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RESEARCH ARTICLE

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Migration studies and chemical characterization of low molecular weight cyclic polyester oligomers from food packaging lamination adhesives

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Laminate structures are widely used for food packaging applications. Polyester urethane-based adhesives are very common materials for bonding the layers of such laminates together. Unintended by-products of polyester synthesis include low molecular weight cyclic polyester oligomers (cyclic oligoesters) that lack the required hydroxyl functionality to react with isocyanates to form the intended high molecular weight polyurethane polymer and remain as impurities with high migration potential. Our investigation conducted migration studies of 537 commercial and/or developmental food packaging laminate structures by using food simulants with gas chromatography-mass spectrometry analyses of the extracts. A subset of the extracts were also analysed by high-performance liquid chromatography-mass spectrometry and gas chromatography-mass spectrometry with chemical ionization. Migration of cyclic oligoesters of diverse chemical structure was observed in nearly all of the samples analysed. Aside from migrants originating directly from polyolefin sealant films on the food-contact side of the laminates, cyclic oligoesters were the migrants detected at next highest concentration. This report presents electron ionization mass spectra and molecular structures of 106 cyclic oligoesters including a series of novel as well as previously identified species. Fifty-six cyclic oligoesters migrated from the 537 laminate samples analysed were evaluated for frequency of occurrence and migration concentration range. The most commonly observed cyclic oligoester migrants were those derived from combinations of the polyhydric alcohols, diethylene glycol, and neopentyl glycol and the dibasic acids, adipic, and phthalic/isophthalic.

KEYWORDS

cyclic oligoester, GC-MS, HPLC-MS, laminates, migration, polyurethane adhesive

1 | INTRODUCTION

Flexible laminate structures are widely used in food packaging applications. This multilayer packaging format has been adopted by the packaging industry to improve the barrier properties, mechanical strength, heat sealing, and printing properties of the substrates allowing a better preservation of food products. Polyurethane (PU) is the most common adhesive used for flexible laminate structures due to its excellent adhesion properties, chemical resistance, temperature resistance, and its ease of application at fast roll-to-roll lamination speeds.[1] For flexible laminate applications, PU lamination adhesives are commonly synthesized by reacting polyester or polyester polyol with di-isocyanates, polyfunctional isocyanates, or isocyanate-prepolymers to introduce soft chain segments, which impart desirable rheological properties.[2] Polyesters or polyester polyols are synthesized by a polycondensation reaction between diols and dicarboxylic acids requiring a continuous removal of water to shift the equilibrium to favour production of linear high molecular weight (mw) polyester chains. In addition, an excess of diol is used to generate terminal hydroxyl groups for polyester polyols.[3] Because of the mass transfer limitation influencing the reaction rate, the removal of water and extra diols becomes difficult. Consequently, the stoichiometry of the reaction leads to the formation of short-chain cyclic oligoesters in addition to linear polyesters.[4] Another mechanism for cyclic oligoester formation involves thermal

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degradation of polyester backbone and transesterification reaction. Therefore, both polyester or polyester polyol synthesis and degradation contribute to the total amounts of cyclic oligoesters in PU laminating adhesives.[5]

From an industrial point of view, short-chain cyclic oligoesters can adversely affect physical properties, as they do not have free hydroxyl groups for further polycondensation and polyaddition reactions to build high mw polymers.[4] Several patents have suggested procedures to reduce cyclic oligoester contents in polyesters and polyester polyol.[6,7] From a food packaging perspective, low mw cyclic oligoesters are undesirable as they have high migration potential.[8] The combination of low mw, hydrophobicity, and lack of hydroxyl functionality such that they could be scavenged by isocyanate groups during urethane cure gives the molecules a high migration potential, and the right size and structure to readily diffuse through polyolefin food contact layers.[9]

Although there is considerable toxicological data available for monomers used in polyester production, there is scant public data available for dietary risk assessment of low mw cyclic oligoesters. Neither the US Food and Drug Administration (FDA) nor the European Union (EU) currently provides any specific migration threshold limits for low mw oligoesters. In Europe, unexpected substances that present in food packaging materials with migration concern are referred to as non-intentionally added substances (NIAS). NIAS impurities of raw materials, decomposition, or side-reaction products of the food contact material and polymerization by-products such as oligomers.[10,11] According to the European Commission regulations, NIAS need to be considered in the risk assessment of the final product.[12] EU (No.) 10/2011 defined 0.01 mg/kg as the conventional detection limit and migration limit for substances not present in the contained positive list.[13] When cyclic oligoesters are found in migration test at a higher level, a risk assessment approach, based on data from manufacturer studies, is generally taken. In the United States, the FDA considers unintentionally added substances according to anticipated exposure levels through a combination of how much is detected in a sample and calculated to be present in the daily diet, versus such factors as potential toxicity or carcinogenicity (per the virtually safe dose).[14] Currently, identified short-chain cyclic oligoesters are generally in the mass range less than 1000 Da and their toxicity and pharmacokinetic properties have not been published. In general, regulatory authorities are most concerned with packaging migrants below mass 1000 Da because this is the fraction most likely to be absorbed in the gastrointestinal tract. It was reported that absorption of molecules above 1000 Da was less than 1%.[15]

In previous studies, 24 low mw cyclic oligoester migrants from laminates have been identified mainly by using extraction methods with organic solvents, water, or modified polyphenylene oxide (MPPO a/k/a Tenax).[5,16-20] The identified migrants were mostly derived from diols, namely, diethylene glycol (DEG), ethylene glycol (EG), and neopentyl glycol (NPG), and diacids like adipic acid (AA), isophthalic acid (IPA), and phthalic acid (PA). Several cyclic oligoesters also have been reported from migration studies of polyester-based can coatings, bottles, and trays.[15,21-25] Though the available data on cyclic oligoesters are not exhaustive, all previously conducted studies indicate that a wide variety of cyclic oligoesters are pervasive migrants from polyester-PU or polyester polyol-PU packaging materials.

There are only a few studies available on the migration of these compounds into actual food systems or common liquid food simulants recommended by regulatory agencies. For many years, our laboratories have been engaged in routine migration testing of commercial laminate structures to assist the packaging industry with quality assurance and regulatory compliance. In this context, many migration studies have been conducted on developmental lamination adhesives in support of global regulatory petitions for use in food packaging applications. This report presents data of 537 analysed samples in which 56 low mw cyclic oligoester migrants have been detected and identified with respect to their molecular structure, migration concentration range, frequency of occurrence, and electron ionization (EI) mass spectra. Furthermore, EI mass spectra for 50 additional cyclic oligoesters derived from direct extraction of polyester and/or cured adhesives, not as of yet identified as migrating species from laminates, are presented. Examples of selected chemical ionization (CI) and high-performance liquid chromatography-mass spectrometry (HPLC-MS) spectra are included. Mass spectra of these migrants serve as a useful reference for known cyclic oligoesters, and many novel structures are reported for the first time in this study.

2 | MATERIALS AND METHODS

2.1 | Test samples

In this study, 537 different PU adhesive-containing laminate samples for food packaging were analysed. Sources of laminates for extraction and analysis include commercial food packaging laminates and developmental PU adhesive-based laminates from adhesive manufacturers. The developmental samples were mainly provided for migration testing in support of regulatory petitions. A complete description of each laminate structure analysed in this study (film types, film thickness/gauge, number of plies, barrier web, adhesive layers and coating weights, etc.) is beyond the scope of this publication. Many commercial samples were submitted without specifications because of proprietary concerns of manufacturers. However, all 537 laminates analysed contained polyethylene, polypropylene, or polyolefin co-extrusion films as the sealant plies (food-contact plies) with PU adhesives applied on the non-food contact side binding outer plies.

2.2 | Reagents, reference standards, and materials

Anthracene-d_{10} (CAS No. 1719-06-8, 98% isotopic purity) used as an internal standard was purchased from Sigma-Aldrich (Milwaukee, WI, USA). Ethanol 190 Proof (USP grade) was purchased from Pharmco Products (Brookfield, CT, USA) and was redistilled prior to use. Methylene chloride (Optima grade), n-hexane (HPLC grade), acetonitrile (Optima grade), methanol (Optima grade), water (HPLC grade), and formic acid (Optima LC/MS grade) were from Thermo Fischer Scientific (Fair Lawn, NJ, USA). Distilled and deionized water was prepared in house by double distillation in a glass-lined still followed by deionization and activated carbon filtration in a Millipore Milli-Q purification system. Cyclic oligoester standards based on DEG, NPG, AA, and PA

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including DEG, AA cyclic diester (cyclic DEG-AA), DEG, PA cyclic diester (cyclic DEG-PA), and NPG, AA cyclic oligoester dimer (cyclic NPG-AA-NPG-AA) were provided by C.O.I.M. S.p.A. (Via Ricengo 21/23, 26010 Offanengo CR, Italy). They were obtained by vacuum steam distillation of polyester followed by preparative HPLC purification.

2.3 | Migration cell extraction testing

Migration testing was conducted by using 0.5 dm^2 surface area, single-side migration cells constructed of stainless steel plates, and Teflon gasket assemblies with filling and draining ports bolted together with 12 cap screws. Details of the migration cells have been described previously.[26-28]

Sections of laminate samples were cut and placed into the migration cells with the sealant film side of the laminations (food-contact side) exposed to the food simulant. Food simulants used for the studies were most commonly 10% ethanol (ETOH) and 95% ETOH with 50% ETOH and 3% acetic acid sometimes used. Depending on the specific packaging type or application, food simulant solvent volume to surface area ratios were typically 0.78 mL/cm^2 for retort pouches (corresponding to 5.0 $mL/inch^2$, which is the maximum fill capacity for pouches) or 1.57 mL/cm^2 (corresponding to FDA default recommendation of 10 $mL/inch^2$ for food packaging migration testing). A ratio of 1.66 mL/cm^2 corresponding to the 6 dm^2/kg "EU cube" model was also occasionally used for food packaging targeting the European market. Cells were incubated corresponding to US FDA Condition of Use A-H and/or EU 10/2011 guidance for food packaging migration studies.[13,14] The specific conditions were selected based on the intended packaging applications.

For laminate samples analysed, control samples of unlaminated sealant films and unprinted laminates were provided so the source of migrants could be readily pinpointed. Method blanks consisting of empty extraction cells with food simulants were routinely prepared and analysed. Compounds detected in the method blanks were disregarded in the data treatment of the test samples.

2.4 | Sample preparation for gas chromatography-mass spectrometry analysis

Following incubation, the food simulants were drained into borosilicate glass test tubes or glass media bottles sealed with Teflon-lined, screw cap closures and stored from light at room temperature prior to analysis. Simulant extracts were visually observed, and any cloudiness or precipitates were noted.

In preparation for gas chromatography-mass spectrometry (GC-MS) analysis, methylene chloride back extraction is used to minimize potential evaporative loss during concentration process. Cyclic oligoesters are relative hydrophobic and preferentially soluble in methylene chloride rather than aqueous solvents. Such solvent partition technique was also utilized to purify the cyclic oligoester standards from their polar monomer residues. Aliquots of 10% ETOH or 3% acetic acid simulant extracts (40 mL) were transferred to borosilicate glass test tubes sealed with Teflon-lined, screw cap closures and matrix-spiked with 100 parts per billion w/v (ppb w/v) anthracene-d_{10} via the addition of 4.0 μL of a 1.0 mg/mL stock solution in methylene chloride. Methylene chloride (5.0 mL) were added, and the tubes were tightly stoppered, vigorously extracted, and then centrifuged at 2500 rpm for 30 minutes to promote complete phase separation. Following centrifugation, the lower methylene chloride layers were aspirated by using a Pasteur pipet, transferred to 5.0 mL size, tapered, borosilicate glass Reacti-Vials and carefully concentrated to a final volume of approximately 0.1 to 0.5 mL under a gentle stream of nitrogen at room temperature without reaching dryness. For 95% or 50% ETOH extracts, the above procedures were repeated but the ETOH concentration was adjusted to 10% via dilution with distilled water prior to the methylene chloride extraction step and the ratio of 10% ETOH to methylene chloride maintained at a constant 8:1 ratio to avoid alteration of aqueous-organic partition coefficients. Concentrated extracts were then analysed by GC-MS using conditions described in the following section.

2.5 | Sample preparation for HPLC-MS analysis

In preparation for HPLC-MS, simulant extracts were concentrated to dryness in borosilicate glass round-bottomed flasks by using a rotary evaporator operated under reduced temperature and pressure. Immediately upon reaching dryness, the residues were redissolved in methanol and/or methanol: methylene chloride (1:1) and quantitatively transferred to tapered glass Reacti-Vials. The solvents were removed under a gentle stream of nitrogen, and then, the residues redissolved in a volume of acetonitrile: water (1:1) with 0.1% formic acid (for 3% acetic acid and 10% ETOH extracts) or acetonitrile with 0.1% formic acid (for 50% and 95% ETOH extracts), the final volume being adjusted as to provide a 100X concentration factor based on the original volume of extract subjected to evaporative concentration.

2.6 | GC-MS analysis methodology

In this study, different GC-MS and HPLC-MS instrument models were used because the data were accumulated over a 10-year period by using different instruments in service at our laboratories. Adhesive manufacturers also shared data from their own instruments as references. Nevertheless, the EI mass spectra presented are equivalent regardless of the instruments upon which they were acquired.

GC-MS analyses were mainly conducted by using a Varian 3400 GC directly interfaced to 1 of 2 different mass spectrometers, a Thermo-Finnigan TSQ-7000 triple stage quadrupole tandem mass spectrometer equipped with an X-calibur data system or a Finnigan MAT 8230 double focusing, magnetic sector, high-resolution mass spectrometer equipped with a Finnigan MAT SS300 data system. The GC on each MS was equipped with a 30 m × 0.32 mm I.D. Guardian-ZB-5MS (Phenomonex) (5% phenyl, poly-dimethylphenylsiloxane) capillary column with a 0.25 μm film thickness. Injection volume was 1.0 μL. The injector temperature was 300°C (splitless mode with a 100:1 split activated 0.5-min post-injection to serve as a septum purge). The GC column temperature was programmed from 50°C (hold 3 min) to 320°C at a rate of 10°C/min with a 10 minutes hold at the upper limit. The upper limit was occasionally extended to 340°C for samples containing high boiling migrants. The GC-MS transfer line temperature was 320°C (or 340°C). The TSQ-7000 mass spectrometer was operated in EI mode

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(70 eV) scanning masses 35 to 1000 *m/z* once each second. The magnetic sector MS was operated in EI mode scanning masses 35 to 750 *m/z* at a scan rate of 0.6 seconds per decade with an inter scan time (magnet reset time) of 0.8 seconds. Many of the cyclic oligoesters yield low intensity or nonexistent molecular ions in their EI spectra. The mw of all cyclic oligoesters with weak or nonexistent molecular ions in their EI spectra were confirmed by CI. Analyses in CI mode were conducted exclusively by using the magnetic sector instrument with isobutane CI reagent gas at a source pressure of 0.8 torr. For data management, total ion current (TIC) chromatograms were integrated with the system software and the peak lists and area integration values were pasted into spreadsheet-based templates. Semiquantitative concentration values for cyclic oligoesters were calculated via TIC peak area ratio relative to the anthracene-d_{10} matrix-spiked internal standard assuming a detector response factor of 1.0.

2.7 | HPLC-MS analysis methodology

A subset of the laminate food-contact side extracts (all migration studies in support of regulatory petitions, approximately 10% of total) were analysed by HPLC-MS to screen extracts for potential nonvolatile cyclic oligoesters not amenable to GC-MS analysis. High-performance liquid chromatography-mass spectrometry analyses were conducted by using a Shimadzu LC-10 AD HPLC with SCL-10 controller and SIL-10A autosampler interfaced to a Waters Micromass Quattro triple stage quadrupole tandem mass spectrometer and/or a Thermo-Finnigan Surveyor HPLC system interfaced to Thermo-Finnigan LCQ ion trap mass spectrometer. Sample injections (1.0-5.0 μL) were made in loop injection mode (column bypass mode) with a column flow rate of 0.1 to 0.4 mL/min and an isocratic mobile phase consisting of water: acetonitrile (1:1) containing 0.1% formic acid. Loop injection is a fast and highly efficient technique in analyzing the unknown oligomers from developmental adhesives and laminate extracts matrix. It can map out different oligomer clusters and detect any compounds that may co-elute with each other or interact with the active site of HPLC columns. Ionization mode was positive ion electrospray (electrospray ionization) or atmospheric pressure chemical ionization scanning masses 50 to 2000 *m/z* once per second. Data were acquired and processed by using MassLynx and/or Xcalibur data systems.

2.8 | Determination of upper molecular weight limit of cyclic oligoester migration through sealant films

It has been argued that the upper mw limit of cyclic oligoester migration observed via GC-MS analyses of laminate extracts may be limited by volatility and that higher mw, nonvolatile species not amenable to GC may be present in extracts but not detectable. In these instances, HPLC-MS analysis methodology, which is not limited by volatility, would be indicated. The following experiments involving both GC-MS and HPLC-MS analyses were conducted to define the upper mw limit of cyclic oligoesters through laminate sealant films (food-contact films).

Laminate structures with sealant films of varying barrier properties were evaluated in this study. The thinnest gauge sealant films with lowest barrier properties were 25.4 μm linear low-density polyethylene films. The thickest gauge sealant films with highest barrier properties were 76.2 μm cast polypropylene (CPP) films. Laminates prepared with these films were used for these evaluations. Experiments were conducted to evaluate the upper mw limit of cyclic oligoester migration through these 2 extreme examples. Migration studies of laminate structures were conducted by using both 10% ETOH and 95% ETOH food simulants with retort condition extraction (2 h at 121°C). Extracts were analysed by both GC-MS and HPLC-MS by using conditions described above. Samples of the specific polyester resin used in the PU lamination adhesive formulation of these laminate structures were subjected to extraction with n-hexane. High mw polyester is n-hexane insoluble, while low mw oligomers (<2000 Da) are n-hexane soluble. Polyester (1.0 g) was extracted with 10.0 mL of n-hexane for 24 hours at 40°C with constant agitation. After cooling to room temperature, samples were centrifuged and the upper n-hexane layers were decanted into tared vials. The n-hexane was evaporated to dryness under a gentle stream of nitrogen; residues were weighed and then redissolved in methylene chloride (for GC-MS) or methanol (for HPLC-MS) at 10.0 mg/mL concentration. The polyester n-hexane extracts were directly analysed by GC-MS and HPLC-MS to fingerprint the particular species available for migration within the adhesives as well as to define the upper weight limit of the short chain cyclic oligoesters present in the polyester. The GC-MS and HPLC-MS analysis data of food-contact side laminate extracts and polyester n-hexane extracts were compared to determine the upper limit of mw migration of cyclic oligoesters through the films.

3 | RESULTS AND DISCUSSION

3.1 | Identification of cyclic oligoesters

The results of migration study performed on 537 commercially manufactured laminates are reported. The data illustrate a variety of cyclic oligoesters migrate from the food-contact side of the laminate packaging to food simulant. The complete list of identified cyclic oligoesters is summarized in Table 1 with the percent relative abundance of their corresponding molecular ions and 10 major mass fragments from EI mass spectra. The structures of the cyclic oligoesters were derived from interpretation of the EI mass spectral fragmentation patterns (see the Supporting Information) and mw confirmation by CI and/or HPLC-MS data. Formulation information provided directly by adhesive manufacturers assisted with the structure confirmation and constituent monomers (of which MS library spectra are readily available) were confirmed. The source of cyclic oligoesters was verified to be the lamination adhesive as opposed to other components of the laminations by analyzing control (unlaminated) sealant films and/or unprinted laminate controls. Furthermore, direct extractions of raw materials of PU laminating adhesives themselves prepared as cured films on glass plates were prepared and analysed. Compounds are listed in Table 1 in order of mw from lowest to highest. The mw of the identified cyclic oligoesters ranged from 170 to 650 Da. Among 106 identified compounds, 85 are newly detected short-chain cyclic oligoesters from food packaging lamination adhesives, which are

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TABLE 1 Identification of low molecular weight (<650 Da) cyclic oligoester migrants from polyurethane lamination adhesives (name, molecular formula, molecular ion $[M]^+$ percent abundance, and 10 major EI mass spectra fragment ion peaks percent abundance)

Name[a]	Molecular Formula	$[M]^+$ Ion (% Abundance)	10 Major EI Mass Spectra Fragment Ion Peaks (% Abundance)
Cyclic EG-AA[b]	$C_8H_{12}O_4$	172(0.00)[e,f]	55(100.00) 112(68.04) 142(64.00) 84(57.31) 41(42.79) 56 (37.00) 144 (33.60) 113(33.48) 42(29.43) 39(21.16)
Cyclic PG-AA[c,d]	$C_9H_{14}O_4$	186(6.31)	55(100.00) 129(77.78) 41(65.37) 56(52.25) 111(40.64) 39(38.64) 101(26.53) 42(26.13) 83(21.52) 43(14.51)
Cyclic 1,4-BD-AA[b]	$C_{10}H_{16}O_4$	200(0.21)[e,f]	55(100.00) 54(99.79) 129(46.55) 100(45.00) 84(43.83) 41(42.69) 111(32.24) 56(27.84) 42(26.27) 71(21.98)
Cyclic EG-SuA[c]	$C_{10}H_{16}O_4$	200(0.00)[e]	138(100.00) 55(46.44) 41(45.49) 139(44.24) 68(33.70) 69(31.92) 86(28.99) 42(28.47) 157(24.97) 84(21.66)
Cyclic MP-diol-AA[c]	$C_{10}H_{16}O_4$	200(0.56)[e,f]	129(100.00) 111(83.88) 55(55.83) 101 (29.99) 41 (26.17) 83 (24.63) 172(22.46) 42(13.88) 39(13.11) 112(12.80)
Cyclic EG-AzA[c]	$C_{11}H_{18}O_4$	214(0.27)[e]	152(100.00) 55(87.45) 41(52.12) 98(49.45) 171(48.99) 83(30.76) 86(30.62) 84(26.78) 124(24.98) 42(23.34)
Cyclic NPG-AA[b]	$C_{11}H_{18}O_4$	214(1.09)[f]	129(100.00) 55 (47.72) 111(46.44) 56(45.24) 41(26.35) 101(20.03) 83(17.11) 43(11.49) 69(10.05) 112(9.05)
Cyclic DEG-AA[b]	$C_{10}H_{16}O_5$	216(0.26)[e,f]	173(100.00) 55(78.00) 99(35.86) 84(32.54) 56(25.04) 111(24.12) 42(22.06) 41(22.03) 45(19.67) 83(16.94)
Cyclic 1,6-HD-AA[b]	$C_{12}H_{20}O_4$	228(0.85)[e,f]	55(100.00) 82(53.55) 111(53.28) 129(49.05) 83(44.07) 41(41.78) 101(39.87) 100(34.24) 54(26.01) 67(25.32)
Cyclic EG-SeA[c]	$C_{12}H_{20}O_4$	228(0.22)[e,f]	185(100.00) 55(76.00) 98(72.72) 138(52.46) 166(45.21) 41(44.93) 97(29.27) 86(25.12) 99(24.20) 83(23.74)
Cyclic PG-AzA[c,d]	$C_{12}H_{20}O_4$	228(1.30)	152(100.00) 98(83.38) 171(66.67) 55(65.77) 41(48.15) 42(39.04) 154(30.33) 100(28.83) 97(28.63) 113(26.03)
Cyclic NPG-PA[c,d]	$C_{13}H_{14}O_4$	234(0.50)[e]	149(100.00) 56(47.15) 76(35.04) 41(21.72) 50(17.82) 104(17.32) 39(14.71) 65(11.71) 55(9.51) 74(9.41)
Cyclic DEG-IPA[b]	$C_{12}H_{12}O_5$	236(0.07)[e,f]	193(100.00) 149(75.16) 104(19.90) 132(13.41) 76(12.25) 194 (10.90) 148(7.17) 176(6.70) 150(5.95) 50(3.79)
Cyclic DEG-PA[b]	$C_{12}H_{12}O_5$	236(0.05)[e]	149 (100.00) 193 (98.57) 104 (33.37) 76(24.76) 148(17.20) 132(12.99) 194(9.89) 176(8.27) 190 (7.79) 150(6.17)
Cyclic NPG-SuA[c]	$C_{13}H_{22}O_4$	242(0.11)[e,f]	157(100.00) 111(25.22) 175(23.44) 129(20.66) 55(13.49) 41(11.76) 215(10.46) 56(9.37) 158(8.52) 43(6.41)
Cyclic PG-SeA[c,d]	$C_{13}H_{22}O_4$	242(0.70)[e]	55(100.00) 98(89.39) 41(81.88) 185(53.15) 42(45.05) 43(31.53) 97(31.03) 69(29.13) 113(29.13) 39(28.83)
Cyclic DPG-AA[b,d]	$C_{12}H_{20}O_5$	244(0.20)[e]	55(100.00) 187(93.79) 111(57.06) 41(51.45) 84(47.65) 42(40.04) 101(37.14) 83(32.43) 56(31.43) 113(30.33)
Cyclic 1,6-HD–PA[c]	$C_{14}H_{16}O_4$	248(3.01)	149(100.00) 82(12.44) 150(11.00) 100(8.64) 54(6.51) 71(6.08) 67(5.85) 76(4.54) 42(3.61) 41(3.47) 248(3.01)
Cyclic MP-diol-SeA[c]	$C_{14}H_{24}O_4$	256(7.11)[f]	185(100.00) 55(97.91) 41(59.62) 98(59.42) 166(56.47) 138(46.36) 183(38.27) 165 (35.05) 114(34.62) 42(30.52)
Cyclic NPG-AzA[c]	$C_{14}H_{24}O_4$	256(0.27)[e]	55(100.00) 171(98.12) 152(82.61) 41(82.18) 56(44.35) 69(36.75) 42(35.46) 97(28.73) 83(27.10) 98(22.32)
Cyclic NPG-SeA[c]	$C_{15}H_{26}O_4$	270(1.66)[f]	185(100.00) 55(49.27) 41(37.72) 98(31.08) 141(23.51) 56(22.84) 166(22.54) 138(22.04) 69(20.97) 128(17.53)
Cyclic DPG-AzA[c,d]	$C_{15}H_{26}O_5$	286(0.40)[e]	113(100.00) 55(66.77) 229(65.67) 98(39.84) 100(36.64) 97(17.52) 83(16.22) 69(15.02) 59(14.11) 56(13.11)
Cyclic DPG-SeA[c,d]	$C_{16}H_{28}O_5$	300(0.30)[e]	243(100.00) 55(42.54) 41(35.64) 98(35.04) 113(28.13) 42(23.82) 43(17.02) 97(16.72) 69(16.52) 84(15.42)
Cyclic TPG-AA[c,d]	$C_{15}H_{26}O_6$	302(0.40)[e]	113(100.00) 187(54.85) 55(37.44) 59(29.13) 41(26.43) 42(17.62) 111(16.62) 43(14.11) 57(13.51) 56(12.01)
Cyclic TPG-PA[c,d]	$C_{17}H_{22}O_6$	322(0.40)[e]	162(100.00) 104(62.26) 76(32.93) 207(30.93) 149(21.32) 279(15.12) 204(12.41) 163(11.51) 41(8.51) 105(7.01)
Cyclic EG-AA-EG-AA[b]	$C_{16}H_{24}O_8$	344(7.54)[f]	173(100.00) 99(61.02) 55(41.78) 113(32.68) 111(24.45) 86(21.16) 217(20.63) 155(17.34) 129(10.15) 56(10.02)
Cyclic EG-AA-PG-AA[c,d]	$C_{17}H_{26}O_8$	358(6.81)	55(100.00) 113(62.26) 173(42.04) 111(34.53) 99(34.43) 187(26.23) 83(26.03) 56(25.83) 41(21.42) 45(20.92)
Cyclic EG-AA-EG-IPA[b]	$C_{18}H_{20}O_8$	364(8.87)[f]	193(100.00) 149(20.47) 237(20.35) 104(14.47) 148(11.03) 194(11.00) 364(8.87) 99(6.90) 321(6.85) 55(6.11)
Cyclic EG-AA-1,4-BD-AA[c,d]	$C_{18}H_{28}O_8$	372(6.71)	55(100.00) 173(51.25) 99(46.25) 111(34.93) 129(25.83) 83(23.52) 54(23.32) 41(22.72) 113(21.42) 56(20.22)

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TABLE 1 (Continued)

Name[a]	Molecular Formula	$[M]^+$ Ion (% Abundance)	10 Major EI Mass Spectra Fragment Ion Peaks (% Abundance)
Cyclic PG-AA-PG-AA[c]	$C_{18}H_{28}O_8$	372(11.05)	187(100.00) 55(78.96) 113(69.18) 111(60.37) 127(38.56) 56(22.50) 41(19.02) 201(18.58) 100(17.44) 84(17.13)
Cyclic EG-AA-PG-PA[c,d]	$C_{19}H_{22}O_8$	378(4.00)	104(100.00) 76(75.68) 193(71.87) 55(71.77) 149(58.66) 148(34.03) 41(23.92) 207(21.92) 162(20.22) 105(16.52)
Cyclic EG-IPA-EG-IPA[b]	$C_{20}H_{16}O_8$	384(0.18)[e,f]	341(100.00) 76(60.92) 208(53.91) 104 (41.24) 149(22.47) 342(22.24) 152(15.82) 324(13.58) 236(12.07) 266(8.91)
Cyclic EG-TPA-EG-TPA[c]	$C_{20}H_{16}O_8$	384(0.65)[e,f]	341(100.00) 338(30.67) 208(22.97) 342(19.91) 104(8.24) 162(7.45) 152 (7.24) 236(6.54) 266(6.20) 76(5.17)
Cyclic DEG-AA-EG-AA[b]	$C_{18}H_{28}O_9$	388(0.37)[e,f]	345(100.00) 55 (92.41) 99(86.42) 173(70.59) 155(55.31) 111(40.26) 113(33.30) 217 (30.67) 86(29.50) 346(23.97)
Cyclic PG-AA-PG-IPA[c]	$C_{20}H_{24}O_8$	392(7.93)	207(100.00) 162(49.58) 149(42.61) 104(37.24) 220(19.97) 55(14.79) 76(14.71) 208(11.54) 111(11.38) 190(10.50)
Cyclic EG-PA-PG-PA[c,d]	$C_{21}H_{18}O_8$	398(0.50)[e]	208(100.00) 341(97.40) 324(73.27) 76(54.85) 104(44.24) 236(40.54) 354(32.33) 266(31.73) 149(21.92) 355(19.42)
Cyclic 1,4-BD-AA-1,4-BD-AA[b]	$C_{20}H_{32}O_8$	400(5.51)[f]	55(100.00) 129(90.74) 201(85.00) 111(61.96) 54(53.92) 127(46.27) 141(38.76) 71(36.38) 84(25.00) 41(23.47)
Cyclic NPG-AA-PG-AA[c]	$C_{20}H_{32}O_8$	400(14.89)	187(100.00) 55(41.57) 111(29.51) 215(24.46) 129(21.04) 113(20.89) 56(18.30) 141(15.15) 400(14.89) 41(13.93)
Cyclic MP-diol-AA- MP-diol-AA[c]	$C_{20}H_{32}O_8$	400(11.56)[f]	201(100.00) 127(18.51) 111(15.42) 400(11.56) 329(10.41) 202(10.22) 341(8.85) 55(8.41) 114(6.64) 129(6.13)
Cyclic DEG-AA-PG-AA[c,d]	$C_{19}H_{30}O_9$	402(0.00)[e]	55(100.00) 99(44.84) 359(36.34) 113(31.43) 111(31.13) 83(26.73) 41(23.42) 56(23.02) 155(21.12) 45(21.02)
Cyclic EG-AA-NPG-PA[c,d]	$C_{21}H_{26}O_8$	406(4.30)	193(100.00) 104(91.09) 55(73.87) 149(73.17) 76(58.56) 56(54.85) 41(38.44) 69(17.12) 235(16.02) 111(15.22)
Cyclic EG-AA-DEG-IPA[b]	$C_{20}H_{24}O_9$	408(0.13)[e,f]	365(100.00) 193(22.18) 149(11.59) 148(11.56) 104(10.31) 366(7.89) 237(6.76) 55(5.55) 99(4.42) 155(4.20)
Cyclic EG-IPA-MP-diol-IPA[c]	$C_{22}H_{20}O_8$	412(1.10)[f]	341(100.00) 340(76.24) 207(28.03) 342(23.55) 208(23.50) 334(23.22) 104(16.79) 76(14.06) 149(12.72) 328(12.16)
Cyclic PG-PA-PG-PA[c,d]	$C_{22}H_{20}O_8$	412(0.80)[e]	208(100.00) 355(69.77) 76(50.35) 104(48.95) 236(47.45) 338(46.45) 266(44.34) 149(30.33) 368(23.62) 280(22.82)
Cyclic 1,6-HD-AA-PG-AA[c]	$C_{21}H_{34}O_8$	414(16.62)	55(100.00) 187(96.91) 111(59.29) 113(57.60) 129(43.13) 83(38.44) 268(28.72) 127(26.64) 41(26.14) 101(24.90)
Cyclic EG-SeA-EG-IPA[c]	$C_{22}H_{28}O_8$	420(9.11)[f]	237(100.00) 193(38.47) 149(34.12) 166(26.70) 104(20.11) 148(18.31) 132(17.45) 98(14.77) 377(14.33) 337(9.99)
Cyclic PG-AA-DEG-IPA[c,d]	$C_{21}H_{26}O_9$	422(0.85)[e]	207(100.00) 236(63.76) 149(56.21) 104(31.97) 206(27.57) 55(19.48) 190(17.37) 41(16.52) 76(14.17) 420(13.84)
Cyclic EG-IPA-NPG-IPA[c]	$C_{23}H_{22}O_8$	426(4.56)[f]	341(100.00) 339(47.72) 208(24.22) 342(19.99) 333(15.86) 206(10.63) 104(9.88) 76(9.63) 149(8.42) 327(8.09)
Cyclic NPG-AA-NPG-AA[c]	$C_{22}H_{36}O_8$	428(29.65)[f]	215 (100.00) 55(34.04) 428(29.65) 343(22.97) 56(21.95) 129(21.21) 111(15.62) 216(14.68) 141(12.71) 69(11.69)
Cyclic EG-AzA-EG-AzA[c]	$C_{22}H_{36}O_8$	428(20.36)	99(100.00) 55(76.36) 385(66.19) 215(57.02) 384(42.29) 86(37.61) 152(36.04) 155(33.57) 83(25.35) 259(24.54)
Cyclic DEG-IPA-EG-IPA[b]	$C_{22}H_{20}O_9$	428(0.13)[e,f]	385(100.00) 208(36.15) 386(34.30) 149(16.42) 104(13.66) 76(12.88) 341(10.97) 297(10.92) 162 (8.42) 193(7.96)
Cyclic DEG-AA-NPG-AA[b,d]	$C_{21}H_{34}O_9$	430(0.00)[e]	55(100.00) 387(54.75) 173(53.55) 56(49.55) 99(47.25) 111(44.54) 83(42.04) 217(39.14) 41(36.54) 155(31.93)
Cyclic DPG-AA-PG-AA[c,d]	$C_{21}H_{34}O_9$	430(0.10)[e]	187(100.00) 111(64.96) 373(53.55) 55(49.65) 129(38.64) 245(33.33) 113(30.93) 101(28.93) 45(23.62) 83(22.72)
Cyclic DEG-AA-DEG-AA[b]	$C_{20}H_{32}O_{10}$	432(0.19)[e,f]	173(100.00) 389(72.33) 99(62.74) 155(55.25) 55(38.25) 111(28.20) 243(24.33) 217(24.29) 113(13.48) 86(12.19)
Cyclic MP-diol-IPA-MP-diol-IPA[c]	$C_{24}H_{24}O_8$	440(1.67)[f]	369(100.00) 365(34.86) 208(29.56) 149(18.50) 370(18.38) 360(14.62) 104(14.33) 297(12.49) 221(12.11) 372(11.97)
Cyclic NPG-AA-1,6-HD-AA[c]	$C_{23}H_{38}O_8$	442(10.65)	55(100.00) 129(65.34) 215(51.54) 229(42.61) 83(41.86) 111(34.15) 41(30.53) 141(29.83) 56(27.28) 101(23.02)
Cyclic DEG-AA-1,6-HD-AA[c,d]	$C_{22}H_{36}O_9$	444(0.60)[e]	55(100.00) 99(79.18) 401(63.46) 111(59.96) 173(59.66) 83(52.05) 129(40.44) 217(38.54) 155(27.83) 101(27.13)
Cyclic NPG-AA-NPG-IPA[c]	$C_{24}H_{32}O_8$	448(7.29)[f]	235(100.00) 149(44.59) 237(25.23) 69(24.10) 104(17.10) 56(16.50) 363(15.56) 231(14.84) 55(14.66) 41(14.08)

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TABLE 1 (Continued)

Name[a]	Molecular Formula	$[M]^+$ Ion (% Abundance)	10 Major EI Mass Spectra Fragment Ion Peaks (% Abundance)
Cyclic EG-SeA-MP-diol-IPA[c]	$C_{24}H_{32}O_8$	448(28.26)	149(100.00) 377(71.75) 193(66.02) 104(50.00) 265(42.93) 55(41.62) 375(35.76) 448(28.26) 76(22.87) 447(21.55)
Cyclic PG-SeA-PG-PA[c,d]	$C_{24}H_{32}O_8$	448(16.42)	149(100.00) 104(91.39) 207(55.56) 55(44.24) 76(40.64) 391(40.34) 41(28.93) 113(26.03) 162(25.93) 265(21.92)
Cyclic DEG-AA-NPG-PA[b,d]	$C_{23}H_{30}O_9$	450(0.00)[e]	104(100.00) 149(85.99) 407(76.18) 55(66.27) 76(64.46) 56(48.15) 193(39.34) 41(35.04) 69(25.23) 111(20.52)
Cyclic DPG-AA-PG-PA[c,d]	$C_{23}H_{30}O_9$	450(0.00)[e]	393(100.00) 104(79.68) 149(71.37) 55(65.27) 207(64.16) 162(52.05) 113(42.94) 76(42.14) 111(26.03) 394(20.92)
Cyclic DEG-AA-DEG-IPA[b]	$C_{22}H_{28}O_{10}$	452(0.16)[e,f]	409(100.00) 193 (49.09) 104(22.61) 149(21.55) 410 (18.88) 148(14.16) 237(12.49) 406(12.33) 155(12.31) 55(10.87)
Cyclic EG-SeA-EG-SeA[c]	$C_{24}H_{40}O_8$	456(28.11)[f]	413(10.00) 229(53.40) 99(50.70) 169(35.16) 55(31.12) 456(28.11) 273(26.35) 411(21.98) 414(21.95) 155(20.54)
Cyclic 1,6-HD-AA-1,6-HD-AA[c]	$C_{24}H_{40}O_8$	456(2.88)[f]	55(100.00) 229(75.57) 129(62.95) 83(60.72) 82(49.84) 111(45.82) 211(37.66) 101(31.00) 41(28.12) 67(15.92)
Cyclic NPG-AA-NPG-SuA[c]	$C_{24}H_{40}O_8$	456(0.04)[e]	215(100.00) 243(93.56) 429(77.29) 157(39.64) 129(25.69) 389(19.95) 430(18.64) 371(16.84) 111(16.46) 343(15.01)
Cyclic DEG-AA-DPG-AA[c,d]	$C_{22}H_{36}O_{10}$	460(0.60)[e]	111(100.00) 173(80.58) 55(67.47) 169(55.66) 213(45.95) 41(43.94) 155(35.94) 231(34.43) 99(33.13) 83(29.03)
Cyclic EG-SeA-NPG-IPA[c]	$C_{25}H_{34}O_8$	462(33.77)[f]	149(100.00) 378(90.55) 193(82.16) 377(65.47) 148(52.05) 104(49.93) 279(36.34) 190(36.33) 462(33.77) 55(31.72)
Cyclic DEG-AzA-PG-PA[c,d]	$C_{24}H_{32}O_9$	464(1.60)	104(100.00) 149(99.80) 55(69.97) 421(60.96) 76(54.55) 193(51.15) 99(37.64) 148(34.73) 41(31.13) 207(21.52)
Cyclic NPG-IPA-NPG-IPA[c]	$C_{26}H_{28}O_8$	468(13.54)[f]	383(100.00) 380(38.81) 208(29.11) 149(22.38) 384(21.60) 297(21.53) 374(16.45) 104(14.74) 296(13.82) 468(13.54)
Cyclic DPG-PA-PG-PA[c,d]	$C_{25}H_{26}O_9$	470(0.10)[e]	413(100.00) 208(78.78) 104(70.97) 76(50.05) 149(46.15) 311(30.33) 189(28.23) 414(24.52) 105(24.02) 236(21.62)
Cyclic DEG-IPA-DEG-IPA[b]	$C_{24}H_{24}O_{10}$	472(0.03)[e,f]	429(100.00) 430(46.41) 208(15.58) 297(13.80) 149(12.97) 104(10.64) 425(8.43) 193(7.17) 237(6.90) 263(5.55)
Cyclic DEG-PA-DEG-PA[b,d]	$C_{24}H_{24}O_{10}$	472(0.00)[e]	193(100.00) 149(83.48) 104(44.34) 148(39.44) 76(20.62) 105(17.12) 176(12.01) 194(11.31) 281(9.81) 237(9.71)
Cyclic DPG-AA-1,6-HD-AA[c,d]	$C_{24}H_{40}O_9$	472(0.30)[e]	113(100.00) 55(67.27) 415(49.55) 111(37.04) 83(26.13) 187(22.72) 129(22.62) 101(20.92) 41(15.32) 127(14.61)
Cyclic DEG-AA-DEG-AzA[c]	$C_{23}H_{38}O_{10}$	474(0.50)[e]	99(100.00) 55(81.88) 173(30.13) 155(29.63) 86(27.43) 215(26.63) 431(26.33) 83(25.23) 111(19.62) 41(18.72)
Cyclic MP-diol-SeA-MP-diol-IPA[c]	$C_{26}H_{36}O_8$	476(16.67)[f]	405(100.00) 149(56.82) 221(48.08) 104(32.96) 55(32.75) 218(24.54) 399(20.69) 293(18.82) 476(16.67) 406(16.23)
Cyclic 1,6-HD-AA-1,6-HD-PA[c,d]	$C_{26}H_{36}O_8$	476(9.01)	149(100.00) 55(82.08) 82(57.86) 83(53.95) 104(41.74) 41(28.63) 111(24.82) 76(21.42) 377(19.62) 359(19.42)
Cyclic EG-SeA-MP-diol-SeA[c]	$C_{26}H_{44}O_8$	484(32.97)[f]	55(100.00) 413(62.89) 99(52.63) 127(52.18) 229(45.18) 69(42.13) 441(40.18) 484(32.97) 114(32.90) 98(30.24)
Cyclic PG-SeA-PG-SeA[c,d]	$C_{26}H_{44}O_8$	484(17.22)	113(100.00) 55(84.88) 183(58.86) 427(58.76) 98(52.25) 69(46.35) 100(46.05) 41(36.64) 243(32.33) 97(31.93)
Cyclic DEG-AzA-NPG-PA[c]	$C_{26}H_{36}O_9$	492(0.00)[e]	149(100.00) 449(96.20) 104(88.59) 55(71.57) 76(46.85) 56(45.65) 69(43.24) 193(42.54) 148(38.94) 41(36.44)
Cyclic DPG-AzA-PG-PA[c,d]	$C_{26}H_{36}O_9$	492(0.00)[e]	435(100.00) 104(91.59) 149(69.97) 207(55.06) 162(41.14) 76(36.14) 436(26.03) 55(21.32) 189(20.22) 105(20.12)
Cyclic DEG-AzA-DEG-PA[c,d]	$C_{25}H_{34}O_{10}$	494(0.00)[e]	104(100.00) 451(94.69) 149(81.68) 193(75.58) 148(52.65) 55(50.85) 76(42.74) 99(35.64) 105(31.93) 83(27.03)
Cyclic 1,6-HD-PA-1,6-HD-PA[c]	$C_{28}H_{32}O_8$	496(2.96)	149(100.00) 249(49.22) 101(21.48) 82(19.04) 150(15.82) 55(15.12) 230(13.94) 397(13.09) 83(13.03) 202(10.04)
Cyclic EG-SeA-NPG-SeA[c]	$C_{27}H_{46}O_8$	498(37.82)[f]	413(100.00) 55(54.16) 411(49.87) 69(44.50) 498(37.82) 455(34.81) 229(34.08) 99(31.60) 141(29.37) 185(27.45)
Cyclic NPG-SeA-NPG-IPA[c]	$C_{28}H_{40}O_8$	504(29.94)[f]	419(100.00) 418(53.66) 149(43.61) 235(36.16) 504(29.94) 420(28.21)5 321(19.29) 104(15.60) 69(14.61) 503(12.44)
Cyclic DEG-PA-NPG-SeA[c,d]	$C_{27}H_{38}O_9$	506(1.60)	149(100.00) 104(72.17) 55(43.74) 463(40.54) 69(38.34) 193(37.84) 99(31.73) 76(30.13) 148(25.93) 56(24.12)
Cyclic PG-SeA-DPG-PA[c,d]	$C_{27}H_{38}O_9$	506(1.20)	449(100.00) 149(89.79) 104(83.68) 113(68.57) 207(56.26) 55(53.75) 162(46.85) 41(32.23) 76(32.03) 69(29.73)

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TABLE 1 (Continued)

Name[a]	Molecular Formula	$[M]^+$ Ion (% Abundance)	10 Major EI Mass Spectra Fragment Ion Peaks (% Abundance)
Cyclic MP-diol-SeA-MP-diol-SeA[c]	$C_{28}H_{48}O_8$	512(28.77)[f]	441(100.00) 55(68.58) 440(60.09) 127(51.90) 114(39.21) 257(36.49) 69(31.09) 512(28.77) 40(24.31) 185(24.14)
Cyclic PG-SeA-NPG-SeA[c,d]	$C_{28}H_{48}O_8$	512(20.62)	113(100.00) 55(78.68) 455(49.35) 69(45.85) 98(45.75) 100(44.34) 41(34.53) 169(34.53) 211(33.63) 83(31.93)
Cyclic EG-AA-EG-AA-EG-AA[c,d]	$C_{24}H_{36}O_{12}$	516(5.51)	99(100.00) 55(72.97) 345(51.95) 173(45.95) 113(37.64) 155(36.14) 111(35.14) 83(25.03) 86(23.42) 112(20.22)
Cyclic DPG-PA-DPG-PA[c,d]	$C_{28}H_{32}O_{10}$	528(0.00)[e]	471(100.00) 149(57.86) 104(50.25) 208(48.45) 76(32.53) 207(30.43) 472(27.53) 162(19.42) 297(15.52) 65(14.21)
Cyclic NPG-SeA-NPG-SeA[c]	$C_{30}H_{52}O_8$	540(26.37)[f]	455(100.00) 456(54.69) 540(26.37) 141(15.40) 450(13.77) 69(13.74) 271(12.61) 185(11.64) 128(10.78) 55(9.93)
Cyclic PG-SeA-DPG-SeA[c,d]	$C_{29}H_{50}O_9$	542(4.00)	485(100.00) 113(95.50) 55(75.08) 243(62.06) 98(50.65) 69(45.35) 183(40.84) 100(35.14) 41(34.53) 43(32.53)
Cyclic DEG-SeA-DEG-SeA[c,d]	$C_{28}H_{48}O_{10}$	544(1.00)	99(100.00) 229(53.05) 55(41.24) 273(33.43) 86(28.13) 69(26.03) 501(21.72)141(20.72) 98(20.62) 155(19.92)
Cyclic EG-AA-EG-AA-1,4-BD-AA[c,d]	$C_{26}H_{40}O_{12}$	544(6.81)	55(100.00) 99(84.88) 173(62.96) 111(49.75) 113(33.83) 83(31.93) 155(31.63) 373(26.53) 129(22.82) 84(22.72)
Cyclic PG-AA-PG-AA-PG-AA[c,d]	$C_{27}H_{42}O_{12}$	558(3.60)	113(100.00) 530(71.17) 55(68.17) 111(57.76) 187(50.35) 57(45.55) 373(37.84) 219(37.34) 127(34.03) 515(28.23)
Cyclic 1,4-BD-AA-1,4-BD-AA-EG-AA[c,d]	$C_{28}H_{44}O_{12}$	572(6.21)	55(100.00) 111(53.95) 99(43.24) 173(42.44) 129(38.84) 83(29.43) 54(23.62) 84(22.82) 373(22.72) 71(22.32)
Cyclic NPG-AA-PG-AA-PG-AA[c,d]	$C_{29}H_{46}O_{12}$	586(10.01)	113(100.00) 111(91.29) 187(84.58) 55(77.68) 373(60.76) 127(40.14) 401(37.64) 83(34.53) 501(34.13) 56(34.03)
Cyclic DEG-AA-PG-AA-PG-AA[c,d]	$C_{28}H_{44}O_{13}$	588(1.10)	55(100.00) 113(85.49) 111(77.18) 187(59.06) 99(52.85) 83(42.54) 155(29.63) 127(28.73) 173(27.73) 84(27.53)
Cyclic DPG-SeA-DPG-SeA[c,d]	$C_{32}H_{56}O_{10}$	600(0.90)[e]	543(100.00) 113(87.29) 243(77.58) 55(52.25) 98(36.74) 69(34.33) 544(31.83) 183(30.13) 100(27.93) 41(27.33)
Cyclic NPG-AA-NPG-AA-PG-AA[c,d]	$C_{31}H_{50}O_{12}$	614(14.31)	401(100.00) 111(97.30) 55(73.27) 187(65.67) 529(60.46) 129(55.76) 215(54.95) 113(53.75) 69(46.75) 56(43.94)
Cyclic DEG-AA-DEG-AA-PG-AA[c,d]	$C_{29}H_{46}O_{14}$	618(0.00)[e]	99(100.00) 55(84.38) 173(81.08) 111(75.98) 155(60.56) 113(55.66) 187(44.24) 83(37.34) 217(32.73) 100(30.23)
Cyclic TPG-AA-TPG-PA[c,d]	$C_{32}H_{48}O_{12}$	624(0.00)[e]	162(100.00) 104(88.59) 207(85.89) 113(81.58) 149(74.07) 187(41.74) 55(35.54) 509(34.23) 111(29.53) 41(26.53)
Cyclic NPG-AA-NPG-AA-NPG-AA[c]	$C_{33}H_{54}O_{12}$	642(0.59)[e,f]	429(100.00) 215(50.02) 430(24.32) 129(13.67) 301(11.81) 343(5.86) 111(5.53) 216(5.45) 55(5.25) 56(4.45)
Cyclic NPG-AA-NPG-AA-DEG-AA[c,d]	$C_{32}H_{52}O_{13}$	644(1.00)	111(100.00) 55(78.88) 215(70.17) 431(62.16) 99(59.06) 129(57.56) 69(55.36) 173(52.85) 155(51.85) 56(43.84)
Cyclic DEG-AA-DEG-AA-DEG-AA[c,d]	$C_{30}H_{48}O_{15}$	648(0.20)[e]	173(100.00) 99(96.30) 155(68.57) 55(57.46) 111(51.55) 217(37.84) 389(32.03) 243(31.83) 83(30.23) 605(26.33)

[a]EG, ethylene glycol; 1,4-BD, 1,4 butanediol; MP-diol, 2-methyl-1, 3-propanediol; DEG, diethylene glycol; 1,6-HD, 1,6 hexanediol; NPG, neopentyl glycol; PG, propylene glycol; DPG, dipropylene glycol; TPG, tripropylene glycol; AA, adipic acid; AzA, azelaic acid; SeA, sebacic acid; SuA, suberic acid; PA, phthalic acid; IPA, isophthalic acid; TPA, terephthalic acid.

[b]Already identified cyclic oligoester by previous studies.

[c]Newly identified cyclic oligoester in this present study.

[d]Cyclic oligoester identified from direct extraction of polyurethane adhesive raw materials.

[e]Cyclic oligoester molecular ion confirmed with gas chromatography-mass spectrometry (GC-MS) chemical ionization (CI) analysis.

[f]Cyclic oligoester molecular ion confirmed with high-performance liquid chromatography-mass spectrometry (HPLC-MS) analysis.

reported in the open literature for or the first time. The report includes the mass spectra of previously identified 21 cyclic oligoesters as well, since they belong to the detected migrants in the analysed samples. Fifty of the identified cyclic oligoesters were from direct extraction of developmental adhesive raw materials and were not observed as migrants from laminate samples thus far as they represent new adhesive formulations that have not been commercially marketed or were only recently introduced. However, they all have migration potential because of their low mw.

Most of the cyclic oligoesters yield EI mass spectra with intact molecular ions. However, some of the molecular ions are low intensity or absent in the EI spectra. In these cases, CI analysis and/or HPLC-MS (+ ion electrospray ionization or atmospheric pressure chemical ionization) were performed to verify mw. Diethylene glycol is illustrated as a typical example: The molecular ion $[M]^+$ percent abundance of cyclic DEG-AA at 216 is low intensity in the EI spectrum because of the labile ether linkages from DEG (Figure 1), but under CI analysis, a strong protonated ion $[M + H]^+$ at 217 is produced (Figure 2), whereas under HPLC-MS analysis, an additional sodium adduct ion $[M + Na]^+$ at 239 is present in addition to the $[M + H]^+$ (Figure 3). Some cyclic oligoesters also undergo self CI and yield a low intensity protonated ions $[M + H]^+$ under EI conditions owing to the strong basicity of the carbonyls in

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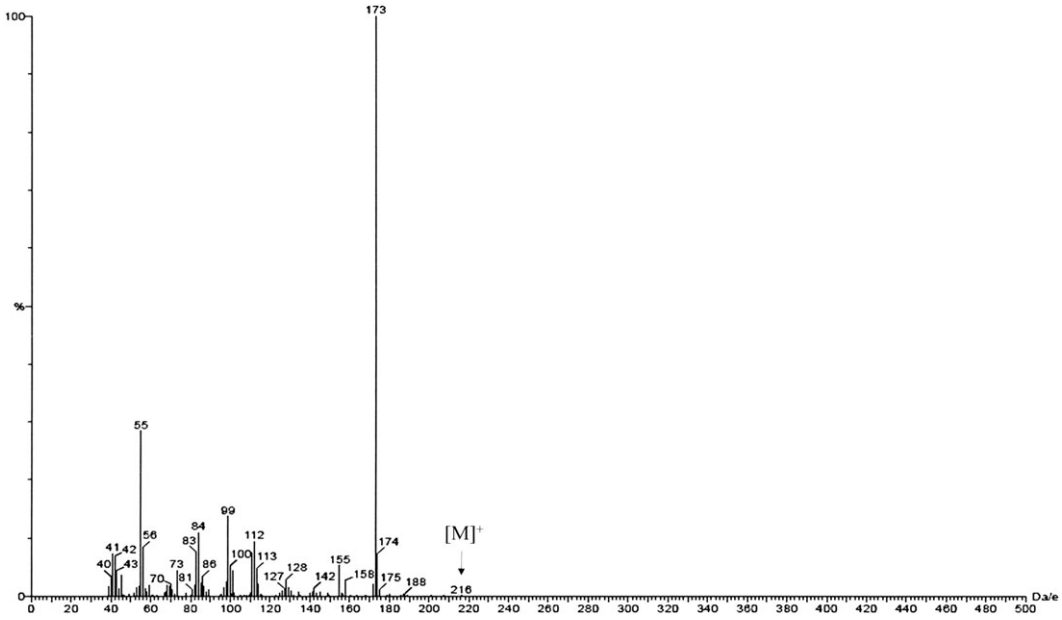


FIGURE 1 Electron ionization (EI) mass spectrum of cyclic diethylene glycol-adipic acid diester (DEG-AA)

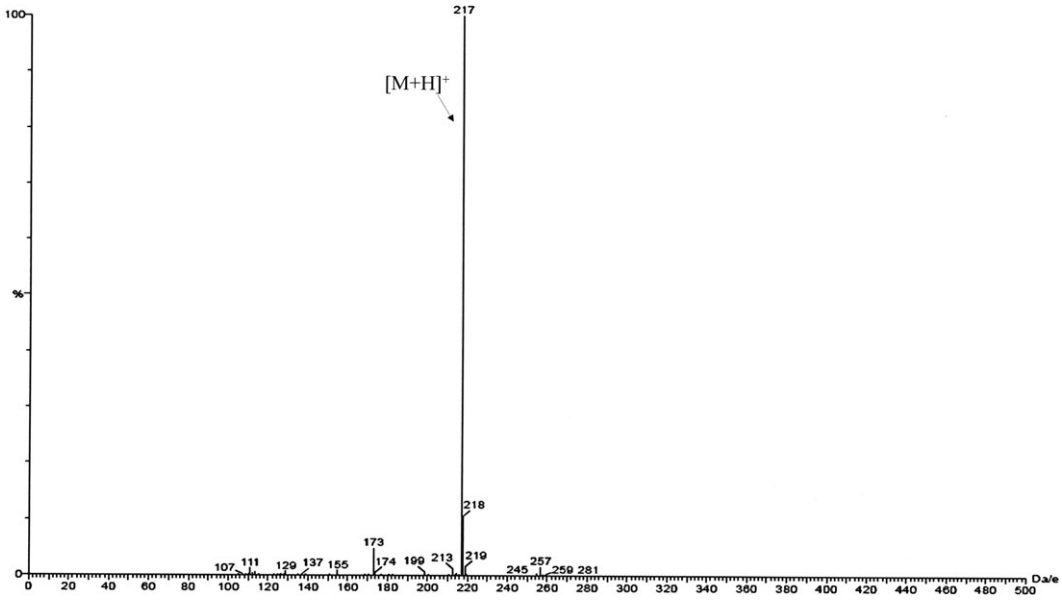


FIGURE 2 Chemical ionization (CI) mass spectrum of cyclic diethylene glycol-adipic acid diester (DEG-AA)

their structures. Ions at $[M-18]^+$ were occasionally observed in cyclic oligoesters likely as a consequence of ring cleavage possibly followed by a Mclafferty rearrangement accompanied by neutral loss of water.

Fragment ions at *m/z* 55 $[C_4H_7]^+$ and 111 $[C_6H_7O_2]^+$ were characteristic ions for cyclic oligoesters based on aliphatic diacids. For aromatic type cyclic oligoesters (phthalate, isophthalate, or terephthalate), 149 $[C_8H_5O_3]^+$ and 104 $[C_7H_4O]^+$ were the common fragment ions. Cyclic oligoesters that contain both aromatic and aliphatic acids exhibited mixed fragmentation characteristics. In the case of cyclic NPG-AA-NPG-IPA, the major fragment ions were observed at *m/z* 55, 104, and 149. Cyclic oligoesters from AA usually had a fragment ion at 129 $[C_6H_9O_3]^+$. Cyclic oligoesters from suberic acid generally had a fragment ion at 157 $[C_8H_{13}O_3]^+$ because suberic acid has 2 more $-CH_2$ units in the alkyl chain than AA and their fragmentation patterns are similar. Azelaic acid (AzA) has 3 more $-CH_2$ units than AA in the alkyl chain. Therefore, its cyclic oligoesters often showed a fragment ion at 171 $[C_9H_{15}O_3]^+$. Sebacic acid (SeA) has 4 more $-CH_2$ units than AA in the alkyl chain, and its cyclic oligoesters showed a characteristic fragment ion at 185 $[C_{10}H_{17}O_3]^+$. Neutral loss of 71 generally occurs for cyclic oligoesters based on 1,4-butanediol (1,4-BD) and 2-methyl-1, 3-propanediol (MP-diol); a loss of 43 usually occurs for cyclic oligoesters based on EG and DEG; and a loss of 57 often occurs for propylene glycol (PG), dipropylene glycol, and tripropylene glycol; a loss of 85 and 99 is common for NPG and 1,6-hexanediol (1,6-HD), respectively. The cyclic polyester dimers with 2 units of same diols and 2 units of same diacids showed characteristic ions at half of

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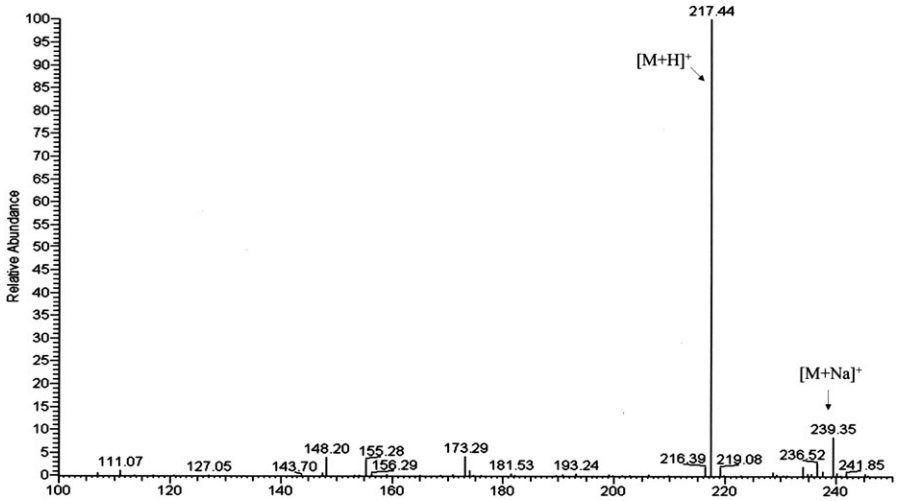


FIGURE 3 Electrospray ionization (ESI) mass spectrum of cyclic diethylene glycol-adipic acid diester (DEG-AA)

the mw plus one. Cyclic EG-AA-EG-AA (mw 344) showed a major fragment ion at 173; cyclic PG-AA-PG-AA (mw 372) showed 187; cyclic DEG-AA-DEG-AA (mw 432) showed 217; cyclic NPG-IPA-NPG-IPA (mw 468) showed 235; cyclic DEG-IPA-DEG-IPA (mw 472) showed 237; cyclic1,6-HD-PA-1,6-HD-PA (mw 496) showed 249; cyclic MP-diol-SeA-MP-diol-SeA (mw 512) showed 257; and cyclic NPG-SeA-NPG-SeA (mw 540) showed 271. Cyclic 1,4-BD-AA-1,4-BD-AA and cyclic MP-diol-AA-MP-diol-AA that both have mw 400 showed a major fragment ion at 201; cyclic NPG-AA-NPG-AA and cyclic EG-AzA-EG-AzA that both have mw 428 showed 215; cyclic EG-SeA-EG-SeA and cyclic 1,6-HD-AA-1,6-HD-AA that both have mw 456 showed 229; and cyclic EG-terephthalic acid (TPA)-EG-TPA and cyclic EG-IPA-EG-IPA that both have mw 384 showed 193.

