Electronic Supplementary Information (ESI)

Highly Regioselective Opening of Zirconacyclopentadienes by Remote Coordination: Concise Synthesis of the Furan Core of the Leupyrrins

Thomas Debnar,† Sandra Dreisigacker† and Dirk Menche*,‡

† *Universität Heidelberg, Institut für Organische Chemie, INF 270, D-69120 Heidelberg, Germany and*
‡ *Kekulé-Institut für Organische Chemie und Biochemie der Universität Bonn, Gerhard-Domagk-Str. 1, D-53121 Bonn, Germany.*

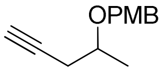
E-mail: *dirk.menche@uni-bonn.de*

Contents

General Remarks: Optical rotations were determined on a Perkin-Elmer 241 instrument. UV spectra were recorded on a Shimadzu UV-2102 PC scanning spectrometer. IR spectra were measured with a Nicolet 20DXB FT-IR spectrometer. NMR spectra were recorded in $CDCl_3$ on a Bruker AM 300, AM 400 and DMX-600 spectrometer. EI and DCI mass spectra (reactant gas ammonia) were obtained on a Finnigan MAT 95 spectrometer, high resolution data were aquired using peak matching (M/DM = 10000). Analytical TLC (TLC aluminium sheets silica gel Si 60 F_{254} (Merck), solvent: mixtures of ethylacetate/*n*-haxane, detection: UV absorption at 254 nm, dark blue spots on staining with cerium(IV)sulfate- phosphomolybdic acid in sulfuric acid followed by charring.

I. EXPERIMENTAL DETAILS AND CHARACTERIZATION DATA

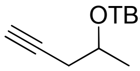
1-Methoxy-4-((pent-4-yn-2-yloxy)methyl)benzene (S1)



Chemical Formula: $C_{13}H_{16}O_2$
Exact Mass: 204,1150
Molecular Weight: 204,2649

To a suspension of 380 mg (9.51 mmol, 1.60 eq.) of 60 % sodium hydride dispersion in mineral oil in THF (15.0 ml) at 0 °C was slowly added pent-4-yn-2-ol (500 mg, 5.94 mmol, 1.00 eq.). The resulting heterogeneous mixture was stirred at room temperature for 3 h whereupon 1.10 g (2.97 mmol, 0.50 eq.) of tetrabutylammonium iodide and 1.86 g (11.9 mmol, 2.0 eq.) of *p*-methoxybenzyl chloride were successively added. After stirring at room temperature for 16 h, the mixture was quenched by addition of water (20.0 ml) followed by dilution with diethyl ether(50.0 ml). The resulting clear layers were separated, the aqueous portion was extracted with diethyl ether (3 x 20.0 ml) and the combined organic extracts were washed with brine (20.0 ml), dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography (70.0 g SiO_2, *n*-hexane/ethyl acetate 20:1) afforded the protected alcohol **S1** (948 mg, 4.64 mmol, 78 %) as a colourless oil. $R_f = 0.42$ (*n*-hexane/ethyl acetate 10:1); ^{1}H-NMR (300 MHz, $CDCl_3$) δ ppm 1.32 (d, J = 6.2 Hz, 3H), 2.03 (t, J = 2.6 Hz, 1H), 2.37 (ddd, J = 16.8, 7.0, 2.6 Hz, 1H), 2.51 (ddd, J = 16.5, 4.8, 2.6 Hz, 1H), 3.70 (tq, J = 6.9, 5.6 Hz, 1H), 3.82 (s, 3H), 4.52 (s, 2H), 6.89 (m, 2H), 7.30 (m, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ ppm 19.53, 26.02, 55.29, 69.91, 70.35, 72.81, 81.29, 113.79, 129.23, 130.57, 159.16; MS (ESI) *m/z*: 227.1 $[M+Na]^+$. The spectroscopic data were in agreement with those previously reported.[1]

tert-Butyldimethyl(pent-4-yn-2-yloxy)silane (S2)



Chemical Formula: $C_{11}H_{22}OSi$
Exact Mass: 198,1440
Molecular Weight: 198,3773

---

[1] Y. Kobayashi, M. Asano, S. Yoshida, A. Takeuchi, *Org. Lett.* **2005**, 7, 1533.

To a solution of pent-4-yn-2-ol (1.00 g, 11.9 mmol, 1.00 eq.) in DMF (30.0 ml) at 0 °C was added *tert*-butyldimethylsilyl chloride (2.69 g, 17.8 mmol, 1.50 eq), then imidazole (1.21 g, 17.8 mmol, 1.50 eq). The resulting solution was stirred at room temperature for 12 h. Then 30.0 ml of water were added and the suspension was extracted with diethyl ether (3 x 30.0 ml). The combined organic layers were washed with water (50.0 ml), dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. Purification by flash chromatography (50.0 g SiO_2, *n*-hexane/ethyl acetate 20:1) afforded 2.24 g (11.3 mmol, 95 %) of **S2** as a colourless liquid. R_f = 0.52 (*n*-hexane/ethyl acetate 10:1); ^{1}H-NMR (300 MHz, $CDCl_3$) δ ppm 0.08 (s, 3H), 0.09 (s, 3H), 0.90 (s, 9H), 1.24 (d, *J* = 6.2 Hz, 3H), 1.98 (t, *J* = 2.6 Hz, 1H), 2.22 (ddd, *J* = 16.5, 7.3, 2.6, 1H), 2.34 (ddd, *J* = 16.5, 5.5, 2.6 Hz, 1H), 3.95 (tq, *J* = 6.7, 5.5 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ ppm -4.76, -4.68, 18.13, 23.24, 25.82, 29.37, 67.51, 69.68, 81.94; MS (EI+) *m/z* (%): 198.1 (M^+, 0.03), 159.1 (16). The spectroscopic data were in agreement with those previously reported.[2]

General Procedure for the Preparation of Propargylic Alcohols S3 – S7:

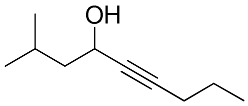
To a solution of 1.00 eq. of the corresponding alkyne in dry THF at -78 °C was slowly added *n*-butyllithium (1.20 eq., 2.0 M in cyclohexane). The resulting solution was stirred at this temperature for 1 h, and then 1.10 eq. of 3-methylbutanal were added via syringe. After 1 h of stirring, the reaction mixture was allowed to warm to room temperature and stirred for an additional hour. The reaction mixture was quenched with a saturated solution of ammonium chloride and the phases were separated. The aqueous layer was extracted with Et_2O, the combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. Purification by flash chromatography afforded the corresponding Propargylic Alcohols **S3 – S7** in variable yields given below.

