Supporting information

Exo-Selective Reductive Macrocyclization of Ynals

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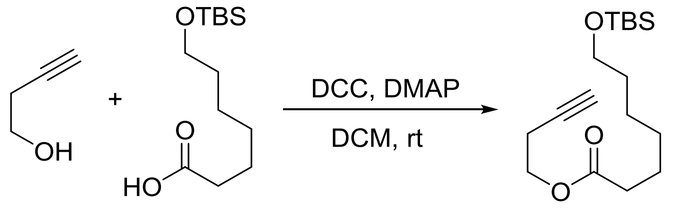
General Methods: Unless otherwise noted, all reactions were conducted in flame-dried or oven-dried glassware with magnetic stirring under an atmosphere of dry nitrogen. Solvents were purified under nitrogen using a solvent purification system (Innovative Technology, inc., Model #SPS-400-3 and PS-400-3). Unless otherwise noted, all other chemical reagents were obtained from commercial sources and used as received. Silanes were purified by passing through alumina. $Ni(COD)_2$ (Strem Chemicals, Inc.), all *N*-heterocyclic carbene salts (Aldrich), potassium *tert*-butoxide (Strem Chemicals, Inc.) were stored and weighed in an inert atmosphere glovebox. Reaction temperatures were controlled by a JKEM Scientific (Model 210) temperature modulator. Analytical thin layer chromatography (TLC) was performed on SiliaPlate TLC 60Å F-254 (250 μm silica gel) and compounds were visualized with phosphomolybdic acid, ceric ammonium molybdate, or aqueous $KMnO_4$ stain. Flash column chromatography was performed using SiliaFlash® P60 (230-400 mesh) silica gel.

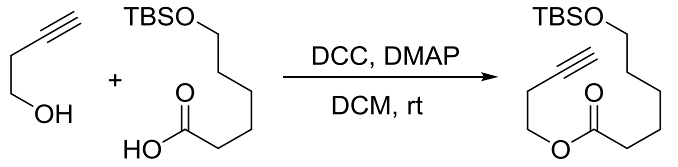
^{1}H-Nuclear Magnetic Resonance (^{1}H-NMR) and ^{13}C Nuclear Magnetic Resonance (^{13}C-NMR) spectra were recorded on Varian MR 400, Vnmrs 500, INOVA 500 and Vnmrs 700 MHz. NMR spectra were recorded in deuterated chloroform ($CDCl_3$) at room temperature unless otherwise stated. The NMR data were presented as follows: chemical shift in ppm with the proton signal of the residual of chloroform (δ 7.26 for ^{1}H-NMR) and ($\delta = 77.0$ ppm for ^{13}C-NMR) as internal standards, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet, br. = broad), coupling constant (*J*/Hz), integration. High resolution mass spectra were recorded on a VG 70-250-s spectrometer manufactured by Micromass Corp. (Manchester UK) at the University of Michigan Mass Spectrometry Laboratory. IR spectra were collected on a Spectrum BX FTIR from Perkin-Elmer and reported in unit of cm^{-1}.

General procedure (A) for the DCC coupling reaction: To a solution of a carboxylic acid (5 mmol, 1 equiv) and an alcohol (9 mmol, 1.8 equiv) in dichloromethane (20 mL) at rt was added a solution of *N*,*N*′-dicyclohexylcarbodiimide (DCC, 5.5 mmol, 1.1 equiv) in dichloromethane (5 mL) and 4-(dimethylamino)pyridine (DMAP, 1 mmol, 0.2 equiv) subsequently. The reaction was then stirred overnight at rt. Hexanes (25 mL) were added and the resulting solution was filtered. The filtrate was concentrated in vacuo and the crude reaction mixture was purified by flash chromatography.



SA-1

But-3-yn-1-yl 7-((*tert*-butyldimethylsilyl)oxy)heptanoate (SA-1): Following the general procedure (**A**), the reaction of 7-((*tert*-butyldimethylsilyl)oxy)heptanoic acid[1] (1.5055 g, 0.00578 mol, 1 equiv), 3-butyn-1-ol (0.79 mL, 0.0104 mol, 1.8 equiv), DCC (1.3287 g, 0.00644 mol, 1.1 equiv) and DMAP (0.1475 g, 0.00121 mol, 0.2 equiv) afforded the product as a colorless oil (1.3129 g, 73% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 10:1). FTIR (KBr): 3313, 2932, 2858, 1741, 1641, 1256, 1160, 1100 cm^{-1}; ^{1}H-NMR (500 MHz, CDCl$_3$) δ 4.18 (t, *J* = 6.8 Hz, 2H), 3.59 (t, *J* = 6.5 Hz, 2H), 2.53 (td, *J* = 6.8, 2.7 Hz, 2H), 2.33 (t, *J* = 7.5 Hz, 2H), 2.00 (t, *J* = 2.6 Hz, 1H), 1.68 – 1.59 (m, 2H), 1.55 – 1.46 (m, 2H), 1.38 – 1.30 (m, 4H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C-NMR (100 MHz, CDCl$_3$) δ 173.1, 79.8, 69.7, 62.9, 61.7, 33.9, 32.5, 28.7, 25.8, 25.3, 24.2, 18.8, 18.1, -5.5; HRMS (ESI) *m*/*z*: [M+H]$^+$ calcd. for $C_{17}H_{33}O_3{}^{28}Si_1$, 313.2193; found, 313.2197.



SA-2

But-3-yn-1-yl 6-((*tert*-butyldimethylsilyl)oxy)hexanoate (SA-2): Following the general procedure (**A**), the reaction of 6-((*tert*-butyldimethylsilyl)oxy)hexanoic acid[1] (1.7396 g, 0.00706 mol, 1 equiv), 3-butyn-1-ol (0.96 mL, 0.0127 mol, 1.8 equiv), DCC (1.6509 g, 0.00800 mol, 1.1 equiv) and DMAP (0.1713 g, 0.00140 mol, 0.2 equiv) afforded the product as a colorless oil (1.5173 g, 72% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 20:1). FTIR (neat): 3313, 2930, 2857, 1738, 1254, 1159, 1095 cm^{-1}; ^{1}H-NMR (500 MHz, CDCl$_3$) δ 4.18 (t, *J* = 6.8 Hz, 2H), 3.60 (t, *J* = 6.5 Hz, 2H), 2.53 (td, *J* = 6.8, 2.7 Hz, 2H), 2.34 (t, *J* = 7.6 Hz, 2H), 2.00 (t, *J* = 2.7 Hz, 1H), 1.69 – 1.61 (m, 2H), 1.56 – 1.49 (m, 2H), 1.41 – 1.33 (m, 2H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C-NMR

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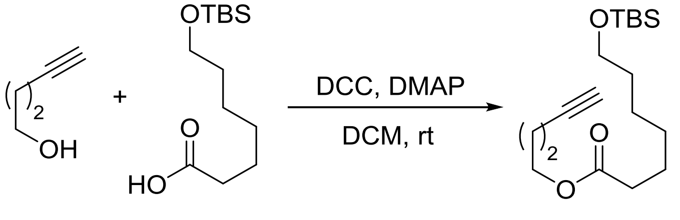
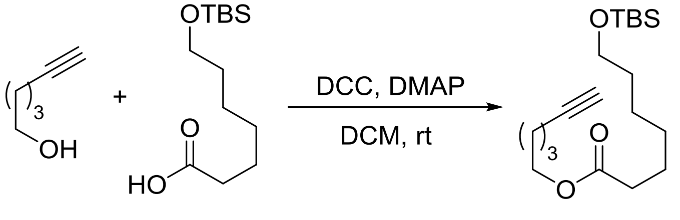
(1) Samorì, C.; Ali-Boucetta, H.; Sainz, R.; Guo, C.; Toma, M. F.; Fabbro, C.; Da Ros, T.; Prato, M.; Kostarelos, K.; Bianco, A. *Chem. Commun.* **2010**, *46*, 1494–1496.

(100 MHz, $CDCl_3$) δ 173.0, 79.8, 69.7, 62.6, 61.7, 33.9, 32.3, 25.7, 25.2, 24.5, 18.8, 18.1, -5.5; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{16}H_{31}O_3{}^{28}Si_1$, 299.2037; found, 299.2047.



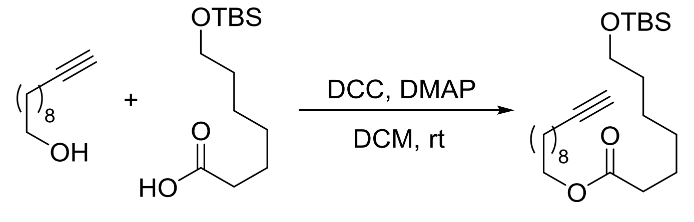
SA-3

Pent-4-yn-1-yl 7-((tert-butyldimethylsilyl)oxy)heptanoate (SA-3): Following the general procedure (**A**), the reaction of 7-((*tert*-butyldimethylsilyl)oxy)heptanoic acid (1.8392 g, 7.06 mmol, 1 equiv), 4-pentyn-1-ol (0.70 mL, 7.52 mmol, 1.07 equiv), DCC (1.6151 g, 7.83 mmol, 1.1 equiv) and DMAP (0.1699 g, 1.39 mmol, 0.2 equiv) afforded the product as a colorless oil (1.2163 g, 53% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 20:1 then 10:1). FTIR (KBr): 3314, 2932, 2858, 1739, 1256, 1165, 1100 cm^{-1}; ^1H-NMR (500 MHz, $CDCl_3$) δ 4.17 (t, *J* = 6.3 Hz, 2H), 3.59 (t, *J* = 6.5 Hz, 2H), 2.33 – 2.25 (m, 4H), 1.97 (t, *J* = 2.6 Hz, 1H), 1.90 – 1.82 (m, 2H), 1.68 – 1.58 (m, 2H), 1.55 – 1.46 (m, 2H), 1.39 – 1.27 (m, 4H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.4, 82.7, 68.9, 62.9, 62.5, 34.0, 32.5, 28.8, 27.4, 25.8, 25.3, 24.8, 18.2, 15.0, -5.5; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{18}H_{35}O_3{}^{28}Si_1$, 327.2350; found, 327.2354.



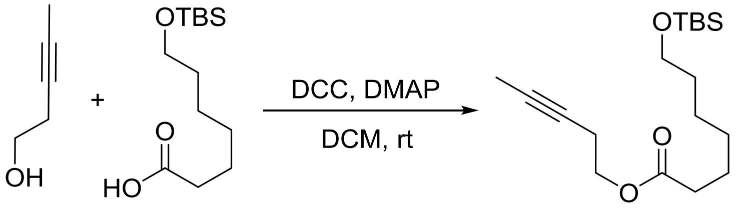
SA-4

Hex-5-yn-1-yl 7-((*tert*-butyldimethylsilyl)oxy)heptanoate (SA-4): Following the general procedure (**A**), the reaction of 7-((*tert*-butyldimethylsilyl)oxy)heptanoic acid (1.7887 g, 6.87 mmol, 1 equiv), 5-hexyn-1-ol (0.80 mL, 7.25 mmol, 1.06 equiv), DCC (1.5773 g, 7.64 mmol, 1.1 equiv) and DMAP (0.1703 g, 1.39 mmol, 0.2 equiv) afforded the product as a colorless oil (1.2157 g, 52% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 20:1 then 10:1). FTIR (KBr): 3313, 2932, 2858, 1737, 1256, 1167, 1101 cm^{-1}; ^1H-NMR (500 MHz, $CDCl_3$) 4.09 (t, *J* = 6.5 Hz, 2H), 3.59 (t, *J* = 6.5 Hz, 2H), 2.30 (t, *J* = 7.6 Hz, 2H), 2.23 (td, *J* = 7.0, 2.6 Hz, 2H), 1.96 (t, *J* = 2.6 Hz, 1H), 1.79 – 1.72 (m, 2H), 1.66 – 1.56 (m, 4H), 1.55 – 1.47 (m, 2H), 1.37 – 1.30 (m, 4H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.5, 83.6, 68.6, 63.5, 62.9, 34.1, 32.5, 28.8, 27.6, 25.8, 25.4, 24.8 (2xC), 18.2, 17.9, -5.4; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{19}H_{37}O_3{}^{28}Si_1$, 341.2506; found, 341.2511.



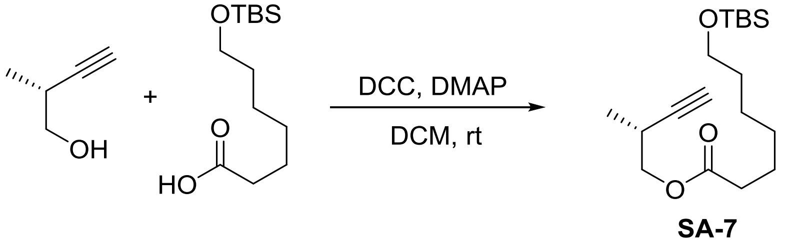
SA-5

Undec-10-yn-1-yl 7-((*tert*-butyldimethylsilyl)oxy)heptanoate (SA-5): Following the general procedure **(A)**, the reaction of 7-((*tert*-butyldimethylsilyl)oxy)heptanoic acid (0.8894 g, 3.415 mmol, 1 equiv), 10-undecyn-1-ol (0.8582 g, 5.100 mmol, 1.5 equiv), DCC (0.7888 g, 3.823 mmol, 1.1 equiv) and DMAP (0.0782 g, 0.640 mmol, 0.2 equiv) afforded the product as a colorless oil (0.8563 g, 61% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 20:1 then 10:1). FTIR (KBr): 3313, 2931, 2857, 1737, 1256, 1169, 1100 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.05 (t, *J* = 6.7 Hz, 2H), 3.59 (t, *J* = 6.5 Hz, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 2.18 (td, *J* = 7.1, 2.6 Hz, 2H), 1.94 (t, *J* = 2.6 Hz, 1H), 1.70 – 1.57 (m, 4H), 1.54 – 1.46 (m, 4H), 1.44 – 1.23 (m, 14H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.3, 84.1, 68.0, 64.0, 62.8, 34.0, 32.4, 29.1, 29.0, 28.8, 28.7, 28.5, 28.4, 28.3, 25.72, 25.69, 25.3, 24.8, 18.13, 18.05, -5.5; HRMS (ESI) *m/z*: [M+H]$^+$ calcd. for $C_{24}H_{47}O_3{}^{28}Si_1$, 411.3289; found, 411.3291.



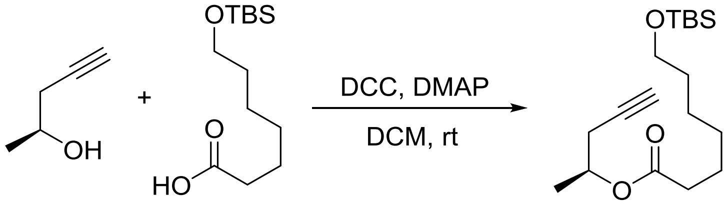
SA-6

Pent-3-yn-1-yl 7-((*tert*-butyldimethylsilyl)oxy)heptanoate (SA-6): Following the general procedure **(A)**, the reaction of 7-((*tert*-butyldimethylsilyl)oxy)heptanoic acid (1.6069 g, 0.00617 mol, 1 equiv), 3-pentyn-1-ol (1.00 mL, 0.0108 mol, 1.8 equiv), DCC (1.7598 g, 0.00853 mol, 1.4 equiv) and DMAP (0.1521 g, 0.00125 mol, 0.2 equiv) afforded the product as a colorless oil (1.6042 g, 80% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 20:1; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.13 (t, *J* = 6.9 Hz, 2H), 3.59 (t, *J* = 6.5 Hz, 2H), 2.49 – 2.42 (m, 2H), 2.32 (t, *J* = 7.5 Hz, 2H), 1.78 (t, *J* = 2.5 Hz, 3H), 1.67 – 1.59 (m, 2H), 1.54 – 1.47 (m, 2H), 1.37 – 1.31 (m, 4H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 173.3, 77.0, 74.6, 63.0, 62.5, 34.0, 32.5, 28.8, 25.8, 25.4, 24.8, 19.1, 18.2, 3.3, -5.4; HRMS (ESI) *m/z*: [M+H]$^+$ calcd. for $C_{18}H_{35}O_3{}^{28}Si_1$, 327.2350; found, 327.2354.



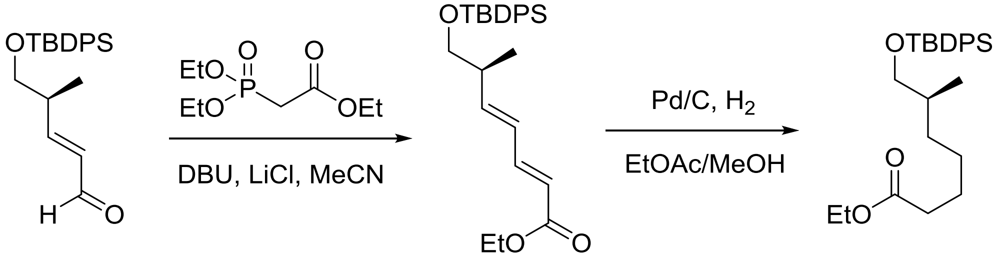
SA-7

(*R*)-2-Methylbut-3-yn-1-yl 7-((*tert*-butyldimethylsilyl)oxy)heptanoate (SA-7): Following the general procedure **(A)**, the reaction of 7-((*tert*-butyldimethylsilyl)oxy)heptanoic acid (0.6990 g, 0.00268 mol, 1 equiv), (*R*)-2-methylbut-3-yn-1-ol[2] (~0.0038 mol, ~1.8 equiv), DCC (0.6298 g, 0.00352 mol, 1.1 equiv) and DMAP (0.0670 g, 0.000548 mol, 0.2 equiv) afforded the product as a colorless oil (0.3235 g, 37% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 20:1). FTIR (neat): 3312, 2928, 2856, 1738, 1462, 1388, 1254, 1155 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.09 (dd, *J* = 10.6, 6.8 Hz, 1H), 4.01 (dd, *J* = 10.6, 6.8 Hz, 1H), 3.59 (t, *J* = 6.5 Hz, 2H), 2.84 – 2.74 (m, 1H), 2.34 (t, *J* = 7.5 Hz, 2H), 2.08 (d, *J* = 2.4 Hz, 1H), 1.69 – 1.59 (m, 2H), 1.55 – 1.45 (m, 2H), 1.39 – 1.29 (m, 4H), 1.22 (d, *J* = 6.9 Hz, 3H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 173.3, 84.9, 69.5, 66.9, 63.0, 34.0, 32.5, 28.8, 25.9, 25.6, 25.4, 24.8, 18.2, 17.3, -5.4; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{18}H_{35}O_3{}^{28}Si_1$, 327.2350; found, 327.2350.



SA-8

(*S*)-Pent-4-yn-2-yl 7-((*tert*-butyldimethylsilyl)oxy)heptanoate (SA-8): Following the general procedure **(A)**, the reaction of 7-((*tert*-butyldimethylsilyl)oxy)heptanoic acid (1.5232 g, 0.00585 mol, 1 equiv), (*S*)-pent-4-yn-2-ol[3] (0.8976 g, 0.0107 mol, 1.8 equiv), DCC (1.3570 g, 0.00658 mol, 1.1 equiv) and DMAP (0.1505 g, 0.00123 mol, 0.2 equiv) afforded the product as a colorless oil (1.1394 g, 60% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 10:1). FTIR (neat): 3313, 2932, 2858, 1734, 1463, 1382, 1252, 1091 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.08 – 4.97 (m, 1H), 3.59 (t, *J* = 6.5 Hz, 2H), 2.49 – 2.42 (m, 2H), 2.30 (t, *J* = 7.5 Hz, 2H), 2.00 (t, *J* = 2.7 Hz, 1H), 1.68 – 1.57 (m, 2H), 1.54 – 1.46 (m, 2H), 1.37 – 1.30 (m, 7H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 172.6, 79.4, 70.3, 68.0, 62.8, 34.2, 32.4, 28.7, 25.8, 25.31, 25.28, 24.8, 18.9, 18.2, -5.5; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{18}H_{35}O_3{}^{28}Si_1$, 327.2350; found, 327.2363.



S1 **S2** **S3**

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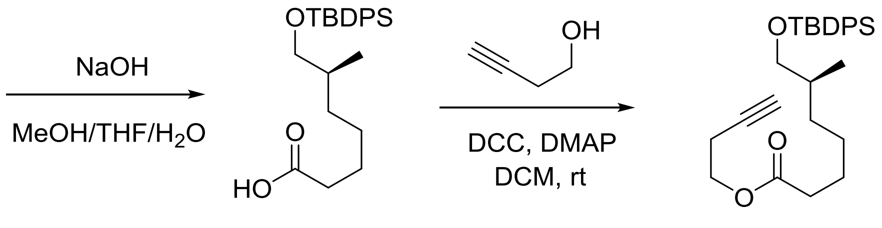
[2] Kong, K.; Moussa, Z.; Lee, C.; Romo, D. *J. Am. Chem. Soc.* **2011**, *133*, 19844–19856.

[3] Yuen, T.-Y.; Brimble, M. A. *Org. Lett.* **2012**, *14*, 5154–5157.



S4 **SA-9**

Ethyl (*S*,2*E*,4*E*)-7-((*tert*-butyldiphenylsilyl)oxy)-6-methylhepta-2,4-dienoate (S2): Under nitrogen atmosphere, to a mixture of lithium chloride (0.6323 g, 0.0149 mol, 1.2 equiv) and acetonitrile (90 mL) at rt was added triethyl phosphonoacetate (2.60 mL, 0.0130 mol, 1.05 equiv) followed by 1,8-diazabicyclo[5.4.0]undec-7-ene (2.20 mL, 0.0147 mol, 1.2 equiv). After stirring for 10 min, a solution of (*S,E*)-5-((*tert*-butyldiphenylsilyl)oxy)-4-methylpent-2-enal[4] (4.3680 g, 0.0124 mol 1 equiv) in acetonitrile (20 mL) was added slowly. The resulting reaction mixture was stirred overnight at rt and then quenched with saturated aqueous sodium bicarbonate solution. It was extracted with diethyl ether three times. The combined organic layers were dried over magnesium sulfate. After filtering the solution, the filtrate was concentrated in vacuo and then dried over a vacuum line to give the crude product **S2** as a pale yellow oil, which was used in the subsequent reaction directly without further purification.

Ethyl (*S*)-7-((*tert*-butyldiphenylsilyl)oxy)-6-methylheptanoate (S3): The crude **S2** was dissolved in 20 mL ethyl acetate/methanol (v/v = 1/4) and added to a suspension of Pd/C in 5 mL ethyl acetate/methanol (v/v = 1/4). The resulting mixture was shaken for 24 h in a Parr reactor at 40 psi hydrogen atmosphere. The solution was then filtered through silica gel and washed with diethyl ether. The filtrate was concentrated in vacuo and then dried over a vacuum line to give the crude ester **S3** as a pale yellow oil (4.4597g, 84% yield over 2 steps), which was used in the subsequent reaction directly without further purification.

(*S*)-7-((*tert*-Butyldiphenylsilyl)oxy)-6-methylheptanoic acid (S4): To a solution of ester **S3** (1.4396 g, 3.374 mmol, 1 equiv) in methanol (20 mL) and tetrahydrofuran (13 mL) at 0 ˚C was added 2*N* aqueous sodium hydroxide solution (6.8 mL, 13.6 mmol, 4 equiv) slowly. The resulting mixture stirred at 0 ˚C for 1 h then rt for 3 h. TLC showed there was still starting material left, so additional 2*N* aqueous sodium hydroxide solution (6.8 mL, 13.6 mmol, 4 equiv) was added and the reaction was stirred at rt for 2h. It was then diluted with water and acidified with aqueous potassium bisulfate solution. The resulting mixture was extracted with ethyl acetate three times and the combined organic layers were dried over magnesium sulfate. After filtering the solution, the filtrate was concentrated in vacuo and then dried over a vacuum line to give the crude carboxylic acid **S4** (1.2988 g, 97% yield) as a pale yellow oil, which was used in the subsequent reaction directly without further purification.

(*S*)-But-3-yn-1-yl 7-((*tert*-butyldiphenylsilyl)oxy)-6-methylheptanoate (SA-9): Following the general procedure **(A)**, the reaction of carboxylic acid **S4** (1.2988 g, 0.00326 mol, 1 equiv), 3-butyn-1-ol (1.0 mL, 0.0132 mol, 4 equiv), DCC (0.9242 g, 0.00448 mol, 1.4 equiv) and DMAP (0.3945 g, 0.323 mol, 1 equiv) afforded the product as a colorless oil (0.0.8637 g, 59% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 20:1 then 10:1). FTIR (neat): 3293, 2929, 2855, 1737, 1471, 1427,

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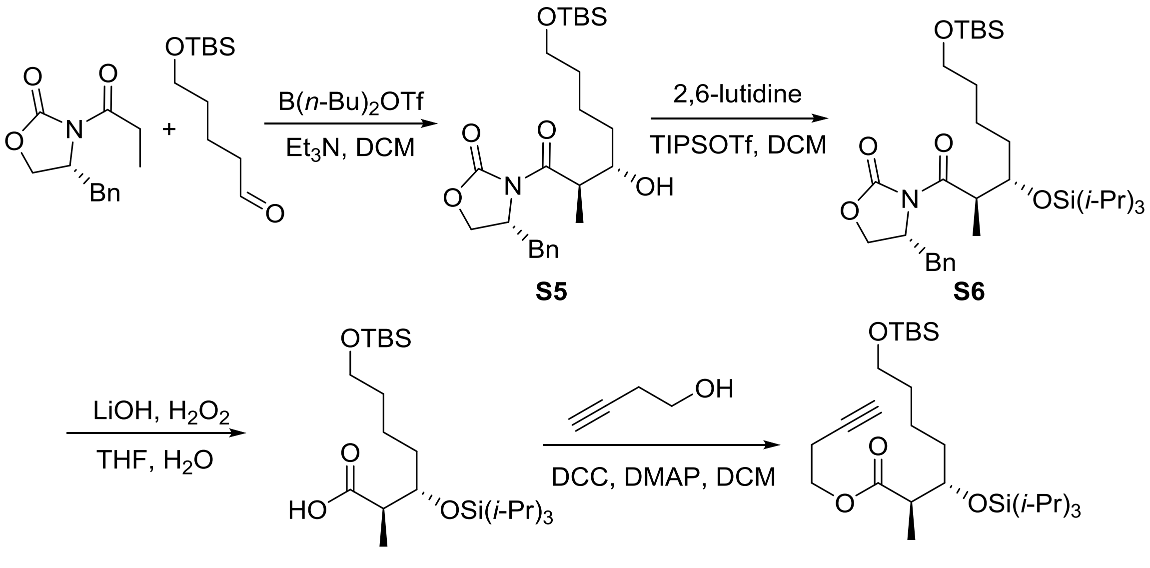
(4) Marshall, J. A.; Herold, M.; Eidam, H. S.; Eidam, P. *Org. Lett.* **2006**, 8, 5505–5508.

1388, 1164, 1100 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.66 (dd, J = 7.8, 1.5 Hz, 4H), 7.46 – 7.33 (m, 6H), 4.18 (t, J = 6.8 Hz, 2H), 3.53 – 3.39 (m, 2H), 2.52 (td, J = 6.8, 2.7 Hz, 2H), 2.30 (t, J = 7.6 Hz, 2H), 1.98 (t, J = 2.7 Hz, 1H), 1.72 – 1.55 (m, 3H), 1.51 – 1.38 (m, 1H), 1.39 – 1.18 (m, 2H), 1.18 – 1.07 (m, 1H), 1.05 (s, 9H), 0.90 (d, J = 6.7 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 173.4, 135.5, 134.0, 129.4, 127.5, 80.2, 69.8, 68.7, 61.8, 35.5, 34.1, 32.7, 26.8, 26.4, 25.1, 19.3, 18.9, 16.8; HRMS (ESI) *m/z*: $[M+NH_4]^+$ calcd. for $C_{28}H_{42}{}^{14}N_1O_3{}^{28}Si_1$, 468.2928; found, 468.2929.



S5 **S6** **S7** **SA-10**

(*R*)-4-Benzyl-3-((2*R*,3*S*)-7-((*tert*-butyldimethylsilyl)oxy)-3-hydroxy-2-methylheptanoyl)oxazolidin-2-one (S5): To a solution of (*4R*)-3-propionyl-4-benzyl-2-oxazolidinone (418 mg, 1.77 mmol, 1.2 equiv) in CH_2Cl_2 (3.3 mL) was added dibutylboron triflate (448 μL, 1.85 mmol, 1.25 equiv), followed by triethylamine (309 μL, 2.22 mmol, 1.5 equiv) dropwise at 0 ˚C and stirred for 20 min. The solution was then cooled to -78 ˚C. To this solution was added a solution of 5-((*tert*-butyldimethylsilyl)oxy)pentanal[5] (320 mg, 1.48 mmol, 1 equiv) in CH_2Cl_2 (3.9 mL) at -78 ˚C. The resulting solution was stirred for 20 min at -78 ˚C. The reaction mixture was then warmed up to rt and stirred for 5 h. The reaction was terminated by adding 3 mL pH 7 aqueous phosphate buffer solution and methanol (9 mL) at 0 ˚C. To this cloudy solution was added a solution of methanol and 30% hydrogen peroxide (2:1, 9 mL) and the resulting solution was stirred for 1 h at 0 ˚C. Then the reaction mixture was concentrated to remove organic solvents, and the resulting mixture was extracted three times with diethyl ether. The organic layer was washed with saturated aqueous sodium bicarbonate and saturated aqueous NaCl, dried over Na_2SO_4, filtered and concentrated. The crude residue was purified by silica column chromatography (30% EtOAc in hexanes) to yield 635 mg (96%) of the desired aldol product as a colorless oil. ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.34 (t, J =7.7 Hz, 2H), 7.29 (t, J = 7.7 Hz, 1H), 7.21 (d, J = 7.0 Hz, 2H), 4.73 – 4.68 (m, 1H), 4.23 (dd, J = 9.1, 9.1 Hz, 1H), 4.19 (dd, J = 9.1, 2.8 Hz, 1H), 3.98 – 3.93 (m, 1H), 3.76 (qd, J = 6.3, 2.5 Hz, 1H), ^{13}C NMR (175 MHz, $CDCl_3$) δ 177.5, 153.0, 135.0, 129.4, 128.9, 127.4, 71.4, 66.1, 63.1, 55.1, 42.1, 37.8, 33.5, 32.6,

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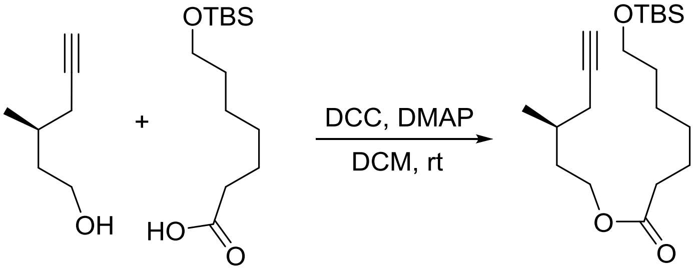
[5] Cran, J. W.; Krafft, M. E. *Angew. Chem., Int. Ed.* **2012**, *51*, 9398 –9402.

25.9, 22.3, 18.3, 10.4, -5.3. IR (thin film) 3524, 2930, 2858, 1784, 1698, 1456, 1386, 1210, 1104 cm^{-1}. HRMS (ESI) *m/z* calculated for [M+H]$^+$ 450.2676, found 450.2678.

(*R*)-4-Benzyl-3-((2*R*,3*S*)-7-((*tert*-butyldimethylsilyl)oxy)-2-methyl-3-((triisopropyl silyl)oxy)heptanoyl)oxazolidin-2-one (S6): A solution of **S5** (592 mg, 1.32 mmol, 1 equiv) in CH_2Cl_2 (6.6 mL) was cooled to 0 ˚C before 2,6-lutidine (341 μL, 3.00 mmol, 2.3 equiv) was added followed by TIPSOTf (586 μL, 2.11 mmol, 1.6 equiv). The reaction solution was stirred from 0 ˚C to rt for 3 h, before it was quenched by the addition of saturated aqueous $NaHCO_3$ solution. The organic solution was separated, washed with saturated aqueous NaCl, dried over Na_2SO_4 and filtered. After concentration, the residue was chromatographed over silica gel (7% EtOAc in hexanes) to give 836 mg of the desired silyl ether (100% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (t, *J* = 6.8 Hz, 2H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.22 (d, *J* = 6.8 Hz, 2H), 4.61 – 4.53 (m, 1H), 4.26 – 4.20 (m, 1H), 4.16 (dd, *J* = 9.2, 2.9 Hz, 1H), 4.11 (t-like, *J* = 8.2 Hz, 1H), 3.86 (qd, *J* = 6.0, 4.0 Hz, 1H), 3.59 (t, *J* = 6.6 Hz, 2H), 3.31 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.77 (dd, *J* = 13.4, 9.8 Hz, 1H), 1.68 – 1.46 (m, 4H), 1.42 – 1.31 (m, 2H), 1.22 (d, *J* = 6.8 Hz, 3H), 1.10 – 1.01 (m, 21H), 0.89 (s, 9H), 0.04 (s, 6H) ^{13}C NMR (175 MHz, $CDCl_3$) δ 175.1, 153.1, 135.5, 129.5, 128.9, 127.3, 73.2, 66.0, 63.0, 55.9, 42.5, 37.6, 35.6, 33.2, 25.9, 21.2, 18.3, 18.2, 18.1, 17.7, 13.0, 12.2, 10.2, -5.3. IR (thin film, cm^{-1}) 2942, 2864, 1782, 1705, 1462, 1381. HRMS (ESI) *m/z* calculated for [M+H]$^+$ 606.4010, found 606.4005.

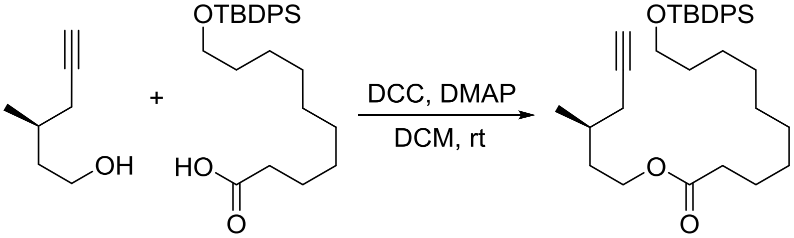
(2*R*,3*S*)-7-((*tert*-Butyldimethylsilyl)oxy)-2-methyl-3-((triisopropylsilyl)oxy)heptanoic acid (S7): To an ice cooled solution of **S6** (690 mg, 1.14 mmol, 1 equiv) in 11.4 mL of a 4:1 mixture of THF:H_2O was added 30% solution of H_2O_2 (930 μL, 9.10 mmol, 7.9 equiv), followed by LiOH (83.4 mg, 3.41 mmol, 3 equiv). The reaction mixture was stirred from 0 ˚C to rt for 12 h before it was quenched by the addition of 6 mL of saturated aqueous $Na_2S_2O_3$ solution and 6 mL of saturated aqueous NH_4Cl solution. The mixture was transferred to a separatory funnel and the aqueous layer was extracted three times with EtOAc. The combined organic extracts were dried over sodium sulfate, filtered and concentrated. The crude residue was chromatographed over silica gel (15% EtOAc in hexanes) to yield 508 mg (95%) of the desired acid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.11 (td, *J* = 5.5, 4.5 Hz, 1H), 3.60 (t, *J* = 6.0 Hz, 2H), 2.72 (qd, *J* = 7.0, 4.0 Hz, 1H), 1.66 – 1.34 (m, 6H), 1.19 – 1.04 (m, 24 H), 0.89 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (175 MHz, $CDCl_3$) δ 181.4, 73.9, 62.9, 44.1, 35.2, 33.2, 26.1, 21.9, 18.5, 18.4, 18.4, 13.2, 9.9, -5.2. IR (thin film, cm^{-1}) 2945, 2867, 1464, 1387. HRMS (ESI) *m/z* calculated for [M+H]$^+$ 447.3326, found 447.3338.

But-3-yn-1-yl (2*R*,3*S*)-7-((tert-butyldimethylsilyl)oxy)-2-methyl-3-((triisopropylsilyl) oxy)heptanoate (SA-10): S7 (508 mg, 1.14 mmol,1 equiv), DCC (261 mg, 1.25 mmol, 1.1 equiv), DMAP (155 mg, 1.25 mmol, 1.1 equiv) and 3-butyn-1-ol (140 μL, 1.83 mmol, 1.6 equiv) were dissolved in 14 mL of CH_2Cl_2 and stirred at rt for 96 h. The reaction mixture was filtered through cotton, the filtrate concentrated and the crude residue was chromatographed over silica gel (eluent 20% EtOAc in hexanes) to yield 522 mg (92%) of the desired product as a colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.28-4.18 (m, 2H), 4.15-4.08 (m, 1H), 3.60 (t, *J* =6.5 Hz, 2H), 2.58 (qd, *J* = 7.0, 4.0 Hz, 1H), 2.52 (td, *J* = 7.0, 2.5 Hz, 2H), 1.98 (t, *J* = 2.3 Hz, 1H), 1.65 – 1.47 (m, 4H), 1.39 – 1.29 (m, 2H), 1.15 (d, *J* = 7.0 Hz, 3H), 1.04 (s, 21H), 0.89 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (175 MHz, $CDCl_3$) δ 174.8, 80.0, 73.5, 69.8, 62.9, 62.0, 43.8, 35.0, 33.0, 25.9, 21.5, 18.9, 18.3, 18.2, 18.1, 12.9, 10.0, -5.3. IR (thin film, cm^{-1}) 3312, 2921, 2854, 1711, 1454. HRMS (ESI) *m/z* calculated for $[M+H]^+$ 499.3639, found 499.3632.



SA-11

(*S*)-3-Methylhex-5-yn-1-yl 7-((*tert*-butyldimethylsilyl)oxy)heptanoate (SA-11): Following the general procedure **(A)**, the reaction of 7-((*tert*-butyldimethylsilyl)oxy)heptanoic acid (0.7244 g, 2.781 mmol, 1 equiv), (*S*)-3-methylhex-5-yn-1-ol[6] (0.2796, 2.494 mmol, 1.1 equiv), DCC (0.6453 g, 3.128 mmol, 1.3 equiv) and DMAP (61.4 mg, 0.503 mmol, 0.2 equiv) afforded the product as a colorless oil (0.5260 g, 59% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 20:1). FTIR (neat): 3297, 2929, 2857, 1735, 1462, 1253, 1168, 1097 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.19 – 4.04 (m, 2H), 3.59 (t, *J* = 6.5 Hz, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 2.25 – 2.07 (m, 2H), 1.97 (t, *J* = 2.6 Hz, 1H), 1.87 – 1.70 (m, 2H), 1.67 – 1.57 (m, 2H), 1.57 – 1.47 (m, 3H), 1.38 – 1.30 (m, 4H), 1.03 (d, *J* = 6.6 Hz, 3H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.0, 82.1, 69.6, 62.9, 62.1, 34.2, 34.1, 32.5, 29.2, 28.8, 25.8, 25.4, 25.3, 24.8, 19.0, 18.1, -5.5; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{20}H_{39}O_3{}^{28}Si_1$, 355.2663; found, 355.2674.



SA-12

(*S*)-3-Methylhex-5-yn-1-yl 10-((*tert*-butyldiphenylsilyl)oxy)decanoate (SA-12): Following the general procedure **(A)**, the reaction of 10-((*tert*-butyldiphenylsilyl)oxy)decanoic acid[7] (0.8134 g, 1.906 mmol，1 equiv), (*S*)-3-methylhex-5-yn-1-ol (0.3178, 2.83 mmol, 1.5 equiv), DCC (0.6285 g, 3.046 mmol, 1.6 equiv) and DMAP (50.2 mg, 0.411 mmol, 0.2 equiv) afforded the product as a colorless oil (0.7100 g, 72% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 20:1). FTIR (neat): 3306, 2929, 2856, 2118, 1734, 1458, 1428, 1172, 1106 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.69 – 7.64 (m, 4H), 7.44 – 7.35 (m, 6H), 4.19 – 4.07 (m, 2H), 3.68 – 3.60 (m, 2H), 2.29 (td, *J* = 7.6, 5.7 Hz, 2H), 2.20 – 2.15 (m, 1H), 1.99 – 1.88 (m, 1H), 1.88 – 1.69 (m, 2H), 1.66 – 1.50 (m, 5H), 1.41 – 1.16 (m, 11H), 1.10 – 0.99 (m, 12H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.5, 135.4, 134.0, 129.3, 127.4, 82.2, 69.6, 63.8, 62.1, 34.3,

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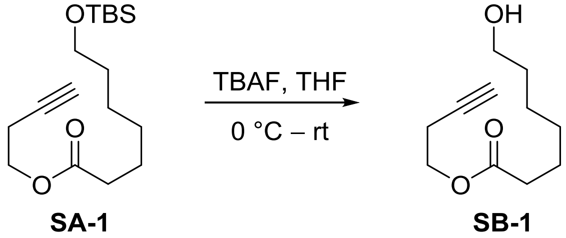
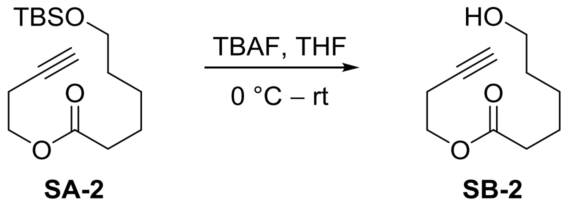
(6) García-Fortaneta, J.; Formentína, P.; Díaz-Oltra, S.; Murga, J.; Carda, M.; Marco, J. A. *Tetrahedron* **2013**, *69*, 3192-3196.
(7) Knapp-Reed, B.; Mahandru, G. M.; Montgomery, J. *J. Am. Chem. Soc.* **2005**, *127*, 13156-13157.

34.2, 32.4, 29.3, 29.21, 29.15, 29.1, 29.0, 26.7, 25.6, 25.5, 24.8, 19.07, 19.06; HRMS (ESI) *m/z*: $[M+NH_4]^+$ calcd. for $C_{33}H_{52}O_3{}^{14}N_1{}^{28}Si_1$, 538.3711; found, 538.3728.

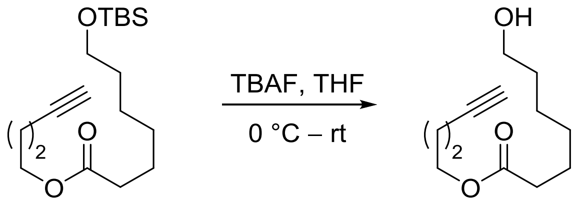
General procedure (B) for the removal of TBS: To a solution of TBS ether (4 mmol, 1 equiv) in tetrahydrofuran (9 mL) at 0 ˚C was added tetrabutylammonium fluoride (TBAF, 1.0 M in THF, 9 mL, 9.0 mmol, 2.25 equiv) slowly. The reaction was stirred at 0 ˚C for 1 h and then rt for 1 h. Water was added and the resulting mixture was extracted with diethyl ether three times. The combined organic layers were dried over magnesium sulfate. After filtering the solution, the filtrate was concentrated in vacuo. The crude residue was purified by flash chromatography to give the alcohol product.



Pent-4-yn-1-yl 7-hydroxyheptanoate (SB-1): Following the general procedure **(B)**, the reaction of **SA-1** (1.3129 g, 4.20 mmol, 1 equiv), TBAF (1.0 M in THF, 9.5 mL, 9.5 mmol, 2.26 equiv) afforded the product as a colorless oil (0.6444 g, 77% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 1:1 then 1:2). FTIR (KBr): 3400 (br.), 3294, 2935, 2861, 1733, 1253, 1176 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.18 (t, J = 6.8 Hz, 2H), 3.64 (t, J = 6.6 Hz, 2H), 2.53 (td, J = 6.8, 2.7 Hz, 2H), 2.34 (t, J = 7.5 Hz, 2H), 2.00 (t, J = 2.6 Hz, 1H), 1.69 – 1.62 (m, 2H), 1.60 – 1.54 (m, 2H), 1.43 – 1.33 (m, 4H), 1.24 (s, 1H); ^{13}C-NMR (175 MHz, $CDCl_3$) δ 173.3, 79.8, 69.7, 62.0, 61.7, 33.7, 32.1, 28.5, 25.1, 24.5, 18.6; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{11}H_{18}O_3{}^{23}Na_1$, 221.1148; found, 221.1148.

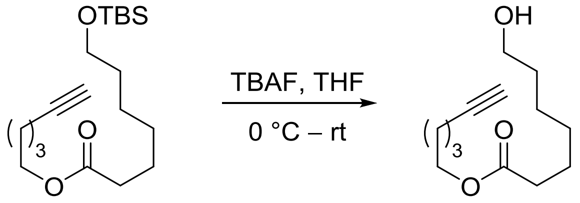


But-3-yn-1-yl 6-hydroxyhexanoate (SB-2): Following the general procedure **(B)**, the reaction of **SA-2** (0.9084 g, 3.04 mmol, 1 equiv), TBAF (1.0 M in THF, 6.90 mL, 6.90 mmol, 2.27 equiv) afforded the product as a colorless oil (0.4948 g, 88% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 1:1). FTIR (neat): 3420 (br.), 3288, 2936, 1731, 1457, 1170, 1052 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.19 (t, J = 6.8 Hz, 2H), 3.68 – 3.62 (m, 2H), 2.53 (td, J = 6.8, 2.7 Hz, 2H), 2.35 (t, J = 7.4 Hz, 2H), 2.00 (dd, J = 2.9, 2.3 Hz, 1H), 1.74 – 1.63 (m, 2H), 1.63 – 1.57 (m, 2H), 1.47 – 1.37 (m, 2H), 1.28 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.3, 79.7, 69.7, 61.7, 61.6, 33.7, 31.8, 24.9, 24.2, 18.5; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{10}H_{17}O_3$, 207.0992; found, 207.0995.



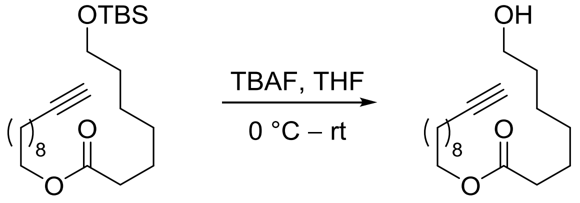
SA-3 **SB-3**

Pent-4-yn-1-yl 7-hydroxyheptanoate (SB-3): Following the general procedure **(B)**, the reaction of **SA-3** (1.2126 g, 3.71 mmol, 1 equiv), TBAF (1.0 M in THF, 9.50 mL, 9.50 mmol, 2.5 equiv) afforded the product as a colorless oil (0.6971 g, 88% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 1:1 then 1:2). FTIR (KBr): 3409 (br.), 3296, 2935, 2861, 1734, 1257, 1178, 1080, 1057, 1032 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.17 (t, *J* = 6.3 Hz, 2H), 3.64 (t, *J* = 6.2 Hz, 2H), 2.33 – 2.26 (m, 4H), 1.97 (t, *J* = 2.7 Hz, 1H), 1.90 – 1.82 (m, 2H), 1.68 – 1.61 (m, 2H), 1.60 – 1.53 (m, 2H), 1.43 – 1.31 (m, 4H), 1.27 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.5, 82.6, 68.8, 62.4, 62.0, 33.8, 32.1, 28.5, 27.1, 25.1, 24.5, 14.8; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{12}H_{20}O_3{}^{23}Na_1$, 235.1305; found, 235.1307.



