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Supporting Information

69451 Weinheim, Germany

Synthesis of Rhazinocine via an Iterative and Regioselective Metal Catalyzed C-H Bond Functionalization Strategy.

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Supporting Information

Experimental procedures and data

^{1}H and ^{13}C NMR spectra

EXPERIMENTAL PROCEDURES

Solvents: Diethyl ether and tetrahydrofuran were distilled from lithium aluminium hydride; acetonitrile, toluene, dichloromethane and toluene from calcium hydride. Anhydrous *N,N*-dimethyl formamide, dimethylsulphoxide and pyridine were used as supplied. Petrol refers to petroleum ether b.p. 40-60 ˚C and ether to diethyl ether, which were distilled before use.

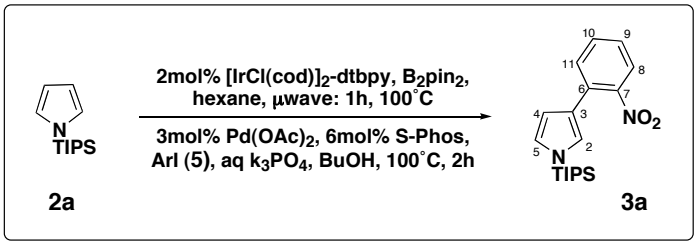
Reagents: All reactions were performed under a nitrogen atmosphere unless otherwise stated. Reagents were used as supplied or purified using standard procedures as necessary.

Chromatography: Flash column chromatography was carried out using Merck Kieselgel 230-400 mesh under pressure unless otherwise indicated. Analytical thin layer chromatography was performed using pre-coated glass-backed plates (Merck Kieselgel 60 F254) and visualised by ultra-violet radiation (254 nm), acidic ammonium molybdate (VI), or acidic potassium permanganate solutions as appropriate.

Data Collection: Infra-red spectra were recorded as thin films on a Perkin Elmer Spectrum One FT-IR spectrometer. Absorption maxima (υ_{max}) are reported in wave numbers (cm^{-1}). ^{1}H NMR spectra were recorded on Bruker DPX-400 and Bruker DPX-500 spectrometers and are reported (based on appearance rather than interpretation) as follows: chemical shift δ/ppm (number of protons, multiplicity, coupling constant *J* /Hz, assignment). Residual protic solvents; chloroform (δH=7.26 ppm) was used as an internal reference. ^{13}C spectra were recorded at 100MHz on Bruker DPX-400 spectrometers. High resoltion mass measurements were made by the EPSRC mass spectrometry service (Swansea) or recorded in-house using a Micromass Quadropole-Time of Flight (Q-ToF) spectrometer.

Equipment: A CEM Discover microwave synthesiser (150W) was used for all reactions that required microwave heating.

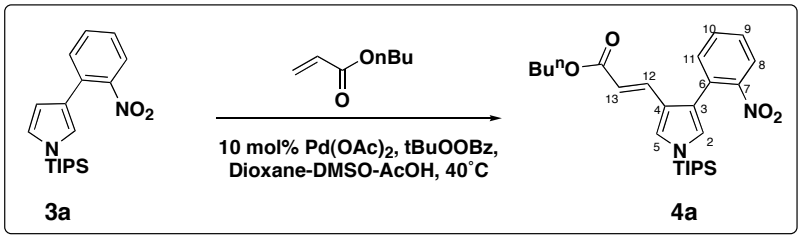
3-(2-nitrophenyl)-1-(triisopropylsilyl)-1H-pyrrole, **3a**



Hexane (2mL) was added to a glass microwave tube containing 1-*t*riisopropylsilyl pyrole **2a** (90mg, 0.4mmol, 1.0eq), bis(picinolato)diboron (103mg, 0.4mmol, 1.0eq), 2 mol% $[IrCl(COD)]_2$ (5mg, 0.01mmol) and 4 mol% 4,4'-di*tert*butyl-2,2'-bipyridine (4mg, 0.02mmol). The reaction mixture was heated at 100˚C for 50mins in a 150W microwave. After cooling to room temperature 2-iodo-nitrobenzene (100mg, 0.4, 1.0eq), 1M aqueous potassium phosphate (127mg, 0.6mmol, 1.5eq) 3 mol% palladium acetate (3mg, 0.01mmol), 6 mol% S-Phos ligand (10mg, 0.02mmol) and butanol (2mL) was added to the crude reaction mixture. The reaction mixture was stirred for a further 2h at 100˚C. The reaction was allowed to cool to room temperature, diluted with ethyl acetate (40mL) and washed with water (10mL) and brine (10mL). The organic layers were dried ($MgSO_4$) and evaporated. The crude reaction mixture was purified by flash column chromatography, eluting over a gradient of 0-10% diethylether/hexane, to give 1-triisopropylsilyl-3-(2-nitrophenyl) *pyrrole* **3a** (114mg, 0.33mmol, 82%) as a yellow oil.

TLC R_f 0.85 (10% diethylether/cyclohexane); ν_{max}/cm^{-1} (film): 2948-2869 (C-H), 1608 (Ar), 1529 and 1361 (NO_2), 1489, 1464; δH (400MHz, d_1-chloroform) 7.57 (1H, dd, *J* 8.0, 1.0, H8), 7.54 (1H, dd, *J* 7.8, 1.4, H11), 7.47 (1H, dt, *J* 7.6, 1.2, H10), 7.27 (1h, dt, *J* 7.4, 1.5, H9), 6.90, (1H, t, *J* 1.7, H5), 6.79 (1H, t, *J* 4.8, H2), 6.40 (1H, dd, *J* 2.7, 1.5, H4), 1.45 (3H, septet, *J* 7.5, SiC<u>H</u>$(CH_3)_2$), 1.11 (18H, d, *J* 7.5, SiCH$(C\underline{H}_3)_2$); δC (100MHz, d_1-chloroform) 149.2, 131.3, 130.8, 129.9, 126.0, 125.0, 123.2, 122.9, 120.8, 110.4, 17.7, 11.6; m/z HRMS (ESI) found $[M+H]^+$ 345.1999, $C_{19}H_{29}N_2O_2Si$ requires 345.1993

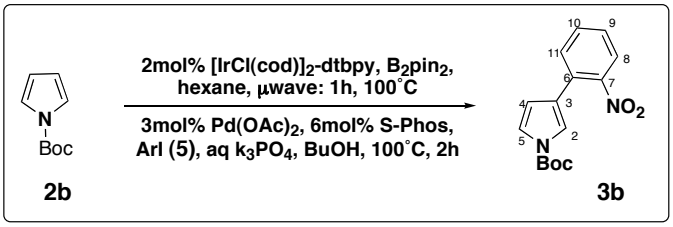
(E) 4-(3-butoxy-3-oxoprop-1-enyl)-3-(2-nitrophenyl)-1-(triisopropylsilyl)-1H-pyrrole, **4a**



Palladium acetate (2mg, 0.01mmol, 10mol%), *n*-butyl acrylate (7mg, 0.05mmol, 1.0eq) and *t*-butylperoxybenzoate (10mg, 0.05mmol, 1.0eq) were added to 1-triisopropylsilyl-3-(2-nitrophenyl) pyrrole **3a** (34mg, 0.10mmol, 2.0eq) dissolved in dioxane-dimethylsulfoxide-acetic acid (9:1:3, 0.5M). The reaction mixture was heated at 40˚C in a sealed reaction vessel for 24h. The crude mixture was then filtered through a plug of Celite and diluted with ethyl acetate (50mL). The organic layer was washed with saturated aqueous sodium bicarbonate (2x 10mL) and brine (10mL) then dried ($MgSO_4$) and evaporated. The crude product was purified by flash column chromatography, eluting over a gradient of 0-20% diethylether/cyclohexane, to give *pyrrole* **4a** (17mg, 0.04mmol, 75%) as a yellow oil.

TLC R_f 0.50 (10% diethylether/cyclohexane); ν_{max}/cm^{-1} (film): 2950-2868 (C-H), 1702 (C=O) 1628 (Ar), 1572, 1526 and 1347 (NO_2), 1463, 1386; δH (400MHz, d_1-chloroform) 7.81 (1H, dd, *J* 7.9, 1.3, H^8), 7.56 (1H, dt, *J* 7.5, 1.1, H^{10}), 7.50 (1H, d, *J* 16.0, H^{12}), 7.46-7.41 (2H, m, $H^{9,11}$), 7.11 (1H, d, *J* 2.1, H^5), 6.70 (1H, d, *J* 2.1, H^2), 5.82 (1H, d, *J* 16.0, H^{13}), 4.10 (2H, t, *J* 6.7, $CO_2C\underline{H}_2$), 1.60 (2H, quintet, *J* 6.7, $CO_2CH_2C\underline{H}_2$), 1.45 (2H, sextet, *J* 7.2, $C\underline{H}_2CH_3$), 1.40 (3H, septet, *J* 7.5, $SiC\underline{H}(CH_3)_2$), 1.11 (18H, d, *J* 7.5, $SiCH(C\underline{H}_3)_2$), 0.92 (3H, t, *J* 7.2, $C\underline{H}_3$); δC (100MHz, d_1-chloroform) 167.8, 150.4, 137.5, 133.1, 131.7, 129.4, 127.8, 126.8, 125.0, 123.7, 121.2, 121.1, 63.9, 30.8, 19.2, 17.6, 13.7, 11.5; m/z HRMS (ESI) found [M+H]+ 471.2698, $C_{26}H_{39}N_2O_4Si$ requires 471.2679.

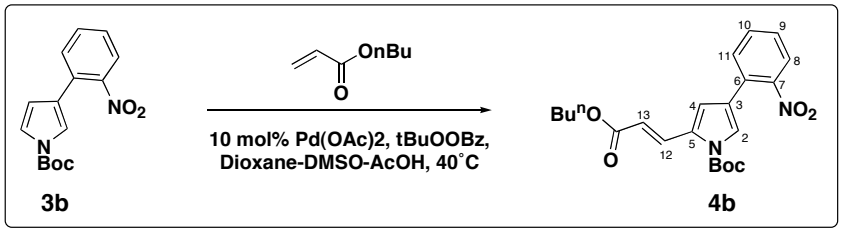
tert-butyl 3-(2-nitrophenyl)-1H-pyrrole-1-carboxylate, **3b**



Hexane (2mL) was added to a microwave flask with 1-*tert*-butylpyrole carboxyate **2b** (67mg, 0.4mmol, 1.0eq), bis(picinolato)diboron (103mg, 0.4mmol, 1.0eq), 2 mol% $[IrCl(COD)]_2$ (5mg, 0.01mmol) and 4 mol% 4,4'-di*tert*butyl-2,2'-bipyridine (4mg, 0.02mmol). The reaction mixture was heated at 100˚C for 50mins in a 150W microwave a 150W microwave. After cooling to room temperature 2-iodo-nitrobenzene 2-iodo-nitrobenzene (100mg, 0.4, 1.0eq), 1M aqueous potassium phosphate (127mg, 0.6mmol, 1.5eq) 3 mol% palladium acetate (3mg, 0.01mmol), 6 mol% S-Phos ligand (10mg, 0.02mmol) and butanol (2mL) were added to the crude reaction mixture. The reaction mixture was stirred for a further 2h at 100˚C. The reaction was allowed to cool to room temperature, diluted with ethyl acetate (40mL) and washed with water (10mL) and brine (10mL). The organic layers were dried ($MgSO_4$) and evaporated. The crude reaction mixture was purified by flash column chromatography, eluting over a gradient of 0-10% diethylether/hexane, to give 1-tert-butyl-3-(2-nitrophenyl) *pyrrole* **3b** (78mg, 0.27mmol, 68%) as a yellow oil.

TLC R_f 0.75 (10% diethylether/cyclohexane); ν_{max}/cm^{-1} (film): 2980-2899 (C-H), 1743 (C=O), 1611 (Ar), 1526 and 1364 (NO_2), 1498, 1475, 1458, 1389, 1278, 1255; δH (400MHz, d_1-chloroform) 7.71 (1H, dd, *J* 8.2, 1.2, H^8), 7.54 (1H, dt, *J* 7.8, 1.3, H^{10}), 7.48 (1H, dd, *J* 7.8, 1.7, H^{11}), 7.38 (1H, dt, *J* 7.8, 1.7, H^9), 7.38 (1H, d, *J* 1.6, H^2), 7.27 (1H, dd, *J* 3.3, 2.3, H^5), 6.26 (1H, dd, *J* 3.3, 1.7, H^4), 1.61 (9H, s, $C(C\underline{H}_3)_3$); δC (100MHz, d_1-chloroform)149.1, 148.4, 132.0, 131.2, 128.9, 127.6, 123.7, 122.7, 120.8, 118.2, 111.8, 84.3, 27.9; m/z HRMS (ESI) found [M+H]+ 289.1183, $C_{15}H_{16}N_2O_4$ requires 289.1183.

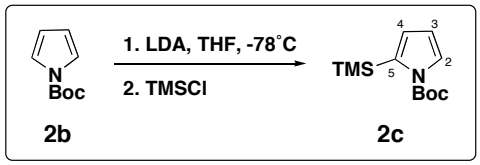
(E)-tert-butyl 5-(3-butoxy-3-oxoprop-1-enyl)-3-(2-nitrophenyl)-1H-pyrrole-1-carboxylate, **4b**



Palladium acetate (2mg, 0.01mmol, 10mol%) *n*-butyl acryalte (13mg, 0.10mmol, 1.0eq) and *t*-butylperoxybenzoate (19mg, 0.10mmol, 1.0eq) were added to 1-*tert*-butyl-3-(2-nitrophenyl)pyrrole carboxylate **3b** (58mg, 0.20mmol, 2.0eq) dissolved in dioxane-dimethylsulfoxide-acetic acid (9:1:3, 0.5M). The reaction mixture was heated at 40˚C in a sealed reaction vessel for 24h. The crude mixture was then filtered through a plug of Celite and diluted with ethyl acetate (50mL). The organic layer was washed with saturated aqueous sodium bicarbonate (2x 10mL) and brine (10mL) then dried ($MgSO_4$) and evaporated. The crude product was purified by flash column chromatography, eluting over a gradient of 0-20% diethylether/cyclohexane, to give *pyrrole* **4b** (9:1, C5:C2) (30mg, 0.07mmol, 72%) as a yellow oil.

TLC R_f 0.50 (10% diethylether/cyclohexane); ν_{max}/cm^{-1} (film): 2960-2873 (C-H), 1747 (C=O), 1705 (C=O), 1623 (Ar), 1582, 1526 and 1337 (NO_2), 1465, 1370, 1247; δH (400MHz, d_1-chloroform) 8.24 (1H, d, *J* 15.9, H^{12}), 7.76 (1H, dd, *J* 8.0, 1.1, H^8), 7.57 (1H, dt, *J* 7.5, 1.2, H^{10}), 7.52 (1H, d, *J* 1.9, H^2), 7.47 (1H, dd, *J* 7.8, 1.4, H^{11}), 7.43 (1H, dt, *J* 7.6, 1.4, H^9), 6.70 (1H, d, *J* 1.9, H^4), 6.24 (1H, d, *J* 16.0, H^{13}), 4.19 (2H, t, *J* 6.6, $CO_2C\underline{H}_2$), 1.67 (2H, quintet, *J* 6.9, $CO_2CH_2C\underline{H}_2$), 1.64 (9H, s, $C(CH_3)_3$), 1.43 (2H, sextet, *J* 7.5, $C\underline{H}_2CH_3$), 0.96 (3H, t, *J* 7.5, $C\underline{H}_3$); δC (100MHz, d_1-chloroform) 167.0, 149.1, 148.5, 134.3, 132.2, 131.7, 131.2, 128.1, 128.0, 123.9, 122.7, 122.1, 117.9, 114.0, 85.6, 64.3, 30.8, 28.0, 19.2, 13.7; m/z HRMS (ESI) found [M+H]+ 415.1875, $C_{22}H_{27}N_2O_6$ requires 415.1869.

tert-butyl-5-(trimethylsilyl)-1H-pyrrole-1-carboxylate, **2c**



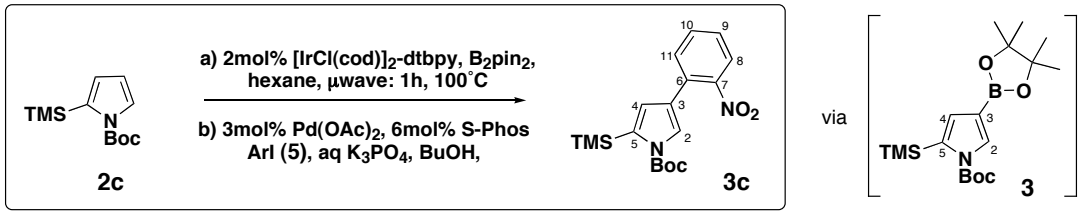
Freshly distilled diisopropylamine (0.94mL, 6.60mmol, 1.1eq) in THF (10mL) was cooled to -78˚C under a nitrogen atmosphere. *n*-Butyl lithium, 1.6M in hexanes (4.12mL, 6.60mmol, 1.1eq) was added slowly and the reaction mixture allowed to warm to 0˚C for 1h before re-cooling to -78˚C.

1-*t*-butyl pyrrole carboxylate **2b** (1.0g, 6.00mmol, 1.0eq) in THF (20mL) was cooled to -78˚C under a nitrogen atmosphere. The LDA solution was added via cannula over 20 mins at -78˚C. The reaction mixture was stirred at -78˚C for a further 6h before trimethylsilylchoride (1.0mL, 7.80mmol, 1.4eq) was added and the mixture allowed to slowly warm to room temperature over 10h. The reaction was recooled to 0˚C and poured into ice cold water (40mL) then extracted with ethyl acetate (2x60mL). The combined organic layers were dried ($MgSO_4$) and evaporated. The crude reaction mixture was purified by flash column chromatography, eluting over a gradient of 0-10% diethylether/hexane, to give 1-*t*-butyl-2-trimethylsilyl pyrrole carboxylate **2c** (1.30g, 5.46mmol, 91%) as a colourless oil.

TLC R_f 0.75 (25% diethylether/cyclohexane); δH (400MHz, d_1-chloroform) 7.39 (1H, dd, *J* 3.0, 1.5, H^2), 6.47 (1H, dd, *J* 3.0, 1.5, H^4), 6.22 (1H, t, *J* 3.0, H^3), 1.60 (9H, s, $C(CH_3)_3$), 0.27 (9H, s, $Si(CH_3)_3$); δC (100MHz, d_1-chloroform) 149.6, 134.9, 124.5, 123.4, 111.6, 83.3, 28.0, -0.4.

Data consistent with literature. Ref: *J. Org. Chem.* **1981**, *46,* 157-164

tert-butyl-3-(2-nitrophenyl)- 5-(trimethylsilyl)-1H-pyrrole-1-carboxylate, **3c**

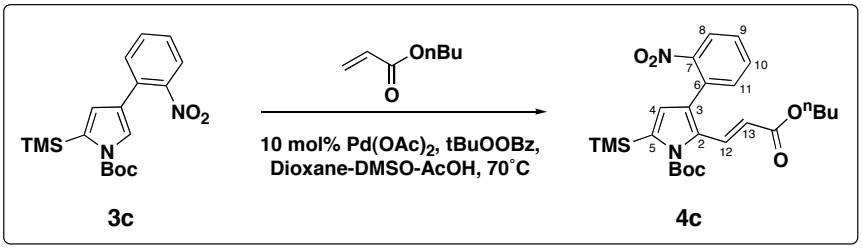


One-pot method: Hexane (3mL) was added to a microwave flask with 1-*t*-butyl-5-trimethylsilyl-pyrrole carboxylate **2c** (375mg, 1.55mmol, 1.0eq), bis(picinolato)diboron (398mg, 1.55mmol, 1.0eq), 2 mol% $[IrCl(COD)]_2$ (20mg, 0.03mmol) and 4 mol% 4,4'-di*tert*butyl-2,2'-bipyridine (18mg, 0.06mmol). The reaction mixture was heated at 100˚C for 50mins in a 150W microwave. After cooling to room temperature 2-iodo-nitrobenzene (386mg, 1.55mmol, 1.0eq), 1M aqueous potassium phosphate (213mg, 2.01mmol, 1.3eq) 3 mol% palladium acetate (11mg, 0.05mmol), 6 mol% S-Phos ligand (42mg, 0.09mmol) and butanol (6mL) were added to the crude reaction mixture. The reaction mixture was heated for a further 2h at 100˚C. The reaction was allowed to cool to room temperature, diluted with ethyl acetate (80mL) and washed with water (20mL) and brine (20mL). The organic layers were dried ($MgSO_4$) and evaporated. The crude reaction mixture was purified by flash column chromatography, eluting over a gradient of 0-20% diethylether/hexane, to give 1-*t*-butyl-2-trimethylsilyl-3-(2-nitrophenyl) *pyrrole* **3c** (435mg, 1.21mmol, 78%) as a yellow oil.

TLC R_f 0.75 (25% diethylether/cyclohexane); ν_{max}/cm^{-1} (film): 2978-2863 (C-H), 1743 (C=O), 1611 (Ar), 1568, 1528 and 1367 (NO_2), 1479, 1459, 1271; δH (400MHz, d_1-chloroform) 7.70 (1H, dd, *J* 8.1, 1.1, H^8), 7.53 (1H, dt, *J* 7.8, 1.0, H^{10}), 7.50 (1H, d, *J* 1.7, H^2), 7.49 (1H, dd, *J* 7.7, 1.8, H^{11}), 7.37 (1H, dt, *J* 7.5, 1.7, H^9), 6.47 (1H, d *J* 1.6, H^4), 1.61 (9H, s, $C(CH_3)_3$), 0.29 (9H, s, $Si(CH_3)_3$); δC (100MHz, d_1-chloroform) 149.3, 149.1, 136.1, 131.8, 131.3, 129.0, 127.3, 123.7, 123.0, 122.7, 122.4, 84.0, 27.9, -0.4; m/z HRMS (EI) found [M]+ 360.1503, $C_{18}H_{24}N_2O_4Si$ requires 360.1500.

Tert-butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(trimethylsilyl)-1H-pyrrole-1-carboxylate, **3.** TLC R_f 0.80 (25% diethylether/cyclohexane); ν_{max}/cm^{-1} (film): 2979-2810 (C-H), 1744 (C=O), 1563, 1458, 1393, 1371, 1351, 1330; δH (400MHz, d_1-chloroform) 8.24 (1H, d, *J* 1.3, H^2), 7.33 (1H, d, *J* 1.3, H^4), 1.27 (9H, s, $C(CH_3)_3$), 1.25 (12H, s, $OC(CH_3)_2$) 0.53 (9H, s, $Si(CH_3)_3$); δC (100MHz, d_1-chloroform) 149.7, 135.6, 133.8, 129.3, 128.4, 83.0, 27.3, 24.7, -0.4; m/z HRMS (ESI) found [M+H]+ 366.2266, $C_{18}H_{32}NO_4SiB$ requires 366.2266.

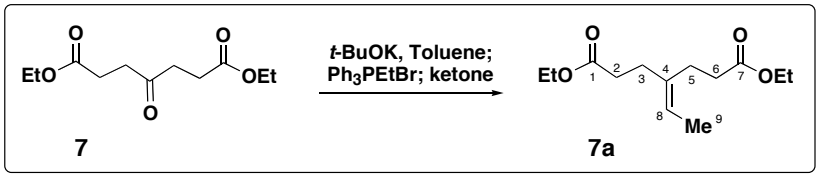
(E)-tert-butyl 2-(3-butoxy-3-oxoprop-1-enyl)-3-(2-nitrophenyl)-5-(trimethylsilyl)-1H-pyrrole-1-carboxylate, **4c**



Palladium acetate (2mg, 0.01mmol, 10mol%), *n*-butyl acrylate (26mg, 0.20mmol, 2eq) and *t*-butylperoxybenzoate (19mg, 0.10mmol, 1.0eq) were added to 1-*t*-butyl-3-(2-nitrophenyl) pyrrole carboxylate **3c** (36mg, 0.10mmol, 1.0eq) dissolved in dioxane-dimethylsulfoxide-acetic acid (9:1:3, 0.5M). The reaction mixture was heated at 70˚C in a sealed reaction vessel for 24h. The crude mixture was then filtered through a plug of Celite and diluted with ethyl acetate (50mL). The organic layer was washed with saturated aqueous sodium bicarbonate (2x 10mL) and brine (10mL) then dried ($MgSO_4$) and evaporated. The crude product was purified by flash column chromatography, eluting over a gradient of 0-20% diethylether/cyclohexane, to give **4c** (29mg, 0.06mmol, 60%) as a yellow oil.

