Electronic Supplementary Information

for

Bioinspired Total Synthesis of Boneratamides A–C

Kaito Ooka,[a] Keisuke Nakanishi,[a] Yutaro Udagawa,[a] Yoshiyasu Ichikawa,*[b] and Seijiro Hosokawa*[a]

[a] Department of Applied Chemistry, Faculty of Advanced Science and Engineering, Waseda University,

3-4-1 Ohkubo, Shinjuku-ku, Tokyo 169-8555, Japan

[b] Faculty of Science, Kochi University,

Akebono-cho, Kochi 780-8520, Japan

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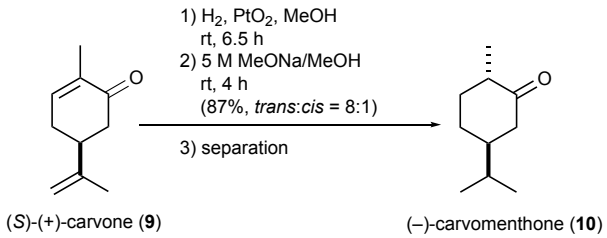
General Information

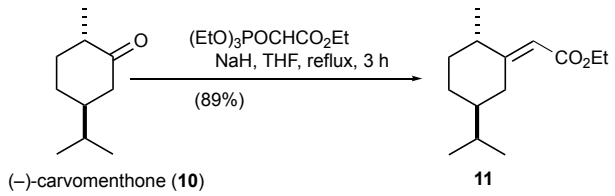
Melting points (Mp) were recorded on a Yanaco MP-S3 melting point apparatus and are not corrected. Optical rotations were measured on a JASCO P-2200 digital polarimeter at the sodium D line with a 100 mm path length cell, and are reported as follows:$[\alpha]_D^T$, concentration (g/100 mL), and solvent. Infrared spectra (IR), recorded on a JASCO FT/IR-460 spectrophotometer and Thermo Fisher Scientific Nicolet 6700 FT-IR spectrometer, are reported in wave number (cm^{-1}). Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on JEOL LA 500 (500 MHz), JEOL ECS-400 (400 MHz) and JEOL ECZ 500 (500 MHz) spectrometers. ^{1}H NMR chemical shifts (δ_H) are reported in parts per million (ppm) with the solvent resonance as the internal standard relative to chloroform (δ = 7.26), CHD_2OD (δ = 3.31), benzene (δ = 7.15) and DMSO (δ = 2.50). Data are reported as follows: chemical shift (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broadened, m = multiplet), coupling constants (*J*, given in Hz) and number of protons. ^{13}C NMR chemical shifts (δ) are recorded in parts per million (ppm) relative to the residual solvent peaks of $CDCl_3$ (δ = 77.16), CD_3OD (δ = 49.9), C_6D_6 (δ = 128.06) and DMSO-d_6 (δ = 39.5) as internal standards. High-resolution mass spectra (HRMS), measured on a BRUKER, FT-ICRMS, solariX XR, Thermo Fisher Scientific Exactive™ Plus, JEOL JMS-GCMATEII and JEOL JMS-T100CS AccuTOF spectrometer, are reported in *m/z*. Reactions were monitored by thin-layer chromatography on glass plates 0.25 mm coated with silica gel 60 F_{254} (MERCK 1.05715). Open-column chromatography was carried out with Silica gel 60 (particle size 0.063-0.200 mm, 70-230 mesh ASTM). Reactions were run under atmosphere of argon when the reactions were sensitive to moisture or oxygen. THF was distilled from $LiAlH_4$ before use. Dichloromethane was dried over molecular sieves 3 Å. Pyridine and triethylamine were stocked over anhydrous KOH. All other commercially available reagents were used as CH_2Cl_2

Experimental Section



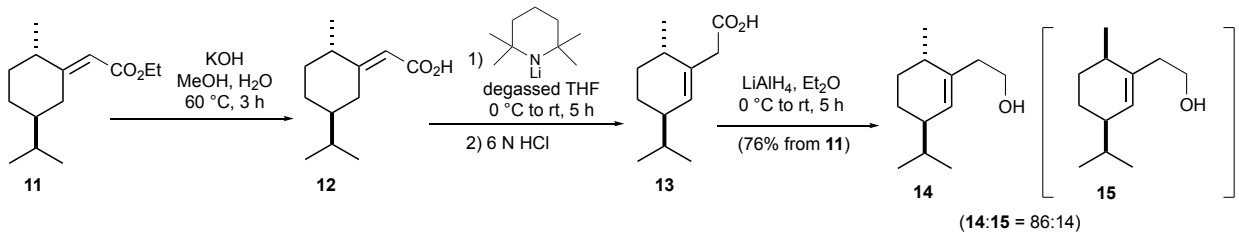
(*S*)-(+)-carvone (**9**) (–)-carvomenthone (**10**)

(–)-(2*S*,5*S*)-5-Isopropyl-2-methylcyclohexanone [(–)-carvomenthone] (10). A solution of (*S*)-(+)-carvone (**9**) (60.0 g, 26.6 mmol) dissolved in methanol (240 mL) in the presence of platinum oxide (120 mg, 0.13 mol%) was vigorously stirred at room temperature under hydrogen atmosphere for 6.5 h. The solution was filtered on the pad of Celite and concentrated under reduced pressure to afford a mixture of (–)-carvomenthone (**10**) (57.4 g). This mixture was treated with a solution of sodium methoxide (5.0 M solution in methanol, 3.4 mL). After standing at room temperature for 3.5 h, the reaction mixture was diluted with water. The aqueous layer was extracted with ether (×2). The combined organic layers were washed with water and brine, and dried (Na_2SO_4). Concentration under reduced pressure gave the residue (55.75 g), which was subjected to Kugelrohr distillation (oven temperature 85 °C/0.1 mmHg) to afford (–)-carvomenthone (**10**) (53.5 g, t*rans*:*cis* = 8:1, 87%). A portion of this product (25.0 g) was separated by silica-gel column chromatography (Et_2O/hexane 1:40→1:20) to afford the trans-isomer **10** as a colorless liquid (15.0 g). The ^{1}H NMR data obtained for **10** were in agreement with values previously reported for *ent*-(+)-**10**.[1] $[\alpha]_D^{22}$ = –11.9 (*c* = 3.17, EtOH) {Literature: $[\alpha]_D^{22}$ = –15.5 (*c* = 3, EtOH)[1]}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.40 (ddd, *J* = 13.0, 3.5, 2.5 Hz, 1H), 2.33 (dqd, *J* = 13.0, 6.5, 1.0 Hz, 1H), 2.13–2.01 (m, 2H), 1.85 (dddd, *J* = 12.5, 5.5, 2.5, 2.5 Hz, 1H), 1.61–1.51 (m, 2H), 1.44 (dddd, *J* = 13.0, 13.0, 11.5, 3.5 Hz, 1H), 1.30 (qd, *J* = 13.0, 3.5 Hz, 1H), 1.01 (d, *J* = 6.5 Hz, 3H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.89 (d, *J* = 6.5 Hz, 3H).



(–)-carvomenthone (**10**) **11**

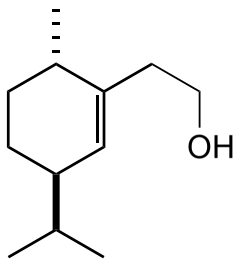
(*E*)-Ethyl 2-((2*S*,5*S*)-5-isopropyl-2-methylcyclohexylidene)acetate (11). A solution of (–)-carvomenthone (**10**) (9.90 g, 64.2 mmol) in THF (15 mL) was added to a solution of sodium trimethylphosphonoacetate {prepared from trimethylphosphonoacetate (43.2 g, 193 mmol) and sodium hydride (5.13 g; 60% in oil, washed with hexane, 128 mmol) in THF 80 mL)}. After heating at reflux for 3 h, The reaction mixture was cooled to room temperature and diluted with saturated aqueous NH_4Cl. The separated aqueous layer was extracted with Et_2O (×2), and the combined organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to afford the product (18.4 g). A portion of this crude product (11.4 g) was purified by column chromatography on silica gel eluting with EtOAc/hexane (1:40) to afford **11** (7.95 g, 89%) as a colorless oil. The ^{1}H NMR data obtained for **11** were in agreement with values previously reported for *ent*-**11**.[3] ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 5.54 (brs, 1H), 4.16 (qd, *J* = 7.0, 2.0 Hz, 2H), 3.94 (brddd, *J* = 13.0, 2.5, 2.0 Hz, 1H), 2.18–2.04 (m, 1H), 1.94 (ddd, *J* = 12.5, 7.0, 2.0 Hz, 1H), 1.80–1.70 (m, 1H), 1.55–1.45 (m, 2H), 1.29 (t, *J* = 7.0 Hz, 3H), 1.29–1.23 (m, 2H), 1.17–1.08 (m, 1H), 1.04 (d, *J* = 6.5 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H), 0.90 (d, *J* = 7.0 Hz, 3H).



2-((3*R*,6*S*)-3-Isopropyl-6-methylcyclohex-1-enyl)ethanol (14). To a solution of ester **11** (2.50 g, 11.1 mmol) dissolved in a mixture of methanol (16 mL) and water (12 mL) was added potassium hydroxide (4.06 g, 72.4 mmol). The solution was heated at 60 °C for 3 h and washed with Et_2O (×3). The aqueous layer was acidified with 6 N HCl, and extracted with EtOAc (×3). The combined organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to afford the crude product **12** (2.44 g), which was used for the subsequent reactions without purification.

A solution of 2,2,6,6-tetramethylpiperidine (15 mL, 89.1 mmol) in THF (46 mL) was degassed by three freeze-thaw cycles. To this solution cooled to –20 °C (a sodium chloride/ice bath) under argon atmosphere was added a solution of *n*-butyllithium (1.15 M in hexane, 39 mL, 44.6 mmol) dropwise. The solution was warmed to 0 °C and stirred at 0 °C for 50 minutes. To this solution was added **12** (2.44 g) in THF (10 mL) at 0 °C. The cooling bath was removed and stirring continued at room temperature for 5 h. The reaction mixture was acidified with aqueous 6 N HCl, and the separated aqueous layer was extracted with ether (×3). The combined organic layer was extracted with aqueous 1 N NaOH. The separated aqueous layer was washed with Et_2O (×3), acidified with 6 M HCl, and extracted with EtOAc (×3). The combined organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to afford the crude product **13** (2.29 g) , which was used for the subsequent reactions without purification. To a suspension of lithium aluminum hydride (1.27 g, 33.4 mmol) in Et_2O (45 mL) cooled to 0 °C under nitrogen atmosphere was added a solution of **13** (2.29 g) in Et_2O (15 mL). The cooling bath was removed and stirring was continued for 5 h at room temperature. The reaction mixture was cooled to 0 °C and treated with several drops of ethanol to quench the

reaction and aqueous potassium sodium (+)-tartrate tetrahydrate solution (12.6 g). After stirring at room temperature for 1 h, the solution was filtered on the pad of Celite. The separated aqueous layer was extracted with Et_2O (×3). The combined organic extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure to afford crude residue, which was purified by silica-gel column chromatography (EtOAc/hexane 1:7) to provide **14** (1.54 g, 12.5 mmol, 76% for three steps) as a pale yellow oil. The ^1H and ^{13}C NMR data obtained for **14** are in good agreement with values previously reported.[1] $[\alpha]_D^{23}$ = –39.6 (*c* = 1.15, CH_2Cl_2) {Literature reported for *ent*-(+)-**14**: $[\alpha]_D^{25}$ = +39.3 (*c* = 1, CH_2Cl_2)[1]}{Literature reported for *ent*-(+)-**14**: $[\alpha]_D^{20}$ = +34 (*c* = 2.20, $CHCl_3$)[2]}; IR (KBr): ν_{max} = 3327, 2956, 2930, 2871, 1463, 1446, 1385, 1367, 1043 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 5.39 (brs, 1H), 3.71–3.57 (m, 2H), 2.47–2.39 (m, 1H), 2.17 (dq, *J* = 8.5, 7.0 Hz, 1H), 2.14–2.06 (m, 1H), 1.97–1.90 (m, 1H), 1.84 (dddd, *J* = 9.5, 5.0, 4.5, 2.0 Hz, 1H), 1.66 (dddd, *J* = 10.0, 5.0, 5.0, 1.0 Hz, 1H), 1.61–1.51 (m, 1H), 1.23 (dddd, *J* = 11.0, 9.5, 6.5, 2.0 Hz, 1H), 1.19 (dddd, *J* = 10.5, 9.5, 6.5, 2.0 Hz, 1H), 0.99 (d, *J* = 7.0 Hz, 3H), 0.88 (d, *J* = 7.0 Hz, 3H), 0.85 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 138.2, 129.0, 60.4, 42.3, 38.1, 32.3, 32.2, 32.0, 24.7, 19.9, 19.7, 19.4; HRMS (ESI): m/z calcd for $C_{12}H_{23}O$ $[M+H]^+$, 183.1743, found 183. 1745.



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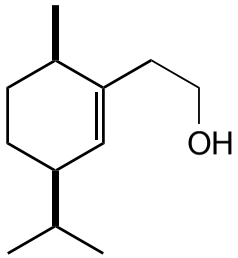

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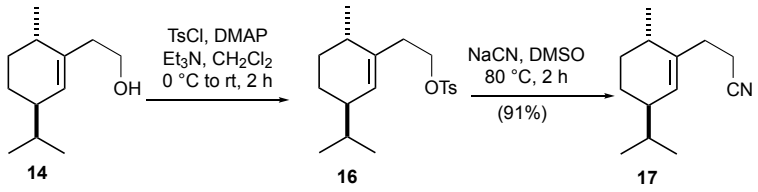
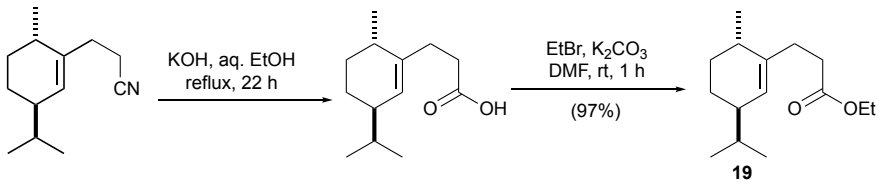
14:**15** = 86:14



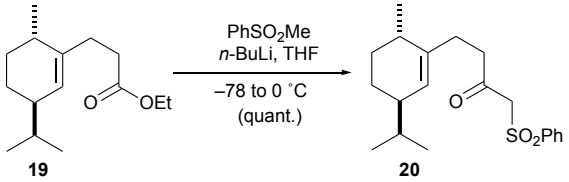
3-((3*R*,6*S*)-3-Isopropyl-6-methylcyclohex-1-enyl)propanenitrile (17). To a solution of *p*-toluenesulfonyl chloride (3.92 g, 20.6 mmol), 4-dimethylaminopyridine (251 mg, 2.05 mmol) and triethylamine (4.4 mL, 32 mmol) dissolved in CH_2Cl_2 (75 mL) cooled to 0 °C was added a solution of **14** (2.50 g, 13.7 mmol) in CH_2Cl_2 (5.0 mL). After stirring at room temperature for 2 h, saturated aqueous $NaHCO_3$ was added. The separated aqueous layer was extracted with Et_2O (×3). The combined organic layers were dried over Na_2SO_4. Concentration under reduced pressure gave **16**, which was successively dissolved in DMSO (75 mL). This solution was treated with sodium cyanide (1.21 g, 24.7 mmol), and heated at 80 ˚C for 2 h. After cooling to room temperature, the reaction mixture was diluted with H_2O and extracted with EtOAc (×3). The combined organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to afford a residue, which was purified by silica-gel column chromatography (EtOAc/hexane 1:10) to provide **17** (2.39 g, 12.5 mmol, 91% for two steps) as a pale yellow oil. 2-((3*R*,6*S*)-3-Isopropyl-6-methylcyclohex-1-enyl)ethyl 4-methylbenzenesulfonate (**16**): $[\alpha]_D^{24}$ = –23.4 (*c* = 2.66, $CHCl_3$); IR (KBr): ν_{max} = 2957, 2929, 2871, 1599, 1463, 1362, 1177, 961, 909, 815 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.79 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 5.27 (brs, 1H), 4.07 (ddd, *J* = 14.5, 9.5, 8.0 Hz, 1H), 4.06 (ddd, *J* = 14.5, 9.5, 7.5 Hz, 1H), 2.45 (s, 1H), 2.44–2.36 (m, 1H), 2.28 (ddd, *J* = 14.0, 8.0, 7.5 Hz, 1H), 2.01–1.92 (m, 1H), 1.88–1.81 (m, 1H), 1.77 (dddd, *J* = 10.0, 5.0, 4.5, 2.0 Hz, 1H), 1.60 (dddd, *J* = 10.0, 5.0, 4.5, 1.0 Hz, 1H), 1.50 (qd, *J* = 6.5, 1.5 Hz, 1H), 1.15 (dddd, *J* = 11.0, 10.0, 6.5, 2.0 Hz, 1H), 1.13 (dddd, *J* = 11.5, 10.0, 6.5, 1.0 Hz, 1H), 0.90 (d, *J* = 7.0 Hz, 3H), 0.84 (d, *J* = 6.5 Hz, 3H), 0.81 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 144.7, 136.7, 133.4, 129.8, 129.1, 127.9, 69.4, 42.2, 34.2, 32.3, 32.2, 24.3, 21.7, 19.8, 19.7, 19.3; HRMS (ESI): m/z calcd for $C_{19}H_{28}O_3NaS$ $[M+Na]^+$, 359.1655, found 359.1650. Compound **17**: $[\alpha]_D^{25}$ = –26.1 (*c* = 2.20, $CHCl_3$); IR (KBr): ν_{max} =

2957, 2931, 2871, 2246, 1463, 1445, 1385, 1368 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 5.41 (brs, 1H), 2.51–2.26 (m, 4H), 2.16–2.06 (m, 1H), 1.96–1.89 (m, 1H), 1.86 (dddd, *J* = 10.0, 5.5, 5.0, 2.0 Hz, 1H), 1.66 (dddd, *J* = 10.0, 5.5, 5.0, 1.5 Hz, 1H), 1.59 (qd, *J* = 7.0, 1.5 Hz, 1H),1.25 (dddd, *J* = 11.5, 10.0, 6.0, 2.0 Hz, 1H), 1.21 (dddd, *J* = 12.0, 10.0, 6.0, 1.5 Hz, 1H), 0.99 (d, *J* = 7.0 Hz, 3H), 0.91 (d, *J* = 7.0 Hz, 3H), 0.87 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (C_6D_6, 100 MHz) δ = 138.4, 128.4, 119.7, 42.2, 32.3, 32.0, 31.9, 30.6, 21.3, 19.8, 19.6, 19.3, 16.5; HRMS (ESI): m/z calcd for $C_{13}H_{22}N$ $[M+H]^+$, 192.1747, found 192.1748.



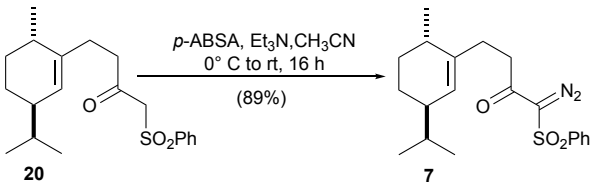
Ethyl 3-((3*R*,6*S*)-3-isopropyl-6-methylcyclohex-1-enyl)propanoate (19). A solution of **17** (1.80 g, 9.40 mmol) and potassium hydroxide (2.64g, 47.0 mmol) dissolved in a mixture of EtOH (25 mL) and H_2O (25 mL) was heated at 100 ˚C for 22 h. After cooling to room temperature, the reaction mixture was extracted with Et_2O (×3). The aqueous layer was acidified with 1 M HCl (10 mL), and then extracted with EtOAc (×3). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure to afford crude carboxylic acid **18**, which was dissolved in DMF (62 mL). To this solution was added solid K_2CO_3 (6.49 g, 47.0 mmol). After stirring at room temperature for 1 h, ethyl bromide (0.84 mL, 11.3 mmol) was added. The reaction mixture was stirred at room temperature for 2 h, diluted with H_2O, neutralized with 1 M HCl, and then extracted with a 3:1 mixture of hexane and EtOAc (×3). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by silica-gel column chromatography (EtOAc/hexane 1:30) to provide **19** (1.84 g, 97% calculated based on consumed **18**) and recovered **18** (275 mg, 15%). 3-((3*R*,6*S*)-3-Isopropyl-6-methylcyclohex-1-en-1-yl)propanoic acid (**18**): $[\alpha]_D^{25}$ = –3.9 (c = 4.30, $CHCl_3$); IR (KBr): ν_{max} = 2957, 2930, 2872, 2660, 1713, 1445, 1297, 934 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 5.32 (brs, 1H), 2.55–2.27 (m, 4H), 2.16–2.07 (m, 1H), 1.94–1.87 (m, 1H), 1.87–1.79 (m, 1H), 1.67–1.59 (m, 1H), 1.55 (qd, J = 7.0, 1.5 Hz, 1H), 1.21 (dddd, J = 12.0, 10.0, 6.0, 2.0 Hz, 1H),1.18 (dddd, J = 12.5, 10.0, 6.0, 2.0 Hz, 1H), 0.99 (d, J = 7.0 Hz, 3H), 0.86 (d, J = 7.0 Hz, 3H), 0.83 (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 180.2, 140.1, 126.5, 77.4, 77.1, 76.8, 42.1, 33.1, 32.4, 32.3, 32.3, 30.0, 24.5, 19.7, 19.7, 19.3; HRMS (ESI): m/z calcd for $C_{13}H_{21}O_2$ $[M–H]^-$, 209.1547, found 209.1538. The characterization data obtained for compound **19** are in agreement with values

previously reported.[4] Compound **19**: $[\alpha]_D^{25}$ = −10.9 (*c* = 3.18, $CHCl_3$); IR (KBr): ν_{max} = 2957, 2931, 2872, 1739, 1463, 1445, 1369, 1162, 1045 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 5.30 (brs, 1H), 4.12 (q, *J* = 7.0 Hz, 2H), 2.50–2.27 (m, 4H), 2.15–2.06 (m, 1H), 1.92–1.78 (m, 2H), 1.66–1.59 (m, 1H), 1.57–1.49 (m, 1H), 1.25 (t, *J* = 7.0 Hz, 3H), 1.24–1.15 (m, 2H), 0.99 (d, *J* = 7.0 Hz, 3H), 0.86 (d, *J* = 7.0 Hz, 3H), 0.83 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 173.7, 140.5, 126.0, 60.3, 42.1, 33.4, 32.4, 32.3, 30.2, 24.6, 19.7, 19.4, 14.3; HRMS (ESI): m/z calcd for $C_{15}H_{27}O_2$ $[M+H]^+$, 239.2006, found 239.2004.

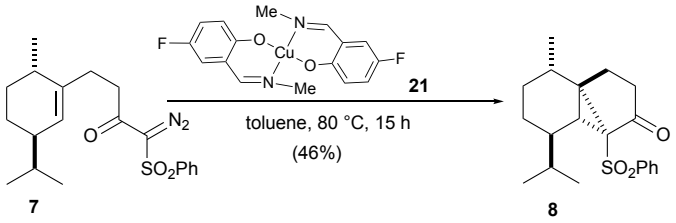


19 20

4-((3*R*,6*S*)-3-Isopropyl-6-methylcyclohex-1-enyl)-1-(phenylperoxythio)butan-2-one (20). Methyl phenyl sulfone (4.22 g, 27.0 mmol) was dissolved in toluene and the solvent is removed azeotropically by rotary evaporation (×3). After this procedure followed by drying under vacuum, methyl phenyl sulfone was dissolved in THF (85 mL). To this solution cooled to –78 °C under nitrogen atmosphere, *n*-butyllithium (1.5 M solution in hexane, 15.4 mL, 23.2 mmol) was added. The solution was warmed to 0 °C and stirred at 0 °C for 30 min. To this solution cooled to –78 °C was added a solution of ester **19** (1.84 g, 7.72 mmol) in THF (5.0 mL). The reaction mixture was stirred at –78 °C for 30 min and warmed at 0 °C. After stirring at 0 °C for 30 min, saturated aqueous ammonium chloride was added. The separated aqueous layer was extracted with EtOAc (×3). The combined organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel eluting with EtOAc/hexane (1:4) to afford **20** (2.72g, quant.) as a colorless oil. The characterization data obtained for **20** are in agreement with values previously reported.[4]



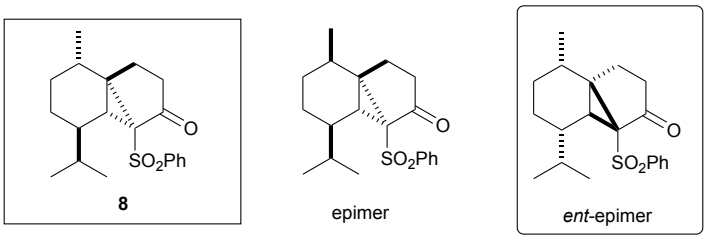
1-Diazo-4-((3*R*,6*S*)-3-isopropyl-6-methylcyclohex-1-enyl)-1-(phenylperoxythio)butan-2-one (7). To a solution of **20** (4.22 g, 12.1 mmol) and *p*-acetamidobenzenesulfonyl azide (3.20 g, 13.3 mmol) dissolved in acetonitrile (120 mL) cooled to 0 ˚C was added triethylamine (5.10 mL, 36.3 mmol) dropwise under nitrogen atmosphere. The reaction mixture was stirred at room temperature for 16 h and then filtered through a pad of Celite. The filtered cake was washed with a 1:5 mixture of EtOAc and hexane. The combined filtrate was concentrated under reduced pressure, and the resulting crude product was purified by silica-gel column chromatography (EtOAc/hexane, 1:5) to afford **7** (4.04 g, 89%) as a yellow oil. The characterization data obtained for compound **7** are in agreement with values previously reported.[4]



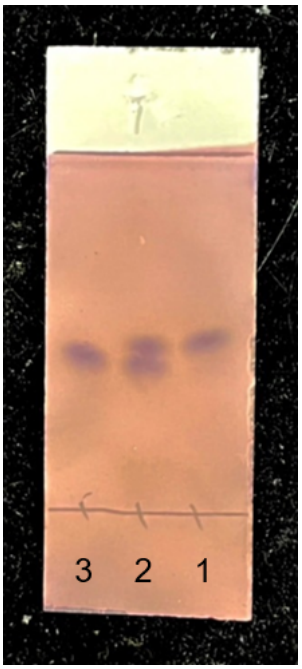
(3b*R*,4*R*,7*S*,7a*S*)-4-Isopropyl-7-methyl-3a-(phenylsulfonyl)octahydro-3*H*-cyclopenta[1,3]cyclopropa[1,2]benzen-3-one (8). To a solution of bis-(5-fluoro-(*N*-methylsalicyl aldiminato))copper (II) (**21**) (63 mg, 0.17 mmol) in toluene (60 mL) was added a solution of diazo compound **7** (800 mg, 2.14 mmol) dissolved in toluene (20 mL). The solution was heated at 80 ˚C for 15 h under nitrogen atmosphere, cooled to room temperature and concentrated under reduced pressure. The crude product was purified by silica-gel column chromatography (EtOAc/hexane 1:8 and EtOAc/ toluene 1:30) to afford **8** (344 mg, 46%) as a white solid. The characterization data obtained for compound **8** are in agreement with values previously reported.[4]

Separation of cyclopropane intermediate **8** and its *ent*-epimer

ent-Epimer of **8** is an intermediate in our previously reported synthesis of exigurin.[4]

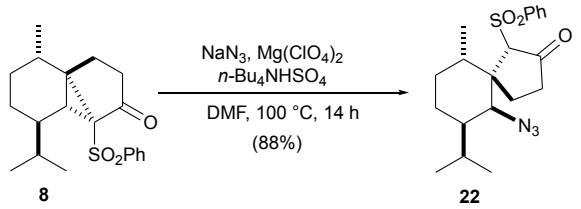


A solution of the substance to be examined was spotted on a 0.25 mm E. Merck silica plate (60F-254). The plate was inserted into a developing chamber containing a mixture of v/v 8:1 hexane/ethyl acetate. After the solvent had risen to near the top of the plate, the plate was removed from the developing chamber and the solvent front was marked with a pencil. The resulting plate was returned to the chamber, developed, removed from the chamber, and allow the solvent to evaporate. After one more cycle of this process, we observed two cleanly separated spots (line 2).

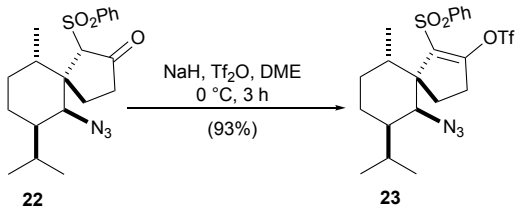


Lane 1: Cyclopropane intermediate **8**
Lane 2: Co-spot.
Lane 3: *ent*-epimer

Visualizing agent: *p*-anisaldehyde

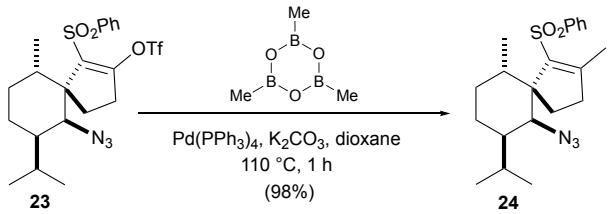


(1*R*,5*S*,6*S*,7*R*,10*S*)-6-Azido-7-isopropyl-10-methyl-1-(phenylsulfonyl)spiro[4.5]decan-2-one (22). To a solution of **8** (610 mg, 1.77 mmol) dissolved in DMF (24 mL) were added sodium azide (2.53 g, 38.9 mmol), magnesium perchlorate (1.18 g, 5.30 mmol) and tetrabutylammonium hydrogen sulfate (7.20 g, 21.2 mmol). The mixture was heated under nitrogen atmosphere at 100 ˚C for 14 h. After cooling to room temperature, the reaction mixture was diluted with water (125 mL) and then extracted with EtOAc (×3). The combined organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by silica-gel column chromatography (EtOAc/hexane 1:6) to afford **22** (528 mg, 88%, calculated based on consumed **8**) as a white solid and recovered **8** (76 mg, 12%). Mp 40–41 °C; $[\alpha]_D^{25}$ = –36.3 (c = 1.54, $CHCl_3$); IR (KBr): ν_{max} = 2961, 2928, 2881, 2101, 1747, 1448, 1311, 1141, 712 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.80–7.76 (m, 2H), 7.72–7.67 (m, 1H), 7.60–7.54 (m, 2H), 4.80 (s, 1H), 3.61 (s, 1H), 2.87–2.66 (m, 2H), 2.41–2.29 (m, 1H), 2.20–2.12 (m, 2H), 2.04–1.94 (m, 2H), 1.76–1.63 (m, 2H), 1.50 (ddd, J = 14.0, 6.0, 3.0 Hz, 1H), 1.34–1.22 (m, 1H), 1.14 (d, J = 6.5 Hz, 3H), 1.11–1.03 (m, 1H), 1.01 (d, J = 6.5 Hz, 3H), 0.61 (d, J = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 209.0, 137.8, 134.4, 129.1, 128.9, 75.5, 68.9, 54.0, 37.9, 36.7, 33.4, 31.5, 30.5, 24.2, 20.9, 20.4, 17.1; HRMS (ESI): m/z calcd for $C_{20}H_{27}O_3N_3NaS$ $[M+Na]^+$, 412.1665, found 412.1664.

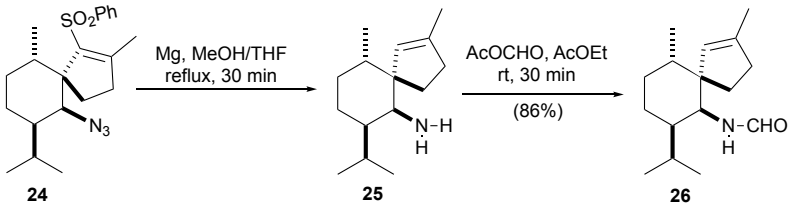


22 23

(5*S*,6*S*,7*R*,10*S*)-6-Azido-7-isopropyl-10-methyl-1-(phenylsulfonyl)spiro[4.5]dec-1-en-2-yl trifluoromethanesulfonate (23). To a solution of **22** (519 mg, 1.33 mmol) in 1,2-dimethoxyethane (24 mL) was added sodium hydride (55% dispersion in mineral oil, 240 mg, 6.65 mmol). The mixture was heated under nitrogen atmosphere at 40 ˚C for 30 min. After cooling to 0 ˚C, trifluoromethanesulfonic anhydride (0.75mL, 2.66 mmol) was added dropwise. After stirring at 0 ˚C for 3 h, saturated aqueous NH_4Cl was added. The separated aqueous layer was extracted with EtOAc (×3), and the combined organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by silica-gel column chromatography (EtOAc/hexane 1:7) to furnish **23** (643 mg, 93%). Mp 93–94 °C; $[\alpha]_D^{25}$ = +15.3 (c = 1.39, $CHCl_3$); IR (KBr): ν_{max} = 2959, 2925, 2872, 2102, 1607, 1434, 1331, 1217, 1152, 950, 812 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.99–7.94 (m, 2H), 7.68–7.62 (m, 1H), 7.59–7.54 (m, 2H), 4.06 (brs, 1H), 2.81 (ddd, J = 13.0, 9.0, 6.5 Hz, 1H), 2.66 (ddd, J = 18.0, 9.0, 5.5 Hz, 1H), 2.25 (ddd, J = 13.5, 9.5, 6.5 Hz, 1H), 2.14–2.04 (m, 2H), 2.00–1.53 (m, 5H), 1.49–1.38 (m, 1H), 1.17 (d, J = 6.5 Hz, 3H), 1.00 (d, J = 7.0 Hz, 3H), 0.98 (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 157.2, 142.2, 138.1, 133.9, 129.2, 127.8, 119.8, 116.1, 68.6, 61.8, 44.3, 36.2, 34.0, 29.6, 29.3, 23.3, 21.5, 21.0, 17.5, 14.2; HRMS (ESI): m/z calcd for $C_{21}H_{26}O_5N_3F_3NaS_2$ $[M+Na]^+$, 544.1158 , found 544.1159.