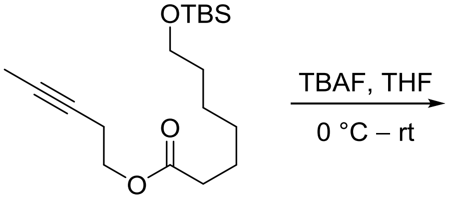
SA-4 **SB-4**

Hex-5-yn-1-yl 7-hydroxyheptanoate (SB-4): Following the general procedure **(B)**, the reaction of **SA-4** (1.2335 g, 3.62 mmol, 1 equiv), TBAF (1.0 M in THF, 9.50 mL, 9.50 mmol, 2.6 equiv) afforded the product as a colorless oil (0.6852 g, 84% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 1:1 then 1:2). FTIR (KBr): 3410, 3296, 2936, 2863, 1733, 1256, 1178, 1079, 1056 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.09 (t, *J* = 6.4 Hz, 2H), 3.64 (t, *J* = 6.6 Hz, 2H), 2.31 (t, *J* = 7.5 Hz, 2H), 2.23 (td, *J* = 7.0, 2.7 Hz, 2H), 1.96 (t, *J* = 2.7 Hz, 1H), 1.82 – 1.70 (m, 2H), 1.69 – 1.51 (m, 6H), 1.45 – 1.31 (m, 4H), 1.23 (s, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 173.7, 83.6, 68.5, 63.5, 62.2, 34.0, 32.2, 28.6, 27.4, 25.2, 24.7, 24.6, 17.8; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{13}H_{22}O_3{}^{23}Na_1$, 249.1461; found, 249.1464.



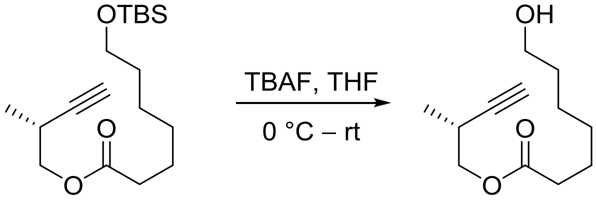
SA-5 **SB-5**

Undec-10-yn-1-yl 7-hydroxyheptanoate (SB-5): Following the general procedure **(B)**, the reaction of **SA-5** (0.7362 g, 1.79 mmol, 1 equiv), TBAF (1.0 M in THF, 4.0 mL, 4.0 mmol, 2.23 equiv) afforded the product as a colorless oil (0.525 g, 99% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 3:1). FTIR (KBr): 3400 (br.), 3310, 2932, 2857, 1734, 1257, 1179, 1057 cm^{-1}; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 4.05 (t, J = 6.7 Hz, 2H), 3.64 (t, J = 6.6 Hz, 2H), 2.30 (t, J = 7.5 Hz, 2H), 2.18 (td, J = 7.1, 2.7 Hz, 2H), 1.94 (t, J = 2.6 Hz, 1H), 1.68 – 1.48 (m, 8H), 1.44 – 1.22 (m, 15H); ^{13}C-NMR (100 MHz, CDCl$_3$) δ 173.9, 84.7, 68.1, 64.4, 62.7, 34.2, 32.5, 29.3, 29.1, 28.9, 28.8, 28.63, 28.55, 28.4, 25.8, 25.4, 24.9, 18.3; HRMS (ESI) *m/z*: [M+Na]$^+$ calcd. for $C_{18}H_{32}O_3{}^{23}Na_1$, 297.2424; found, 297.2426.



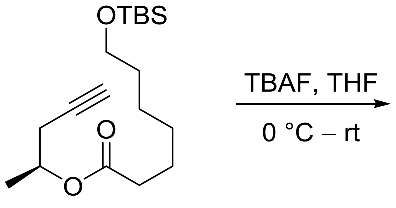
SA-6 **SB-6**

Pent-3-yn-1-yl 7-hydroxyheptanoate (SB-6): Following the general procedure **(B)**, the reaction of **SA-6** (0.8398 g, 2.57 mmol, 1 equiv), TBAF (1.0 M in THF, 5.8 mL, 5.8 mmol, 2.26 equiv) afforded the product as a colorless oil (0.3958 g, 73% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 1:1). FTIR (KBr): 3368 (br.), 2929, 2932, 2859, 1734, 1456, 1389, 1340, 1169, 1055 cm^{-1}; ^{1}H-NMR (500 MHz, CDCl$_3$) δ 4.12 (t, J = 6.9 Hz, 2H), 3.64 (t, J = 6.6 Hz, 2H), 2.49 – 2.42 (m, 2H), 2.32 (t, J = 7.5 Hz, 2H), 1.77 (t, J = 2.5 Hz, 3H), 1.68 – 1.61 (m, 2H), 1.61 – 1.53 (m, 2H), 1.42 – 1.32 (m, 4H), 1.29 (s, 1H); ^{13}C-NMR (100 MHz, CDCl$_3$) δ 173.5, 77.1, 74.6, 62.5 (2xC), 34.0, 32.4, 28.7, 25.3, 24.7, 19.1, 3.3; HRMS (ESI) *m/z*: [M+H]$^+$ calcd. for $C_{12}H_{21}O_3$, 213.1485; found, 213.1484.



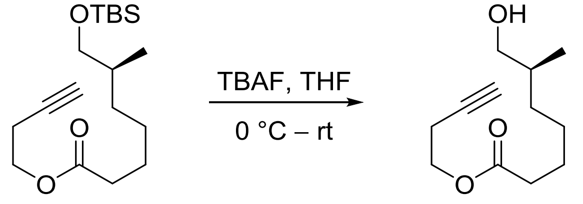
SA-7 **SB-7**

(*R*)-2-Methylbut-3-yn-1-yl 7-hydroxyheptanoate (SB-7): Following the general procedure **(B)**, the reaction of **SA-7** (0.2689 g, 0.823 mmol, 1 equiv), TBAF (1.0 M in THF, 1.90 mL, 1.90 mmol, 2.31 equiv) afforded the product as a colorless oil (0.1742 g, 99.7% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 2:1, then 1:1). FTIR (KBr): 3410 (br.), 2991, 2933, 2859, 1732, 1461, 1373, 1258, 1172 cm^{-1}; ^{1}H-NMR (500 MHz, CDCl$_3$) δ 4.09 (dd, J = 10.6, 6.8 Hz, 1H), 4.02 (dd, J = 10.6, 6.7 Hz, 1H), 3.64 (t, J = 6.6 Hz, 2H), 2.85 – 2.75 (m, 1H), 2.35 (t, J = 7.5 Hz, 2H), 2.08 (d, J = 2.4 Hz, 1H), 1.72 – 1.61 (m, 2H), 1.61 – 1.52 (m, 2H), 1.43 – 1.34 (m, 5H), 1.22 (d, J = 7.0 Hz, 3H); ^{13}C-NMR (125 MHz, CDCl$_3$) δ 173.4, 84.9, 69.5, 66.9, 62.3, 33.9, 32.3, 28.7, 25.5, 25.2, 24.7, 17.2; HRMS (ESI) *m/z*: [M+H]$^+$ calcd. for $C_{12}H_{21}O_3$, 213.1485; found, 213.1484.



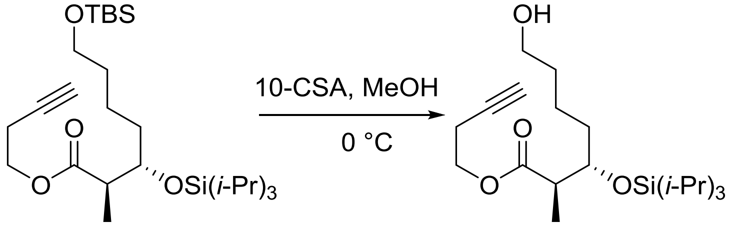
SA-8 **SB-8**

(*S*)-Pent-4-yn-2-yl 7-hydroxyheptanoate (SB-8): Following the general procedure **(B)**, the reaction of **SA-8** (1.1342 g, 3.473 mmol, 1 equiv), TBAF (1.0 M in THF, 7.80 mL, 7.80 mmol, 2.25 equiv) afforded the product as a colorless oil (0.580 g, 79% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 2:1). FTIR (neat): 3415 (br.), 3289, 2935, 2860, 1728, 1177, 1053 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.06 – 4.97 (m, 1H), 3.64 (t, J = 6.5 Hz, 2H), 2.49 – 2.42 (m, 2H), 2.31 (t, J = 7.5 Hz, 2H), 2.02 – 1.99 (m, 1H), 1.70 – 1.61 (m, 2H), 1.60 – 1.53 (m, 2H), 1.42 – 1.35 (m, 4H), 1.33 (d, J = 6.3 Hz, 3H), 1.24 (s, 1H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 172.9, 79.3, 70.3, 68.0, 62.0, 34.0, 32.1, 28.5, 25.13, 25.07, 24.5, 18.7; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{12}H_{20}O_3{}^{23}Na_1$, 235.1305; found, 235.1312.



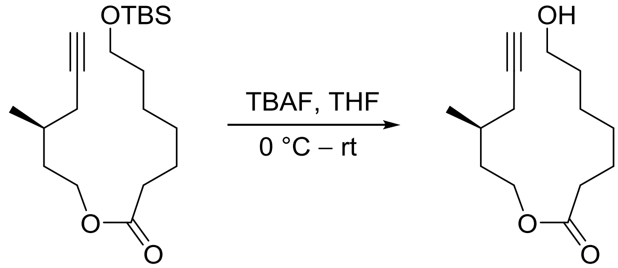
SA-9 **SB-9**

(*S*)-But-3-yn-1-yl 7-hydroxy-6-methylheptanoate (SB-9): Following the general procedure **(B)**, the reaction of **SA-9** (1.3566 g, 3.01 mmol, 1 equiv), TBAF (1.0 M in THF, 6.8 mL, 6.8 mmol, 2.26 equiv) afforded the product as a colorless oil (0.5599 g, 88% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 2:1). FTIR (neat): 3415 (br.), 3289, 2935, 2860, 1728, 1177, 1053 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.19 (t, J = 6.7 Hz, 2H), 3.50 (dd, J = 10.5, 5.9 Hz, 1H), 3.43 (dd, J = 10.5, 6.3 Hz, 1H), 2.53 (td, J = 6.8, 2.7 Hz, 2H), 2.34 (t, J = 7.5 Hz, 2H), 2.00 (t, J = 2.6 Hz, 1H), 1.69 – 1.56 (m, 3H), 1.50 – 1.22 (m, 4H), 1.21 – 1.08 (m, 1H), 0.91 (d, J = 6.7 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 173.3, 79.8, 69.7, 67.5, 61.7, 35.2, 33.8, 32.4, 26.1, 24.8, 18.6, 16.3; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{12}H_{21}O_3$, 213.1485; found, 213.1485.



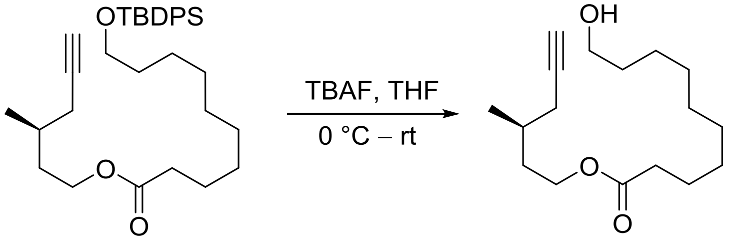
SA-10 **SB-10**

But-3-yn-1-yl (*2R,3S*)-7-hydroxy-2-methyl-3-((triisopropylsilyl)oxy)heptanoate (SB-10): To an ice cooled solution of **SA-10** (522 mg, 1.05 mmol, 1 equiv) in 20 mL of MeOH was added 10-camphorsulphonic acid (61.4 mg, 0.262 mmol, 0.25 equiv). The reaction mixture was allowed to stir at 0 ˚C for 1 h and then quenched by the addition of saturated aqueous $NaHCO_3$ solution. After transferring to a separatory funnel, the aqueous layer was extracted three times with EtOAc. The combined organic extracts were washed with brine, dried over sodium sulfate, filtered and concentrated. The crude residue was purified over silica gel (30% EtOAc in hexanes) to yield 347 mg (86%) of the desired compound as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.28 – 4.18 (m, 2H), 4.16 – 4.08 (m, 1H), 4.12 (dt, J = 10.4, 6.8 Hz, 1H), 3.69 – 3.61 (m, 2H), 2.59 (qd, J = 6.8, 4.0 Hz, 1H), 2.53 (td, J = 6.8, 2.4 Hz, 2H), 1.99 (t, J = 2.4 Hz, 1H), 1.67 – 1.51 (m, 4H), 1.43 – 1.31 (m, 2H), 1.28 – 1.19 (m, 3H), 1.16 (d, J = 7.0 Hz, 3H), 1.05 (s, 18H). ^{13}C NMR (175 MHz, $CDCl_3$) δ 174.8, 80.1, 73.3, 69.8, 62.7, 62.0, 43.8, 34.9, 32.8, 21.3, 18.9. 18.4, 18.1, 12.8, 10.2. IR (thin film, cm^{-1}) 3313, 2942, 2866, 1732, 1462. HRMS (ESI) *m/z* calculated for [M+H]$^+$ 385.2769, found 385.2769.



SA-11 **SB-11**

(*S*)-3-Methylhex-5-yn-1-yl 7-hydroxyheptanoate (SB-11): Following the general procedure **(B)**, the reaction of **SA-11** (0.512 g, 1.30 mmol, 1 equiv), TBAF (1.0 M in THF, 2.90 mL, 2.90 mmol, 2.23 equiv) afforded the product as a colorless oil (0.3296 g, 95% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 3:1 then 1:1). FTIR (neat): 3396 (br.), 3292, 2933, 2857, 1731, 1459, 1432, 1352, 1254, 1175, 1054 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.21 – 4.05 (m, 2H), 3.64 (t, J = 6.6 Hz, 2H), 2.30 (t, J = 7.5 Hz, 2H), 2.25 – 2.09 (m, 2H), 1.98 (t, J = 2.7 Hz, 1H), 1.88 – 1.74 (m, 2H), 1.69 – 1.48 (m, 5H), 1.43 – 1.30 (m, 4H), 1.25 (br.s, 1H), 1.03 (d, J = 6.7 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 173.7, 82.2, 69.5, 62.2, 62.1, 34.0, 33.9, 32.1, 29.0, 28.6, 25.3, 25.1, 24.6, 18.9; HRMS (ESI) *m/z*: [M+Na]$^+$ calcd. for $C_{14}H_{24}O_3{}^{23}Na_1$, 263.1618; found, 263.1622.

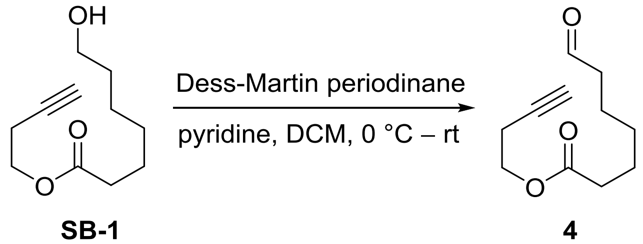


SA-12 **SB-12**

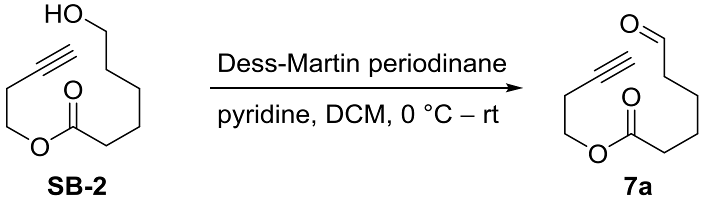
(*S*)-3-Methylhex-5-yn-1-yl 10-hydroxydecanoate (SB-12): Following the general procedure **(B)**, the reaction of **SA-12** (0.7077 g, 1.36 mmol, 1 equiv), TBAF (1.0 M in THF, 3.10 mL, 3.10 mmol, 2.28 equiv) afforded the product as a colorless oil (0.2847 g, 74% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate =

3:1). FTIR (neat): 3458 (br.), 3308, 2927, 2854, 1732, 1458, 1354, 1173, 1057 cm^{-1}; ^{1}H-NMR (500 MHz, CDCl$_3$) δ 4.18 – 4.07 (m, 2H), 3.66 – 3.61 (m, 2H), 2.30 (td, J = 7.5, 5.7 Hz, 2H), 2.24 – 2.10 (m, 2H), 2.01 – 1.95 (m, 1H), 1.87 – 1.74 (m, 2H), 1.66 – 1.49 (m, 5H), 1.38 – 1.27 (m, 10H), 1.20 (t, J = 5.6 Hz, 1H), 1.03 (d, J = 6.7 Hz, 3H); ^{13}C-NMR (100 MHz, CDCl$_3$) δ 173.6, 82.1, 69.5, 62.2, 62.1, 34.03, 33.98, 32.4, 29.09, 29.07, 29.01, 28.87, 28.78, 25.5, 25.3, 24.6, 18.9; HRMS (ESI) *m/z*: [M+H]$^+$ calcd. for $C_{17}H_{31}O_3$, 305.2087; found, 305.2093.

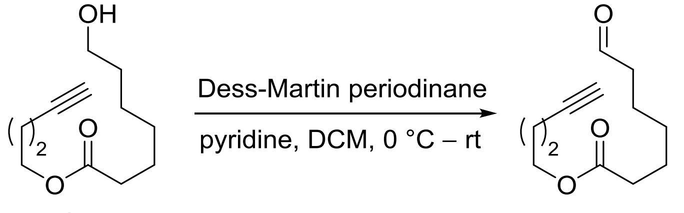
General procedure (C) for the Dess-Martin oxidation: To a solution of alcohol (1 mmol, 1 equiv) in dichloromethane (10 mL) at 0 ˚C was added pyridine (5 mmol, 5 equiv) and Dess–Martin periodinane (2.5 mmol, 2.5 equiv) subsequently. The reaction was then stirred at 0 ˚C for 10 min before adding wet dichloromethane (0.5 mL). The ice-water bath was then removed, and the resulting mixture was stirred at rt for 1 h. A mixture of saturated aqueous sodium thiosulfate and sodium bicarbonate solution (v/v=1:1) was added. After an additional 30 min stirring at rt, the mixture was transferred to separatory funnel and extracted with diethyl ether three times. The combined organic layers were dried over magnesium sulfate. After filtering the solution, the filtrate was concentrated in vacuo. The crude residue was purified by flash chromatography to give the ynal product.



But-3-yn-1-yl 7-oxoheptanoate (4): Following the general procedure **(C)**, the reaction of **SB-1** (0.2153 g, 1.09 mmol, 1 equiv), pyridine (0.44 mL, 5.44 mmol, 5 equiv) and Dess-Martin periodinane (1.1673 g, 2.75 mmol, 2.5 equiv) afforded the product as a colorless oil (0.1678 g, 79% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 4:1). FTIR (KBr): 3288, 2940, 2865, 2726, 1733, 1225, 1176, 1097 cm^{-1}; ^{1}H-NMR (500 MHz, CDCl$_3$) δ 9.76 (s, 1H), 4.18 (t, J = 6.8 Hz, 2H), 2.53 (td, J = 6.8, 2.7 Hz, 2H), 2.44 (td, J = 7.3, 1.7 Hz, 2H), 2.34 (t, J = 7.4 Hz, 2H), 2.00 (t, J = 2.7 Hz, 1H), 1.71 – 1.60 (m, 4H), 1.42 – 1.33 (m, 2H); ^{13}C-NMR (100 MHz, CDCl$_3$) δ 202.0, 172.8, 79.0, 69.7, 61.6, 43.3, 33.5, 28.2, 24.3, 21.3, 18.6; HRMS (EI) *m/z*: [M-H$_2$+H]$^+$ calcd. for $C_{11}H_{15}O_3$, 195.1021; found, 195.1030.

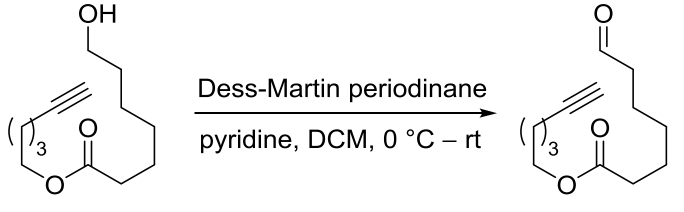


But-3-yn-1-yl 6-oxohexanoate (7a): Following the general procedure **(C)**, the reaction of **SB-2** (0.1054 g, 0.57 mmol, 1 equiv), pyridine (0.23 mL, 2.84 mmol, 5 equiv) and Dess-Martin periodinane (0.6141 g, 1.45 mmol, 2.5 equiv) afforded the product as a colorless oil (0.0844 g, 81% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 4:1). FTIR (KBr): 3284, 2929, 2727, 1721, 1457, 1390, 1231, 1152, 1091 cm^{-1}; ^{1}H-NMR (500 MHz, CDCl$_3$) δ 9.77 (t, *J* = 1.6 Hz, 1H), 4.18 (t, *J* = 6.7 Hz, 2H), 2.53 (td, *J* = 6.7, 2.7 Hz, 2H), 2.50 – 2.43 (m, 2H), 2.40 – 2.33 (m, 2H), 2.00 (t, *J* = 2.6 Hz, 1H), 1.74 – 1.62 (m, 4H); ^{13}C-NMR (125 MHz, CDCl$_3$) δ 201.8, 172.8, 79.9, 69.8, 61.9, 43.3, 33.7, 24.2, 21.1, 18.8; HRMS (ESI) *m/z*: [M+Na]$^+$ calcd. for $C_{10}H_{14}O_3{}^{23}Na_1$, 205.0835; found, 205.0837.



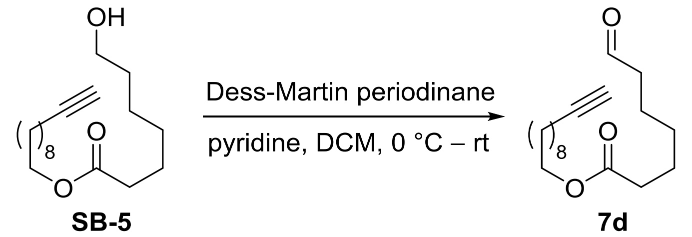
SB-3 **7b**

Pent-4-yn-1-yl 7-oxoheptanoate (7b): Following the general procedure (**C**), the reaction of **SB-3** (0.2163 g, 1.02 mmol, 1 equiv), Dess-Martin periodinane (1.0915 g, 2.58 mmol, 2.5 equiv) and pyridine (0.41 mL, 5.07 mmol, 5 equiv) afforded the product as a colorless oil (0.1513 g, 71% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 4:1). FTIR (KBr): 3282, 2938, 2862, 1722, 1462, 1391, 1363, 1249, 1171, 1151 cm^{-1}; ^{1}H-NMR (500 MHz, CDCl$_3$) δ 9.77 (t, *J* = 1.7 Hz, 1H), 4.17 (t, *J* = 6.3 Hz, 2H), 2.44 (td, *J* = 7.3, 1.7 Hz, 2H), 2.36 – 2.23 (m, 4H), 1.97 (t, *J* = 2.6 Hz, 1H), 1.92 – 1.81 (m, 2H), 1.70 – 1.59 (m, 4H), 1.43 – 1.29 (m, 2H); ^{13}C-NMR (125 MHz, CDCl$_3$) δ 202.2, 173.2, 82.8, 68.9, 62.6, 43.4, 33.8, 28.4, 27.3, 24.5, 21.5, 15.0; HRMS (ESI) *m/z*: [M+Na]$^+$ calcd. for $C_{12}H_{18}O_3{}^{23}Na_1$, 233.1148; found, 233.1145.

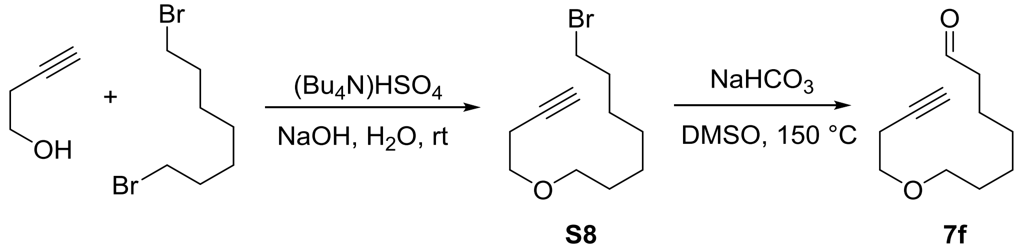


SB-4 **7c**

Hex-5-yn-1-yl 7-oxoheptanoate (7c): Following the general procedure (**C**), the reaction of **SB-4** (0.2353 g, 1.040 mmol, 1 equiv), Dess-Martin periodinane (1.1100 g, 2.50 mmol, 2.5 equiv) and pyridine (0.42 mL, 5.19 mmol, 5 equiv) afforded the product as a colorless oil (0.1516 g, 65% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 4:1). FTIR (KBr): 3288, 2943, 2866, 2724, 1730, 1249, 1178, 1096 cm^{-1}; ^{1}H-NMR (500 MHz, CDCl$_3$) δ 9.75 (t, *J* = 1.6 Hz, 1H), 4.08 (t, *J* = 6.5 Hz, 2H), 2.43 (t, *J* = 7.3 Hz, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 2.22 (td, *J* = 7.1, 2.7 Hz, 2H), 1.95 (t, *J* = 2.6 Hz, 1H), 1.79 – 1.69 (m, 2H), 1.69 – 1.53 (m, 6H), 1.41 – 1.29 (m, 2H); ^{13}C-NMR (125 MHz, CDCl$_3$) δ 202.3, 173.5, 83.8, 68.7, 63.7, 43.6, 34.0, 28.6, 27.6, 24.9, 24.6, 21.7, 18.0; HRMS (EI) *m/z*: [M+H]$^+$ calcd. for $C_{13}H_{21}O_3$, 225.1491; found, 225.1496.

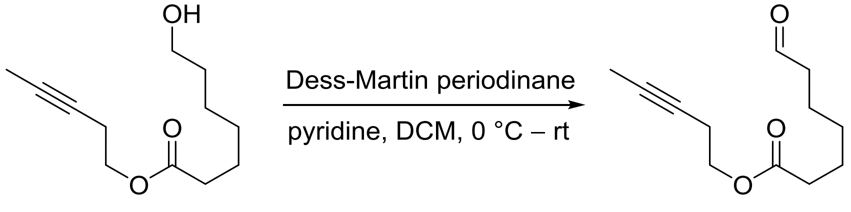


Undec-10-yn-1-yl 7-oxoheptanoate (7d): Following the general procedure **(C)**, the reaction of **SB-5** (0.1454 g, 0.49 mmol, 1 equiv), Dess-Martin periodinane (0.5058 g, 1.19 mmol, 2.4 equiv) and pyridine (0.10 mL, 2.47 mmol, 5 equiv) afforded the product as a colorless oil (100.9 mg, 70% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 5:1). FTIR (neat): 3288, 2927, 2855, 1725, 1462, 1389, 1356, 1173 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.77 (t, J = 1.7 Hz, 1H), 4.05 (t, J = 6.7 Hz, 2H), 2.44 (td, J = 7.3, 1.8 Hz, 2H), 2.31 (t, J = 7.5 Hz, 2H), 2.24 – 2.13 (m, 2H), 1.94 (t, J = 2.6 Hz, 1H), 1.70 – 1.58 (m, 6H), 1.55 – 1.46 (m, 2H), 1.44 – 1.25 (m, 12H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 202.2, 173.4, 84.5, 68.0, 64.3, 43.5, 33.9, 29.2, 29.0, 28.9, 28.54, 28.48, 28.46, 28.3, 25.8, 24.5, 21.6, 18.2; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{18}H_{31}O_3$, 317.2087; found, 317.2083.



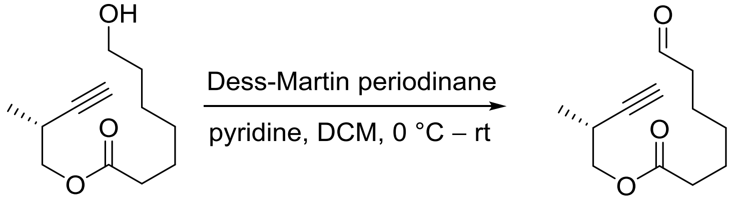
1-Bromo-7-(but-3-yn-1-yloxy)heptane (S8): Under nitrogen atmosphere, to a mixture of 1,7-dibromoheptane (9.6788 g, 0.038 mol, 3 equiv), 3-butyn-1-ol (0.8873 g, 0.0127 mol, 1 equiv) and tetrabutylammonium bisulfate (0.0867 g, 0.255 mmol, 0.02 equiv) at rt was added a solution of sodium hydroxide (5.0770 g, 0.127 mol, 10 equiv) in water (13 mL). The reaction was stirred at rt for 60 h and then diluted with water. The reaction mixture was extracted with diethyl ether three times. The combined organic layers were dried over magnesium sulfate. The solution was filtered, and the filtrate was concentrated in vacuo. The crude residue was purified by flash chromatograph (silica gel, hexanes:ethyl acetate = 20:1 then 10:1) to afford the product as a colorless oil (2.3157 g, 74% yield). FTIR (KBr): 3300, 2934, 2859, 1464, 1436, 1364, 1256, 1116 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.55 (t, J = 7.0 Hz, 2H), 3.45 (t, J = 6.6 Hz, 2H), 3.40 (t, J = 6.8 Hz, 2H), 2.46 (td, J = 7.0, 2.6 Hz, 2H), 1.98 (t, J = 2.7 Hz, 1H), 1.90 – 1.79 (m, 2H), 1.64 – 1.52 (m, 2H), 1.49 – 1.39 (m, 2H), 1.39 – 1.27 (m, 4H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 81.0, 70.5, 69.0, 68.4, 33.5, 32.4, 29.2, 28.1, 27.8, 25.6, 19.5; HRMS (EI) *m/z*: $[M-C_3H_3]^+$ calcd. for $C_8H_{16}O^{79}Br_1$, 207.0384; found, 207.0386.

7-(But-3-yn-1-yloxy)heptanal (7f): Under nitrogen atmosphere, to a mixture of sodium bicarbonate (1.0097 g, 12.02 mmol, 6 equiv) and dimethyl sulfoxide (8 mL) in a 150 ˚C oil bath was added a solution of **S8** (0.4981 g, 2.02 mmol, 1 equiv) in dimethyl sulfoxide (2 mL). The resulting mixture was stirred at 150 ˚C for 20 min before allowing to cool down to rt. It was diluted with water and extracted with diethyl ether three times. The combined organic layers were dried over magnesium sulfate. The solution was filtered, and the filtrate was concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, hexanes:ethyl acetate = 10:1) to afford the product as a colorless oil (0.1748 g, 48% yield). FTIR (KBr): 3291, 2937, 2862, 2724, 1724, 1636, 1464, 1365, 1116 cm^{-1}; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 9.76 (t, J = 1.9 Hz, 1H), 3.54 (t, J = 7.0 Hz, 2H), 3.45 (t, J = 6.5 Hz, 2H), 2.52 – 2.37 (m, 4H), 1.98 (t, J = 2.7 Hz, 1H), 1.70 – 1.50 (m, 4H), 1.43 – 1.28 (m, 4H); ^{13}C-NMR (125 MHz, CDCl$_3$) ^{13}C NMR (125 MHz, CDCl$_3$) δ 202.6, 81.3, 70.8, 69.1, 68.7, 43.7, 29.3, 28.8, 25.8, 21.9, 19.7; HRMS (ESI) *m/z*: [M+H]$^+$ calcd. for $C_{11}H_{19}O_2$, 183.1380; found, 183.1374.



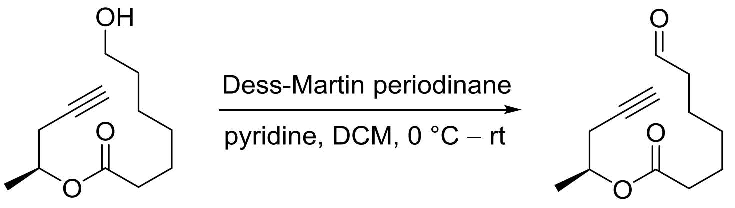
SB-6 **7g**

Pent-3-yn-1-yl 7-oxoheptanoate (7g): Following the general procedure (**C**), the reaction of **SB-6** (0.1649 g, 0.78 mmol, 1 equiv), Dess-Martin periodinane (0.8294 g, 1.96 mmol, 2.5 equiv) and pyridine (0.31 mL, 3.83 mmol, 5 equiv) afforded the product as a colorless oil (0.1108 g, 68% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 4:1). FTIR (neat): 3288, 2927, 2855, 1725, 1462, 1389, 1356, 1173 cm^{-1}; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 9.76 (t, J = 1.7 Hz, 1H), 4.12 (t, J = 6.9 Hz, 2H), 2.51 – 2.39 (m, 4H), 2.33 (t, J = 7.4 Hz, 2H), 1.77 (t, J = 2.5 Hz, 3H), 1.70 – 1.59 (m, 4H), 1.42 – 1.31 (m, 2H); ^{13}C-NMR (100 MHz, CDCl$_3$) δ 202.4, 173.3, 77.2, 74.7, 62.7, 43.6, 33.9, 28.5, 24.6, 21.7, 19.2, 3.5; HRMS (ESI) *m/z*: [M+Na]$^+$ calcd. for $C_{12}H_{18}O_3{}^{23}Na_1$, 233.1148; found, 233.1151.



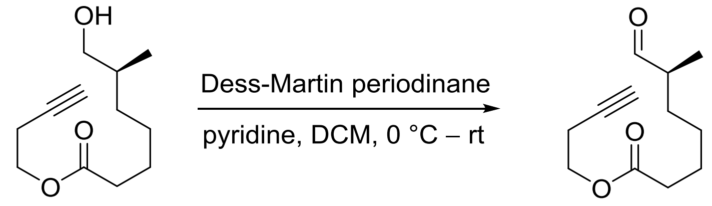
SB-7 **9a**

(*R*)-2-Methylbut-3-yn-1-yl 7-oxoheptanoate (9a): Following the general procedure (**A**), the reaction of **SB-7** (0.1111 g, 0.523 mmol, 1 equiv), Dess-Martin periodinane (0.5634 g, 1.328 mmol, 2.5 equiv) and pyridine (0.21 mL, 2.596 mmol, 5 equiv) afforded the product as a colorless oil (0.0837 g, 76% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 4:1). FTIR (neat): 3288, 2927, 2855, 1725, 1462, 1389, 1356, 1173 cm^{-1}; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 9.77 (t, J = 1.7 Hz, 1H), 4.09 (dd, J = 10.6, 6.8 Hz, 1H), 4.02 (dd, J = 10.6, 6.7 Hz, 1H), 2.86 – 2.72 (m, 1H), 2.45 (td, J = 7.3, 1.8 Hz, 2H), 2.36 (t, J = 7.4 Hz, 2H), 2.08 (d, J = 2.5 Hz, 1H), 1.74 – 1.60 (m, 4H), 1.46 – 1.31 (m, 2H), 1.22 (d, J = 7.0 Hz, 3H); ^{13}C-NMR (125 MHz, CDCl$_3$) δ 202.3, 173.1, 84.9, 69.5, 67.0, 43.5, 33.8, 28.4, 25.6, 24.5, 21.5, 17.2; HRMS (ESI) *m/z*: [M+H]$^+$ calcd. for $C_{12}H_{19}O_3$, 211.1329; found, 211.1326.



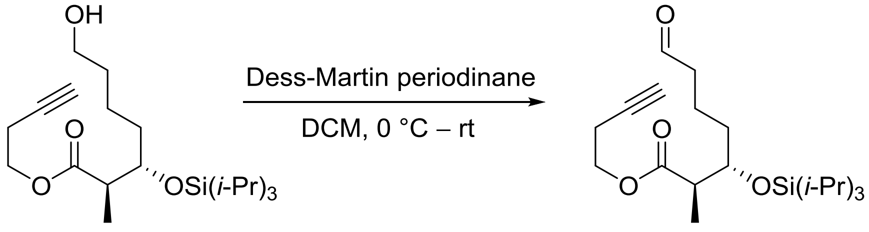
SB-8 **9b**

(*S*)-Pent-4-yn-2-yl 7-oxoheptanoate (9b): Following the general procedure **(A)**, the reaction of **SB-8** (0.2104 g, 0.991 mmol, 1 equiv), Dess-Martin periodinane (0.9486 g, 2.237 mmol, 2.26 equiv) and pyridine (0.40 mL, 4.946 mmol, 5 equiv) afforded the product as a colorless oil (0.1708 g, 82% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 4:1). FTIR (neat): 3288, 2936, 1724, 1457, 1380, 1175, 1133, 1054 $\mathrm{cm^{-1}}$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.74 (t, J = 1.7 Hz, 1H), 5.04 – 4.94 (m, 1H), 2.48 – 2.39 (m, 4H), 2.29 (t, J = 7.4 Hz, 2H), 1.99 (t, J = 2.7 Hz, 1H), 1.69 – 1.57 (m, 4H), 1.42 – 1.32 (m, 2H), 1.31 (d, J = 6.3 Hz, 3H); ^{13}C-NMR (175 MHz, $CDCl_3$) δ 202.2, 172.6, 79.6, 70.3, 68.2, 43.4, 34.0, 28.3, 25.3, 24.5, 21.5, 18.9; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{12}H_{18}O_3{}^{23}Na_1$, 233.1148; found, 233.1149.



SB-9 **9c**

(*S*)-But-3-yn-1-yl 6-methyl-7-oxoheptanoate (9c): Following the general procedure **(C)**, the reaction of **SB-9** (73.4 mg, 0.35 mmol, 1 equiv), Dess-Martin periodinane (0.3680 g, 0.87 mmol, 2.5 equiv) and pyridine (0.14 mL, 1.73 mmol, 5 equiv) afforded the product as a colorless oil (41.7 mg, 57% yield) after purification by flash chromatography (silica gel, hexanes:ethyl acetate = 4:1). FTIR (neat): 3288, 2935, 2855, 1730, 14659, 1234, 1166 $\mathrm{cm^{-1}}$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 9.61 (d, J = 1.9 Hz, 1H), 4.19 (t, J = 6.8 Hz, 2H), 2.53 (td, J = 6.8, 2.7 Hz, 2H), 2.39 – 2.28 (m, 3H), 2.00 (t, J = 2.7 Hz, 1H), 1.78 – 1.60 (m, 3H), 1.44 – 1.32 (m, 3H), 1.10 (d, J = 7.0 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 204.8, 173.1, 80.0, 69.8, 61.9, 46.0, 33.8, 30.0, 26.3, 24.7, 18.9, 13.2; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{12}H_{18}O_3{}^{23}Na_1$, 233.1148; found, 233.1149.

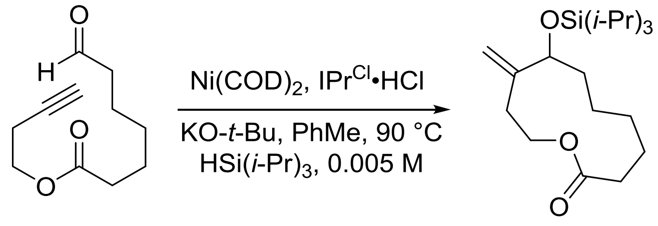


SB-10 **9d**

But-3-yn-1-yl (*2R,3S*)-2-methyl-7-oxo-3-((triisopropylsilyl)oxy)heptanoate (SC-11): Dess-Martin periodinane (46 mg, 0.11 mmol) was added to a solution of but-3-yn-1-ol **SB-10** (28 mg, 0.072 mmol) in 1 mL of CH_2Cl_2 at 0 ˚C. The mixture was allowed to stir for

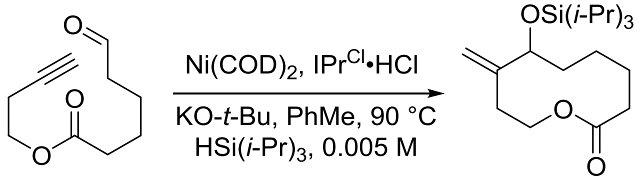
3.5 h as it warmed gradually to rt, then it was quenched with saturated sodium bicarbonate solution and stirred for an additional 10 min before it was transferred to a separatory funnel. The aqueous layer was washed three times with EtOAc, and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by column chromatography (SiO_2, 30% EtOAc in hexanes) to yield 26 mg (95%) of the aldehyde as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.77 (t, J = 1.6 Hz, 1H), 4.27 – 4.09 (m, 3H), 2.61 (qd, J = 7.0, 4.2 Hz, 1H), 2.53 (td, J = 7.0, 2.8 Hz, 2H), 2.46 (td, J = 7.0, 1.6 Hz, 2H), 1.99 (t, J = 2.8 Hz, 1H), 1.73 – 1.50 (m, 4H), 1.17 (d, J = 7.0 Hz, 3H), 1.10 – 0.98 (m, 21H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.8, 174.5, 80.0, 73.1, 69.8, 62.0, 43.9, 43.8, 34.5, 18.9, 18.12, 18.10, 17.6, 12.8, 10.7; IR (thin film, cm^{-1}) 3310, 2942, 2864, 2718, 1726, 1461, 1385. HRMS (ESI) m/z calculated for $[M+H]^+$ 385.2769, found 385.2769.

General procedure (D) for the macrocyclization: In a glovebox, an oven-dried round-bottom flask was charged with $Ni(COD)_2$ (0.033 mmol, 0.33 equiv), $IPr^{Cl}\cdot HCl$ (0.030 mmol, 0.3 equiv) and potassium *tert*-butoxide (0.40 mmol, 0.4 equiv). The round-bottom flask was capped with a septum and removed from the glovebox. After connecting to a nitrogen line, toluene (3 mL) was added, and the resulting mixture was stirred at rt for 20 min to form a red solution. The reaction was then diluted with toluene (15 mL) and placed into a 90 ˚C oil bath. Triisopropylsilane (0.5 mmol, 5 equiv) was added in one portion, followed by the slow addition of a solution of ynal (0.1 mmol, 1 equiv) in toluene (2 mL) over 1 h by syringe drive. The reaction mixture was stirred overnight at 90 ˚C (usually 12 h after the addition of ynal). After allowing to cool to rt, the volatiles were removed under vacuum. The reaction residue was passed through a plug of silica gel and washed with a 1:1 mixture of hexanes/ethyl acetate. A crude ^{1}H-NMR spectrum was taken to determine the regioselectivity, and the crude residue was purified by the flash chromatography to give the product.



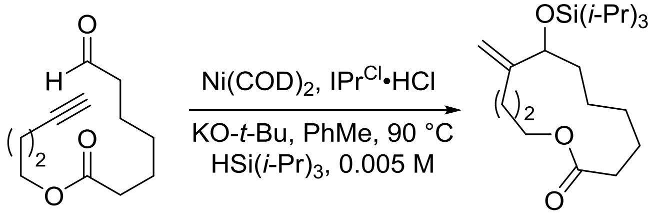
4 **5**

9-Methylene-8-((triisopropylsilyl)oxy)oxacycloundecan-2-one (5): Following the general procedure **(D)**, the reaction of **4** (152.5 mg, 0.777 mmol, 1 equiv), $Ni(COD)_2$ (68.1 mg, 0.248 mmol, 0.32 equiv), $IPr^{Cl}\cdot HCl$ (114.8 mg, 0.232 mmol, 0.30 equiv), potassium *tert*-butoxide (34.8 mg, 0.0310 mmol, 0.40 equiv) and triisopropylsilane (0.80 mL, 3.905 mmol, 5 equiv) afforded the product as a colorless oil (189.9 mg, 69% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether= 30:1 then 20:1). FTIR (KBr): 2944, 2867, 1734, 1465, 1382, 1272, 1233, 1088, 1058 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.09 (s, 1H), 5.04 (s, 1H), 4.66 (t, J = 11.2 Hz, 1H), 4.18 – 4.05 (m, 2H), 2.69 – 2.57 (m, 1H), 2.43 (dd, J = 16.1, 8.1 Hz, 1H), 2.25 – 2.06 (m, 2H), 2.01 – 1.86 (m, 1H), 1.81 – 1.69 (m, 1H), 1.69 – 1.58 (m, 1H), 1.52 – 1.39 (m, 3H), 1.38 – 1.27 (m, 1H), 1.23 – 1.15 (m, 1H), 1.11 – 0.88 (m, 21H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 173.9, 147.8, 113.9, 77.4, 64.3, 35.1, 31.8, 28.4, 27.7, 21.0, 20.3, 18.1, 18.0, 12.3; HRMS (EI) *m/z*: $[M]^+$ calcd. for $C_{20}H_{38}O_3{}^{28}Si_1$, 354.2590; found, 354.2595.



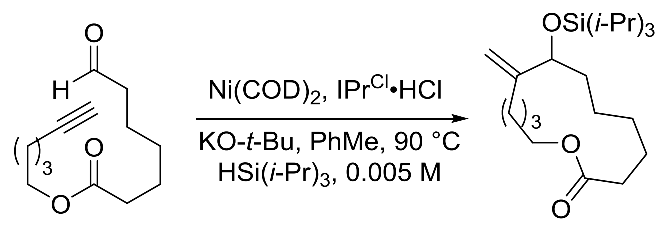
7a **8a**

8-Methylene-7-((triisopropylsilyl)oxy)oxecan-2-one (8a): Following the general procedure **(D)**, the reaction of **7a** (21.4 mg, 0.117 mmol, 1 equiv), $Ni(COD)_2$ (10.1 mg, 0.0367 mmol, 0.31 equiv), $IPr^{Cl}{\cdot}HCl$ (18.2 mg, 0.0368 mmol, 0.31 equiv), potassium *tert*-butoxide (5.4 mg, 0.0481 mmol, 0.41 equiv) and triisopropylsilane (0.12 mL, 0.586 mmol, 5 equiv) afforded the product as a colorless oil (18.1 mg, 45% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether= 30:1 then 20:1). FTIR (neat): 2942, 2865, 1737, 1462, 1369, 1347, 1326, 1256, 1207, 1134, 1066 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.13 (s, 1H), 5.08 (s, 1H), 4.44 – 4.35 (m, 1H), 4.28 (td, *J* = 10.2, 3.8 Hz, 1H), 4.13 (dd, *J* = 9.1, 4.1 Hz, 1H), 2.64 – 2.53 (m, 1H), 2.38 – 2.26 (m, 2H), 2.15 (dt, *J* = 15.0, 4.6 Hz, 1H), 1.85 – 1.71 (m, 1H), 1.69 – 1.39 (m, 4H), 1.32 – 1.26 (m, 1H), 1.03 (s-like, 21H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 173.6, 148.1, 114.7, 76.3, 64.8, 34.1, 33.5, 28.9, 22.9, 21.4, 18.1, 12.4; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{19}H_{37}O_3{}^{28}Si_1$, 341.2506; found, 341.2504.



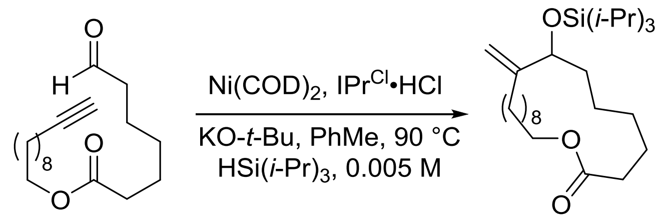
7b **8b**

9-Methylene-8-((triisopropylsilyl)oxy)oxacyclododecan-2-one (8b): Following the general procedure **(D)**, the reaction of **7b** (22.3 mg, 0.106 mmol, 1 equiv), $Ni(COD)_2$ (10.1 mg, 0.0367 mmol, 0.35 equiv), $IPr^{Cl}{\cdot}HCl$ (15.7 mg, 0.0318 mmol, 0.30 equiv), potassium *tert*-butoxide (4.4 mg, 0.0392 mmol, 0.37 equiv) and triisopropylsilane (0.11 mL, 0.537 mmol, 5 equiv) afforded the product as a colorless oil (21.0 mg, 54% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether= 30:1 then 20:1). FTIR (KBr): 2943, 2866, 1734, 1462, 1258, 1152, 1083 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.05 (s, 1H), 4.79 (d, *J* = 1.7 Hz, 1H), 4.33 (ddd, *J* = 11.2, 9.0, 3.7 Hz, 1H), 4.18 (dd, *J* = 9.0, 4.1 Hz, 1H), 3.98 (ddd, *J* = 10.9, 5.9, 4.1 Hz, 1H), 2.40 (ddd, *J* = 14.2, 7.5, 3.4 Hz, 1H), 2.35 – 2.26 (m, 1H), 2.26 – 2.19 (m, 1H), 2.19 – 2.11 (m, 1H), 2.08 – 1.90 (m, 2H), 1.89 – 1.79 (m, 1H), 1.80 – 1.70 (m, 1H), 1.70 – 1.51 (m, 2H), 1.49 – 1.35 (m, 2H), 1.31 – 1.11 (m, 2H), 1.09 – 0.97 (m, 21H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 174.6, 148.0, 110.8, 77.2, 61.9, 35.6, 33.9, 28.0, 23.7, 23.3, 22.0, 21.56, 18.08, 18.06, 12.3; HRMS (APCI) *m/z*: $[M+H]^+$ calcd. for $C_{21}H_{41}O_3{}^{28}Si_1$, 369.2819; found, 369.2822.