TLC R_f 0.50 (10% diethylether/cyclohexane); ν_{max}/cm^{-1} (film): 2961-2873 (C-H), 1742 (C=O), 1713 (C=O), 1628 (Ar), 1529 and 1337 (NO_2), 1460, 1372, 1259; δH (400MHz, d_1-chloroform) 7.92 (1H, dd, *J* 8.1, 1.2, H^8), 7.90 (1H, d, *J* 16.1, H^{12}), 7.58 (1H, dt, *J* 7.6, 1.3, H^{10}), 7.47 (1H, dt, *J* 7.8, 1.5, H^9), 7.35 (1H, dd, *J* 7.7, 1.4, H^{11}), 6.36 (1H, s, H^4), 5.40 (1H, d, *J* 16.1, H^{13}), 4.07 (2H, t, *J* 6.7, $CO_2C\underline{H}_2$), 1.64 (9H, s, $C(CH_3)_3$), 1.59 (2H, quintet, *J* 6.9, $CO_2CH_2C\underline{H}_2$), 1.34 (2H, sextet, *J* 7.4, $C\underline{H}_2CH_3$), 0.90 (3H, t, *J* 7.4, $C\underline{H}_3$), 0.28 (9H, s, $Si(CH_3)_3$); δC (100MHz, d_1-chloroform) 166.6, 150.1, 149.3, 139.7, 134.9, 132.8, 132.6, 130.6, 129.8, 128.4, 126.2, 124.5, 124.0, 119.3, 85.5, 64.2, 30.7, 27.9, 19.1, 13.7, -0.2; m/z HRMS (ESI) found [M+H]+ 487.2272, $C_{25}H_{35}N_2O_6Si$ requires 487.2264.

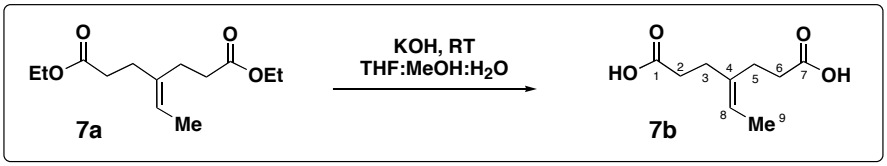
Diethyl 4-ethylideneheptanedioate, **7a**



A suspension of sublimed potassium *tert*-butoxide (2.92g, 26.0mmol, 3eq) in dry toluene (200mL) was stirred at room temperature for 0.5h. Triphenylphosphonium ethyl bromide (9.68g, 26.0mmol, 3eq) was added portion-wise to the reaction mixture and stirred at room temperature for a further 0.5h at which time the reaction had reached a scarlet color. A solution of diethyl-4-oxo-pimelate **7** (2.00g, 8.68mmol, 1eq) in toluene (40mL) was added to the ylid solution and stirred for a further 4h. The reaction mixture was poured into saturated aqueous ammonium chloride solution (200mL) and extracted with ethyl acetate (2x200mL). The organic layers were combined, dried ($MgSO_4$) and evaporated. The crude product was purified by flash column chromatography, eluting over a gradient of 0-20% ethylacetate/hexane, to give *olefin* **7a** (1.68g, 6.96mmol, 80%) as a colorless oil.

TLC R_f 0.55 (25% ethylacetate/cyclohexane); ν_{max}/cm^{-1} (film): 2980-2872 (C-H), 1735 (C=O), 1463, 1446, 1370, 1344, 1296; δH (400MHz, d_1-chloroform) 5.27 (1H, q, *J* 6.8, H^8), 4.12 (2H, q, *J* 7.1, $CO_2C\underline{H}_2$), 4.11 (2H, q, *J* 7.1, $CO_2C\underline{H}_2$'), 2.41-2.28 (8H, m, $CH_2^{2,3,5,6}$), 1.59 (3H, d, *J* 6.8, CH_3^9), 1.25 (3H, t, *J* 7.1, $CO_2CH_2C\underline{H}_3$), 1.24 (3H, t, *J* 7.1, $CO_2CH_2C\underline{H}_3$'); δC (100MHz, d_1-chloroform) 173.3, 173.2, 136.5, 120.9, 60.4, 60.3, 33.2, 32.9, 31.5, 25.2, 14.2, 13.2; m/z HRMS (ESI) found [M+Na]+ 265.1422. $C_{13}H_{22}O_4Na$ requires 265.1416.

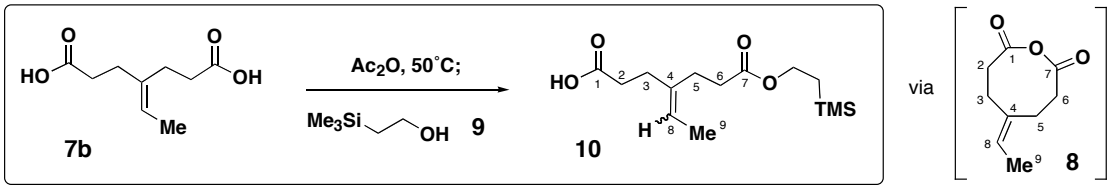
4-ethylideneheptanedioic acid, **7b**



Sodium hydroxide powder (2.97g, 55mmol, 2.1eq) was added to a solution of Wittig product **7a** (6.25g, 26mmol, 1eq) in water:THF:methanol (2:1:1, 120mL). After stirring for 6h at room temperature the reaction mixture was extracted with ethyl acetate (2x150mL). Aqueous sodium bisulphate was added to the aqueous layer until it reached pH 2 when it was further extracted with ethyl acetate (2x1500mL). The combined organic layers were dried ($MgSO_4$) and evaporated to give the crude *diacid* **7b** (4.84g, 26mmol, 100%) as a colourless solid.

TLC R_f 0.10 (50% ethylacetate/cyclohexane); ν_{max}/cm^{-1} (film): 3400-2500 broad (COO-H), 3034-2872 (C-H), 1700 (C=O), 1423, 1410, 1290, 1252, 1210, 1180; δH (400MHz, d_1-chloroform) 5.33 (1H, q, *J* 6.7, H^8), 2.50-2.31 (8H, m, $H^{2,3,5,6}$), 1.69 (3H, d, *J* 6.7, H^9); δC (100MHz, d_1-chloroform) 168.8, 168.7, 134.8, 122.2, 33.9, 33.7, 30.5, 24.4, 13.3; m/z HRMS (ESI) found [M+Na]+ 209.0783. $C_9H_{14}O_4Na$ requires 209.0784.

4-ethylidene-7-oxo-7-(2-(trimethylsilyl)ethoxy)heptanoic acid, **10**



The diacid **7b** (1.00g, 5.4mmol, 1eq) was heated in acetic anhydride (5mL) at 50˚C for 2h. The acetic anhydride was removed *in vacuo*, trimethylsilyl-ethanol **9** (637mg, 5.4mmol, 1eq) was added and the reaction heated at 50˚C for a further 2h. The crude product was purified by flash column chromatography, eluting over a gradient of 0-70% ethylaceate/cyclohexane to give the *acid* **10** (850mg, 2.97mmol, 55%) as a colourless oil.

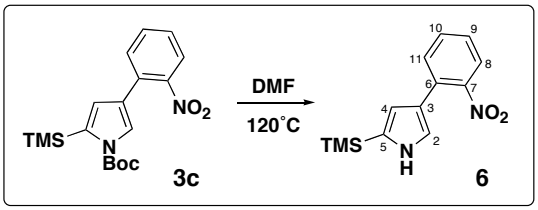
5-ethylideneoxocane-2,8-dione, **8**

ν_{max}/cm^{-1} (film): 2990-2854 (C-H), 1812 and 1744 (C=O), 1440, 1415, 1359, 1026 (C-O-C); δH (400MHz, d_1-chloroform) 5.34 (1H, q, *J* 6.7, H^8), 2.56 (2H, dt, *J* 7.6, 1.0, CH_2^2), 2.52 (2H, dt, *J* 7.8, 1.0, CH_2^6), 2.40 (2H. t, *J* 7.7, CH_2^3), 2.34 (2H, t, *J* 7.4, CH_2^5) 1.61 (3H, d, *J* 6.7, H^9); δC (100MHz, d_1-chloroform) 168.8, 168.7, 134.8, 122.2, 33.9, 33.7, 30.5, 24.4, 13.3.

4-ethylidene-7-oxo-7-(2-(trimethylsilyl)ethoxy)heptanoic acid, **10**

TLC R_f 0.55 (50% ethylacetate/cyclohexane); ν_{max}/cm^{-1} (film): 3300-2500 (COO-H), 2950-2850 (C-H), 1731 (C=O) and 1705 (C=O), 1415, 1244, 1182 (C-O), 834; δH (400MHz, d_1-chloroform) 11.16 (1H, br s, OH), 5.28 (1H, q, *J* 6.7, H^8), 4.17-4.12 (2H, m, O$C\underline{H}_2$), 2.46-2.28 (8H, m, $CH_2^{2,3,5,6}$) 1.59 (3H, d, *J* 6.7, H^9), 0.99-0.94 (2H, m, $C\underline{H}_2$TMS), 0.02 (9H, s, Si($C\underline{H}_3$)$_3$) ; δC (100MHz, d_1-chloroform) 179.4 (2), 173.5, 173.4, 136.2, 136.1, 121.2, 121.0, 62.7, 62.6, 33.3, 33.0, 32.8, 32.6, 31.4, 31.1, 25.2, 24.9, 17.3 (2), 13.2 (2), -1.5 (2); m/z HRMS (ESI) found [M+Na]+ 309.1501. $C_{14}H_{26}O_4SiNa$ requires 309.1498.

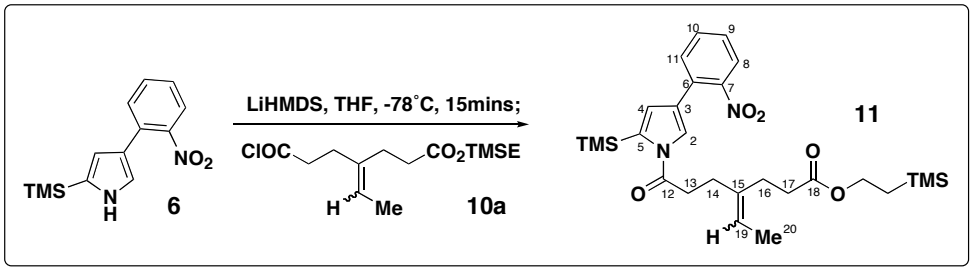
3-(2-nitrophenyl)-5-(trimethylsilyl)-1H-pyrrole, **6**



A solution of 1-*t*-butyl-2-trimethylsilyl-3-(2-nitrophenyl) pyrrole carboxylate **3c** (300mg, 0.83mmol, 1eq) in *N,N*-dimethylformamide (5mL) was heated at 120˚C for 3h under a nitrogen atmosphere. The reaction mixture was cooled to room temperature and poured into water. The aqueous layer was extracted with ethylacetate (2x30mL) and combined organic extracts washed with brine (3-20mL), dried ($MgSO_4$) and evaporated. The crude reaction mixture was purified by flash column chromatography, eluting over a gradient of 25% diethylether/hexane, to give 1-*H*-2-trimethylsilyl-3-(2-nitrophenyl) *pyrrole* **6** (198mg, 0.76mmol, 91%) as a yellow oil.

TLC R_f 0.45 (25% diethylether/cyclohexane); ν_{max}/cm^{-1} (film): 3417 (N-H), 2955-2899 (C-H), 1607 (Ar), 1559, 1521 and 1362 (NO_2), 1249; δH (400MHz, d_1-chloroform) 8.37 (1H, br s, N-H), 7.60 (1H, dd, *J* 8.0, 1.0, H^8), 7.52 (1H, dt, *J* 7.8, 1.0, H^{10}), 7.48 (1H, dd, *J* 7.8, 1.0, H^{11}), 7.29 (1H, ddd, *J* 8.0, 7.2, 1.6, H^9), 7.13 (1H, dd, *J* 2.7, 1.5, H^2), 6.49 (1H, dd, *J* 2.6, 1.5, H^4), 0.28 (9H, s, $Si(CH_3)_3$); δC (100MHz, d_1-chloroform) 149.0, 132.1, 131.5, 131.0, 129.7, 126.2, 123.3, 120.6, 119.6, 117.0, -0.9; m/z HRMS (ESI) found [M+H]+ 261.1069, $C_{13}H_{17}N_2O_2Si$ requires 261.1059.

(E/Z) 2-(trimethylsilyl)ethyl 4-ethylidene-7-(3-(2-nitrophenyl)-5-(trimethylsilyl)-1H-pyrrol-1-yl)-7-oxoheptanoate, **11**

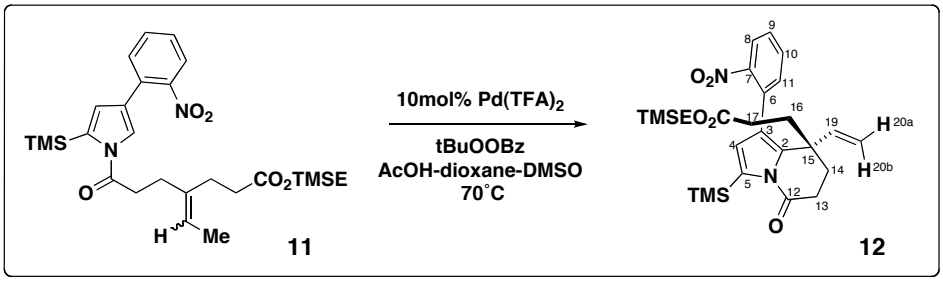


i) *N,N*-dimethylformamide (2 drops) and oxalyl chloride (404μL, 4.56mmol, 1.3eq) were added to a solution of acid **10** (1.00g, 3.50mmol, 1eq) in dichloromethane (10mL). The reaction was stirred at 0˚C for a further 2.5h before solvents were removed *in vacuo* to give the crude acid chloride **10a** as a colorless oil.

ii) Lithium bis(trimethylsilyl)amide (1.0M in THF) (1.75mL, 1.75mmol, 1.0eq) was added to a stirred solution of pyrrole **6** (455mg, 1.75mmol, 1.0eq) in THF (10mL) at -78˚C. After stirring for 10 mins at -78˚C the crude acid chloride **10a** (1.06g, 3.5mmol, 2.0eq) dissolved in THF (20mL) was added and the reaction mixture stirred for a further 30 mins at -78˚C before being allowed to warm to 0˚C. The reaction mixture was poured into ice cold water and extracted with ethyl acetate (50mL). The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated. The crude reaction mixture was purified by flash column chromatography, eluting over a gradient of 0-20% diethylether/cyclohexane, to give *acyl-pyrrole* **11** (702mg, 1.33mmol, 76%) as a yellow oil.

TLC R_f 0.70 (25% diethylether/cyclohexane); ν_{max}/cm^{-1} (film): 2953-2899 (C-H), 1720 (C=O), 1610 (Ar), 1576, 1527 and 1366 (NO_2), 1246; δH (400MHz, d_1-chloroform) 7.72 (2x1H, 2xd, *J* 8.1, H^8), 7.55 (2x1H, 2xdt, *J* 7.7, 1.3, H^{10}), 7.50 and 7.51(2x1H, 2xdd, *J* 7.7, 1.8, H^{11}), 7.44 and 7.43 (2x1H, 2xd, *J* 1.5, H^2), 7.40 (2x1H, 2xddd, *J* 8.0, 7.4, 1.6, H^9), 6.54 (2x1H, 2xd, *J* 1.4, H^4), 5.32 (2x1H, 2xq, *J* 6.1, H^{19}), 4.15 (2x2H, m, $CO_2C\underline{H}_2$), 2.94 (2x2H, 2xt, *J* 7.8, $C\underline{H}_2{}^{13}$), 2.52-2.35 (2x6H, m, $C\underline{H}_2{}^{14,16,17}$), 1.62 and 1.60, (2x3H, 2xd, *J* 6.1, $C\underline{H}_3{}^{20}$), 0.98 (2x2H, m, $C\underline{H}_2TMS$), 0.27 and 0.25 (2x9H, 2xs, $Si(C\underline{H}_3)_3$), 0.03 (2x9H, 2xs, $CO_2CH_2CH_2Si(C\underline{H}_3)_3$); δC (100MHz, d_1-chloroform) 173.4 (2), 170.6 (2), 149.1 (2), 136.1 (3), 136.0, 132.0 (2), 131.2 (2), 128.5 (2), 127.7 (2), 124.2, 124.1, 124.0, 123.9, 123.8 (2), 121.7, 121.6, 121.5, 121.4, 62.7, 62.6, 33.7, 33.3 (2), 33.0, 31.6, 31.1, 25.2, 24.9, 17.3 (2), 13.3 (2), -0.45, -0.46, -1.49 (2); m/z HRMS (ESI) found [M+H]+ 529.2557, $C_{27}H_{41}N_2O_5Si_2$ requires 529.2554.

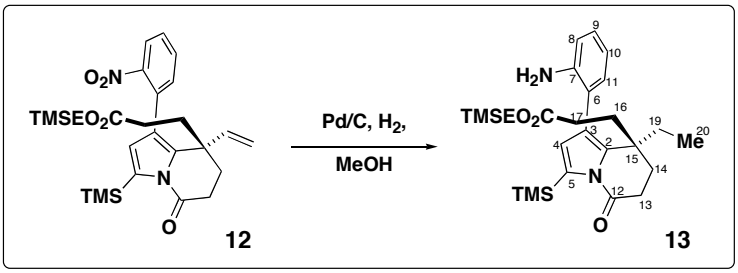
2-(trimethylsilyl)ethyl 3-(-(2-nitrophenyl)-5-oxo3-(trimethylsilyl)-8-vinyl-5,6,7,8-tetrahydroinindolozin-8-yl) propanoate, **12**



Solutions of acyl-pyrrole **11** (35mg, 0.07mmol, 0.9eq) in dioxane-dimethylsulfoxide (9:1, 0.35mL) and *t*-butylperoxybenzoate (15mg, 0.08mmol, 1.0eq) in dioxane-AcOH (3:1, 0.35mL) were added dropwise over 18h to a sealed flask containing palladium trifluoroacetate (2.5mg, 0.01mmol, 10mol%), *t*-butylperoxybenzoate (3mg, 0.02mmol, 0.2eq) and acyl-pyrrole **11** (5mg, 0.01mmol, 0.1eq). The reaction mixture was heated at 70˚C for a total 24h (85% conversion). The crude mixture was then filtered through a plug of celite and diluted with ethyl acetate (50mL). The organic layer was washed with saturated aqueous sodium bicarbonate (2x 10mL) and brine (10mL) then dried ($MgSO_4$) and evaporated. The crude product was purified by flash column chromatography, eluting with 15% diethylether/40-60 petroleum ether, to give *pyrrole* **12** (21mg, 0.04mmol, 53%) as a yellow oil.

TLC R_f 0.50 (25% diethylether/cyclohexane); ν_{max}/cm^{-1} (film): 2954-2899 (C-H), 1718 (C=O), 1615 (Ar), 1572, 1527 and 1355 (NO_2), 1318, 1246, 1165; δH (500MHz, d_6-dimethylsulfoxide at 373 K) 7.96 (1H, d *J* 8.0, H^8), 7.65 (1H, t, *J* 7.3, H^{10}), 7.59 (1H, t, *J* 7.4, H^9), 7.48 (1H, d, *J* 7.5, H^{11}), 6.34 (1H, s, H^4), 5.82 (1H, dd, *J*, 17.4, 10.7, H^{19}), 5.11 (1H, d, *J* 10.7, H^{20a}), 4.73, (1H, d, *J* 17.4, H^{20b}), 4.01 (2H, t, *J* 8.0, $CO_2C\underline{H}_2$), 2.75 (2H, t, *J* 5.6, $C\underline{H}_2{}^{13}$), 2.17 (2H, t, *J* 7.9, $\underline{H}^{16',17'}$), 2.08 (1H, quintet, *J* 7.5, H^{14}), 1.93-1.85 (2H, m, $H^{17,14'}$), 1.76 (1H, m, H^{16}), 0.86 (2H, t, *J* 8.0, $C\underline{H}_2$TMS), 0.24 (9H, s, TMS), 0.02 (9H, s, CO_2Et-TMS); δH (400MHz, d_1-chloroform at RT) 7.90 (1H, d, *J* 7.3, H^8), 7.54-7.43 (3H, m, $H^{9,10,11}$), 6.30 (1H, br s, H^4), 5.76 (1H, br s, H^{19}), 5.22 (1H, br s, H^{20A}), 4.75 (1H, d, *J* 17.3, H^{20B}), 3.99 (2H, br t, *J* 7.8, $CO_2C\underline{H}_2$), 2.81 (1H, ddd, *J* 17.3, 11.9, 5.0, H^{13A}), 2.68 (1H, dt, *J* 17.6, 4.2, H^{13B}), 2.38-1.95 (4H, br m, $H^{17, 17', 16', 14}$), 1.93-1.70 (2H, br m, $H^{16, 14'}$), 0.87 (2H, br t, *J* 7.8, $C\underline{H}_2$TMS), 0.25 (9H, s, $Si(C\underline{H}_3)_3$), 0.01 (9H, s, $CO_2EtSi(C\underline{H}_3)_3$); δC (100MHz, d_6-dimethylsulfoxide at 373 K) 172.5, 168.8, 149.9, 142.6, 136.9, 133.5, 132.5, 132.0, 130.4, 129.4, 126.6, 124.4, 121.2, 115.5, 62.1, 42.9, 32.2, 29.9, 29.5, 29.2, 17.5, 0.3, -1.1; m/z HRMS (ESI) found [M+H]+ 527.2390, $C_{27}H_{39}N_2O_5Si_2$ requires 527.2392.

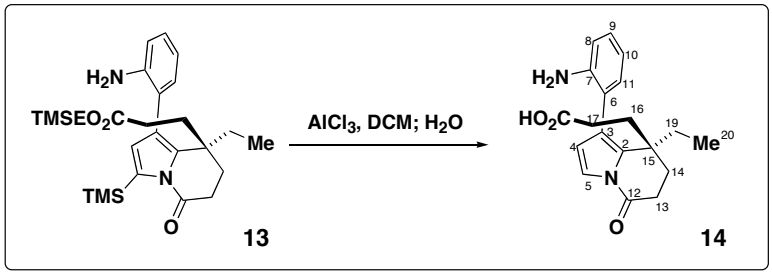
2-(trimethylsilyl)ethyl 3-(1-(2-aminophenyl)-8-ethyl-5-oxo-3-(trimethylsilyl)-5,6,7,8-tetrahydroindolizin-8-yl) propanoate, **13**



Pyrrole **12** (52mg, 0.10mmol, 1.0eq) was dissolved in methanol (3mL) and added to a sealed flask with 10% palladium on activated carbon (5mg). The flask was flushed with hydrogen gas and the reaction mixture stirred under a hydrogen atmosphere for 1h. The crude reaction mixture was filtered through a plug of Celite and solvents evaporated to give *pyrrole* **13** (50mg, 0.10mmol, 100%) as a colorless oil.

TLC R_f 0.70 (25% diethylether/cyclohexane); ν_{max}/cm^{-1} (film): 3474 and 3377 (NH_2), 2959-2850 (C-H), 1717 (C=O), 1616 (Ar), 1578, 1495, 1456, 1417, 1363, 1317, 1260, 1249; Starts to decompose (-TMS) at temperatures above 373 K, rotameric at temperatures below 373 K. δH (500MHz, d_6-dimethylsulfoxide at 403 K) 7.04 (1H, dd, *J* 7.0, 1.5, H^{11}), 6.98 (1H, dt, *J* 6.6, 1.7, H^{9}), 6.73 (1H, dd, *J* 8.0, 1.0, H^{8}), 6.59 (1H, dt, *J* 7.4, 1.2, H^{10}), 6.29 (1H, s, H^{4}), 4.09 (2H, t, *J* 8.0, $CO_2C\underline{H}_2$), 2.77 (2H, t, *J* 6.3, $C\underline{H}_2{}^{13}$), 2.51-2.12 (2H, m, $H^{16,17}$), 1.97-1.85 (4H, m, $H^{16', 17', 14, 14'}$), 1.70 (1H, dq, *J* , H^{19}), 1.59 (1H, dq, *J* , H19'), 0.93 (2H, t, *J* 8.0, $C\underline{H}_2$TMS), 0.78 (3H, t, *J* , $C\underline{H}_3{}^{20}$), 0.25 (9H, s, TMS), 0.04 (9H, s, $CO_2Et\underline{TMS}$); δH (400MHz, d_1-chloroform at 300K) 7.12 and 7.11 (2x1H, 2xdt, *J* 7.4, 1.6, H^{9}), 7.08 (2x1H, 2xd, *J* 7.4, H^{11}), 6.74-6.68 (2x2H, m, $H^{8,10}$), 6.37 and 6.33 (2x1H, 2xs, H^{2}), 4.11 and 4.03 (2x2H, 2xdd, *J* 8.6, 10.2, $CO_2C\underline{H}_2$), 3.66 and 3.61 (2x2H, br s, NH_2), 2.78-2.73 (2x2H, m, $C\underline{H}_2{}^{13}$), 2.21-2.14 (2x2H, m, $C\underline{H}_2{}^{17}$), 1.95-1.82 (2x4H, m, $H^{14,16}$), 1.66-1.61 (2x2H, m, $C\underline{H}_2CH_3$), 1.62 and 1.60, (2x3H, 2xd, *J* 6.1, $C\underline{H}_3{}^{20}$), 0.96 and 0.78 (2x2H, 2xt, *J* 7.4, $C\underline{H}_2$TMS), 0.88 (2x3H, 2xt, *J* 7.6, $CH_2C\underline{H}_3$), 0.25 (2x9H, 2xs, $Si(C\underline{H}_3)_3$), 0.04 and 0.02 (2x9H, 2xs, $CO_2CH_2CH_2Si(C\underline{H}_3)_3$); δC (100MHz, d_1-chloroform at 300K) 173.7, 173.5, 168.8, 144.0 (br), 139.2, 133.2, 131.0, 130.8, 128.7 (2), 127.4, 127.1, 121.4 (t, 3), 118.1 (br), 115.5 (br), 62.7, 62.6, 39.1, 39.0, 32.3, 31.9, 30.6, 30.2, 29.5, 29.2, 28.0, 27.8, 17.3 (2), 9.0, 8.5, -0.2, -1.5; m/z HRMS (ESI) found [M+H]+ 499.2829, $C_{27}H_{43}N_2O_3Si_2$ requires 499.2812.