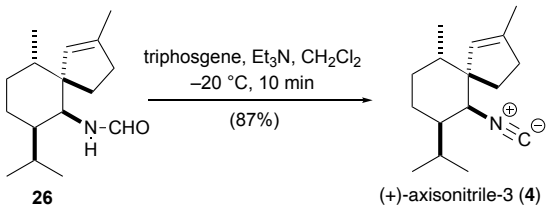


(5*S*,6*S*,7*R*,10*S*)-6-Azido-7-isopropyl-2,10-dimethyl-1-(phenylsulfonyl)spiro[4.5]dec-1-ene (24). To a solution of **23** (420 mg, 0.805 mmol) in 1,4-dioxane (7.0 mL, argon was bubbled through the solution for 60 min) was added tetrakis(triphenylphosphine)palladium (93 mg, 0.81 mmol). After stirring at room temperature for 5 min under argon atmosphere, potassium carbonate (333 mg, 2.42 mmol) and trimethylboroxine (0.12 mL, 0.81 mmol) were added. The reaction mixture was heated at 110 ˚C for 1 h, diluted with THF and filtered through a pad of silica-gel. Concentration of the filtrate under reduced pressure followed by purification by silica-gel column chromatography (EtOAc/hexane 1:12) provided **24** (304 mg, 98%) as a white solid. Mp 123–124 °C; $[\alpha]_D^{25}$ = +15.1 (*c* = 1.74, $CHCl_3$); IR (KBr): ν_{max} = 2960, 2931, 2871, 2098, 1463, 1446, 1302, 1146, 725, 689 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.91–7.87 (m, 2H), 7.60–7.49 (m, 3H), 4.00 (brs, 1H), 2.54 (ddd, *J* = 18.0, 7.5, 7.5 Hz, 1H), 2.45 (ddd, *J* = 17.5, 7.5, 6.0 Hz, 1H), 2.17 (ddd, *J* = 13.0, 8.0, 6.5 Hz, 1H), 2.04 (ddd, *J* = 13.0, 8.0, 6.0 Hz, 1H), 1.95 (s, 3H), 1.92–1.78 (m, 3H), 1.72–1.31 (m, 4H), 1.13 (d, *J* = 7.0 Hz, 3H), 0.88 (d, *J* = 6.5 Hz, 3H), 0.80 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 162.1, 144.3, 140.7, 132.7, 129.2, 126.3, 69.0, 64.9, 44.0, 37.8, 36.2, 35.9, 29.5, 29.1, 23.4, 21.4, 20.8, 18.6, 17.5; HRMS (ESI): m/z calcd for $C_{21}H_{29}O_2N_3NaS$ $[M+Na]^+$, 410.1873, found 410.1871.



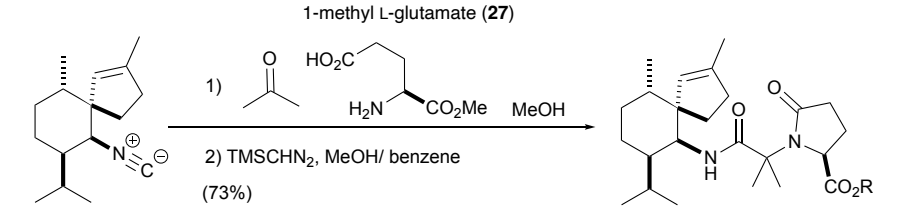
***N*-((5*R*,6*S*,7*R*,10*S*)-7-isopropyl-2,10-dimethylspiro[4.5]dec-1-en-6-yl)formamide (26)**. To a suspension of magnesium powder (941 mg, 38.7 mmol, activated by washing with 1N HCl and acetone before use) in MeOH (7.5 mL) under nitrogen atmosphere was added a solution of **24** (300 mg, 0.77 mmol) in THF (2.1 mL). The solution was heated to reflux for 30 min, diluted with EtOAc and then filtered through a pad of Celite. The filtrate was concentrated under reduced pressure to give crude amine **25**, which was dissolved in EtOAc (15 mL). The solution was treated with acetic formic anhydride (0.15 mL, 1.94 mmol). After stirring at room temperature for 60 min, saturated aqueous $NaHCO_3$ was added. The separated aqueous layer was extracted with EtOAc (×3), and the combined organic layer was dried (Na_2SO_4). Concentration under reduced pressure gave a residue, which was purified by silica-gel column chromatography (EtOAc/hexane 1:3 → 1:2) to provide **26** (167 mg, 86% for two steps). Formamide **26** exists as a mixture of amide rotamers on the ^1H and ^{13}C NMR time scale. When two rotamers are observed, signals for the minor rotamers are given in braces. (5*R*,6*S*,7*R*,10*S*)-7-Isopropyl-2,10-dimethylspiro[4.5]dec-1-en-6-amine (**25**): $[\alpha]_D^{25}$ = +14.2 (*c* = 1.18, $CHCl_3$); IR (KBr): ν_{max} = 2955, 2925, 2870, 1613, 1462, 1375, 846, 819 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 5.30 (brs, 1H), 2.72 (brs, 1H), 2.22–2.15 (m, 1H), 1.83–1.77 (m, 1H), 1.74 (d, *J* = 1.0 Hz, 3H), 1.72–1.64 (m, 2H), 1.51–1.38 (m, 2H), 1.37–1.16 (m, 6H), 1.14–1.03 (m, 1H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.89 (d, *J* = 6.5 Hz, 3H), 0.74 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 141.8, 126.8, 58.7, 58.0, 45.3, 36.6, 35.2, 34.1, 31.8, 29.4, 24.4, 21.5, 20.7, 17.1, 16.4; HRMS (ESI): m/z calcd for $C_{15}H_{28}N$ $[M+H]^+$, 222.2216, found 222.2216. Compound **26**: Mp 96–98 °C; $[\alpha]_D^{25}$ = –13.9 (*c* = 1.55, $CHCl_3$); IR (KBr): ν_{max} = 3306, 3044, 2957, 2929, 2870, 1659, 1538, 1463, 1384, 739 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 8.27 (d,

J = 1.5 Hz, 1H), {8.05 (d, *J* = 12.0 Hz, 1H)}, {5.72–5.64 (m, 1H)}, 5.57–5.49 (m, 1H), 5.26 (brs, 1H), 4.23 (brd, *J* = 11.5 Hz, 1H), {3.30 (brdd, *J* = 11.5, 2.5 Hz, 1H)}, 2.32–2.08 (m, 2H), {2.32–2.08 (m, 2H)}, 1.89–1.81 (m, 2H), {1.89–1.81 (m, 2H)}, {1.75 (brs, 3H)}, 1.73 (brs, 3H), {1.72–1.61 (m, 1H)}, 1.64 (ddd, *J* = 13.5, 9.5, 4.0 Hz, 1H), 1.53–1.47 (m, 1H), {1.53–1.47 (m, 1H)}, 1.43–1.25 (m, 4H), {1.43–1.25 (m, 4H)}, 1.22–1.10 (m, 1H), {1.22–1.10 (m, 1H)}, 0.92 (d, *J* = 6.0 Hz, 3H), {0.90 (d, *J* = 6.5 Hz, 3H)}, 0.88 (d, *J* = 6.0 Hz, 3H), {0.85 (d, *J* = 6.5 Hz, 3H)}, 0.77 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = {164.4}, 161.1, {143.8}, 143.6, {125.2}, 125.1, {59.5}, 58.1, {57.9}, 54.0, 44.3, {44.1}, {36.2}, 36.1, {36.0}, 35.7, {34.7}, 33.7, 31.6, {31.3}, 29.6, {28.8}, 25.4, {25.1}, 21.3, 21.0, {20.8}, {20.7}, 17.1, {17.0}, 16.3, {16.2}; HRMS (ESI): m/z calcd for $C_{16}H_{28}ON$ $[M+H]^+$, 250.2165, found 250.2165.

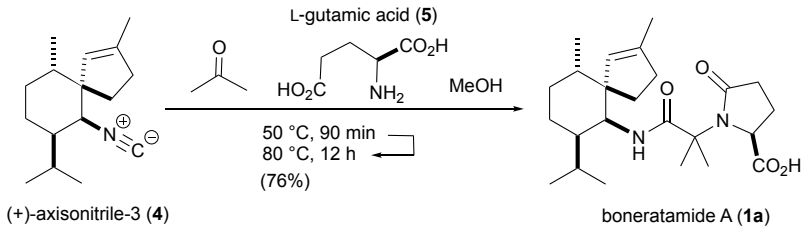


26 (+)-axisonitrile-3 (**4**)

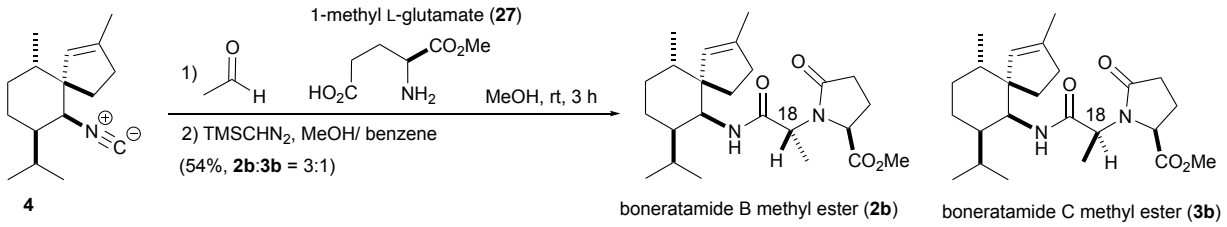
(+)-Axisonitrile- 3 (4). To a solution of **26** (165 mg, 0.66 mol) and triethylamine (0.65 mL, 4.63 mmol) dissolved in CH_2Cl_2 (2.4 mL) cooled to –20 ˚C was added triphosgene (118 mg, 0.40 mmol). After stirring at –20 ˚C for 10 min, the reaction mixture was warmed to 0 ˚C and then treated with saturated aqueous of $NaHCO_3$ and CH_2Cl_2. After vigorous stirring at 0 ˚C for 1 h, the separated aqueous layer was extracted with EtOAc (×3). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was purified by silica-gel column chromatography (EtOAc/hexane 1:10) to afford (+)-axisonitrile-3 (**4**) (133 mg, 87%) as a white crystalline mass. Mp 99–100 °C (Literature: 101–103 °C[5]) (Literature: 99–102 °C[6]) (Literature: 94–95°C[7]); $[\alpha]_D^{22}$ = +89.2 (c = 1.0, $CHCl_3$) {Literature: $[\alpha]_D^{22}$ = +68.4 (c = 1, $CHCl_3$)[5]}{Literature: $[\alpha]_D^{22}$ = +43.4 (c = 0.006, $CHCl_3$)[6]}{Literature: $[\alpha]_D^{22}$ = +54.4 (c = 0.10, $CHCl_3$)[7]}; IR (KBr): ν_{max} = 2959, 2920, 2893, 2853, 2133, 1655, 1458, 1442, 1373, 1328 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 5.13 (q, J = 1.0 Hz, 1H), 3.59 (brs, 1H), 2.28–2.20 (m, 2H), 1.98–1.92 (m, 2H), 1.84–1.76 (m, 2H), 1.74 (brs, 3H), 1.59 (qd, J = 6.5, 2.5 Hz, 1H), 1.54–1.48 (m, 1H), 1.40–1.27 (m, 1H), 1.21–1.10 (m, 2H), 0.94 (d, J = 6.5 Hz, 3H), 0.91 (d, J = 6.5 Hz, 3H), 0.76 (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 155.7 (t), 144.8, 123.7, 64.6 (t), 57.1, 43.8, 35.9, 35.0, 34.4, 31.2, 29.8, 24.9, 20.8, 20.4, 17.0, 16.1; HRMS (ESI): m/z calcd for $C_{16}H_{29}N_2$ $[M+NH_4]^+$, 249.2325 , found 249.2325.



Boneratamide A methyl ester (1b). A solution of L-glutamic acid 1-methyl ester (**27**) (10 mg, 0.065 mmol) and acetone (0.030 mL, 0.43 mmol) in MeOH (0.60 mL) under nitrogen atmosphere was heated at 50 ˚C for 60 min. To this mixture was added (+)-axisonitrile-3 (**4**) (10 mg, 0.043 mmol). After stirring at 50 ˚C for 60 min and at 80 ˚C for 120 min, the reaction mixture was cooled to room temperature and diluted with H_2O. The aqueous layer was extracted with EtOAc (×3), and the combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. The resulting crude mixture of **1a** and **1b** was dissolved in a mixture of benzene (0.40 mL) and methanol (0.20 mL), and then treated with trimethylsilyldiazomethane (2.0 M solution in ether, 0.21mL, 0.42 mmol). After stirring at room temperature for 16 h, the solution was concentrated under reduced pressure to afford a crude product, which was purified by silica-gel chromatography (EtOAc/hexane 1:3) to furnish boneratamide A methyl ester (**1b)** (14 mg, 73%) as a white solid. Mp 165–166 °C (recrystallized from AcOEt/hexane); $[\alpha]_D^{28}$ = +2.6 (*c* = 1.31, CH_2Cl_2), $[\alpha]_D^{20}$ = +8.8 (*c* = 1.73, MeOH); IR (KBr): ν_{max} = 3366, 2956, 2929, 2871, 1732, 1708, 1673, 1530, 1463, 1439, 1393, 1220, 1180 cm^{-1}; ^1H NMR (C_6D_6, 400 MHz) δ = 7.51 (d, *J* = 10.5 Hz, 1H), 5.41 (q, *J* = 1.0 Hz, 1H), 4.66 (dd, *J* = 10.5, 2.5 Hz, 1H), 3.76 (dd, *J* = 10.0, 1.5 Hz, 1H), 3.16 (s, 3H), 2.66 (ddd, *J* = 13.5, 9.5, 5.5 Hz, 1H), 2.47–2.37 (m, 1H), 2.21–2.04 (m, 3H), 1.95–1.88 (m, 1H), 1.86–1.68 (m, 3H), 1.79 (ddd, *J* = 16.5, 9.5, 1.5 Hz, 1H), 1.66 (s, 3H), 1.62 (d, *J* = 1.0 Hz, 3H), 1.51–1.39 (m, 3H), 1.36–1.25 (m, 2H), 1.24 (s, 3H), 1.17 (d, *J* = 6.5 Hz, 3H), 0.98 (d, *J* = 6.5 Hz, 6H); ^{13}C NMR (C_6D_6, 100 MHz) δ = 175.5, 175.3, 175.1, 143.7, 126.3, 60.5, 58.9, 56.3, 45.6, 36.6, 35.6, 34.1, 32.4, 32.0, 30.2, 30.1, 25.6, 23.3, 23.1, 21.8, 17.2, 17.1, 14.4; HRMS (ESI): m/z calcd for $C_{25}H_{41}O_4N_2$ $[M+H]^+$, 433.3061, found 433.3061.

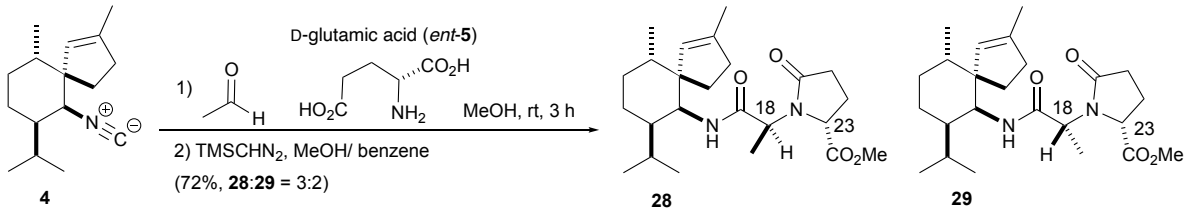


Boneratamide A (1a). A suspension of L-glutamic acid (**5**) (11 mg, 0.072 mmol), acetone (0.10 mL, 1.30 mmol) and MeOH (0.60 mL) in a sealed test tube under nitrogen atmosphere was heated at 50 ˚C for 2 h. To this mixture was added (+)-axisonitrile-3 (**4**) (10 mg, 0.043 mmol) at room temperature. The reaction mixture was heated at 50 ˚C for 90 min and then at 80 ˚C for 12 h . After cooling at room temperature, concentration under reduced pressure afforded a residue, which was purified by silica-gel chromatography ($CHCl_3$/MeOH 7:1) to furnish boneratamide A (**1a)** (14 mg, 76%) as a white solid. Mp 222–223 °C; $[\alpha]_D^{28}$ = +13.8 (c = 0.54, CH_2Cl_2); IR (KBr): ν_{max} = 3330, 2956, 2927, 2870, 1716, 1654, 1541, 1463, 1386, 1229 cm^{-1}; ^1H NMR (C_6D_6, 400 MHz) δ = 7.36–7.22 (m, 1H), 5.31 (brs, 1H), 4.50 (brd, J = 10.0 Hz, 1H), 4.04 (brd, J = 9.5 Hz, 1H), 2.37–2.06 (m, 5H), 1.91–1.65 (m, 5H), 1.63 (brs, 3H), 1.49 (brs, 3H), 1.40–1.25 (m, 5H), 1.23 (brs, 3H), 1.15 (d, J = 6.5 Hz, 3H), 0.97 (d, J = 6.5 Hz, 3H), 0.91 (d, J = 6.5 Hz, 3H); ^1H NMR ($CDCl_3$, 400 MHz) δ = 6.31 (brd, J = 10.5 Hz, 1H), 5.24 (brs, 1H), 4.41 (d, J = 8.5 Hz, 1H), 4.16 (dd, J = 10.5, 2.5 Hz, 1H), 2.55–2.08 (m, 6H), 1.96–1.87 (m, 1H), 1.79–1.71 (m, 1H), 1.74 (brs, 3H), 1.68 (s, 3H), 1.65–1.50 (m, 3H), 1.48 (s, 3H), 1.38–1.26 (m, 2H), 1.24–1.12 (m, 1H), 1.04–0.92 (m, 1H), 0.90 (d, J = 6.5 Hz, 3H), 0.89 (d, J = 6.5 Hz, 3H), 0.78 (d, J = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 176.3, 175.4, 175.3, 143.6, 125.4, 60.2, 58.5, 58.4, 56.1, 44.9, 36.3, 35.6, 33.6, 31.8, 30.0, 29.8, 29.5, 25.9, 25.7, 25.2, 23.1, 21.4, 17.1, 16.5; HRMS (ESI): m/z calcd for $C_{24}H_{39}O_4N_2$ $[M+H]^+$, 419.2904, found 419.2904.



Methyl esters of boneratamide B (2b) and C (3b). A solution of L-glutamic acid 1-methyl ester (**27**) (8 mg, 0.048 mmol) and acetaldehyde (0.075 mL, 1.30 mmol) in MeOH (0.30 mL) was stirred at room temperature for 60 min. To this mixture was added a solution of axisonitrile-3 (**4**) (10 mg, 0.043 mmol) dissolved in a mixture of benzene (0.025 mL) and methanol (0.10 mL). The reaction mixture was stirred at room temperature for 3 h, and then diluted with water. The aqueous layer was extracted with EtOAc (×3), and the combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to afford a residue, which was dissolved in a mixture of benzene (0.44 mL) and methanol (0.21 mL). The solution was treated with trimethylsilyldiazomethane (2.0 M solution in ether, 0.21mL, 0.42 mmol), stirred at room temperature for 12 h and then concentrated under reduced pressure. The crude product was purified by silica-gel chromatography (EtOAc/hexane 1:2) to furnish boneratamide B methyl ester (**2b)** (7.1 mg, 39%) as a colorless oil and boneratamide C methyl ester (**3b)** (2.8 mg, 15%) as a white solid. Boneratamide B methyl ester (**2b)**: $[\alpha]_D^{26}$ = +15.2 (c = 2.15, CH_2Cl_2), $[\alpha]_D^{26}$ = +19.9 (c = 2.07, $CHCl_3$); IR (KBr): ν_{max} = 3338, 2955, 2930, 2871, 1746, 1667, 1537, 1438, 1416, 1204, 1179 cm^{-1}; ^1H NMR (C_6D_6, 400 MHz) δ = 6.92 (d, J = 10.5 Hz, 1H), 5.30 (q, J = 1.5 Hz, 1H), 4.48 (dd, J = 10.5, 2.5 Hz, 1H), 4.46 (q, J = 7.0 Hz, 1H), 4.11 (dd, J = 9.5, 2.0 Hz, 1H), 3.22 (s, 3H), 2.31–2.21 (m, 2H), 2.16–2.08 (m, 2H), 1.87 (ddd, J = 17.0, 10.0, 2.5 Hz, 1H), 1.75–1.62 (m, 4H), 1.61 (d, J = 1.0 Hz, 3H), 1.53–1.40 (m, 3H), 1.37 (d, J = 7.0 Hz, 3H), 1.32–1.27 (m, 1H), 1.20–1.12 (m, 2H), 1.11 (d, J = 7.0 Hz, 3H), 0.90 (d, J = 6.5 Hz, 3H), 0.86 (d, J = 6.5 Hz, 3H); ^{13}C NMR (C_6D_6, 100 MHz) δ = 175.4 173.2, 170.5, 142.8, 126.0, 58.7, 58.6, 55.0, 52.9, 51.6, 44.8, 36.0, 35.2, 33.4, 32.0, 29.7, 29.5, 25.3, 24.1, 21.4, 21.0,

16.7, 16.5, 14.2; HRMS (ESI): m/z calcd for $C_{24}H_{39}O_4N_2$ $[M+H]^+$, 419.2904, found 419.2904. Boneratamide C methyl ester (**3b)**: Mp 103−104 °C (recrystallized from benzene/hexane); $[\alpha]_D^{26}$ = –29.5 (*c* = 1.00, CH_2Cl_2), $[\alpha]_D^{27}$ = –35.7 (*c* = 1.00, $CHCl_3$); IR (KBr): ν_{max} = 3339, 2954, 2927, 2870, 1746, 1666, 1541, 1438, 1208, 1178 cm^{-1}; ^1H NMR (C_6D_6, 400 MHz) δ = 7.21 (d, *J* = 11.0 Hz, 1H), 5.32 (q, *J* = 1.5 Hz, 1H), 4.53 (q, *J* = 7.0 Hz, 1H), 4.46 (brd, *J* = 11.0 Hz, 1H), 3.86 (dd, *J* = 9.0, 3.0 Hz, 1H), 3.34 (s, 3H), 2.34–2.03 (m, 4H), 1.84 (ddd, *J* = 17.0, 9.5, 3.5 Hz, 1H), 1.82–1.76 (m, 1H), 1.77 (ddd, *J* = 13.0, 9.0, 4.0 Hz, 1H), 1.64–1.60 (m, 2H), 1.59 (d, *J* = 1.0 Hz, 3H), 1.53–1.50 (m, 1H), 1.46–1.35 (m, 2H), 1.34 (d, *J* = 7.0 Hz, 3H), 1.33–1.27 (m, 2H), 1.17 (d, *J* = 6.5 Hz, 3H), 1.15–1.10 (m, 1H), 0.98 (d, *J* = 6.5 Hz, 3H), 0.84 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (C_6D_6, 100 MHz) δ = 175.8 172.3, 170.0, 143.1, 126.3, 59.2, 58.0, 55.3, 53.3, 51.9, 45.2, 36.2, 35.4, 33.7, 32.3, 29.8, 29.4, 25.5, 23.8, 22.3, 21.4, 17.0, 16.8, 14.7; HRMS (ESI): m/z calcd for $C_{24}H_{39}O_4N_2$ $[M+H]^+$, 419.2904, found 419.2904.



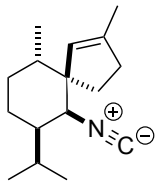
Methyl (*R*)-1-((*S*)-1-(((5*R*,6*S*,7*R*,10*S*)-7-isopropyl-2,10-dimethylspiro[4.5]dec-1-en-6-yl) amino)-1-oxopropan-2-yl)-5-oxopyrrolidine-2-carboxylate (28) and methyl (*R*)-1-((*R*)-1 -(((5*R*,6*S*,7*R*,10*S*)-7-isopropyl-2,10-dimethylspiro[4.5]dec-1-en-6-yl)amino)-1-oxopropan-2-yl)-5-oxopyrrolidine-2-carboxylate (29). A solution of D-glutamic acid (*ent*-**5**) (9.5 mg, 0.065 mmol) and acetaldehyde (0.075 mL, 1.30 mmol) in MeOH (0.30 mL) was stirred at room temperature for 3 h. To this mixture was added a solution of (+)-axisonitrile-3 (**4**) (10 mg, 0.043 mmol) dissolved in a mixture of benzene (0.050 mL) and methanol (0.10 mL). The reaction mixture was stirred at room temperature for 19 h and diluted with water. The aqueous layer was extracted with EtOAc (×3), and the combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to afford a residue, which was dissolved in a mixture of benzene (0.44 mL) and methanol (0.22 mL). The solution was treated with trimethylsilyldiazomethane (2.0 M solution in ether, 0.21 mL, 0.42 mmol), stirred at room temperature for 20 h and then concentrated under reduced pressure. The crude product was purified by silica-gel chromatography (EtOAc/hexane 1:2) to furnish **28** (9.2 mg, 51%) as a white solid and **29** (3.8 mg, 21%) as a colorless oil.

Methyl (*R*)-1-((*S*)-1-(((5*R*,6*S*,7*R*,10*S*)-7-isopropyl-2,10-dimethylspiro[4.5]dec-1-en-6-yl)amino) -1-oxopropan-2-yl)-5-oxopyrrolidine-2-carboxylate **(28)**: Mp 70–71 °C; $[\alpha]_D^{25}$ = –51.1 (*c* = 1.77, CH_2Cl_2); IR (KBr): ν_{max} = 3341, 2955, 2930, 2871, 1746, 1667, 1538, 1438, 1415, 1205, 1179 cm^{-1}; ^1H NMR (C_6D_6, 500 MHz) δ = 6.78 (brd, *J* = 10.5 Hz, 1H), 5.28 (q, *J* = 1.5 Hz, 1H), 4.59 (q, *J* = 7.0 Hz, 1H), 4.44 (dd, *J* = 11.0, 2.0 Hz, 1H), 4.19 (dd, *J* = 9.5, 1.5 Hz, 1H), 3.22 (s, 3H), 2.34–2.25 (m, 2H), 2.18–2.04 (m, 2H), 1.87 (ddd, *J* = 17.0, 9.5, 2,5 Hz, 1H), 1.78–1.63 (m,

3H), 1.53–1.41 (m, 3H), 1.36 (d, *J* = 7.0 Hz, 3H), 1.35–1.16 (m, 3H), 1.14–1.07 (m, 1H), 1.04 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.5 Hz, 3H), 0.81 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (C_6D_6, 100 MHz) δ = 175.8, 173.7, 170.6, 170.5, 143.3, 126.2, 58.9, 58.5, 55.3, 52.7, 51.9, 45.1, 36.3, 35.4, 33.7, 32.2, 30.1, 29.7, 25.6, 24.4, 21.6, 21.4, 17.1, 16.8, 14.6, 14.4; HRMS (ESI): m/z calcd for $C_{24}H_{39}O_4N_2$ $[M+H]^+$, 419.2904 , found 419.2904.

Methyl (*R*)-1-((*R*)-1-(((5*R*,6*S*,7*R*,10*S*)-7-isopropyl-2,10-dimethylspiro[4.5]dec-1-en-6-yl)amino) -1-oxopropan-2-yl)-5-oxopyrrolidine-2-carboxylate (**29**): $[\alpha]_D^{26}$ = +8.4 (*c* = 0.60, CH_2Cl_2); IR (KBr): ν_{max} = 3336, 2955, 2928, 2871, 1748, 1689, 1664, 1541, 1438, 1419, 1209, 1178 cm^{-1}; ^{1}H NMR (C_6D_6, 500 MHz) δ = 7.22 (brd, *J* = 10.5 Hz, 1H), 5.33 (q, *J* = 1.5 Hz, 1H), 4.50 (q, *J* = 7.0 Hz, 1H), 4.42 (dd, *J* = 10.5, 2.5 Hz, 1H), 3.89 (dd, *J* = 8.5, 3.0 Hz, 1H), 3.36 (s, 3H), 2.40–2.33 (m, 1H), 2.28 (ddd, *J* = 17.0, 10.0, 10.0 Hz, 1H), 2.22–2.14 (m, 2H), 1.84 (ddd, *J* = 17.0, 9.5, 3.5 Hz, 1H), 1.83 (ddd, *J* = 17.0, 4.5, 4.5 Hz, 1H), 1.79–1.70 (m, 2H), 1.64 (s, 3H), 1.55–1.38 (m, 4H), 1.33 (d, *J* = 7.0 Hz, 3H), 1.31–1.15 (m, 3H), 1.13 (d, *J* = 6.5 Hz, 3H), 0.91 (d, *J* = 6.5 Hz, 3H), 0.88 (d, *J* = 6.5 Hz, 3H);^{13}C NMR (C_6D_6, 100 MHz) δ = 175.8, 172.3, 170.0, 143.0, 126.6, 58.7, 58.3, 55.5, 53.3, 52.0, 45.4, 36.6, 35.4, 33.8, 32.4, 30.1, 29.9, 25.7, 23.9, 21.8, 21.4, 17.1, 17.0, 14.8, 14.4; HRMS (ESI): m/z calcd for $C_{24}H_{39}O_4N_2$ $[M+H]^+$, 419.2904 , found 419.2904.

Comparison of ^{1}H NMR data of synthetic and isolated (+)-axisonitrile-3 (**4**)

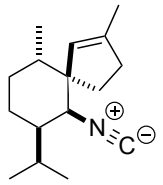


(+)-axisonitrile-3 (**4**)

^{1}H NMR (δ) Synthetic Sample (400 MHz, $CDCl_3$)	^{1}H NMR (δ) Natural Sample[6] (400 MHz, $CDCl_3$)
5.13 (1H, q, *J* = 1.0)	5.11 (1H, br s, H-1)
3.59 (1H, brs)	3.57 (1H, br s, H-6)
2.20–2.28 (2H, m)	2.21 (2H, m, H-3a, H-3b)
1.92–1.98 (2H, m)	1.93 (2H, m, H-4a, H-4b)
1.76–1.84 (2H, m)	1.77 (2H, m, H-8a, H-10)
1.74 (3H, brs)	1.72 (3H, br s, H-14)
1.59 (1H, qd, *J* = 6.5, 2.5)	1.57 (1H, m, H-11)
1.48–1.54 (1H, m)	1.48 (1H, m, H-9a)
1.27–1.40 (1H, m)	1.33 (1H, ddd, *J* = 13.0, 13.0, 4.0)
1.10–1.21 (2H, m)	1.13 (1H, m, H-7)
–	1.04 (1H, m, H-9b)
0.94 (3H, d, *J* = 6.5)	0.92 (3H, d, *J* = 6.6, H-12)
0.91 (3H, d, *J* = 6.5)	0.89 (3H, d, *J* = 6.6, H-13)
0.76 (3H, d, *J* = 7.0)	0.74 (3H, d, *J* = 7.0, H-15)

Coupling constants, $J_{H–H}$ (in Hz), are given in parentheses.

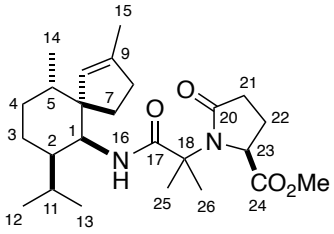
Comparison of ^{13}C NMR data of synthetic and isolated (+)-axisonitrile-3 (**4**)



(+)-axisonitrile-3 (**4**)

Position	^{13}C NMR (δ) Synthetic Sample (100 MHz, $CDCl_3$)	^{13}C NMR (δ) Natural Sample[6] (100 MHz, $CDCl_3$)	Δδ
1	123.7	123.6	+0.1
2	144.8	144.8	0
3	35.9	35.8	+0.1
4	35.0	34.9	+0.1
5	57.1	57.0	+0.1
6	64.6	64.5	+0.1
7	43.8	43.8	0
8	24.9	24.9	0
9	31.2	31.2	0
10	34.4	34.3	+0.1
11	29.8	29.7	+0.1
12	20.8	20.7	+0.1
13	20.4	20.3	+0.1
14	17.0	16.9	+0.1
15	16.1	16.0	+0.1
16	156.4	155.6	–0.2

Comparison of ^{1}H NMR data of synthetic and isolated boneratamide A methyl ester

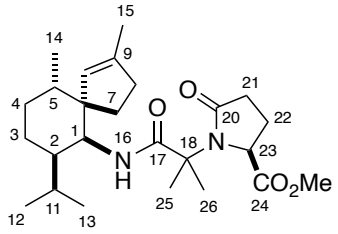


methyl ester of boneratamide A (**1b**)

Position	^{1}H NMR (δ) Synthetic Sample (400 MHz, C_6D_6)	^{1}H NMR (δ) Natural Sample[8] (500 MHz, C_6D_6)
1	4.66 (dd, *J* = 10.5, 2.5)	4.65 (dd, *J* = 10.4, 2.3)
2	***	1.42–1.50 (m)
3a	**	1.68 (m)
3b	1.88–1.95 (m)	1.91 (dm, *J* = 12.1)
4a	****	1.28 (m)
4b	**	1.70 (m)
5	**	1.81 (m)
6		
7a	*	2.07 (ddd, *J* = 13.7, 9.3, 4.3)
7b	2.66 (ddd, *J* = 13.5, 9.5, 5.5)	2.65 (ddd, *J* = 13.7, 9.8, 5.9)
8a	*	2.14 (m)
8b	2.37–2.47 (m)	2.42 (m)
10	5.41 (q, *J* = 1.0)	5.41 (brs)
11	***	1.42–1.50
12	1.17 (d, *J* = 6.5)	1.17 (d, *J* = 6.4)
13	0.98 (d, *J* = 6.5)	0.98 (d, *J* = 6.4)
14	0.98 (d, *J* = 6.5)	0,97 (d, *J* = 6.5)
15	1.62 (d, *J* = 1.0)	1.62 (brs)
16 NH	7.51 (d, *J* = 10.5)	7.49 (d, *J* = 10.4)
18		
21a	1.79 (ddd, *J* = 16.5, 9.5, 1.5)	1.79 (ddd, *J* = 16.4, 9.5, 1.9)
21b	*	2.14 (m)
22a	****	1.30 (m)
22b	***	1.42–1.50
23	3.76 (dd, *J* = 10.0, 1.5)	3.78 (dd, *J* = 9.8, 1.5)
25	1.66 (s)	1.66 (s)
26	1.24 (s)	1.25 (s)
OMe	3.16 (s)	3.17 (s)

*2.04–2.21(m), 3H; **1.68–1.86 (m), 3H; ***1.39–1.51 (m), 3H; ****1.25–1.36 (m), 2H.