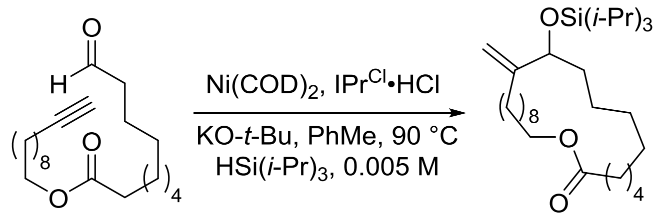
7c **8c**

9-Methylene-8-((triisopropylsilyl)oxy)oxacyclotridecan-2-one (8c): Following the general procedure **(D)**, the reaction of **7c** (49.6 mg, 0.22 mmol, 1 equiv), Ni(COD)$_2$ (20.4 mg, 0.074 mmol, 0.34 equiv), IPr^{Cl}·HCl (32.0 mg, 0.065 mmol, 0.29 equiv), potassium *tert*-butoxide (7.8 mg, 0.70 mmol, 0.31 equiv) and triisopropylsilane (0.23 mL, 1.10 mmol, 5 equiv) afforded the product as a colorless oil (56.1 mg, 66% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether= 30:1 then 20:1). FTIR (KBr): cm^{-1}; ^{1}H-NMR (500 MHz, CDCl$_3$) δ 5.02 (s, 1H), 4.78 (s, 1H), 4.30 (ddd, J = 10.4, 6.9, 3.1 Hz, 1H), 4.18 – 4.13 (m, 1H), 4.05 (ddd, J = 10.9, 8.4, 2.5 Hz, 1H), 2.38 – 2.23 (m, 3H), 1.97 – 1.88 (m, 1H), 1.87 – 1.72 (m, 2H), 1.70 – 1.59 (m, 4H), 1.48 – 1.26 (m, 4H), 1.21 – 1.14 (m, 2H), 1.07 – 0.98 (m, 21H); ^{13}C-NMR (125 MHz, CDCl$_3$) δ 174.3, 149.8, 112.6, 76.6, 64.2, 36.8, 35.0, 29.9, 28.7, 26.6, 24.2 (2xC), 23.6, 18.1, 12.4; HRMS (EI) *m/z*: [M-*i*-Pr]$^+$ calcd. for $C_{22}H_{43}O_3{}^{28}Si_1$, 339.2355; found, 339.2355.



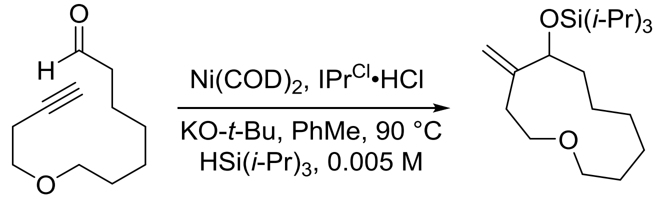
7d **8d**

9-Methylene-8-((triisopropylsilyl)oxy)oxacyclooctadecan-2-one (8d): Following the general procedure **(D)**, the reaction of **7d** (30.4 mg, 0.103 mmol, 1 equiv), Ni(COD)$_2$ (10.8 mg, 0.0393 mmol, 0.38 equiv), IPr^{Cl}·HCl (15.8 mg, 0.0320 mmol, 0.31 equiv), potassium *tert*-butoxide (4.1 mg, 0.537 mmol, 5 equiv) and triisopropylsilane (0.11 mL, 0.537 mmol, 5 equiv) afforded the product as a colorless oil (29.1 mg, 62% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether= 50:1 then 30:1). FTIR (KBr): 2932, 2865, 1737, 1463, 1384, 1258, 1143, 1088, 1063 cm^{-1}; ^{1}H-NMR (500 MHz, CDCl$_3$) δ 4.94 (s, 1H), 4.80 (d, J = 1.9 Hz, 1H), 4.20 – 4.15 (m, 1H), 4.15 – 4.05 (m, 2H), 2.36 – 2.22 (m, 2H), 2.07 – 1.86 (m, 2H), 1.68 – 1.45 (m, 7H), 1.42 – 1.16 (m, 15H), 1.07 – 0.99 (m, 21H); ^{13}C-NMR (100 MHz, CDCl$_3$) δ 173.8, 150.8, 109.8, 76.9, 63.9, 35.4, 35.1, 29.0, 28.8, 28.2, 28.1, 27.9, 27.8, 27.3, 26.5, 25.24, 25.22, 24.2, 18.11, 18.10, 12.4; HRMS (ESI) *m/z*: [M+Na]$^+$ calcd. for $C_{27}H_{52}O_3{}^{28}Si_1{}^{23}Na_1$, 475.3578; found, 475.3576.



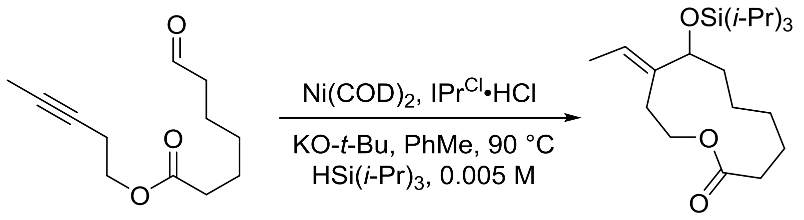
7e **8e**

12-Methylene-11-((triisopropylsilyl)oxy)oxacyclohenicosan-2-one (8e): Following the general procedure **(D)**, the reaction of **7e**[7] (84.5 mg, 0.25 mmol, 1 equiv), Ni(COD)$_2$ (19.1 mg, 0.069 mmol, 0.28 equiv), IPr^{Cl}·HCl (34.3 mg, 0.069 mmol, 0.28 equiv), potassium *tert*-butoxide (11.2 mg, 0.10 mmol, 0.40 equiv) and triisopropylsilane (0.24 mL, 1.17 mmol, 5 equiv) afforded the product as a colorless oil (86.3 mg, 69% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether= 50:1 then 30:1). FTIR (neat): 2926, 2856, 1736, 1463, 1384, 1238, 1153, 1088, 1063 cm^{-1}; ^{1}H-NMR (500 MHz, CDCl$_3$) δ 4.91 (s, 1H), 4.81 (d, J = 1.7 Hz, 1H), 4.17 – 4.07 (m, 3H), 2.30 (t, J = 7.0 Hz, 2H), 2.15 – 2.04 (m, 1H), 1.98 – 1.86 (m, 1H), 1.67 – 1.58 (m, 4H), 1.57 – 1.50 (m, 2H), 1.50 – 1.42 (m, 2H), 1.38 – 1.15 (m, 20H), 1.06 – 0.97 (m, 21H); ^{13}C-NMR (100 MHz, CDCl$_3$) δ 174.0, 150.9, 110.3, 77.3, 64.2, 36.0, 34.8, 29.7, 29.4, 29.3, 29.20 (2xC), 29.15, 29.03, 28.95, 28.8, 28.7, 27.8, 26.2, 25.3, 24.5, 18.1, 12.4; HRMS (ESI) *m/z*: [M+Na]$^+$ calcd. for $C_{30}H_{58}O_3{}^{28}Si_1{}^{23}Na_1$, 517.4047; found, 517.4043.



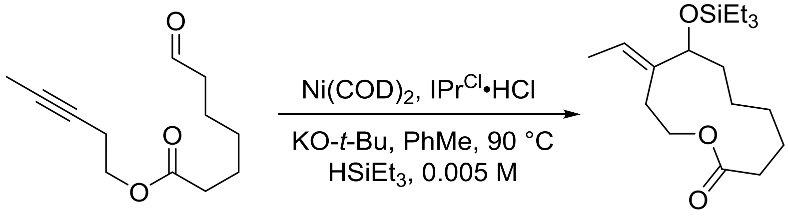
7f **8f**

Triisopropyl((4-methyleneoxacycloundecan-5-yl)oxy)silane (8f): Following the general procedure **(D)**, the reaction of **7f** (36.8 mg, 0.20 mmol, 1 equiv), Ni(COD)$_2$ (18.2 mg, 0.066 mmol, 0.33 equiv), IPr^{Cl}·HCl (28.8 mg, 0.058 mmol, 0.29 equiv), potassium *tert*-butoxide (7.7 mg, 0.69 mmol, 0.35 equiv) and triisopropylsilane (0.21 mL, 1.03 mmol, 5 equiv) afforded the product as a colorless oil (35.2 mg, 51% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether= 50:1 then 30:1). FTIR (KBr): 2942, 2866, 1645, 1464, 1360, 1260, 1111, 1091, 1063 cm^{-1}; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 5.02 (s, 1H), 4.96 (s, 1H), 4.20 (dd, J = 9.4, 4.1 Hz, 1H), 3.70 – 3.62 (m, 1H), 3.53 (ddd, J = 9.3, 9.0, 2.8 Hz, 1H), 3.47 (ddd, J = 10.3, 6.8, 3.4 Hz, 1H), 3.44 – 3.36 (m, 1H), 2.47 (ddd, J = 14.8, 8.5, 3.0 Hz, 1H), 2.08 (ddd, J = 14.6, 6.3, 2.3 Hz, 1H), 1.92 – 1.78 (m, 1H), 1.70 – 1.58 (m, 1H), 1.55 – 1.40 (m, 6H), 1.38 – 1.29 (m, 1H), 1.25 – 1.16 (m, 1H), 1.07 – 1.00 (m, 21H); ^{13}C-NMR (175 MHz, CDCl$_3$) δ 151.6, 112.9, 71.9, 71.5, 33.2, 31.8 (br., 2xC), 28.5, 27.5, 23.4, 22.5, 18.11, 18.09, 12.4; HRMS (EI) *m/z*: [M]$^+$ calcd. for $C_{20}H_{40}O_2{}^{28}Si_1$, 340.2798; found, 340.2796.



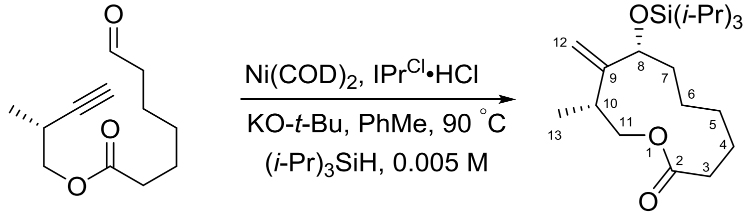
7g **8g**

(*E*)-9-Ethylidene-8-((triisopropylsilyl)oxy)oxacycloundecan-2-one 8g): Following the general procedure **(D)**, the reaction of **7g** (20.6 mg, 0.098 mmol, 1 equiv), $Ni(COD)_2$ (8.9 mg, 0.032 mmol, 0.33 equiv), $IPr^{Cl}\cdot HCl$ (14.9 mg, 0.030 mmol, 0.31 equiv), potassium *tert*-butoxide (4.7 mg, 0.042 mmol, 0.43 equiv) and triisopropylsilane (0.10 mL, 0.49 mmol, 5 equiv) afforded the product as a colorless oil (24.8 mg, 69% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 30:1). FTIR (neat): 2941, 2863, 1731, 1463, 1268, 1233, 1080, 1069, 1050 cm^{-1}; ^1H-NMR (500 MHz, $CDCl_3$) δ 5.40 (q, J = 6.8 Hz, 1H), 4.99 – 4.82 (m, 1H), 4.00 – 3.82 (m, 2H), 2.69 (ddd, J = 16.0, 12.2, 3.9 Hz, 1H), 2.48 (dd, J = 15.9, 6.9 Hz, 1H), 2.22 (d, J = 15.5 Hz, 1H), 2.14 (dd, J = 17.0, 12.8 Hz, 1H), 2.07 – 1.94 (m, 1H), 1.93 – 1.80 (m, 1H), 1.70 (d, J = 7.0 Hz, 3H), 1.63 – 1.54 (m, 1H), 1.53 – 1.42 (m, 2H), 1.42 – 1.28 (m, 1H), 1.23 – 1.11 (m, 1H), 1.08 – 0.92 (m, 22H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 174.0, 138.5, 125.2, 79.1, 61.9, 35.3, 32.9, 28.6, 24.9, 21.6, 20.0, 18.04, 17.97, 13.4, 12.3; HRMS (EI) *m/z*: $[M]^+$ calcd. for $C_{21}H_{40}O_3{}^{28}Si_1$, 368.2747; found, 368.2737.



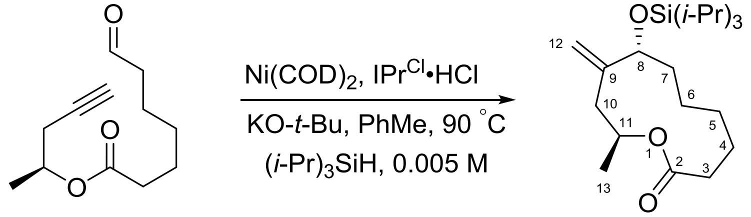
7g **8h**

(*E*)-9-Ethylidene-8-((triethylsilyl)oxy)oxacycloundecan-2-one (8h): Following the general procedure **(D)**, the reaction of **7g** (17.7 mg, 0.084 mmol, 1 equiv), $Ni(COD)_2$ (7.7 mg, 0.028 mmol, 0.33 equiv), $IPr^{Cl}\cdot HCl$ (12.7 mg, 0.026 mmol, 0.31 equiv), potassium *tert*-butoxide (3.8 mg, 0.034 mmol, 0.40 equiv) and triethylsilane (0.07 mL, 0.44 mmol, 5 equiv) afforded the product as a colorless oil (20.4 mg, 74% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 30:1). FTIR (neat): 2953, 2874, 1730, 1458, 1230, 1070, 1041, 1002 cm^{-1}; ^1H-NMR (400 MHz, $CDCl_3$) δ 5.41 (q, J = 6.9 Hz, 1H), 4.86 (t, J = 11.0 Hz, 1H), 3.96 – 3.80 (m, 2H), 2.65 (ddd, J = 16.1, 12.5, 4.0 Hz, 1H), 2.48 (dd, J = 15.7, 6.5 Hz, 1H), 2.22 (d, J = 16.3 Hz, 1H), 2.19 – 2.09 (m, 1H), 2.10 – 1.94 (m, 1H), 1.94 – 1.81 (m, 1H), 1.69 (d, J = 6.9 Hz, 3H), 1.62 – 1.40 (m, 3H), 1.39 – 1.27 (m, 1H), 1.23 – 1.10 (m, 1H), 1.03 – 0.86 (m, 10H), 0.54 (q, J = 7.6 Hz, 6H); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 174.0, 138.6, 125.3, 78.9, 62.0, 35.3, 32.9, 28.6, 24.9, 21.6, 20.0, 13.5, 6.8, 4.8; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{18}H_{34}O_3{}^{28}Si_1{}^{23}Na_1$, 349.2169; found, 349.2174.



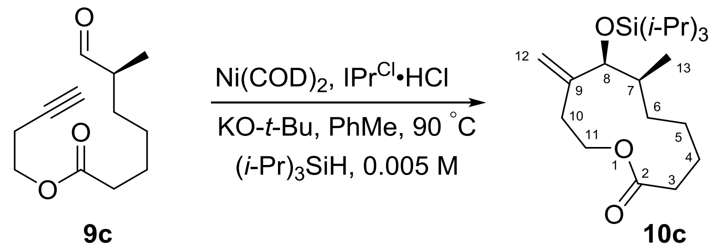
9a **10a**

(8*R*,10*R*)-10-Methyl-9-methylene-8-((triisopropylsilyl)oxy)oxacycloundecan-2-one (10a): Following the general procedure (**D**), the reaction of **9a** (20.7 mg, 0.0984 mmol, 1 equiv), Ni(COD)$_2$ (9.7 mg, 0.0353 mmol, 0.36 equiv), IPr^{Cl}·HCl (15.7 mg, 0.0318 mmol, 0.32 equiv), potassium *tert*-butoxide (4.9 mg, 0.0437 mmol, 0.44 equiv) and triisopropylsilane (0.10 mL, 0.488 mmol, 5 equiv) afforded the product as a colorless oil (21.0 mg, 58% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 20:1). FTIR (neat): 2941, 2865, 1733, 1462, 1258, 1102, 1061, 1061 cm^{-1}; ^{1}H-NMR (500 MHz, CDCl$_3$) δ 5.36 (d, J = 1.6 Hz, 1H), 5.13 (s, 1H), 4.63 (dd, J = 12.0, 10.5 Hz, 1H, H-11a), 4.33 (d, J = 3.2 Hz, 1H, H-8), 3.80 (dd, J = 10.5, 3.9 Hz, 1H, H-11b), 2.47 (ddd, J = 16.1, 7.9, 1.6 Hz, 1H), 2.40 – 2.27 (m, 1H, H-10), 2.12 – 2.04 (m, 1H), 1.99 – 1.87 (m, 1H), 1.86 – 1.75 (m, 1H), 1.62 – 1.37 (m, 4H), 1.35 – 1.14 (m, 2H), 1.09 – 1.03 (m, 21H), 1.02 (d, J = 7.1 Hz, 3H, Me-13); ^{13}C-NMR (125 MHz, CDCl$_3$) δ 173.7, 153.1, 109.4, 74.1, 69.0, 35.1, 34.9, 29.8, 28.2, 20.6, 19.0, 18.11, 18.08, 17.0, 12.3; HRMS (ESI) *m/z*: [M+H]$^+$ calcd. for $C_{21}H_{41}O_3{}^{28}Si_1$, 369.2819; found, 369.2819.



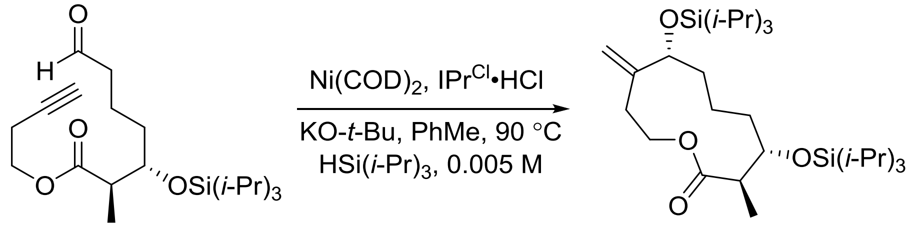
9b **10b**

(8*R*,11*S*)-11-methyl-9-methylene-8-((triisopropylsilyl)oxy)oxacycloundecan-2-one (10b): Following the general procedure (**D**), the reaction of **9b** (41.9 mg, 0.199 mmol, 1 equiv), Ni(COD)$_2$ (17.8 mg, 0.0647 mmol, 0.33 equiv), IPr^{Cl}·HCl (30.0 mg, 0.0607 mmol, 0.31 equiv), potassium *tert*-butoxide (8.8 mg, 0.0784 mmol, 0.39 equiv) and triisopropylsilane (0.20 mL, 0.976 mmol, 5 equiv) afforded the product as a colorless oil (45.2 mg, 62% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 20:1). FTIR (neat): 2938, 2866, 1728, 1462, 1359, 1250, 1107, 1069, 1038 cm^{-1}; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 5.45 – 5.37 (m, 1H, H-11), 5.35 (s, 1H, H-12a), 5.14 (s, 1H, H-12b), 4.30 (s, 1H, H-8), 2.50 (dd, J = 16.7, 6.8 Hz, 1H), 2.36 (d, J = 14.9 Hz, 1H, H-10a), 2.18 – 2.05 (m, 1H), 2.04 – 1.83 (m, 3H), 1.53 – 1.36 (m, 5H), 1.33 – 1.19 (m, 4H), 1.11 – 0.99 (m, 21H); ^{13}C-NMR (125 MHz, CDCl$_3$) δ 173.1, 146.7, 112.5, 74.9, 72.1, 38.4, 35.5, 29.5, 28.3, 21.2, 19.9, 18.10, 18.07, 17.6, 12.4; HRMS (ESI) *m/z*: [M+H]$^+$ calcd. for $C_{21}H_{41}O_3{}^{28}Si_1$, 369.2819; found, 369.2818.



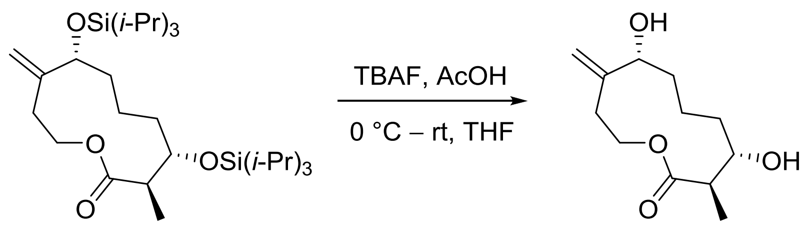
9c **10c**

(7*R*,8*R*)-7-methyl-9-methylene-8-((triisopropylsilyl)oxy)oxacycloundecan-2-one (10c): Following the general procedure (**D**), the reaction of **9c** (106.4 mg, 0.51 mmol, 1 equiv), Ni(COD)$_2$ (43.1 mg, 0.16 mmol, 0.31 equiv), IPr^{Cl}·HCl (73.6 mg, 0.15 mmol, 0.29 equiv), potassium *tert*-butoxide (22.9 mg, 0.204 mmol, 0.40 equiv) and triisopropylsilane (0.51 mL, 2.49 mmol, 5 equiv) afforded the product as a colorless oil (93.4 mg, 50% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 20:1). FTIR (neat): 2940, 2864, 1732, 1462, 1369, 1264, 1137, 1102, 1053 cm^{-1}; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 5.33 (s, 1H), 5.18 (s, 1H), 5.01 (ddd, *J* = 13.2, 10.9, 2.6 Hz, 1H, H-11a), 4.16 (s, 1H, H-8), 3.93 – 3.87 (m, 1H, H-11b), 2.48 (dd, *J* = 17.3, 7.5 Hz, 1H), 2.35 (d, *J* = 16.7 Hz, 1H, H-10b), 2.15 – 2.02 (m, 2H), 1.97 – 1.79 (m, 2H), 1.64 – 1.47 (m, 3H), 1.46 – 1.28 (m, 2H), 1.09 – 1.04 (m, 21H), 1.01 (d, *J* = 6.8 Hz, 3H, Me-13); ^{13}C-NMR (125 MHz, CDCl$_3$) δ 173.8, 147.2, 112.1, 81.2, 63.6, 35.4, 31.0, 30.5, 25.9, 23.8, 20.3, 18.3, 18.2, 17.4, 13.2; HRMS (ESI) *m/z*: [M+H]$^+$ calcd. for $C_{21}H_{41}O_3{}^{28}Si_1$, 369.2819; found, 369.2817.



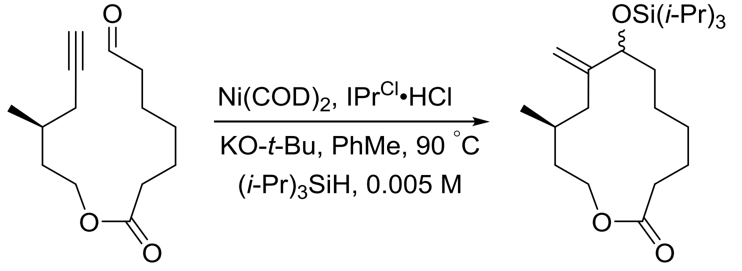
9d **10d**

(3*R*,4*S*,8*R*)-3-Methyl-9-methylene-4,8-bis((triisopropylsilyl)oxy)oxacycloundecan-2-one (10d): Following the general procedure (**D**), the reaction of **9d** (38.8 mg, 0.10 mmol, 1 equiv), Ni(COD)$_2$ (8.6 mg, 0.031 mmol, 0.31 equiv), IPr^{Cl}·HCl (15.4 mg, 0.031 mmol, 0.31 equiv), potassium *tert*-butoxide (4.3 mg, 0.038 mmol, 0.38 equiv) and triisopropylsilane (0.10 mL, 0.49 mmol, 5 equiv) afforded the product as a colorless oil (33.1 mg, 61% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether= 40:1 then 20:1). FTIR (neat): 2942, 2865, 1733, 1462, 1383, 1232, 1090, 1057 cm^{-1}; ^{1}H-NMR (500 MHz, CDCl$_3$) δ 5.23 (s, 1H), 5.15 (s, 1H), 4.57 (t, *J* = 10.0 Hz, 1H), 4.31 (s, 1H), 4.17 (d, *J* = 6.4 Hz, 1H), 4.00 (td, *J* = 9.0, 2.5 Hz, 1H), 2.54 – 2.37 (m, 2H), 2.19 – 2.06 (m, 1H), 1.89 – 1.69 (m, 2H), 1.68 – 1.55 (m, 2H), 1.31 – 1.17 (m, 5H), 1.10 – 1.07 (m, 21H), 1.06 – 1.00 (m, 21H); ^{13}C-NMR (125 MHz, CDCl$_3$) δ 175.5, 147.6, 113.4, 75.3, 72.8, 64.5, 48.3, 37.2, 32.9, 29.9, 18.3, 18.2, 18.1, 18.02, 17.99, 16.4, 12.9, 12.3; HRMS (EI) *m/z*: [M-C$_3$H$_7$]$^+$ calcd. for $C_{30}H_{60}O_4{}^{28}Si_2$, 497.3482; found, 497.3474.



10d **S9**

(3*R*,4*S*,8*R*)-4,8-dDihydroxy-3-methyl-9-methyleneoxacycloundecan-2-one (S9): To a solution of **10d** (26.7 mg, 0.049 mmol, 1 equiv) in tetrahydrofuran (4 mL) at 0 °C was added acetic acid (8 μL, 0.14 mmol, 2.9 equiv) and TBAF (1.0 M in THF, 0.62 mL, 0.62 mmol, 13 equiv) subsequently. The reaction was warmed up slowly to rt in the ice/water bath and stirred overnight. It was then diluted with water and extracted with ethyl acetate three times. The combined organic layers were dried over magnesium sulfate. The solution was filtered, and the filtrate was concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, ethyl acetate) to afford the product as a white solid (9.0 mg, 80% yield). FTIR (neat): 3280 (br.), 2921, 1724, 1458, 1262, 1232, 1074, 1018 cm^{-1}; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 5.25 (s, 1H), 5.19 (s, 1H), 4.69 – 4.58 (m, 1H), 4.29 – 4.20 (m, 1H), 4.16 (dd, *J* = 7.7, 2.2 Hz, 1H), 3.87 – 3.76 (m, 1H), 2.57 – 2.39 (m, 2H), 2.30 – 2.18 (m, 1H), 1.90 – 1.46 (m, 6H), 1.42 – 1.28 (m, 2H), 1.26 (d, *J* = 6.9 Hz, 3H); ^{13}C-NMR (125 MHz, CDCl$_3$) δ 174.8, 148.2, 113.0, 73.7, 71.8, 64.2, 46.9, 35.6, 31.3, 30.8, 17.6, 15.4; HRMS (ESI) *m/z*: [M+Na]$^+$ calcd. for $C_{12}H_{20}O_4{}^{23}Na_1$, 251.1254; found, 251.1256.



dr (**10ea**:**10eb**) = 69:31

9e **10e**

(11*S*)-11-methyl-9-methylene-8-((triisopropylsilyl)oxy)oxacyclotridecan-2-one (10e): Following the general procedure **(D)**, the reaction of **9e**[8] (49.4 mg, 0.207 mmol, 1 equiv), Ni(COD)$_2$ (20.7 mg, 0.0753 mmol, 0.36 equiv), IPr^{Cl}·HCl (30.1 mg, 0.0609 mmol, 0.29 equiv), potassium *tert*-butoxide (9.0 mg, 0.0802 mmol, 0.39 equiv) and triisopropylsilane (0.18 mL, 0.879 mmol, 4 equiv) afforded the product as a colorless oil (46.0 mg, 56% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 30:1). FTIR (neat): 2937, 2865, 1734, 1461, 1250, 1144, 1084, 1060 cm^{-1}; ^{1}H-NMR (500 MHz, CDCl$_3$) δ 5.20 (s, 1H$_{\mathbf{10ea}}$), 4.92 (d, *J* = 2.2 Hz, 1H$_{\mathbf{10eb}}$), 4.81 (s, 1H$_{\mathbf{10ea}}$), 4.76 (d, *J* = 2.3 Hz, 1H$_{\mathbf{10eb}}$), 4.40 (dt, *J* = 11.0, 3.4 Hz, 1H$_{\mathbf{10eb}}$), 4.27 – 4.15 (m, 3H$_{\mathbf{10ea}}$), 4.09 (dd, *J* = 9.8, 5.2 Hz, 1H$_{\mathbf{10eb}}$), 4.07 – 4.01 (m, 1H$_{\mathbf{10eb}}$), 2.47 (d, *J* = 9.9 Hz, 1H$_{\mathbf{10eb}}$), 2.43 – 2.34 (m, 1H$_{\mathbf{10ea}}$), 2.33 – 2.22 (m, 2H$_{\mathbf{10ea}}$), 2.21 – 2.11 (m, 1H$_{\mathbf{10eb}}$), 2.10 – 2.01 (m, 2H$_{\mathbf{10eb}}$), 2.01 – 1.85 (m, 2H$_{\mathbf{10ea}}$), 1.85 – 1.75 (m, 1H$_{\mathbf{10eb}}$), 1.73 – 1.11 (m, 10H$_{\mathbf{10ea}}$ +10H$_{\mathbf{10eb}}$), 1.08 – 1.01 (m, 21H$_{\mathbf{10ea}}$

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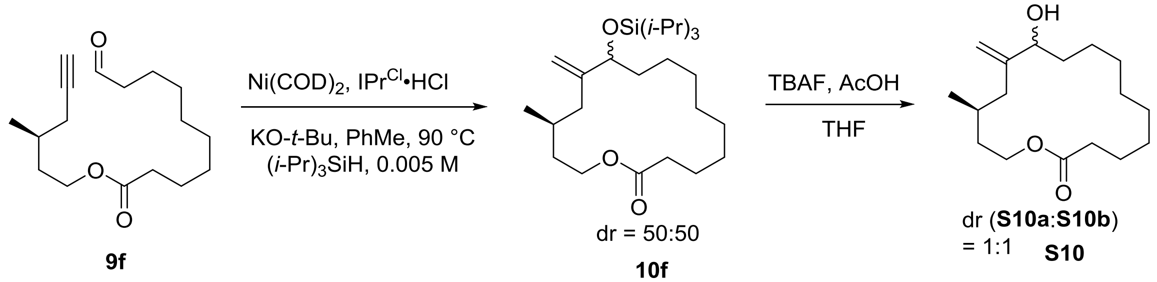
(8) Synthesized with general procedure (**C**) and used without characterization.

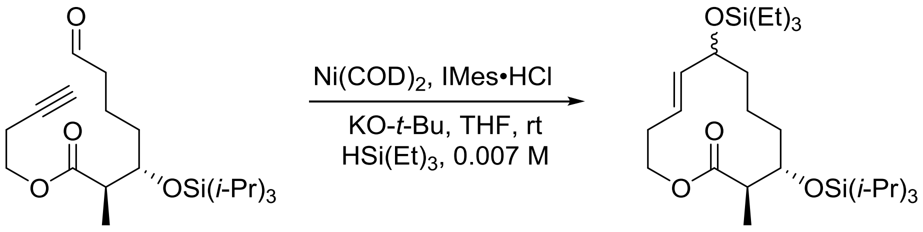
+21H_{10eb}), 0.99 (d, J = 6.0 Hz, 3H_{10eb}), 0.97 (d, J = 6.6 Hz, 3H_{10ea}); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 174.3 (C_{10eb}), 174.1 (C_{10ea}), 148.7 (C_{10ea}), 147.9 (C_{10eb}), 115.9 (C_{10eb}), 112.7 (C_{10ea}), 78.3 (C_{10eb}), 74.5 (C_{10ea}), 62.7 (C_{10ea}), 61.9 (C_{10eb}), 41.6 (C_{10ea}), 38.6 (C_{10eb}), 37.3 (C_{10eb}) , 35.9 (C_{10ea}), 35.4 (C_{10eb}), 34.8 (C_{10ea}), 34.6 (C_{10ea}), 33.8 (C_{10eb}), 29.2 (C_{10eb}), 28.2 (C_{10ea}), 28.1 (C_{10ea}), 27.9 (C_{10eb}), 24.2 (C_{10eb}), 24.0 (C_{10ea}), 23.9 (C_{10eb}), 22.7 (C_{10ea}), 21.1 (C_{10ea}), 20.9 (C_{10eb}), 18.15 (C_{10ea}), 18.14 (C_{10ea}), 18.10 (C_{10eb}), 18.06 (C_{10eb}), 12.5 (C_{10ea}), 12.3 (C_{10eb}); HRMS (ESI) m/z: $[M+Na]^+$ calcd. for $C_{23}H_{44}O_3{}^{28}Si_1{}^{23}Na_1$, 419.2952; found, 3419.2944.



(14S)-14-methyl-12-methylene-11-((triisopropylsilyl)oxy)oxacyclohexadecan-2-one (10f): Following the general procedure **(D)**, the reaction of **9f**^{8} (56.0 mg, 0.200 mmol, 1 equiv), $Ni(COD)_2$ (18.2 mg, 0.0662 mmol, 0.33 equiv), $IPr^{Cl}\cdot HCl$ (30.4 mg, 0.0615 mmol, 0.31 equiv), potassium *tert*-butoxide (9.2 mg, 0.0820 mmol, 0.41 equiv) and triisopropylsilane (0.18 mL, 0.879 mmol, 4 equiv) afforded the product as a colorless oil (66.0 mg, 75% yield) after purification by flash chromatography (silica gel, hexanes:diethyl ether = 30:1). The products were characterized as the corresponding alcohols as shown below.

(14S)-11-hydroxy-14-methyl-12-methyleneoxacyclohexadecan-2-one (S10): To a solution of **10f** (104.5 mg, 0.238 mmol, 1 equiv) in tetrahydrofuran (25 mL) at 0 °C was added acetic acid (28 μL, 0.490 mmol, 2 equiv) and TBAF (1.0 M solution in THF, 2.9 mL, 2.9 mmol, 12 equiv). The reaction was slowly warmed up to rt and stirred overnight. It was then diluted with water and extracted with diethyl ether three times. The combine organic layers were washed with brine and dried over magnesium sulfate. The solution was filtered, and the filtrate was concentrated in vacuo. The crude residue was purified by flash chromatography (silica gel, hexanes:diethyl ether = 3:1) to afford four fractions: fr.1 (4.4 mg, **S10a**: **S10b** = 10:1), fr.2 (12.3 mg, **S10a**: **S10b** = 3:1), fr.3 (9.9 mg, **S10a**: **S10b** = 1:1.3) and fr.4 (12.1 mg, **S10a**: **S10b** =1:3). Combine yield (38.7 mg, 58% yield). **S10a** was characterized with fr.1 and **S10b** was characterized with fr.4. FTIR (neat): 3424 (br.), 2927, 2858, 1732, 1458, 1348, 1235, 1170, 1069, 1098 cm^{-1}; **S10a** (characterized with fr.1): ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.11 (d, J = 1.5 Hz, 1H), 4.86 (s, 1H), 4.27 (ddd, J = 11.0, 6.2, 4.7 Hz, 1H), 4.12 – 4.01 (m, 2H), 2.43 – 2.24 (m, 2H), 2.26 – 2.13 (m, 1H), 1.94 – 1.81 (m, 2H), 1.71 – 1.27 (m, 17H), 0.91 (d, J = 6.2 Hz, 3H); ^{13}C-NMR (175 MHz, $CDCl_3$) δ 173.9, 150.3, 111.2, 73.0, 61.9, 40.7, 36.2, 34.3, 33.8, 27.4, 27.1, 26.8, 26.7, 26.6, 24.5, 23.9, 18.8; **S10b** (characterized with fr.4): ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.14 (s, 1H_{S10b}), 5.10 (d, J = 1.6 Hz, 1H_{S10a}), 4.88 (d, J = 1.4 Hz, 1H_{S10b}), 4.86 (s, 1H_{S10a}), 4.27 (ddd, J = 11.0, 6.2, 4.7 Hz, 1H_{S10a}), 4.25 – 4.09 (m, 2H_{S10b}), 4.10 – 4.01 (m, 1H_{S10b}+2H_{S10a}), 2.37 – 2.27 (m, 1H_{S10b}+2H_{S10a}), 2.22 – 2.14 (m, 1H_{S10a}), 2.12 – 2.04 (m, 1H_{S10b}), 1.99 (dd, J = 14.0, 8.0 Hz, 1H_{S10b}), 1.92 – 1.27 (m, 19H_{S10b}+19H_{S10a}), 0.93 – 0.88 (m, 3H_{S10b}+3H_{S10a});

^{13}C-NMR (175 MHz, $CDCl_3$) δ 174.04 (C_{S10b}), 173.92 (C_{S10a}), 150.32 (C_{S10b}), 150.25 (C_{S10a}), 111.6 (C_{S10b}), 111.2 (C_{S10a}), 73.4 (C_{S10b}), 73.0 (C_{S10a}), 62.0 (C_{S10b}), 61.9 (C_{S10a}), 42.2 (C_{S10b}), 40.7 (C_{S10a}), 36.2 (C_{S10a}), 35.5 (C_{S10b}), 34.2 (C_{S10a}), 34.08 (C_{S10b}), 34.05 (C_{S10b}), 33.8 (C_{S10a}), 27.7 (C_{S10b}), 27.41 (C_{S10b}), 27.37 (C_{S10a}), 27.1 (C_{S10a}), 26.8 (C_{S10a}), 26.70 (C_{S10b}), 26.67 (C_{S10a}), 26.60 (C_{S10b}), 26.59 (C_{S10b}), 26.56 (C_{S10a}), 24.60 (C_{S10b}), 24.5 (C_{S10a}), 23.9 (C_{S10a}), 23.3 (C_{S10b}), 18.9 (C_{S10b}), 18.8 (C_{S10a}). HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{17}H_{30}O_3{}^{23}Na_1$, 305.2087; found, 305.2084.

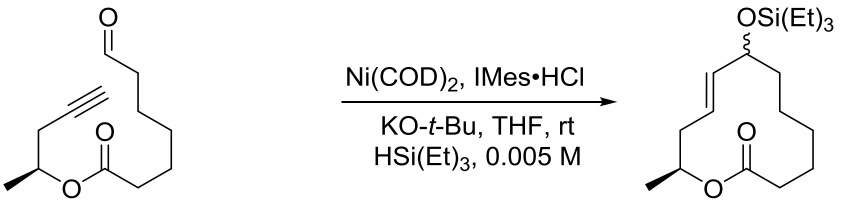


9d

11

endo:exo = <5:95
dr of endo (**11a**:**11b**) = 80:20

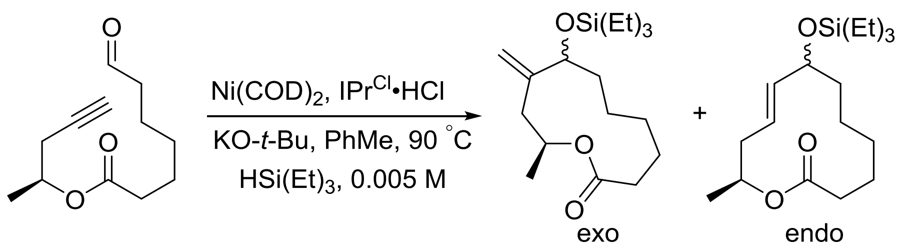
(3*R*,4*S*,*E*)-3-methyl-8-((triethylsilyl)oxy)-4-((triisopropylsilyl)oxy)oxacyclododec-9-en-2-one (11): In a glovebox, an oven-dried round-bottom flask was charged with $Ni(COD)_2$ (57.9 mg, 0.206 mmol, 0.30 equiv), IMes·HCl (72.5 mg, 0.206 mmol, 0.30 equiv) and potassium *tert*-butoxide ((23.6 mg, 0.206 mmol, 0.30 equiv). The round-bottom flask was capped with a septum and removed from the glovebox. After connecting to a nitrogen line, tetrahydrofuran (50 mL) was added. The resulting mixture was stirred at rt for 15 min to give a dark blue solution. Triethylsilane (220 μL, 1.38 mmol, 2 equiv) was added in one portion. A solution of **9d** (263 mg, 0.688 mmol, 1 equiv) in tetrahydrofuran (50 mL) was added over 3 h by syringe drive. The resulting mixture was stirred overnight at rt. The volatiles were removed under vacuum. The reaction residue was passed through a plug of silica gel and washed with a 1:1 mixture of hexanes/ethyl acetate. The filtrate was concentrated in vacuo to give the crude product. A crude ^{1}H-NMR spectrum was taken to determine the diastereoselectivity, and the crude mixture was purified by flash chromatography (silica gel, hexanes:diethyl ether = 30:1) to give a mixture of diastereomers of endo-selective macrocycles as a colorless oil (151 mg, 44% yield). FTIR (thin film): 2944, 2867, 1730, 1456, 1380 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 5.53 – 5.24 (m, $2H_{11a}$+$2H_{11b}$), 4.93 (td, J = 11.4, 4.1 Hz, $1H_{11a}$), 4.68 (ddd, J = 11.0, 8.1, 4.8 Hz, $1H_{11b}$), 4.29 – 4.19 (m, $1H_{11b}$), 4.10 – 3.95 (m, $2H_{11a}$), 3.94 – 3.88 (m, $1H_{11b}$), 3.88 – 3.81 (m, $1H_{11b}$), 3.68 (ddd, J = 11.0, 4.7, 2.0 Hz, $1H_{11a}$), 2.61 – 2.48 (m, $1H_{11a}$ +$1H_{11b}$), 2.48 – 2.33 (m, $2H_{11a}$ +$2H_{11b}$), 1.80 – 1.18 (m, $9H_{11a}$ +$9H_{11b}$), 1.17 – 1.01 (m, $21H_{11a}$ +$21H_{11b}$), 0.99 – 0.82 (m, $9H_{11a}$ +$9H_{11b}$), 0.67 – 0.47 (m, $6H_{11a}$ +$6H_{11b}$); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 175.9 (C_{11a}), 175.5 (C_{11b}), 136.1 (C_{11a}), 135.5 (C_{11b}), 127.8 (C_{11a}), 125.1 (C_{11b}), 74.3 (C_{11b}), 74.0 (C_{11a}), 72.9 (C_{11a}), 72.3 (C_{11b}), 61.6 (C_{11b}), 60.4 (C_{11a}), 45.3 (C_{11b}), 44.8 (C_{11a}), 35.4 (C_{11a}), 35.2 (C_{11b}), 34.9 (C_{11b}), 33.4 (C_{11a}), 32.7 (C_{11b}), 32.1 (C_{11a}), 18.2 ($1xC_{11a}$, $1xC_{11b}$), 18.2 (C_{11b}), 18.2 (C_{11a}), 17.3 (C_{11a}), 17.2 (C_{11b}), 16.3 (C_{11a}), 16.2 (C_{11b}), 12.9 (C_{11b}), 12.8 (C_{11a}), 6.84 (C_{11b}), 6.77 (C_{11a}), 4.9 (C_{11a}), 4.8 (C_{11b}); HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{27}H_{55}O_4{}^{28}Si_2$, 499.3639; found, 499.3633.