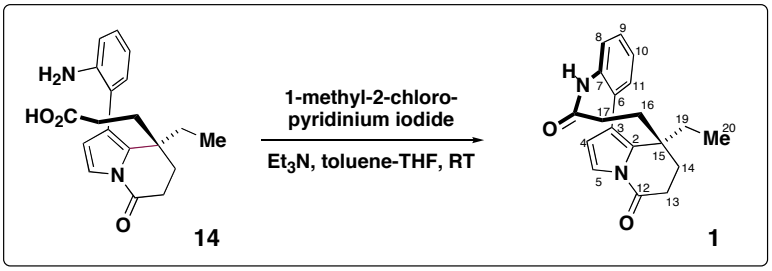
3-(1-(2-aminophenyl)-8-ethyl-5-oxo-5,6,7,8-tetrahydroindolizin-8-yl)propanoic acid, **14**



Aluminium chloride (68mg, 0.50mmol, 5.0eq) was added to a solution of pyrrole **13** (50mg, 0.10mmol, 1.0eq) in dichloromethane (5mL) at 0˚C. The reaction mixture was stirred at 0˚C for a further 2h before water (10mL) was added. The mixture was extracted with ethyl acetate (2x100mL) and organic layers were combined, dried ($MgSO_4$) and evaporated. The amino-acid product **14** could be used crude or purified by flash column chromatography, eluting over a gradient of 0-20% methanol/dichloromethane to give *amino acid* **14** (29mg, 0.09mmol, 90%) as a colorless oil.

TLC R_f 0.40 (10% methanol/dichloromethane); ν_{max}/cm^{-1} (film): 3520 and 3480 br (N-H), 2941-2875 (C-H), 1711 (C=O), 1617, 1583, 1504, 1481, 1451, 1396, 1372, 1307; δH (500MHz, d_6-dimethylsulfoxide at 373K) 7.42 (1H, d, *J* 3.3, H^5), 7.04 (1H, ddd, *J* 8.0, 7.5, 1.5, H^9), 6.98 (1H, dd, *J* 7.5, 1.5, H^{11}), 6.72 (1H, dd, *J* 8.0, 1.0, H^8), 6.58 (1H, dt, *J* 7.3, 1.1, H^{10}), 6.10 (1H, d, *J* 3.3, H^4), 3.00 (3H, br s, O<u>H</u>, N<u>H</u>$_2$), 2.75 (1H, t, *J* 6.6, CH_2^{13}), 2.19-2.07 (2H, m, CH_2^{17}), 1.96-1.79 (4H, m, $CH_2^{14,16}$), 1.68 (1H, dq, *J* 14.8, 7.3, $H^{19'}$), 1.56 (1H, dq, *J* 14.8, 7.3, H^{19}), 0.76 (3H, t, *J* 7.3, C<u>H</u>$_3^{20}$); δC (100MHz, d_6-dimethylsulfoxide at 373K) 174.4, 168.3, 146.5, 135.3, 130.8, 128.6, 121.5, 120.9, 116.7, 116.4, 116.0, 115.0, 55.1, 49.0, 38.9, 29.7, 28.8, 20.0, 9.2; m/z HRMS (ESI) found [M+H]+ 327.1712. $C_{19}H_{23}N_2O_3$ requires 327.1709.

3-*oxo-rhazinilam*, **1**



Crude amino-acid pyrrole **14** (30mg, 0.09mmol, 1.0eq) dissolved in THF:toluene (3:2,17mL) was added dropwise via a syringe pump over 12h to a stirred solution of 1-methyl-2-chloro-pyridinium iodide (234mg, 0.90mmol, 10eq) and triethylamine (250μL, 1.80mmol, 20eq) in toluene (12mL). The reaction mixture was stirred for a further 2h at room temperature, before being was filtered and washed with toluene. The filtrate was evaporated and the crude product purified by flash column chromatography, eluting over a gradient of 0-10% methanol in dichloromethane, to give 3-oxo-rhazinilam **1** (22mg, 0.07mmol, 74% over 3 steps) as a brown oil.

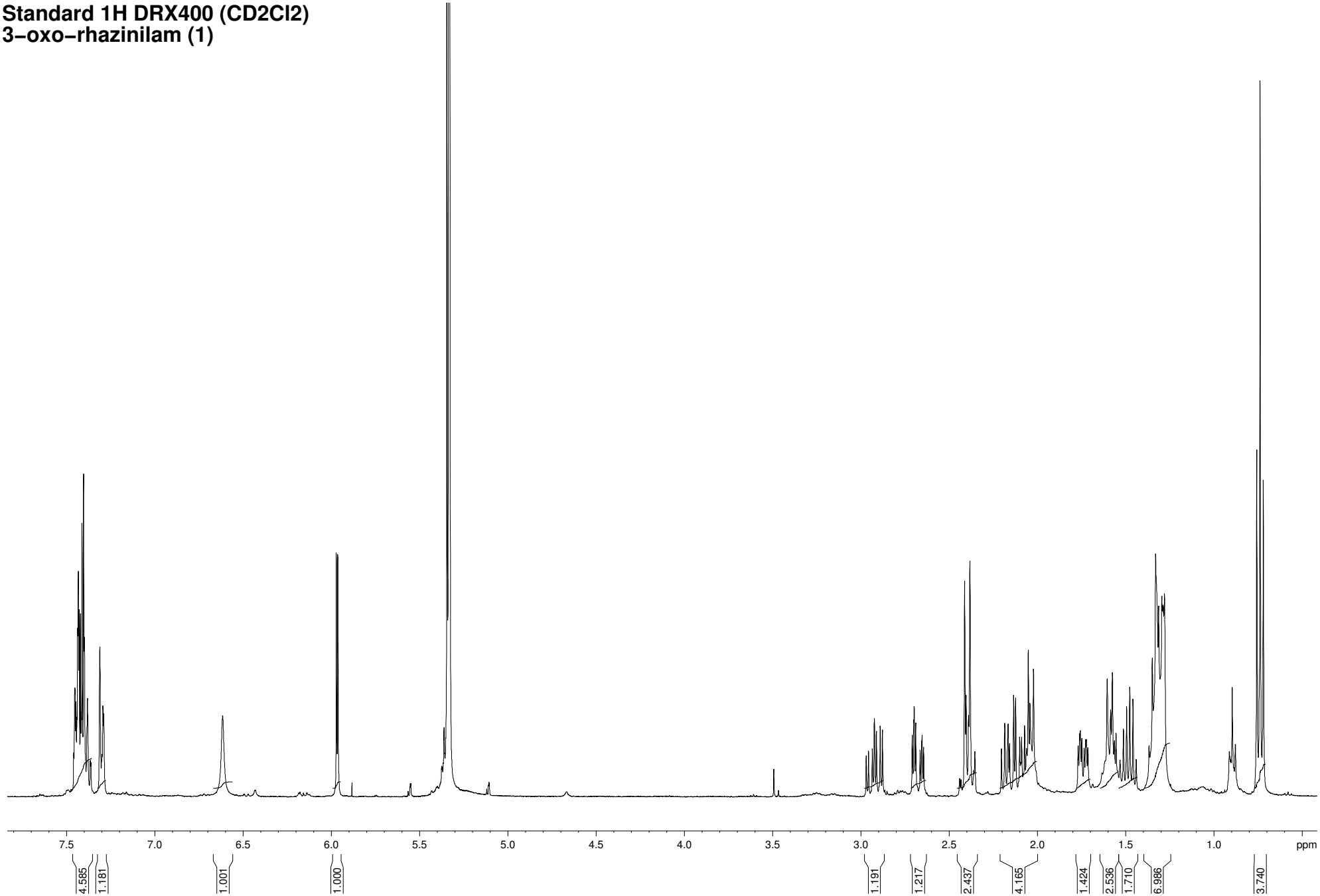
TLC R_f 0.25 (70% ethylacetate/cyclohexane); ν_{max}/cm^{-1} (film): 3240 br (N-H), 2972-2875 (C-H), 1718 (C=O), 1667 (amide C=O), 1579, 1506, 1445, 1403, 1370, 1313; δH (700MHz, d_2-dichloromethane) 7.41-7.44 (2H, m, H^9 and H^{11}), 7.39 (1H, d, *J* 3.3, H^5), 7.37 (1H, ddt, *J* 7.5, 1.4, 0.6, H^{10}), 7.29 (1H, m, H^8), 6.61 (1H, br s, N-H), 5.95 (1H, d, *J* 3.3, H^4), 2.91 (1H, ddd, *J* 17.9, 13.7, 5.2, H^{13a}), 2.66 (1H, ddd, *J* 17.9, 4.5, 3.3, H^{13b}), 2.40 (2H, m, $H^{16'}$, $H^{17'}$), 2.11 (1H, dt, *J* 13.7, 4.6, H^{14a}), 2.03 (1H, dd, *J* 12.3, 8.1, H^{17}), 1.72 (1H, ddd, *J* 13.6, 5.0, 3.3, H^{14b}), 1.57 (1H, dd, *J* 12.4, 8.0, H^{16}), 1.47 (1H, dq, *J* 14.8, 7.4, $H^{19'}$), 1.32 (1H, m, H^{19}), 0.74 (3H, t, *J* 7.4, $C\underline{H}_3{}^{20}$); δC (100MHz, d_2-dichloromethane) 176.4, 168.3, 137.9, 137.6, 134.1, 130.8, 129.3, 128.1, 128.1, 122.5, 116.5, 115.1, 38.7, 34.0, 32.2, 30.0, 29.5, 28.6, 8.2; m/z HRMS (ESI) found [M+H]+ 309.1606. $C_{19}H_{21}N_2O_2$ requires 309.1603.

Data consistent with natural product literature. Ref: *J. Nat. Prod.* **2001**, *64,* 114-116

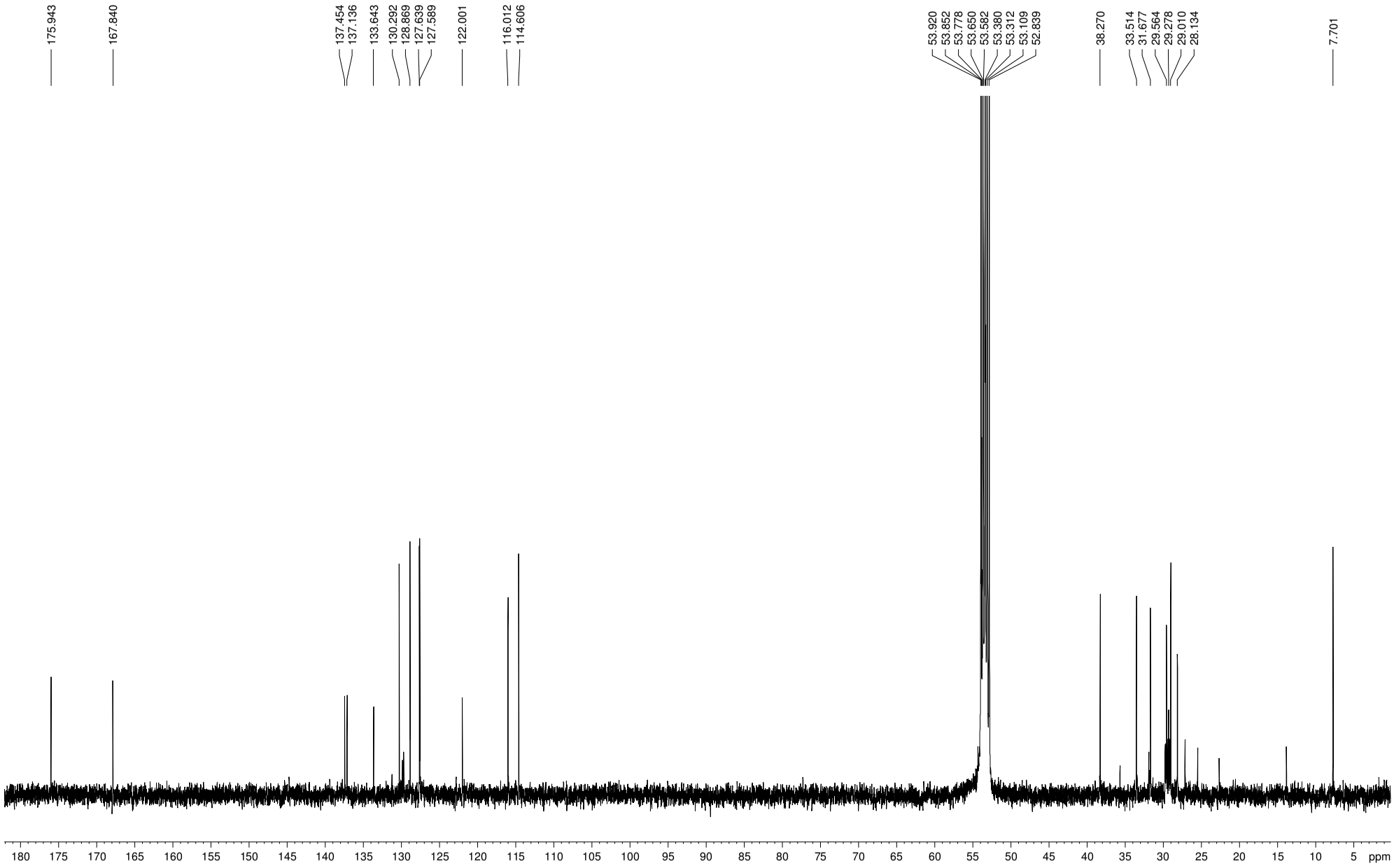
Comparison of ^{13}C NMR spectra for the natural and synthetic samples of 3-oxo-rhazinilam

Carbon no.	Natural δ (ppm)	Synthetic δ (ppm)	δδ (ppm)
18	176.4	176.4	0.0
12	168.3	168.3	-0.1
7	138.0	137.9	-0.1
2	137.7	137.6	0.0
6	134.1	134.1	0.0
9	130.8	130.8	0.0
11	129.3	129.3	0.0
10	128.1	128.1	0.0
8	128.1	128.1	0.0
3	122.5	122.5	0.0
5	116.5	116.5	0.0
4	115.1	115.1	0.0
15	38.8	38.7	-0.1
16	34.0	34.0	0.0
14	32.2	32.2	0.0
19	30.1	30.0	-0.1
13	29.5	29.5	0.0
17	28.7	28.6	-0.1
20	8.1	8.2	+0.1

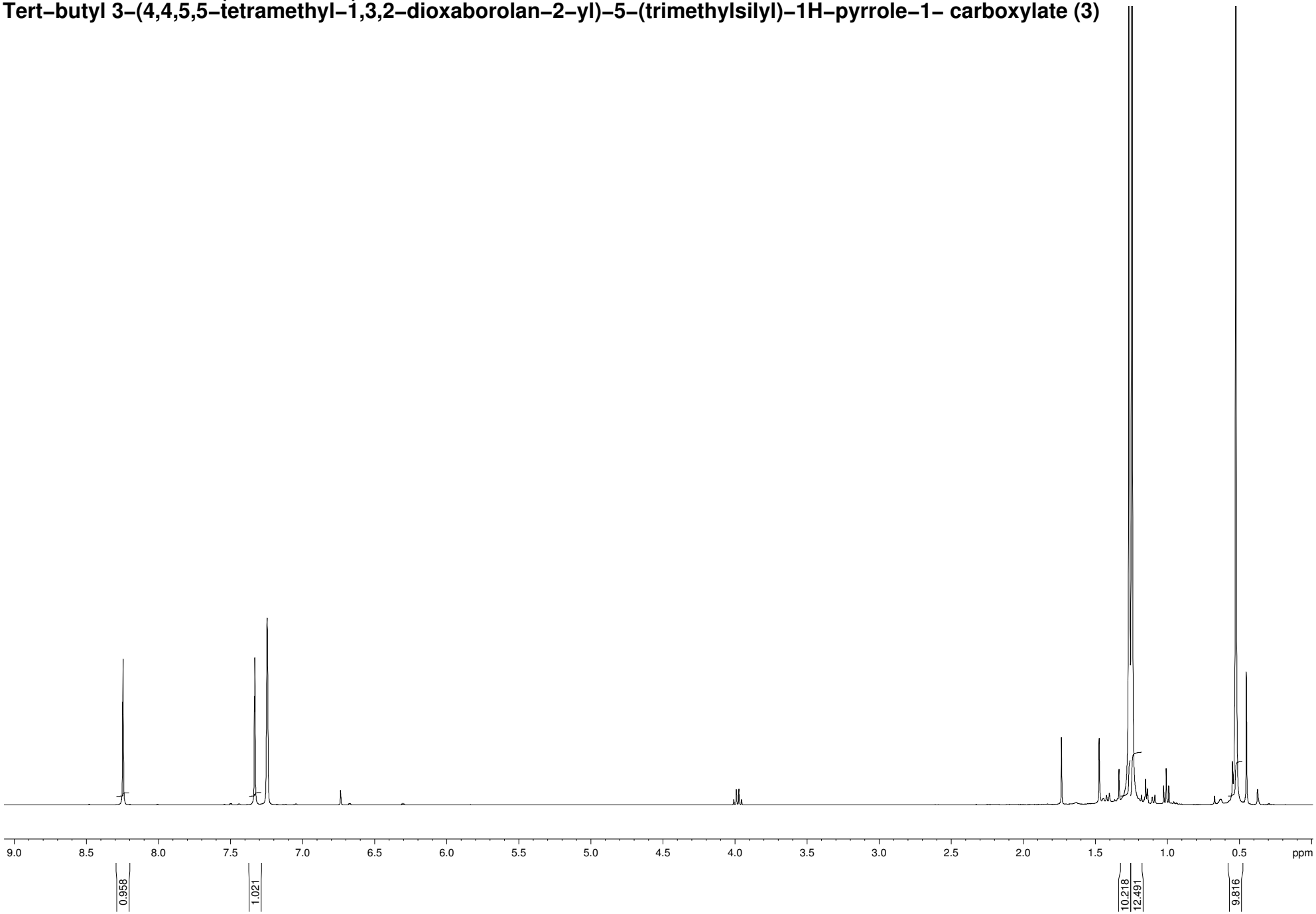
Standard 1H DRX400 (CD2Cl2)
3−oxo−rhazinilam (1)



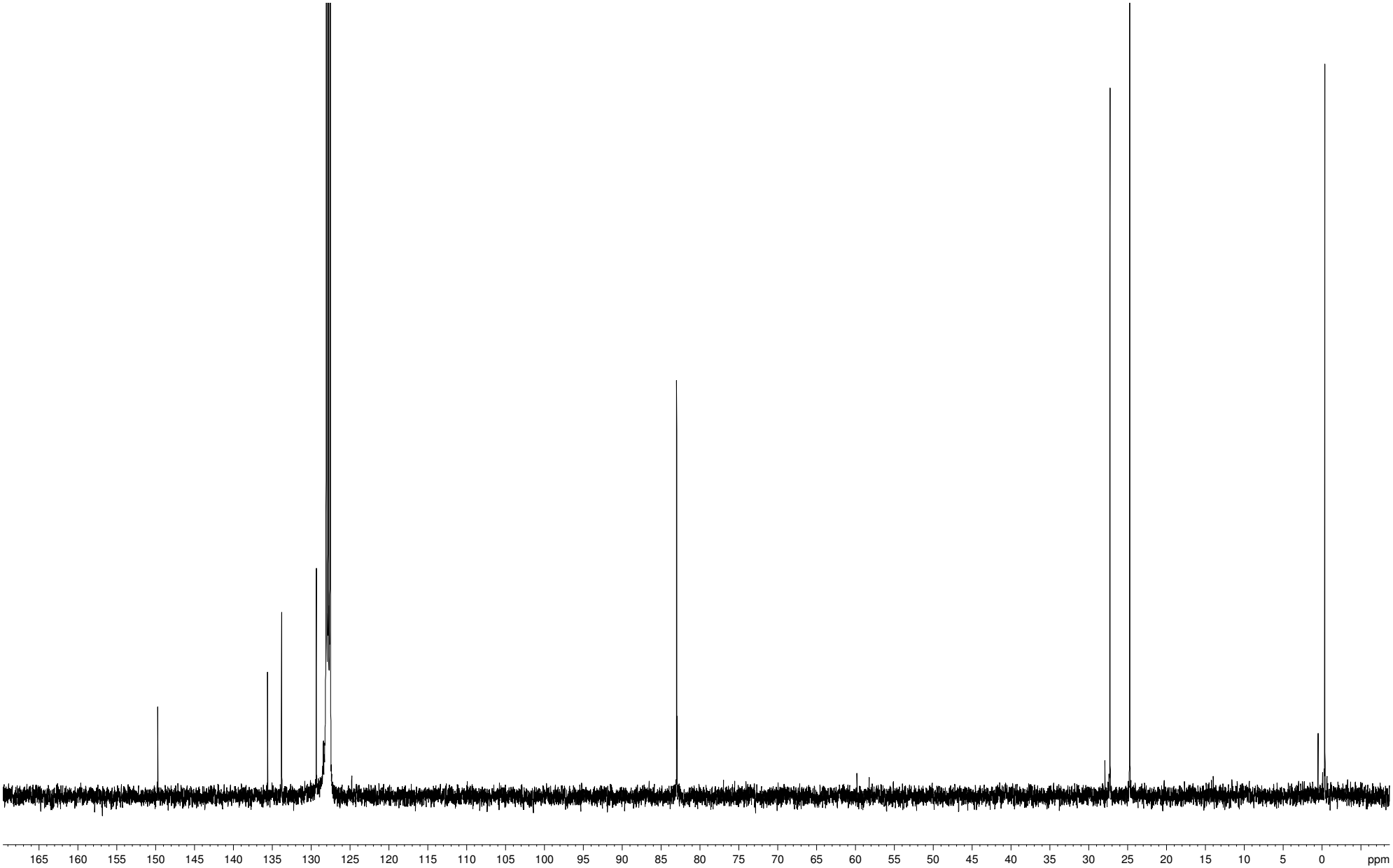
Standard 13C DRX400 (CD2Cl2)
3−oxo−rhazinilam (1)



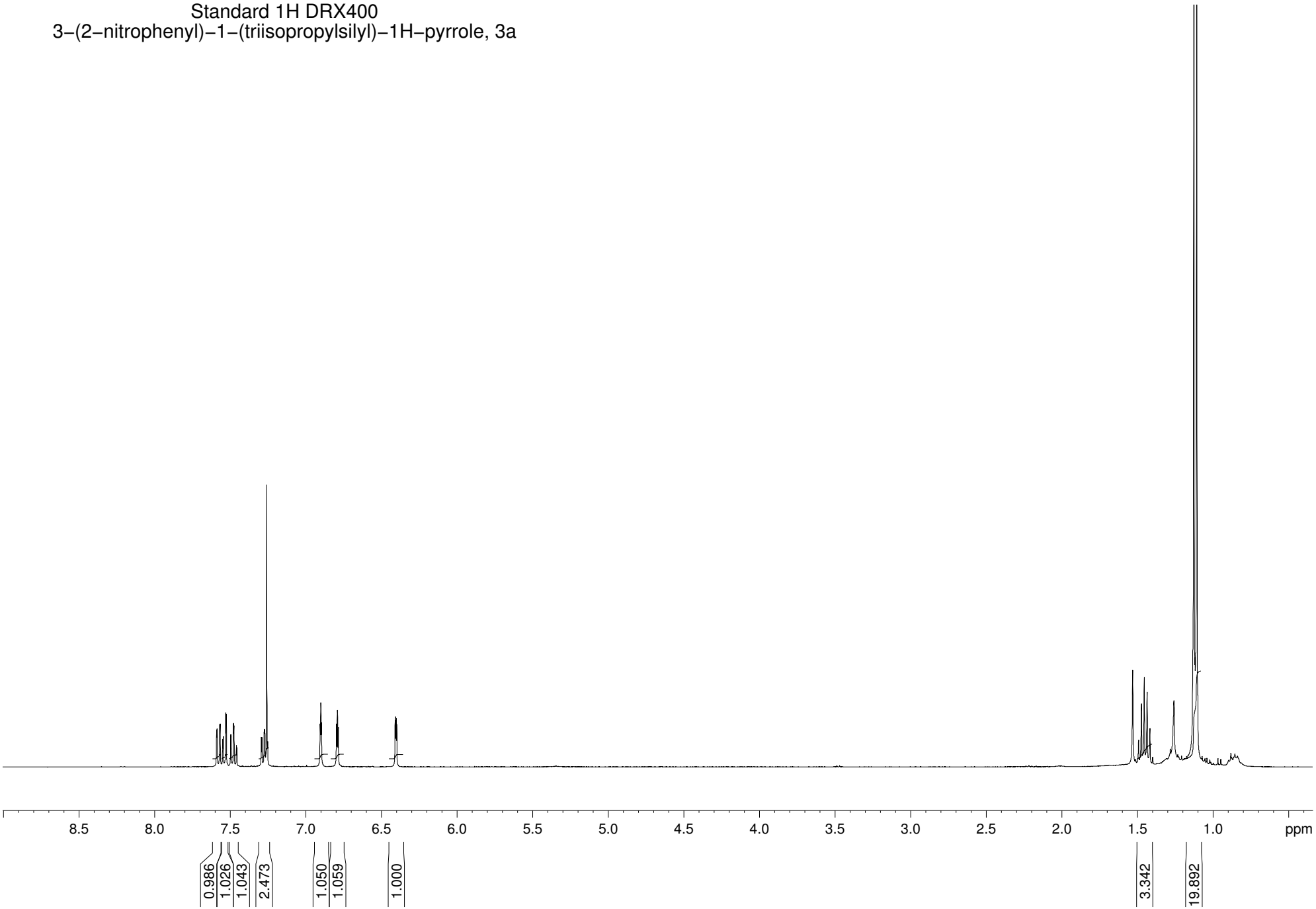
Standard 1H DRX400 (D6-benzene)
Tert-butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5-(trimethylsilyl)-1H-pyrrole-1- carboxylate (3)