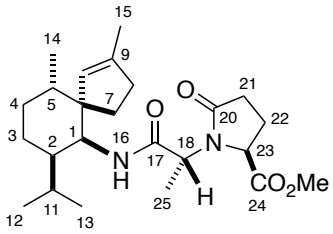
Comparison of ^{13}C NMR data of synthetic and isolated boneratamide A methyl ester



methyl ester of boneratamide A (**1b**)

Position	^{13}C NMR (δ) Synthetic Sample (100 MHz, C_6D_6)	^{13}C NMR (δ) Natural Sample[8] (125 MHz, C_6D_6)	Δδ (ppm)
1	55.4	55.3	+0.1
2	45.5	45.6	–0.1
3	25.6	25.7	–0.1
4	32.6	32.7	–0.1
5	35.6	35.6	0
6	59.1	59.2	–0.1
7	33.9	33.9	0
8	36.6	36.6	0
9	143.6	143.6	0
10	126.4	126.4	0
11	30.3	30.3	0
12	21.7	21.7	0
13	21.6	21.6	0
14	17.1	17.1	0
15	17.1	17.2	–0.1
16	–	–	
17	172.8	172.7	+0.1
18	60.9	60.9	0
19	–	–	
20	174.1	174.0	+0.1
21	30.0	30.0	0
22	24.5	24.5	0
23	57.7	57.8	–0.1
24	175.7	175.5	+0.2
25	23.7	23.8	–0.1
26	25.6	25.6	0
OMe	52.3	52.2	+0.1

Comparison of ^{1}H NMR data of synthetic and isolated boneratamide B methyl ester

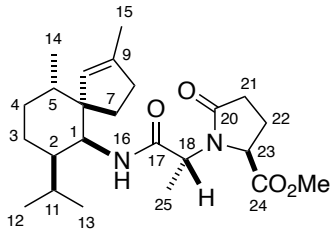


methyl ester of boneratamide B (**2b**)

Position	^{1}H NMR (δ) Synthetic Sample (400 MHz, C_6D_6)	^{1}H NMR (δ) Natural Sample[8] (500 MHz, C_6D_6)
1	4.48 (dd, *J* = 10.5, 2.5)	4.48 (dd, *J* = 10.8, 2.6)
2	1.27–1.32 (m)	1.28 (m)
3a	*****	1.14 (m)
3b	***	1.73 (m)
4a	*****	1.12 (m)
4b	****	1.49 (m)
5	***	1.61 (m)
6		
7a	***	1.71 (m)
7b	**	2.12 (m)
8a	**	2.11 (m)
8b	*	2.28 (m)
10	5.30 (q, *J* = 1.5)	5.30 (brs)
11	****	1.47 (m)
12	1.11 (d, *J* = 7.0)	1.11 (d, *J* = 6.6)
13	0.90 (d, *J* = 6.5)	0.90 (d, *J* = 6.7)
14	0.86 (d, *J* = 6.5)	0.86 (d, *J* = 6.6)
15	1.61 (d, *J* = 1.0)	1.61 (brs)
16 NH	6.92 (d, *J* 10.5)	6.91 (d, *J* = 10.8)
18	4.46 (q, *J* = 7.0)	4.46 (q, *J* = 7.2)
21a	1.87 (ddd, *J* = 17.0, 10.0, 2.5)	1.87 (ddd, *J* = 16.6, 9.6, 2.4)
21b	*	2.26 (m)
22a	****	1.42 (m)
22b	***	1.67 (m)
23	4.11 (dd, *J* = 9.5, 2.0)	4.11 (dd, *J* = 9.5, 1.8)
25	1.37 (d, *J* = 7.0)	1.37 (d, *J* = 7.2)
OMe	3.22 (s)	3.22 (s)

*2.21–2.31(m), 2H; **2.08–2.16 (m), 2H; ***1.62–1.75 (m), 4H; ****1.40–1.53 (m), 3H; *****1.12–1.20 (m), 2H.

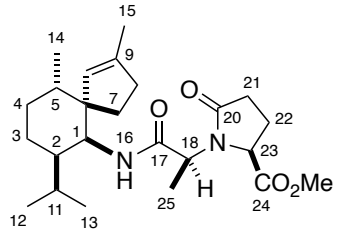
Comparison of ^{13}C NMR data of synthetic and isolated boneratamide B methyl ester



methyl ester of boneratamide B (**2b**)

Position	^{13}C NMR (δ) Synthetic Sample (100 MHz, C_6D_6)	^{13}C NMR (δ) Natural Sample[8] (125 MHz, C_6D_6)	Δδ (ppm)
1	55.0	55.2	–0.2
2	44.8	45.1	–0.3
3	25.3	25.7	–0.4
4	32.0	32.2	–0.2
5	35.2	35.6	–0.4
6	58.7	59.0	–0.3
7	33.4	33.6	–0.2
8	36.0	36.3	–0.3
9	142.8	143.1	–0.3
10	126.0	126.2	–0.2
11	29.7	30.0	–0.3
12	21.4	21.7	–0.3
13	21.0	21.3	–0.3
14	16.5	16.8	–0.3
15	16.7	17.0	–0.3
16	–	–	
17	170.3	170.2	+0.1
18	52.9	53.3	–0.4
19	–	–	
20	175.4	175.6	–0.2
21	29.5	29.7	–0.2
22	24.1	24.3	–0.2
23	58.6	58.8	–0.2
24	173.3	173.4	–0.1
25	14.2	14.1	+0.1
OMe	51.6	51.9	–0.3

Comparison of ^{1}H NMR data of synthetic and isolated boneratamide C methyl ester

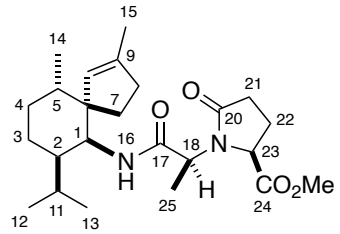


methyl ester of boneratamide C (**3b**)

Position	^{1}H NMR (δ) Synthetic Sample (400 MHz, C_6D_6)	^{1}H NMR (δ) Natural Sample[8] (500 MHz, C_6D_6)
1	4.46 (brd *J* = 10.8)	4.46 (bd, *J* = 10.9)
2	****	1.32 (m)
3a	****	1.30 (m)
3b	1.76–1.82 (m)	1.78 (m)
4a	1.10–1.15 (m)	1.14 (m)
4b	1.50–1.53 (m)	1.51 (m)
5	**	1.61 (m)
6		
7a	1.77 (ddd, *J* = 13.0, 9.0, 4.0)	1.76 (ddd, *J* = 13.2, 9.2, 3.9)
7b	*	2.18 (m)
8a	*	2.10 (m)
8b	*	2.31 (m)
10	5.32 (q, *J* = 1.5)	5.32 (br)
11	**	1.61 (m)
12	1.17 (d, *J* = 6.5)	1.17 (d, *J* = 6.4)
13	0.98 (d, *J* = 6.5)	0.98 (d, *J* = 6.7)
14	0.84 (d, *J* = 6.5)	0.84 (d, *J* = 6.6)
15	1.59 (d, *J* = 1.0)	1.59 (brs)
16 NH	7.21 (d, *J* = 11.0)	7.20 (d, *J* = 10.9)
18	4.53 (q, *J* = 7.0)	4.52 (q, *J* = 7.3)
21a	1.84 (ddd, *J* = 17.0, 9.5, 3.5)	1.84 (ddd, *J* = 16.8, 9.6, 3.3)
21b	*	2.27 (m)
22a	***	1.42 (m)
22b	***	1.45 (m)
23	3.86 (dd, *J* = 9.0, 3.0)	3.86 (dd, *J* = 8.8, 2.8)
25	1.34 (d, *J* = 7.0)	1.34 (d, *J* = 7.2)
OMe	3.34 (s)	3.34 (s)

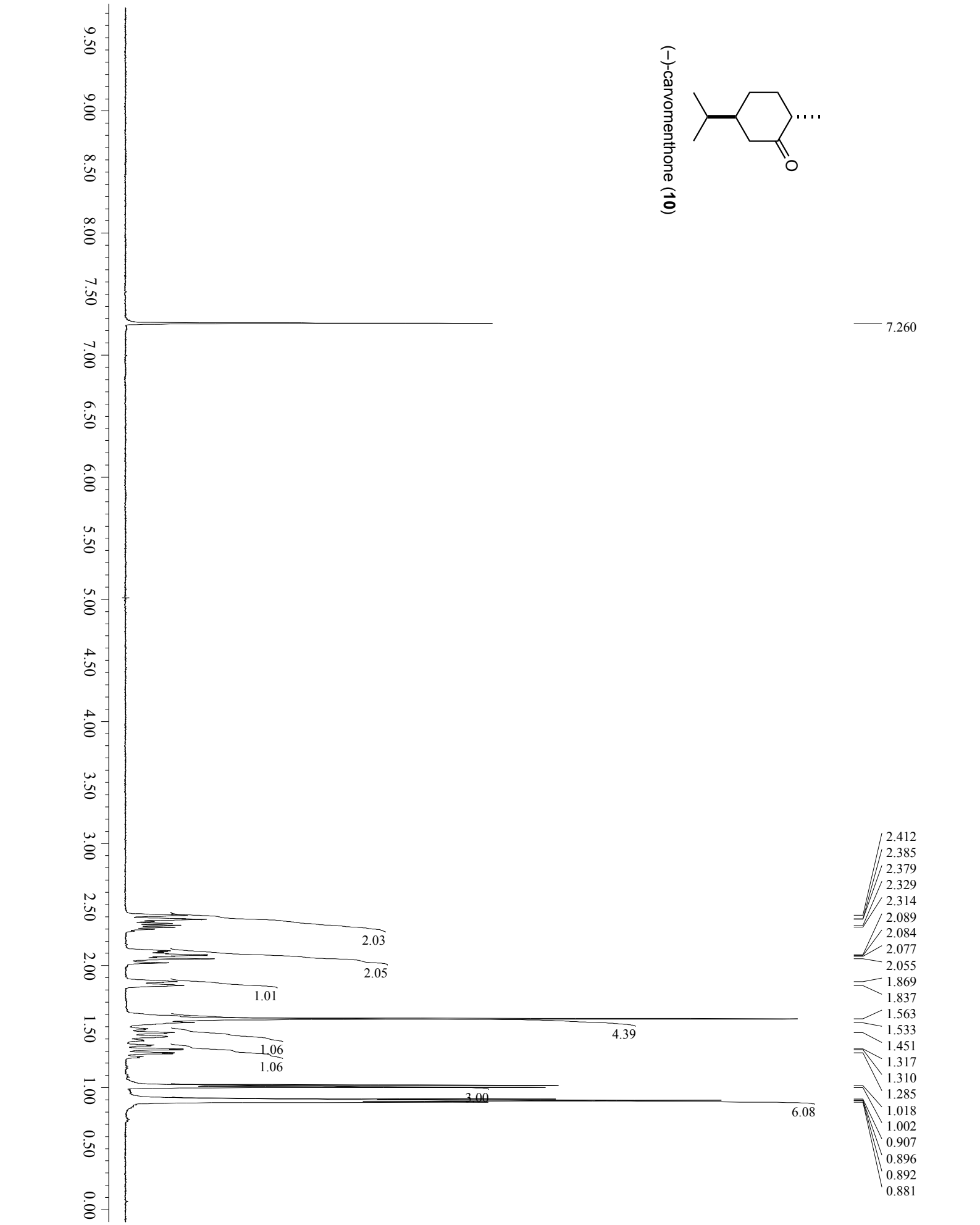
*2.03–2.34 (m), 4H; **1.60–1.64 (m), 2H; ***1.35–1.46 (m), 2H; ****1.27–1.33 (m), 2H.

Comparison of ^{13}C NMR data of synthetic and isolated boneratamide C methyl ester



methyl ester of boneratamide C (**3b**)

Position	^{13}C NMR (δ) Synthetic Sample (100 MHz, C_6D_6)	^{13}C NMR (δ) Natural Sample[8] (125 MHz, C_6D_6)	Δδ (ppm)
1	55.3	55.4	–0.1
2	45.2	45.3	–0.1
3	25.5	25.5	0
4	32.3	32.3	0
5	35.4	35.5	–0.1
6	59.2	58.9	+0.3
7	33.7	33.7	0
8	36.2	36.3	–0.1
9	143.1	143.5	–0.4
10	126.3	126.5	–0.2
11	29.4	29.4	0
12	22.3	22.3	0
13	21.4	21.4	0
14	16.8	17.1	–0.3
15	17.0	17.2	–0.2
16	–	–	
17	170.0	170.0	0
18	53.3	53.5	–0.2
19	–	–	
20	175.8	175.9	–0.1
21	29.8	29.9	–0.1
22	23.8	23.7	+0.1
23	58.0	58.1	–0.1
24	172.3	172.4	–0.1
25	14.7	14.4	+0.3
OMe	51.9	52.0	–0.1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8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
7.260
2.412
2.385
2.379
2.329
2.314
2.089
2.084
2.077
2.055
1.869
1.837
1.563
1.533
1.451
1.317
1.310
1.285
1.018
1.002
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0.892
0.881
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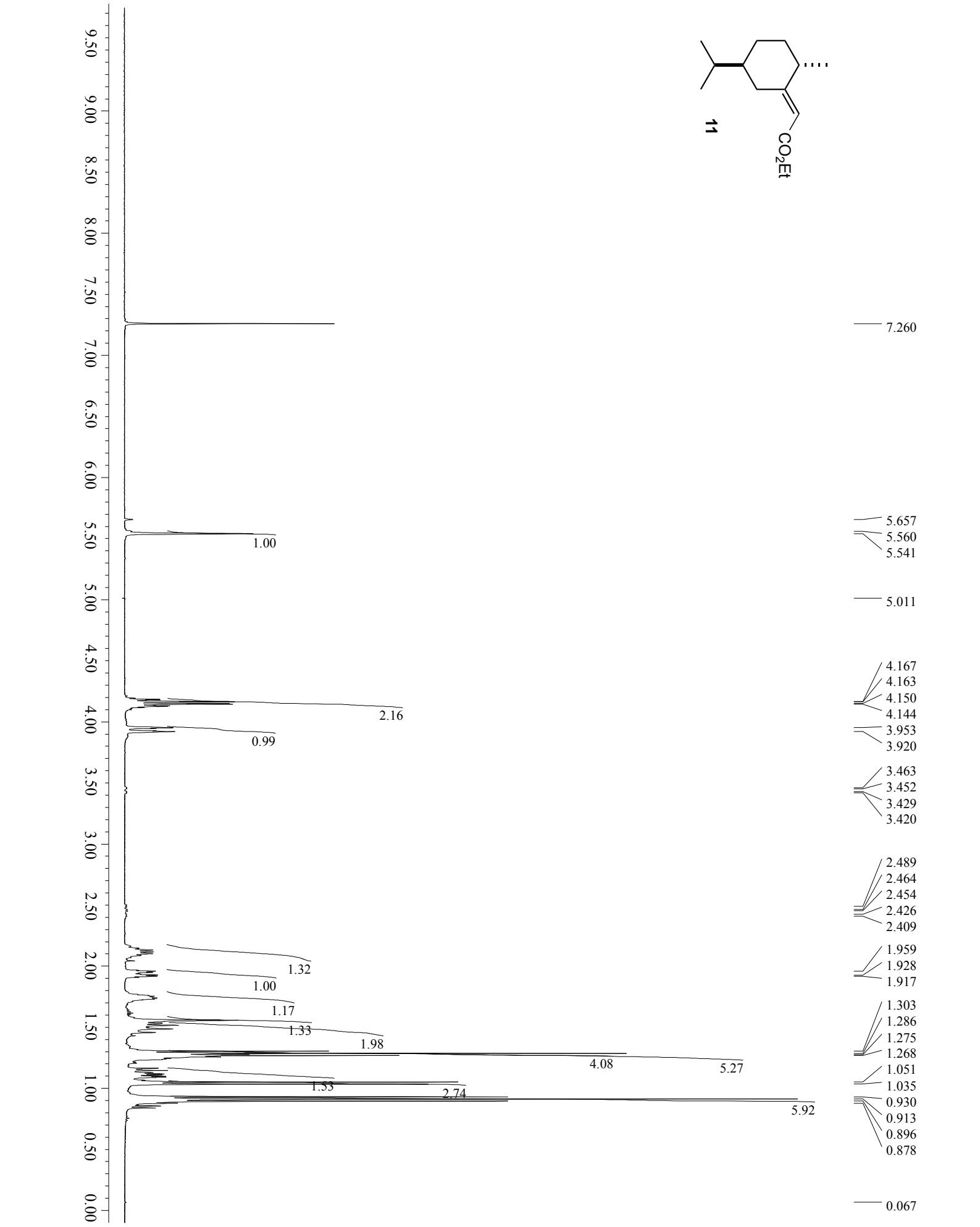
2.05
1.01
4.39
1.06
1.06
3.00
6.08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CO2Et
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7.50
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6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
7.260
5.657
5.560
5.541
5.011
4.167
4.163
4.150
4.144
3.953
3.920
3.463
3.452
3.429
3.420
2.489
2.464
2.454
2.426
2.409
1.959
1.928
1.917
1.303
1.286
1.275
1.268
1.051
1.035
0.930
0.913
0.896
0.878
0.067
1.00
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1.00
1.17
1.33
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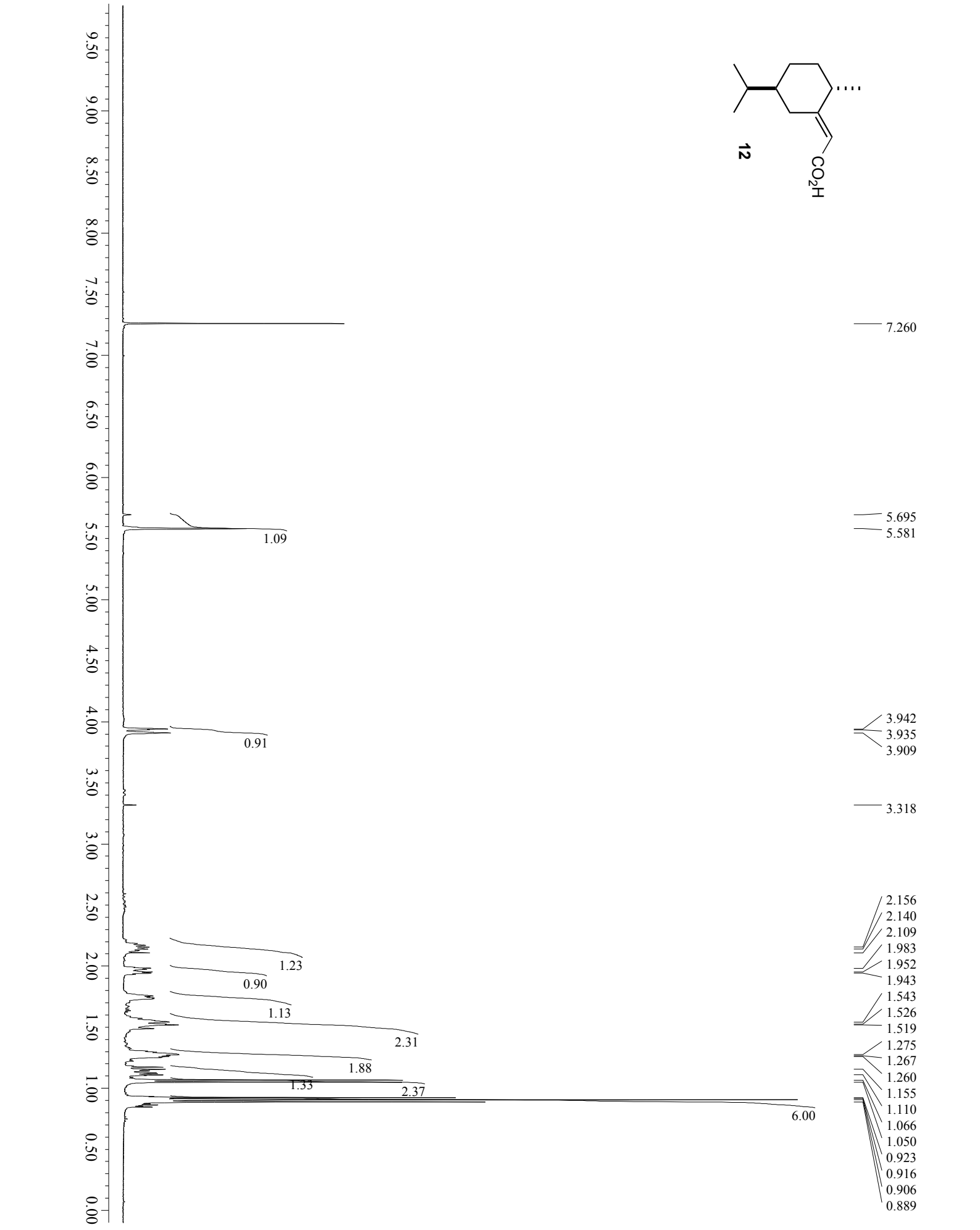
4.08
5.27
1.53
2.74
5.92


12
CO2H
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8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
7.260
5.695
5.581
3.942
3.935
3.909
3.318
2.156
2.140
2.109
1.983
1.952
1.943
1.543
1.526
1.519
1.275
1.267
1.260
1.155
1.110
1.066
1.050
0.923
0.916
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0.91
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0.90
1.13
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1.33
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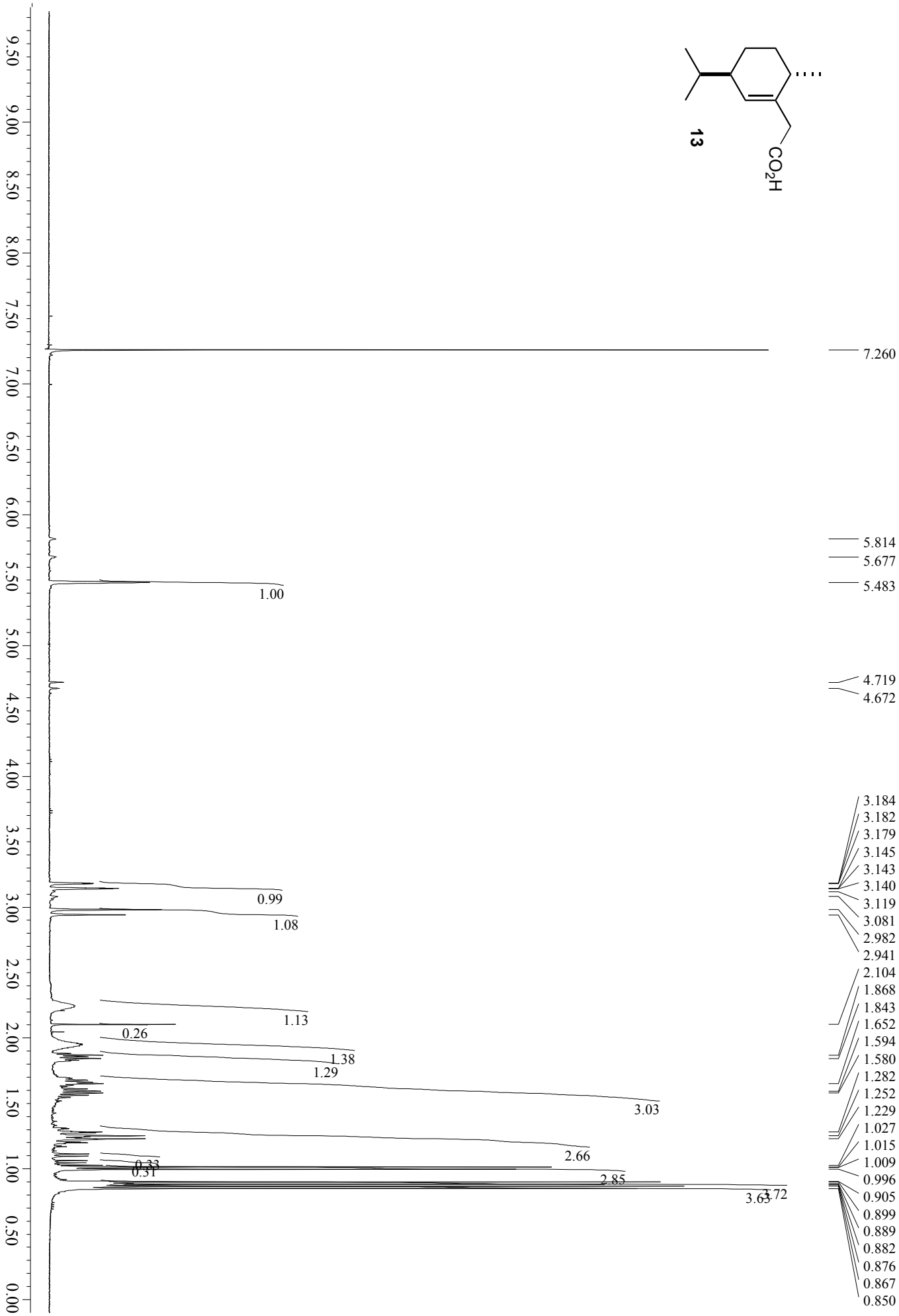
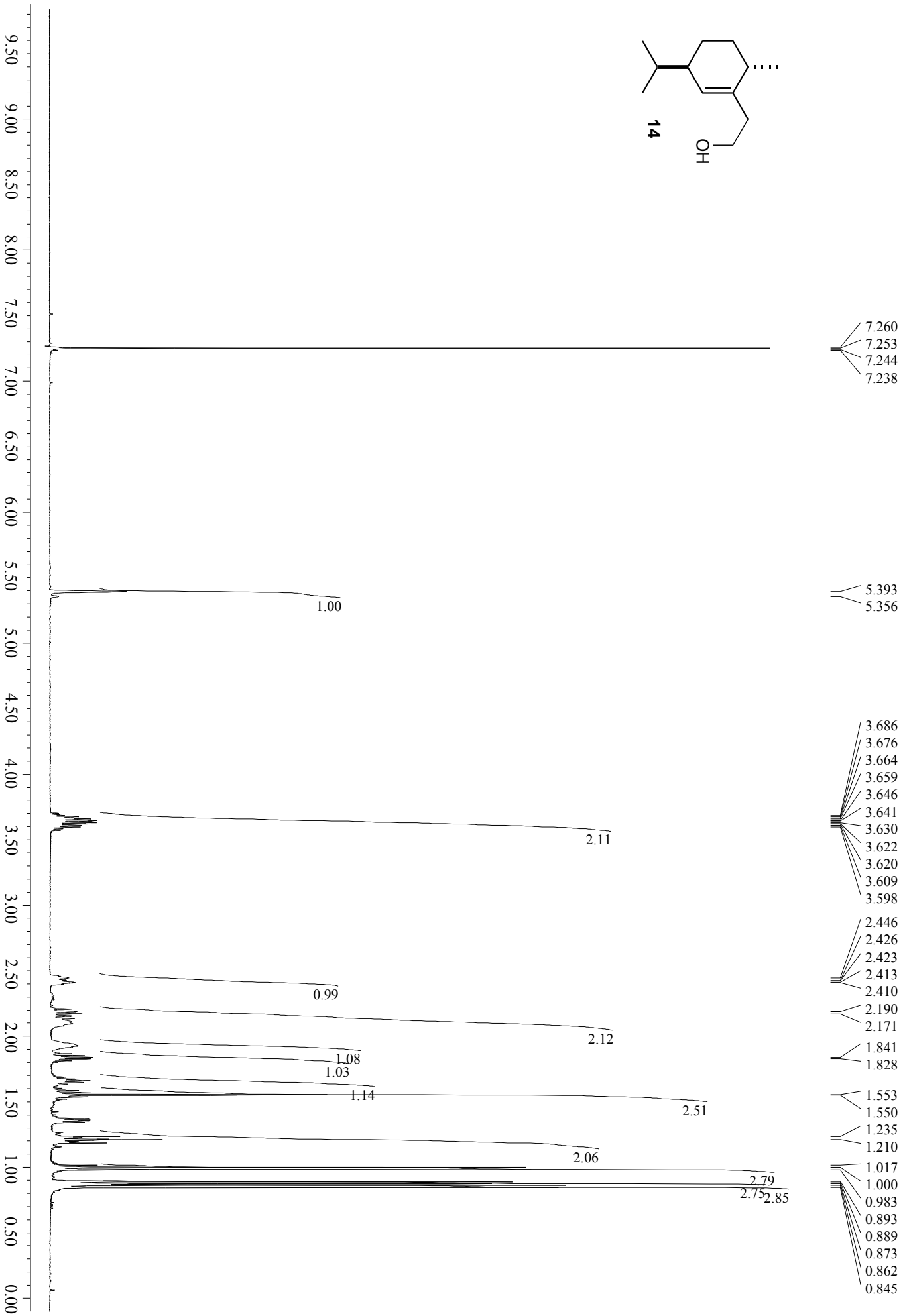
6.00


13
CO2H
9.50
9.00
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
7.260
5.814
5.677
5.483
4.719
4.672
3.184
3.182
3.179
3.145
3.143
3.140
3.119
3.081
2.982
2.941
2.104
1.868
1.843
1.652
1.594
1.580
1.282
1.252
1.229
1.027
1.015
1.009
0.996
0.905
0.899
0.889
0.882
0.876
0.867
0.850
1.00
0.99
1.08
1.13
0.26
1.38
1.29
3.03
2.66
0.33
0.31
2.85
3.72
3.63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8.00
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7.00
6.50
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5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
1.00
2.11
0.99
2.12
1.08
1.03
1.14
2.51
2.06
2.79
2.75
2.85
7.260
7.253
7.244
7.238
5.393
5.356
3.686
3.676
3.664
3.659
3.646
3.641
3.630
3.622
3.620
3.609
3.598
2.446
2.426
2.423
2.413
2.410
2.190
2.171
1.841
1.828
1.553
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1.017
1.000
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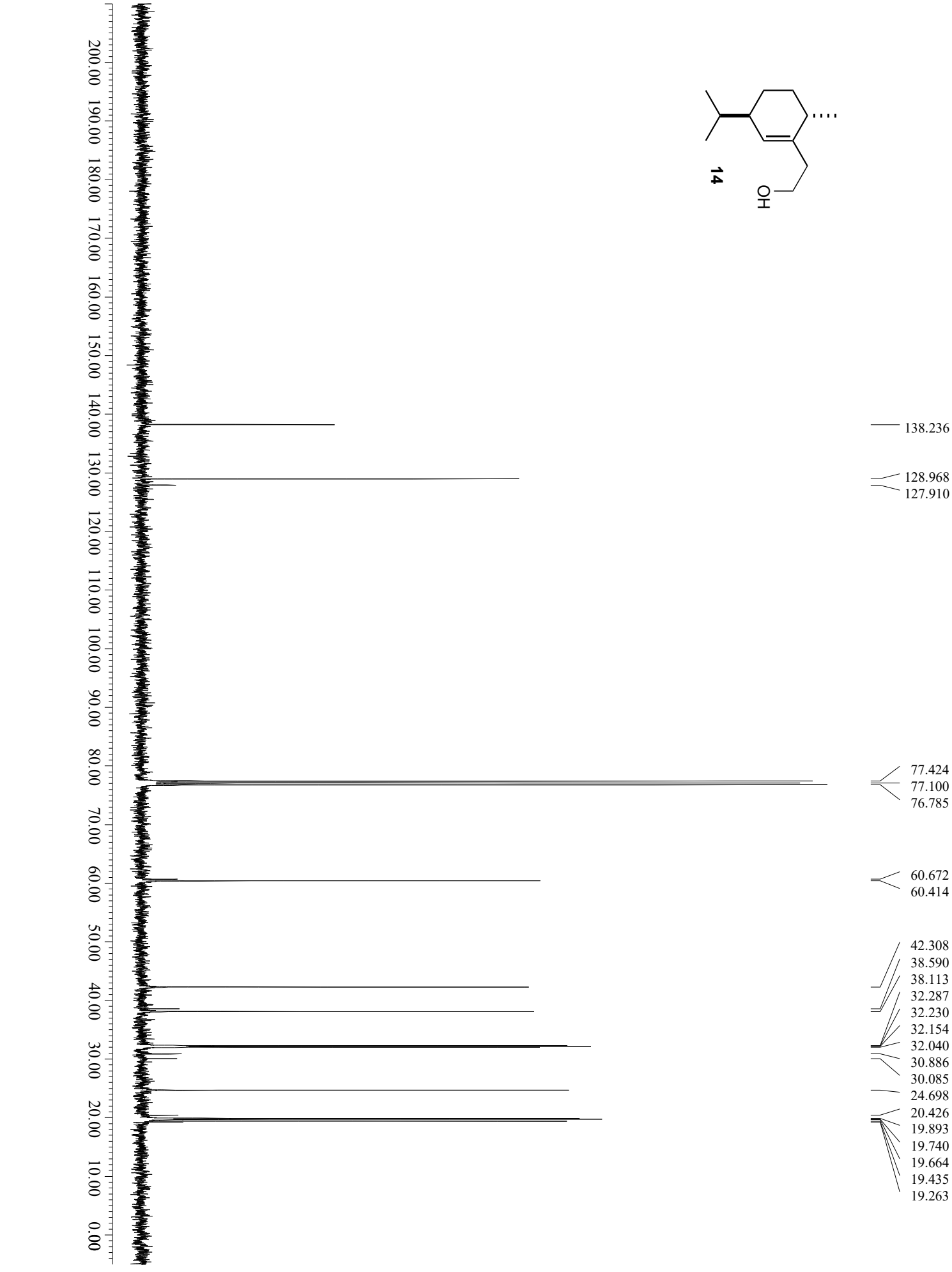
0.893
0.889
0.873
0.862
0.845