9b

17
endo:exo = >95:5
dr of endo (**17a**:**17b**) = 74:26

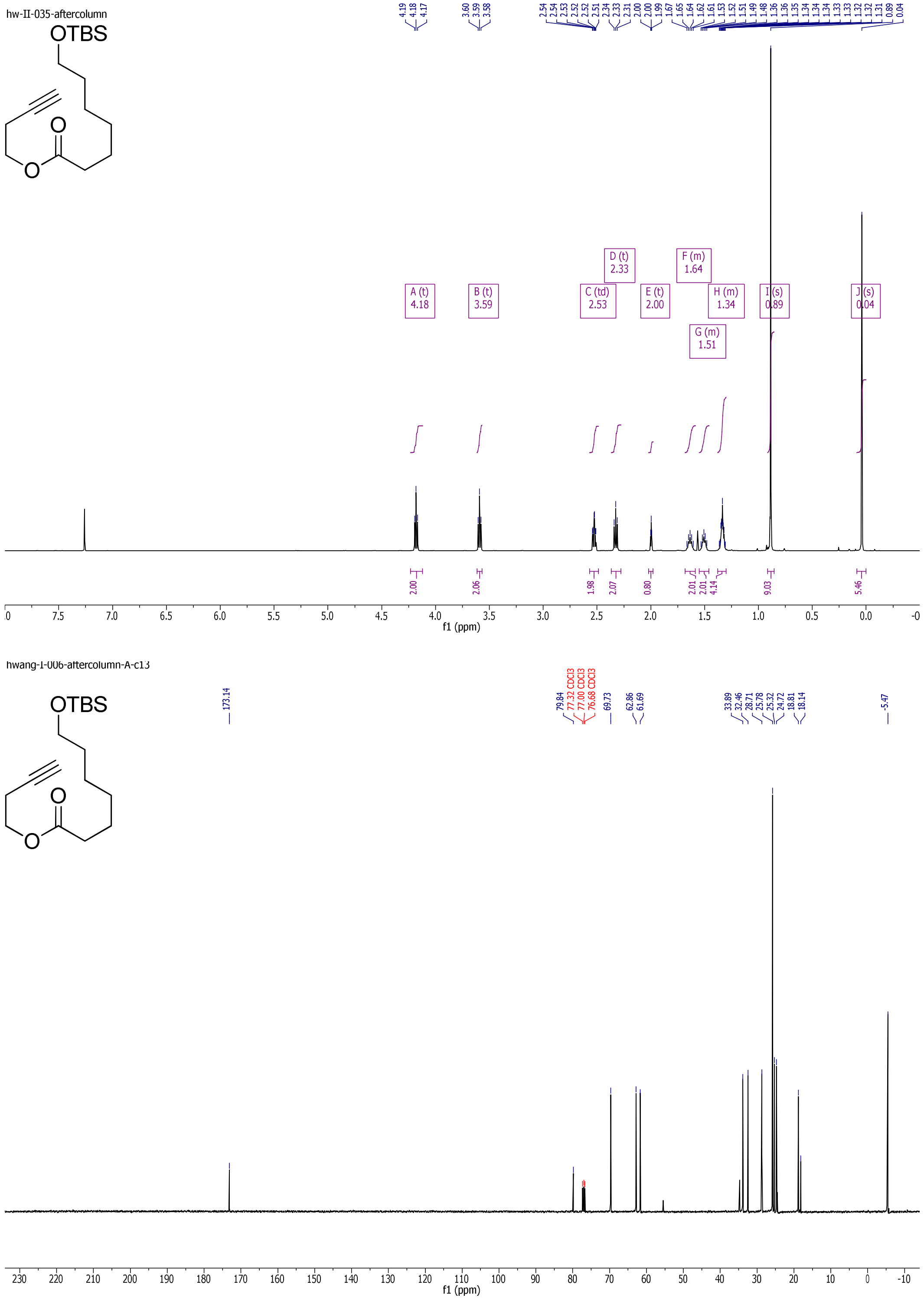
(12*S*,*E*)-12-methyl-8-((triethylsilyl)oxy)oxacyclododec-9-en-2-one (17): In a glovebox, an oven-dried round-bottom flask was charged with $Ni(COD)_2$ (18.7 mg, 0.0680 mmol, 0.34 equiv), IMes·HCl (20.4 mg, 0.0598 mmol, 0.30 equiv) and potassium *tert*-butoxide (10.8 mg, 0.0962 mmol, 0.48 equiv). The round-bottom flask was capped with a septum and removed from the glovebox. After connecting to a nitrogen line, tetrahydrofuran (5 mL) was added, and the resulting mixture was stirred at rt for 15 min to give a dark blue solution. The reaction was then diluted with tetrahydrofuran (33 mL) before adding triethylsilane (0.16 mL, 1.00 mmol, 5 equiv) in one portion. A solution of **9b** (42.2 mg, 0.20 mmol, 1 equiv) in tetrahydrofuran (2 mL) was added over 1 h by syringe drive. The resulting mixture was stirred overnight at rt. The volatiles were then removed under vacuum. The reaction residue was passed through a plug of silica gel and washed with a 1:1 mixture of hexanes/ethyl acetate. The filtrate was concentrated in vacuo to give the crude product. GC-MS and ^{1}H-NMR analysis of the crude showed that the product is mainly a mixture of diastereomers of endocyclization products (endo:exo = 99:1, dr of endo-products = 2.8:1). The crude mixture was purified by flash chromatography (silica gel, hexanes:diethyl ether = 30:1) to give a mixture of diastereomers of endocyclization products as a colorless oil (14.3 mg, 22% yield). FTIR (neat): 2936, 1730, 1457, 1364, 1259, 1156, 1058 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.61 – 5.51 (m, $1H_{\mathbf{17a}}$), 5.46 (dd, *J* = 15.2, 4.3 Hz, $1H_{\mathbf{17a}}$), 5.41 – 5.33 (m, $2H_{\mathbf{17b}}$), 5.24 – 5.14 (m, $1H_{\mathbf{17b}}$), 5.10 – 5.00 (m, $1H_{\mathbf{17a}}$), 4.27 (br.s, $1H_{\mathbf{17a}}$), 4.08 – 3.99 (m, $1H_{\mathbf{17b}}$), 2.49 – 2.12 (m, $4H_{\mathbf{17a}}$ +$4H_{\mathbf{17b}}$), 1.88 – 1.76 (m, $1H_{\mathbf{17b}}$), 1.73 – 1.60 (m, $2H_{\mathbf{17a}}$ +$1H_{\mathbf{17b}}$), 1.55 – 1.21 (m, $9H_{\mathbf{17a}}$+$9H_{\mathbf{17b}}$), 1.01 – 0.80 (m, $9H_{\mathbf{17a}}$ +$9H_{\mathbf{17b}}$), 0.61 – 0.49 (m, $6H_{\mathbf{17a}}$ +$6H_{\mathbf{17b}}$). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 173.44 ($C_{\mathbf{17a}}$), 173.39 ($C_{\mathbf{17b}}$), 136.6 ($C_{\mathbf{17a}}$), 135.9 ($C_{\mathbf{17b}}$), 128.3 ($C_{\mathbf{17b}}$), 123.9 ($C_{\mathbf{17a}}$), 73.4 ($C_{\mathbf{17b}}$), 71.6 ($C_{\mathbf{17a}}$), 69.1 ($C_{\mathbf{17a}}$), 68.4 ($C_{\mathbf{17b}}$), 40.6 ($C_{\mathbf{17b}}$), 39.2 ($C_{\mathbf{17a}}$), 35.6 ($C_{\mathbf{17b}}$), 34.3 ($C_{\mathbf{17a}}$), 34.0 ($C_{\mathbf{17a}}$), 32.6 ($C_{\mathbf{17b}}$), 26.4 ($C_{\mathbf{17a}}$), 24.5 ($C_{\mathbf{17a}}$), 24.3 ($C_{\mathbf{17b}}$), 23.9 ($C_{\mathbf{17b}}$), 23.1 ($C_{\mathbf{17a}}$), 23.0 ($C_{\mathbf{17b}}$), 20.6 ($C_{\mathbf{17b}}$), 20.5 ($C_{\mathbf{17a}}$), 6.9 ($C_{\mathbf{17a}}$), 6.8 ($C_{\mathbf{17b}}$), 4.93 ($C_{\mathbf{17b}}$), 4.86 ($C_{\mathbf{17a}}$); HRMS (ESI) *m*/*z*: $[M+Na]^+$ calcd. for $C_{18}H_{34}O_3{}^{28}Si_1{}^{23}Na_1$, 349.2169; found, 349.2166.



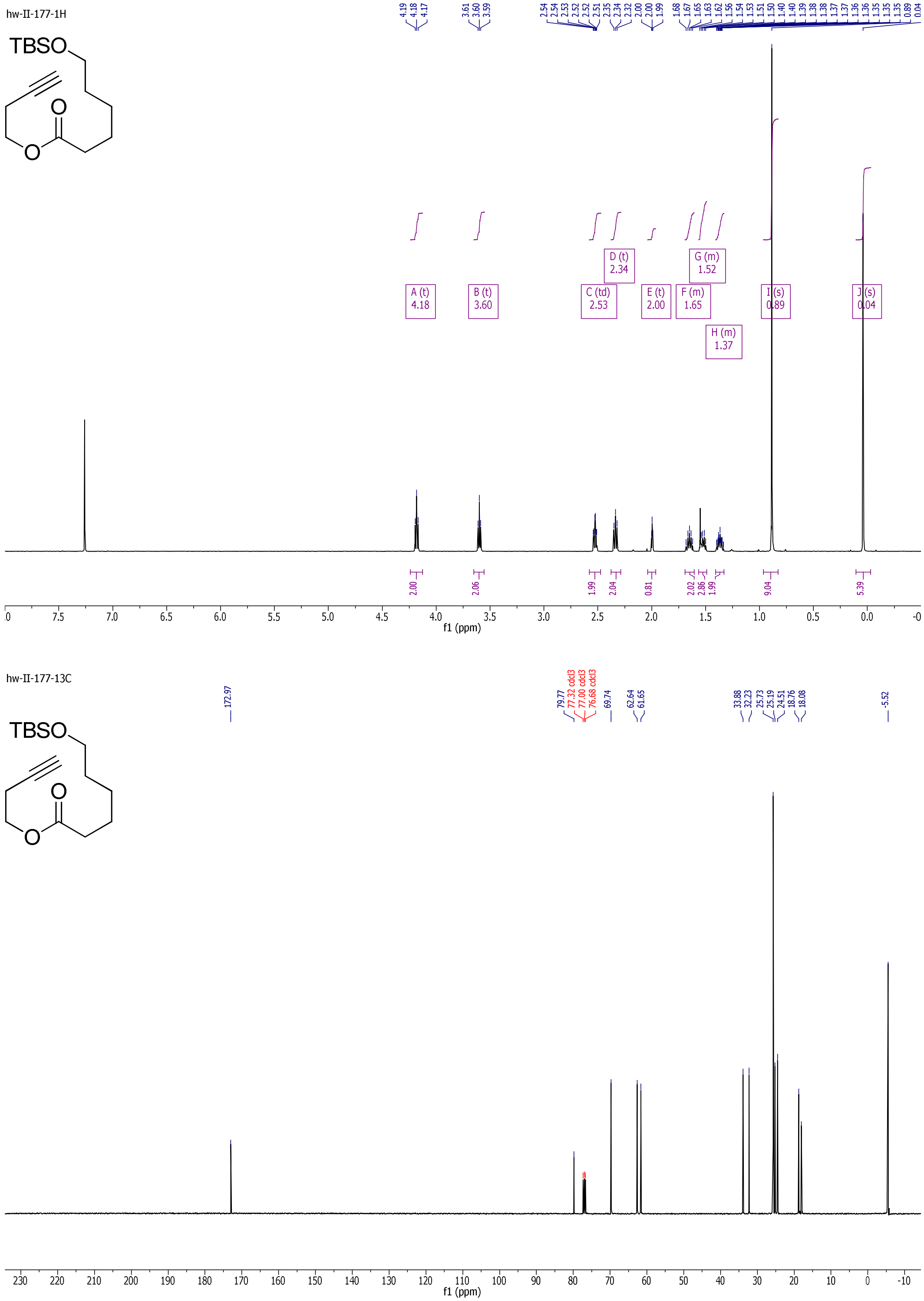
9b **16** **17**

exo:endo **16**:(**17a**+**17b**) = 33:66
dr of endo (**17a**:**17b**) = 1:2.4
dr of exo = >95:5

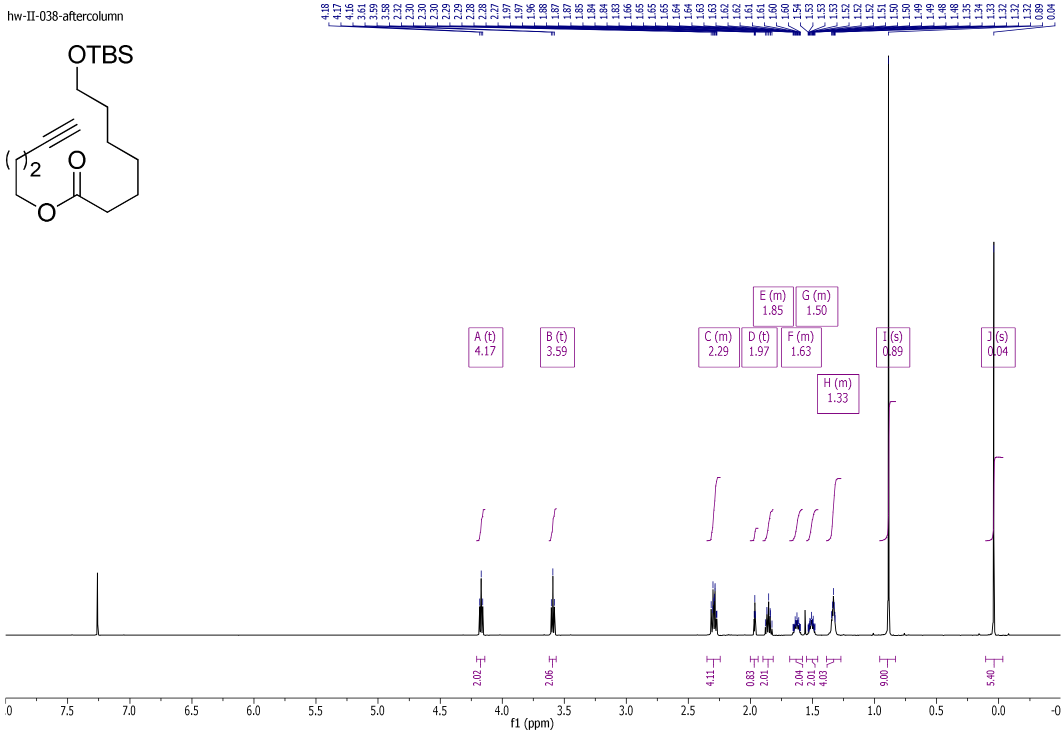
((11*S*)-11-methyl-9-methylene-8-((triethylsilyl)oxy)oxacycloundecan-2-one (16): Following the general procedure **(D)**, the reaction of **9b** (44.1 mg, 0.210 mmol, 1 equiv), Ni(COD)$_2$ (20.0 mg, 0.0727 mmol, 0.35 equiv), IPr^{Cl}·HCl (32.4 mg, 0.0656 mmol, 0.31 equiv), potassium *tert*-butoxide (9.4 mg, 0.0838 mmol, 0.40 equiv) and triethylsilane (0.16 mL, 1.002 mmol, 5 equiv) afforded the crude product. GC-MS and ^{1}H-NMR analysis of the crude showed the product was a mixture of diastereomers of endo- and exocyclization products (endo:exo = 67:33, dr of endo-products: 1:2.4, dr of exo-products: >95:5). The crude mixture was purified by flash chromatography (silica gel, hexanes:diethyl ether = 30:1) to give a mixture exo- and endo-cyclization products (**16** and **17**) as a colorless oil (20.2 mg, 29% yield). FTIR (neat): 2952, 2876, 1730, 1457, 1363, 1250, 1155, 1080, 1014 cm^{-1}; ^{1}H-NMR (500 MHz, CDCl$_3$) δ 5.60 – 5.51 (m, 1H$_{\mathbf{17a}}$), 5.49 – 5.43 (m, 1H$_{\mathbf{17a}}$ 5.41 – 5.37 (m, 2H$_{\mathbf{17b}}$), 5.36 – 5.32 (m, 1H$_{\mathbf{16}}$), 5.31 – 5.27 (m, 1H$_{\mathbf{16}}$), 5.23 – 5.15 (m, 1H$_{\mathbf{17b}}$), 5.09 (d, *J* = 1.7 Hz, 1H$_{\mathbf{16}}$), 5.08 – 5.01 (m, 1H$_{\mathbf{17a}}$), 4.29 – 4.24 (m, 1H$_{\mathbf{17a}}$), 4.20 (br.d, *J* = 5.0 Hz, 1H$_{\mathbf{17b}}$), 4.07 – 4.00 (m, 1H$_{\mathbf{16}}$), 2.53 – 2.45 (m, 1H$_{\mathbf{16}}$), 2.45 – 2.13 (m, 4H$_{\mathbf{17b}}$+4H$_{\mathbf{17a}}$+1H$_{\mathbf{16}}$), 2.12 – 2.06 (m, 2H$_{\mathbf{16}}$), 2.03 – 1.88 (m, 2H$_{\mathbf{16}}$), 1.88 – 1.77 (m, 1H$_{\mathbf{17b}}$), 1.71 – 1.62 (m, 1H$_{\mathbf{17b}}$+2H$_{\mathbf{17a}}$), 1.58 – 1.18 (m, 9H$_{\mathbf{17b}}$+9H$_{\mathbf{17a}}$+9H$_{\mathbf{16}}$), 0.98 – 0.87 (m, 9H$_{\mathbf{17b}}$+9H$_{\mathbf{17a}}$+9H$_{\mathbf{16}}$), 0.62 – 0.50 (m, 6H$_{\mathbf{17b}}$+6H$_{\mathbf{17a}}$+6H$_{\mathbf{16}}$); ^{13}C-NMR (125 MHz, CDCl$_3$) δ 173.45 (C$_{\mathbf{17a}}$), 173.39 (C$_{\mathbf{17b}}$), 173.19 (C$_{\mathbf{16}}$), 147.0 (C$_{\mathbf{16}}$), 136.57 (C$_{\mathbf{17a}}$), 135.90 (C$_{\mathbf{17b}}$), 128.30 (C$_{\mathbf{17b}}$), 123.87 (C$_{\mathbf{17a}}$), 112.33 (C$_{\mathbf{16}}$), 74.29 (C$_{\mathbf{16}}$), 73.36 (C$_{\mathbf{17b}}$), 72.36 (C$_{\mathbf{16}}$), 71.60 (C$_{\mathbf{17a}}$), 69.12 (C$_{\mathbf{17a}}$), 68.39 (C$_{\mathbf{17b}}$), 40.57 (C$_{\mathbf{17b}}$), 39.19 (C$_{\mathbf{17a}}$), 38.42 (C$_{\mathbf{16}}$), 35.58 (C$_{\mathbf{17b}}$), 35.53 (C$_{\mathbf{16}}$), 34.33 (C$_{\mathbf{17a}}$), 33.97 (C$_{\mathbf{17a}}$), 32.64 (C$_{\mathbf{17b}}$), 29.84 (C$_{\mathbf{16}}$), 28.26 (C$_{\mathbf{16}}$), 26.35 (C$_{\mathbf{17a}}$), 24.50 (C$_{\mathbf{17a}}$), 24.27 (C$_{\mathbf{17b}}$), 23.90 (C$_{\mathbf{17b}}$), 23.07 (C$_{\mathbf{17a}}$), 23.00 (C$_{\mathbf{17b}}$), 21.13 (C$_{\mathbf{16}}$), 20.56 (C$_{\mathbf{17b}}$), 20.46 (C$_{\mathbf{17a}}$), 19.98 (C$_{\mathbf{16}}$), 17.93 (C$_{\mathbf{16}}$), 6.89 (C$_{\mathbf{16}}$), 6.88 (C$_{\mathbf{17a}}$), 6.78 (C$_{\mathbf{17b}}$), 4.92 (C$_{\mathbf{17b}}$), 4.86 (C$_{\mathbf{17a}}$), 4.81 (C$_{\mathbf{16}}$). HRMS (ESI) *m*/*z*: [M+Na]$^+$ calcd. for $C_{18}H_{34}O_3{}^{28}Si_1{}^{23}Na_1$, 349.2169; found, 349.2167.

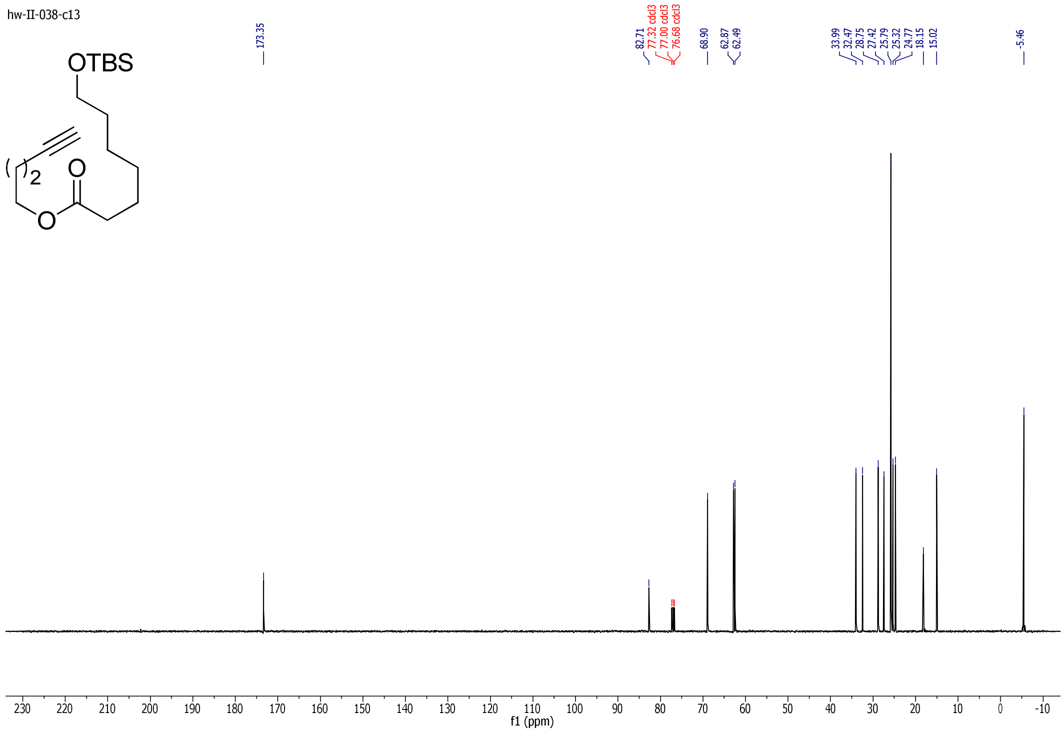


^{1}H- and ^{13}C-NMR spectra of compound **SA-1**

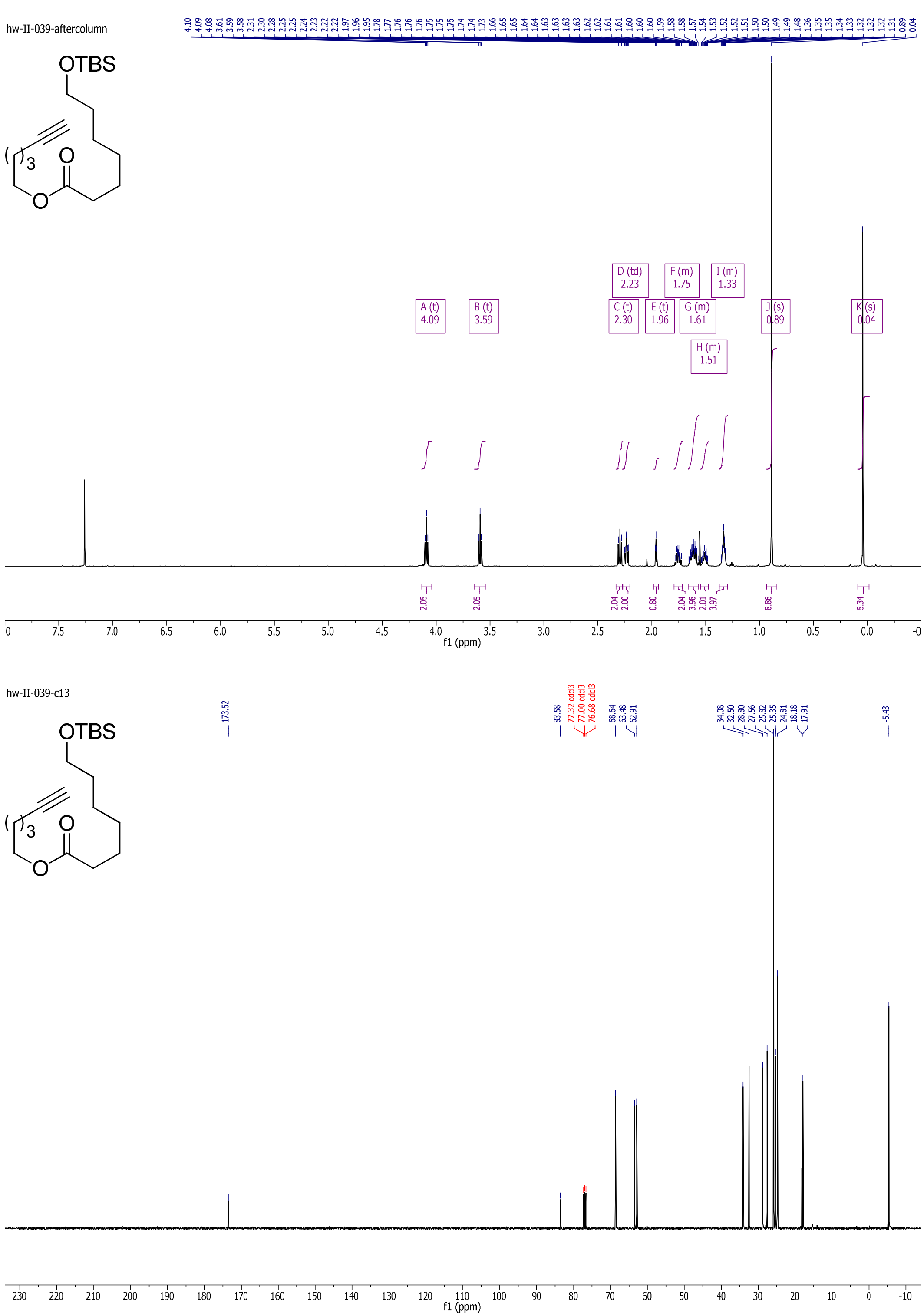


^{1}H- and ^{13}C-NMR spectra of compound **SA-2**



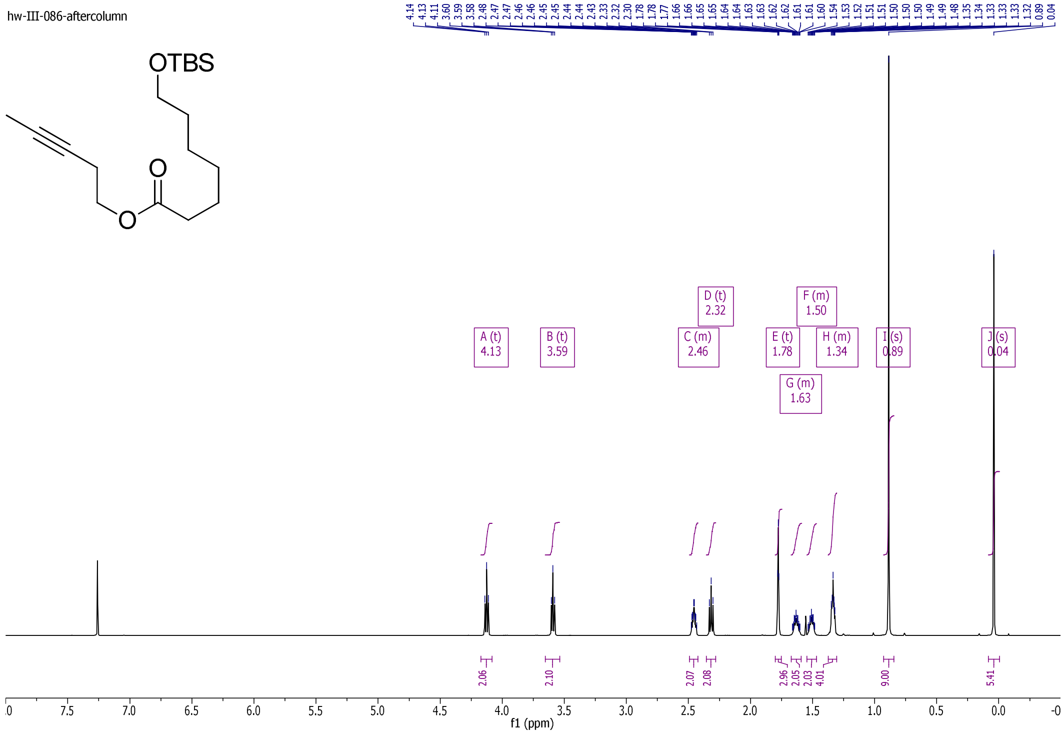


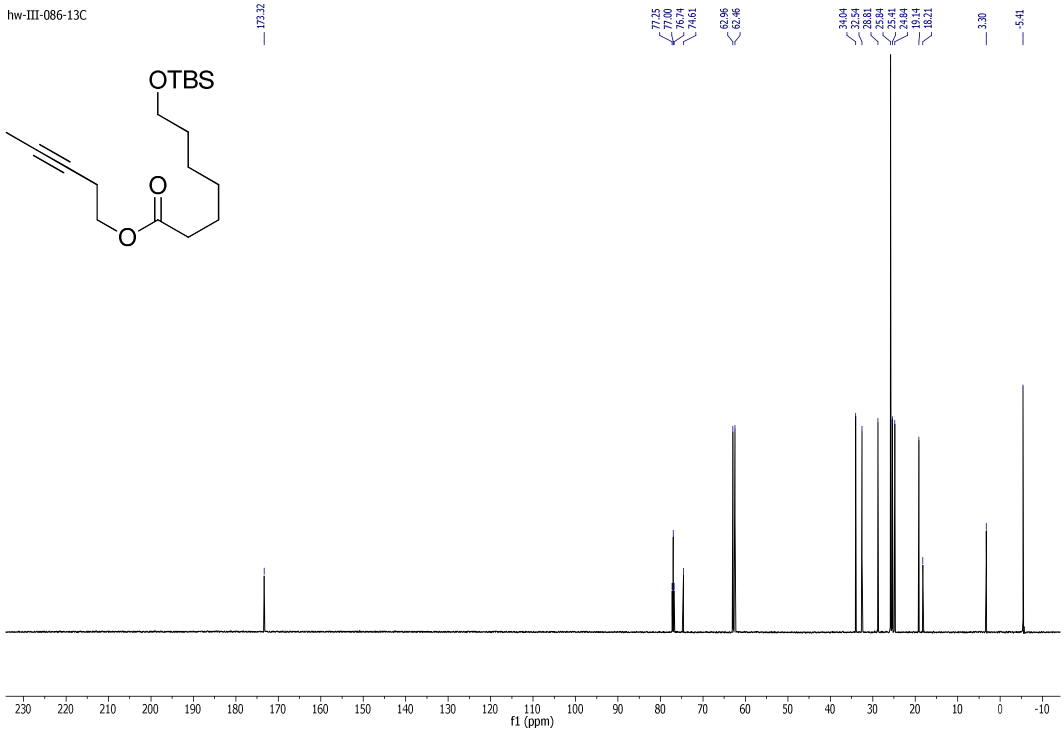
^{1}H- and ^{13}C-NMR spectra of compound **SA-3**



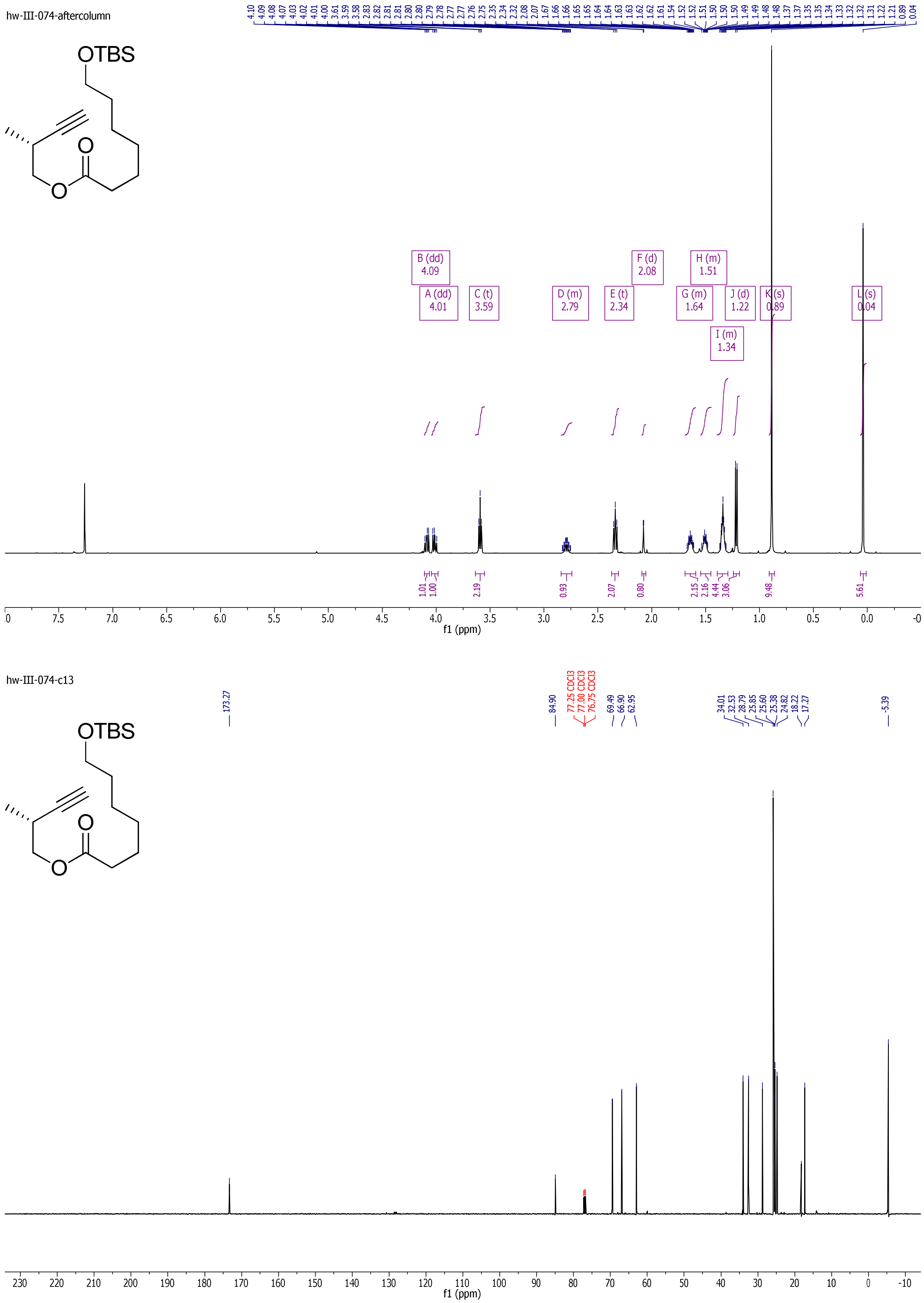
^{1}H- and ^{13}C-NMR spectra of compound **SA-4**

^{1}H- and ^{13}C-NMR spectra of compound **SA-5**



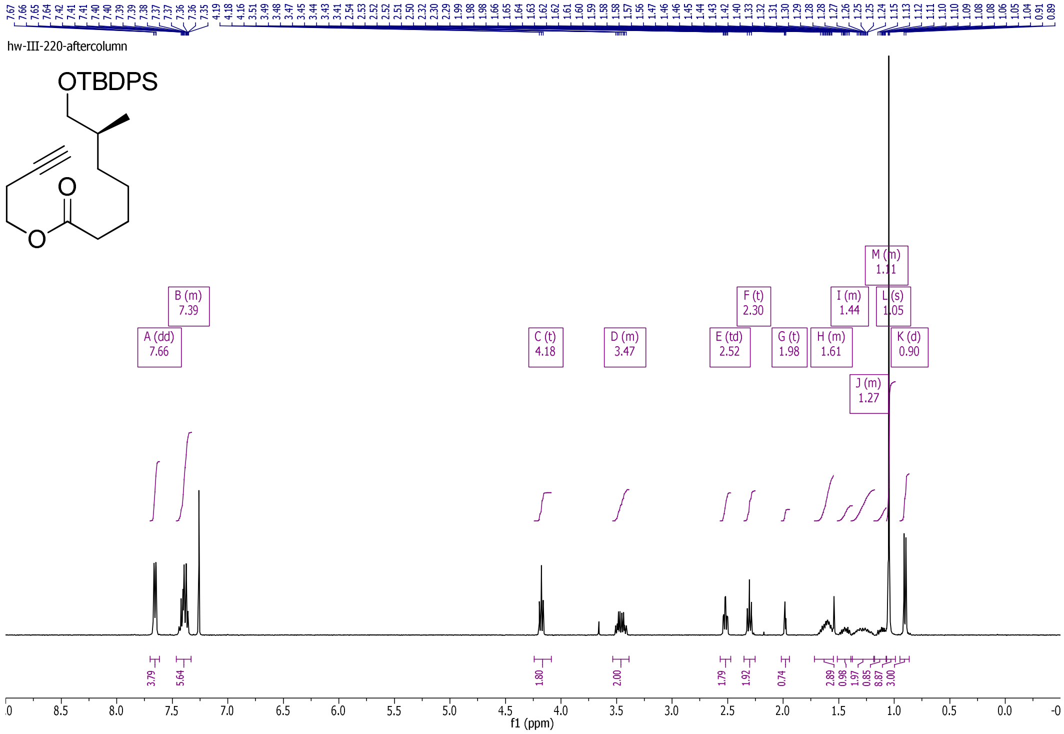


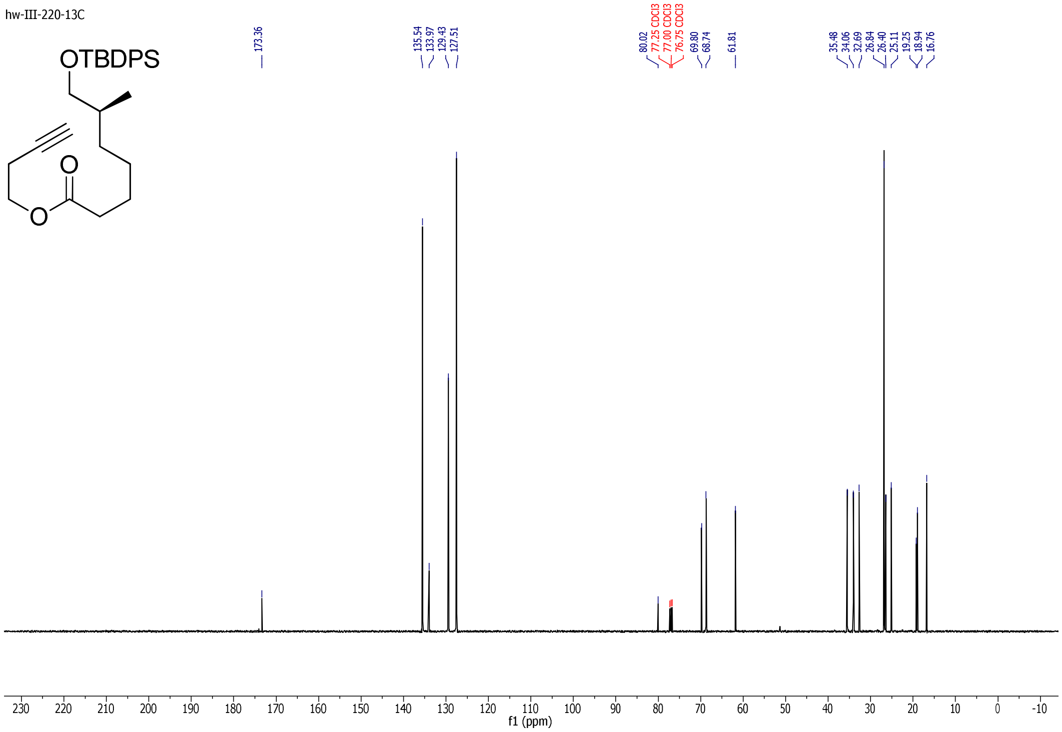
^{1}H- and ^{13}C-NMR spectra of compound **SA-6**



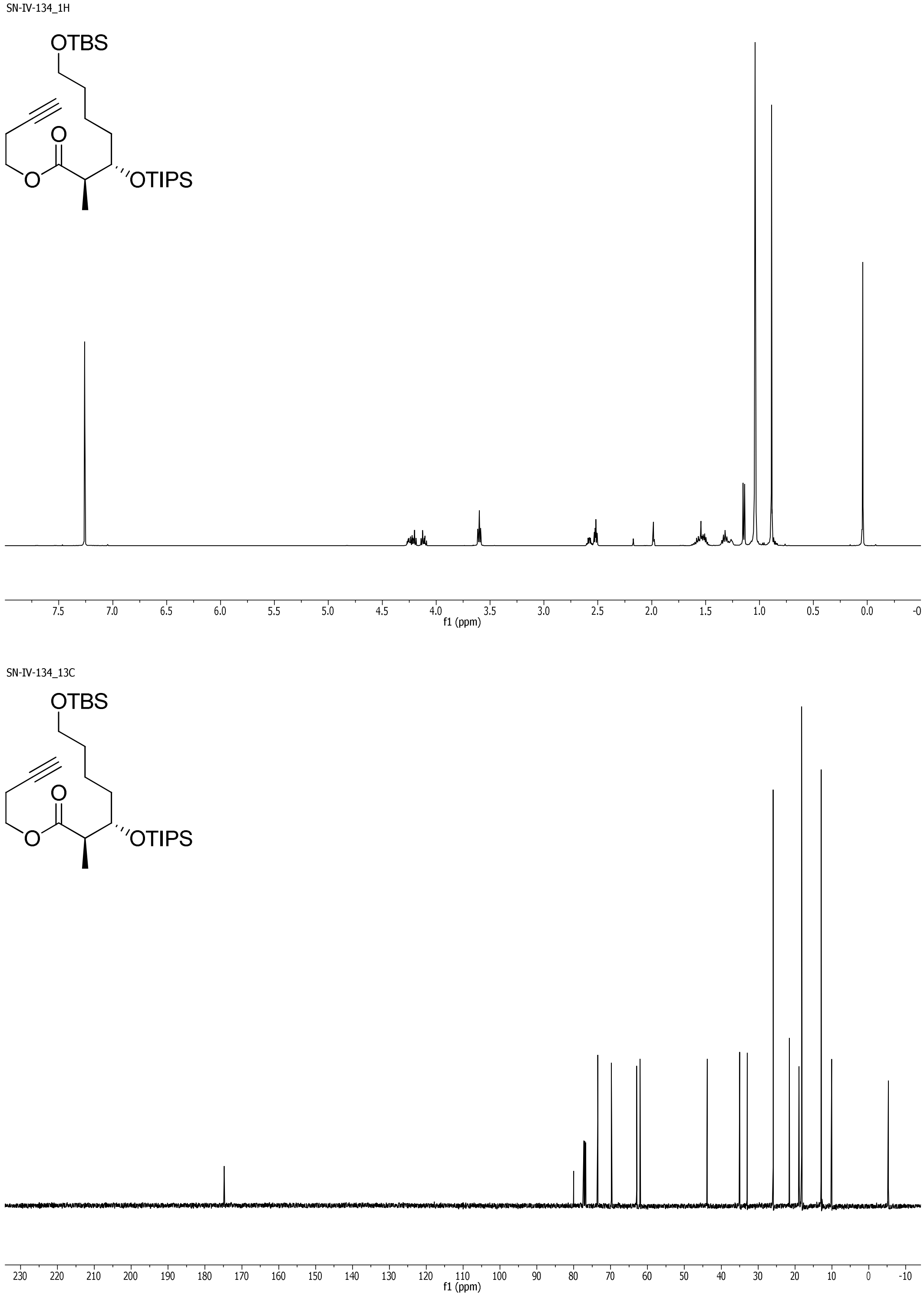
^{1}H- and ^{13}C-NMR spectra of compound **SA-7**

^{1}H- and ^{13}C-NMR spectra of compound **SA-8**



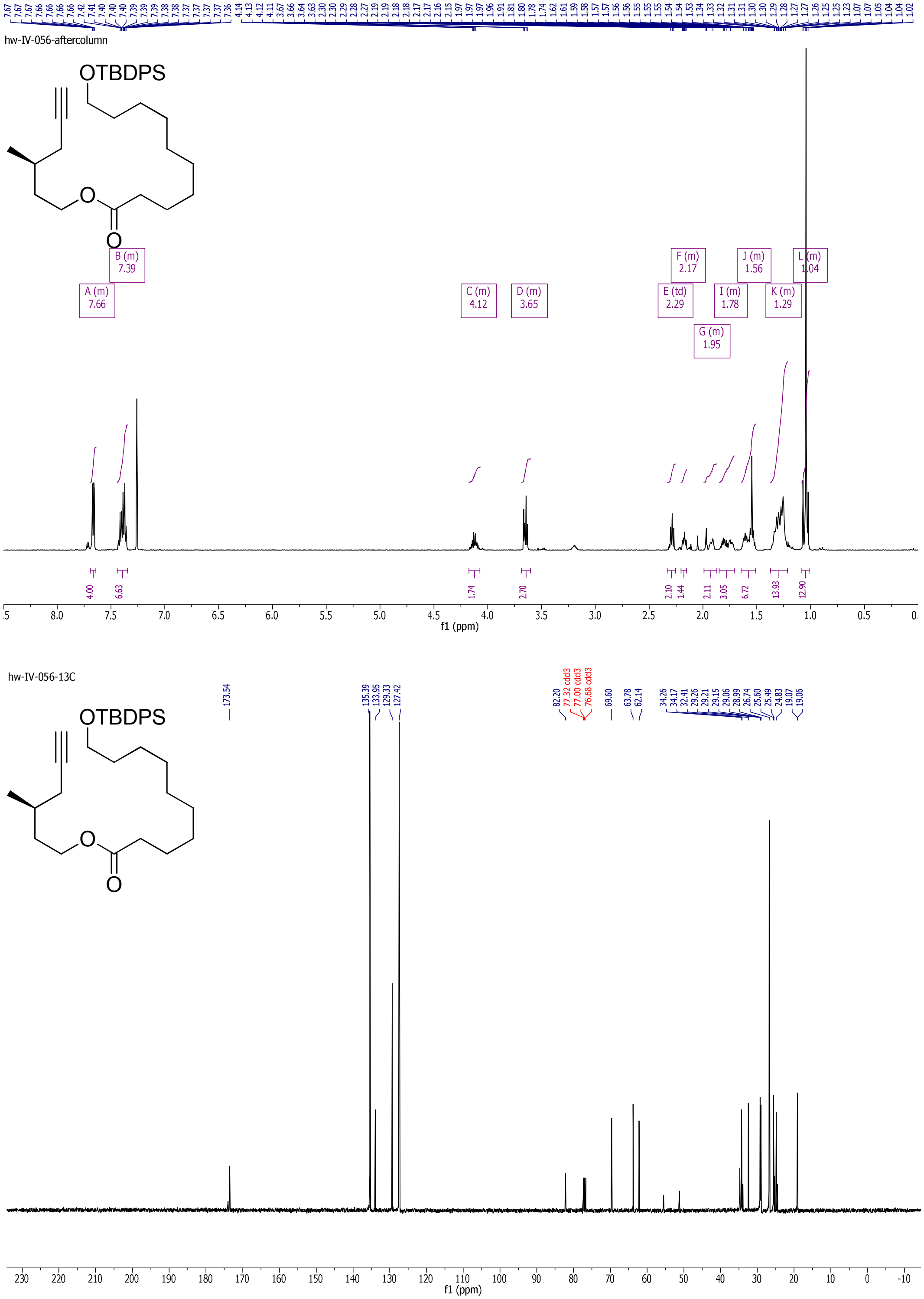


^{1}H- and ^{13}C-NMR spectra of compound **SA-9**

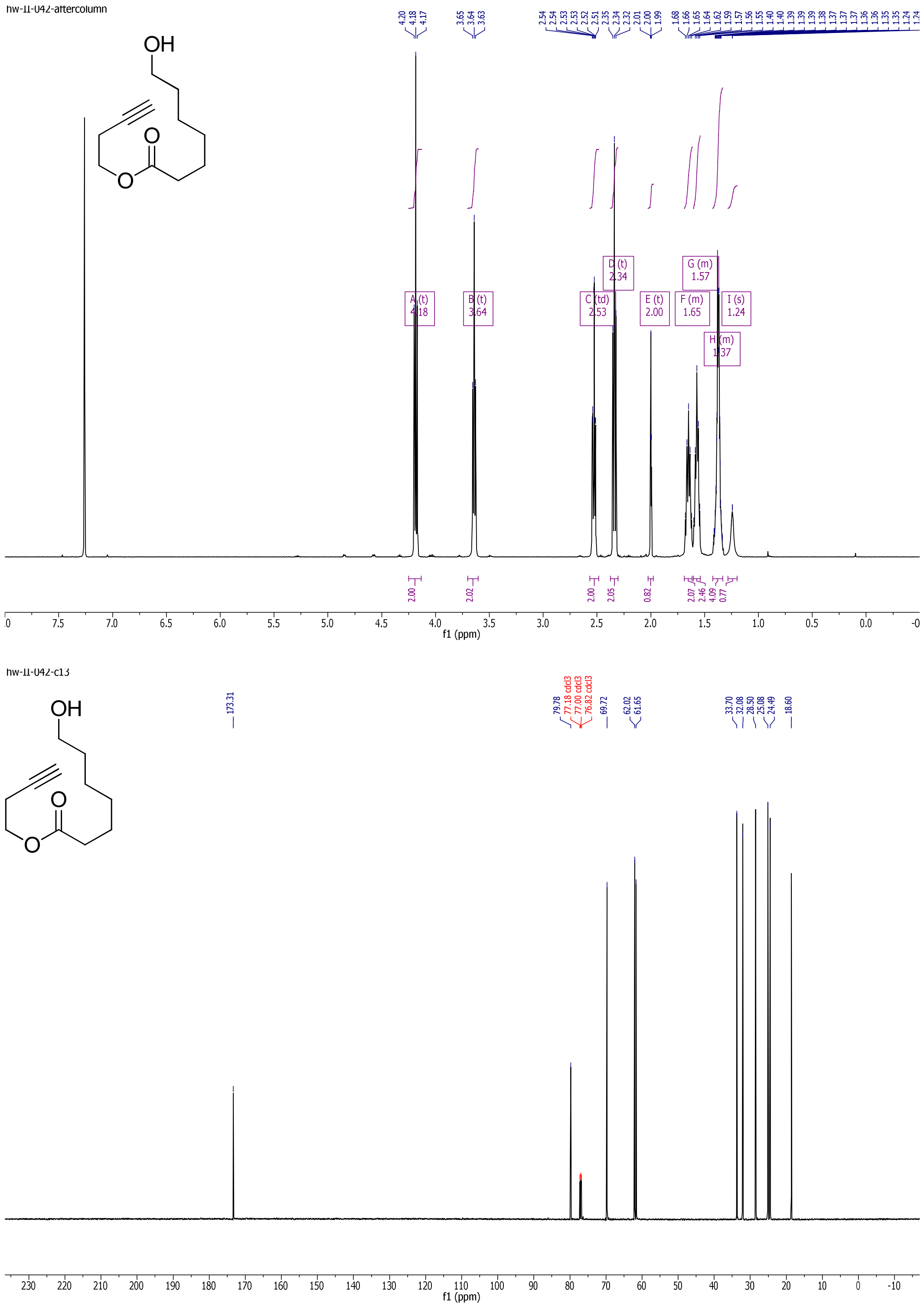


、 ^{1}H- and ^{13}C-NMR spectra of compound **SA-10**

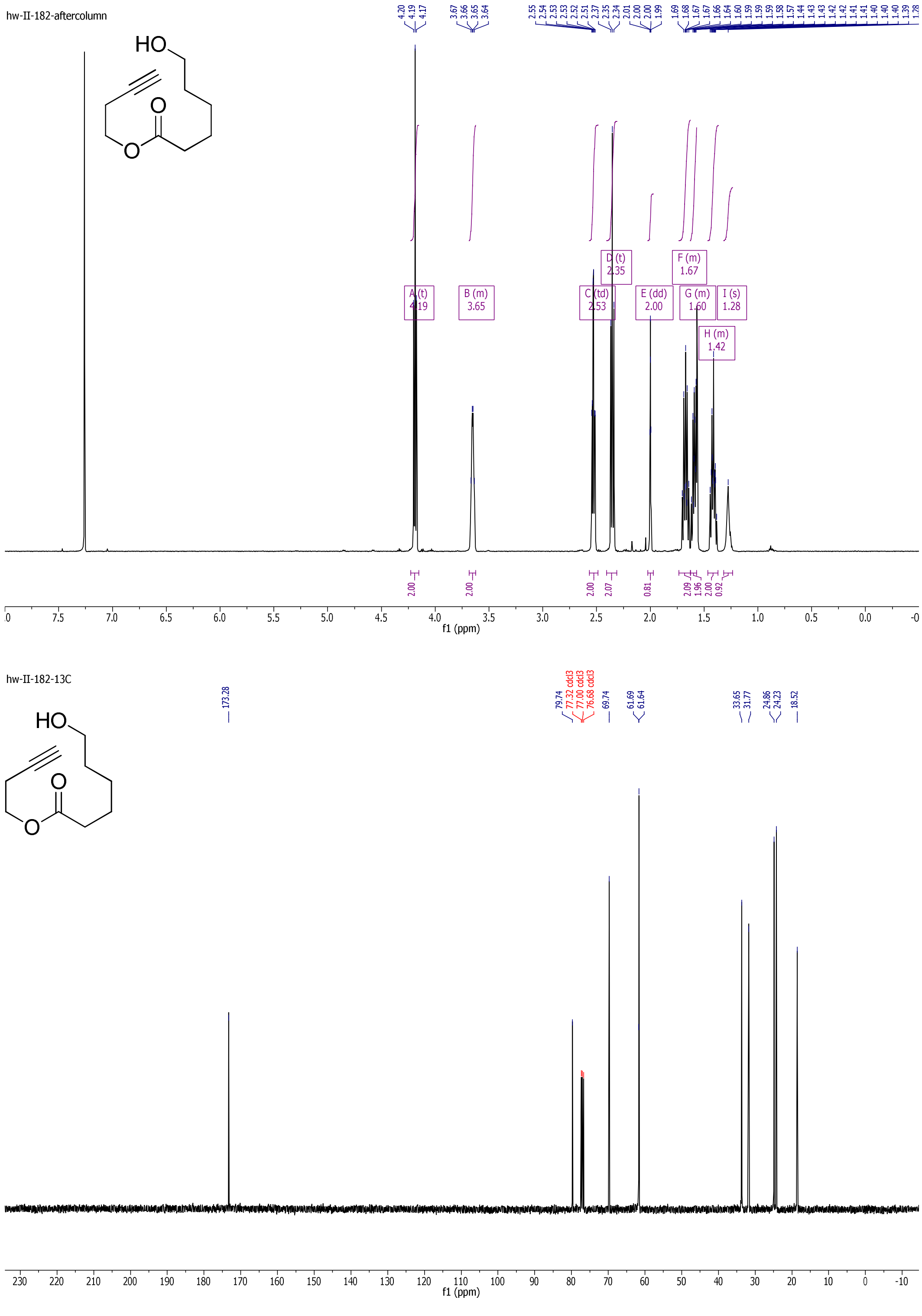
^{1}H- and ^{13}C-NMR spectra of compound **SA-11**



