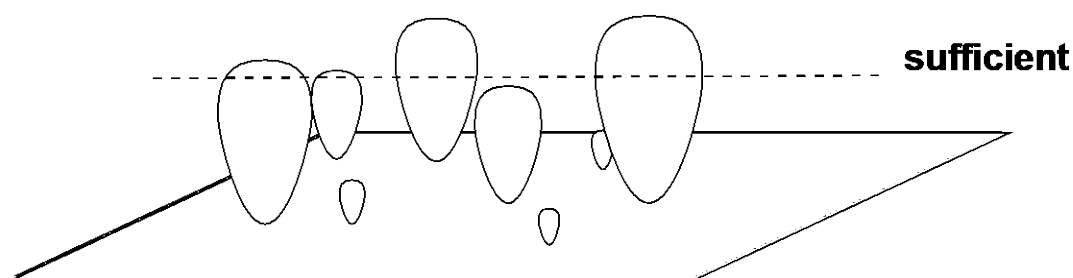


Figure 6: Optimization of two variables

53. A POSITA would know and understand that commercial scale dehydration reactions are common and have been carried out for decades. For example, SASOL, a chemical company, has been commercially producing 1-octene

via dehydration of 1-octanol for many years, and certainly before the Priority Date of the '803 Patent. *See, e.g.*, De Bruyn. The process at commercial scale is well-understood and predictable.

D. Second Reaction Described by the '803 Patent: 1-alkene to 1,2- diol conversion

54. The second reaction undertaken is the conversion of the 1-alkene to its corresponding diol (commonly referred to as a 1,2-alkanediol or glycol). A POSITA would understand that many processes for converting the 1-alkene to the 1,2-diol were well-known and well-understood in the art. The various reagents and protocols were well-described. Among the many ways to convert the 1-alkene to the corresponding 1,2-diol were Swern (conversion using formic acid/H₂O₂; KOH), Sarma (conversion using H₂O₂/ethyl acetate/lipase), Wang (conversion using O₂/acetic acid/Pd catalyst to make diacetate), Fristad (conversion using ammonium persulfate/acetic acid/Fe catalyst to make diacetate), Ho (conversion using NaIO₄/H₂SO₄/Ru catalyst), Sakurada (conversion using bis (trimethylsilyl) peroxide/trimethylsilyl acetate/acetic acid/Sn catalyst to make monoacetate), Herrmann (conversion using H₂O₂/H₂O/Re catalyst), Williams (conversion using potassium ferricyanide/Os catalyst), Adam (conversion using peroxy lactone to make the 1,4-dioxane-2-one), Miyaura (conversion using chromyl nitrate to make epoxide). The POSITA would be motivated by, *e.g.*, ease of operation and the

minimal cost to first explore the combination of a peracid with water to effect this transformation. *See, e.g., Swern; see also Sarma.*

55. The POSITA reading Swern and Sarma would understand that the epoxide opening step would be accompanied by some ester formation. One well-known method of maximizing yield of the diol from this reaction is to add a hydrolysis step, *e.g.,* add hydroxide [Swern; Sarma; and Wade] to the reaction mixture, to maximize the yield of the bio-1,2-diol created from the bio-1-alkene.

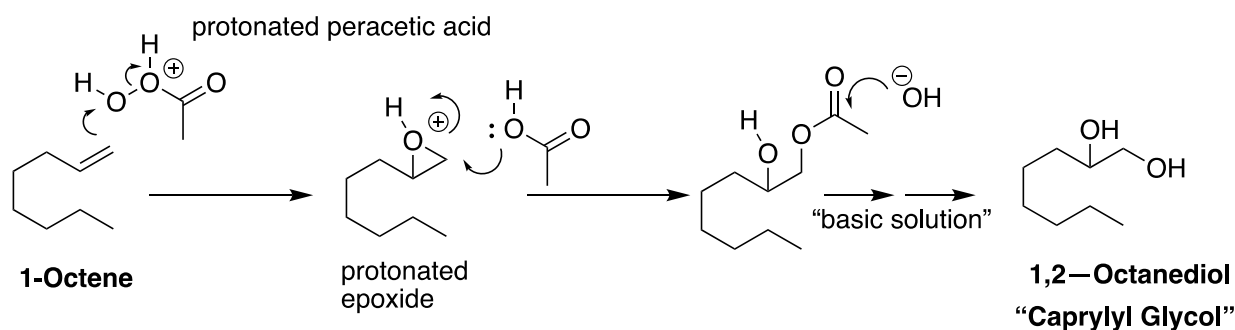


Figure 7: Conversion of 1-octene to 1,2-octanediol

56. To illustrate the protocol of Swern and Sarma that a POSITA would use to convert the 1-octene to the 1,2-octanediol, the 1-octene is epoxidized [Swern; Wade at 360-361; and Fringuelli 1939-1942], then the epoxide is opened with water [Wade at 362] or with *e.g.,* the carboxylic acid. Further treatment with basic solution ("saponification") is important if the epoxide is opened by the carboxylic acid rather than by water or if there is some residual epoxide [Swern; and Sarma].

57. In the '803 patent, the 1-alcohol is referred to as a “bio-1-alcohol”. '803 patent at 9:7-10. A POSITA would understand that a bio-1-alcohol is defined as being derived from current vegetable or animal origins rather than being derived from petroleum or coal. Bio-alcohols used as the starting materials for commercial chemical production were well known when the '803 patent was filed and small differences in isotope substitution between new and fossil carbon compounds would have negligible impact on any reaction taking place.

VII. THE PROCESSES DESCRIBED IN THE '803 PATENT WERE WELL KNOWN

A. Claims 1-7, 9-11, 24-26 and 28-29 are rendered obvious under 35 U.S.C. § 103 by Cheng in view of Le

58. A POSITA understands Cheng to describe a “commercially attractive way” for generating 1,2-alkanediols from 1-alkenes. Cheng at 1:40-45. A POSITA would understand that Cheng’s conversion process from alkenes to diols can use Le’s bio-1-alkenes having 6 to 9 carbon atoms derived from “renewable materials”. Le at [0002]. A POSITA would be motivated to convert the bio-alkenes of Le into 1,2-bio-alkanediols according to Cheng’s process because “...vicinal alkanediols, such as 1,2-alkane diols...” are useful in commercial applications, and Cheng’s method is a “commercially attractive way[]” for carrying out the conversion without objectionable odors commonly associated with the 1,2-alkanediols. Cheng at 1:6-10 and 1:40-48. Further, a POSITA understands that the choice of bio-based versus

petroleum starting materials would likely be driven by many considerations, *e.g.*, marketing, cost, and availability. *See, e.g.*, Vermeirin at 1:19-28; *see also* Koivusalmi at 1:51-2:8.

59. A POSITA would be motivated to prepare the bio-1,2-alkanediol from the bio-1-alkenes of Le (derived from current biomass) instead of petrochemically derived 1-alkenes given the growing demand in the market for renewable products and desires to reduce reliance on petroleum products. Parekh at 1:14-16; Alibhai at 1:31-4:44. In addition, a POSITA would be motivated to use bio-1-alkenes of Le (derived from natural feedstocks) instead of petrochemically derived 1-alkenes because this was a known solution to solve the known problem of detrimental environmental impacts associated with fossil fuel production and use. Le at [0009]-[0013].

60. A POSITA would also understand that a 1-alcohol, regardless of whether it is from current biomass or petroleum will predictably dehydrate to the corresponding 1-alkene that can then be converted to the corresponding 1,2-alkanediol based on the well-known protocols previously discussed.

61. Accordingly, it would be obvious to a person of skill in the art to use the bio-1-alkenes of Le to produce bio-1,2-alkanediols according to the procedures outlined by Cheng.

1. Claim 1

A process for the synthesis of bio-1,2-alkanediols, comprising: providing a bio-alkene having a carbon chain of about 5 to about 20 carbon atoms and a bio-1-alkene regioselectivity of at least about 80%; and

62. A POSITA would understand that at the time of the filing of the '803 patent the conversion of alkenes to 1,2-diols was a well-known and well-understood process. As one example, Cheng teaches how to convert alkenes having carbon chain length of 2 to 12 carbon atoms to their corresponding 1,2-alkanediols. Cheng at 2:44-67, 6:29-67, 7:1-40, 7:47-8:9, 11:20-41, 13:40-50, 13:58-18:59. In Cheng, examples provide POSITA guidance on the conversion of 1-hexene. First, Cheng epoxidizes 1-hexene to 1,2-epoxyhexane, which is subsequently converted to 1,2-hexanediol. A POSITA understands and Cheng teaches that the process works equivalently to produce 1,2-alkanediols having a carbon chain length of 2 to 12 carbon atoms, based on the starting alkenes having a corresponding carbon chain length of 2 to 12 carbon atoms.

63. Cheng can be combined with Le which describes alkenes “obtained from a fatty substance consisting of a plant oil...extracted from renewable resources.” Le at [0023]; *see also* [0027]-[0028], [0036]-[0037], [0053]-[0057], [0062]-[0063] and [0086]-[0089]. In one example, Le teaches, “plant oil comprising ricinoleic acid” which includes castor oil, is processed to obtain heptan-1-ol (1-heptanol), which is then dehydrated “so as to form 1-heptene.” Le at [0101]-[0105].

A POSITA would have understood that the alcohol (*e.g.*, 1-heptanol) and the alkene (*e.g.*, 1-heptene) in Le's method are a bio-alcohol and a bio-alkene, respectively, because they are derived from renewable plant oils and/or animal fats rather than petroleum or other fossil fuel sources.

64. A POSITA would understand that because the starting materials produced by Le are derived from renewable plant oils and/or fatty substances, the initial alcohol is a bio-1-alcohol and the product is a bio-1-alkene. '803 Patent at 13:53-55 ("bio-alkenes may be bio-1-pentene, bio-1-iso-pentene, bio-1-hexene, bio-1-heptene, ..."). In my opinion the alkenes produced by Le fit within the definition of "bio" provided by the '803 Patent, because they are "derived from the carbon of plant sources." '803 Patent at 3:26-56.

65. Le describes "an olefin, derived from renewable materials, having a number of carbon atoms included in the range of from 6 to 9." Le at [0002]; *see also* [0007], [0019]-[0020], [0059] and [0117]. The term "olefin" used in Le is another name for alkene while an alpha-olefin is another name for a 1-alkene. Le provides specific examples teaching a POSITA how to dehydrate C₆-C₉ alcohols to their respective alkenes. Le at [0094]-[0105], [0110]-[0114] and [0117]; *see also* [0168]-[0174] (dehydrating bio-1-heptanol derived from castor oil to produce bio-1-heptene). The chain lengths of bio-1-hexene, bio-1-heptene, and bio-1-nonene are respectively 6, 7 and 9 carbon atoms.

66. While Le does not use the word “regioselectivity”, a POSITA knows that regioselectivity merely describes the preference of a process to form one specific regioisomer over another regioisomer. Wade at 339. For example, when there are multiple regiosomeric products available for a reaction, and one of those regioisomers is favored, a POSITA would understand the reaction to be regioselective. A POSITA would recognize that the product 1-alkene from the dehydration can be isomerized under the reaction conditions to the 2-alkene. A POSITA would consider a protocol that converted a 1-alcohol primarily to the 1-alkene to be regioselective.

67. Le discloses a known process that “makes it possible to produce predominantly one olefin with a very limited number of isomers.” Le at [0012] and [0021]. Le states that when a 1-alcohol is dehydrated “a single isomer (an alpha-olefin) is obtained” contrasted to “when the saturated alcohol is not in the alpha-position, a mixture of two isomers is formed.” Le at [0068]. An alpha-olefin is another term for a 1-alkene. Finally, Le describes a purifying step for the bio-1-alcohol before dehydration to the corresponding bio-1-alkene. Le at [0171] and [0172]. Thus, a POSITA would understand Le to teach that the pure bio-1-alcohol (pure bio-1-heptanol) is dehydrated to “a single isomer” (bio-1-alkene) which would have a regioselectivity of at least about 80%.

68. The bio-1-alkene is the initial product from the dehydration of the bio-1-alcohol. Formation of other regioisomers (bio-2-alkene, bio-3-alkene) would arise from isomerization of the initially formed bio-1-alkene on the catalyst. As the product bio-1-alkene is removed quickly from the catalyst, isomerization is minimal. Accordingly, a POSITA would understand that even though Le does not actually use the term “regioselectivity,” Le’s method of obtaining a “single isomer” of the bio-1-alkene from pure 1-alcohol results in a high preference for the production of the bio-1-alkene.

69. Le provides specific examples for forming single isomers of bio-1-hexene, bio-1-heptene, and bio-1-nonene. When Le forms a mixture that includes two isomers, they are expressly identified. For example, when starting with 2-octanol, Le reports forming a mixture of 1-octene and 2-octene. Le at [0109]. A POSITA would understand that a 5% byproduct of a regioisomer *e.g.*, 2-alkene, would be easily detectable in the final product by magnetic resonance analysis. Accordingly, a POSITA would understand that Le’s “single isomer” is at least 95% 1-alkene because if there were any significant isomerization Le would have readily found and reported the byproduct. Therefore, a POSITA would understand that although Le does not use the term regioselectivity, Le’s method of obtaining a single isomer of the bio-1-alkene results in a bio-1-alkene regioselectivity of greater than 95%, which is “at least about 80%.”

converting the bio-alkene to a bio-1,2-alkanediol having a carbon chain length of about 5 to about 20 carbon atoms.

70. Patent Owner acknowledges, and I agree, that converting a bio-1-alkene to a corresponding bio-1,2-alkanediol having a carbon chain length of about 5 to about 20 carbon atoms was well-known in the art prior to filing the '803 Patent. '803 Patent at 18:30-43. I understand that during patent prosecution the Patent Owner identified as well-known the specific steps claimed in the '803 patent that convert a 1-alkene to a 1,2-alkanediol. '803 Patent at 18:30-43. Patent Owner explained that one well-known sequence for this conversion was:

Various chemical reactions may be used for this conversion as are known for use in standard alkene to alkanediol conversions using petrochemically derived starting materials and/or that are used for smaller chain bio-alkanes. For example, the bio-1-alkene is reacted in the presence of at least one of formic acid or acetic acid, and a peroxide such as hydrogen peroxide to form an intermediate solution including a bio-1,2-epoxyalkane, bio-1,2-alkanediol, and other components. This is then further contacted with a base solution, such as a sodium hydroxide or another suitable base solution, to complete formation of the bio-1,2-alkanediol. The process noted above preferably yields about 60% to about 99%, and more preferably about 70% to about 99% or about 75% to about 99% of bio-1,2-alkanediol.

'803 Patent at 18:30-43.

71. Cheng also describes converting alkenes having carbon chain lengths of 2 to 12 into the corresponding 1,2-alkanediols. Cheng at 2:44-67, 6:29-67, 7:1-40, 7:47-8:9, 11:20-41 and 13:40-50; *see also* 13:58-18:59 (Example 1 converts 1-hexene to an intermediate 1,2-epoxyhexane and Examples 2-6 convert the

intermediate 1,2-epoxyhexane into 1,2-hexanediol). Cheng states, “[i]n Examples 3-5, 1,2-hexanediol is produced by hydrolysis from 1,2-epoxyhexane which in turn was produced in Example 1 by oxidation of 1-hexene with hydrogen peroxide using a peroxotungstate catalyst.” Cheng at 13:40-43. Cheng also provides that “various epoxidizable olefinic compounds can be epoxidized and purified in the practice of this invention.” Cheng at 11:29-30. Cheng specifically identifies 1-alkenes having 2 to 12 carbon atoms, including:

ethylene, 1-propene, 2-methyl-1-propene, 1-butene, 1-pentene, 4-methyl-1-pentene, 1-hexene, 3-ethyl-1-hexene, 4-n-propyl-1-heptene, 1-octene, 1-nonene, 1-unadecene, 1-dodecene, 5-methyl-1-dodecene, 1-tetradecene, 1-hexadecene, and the like. Preferred alkenes are 1-pentene, 1-hexene, 1-heptene, and 1-octene; highly preferred is 1-hexene.

Cheng at 11:35-41.

72. A POSITA would understand Cheng’s process for converting 1-hexene to 1,2-hexanediol refers to a starting and final product having a carbon chain length of 6 carbon atoms. Likewise, a POSITA would understand based on the knowledge of skill in the art and because Cheng explicitly refers to alkenes having carbon chain lengths of 2 to 12, that Cheng’s process for creating 1,2-alkanediols would predictably yield 1,2-alkanediols having chain lengths of 2 to 12 carbon atoms. Cheng at 11:35-41. Accordingly, it is my opinion that a POSITA would understand that Cheng’s process forms 1,2-alkanediols with carbon chain lengths of 2 to 12

carbon atoms. Cheng at 11:35-41. Further, a POSITA would understand that beginning with one of the bio-1-alkenes from Le, the selected 1,2-alkanediol formed by the Cheng process would be the corresponding bio-1,2-alkanediol.

2. Claims 2-5

Claim 2. The process of claim 1, wherein the bio-alkene and the bio-1,2-alkanediol each have a carbon chain of about 6 to about 14 carbon atoms.

Claim 3. The process according to claim 2, wherein the bio-alkene and the bio-1,2-alkanediol each have a carbon chain length of about 6 to about 10 carbon atoms.

Claim 4. The process according to claim 3, wherein the bio-alkene and the bio-1,2-alkanediol each have a carbon chain length of about 6 to about 8 carbon atoms.

Claim 5. The process according to claim 1, wherein the bio-alkene is bio-octene and the bio-1,2-alkane diol is bio-1,2-octanediol.

73. A POSITA would understand that Le teaches “an olefin [alkene], derived from a renewable materials, having a number of carbon atoms included in the range of from 6 to 9.” Le at [0002]; *see also* [0007], [0019-0020], [0059] and [0117] (describing Le’s invention producing alkenes with 6 to 9 carbon atoms).