14
OH
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77.424
77.100
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60.672
60.414
42.308
38.590
38.113
32.287
32.230
32.154
32.040
30.886
30.085
24.698
20.426
19.893
19.740
19.664
19.435
19.263
200.00
190.00
180.00
170.00
160.00
150.00
140.00
130.00
120.00
110.00
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90.00
80.00
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50.00
40.00
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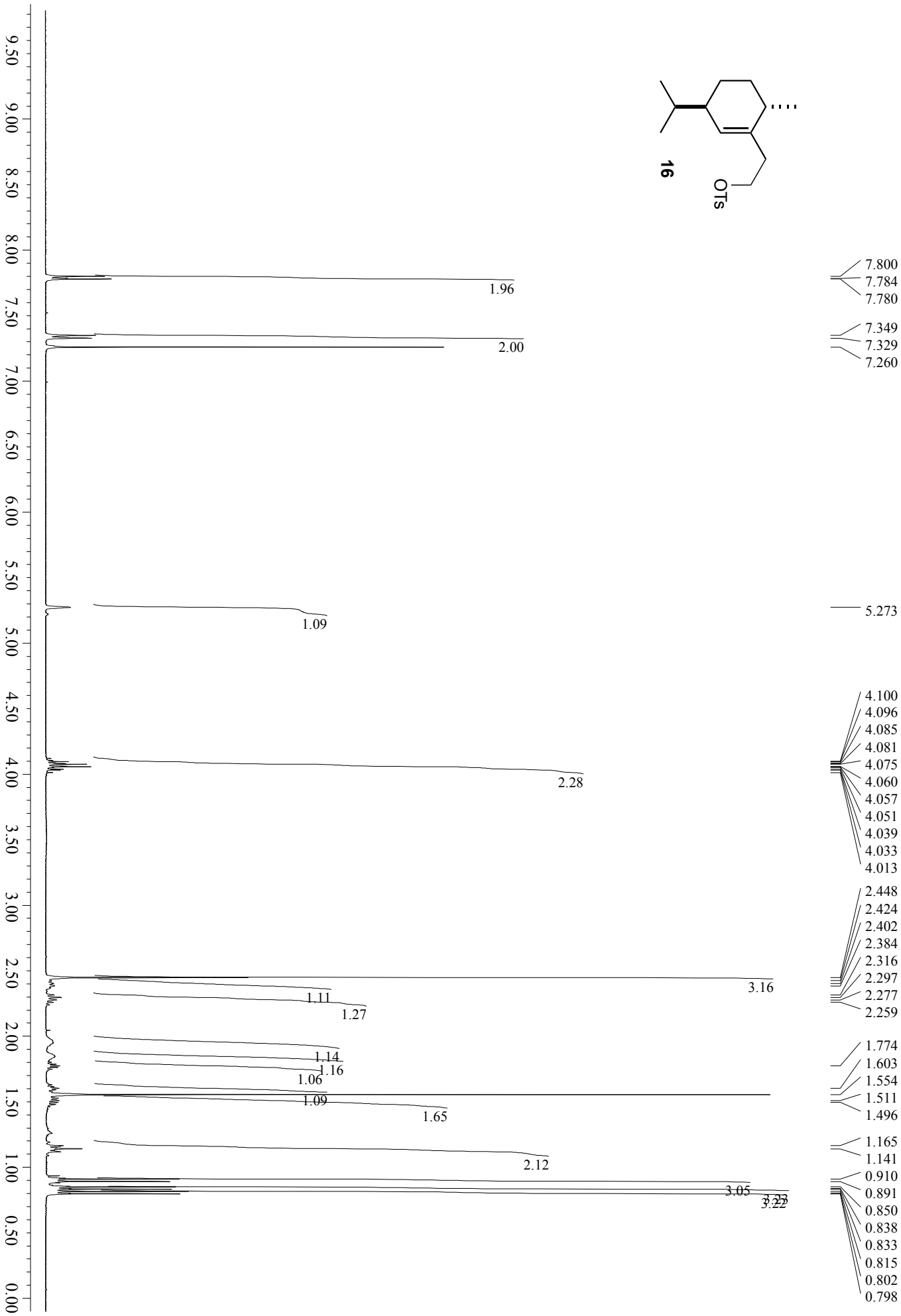
20.00
10.00
0.00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5.50
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4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
1.96
2.00
1.09
2.28
3.16
1.11
1.27
1.14
1.16
1.06
1.09
1.65
2.12
3.05
3.22
7.800
7.784
7.780
7.349
7.329
7.260
5.273
4.100
4.096
4.085
4.081
4.075
4.060
4.057
4.051
4.039
4.033
4.013
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2.402
2.384
2.316
2.297
2.277
2.259
1.774
1.603
1.554
1.511
1.496
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1.141
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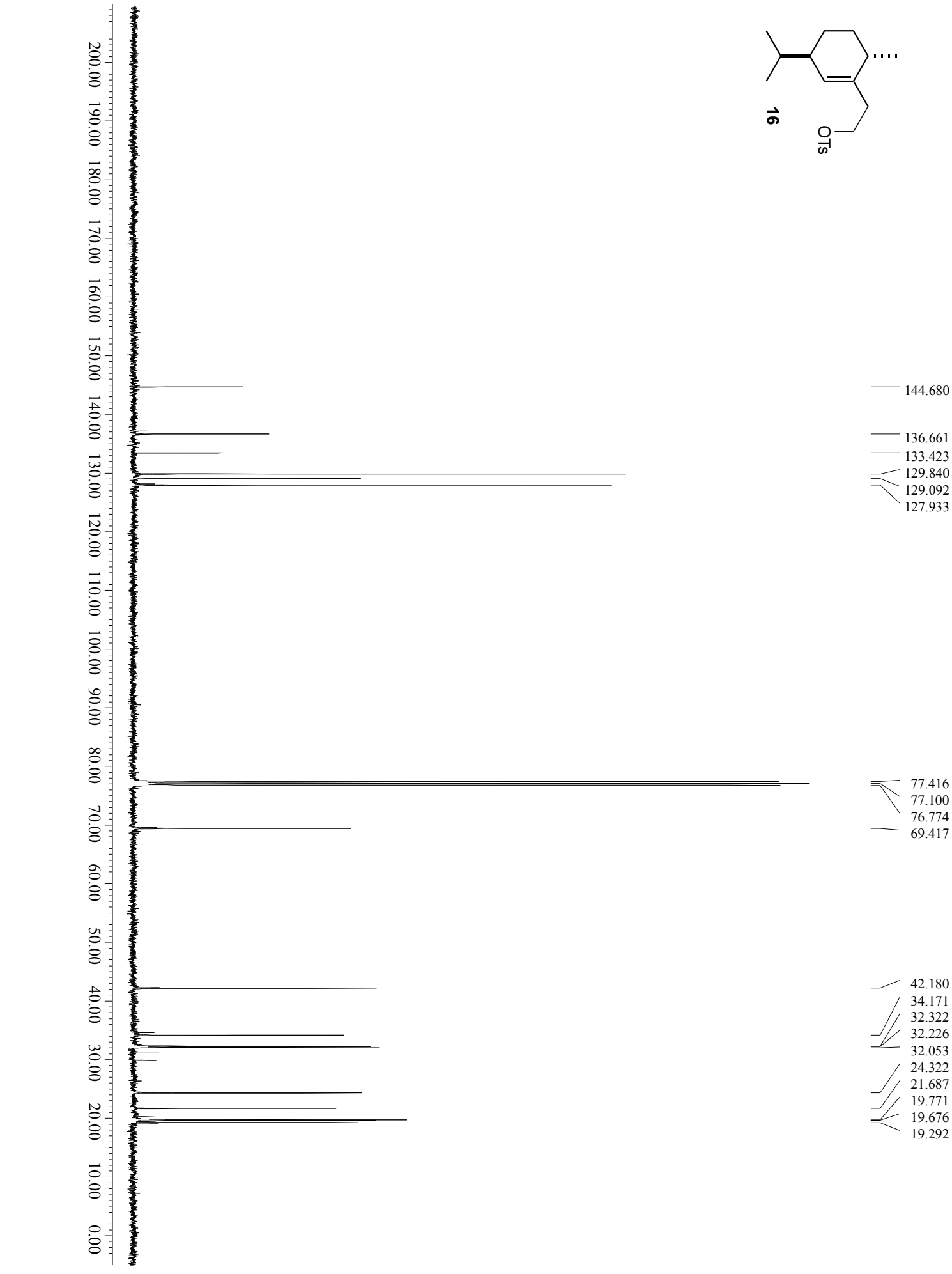
0.891
0.850
0.838
0.833
0.815
0.802
0.798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42.180
34.171
32.322
32.226
32.053
24.322
21.687
19.771
19.676
19.292
200.00
190.00
180.00
170.00
160.00
150.00
140.00
130.00
120.00
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60.00
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40.00
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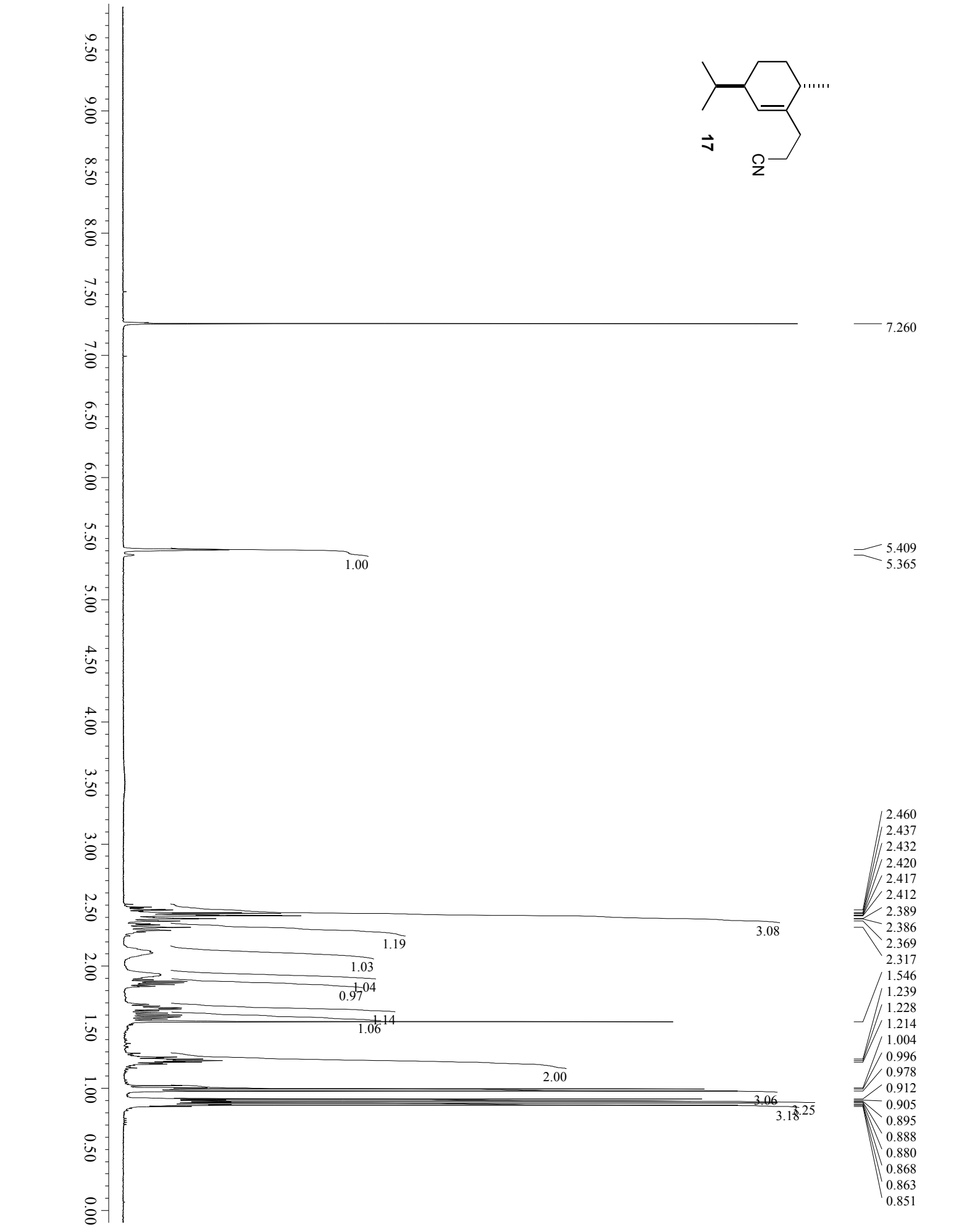
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CN
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7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
7.260
5.409
5.365
1.00
2.460
2.437
2.432
2.420
2.417
2.412
2.389
2.386
2.369
2.317
3.08
1.19
1.03
1.04
0.97
1.14
1.06
1.546
1.239
1.228
1.214
1.004
0.996
0.978
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0.880
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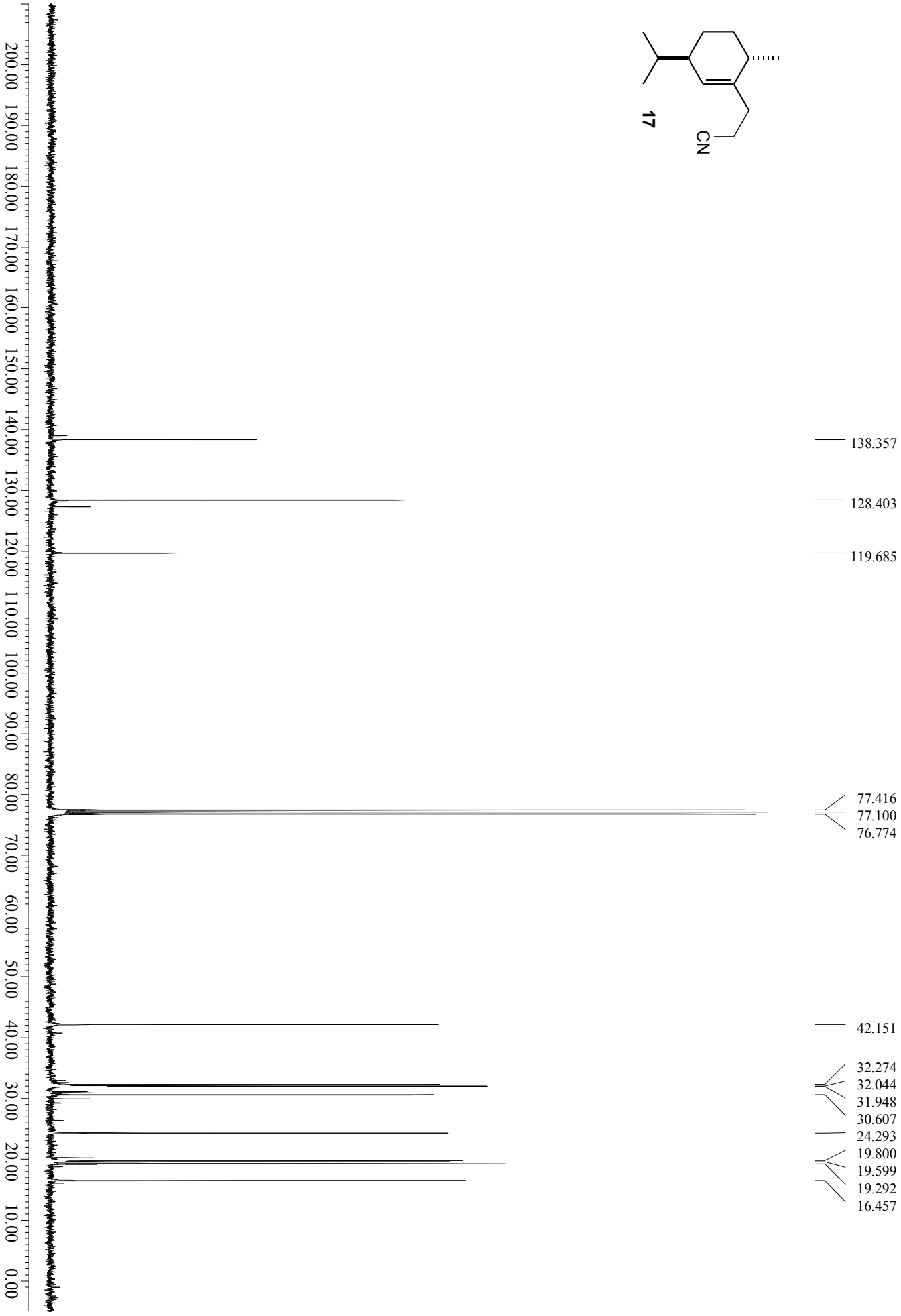
3.18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130.00
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100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
CN
17
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128.403
119.685
77.416
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32.274
32.044
31.948
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24.293
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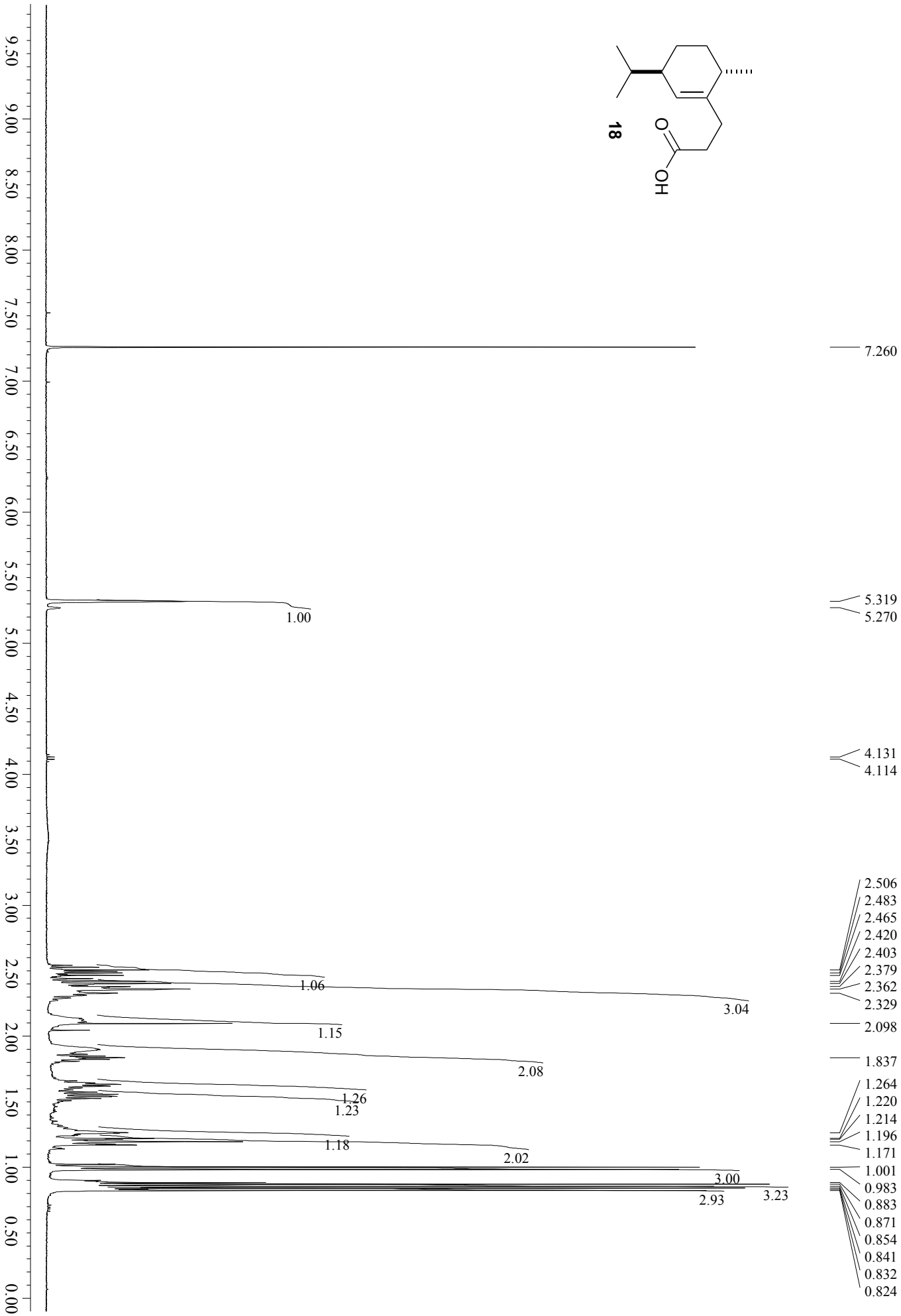
19.292
16.457


18
OH
O
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8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
7.260
5.319
5.270
4.131
4.114
2.506
2.483
2.465
2.420
2.403
2.379
2.362
2.329
2.098
1.837
1.264
1.220
1.214
1.196
1.171
1.001
0.983
0.883
0.871
0.854
0.841
0.832
0.824
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3.04
1.15
2.08
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1.23
1.18
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3.00
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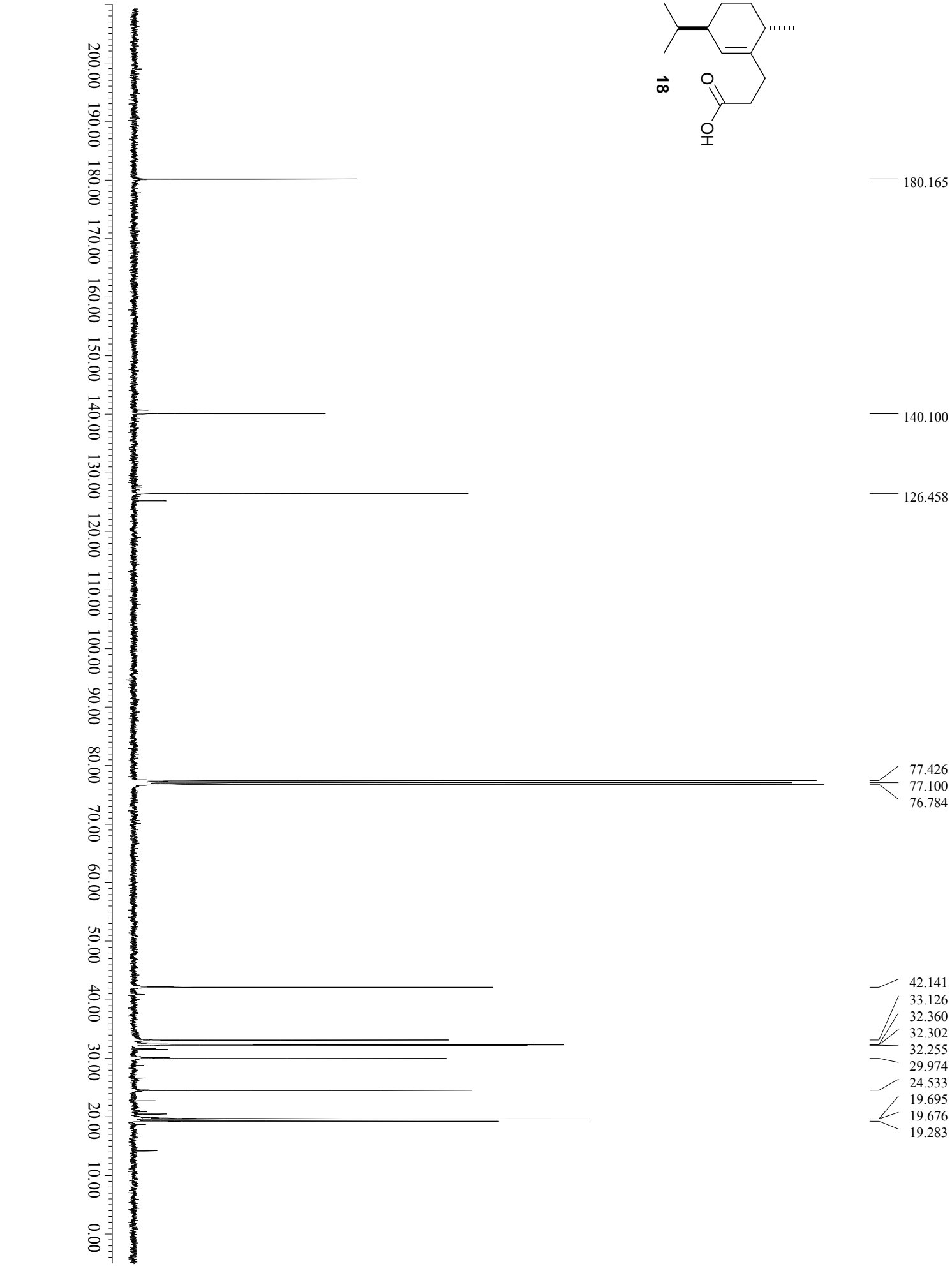
3.23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150.00
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130.00
120.00
110.00
100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
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77.426
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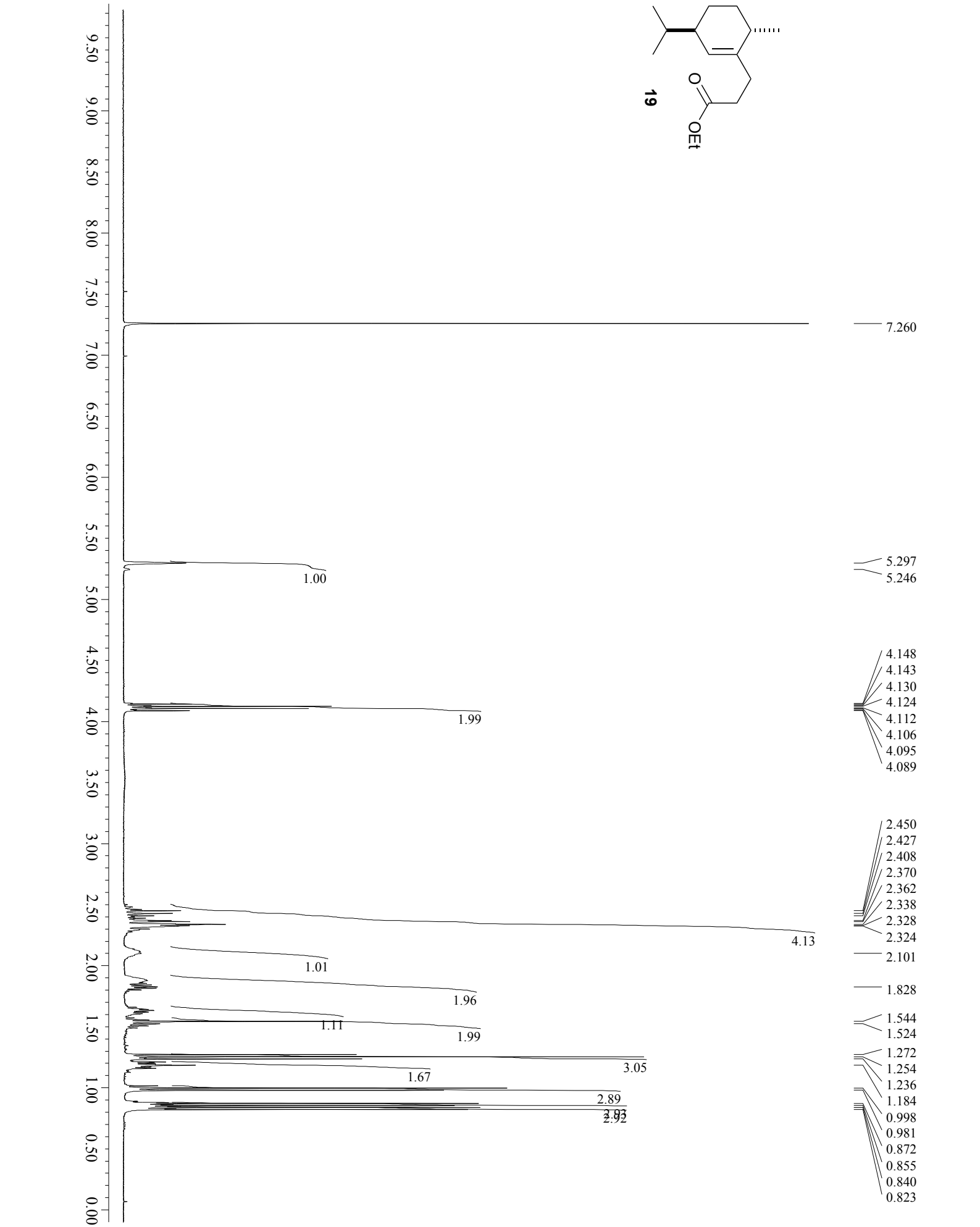
19.283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OEt
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8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
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5.246
4.148
4.143
4.130
4.124
4.112
4.106
4.095
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2.427
2.408
2.370
2.362
2.338
2.328
2.324
2.101
1.828
1.544
1.524
1.272
1.254
1.236
1.184
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0.981
0.872
0.855
0.840
0.823
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1.01
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1.11
1.99
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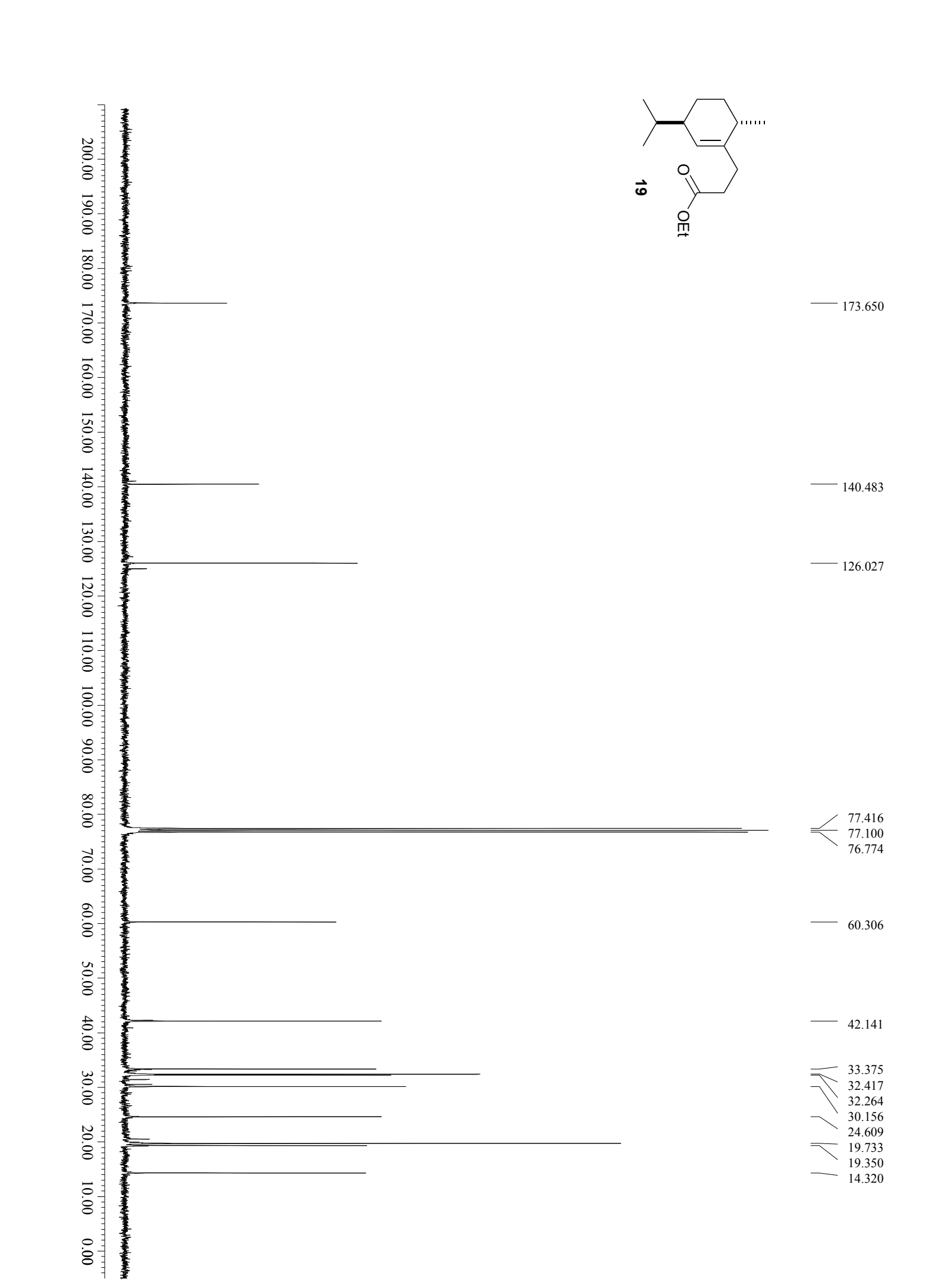
2.92