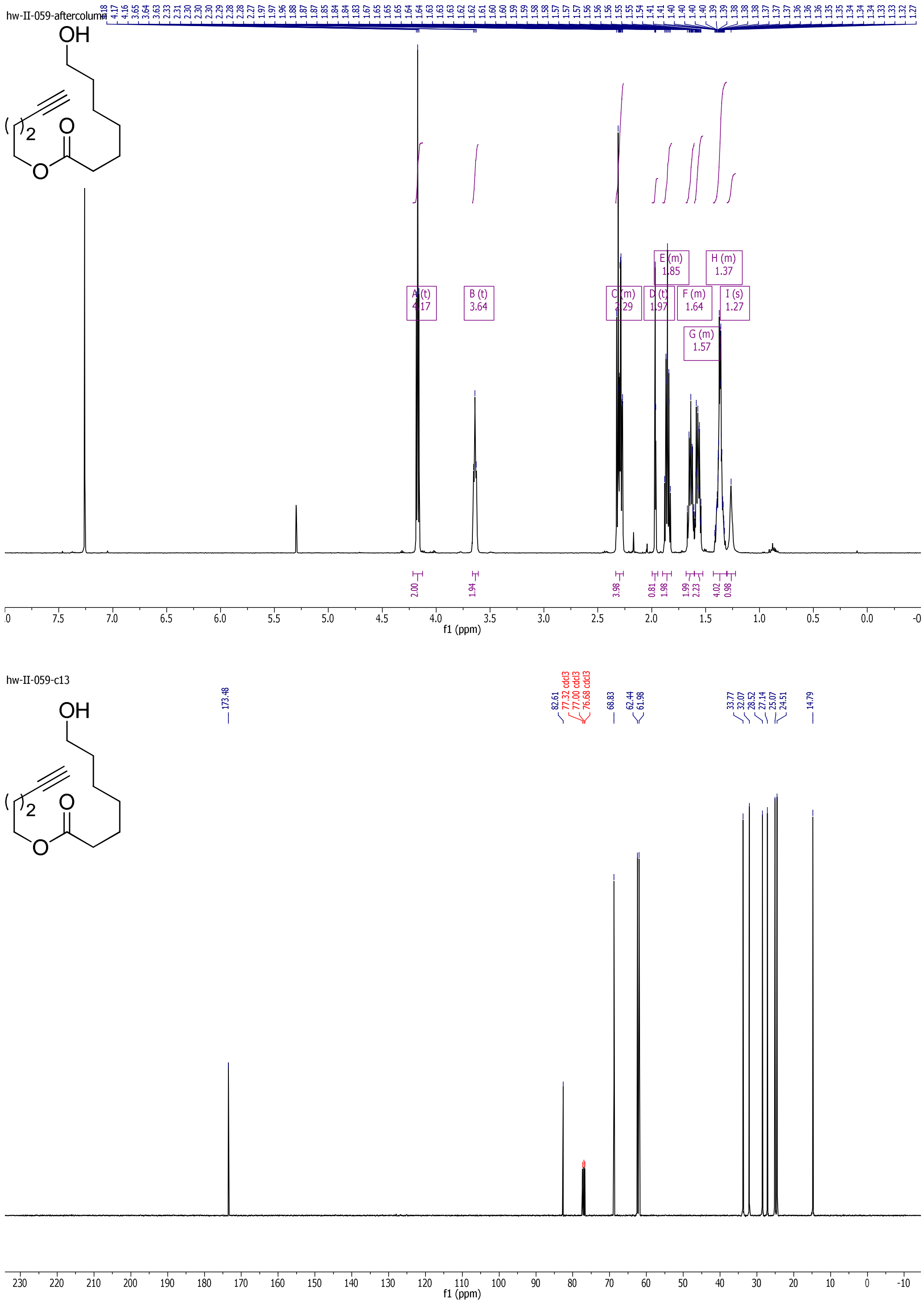
^{1}H- and ^{13}C-NMR spectra of compound **SA-12**



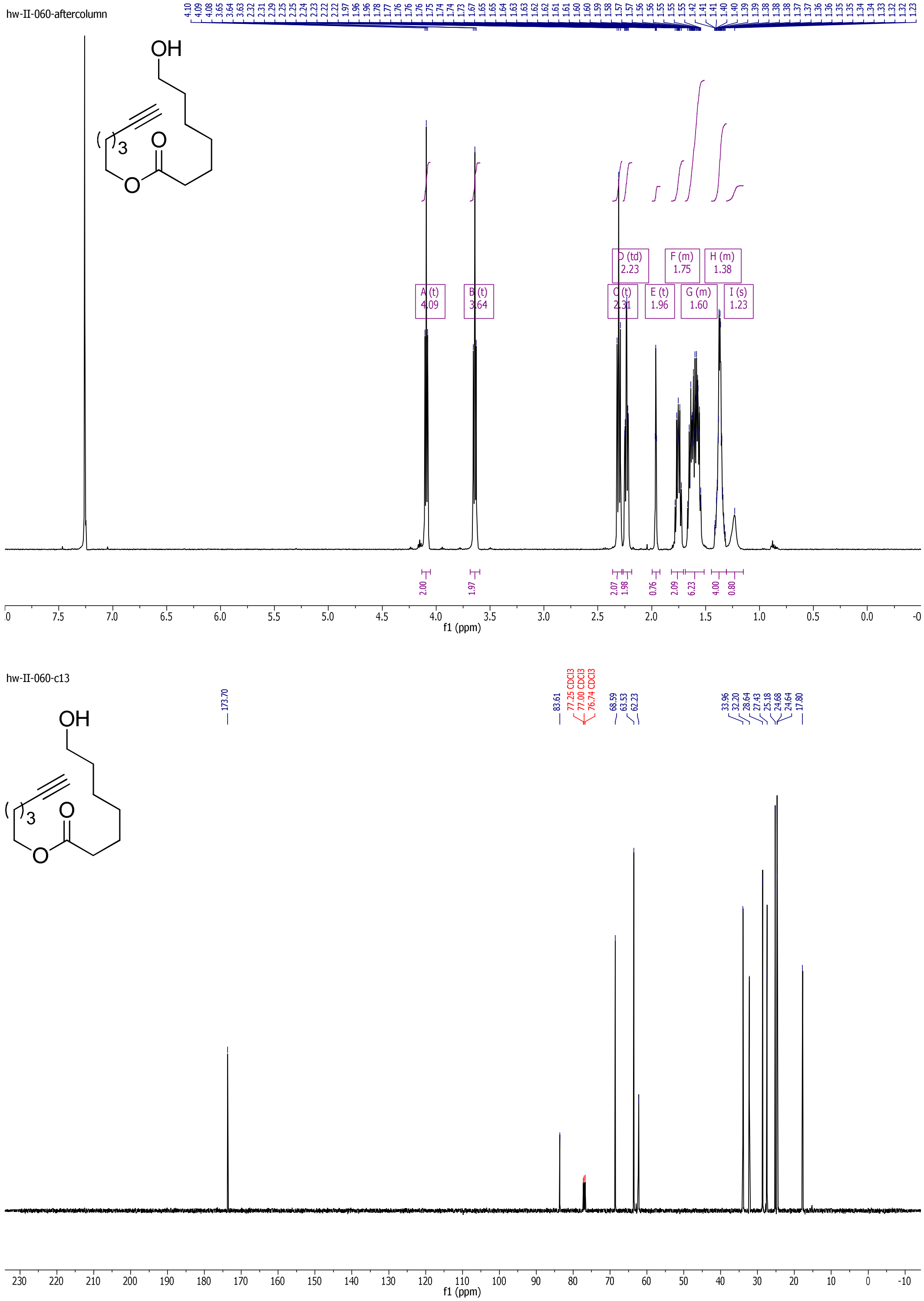
^{1}H- and ^{13}C-NMR spectra of compound **SB-1**



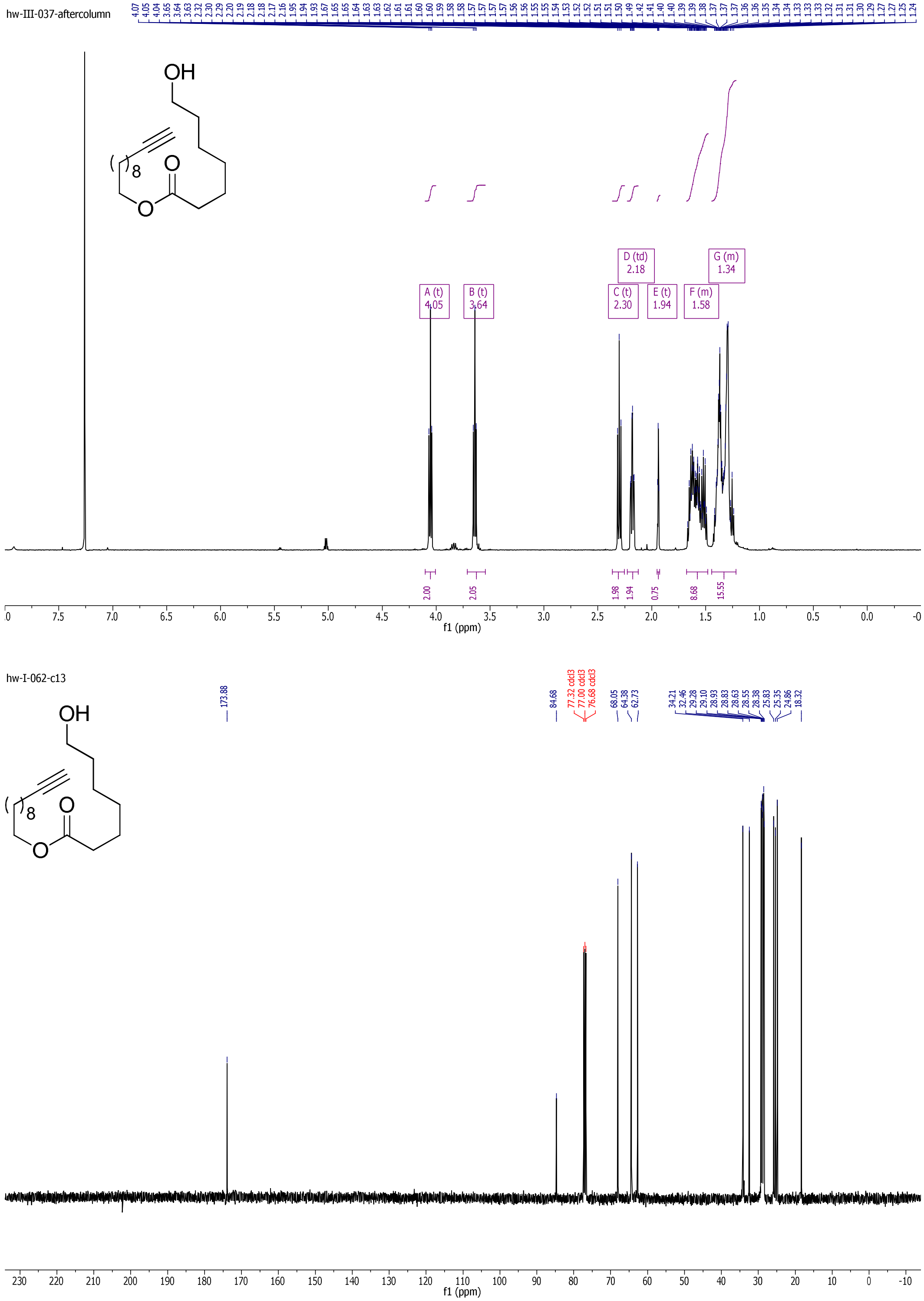
^{1}H- and ^{13}C-NMR spectra of compound **SB-2**



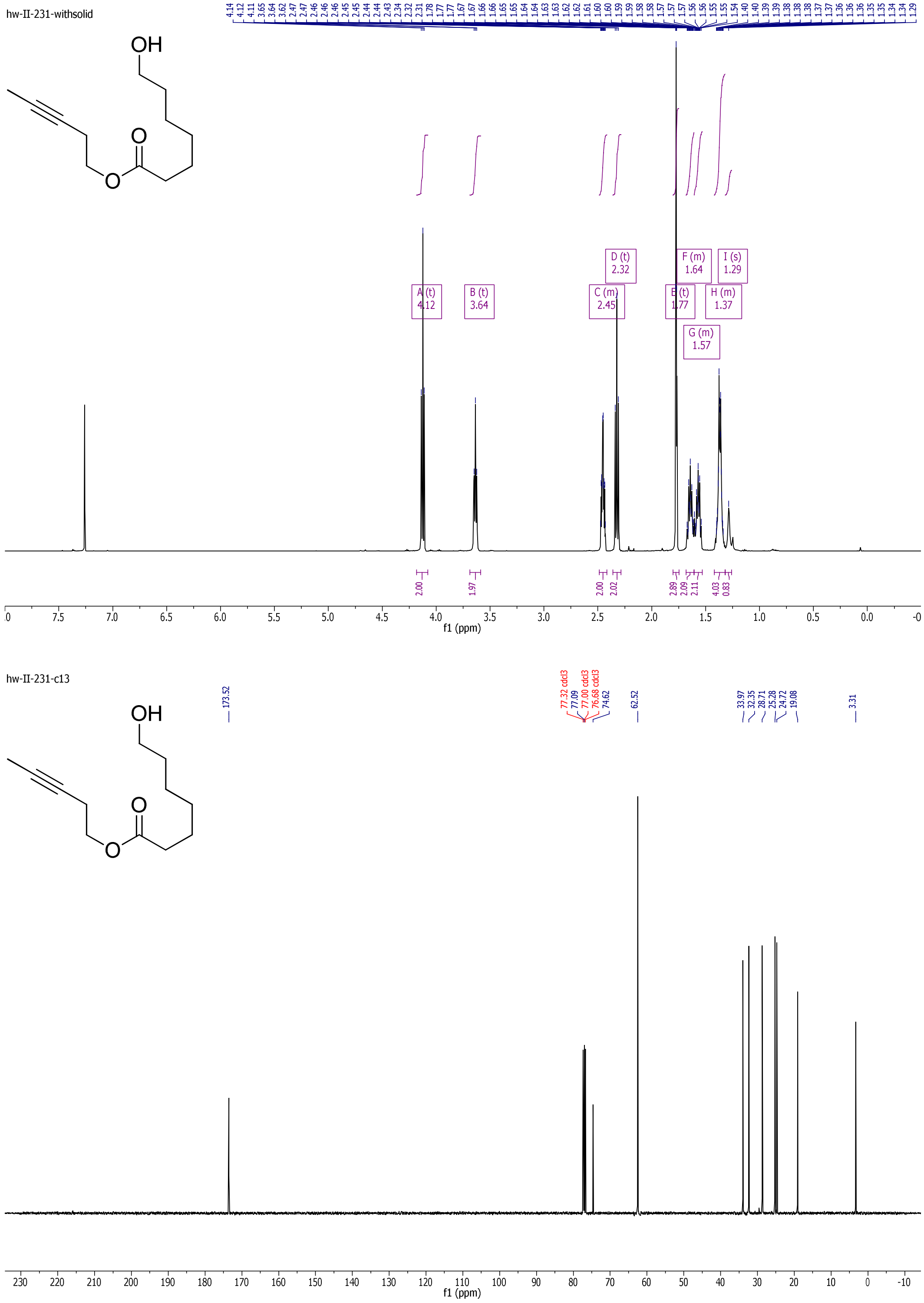
^1H- and ^{13}C-NMR spectra of compound **SB-3**



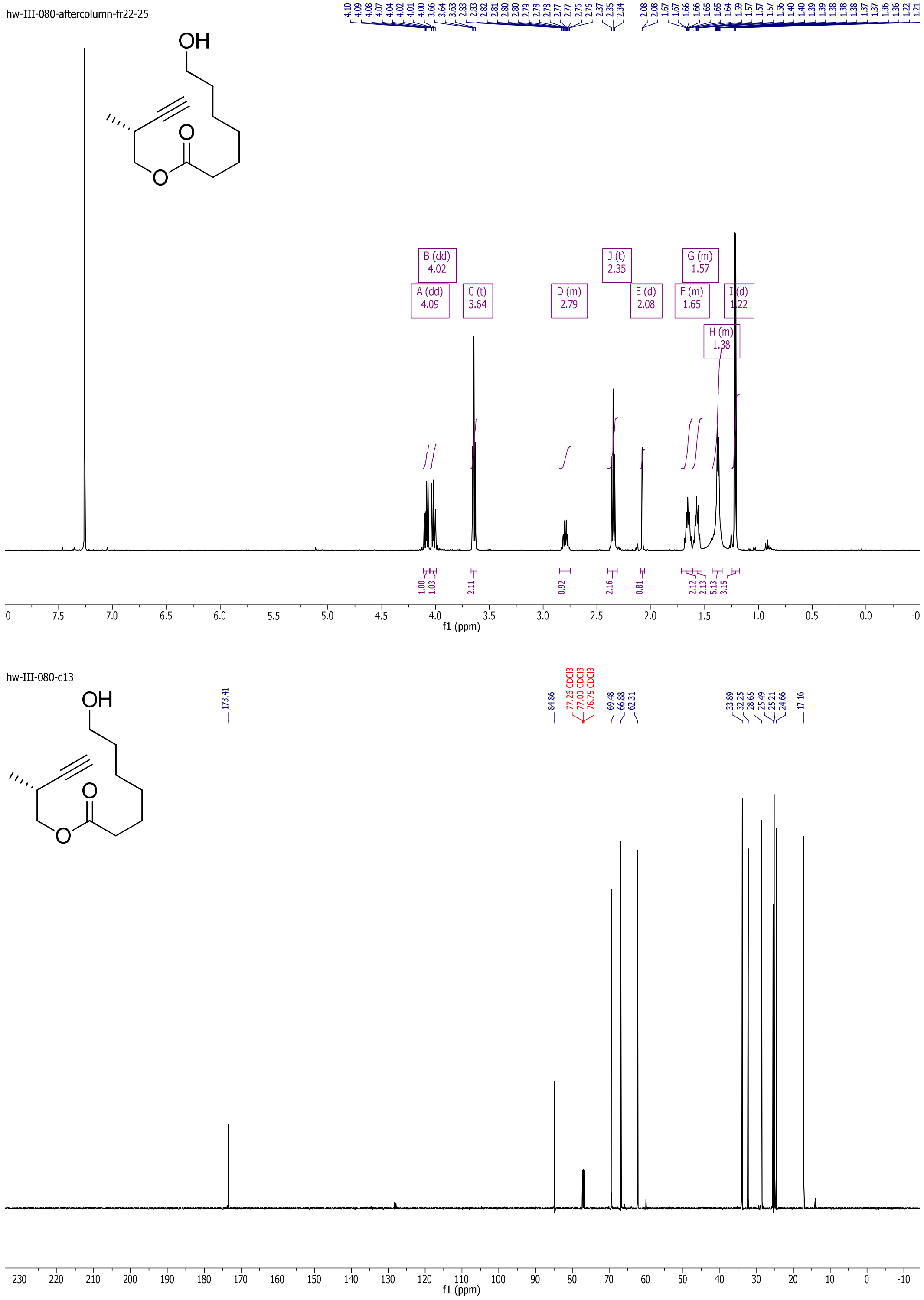
^{1}H- and ^{13}C-NMR spectra of compound **SB-4**



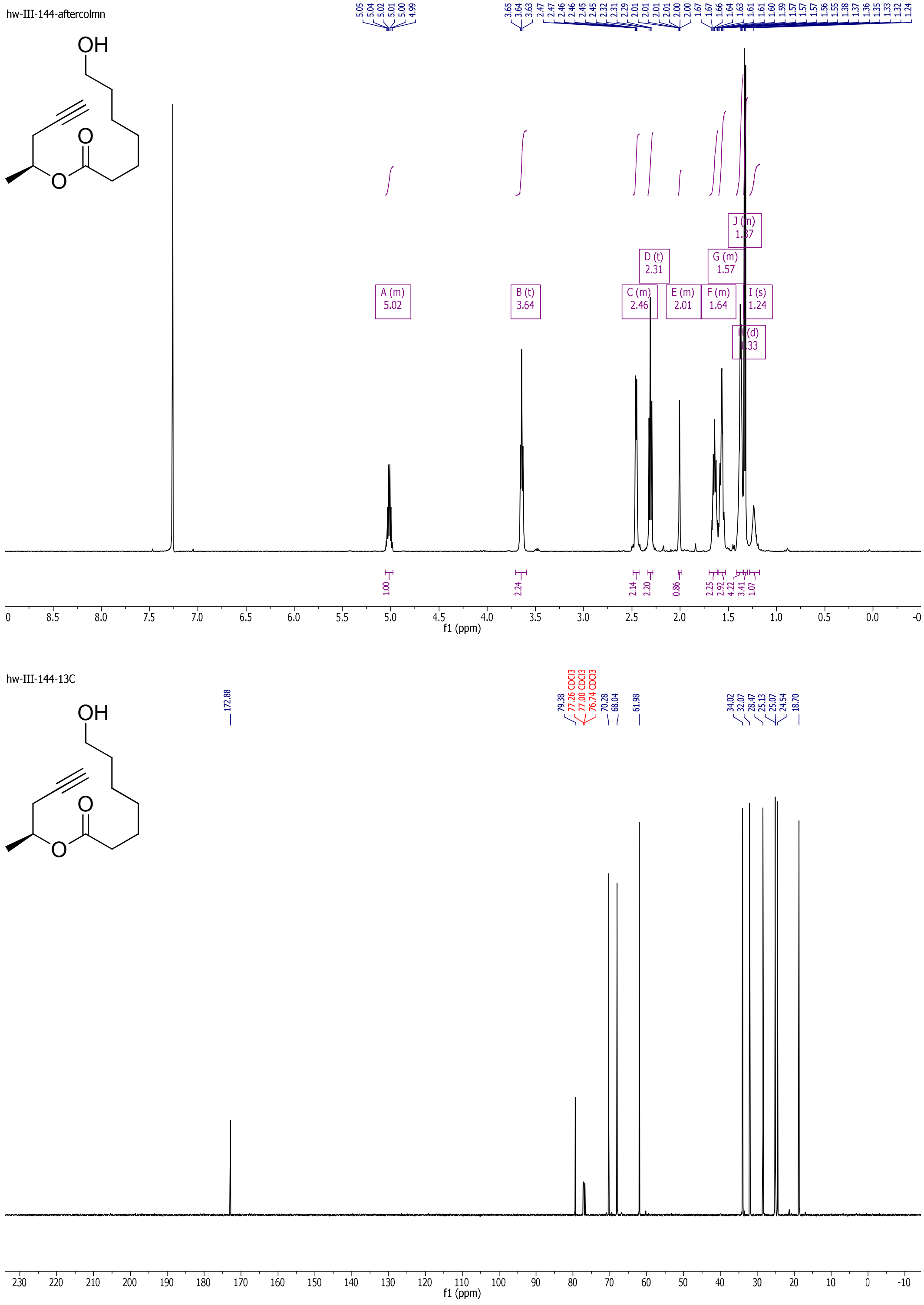
^{1}H- and ^{13}C-NMR spectra of compound **SB-5**



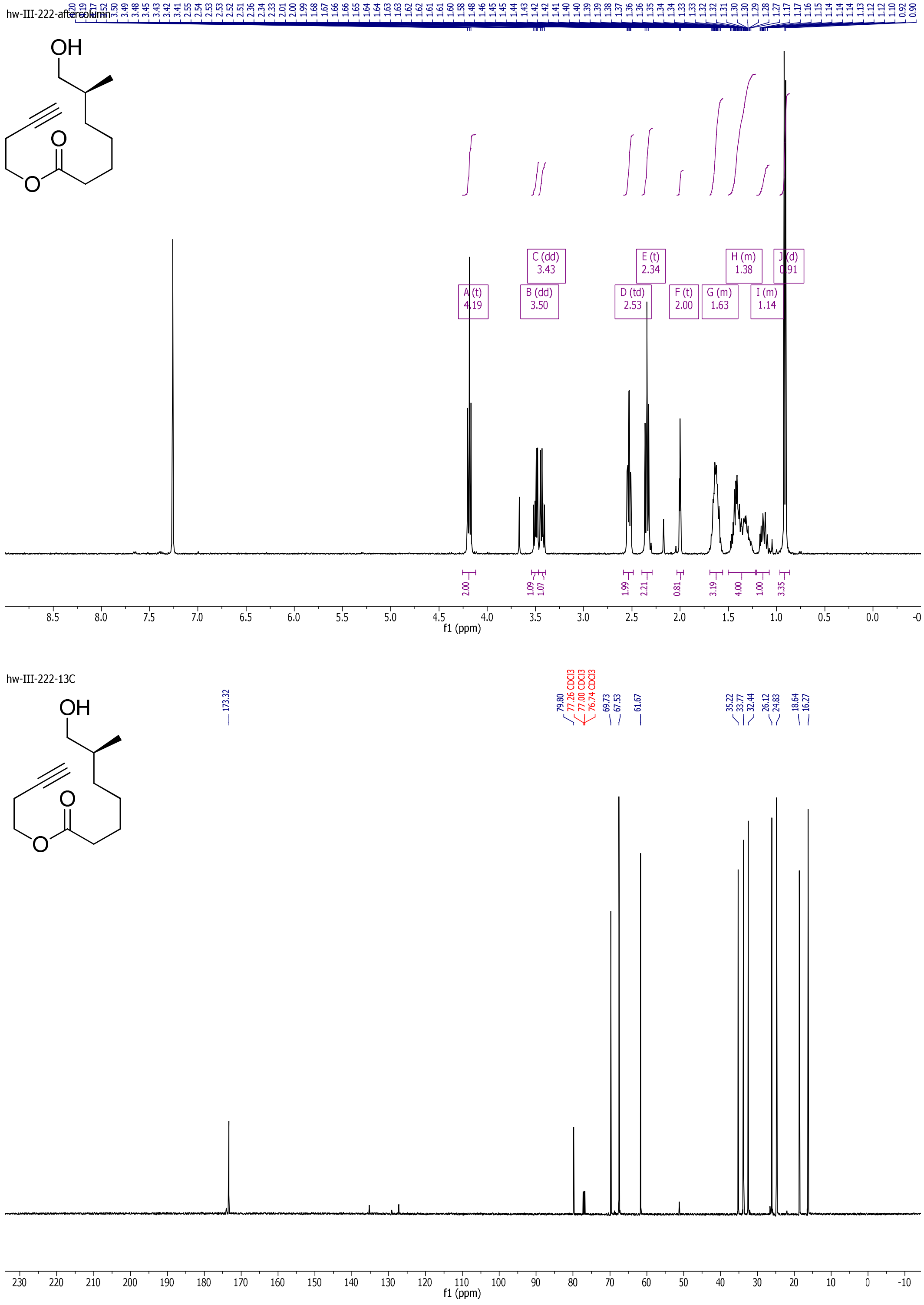
^{1}H- and ^{13}C-NMR spectra of compound **SB-6**



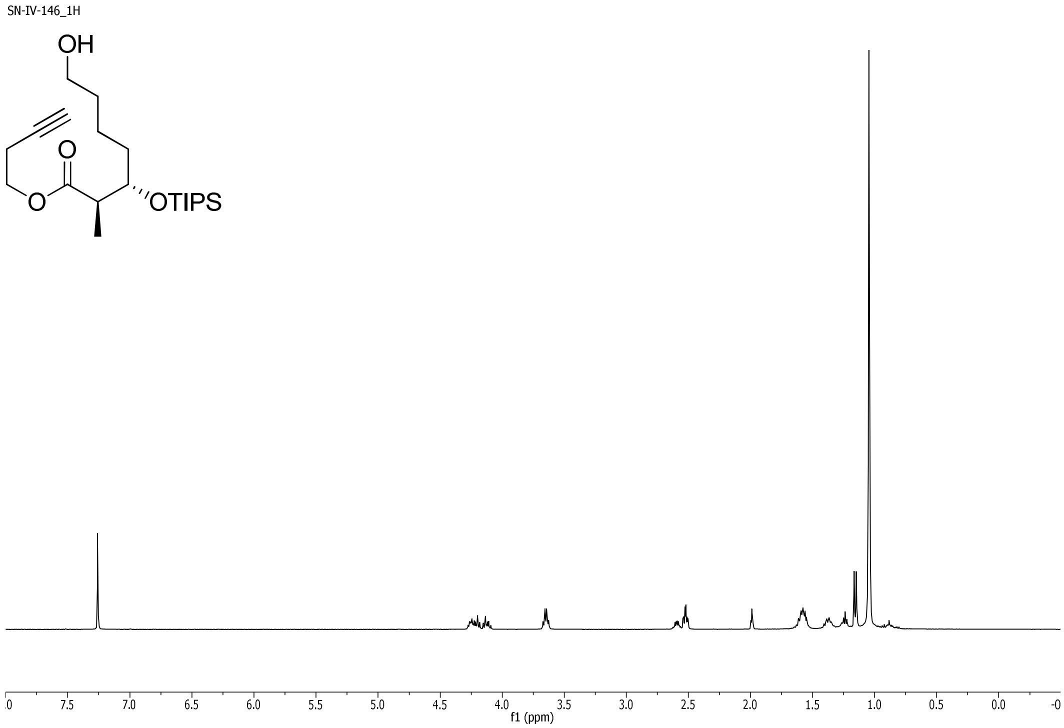
^{1}H- and ^{13}C-NMR spectra of compound **SB-7**

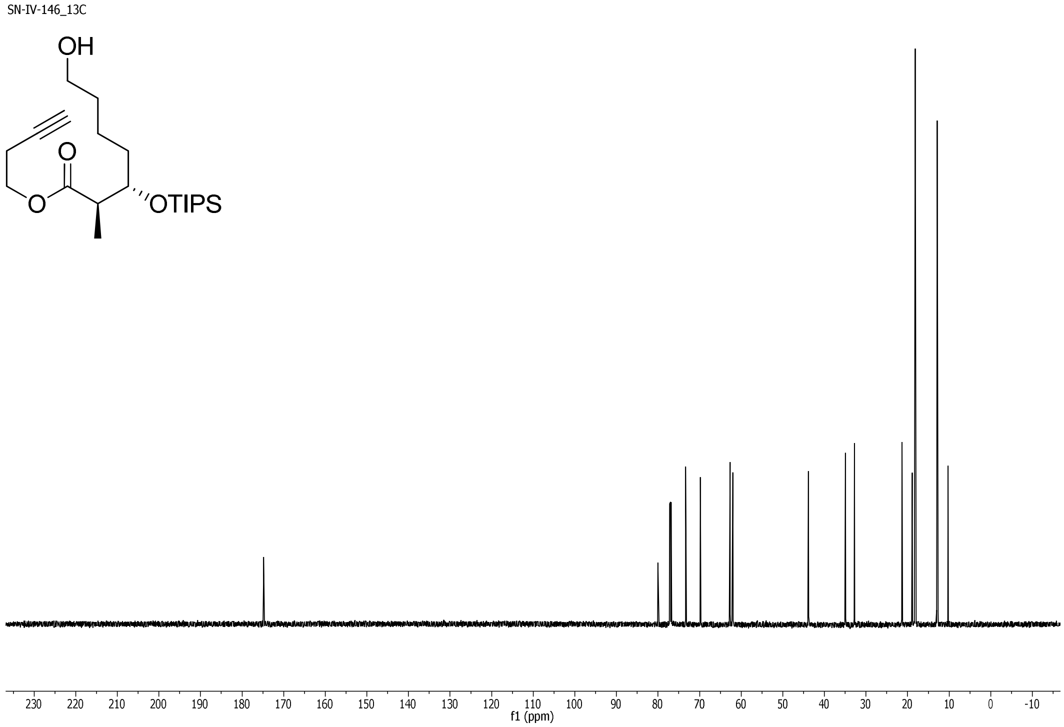


^{1}H- and ^{13}C-NMR spectra of compound **SB-8**

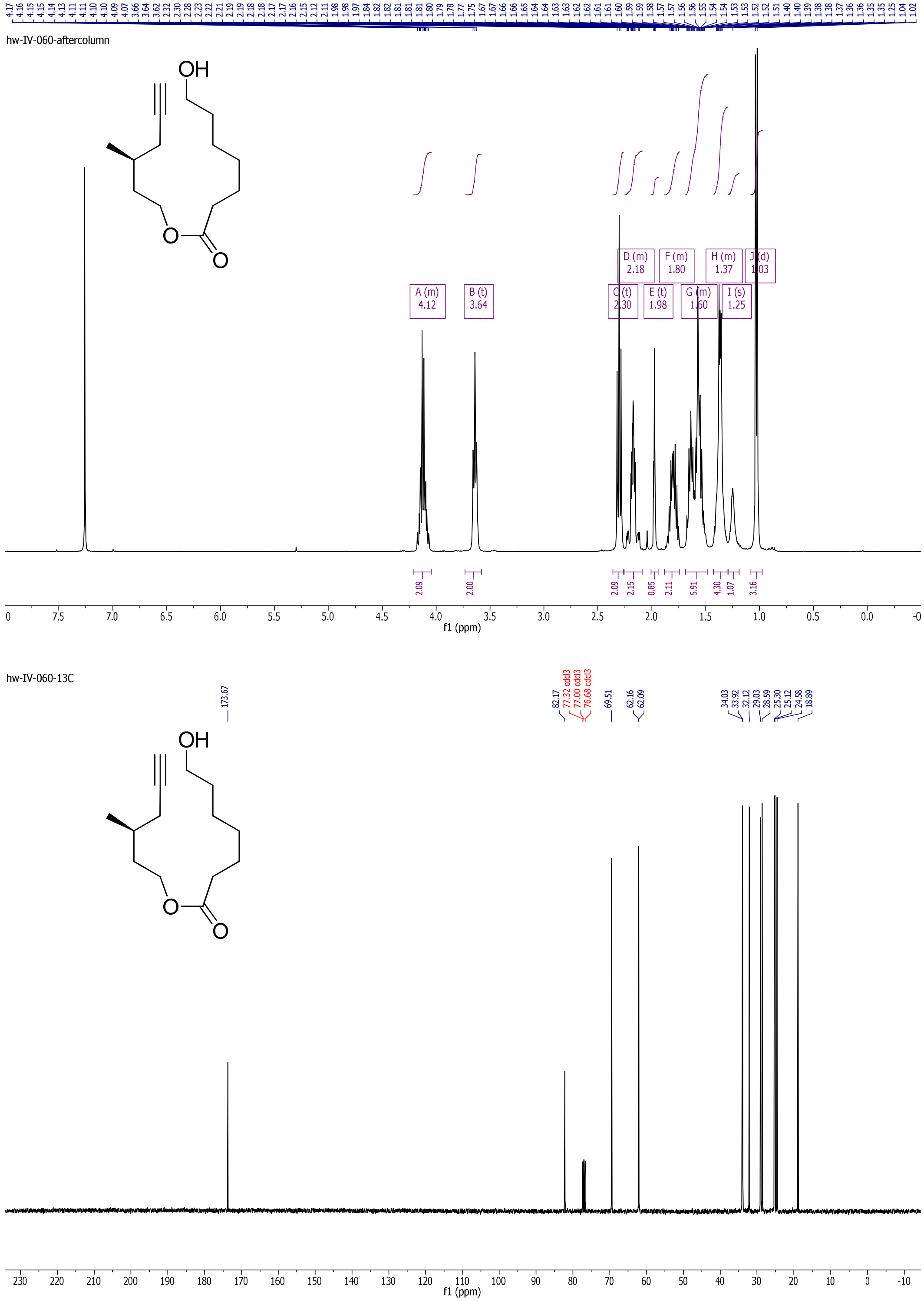


^{1}H- and ^{13}C-NMR spectra of compound **SB-9**

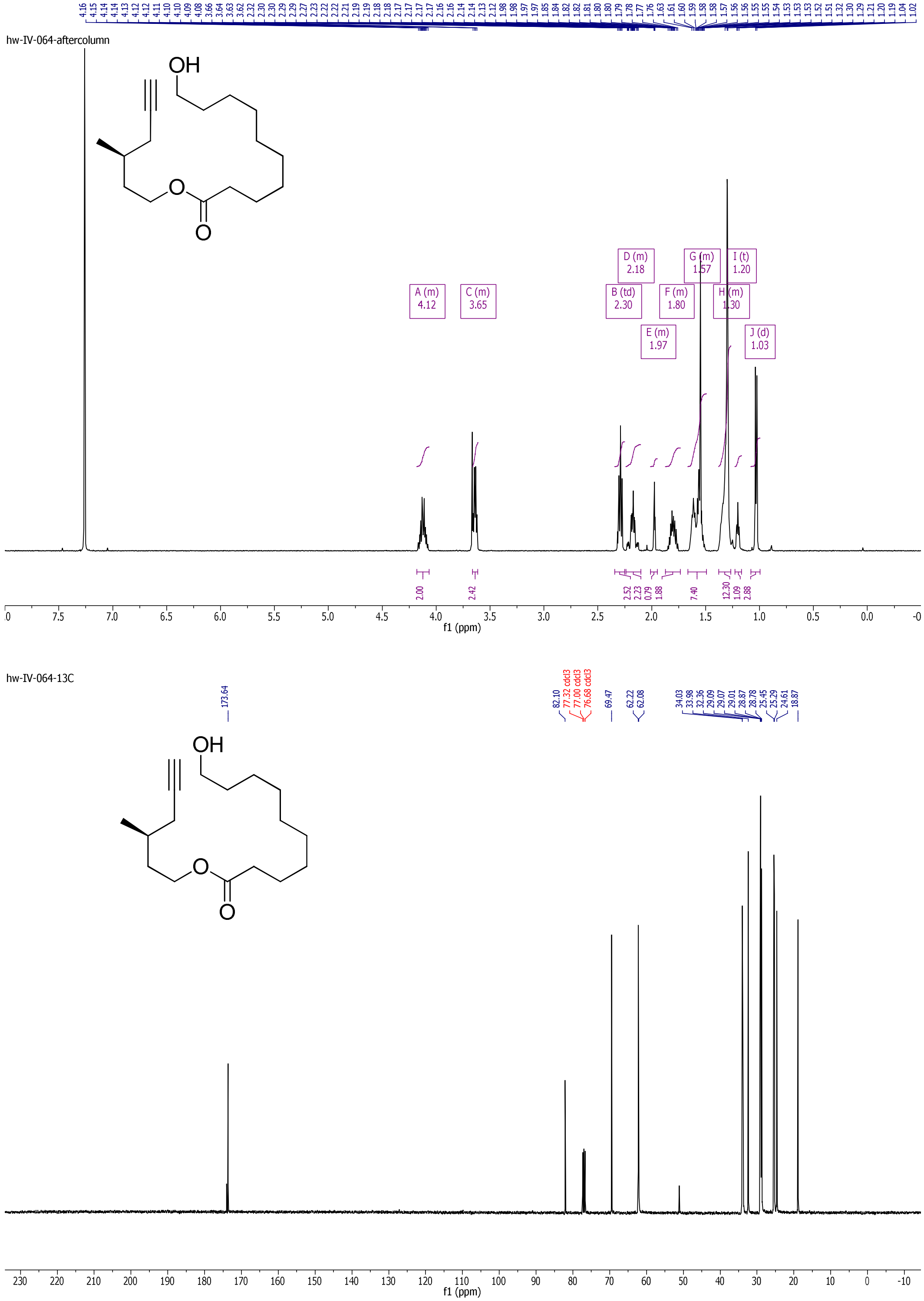




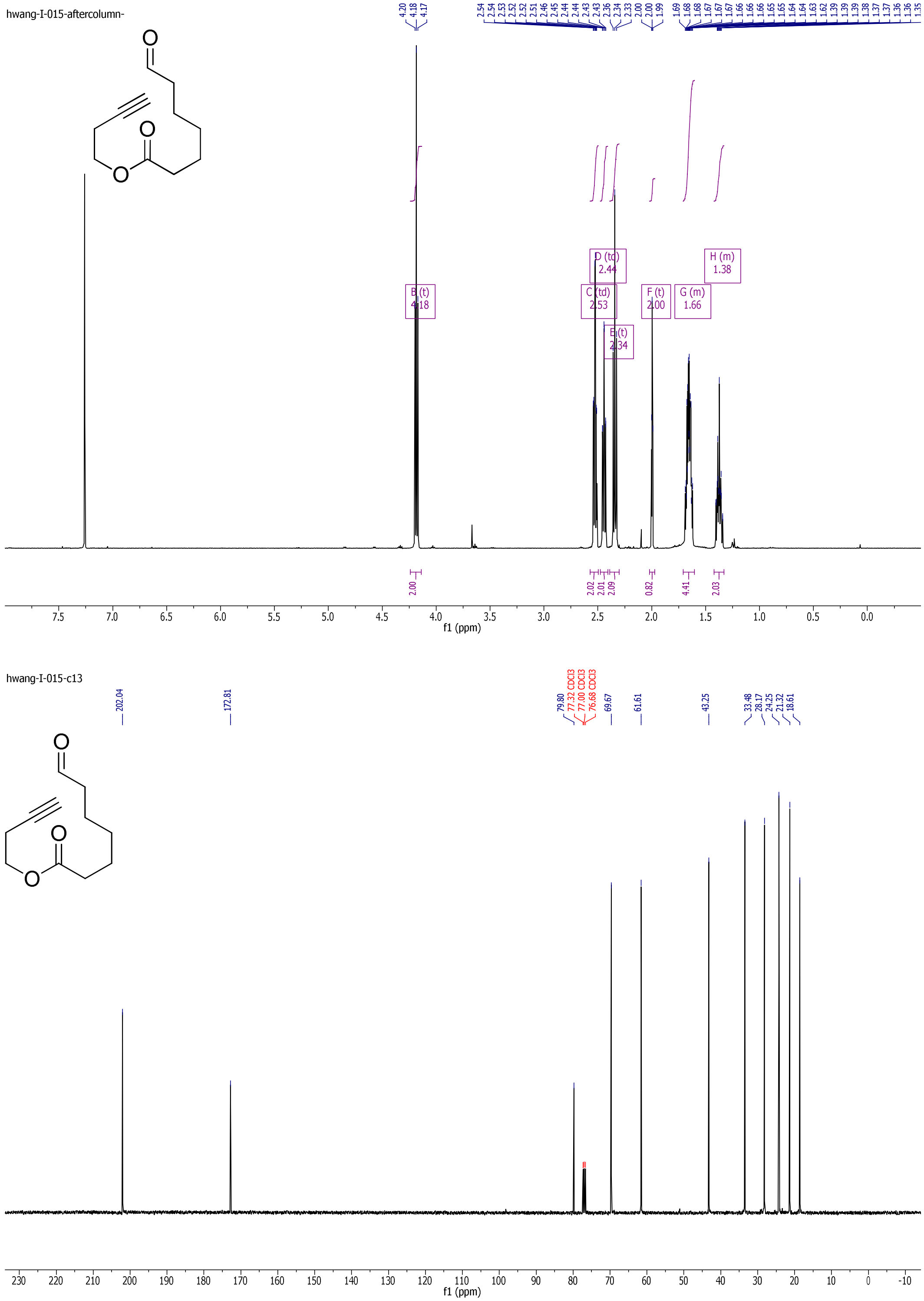
^{1}H- and ^{13}C-NMR spectra of compound **SB-10**



