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ACCESSORY PUBLICATION

Synthesis of diyne substituted 2-hydroxy acids, esters and amides

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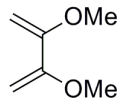
1. Experiment Details and Data for Compounds 4 - 34

General: All melting points were obtained on an electrothermal apparatus and are uncorrected. Proton NMR and Carbon NMR spectra were obtained on *Bruker DRX500*, *Bruker AV400* and *Bruker AV200* spectrometer, operating at 500 MHz, 400 MHz and 200 MHz. All spectra were obtained at 23°C unless specified. Chemical shifts are reported in parts per million (ppm) on the δ scale and relative to the chloroform peak at 7.26 ppm (^{1}H) or 77.1 ppm (^{13}C), the methanol peak at 3.31 ppm (^{1}H) or 49.0 ppm (^{13}C) and the dimethyl sulfoxide peak at 2.50 ppm (^{1}H) or 39.5 ppm (^{13}C). Positive ion EI mass spectra were run on a ThermoQuest MAT95XL mass spectrometer using an ionization energy of 70eV. Accurate mass measurements were obtained with a resolution of 5000-10000 using PFK as the reference compound. Oven dried glassware was used in all reactions carried out under an inert atmosphere (either dry nitrogen or argon). All starting materials and reagents were obtained commercially unless otherwise stated. Removal of solvents "*under reduced pressure*" refers to the process of bulk solvent removal by rotary evaporation (low vacuum pump) followed by application of high vacuum pump (oil pump) for a minimum of 30 min. Analytical thin layer chromatography (TLC) was performed on plastic-backed Merck Kieselgel KG60F_{254} silica plates and visualised using short wave ultraviolet light, potassium permanganate or phosphomolybdate dip. Flash chromatography was performed using 230-400 mesh Merck Silica Gel 60 following established guidelines under positive pressure. Tetrahydrofuran and dichloromethane were obtained from a solvent dispensing system under an inert atmosphere. All other reagents and solvents were used as purchased.

Synthesis of 2, 3-Dimethoxy-1,3-butadiene-diene[1]



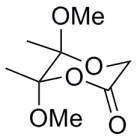
A mixture of biacetyl (17.2 g, 0.2 mol), absolute methanol (25 ml, 1.25 mol), trimethyl orthoformate (63.6 g, 0.6 mol) and concentrated sulfuric acid (95 drops) was refluxed for 10 h. The excess of reagents were distilled of and the remaining liquid was vacuum-distilled. Ammonium dihydrogenphosphate (25 mg) and a few crystals of hydroquinone were added and the liquid was heated at 100°C to 110°C. Methanol slowly distilled over, together with some remaining orthoformate. The oil bath temperature was raised (160°C to 170°C) and the colourless oily liquid collected between 129°C and 132°C (17.3 g or 76 % of crude diene). Redistillation gave 2,3-dimethoxy-1, 3-butadiene (15.5 g, 68 %), b. p. 132°C – 132.5°C.

^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 4.57 (2H, d, J = 1.5 Hz), 3.57 (6H, s), 4.02 (2H, d, J = 1.5 Hz)

[1] Reichwagen, J.; Hopf, H.; Del Guerzo, A.; Belin, C.; Bouas-Laurent, H.; Desvergne, J.-P. *Org. Lett.* **2005**, *7(6)*, 971-974

The spectral data agree with the data given in the literature[2].

Synthesis of (±) 5,6-Dimethoxy-5,6-dimethyl-[1, 4]dioxane-2-one (**16**)[3]



Triphenylphosphine hydrobromide (0.41 g, 1.20 mmol) was added to a stirred solution of hydroxy-acetic acid (0.68 g, 8.88 mmol) and 2,3-dimethoxy-1,3-butadiene (1.22 g, 5.73 mmol) in CH_2Cl_2 (40 ml) at room temperature. After 3 h, the reaction mixture was diluted with CH_2Cl_2 (80 ml). The organic phase was washed with saturated aqueous $NaHCO_3$ (80 ml), dried (Na_2SO_4), filtered and concentrated *in vacuo*. The residue was purified by flash chromatography (hexane - EtOAc 4:1) to give the lactone as a white solid (1.40 g, 83 %).

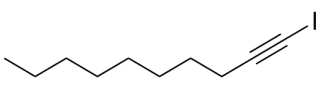
^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 4.28 (1H, d, J = 17.6), 4.14 (1H, d, J = 17.6 Hz), 3.43 (3H, s), 3.30 (3H, s),1.49 (3H, s), 1.38 (3H, s)

The spectral data agree with the data given in the literature[3].

General Procedure A: Iodination of terminal alkynes[4]

N-BuLi (1.6 M in hexane, 1.3 equiv) was added slowly to a solution of a terminal alkyne (1 equiv) in dry THF at -20°C under argon. The reaction mixture was stirred for one hour and then cooled to -40°C. Iodide (1.05 equiv) was added slowly und argon. After stirring for 12 h at room temperature the reaction mixture was quenched with saturated ammonium chloride solution and extracted with ethyl acetate. The combined organic layers were washed with saturated sodium thiosulfate solution, and dried over sodium sulfate. Removal of the solvent left the product that was used without further purification in the next reaction step.

Synthesis of 1-iododec-1-yne (**4**)



[2] Pozzo, J.-L.; Clavier, G. M.; Colomes, M.; Bouas-Laurent, H. *Tetrahedron*, **1997**, *53*, 6377-6390

[3] Ley, S. V.; Diez, E.; Dixon, D. J.; Guy, R. T.; Michel, P.; Nattrass, G. L.; Sheppard, T. D. *Org. Biomol. Chem.*, **2004**, *2*, 3608-3617

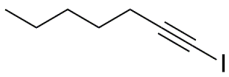
[4] Coleman, B. E.; Cwynar, V.; Hart, D. J.; Havas, F.; Mohan, J. M.; Patterson, S.; Ridenour, S.; Schmidt, M.; Smith, E.; Wells, A. J. *Synlett* **2004**, *8*, 1339-1342.

N-BuLi (25.3 ml, 40.6 mmol), dec-1-yne (5.6 ml, 31.2 mmol) and iodide (8.3 g, 32.8 mmol) in dry THF (100 ml) were reacted accordingly to general procedure A. The aqueous work up with saturated ammonium chloride solution (200 ml), ethyl acetate (3 x 100 ml) and saturated sodium thiosulfate solution (100 ml) resulted in 1-iododec-1-yne (7.5 g, 28.4 mmol, 91 %).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 2.35 (2H, t, J = 6.9 Hz), 1.29 – 1.64 (12H, m), 0.88 (3H, t, J = 7.5 Hz)

The spectral data agree with the data given in the literature[4]

Synthesis of 1-iodohept-1-yne (**5**)

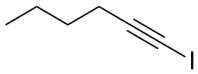


N-BuLi (25.3 ml, 40.6 mmol), hept-1-yne (4.1 ml, 31.2 mmol) and iodide (8.3 g, 32.8 mmol) in dry THF (100 ml) were reacted accordingly to general procedure A. The aqueous work up with saturated ammonium chloride solution (200 ml), ethyl acetate (3 x 100 ml) and saturated sodium thiosulfate solution (100 ml) resulted in 1-iodohept-1-yne (6.6 g, 29.6 mmol, 95 %).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 2.35 (2H, t, J = 6.9 Hz), 1.32 – 1.59 (6H, m), 0.88 (3H, t, J = 7.5 Hz)

The spectral data agree with the data given in the literature[4]

Synthesis of 1-iodohex-1-yne (**6**)

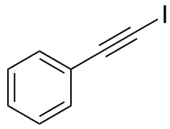


N-BuLi (25.3 ml, 40.6 mmol), hex-1-yne (3.6 ml, 31.2 mmol) and iodide (8.3 g, 32.8 mmol) in dry THF (100 ml) were reacted accordingly to general procedure A. The aqueous work up with saturated ammonium chloride solution (200 ml), ethyl acetate (3 x 100 ml) and saturated sodium thiosulfate solution (100 ml) resulted in 1-iodohex-1-yne (6.1 g, 29.3 mmol, 94 %).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 2.35 (2H, t, J = 6.9 Hz), 1.35 – 1.51 (4H, m), 0.89 (3H, t, J = 7.4 Hz)

The spectral data agree with the data given in the literature[4]

Synthesis of 1-iodo-2-phenylacetylene (**7**)



N-BuLi (25.3 ml, 40.6 mmol), dec-1-yne (3.4 ml, 31.2 mmol) and iodide (8.3 g, 32.8 mmol) in dry THF (100 ml) were reacted accordingly to general procedure A. The aqueous work up with saturated ammonium chloride solution (200 ml), ethyl acetate (3 x 100 ml) and saturated sodium thiosulfate solution (100 ml) resulted in 1-iodo-2-phenylacetylene (6.6 g, 29.0 mmol, 93 %).

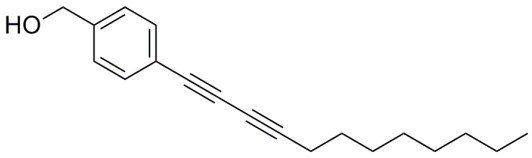
^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 7.46 – 7.39 (m, 2H), 7.35 – 7.25 (m, 3H)

The spectral data agree with the data given in the literature[5]

General Procedure B: Synthesis of unsymmetrical conjugated diyne alcohols[6]

To a stirred solution of iodo-alkyne and alkynol in pyrrolidine under an argon atmosphere, was added copper(I) iodide. After stirring at room temperature for 30 min, the mixture was hydrolysed with a saturated aqueous solution of ammonium chloride and extracted with diethyl ether. The organic extract was dried over magnesium sulfate and the solvent was removed in vacuo. Column chromatography afforded the pure compounds.

Synthesis of (4-Dodeca-1,3-diynyl-phenyl)-methanol (**8**)



1-iododecyne (3.00 g, 11.4 mmol), (4-ethynyl-phenyl)-methanol (0.50 g, 3.8 mmol) and copper(I)iodide (72.0 mg, 0.4 mmol) in pyrrolidine (10 ml) were reacted accordingly to general procedure B. 30 ml of an aqueous solution of ammonium chloride and diethyl ether (3 x 20 ml) were used for the aqueous work up. Column chromatography (ethyl acetate/hexane 15:85) gave 0.44 g (1.6 mmol, 43 %) of pure (4-dodeca-1,3-diynyl-phenyl)-methanol.

^{1}H-NMR ($CDCl_3$, 200 MHz): δ[ppm] = 7.47 (d, 2H, J = 8.2 Hz), 7.30 (d, 2H, J = 8.2 Hz), 4.70 (d, 2H, J = 5.9 Hz), 2.36 (tr, 2H, J = 6.9 Hz), 1.75 – 1.17 (m, 13 H), 0.85 (tr, 3H, J = 6.7 Hz)

^{13}C-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 141.6, 132.7, 126.7, 121.3, 85.0, 77.2, 74.5, 65.0, 64.9, 31.8, 29.1, 29.1, 28.9, 28.3, 22.6, 19.6, 14.1

IR (film) [cm^{-1}]: = 3268, 2932, 2853, 2245, 1913, 1455, 1040, 908, 733

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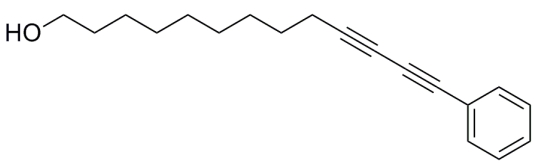
[5] Kunishima, M.; Nakata, D.; Tanaka, S.; Hioki, K.; Tani, S. *Tetrahedron*, **2000**, *56*, 9927 - 9935

[6] Alami, M.; Ferri, F. *Tetrahedron Lett.* **1996**, *37(16)*, 2763-2766

HR-MS (EI): 268.1822 (M^+, $C_{19}H_{24}O^+$; calc. 268.1822)

Synthesis of 13-Phenyl-trideca-10, 12-diyn-1-ol (**9**)



1-iodo-2-phenylacetylene (6.80 g, 29.8 mmol), undec-10-yn-1-ol (2.94 g, 17.5 mmol) and copper(I) iodide (0.57 g, 3.0 mmol) in pyrrolidine (50 ml) were reacted accordingly to general procedure B. 200 ml of an aqueous solution of ammonium chloride and diethyl ether (3 x 200 ml) were used for the aqueous work up. Column chromatography (ethyl acetate/hexane 34:66) gave 2.96 g (11.0 mmol, 63 %) of pure 13-phenyl-trideca-10, 12-diyn-1-ol.

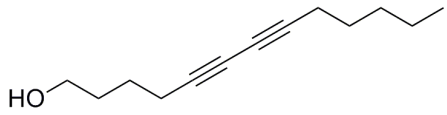
^{1}H-NMR ($CDCl_3$, 200 MHz): δ[ppm] = 7.52 – 7.42 (m, 2 H), 7.36 – 7.22 (m, 3 H), 3.64 (2H, J = 5.5 Hz, J = 6.4 Hz), 2.36 (tr, 2H, J = 6.8 Hz),1.66 – 1.07 (m, 14 H),

^{13}C-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 132.5, 128.8, 128.3, 122.1, 84.8, 77.2, 74.7, 65.1, 63.1, 32.8, 29.4, 29.3, 29.0, 28.8, 28.2, 25.7, 19.6

IR (film) [cm^{-1}]: = 3340, 3058, 2929, 2856, 2244, 1595, 1442, 1336, 1056, 755

HR-MS (EI): 268.1816 (M^+, $C_{19}H_{24}O^+$; calc. 268.1822)

Synthesis of trideca-5,7-diyne-1-ol (**10**)



1-iodo-hept-1-yne (9.60 g, 43.3 mmol), hex-5-yn-1-ol (2.50 g, 25.5 mmol) and copper(I) iodide (0.82 g, 4.3 mmol).in pyrrolidine (60 ml) were reacted accordingly to general procedure B. 150 ml of an aqueous solution of ammonium chloride and diethyl ether (3 x 150 ml) were used for the aqueous work up. Column chromatography (ethyl acetate/hexane 34:66) gave 2.90 g (15.10 mmol, 60 %) of pure trideca-5,7-diyn-1-ol.

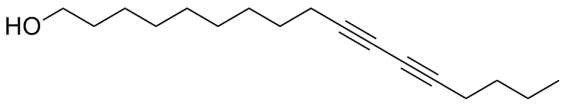
^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 3.65 (2H, t, J = 6.1 Hz), 2.29 (2H, t, J = 6.8 Hz), 2.23 (2H, t, J = 7.0 Hz), 1.71 – 1.26 (10H, m), 0.88 (3H, t, J = 7.1 Hz)

^{13}C-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 77.7, 76.9, 65.7, 65.1, 62.3, 31.7, 31.0, 28.0, 24.6, 22.1, 19.1, 19.0, 13.9

IR (film) [cm^{-1}]: = 3314, 2934, 2864, 2256, 2156, 1457, 1325, 1061

HR-MS (EI): 192.1502 (M^+, $C_{13}H_{20}O^+$; calc. 192.1509)

Synthesis of heptadeca-10,12-diyne-1-ol (**11**)



1-iodo-hex-1-yne (6.20 g, 29.8 mmol), undec-10-yn-1-ol (2.95 g, 17.5 mmol) and copper(I) iodide (0.57 g, 3.0 mmol).in pyrrolidine (50 ml) were reacted accordingly to general procedure B. 100 ml of an aqueous solution of ammonium chloride and diethyl ether (3 x 50 ml) were used for the aqueous work up. Column chromatography (ethyl acetate/hexane 34:66) gave 3.77 g (15.19 mmol, 87 %) of pure heptadeca-10,12-diyn-1-ol.

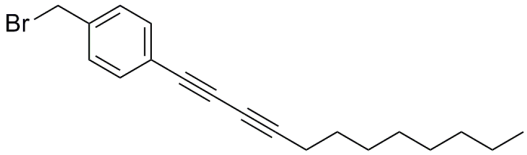
^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 3.62 (2H, t, J = 7.0 Hz), 2.27 – 2.21 (4H, m), 1.62 – 1.26 (18H, m), 0.89 (3H, t, J = 7.3 Hz)

^{13}C-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 77.5, 77.5, 65.3, 65.2, 63.1, 32.8, 30.4, 29.4, 29.3, 29.0, 28.8, 28.3, 25.7, 21.9, 19.2, 18.9, 13.5

IR (film) [cm^{-1}]: = 3333, 2929, 2855, 1780, 1464, 1323, 1058, 723

HR-MS (EI): 248.2125 (M^+, $C_{17}H_{28}O^+$; calc. 248.2135)

Synthesis of 1-Bromomethyl-4-dodeca-1,3-diynyl-benzene (**12**)[7]



To a solution of (4-dodeca-1,3-diynyl-phenyl)-methanol (2.97 g, 11.0 mmol) and pyridine (17.7 mmol, 1.40 ml) in acetonitrile (30 ml) was added at 0°C in 10 min solid PPh_3Br_2 (6.10 g, 14.4 mmol). After stirring at room temperature for 1 h (disappearance of alcohol is checked by TLC), the reaction mixture was filtered through a short pad of silica gel and rinsed with ether-pentane 1/10 (200 ml) to give the pure bromide (3.10 g, 9.36 mmol, 85 %).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 7.44 (d, 2H, J = 8.3 Hz), 7.32 (d, 2H, J = 8.3 Hz), 4.46 (s, 2H), 2.36 (tr, 2H, J = 6.8 Hz), 1.67 – 1.11 (m, 12H), 0.88 (tr, 3H, J = 6.0 Hz)

^{13}C-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 138.3, 132.8, 129.0, 122.3, 85.7, 77.2, 75.2, 74.0, 65.0, 32.8, 31.8, 29.1, 29.0, 28.9, 28.2, 22.6, 19.6, 14.1

IR (film) [cm^{-1}]: = 2922, 2854, 2242, 1923, 1466, 1409, 1225, 1199, 835

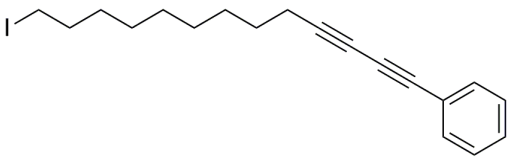
HR-MS (EI): 330.0978 (M^+, $C_{19}H_{23}Br^+$; calc. 330.0978)

[7] Sandri, J.; Viala, J. *Synth. Commun.* **1992**, *22(20)*, 2945-2948.

General Procedure C: Conversion of diyne alcohols into diyne iodides[8]

To a solution of diyne alcohols (1 equiv), triphenylphosphine (1.1 equiv) and imidazole (1.2 equiv) in dichloromethane was added iodine (1.05 equiv) in small portions at -10°C. The solution was stirred at -10°C for 1 h before it was quenched with saturated aqueous amonium thiosulfate. The organic phase was separated and the aqueous phase was extracted with dichloromethane. The combined organic phases were dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography

Synthesis of (13-Iodo-trideca-1,3-diynyl)-benzene (**13**)



13-phenyl-trideca-10,12-diyn-1-ol (0.50 g, 1.9 mmol), triphenylphosphine (0.54 g, 2.1 mmol), imidazole (0.15 g, 2.2 mmol) and iodine (0.50 g, 2.0 mmol) in dichloromethane (50 ml) were reacted accordingly to general procedure C. For the work up a saturated aqueous solution of amonium thiosulfate (30 ml) and dichloromethane (3 x 20 ml) were used. The residue was purified by flash silica gel column chromatography (gradient eluent 0 % to 2 % ethyl acetate in hexanes) to provide pure (13-Iodo-trideca-1,3-diynyl)-benzene (0.43 g, 1.13 mmol, 61 %).

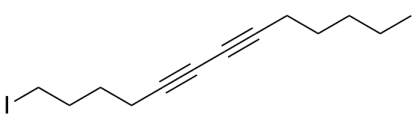
^{1}H-NMR ($CDCl_3$, 200 MHz): δ[ppm] = 7.38 – 7.24 (m, 3H), 7.53 – 7.42 (m, 2H), 3.19 (tr, 2H, J = 7.0 Hz), 2.36 (tr, 2H, J = 6.8 Hz), 1.91 – 1.68 (m, 2H), 1.66 – 1.05 (m, 13 H)

^{13}C-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 132.4, 128.7, 128.3, 122.0, 84.7, 74.7, 74.4, 65.1, 29.2, 28.9, 28.7, 28.4, 28.2, 19.5, 7.2

IR (film) [cm^{-1}]: = 3033, 2928, 2854, 2244, 1595, 1461, 1442, 1178, 755

HR-MS (EI): 378.0823 (M^+, $C_{19}H_{23}I^+$; calc. 378.0839)

Synthesis of 1-iodotrideca-5,7-diyne (**14**)



[8] Liu, J.; Swidorski, J. J.; Peters, S. D.; Hsung, R. P. *J. Org. Chem.* **2005**, *70(10)*, 3898-3902

1-Trideca-5,7-diyne-1-ol (2.82 g, 14.7 mmol), triphenylphosphine (4.23 g, 16.1 mmol), imidazole (1.20 g, 17.60 mmol) and iodine (3.91 g, 15.4 mmol) in dichloromethane (200 ml) were reacted accordingly to general procedure C. For the work up a saturated aqueous solution of amonium thiosulfate (80 ml) and dichloromethane (3 x 80 ml) were used. The residue was purified by flash silica gel column chromatography (gradient eluent 0 % to 2 % ethyl acetate in hexanes) to provide pure 1-iodotrideca-5,7-diyne (4.12 g, 13.6 mmol, 93 %).

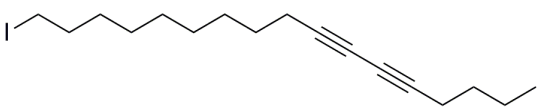
^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 3.18 (2H, t, J = 6.9 Hz), 2.28 (2H, t, J = 6.9 Hz), 2.22 (2H, t, J = 7.0 Hz), 1.92 (2H, quint, J = 7.1 Hz), 1.62 (2H, quint, J = 7.7 Hz), 1.51 (2H, quint, J = 7.8 Hz), 1.39 – 1.25 (4H, m), 0.87 (3H, t, J = 7.1 Hz)

^{13}C-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 77.9, 76.1, 66.0, 65.0, 32.2, 30.9, 29.0, 27.9, 22.1, 19.1, 18.1, 13.9, 5.8

IR (film) [cm^{-1}]: = 2954, 2932, 2861, 2650, 2255, 1455, 1211, 728

HR-MS (EI): 302.0523 (M^+, $C_{13}H_{19}I^+$; calc. 302.0526)

Synthesis of 17-Iodo-heptadeca-10,12-diyne (**15**)



Heptadeca-10,12-diyn-1-ol (2.93 g, 11.8 mmol), triphenylphosphine (3.40 g, 13.0 mmol), imidazole (0.96 g, 14.2 mmol) and iodine (3.14 g, 12.4 mmol) in dichloromethane (60 ml) were reacted accordingly to general procedure C. For the work up a saturated aqueous solution of amonium thiosulfate (80 ml) and dichloromethane (3 x 80 ml) were used. The residue was purified by flash silica gel column chromatography (gradient eluent 0 % to 2 % ethyl acetate in hexanes) to provide pure 17-iodo-heptadeca-10,12-diyne (3.90 g, 10.9 mmol, 92 %).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 3.18 (2H, t, J = 7.1 Hz), 2.27 – 2.20 (4H, m), 1.81 (2H, quint, J = 6.9 Hz), 1.54 – 1.29 (16H, m), 0.90 (3H, t, J = 7.3 Hz)

^{13}C-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 77.5, 77.4, 65.3, 65.2, 33.5, 30.4, 30.4, 29.2, 28.9, 28.7, 28.4, 28.3, 21.9, 19.2, 18.9, 13.5, 7.2

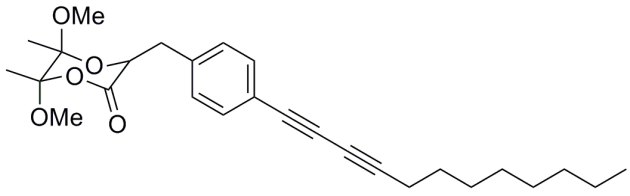
IR (film) [cm^{-1}]: = 2931, 2858, 2251, 1462, 1427, 1378, 1218, 1100, 908, 737

HR-MS (EI): 358.1137 (M^+, $C_{17}H_{27}I^+$; calc. 358.1152)

General Procedure D: Alkylation of butane-2,3-diacetal with diyne halides[3]

Lithium bis(trimethylsilyl)amide (1M in THF) was added to a stirred solution of 5,6-dimethoxy-5,6-dimethyl-[1, 4] dioxan-2-one in dry THF at -78 °C. After 15 min a diyne halide was added and the solution stirred at -78°C for 1 h and then warmed to -20°C for 2.5 h. The reaction was quenched at -20°C with acetic acid then diethyl ether was added and the precipitated salts removed by filtration through a plug of silica. The crude product was purified through column chromatography

Synthesis of 3-(4-Dodeca-1,3-diynyl-benzyl)-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxan-2-one (**17**)



Lithium bis(trimethylsilyl)amide (3.12 ml, 3.12 mmol), 5,6-Dimethoxy-5,6-dimethyl-[1, 4] dioxan-2-one (0.50 g, 2.4 mmol) and 1-bromomethyl-4-dodeca-1,3-diynyl-benzene (3.10 g, 9.4 mmol) were reacted in THF (20 ml) accordingly to general procedure D. For the work up acetic acid (0.36 ml, 6.2 mmol) and diethyl ether (20 ml) were used. The crude product was purified through column chromatography (Et_2O/petrol 8:1) to give the lactone as a colourless oil (1.21 g, 2.8 mmol, 88 %).

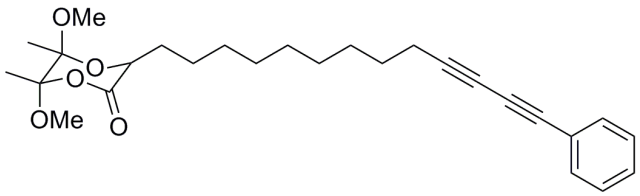
^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 0.89 (tr, 3H, J = 6.6 Hz), 1.46 – 1.22 (m, 16H), 1.62 – 1.52 (m, 2H), 2.35 (tr, 2H, J = 7.0 Hz), 3.06 (s, 3H), 3.15 (d, 2H, J = 5.5 Hz), 3.24 (s, 3H), 4.37 (tr, 1H, J = 5.0 Hz), 7.22 (d, 2H, J = 8.3 Hz), 7.38 (d, 2H, J = 8.3 Hz)

^{13}C-NMR ($CDCl_3$, 200 MHz): δ[ppm] = 169.3, 137.9, 132.1, 130.2, 120.2, 105.0, 98.2, 84.7, 74.8, 74.2, 71.2, 65.1, 49.6, 49.0, 38.2, 31.8, 29.1, 29.0, 28.9, 28.3, 22.6, 19.6, 17.8, 16.9, 14.1

IR (film) [cm^{-1}]: = 3480, 2929, 2243, 1751, 1460, 1379, 1275, 1148, 1037, 865

HR-MS (EI): 440.2564 (M^+, $C_{27}H_{36}O_5^+$; calc. 440.2557)

Synthesis of 5,6-Dimethoxy-5,6-dimethyl-3-(13-phenyl-trideca-10,12-diynyl)-[1,4]dioxan-2-one (**18**)



Lithium bis(trimethylsilyl)amide (2.36 ml, 2.36 mmol), 5,6-Dimethoxy-5,6-dimethyl-[1, 4] dioxan-2-one (0.50 g, 2.4 mmol) and (13-iodo-trideca-1,3-diynyl)-benzene (2.98 g, 7.9 mmol) were reacted in THF (20 ml) accordingly to general procedure D. For the work up acetic acid (0.31 ml, 5.3 mmol) and

diethyl ether (20 ml) were used. The crude product was purified through column chromatography (Et_2O/petrol 8:1) to give the lactone as a colourless oil 0.41 g (0.9 mmol, 39 %).