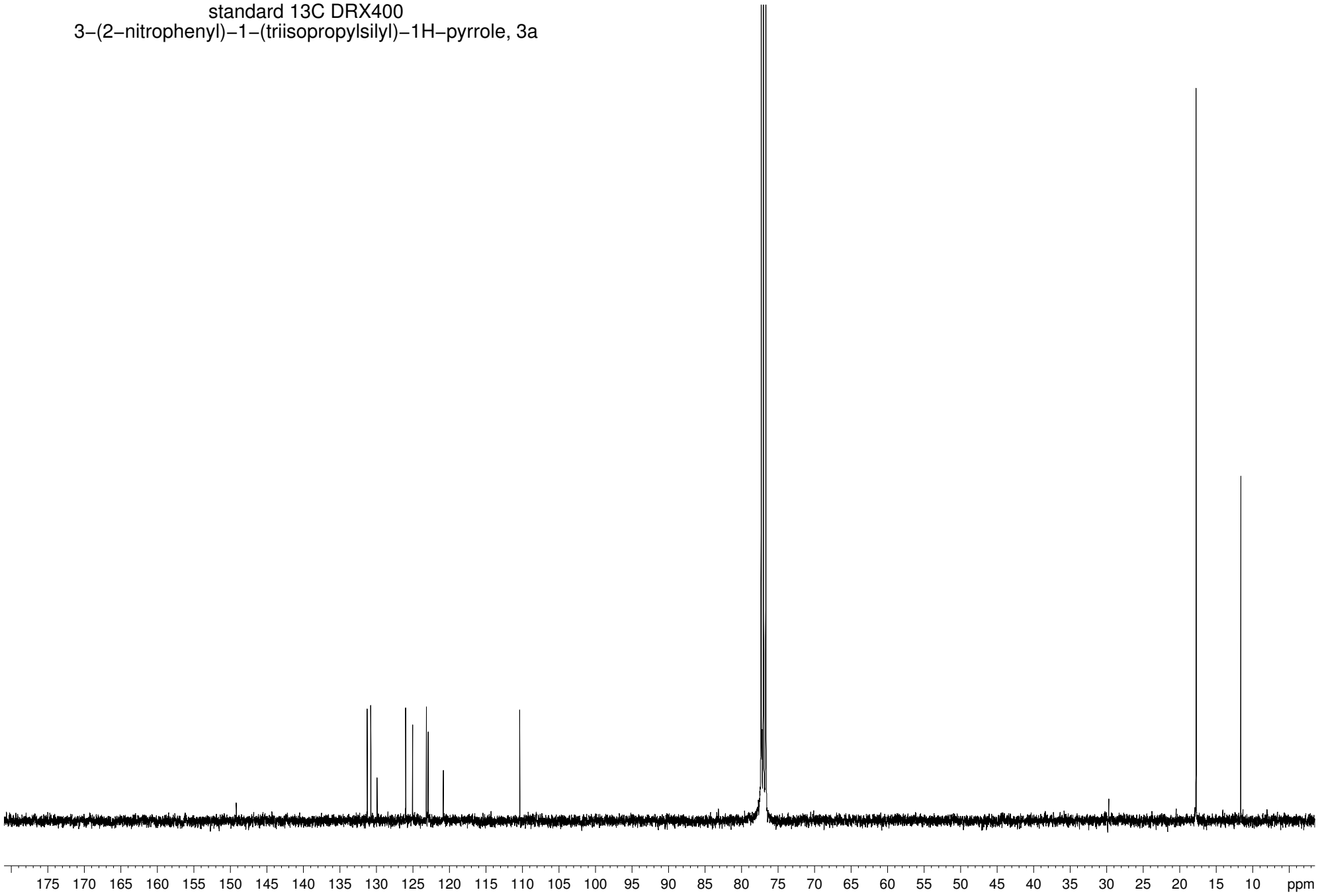


Standard 13C DRX400 (D6–benzene)
Tert–butyl 3–(4,4,5,5–tetramethyl–1,3,2–dioxaborolan–2–yl)–5–(trimethylsilyl)–1H–pyrrole–1– carboxylate (3)

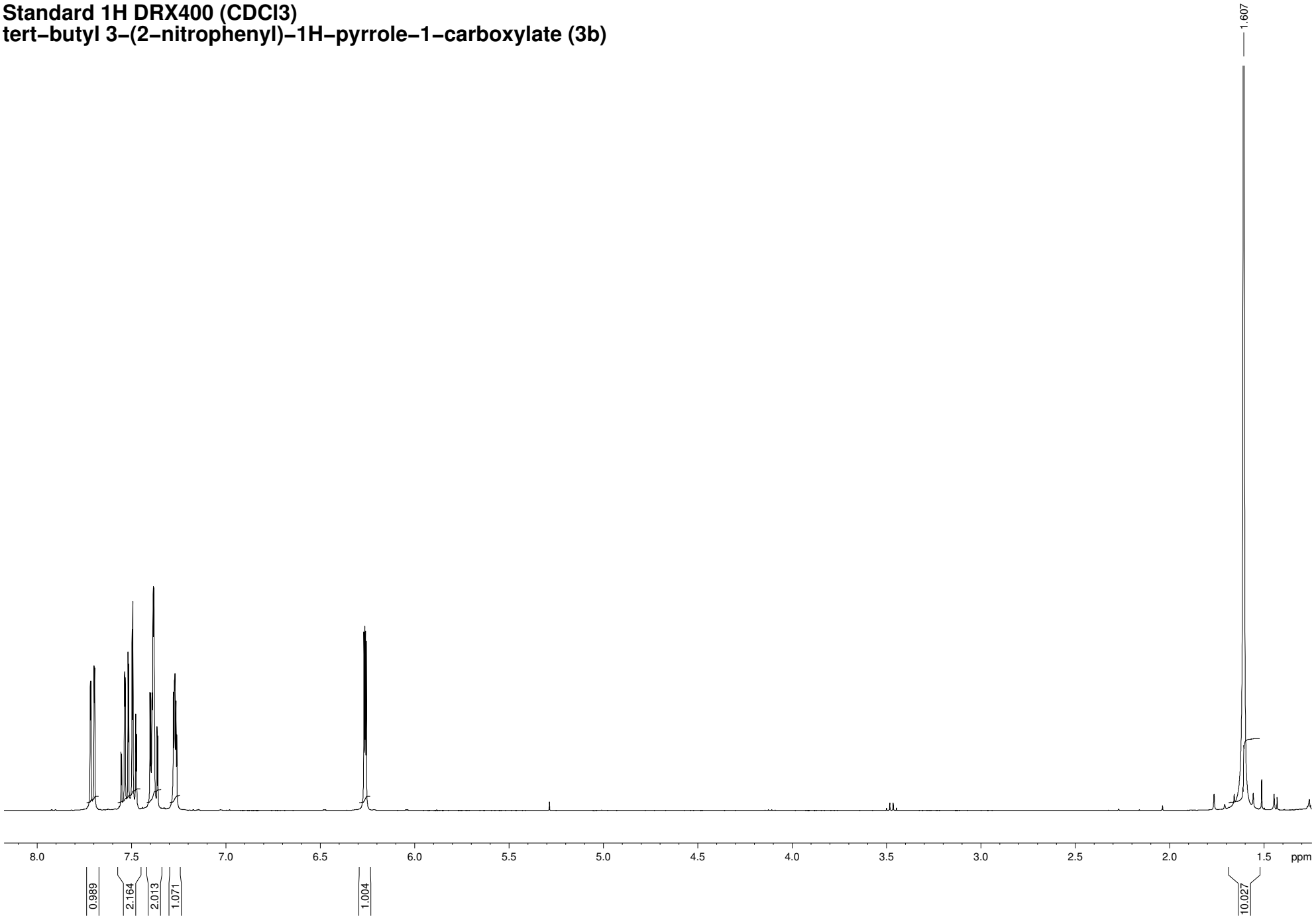


Standard 1H DRX400
3–(2–nitrophenyl)–1–(triisopropylsilyl)–1H–pyrrole, 3a

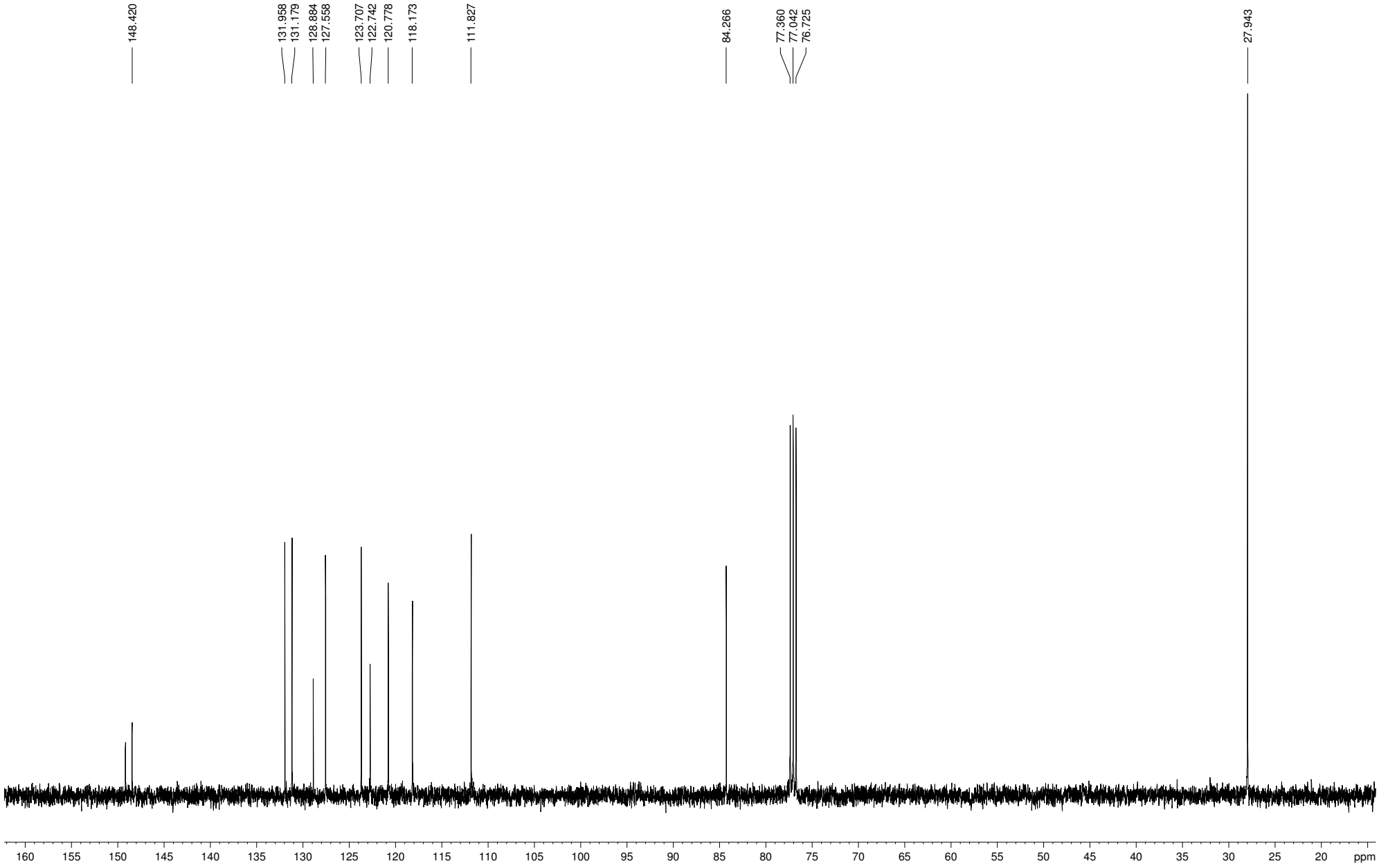



standard 13C DRX400
3–(2–nitrophenyl)–1–(triisopropylsilyl)–1H–pyrrole, 3a
175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 ppm

Standard 1H DRX400 (CDCl3)
tert−butyl 3−(2−nitrophenyl)−1H−pyrrole−1−carboxylate (3b)

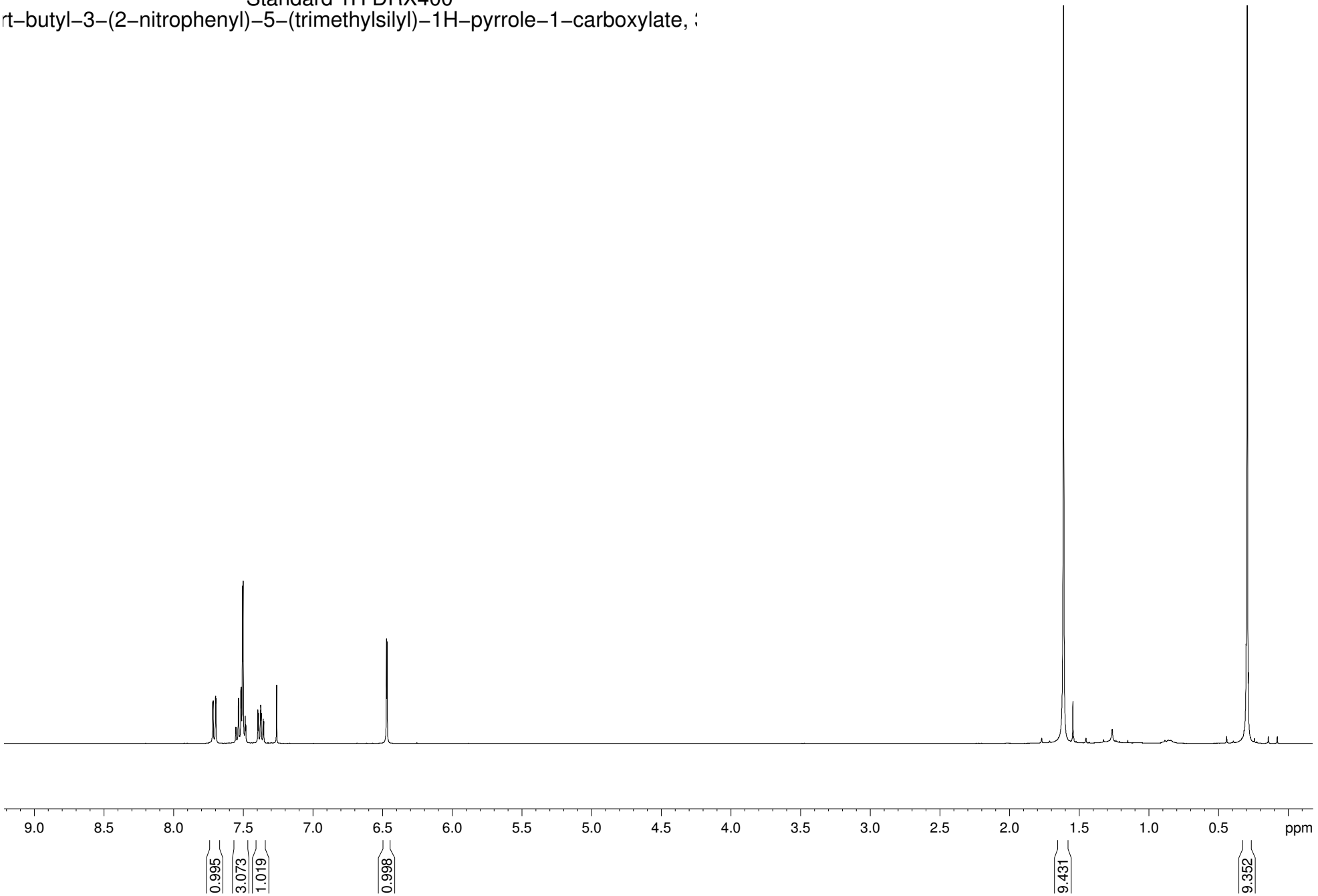


Standard 13C DRX400 (CDCl3)
tert−butyl 3−(2−nitrophenyl)−1H−pyrrole−1−carboxylate (3b)

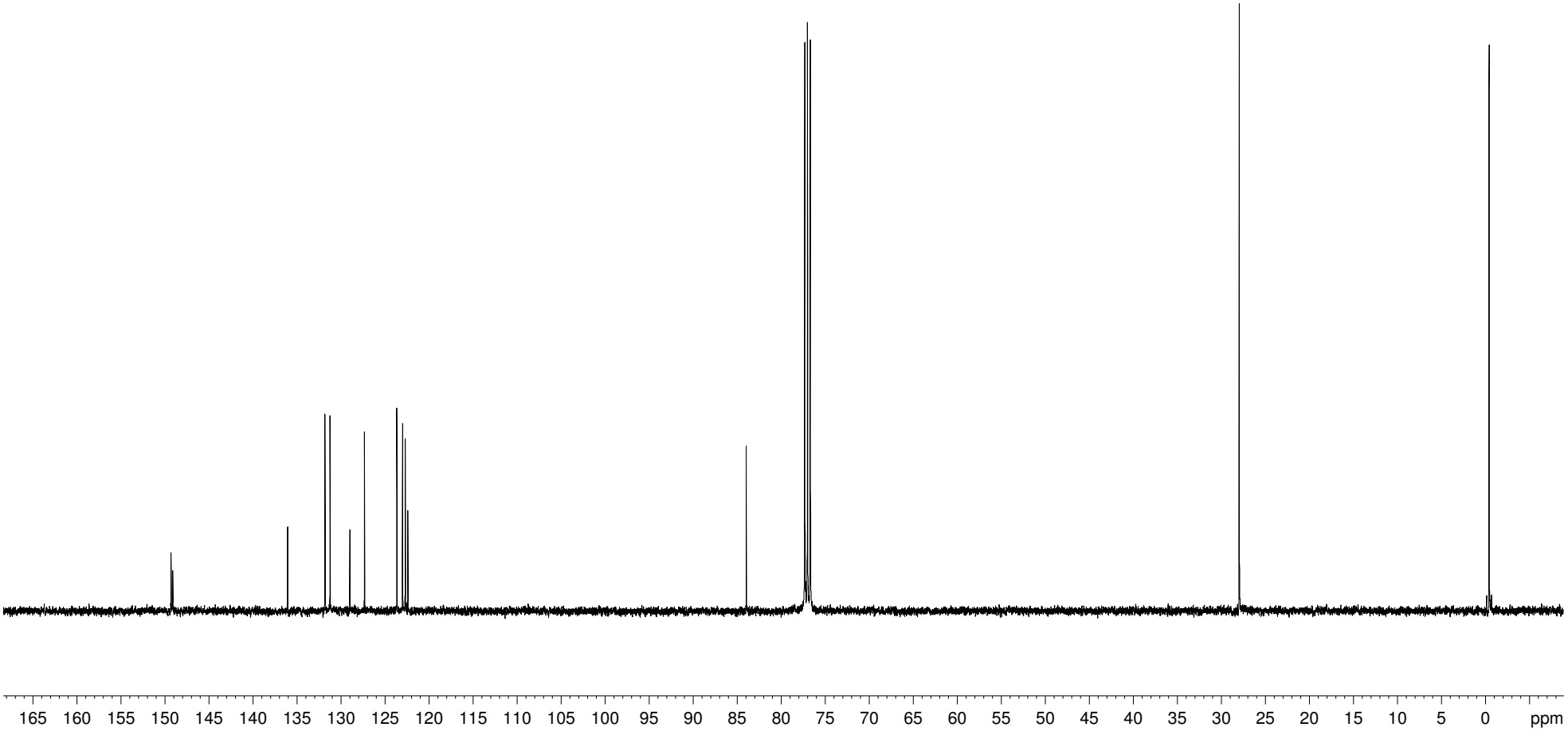


Standard 1H DRX400

rt–butyl–3–(2–nitrophenyl)–5–(trimethylsilyl)–1H–pyrrole–1–carboxylate, 3

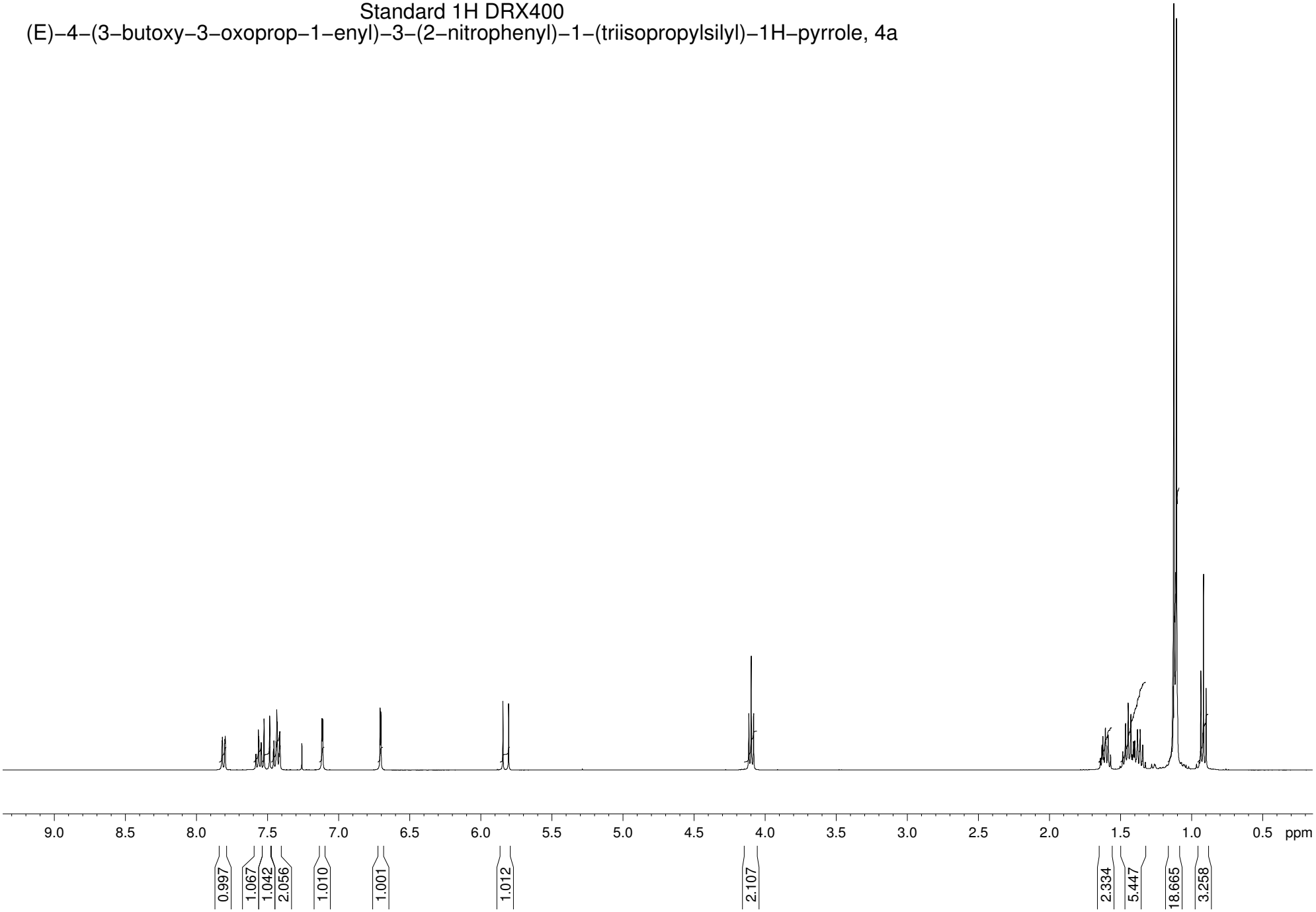


Standard 13C DRX400
tert−butyl−3−(2−nitrophenyl)−5−(trimethylsilyl)−1H−pyrrole−1−carboxylate, 3c

