

Supplementary Information

Unified synthesis of tirandamycins and streptolydigin

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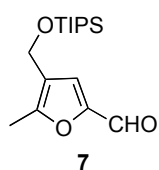
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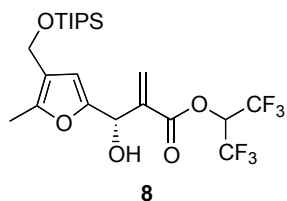
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General. Where appropriate, reactions were performed in flame-dried glassware under argon atmosphere. All extracts were dried over MgSO₄ and concentrated by rotary evaporation below 30 °C at 25 Torr unless otherwise noted. Commercial reagents and solvents were used as supplied with following exceptions. Acetonitrile (MeCN), benzene, dichloromethane (CH₂Cl₂), *N,N*-dimethylformamide (DMF), methanol (MeOH), triethylamine (NEt₃), and toluene were distilled from CaH₂. Thin layer chromatography (TLC) was performed using precoated silica gel plates (0.2 or 0.5 mm thickness) and silica gel 60 RP-18 (0.25 mm thickness). Column chromatography was performed using silica gel (particle size 100-210 μm (regular), 40-50 μm (flash), 74-210 μm (ODS)). Optical rotations were recorded on digital polarimeter at ambient temperature. Infrared spectra (FTIR) were measured on a Fourier transform infrared spectrometer. ¹H NMR (400 and 500 MHz) and ¹³C NMR (100 and 125 MHz) spectra were measured using CDCl₃, CD₂Cl₂, CD₃OD as solvent, and chemical shifts are reported as δ values in ppm based on internal CHCl₃ (¹H: 7.26 ppm; ¹³C: 77.0 ppm), CD₂Cl₂ (¹H: 5.32 ppm; ¹³C: 53.8 ppm), CD₃OD (¹H: 3.31 ppm; ¹³C: 49.0 ppm). Mass (MS) and high resolution mass (HRMS) spectra were taken in ESI, EI or FAB mode.



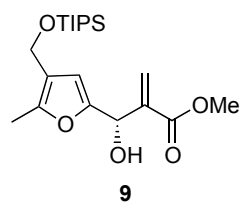
5-Methyl-4-(((triisopropylsilyloxy)methyl)furan-2-carbaldehyde (7). To an ice-cooled suspension of LiAlH₄ (9.0 g, 288 mmol) in Et₂O (216 mL) was slowly added a solution of ethyl 2-methyl-3-furancarboxylate (30 g, 192 mmol) in Et₂O (192 mL). After stirring at 0 °C for 1 h, the reaction was carefully quenched with H₂O (15 mL) and the mixture was stirred at room temperature for 1 h. The mixture was filtered through Celite which was thoroughly washed with Et₂O. The combined filtrate and washings are dried and concentrated to give the corresponding alcohol (25 g) which was used for the next reaction without purification. To a solution of the crude alcohol (25 g) in CH₂Cl₂ (180 mL) was added imidazole (33 g, 480 mmol) and TIPSCl (61 mL, 288 mmol). After being stirred at room temperature for 12 h, the mixture was diluted with saturated NH₄Cl (200 mL) at 0 °C, extracted with AcOEt, dried, and concentrated. The residue was purified by column chromatography (SiO₂ 1 kg, hexane/AcOEt = 100:1) to give the TIPS ether (63 g) containing silicon impurities, which was used for the next reaction without further purification. To a solution of the TIPS ether (63 g) in THF (1.2 L) were added *sec*-BuLi (1.04 M in hexane, 200 mL, 208 mmol) at -78 °C. After stirring at -78 °C for 1 h, a solution of DMF (72 mL, 900 mmol) in THF (120 mL) was added dropwise over 1 h, and the mixture was stirred at -78 °C for 1 h and then at -50 °C for 1 h. The reaction was quenched with saturated NH₄Cl (200 mL) at 0 °C and the mixture was extracted with AcOEt. The extract was washed with brine, dried, concentrated, and chromatographed (SiO₂ 1 kg,

hexane/AcOEt = 15:1 to 10:1) to give **7** (50 g, 88%) as a yellow oil: ^1H NMR (400 MHz, CDCl_3) δ 9.50 (s, 1H), 7.22 (s, 1H), 4.63 (s, 2H), 2.39 (s, 3H), 1.20-1.05 (m, 21H); ^{13}C NMR (100 MHz, CDCl_3) δ 176.4, 155.0, 150.1, 123.4, 122.8, 56.7, 17.6, 12.1, 11.6; FT-IR (neat) 2943, 2864, 1680, 1525, 1461, 1132, 1075, 881, 683 cm^{-1} ; MS (ESI) m/z 319 [(M+Na) $^+$]; HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{28}\text{NaO}_3\text{Si}$ [(M+Na) $^+$] 319.1705, found 319.1694.



(S)-1,1,1,3,3,3-Hexafluoropropan-2-yl 2-(Hydroxy(5-methyl-4-(((triisopropylsilyloxy)-methyl)furan-2-yl)methyl)acrylate (8**).**

β -ICD (1.04 g, 1.4 mmol) was dissolved in THF (10 mL) and the solution was evaporated. After repeating this operation three times, the amorphous residue was dried under vacuum at room temperature for 20 min. A solution of the dried β -ICD and aldehyde **7** (5.0 g, 16.9 mmol) in DMF (56 mL) was cooled to -55 $^\circ\text{C}$, and HFIPA (3.7 mL, 22.0 mmol) was then added. After the mixture was stirred at -55 $^\circ\text{C}$ for 3 days, the reaction was quenched by the addition of 0.1 M HCl (50 mL). The mixture was extracted with EtOAc, washed with saturated NaHCO_3 and brine, dried, and concentrated. The residue was purified by column chromatography (SiO_2 200 g, hexane/AcOEt = 20:1) to give **8** (6.14 g, 70%) as a colorless oil: $[\alpha]_{\text{D}}^{22}$ -28.4 (c 1.00, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 6.61 (s, 1H), 6.31 (s, 1H), 6.20 (s, 1H), 5.80 (septet, J = 6.0 Hz, 1H), 5.58 (d, J = 5.2 Hz, 1H), 4.52 (s, 2H), 2.23 (s, 3H), 1.18-1.02 (m, 21H); ^{13}C NMR (100 MHz, CDCl_3) δ 162.3, 150.5, 148.3, 137.4, 130.0, 123.4 (q, $^1J_{\text{C},\text{F}}$ = 281 Hz), 120.4, 109.1, 66.6 (septet, $^1J_{\text{C},\text{F}}$ = 35 Hz), 66.2, 57.3, 17.9, 11.9, 11.7; FTIR (neat) 3382, 2946, 2868, 1757, 1638, 1464, 1385, 1230, 1203, 1117 cm^{-1} ; MS (ESI) m/z 541 [(M+Na) $^+$]; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{32}\text{F}_6\text{NaO}_5\text{Si}$ [(M+Na) $^+$] 541.1820, found 541.1813.

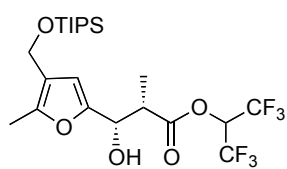


(S)-Methyl 2-(Hydroxy(5-methyl-4-(((triisopropylsilyloxy)methyl)-furan-2-yl)methyl)acrylate (9**).** To a solution of **8** (5.19 g, 10.0 mmol) in MeOH (100 mL) was added NEt_3 (6.9 mL, 50 mmol) at 0 $^\circ\text{C}$. After stirring at room temperature for 1 h, the reaction was quenched by the

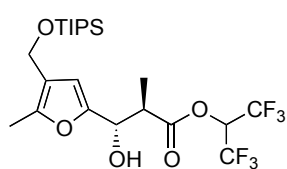
addition of Dowex-50 (5 g) at 0 $^\circ\text{C}$. The mixture was filtered, concentrated, and chromatographed (flash, SiO_2 100 g, hexane/AcOEt = 10:1) to give **9** (3.83 g, 100%) as a yellow oil which was determined to be 99% ee by HPLC analysis on a chiral stationary phase: $[\alpha]_{\text{D}}^{23}$ -13.5 (c 1.00, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 6.35 (s, 1H), 6.16 (s, 1H), 5.95 (s, 1H), 5.50 (s, 1H), 4.51 (s, 2H), 3.73 (s, 3H), 3.10 (brs, 1H), 2.23 (s, 3H), 1.18-1.01 (m, 21H); ^{13}C NMR (100 MHz, CDCl_3) δ 166.4, 151.4, 147.8, 139.5, 130.0, 126.4, 120.1, 108.6, 67.0, 57.4, 51.9, 17.9, 11.9, 11.8; FTIR (neat) 3448, 2943, 2865, 1725, 1630, 1437, 1219, 1144,

1062 cm^{-1} ; MS (ESI) m/z 405 $[(M+Na)^+]$; HRMS (ESI) calcd for $\text{C}_{20}\text{H}_{34}\text{NaO}_5\text{Si}$ $[(M+Na)^+]$ 405.2073, found 405.2080. HPLC conditions: Danicel Chiralcel AD-H, 2-propanol/hexane = 1/100 (1 mm/min), t_R = 17.8 min (*S*) and 20.8 min (*R*).

Hydrogenation of Ester 8 (Entry 1). To an ice-cooled solution of **8** (52 mg, 0.10 mmol) in CH_2Cl_2 (2 mL) were added 10% Pd/C (5 mg). After being stirred under hydrogen atmosphere at 0 °C for 1 h, the mixture was filtered through Celite which was washed with CH_2Cl_2 . The combined filtrate and washings were concentrated and purified by preparative TLC (hexane/AcOEt = 5:1) to give the corresponding *syn*-product (13 mg, 24%) and *anti*-product (37 mg, 72%).

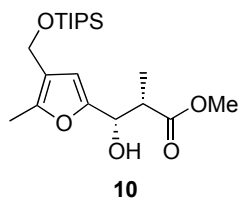


syn-Product, a colorless oil: $[\alpha]_D^{27}$ -1.6 (c 0.78, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 6.26 (s, 1H), 5.73 (septet, J = 6.0 Hz, 1H), 4.96 (d, J = 6.4 Hz, 1H), 4.52 (s, 2H), 3.20-3.10 (m, 1H), 2.30-2.21 (m, 4H), 1.34 (d, J = 6.8 Hz, 3H), 1.12-1.05 (m, 21H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.1, 150.7, 147.8, 120.3 (q, $^1J_{C,F}$ = 282 Hz), 120.2, 108.8, 68.3, 66.4 (septet, $^1J_{C,F}$ = 34 Hz), 57.4, 44.1, 17.9, 12.0, 11.9, 11.7; FTIR (neat) 3412, 2946, 2863, 1779, 1467, 1384, 1292, 1234, 1115 cm^{-1} ; MS (EI) m/z 103, 131, 253, 329, 459, 477(100), 520 (M) $^+$; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{34}\text{F}_6\text{O}_5\text{Si}$ (M) $^+$ 520.2087, found 520.2080.

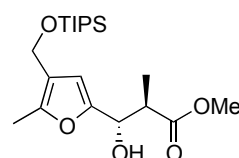


anti-Product, a colorless oil: $[\alpha]_D^{27}$ -14.5 (c 1.00, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 6.30 (s, 1H), 5.83 (septet, J = 6.0 Hz, 1H), 4.76 (d, J = 8.4 Hz, 1H), 4.55 (s, 2H), 3.26-3.19 (m, 1H), 2.46 (brs, 1H), 2.24 (s, 3H), 1.14 (d, J = 6.8 Hz, 3H), 1.12-1.00 (m, 21H); ^{13}C NMR (100 MHz, CDCl_3) δ 171.9, 150.2, 148.1, 120.4 (q, $^1J_{C,F}$ = 279 Hz), 120.2, 109.8, 69.4, 66.4 (septet, $^1J_{C,F}$ = 35 Hz), 57.3, 44.6, 17.9, 13.8, 11.9, 11.8; FTIR (neat) 3461, 2946, 2866, 1735, 1459, 1376, 1205, 1065, 885, 807 cm^{-1} ; MS (ESI) m/z 543 $[(M+Na)^+]$; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{34}\text{F}_6\text{NaO}_5\text{Si}$ $[(M+Na)^+]$ 543.2079, found 543.2053.

Hydrogenation of Ester 9 (Entry 2). To an ice-cooled solution of **9** (38 mg, 0.10 mmol) in CH_2Cl_2 (2 mL) were added 10% Pd/C (4 mg). After being stirred under hydrogen atmosphere at 0 °C for 1 h, the mixture was filtered through Celite which was washed with CH_2Cl_2 . The combined filtrate and washings were concentrated, and purified by preparative TLC (hexane/AcOEt = 5:1) to give the corresponding *syn*-product **10** (10 mg, 26%) and *anti*-product (27 mg, 72%).



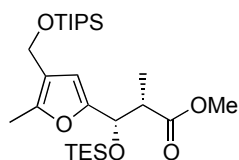
***syn*-Product 10**, a colorless oil: $[\alpha]_D^{22} -1.9$ (*c* 1.00, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.22 (s, 1H), 4.91 (t, *J* = 5.4 Hz, 1H), 4.53 (s, 2H), 3.69 (s, 3H), 2.93 (qd, *J* = 5.4, 6.8 Hz, 1H), 2.87 (d, *J* = 5.4 Hz, 1H), 2.23 (s, 3H), 1.25 (d, *J* = 6.8 Hz, 3H), 1.18-1.00 (m, 21H); ¹³C NMR (100 MHz, CDCl₃) δ 175.3, 151.4, 147.2, 119.9, 108.0, 68.7, 57.4, 51.8, 44.0, 17.9, 11.9, 11.8, 11.7; FTIR (neat) 3461, 2946, 2866, 1735, 1459, 1376, 1205, 1065 cm⁻¹; MS (ESI) *m/z* 407 [(M+Na)⁺]; HRMS (ESI) calcd for C₂₀H₃₆NaO₅Si [(M+Na)⁺] 407.2229, found 407.2206.



***anti*-Product**, a colorless oil: $[\alpha]_D^{27} -23.0$ (*c* 1.00, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.25 (s, 1H), 4.69 (dd, *J* = 6.4, 7.6 Hz, 1H), 4.54 (s, 2H), 3.74 (s, 3H), 3.00 (qd, *J* = 7.6, 14.2 Hz, 1H), 2.93 (d, *J* = 6.4 Hz, 1H), 1.18-1.01 (m, 24H); ¹³C NMR (100 MHz, CDCl₃) δ 175.9, 151.2, 147.6, 120.0, 109.1, 69.8, 57.4, 51.9, 44.4, 17.9, 14.3, 11.9, 11.8; FTIR (neat) 3473, 2944, 2866, 1740, 1461, 1378, 1169, 1063, 883, 804 cm⁻¹; MS (ESI) *m/z* 407 [(M+Na)⁺]; HRMS (ESI) calcd for C₂₀H₃₆NaO₅Si [(M+Na)⁺] 407.2229, found 407.2226.

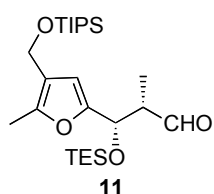
MgBr₂-mediated Hydrogenation of Ester 8 (Entry 3). To an ice-cooled solution of **8** (56 mg, 0.11 mmol) in CH₂Cl₂ (1 mL) were added MgBr₂ (30 mg, 0.16 mmol) and 10% Pd/C (28 mg). After being stirred under hydrogen atmosphere at 0 °C for 5 h and then at room temperature for 1 h, the mixture was filtered through Celite which was washed with CH₂Cl₂. The combined filtrate and washings were washed with saturated NaHCO₃ and brine, dried, concentrated, and purified by preparative TLC (hexane/AcOEt = 5:1) to give the corresponding the *syn*-product (28 mg, 49%) and the *anti*-product (28 mg, 49%) as a colorless oil, respectively.

Synthesis of Compound 10 by MgBr₂-mediated Hydrogenation of Ester 9 (Entry 4). To an ice-cooled solution of **9** (27.6 g, 72 mmol) in CH₂Cl₂ (500 mL) were added MgBr₂ (20.0 g, 108 mmol) and 10% Pd/C (14.0 g). After being stirred under hydrogen atmosphere at 0 °C for 5 h and then at room temperature for 1 h, the mixture was filtered through Celite which was washed with CH₂Cl₂. The combined filtrate and washings were washed with saturated NaHCO₃ and brine, dried, concentrated, and chromatographed (SiO₂ 350 g, hexane/AcOEt = 7:1) to give **10** (26.0 g, 94%) as a colorless oil.



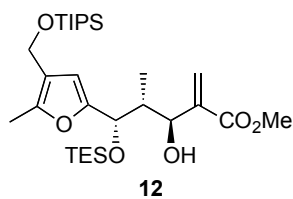
(2S,3S)-Methyl 2-Methyl-3-(5-methyl-4-(((triisopropylsilyl)oxy)methyl)furan-2-yl)-3-(((triethylsilyl)oxy)propanoate.

To an ice-cooled solution of **10** (23.8 g, 62 mmol) in CH₂Cl₂ (124 mL) were added TESCl (25.8 mL, 155 mmol), DIPEA (42.2 mL, 248 mmol), and DMAP (0.76 g, 6.2 mmol), and the mixture was stirred at 0 °C for 30 min. The mixture was diluted with CH₂Cl₂, and washed with saturated NH₄Cl, dried, concentrated, and chromatographed (SiO₂ 300 g, hexane/AcOEt = 70:1) to give the TES ether (29.6 g, 96%) as a colorless oil: $[\alpha]_D^{28} -21.1$ (*c* 1.00, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.14 (s, 1H), 4.90 (d, *J* = 6.7 Hz, 1H), 4.51 (s, 2H), 3.58 (s, 3H), 2.86 (qd, *J* = 6.7, 6.8 Hz, 1H), 2.20 (s, 3H), 1.21 (d, *J* = 6.8 Hz, 3H), 1.17-1.00 (m, 21H), 0.87 (t, *J* = 8.1 Hz, 9H), 0.52 (q, *J* = 8.1 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 174.5, 152.6, 146.6, 119.9, 108.0, 69.6, 57.5, 51.4, 45.9, 17.9, 12.2, 11.9, 11.7, 6.6, 4.6; FTIR (neat) 2946, 2868, 1742, 1460, 1248, 1140, 1066 cm⁻¹; MS (EI) *m/z* 73, 135, 193, 265, 267, 325, 367, 411, 441, 498 (M⁺); HRMS (EI) calcd for C₂₆H₅₀O₅Si₂ (M⁺) 498.3197, found 498.3175.



(2S,3S)-2-Methyl-3-(5-methyl-4-(((triisopropylsilyl)oxy)methyl)furan-2-yl)-3-(((triethylsilyl)oxy)propanal (11).

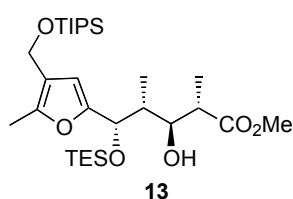
To a solution of the TES ether (14.2 g, 28.5 mmol) in CH₂Cl₂ (285 mL) was added DIBAL-H (1.02 M in hexane, 50 mL, 51.3 mol) at -94 °C. After stirring at -94 °C for 1 h, the reaction was quenched by the addition of isopropanol (2 M in CH₂Cl₂, 200 mL, 400 mol) and the mixture was allowed to warm to 0 °C. Saturated Rochelle salt (100 mL) was added and the mixture was vigorously stirred at room temperature for 6 h. The mixture was extracted with AcOEt, dried over Na₂SO₄, concentrated, and chromatographed (SiO₂ 450 g, hexane/AcOEt = 50:1) to afford **11** (13.0 g, 98%) as colorless oil: $[\alpha]_D^{28} -18.4$ (*c* 1.00, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 9.82 (s, 1H), 6.18 (s, 1H), 4.94 (d, *J* = 5.2 Hz, 1H), 4.53 (s, 2H), 2.76 (qd, *J* = 5.2, 6.8 Hz, 1H), 2.20 (s, 3H), 1.17-1.02 (m, 24H), 0.88 (t, *J* = 7.8 Hz, 9H), 0.53 (q, *J* = 7.8 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 204.0, 151.7, 147.1, 120.1, 109.0, 68.6, 57.4, 52.1, 17.9, 12.0, 11.8, 9.2, 6.6, 4.6; FTIR (neat) 2949, 2872, 1728, 1460, 1387, 1227, 1071, 1009 cm⁻¹; MS (EI) *m/z* 73, 103, 115, 181, 238, 253, 337, 411(100), 425, 468 (M⁺); HRMS (EI) calcd for C₂₅H₄₈O₄Si₂ (M⁺) 468.3091, found 468.3089.



(3S,4R,5S)-Methyl 3-Hydroxy-4-methyl-5-(5-methyl-4-(((triisopropylsilyl)oxy)methyl)furan-2-yl)-2-methylene-5-(((triethylsilyl)oxy)pentanoate (12).

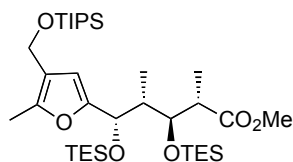
α -ICPN (62 mg, 0.2 mmol) was dissolved in THF (2 mL) and the solution was evaporated at room temperature. After repeating this operation three times, the amorphous residue was dried

under vacuum at room temperature for 10 min. A solution of the dried α -ICPN and **11** (468 mg, 1.0 mmol) in DMF (3.3 mL) was cooled to $-55\text{ }^{\circ}\text{C}$, and HFIPA (680 μL , 4.0 mmol) was then added. After stirring at $-55\text{ }^{\circ}\text{C}$ for 3 days, the reaction was quenched by the addition of 0.1 M HCl (4 mL). The mixture was extracted with AcOEt, washed with saturated NaHCO_3 and brine, dried, and concentrated. Short column chromatography (SiO_2 10 g, hexane/AcOEt = 75:1 to 20:1) gave the recovered **11** (114 mg, 20%) and the impure HFIPA ester (450 mg), the latter of which was dissolved into MeOH (2 mL). The solution was stirred at room temperature for 6 h, concentrated, and chromatographed (SiO_2 6 g, hexane/AcOEt = 30:1 to 20:1) to give **12** (376 mg, 68%; 86% based on the recovered **11**) as a colorless oil: $[\alpha]_{\text{D}}^{27} -24.7$ (c 1.00, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 6.28 (s, 1H), 6.18 (s, 1H), 5.84 (s, 1H), 5.04 (d, $J = 2.4$ Hz, 1H), 4.54 (s, 2H), 4.41 (t, $J = 7.1$ Hz, 1H), 3.91 (d, $J = 6.6$ Hz, 1H), 3.76 (s, 3H), 2.202 (s, 3H), 2.15 (ddt, $J = 2.4, 6.6, 7.2$ Hz, 1H), 1.17-1.06 (m, 21H), 0.91 (t, $J = 8.1$ Hz, 9H), 0.85 (d, $J = 7.2$ Hz, 3H), 0.55 (q, $J = 8.0$ Hz, 6H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 167.0, 152.8, 146.5, 141.6, 126.7, 119.9, 108.5, 74.9, 69.8, 57.5, 51.8, 42.9, 17.9, 12.0, 11.8, 11.7, 6.7, 4.6; FTIR (neat) 3509, 2948, 2870, 1723, 1461, 1221, 1083 cm^{-1} ; MS (ESI) m/z 577 $[(\text{M}+\text{Na})^+]$; HRMS (ESI) calcd for $\text{C}_{29}\text{H}_{54}\text{NaO}_6\text{Si}_2$ $[(\text{M}+\text{Na})^+]$ 577.3356, found 577.3344.



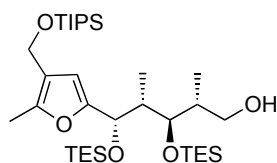
(2S,3S,4R,5S)-Methyl 3-Hydroxy-2,4-dimethyl-5-(5-methyl-4-(((triisopropylsilyloxy)methyl)furan-2-yl)-5-((triethylsilyloxy)-pentanoate (13). A mixture of **12** (19.6 g, 35.3 mmol) and bicyclo[2.2.1]hepta-2,5-diene 1,4-bis(diphenylphosphino)butane-

rhodium trifluoromethanesulfonate (816 mg, 1.06 mmol) in CH_2Cl_2 (137 mL) was stirred at $0\text{ }^{\circ}\text{C}$ under hydrogen atmosphere. After being stirred at $0\text{ }^{\circ}\text{C}$ for 1 h, the mixture was filtered through SiO_2 which was washed with AcOEt. The filtrate and washings were concentrated and chromatographed (SiO_2 600 g, hexane/AcOEt = 50:1) to give **13** (17.2 g, 87%) as a colorless oil: $[\alpha]_{\text{D}}^{29} -17.2$ (c 1.00, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 6.17 (s, 1H), 5.01 (d, $J = 2.7$ Hz, 1H), 4.54 (s, 2H), 3.67 (s, 3H), 3.66-3.55 (m, 1H), 2.71-2.64 (m, 1H), 2.21 (s, 3H), 1.97-1.91 (m, 1H), 1.27 (d, $J = 7.1$ Hz, 3H), 1.18-1.02 (m, 21H), 0.93-0.88 (m, 12H), 0.54 (q, $J = 8.1$ Hz, 6H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 175.9, 153.0, 146.3, 119.9, 108.3, 75.8, 70.3, 57.5, 51.5, 42.3, 41.9, 17.9, 14.8, 12.0, 11.8, 11.5, 6.6, 4.6; FTIR (neat) 3516, 2949, 2873, 1723, 1459, 1375, 1070 cm^{-1} ; MS (ESI) m/z 579 $[(\text{M}+\text{Na})^+]$; HRMS (ESI) calcd for $\text{C}_{29}\text{H}_{56}\text{NaO}_6\text{Si}_2$ $[(\text{M}+\text{Na})^+]$ 579.3513, found 579.3532.



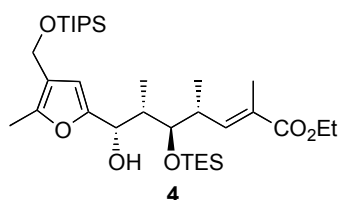
(2*S*,3*S*,4*R*,5*S*)-Methyl 2,4-Dimethyl-5-(5-methyl-4-(((triisopropylsilyloxy)methyl)furan-2-yl)-3,5-bis((triethylsilyloxy)oxy)pentanoate.

To an ice-cooled solution of **13** (104 mg, 0.187 mmol) in CH₂Cl₂ (1 mL) were added TESOTf (136 μL, 0.56 mmol) and 2,6-lutidine (130 μL, 1.12 mmol), and the mixture was stirred at 0 °C for 30 min. The mixture was extracted with AcOEt, and the extract was washed with saturated NH₄Cl, dried, and concentrated. The residue was purified by column chromatography (SiO₂ 10 g, hexane/AcOEt = 40:1) to afford the bis-TES ether (114 mg, 91%) as a colorless oil: [α]_D²⁹ -4.1 (*c* 1.00, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.11 (s, 1H), 4.55 (d, *J* = 8.6 Hz, 1H), 4.54 (s, 2H), 3.76 (dd, *J* = 3.4, 7.2 Hz, 1H), 3.60 (s, 3H), 2.42-2.35 (m, 1H), 2.24-2.18 (m, 4H), 1.18-1.03 (m, 24H), 1.01 (d, *J* = 7.6 Hz, 3H), 0.94-0.82 (m, 18H), 0.60-0.45 (m, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 175.7, 153.3, 146.4, 120.0, 108.9, 75.6, 68.9, 57.5, 51.6, 43.9, 43.8, 17.9, 13.8, 12.2, 12.0, 11.7, 6.8, 6.7, 5.1, 4.8; FTIR (neat) 2950, 2875, 1740, 1460, 1376, 1241, 1065, 1008 cm⁻¹; MS (ESI) *m/z* 693 [(M+Na)⁺]; HRMS (ESI) calcd for C₃₅H₇₀NaO₆Si₃ [(M+Na)⁺] 693.4377, found 693.4359.



(2*R*,3*R*,4*R*,5*S*)-2,4-Dimethyl-5-(5-methyl-4-(((triisopropylsilyloxy)methyl)furan-2-yl)-3,5-bis((triethylsilyloxy)oxy)pentan-1-ol.

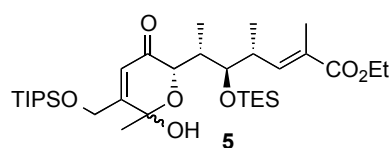
To a solution of the bis-TES ether (90 mg, 0.134 mmol) in CH₂Cl₂ (1.4 mL) were added DIBAL-H (1.04 M in hexane, 0.27 mL, 0.28 mol) at -78 °C, and the mixture was stirred at -78 °C for 1 h. The reaction was quenched with saturated Rochelle salt (2 mL), and the mixture was stirred vigorously at room temperature for 6 h. The mixture was extracted with CH₂Cl₂, dried, concentrated, and chromatographed (SiO₂ 5 g, hexane/AcOEt = 25:1) to give the alcohol (74 mg, 87%) as a colorless oil: [α]_D²⁹ -29.4 (*c* 1.00, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.09 (s, 1H), 4.54 (s, 2H), 4.33 (d, *J* = 9.2 Hz, 1H), 3.76-3.69 (m, 1H), 3.55-3.47 (m, 1H), 3.40 (t, *J* = 4.0 Hz, 1H), 2.91 (t, *J* = 6.4 Hz, 1H), 2.32-2.23 (m, 1H), 2.23 (s, 3H), 1.71 (brs, 1H), 1.13 (d, *J* = 7.2 Hz, 3H), 1.11-1.03 (m, 21H), 0.96-0.81 (m, 21H), 0.58 (q, *J* = 8.0 Hz, 6H), 0.49 (q, *J* = 8.0 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 152.8, 146.6, 120.0, 109.0, 78.4, 69.8, 66.6, 57.4, 46.2, 35.6, 17.9, 16.9, 11.9, 11.7, 11.3, 6.8, 6.7, 4.8, 4.7; FTIR (neat) 3455, 2951, 2875, 1461, 1415, 1238, 1059, 1008 cm⁻¹; MS (ESI) *m/z* 665 [(M+Na)⁺]; HRMS (ESI) calcd for C₃₄H₇₀NaO₅Si₃ [(M+Na)⁺] 665.4428, found 665.4417.



(4*R*,5*R*,6*S*,7*S*,*E*)-Ethyl 7-Hydroxy-2,4,6-trimethyl-7-(5-methyl-4-(((triisopropylsilyloxy)methyl)furan-2-yl)-5-((triethylsilyloxy)oxy)hept-2-enoate (4**).**

To a mixture of the alcohol

(850 mg, 1.32 mmol) and molecular sieves 4 Å (8.5 g, preactivated at 200 °C for 2 h) in CH₂Cl₂ (40 mL) were added NMO (323 mg, 2.64 mmol) and TPAP (146 mg, 0.396 mmol) at 0 °C. After being stirred at room temperature for 1 h, the mixture was filtered through Celite which was washed with CH₂Cl₂. The combined filtrate and washings were concentrated to give the aldehyde. The crude aldehyde was dissolved in toluene (30 mL) and ethyl 2-(triphenylphosphoranylidene)propionate (1.4 g, 3.96 mmol) was added. After being heated at reflux for 16 h, the mixture was cooled to room temperature, concentrated, and chromatographed (SiO₂ 50 g, hexane/AcOEt, 30:1) to give the corresponding α,β-unsaturated ester (840 mg) as a little impure yellow oil which was used for the next reaction without further purification. The α,β-unsaturated ester (840 mg) was dissolved in THF (17 mL), and H₂O (1.7 mL) and AcOH (5 mL) were added at room temperature. After being stirred at room temperature for 36 h, the mixture was diluted with saturated NaHCO₃ (20 mL) at 0 °C, extracted with AcOEt, dried, and concentrated. The residue was purified by column chromatography (SiO₂ 30 g, hexane/AcOEt = 20:1 to 5:1) to give **4** (708 mg, 74%) as a colorless oil: $[\alpha]_D^{27} +20.8$ (*c* 1.00, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.78 (dd, *J* = 1.4, 10.0 Hz, 1H), 6.18 (s, 1H), 5.04 (s, 1H), 4.54 (s, 2H), 4.25-4.15 (m, 2H), 3.70 (dd, *J* = 3.8, 6.3 Hz, 1H), 3.07 (s, 1H), 2.89-2.80 (m, 1H), 2.24 (s, 3H), 2.10-2.02 (m, 1H), 1.87 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.18-0.94 (m, 36H), 0.65 (q, *J* = 8.4 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 168.1, 153.2, 146.4, 144.8, 127.6, 119.9, 107.2, 80.9, 68.3, 60.4, 57.6, 39.7, 37.5, 18.0, 17.3, 14.2, 12.6, 12.0, 11.8, 11.6, 6.9, 5.3; FTIR (neat) 3498, 2950, 2870, 1709, 1461, 1379, 1237, 1090, 738 cm⁻¹; MS (ESI) *m/z* 633 [(M+Na)⁺]; HRMS (ESI) calcd for C₃₃H₆₂NaO₆Si₂ [(M+Na)⁺] 633.3982, found 633.3972.

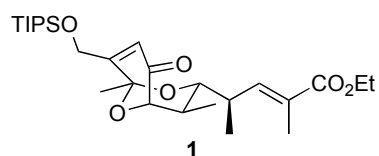


(4*R*,5*R*,6*S*,*E*)-Ethyl 6-((2*S*)-6-Hydroxy-6-methyl-3-oxo-5-(((triisopropylsilyl)oxy)methyl)-3,6-dihydro-2*H*-pyran-2-yl)-2,4-dimethyl-5-((triethylsilyl)oxy)hept-2-enoate (5).

To an ice-cooled solution of **4** (7.5 g, 12.2 mmol) in CH₂Cl₂ (407 mL) was added *m*CPBA (75% purity, 4.8 g, 20.7 mmol). After stirring at 0 °C for 2 h, the reaction was quenched with saturated NaHSO₃ (200 mL) and the mixture was extracted with CH₂Cl₂. The extract was washed with saturated NaHCO₃ and brine, dried, concentrated, chromatographed (SiO₂ 30 g, hexane/AcOEt = 5:1) to give **5** (7.6 g, 92%), a colorless oil, as a 6:1 epimeric mixture.

Major epimer: $[\alpha]_D^{27} +10.7$ (*c* 1.00, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.02 (dd, *J* = 1.4, 10.0 Hz, 1H), 6.24-6.22 (m, 1H), 4.63 (s, 1H), 4.48-4.47 (m, 2H), 4.25-4.15 (m, 2H), 3.75 (dd, *J* = 2.2, 8.0 Hz, 1H), 3.07 (s, 1H), 2.77-2.71 (m, 1H), 2.42-2.33 (m, 1H), 2.10-2.02 (m, 1H), 1.84 (d, *J* = 1.4 Hz, 3H), 1.57 (s, 3H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.18-0.98 (m, 30H), 0.73-0.67

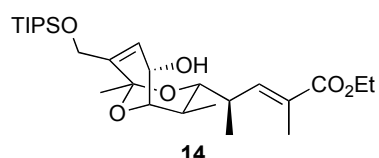
(m, 9H); ^{13}C NMR (100 MHz, CDCl_3) δ 197.7, 168.7, 160.8, 143.7, 126.9, 121.4, 107.2, 93.4, 74.9, 61.5, 60.4, 39.3, 36.8, 26.5, 17.9, 14.1, 12.5, 11.8, 10.8, 7.0, 5.5; FTIR (neat) 3410, 2944, 2873, 1710, 1683, 1458, 1379, 1219, 1137 cm^{-1} ; MS (ESI) m/z 649 [(M+Na) $^+$]; HRMS (ESI) calcd for $\text{C}_{33}\text{H}_{62}\text{NaO}_7\text{Si}_2$ [(M+Na) $^+$] 649.3931, found 649.3938.



(4R,E)-Ethyl 4-((3R,4R)-1,4-Dimethyl-6-oxo-8-(((triisopropylsilyloxy)methyl)-2,9-dioxabicyclo[3.3.1]non-7-en-3-yl)-2-methylpent-2-enoate (1).

Method A: To a solution of **5** (50 mg, 80 μmol) in MeCN (19 mL) were added 48% HF (5.0 μL , 0.12 mmol) and 25% H_2SiF_6 (5.4 μL , 0.12 mmol) at room temperature. After stirring at room temperature for 20 min, saturated K_2CO_3 (1 mL) was added and the mixture was extracted with AcOEt. The extract was washed with H_2O and brine, dried, concentrated, and purified by preparative TLC (hexane/AcOEt = 10:1) to give **1** (29 mg, 74%) as a colorless oil.

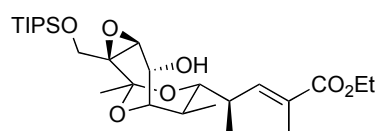
Method B: To a solution of **5** (7.1 g, 11.3 mmol) in Ac_2O (110 mL) was added I_2 (1.47 g, 5.3 mmol) at -10°C . After stirring at -10°C for 3 h, the reaction was quenched with saturated $\text{Na}_2\text{S}_2\text{O}_3$ (50 mL) and the mixture was extracted with AcOEt. The extract was washed with saturated NaHCO_3 and brine, dried, and concentrated. The residue was purified by flash column chromatography (SiO_2 300 g, hexane/AcOEt = 10:1) to give **1** (3.0 g, 54%) as a colorless oil: $[\alpha]_{\text{D}}^{28} -110.5$ (c 1.00, CHCl_3) [lit. 1 $[\alpha]_{\text{D}}^{28} +105.5$ (c 1.45, CHCl_3) (enantiomer)]; ^1H NMR (400 MHz, CDCl_3) δ 6.90 (dd, $J = 1.4, 10.3$ Hz, 1H), 6.53 (s, 1H), 4.52 (dd, $J = 2.2, 18.2$ Hz, 1H), 4.25-4.15 (m, 2H), 4.04 (d, $J = 6.1$ Hz, 1H), 3.44 (dd, $J = 2.2, 11.5$ Hz, 1H), 2.85-2.73 (m, 1H), 2.06-1.96 (m, 1H), 1.85 (d, $J = 1.4$ Hz, 3H), 1.53 (s, 3H), 1.32 (t, $J = 7.1$ Hz, 3H), 1.14-1.05 (m, 21H), 1.02 (d, $J = 6.9$ Hz, 3H), 0.73 (d, $J = 7.1$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 195.4, 168.0, 158.2, 141.3, 128.5, 123.3, 94.7, 78.9, 76.7, 60.8, 60.6, 34.0, 33.4, 24.0, 17.9, 17.6, 16.4, 14.2, 12.4, 12.2, 11.8, 11.6; FTIR (neat) 2942, 2866, 1709, 1686, 1459, 1383, 1252, 1138 cm^{-1} ; MS (ESI) m/z 517 [(M+Na) $^+$]; HRMS (ESI) calcd for $\text{C}_{27}\text{H}_{46}\text{NaO}_6\text{Si}$ [(M+Na) $^+$] 517.2961, found 517.2958.



(4R,E)-Ethyl 4-((3R,4R,6R)-6-Hydroxy-1,4-dimethyl-8-(((triisopropylsilyloxy)methyl)-2,9-dioxabicyclo[3.3.1]non-7-en-3-yl)-2-methylpent-2-enoate (14).

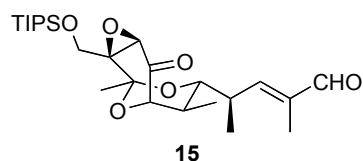
To an ice-cooled solution of **1** (960 mg, 1.94 mmol) in MeOH (96 mL) were added CeCl_3 (513 mg, 1.94 mmol) and NaBH_4 (581 mg, 15.5 mmol), and the mixture was stirred at 0°C for 5 min. The reaction was quenched with 10% HCl (10 mL) and added water (50 mL), then the mixture was extracted with AcOEt. The extract was washed with saturated NaHCO_3 , dried, concentrated,

and purified by flash column chromatography (SiO₂ 50 g, toluene/AcOEt = 20:1) to give **14** (950 mg, 95%) as a colorless oil: $[\alpha]_D^{28} +2.4$ (*c* 1.00, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.92 (dd, *J* = 1.4, 10.3 Hz, 1H), 6.13-6.12 (m, 1H), 4.89 (brs, 1H), 4.30 (dd, *J* = 2.2, 3.4 Hz, 1H), 4.22-4.28 (m, 2H), 4.00 (d, *J* = 4.4 Hz, 1H), 3.75 (dd, *J* = 2.3, 11.2 Hz, 1H), 2.83-2.72 (m, 1H), 2.08-1.99 (m, 1H), 1.85 (d, *J* = 1.4 Hz, 3H), 1.38 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.14-1.08 (m, 21H), 1.01 (d, *J* = 7.1 Hz, 3H), 0.95 (d, *J* = 7.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 168.2, 142.1, 136.3, 128.0, 126.0, 94.6, 76.1, 73.2, 68.8, 60.8, 60.4, 36.0, 34.1, 24.2, 18.0, 16.4, 14.2, 12.9, 12.3, 11.9; FTIR (neat) 3472, 2941, 2866, 1708, 1459, 1379, 1252, 1038 cm⁻¹; MS (ESI) *m/z* 519 [(M+Na)⁺]; HRMS (ESI) calcd for C₂₇H₄₈NaO₆Si [(M+Na)⁺] 519.3117, found 519.3127.



(4*R,E*)-Ethyl 4-((2*S,4R,5S,7R,8R*)-5-Hydroxy-1,7-dimethyl-2-(((triisopropylsilyl)oxy)methyl)-3,9,10-trioxatricyclo-[4.3.1.0^{2,4}]decan-8-yl)-2-methylpent-2-enoate.

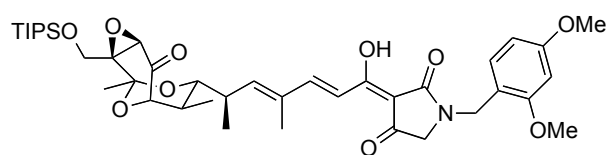
To an ice-cooled solution of **14** (45 mg, 91 μmol) in CH₂Cl₂ (2 mL) and H₂O (61 μL) were added NaH₂PO₃ (13.6 mg, 0.113 mmol) and *m*CPBA (75% purity, 26.4 mg, 0.115 mmol). After stirring at room temperature for 24 h, the reaction was quenched with saturated NaHSO₃ (10 mL) and the mixture was extracted with AcOEt. The extract was washed with saturated NaHCO₃ and brine, dried, concentrated, and purified by preparative TLC (hexane/AcOEt = 5:1) to give the epoxy alcohol (36 mg, 77%) as a colorless oil: $[\alpha]_D^{28} +17.7$ (*c* 0.51, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.90 (dd, *J* = 1.4, 10.3 Hz, 1H), 4.42 (dd, *J* = 5.2, 7.1 Hz, 1H), 4.22-4.18 (m, 2H), 4.08-3.98 (m, 3H), 3.94 (dd, *J* = 2.2, 11.6 Hz, 1H), 3.56 (d, *J* = 1.0 Hz, 1H), 2.83-2.76 (m, 1H), 2.08-2.01 (m, 1H), 1.86 (d, *J* = 1.4 Hz, 3H), 1.41 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.14-1.07 (m, 24H), 0.95 (d, *J* = 7.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 168.1, 140.9, 128.3, 95.3, 75.6, 71.3, 67.0, 60.5, 59.3, 59.1, 59.0, 36.1, 34.3, 22.9, 17.9, 16.4, 14.2, 12.9, 12.3, 11.8; FTIR (neat) 3498, 2941, 2866, 1705, 1459, 1379, 1248, 1038 cm⁻¹; MS (ESI) *m/z* 535 [(M+Na)⁺]; HRMS (ESI) calcd for C₂₇H₄₈NaO₇Si [(M+Na)⁺] 535.3067, found 535.3079.



(4*R,E*)-4-((2*S,4S,7R,8R*)-1,7-Dimethyl-5-oxo-2-(((triisopropylsilyl)oxy)methyl)-3,9,10-trioxatricyclo[4.3.1.0^{2,4}]-decan-8-yl)-2-methylpent-2-enal (15**).**

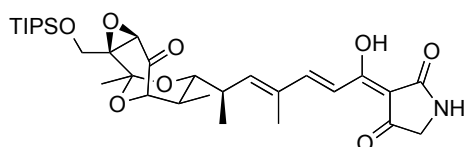
To a solution of the epoxy alcohol (31 mg, 61 μmol) in CH₂Cl₂ (4.3 mL) was added DIBAL-H (1.04 M in hexane, 0.29 mL, 0.30 mmol) at -78 °C, and the mixture was stirred at -78 °C for 1 h. The reaction was quenched with saturated Rochelle salt (4 mL), and the mixture was stirred at room

temperature for 6 h. The mixture was extracted with CH₂Cl₂, dried, and concentrated. The crude diol was dissolved in CH₂Cl₂ (4.3 mL) and molecular sieves 4 Å (300 mg, preactivated at 200 °C for 2 h) and PDC (183 mg, 0.49 mmol) were added at room temperature. After being stirred at room temperature for 1 h, the mixture was filtered through Celite which was washed with CH₂Cl₂. The combined filtrate and washings were concentrated and purified by preparative TLC (hexane/AcOEt = 3:1) to give **15** (27 mg, 95%) as a colorless oil: $[\alpha]_D^{26} +3.9$ (*c* 0.33, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 9.46 (s, 1H), 6.63 (dd, *J* = 1.1, 10.1 Hz, 1H), 4.15 (d, *J* = 12.0 Hz, 1H), 4.06 (d, *J* = 12.0 Hz, 1H), 4.05 (d, *J* = 12.0 Hz, 1H), 3.72 (s, 1H), 3.67 (dd, *J* = 1.9, 11.7 Hz, 1H), 3.00-2.94 (m, 1H), 2.02-1.91 (m, 1H), 1.77 (d, *J* = 1.3 Hz, 3H), 1.56 (s, 3H), 1.17 (d, *J* = 7.1 Hz, 3H), 1.08-1.14 (m, 21H), 0.75 (d, *J* = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 202.1, 195.0, 151.9, 140.0, 96.0, 78.5, 76.7, 60.1, 58.2, 56.4, 34.6, 34.3, 23.3, 17.9, 16.4, 11.7, 11.4, 9.3; FTIR (neat) 2941, 2866, 1726, 1689, 1463, 1375, 1140, 1008 cm⁻¹; MS (EI) *m/z* 466 (M⁺); HRMS (EI) calcd for C₂₅H₄₂O₆Si (M⁺) 466.2750, found 466.2758.



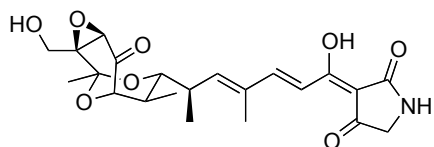
N-(2,4-Dimethoxybenzyl)tirandamycin B TIPS Ether. To an ice-cooled solution of phosphonate **16** (60 mg, 0.14 mmol) in THF

(2 mL) was stirred was added KO^tBu (27 mg, 0.24 mmol), and the mixture was stirred at 0 °C for 2 h. A solution of **10** (32 mg, 70 μmol) in THF (0.5 mL) was added at 0 °C and stirring was continued at 0 °C for 24 h. The reaction was quenched with 1% HCl (2 mL) and the mixture was extracted with Et₂O. The extract was washed with brine, filtered using a glass funnel plugged with lab wiper, concentrated, and chromatographed (ODS 5 g, MeCN/H₂O = 10:1) to give the title compound (45 mg, 80%) as a yellow oil: $[\alpha]_D^{25} -14.1$ (*c* 1.00, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.50 (d, *J* = 15.6 Hz, 1H), 7.19-7.11 (m, 2H), 6.47-6.43 (m, 2H), 6.14 (d, *J* = 10.1 Hz, 1H), 4.50 (s, 2H), 4.13-3.99 (m, 3H), 3.80 (s, 3H), 3.79 (s, 3H), 3.67-3.54 (m, 4H), 2.84-2.76 (m, 1H), 2.01-1.88 (m, 4H), 1.53 (s, 3H), 1.09-1.00 (m, 24H), 0.71 (d, *J* = 6.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 202.4, 192.0, 173.6, 173.3, 160.9, 158.5, 148.5, 142.5, 134.8, 131.2, 116.9, 116.2, 104.3, 101.0, 98.5, 95.8, 78.6, 77.2, 60.1, 58.1, 56.4, 55.6, 55.3, 40.0, 34.5, 34.4, 23.3, 17.9, 17.7, 16.9, 12.2, 11.7, 11.3; FTIR (neat) 3420, 2940, 2866, 1726, 1702, 1644, 1617, 1572, 1508, 1468, 1376, 1294, 1272, 1136, 1003 cm⁻¹; MS (ESI) *m/z* 762 [(M+Na)⁺]; HRMS (ESI) calcd for C₄₀H₅₇NNaO₁₀Si [(M+Na)⁺] 762.3649, found 762.3675.



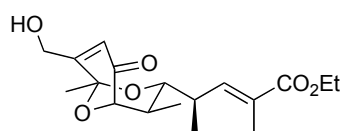
Tirandamycin B TIPS Ether. To a solution of *N*-(2,4-dimethoxybenzyl)tirandamycin B TIPS ether (90 mg, 123 μmol) in CH_2Cl_2 (4.5 mL) were added

thioanisole (720 μL , 6 mmol) and TFA (4.5 mL) at room temperature. After being stirred at room temperature for 2 h, the mixture was diluted with ice water (15 mL), extracted with CH_2Cl_2 , washed with saturated NaHCO_3 , filtered using a glass funnel plugged with lab wiper, and concentrated. The residue was purified by reverse phase column chromatography (ODS 15 g, $\text{MeCN}/\text{H}_2\text{O}$ = 10:1 to 2:1) to give the title compound (58.2 mg, 81%) as a yellow oil: $[\alpha]_{\text{D}}^{26}$ -21.8 (c 0.485, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.57 (d, J = 15.8 Hz, 1H), 7.16 (d, J = 15.8 Hz, 1H), 6.20 (d, J = 10.4 Hz, 1H), 5.80 (brs, 1H), 4.14 (d, J = 12.4 Hz, 1H), 4.05 (d, J = 12.0 Hz, 1H), 4.03 (d, J = 5.6 Hz, 1H), 3.82 (s, 2H), 3.63 (s, 2H), 3.62 (d, J = 12.0 Hz, 1H), 2.87-2.80 (m, 1H), 2.02-1.90 (m, 4H), 1.54 (s, 3H), 1.15-1.01 (m, 24H), 0.73 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 202.4, 192.6, 176.5, 174.9, 149.5, 143.4, 134.9, 116.7, 100.1, 95.9, 78.6, 77.2, 60.1, 58.1, 56.4, 51.6, 34.6, 34.4, 23.3, 17.8, 16.9, 12.2, 11.7, 11.4; FTIR (neat) 3442, 2860, 1725, 1658, 1617, 1566, 1455, 1215, 1139, 1062, 1001 cm^{-1} ; MS (ESI) m/z 612 $[(\text{M}+\text{Na})^+]$; HRMS (ESI) calcd for $\text{C}_{31}\text{H}_{47}\text{NNaO}_8\text{Si}$ $[(\text{M}+\text{Na})^+]$ 612.2968, found 612.2984.



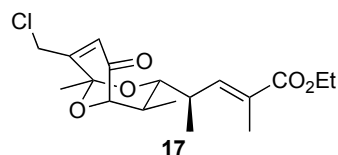
(-)-Tirandamycin B. To a solution of tirandamycin B TIPS ether (58 mg, 98 μmol) in MeCN (18 mL) was added HF·pyridine (630 μL) at room temperature. After

being stirred at room temperature for 24 h, the mixture was diluted with ice water (20 mL), extracted with AcOEt , washed with saturated NaHCO_3 , filtered using a glass funnel plugged with lab wiper, and concentrated. The residue was purified by reverse phase column chromatography (ODS 15 g, $\text{MeCN}/\text{H}_2\text{O}$ = 1:1) to give tirandamycin B (35 mg, 82%) as a yellow oil: $[\alpha]_{\text{D}}^{24}$ -8.1 (c 0.36, EtOH) [lit.² $[\alpha]_{\text{D}}^{25}$ -8.0 (c 0.55, EtOH)]; ^1H NMR (500 MHz, CDCl_3) δ 7.56 (d, J = 15.5 Hz, 1H), 7.16 (d, J = 15.5 Hz, 1H), 6.18 (d, J = 10.0 Hz, 1H), 6.29 (brs, 1H), 4.04 (d, J = 6.0 Hz, 1H), 3.99 (brs, 1H), 3.98 (brs, 1H), 3.80 (s, 1H), 3.70 (s, 1H), 3.66 (d, J = 7.0 Hz, 1H), 2.90-2.80 (m, 1H), 2.03-1.97 (m, 1H), 1.91 (s, 3H), 1.57 (s, 3H), 1.12 (d, J = 7.0 Hz, 3H), 0.72 (d, J = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 201.4, 192.6, 176.5, 175.1, 149.6, 143.3, 135.0, 116.8, 100.1, 95.9, 78.7, 77.3, 59.3, 58.0, 56.8, 51.6, 34.5, 34.5, 23.3, 16.9, 12.3, 11.4; FTIR (neat) 3450, 2968, 2928, 2864, 1718, 1658, 1617, 1566, 1455, 1144, 1112, 1013, cm^{-1} ; MS (EI) m/z 75, 93, 185, 255, 257, 369, 433 (M^+); HRMS (EI) calcd for $\text{C}_{22}\text{H}_{27}\text{NO}_8$ (M^+) 433.1737, found 433.1757.



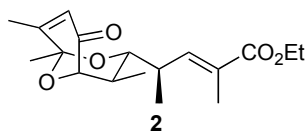
(4R,E)-Ethyl 4-((3R,4R)-8-(Hydroxymethyl)-1,4-dimethyl-6-oxo-2,9-dioxabicyclo[3.3.1]non-7-en-3-yl)-2-methylpent-2-enoate. To a solution of **1** (750 mg, 1.53 mmol) in MeCN (300

mL) was added HF·pyridine (9.0 mL) at room temperature. After being stirred for 1 day, the mixture was basified with saturated NaHCO₃, extracted with AcOEt, washed with brine, dried, and concentrated. The residue was purified by column chromatography (SiO₂ 30 g, hexane/AcOEt = 2:1 to 3:2) to give the title compound (503 mg, 97%) as a colorless oil: $[\alpha]_D^{23}$ -144.6 (*c* 1.00, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.90 (dd, *J* = 1.6, 10.4 Hz, 1H), 6.45 (s, 1H), 4.45 (d, *J* = 17.2 Hz, 1H), 4.28-4.20 (m, 3H), 4.06 (d, *J* = 6.0 Hz, 1H), 3.49 (dd, *J* = 2.0, 11.6 Hz, 1H), 2.83-2.73 (m, 1H), 2.05-1.98 (m, 1H), 1.96-1.84 (m, 4H), 1.53 (s, 3H), 1.32 (t, *J* = 7.2 Hz, 3H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.72 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 195.2, 168.1, 157.5, 141.2, 128.5, 123.6, 94.8, 78.8, 76.9, 60.6, 60.5, 34.0, 33.4, 24.0, 16.4, 14.2, 12.4, 11.6; FTIR (neat) 3474, 2971, 2937, 1709, 1682, 1451, 1387, 1292, 1255, 1125 cm⁻¹; MS (ESI) *m/z* 361 [(M+Na)⁺]; HRMS (ESI) calcd for C₁₈H₂₆NaO₆ [(M+Na)⁺] 361.1627, found 361.1619.



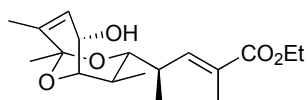
(4R,E)-Ethyl 4-((3R,4R)-8-(Chloromethyl)-1,4-dimethyl-6-oxo-2,9-dioxabicyclo[3.3.1]non-7-en-3-yl)-2-methylpent-2-enoate (17**).** To a solution of the alcohol (319 mg, 0.941 mmol) in

DMF (9.4 mL) were added NEt₃ (524 μL, 3.76 mmol), LiCl (120 mg, 2.82 mmol) and MsCl (146 μL, 1.88 mmol) at -40 °C, and the mixture was stirred at -40 °C for 30 min and then at room temperature for 90 min, the reaction was quenched with saturated NH₄Cl (10 mL) and extracted with AcOEt. The extract was washed with brine, dried, concentrated, and chromatographed (SiO₂ 30 g, hexane/AcOEt = 7:1) to give **17** (287 mg, 85%) as a colorless oil: $[\alpha]_D^{23}$ -195.5 (*c* 1.00, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.90 (d, *J* = 10.4 Hz, 1H), 6.47 (s, 1H), 4.28-4.19 (m, 3H), 4.23-4.06 (m, 2H), 3.46 (dd, *J* = 2.0, 11.6 Hz, 1H), 2.83-2.75 (m, 1H), 2.08-1.99 (m, 1H), 1.85 (d, *J* = 1.2 Hz, 3H), 1.61 (s, 3H), 1.32 (t, *J* = 7.2 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.72 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 194.9, 167.9, 151.9, 141.0, 128.6, 127.5, 95.3, 78.8, 76.9, 60.6, 41.7, 34.0, 33.5, 24.2, 16.4, 14.2, 12.4, 11.5; FTIR (neat) 2976, 2933, 1704, 1650, 1455, 1380, 1254, 1123, 1003 cm⁻¹; MS (EI) *m/z* 43, 67, 95, 109, 141, 181, 215, 311, 356 (M⁺); HRMS (EI) calcd for C₁₈H₂₅ClO₅ (M⁺) 356.1391, found: 356.1399.