74. In addition to teaching bio-alkenes of 6 to 9 carbon atoms, A POSITA would understand that Le also teaches specific examples for dehydrating bio-1-hexanol, bio-1-heptanol, and bio-1-nonanol into bio-1-hexene, bio-1-heptene, and bio-1-nonene. Le at [0094]-[0105]; *see also* [0168-0174] (providing an example involving dehydrating bio-1-heptanol derived from castor oil to make bio-1-

heptene). The carbon chain lengths of bio-1-hexene, bio-1-heptene, and bio-1-nonene are 6, 7, and 9, respectively. Carbon chains of 6 to 9 carbon atoms are within the ranges of 6 to 14 (claim 2), 6 to 10 (claim 3), 6 to 8 (claim 4), and 8 carbon (claim 5).

75. Le provides a specific example of dehydrating bio-2-octanol into a mixture of bio-1-octene and bio-2-octene. Le at [0106]-[0109]. While this example uses bio-2-octanol instead of bio-1-octanol, Le is not limited. A POSITA would understand that dehydration of bio-2-octanol would lead to two regioisomers, bio-1-octene and bio-2-octene, because the alcohol in the 2 position could dehydrate in either direction, towards the 1 position to give the bio-1-octene or towards the 3 position to give the bio-2-octene. Le presumably used bio-2-octanol because it was readily available at low cost, not because of any technical difficulty using bio-1-octanol. Le at [0068]. A POSITA would expect that using the process of Le with bio-1-octanol instead of the bio-2-octanol, would produce “a single isomer (an alpha-olefin)”, bio-1-octene. Le at [0068]. Therefore, a POSITA would understand that if the desired end-product were bio-1-octene (instead of a mixture of bio-1-octene and bio-2-octene), starting with bio-1-octanol, also taught by Le, would result in formation of “a single isomer” of bio-1-octene.

76. Cheng teaches “[i]n Examples 3-5, 1,2-hexanediol is produced by hydrolysis of 1,2-epoxyhexane which in turn was produced in Example 1 by

oxidation of 1-hexene with hydrogen peroxide using a peroxotungstate catalyst.” Cheng at 13:40-43. A POSITA would understand that Cheng’s disclosure of a process for converting 1-hexene to 1,2-hexanediol refers to a product having a chain length of 6 carbon atoms. Cheng also explicitly discloses the conversion of 1-octene to 1,2-octanediol, which both have carbon chain lengths of 8 carbon atoms. Cheng at 11:35-41 (starting alkenes include 1-octene).

77. Finally, a POSITA would understand that the process for synthesizing 1,2-alkanediols provided by Cheng would predictably yield 1,2-alkanediols having various chain lengths from 2 to 12 because Cheng explicitly refers to 1-alkenes having a chain length of 2 to 12 carbon atoms. Cheng at 11:35-41 (including starting with *e.g.*, 1-octene). A POSITA would understand that using Le’s bio-1-octene in Cheng’s conversion process would predictably result in bio-1,2-octanediol.

3. Claim 6

The process according to claim 1, wherein the bio-alkene results from a process wherein a bio-1-alcohol is dehydrated by heating the bio-1-alcohol in a reactor with a catalyst.

78. Le teaches an alkene/olefin “is obtained from a fatty substance consisting of a plant oil...extracted from renewable resources.” Le at [0023]; *see also* [0036]-[0037], [0053]-[0057], [0062]-[0063], [0086]-[0089] and [0094]-[0117]. In one example, Le explains, “oil comprising ricinoleic acid, preferably castor oil” is processed to obtain heptan-1-ol (1-heptanol), which is then dehydrated

“so as to form 1-heptene.” Le at [0101-0105]. A POSITA understands the alcohol (*e.g.*, 1-heptanol) and the alkene (*e.g.*, 1-heptene) in Le’s method are a bio-alcohol and a bio-alkene because they are derived from renewable plant oils, rather than petroleum or other fossil fuel sources. ’803 Patent at 13:53-55 (“bio-alkenes may be bio-1-pentene, bio-1-iso-pentene, bio-1-hexene, bio-1-heptene, ...”). Indeed, the ’803 Patent expressly notes that non-petrochemically derived products are known in the art as “bio” products, such as products “derived from the carbon of plant sources.” ’803 Patent at 3:26-56.

79. With regards to dehydrating the bio-alcohol, Le teaches:

In order to form the olefin (a) according to the process of the invention, **a dehydration step is carried out in a reactor** so as to form a mixture of alkene and water. This dehydration step can be carried out **in the presence of a dehydration catalyst**, for example a γ -alumina-based catalyst, which may be acidic or basic, in the presence of the **alcohols obtained from the starting materials of renewable origin**.

Le at [0062]-[0063] (emphasis added). The alcohol is dehydrated in the reactor by heating it at least within the exemplary temperature range of 250 to 400 °C. Le at [0065] and [0171].

80. Le’s numerous examples disclose dehydrating 1-hexanol, 1-heptanol, and 1-nonanol (all 1-alcohols) derived from plant oils into their respective 1-alkenes, *i.e.*, 1-hexene, 1-heptene, and 1-nonene. Le at [0094]-[0105], [0110]-[0114] and [0117]; *see also* [0168]-[0174] (dehydrating 1-heptanol derived from castor oil to 1-heptene).

81. Finally, the catalyst used in the dehydration reaction may be γ -alumina that is acidic, basic, doped, powder, or granules, and having various pore sizes. Le at [0062]-[0064], [0066], [0119] and [0171]. Specific examples of commercially available catalysts referenced in Le are “ESM 110®” produced by Eurosupport and “Pural® KR1” produced by Sasol®. Le at [0064] and [0066].

82. Therefore, a POSITA understands that Le teaches dehydrating a bio-1-alcohol (e.g., 1-hexanol or 1-heptanol derived from plant oil) by heating the bio-1-alcohol in a reactor (e.g., at 250 to 400 °C) with a catalyst (e.g., a γ -alumina catalyst) to form a bio-1-alkene (e.g., 1-hexene or 1-heptene derived from plant oil).

4. Claim 7

The process according to claim 6, wherein the reactor is a fixed bed reactor.

83. Le teaches an example using a tubular reactor with a catalytic bed to dehydrate 1-heptanol to 1-heptene. Le at [0171]. A POSITA understands that the reactor taught by Le would be a fixed bed reactor because the catalytic bed is a fixed layer of “ESM110® alumina” within the tubular reactor that promotes the dehydration of the 1-heptanol.

5. Claim 9

The process according to claim 6, wherein the catalyst is selected from ZnAl_2O_4 and a γ -alumina catalyst.

84. Le teaches the catalyst used in the dehydration reaction can be γ -alumina with varying parameters, such as the catalyst being acidic, basic, doped,

powder, granules, and having various pore sizes. Le at [0062]-[0064], [0066], [0119] and [0171]. Specific examples of commercially available catalysts that can be used with Le are “ESM 110®” produced by Eurosupport and “Pural® KR1” produced by Sasol. Le at [0064] and [0066]. A POSITA would understand that the commercially available catalysts are γ -alumina catalysts.

6. Claims 10-11

10. The process according to claim 9, wherein the bio-alkene has a bio-1-alkene regioselectivity of about 92% to about 99%.

11. The process according to claim 10, wherein the bio-alkene have a bio-1-alkene regioselectivity of about 95% to about 99%.

85. As discussed above with respect to Claim 1, a POSITA would understand that Le’s method to obtain a single isomer of the bio-alkene comprises a bio-1-alkene regioselectivity greater than 95%, which a POSITA would understand is at least about 92% to 99% and at least 95% to about 99%. Le expressly teaches “an olefin, derived from renewable materials, having a number of carbon atoms included in the range of from 6 to 9.” Le at [0002]; *see also* Le at [0007], [0019]-[0020], [0059] and [0117] (Le produced alkenes with 6 to 9 carbon atoms).

86. While Le does not use the word “regioselectivity”, a POSITA knows that regioselectivity merely describes the preference of a process to form one specific regioisomer over another regioisomer. Wade at 339. For example, when there are multiple regioisomeric products available for a reaction, and one of those regioisomers is favored, a POSITA would understand the reaction to be

regioselective. A POSITA would recognize that the product 1-alkene from the dehydration can isomerize and therefore could optimize reaction conditions to avoid isomerization. A POSITA would also understand and know how to design a protocol that converts a 1-alcohol primarily to the 1-alkene, with high regioselectivity.

87. A POSITA would have also understood that Le's invention teaches the production of the *bio*-alpha-olefin with very limited contamination by regioisomers. Le at [0012] and [0021]. Le also teaches that "when the saturated alcohol is not in the alpha-position, a mixture of two or more regioisomers is formed." Le at [0068]. A POSITA therefore would have understood the importance of using the bio-1-alcohol in the dehydration to make the bio-1-alkene, as the bio-1-alkene is the kinetic product from the dehydration of the bio-1-alcohol.

88. The high preference for 1-alkene formation on dehydration of 1-alcohols with γ -alumina catalysts had been known for more than 50 years prior to the filing of the '803 Patent. A POSITA would therefore expect that the conditions of the dehydration reaction taught by Le would lead to the bio-1-alkene product with high regioselectivity. The POSITA would also observe that Le easily distinguished between the 1-octene and the 2-octene obtained when the starting alcohol was 2-alcohol. Le at [0108]-[0109].

89. A POSITA would also understand that if impurity production increased above 5%, the impurities would be easily detectable by magnetic resonance analysis.

Accordingly, a POSITA would understand that Le's "single isomer" is at least 95% bio-1-alkene because if there were any significant impurity production it would have been readily apparent and reported. Therefore, a POSITA would understand that although Le does not use the term regioselectivity, Le's method of obtaining a single isomer of the bio-1-alkene results in a bio-1-alkene regioselectivity of greater than 95%.

90. A POSITA would expect that significant unexpected impurities would be addressed by the author of a paper and/or patent. Therefore, based on the known outcomes of the bio-1-alcohol dehydration reactions as well as the disclosure of Le failing to identify any regioisomeric product, a POSITA would have understood that the 1-heptene and 1-nonene reported were not contaminated with significant amounts (*e.g.*, greater than 5%) of reaction impurities.

91. A POSITA would have understood purification was a common process step before, during, and after a reaction. Further, Le provides at least one example where the bio-1-alcohol was purified prior to dehydration to form the corresponding bio-1-alkene. Le at [0171] ("After separation of 1-heptanol from the other compounds, the 1-heptanol is injected, in order to dehydrate it...") and [0172] ("the mixture of water and 1-heptene produced").

92. Therefore, a POSITA would understand that Le's described process results in the production of a single regioisomer of the bio-1-alkene with a

regioselectivity of greater than 95%. Accordingly, claims 10 and 11 are rendered obvious for the same reasons as discussed with respect to claim 1.

7. Claim 24

The process according to claim 6, wherein the bio-alkene undergoes a distillation step to refine the bio-alkene prior to converting the bio-alkene to the bio-1,2-alkanediol.

93. A POSITA would understand and Le teaches that the alpha olefin (1-alkene) can be purified using known techniques, including “a distillation step” that refines the 1-alkene to be used in further processing. Le at [0067]; *see also* [0173] (example with step of purifying 1-heptene). A POSITA would have refined the bio-1-alkene from Le prior to converting it to a bio-1,2-alkanediol in order to purify the input material to Cheng’s process thereby improving the efficiency and yield of Cheng’s process.

94. Cheng also describes a distillation step to separate the bio-alkene from the epoxide, so that the 1-hexene can be recycled back to the reactor to improve the overall conversion to the 1,2-hexanediol. Cheng at 6:29-67; *see also* 7:1-40 and FIG. 1 (“recycle hexene”). A POSITA would understand that the intermediate product mixture is distilled to separate the unreacted 1-hexene from the epoxide prior to the conversion of the latter to the 1,2-alkanediol. Distillation of an intermediate is also commonly used to improve the purity of a final product.

8. Claim 25

The process according to claim 6, wherein the bio-1,2-alkanediol formed from the bio-alkene undergoes a final distillation step to refine the bio-1,2-alkanediol.

95. A POSITA would understand and Cheng describes a distillation step for the 1,2-alkanediol. *See, e.g.*, Le at Examples 2-5 and 14:61-17:63. In particular, in Example 2, part (c) “[a] batch distillation column” is used to refine the 1,2-hexanediol. Le at 15:25-36 (98.9% 1,2-[hexanediol] “was then recovered in the distillate.”). A POSITA would likewise utilize this distillation step in the combination of Le and Cheng to refine the bio-1,2-alkanediol into a purer 1,2-alkanediol product and/or for use as a more efficient input into additional chemical processes.

9. Claim 26

The process according to claim 1, wherein the bio-alkene results from a process wherein the bio-1-alcohol in water is dehydrated by heating the bio-1-alcohol with a catalyst under a purge gas.

96. Le describes dehydrating a bio-alcohol in the presence of a catalyst under a purge gas, such as “nitrogen, helium, argon, water, methane, propane, butane and the other aliphatic or aromatic hydrocarbons.” Le at [0065]-[0066]. Water was used earlier in the process, e.g., during cracking step. Le at [0169]-[0171]. A POSITA would understand that in absence of explicit drying that some water would be present in the starting bio-1-alcohol. Le does not explicitly dry the starting bio-1-alcohol, therefore water will be present. Further, the bio-1-alcohol of Le is also in

water because the dehydration process generates water in the mixture being dehydrated. Le at [0062].

10. Claims 28-29

Claim 28: The process according to claim 1, wherein the process yields at least about 60% to about 99% of the bio-1,2-alkanediol.

Claim 29: The process according to claim 28, wherein the process yields at least about 72% to about 99% of the bio-1,2-alkanediol.

97. Cheng describes an 83% yield for the epoxidation reaction. *See* Cheng at 14:53 (molecular weight of epoxyhexane is 100 and the molecular weight of 1,2-hexanediol, the end product, is 118). Further, following Example 2 of Cheng, 318 g of epoxyhexane is 3.18 mols, and the distilled product, 1,2-hexanediol, weighed 316.5 g, which is 2.68 mols representing an 84.3% yield. However, the product was 96.8% pure. Therefore, the yield for the hydrolysis reaction was 81.6%. Putting the two together, the overall yield for the conversion from alkene to alkanediol was 69%.

98. A POSITA would also understand this is within experimental variation of 72% overall yield. Further, a POSITA would understand the process can be easily optimized for higher overall yields, if desired, for instance by increasing the salt concentration of the aqueous washes in the work up. A POSITA would expect that increasing the salt concentration of the aqueous washes would maximize the partitioning of the diol into the organic phase, leading to higher overall yield.

**B. Claims 1-7, 9-11, 24-26, 28, and 29 are rendered obvious under 35
U.S.C. § 103 by Cheng in view of Wright ‘788**

99. A POSITA understands Cheng to describe a “commercially attractive way” for generating 1,2-alkanediols from 1-alkenes. Cheng at 1:40-45. A POSITA would understand that Cheng’s conversion process from alkenes to diols can use the product from Wright ‘788’s method for a dehydrating bio-1-alcohol to produce bio-1-alkene with high selectivity (>95%). Wright ‘788 at [0018]; *see also* [0003] (producing α -olefin with 92-99% regiochemical selectivity). A POSITA would be motivated to convert the bio-alkenes of Wright ‘788 into 1,2-bio-alkanediols according to Cheng’s process because “...vicinal alkanediols, such as 1,2-alkane diols...” are useful in commercial applications, and Cheng’s method is a “commercially attractive way[]” for carrying out the conversion without objectionable odors commonly associated with the 1,2-alkanediols. Cheng at 1:6-10 and 1:40-48.

100. A POSITA would understand the advantages of using the natural feedstocks taught by Wright ‘788 with the 1,2-alkanediol process conducted by Cheng. A POSITA would also understand that a 1-alcohol, regardless of whether it is from current biomass or petroleum will predictably dehydrate to the corresponding 1-alkene that can then be converted to the corresponding 1,2-alkanediol based on the well-known protocols (*e.g.*, Cheng) previously discussed. A POSITA would understand that the choice of bio-based versus petroleum starting materials might be

driven by many considerations, e.g., marketing, cost, availability. *See, e.g.*, Vermeirin at 1:19-28; Koivusalmi at 1:51-2:8.

101. A POSITA would be motivated to prepare the bio-1,2-alkanediol from the bio-1-alkenes of Wright '788 (derived from current biomass) instead of petrochemically derived 1-alkenes given the growing demand in the market for renewable products and desires to reduce reliance on petroleum products. Parekh at 1:14-16; Alibhai at 1:31-4:44.

102. Further, a POSITA would be motivated to use the natural feedstocks given the environmental impacts associated with using petroleum derived starting materials. *See, e.g.*, Vermeirin at 1:19-28; Koivusalmi at 1:51-2:8. Accordingly, it would be obvious to a person of skill in the art to form a bio-1-alkene using the bio-alcohols of Wright and convert the bio-1-alkenes so formed to bio-1,2-alkanediols following Cheng.

1. Claim 1

**A process for the synthesis of bio-1,2-alkanediols, comprising:
providing a bio-alkene having a carbon chain of about 5 to about
20 carbon atoms and a bio-1-alkene regioselectivity of at least about
80%;**

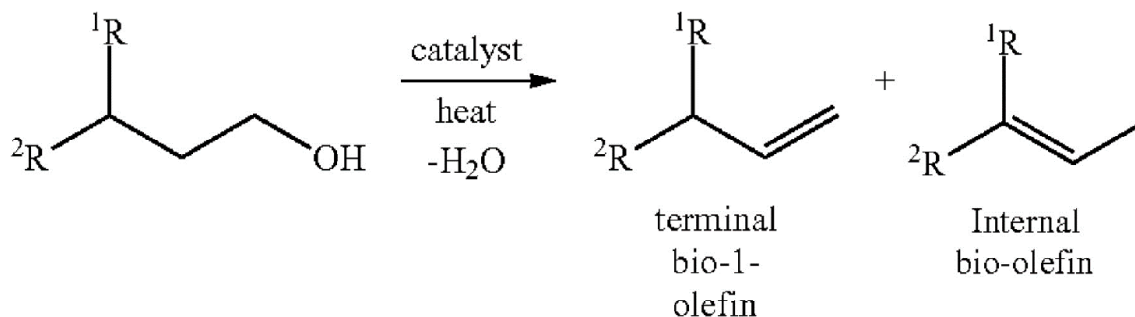
103. A POSITA would understand that at the time of the filing of the '803 patent the conversion of alkenes to 1,2-diols was a well-known and well-understood process. As one example, Cheng teaches how to convert alkenes having carbon chain length of 2 to 12 carbon atoms to their corresponding 1,2-alkanediols. Cheng at 2:44-

67, 6:29-67, 7:1-40, 7:47-8:9, 11:20-41, 13:40-50, and 13:58-18:59. In Cheng, examples provide a POSITA guidance on the conversion of 1-hexene. First Cheng epoxidizes 1-hexene to 1,2-epoxyhexane, which is subsequently converted to 1,2-hexanediol. A POSITA understands and Cheng teaches that the process works equivalently to produce 1,2-alkanediols having a carbon chain length of 2 to 12 carbon atoms, based on the starting alkenes having a corresponding carbon chain length of 2 to 12 carbon atoms.