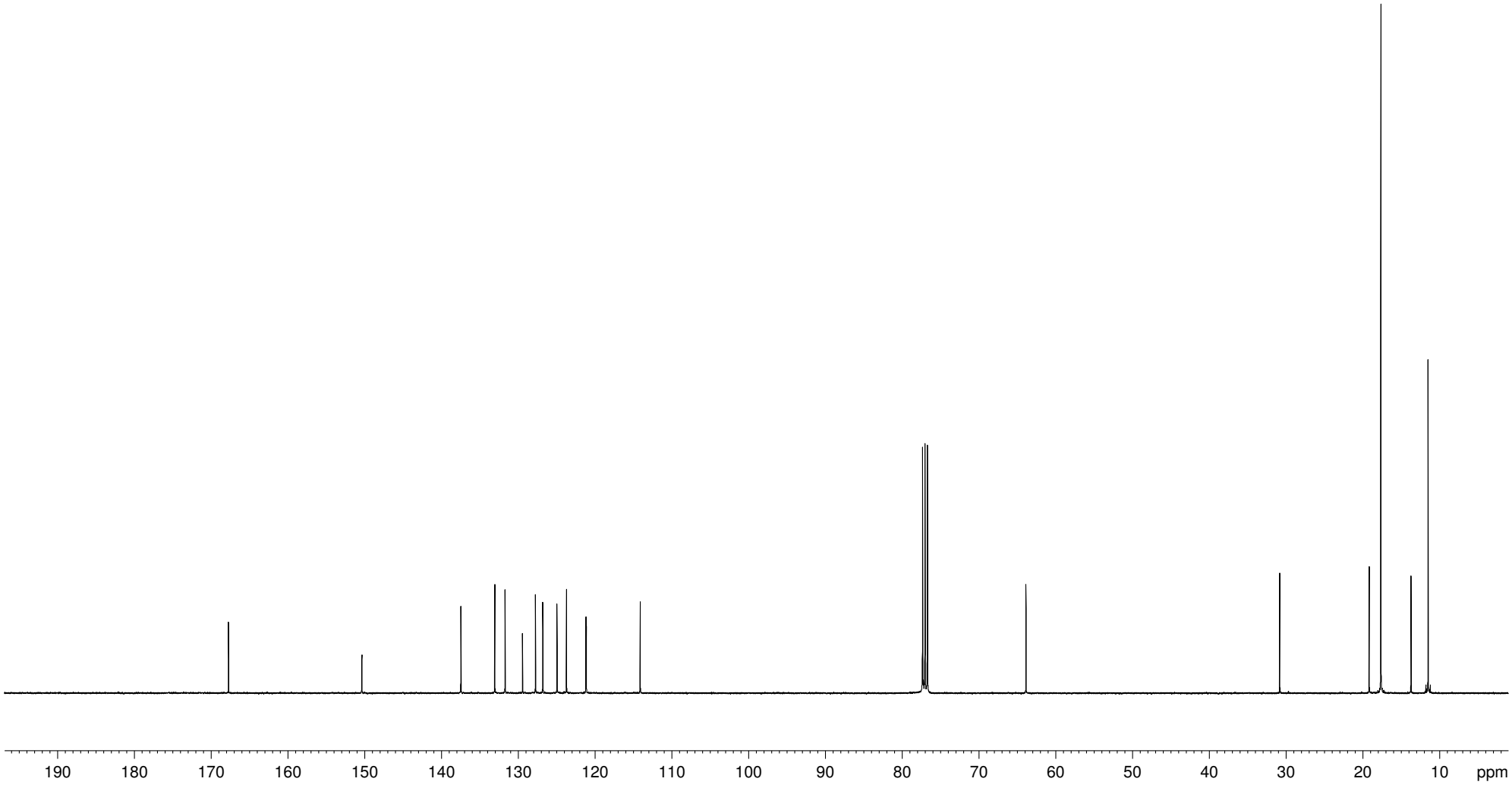


Standard 1H DRX400

(E)−4−(3−butoxy−3−oxoprop−1−enyl)−3−(2−nitrophenyl)−1−(triisopropylsilyl)−1H−pyrrole, 4a

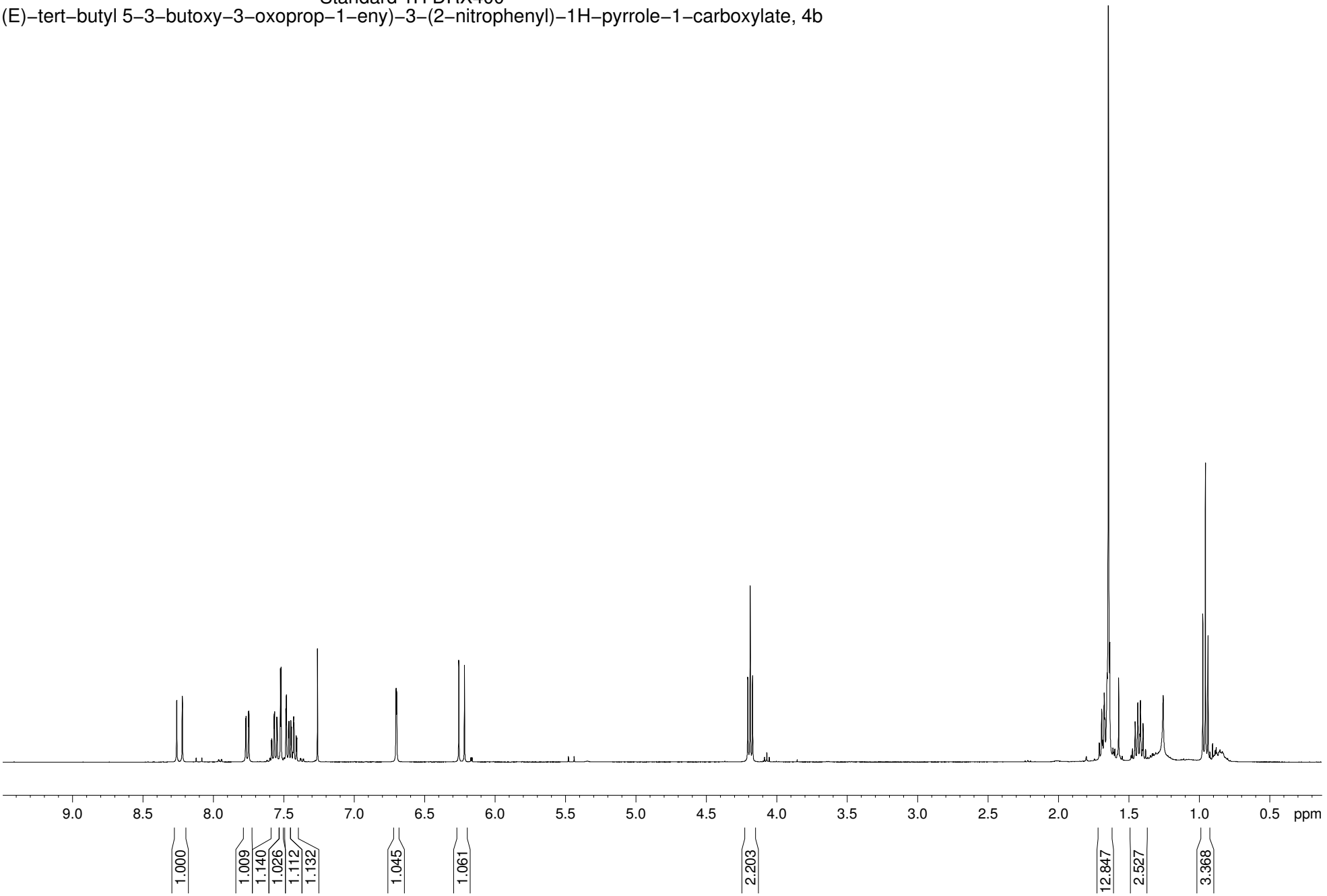


Standard 1H DRX400 (CDCl3)
–(3–butoxy–3–oxoprop–1–enyl)–3–(2–nitrophenyl)–1–(triisopropylsilyl)–1H–pyrro

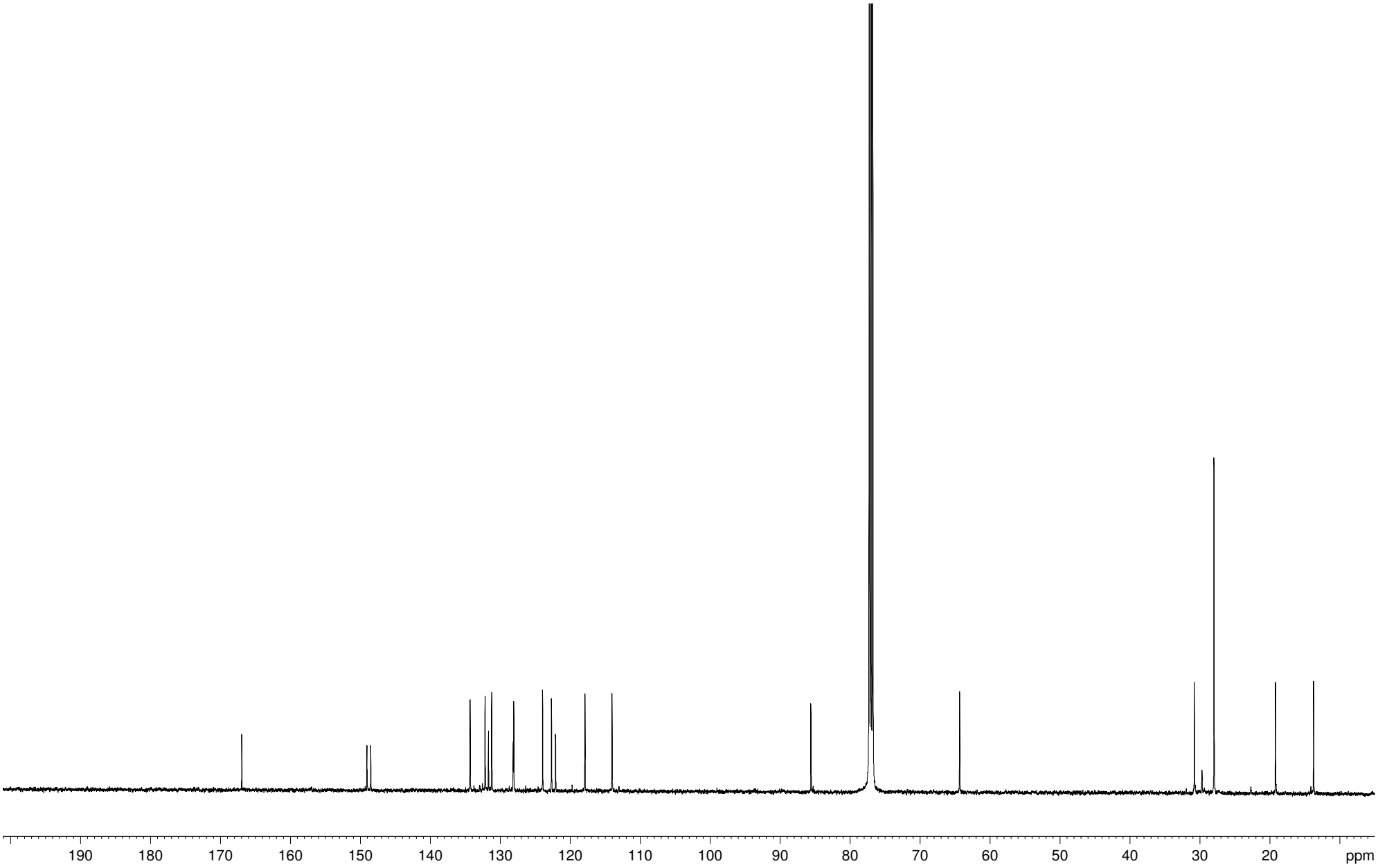


Standard 1H DRX400

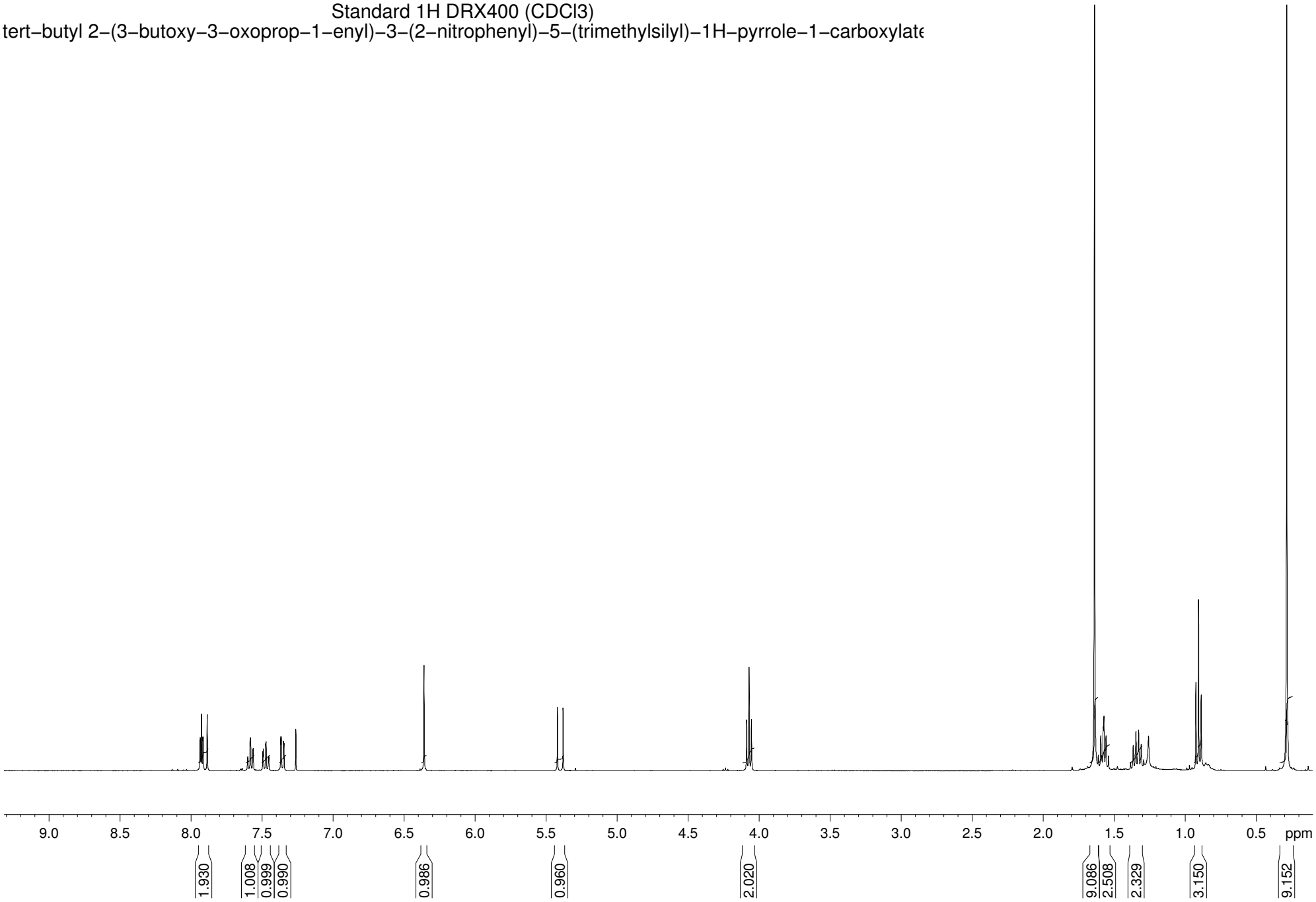
(E)−tert−butyl 5−3−butoxy−3−oxoprop−1−eny)−3−(2−nitrophenyl)−1H−pyrrole−1−carboxylate, 4b



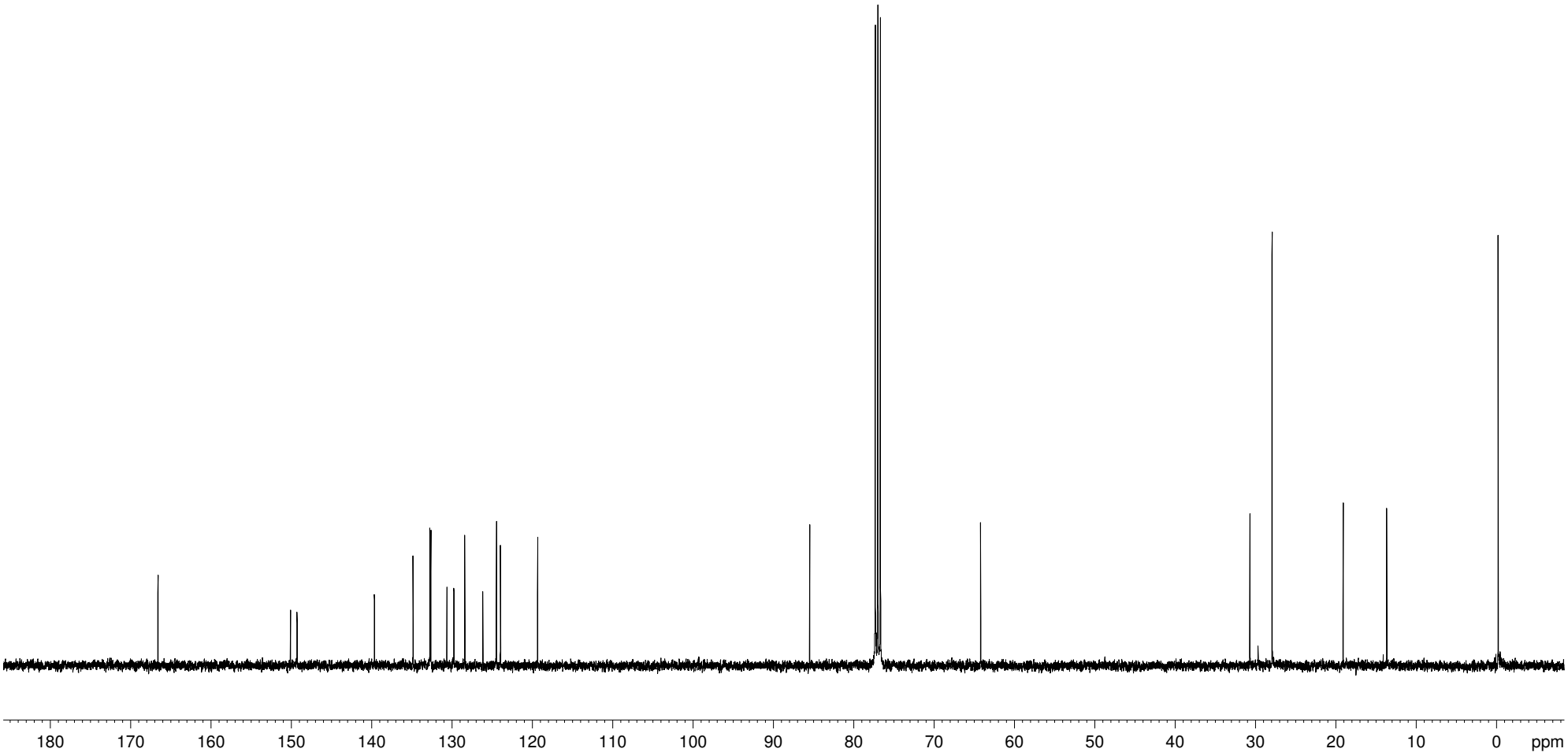
Standard ATM BB DRX500 13C (CDCl3)
(E)−tert−butyl 5−(3−butoxy−3−oxoprop−1−enyl)−3−(2−nitrophenyl)−1H−pyrrole−1−carboxylate, 4b



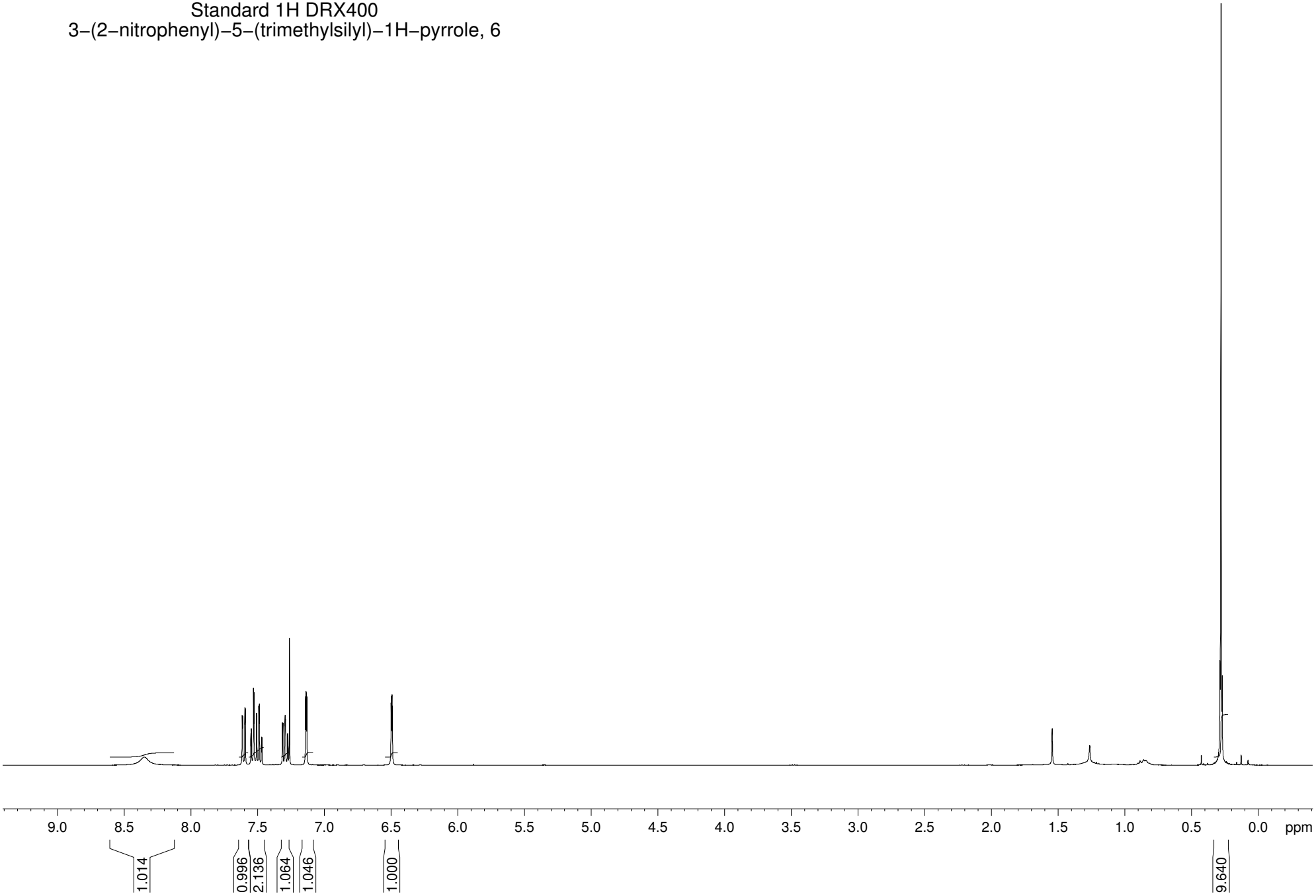
Standard 1H DRX400 (CDCl3)
tert–butyl 2–(3–butoxy–3–oxoprop–1–enyl)–3–(2–nitrophenyl)–5–(trimethylsilyl)–1H–pyrrole–1–carboxylate