---

[2] J. J. De Voss, B. D. Schwartz, P. Y. Hayes, W. Kitching, *J. Org. Chem.* **2005**, 70, 3054.

Alkyne	*n*-BuLi	Aldehyde	THF	Product	Purification
1-Pentyne 300 mg (4.40 mmol)	2.64 ml (5.28 mmol)	420 mg (4.84 mmol)	10.0 ml	**S3**	40.0 g SiO_2, *n*-hexane/ethyl acetate (10:1)
4-Methyl-1-pentyne 300 mg (3.65 mmol)	2.19 ml (4.38 mmol)	346 mg (4.02 mmol)	10.0 ml	**S4**	40.0 g SiO_2, *n*-hexane/ethyl acetate (10:1)
S9 100 mg (1.02 mmol)	0.61 ml (1.22 mmol)	96.5 mg (1.12 mmol)	5.00 ml	**S5**	20.0 g SiO_2, *n*-hexane/ethyl acetate (10:1)
S1 500 mg (2.52 mmol)	1.52 ml (3.02 mmol)	239 mg (2.77 mmol)	15.0 ml	**S6**	60.0 g SiO_2, *n*-hexane/ethyl acetate (10:1)
S2 300 mg (1.47 mmol)	0.88 ml (1.76 mmol)	140 mg (1.62 mmol)	10.0 ml	**S7**	50.0 g SiO_2, *n*-hexane/ethyl acetate (5:1)

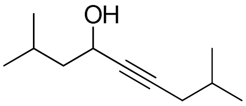
2-Methylnon-5-yn-4-ol (S3)



Chemical Formula: $C_{10}H_{18}O$
Exact Mass: 154,1358
Molecular Weight: 154,2493

Yield 69 % (466 mg, 3.02 mmol).[3] R_f = 0.29 (*n*-hexane/ethyl acetate 10:1); ^{1}H-NMR (300 MHz, $CDCl_3$) δ ppm 0.97 (d, *J* = 6.8 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H), 1.03 (t, *J* = 7.4 Hz, 3H), 1.52 – 1.70 (m, 2H), 1.57 (sxt, *J* = 7.3 Hz, 2H), 1.89 (spt, *J* = 6.8 Hz, 1H), 2.23 (dt, *J* = 7.0, 1.9 Hz, 2H), 4.45 (tt, *J* = 7.2, 1.9 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ ppm 13.44, 20.63, 22.08, 22.50, 22.54, 24.79, 47.31, 61.27, 81.63, 85.27; HRMS (EI+) calculated for $C_{10}H_{17}O$ [M-H$^+$]: 153.1279, found: 153.1289.

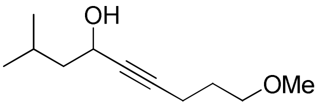
2,8-Dimethylnon-5-yn-4-ol (S4)



Chemical Formula: $C_{11}H_{20}O$
Exact Mass: 168,1514
Molecular Weight: 168,2759

Yield 65 % (397 mg, 2.36 mmol).[4] R_f = 0.31 (*n*-hexane/ethyl acetate 10:1); ^{1}H-NMR (300 MHz, $CDCl_3$) δ ppm 0.87 (d, *J* = 6.9 Hz, 6H), 0.90 (d, *J* = 6.6 Hz, 6H), 1.48 (m, 2H), 1.73 (spt, *J* = 6.6 Hz, 1H), 1.78 (spt, *J* = 6.9 Hz, 1H), 2.03 (dd, *J* = 6.6, 2.2 Hz, 2H), 4.34 (tt, *J* = 6.9, 1.8 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ ppm 21.94, 22.52, 22.54, 24.84, 27.85, 27.81, 47.34, 61.31, 82.41, 84.34; HRMS (EI+) calculated for $C_{10}H_{17}O$ [M-H$^+$]: 153.1279, found: 153.1289.

9-Methoxy-2-methylnon-5-yn-4-ol (S5)



Chemical Formula: $C_{11}H_{20}O_2$
Exact Mass: 184,1463
Molecular Weight: 184,2753

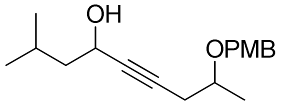
---

[3] Product contained a minor impurity which was easily removed after etherification (^{1}H-NMR δ ppm 1.22 – 1.51, 3.72, 3.80; ^{13}C-NMR δ ppm 14.08, 22.04, 22.75, 23.51, 24.61, 27.79, 37.76, 46.79, 69.98).

[4] Product contained a minor impurity which was easily removed after etherification (^{1}H-NMR δ ppm 1.10 – 1.40, 3.60; ^{13}C-NMR δ ppm 14.09, 22.05, 22.77, 23.53, 24.62, 27.99, 37.78, 46.80, 69.89).

Yield 48 % (89.0 mg, 0.49 mmol). R_f = 0.33 (*n*-hexane/ethyl acetate 5:1); ^{1}H-NMR (300 MHz, $CDCl_3$) δ ppm 0.85 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.2 Hz, 3H), 1.45 (ddd, *J* = 13.3, 7.0, 7.3 Hz, 1H), 1.54 (ddd, *J* = 13.3, 7.0, 7.3 Hz, 1H), 1.69 (quin, *J* = 6.9 Hz, 2H), 1.77 (spt, *J* = 6.9 Hz, 1H), 2.23 (dt, *J* = 6.9, 1.8 Hz, 2H), 3.27 (s, 3H), 3.38 (t, *J* = 6.2 Hz, 2H), 4.33 (tt, *J* = 7.3, 2.2 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ ppm 15.45, 22.51, 22.55, 24.81, 28.64, 47.27, 58.63, 61.25, 71.17, 81.83, 84.60; HRMS (ESI+) calculated for $C_{11}H_{20}O_2Na$ $[M+Na]^+$: 207.1361, found: 207.1362.