104. Accordingly, a POSITA would understand that Cheng discloses a process for synthesizing a 1,2-alkanediol from 1-alkenes of chain lengths from 2 to about 12 carbon atoms.

105. A POSITA would understand that Cheng can be combined with Wright '788 which teaches a highly regioselective conversion of a bio-1-alcohol to a bio-1-alkene. Wright '788 characterizes its invention as “a catalyst system and approach that lead to high regiochemical dehydration of 1-bioalcohols” in a reactor chamber to “optimize bio-1-alkene production.” Wright '788 at [0027] and [0030].

106. A POSITA would understand that Wright '788 describes creating bio-1-alkenes having a chain length of 6 to 20 carbon atoms, as shown below, where ¹R and ²R can be “hydrogen, an alkyl radical of C1 to C20, and any combination thereof.” Wright '788 at [0003] and [0016]-[0017].



Wright '788 at [0016]

107. A POSITA would understand that the primary example in Wright '788 describes the dehydration of bio-1-butanol to bio-1-butene, each of which have a chain length of 4 carbon atoms. Wright '788 at [0027], [0034] and claim 2. I have been informed that a chain length of 4 carbon atoms may fall within the scope of “about 5” carbon atoms as the number of carbon atoms in a chemical composition must be a whole number.

108. Wright '788 also includes embodiments producing bio-1-alkenes having carbon chain lengths of 6 carbon atoms up to longer carbon chains lengths of 16 carbon atoms. Wright '788 at [0022] and claims 11-12. A POSITA understands the corresponding terminal alkene for 1-hexanol is 1-hexene because both have a chain length of 6 carbon atoms. Wright '788 also explains, “[e]mbodiments of the invention...produce the respective α -olefin with 92-99% regiochemical selectivity.” Wright '788 at [0008], [0016] (“high selectivity (>92%)”), and [0018] (“high selectivity (>95%)”).

109. A POSITA would understand that when combined, Cheng in view of Wright '788 teaches providing a bio-alkene having a carbon chain of about 5 to about 20 carbon atoms and a bio-1-alkene regioselectivity of at least about 80% as presently claimed.

Converting the bio-alkene to a bio-1,2-alkanediol having a carbon chain length of about 5 to about 20 carbon atoms.

110. Patent Owner acknowledges, and I agree, that converting a bio-1-alkene to a corresponding bio-1,2-alkanediol having a carbon chain length of about 5 to about 20 carbon atoms was well-known in the art prior to filing the '803 Patent. '803 Patent at 18:30-43. I understand that during patent prosecution the Patent Owner identified as well-known the specific steps claimed in the '803 patent that convert a 1-alkene to a 1,2-alkanediol. '803 Patent at 18:30-43. Patent Owner explained that one well-known sequence for this conversion was:

Various chemical reactions may be used for this conversion as are known for use in standard alkene to alkanediol conversions using petrochemically derived starting materials and/or that are used for smaller chain bio-alkanes. For example, the bio-1-alkene is reacted in the presence of at least one of formic acid or acetic acid, and a peroxide such as hydrogen peroxide to form an intermediate solution including a bio-1,2-epoxyalkane, bio-1,2-alkanediol, and other components. This is then further contacted with a base solution, such as a sodium hydroxide or another suitable base solution, to complete formation of the bio-1,2-alkanediol. The process noted above preferably yields about 60% to about 99%, and more preferably about 70% to about 99% or about 75% to about 99% of bio-1,2-alkanediol.

'803 Patent at 18:30-43.

111. Cheng also describes converting alkenes having carbon chain lengths of 2 to 12 into the corresponding 1,2-alkanediols. Cheng at 2:44-67; 6:29-67; 7:1-40; 7:47-8:9; 11:20-41; 13:40-50; *see also* 13:58-18:59 (Example 1 converts 1-hexene to an intermediate 1,2-epoxyhexane and Examples 2-6 convert the intermediate 1,2-epoxyhexane into 1,2-hexanediol). Cheng states, “[i]n Examples 3-5, 1,2-hexanediol is produced by hydrolysis from 1,2-epoxyhexane which in turn was produced in Example 1 by oxidation of 1-hexene with hydrogen peroxide using a peroxotungstate catalyst.” Cheng at 13:40-43. Cheng also provides that “various epoxidizable olefinic compounds can be epoxidized and purified in the practice of this invention.” Cheng at 11:29-30. Cheng specifically identifies 1-alkenes having 2 to 12 carbon atoms, including:

ethylene, 1-propene, 2-methyl-1-propene, 1-butene, 1-pentene, 4-methyl-1-pentene, 1-hexene, 3-ethyl-1-hexene, 4-n-propyl-1-heptene, 1-octene, 1-nonene, 1-unadecene, 1-dodecene, 5-methyl-1-dodecene, 1-tetradecene, 1-hexadecene, and the like. Preferred alkenes are 1-pentene, 1-hexene, 1-heptene, and 1-octene; highly preferred is 1-hexene.

Cheng at 11:35-41.

112. A POSITA would understand Cheng’s process for converting 1-hexene to 1,2-hexanediol refers to a starting and final product having a carbon chain length of 6 carbon atoms. Likewise, a POSITA would understand based on the knowledge of skill in the art and because Cheng explicitly refers to alkenes having carbon chain

lengths of 2 to 12, that Cheng's process for creating 1,2-alkanediols would predictably yield 1,2-alkanediols having chain lengths of 2 to 12 carbon atoms. Cheng at 11:35-41.

113. Accordingly, it is my opinion that a POSITA would understand that Cheng's process forms 1,2-alkanediols with carbon chain lengths of 2 to 12 carbon atoms. Cheng at 11:35-41. Further, a POSITA would understand that beginning with the bio-1-alkene from Wright, the 1,2-alkanediols formed by the Cheng process would be bio-1,2-alkanediols.

2. Claims 2-5

Claim 2. The process of claim 1, wherein the bio-alkene and the bio-1,2-alkanediol each have a carbon chain of about 6 to about 14 carbon atoms.

Claim 3. The process according to claim 2, wherein the bio-alkene and the bio-1,2-alkanediol each have a carbon chain length of about 6 to about 10 carbon atoms.

Claim 4. The process according to claim 3, wherein the bio-alkene and the bio-1,2-alkanediol each have a carbon chain length of about 6 to about 8 carbon atoms.

Claim 5. The process according to claim 1, wherein the bio-alkene is bio-octene and the bio-1,2-alkane diol is bio-1,2-octanediol.

114. A POSITA would understand that Wright '788 includes embodiments describing the production of a range of bio-1-alkenes from bio-1-hexene to bio-1-hexadecene. Bio-1-hexene has a chain length of 6 carbon atoms and bio-1-hexadecene has a chain length of 16 carbon atoms. Wright '788 at [0022] and claims

11-12. In addition, Wright '788 teaches bio-1-alkenes of any chain length from 6 and 20 carbon atoms, including bio-1-hexene (6 carbon atoms) and bio-1-octene (eight carbon atoms). Wright '788 at [0003] and [0016]-[0017].

115. Cheng teaches “In Examples 3-5, 1,2-hexanediol is produced by hydrolysis from 1,2-epoxyhexane which in turn was produced in Example 1 by oxidation of 1-hexene with hydrogen peroxide using a peroxotungstate catalyst.” Cheng at 13:40-43. A POSITA understands that Cheng’s disclosure of a process for converting 1-hexene to 1,2-hexanediol refers to a carbon chain length of 6 carbon atoms. Cheng also explicitly discloses the conversion of 1-octene to 1,2-octanediol, which both have carbon chain lengths of 8 carbon atoms. Cheng at 11:35-41 (starting alkenes include 1-octene).

116. Finally, a POSITA would understand that the process for synthesizing 1,2-alkanediols provided by Cheng would predictably yield 1,2-alkanediols having various chain lengths from 2 to 12 because Cheng explicitly refers to 1-alkenes having a chain length of 2 to 12 carbon atoms. Cheng at 11:35-41 (including starting with e.g., 1-octene). A POSITA would understand that using Wright ‘788’s bio-1-octene in Cheng’s conversion process would predictably result in bio-1,2-octanediol.

3. Claim 6

Claim 6. The process according to claim 1, wherein the bio-alkene results from a process wherein a bio-1-alcohol is dehydrated by heating the bio-1-alcohol in a reactor with a catalyst.

117. A POSITA would understand that Wright '788 characterizes its invention as “a catalyst system and approach that lead to high regiochemical dehydration of 1-bioalcohols” in a reactor chamber to “optimize bio-1-alkene production.” Wright '788 at [0027] and [0030]. In one example, Wright describes “the dehydration of bio-1-butanol” with a γ -alumina catalyst with the bio-1-alcohol heated at 200° C to 400° C in a fixed-bed continuous flow reactor to produce “bio-1-butene.” Wright '788 at [0008] and [0034].

118. Further, a POSITA would understand that the published claims of Wright '788 disclose “A bio-1-alkene product, comprising: at least one bio-1-alcohol; at least one desired catalyst, wherein said bio-1-alcohol is subjected and heated to at least one desired catalyst; ...to produce bio-1-alkene product.” Wright '788 at Claim 1. I also have been informed that the Patent Owner has argued that Wright '788 requires the catalyst to be treated with a silanizing agent. A POSITA reading Wright '788 would understand the teachings to include multiple different embodiments with multiple variables that are available to optimize the dehydration. One variable taught by Wright '788 includes the treatment of the catalyst with silanizing agent. This was a known technique in the art. Wright '788 also teaches a

catalyst treated with a base, the use of a γ -alumina catalyst and a ZnAl_2O_4 catalyst. Wright '788 at [0020], [0022], [0024], claim 7, and claims 19-20. A POSITA would consider changing and/or eliminating any or all of the available variables to achieve his or her desired outcome.

119. Therefore, a POSITA would understand that Cheng in view of Wright '788 teaches a process of dehydrating a bio-1-alcohol by heating the bio-1-alcohol in a reactor with a catalyst to create a bio-1-alkene that can be converted to a bio-1,2-alkanediol.

4. Claim 7

The process according to claim 6, wherein the reactor is a fixed bed reactor.

120. A POSITA would understand that Wright '788 describes using a “fixed-bed continuous flow reactor” to dehydrate a bio-1-alcohol to the corresponding bio-1-alkene. Wright '788 at [0034]. A POSITA understands that the reactor taught by Wright '788 would be a fixed bed reactor because it is expressly so described by the reference.

5. Claim 9

The process according to claim 6, wherein the catalyst is selected from ZnAl_2O_4 and a γ -alumina catalyst.

121. A POSITA would understand that Wright '788 teaches the use of a γ -alumina catalyst and a ZnAl_2O_4 catalyst. Wright '788 at [0020], [0024], claim 7, and claims 19-20. The catalyst of Wright '788 can also be a combination of γ -alumina

and zinc oxide (ZnAl_2O_4). Wright '788 at [0019], [0022] and claim 21-22. A POSITA would understand Wright '788 teaches that the catalyst is selected from ZnAl_2O_4 and a γ -alumina catalyst.

6. Claims 10-11

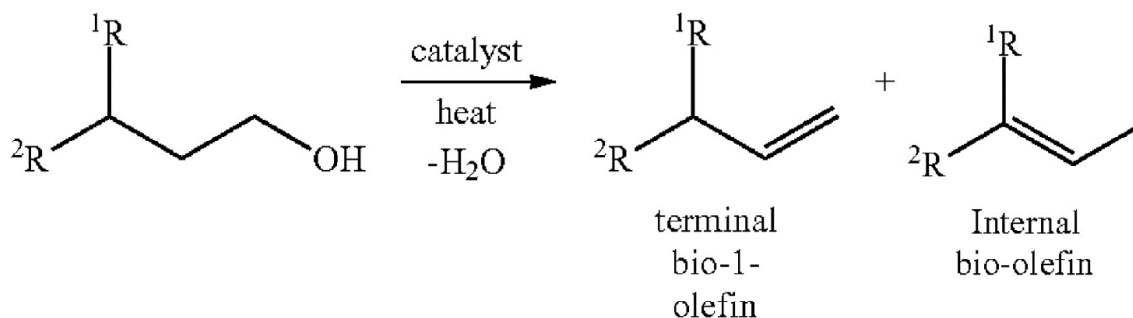
10. The process according to claim 9, wherein the bio-alkene has a bio-1-alkene regioselectivity of about 92% to about 99%.

11. The process according to claim 10, wherein the bio-alkene have a bio-1-alkene regioselectivity of about 95% to about 99%.

122. As discussed with claim 1, Wright '788 explains, “[e]mbodiments of the invention...produce the respective α -olefin with 92-99% regiochemical selectivity.” Wright '788 at [0008], [0016] (“high selectivity (>92%)”), [0018] (“high selectivity (>95%)”). Furthermore, based on the claim construction including bio-1-butene, the regioselectivity for bio-1-butene is 94-95%. Wright '788 at [0034].

123. Although the primary example provided in Wright '788 is of dehydrating 1-butanol, which is a four-carbon alcohol, a POSITA would understand the teachings of Wright '788 to include dehydrating 1-alcohols with longer carbon chains to the corresponding 1-alkenes. Wright '788 at [0016]-[0017]. Wright '788 teaches dehydrating 1-alcohols with a carbon chain length of six (“bio-1-hexanol”) or longer carbon chains including a specific example of a carbon chain length of sixteen (“1-hexadecanol”). Wright '788 at [0022] and claims 11-12. A POSITA would have understood that Wright '788 further teaches that these bio-1-alcohols would be converted into bio-1-alkenes with any carbon chain length between 4

carbons and 23 carbons with high regioselectivity. This is illustrated by the below reaction where ^1R and ^2R can be “hydrogen, an alkyl radical of C1 to C20, and any combination thereof.” Wright ’788 at [0016]-[0017].



Wright ’788 at [0016]

124. A POSITA would understand that Wright ’788 includes embodiments describing the dehydration of bio-1-alcohols having a chain length of 6 carbon atoms (“bio-1-hexanol”) or longer carbon chains lengths of up through 23 carbon atoms (“bio-1-tricosanol”). Wright ’788 at [0022] and claims 11-12. A POSITA understands the corresponding terminal alkene for 1-hexanol is 1-hexene because both have a chain length of 6 carbon atoms. Based on the teachings of Wright ‘788, the regioselectivity would not be impacted by the chain length. Therefore, a POSITA would be confident that dehydration of longer chain bio-1-alcohols would give the same regioselectivity as that observed for the dehydration of bio-1-butanol. Indeed, this has been known since 1945. *See, e.g.,* Komarewsky.

125. A POSITA, based on the disclosure of Wright '788, would have expected that dehydration of, e.g., bio-1-octanol would result in the same high yields and regioselectivity as bio-1-butanol, i.e., in excess of 95% regioselectivity.

7. Claim 24

The process according to claim 6, wherein the bio-alkene undergoes a distillation step to refine the bio-alkene prior to converting the bio-alkene to the bio-1,2-alkanediol.

126. A POSITA would understand that the combination of Wright '788 and Cheng teaches multiple steps where the bio-1-alkene is distilled and refined prior to converting it to the bio-1,2-alkanediol. Wright '788 discloses distilling the bio-1-alkene product to refine it by separating it from water. Wright '788 at [0032].

127. Cheng also describes a distillation step to separate the bio-alkene from the epoxide, so that the 1-hexene can be recycled back to the reactor to improve the overall conversion to the 1,2-hexanediol. Cheng at 6:29-67, 7:1-40 and FIG. 1 ("recycle hexene"). A POSITA would understand that the intermediate product mixture is distilled to separate the unreacted 1-hexene from the epoxide prior to the conversion of the latter to the 1,2-alkanediol. Distillation of an intermediate is also commonly used to improve the purity of a final product.

8. Claim 25

The process according to claim 6, wherein the bio-1,2-alkanediol formed from the bio-alkene undergoes a final distillation step to refine the bio-1,2-alkanediol.

128. A POSITA would understand and Cheng describes a distillation step for the 1,2-alkanediol. *See, e.g.*, Le at Examples 2-5 at 14:61-17:63. In particular, in Example 2, part (c) “[a] batch distillation column” is used to refine the 1,2-hexanediol. *Id* at 15:25-36 (98.9% 1,2-[hexanediol] “was then recovered in the distillate.”). A POSITA would likewise utilize this distillation step in the combination of Wright ‘788 and Cheng to refine the bio-1,2-alkanediol into a purer 1,2-alkanediol product and/or for use as a more efficient input into additional chemical processes.

9. Claim 26

The process according to claim 1, wherein the bio-alkene results from a process wherein the bio-1-alcohol in water is dehydrated by heating the bio-1-alcohol with a catalyst under a purge gas.

129. A POSITA would understand that Wright ’788 discloses dehydrating a “bio-1-alcohol having from 1 ppm to 90% water, ...with at least one purge gas at a rate of about 0.01 to about 1.0 per mass of said catalyst/hour to produce bio-1-alkene with high selectivity (>95%).” Wright ’788 at [0018]; *see also* [0021-0022] (discussing dehydration of bio-1-alcohol where “the purge gas is nitrogen, argon, or a mixture of the two gases”).