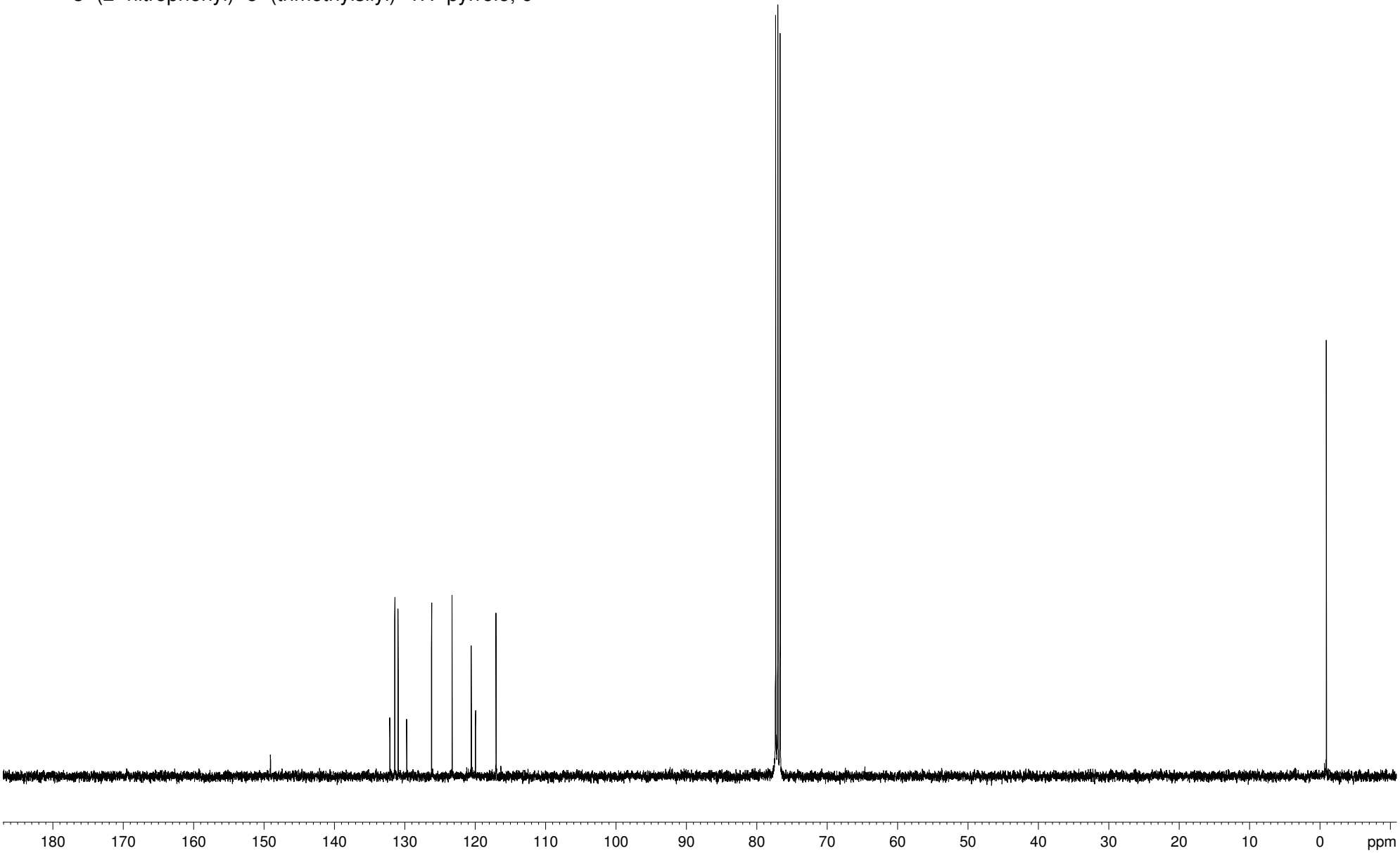
Standard 13C DRX400 (CDCl3)
tert–butyl 2–(3–butoxy–3–oxoprop–1–enyl)–3–(2–nitrophenyl)–5–(trimethylsilyl)–1H–pyrrole–1–carboxylate



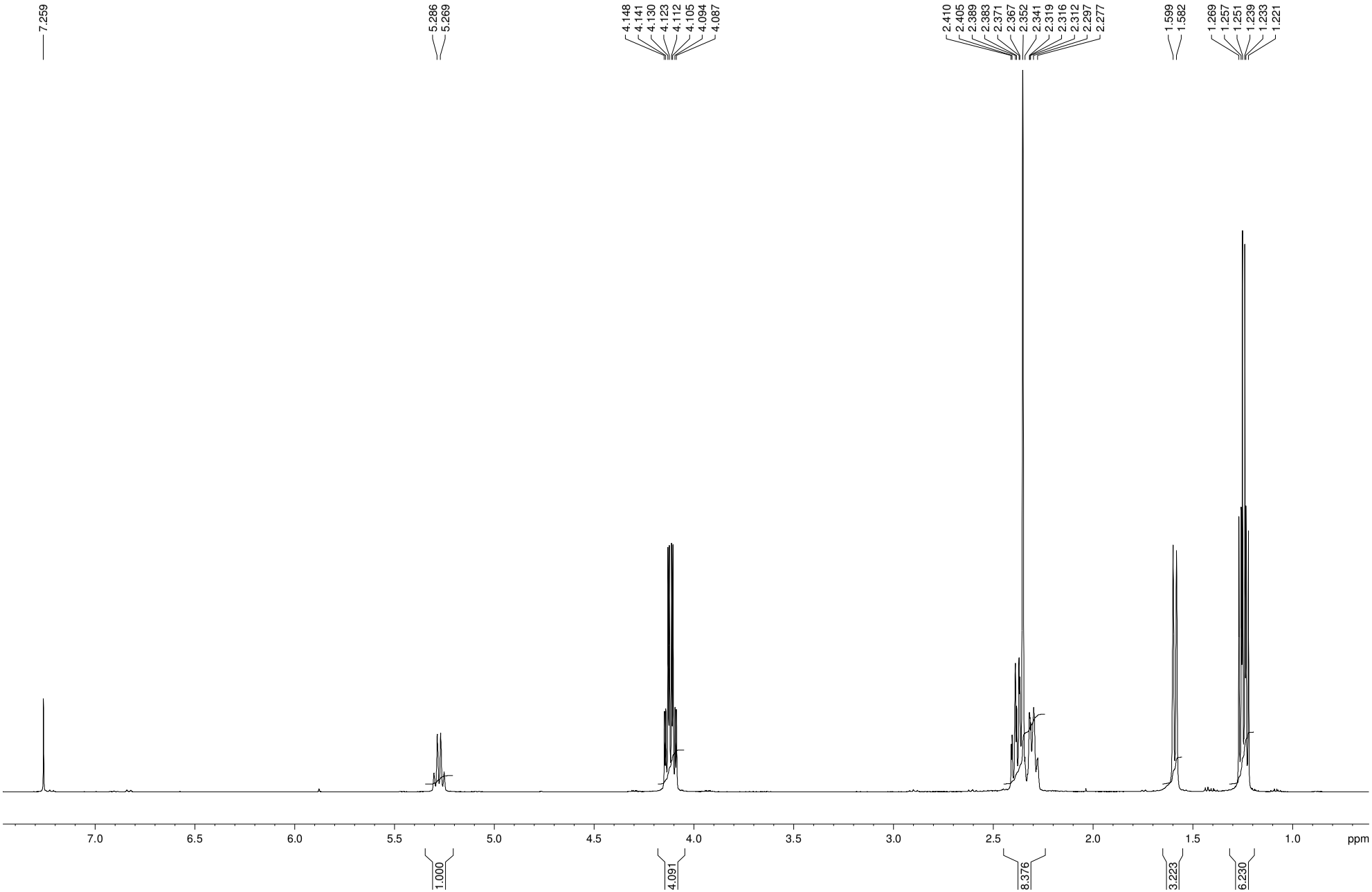
Standard 1H DRX400
3–(2–nitrophenyl)–5–(trimethylsilyl)–1H–pyrrole, 6



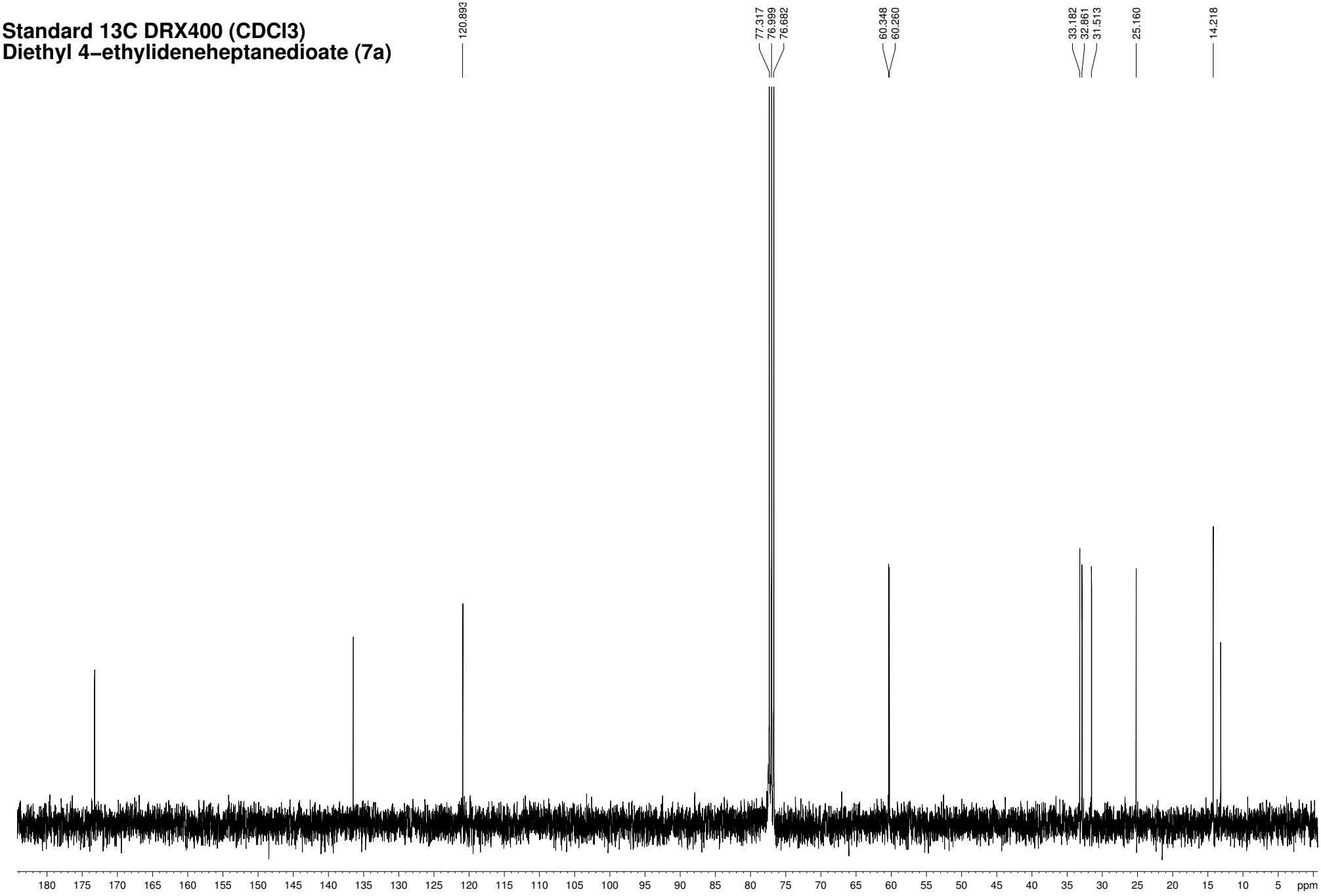
Standard 13C DRX400
3–(2–nitrophenyl)–5–(trimethylsilyl)–1H–pyrrole, 6



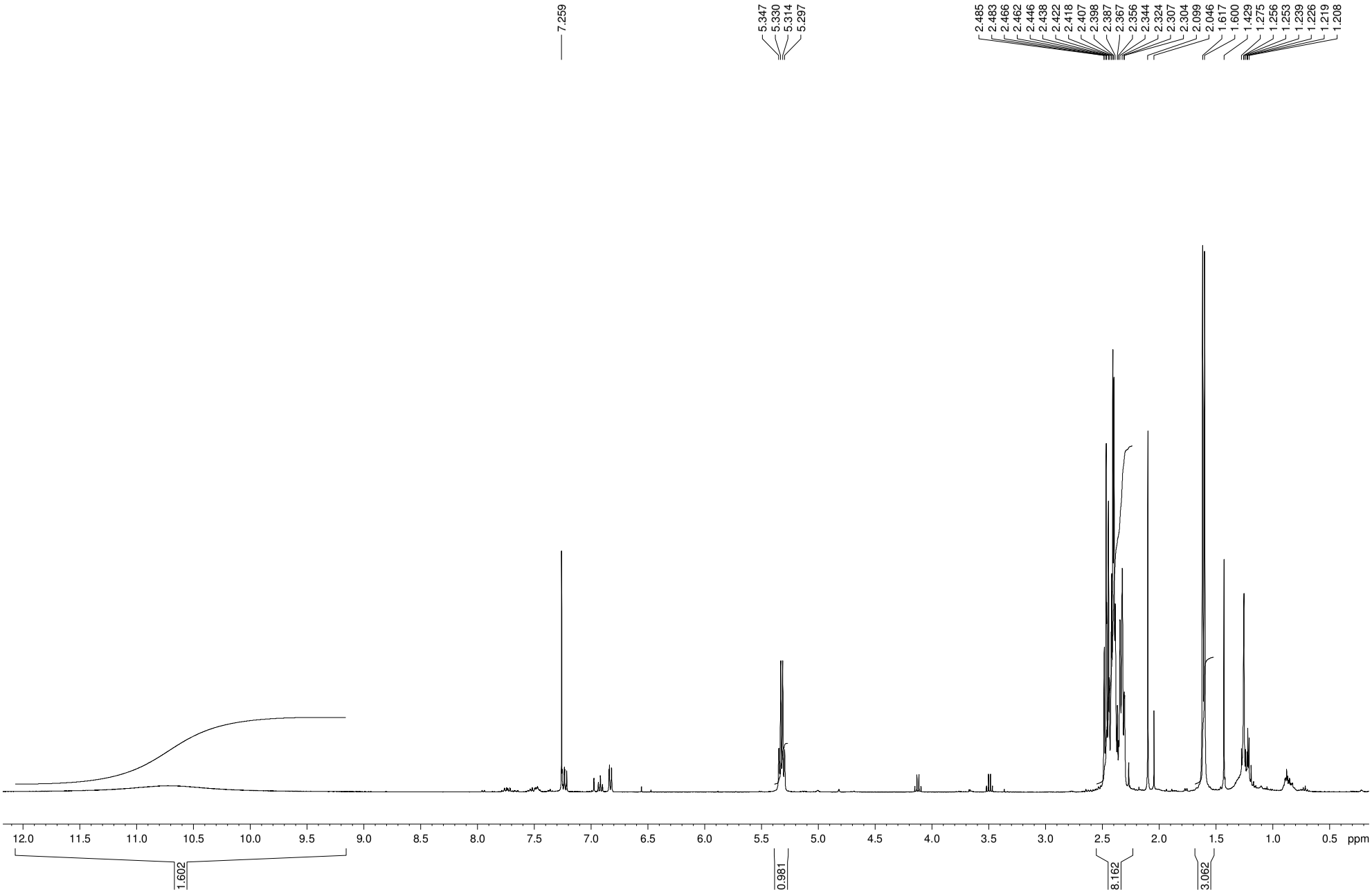
Standard 1H DRX400 (CDCl3)
Diethyl 4–ethylideneheptanedioate (7a)



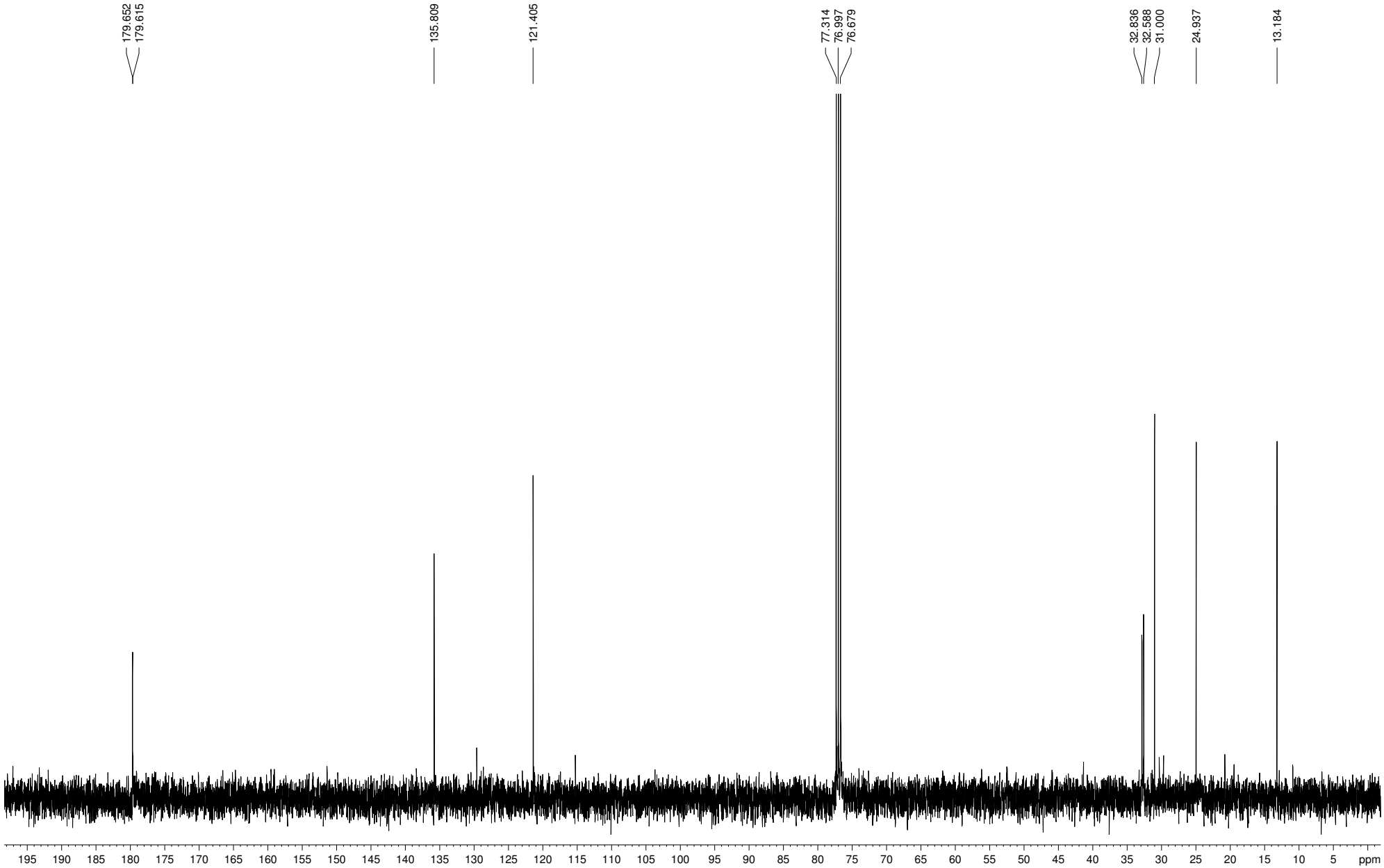
Standard 13C DRX400 (CDCl3)
Diethyl 4–ethylideneheptanedioate (7a)



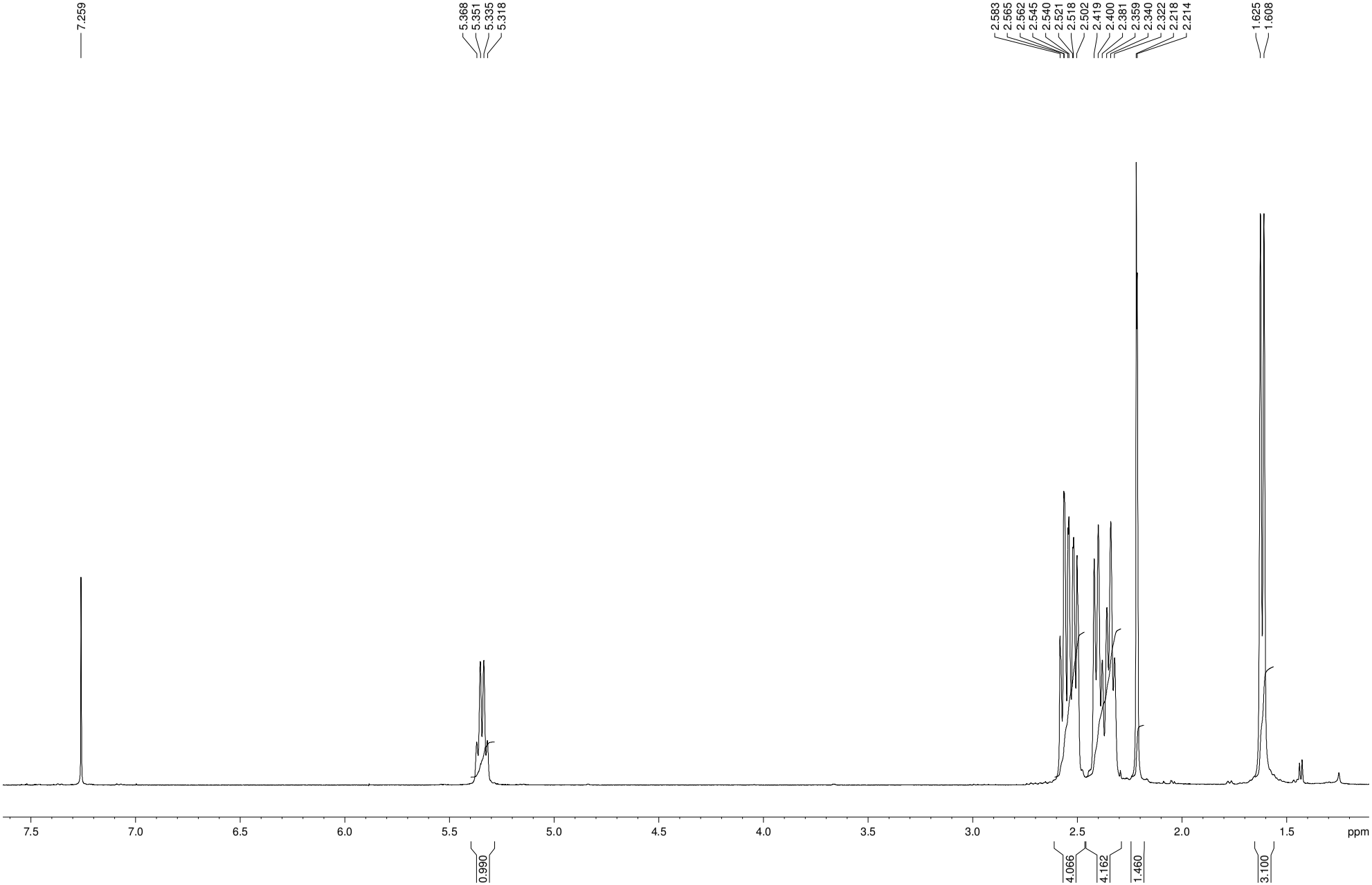
Standard 1H DRX400 (CDCl3)
4–ethylideneheptanedioic acid (7b)



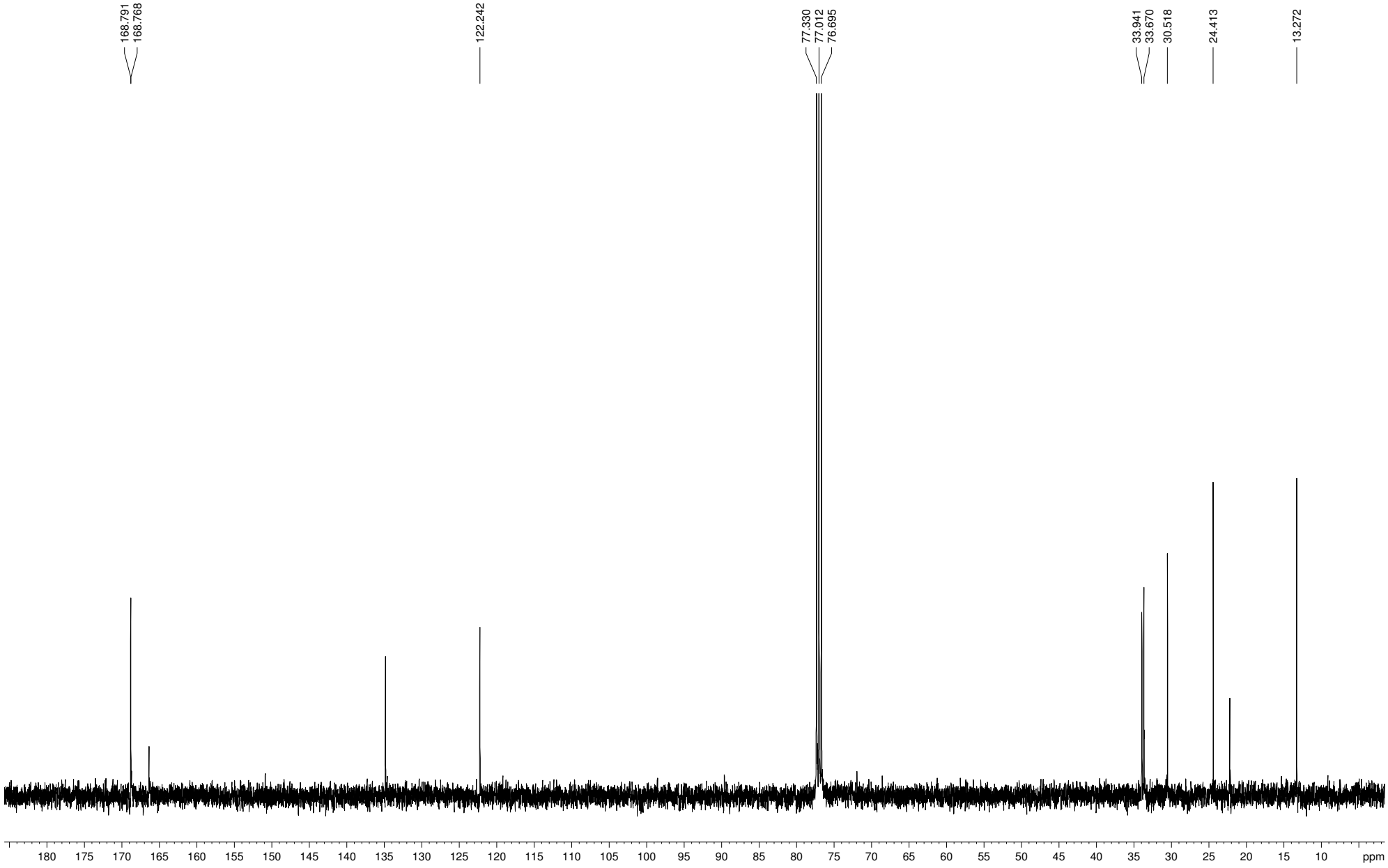
Standard 13C DRX400 (CDCl3)
4–ethylideneheptanedioic acid (7b)