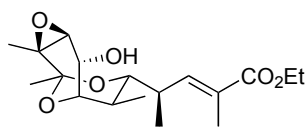
(4*R,E*)-ethyl 2-methyl-4-((3*R,4R*)-1,4,8-trimethyl-6-oxo-2,9-dioxabicyclo[3.3.1]non-7-en-3-yl)pent-2-enoate (2). To a solution of **17** (128 mg, 0.36 mmol) in benzene (6 mL) were added AIBN

(8.8 mg, 54 μ mol) and $^n\text{Bu}_3\text{SnH}$ (194 μ L, 0.72 mol) at room temperature, and the mixture was heated at reflux for 40 min. The mixture was cooled to room temperature and additional AIBN (6.8 mg, 42 μ mol) was added, and the mixture was heated at reflux for 50 min. After being cooled to room temperature, the mixture was evaporated and chromatographed (toluene/AcOEt = 20:1) to give **2** (102 mg, 88%) as a colorless oil: $[\alpha]_{\text{D}}^{27} -172.2$ (c 0.40, CHCl_3) [lit.³ $[\alpha]_{\text{D}} -185.2$ (c 1.50, CHCl_3)]; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 6.91 (d, $J = 1.2$, 10.6 Hz, 1H), 6.11 (s, 1H), 4.22 (q, $J = 7.2$ Hz, 2H), 4.03 (d, $J = 6.4$ Hz, 1H), 3.41 (dd, $J = 2.0$, 11.2 Hz, 1H), 2.81-2.72 (m, 1H), 2.05-1.93 (m, 4H), 1.85 (d, $J = 1.2$ Hz, 3H), 1.56 (s, 3H), 1.32 (t, $J = 6.8$ Hz, 3H), 1.04 (d, $J = 6.8$ Hz, 3H), 0.76 (d, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 195.2, 168.1, 155.8, 141.3, 128.5, 127.1, 96.0, 79.0, 60.6, 34.0, 33.5, 24.4, 19.2, 16.5, 14.3, 12.4, 11.6; FTIR (neat) 2976, 1708, 1684, 1455, 1378, 1243, 1217, 1008 cm^{-1} ; MS (EI) m/z 43, 99, 169, 181, 277, 322 (M^+); HRMS (EI) calcd for $\text{C}_{18}\text{H}_{26}\text{O}_5$ (M^+) 322.178, found: 322.1773.



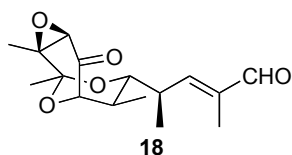
(4*R,E*)-ethyl 4-((3*R,4R,6R*)-6-hydroxy-1,4,8-trimethyl-2,9-dioxabicyclo[3.3.1]non-7-en-3-yl)-2-methylpent-2-enoate.

To an ice-cooled solution of **2** (80 mg, 249 μ mol) in MeOH (12.4 mL) were added CeCl_3 (66 mg, 249 μ mol) and NaBH_4 (74.9 mg, 1.98 mmol), and the mixture was stirred at 0 $^\circ\text{C}$ for 5 min. The reaction was quenched with 10% HCl (0.5 mL) and the mixture was extracted with AcOEt. The extract was washed with saturated NaHCO_3 , dried, concentrated, and chromatographed (SiO_2 5 g, hexane/AcOEt = 2:1) to give the title compound (79.6 mg, 99%) as a colorless oil: $[\alpha]_{\text{D}}^{24} +1.9$ (c 1.00, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 6.93 (d, $J = 10.4$ Hz, 1H), 5.71 (s, 1H), 4.78 (brs, 1H), 4.25-4.15 (m, 2H), 3.96 (t, $J = 5.6$ Hz, 1H), 3.71 (dd, $J = 1.6$, 11.0 Hz, 1H), 2.82-2.72 (m, 1H), 2.08-1.98 (m, 1H), 1.85 (s, 3H), 1.63 (s, 3H), 1.42 (s, 3H), 1.31 (t, $J = 7.2$ Hz, 3H), 1.03 (d, $J = 6.8$ Hz, 3H), 0.94 (d, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 168.3, 142.4, 133.6, 128.2, 128.0, 95.8, 76.3, 73.4, 68.8, 60.5, 36.1, 34.1, 24.2, 17.7, 16.5, 14.3, 12.9, 12.4; FTIR (neat) 3470, 2978, 1707, 1446, 1375, 1304, 1243, 1107 cm^{-1} ; MS (EI) m/z 58, 91, 114, 137, 165, 183, 211, 261, 279, 324 (M^+); HRMS (EI) calcd for $\text{C}_{18}\text{H}_{28}\text{O}_5$ (M^+) 324.1937, found: 324.1941.



(4*R,E*)-Ethyl 4-((2*S*,4*R*,5*S*,7*R*,8*R*)-5-Hydroxy-1,2,7-trimethyl-3,9,10-trioxatricyclo[4.3.1.0^{2,4}]decan-8-yl)-2-methylpent-2-

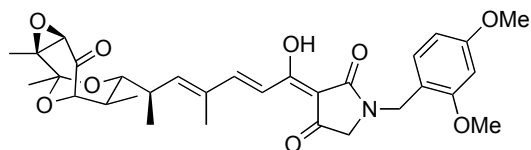
enoate. To an ice-cooled solution of the allylic alcohol (12 mg, 36 μmol) in CH_2Cl_2 (2.8 mL) and H_2O (24 μL) were added NaH_2PO_3 (6.8 mg, 57 μmol) and *m*CPBA (75% purity, 12.3 mg, 54 μmol). After stirring at room temperature for 24 h, the reaction was quenched with saturated NaHSO_3 (5 mL), and the mixture was extracted with AcOEt. The extract was washed with saturated NaHCO_3 and brine, dried, concentrated, and purified by preparative TLC (hexane/AcOEt = 2:1) to give the title epoxide (10 mg, 82%) as a colorless oil: $[\alpha]_{\text{D}}^{25} +13.9$ (*c* 0.50, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 6.91 (dd, *J* = 1.2, 10.4 Hz, 1H), 4.41 (dd, *J* = 5.2, 7.6 Hz, 1H), 4.25-4.18 (m, 2H), 3.98 (t, *J* = 5.2 Hz, 1H), 3.90 (dd, *J* = 2.0, 11.6 Hz, 1H), 3.18 (s, 1H), 2.84-2.76 (m, 1H), 2.10-2.01 (m, 1H), 1.86 (d, *J* = 1.2 Hz, 1H), 1.76 (brs, 1H), 1.42 (s, 3H), 1.39 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 3H), 1.12 (d, *J* = 6.8 Hz, 3H), 0.95 (d, *J* = 7.6 Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 168.2, 141.2, 128.2, 96.2, 75.6, 71.6, 66.9, 64.0, 60.6, 56.2, 36.1, 34.3, 21.9, 16.5, 16.3, 14.2, 12.9, 12.4; FTIR (neat) 3479, 2978, 1708, 1451, 1375, 1304, 1240, 1129 cm^{-1} ; MS (EI) *m/z* 43, 98, 125, 142, 165, 199, 295, 340 (M^+); HRMS (EI) calcd for $\text{C}_{18}\text{H}_{26}\text{O}_6$ (M^+) 340.1886, found: 340.1878.



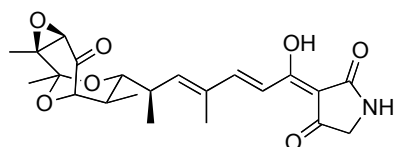
(4*R,E*)-2-Methyl-4-((2*S*,4*S*,7*R*,8*R*)-1,2,7-trimethyl-5-oxo-3,9,10-trioxatricyclo[4.3.1.0^{2,4}]decan-8-yl)pent-2-enal (18).

To a solution of the epoxy ester (35 mg, 102 μmol) in CH_2Cl_2 (7 mL) were added DIBAL-H (1.02 M in hexane, 0.5 mL, 0.51 mmol) at -78 $^\circ\text{C}$, and the mixture was stirred at -78 $^\circ\text{C}$ for 1 h. The reaction was quenched with saturated Rochelle salt (5 mL) and the mixture was stirred at room temperature for 6 h. The mixture was extracted with CH_2Cl_2 , dried, and concentrated. The residue was dissolved in CH_2Cl_2 (7 mL), and molecular sieves 4 \AA (350 mg, preactivated at 200 $^\circ\text{C}$ for 2 h) and PDC (305 mg, 0.8 mmol) were added at room temperature. After being stirred at room temperature for 1 h, the mixture was filtered through Celite which was washed with CH_2Cl_2 . The combined filtrate and washings were concentrated, and purified by preparative TLC (hexane/AcOEt = 2:1) to give **18** (17.4 mg, 58%) as a colorless oil: $[\alpha]_{\text{D}}^{22} +23.8$ (*c* 0.245, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 9.46 (s, 1H), 6.65 (dd, *J* = 1.2, 10.4 Hz, 1H), 4.04 (d, *J* = 6.0 Hz, 1H), 3.63 (dd, *J* = 2.0, 11.6 Hz, 1H), 3.30 (s, 1H), 3.01-2.93 (m, 1H), 2.00-1.91 (m, 1H), 1.77 (d, *J* = 1.2 Hz, 1H), 1.59 (s, 3H), 1.49 (s, 3H), 1.19 (d, *J* = 6.8 Hz, 3H), 0.74 (d, *J* = 6.8 Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 202.8, 195.1, 152.0, 140.0, 96.9, 78.6, 77.2, 61.2, 57.0, 34.8, 34.3, 22.6, 16.5, 15.6, 11.4, 9.3; FTIR (neat) 2974, 2937, 1725, 1685, 1451, 1379, 1142, 1008 cm^{-1} ; MS (EI) *m/z* 69, 109, 137, 155, 181, 197, 237, 252, 294 (M^+); HRMS (EI) calcd for $\text{C}_{16}\text{H}_{22}\text{O}_5$ (M^+) 294.1467,

found: 294.1457.

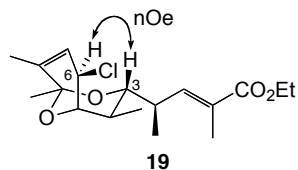


***N*-(2,4-Dimethoxybenzyl)tirandamycin A.** To an ice-cooled solution of phosphonate **16** (14 mg, 32 μmol) in THF (1 mL) was added KO^tBu (7.3 mg, 65 μmol), and the mixture was stirred at 0 °C for 2 h. A solution of **18** (4.8 mg, 16 μmol) in THF (0.5 mL) was added at 0 °C and stirring was continued at 0 °C for 24 h. The reaction was quenched with 1% HCl (0.5 mL) and the mixture was extracted with Et_2O . The extract was washed with brine, filtered using a glass funnel plugged with lab wiper, concentrated, and purified by reverse phase preparative TLC ($\text{MeCN}/\text{H}_2\text{O} = 5:1$) to give the title compound (5.7 mg, 62%) as a yellow oil: $[\alpha]_{\text{D}}^{28} -8.5$ (c 0.500, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.52 (d, $J = 15.6$ Hz, 1H), 7.18 (d, $J = 5.2$ Hz, 1H), 7.12 (d, $J = 15.6$ Hz, 1H), 6.45 (m, 2H), 6.17 (d, $J = 9.6$ Hz, 1H), 4.57 (s, 2H), 4.01 (d, $J = 6.0$ Hz, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.65 (s, 2H), 3.56 (dd, $J = 1.6, 11.6$ Hz, 1H), 3.27 (s, 1H), 2.87-2.80 (m, 1H), 2.02-1.86 (m, 4H), 1.56 (s, 3H), 1.46 (s, 3H), 1.12 (d, $J = 7.2$ Hz, 3H), 0.71 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 202.5, 192.1, 173.6, 173.4, 160.9, 158.6, 148.6, 142.7, 134.8, 131.3, 116.9, 116.1, 104.4, 101.1, 98.5, 96.8, 78.7, 77.2, 61.2, 57.0, 55.6, 55.4, 40.0, 34.7, 34.4, 22.6, 16.9, 15.6, 12.2, 11.4; FTIR (neat) 2965, 2853, 1705, 1618, 1578, 1463, 1292, 1212, 1148, 1013 cm^{-1} ; MS (FAB) m/z 79, 154, 232, 307, 430, 567 (M^+); HRMS (FAB) calcd for $\text{C}_{31}\text{H}_{37}\text{NO}_9$ (M^+) 567.2468, found: 567.2463.



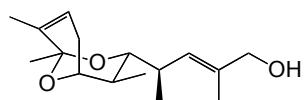
(+)-Tirandamycin A. To a solution of *N*-(dimethoxybenzyl)-tirandamycin A (7.6 mg, 13 μmol) was added TFA (1 mL) at room temperature, and the mixture was stirred for 30 min. The mixture was diluted with ice water (2 mL), extracted with CH_2Cl_2 , washed with saturated NaHCO_3 , filtered using a glass funnel plugged with lab wiper, and concentrated. The residue was purified by reverse phase column chromatography (ODS 2 g, $\text{CH}_3\text{CN}:\text{H}_2\text{O}$, 2:1) to give tirandamycin A (4.6 mg, 82%) as a yellow oil: $[\alpha]_{\text{D}}^{28} +3.7$ (c 0.251, EtOH) [lit.² $[\alpha]_{\text{D}}^{25} +4$ (c 0.5, EtOH)]; ^1H NMR (500 MHz, CD_2Cl_2) δ 7.58 (d, $J = 15.5$ Hz, 1H), 7.15 (d, $J = 16$ Hz, 1H), 6.24 (d, $J = 10.0$ Hz, 1H), 5.77 (brs, 1H), 3.98 (d, $J = 6.0$ Hz, 1H), 3.78 (s, 2H), 3.60 (d, $J = 10.0$ Hz, 1H), 3.25 (s, 1H), 2.89-2.83 (m, 1H), 2.00-1.91 (m, 4H), 1.53 (s, 3H), 1.45 (s, 3H), 1.13 (d, $J = 7.0$ Hz, 3H), 0.70 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 202.9, 192.8, 176.7, 175.0, 149.7, 144.2, 135.2, 116.8, 97.1, 79.2, 77.2, 61.4, 57.3, 51.9, 35.0, 34.8, 22.7, 17.0, 15.7, 12.3, 11.5; FTIR (neat) 3400, 2924, 1722, 1654, 1614, 1574, 1472, 1143, 1005 cm^{-1} ; MS (ESI) m/z 440 [$(\text{M}+\text{Na})^+$]; HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{27}\text{NNaO}_7$ [$(\text{M}+\text{Na})^+$]

440.1695, found 440.1685.



(*R,2E*)-Ethyl 4-((*1S,3R,5R,6R*)-6-chloro-1,4,8-trimethyl-2,9-dioxabicyclo[3.3.1]non-7-en-3-yl)-2-methylpent-2-enoate (19).

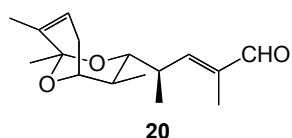
To an ice-cooled solution of the above-mentioned allylic alcohol (80 mg, 0.25 mmol), prepared by Luche reduction of **2**, in THF (6 mL) were added NEt_3 (116 μL , 1.5 mmol), MsCl (311 μL , 2.2 mmol) and LiCl (79 mg, 1.8 mmol). After being heated at reflux for 3 h, the mixture was diluted with AcOEt , washed with saturated NH_4Cl and brine, dried, and concentrated. The residue was purified by column chromatography (SiO_2 5 g, toluene/ AcOEt = 30:1) to give **19** (54 mg, 66%) as a colorless oil: $[\alpha]_{\text{D}}^{23}$ -152.9 (c 1.00, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 6.89 (dd, J = 1.2, 10.0 Hz, 1H), 5.90 (d, J = 4.8 Hz, 1H), 4.38 (d, J = 4.8 Hz, 1H), 4.21 (qd, J = 1.2, 6.8 Hz, 2H), 4.14 (d, J = 15.6 Hz, 1H), 3.32 (dd, J = 2.4, 11.6 Hz, 1H), 2.75-2.68 (m, 1H), 2.00-1.93 (m, 1H), 1.84 (d, J = 1.2 Hz, 3H), 1.71 (s, 3H), 1.50 (s, 3H), 1.32 (t, J = 6.8 Hz, 3H), 1.02 (d, J = 7.6 Hz, 3H), 0.77 (d, J = 7.2 Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 168.0, 141.6, 136.6, 128.2, 123.8, 95.2, 77.9, 75.8, 60.5, 51.3, 34.3, 34.1, 23.8, 18.1, 16.3, 14.2, 12.8, 12.4; FTIR (neat) 2971, 1710, 1452, 1382, 1303, 1247, 1132, 1056 cm^{-1} ; MS (EI) m/z 43, 109, 137, 143, 201, 297, 307, 342 (M^+); HRMS (EI) calcd for $\text{C}_{18}\text{H}_{27}^{35}\text{ClO}_4$ (M^+) 342.1598, found: 342.1593. The stereostructure was determined by the significant nOe between C3-H and C6-H in the NOESY spectrum.



(*R,E*)-2-Methyl-4-((*1R,3R,4S,5R*)-1,4,8-trimethyl-2,9-dioxabicyclo[3.3.1]non-7-en-3-yl)pent-2-en-1-ol.

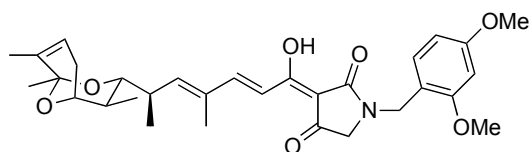
To a solution of **19** (30 mg, 32 μmol) in benzene (1.5 mL) were added AIBN (3.5 mg, 8 μmol) and $^n\text{Bu}_3\text{SnH}$ (47 μL , 32 μmol) at room temperature, and the mixture was heated at reflux for 1 h. After being cooled to room temperature, the mixture was evaporated and chromatographed (SiO_2 5 g, toluene/ AcOEt = 20:1) to give the dechlorinated compound (28 mg) contaminated by some impurities, which was used for the next reaction without purification. To a solution of crude product (28 mg) in CH_2Cl_2 (1 mL) were added DIBAL-H (1.02 M in hexane, 70 μL , 67 μmol) at -78 $^\circ\text{C}$, and the mixture was stirred at -78 $^\circ\text{C}$ for 1 h. The reaction was quenched with saturated Rochelle salt (1 mL) at -78 $^\circ\text{C}$, and the mixture was allowed to warm to room temperature and stirred for 6 h. The mixture was extracted with CH_2Cl_2 , dried, concentrated, and chromatographed (SiO_2 5 g, toluene/ AcOEt = 5:1) to give the alcohol (23 mg, 69%) as a colorless oil: $[\alpha]_{\text{D}}^{27}$ -47.2 (c 0.55, CHCl_3) [lit.⁴ $[\alpha]_{\text{D}}^{29}$ -44.3 (c 1.00, CHCl_3)] ; $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 5.69 (d, J = 1.6 Hz, 1H), 5.60 (dd, J = 1.2, 10.0 Hz, 1H), 4.03 (d, J = 5.2 Hz,

2H), 3.95 (t, $J = 6.4$ Hz, 1H), 3.43 (dd, $J = 2.0, 11.0$ Hz, 1H), 2.65-2.55 (m, 1H), 2.45-2.32 (m, 1H), 1.99-1.92 (m, 1H), 1.69 (d, $J = 1.6$ Hz, 3H), 1.61 (s, 3H), 1.41 (s, 3H), 0.98 (d, $J = 7.2$ Hz, 3H), 0.68 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 135.1, 132.7, 127.2, 123.1, 95.3, 77.3, 71.1, 69.3, 34.6, 33.0, 24.4, 24.2, 18.4, 17.6, 13.7, 13.4; FTIR (neat) 3466, 2960, 2933, 1447, 1375, 1228, 1192, 1120, 1049 cm^{-1} ; MS (EI) m/z 43, 109, 167, 235, 266 (M^+); HRMS (EI) calcd for $\text{C}_{16}\text{H}_{26}\text{O}_3$ (M^+) 266.1882, found: 266.1877.



(*R,E*)-2-Methyl-4-((1*R*,3*R*,4*S*,5*R*)-1,4,8-trimethyl-2,9-dioxabicyclo[3.3.1]non-7-en-3-yl)pent-2-ena (20).

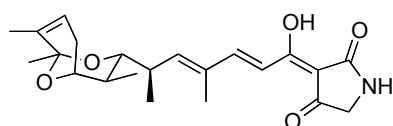
To a stirred solution of the alcohol (20.5 mg, 77 μmol) and iodobenzene diacetate (37.2 mg, 115 μmol) in CH_2Cl_2 (1 mL) was added TEMPO (1.2 mg, 8 μmol) at room temperature, and the mixture was stirred for 1 h. The reaction was quenched by the addition of saturated NaHCO_3 (5 mL) followed by saturated $\text{Na}_2\text{S}_2\text{O}_3$ (5 mL). The mixture was extracted with CH_2Cl_2 , dried over Na_2SO_4 , concentrated, and chromatographed (SiO_2 3 g, hexane/ $\text{AcOEt} = 5:1$) to give **20** (19 mg, 94%) as a pale yellow oil: $[\alpha]_{\text{D}}^{28} -44.2$ (c 1.05, CHCl_3) [lit.⁴ $[\alpha]_{\text{D}}^{29} -40.2$ ($c = 0.7$, CHCl_3)]; ^1H NMR (400 MHz, CDCl_3): δ 9.46 (s, 1H), 6.75 (dd, $J = 1.2, 10.4$ Hz, 1H), 5.71 (br s, 1H), 3.96 (t, $J = 6.4$ Hz, 1H), 3.54 (dd, $J = 2.0, 11.2$ Hz, 1H), 2.95-2.86 (m, 1H), 2.45-2.36 (m, 1H), 2.00-1.92 (m, 1H), 1.90-1.81 (m, 1H), 1.76 (d, $J = 2.0$ Hz, 3H), 1.63 (s, 3H), 1.43 (s, 3H), 1.09 (d, $J = 6.8$ Hz, 3H), 0.70 (d, $J = 7.2$, Hz, 3H) ppm; ^{13}C NMR (100 MHz, CDCl_3): δ 195.6, 155.2, 139.2, 132.3, 123.3, 95.5, 76.2, 70.9, 35.2, 34.4, 24.2, 24.1, 18.3, 16.5, 13.2, 9.2; FTIR (neat): 2967, 2937, 1679, 1455, 1379, 1336, 1267, 1195, 1159, 1124 cm^{-1} ; MS (EI) m/z 43, 95, 109, 167, 204, 264 (M^+); HRMS (EI) m/z calcd for $\text{C}_{16}\text{H}_{24}\text{O}_3$ (M^+): 264.1725, found: 264.1723.



***N*-(2,4-Dimethoxybenzyl)tirandamycin C.**

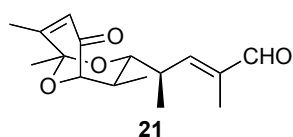
To an ice-cooled solution of phosphonate **16** (74 mg, 174 μmol) in THF (2 mL) was added KO^tBu (39 mg, 357 μmol), and the mixture was stirred at 0 $^\circ\text{C}$ for 2 h. A solution of **20** (19 mg, 72 μmol) in THF (1 mL) was added at 0 $^\circ\text{C}$ and stirring was continued at 0 $^\circ\text{C}$ for 18 h. The reaction was quenched with saturated NH_4Cl (3 mL) and the mixture was extracted with AcOEt . The extract was filtered using a glass funnel plugged with lab wiper, concentrated, and chromatographed (SiO_2 5 g, hexane/ $\text{AcOEt} = 1:1$) to give the title compound (34 mg, 90%) as a pale yellow oil: $[\alpha]_{\text{D}}^{26} -59.3$ (c 0.500, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 7.57 (d, $J = 15.6$ Hz, 1H), 7.18 (d, $J = 8.8$ Hz, 1H), 7.09 (d, $J = 15.6$ Hz, 1H), 6.48-6.44 (m, 2H), 6.29 (d, $J = 10.0$ Hz, 1H), 5.70 (brs, 1H), 4.57 (s, 2H), 3.94 (t, $J = 6.4$ Hz, 1H), 3.81 (s, 3H), 3.80 (s,

3H), 3.64 (s, 2H), 3.48 (d, $J = 11.2$ Hz, 1H), 2.85-2.75 (m, 1H), 2.43-2.35 (m, 1H), 1.98–1.84 (m, 5H), 1.62–1.59 (m, 3H), 1.42 (s, 3H), 1.04 (d, $J = 6.8$ Hz, 3H), 0.67 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 192.1, 174.0, 173.5, 160.9, 158.6, 149.6, 146.2, 134.0, 132.5, 131.2, 123.2, 116.1, 116.0, 104.3, 100.7, 98.5, 95.4, 76.6, 71.0, 55.6, 55.4, 40.0, 35.0, 34.5, 24.3, 24.1, 18.3, 17.0, 13.2, 12.2; FTIR (neat) 3426, 2933, 2877, 1701, 1615, 1468, 1372, 1295, 1208, 1159, 1116, 1041, 869 cm^{-1} ; MS (FAB) m/z 79, 154, 289, 307, 460, 538 (100) $[(\text{M}+\text{H})^+]$; HRMS (FAB) calcd for $\text{C}_{31}\text{H}_{40}\text{NO}_7$ $[(\text{M}+\text{H})^+]$ 538.2782, found: 538.2798.



(-)-Tirandamycin C. To a solution of *N*-(dimethoxybenzyl)-tirandamycin C (33.7 mg, 63 μmol) in CH_2Cl_2 (2 mL) was added TFA (1 mL) and the mixture was stirred for 30 min.

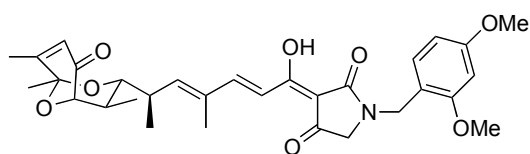
The mixture was diluted with ice water (2 mL), extracted with CH_2Cl_2 , filtered using a glass funnel plugged with lab wiper, and concentrated. The residue was purified by reverse phase column chromatography (ODS 3 g, $\text{CH}_3\text{CN}/\text{H}_2\text{O} = 2:1$) to give tirandamycin C (13.6 mg, 56%) as a yellow oil: $[\alpha]_{\text{D}}^{26} -59.7$ (c 0.10, EtOH) [lit.² $[\alpha]_{\text{D}}^{25} -59$ (c 0.11, EtOH)]; ^1H NMR (500 MHz, CD_2Cl_2) δ 7.62 (d, $J = 15.5$ Hz, 1H), 7.12 (d, $J = 15.5$ Hz, 1H), 6.32 (d, $J = 10.0$ Hz, 1H), 6.11 (brs, 1H), 5.70 (brs, 1H), 3.90 (brt, $J = 6.0$ Hz, 1H), 3.78 (s, 2H), 3.49 (d, $J = 11.0$ Hz, 1H), 2.87-2.79 (m, 1H), 2.38-2.28 (m, 1H), 2.00-1.81 (m, 5H), 1.61 (m, 3H), 1.38 (s, 3H), 1.04 (d, $J = 7.0$ Hz, 3H), 0.68 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 192.8, 176.9, 175.3, 150.4, 147.4, 134.5, 132.9, 123.7, 116.1, 100.3, 95.8, 77.0, 71.3, 52.0, 35.5, 34.9, 24.5, 24.5, 18.4, 17.2, 13.3, 12.3; FTIR (neat) 3253, 2952, 2928, 2853, 1617, 1568, 1455, 1378, 1289, 1237, 1120 cm^{-1} ; MS (FAB) m/z 109, 154, 232, 288, 307, 387 (100) (M^+); HRMS (FAB) calcd for $\text{C}_{22}\text{H}_{29}\text{NO}_5$ (M^+) 387.2046, found: 387.2057.



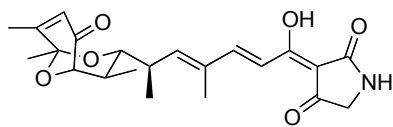
(4*R*,*E*)-2-Methyl-4-((3*R*,4*R*)-1,4,8-trimethyl-6-oxo-2,9-dioxabicyclo[3.3.1]non-7-en-3-yl)pent-2-enal (21). To a solution of **2** (48.6 mg, 0.15 mmol) in CH_2Cl_2 (2 mL) were added DIBAL-H (1.02

M in hexane, 0.74 mL, 0.75 mmol) at -78 $^\circ\text{C}$, and the mixture was stirred at -78 $^\circ\text{C}$ for 1 h. The reaction was quenched with saturated Rochelle salt (1.5 mL), and the mixture was stirred at room temperature for 6 h. The mixture was extracted with CH_2Cl_2 , dried, and concentrated. The residue was dissolved in CH_2Cl_2 (10 mL), and NaHCO_3 (378 mg, 4.5 mmol) and Dess-Martin periodinane (381 mg, 0.9 mmol) were added at room temperature. After stirring at room temperature for 2 h, the reaction was quenched with 50% $\text{Na}_2\text{S}_2\text{O}_4$ (10 mL) and the mixture was extracted with AcOEt. The extract was washed with saturated NaHCO_3 , dried over Na_2SO_4 , concentrated, and chromatographed (SiO_2 3 g, hexane/AcOEt = 8:1) to give **21**

(39 mg, 94%) as a colorless oil: $[\alpha]_D^{26} -225.6$ (c 0.47, CHCl_3); $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 9.47 (s, 1H), 6.70 (dd, $J = 1.2, 10.2$ Hz, 1H), 6.13 (s, 1H), 4.04 (d, $J = 6.0$ Hz, 1H), 3.48 (dd, $J = 2.0, 11.6$ Hz, 1H), 3.02-2.95 (m, 1H), 2.00-1.91 (m, 4H), 1.77 (d, $J = 1.2$ Hz, 3H), 1.58 (s, 3H), 1.11 (d, $J = 7.2$ Hz, 3H), 0.73 (d, $J = 7.2$ Hz, 3H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 195.2, 194.8, 155.6, 153.5, 139.6, 127.1, 96.1, 78.8, 76.9, 34.1, 33.7, 24.3, 19.2, 16.5, 11.6, 9.3; FTIR (neat) 2976, 2873, 1673, 1638, 1455, 1435, 1383, 1232, 1120 cm^{-1} ; MS (EI) m/z 43, 69, 95, 111, 181, 256, 278 (M^+); HRMS (EI) calcd for $\text{C}_{16}\text{H}_{22}\text{O}_4$ (M^+) 278.1518, found: 278.1510.

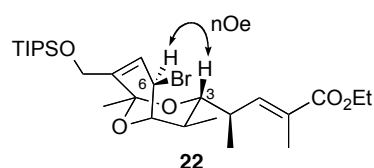


***N*-(2,4-Dimethoxybenzyl)tirandamycin D.** To an ice-cooled solution of phosphonate **16** (80 mg, 188 μmol) in THF (2 mL) was added KO^tBu (42 mg, 376 μmol), and the mixture was stirred at 0 $^\circ\text{C}$ for 2 h. A solution of **18** (22 mg, 79 μmol) in THF (1 mL) was added at 0 $^\circ\text{C}$ and stirring was continued at 0 $^\circ\text{C}$ for 24 h. The reaction was quenched with 1% HCl (1.3 mL) and the mixture was extracted with Et_2O . The extract was washed with brine, filtered using a glass funnel plugged with lab wiper, concentrated, and purified by reverse phase column chromatography (ODS 3 g, $\text{MeCN}/\text{H}_2\text{O} = 2:1$) to give the title compound (24 mg, 54%) as a yellow oil: $[\alpha]_D^{28} -118.9$ (c 0.500, CHCl_3); $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.55 (d, $J = 16.0$ Hz, 1H), 7.18 (d, $J = 9.0$ Hz, 1H), 7.12 (d, $J = 15.5$ Hz, 1H), 6.46 (m, 2H), 6.23 (d, $J = 10.0$ Hz, 1H), 6.11 (s, 1H), 4.58 (s, 2H), 4.01 (d, $J = 5.5$ Hz, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.66 (s, 2H), 3.42 (dd, $J = 2.0, 11.5$ Hz, 1H), 2.89-2.81 (m, 1H), 2.00-1.93 (m, 1H), 1.93 (s, 3H), 1.89 (s, 3H), 1.55 (s, 3H), 1.06 (d, $J = 7.0$ Hz, 3H), 0.71 (d, $J = 7.0$ Hz, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 195.2, 192.1, 173.7, 173.5, 160.9, 158.6, 155.8, 148.9, 144.3, 134.5, 131.3, 127.0, 116.7, 116.1, 104.4, 100.9, 98.5, 96.0, 79.1, 55.6, 55.4, 40.0, 34.3, 33.6, 24.4, 19.2, 17.0, 12.2, 11.6; FTIR (neat) 3410, 2944, 1690, 1618, 1570, 1465, 1238, 1120, 997 cm^{-1} ; MS (FAB) m/z 79, 154, 307, 414, 551 (100) (M^+); HRMS (FAB) calcd for $\text{C}_{31}\text{H}_{37}\text{NO}_8$ (M^+) 551.2519, found: 551.2494.



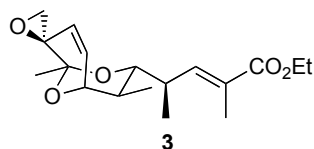
(-)-Tirandamycin D. To a solution of *N*-(2,4-dimethoxybenzyl)tirandamycin D (22 mg, 40 μmol) was added TFA (2 mL) at room temperature, and the mixture was stirred for 30 min. The mixture was diluted with ice water (4 mL) and extracted with CH_2Cl_2 . The extract was washed with saturated NaHCO_3 , filtered using a glass funnel plugged with lab wiper, and concentrated. The residue was purified by reverse phase column chromatography (ODS 2 g, $\text{CH}_3\text{CN}/\text{H}_2\text{O} = 2:1$) to give titled compound (13 mg, 78%) as a yellow oil: $[\alpha]_D^{28} -95.8$ (c 0.250, EtOH) [lit.² $[\alpha]_D^{25} -60$ (c 0.55, EtOH)]; $^1\text{H NMR}$ (500 MHz, CD_2Cl_2) δ 7.61 (d, $J =$

15.6 Hz, 1H), 7.14 (d, $J = 16.0$ Hz, 1H), 6.29 (d, $J = 10.5$ Hz, 1H), 6.08 (s, 1H), 6.08 (brs, 1H), 3.97 (d, $J = 6.0$ Hz, 1H), 3.78 (s, 2H), 3.44 (dd, $J = 2.0, 11.5$ Hz, 1H), 2.89 (m, 1H), 1.97 (m, 1H), 1.92 (s, 3H), 1.91 (d, $J = 1.1$ Hz, 3H), 1.53 (s, 3H), 1.06 (d, $J = 7.0$ Hz, 3H), 0.69 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 195.4, 192.8, 176.8, 175.2, 156.3, 149.9, 145.7, 134.9, 127.3, 116.6, 96.4, 79.4, 77.6, 52.0, 34.7, 33.9, 24.6, 19.4, 17.1, 12.4, 11.8; FTIR (neat) 3285, 2932, 1682, 1614, 1568, 1455, 1378, 1242, 1119 cm^{-1} ; MS (FAB) m/z 93, 185, 277, 369, 415 (M^+); HRMS (FAB) calcd for $\text{C}_{23}\text{H}_{29}\text{NO}_6$ (M^+) 415.1995, found: 415.1979.



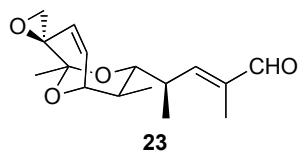
(*R,E*)-Ethyl 4-((1*S*,3*R*,4*R*,5*S*,6*S*)-6-Bromo-1,4-dimethyl-8-(((triisopropylsilyl)oxy)methyl)-2,9-dioxabicyclo[3.3.1]-non-7-en-3-yl)-2-methylpent-2-enoate (22).

To an ice-cooled solution of **14** (302 mg, 0.6 mmol) in THF (9 mL) were added NEt_3 (635 μL , 4.6 mmol) and MsCl (273 μL , 3.5 mmol). After being stirred at room temperature for 3 h, the mixture was diluted with AcOEt , washed with saturated NH_4Cl and brine, dried, and concentrated. The residue was purified by column chromatography (SiO_2 9 g, hexane/ AcOEt = 5:1) to give the mesylate as a colorless oil (380 mg) which was very labile. The mesylate (380 mg) thus obtained was immediately dissolved in THF (12 mL), and NEt_3 (1 mL, 7.3 mmol) and LiBr (317 mg, 3.7 mmol) were added. After being heated at reflux for 5 h, the mixture was cooled to room temperature, diluted with saturated NH_4Cl , and extracted with AcOEt . The extract was washed with brine, dried, concentrated, and chromatographed (SiO_2 15 g, hexane/ AcOEt = 30:1) to give **22** (240 mg, 70%) as a colorless oil: $[\alpha]_{\text{D}}^{28} -95.0$ (c 2.00, CHCl_3); ^1H NMR (400 MHz, CDCl_3) δ 6.87 (d, $J = 10.0$ Hz, 1H), 6.37 (d, $J = 4.4$ Hz, 1H), 4.72 (d, $J = 4.4$ Hz, 1H), 4.34 (d, $J = 16.0$ Hz, 1H), 4.27 (d, $J = 6.4$ Hz, 1H), 4.21 (qd, $J = 1.6, 7.0$ Hz, 2H), 4.08 (d, $J = 15.6$ Hz, 1H), 2.75-2.68 (m, 1H), 1.98-1.91 (m, 1H), 1.84 (d, $J = 1.2$ Hz, 3H), 1.44 (s, 3H), 1.31 (t, $J = 6.8$ Hz, 3H), 1.18-1.08 (m, 21H), 0.99 (d, $J = 7.2$ Hz, 3H), 0.78 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 168.0, 141.6, 138.5, 128.2, 122.4, 93.9, 77.9, 75.8, 60.6, 60.5, 42.9, 34.9, 34.0, 23.8, 18.0, 16.3, 14.2, 12.9, 12.4, 11.9; FTIR (neat) 2945, 2864, 1710, 1458, 1379, 1303, 1247, 1132, 1065 cm^{-1} ; MS (EI) m/z 43, 69, 87, 187, 278, 417, 558 (M^+); HRMS (EI) calcd for $\text{C}_{27}\text{H}_{47}^{79}\text{BrO}_5\text{Si}$ (M^+) 558.2376, found: 558.2379. The stereostructure was determined by the significant nOe between C3-H and C6-H in the NOESY spectrum.



(*R,E*)-Ethyl 4-((1*R*,2'*R*,3*R*,4*S*,5*R*)-1,4-Dimethyl-2,9-dioxaspiro[bicyclo[3.3.1]non[6]ene-8,2'-oxiran]-3-yl)-2-methylpent-2-enoate (3**).**

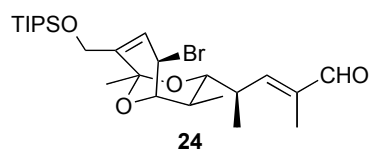
To an ice-cooled solution of **22** (230 mg, 0.41 mmol) in THF (21 mL) was added TBAF (1.0 M in THF, 0.5 mL, 0.5 mmol), and the mixture was stirred at 0 °C for 20 min. The mixture was then heated at reflux for 2 h and cooled to room temperature. The mixture was diluted with AcOEt and washed with saturated NH₄Cl and brine, dried, and concentrated. The residue was purified by column chromatography (SiO₂ 8 g, hexane/AcOEt = 6:1) to give **3** (112 mg, 85%) as a colorless oil: $[\alpha]_D^{26} +173.8$ (*c* 0.500, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 6.88 (dd, *J* = 1.2, 10.2 Hz, 1H), 6.36 (dd, *J* = 4.8, 10.0 Hz, 1H), 5.63 (d, *J* = 10.0 Hz, 1H), 4.36 (t, *J* = 4.8 Hz, 1H), 4.24-4.17 (m, 2H), 3.64 (dd, *J* = 1.6, 10.6 Hz, 1H), 2.99 (d, *J* = 6.4 Hz, 1H), 2.82 (d, *J* = 4.8 Hz, 1H), 2.75-2.68 (m, 1H), 2.00-1.94 (m, 1H), 1.84 (d, *J* = 1.6 Hz, 3H), 1.31 (t, *J* = 7.4 Hz, 3H), 1.24 (s, 3H), 1.04 (d, *J* = 6.8 Hz, 3H), 0.70 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 168.1, 141.7, 133.8, 130.6, 127.8, 98.8, 75.9, 71.5, 60.5, 55.0, 50.5, 34.9, 33.8, 22.1, 16.5, 14.2, 12.5, 12.4; FTIR (neat) 2970, 1709, 1650, 1298, 1243, 1135, 1043, 1004 cm⁻¹; MS (EI) *m/z* 95, 109, 121, 140, 181, 263, 277, 322 (M⁺); HRMS (EI) calcd for C₁₈H₂₆O₅ (M⁺) 322.178, found: 322.1792.



(*R,E*)-4-((1*R*,2'*R*,3*R*,4*S*,5*R*)-1,4-Dimethyl-2,9-dioxaspiro[bicyclo[3.3.1]non[6]ene-8,2'-oxiran]-3-yl)-2-methylpent-2-enal (23**).**

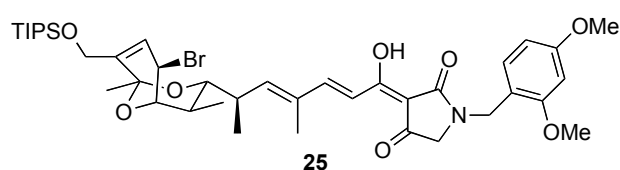
To a solution of **3** (84.7 mg, 267 μmol) in CH₂Cl₂ (18 mL) were added DIBAL-H (1.02 M in hexane, 0.68 mL, 0.69 mmol) at -78 °C. After stirring at -78 °C for 1 h, the reaction was quenched with saturated Rochelle salt (7 mL), and the mixture was stirred at room temperature for 6 h. The mixture was extracted with CH₂Cl₂, dried, and concentrated. The residue was dissolved in CH₂Cl₂ (18 mL), and NaHCO₃ (441 mg, 5.2 mmol) and Dess-Martin periodinane (223 mg, 0.52 mmol) were added at room temperature. After stirring at room temperature for 2 h, the reaction was quenched with 50% Na₂S₂O₄ (1.2 mL) and the mixture was extracted with AcOEt. The extract was washed with saturated NaHCO₃, dried over Na₂SO₄, concentrated, and chromatographed (SiO₂ 5 g, hexane/AcOEt = 5:1) to give **23** (73 mg, 100%) as a colorless oil: $[\alpha]_D^{26} +192.0$ (*c* 0.35, CHCl₃) [lit.⁵ $[\alpha]_D^{24.3} +196.1$ (*c* 0.8, CHCl₃)]; ¹H NMR (400 MHz, CDCl₃) δ 9.44 (s, 1H), 6.67 (dd, *J* = 1.6, 10.2 Hz, 1H), 6.35 (dd, *J* = 4.6, 10.4 Hz, 1H), 5.64 (d, *J* = 10.4 Hz, 1H), 4.36 (t, *J* = 4.6 Hz, 1H), 3.70 (dd, *J* = 2.0, 10.6 Hz, 1H), 2.99 (d, *J* = 4.8 Hz, 1H), 2.88 (m, 2H), 1.90 (m, 1H), 1.75 (s, 3H), 1.24 (s, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 0.71 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 195.4, 154.1, 139.1, 133.6, 130.6, 98.9, 75.8, 71.3, 54.9, 50.5, 35.2, 33.9, 22.2, 16.6, 12.5, 9.2; FTIR (neat) 2930, 1685, 1642, 1456, 1385, 1219, 1200, 1132,

1042 cm⁻¹; MS (EI) *m/z* 67, 81, 95, 109, 121, 145, 160, 175, 203, 218, 236, 278 (M⁺); HRMS (EI) calcd for C₁₆H₂₂O₄ (M⁺) 278.1518, found: 278.1527.



(*R,2E*)-4-(((1*S*,3*R*,5*R*,6*R*)-6-Bromo-8-(((triisopropylsilyl)oxymethyl)-1,4-dimethyl-2,9-dioxabicyclo[3.3.1]non-7-en-3-yl)-2-methylpent-2-enal(24). To a solution of **22** (136 mg,

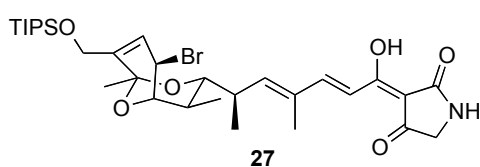
243 μmol) in CH₂Cl₂ (8 mL) was added DIBAL-H (1.02 M in hexane, 0.6 mL, 0.60 mmol) at -78 °C. After stirring at -78 °C for 1 h, the reaction was quenched with saturated Rochelle salt (6 mL), and the mixture was stirred at room temperature for 6 h. The mixture was extracted with CH₂Cl₂, dried, and concentrated. The residue (137 mg) was dissolved in CH₂Cl₂ (4 mL), and NaHCO₃ (408 mg, 4.9 mmol) and Dess-Martin periodinane (206 mg, 0.48 mmol) were added at room temperature. After stirring at room temperature for 30 min, the reaction was quenched with 50% Na₂S₂O₄ (4 mL) and the mixture was extracted with AcOEt. The extract was washed with saturated NaHCO₃, dried over Na₂SO₄, concentrated, and chromatographed (SiO₂ 5 g, hexane/AcOEt = 15:1) to give **24** (128 mg, 100%) as a colorless oil: [α]_D²⁷ -129.0 (*c* 0.98, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 9.46 (s, 1H), 6.67 (d, *J* = 10.0 Hz, 1H), 6.39 (d, *J* = 5.2 Hz, 1H), 4.72 (d, *J* = 4.8 Hz, 1H), 4.35 (d, *J* = 15.6 Hz, 1H), 4.28 (d, *J* = 6.0 Hz, 1H), 4.09 (d, *J* = 15.6 Hz, 1H), 3.43 (d, *J* = 11.6 Hz, 1H), 2.95-2.87 (m, 1H), 1.96-1.88 (m, 1H), 1.76 (s, 3H), 1.46 (s, 3H), 1.19-1.05 (m, 24H), 0.81 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 195.3, 153.9, 139.5, 138.3, 122.6, 93.9, 77.8, 75.7, 60.8, 42.5, 35.1, 34.2, 23.8, 18.0, 16.4, 12.9, 12.4, 11.9, 9.2; FTIR (neat) 2942, 2866, 1688, 1460, 1383, 1316, 1231, 1196, 1132, 1063 cm⁻¹; MS (EI) *m/z* 107, 314, 471, 514 (M⁺); HRMS (EI) calcd for C₂₅H₄₃⁷⁹BrO₄Si (M⁺) 514.2114, found: 514.2108.



(*3Z*)-1-(2,4-Dimethoxybenzyl)-3-(((*R,2E,4E*)-6-(((1*S*,3*R*,5*R*,6*R*)-6-bromo-8-(((triisopropylsilyl)oxy)methyl)-1,4-dimethyl-2,9-dioxabicyclo[3.3.1]non-

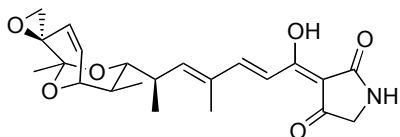
7-en-3-yl)-1-hydroxy-4-methylhepta-2,4-dienylidene)pyrrolidine-2,4-dione (25**).** To an ice-cooled solution of phosphonate **16** (256 mg, 0.60 mmol) in THF (4 mL) was stirred was added KO^tBu (135 mg, 1.20 mmol), and the mixture was stirred at 0 °C for 2 h. A solution of **24** (110 mg, 213 μmol) in THF (1 mL) was added at 0 °C and stirring was continued at 0 °C for 24 h. The reaction was quenched with saturated NH₄Cl (5 mL) and the mixture was extracted with Et₂O. The extract was washed with brine, filtered using a glass funnel plugged with lab wiper, concentrated, and purified by reverse phase column chromatography (ODS 9

g, CH₃CN/H₂O = 3:1 to 1:0) to give **25** (165 mg, 98%) as a yellow oil: $[\alpha]_D^{26} -97.6$ (*c* 1.00, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.54 (d, *J* = 15.6 Hz, 1H), 7.18 (d, *J* = 8.8 Hz, 1H), 7.10 (d, *J* = 15.6 Hz, 1H), 6.47-6.44 (m, 2H), 6.37 (d, *J* = 3.6 Hz, 1H), 6.20 (d, *J* = 9.6 Hz, 1H), 4.71 (d, *J* = 3.6 Hz, 1H), 4.57 (s, 2H), 4.33 (d, *J* = 16.0 Hz, 1H), 4.26 (d, *J* = 6.0 Hz, 1H), 4.07 (d, *J* = 16.0 Hz, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.65 (s, 2H), 3.36 (dd, *J* = 1.2, 11.2 Hz, 1H), 2.95-2.87 (m, 4H), 1.99-1.87 (m, 4H), 1.44 (s, 3H), 1.18-1.07 (m, 21H), 0.99 (d, *J* = 7.2 Hz, 3H), 0.78 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 192.0, 173.8, 173.4, 160.9, 158.6, 149.1, 144.7, 138.5, 134.3, 131.2, 122.4, 116.5, 116.1, 104.3, 100.9, 98.5, 93.9, 77.9, 76.1, 60.8, 55.6, 55.3, 42.9, 39.9, 35.0, 34.3, 23.8, 18.0, 16.9, 12.9, 12.2, 11.9; FTIR (neat) 3490, 2941, 2865, 1702, 1622, 1466, 1380, 1239, 1131, 1038 cm⁻¹; MS (FAB) *m/z* 136, 151, 282, 307, 460, 788 (100) [(M+H)⁺]; HRMS (FAB) calcd for C₄₀H₅₉⁷⁹BrO₈Si [(M+H)⁺] 788.3193, found: 788.3187.



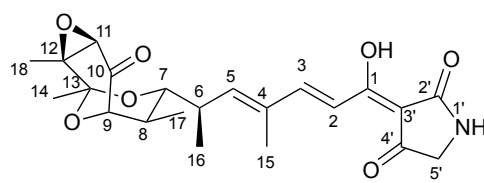
(3Z)-3-((R,2E,4E)-6-((1S,3R,5R,6R)-6-bromo-8-(((triiisopropylsilyl)oxy)methyl)-1,4-dimethyl-2,9-dioxa-bicyclo[3.3.1]non-7-en-3-yl)-1-hydroxy-4-methylhepta-2,4-dienylidene)pyrrolidine-2,4-dione (27). To

a solution of **25** (43 mg, 55 μmol) in CH₂Cl₂ (6 mL) were added phosphate buffer (pH = 6.4) (0.2 M, 4 mL, 0.8 mmol) and DDQ (112 mg, 0.5 mmol) at room temperature. After being stirred at 50 °C for 5 days, the mixture was diluted with saturated NaHCO₃ (6 mL) and 10% Na₂S₂O₄ (12 mL), and then extracted with AcOEt. The extract was filtered using a glass funnel plugged with lab wiper, concentrated, and purified by reverse phase preparative TLC (MeCN) to give **27** (13 mg, 37%, 77% brsm) as a yellow oil and **25** (22 mg, 52%): $[\alpha]_D^{26} -118.2$ (*c* 0.490, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.60 (d, *J* = 15.6 Hz, 1H), 7.15 (d, *J* = 15.6 Hz, 1H), 6.38 (d, *J* = 4.0 Hz, 1H), 6.25 (d, *J* = 10.4 Hz, 1H), 5.81 (brs, 1H), 4.71 (d, *J* = 4.4 Hz, 1H), 4.34 (d, *J* = 15.6 Hz, 1H), 4.26 (d, *J* = 6.0 Hz, 1H), 4.08 (d, *J* = 15.6 Hz, 1H), 3.82 (brs, 2H), 3.37 (dd, *J* = 1.6, 11.2 Hz, 1H), 2.93-2.86 (m, 1H), 1.95-1.88 (m, 4H), 1.44 (s, 3H), 1.15-1.01 (m, 24H), 0.79 (d, *J* = 7.6 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 192.5, 176.5, 175.3, 150.2, 145.6, 138.5, 134.4, 122.5, 116.3, 99.9, 93.9, 77.9, 76.1, 60.9, 51.5, 42.9, 35.1, 34.4, 23.8, 18.1, 16.9, 12.9, 12.2, 11.9; FTIR (neat) 3323, 2940, 2865, 1623, 1572, 1460, 1377, 1241, 1126, 1100, 1063 cm⁻¹; MS (FAB) *m/z* 107, 151, 281, 337, 638 [(M+H)⁺]; HRMS (FAB) calcd for C₃₁H₄₉⁷⁹BrO₆Si [(M+H)⁺] 638.2513, found: 638.2513.



(+)-Tirandalydigin. To an ice-cooled solution of **27** (17 mg, 27 μmol) in THF (3.5 mL) was added TBAF (1.0 M in THF, 93 μL , 93 μmol), and the mixture was stirred at 0 °C for 20 min. The mixture was then heated at reflux for 3 h and cooled to room temperature. The mixture was diluted with AcOEt and washed with saturated NH_4Cl and brine, filtered using a glass funnel plugged with lab wiper, and concentrated. The residue was purified by reverse phase preparative TLC (MeCN) to give tirandalydigin (5.3 mg, 50%) as a yellow oil. A solution of tirandalydigin in MeOH (1 mL) was treated with saturated NaHCO_3 (0.1 mL) and concentrated to dryness. The residue was dissolved in MeOH and filtered using a glass funnel plugged with lab wiper, and concentrated to afford a sodium salt of tirandalydigin: $[\alpha]_{\text{D}}^{29} +52$ (c 0.73, MeOH) for Na salt, $[\alpha]_{\text{D}}^{30} +22$ (c 0.63, MeOH) for H form [lit.⁶ $[\alpha]_{\text{D}}^{26} -4.0$ (c 0.50, MeOH)]; ^1H NMR (500 MHz, CDCl_3) δ 7.62 (d, $J = 15.5$ Hz, 1H), 7.27 (d, $J = 15.5$ Hz, 1H), 6.40 (dd, $J = 5.0, 10.2$ Hz, 1H), 5.95 (d, $J = 10.0$ Hz, 1H), 5.62 (d, $J = 10.2$ Hz, 1H), 4.33 (t, $J = 5.0$ Hz, 1H), 3.71 (d, $J = 10.5$ Hz, 1H), 3.59 (s, 2H), 2.99 (d, $J = 5.0$ Hz, 1H), 2.85 (d, $J = 5.0$ Hz, 1H), 2.85-2.79 (m, 1H), 1.94-1.88 (m, 1H), 1.89 (s, 3H), 1.16 (s, 3H), 1.05 (d, $J = 7.0$ Hz, 3H), 0.74 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 197.1, 186.1, 179.9, 144.9, 140.3, 135.5, 135.1, 131.5, 126.7, 104.2, 100.1, 77.8, 72.9, 56.2, 51.3, 50.9, 36.5, 34.8, 22.7, 17.7, 12.9, 12.7; FTIR (neat) 3600-3000, 2963, 2927, 1613, 1463, 1234, 1125, 1041, 1001 cm^{-1} ; MS (FAB) m/z 77, 107, 136, 154, 242, 307, 424 (100) $[(\text{M}+\text{Na})^+]$; HRMS (FAB) calcd for $\text{C}_{22}\text{H}_{27}\text{NO}_6\text{Na}$ $[(\text{M}+\text{Na})^+]$ 424.1736, found: 424.1722.

NMR Comparison of Synthetic Compounds with the Natural Products

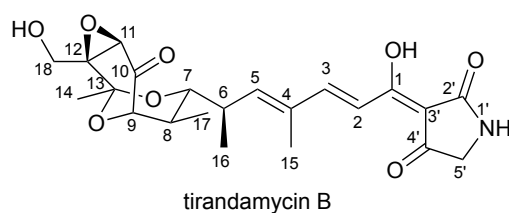


tirandamycin A

Ref 2

*Both synthetic and natural specimens exist as a ca. 4:1 mixture of the $\Delta^{1,3'}$ -enol geometrical isomers. The table shows the peaks corresponding to the major isomer.