10. Claims 28 and 29

Claim 28: The process according to claim 1, wherein the process yields at least about 60% to about 99% of the bio-1,2-alkanediol.

Claim 29: The process according to claim 28, wherein the process yields at least about 72% to about 99% of the bio-1,2-alkanediol.

130. Cheng describes an 83% yield for the epoxidation reaction. *See* Cheng at 14:53 (molecular weight of epoxyhexane is 100 and the molecular weight of 1,2-hexanediol, the end product, is 118). Further, following Example 2 of Cheng, 318 g of epoxyhexane is 3.18 mols, and the distilled product, 1,2-hexanediol, weighed 316.5 g, which is 2.68 mols representing an 84.3% yield. However, the product was 96.8% pure. Therefore, the yield for the hydrolysis reaction was 81.6%. Putting the two together, the overall yield for the conversion from alkene to alkanediol was 69%.

131. A POSITA would also understand this is within experimental variation of 72% overall yield. Further, a POSITA would understand the process can be easily optimized for higher overall yields, if desired, for instance by increasing the salt concentration of the aqueous washes in the work up. A POSITA would expect that increasing the salt concentration of the aqueous washes would maximize the partitioning of the diol into the organic phase, leading to higher overall yield.

**C. Claims 1-7, 9-11, 24-26, 35, and 36 are rendered obvious under 35
U.S.C. § 103 by Furuya in view of Le**

132. Le describes a process for preparing α -olefins (1-alkenes) having 6 to 9 carbon atoms from “renewable materials.” Le at [0002]. A POSITA would understand that Furuya describes a process for converting the α -olefins of Le to different bio-based compounds, including 1,2-alkanediols. Furuya describes preparing 1,2-alkanediols by epoxidizing α -olefins and hydrolyzing the product epoxy compounds to form the 1,2-alkanediols, with controls to minimize malodor in the final product. Furuya at 2:41-47; 2:65-66. Combining Le with Furuya would be obvious to a POSITA to make a route from bio-1-alcohols to bio-1,2-alkanediols suitable for cosmetic use. Furuya at 1:49-67; 3:40-57; *see also* 8:6-9

133. A POSITA would recognize the marketing advantages of using the natural feedstocks taught by Le to form the “natural” version of the 1,2-alkanediols of Furuya. *See, e.g.*, Parekh at 1:14-16; Alibhai at 1:31-4:44. Additionally, a POSITA would be motivated to use bio-1-alkenes of Le (derived from natural feedstocks) instead of petrochemically derived 1-alkenes to reduce the environmental impacts associated fossil fuels. Le at [0009]-[0013]. Combining Le with Furuya would also be obvious to a POSITA because Furuya solves a problem of objectionable odors associated with forming 1,2-alkanediols from 1-alkenes, a known solution to a known problem. Furuya at 1:49-67, 3:40-57 and 8:6-11. Further, a POSITA understands that the choice of bio-based versus petroleum starting

materials would likely be driven by many considerations, *e.g.*, marketing, cost, and availability. *See, e.g.*, Vermeirin at 1:19-28; Koivusalmi at 1:51-2:8.

134. A POSITA would also understand that a 1-alcohol, regardless of whether it is from current biomass or petroleum will predictably dehydrate to the corresponding 1-alkene that can then be converted to the corresponding 1,2-alkanediol based on the well-known protocols previously discussed.

135. Accordingly, it would be obvious to a person of skill in the art to use the bio-1-alkenes of Le to produce bio-1,2-alkanediols according to the procedures outlined by Furuya.

1. Claim 1

A process for the synthesis of bio-1,2-alkanediols, comprising: providing a bio-alkene having a carbon chain of about 5 to about 20 carbon atoms and a bio-1-alkene regioselectivity of at least about 80%; and

136. Furuya converts α -olefins (1-alkenes) having a carbon chain length of 4 or more carbon atoms to the corresponding 1,2-alkanediols. For example, Furuya converts 1-octene (8 carbon atoms), 1-decene (10 carbon atoms), and 1-dodecene (12 carbon atoms) to 1,2-octanediol, 1,2-decanediol, and 1,2-dodecanediol, respectively. Furuya at 1:49-60, 2:41-3:11, 3:40-57; *see also* 8:6-11-9.

137. Furuya can be combined with Le which describes alkenes “obtained from a fatty substance consisting of a plant oil...extracted from renewable resources.” Le at [0023]; *see also* [0036]-[0037], [0053]-[0057], [0062]-[0063] and

[0086]-[0089]. In one example, Le teaches, “plant oil comprising ricinoleic acid” which includes castor oil, is processed to obtain heptan-1-ol (1-heptanol), which is then dehydrated “so as to form 1-heptene.” Le at [0101]-[0105]. A POSITA would have understood that the alcohol (*e.g.*, 1-heptanol) and the alkene (*e.g.*, 1-heptene) in Le’s method are a bio-alcohol and a bio-alkene, respectively, because they are derived from renewable plant oils and/or animal fats rather than petroleum or other fossil fuel sources.

138. A POSITA would understand that because the starting materials produced by Le are derived from renewable plant oils and/or fatty substances, the initial alcohol is a bio-1-alcohol and the product is a bio-1-alkene. ’803 Patent at 13:53-55 (“bio-alkenes may be bio-1-pentene, bio-1-iso-pentene, bio-1-hexene, bio-1-heptene, ...”). In my opinion the alkenes produced by Le fit within the definition of “bio” provided by the ’803 Patent, because they are “derived from the carbon of plant sources.” ’803 Patent at 3:26-56.

139. Le describes “an olefin, derived from renewable materials, having a number of carbon atoms included in the range of from 6 to 9.” Le at [0002]; *see also* [0007], [0019]-[0020], [0059] and [0117]. The term “olefin” used in Le is another name for alkene while an alpha-olefin is another name for a 1-alkene. Le provides specific examples teaching a POSITA how to dehydrate C₆-C₉ alcohols to their respective alkenes. Le at [0094]-[0105], [0110]-[0114], and [0117]; *see also*

[0168]-[0174] (dehydrating bio-1-heptanol derived from castor oil to produce bio-1-heptene). The chain lengths of bio-1-hexene, bio-1-heptene, and bio-1-nonene are respectively 6, 7 and 9 carbon atoms.

140. While Le does not use the word “regioselectivity”, a POSITA knows that regioselectivity merely describes the preference of a process to form one specific regioisomer over another regioisomer. Wade at 339. For example, when there are multiple regiosomeric products available for a reaction, and one of those regioisomers is favored, a POSITA would understand the reaction to be regioselective. A POSITA would recognize that the product 1-alkene from the dehydration can be isomerized under the reaction conditions to the 2-alkene. A POSITA would consider a protocol that converted a 1-alcohol primarily to the 1-alkene to be regioselective.

141. Le discloses a known process that “makes it possible to produce predominantly one olefin with a very limited number of isomers.” Le at [0012] and [0021]. Le states that when a 1-alcohol is dehydrated “a single isomer (an alpha-olefin) is obtained” contrasted to “when the saturated alcohol is not in the alpha-position, a mixture of two isomers is formed.” Le at [0068]. An alpha-olefin is another term for a 1-alkene. Finally, Le describes a purifying step for the bio-1-alcohol before dehydration to the corresponding bio-1-alkene. Le at [0171], [0172]. Thus, a POSITA would understand Le to teach that the pure bio-1-alcohol (pure bio-

1-heptanol) is dehydrated to “a single isomer” (bio-1-alkene) which would have a regioselectivity of at least about 80%.

142. The bio-1-alkene is the initial product from the dehydration of the bio-1-alcohol. Formation of other regioisomers (bio-2-alkene, bio-3-alkene) would arise from isomerization of the initially formed bio-1-alkene on the catalyst. As the product bio-1-alkene is removed quickly from the catalyst, isomerization is minimal. Accordingly, a POSITA would understand that even though Le does not actually use the term “regioselectivity,” Le’s method of obtaining a “single isomer” of the bio-1-alkene from pure 1-alcohol results in a high preference for the production of the bio-1-alkene.

143. Le provides specific examples for forming single isomers of bio-1-hexene, bio-1-heptene, and bio-1-nonene. When Le forms a mixture that includes two isomers, they are expressly identified. For example, when starting with 2-octanol, Le reports forming a mixture of 1-octene and 2-octene. Le at [0109]. A POSITA would understand that a 5% byproduct of an unwanted isomer e.g., 2-alkene, would be easily detectible in the final product by magnetic resonance analysis. Accordingly, a POSITA would understand that Le’s “single isomer” is at least 95% 1-alkene because if there were any significant isomerization Le would have readily found and reported the byproduct. Therefore, a POSITA would understand that although Le does not use the term regioselectivity, Le’s method of

obtaining a single isomer of the bio-1-alkene results in a bio-1-alkene regioselectivity of greater than 95%, which is “at least about 80%.”

Converting the bio-alkene to a bio-1,2-alkanediol having a carbon chain length of about 5 to about 20 carbon atoms.

144. Patent Owner acknowledges, and I agree, that converting a bio-1-alkene to a corresponding bio-1,2-alkanediol having a carbon chain length of about 5 to about 20 carbon atoms was well-known in the art prior to filing the '803 Patent. '803 Patent at 18:30-43. I understand that during patent prosecution the Patent Owner identified as well-known the specific steps claimed in the '803 patent that convert a 1-alkene to a 1,2-alkanediol. '803 Patent at 18:30-43. Patent Owner explained that one well-known sequence for this conversion was:

Various chemical reactions may be used for this conversion as are known for use in standard alkene to alkanediol conversions using petrochemically derived starting materials and/or that are used for smaller chain bio-alkanes. For example, the bio-1-alkene is reacted in the presence of at least one of formic acid or acetic acid, and a peroxide such as hydrogen peroxide to form an intermediate solution including a bio-1,2-epoxyalkane, bio-1,2-alkanediol, and other components. This is then further contacted with a base solution, such as a sodium hydroxide or another suitable base solution, to complete formation of the bio-1,2-alkanediol. The process noted above preferably yields about 60% to about 99%, and more preferably about 70% to about 99% or about 75% to about 99% of bio-1,2-alkanediol.

'803 Patent at 18:30-43.

145. A POSITA would understand that Furuya discloses a process for converting alkenes, with carbon chain lengths of 8, 10, and 12, to the 1,2-alkanediols with respective carbon chain lengths of 8, 10, and 12. Furuya at 1:49-60, 2:41-3:11 and 3:40-57; *see also* 8:6-11-9. A POSITA would therefore understand that bio-1-octanol could be readily converted via the Furuya process to bio-1,2-octanediol, by way of bio-1-octene.

146. A POSITA would understand that in one example, Furuya illustrates forming 1,2-octanediol from 1-octene. Furuya at 8:6-31. Furuya's process for preparing 1,2-octanediol is as follows:

381 g (3.4 mol) α -olefin having eight carbon atoms and 218 g (4.5 mol) of 95% formic acid were charged into a 2000 ml four-neck glass flask with a stirrer, a thermometer, and a nitrogen inlet. Then, 261 g (4.6 mol) of 60% hydrogen peroxide was added dropwise at 60° C. for two hours. After the completion of dropping, the reactant was aged at 60° C. for eight hours. After the reactant was left to stand and a lower aqueous layer was removed, 192 g (1.2 mol) of 25% aqueous sodium hydroxide was added to the reactant. The reactant was stirred at 60° C. for 30 minutes for saponification and was left to stand. A lower aqueous layer was then removed. After the saponification and removal of the aqueous layer were performed one more time, the product was washed with hot water and hexane to yield 380 g of 1,2-octanediol.

Furuya at 8:6-31; *see also* 8:33-45 (further describing the processes for preparing 1,2-decanediol and 1,2-dodecanediol from, respectively, 1-decene and 1-dodecene.)

147. A POSITA would understand that Furuya's process for converting an α -olefin, *e.g.*, 1-octene, to 1,2-octanediol refers to a carbon chain length of 8 carbon atoms. Likewise, a POSITA would understand that this process would predictably yield 1,2-alkanediols having longer and shorter chain lengths based on the 1-alkene used as starting material. Furuya at 8:6-31 and 2:65-66 (the alkanediol used has at least 4 carbon atoms); *see also* 8:6-11 (describing processes using α -olefin's having 8, 10, and 12 carbon atoms). As such, a POSITA would understand Furuya combined with Le describes processes for forming bio-1,2-alkanediols with carbon chain lengths greater than 4, and specifically 8, 10, and 12. *See, e.g.*, Furuya.

2. Claims 2-5

Claim 2. The process of claim 1, wherein the bio-alkene and the bio-1,2-alkanediol each have a carbon chain of about 6 to about 14 carbon atoms.

Claim 3. The process according to claim 2, wherein the bio-alkene and the bio-1,2-alkanediol each have a carbon chain length of about 6 to about 10 carbon atoms.

Claim 4. The process according to claim 3, wherein the bio-alkene and the bio-1,2-alkanediol each have a carbon chain length of about 6 to about 8 carbon atoms.

Claim 5. The process according to claim 1, wherein the bio-alkene is bio-octene and the bio-1,2-alkane diol is bio-1,2-octanediol.

148. A POSITA would understand that Le teaches "an olefin [alkene], derived from a renewable materials, having a number of carbon atoms included in

the range of from 6 to 9.” Le at [0002]; *see also* [0007], [0019-0020], [0059] and [0117] (describing Le’s invention producing alkenes with 6 to 9 carbon atoms).

149. In addition to teaching the formation of bio-1-alkenes of 6 to 9 carbon atoms, a POSITA would understand that Le also teaches specific examples for dehydrating bio-1-hexanol, bio-1-heptanol, and bio-1-nonanol into bio-1-hexene, bio-1-heptene, and bio-1-nonene. Le at [0094]-[0105]; *see also* [0168]-[0174] (example involving dehydrating bio-1-heptanol derived from castor oil to make bio-1-heptene). The carbon chain lengths of bio-1-hexene, bio-1-heptene, and bio-1-nonene are 6, 7, and 9, respectively. Carbon chains of 6 to 9 carbon atoms are within the ranges of 6 to 14 (claim 2), 6 to 10 (claim 3), 6 to 8 (claim 4), and 8 carbon (claim 5).

150. Le provides a specific example of dehydrating bio-2-octanol into a mixture of bio-1-octene and bio-2-octene. Le at [0106]-[0109]. While this example uses bio-2-octanol instead of bio-1-octanol, Le is not limited. A POSITA would understand that dehydration of bio-2-octanol would lead to two regioisomers, bio-1-octene and bio-2-octene, because the alcohol in the 2 position could dehydrate in either direction, towards the 1 position to give the bio-1-octene or towards the 3 position to give the bio-2-octene. Le presumably used bio-2-octanol because it was readily available at low cost, not because of any technical difficulty using bio-1-octanol. Le at [0068]. A POSITA would expect that using the process of Le with

bio-1-octanol instead of the bio-2-octanol, would produce “a single isomer (an alpha-olefin)”, bio-1-octene. Le at [0068]. Therefore, a POSITA would understand that if the desired end-product were bio-1-octene (instead of a mixture of bio-1-octene and bio-2-octene), starting with bio-1-octanol, also taught by Le, would result in formation of “a single isomer” of bio-1-octene.

151. Likewise, a POSITA would understand that Furuya describes converting α -olefins (1-alkenes) having a carbon chain length greater than 4 to a corresponding 1,2-alkanediol. Furuya at 1:49-60, 2:41-3:11, 3:40-57; *see also* 8:6-11 (describing the synthesis and treatment of 1,2-octanediol, 1,2-decanediol, and 1,2-dodecanediol from α -olefin’s having 8, 10, and 12 carbon atoms respectively).

152. A POSITA would understand that Furuya’s process for converting an α -olefin (*e.g.*, 1-octene) to 1,2-octanediol refers to a carbon chain length of 8 carbon atoms. Likewise, a POSITA would understand that this process would predictably yield 1,2-alkanediols having longer and shorter chain lengths based on the 1-alkene used as starting material. Furuya at 1:49-60, 2:41-3:11, 3:40-57; *see also* 2:65-66 (the alkanediol used has at least 4 carbon atoms); 8:6-31 (α -olefin’s having 8, 10, and 12 carbon atoms). As such, a POSITA would understand Furuya describes a process for forming 1,2-alkanediols with carbon chain lengths greater than 4, and specifically carbon chains of 8, 10, and 12 in length. *See, e.g.* Furuya.

153. Accordingly, a POSITA would understand the combination of Le with Furuya provides a process for converting bio-1-alkenes to bio-1,2-alkanediols with carbon chain lengths including a chain length of 8 carbon atoms.

3. Claim 6

The process according to claim 1, wherein the bio-alkene results from a process wherein a bio-1-alcohol is dehydrated by heating the bio-1-alcohol in a reactor with a catalyst.

154. Le teaches an alkene/olefin “is obtained from a fatty substance consisting of a plant oil...extracted from renewable resources.” Le at [0023]; *see also* [0036]-[0037], [0053]-[0057], [0062]-[0063], [0086]-[0089] and [0094]-[0117]. In one example, Le explains, “oil comprising ricinoleic acid, preferably castor oil” is processed to obtain heptan-1-ol (1-heptanol), which is then dehydrated “so as to form 1-heptene.” Le at [0101-0105]. A POSITA understands the alcohol (e.g., 1-heptanol) and the alkene (e.g., 1-heptene) in Le’s method are a bio-alcohol and a bio-alkene because they are derived from renewable plant oils, rather than petroleum or other fossil fuel sources. ’803 Patent at 13:53-55 (“bio-alkenes may be bio-1-pentene, bio-1-iso-pentene, bio-1-hexene, bio-1-heptene, ...”). Indeed, the ’803 Patent expressly notes that non-petrochemically derived products are known in the art as “bio” products, such as products “derived from the carbon of plant sources.” ’803 Patent at 3:26-56.

