Electronic Supplementary Information

for

Total Synthesis of Exigurin:
Ugi Reaction in a Hypothetical Biosynthesis of Natual Products

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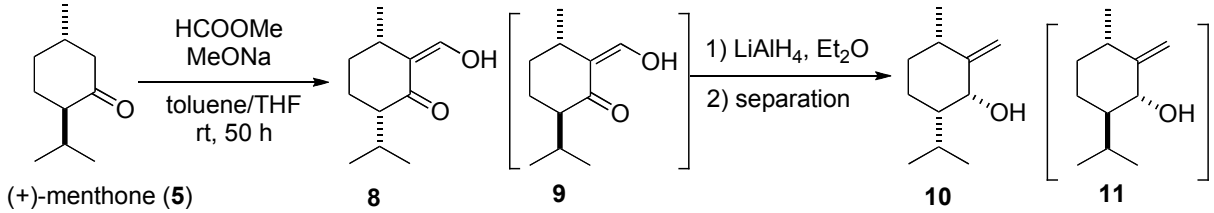
General Information

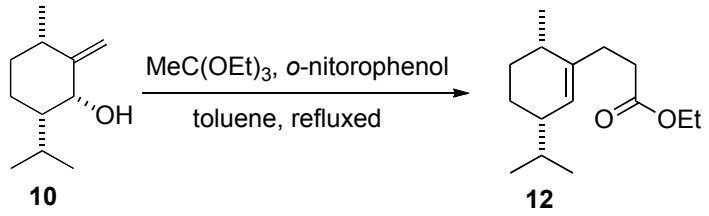
Melting points (Mp) were recorded on a Yanaco MP-S3 melting point apparatus and are not corrected. Optical rotations were measured on a JASCO P-2200 digital polarimeter at the sodium D line with a 100 mm path length cell, and are reported as follows:$[\alpha]_D^T$, concentration (g/100 mL), and solvent. 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) and JEOL ECS-400 (400 MHz) spectrometers. ^{1}H NMR chemical shifts (δ) are reported in parts per million (ppm) with the solvent resonance as the internal standard relative to chloroform (δ_H = 7.27), CHD_2OD (δ_H = 3.31), benzene (δ_H = 7.20) and DMSO (δ_H = 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_C = 77.0), CD_3OD (δ_C = 49.9), C_6D_6 (δ_C = 128.0) and DMSO-d_6 (δ_C = 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 received.

Experimental Section



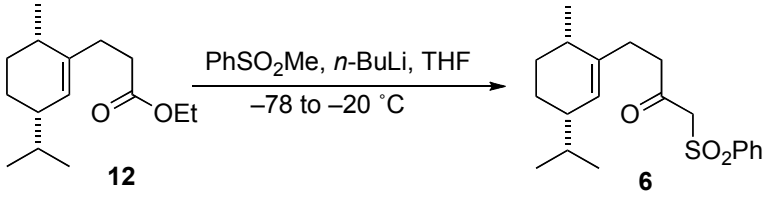
(3*S*,6*R*)-6-Isopropyl-3-methyl-2-methylenecyclohexanol (10). To a suspension of sodium methoxide (17.0 g, 0.31 mol) in a mixture of methyl formate (20.0 ml , 033 mol) and toluene (100 mL) was added a solution of (+)-menthone (**5**) (11.55 g, 74 mmol) in THF (50 mL). After vigorous stirring at room temperature for 14 h, more additional sodium methoxide (7.0 g, 0.13 mol) and THF (30 mL) were added. After stirring at room temperature for 50 h, water (250 mL) and hexane (40 mL) were added in one portion. The aqueous layer was separated and extracted with hexane. The aqueous layer was neutralized with 20% (w/v) aqueous H_2SO_4, and then extracted with ether. The combined organic layers were washed with water, saturated aqueous $NaHCO_3$, and brine, and dried (Na_2SO_4). Concentration under reduced pressure gave crude hydroxymethylene ketone **8** and **9** (11.93 g, 86%, a 93:7 *cis:trans* mixture determined by ^{1}H NMR analysis) as a pale yellow oil, which was used for the next step without further purification.

A solution of hydroxymethylene ketone **8** and **9** (11.93 g, 65.5 mmol) dissolved in ether (40mL) was added dropwise to a stirred solution of lithium aluminum hydride (5.10 g, 134 mmol) in ether (260 mL) at –20 °C. Cooling bath was removed and the solution was stirred at room temperature for 4.5 h and then carefully quenched with methanol (14 mL). Aqueous potassium sodium (+)-tartrate tetrahydrate solution (70 g, 300 mL) was added. After stirring at room temperature for 1 h, separated aqueous layer was extracted with ether. The combined organic layers were washed with brine, dried (Na_2SO_4) and concentrated to afford crude material (10.66 g). Purification by silica-gel chromatography (ether/hexane 1:30 followed by 1:20) afforded **10** (5.75g, 44% calculated from (+)-menthone **5**) and **11** (0.46 g, 4.1%). $[\alpha]_D^{20}$ = +8.9 (*c* = 1.00, $CHCl_3$); IR (KBr) ν_{max} = 3387, 2958, 2933, 2871 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ = 4.88 (s, 1H), 4.81 (s, 1H), 4.37–4.35 (m, 1H), 2.48–2.42 (m, 1H), 1.71–1.63 (m, 2H), 1.59–1.47 (m, 3H), 1.21 (d, *J* = 7.0 Hz, 3H), 1.13–1.07 (m, 1H), 1.00 (d, *J* = 7.0 Hz, 3H), 0.93 (d, *J* = 7.0 Hz. 3H), 0.88 (t, *J* = 6.5 Hz. 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ = 154.6, 110.0, 74.8, 49.4, 36.0, 32.7, 28.2, 21.3, 21.2, 21.0, 14.1.



10 **12**

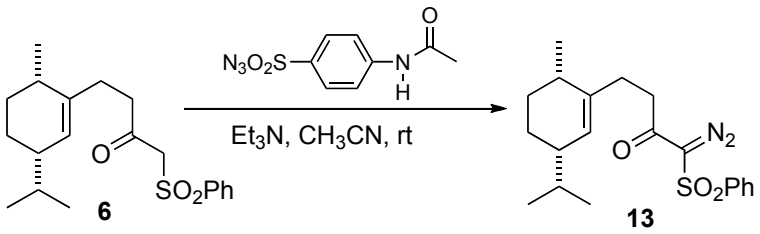
Ethyl 3-((3*S*,6*S*)-3-isopropyl-6-methylcyclohex-1-enyl)propanoate (12). A solution of **10** (5.08 g, 30.6 mmol) and *o*-nitrophenol (200 mg, 1.44 mmol) dissolved in a mixture of ethyl orthoformate (30 mL, 165 mmol) and toluene (30 mL) was heated with stirring at 120 °C for 30 min and at 160 °C for 30 min, until ethanol and toluene no longer distilled from the reaction flask. Excess ethyl orthoformate was removed by evaporation under reduced pressure (approximately 80 °C at 10 mmHg) to afford the yellow residual liquid, which was purified by silica-gel chromatography (AcOEt/hexane 1:50) to afford **12** (5.16g, 71%) as a colorless oil. $[\alpha]_D^{28}$ = –28.4 (*c* = 1.00, $CHCl_3$); IR (KBr) ν_{max} = 1738, 2870, 2933, 2958 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ = 5.24 (s, 1H), 4.12 (q, *J* = 7.0 Hz, 2H), 2.47–2.22 (m, 4H), 2.10–2.05 (m, 1H), 1.90–1.86 (m, 1H), 1.66–1.44 (m, 4H), 1.37–1.29 (m, 1H), 1.25 (t, *J* = 7.0 Hz, 3H), 1.00 (d, *J* = 7.0 Hz, 3H), 0.85 (d, *J* = 7.0 Hz, 3H), 0.82 (d, *J* = 7.0 Hz. 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ = 173.6, 140.9, 124.8, 60.2, 42.1, 33.1, 32.2, 31.3, 30.4, 30.0, 20.4, 19.6, 19.5, 19.1, 14.2; HRMS(ESI): m/z calcd for $C_{15}H_{26}NaO_2$ $[M+Na]^+$ 261.18, found 261.825.



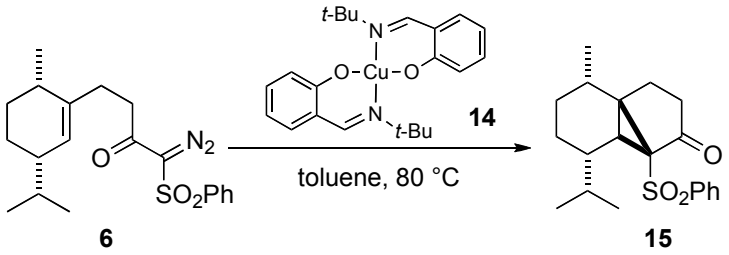
12 **6**

Ethyl 3-((3*S*,6*S*)-3-isopropyl-6-methylcyclohex-1-enyl)propanoate (6). Methyl phenyl sulfone (1.00 g, 7.35 mmol) was dissolved in toluene (20 mL) and the solvent is removed azeotropically by rotary evaporation. After this procedure followed by drying under vacuum, methyl phenyl sulfone was dissolved in THF (15 mL). To this solution cooled to –78 °C under argon atmosphere, *n*-butyl lithium (1.6 M solution in hexanes, 3.80 mL, 6.30 mmol) was added. After stirring at –78 °C for 12 minutes, ester **12** (0.50 g, 2.10 mmol) in THF (3.0 mL) was added. The reaction mixture was stirred at –78 °C for 15 min and at –20 °C (sodium chloride/ice bath) for 25 min. Saturated aqueous ammonium chloride and ether was added, and separated aqueous layer was extracted with ether (×2). The combined organic

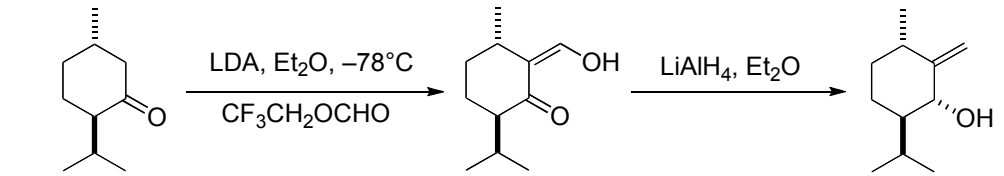
layer was washed with water and brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel eluting with AcOEt/hexane (1:5) to give **6** (686 mg, 99%) as an oil. $[\alpha]_D^{22} = -17.3$ (c = 1.00, $CHCl_3$); IR (KBr) ν_{max} = 1154, 1324, 1720, 2870, 2932, 2957 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ = 7.88 (d, J = 10.5 Hz, 2H), 7.67 (t, J = 10.5 Hz, 1H), 7.56 (t, J = 10.5 Hz, 2H), 5.20 (s, 1H), 4.18 (d, J = 14.0 Hz, 1H), 4.13 (d, J = 14.0 Hz, 1H), 2.85–2.72 (m, 2H), 2.28–2.16 (m, 2H), 2.05–2.00 (m, 1H), 1.89–1.83 (m, 1H), 1.70–1.24 (m, 5H), 0.97 (d, J = 10.0 Hz, 3H), 0.85 (d, J = 9.5 Hz, 3H), 0.82 (d, J = 9.5 Hz. 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ = 198.0, 140.3, 138.7, 134.2, 129.3, 128.2, 125.5, 66.7, 43.1, 42.1, 32.1, 31.3, 29.9, 28.7, 20.3, 19.7, 19.5, 19.1; HRMS(ESI): m/z calcd for $C_{20}H_{28}NaO_3S$ $[M+Na]^+$ 371.17, found 371.1651.



1-Diazo-4-((3*S*,6*S*)-3-isopropyl-6-methylcyclohex-1-enyl)-1-(phenylsulfonyl)butan-2-one (13). To solution of **6** (376 mg, 1.08 mmol) and *p*-acetamidobenzenesulfonyl azide (274 mg, 1.14 mmol) in acetonitrile (10 mL) under argon atmosphere at 0 °C was added triethylamine (0.48 mL, 3.42 mmol). The cooling bath was removed and the reaction mixture was allowed to stir at room temperature for 4 h, and then concentrated under reduced pressure. The resulting residue was suspended in a mixture of ether and hexane (1:1) and filtrated on Celite. Concentration of the filtrate gave the residue, which was purified by silica gel chromatography (AcOEt/Hexane 1:5) afforded **13** (341 mg, 84%). $[\alpha]_D^{28} = -19.5$ (c = 1.00, $CHCl_3$); IR (KBr) ν_{max} = 1156, 1342, 1666, 2109, 2869, 2932, 2957 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ = 7.98 (d, J = 11.0 Hz, 2H), 7.66 (t, J = 11.0 Hz,1H), 7.57 (t, J = 11.0 Hz, 2H), 5.10 (brs, 1H), 2.69–2.57 (m, 2H), 2.26–2.14 (m, 2H), 2.00–1.91 (m, 1H), 1.82–1.80 (m, 1H), 1.60–1.41 (m, 4H), 1.32–1.25 (m, 1H), 0.93 (d, J = 10.0 Hz, 3H), 0.84 (d, J = 10.0 Hz, 3H), 0.81 (d, J = 10.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ = 188.2, 134.1, 142.0, 140.3, 129.4, 127.3, 125.4, 42.0, 38.0, 32.1, 31.3, 29.9, 29.1, 20.2, 19.6, 19.4, 19.0; HRMS(ESI): m/z calcd for $C_{20}H_{27}N_2NaO_3S$ $[M+H]^+$ 375.1742, found 375.1738.



(3b*S*,4*S*,7*S*,7a*R*)-4-isopropyl-7-methyl-3a-(phenylsulfonyl)octahydro-3*H*-cyclopenta[1,3] cyclopropa[1,2]benzen-3-one (15). A solution of **13** (304 mg, 0.81 mmol) in toluene (30 mL) was evacuated by water aspirator and flushed with argon (×3). To this solution bis-(*N*-*t*-butylsalicylaldiminato)copper (II) (3.3 mg, 0.008 mmol) and stirring bar were quickly added. The reaction mixture was evacuated by water aspirator, flushed with argon, heated at 80 °C for 1.5 h, and then concentrated under reduced pressure to afford the residue, which was purified by silica gel chromatography (AcOEt/Hexane 1:10) to afford **15** (212 mg, 75%) as a colorless crystal. Mp 133–134 °C (recrystallized from AcOEt/hexane); $[\alpha]_D^{27} = -49.3$ (c = 1.00, $CHCl_3$); IR (KBr): ν_{max} = 1146, 1309, 1734, 2869, 2954, 3447 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ = 7.98 (d, J = 11.0 Hz, 2H), 7.59 (t, J = 11.0 Hz, 1H), 7.45 (t, J = 11.0 Hz, 2H), 2.84–2.77 (m, 1H), 2.38–2.32 (m, 1H), 2.17–1.99 (m, 3H), 1.93–1.81 (m, 3H), 1.56 (d, J = 11.0 Hz, 1H), 1.33 (oct, J = 9.5 Hz, 1H), 1.38–1.30 (m, 1H), 1.19–1.15 (m, 1H), 1.13 (d, J = 10.0 Hz, 3H), 1.01 (d, J = 9.5 Hz, 3H), 0.90 (d, J = 9.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 205.6. 141,4, 133.4, 128.6, 128.5, 58.1, 46.1, 39.4, 34.8, 33.7, 32.4, 29.0, 24.3, 22.3, 20.5, 19.5, 18.3; HRMS(ESI): m/z calcd for $C_{20}H_{26}NaO_3S$ $[M+Na]^+$ 369.1500, found 369.1495.

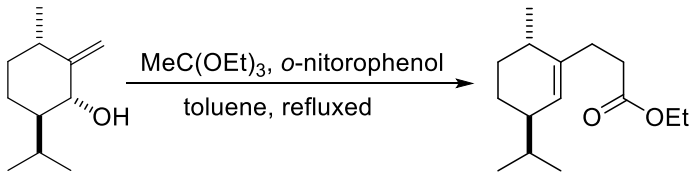


(+)-menthone (**5**) **9** **11**

(1*R*,3*S*,6*R*)-6-Isopropyl-3-methyl-2-methylenecyclohexan-1-ol (11). To a solution of diisopropylamine (36.8 mL, 216 mmol) in ether (380 mL) at –78 °C was added *n*-butyllithium (2.6 M in hexane, 120 mL, 314 mmol) dropwise. After stirring at –78 °C for 10 min, the solution was warmed to 0 °C. After stirring at 0 °C for 30 min, the solution was cooled to –78 °C and then a solution of (+)-menthone (**5**) (20.2 g, 130.1 mmol) in ether (20 mL) was added dropwise. After stirring at –78 °C for 15 min, 2,2,2-trifluoroethyl formate (76.3 mL, 785 mmol) was added over 10 min. The reaction mixture was stirred at –78 °C for 3 h, and then quenched by the addition of saturated aqueous NH_4Cl. The mixture was treated with 10% sulfuric until the mixture became acidic, and then extracted with ether (×3). The combined organic layer was extracted with 1 M aqueous NaOH (×3). The combined aqueous basic extracts were acidified by dropwise addition of 10% sulfuric, and the resulting aqueous layer was extracted with ether (×3). The combined organic layer was washed with water and brine, dried over Na_2SO_4 and concentrated under reduced pressure. Crude product **9** (16.7 g) was used for the next step without further purification.

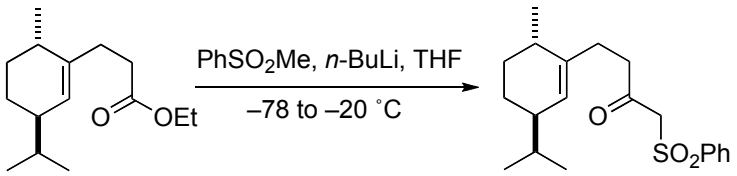
A solution of lithium aluminum hydride (13.9 g, 366.4 mmol) dissolved in ether (480 mL) cooled to –20 ˚C was added a solution of the crude product (16.7 g) in ether (20 mL). The cooling bath was removed. After stirring at room temperature for 14 h, the reaction mixture was cooled to 0 ˚C, and then carefully quenched by the addition of 10% aqueous sodium carbonate. The resulting suspension was filtered over Celite and the filtrate cake was washed with ether. The combined filtrate was concentrated under reduced pressure to afford the crude product, which was purified by silica-gel column chromatography (ether/pentane 1:10) to give compound **11** (3.54 g, 15% over 2 steps) as a colorless solid. Mp 41–42 °C; $[\alpha]_D^{25}$ = +76.9 (*c* = 1.00, $CHCl_3$); IR (KBr): ν_{max} = 3356, 2958, 2933, 2871 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 5.02 (d, *J* = 1.5 Hz, 1H), 4.74–4.71 (m, 1H), 3.83 (br d, *J* = 8.0 Hz, 1H), 2.23 (dqd, *J* = 14.5, 7.0, 2.0 Hz, 1H), 2.03–1.92 (m, 1H), 1.81 (dq, *J* = 12.0, 4.0 Hz, 1H), 1.71–1.61 (m, 1H), 1.29–1.16 (m, 2H), 1.09 (d, *J* = 6.0 Hz, 3H), 1.02–0.93 (m, 1H),

0.93 (d, J = 6.0 Hz, 3H), 0.87 (d, J = 7.0 Hz. 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 156.9, 100.6, 74.3, 52.0, 36.7, 36.0, 26.6, 23.0, 20.9, 18.1, 15.8; HRMS(DART): m/z calcd for $C_{11}H_{24}ON$ $[M+NH_4]^+$, 186.1852, found 186.1852.



11 **16**

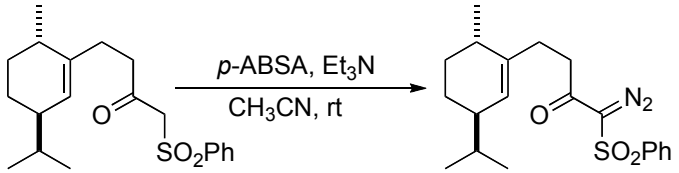
Ethyl 3-((3*R*,6*S*)-3-isopropyl-6-methylcyclohex-1-en-1-yl)propanoate (16). A solution of **11** (3.54 g, 20.9 mmol) and *o*-nitrophenol (1.66 g, 105 mmol) dissolved in a mixture of toluene (21.3 mL) and ethyl orthoacetate (19.1 mL, 0.288 mmol) was heated at 120 ˚C for 2 h, during which time ethanol and toluene distilled from the reaction flask. After cooling to room temperature, concentration of the reaction mixture under reduced pressure, followed by purification using silica-gel column chromatography (EtOAc/hexane 1:30) provided **16** (5.87 g, 85%) as a colorless oil. $[\alpha]_D^{27}$ = −15.4 (c = 1.00, $CHCl_3$); IR (KBr): ν_{max} = 2957, 2930, 2872, 1738 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 5.30 (s, 1H), 4.11 (q, J = 7.0 Hz, 2H), 2.50−2.26 (m, 4H), 2.18−2.05 (m, 1H), 1.93−1.77 (m, 2H), 1.68−1.57 (m, 1H), 1.58−1.48 (m, 1H), 1.25 (t, J = 7.0 Hz, 3H), 1.21−1.15 (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 = 173.5, 140.4, 125.9, 60.2, 42.0, 33.2, 32.3, 32.1, 30.0, 24.5, 19.6, 19.2, 14.2; HRMS(ESI): m/z calcd for $C_{15}H_{27}O_2$ $[M+H]^+$, 239.2004, found 239.2006.



16 **7**

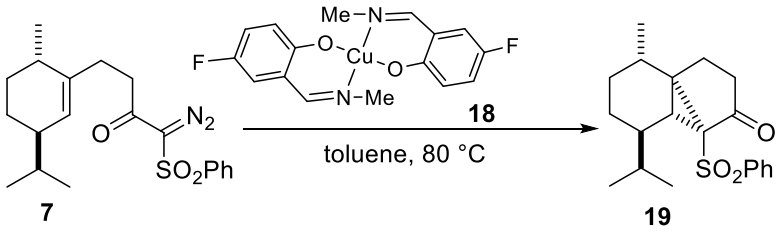
4-((3*R*,6*S*)-3-Isopropyl-6-methylcyclohex-1-en-1-yl)-1-(phenylsulfonyl)butan-2-one (7). Methyl phenyl sulfone (8.24 g, 52.7 mmol) was dissolved in toluene (10 mL) and the solvent was removed azeotropically by rotary evaporation. After this procedure, THF (170 mL) was added. To this solution cooled to −78 ˚C was added *n*-butyllithium (2.60 M in hexane, 17.4 mL, 45.2 mmol). The reaction mixture was warmed to 0 ˚C. After stirring at 0 ˚C for 30 min, the reaction mixture was cooled to −78 ˚C and then treated with a solution of **16** (5.87 g,

24.6 mmol) in THF (9.50 mL). After stirring at −78 ˚C for 30 min followed by at 0 ˚C for 30 min, the reaction was quenched by the addition of saturated aqueous NH_4Cl. The separated aqueous layer was extracted with EtOAc (×3). The combined organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by silica-gel column chromatography (EtOAc/hexane 1:10) to yield **7** (7.06 g, 83%) as a white solid. Mp 33–34 °C; $[\alpha]_D^{26}$ = −3.5 (*c* = 1.00, $CHCl_3$); IR (KBr): ν_{max} = 3064, 2957, 2930, 2870, 1720, 1323, 1154 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.91–7.87 (m, 2H), 7.71–7.66 (m, 1H), 7.60–7.55 (m, 2H), 5.26 (s, 1H), 4.18 (d, *J* = 13.5 Hz, 1H), 4.14 (d, *J* = 13.5 Hz, 1H), 2.83 (ddd, *J* = 18.0, 9.5, 6.0 Hz, 1H), 2.72 (ddd, *J* = 18.0, 9.0, 6.5 Hz, 1H), 2.36–2.18 (m, 2H), 2.13–2.02 (m, 1H), 1.90–1.76 (m, 2H), 1.68–1.46 (m, 2H), 1.30–1.11 (m, 2H), 0.97 (d, *J* = 7.0 Hz, 3H), 0.85 (d, *J* = 7.0 Hz, 3H), 0.81 (d, *J* = 7.0 Hz. 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 198.0, 139.8, 138.7, 134.3, 129.3, 128.3, 126.5, 66.8, 43.1, 42.0, 32.3, 32.3, 32.1, 28.5, 24.4, 19.8, 19.6, 19.3; HRMS(ESI): m/z calcd for $C_{20}H_{28}O_3NaS$ $[M+Na]^+$, 371.1649, found 371.1651.



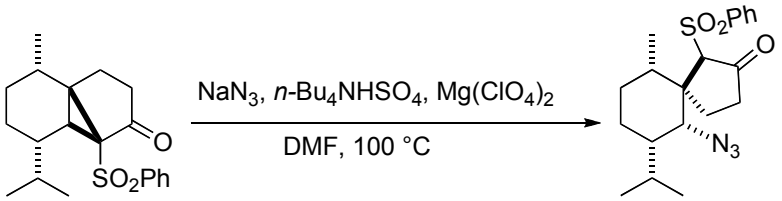
1-Diazo-4-((3*R*,6*S*)-3-isopropyl-6-methylcyclohex-1-en-1-yl)-1-(phenylsulfonyl)butan-2-one (17). To a solution of **7** (2.00 g, 5.74 mmol) and *p*-acetamidobenzenesulfonyl azide (1.52 g, 6.31 mmol) dissolved in acetonitrile (60 mL) cooled to 0 ˚C was added triethylamine (2.40 mL, 17.2 mmol) dropwise. The reaction mixture was stirred at room temperature for 14 h, diluted with water and EtOAc, and concentrated under reduced pressure to remove acetonitrile and EtOAc. The resulting aqueous layer was extracted with EtOAc (×3). The combined organic layer was concentrated under reduced pressure. The resulting residue was suspended in a mixture of hexane and EtOAc (5:1) and then filtered. The filtrate was concentrated under reduced pressure, and the resulting crude product was purified by silica-gel column chromatography (EtOAc/hexane 1:5) to afford **17** (1.79 g, 84%) as a yellow oil. $[\alpha]_D^{26}$ = −3.1 (*c* = 1.00, $CHCl_3$); IR (KBr): ν_{max} = 3065, 2956, 2929, 2870, 2122, 1667, 1342, 1156 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 8.01–7.96 (m, 2H), 7.70–7.65 (m, 1H), 7.61–7.56 (m, 2H), 5.18 (s, 1H), 2.68 (ddd, *J* = 17.0, 9.5, 6.0 Hz, 1H), 2.58 (ddd, *J* = 17.0, 9.0,

6.5 Hz, 1H), 2.28 (ddq, *J* = 16.0, 7.0, 1.0 Hz, 1H), 2.31–2.16 (m, 1H), 2.02–1.93 (m, 1H), 1.89–1.73 (m, 2H), 1.64–1.44 (m, 2H), 1.21–1.09 (m, 2H), 0.91 (d, *J* = 7.0 Hz, 3H), 0.84 (d, *J* = 7.0 Hz, 3H), 0.80 (d, *J* = 7.0 Hz. 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 188.2, 142.1, 139.9, 134.1, 129.5, 127.3, 126.4, 41.9, 38.1, 32.4, 32.2, 32.0, 28.6, 24.3, 19.7, 19.2; HRMS(ESI): m/z calcd for $C_{20}H_{27}N_2O_3S$ $[M+H]^+$, 375.1737, found 375.1737.

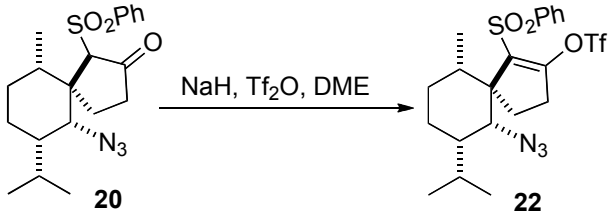


7 **19**

(3b*R*,4*R*,7*S*,7a*S*)-4-Isopropyl-7-methyl-3a-(phenylsulfonyl)octahydro-3H-cyclopenta[1,3]cyclopropa[1,2]benzen-3-one (19). To a solution of bis-(5-fluoro-(*N*-methylsalicylaldiminato))copper (II) (3.9 mg, 0.011 mmol) in toluene (4.5 mL, argon was bubbled through the solution for 30 min) was added diazo compound **7** (50 mg, 0.14 mmol) dissolved in toluene (0.50 mL, argon was bubbled through the solution for 30 min). The solution was heated at 80 ˚C for 2 h under argon atmosphere, cooled to room temperature, and concentrated under reduced pressure. The crude product was purified by silica-gel column chromatography (EtOAc/hexane 1:8) to afford **19** (21 mg, 46%) as a white solid. Mp 128–130 °C (recrystallized from acetone); $[\alpha]_D^{26}$ = –28.1 (*c* = 1.00, $CHCl_3$); IR (KBr): ν_{max} = 3068, 2959, 2937, 2873, 1729, 1310, 1148 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.17–8.12 (m, 2H), 7.62–7.57 (m, 1H), 7.54–7.49 (m, 2H), 2.38 (ddd, *J* = 13.0, 10.0, 10.0 Hz. 1H), 2.27 (ddd, *J* = 19.0, 10.0, 2.0 Hz. 1H), 2.19 (ddd, *J* = 19.0, 10.0, 9.0 Hz. 1H), 2.11–1.99 (m, 2H), 1.96–1.85 (m, 1H), 1.84–1.68 (m, 3H), 1.52–1.44 (m, 2H), 1.41 (d, *J* = 7.0 Hz, 3H), 1.02–0.91 (m, 1H), 0.84 (d, *J* = 7.0 Hz, 3H), 0.76 (d, *J* = 7.0 Hz. 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 206.2, 141.4, 133.3, 129.0, 128.3, 63.1, 49.1, 38.0, 36.1, 33.7, 33.5, 32.8, 28.8, 28.4, 26.3, 19.9, 19.2, 18.2; HRMS(ESI): m/z calcd for $C_{20}H_{27}O_3S$ $[M+H]^+$, 347.1674, found 347.1675.