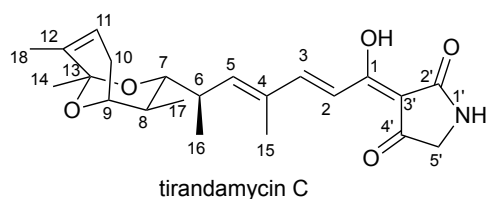
Position	^{13}C (CD_2Cl_2)		^1H (CD_2Cl_2)	
	Natural	Synthetic (125 MHz)	Natural	Synthetic (500 MHz)
1'				5.83 (brs)
2'	176.9	176.7		
3'	not reported	100.5		
4'	193.1	192.8		
5'	52.1	51.9	3.78 (s)	3.78 (s)
1	175.5	175.0		
2	117.1	116.8	7.15 (dd, $J = 0.4, 15.8$)	7.14 (d, $J = 16.0$)
3	150	149.7	7.58 (dd, $J = 0.7, 15.8$)	7.58 (d, $J = 16.0$)
4	135.3	135.2		
5	144.5	144.2	6.24 (d, $J = 9.9$)	6.24 (d, $J = 10.0$)
6	34.9	34.8	2.87 (m)	2.87 (m)
7	77.4	77.2	3.58 (not reported)	3.60 (d, $J = 11.5$)
8	35	35	1.97 (m)	1.97 (m)
9	79.4	79.2	3.98 (d, $J = 6.1$)	3.98 (d, $J = 6.0$)
10	203.2	202.9		
11	61.6	61.4	3.25 (s)	3.25 (s)
12	57.5	57.3		
13	97.4	97.1		
14	22.8	22.7	1.53 (s)	1.53 (s)
15	12.5	12.3	1.91 (d, $J = 1.3$)	1.91 (s)
16	17.2	17.0	1.14 (d, $J = 6.8$)	1.13 (d, $J = 7.0$)
17	11.6	11.5	0.71 (d, $J = 7.0$)	0.70 (d, $J = 7.0$)
18	15.8	15.7	1.46 (s)	1.45 (s)



Ref 7

*Both synthetic and natural specimens exist as a ca. 4:1 mixture of the $\Delta^{1,3'}$ -enol geometrical isomers. The table shows the peaks corresponding to the major isomer.

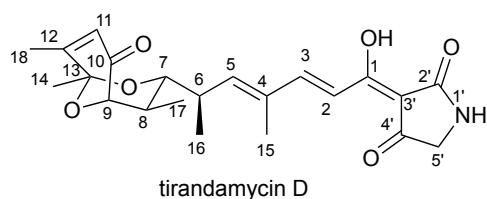
Position	¹³ C (CDCl ₃)		¹ H (CDCl ₃)	
	Natural (125 MHz)	Synthetic (100 MHz)	Natural (500 MHz)	Synthetic (500 MHz)
1'				6.29 (brs)
2'	176.7	176.5		
3'	100.4	100.1		
4'	192.8	192.6		
5'	51.9	51.6	3.83 (s)	3.83 (s)
1	175.4	175.1		
2	117.1	116.8	7.17 (d, <i>J</i> = 15.5)	7.16 (d, <i>J</i> = 15.5)
3	149.9	149.6	7.57 (d, <i>J</i> = 15.5)	7.56 (d, <i>J</i> = 15.5)
4	135.3	135		
5	143.6	143.3	6.19 (d, <i>J</i> = 10.0)	6.18 (d, <i>J</i> = 10.0)
6	34.8	34.5	2.86 (m)	2.85 (m)
7	77.5	77.3	3.67 (d, <i>J</i> = 11.5)	3.66 (d, <i>J</i> = 11.5)
8	34.8	34.5	1.99 (m)	1.99 (m)
9	79	78.7	4.05 (d, <i>J</i> = 6.5)	4.04 (d, <i>J</i> = 6.0)
10	201.7	201.4		
11	58.4	58	3.70 (s)	3.70 (s)
12	57.2	56.8		
13	96.2	95.9		
14	23.6	23.3	1.58 (s)	1.57 (s)
15	12.6	12.3	1.91 (s)	1.91 (s)
16	17.2	16.9	1.13 (d, <i>J</i> = 7.0)	1.12 (d, <i>J</i> = 7.0)
17	11.7	11.4	0.73 (d, <i>J</i> = 7.0)	0.72 (d, <i>J</i> = 7.0)
18	59.6	59.3	4.00 (brs), 3.99 (brs)	3.99 (brs), 3.98 (brs)



Ref 2

*Both synthetic and natural specimens exist as a ca. 4:1 mixture of the $\Delta^{1,3'}$ -enol geometrical isomers. The table shows the peaks corresponding to the major isomer.

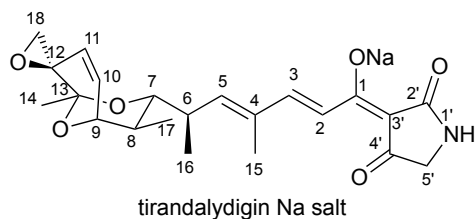
Position	^{13}C (CD_2Cl_2)		^1H (CD_2Cl_2)	
	Natural	Synthetic (100 MHz)	Natural	Synthetic (500 MHz)
1'				6.11 (brs)
2'	177.1	176.9		
3'	not reported	100.3		
4'	193.1	192.8		
5'	51.9	52	3.78 (s)	3.78 (s)
1	175.5	175.3		
2	116.1	116.1	7.12 (dd, $J = 0.4, 15.7$)	7.12 (d, $J = 15.5$)
3	150.4	150.4	7.62 (dd, $J = 0.8, 15.7$)	7.62 (d, $J = 15.5$)
4	134.9	134.5		
5	147.5	147.4	6.32 (d, $J = 10.2$)	6.32 (d, $J = 10.0$)
6	34.9	34.9	2.83 (m)	2.83 (m)
7	77	77	3.49 (dd, $J = 2.1, 11.0$)	3.49 (d, $J = 11.0$)
8	35.5	35.5	1.84 (m)	1.84 (m)
9	71.4	71.3	3.90 (br d, $J = 6.5$)	3.90 (br t, $J = 6.0$)
10	24.5	24.5	2.33 (m), 1.96 (m)	2.33 (m), 1.96 (m)
11	123.6	123.7	5.70 (br s)	5.71 (br s)
12	133.2	132.9		
13	96.1	95.8		
14	24.5	24.5	1.38 (s)	1.38 (s)
15	12.4	12.3	1.91 (d, $J = 1.3$)	1.91 (br s)
16	17.2	17.2	1.05 (d, $J = 7.0$)	1.04 (d, $J = 7.0$)
17	13.2	13.3	0.68 (d, $J = 7.0$)	0.68 (d, $J = 7.0$)
18	18.3	18.4	1.61 (s)	1.61 (s)



Ref 2

*Both synthetic and natural specimens exist as a ca. 4:1 mixture of the $\Delta^{1,3'}$ -geometrical isomers. The table shows the peaks corresponding to the major isomer.

Position	^{13}C (CD_2Cl_2)		^1H (CD_2Cl_2)	
	Natural	Synthetic (100 MHz)	Natural	Synthetic (500 MHz)
1'			5.70 (s)	6.08 (brs)
2'	177	176.8		
3'	not reported	100.3		
4'	193	192.8		
5'	51.9	52.0	3.78 (s)	3.78 (s)
1	175.5	175.2		
2	116.7	116.6	7.15 (dd, $J = 0.4, 15.8$)	7.14 (d, $J = 16.0$)
3	150.2	149.9	7.61 (dd, $J = 0.7, 15.7$)	7.61 (d, $J = 15.5$)
4	135.5	134.9		
5	145.8	145.7	6.30 (d, $J = 10.1$)	6.29 (d, $J = 10.5$)
6	34.8	34.7	2.89 (m)	2.89 (m)
7	77.7	77.6	3.44 (dd, $J = 2.1, 11.3$)	3.44 (dd, $J = 2.0, 11.5$)
8	33.9	33.9	1.97 (m)	1.97 (m)
9	79.5	79.4	3.97 (d, $J = 5.8$)	3.97 (d, $J = 6.0$)
10	195.7	195.4		
11	127.4	127.3	6.08 (s)	6.08 (s)
12	156.7	156.3		
13	96.7	96.4		
14	24.6	24.6	1.54 (s)	1.53 (s)
15	12.4	12.4	1.91 (d, $J = 1.1$)	1.91 (s)
16	17	17.1	1.07 (d, $J = 7.0$)	1.06 (d, $J = 7.0$)
17	11.6	11.8	0.69 (d, $J = 7.2$)	0.69 (d, $J = 7.0$)
18	19.4	19.3	1.92 (s)	1.92 (s)

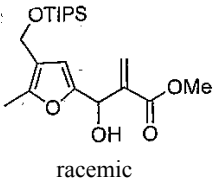


Ref 6

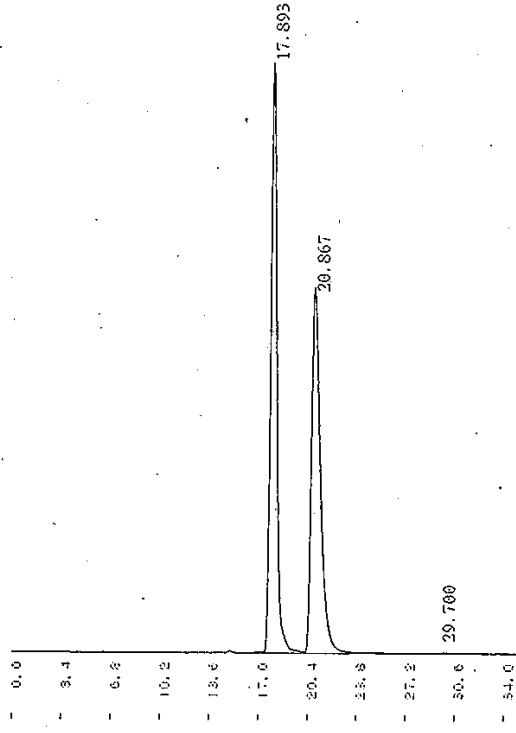
Position	¹³ C (CD ₃ OD)		¹ H (CD ₃ OD)	
	Natural (75.5 MHz)	Synthetic (100 MHz)	Natural (300.1 MHz)	Synthetic (500 MHz)
1'				
2'	179.9	179.9		
3'	104.2	104.2		
4'	197.2	197.1		
5'	50.9	50.9	3.58 (s)	3.59 (s)
1	186.1	186.1		
2	126.6	126.7	7.61 (d, <i>J</i> = 15.3)	7.62 (d, <i>J</i> = 15.5)
3	144.9	144.9	7.26 (d, <i>J</i> = 15.3)	7.27 (d, <i>J</i> = 15.5)
4	135.5	135.5		
5	140.3	140.3	5.94 (d, <i>J</i> = 10.2)	5.95 (d, <i>J</i> = 10.0)
6	34.8	34.8	2.80 (m)	2.80 (m)
7	77.8	77.8	3.70 (dd, <i>J</i> = 2.1, 10.6)	3.71 (d, <i>J</i> = 10.5)
8	36.5	36.5	1.91 (m)	1.94-1.88 (m)
9	72.9	72.9	4.33 (t, <i>J</i> = 5.0)	4.33 (t, <i>J</i> = 5.0)
10	135.1	135.1	6.40 (dd, <i>J</i> = 5.0, 10.2)	6.40 (dd, <i>J</i> = 5.0, 10.2)
11	131.5	131.5	5.62 (d, <i>J</i> = 10.2)	5.62 (d, <i>J</i> = 10.2)
12	56.1	56.2		
13	100.1	100.1		
14	22.7	22.7	1.15 (s)	1.16 (s)
15	12.9	12.9	1.88 (s)	1.89 (s)
16	17.8	17.7	1.04 (d, <i>J</i> = 6.8)	1.05 (d, <i>J</i> = 7.0)
17	12.7	12.7	0.73 (d, <i>J</i> = 7.1)	0.74 (d, <i>J</i> = 6.5)
18	51.4	51.3	2.98 (d, <i>J</i> = 5.2)	2.99 (d, <i>J</i> = 5.0)
			2.84 (d, <i>J</i> = 5.2)	2.85 (d, <i>J</i> = 5.0)

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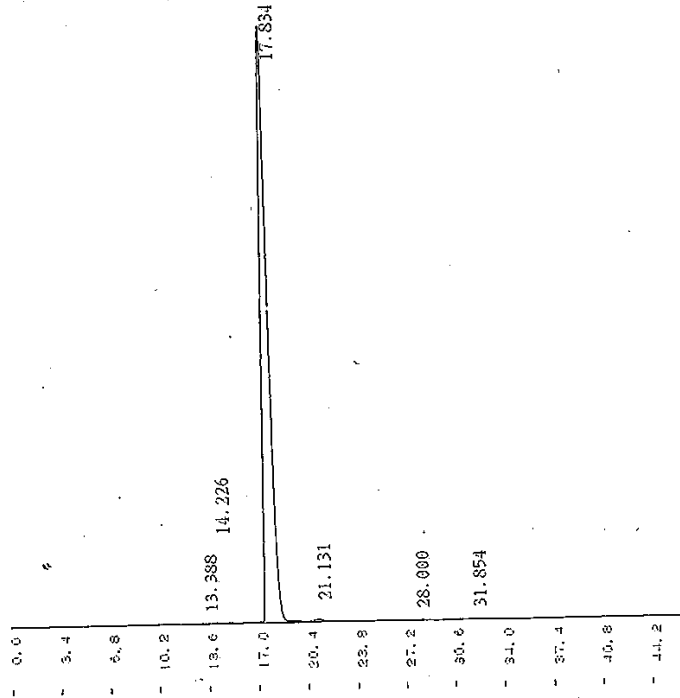
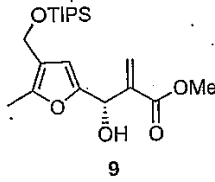
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3	29.7	5933	92	V		0.0941	
TOTAL						6303266	162864

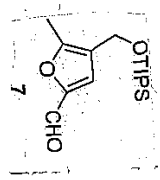
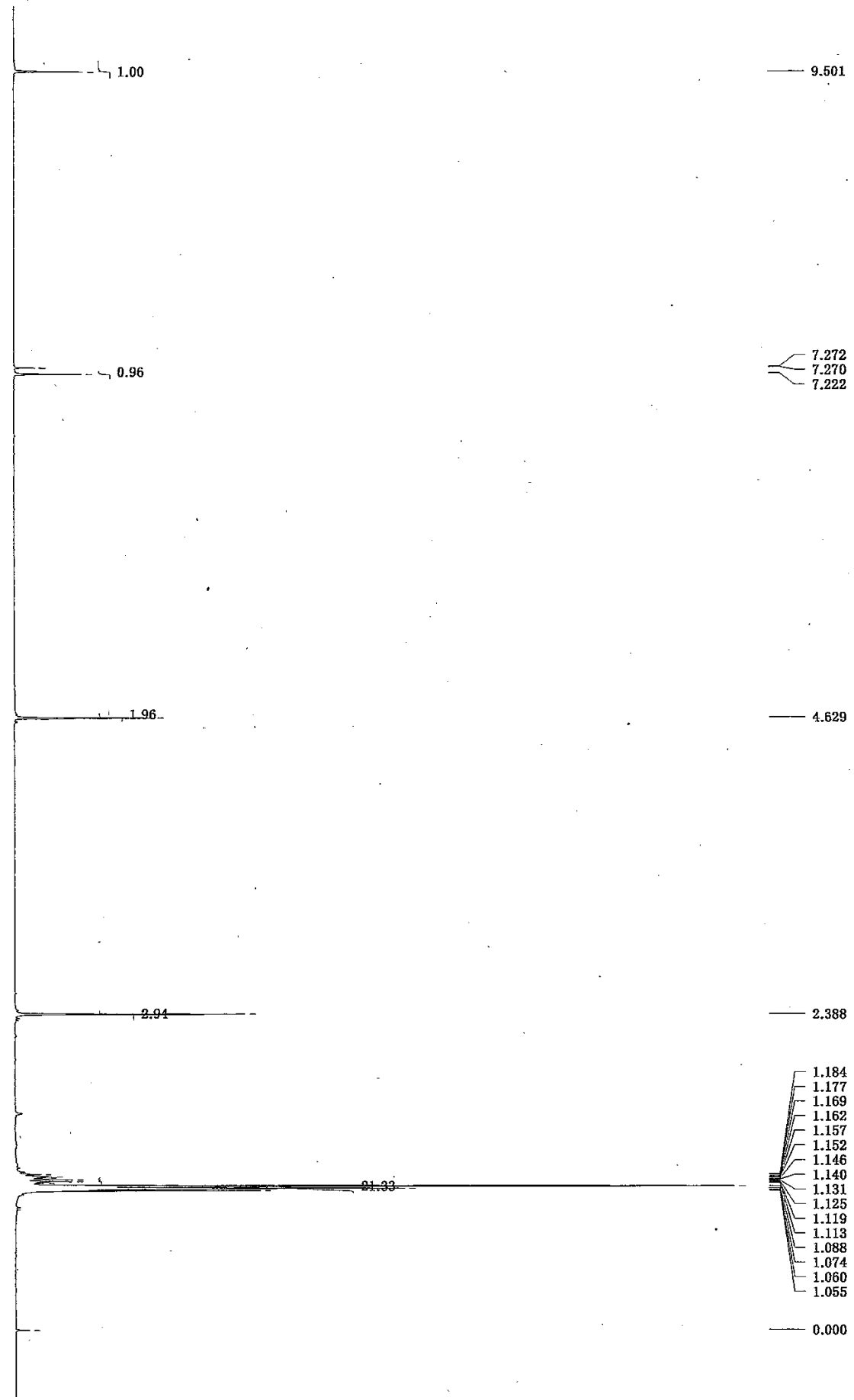
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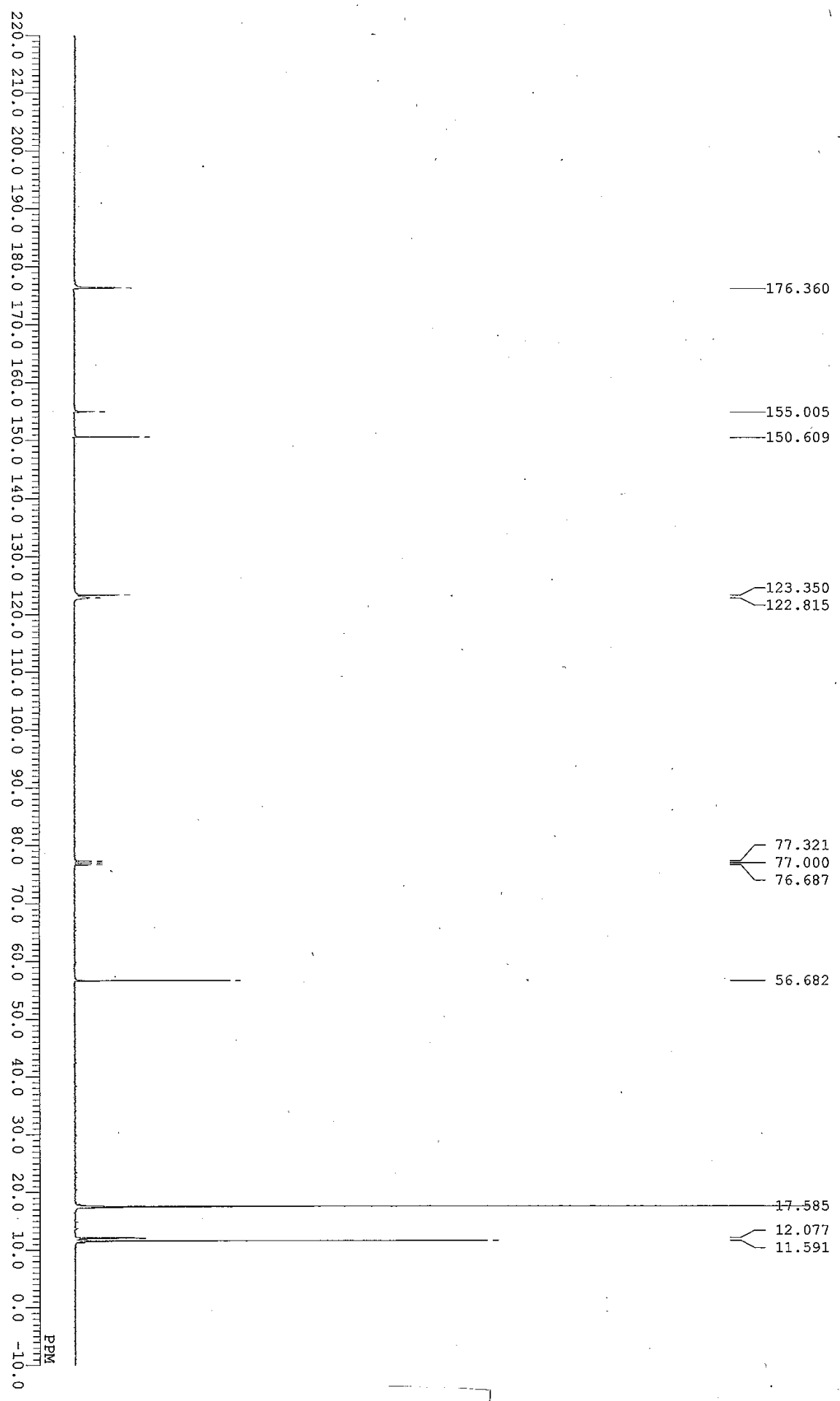
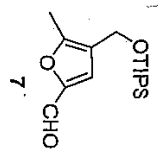


** CALCULATION REPORT **

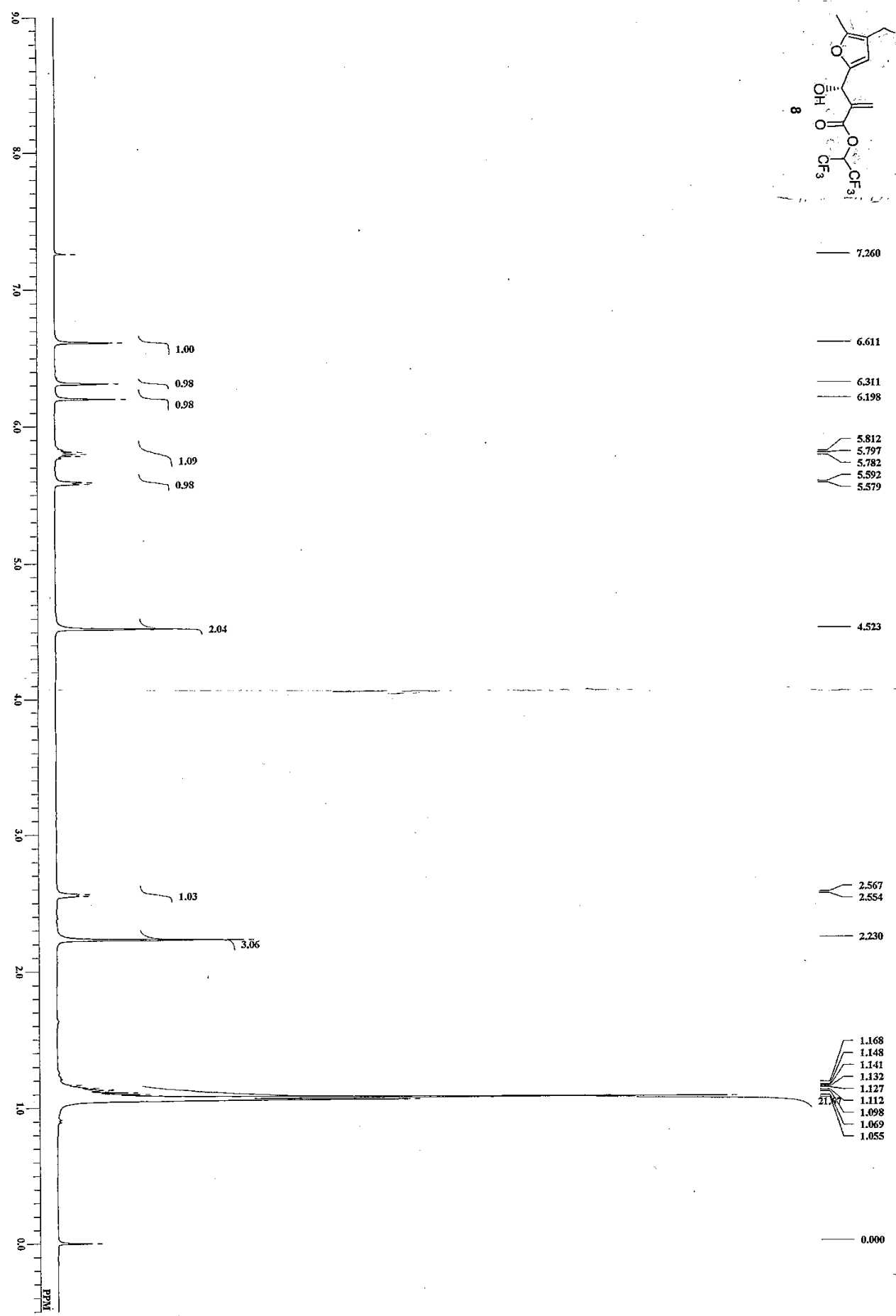
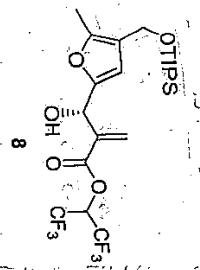
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4	21.131	34622	858	T		0.4867	
5	28	2707	61	T		0.0381	
6	31.854	11779	100	T		0.1656	
TOTAL						7112992	191521

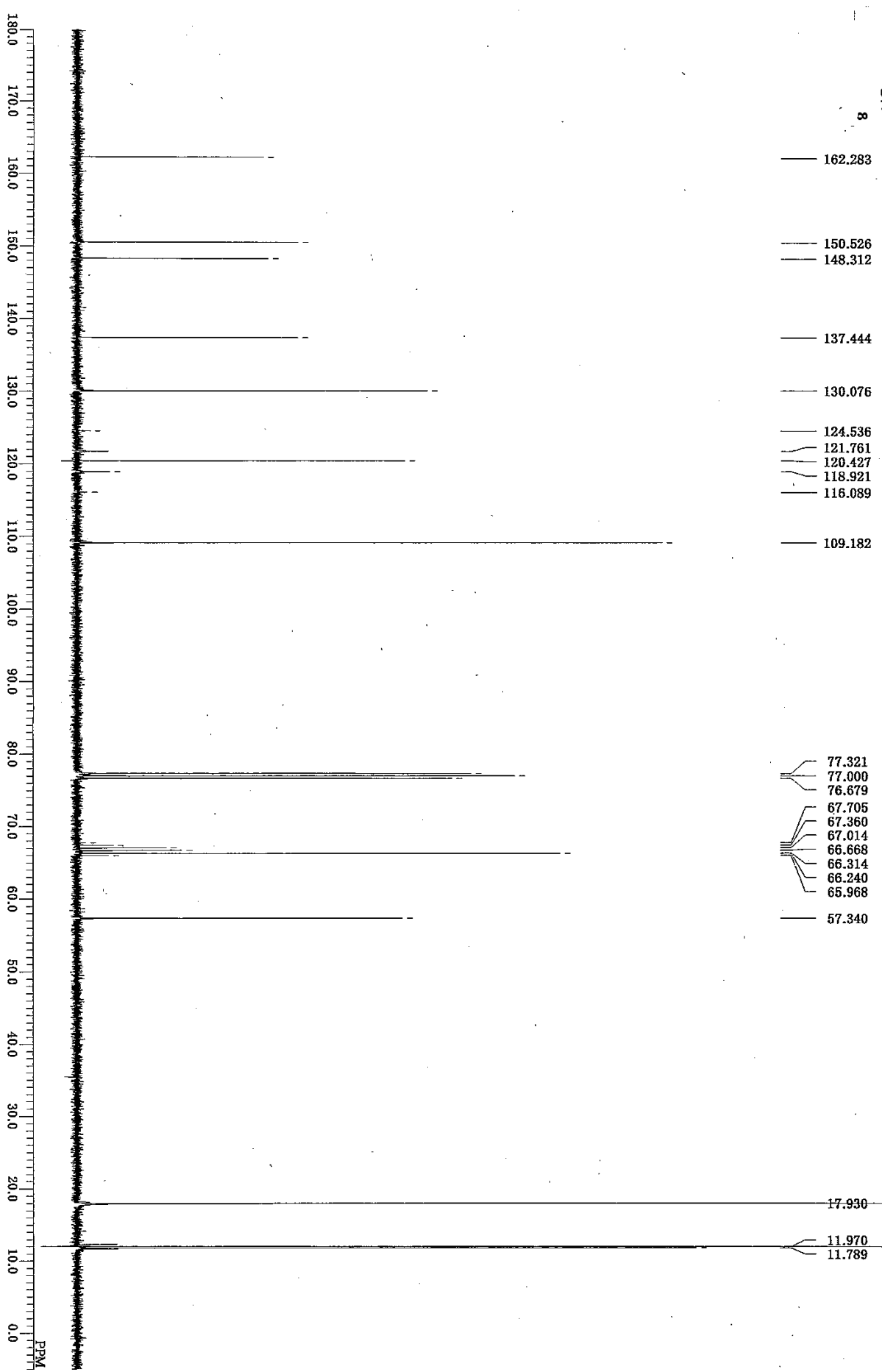
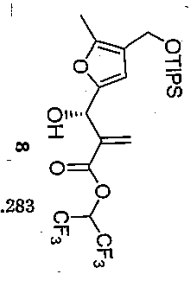
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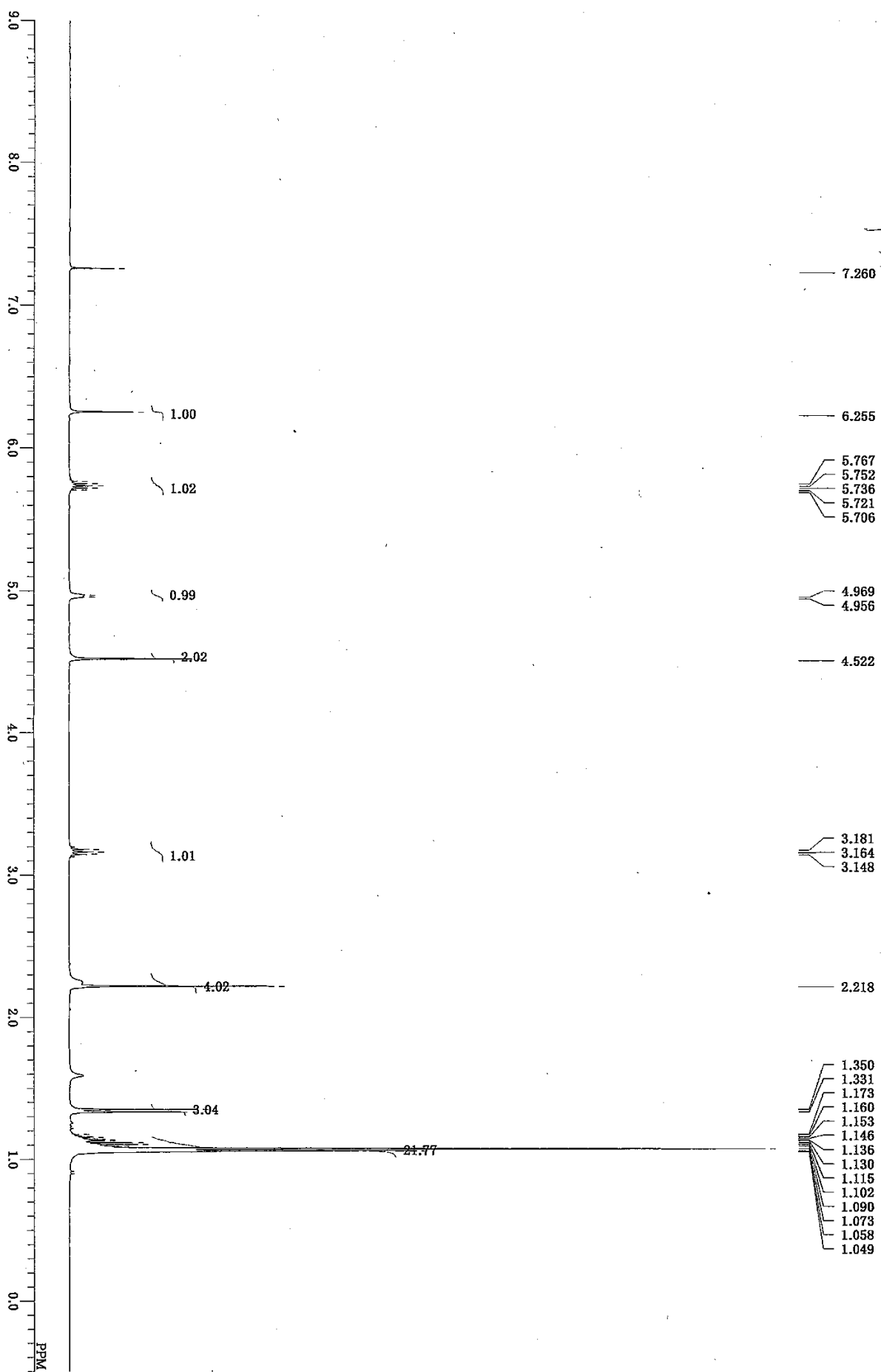
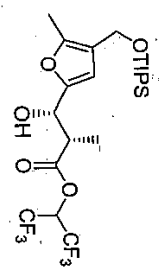


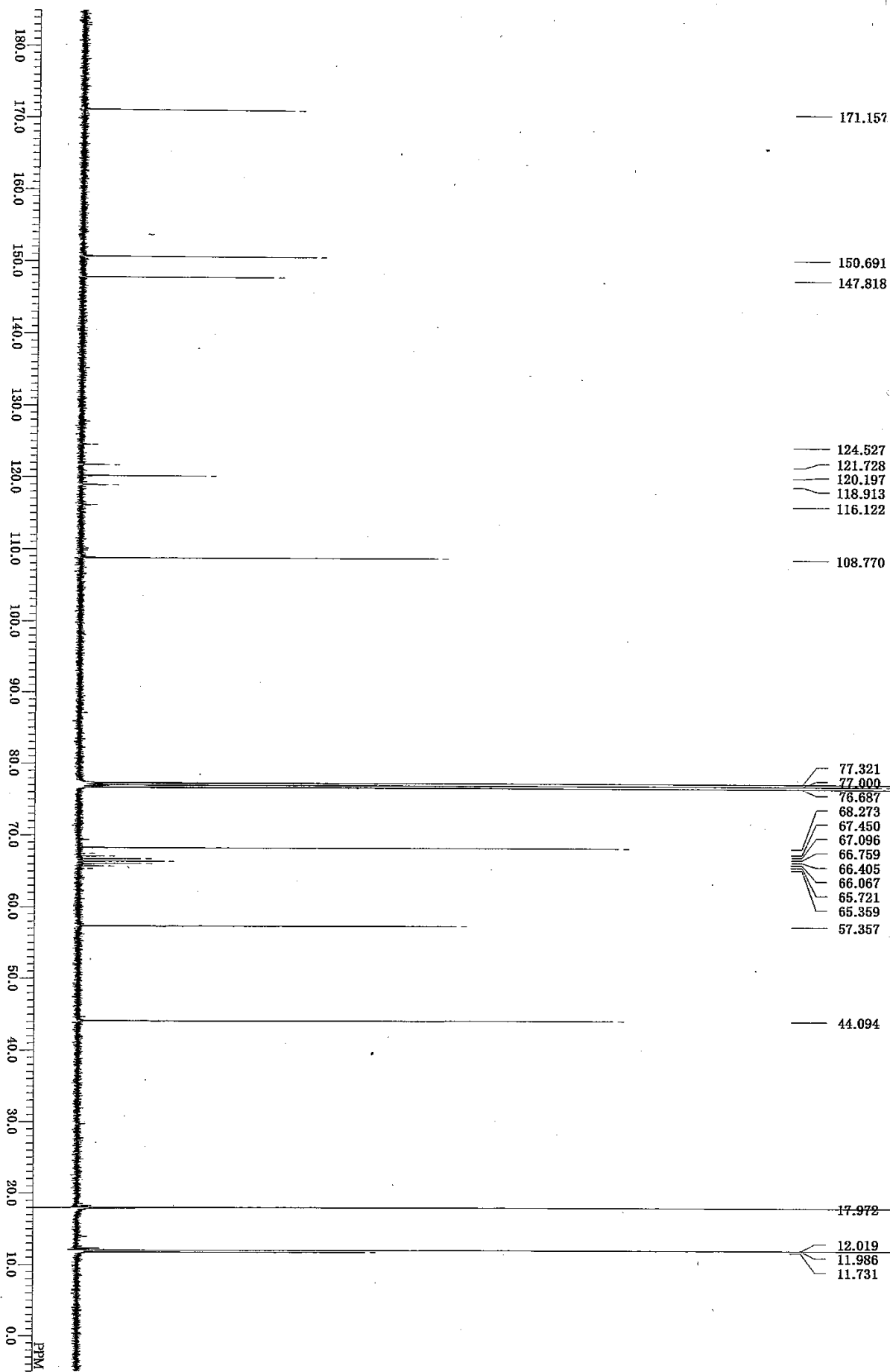
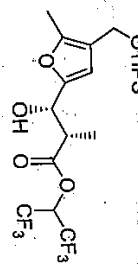


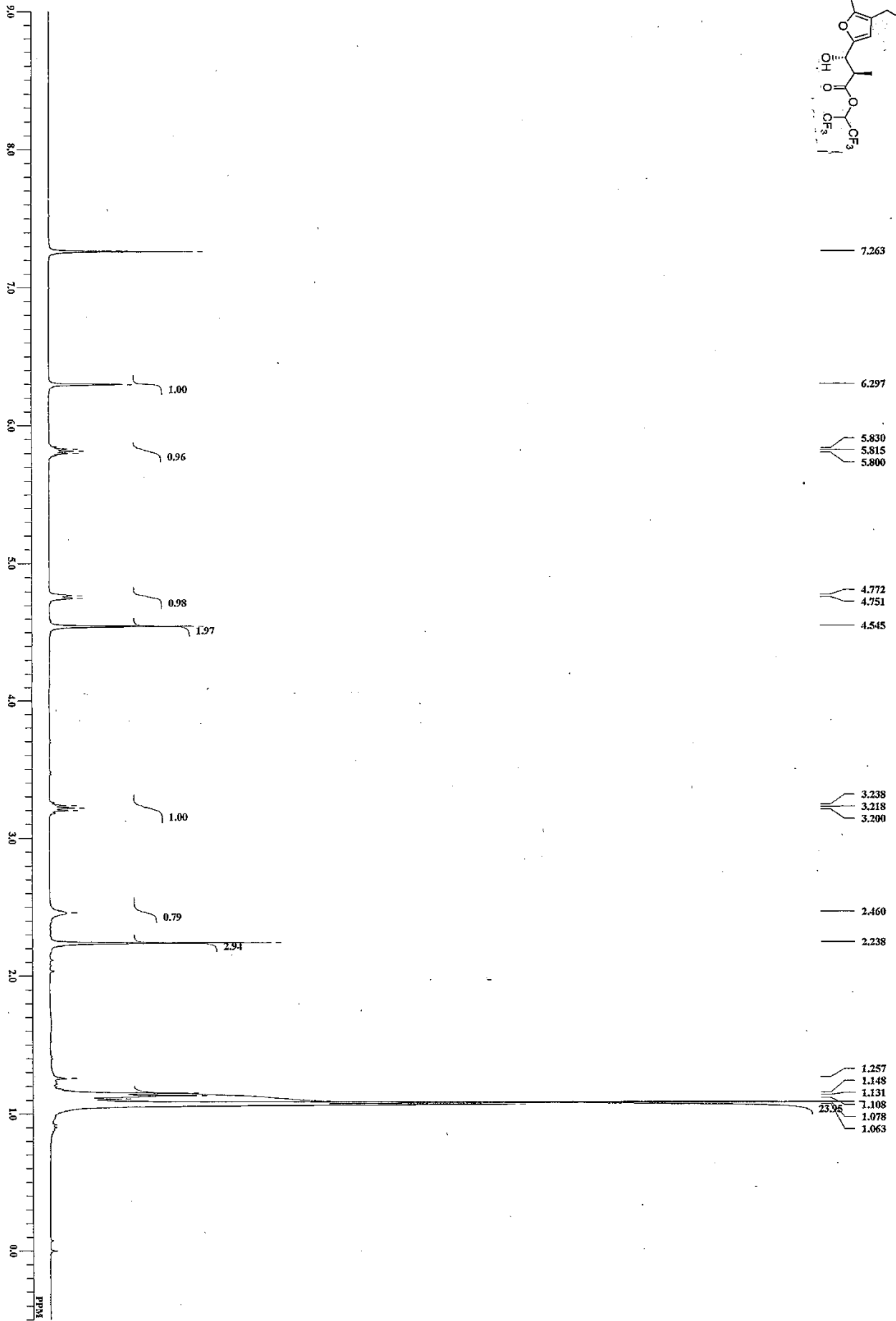
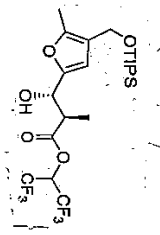
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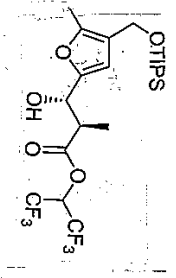
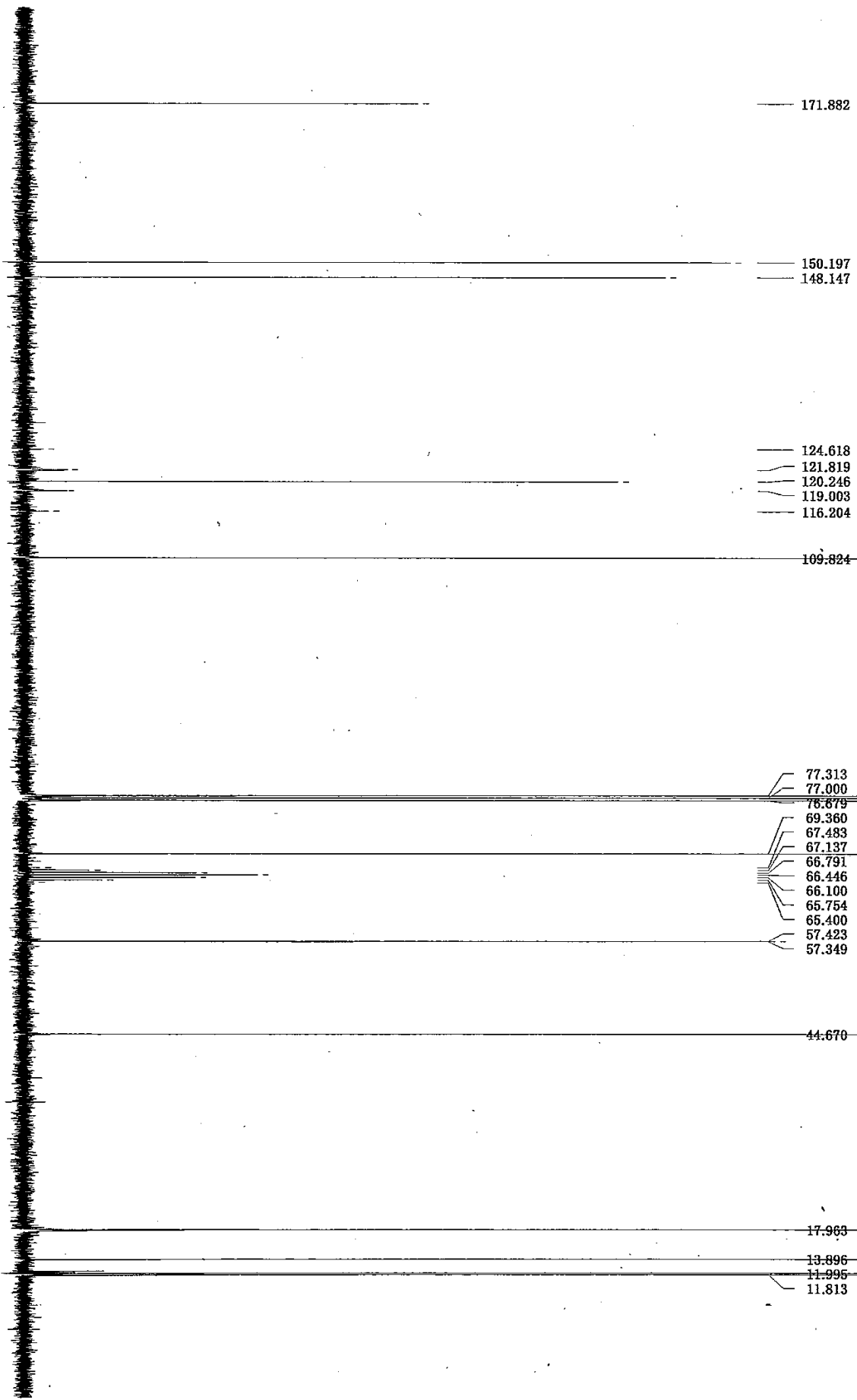


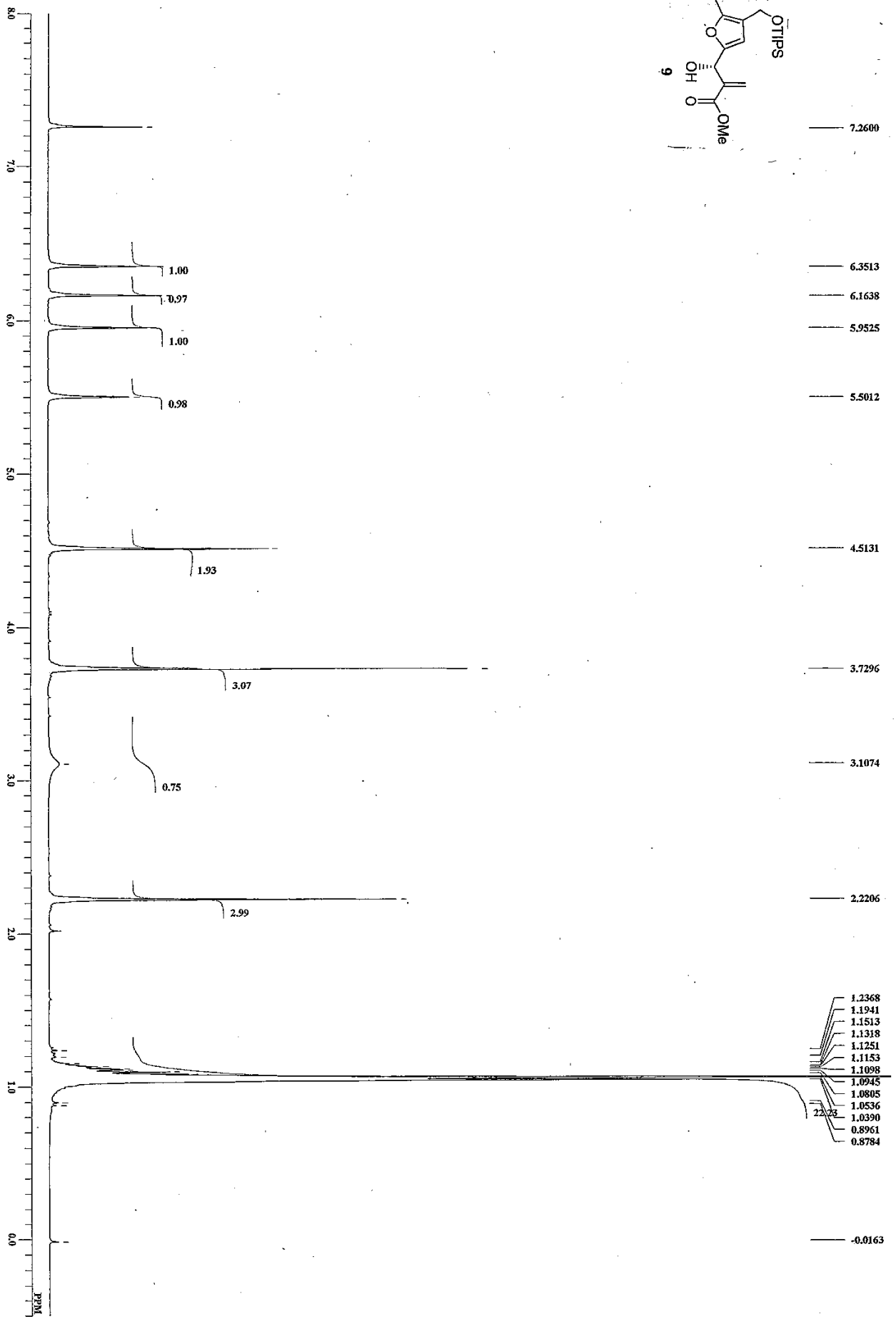




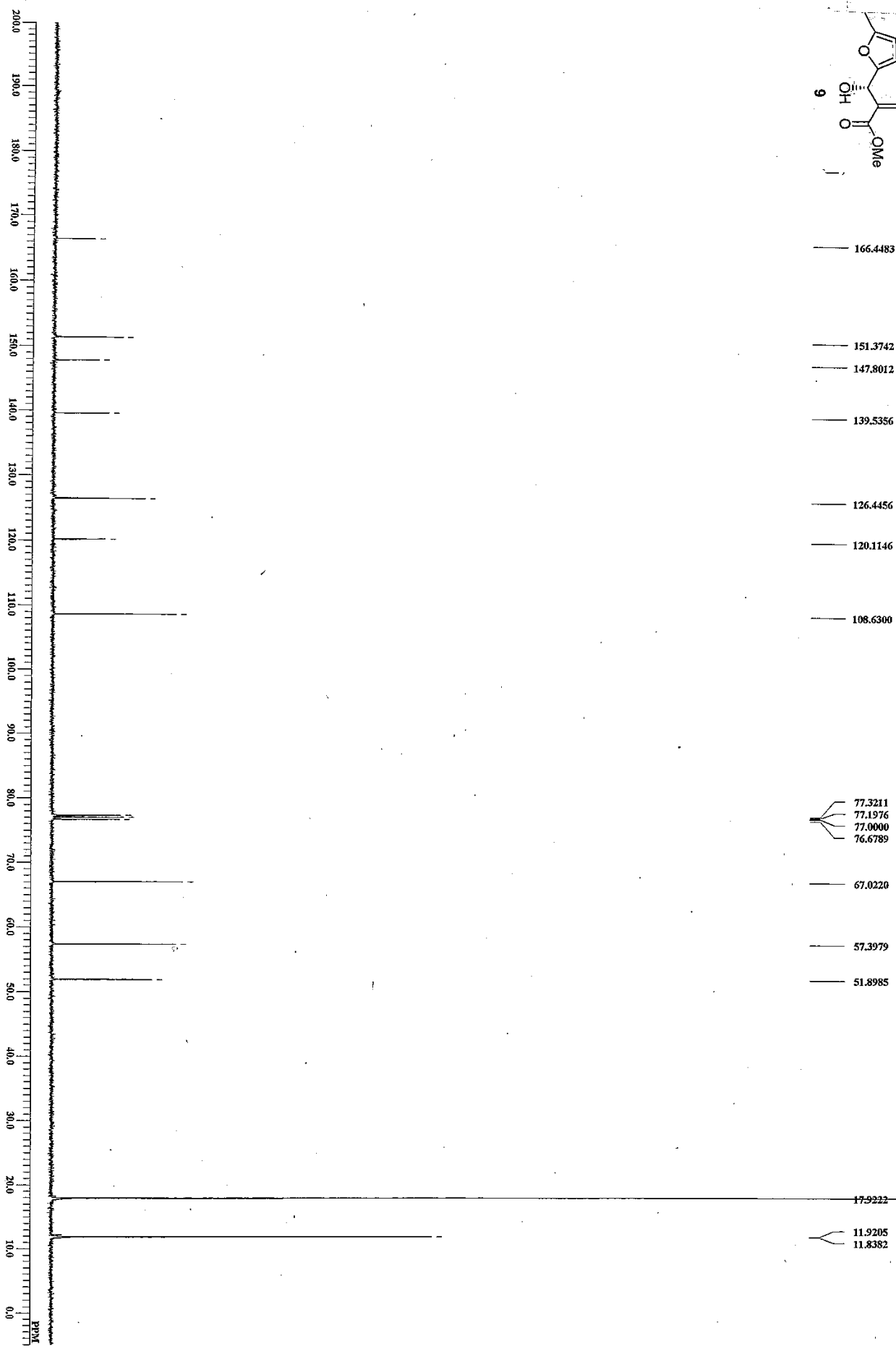
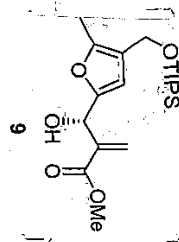


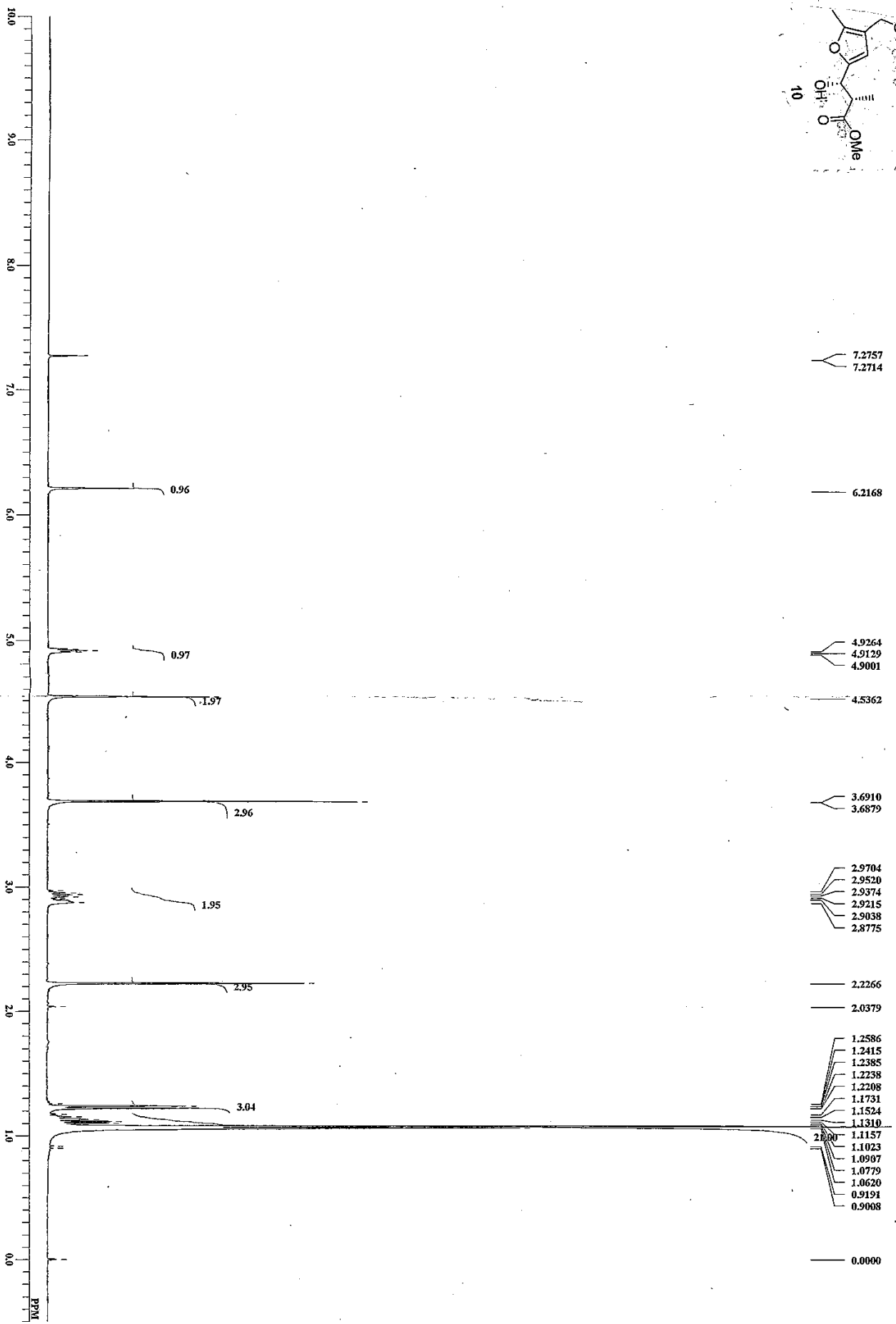
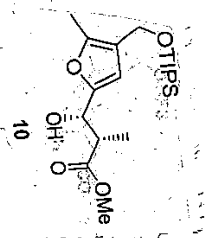
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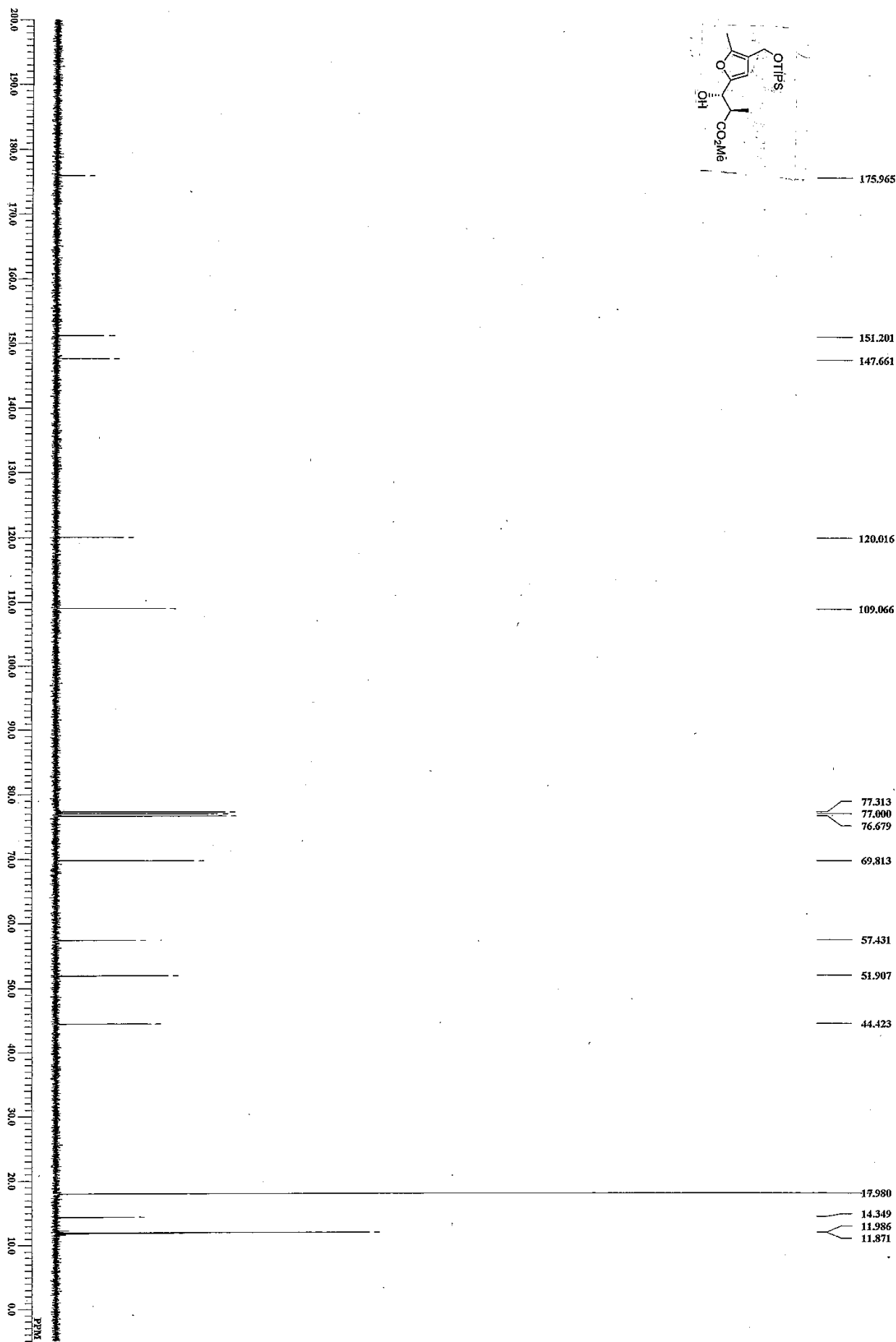