155. With regards to dehydrating the bio-alcohol, Le teaches:

In order to form the olefin (a) according to the process of the invention, **a dehydration step is carried out in a reactor** so as to form a mixture of alkene and water. This dehydration step can be carried out **in the presence of a dehydration catalyst**, for example a γ -alumina-based catalyst, which may be acidic or basic, in the presence of the **alcohols obtained from the starting materials of renewable origin**.

Le at [0062]-[0063] (emphasis added). The alcohol is dehydrated in the reactor by heating it at least within the exemplary temperature range of 250 to 400 °C. Le at [0065] and [0171].

156. Le's numerous examples disclose dehydrating 1-hexanol, 1-heptanol, and 1-nonanol (all 1-alcohols) derived from plant oils into their respective 1-alkenes, i.e., 1-hexene, 1-heptene, and 1-nonene. Le at [0094]-[0105], [0110]-[0114], and [0117]; *see also* [0168]-[0174] (dehydrating 1-heptanol derived from castor oil to 1-heptene).

157. Finally, the catalyst used in the dehydration reaction may be γ -alumina that is acidic, basic, doped, powder, or granules, and having various pore sizes. Le at [0062]-[0064], [0066], [0119], and [0171]. Specific examples of commercially available catalysts referenced in Le are "ESM 110®" produced by Eurosupport and "Pural® KR1" produced by Sasol®. Le at [0064] and [0066].

158. Therefore, a POSITA understands that Le teaches dehydrating a bio-1-alcohol (e.g., 1-hexanol or 1-heptanol derived from plant oil) by heating the bio-1-

alcohol in a reactor (e.g., at 250 to 400 °C) with a catalyst (e.g., a γ -alumina catalyst) to form a bio-1-alkene (e.g., 1-hexene or 1-heptene derived from plant oil).

4. Claim 7

The process according to claim 6, wherein the reactor is a fixed bed reactor.

159. Le teaches an example using a tubular reactor with a catalytic bed to dehydrate 1-heptanol to 1-heptene. Le at [0171]. A POSITA understands that the reactor taught by Le would be a fixed bed reactor because the catalytic bed is a fixed layer of “ESM110® alumina” within the tubular reactor that promotes the dehydration of the 1-heptanol.

5. Claim 9

The process according to claim 6, wherein the catalyst is selected from ZnAl_2O_4 and a γ -alumina catalyst.

160. Le teaches the catalyst used in the dehydration reaction can be γ -alumina with varying parameters, such as the catalyst being acidic, basic, doped, powder, granules, and having various pore sizes. Le at [0062]-[0064], [0066], [0119], and [0171]. Specific examples of commercially available catalysts that can be used with Le are “ESM 110®” produced by Eurosupport and “Pural® KR1” produced by Sasol. Le at [0064] and [0066]. A POSITA would understand that the commercially available catalysts are γ -alumina catalysts.

6. Claims 10-11

10. The process according to claim 9, wherein the bio-alkene has a bio-1-alkene regioselectivity of about 92% to about 99%.

11. The process according to claim 10, wherein the bio-alkene have a bio-1-alkene regioselectivity of about 95% to about 99%.

161. As discussed above with respect to Claim 1, a POSITA would understand that Le's method to obtain a single isomer of the bio-alkene comprises a bio-1-alkene regioselectivity greater than 95%, which a POSITA would understand is at least about 92% to 99% and at least 95% to about 99%. Le expressly teaches "an olefin, derived from renewable materials, having a number of carbon atoms included in the range of from 6 to 9." Le at [0002]; *see also* Le at [0007], [0019]-[0020], [0059], and [0117] (Le produced alkenes with 6 to 9 carbon atoms).

162. While Le does not use the word "regioselectivity", a POSITA knows that regioselectivity merely describes the preference of a process to form one specific regioisomer over another regioisomer. Wade at 339. For example, when there are multiple regioisomeric products available for a reaction, and one of those regioisomers is favored, a POSITA would understand the reaction to be regioselective. A POSITA would recognize that the product 1-alkene from the dehydration can isomerize and therefore could optimize reaction conditions to avoid isomerization. A POSITA would also understand and know how to design a protocol that converts a 1-alcohol primarily to the 1-alkene, with high regioselectivity.

163. A POSITA would have also understood that Le's invention teaches the production of the *bio*-alpha-olefin with very limited contamination by regioisomers. Le at [0012] and [0021]. Le also teaches that "when the saturated alcohol is not in the alpha-position, a mixture of two or more regioisomers is formed." Le at [0068]. A POSITA therefore would have understood the importance of using the bio-1-alcohol in the dehydration to make the bio-1-alkene, as the bio-1-alkene is the kinetic product from the dehydration of the bio-1-alcohol.

164. The high preference for 1-alkene formation on dehydration of 1-alcohols with γ -alumina catalysts had been known for more than 50 years prior to the filing of the '803 Patent. A POSITA would therefore expect that the conditions of the dehydration reaction taught by Le would lead to the 1-alkene product with high regioselectivity. The POSITA would also observe that Le easily distinguished between the 1-octene and the 2-octene obtained when the starting alcohol was 2-alcohol. Le at [0108]-[0109].

165. A POSITA would also understand that if impurity production increased above 5%, the impurities would be easily detectable by magnetic resonance analysis. Accordingly, a POSITA would understand that Le's "single isomer" is at least 95% bio-1-alkene because if there were any significant impurity production it would have been readily apparent and reported. Therefore, a POSITA would understand that although Le does not use the term regioselectivity, Le's method of obtaining a single

isomer of the bio-1-alkene results in a bio-1-alkene regioselectivity of greater than 95%.

166. A POSITA would expect that significant unexpected impurities would be addressed by the author of a paper and/or patent. Therefore, based on the known outcomes of the bio-1-alcohol dehydration reactions as well as the disclosure of Le failing to identify any regioisomeric product, a POSITA would have understood that the 1-heptene and 1-nonene reported were not contaminated with significant amounts (*e.g.*, greater than 5%) of reaction impurities.

167. A POSITA would have understood purification was a common process step before, during, and after a reaction. Further, Le provides at least one example where the bio-1-alcohol was purified prior to dehydration to form the corresponding bio-1-alkene. Le at [0171] (“After separation of 1-heptanol from the other compounds, the 1-heptanol is injected, in order to dehydrate it...”), [0172] (“the mixture of water and 1-heptene produced”).

168. Therefore, a POSITA would understand that Le’s described process results in the production of a single regioisomer of the bio-1-alkene with a regioselectivity of greater than 95%. Accordingly, claims 10 and 11 are rendered obvious for the same reasons as discussed with respect to claim 1.

7. Claim 24

The process according to claim 6, wherein the bio-alkene undergoes a distillation step to refine the bio-alkene prior to converting the bio-alkene to the bio-1,2-alkanediol.

169. A POSITA would understand and Le teaches that the alpha olefin (1-alkene) can be purified using known techniques, including “a distillation step” that refines the 1-alkene to be used in further processing. Le at [0067]; *see also* [0173] (example with step of purifying 1-heptene). A POSITA would have refined the bio-1-alkene from Le prior to converting it to a bio-1,2-alkanediol in order to purify the input material to Furuya’s process thereby improving the efficiency and yield of Furuya’s process.

170. A POSITA would understand that Le in view of Furuya distills the bio-1-alkenes to refine them prior to converting the bio-1-alkene to their corresponding bio-1,2-alkanediols.

8. Claim 25

The process according to claim 6, wherein the bio-1,2-alkanediol formed from the bio-alkene undergoes a final distillation step to refine the bio-1,2-alkanediol.

171. Furuya describes distilling 1,2-octanediol, 1,2-decanediol, and 1,2-dodecanediol to refine these alkanediols. Furuya at 8:63-9:3. Further, Furuya explains that because the alkanediol produced typically has a smell, “the alkanediol composition is usually purified by distillation, which is a common purification method.” Furuya at 1:52-56. A POSITA would likewise utilize this distillation step

in the combination of Le and Furuya to refine the bio-1,2-alkanediol into a purer 1,2-alkanediol product and/or for use as a more efficient input into additional chemical processes.

9. Claim 26

The process according to claim 1, wherein the bio-alkene results from a process wherein the bio-1-alcohol in water is dehydrated by heating the bio-1-alcohol with a catalyst under a purge gas.

172. Le describes dehydrating a bio-alcohol in the presence of a catalyst under a purge gas, such as “nitrogen, helium, argon, water, methane, propane, butane and the other aliphatic or aromatic hydrocarbons.” Le at [0065]-[0066]. Water was used earlier in the process, e.g., during cracking step. Le at [0169]-[0171]. A POSITA would understand that in absence of explicit drying that some water would be present in the starting bio-1-alcohol. Le does not explicitly dry the starting bio-1-alcohol, therefore water will be present. Further, the bio-1-alcohol of Le is also in water because the dehydration process generates water in the mixture being dehydrated. Le at [0062].

10. Claims 28 and 29

Claim 28: The process according to claim 1, wherein the process yields at least about 60% to about 99% of the bio-1,2-alkanediol.

Claim 29: The process according to claim 28, wherein the process yields at least about 72% to about 99% of the bio-1,2-alkanediol.

173. Furuya, in Example 1, starts with “381g (3.4 mol)” of 1-octene with a molecular weight of 112, which provides the quoted 3.4 mol. Furuya at 8:18-19. The

product of the hydroxylation yields 380 grams of 1,2 octanediol, which has a molecular weight of 144. 380 grams of 1,2-octanediol is 2.64 mol. A POSITA would understand that the product 2.64 mol divided by the starting material of 3.4 mol provides 77.6 % yield, which is greater yield than the 60% and 72% claimed.

11. Claims 35 and 36

Claim 35: The process of claim 1, wherein the bio-alkene is converted to the bio-1,2-alkanediol having a carbon chain length of about 5 to about 20 carbon atoms by reacting the bio-alkene in the presence of at least one of a peracid and a hydroxide to form a reaction product, and contacting the reaction product with water and a base to form the bio-1,2-alkanediol.

Claim 36: The process according to claim 35, wherein the bio-alkene is converted to the bio-1,2-alkanediol by reacting the bio-alkene in the presence of at least one of formic acid or acetic acid and a peroxide to form a bio-1,2-epoxyalkane having an epoxy ring, and contacting the 1,2-epoxyalkane with water and sodium hydroxide to form the bio-1,2-alkanediol.

174. A POSITA would understand that Furuya describes a process for reacting an α -olefin with formic acid and hydrogen peroxide. Furuya at 8:6-31. A POSITA would understand that adding formic acid and hydrogen peroxide to the α -olefin, as described by Le and Furuya, would lead initially to the bio-1,2-epoxyalkane, a three-membered ring containing two carbons and an oxygen. A POSITA would also understand that formic acid and hydrogen peroxide are “at least one of a peracid and hydroxide.” A POSITA would understand that under the reaction conditions some of the epoxide would be opened to a mixture of the diol and the esters of the diol. Sarma at 6776-6778.

175. After creation of a bio-1,2-epoxyalkane mixture, a POSITA would understand that Furuya adds aqueous sodium hydroxide (e.g., water and sodium hydroxide) to the solution for complete conversion to bio-1,2-alkanediol. Sarma at 6776-6778.

D. Claims 1-7, 9-11, 24-26, 35, and 36 are rendered obvious under 35 U.S.C. § 103 by Furuya in view of Wright ‘788.

176. A POSITA understands Furuya to describe converting 1-alkenes to their corresponding 1,2-alkanediols. Furuya at 2:41-47; 2:65-66; 8:6-46. Wright ‘788 describes dehydrating bio-1-alcohols to their corresponding bio-1-alkenes with 92-99% regiochemical selectivity. Wright ‘788 at [0003] and [0018]. It would be obvious to a POSITA to use the bio-1-alkenes of Wright to form bio-1,2-alkanediols according to the methods set forth in Furuya. *See, e.g.,* Furuya.

177. A POSITA would understand that Furuya’s conversion process from alkenes to diols can use the product from Wright ‘788’s method for a dehydrating bio-1-alcohol to produce bio-1-alkene with high selectivity (>95%). Wright ‘788 at [0018]; see also [0003] (producing α -olefin with 92-99% regiochemical selectivity). A POSITA would be motivated to convert the bio-alkenes of Wright ‘788 into 1,2-bio-alkanediols according to Furuya’s process because diols are useful in commercial applications, and Furuya’s method for carrying out the conversion reduces objectionable odors commonly associated with the 1,2-alkanediols. Furuya at 1:49-67; 3:40-57; *see also* 8:6-11.

178. A POSITA would understand the advantages of using the natural feedstocks taught by Wright '788 with the 1,2-alkanediol process conducted by Fuyura. Wright '788 at [0018]; *see also* [0003]. A POSITA would also understand that a 1-alcohol, regardless of whether it is from current biomass or petroleum will predictably dehydrate to the corresponding 1-alkene that can then be converted to the corresponding 1,2-alkanediol based on the well-known protocols (*e.g.*, Furuya) previously discussed. A POSITA would understand that the choice of bio-based versus petroleum starting materials might be driven by many considerations, *e.g.*, marketing, cost, availability. *See, e.g.*, Vermeirin at 1:19-28; Koivusalmi at 1:51-2:8.

179. A POSITA would be motivated to prepare the bio-1,2-alkanediol from the bio-1-alkenes of Wright '788 (derived from current biomass) instead of petrochemically derived 1-alkenes given the growing demand in the market for renewable products and desires to reduce reliance on petroleum products. Parekh at 1:14-16; Alibhai at 1:31-4:44. Additionally, a POSITA would be motivated to use bio-1-alkenes of Wright '788 (derived from natural feedstocks) instead of petrochemically derived 1-alkenes to reduce the environmental impacts associated fossil fuels. Combining Wright '788 with Furuya would also be obvious to a POSITA because Furuya solves a problem of objectionable odors associated with

forming 1,2-alkanediols from 1-alkenes, a known solution to a known problem.

Furuya at 1:49-67, 3:40-57 and 8:6-11

180. Accordingly, it would be obvious to a person of skill in the art to form a bio-1-alkene using the bio-alcohols of Wright '788 and convert the bio-1-alkenes so formed to bio-1,2-alkanediols following the procedure of Furuya.

1. Claim 1

A process for the synthesis of bio-1,2-alkanediols, comprising: providing a bio-alkene having a carbon chain of about 5 to about 20 carbon atoms and a bio-1-alkene regioselectivity of at least about 80%;

181. A POSITA understands that Furuya converts α -olefins (1-alkenes) having a carbon chain length of 4 or more carbon atoms to the corresponding 1,2-alkanediols. For example, Furuya converts 1-octene (8 carbon atoms), 1-decene (10 carbon atoms), and 1-dodecene (12 carbon atoms) to 1,2-octanediol, 1,2-decanediol, and 1,2-dodecanediol, respectively. Furuya at 1:49-60, 2:41-3:11 and 3:40-57; *see also* 8:6-11 (describing converting α -olefin's having 8, 10, and 12 carbon atoms to 1,2-alkanediols).

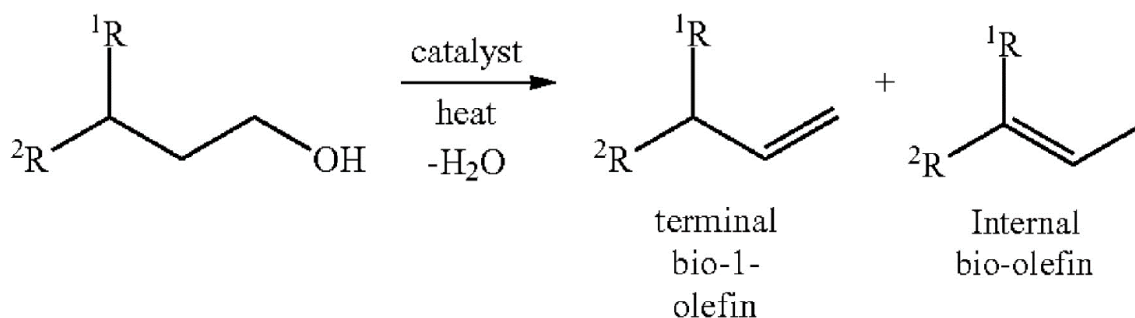
182. A POSITA understands that Furuya creates 1,2-octanediol from an α -olefin having eight carbon atoms (e.g., 1-octene). Furuya at 8:6-31 (producing 1,2-alkanediols from α -olefins having 10 and 12 carbon atoms). Thus, it is my opinion that a POSITA would understand that Furuya discloses a process for synthesizing a

1,2-alkanediols from 1-alkenes having a chain length greater than 4 carbon atoms, including a chain length of 8 carbon atoms.

183. To the extent that Furuya does not specifically characterize its α -olefins (1-alkenes) as “bio”-1-alkenes having a specific regioselectivity, a POSITA would look to Wright ‘788 which explicitly discloses bio-1-alkenes.

184. A POSITA would understand that Wright teaches a highly regioselective conversion of a bio-1-alcohol to a bio-1-alkene. Wright ‘788 characterizes its invention as “a catalyst system and approach that lead to high regiochemical dehydration of 1-bioalcohols” in a reactor chamber to “optimize bio-1-alkene production.” Wright ‘788 at [0027] and [0030].

185. A POSITA would understand that Wright ‘788 describes creating bio-1-alkenes having a chain length of 6 to 20 carbon atoms, as shown below, where ^1R and ^2R can be “hydrogen, an alkyl radical of C1 to C20, and any combination thereof.” Wright ‘788 at [0003] and [0016]-[0017].



Wright ‘788 at [0016]

186. A POSITA would understand that the primary example in Wright '788 dehydrates bio-1-butanol to bio-1-butene, which has a chain length of 4 carbon atoms. Wright '788 at [0027], [0034] and claim 2. A chain length of 4 carbon atoms falls within the scope of "about 5" carbon atoms, as explained above in Section V. Wright '788 includes embodiments producing bio-1-alkenes having a shorter carbon chain length of 6 carbon atoms up to longer carbon chains lengths of 16 carbon atoms. Wright '788 at [0022] and claims 11-12. Wright '788 also explains, "[e]mbodiments of the invention...produce the respective α -olefin with 92-99% regiochemical selectivity." Wright '788 at [0008], [0016] ("high selectivity (>92%)") and [0018] ("high selectivity (>95%)").