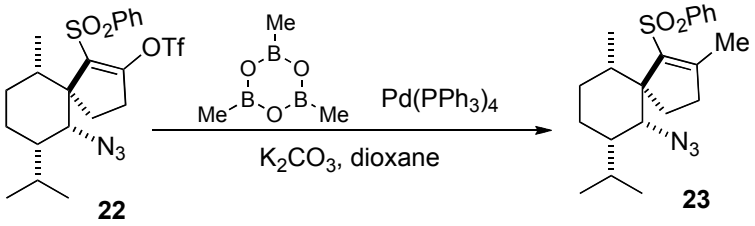


(1*R*,5*R*,6*R*,7*S*,10*S*)-6-Azido-7-isopropyl-10-methyl-1-(phenylsulfonyl)spiro[4.5]decan-2-one (20). To a solution of **15** (100 mg, 0.289 mmol) dissolved in *N,N*-dimethylformamide (4.0 mL) were added sodium azide (424 mg, 6.34 mmol), magnesium perchlorate (177 mg, 0.868 mmol) and tetrabutylammonium hydrogen sulfate (1.18 g, 3.47 mmol). The mixture was heated under argon atmosphere at 100 ˚C for 14 h. After cooling to room temperature, the reaction mixture was diluted with water and then extracted with EtOAc (×3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by silica-gel column chromatography (EtOAc/hexane 1:6) to afford **20** (74 mg, 66%) as a white solid. Mp 158–160 °C; $[\alpha]_D^{22}$ = +55.4 (*c* = 1.00, $CHCl_3$); IR (KBr): ν_{max} = 3068, 2949, 2876, 2105, 1751, 1586, 1447, 1310, 1155 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.78–7.76 (m, 2H), 7.72–7.67 (m, 1H), 7.57 (t, *J* = 8.0 Hz, 2H), 4.80 (s, 1H), 3.60 (s, 1H), 2.78–2.50 (m, 3H), 2.30–2.19 (m, 1H), 1.78–1.65 (m, 2H), 1.64–1.46 (m, 3H), 1.35 (ddd, *J* = 12.0, 4.8 Hz, 1H), 1.19–1.16 (m, 1H), 1.17 (s, 3H), 1.13 (d, *J* = 6.0 Hz, 3H), 1.03 (d, *J* = 6.0 Hz. 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 207.5, 138.2, 134.3, 129.0, 128.8, 78.0, 66.3, 54.4, 45.8, 34.1, 34.0, 30.2, 29.0, 28.9, 20.9, 20.1, 18.9, 16.0; HRMS(ESI): m/z calcd for $C_{20}H_{27}N_3O_3NaS$ $[M+Na]^+$, 412.1665, found 412.1665.



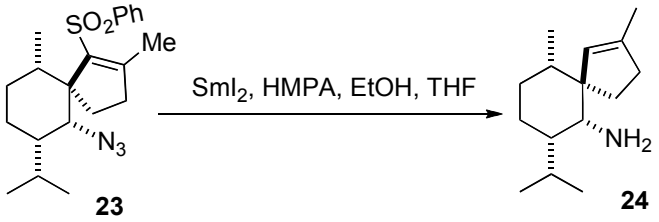
(5*R*,6*R*,7*S*,10*S*)-6-Azido-7-isopropyl-10-methyl-1-(phenylsulfonyl)spiro[4.5]dec-1-en-2-yl trifluoromethanesulfonate (22). To a solution of **20** (64 mg, 0.16 mmol) in 1,2-dimethoxyethane (2.90 mL) was added sodium hydride (55% dispersion in mineral oil, 36 mg, 0.82 mmol). The mixture was heated under argon atmosphere at 40 ˚C for 30 min. After cooling to 0 ˚C, trifluoromethanesulfonic anhydride (0.55 mL, 0.33 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 over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by silica-gel column chromatography (EtOAc/hexane 1:12) to afford **22** (79 mg, 92%) as a white solid. Mp 115–117 °C; $[\alpha]_D^{23}$ = –18.0 (*c* = 1.00, $CHCl_3$); IR (KBr): ν_{max} = 3070, 2965, 2931, 2873, 2100, 1639, 1585, 1327, 1150 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 8.01–7.97 (m, 2H), 7.70–7.64 (m, 1H), 7.63–7.58 (m, 2H), 4.79 (d, *J* = 4.0 Hz, 1H), 2.71 (ddd, *J* = 18.0, 9.0, 9.0 Hz, 1H), 2.62 (ddd, *J* = 18.0, 11.0, 2.5 Hz, 1H), 2.47 (ddq, *J* = 8.0, 7.0, 4.0 Hz, 1H), 2.15–2.05 (m, 1H), 2.01 (ddd, *J* = 14.0, 5.0, 2.5 Hz, 1H), 1.87 (ddd, *J* = 14.0, 9.5, 2.5 Hz, 1H), 1.84–1.73 (m, 2H), 1.55–1.42 (m, 2H), 1.20 (d, *J* = 6.0 Hz, 3H), 1.26–1.12 (m, 1H), 0.92 (d, *J* = 6.0 Hz, 3H), 0.91 (d, *J* = 7.0 Hz. 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 155.2, 141.0, 134.0, 129.1, 127.9, 119.8, 116.5, 67.1, 60.0, 43.7, 38.1, 31.2, 27.5, 26.7, 25.6, 23.4, 23.1, 22.3, 15.9; HRMS(ESI): m/z calcd for $C_{21}H_{26}F_3N_3O_5NaS_2$ $[M+Na]^+$, 544.1157, found 544.1158.



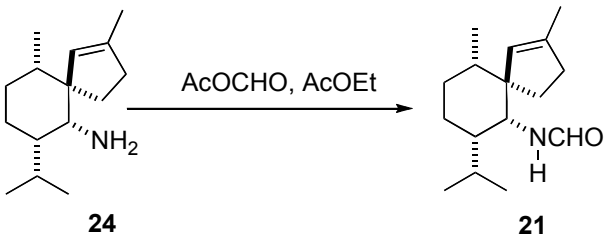
(5*R*,6*R*,7*S*,10*S*)-6-Azido-7-isopropyl-2,10-dimethyl-1-(phenylsulfonyl)spiro[4.5]dec-1-ene (23). To a solution of **22** (150 mg, 0.288 mmol) in 1,4-dioxane (2.50 mL, argon was bubbled through the solution for 15 min) was added tetrakis(triphenylphosphine)palladium (33 mg, 0.29 mmol). After stirring at 0 ˚C for 5 min under argon atmosphere, potassium carbonate (119 mg, 0.863 mmol) and trimethylboroxine (0.406 mL, 0.288 mmol) were added. After stirring at 110 ˚C for 1 h, the mixture was filtered through a pad of Celite, and rinsed with THF. Concentration of the filtrate under reduced pressure followed by purification by silica-gel column chromatography (EtOAc/hexane 1:12) provided **23** (107 mg, 96%) as a white solid. Mp 123–124 °C; $[\alpha]_D^{23}$ = +22.2 (*c* = 1.00, $CHCl_3$); IR (KBr): ν_{max} = 2961, 2931, 2871, 2096, 1617, 1462, 1302, 1144, 1085 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.97–7.92 (m, 2H), 7.61–7.52 (m, 3H), 4.76 (d, *J* = 5.0 Hz, 1H), 2.50–2.31 (m, 3H), 2.09 (s, 3H), 2.01–1.92 (m, 2H), 1.89–1.79 (m, 1H), 1.79–1.70 (m, 2H), 1.49 (tt, *J* = 14.0, 3.5, 1H), 1.43–1.35 (m, 1H), 1.18 (d, *J* = 6.5 Hz, 3H), 1.28–1.11 (m, 1H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.74 (d, *J* = 7.0 Hz. 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 158.4, 143.2, 137.6, 132.9, 129.0,

126.9, 67.8, 64.2, 43.9, 40.1, 38.3, 27.6, 26.6, 26.1, 25.1, 23.0, 22.4, 16.9, 16.2; HRMS(ESI): m/z calcd for $C_{21}H_{29}N_3O_2NaS$ $[M+Na]^+$, 410.1871, found 410.1873.



23 **24**

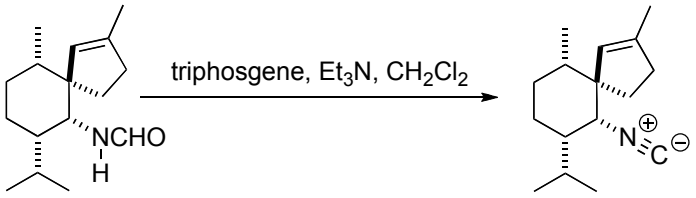
(5*S*,6*R*,7*S*,10*S*)-7-Isopropyl-2,10-dimethylspiro[4.5]dec-1-en-6-amine (24). To a solution of samarium (II) iodide (SmI_2, 0.023 M in THF, 9.15 mL, 0.21 mmol) cooled to –20 ˚C under argon atmosphere were added successively hexamethylphosphoramide (0.19 mL, 1.07 mmol), ethanol (0.11 mL, 1.83 mmol) and a solution of **23** (21 mg, 0.53 mmol) in THF (0.50 mL, argon was bubbled through the solution for 15 min before use). After stirring at -20 ˚C for 30 min, saturated aqueous of NH_4Cl was added. The separated aqueous layer was extracted with EtOAc (×3), and the combined organic layer was washed with saturated aqueous $NaHCO_3$ and saturated aqueous $Na_2S_3O_2$. After drying over Na_2SO_4, concentration under reduced pressure gave a residue, which was purified by silica-gel column chromatography (EtOAc) to provide **24** (6 mg, 50%) as a pale yellow oil. $[\alpha]_D^{23}$ = +20.6 (*c* = 1.00, $CHCl_3$); IR (KBr): ν_{max} = 3043, 2957, 2928, 2869, 1615, 1455, 1375, 1018, 996 cm^{-1}; ^1H NMR (CD_3OD, 400 MHz) δ = 5.51 (br s, 1H), 2.81–2.77 (m, 1H), 2.35–2.24 (m, 1H), 2.24–2.14 (m, 1H), 2.02 (dddd, *J* = 13.0, 8.5, 5.0, 1.5 Hz, 1H), 1.84–1.76 (m, 2H), 1.70 (d, *J* =1.0 Hz, 3H), 1.67–1.40 (m, 6H), 1.33–1.21 (m, 1H), 1.06 (dd, *J* = 7.0, 2.0 Hz, 3H), 0.94 (dd, *J* = 7.0, 2.0 Hz, 3H), 0.89 (dd, *J* = 6.5, 2.0 Hz. 3H); ^{13}C NMR (CD_3OD, 100 MHz) δ = 140.9, 133.5, 58.2, 57.7, 46.7, 38.5, 36.5, 33.3, 30.3, 29.5, 22.0, 21.6, 21.3, 17.4, 16.8; HRMS(ESI): m/z calcd for $C_{15}H_{28}N$ $[M+H]^+$, 222.2216, found 222.2216.



24 **21**

Exiguamide (21). A solution of compound **24** (14 mg, 0.065 mmol) dissolved in EtOAc (0.72 mL) under argon atmosphere was treated with acetic formic anhydride (0.26 mL, 0.32

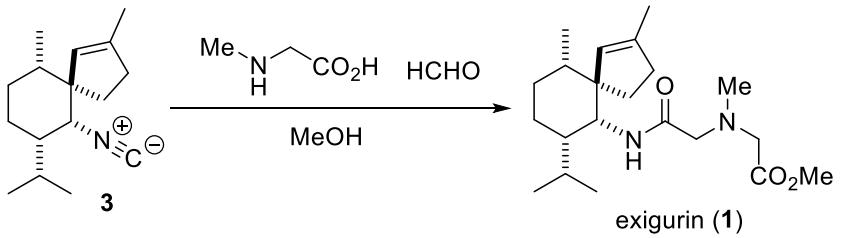
mmol, prepared by treatment of acetic anhydride with formic acid at 50 ˚C for 1 h). After stirring at room temperature for 20 min, the mixture was treated with aqueous $NaHCO_3$. The separated aqueous layer was extracted with EtOAc (×3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by silica-gel column chromatography (EtOAc/hexane 1:2) to give exiguamide (**21**) (11 mg, 68%) as a colorless crystal. Mp 139–141 °C; $[\alpha]_D^{27}$ = +32.9 (c = 1.00, $CHCl_3$); IR (KBr): ν_{max} = 3307, 3043, 2959, 2929, 2870, 1689, 1659, 1530, 1458, 1382, 787 cm^{-1}; ^1H NMR (DMSO-d_6, 400 MHz) δ = 8.08 (d, J = 1.5 Hz, 1H), 7.62 (br d, J = 10.0 Hz, 1H), 5.58 (br s, 1H), 3.82 (dd, J = 10.0, 3.0 Hz, 1H), 2.34 (ddd, J = 16.0, 8.0, 8.0 Hz, 1H), 1.99 (br dd, J = 15.0, 9.0 Hz, 1H), 1.83–1.71 (m, 2H), 1.68 (s, 3H), 1.59–1.51 (m, 1H), 1.51–1.21 (m, 5H), 1.15–1.06 (m, 1H), 0.95 (d, J = 7.0 Hz, 3H), 0.86 (d, J = 6.5 Hz, 3H), 0.68 (d, J = 6.5 Hz. 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ = 161.2, 139.3, 131.8, 56.2, 50.3, 43.4, 36.4, 34.7, 33.8, 29.5, 29.0, 21.1, 20.4, 19.4, 16.9, 15.9; HRMS(ESI): m/z calcd for $C_{16}H_{28}NO$ $[M+H]^+$, 250.2165, found 250.2165.



21 (–)-10-*epi*-axisonitrile-3 (**3**)

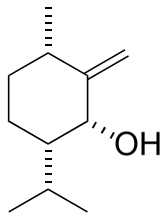
(–)-10-*epi*-Axisonitrile-3 (3). To a solution of exiguamide (**21**) (20 mg, 0.79 mol) and triethylamine (0.77 mL, 0.55 mmol) dissolved in CH_2Cl_2 (0.28 mL) cooled to –20 ˚C was added triphosgene (22 mg, 0.073 mmol). After stirring at –20 ˚C for 10 min, the reaction mixture was warmed to 0 ˚C and then 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 CH_2Cl_2 (×3). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by silica-gel column chromatography (EtOAc/hexane 1:10) to afford (–)-10-*epi*-axisonitrile-3 (**3**) (16 mg, 88%) as a colorless oil. $[\alpha]_D^{26}$ = –39.4 (c = 1.00, $CHCl_3$); IR (KBr): ν_{max} = 3046, 2964, 2931, 2874, 2131, 1655, 1456, 1385 cm^{-1}; ^1H NMR (C_6D_6, 400 MHz) δ = 5.24 (q, J = 1.0 Hz, 1H), 3.51 (br s, 1H), 2.29 (ddd, J = 13.5, 7.5, 3.0 Hz, 1H), 2.15–2.05 (m, 1H), 1.98–1.90 (m, 1H), 1.82 (ddd, J = 13.0, 8.0, 8.0 Hz, 1H), 1.77–1.68 (m, 1H), 1.60–1.54 (m, 2H), 1.51–1.50 (m, 3H), 1.53–1.46 (m,

2H), 1.44–1.37 (m, 1H), 1.30 (d, J = 7.5 Hz, 3H), 1.02–0.89 (m, 1H), 0.85 (d, J = 6.5 Hz, 3H), 0.82 (d, J = 6.5 Hz, 3H); ^{13}C NMR (C_6D_6, 100 MHz) δ = 161.4 (t), 161.4, 161.3, 141.7, 130.2, 59.4, 59.4, 59.4 (t), 55.1, 44.1, 37.1, 35.0, 34.6, 30.0, 29.6, 20.8, 20.0, 19.7, 16.7, 16.3; HRMS(DART): m/z calcd for $C_{16}H_{29}N_2$ $[M+NH_4]^+$, 249.2322, found 249.2325.



3 exigurin (**1**)

Exigurin (1). *N*-Methylglycine (5.7 mg, 0.064 mmol) and aqueous formaldehyde (37%, 22 μL, 0.32 mmol) were dissolved in methanol (0.60 mL). The mixture was heated under argon atmosphere at 50 ˚C for 15 min. To this mixture was added a solution of (–)-10-*epi*-axisonitrile-3 (**3**) (13 mg, 0.058 mmol) in methanol (0.07 mL). After stirring at 50 ˚C for 20 min, the reaction mixture was concentrated under reduced pressure and then extracted with EtOAc (×3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by silica-gel column chromatography (EtOAc/hexane 2:1) to afford exigurin (**1**) (11 mg, 53%) as a colorless oil. $[\alpha]_D^{24}$ = +20.7 (c = 1.00, $CHCl_3$); IR (KBr): ν_{max} = 3367, 3041, 2955, 2926, 2871, 2802, 2731, 1748, 1678, 1514, 1457, 1199, 1064 cm^{-1}; ^{1}H NMR (C_6D_6, 400 MHz) δ = 7.57 (d, J = 10.5 Hz, 1H), 5.66 (br s, 1H), 4.49 (dd, J = 10.5, 2.5 Hz, 1H), 3.27 (s, 3H), 3.07 (d, J = 16.0 Hz, 1H), 3.02 (d, J = 16.0 Hz, 1H), 2.84 (s, 2H), 2.89–2.79 (m, 1H), 2.23 (ddd, J = 13.0, 8.0, 2.0 Hz, 1H), 2.14 (ddq, J = 16.0, 9.0 1.0 Hz, 1H), 2.08 (s, 3H), 1.91-1.80 (m, 1H), 1.69 (br s, 3H), 1.77–1.62 (m, 3H), 1.60–1.30 (m, 4H), 1.14 (d, J = 7.5 Hz, 3H), 1.13 (d, J = 6.5 Hz, 3H), 0.99 (d, J = 6.5 Hz. 3H); ^{13}C NMR (C_6D_6, 100 MHz) δ = 170.7, 169.0, 140.8, 131.8, 61.5, 58.4, 57.1, 52.3, 51.0, 44.7, 43.2, 37.2, 35.5, 34.9, 30.2, 30.1, 21.5, 21.2, 20.3, 17.1, 16.5; HRMS(ESI): m/z calcd for $C_{21}H_{37}N_2O_3$ $[M+H]^+$, 365.2798, found 365.2799.



10

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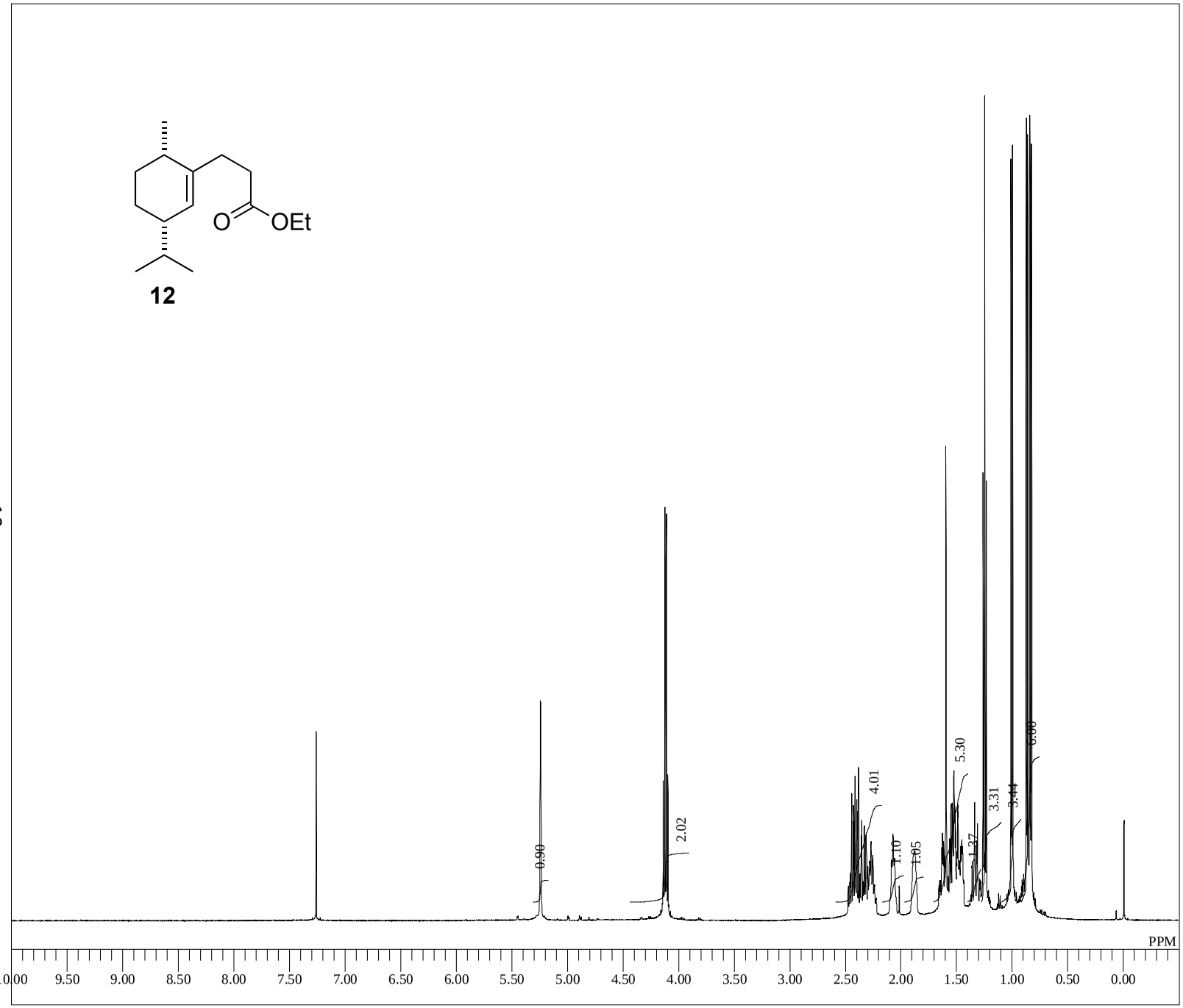

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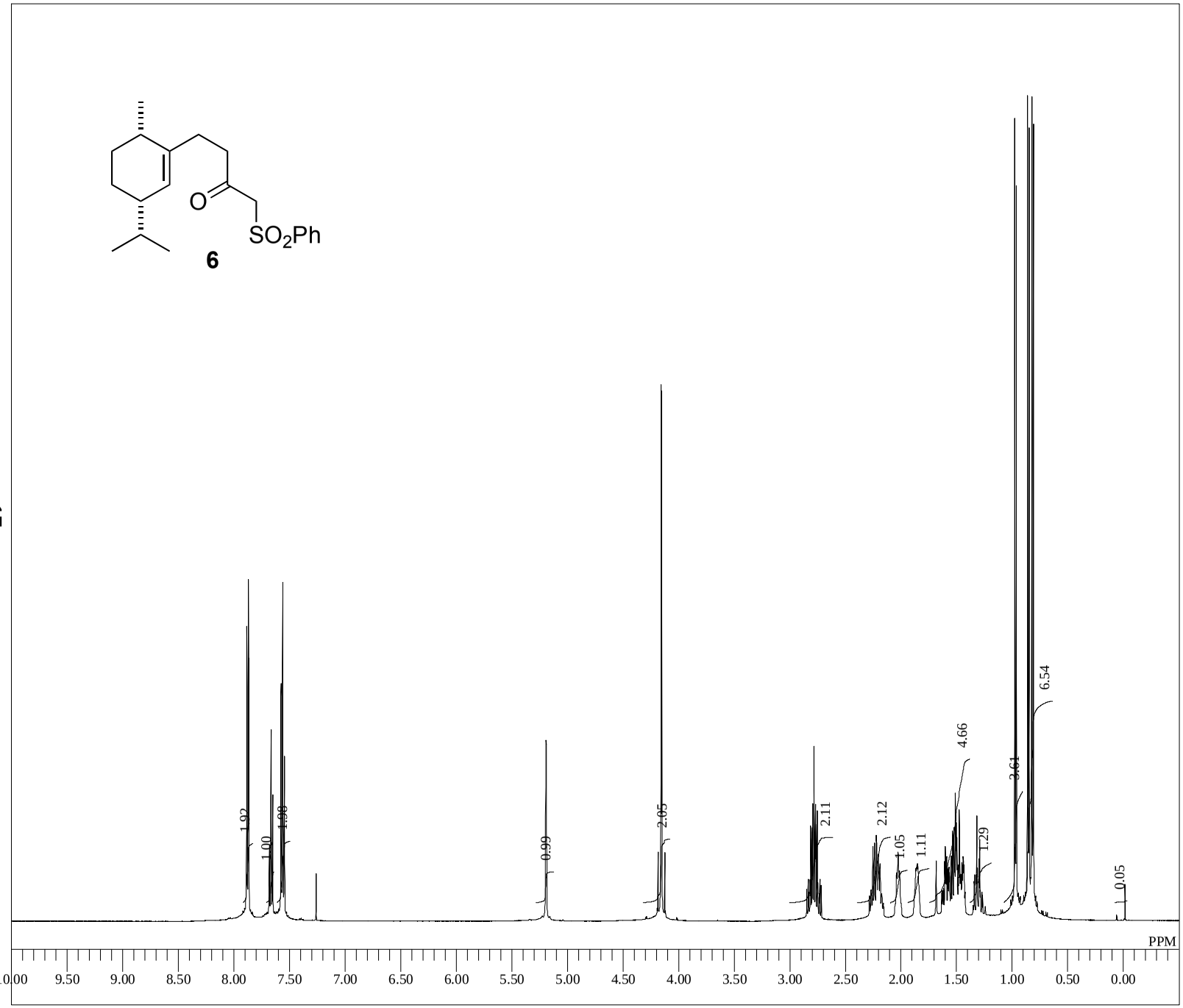
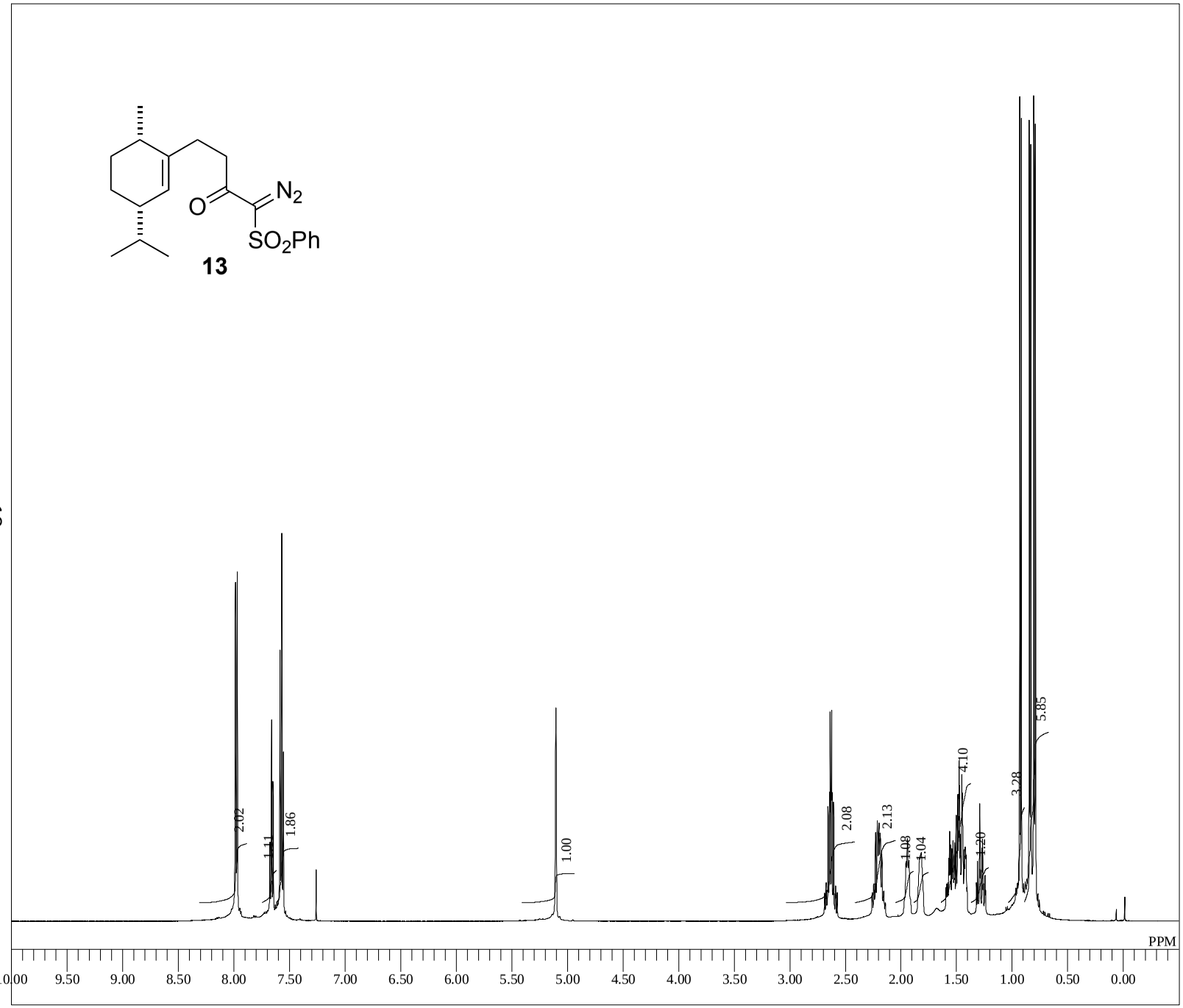
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16384
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	21.2 c
SLVNT	CDCL3
EXREF	7.26 ppm
BF	0.12 Hz
RGAIN	40