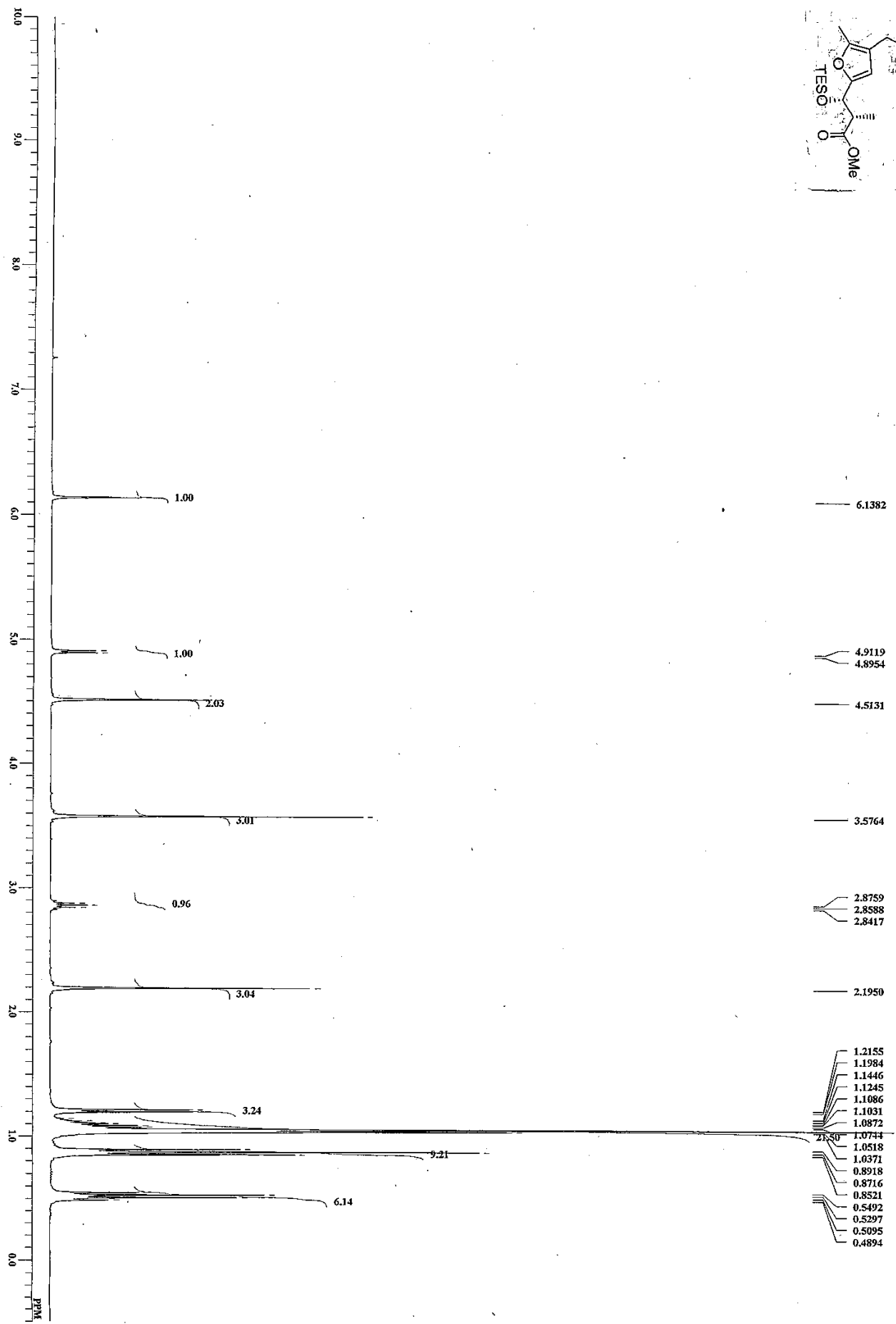
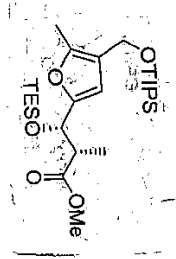


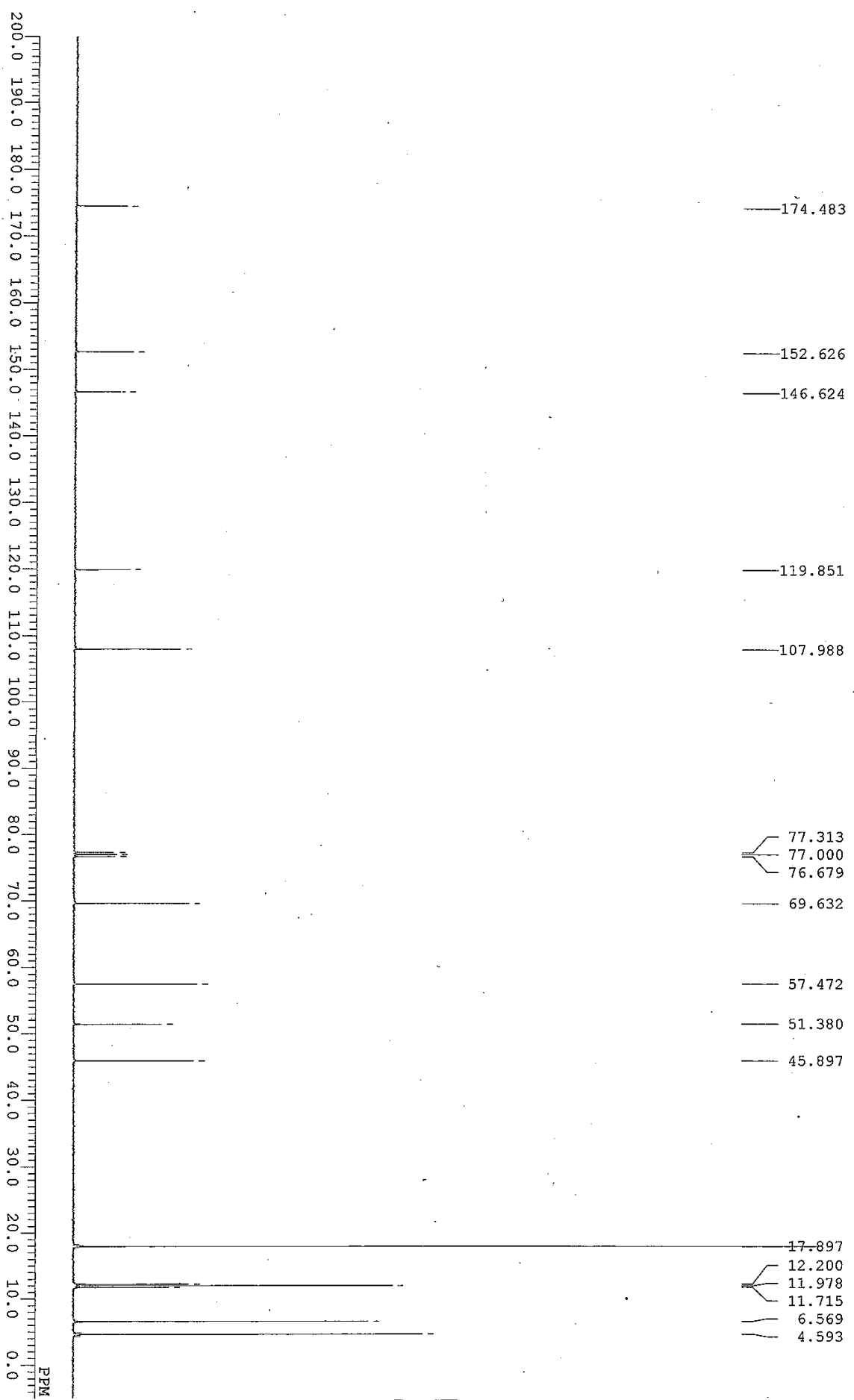
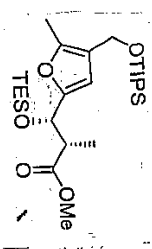
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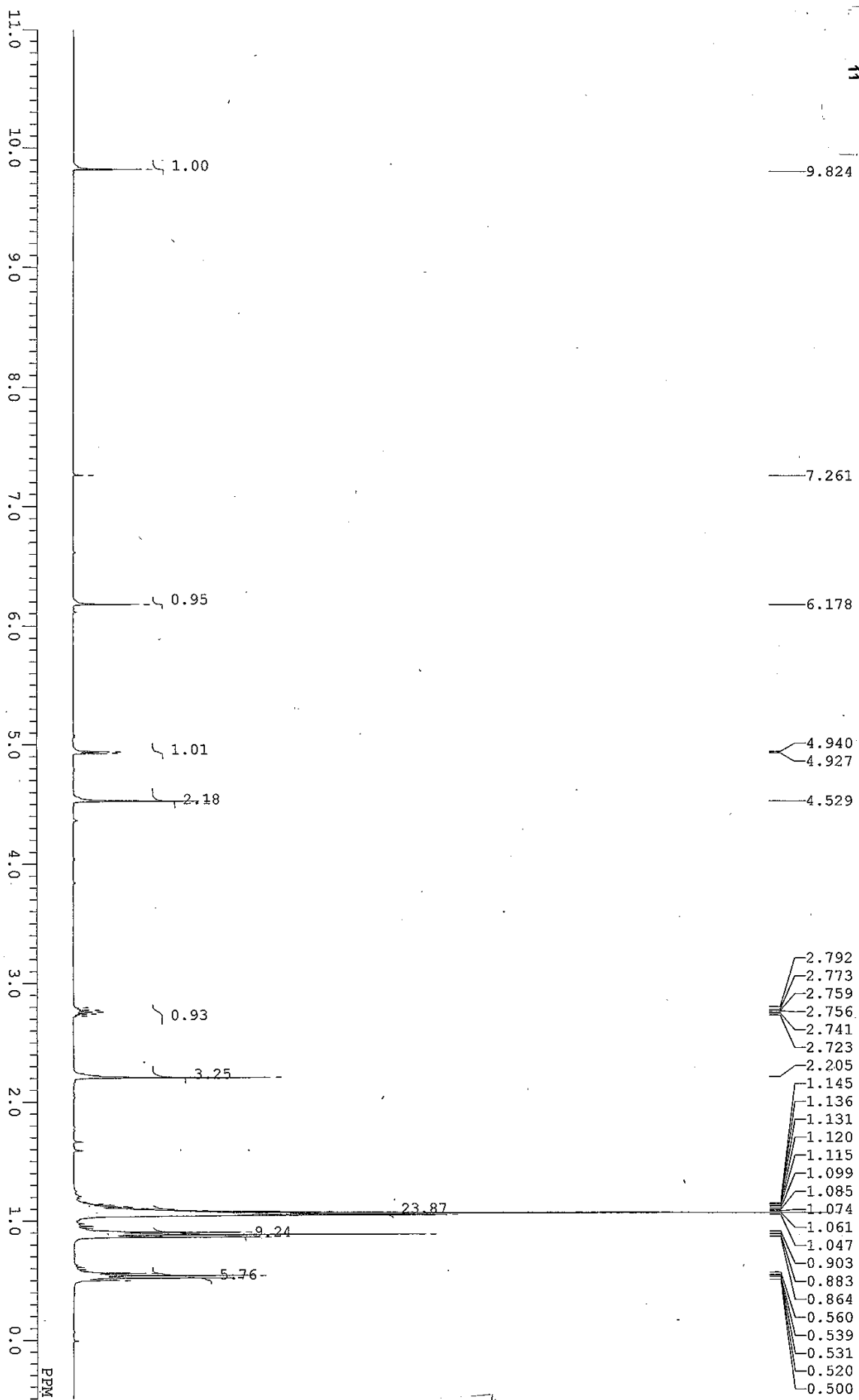
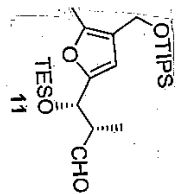


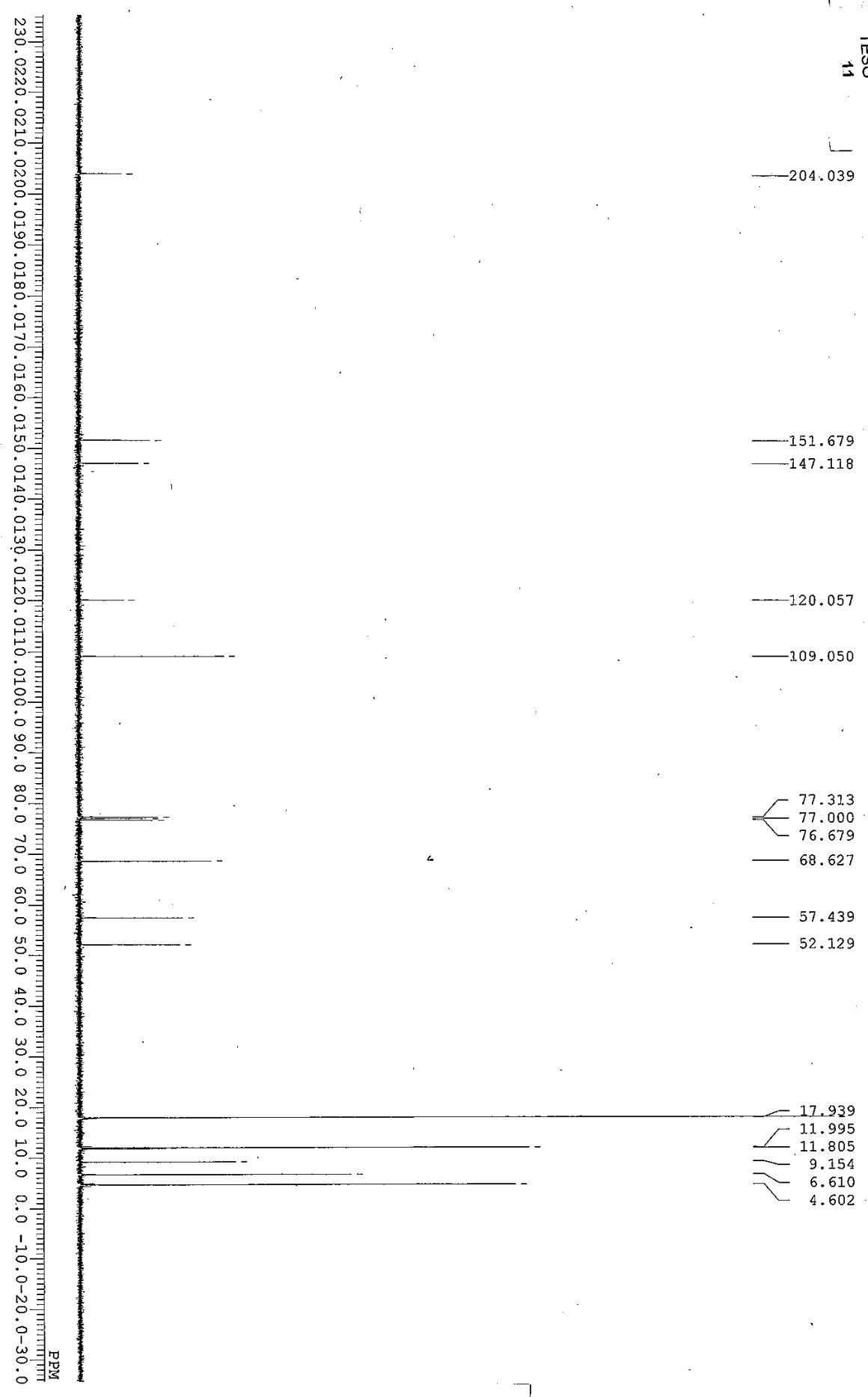
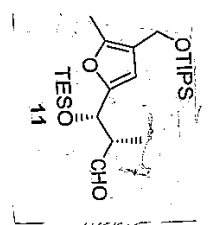




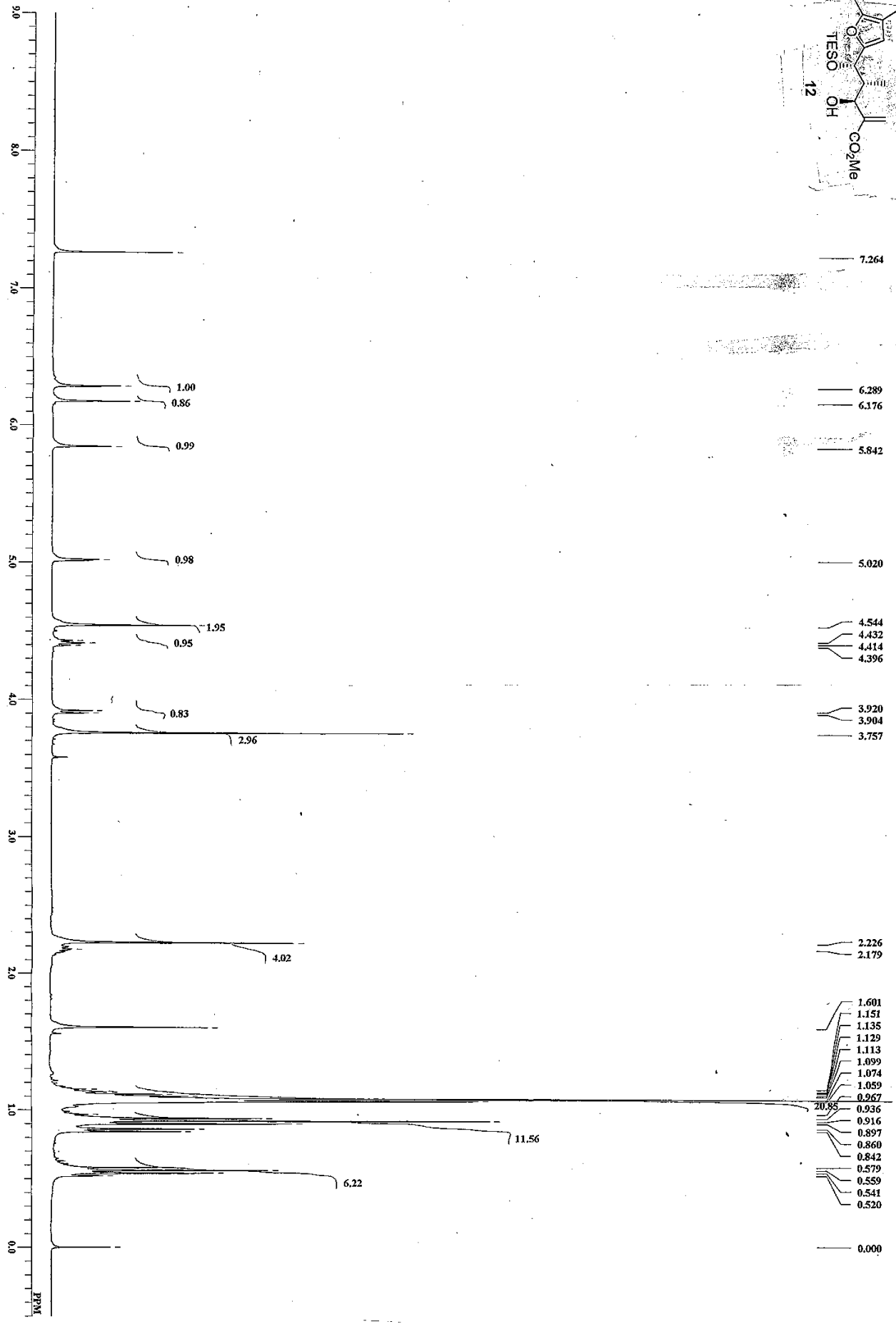
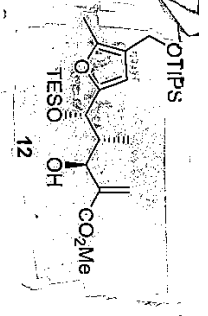


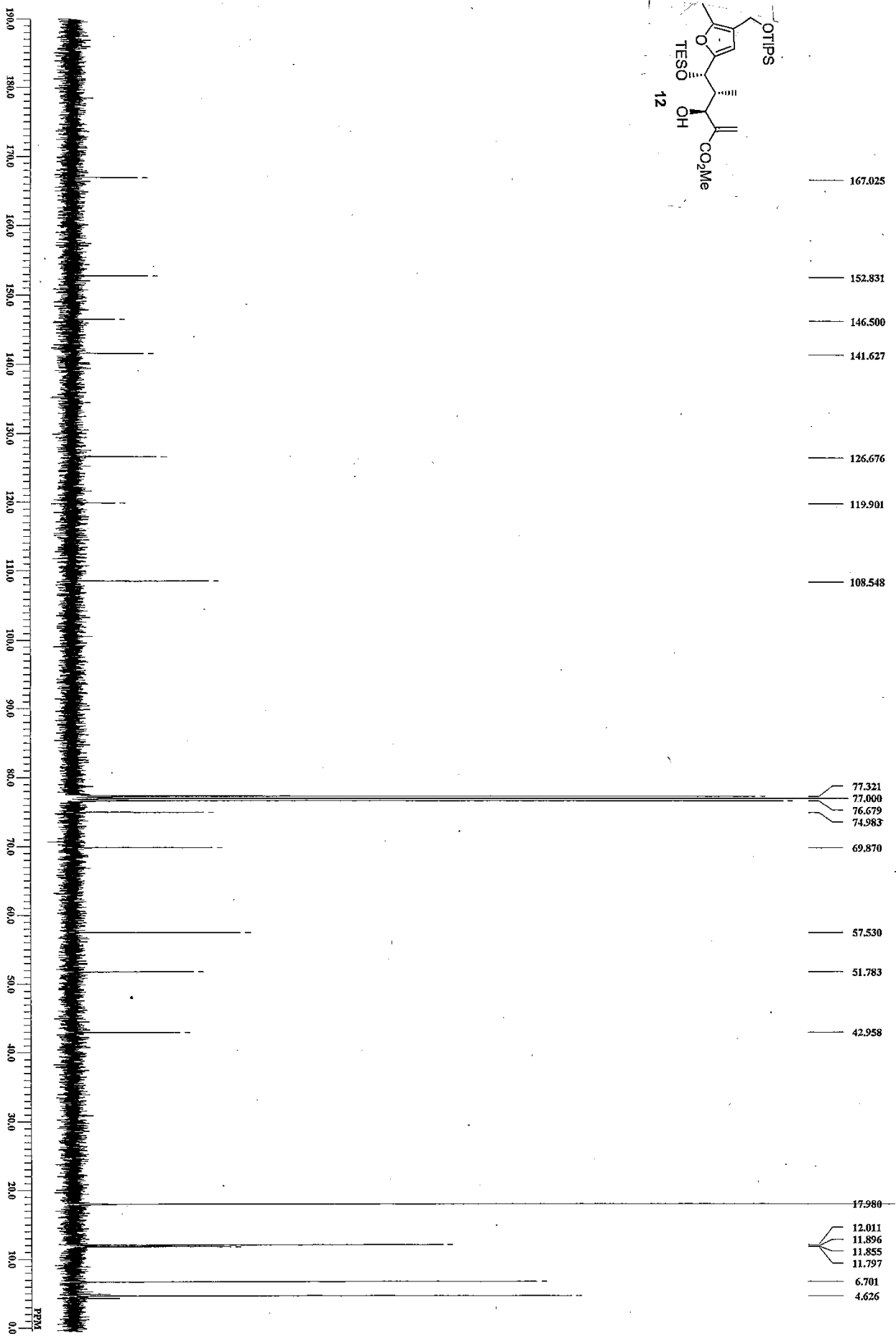
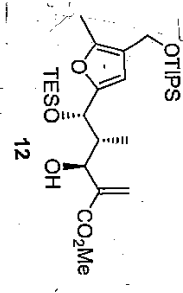




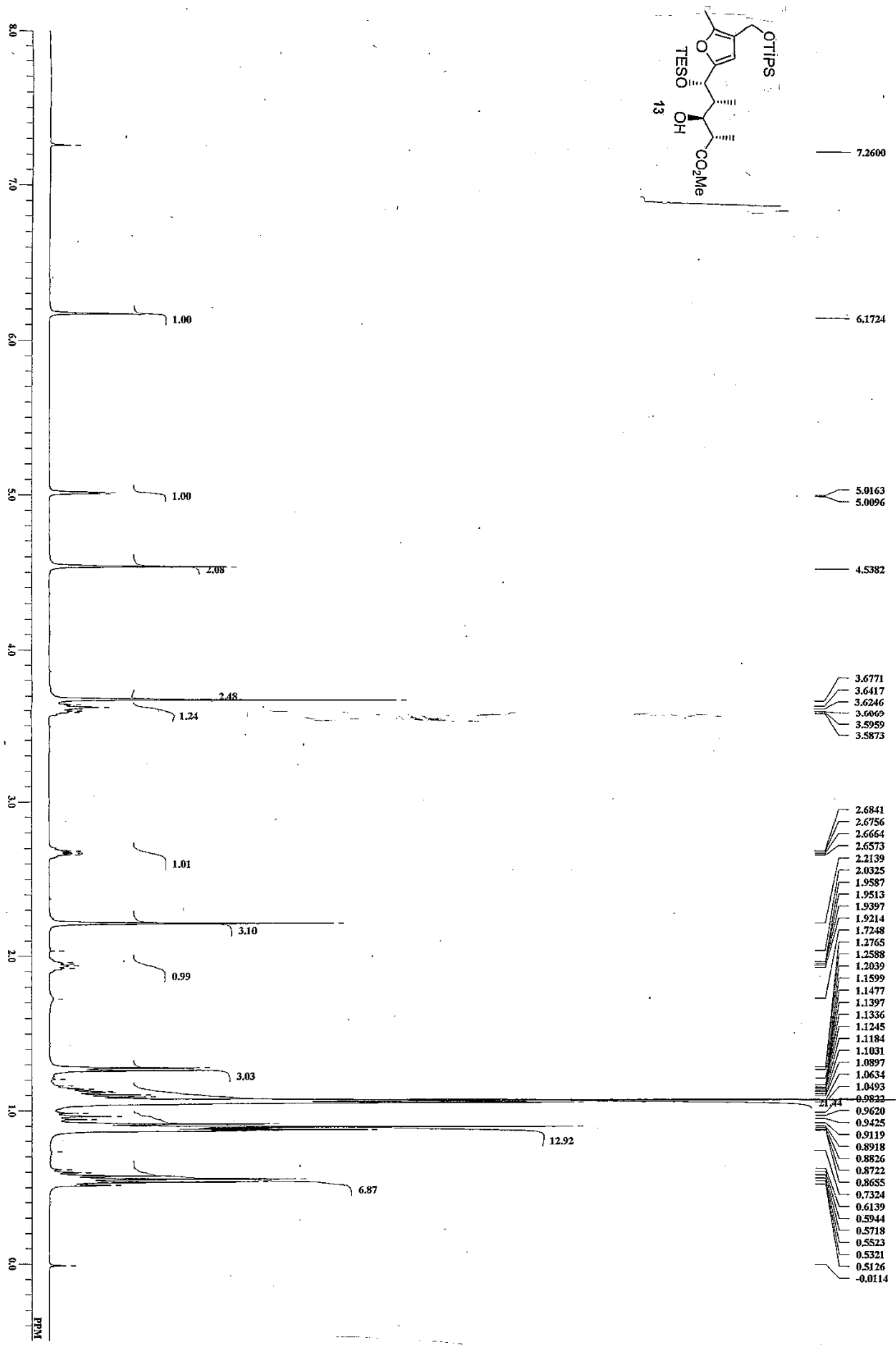


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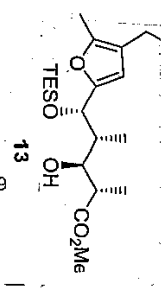
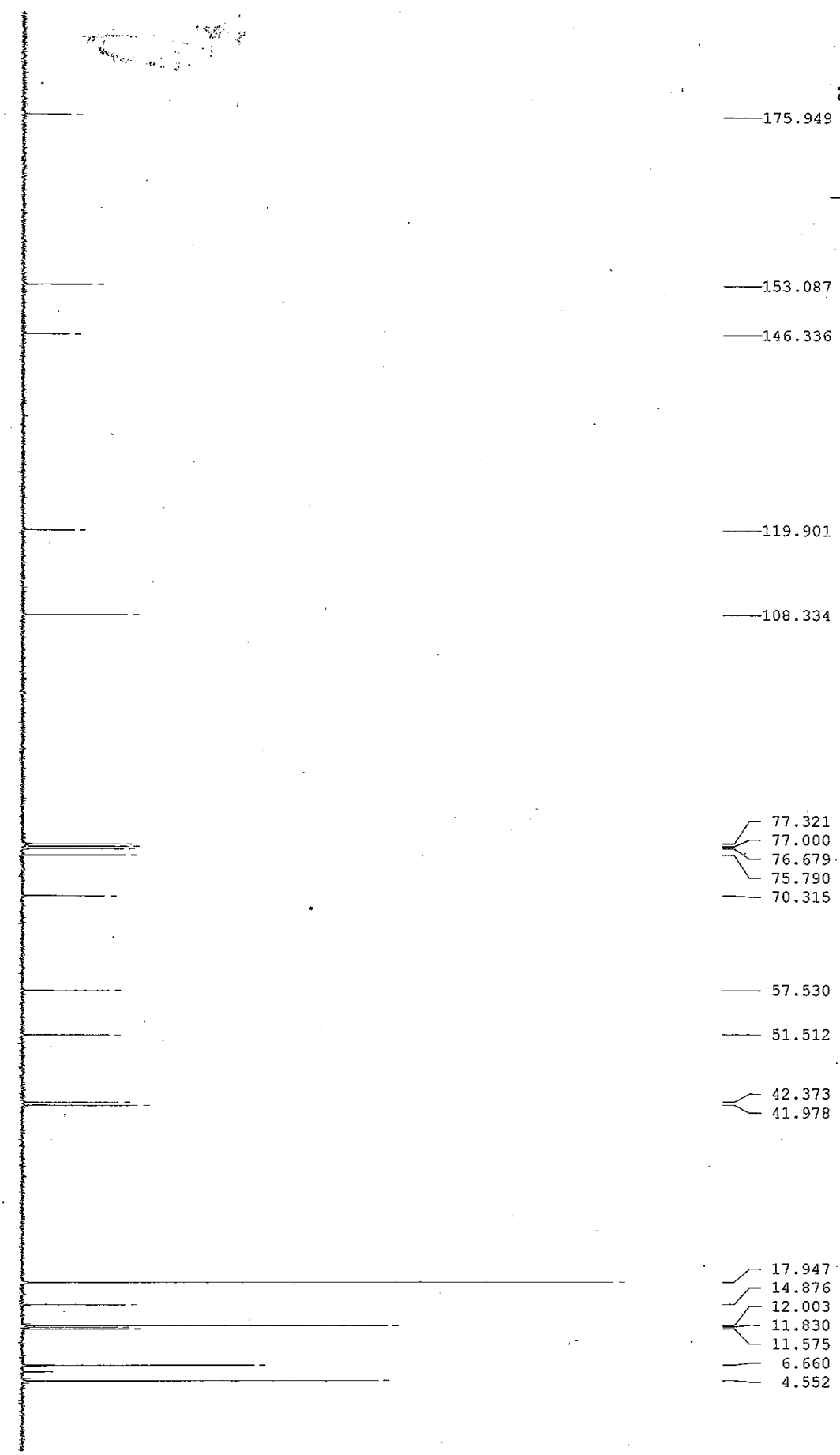


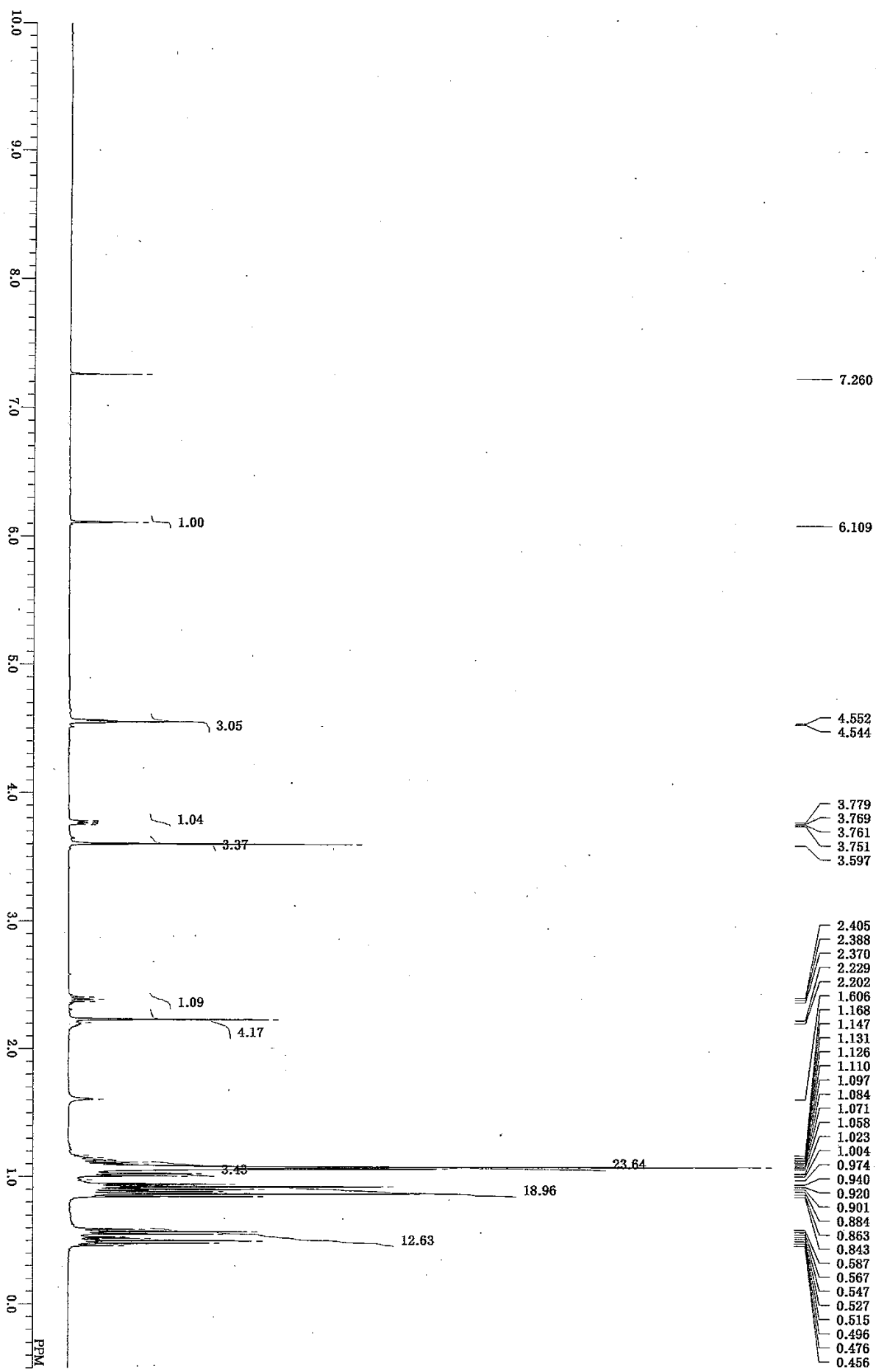
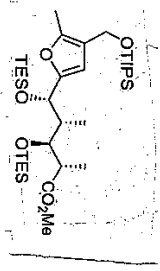
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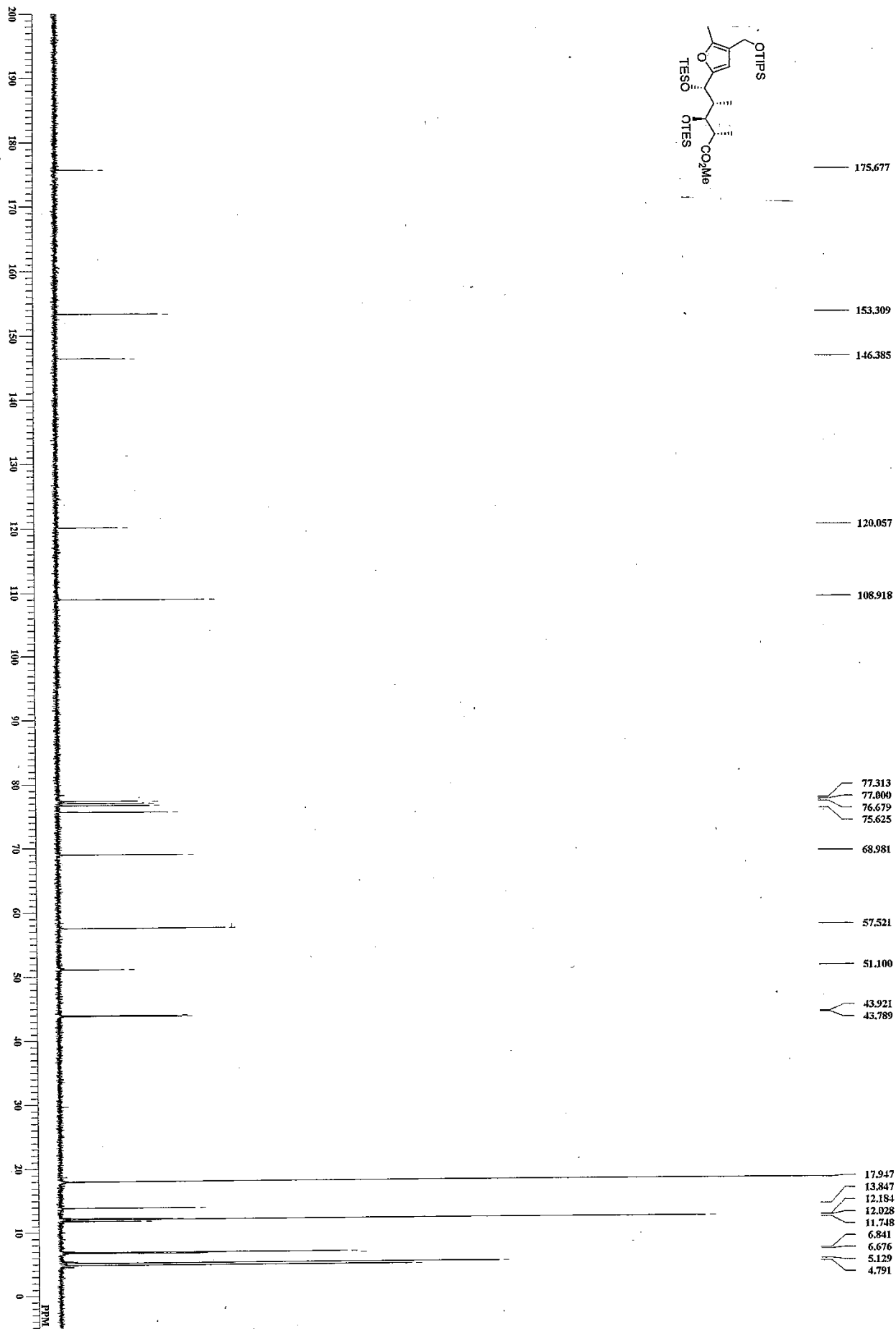


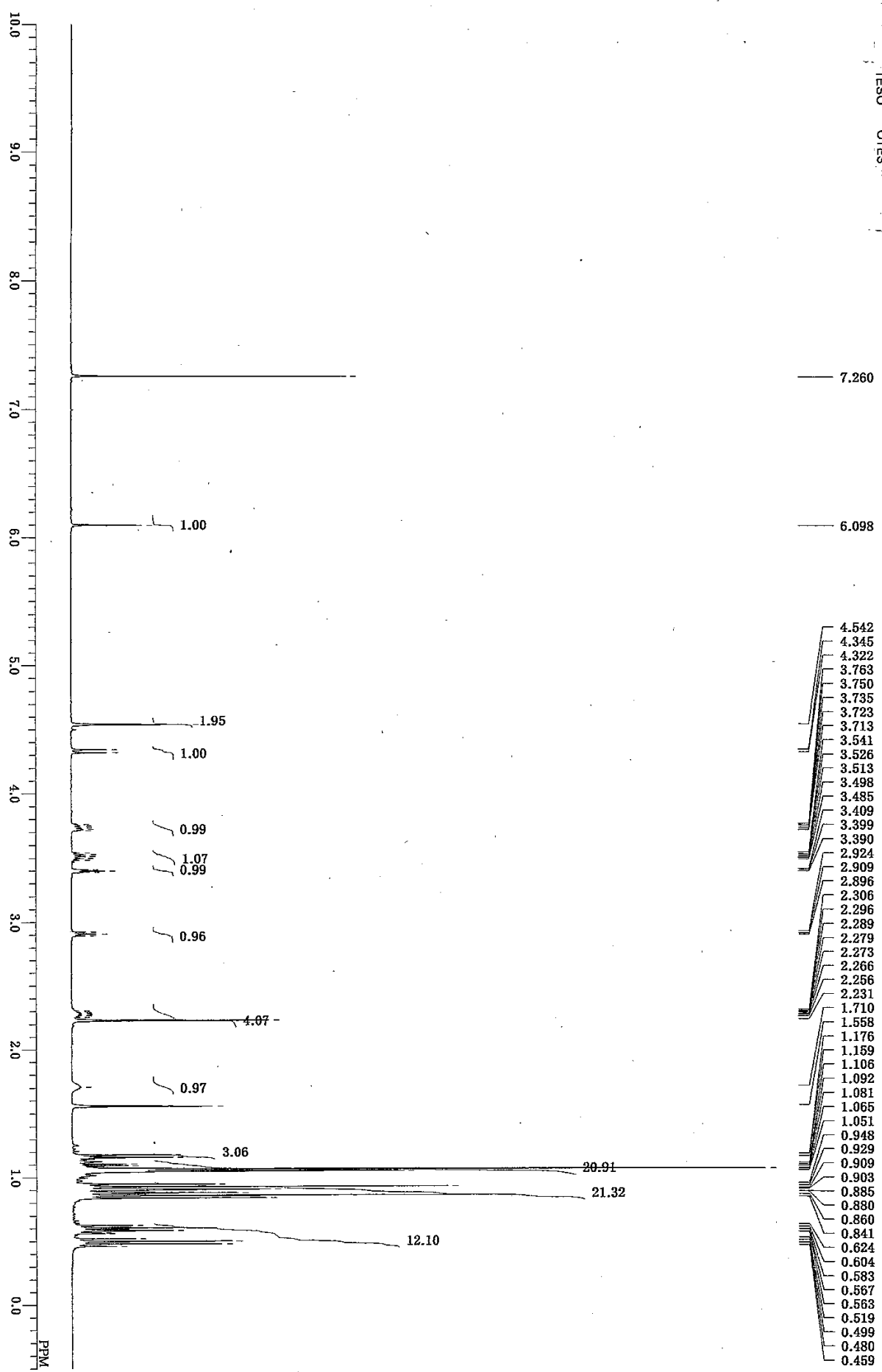
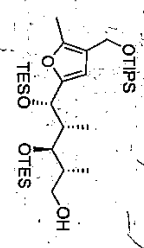
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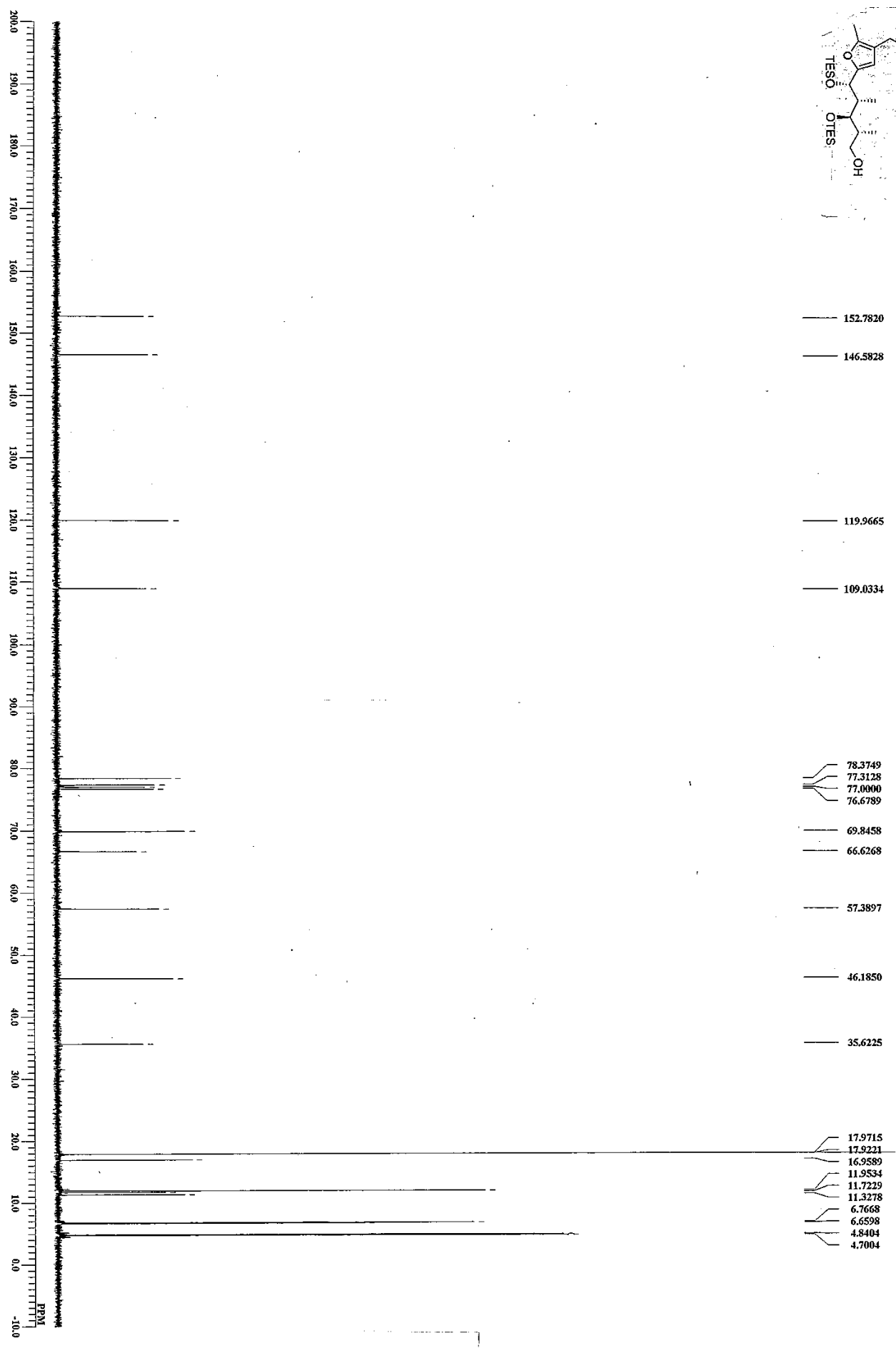
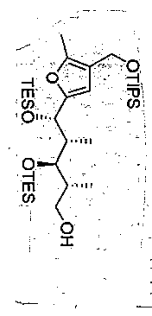
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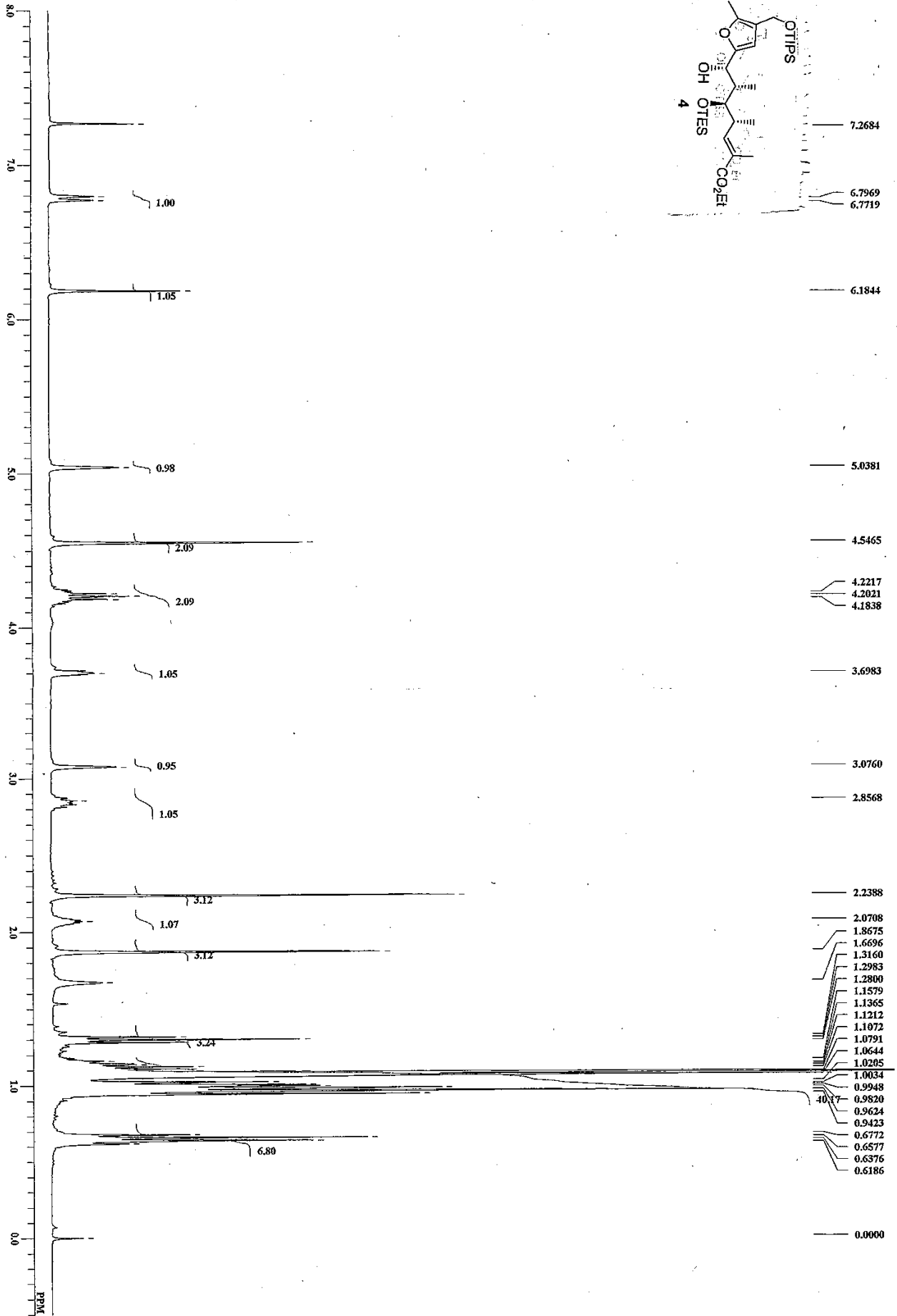




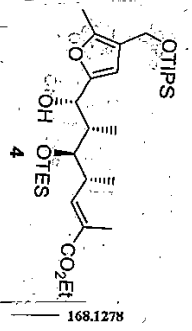
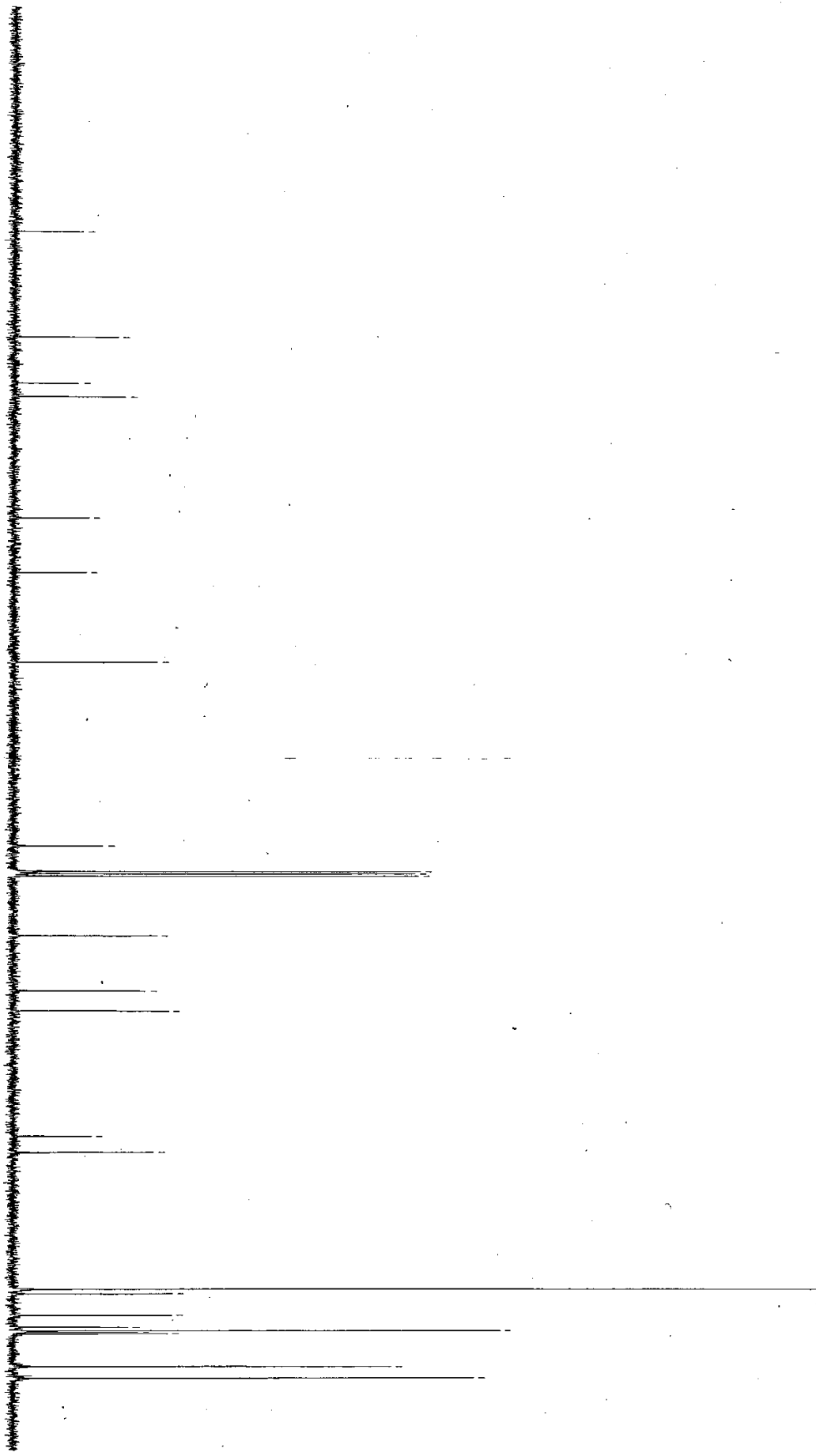