Aromatic type cyclic oligoesters are mainly based on PA, IPA, and TPA. Terephthalic acid contributes to the linearity and crystallinity of the polymer chain, while IPA and PA tend to break up crystallinity and are incorporated to modulate the resulting rheological properties of the adhesive. The cyclic oligoester formed from TPA generally showed a fragment at 162 rather than 149. Isophthalic acid and PA-based cyclic oligoester isomers showed very similar fragmentation pattern, but they were distinguished by raw material formulation information and by GC retention time index (phthalates usually elute before isophthalates).

To elucidate identities of the cyclic oligoesters unequivocally, analysis with authentic standards is required to confirm their structures. We obtained authentic standards of cyclic DEG-AA, cyclic DEG-PA, and cyclic NPG-AA-NPG-AA standards isolated by vacuum distillation of polyester with subsequent purification by HPLC. The synthesis of cyclic oligoesters consisting of different glycols or diacids monomers is not easy because of the difficulties in controlling the complex products formation and purification.

3.2 | Determination of upper molecular weight limit for cyclic oligoesters migration through sealant film

The maximum mw of the cyclic oligoester migrants observed in this study was trimer range (<650 Da) for 25.4 μm LDPE sealant films and dimer range (<540 Da) for 76.2 μm CPP films. These 2 films represent extremes of sealant film thickness used for the construction of most food packaging laminates. The experimentally observed mw cut-offs are not attributed to the volatility limitations of GC-MS analysis since the samples were also analysed by HPLC-MS and higher mw cyclic oligoesters were typically not observed in extracts from migration studies. However, higher mw oligomers are in fact observed in the direct extracts of adhesive raw materials when analysed by HPLC-MS. Therefore, cyclic oligoesters with mw above dimer and trimer range are present in adhesive within laminates but is too high mw to migrate. Figure 4 is a GC-MS TIC chromatogram obtained by analyzing the 10% ETOH food-contact side extract from a polyethylene terephthalate/aluminium/nylon/CPP structure laminate with a MP-diol polyester-based PU adhesives applied between nylon and the 76.2 μm CPP web. Single-side cell migration testing was performed under FDA condition of Use A (2 h at 121°C) for intended high-temperature heat-sterilized food packaging applications. The high mw cyclic migrants observed in this analysis are dimer-type oligoesters including cyclic EG-IPA-EG-IPA, cyclic EG-IPA-MP-diol-IPA, cyclic EG-SeA-MP-diol-IPA, cyclic MP-diol-IPA-MP-diol-IPA, cyclic EG-SeA-MP-diol-SeA, cyclic MP-diol-IPA-MP-diol-SeA, and cyclic MP-diol-SeA-MP-diol-SeA, which is consistent with the full HPLC-MS analysis on the same laminate migrant extract that showed only up to the dimer-type mw range cyclic oligoesters (Figure 5), whereas the full HPLC-MS analysis of the direct extracts of MP-diol polyester raw material used to formulate the lamination adhesive showed even higher mw cyclic oligoester trimer, tetramer, and pentamer clusters (Figure 6). In contrast, same experiments on the 25.4 μm linear low-density polyethylene showed that the maximum mw cut-offs are trimer-type cyclic oligoesters, specifically cyclic NPG-AA-NPG-AA-NPG-AA with mw 642. In general, cyclic oligoesters that have mw above the trimer clusters do not migrate through all the laminate samples we analysed even under extreme temperatures such as retort condition.

3.3 | Cyclic oligoester extraction with different food simulant

In this study, 90% of the laminate samples were tested under FDA-specified condition of use with 10% ETOH, 50% ETOH, and/or 95%

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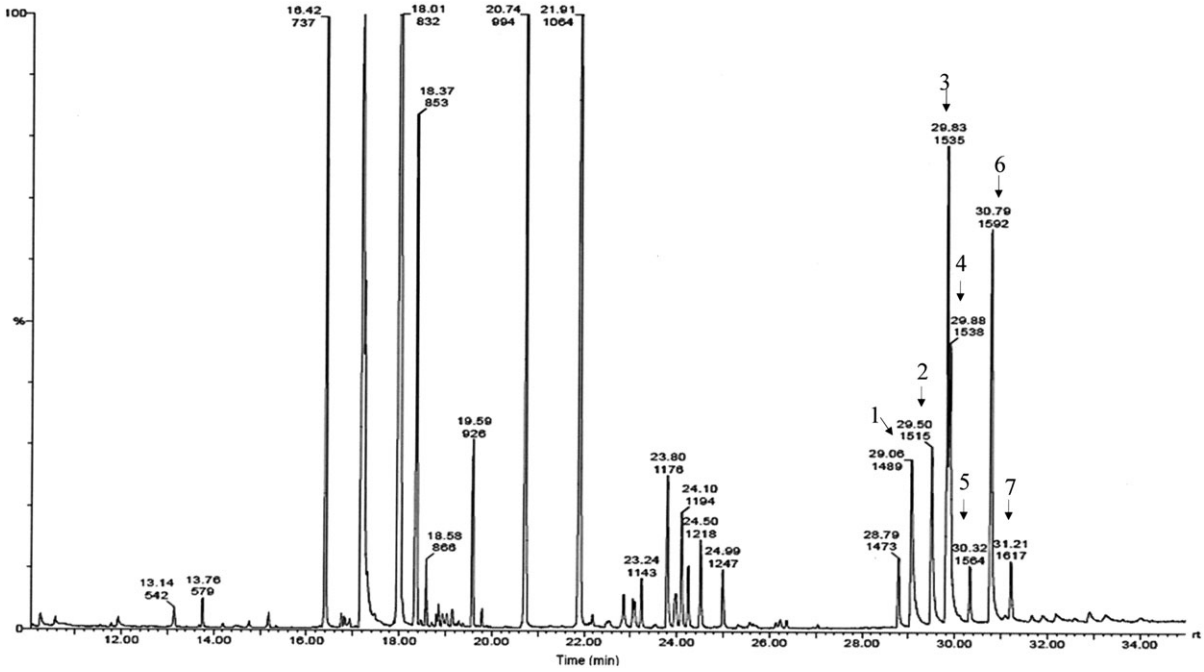


FIGURE 4 Gas chromatography-mass spectrometry (GC-MS) chromatogram of 10% ethanol food-contact side extract from a polyethylene terephthalate (PET)-aluminum-nylon-3mil cast polypropylene (CPP) laminate with MP-diol polyester based polyurethane (PU) adhesive (Peaks 1, 2, 3, 4, 5, 6 and 7 were identified as EG-IPA-EG-IPA, EG-IPA-MP-diol-IPA, EG-SeA-MP-diol-IPA, MP-diol-IPA-MP-diol-IPA, EG-SeA-MP-diol-SeA, MP-diol-IPA-MP-diol-SeA, and MP-diol-SeA-MP-diol-SeA)

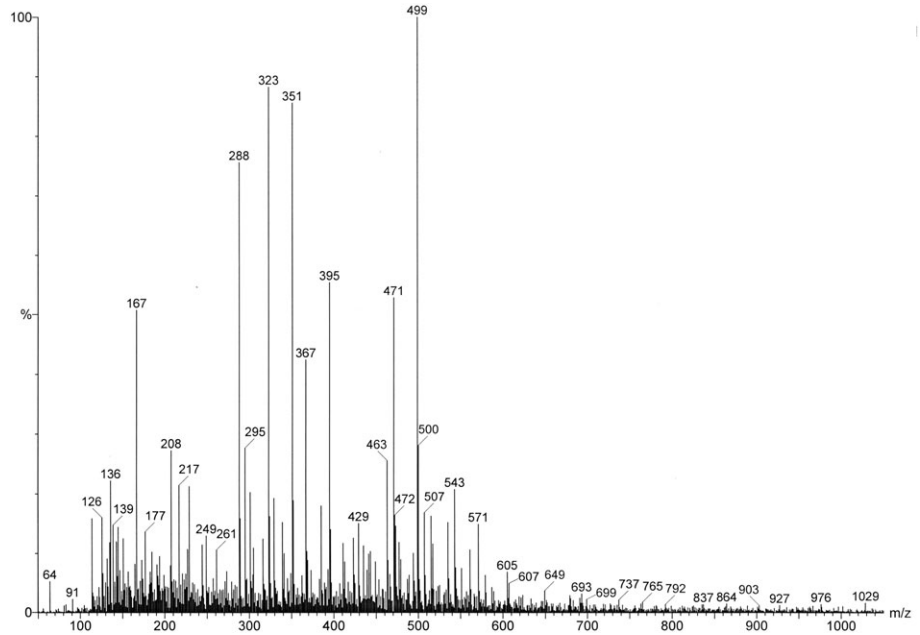


FIGURE 5 Liquid chromatography-mass spectrometry (LC-MS) full spectra of 10% ethanol food-contact side extract from a polyethylene terephthalate (PET)-aluminium-nylon 3mil cast polypropylene (CPP) laminate with MP-diol polyester based polyurethane (PU) adhesive

ETOH as food simulants because most sample suppliers were mainly in the US food packaging market. Acetic acid (3%) was only used for acidic food applications (pH < 4.5) in EU. In United States, the FDA guidance for aqueous-acidic food simulant is 10% ETOH.[14] A recent study indicates that cyclic oligoesters can break down to linear polyester oligomers in 3% acetic acid food simulant.[20] Nevertheless, in all 5 laminate samples that we tested with 3% acetic acid, cyclic oligoester migrants were generally in low concentrations and linear polyester oligomers were not observed in the GC-MS analyses (possibly due to loss of volatility and greater hydrogen-bonding affinity which tends to broaden the GC peak shape and increase detection threshold). We spiked 10% ETOH, 3% acetic acid, and 95% ETOH with cyclic DEG-AA standard at concentrations ranging from 0.1 to 1.0 ppm w/v) to estimate the recovery in these 3 simulants. Using the described methylene chloride extraction protocol for GC-MS analysis, the recovery from 10% ETOH, 95% ETOH, and 3% acetic acid was 98%, 88%, and

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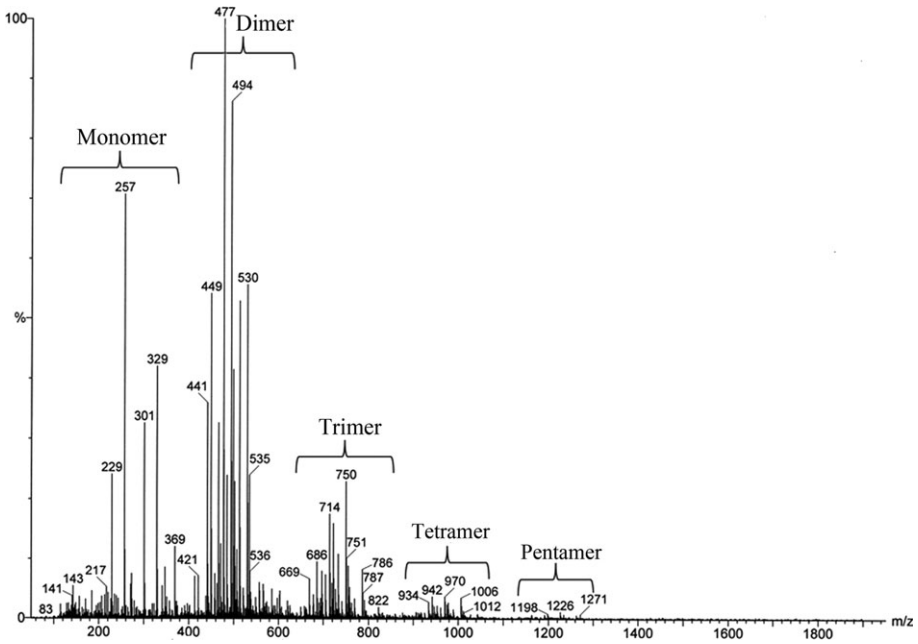


FIGURE 6 Liquid chromatography-mass spectrometry (LC-MS) full spectra of hexane extract of MP-diol polyester raw material used in the polyethylene terephthalate (PET)-aluminum-nylon-3mil cast polypropylene (CPP) laminate (for determination of high molecular weight (mw) cyclic oligoesters)

81%, respectively. The lower recovery associated with the 3% acetic acid may be a consequence of ring hydrolysis.

Our lab uses validated methods to analyse diisocyanate monomers, ethanol reaction products of isocyanates that form in ethanolic food simulants (diethyl carbamates), and hydrolysis products of isocyanates (the corresponding diamines), as they are migrants of high concern. However, manufacturers nowadays have improved their adhesive design, such that these compounds are rarely observed and if detected are at exceedingly trace level concentrations (typically low to sub-ppb). In contrast, cyclic oligoesters are observed in nearly all migration studies performed on laminates made with polyester urethane based adhesive systems.

3.4 | Evaluation of the occurrence and migration level of cyclic oligoesters

The frequency of occurrence of all cyclic oligoester migrants with their individual estimated maximum migration levels from the laminates was compiled and presented in Table 2. The absolute frequency of occurrence for each cyclic oligoester migrant is based on recording the number of laminates that contains that cyclic compound. The relative frequency of occurrence of each cyclic oligoester migrant is based on normalizing the absolute frequency by the total number of laminates evaluated.

As can be observed (Table 2), cyclic DEG-AA is the most prevalent short-chain cyclic oligoester migrant with a relative frequency of occurrence corresponding to 0.669 and a maximum migration level of 159.31 $\mu g/dm^2$. Moreover, cyclic DEG-AA-DEG-AA is the most prevalent dimer-type cyclic oligoester migrant with a relative frequency of occurrence corresponding to 0.236 displaying a maximum migration level of 116.85 $\mu g/dm^2$. Cyclic DEG-IPA is the most prevalent aromatic cyclic oligoester migrant; its relative frequency of occurrence is 0.127 with a maximum migration level of 3683.99 $\mu g/dm^2$. It is noteworthy that the laminate structure with such high migration concentration of cyclic DEG-IPA was the subject of an off-flavour complaint (bitter off-flavour tainting) of confectionary candies stored therein. These 3 prevalent migrants are all based on DEG, which is the common raw material of PU adhesives because of its relative low cost and good functionality.

Neopentyl glycol-based cyclic oligoester migrants are also frequently found in the industry laminates studied, which is to be expected, because NPG is a versatile raw material used in the production of PU adhesives, given the contribution of the 2 methyl groups on the alpha carbon atom that impart improved chemical and thermal stability. Cyclic NPG-AA is the second most prevalent cyclic oligoester migrant with a relative frequency of occurrence of 0.335, and its maximum migration level is 149.56 $\mu g/dm^2$. Cyclic NPG-AA-NPG-AA is the second most prevalent dimer cyclic oligoester migrant with a relative frequency of occurrence estimated to 0.192 and a maximum migration level of 224.86 $\mu g/dm^2$.

Migration is a complex process driven by molecular diffusion directed by both kinetic and thermodynamic control of the mass transfer. The frequency of the occurrence of the migrants, migration concentration, and the rate of their migration are tightly depended on factors such as adhesive formulation, coating weight, efficiency of cure, and type plus thickness of sealant films. In addition, the physicochemical properties of the oligomers such as molecular size, polarity, structure, mw, and vapour pressure are also determining factors that influence their degree of mobility into the food simulants. Moreover, the rate of their diffusion is also dependent on the specific conditions of the migration tests such as time and temperature during extraction. This indicates that migrants could be produced from the packaging materials or as a result of the degradation process causing by sever treatment conditions, namely, processing conditions, storage time, and temperature. Frequency of detected cyclic oligoesters is also directly related to the widespread use of particular polyester types in PU adhesive formulations and their applications for food packaging

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TABLE 2 Occurrence of cyclic oligoester migrants in laminates

Name[a]	Migrant Concentration Range[b] (μg/dm²)	Absolute Frequency of Occurrence	Relative Frequency of Occurrence
Cyclic DEG-AA	0.00[c]-159.31	359	0.669
Cyclic NPG-AA	0.01-149.56	180	0.335
Cyclic 1,6-HD-AA	0.00[c]-32.34	149	0.277
Cyclic DEG-AA-DEG-AA	0.00[c]-116.85	127	0.236
Cyclic 1,4-BD-AA	0.01-11.52	116	0.216
Cyclic NPG-AA-NPG-AA	0.01-224.86	103	0.192
Cyclic EG-AA	0.00[c]-14.95	101	0.188
Cyclic DEG-IPA	0.01-3683.99	68	0.127
Cyclic 1,4-BD-AA-1,4-BD-AA	0.02-7.50	53	0.099
Cyclic 1,6-HD-AA-1,6-HD-AA	0.01-13.48	43	0.080
Cyclic NPG-AzA	0.29-4.75	27	0.050
Cyclic NPG-SeA	0.05-24.69	24	0.045
Cyclic DEG-PA	0.01-125.01	15	0.028
Cyclic EG-AA- EG-AA	0.08-6.82	14	0.026
Cyclic DEG-IPA-DEG-AA	0.64-40.84	14	0.026
Cyclic EG-AzA	0.50-2.79	13	0.024
Cyclic NPG-AA-NPG-AA-NPG-AA	0.02-3.65	13	0.024
Cyclic PG-AA-PG-AA	0.45-1.68	13	0.024
Cyclic NPG-AA-1,6-HD-AA	1.62-11.31	13	0.024
Cyclic 1,6-HD-AA-PG-AA	0.41-7.12	13	0.024
Cyclic NPG-AA-PG-AA	1.18-3.92	12	0.022
Cyclic PG-AA-PG-IPA	0.21-0.60	11	0.020
Cyclic PG-AA-DEG-IPA	0.19-0.38	11	0.020
Cyclic EG-IPA-EG-IPA	16.60-71.18	9	0.017
Cyclic DEG-IPA-DEG-IPA	1.23-74.58	9	0.017
Cyclic DEG-AA-EG-AA	0.42-12.70	9	0.017
Cyclic EG-SeA-NPG-IPA	6.78-66.75	7	0.013
Cyclic NPG-IPA-NPG-SeA	1.67-89.03	7	0.013
Cyclic NPG-AA-NPG-IPA	0.66-25.74	7	0.013
Cyclic EG-SeA	0.58-17.55	7	0.013
Cyclic EG-SeA-DEG-SeA	11.90-24.69	6	0.011
Cyclic NPG-SeA-NPG-SeA	0.12-29.42	6	0.011
Cyclic NPG-IPA-NPG-IPA	0.06-4.84	5	0.009
Cyclic DEG-AA-EG-IPA	29.52-52.96	4	0.007
Cyclic 1,6-HD-PA	21.56-60.71	3	0.006
Cyclic NPG-AA-NPG-SuA	0.67-1.96	3	0.006
Cyclic EG-IPA-EG-AA	19.42-23.08	3	0.006
Cyclic DEG-IPA-EG-IPA	27.01-106.45	3	0.006
Cyclic NPG-SuA	0.03-0.03	2	0.004
Cyclic EG-TPA-EG-TPA	4.08-167.95	2	0.004
Cyclic EG-SuA	0.14-0.25	2	0.004
Cyclic EG-AzA 2 + 2	1.60-4.62	2	0.004
Cyclic MP-diol-SeA	33.88	1	0.002
Cyclic EG-IPA-NPG-IPA	2.20	1	0.002
Cyclic MP-diol-IPA-EG-IPA	2.24	1	0.002
Cyclic MP-diol-IPA -MP-diol-IPA	4.20	1	0.002
Cyclic EG-SeA-MP-diol-IPA	8.22	1	0.002
Cyclic MP-diol-SeA-MP-diol-IPA	4.91	1	0.002
Cyclic EG-SeA-MP-diol-SeA	0.59	1	0.002
Cyclic EG-SeA-NPG-SeA	0.77	1	0.002

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TABLE 2 (Continued)

Name[a]	Migrant Concentration Range[b] (μg/dm^2)	Absolute Frequency of Occurrence	Relative Frequency of Occurrence
Cyclic MP-diol-SeA-MP-diol-SeA	0.67	1	0.002
Cyclic 1,6-HD-PA-1,6-HD-PA	12.00	1	0.002
Cyclic MP-diol-AA	2.84	1	0.002
Cyclic MP-diol-AA-MP-diol-AA	9.11	1	0.002
Cyclic EG-SeA-EG-SeA	4.90	1	0.002
Cyclic EG-SeA-EG-IPA	29.38	1	0.002

[a]EG, ethylene glycol; 1,4-BD, 1,4 butanediol; MP-diol, 2-methyl-1, 3-propanediol; DEG, diethylene glycol; 1,6-HD, 1,6 hexanediol; NPG, neopentyl glycol; AA, adipic acid; AzA, azelaic acid; SeA, sebacic acid; SuA, suberic acid; PA, phthalic acid; IPA, isophthalic acid; TPA, terephthalic acid.

[b]Minimum to maximum migrant concentration in microgram per square decimetre of surface area exposed to extraction is estimated based on the peak area ratio to internal standard.

[c]Minimum concentration less than 0.005 μg/dm[b] (5 ng/dm^2).

are restricted by regulations. The polyester monomers specified in food contact regulations are the ones most commonly observed.

4 | CONCLUSION

Based on our migration testing on 537 commercial and/or developmental laminate samples, 56 short-chain cyclic oligoesters were identified. All detected migrants can occur at high or low concentration levels depending on their physicochemical properties and their initial concentration in the packaging material. The results indicate that DEG, NPG, AA, and IPA-based ester migrants have a relative higher occurrence rate that can be attributed to their extensive usage as laminating adhesive raw materials.

The results of this study regarding cyclic oligoesters, including the molecular structure, migration concentration range, and frequency occurrence, could be of great value for future regulatory risk assessment. The mass spectra of all 106 identified cyclic oligoesters, which migrate or potentially migrate, can provide important database for the food packaging industry to establish a systematic quality control of the food packaging materials.

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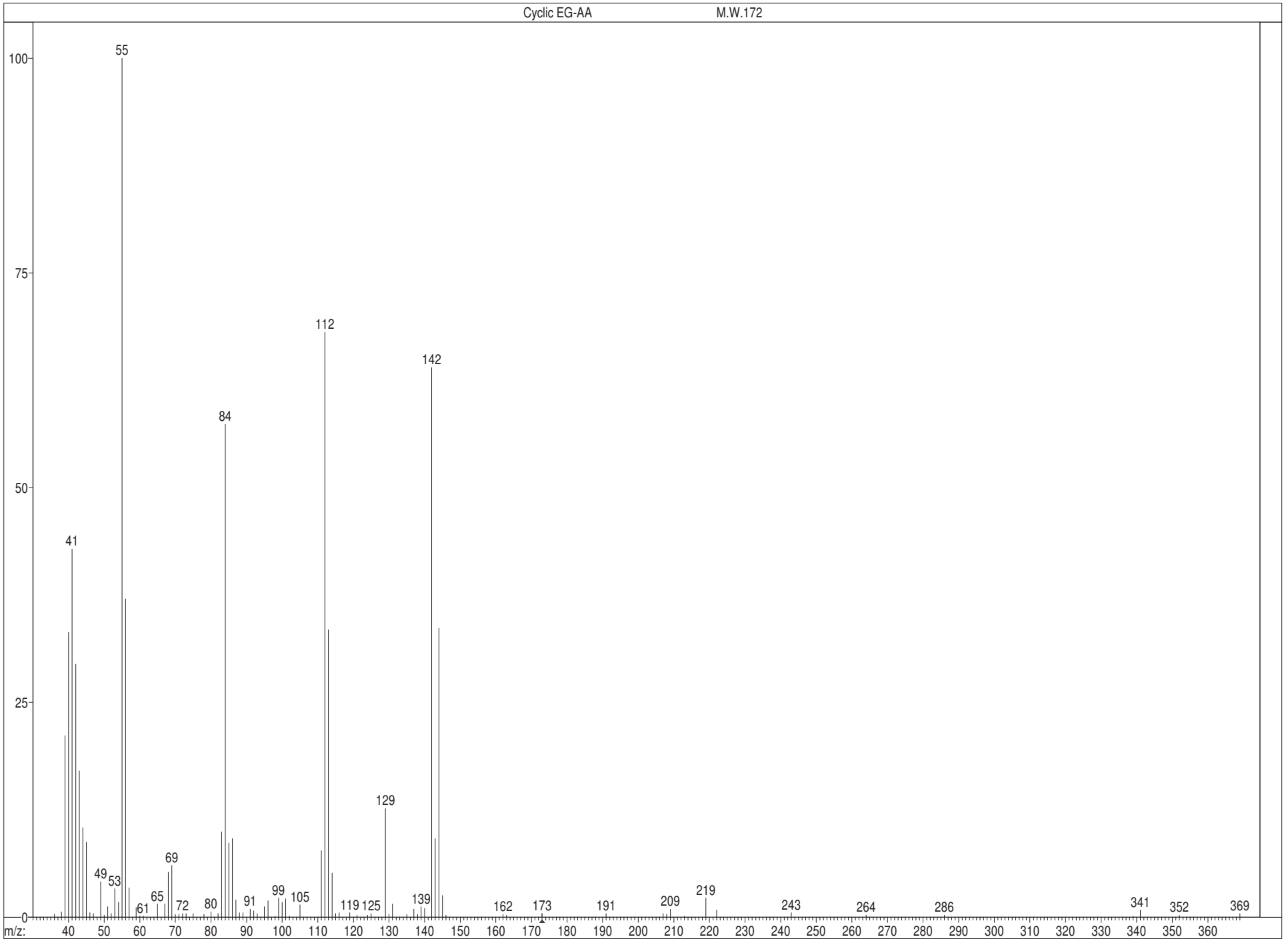
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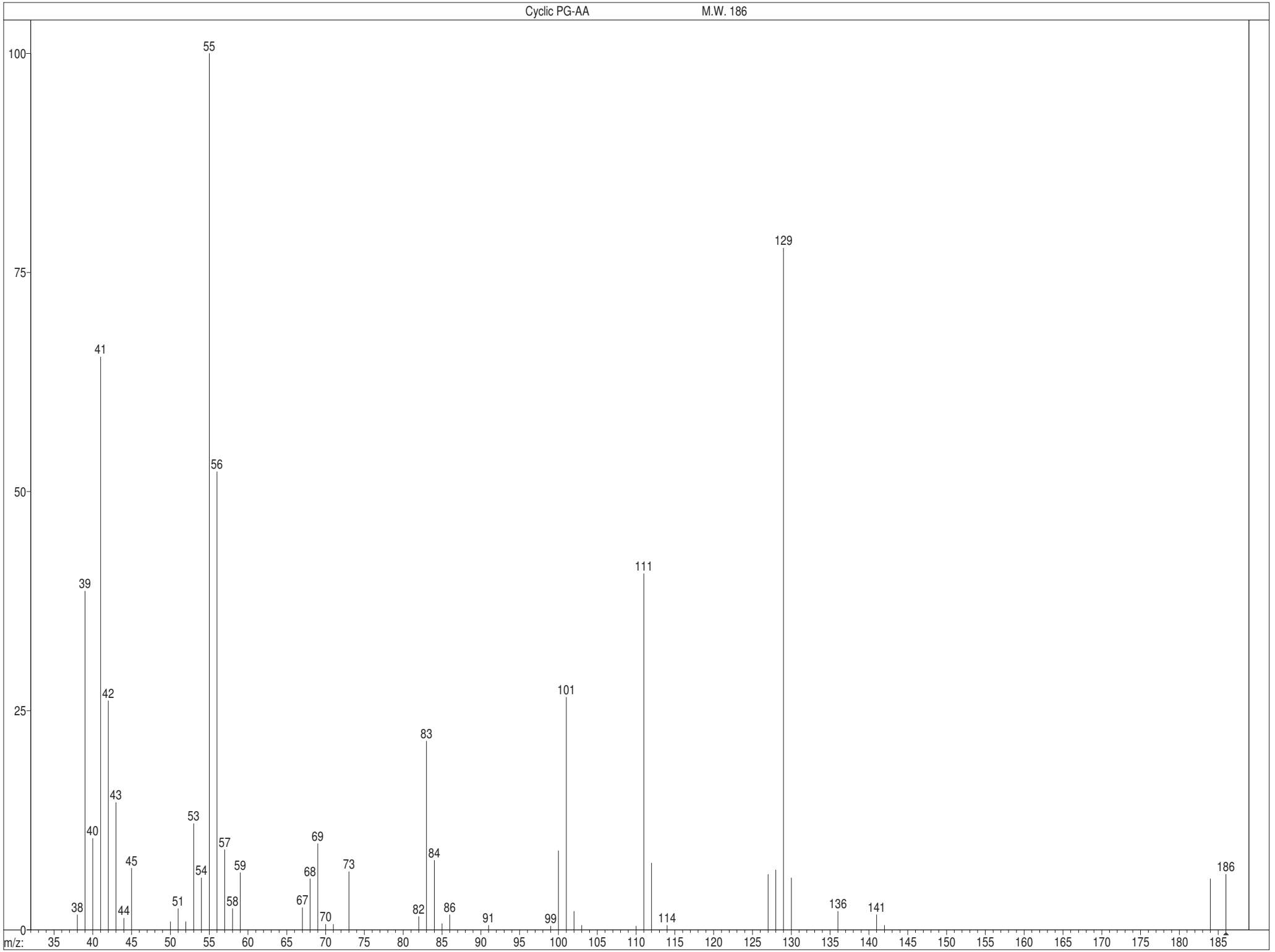
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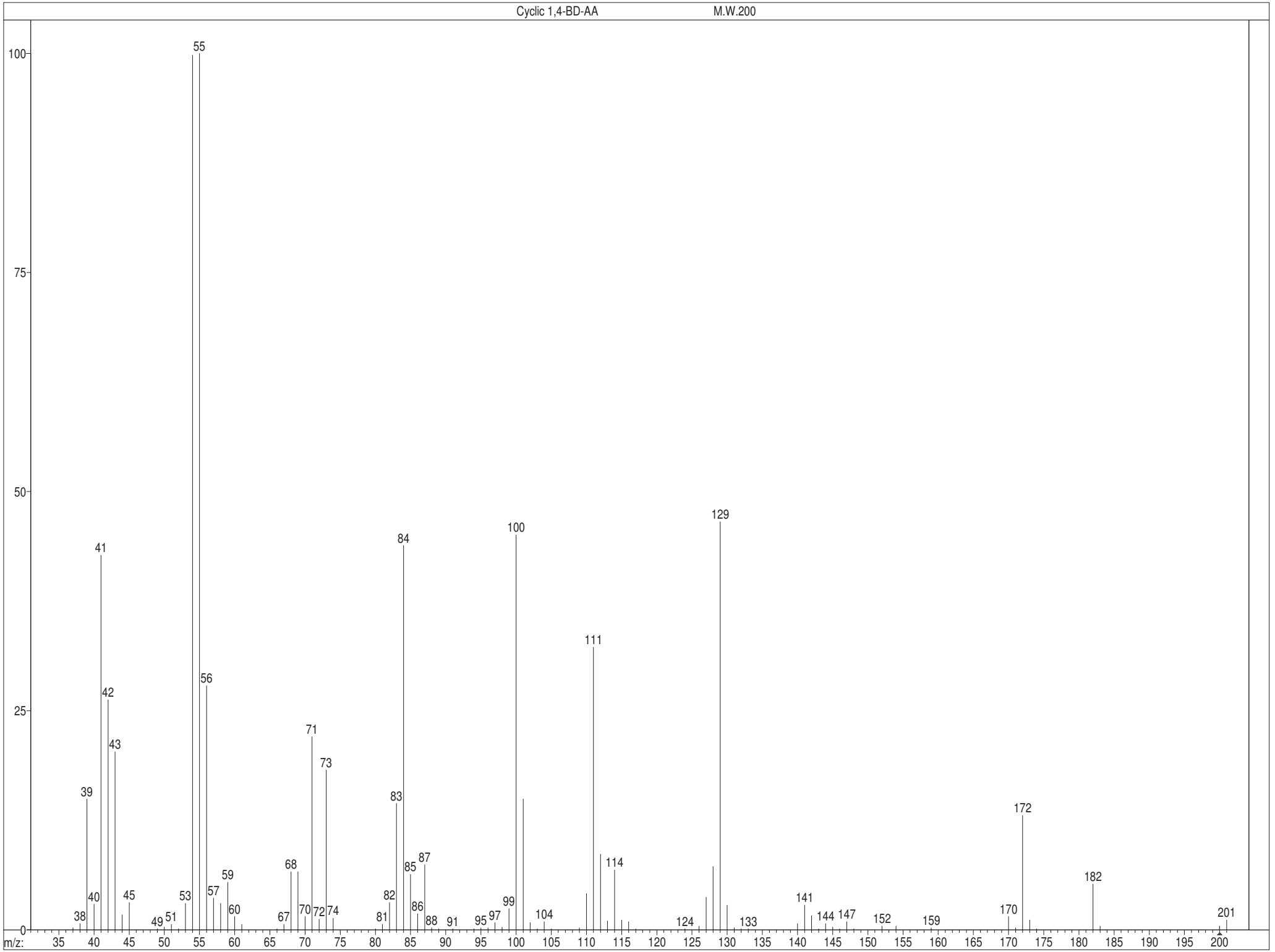


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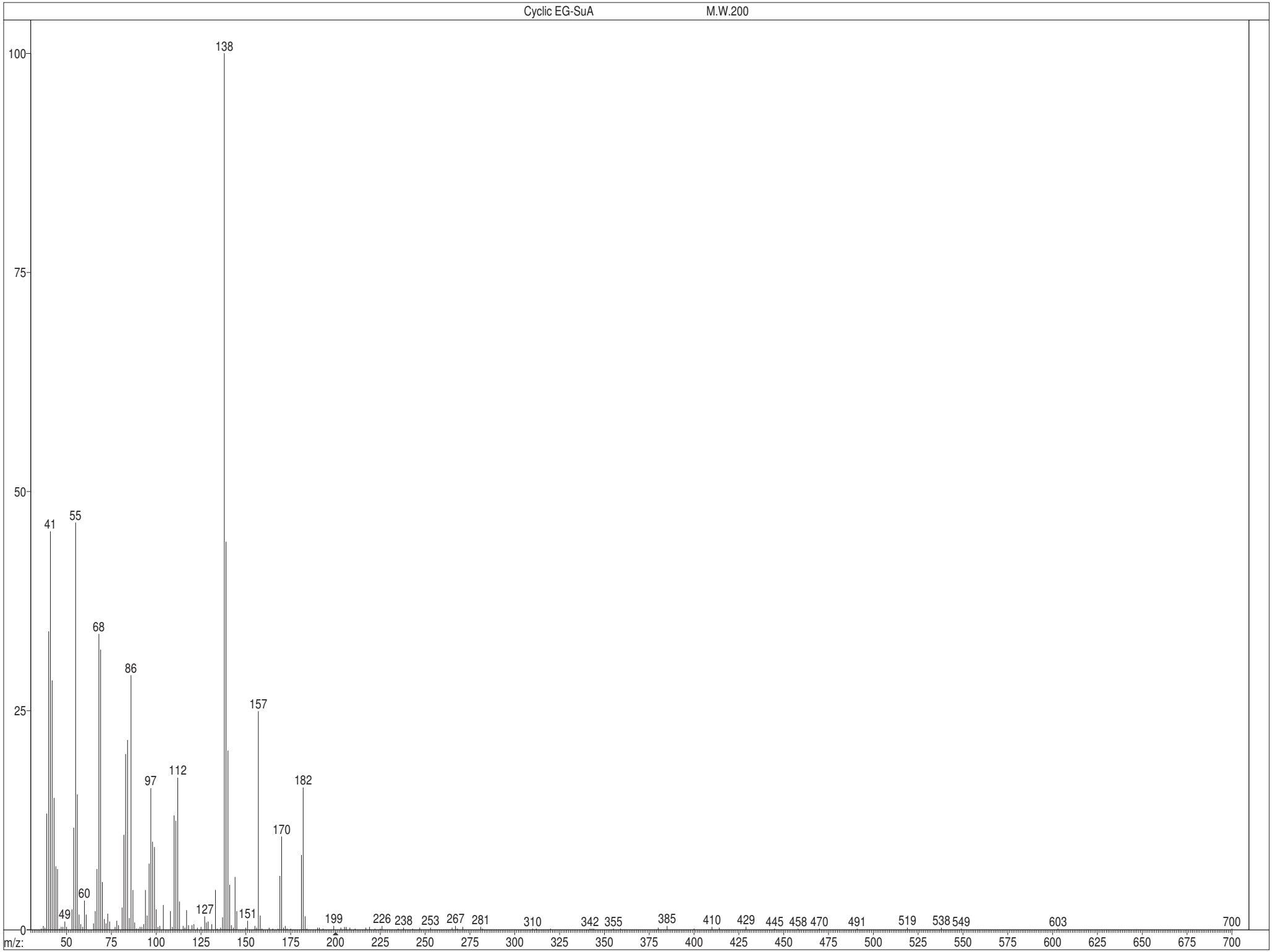
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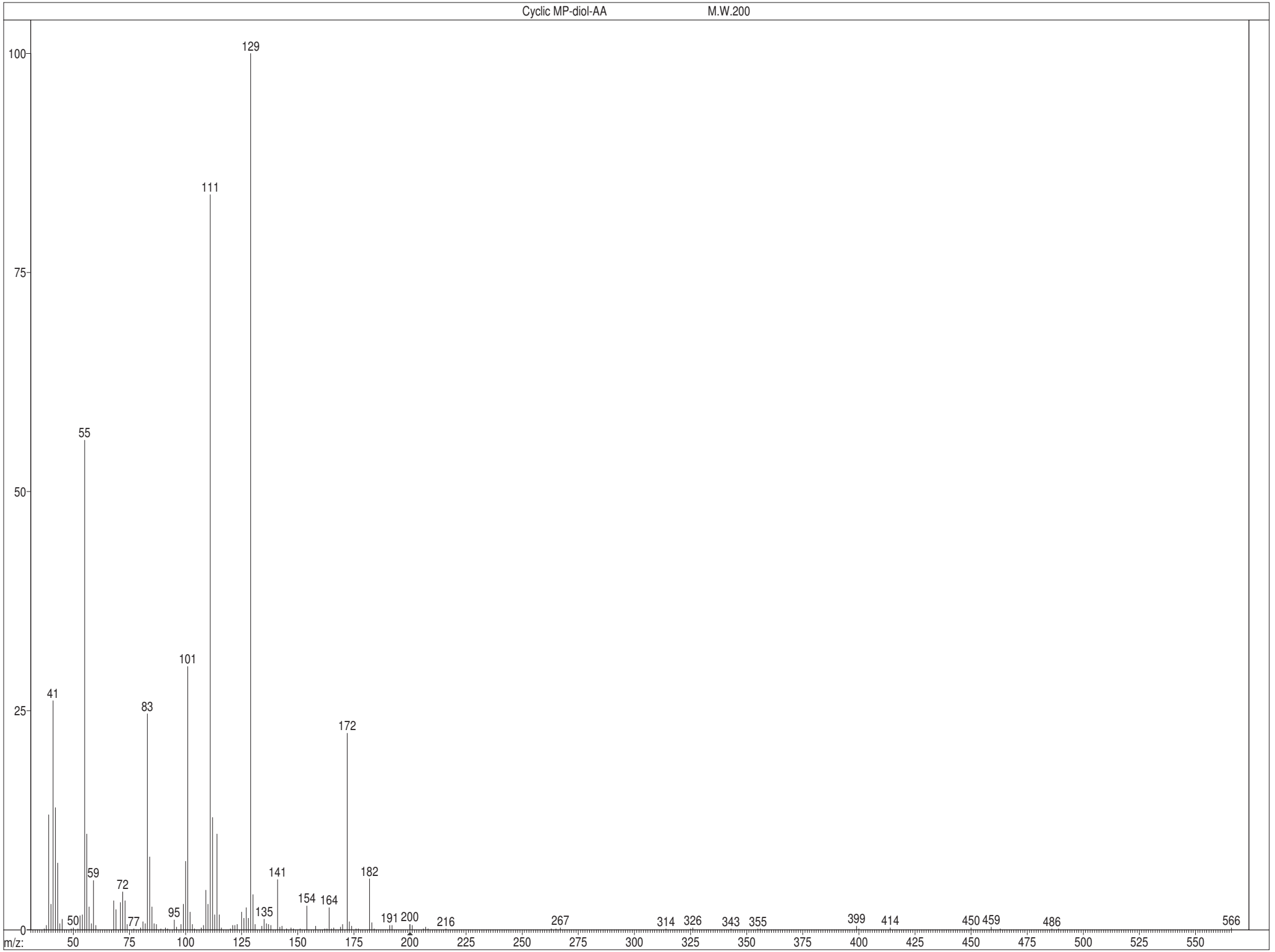


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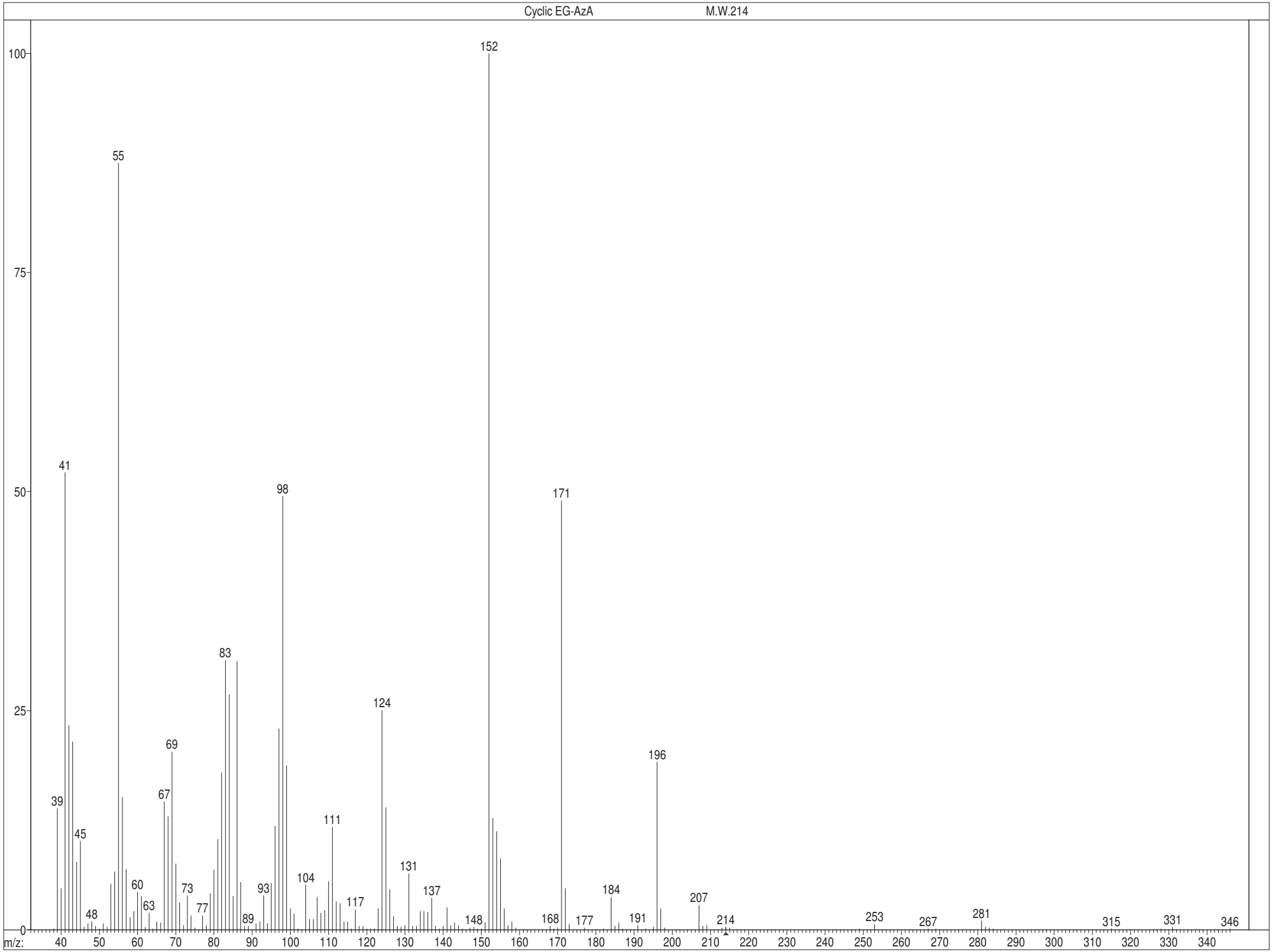
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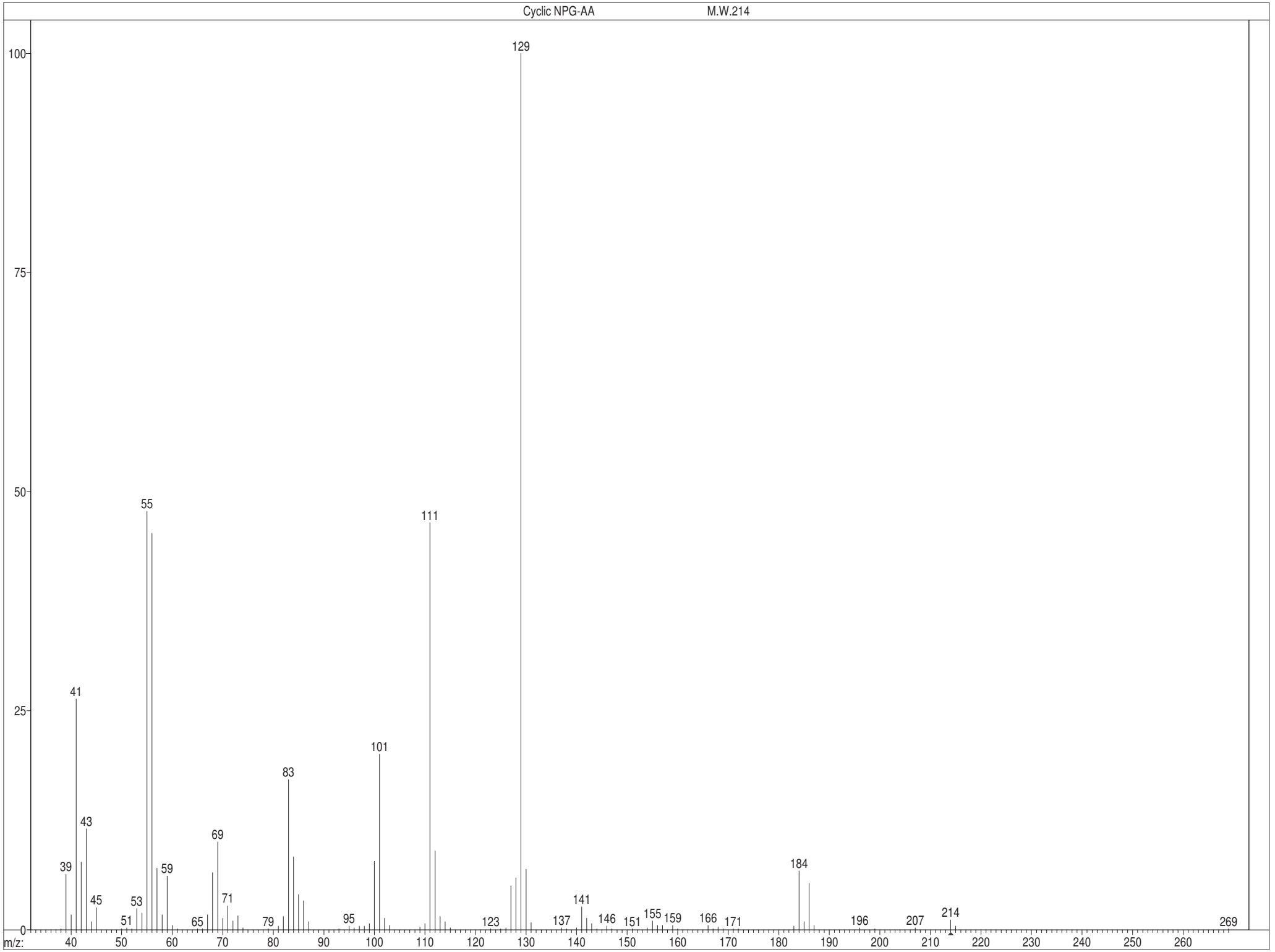
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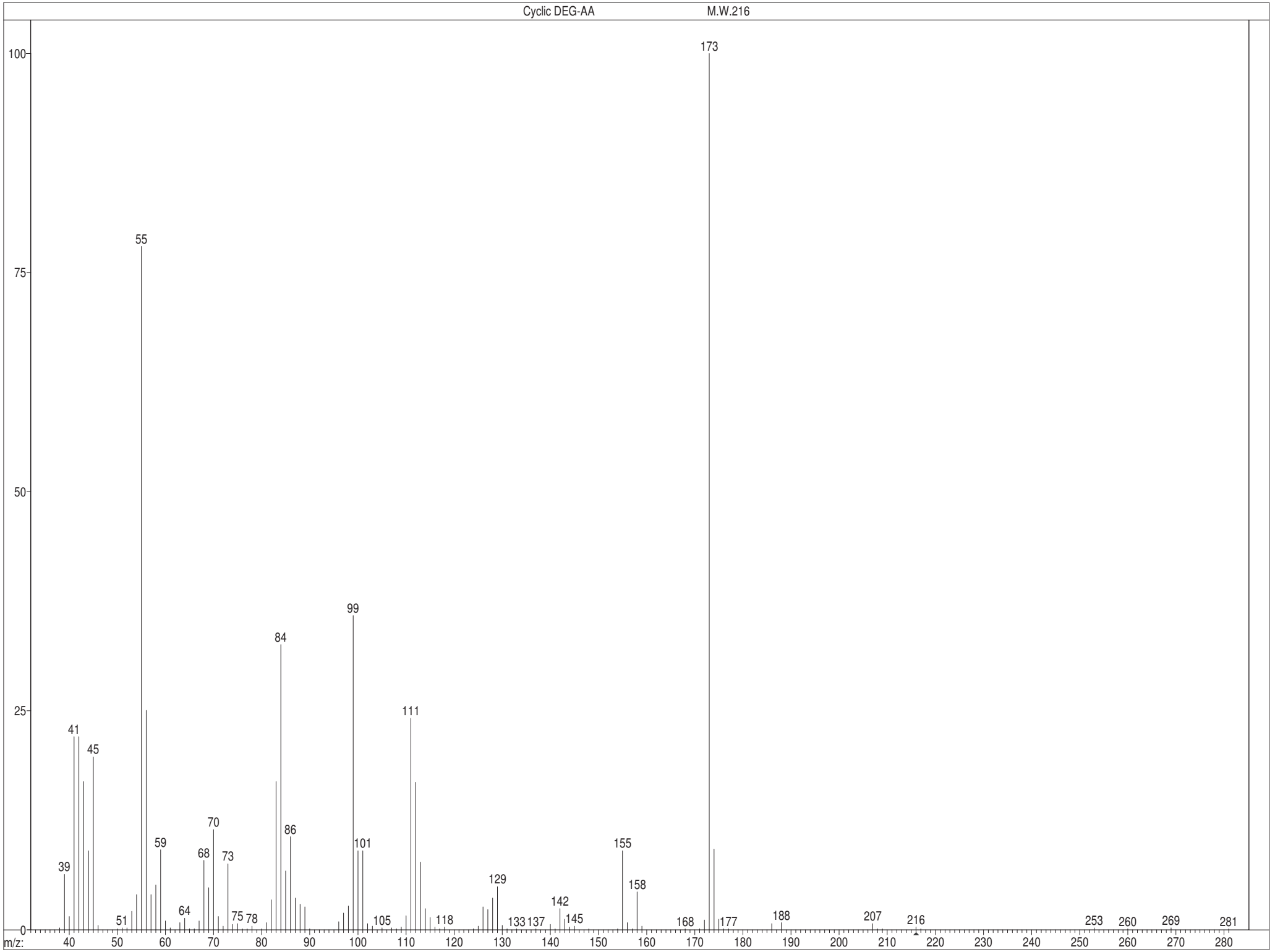
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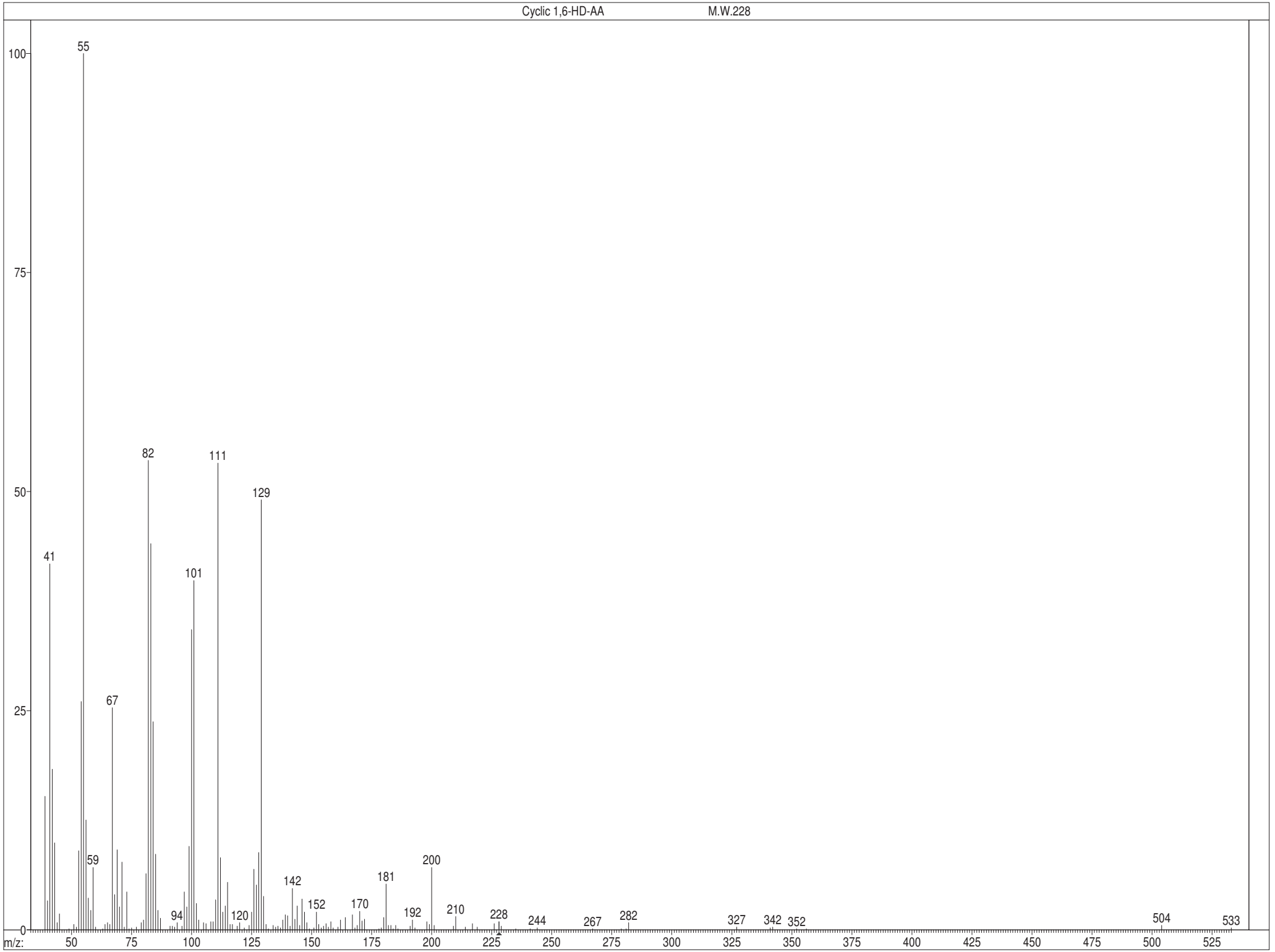
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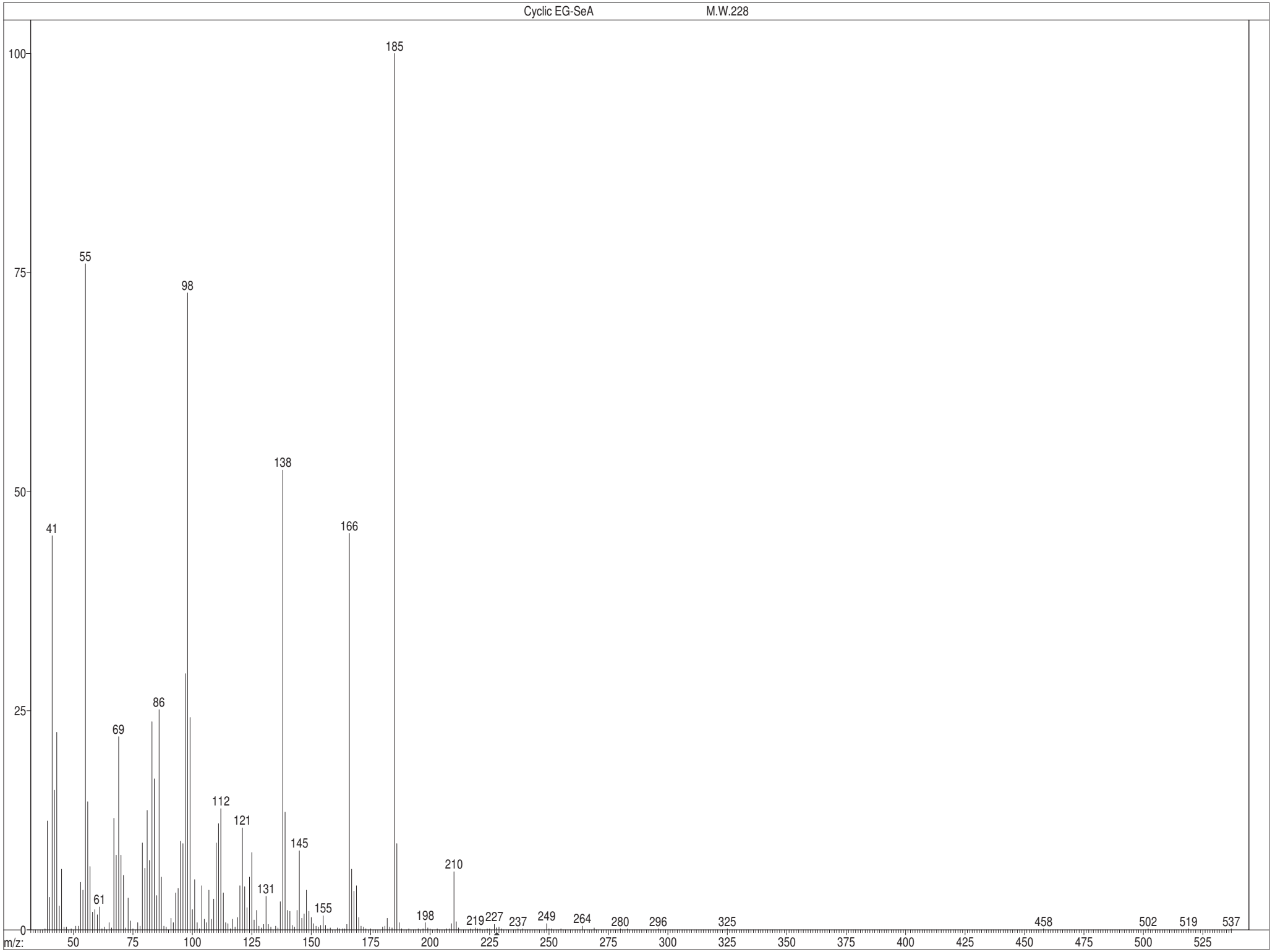