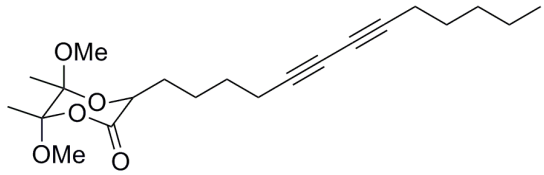
^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 7.51-7.46 (m, 2H), 7.37 – 7.26 (m, 3H), 3.42 (s, 3H), 3.30 (s, 3H), 2.36 (tr, 2H, J = 7.0 Hz), 1.86 (quart, 2H, J = 7.8 Hz), 1.60 – 1.23 (m, 20H).

^{13}C-NMR ($CDCl_3$, 200 MHz): δ[ppm] = 170.4, 132.5, 128.8, 128.3, 122.1, 104.8, 98.0, 84.9, 74.7, 74.4, 70.6, 65.0, 49.9, 49.0, 32.7, 29.4, 29.4, 29.2, 29.0, 28.8, 28.2, 25.1, 19.6, 17.9, 17.0

IR (film) [cm^{-1}]: = 3478, 2929, 2856, 2244, 1751, 1460, 1265, 1147, 1038, 757

HR-MS (EI): 440.2542 (M^+, $C_{27}H_{36}O_5^+$; calc. 440.2563)

Synthesis of (±) 5, 6-Dimethoxy-5, 6-dimethyl-3-(trideca-5,7-diynyl)-1,4-dioxan-2-one (**19**)



Lithium bis(trimethylsilyl)amide (3.15 ml, 3.15 mmol), 5,6-Dimethoxy-5,6-dimethyl-[1, 4] dioxan-2-one (0.60 g, 3.15 mmol) and 1-iodotrideca-5,7-diyne (2.86 g, 9.5 mmol) were reacted in THF (5 ml) accordingly to general procedure D. For the work up acetic acid (0.40 ml, 6.94 mmol) and diethyl ether (20 ml) were used. The crude product was purified through column chromatography (Et_2O/petrol 8:1) to give the lactone as a colourless oil 0.45 g (1.23 mmol, 39 %).

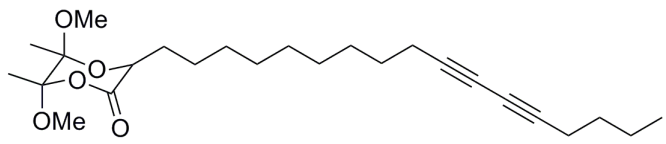
^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 4.14 (1H, t, J = 5.9 Hz), 3.42 (3H, s), 3.30 (3H, s), 2.27 – 2.21 (4H, m), 1.87 (2H, quart, J = 5.9 Hz), 1.48 (3H, s), 1.39 (3H, s), 1.63–1.23 (10H, m), 0.89 (3H, t, J = 7.0 Hz)

^{13}C-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 170.1, 104.8, 98.0, 77.6, 70.3, 68.3, 65.5, 65.2, 49.9, 49.0, 32.1, 30.9, 28.0, 28.0, 24.5, 22.1, 19.1, 19.1, 17.8, 17.0, 13.9,

IR (film) [cm^{-1}]: = 3293, 2935, 2156, 1752, 1460, 1379, 1148, 1038, 862

HR-MS (EI): 364.2234 (M^+, $C_{21}H_{32}O_5^+$; calc. 364.2244)

Synthesis of (±) 5,6-Dimethoxy-5,6-dimethyl-3-heptadeca-10,12-diynyl-[1,4] dioxan-one (**20**)



Lithium bis(trimethylsilyl)amide (1.0 ml, 1.0 mmol), 5,6-Dimethoxy-5,6-dimethyl-[1, 4] dioxan-2-one (0.20 g, 1.1 mmol) and 17-Iodo-heptadeca-5,7-diyne (1.13 g, 3.2 mmol) were reacted in THF (5 ml) accordingly to general procedure D. For the work up acetic acid (0.15 ml, 2.1 mmol) and diethyl ether

(10 ml) were used. The crude product was purified through column chromatography (Et_2O/petrol 8:1) to give the lactone as a colourless oil 0.19 g (0.44 mmol, 42 %).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 4.14 (1H, t, J = 5.9 Hz), 3.42 (3H, s), 3.30 (3H, s), 2.28 – 2.20 (4H, m), 1.86 (2H, quart, J = 7.8 Hz), 1.47 (3H, s), 1.38 (3H, s), 1.56–1.23 (18H, m), 0.90 (3H, t, J = 7.3 Hz)

^{13}C-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 170.4, 104.8, 98.0, 77.5, 77.5, 77.2, 70.6, 65.2, 50.0, 49.0, 32.7, 30.4, 29.4, 29.4, 29.3, 29.0, 28.8, 28.3, 25.1, 21.9, 19.2, 18.9, 17.9, 17.1, 13.5

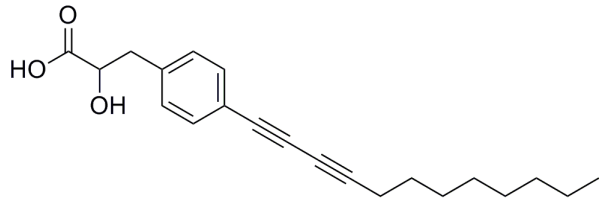
IR (film) [cm^{-1}]: = 3155, 2932, 2859, 2254, 1737, 1463, 1380, 1274, 1149, 1037, 911, 742

HR-MS (EI): 420.2853 (M^+, $C_{25}H_{40}O_5^+$; calc. 420.2870)

General Procedure E: Acid mediated hydrolysis of butane-2,3-diacetals[3]

Butane-2,3-diacetals were dissolved in a solution of TFA-H_2O (9:1) and stirred at room temperature for 45 min. NaOH (2.5 M) was added, the mixture stirred for 15 min, acidified with 3N HCl (pH 2) and then extracted with CH_2Cl_2. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give the pure products.

Synthesis of 3-(4-Dodeca-1,3-diynyl-phenyl)-2-hydroxy-propionic acid (**21**)



3-(4-Dodeca-1,3-diynyl-benzyl)-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxan-2-one (0.17 g, 0.4 mmol) was reacted accordingly to general procedure E in a solution of TFA-H_2O (9:1, 5 ml). For the work up sodium hydroxyde (2.5 M, 5 ml) and CH_2Cl_2 (3 x 20 ml) were used. The pure product was obtained in 93 % yield (0.4 mmol, 0.12 g).

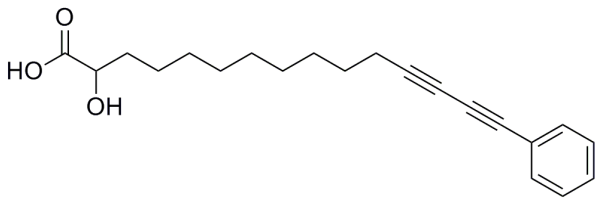
^{1}H-NMR ($CDCl_3$, 200 MHz): δ[ppm] = 7.42 (d, 2H, J = 8.1 Hz), 7.20 (d, 2H, J = 8.1 Hz), 4.51 (dd, 1H, J = 7.0 Hz, J = 3.9 Hz), 3.21 (dd, 1H, J = 14 Hz, J = 3.9 Hz), 2.98 (dd, 1H, J = 14.0 Hz, J = 7.0 Hz), 2.35 (tr, 2H, J = 6.8 Hz), 1.68 – 1.07 (m, 12 H), 0.88 (tr, 3H, J = 6.2 Hz)

^{13}C-NMR ($CDCl_3$, 200 MHz): δ[ppm] = 177.7, 136.9, 132.6, 129.6, 121.0, 85.0, 77.2, 74.6, 74.4, 65.0, 40.0, 31.8, 29.1, 29.1, 28.9, 28.3, 22.6, 19.6, 14.1

IR (film) [cm^{-1}]: = 3508, 2956, 2853, 17421464, 1279, 1110, 815, 733

HR-MS (EI): 326.1873 (M^+, $C_{21}H_{26}O_3^+$; calc. 326.1876)

Synthesis of 2-hydroxy-15-phenyl-pentadeca-12,14-diynoic acid (**22**)



5,6-Dimethoxy-5,6-dimethyl-3-(13-phenyl-trideca-10,12-diynyl)-[1,4]dioxan-2-one (0.29 g, 0.7 mmol) was reacted accordingly to general procedure E in a solution of TFA-H_2O (9:1, 10 ml). For the work up sodium hydroxyde (2.5 M, 10 ml) and CH_2Cl_2 (3 x 20 ml) were used. The pure product was obtained in 93 % yield (0.6 mmol, 0.20 g).

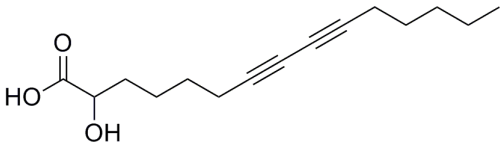
^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 7.53-7.42 (m, 2H), 7.35-7.27 (m, 3H), 4.28 (dd, *J* = 7.2 Hz, *J* = 4.1 Hz , 1H), 2.36 (t, *J* = 7.02 Hz, 2H), 1.92-1.77 (m, 1H), 1.79-1.62 (m, 1H), 1.62-1.22 (m, 14H),

^{13}C-NMR ($CDCl_3$, 200 MHz): δ[ppm] = 179.7, 132.5, 128.8, 128.3, 122.1, 84.8, 74.7, 74.4, 70.3, 65.1, 34.2, 29.3, 29.2, 29.0, 28.8, 28.2, 24.7, 19.6

IR (film) [cm^{-1}]: = 3508, 2917, 2848, 2243, 1740, 1594, 1466, 1291, 1237, 1119, 901, 751

HR-MS (EI): 326.1873 (M^+, $C_{21}H_{26}O_3^+$; calc. 326.1876)

Synthesis of 2-hydroxy-pentadeca-7, 9-diynoic acid (**23**)



(±) 5,6-Dimethoxy-5,6-dimethyl-3-(trideca-5,7-diynyl)-[1,4]-dioxan-2-one (0.17 g, 0.5 mmol) was reacted accordingly to general procedure E in a solution of TFA-H_2O (9:1, 5 ml). For the work up sodium hydroxyde (2.5 M, 5 ml) and CH_2Cl_2 (3 x 20 ml) were used. The pure product was obtained in 91 % yield (0.4 mmol, 0.11 g).

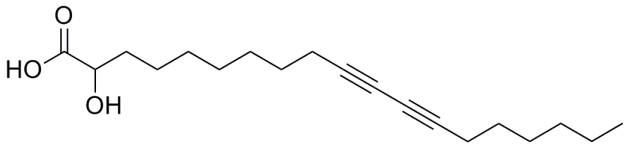
^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 4.34 – 4.21 (1H, m), 2.32 – 2.22 (4H, m), 1.95 – 1.47 (8H, m), 1.42 – 1.23 (4H, m), 0.89 (3H, t, J = 7.1 Hz)

^{13}C-NMR ($CDCl_3$, 200 MHz): δ[ppm] = 179.1, 77.8, 76.8, 70.0, 65.7, 65.1, 33.6, 31.0, 28.0, 28.0, 24.1, 22.1, 19.2, 19.1, 13.9,

IR (film) [cm^{-1}]: = 3507, 2953, 2863, 1740, 1461, 1240, 1113, 892,

HR-MS (EI): 250.1563 (M^+, $C_{15}H_{22}O_3^+$; calc. 250.1563)

Synthesis of 2-hydroxy-nonadeca-10,12-diynoic acid (**24**)



(±) 5,6-Dimethoxy-5, 6-dimethyl-3-heptadeca-10,12-diynyl-[1,4] dioxan-one (0.16 g, 0.4 mmol) was reacted accordingly to general procedure E in a solution of TFA-H_2O (9:1, 5 ml). For the work up sodium hydroxyde (2.5 M, 5 ml) and CH_2Cl_2 (3 x 20 ml) were used. The pure product was obtained in 91 % yield (0.4 mmol, 0.11 g).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 4.28 (1H, dd, J^1 = 4.0, J^2 = 6.9), 2.28 – 2.22 (4H, m), 1.92-1.75 (1H, m), 1.60 – 1.72 (1H, m), 1.57 – 1.18 (18H, m), 0.90 (3H, t, J = 7.3 Hz)

^{13}C-NMR ($CDCl_3$, 200 MHz): δ[ppm] = 179.7, 77.5, 77.3, 70.3, 68.0, 65.2, 34.0, 30.4, 29.4, 29.1, 29.0, 28.8, 28.3, 24.6, 21.7, 19.2, 18.9, 13.5

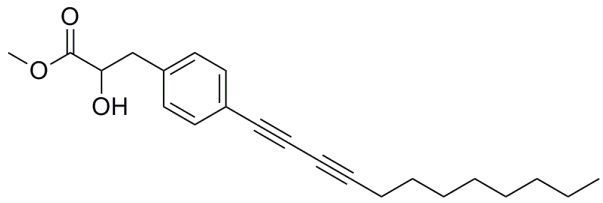
IR (film) [cm^{-1}]: = 3500, 2918, 2849, 1741, 1465, 1294, 1121, 1093, 902

HR-MS (EI): 306.2188 (M^+, $C_{19}H_{30}O_3^+$; calc. 306.2189)

General Procedure F: Synthesis of the 2-hydroxy-diyne ester through transesterification of butane-2,3-diacetals

Butane-2,3-diacetals were dissolved in a 0.5 M solution of TMSCl in alcohol (Reaction time and reaction temperature were modified accordingly to the alcohols used). The reaction was concentrated *in vacuo* and the residue purified by column chromatography to give the pure products.

Synthesis of 3-(4-Dodeca-1,3-diynyl-phenyl)-2-hydroxy-propionic acid methyl ester (**25**)



3-(4-Dodeca-1,3-diynyl-benzyl)-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxan-2-one (0.15 g, 0.3 mmol) was dissolved in a 0.5 M solution of trimethylsilyl chloride (5 mmol, 0.5 g) in methanol (10 ml) and stirred at room temperature for 1 h. The reaction was concentrated *in vacuo* and purified through column chromatography (EtOAc/petrol 1:3), giving the pure product in 95 % yield (0.3 mmol, 0.11 g).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 7.40 (d, 2H, J = 8.1 Hz), 7.15 (d, 2H, J = 8.1 Hz), 4.44 (ddd, 1H, J = 4.5 Hz, J = 6.2 Hz, J = 10.4 Hz), 3.77 (s, 3H), 3.11 (dd, 1H, J = 14.0 Hz, J = 3,9 Hz), 2.95 (dd,

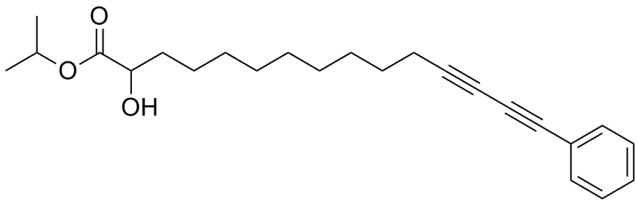
1H, J = 14.0 Hz, J = 7.0 Hz), 2.72 (d, 1H, J = 5.9 Hz), 2.35 (tr, 2H, J = 7.0 Hz), 1.61 – 1.20 (m, 12H), 0.89 (tr, 3H, J = 6.2 Hz),

^{13}C-NMR ($CDCl_3$, 200 MHz): δ[ppm] = 174.3, 137.4, 132.5, 129.5, 120.7, 84.8, 74.5, 74.4, 71.0, 65.0, 52.5, 40.4, 31.8, 29.1, 29.0, 28.9, 28.2, 22.6, 19.6, 14.1

IR (film) [cm^{-1}]: = 3481, 2928, 2856, 2243, 1740, 1509, 1440, 1269, 1221, 1111, 824

HR-MS (EI): 340.2038 (M^+, $C_{22}H_{28}O_3^+$; calc. 340.2033)

Synthesis of 2-hydroxy-15-phenyl-pentadeca-12,14-diynoic acid isopropyl ester (**26**)



5,6-Dimethoxy-5,6-dimethyl-3-(13-phenyl-trideca-10,12-diynyl)-[1,4]dioxan-2-one (0.10 g, 0.3 mmol) was dissolved in a 0.5 M solution of trimethylsilyl chloride (5 mmol, 0.5 g) in ^{i}PrOH (10 ml) and and heated to reflux at 80°C for 45 h. The reaction was concentrated *in vacuo* and purified through column chromatography (EtOAc/petrol 1:3), giving the pure product in 86 % yield (0.2 mmol, 0.09 g).

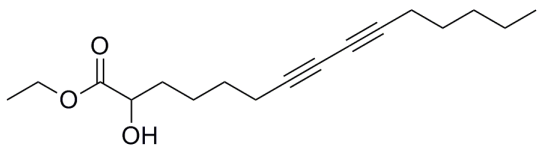
^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 7.50 – 7.46 (m, 2H), 7.35 – 7.26 (m, 3H), 5.10 (hept, 1H, J = 6.3 Hz), 4.12 (dd, 1H, J = 4.3 Hz, J = 2.2 Hz), 2.75 (br, 1H), 2.35 (tr, 2H, J = 7.0 Hz), 1.81 – 1.23 (m, 22H),

^{13}C-NMR ($CDCl_3$, 200 MHz): δ[ppm] = 175.0, 132.5, 128.8, 128.3, 122.1, 84.8, 74.7, 74.4, 70.4, 69.4, 65.0, 34.4, 29.4, 29.3, 29.3, 29.0, 28.8, 28.2, 24.6, 21.8, 19.6

IR (film) [cm^{-1}]: = 3505, 2980, 2856, 2244, 1727, 1464, 1374, 1264, 1106, 756

HR-MS (EI): 368.2339 (M^+, $C_{24}H_{32}O_3^+$; calc. 368.2346)

Synthesis of ethyl 2-hydroxypentadeca-7,9-diynoate (**27**)



(±) 5, 6-Dimethoxy-5, 6-dimethyl-3-(trideca-5,7-diynyl)-1,4-dioxan-2-one (0.16 g, 0.4 mmol) was dissolved in a 0.5 M solution of trimethylsilyl chloride (5.0 mmol, 0.54 g) in ethanol (10 ml) and stirred at room temperature for 12 h. The reaction was concentrated *in vacuo* and purified through column chromatography (EtOAc/petrol 1:3), giving the pure product in 96 % yield (0.4 mmol, 0.12 g).

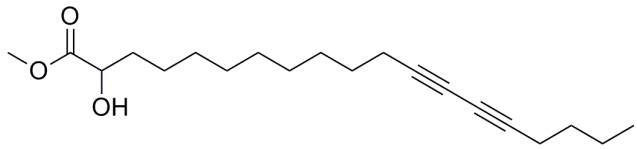
^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 4.31 – 4.21 (m, 2H), 4.15 (dd, 1H, J = 4.0 Hz, J = 2.9 Hz), 2.85 – 2.58 (br, 1H), 2.31 – 2.17 (m, 4H), 1.84 – 1.73 (m, 1H), 1.70 – 1.20 (m, 14H), 0.88 (tr, 3H, J = 7.1 Hz)

^{13}C-NMR ($CDCl_3$, 200 MHz): δ[ppm] = 175.2, 76.8, 70.2, 68.4, 65.6, 65.2, 61.7, 33.8, 31.0, 28.0, 24.0, 22.1, 19.1, 19.0, 14.2, 13.9

IR (film) [cm^{-1}]: = 3492, 2934, 2863, 2156, 1733, 1462, 1215, 1107, 1025

HR-MS (EI): 278.1874 (M^+, $C_{17}H_{26}O_3^+$; calc. 278.1876)

Synthesis of methyl 2-hydroxynonadeca-12, 14-diynoate (**28**)



(±) 5,6-Dimethoxy-5,6-dimethyl-3-heptadeca-10,12-diynyl-[1,4] dioxan-one (0.18 g, 0.4 mmol) was dissolved in a 0.5 M solution of trimethylsilyl chloride (5 mmol, 0.5 g) in Methanol (10 ml) and stirred at room temperature for 25 min. The reaction was concentrated *in vacuo* and purified through column chromatography (EtOAc/petrol 1:3), giving the pure product in 95 % yield (0.4 mmol, 0.11 g).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 4.18 (dd, 1H, J = 5.7 Hz, J = 11.7 Hz), 3.79 (s, 3H), 2.67 (d, 1H, J = 5.7 Hz), 2.23 (quart, 4H, J = 6.4 Hz), 1.83 – 1.74 (m, 1H), 1.67 – 1.58 (m, 1H), 1.56 – 1.20 (m, 18H), 0.90 (tr, 3H, J = 7.3 Hz)

^{13}C-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 175.8, 77.5, 77.5, 70.4, 65.3, 65.2, 52.5, 34.4, 30.4, 29.4, 29.3, 29.2, 29.0, 28.8, 28.3, 24.7, 21.9, 19.2, 18.9, 13.5

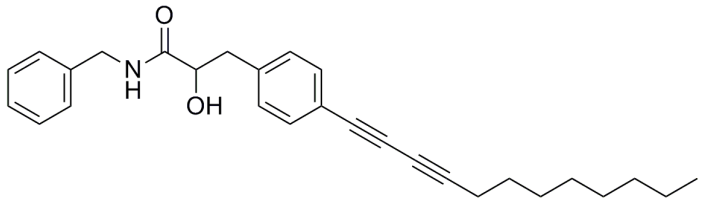
IR (film) [cm^{-1}]: = 3491, 2929, 2857, 2168, 1737, 1458, 1439, 1219, 1143, 1085, 724

HR-MS (EI): 320.2356 (M^+, $C_{20}H_{32}O_3^+$; calc. 320.2346)

General Procedure G: Synthesis of the 2-hydroxy-diyne amides through aminolysis of butane-2,3-diacetals

Butane-2,3-diacetals were dissolved in in the amine used for the aminolysis and stirred at room temperature (The reaction times were modified accordingly to the amines used). A solution of TFA-H_2O (9:1) was added and the mixture was stirred at room temperature for 15 min. The reaction was concentrated *in vacuo* and the residue purified by column chromatography to give the pure products.

Synthesis of N-Benzyl-3-(4-dodeca-1,3-diynyl-phenyl)-2-hydroxy-propionamide (**29**)



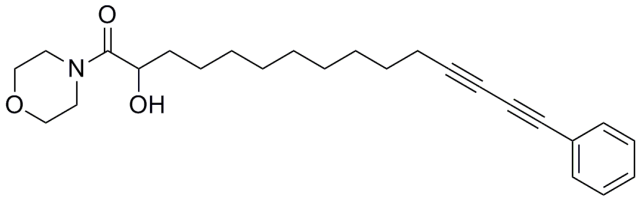
3-(4-Dodeca-1,3-diynyl-benzyl)-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxan-2-one (0.15 g, 0.4 mmol) was dissolved in benzylamine (2 ml) and stirred at room temperature for 72 h. 5 ml of TFA-H_2O (9:1) was added and the mixture was stirred at room temperature for 15 min. The reaction was concentrated in vacuo and the residue purified by column chromatography (EtOAc/petrol 1:1) to give the pure product in 47 % yield (0.2 mmol, 0.06 g).

^{1}H-NMR ($CDCl_3$, 200 MHz): δ[ppm] = 7.41 – 7.09 (m, 10H), 6.80 (tr, 1H, J = 5.8 Hz), 4.51 – 4.29 (m, 3H), 3.18 (dd, 1H, J = 13.9 Hz, J = 4.0 Hz), 2.92 (dd, 1H, J = 13.9 Hz, J = 7.8 Hz), 2.85 – 2.62 (br, 1H), 2.36 (tr, 2H, 6.8 Hz), 1.65 – 1.18 (m, 12H), 0.89 (tr, 3H, J = 5.9 Hz)

^{13}C-NMR ($CDCl_3$, 200 MHz): δ[ppm] = 172.2, 137.8, 137.6, 132.7, 129.7, 128.7, 127.7, 127.6, 120.8, 85.0, 74.6, 74.4, 72.6, 65.0, 43.1, 40.8, 31.8, 29.1, 29.0, 28.9, 28.2, 22.6, 19.6, 14.1

HR-MS (EI): 415.2497 (M^+, $C_{28}H_{33}NO_2^+$; calc. 415.2506)

Synthesis of 2-hydroxy-1-morpholin-4-yl-15-phenyl-pentadeca-12,14-diyn-1-one (**30**)



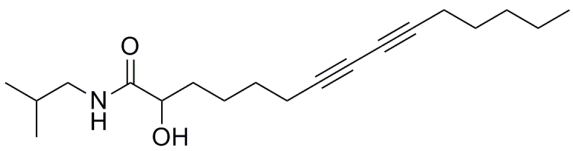
5,6-Dimethoxy-5,6-dimethyl-3-(13-phenyl-trideca-10,12-diynyl)-[1,4]dioxan-2-one (0.08 g, 0.2 mmol) was dissolved in morpholine (2 ml) and stirred at room temperature for 48 h. 5 ml of TFA-H_2O (9:1) was added and the mixture was stirred at room temperature for 15 min. The reaction was concentrated in vacuo and the residue purified by column chromatography (EtOAc/petrol 1:1) to give the pure product in 83 % yield (0.2 mmol, 0.06 g).

^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 7.51 – 7.43 (m, 2H), 7.37 – 7.26 (m, 3H), 4.39 – 4.26 (m, 1H), 3.78 – 3.54 (m, 7H), 3.46 – 3.35 (m, 2H), 2.35 (tr, 2H, J = 7.0 Hz), 1.64 – 1.22 (m, 16H)

^{13}C-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 173.2, 132.4, 128.8, 128.3, 122.1, 84.8, 74.7, 74.4, 67.7, 66.8, 66.4, 65.1, 45.4, 42.8, 35.1, 29.4, 29.3, 29.0, 28.8, 28.2, 24.9, 19.5

HR-MS (EI): 395.2453 (M^+, $C_{25}H_{33}NO_3^+$; calc. 395.2455)

Synthesis of 2-hydroxy-N-isobutylpentadeca-7,9diynamide (**31**)



(±) 5, 6-Dimethoxy-5, 6-dimethyl-3-(trideca-5,7-diynyl)-1,4-dioxan-2-one (0.16 g, 0.4 mmol) was dissolved in isobutylamine (2 ml) and stirred at room temperature for 120 h. 5 ml of TFA-H_2O (9:1) was added and the mixture was stirred at room temperature for 15 min. The reaction was concentrated in vacuo and the residue purified by column chromatography (EtOAc/petrol 1:1) to give the pure product in 78 % yield (0.34 mmol, 0.10 g).

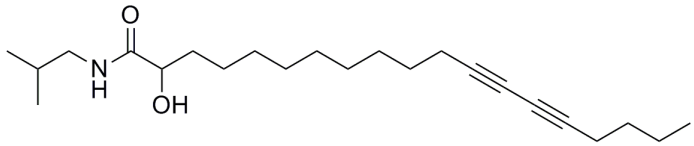
^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 6.57 – 6.52 (br, 1H), 4.13 (dd, 1H, J = 3.6 Hz, J = 7.5 Hz),3.19 – 3.06 (m, 2H), 2.89 – 2.35 (br, 1H), 2.29 – 2.20 (m, 4H), 1.88 – 1.73 (m, 2H), 1.70 – 1.48 (m, 7H), 1.40 – 1.24 (m, 4H), 0.98 – 0.84 (m, 9H)

^{13}C-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 173.5, 77.8, 76.9, 72.0, 65.6, 65.2, 46.5, 34.5, 31.0, 28.5, 28.0, 28.0, 24.2, 22.1, 20.1, 19.2, 19.1, 13.9

IR (film) [cm^{-1}]: = 3324, 2957, 2932, 2870, 2256, 1652, 1539, 1464, 1276, 1160, 1104, 818

HR-MS (EI): 305.2346 (M^+, $C_{19}H_{31}NO_2^+$; calc. 305.2349)

Synthesis of 2-hydroxy-N-isobutylnonadeca-12,14-diynamide (**32**)



(±) 5,6-Dimethoxy-5, 6-dimethyl-3-heptadeca-10,12-diynyl-[1,4] dioxan-one (0.16 g, 0.4 mmol) was dissolved in isobutylamine (2 ml) and stirred at room temperature for 120 h. 5 ml of TFA-H_2O (9:1) was added and the mixture was stirred at room temperature for 15 min. The reaction was concentrated *in vacuo* and the residue purified by column chromatography (EtOAc/petrol 1:1) to give the pure product in 73 % yield (0.3 mmol, 0.10 g).