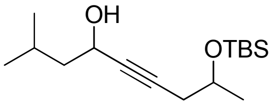
8-(4-Methoxybenzyloxy)-2-methylnon-5-yn-4-ol (S6)



Chemical Formula: $C_{18}H_{26}O_3$
Exact Mass: 290,1882
Molecular Weight: 290,3972

Yield 91 % (389 mg, 1.34 mmol). R_f = 0.17 (*n*-hexane/ethyl acetate 10:1); ^{1}H-NMR (300 MHz, $CDCl_3$) δ ppm 0.92 (d, *J* = 6.6 Hz, 3H), 0.94 (d, *J* = 6.6 Hz, 3H), 1.28 (d, *J* = 6.2 Hz, 3H), 1.53 (ddd, *J* = 13.5, 7.0, 6.2 Hz, 1H), 1.62 (ddd, *J* = 13.5, 7.5, 7.0 Hz, 1H), 1.84 (spt, *J* = 6.6 Hz, 1H), 2.37 (ddd, *J* = 16.5, 7.3, 2.2 Hz, 1H), 2.52 (ddd, *J* = 16.5, 5.1, 1.8 Hz, 1H), 3.66 (sxt, *J* = 6.2 Hz, 1H), 3.80 (s, 3H), 4.40 (t, *J* = 7.1 Hz, 1H), 4.49 (s, 2H), 6.88 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ ppm 19.6, 22.48, 22.53, 24.8, 26.3, 47.2, 55.3, 61.2, 70.3, 73.1, 82.0, 83.2, 113.8, 129.2, 130.6, 159.2; HRMS (ESI+) calculated for $C_{18}H_{26}O_3Na$ $[M+Na]^+$: 313.1780, found: 313.1772.

8-(*tert*-Butyldimethylsilyloxy)-2-methylnon-5-yn-4-ol (S7)

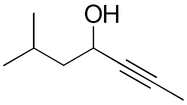


Chemical Formula: $C_{16}H_{32}O_2Si$
Exact Mass: 284,2172
Molecular Weight: 284,5096

Yield 79 % (569 mg, 2.00 mmol). R_f = 0.17 (*n*-hexane/ethyl acetate 10:1); ^{1}H-NMR (300 MHz, $CDCl_3$) δ ppm 0.08 (s, 3H), 0.085 (s, 3H), 0.90 (s, 9H), 0.93 (d, *J* = 7.2 Hz, 3H), 0.95 (d, *J* = 7.0 Hz, 3H), 1.22 (d, *J* = 6.0 Hz, 3H), 1.53 (ddd, *J* = 13.5, 6.9, 6.5 Hz, 1H), 1.61 (ddd, *J* = 13.4, 7.3, 6.5 Hz, 1H), 1.85 (spt, *J* = 6.7 Hz, 1H), 2.27 (ddd, *J* = 16.5, 7.2, 1.9 Hz, 1H), 2.38 (ddd, *J* = 16.2, 5.4, 1.9 Hz, 1H), 3.94 (tq, *J* = 6.4, 5.8 Hz, 1H), 4.40 (tt, *J* = 7.2, 1.8 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ ppm -4.7, -4.6, , 18.1, 22.4, 22.5, 23.3, 24.8, 25.8, 29.6, 47.2, 61.3, 67.6, 82.69/82.71*, 82.92/82.95*; HRMS (ESI+) calculated for $C_{16}H_{32}O_2SiNa$ $[M+Na]^+$: 307.2069, found: 307.2067.

*Diastereomers slightly differ in ^{13}C – chemical shifts.

Methylhept-2-yn-4-ol (S8)



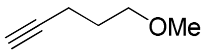
Chemical Formula: $C_8H_{14}O$
Exact Mass: 126,1045
Molecular Weight: 126,1962

Methylacetylene was bubbled into 30.0 ml of dry THF at -78 °C for 25 min. To this solution was slowly added *n*-Butyllithium (5.00 ml, 10.0 mmol, 2.0 M in cyclohexane). The resulting solution was stirred at this temperature for 1 h, and then 3-methylbutanal (718 mg, 8.33 mmol, 1.10 eq.) was added via syringe. After 1 h of stirring, the reaction mixture was allowed to warm to room temperature and stirred for an additional hour. The reaction mixture was quenched with a saturated solution of ammonium chloride (10.0 ml) and the phases were separated. The aqueous layer was extracted with Et_2O (3 x 15.0 ml), the combined organic layers were washed with brine (15.0 ml), dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. Purification by flash chromatography (60.0 g SiO_2, *n*-hexane/ethyl acetate 10:1) afforded **S8** (639 mg, 5.06 mmol, 60 %) as a slightly yellow oil.
R_f = 0.24 (*n*-hexane/ethyl acetate 10:1); ^{1}H-NMR (300 MHz, $CDCl_3$) δ ppm 0.85 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H), 1.49 (m, 2H), 1.76 (spt, *J* = 6.6 Hz, 1H), 1.77 (d, *J* = 2.2 Hz, 3H), 4.31 (m, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ ppm 3.55, 22.49, 22.54, 24.77, 47.20, 61.16, 80.67, 80.86; MS (EI+) *m/z* 125.10 $[M\text{-}H^+]$. The spectroscopic data were in agreement with those previously reported.[5]

---

[5] K. -K. Chan, N. Cohen, J. P. De Noble, A. C. Specian, G. Saucy, *J. Org. Chem.* **1976**, 41, 3497.