187. A POSITA would understand that when combined, Furuya in view of Wright '788 teaches providing a bio-alkene having a carbon chain of about 5 to about 20 carbon atoms and a bio-1-alkene regioselectivity of at least about 80% as presently claimed.

converting the bio-alkene to a bio-1,2-alkanediol having a carbon chain length of about 5 to about 20 carbon atoms.

188. Patent Owner acknowledges, and I agree, that converting a bio-1-alkene to a corresponding bio-1,2-alkanediol having a carbon chain length of about 5 to about 20 carbon atoms was well-known in the art prior to filing the '803 Patent. '803 Patent at 18:30-43. I understand that during patent prosecution the Patent Owner identified as well-known the specific steps claimed in the '803 patent that

convert a 1-alkene to a 1,2-alkanediol. '803 Patent at 18:30-43. Patent Owner explained that one well-known sequence for this conversion was:

Various chemical reactions may be used for this conversion as are known for use in standard alkene to alkanediol conversions using petrochemically derived starting materials and/or that are used for smaller chain bio-alkanes. For example, the bio-1-alkene is reacted in the presence of at least one of formic acid or acetic acid, and a peroxide such as hydrogen peroxide to form an intermediate solution including a bio-1,2-epoxyalkane, bio-1,2-alkanediol, and other components. This is then further contacted with a base solution, such as a sodium hydroxide or another suitable base solution, to complete formation of the bio-1,2-alkanediol. The process noted above preferably yields about 60% to about 99%, and more preferably about 70% to about 99% or about 75% to about 99% of bio-1,2-alkanediol.

'803 Patent at 18:30-43.

189. A POSITA would understand that Furuya discloses a process for converting alkenes, with carbon chain lengths of 8, 10, and 12, to the 1,2-alkanediols with respective carbon chain lengths of 8, 10, and 12. Furuya at 1:49-60, 2:41-3:11 and 3:40-57; *see also* 8:6-11-9. A POSITA would therefore understand that bio-1-octanol could be readily converted via the Furuya process to bio-1,2-octanediol, by way of bio-1-octene.

190. A POSITA would understand that in one example, Furuya illustrates forming 1,2-octanediol from 1-octene. Furuya at 8:6-31. Furuya's process for preparing 1,2-octanediol is as follows:

381 g (3.4 mol) α -olefin having eight carbon atoms and 218 g (4.5 mol)

of 95% formic acid were charged into a 2000 ml four-neck glass flask with a stirrer, a thermometer, and a nitrogen inlet. Then, 261 g (4.6 mol) of 60% hydrogen peroxide was added dropwise at 60° C. for two hours. After the completion of dropping, the reactant was aged at 60° C. for eight hours. After the reactant was left to stand and a lower aqueous layer was removed, 192 g (1.2 mol) of 25% aqueous sodium hydroxide was added to the reactant. The reactant was stirred at 60° C. for 30 minutes for saponification and was left to stand. A lower aqueous layer was then removed. After the saponification and removal of the aqueous layer were performed one more time, the product was washed with hot water and hexane to yield 380 g of 1,2-octanediol.

Furuya at 8:6-31; *see also* 8:33-45 (further describing the processes for preparing 1,2-decanediol and 1,2-dodecanediol from, respectively, 1-decene and 1-dodecene.)

191. A POSITA would understand that Furuya's process for converting an α -olefin, e.g., 1-octene, to 1,2-octanediol refers to a carbon chain length of 8 carbon atoms. Likewise, a POSITA would understand that this process would predictably yield 1,2-alkanediols having longer and shorter chain lengths based on the 1-alkene used as starting material. Furuya at 8:6-45 and 2:65-66 (the alkanediol used has at least 4 carbon atoms); *see also* 8:6-11 (describing processes using α -olefin's having 8, 10, and 12 carbon atoms). As such, a POSITA would understand Furuya when combined with Wright '788 describes processes for forming bio-1,2-alkanediols with carbon chain lengths greater than 4, and specifically 8, 10, and 12. *See, e.g.,* Furuya.

2. Claims 2-5

Claim 2. The process of claim 1, wherein the bio-alkene and the bio-1,2-alkanediol each have a carbon chain of about 6 to about 14 carbon atoms.

Claim 3. The process according to claim 2, wherein the bio-alkene and the bio-1,2-alkanediol each have a carbon chain length of about 6 to about 10 carbon atoms.

Claim 4. The process according to claim 3, wherein the bio-alkene and the bio-1,2-alkanediol each have a carbon chain length of about 6 to about 8 carbon atoms.

Claim 5. The process according to claim 1, wherein the bio-alkene is bio-octene and the bio-1,2-alkane diol is bio-1,2-octanediol.

192. A POSITA would understand that Wright '788 includes embodiments describing the production of a range of bio-1-alkenes from bio-1-hexene to bio-1-hexadecene. Bio-1-hexene has a chain length of 6 carbon atoms and bio-1-hexadecene has a chain length of 16 carbon atoms. Wright '788 at [0022] and claims 11-12. In addition, Wright '788 teaches bio-1-alkenes of any chain length from 6 and 20 carbon atoms, including bio-1-hexene (6 carbon atoms) and bio-1-octene (eight carbon atoms). Wright '788 at [0003] and [0016]-[0017].

193. Likewise, a POSITA understands that Furuya teaches a process for the conversion of α -olefins (1-alkenes) with a carbon chain length greater than 4, to a corresponding 1,2-alkanediol. Furuya at 1:49-60; 2:41-3:11; 3:40-57; *see also* 8:6-11 (describing the synthesis and treatment of 1,2-octanediol, 1,2-decanediol, and 1,2-dodecanediol from α -olefin's having 8, 10, and 12 carbon atoms).

194. A POSITA would understand that Furuya's process for converting an α -olefin (e.g., 1-octene) to a 1,2-alkanediol (e.g., 1,2-octanediol) refers to a carbon chain length of 8 carbon atoms. Likewise, a POSITA would understand that this process would predictably yield 1,2-alkanediols having longer and shorter chain lengths based on the 1-alkene used as starting material. Furuya at 1:49-60, 2:41-3:11, 3:40-57; *see also* Furuya at 2:65-66 (the alkanediol used has at least 4 carbon atoms) and 8:6-31 (α -olefin's having 8, 10, and 12 carbon atoms). As such, a POSITA would understand Furuya describes a process for forming 1,2-alkanediols with carbon chain lengths greater than 4, and specifically carbon chains of 8, 10, and 12 in length. *See, e.g.*, Furuya.

195. Accordingly, a POSITA would understand the combination of Wright '788 with Furuya provides a process for converting bio-1-alkenes to bio-1,2-alkanediols with carbon chain lengths including a chain length of 8 carbon atoms.

3. Claim 6

The process according to claim 1, wherein the bio-alkene results from a process wherein a bio-1-alcohol is dehydrated by heating the bio-1-alcohol in a reactor with a catalyst.

196. Wright '788 describes bio-1-alkenes, including bio-1-alkenes with carbon chain lengths of 6 to 16 carbon atoms in length. Wright '788 at [0022] and claims 11-12.

197. Furthermore, a POSITA would understand that Wright '788 characterizes its invention as “a catalyst system and approach that lead to high regiochemical dehydration of 1-bioalcohols” in a reactor chamber to “optimize bio-1-alkene production.” Wright '788 at [0027] and [0030]. In one example, Wright describes “the dehydration of bio-1-butanol” with a γ -alumina catalyst with the bio-1-alcohol heated at 200° C to 400° C in a fixed-bed continuous flow reactor to produce “bio-1-butene.” Wright '788 at [0008] and [0034].

198. Further, a POSITA would understand that the published claims of Wright '788 disclose “A bio-1-alkene product, comprising: at least one bio-1-alcohol; at least one desired catalyst, wherein said bio-1-alcohol is subjected and heated to at least one desired catalyst; ...to produce bio-1-alkene product.” Wright '788 at Claim 1.

199. Therefore, Furuya in view of Wright '788 teaches a process of dehydrating a bio-1-alcohol by heating the bio-1-alcohol in a reactor with a catalyst to create a bio-1-alkene that can be converted to a 1,2-alkanediol.

4. Claim 7

The process according to claim 6, wherein the reactor is a fixed bed reactor.

200. A POSITA would understand that Wright '788 describes using a “fixed-bed continuous flow reactor” to dehydrate a bio-1-alcohol to a corresponding bio-1-alkene. Wright '788 at [0034]. A POSITA understands that the reactor taught

by Wright '788 would be a fixed bed reactor because it is expressly described by the reference.

5. Claim 9

The process according to claim 6, wherein the catalyst is selected from ZnAl_2O_4 and a γ -alumina catalyst.

201. A POSITA would understand that Wright '788 teaches the use of a γ -alumina catalyst and a ZnAl_2O_4 catalyst. Wright '788 at [0020], [0024], claim 7 and claims 19-20. The catalyst of Wright '788 can also be a combination of γ -alumina and zinc oxide (ZnAl_2O_4). Wright '788 at [0019], [0022] and claim 21-22. A POSITA would understand Wright '788 to explicitly teach a fixed bed reactor. Accordingly, a POSITA would understand Wright '788 teaches that the catalyst is selected from ZnAl_2O_4 and a γ -alumina catalyst.

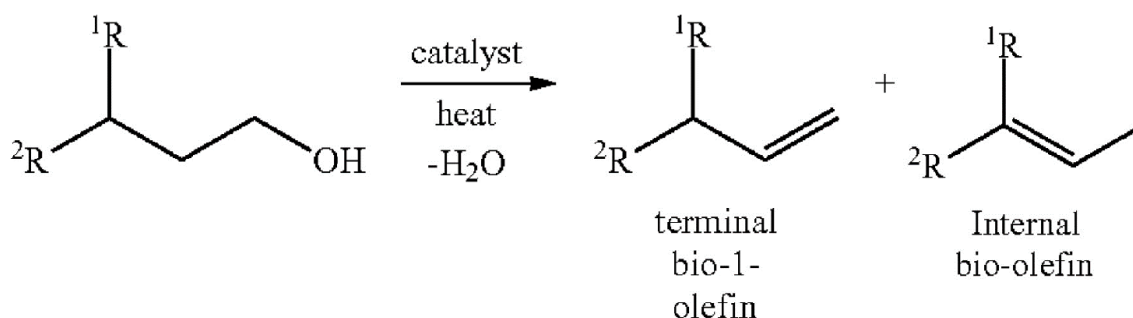
6. Claims 10-11

10. The process according to claim 9, wherein the bio-alkene has a bio-1-alkene regioselectivity of about 92% to about 99%.

11. The process according to claim 10, wherein the bio-alkene have a bio-1-alkene regioselectivity of about 95% to about 99%.

202. As discussed with claim 1, Wright '788 explains, “[e]mbodiments of the invention...produce the respective α -olefin with 92-99% regiochemical selectivity.” Wright '788 at [0008], [0016] (“high selectivity (>92%)”), [0018] (“high selectivity (>95%)”). Furthermore, based on the claim construction, including bio-1-butene, the regioselectivity for bio-1-butene is 94-95%. Wright '788 at [0034].

203. Although the primary example provided in Wright '788 is of dehydrating 1-butanol, which is a four-carbon alcohol, a POSITA would understand the teachings of Wright '788 to include dehydrating 1-alcohols with longer carbon chains to the corresponding 1-alkenes. Wright '788 at [0016]-[0017]. Wright '788 teaches dehydrating 1-alcohols with a carbon chain length of six ("bio-1-hexanol") or longer carbon chains including a specific example of a carbon chain length of sixteen ("1-hexadecanol"). Wright '788 at [0022] and claims 11-12. A POSITA would have understood that Wright '788 further teaches that these bio-1-alcohols would be converted into bio-1-alkenes with any carbon chain length between 4 carbons and 23 carbons with high regioselectivity. This is illustrated by the below reaction where ¹R and ²R can be "hydrogen, an alkyl radical of C1 to C20, and any combination thereof." Wright '788 at [0016]-[0017].



Wright '788 at [0016]

204. A POSITA would understand that Wright '788 includes embodiments describing the dehydration of bio-1-alcohols having a chain length of 6 carbon atoms

(“bio-1-hexanol”) or longer carbon chains lengths of 23 carbon atoms (“bio-1-tricosanol”). Wright ’788 at [0022] and claims 11-12. A POSITA understands the corresponding terminal alkene for 1-hexanol is 1-hexene because both have a chain length of 6 carbon atoms. Based on the teachings of Wright ’788, the regioselectivity would not be impacted by the chain length. Therefore, a POSITA would be confident that dehydration of longer chain bio-1-alcohols would give the same regioselectivity as that observed for the dehydration of bio-1-butanol. Indeed, this has been known since 1945. *See, e.g.,* Komarewsky.

205. A POSITA, based on the disclosure of Wright ’788, would have expected that dehydration of, e.g., bio-1-octanol would result in the same high yields and regioselectivity as bio-1-butanol, *i.e.*, in excess of 95% regioselectivity.

7. Claim 24

The process according to claim 6, wherein the bio-alkene undergoes a distillation step to refine the bio-alkene prior to converting the bio-alkene to the bio-1,2-alkanediol.

206. A POSITA would understand that the combination of Wright ’788 and Furuya teaches multiple steps where the bio-1-alkene is distilled prior to converting it to the bio-1,2-alkanediol. Wright ’788 discloses distilling the bio-alkene product to refine it by separating it from water. Wright ’788 at [0032].

8. Claim 25

The process according to claim 6, wherein the bio-1,2-alkanediol formed from the bio-alkene undergoes a final distillation step to refine the bio-1,2-alkanediol.

207. A POSITA would understand that Furuya teaches distilling 1,2-octanediol, 1,2-decanediol, and 1,2-dodecanediol. Furuya at 8:63-9:3. Further, Furuya explains that because the alkanediol produced by the disclosed process typically has an objectionable odor, “the alkanediol composition is usually purified by distillation, which is a common purification method.” Furuya at 1:52-56.

9. Claim 26

The process according to claim 1, wherein the bio-alkene results from a process wherein the bio-1-alcohol in water is dehydrated by heating the bio-1-alcohol with a catalyst under a purge gas.

208. Wright ’788 discloses dehydrating a “bio-1-alcohol having from 1 ppm to 90% water, ...with at least one purge gas at a rate of about 0.01 to about 1.0 per mass of said catalyst/hour to produce bio-1-alkene with high selectivity (>95%).” Wright ’788 at [0018]; *see also* [0021]-[0022] (discussing dehydration of bio-1-alcohol where “the purge gas is nitrogen, argon, or a mixture of the two gases”). Therefore, a POSITA would understand that the combination of Furuya and Wright ’788 teaches a process “wherein the bio-1-alcohol in water is dehydrated by heating the bio-1-alcohol [i.e., bio-1-hexanol] with a catalyst [i.e., γ -alumina] under a purge gas [i.e., nitrogen, argon, or a mixture of the two gases].”

10. Claims 28 and 29

Claim 28: The process according to claim 1, wherein the process yields at least about 60% to about 99% of the bio-1,2-alkanediol.

Claim 29: The process according to claim 28, wherein the process yields at least about 72% to about 99% of the bio-1,2-alkanediol.

209. Furuya starts with “381g (3.4 mol)” of 1-octene with a molecular weight of 112, which provides the quoted 3.4 mol. Furuya at 8:18-19. The product of the hydroxylation yields 380 grams of 1,2 octanediol, which has a molecular weight of 144. 380 grams of 1,2-octanediol is 2.64 mol. A POSITA would understand that the product 2.64 mol divided by the starting material of 3.4 mol provides 77.6 % yield, which is greater yield than the 60% and 72% claimed.

11. Claims 35-36

Claim 35: The process of claim 1, wherein the bio-alkene is converted to the bio-1,2-alkanediol having a carbon chain length of about 5 to about 20 carbon atoms by reacting the bio-alkene in the presence of at least one of a peracid and a hydroxide to form a reaction product, and contacting the reaction product with water and a base to form the bio-1,2-alkanediol.

Claim 36: The process according to claim 35, wherein the bio-alkene is converted to the bio-1,2-alkanediol by reacting the bio-alkene in the presence of at least one of formic acid or acetic acid and a peroxide to form a bio-1,2-epoxyalkane having an epoxy ring, and contacting the 1,2-epoxyalkane with water and sodium hydroxide to form the bio-1,2-alkanediol.

210. A POSITA would understand that Furuya describes a process for reacting an α -olefin with formic acid and hydrogen peroxide. Furuya at 8:6-31. A POSITA would understand that adding formic acid and hydrogen peroxide to the α -

olefin, as described by Wright '788 and Furuya, would lead initially to the bio-1,2-epoxyalkane, a three-membered ring containing two carbons and an oxygen. A POSITA would also understand that formic acid and hydrogen peroxide are “at least one of a peracid and hydroxide.” A POSITA would understand that under the reaction conditions some of the epoxide would be opened to a mixture of the diol and the esters of the diol. *See, e.g.,* Sarma at 6776-6778.

211. After creation of a bio-1,2-epoxyalkane mixture, a POSITA would understand that Furuya adds aqueous sodium hydroxide (e.g., water and sodium hydroxide) to the solution for complete conversion to bio-1,2-alkanediol. *See, e.g.,* Sarma and Furuya.

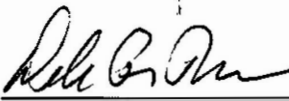
VIII. CONCLUSION

212. In my opinion, and in view of the foregoing, a POSITA would view claims 1-7, 9-11, 24-26, 28, 29, 35 and 36 of U.S. Patent 10,882,803 as obvious at least in light of the combinations of prior art references discussed above.