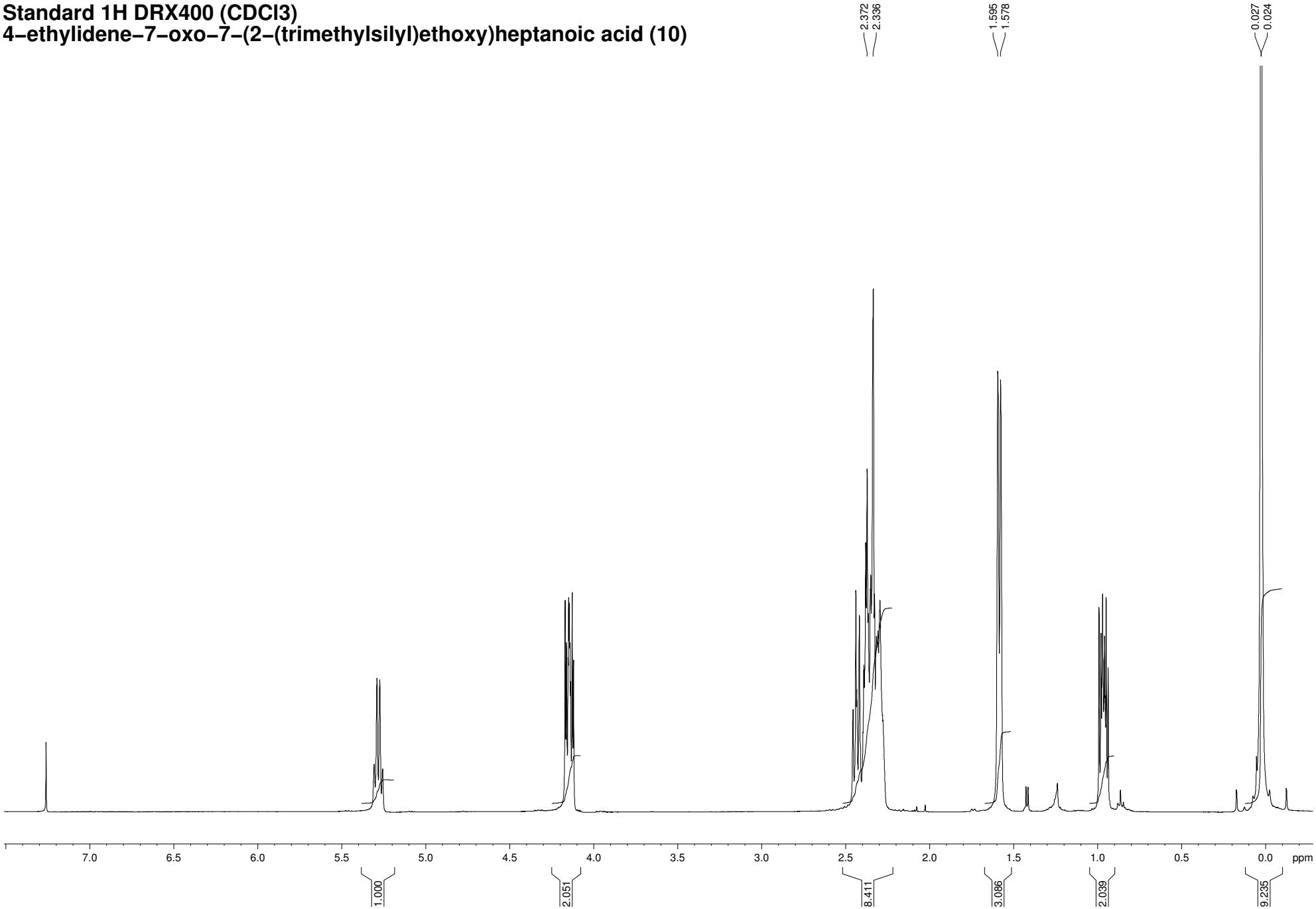
Standard 1H DRX400 (CDCl3)
5−ethylideneoxocane−2,8−dione (8)



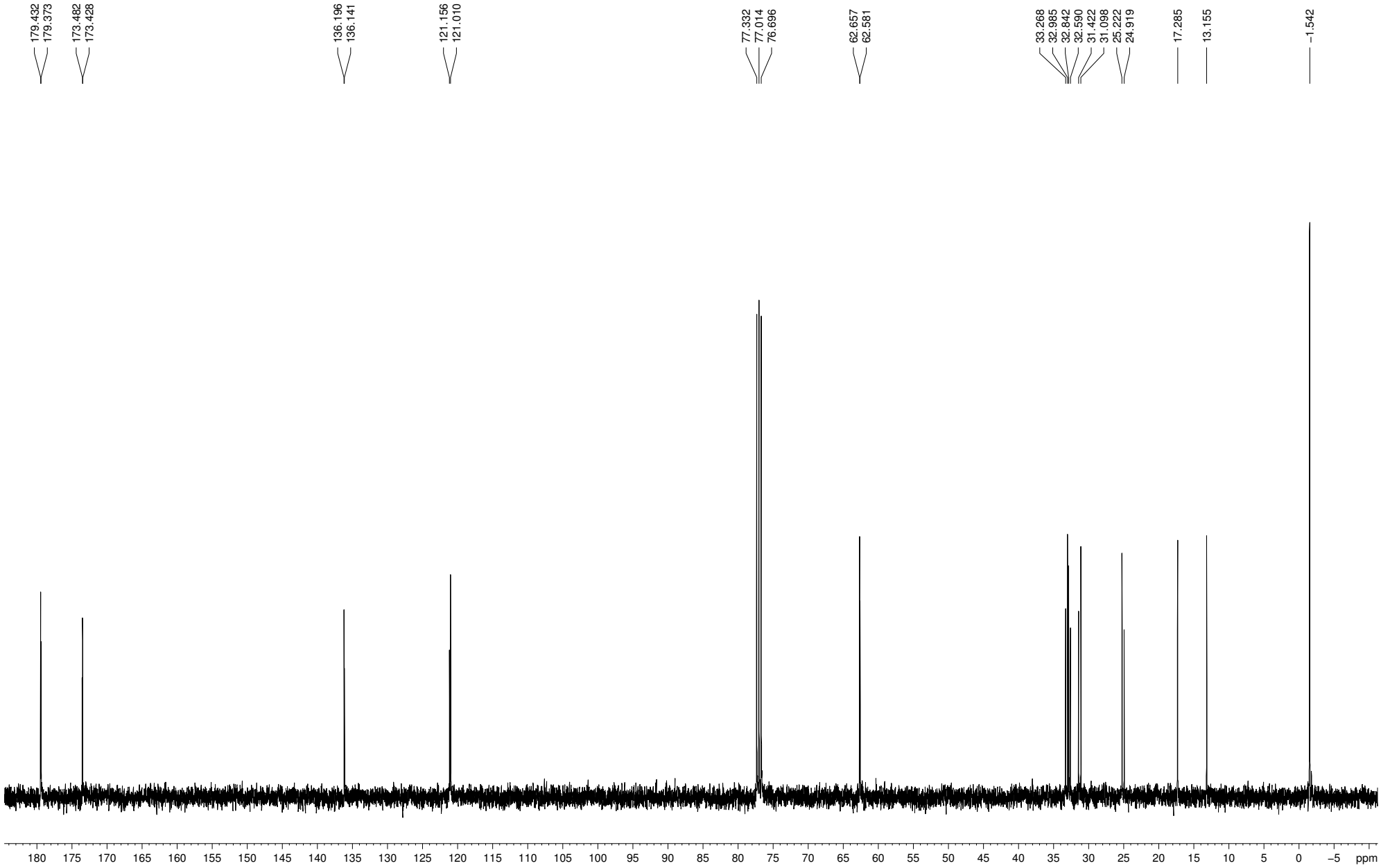
Standard 13C DRX400 (CDCl3)
5−ethylideneoxocane−2,8−dione (8)



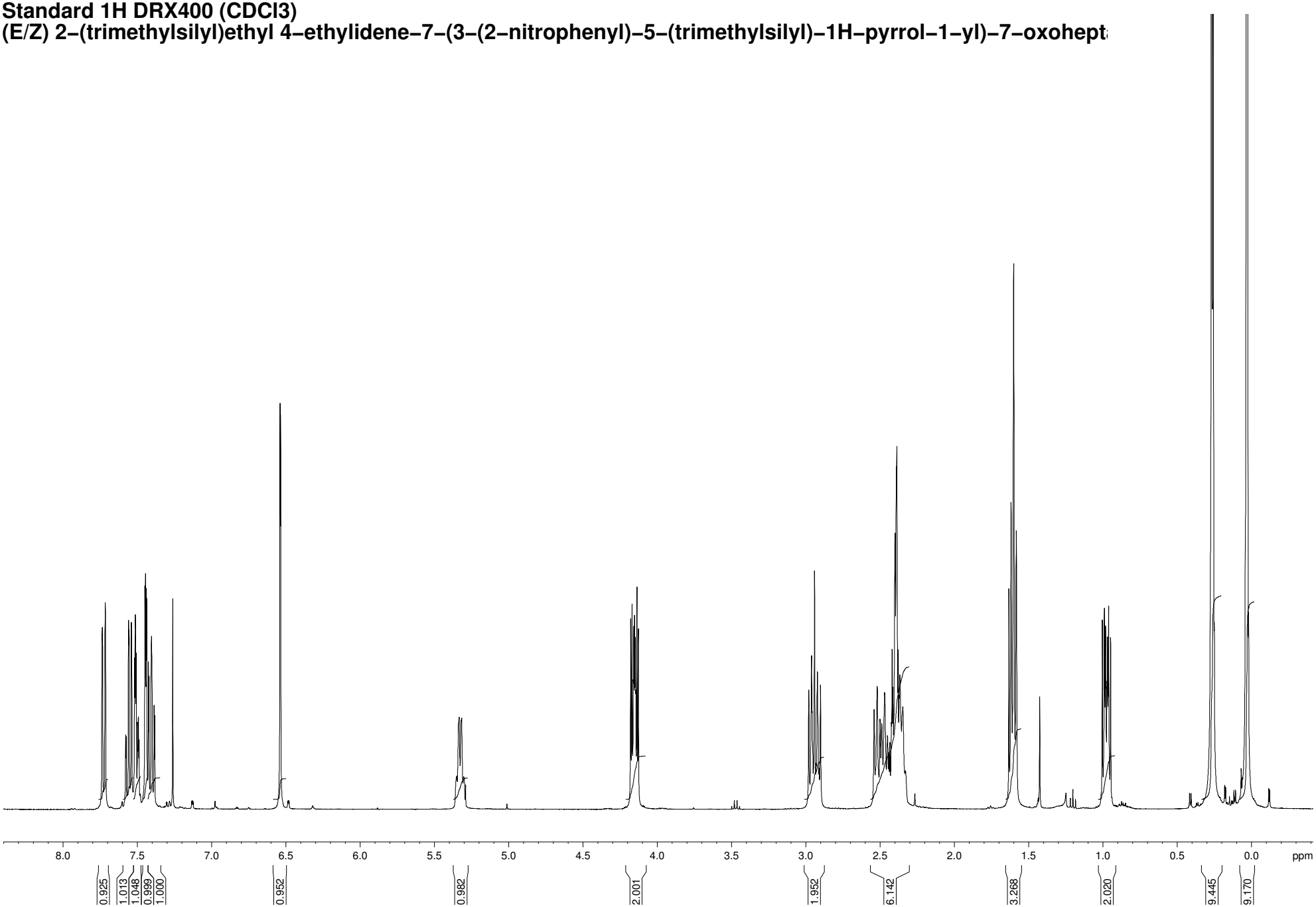
Standard 1H DRX400 (CDCl3)
4–ethylidene–7–oxo–7–(2–(trimethylsilyl)ethoxy)heptanoic acid (10)



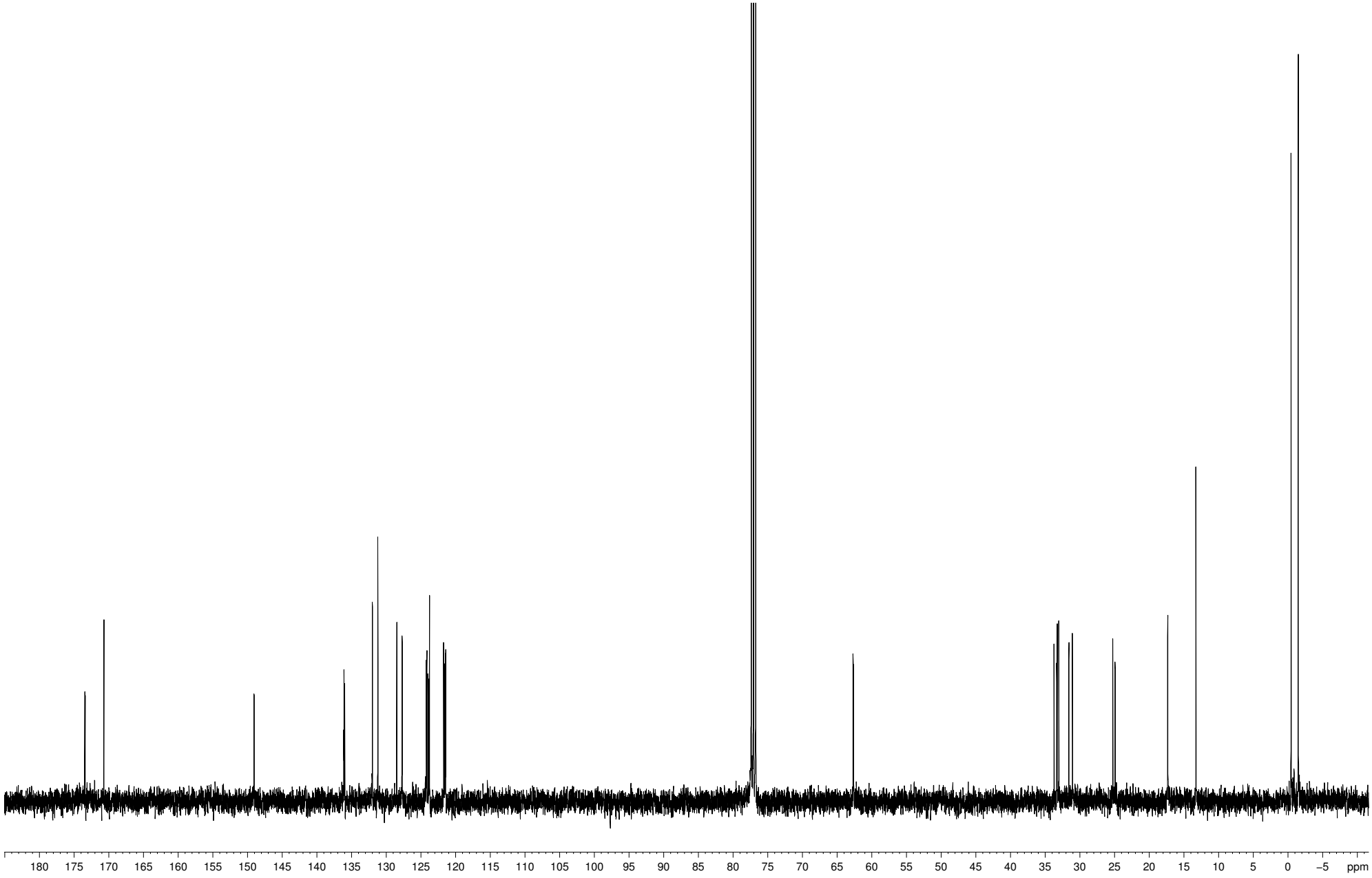
Standard 13C DRX400 (CDCl3)
4−ethylidene−7−oxo−7−(2−(trimethylsilyl)ethoxy)heptanoic acid (10)



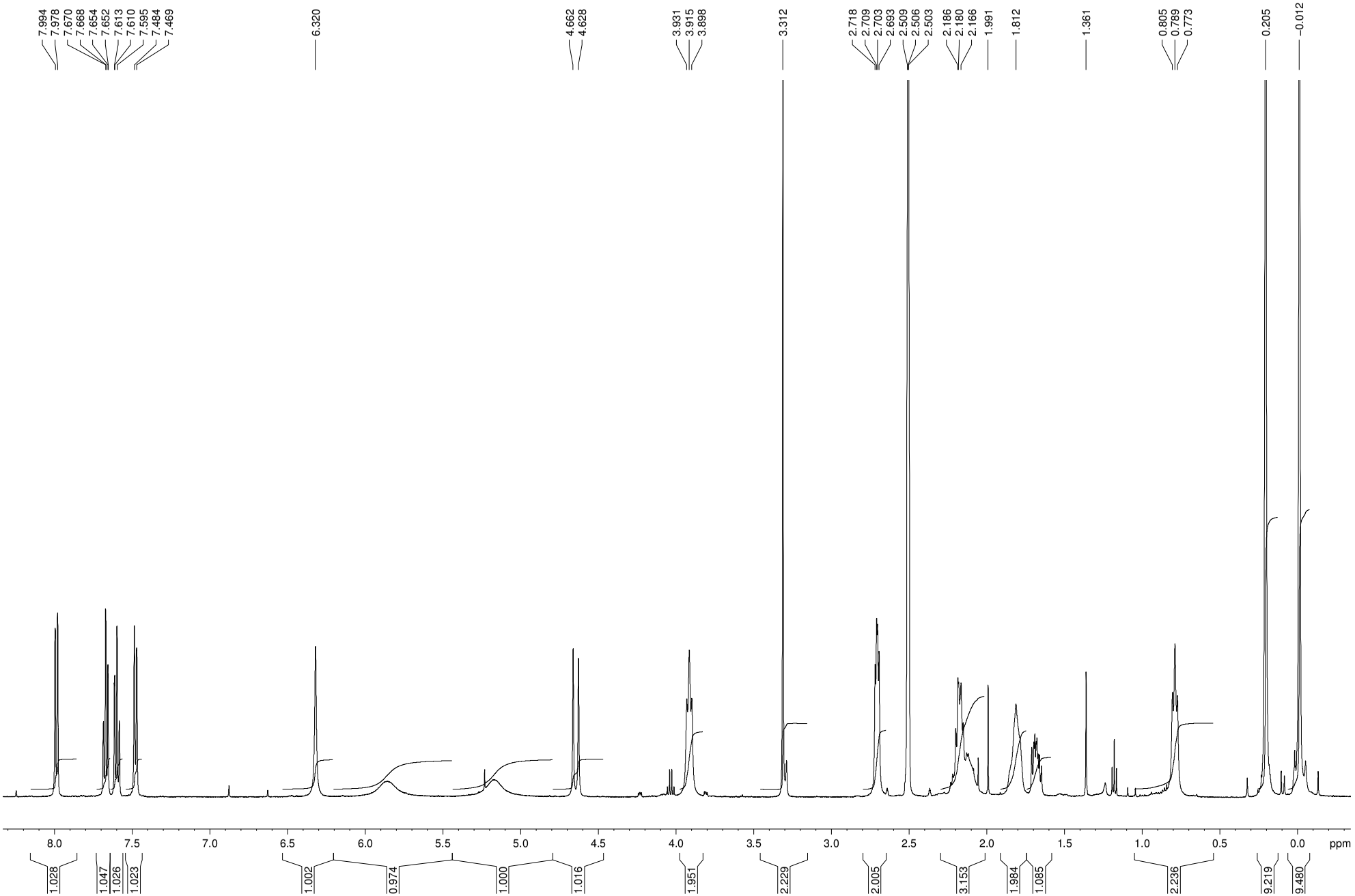
Standard 1H DRX400 (CDCl3)
(E/Z) 2–(trimethylsilyl)ethyl 4–ethylidene–7–(3–(2–nitrophenyl)–5–(trimethylsilyl)–1H–pyrrol–1–yl)–7–oxohept



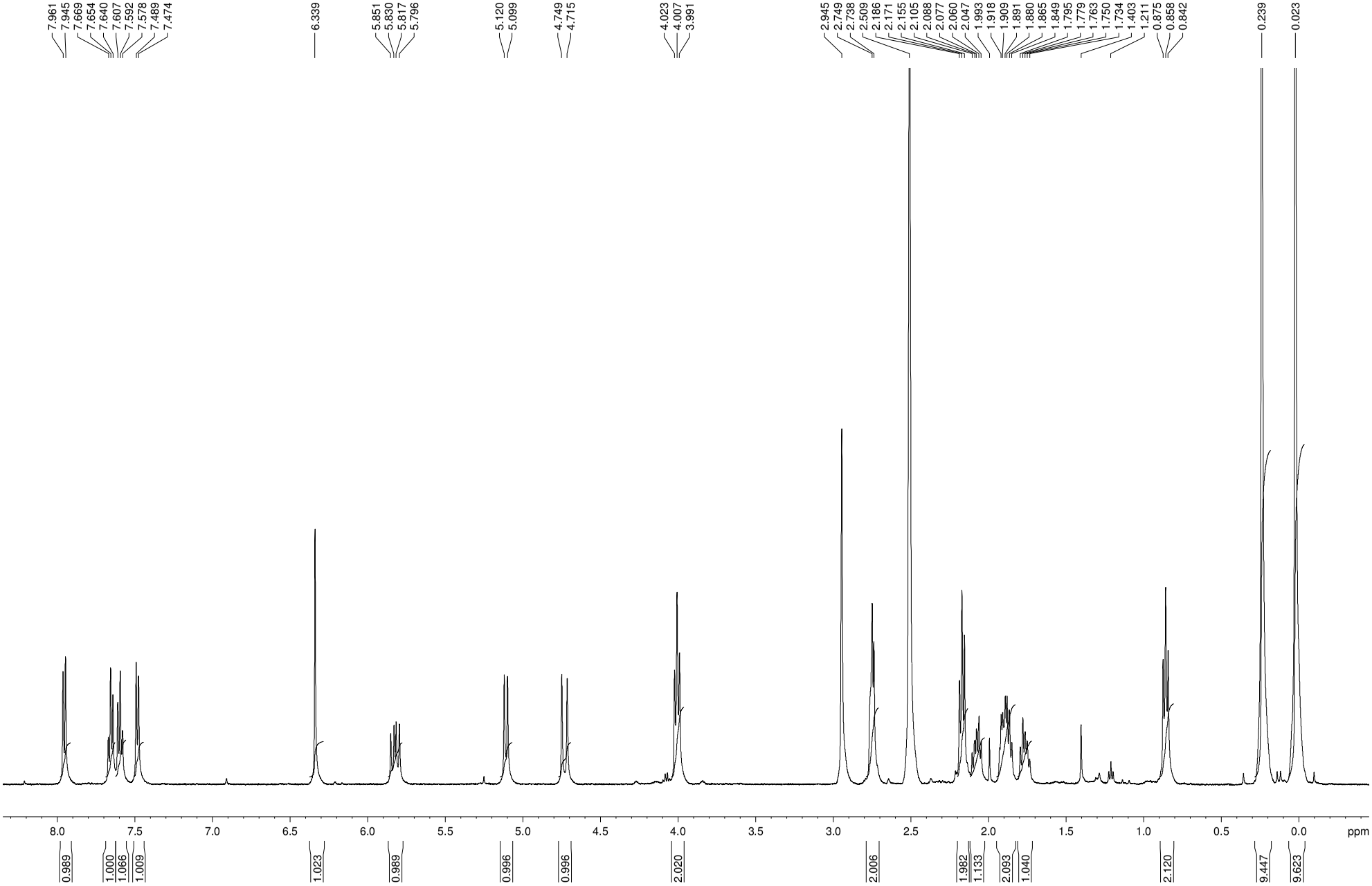
Standard 13C DRX400 (CDCl3)
(E/Z) 2–(trimethylsilyl)ethyl 4–ethylidene–7–(3–(2–nitrophenyl)–5–(trimethylsilyl)–1H–pyrrol–1–yl)–7–oxoheptanoate (11)