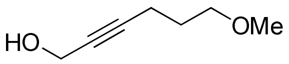
5-Methoxypent-1-yne (S9)



Chemical Formula: $C_6H_{10}O$
Exact Mass: 98,0732
Molecular Weight: 98,1430

To a mixture of iodomethane (20.1 g, 141 mmol, 1.70 eq.) and sodium hydride (5.33 g, 1.33 mol, 1.60 eq., 60 % in mineral oil) in dry THF (150 ml) was added dropwise within 15 min under Ar and at room temperature, pent-4-yn-l-ol (7.00 g, 83.2 mmol, 1.00 eq.). The mixture was then heated to 50 °C for 1 h, cooled to room temperature, and poured into 70.0 ml of water. The aqueous layer was extracted with Et_2O, the extract dried over $MgSO_4$ and evaporated. Distillation (b.p. 107-115 °C) afforded of 2.98 g (30.4 mmol, 37 %) of **S9** as a colourless liquid. ^{1}H-NMR (300 MHz, $CDCl_3$) δ ppm 1.67 – 1.76 (quin, J = 6.9 Hz, 2H), 1.88 (t, J = 2.7, 1H), 2.22 (dt, J = 7.2, 2.7 Hz, 2H), 3.27 (s, 3H), 3.40 (t, J = 6.1 Hz, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ ppm 15.59, 28.86, 50.31, 58.99, 68.79, 71.42; MS (EI+) m/z = 98.1 [M^+]. The spectroscopic data were in agreement with those previously reported.[6]

5-Methoxyhex-2-yn-1-ol (S10)



Chemical Formula: $C_7H_{12}O_2$
Exact Mass: 128,0837
Molecular Weight: 128,1690

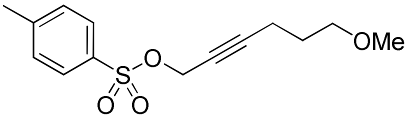
5-methoxypent-1-yn (**S9**) (2.00 g, 20.4 mmol, 1.00 eq.) was dissolved in dry THF (90.0 ml) and cooled to -78 °C. Then *n*-butyllithium (9.78 ml, 24.5 mmol, 1.20 eq., 2.5 M in *n*-hexane) was slowly added. The resulting mixture was stirred at this temperature for 15 min, then allowed to warm to room temperature and transferred by cannula into a solution of paraformaldehyde (2.38 g, 26.5 mmol, 1.30 eq.) in dry THF (40.0 ml). After stirring for further 15 min the reaction mixture was quenched with a saturated solution of ammonium chloride (30.0 ml). The phases were separated and the organic layer was extracted with ethyl acetate (3 x 30.0 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and the solvent was removed *in vacuo*. Purification by flash chromatography (50.0 g SiO_2, *n*-hexane/ethyl acetate 10:1) afforded 1.88 g (14.7 mmol, 72 %) of **S10** as a colourless liquid. R_f = 0.18 (*n*-hexane/ethyl acetate 3:1); ^{1}H-NMR (300

---

[6] P. Müller, C. Gränicher, *Helv. Chim. Act.* **1995**, *78*, 129.

MHz, $CDCl_3$) δ ppm 1.19 (t, *J* = 7.0 Hz, 1H), 1.71 (quin, *J* = 7.0 Hz, 2H), 2.24 (tt, *J* = 7.0, 2.20 Hz, 2H), 3.27 (s, 3H), 3.39 (t, *J* = 6.2 Hz, 2H), 4.18 (dt, *J* = 6.2, 2.2 Hz, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ ppm 15.49, 28.52, 51.30, 58.60,71.15, 78.66, 85.62; HR-MS (EI+) calculated for $C_7H_{11}O_2$ $[M\text{-H}]^+$: 127.0764, found: 127.0758.

6-Methoxyhex-2-ynyl-4-methylbenzenesulfonate (S11)



Chemical Formula: $C_{14}H_{18}O_4S$
Exact Mass: 282,0926
Molecular Weight: 282,3553

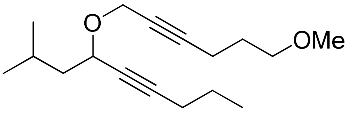
To a solution of alcohol **S10** (500 mg, 3.90 mmol, 1.00 eq.) in dry Et_2O (50.0 ml) was added 4-methylbenzenesulfonyl chloride (817 mg, 4.29 mmol, 1.10 eq.). The resulting mixture was cooled to -5°C and at this temperature potassium hydroxide (1.53 g, 27.3 mmol, 7.00 eq.) was added in portions over 2 h. After an additional hour of stirring at -5 °C the reaction mixture was poured into ice water (50.0 ml), the layers were separated and the aqueous layer was extracted with Et_2O (2 x 20.0 ml). The combined organic layers were dried over anhydrous $MgSO_4$ and the solvent was removed *in vacuo*. Purification by flash chromatography (60.0 g SiO_2, *n*-hexane/ethyl acetate 3:1) afforded **S11** (968 mg, 3.43 mmol, 88 %) as a colourless liquid. R_f = 0.56 (*n*-hexane/ethyl acetate 1:1); ^{1}H-NMR (300 MHz, $CDCl_3$) δ ppm 1.57 (quin, *J* = 6.6 Hz, 2H), 2.11 (tt, *J* = 6.9, 2.2 Hz, 2H), 2.38 (s, 3H), 3.24 (s, 3H), 3.28 (t, *J* = 6.2 Hz, 2H), 4.63 (t, *J* = 2.2 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.75 (d, *J* = 8.4 Hz, 2H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ ppm 15.44, 21.63, 28.10, 58.61, 70.89. 72.14, 77.21, 89.79, 128.11, 129.73, 133.43, 144.88; HR-MS (ESI) calculated for $C_{14}H_{18}O_4SNa$ $[M\text{+Na}]^+$: 305.0824, found: 305.0818.