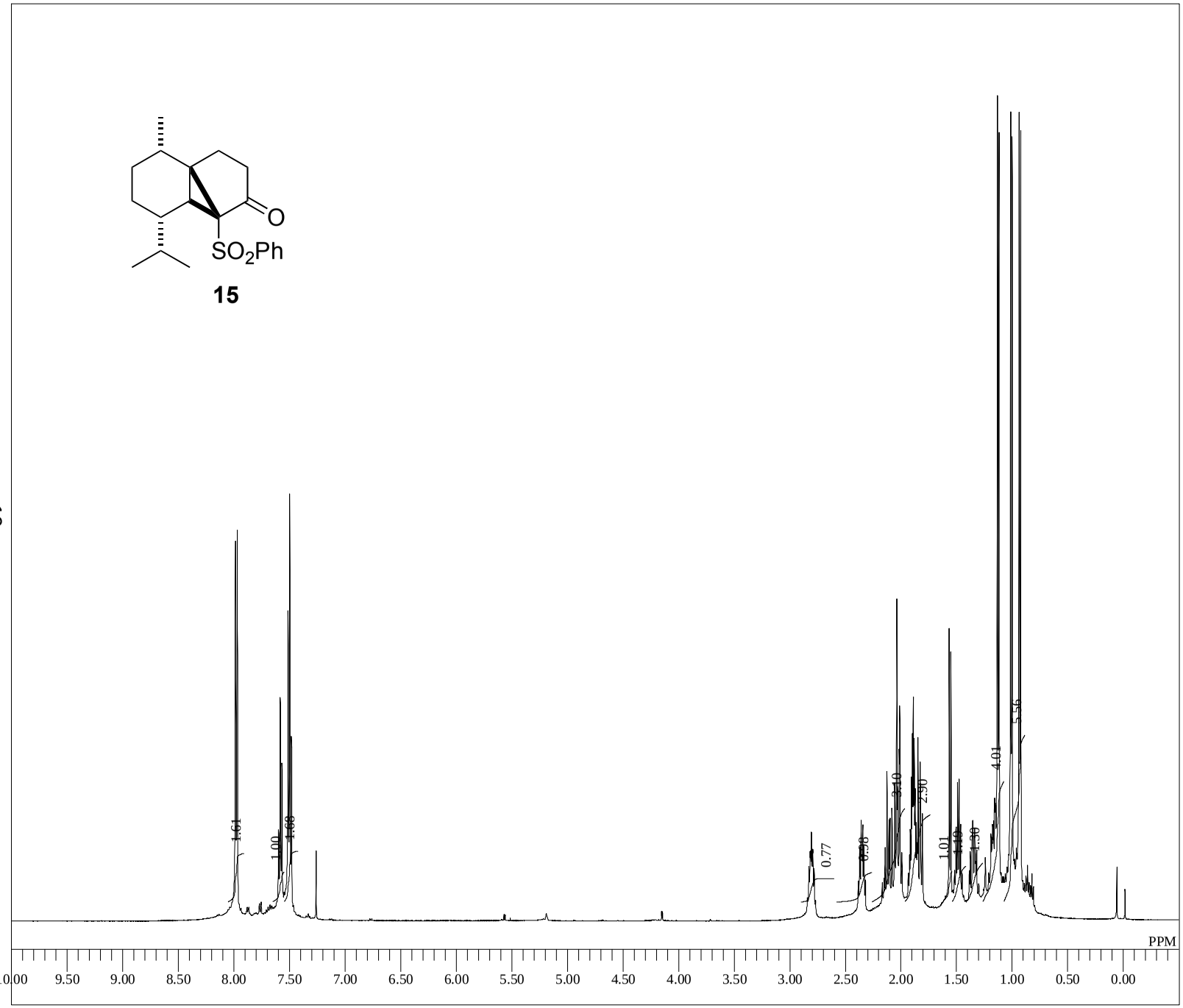


17

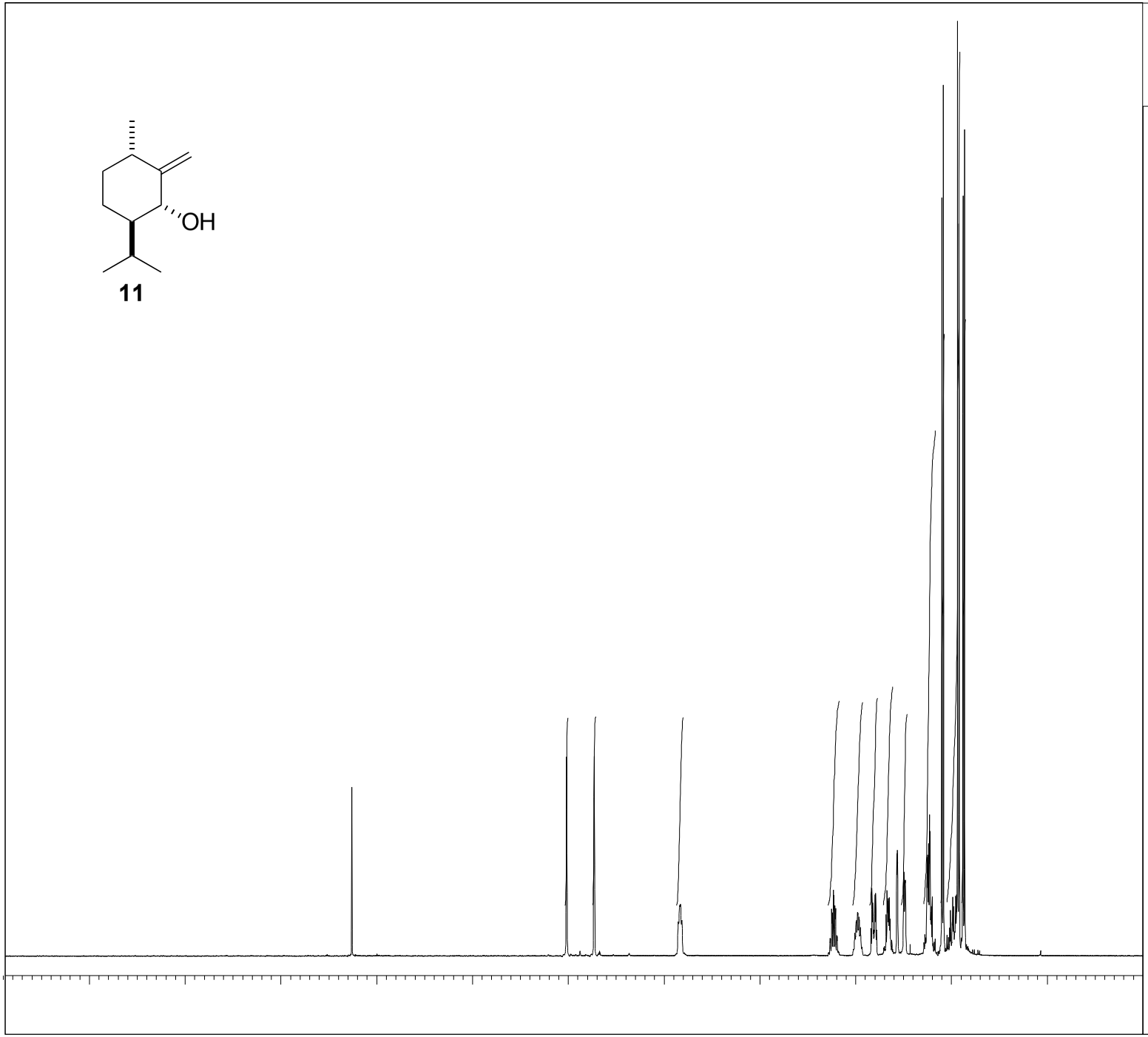
DFILE	MAE-2181-column-data2_proton-1-1.jdf
COMNT	single_pulse
DATIM	2017-08-04 10:25:26
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16384
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	23.3 c
SLVNT	CDCL3
EXREF	7.26 ppm
BF	0.12 Hz
RGAIN	28



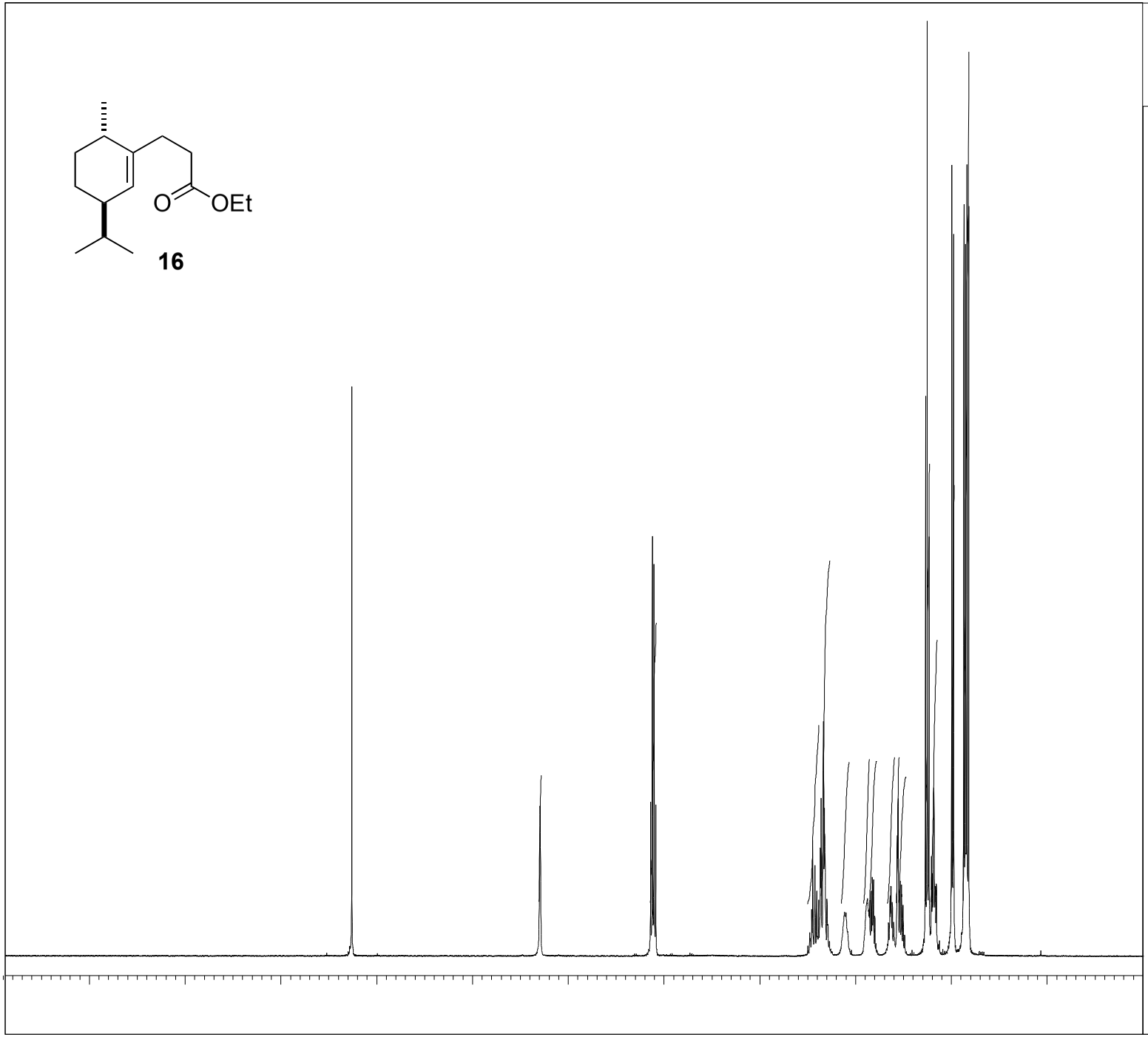
DFILE	MAE-2187-column_proton-3-1.jdf
COMNT	single_pulse
DATIM	2017-08-24 14:45:24
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16384
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	23.3 c
SLVNT	CDCL3
EXREF	7.26 ppm
BF	0.12 Hz
RGAIN	30



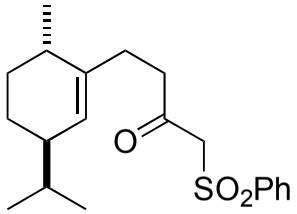
DFILE	MAE-2189-column_proton-1-1.jdf
COMNT	single_pulse
DATIM	2017-09-01 15:23:26
OBNUC	1H
EXMOD	proton.jxp
OBFRQ	500.16 MHz
OBSET	2.41 KHz
OBFIN	6.01 Hz
POINT	16384
FREQU	9384.38 Hz
SCANS	8
ACQTM	1.7459 sec
PD	5.0000 sec
PW1	4.68 usec
IRNUC	1H
CTEMP	22.1 c
SLVNT	CDCL3
EXREF	7.26 ppm
BF	0.12 Hz
RGAIN	32




```
Filename          = 9KN_11_1H_CDCl3_400MHz_2019_
Author            = delta
Experiment        = single_pulse.ex2
Sample_Id         = 1
Solvent           = CHLOROFORM-D
Creation_Time     =  3-JUN-2019 12:27:35
Revision_Time     =  5-NOV-2019 21:48:07
Current_Time      =  5-NOV-2019 21:49:27

Comment           = single_pulse
Data_Format       = 1D COMPLEX
Dim_Size          = 13107
Dim_Title         = 1H
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.389766[T] (400[MHz])
X_Acq_Duration    = 1.31072[s]
X_Domain          = 1H
X_Freq            = 399.78219838[MHz]
X_Offset          = 5[ppm]
X_Points          = 16384
X_Prescans        = 1
X_Resolution      = 0.76293945[Hz]
X_Sweep           = 12.5[kHz]
Irr_Domain        = 1H
Irr_Freq          = 399.78219838[MHz]
Irr_Offset        = 5[ppm]
Tri_Domain        = 1H
Tri_Freq          = 399.78219838[MHz]
Tri_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 8
Total_Scans       = 8

Relaxation_Delay = 5[s]
Recvr_Gain        = 30
Temp_Get          = 25[dC]
X_90_Width        = 12.2[us]
X_Acq_Time        = 1.31072[s]
X_Angle           = 45[deg]
X_Atn             = 3.5[dB]
X_Pulse           = 6.1[us]
Irr_Mode          = Off
Tri_Mode          = Off
Dante_Presat      = FALSE
Initial_Wait      = 1[s]
Repetition_Time   = 6.31072[s]
```

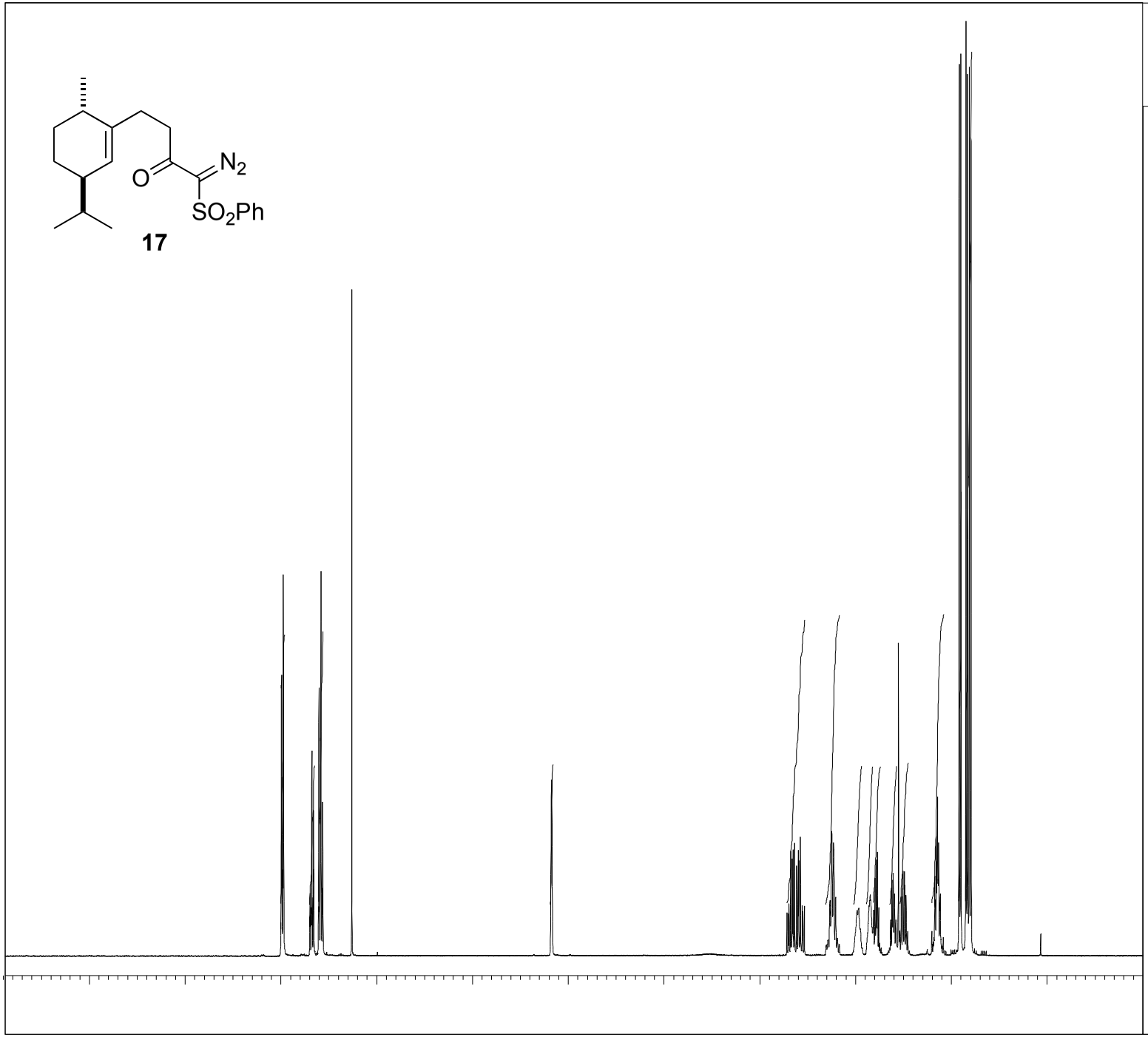



```
Filename          = 9KN_16_1H_CDCl3_400MHz_2019_
Author            = delta
Experiment        = single_pulse.ex2
Sample_Id         = 1
Solvent           = CHLOROFORM-D
Creation_Time     = 22-JUL-2019 10:00:47
Revision_Time     =  5-NOV-2019 21:52:02
Current_Time      =  5-NOV-2019 21:52:29

Comment           = single_pulse
Data_Format       = 1D COMPLEX
Dim_Size          = 13107
Dim_Title         = 1H
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 2.20725248[s]
X_Domain          = 1H
X_Freq            = 395.88430144[MHz]
X_Offset          = 5[ppm]
X_Points          = 16384
X_Prescans        = 1
X_Resolution      = 0.45305193[Hz]
X_Sweep           = 7.42280285[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Tri_Domain        = 1H
Tri_Freq          = 395.88430144[MHz]
Tri_Offset        = 5[ppm]
Clipped           = TRUE
Scans             = 8
Total_Scans       = 8

Relaxation_Delay = 5[s]
Recvr_Gain        = 50
Temp_Get          = 21.8[dC]
X_90_Width        = 13.25[us]
X_Acq_Time        = 2.20725248[s]
X_Angle           = 45[deg]
X_Atn             = 2.5[dB]
X_Pulse           = 6.625[us]
Irr_Mode          = Off
Tri_Mode          = Off
Dante_Presat      = FALSE
Initial_Wait      = 1[s]
Repetition_Time   = 7.20725248[s]
```



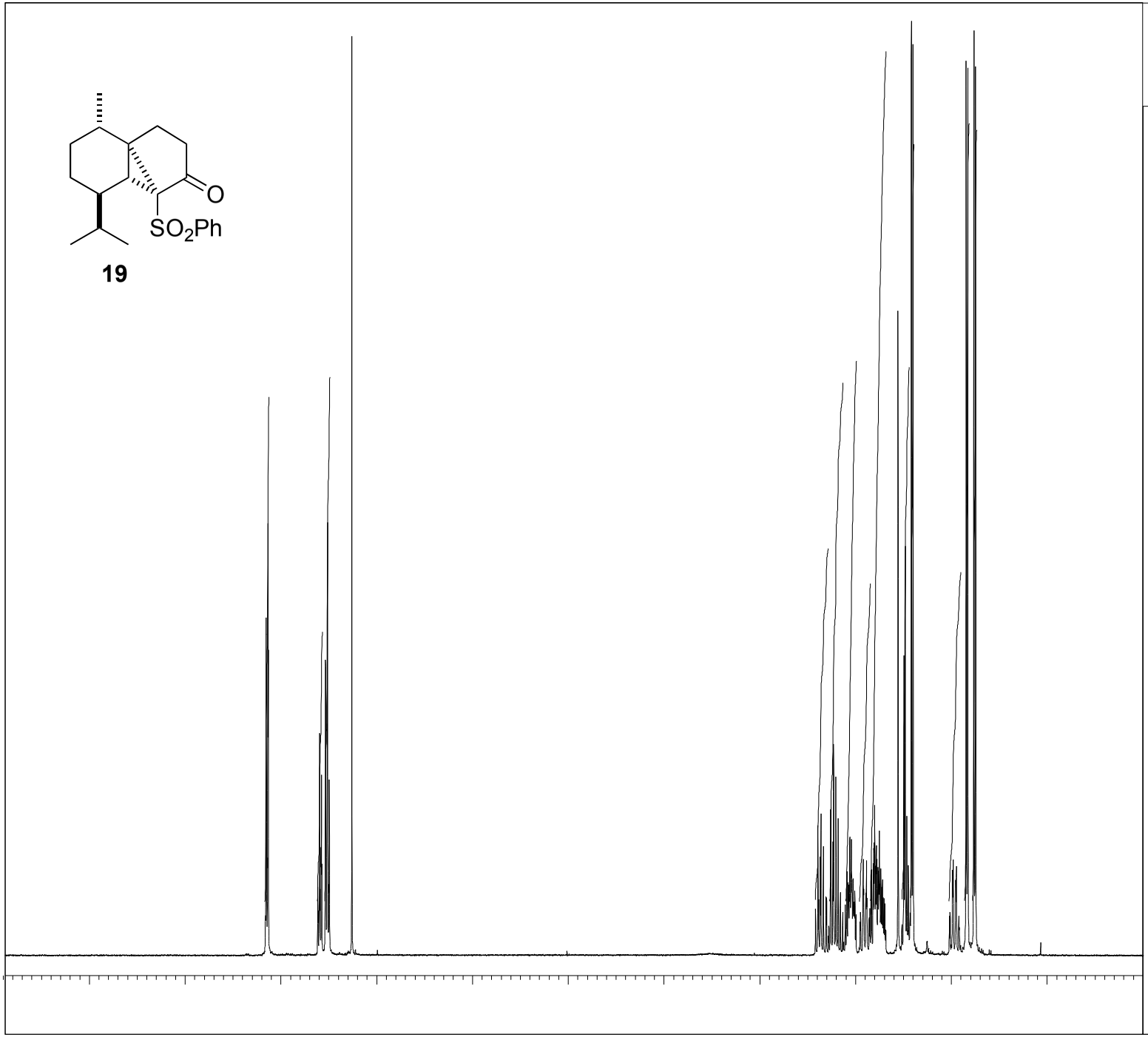
7


```
Filename          = 9KN_17_1H_CDCl3_400MHz_2019_
Author            = delta
Experiment        = single_pulse.ex2
Sample_Id         = 1
Solvent           = CHLOROFORM-D
Creation_Time     = 14-MAY-2019 11:28:42
Revision_Time     =  5-NOV-2019 21:53:46
Current_Time      =  5-NOV-2019 21:54:04

Comment           = single_pulse
Data_Format       = 1D COMPLEX
Dim_Size          = 13107
Dim_Title         = 1H
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 2.20725248[s]
X_Domain          = 1H
X_Freq            = 395.88430144[MHz]
X_Offset          = 5[ppm]
X_Points          = 16384
X_Prescans        = 1
X_Resolution      = 0.45305193[Hz]
X_Sweep           = 7.42280285[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Tri_Domain        = 1H
Tri_Freq          = 395.88430144[MHz]
Tri_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 8
Total_Scans       = 8

Relaxation_Delay = 5[s]
Recvr_Gain        = 36
Temp_Get          = 22[dC]
X_90_Width        = 11.1[us]
X_Acq_Time        = 2.20725248[s]
X_Angle           = 45[deg]
X_Atn             = 2[dB]
X_Pulse           = 5.55[us]
Irr_Mode          = Off
Tri_Mode          = Off
Dante_Presat      = FALSE
Initial_Wait      = 1[s]
Repetition_Time   = 7.20725248[s]
```



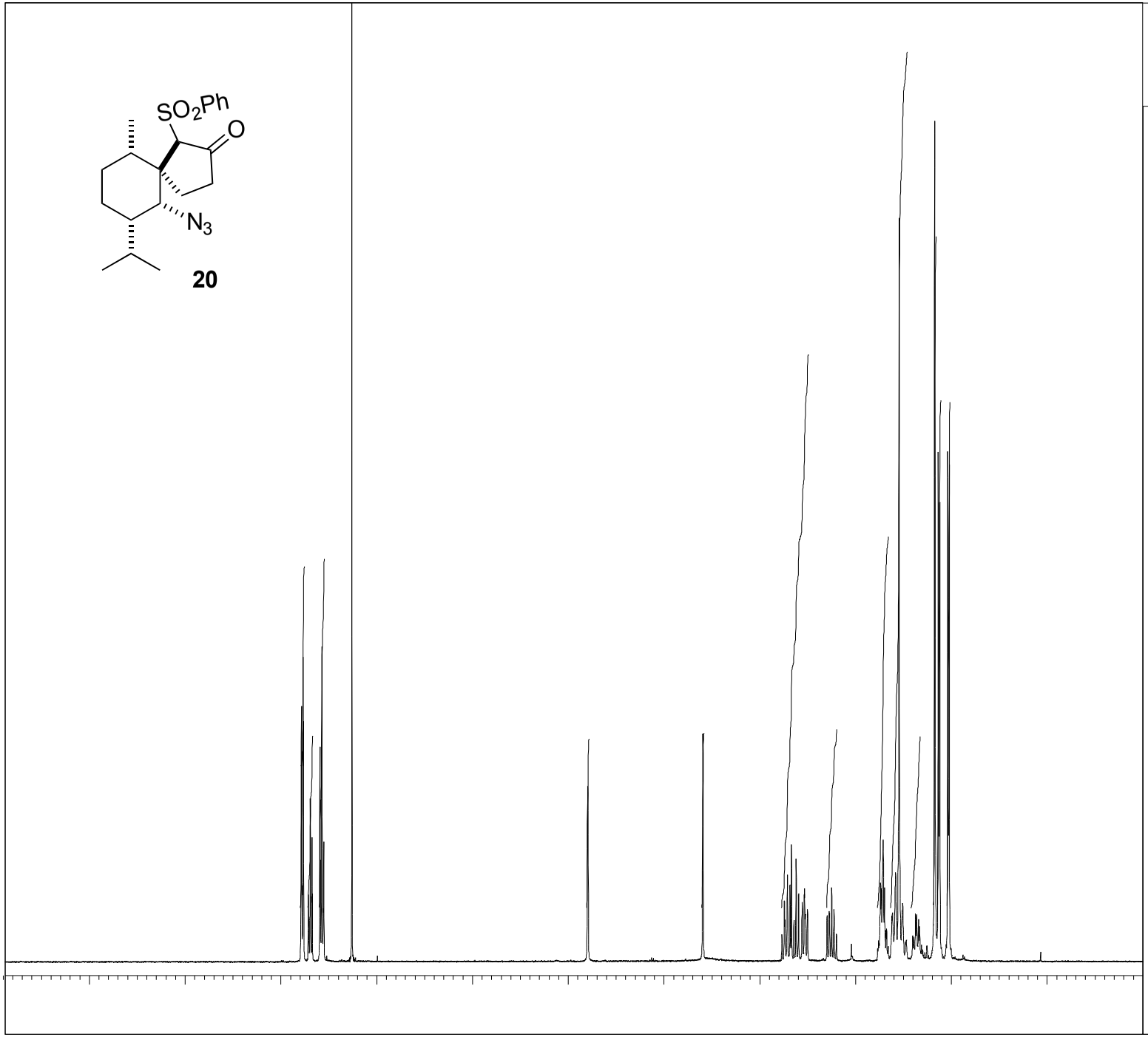
17

```
Filename          = 9KN_7_1H_CDCl3_400MHz_2019_0
Author            = delta
Experiment        = single_pulse.ex2
Sample_Id         = 1
Solvent           = CHLOROFORM-D
Creation_Time     = 16-MAY-2019 23:59:26
Revision_Time     =  5-NOV-2019 21:46:03
Current_Time      =  5-NOV-2019 21:47:04

Comment           = single_pulse
Data_Format       = 1D COMPLEX
Dim_Size          = 13107
Dim_Title         = 1H
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 2.20725248[s]
X_Domain          = 1H
X_Freq            = 395.88430144[MHz]
X_Offset          = 5[ppm]
X_Points          = 16384
X_Prescans        = 1
X_Resolution      = 0.45305193[Hz]
X_Sweep           = 7.42280285[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Tri_Domain        = 1H
Tri_Freq          = 395.88430144[MHz]
Tri_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 8
Total_Scans       = 8

Relaxation_Delay = 5[s]
Recvr_Gain        = 42
Temp_Get          = 22.6[dC]
X_90_Width        = 11.1[us]
X_Acq_Time        = 2.20725248[s]
X_Angle           = 45[deg]
X_Atn             = 2[dB]
X_Pulse           = 5.55[us]
Irr_Mode          = Off
Tri_Mode          = Off
Dante_Presat      = FALSE
Initial_Wait      = 1[s]
Repetition_Time   = 7.20725248[s]
```



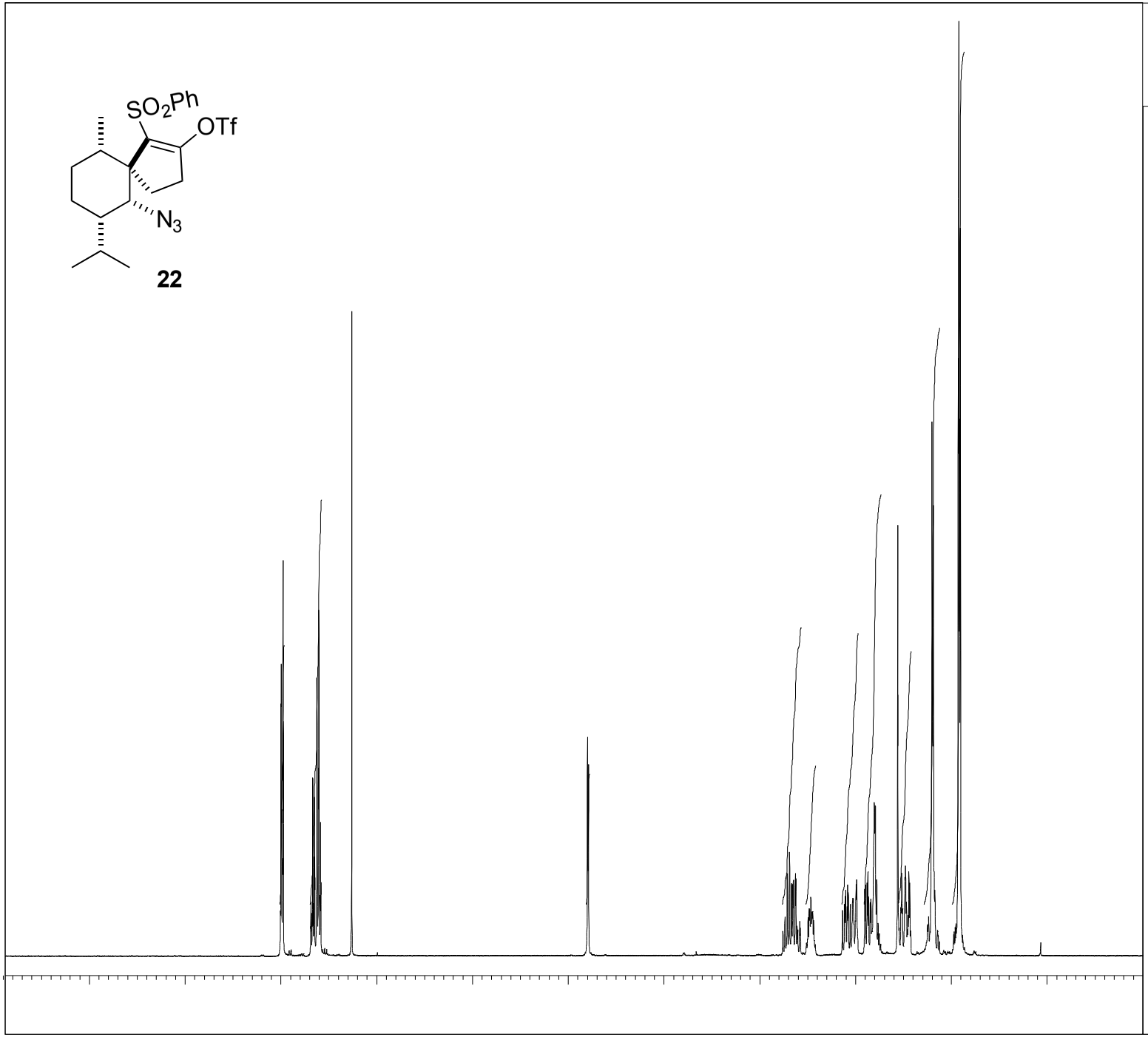
19

```
Filename          = 9KN_19_1H_CDCl3_400MHz_2019_
Author            = delta
Experiment        = single_pulse.ex2
Sample_Id         = 1
Solvent           = CHLOROFORM-D
Creation_Time     = 19-JUN-2019 14:31:41
Revision_Time     =  5-NOV-2019 21:55:14
Current_Time      =  5-NOV-2019 21:56:03

Comment           = single_pulse
Data_Format       = 1D COMPLEX
Dim_Size          = 13107
Dim_Title         = 1H
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 2.20725248[s]
X_Domain          = 1H
X_Freq            = 395.88430144[MHz]
X_Offset          = 5[ppm]
X_Points          = 16384
X_Prescans        = 1
X_Resolution      = 0.45305193[Hz]
X_Sweep           = 7.42280285[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Tri_Domain        = 1H
Tri_Freq          = 395.88430144[MHz]
Tri_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 8
Total_Scans       = 8

Relaxation_Delay = 5[s]
Recvr_Gain        = 36
Temp_Get          = 23[dC]
X_90_Width        = 13.25[us]
X_Acq_Time        = 2.20725248[s]
X_Angle           = 45[deg]
X_Atn             = 2.5[dB]
X_Pulse           = 6.625[us]
Irr_Mode          = Off
Tri_Mode          = Off
Dante_Presat      = FALSE
Initial_Wait      = 1[s]
Repetition_Time   = 7.20725248[s]
```