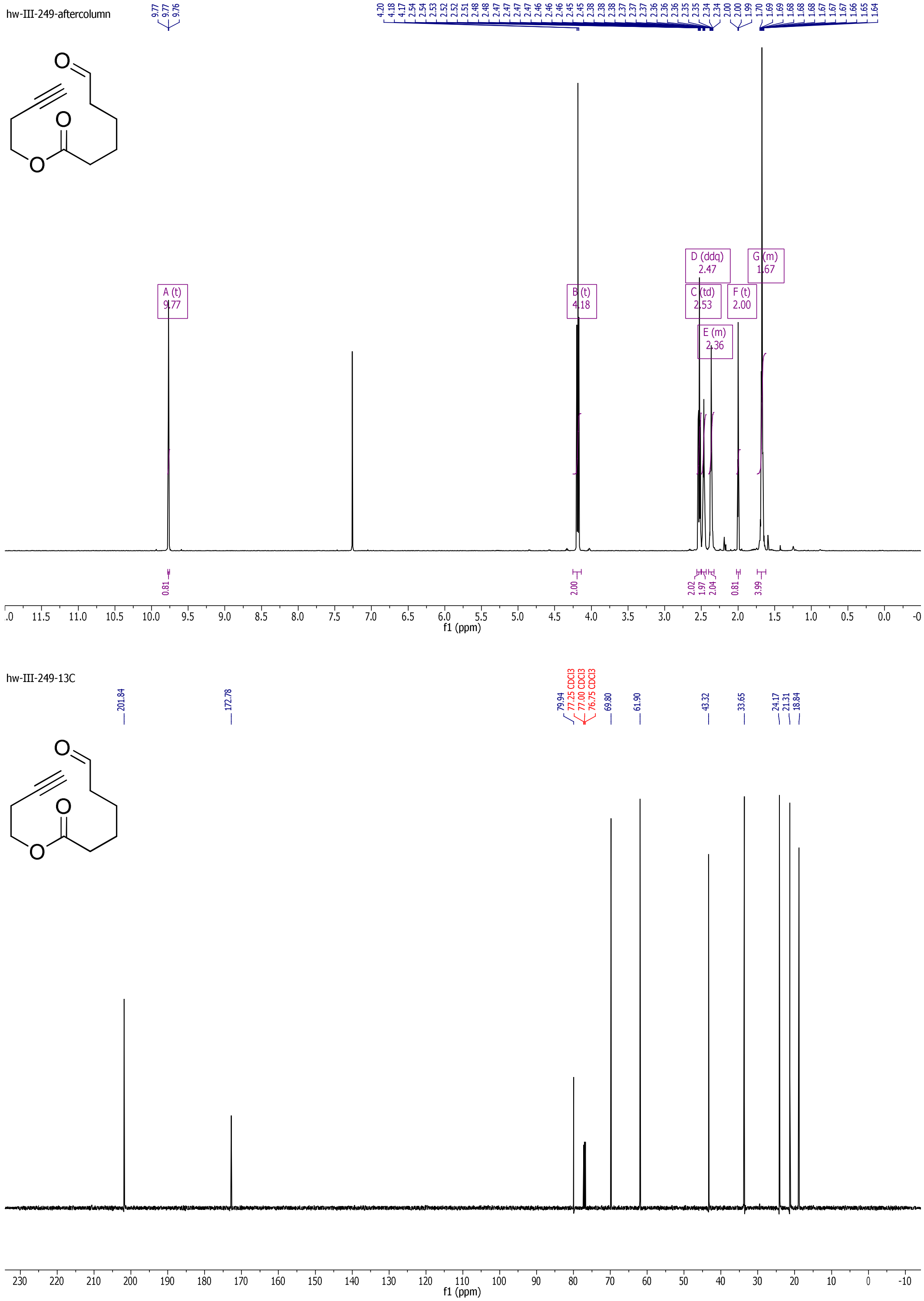
^{1}H- and ^{13}C-NMR spectra of compound **SB-11**



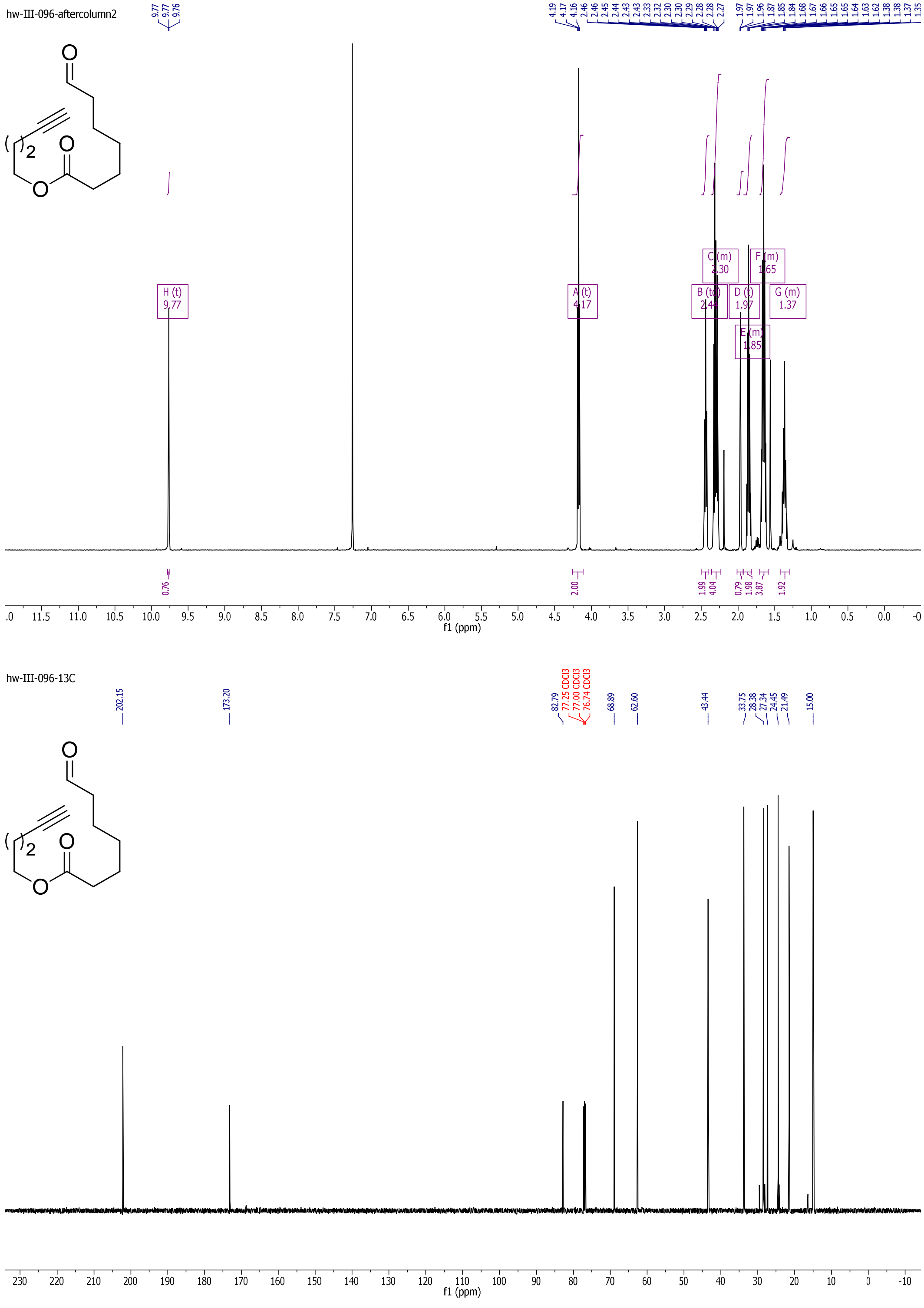
^{1}H- and ^{13}C-NMR spectra of compound **SB-12**



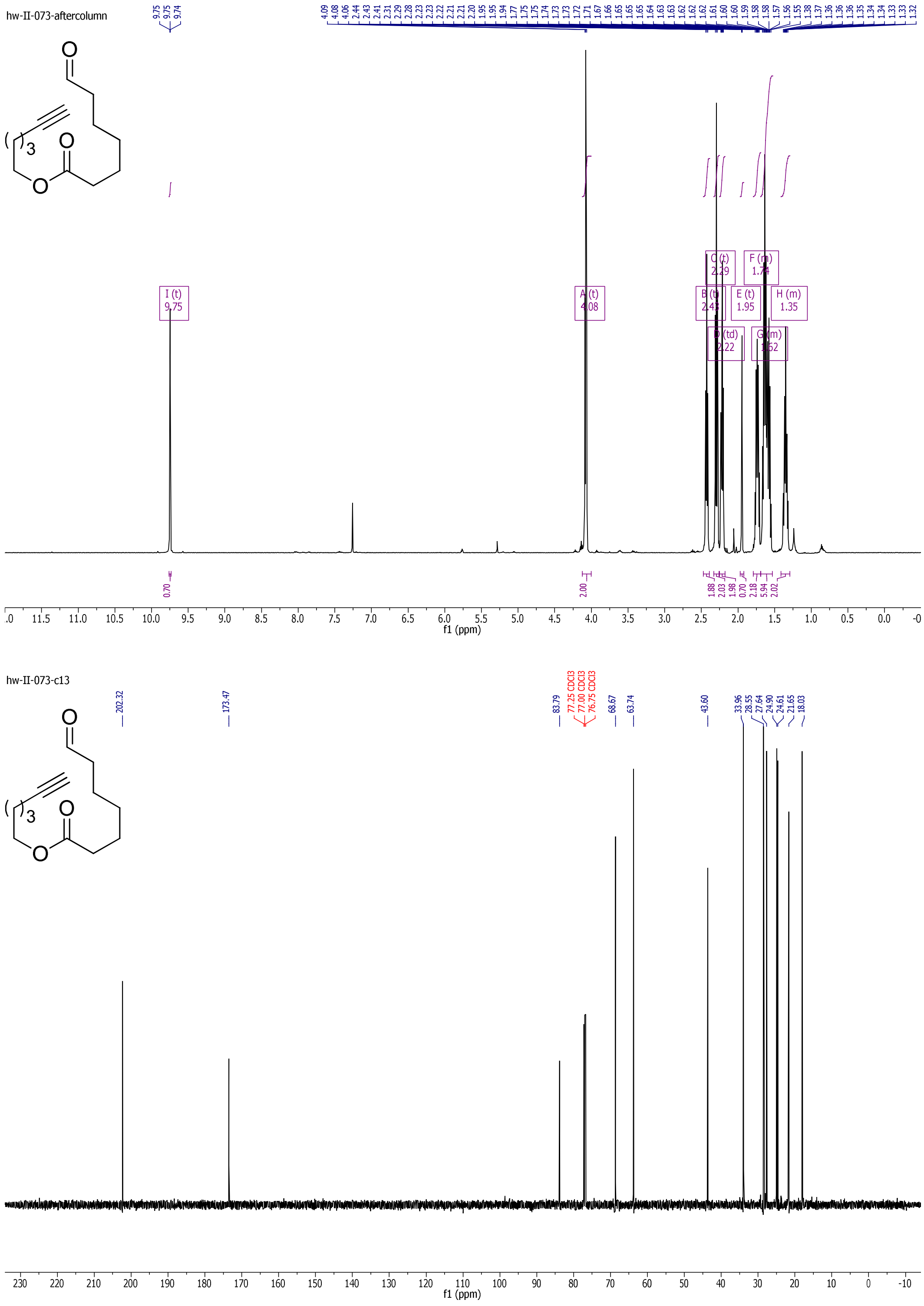
^{1}H- and ^{13}C-NMR spectra of compound **4**



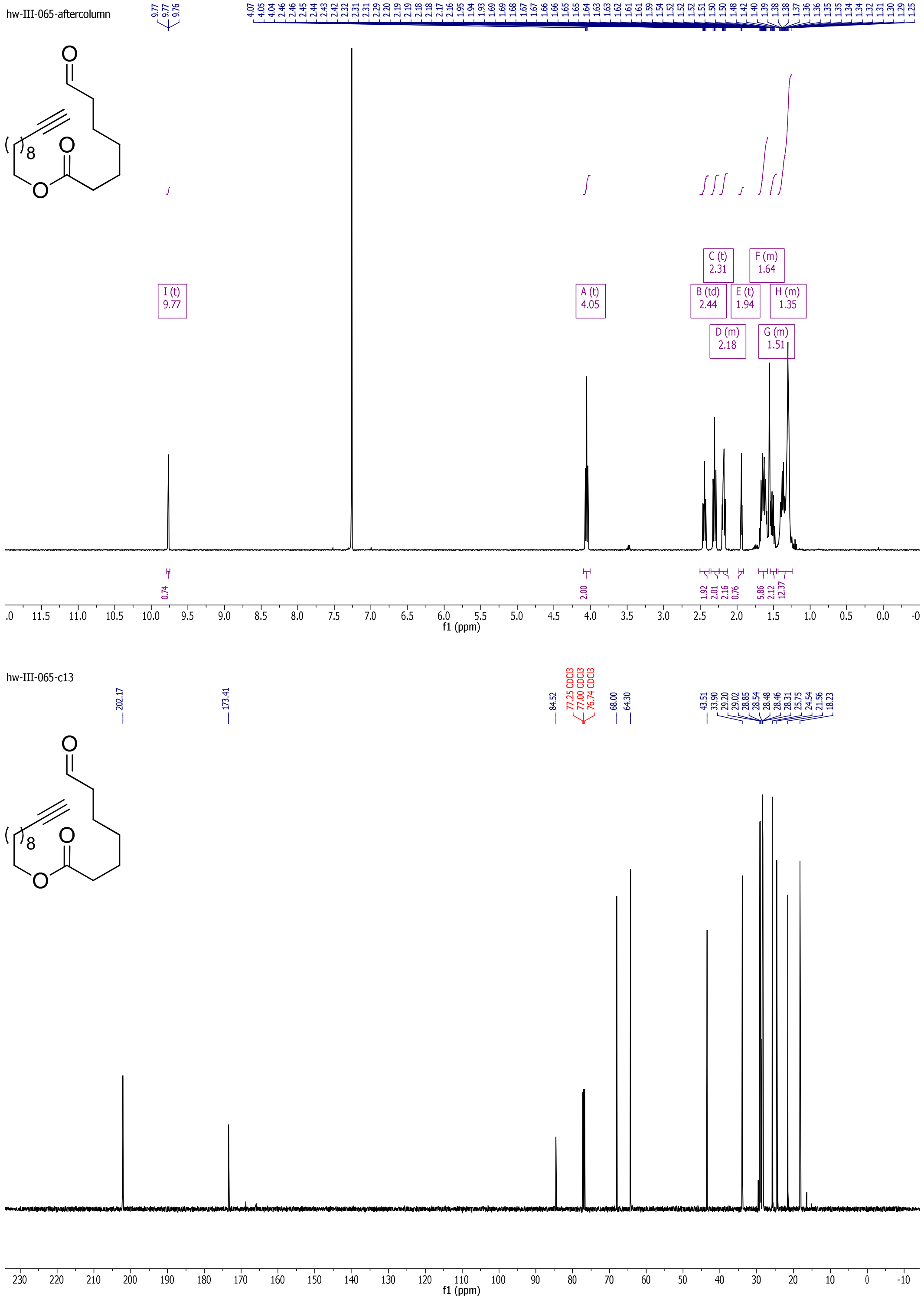
^{1}H- and ^{13}C-NMR spectra of compound **7a**



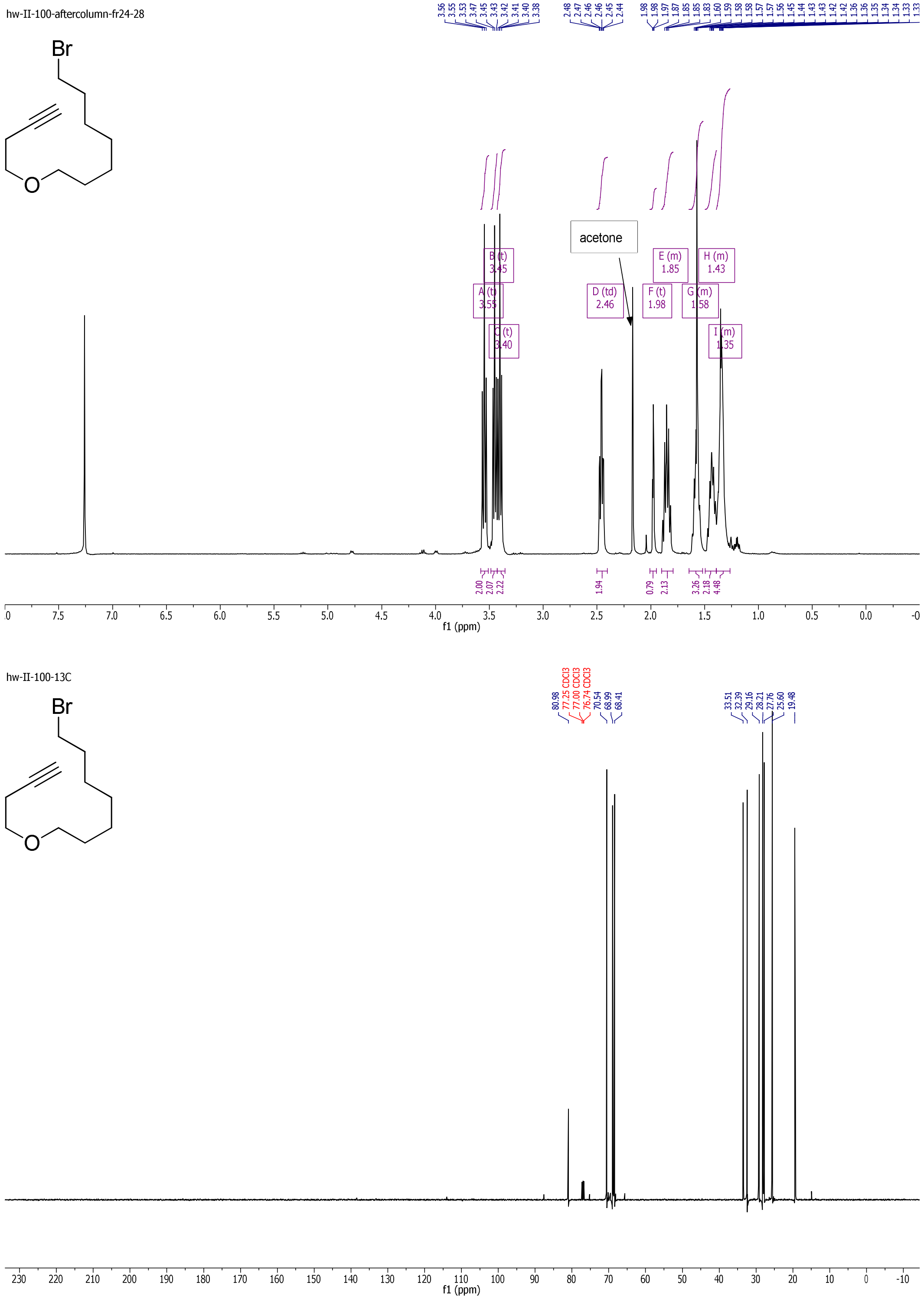
^{1}H- and ^{13}C-NMR spectra of compound **S7b**



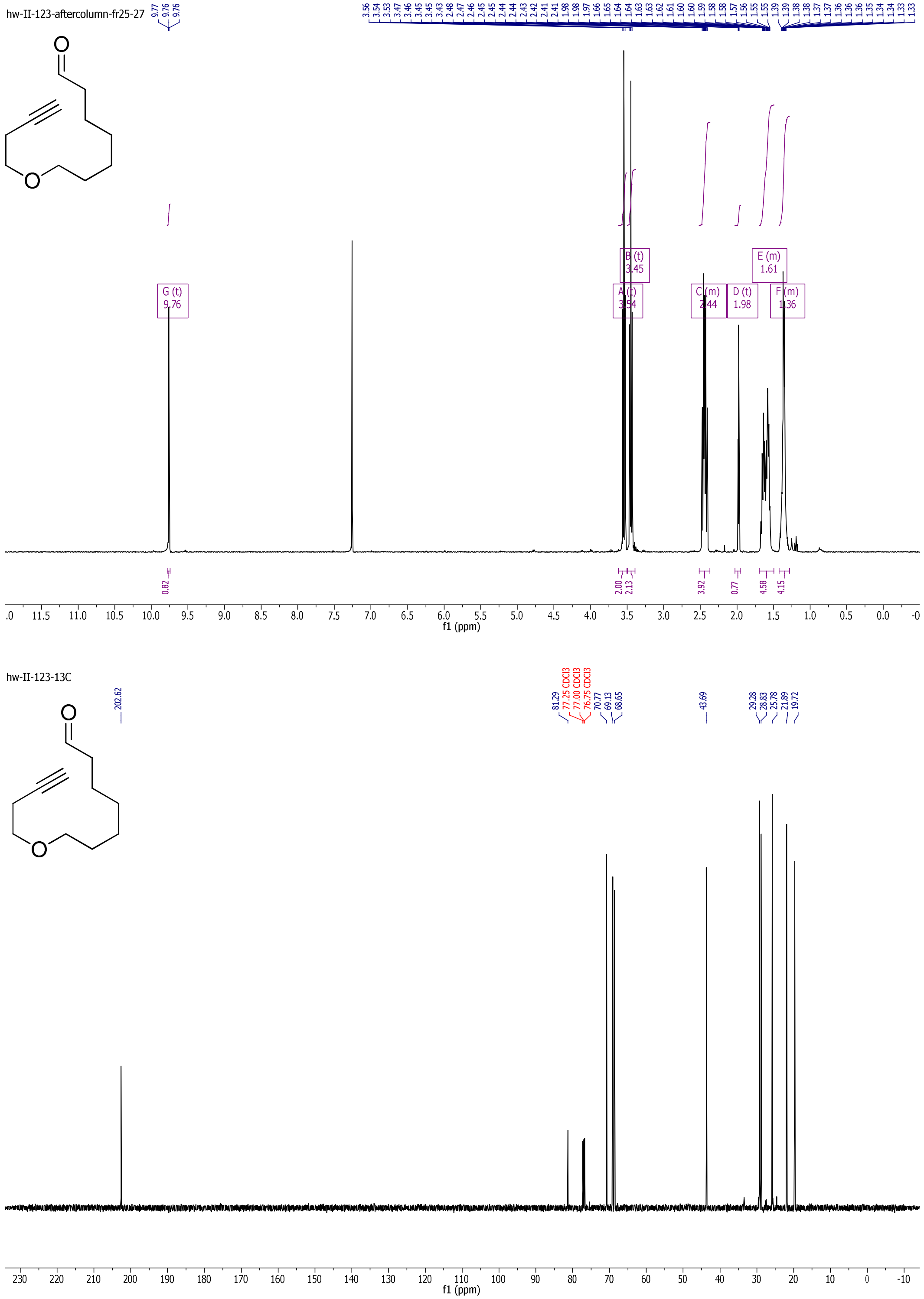
^{1}H- and ^{13}C-NMR spectra of compound **7c**



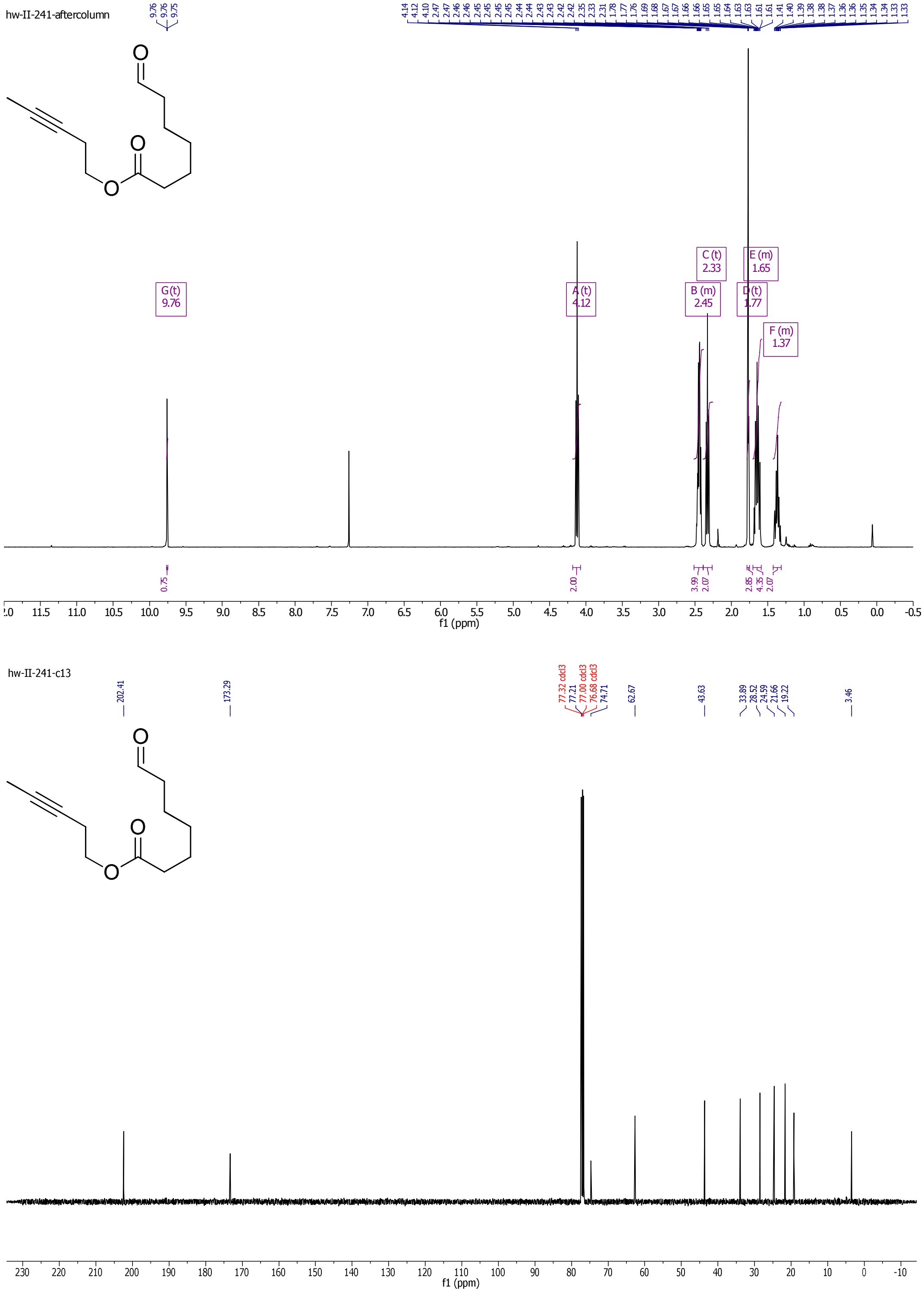
^{1}H- and ^{13}C-NMR spectra of compound **7d**



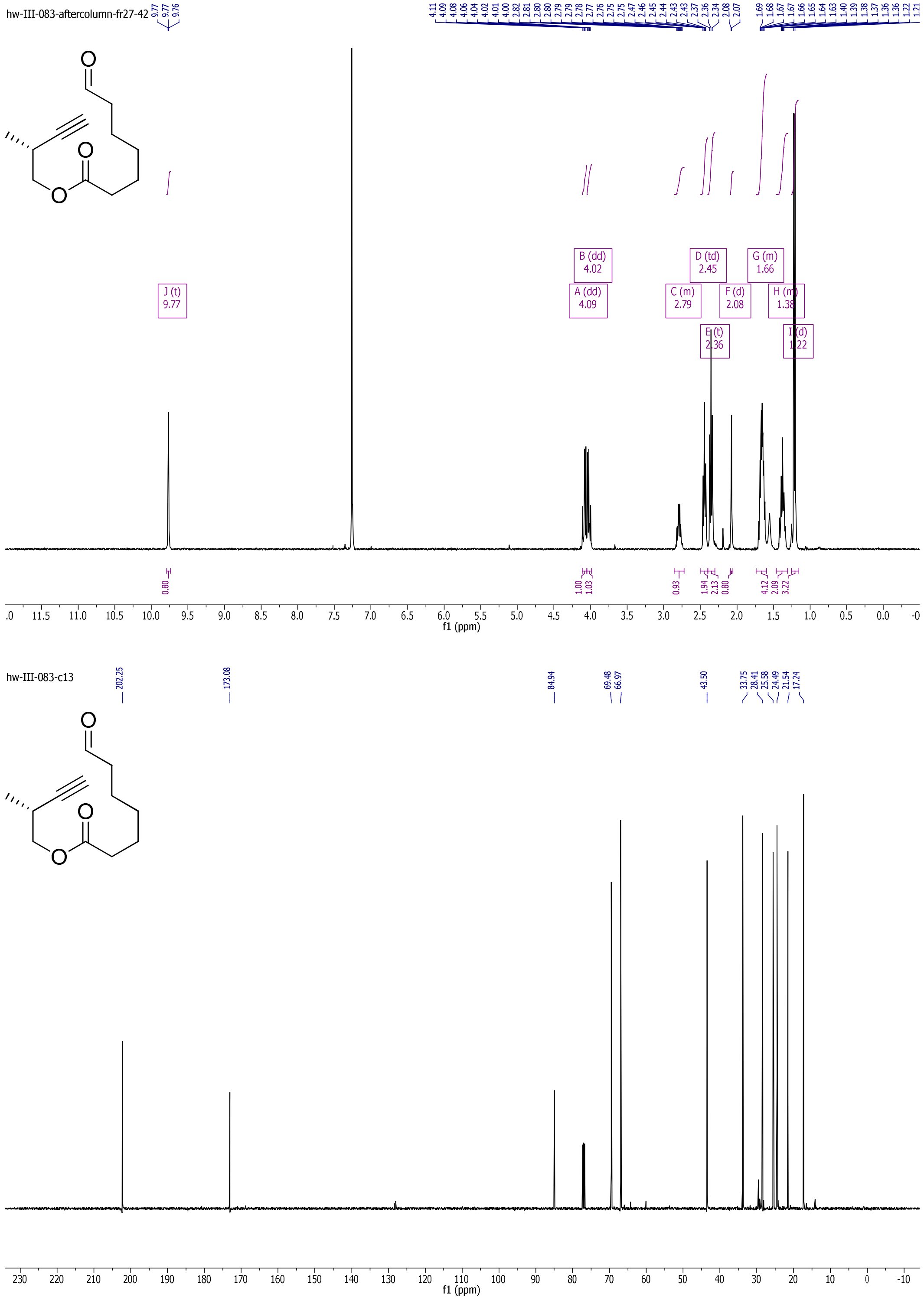
^{1}H- and ^{13}C-NMR spectra of compound **S8**



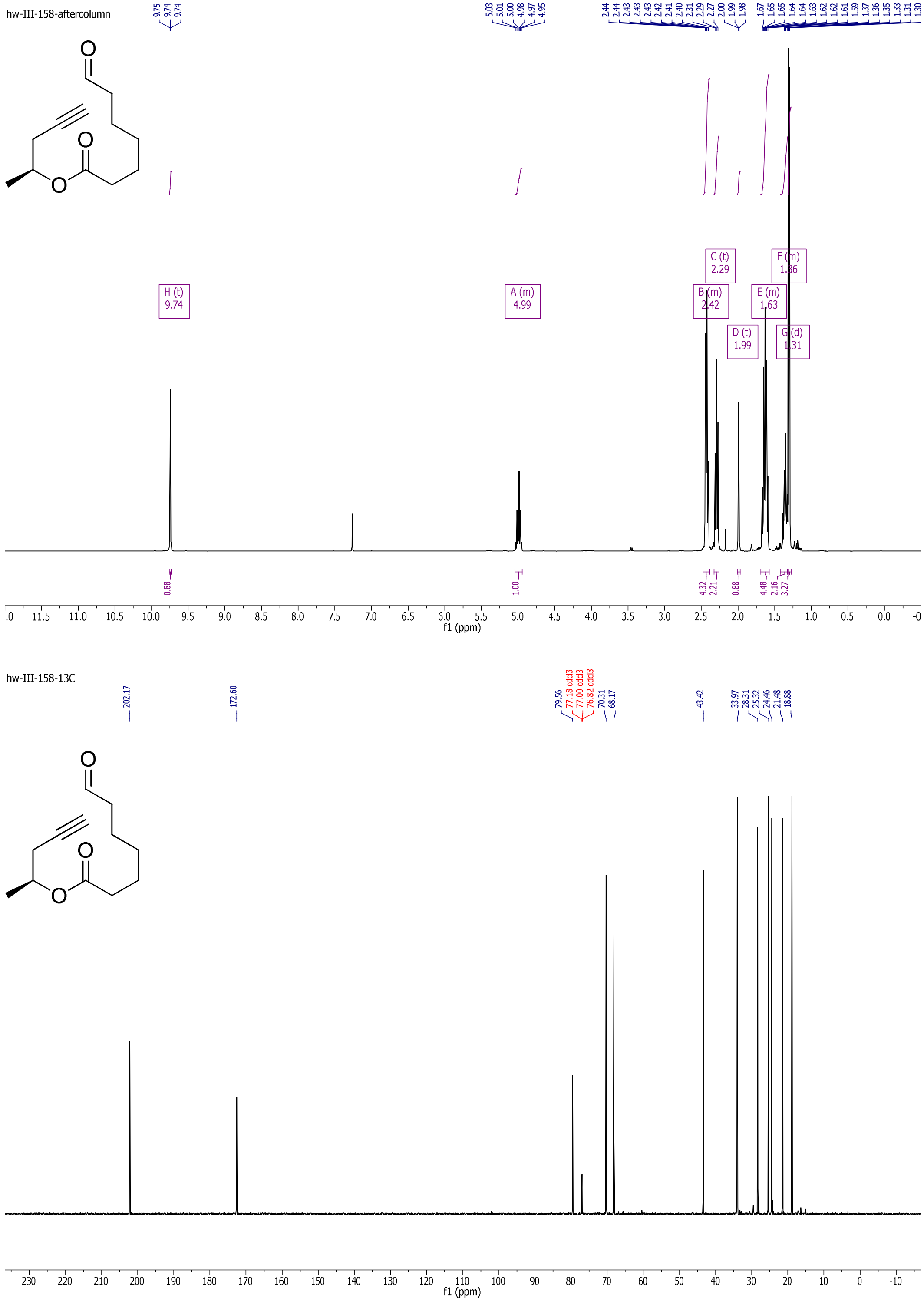
^{1}H- and ^{13}C-NMR spectra of compound **7f**



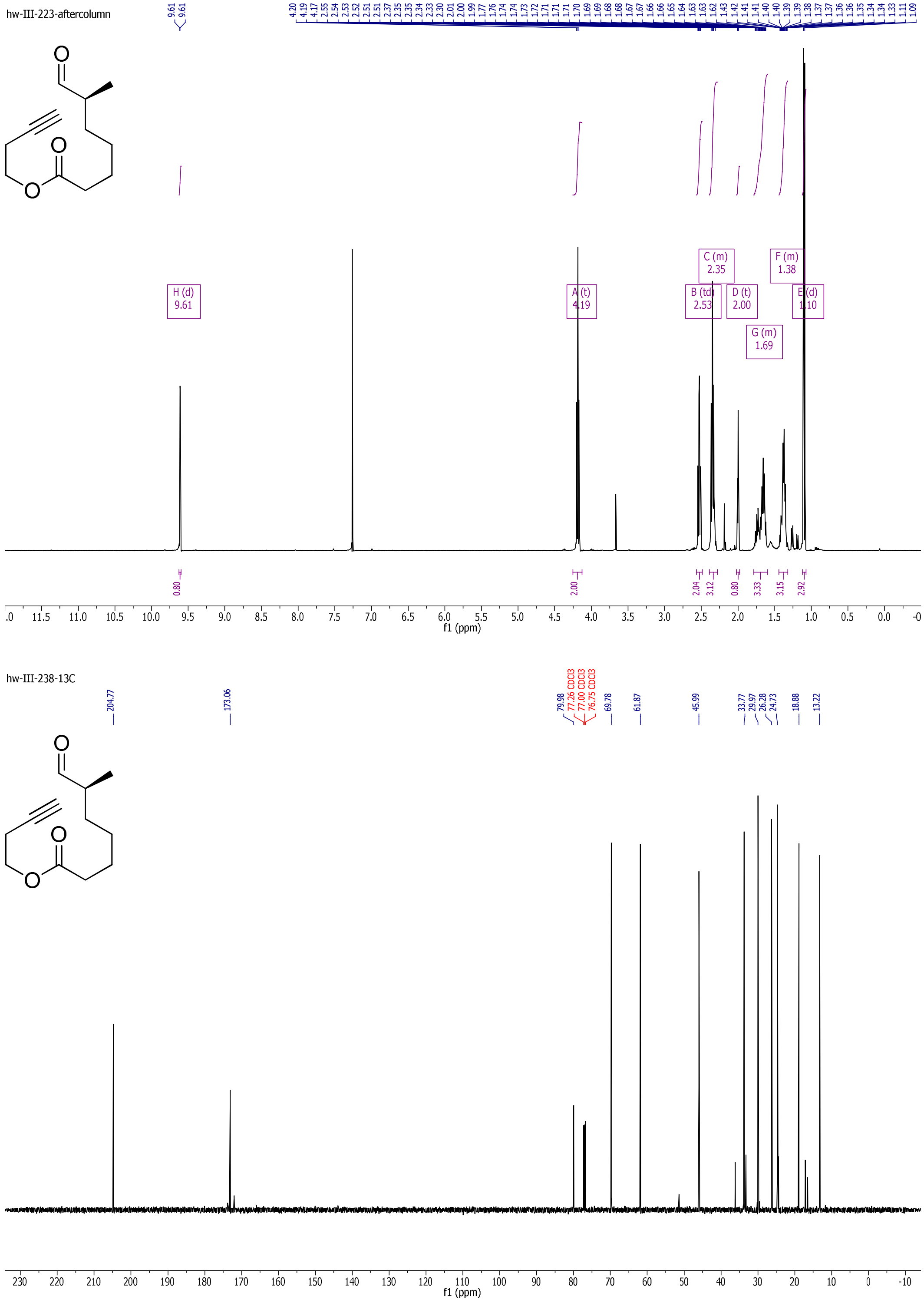
^{1}H- and ^{13}C-NMR spectra of compound **7g**



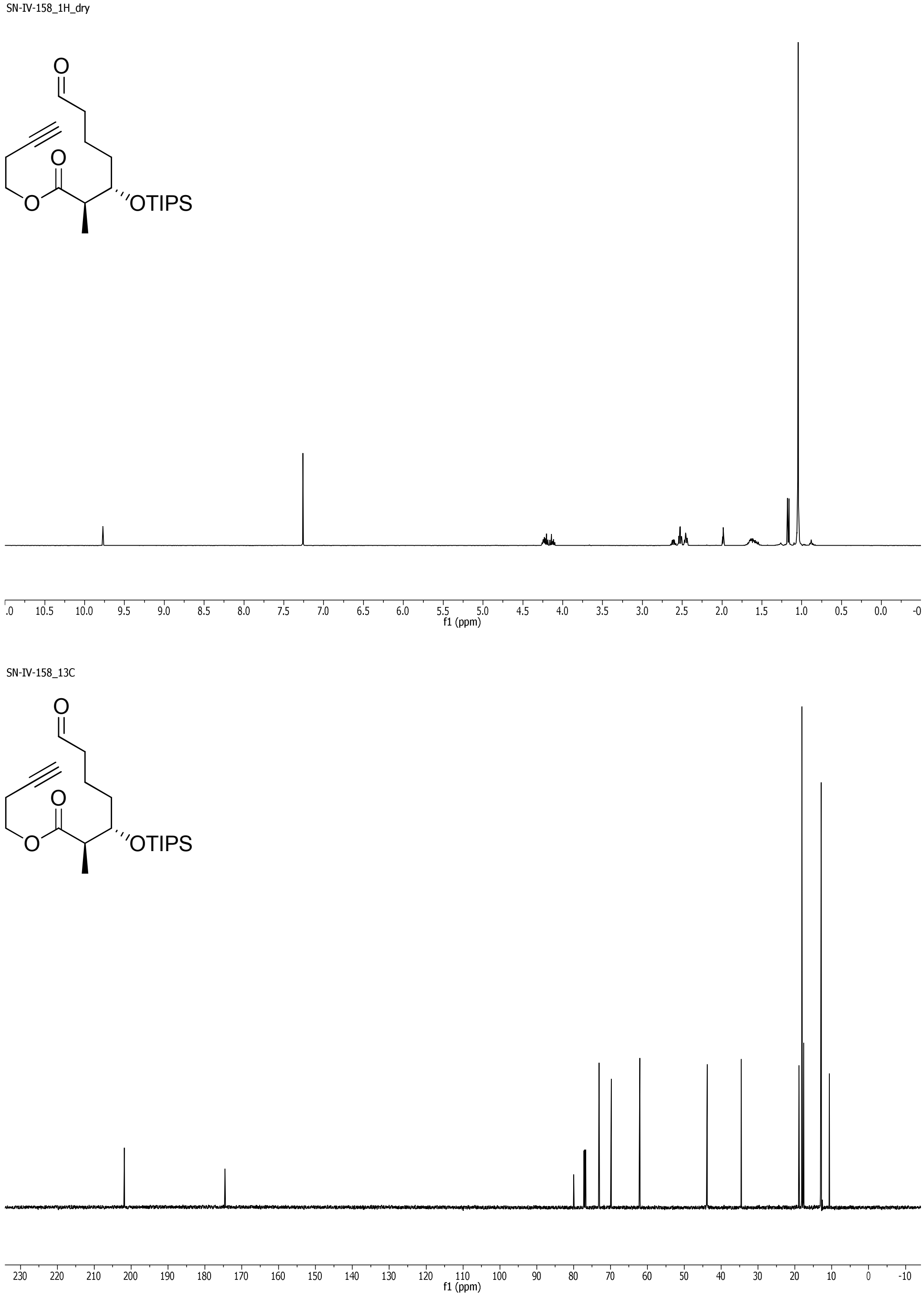
^{1}H- and ^{13}C-NMR spectra of compound **9a**



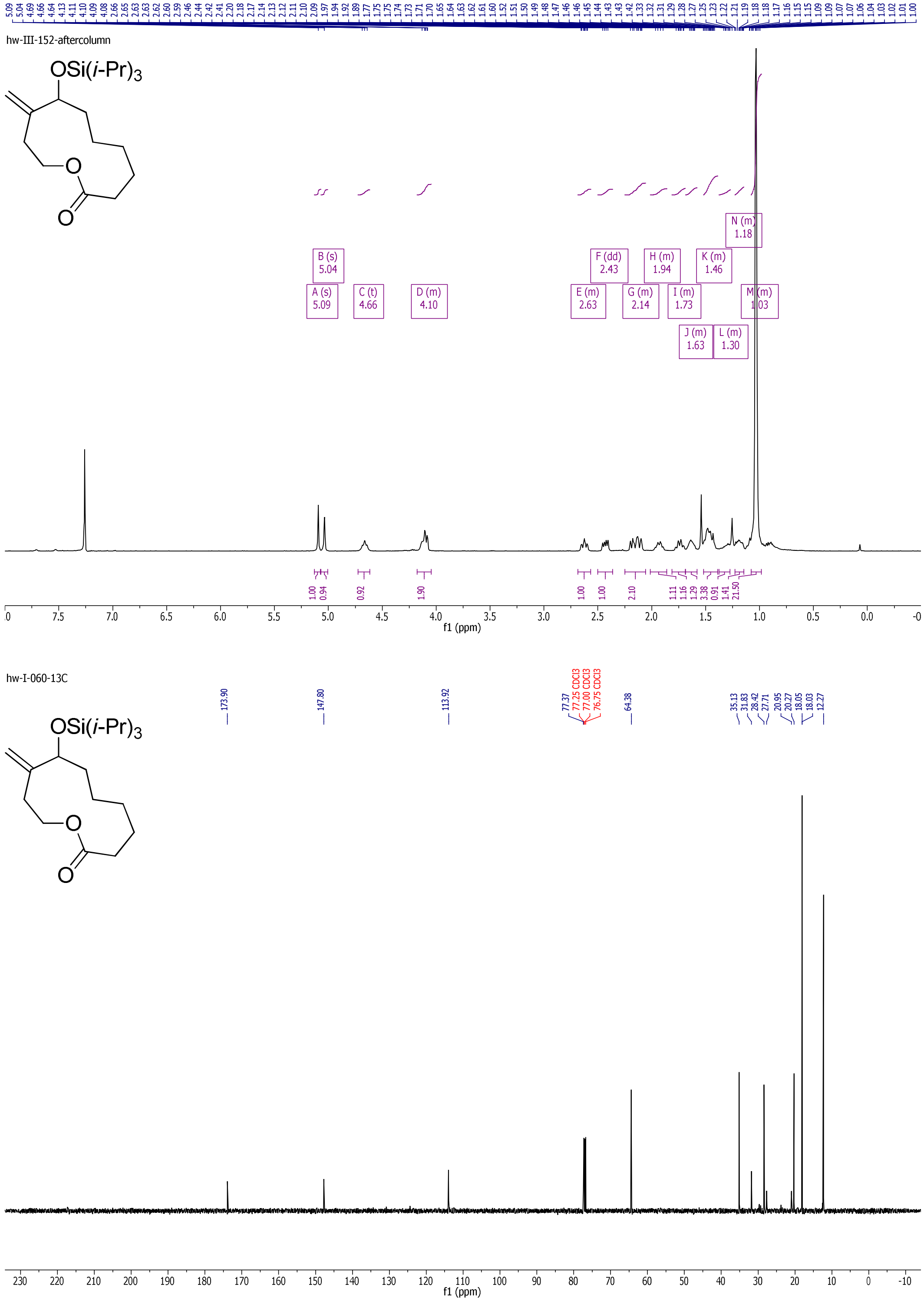
^{1}H- and ^{13}C-NMR spectra of compound **9b**