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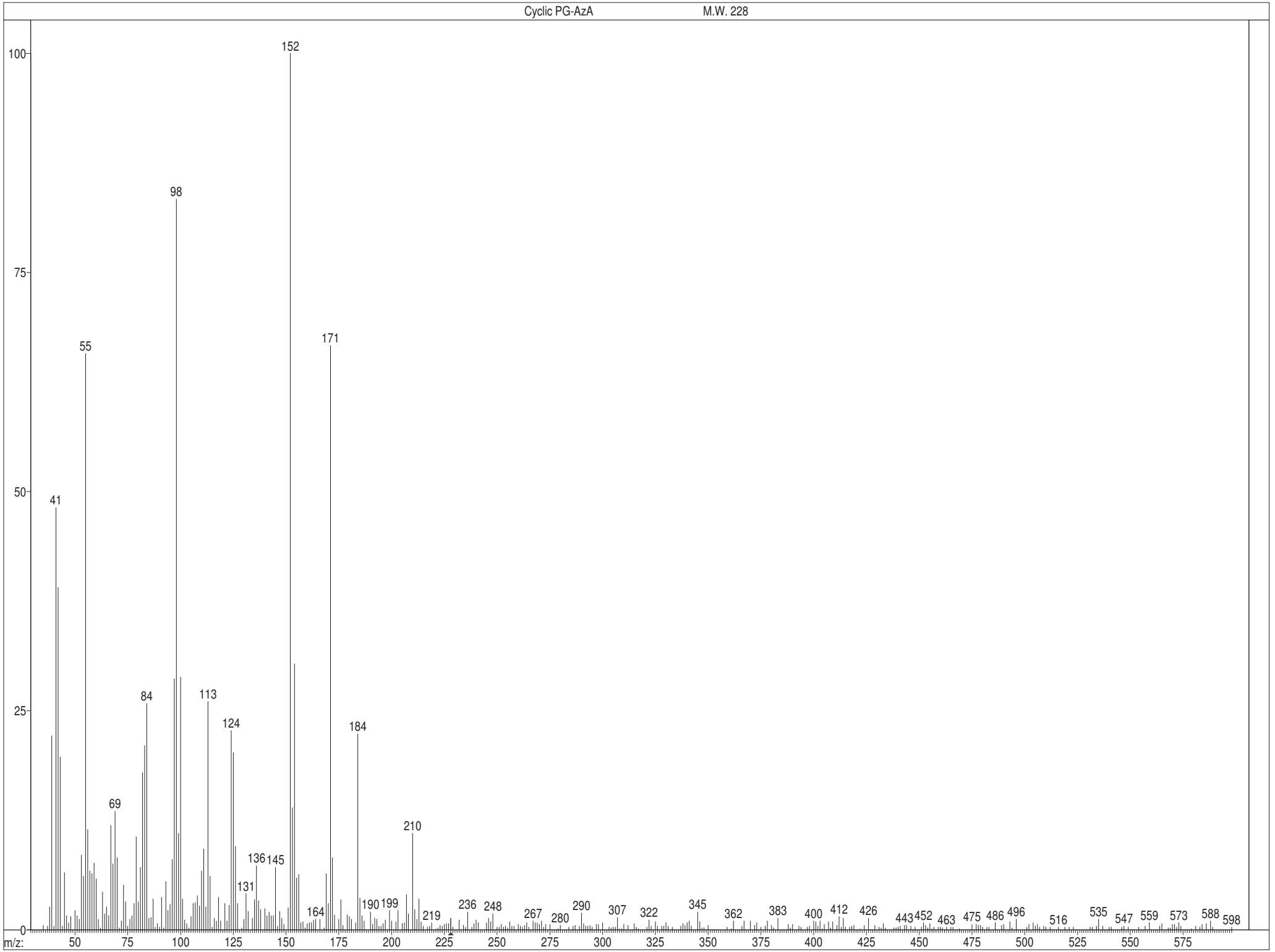


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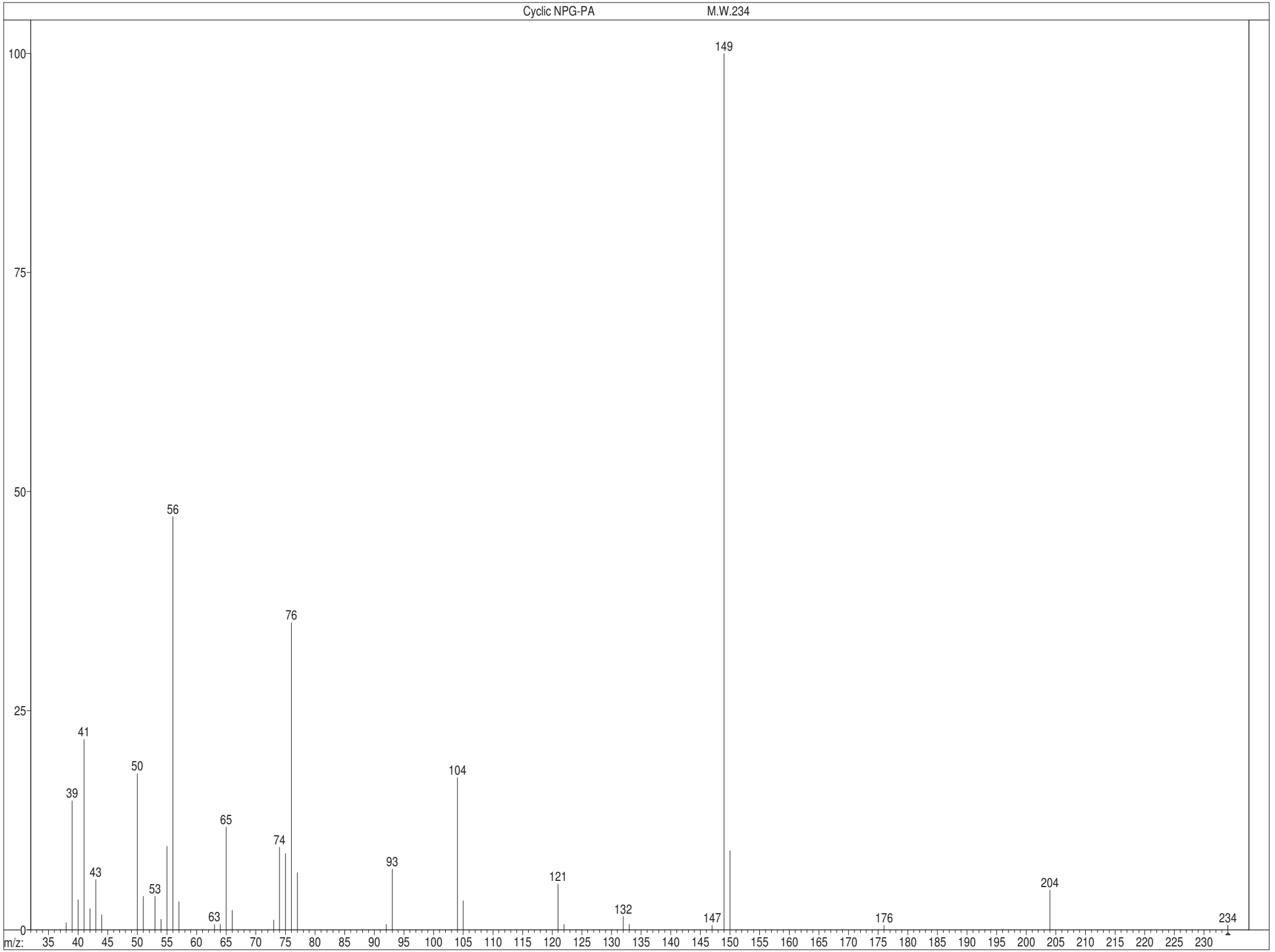


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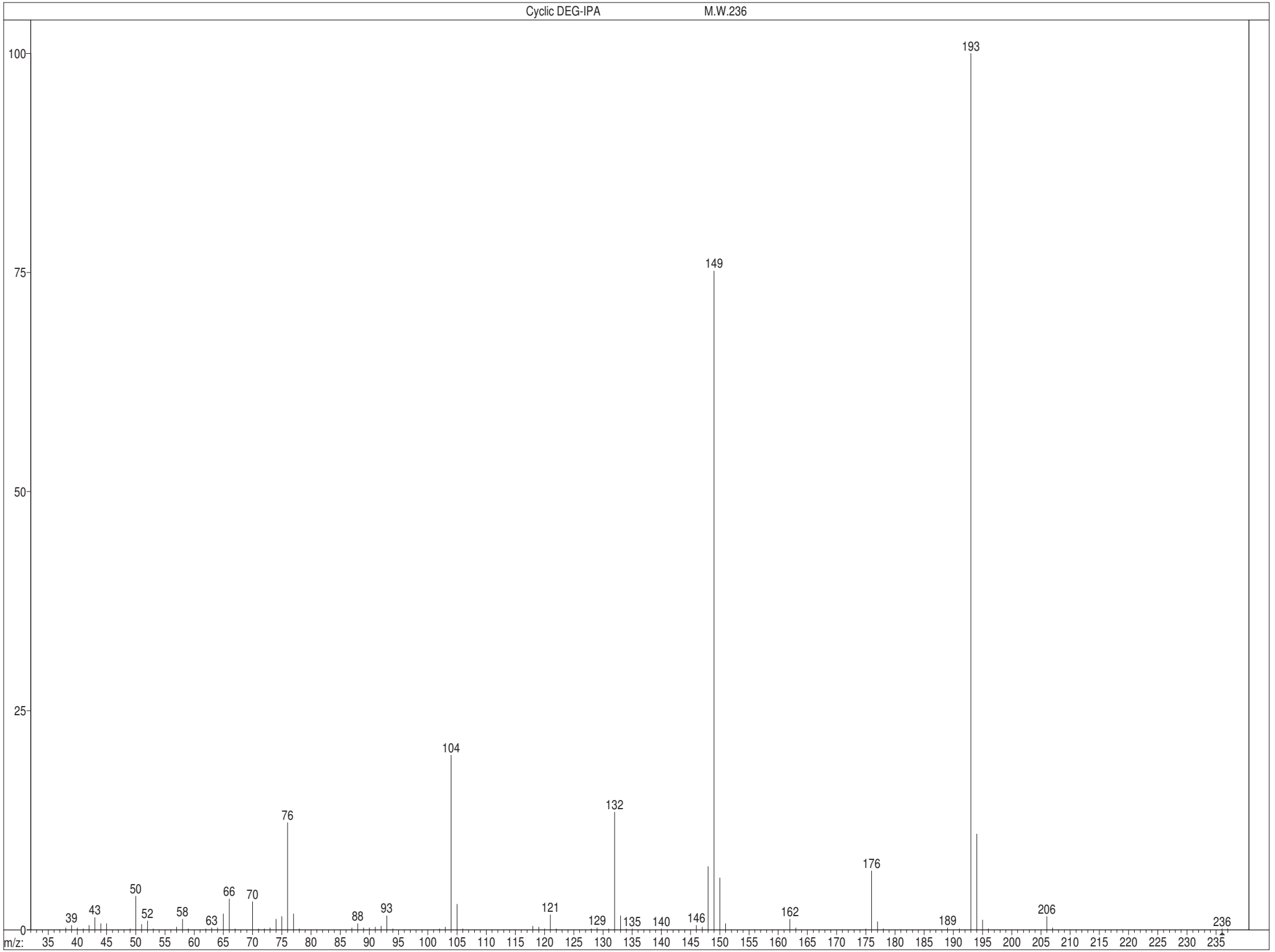


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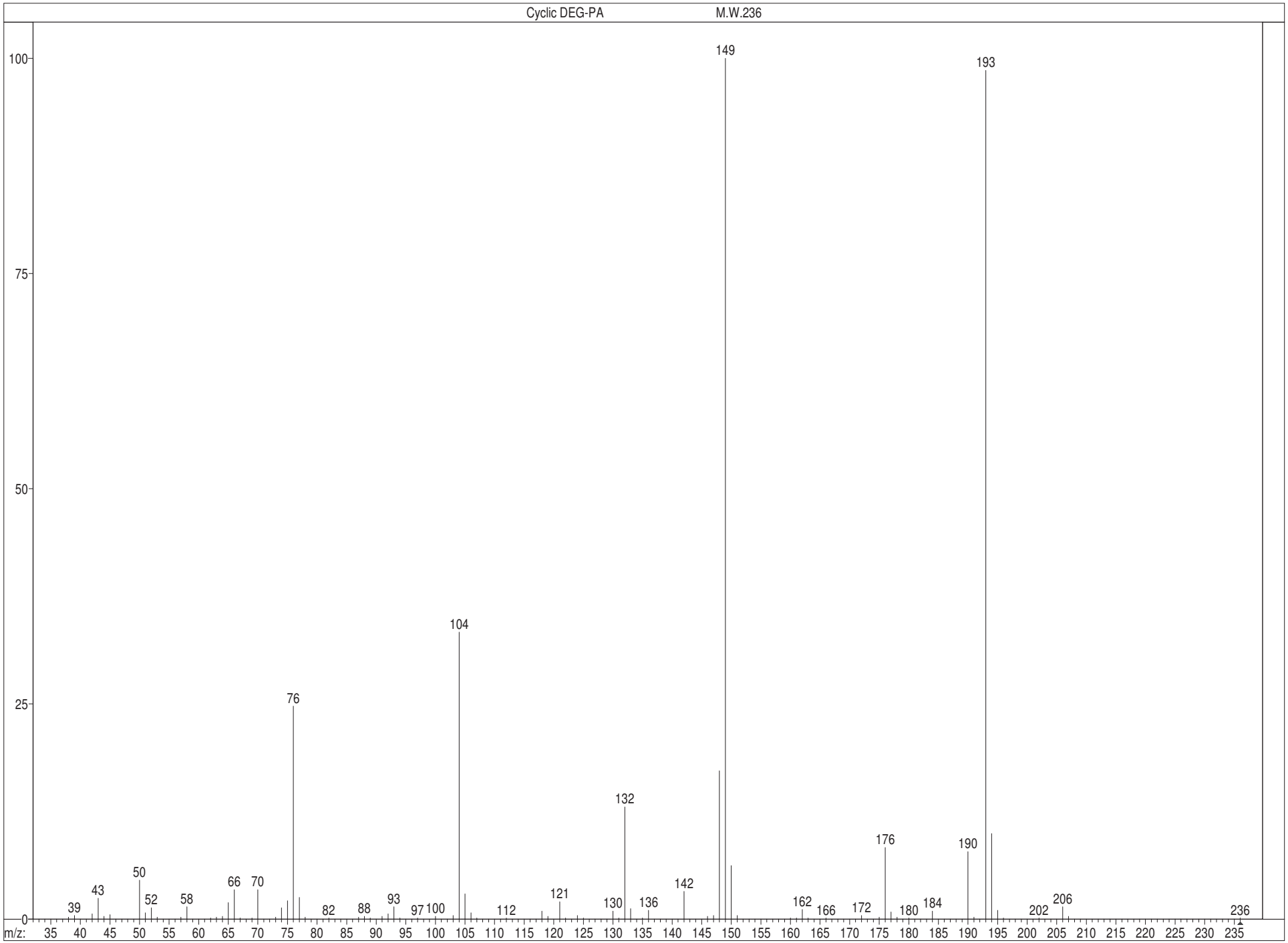
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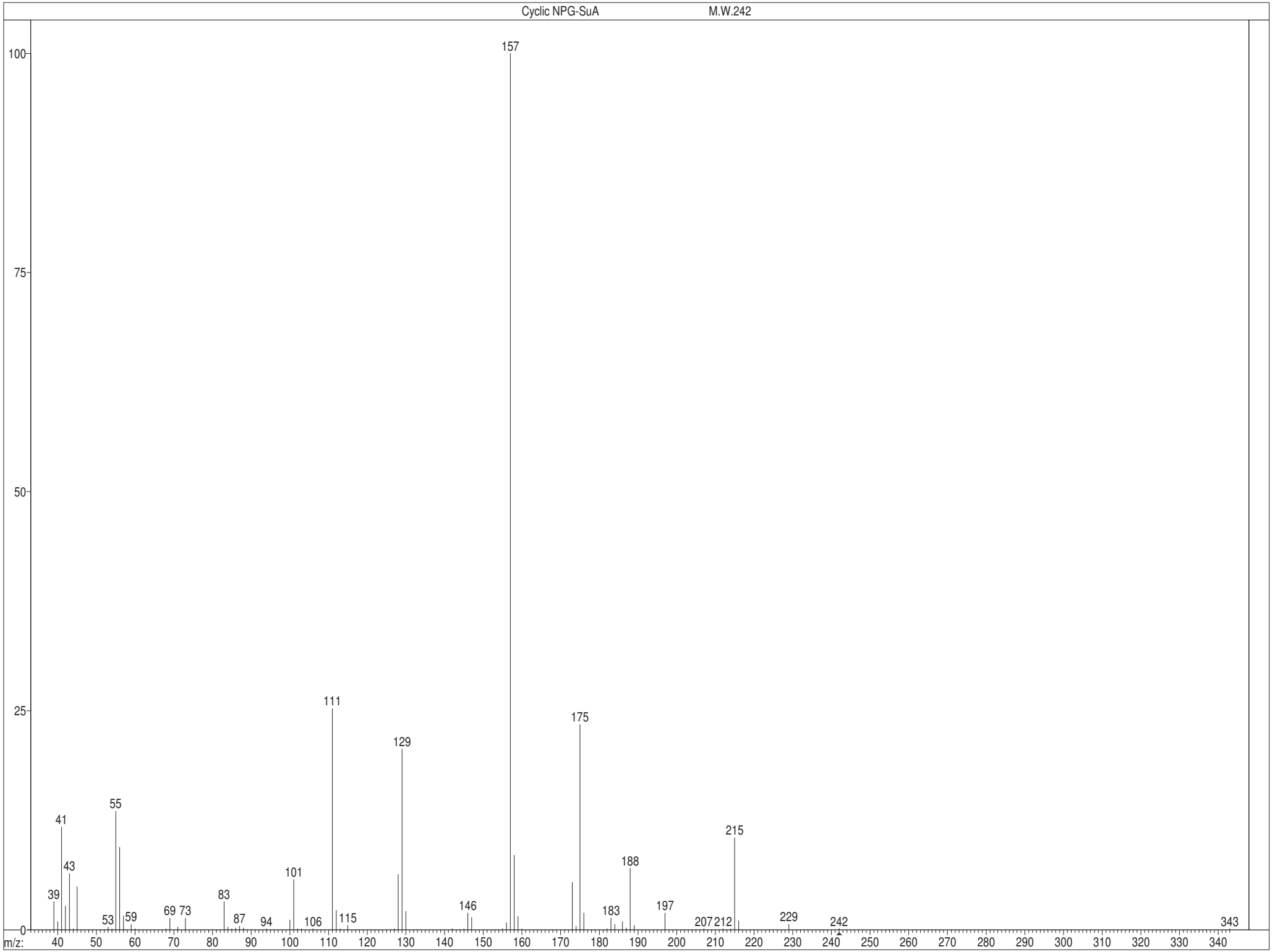
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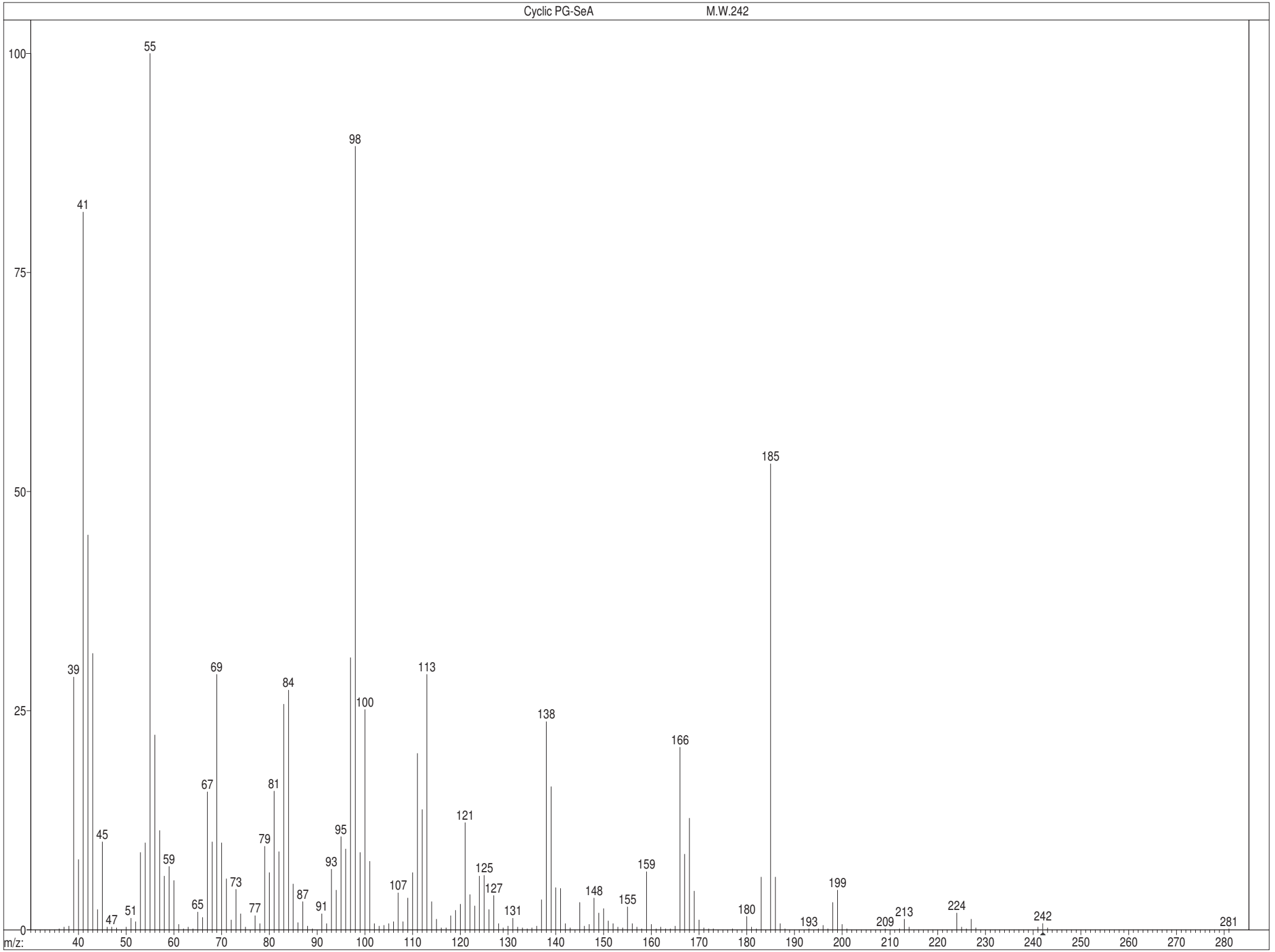
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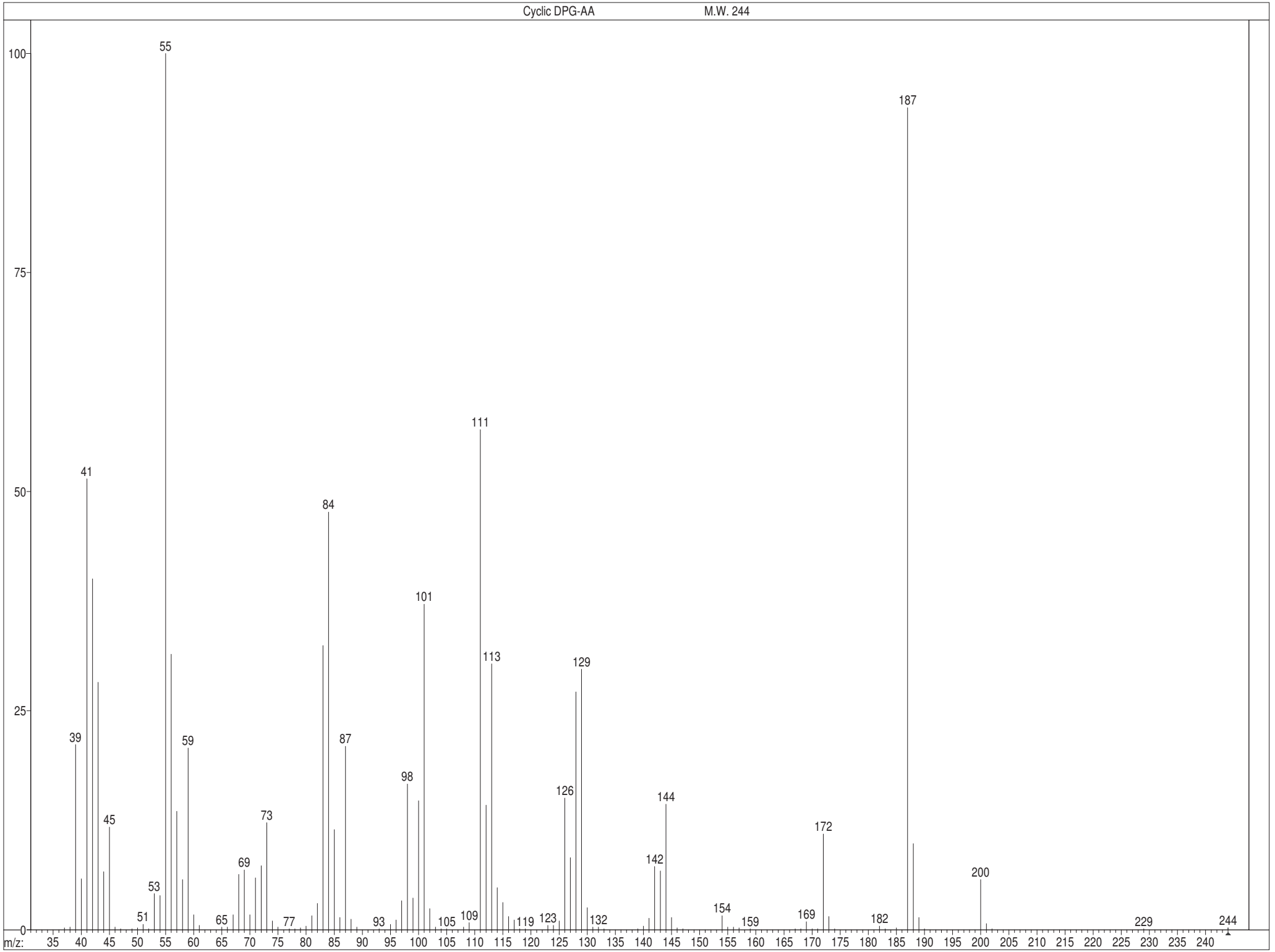


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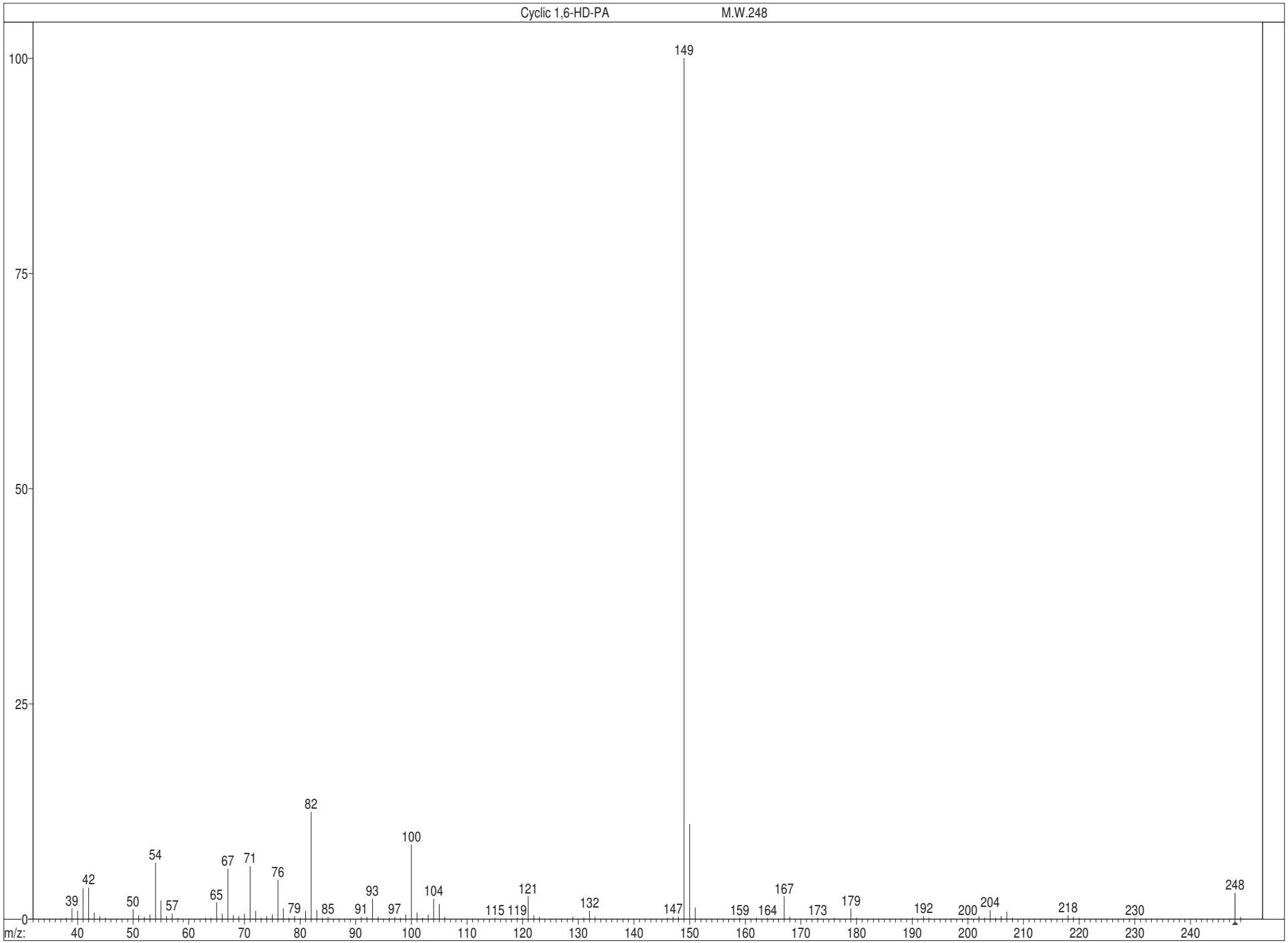


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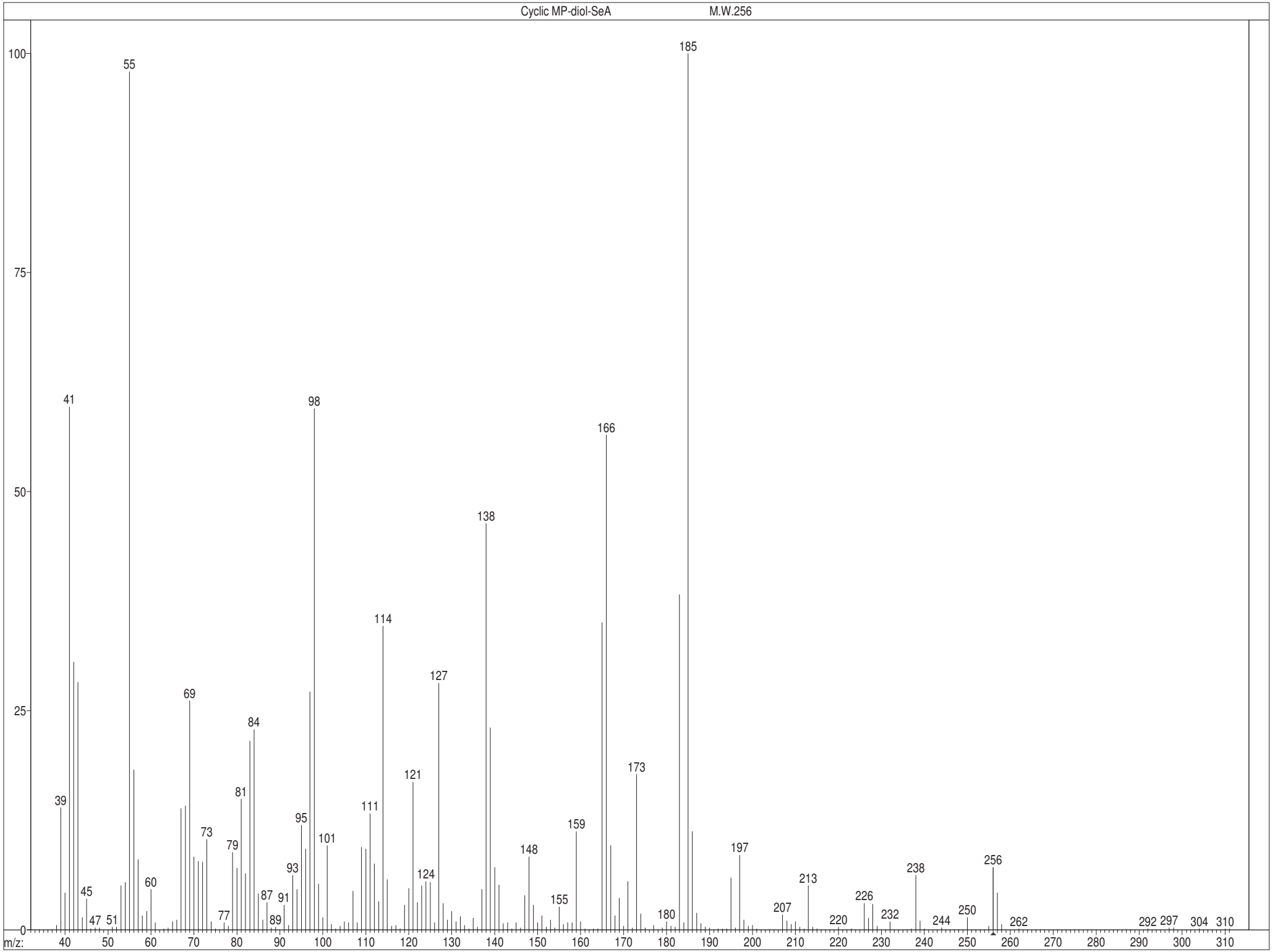
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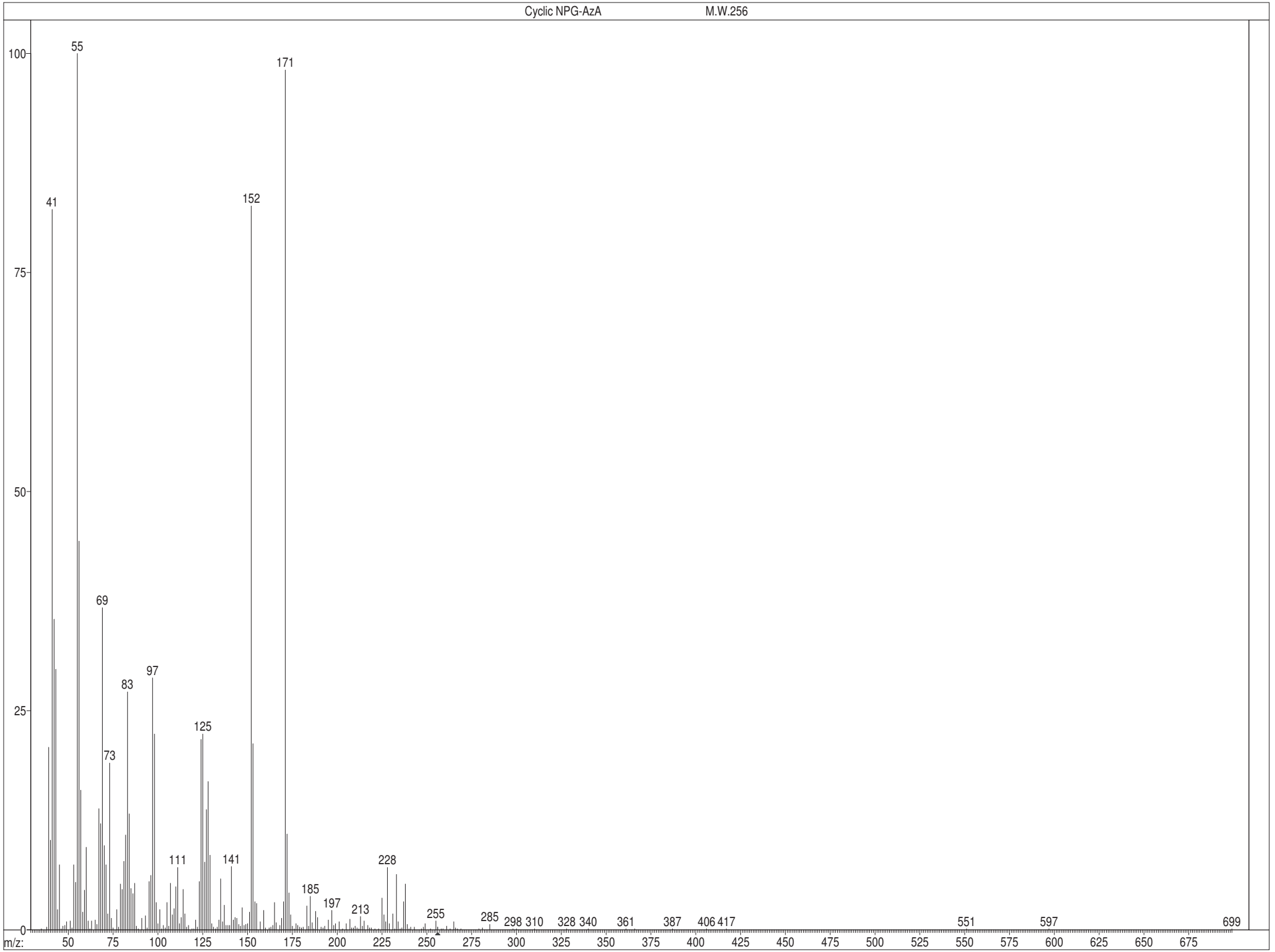


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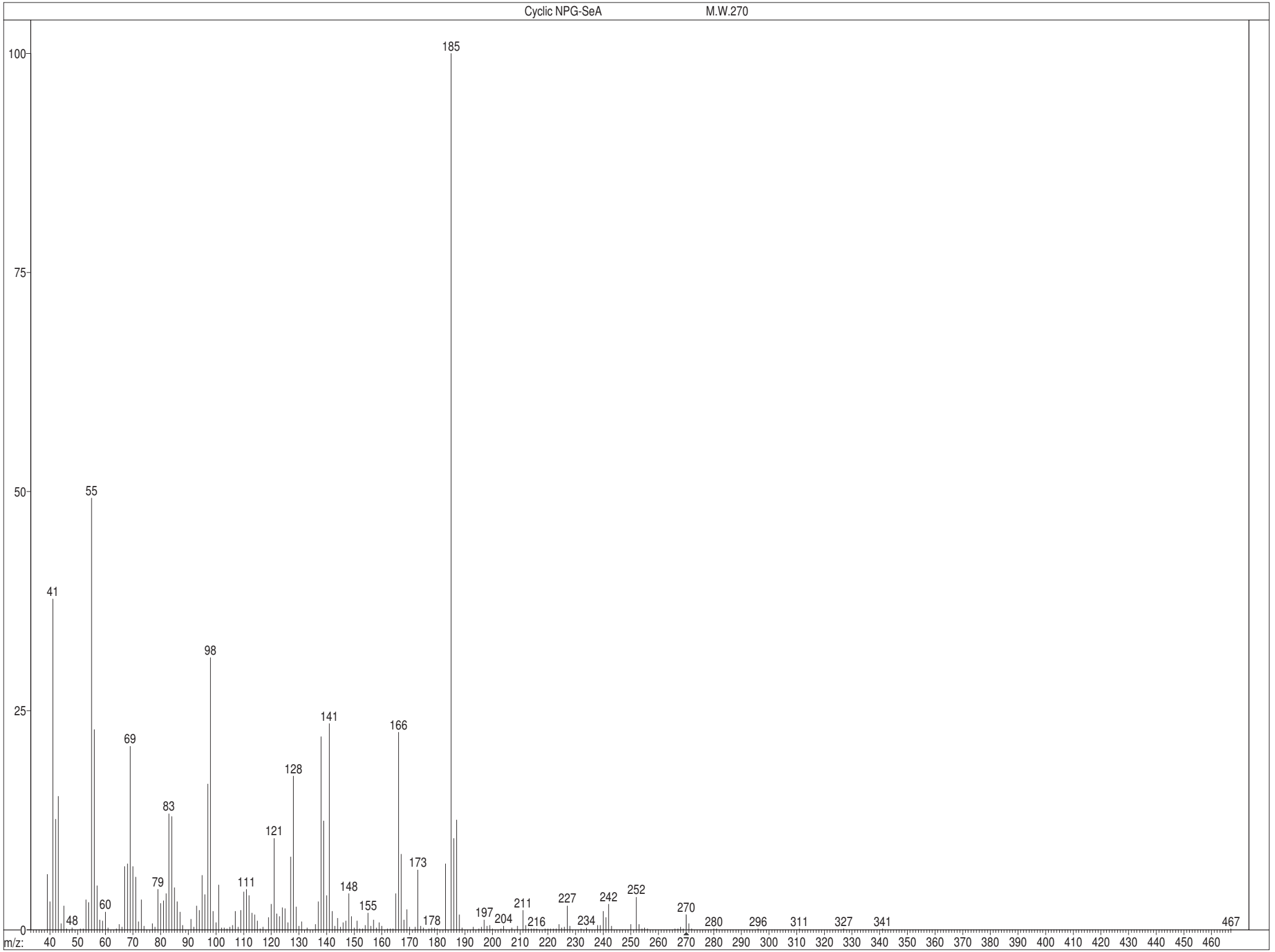


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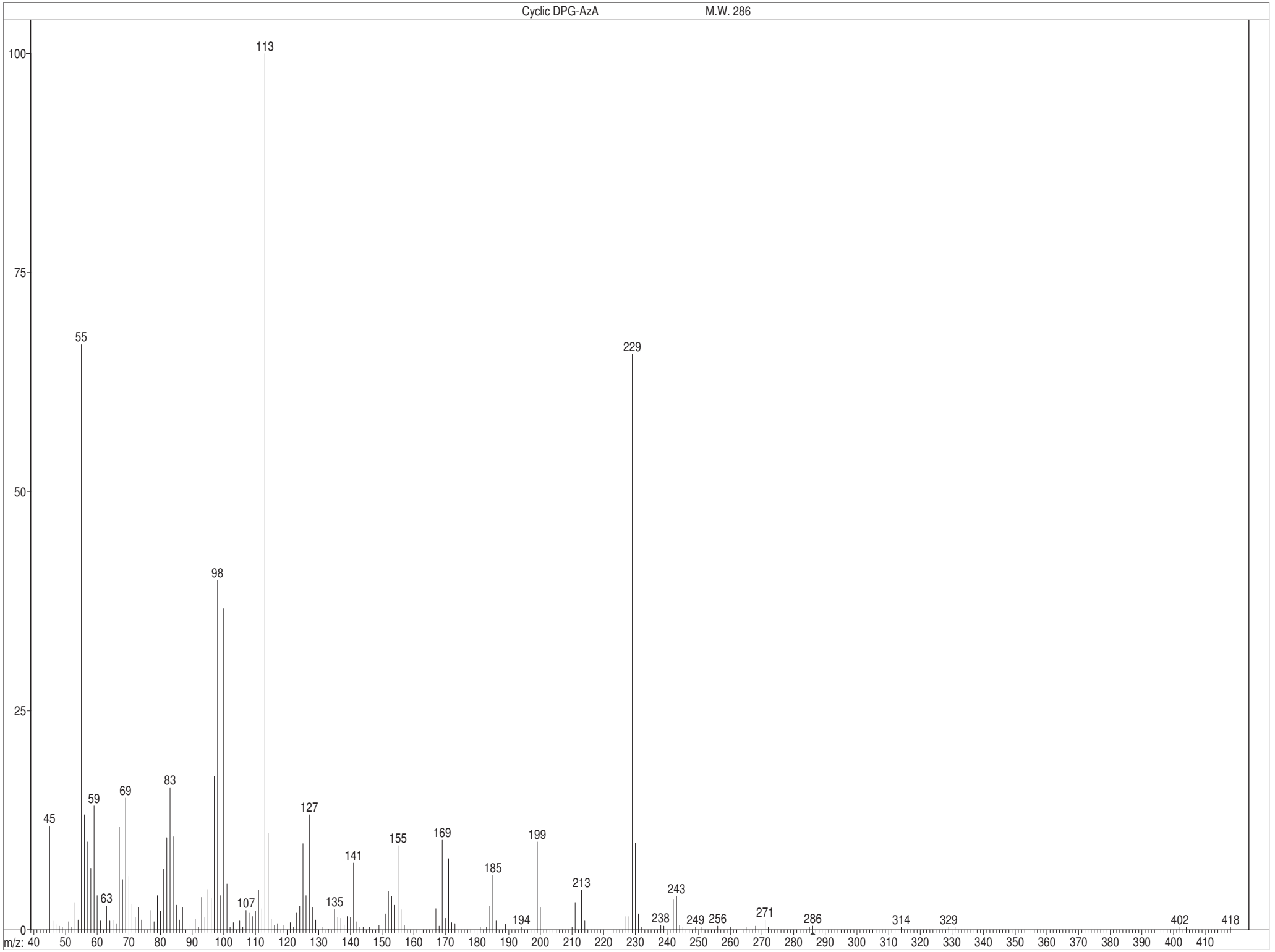
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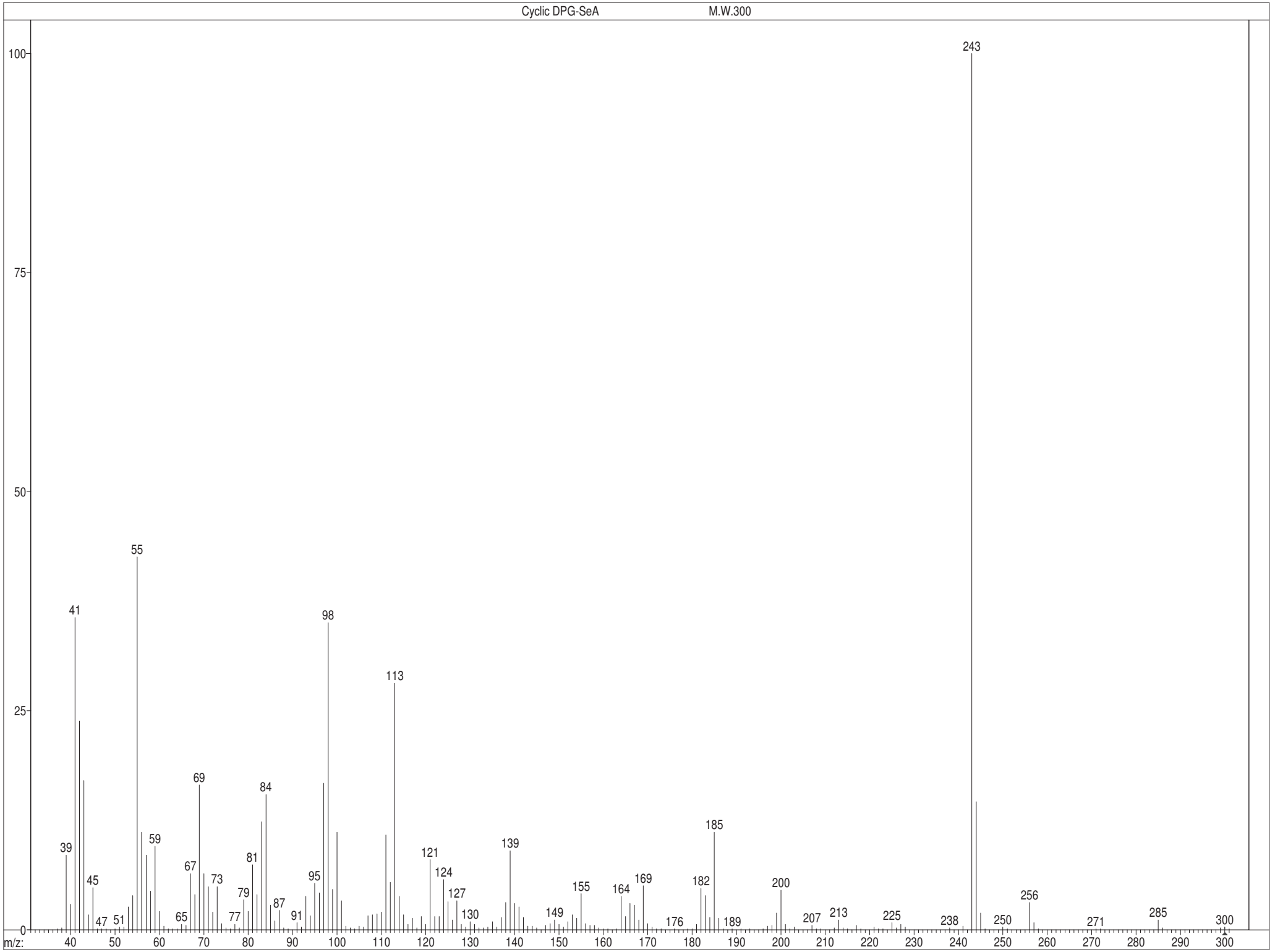


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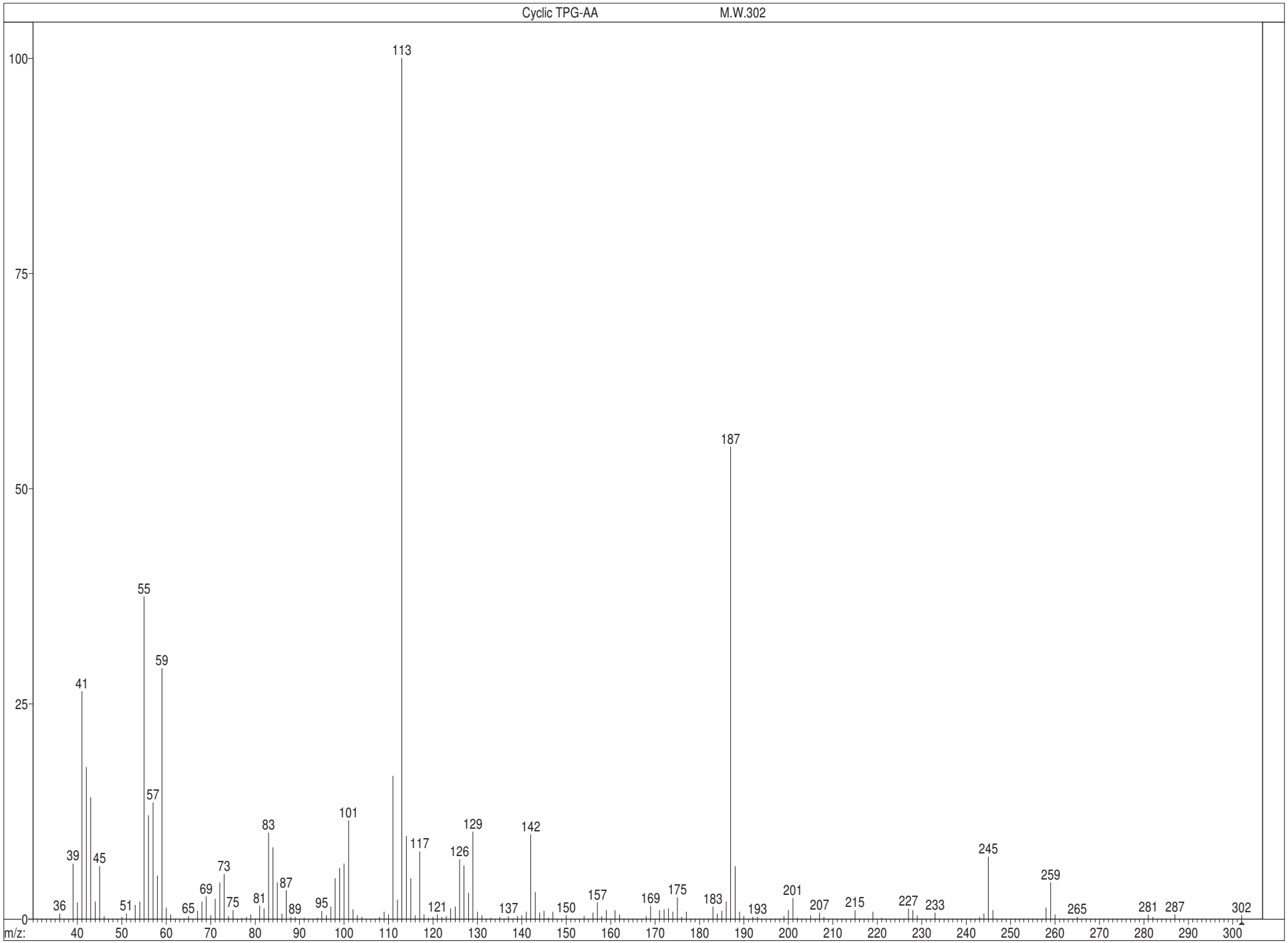
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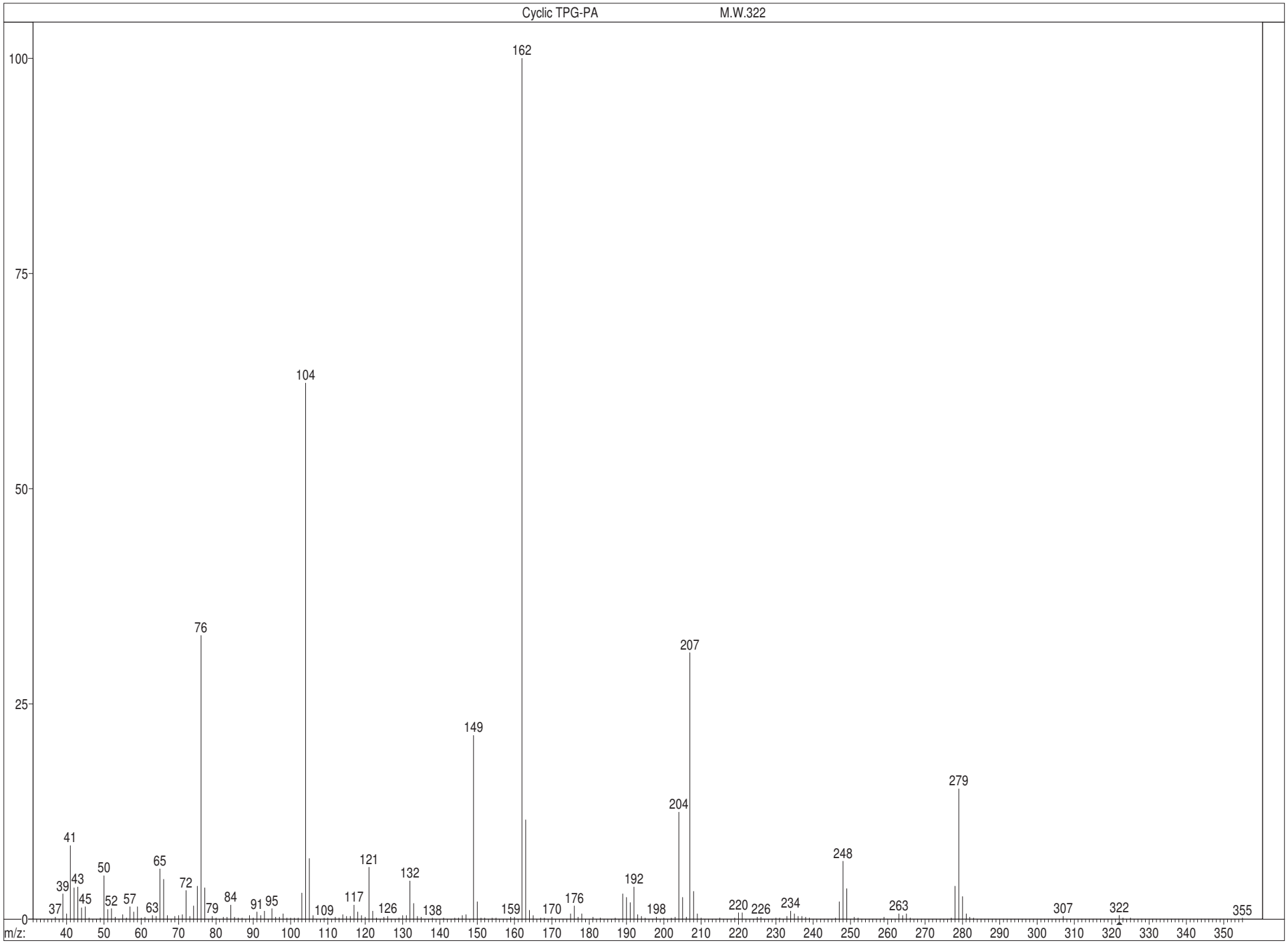