19
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OEt
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170.00
160.00
150.00
140.00
130.00
120.00
110.00
100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
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140.483
126.027
77.416
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32.417
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30.156
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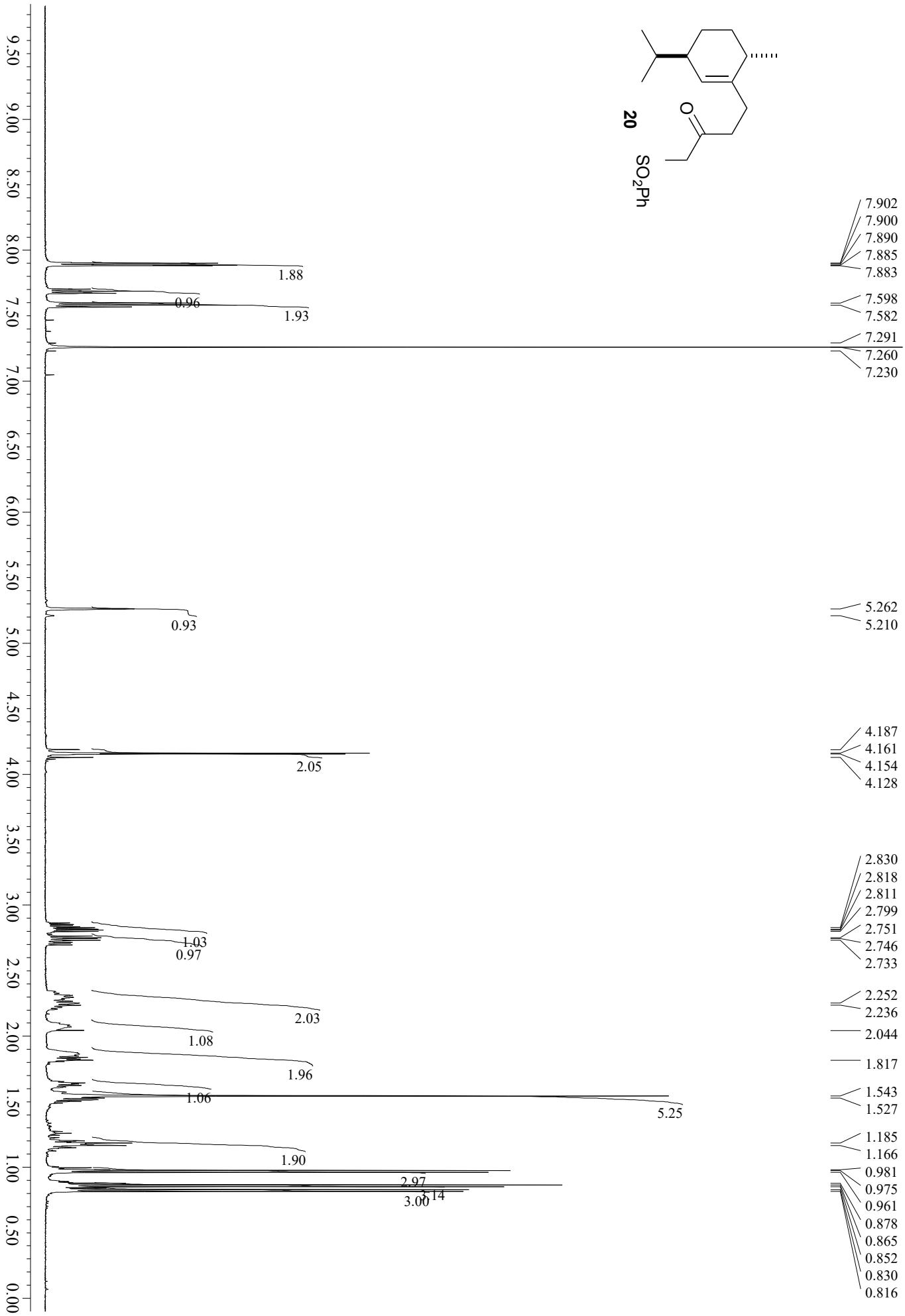
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O
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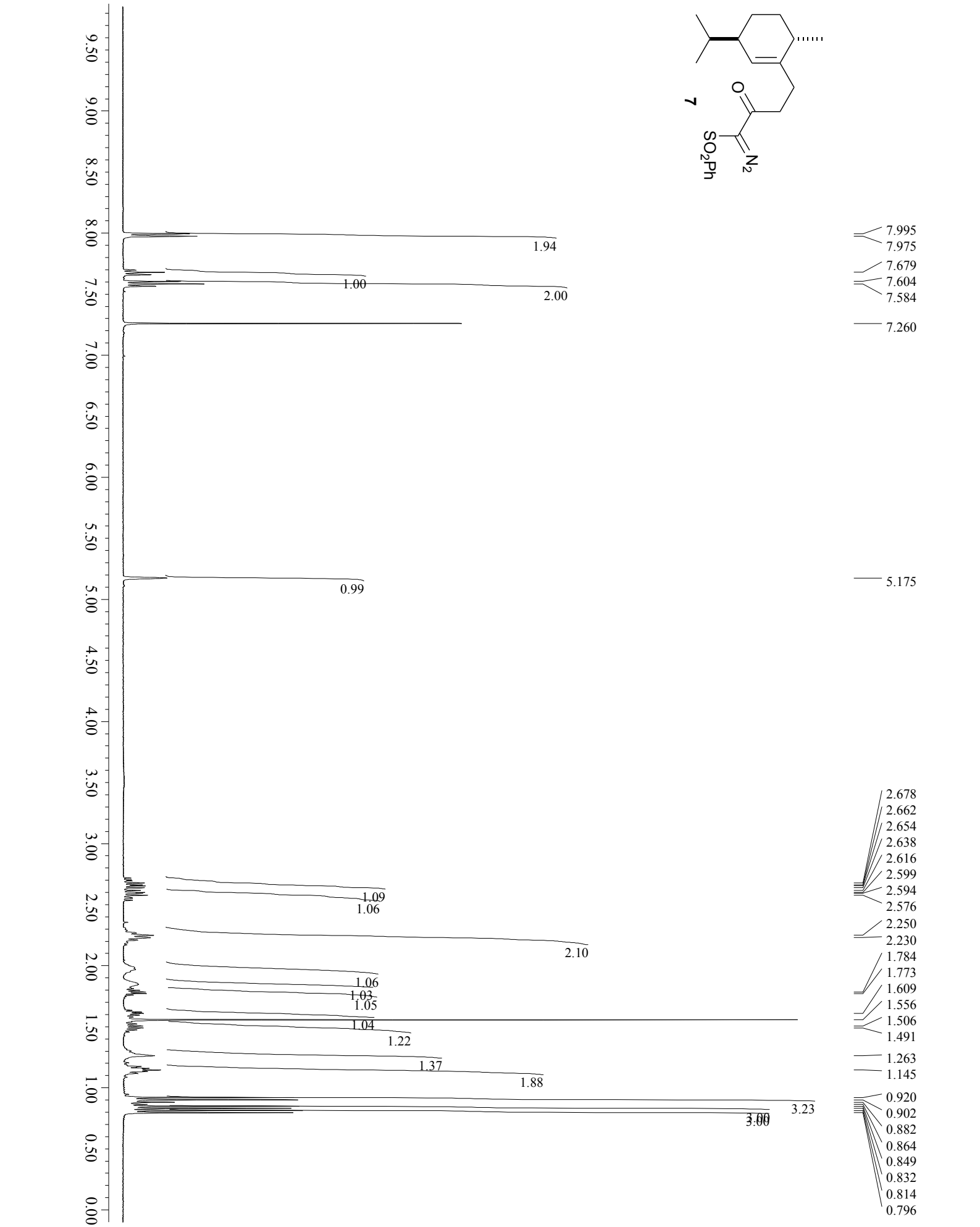
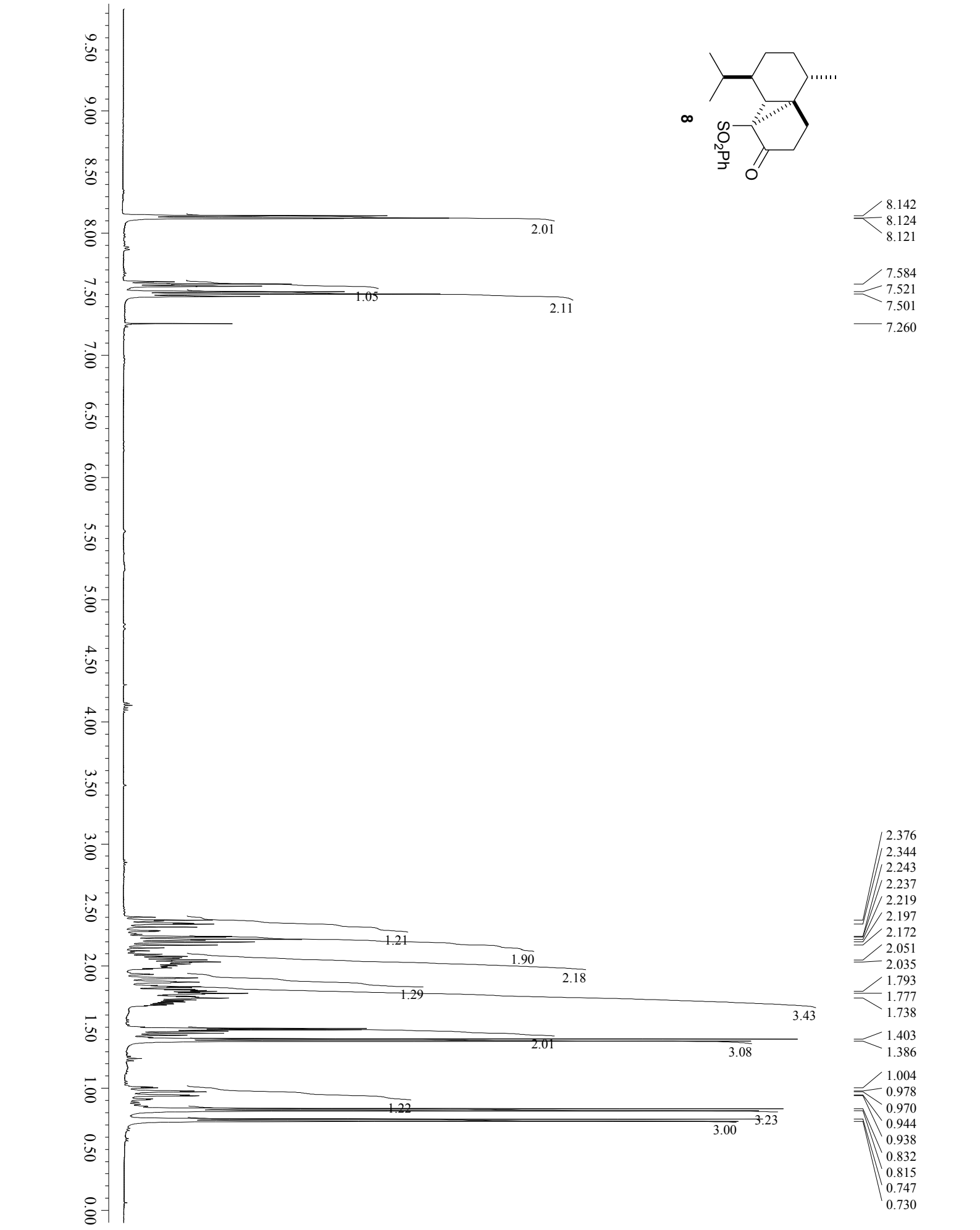
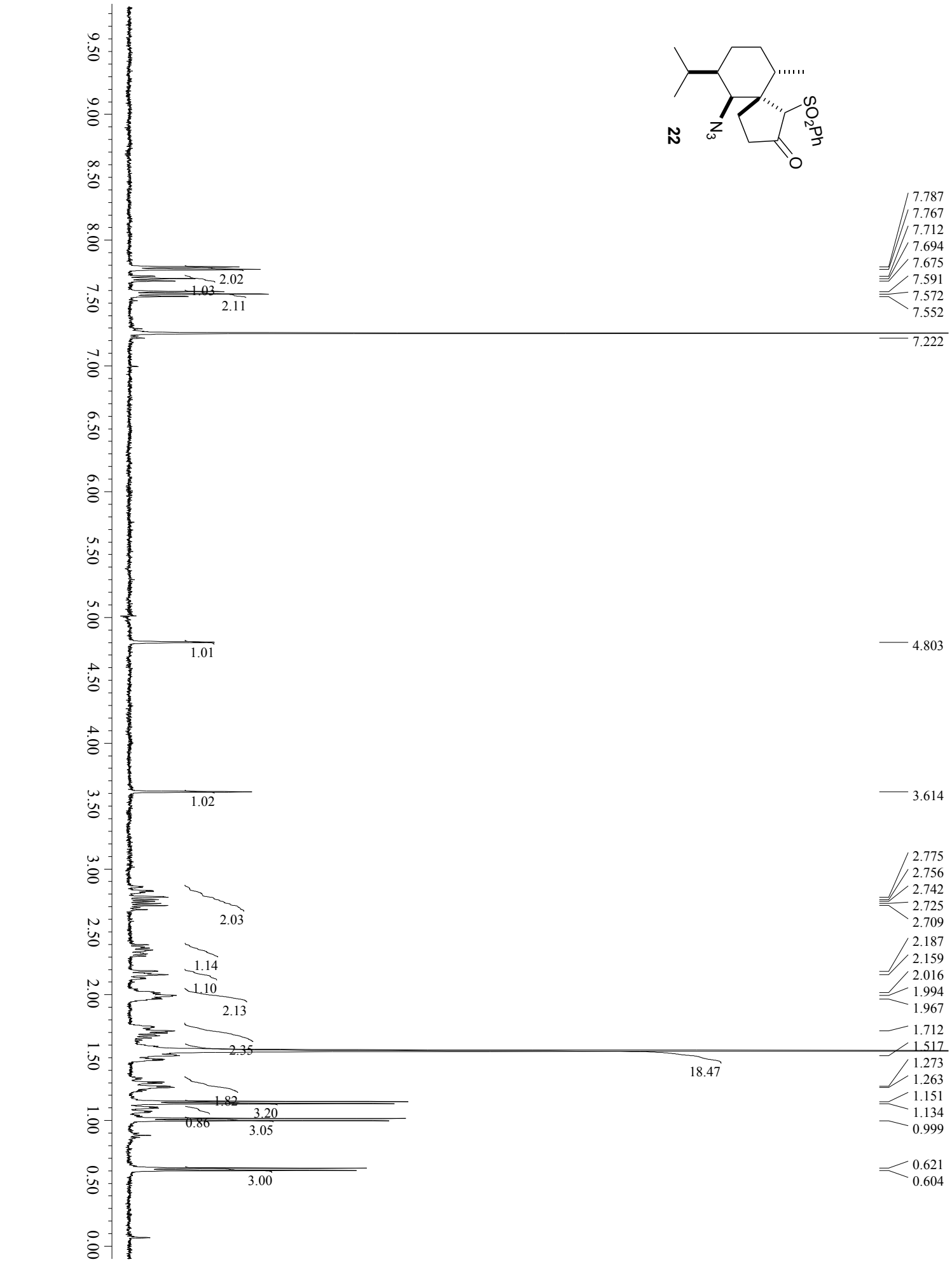
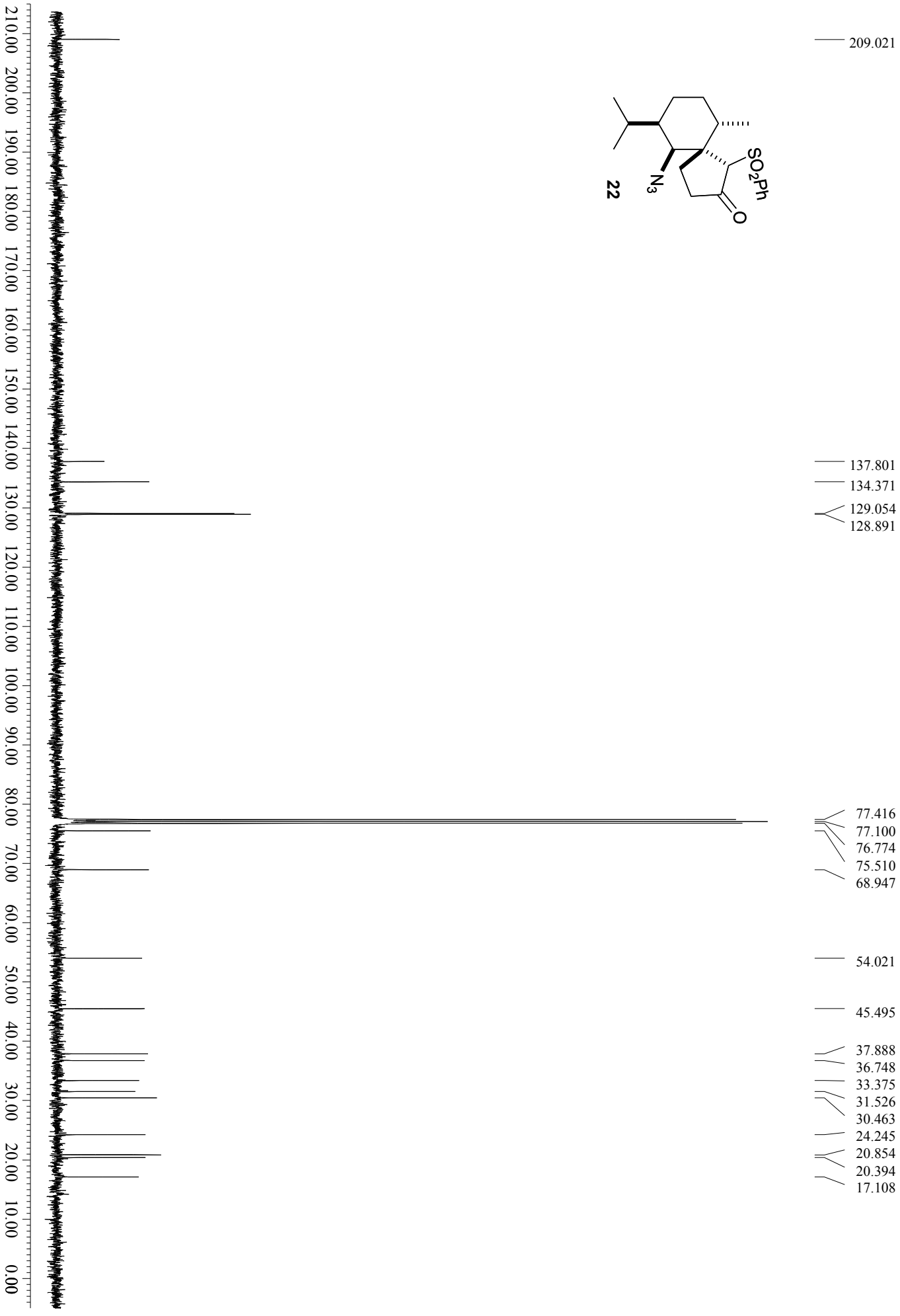
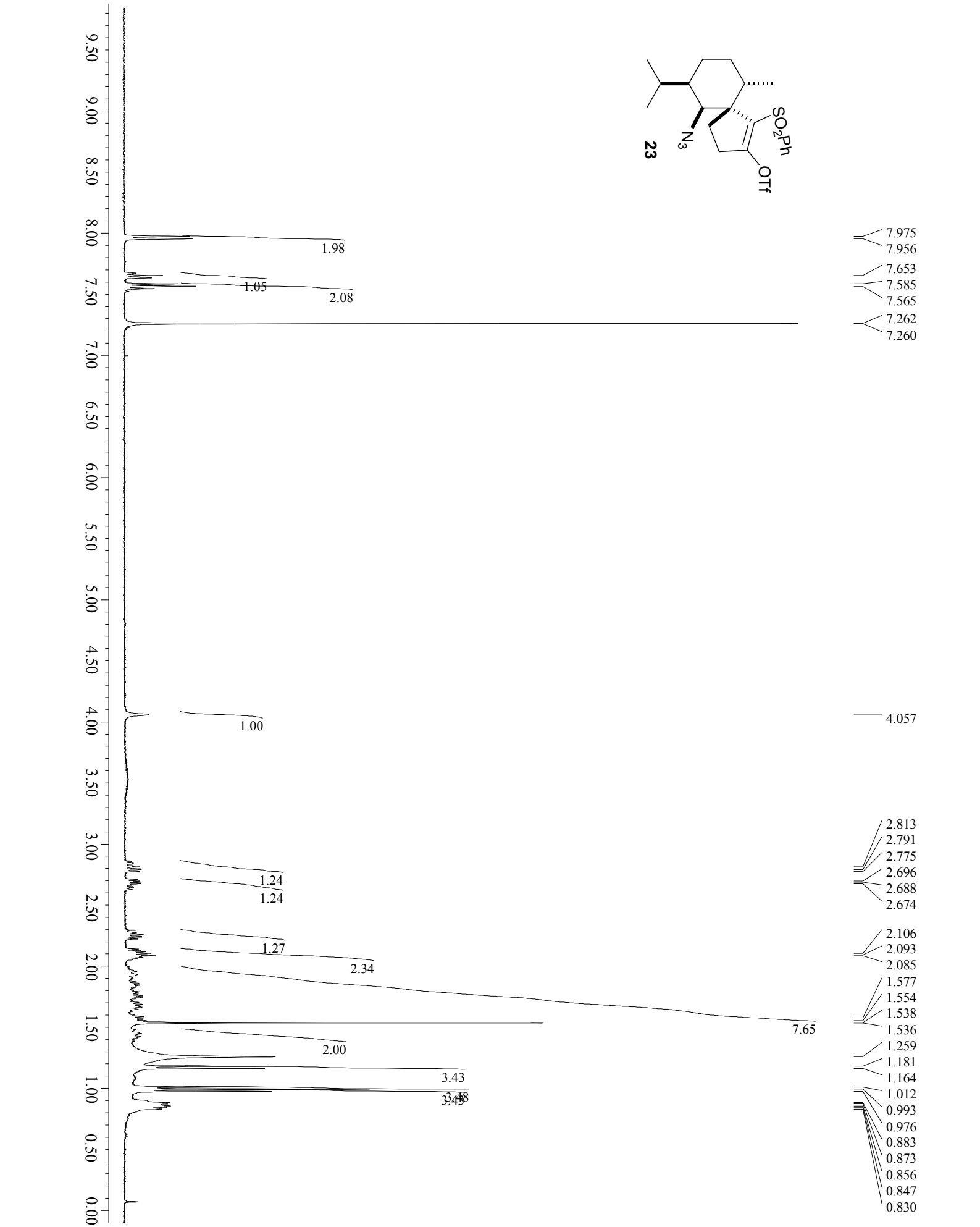
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
1.88
0.96
1.93
0.93
2.05
1.03
0.97
2.03
1.08
1.96
1.06
5.25
1.90
2.97
3.00
5.14
7.902
7.900
7.890
7.885
7.883
7.598
7.582
7.291
7.260
7.230
5.262
5.210
4.187
4.161
4.154
4.128
2.830
2.818
2.811
2.799
2.751
2.746
2.733
2.252
2.236
2.044
1.817
1.543
1.527
1.185
1.166
0.981
0.975
0.961
0.878
0.865
0.852
0.830
0.816

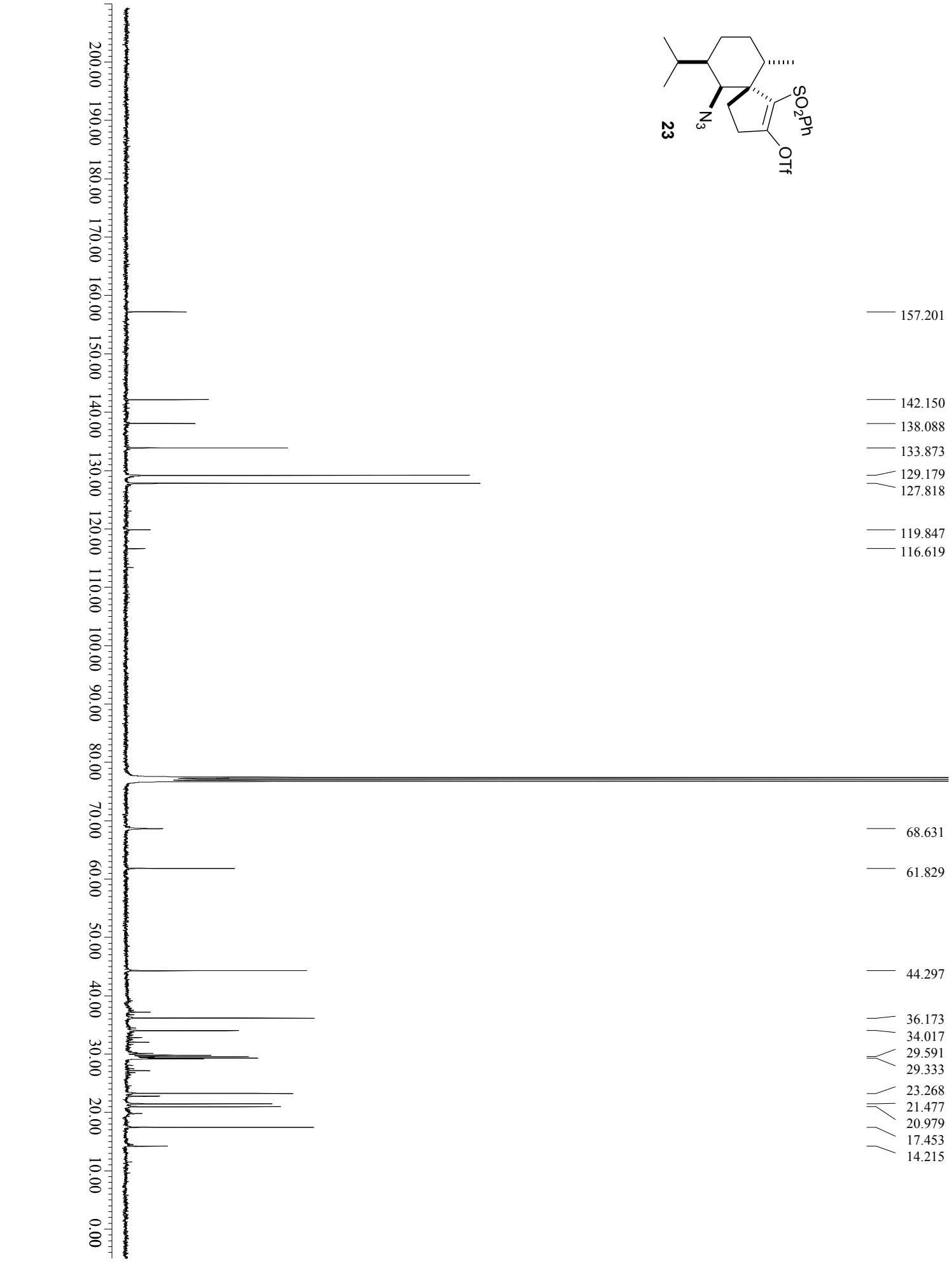

7
O
N2
SO2Ph
9.50
9.00
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
1.94
1.00
2.00
0.99
1.09
1.06
2.10
1.06
1.03
1.05
1.04
1.22
1.37
1.88
3.23
3.00
7.995
7.975
7.679
7.604
7.584
7.260
5.175
2.678
2.662
2.654
2.638
2.616
2.599
2.594
2.576
2.250
2.230
1.784
1.773
1.609
1.556
1.506
1.491
1.263
1.145
0.920
0.902
0.882
0.864
0.849
0.832
0.814
0.796

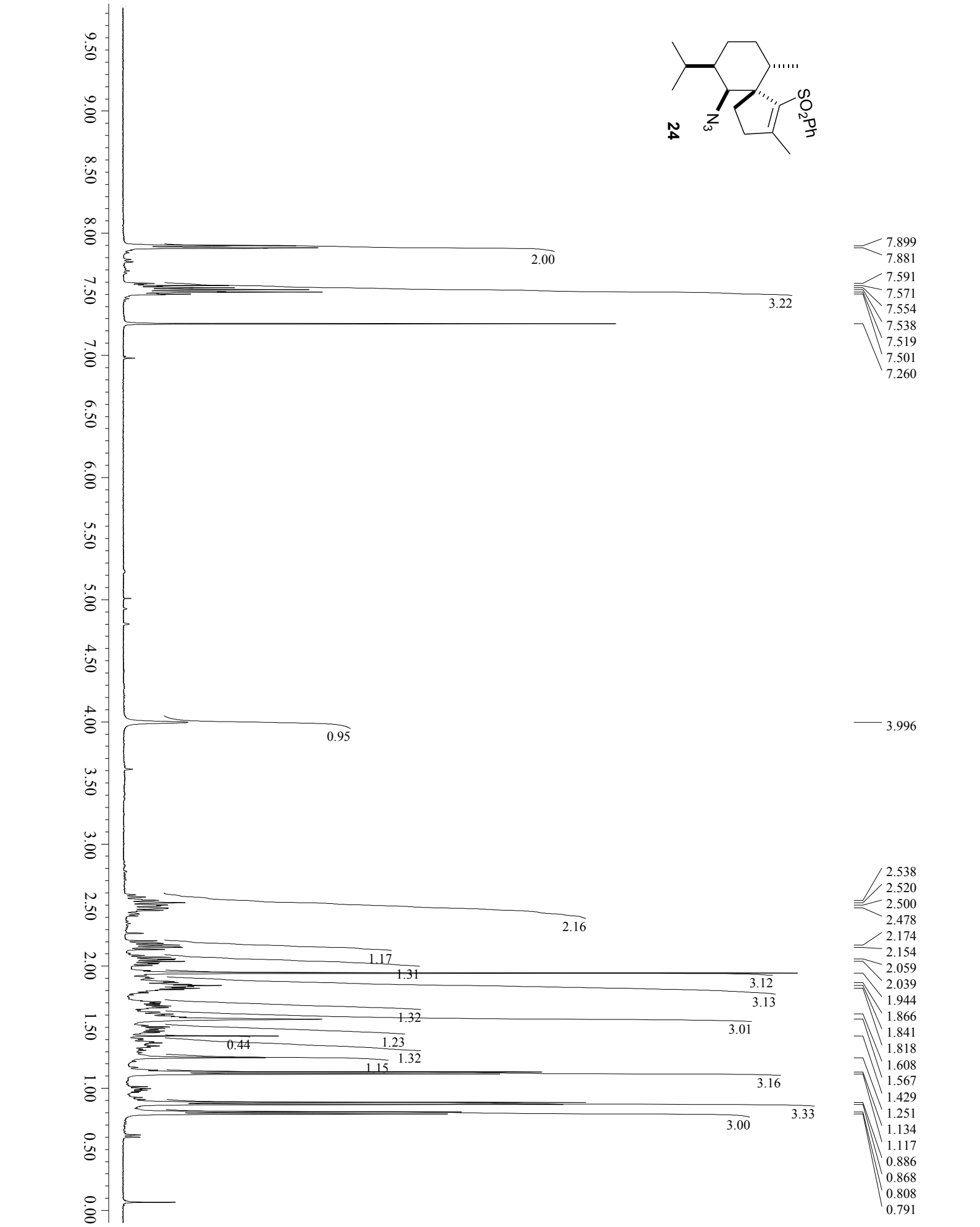

8
SO2Ph
O
8.142
8.124
8.121
7.584
7.521
7.501
7.260
2.376
2.344
2.243
2.237
2.219
2.197
2.172
2.051
2.035
1.793
1.777
1.738
1.403
1.386
1.004
0.978
0.970
0.944
0.938
0.832
0.815
0.747
0.730
2.01
1.05
2.11
1.21
1.90
2.18
1.29
3.43
2.01
3.08
1.22
3.23
3.00
9.50
9.00
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00

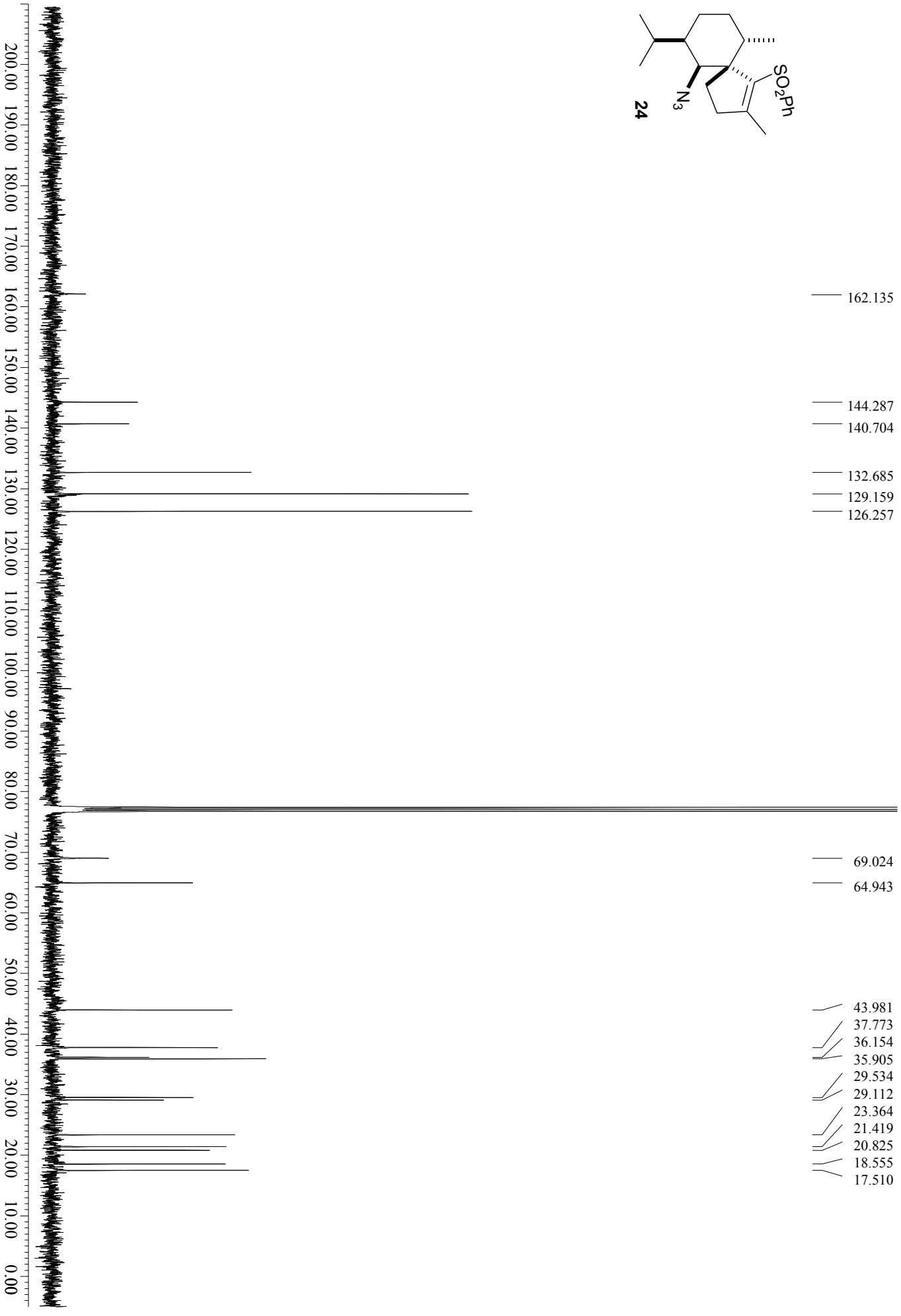

22
N3
SO2Ph
O
7.787
7.767
7.712
7.694
7.675
7.591
7.572
7.552
7.222
4.803
3.614
2.775
2.756
2.742
2.725
2.709
2.187
2.159
2.016
1.994
1.967
1.712
1.517
1.273
1.263
1.151
1.134
0.999
0.621
0.604
2.02
1.03
2.11
1.01
1.02
2.03
1.14
1.10
2.13
2.35
18.47
1.82
3.20
0.86
3.05
3.00