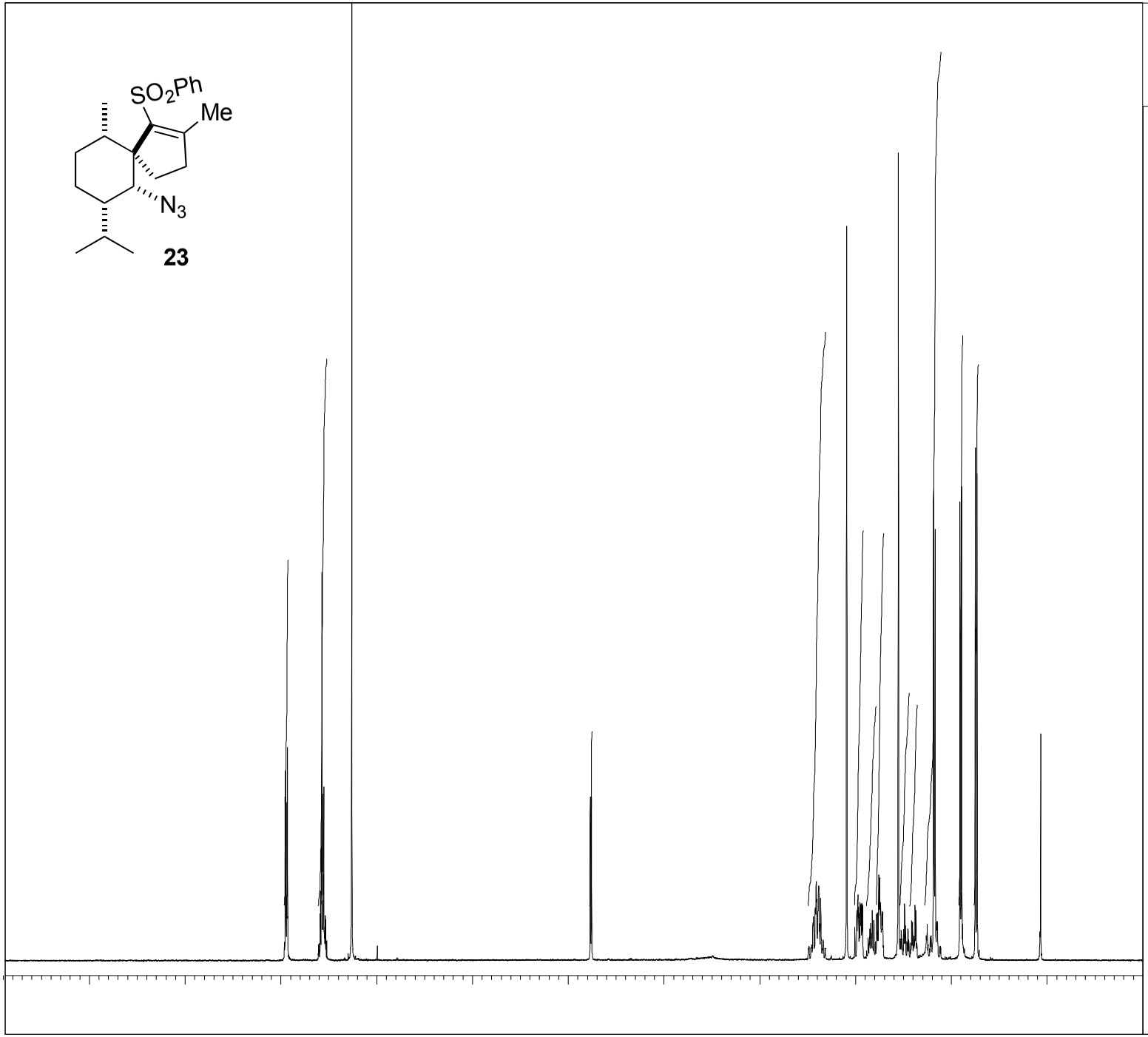


20

```
Filename          = 9KN_21_1H_CDCl3_400MHz_2019_
Author            = delta
Experiment        = single_pulse.ex2
Sample_Id         = 1
Solvent           = CHLOROFORM-D
Creation_Time     = 31-MAY-2019 11:44:50
Revision_Time     =  5-NOV-2019 21:42:22
Current_Time      =  5-NOV-2019 21:43:01

Comment           = single_pulse
Data_Format       = 1D COMPLEX
Dim_Size          = 13107
Dim_Title         = 1H
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 2.20725248[s]
X_Domain          = 1H
X_Freq            = 395.88430144[MHz]
X_Offset          = 5[ppm]
X_Points          = 16384
X_Prescans        = 1
X_Resolution      = 0.45305193[Hz]
X_Sweep           = 7.42280285[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Tri_Domain        = 1H
Tri_Freq          = 395.88430144[MHz]
Tri_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 8
Total_Scans       = 8

Relaxation_Delay = 5[s]
Recvr_Gain        = 48
Temp_Get          = 22.8[dC]
X_90_Width        = 11.1[us]
X_Acq_Time        = 2.20725248[s]
X_Angle           = 45[deg]
X_Atn             = 2[dB]
X_Pulse           = 5.55[us]
Irr_Mode          = Off
Tri_Mode          = Off
Dante_Presat      = FALSE
Initial_Wait      = 1[s]
Repetition_Time   = 7.20725248[s]
```

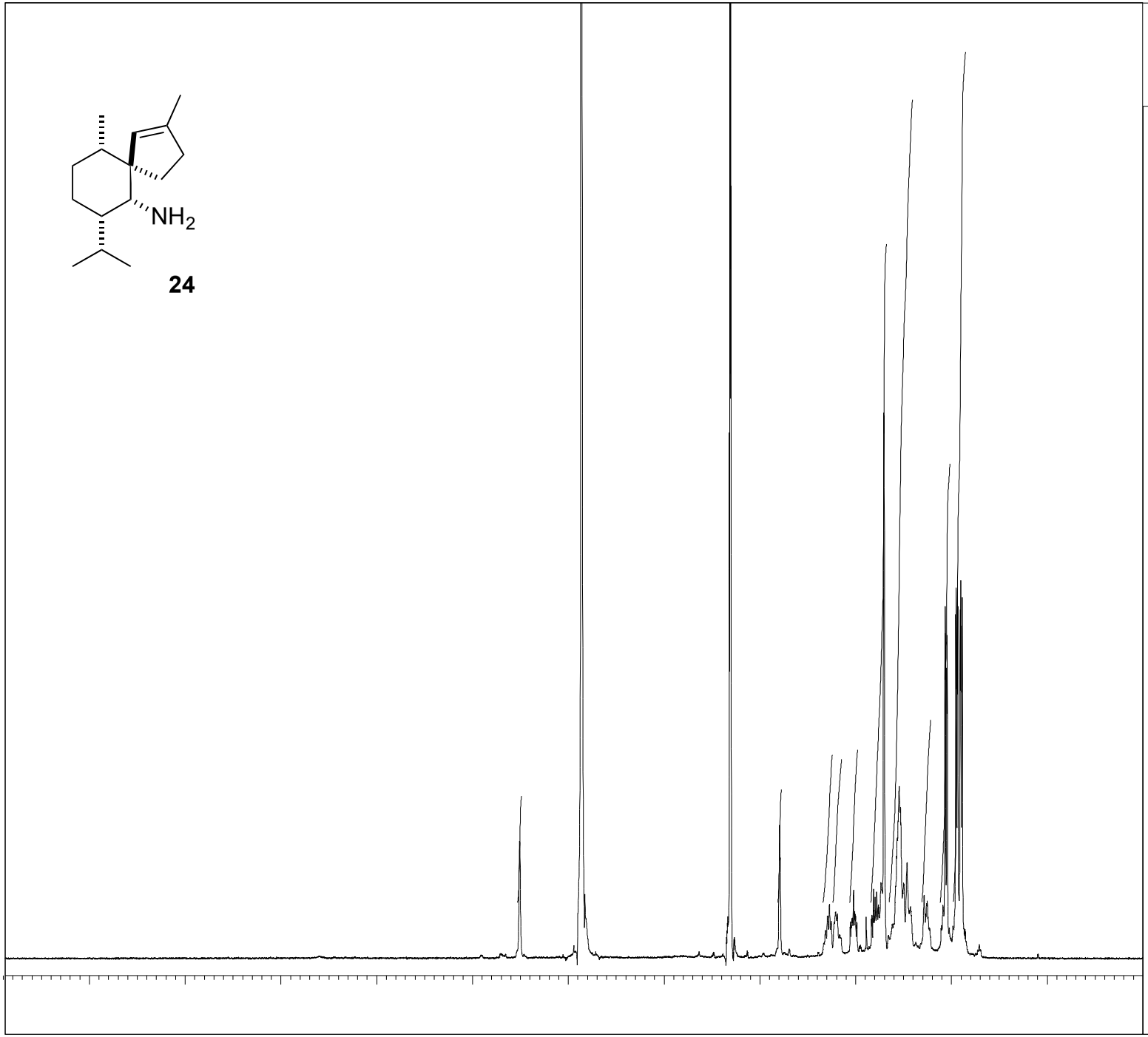



```
Filename          = 9KN_23_1H_CDCl3_400MHz_2019_
Author            = delta
Experiment        = single_pulse.ex2
Sample_Id         = 1
Solvent           = CHLOROFORM-D
Creation_Time     = 21-MAR-2019 09:46:37
Revision_Time     =  5-NOV-2019 21:19:29
Current_Time      =  5-NOV-2019 21:20:19

Comment           = single_pulse
Data_Format       = 1D COMPLEX
Dim_Size          = 13107
Dim_Title         = 1H
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 2.20725248[s]
X_Domain          = 1H
X_Freq            = 395.88430144[MHz]
X_Offset          = 5[ppm]
X_Points          = 16384
X_Prescans        = 1
X_Resolution      = 0.45305193[Hz]
X_Sweep           = 7.42280285[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Tri_Domain        = 1H
Tri_Freq          = 395.88430144[MHz]
Tri_Offset        = 5[ppm]
Clipped           = TRUE
Scans             = 8
Total_Scans       = 8

Relaxation_Delay = 5[s]
Recvr_Gain        = 50
Temp_Get          = 19.8[dC]
X_90_Width        = 11.1[us]
X_Acq_Time        = 2.20725248[s]
X_Angle           = 45[deg]
X_Atn             = 2[dB]
X_Pulse           = 5.55[us]
Irr_Mode          = Off
Tri_Mode          = Off
Dante_Presat      = FALSE
Initial_Wait      = 1[s]
Repetition_Time   = 7.20725248[s]
```



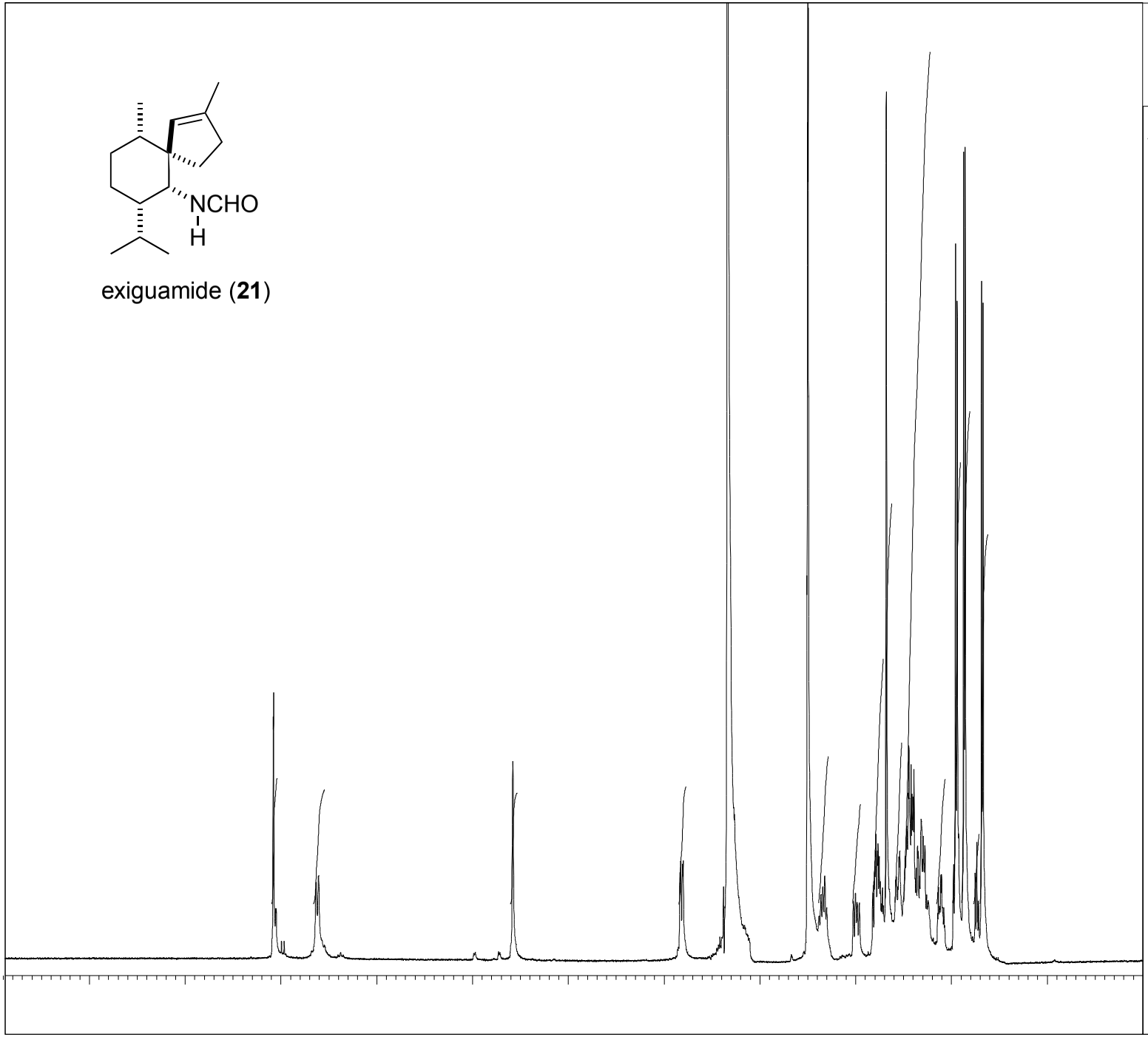
23

```
Filename          = 9KN_24_1H_CDCl3_400MHz_2018_
Author            = delta
Experiment        = single_pulse.ex2
Sample_Id         = 1
Solvent           = CHLOROFORM-D
Creation_Time     =  6-NOV-2018 07:40:54
Revision_Time     =  5-NOV-2019 21:21:29
Current_Time      =  5-NOV-2019 21:23:25

Comment           = single_pulse
Data_Format       = 1D COMPLEX
Dim_Size          = 13107
Dim_Title         = 1H
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 2.20725248[s]
X_Domain          = 1H
X_Freq            = 395.88430144[MHz]
X_Offset          = 5[ppm]
X_Points          = 16384
X_Prescans        = 1
X_Resolution      = 0.45305193[Hz]
X_Sweep           = 7.42280285[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Tri_Domain        = 1H
Tri_Freq          = 395.88430144[MHz]
Tri_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 8
Total_Scans       = 8

Relaxation_Delay = 5[s]
Recvr_Gain        = 48
Temp_Get          = 22[dC]
X_90_Width        = 11.1[us]
X_Acq_Time        = 2.20725248[s]
X_Angle           = 45[deg]
X_Atn             = 2[dB]
X_Pulse           = 5.55[us]
Irr_Mode          = Off
Tri_Mode          = Off
Dante_Presat      = FALSE
Initial_Wait      = 1[s]
Repetition_Time   = 7.20725248[s]
```



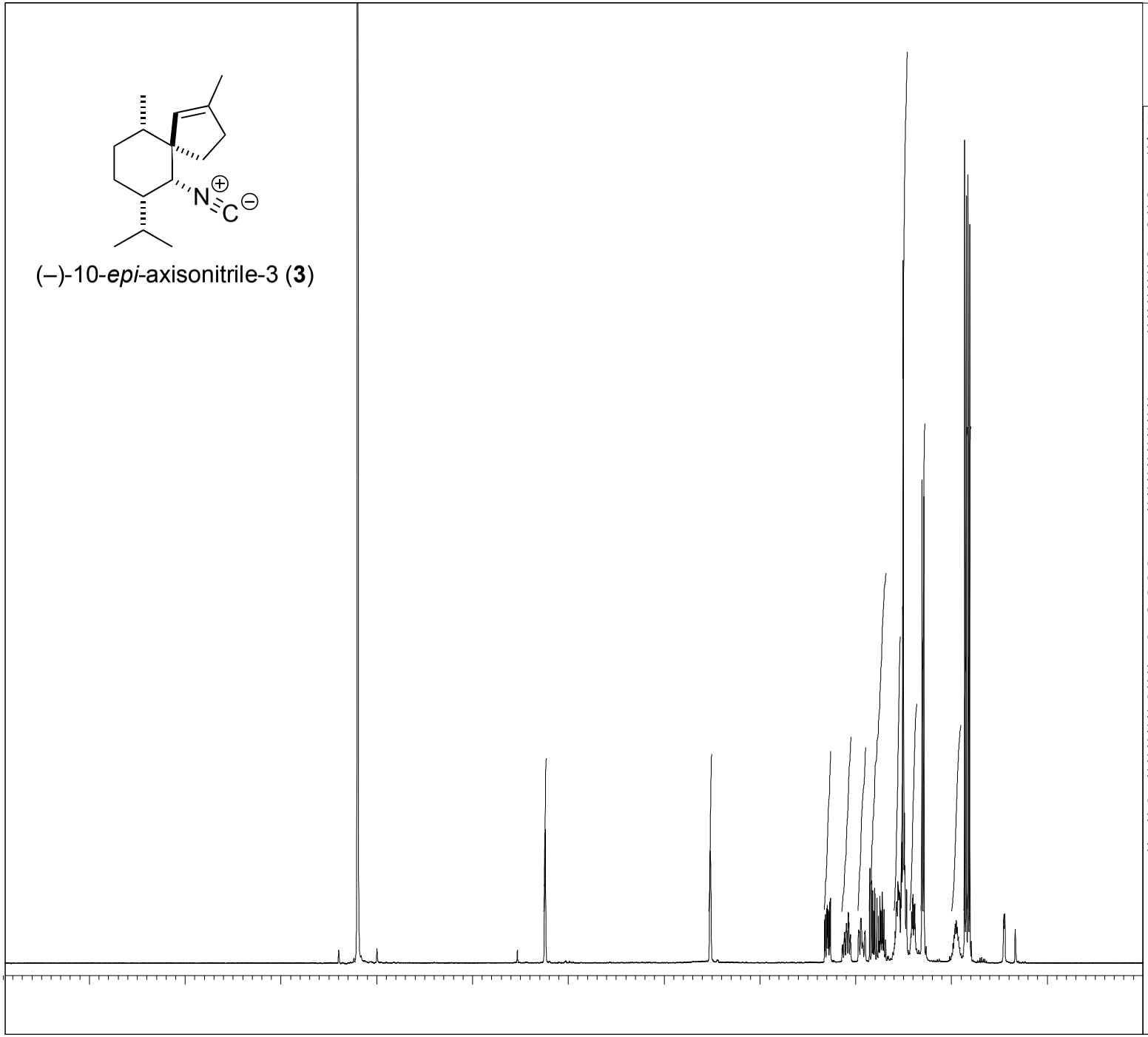
24

```
Filename          = 9KN_25_1H_CD3OD_400MHz_2019_
Author            = delta
Experiment        = single_pulse.ex2
Sample_Id         = 1
Solvent           = METHANOL-D3
Creation_Time     = 25-JUN-2019 19:20:46
Revision_Time     =  5-NOV-2019 21:24:15
Current_Time      =  5-NOV-2019 21:29:24

Comment           = single_pulse
Data_Format       = 1D COMPLEX
Dim_Size          = 13107
Dim_Title         = 1H
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 2.20725248[s]
X_Domain          = 1H
X_Freq            = 395.88430144[MHz]
X_Offset          = 5[ppm]
X_Points          = 16384
X_Prescans        = 1
X_Resolution      = 0.45305193[Hz]
X_Sweep           = 7.42280285[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Tri_Domain        = 1H
Tri_Freq          = 395.88430144[MHz]
Tri_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 8
Total_Scans       = 8

Relaxation_Delay = 5[s]
Recvr_Gain        = 36
Temp_Get          = 23.1[dC]
X_90_Width        = 13.25[us]
X_Acq_Time        = 2.20725248[s]
X_Angle           = 45[deg]
X_Atn             = 2.5[dB]
X_Pulse           = 6.625[us]
Irr_Mode          = Off
Tri_Mode          = Off
Dante_Presat      = FALSE
Initial_Wait      = 1[s]
Repetition_Time   = 7.20725248[s]
```



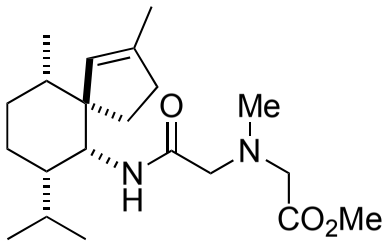
exiguamide (**21**)

```
Filename          = 9KN_exiguamide (22)_1H_DMSO-
Author            = delta
Experiment        = single_pulse.ex2
Sample_Id         = 1
Solvent           = DMSO-D6
Creation_Time     =  1-JUL-2019 14:43:08
Revision_Time     =  5-NOV-2019 21:32:55
Current_Time      =  5-NOV-2019 21:34:07

Comment           = single_pulse
Data_Format       = 1D COMPLEX
Dim_Size          = 13107
Dim_Title         = 1H
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 2.20725248[s]
X_Domain          = 1H
X_Freq            = 395.88430144[MHz]
X_Offset          = 5[ppm]
X_Points          = 16384
X_Prescans        = 1
X_Resolution      = 0.45305193[Hz]
X_Sweep           = 7.42280285[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Tri_Domain        = 1H
Tri_Freq          = 395.88430144[MHz]
Tri_Offset        = 5[ppm]
Clipped           = TRUE
Scans             = 8
Total_Scans       = 8

Relaxation_Delay = 5[s]
Recvr_Gain        = 50
Temp_Get          = 22.9[dC]
X_90_Width        = 13.25[us]
X_Acq_Time        = 2.20725248[s]
X_Angle           = 45[deg]
X_Atn             = 2.5[dB]
X_Pulse           = 6.625[us]
Irr_Mode          = Off
Tri_Mode          = Off
Dante_Presat      = FALSE
Initial_Wait      = 1[s]
Repetition_Time   = 7.20725248[s]
```



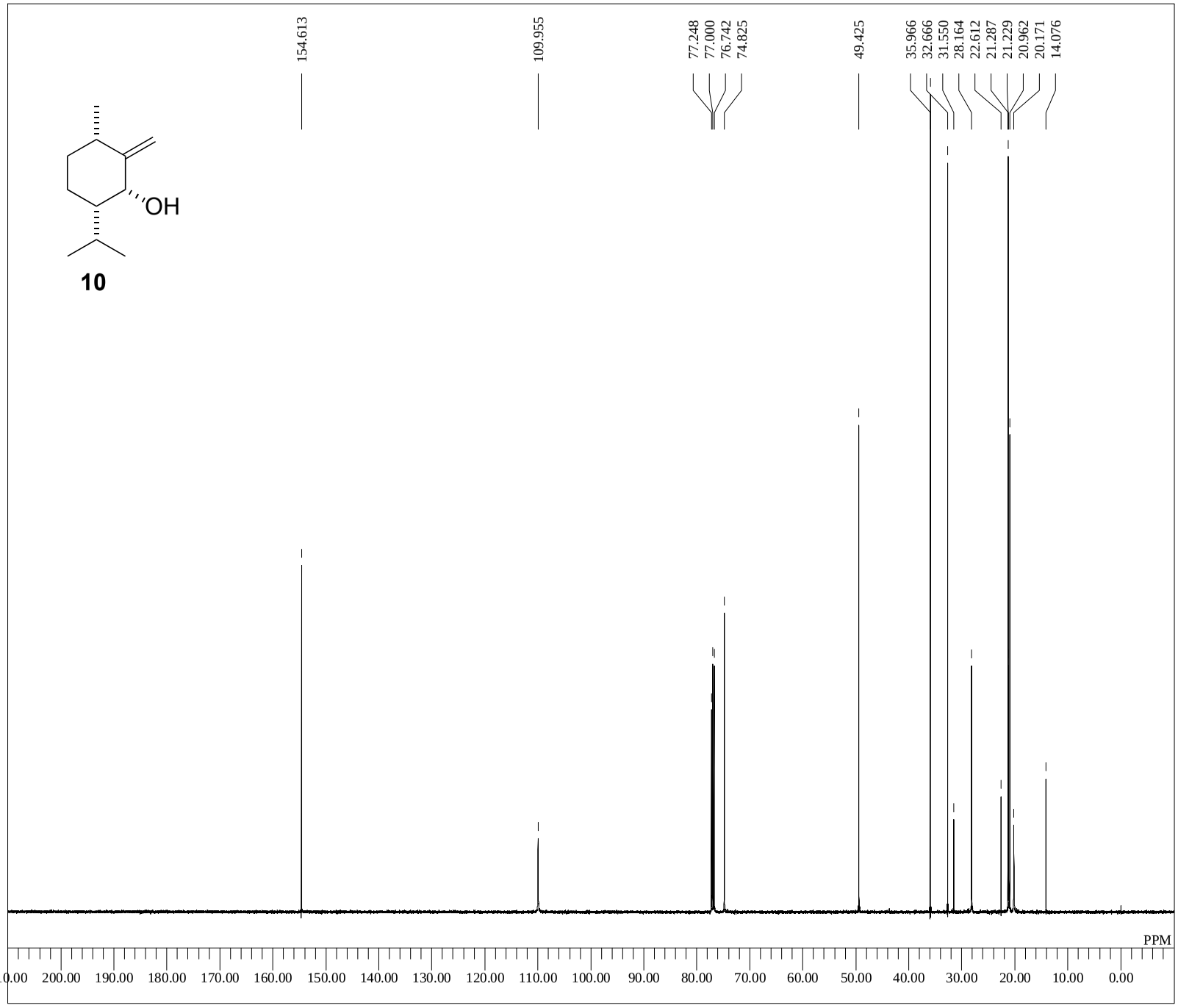
(–)-10-*epi*-axisonitrile-3 (**3**)

```
Filename          = 9KN_(—)-10-epi-axisonitrile
Author            = delta
Experiment        = single_pulse.ex2
Sample_Id         = 1
Solvent           = BENZENE-D6
Creation_Time     = 14-DEC-2018 09:32:17
Revision_Time     =  5-NOV-2019 21:36:07
Current_Time      =  5-NOV-2019 21:37:12

Comment           = single_pulse
Data_Format       = 1D COMPLEX
Dim_Size          = 13107
Dim_Title         = 1H
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 2.20725248[s]
X_Domain          = 1H
X_Freq            = 395.88430144[MHz]
X_Offset          = 5[ppm]
X_Points          = 16384
X_Prescans        = 1
X_Resolution      = 0.45305193[Hz]
X_Sweep           = 7.42280285[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Tri_Domain        = 1H
Tri_Freq          = 395.88430144[MHz]
Tri_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 8
Total_Scans       = 8

Relaxation_Delay = 5[s]
Recvr_Gain        = 42
Temp_Get          = 20.8[dC]
X_90_Width        = 11.1[us]
X_Acq_Time        = 2.20725248[s]
X_Angle           = 45[deg]
X_Atn             = 2[dB]
X_Pulse           = 5.55[us]
Irr_Mode          = Off
Tri_Mode          = Off
Dante_Presat      = FALSE
Initial_Wait      = 1[s]
Repetition_Time   = 7.20725248[s]
```

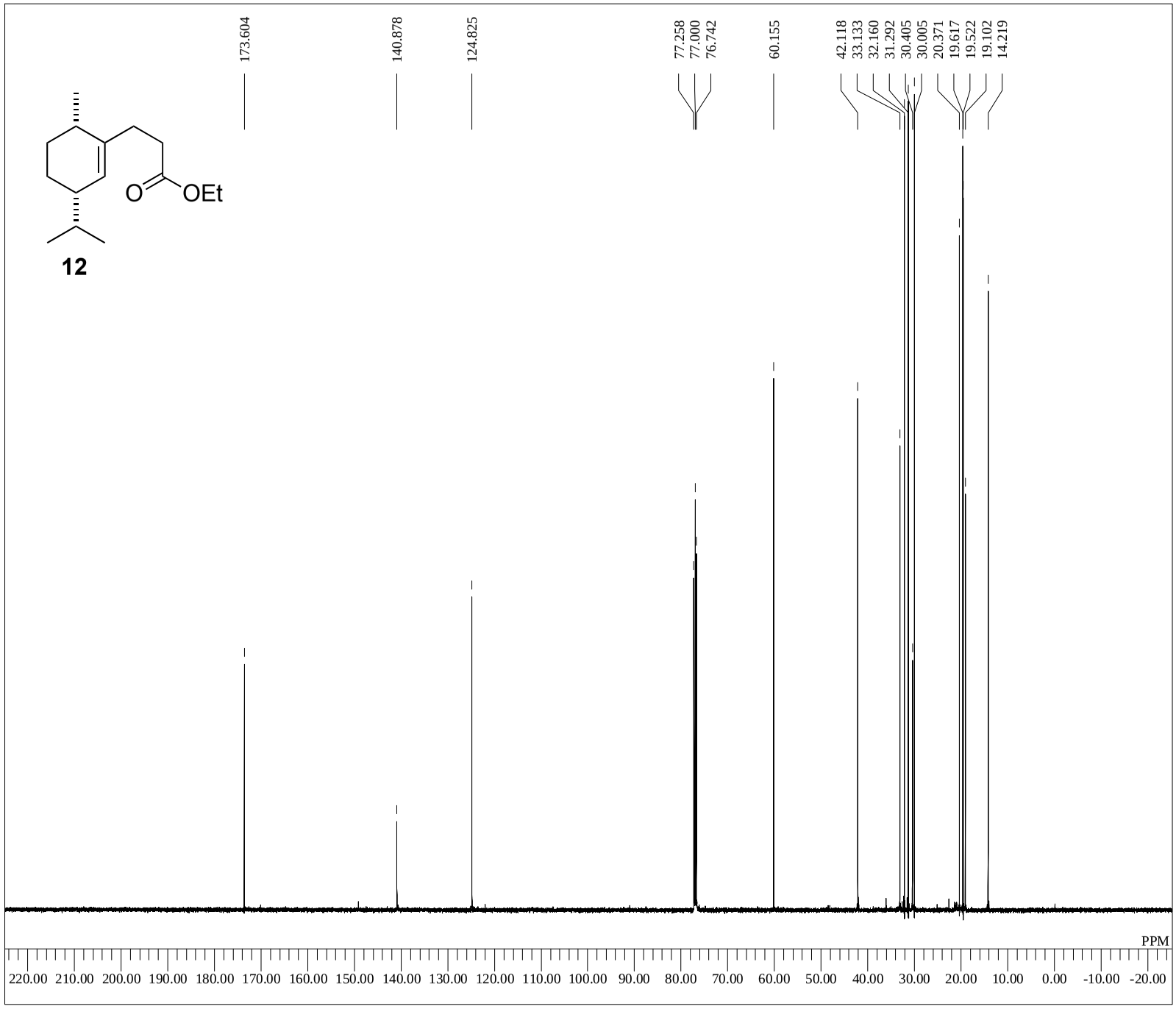


exigurin (**1**)