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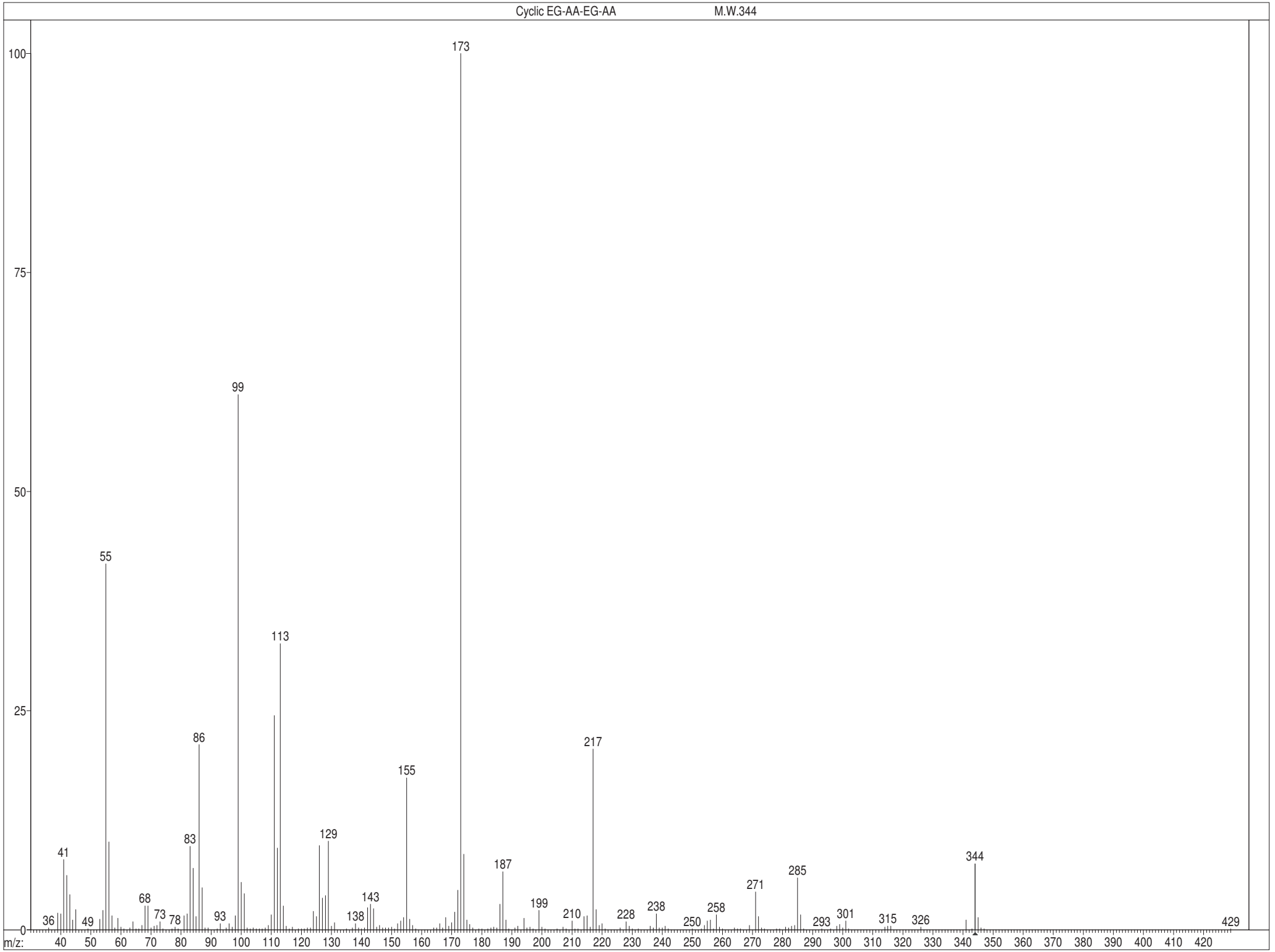
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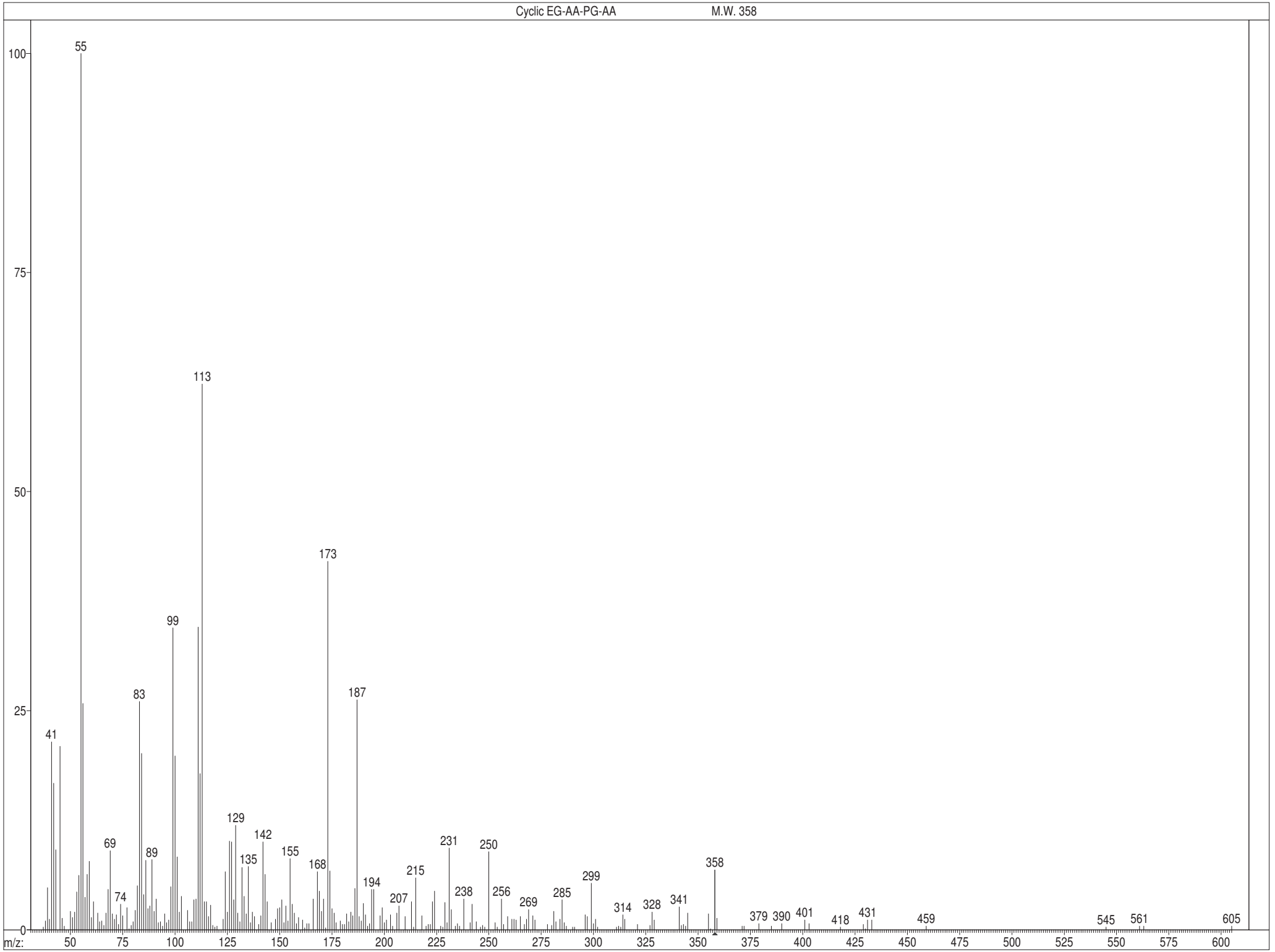
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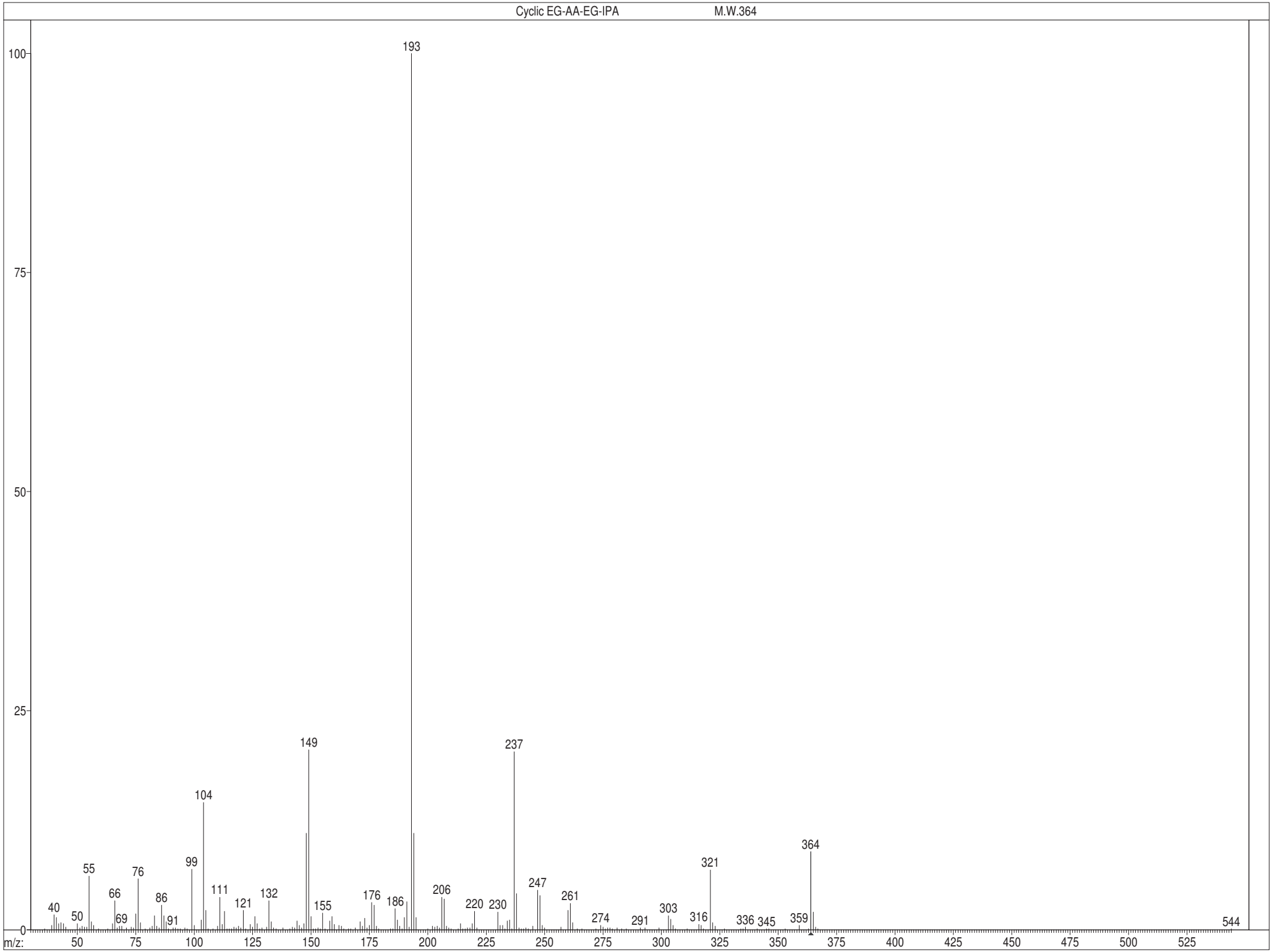
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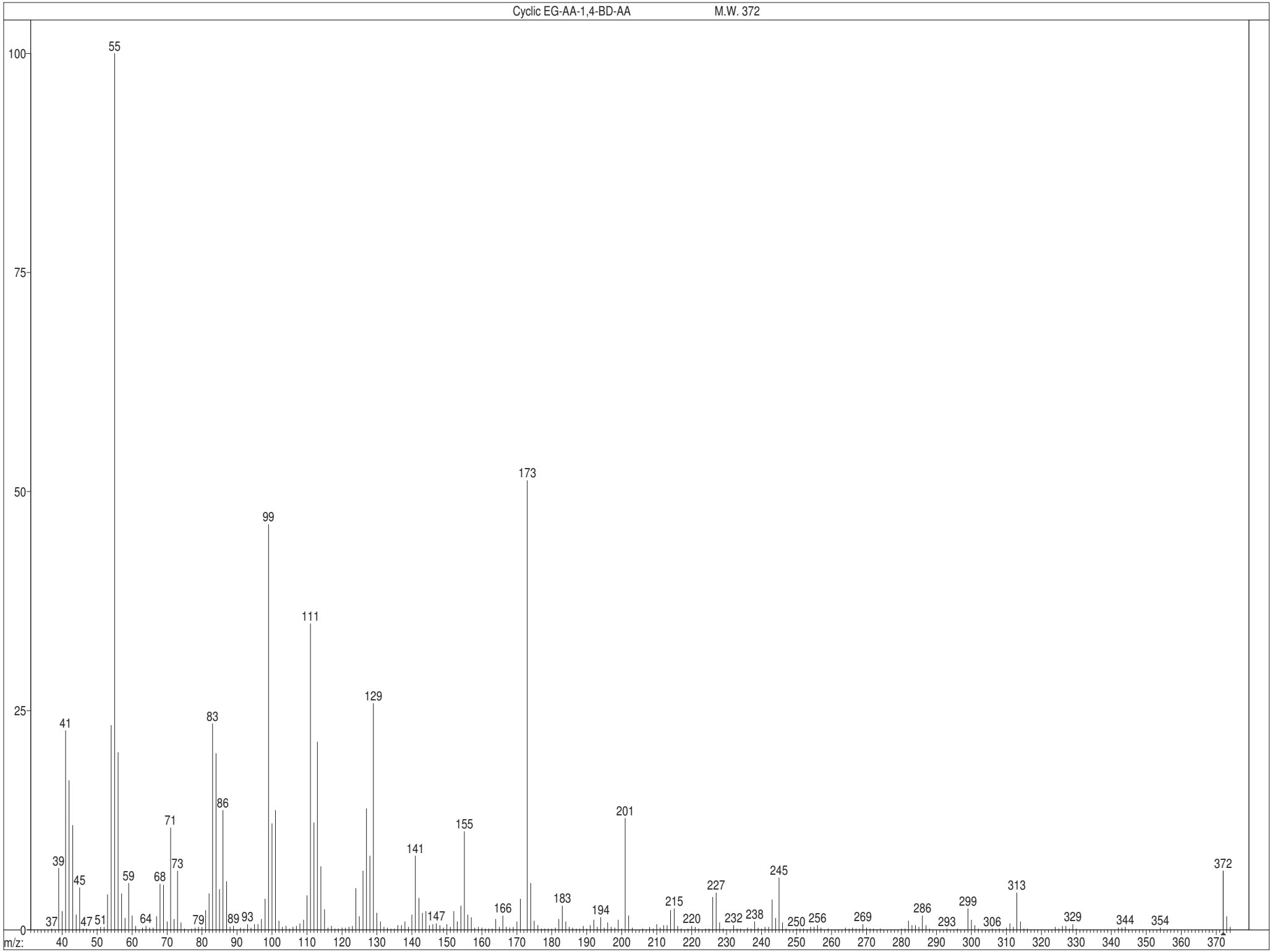
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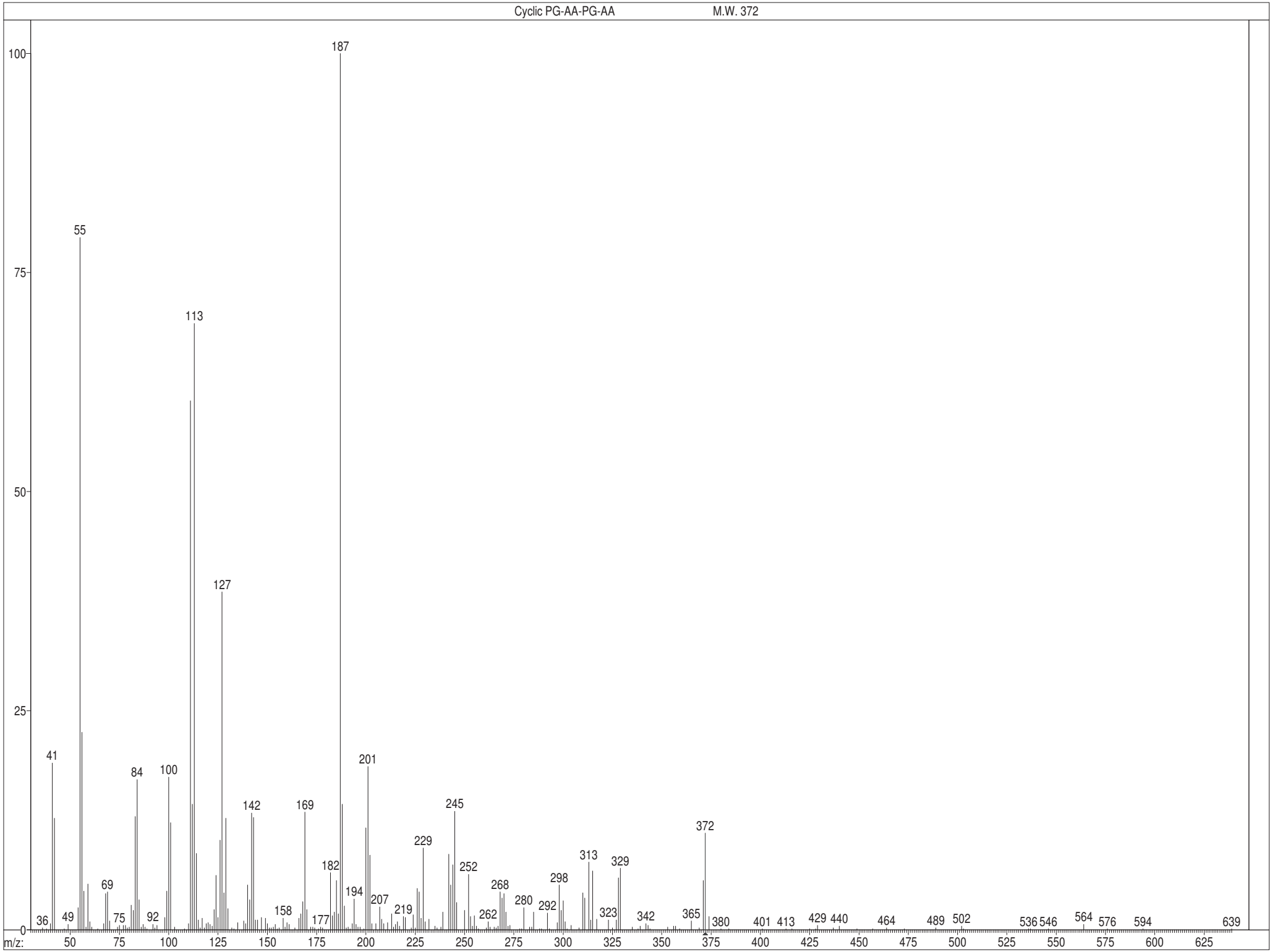


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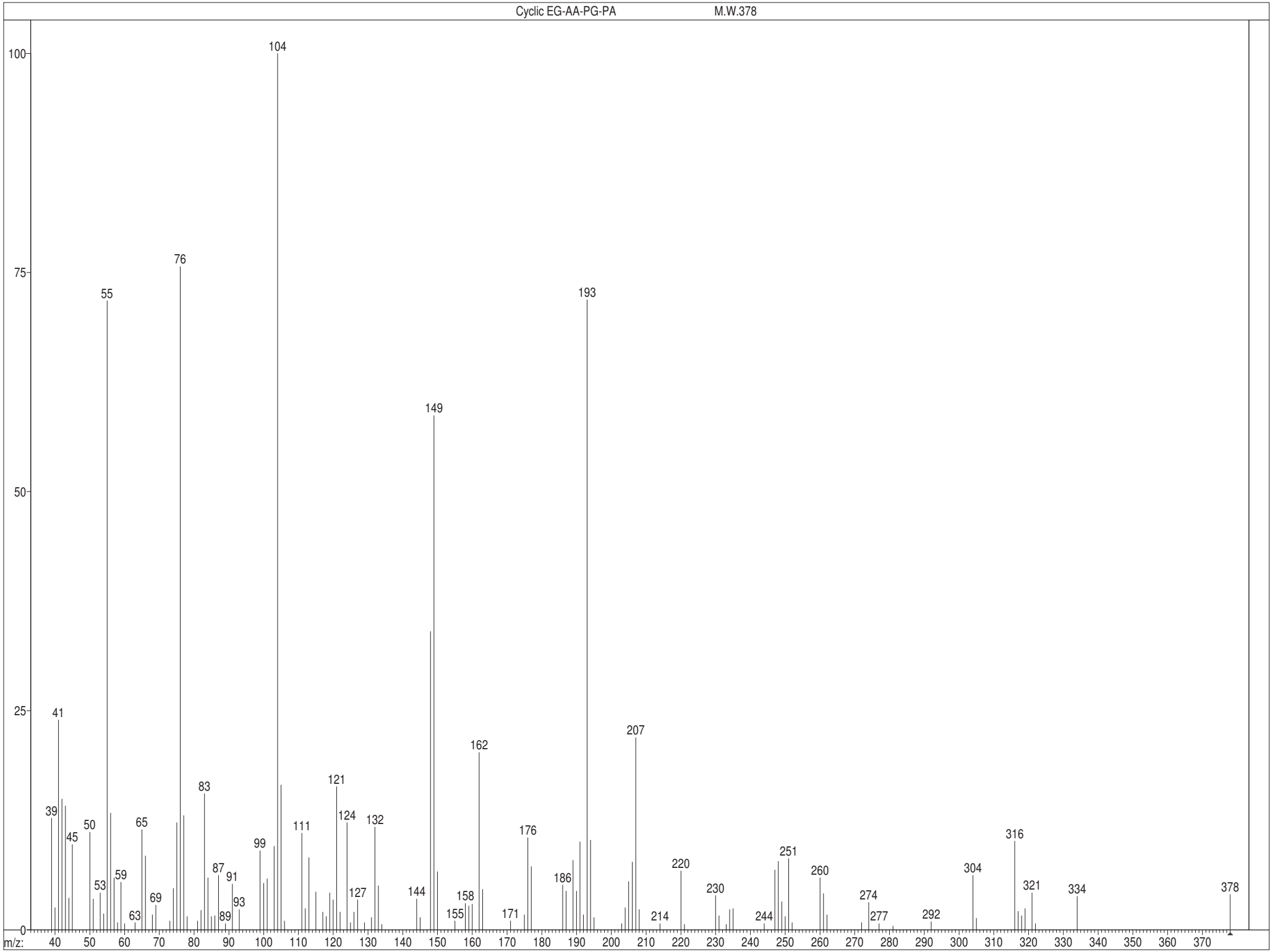
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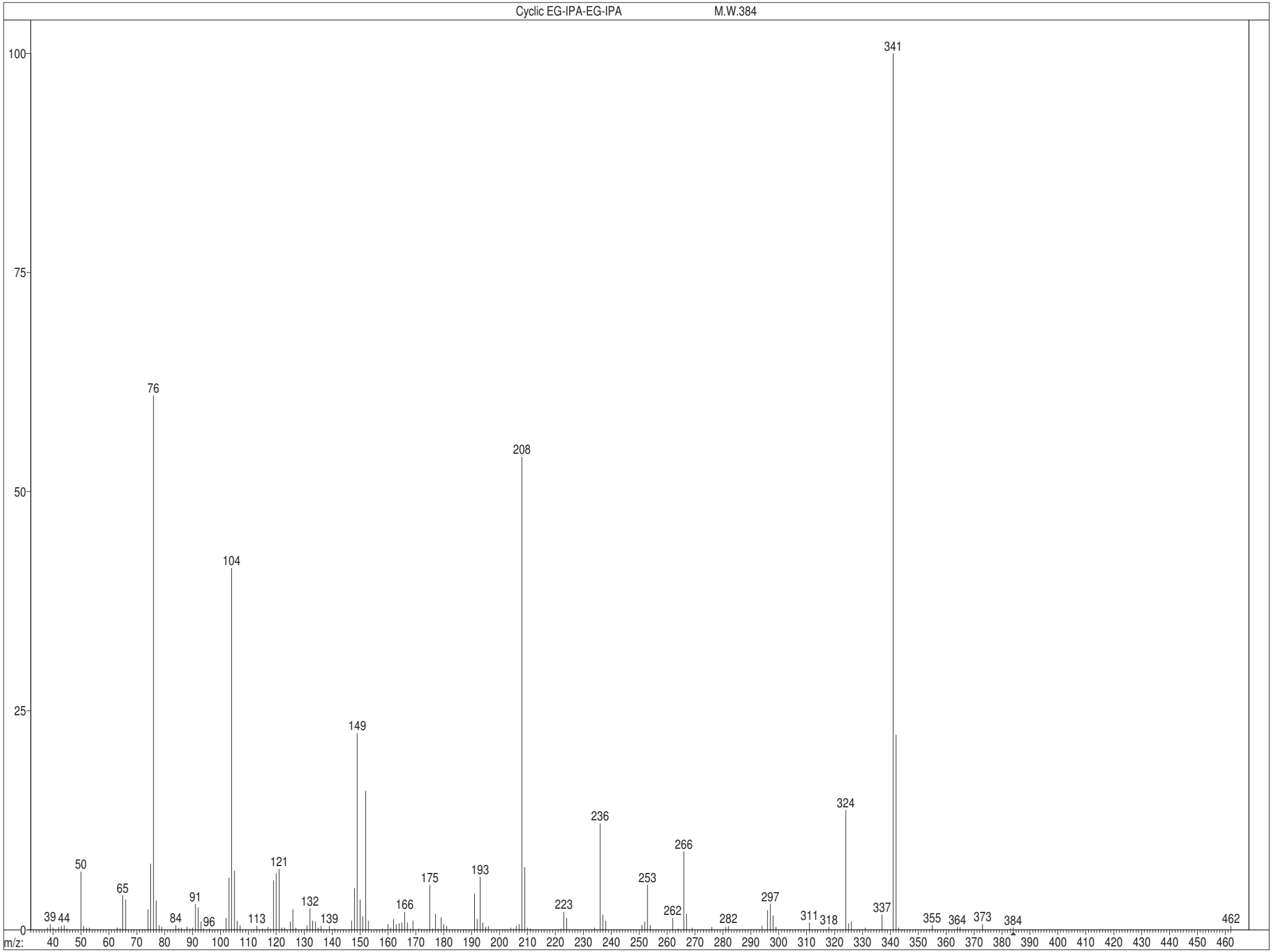
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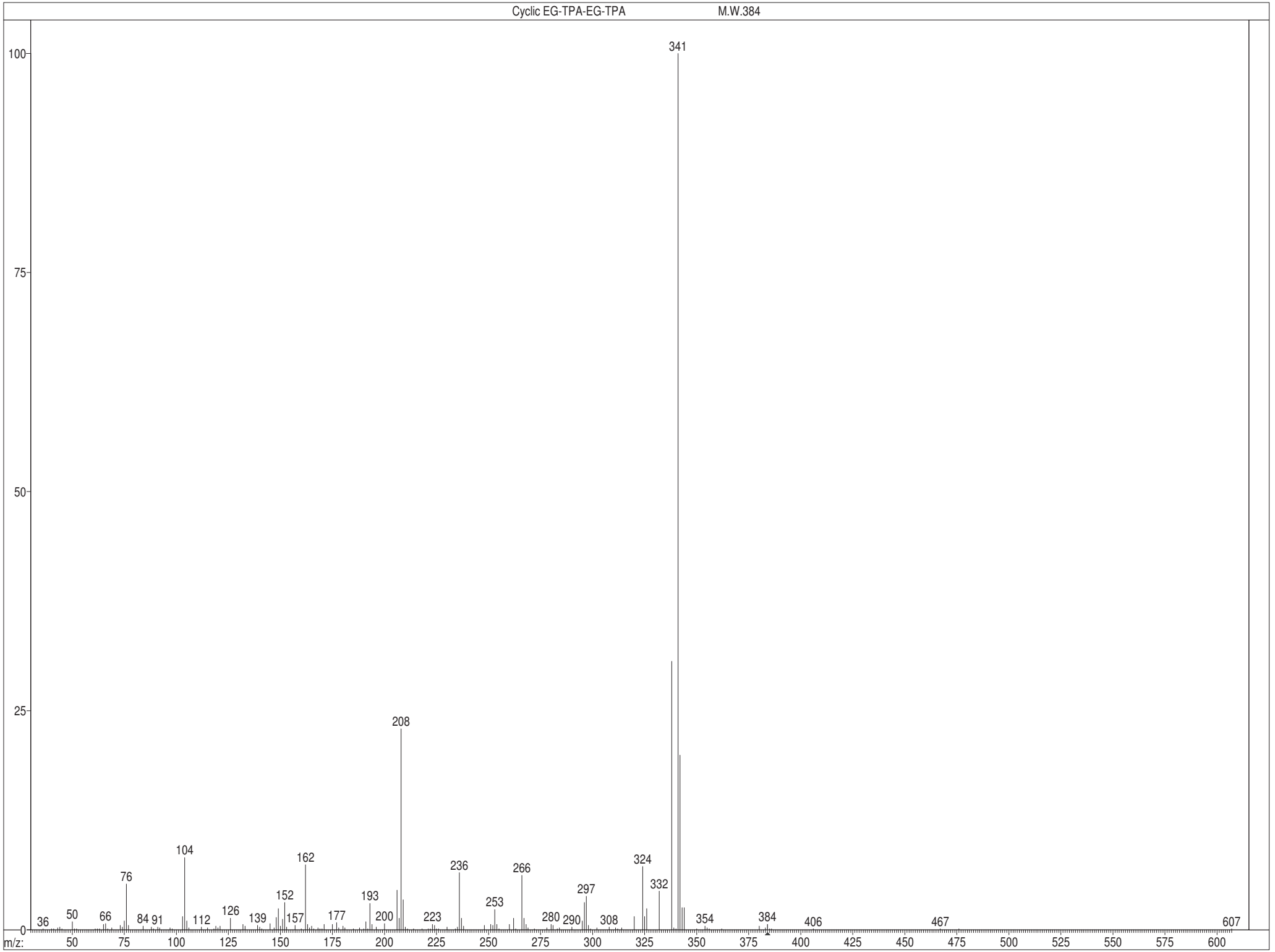
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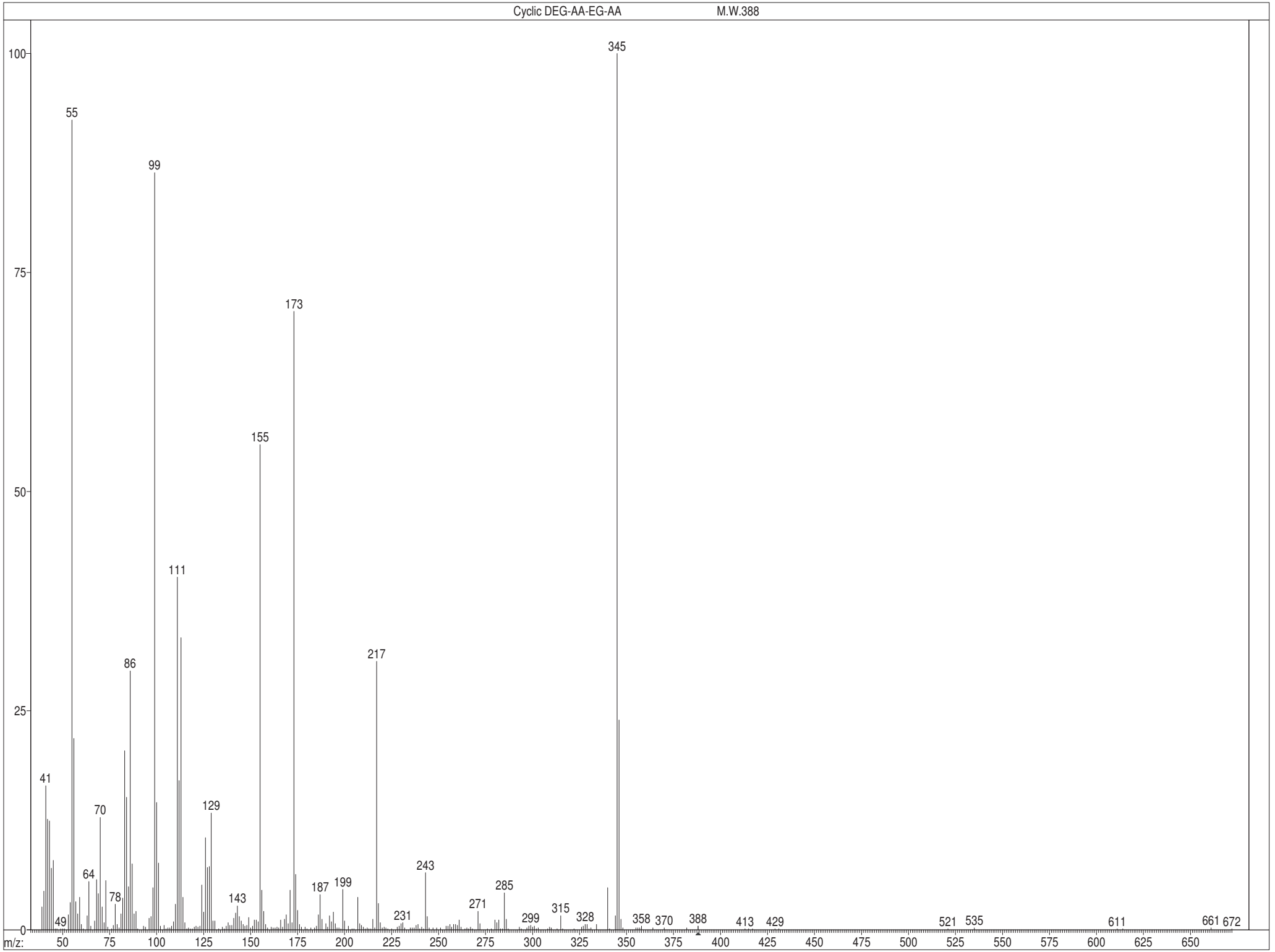


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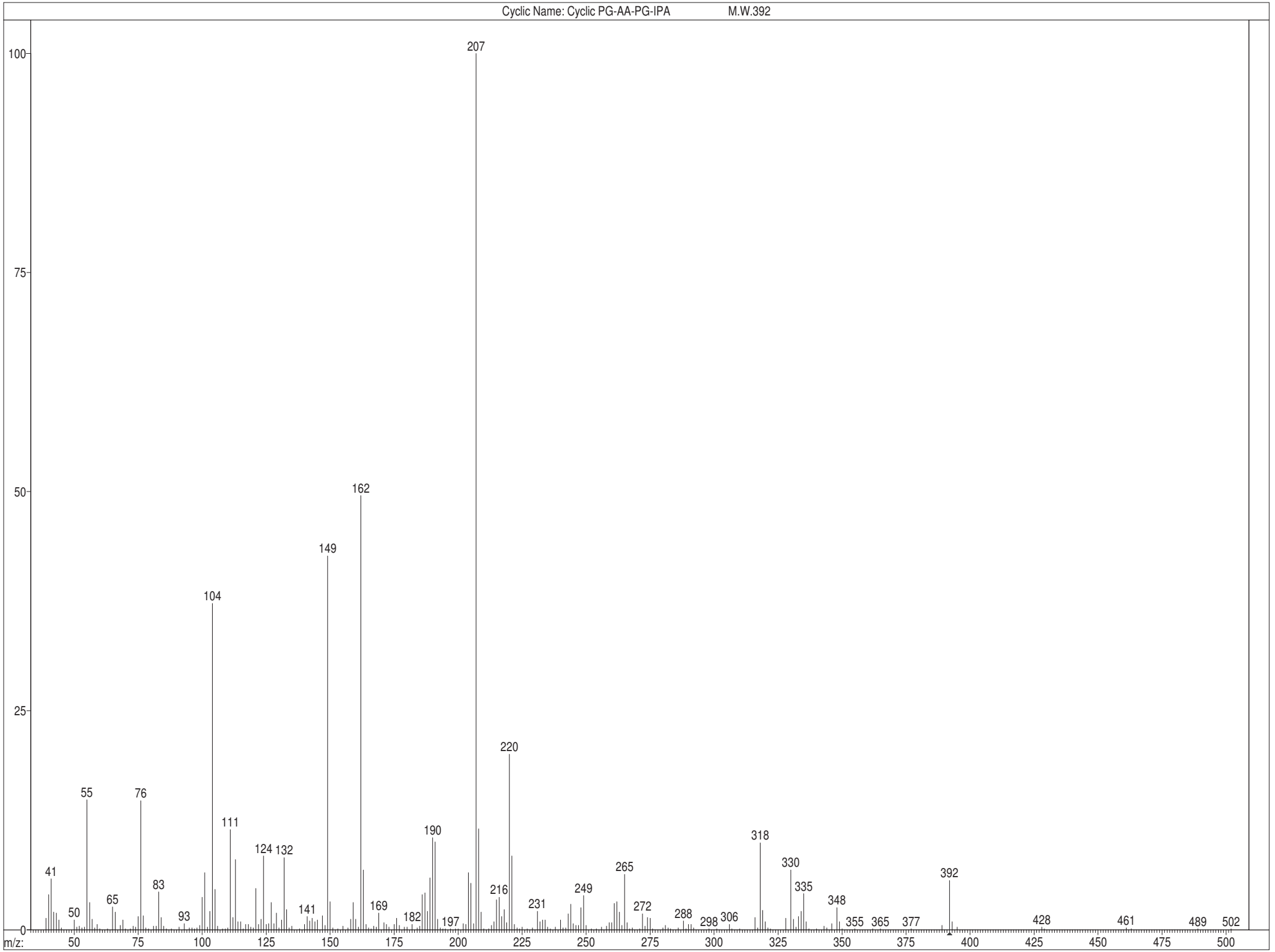
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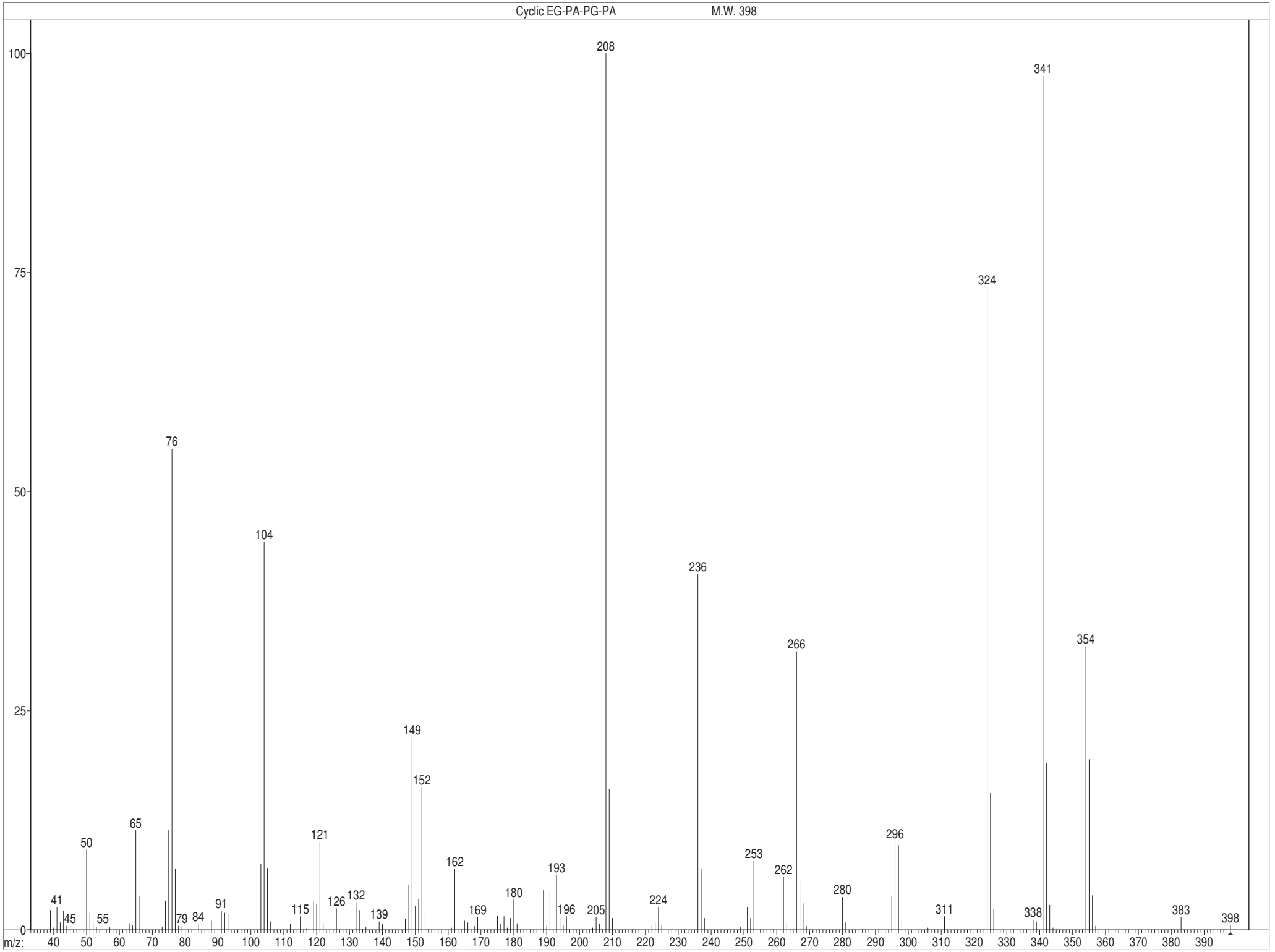
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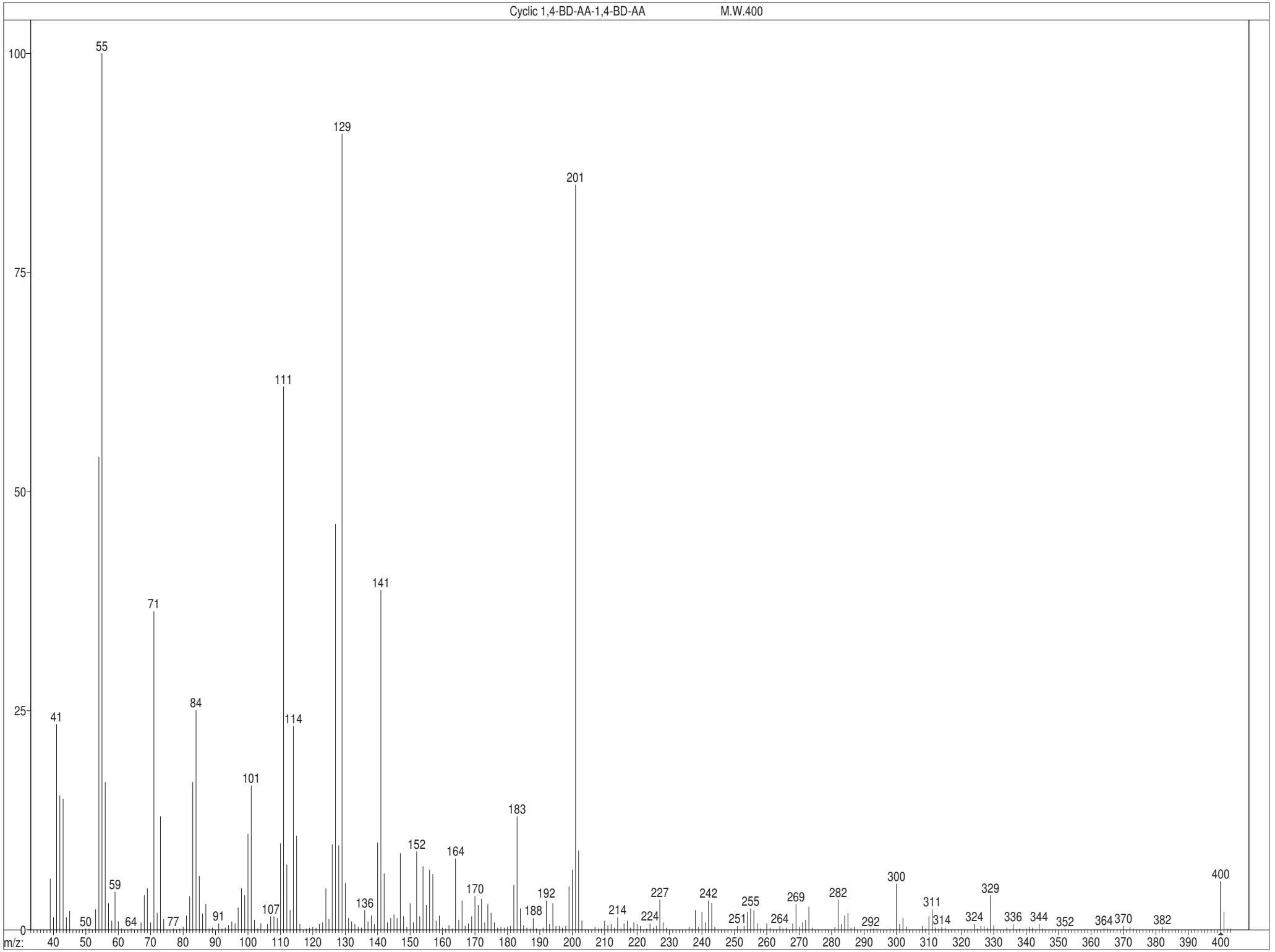


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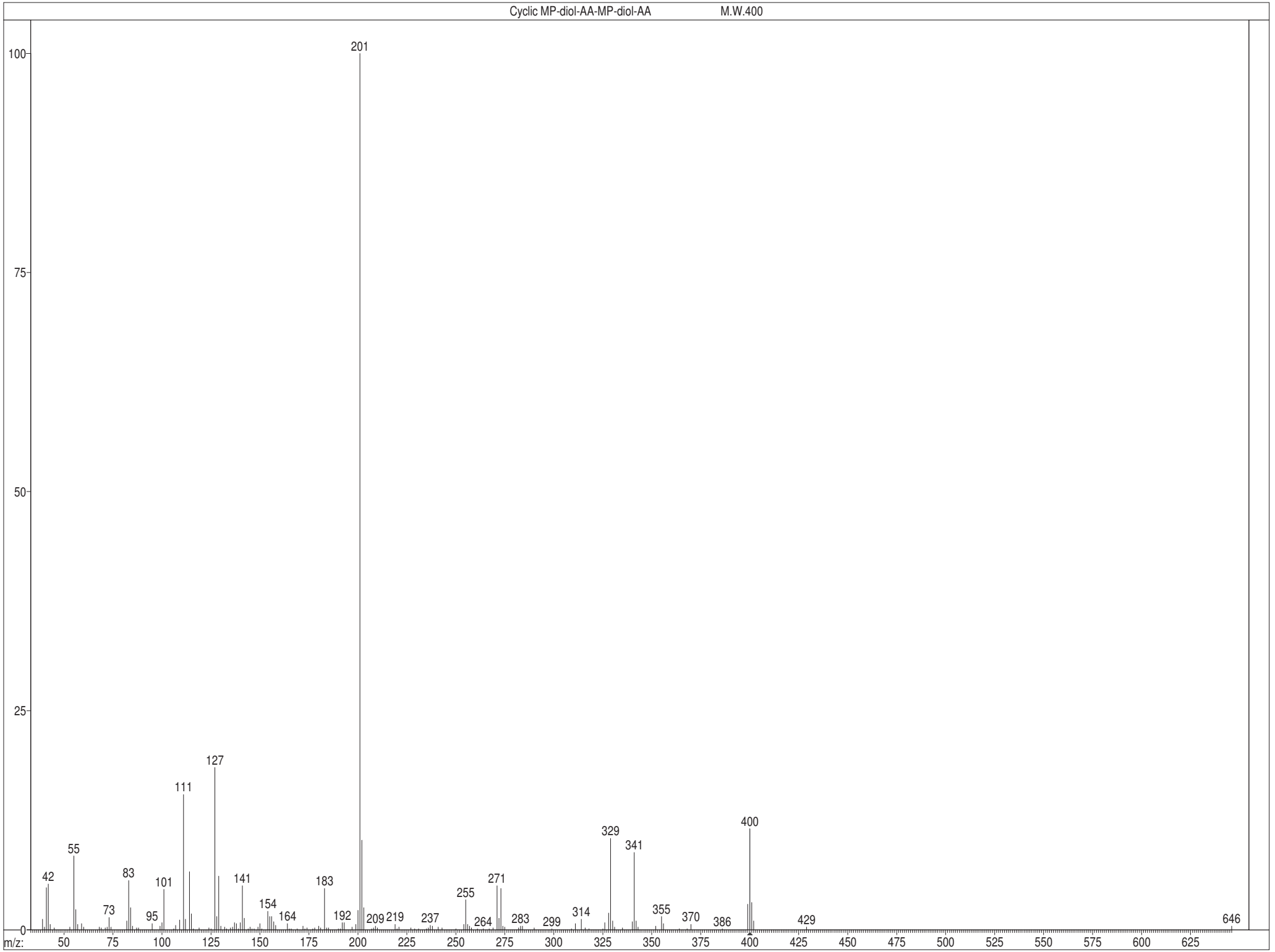


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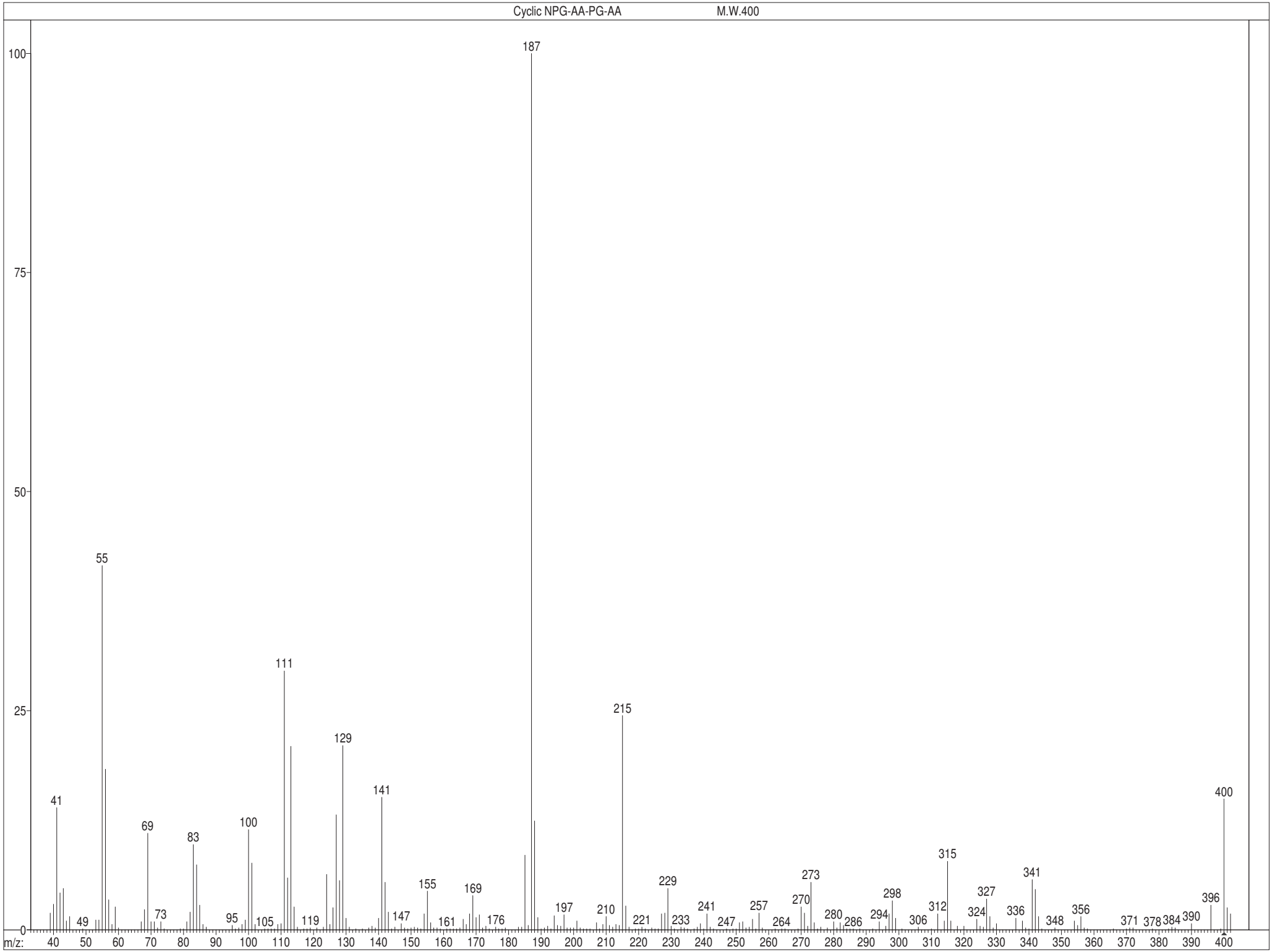
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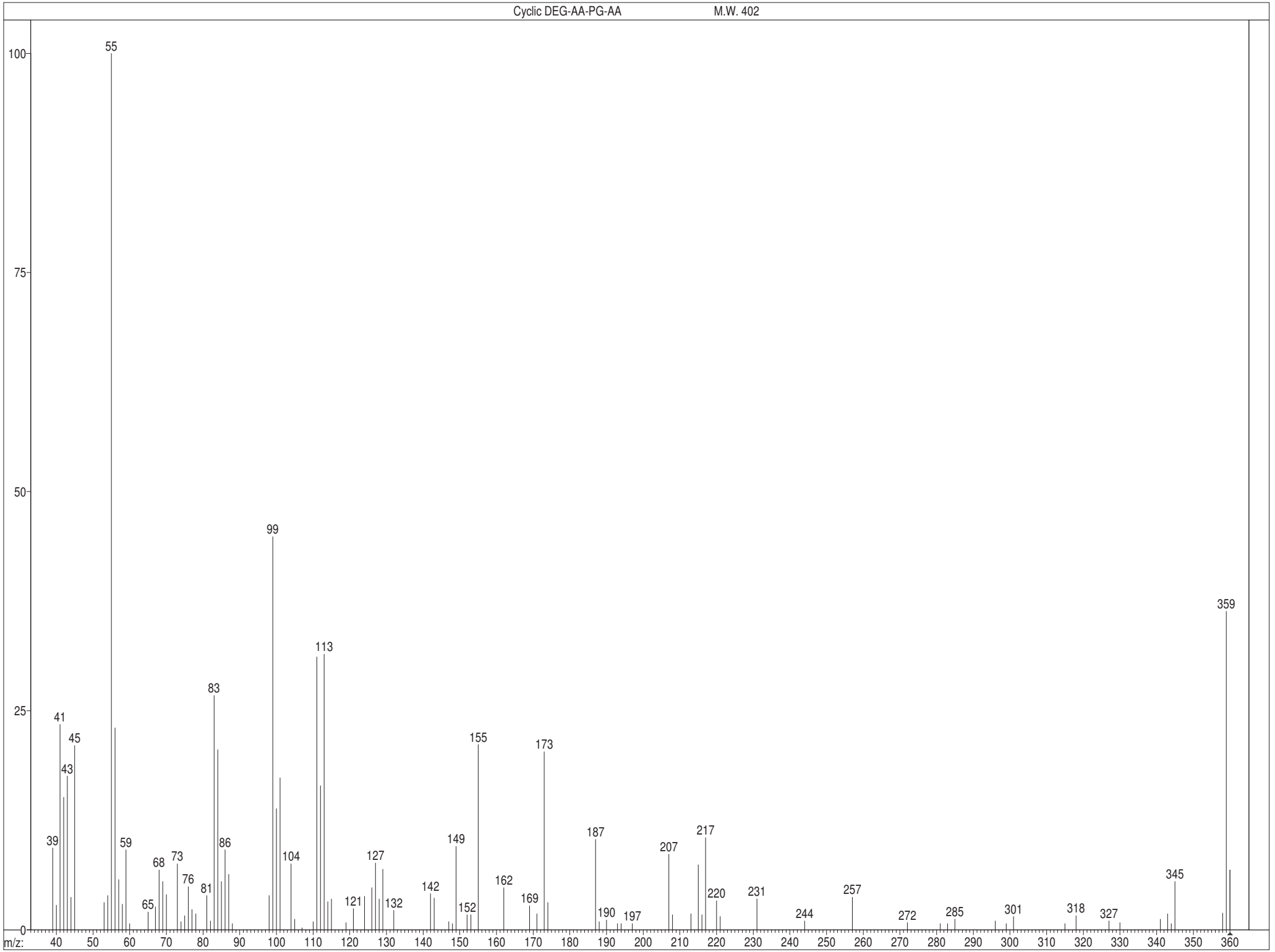


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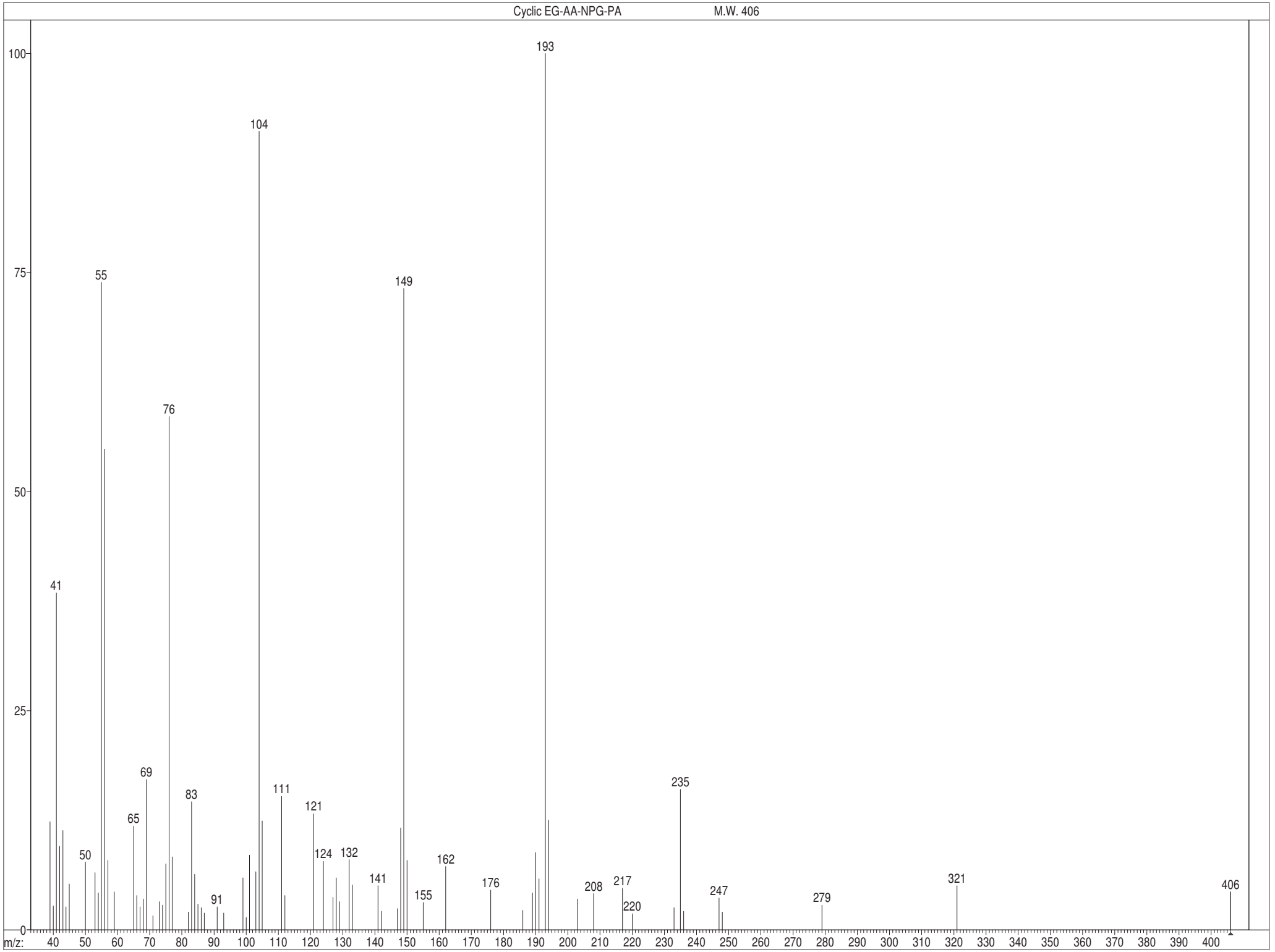


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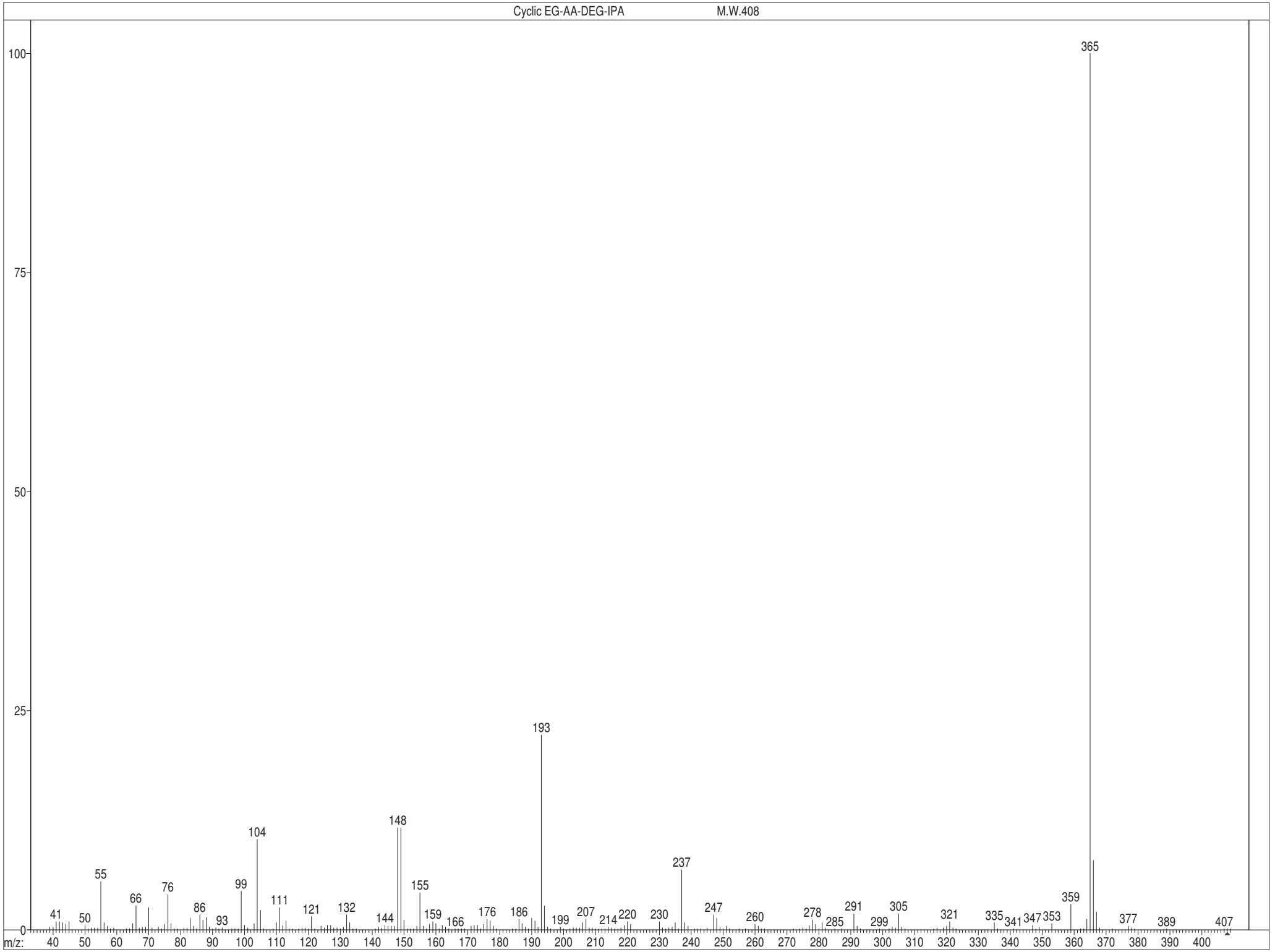
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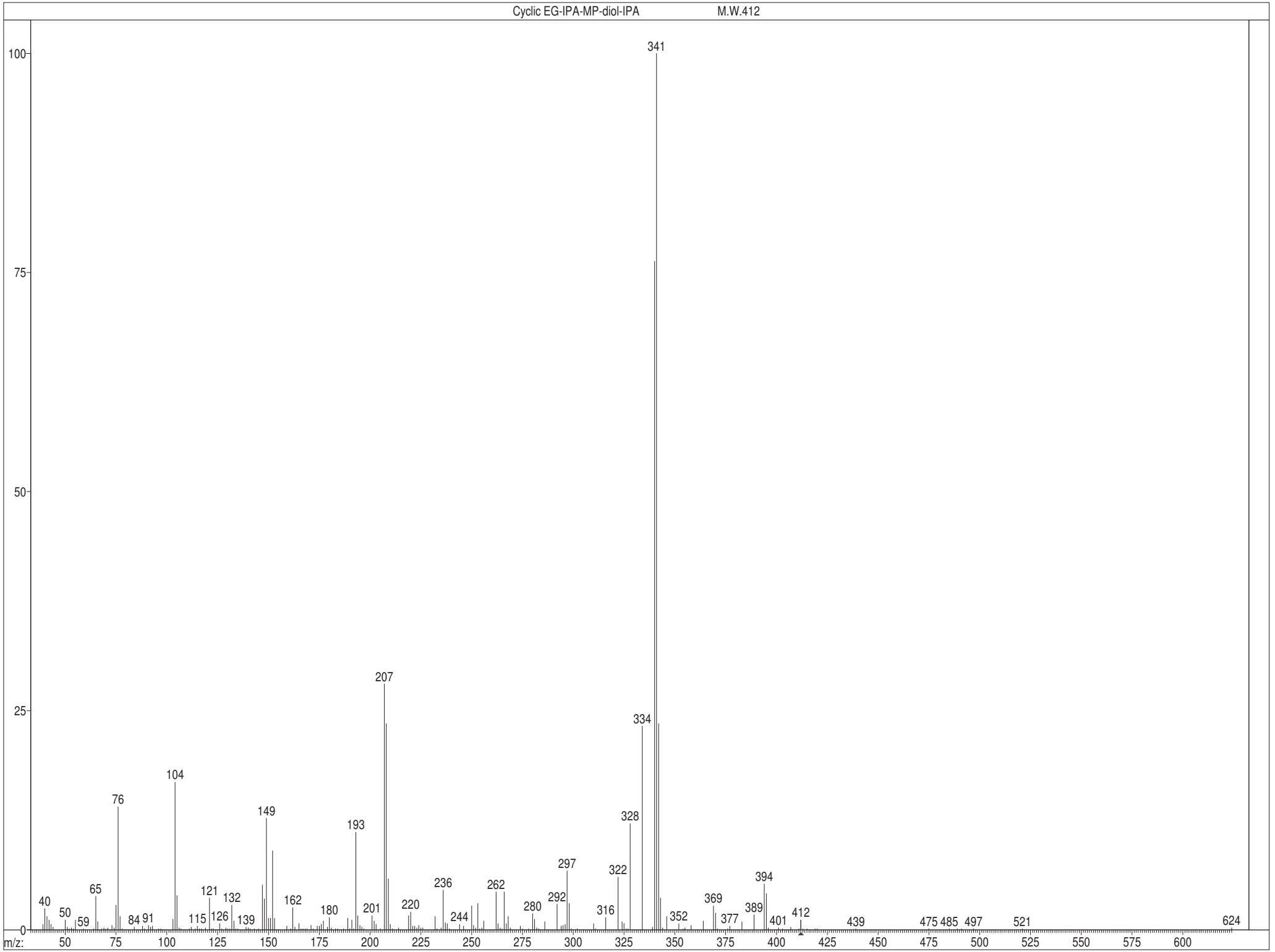