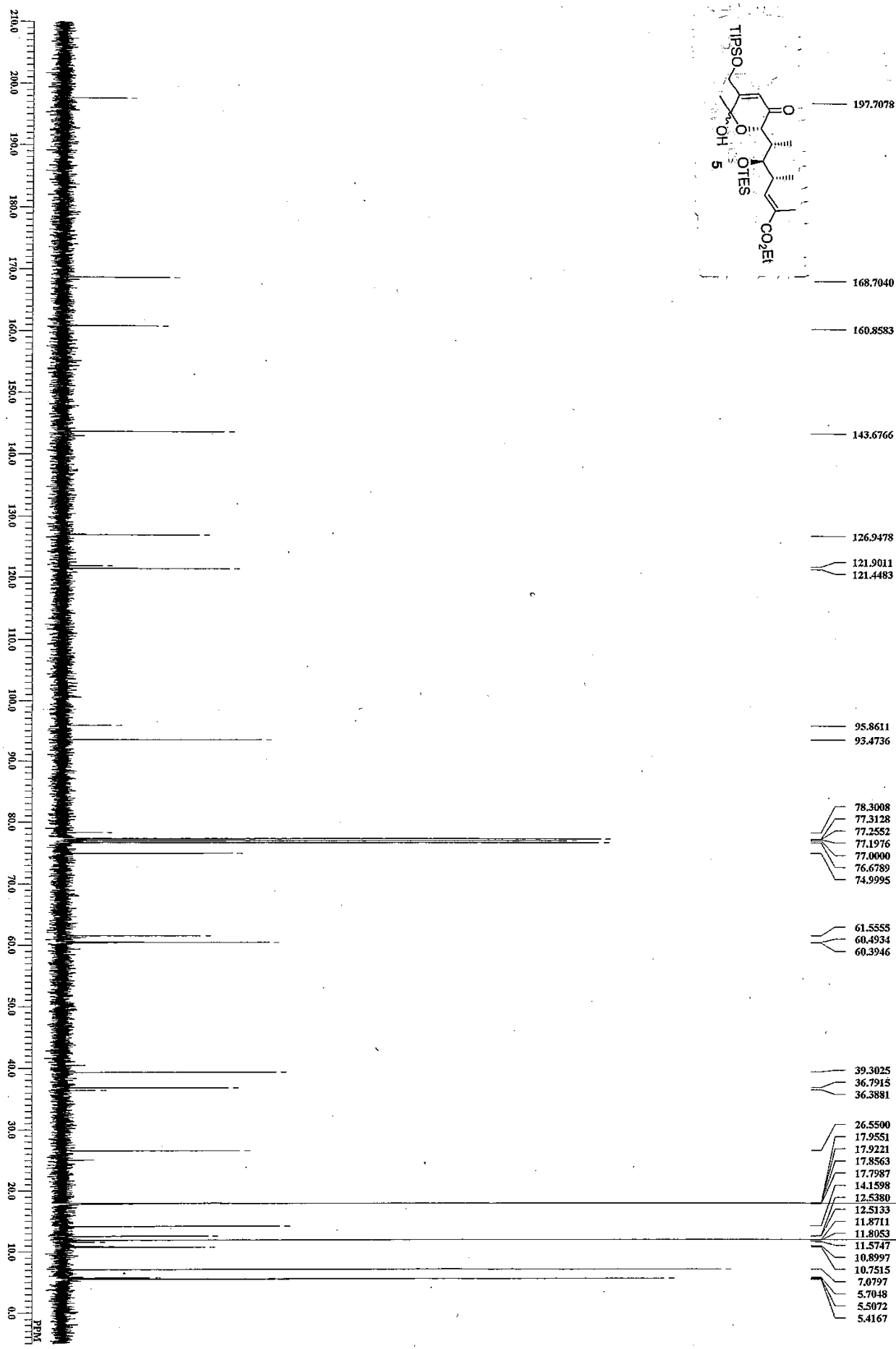


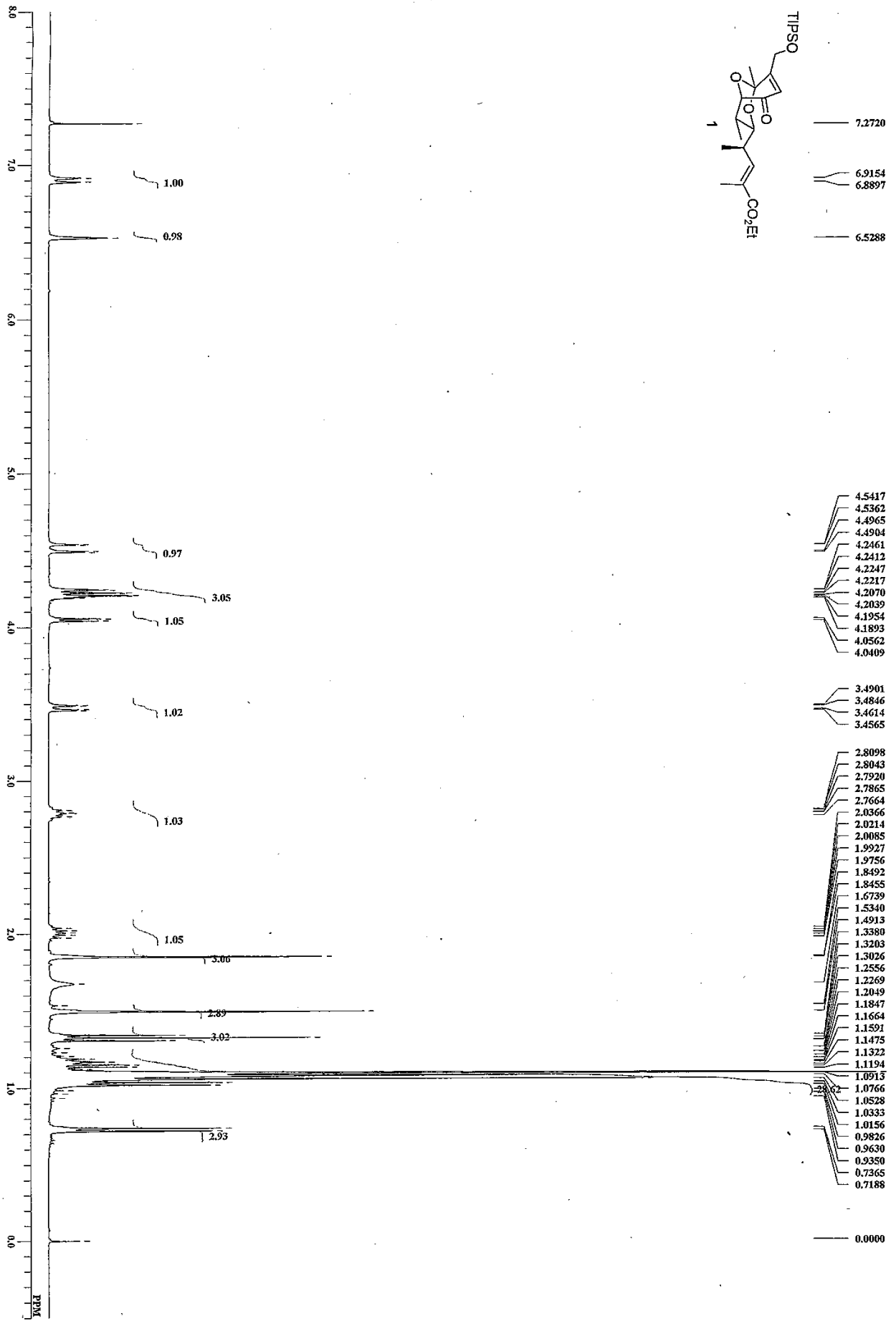


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130.0
120.0
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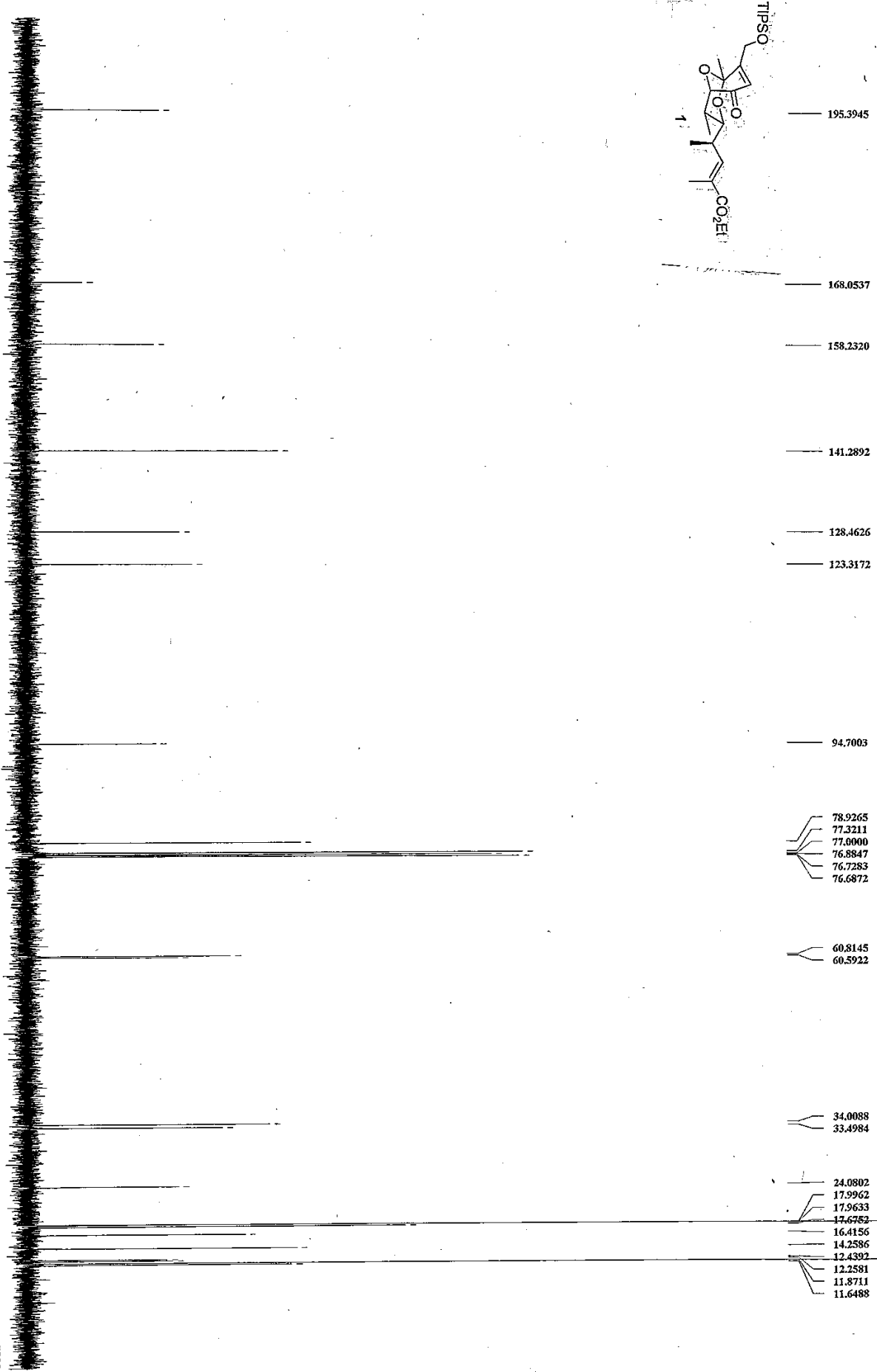


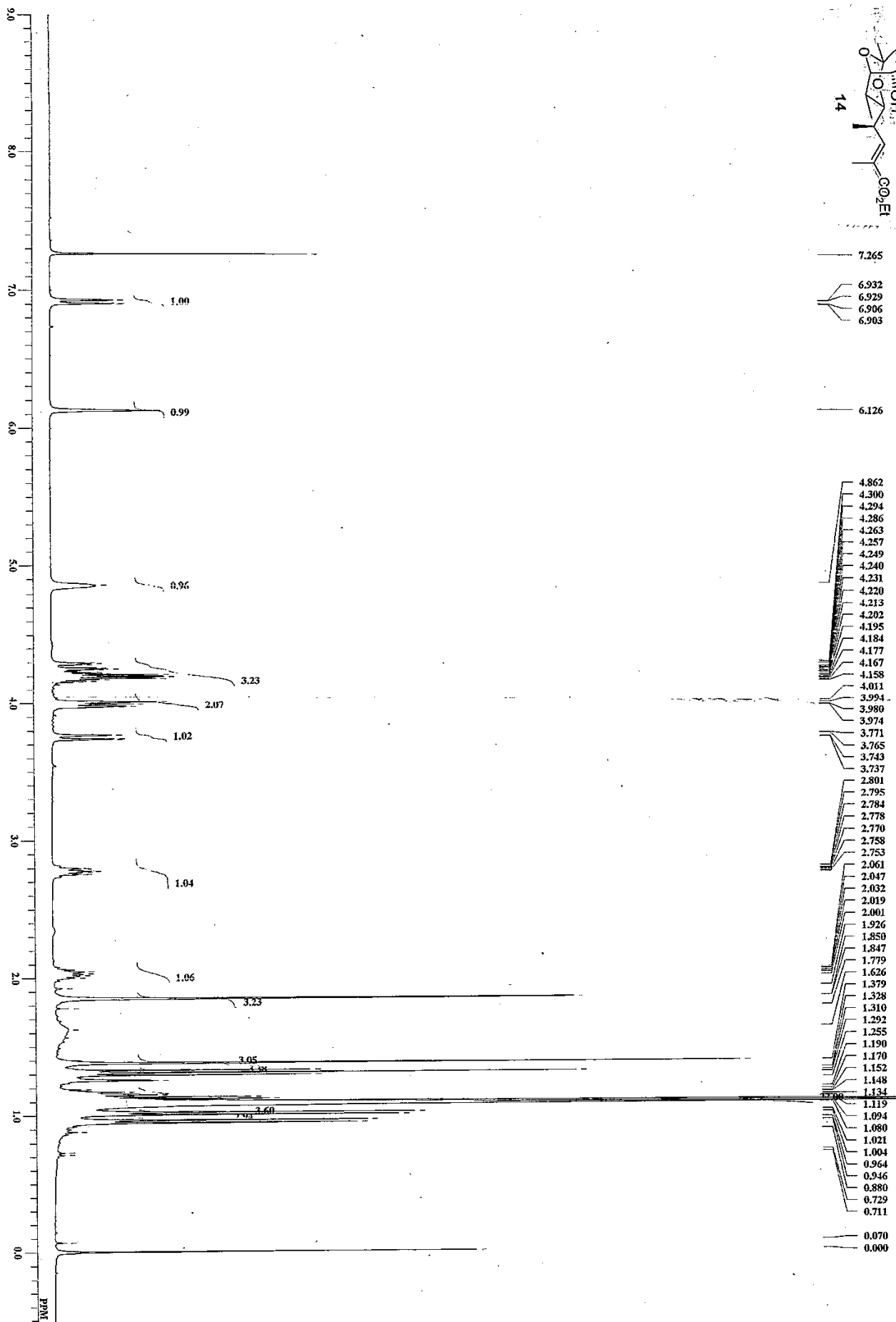
- 168.1278
- 153.2348
- 146.6404
- 144.7633
- 127.6146
- 119.8512
- 107.2140
- 80.9352
- 77.3211
- 77.0000
- 76.6872
- 68.2569
- 60.4276
- 57.5626
- 39.7306
- 37.4666
- 18.0045
- 17.3212
- 14.2421
- 12.5627
- 12.0111
- 11.8464
- 11.6077
- 6.9480
- 5.2850

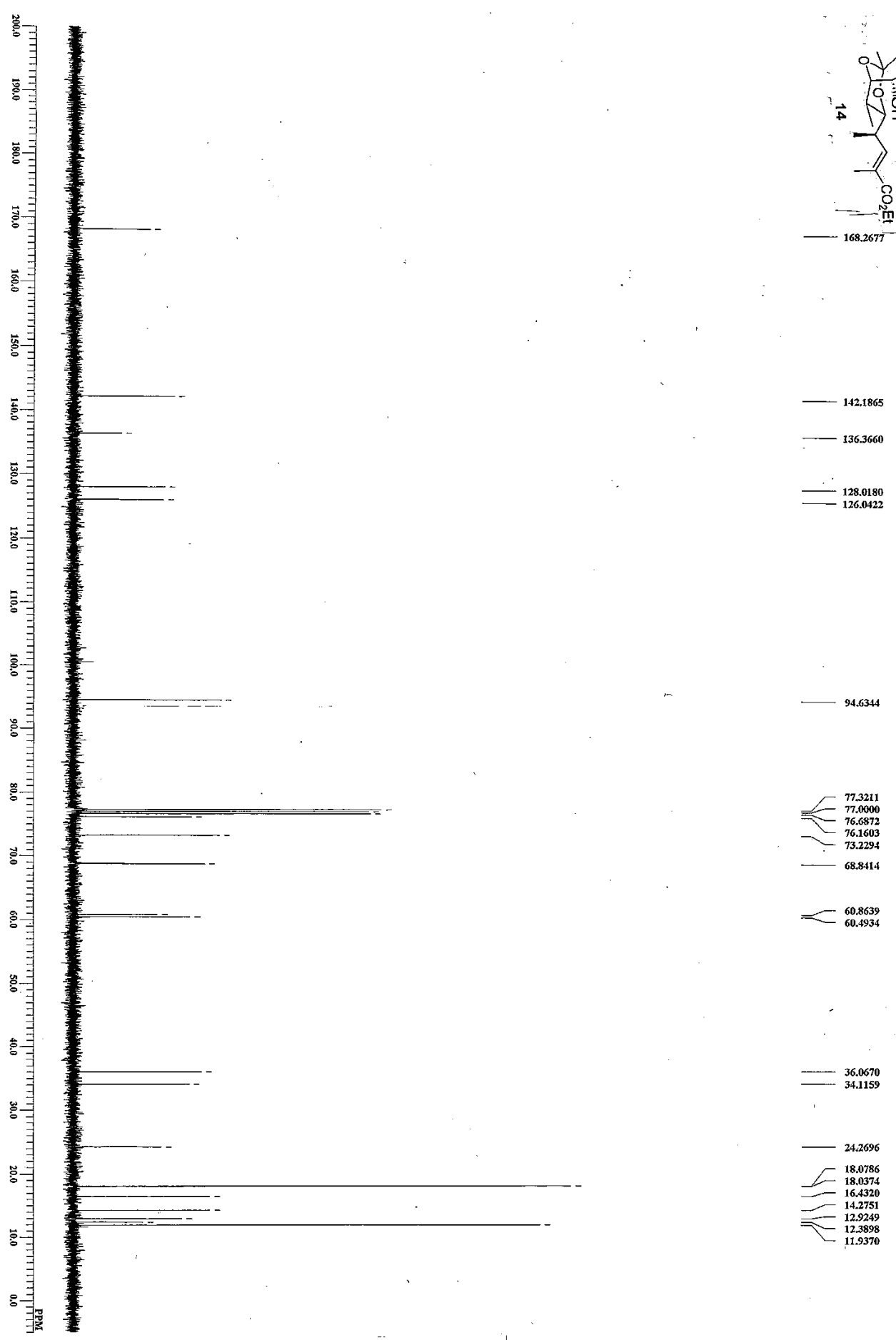
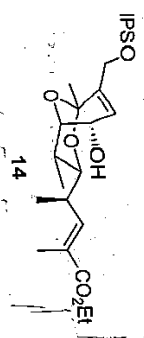


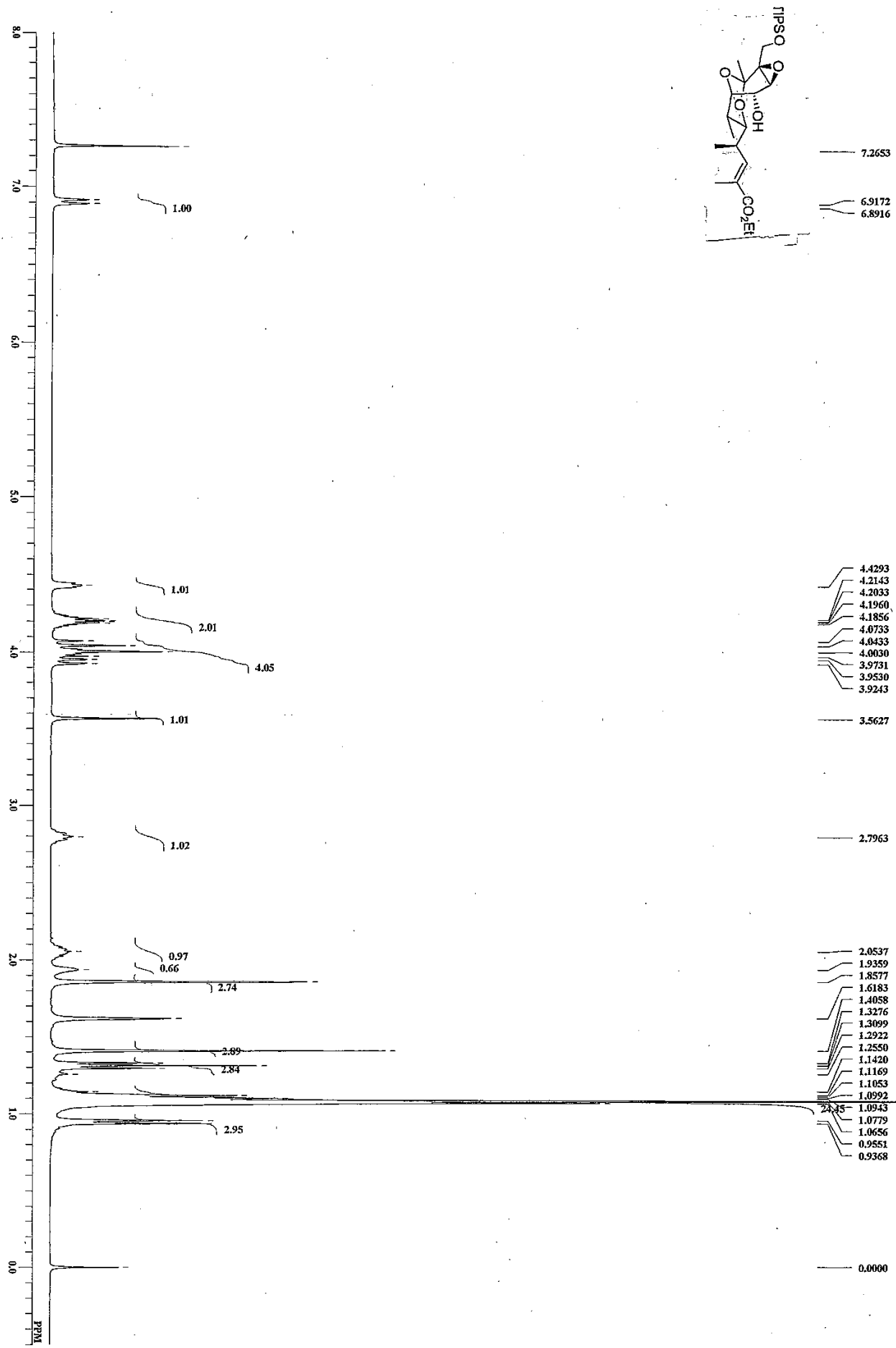


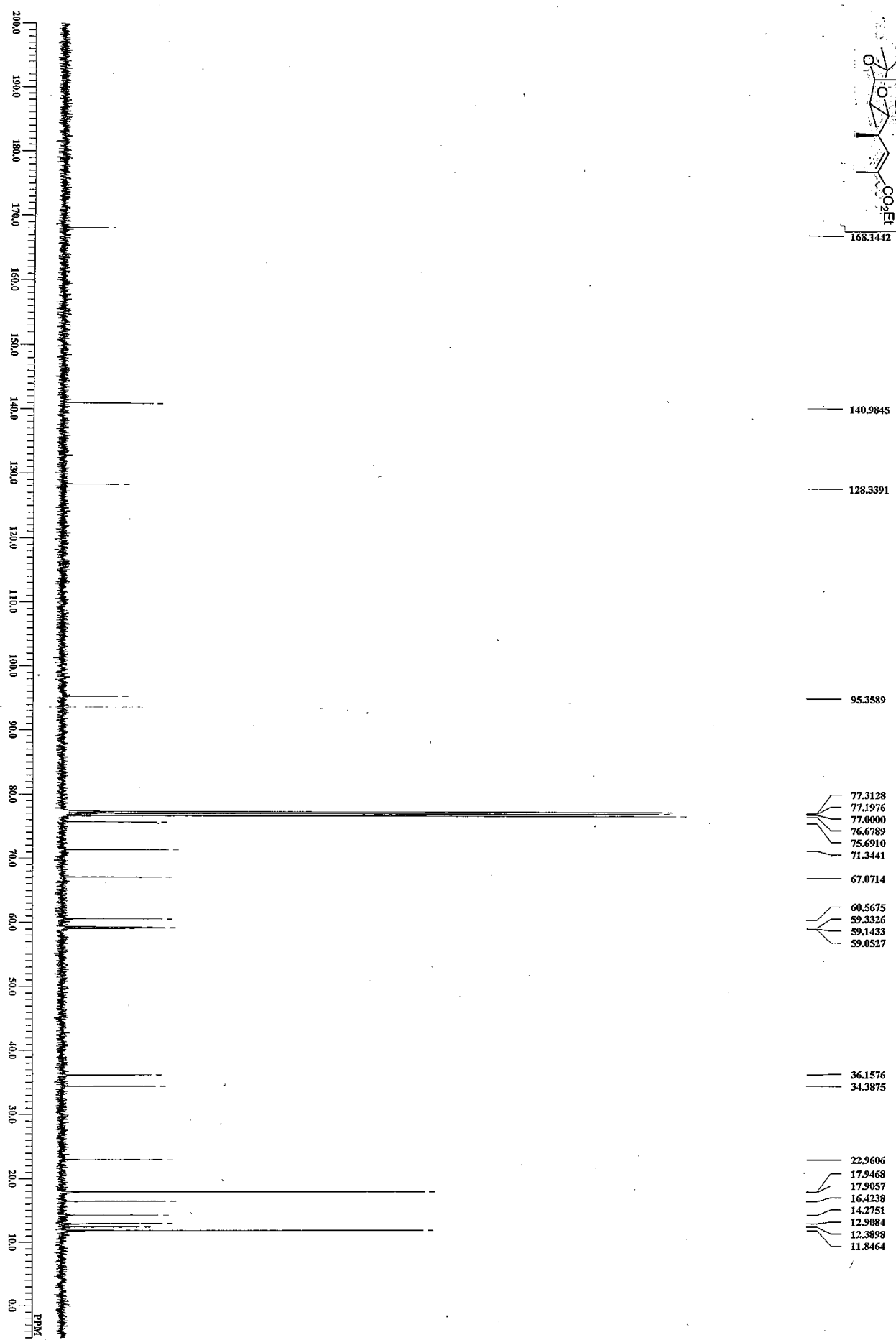
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PPM

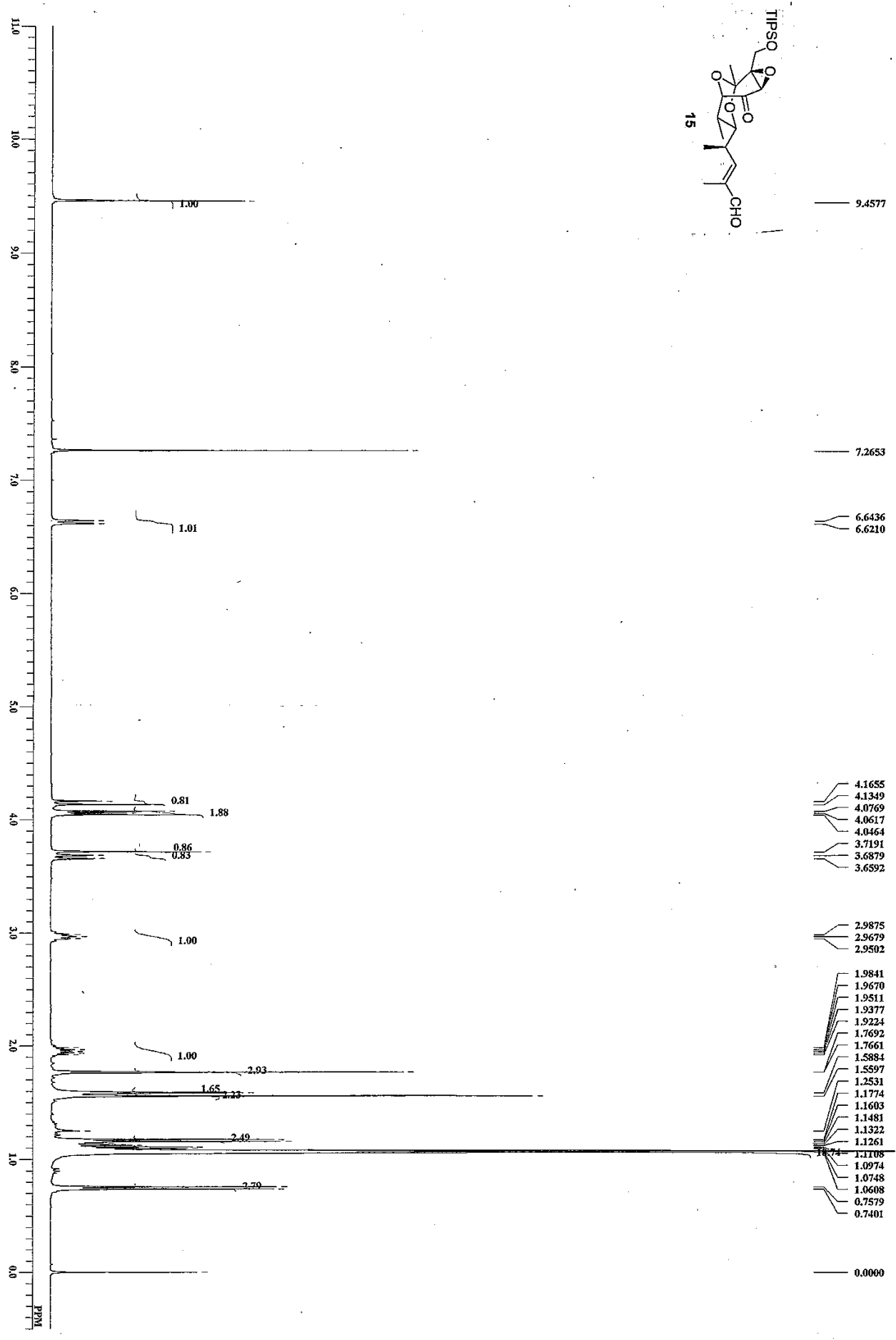
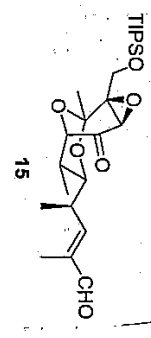


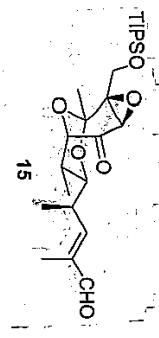




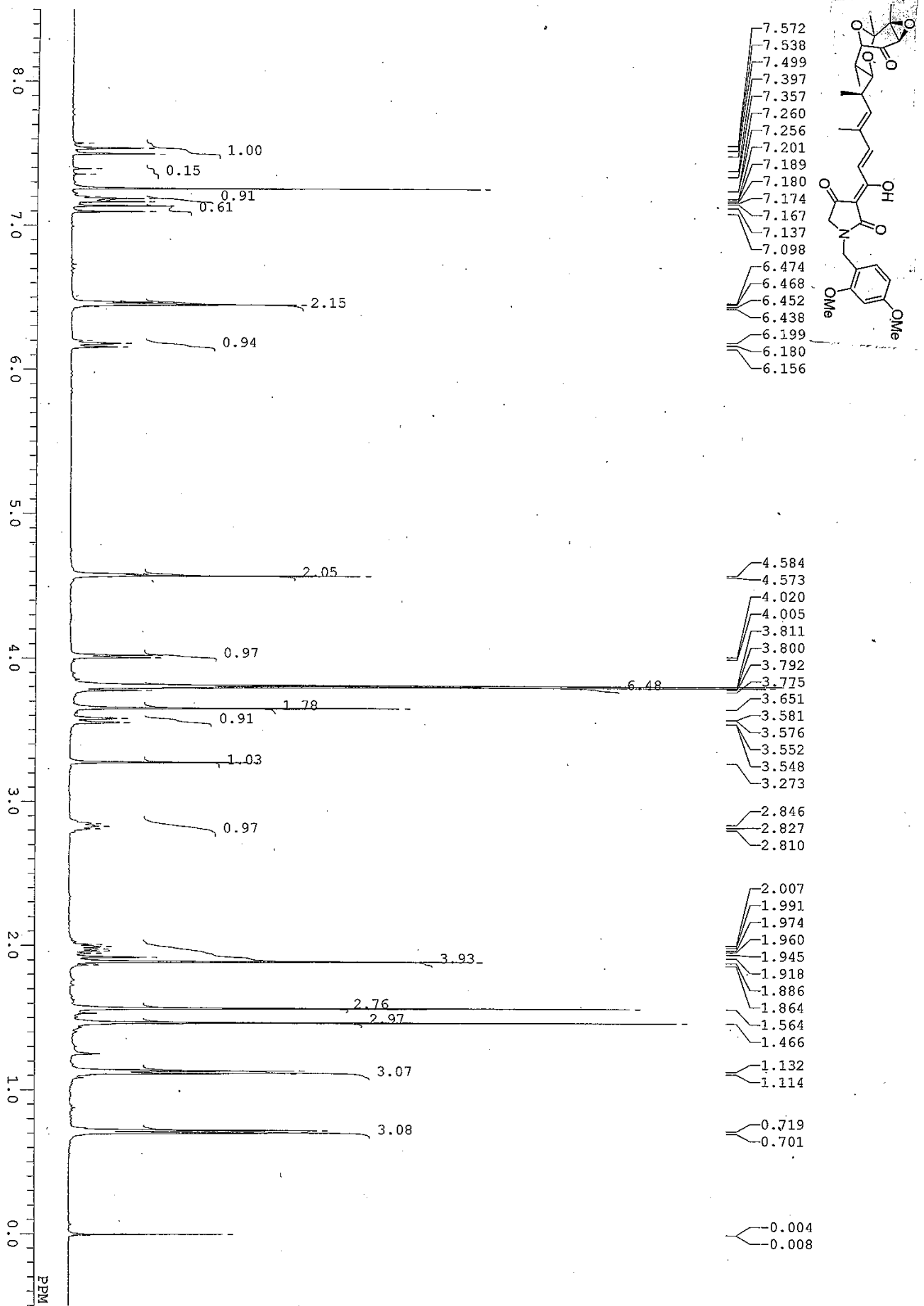


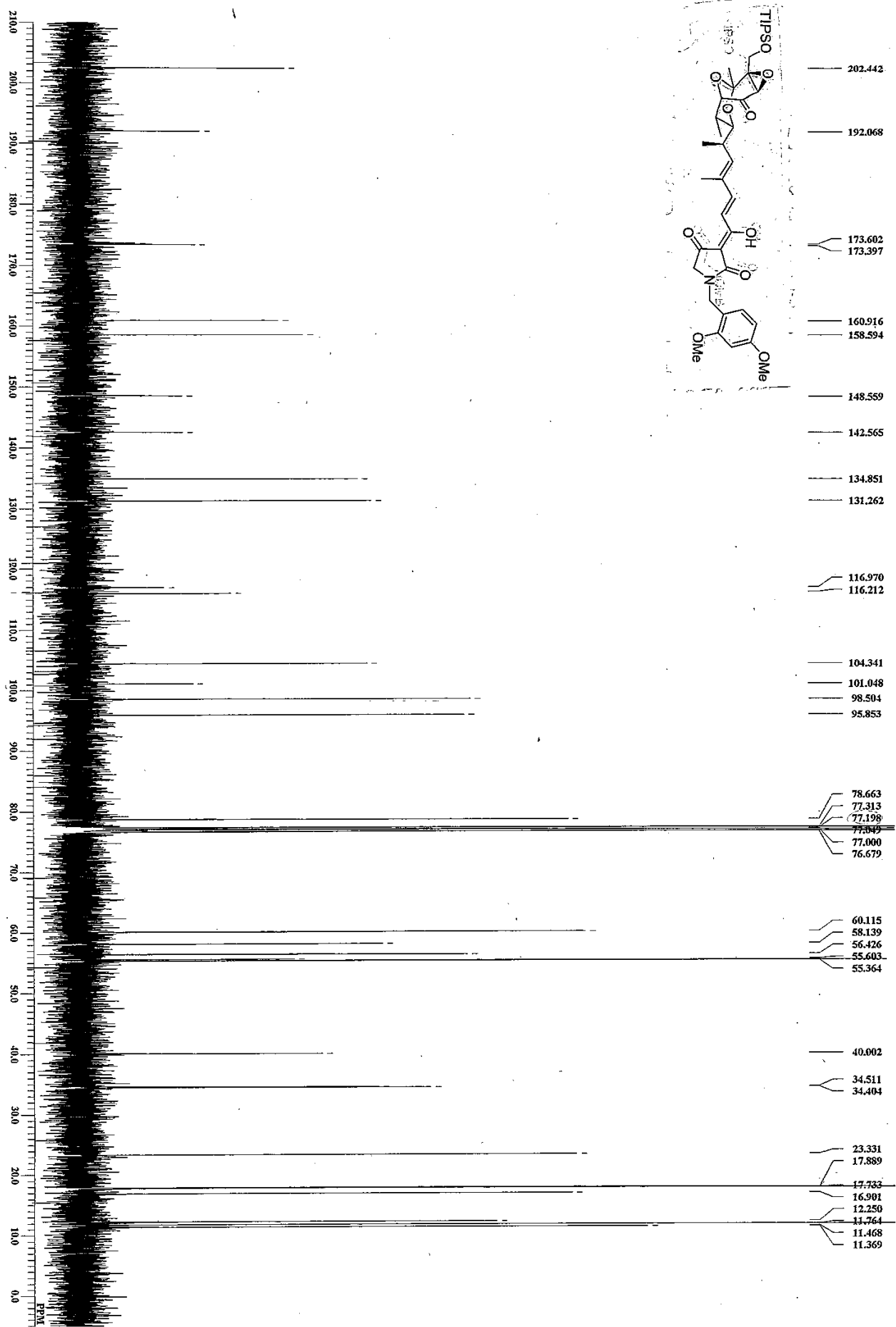


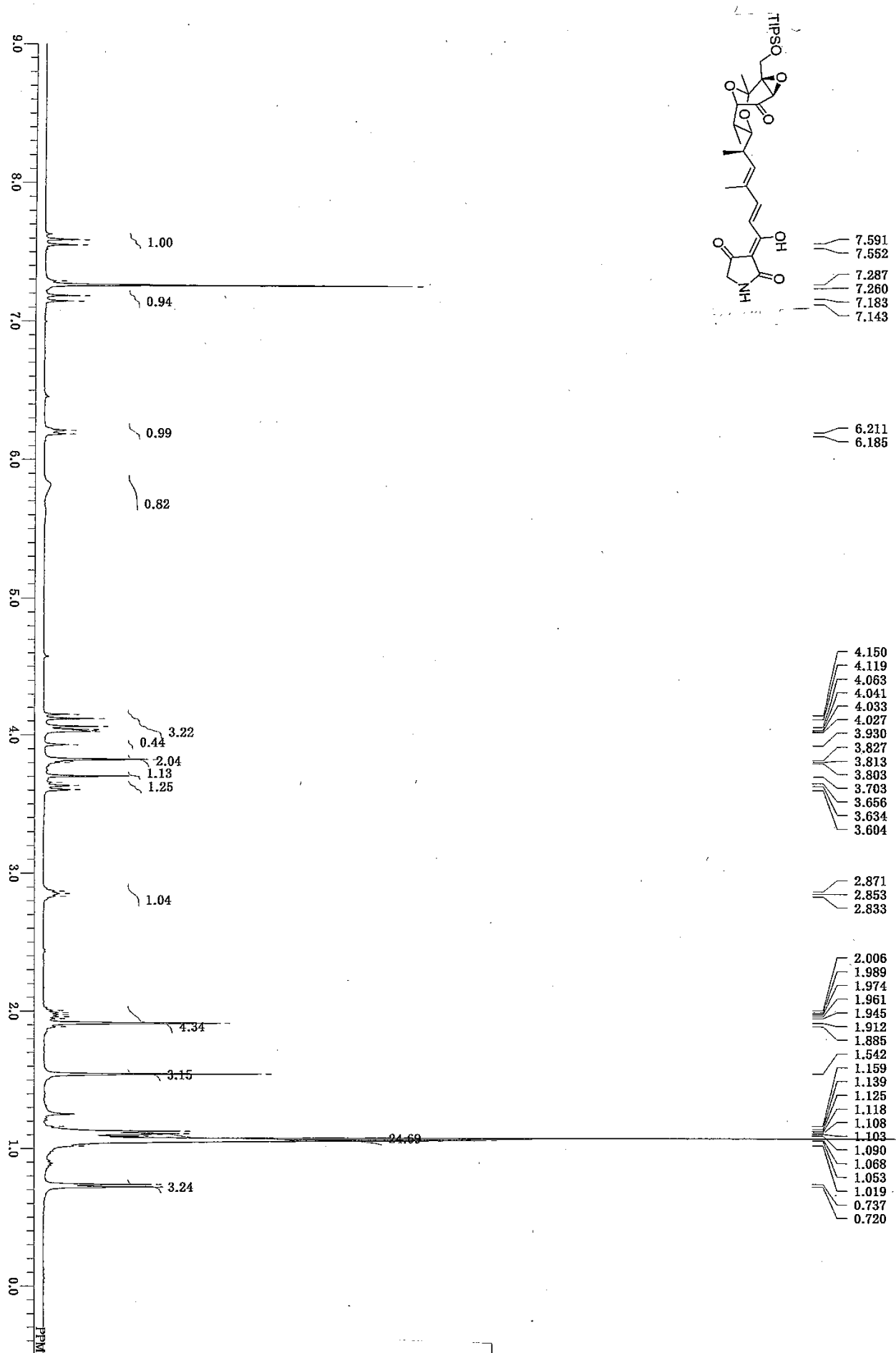




- 202.178
- 195.049
- 151.975
- 140.021
- 96.018
- 78.581
- 77.321
- 77.000
- 76.737
- 76.687
- 60.131
- 58.213
- 56.484
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- 34.371
- 23.372
- 17.914
- 17.856
- 16.391
- 11.789
- 11.435
- 9.319

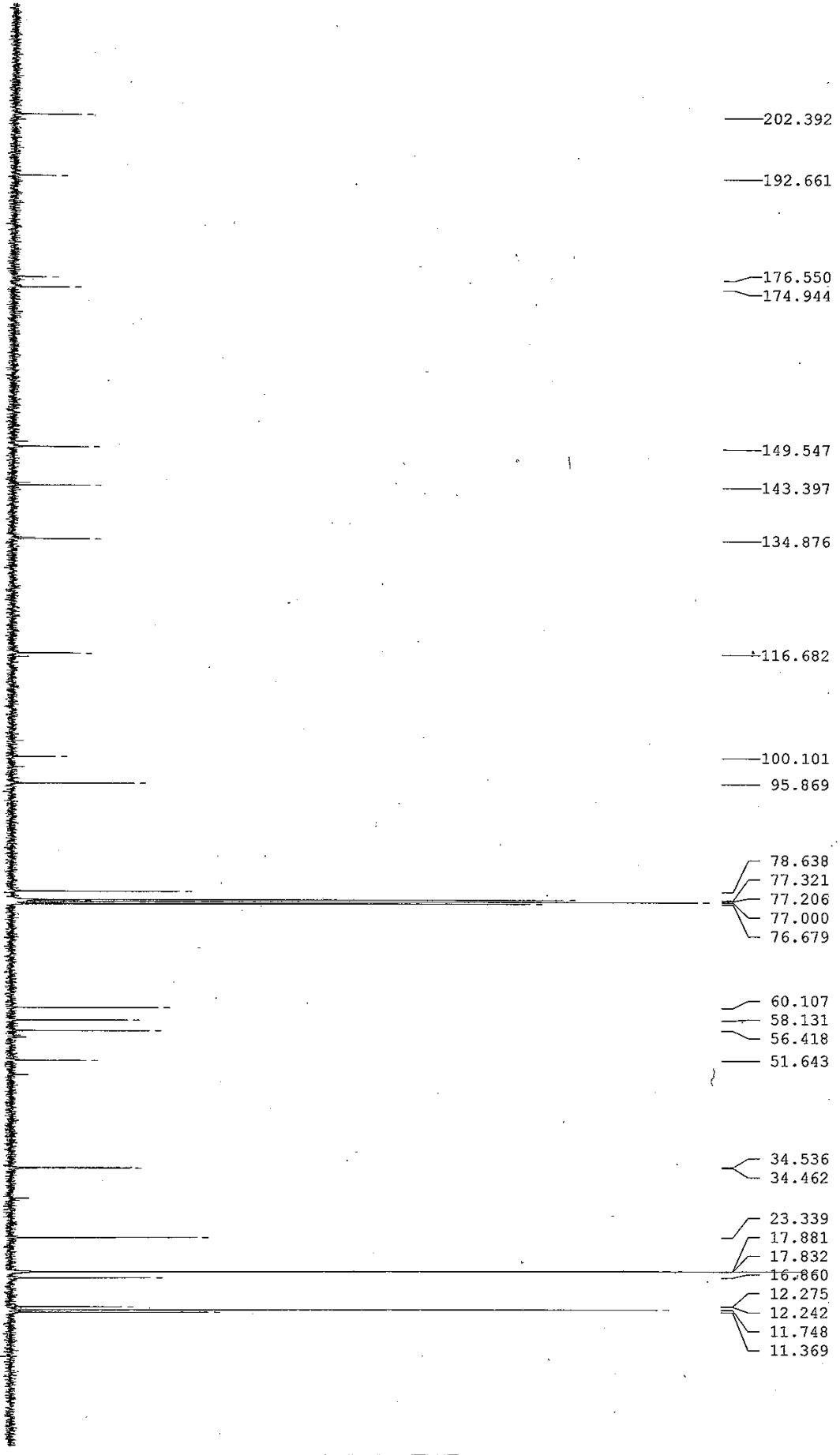






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PPM



- 202.392
- 192.661
- 176.550
- 174.944

- 149.547
- 143.397
- 134.876

- 116.682

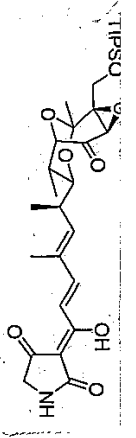
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- 95.869

- 78.638
- 77.321
- 77.206
- 77.000
- 76.679

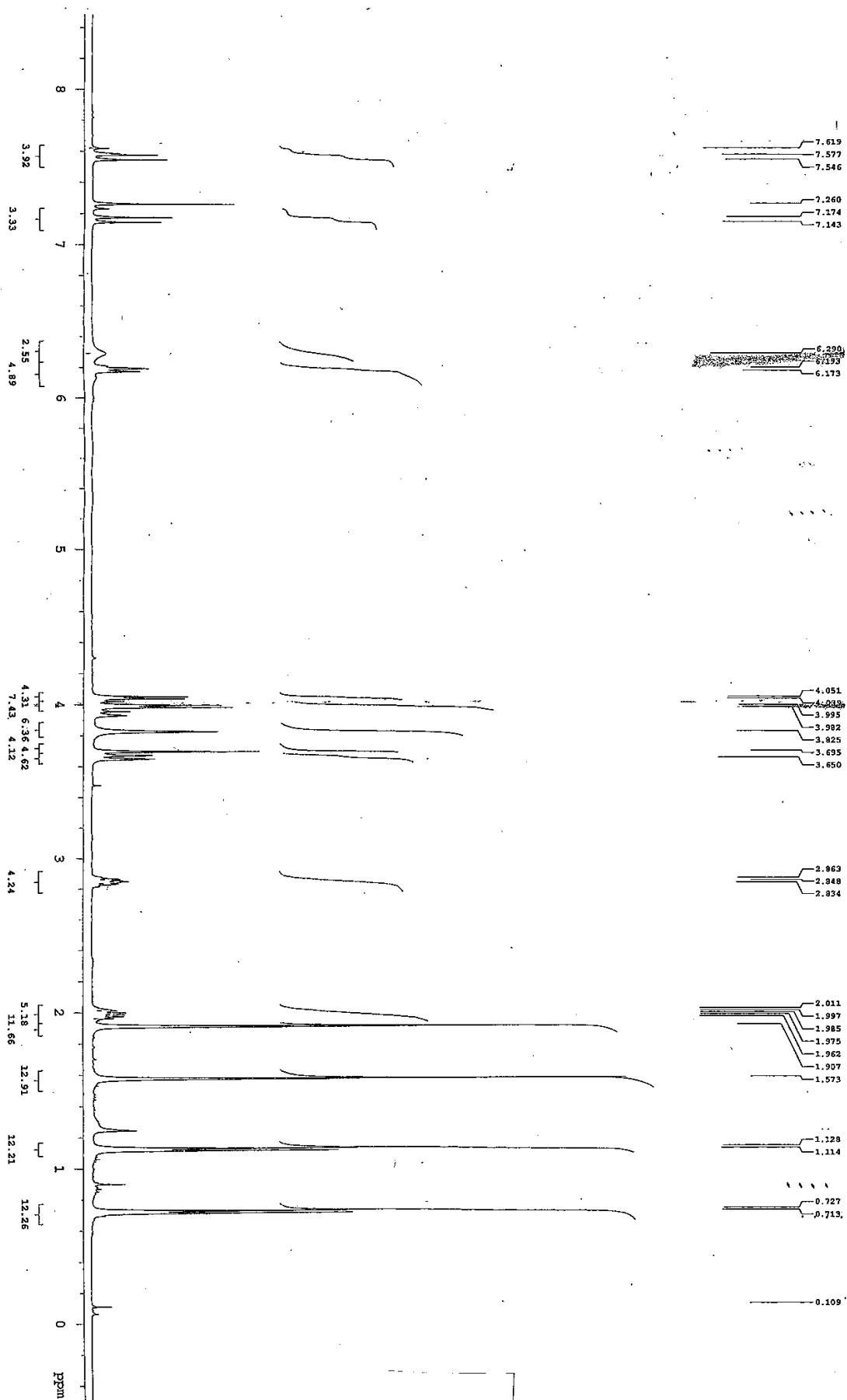
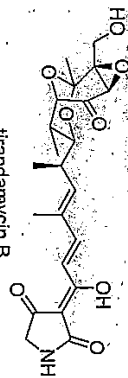
- 60.107
- 58.131
- 56.418
- 51.643

- 34.536
- 34.462

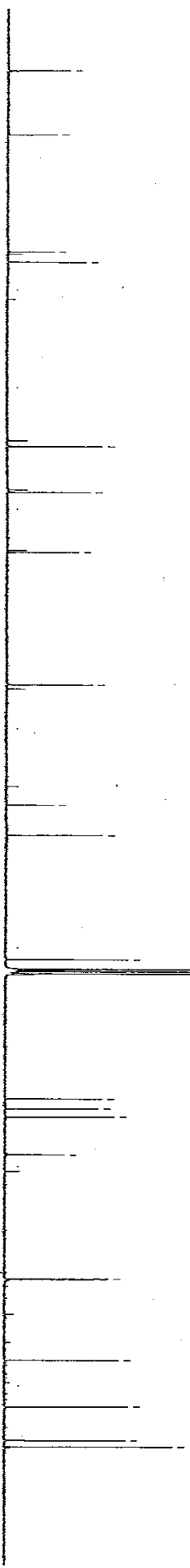
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- 17.881
- 17.832
- 16.860
- 12.275
- 12.242
- 11.748
- 11.369



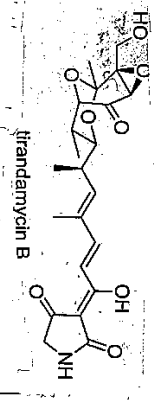
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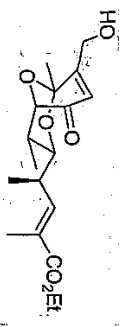
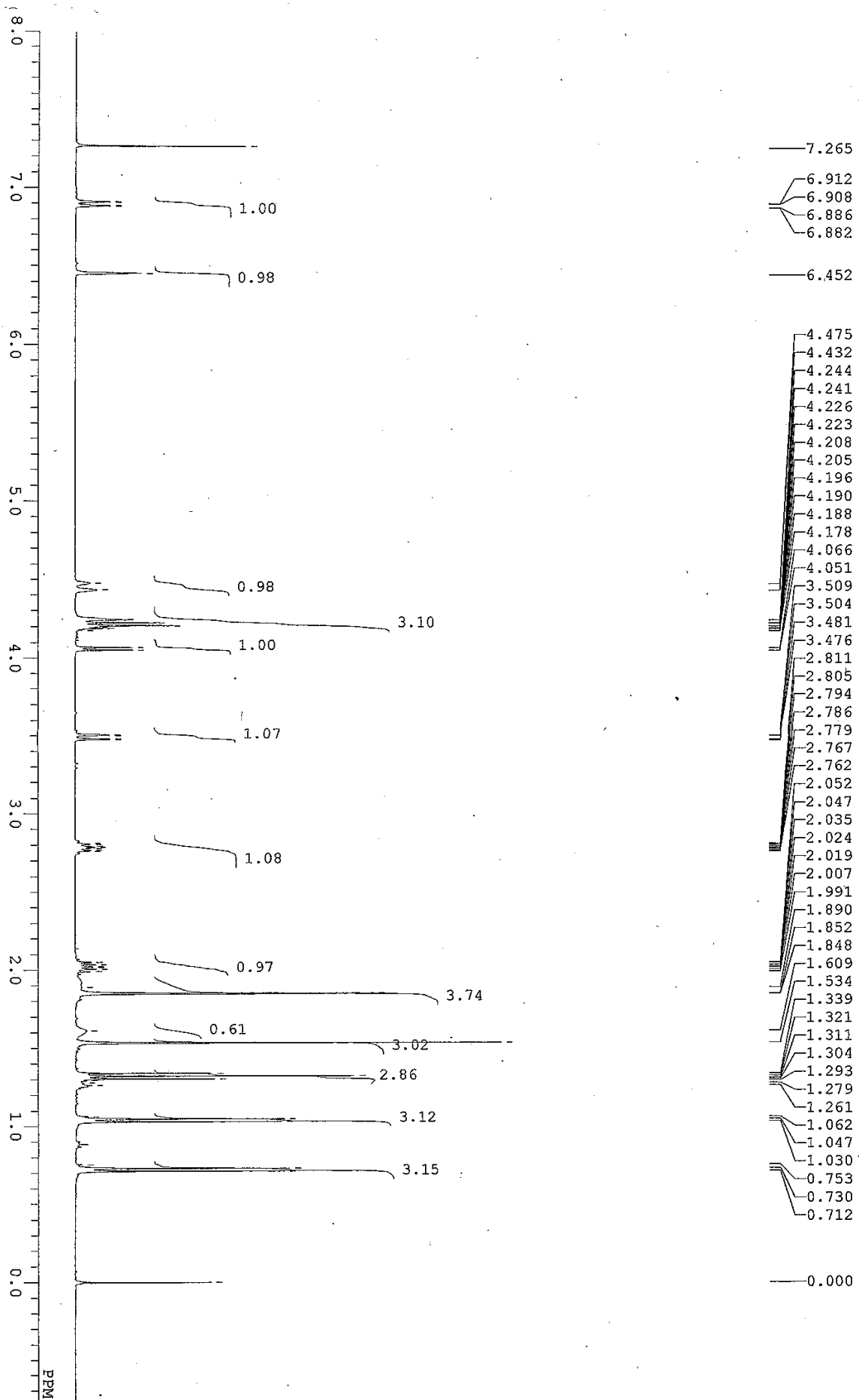