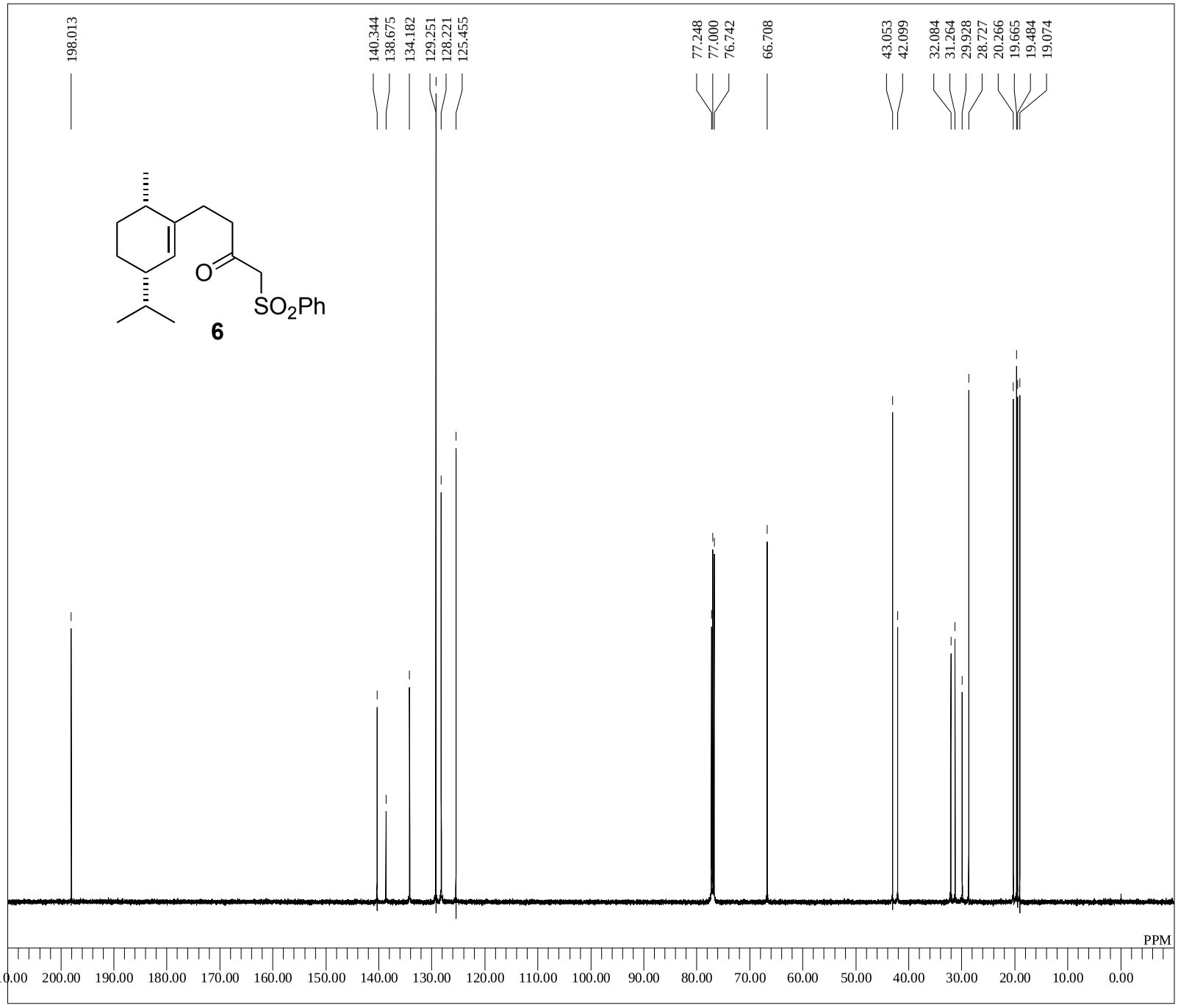

```
Filename          = 9KN_exigurin (1)_1H_C6D6_400
Author            = delta
Experiment        = single_pulse.ex2
Sample_Id         = 1
Solvent           = BENZENE-D6
Creation_Time     = 10-JUL-2019 17:53:28
Revision_Time     =  5-NOV-2019 21:38:43
Current_Time      =  5-NOV-2019 21:39:43

Comment           = single_pulse
Data_Format       = 1D COMPLEX
Dim_Size          = 13107
Dim_Title         = 1H
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 2.20725248[s]
X_Domain          = 1H
X_Freq            = 395.88430144[MHz]
X_Offset          = 5[ppm]
X_Points          = 16384
X_Prescans        = 1
X_Resolution      = 0.45305193[Hz]
X_Sweep           = 7.42280285[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Tri_Domain        = 1H
Tri_Freq          = 395.88430144[MHz]
Tri_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 24
Total_Scans       = 24

Relaxation_Delay = 5[s]
Recvr_Gain        = 36
Temp_Get          = 21.2[dC]
X_90_Width        = 13.25[us]
X_Acq_Time        = 2.20725248[s]
X_Angle           = 45[deg]
X_Atn             = 2.5[dB]
X_Pulse           = 6.625[us]
Irr_Mode          = Off
Tri_Mode          = Off
Dante_Presat      = FALSE
Initial_Wait      = 1[s]
Repetition_Time   = 7.20725248[s]
```



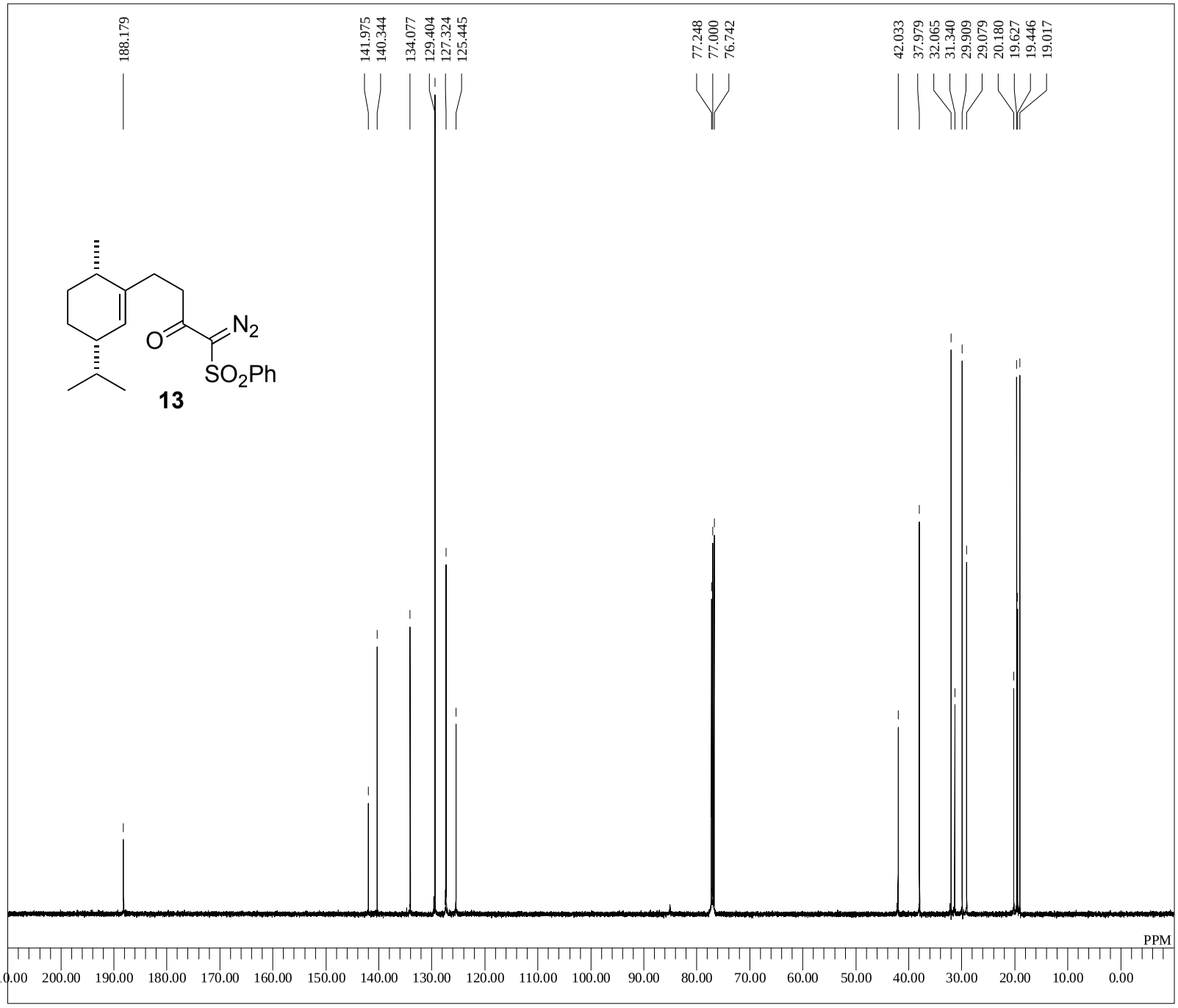
DFILE	ichikawa-1077_Carbon-1-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2017-01-25 16:24:31
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32767
FREQU	39308.18 Hz
SCANS	1024
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	20.5 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	58



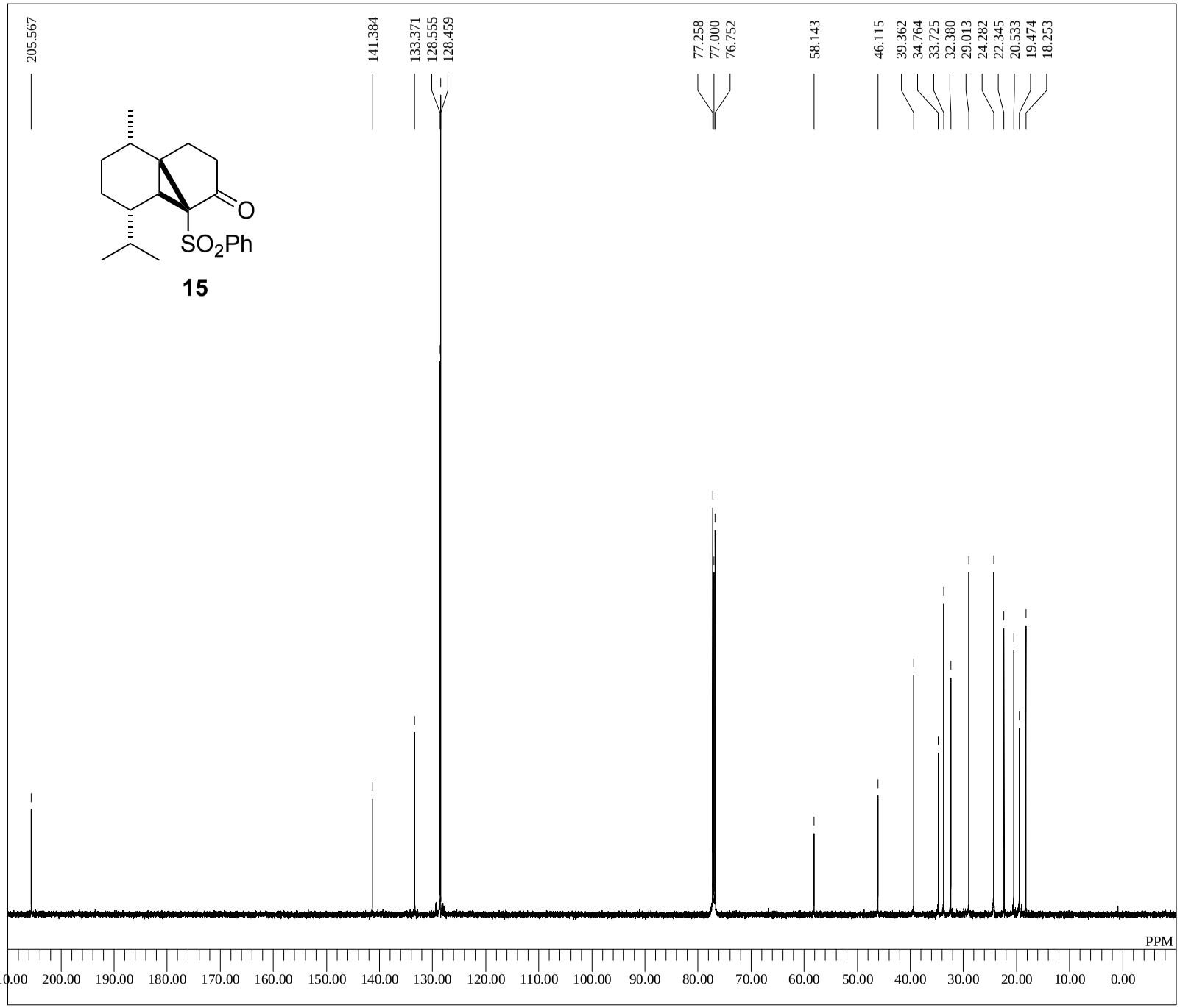
DFILE	MAE-2179-column_Carbon-1-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2017-02-28 15:25:05
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32767
FREQU	39308.18 Hz
SCANS	1024
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	18.4 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50



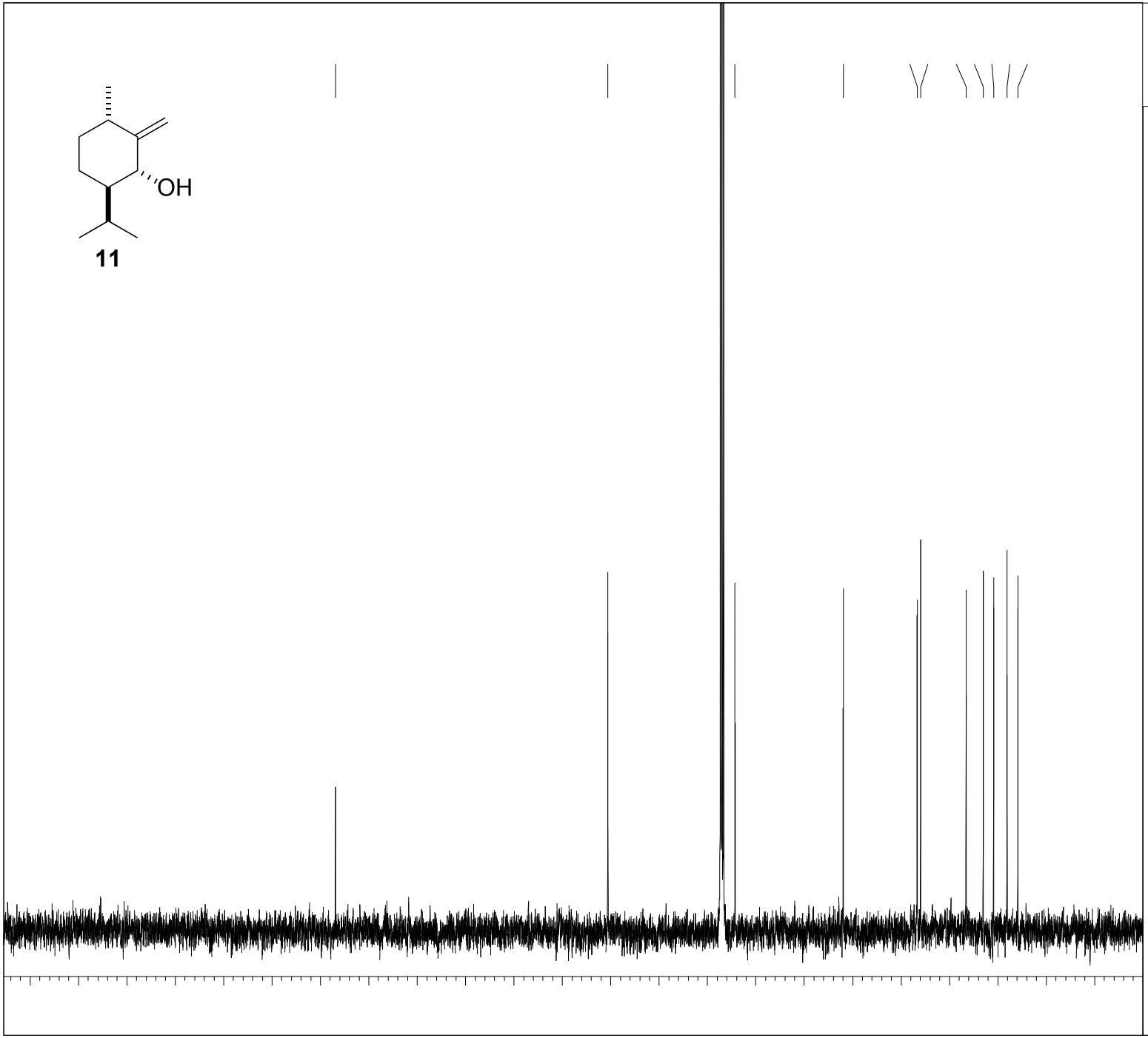
DFILE	MAE-2181-column-data2_Carbon-1-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2017-08-04 10:26:52
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32767
FREQU	39308.18 Hz
SCANS	1024
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	24.1 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	56



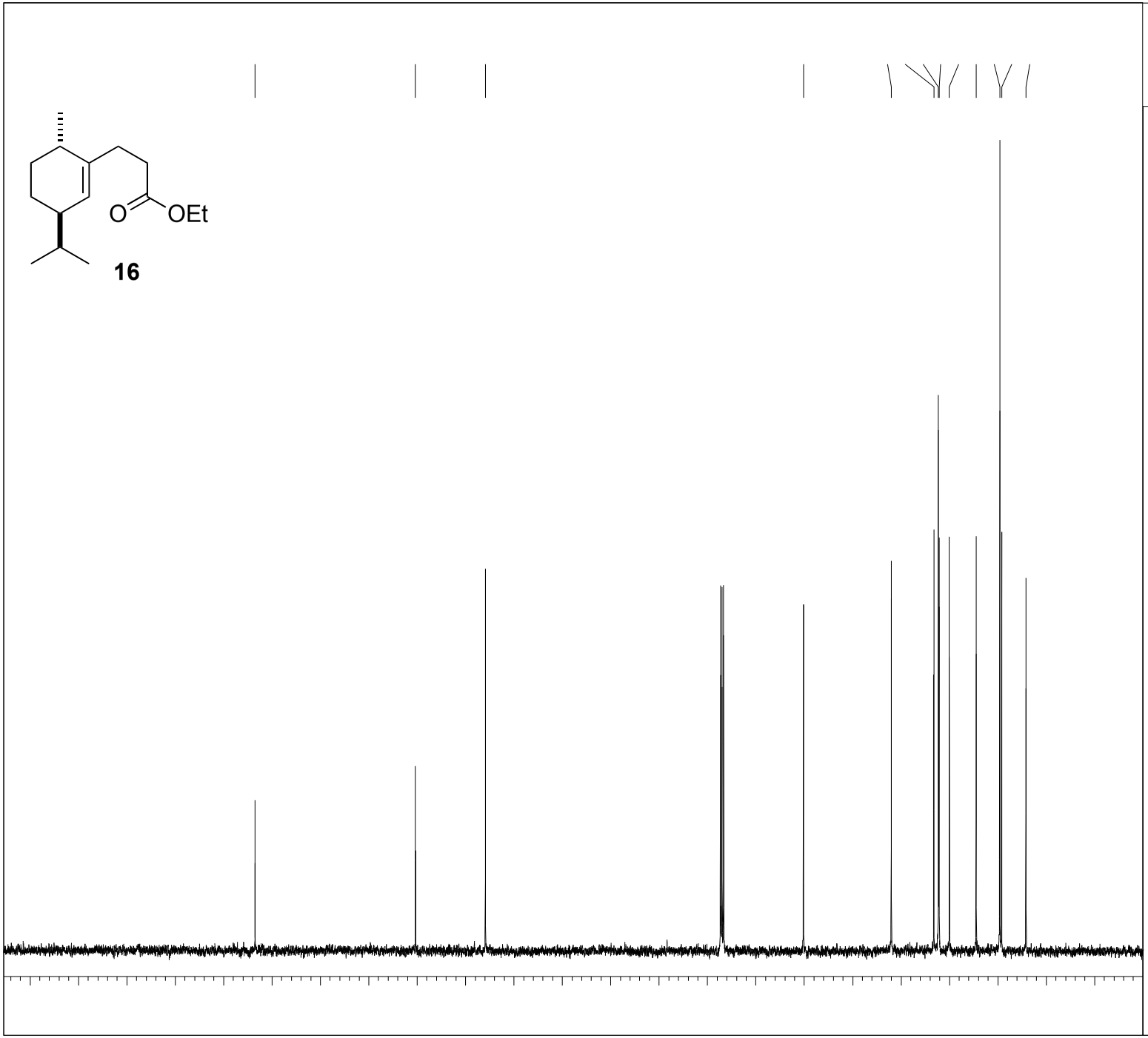
DFILE	MAE-2187-column_Carbon-1-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2017-08-23 15:52:53
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32767
FREQU	39308.18 Hz
SCANS	1024
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	24.1 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	56



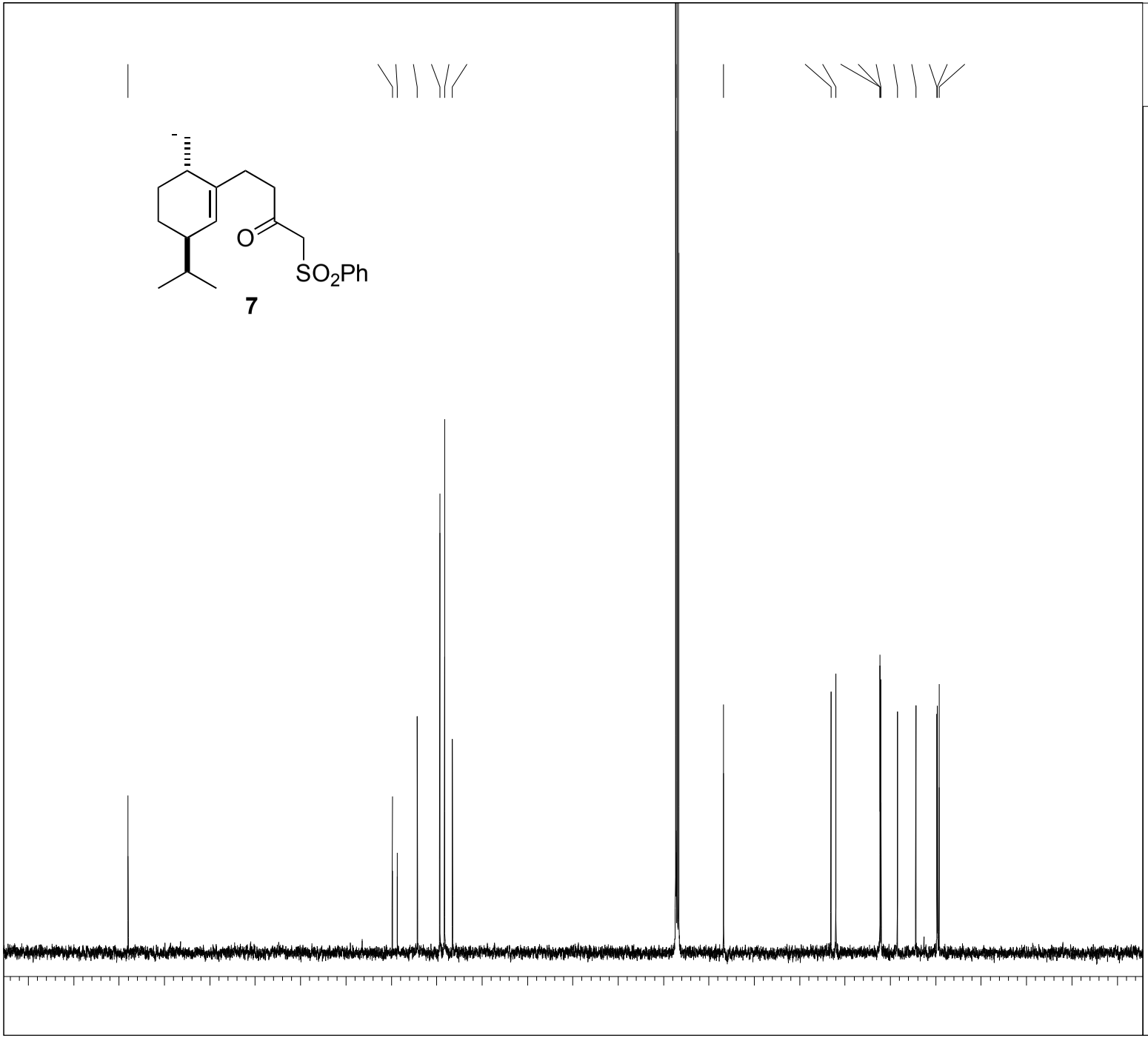
DFILE	MAE-2189-column_Carbon-1-1.jdf
COMNT	single pulse decoupled gated NOE
DATIM	2017-09-01 15:24:58
OBNUC	13C
EXMOD	carbon.jxp
OBFRQ	125.77 MHz
OBSET	7.87 KHz
OBFIN	4.21 Hz
POINT	32767
FREQU	39308.18 Hz
SCANS	1024
ACQTM	0.8336 sec
PD	2.0000 sec
PW1	2.72 usec
IRNUC	1H
CTEMP	23.1 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	54



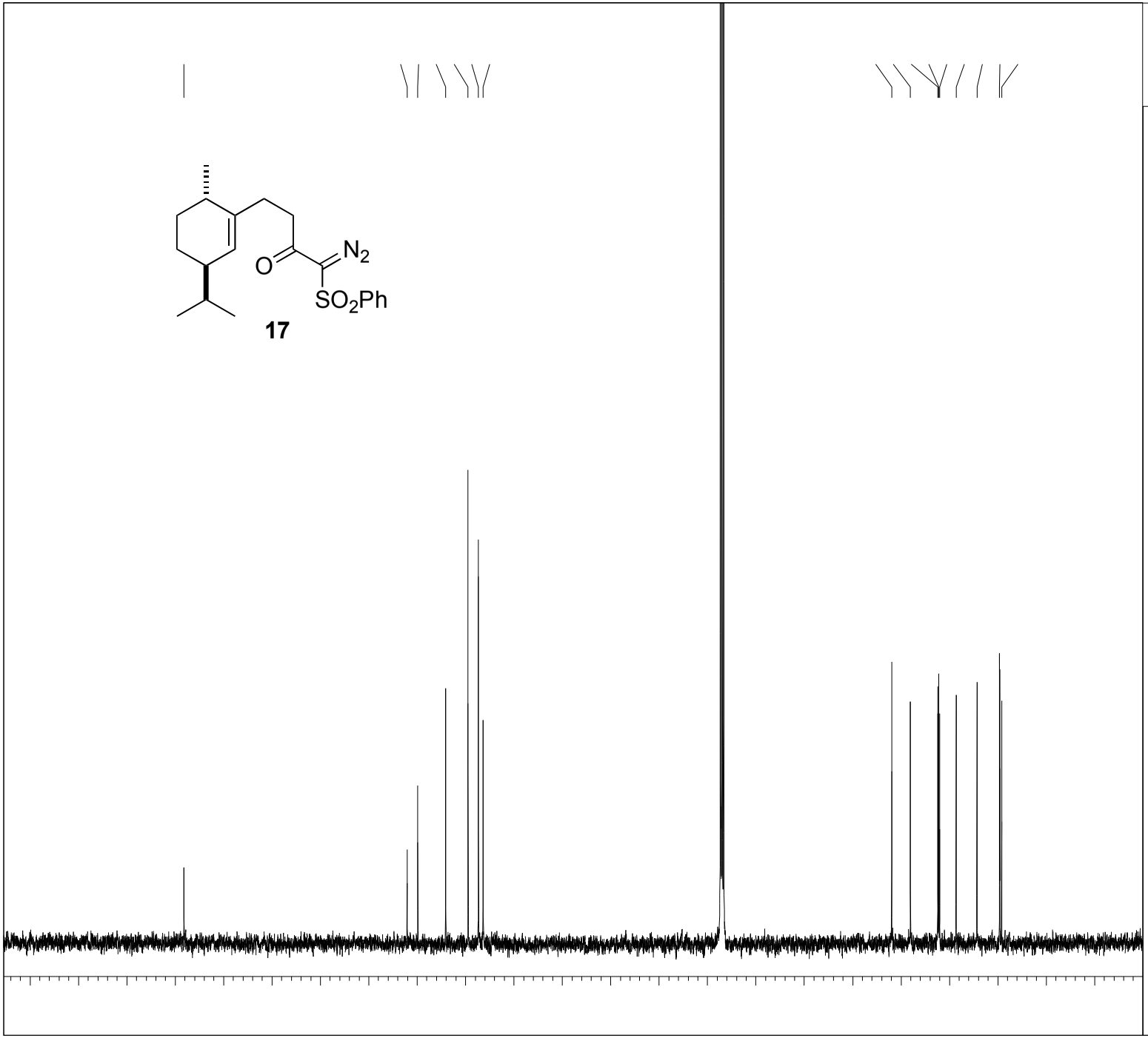

```
Filename          = 9KN_11_13C_CDCl3_400MHz_2019
Author            = delta
Experiment        = single_pulse_dec
Sample_Id         = 1
Solvent           = CHLOROFORM-D
Creation_Time     =  3-JUN-2019 13:20:22
Revision_Time     =  5-NOV-2019 22:24:18
Current_Time      =  5-NOV-2019 22:26:08

Comment           = single pulse decoupled gated
Data_Format       = 1D COMPLEX
Dim_Size          = 26214
Dim_Title         = 13C
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 1.048576[s]
X_Domain          = 13C
X_Freq            = 99.54517646[MHz]
X_Offset          = 100[ppm]
X_Points          = 32768
X_Prescans        = 4
X_Resolution      = 0.95367432[Hz]
X_Sweep           = 31.25[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 442
Total_Scans       = 442

Relaxation_Delay = 2[s]
Recvr_Gain        = 60
Temp_Get          = 23.4[dC]
X_90_Width        = 9.2[us]
X_Acq_Time        = 1.048576[s]
X_Angle           = 30[deg]
X_Atn             = 4.2[dB]
X_Pulse           = 3.06666667[us]
Irr_Atn_Dec       = 22.4[dB]
Irr_Atn_Noe       = 22.4[dB]
Irr_Noise         = WALTZ
Decoupling        = TRUE
Initial_Wait      = 1[s]
Noe               = TRUE
Noe_Time          = 2[s]
Repetition_Time   = 3.048576[s]
```




```
Filename          = 9KN_16_13C_CDCl3_100MHz_201
Author            = delta
Experiment        = single_pulse_dec
Sample_Id         = 1
Solvent           = CHLOROFORM-D
Creation_Time     = 24-JUL-2019 15:38:04
Revision_Time     =  5-NOV-2019 22:26:50
Current_Time      =  5-NOV-2019 22:28:16

Comment           = single pulse decoupled gated
Data_Format       = 1D COMPLEX
Dim_Size          = 26214
Dim_Title         = 13C
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 1.048576[s]
X_Domain          = 13C
X_Freq            = 99.54517646[MHz]
X_Offset          = 100[ppm]
X_Points          = 32768
X_Prescans        = 4
X_Resolution      = 0.95367432[Hz]
X_Sweep           = 31.25[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 131
Total_Scans       = 131

Relaxation_Delay = 2[s]
Recvr_Gain        = 50
Temp_Get          = 23.1[dC]
X_90_Width        = 11[us]
X_Acq_Time        = 1.048576[s]
X_Angle           = 30[deg]
X_Atn             = 4.5[dB]
X_Pulse           = 3.66666667[us]
Irr_Atn_Dec       = 20.873[dB]
Irr_Atn_Noe       = 20.873[dB]
Irr_Noise         = WALTZ
Decoupling        = TRUE
Initial_Wait      = 1[s]
Noe               = TRUE
Noe_Time          = 2[s]
Repetition_Time   = 3.048576[s]
```




```
Filename          = 9KN_17_13C_CDCl3_400MHz_201
Author            = delta
Experiment        = single_pulse_dec
Sample_Id         = 1
Solvent           = CHLOROFORM-D
Creation_Time     = 14-MAY-2019 11:58:31
Revision_Time     =  5-NOV-2019 22:29:36
Current_Time      =  5-NOV-2019 22:30:49

Comment           = single pulse decoupled gated
Data_Format       = 1D COMPLEX
Dim_Size          = 26214
Dim_Title         = 13C
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 1.048576[s]
X_Domain          = 13C
X_Freq            = 99.54517646[MHz]
X_Offset          = 100[ppm]
X_Points          = 32768
X_Prescans        = 4
X_Resolution      = 0.95367432[Hz]
X_Sweep           = 31.25[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 500
Total_Scans       = 500

Relaxation_Delay  = 2[s]
Recvr_Gain        = 60
Temp_Get          = 22.4[dC]
X_90_Width        = 9.2[us]
X_Acq_Time        = 1.048576[s]
X_Angle           = 30[deg]
X_Atn             = 4.2[dB]
X_Pulse           = 3.06666667[us]
Irr_Atn_Dec       = 22.4[dB]
Irr_Atn_Noe       = 22.4[dB]
Irr_Noise         = WALTZ
Decoupling        = TRUE
Initial_Wait      = 1[s]
Noe               = TRUE
Noe_Time          = 2[s]
Repetition_Time   = 3.048576[s]
```