IX. OATH

213. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

Dated: Sep. 22, 2023

By: 

Appendix A

CURRICULUM VITAE

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Date and Place of Birth: November 11, 1948: Berkeley, CA

Marital Status: Married, six children

Education:

1970 B.S. Stanford University (Honors in Chemistry)

1974 Ph.D. Columbia University (Organic Chemistry)

Research Interests:

1969-70 Undergraduate Research, L. J. Altman, Stanford University: Preparation of 9,10-cyclopentaphenanthrene; Preparation and reactions of 1,1-dihaloepoxides.

1970-74 Graduate Research, G. Stork, Columbia University: Intramolecular Michael reactions to produce cis-fused bicyclic systems; Applications to the synthesis of gibberellins.

1974-75 Postdoctoral Research, B. M. Trost, University of Wisconsin: Applications of sulfonium chemistry to natural products synthesis.

1975 - 2014 Research: Stereoselective synthesis of natural products; New methods in synthetic organic chemistry; Computational organometallic chemistry.

Professional Experience:

1974-75 Research Associate, Department of Chemistry, University of Wisconsin

1975-77 Research Instructor, Department of Pharmacology, Vanderbilt University

1977-82	Assistant Professor, Department of Pharmacology, Vanderbilt University
1978-82	Research Assistant Professor, Department of Chemistry, Vanderbilt University
1982-84	Assistant Professor, Department of Chemistry, University of Delaware
1984-93	Associate Professor, Department of Chemistry, University of Delaware
1993-2014	Professor, Department of Chemistry, University of Delaware
2014-	Professor Emeritus, Department of Chemistry, University of Delaware

Professional Service:

1985	NCI SBIR Study Section, May 1985
1986	Chairman, Local Organizing Committee, 29 th National Organic Chemistry Symposium, Newark, DE 1985
1984-87	Consultant, Helix Associates, Newark, DE (2 days/year)
1982-1992	Consultant, Division of Clinical Pharmacology, Vanderbilt University (5 days/year)
1985-88	Invited monthly column, "Organic Chemistry Review," Industrial Chemist
1987-2009	Wallace Carothers Award Committee, Delaware Section, American Chemical Society
1988-89	Visiting Research Scientist, Du Pont Central Research
1991	NIH SBIR Study Section, July 1991
1991	State Department/AID Review Panel, Oct 1991
1992	Visiting Professor, Universidad Autonoma Nuevo Leon, Monterrey, Mexico June 7-13
1992	Ad Hoc member, Medicinal Chemistry A Study Section, NIH Oct 14-16
1993	Member, Medicinal Chemistry Special Study Section, NIH, Nov 30
1992-93	Expert witness, Phoenix Petroleum, King of Prussia, PA
1993-94	Expert witness, Rothwell, Figg, Ernst and Kurz, Washington, D.C.

1994	Consultant, Bausch & Lomb Pharmaceuticals, Tampa, Florida
1995-2002	Consultant, Dupont Company
1995-96	Visiting Research Scientist, Dupont Merck Pharmaceuticals
1996	Symposium Organizer, “Guided Inquiry in the Organic Lecture and Laboratory”, 14 th Biennial Conference on Chemical Education, Clemson University
1998	Member, Fellowship Review Panel, NIH, March 23-24
1998	Symposium Organizer, “Practical Applications of Computational Organometallic Chemistry”, American Chemical Society National Meeting, Boston, August 26
2000	Reviewer, National Research Council
2000	Expert Witness, Kenyon & Kenyon, New York, NY
2001	Visiting Professor, South China Agricultural University, Guangzhou, Jan. 6-10
2001-03	Short Course, “Intermediate Organic”, Dupont Agricultural Chemistry.
2003	Member, Fellowship Review Panel, NIH, July 8-9, Nov. 12
2003	Member, Ernest Guenther Award Canvassing Committee, ACS
2004	Member (ad hoc), BNP Study Section, NIH, March 8-9
2007	Expert Witness, Sterne, Kessler, Goldstein, Fox, Washington, DC
2007	ACS short course, “Recent Developments in Organic Synthesis”, New Brunswick, NJ, June 2007
2007	ACS short course, “Recent Developments in Organic Synthesis”, Boston, MA August 2007
2009	National Defense Science and Engineering Graduate Fellowship review panel, Arlington, VA
2009-2010	Expert Witness, Montgomery, McCracken, Walker & Rhoads, Philadelphia, PA

2010	Expert Witness, Winston & Strawn, Chicago, IL
2010	Expert Witness, Morrison & Foerster, San Diego, CA
2014	Visiting Professor, University of Science and Technology, Hefei, China
2014-2015	Expert Witness, Department of Justice, Washington, DC

Honors and Awards:

1967-70	Dean's List, Stanford University
1968	NSF Undergraduate Research Participant
1969	Elected to Phi Lambda Upsilon
1970-73	NSF Graduate Fellow
1974	Elected to Sigma Xi
1976-84	National Institutes of Health Research Grant, CA 34383
1978	Invited participant, National Science Foundation Workshop on Organic Synthesis and Natural Products Chemistry
1979-83	Petroleum Research Fund AC Research Grants
1980-81	Research Grant, Vanderbilt University Research Council
1983-86	National Institutes of Health Research Grant, GM 32027
1983-87	Fellow of the Alfred P. Sloan Foundation
1983	Research Grant, University of Delaware Research Foundation
1983-86	National Science Foundation Research Grant, CHE 8306692
1984	Invited participant, Symposium, "Latest Trends in Organic Synthesis," Blacksburg, VA
1985	National Science Foundation Travel Grant, IUPAC Symposium on Organometallics in Organic Synthesis, Kyoto, Japan
1985-87	Petroleum Research Fund A/C Research Grant

- 1988 National Science Foundation Travel Grant, IUPAC Symposium on Natural Products Chemistry, Kyoto, Japan
- 1989 Invited speaker, 5th International Symposium on Carbene Chemistry, Kyoto, Japan
- 1991 National Science Foundation Travel Grant, IUPAC Symposium on Organometallics in Organic Synthesis, Utrecht
- 1991-93 Research Grant, Allergan, Inc., Irvine, CA (\$50,828/year) one postdoctoral
- 1991-93 Petroleum Research Fund A/C Research Grant (\$20,000/year) one Ph.D. student
- 1991-93 Research Contract, DoD/Aberdeen, MD (\$25,000/first year, \$49,600 second year) one Ph.D. student
- 1991-92 Research Contract, NIH/NiAAA, Bethesda, MD (\$25,000/year) one Ph.D. student
- 1992-94 National Institutes of Health research grant, GM 46762, "Synthesis of Taxol" \$171,410/year, two postdoctorals, one graduate student
- 1993-2011 National Institutes of Health research grant, GM42056 "Structural Investigation of Prostaglandin Conjugates", \$114,461/year, one postdoctoral, one Ph.D. student (NIH MERIT Award).
- 1994 Invited speaker, ACS National Meeting, Denver
- 1993 National Science Foundation Travel Grant, Joint USA-Japan-China Symposium on Catalysis, Beijing
- 1993 Invited speaker, Scientific Conference on Chemical Defense Research, Aberdeen, MD
- 1994 Research Grant, Zeneca Pharmaceuticals, \$15,000
- 1995 Invited speaker, Symposium on Organometallics in Organic Synthesis, 78th Canadian Society for Chemistry Conference and Exhibition
- 1995-1996 National Science Foundation, GOALI program, \$60,000 Sabbatical support
- 1995-97 Petroleum Research Fund A/C Research Grant (\$25,000/year) one Ph.D. student

- 1996 Invited speaker, 11th International Conference on Organic Synthesis (ICOS-11), Amsterdam
- 1997 Invited speaker, South East Regional Meeting, American Chemical Society
- 1997 Invited speaker, IUPAC International Conference on Biodiversity and Bioresources, Phuket, Thailand
- 1998 Organizer, "Practical Applications of Computational Organometallic Chemistry", National American Chemical Society meeting, Boston
- 1998 Invited speaker, Symposium, "Latest Trends in Organic Synthesis," Gainesville, FL
- 1999 Invited speaker, Middle Atlantic Regional Meeting, American Chemical Society
- 1999 Invited speaker, Organometallics in Organic Synthesis (OMCOS 10), Versailles, France July 21
- 1999 Invited speaker, Gordon Research Conference on Natural Products, Henniker, NH
- 1999-2000 Petroleum Research Fund A/C Research Grant (\$30,000/year) one Ph.D. student
- 1999 Invited speaker, South East Regional Meeting, American Chemical Society
- 2000-2008 National Institutes of Health research grant, GM 60287, "Physiologically Active Natural Products" \$256,700 / year, one postdoctoral, three Ph.D. students
- 2000 Invited speaker, 11th International Conference on Organic Synthesis (ICOS-13), Warsaw
- 2001 Invited speaker, Organometallics in Organic Synthesis (OMCOS 11), Taipei, Taiwan
- 2003 Elected Fellow, American Association for the Advancement of Science
- 2004 Invited speaker, ACS National Meeting, Anaheim, March 2004
- 2004 Invited speaker, International Conference, Chemistry Biology Interface: Synergistic New Frontiers, Delhi, India, Nov. 22-77, 2004.

- 2005 Invited speaker, Symposium on the Chemistry and Biology of Biomolecules, Montpellier, France March 20-25, 2005.
- 2005 Invited speaker, Singapore International Chemical Conference 4 Dec. 8-10, 2005.
- 2006 Invited speaker, ACS National Meeting, Atlanta, March 2006
- 2006 Invited speaker, ACS Middle Atlantic Regional Meeting, Hershey, PA June 2006
- 2007 Invited speaker, Symposium, C-H Activation in Organic Synthesis, Loughborough, England April 2007
- 2008 Lead speaker, Symposium “Innovations in the Organic Chemistry Curriculum” 20th Biennial Conference on Chemical Education, Bloomington, IN July 2008
- 2009 Invited speaker, 2nd Pennsylvania Organic Chemistry Curriculum Development Conference, Immaculata University, Immaculata, PA May 27th
- 2009 Invited speaker, meeting on the Schweinfurthins and Related Natural Products, NIH/Frederick, December 11, 2009
- 2010 Invited speaker, 1st Annual Congress of Catalytic Asymmetric Synthesis, Beijing
- 2010 Invited speaker, ACS National Meeting, Boston
- 2011 Invited speaker, Fifth International Symposium “The Chemistry of Aliphatic Diazo Compounds: Advances and Outlook” St. Petersburg, Russia
- 2011 Invited speaker, Gordon Research Conference on Natural Products
- 2011 Allan R. Day Award, Philadelphia Organic Chemists Club
- 2014 Visiting Professor, University of Science and Technology, Hefei, China
- 2016 Plenary speaker, 23rd Conference on Isoprenoids, Minsk, Belarus
- 2020 Invited speaker, International Conference on Chemical Science for Drug Discovery & Therapy, VNIT Nagpur, India

Publications:

1. Taber, D. F. A simple synthesis of 2-alkyl cyclohexenones. *J. Org. Chem.* 41: 2649, 1976.
2. Trost, B. M.; Taber, D. F.; and Alper, J. B. An approach to the stereocontrolled creation of an acyclic side chain of some natural products. *Tetrahedron Lett.*: 3857, 1976.
3. Taber, D. F. Cyclopentanone ring formation with control of side chain stereochemistry: a simple stereoselective route to the prostaglandins. *J. Am. Chem. Soc.* 99: 3513, 1977.
4. Harbison, R. D.; MacDonald, J.S.; Sweetman, B. J.; ;Taber, D. F. Proposed mechanism for diphenylhydantoin-induced teratogenesis. *Pharmacologist* 19: 179-179 (1977).
5. Taber, D. F., and Lee, C. H. The preparation of dimethyl (7-²H₃-2-oxoheptyl) phosphonate, a reagent for the synthesis of 20-²H₃ prostaglandins and thromboxanes. *J. Labelled Compounds and Radiopharmaceuticals* 14: 599, 1978.
6. Stork, G.; Taber, D. F.; and Marx, M. Intramolecular Michael addition as a route to angularly substituted cis hydroindanes. *Tetrahedron Lett.*: 2445, 1978.
7. Wilson, J. T.; Howell, R. L.; Holladay, M. W.; Brillis, G. M.; Chrastil, H.; Watson, J. T.; and Taber, D. F. Gentisuric acid (GU): metabolic formation and identification as a metabolite of aspirin in man. *Clin. Pharmacol. Ther.* 23: 634-643, 1978.
8. Taber, D. F., and Korsmeyer, R. A simple stereoselective synthesis of (±)-oplopanone. *J. Org. Chem.* 43: 4925-4927, 1978.
9. Jernigan, J.; Taber, D.; Harbison, R. D. General method for the in vitro production and identification of N-dealkylated metabolites. *Tox. App. Pharm.* 48: A164-A164, 1979.
10. Taber, D. F., and Gunn, B. P. Branching strategy in organic synthesis. A versatile ketone to enone homologation. *J. Org. Chem.* 44: 450, 1979.
11. Taber, D. F.; Jernigan, J. D.; Watson, J. T.; Carr, K.; and Woosley R. L. N-Desethylacecainide is a metabolite of procainamide in man: convenient method for the preparation of an N-dealkylated drug metabolite. *Drug Metabol. Disp.* 7: 346, 1979.
12. Taber, D. F. and Gunn, B. P.: Control elements in the intramolecular Diels-Alder Reaction: synthesis of (±)-torreyol. *J. Am. Chem. Soc.* 101: 3992, 1979.

13. Stork, G.; Boeckmann, R. K., Jr.; Taber, D. F.; Still, W. C. and Singh, J. Reductive cyclization of ethynyl ketones in the construction of a significant tricyclic intermediate for the synthesis of gibberellic acid. *J. Am. Chem. Soc.* 101: 7107, 1979.
14. Oates, J. A.; Roberts, L. J., II; Sweetman, B. M.; Maas, R. L.; Gerkens, J. F.; and Taber, D.F. Metabolism of the prostaglandins and thromboxanes, in: *Advances in Prostaglandin and Thromboxane Research*, Vol. 6 (B. Samuelsson, P. E. Ramwell and R. Paoletti, Eds.) Raven Press, NY, 1980, p. 35.
15. Verbeeck, R. K.; James, R. C.; Taber, D. F.; Sweetman, B. J.; and Wilkinson, G. R. The determination of meperidine, normeperidine and deuterated analogs in blood and plasma by gas chromatography mass spectrometry selected ion monitoring. *Biomedical Mass Spectrometry* 7: 58, 1980.
16. Taber, D. F., and Anthony, J. M. Stereoselective synthesis of ($\pm$)-laurene. *Tetrahedron Lett.*: 2779, 1980.
17. Taber, D. F., and Saleh, S. A. Intramolecular Diels-Alder route to angularly substituted perhydrophenanthrenes: synthesis of ($\pm$) fichtelite. *J. Am. Chem. Soc.* 102: 5085, 1980.
18. Taber, D. F.; Saleh, S. A.; and Korsmeyer, R. W. Preparation of cyclohexanones and cyclopentanones of high optical purity. *J. Org. Chem.* 45: 4699, 1980.
19. Maas, R.L.; Roberts, L.J.; Taber, D.F.; Oates, J.A. Urinary dinor thromboxane B₂ levels in normal males and cardiovascular disease. *Clinical Res.* 28: A319-A319, 1980.
20. Taber, D. F.; Phillips, M. A.; and Hubbard, W. C. Preparation of deuterated arachidonic acid. *Prostaglandins*, 22: 349, 1981.
21. Taber, D. F.; Campbell, C.; Gunn, B. P.; Chiu, I.-C. The intramolecular Diels-Alder reaction: stereocontrol through non-synchronous bond formation? *Tetrahedron Lett.* 22: 5141, 1981.
22. Taber, D. F., and Saleh, S. A. Branching strategy in organic synthesis. II: Reversal of olefin polarization with concomitant carbon-carbon bond formation. *J. Org. Chem.* 46:4817, 1981.
23. Hubbard, W. C.; Phillips, M. A.; and Taber, D. F. Selective synthesis of octadeuterated ($\pm$)-5-HETE for use in GC-MS quantitation of 5-HETE. *Prostaglandins* 23: 61, 1982.
24. Taber, D. F.; Phillips, M. A.; and Hubbard, W. C. Preparation of deuterated

- arachidonic acid. *Methods in Enzymology*, Eds. W. E. Lands and W. L. Smith, New York, NY, Academic Press, 1982. V. 86, p. 366.
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 26. Taber, D. F. TLC mesh column chromatography. *J. Org. Chem.* 47: 1351, 1982.
 27. Taber, D. F., and Saleh, S. A. Control elements in the intramolecular Diels-Alder reactions: synthesis of α -eudesmol. *Tetrahedron Lett.* 23: 2361, 1982.
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 29. Taber, D. F., and Petty, E. H. A general route to highly functionalized cyclopentane derivatives by intramolecular C-H insertion. *J. Org. Chem.* 47: 4808, 1982.
 30. Taber, D. F.; Gunn, B. P.; and Chiu, I.-C. Preparation of 2-heptyl cyclohexenone. *Org. Syn.* 61: 59, 1983. Coll. Vol. VII, p. 249 (1990).
 31. Hubbard, W. C., and Taber, D. F. Analysis of hydroxy acids, *Proceedings of the Ninth International School of Pharmacology: Prostaglandins and Leukotrienes*, Plenum, 1983.
 32. Taber, D. F., and Raman, K. Enantioselective carbocyclization: a facile route to chiral cyclopentanes. *J. Am. Chem. Soc.*, 105: 5935, 1983.
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40. Taber, D. F.; Amedio, J. C., Jr.; and Sherrill, R. G. Pd-mediated diazo insertions: preparation of 3-alkyl 2-carbomethoxy cyclopentenones. *J. Org. Chem.* 51: 3382, 1986.
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42. Taber, D. F., and Ruckle, Robert E., Jr.: Cyclopentane construction by Rh₂(OAc)₄-mediated intramolecular C-H insertion: steric and electronic effects. *J. Am. Chem. Soc.* 108: 7686, 1986.
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44. Taber, D. F. and Schuchardt, J. S. Symmetry in retrosynthetic analysis: synthesis of pentalenolactone E methyl ester. *Tetrahedron* 43: 5677, 1987.
45. Prakash, C.; Roberts, L. J. II; Saleh, S. A.; Taber, D. F.; and Blair, I. A. Synthesis of Putative Prostaglandin D₂ Metabolites. *Advances in Prostaglandin, Thromboxane and Leukotriene Research*, Samuelsson, B., Paoletti, R., and Ramswell, P. W., Eds., Raven Press, NY, 1987, V. 17, p. 781.
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47. Taber, D. F.; Amedio, J. C., Jr.; and Jung, K.-Y. P₂O₅/DMSO/Triethylamine (PDT): a convenient procedure for oxidation of alcohols to ketones and aldehydes. *J. Org. Chem.* 52: 5621, 1987.
48. Taber, D.F.; Deker, P.B.; Fales, H.M.; Jones, T.H.; and Lloyd, H.A. Enantioselective construction of heterocycles: synthesis of (R,R)-solenopsin B. *J. Org. Chem.* 53: 2968, 1988.
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Org. Chem. 53:2984-2990, 1988.