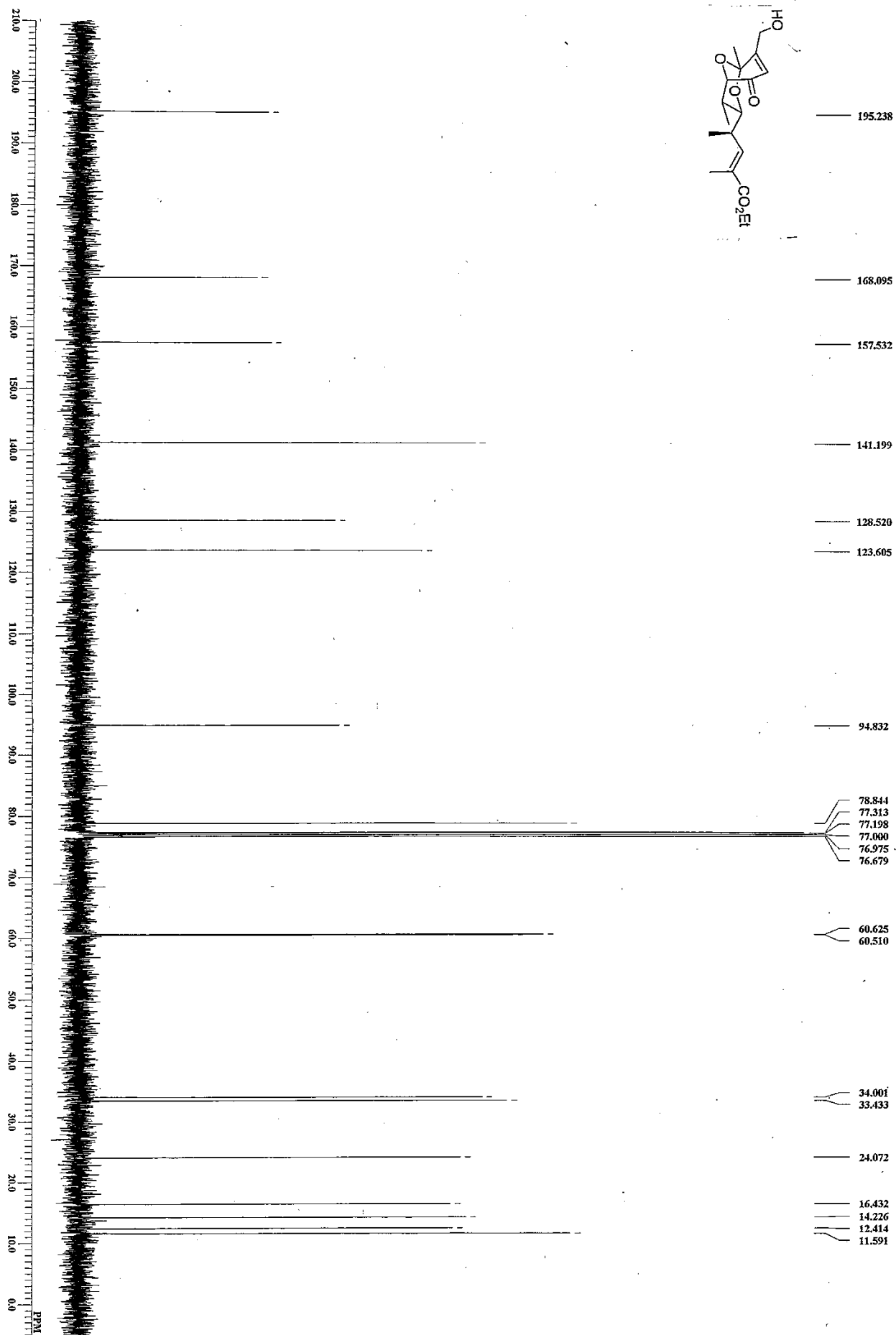
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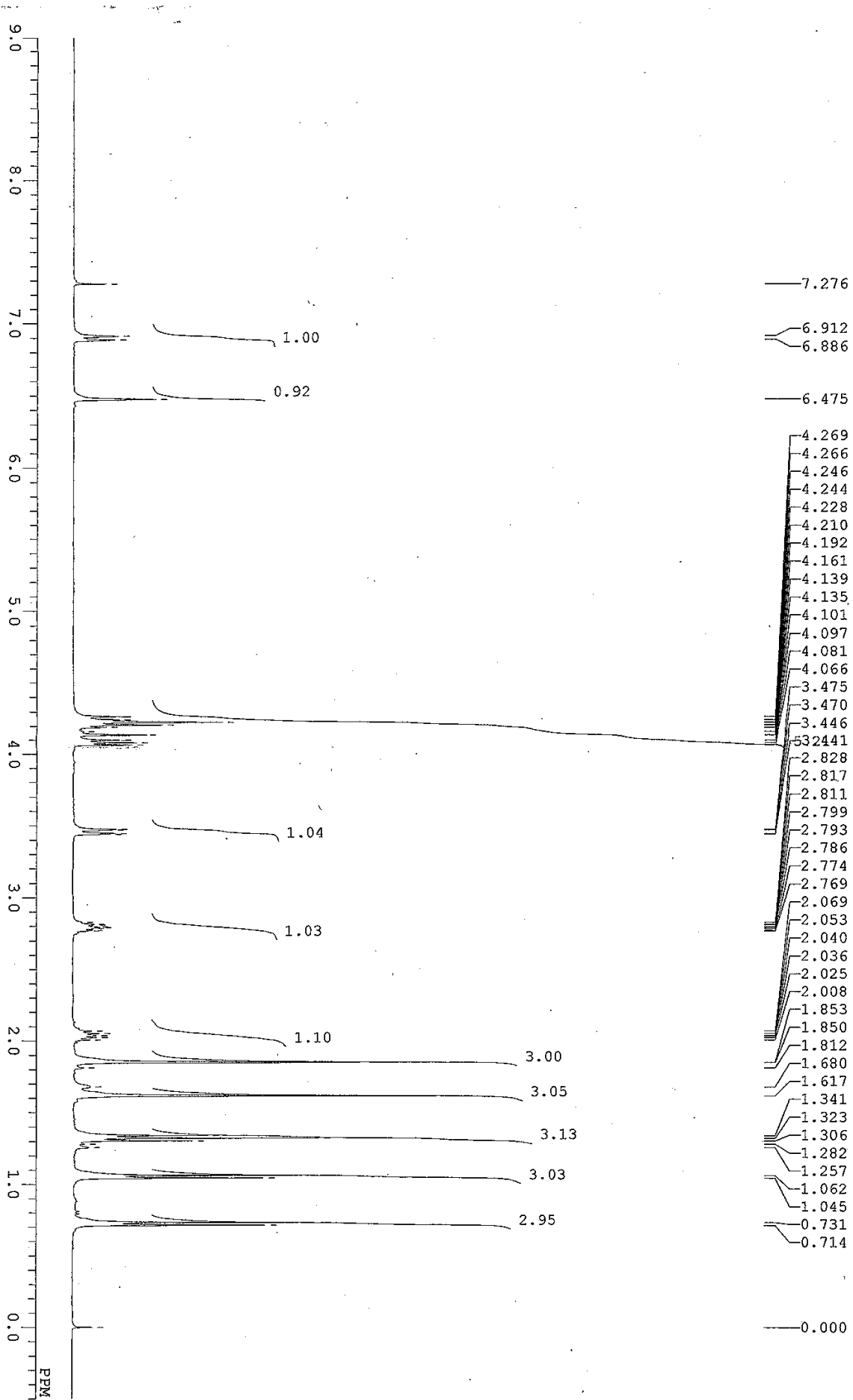
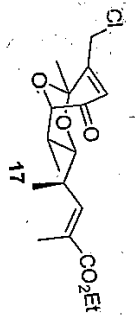


- 201.437
- 192.604
- 176.484
- 175.051
- 149.621
- 143.273
- 134.999
- 116.756
- 100.101
- 95.861
- 78.663
- 77.321
- 77.156
- 77.000
- 76.687
- 59.374
- 57.991
- 56.838
- 51.619
- 34.528
- 34.503
- 34.462
- 23.323
- 16.893
- 12.275
- 11.369



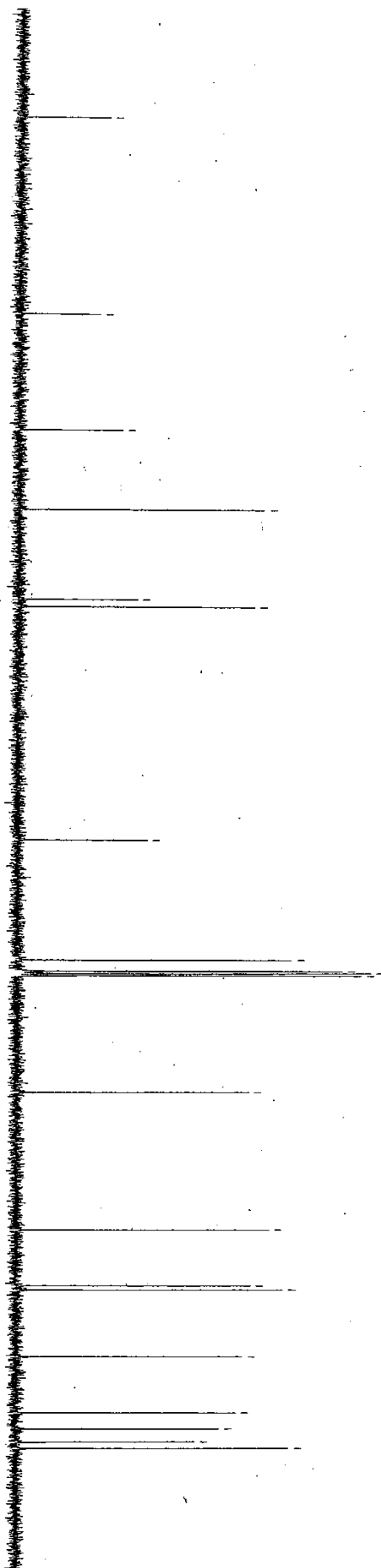




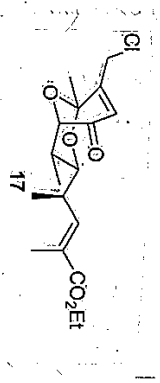


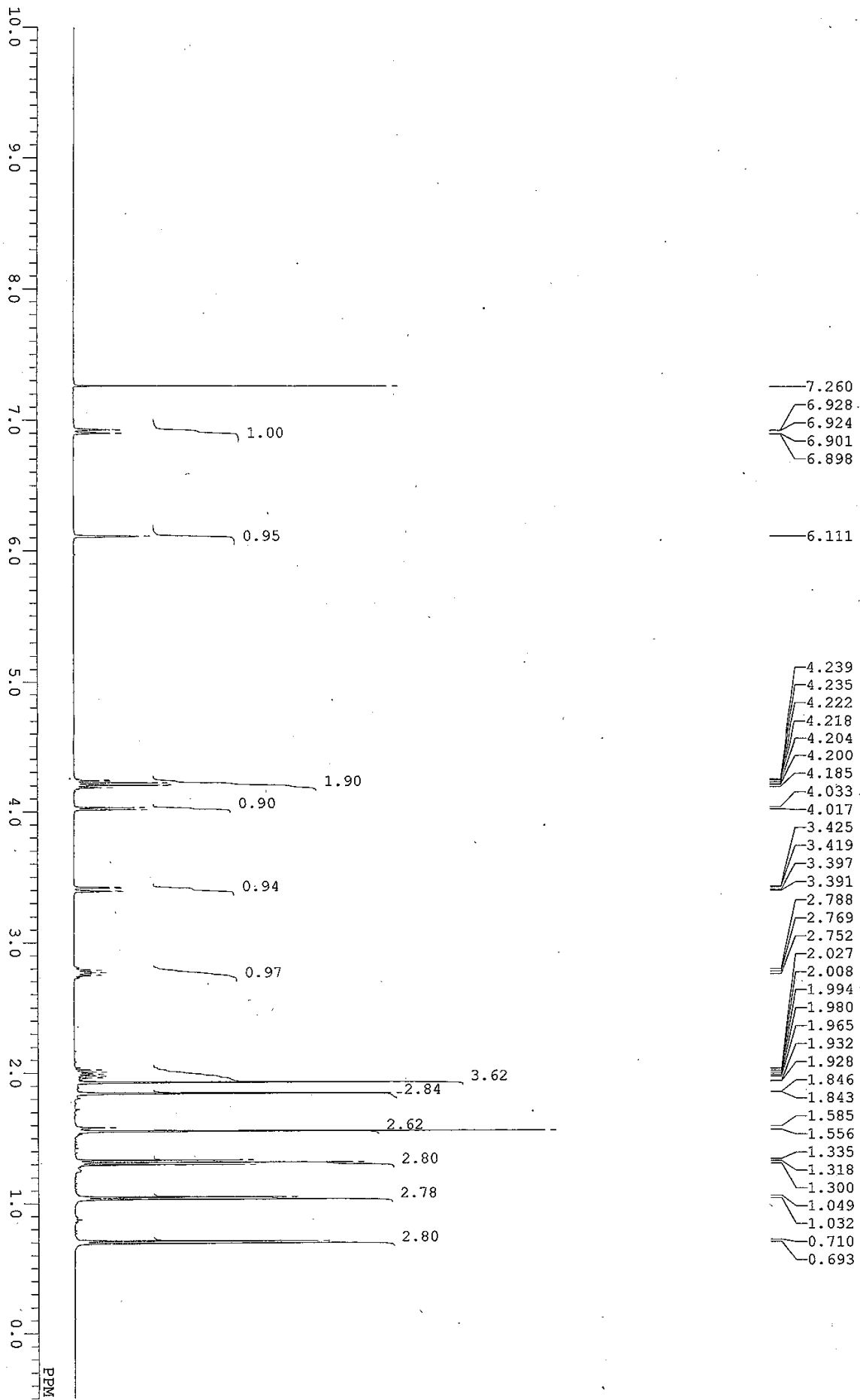
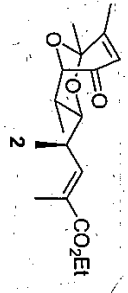
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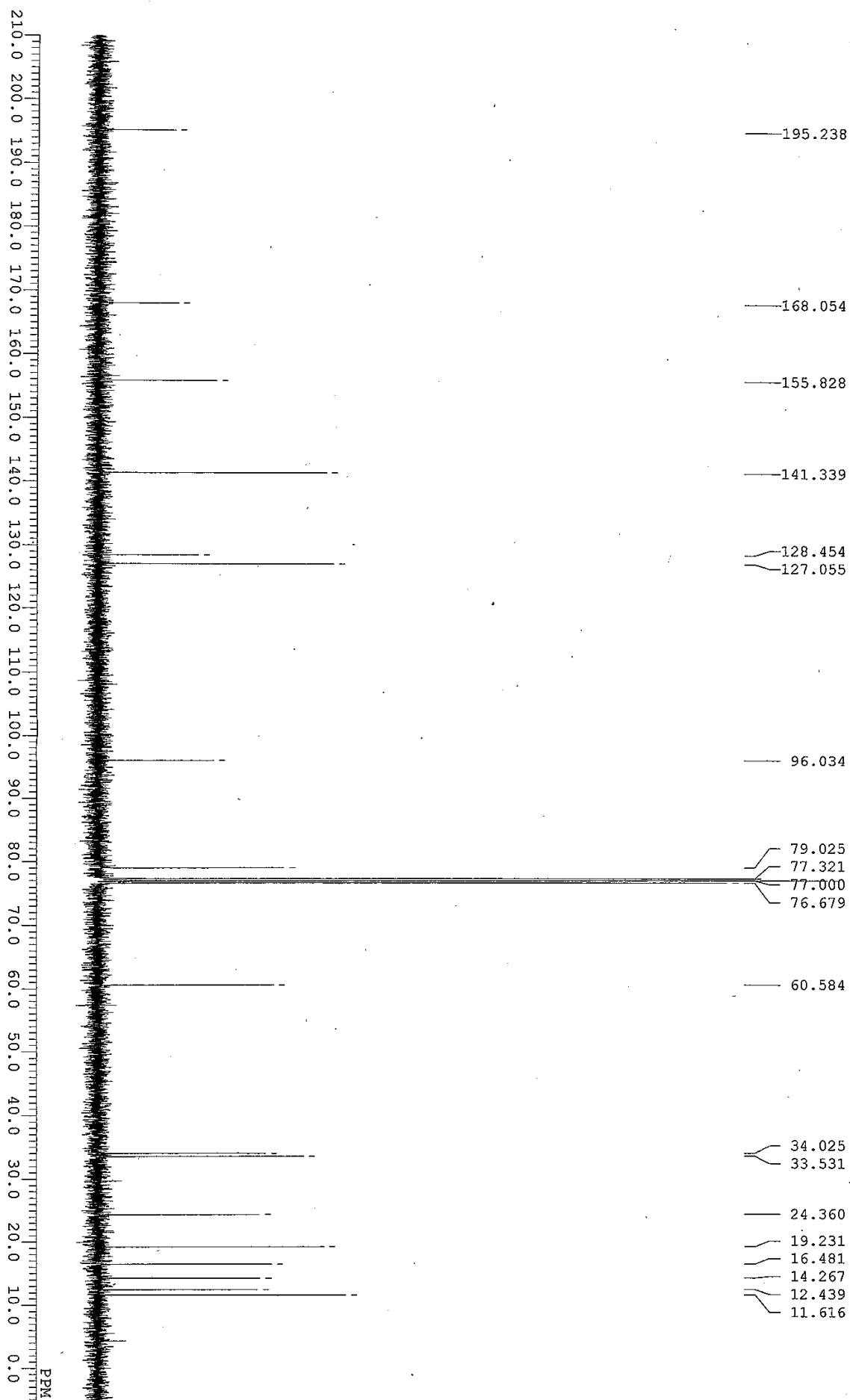
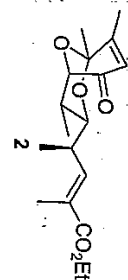
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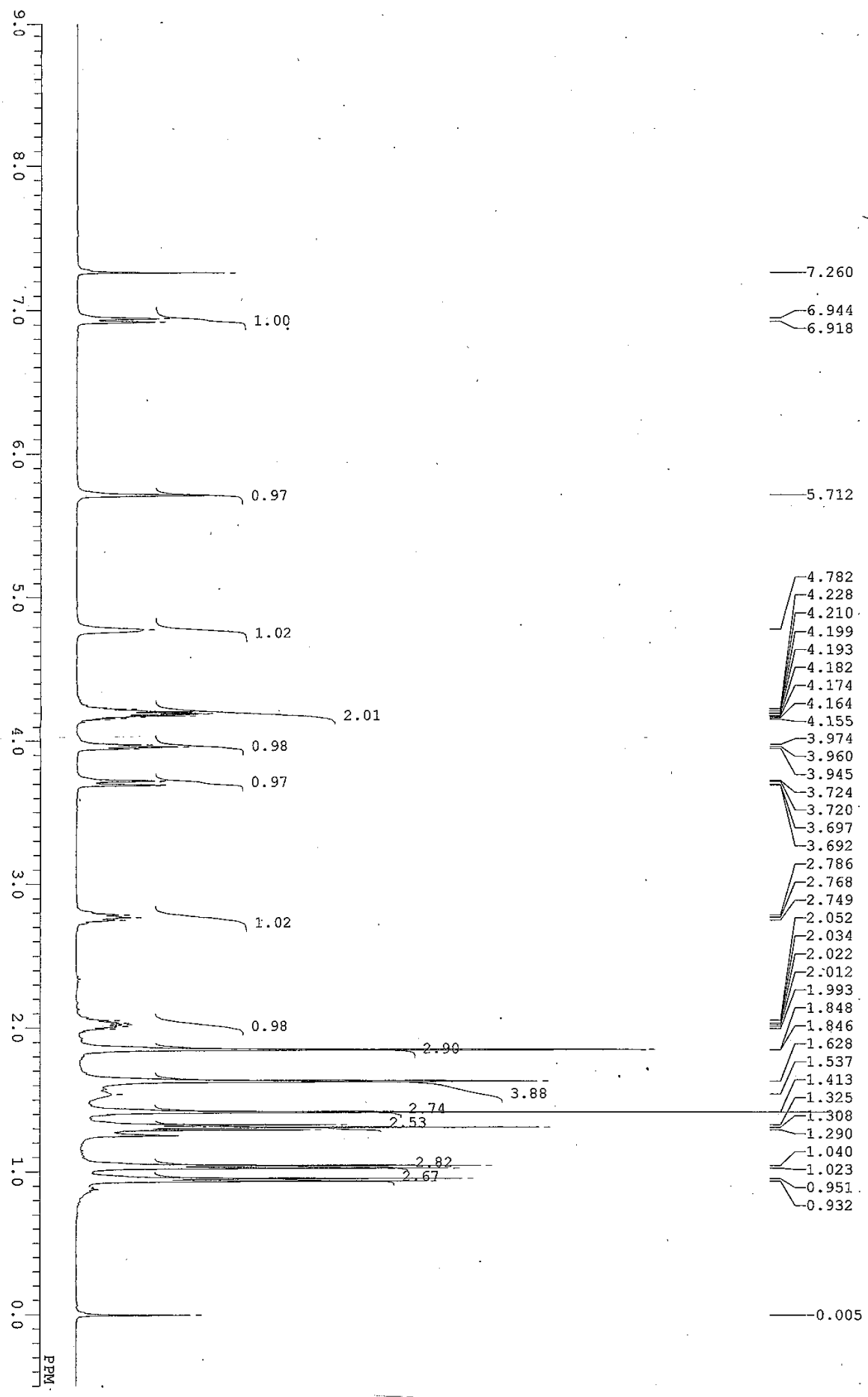
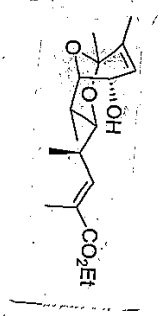


- 194.991
- 167.980
- 151.983
- 141.042
- 128.586
- 127.573
- 95.375
- 78.852
- 77.313
- 77.000
- 76.909
- 76.679
- 60.584
- 41.772
- 34.075
- 33.498
- 24.228
- 16.473
- 14.242
- 12.431
- 11.550



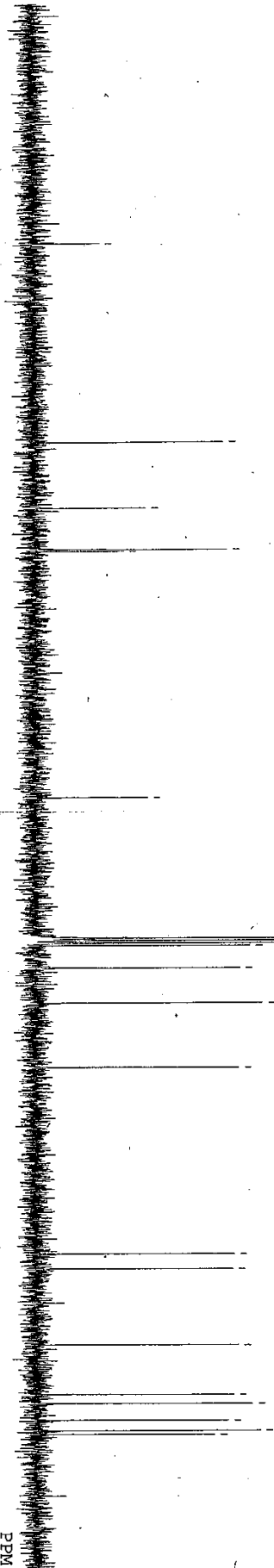






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PPM



—168.259

—142.244

—133.682

—128.232

—128.018

—95.878

77.313

77.000

76.679

76.325

73.411

68.850

—60.469

—36.059

—34.141

—24.163

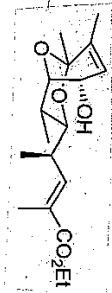
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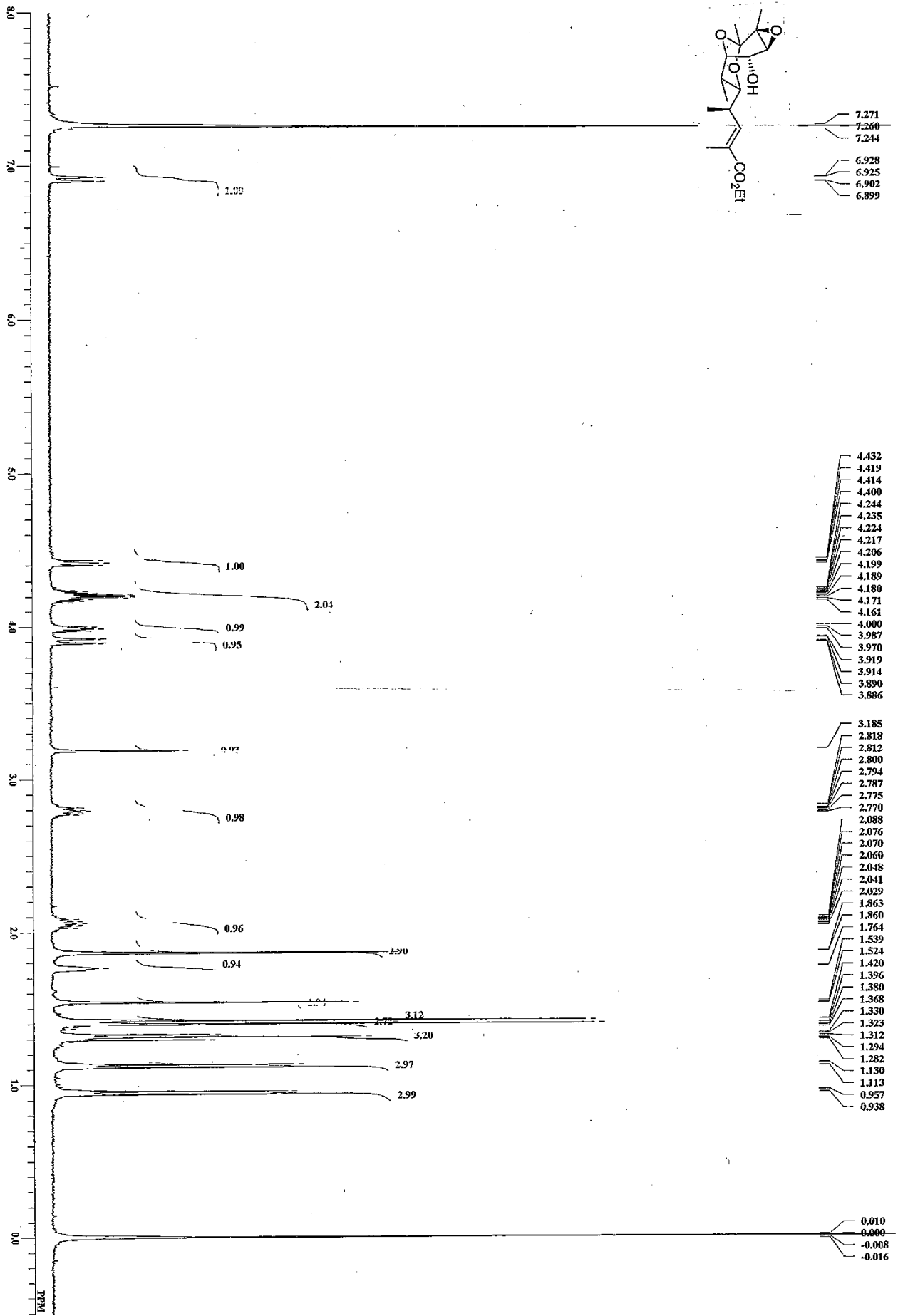
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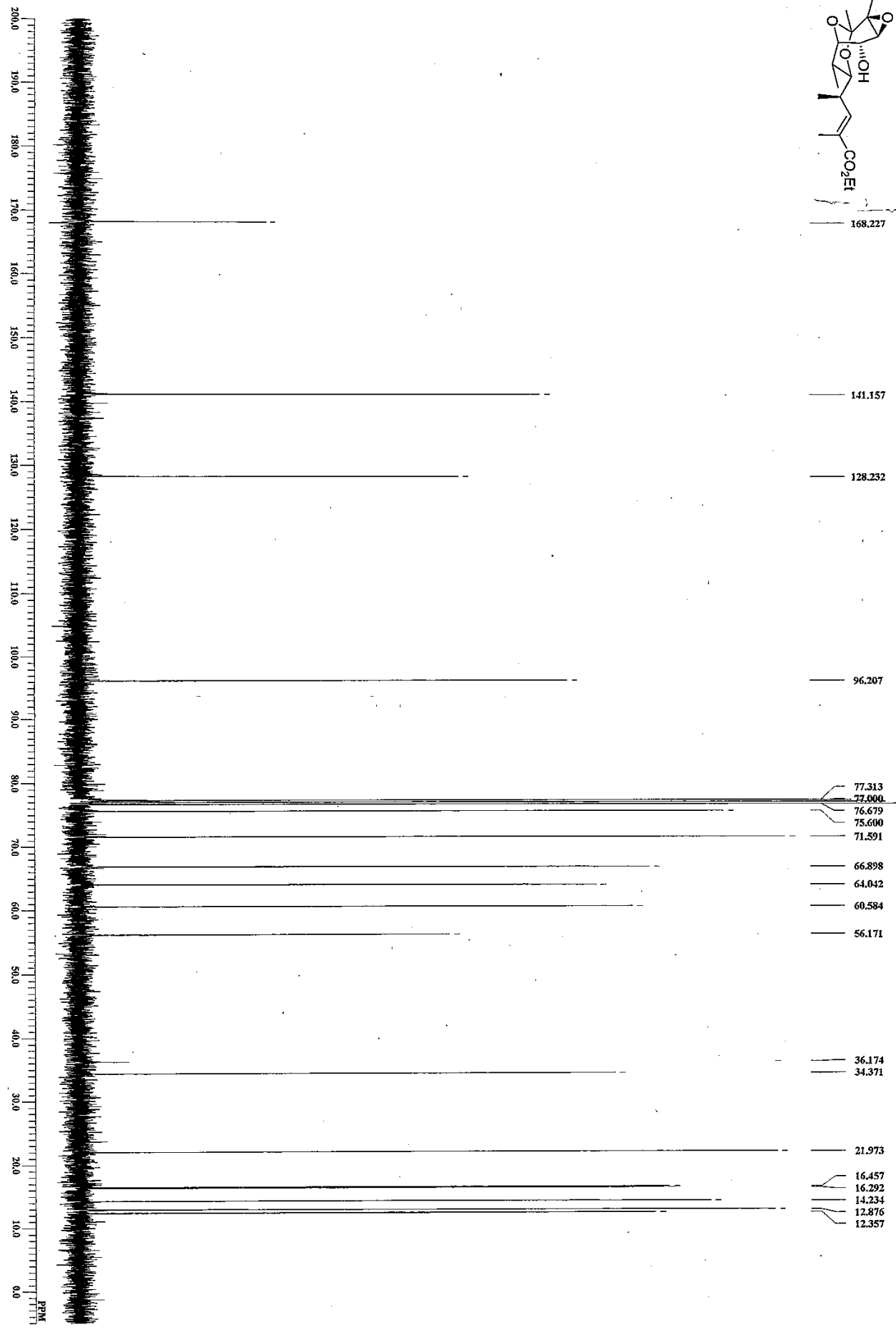
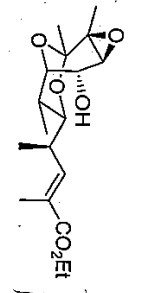
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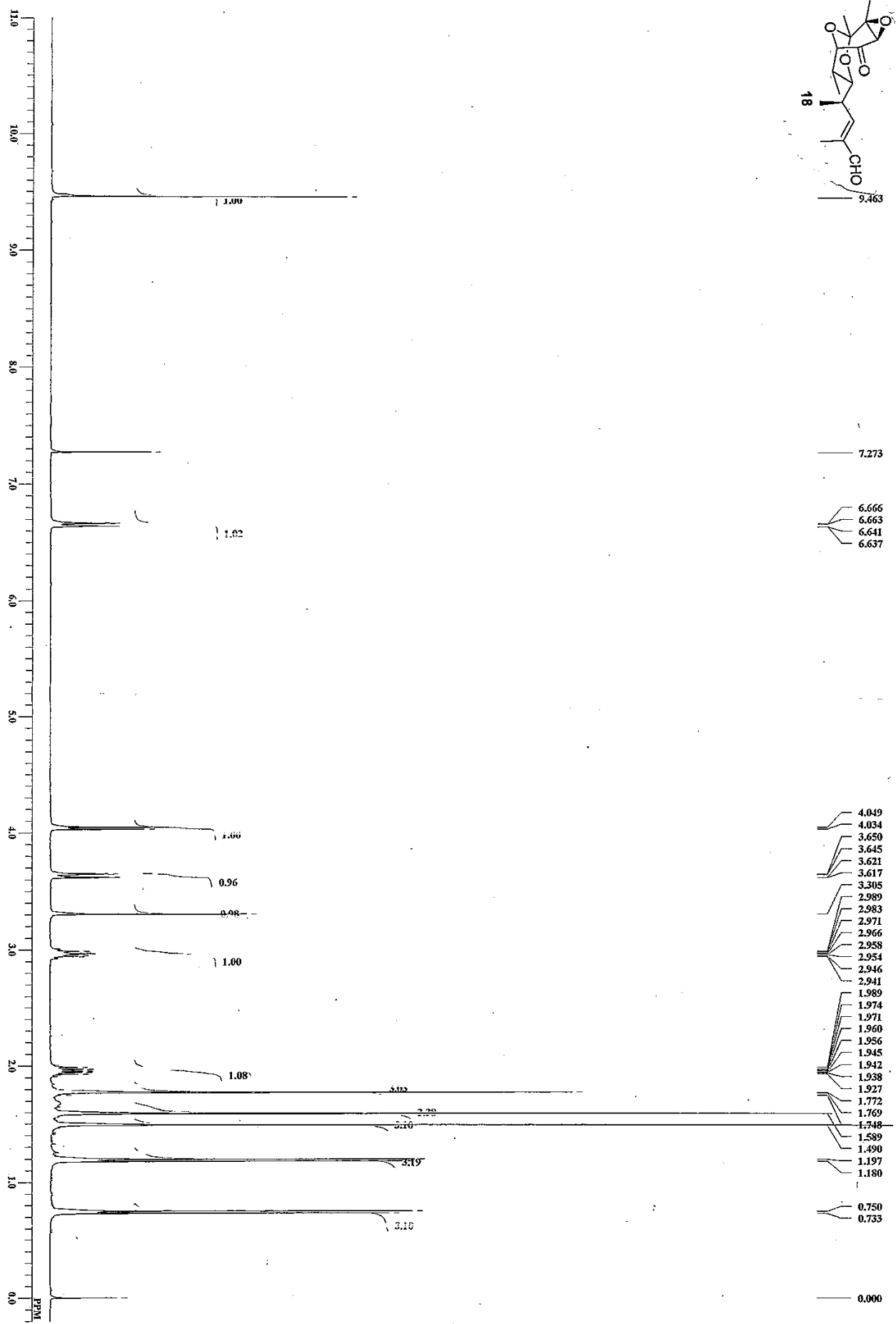
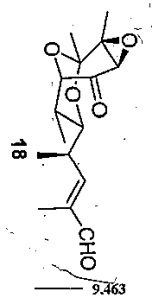
—12.892

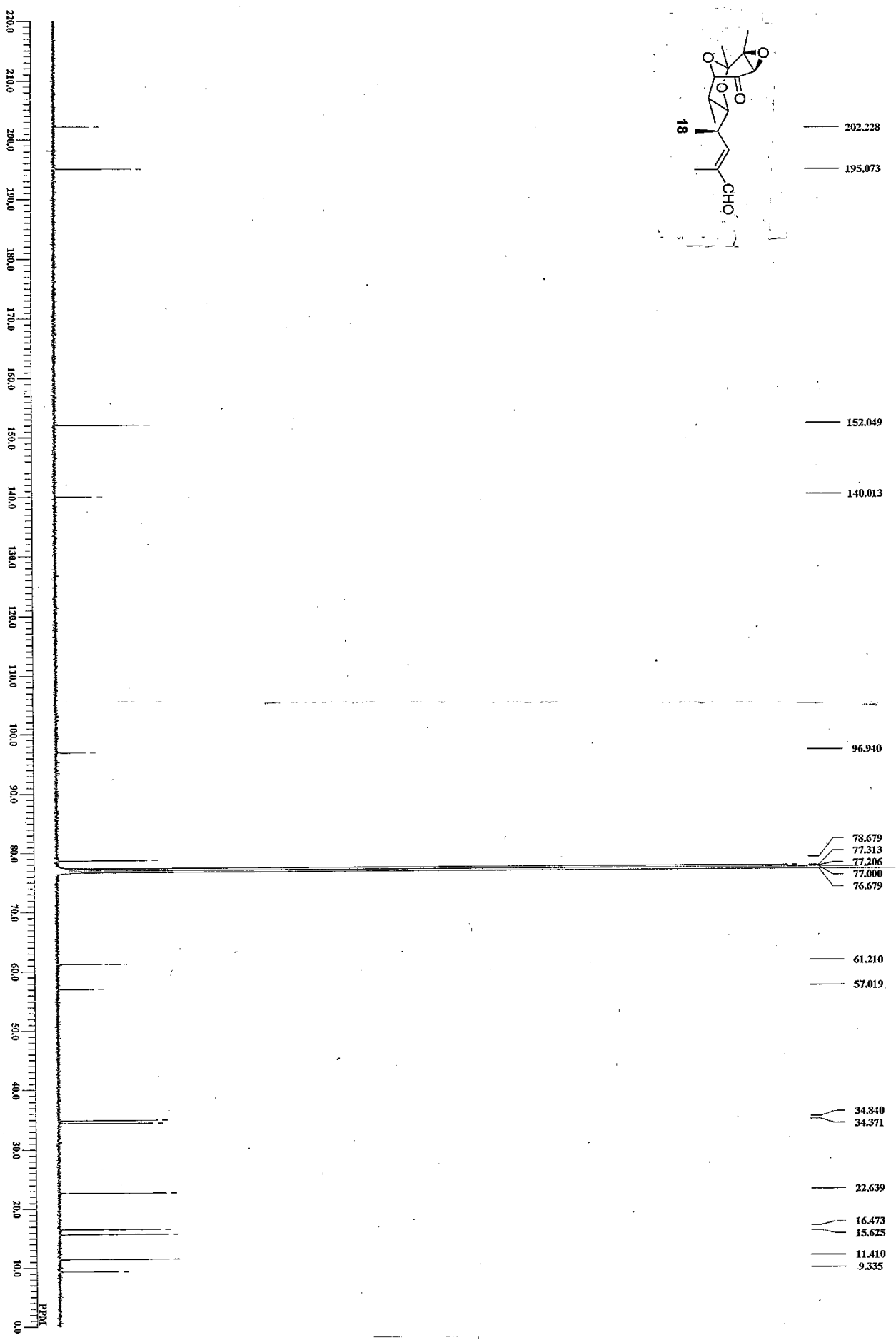
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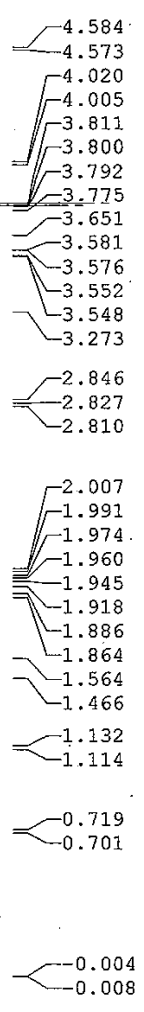
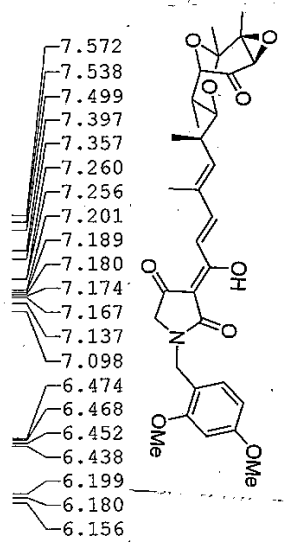
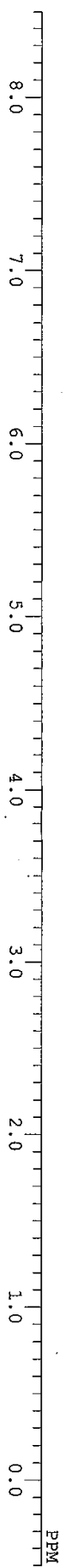






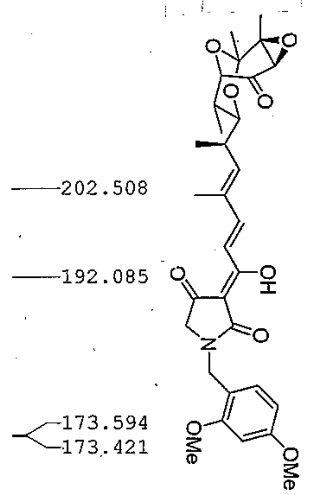
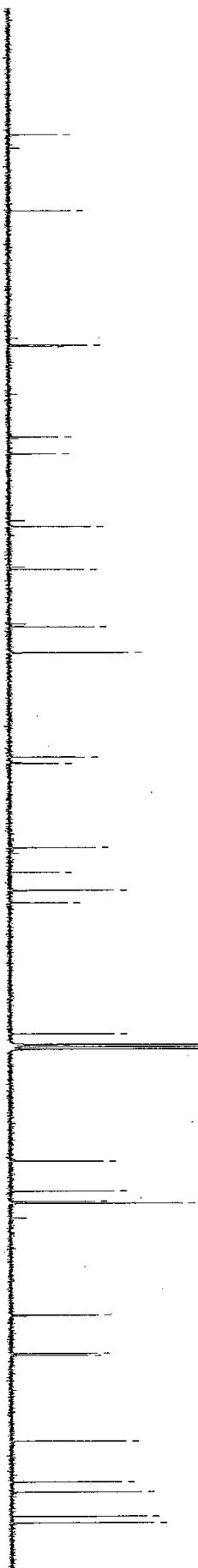




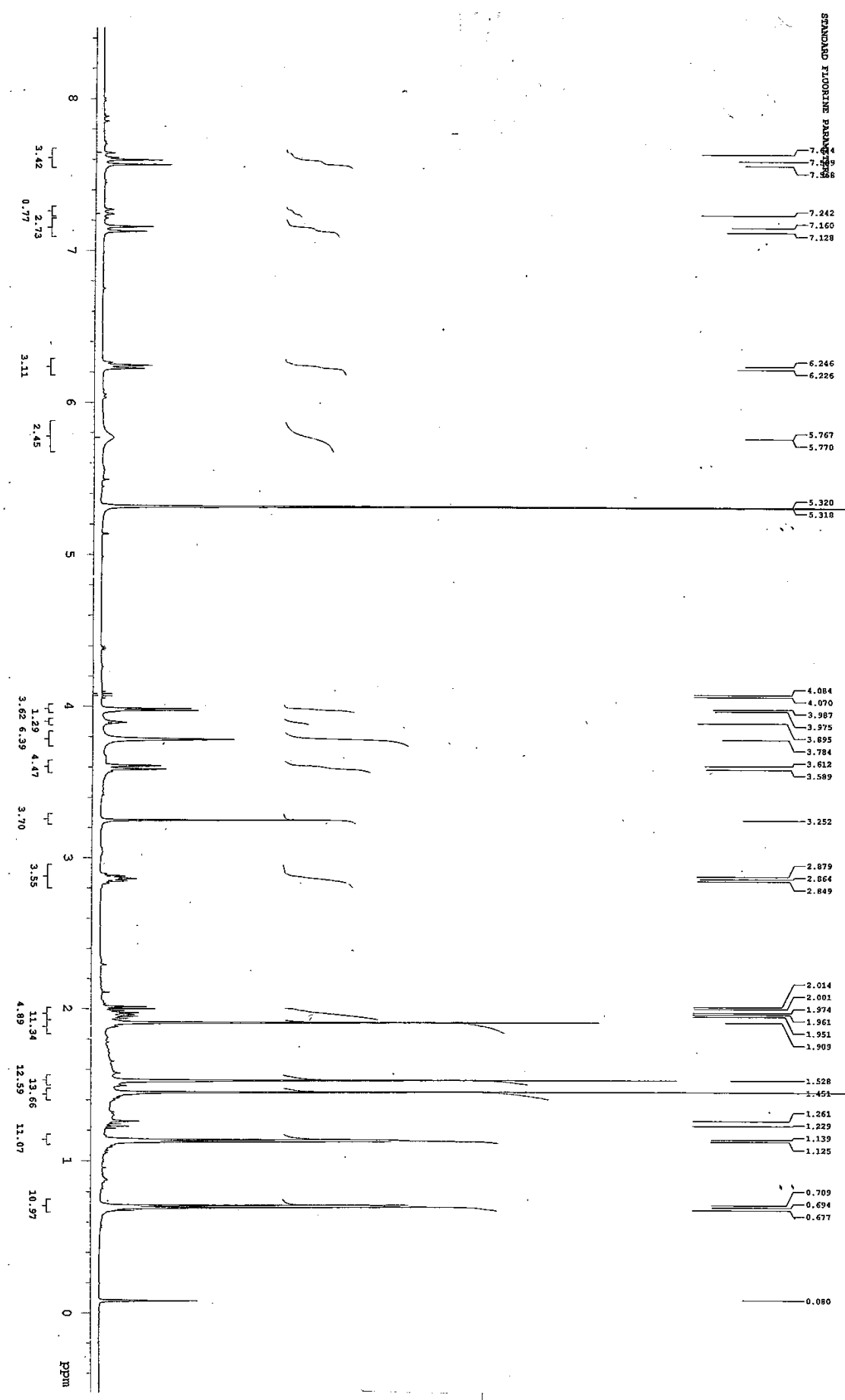
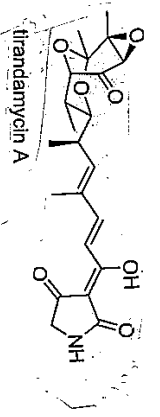


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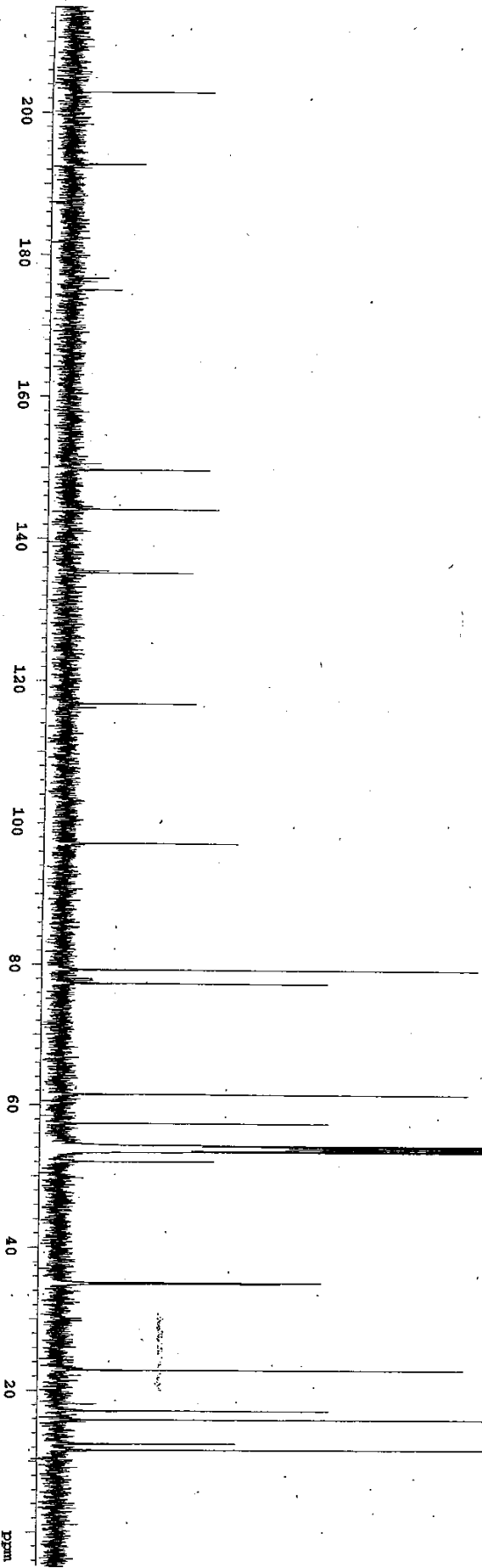
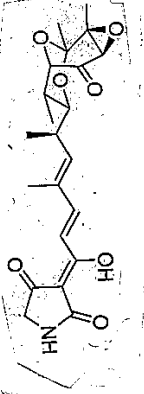
PPM

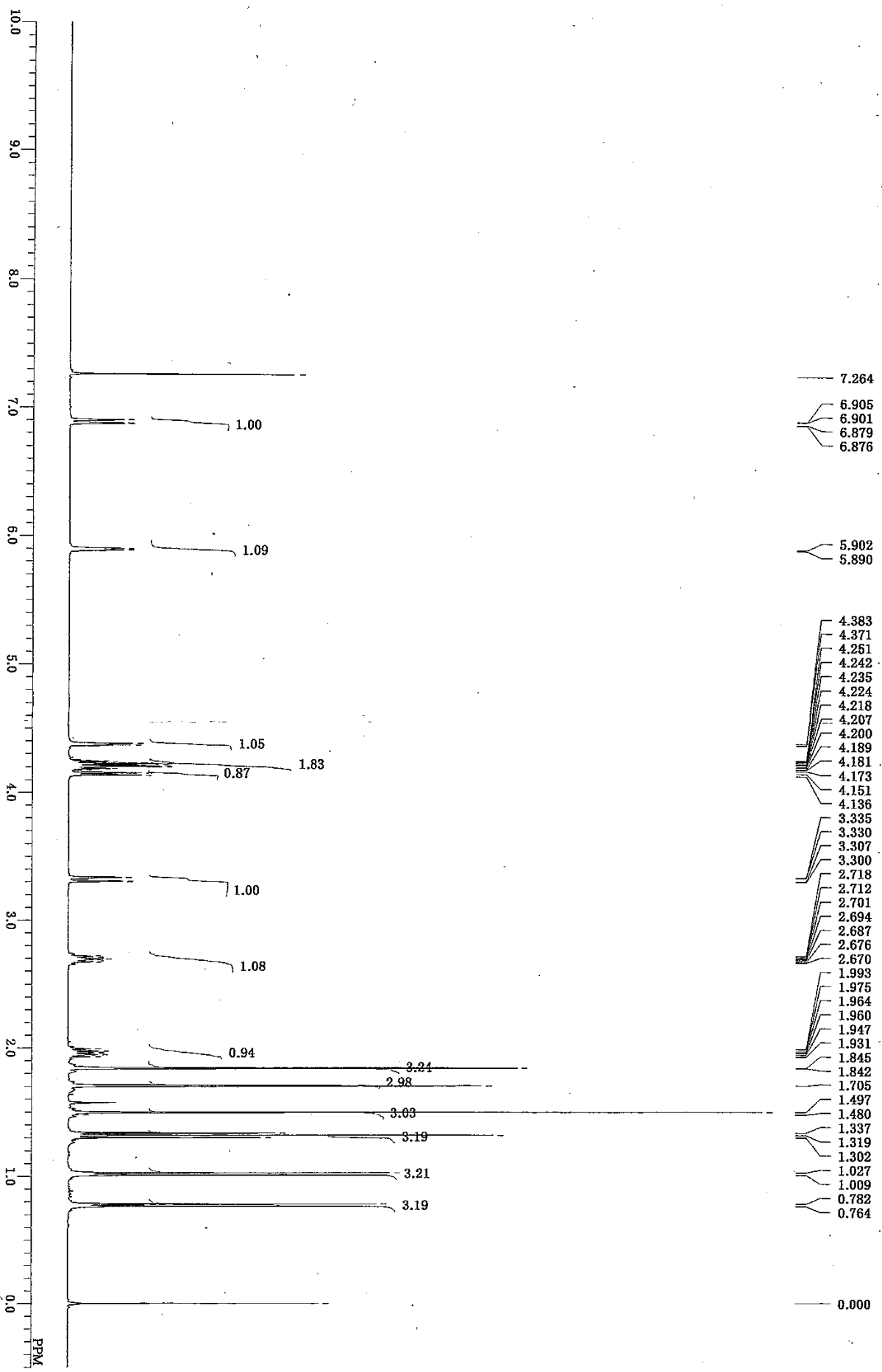
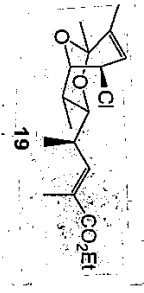


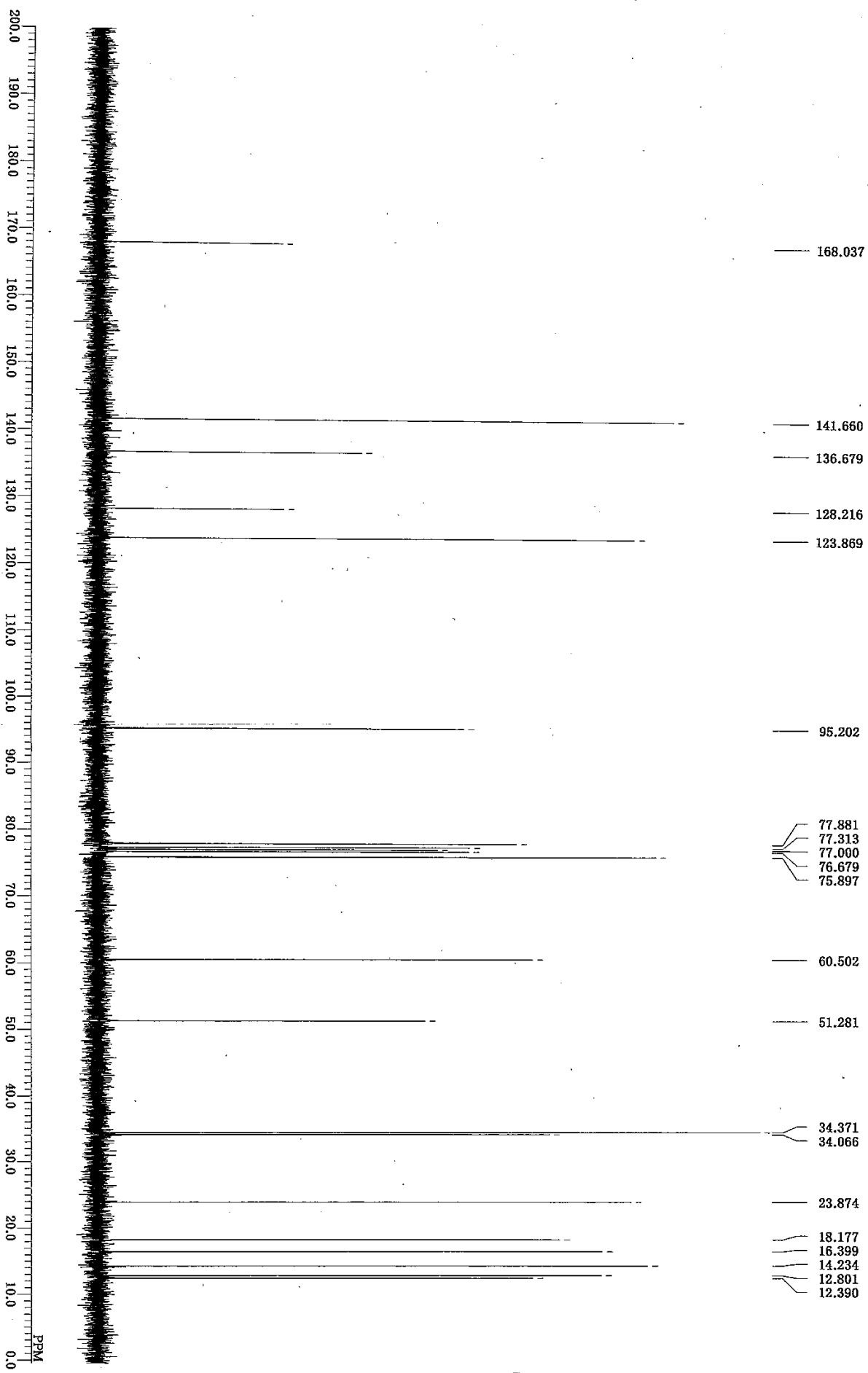
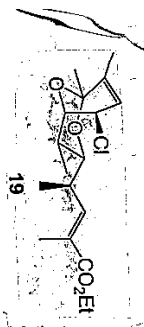
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- 192.085
- 173.594
- 173.421
- 160.957
- 158.635
- 148.657
- 142.705
- 134.843
- 131.303
- 116.912
- 116.064
- 104.365
- 101.056
- 98.537
- 96.808
- 78.778
- 77.321
- 77.206
- 77.000
- 76.679
- 61.210
- 57.060
- 55.644
- 55.406
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- 34.684
- 34.437
- 22.623
- 16.992
- 15.617
- 12.275
- 11.369