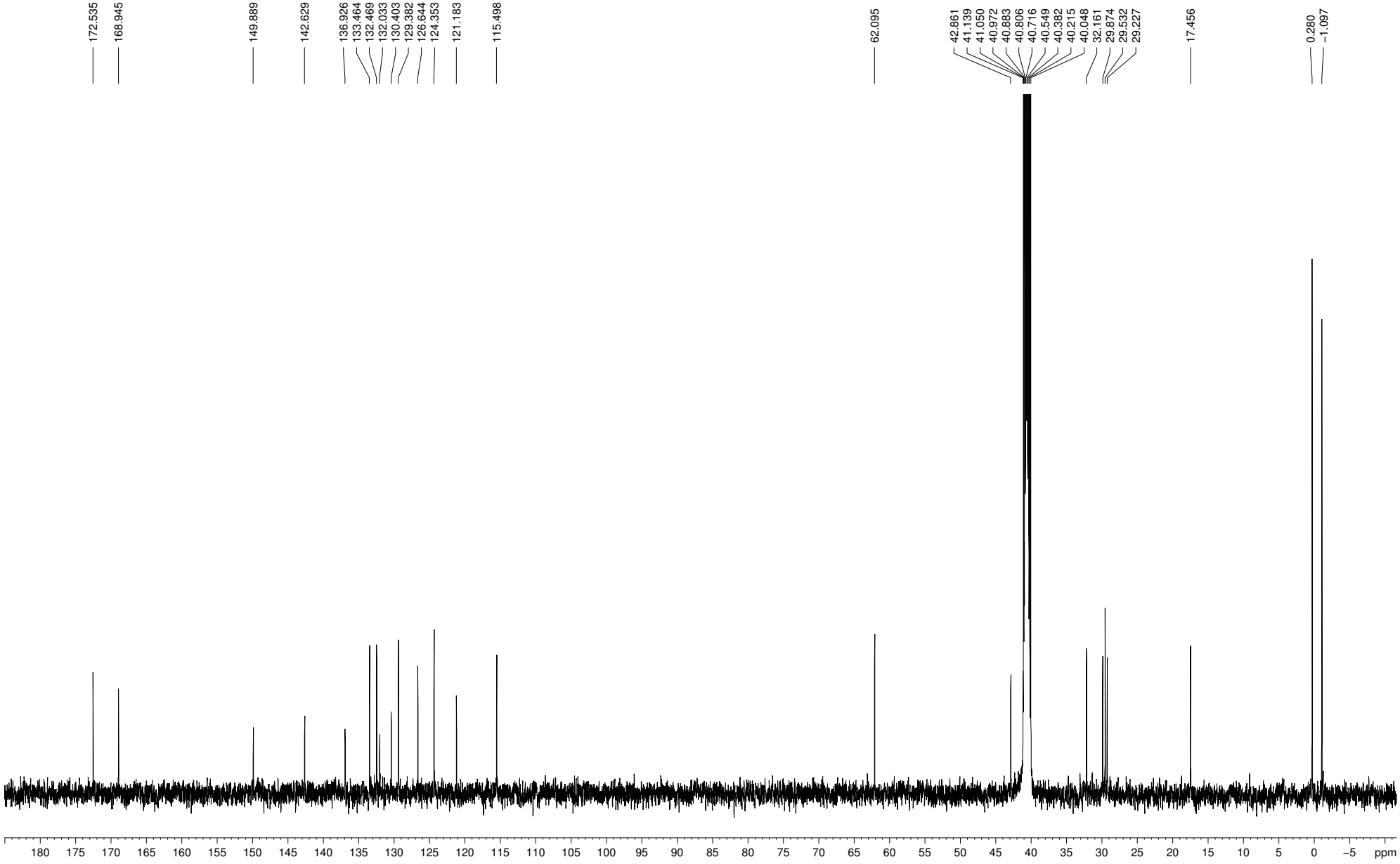
Standard ATM BB DRX500 1H (d6-DMSO)
2-(trimethylsilyl)ethyl 3-(-(2-nitrophenyl)-5-oxo3-(trimethylsilyl)-8-vinyl-5,6,7,8-tetrahydroinindolozin-8-yl) propanoate (12)



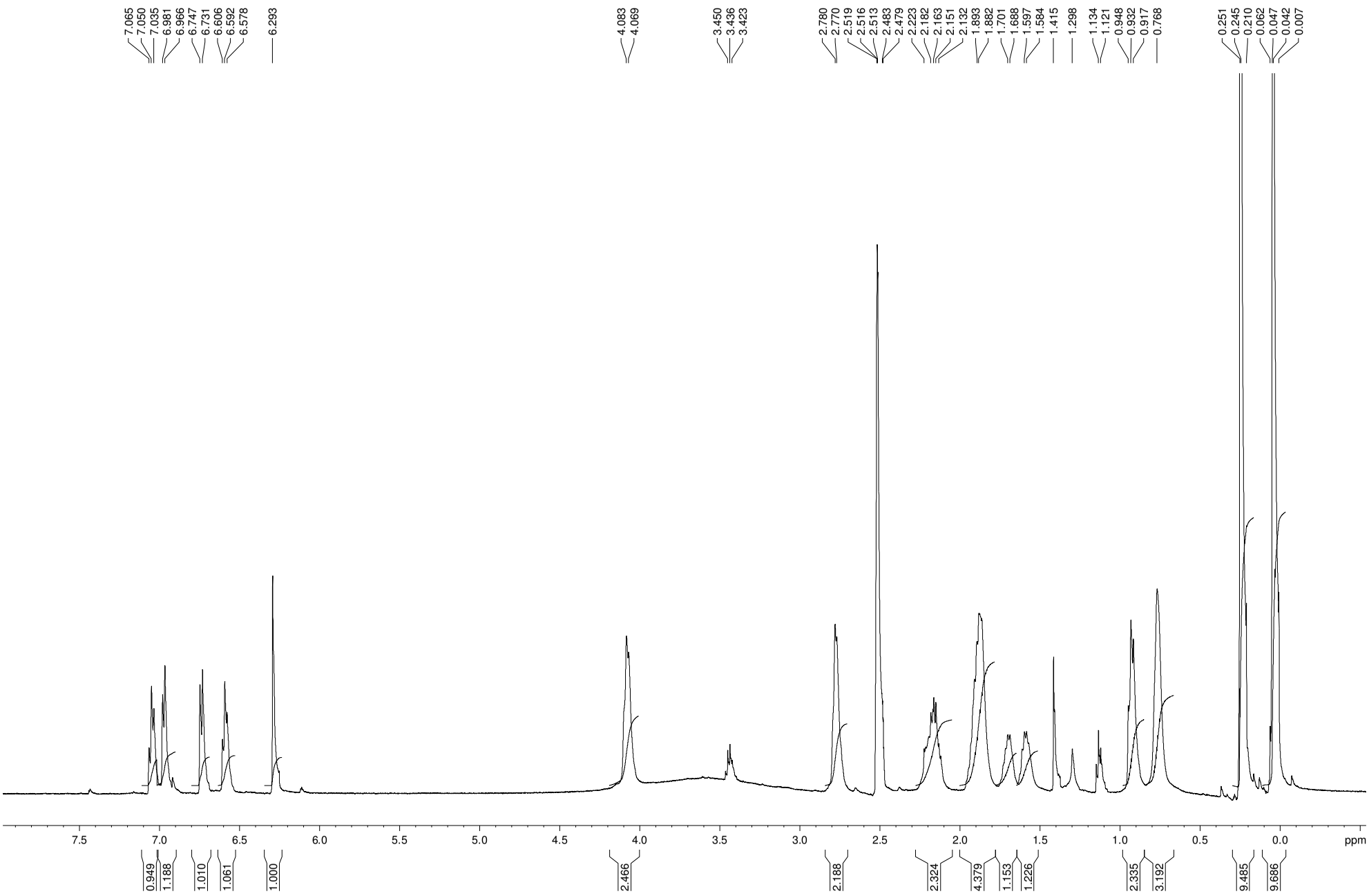
Standard Avance 500 MHz Proton (D6–DMSO at 373 K)
2–(trimethylsilyl)ethyl 3–(–(2–nitrophenyl)–5–oxo3–(trimethylsilyl)–8–vinyl–5,6,7,8–tetrahydroinindolozin–8–yl) propanoate (12)



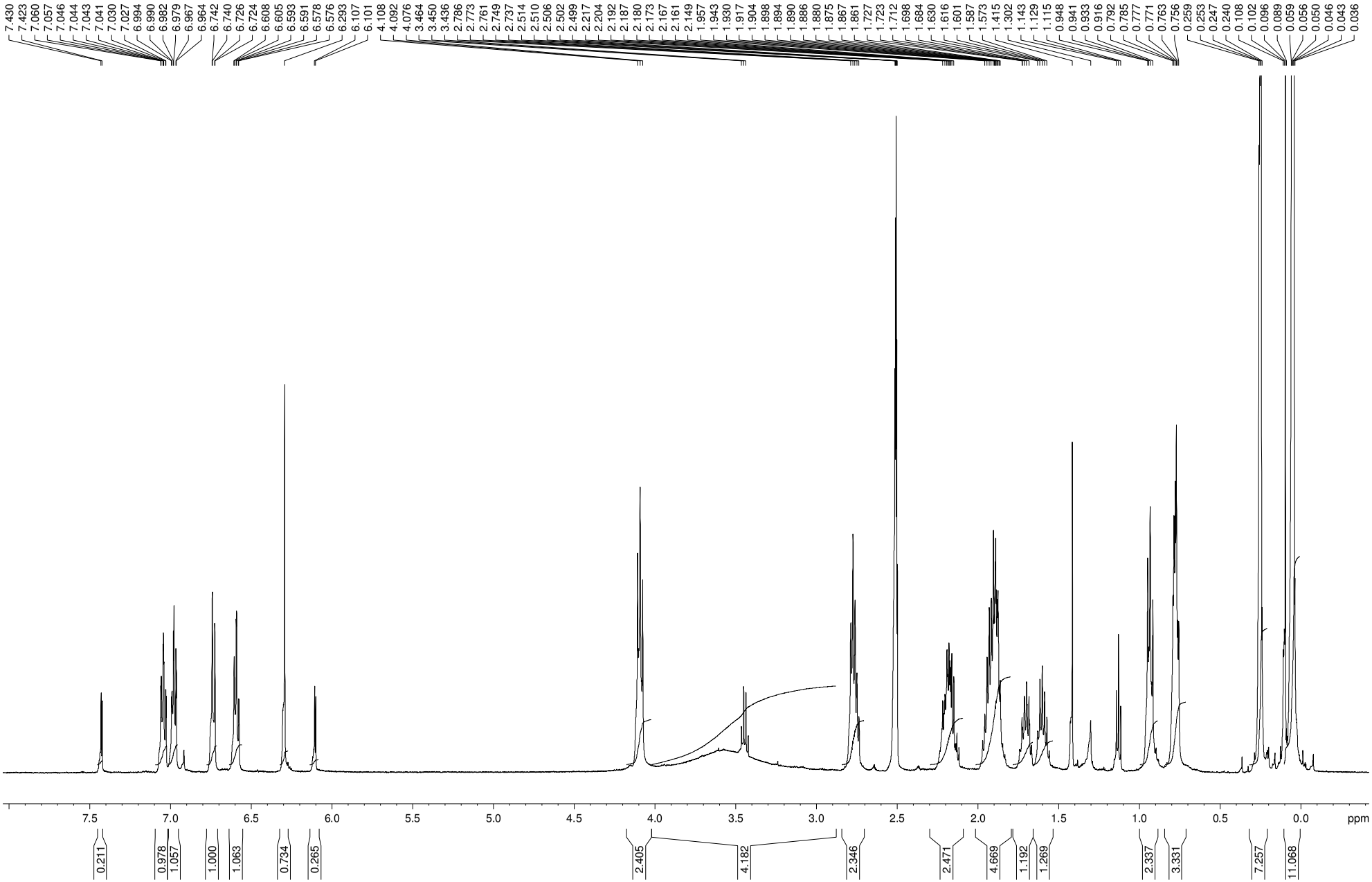
Standard ATM BB DRX500 13C (D6–DMSO at 373 K)
2–(trimethylsilyl)ethyl 3–(–(2–nitrophenyl)–5–oxo3–(trimethylsilyl)–8–vinyl–5,6,7,8–tetrahydroinindolozin–8–yl) propanoate (12)



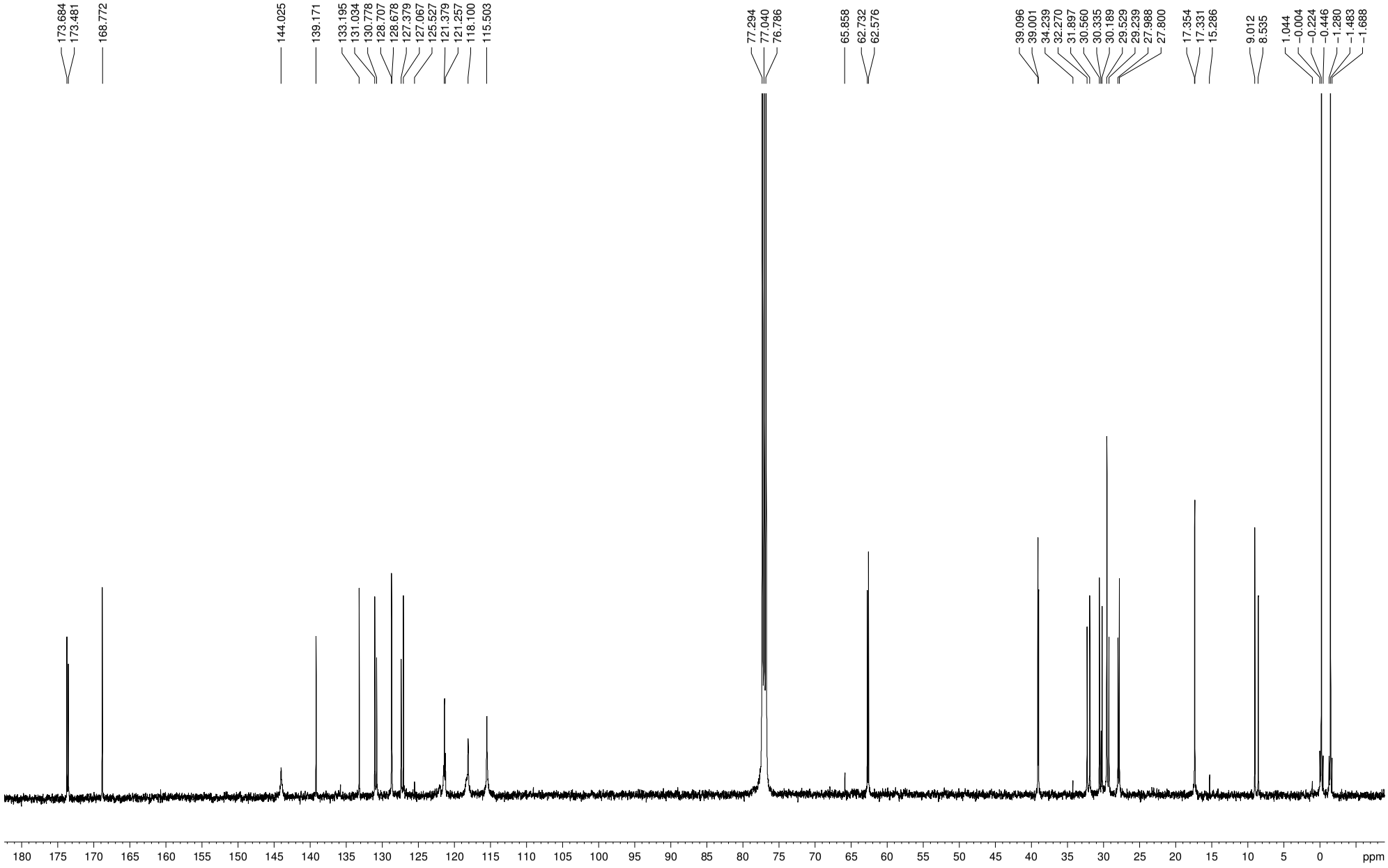
Standard Avance 500 MHz Proton (D6–DMSO 373 K)
2–(trimethylsilyl)ethyl 3–(1–(2–aminophenyl)–8–ethyl–5–oxo–3–(trimethylsilyl)–5,6,7,8–tetrahydroindolizin–8–yl) propanoate (1



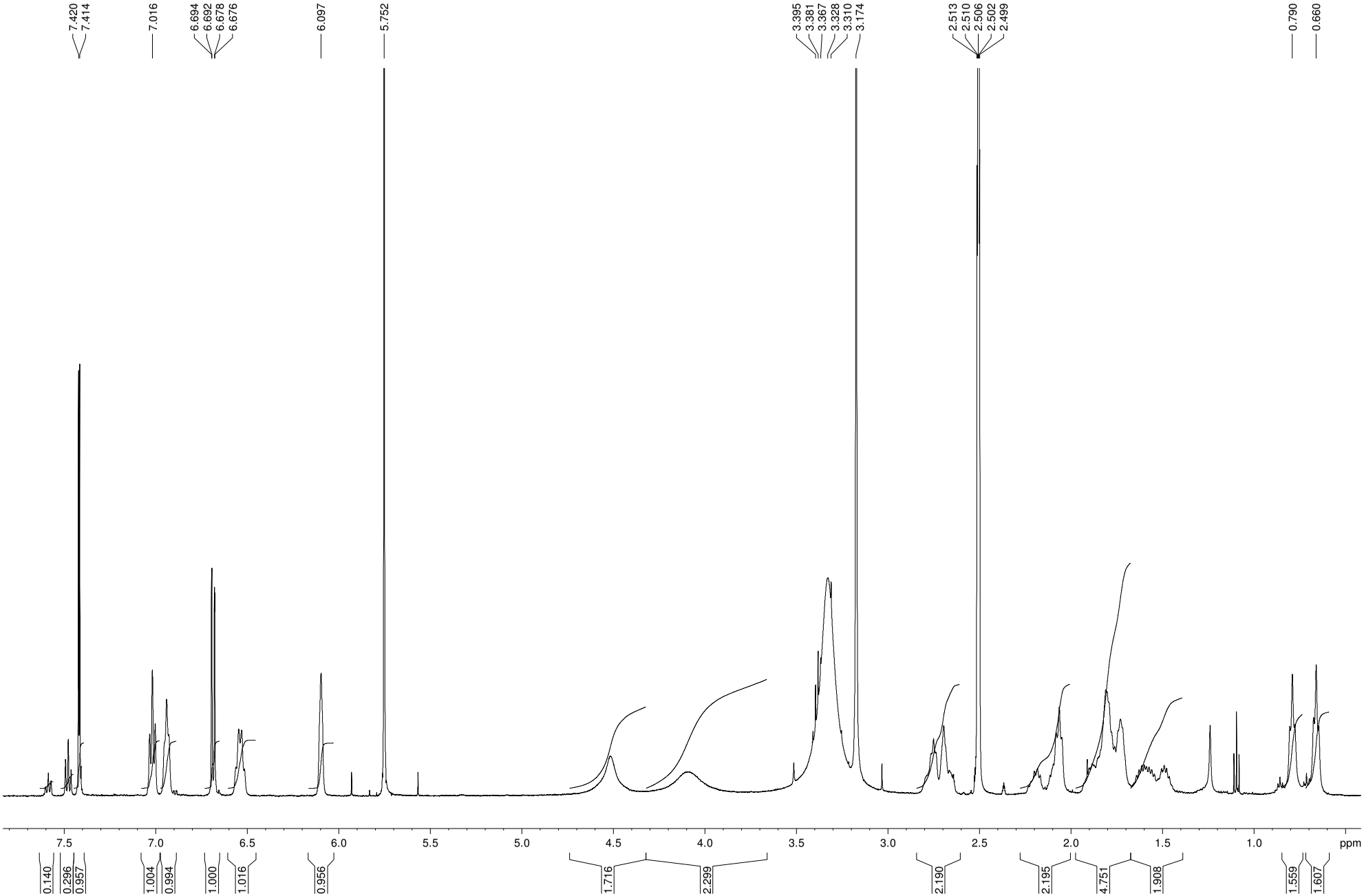
2-(trimethylsilyl)ethyl 3-(1-(2-aminophenyl)-8-ethyl-5-oxo-3-(trimethylsilyl)-5,6,7,8-tetrahydroindolizin-8-yl) propa



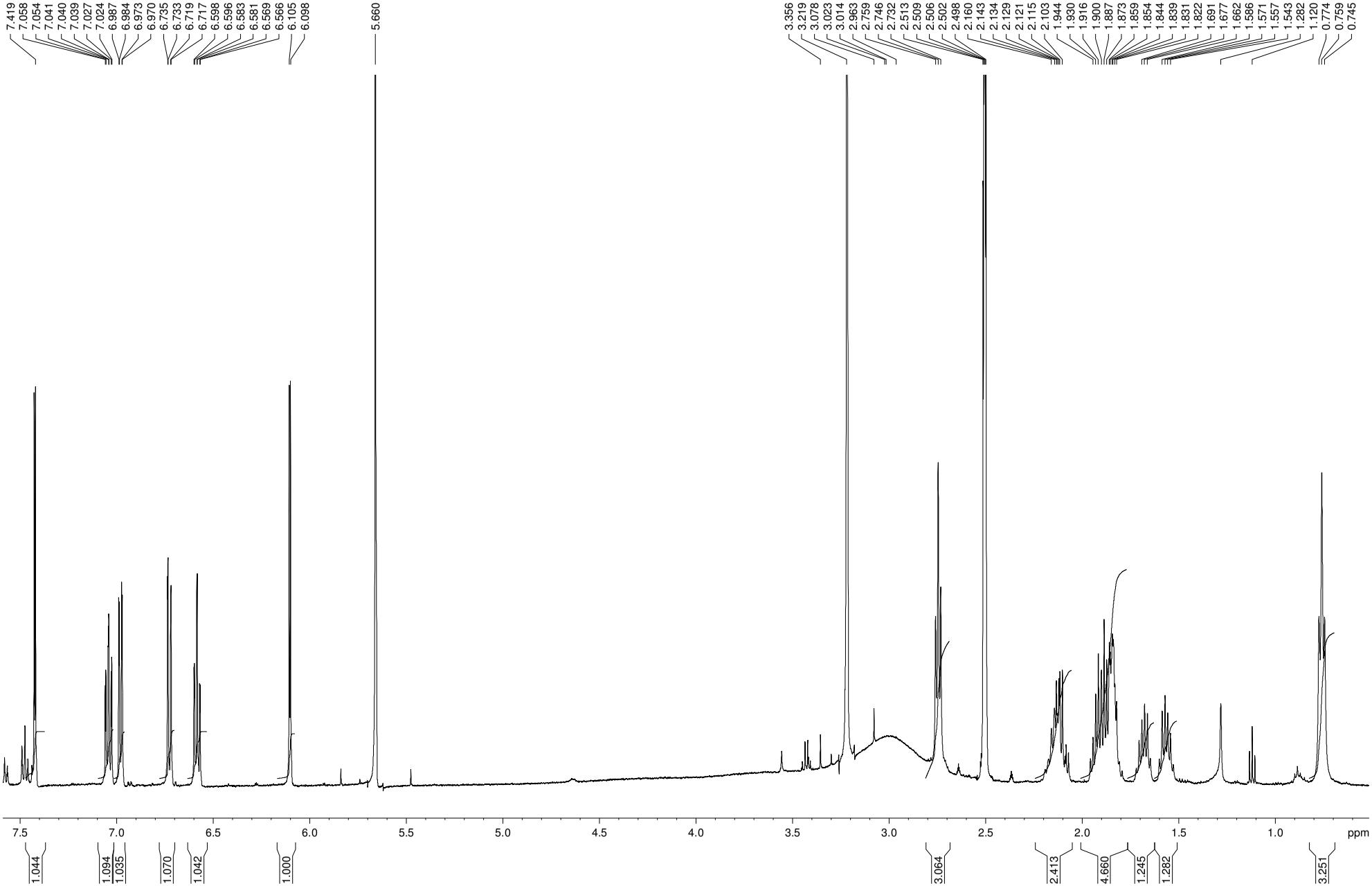
Standard ATM BB DRX500 13C (CDCl3)
2–(trimethylsilyl)ethyl 3–(1–(2–aminophenyl)–8–ethyl–5–oxo–3–(trimethylsilyl)–5,6,7,8–tetrahydroindolizin–8–yl) propanoate (1



Standard ATM BB DRX500 1H, (d6-DMSO at RT)
3-(1-(2-aminophenyl)-8-ethyl-5-oxo-5,6,7,8-tetrahydroindolizin-8-yl)propanoic acid (14)



Standard ATM BB DRX500 1H (d6–dimethylsulfoxide at 373K)
3–(1–(2–aminophenyl)–8–ethyl–5–oxo–5,6,7,8–tetrahydroindolizin–8–yl)propanoic acid (14)



Standard ATM BB DRX500 13C (D6–DMSO at 373K)
3–(1–(2–aminophenyl)–8–ethyl–5–oxo–5,6,7,8–tetrahydroindolizin–8–yl)propanoic acid (14)