50. Prakash, P.; Saleh, S.; Roberts, L.J. III; Blair, I.A.; Taber, D.F. Synthesis of the major urinary metabolite of prostaglandin D₂. J. Chem. Soc. Perkin Trans. I, 1988, 2821.
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52. Prakash, C.; Saleh, S.; Sweetman, B. J.; Taber, D. F.; Blair, I. A. A synthon for C-20 trideuterated eicosanoids: Preparation of [²H₃]-arachidonic acid. J. Labelled Cmpds. and Radiopharm. XXVII: 539, 1989
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54. Taber, D. F. Mack, J. F., Rheingold, A. L. and Geib, S. J. Enantioselective Robinson annulation: synthesis of (+)-O-methyljoubertiamine. J. Org. Chem. 54: 3831, 1989.
55. Nugent, W. A. and Taber, D. F. Zirconium-mediated ring construction from dienes: remarkable effect of ligands on stereochemistry. J. Am. Chem. Soc. 111: 6435, 1989.
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63. Taber, D.F.; Silverberg, L.J.; Robinson, E.D. Cyclopentane construction with control of side-chain configuration: Synthesis of (+)-brefeldin A. *J. Am. Chem. Soc.* 113: 6639, 1991.
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67. Taber, D.F.; Rahimizadeh, M. Amide to ester conversion: A practical route to the carfentanil class of analgetics. *J. Org. Chem.* 57: 4037, 1992.
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72. Taber, D.F.; Wang, Y. Stachel, S.J. Alkyl radical generation by reduction of a ketone tosylhydrazone. *Tetrahedron Letters* 34: 6209, 1993.
73. Taber, D.F.; Wang, Y. Preparation of 2-chloroethyl-1,1-d₂ phenyl sulfide without appreciable scrambling. *J. Org. Chem.* 58: 6470, 1993.
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Taber, D.F.; Lahuerta, P.; Louey, J.P.; Malcolm, S.C.; Meagley, R.P.; Stiriba, S.-e.; You, K.K. Rhodium-Mediated Intramolecular C-H Insertion: Probing the Geometry of the Transition State. Computational Organometallic Chemistry, T.R. Cundari, Ed. . Marcel Dekker, Inc., New York, 2001, pp. 217-236.

Taber, D.F.; Joshi, P. V. Cyclopentane Construction by Rhodium(II)-Mediated Intramolecular C-H Insertion. Modern Rhodium-Catalyzed Organic Reactions. P. A. Evans, Ed. Wiley-VCH, Weinheim, 2005. pp. 357-377.

Invited Lectures

- 1976 Vanderbilt University August 1
- 1977 Vanderbilt University Medical School February 8
- 1977 Vanderbilt University March 17
- University of Oklahoma April 14
- Vanderbilt University September 14
- 1979 Gordon Research Conference on Natural Products July 27
- 1980 Vanderbilt University January 24
- University of Utah July 29
- Utah State University August 7
- 1982 Dupont Experimental Station, Wilmington, DE, January 26
- University of Delaware January 27
- Vanderbilt University February 25
- Oklahoma State University March 12
- Johns Hopkins University, Baltimore, MD, October 13
- Temple University, Philadelphia, PA, October 21
- ICI Americas, Wilmington, DE, November 2
- 1983 NIADDK-NHLBI Organic Chemistry Discussion Group, Jan 4
- Vanderbilt University, Nashville, TN, March 31
- 1984 Symposium, "Latest Trends in Organic Synthesis," Blacksburg, VA, May 30
- Columbia University, New York, NY, July 5
- Millersville University, Millersville, PA, October 10
- Dupont Experimental Station, Wilmington, DE, November

St. Joseph's University, Philadelphia, PA, November 28

1985 Rutgers, Newark, NJ, March 28

Schering Corporation, Bloomfield, NJ, April 17

Philadelphia Organic Chemists' Club, Philadelphia, PA,

Tohoku College of Pharmacy, Sendai, Japan, July 9

University of Tokyo, Tokyo, Japan, July 17

Tokyo Institute of Technology, Tokyo, Japan, July 19

SUNY Stony Brook, Stony Brook, NY, October 3

CUNY, Queens College, Flushing, NY, October 23

Aberdeen Proving Ground, MD, October 30

University of Virginia, Charlottesville, VA, November 1

Dickinson College, Carlisle, PA, November 15

1986 College of William and Mary, Williamsburg, VA, Jan 17

Hoffmann-LaRoche, Nutley, NJ, January 23

Lederle Laboratories, Pearl River, NY, January 24

Sandoz Research Institute, East Hanover, NJ, March 31

University of Grenoble, Grenoble, France, May 23

ETH, Zurich, Switzerland, June 2

Ruprecht-Karls Univ., Heidelberg, W. Germany, June 4

University of Reims, Reims, France, June 5

Dupont Central Research, Wilmington, DE, August 26

Susquehanna Valley Section, ACS, Wilkes-Barre, PA,

Stuart Pharmaceuticals, Wilmington, DE, December 9 1

1987 Dupont Biomedical Products, Wilmington, DE, March 25

Givaudan Corporation, Clifton, NJ, March 27

Bryn Mawr College, Bryn Mawr, PA, April 10

Middle Atlantic Regional Meeting, ACS, Pomona, NJ, May

American Cyanamid, Bound Brook, NJ June

- Shippensburg University, Shippensburg, PA October 23
Dupont Jackson Labs, Deepwater, NJ October 30
University of Rochester, Rochester, NY, December 2
- 1988 Pennsylvania State University, State College, PA,
University of Houston, Houston, TX, April 22
Organic Reactions Catalysis Society, San Antonio, TX,
Takasago International Corp., Tokyo, Japan, May 24
Tokyo Institute of Technology, Tokyo, Japan, May 25
Sagami Chemical Research Center, Kanagawa, Japan, May
Kyoto Institute of Technology, Kyoto, Japan, June 3
Kyushu Symposium on Natural Products Chemistry,
Kyushu University, Fukuoka, Japan, June 7
Du Pont Central Research, Wilmington, DE, September 23
Kansas State University, Manhattan, KS, November 3
University of Kansas, Lawrence, Kansas, November 4
- 1989 CRDCC, U. S. Army, Aberdeen, MD, January 19
Hunter College, New York, NY, March 3
Ciba-Geigy, Summit, NJ, April 6
Ciba-Geigy, Basel, Switzerland, May 9
Howard University, Washington, D.C., Sept. 15
SUNY, Binghamton, NY, October 20
Allergan, Inc., Irvine, CA., November 3
Kyowa Hakko Co., Shizuoka, Japan, November 6
Nagoya University, Nagoya, Japan, November 7
International Symposium on Carbene Chemistry, Kyoto Japan, Nov. 9
Southeast Regional Meeting, ACS, Baton Rouge, LA,
- 1990 Lycoming College, Williamsport, PA, Feb. 14
UMBC, Baltimore, MD, March 6
Emory University, Atlanta, GA, April 17
Middle Atlantic Regional Meeting, ACS, Madison, NJ,

- Eli Lilly & Co., Indianapolis, IN, June 26
- Rutgers University, Newark, NJ, October 11
- University of Pennsylvania, Philadelphia, October 29
- 1991 New York Academy of Sciences, New York, NY Jan 8
- Brigham Young University, Provo, Utah March 21
- Hoffmann-La Roche, Basel, August 19
- University of Basel August 20
- University of Konstanz August 21
- Academy of Sciences, Berlin, August 23
- 1992 Columbia University, New York, Jan 16
- Dupont Central Research & Development, Feb 14
- Allergan, Inc., Irvine, CA, 10 March
- Stanford University, Stanford, CA April 22
- ICI Americas, Richmond, CA April 23
- Texas A&M, College Station, TX May 13
- University of Monterrey, Mexico June 12
- Adelphi University, Garden City, NY Sep 17
- University of Maryland, College Park, MD Sep 22
- Fordham University, Bronx, NY Oct. 20
- Georgetown University, Washington, D.C. Oct.27
- Crystal City,
- 1993 E. Stroudsburg State Univ.; East Stroudsburg, PA Feb. 2
- ACS National Meeting, Denver, March 29
- Peking University, Beijing, June 7
- USA-Japan-China Symposium on Catalysis, Beijing, June 10
- Shanghai Institute of Organic Chemistry, June 16

- Fudan University, Shanghai, June 17
- SUNY Albany Oct 5
- SUNY Stony Brook Oct 28
- Scientific Conference on Chemical Defense Research, Aberdeen, MD Nov
- 1994 Syracuse University, Syracuse, NY Sep 20
- Western Maryland College, November 28
- SmithKline Beecham, King of Prussia, PA Dec 6
- University of Delaware, Newark, DE Dec 7
- 1995 Syntex Pharmaceuticals, Palo Alto, CA April 20
- University of California, Davis April 21
- DuPont Central Research April 24
- 78th Canadian Society for Chemistry Conference and Exhibition, Guelph, May 31
(Invited speaker)
- Drexel University, Philadelphia, PA June 7
- Swarthmore College, Swarthmore, PA September 25
- Dupont Merck Pharmaceuticals, Deepwater, NJ Oct 3
- Rensselaer Polytechnic, Troy, NY Oct 12
- GE Central Research, Schenectady, NY Oct 13
- University of Victoria, Victoria, BC Oct 19
- University of British Columbia, Vancouver, BC Oct 20
- The Upjohn Company, Kalamazoo, Michigan Nov 10
- 1996 Towson State University, Towson, MD April 18
- Middle Atlantic Regional Meeting, American Chemical Society, Villanova, PA
(Invited speaker)

SIPSYS, Avrille, France, June 25
Ecole Nationale Supérieure, Paris, June 26
Gif-sur-Yvette, June 28th
International Conference on Organic Synthesis, Amsterdam, June 30- July 4
(Invited speaker)
14th Biennial Conference on Chemical Education, Clemson University, Aug 4-8
(Invited speaker)
Schering-Plough, Kenilworth, NJ, Sep. 26
Abbott Labs, Chicago, IL, Nov. 7
Rider College, Lawrenceville, NJ, Nov. 18
1997 Pharmacopeia, Inc., Princeton, NJ Jan. 16
Manhattan College, New York City, Jan. 22
North Jersey ACS Organic Section, Union College, Cranford, NJ April 28
Bryn Mawr College, Bryn Mawr, PA Oct. 3rd
Southeast Regional Meeting, American Chemical Society, Roanoke, VA, Oct. 21
(Invited speaker)
IUPAC International Conference on Biodiversity and Bioresources, Phuket, Thailand
(Invited speaker)
Rowan University, Glassboro, NJ December 2
1998 Dickinson College, Carlisle, PA March 5
U. of Barcelona, Spain June 30
Johnson-Matthey, West Deptford, NJ August 13
ACS National Meeting, Boston, MA August 26 (invited speaker)
Lafayette College, Easton, PA September 8
Symposium, "Latest Trends in Organic Synthesis," Gainesville, FL, Oct 30
(invited speaker)
Smith Kline Beecham, November 17
1999 University of Hong Kong January 15
Chinese University of Hong Kong January 19

University of Science and Technology, Hong Kong January 20

Middle Atlantic Regional Meeting, American Chemical Society, May 17 (invited speaker)

Organometallics in Organic Synthesis (OMCOS), Versailles, France July 21 (invited speaker)

Gordon Research Conference on Natural Products, Henniker, NH July 26 (invited speaker)

University of Delaware, Newark, Sep. 17

Elizabethtown College, Elizabethtown, PA Sept. 29

Franklin & Marshall College, Lancaster, PA Sept. 29

Florida State University, Tallahassee, Oct. 5

SERMACS (Southeast Regional Meeting), Knoxville, TN Oct. 19 (invited speaker)

Sloan-Kettering, New York, NY Oct. 26

Salisbury State University, Salisbury, MD Nov. 2

2000 National Institutes of Health, Bethesda, MD March 9

International Conference on Organic Synthesis, Warsaw, July 1- July 5 (Invited speaker)

Stockton State University, Pomona, NJ Oct. 9

Johns Hopkins University, Baltimore, MD Oct 10

2001 Brigham Young University, Provo, UT January 24

Reed College, Portland, OR January 26

Oregon State University, Corvallis, OR January 29

Wyeth-Ayerst, Pearl River, NY March 29

CB Research, New Castle, DE June 12

OMCOS-11, Taipei, Taiwan July 23

Research Review, Center for Catalytic Science and Technology, University of Delaware, Oct.11

- Indiana U. of Pennsylvania, Indiana, PA Nov. 7
- Allegheny College, Meadville, PA Nov. 8
- Edinboro U. of Pennsylvania, Edinboro, PA Nov. 8
- Duquesne University, Pittsburgh, PA Nov. 9
- Ursinus College, Collegeville, PA Nov. 16
- 2002 South China Agricultural University, Guangzhou, Jan. 7
- Temple University, Philadelphia, PA March 28
- Sphinx Pharmaceuticals, Research Triangle Park, NC June 7
- UC Irvine, Sept. 12
- Scripps Institute, San Diego, CA Sept. 13
- CalTech, Pasadena, CA Sept. 16
- 2003 KAIST, Daejon, Korea March 17
- Korea University, Seoul, March 19
- Seoul National University, March 20
- ACS National Meeting, New Orleans, March 24
- Philadelphia Organic Chemists' Club, April 24 (invited speaker)
- Salisbury University, Nov. 5
- 2004 Rutgers University, January 20
- Lehigh University, February 4
- Concurrent Pharmaceuticals, February 12
- ACS National Meeting, Anaheim, March 29 (invited speaker)
- Bristol-Myers Squibb, New Brunswick, NJ June 3
- International Conference, Chemistry Biology Interface: Synergistic New
Frontiers, Delhi, India, Nov. 22-77 (plenary lecturer)

- 2005 Rowan University Feb 28
- Symposium on the Chemistry and Biology of Biomolecules, Montpellier, France
March 20-25 (invited speaker)
- UT Southwestern, Dallas Sep 21
- Southern Methodist University, Dallas, TX September 22
- UT Arlington, Arlington, TX September 23
- Singapore International Chemical Conference 4 Dec. 8-10 (invited speaker)
- 2006 Lilly Pharmaceuticals, Indianapolis, IN Jan. 17
- IUPUI, Indianapolis, IN Jan 18
- Notre Dame University, South Bend, IN Jan 19
- Merck Process, Rahway, NJ Feb. 1
- ACS National Meeting, Atlanta, GA (invited speaker), H.C. Brown Award
Symposium, March 29
- ACS Middle Atlantic Regional Meeting, Hershey, PA (invited symposium
speaker), June 4
- Morgan State University, Oct. 9
- 2007 University of Oxford, April 24
- University of Nottingham, April 25
- Symposium on C-H Activation in Organic Synthesis, Loughborough, England,
April 26 (invited speaker)
- AstraZeneca Macclesfield, April 27th
- IUPAC Organometallics in Organic Synthesis, Nara, Japan August 2nd
- University of the Sciences, Philadelphia Sept. 24th
- Rochester Institute of Technology, Oct. 24th

2008

University of Munich Jan 16th

University of Illinois, Chicago March 13

Infinity Pharmaceuticals, Cambridge, MA June 24

University of Florence July 7

2008 Lead speaker, Symposium “Innovations in the Organic Chemistry Curriculum” 20th Biennial Conference on Chemical Education, Bloomington, IN July 2008

2009

University of Delaware March 6th

Schering-Plough April 16th

2nd Pennsylvania Organic Chemistry Curriculum Development Conference, Immaculata University, Immaculata, PA May 27th (invited speaker)

Invited speaker, meeting on the Schweinfurthins and Related Natural Products, NIH/Frederick, December 11, 2009

2010

West China School of Pharmacy, Chengdu, May 10th

USTC, Hefei, May 13th

University of Science and Technology, Qingdao, May 15th

Institute of Materia Medica, Beijing, May 17th

Peking University, Beijing, May 18th

1st Annual World Congress of Catalytic Asymmetric Synthesis-2010, Beijing, May 20th (invited speaker)

University of Utah, Salt Lake City, UT June 11th

ACS National Meeting, Boston, August 21st (invited speaker)

Cephalon, Inc. West Chester, PA Oct. 26th

Pacificchem, Honolulu, December 15, 19

2011

Fifth International Symposium “The Chemistry of Aliphatic Diazo Compounds: Advances and Outlook” St. Petersburg, Russia, June 7-8 (Invited Speaker)

Gordon Research Conference on Natural Products, July 24-29 (Invited Speaker)

West Virginia University, Oct 5

Philadelphia Organic Chemists Club, Oct 27 (Allan R. Day Award)

University of New Orleans, Nov 11

2013

University of Delaware May 10th

2015

1st International Caparica Christmas Conference on Translational Chemistry
December 8th

2016

23rd Conference on Isoprenoids, Minsk, Belarus September 5th

2020

International Conference on Chemical Science for Drug Discovery & Therapy,
VNIT Nagpur, India July 22-26 (online)