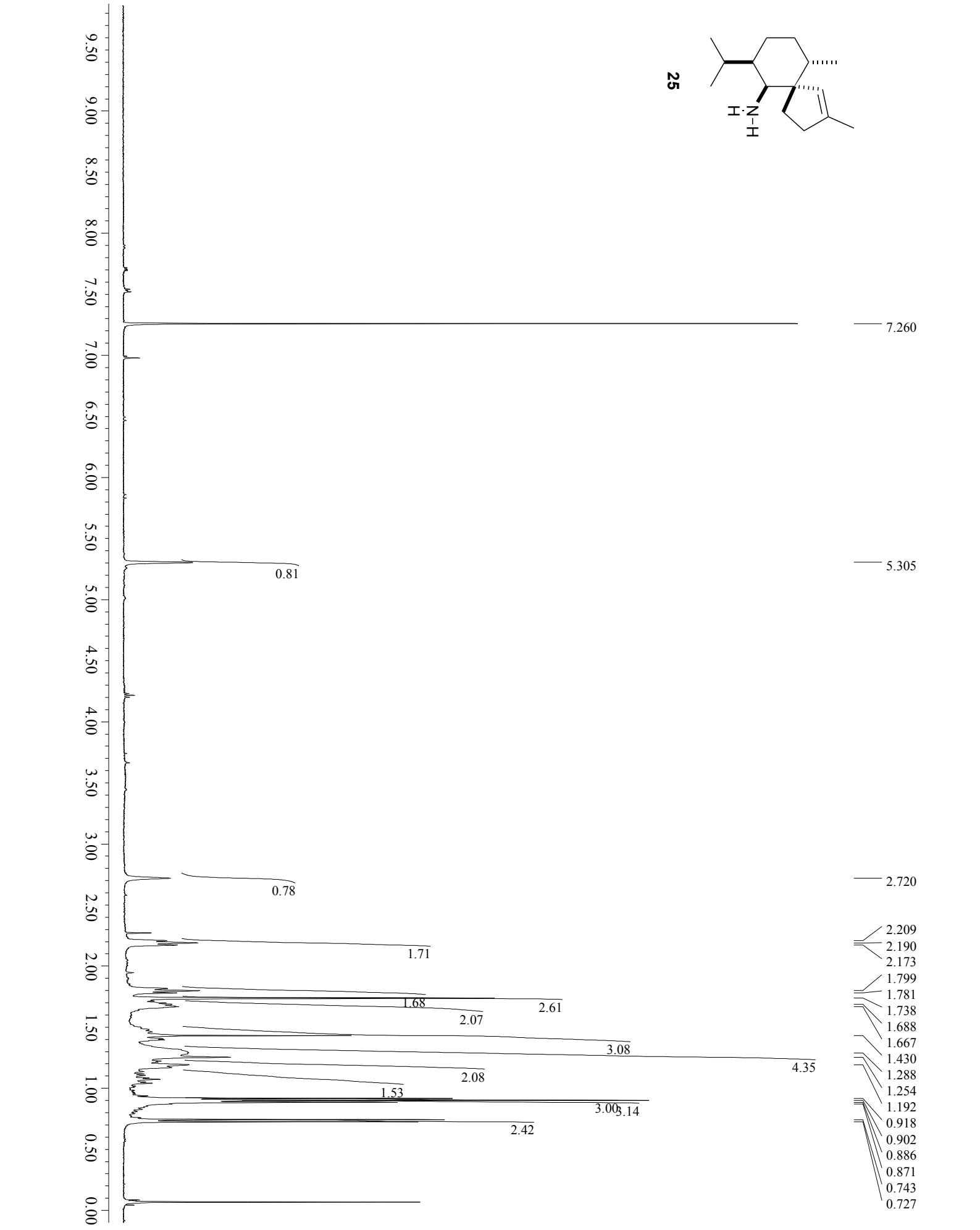

209.021
137.801
134.371
129.054
128.891
77.416
77.100
76.774
75.510
68.947
54.021
45.495
37.888
36.748
33.375
31.526
30.463
24.245
20.854
20.394
17.108
210.00 200.00 190.00 180.00 170.00 160.00 150.00 140.00 130.00 120.00 110.00 100.00 90.00 80.00 70.00 60.00 50.00 40.00 30.00 20.00 10.00 0.00
SO2Ph
N3
O
22

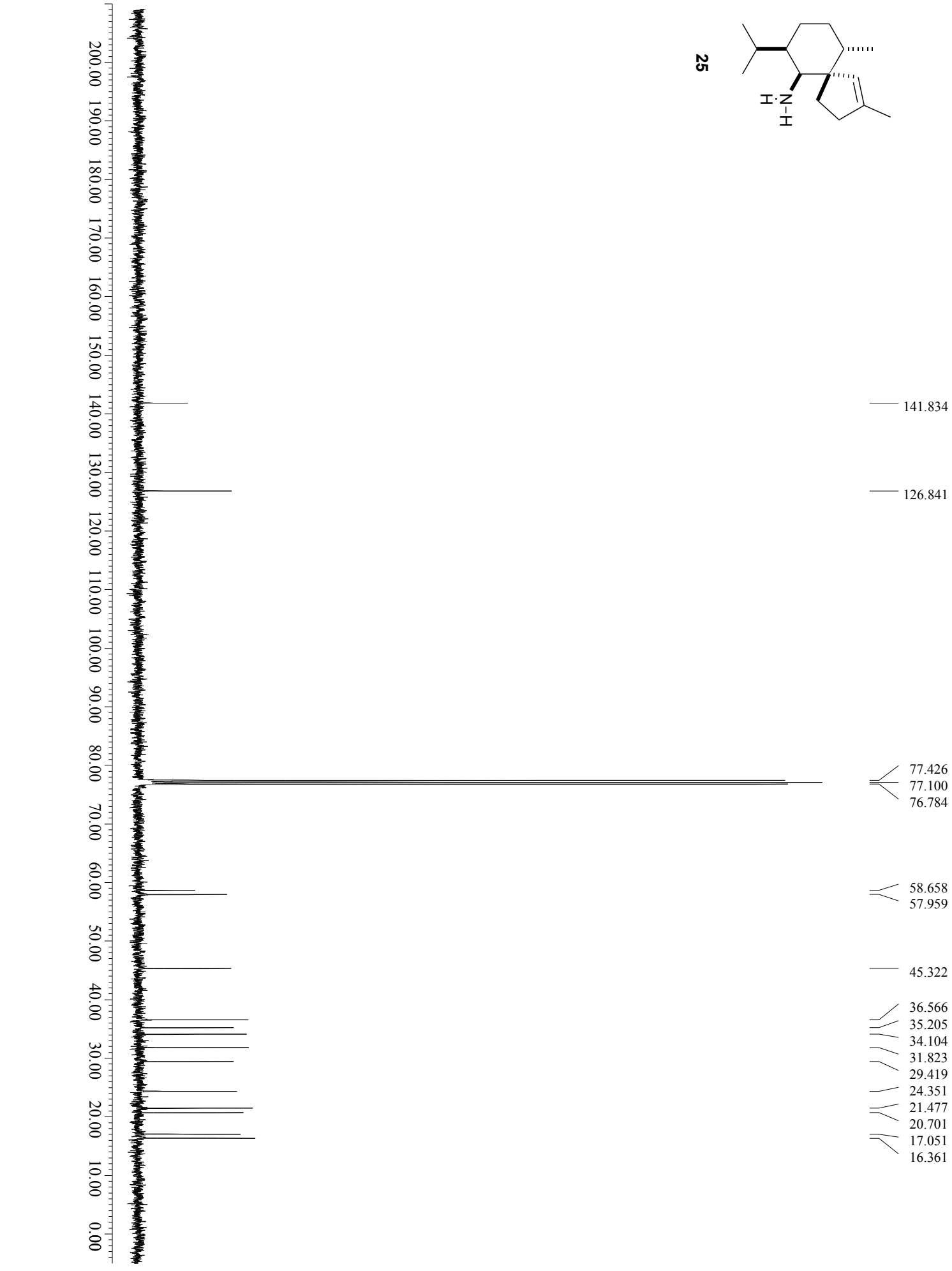

23
N3
SO2Ph
OTf
9.50
9.00
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
1.98
1.05
2.08
1.00
1.24
1.24
1.27
2.34
7.65
2.00
3.43
3.48
3.45
7.975
7.956
7.653
7.585
7.565
7.262
7.260
4.057
2.813
2.791
2.775
2.696
2.688
2.674
2.106
2.093
2.085
1.577
1.554
1.538
1.536
1.259
1.181
1.164
1.012
0.993
0.976
0.883
0.873
0.856
0.847
0.830


23
N3
SO2Ph
OTf
157.201
142.150
138.088
133.873
129.179
127.818
119.847
116.619
68.631
61.829
44.297
36.173
34.017
29.591
29.333
23.268
21.477
20.979
17.453
14.215


24
N3
SO2Ph
9.50
9.00
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
2.00
3.22
0.95
2.16
1.17
1.31
3.12
3.13
1.32
3.01
0.44
1.23
1.32
1.15
3.16
3.33
3.00
7.899
7.881
7.591
7.571
7.554
7.538
7.519
7.501
7.260
3.996
2.538
2.520
2.500
2.478
2.174
2.154
2.059
2.039
1.944
1.866
1.841
1.818
1.608
1.567
1.429
1.251
1.134
1.117
0.886
0.868
0.808
0.791


24
N3
SO2Ph
162.135
144.287
140.704
132.685
129.159
126.257
69.024
64.943
43.981
37.773
36.154
35.905
29.534
29.112
23.364
21.419
20.825
18.555
17.510
200.00
190.00
180.00
170.00
160.00
150.00
140.00
130.00
120.00
110.00
100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00


25
9.50
9.00
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
0.81
0.78
1.71
1.68
2.61
2.07
3.08
4.35
2.08
1.53
3.00
3.14
2.42
7.260
5.305
2.720
2.209
2.190
2.173
1.799
1.781
1.738
1.688
1.667
1.430
1.288
1.254
1.192
0.918
0.902
0.886
0.871
0.743
0.727


25
141.834
126.841
77.426
77.100
76.784
58.658
57.959
45.322
36.566
35.205
34.104
31.823
29.419
24.351
21.477
20.701
17.051
16.361
200.00
190.00
180.00
170.00
160.00
150.00
140.00
130.00
120.00
110.00
100.00
90.00
80.00
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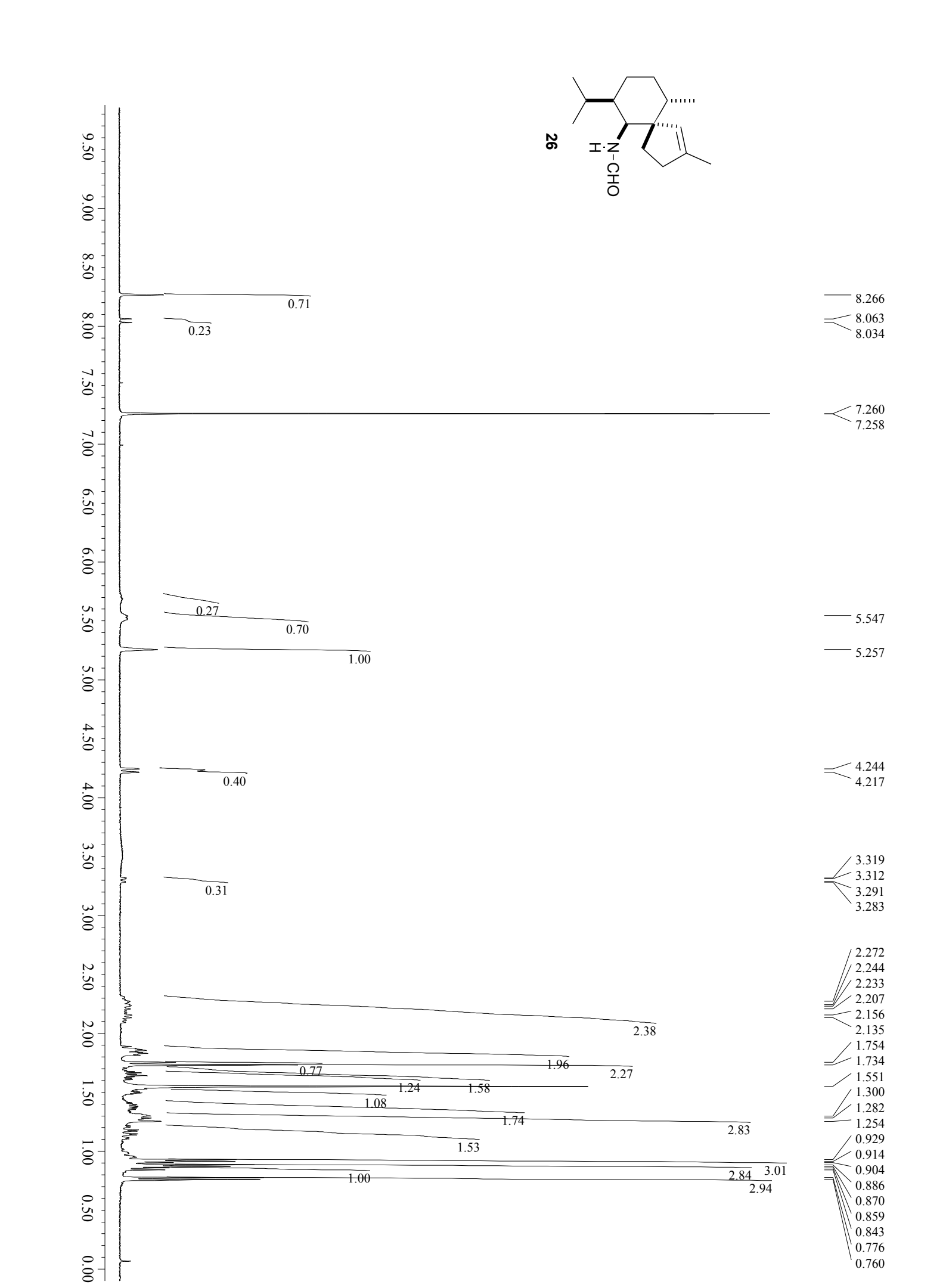
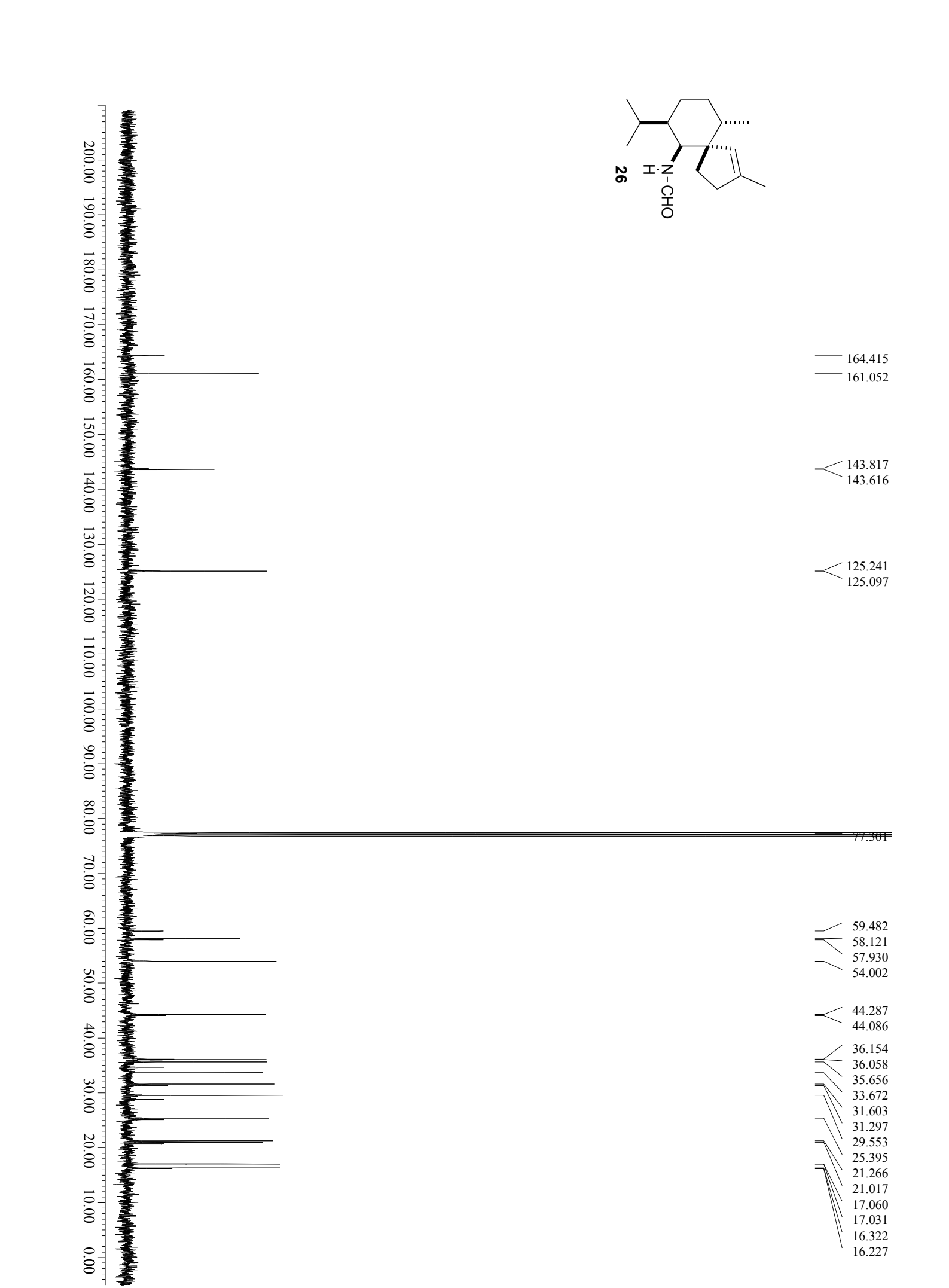
60.00
50.00
40.00
30.00
20.00
10.00
0.00


26
H
N-CHO
9.50
9.00
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
0.71
0.23
0.27
0.70
1.00
0.40
0.31
2.38
1.96
2.27
0.77
1.24
1.58
1.08
1.74
2.83
1.53
3.01
1.00
2.84
2.94
8.266
8.063
8.034
7.260
7.258
5.547
5.257
4.244
4.217
3.319
3.312
3.291
3.283
2.272
2.244
2.233
2.207
2.156
2.135
1.754
1.734
1.551
1.300
1.282
1.254
0.929
0.914
0.904
0.886
0.870
0.859
0.843
0.776
0.760


26
N-CHO
H
164.415
161.052
143.817
143.616
125.241
125.097
77.301
59.482
58.121
57.930
54.002
44.287
44.086
36.154
36.058
35.656
33.672
31.603
31.297
29.553
25.395
21.266
21.017
17.060
17.031
16.322
16.227
200.00
190.00
180.00
170.00
160.00
150.00
140.00
130.00
120.00
110.00
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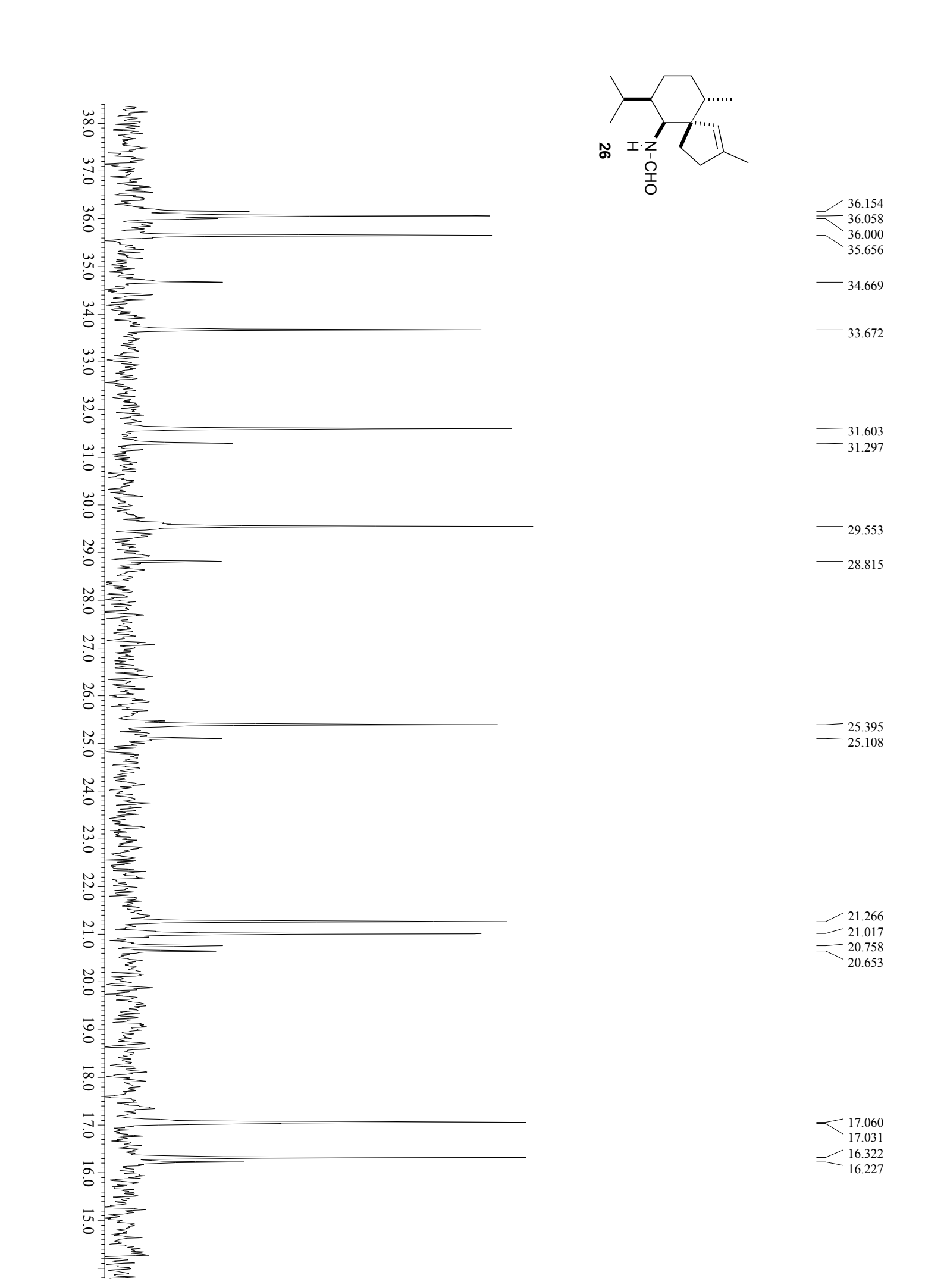
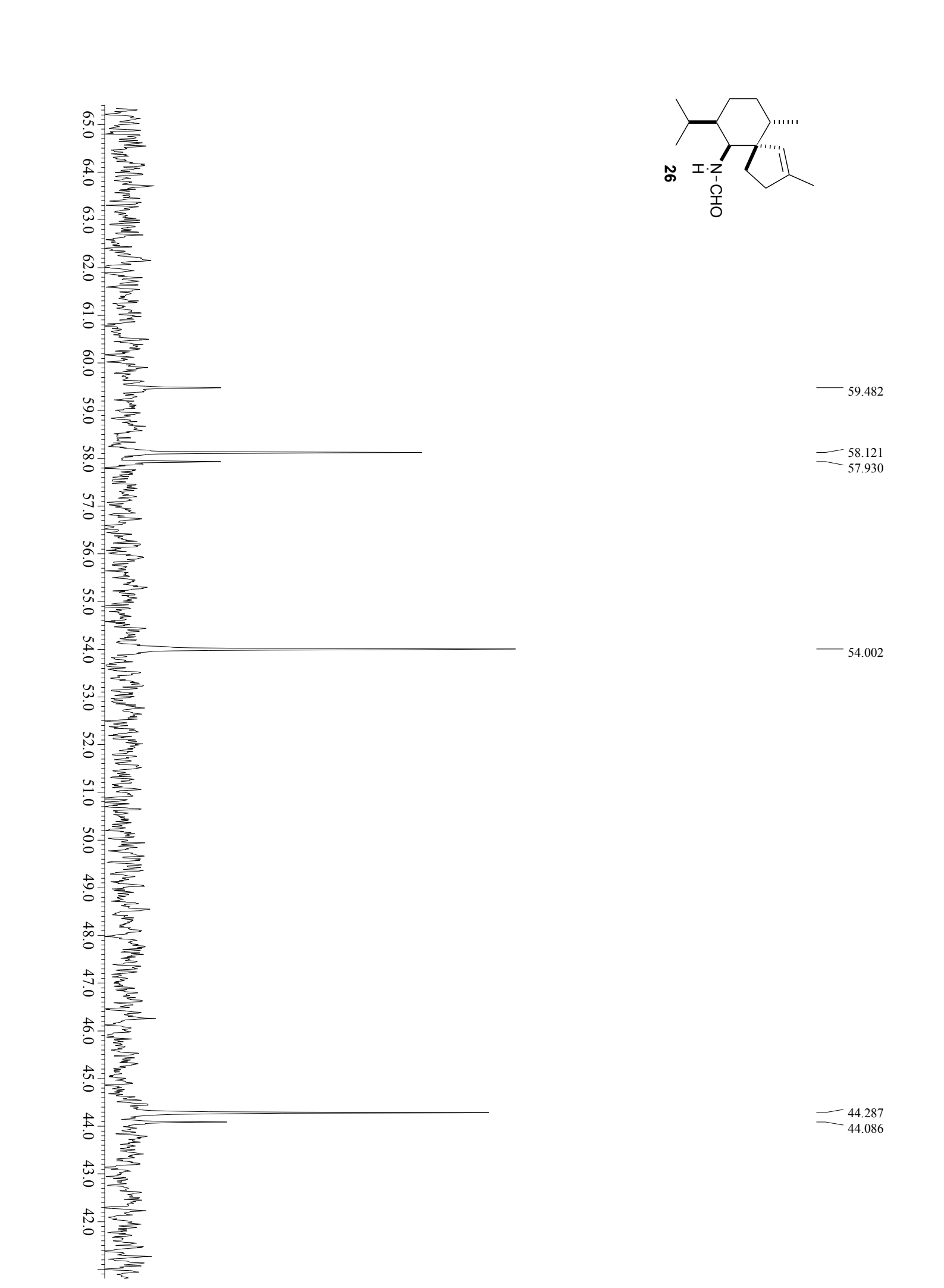
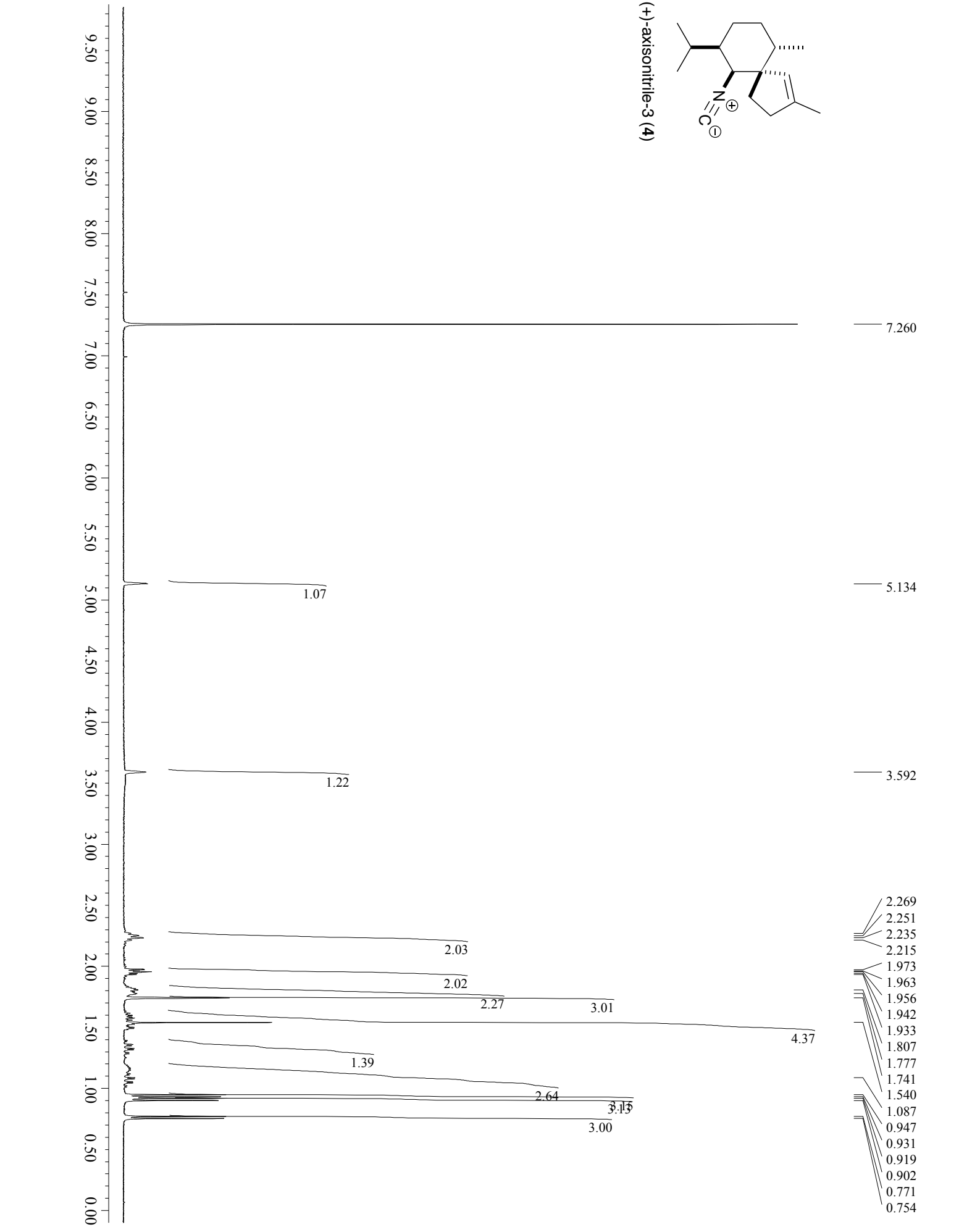
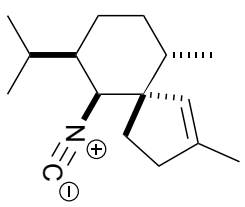
50.00
40.00
30.00
20.00
10.00
0.00

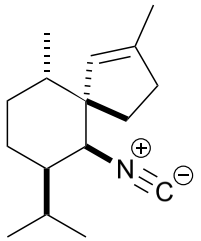

26
N-CHO
H
38.0
37.0
36.0
35.0
34.0
33.0
32.0
31.0
30.0
29.0
28.0
27.0
26.0
25.0
24.0
23.0
22.0
21.0
20.0
19.0
18.0
17.0
16.0
15.0
36.154
36.058
36.000
35.656
34.669
33.672
31.603
31.297
29.553
28.815
25.395
25.108
21.266
21.017
20.758
20.653
17.060
17.031
16.322
16.227


26
N-CHO
H
65.0
64.0
63.0
62.0
61.0
60.0
59.0
58.0
57.0
56.0
55.0
54.0
53.0
52.0
51.0
50.0
49.0
48.0
47.0
46.0
45.0
44.0
43.0
42.0
59.482
58.121
57.930
54.002
44.287
44.086

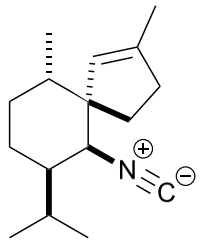

(+)-axisonitrile-3 (4)
9.50
9.00
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
7.260
5.134
3.592
1.07
1.22
2.03
2.02
2.27
3.01
4.37
1.39
2.64
3.15
3.13
3.00
2.269
2.251
2.235
2.215
1.973
1.963
1.956
1.942
1.933
1.807
1.777
1.741
1.540
1.087
0.947
0.931
0.919
0.902
0.771
0.754

(+)-axisonitrile-3 (**4**)