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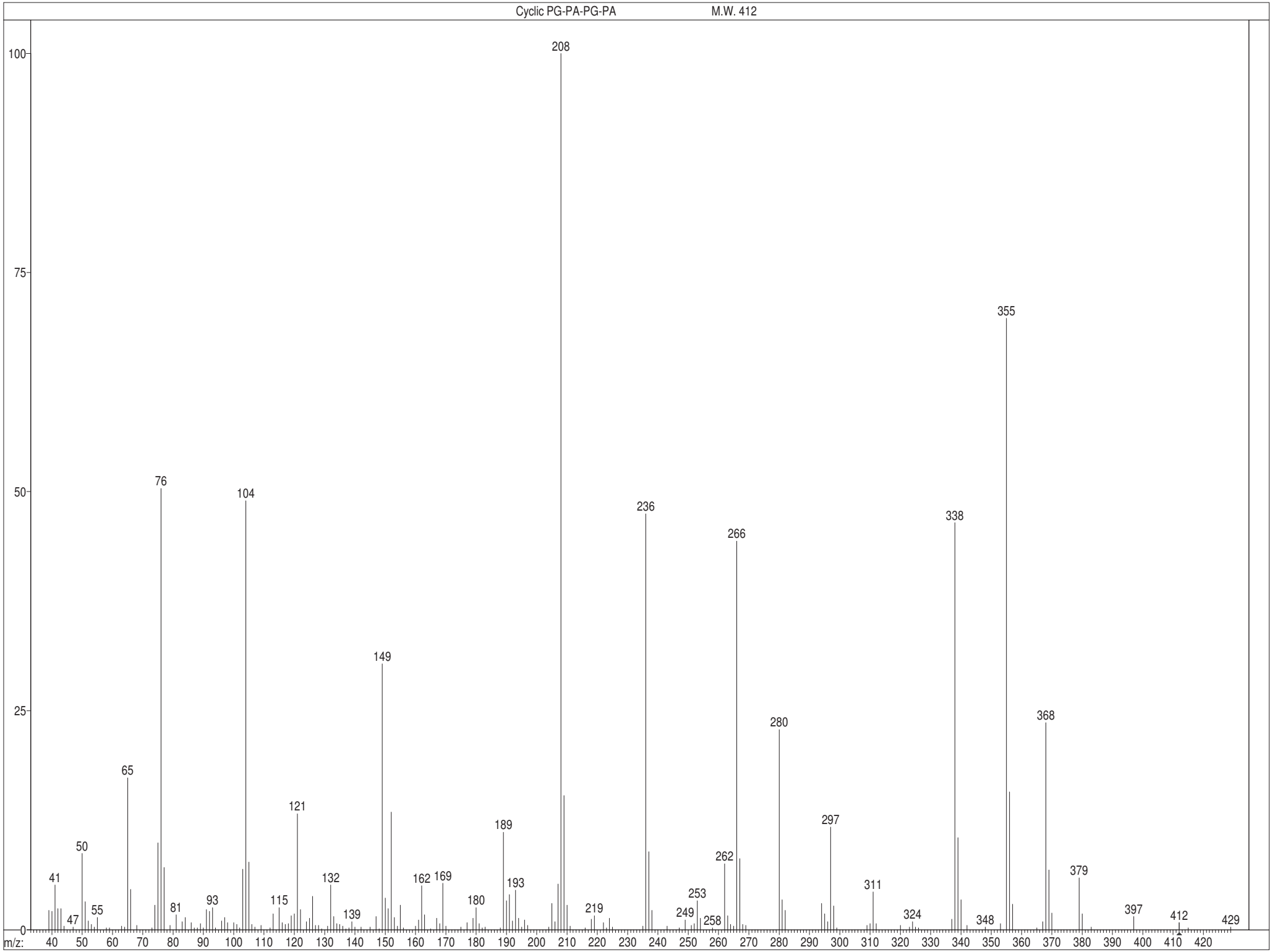


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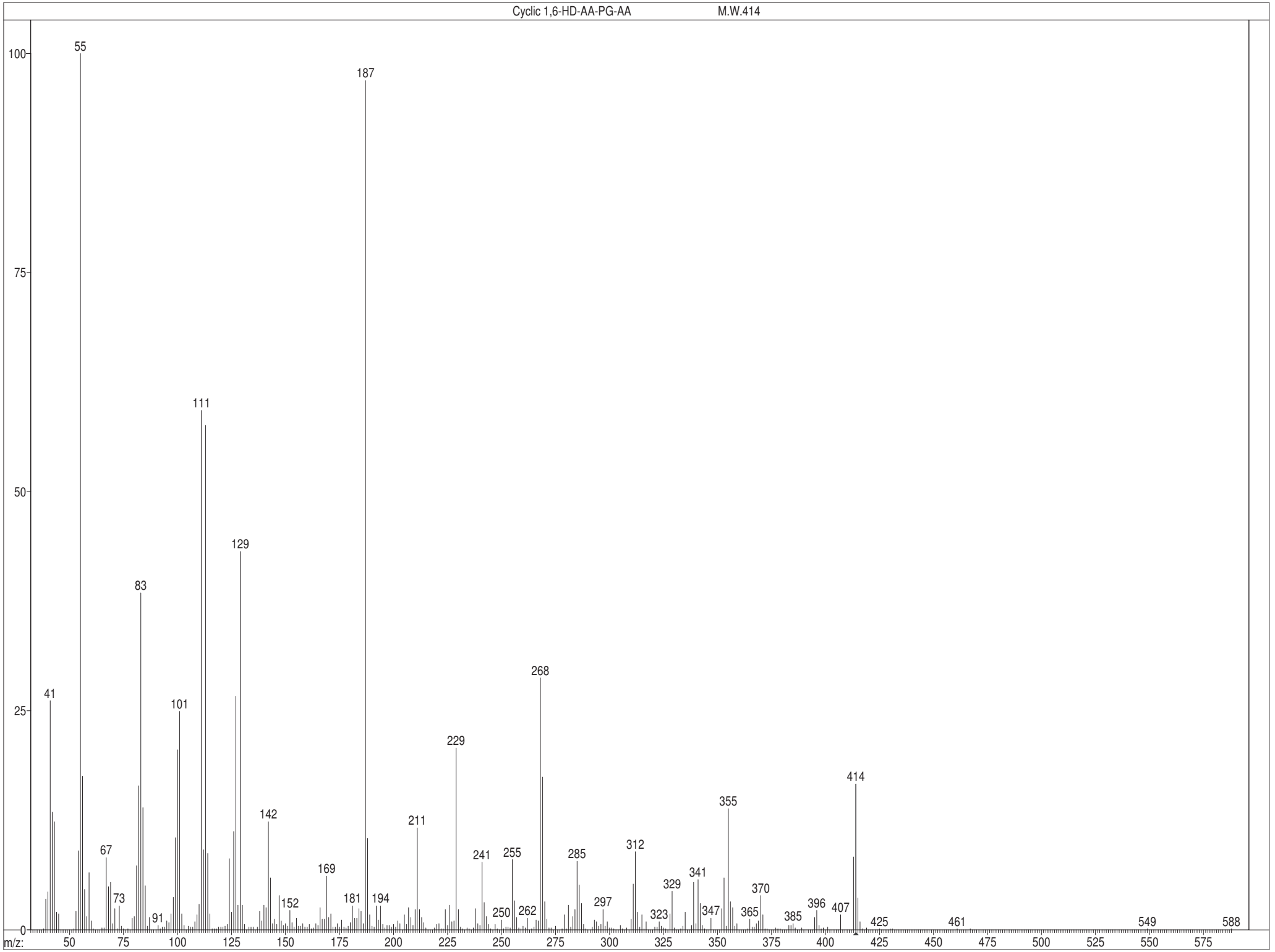


Mass Spectrum for



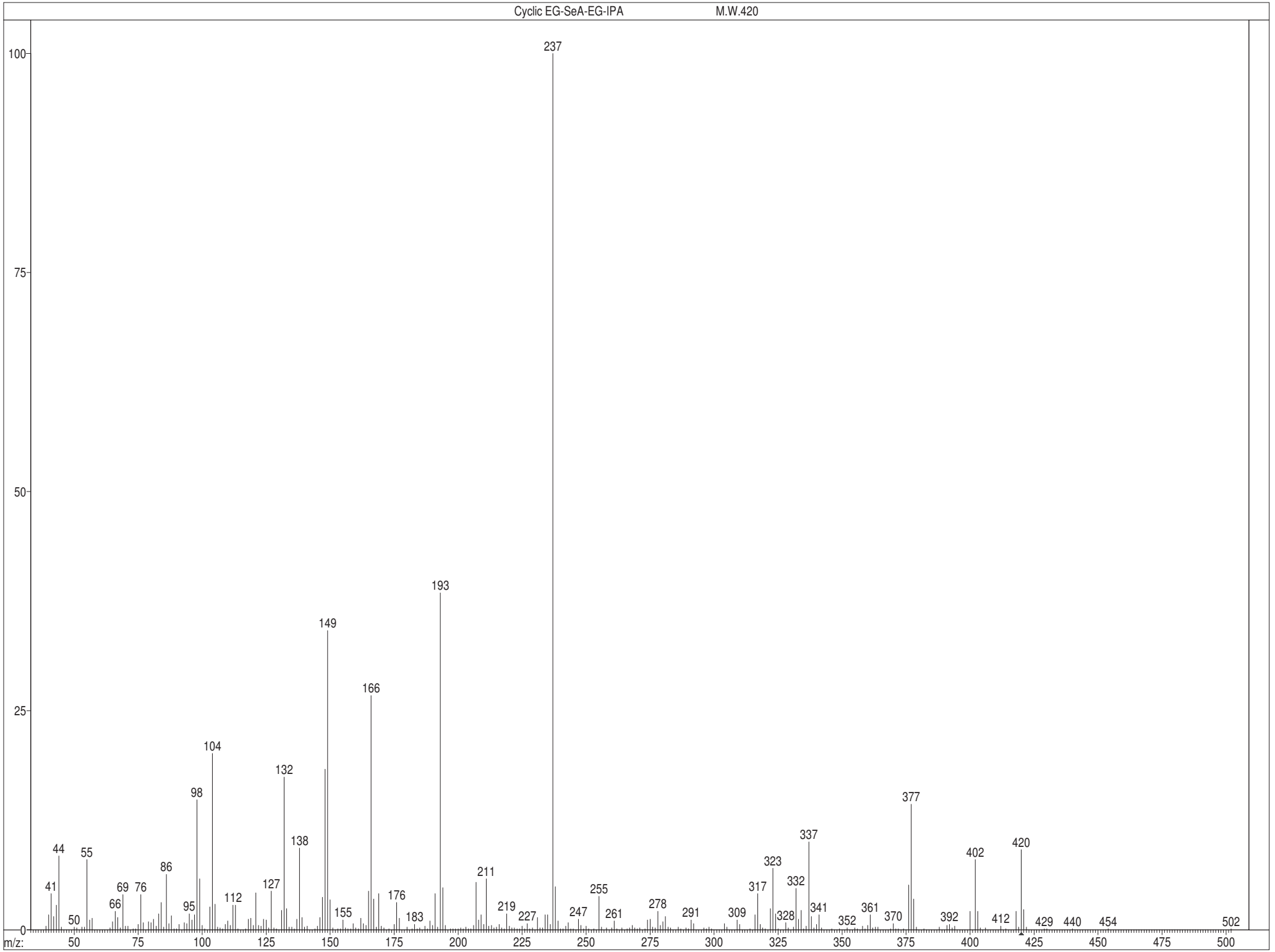
0255

Mass Spectrum for

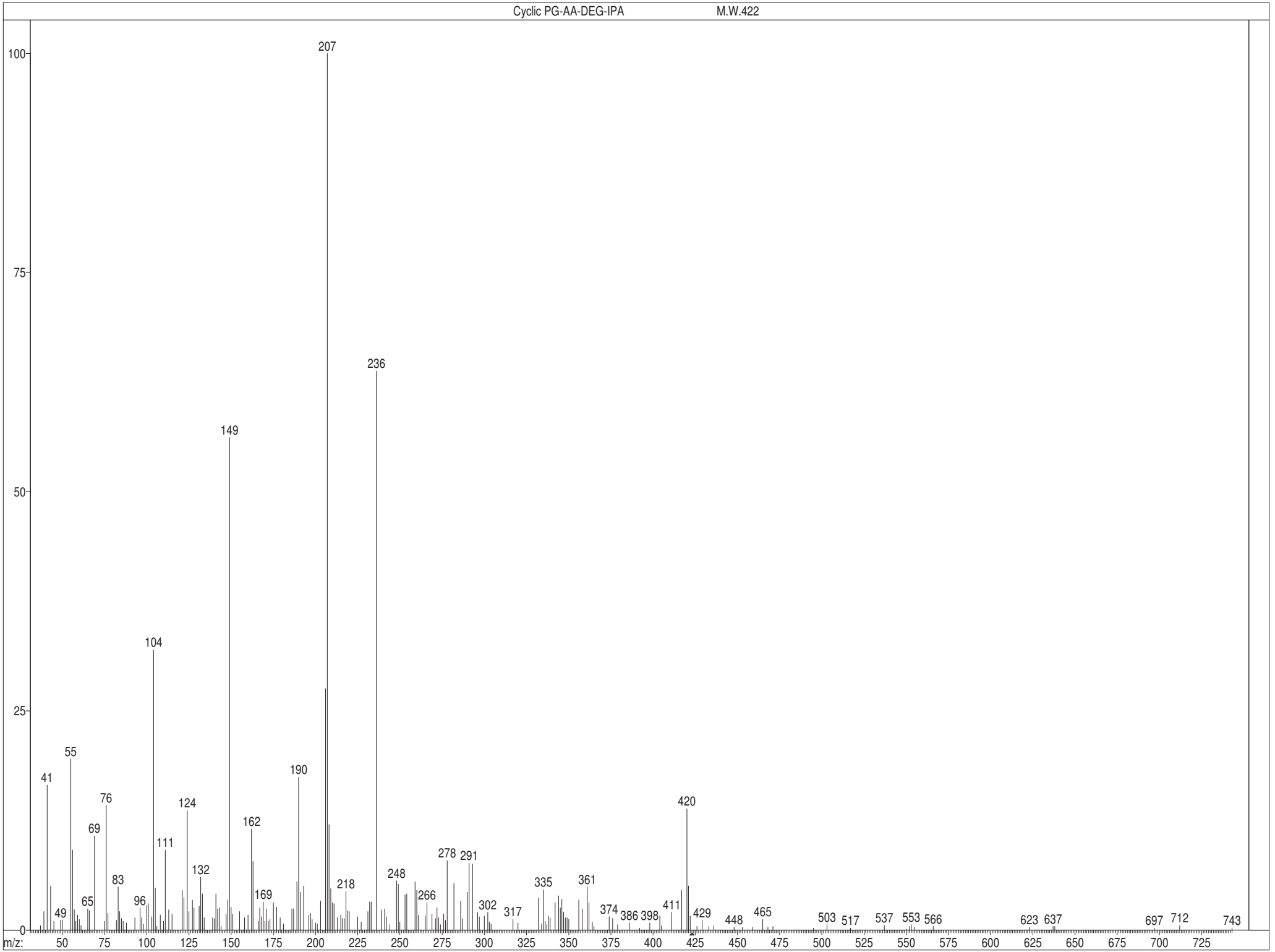


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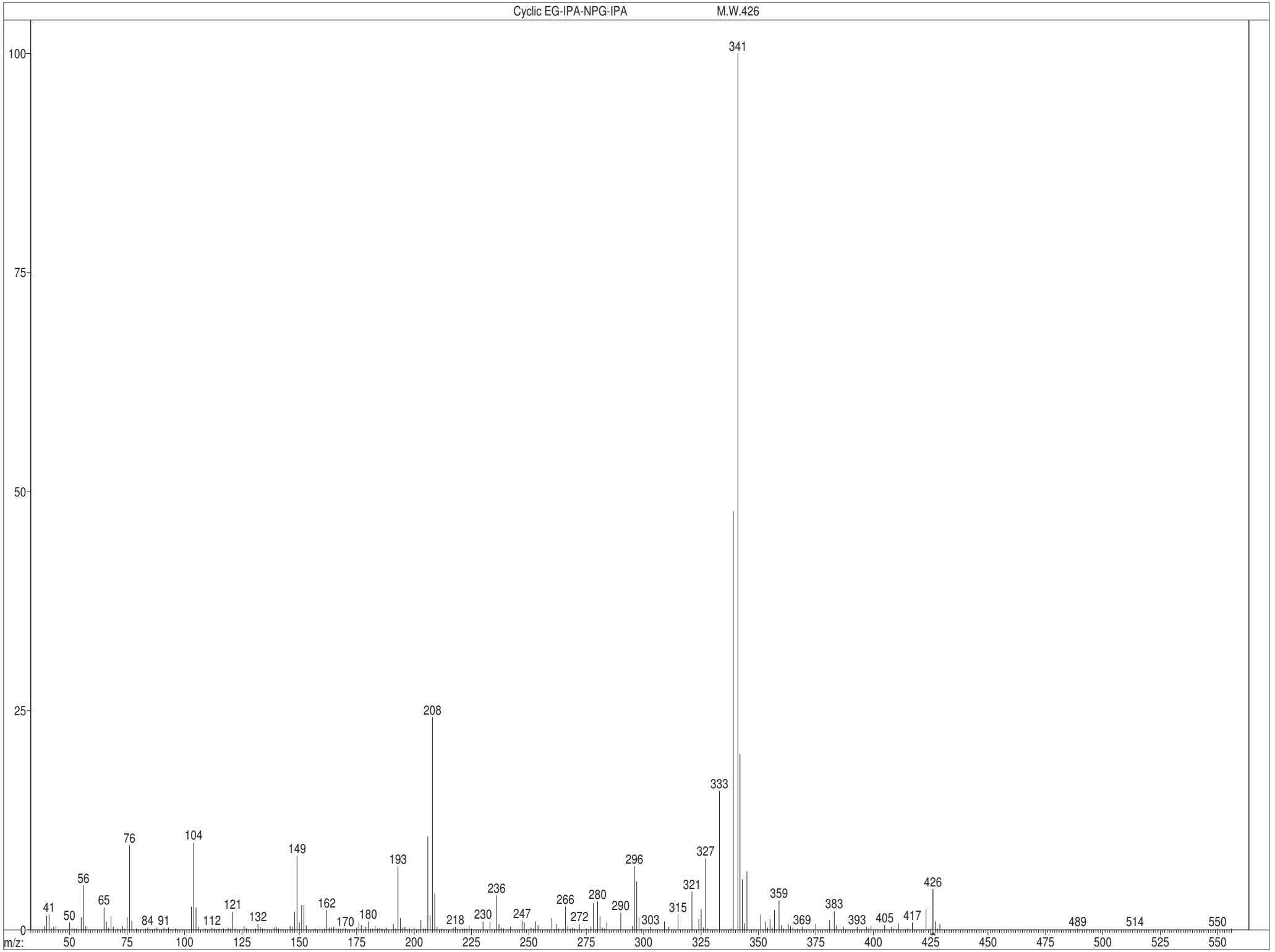
Mass Spectrum for



Mass Spectrum for

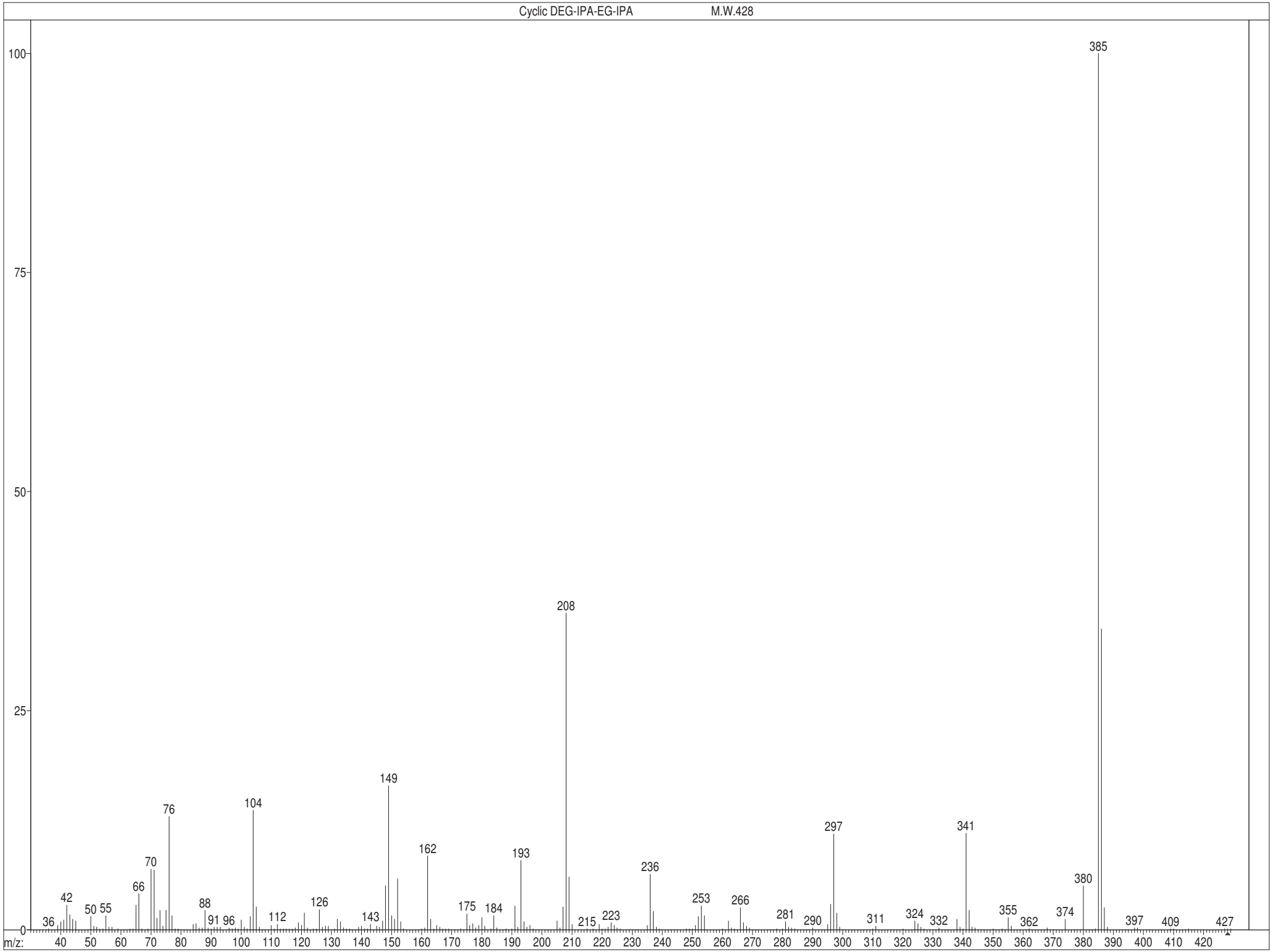


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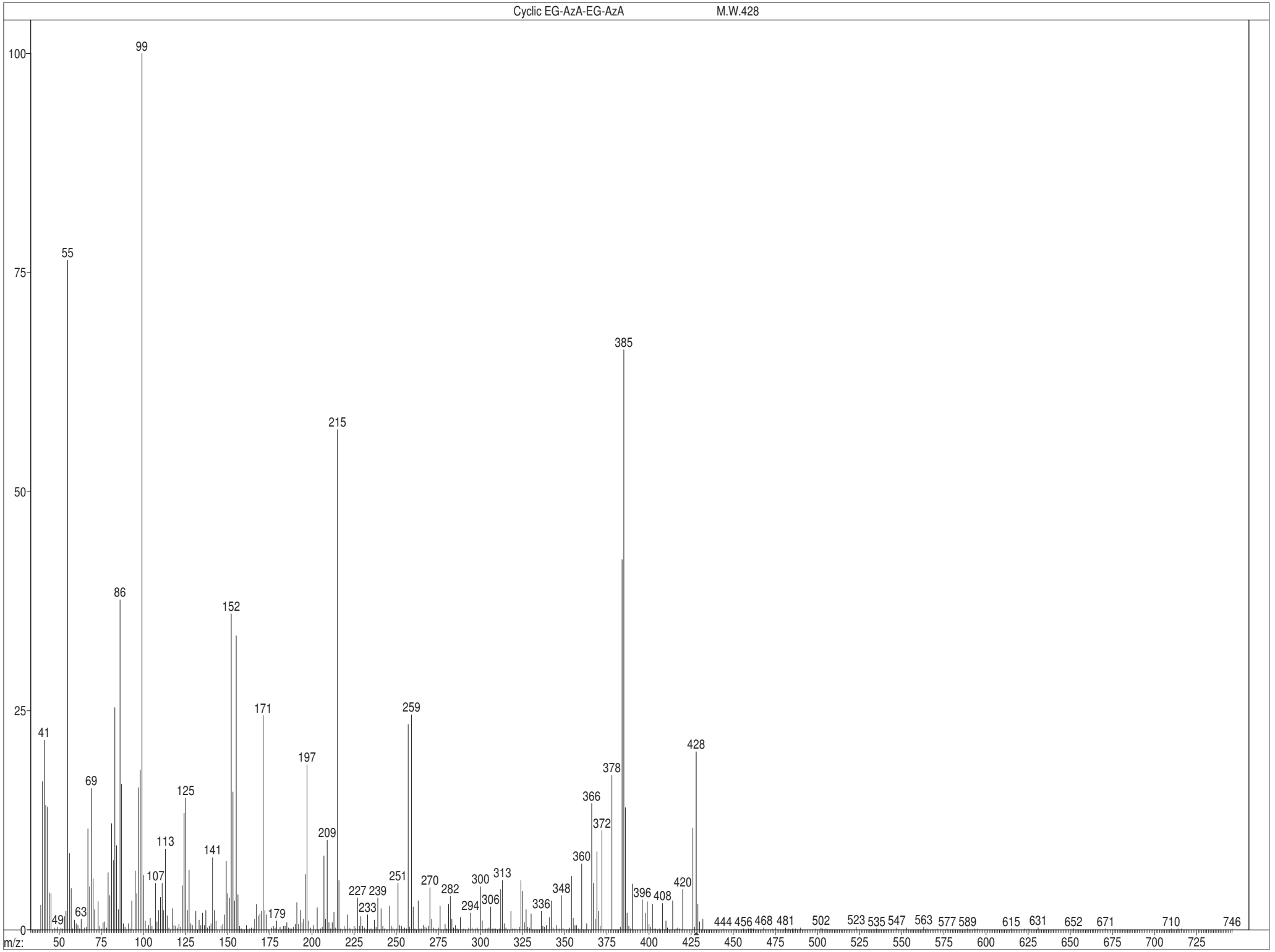
0259

Mass Spectrum for

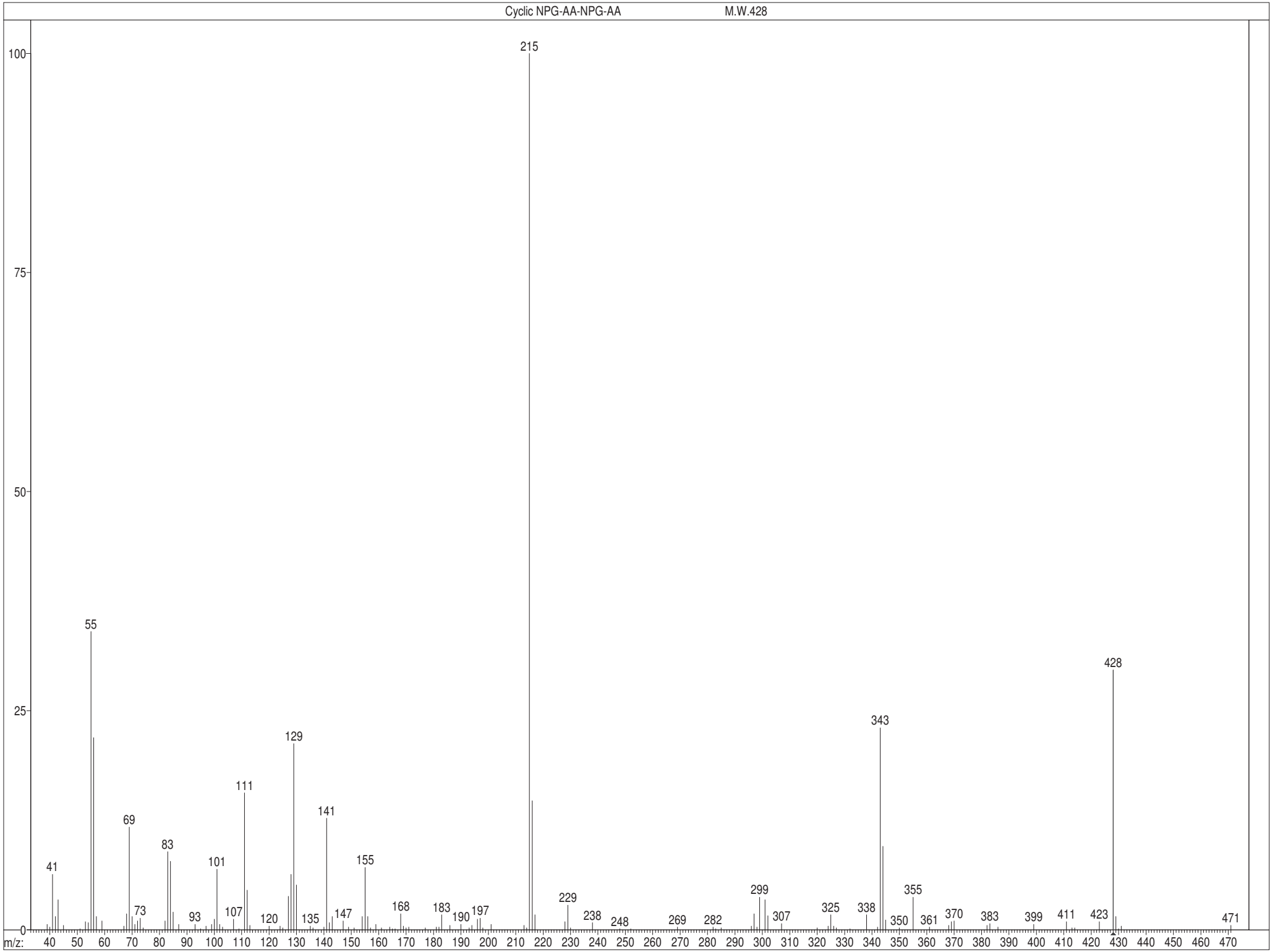


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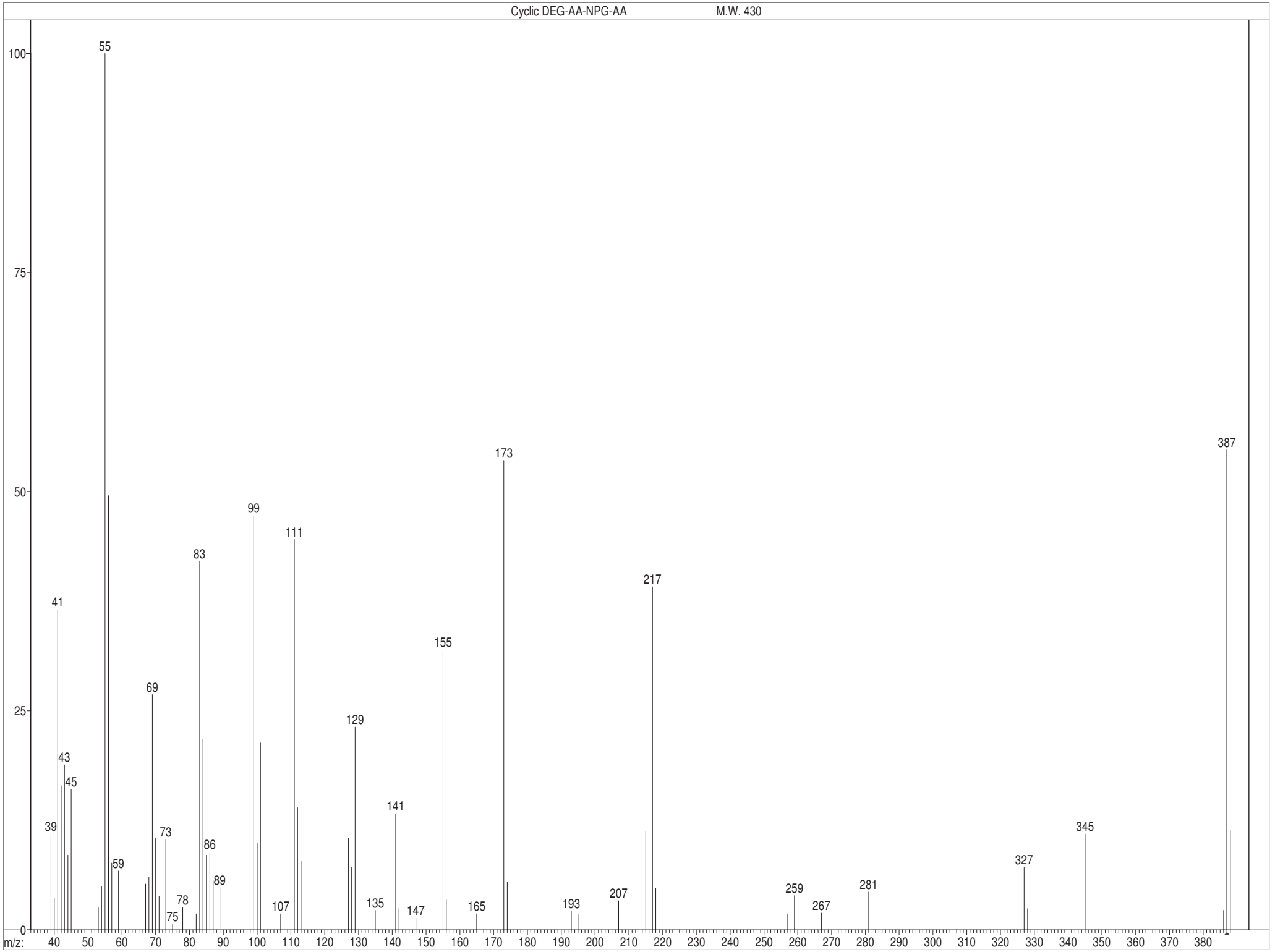
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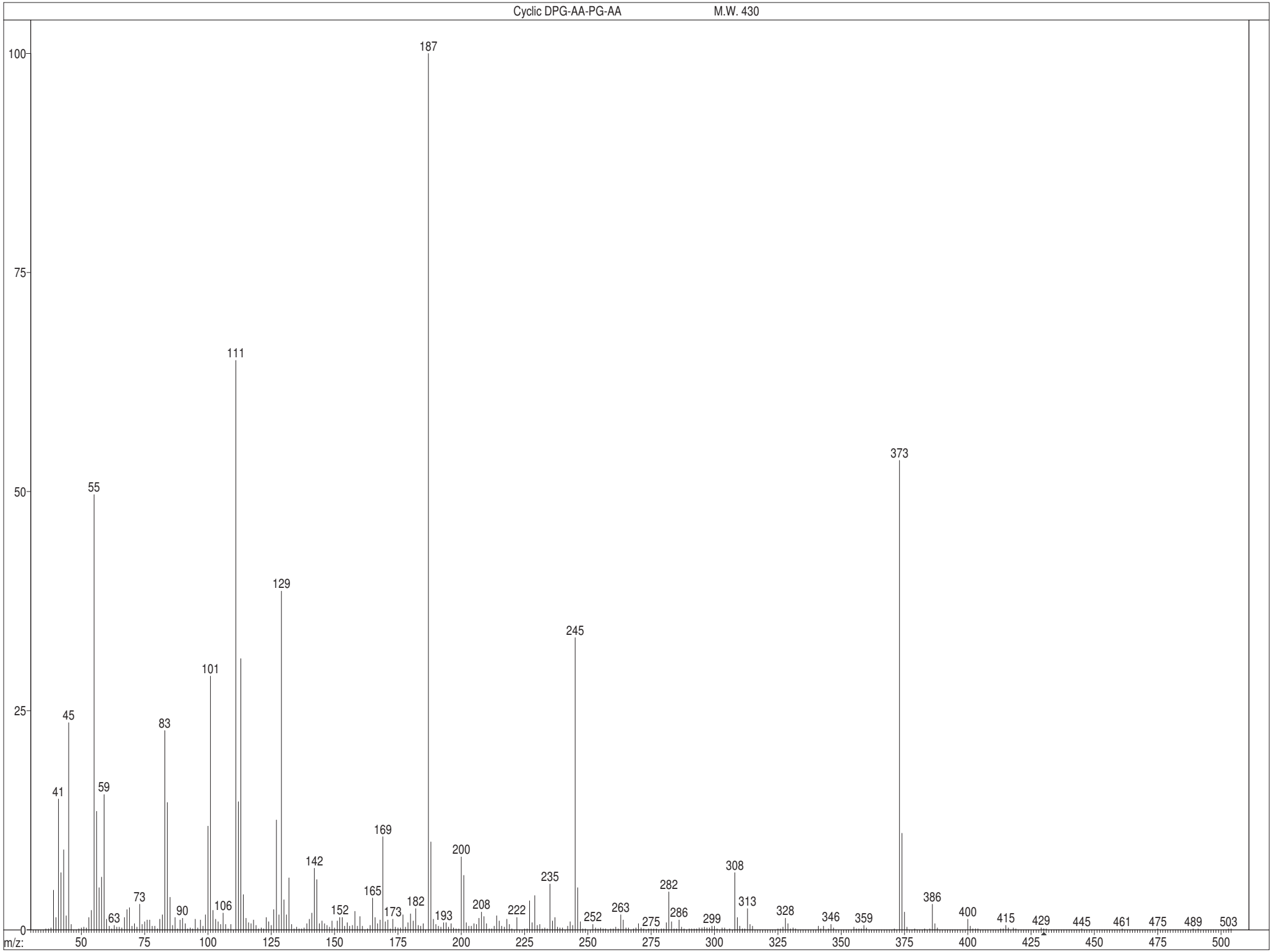
Mass Spectrum for