General Procedure for the Preparation of 1,6-Diynes 5a-f:

To a suspension of sodium hydride (1.60 eq., 60 % dispersion in mineral oil) in acetonitrile at 0 °C was slowly added 1.00 eq. of the corresponding alcohol. The resulting heterogeneous mixture was stirred at room temperature for 1 h whereupon 1.20 eq. of 6-methoxyhex-2-ynyl-4-methylbenzene-sulfonate (**S11**) were successively added. After stirring at room temperature for 24 h, the mixture was quenched by a saturated solution of ammonium chloride, phases were separated and the aqueous layer was extracted with diethyl ether. The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography afforded the corresponding 1,6-diynes in variable yields given below.

Alcohol	Tosylate	NaH	CH_3CN	Product	Purification
S3 200 mg (1.30 mmol)	440 mg (1.56 mmol)	83.2 mg (2.08 mmol)	15.0 ml	**5a**	30.0 g SiO_2, *n*-hexane/ethyl acetate (30:1)
S4 200 mg (1.19 mmol)	403 mg (1.43 mmol)	76.0 mg (1.90 mmol)	15.0 ml	**5b**	30.0 g SiO_2, *n*-hexane/ethyl acetate (30:1)
S8 150 mg (1.19 mmol)	403 mg (1.43 mmol)	76.0 mg (1.90 mmol)	15.0 ml	**5c**	30.0 g SiO_2, *n*-hexane/ethyl acetate (30:1)
S5 45.0 mg (0.24 mmol)	82.7 mg (0.29 mmol)	15.4 mg (0.38 mmol)	5.00 ml	**5d**	10.0 g SiO_2, *n*-hexane/ethyl acetate (30:1)
S6 200 mg (0.69 mmol)	233 (0.83 mmol)	44.0 mg (1.10 mmol)	10.0 ml	**5e**	20.0 g SiO_2, *n*-hexane/ethyl acetate (10:1)
S7 200 mg (0.70 mmol)	237 mg (0.84 mmol)	44.9 mg (1.12 mmol)	10.0 ml	**5f**	20.0 g SiO_2, *n*-hexane/ethyl acetate (30:1)

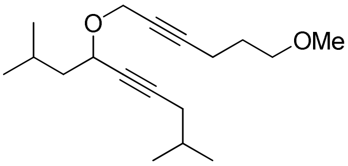
6-(6-Methoxyhex-2-ynyloxy)-8-methylnon-4-yne (5a)



Chemical Formula: $C_{17}H_{28}O_2$
Exact Mass: 264,2089
Molecular Weight: 264,4030

Yield 80 % (260 mg, 1.04 mmol). R_f = 0.43 (*n*-hexane/ethyl acetate 10:1); ^{1}H-NMR (300 MHz, $CDCl_3$) δ ppm 0.92 (d, *J* = 6.6 Hz, 3H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.99 (t, *J* = 7.3 Hz, 3H), 1.53 (quin, *J* = 7.3 Hz, 2H), 1.55 (ddd, *J* = 13.6, 8.3, 7.3 Hz, 1H), 1.67 (ddd, *J* = 13.4, 7.9, 6.8 Hz, 1H), 1.78 (quin, *J* = 7.3 Hz, 2H), 1.87 (spt, *J* = 6.6 Hz, 1H), 2.20 (dt, *J* = 7.3, 2.2 Hz, 2H), 2.32 (tt, *J* = 7.3, 2.2 Hz, 2H), 3.34 (s, 3H), 3.46 (t, *J* = 6.2 Hz, 2H), 4.21 (td, *J* = 15.4, 2.2 Hz, 1H), 4.30 (tt, *J* = 7.1, 2.0 Hz, 1H), 4.32 (td, *J* = 15.4, 2.2 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ ppm 13.44, 15.56, 20.69, 22.13, 22.37, 22.60, 24.64, 28.60, 44.89, 55.94, 58.60, 66.78, 71.20, 76.29, 78.82, 85.83, 86.34; HR-MS (ESI) calculated for $C_{17}H_{28}O_2Na$ [*M*+Na]$^+$: 287.1987, found: 287.1981.

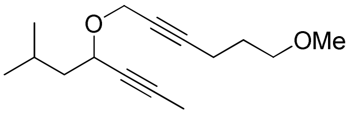
6-(6-Methoxyhex-2-ynyloxy)-2,8-dimethylnon-4-yne (5b)



Chemical Formula: $C_{18}H_{30}O_2$
Exact Mass: 278,2246
Molecular Weight: 278,4296

Yield 54 % (180 mg, 0.65 mmol). R_f = 0.43 (*n*-hexane/ethyl acetate 10:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.92 (d, *J* = 6.7 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H), 0.98 (d, *J* = 6.5 Hz, 6H), 1.53 (ddd, *J* = 13.5, 7.1, 6.6 Hz, 1 H), 1.67 (ddd, *J* = 13.5, 7.2, 6.9 Hz, 1H), 1.78 (tt, *J* = 6.7 Hz, 2H), 1.79 (spt, *J* = 6.5 Hz, 1H), 1.88 (spt, *J* = 6.8 Hz, 1H), 2.12 (dd, *J* = 6.5, 1.9 Hz, 2H), 2.32 (tt, *J* = 7.0, 2.2 Hz, 2H), 3.34 (s, 3H), 3.46 (t, *J* = 6.3 Hz, 2H), 4.22 (td, *J* = 15.3, 2.1 Hz, 1H), 4.31 (dddd, *J* = 7.4, 6.9, 2.1, 2.0 Hz, 1H), 4.32 (td, *J* = 15.1, 2.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 15.6, 21.9, 22.4, 22.6, 24.7, 27.9, 28.0, 28.6, 44.9, 55.9, 58.6, 66.8, 71.2, 76.3, 79.6, 85.4, 85.8; HR-MS (ESI) calculated for $C_{18}H_{30}O_2Na$ [*M*+Na]$^+$: 301.2143, found: 301.2134.