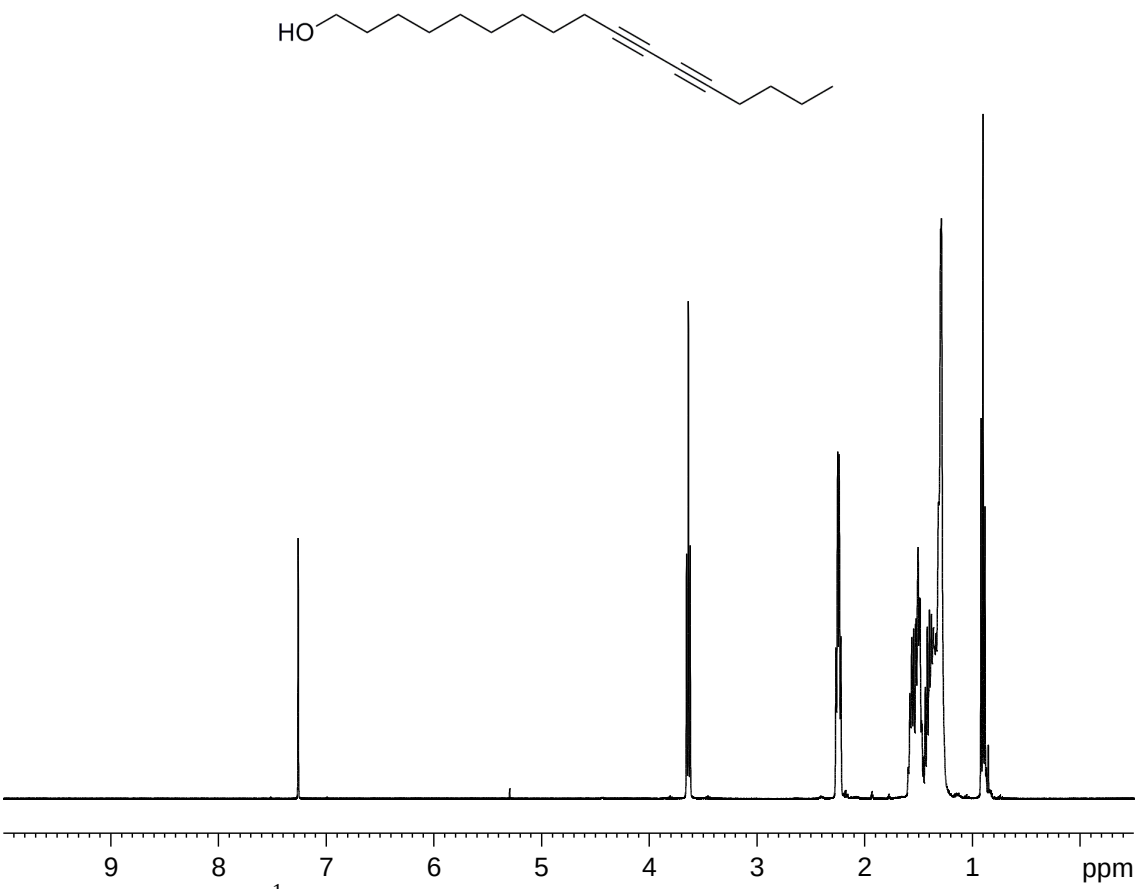
^{1}H-NMR ($CDCl_3$, 400 MHz): δ[ppm] = 6.54 – 6.50 (br, 1H), 4.11 (dd, 1H, J = 3.6 Hz, J = 7.8 Hz), 2.17 – 3.05 (m, 2H), 2.71 – 2.52 (br, 1H), 2.26 – 2.21 (m, 4H), 1.88 – 1.74 (m, 2H), 1.67 – 1.58 (m, 1H), 1.56 – 1.21 (m, 18H), 0.93 – 0.82 (m, 9H)

^{13}C-NMR ($CDCl_3$, 200 MHz): δ[ppm] = 173.7, 77.5, 72.2, 65.2, 46.4, 35.1, 30.4, 29.4, 29.3, 29.0, 28.8, 28.5, 28.3, 24.9, 21.9, 20.1, 19.2, 18.9, 13.5

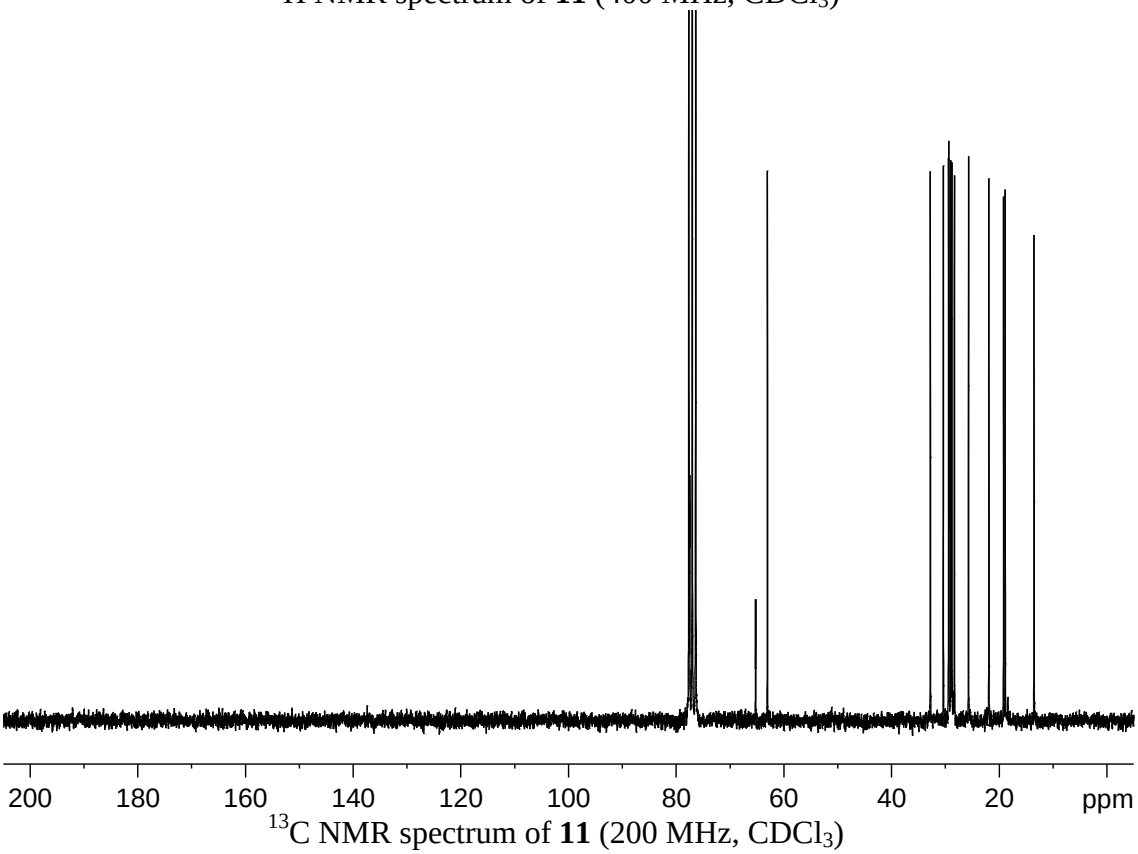
IR (film) [cm^{-1}]: = 3317, 2928, 2857, 2170, 1652, 1538, 1465, 1275, 1159, 1069, 723

HR-MS (EI): 361.2972 (M^+, $C_{23}H_{39}NO_2^+$; calc. 361.2975)

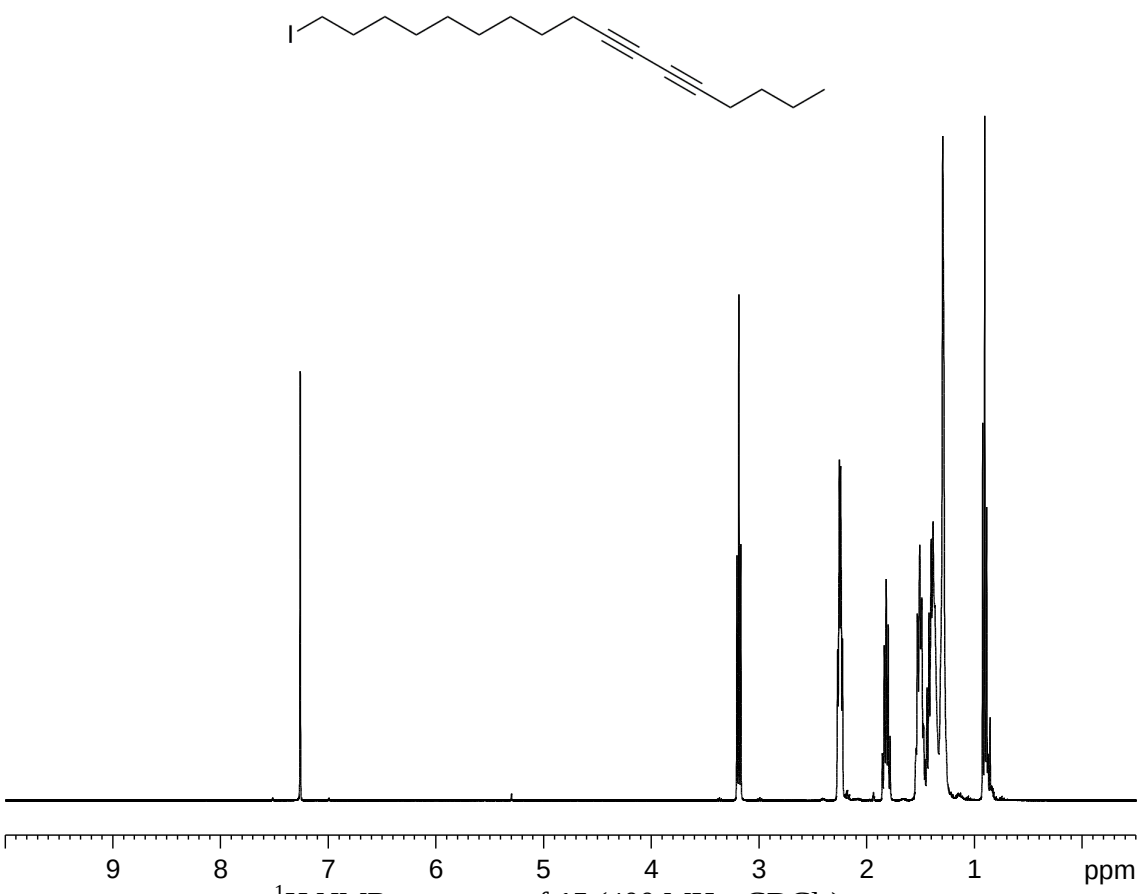
2. ^{1}H and ^{13}C NMR spectra for compounds 8 – 32



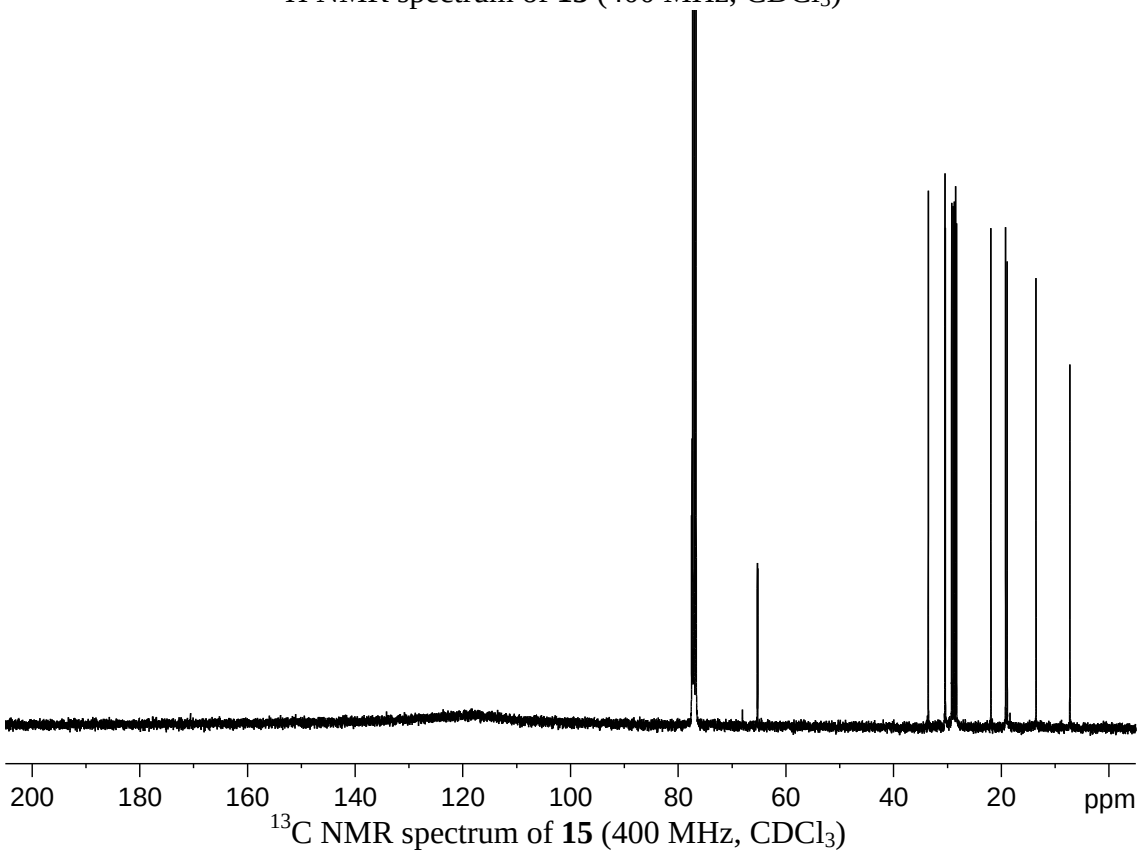
^{1}H NMR spectrum of **11** (400 MHz, $CDCl_3$)



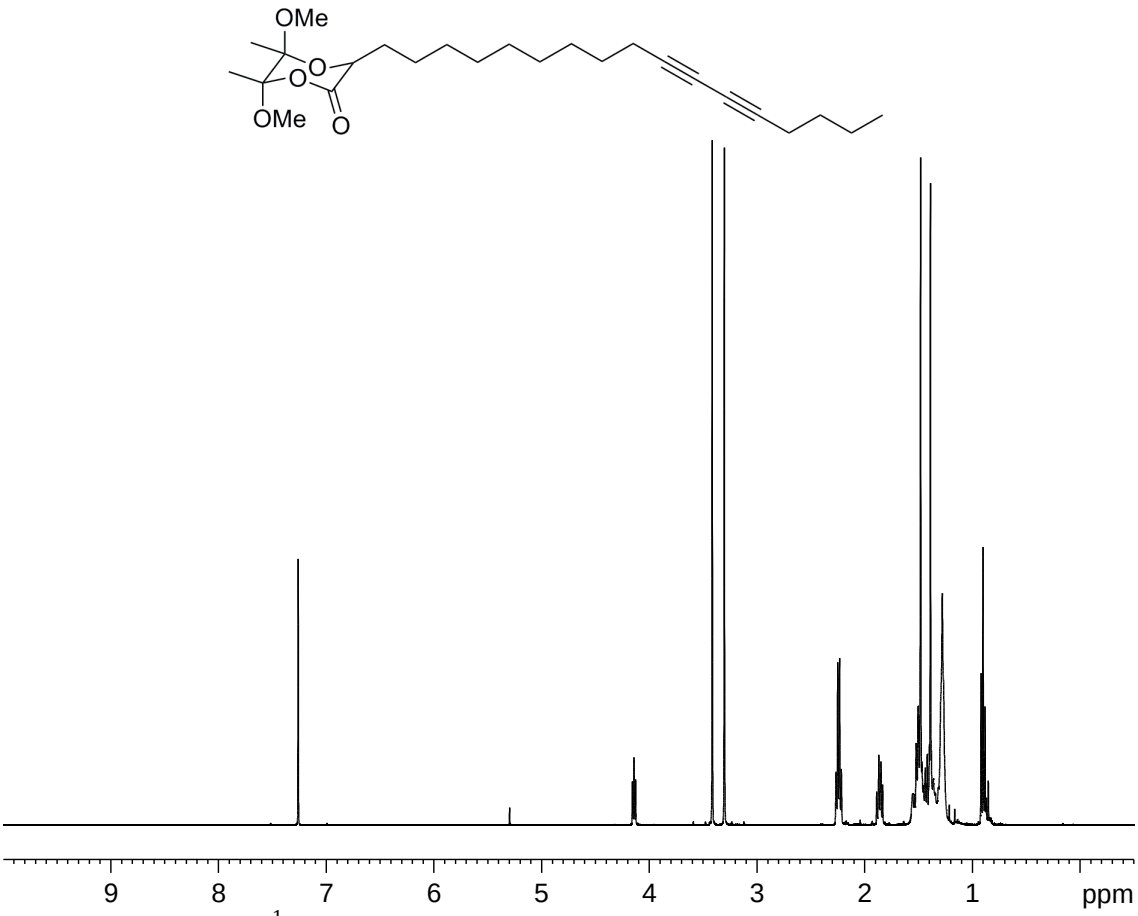
^{13}C NMR spectrum of **11** (200 MHz, $CDCl_3$)



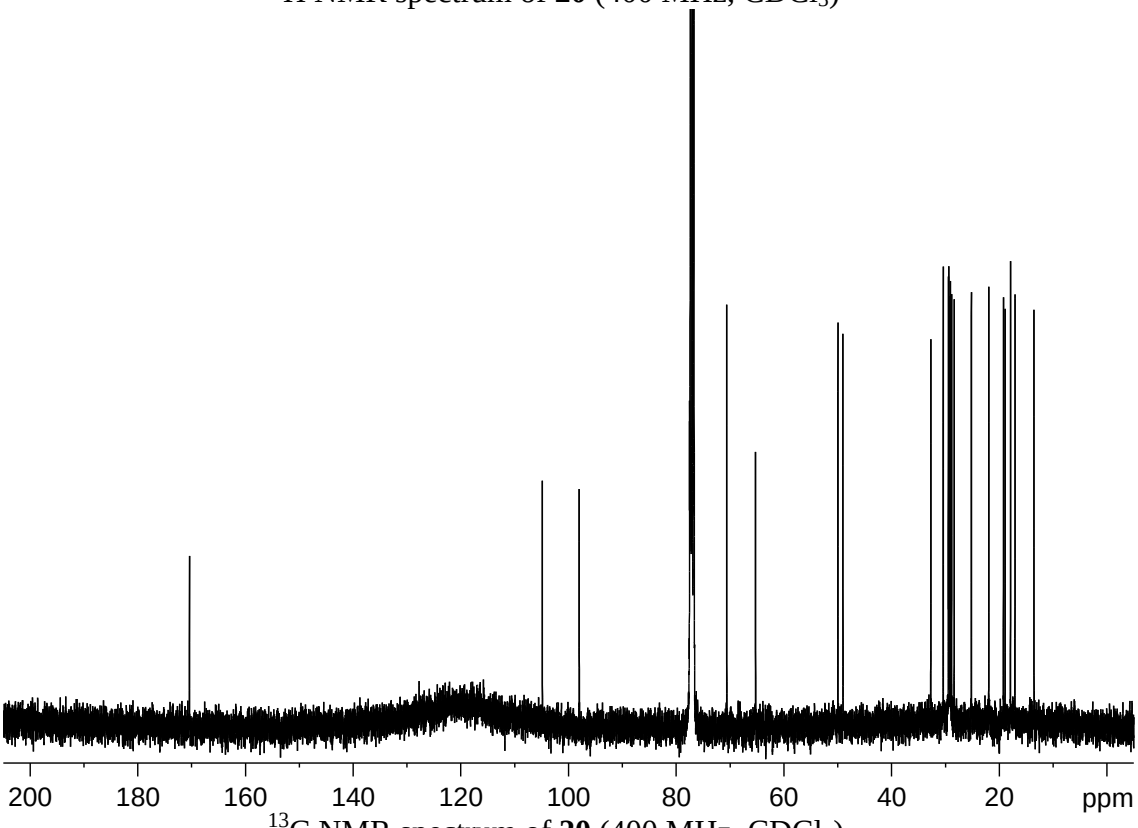
^{1}H NMR spectrum of **15** (400 MHz, $CDCl_3$)



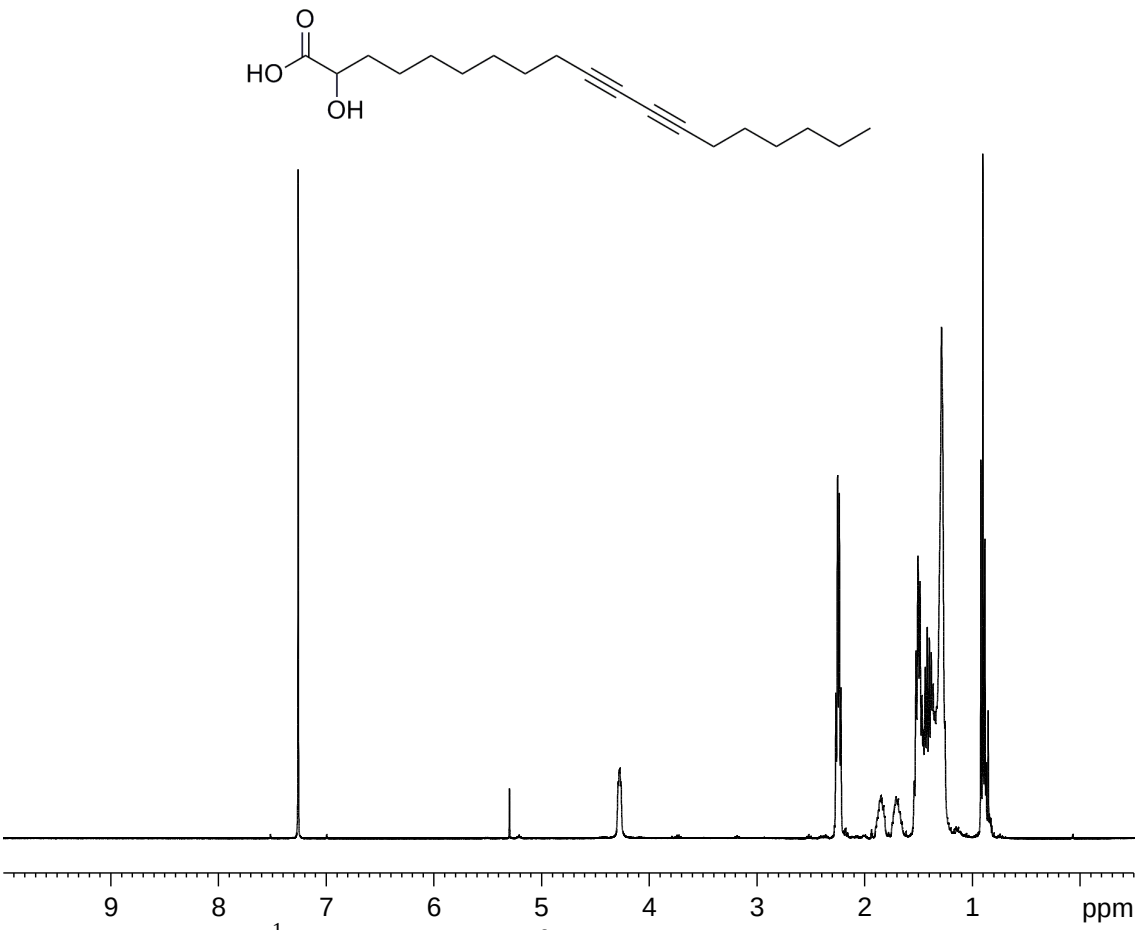
^{13}C NMR spectrum of **15** (400 MHz, $CDCl_3$)



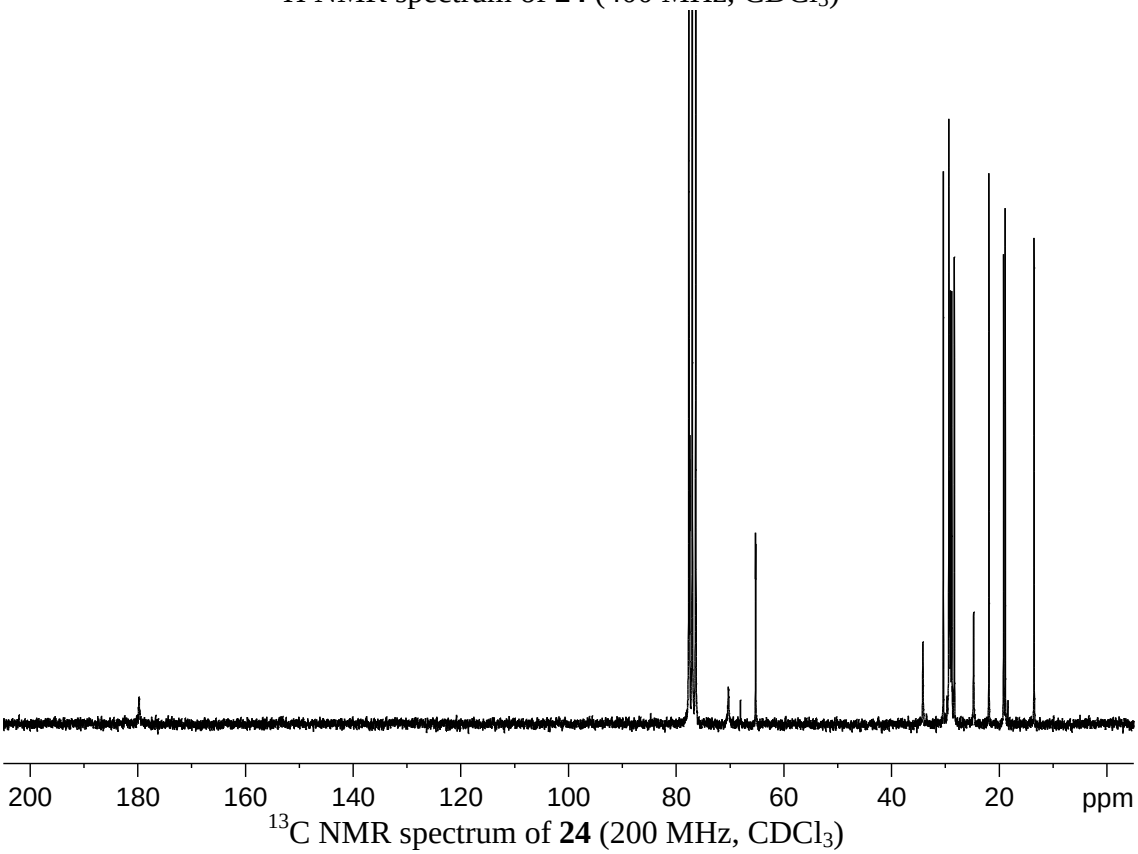
^{1}H NMR spectrum of **20** (400 MHz, $CDCl_3$)