Mass Spectrum for

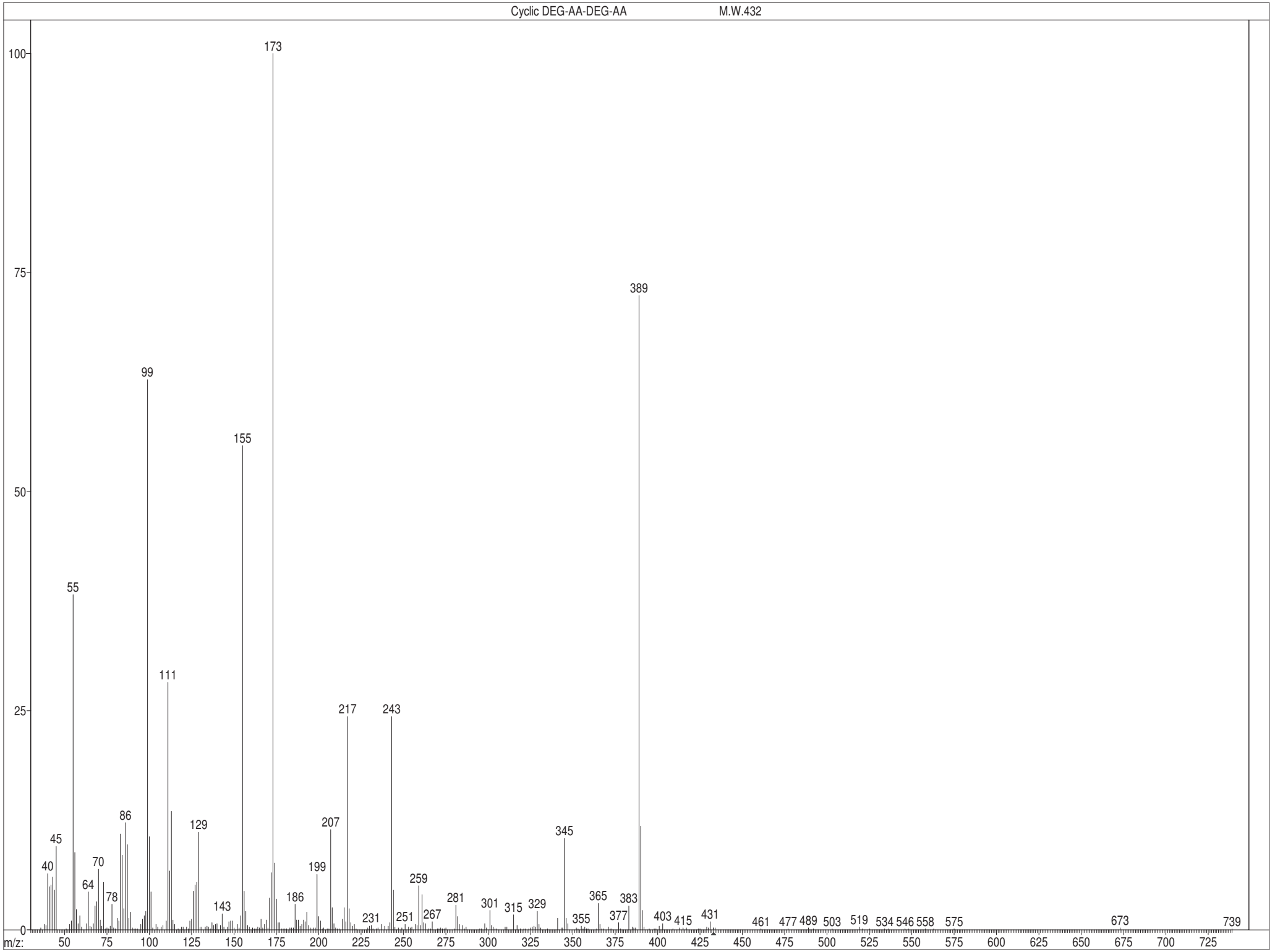


Mass Spectrum for

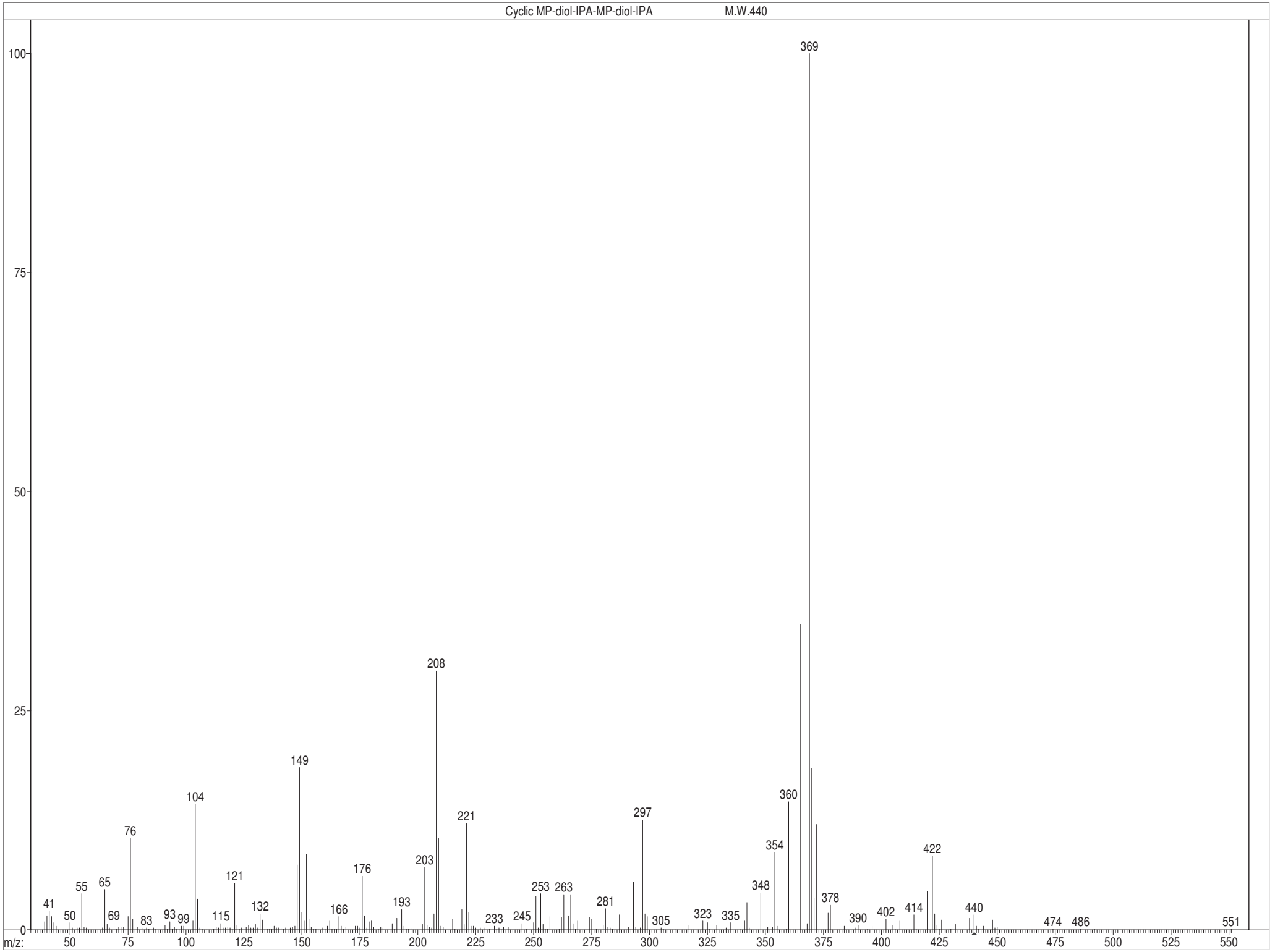


0264

Mass Spectrum for

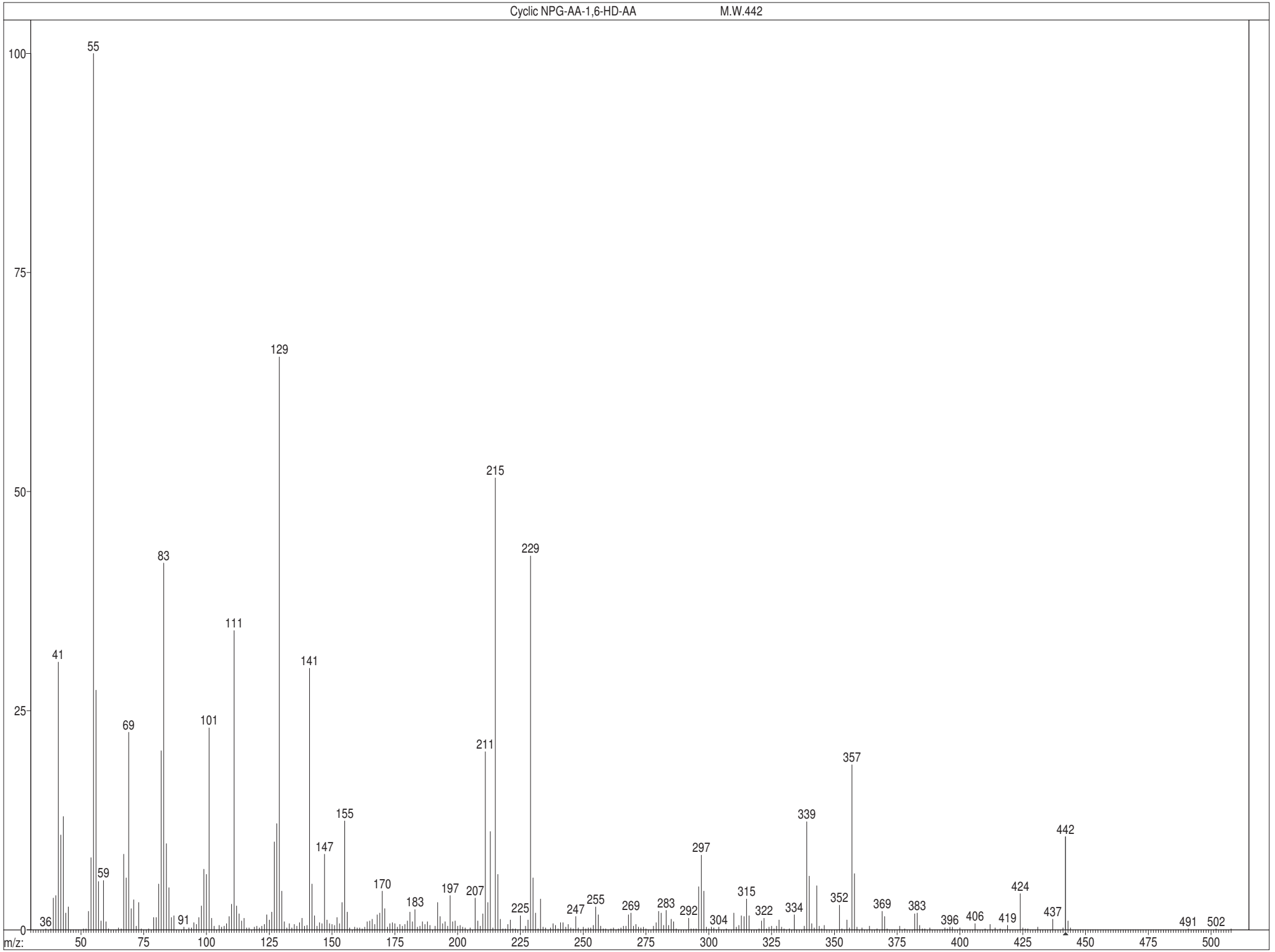


Mass Spectrum for



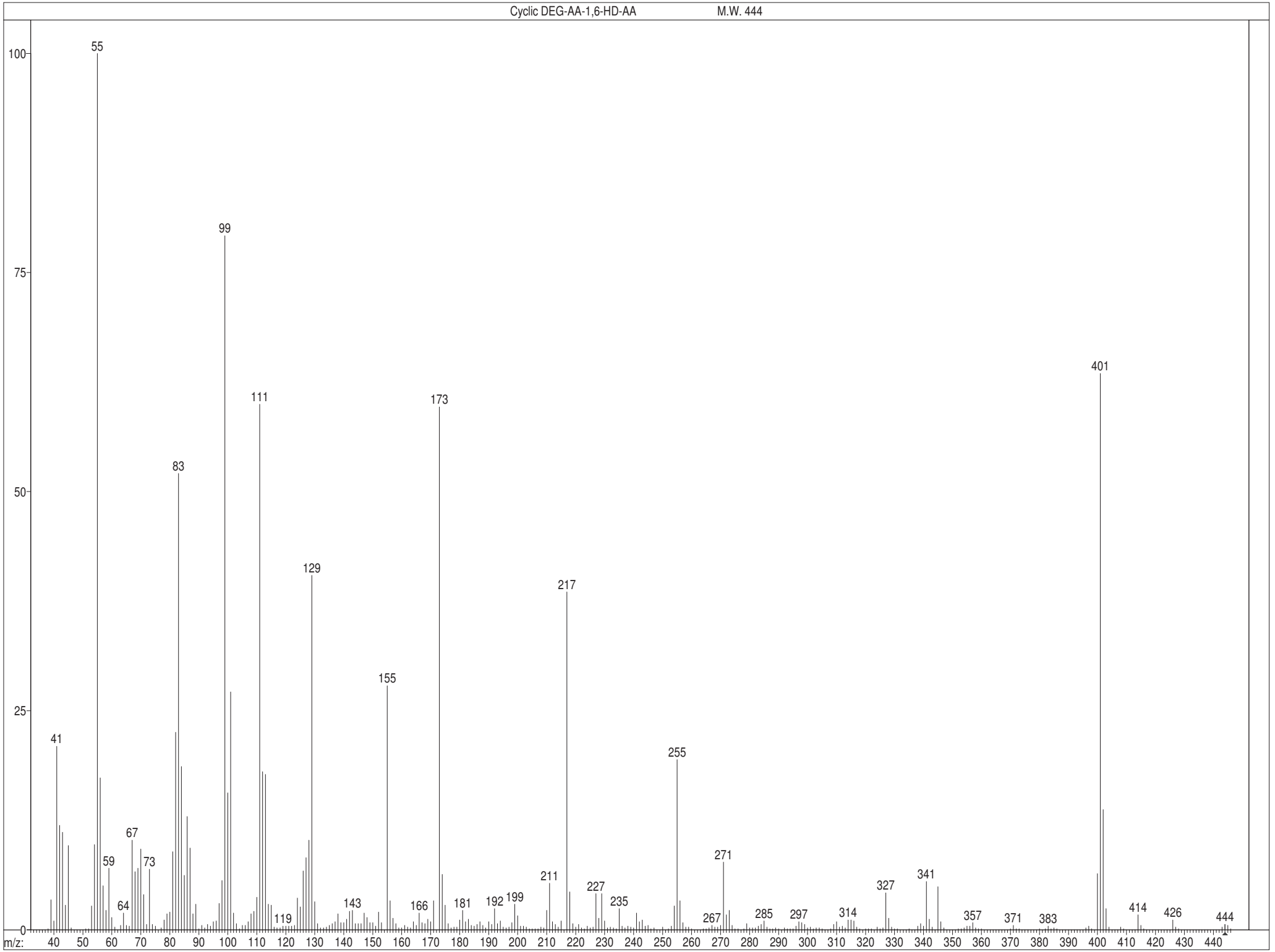
0266

Mass Spectrum for



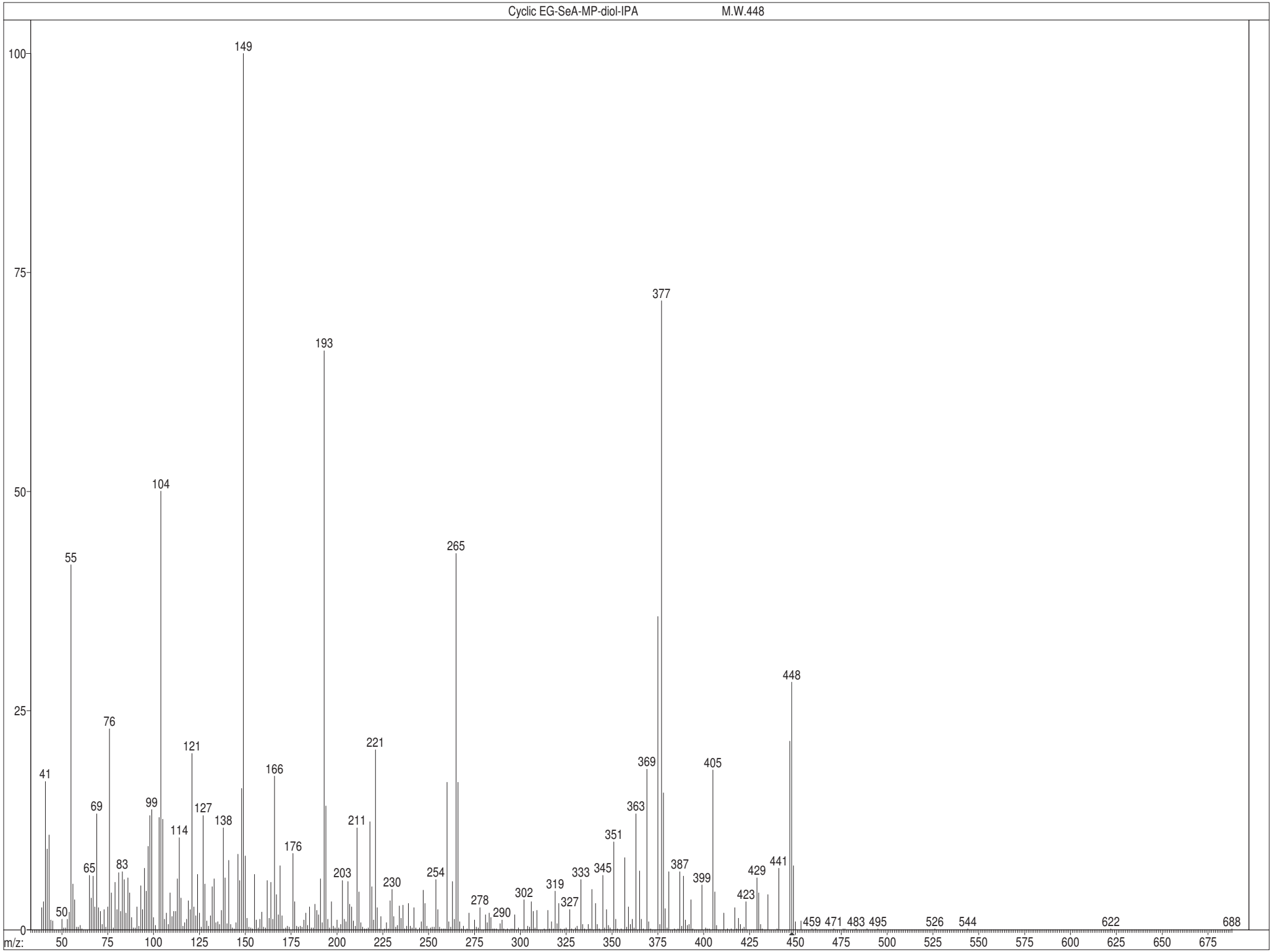
0267

Mass Spectrum for

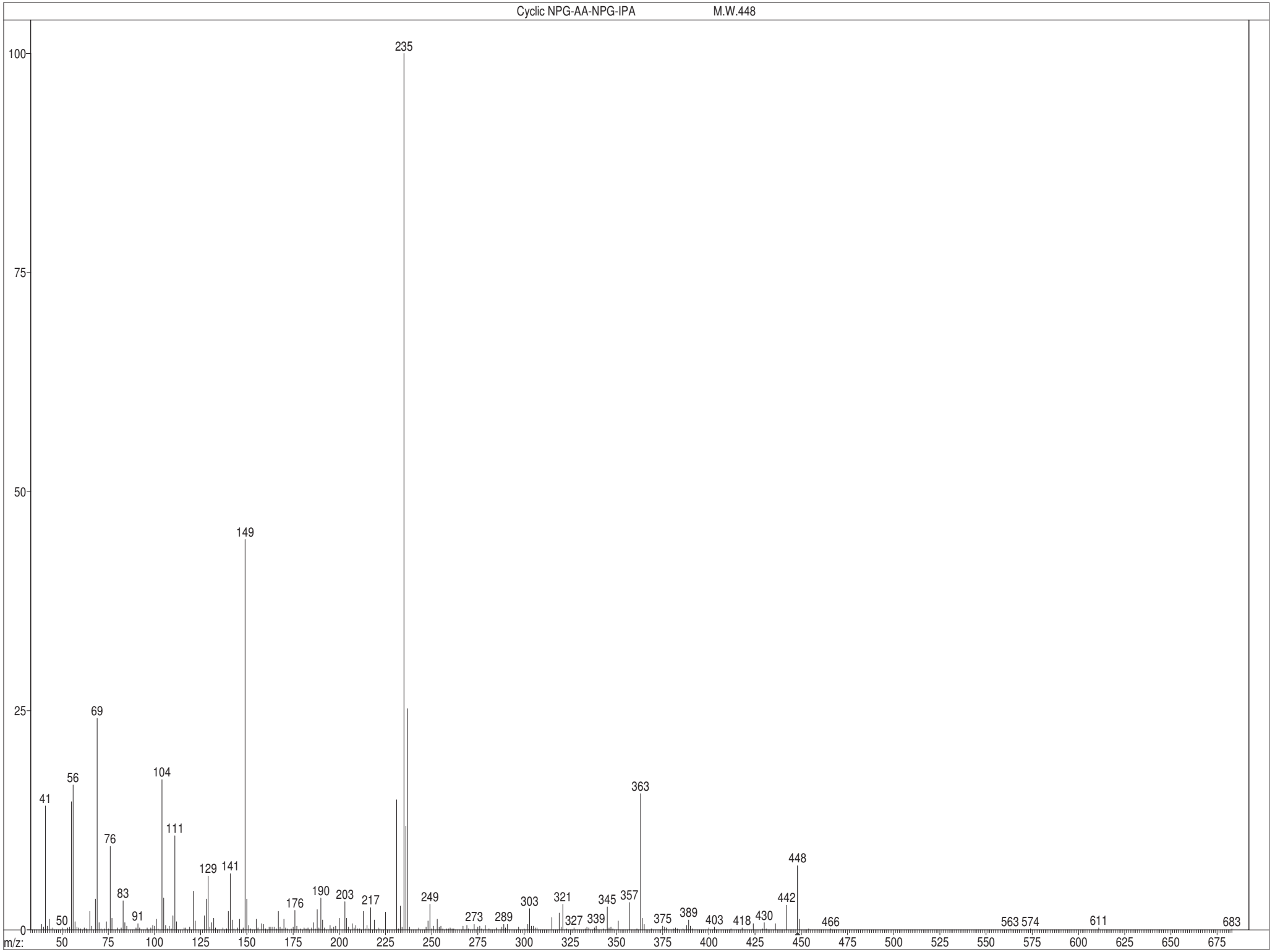


Mass Spectrum for

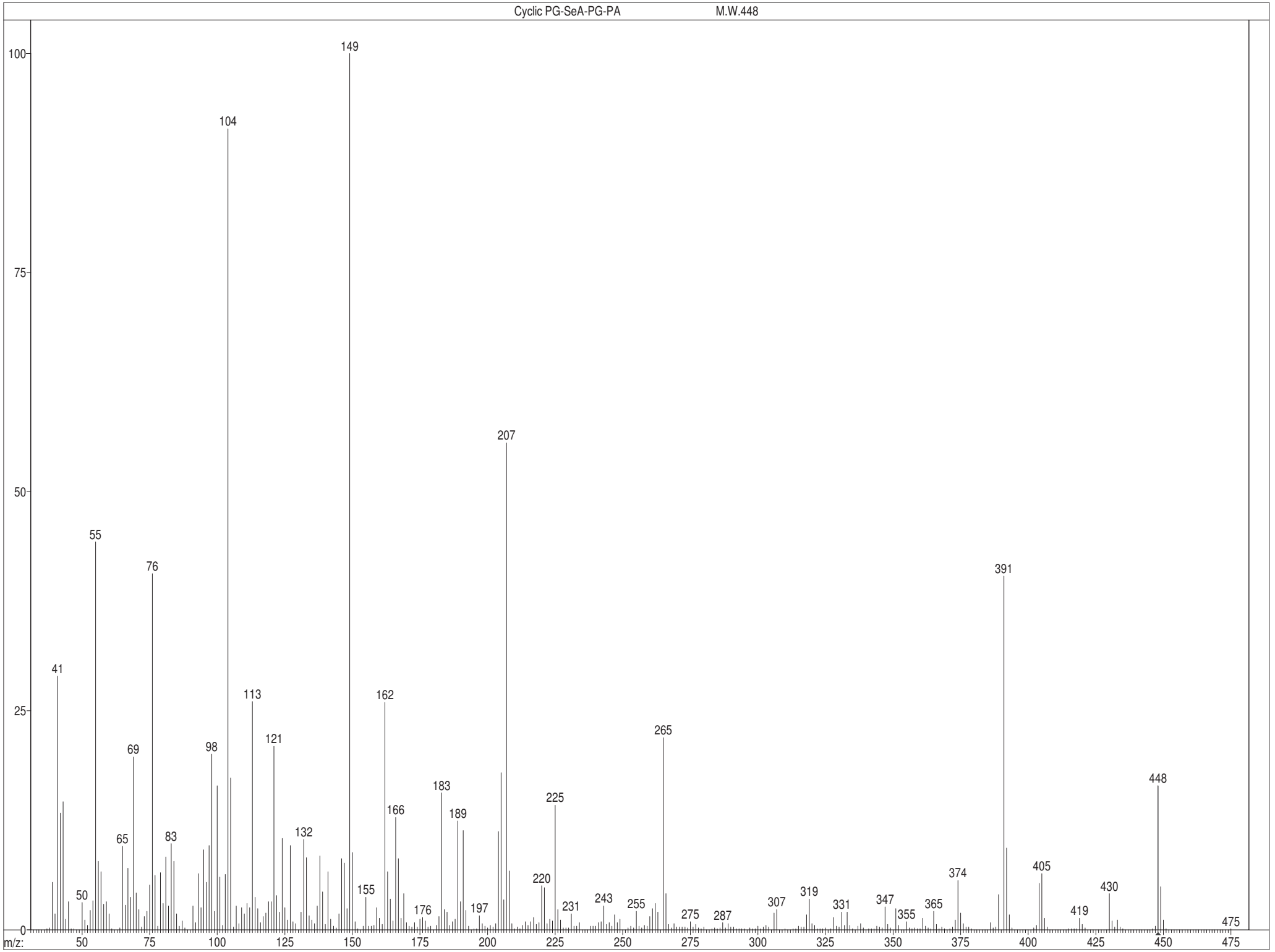
Cyclic EG-SeA-MP-diol-IPA M.W.448



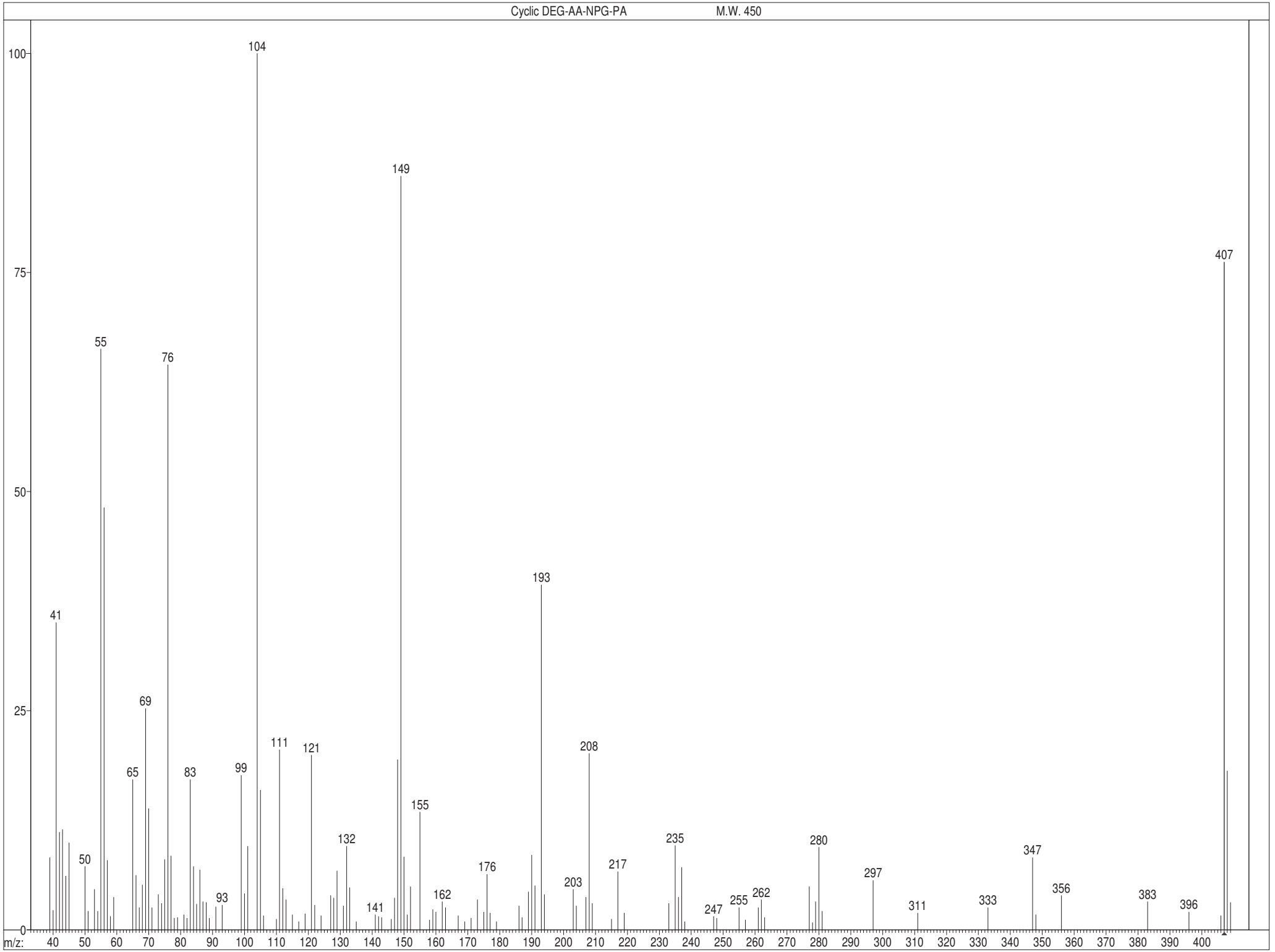
Mass Spectrum for



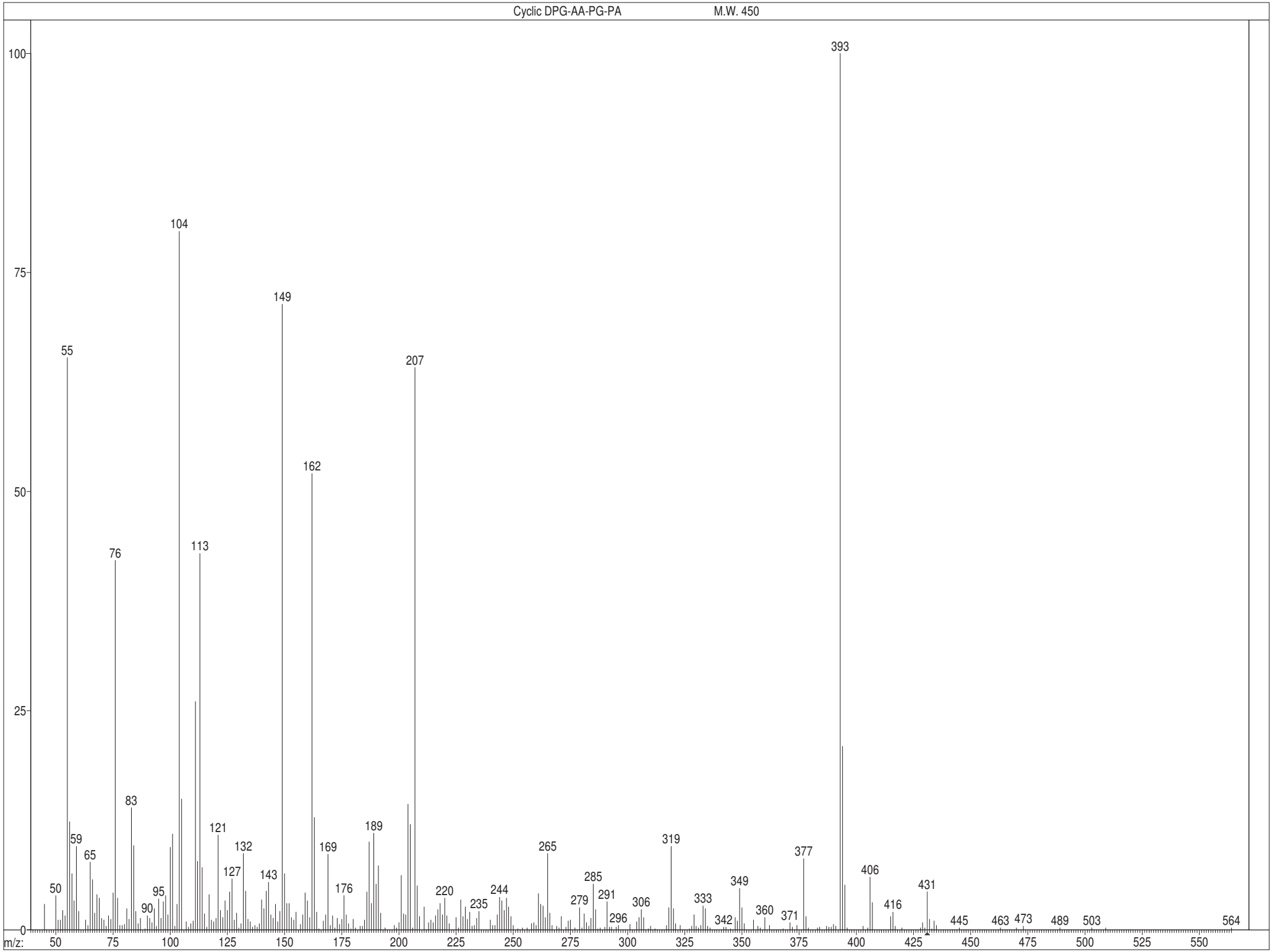
Mass Spectrum for



Mass Spectrum for

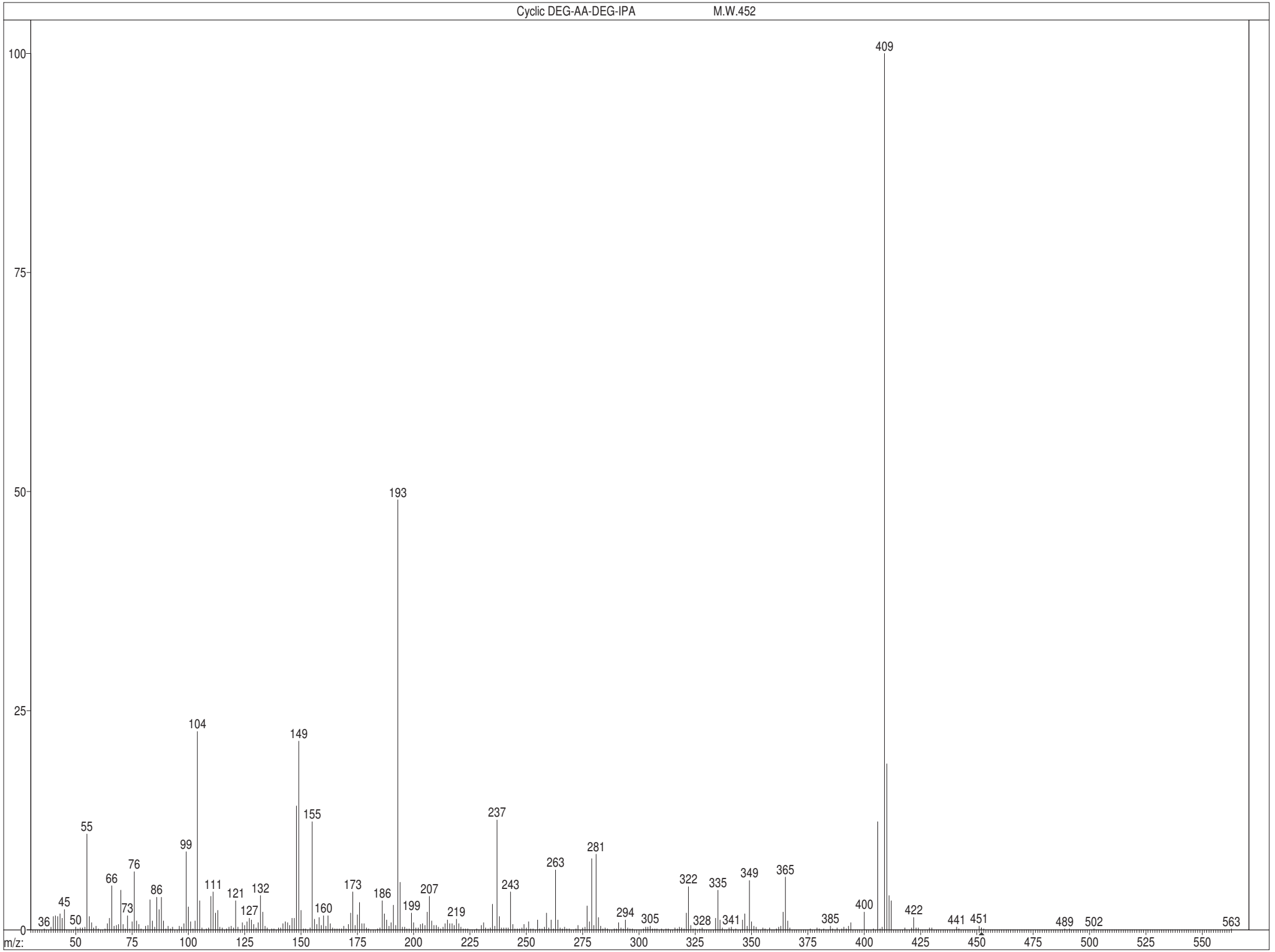


Mass Spectrum for



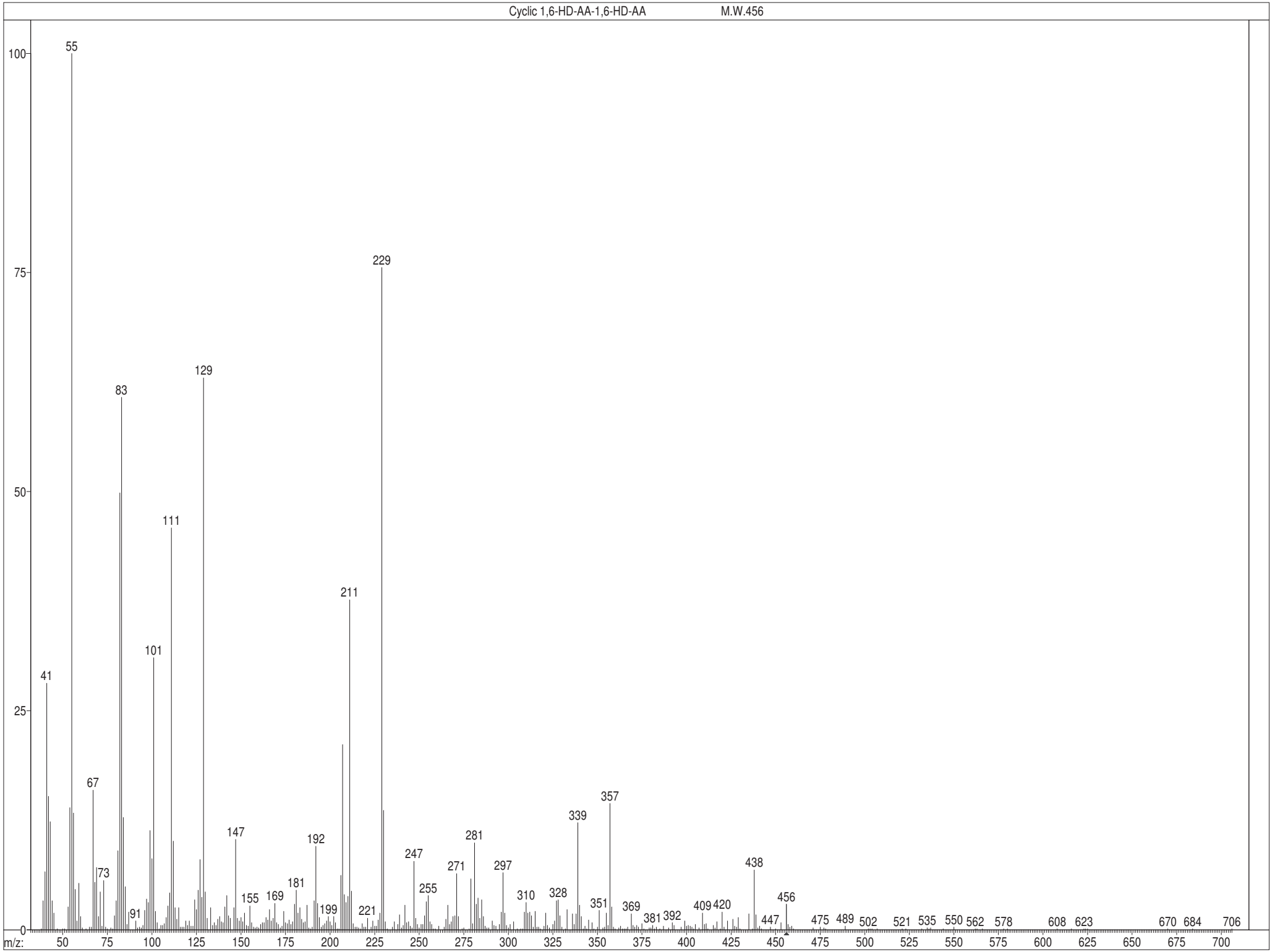
0273

Mass Spectrum for



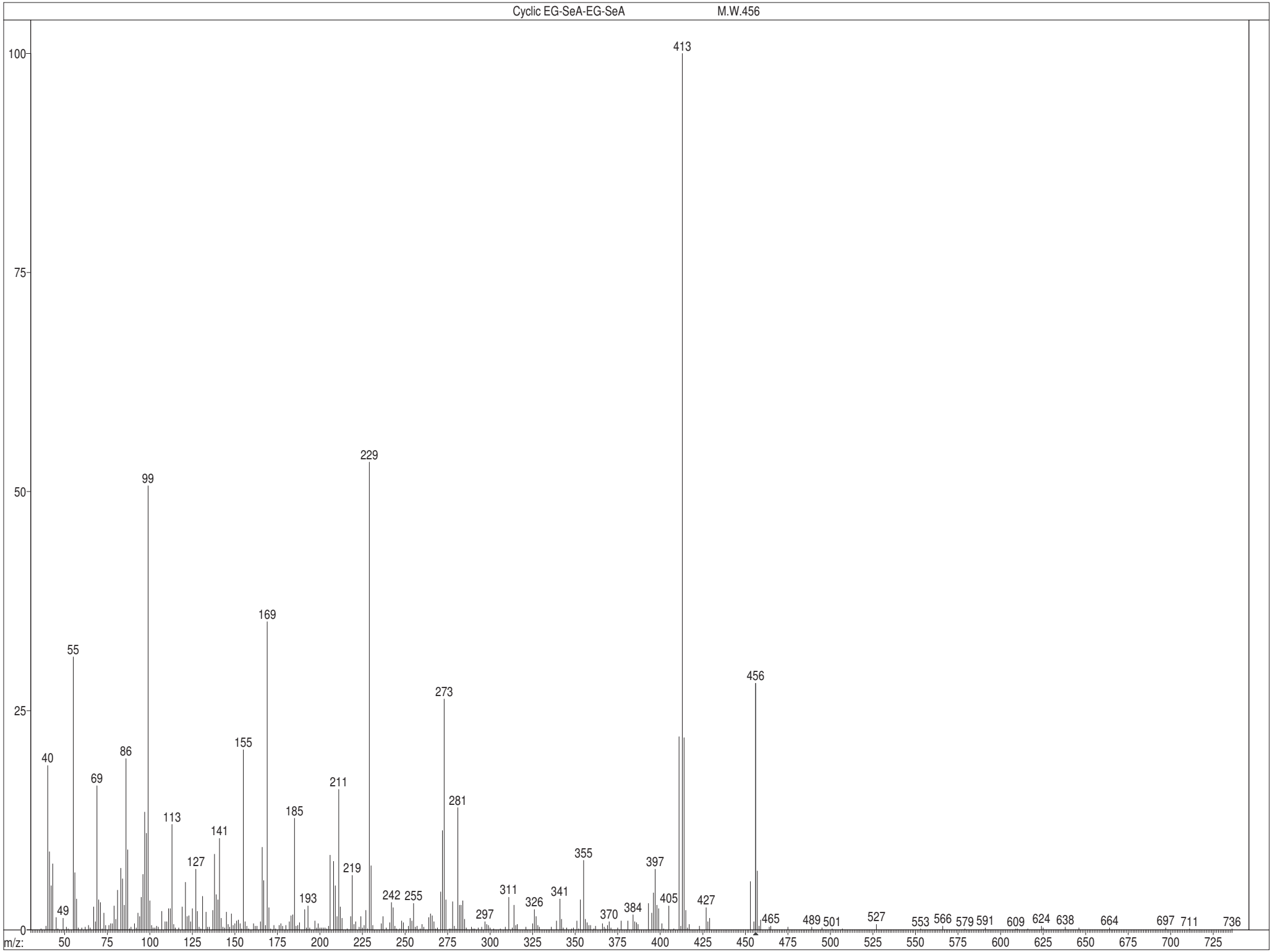
0274

Mass Spectrum for



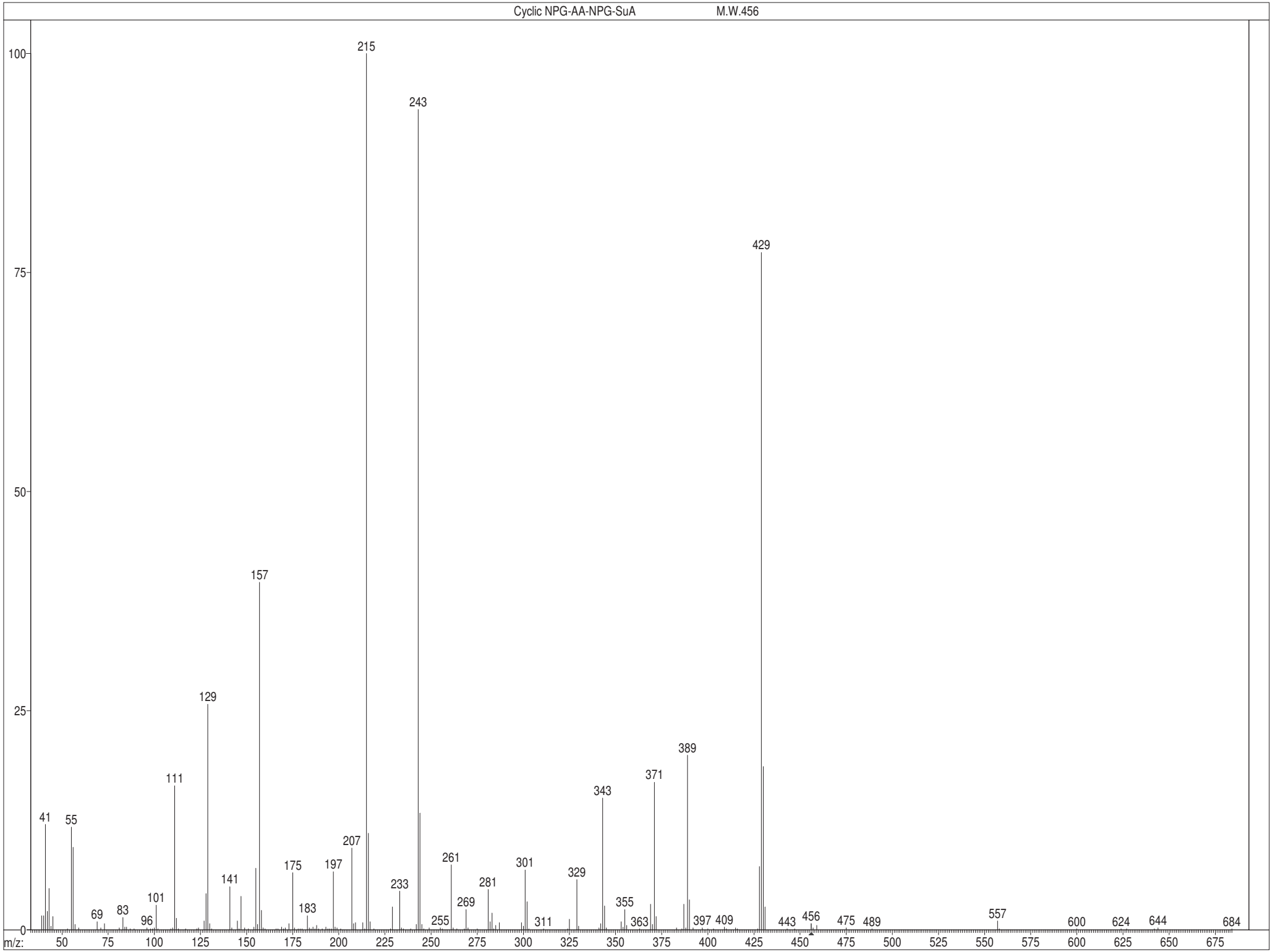
0275

Mass Spectrum for



0276

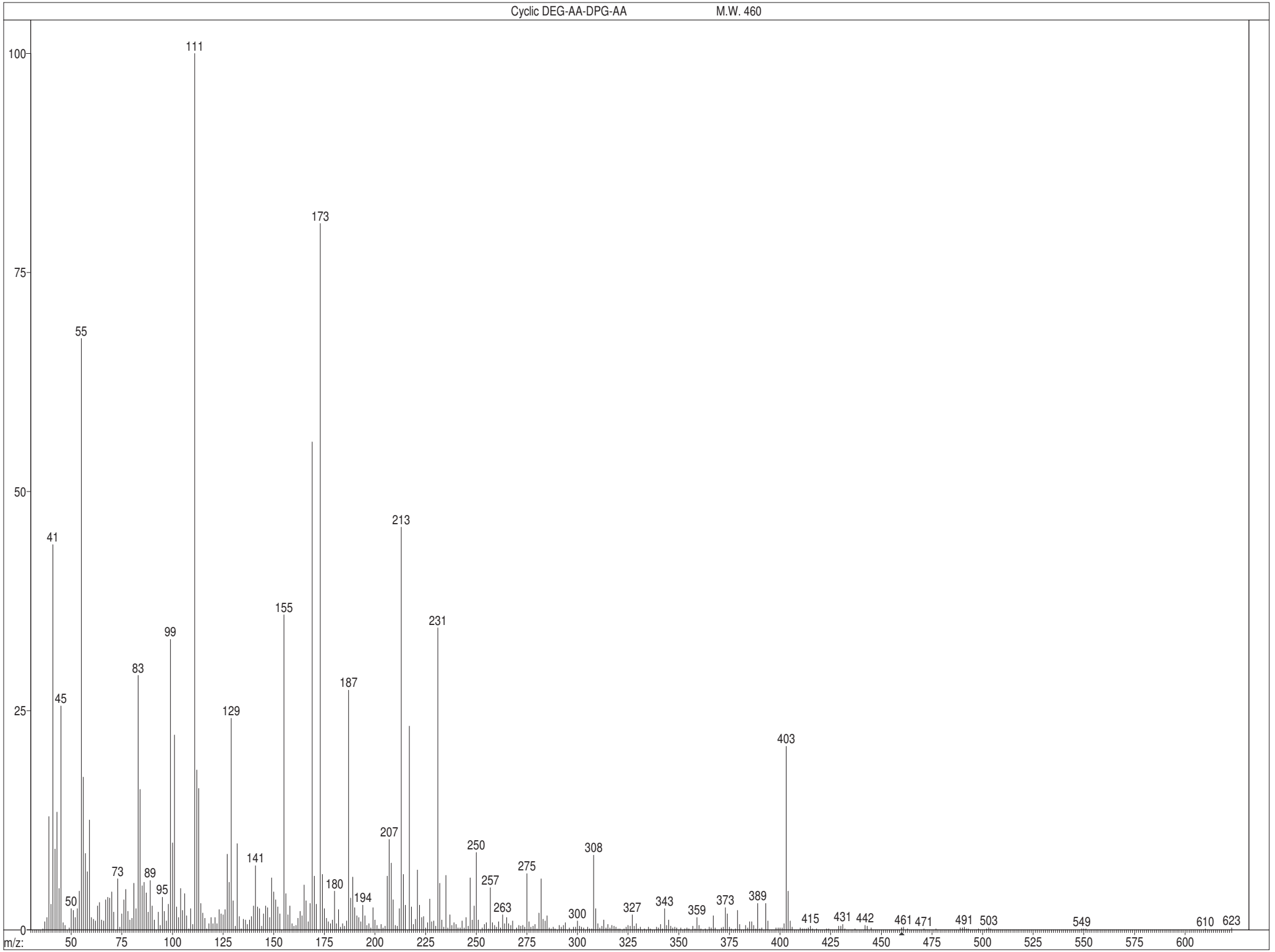
Mass Spectrum for



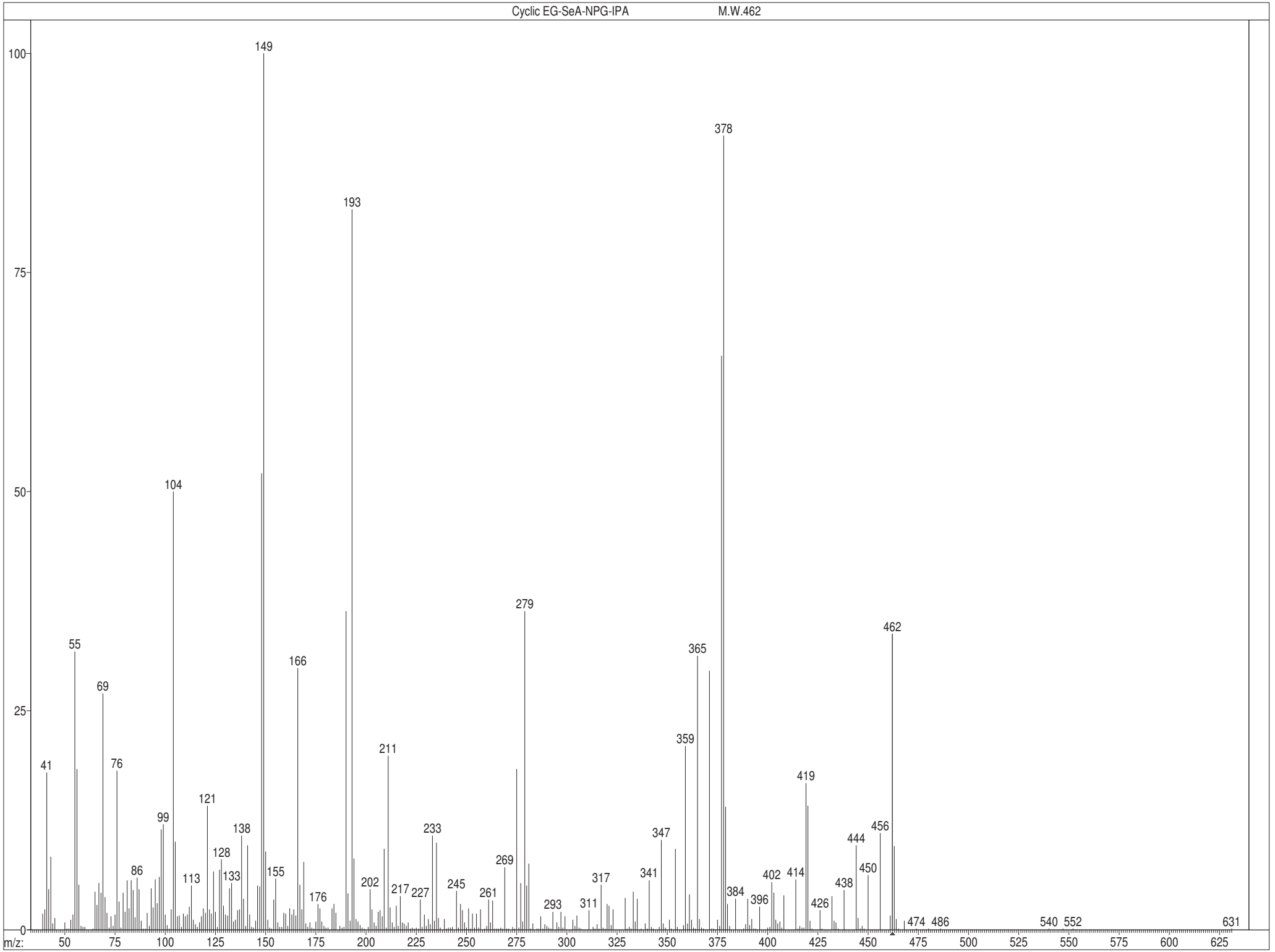
0277

Mass Spectrum for

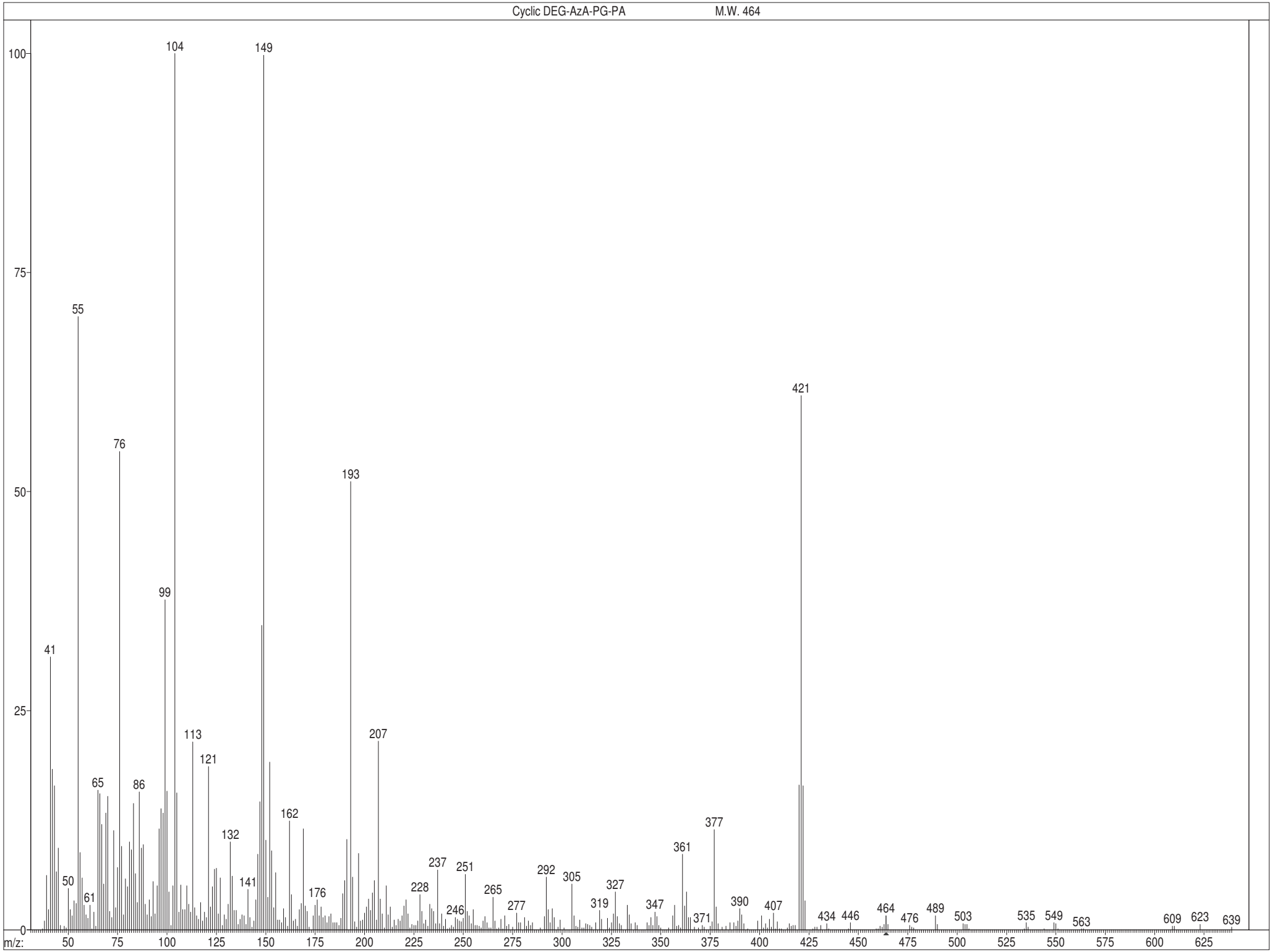
Cyclic DEG-AA-DPG-AA M.W. 460



Mass Spectrum for

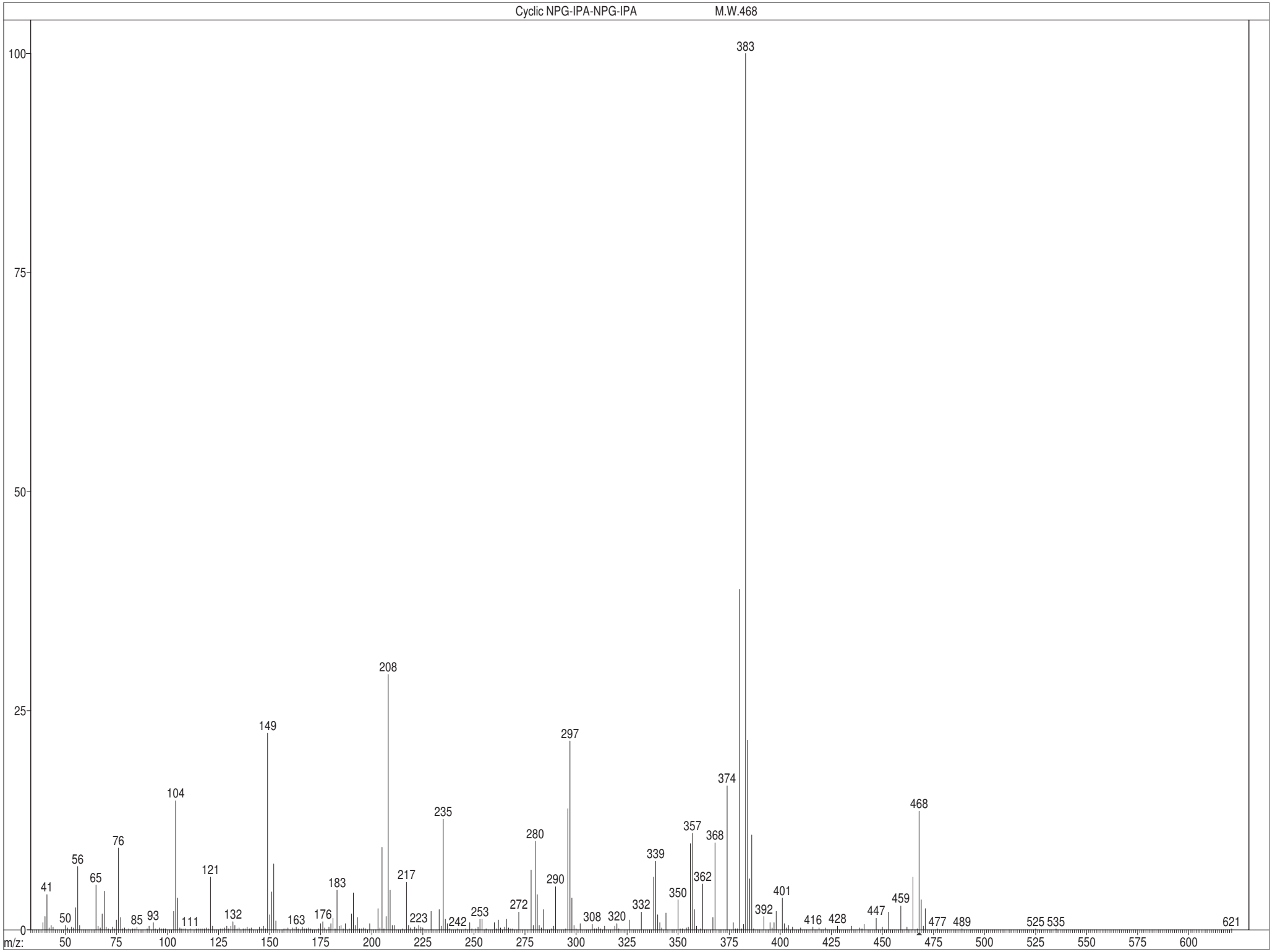


Mass Spectrum for



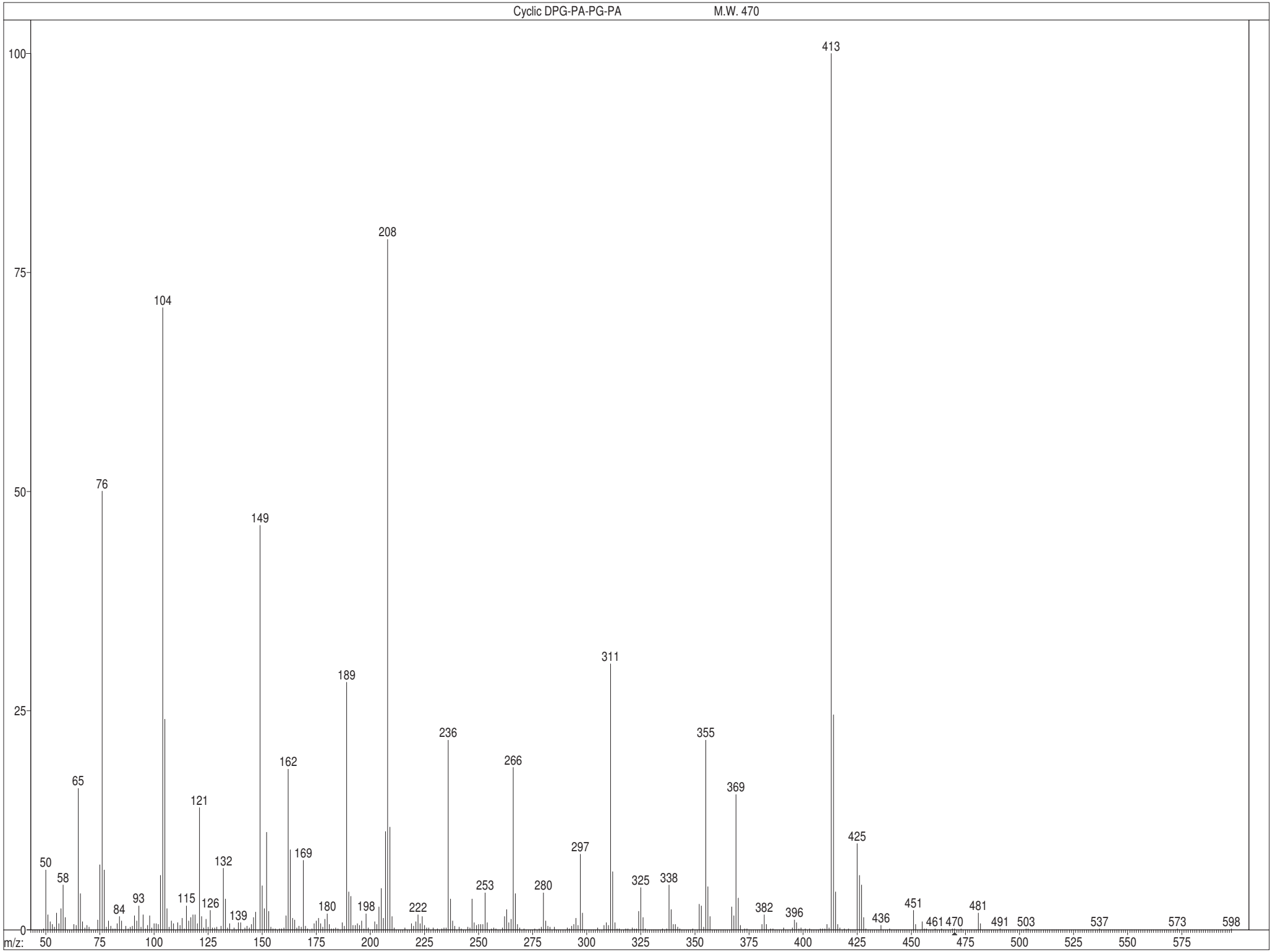
0280

Mass Spectrum for



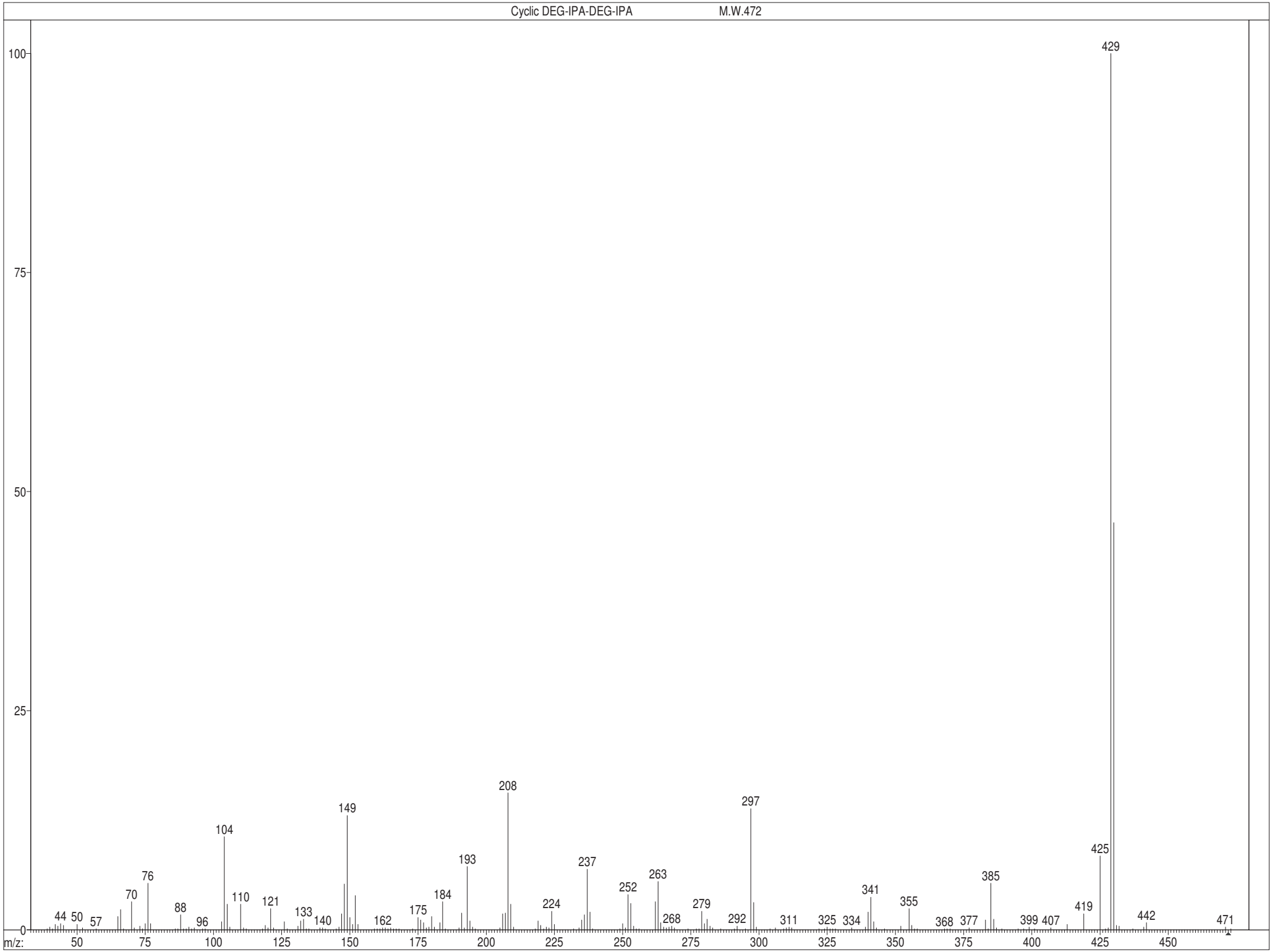
0281