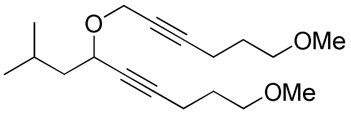
4-(6-Methoxyhex-2-ynyloxy)-6-methylhept-2-yne (5c)



Chemical Formula: $C_{15}H_{24}O_2$
Exact Mass: 236,1776
Molecular Weight: 236,3499

Yield 56 % (159 mg, 0.67 mmol). R_f = 0.42 (*n*-hexane/ethyl acetate 10:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.92 (d, *J* = 6.6 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 1.51 (ddd, *J* = 13.5, 7.1, 6.7 Hz, 1H), 1.66 (ddd, *J* = 13.7, 7.8, 6.5 Hz, 1H), 1.78 (quin, *J* = 6.7 Hz, 2H), 1.87 (spt, *J* = 6.7 Hz, 1H), 1.86 (d, *J* = 2.2 Hz, 3H), 2.32 (tt, *J* = 7.1, 2.2 Hz, 2H), 3.34 (s, 3H), 3.46 (t, *J* = 6.3 Hz, 2H), 4.21 (td, *J* = 15.3, 2.1 Hz, 1H), 4.27 (dddd, *J* = 7.4, 6.7, 2.2, 2.0 Hz, 1H), 4.31 (td, *J* = 15.4, 2.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 3.6, 15.6, 22.3, 22.6, 24.6, 28.6, 44.8, 56.0, 58.6, 66.7, 71.2, 76.3, 77.9, 81.8, 85.9; HR-MS (ESI) calculated for $C_{15}H_{24}O_2Na$ $[M+Na]^+$: 259.1674, found: 259.1669.

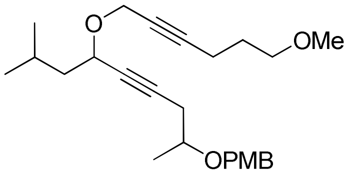
1-Methoxy-6-(6-methoxyhex-2-ynyloxy)-8-methylnon-4-yne (5d)



Chemical Formula: $C_{18}H_{30}O_3$
Exact Mass: 294,2195
Molecular Weight: 294,4290

Yield 68 % (49.0 mg, 0.17 mmol). R_f = 0.45 (*n*-hexane/ethyl acetate 10:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 0.92 (d, *J* = 6.9 Hz, 3H), 0.94 (d, *J* = 7.0 Hz, 3H), 1.52 (ddd, *J* = 13.5, 7.2, 6.7 Hz, 1H), 1.66 (ddd, *J* = 13.8, 7.9, 6.5 Hz, 1H), 1.78 (quin, *J* = 6.7, 6.6 Hz, 2H), 1.78 (quin, *J* = 6.7, 6.6 Hz, 2H), 1.86 (spt, *J* = 6.7 Hz, 1H), 2.32 (tt, *J* = 7.1, 2.3 Hz, 2H), 2.32 (dt, *J* = 7.1, 2.2 Hz, 2H), 3.35 (s, 3H), 3.34 (s, 3H), 3.46 (t, *J* = 6.3 Hz, 2H), 3.46 (t, *J* = 6.3 Hz, 2H), 4.21 (td, *J* = 15.2, 2.0 Hz, 1H), 4.29 (dddd, *J* = 7.8, 6.2, 2.0, 1.8 Hz, 1H), 4.31 (td, *J* = 15.2, 2.1 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ ppm 15.5, 15.6, 22.4, 22.6, 24.6, 28.6, 28.7, 44.8, 56.0, 58.6, 58.6, 66.7, 71.2, 71.2, 76.2, 79.0, 85.7, 85.9; HR-MS (ESI) calculated for $C_{18}H_{30}O_3Na$ $[M+Na]^+$: 317.2093, found: 317.2088.

1-Methoxy-4-((6-(6-methoxyhex-2-ynyloxy)-8-methylnon-4-yn-2-yloxy)methyl)benzene (5e)

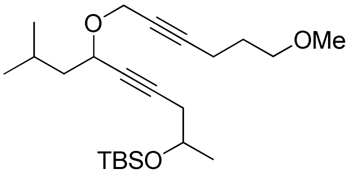


Chemical Formula: $C_{25}H_{36}O_4$
Exact Mass: 400,2614
Molecular Weight: 400,5509

Yield 90 % (248 mg, 0.62 mmol). R_f = 0.24 (*n*-hexane/ethyl acetate 10:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.92 (d, *J* = 6.6 Hz, 3H), 0.94 (d, *J* = 6.6 Hz, 3H), 1.29 (d, *J* = 6.2 Hz, 3H), 1.53 (ddd, *J* = 13.4, 7.2, 6.4 Hz, 1H), 1.68 (ddd, *J* = 13.9, 7.5, 6.4 Hz, 1H), 1.78 (quin, *J* = 6.7 Hz, 2H), 1.87 (spt, *J* = 6.7 Hz, 1H), 2.37 (ddd, *J* = 16.5, 7.2, 2.0 Hz, 1H), 2.32 (tt, *J* = 7.1, 2.1 Hz, 2H), 2.55 (ddd, *J* = 16.6, 5.1, 1.9 Hz, 1H), 3.34 (s, 3H), 3.46 (t, *J* = 6.2 Hz, 2H), 3.67 (tq, *J* = 6.4, 5.9 Hz, 1H), 3.81 (s, 3H), 4.21 (td, *J* = 15.2, 2.1 Hz, 1H), 4.31 (dddd, *J* = 7.5, 6.4, 2.1, 2.0 Hz, 1H), 4.32 (td, *J* = 15.2, 2.1 Hz, 1H), 4.50 (s, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 7.28 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 15.6, 19.7/19.8*, 22.4, 22.6, 24.6, 26.4, 26.9, 28.6, 44.8, 55.3, 56.1, 58.6, 66.7, 70.3/70.4*, 71.2, 73.2, 76.2, 80.4/80.4*, 83.1, 86.0, 113.8, 129.2, 130.6, 159.1; HR-MS (ESI) calculated for $C_{25}H_{36}O_4Na$ $[M+Na]^+$: 423.2511, found: 423.2506.

*Diastereomers slightly differ in ^{13}C – chemical shifts.