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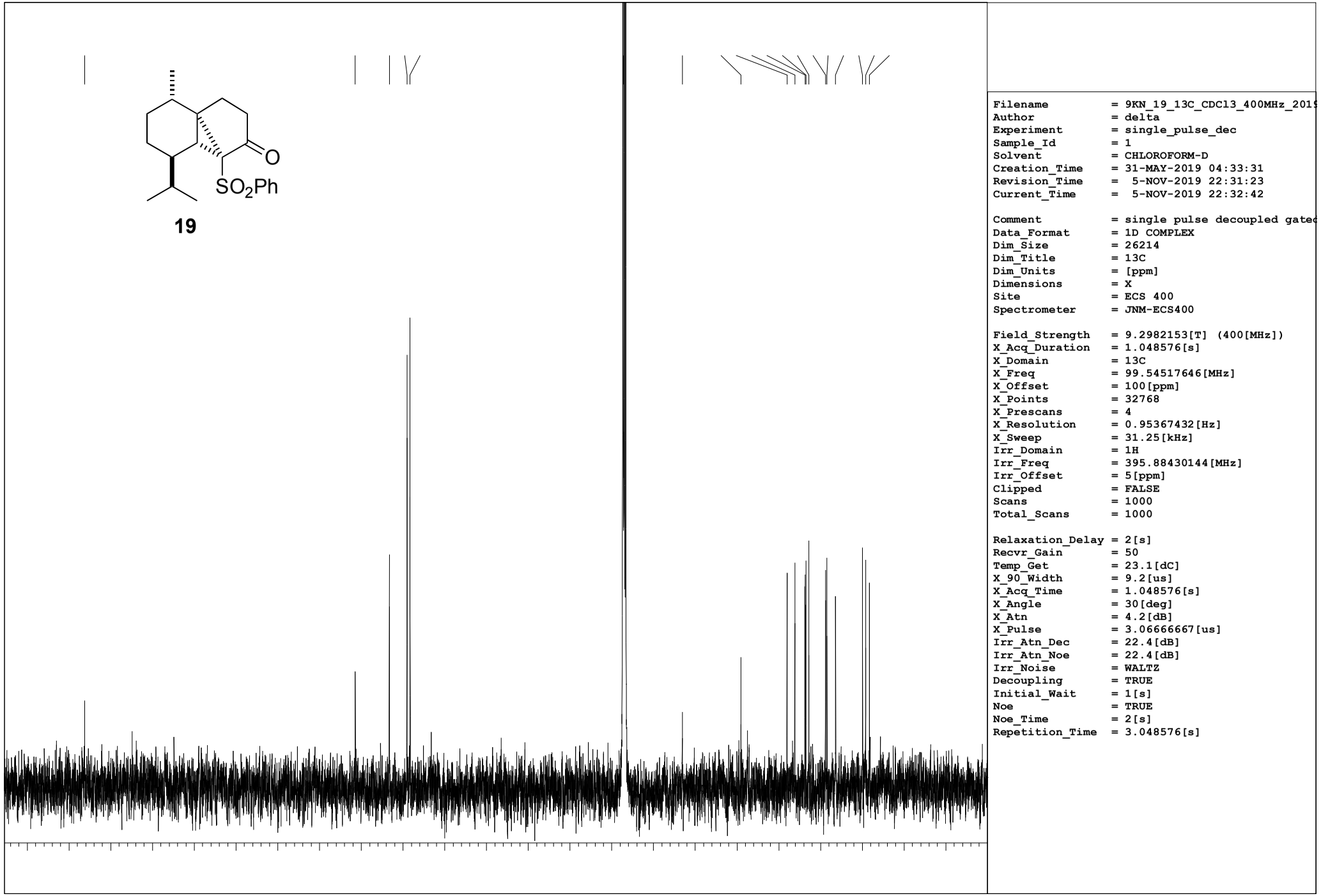
```
Filename          = 9KN_7_13C_CDCl3_400MHz_2019_
Author            = delta
Experiment        = single_pulse_dec
Sample_Id         = 1
Solvent           = CHLOROFORM-D
Creation_Time     = 17-MAY-2019 02:24:23
Revision_Time     =  5-NOV-2019 22:21:05
Current_Time      =  5-NOV-2019 22:23:18

Comment           = single pulse decoupled gated
Data_Format       = 1D COMPLEX
Dim_Size          = 26214
Dim_Title         = 13C
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 1.048576[s]
X_Domain          = 13C
X_Freq            = 99.54517646[MHz]
X_Offset          = 100[ppm]
X_Points          = 32768
X_Prescans        = 4
X_Resolution      = 0.95367432[Hz]
X_Sweep           = 31.25[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 1500
Total_Scans       = 1500

Relaxation_Delay = 2[s]
Recvr_Gain        = 60
Temp_Get          = 22.9[dC]
X_90_Width        = 9.2[us]
X_Acq_Time        = 1.048576[s]
X_Angle           = 30[deg]
X_Atn             = 4.2[dB]
X_Pulse           = 3.06666667[us]
Irr_Atn_Dec       = 22.4[dB]
Irr_Atn_Noe       = 22.4[dB]
Irr_Noise         = WALTZ
Decoupling        = TRUE
Initial_Wait      = 1[s]
Noe               = TRUE
Noe_Time          = 2[s]
Repetition_Time   = 3.048576[s]
```

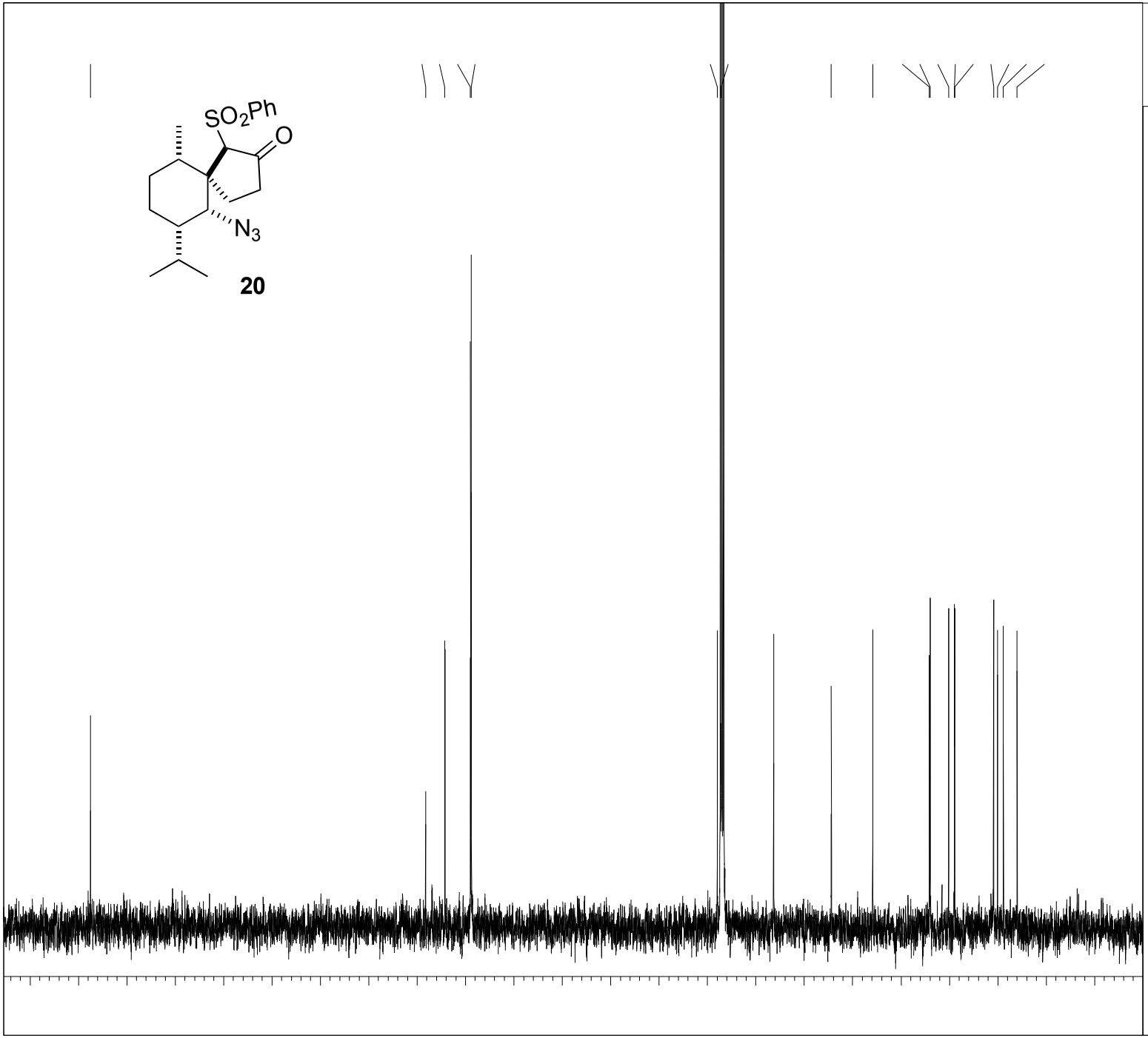



```
Filename          = 9KN_19_13C_CDCl3_400MHz_2019
Author            = delta
Experiment        = single_pulse_dec
Sample_Id         = 1
Solvent           = CHLOROFORM-D
Creation_Time     = 31-MAY-2019 04:33:31
Revision_Time     =  5-NOV-2019 22:31:23
Current_Time      =  5-NOV-2019 22:32:42

Comment           = single pulse decoupled gated
Data_Format       = 1D COMPLEX
Dim_Size          = 26214
Dim_Title         = 13C
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 1.048576[s]
X_Domain          = 13C
X_Freq            = 99.54517646[MHz]
X_Offset          = 100[ppm]
X_Points          = 32768
X_Prescans        = 4
X_Resolution      = 0.95367432[Hz]
X_Sweep           = 31.25[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 1000
Total_Scans       = 1000

Relaxation_Delay = 2[s]
Recvr_Gain        = 50
Temp_Get          = 23.1[dC]
X_90_Width        = 9.2[us]
X_Acq_Time        = 1.048576[s]
X_Angle           = 30[deg]
X_Atn             = 4.2[dB]
X_Pulse           = 3.06666667[us]
Irr_Atn_Dec       = 22.4[dB]
Irr_Atn_Noe       = 22.4[dB]
Irr_Noise         = WALTZ
Decoupling        = TRUE
Initial_Wait      = 1[s]
Noe               = TRUE
Noe_Time          = 2[s]
Repetition_Time   = 3.048576[s]
```



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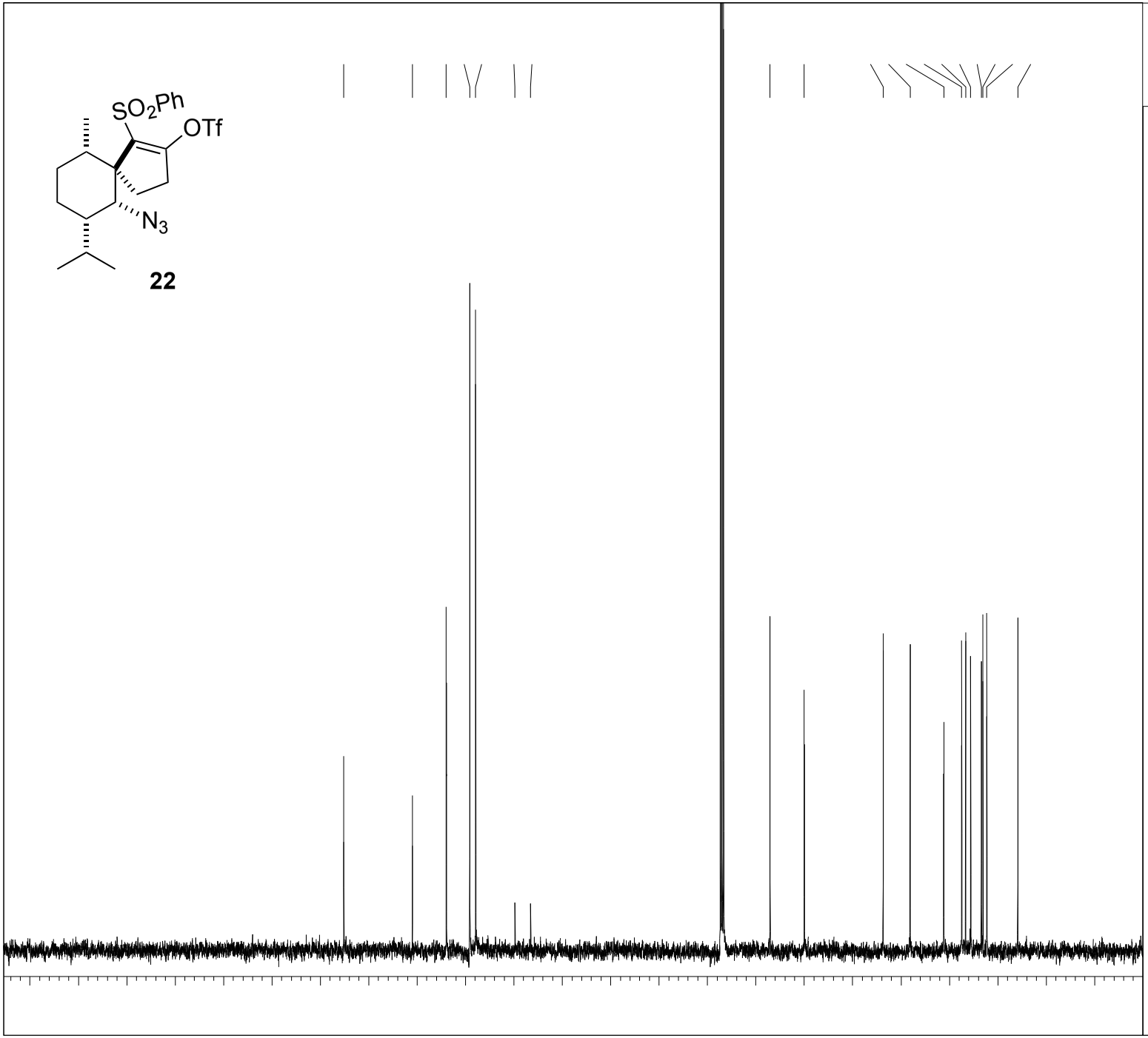
```
Filename          = 9KN_21_13C_CDCl3_400MHz_2018
Author            = delta
Experiment        = single_pulse_dec
Sample_Id         = 1
Solvent           = CHLOROFORM-D
Creation_Time     = 12-MAR-2019 03:43:32
Revision_Time     =  5-NOV-2019 21:58:29
Current_Time      =  5-NOV-2019 22:00:52

Comment           = single pulse decoupled gated
Data_Format       = 1D COMPLEX
Dim_Size          = 26214
Dim_Title         = 13C
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 1.048576[s]
X_Domain          = 13C
X_Freq            = 99.54517646[MHz]
X_Offset          = 100[ppm]
X_Points          = 32768
X_Prescans        = 4
X_Resolution      = 0.95367432[Hz]
X_Sweep           = 31.25[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 500
Total_Scans       = 500

Relaxation_Delay  = 2[s]
Recvr_Gain        = 50
Temp_Get          = 19.7[dC]
X_90_Width        = 9.2[us]
X_Acq_Time        = 1.048576[s]
X_Angle           = 30[deg]
X_Atn             = 4.2[dB]
X_Pulse           = 3.06666667[us]
Irr_Atn_Dec       = 22.4[dB]
Irr_Atn_Noe       = 22.4[dB]
Irr_Noise         = WALTZ
Decoupling        = TRUE
Initial_Wait      = 1[s]
Noe               = TRUE
Noe_Time          = 2[s]
Repetition_Time   = 3.048576[s]
```

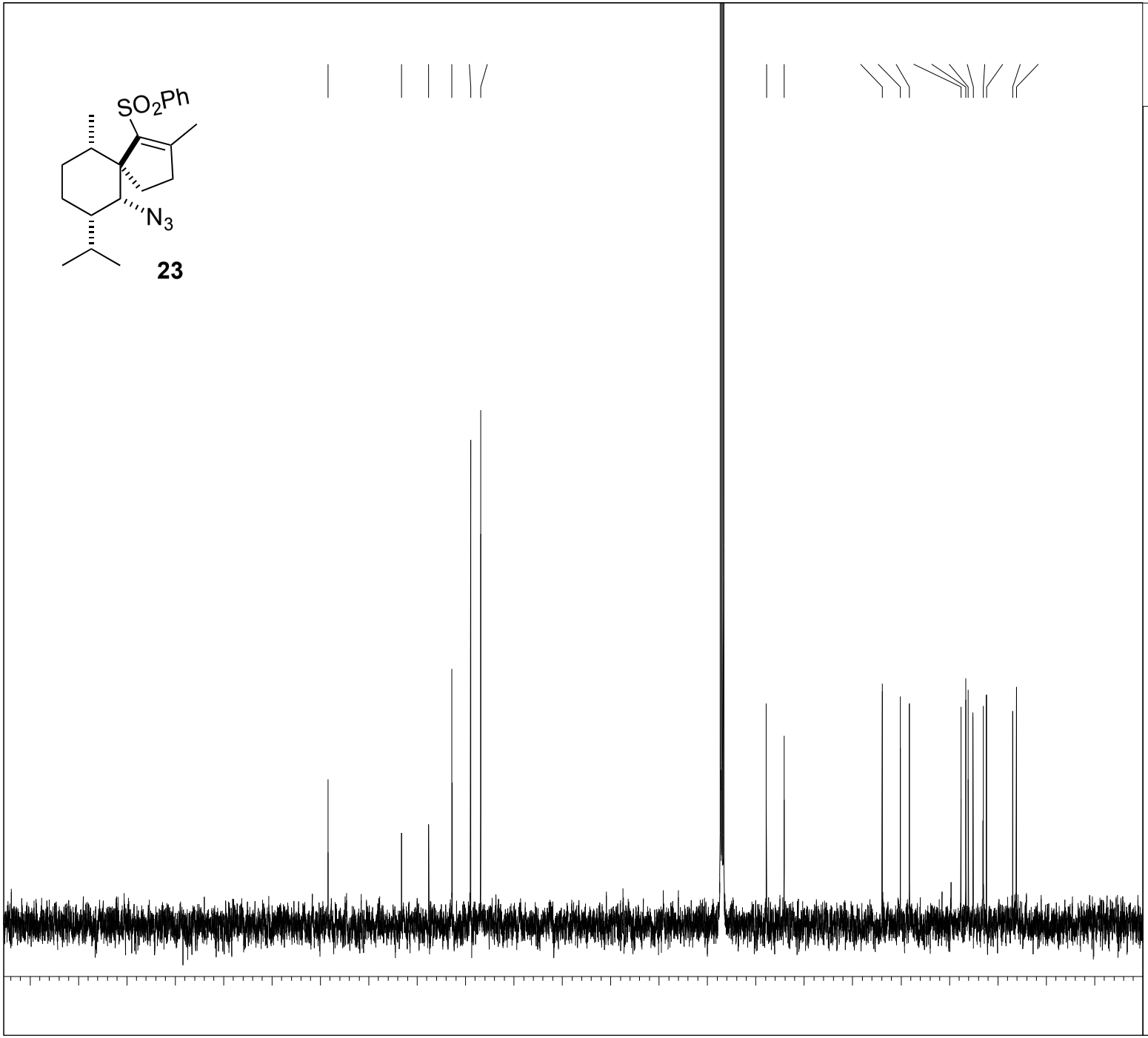



```
Filename          = 9KN_23_13C_CDCl3_400MHz_2018
Author            = delta
Experiment        = single_pulse_dec
Sample_Id         = 1
Solvent           = CHLOROFORM-D
Creation_Time     = 10-JAN-2019 10:15:01
Revision_Time     =  5-NOV-2019 22:01:27
Current_Time      =  5-NOV-2019 22:02:28

Comment           = single pulse decoupled gated
Data_Format       = 1D COMPLEX
Dim_Size          = 26214
Dim_Title         = 13C
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 1.048576[s]
X_Domain          = 13C
X_Freq            = 99.54517646[MHz]
X_Offset          = 100[ppm]
X_Points          = 32768
X_Prescans        = 4
X_Resolution      = 0.95367432[Hz]
X_Sweep           = 31.25[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 239
Total_Scans       = 239

Relaxation_Delay = 2[s]
Recvr_Gain        = 60
Temp_Get          = 19.8[dC]
X_90_Width        = 9.2[us]
X_Acq_Time        = 1.048576[s]
X_Angle           = 30[deg]
X_Atn             = 4.2[dB]
X_Pulse           = 3.06666667[us]
Irr_Atn_Dec       = 22.4[dB]
Irr_Atn_Noe       = 22.4[dB]
Irr_Noise         = WALTZ
Decoupling        = TRUE
Initial_Wait      = 1[s]
Noe               = TRUE
Noe_Time          = 2[s]
Repetition_Time   = 3.048576[s]
```

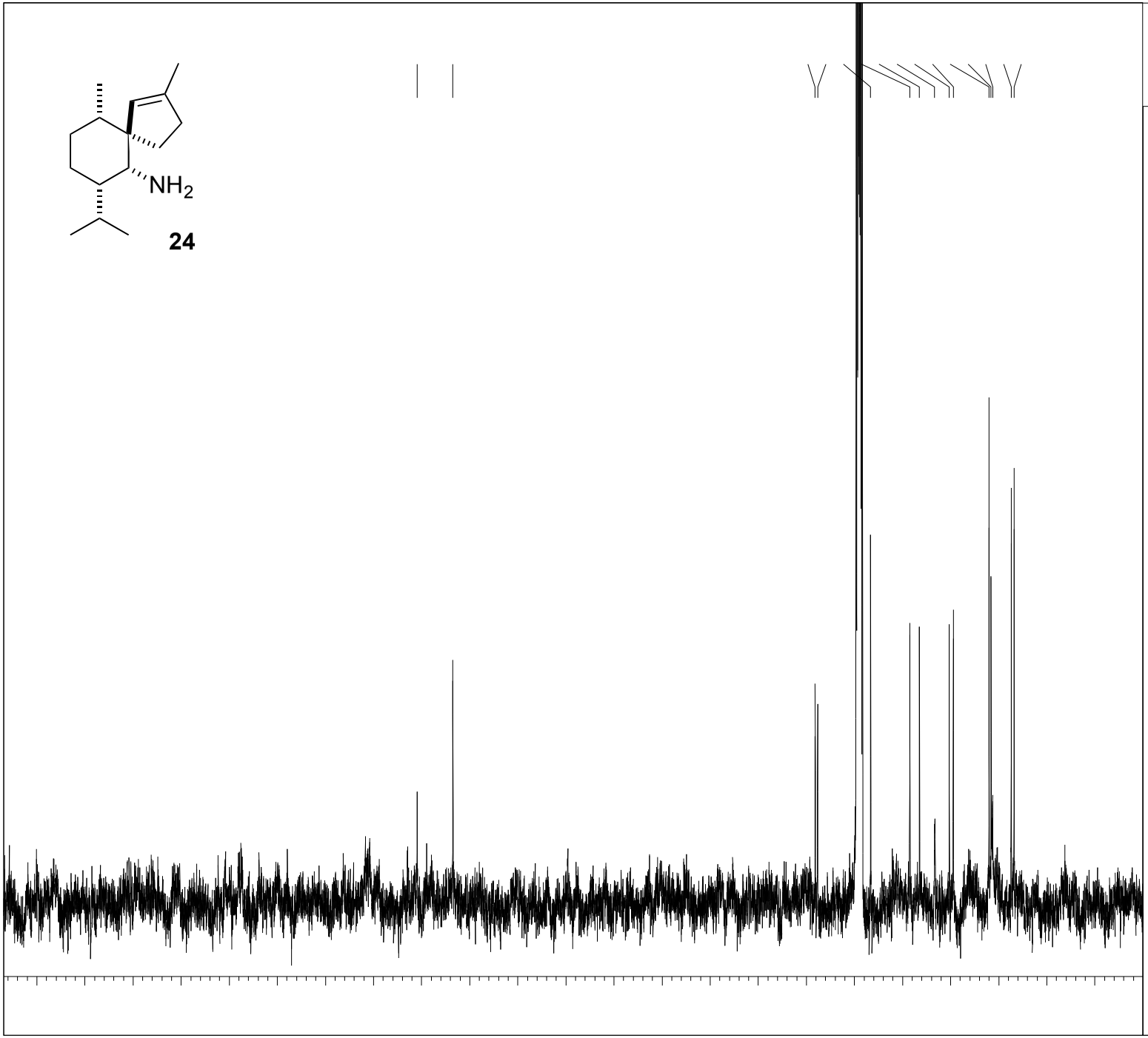



```
Filename          = 9KN_24_13C_CDCl3_400MHz_2018
Author            = delta
Experiment        = single_pulse_dec
Sample_Id         = 1
Solvent           = CHLOROFORM-D
Creation_Time     =  5-JAN-2019 13:30:18
Revision_Time     =  5-NOV-2019 22:07:36
Current_Time      =  5-NOV-2019 22:08:25

Comment           = single pulse decoupled gated
Data_Format       = 1D COMPLEX
Dim_Size          = 26214
Dim_Title         = 13C
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 1.048576[s]
X_Domain          = 13C
X_Freq            = 99.54517646[MHz]
X_Offset          = 100[ppm]
X_Points          = 32768
X_Prescans        = 4
X_Resolution      = 0.95367432[Hz]
X_Sweep           = 31.25[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 290
Total_Scans       = 290

Relaxation_Delay = 2[s]
Recvr_Gain        = 60
Temp_Get          = 20.3[dC]
X_90_Width        = 9.2[us]
X_Acq_Time        = 1.048576[s]
X_Angle           = 30[deg]
X_Atn             = 4.2[dB]
X_Pulse           = 3.06666667[us]
Irr_Atn_Dec       = 22.4[dB]
Irr_Atn_Noe       = 22.4[dB]
Irr_Noise         = WALTZ
Decoupling        = TRUE
Initial_Wait      = 1[s]
Noe               = TRUE
Noe_Time          = 2[s]
Repetition_Time   = 3.048576[s]
```