Mass Spectrum for



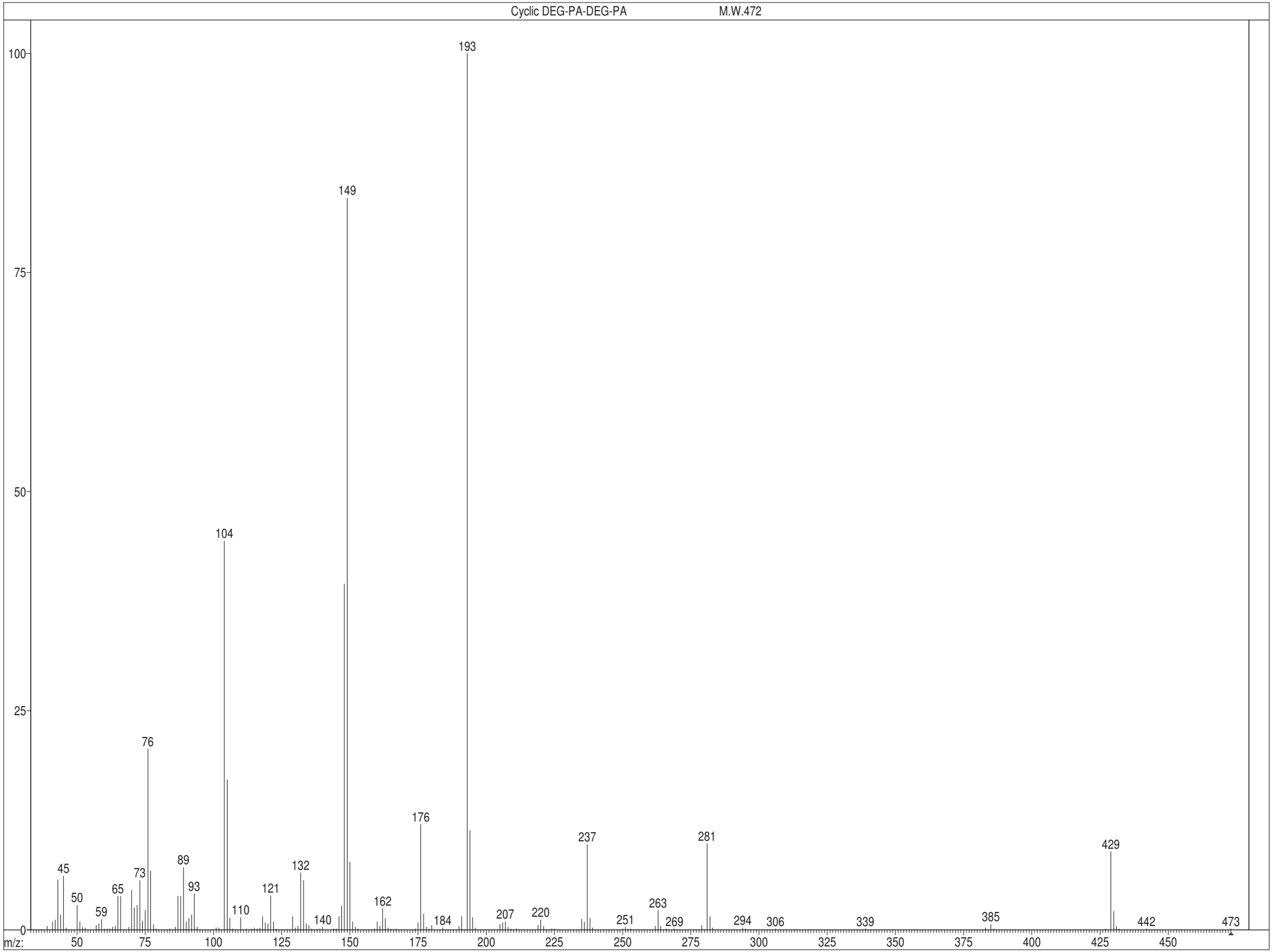
0282

Mass Spectrum for



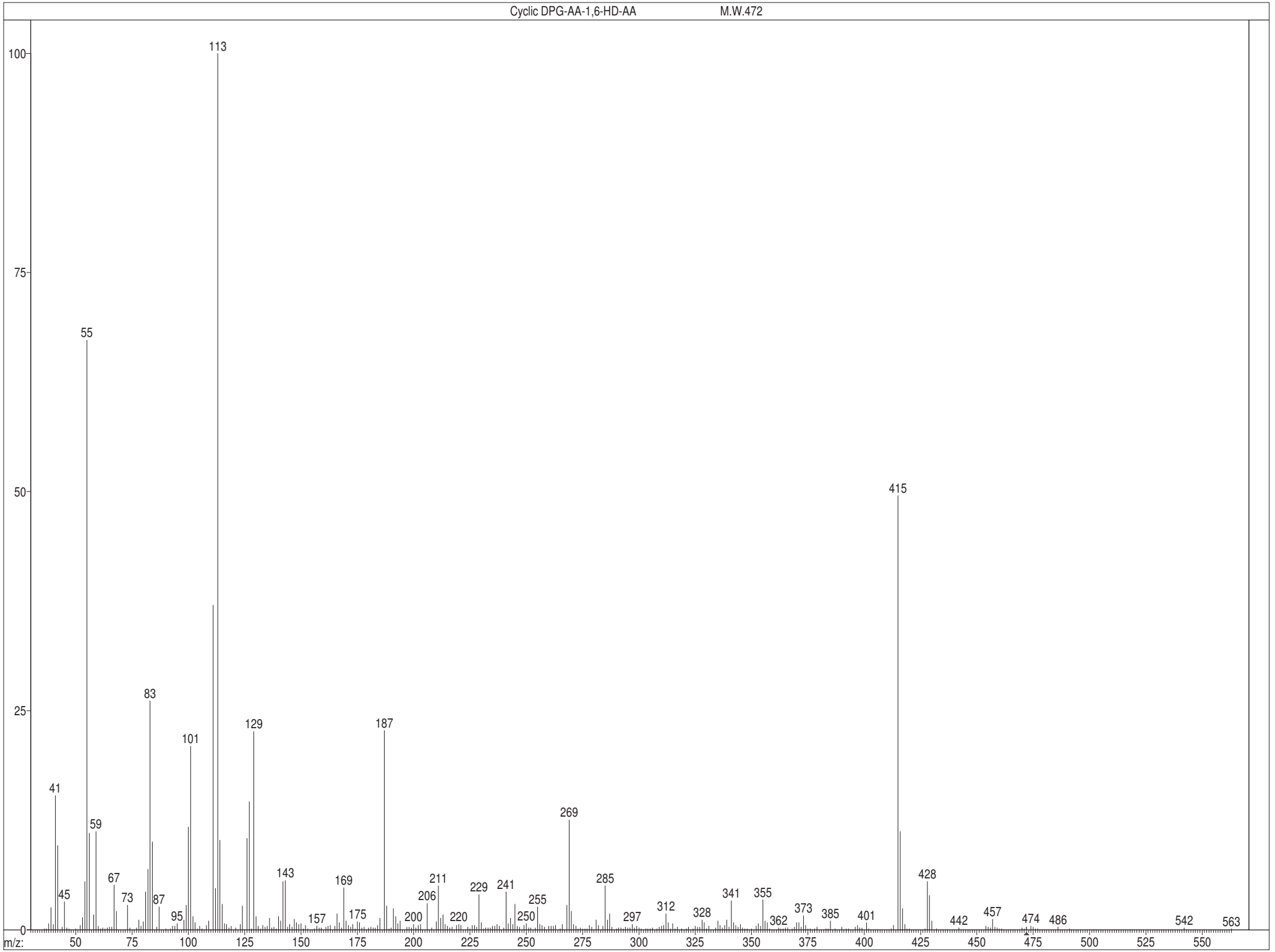
0283

Mass Spectrum for

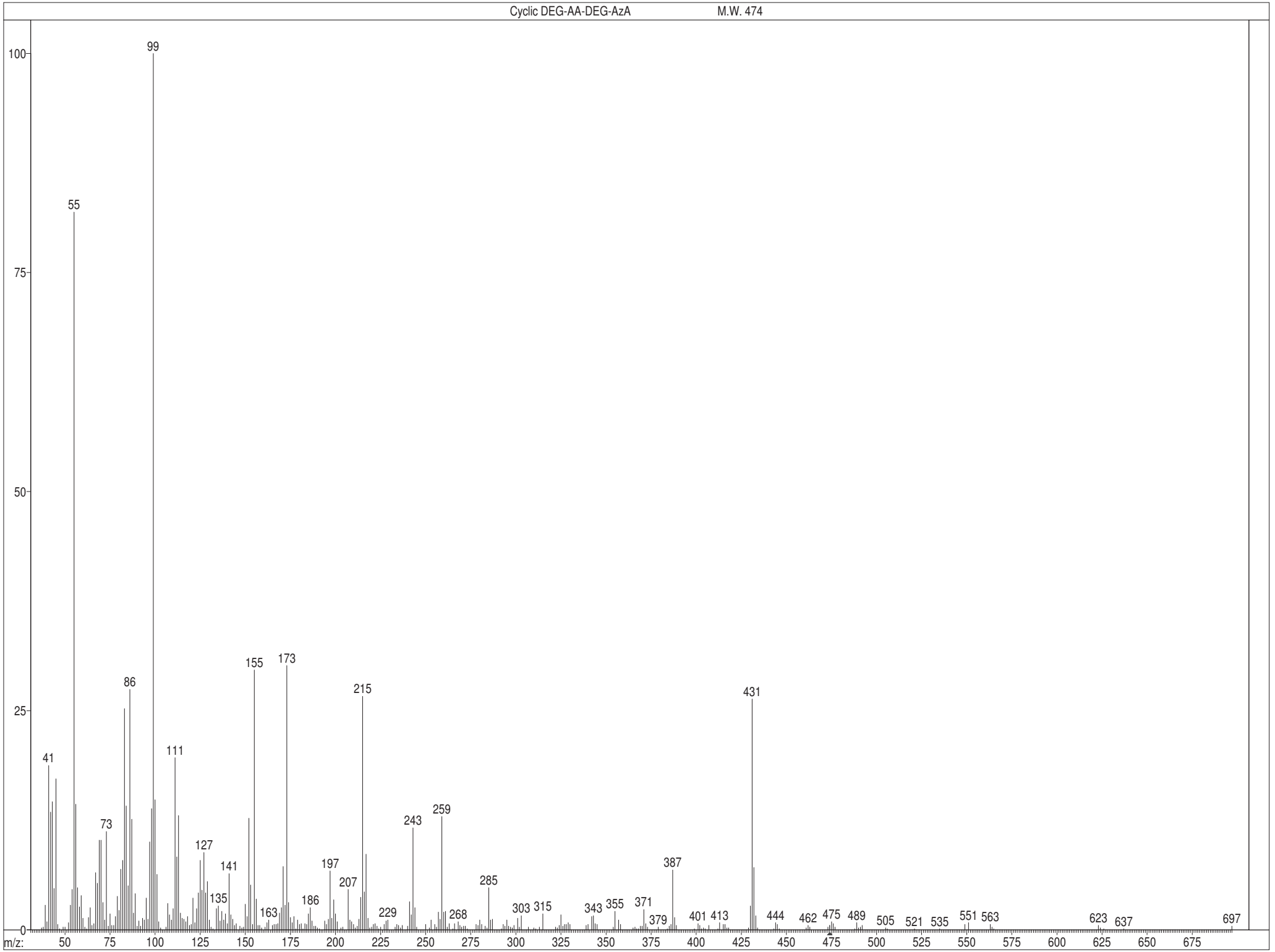


Mass Spectrum for

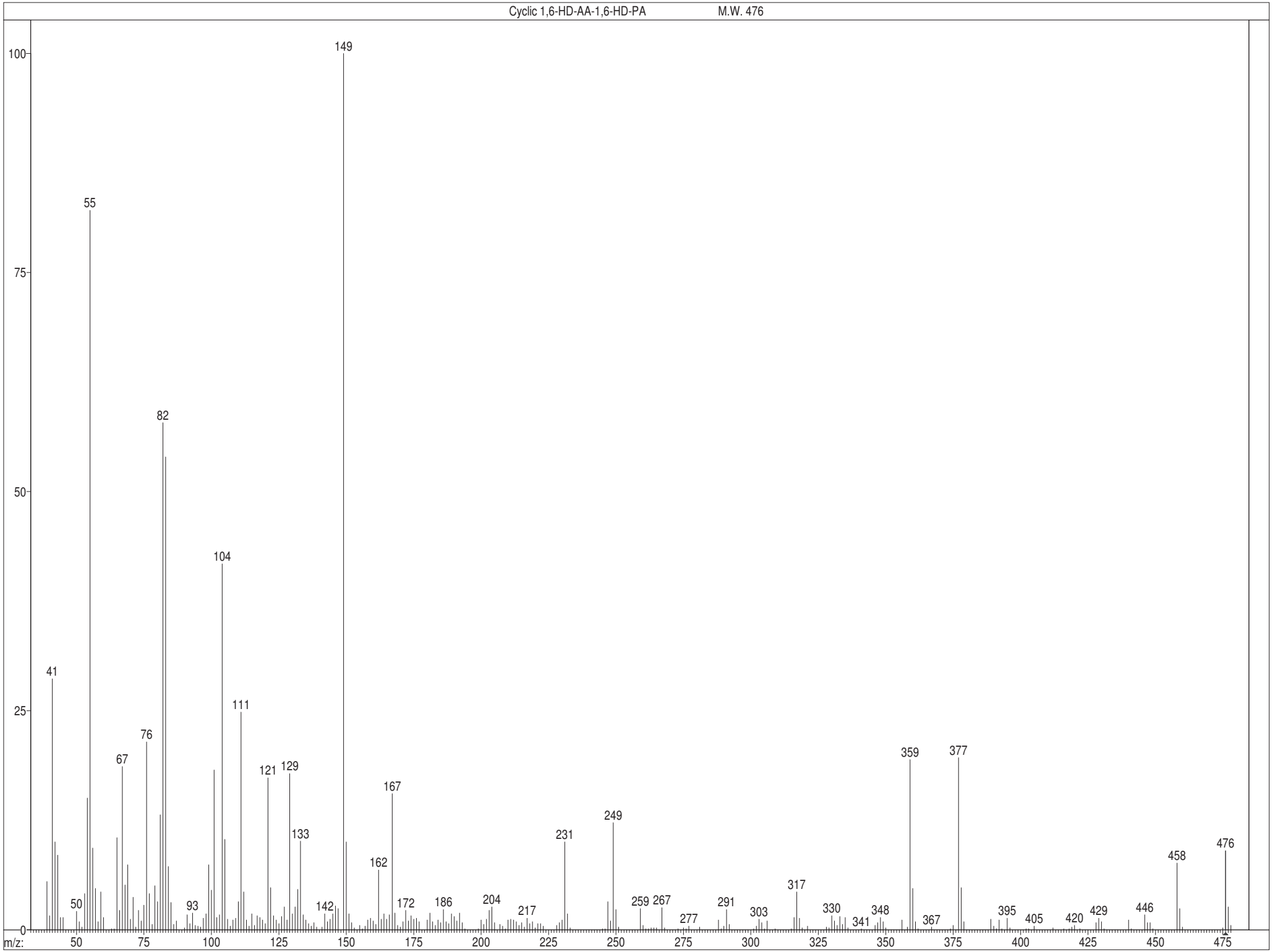
Cyclic DPG-AA-1,6-HD-AA M.W.472



Mass Spectrum for

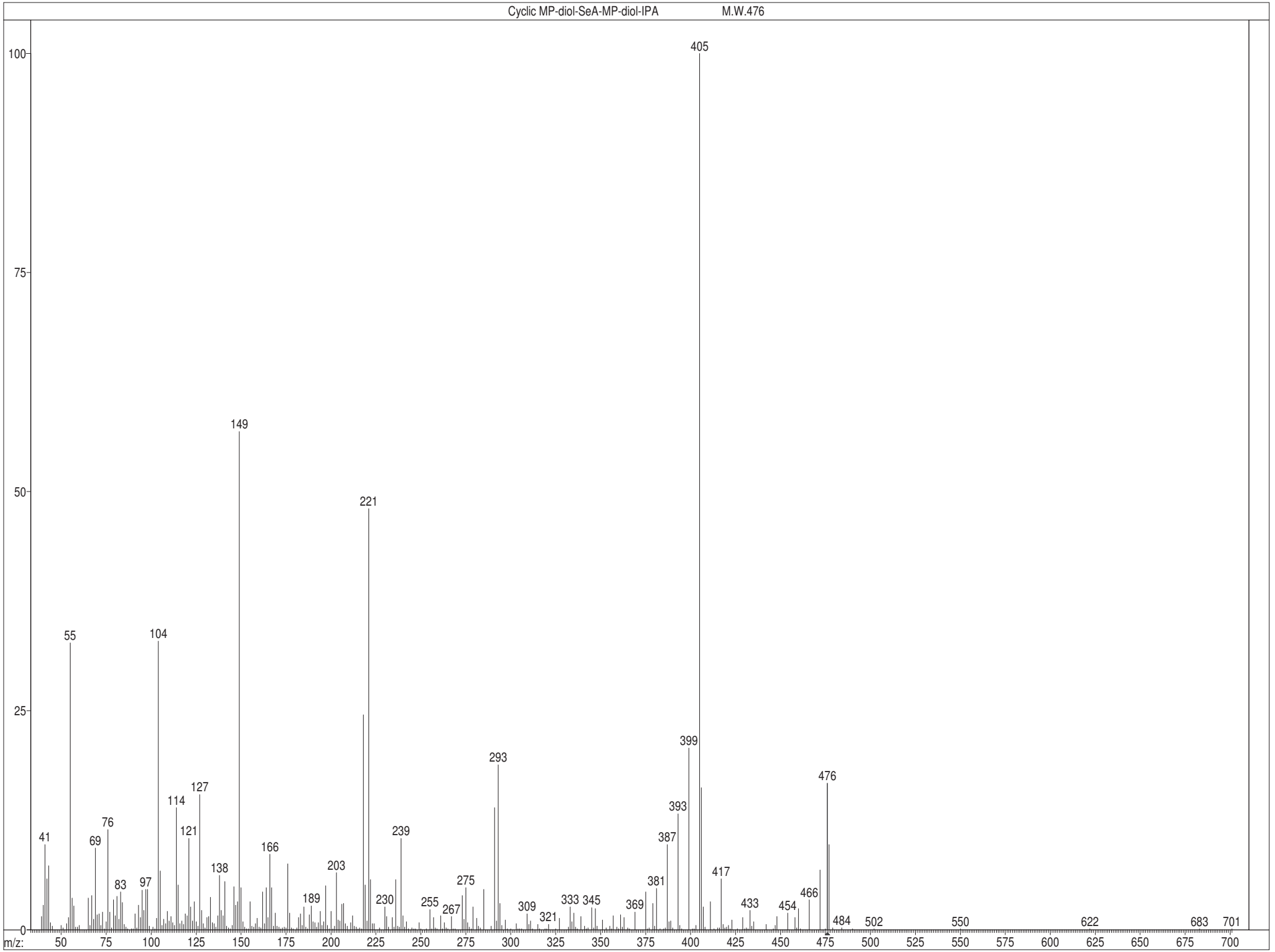


Mass Spectrum for

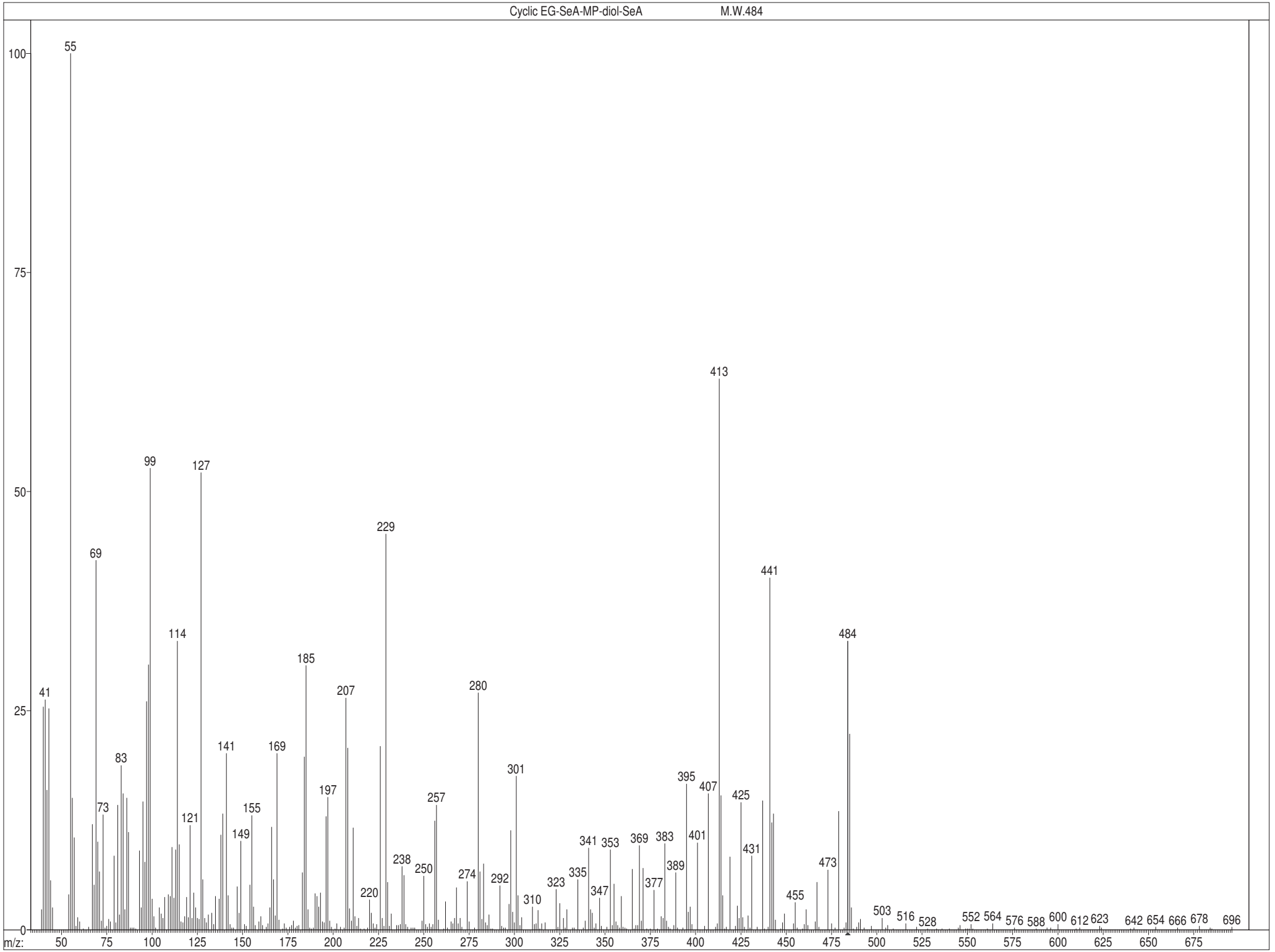


0287

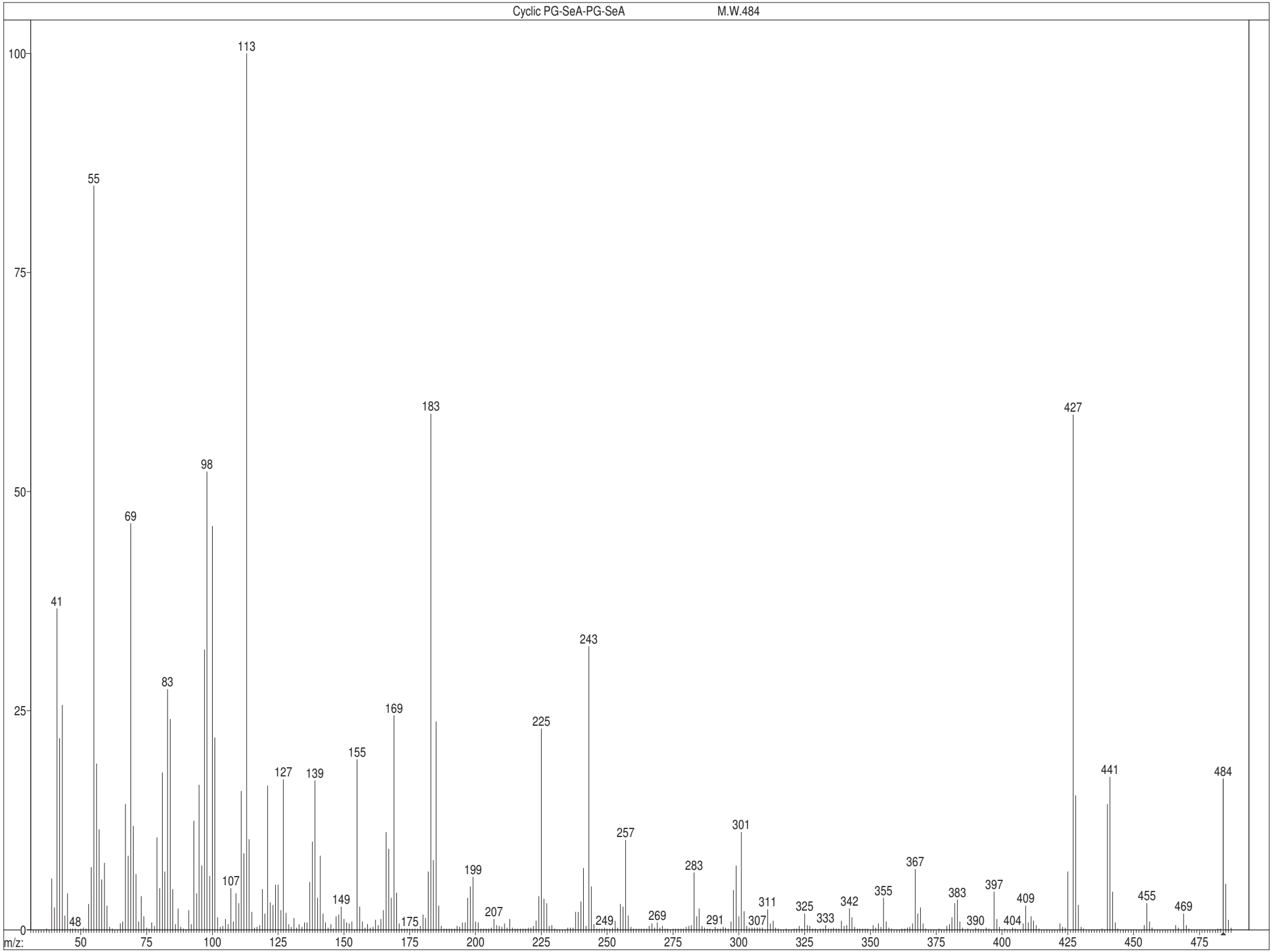
Mass Spectrum for



Mass Spectrum for



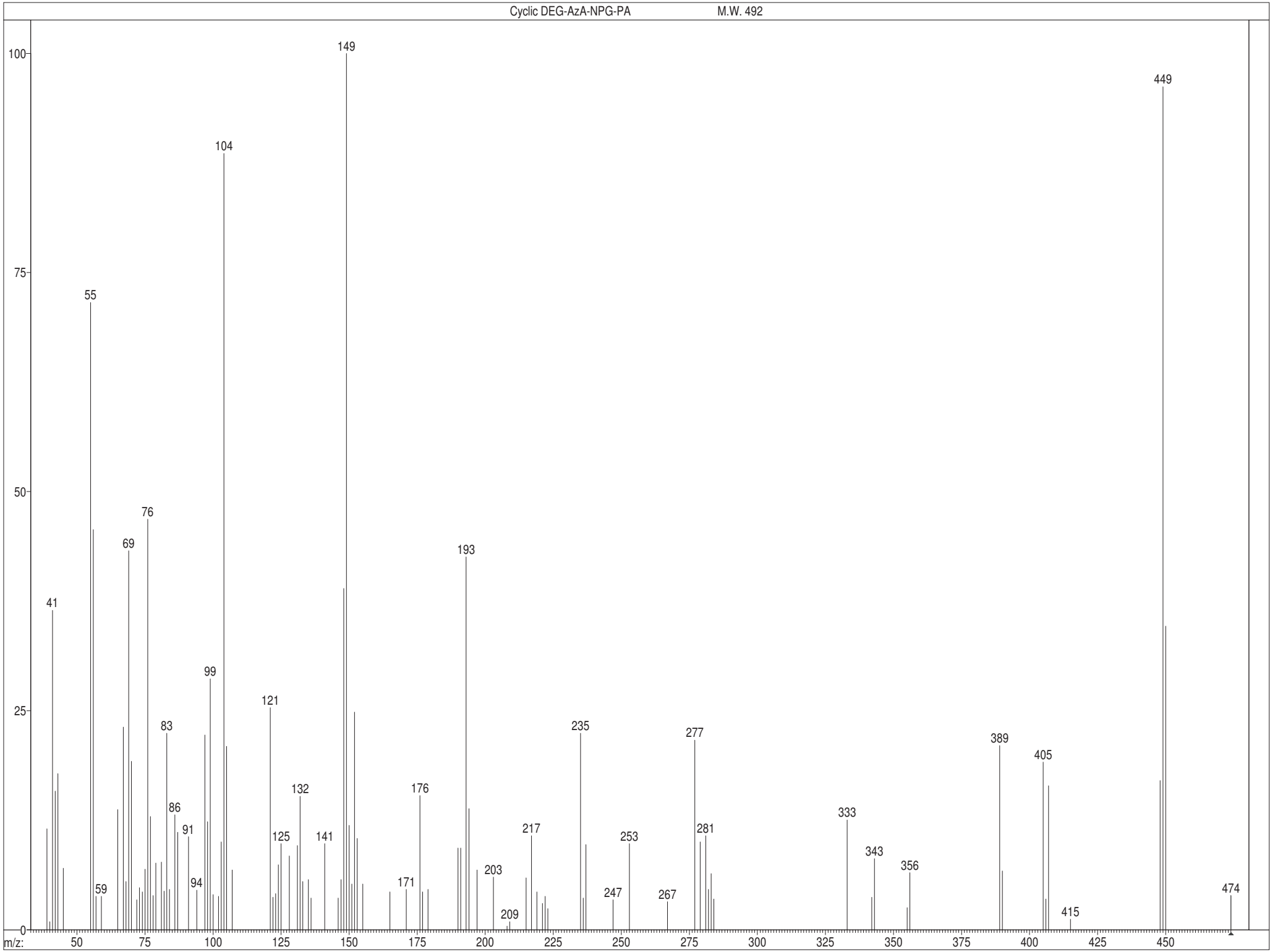
Mass Spectrum for



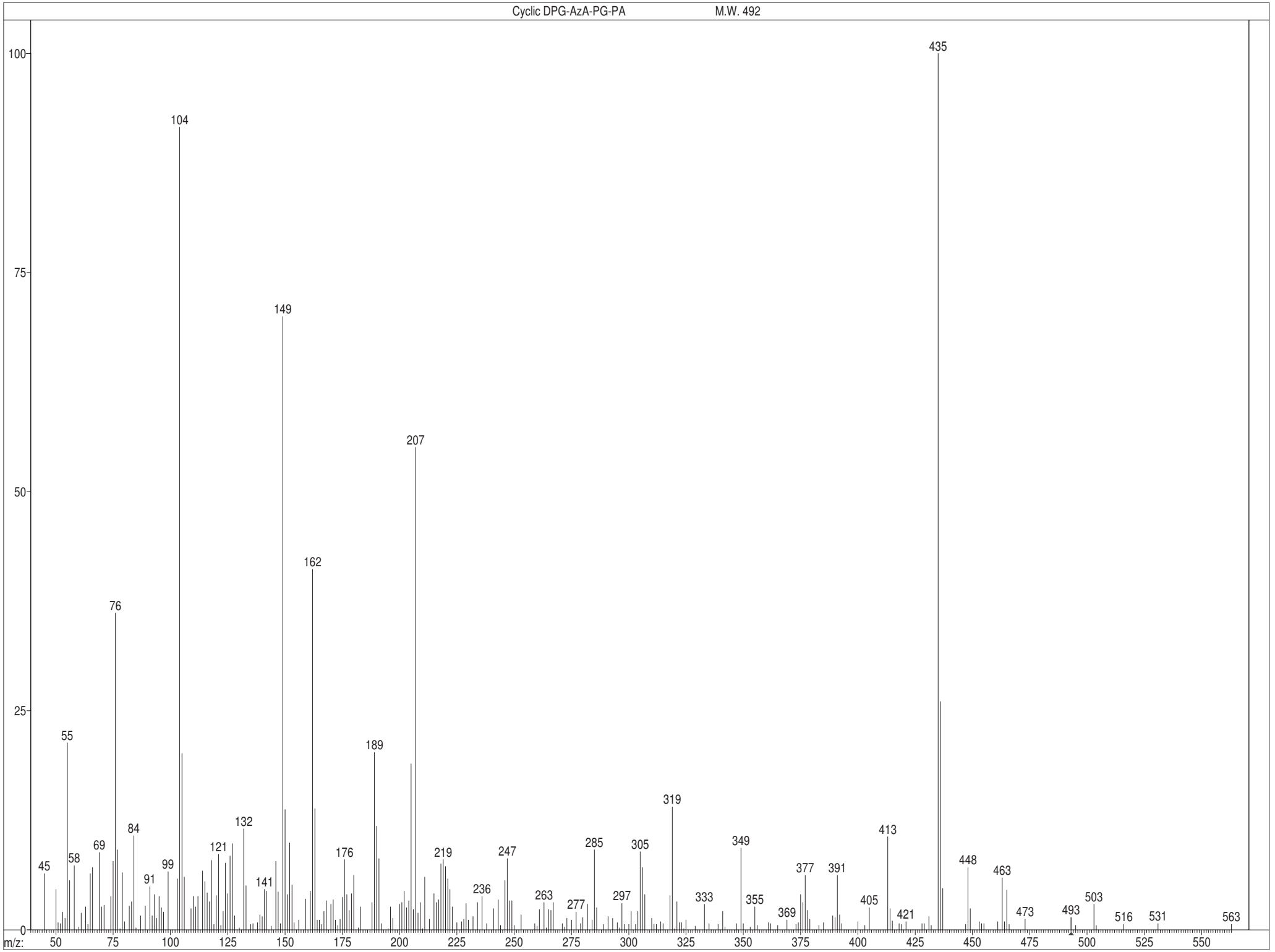
0290

Mass Spectrum for

Cyclic DEG-AzA-NPG-PA M.W. 492

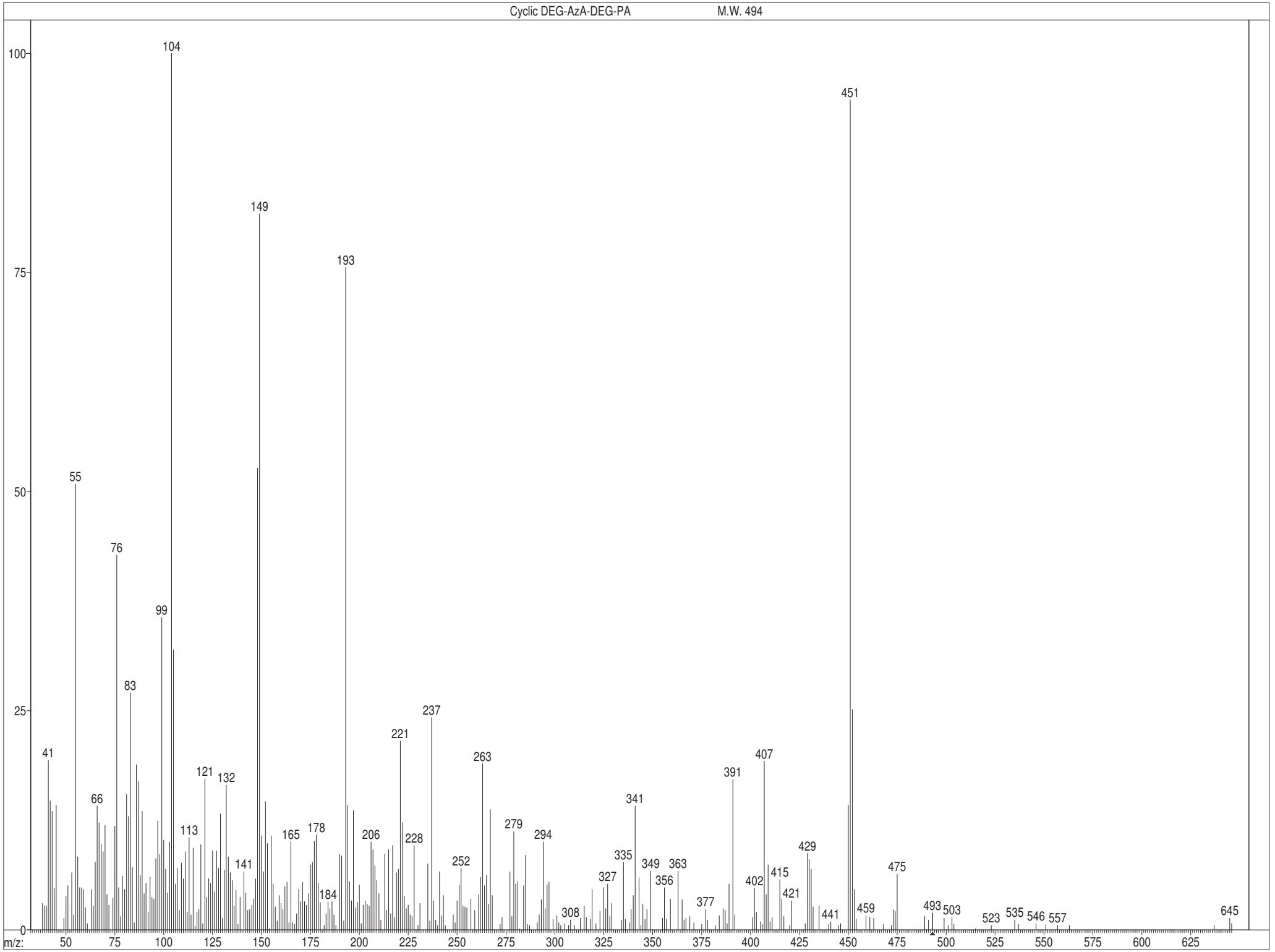


Mass Spectrum for

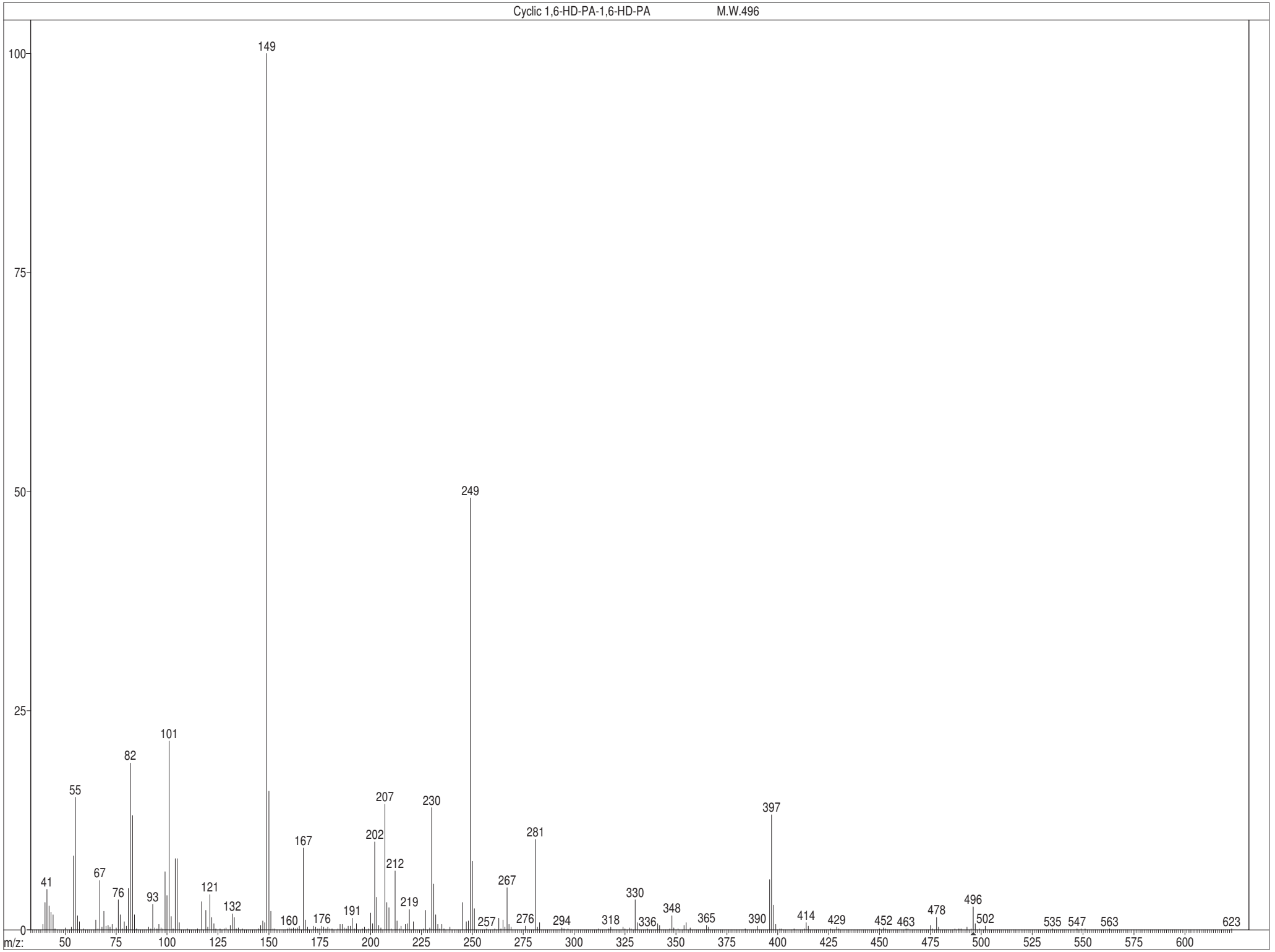


0292

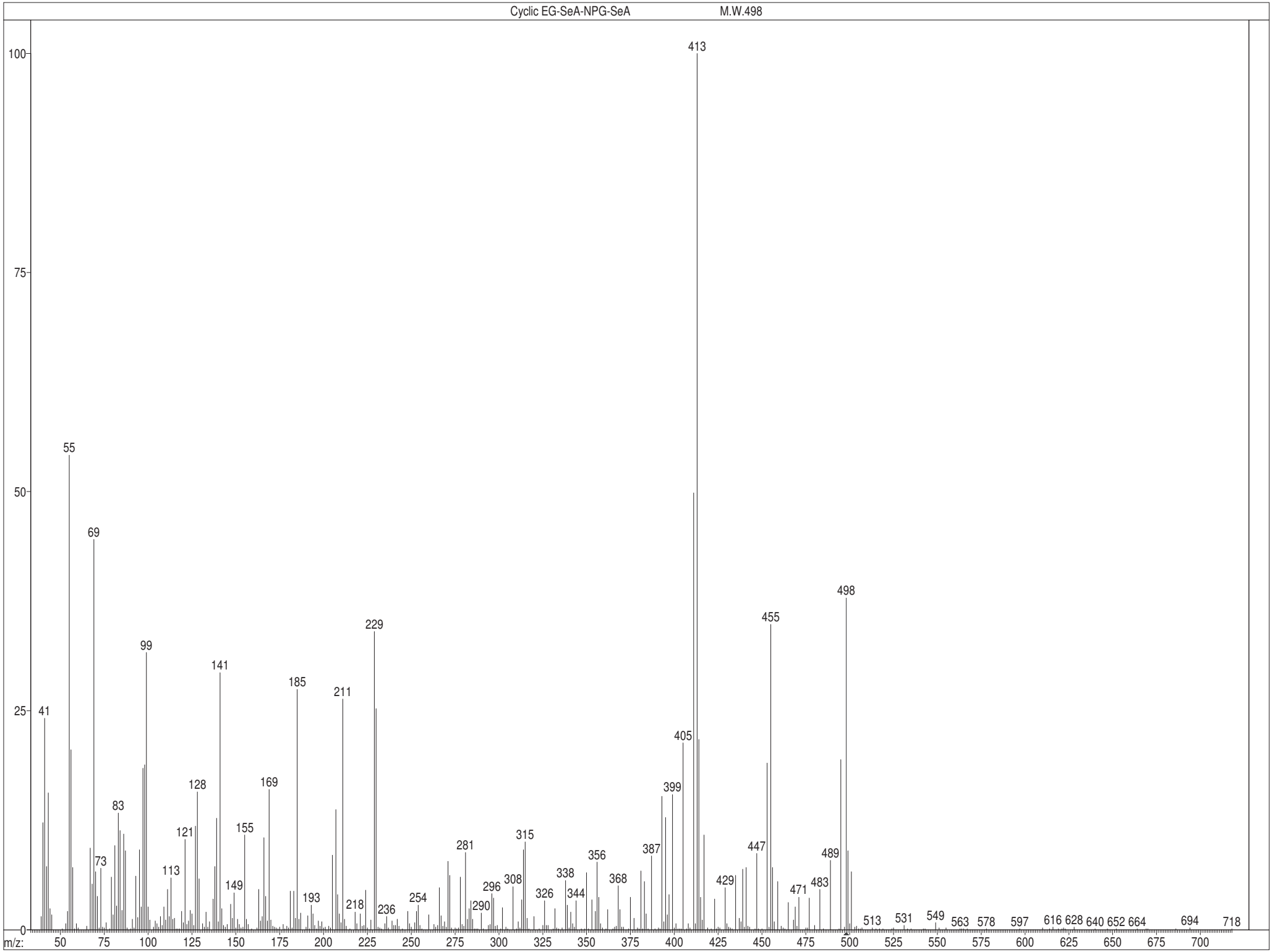
Mass Spectrum for



Mass Spectrum for

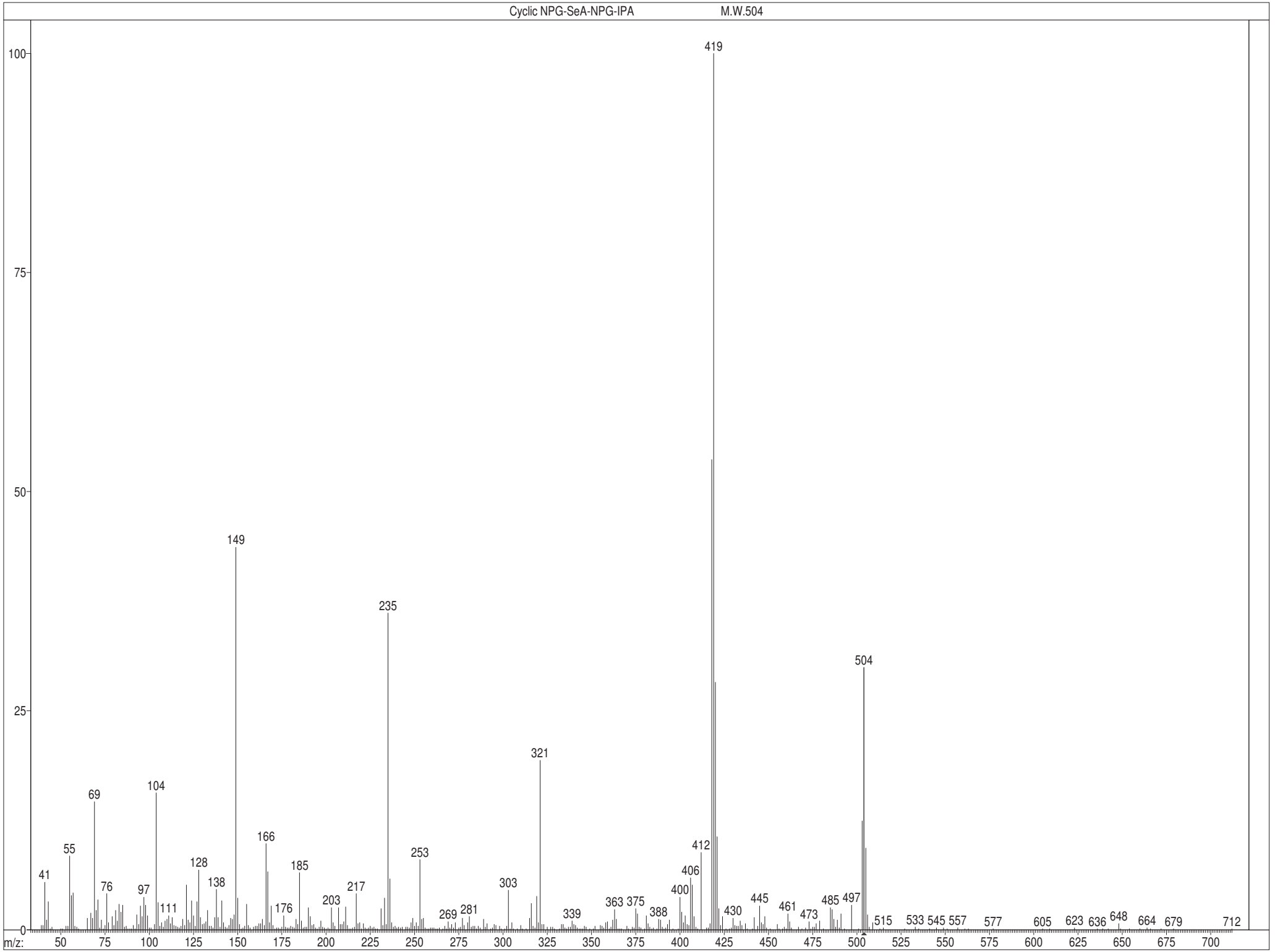


Mass Spectrum for

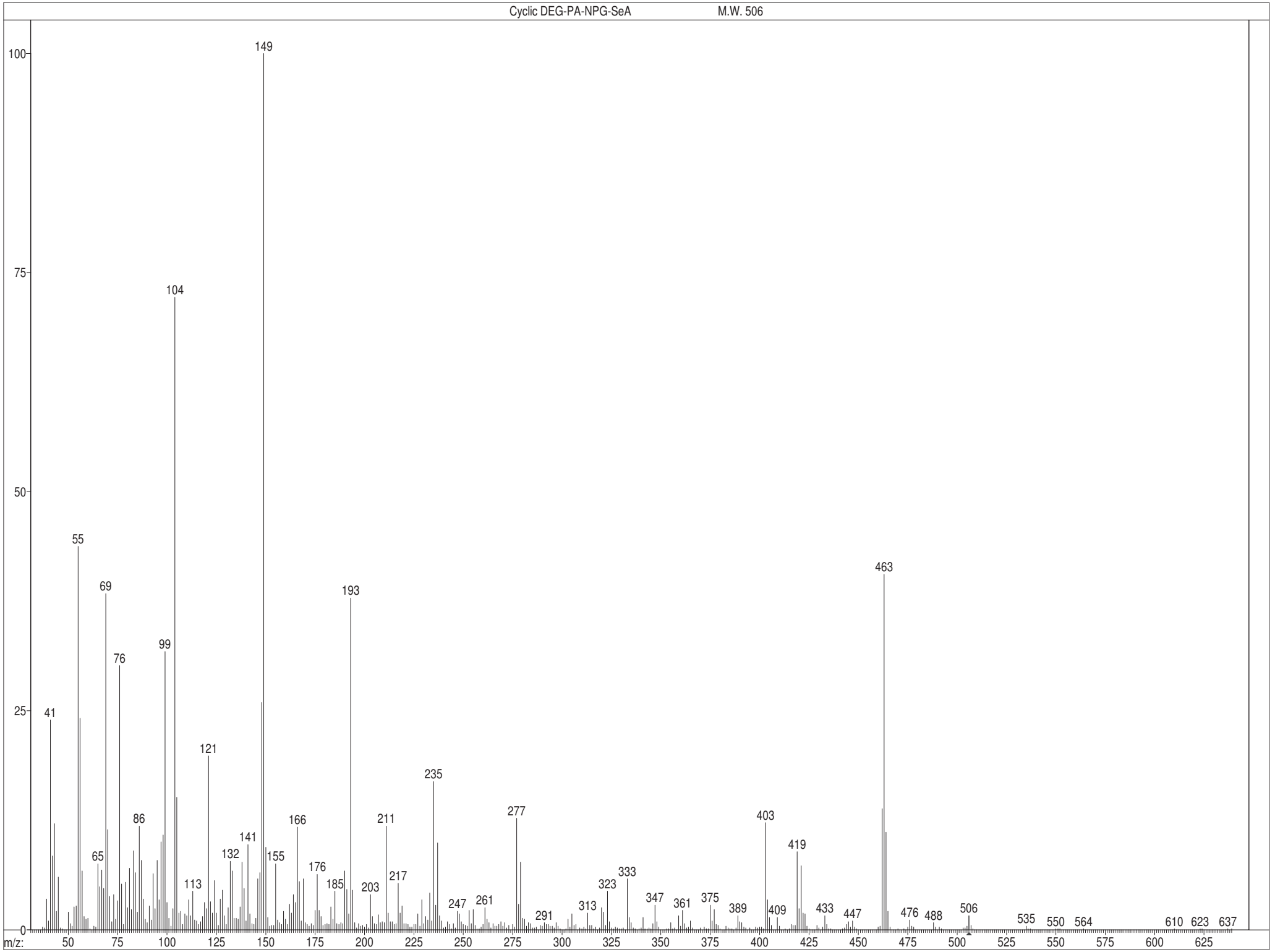


Mass Spectrum for

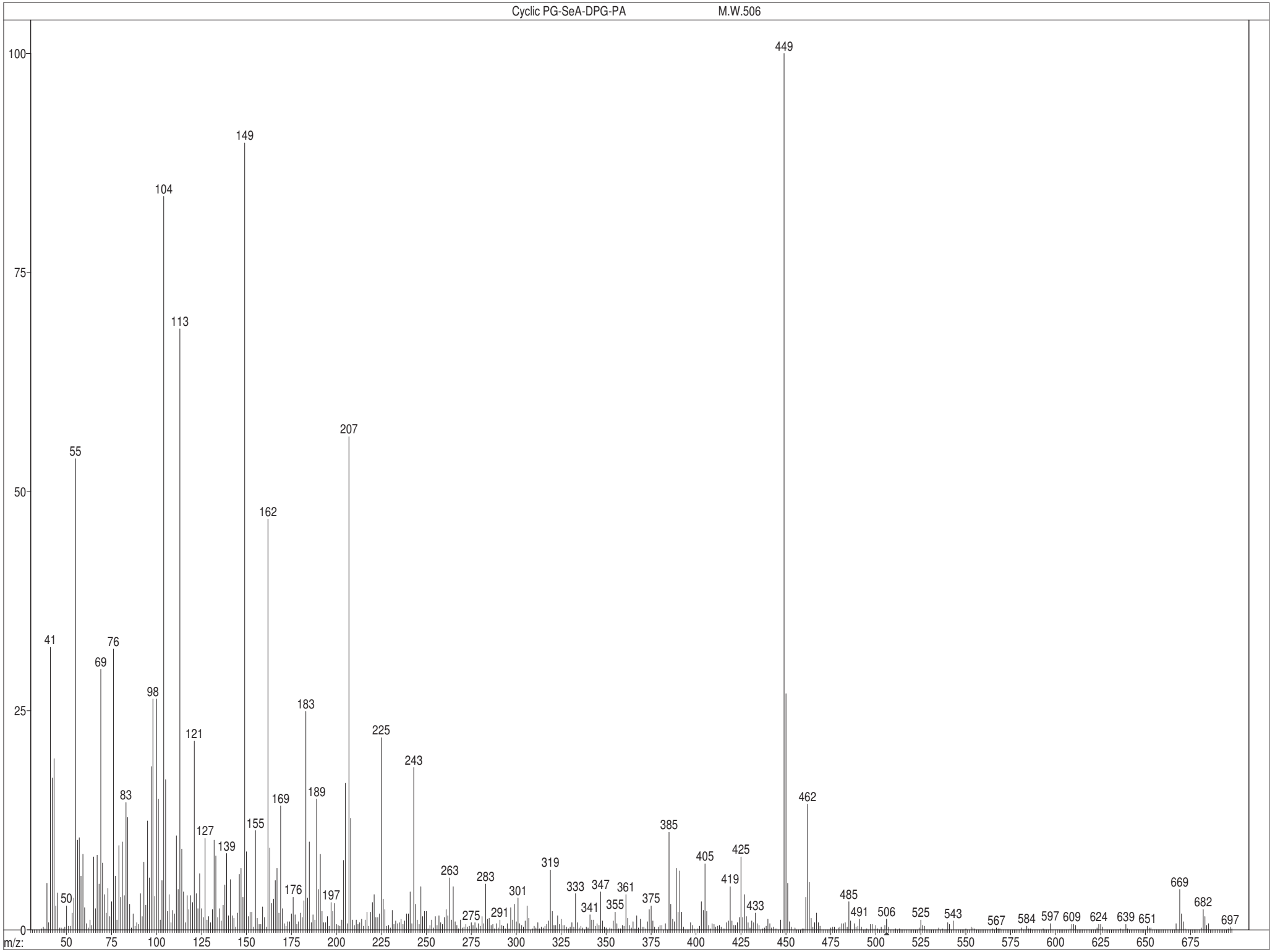
Cyclic NPG-SeA-NPG-IPA M.W.504



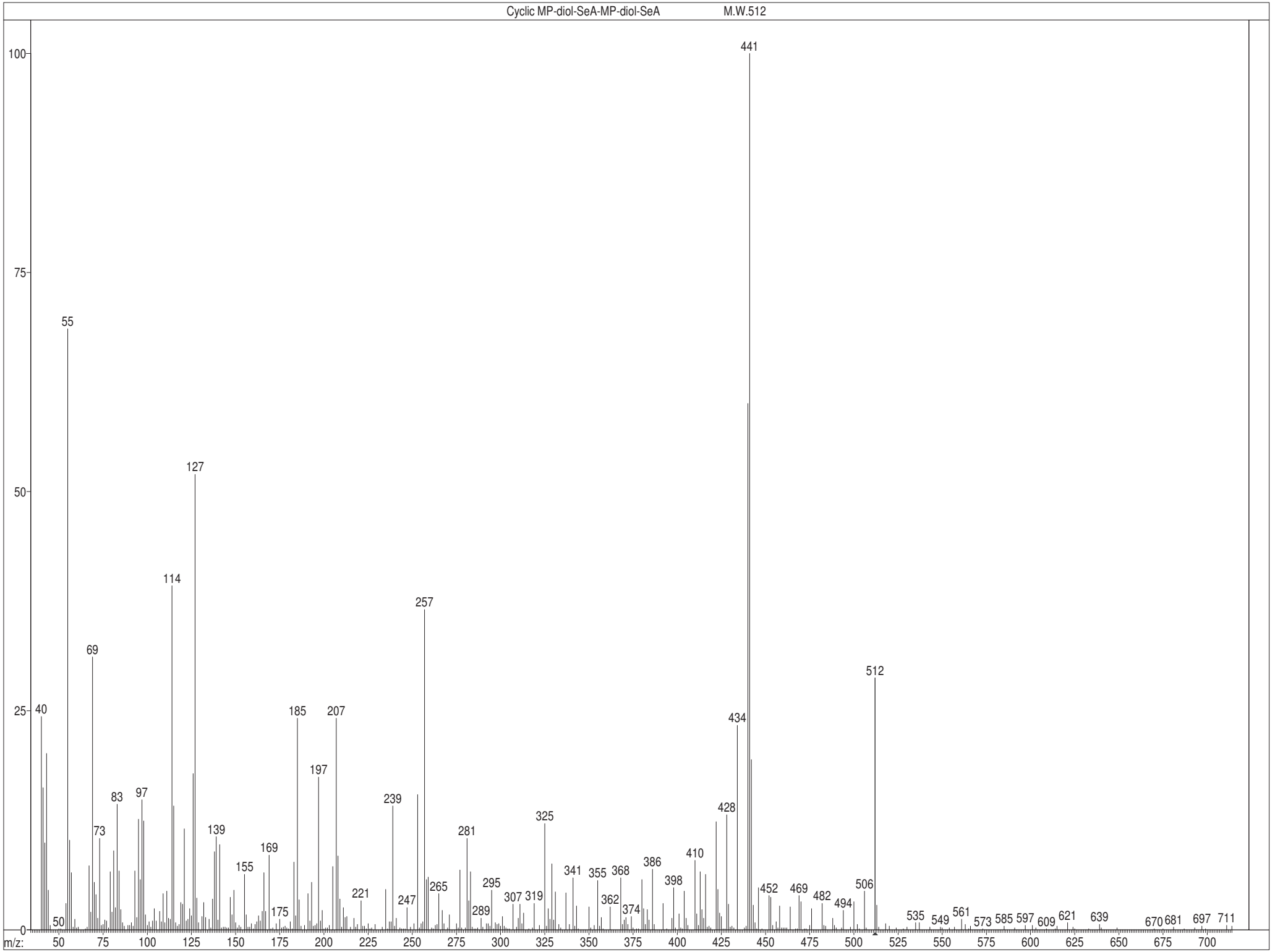
Mass Spectrum for



Mass Spectrum for

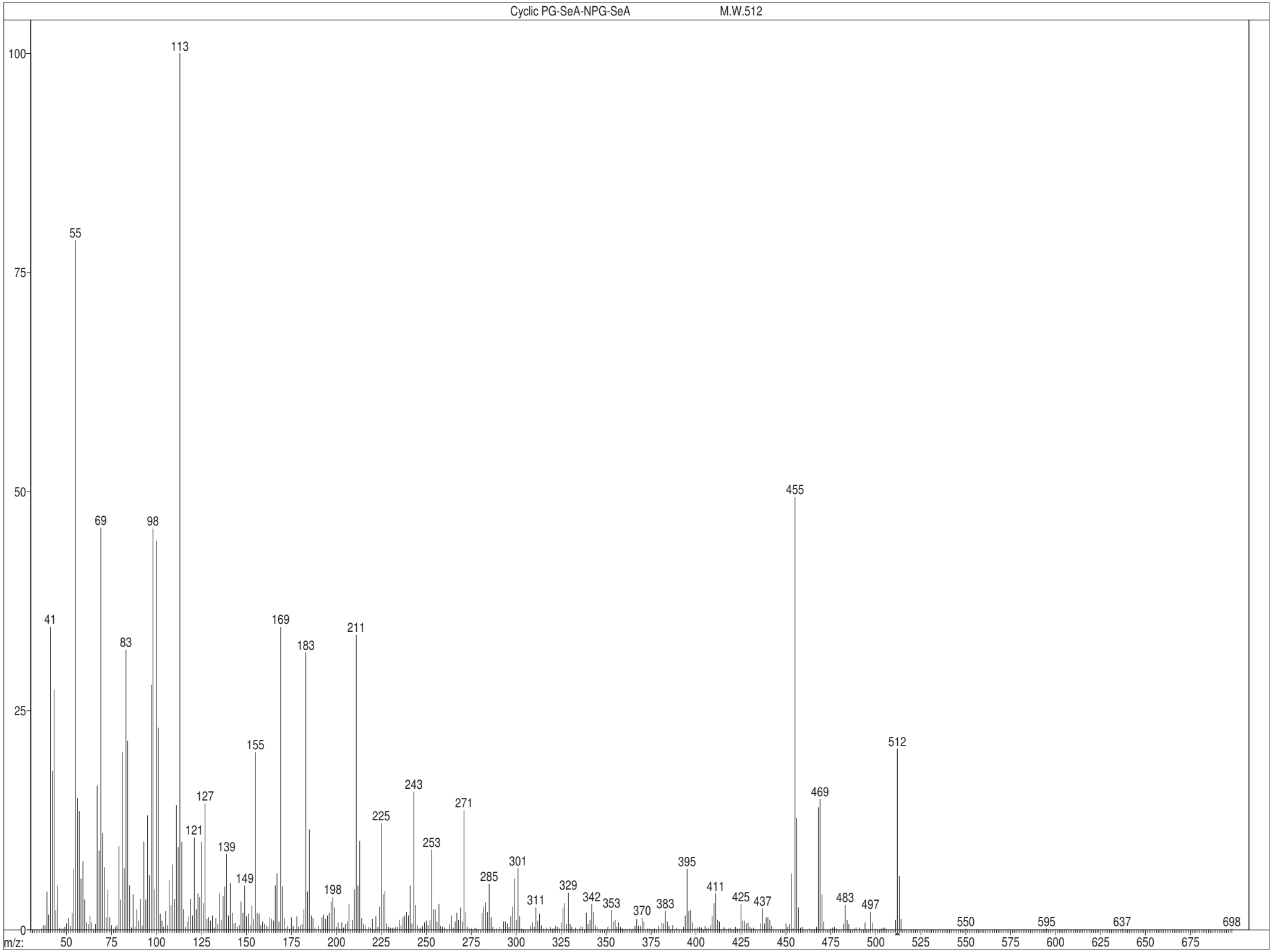


Mass Spectrum for



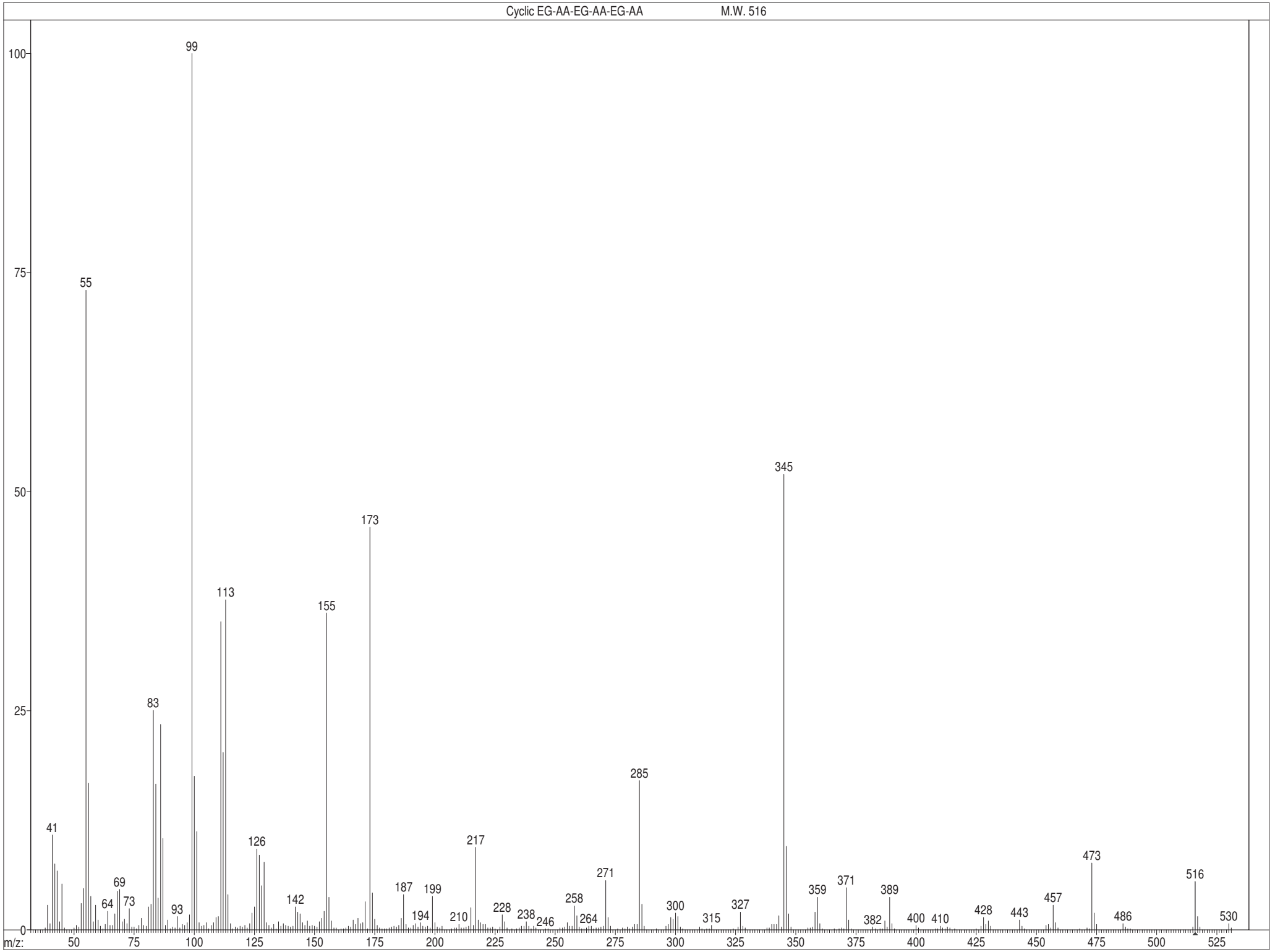
0299

Mass Spectrum for



0300

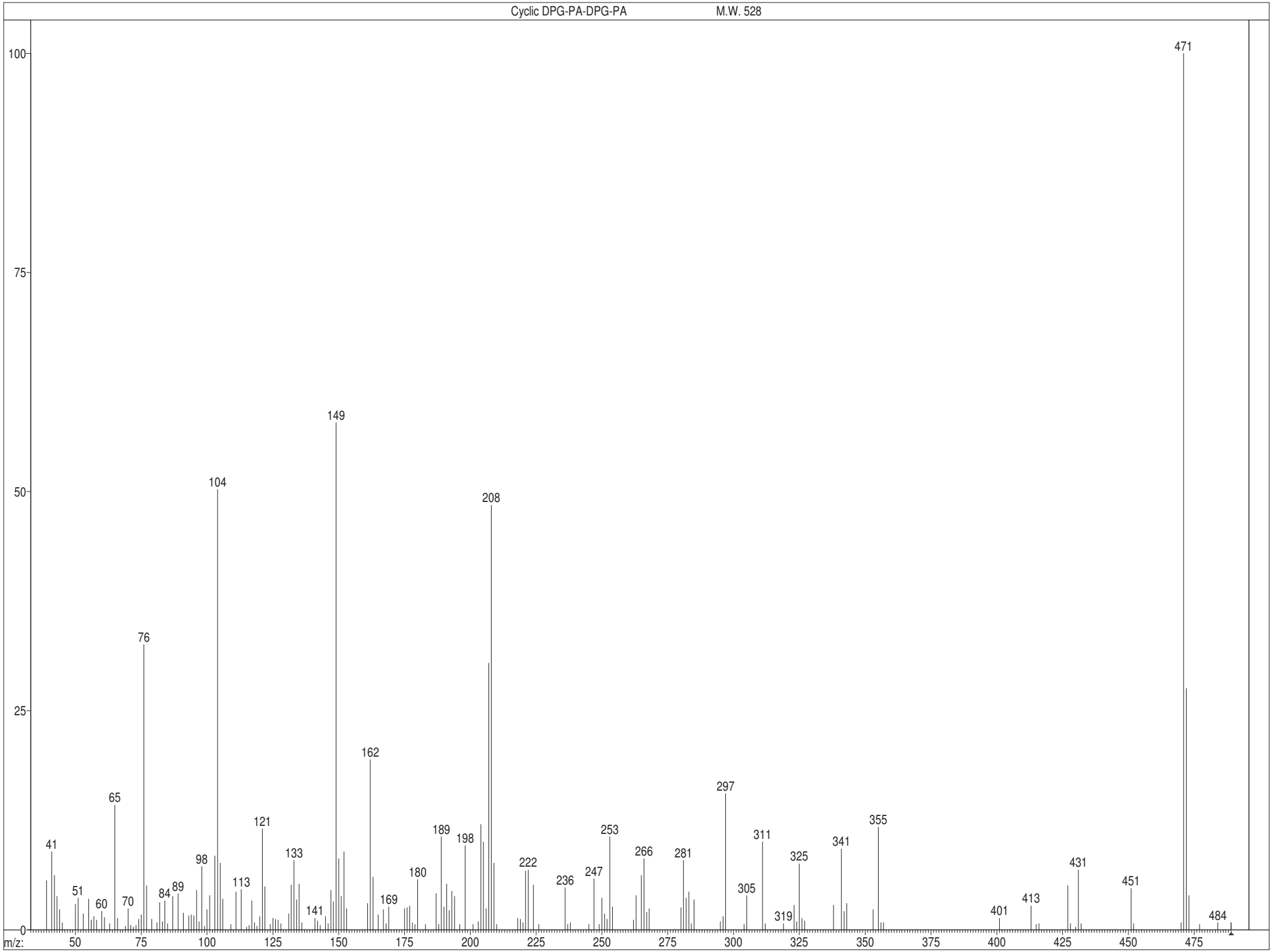