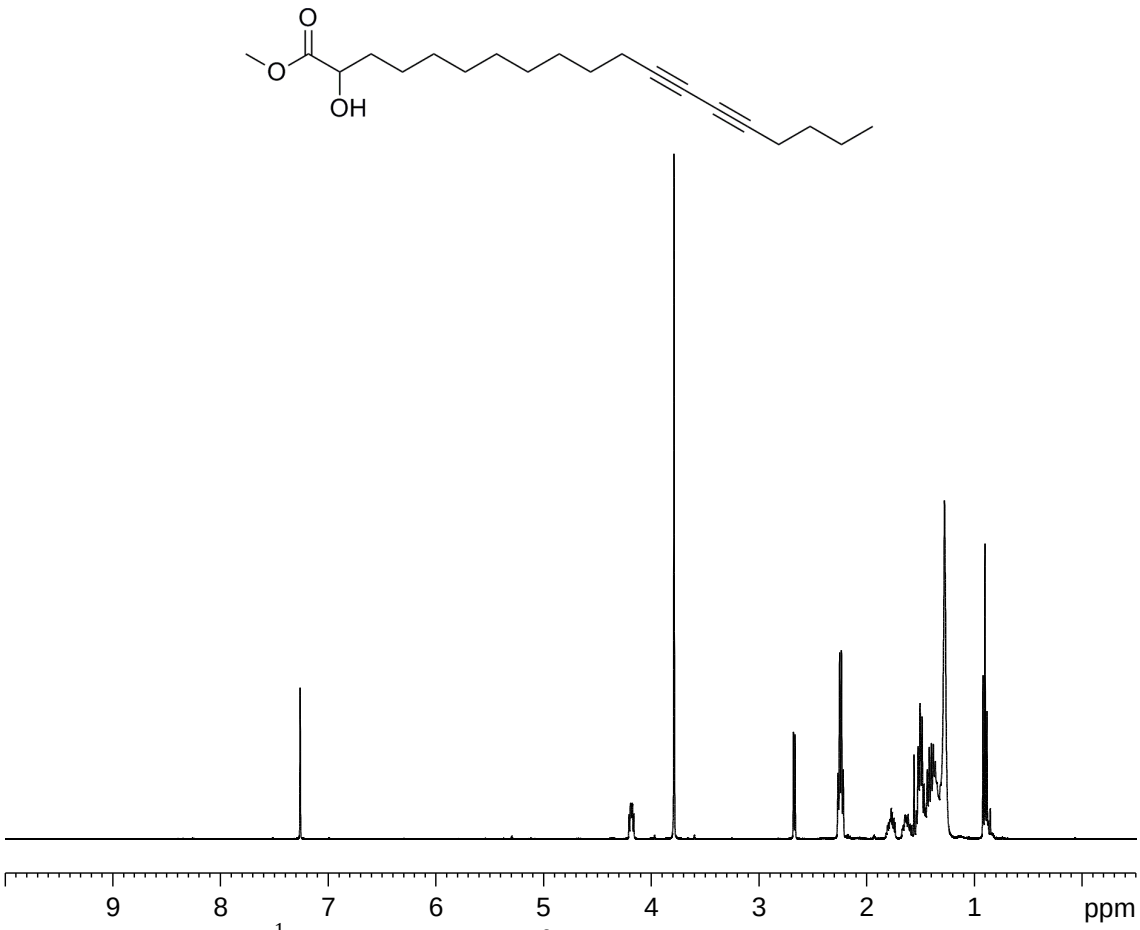
^{13}C NMR spectrum of **20** (400 MHz, $CDCl_3$)



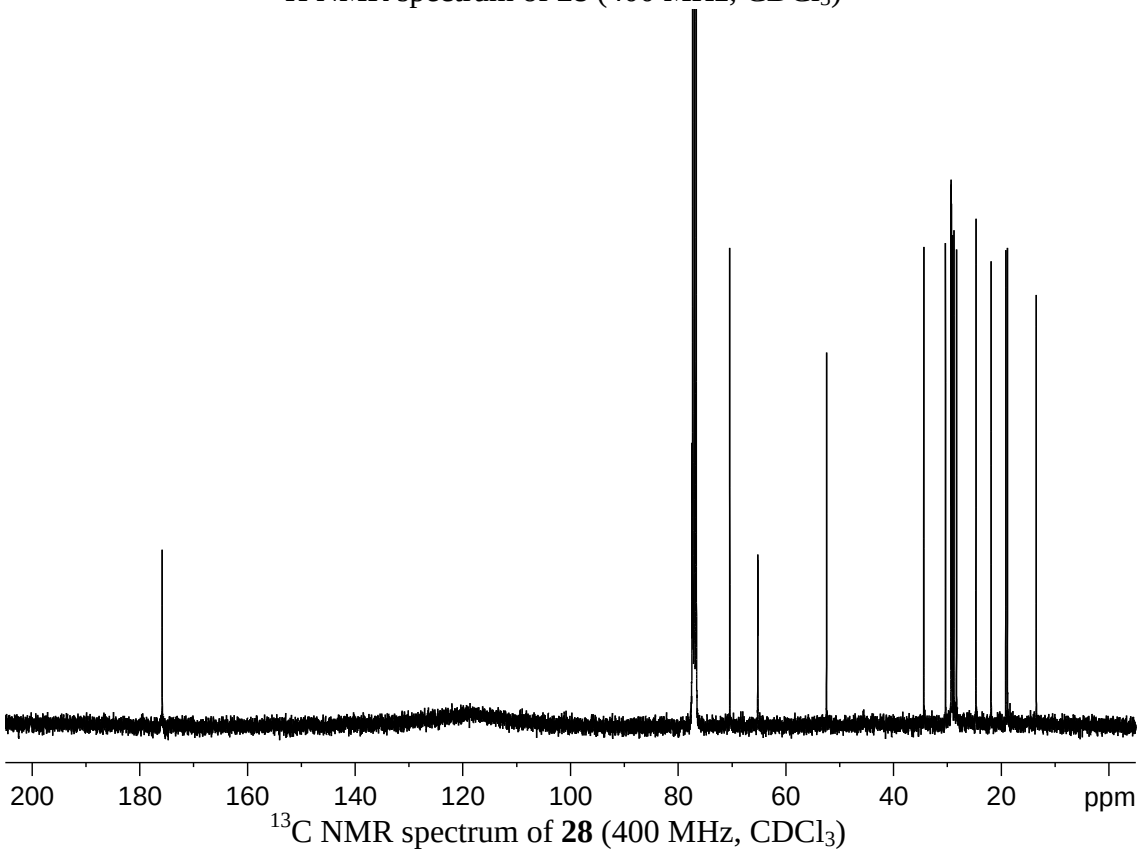
^{1}H NMR spectrum of **24** (400 MHz, $CDCl_3$)



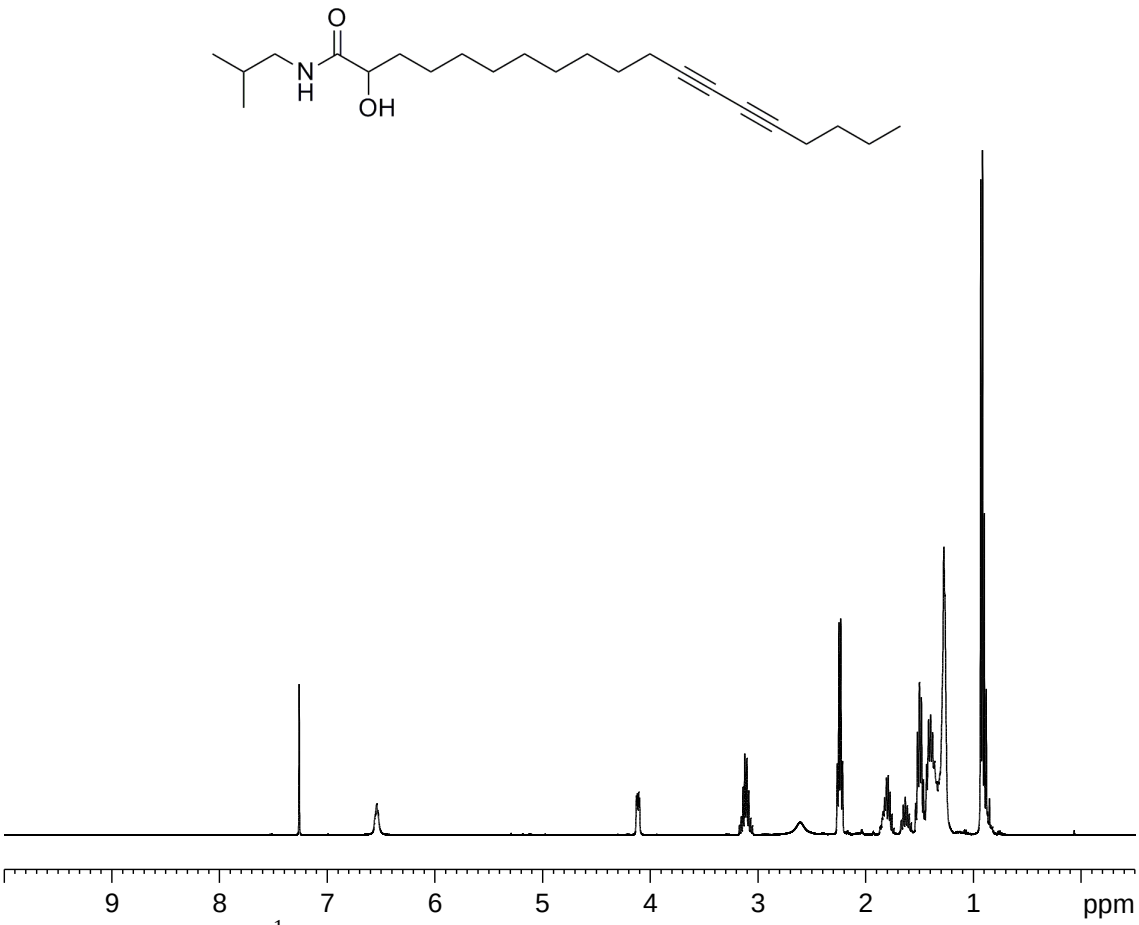
^{13}C NMR spectrum of **24** (200 MHz, $CDCl_3$)



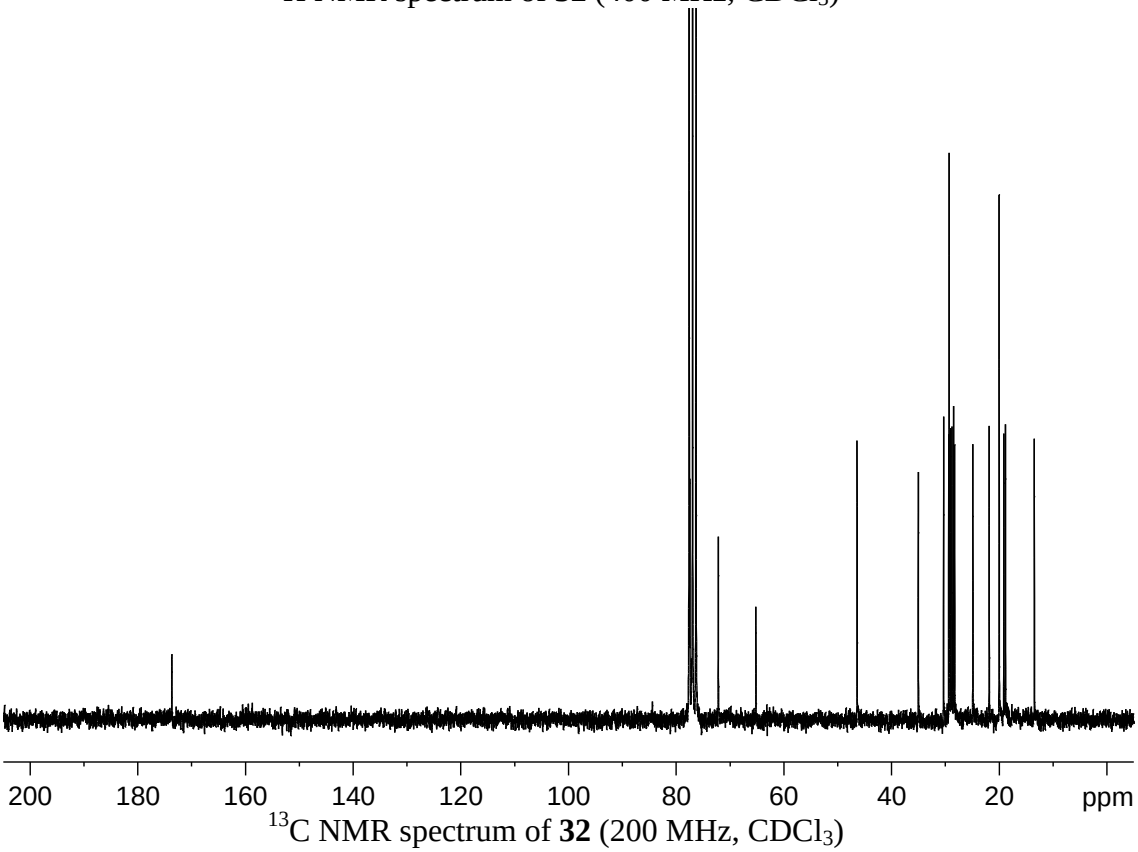
^{1}H NMR spectrum of **28** (400 MHz, $CDCl_3$)



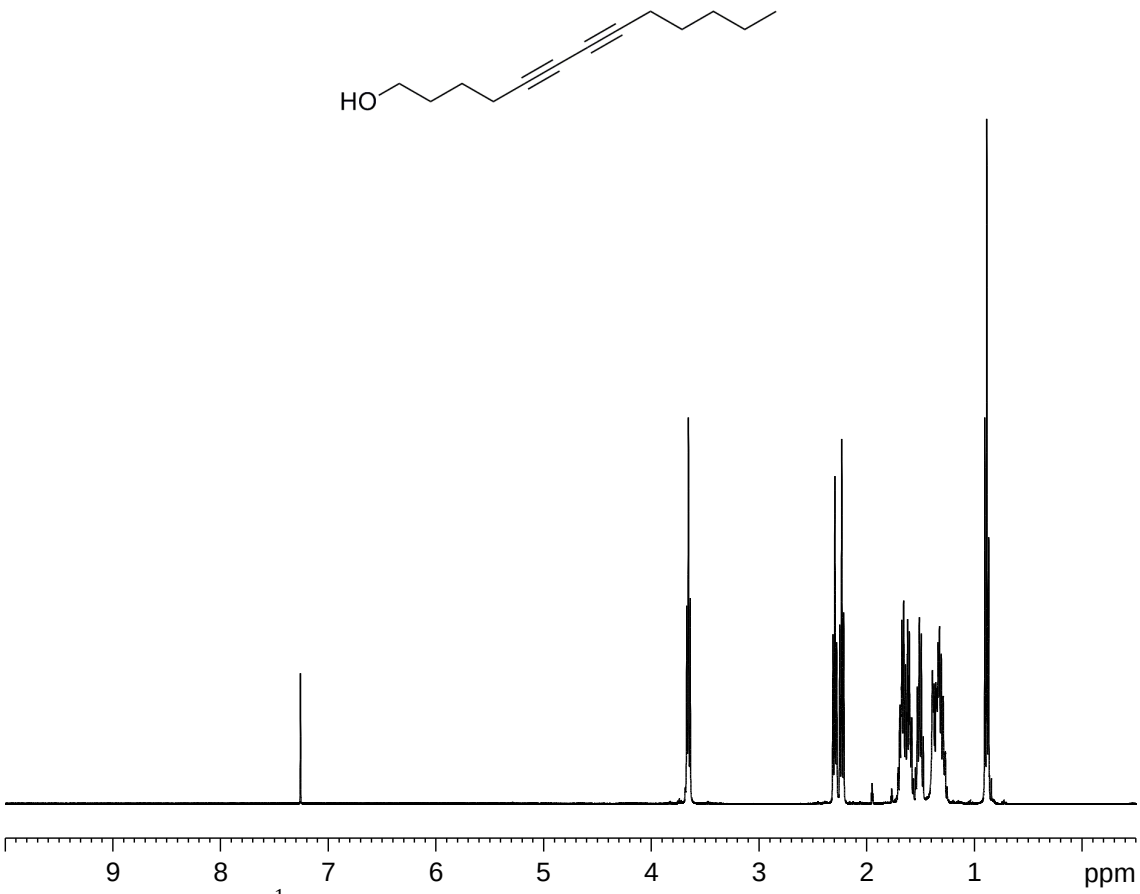
^{13}C NMR spectrum of **28** (400 MHz, $CDCl_3$)



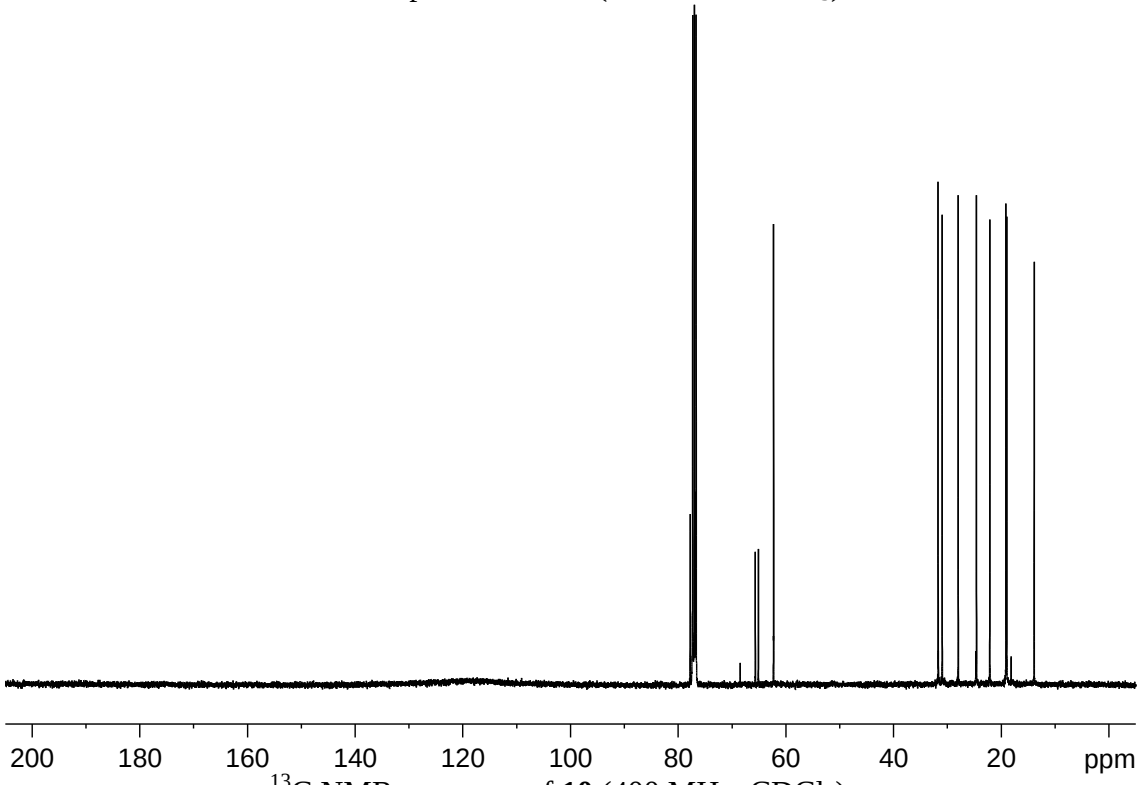
^{1}H NMR spectrum of **32** (400 MHz, $CDCl_3$)



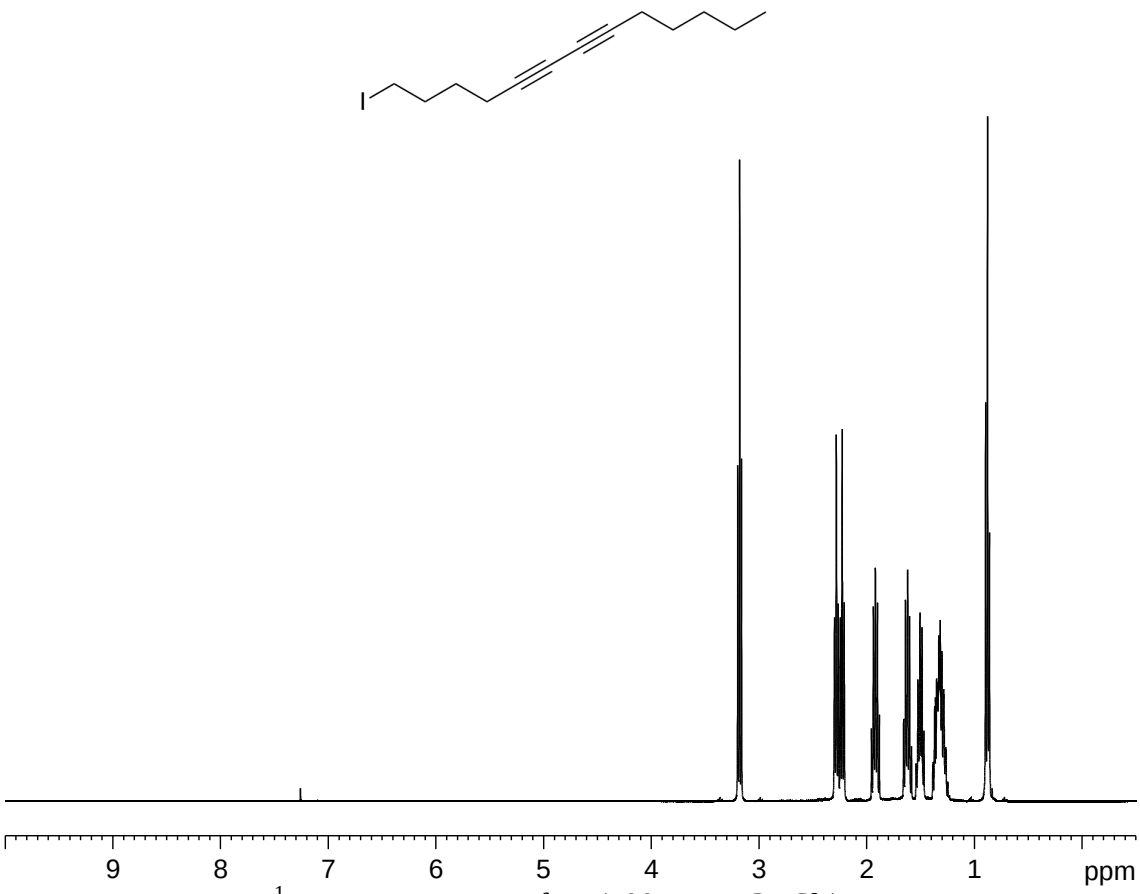
^{13}C NMR spectrum of **32** (200 MHz, $CDCl_3$)



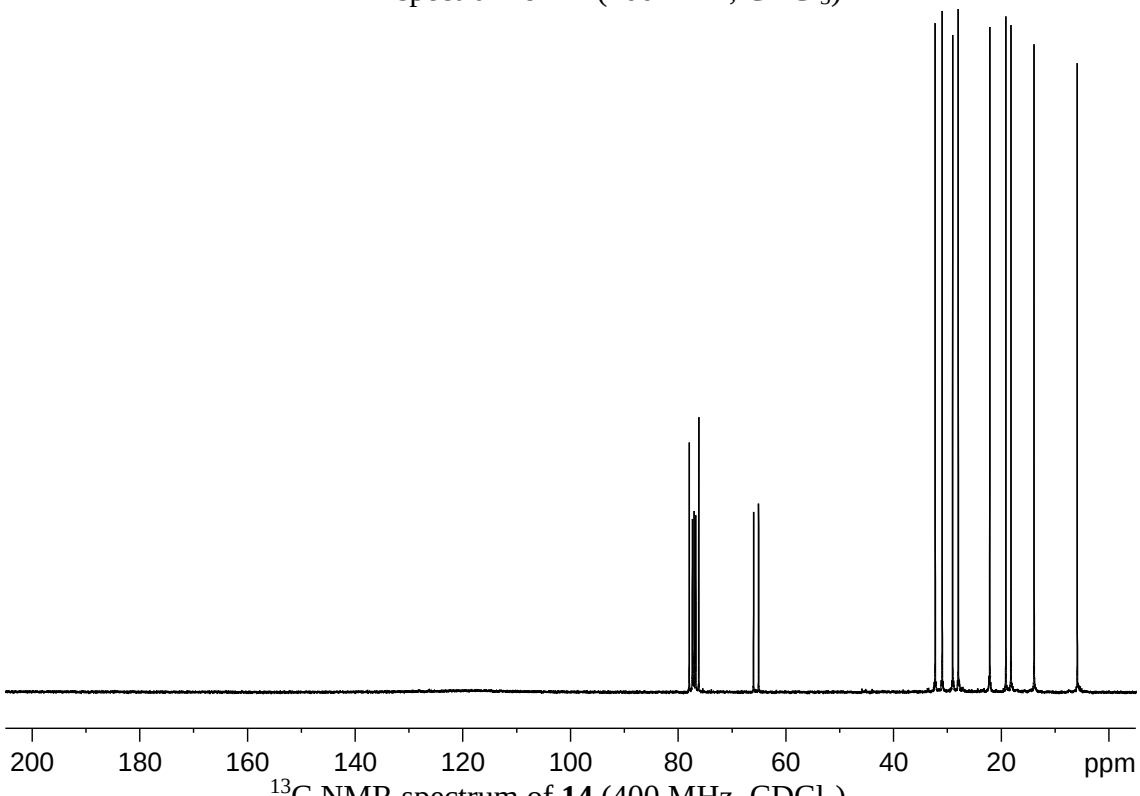
^{1}H NMR spectrum of **10** (400 MHz, $CDCl_3$)



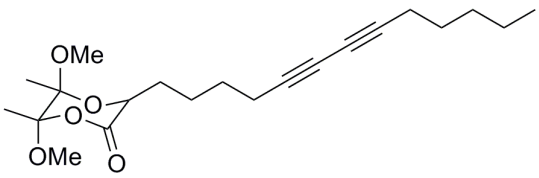
^{13}C NMR spectrum of **10** (400 MHz, $CDCl_3$)

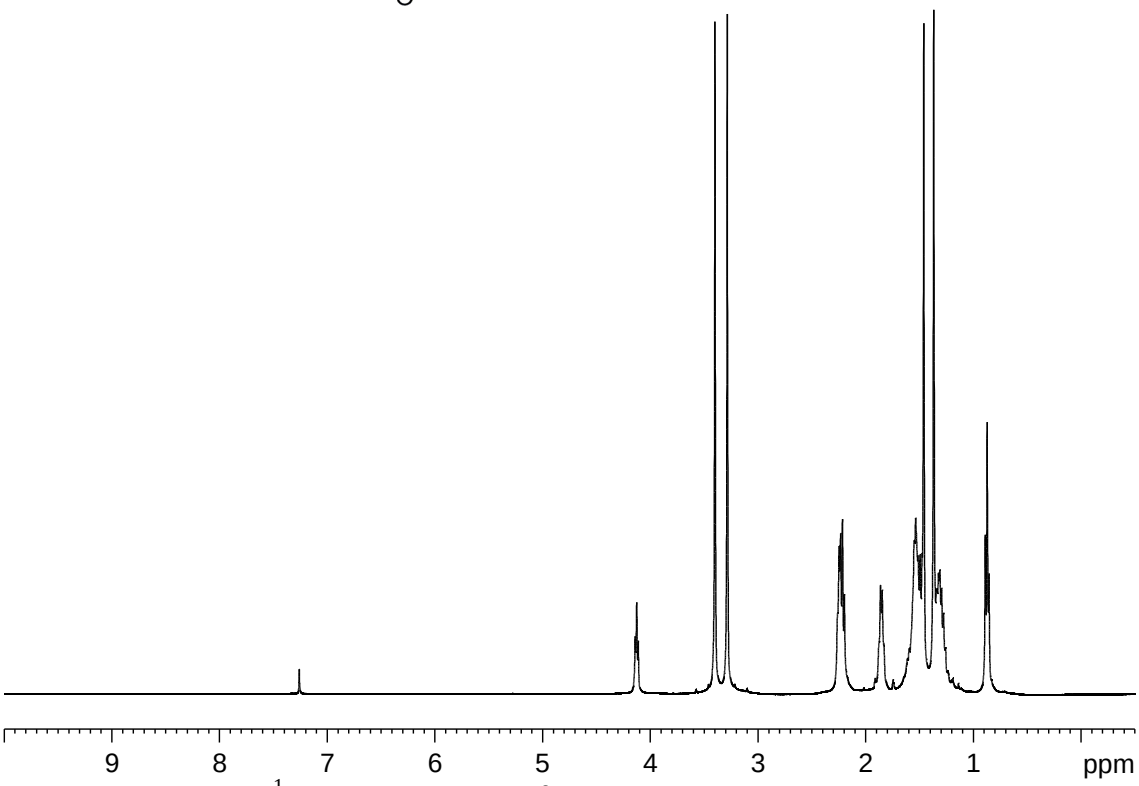


^{1}H NMR spectrum of **14** (400 MHz, $CDCl_3$)