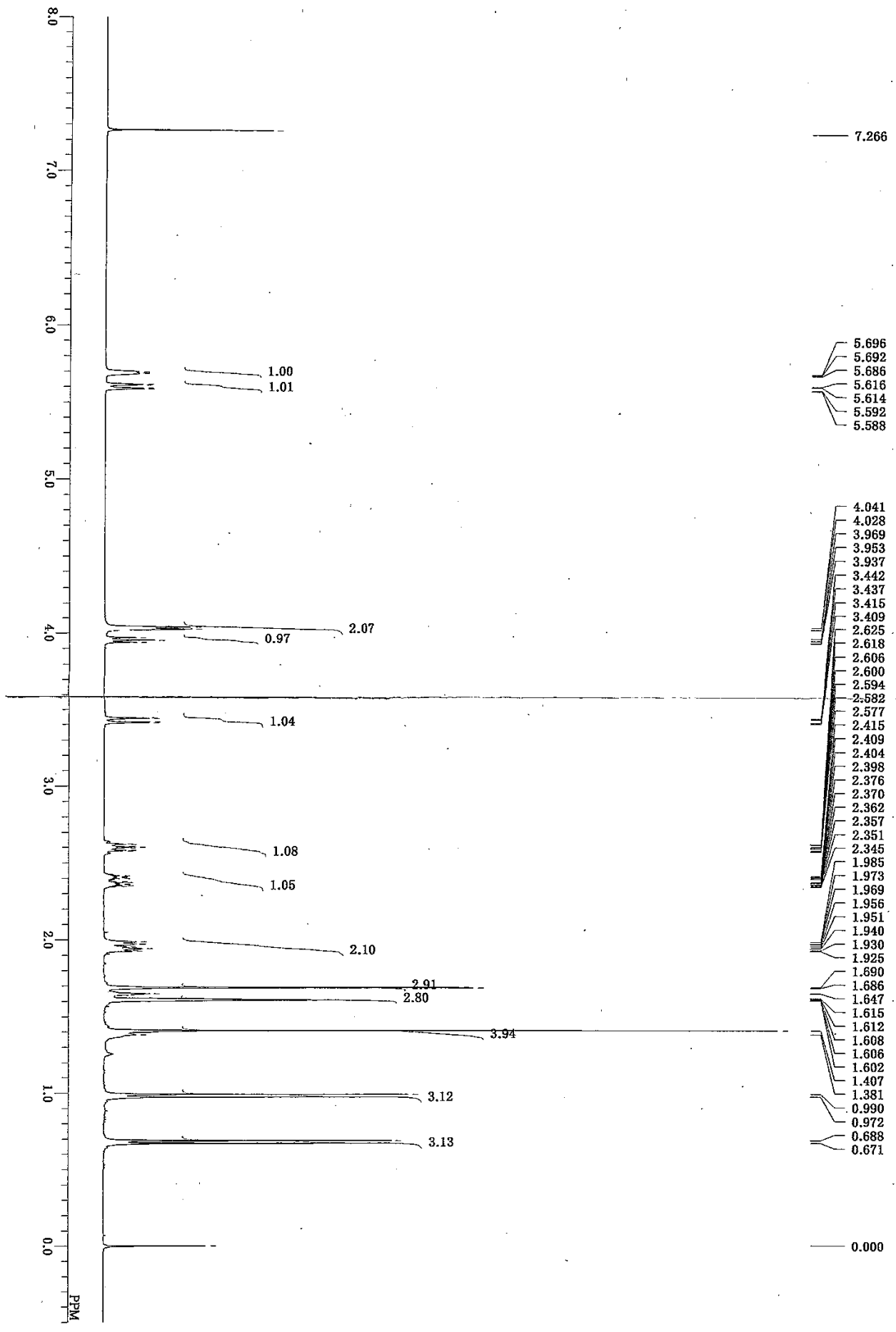
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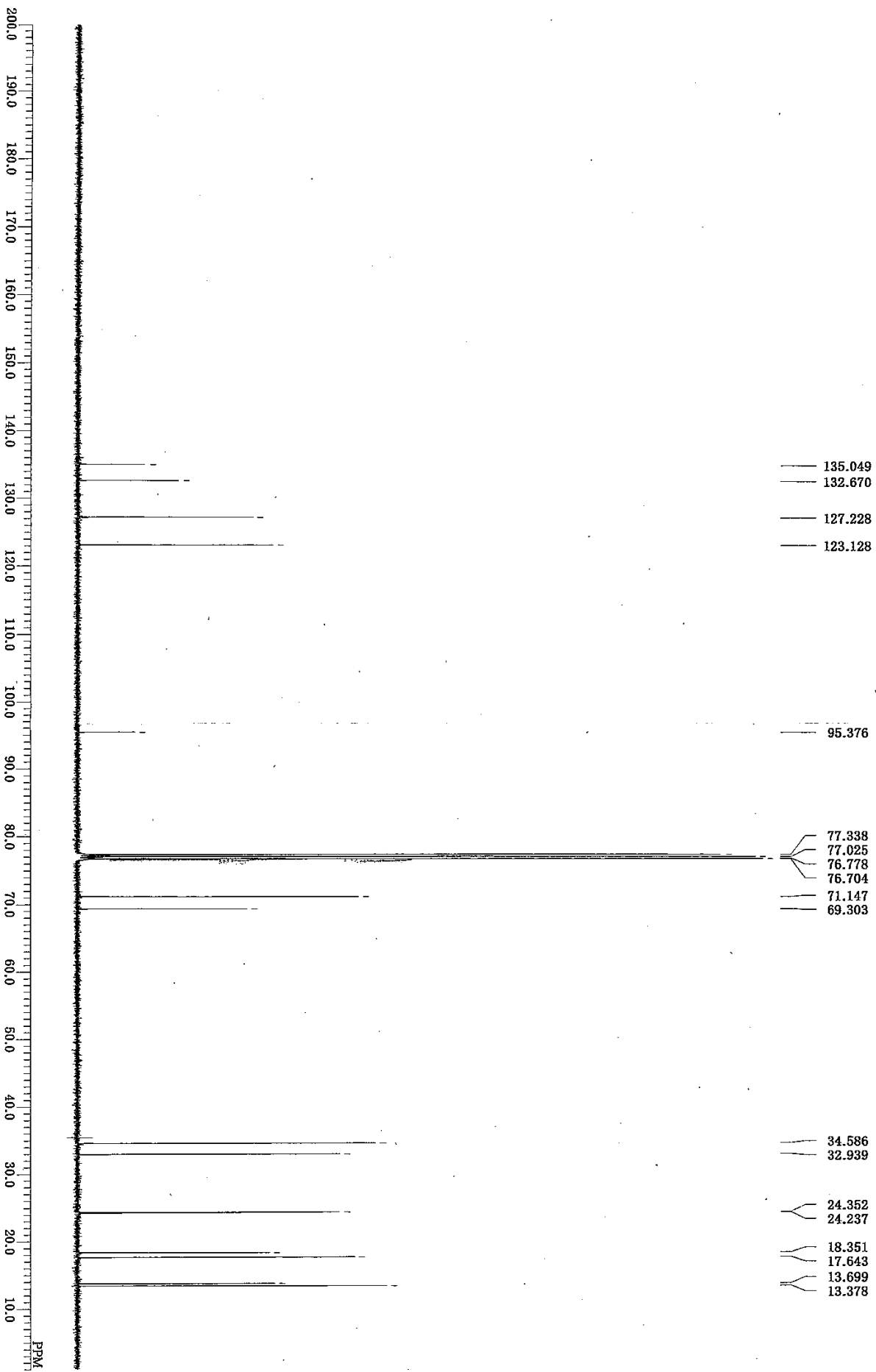
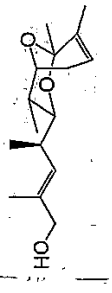


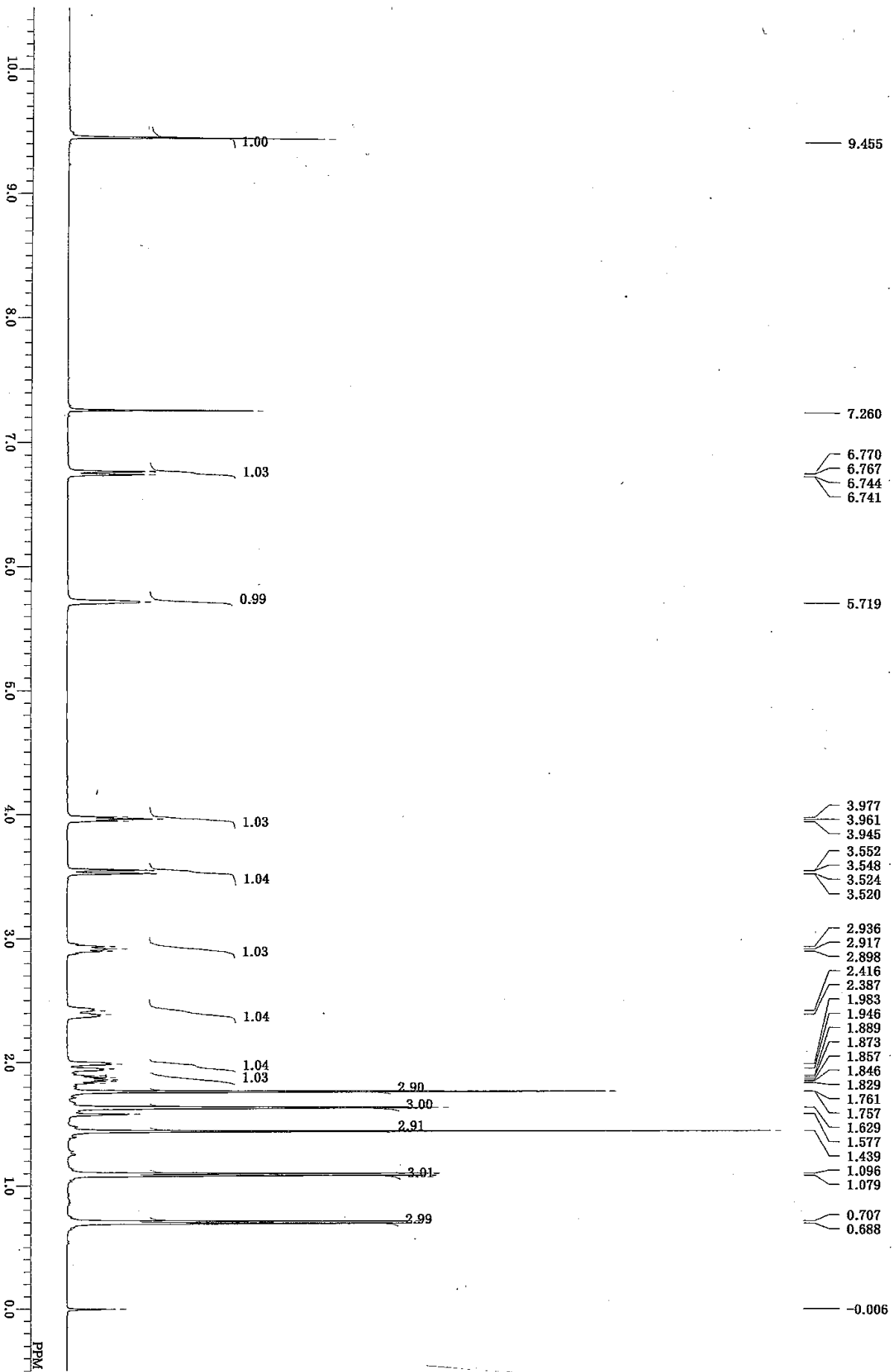
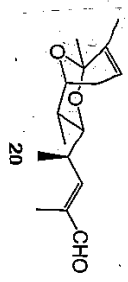


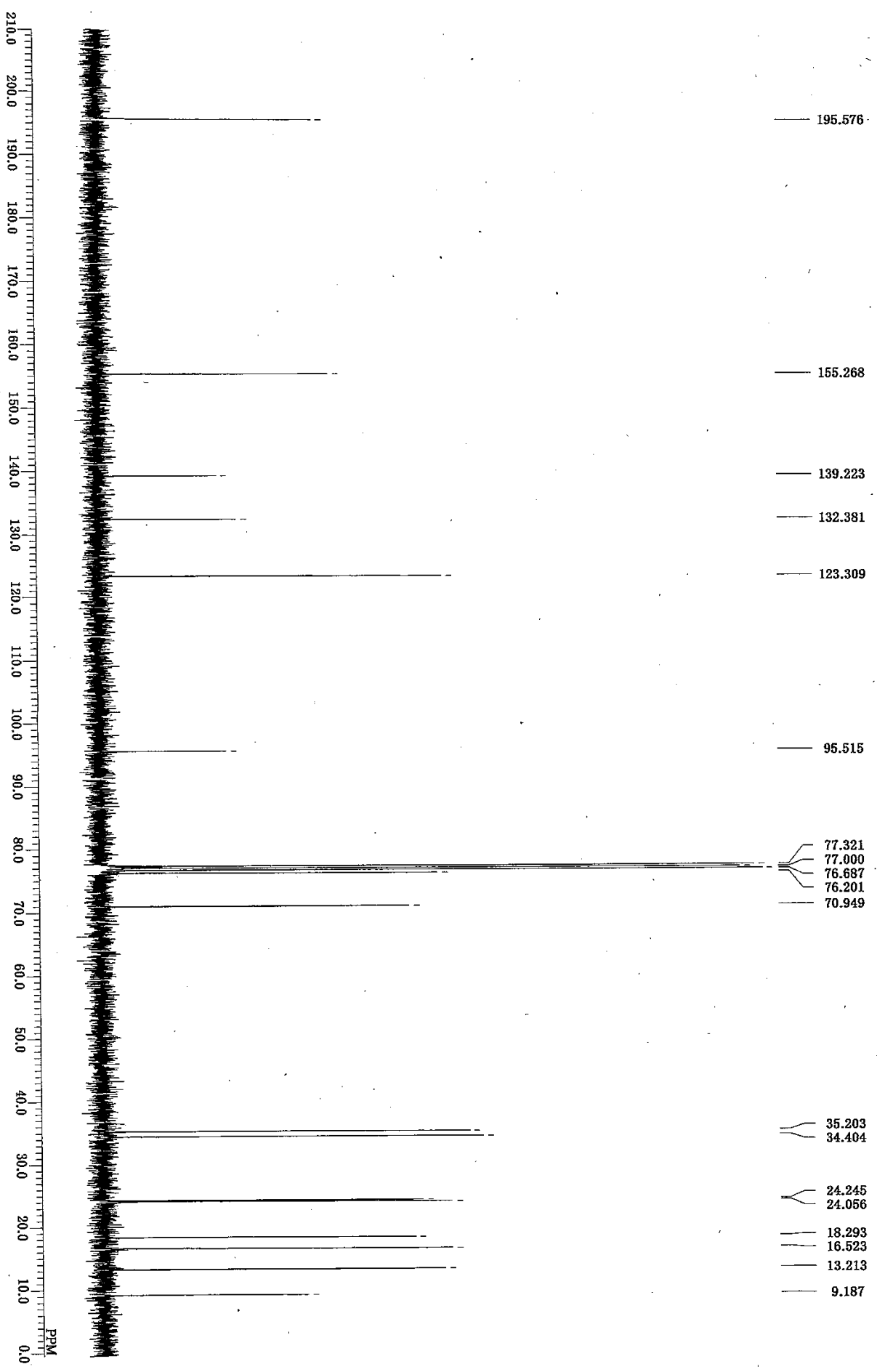
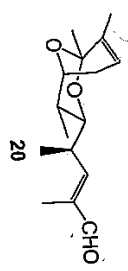


S95

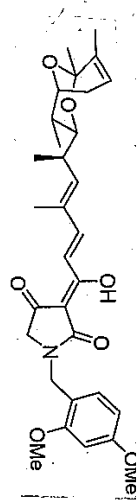
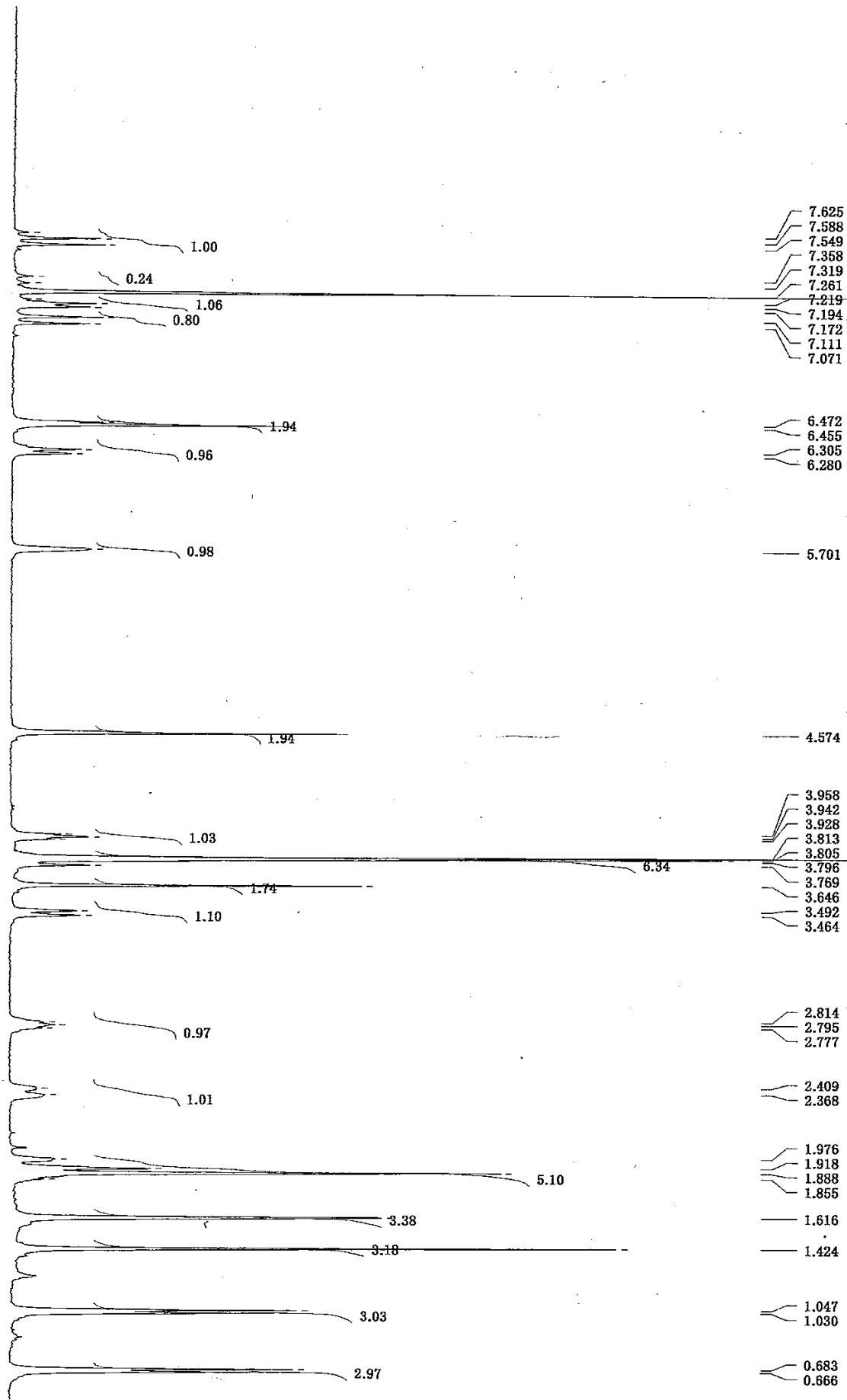






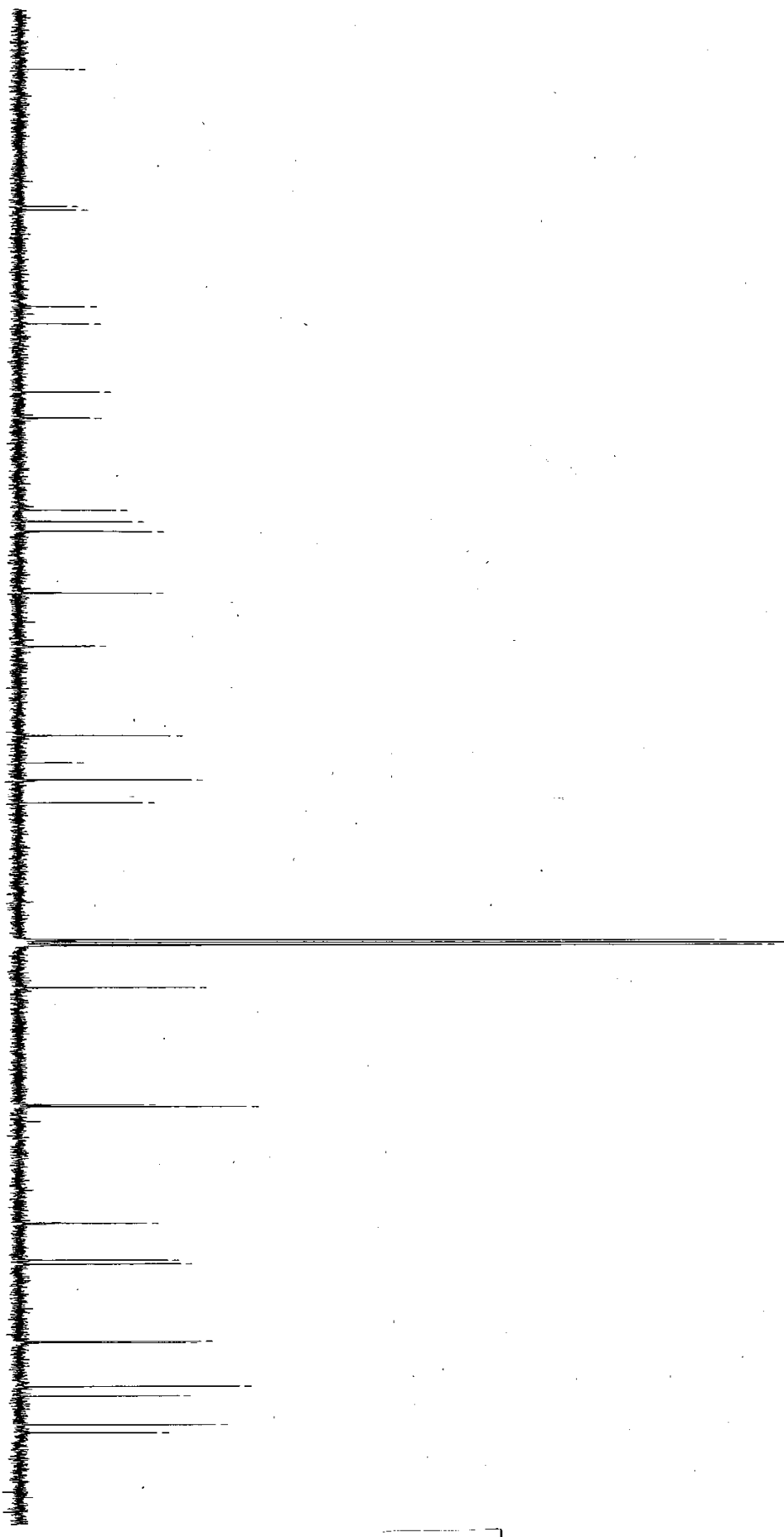


9.0
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2.0
1.0
PPM

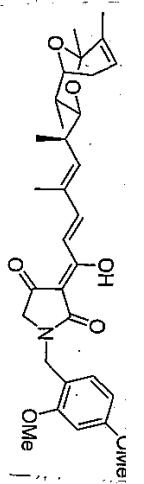


S100

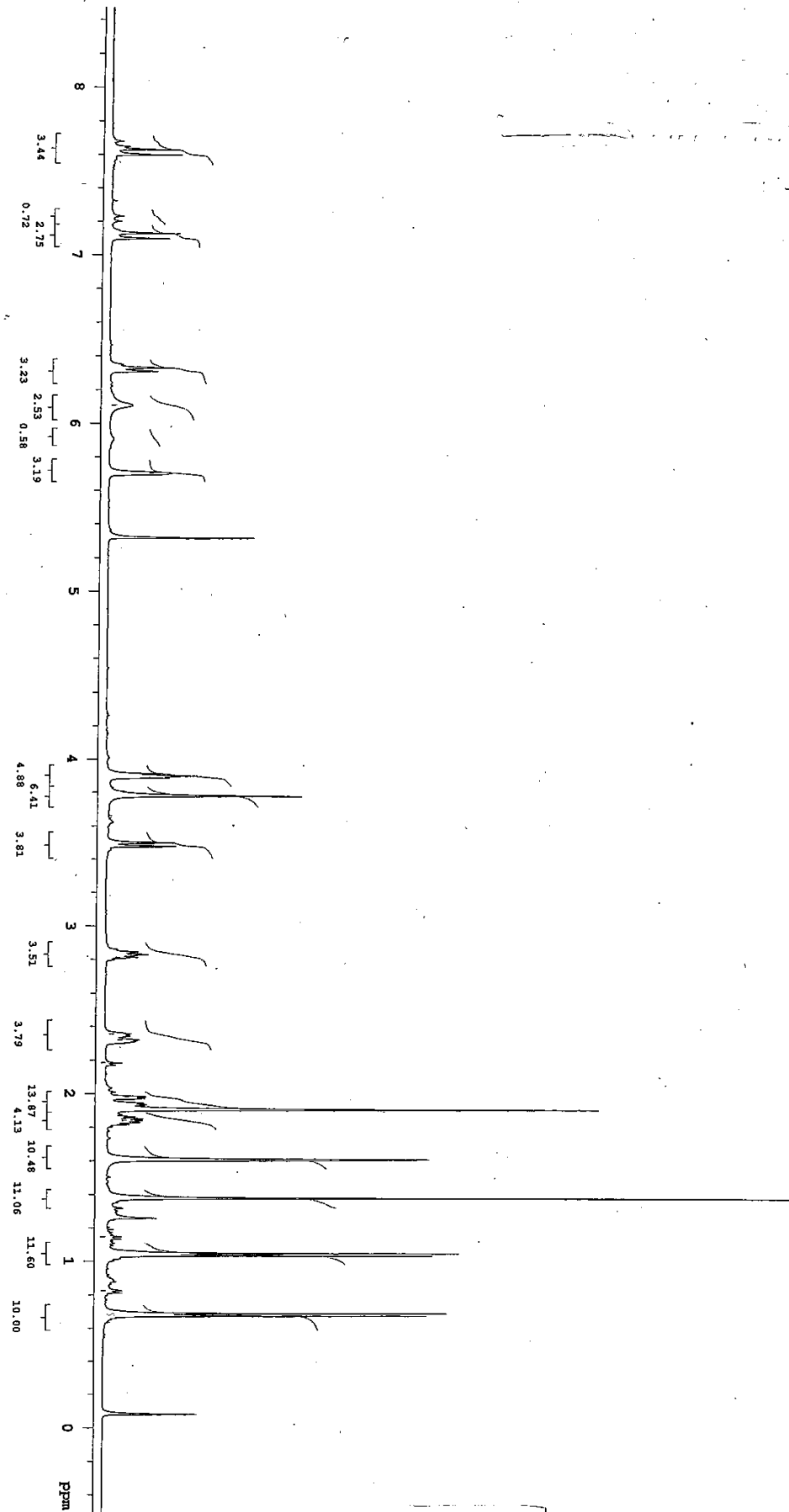
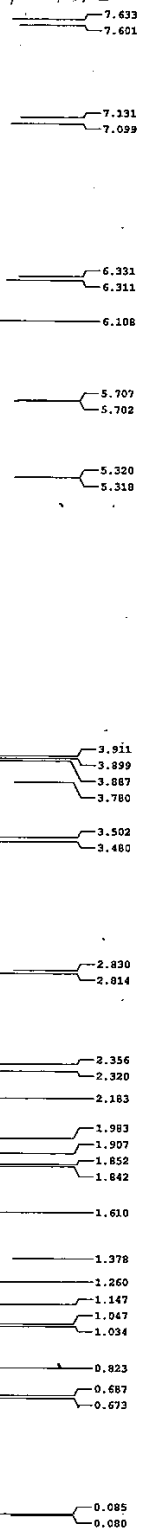
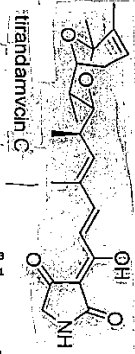
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70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
PPM



- 192.101
- 174.039
- 173.553
- 160.891
- 158.611
- 149.612
- 146.196
- 134.028
- 132.521
- 131.262
- 123.185
- 116.163
- 116.056
- 104.333
- 100.751
- 98.512
- 95.433
- 77.313
- 77.000
- 76.679
- 76.547
- 71.007
- 55.587
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- 24.278
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- 18.309
- 17.049
- 13.230
- 12.184

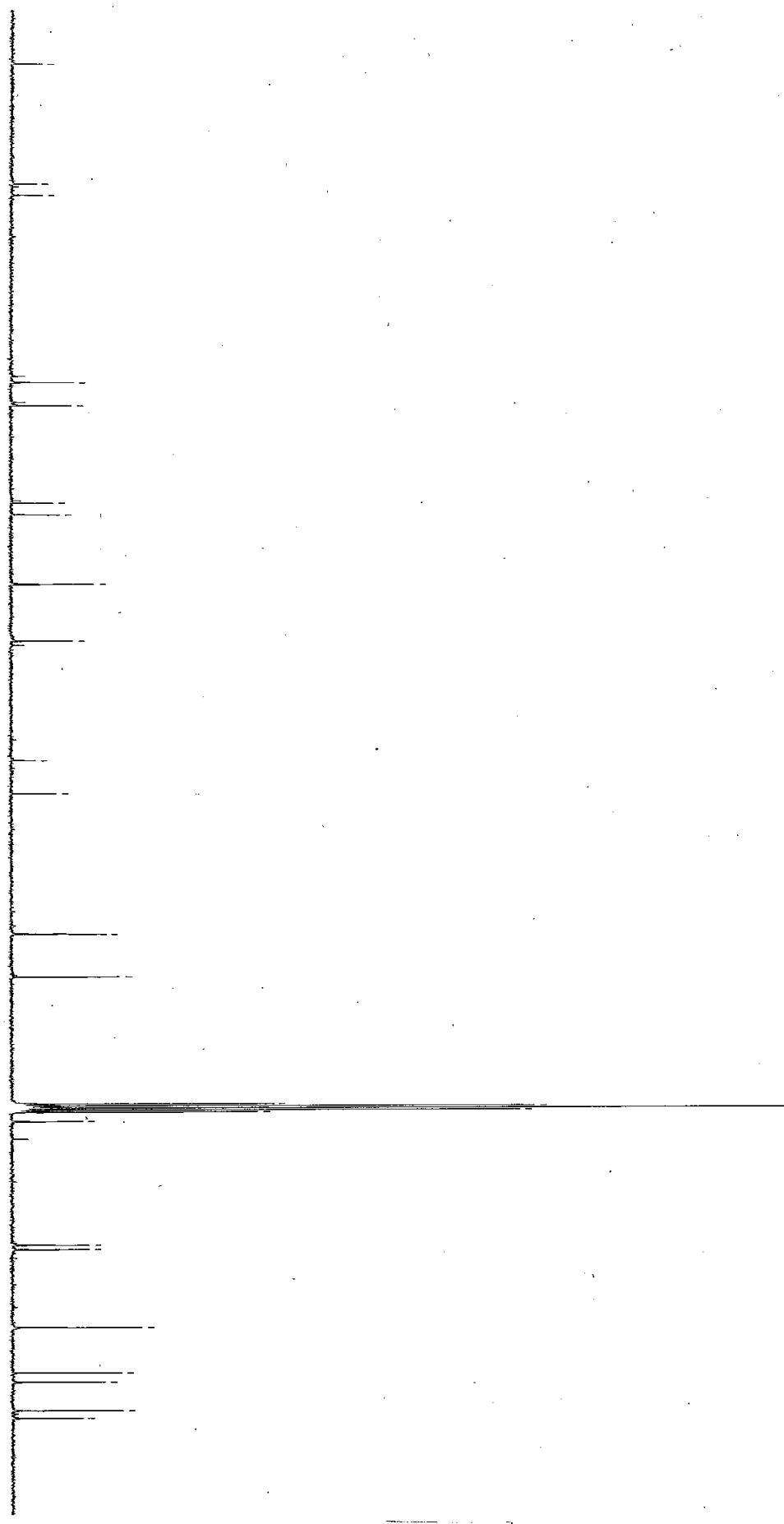


S101



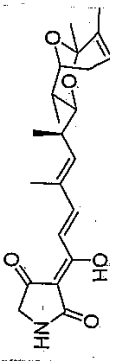
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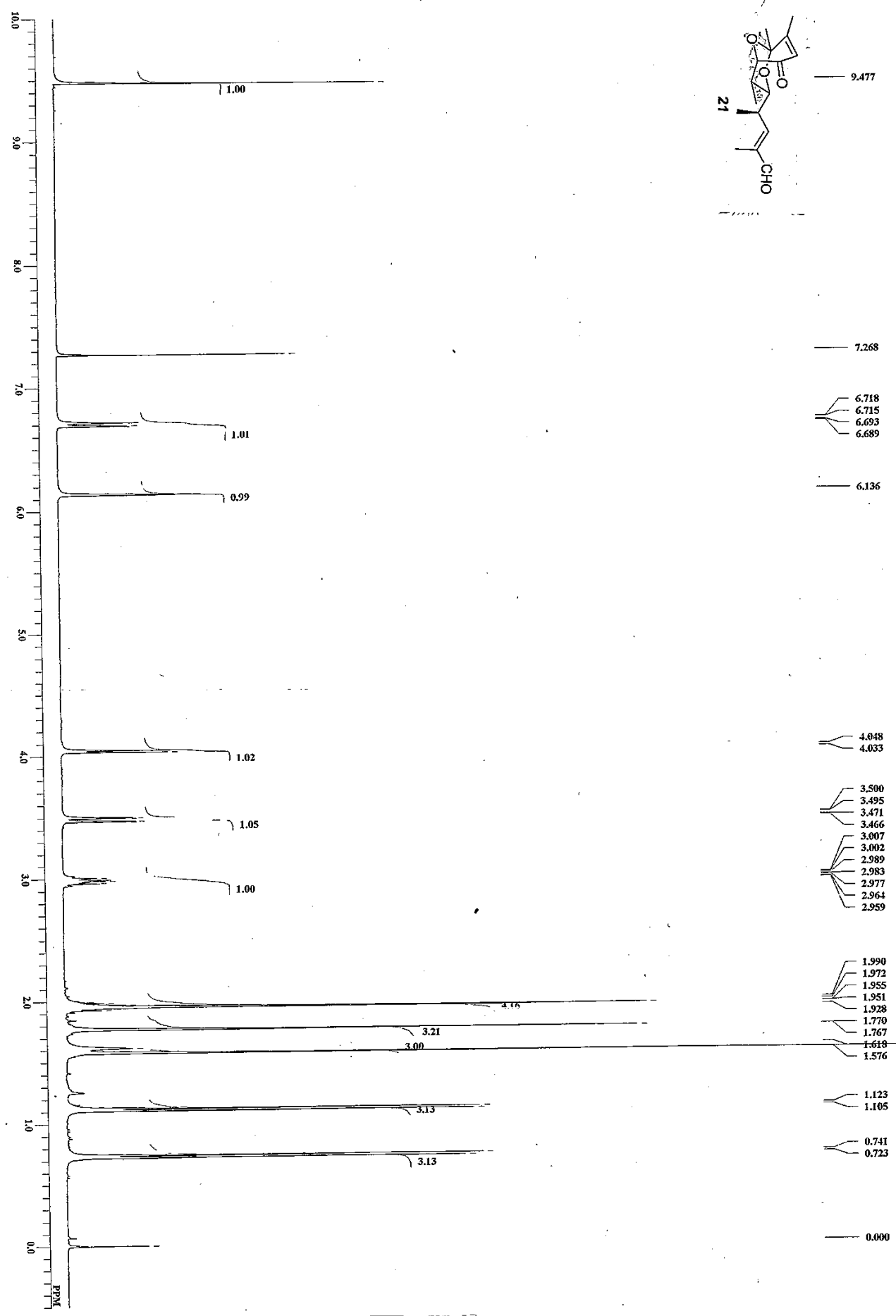
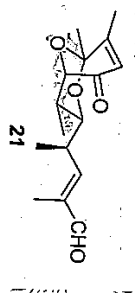
PPM



- 192.809
- 176.871
- 175.348
- 150.444
- 147.389
- 134.480
- 132.916
- 123.671
- 116.072
- 100.257
- 95.754
- 76.992
- 71.303
- 54.343
- 54.277
- 54.072
- 53.800
- 53.528
- 53.257
- 51.997
- 35.540
- 34.939
- 24.516
- 24.492
- 18.416
- 17.197
- 13.344
- 12.332

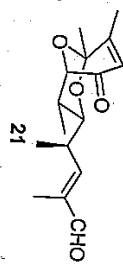
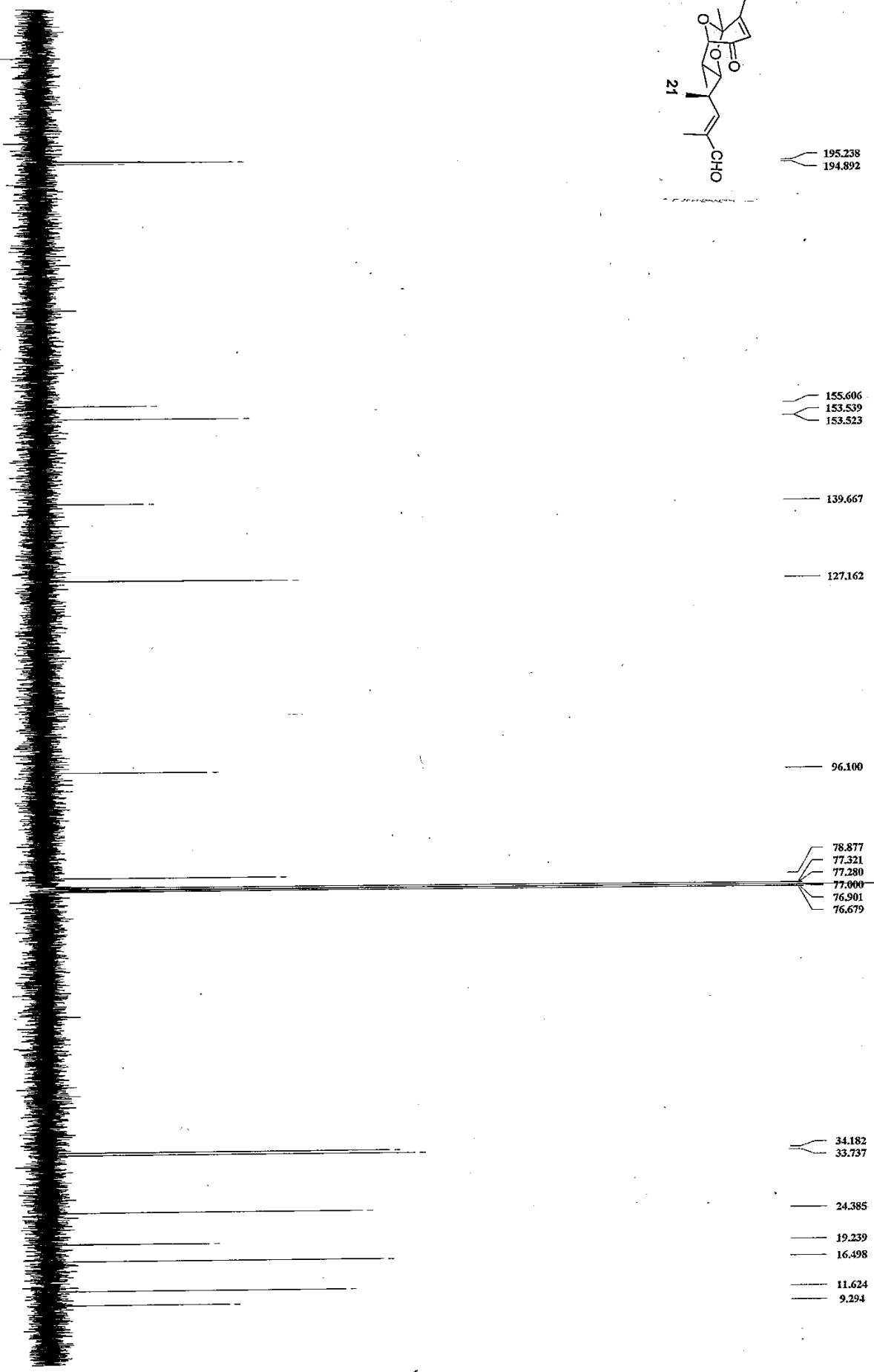
tirandaryoln C



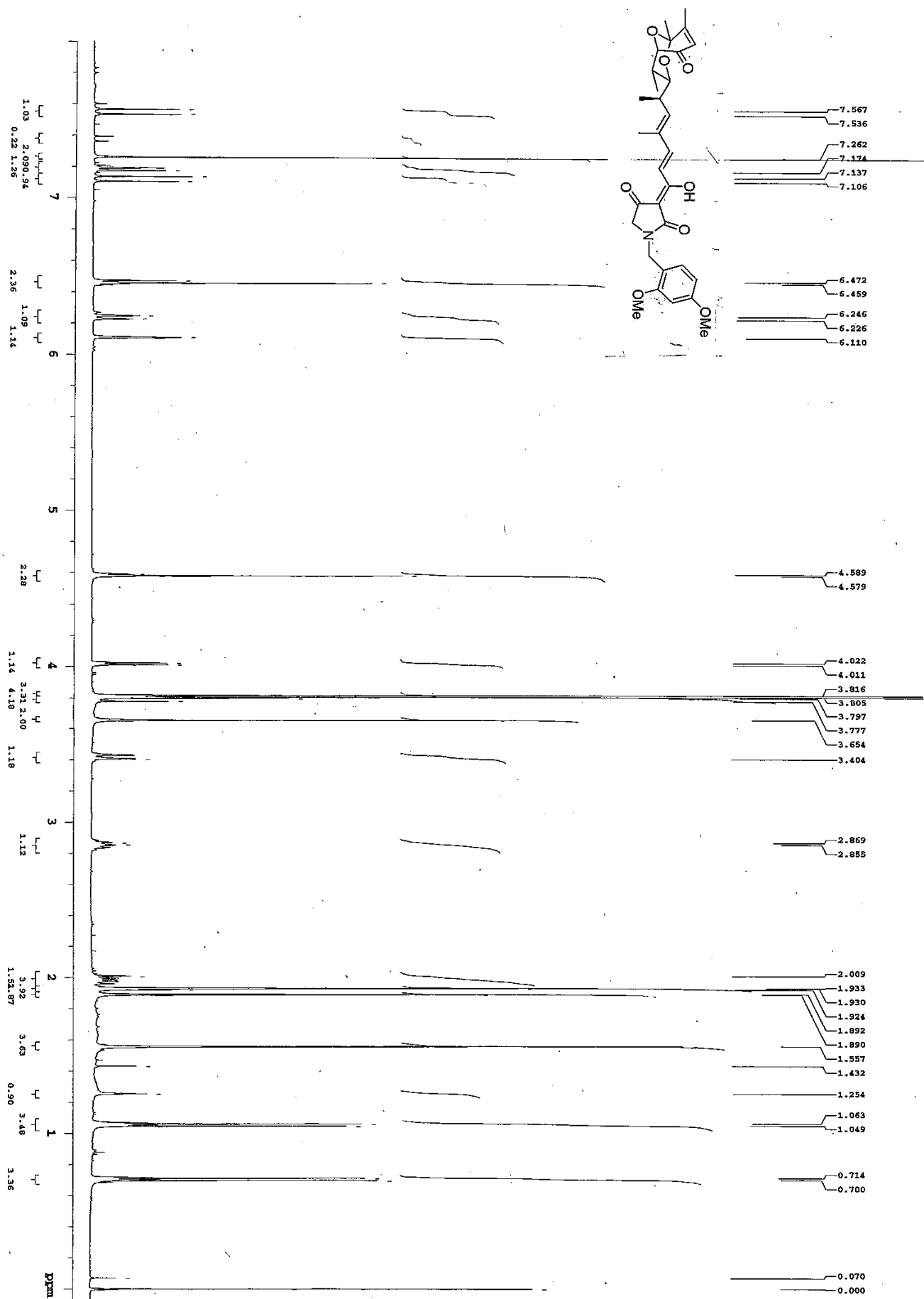


S104

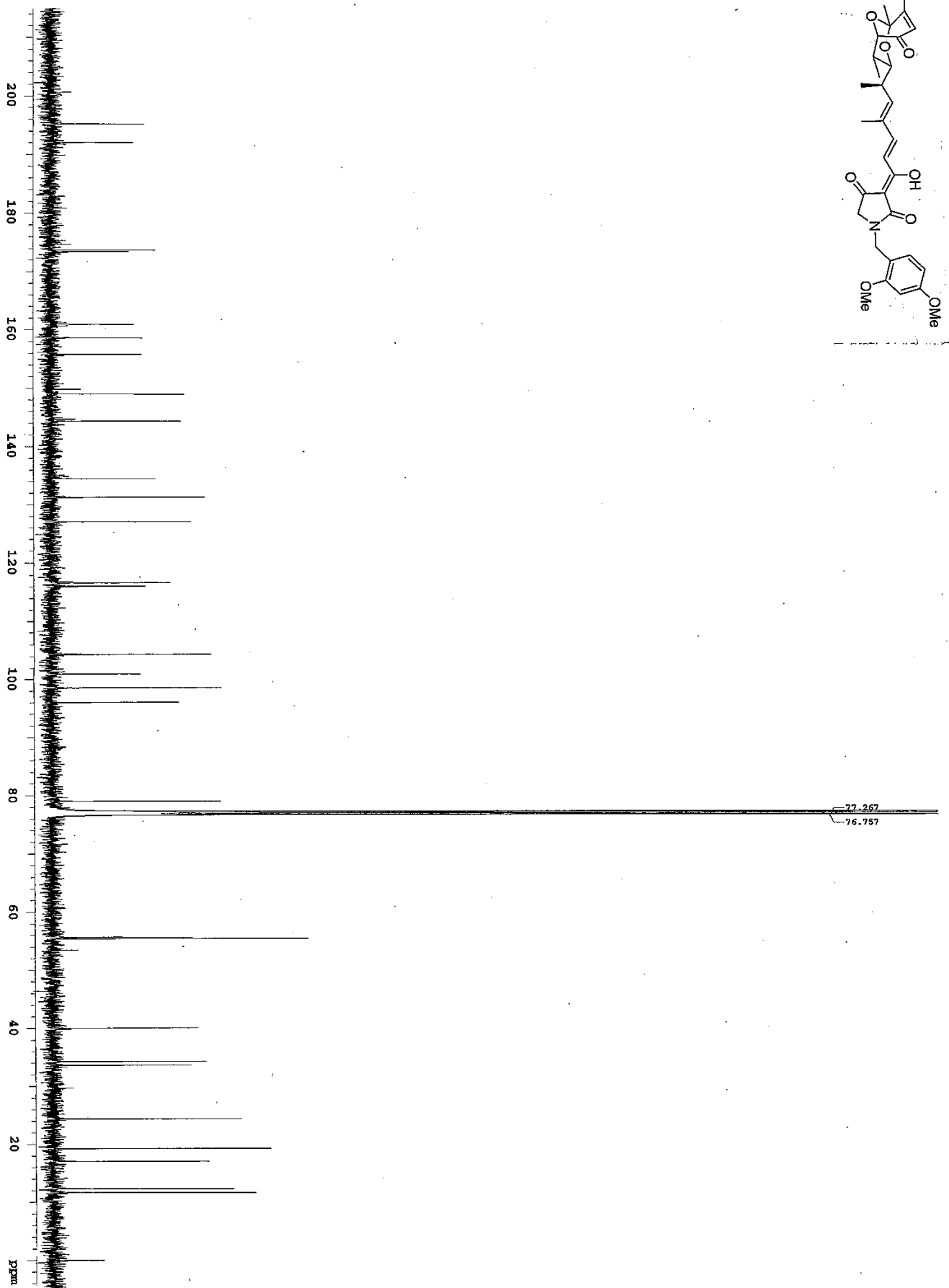
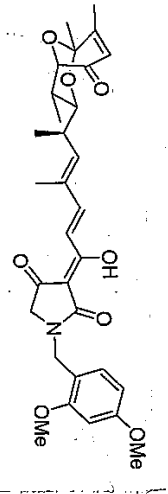
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200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
PPM



S105

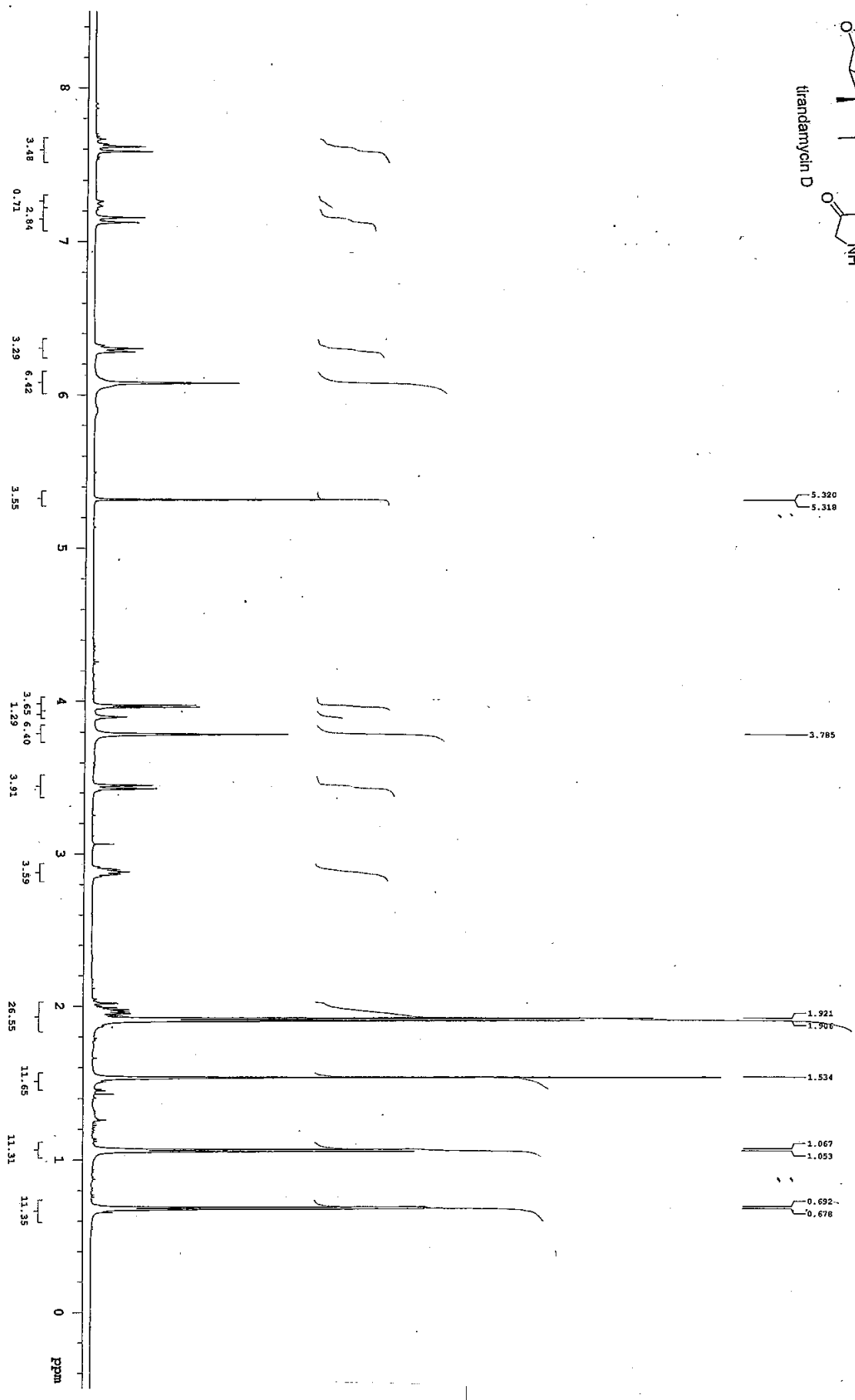
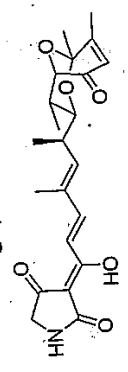