10-Isobutyl-14,16,16,17,17-pentamethyl-2,9,15-trioxa-16-silaoctadeca-6,11-diyne (5f)



Chemical Formula: $C_{23}H_{42}O_3Si$
Exact Mass: 394,2903
Molecular Weight: 394,6633

Yield 67 % (185 mg, 0.47 mmol). R_f = 0.37 (*n*-hexane/ethyl acetate 10:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.07 (s, 3H), 0.08 (s, 3H), 0.89 (s, 9H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.93 (d, *J* = 6.6 Hz, 3H), 1.23 (d, *J* = 6.1 Hz, 3H), 1.52 (ddd, *J* = 13.5, 7.2, 6.8 Hz, 1H), 1.67 (ddd, *J* =

13.4, 7.4, 6.8 Hz, 1H), 1.78 (quin, *J* = 6.7 Hz, 2H), 1.87 (spt, *J* = 6.7 Hz, 1H), 2.28 (ddd, *J* = 15.0, 7.2, 2.0 Hz, 1H), 2.32 (tt, *J* = 7.2, 2.1 Hz, 2H), 2.39 (ddd, *J* = 16.6, 5.3, 1.8 Hz, 1H), 3.34 (s, 3H), 3.46 (t, *J* = 6.2 Hz, 2H), 3.94 (tq, *J* = 7.0, 5.5 Hz, 1H), 4.21 (td, *J* = 15.1, 2.0 Hz, 1H), 4.30 (dddd, *J* = 7.2, 6.9, 2.2, 2.0 Hz, 1H), 4.31 (td, *J* = 15.1, 2.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm -4.4, -4.3, 16.0, 22.8, 23.0, 23.7/23.7*, 25.0, 26.2, 29.0, 30.1, 45.2, 56.4, 59.0, 67.1, 68.0/68.0*, 71.6, 76.6, 80.6/80.6*, 84.0/84.1*, 86.3; HR-MS (ESI) calculated for $C_{23}H_{42}O_3SiNa$ [*M*+Na]$^+$: 417.2801, found: 417.2797.

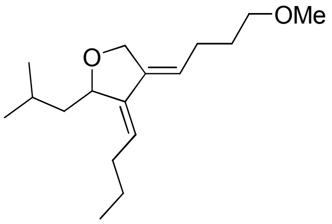
*Diastereomers slightly differ in ^{13}C – chemical shifts.

General Procedure for the Preparation of 3,4-Bisalkylidene-substituted Tetrahydrofurans from 1,6-Diynes 5a-f:

1.00 eq. of Cp_2ZrCl_2 was dissolved in extra dry THF and cooled under argon to -78 °C. Then, 2.00 eq. of *n*-butyllithium (2.0 M in cyclohexane) were added via syringe and the resulting yellow solution was stirred at -78 °C. After 30 min of stirring, 1.00 eq. of the pre-dried 1,6-diyne in extra dry THF was successively added, the solution was allowed to warm to room temperature and stirred for additional 2 h. The reaction mixture was then quenched with 1N HCl, extracted with diethyl ether, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography afforded the corresponding 3,4-bisalkylidene substituted tetrahydrofurans **6a-f** in variable yields given below.

1,6-Diyne	Cp_2ZrCl_2	*n*-BuLi	THF	Product	Purification
5a 20.0 mg (76.0 µmol)	22.3 mg (76.0 µmol)	76.0 µl (152 µmol)	0.3 + 0.3 ml	**6a**	10.0 g SiO_2, *n*-hexane/ethyl acetate (40:1)
5b 15.0 mg (54.0 µmol)	16.0 mg (54.0 µmol)	54.0 µl (108 µmol)	0.2 + 0.2 ml	**6b**	10.0 g SiO_2, *n*-hexane/ethyl acetate (40:1)
5c 13.0 mg (54.0 µmol)	16.0 mg (54.0 µmol)	54.0 µl (108 µmol)	0.2 + 0.2 ml	**6c**	10.0 g SiO_2, *n*-hexane/ethyl acetate (40:1)
5d 3.60 mg (12.0 µmol)	4.00 mg (12.0 µmol)	12.0 µl (24.0 µmol)	0.1 + 0.1 ml	**6d**	5.00 g SiO_2, *n*-hexane/ethyl acetate (40:1)
5e 20.0 mg (50.0 µmol)	15.0 mg (50.0 µmol)	63.0 µl (100 µmol)	0.2 + 0.2 ml	**6e**	10.0 g SiO_2, *n*-hexane/ethyl acetate (20:1)
5f 21.0 mg (54.0 µmol)	16.0 mg (54.0 µmol)	54.0 µl (108 µmol)	0.2 + 0.2 ml	**6f**	10.0 g SiO_2, *n*-hexane/ethyl acetate (40:1)

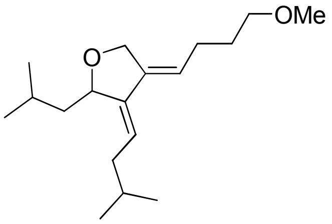
(3*Z*, 4*Z*)-3-Butylidene-2-isobutyl-4-(4-methoxybutylidene)tetrahydrofuran (6a)



Chemical Formula: $C_{17}H_{30}O_2$
Exact Mass: 266,2246
Molecular Weight: 266,4189

Yield 84 % (17.0 mg, 64.0 µmol). R_f = 0.36 (*n*-hexane/ethyl acetate 10:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.95 (d, *J* = 6.7 Hz, 3H), 0.94 (t, *J* = 7.4 Hz, 3H), 0.98 (d, *J* = 6.6 Hz, 3H), 1.15 (ddd, *J* = 14.1, 9.6, 2.8 Hz, 1H), 1.45 (tq, *J* = 7.3, 7.2 Hz, 2H), 1.49 (ddd, *J* = 14.2, 10.4, 4.2 Hz, 2H), 1.58 - 1.59 (m, 1H), 1.69 (quin, *J* = 6.9 Hz, 2H), 1.78 - 1.93 (m, 1H), 2.03 (dt, *J* = 15.4, 7.5 Hz, 2H), 2.05 (dt, *J* = 15.7, 7.7 Hz, 2H), 3.34 (s, 3H), 3.38 (t, *J* = 6.4 Hz, 2H), 4.46 (br. s., 2H), 4.79 (td, *J* = 10.4, 2.4 Hz, 1H), 5.49 - 5.75 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 13.9, 21.6, 22.8, 23.8, 24.9, 26.1, 29.3, 31.3, 43.1, 58.6, 68.4, 72.0, 79.2, 116.4, 117.5, 137.3, 140.3; HR-MS (ESI) calculated for $C_{17}H_{30}O_2Na$ $[M+Na]^+$: 289.2143, found: 289.2140.