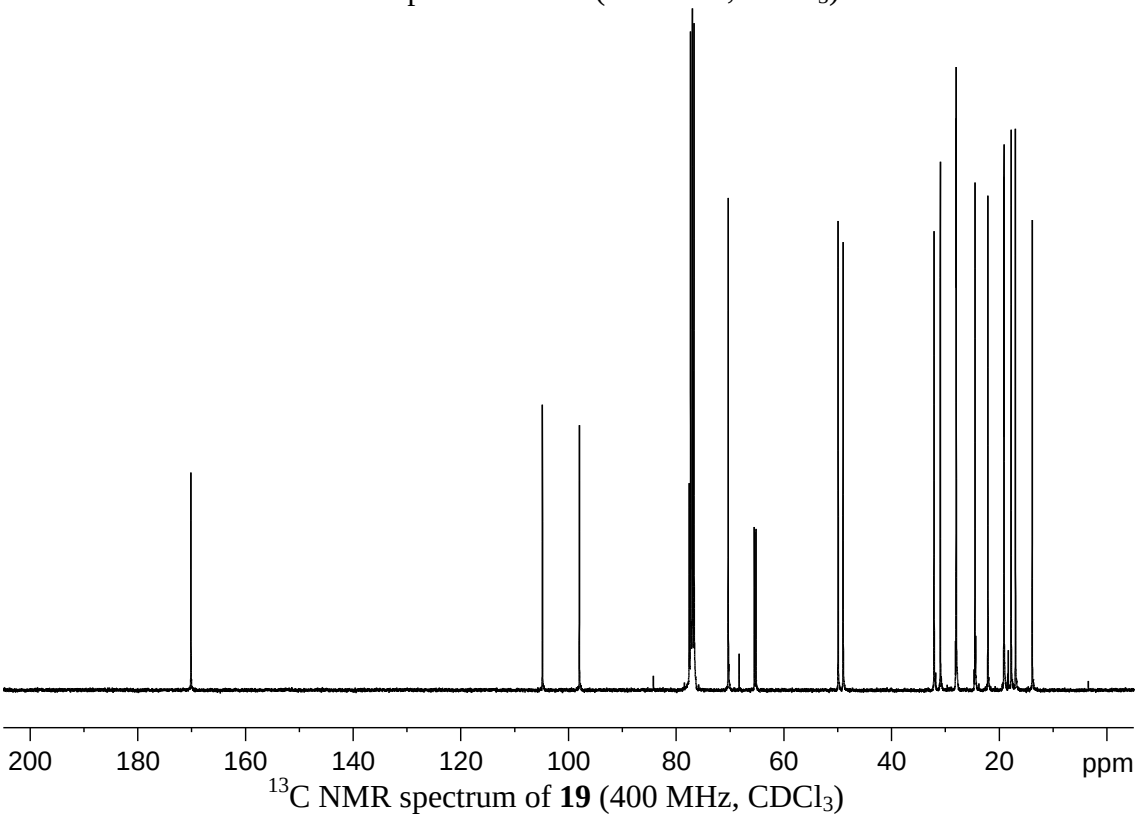


^{13}C NMR spectrum of **14** (400 MHz, $CDCl_3$)

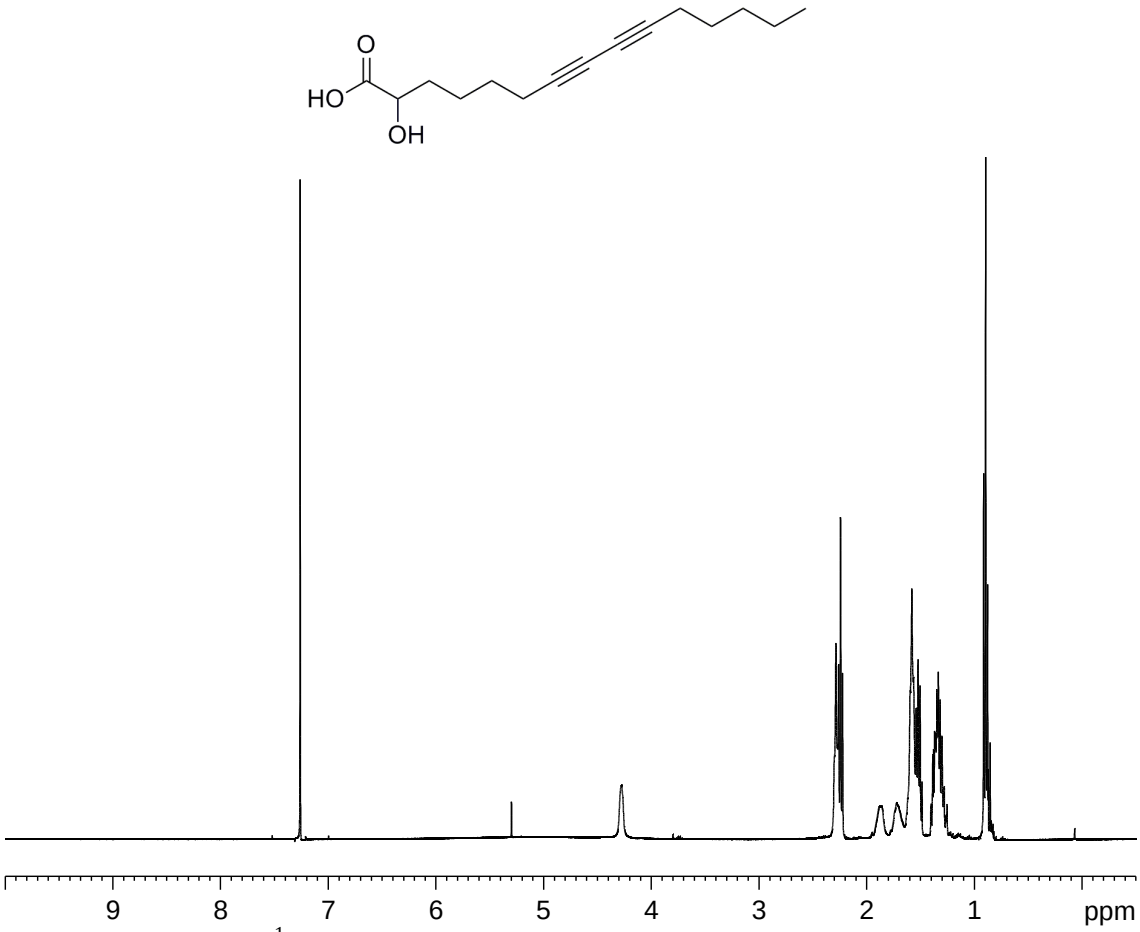




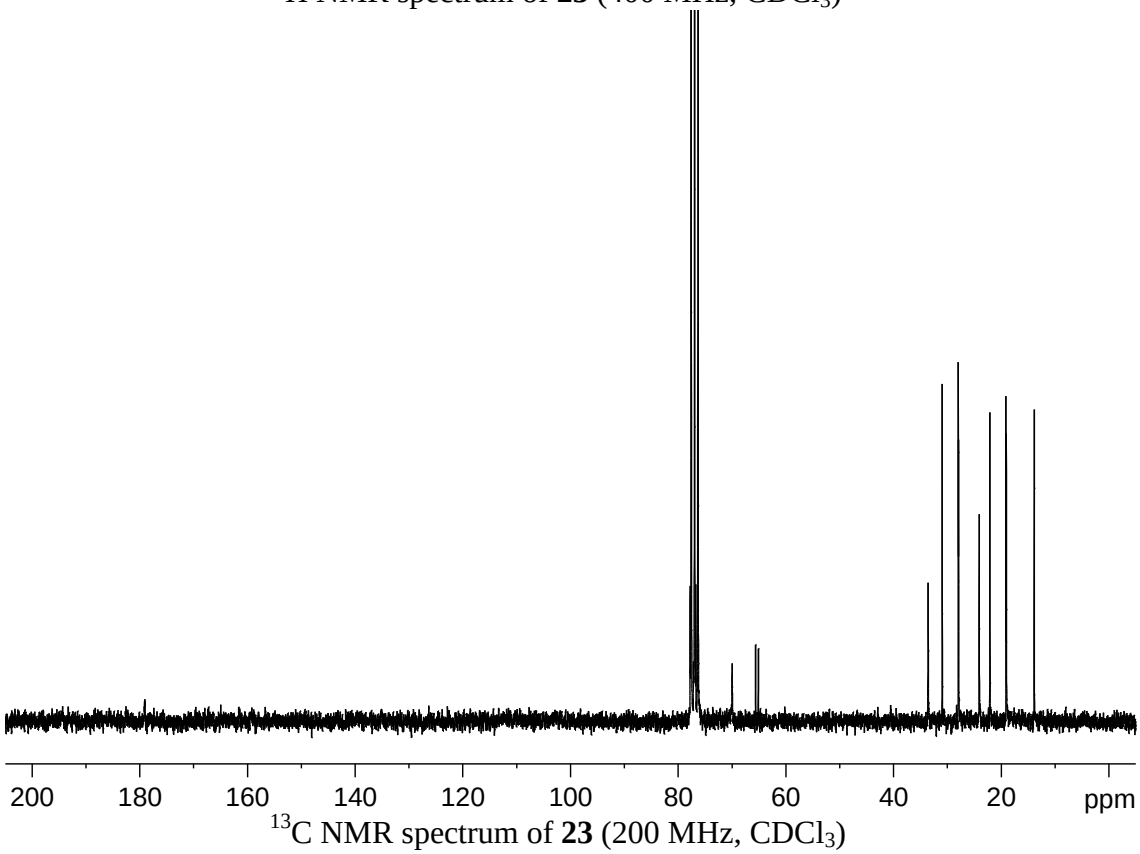
^{1}H NMR spectrum of **19** (400 MHz, $CDCl_3$)



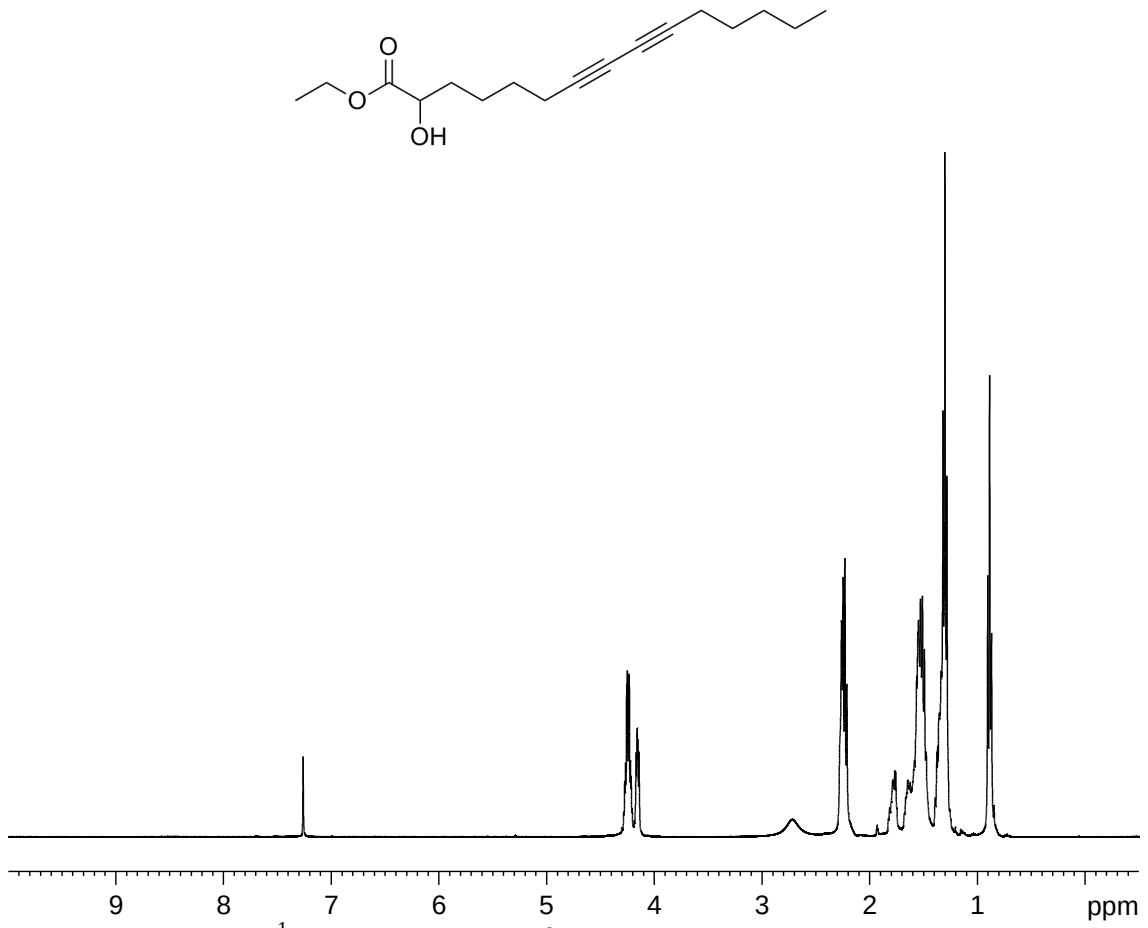
^{13}C NMR spectrum of **19** (400 MHz, $CDCl_3$)



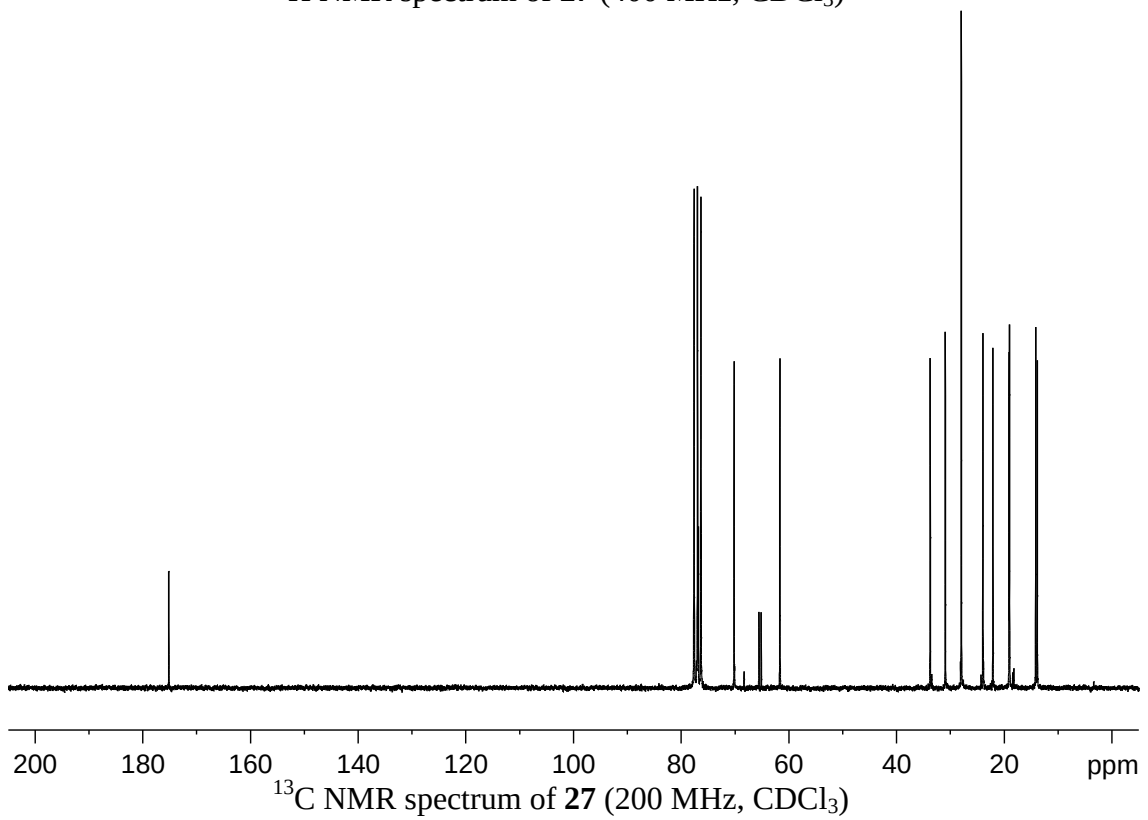
^{1}H NMR spectrum of **23** (400 MHz, $CDCl_3$)



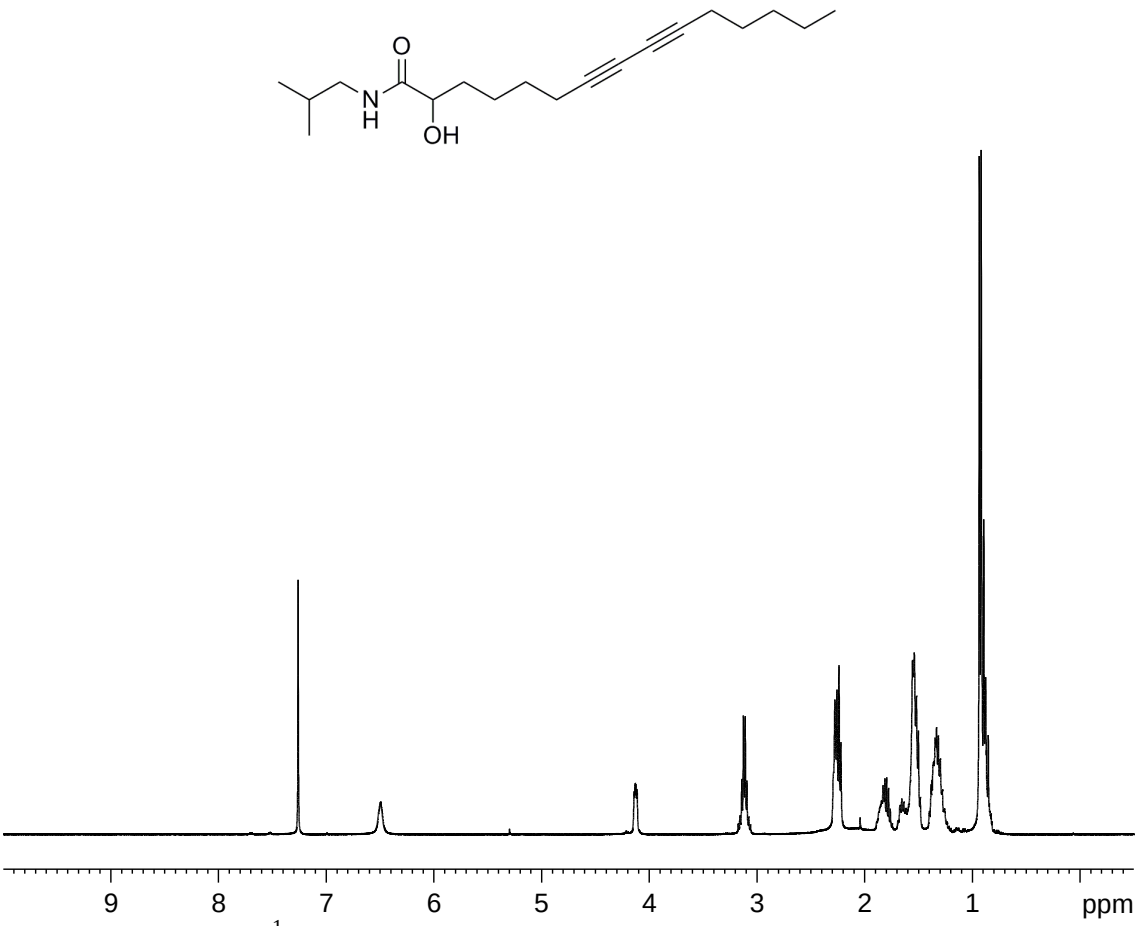
^{13}C NMR spectrum of **23** (200 MHz, $CDCl_3$)



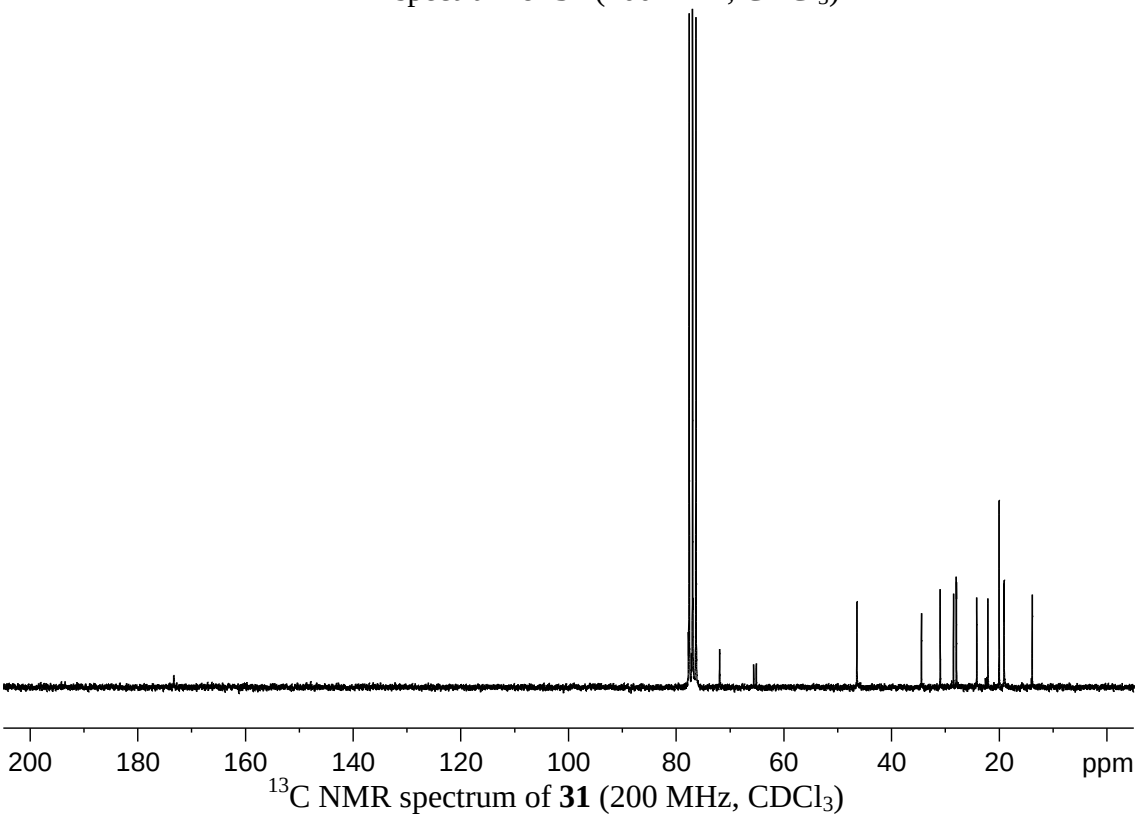
^{1}H NMR spectrum of **27** (400 MHz, $CDCl_3$)



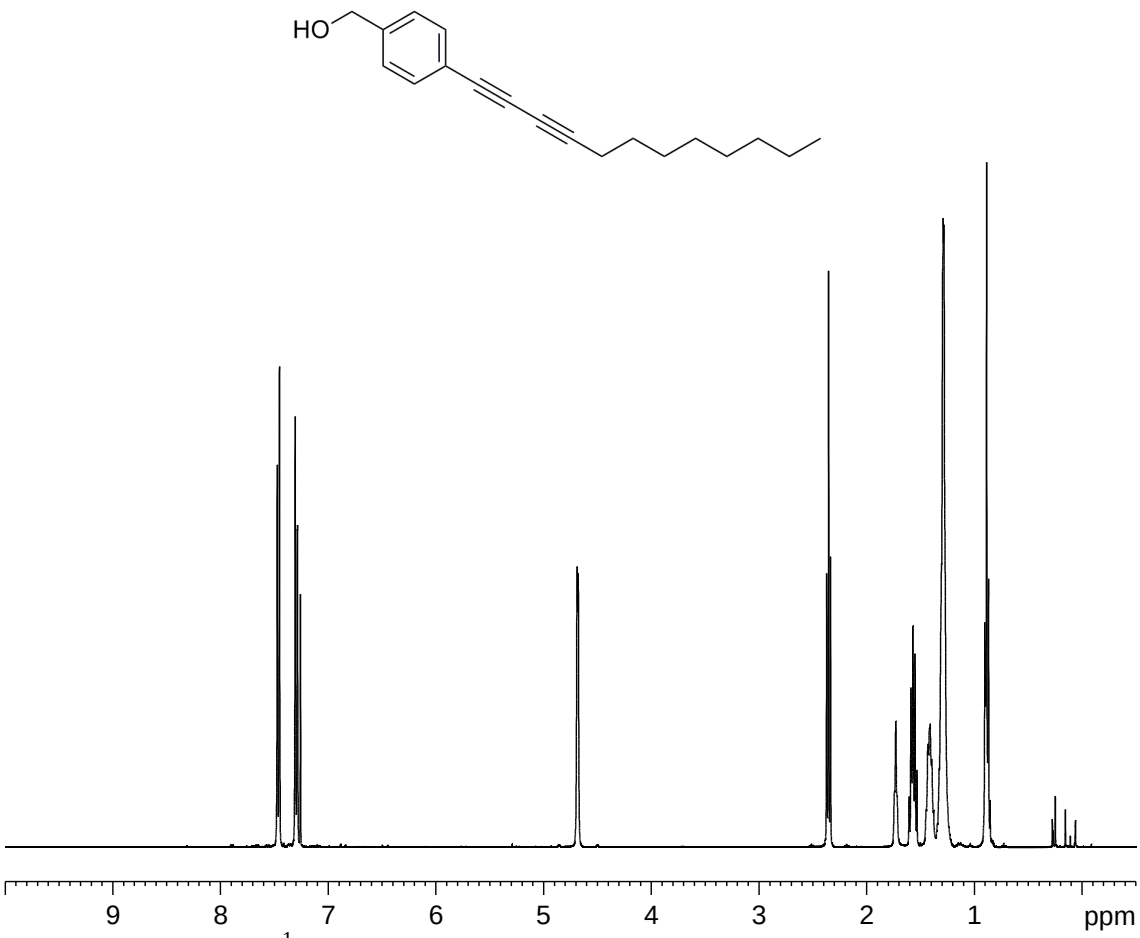
^{13}C NMR spectrum of **27** (200 MHz, $CDCl_3$)



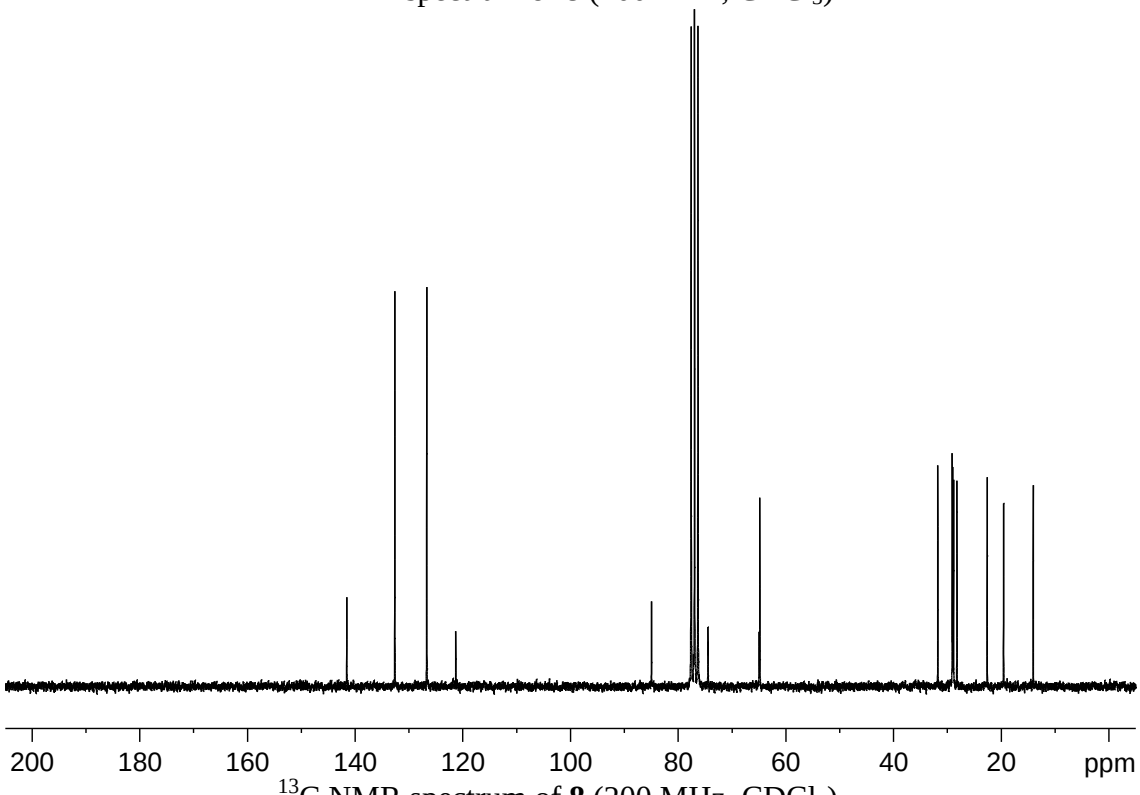
^{1}H NMR spectrum of **31** (400 MHz, $CDCl_3$)