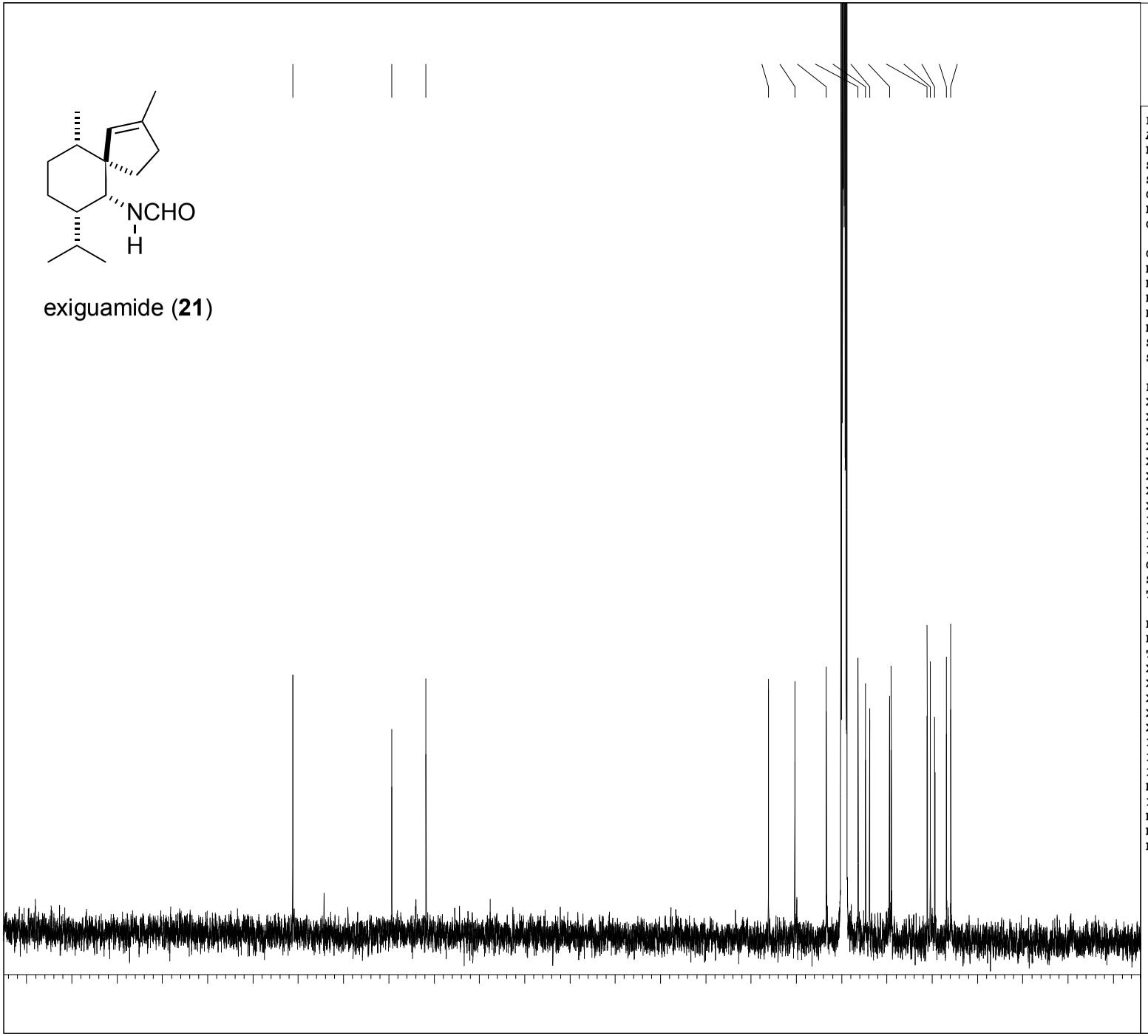
24

```
Filename          = 9KN_25_13C_CDCl3_400MHz_201
Author            = delta
Experiment        = single_pulse_dec
Sample_Id         = 1
Solvent           = METHANOL-D3
Creation_Time     = 24-JUL-2019 07:40:21
Revision_Time     =  5-NOV-2019 22:09:30
Current_Time      =  5-NOV-2019 22:10:13

Comment           = single pulse decoupled gated
Data_Format       = 1D REAL
Dim_Size          = 26214
Dim_Title         = 13C
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 1.048576[s]
X_Domain          = 13C
X_Freq            = 99.54517646[MHz]
X_Offset          = 100[ppm]
X_Points          = 32768
X_Prescans        = 4
X_Resolution      = 0.95367432[Hz]
X_Sweep           = 31.25[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 4842
Total_Scans       = 4842

Relaxation_Delay = 2[s]
Recvr_Gain        = 50
Temp_Get          = 22.6[dC]
X_90_Width        = 11[us]
X_Acq_Time        = 1.048576[s]
X_Angle           = 30[deg]
X_Atn             = 4.5[dB]
X_Pulse           = 3.66666667[us]
Irr_Atn_Dec       = 20.873[dB]
Irr_Atn_Noe       = 20.873[dB]
Irr_Noise         = WALTZ
Decoupling        = TRUE
Initial_Wait      = 1[s]
Noe               = TRUE
Noe_Time          = 2[s]
Repetition_Time   = 3.048576[s]
```



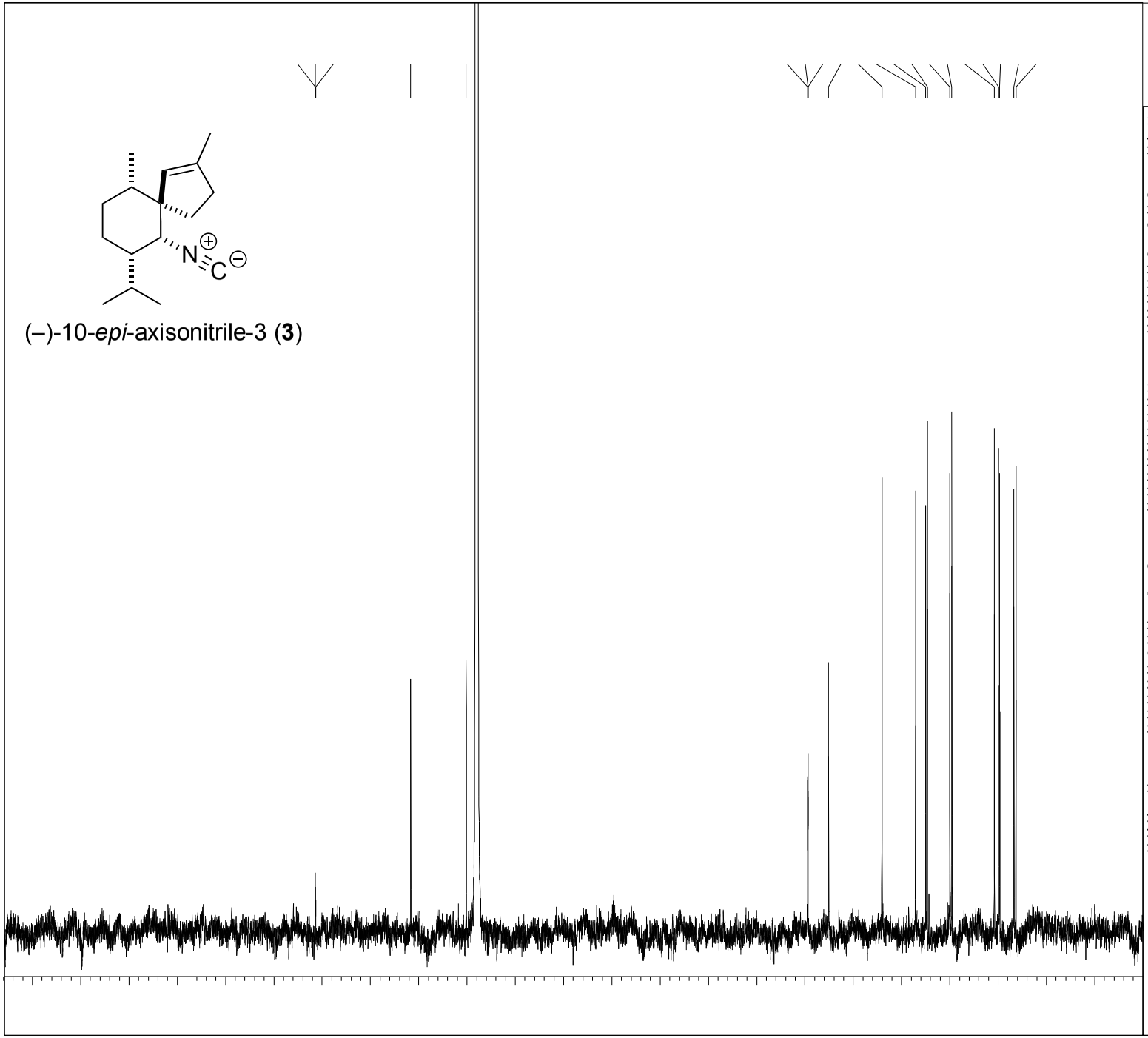
exiguamide (**21**)

```
Filename          = 9KN_exiguamide (22)_13C_DMSO
Author            = delta
Experiment        = single_pulse_dec
Sample_Id         = 1
Solvent           = DMSO-D6
Creation_Time     = 10-JUL-2019 03:10:38
Revision_Time     =  5-NOV-2019 22:10:42
Current_Time      =  5-NOV-2019 22:11:27

Comment           = single pulse decoupled gated
Data_Format       = 1D COMPLEX
Dim_Size          = 52428
Dim_Title         = 13C
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 2.097152[s]
X_Domain          = 13C
X_Freq            = 99.54517646[MHz]
X_Offset          = 100[ppm]
X_Points          = 65536
X_Prescans        = 4
X_Resolution      = 0.47683716[Hz]
X_Sweep           = 31.25[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 1700
Total_Scans       = 1700

Relaxation_Delay = 2[s]
Recvr_Gain        = 60
Temp_Get          = 21.3[dC]
X_90_Width        = 11[us]
X_Acq_Time        = 2.097152[s]
X_Angle           = 30[deg]
X_Atn             = 4.5[dB]
X_Pulse           = 3.66666667[us]
Irr_Atn_Dec       = 20.873[dB]
Irr_Atn_Noe       = 20.873[dB]
Irr_Noise         = WALTZ
Decoupling        = TRUE
Initial_Wait      = 1[s]
Noe               = TRUE
Noe_Time          = 2[s]
Repetition_Time   = 4.097152[s]
```

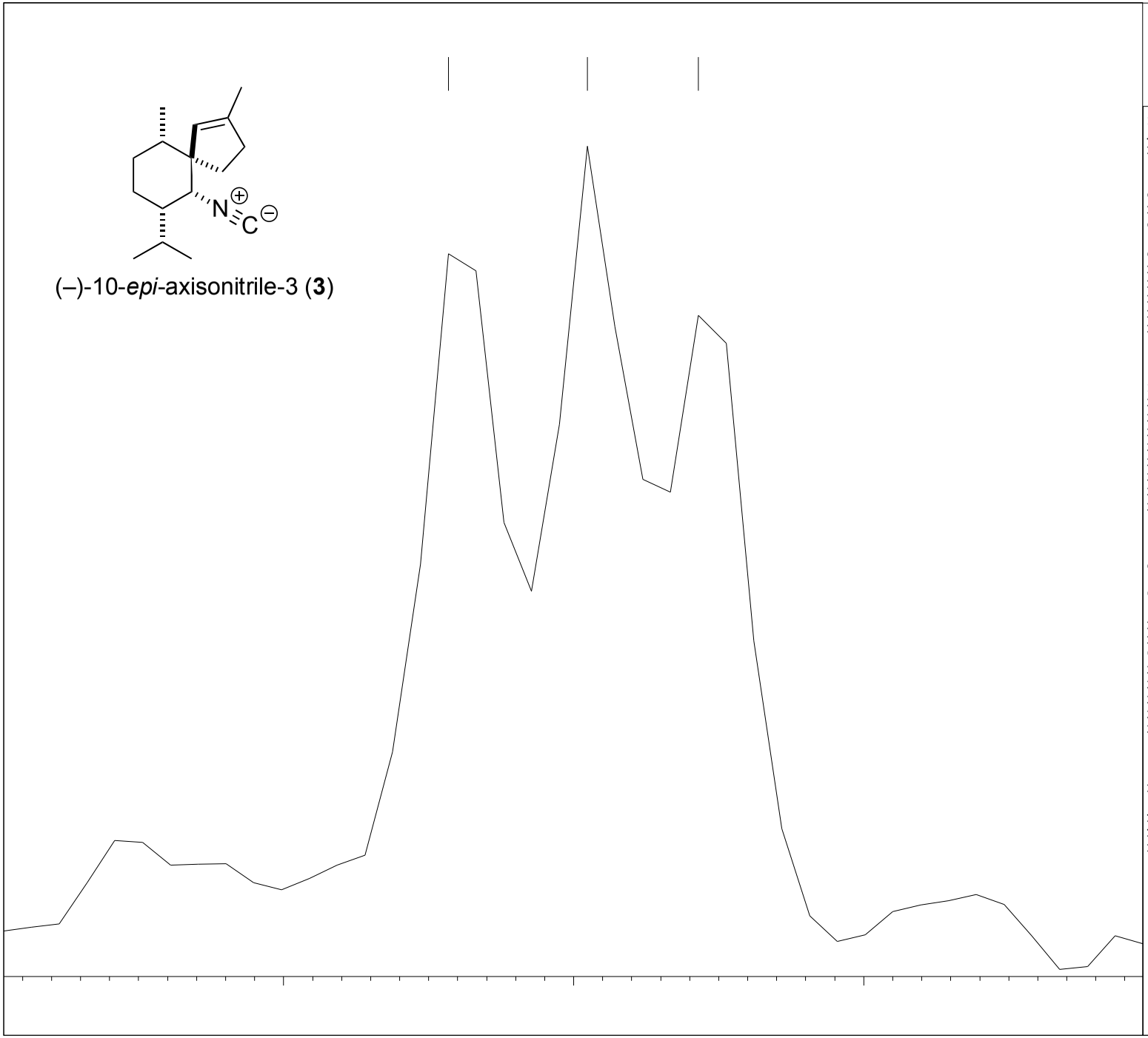



```
Filename          = 9KN_(—)-10-epi-axisonitril-
Author            = delta
Experiment        = single_pulse_dec
Sample_Id         = 1
Solvent           = BENZENE-D6
Creation_Time     =  8-FEB-2019 11:40:47
Revision_Time     =  5-NOV-2019 22:12:40
Current_Time      =  5-NOV-2019 22:13:34

Comment           = single pulse decoupled gated
Data_Format       = 1D REAL
Dim_Size          = 26214
Dim_Title         = 13C
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 1.048576[s]
X_Domain          = 13C
X_Freq            = 99.54517646[MHz]
X_Offset          = 100[ppm]
X_Points          = 32768
X_Prescans        = 4
X_Resolution      = 0.95367432[Hz]
X_Sweep           = 31.25[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 828.0
Total_Scans       = 828.0

Relaxation_Delay = 2[s]
Recvr_Gain        = 50
Temp_Get          = 19[dC]
X_90_Width        = 9.2[us]
X_Acq_Time        = 1.048576[s]
X_Angle           = 30[deg]
X_Atn             = 4.2[dB]
X_Pulse           = 3.06666667[us]
Irr_Atn_Dec       = 22.4[dB]
Irr_Atn_Noe       = 22.4[dB]
Irr_Noise         = WALTZ
Decoupling        = TRUE
Initial_Wait      = 1[s]
Noe               = TRUE
Noe_Time          = 2[s]
Repetition_Time   = 3.048576[s]
```



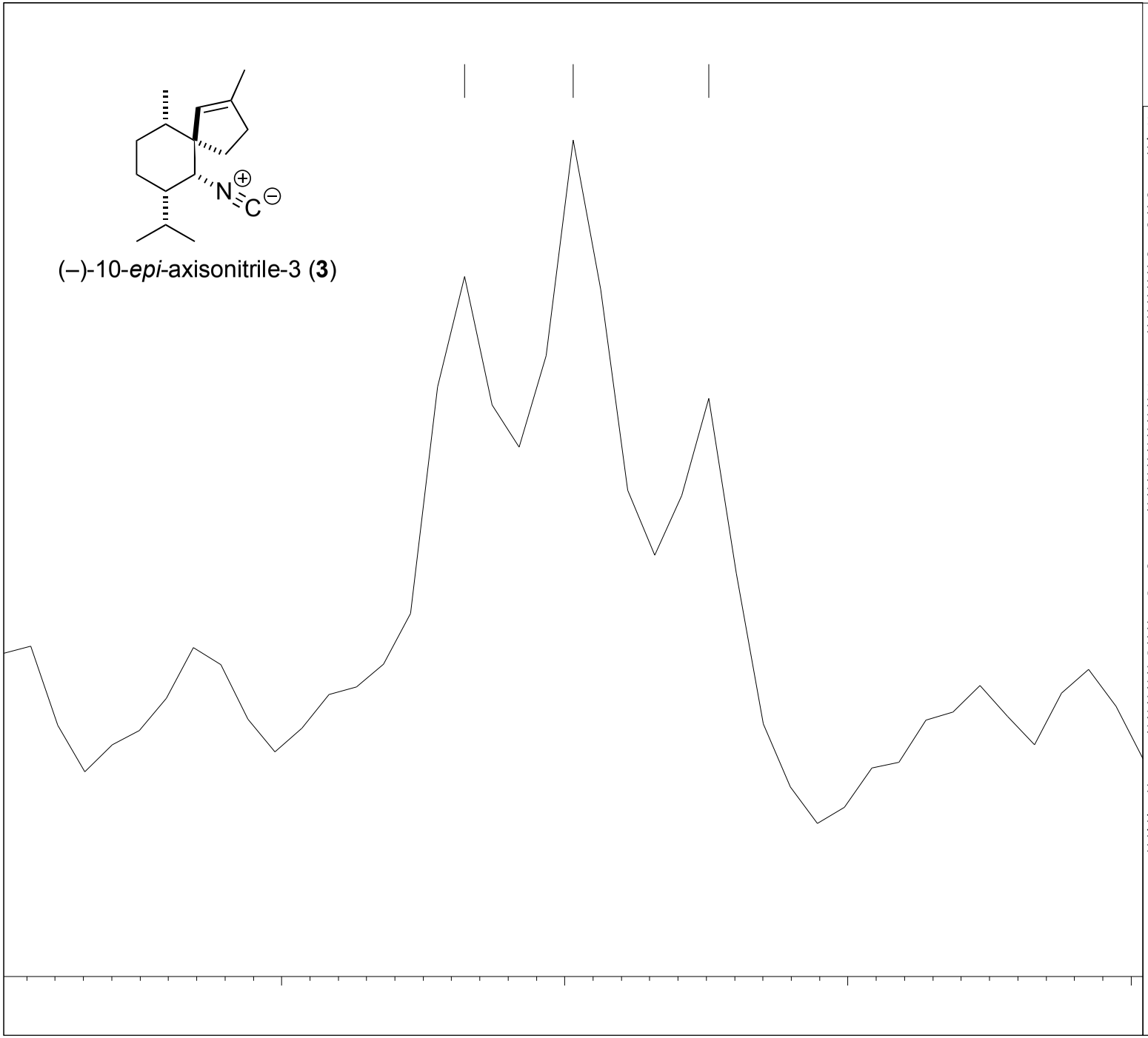
(–)-10-*epi*-axisonitrile-3 (**3**)

```
Filename          = 9KN_(—)-10-epi-axisonitril-
Author            = delta
Experiment        = single_pulse_dec
Sample_Id         = 1
Solvent           = BENZENE-D6
Creation_Time     =  8-FEB-2019 11:40:47
Revision_Time     =  5-NOV-2019 22:16:24
Current_Time      =  5-NOV-2019 22:20:08

Comment           = single pulse decoupled gated
Data_Format       = 1D COMPLEX
Dim_Size          = 26214
Dim_Title         = 13C
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 1.048576[s]
X_Domain          = 13C
X_Freq            = 99.54517646[MHz]
X_Offset          = 100[ppm]
X_Points          = 32768
X_Prescans        = 4
X_Resolution      = 0.95367432[Hz]
X_Sweep           = 31.25[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 828.0
Total_Scans       = 828.0

Relaxation_Delay = 2[s]
Recvr_Gain        = 50
Temp_Get          = 19[dC]
X_90_Width        = 9.2[us]
X_Acq_Time        = 1.048576[s]
X_Angle           = 30[deg]
X_Atn             = 4.2[dB]
X_Pulse           = 3.06666667[us]
Irr_Atn_Dec       = 22.4[dB]
Irr_Atn_Noe       = 22.4[dB]
Irr_Noise         = WALTZ
Decoupling        = TRUE
Initial_Wait      = 1[s]
Noe               = TRUE
Noe_Time          = 2[s]
Repetition_Time   = 3.048576[s]
```

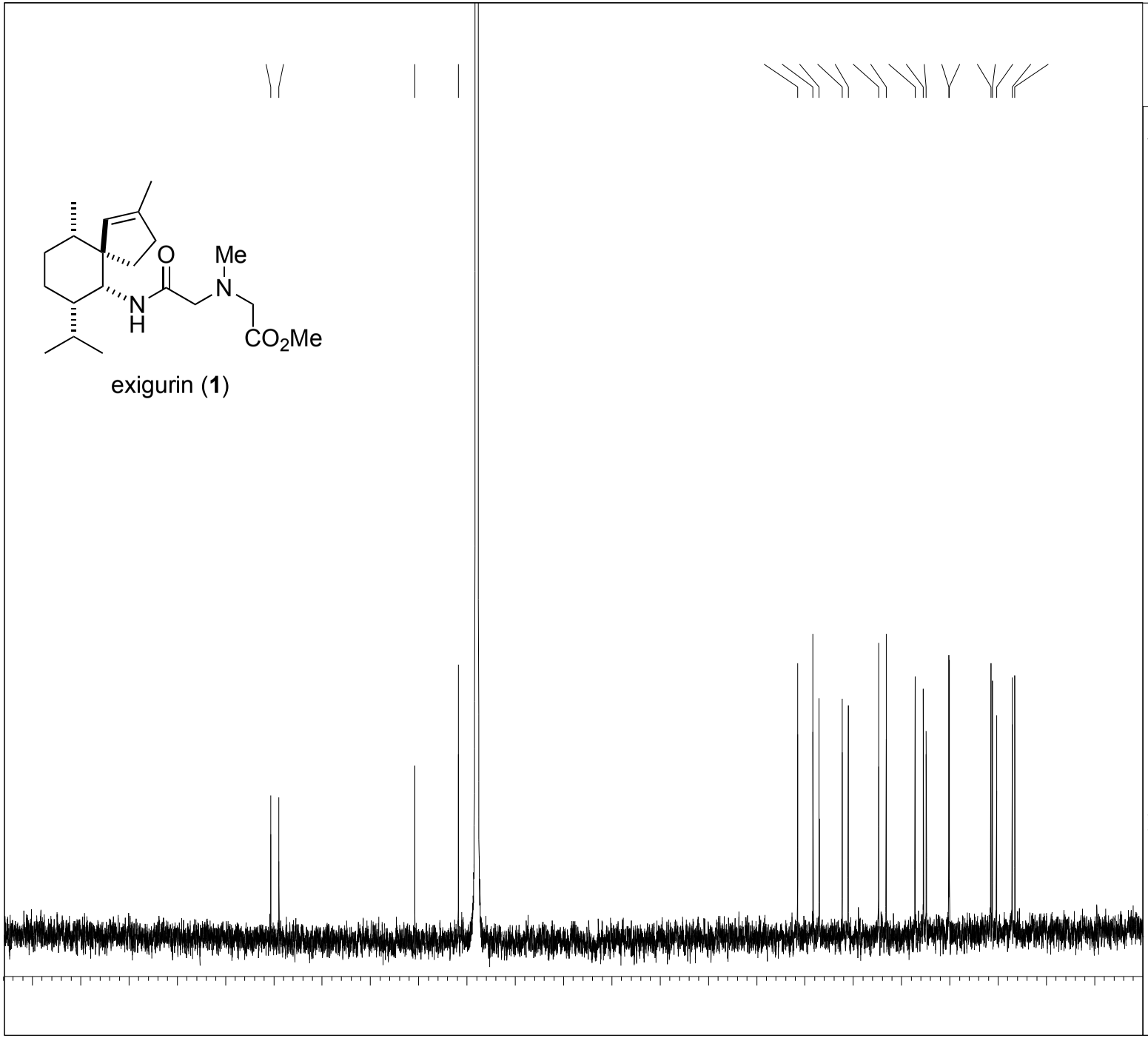



```
Filename          = 9KN_(—)-10-epi-axisonitril-
Author            = delta
Experiment        = single_pulse_dec
Sample_Id         = 1
Solvent           = BENZENE-D6
Creation_Time     =  8-FEB-2019 11:40:47
Revision_Time     =  5-NOV-2019 22:16:24
Current_Time      =  5-NOV-2019 22:17:40

Comment           = single pulse decoupled gated
Data_Format       = 1D COMPLEX
Dim_Size          = 26214
Dim_Title         = 13C
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 1.048576[s]
X_Domain          = 13C
X_Freq            = 99.54517646[MHz]
X_Offset          = 100[ppm]
X_Points          = 32768
X_Prescans        = 4
X_Resolution      = 0.95367432[Hz]
X_Sweep           = 31.25[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 828.0
Total_Scans       = 828.0

Relaxation_Delay = 2[s]
Recvr_Gain        = 50
Temp_Get          = 19[dC]
X_90_Width        = 9.2[us]
X_Acq_Time        = 1.048576[s]
X_Angle           = 30[deg]
X_Atn             = 4.2[dB]
X_Pulse           = 3.06666667[us]
Irr_Atn_Dec       = 22.4[dB]
Irr_Atn_Noe       = 22.4[dB]
Irr_Noise         = WALTZ
Decoupling        = TRUE
Initial_Wait      = 1[s]
Noe               = TRUE
Noe_Time          = 2[s]
Repetition_Time   = 3.048576[s]
```



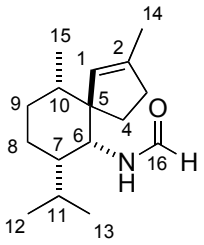
exigurin (**1**)

```
Filename          = 9KN_exigurin (1)_13C_C6D6_40
Author            = delta
Experiment        = single_pulse_dec
Sample_Id         = 1
Solvent           = BENZENE-D6
Creation_Time     = 23-FEB-2019 08:28:09
Revision_Time     =  5-NOV-2019 22:15:03
Current_Time      =  5-NOV-2019 22:15:36

Comment           = single pulse decoupled gated
Data_Format       = 1D COMPLEX
Dim_Size          = 26214
Dim_Title         = 13C
Dim_Units         = [ppm]
Dimensions        = X
Site              = ECS 400
Spectrometer      = JNM-ECS400

Field_Strength    = 9.2982153[T] (400[MHz])
X_Acq_Duration    = 1.048576[s]
X_Domain          = 13C
X_Freq            = 99.54517646[MHz]
X_Offset          = 100[ppm]
X_Points          = 32768
X_Prescans        = 4
X_Resolution      = 0.95367432[Hz]
X_Sweep           = 31.25[kHz]
Irr_Domain        = 1H
Irr_Freq          = 395.88430144[MHz]
Irr_Offset        = 5[ppm]
Clipped           = FALSE
Scans             = 728
Total_Scans       = 728

Relaxation_Delay = 2[s]
Recvr_Gain        = 58
Temp_Get          = 18.8[dC]
X_90_Width        = 9.2[us]
X_Acq_Time        = 1.048576[s]
X_Angle           = 30[deg]
X_Atn             = 4.2[dB]
X_Pulse           = 3.06666667[us]
Irr_Atn_Dec       = 22.4[dB]
Irr_Atn_Noe       = 22.4[dB]
Irr_Noise         = WALTZ
Decoupling        = TRUE
Initial_Wait      = 1[s]
Noe               = TRUE
Noe_Time          = 2[s]
Repetition_Time   = 3.048576[s]
```



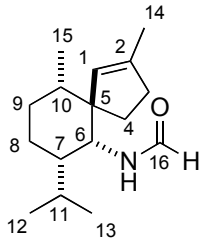
exiguamide (**21**)

: Comparison of ^{1}H-NMR of synthetic and natural exiguamide

Position	(400 MHz, DMSO-d_6)	** (500 MHz, DMSO-d_6)
1	5.58 (brs)	5.58 (brs)
3a	2.34 (ddd, J =16.0, 8.0, 8.0 Hz)	2.34 (ddd, J = 15.8, 8.8, 7.5 Hz)
3b	1.99 (dd, J = 15.0, 9.0 Hz)	1.99 (dd, J = 15.8, 8.8 Hz)
4a	1.83–1.76 (m)	1.80 (ddd, J = 12.6, 7.5, 2.1 Hz)
4b	*	1.42 (ddd, J = 12.6, 8.8, 8.8 Hz)
6	3.82 (dd (10.0, 3.0)	3.82 (dd, J = 10.5, 3.5 Hz)
7	1.15–1.06 (m)	1.11 (m)
8ax	*	1.31 (m)
8eq	1.59–1.51 (m)	1.56 (m)
9ax	1.76–1.70 (m)	1.74 (tt, J = 13.5, 5.4 Hz)
9eq	*	1.44 (m)
10	*	1.47 (m)
11	*	1.30 (m)
12	0.86 (d, J = 6.5 Hz)	0.86 (d, J = 6.5 Hz)
13	0.68 (d, J = 6.5 Hz)	0.68 (d, J = 6.5 Hz)
14	1.68 (s)	1.68 (brs)
15	0.95 (d, J = 7.0 Hz)	0.95 (d, J = 7.5 Hz)
16	8.08 (d, J = 1.5 Hz)	8.08 (brs)
NH	7.62 (brd, J = 10.0 Hz)	7.62 (brd, J = 10.5 Hz)

* 1.51–1.21 (m) 5H

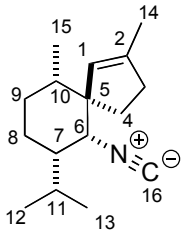
** NMR data are reproduced from the isolation paper, see: Uy, M. M.; Ohta, S.; Yanai, M.; Ohta, E.; Hirata, T.; Ikegami, S. *Tetrahedron* , *59*, 731.



exiguamide (**21**)

: Comparison of ^{13}C-NMR of synthetic and natural exiguamide

Position	(100 MHz, DMSO-d_6)	(125 MHz, DMSO-d_6)	Δδ [ppm]
1	131.82	131.77	+0.05
2	139.35	139.29	+0.06
3	34.71	34.67	+0.04
4	33.83	33.76	+0.07
5	56.19	56.16	+0.03
6	50.34	50.33	+0.01
7	43.38	43.37	+0.01
8	19.44	19.41	+0.03
9	29.46	29.42	+0.04
10	36.39	36.34	+0.05
11	29.05	28.99	+0.06
12	21.12	21.05	+0.07
13	20.41	20.36	+0.05
14	16.86	16.78	+0.08
15	15.91	15.87	+0.04
16	161.21	161.16	+0.05

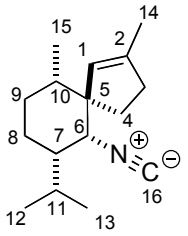


(–)-10-*epi*-axisonitrile-3 (**3**)

: Comparison of ^{1}H-NMR of synthetic and natural (–)-10-*epi*-axisonitrile-3

Position	(400 MHz, C_6D_6)	* (500 MHz, C_6D_6)
1	5.24 (q, *J* = 1.0)	5.25 (brs)
3a	2.15–2.05 (m)	2.11 (ddd, *J* = 16.4, 8.1, 8.1 Hz)
3b	1.98–1.90 (m)	1.95 (ddd , *J* = 6.4, 9.0, 2.9 Hz)
4a	2.29 (ddd, *J* = 13.5, 7.5, 3.0 Hz)	2.28 (ddd, *J* = 13.0, 8.1, 2.9 Hz)
4b	1.82 (ddd, *J* = 13.0, 8.0, 8.0 Hz)	1.82 (ddd, *J* = 13.0, 9.0, 8.1 Hz)
6	3.51 (brs)	3.51 (brs)
7	1.02–0.89 (m)	0.96 (m)
8ax	1.53–1.46 (m)	1.49 (m)
8eq	1.53–1.46 (m)	1.49 (m)
9ax	1.60–1.54 (m)	1.56 (m)
9eq	1.44–1.37 (m)	1.42 (m)
10	1.56–1.52 (m)	1.55 (m)
11	1.77–1.68 (m)	1.72 (m)
12	0.85 (d, *J* = 6.5 Hz)	0.86 (d, *J* = 6.6 Hz)
13	0.82 (d, *J* = 6.5 Hz)	0.82 (d, *J* = 6.6 Hz)
14	1.51–1.50 (m)	1.51 (brs)
15	1.30 (d, *J* = 7.5 Hz)	1.29 (d, *J* = 7.8 Hz)

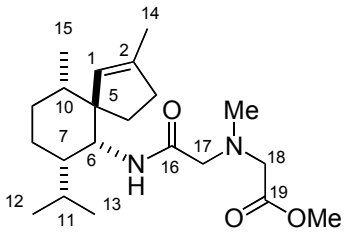
* NMR data are reproduced from the isolation paper, see: Uy, M. M.; Ohta, S.; Yanai, M.; Ohta, E.; Hirata, T.; Ikegami, S. *Tetrahedron* , *59*, 731.