^{1}H- and ^{13}C-NMR spectra of compound **9c**

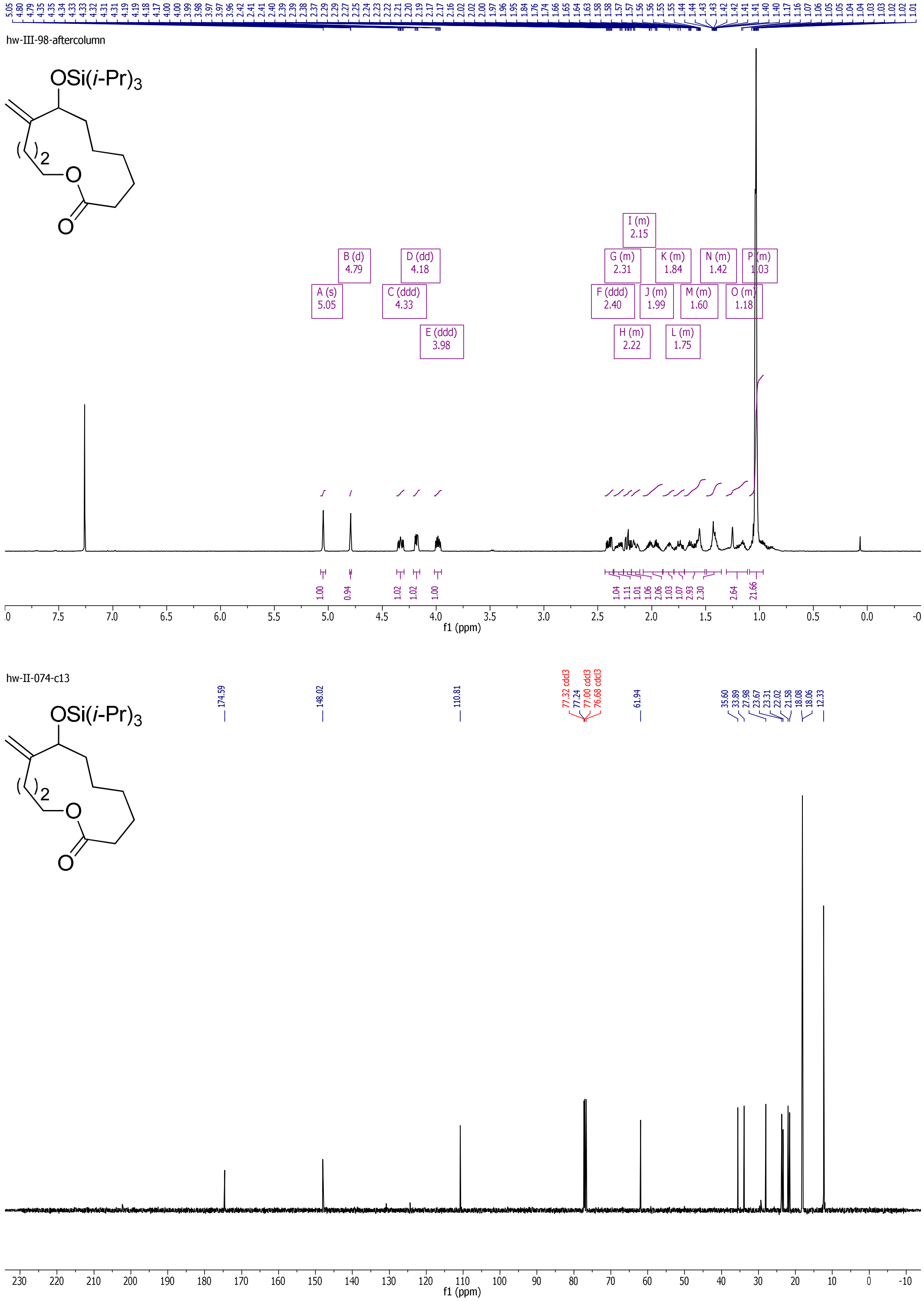


^{1}H- and ^{13}C-NMR spectra of compound **9d**

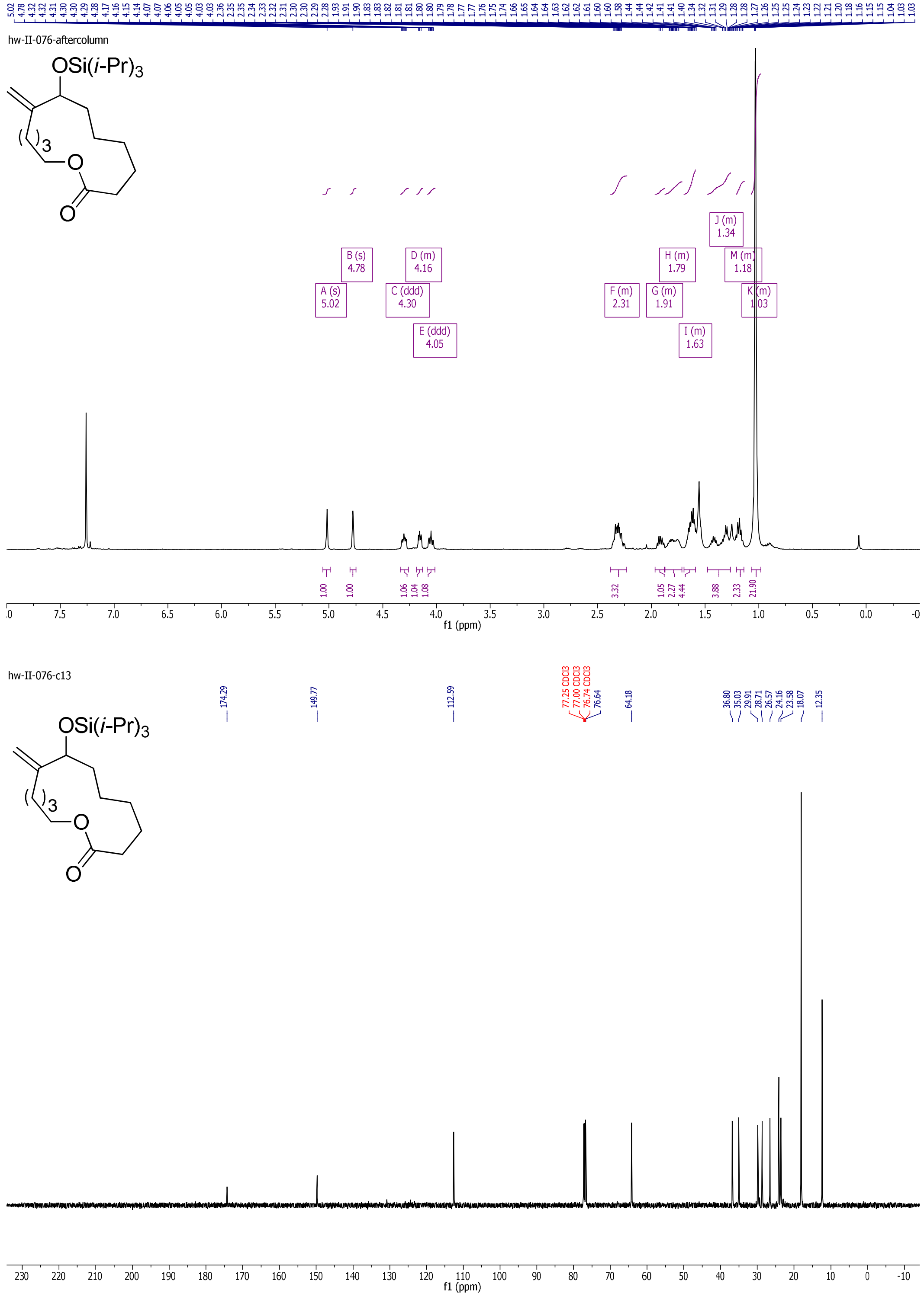


^{1}H- and ^{13}C-NMR spectra of compound **5**

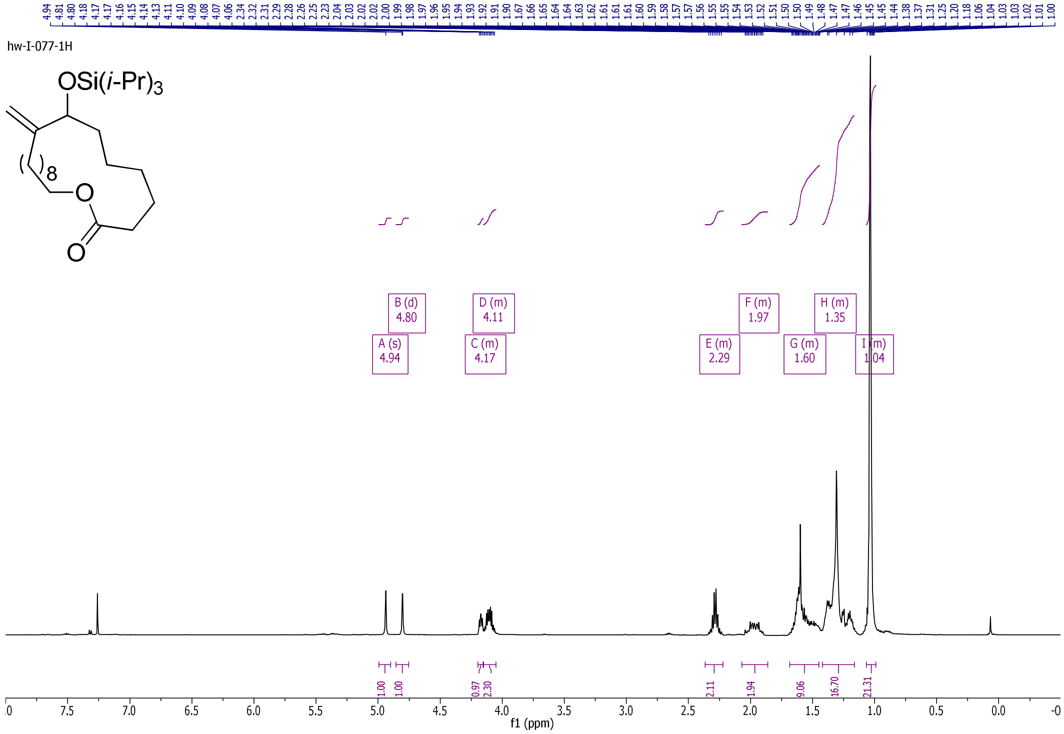
^{1}H- and ^{13}C-NMR spectra of compound **8a**

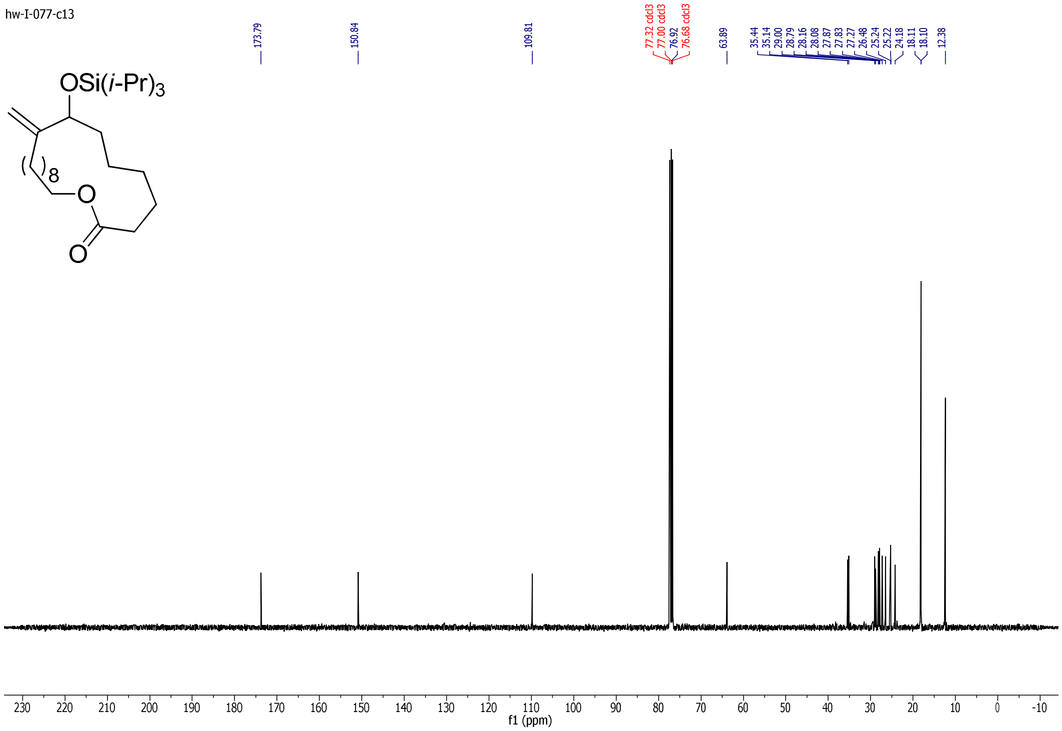


^{1}H- and ^{13}C-NMR spectra of compound **8b**

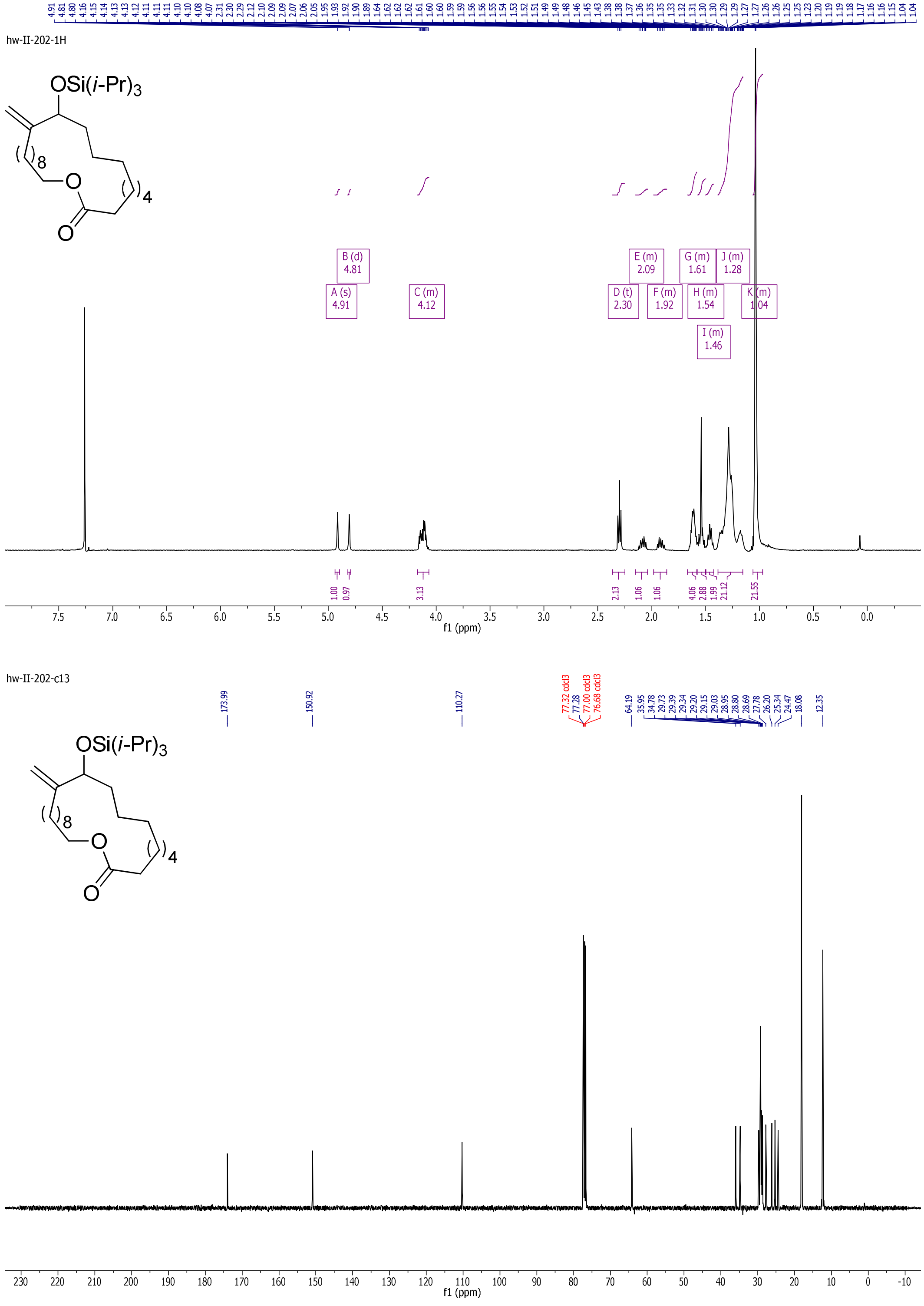


^{1}H- and ^{13}C-NMR spectra of compound **8c**

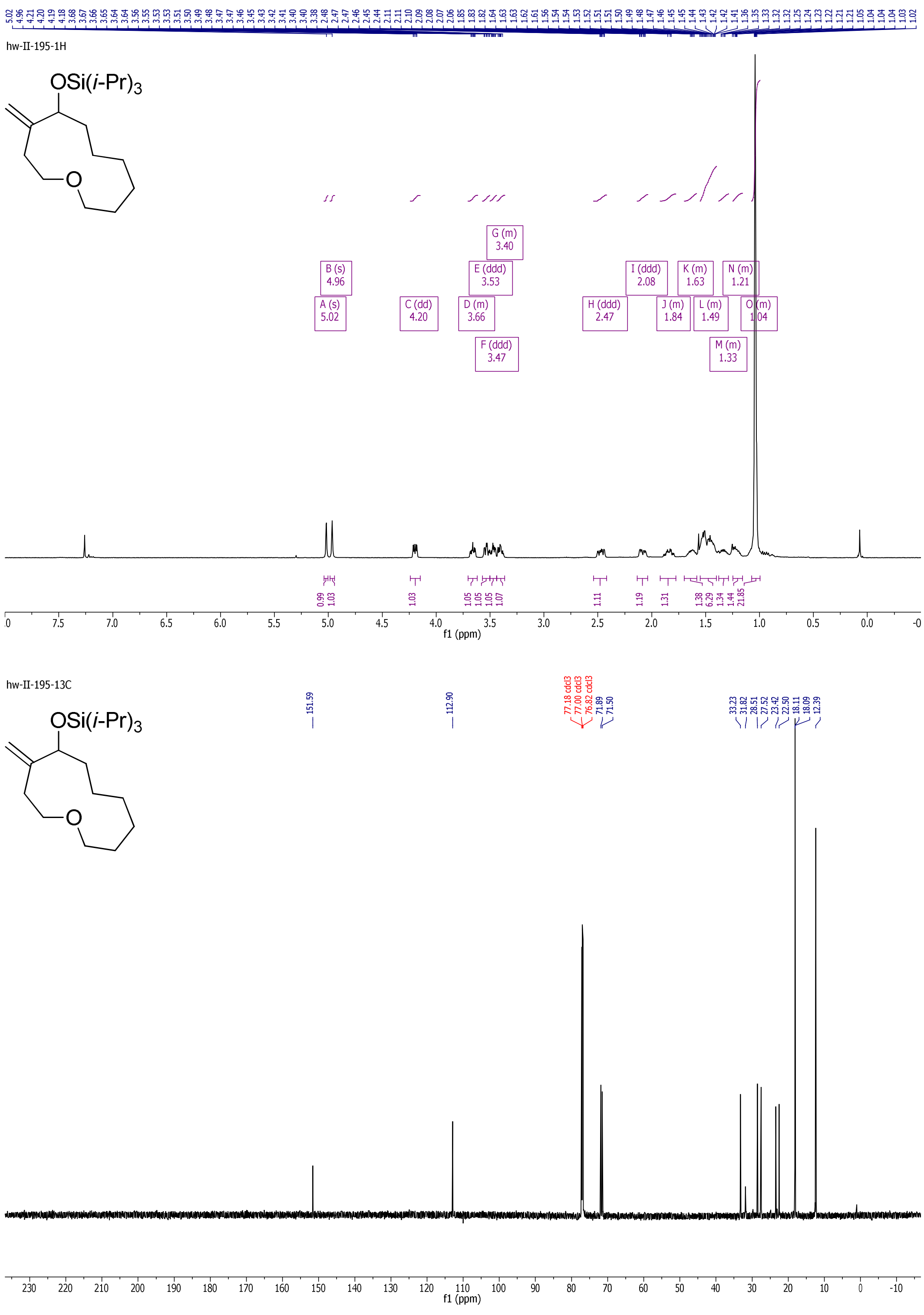




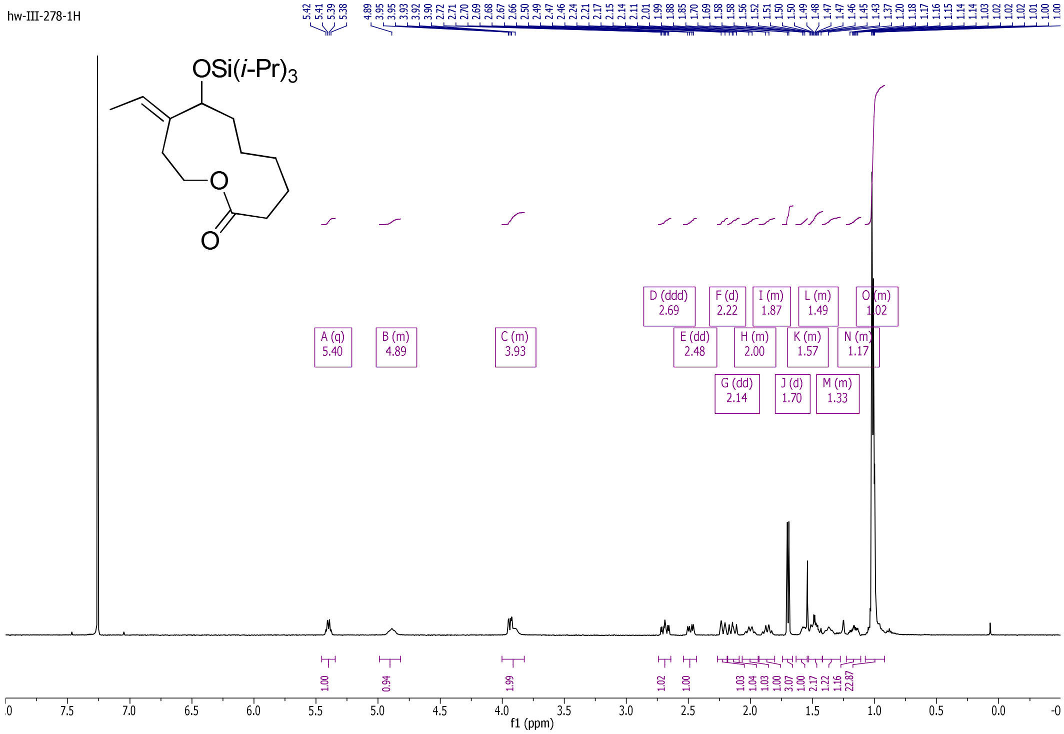
^{1}H- and ^{13}C-NMR spectra of compound **8d**

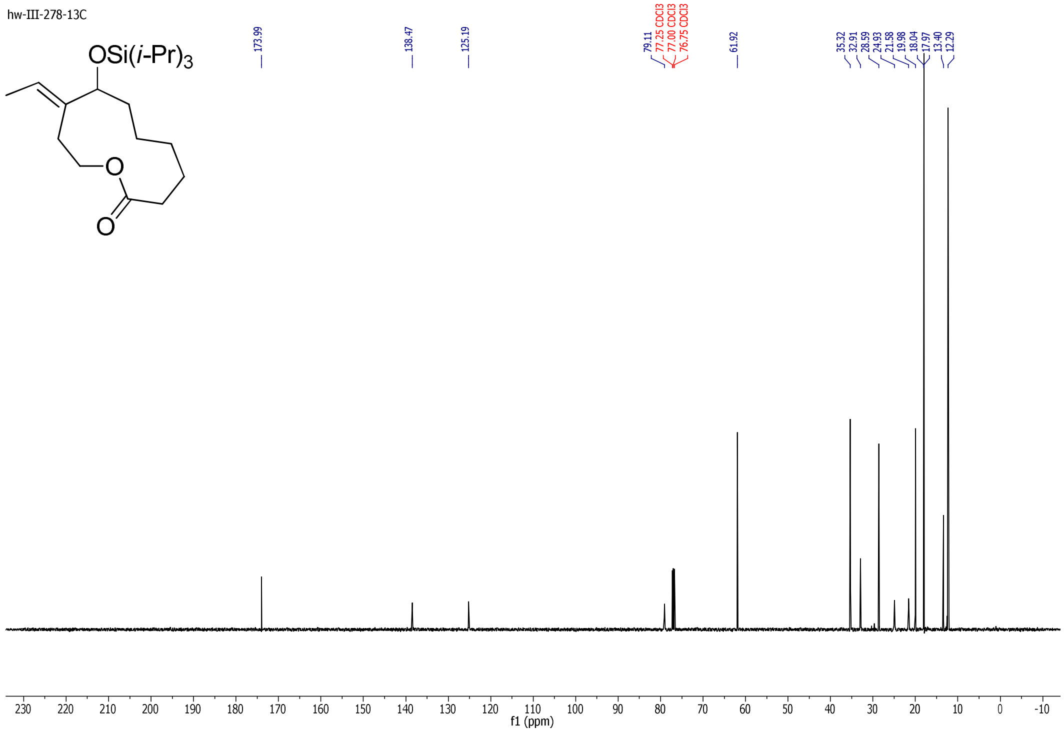


^{1}H- and ^{13}C-NMR spectra of compound **8e**

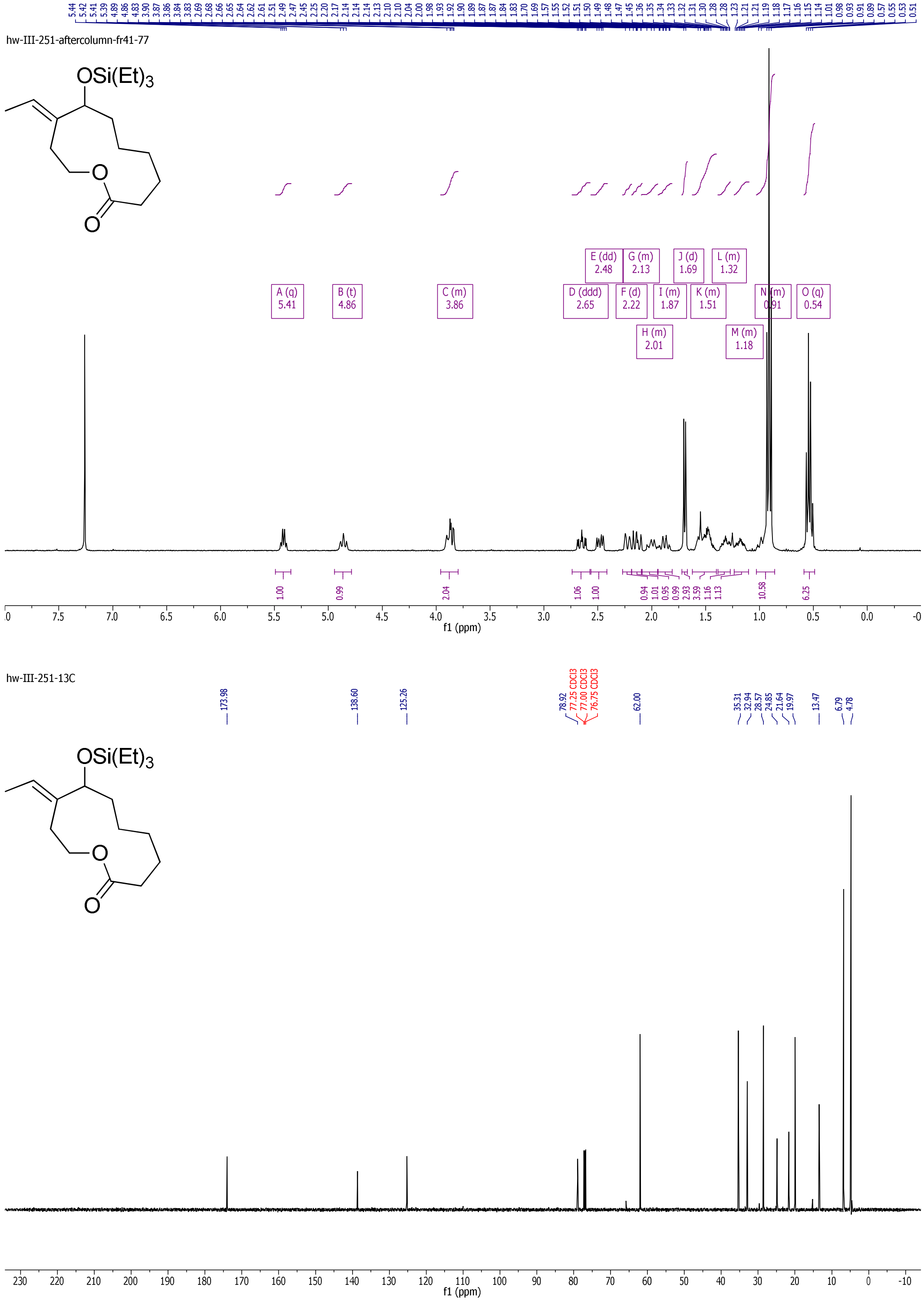


^{1}H- and ^{13}C-NMR spectra of compound **8f**

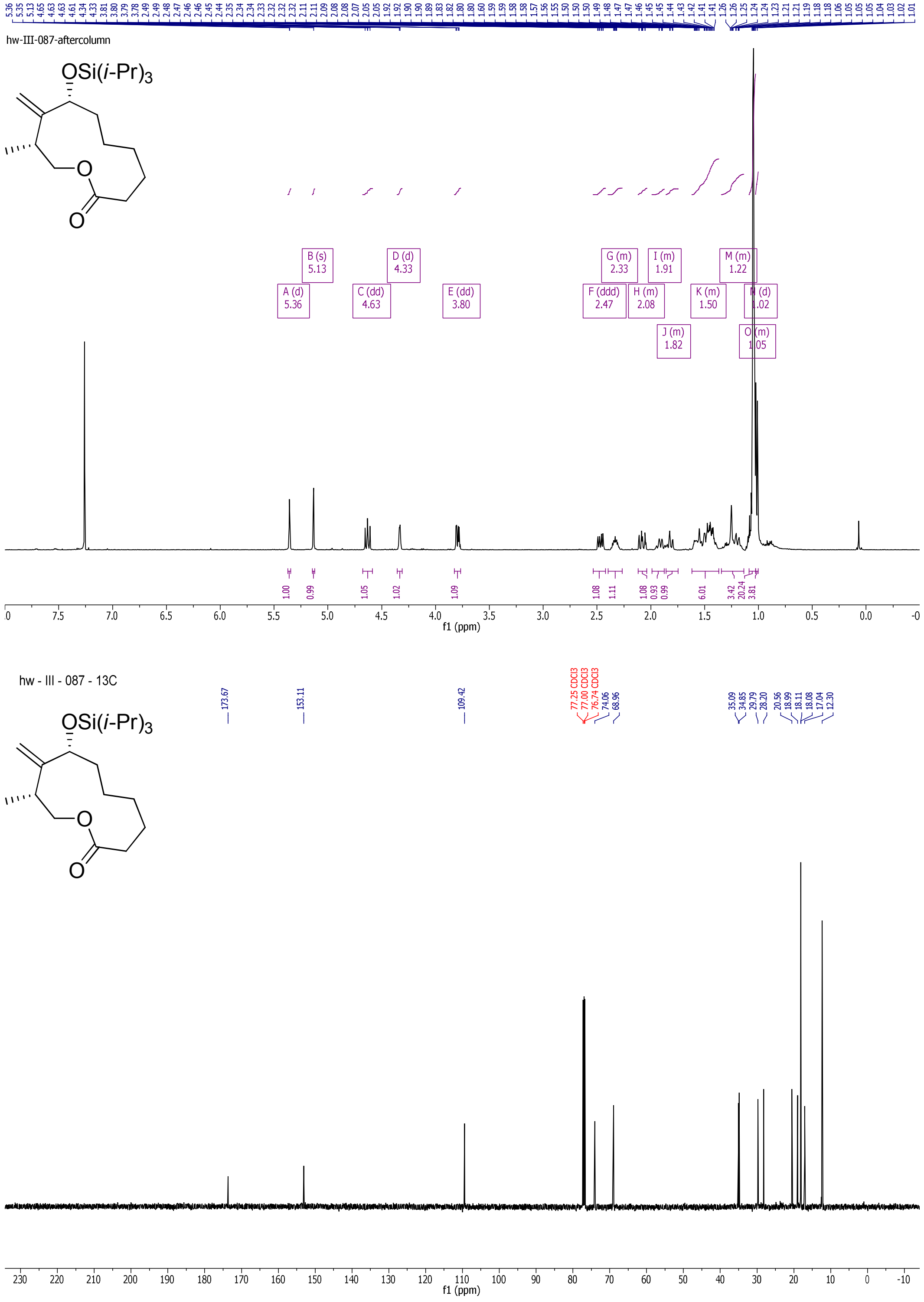




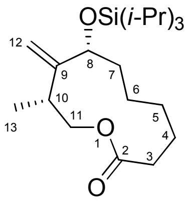
^{1}H- and ^{13}C-NMR spectra of compound **8g**

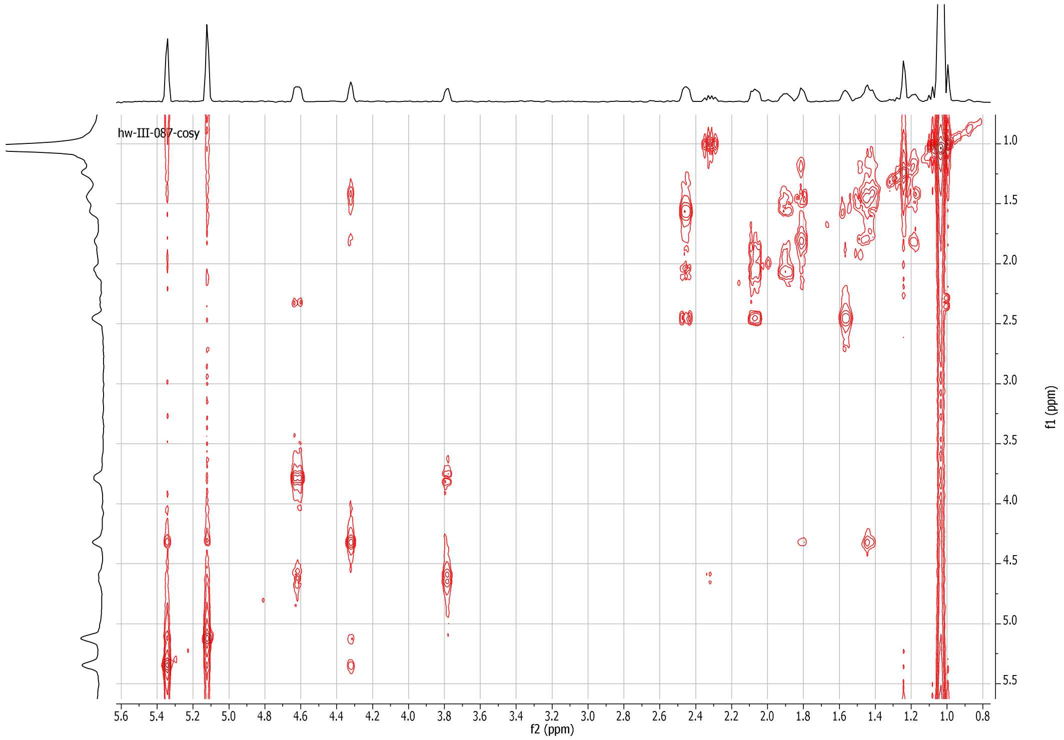


^{1}H- and ^{13}C-NMR spectra of compound **8h**

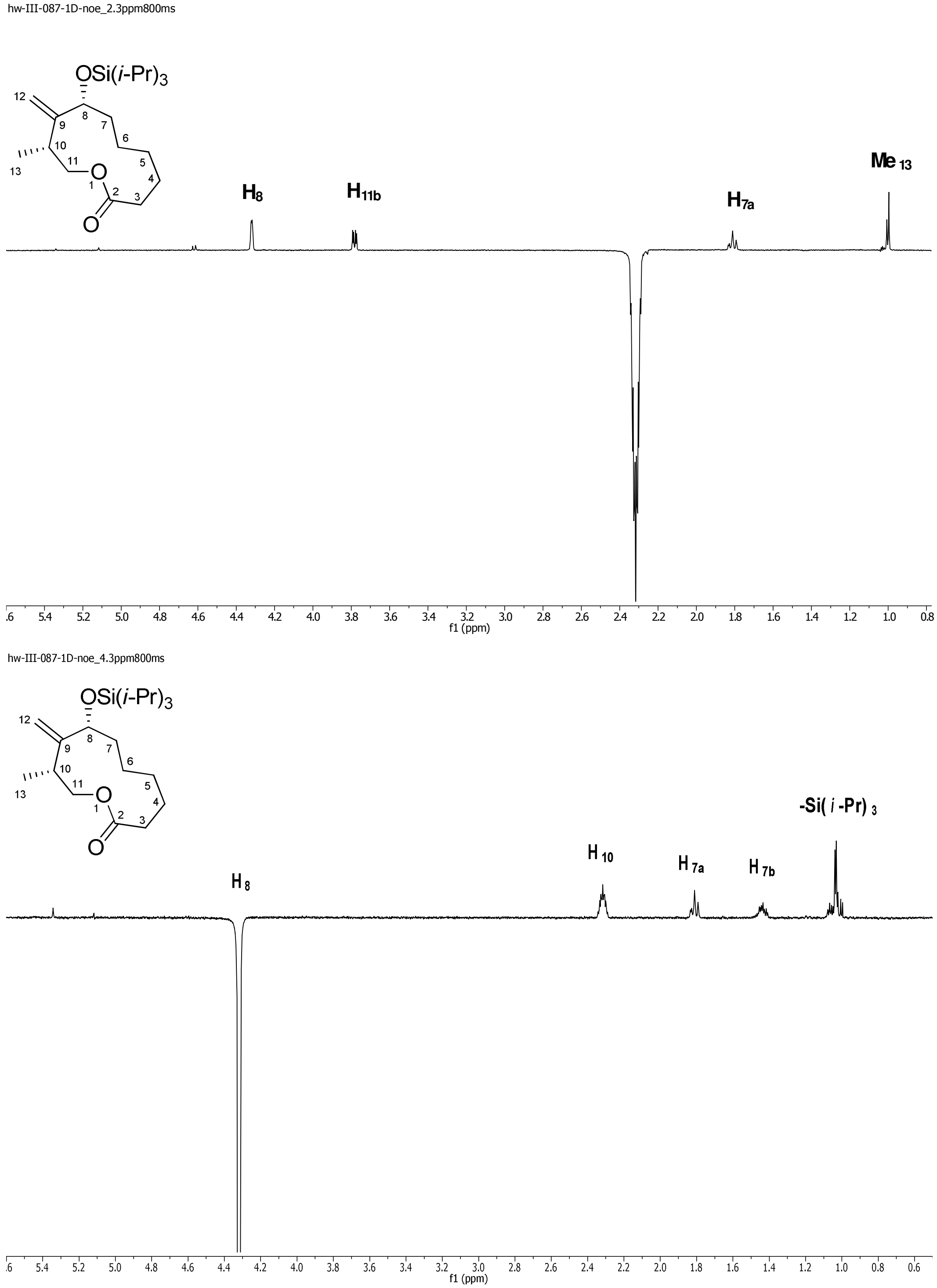


^{1}H- and ^{13}C-NMR spectra of compound **10a**

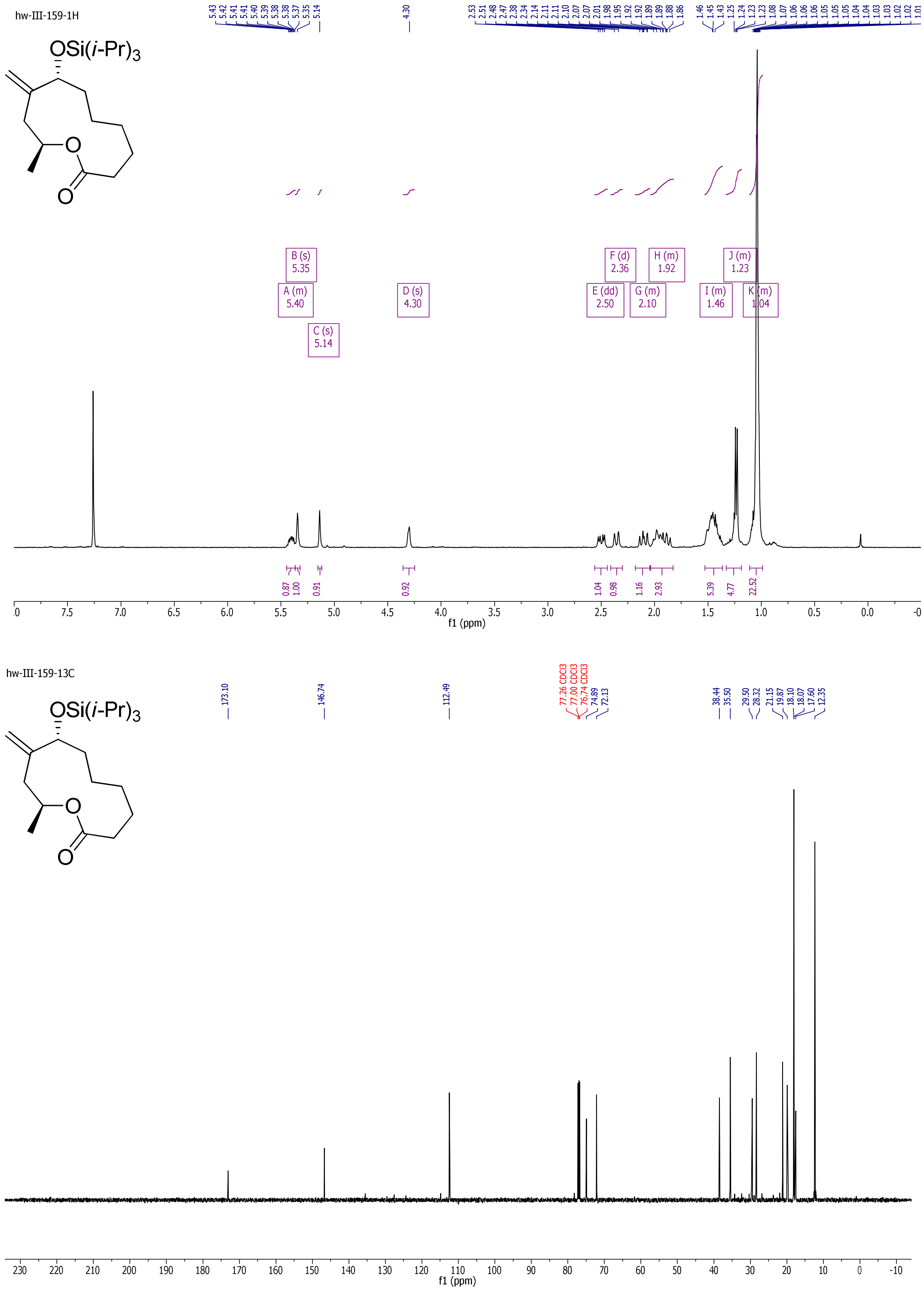




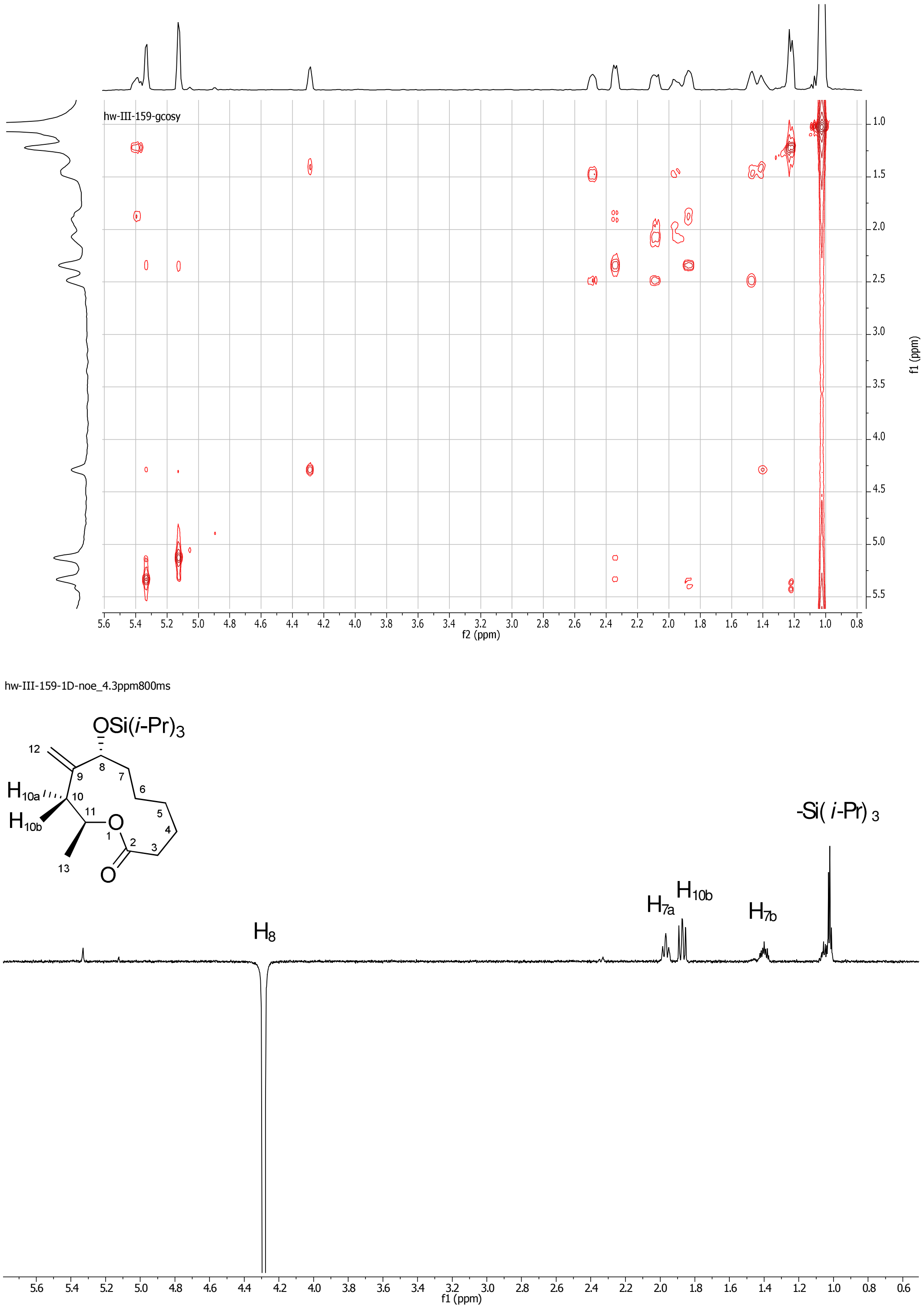
COSY spectra of compound **10a**



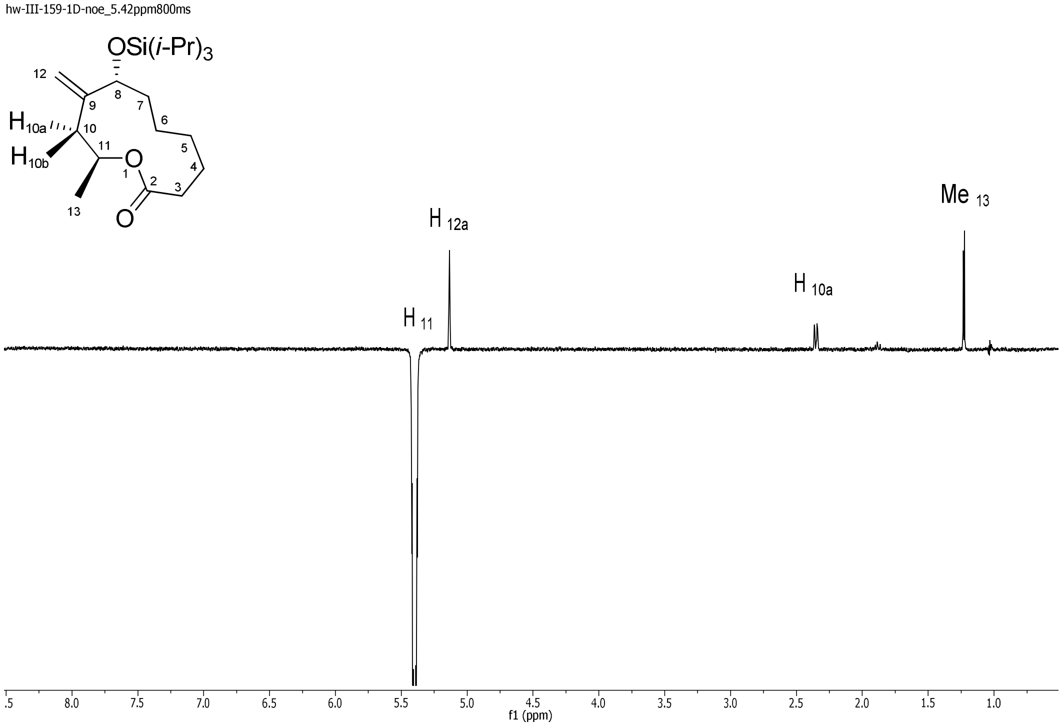
NOE Spectra of compound **10a**

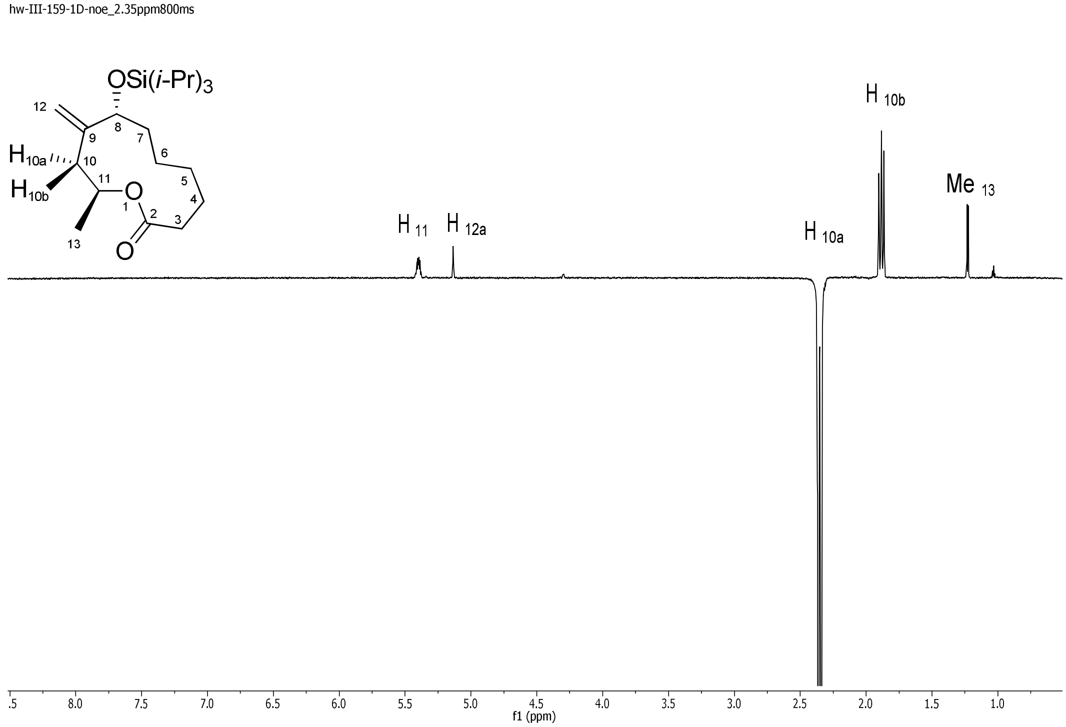


^{1}H- and ^{13}C-NMR spectra of compound **10b**

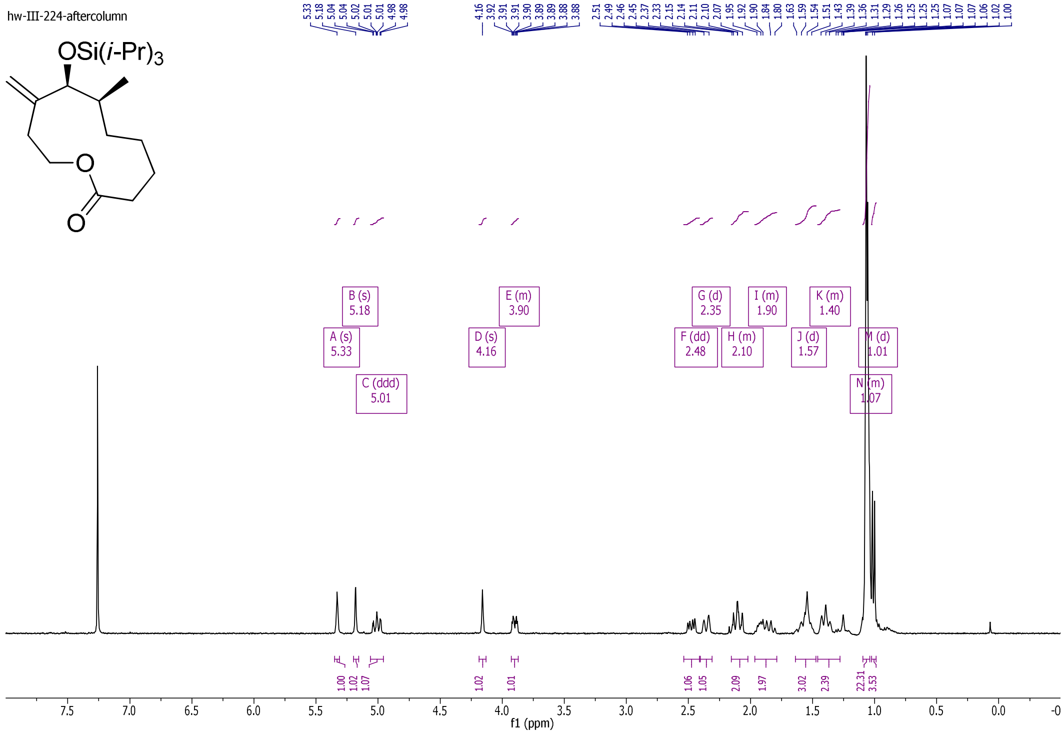


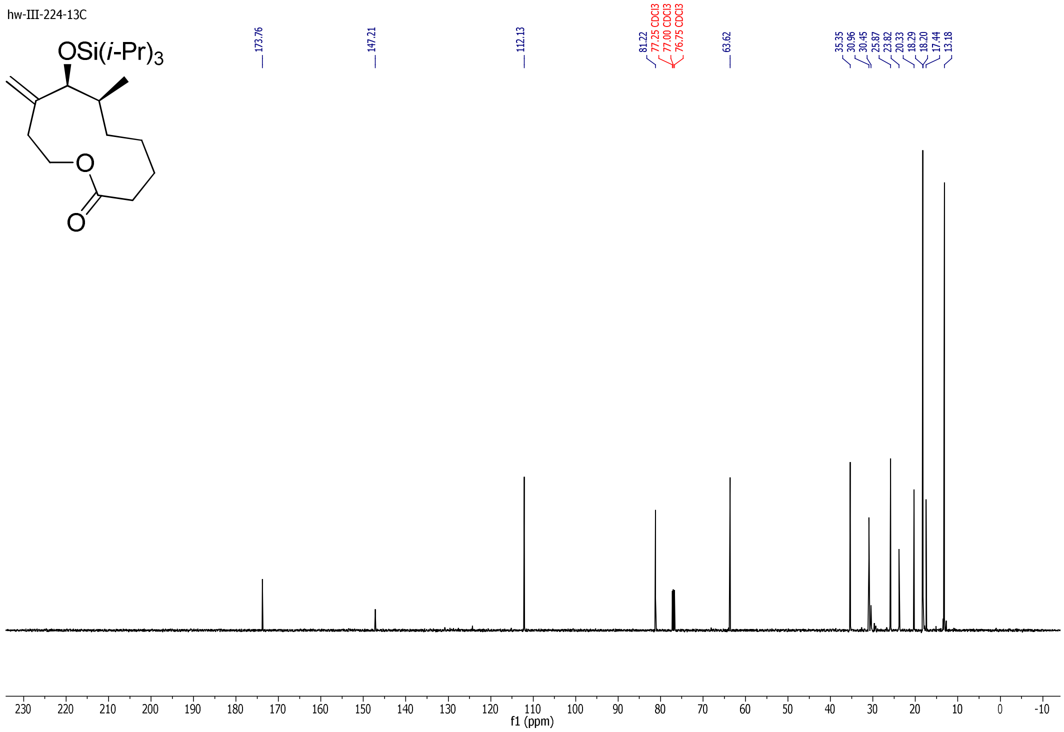
COSY and NOE spectra of compound **10b**