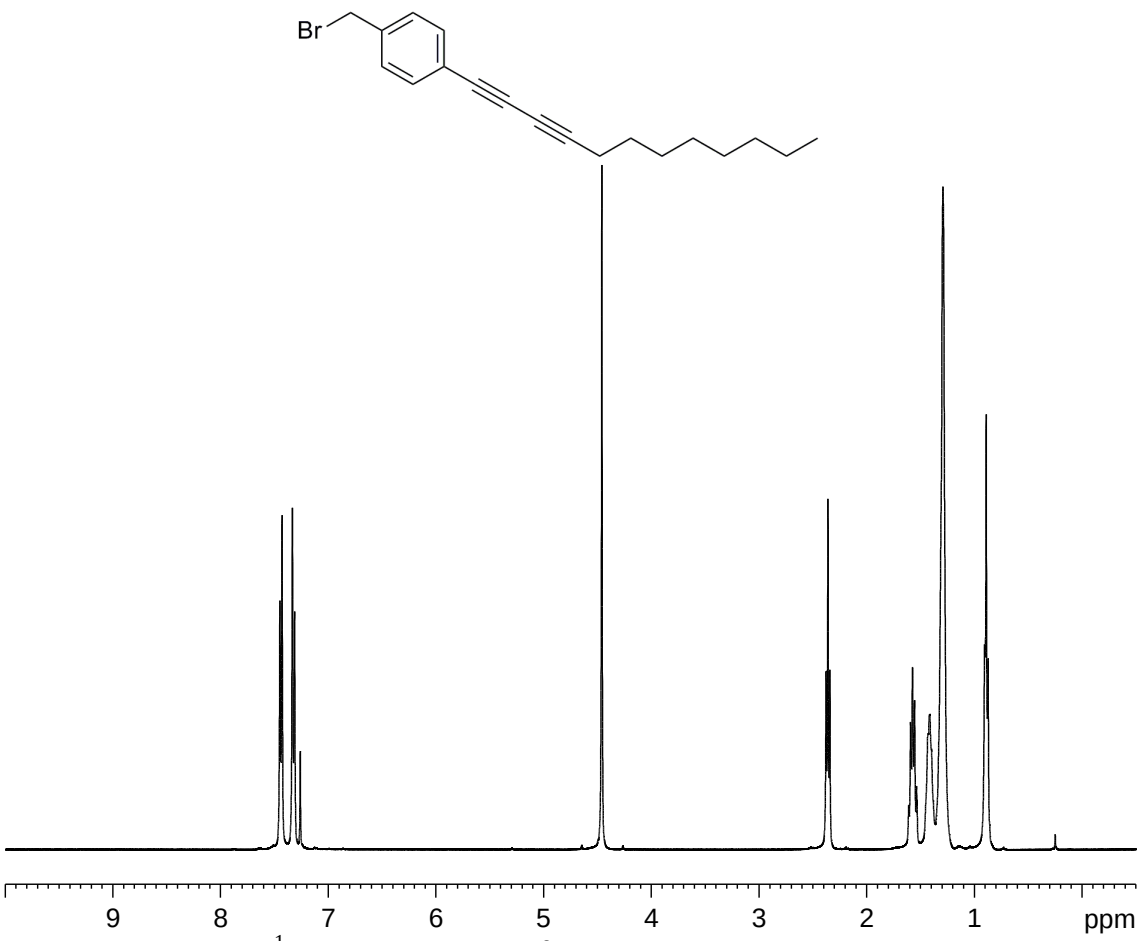
^{13}C NMR spectrum of **31** (200 MHz, $CDCl_3$)



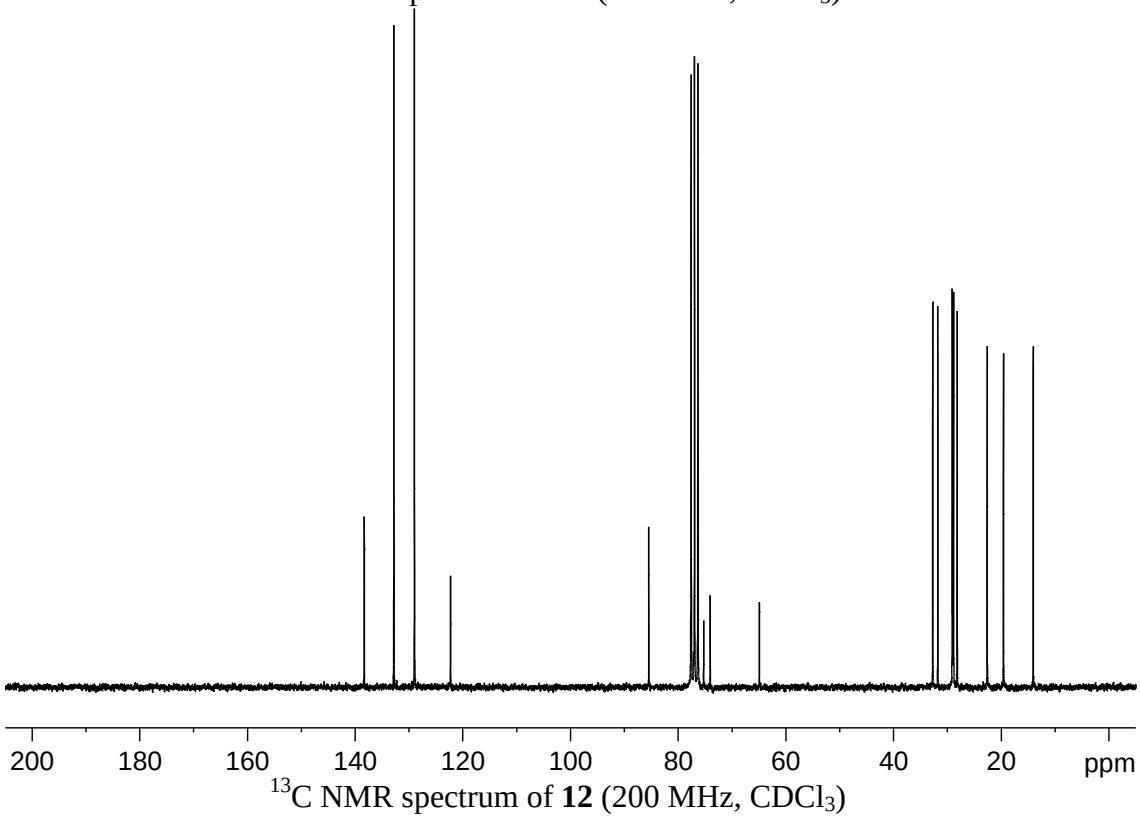
^{1}H NMR spectrum of **8** (400 MHz, $CDCl_3$)



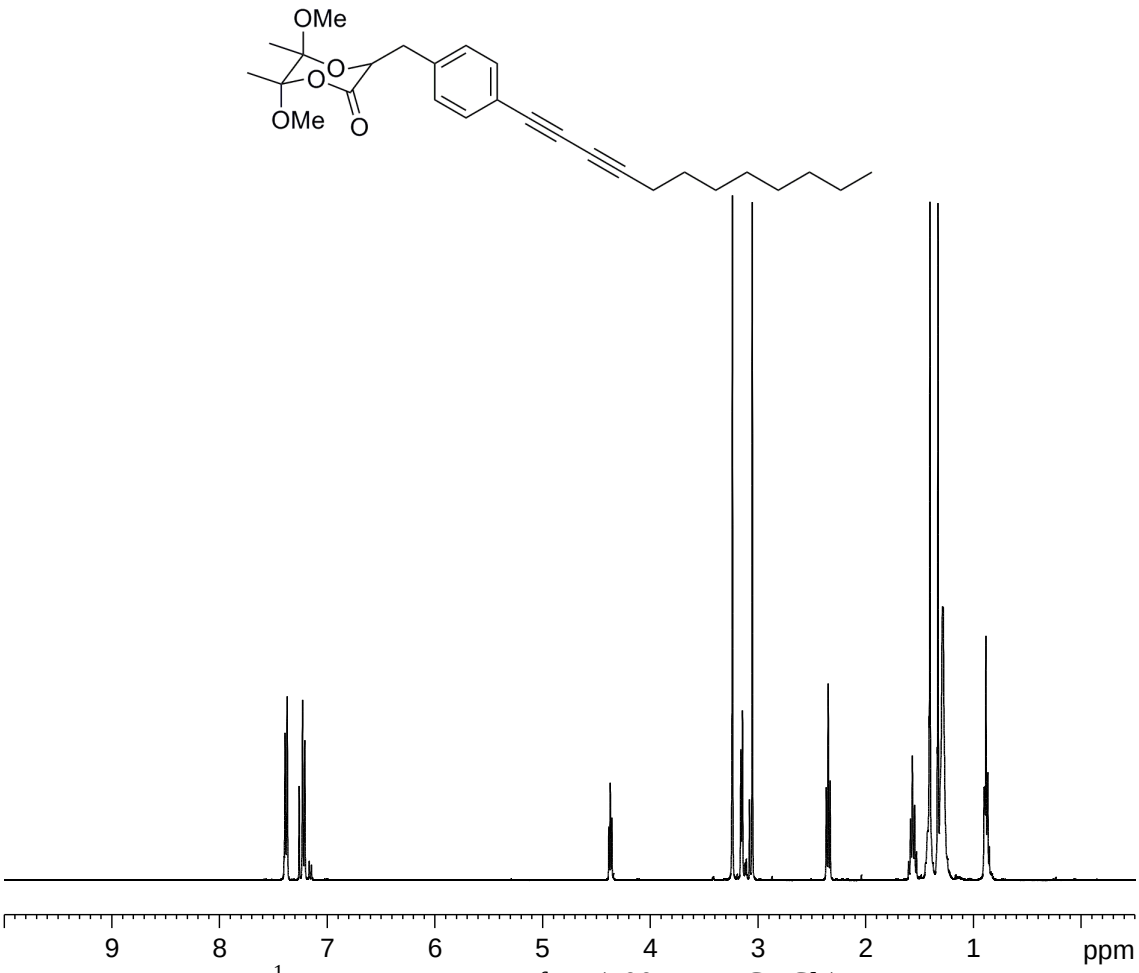
^{13}C NMR spectrum of **8** (200 MHz, $CDCl_3$)



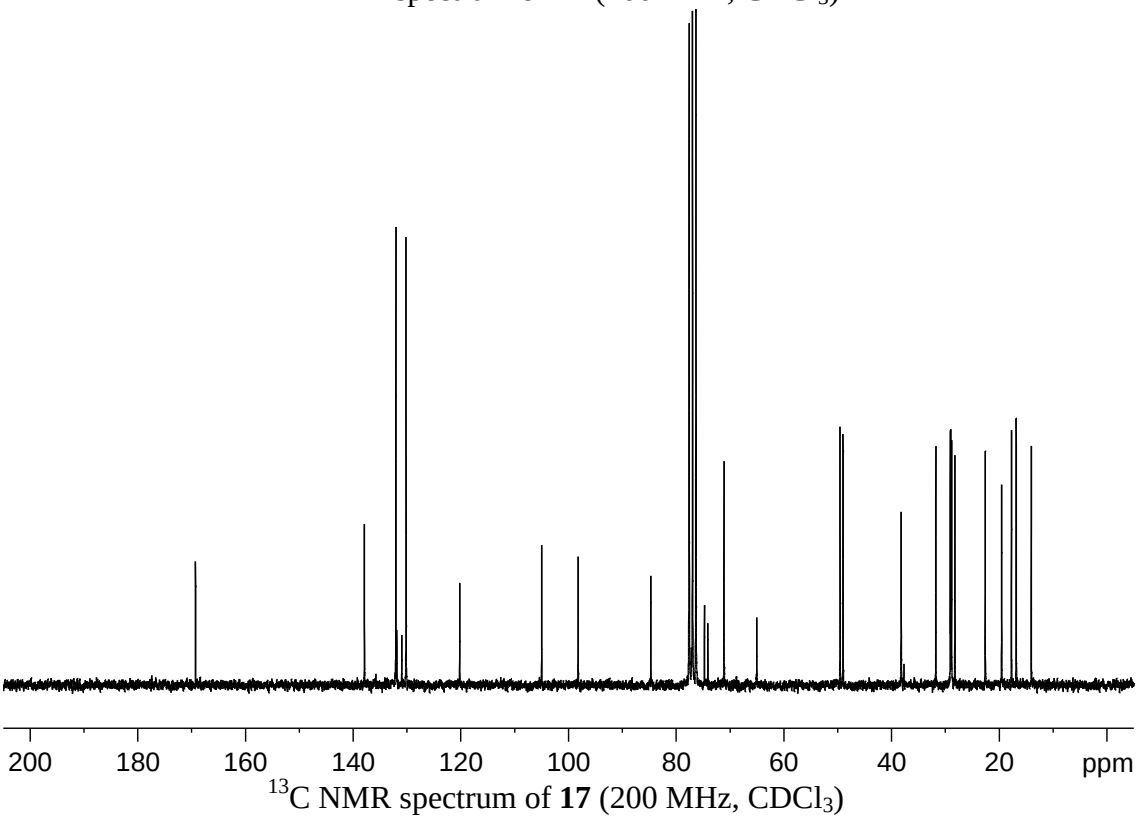
^{1}H NMR spectrum of **12** (400 MHz, $CDCl_3$)



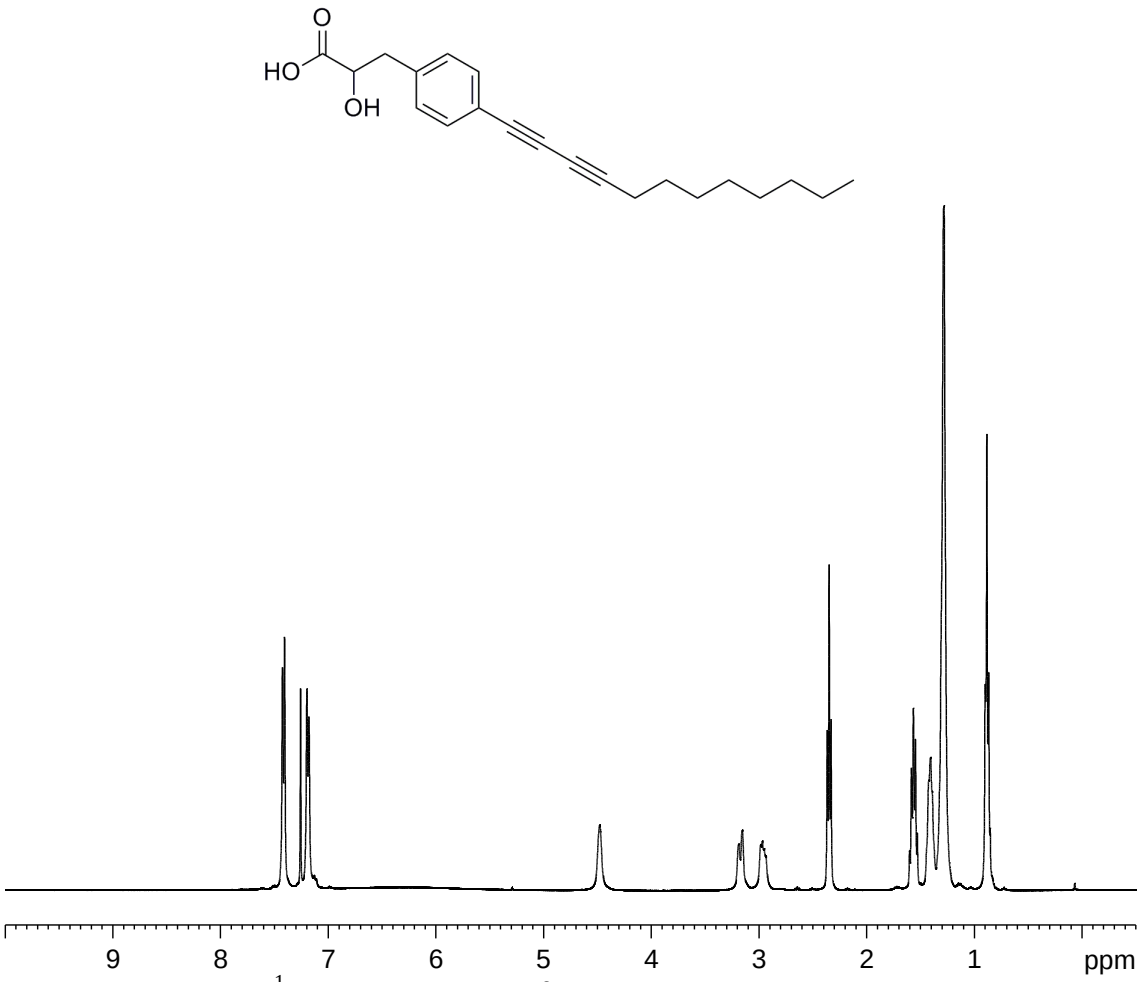
^{13}C NMR spectrum of **12** (200 MHz, $CDCl_3$)



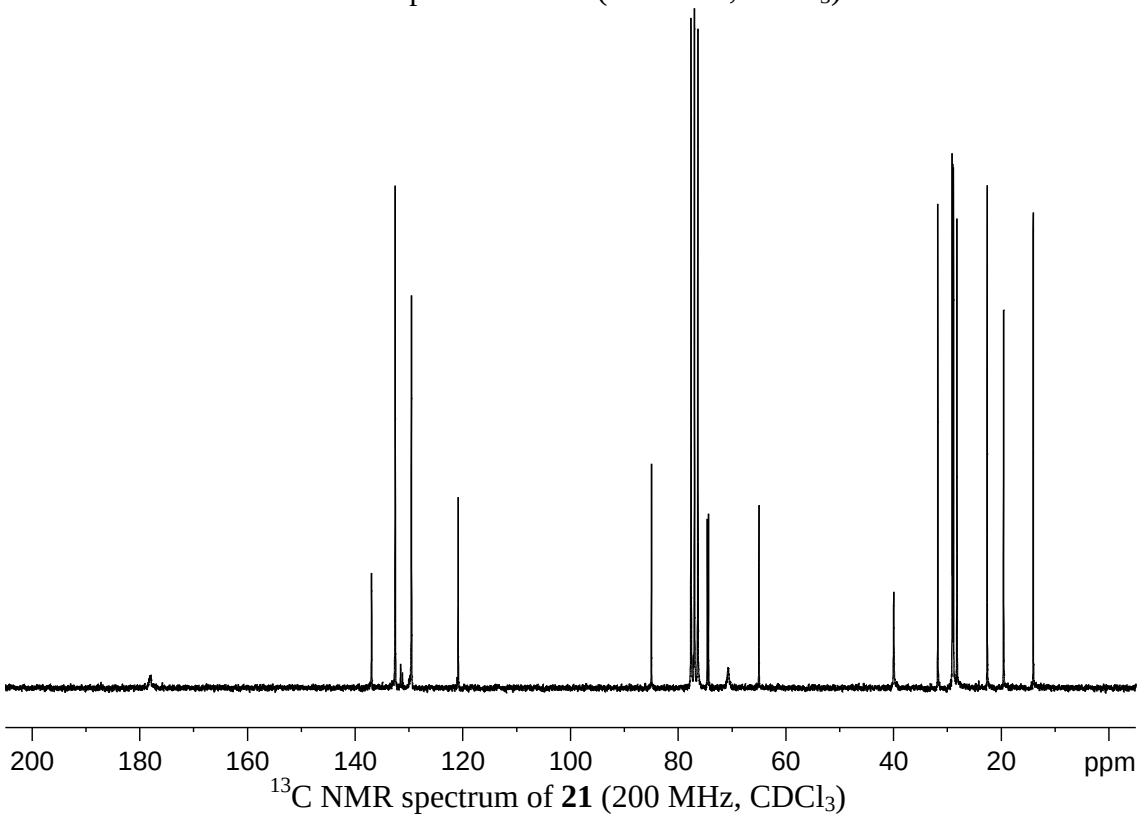
^{1}H NMR spectrum of **17** (400 MHz, $CDCl_3$)



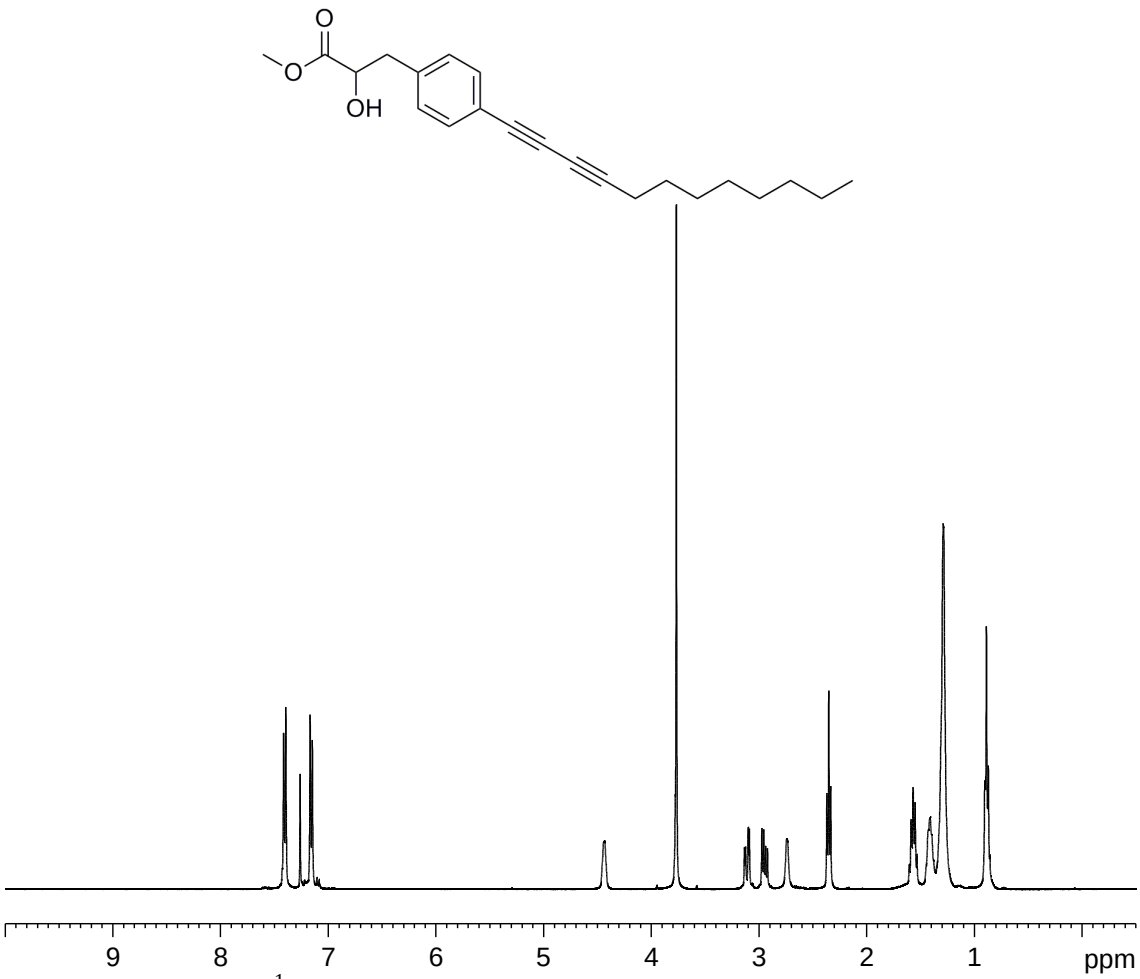
^{13}C NMR spectrum of **17** (200 MHz, $CDCl_3$)



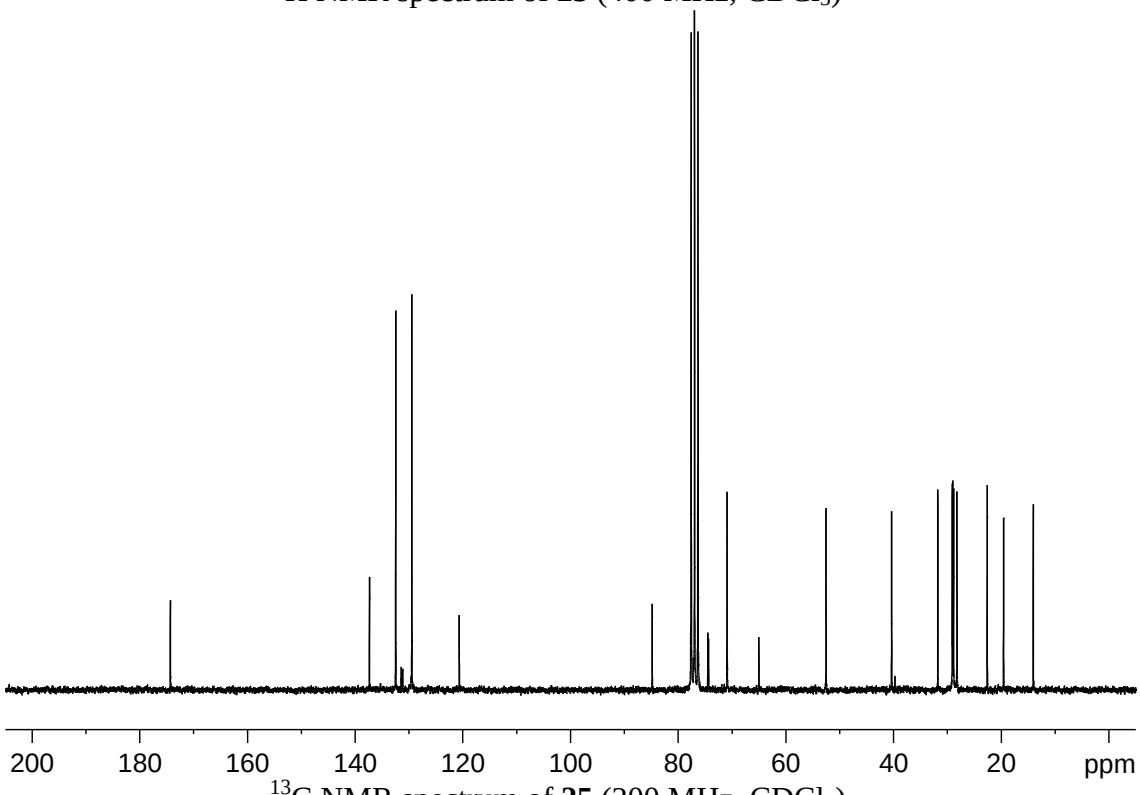
^{1}H NMR spectrum of **21** (400 MHz, $CDCl_3$)