Mass Spectrum for



0301

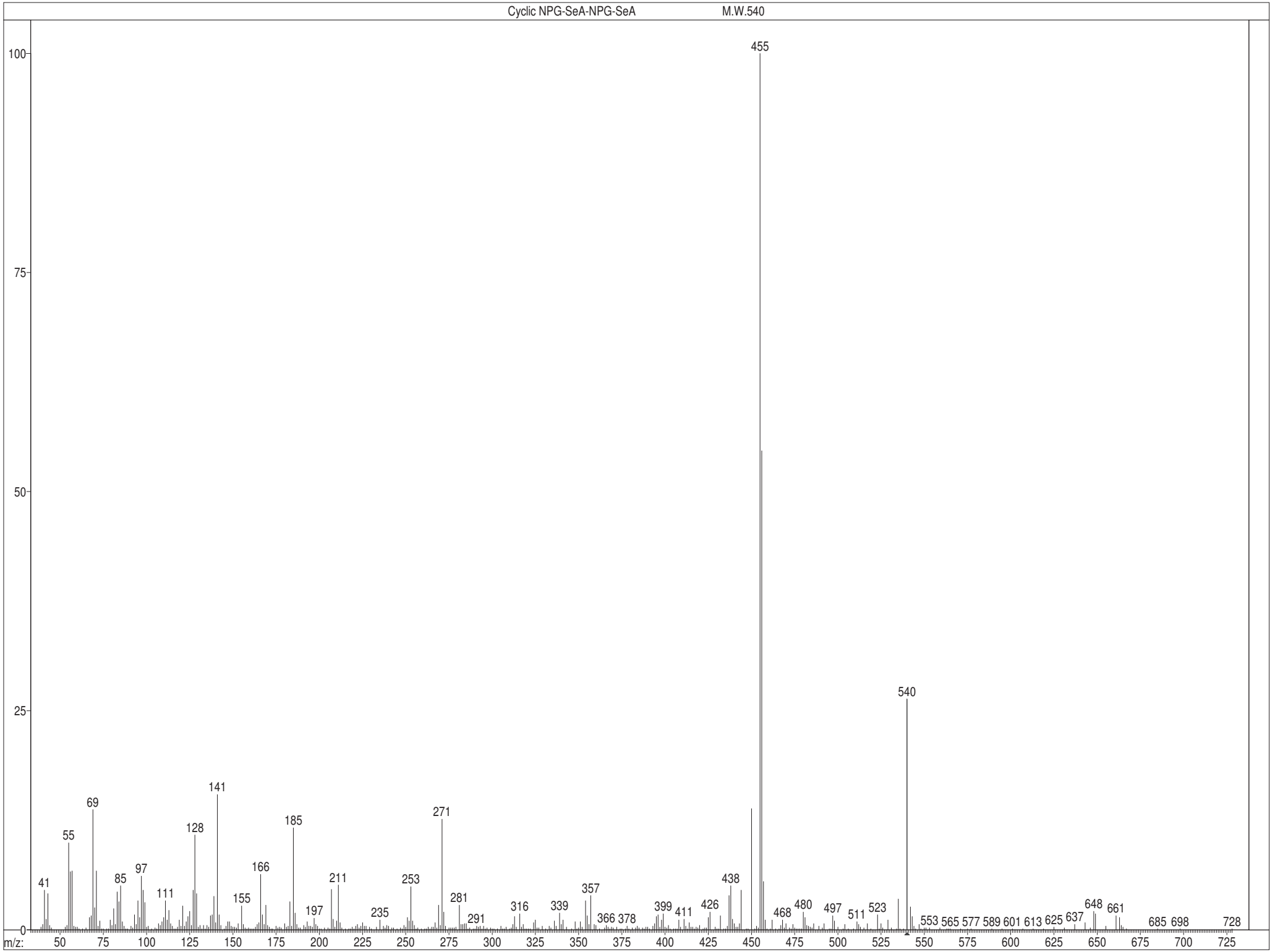
Mass Spectrum for

Cyclic DPG-PA-DPG-PA M.W. 528



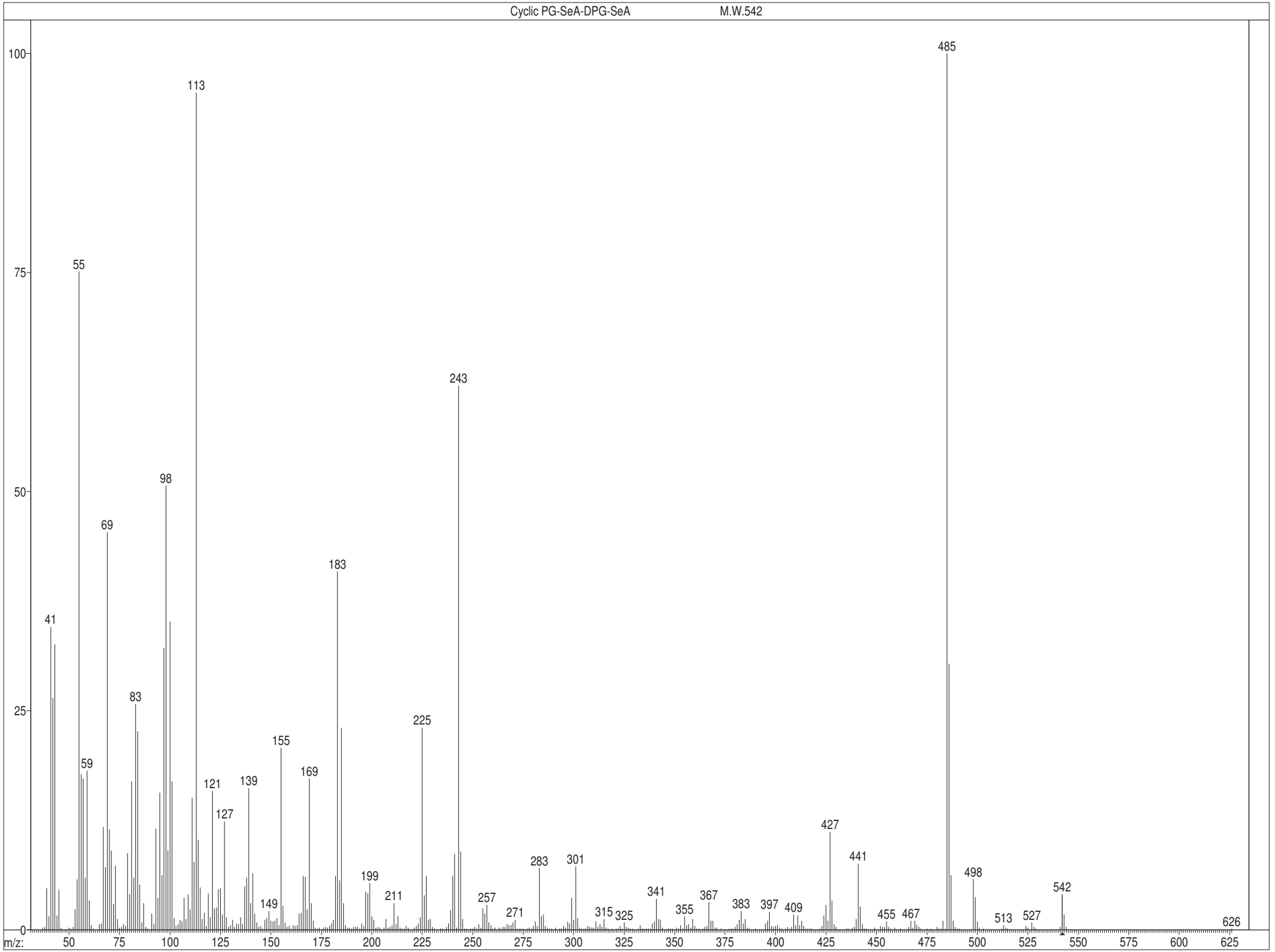
0302

Mass Spectrum for



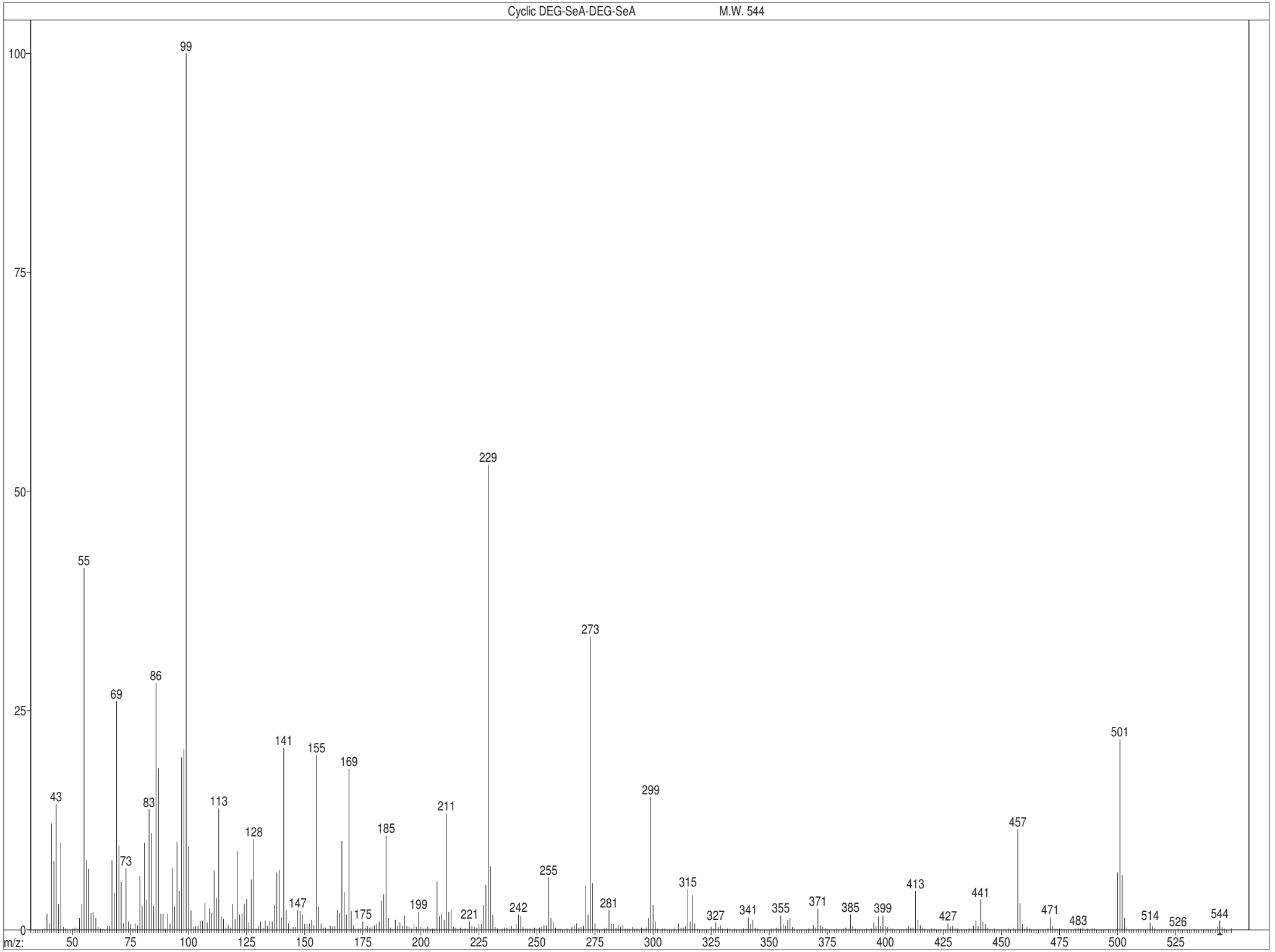
0303

Mass Spectrum for



0304

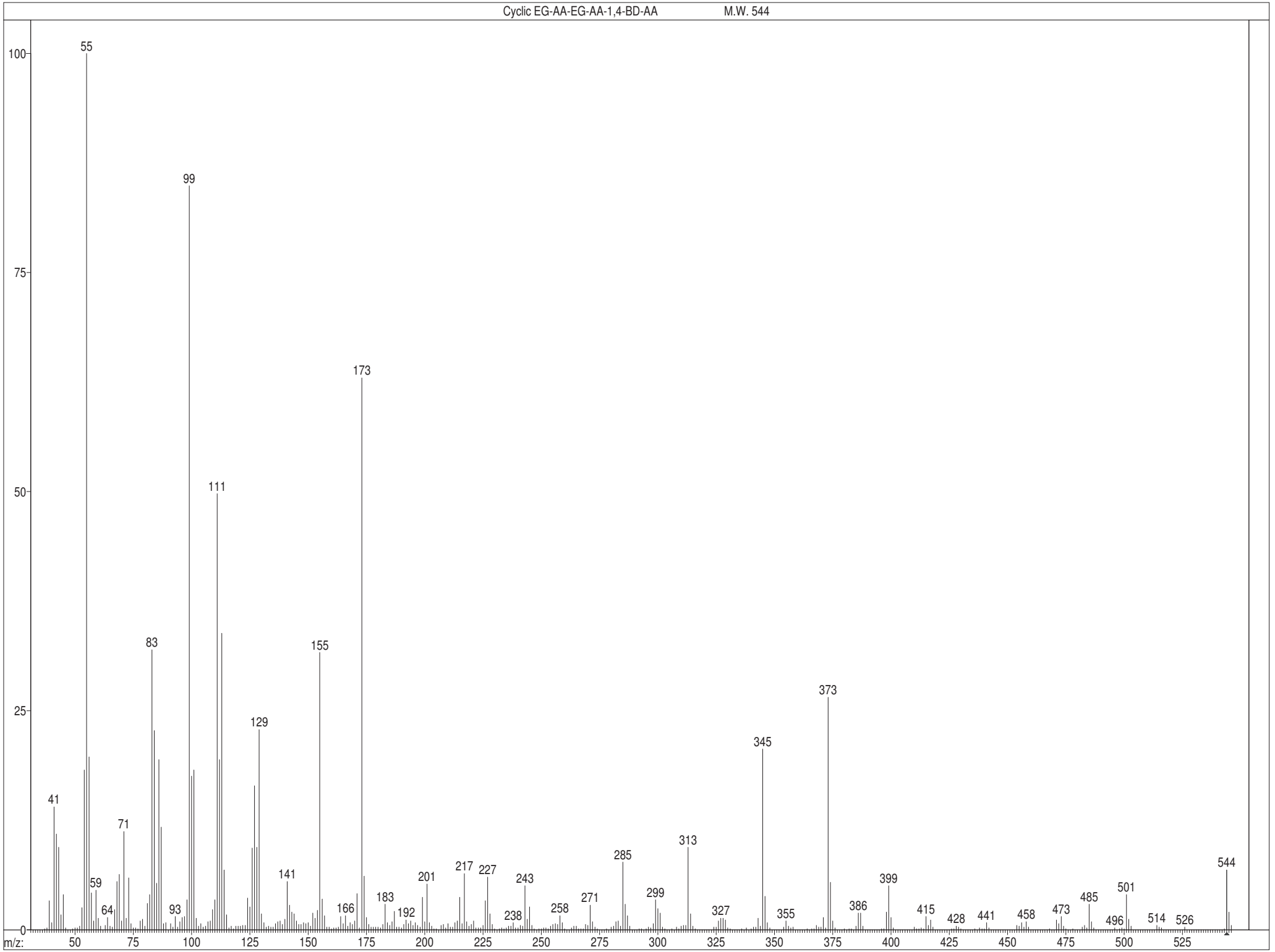
Mass Spectrum for



0305

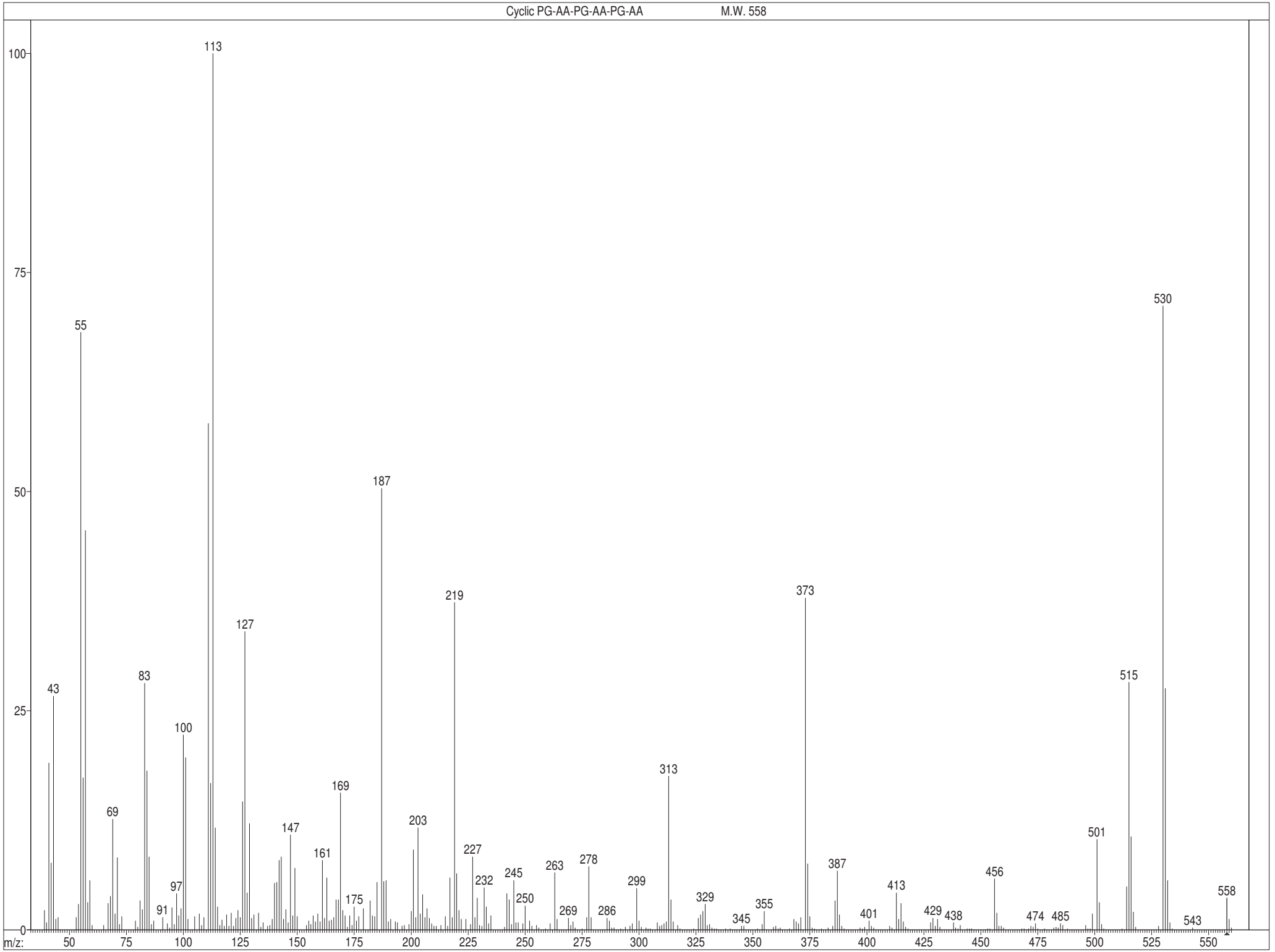
Mass Spectrum for

Cyclic EG-AA-EG-AA-1,4-BD-AA M.W. 544



0306

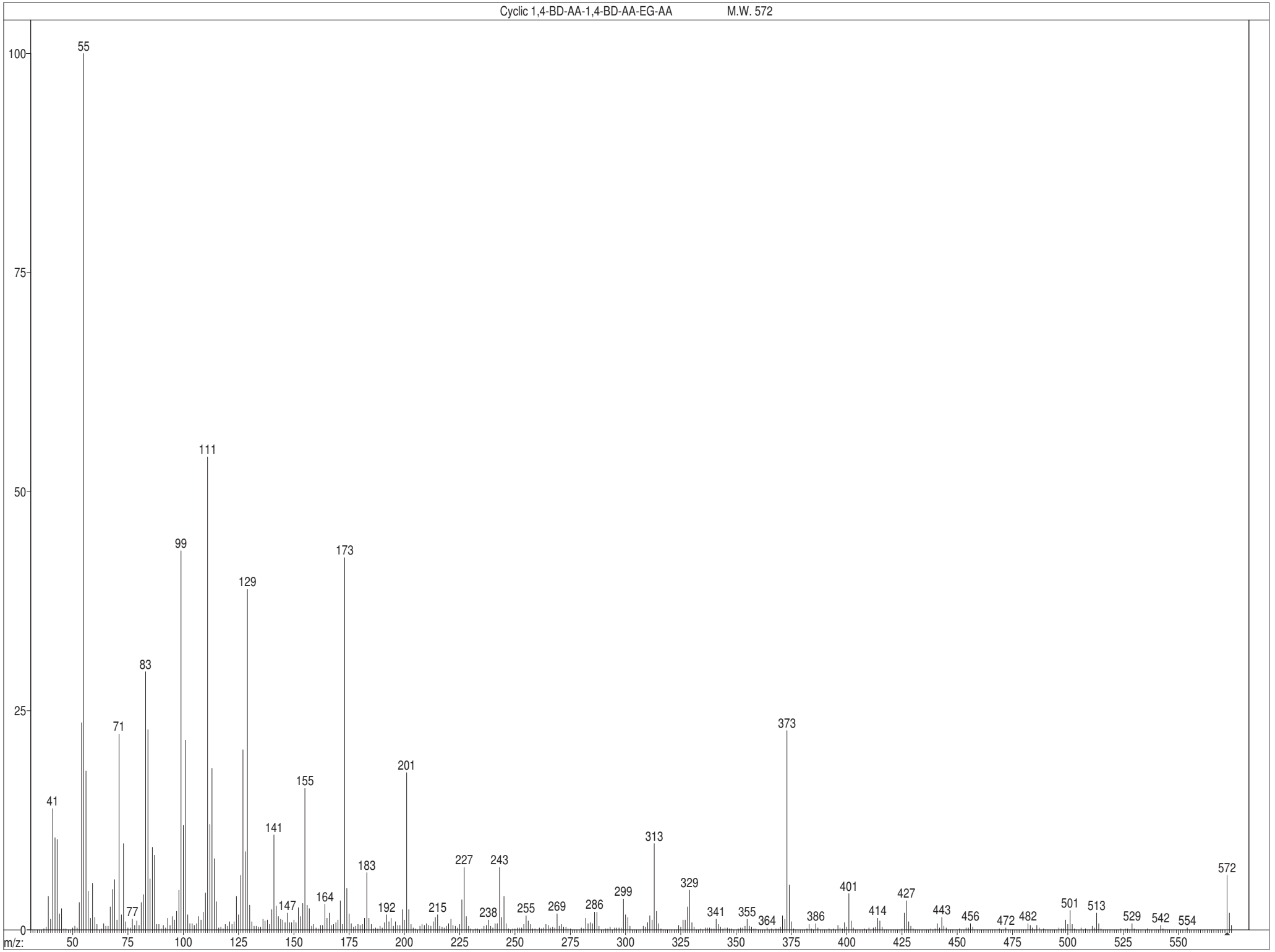
Mass Spectrum for



0307

Mass Spectrum for

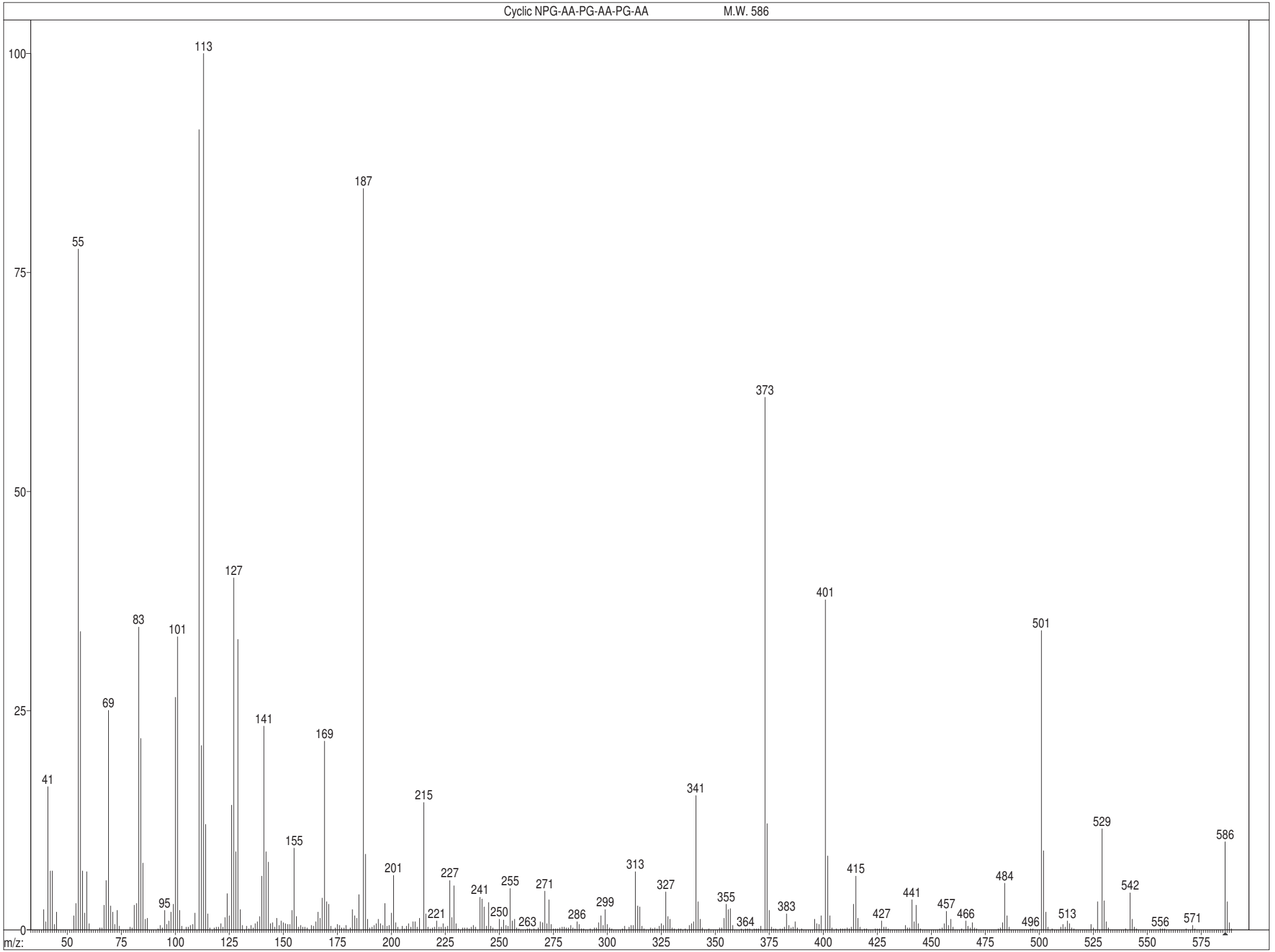
Cyclic 1,4-BD-AA-1,4-BD-AA-EG-AA M.W. 572



0308

Mass Spectrum for

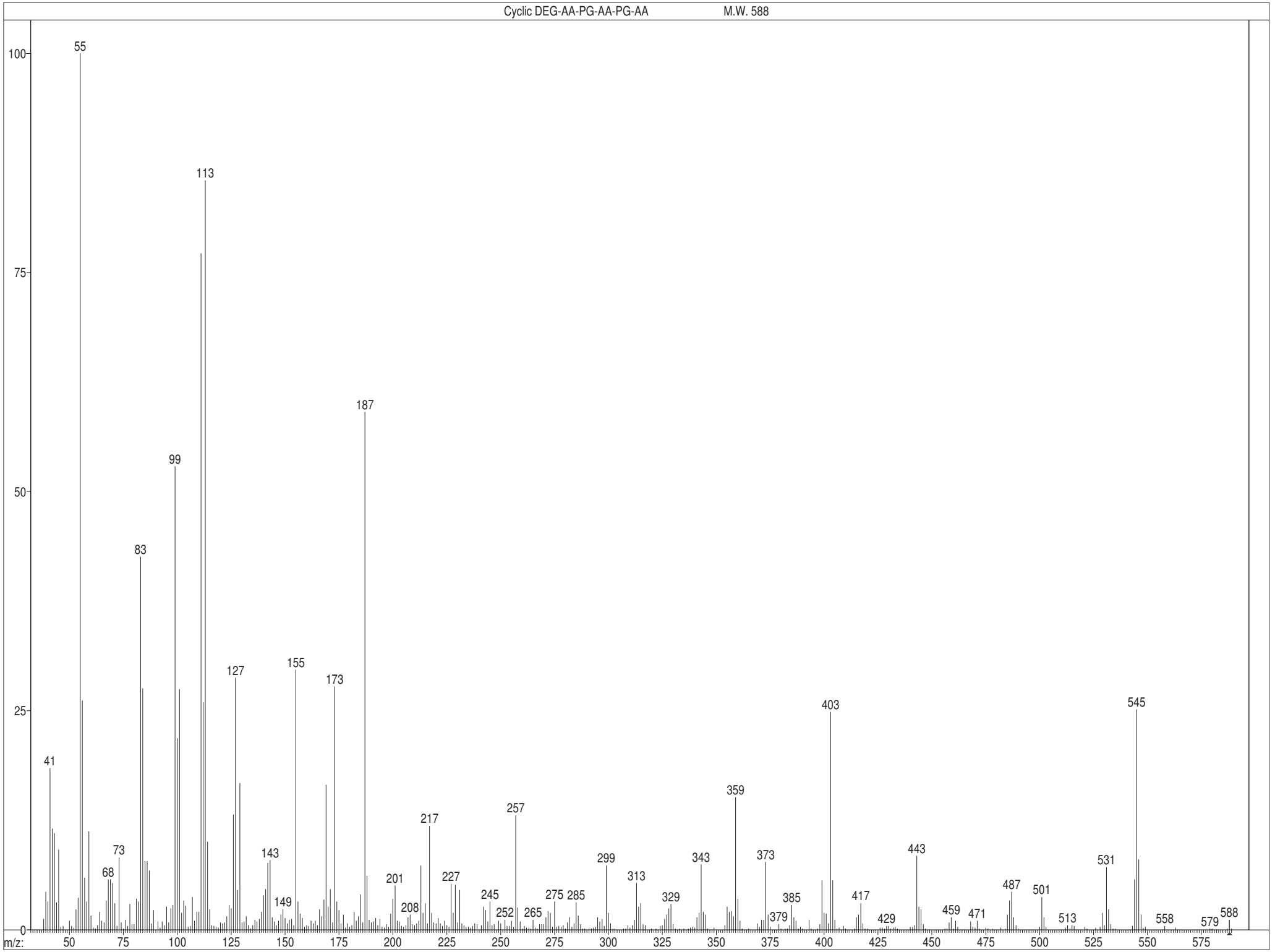
Cyclic NPG-AA-PG-AA-PG-AA M.W. 586



0309

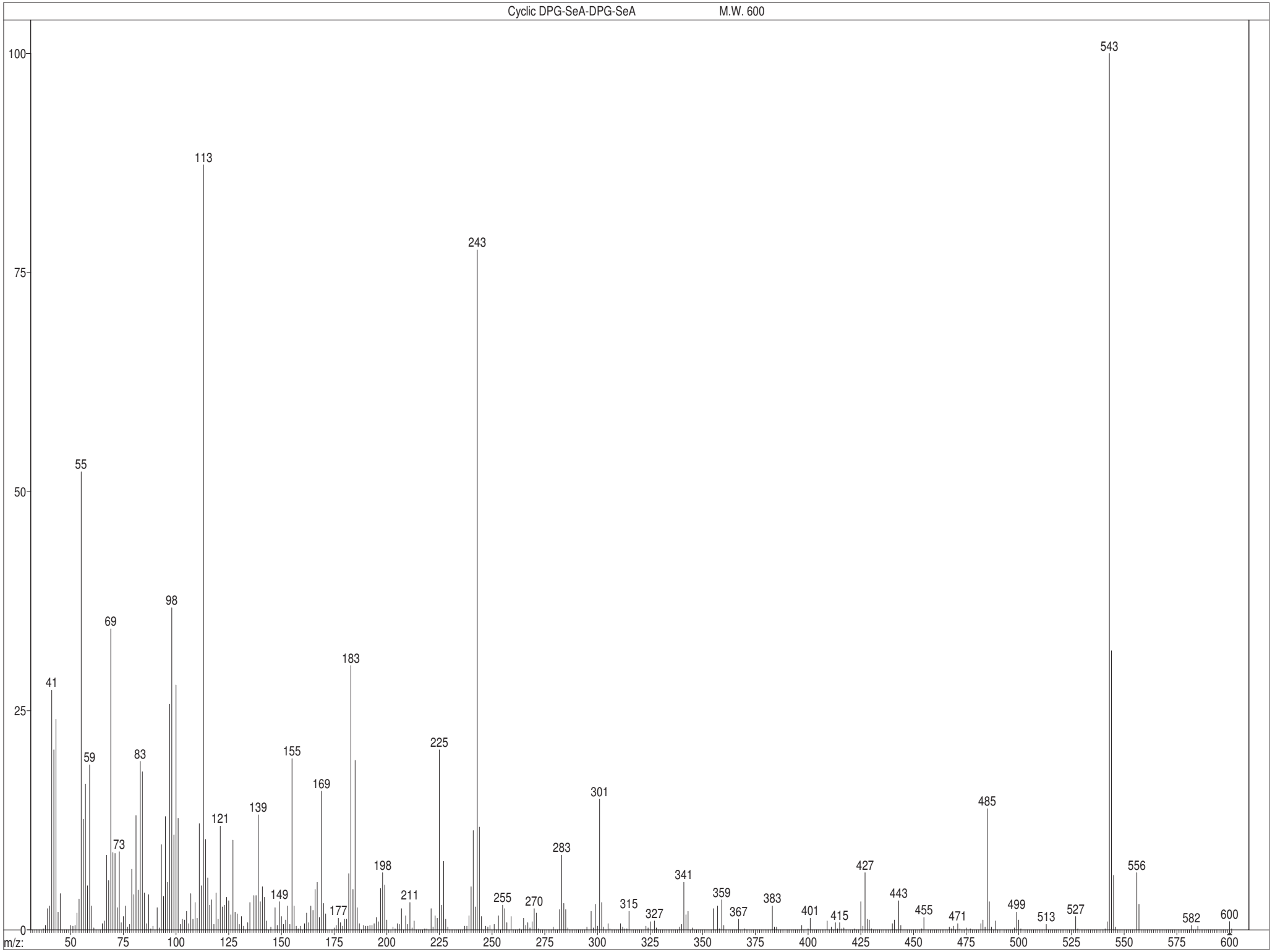
Mass Spectrum for

Cyclic DEG-AA-PG-AA-PG-AA M.W. 588



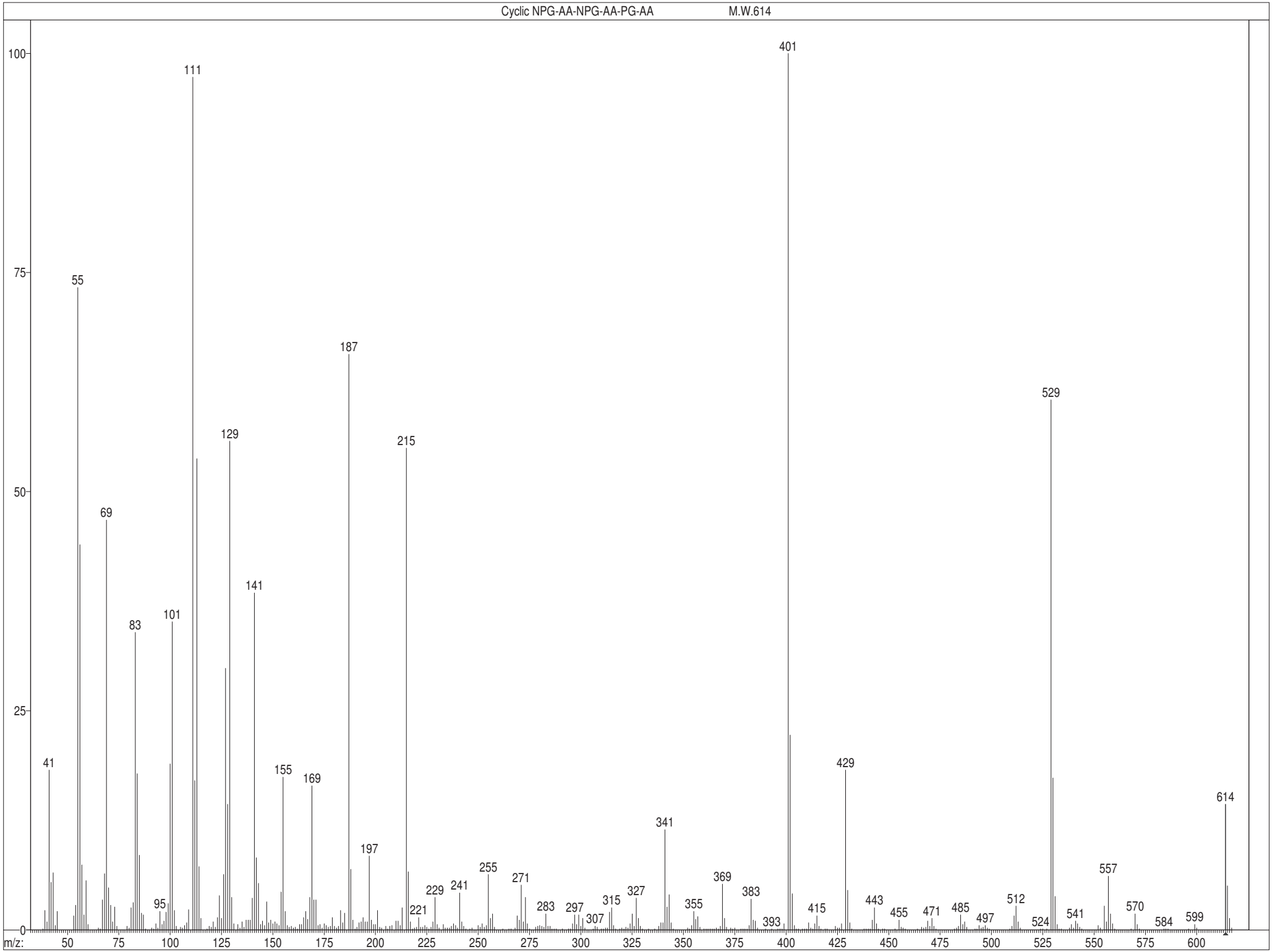
0310

Mass Spectrum for



0311

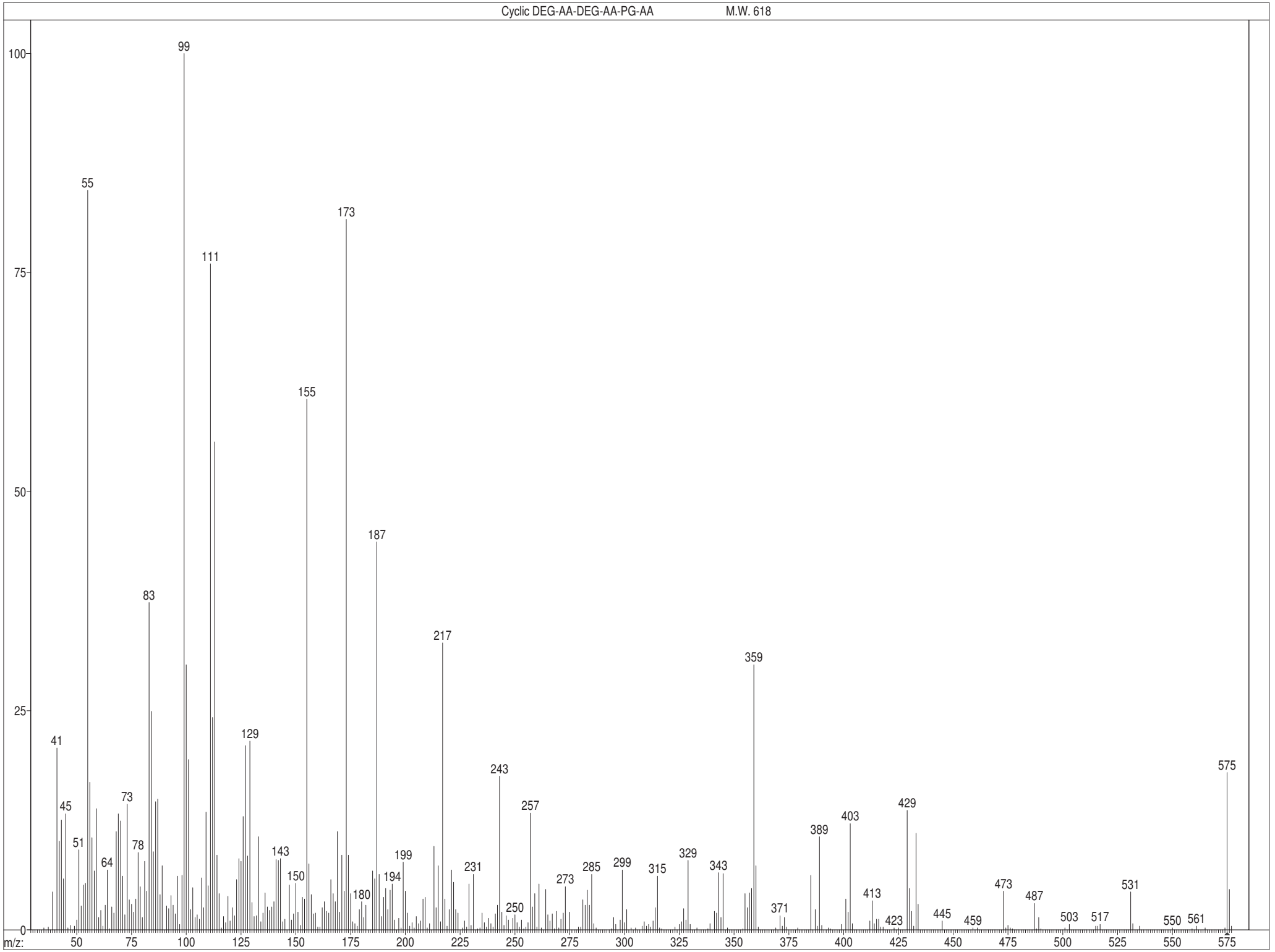
Mass Spectrum for



0312

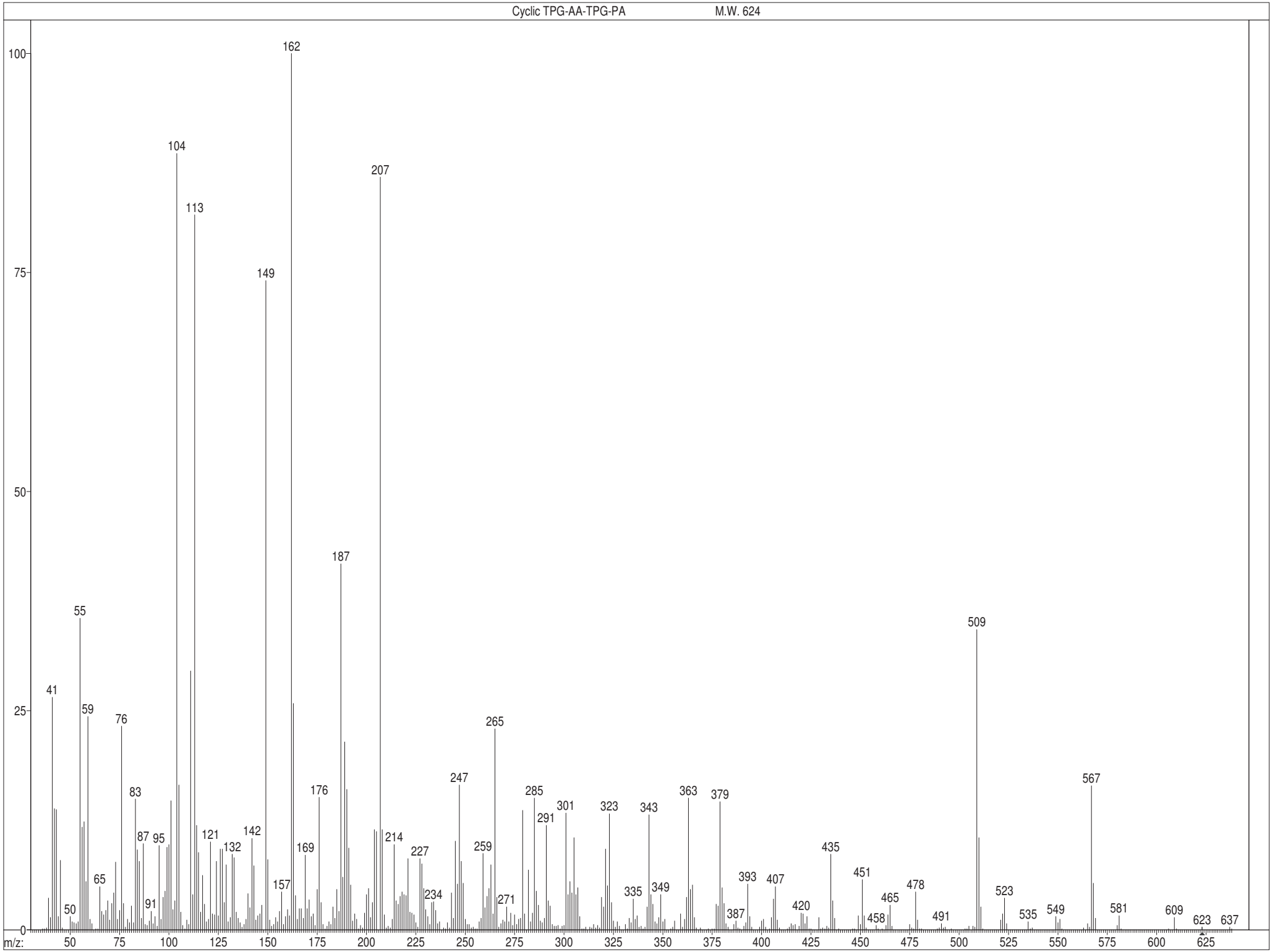
Mass Spectrum for

Cyclic DEG-AA-DEG-AA-PG-AA M.W. 618



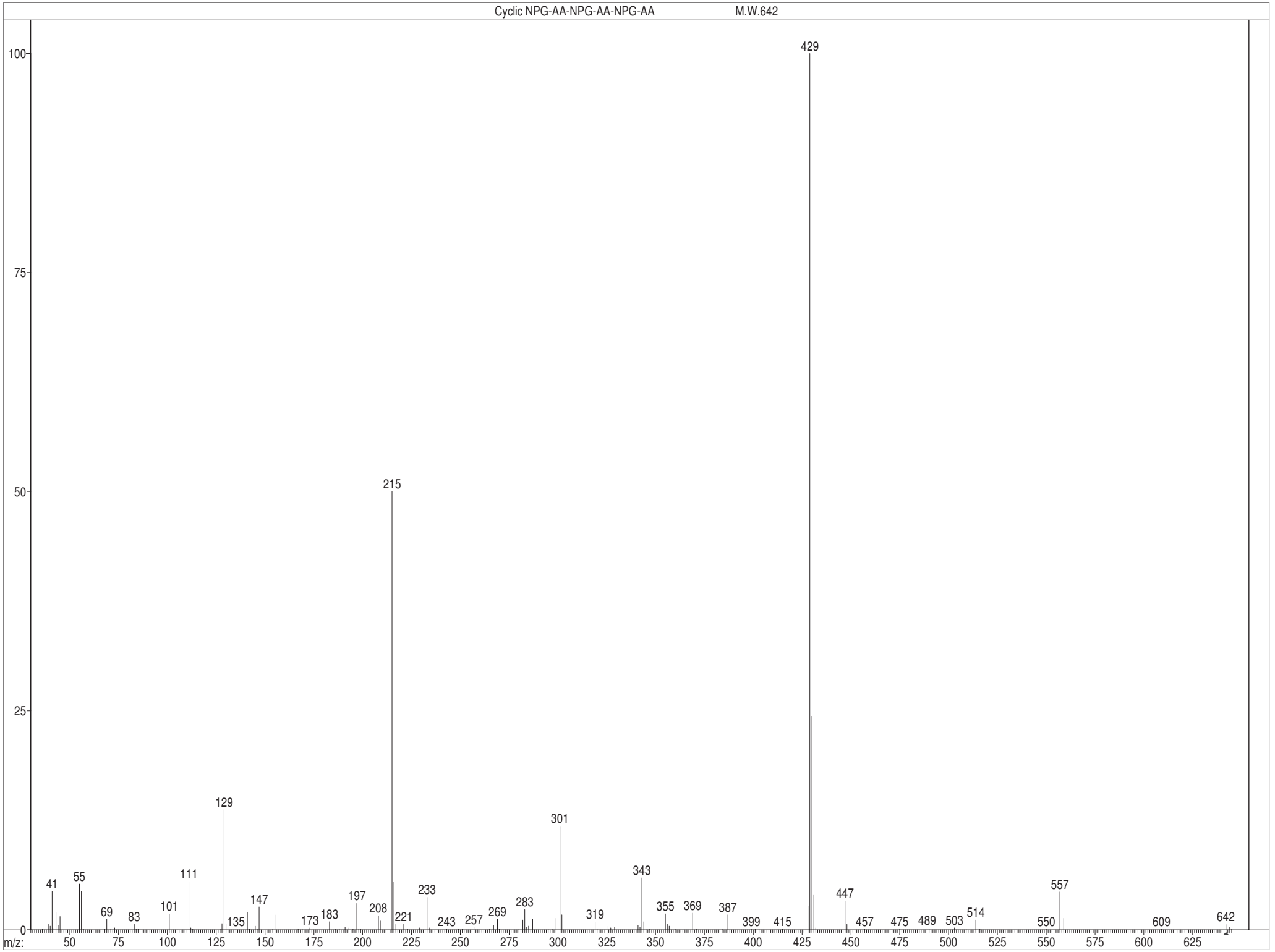
0313

Mass Spectrum for

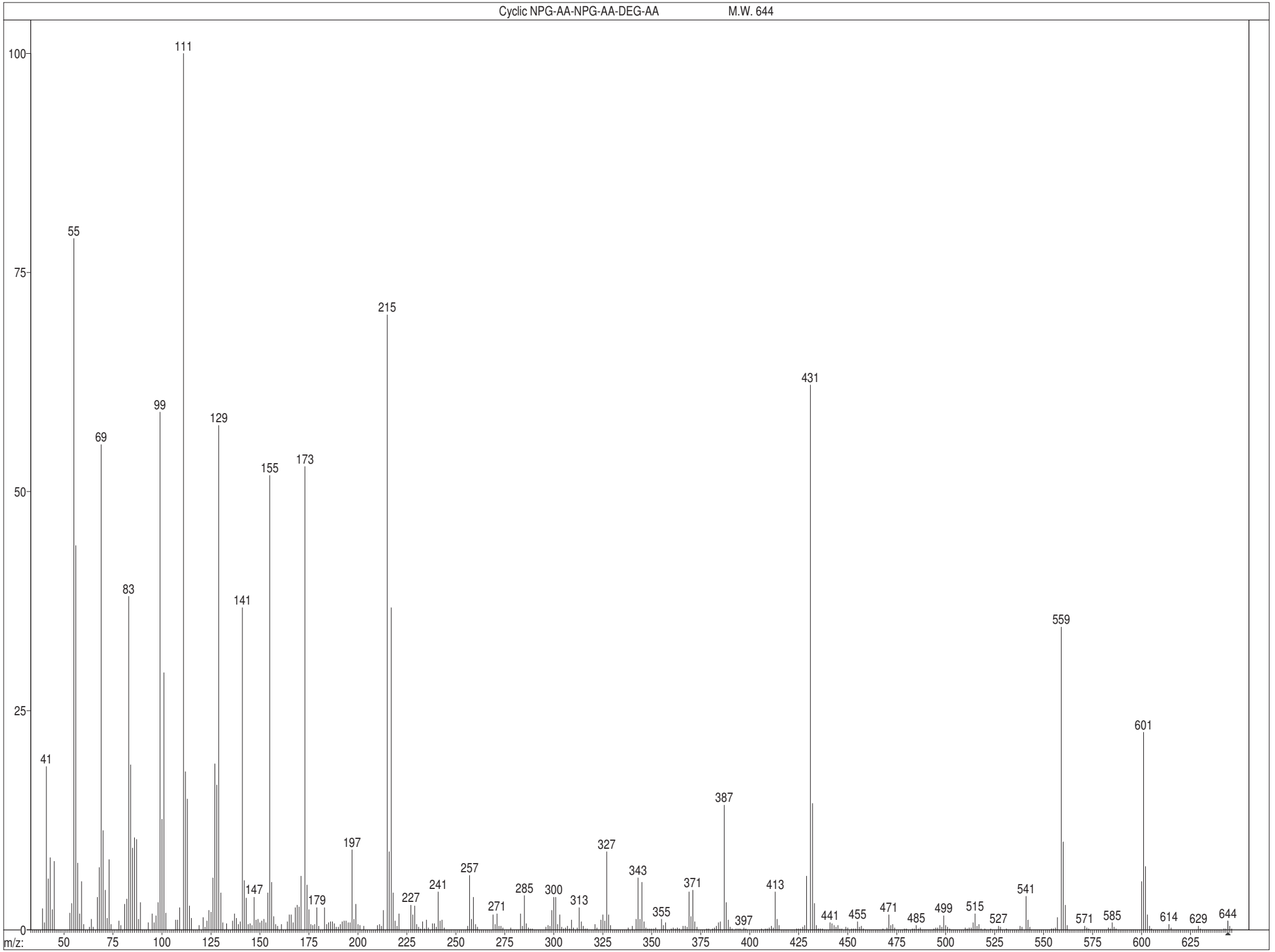


0314

Mass Spectrum for

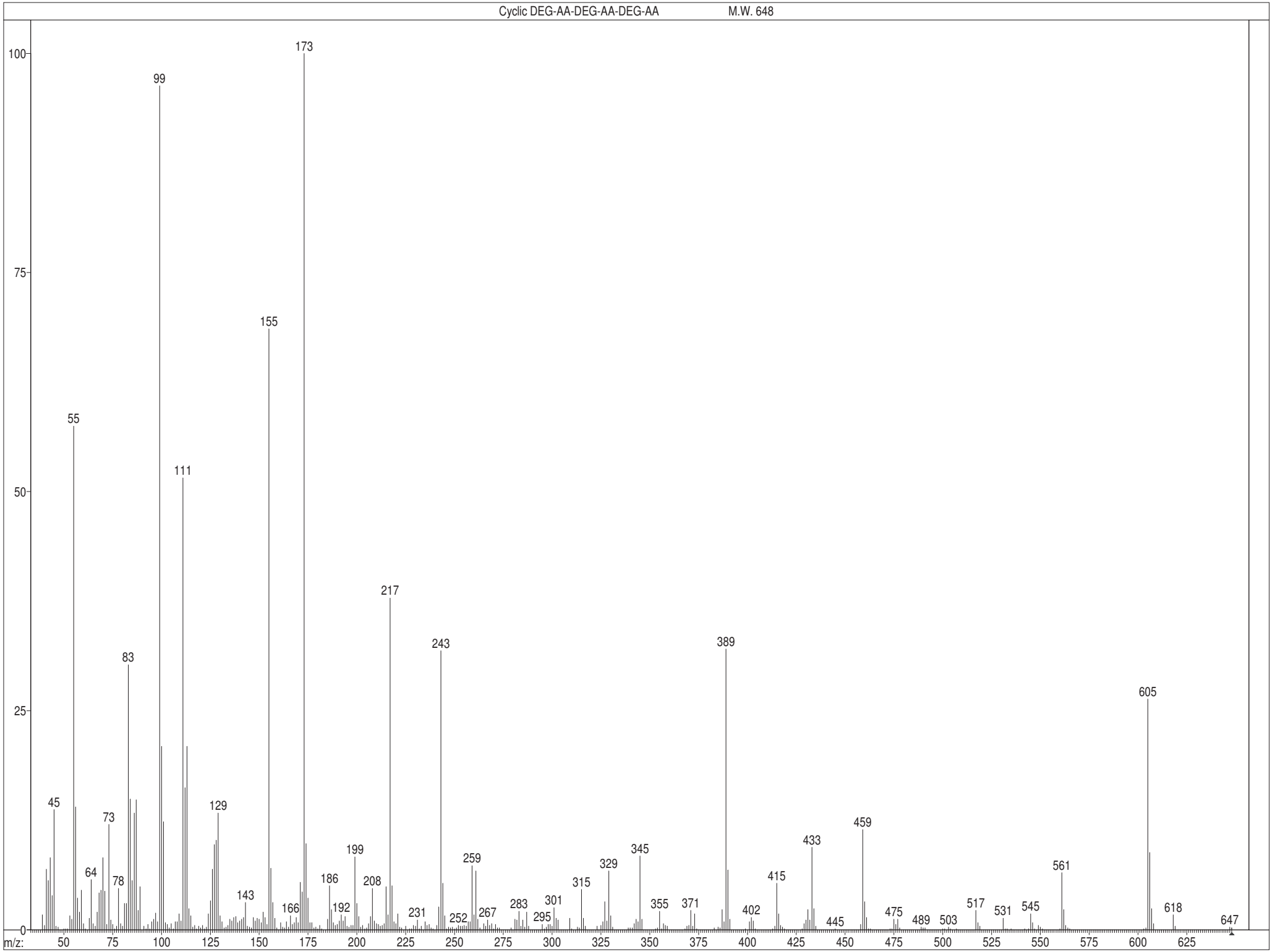


Mass Spectrum for



0316

Mass Spectrum for



0317