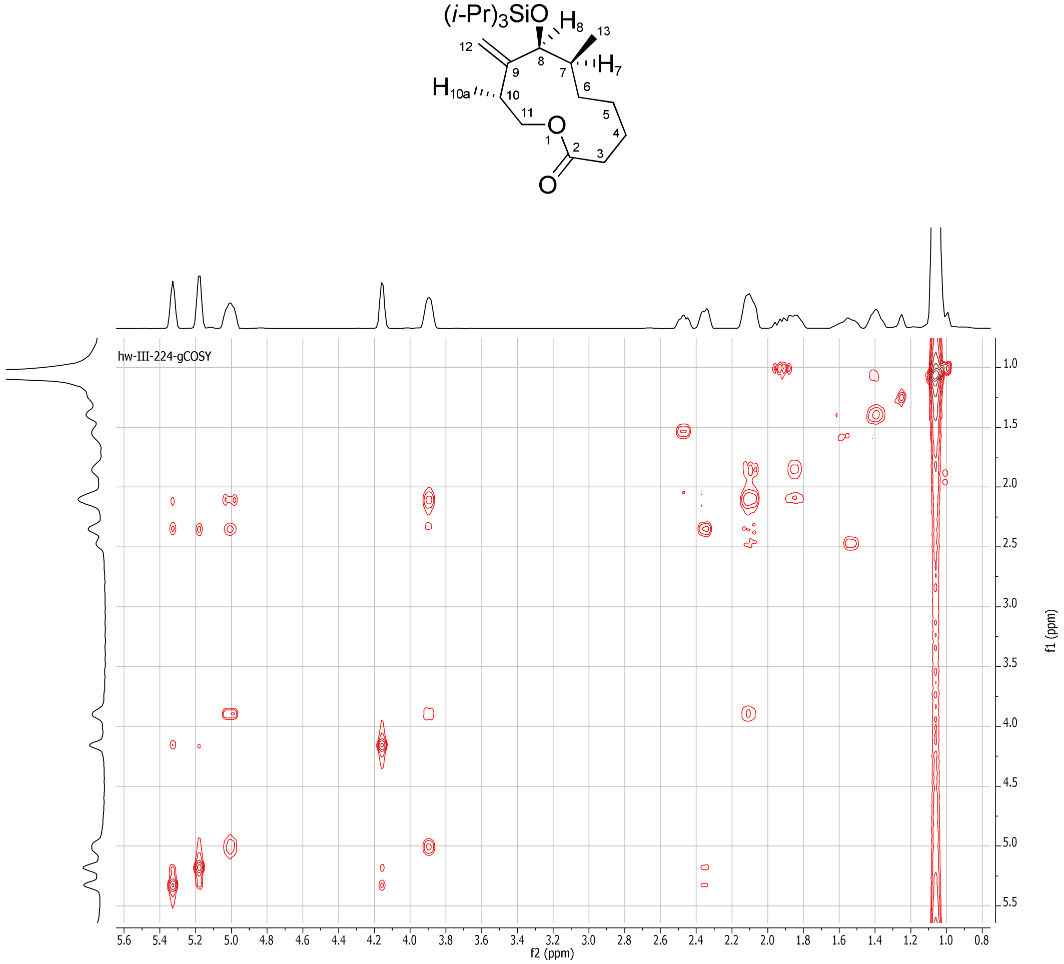


NOE spectra of compound **10b**

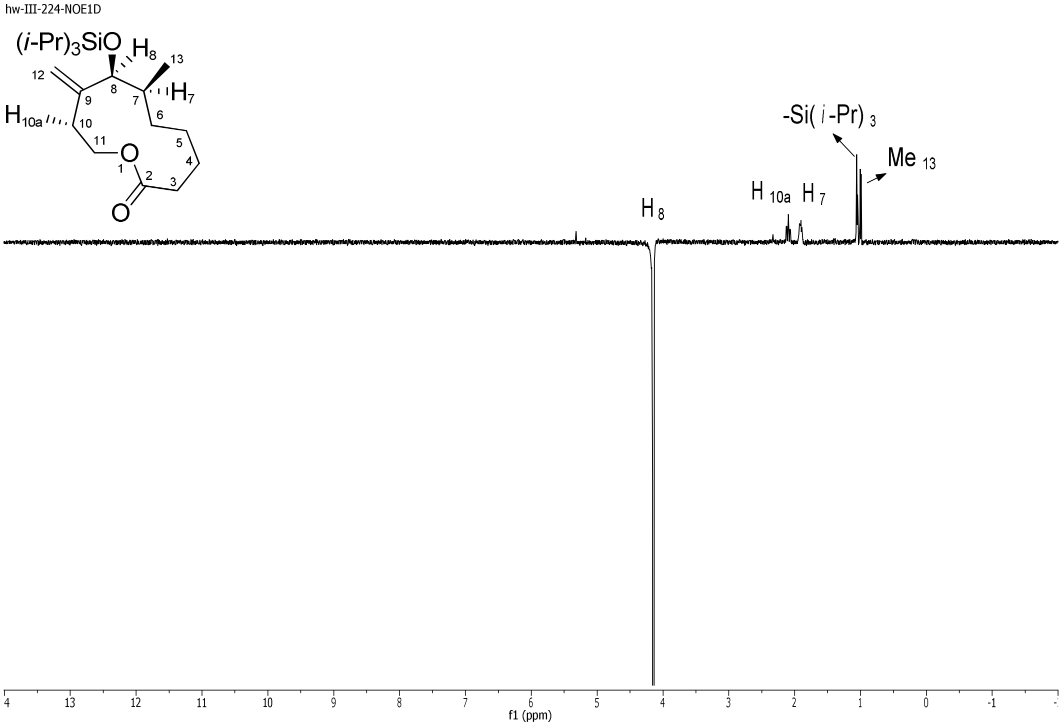


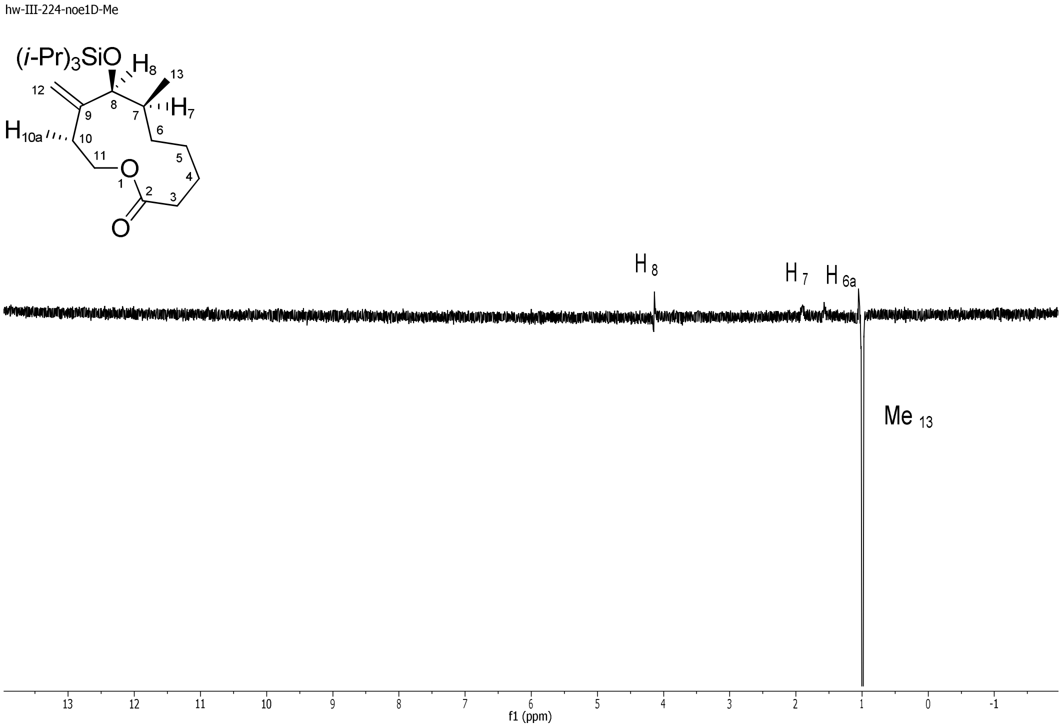


^{1}H- and ^{13}C-NMR spectra of compound **10c**

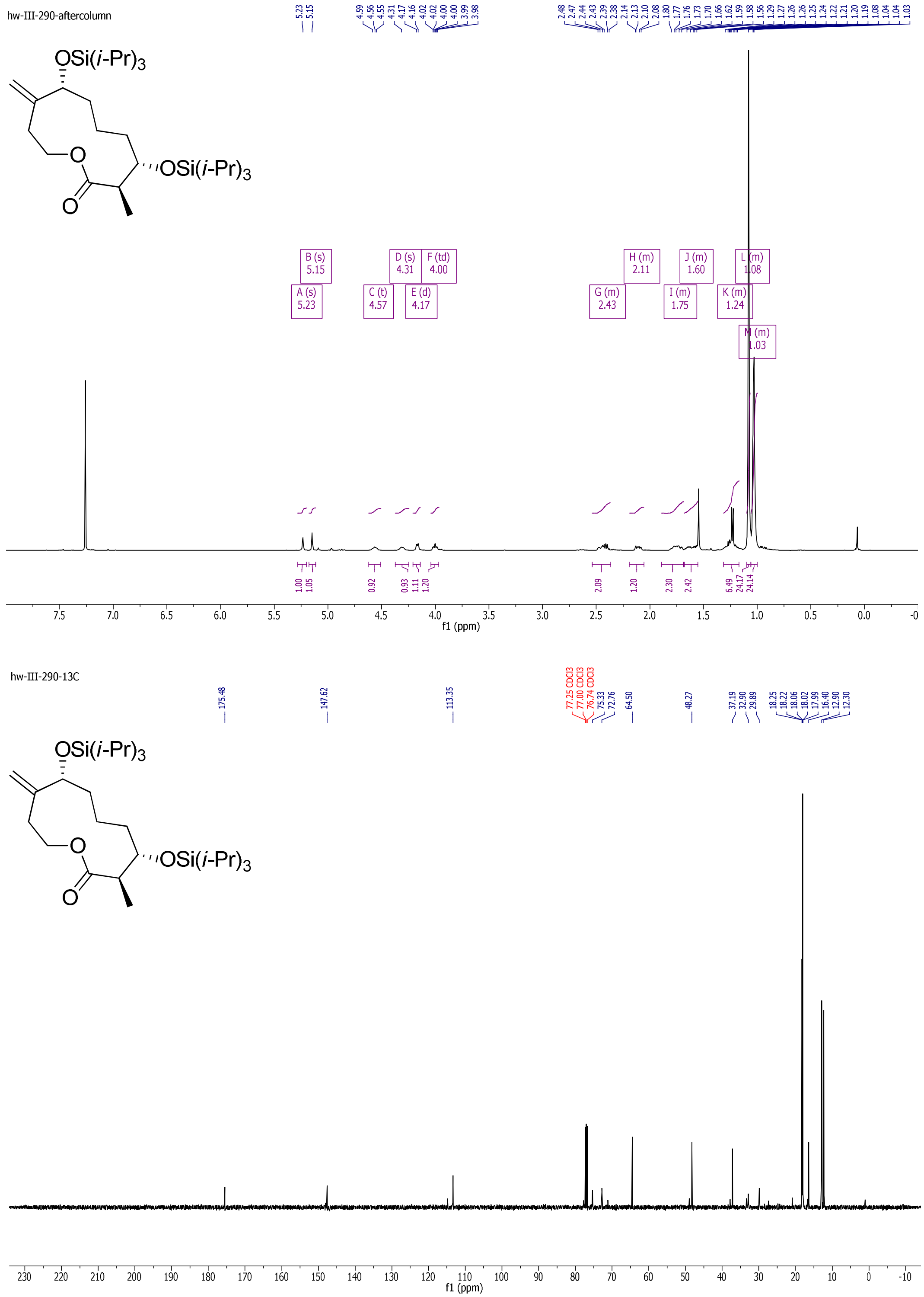


COSY spectrum of compound **10c**

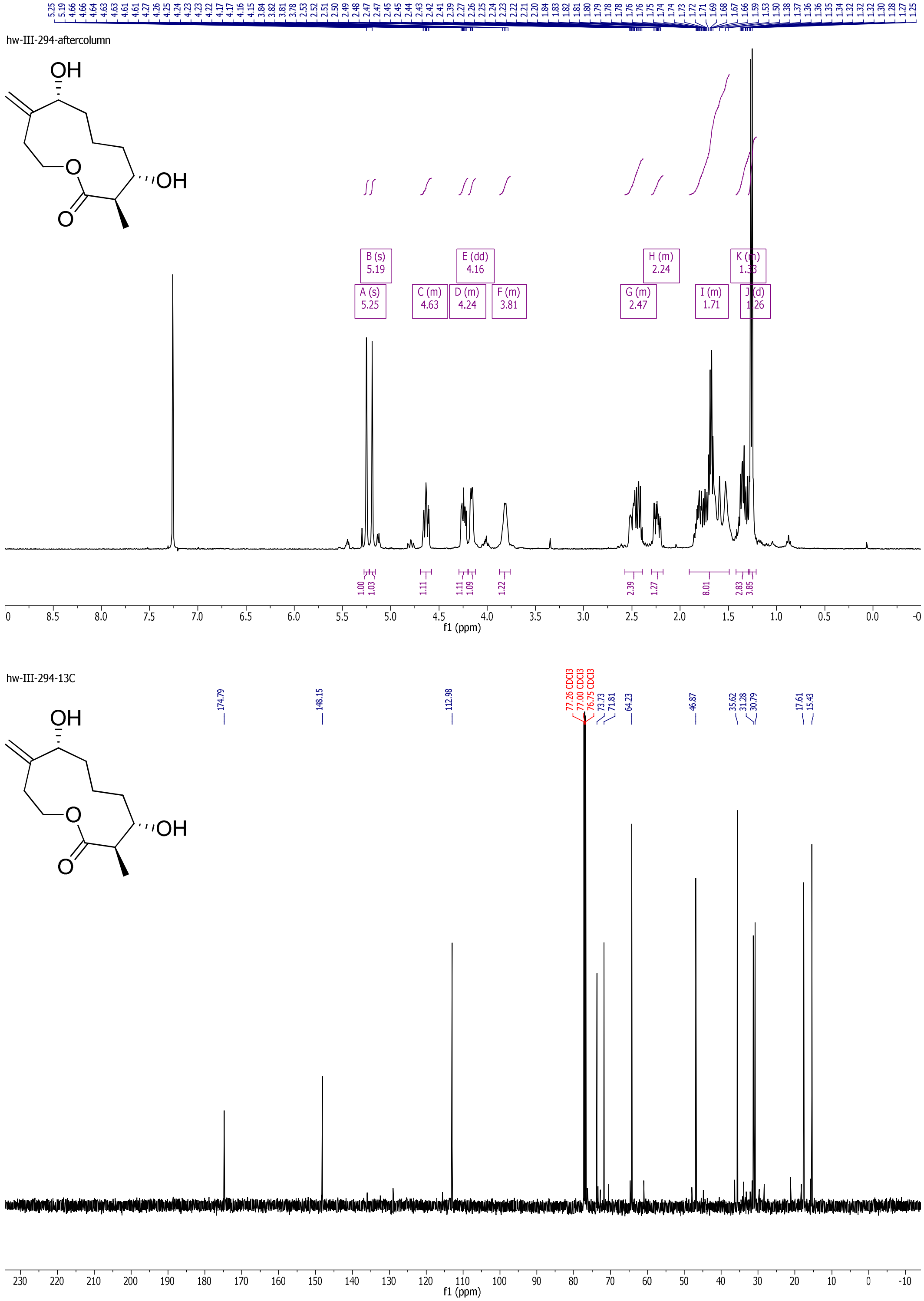




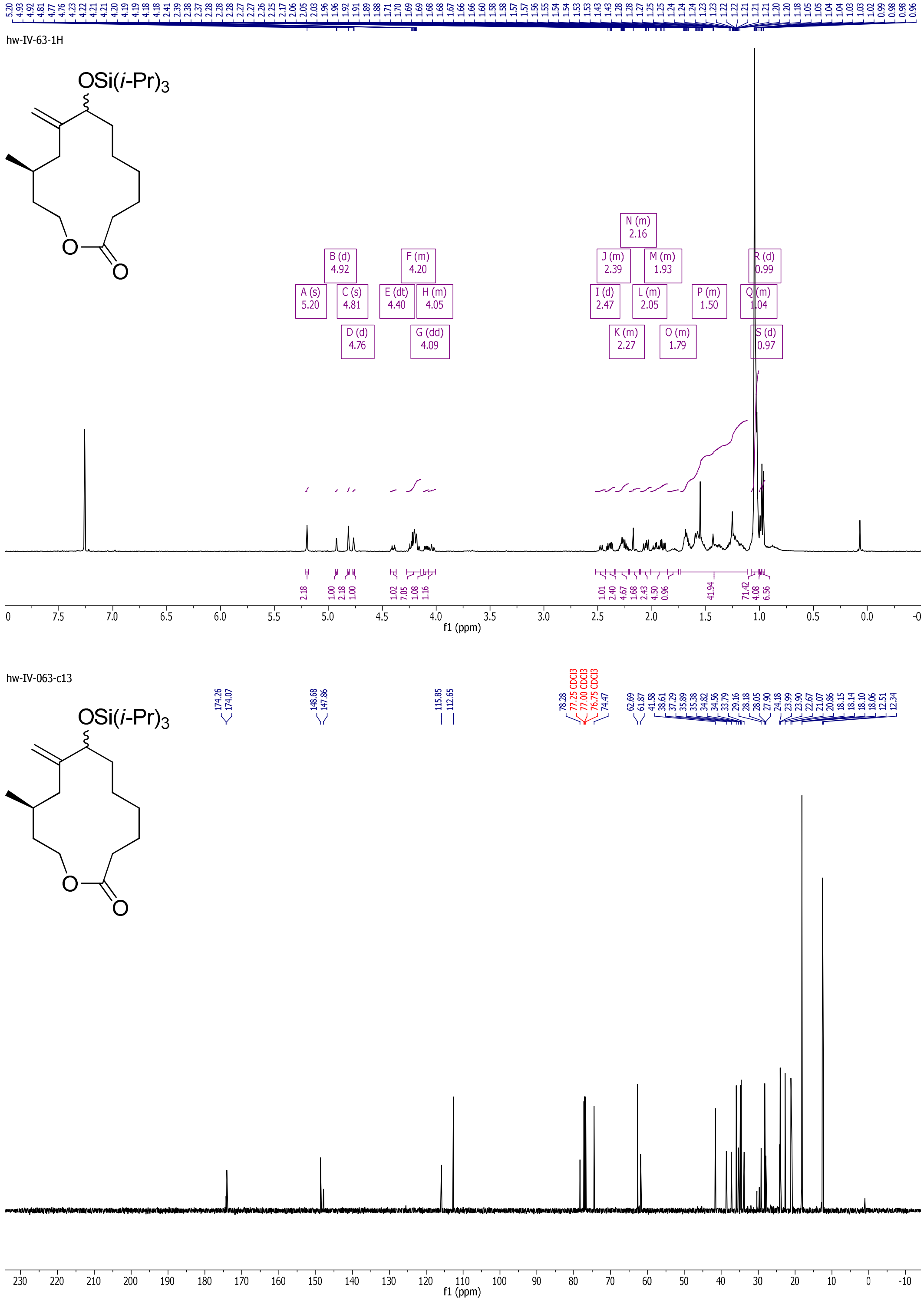
NOE spectra of compound **10c**



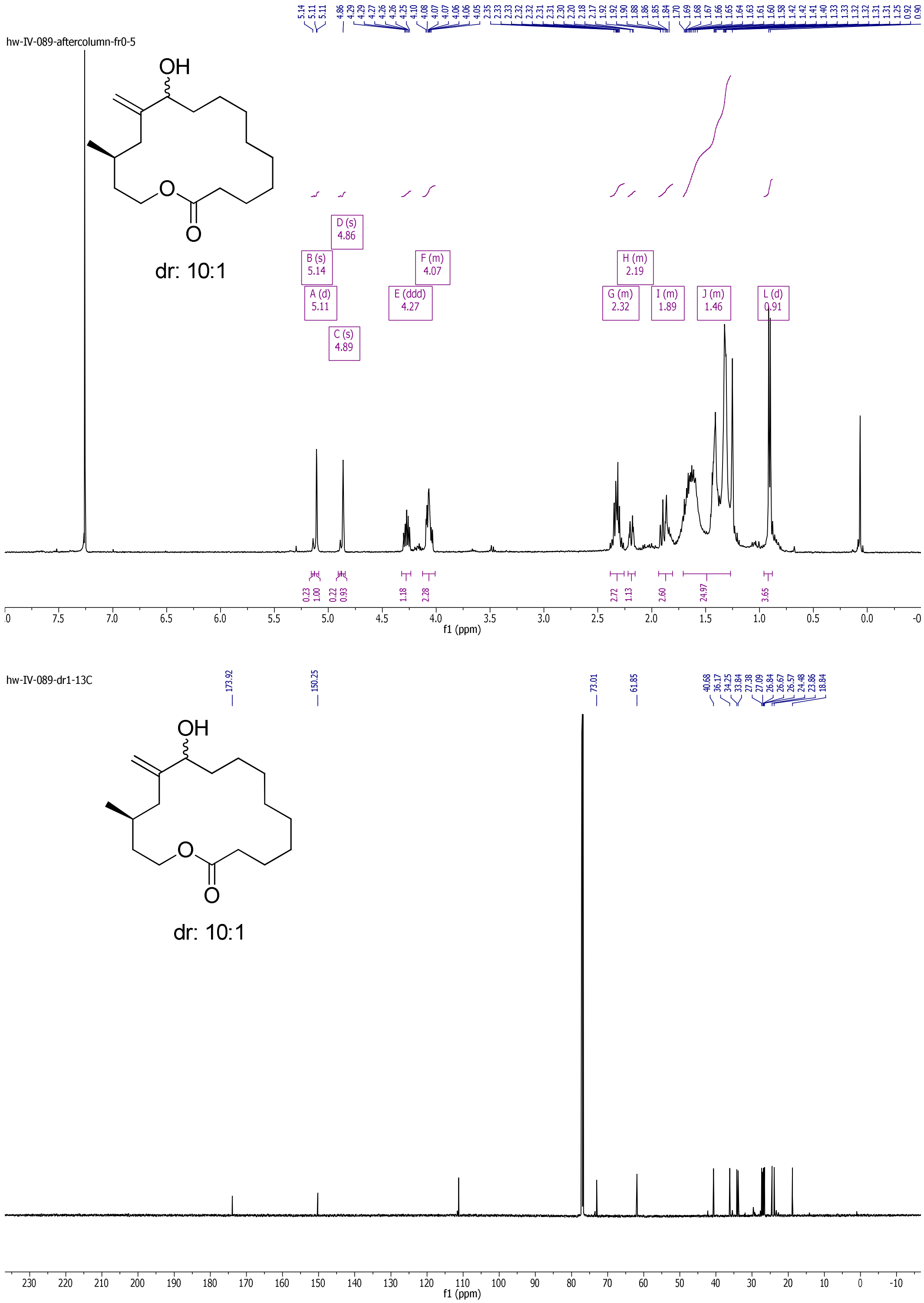
^{1}H- and ^{13}C-NMR spectra of compound **10d**



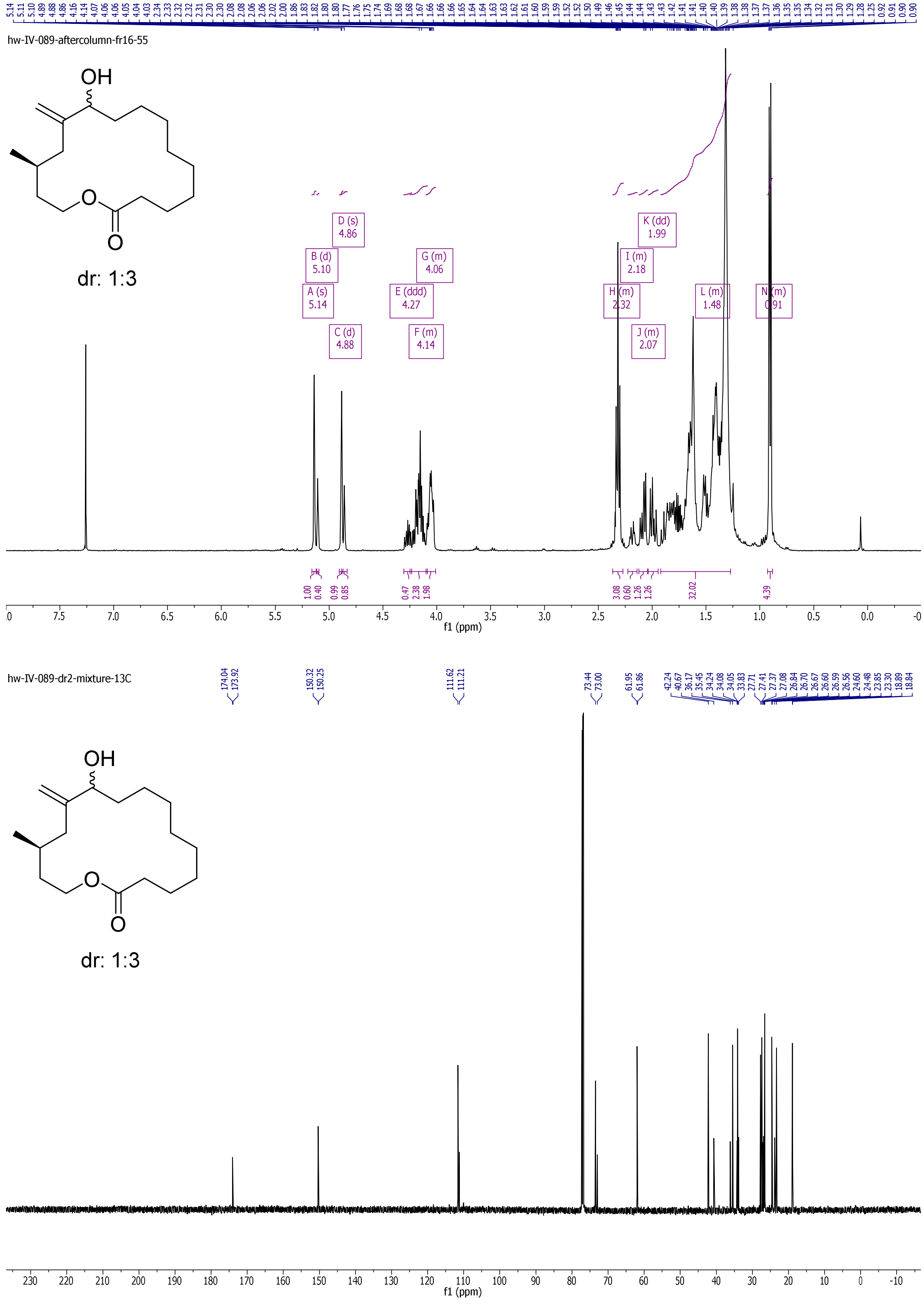
^{1}H- and ^{13}C-NMR spectra of compound **S9**



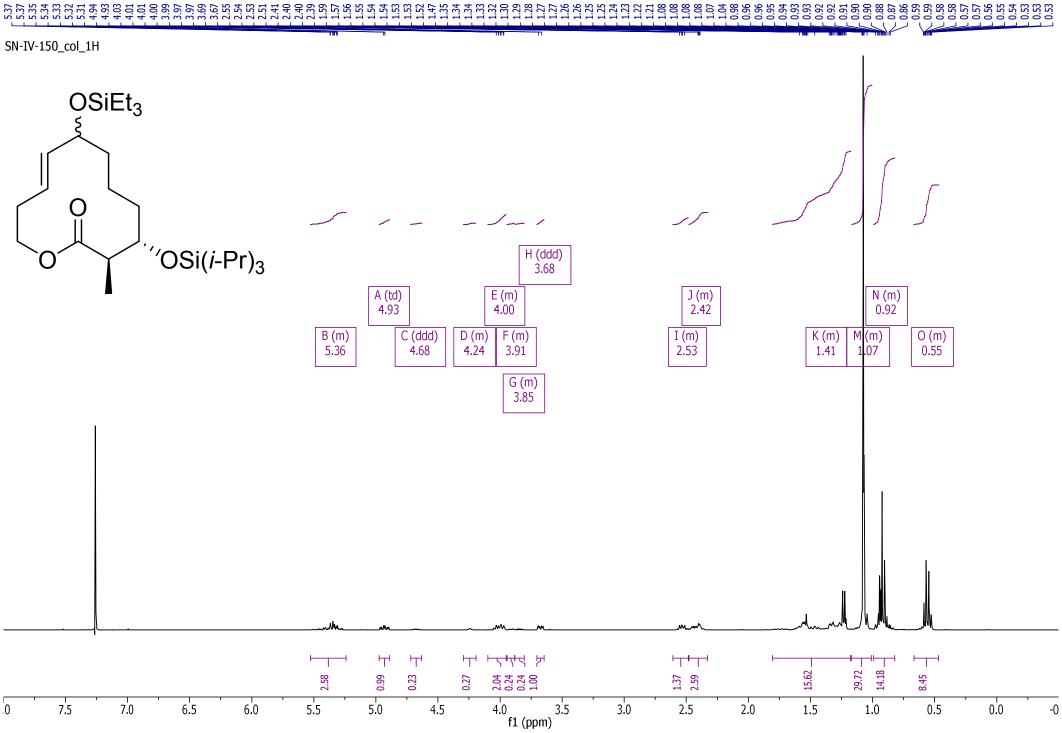
^{1}H- and ^{13}C-NMR spectra of compound **10e**

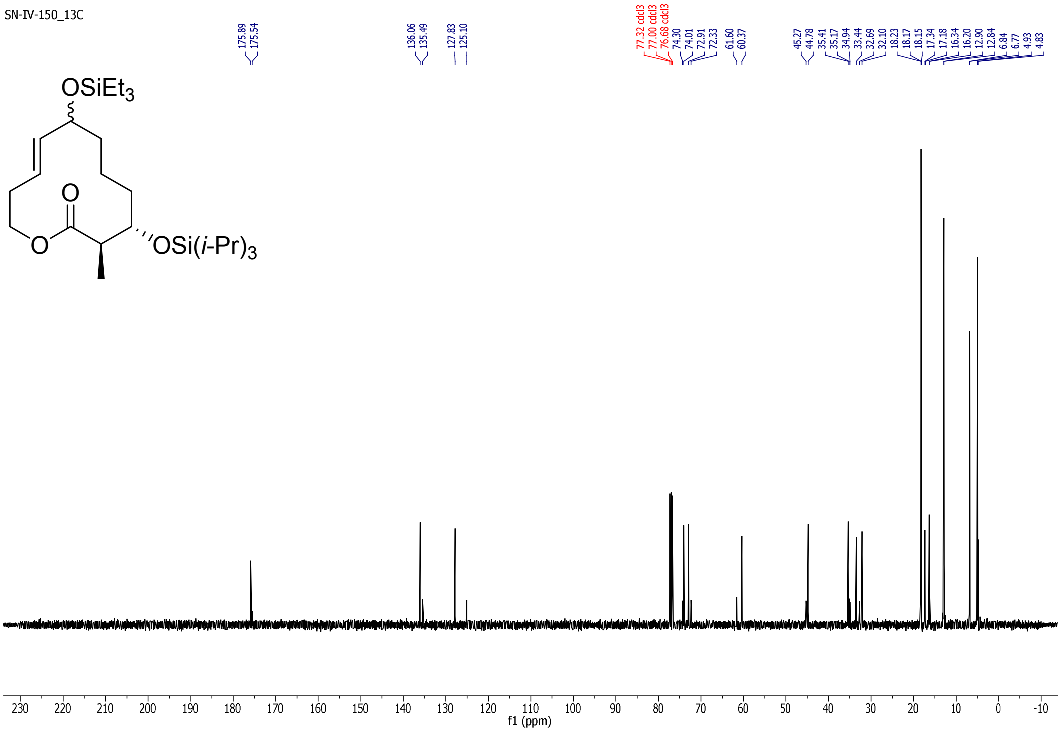


^{1}H- and ^{13}C-NMR spectra of compound **S10a (fr.1)**

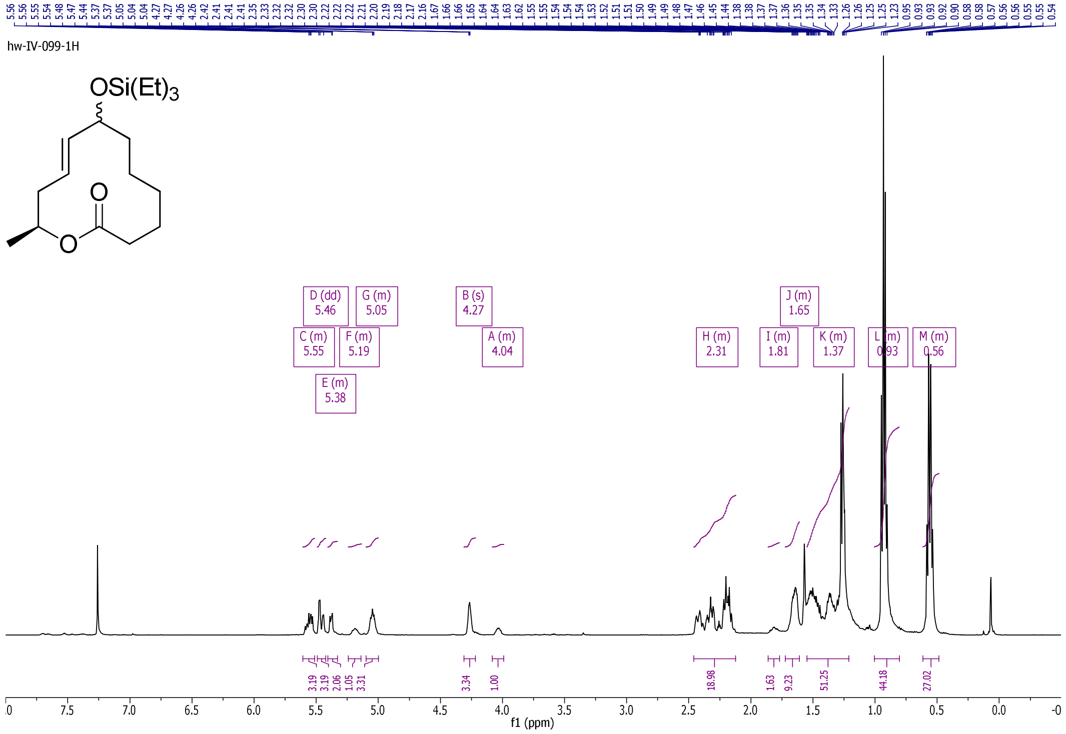


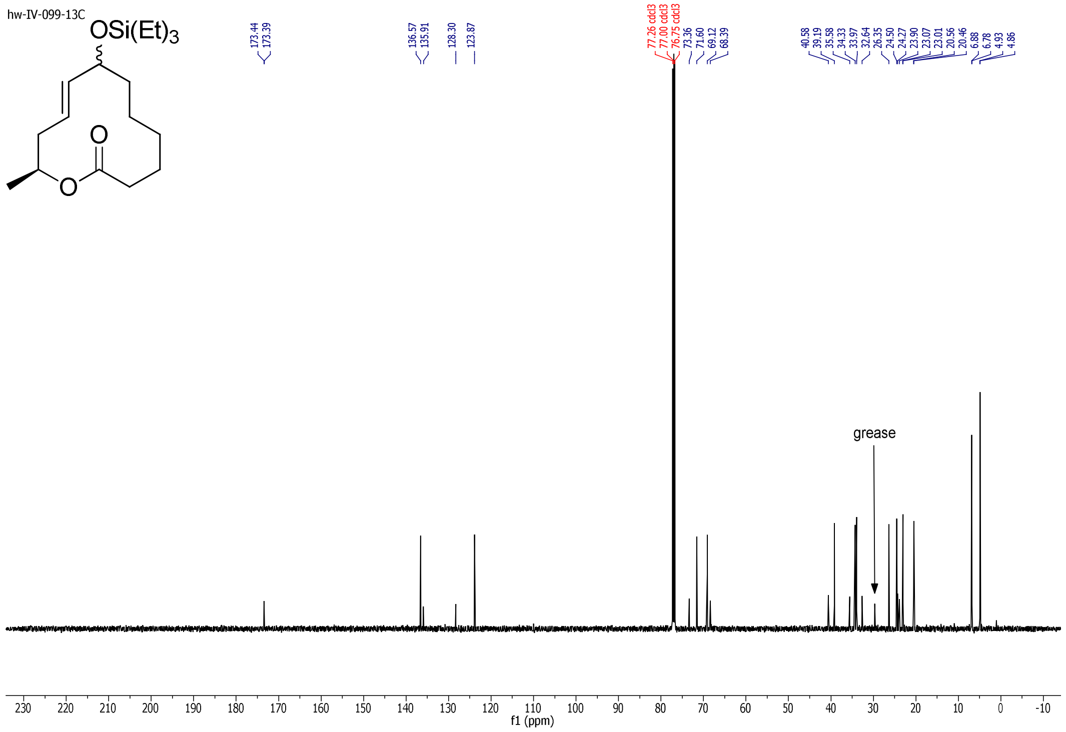
^{1}H- and ^{13}C-NMR spectra of a mixture of compounds **S10a** (minor) and **S10b** (major)



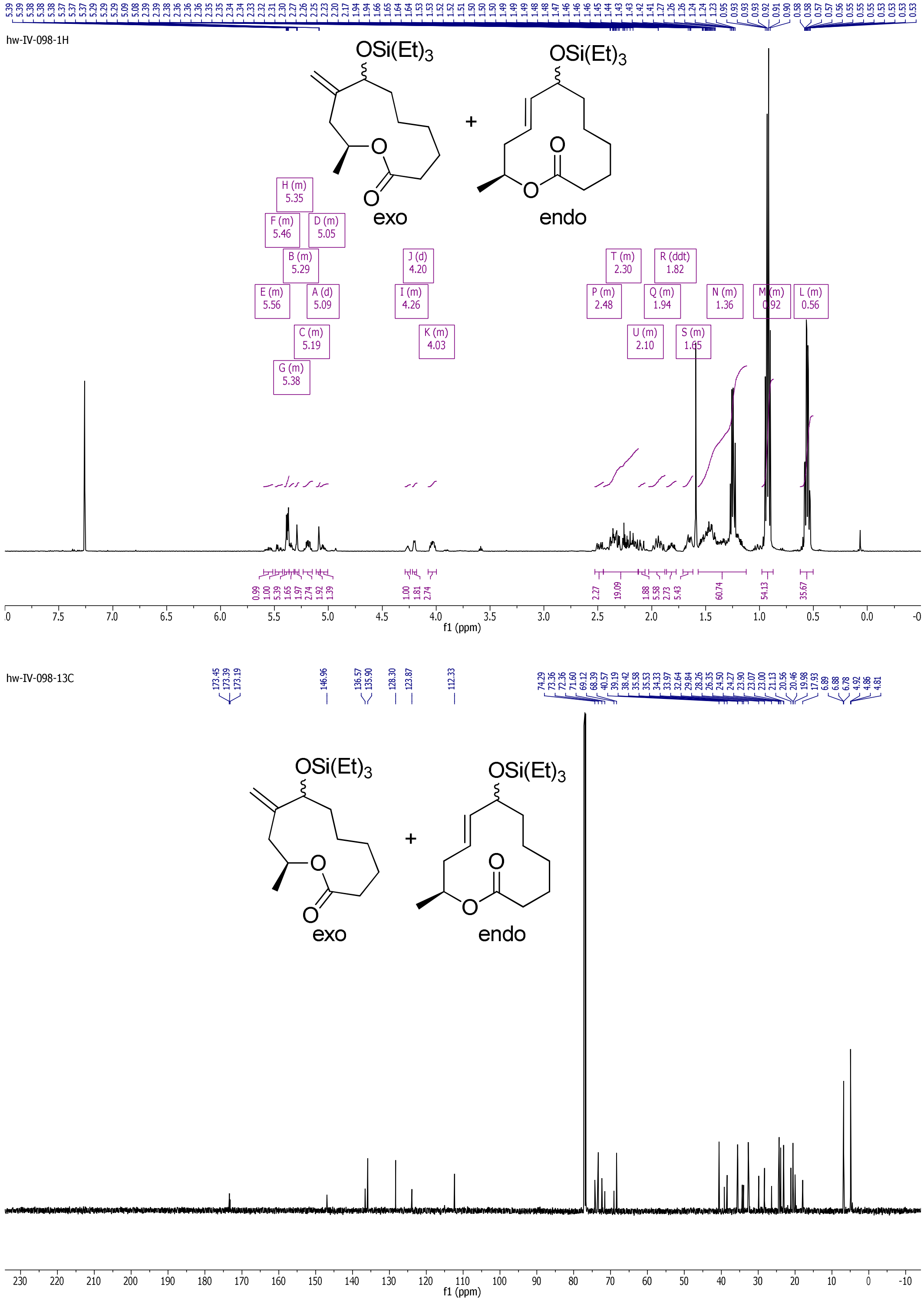


^{1}H- and ^{13}C-NMR spectra of compound **11**





^{1}H- and ^{13}C-NMR spectra of compound **17**



^{1}H- and ^{13}C-NMR spectra of compound **16** and **17**