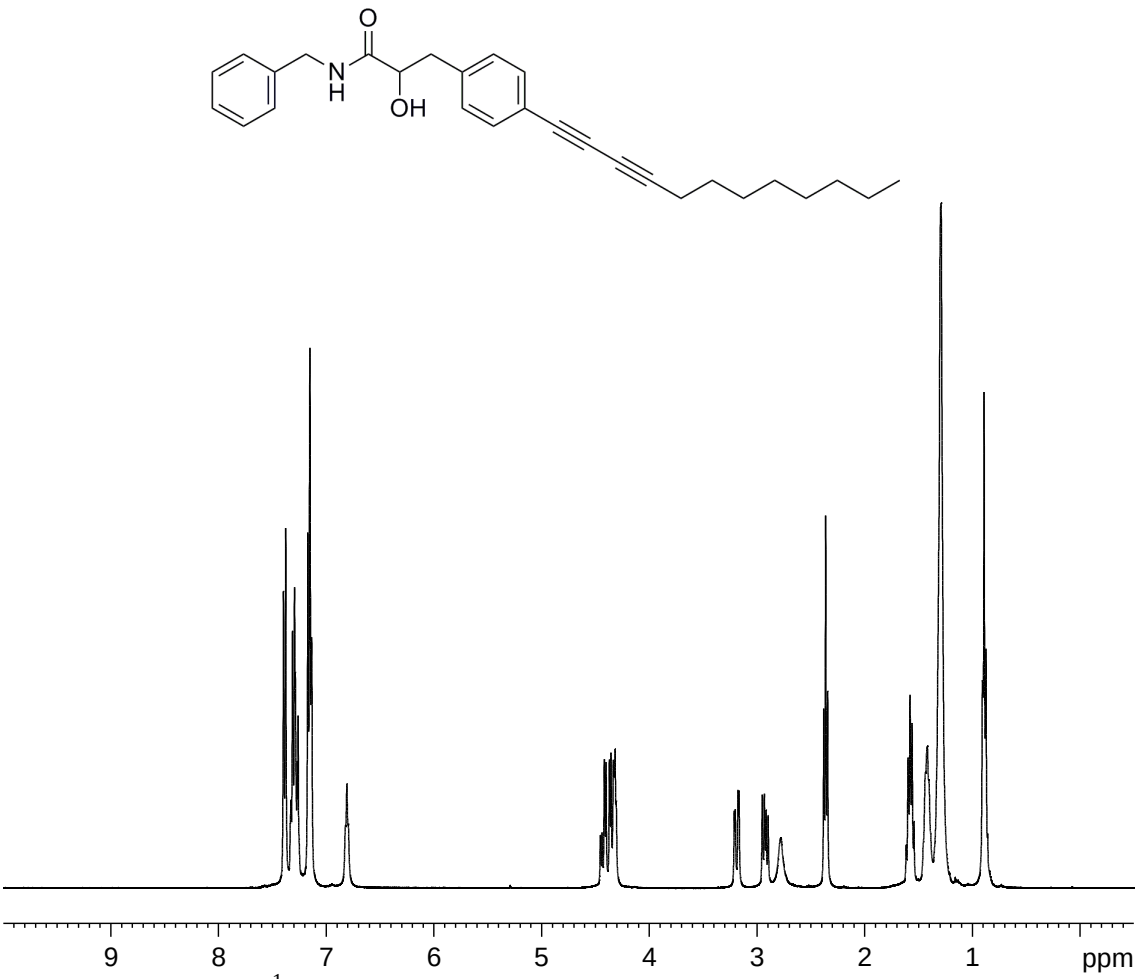
^{13}C NMR spectrum of **21** (200 MHz, $CDCl_3$)



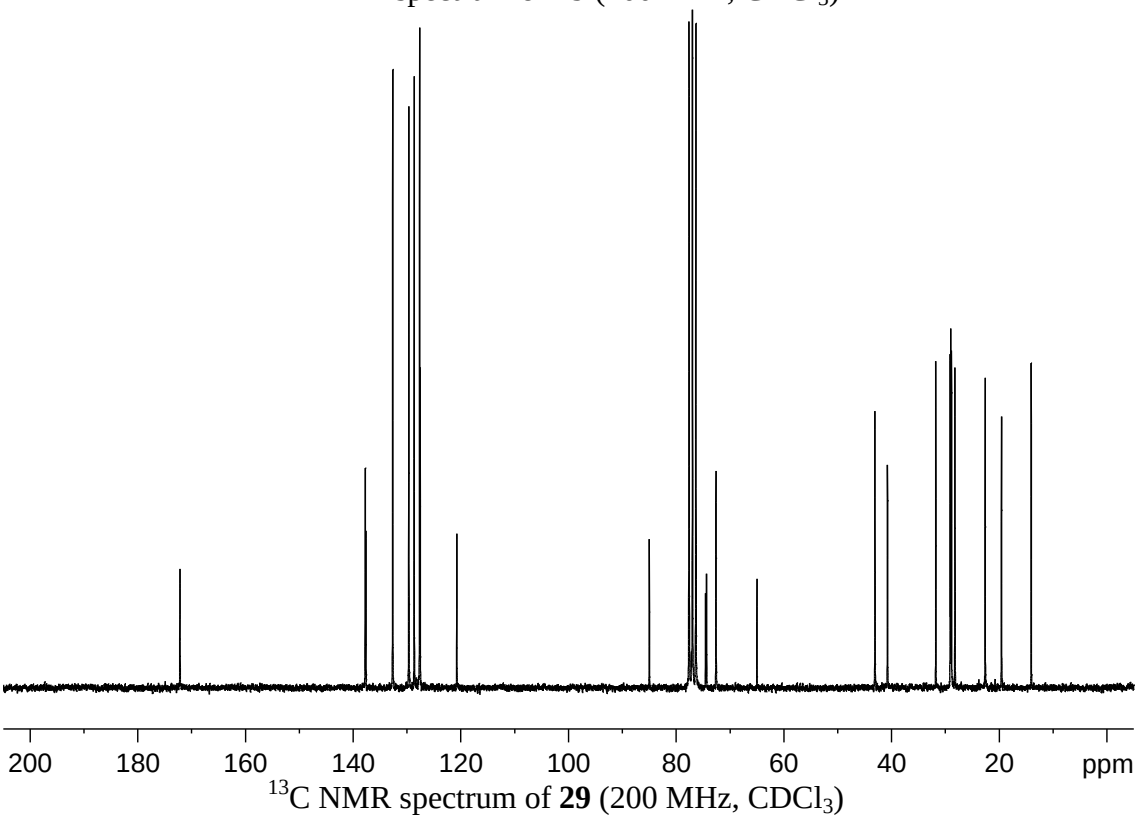
^{1}H NMR spectrum of **25** (400 MHz, $CDCl_3$)



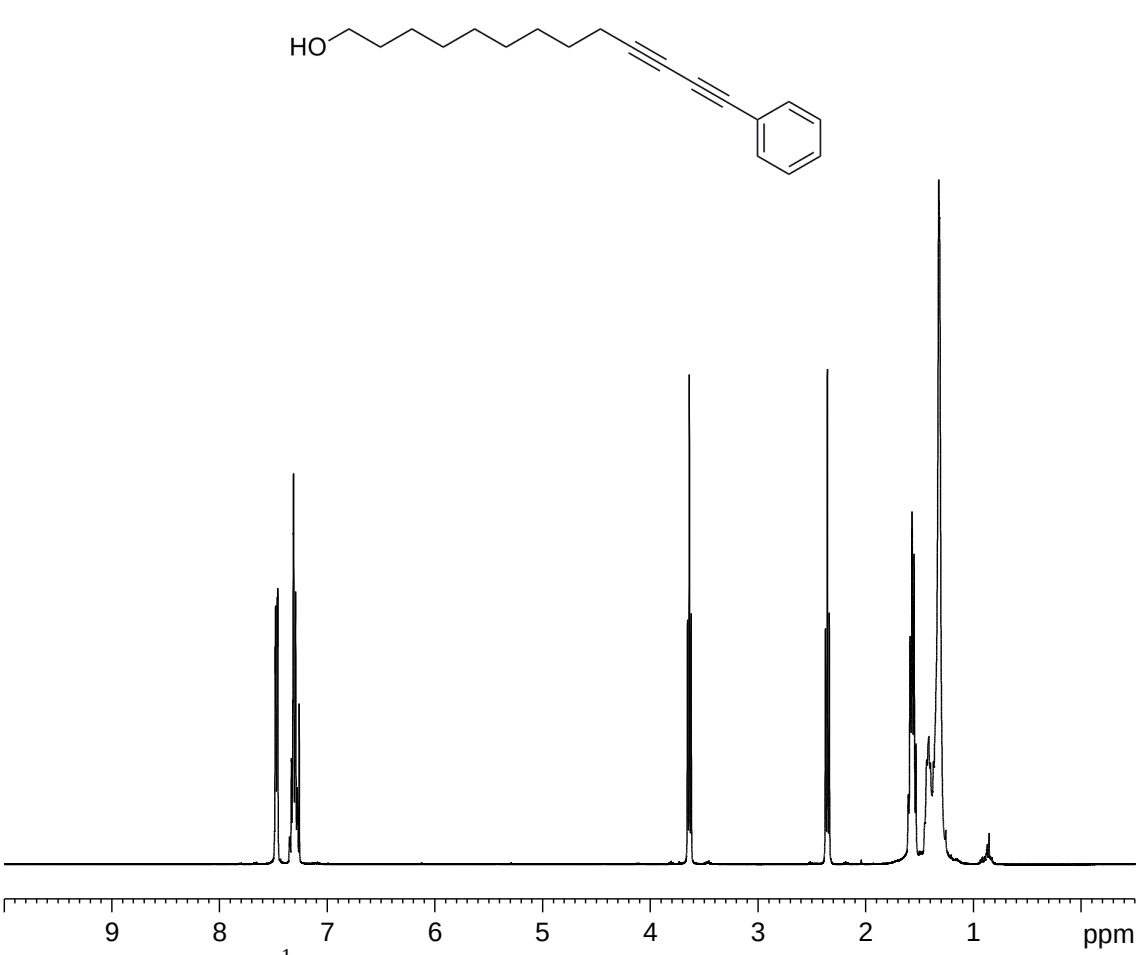
^{13}C NMR spectrum of **25** (200 MHz, $CDCl_3$)



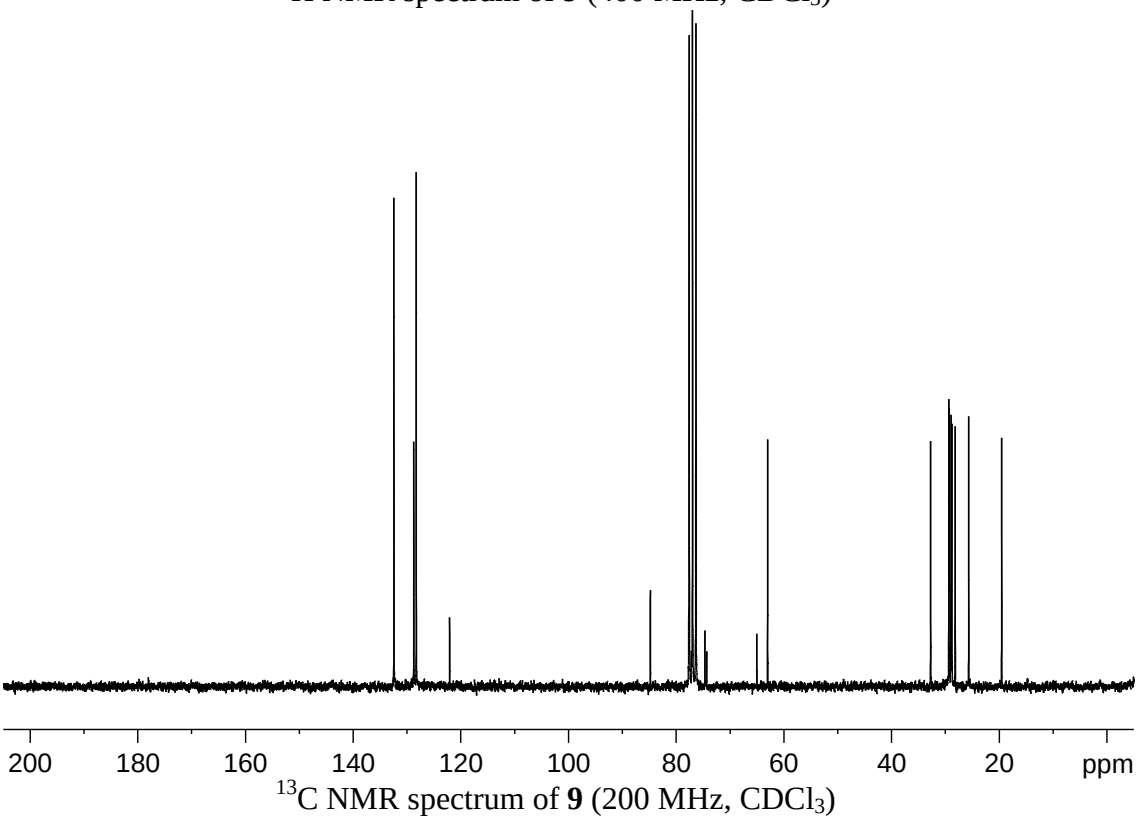
^{1}H NMR spectrum of **29** (400 MHz, $CDCl_3$)



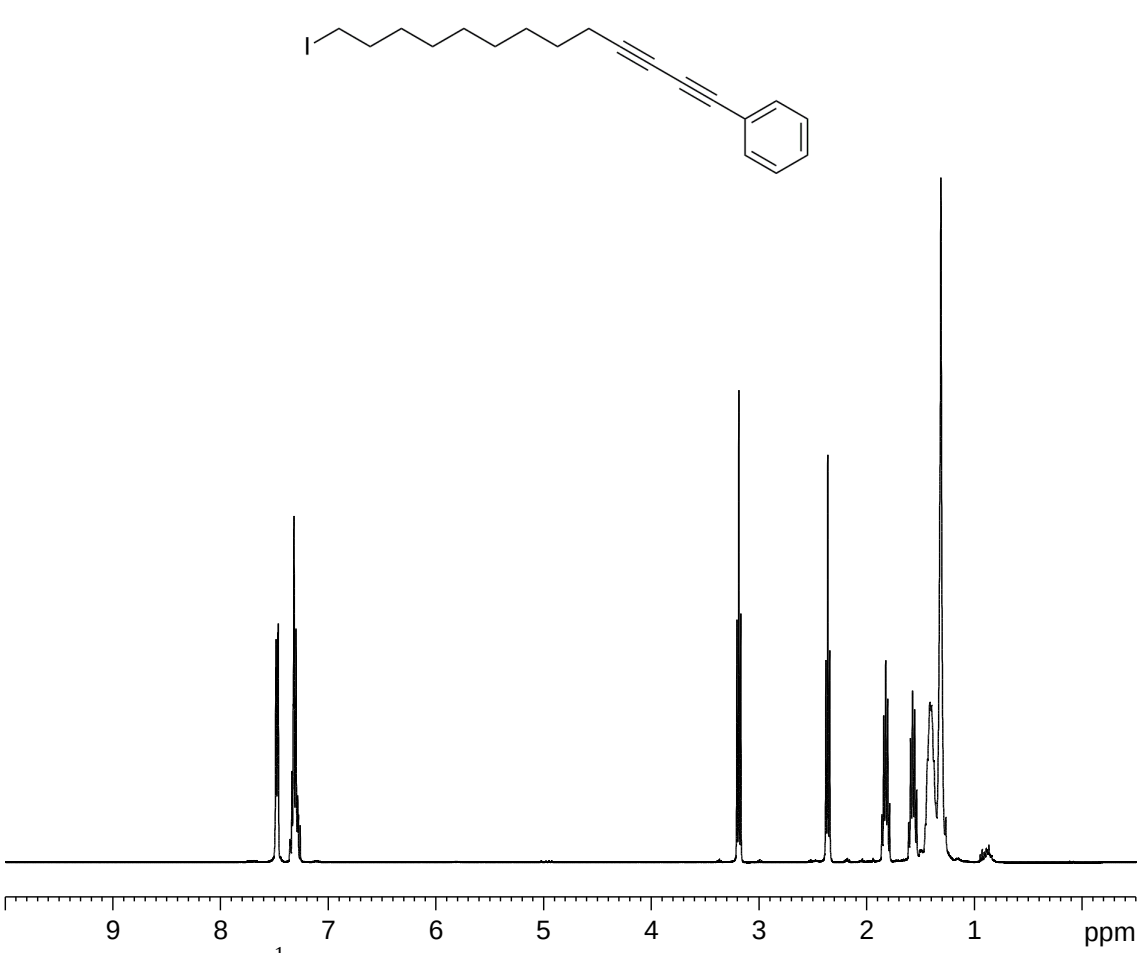
^{13}C NMR spectrum of **29** (200 MHz, $CDCl_3$)



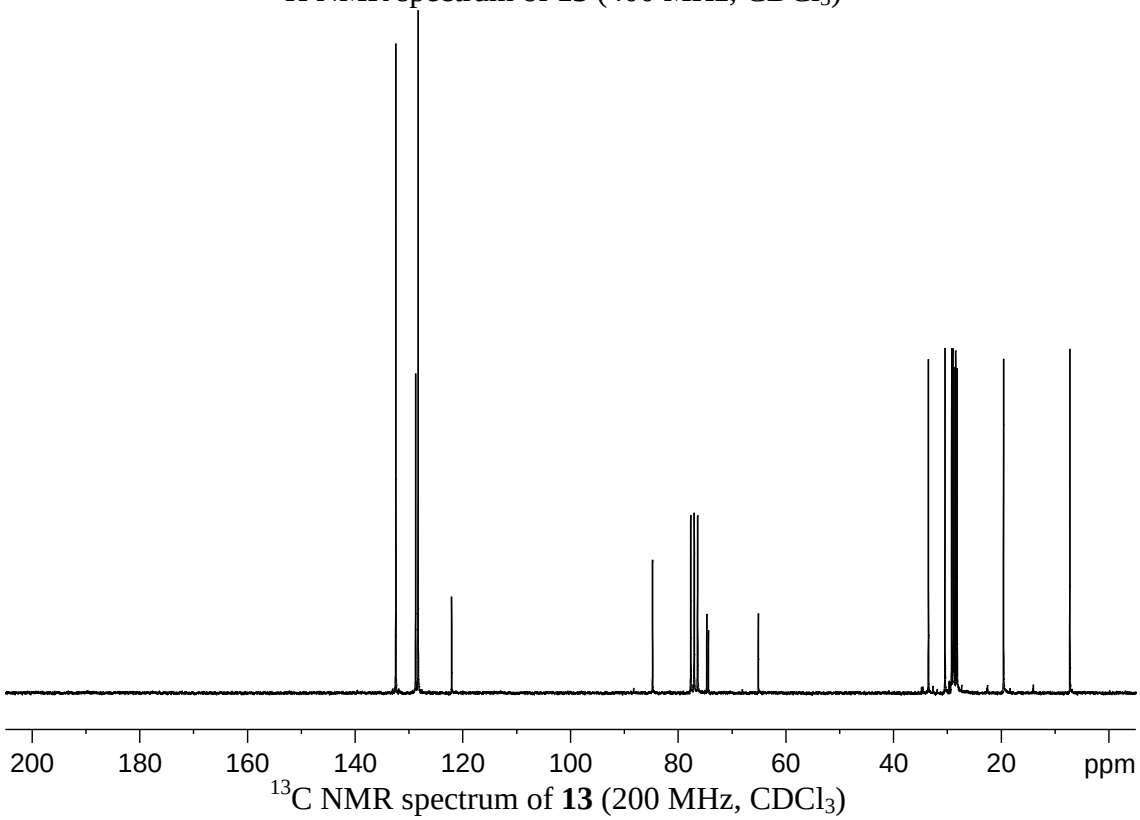
^{1}H NMR spectrum of **9** (400 MHz, $CDCl_3$)



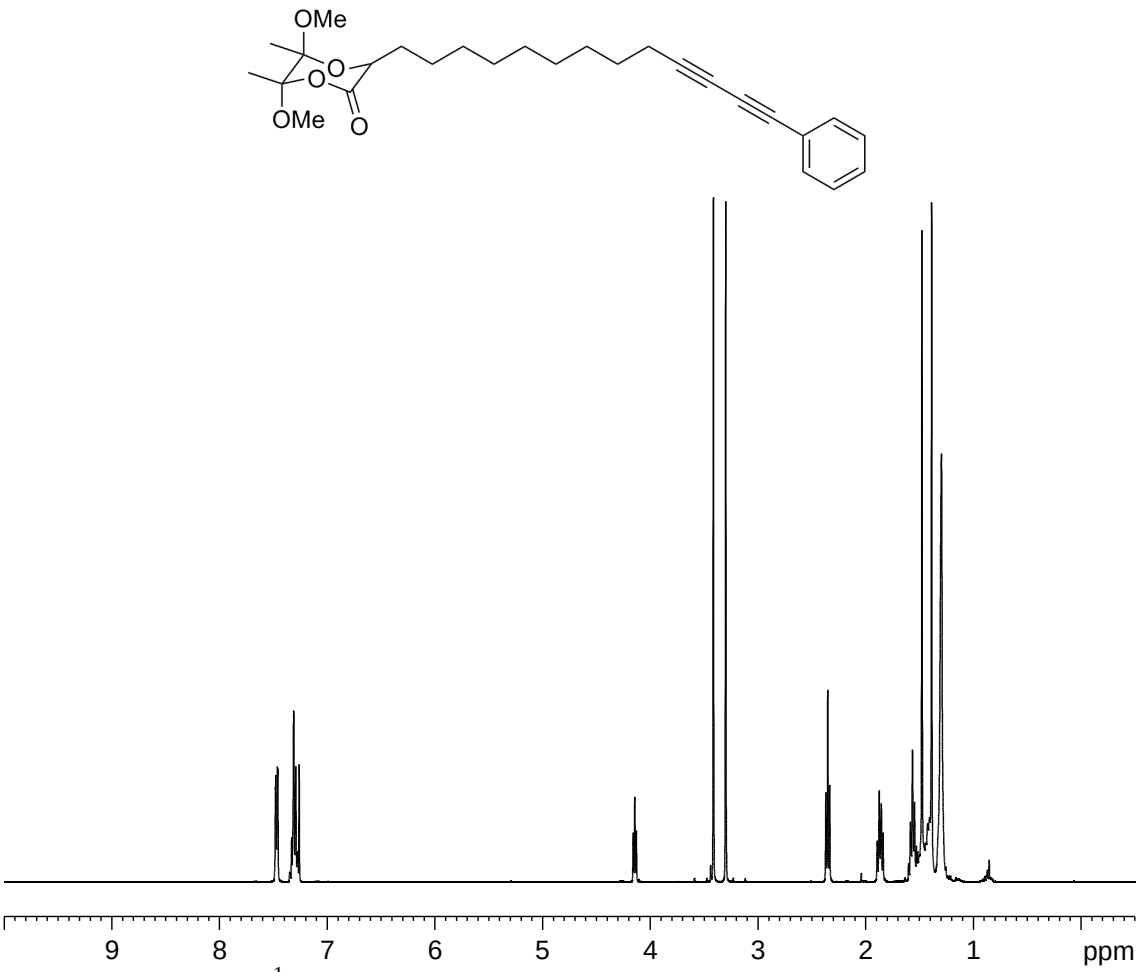
^{13}C NMR spectrum of **9** (200 MHz, $CDCl_3$)



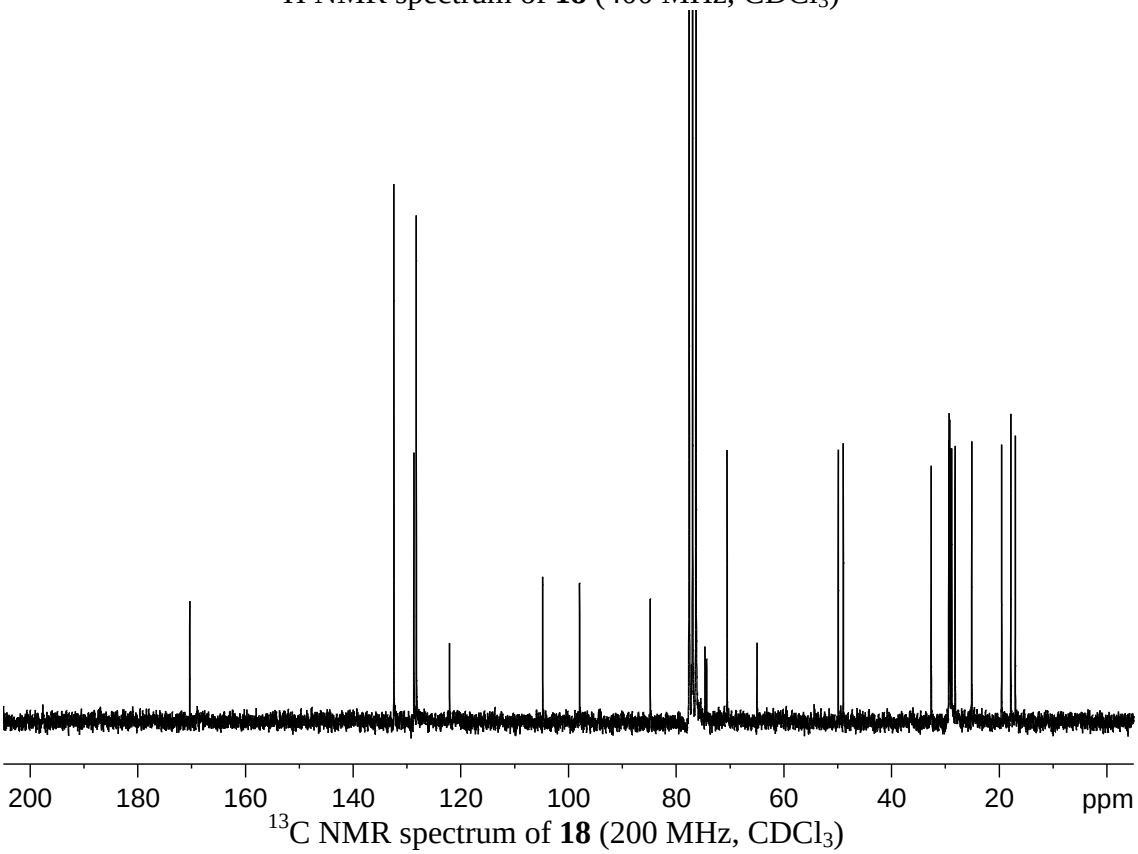
^{1}H NMR spectrum of **13** (400 MHz, $CDCl_3$)



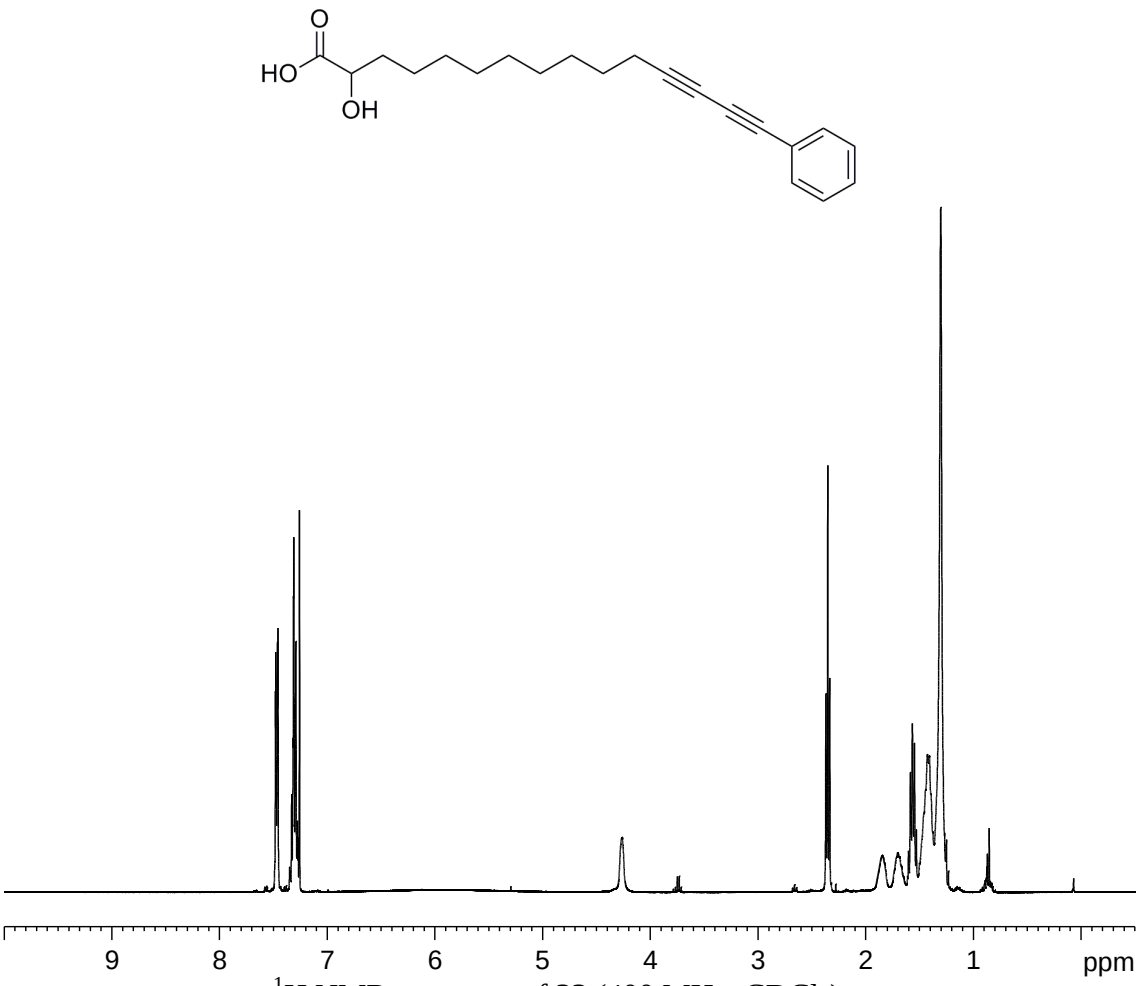
^{13}C NMR spectrum of **13** (200 MHz, $CDCl_3$)