(–)-10-*epi*-axisonitrile-3 (**3**)

: Comparison of ^{13}C-NMR of synthetic and natural (–)-10-*epi*-axisonitrile-3

Position	(100 MHz, C_6D_6)	(125 MHz, C_6D_6)	Δδ [ppm]
1	130.18	130.2	–0.02
2	141.66	141.67	–0.01
3	34.65	34.69	–0.04
4	34.98	34.99	–0.01
5	55.10	55.14	–0.04
6	59.40	59.43	–0.03
7	44.06	44.07	–0.01
8	19.95	19.7	+0.25
9	29.59	29.62	–0.03
10	37.11	37.12	–0.01
11	29.99	30.02	–0.03
12	20.79	20.78	+0.01
13	19.67	19.98	–0.31
14	16.73	16.72	+0.01
15	16.31	16.31	+0.00
16	161.40	161.44	–0.04

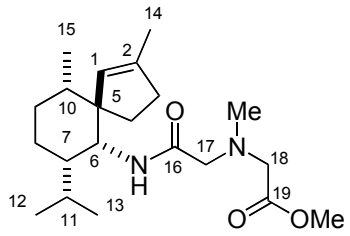


exigurin (**1**)

: Comparison of ^{1}H-NMR of synthetic and natural exigurin

Position	(400 MHz, C_6D_6)	* (500 MHz, C_6D_6)
1	5.66 (brs)	5.67 (brs)
3a	2.89–2.79 (m)	2.82 (m)
3b	2.14 (ddq, *J* = 16.0, 9.0, 1.0 Hz)	2.14 (ddd, *J* = 15.6, 8.8, 2.5 Hz)
4a	2.23 (ddd, *J* = 13.0, 8.0, 2.0 Hz)	2.23 (ddd, *J* = 12.2, 7.5, 2.5 Hz)
4b	1.66-1.62 (m)	1.64 (m)
6	4.49 (dd, *J* = 10.5, 2.5 Hz)	4.48 (dd, *J* = 11.1, 3.5 Hz)
6-NH	7.57 (d, *J* = 10.5 Hz)	7.56 (d, *J* = 11.1 Hz)
7	1.40-1.31 (m)	1.36 (m)
8ax	1.55-1.50 (m)	1.02 (m)
8eq	1.68-1.64 (m)	1.66 (m)
9ax	1.91–1.80 (m)	1.84 (m)
9eq	1.49-1.37 (m)	1.43 (m)
10	1.75-1.67 (m)	1.71 (m)
11	1.58-1.52 (m)	1.55 (m)
12	0.99 (d, *J* = 6.5)	0.98 (d, *J* = 6.6 Hz)
13	1.13 (d, *J* = 6.5)	1.12 (d, *J* = 6.6 Hz)
14	1.69 (brs)	1.68 (brs)
15	1.14 (d, *J* = 7.5 Hz)	1.14 (d, *J* = 7.5 Hz)
17	3.07 (d, *J* = 16.0 Hz, 1H), 3.02 (d, *J* = 16.0 Hz, 1H)	3.05 (s, 2H)
17-NCH_3	2.08 (s)	2.09 (s)
18	2.84 (s, 2H)	2.85 (s, 2H)
19-OCH_3	3.27 (s)	3.28 (s)

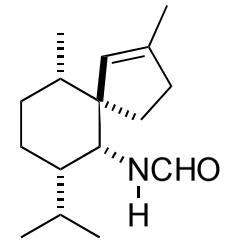
* NMR data are reproduced from the isolation paper, see: Uy, M. M.; Ohta, S.; Yanai, M.; Ohta, E.; Hirata, T.; Ikegami, S. *Tetrahedron* , *59*, 731.



exigurin (**1**)

: Comparison of ^{13}C-NMR of synthetic and natural exigurin

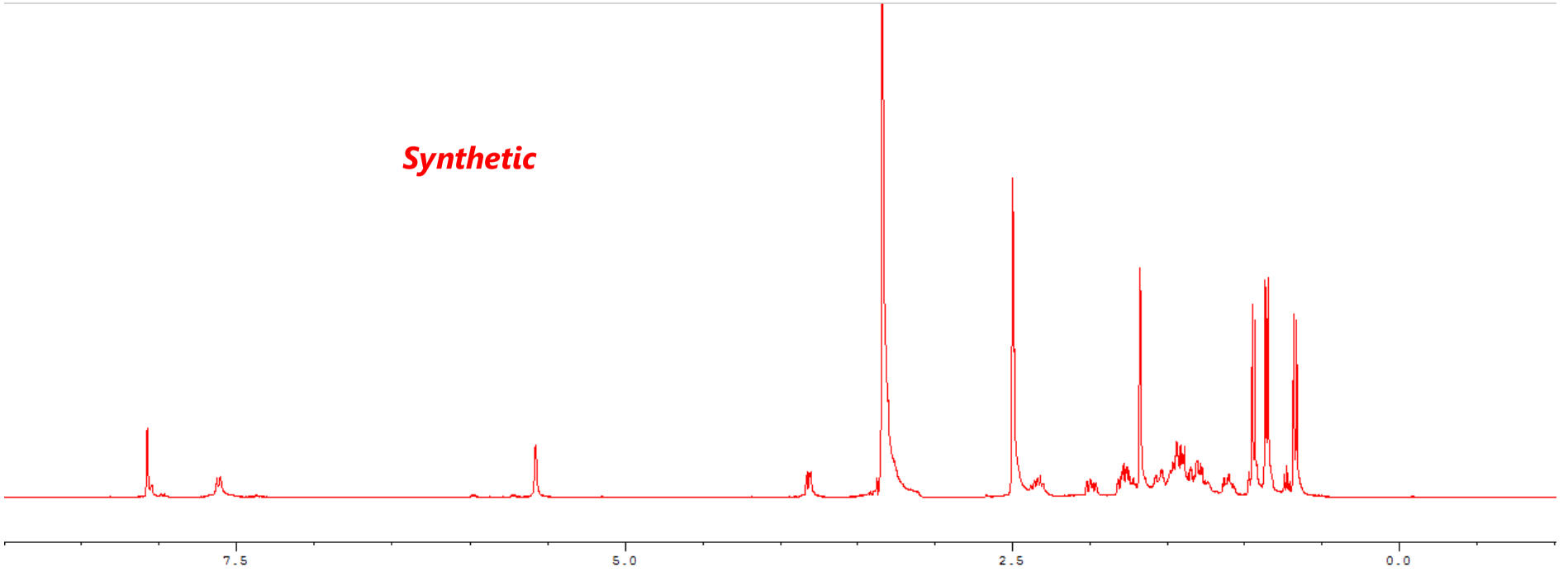
Position	(100 MHz, C_6D_6)	(125 MHz, C_6D_6)	Δδ [ppm]
1	131.79	131.82	–0.03
2	140.80	140.81	–0.01
3	35.46	35.48	–0.02
4	34.88	34.85	+0.03
5	57.06	57.1	–0.04
6	52.30	52.39	–0.09
7	44.73	44.77	–0.04
8	20.34	20.36	–0.02
9	30.12	30.15	–0.03
10	37.22	37.24	–0.02
11	20.23	30.2	+0.03
12	21.52	21.51	+0.01
13	21.21	21.22	-0.01
14	17.09	17.07	+0.02
15	16.52	16.54	–0.02
16	168.96	168.98	–0.02
17	61.52	61.55	–0.03
17-NCH_3	43.19	43.19	–0.00
18	58.35	58.41	–0.06
19	170.65	170.64	+0.01
19-OCH_3	51.04	51.03	+0.01

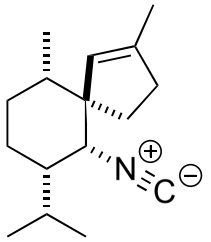


exiguamide (**21**)

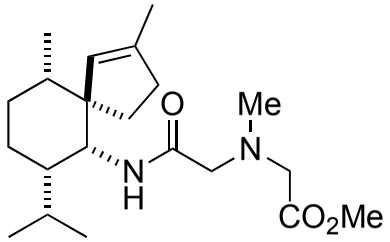
Natural

Synthetic

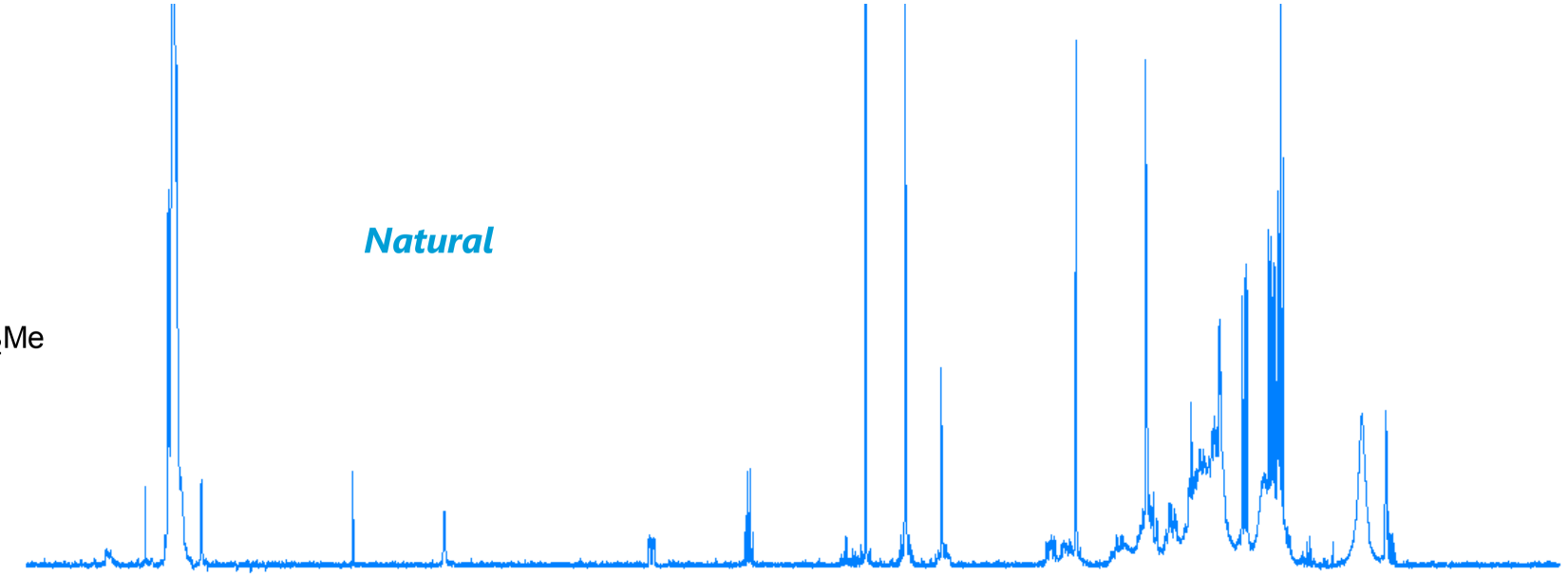


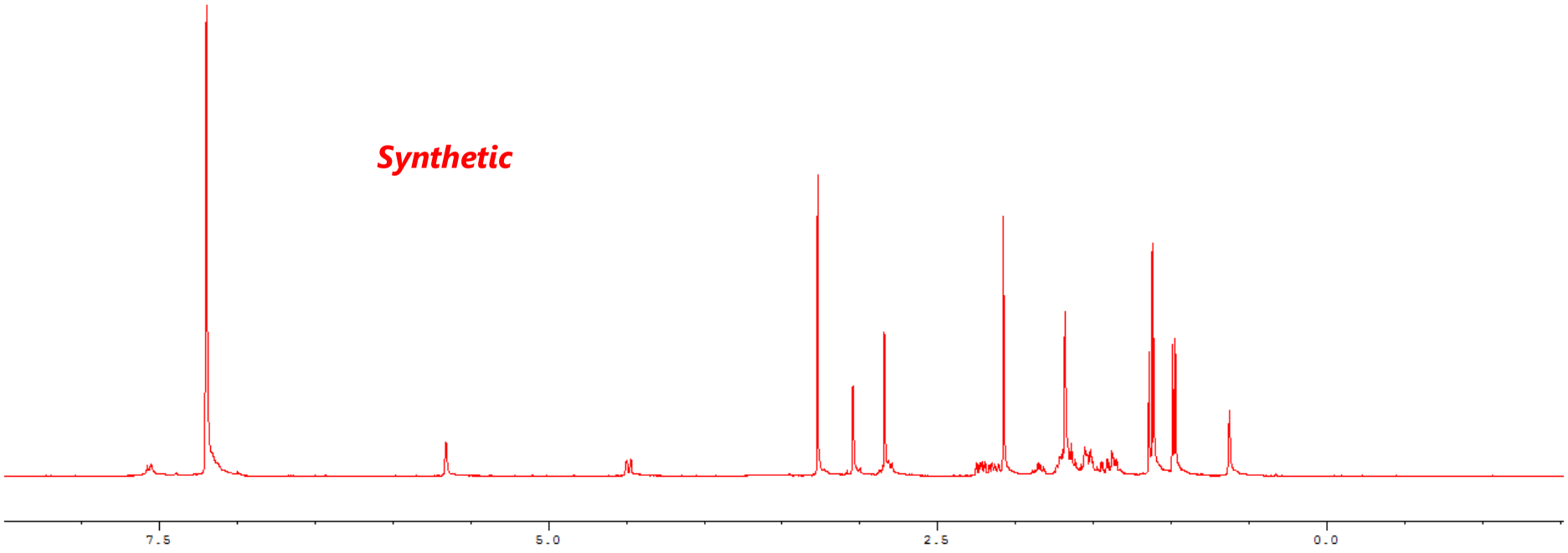


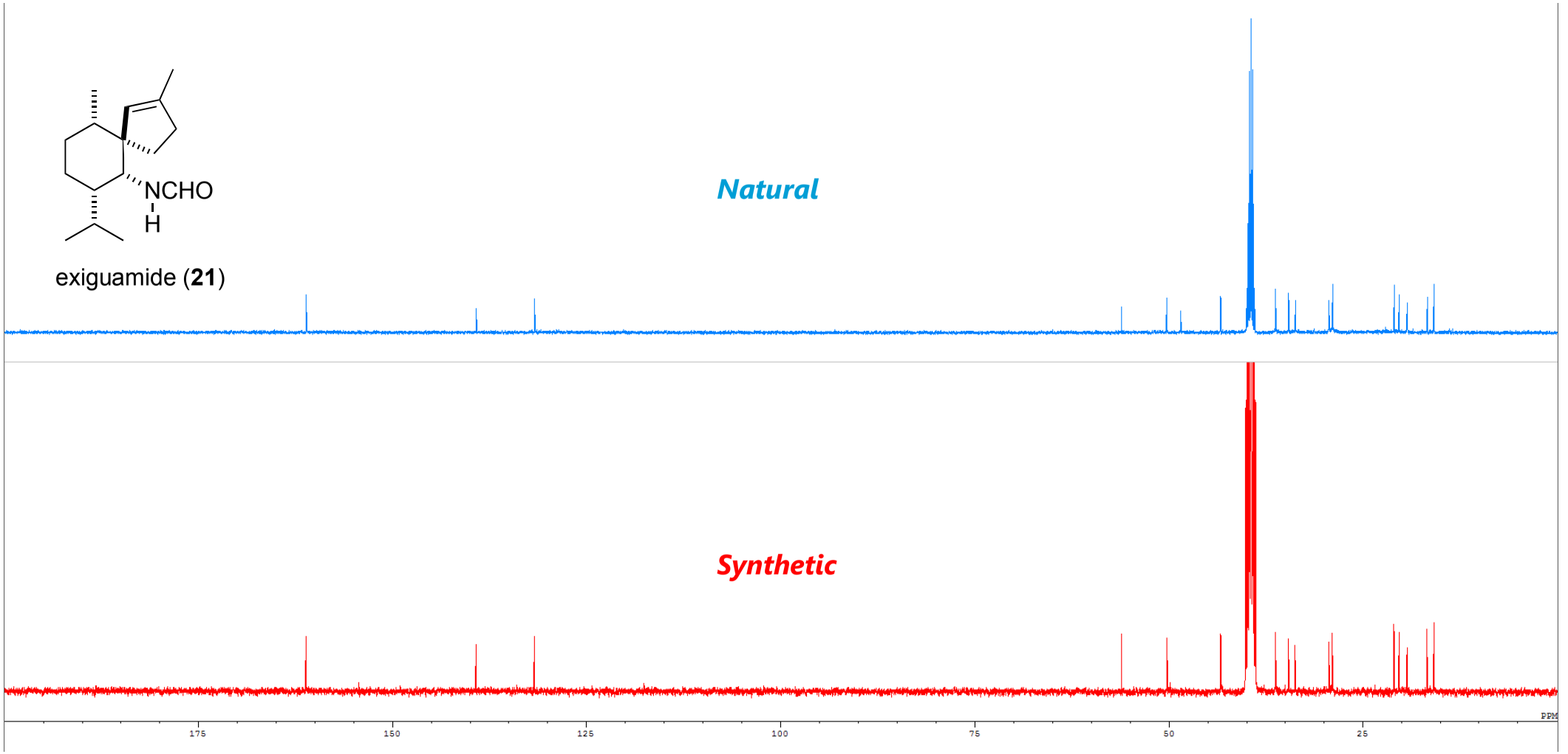
(–)-10-*epi*-axisonitrile-3 (**3**)

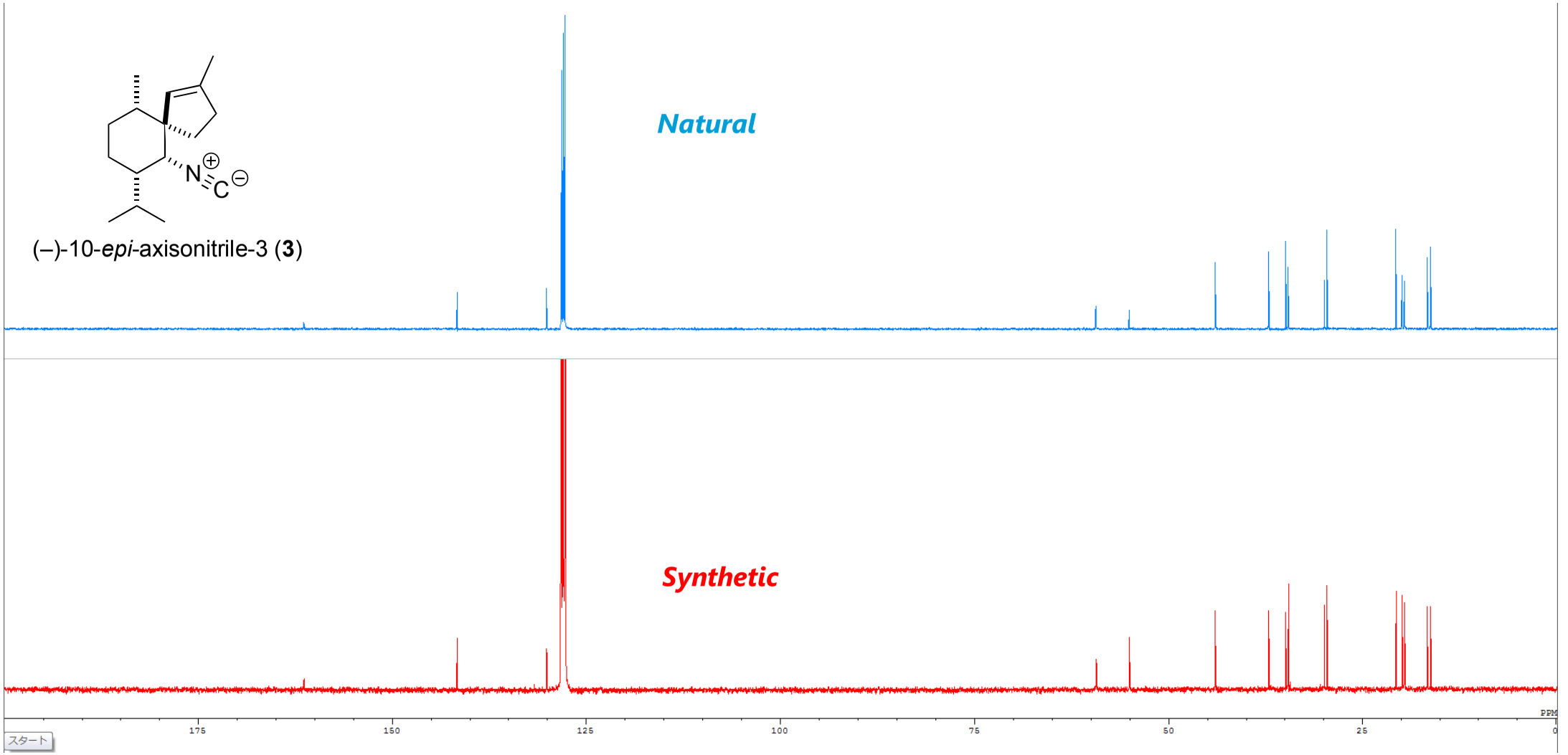


exigurin (**1**)

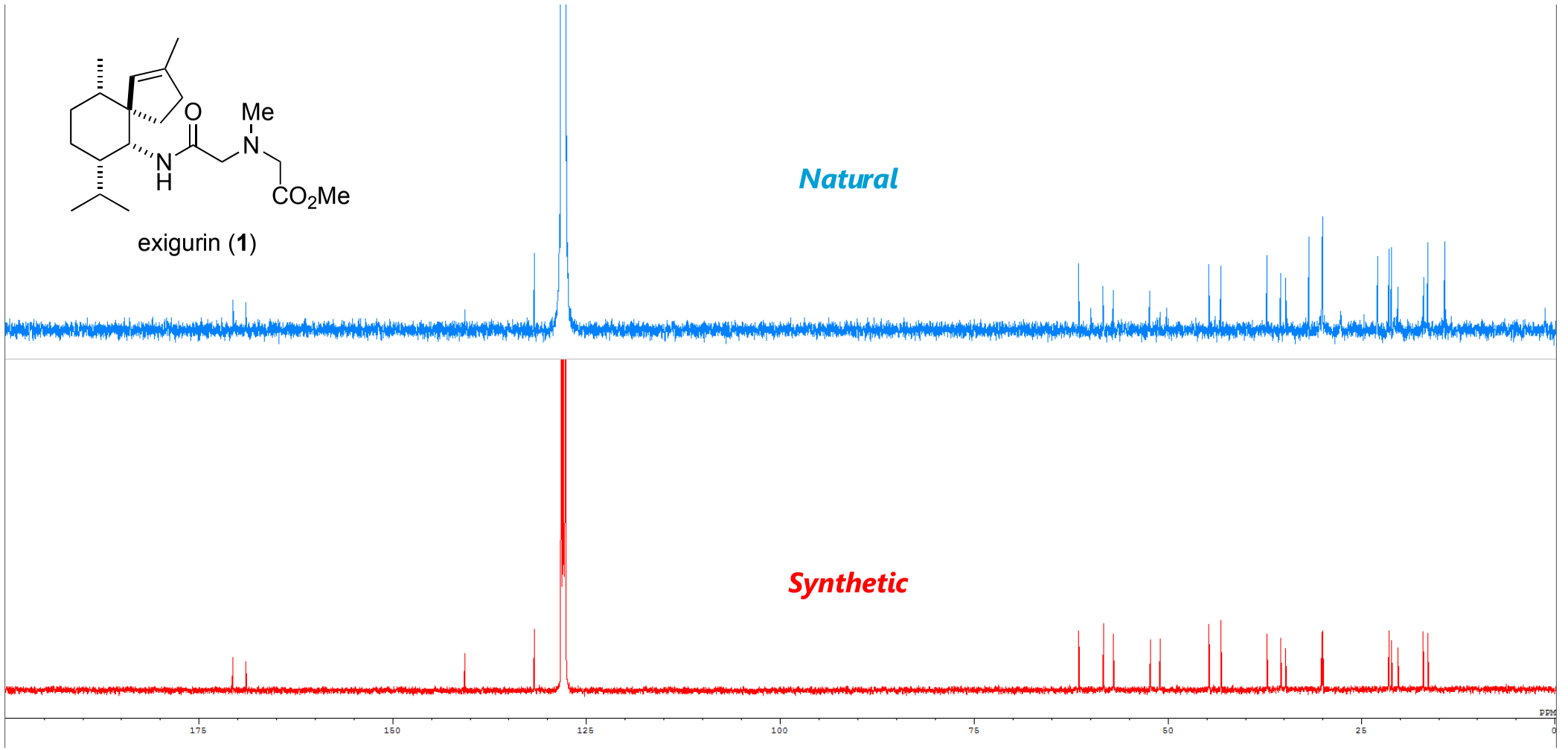




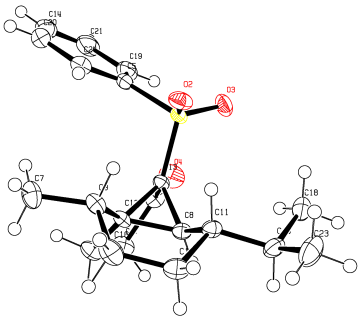

NCHO
H
exiguamide (21)
Natural
Synthetic
175
150
125
100
75
50
25
PPM

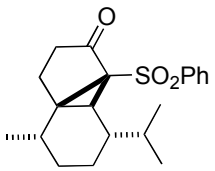


(–)-10-*epi*-axisonitrile-3 (**3**)


O
Me
N
N
H
CO2Me
exigurin (1)
Natural
Synthetic
175
150
125
100
75
50
25
0
PPM

X-ray crystallograpphic structure of





15

CCDC 1943181

Empirical Formula	$C_{20}H_{26}O_3S$
Formula Weight	346.48
Crystal Color, Habit	colorless, block
Crystal Dimensions	0.800 X 0.700 X 0.600 mm
Crystal System	hexagonal
Lattice Type	Primitive
Lattice Parameters	a = 8.0090(4) Å c = 49.0398(13) Å V = 2724.2(2) Å^3
Space Group	$P6_1$ (#169)
Z value	6
D_{calc}	1.267 g/cm^3
F_{000}	1116.00
μ(CuKα)	16.957 cm^{-1}

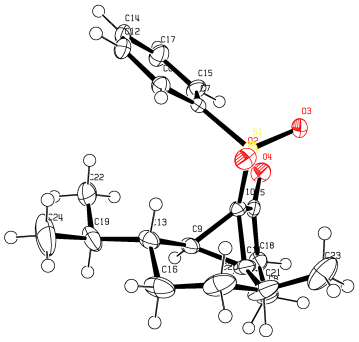
B. Intensity Measurements

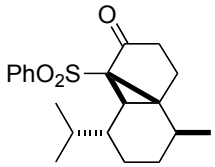
Diffractometer	R-AXIS RAPID
Radiation	CuKα (λ = 1.54187 Å) graphite monochromated
Voltage, Current	50kV, 100mA
Temperature	23.0°C
Detector Aperture	460.0 x 256.0 mm
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	136.4°
No. of Reflections Measured	Total: 31493 Unique: 3339 (R_{int} = 0.0857) Parsons quotients (Flack x parameter): 1622
Corrections	Lorentz-polarization Absorption (trans. factors: 0.197 - 0.362)

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SHELXT Version 2014/4)
Refinement	Full-matrix least-squares on F^2
Function Minimized	$\Sigma\ w\ (Fo^2 - Fc^2)^2$
Least Squares Weights	$w = 1/ [\ \sigma^2(Fo^2) + (0.0590 \cdot P)^2 + 0.1987 \cdot P\ ]$ where $P = (Max(Fo^2,0) + 2Fc^2)/3$
$2\theta_{max}$ cutoff	136.4^o
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	3339
No. Variables	217
Reflection/Parameter Ratio	15.39
Residuals: R1 (I>2.00σ(I))	0.0357
Residuals: R (All reflections)	0.0358
Residuals: wR2 (All reflections)	0.0903
Goodness of Fit Indicator	1.176
Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	$0.22\ e^-/Å^3$
Minimum peak in Final Diff. Map	$-0.51\ e^-/Å^3$

X-ray crystallograpphic structure of





19

CCDC 1943176

Empirical Formula	$C_{20}H_{26}O_3S$
Formula Weight	346.48
Crystal Color, Habit	colorless, block
Crystal Dimensions	0.800 X 0.600 X 0.300 mm
Crystal System	orthorhombic
Lattice Type	Primitive
Lattice Parameters	a = 7.14999(13) Å b = 12.6963(2) Å c = 20.1516(4) Å V = 1829.33(6) Å^3
Space Group	$P2_12_12_1$ (#19)
Z value	4
D_{calc}	1.258 g/cm^3
F_{000}	744.00
μ(CuKα)	16.835 cm^{-1}

B. Intensity Measurements

Diffractometer	R-AXIS RAPID
Radiation	CuKα (λ = 1.54187 Å) graphite monochromated
Voltage, Current	50kV, 100mA
Temperature	23.0°C
Detector Aperture	460.0 x 256.0 mm
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2\theta_{max}$	136.4°
No. of Reflections Measured	Total: 20894 Unique: 3213 (R_{int} = 0.0901) Parsons quotients (Flack x parameter): 1296
Corrections	Lorentz-polarization Absorption (trans. factors: 0.387 - 0.603)

C. Structure Solution and Refinement

Structure Solution	Direct Methods (SHELXT Version 2014/4)
Refinement	Full-matrix least-squares on F^2
Function Minimized	$\Sigma\ w\ (Fo^2 - Fc^2)^2$
Least Squares Weights	$w = 1/ [\ \sigma^2(Fo^2) + (0.0629 \cdot P)^2 + 0.6196 \cdot P\ ]$ where $P = (Max(Fo^2,0) + 2Fc^2)/3$
$2\theta_{max}$ cutoff	136.4^o
Anomalous Dispersion	All non-hydrogen atoms
No. Observations (All reflections)	3213
No. Variables	217
Reflection/Parameter Ratio	14.81
Residuals: R1 (I>2.00σ(I))	0.0369
Residuals: R (All reflections)	0.0371
Residuals: wR2 (All reflections)	0.0967
Goodness of Fit Indicator	1.015
Max Shift/Error in Final Cycle	0.000
Maximum peak in Final Diff. Map	$0.25\ e^-/Å^3$
Minimum peak in Final Diff. Map	$-0.52\ e^-/Å^3$