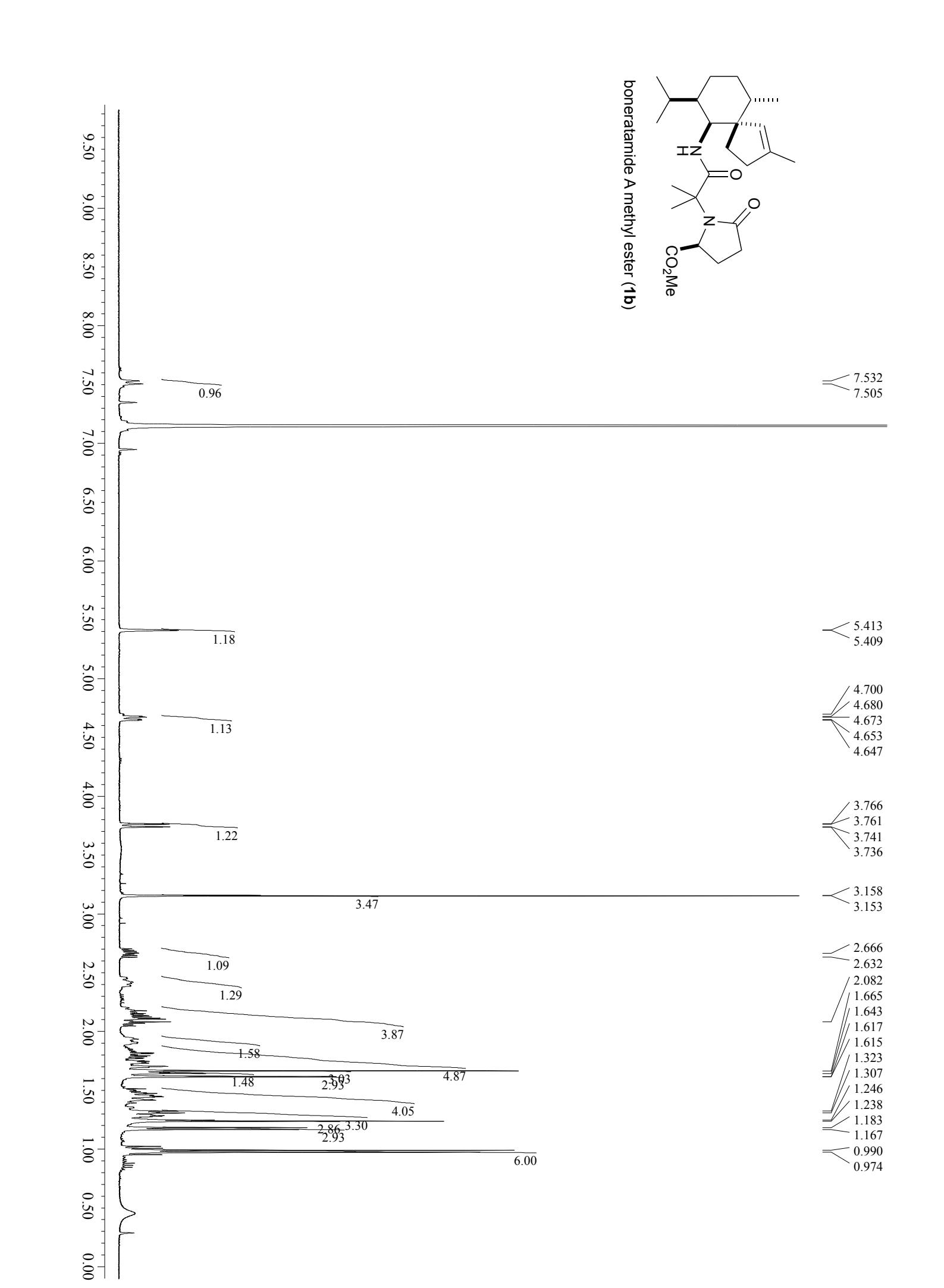


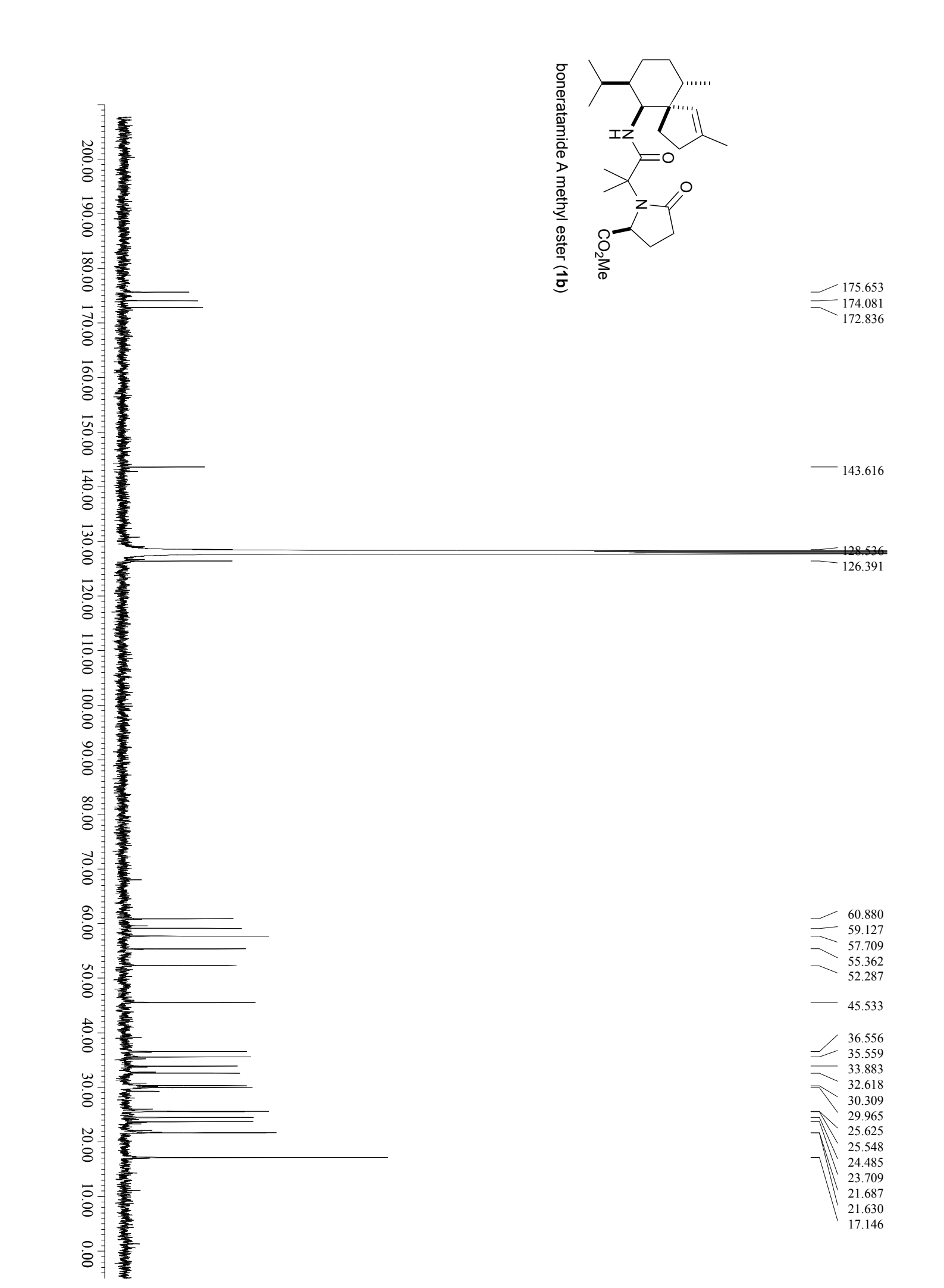


(+)-axisonitrile-3 (**4**)



(+)-axisonitrile-3 (**4**)


boneratamide A methyl ester (1b)
N
H
O
O
N
CO2Me
9.50
9.00
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
0.96
1.18
1.13
1.22
3.47
1.09
1.29
3.87
1.58
4.87
1.48
3.03
2.93
4.05
3.30
2.86
2.93
6.00
7.532
7.505
5.413
5.409
4.700
4.680
4.673
4.653
4.647
3.766
3.761
3.741
3.736
3.158
3.153
2.666
2.632
2.082
1.665
1.643
1.617
1.615
1.323
1.307
1.246
1.238
1.183
1.167
0.990
0.974


boneratamide A methyl ester (1b)
HN
O
N
O
CO2Me
175.653
174.081
172.836
143.616
128.536
126.391
60.880
59.127
57.709
55.362
52.287
45.533
36.556
35.559
33.883
32.618
30.309
29.965
25.625
25.548
24.485
23.709
21.687
21.630
17.146
200.00
190.00
180.00
170.00
160.00
150.00
140.00
130.00
120.00
110.00
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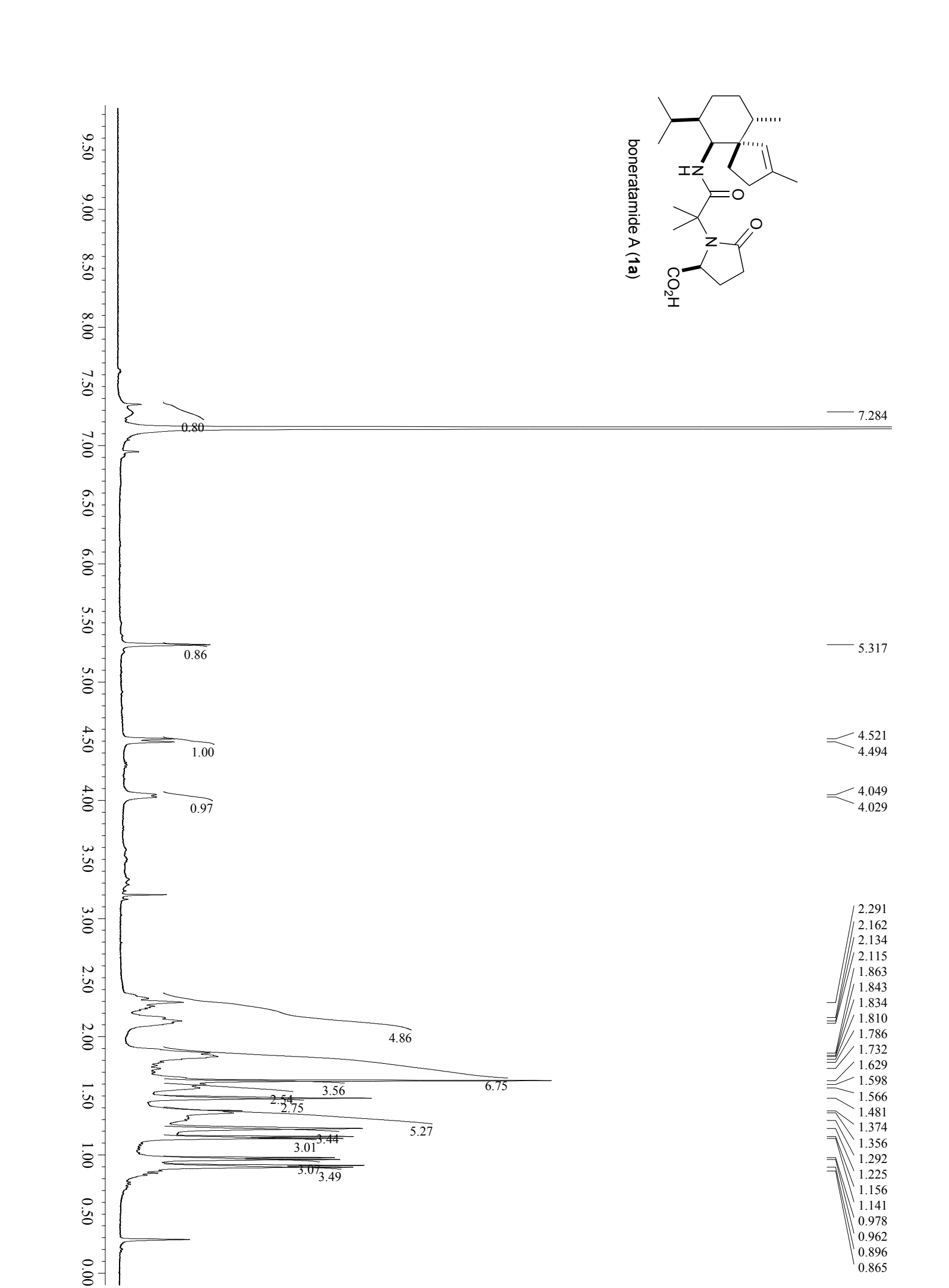
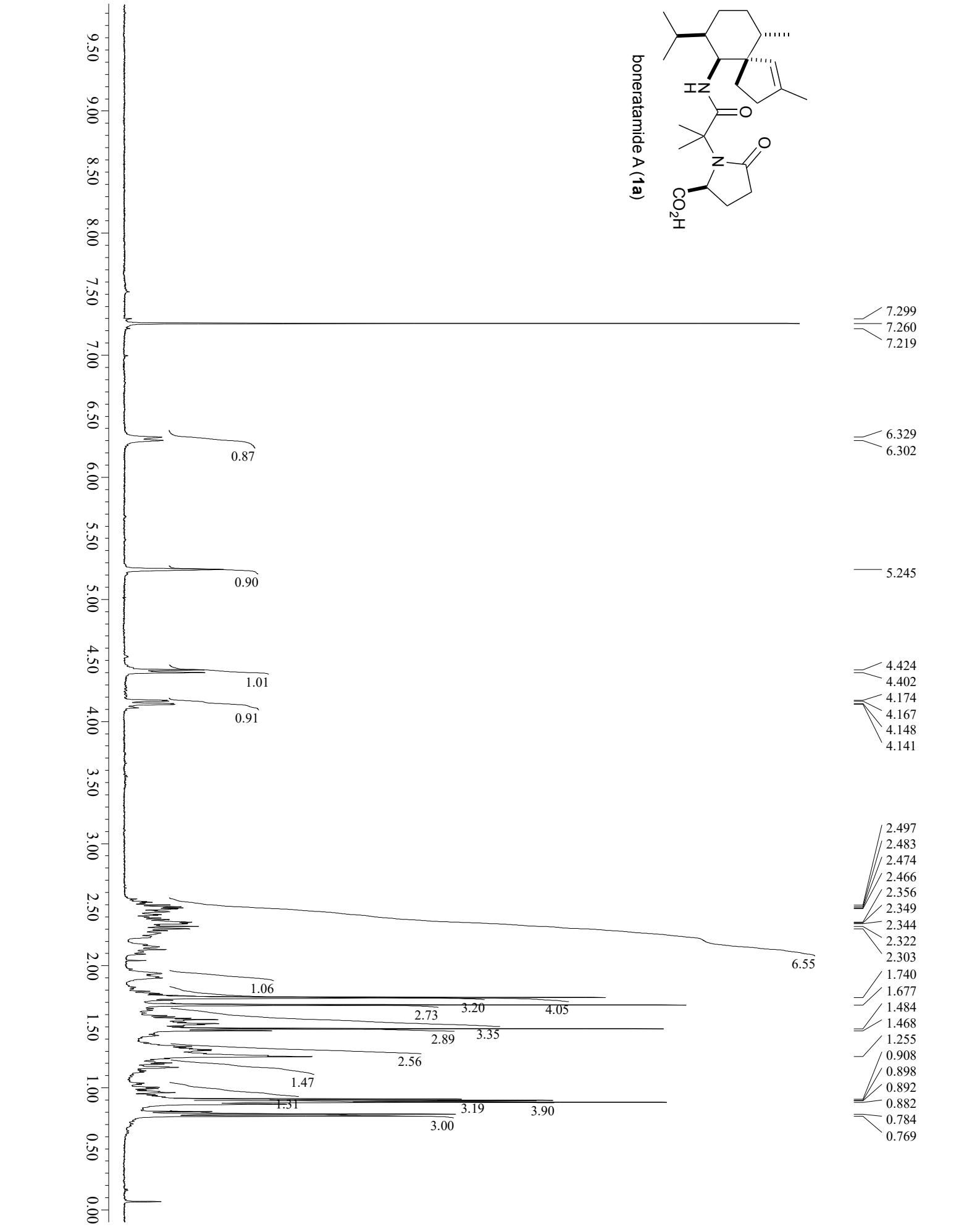
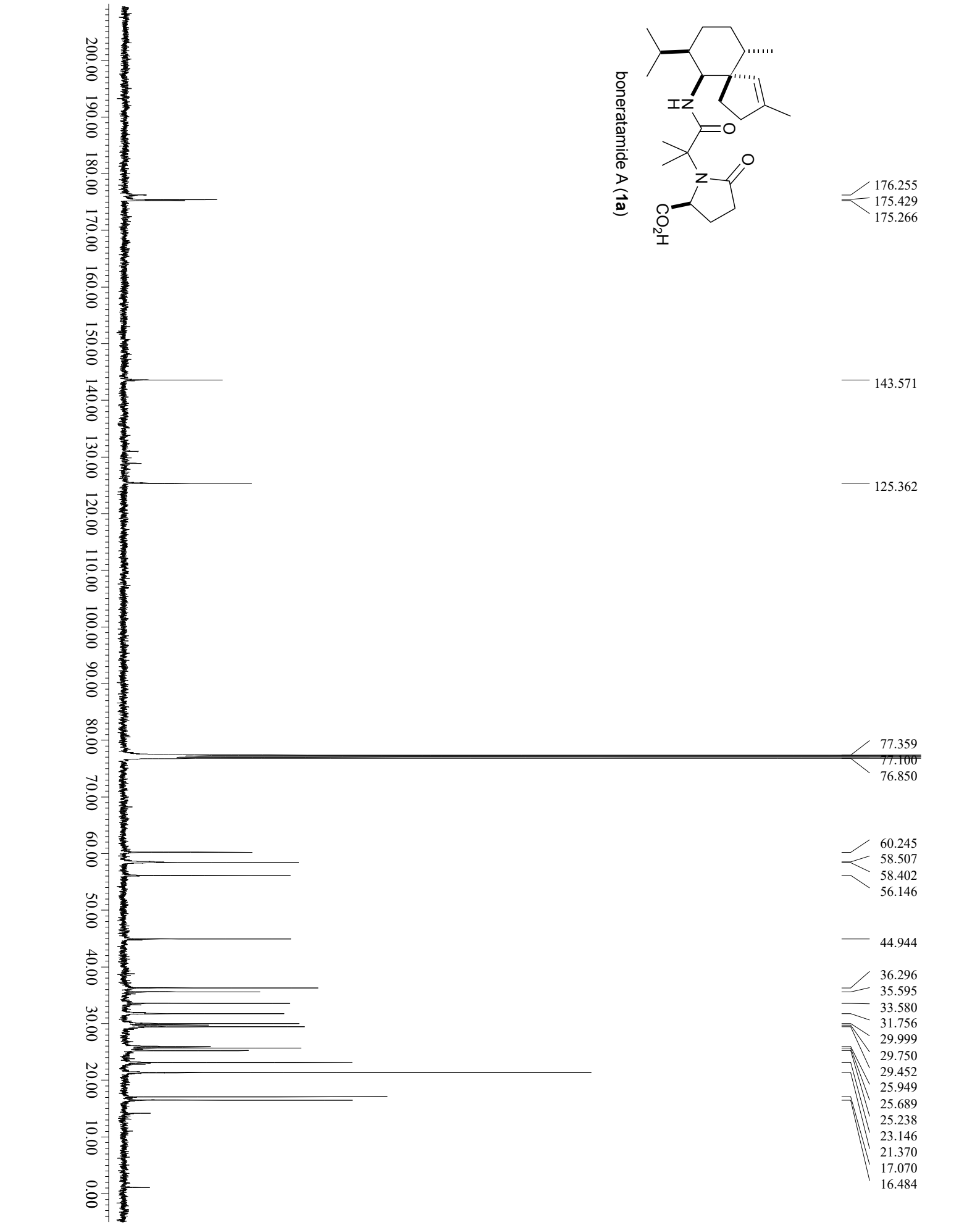
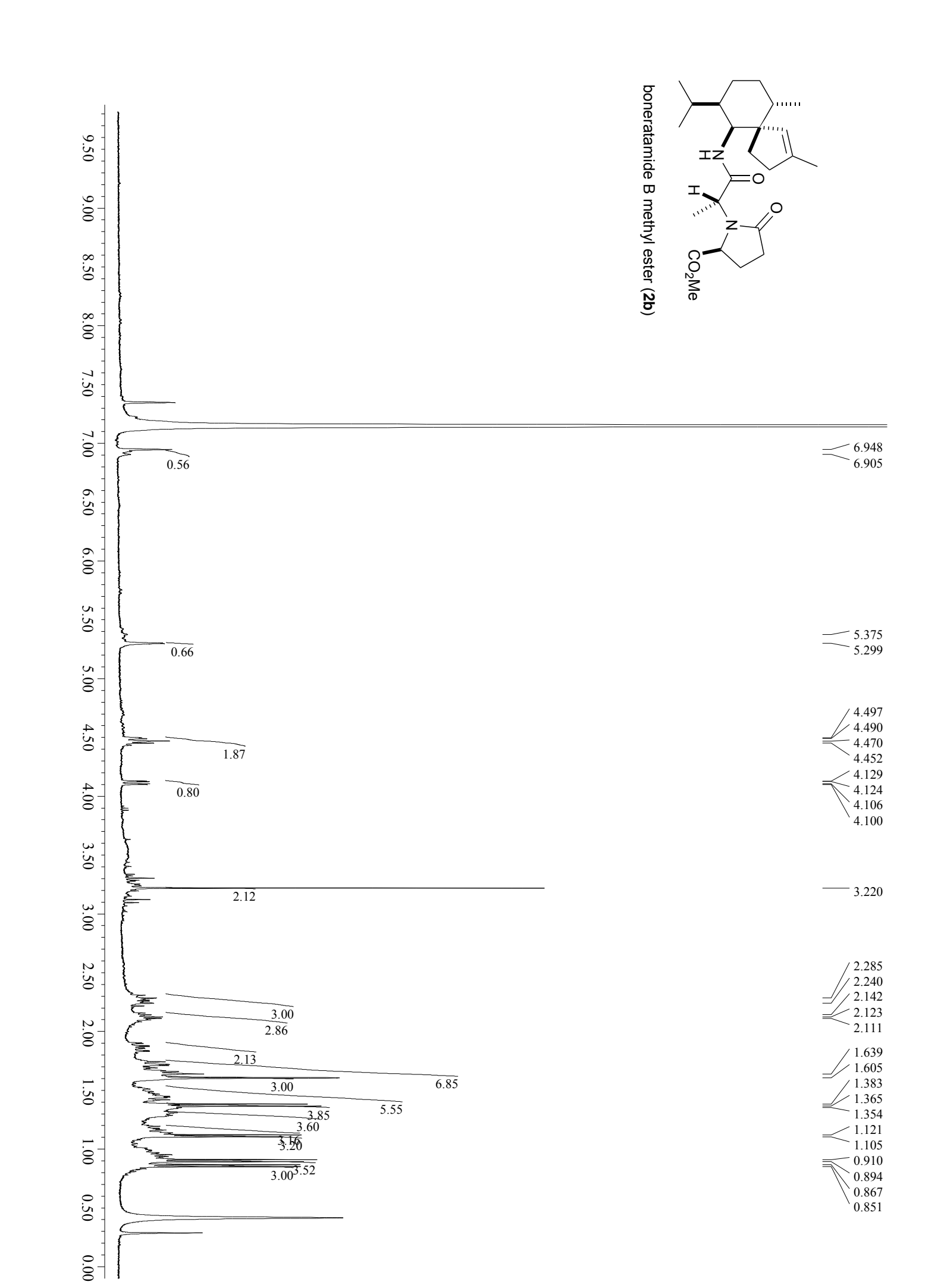
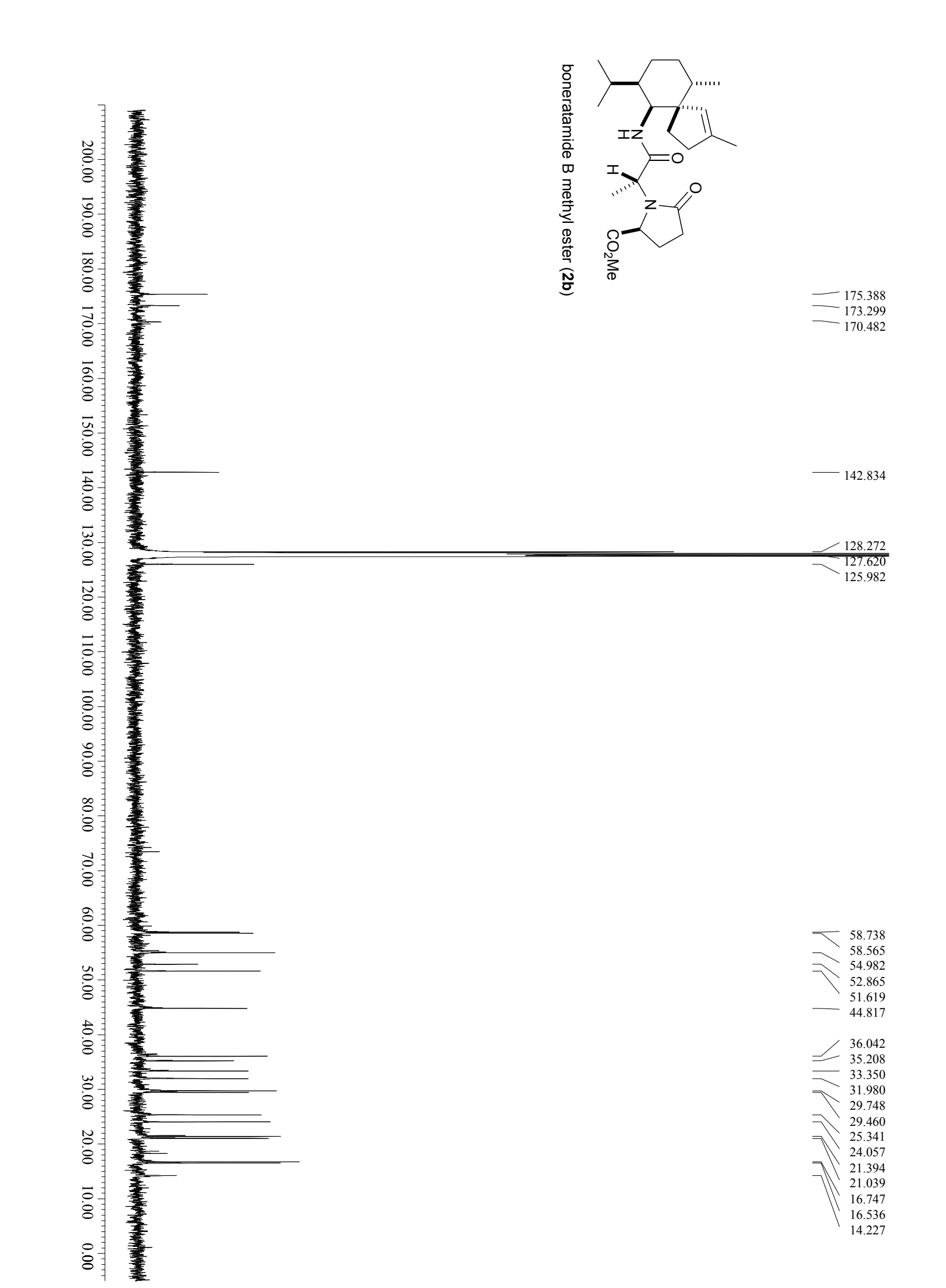
50.00
40.00
30.00
20.00
10.00
0.00


boneratamide A (1a)
9.50
9.00
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
0.80
0.86
1.00
0.97
4.86
6.75
3.56
2.54
2.75
5.27
3.44
3.01
3.07
3.49
7.284
5.317
4.521
4.494
4.049
4.029
2.291
2.162
2.134
2.115
1.863
1.843
1.834
1.810
1.786
1.732
1.629
1.598
1.566
1.481
1.374
1.356
1.292
1.225
1.156
1.141
0.978
0.962
0.896
0.865


boneratamide A (1a)
9.50
9.00
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
0.87
0.90
1.01
0.91
6.55
1.06
2.73
3.20
4.05
2.89
3.35
2.56
1.47
1.31
3.19
3.90
3.00
7.299
7.260
7.219
6.329
6.302
5.245
4.424
4.402
4.174
4.167
4.148
4.141
2.497
2.483
2.474
2.466
2.356
2.349
2.344
2.322
2.303
1.740
1.677
1.484
1.468
1.255
0.908
0.898
0.892
0.882
0.784
0.769


boneratamide A (1a)
176.255
175.429
175.266
143.571
125.362
77.359
77.100
76.850
60.245
58.507
58.402
56.146
44.944
36.296
35.595
33.580
31.756
29.999
29.750
29.452
25.949
25.689
25.238
23.146
21.370
17.070
16.484


boneratamide B methyl ester (2b)
CO2Me
9.50 9.00 8.50 8.00 7.50 7.00 6.50 6.00 5.50 5.00 4.50 4.00 3.50 3.00 2.50 2.00 1.50 1.00 0.50 0.00
0.56
0.66
1.87
0.80
2.12
3.00
2.86
2.13
6.85
3.00
5.55
3.85
3.60
3.16
3.20
3.00
3.52
6.948
6.905
5.375
5.299
4.497
4.490
4.470
4.452
4.129
4.124
4.106
4.100
3.220
2.285
2.240
2.142
2.123
2.111
1.639
1.605
1.383
1.365
1.354
1.121
1.105
0.910
0.894
0.867
0.851