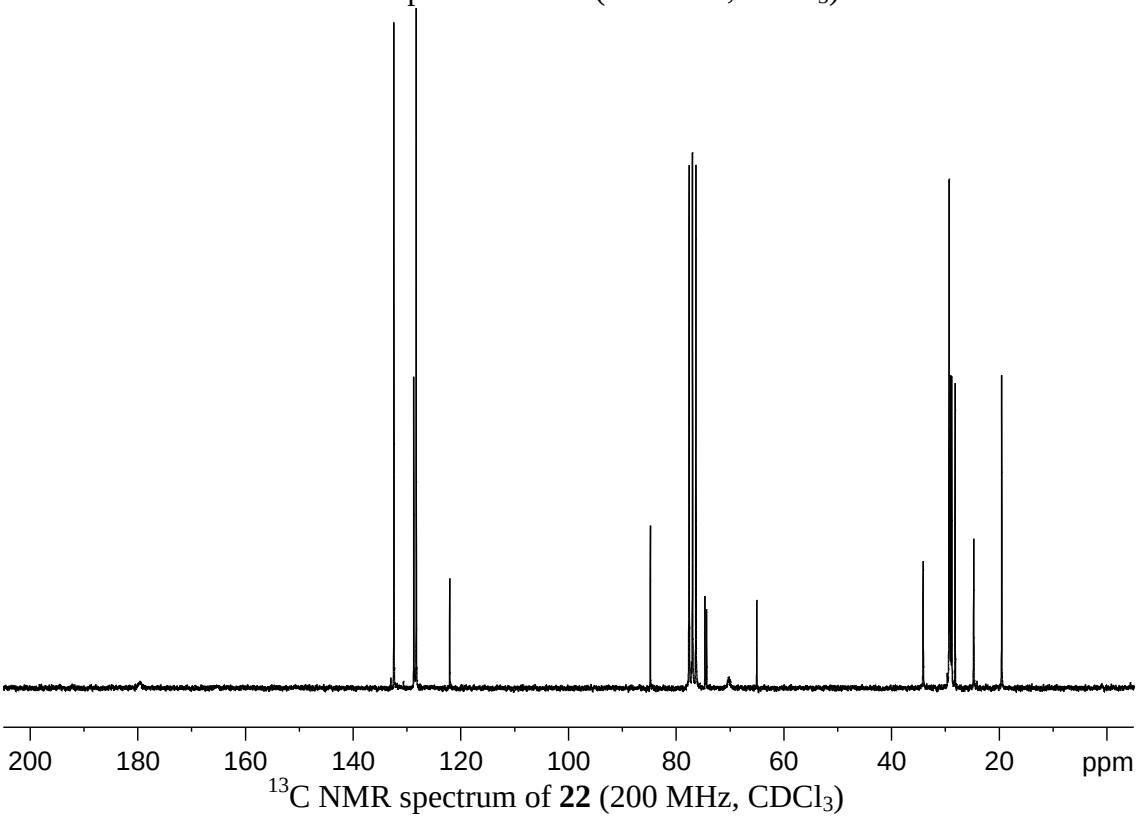
^{1}H NMR spectrum of **18** (400 MHz, $CDCl_3$)



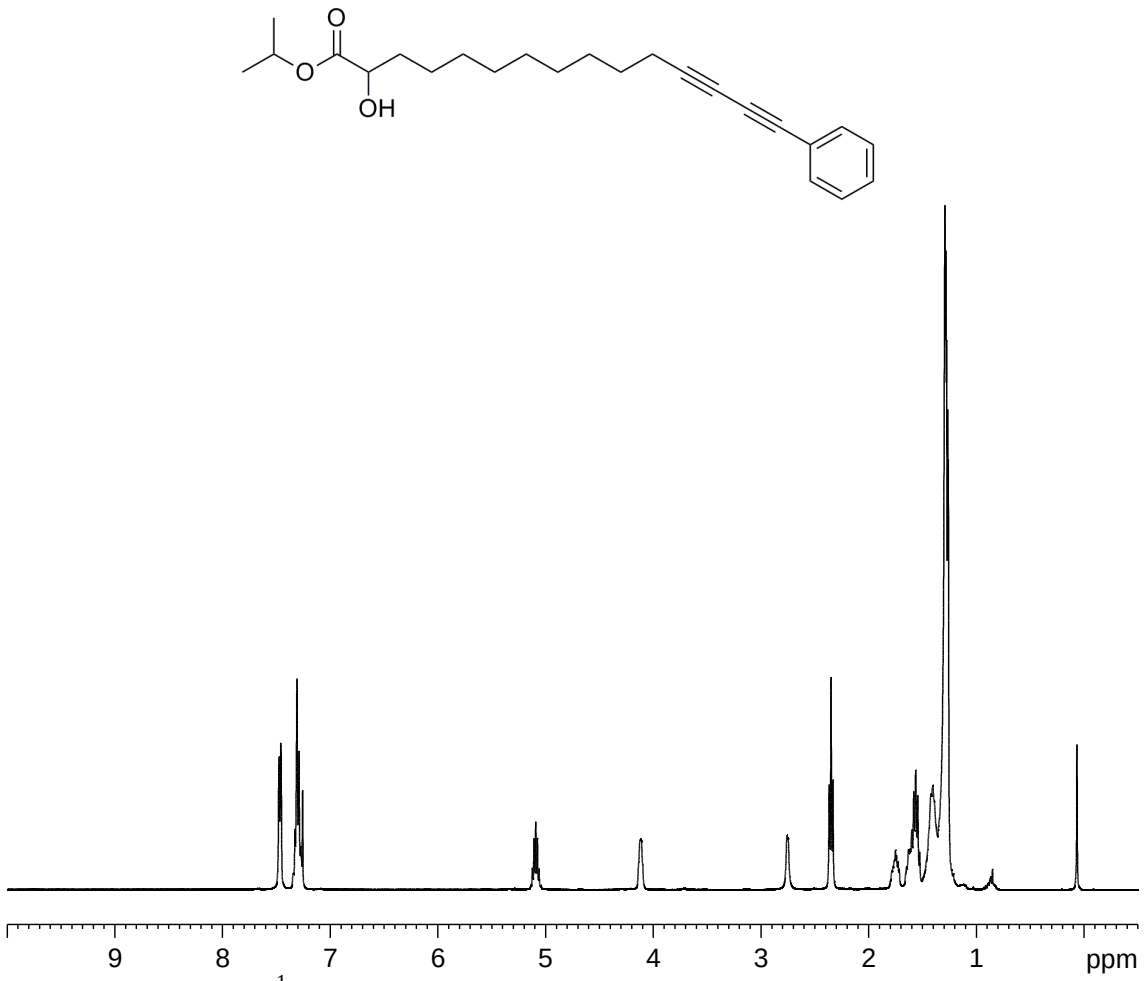
^{13}C NMR spectrum of **18** (200 MHz, $CDCl_3$)



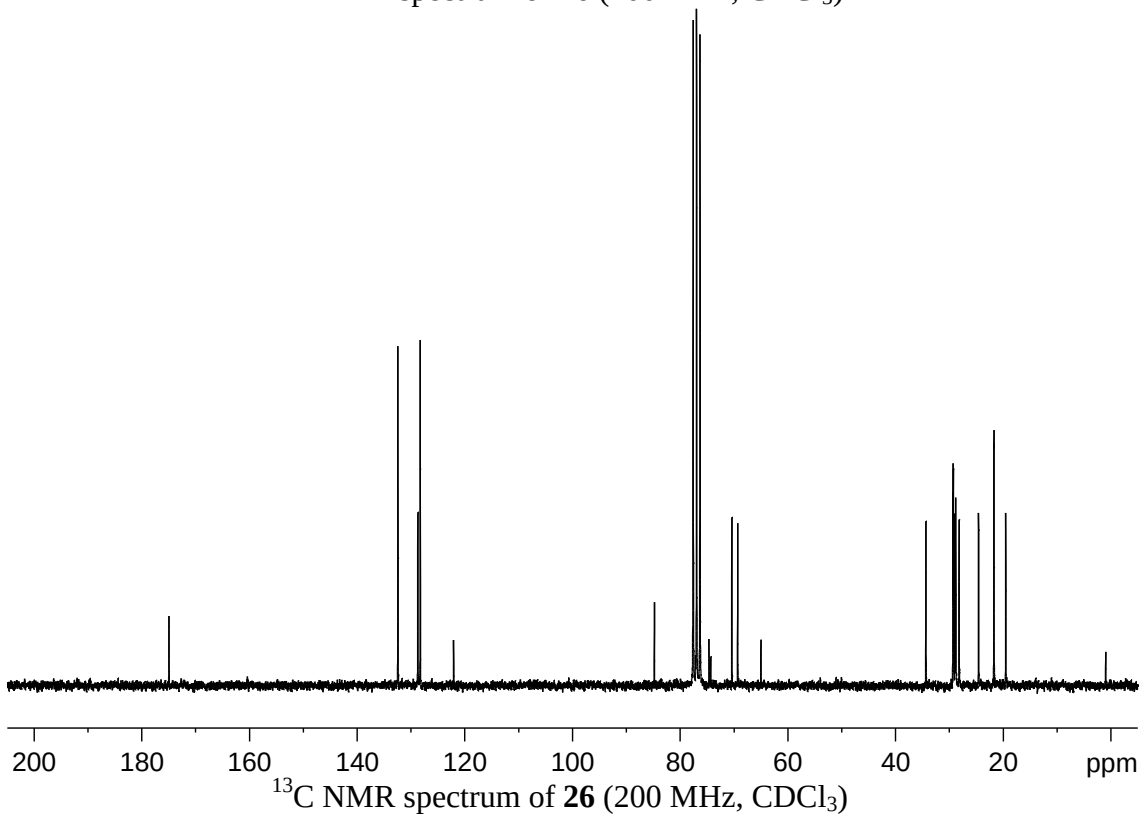
^{1}H NMR spectrum of **22** (400 MHz, $CDCl_3$)



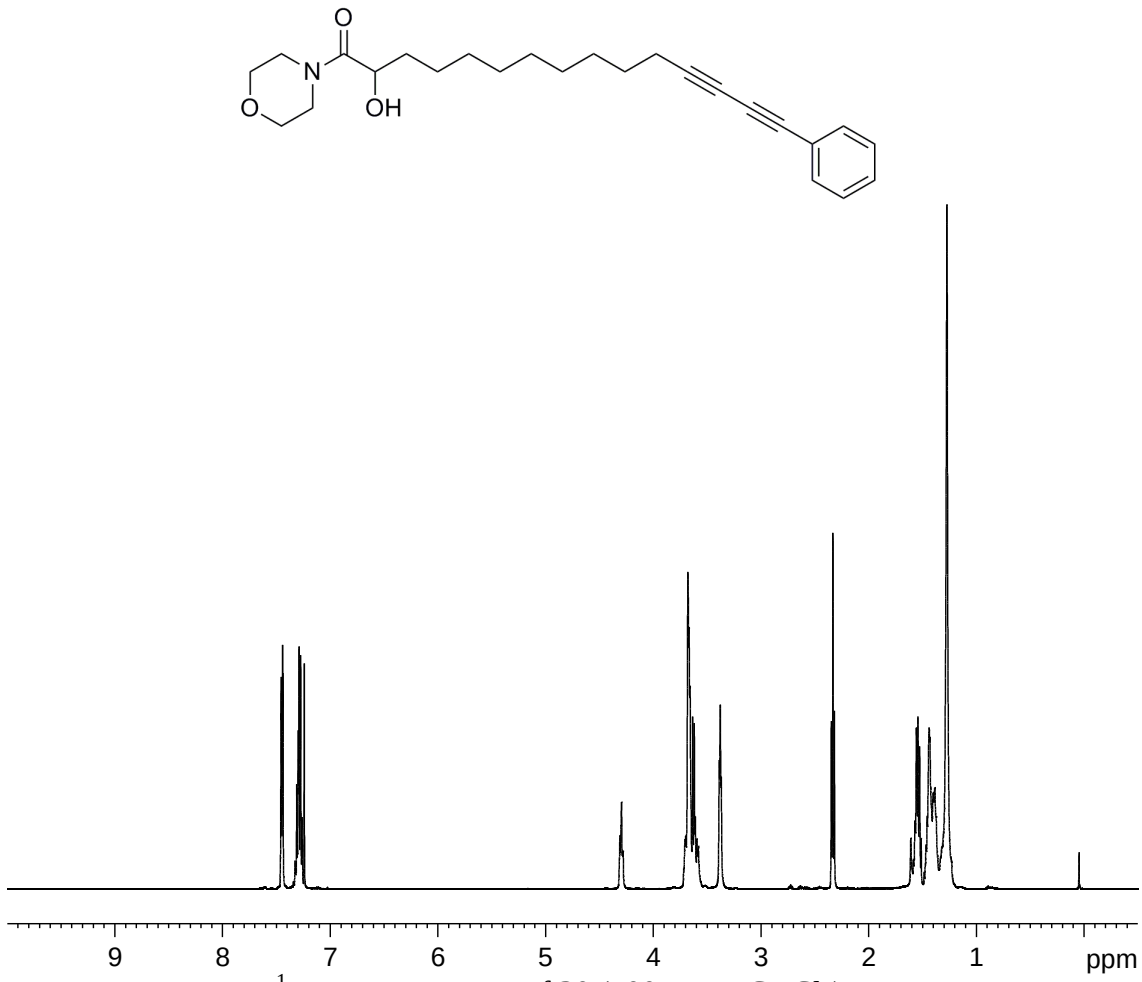
^{13}C NMR spectrum of **22** (200 MHz, $CDCl_3$)



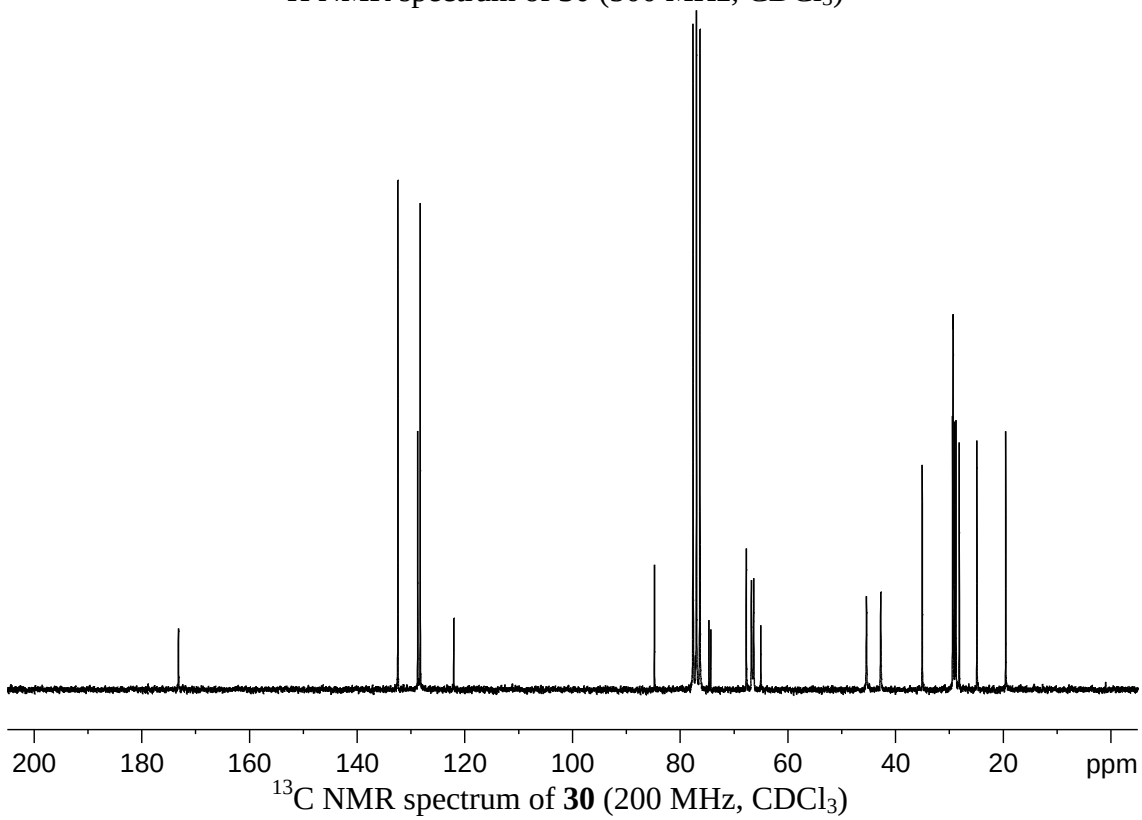
^{1}H NMR spectrum of **26** (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of **26** (200 MHz, $CDCl_3$)

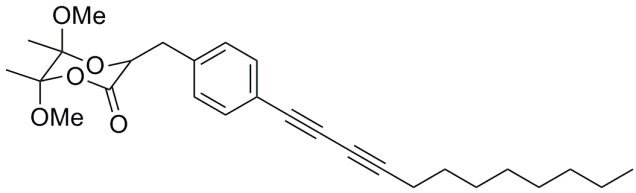


^{1}H NMR spectrum of **30** (500 MHz, $CDCl_3$)

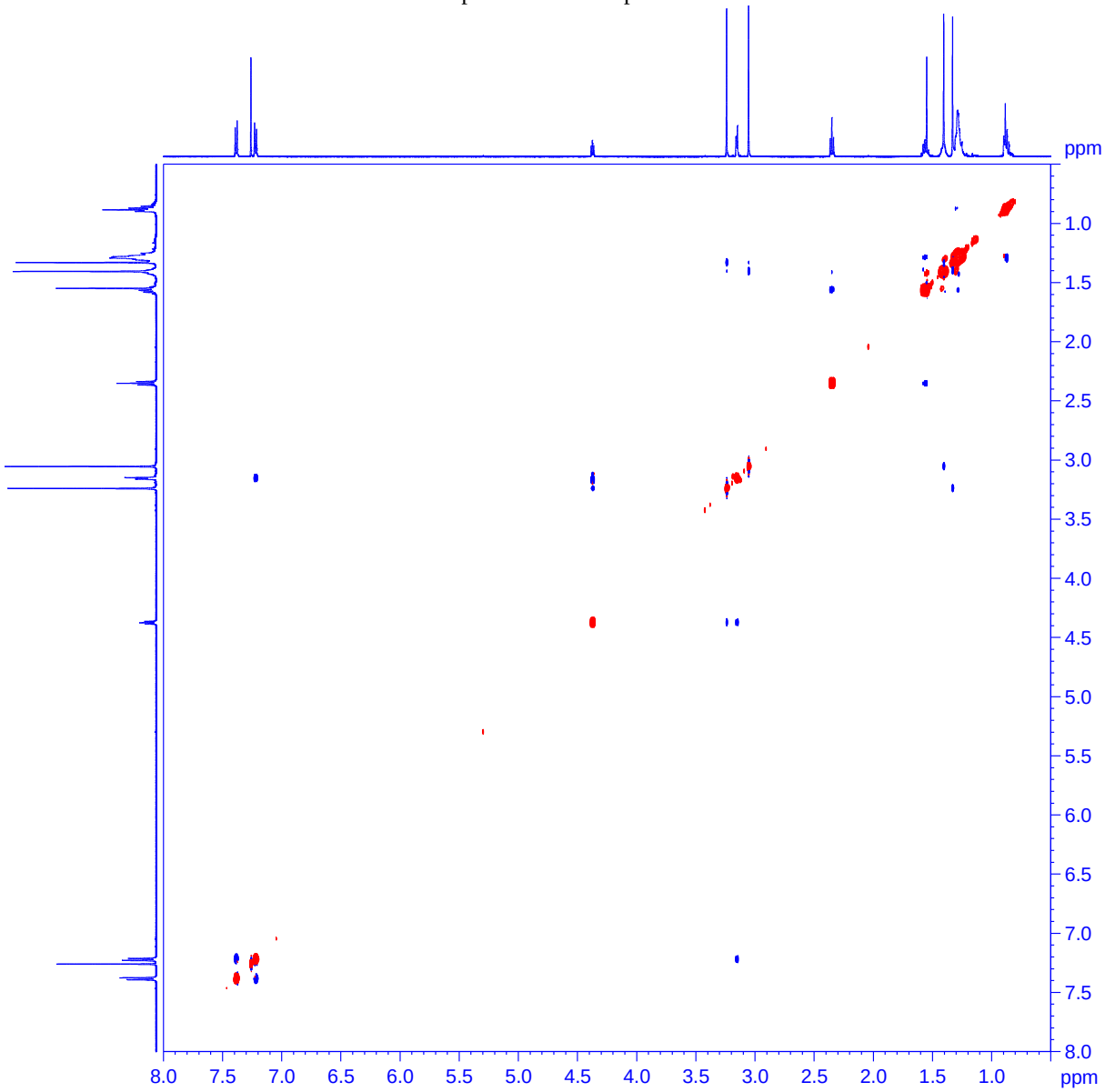


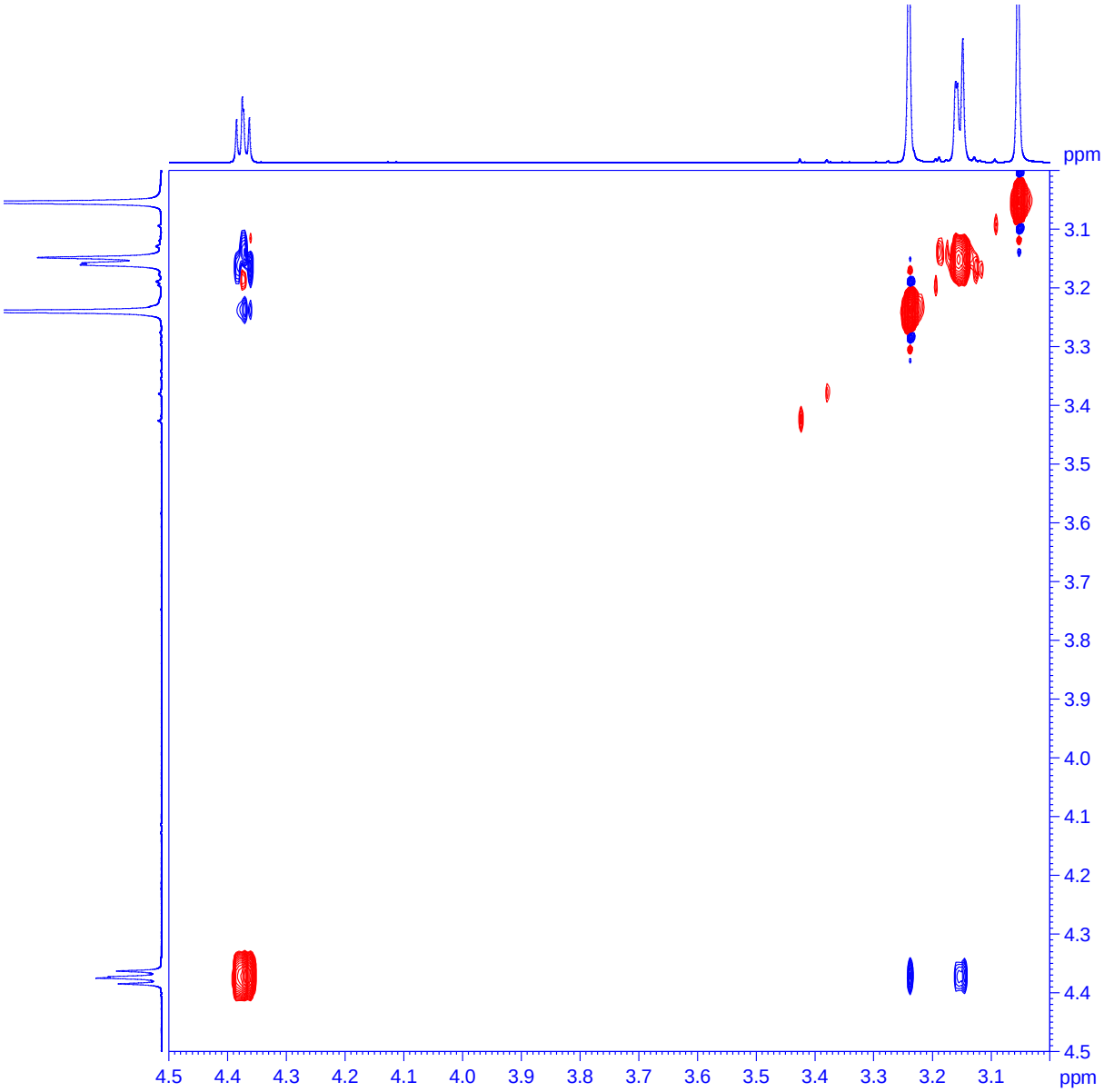
^{13}C NMR spectrum of **30** (200 MHz, $CDCl_3$)

3. ^{1}H–^{1}H NOESY experiment for 17



The ^{1}H–^{1}H NOESY experiment was performed on a Bruker DRX500 NMR spectrometer equipped with a 5 mm ^{1}H–^{13}C–^{15}N triple-resonance inverse probe with *z*-gradient. Data were acquired using a gradient-enhanced NOESY sequence with States phase selection. 512 F1 experiments were acquired, each with 4096 data points acquired for the FID in the F2-dimension. The spectral width was 5000 Hz (1.22 Hz/pt in F2) in both dimensions. Each experiment was summed over 8 scans with a 1.5 s relaxation delay and 1200 ms mixing time. The data were zero-filled in F1 to 2,048 × 2,048 data points and a $/_2$-shifted sine-squared bell window function was applied in both dimensions prior to the two-dimensional Fourier transform. The data were processed in the phase-sensitive mode.




ppm
3.1
3.2
3.3
3.4
3.5
3.6
3.7
3.8
3.9
4.0
4.1
4.2
4.3
4.4
4.5
4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1
ppm

4. Crystallisation and polymerisation of 23

A solution of compound **23** (100 mg) in methanol (30 ml) was reduced in volume to 1 ml under vacuum at 40^{o}C and had added to it a hydrochloric acid solution in tetrahydrofuran (1 M aq. HCl, 20 ml in 20 ml THF). The solution was stirred overnight at room temperature, after which the solvent was removed to give a clear oil. This was dissolved in dichloromethane (1 ml) into which hexane was then introduced by slow vapour diffusion in a sealed system at -10^{o}C. After 3 days well-formed crystals of 2-hydroxy-heptadecadiynoic acid had appeared in the dichloromethane.

Several single crystals prepared as outlined above were taken and exposed to UV radiation (254 nm) (from a handheld UV lamp in a fluorescence analysis cabinet). After a few seconds exposure the crystals turned a deep blue. Upon exposure to organic solvents or high temperatures the crystals turned a deep red colour. After storage at -10^{o}C for a week, the clear crystals had taken on a light blue hue, due to the thermal polymerisation of the diacetylene groups.