S106

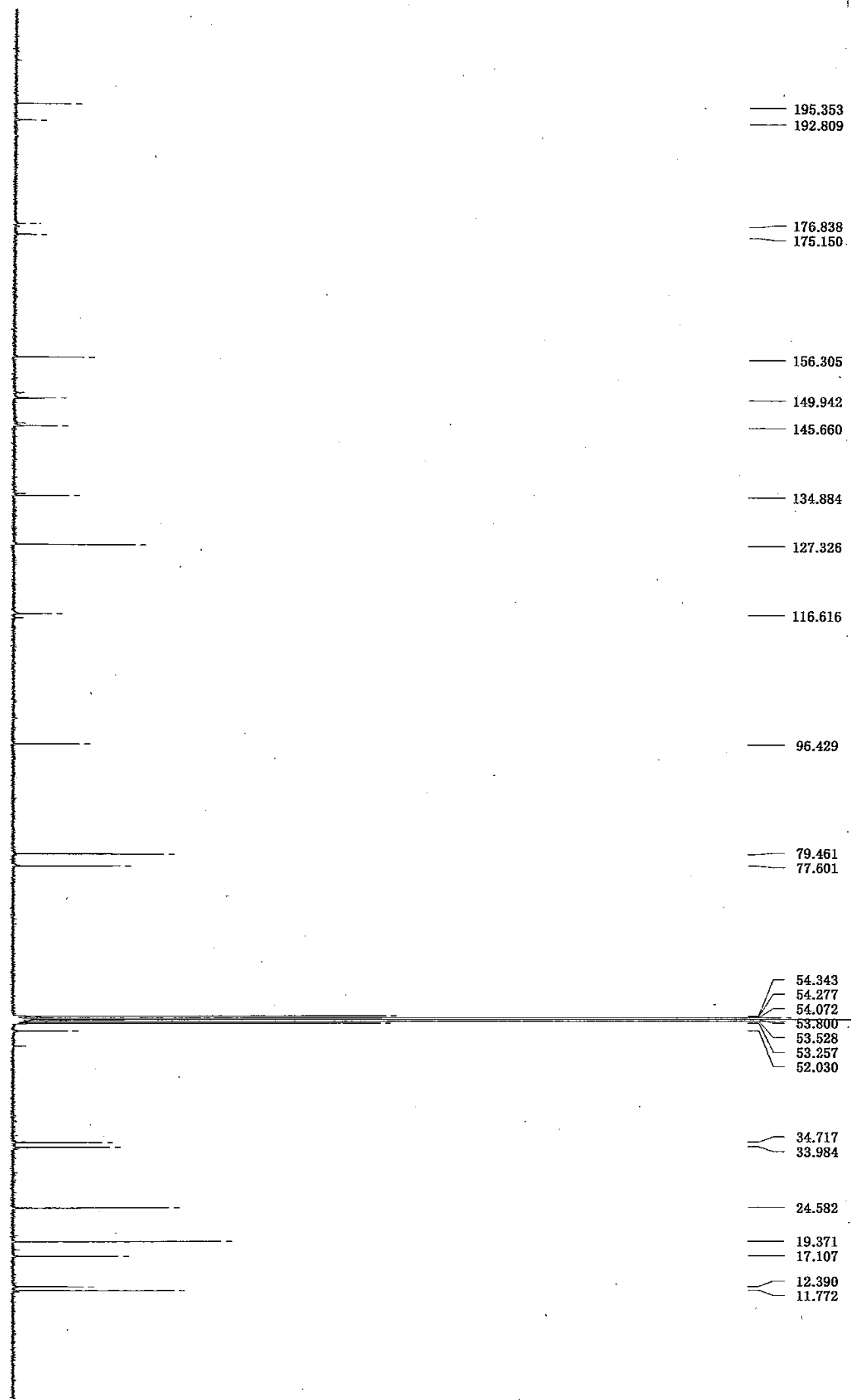


S107

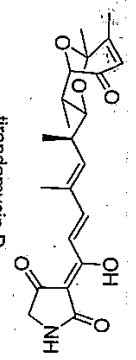
titandarycin D

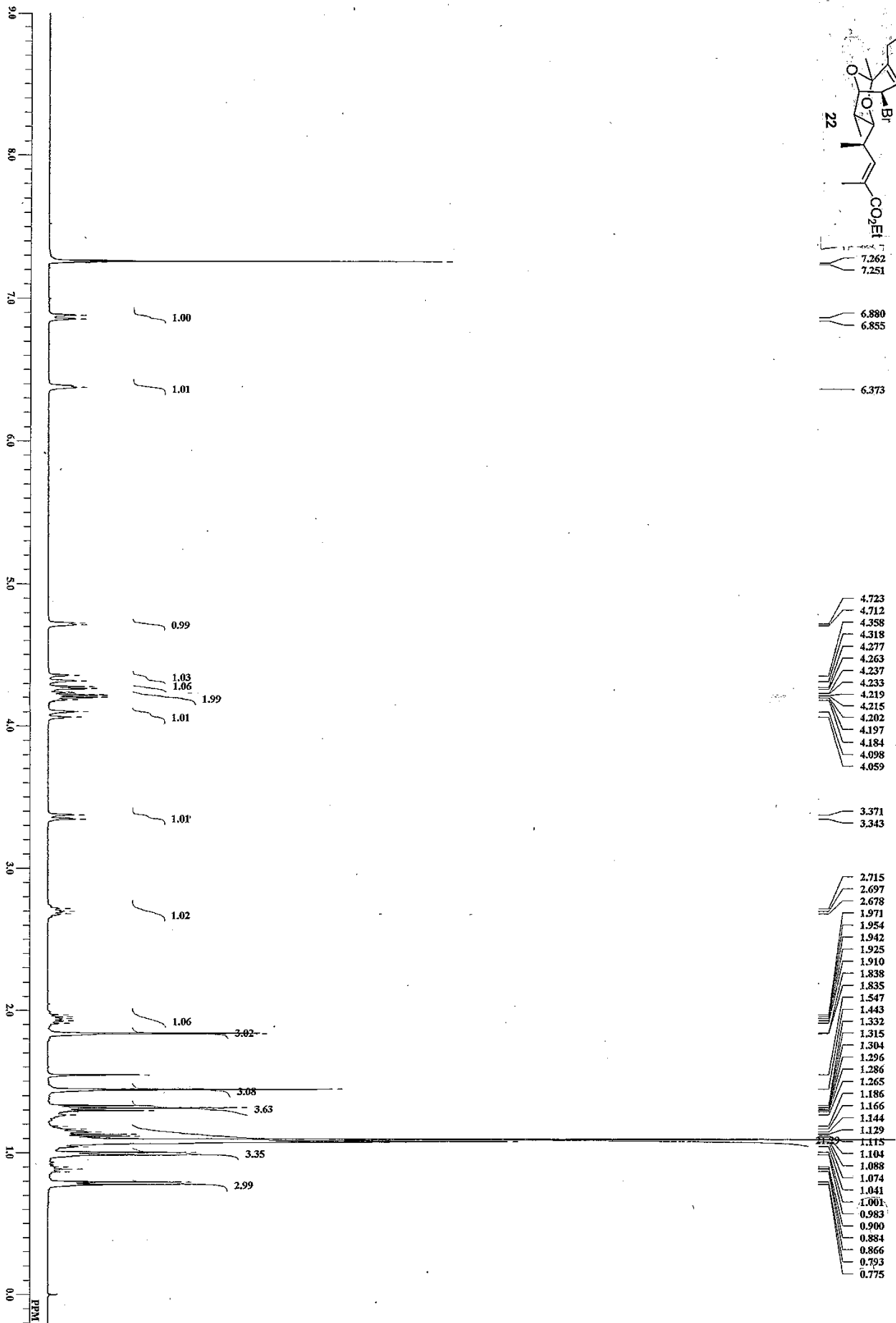


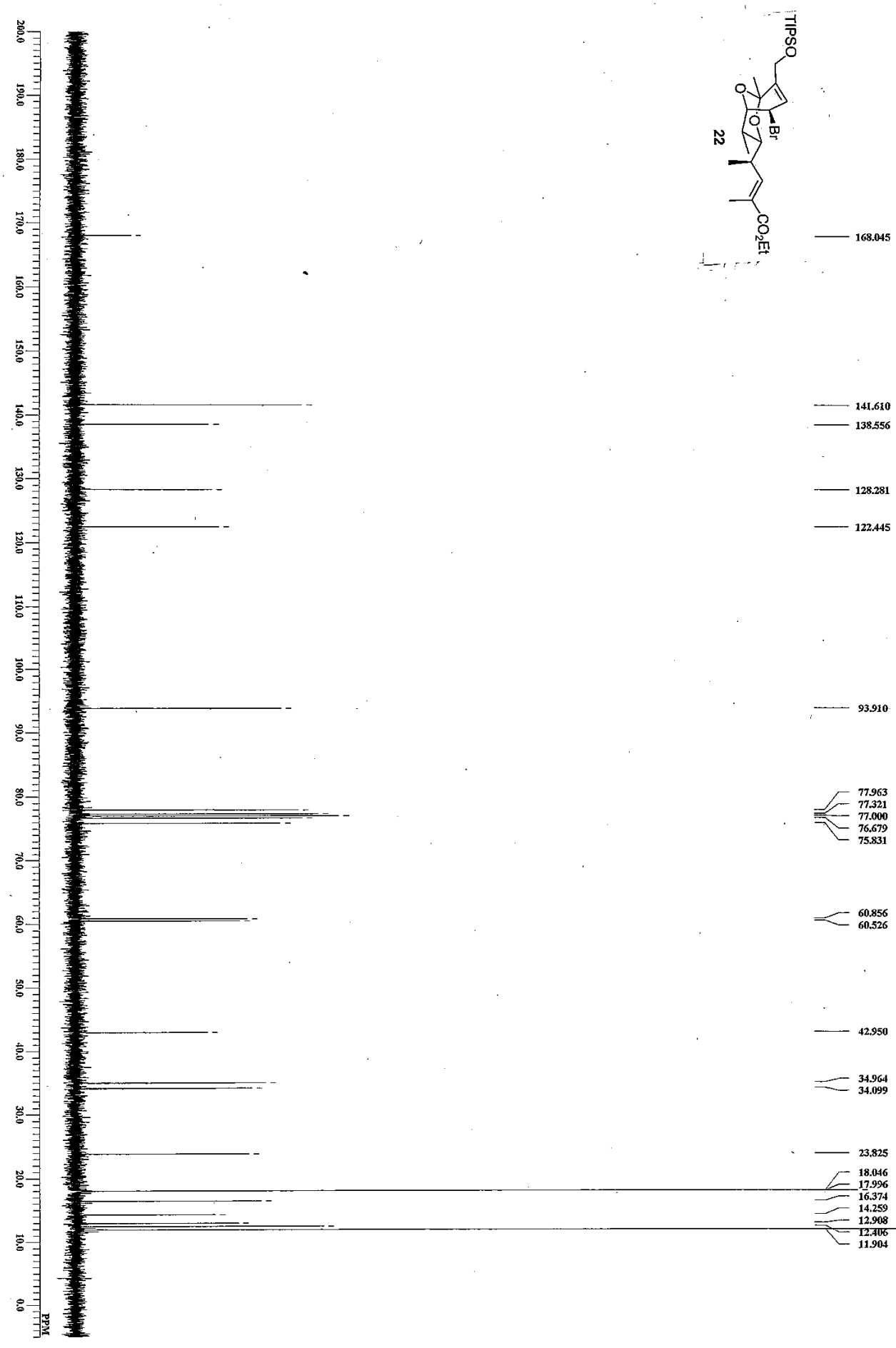
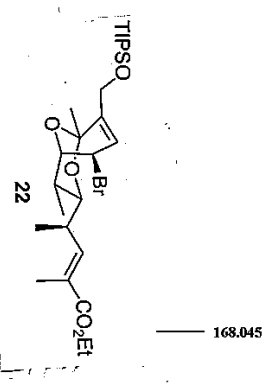
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200.0
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180.0
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160.0
150.0
140.0
130.0
120.0
110.0
100.0
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50.0
40.0
30.0
20.0
10.0
0.0
ppm

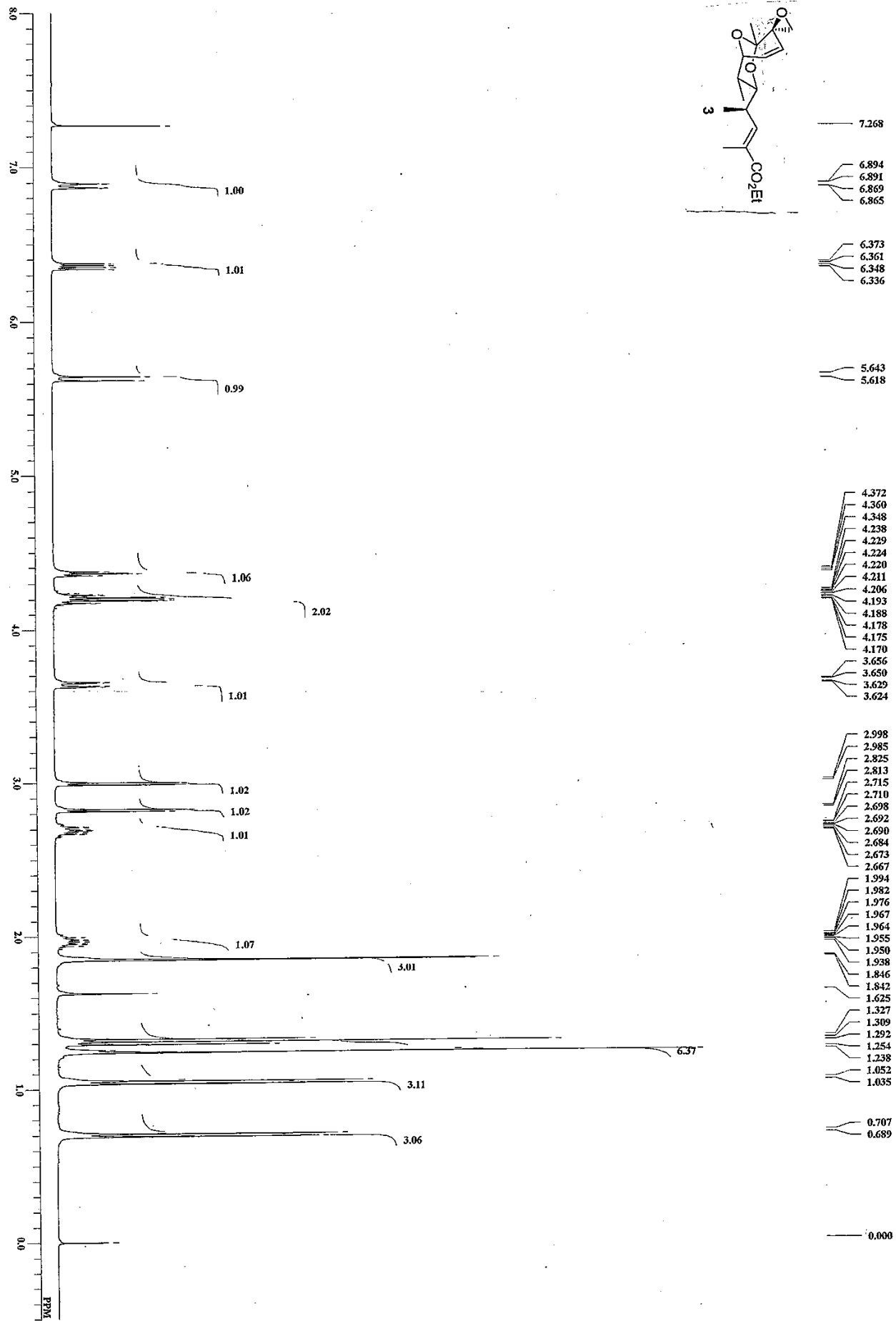


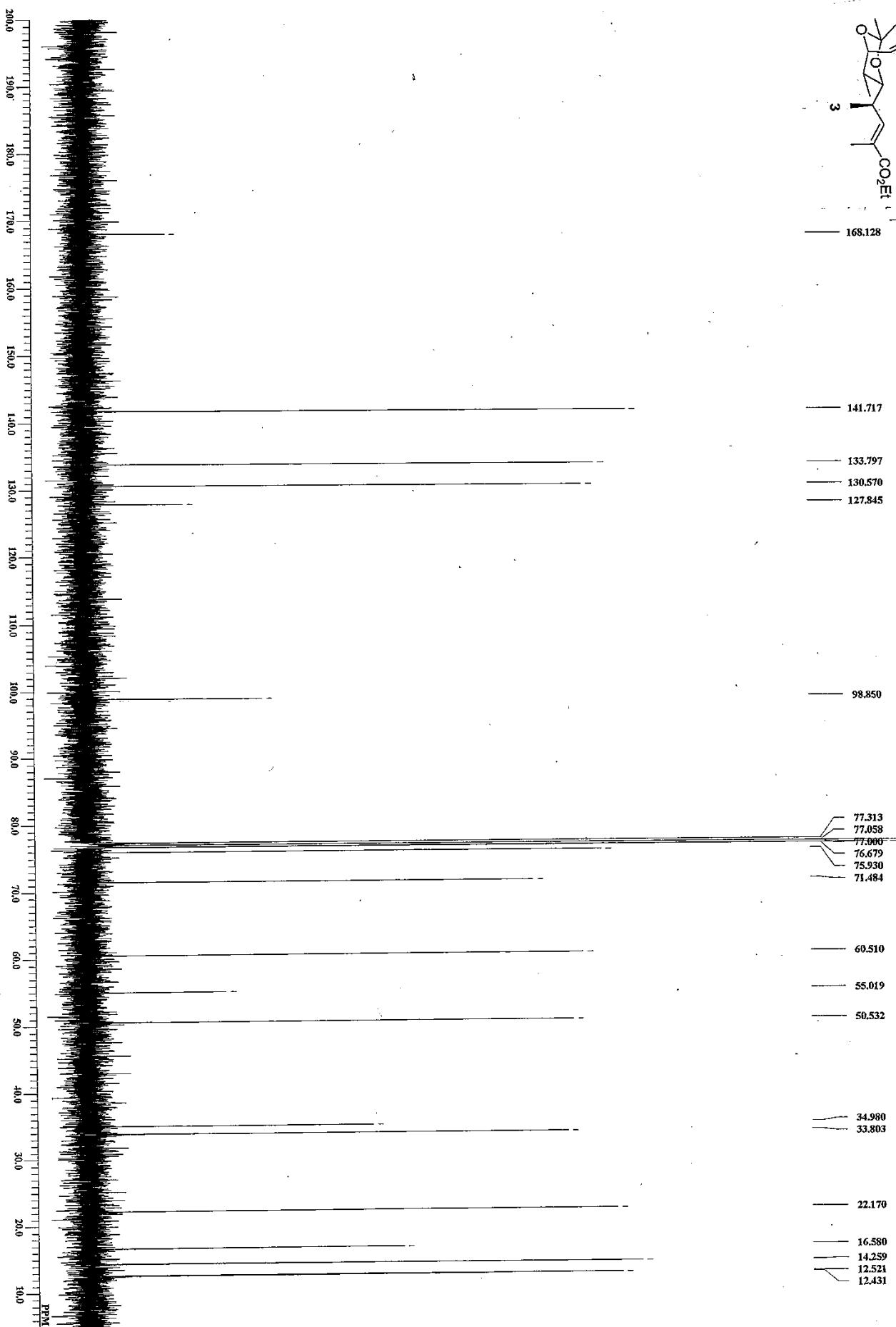
tirandamycin D

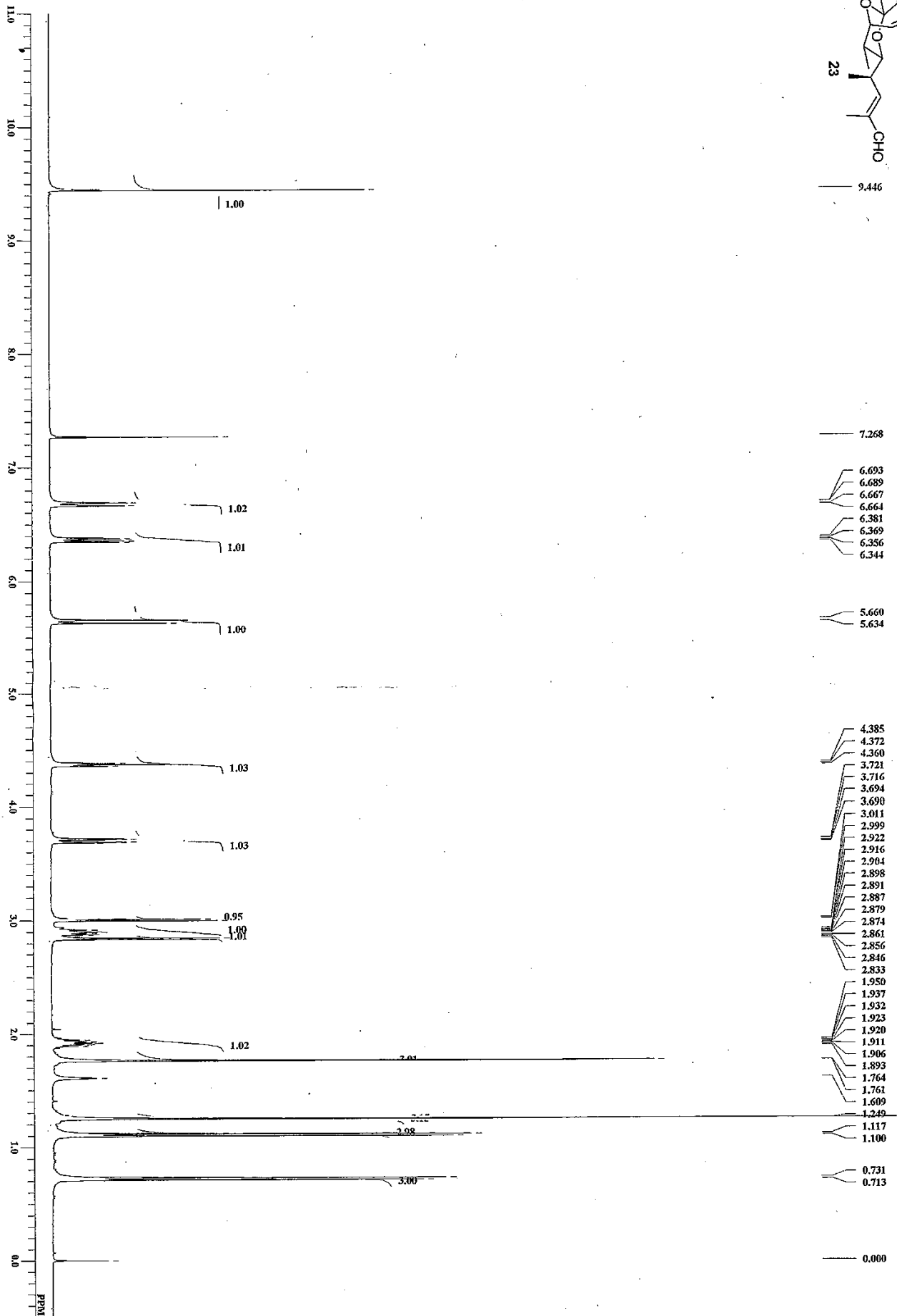
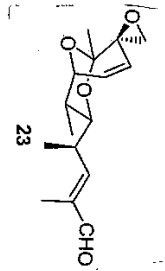






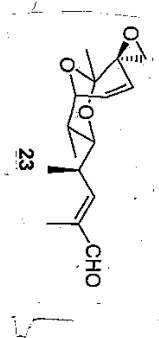
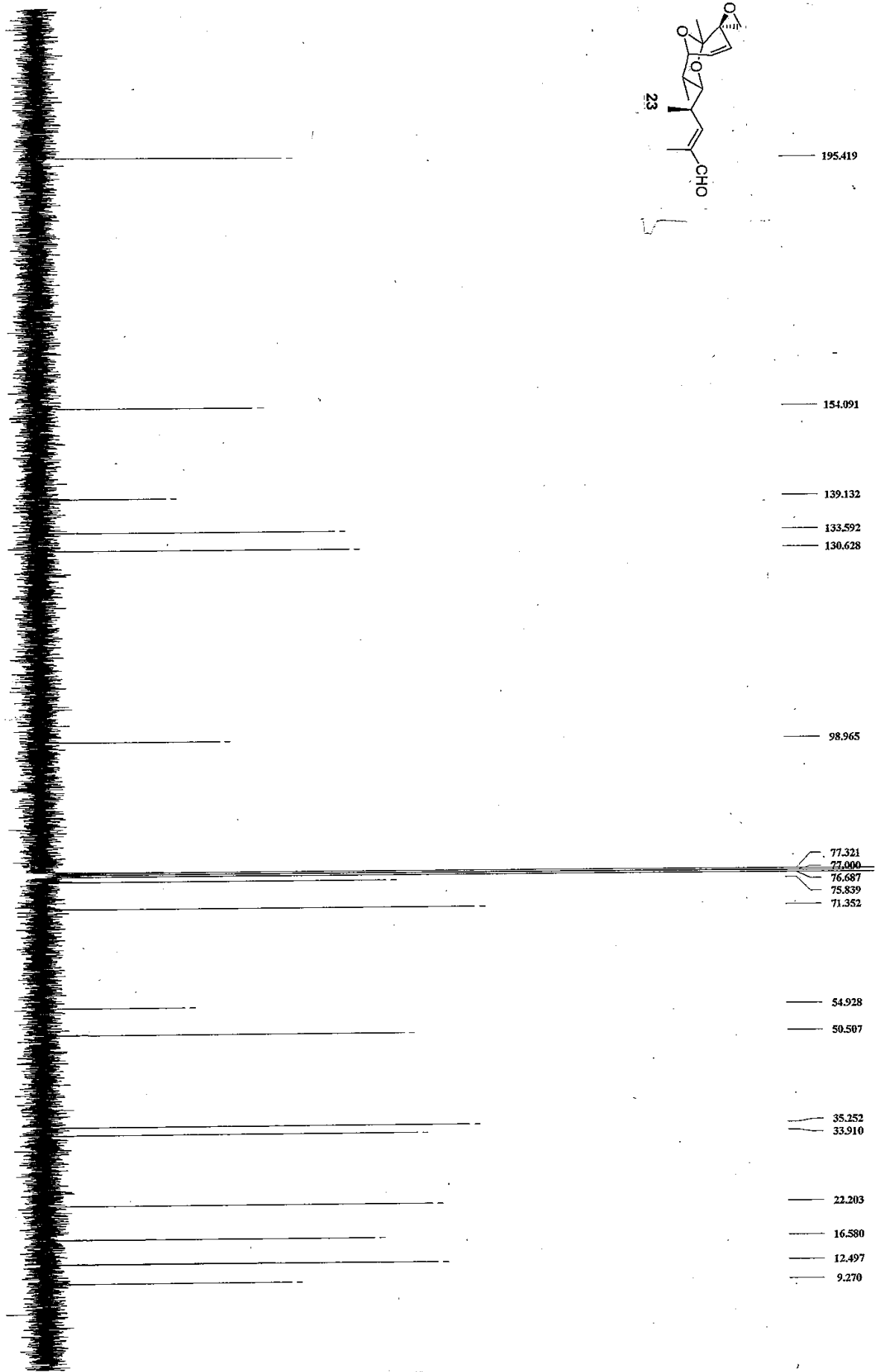


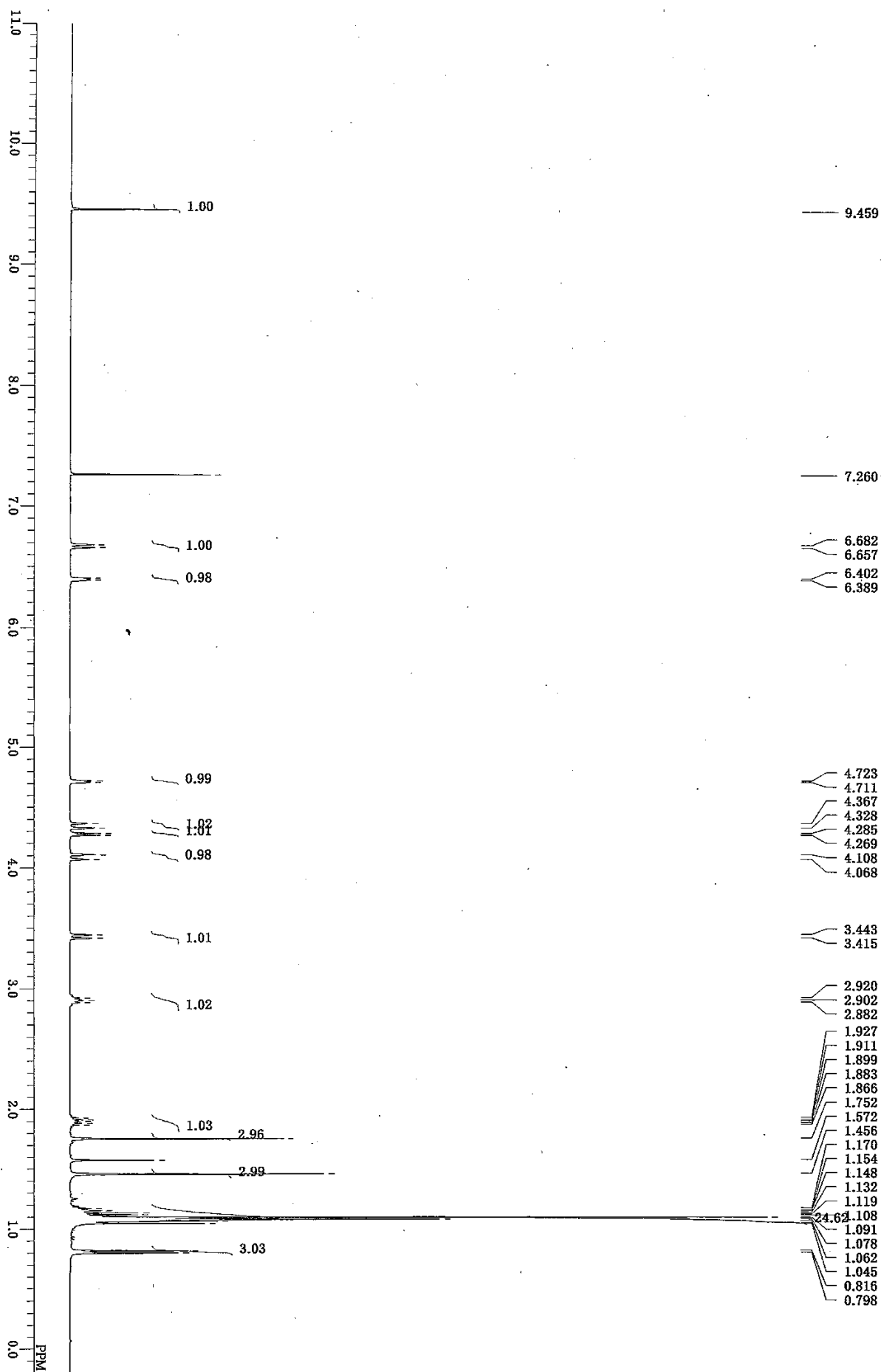
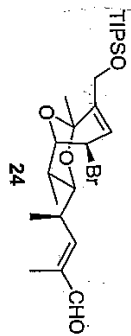




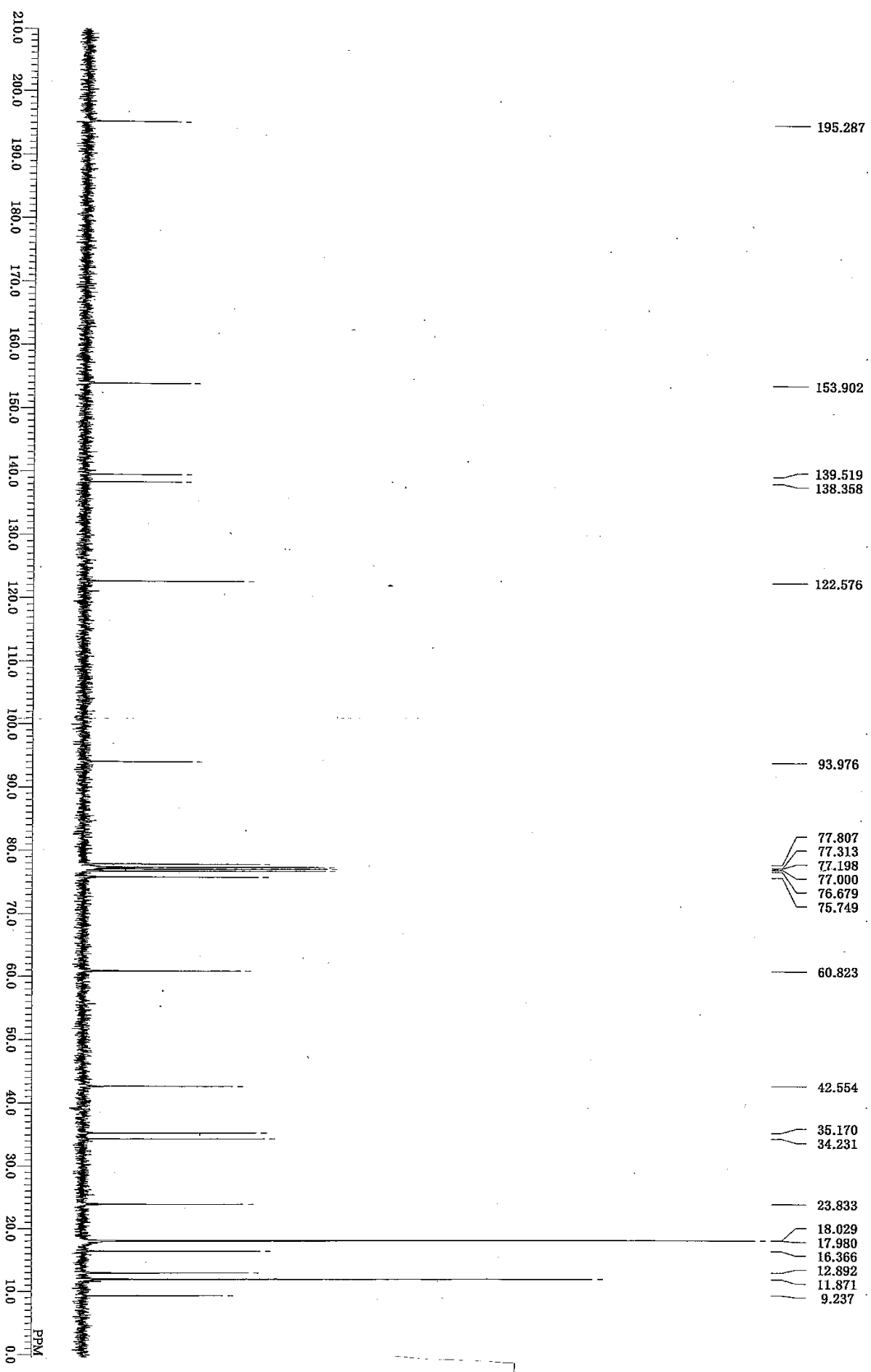
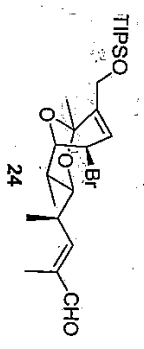
S114

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190.0
180.0
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160.0
150.0
140.0
130.0
120.0
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60.0
50.0
40.0
30.0
20.0
10.0
0.0



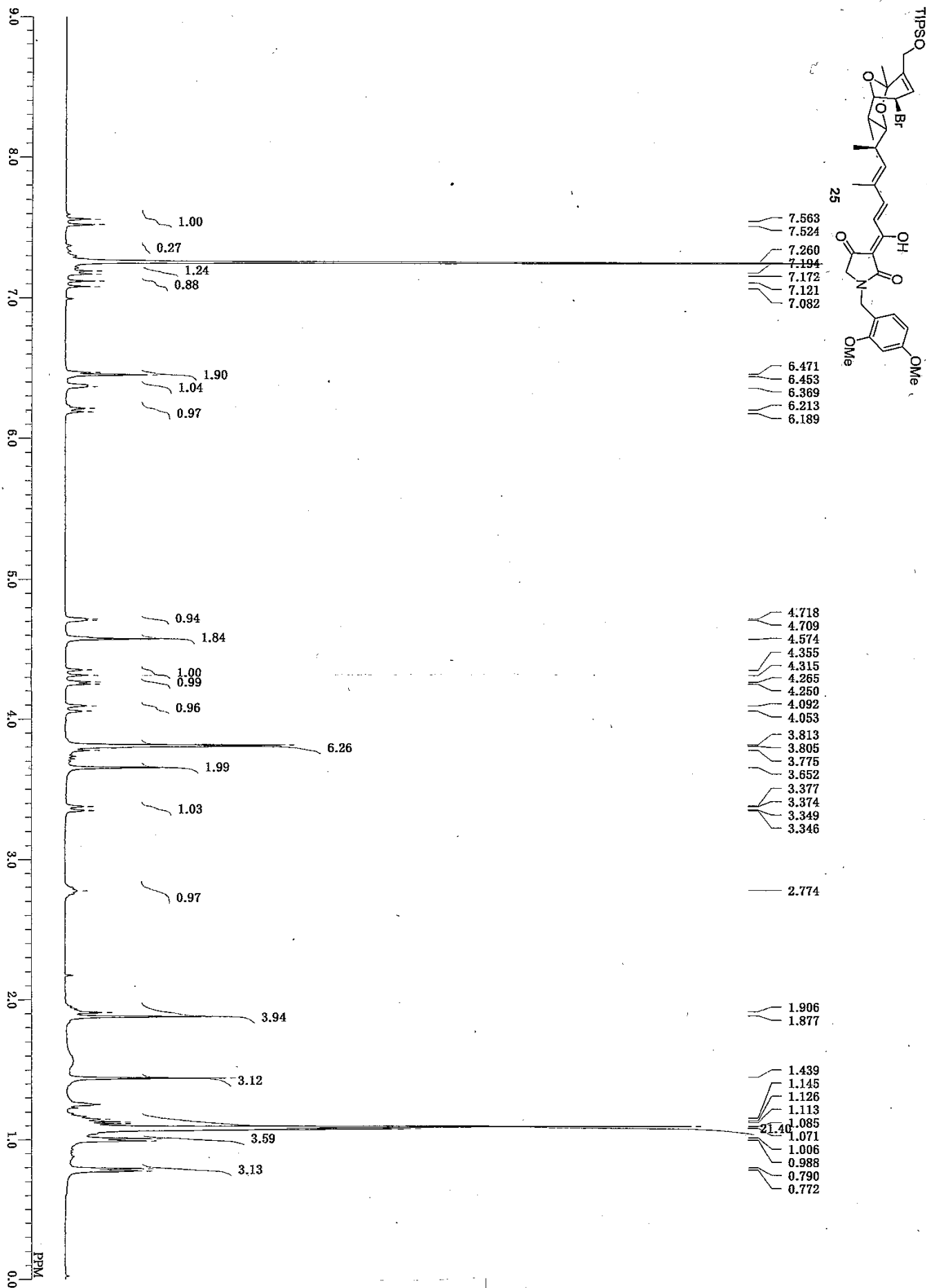


S116

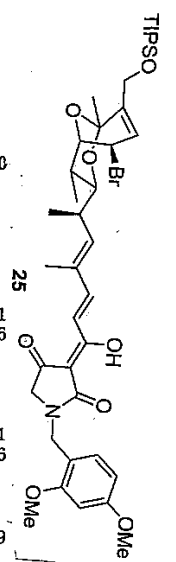
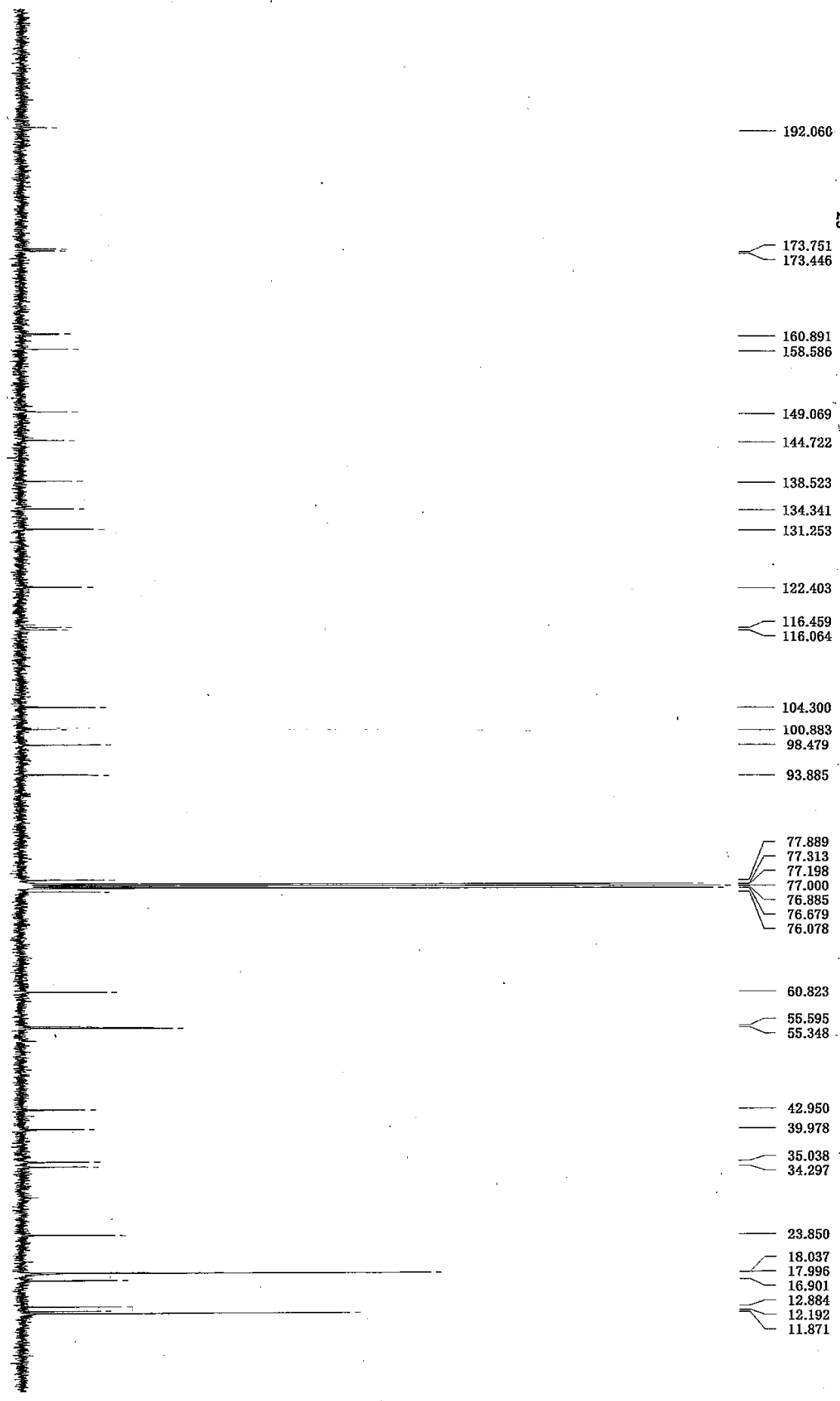


- 195.287
- 153.902
- 139.519
- 138.358
- 122.576
- 93.976
- 77.807
- 77.313
- 77.198
- 77.000
- 76.679
- 75.749
- 60.823
- 42.554
- 35.170
- 34.231
- 23.833
- 18.029
- 17.980
- 16.366
- 12.892
- 11.871
- 9.237

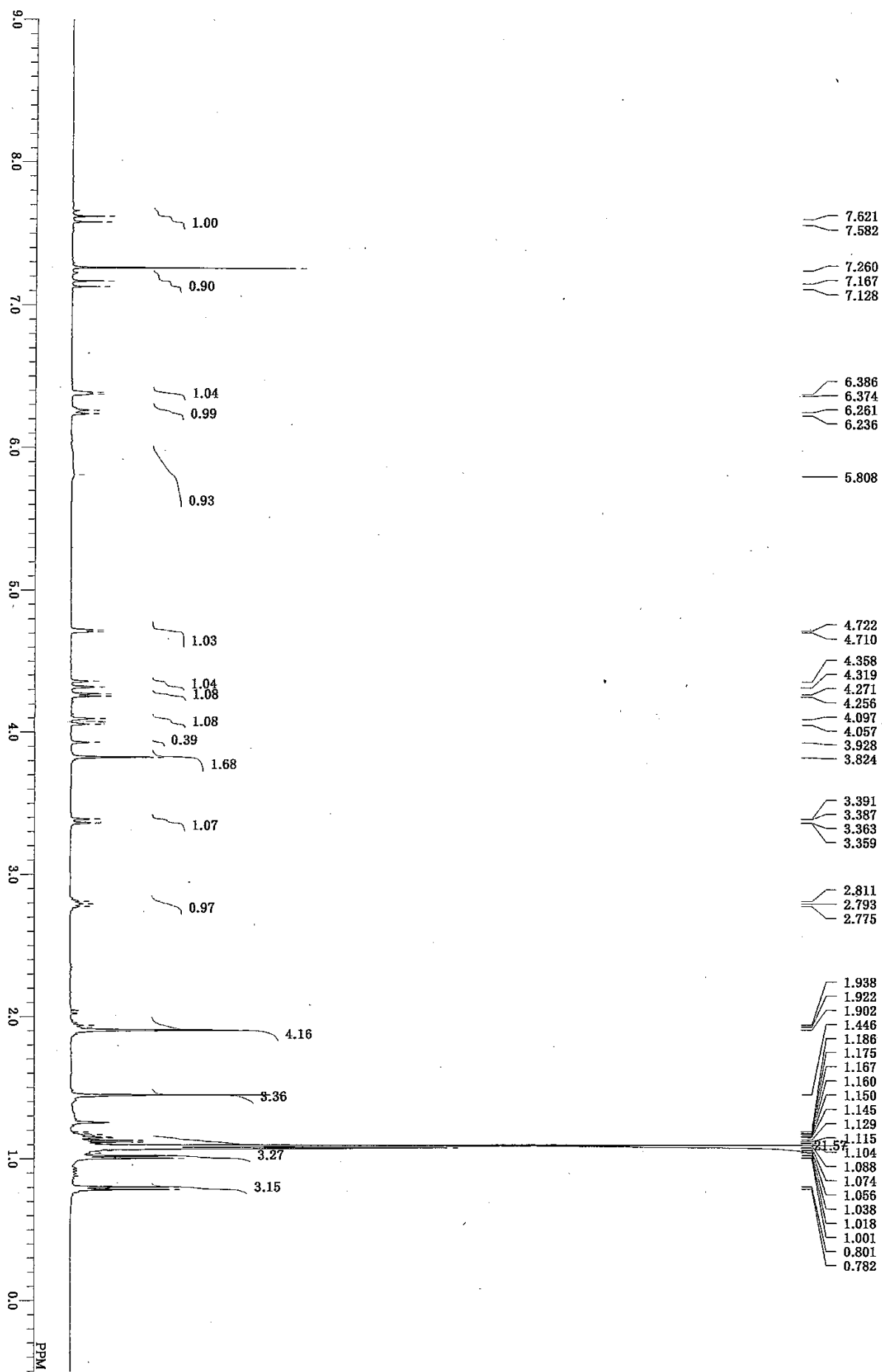
S117



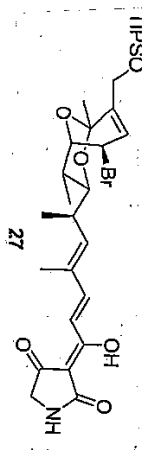
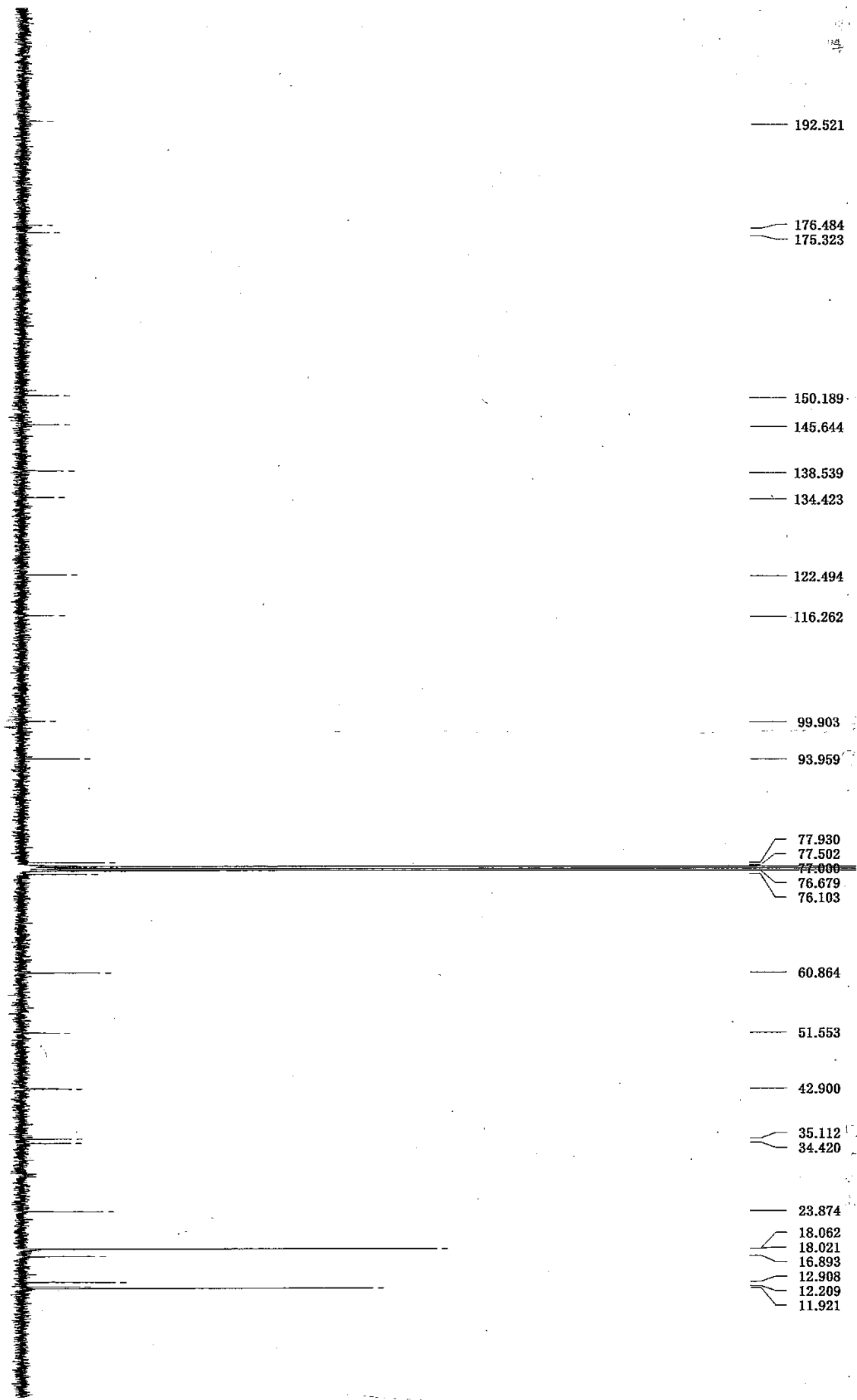
210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0.0
PPM



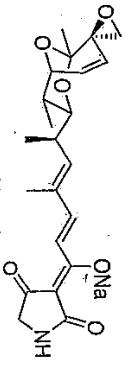
- 192.060
- 173.751
- 173.446
- 160.891
- 158.586
- 149.069
- 144.722
- 138.523
- 134.341
- 131.253
- 122.403
- 116.459
- 116.064
- 104.300
- 100.883
- 98.479
- 93.885
- 77.889
- 77.313
- 77.198
- 77.000
- 76.885
- 76.679
- 76.078
- 60.823
- 55.595
- 55.348
- 42.950
- 39.978
- 35.038
- 34.297
- 23.850
- 18.037
- 17.996
- 16.901
- 12.884
- 12.192
- 11.871



210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0.0 PPM

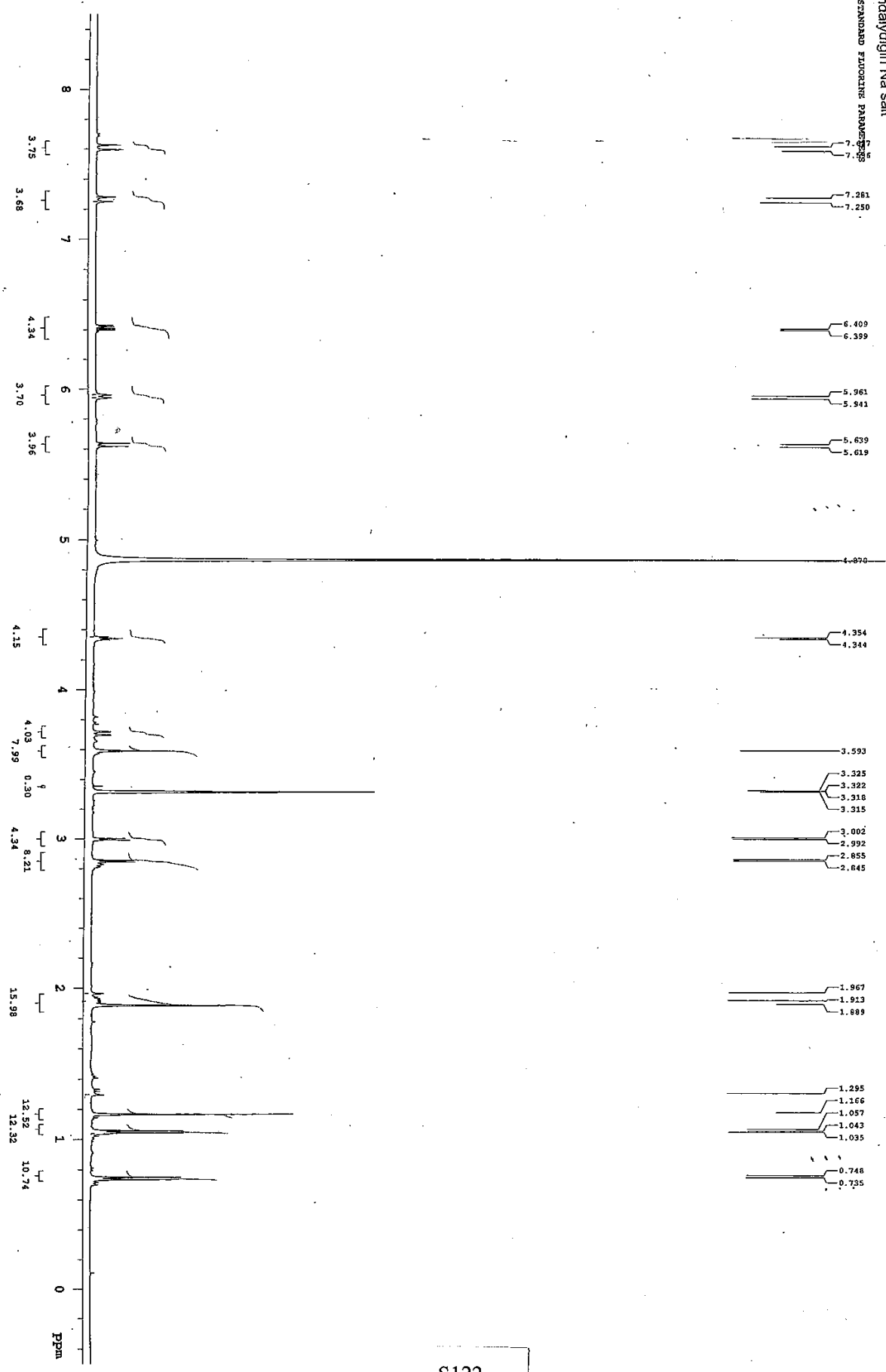


- 192.521
- 176.484
- 175.323
- 150.189
- 145.644
- 138.539
- 134.423
- 122.494
- 116.262
- 99.903
- 93.959
- 77.930
- 77.502
- 77.000
- 76.679
- 76.103
- 60.864
- 51.553
- 42.900
- 35.112
- 34.420
- 23.874
- 18.062
- 18.021
- 16.893
- 12.908
- 12.209
- 11.921

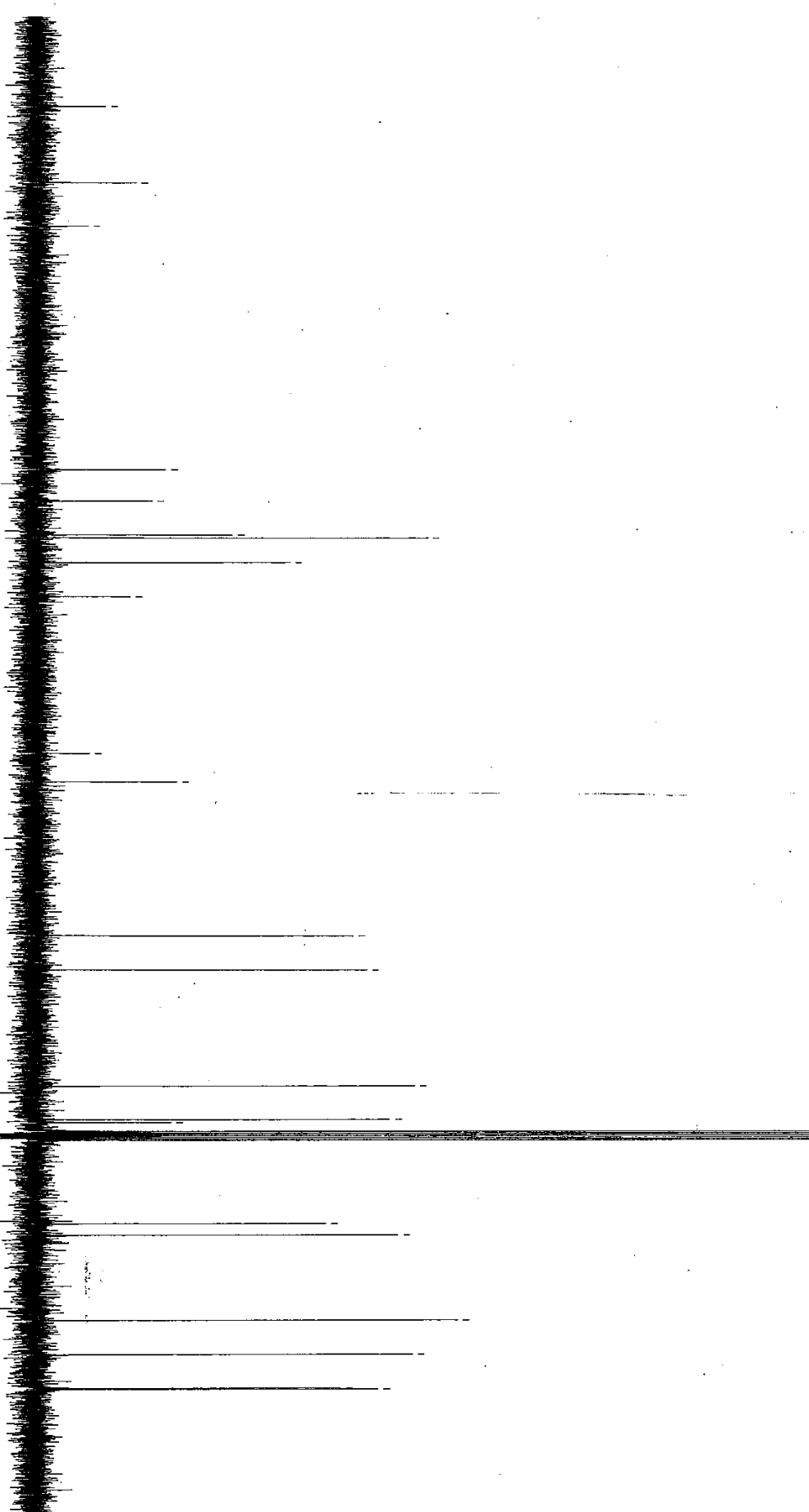


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STANDARD FLUORENE PARAMETERS



210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0.0 PPM



197.131
186.124
179.884

144.895
140.325
135.509
135.089
131.541
126.684

104.167
100.109

77.814
72.875
56.162
51.346
50.910
49.642
49.428
49.395
49.247
49.214
49.181
49.016
49.000
48.959
48.802
48.786
48.737
48.588
48.572
48.358

36.470
34.823
22.672
17.749
12.883
12.735