boneratamide B methyl ester (2b)
HN
O
H
N
O
CO2Me
175.388
173.299
170.482
142.834
128.272
127.620
125.982
58.738
58.565
54.982
52.865
51.619
44.817
36.042
35.208
33.350
31.980
29.748
29.460
25.341
24.057
21.394
21.039
16.747
16.536
14.227
200.00
190.00
180.00
170.00
160.00
150.00
140.00
130.00
120.00
110.00
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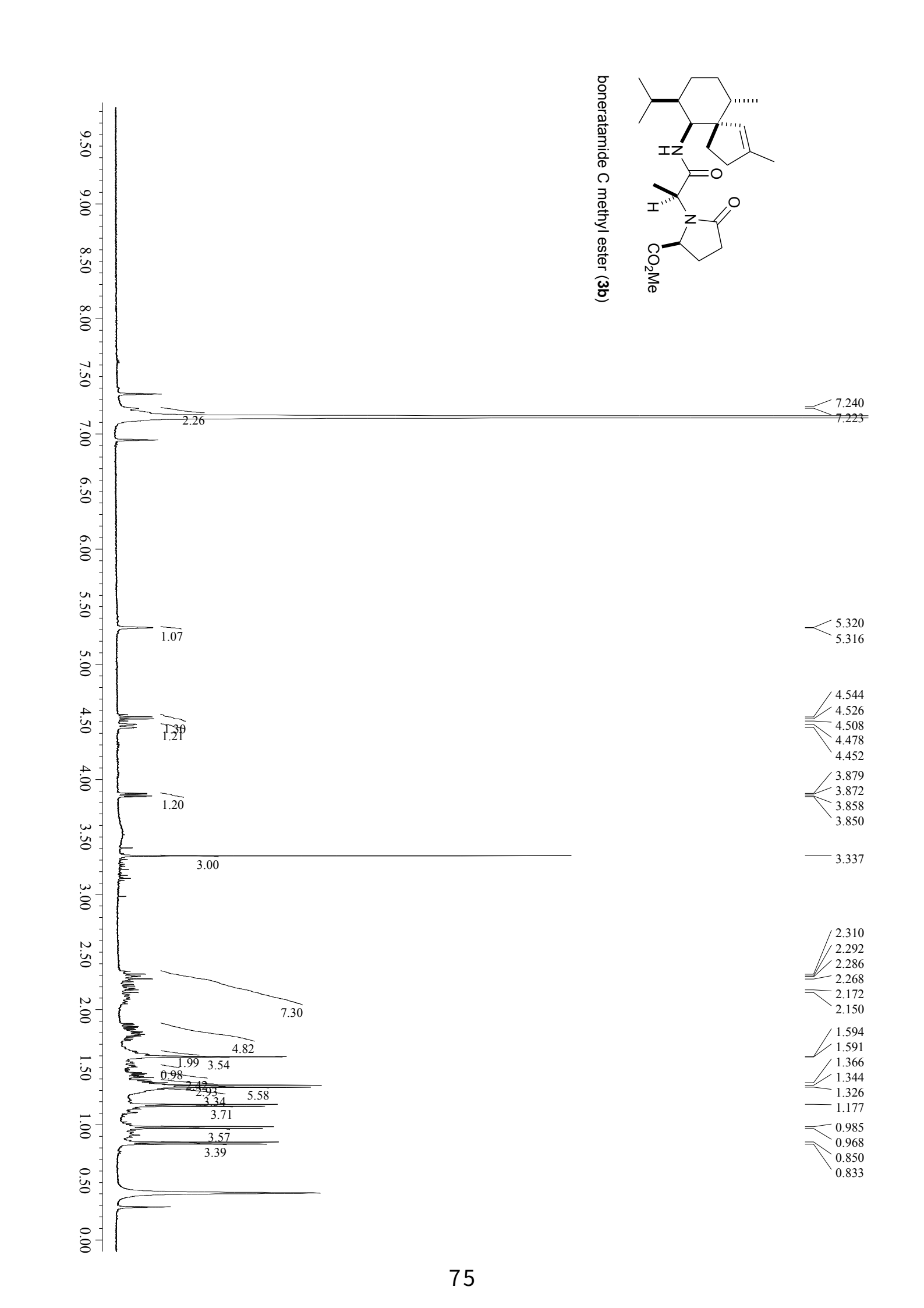
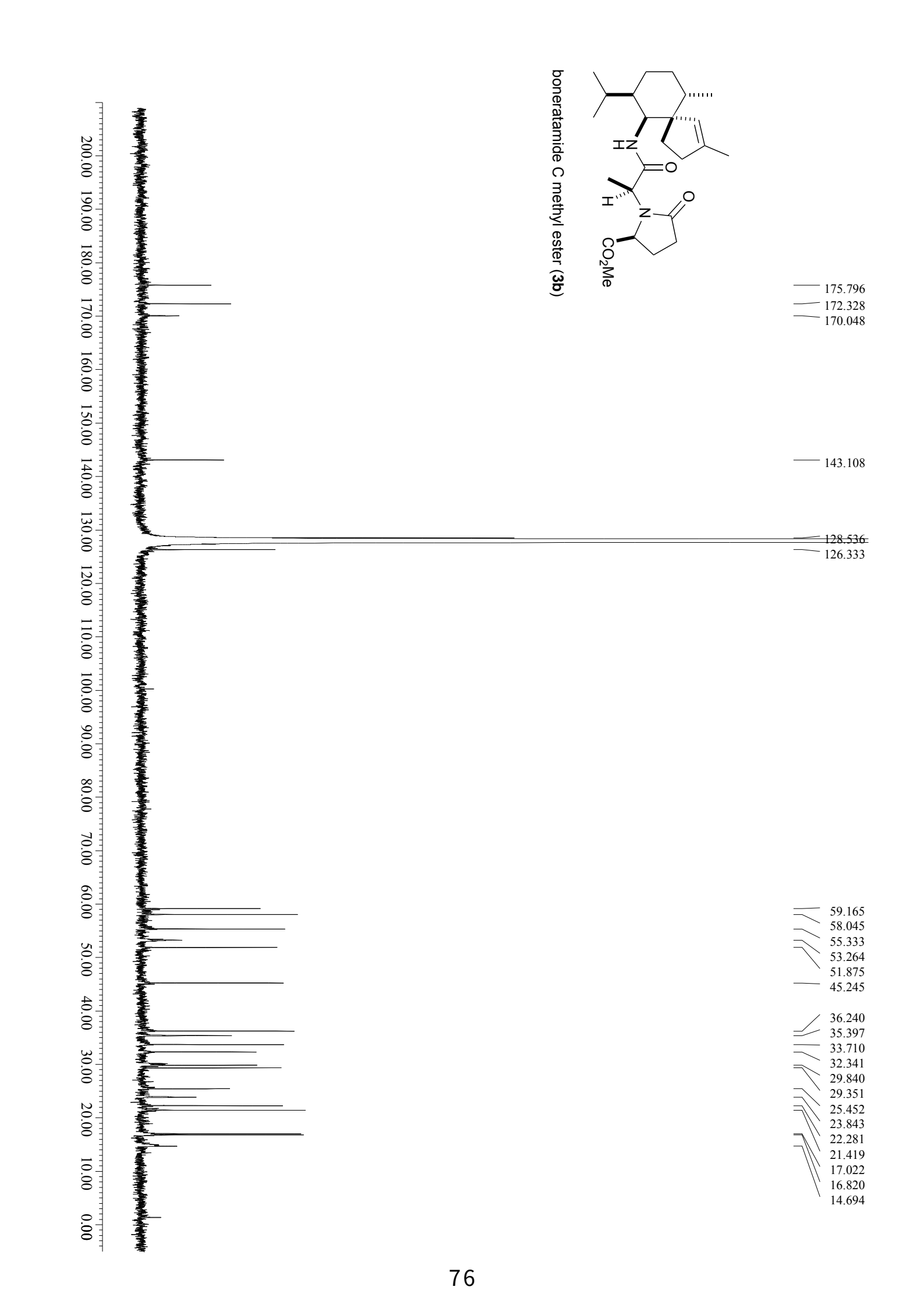
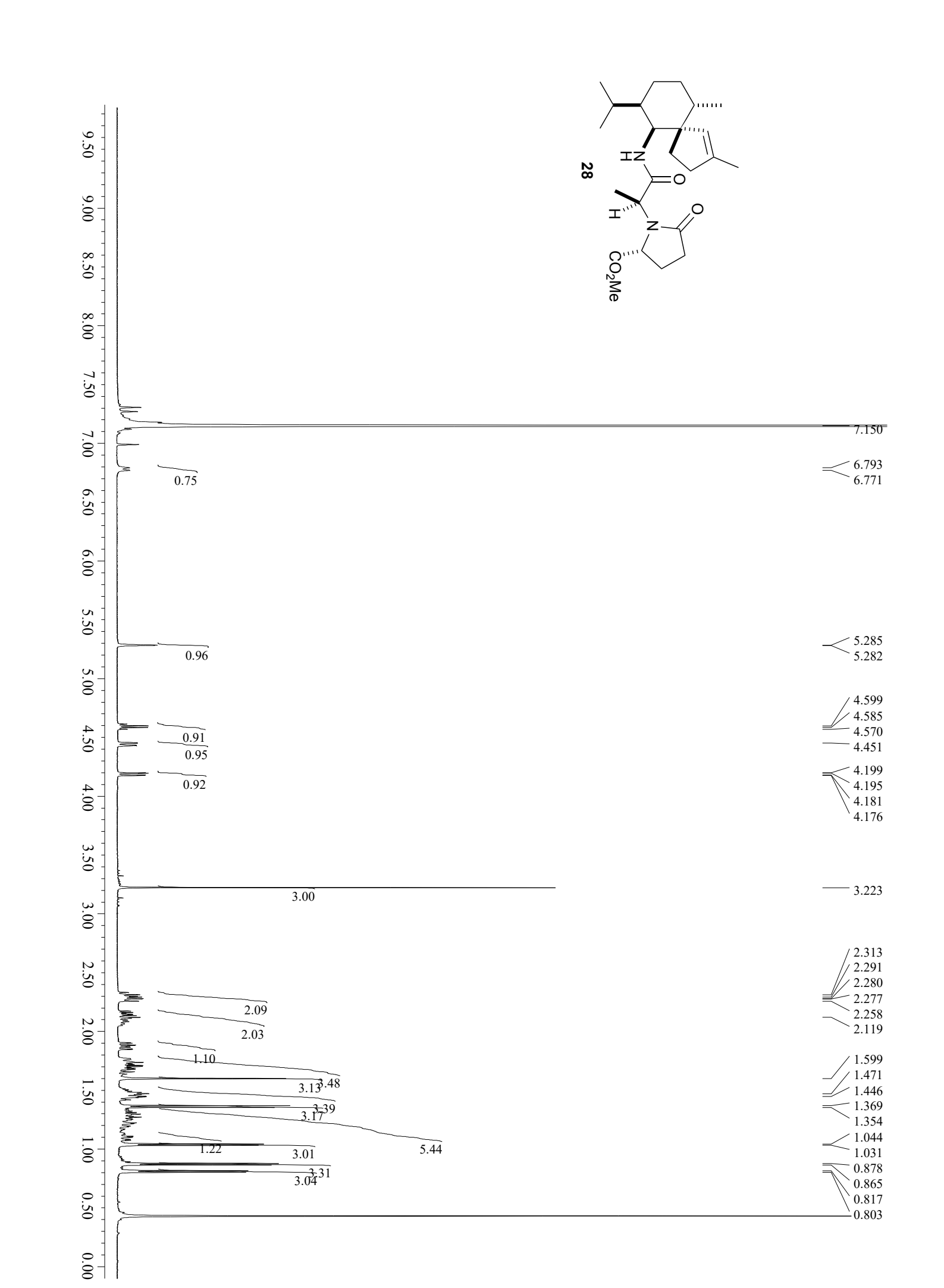
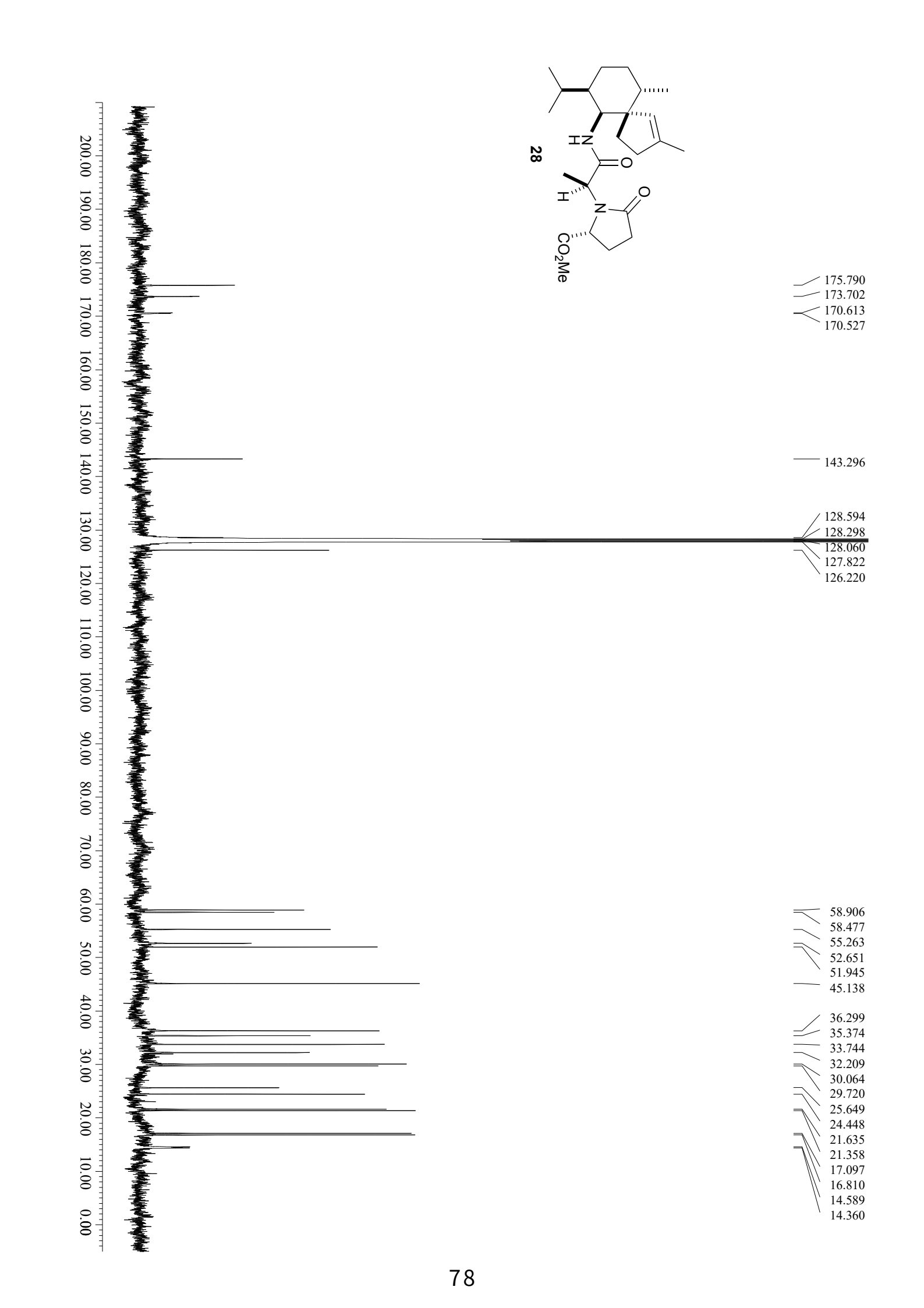
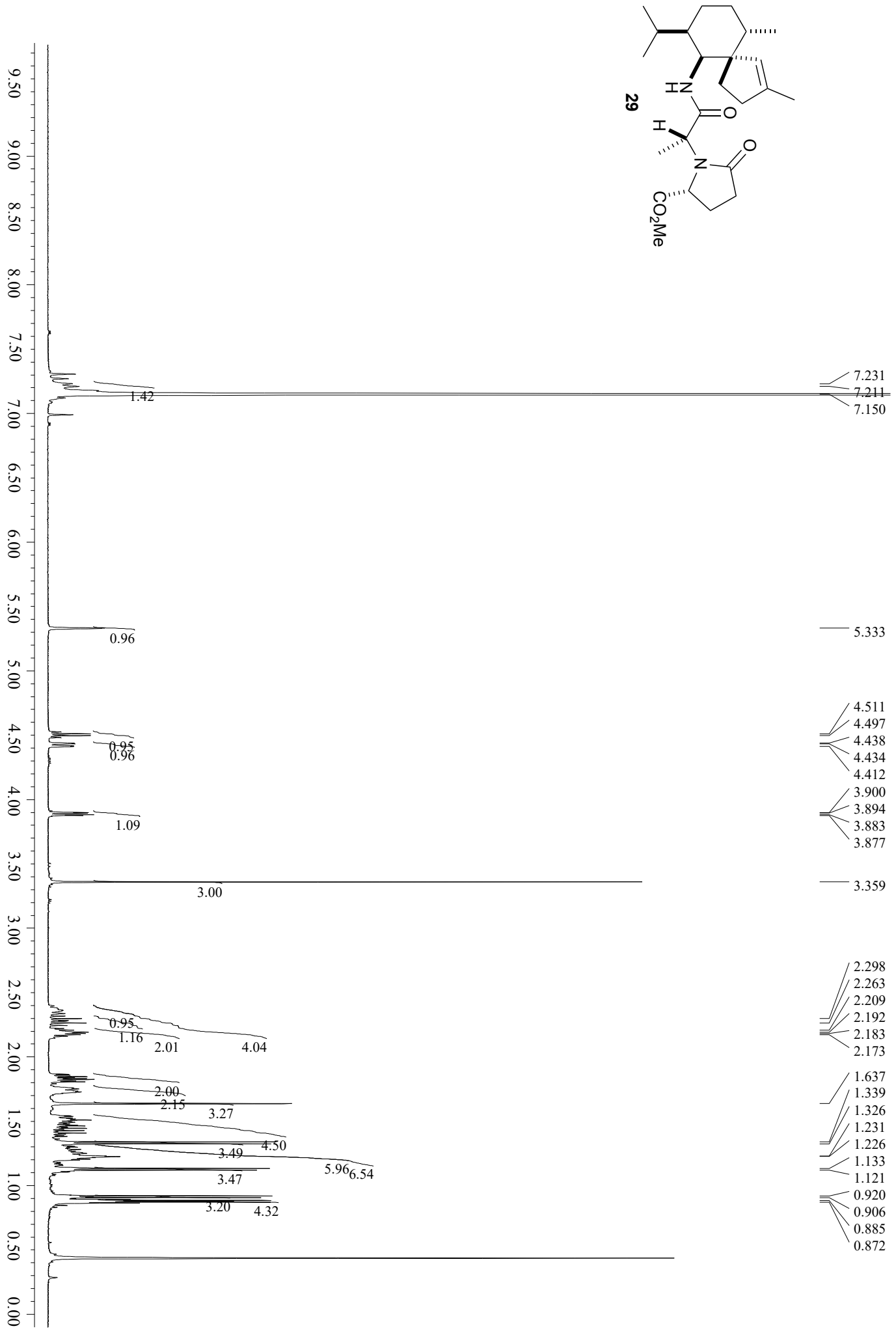
50.00
40.00
30.00
20.00
10.00
0.00

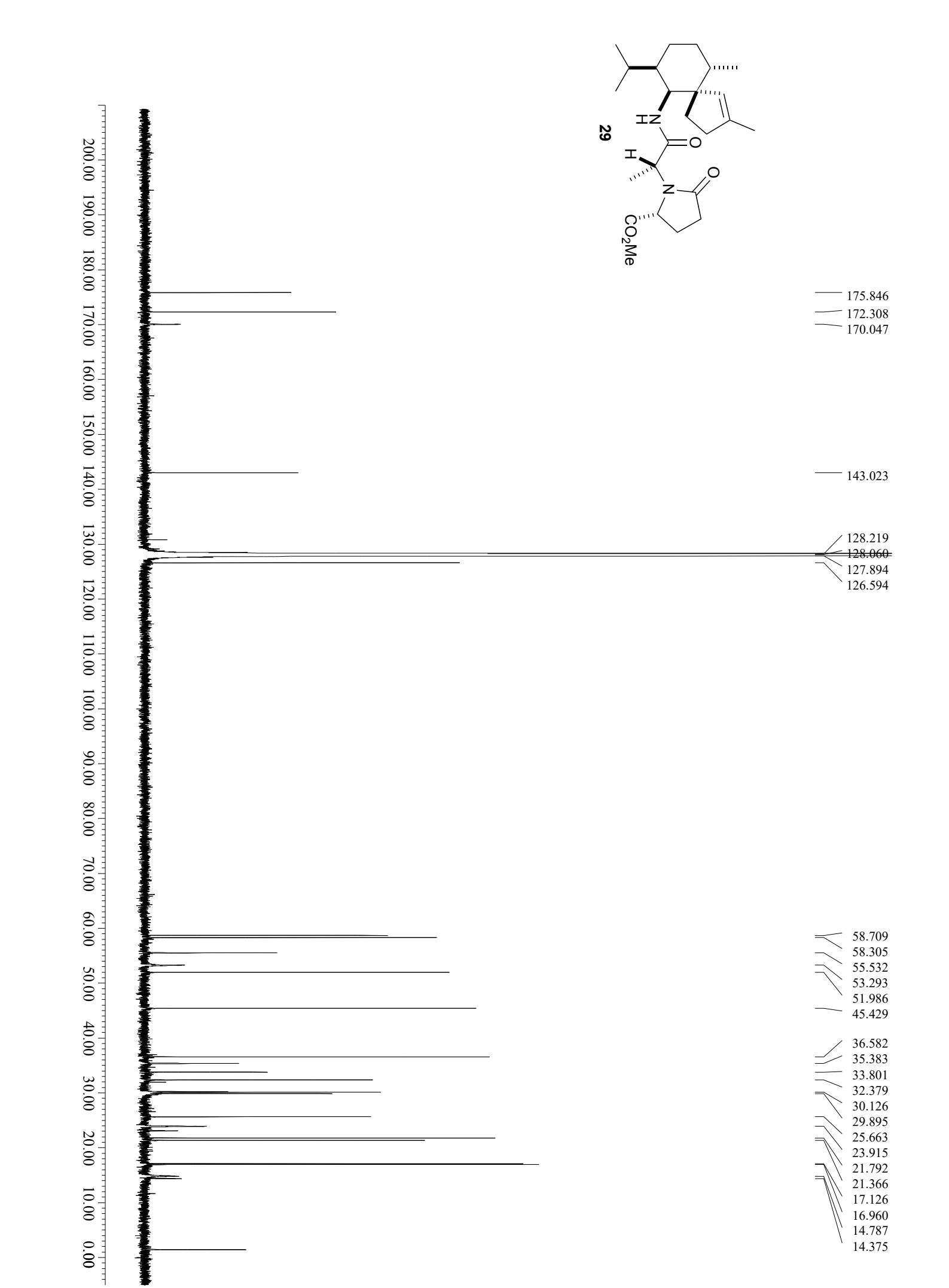

boneratamide C methyl ester (3b)
7.240
7.223
5.320
5.316
4.544
4.526
4.508
4.478
4.452
3.879
3.872
3.858
3.850
3.337
2.310
2.292
2.286
2.268
2.172
2.150
1.594
1.591
1.366
1.344
1.326
1.177
0.985
0.968
0.850
0.833
2.26
1.07
1.30
1.21
1.20
3.00
7.30
4.82
1.99
3.54
0.98
2.43
2.53
5.58
3.34
3.71
3.57
3.39


boneratamide C methyl ester (3b)
175.796
172.328
170.048
143.108
128.536
126.333
59.165
58.045
55.333
53.264
51.875
45.245
36.240
35.397
33.710
32.341
29.840
29.351
25.452
23.843
22.281
21.419
17.022
16.820
14.694
200.00 190.00 180.00 170.00 160.00 150.00 140.00 130.00 120.00 110.00 100.00 90.00 80.00 70.00 60.00 50.00 40.00 30.00 20.00 10.00 0.00

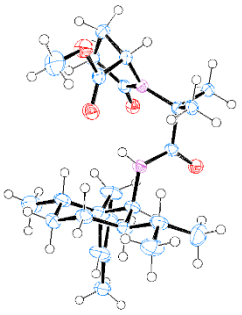

28
H
N
O
H
N
O
CO2Me
9.50
9.00
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
7.150
6.793
6.771
5.285
5.282
4.599
4.585
4.570
4.451
4.199
4.195
4.181
4.176
3.223
2.313
2.291
2.280
2.277
2.258
2.119
1.599
1.471
1.446
1.369
1.354
1.044
1.031
0.878
0.865
0.817
0.803
0.75
0.96
0.91
0.95
0.92
3.00
2.09
2.03
1.10
3.48
3.13
3.39
3.17
5.44
1.22
3.01
3.31
3.04

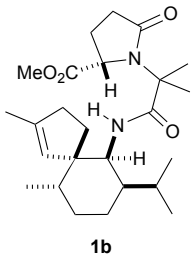

28
175.790
173.702
170.613
170.527
143.296
128.594
128.298
128.060
127.822
126.220
58.906
58.477
55.263
52.651
51.945
45.138
36.299
35.374
33.744
32.209
30.064
29.720
25.649
24.448
21.635
21.358
17.097
16.810
14.589
14.360


29
HN
O
H
N
O
CO2Me
9.50
9.00
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
1.42
0.96
0.95
0.96
1.09
3.00
0.95
1.16
2.01
4.04
2.00
2.15
3.27
4.50
3.49
3.47
5.96
6.54
3.20
4.32
7.231
7.211
7.150
5.333
4.511
4.497
4.438
4.434
4.412
3.900
3.894
3.883
3.877
3.359
2.298
2.263
2.209
2.192
2.183
2.173
1.637
1.339
1.326
1.231
1.226
1.133
1.121
0.920
0.906
0.885
0.872


29
HN
O
H
N
O
CO2Me
175.846
172.308
170.047
143.023
128.219
128.060
127.894
126.594
58.709
58.305
55.532
53.293
51.986
45.429
36.582
35.383
33.801
32.379
30.126
29.895
25.663
23.915
21.792
21.366
17.126
16.960
14.787
14.375
200.00
190.00
180.00
170.00
160.00
150.00
140.00
130.00
120.00
110.00
100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00

X-ray crystallographic structure of **1b**





1b

CCDC 2144949

Empirical Formula	$C_{25}H_{40}N_2O_4$
Formula Weight	432.60
Crystal Color, Habit	colorless, block
Crystal Dimensions	0.700 X 0.350 X 0.300 mm
Crystal System	orthorhombic
Lattice Type	Primitive
Lattice Parameters	a = 7.9942(2) Å b = 10.5274(3) Å c = 29.6819(8) Å V = 2497.98(12) Å^3
Space Group	$P2_12_12_1$ (#19)
Z value	4
D_{calc}	1.150 g/cm^3
F_{000}	944.00
μ(CuKα)	6.154 cm^{-1}

B. Intensity Measurements

Diffractometer	R-AXIS RAPID
Radiation	CuKα (λ = 1.54187 Å) graphite monochromated
Voltage, Current	50kV, 100mA
Temperature	-180.0^{o}C
Detector Aperture	460.0 x 256.0 mm
Data Images	450 exposures
ω oscillation Range (χ=54.0, ϕ=0.0)	80.0 - 260.0^{o}
Exposure Rate	10.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=90.0)	80.0 - 260.0^{o}
Exposure Rate	10.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=180.0)	80.0 - 260.0^{o}
Exposure Rate	10.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=270.0)	80.0 - 260.0^{o}
Exposure Rate	10.0 sec./^{o}
ω oscillation Range (χ=10.0, ϕ=60.0)	80.0 - 260.0^{o}
Exposure Rate	10.0 sec./^{o}

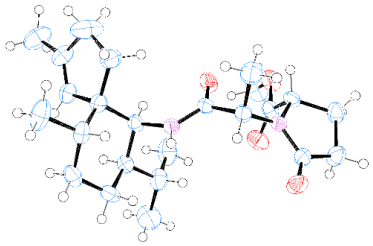
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	136.4°
No. of Reflections Measured	Total: 28338 Unique: 4564 (R_{int} = 0.0711) Parsons quotients (Flack x parameter): 1834
Corrections	Lorentz-polarization Absorption (trans. factors: 0.710 - 0.831)

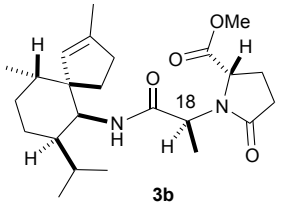
C. Structure Solution and Refinement

Structure Solution Version 2014/4)	Direct Methods (SHELXT
Refinement	Full-matrix least-squares on F^2
Function Minimized	Σ w $(Fo^2 - Fc^2)^2$
Least Squares Weights	$w = 1/ [\sigma^2(Fo^2) + (0.0758 \cdot P)^2 + 1.0018 \cdot P]$ where $P = (Max(Fo^2,0) + 2Fc^2)/3$
$2\theta_{max}$ cutoff	136.4°
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	4564
No. Variables	280
Reflection/Parameter Ratio	16.30
Residuals: R1 (I>2.00σ(I))	0.0468
Residuals: R (All reflections)	0.0479
Residuals: wR2 (All reflections)	0.1305
Goodness of Fit Indicator	1.051
Flack parameter (Parsons' quotients = 1834)	0.09(7)

Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	0.62 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.40 $e^-/Å^3$

X-ray crystallographic structure of **3b**





3b

CCDC 2144950

Empirical Formula	$C_{27}H_{41}N_2O_4$
Formula Weight	457.63
Crystal Color, Habit	colorless, block
Crystal Dimensions	0.600 X 0.500 X 0.300 mm
Crystal System	monoclinic
Lattice Type	C-centered
Lattice Parameters	a = 17.0655(8) Å b = 10.6435(5) Å c = 16.6001(8) Å β = 116.597(8) ^{o} V = 2696.1(3) Å^3
Space Group	C2 (#5)
Z value	4
D_{calc}	1.127 g/cm^3
F_{000}	996.00
μ(CuKα)	5.969 cm^{-1}

B. Intensity Measurements

Diffractometer	R-AXIS RAPID
Radiation	CuKα (λ = 1.54187 Å) graphite monochromated
Voltage, Current	50kV, 100mA
Temperature	-100.0^{o}C
Detector Aperture	460.0 x 256.0 mm
Data Images	180 exposures
ω oscillation Range (χ=54.0, ϕ=0.0)	80.0 - 260.0^{o}
Exposure Rate	10.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=90.0)	80.0 - 260.0^{o}
Exposure Rate	10.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=180.0)	80.0 - 260.0^{o}
Exposure Rate	10.0 sec./^{o}
ω oscillation Range (χ=54.0, ϕ=270.0)	80.0 - 260.0^{o}
Exposure Rate	10.0 sec./^{o}
ω oscillation Range (χ=0.0, ϕ=0.0)	80.0 - 260.0^{o}
Exposure Rate	10.0 sec./^{o}

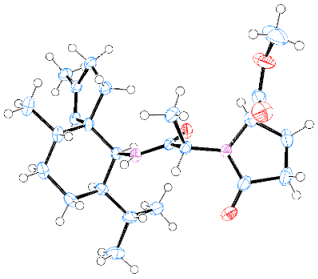
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	136.5°
No. of Reflections Measured	Total: 15545 Unique: 4797 (R_{int} = 0.0333) Parsons quotients (Flack x parameter): 2053
Corrections	Lorentz-polarization Absorption (trans. factors: 0.671 - 0.836)

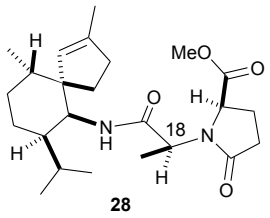
C. Structure Solution and Refinement

Structure Solution Version 2014/4)	Direct Methods (SHELXT
Refinement	Full-matrix least-squares on F^2
Function Minimized	Σ w $(Fo^2 - Fc^2)^2$
Least Squares Weights	$w = 1/ [\sigma^2(Fo^2) + (0.1032 \cdot P)^2 + 1.5528 \cdot P]$ where $P = (Max(Fo^2,0) + 2Fc^2)/3$
$2\theta_{max}$ cutoff	136.5°
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	4797
No. Variables	299
Reflection/Parameter Ratio	16.04
Residuals: R1 (I>2.00σ(I))	0.0543
Residuals: R (All reflections)	0.0559
Residuals: wR2 (All reflections)	0.1571
Goodness of Fit Indicator	1.064
Flack parameter (Parsons' quotients = 2053)	0.11(5)

Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	0.63 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.39 $e^-/Å^3$

X-ray crystallographic structure of **28**



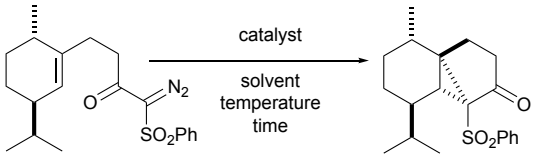


28

CCDC 2183045	
Empirical formula	$C_{24}H_{40}N_2O_5$
Formula weight	436.58
Temperature/K	100.01(10)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	13.2329(2)
b/Å	6.99870(10)
c/Å	14.9696(3)
α/°	90
β/°	115.326(2)
γ/°	90
Volume/Å^3	1253.13(4)
Z	2
ρ_{calc}g/cm^3	1.157
μ/mm^{-1}	0.646
F(000)	476.0
Crystal size/mm^3	0.361 × 0.137 × 0.047
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	6.532 to 149.21
Index ranges	-15 ≤ h ≤ 16, -7 ≤ k ≤ 8, -18 ≤ l ≤ 18
Reflections collected	15311
Independent reflections	4609 [R_{int} = 0.0346, R_{sigma} = 0.0347]
Data/restraints/parameters	4609/1/290

Goodness-of-fit on F^2	1.041
Final R indexes [I>=2σ (I)]	R_1 = 0.0315, wR_2 = 0.0815
Final R indexes [all data]	R_1 = 0.0332, wR_2 = 0.0826
Largest diff. peak/hole / e $Å^{-3}$	0.24/-0.20
Flack parameter	-0.08(8)

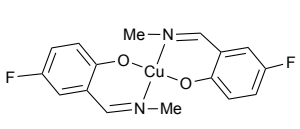
Catalyst Screening for Cyclopropanation [a]



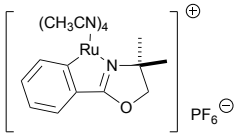
7 8

Entry	Catalyst (mol%)	Solvent	Temperature	Time	Yield (%)[b]
1	copper (Ⅱ) catalyst **1** (8)	toluene	80 ˚C	15 h	46
2	copper (Ⅱ) catalyst **1** (8) - BF_3･OEt_2 (1)	toluene	r.t. to 80 ˚C	4 h	20
3	$Cu(acac)_2$ (2)	toluene	80 ˚C	6 h	33
4 [9]	$Cu(acac)_2$ (1) - BF_3･OEt_2 (1)	CH_2Cl_2	r.t.	6 h	49
5 [9]	$CuOTf(C_6H_6)_{0.5}$ (2)	CH_2Cl_2	r.t. to 40 ˚C	6 h	no reaction
6	$CuOTf(C_6H_6)_{0.5}$ (5)	toluene	80 ˚C	18 h	18
7	CuOAc (2) - BF_3･OEt_2 (1)	CH_2Cl_2	r.t.	68 h	<5
8	$Cu(OTf)_2$ (2)	CH_2Cl_2	r.t.	68 h	<5
9	$Cu(OTf)_2$ (2) - BF_3･OEt_2 (1)	CH_2Cl_2	r.t.	48 h	<5
10	$Cu(TFA)_2$ (2)	toluene	80 ˚C	48 h	8
11	$Cu(TFA)_2$ (2) - BF_3･OEt_2 (1)	CH_2Cl_2	r.t.	24 h	22
12	Cu powder (60)	toluene	80 ˚C	3 h	<5
13	CuCl (100)	toluene	80 ˚C	3 h	45
14	CuBr (100)	toluene	80 ˚C	18 h	33
15	CuI (100)	toluene	80 ˚C	20 h	25
16 [10]	$[RuCl_2(C_6H_6)]_2$ (1)	CH_2Cl_2	r.t. to 40 ˚C	3 d	no reaction
17 [11]	ruthenium (Ⅱ) catalyst **2** (1)	CH_2Cl_2	r.t. to 40 ˚C	3 d	<5
18	$Rh_2(OAc)_4$ (5)	CH_2Cl_2	r.t.	5 min	42
19	$Rh_2(OAc)_4$ (5)	$ClCH_2CH_2Cl$	r.t.	5 min	38
20	$Rh_2(OAc)_4$ (1)	toluene	r.t.	30 min	46
21	$Rh_2(Opiv)_2$ (1)	CH_2Cl_2	r.t.	5 min	0
22	$Rh_2(Opiv)_2$ (1)	toluene	−40 ˚C	30 min	0
23	$Pd(OAc)_2$ (2)	CH_2Cl_2	r.t.	39 h	no reaction
24 [12]	$Pd(OAc)_2$ (5)	toluene	80 ˚C	21 h	15
25 [12]	$Pd(PPh_3)_4$ (5)	toluene	80 ˚C	21 h	13
26	$PdCl_2$ (10)	toluene	80 ˚C	24 h	27

[a]All reactions were performed on 10 mg scale and run under nitrogen atmosphere. [b]Isolated yields.

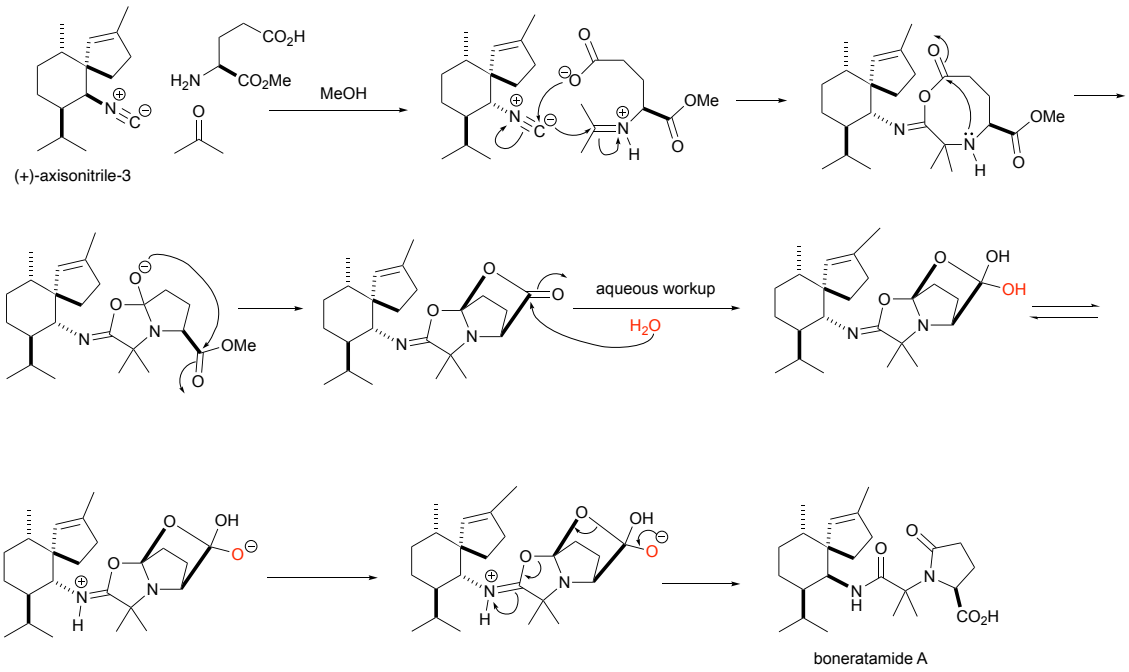


copper (II) catalyst **1**



ruthenium(II) catalyst **2**

A Plausible reaction mechanism for formation of boneratamide A



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