(3*Z*, 4*Z*)-2-Isobutyl-4-(4-methoxybutylidene)-3-(3-methylbutylidene)tetrahydrofuran (6b)

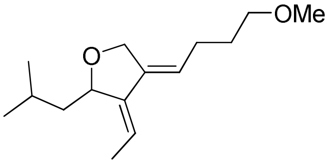


Chemical Formula: $C_{18}H_{32}O_2$
Exact Mass: 280,2402
Molecular Weight: 280,4455

Yield 63 % (9.50 mg, 34.0 µmol). R_f = 0.36 (*n*-hexane/ethyl acetate 10:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ ppm 0.93 (d, *J* = 6.4 Hz, 3H), 0.95 (d, *J* = 6.6 Hz, 6H), 0.99 (d, *J* = 6.6 Hz, 3H), 1.15 (ddd, *J* = 14.4, 9.7, 2.6 Hz, 1H), 1.48 (ddd, *J* = 14.2, 10.4, 4.2 Hz, 1H), 1.58 - 1.67 (m, 1H), 1.69 (quin, *J* = 6.9 Hz, 2H), 1.81 - 1.90 (m, 1H), 1.85 (ddd, *J* = 15.2, 9.8, 7.2 Hz, 1H), 1.93 (ddd, *J* = 15.3, 9.0, 7.7 Hz, 1H), 2.07 (dt, *J* = 8.6, 7.1 Hz, 2H), 3.34 (s, 3H), 3.38 (t, *J* = 6.5 Hz, 2H), 4.46 (m, 2H), 4.77 (td, *J* = 10.6, 2.3 Hz, 1H), 5.64 - 5.70 (m, 2H); ^{13}C NMR

(151 MHz, $CDCl_3$) δ ppm 21.6, 22.3, 22.7, 23.8, 24.9, 26.1, 28.9, 29.3, 38.3, 42.9, 58.6, 68.3, 72.0, 79.2, 116.4, 116.5, 137.3, 140.7; HR-MS (ESI) calculated for $C_{18}H_{32}O_2Na$ [*M*+Na]$^+$: 303.2300, found: 303.2294.

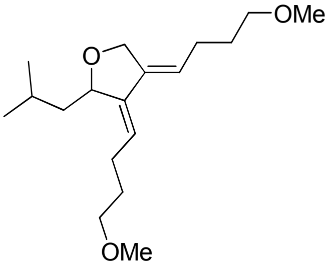
(3*Z*, 4*Z*)-3-Ethylidene-2-isobutyl-4-(4-methoxybutylidene)tetrahydrofuran (6c)



Chemical Formula: $C_{15}H_{26}O_2$
Exact Mass: 238,1933
Molecular Weight: 238,3657

Yield 60 % (7.70 mg, 32.0 μmol). R_f = 0.35 (*n*-hexane/ethyl acetate 10:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ ppm 0.95 (d, *J* = 6.8 Hz, 3H), 0.99 (d, *J* = 6.6 Hz, 3H), 1.18 (ddd, *J* = 14.2, 9.6, 2.6 Hz, 1H), 1.48 (ddd, *J* = 14.2, 10.4, 4.0 Hz, 1H), 1.68 (quin, *J* = 6.9 Hz, 2H), 1.69 (d, *J* = 7.3 Hz, 3H), 1.82 - 1.90 (m, 1H), 2.06 (dt, *J* = 7.6, 7.5 Hz, 2H), 3.33 (s, 3H), 3.37 (t, *J* = 6.4 Hz, 2H), 4.41 - 4.51 (m, 2H), 4.82 (d, *J* = 10.4 Hz, 1H), 5.64 (tt, *J* = 7.6, 2.6 Hz, 1H), 5.73 (dq, *J* = 7.2, 2.2 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ ppm 14.6, 21.5, 23.8, 24.8, 26.1, 29.3, 42.5, 58.6, 68.4, 72.0, 79.0, 111.7, 116.3, 137.3, 141.2; HR-MS (ESI) calculated for $C_{15}H_{26}O_2Na$ [*M*+Na]$^+$: 261.1830, found: 261.1836.

(3*Z*, 4*Z*)-2-Isobutyl-3,4-bis(4-methoxybutylidene)tetrahydrofuran (6d)

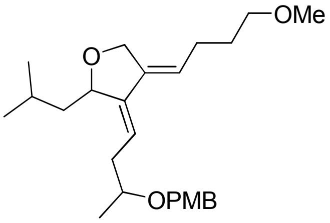


Chemical Formula: $C_{18}H_{32}O_3$
Exact Mass: 296,2351
Molecular Weight: 296,4449

Yield 75 % (2.60 mg, 9.00 μmol). R_f = 0.37 (*n*-hexane/ethyl acetate 10:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ ppm 0.94 (d, *J* = 6.7 Hz, 3H), 0.99 (d, *J* = 6.7 Hz, 3H), 1.16 (ddd, *J* = 14.3, 9.6, 2.7 Hz, 1H), 1.49 (ddd, *J* = 14.1, 10.5, 4.2 Hz, 1H), 1.69 (quin, *J* = 6.9 Hz, 2H), 1.69

(quin, *J* = 6.7 Hz, 2H), 1.81 - 1.92 (m, 1H), 2.07 (dt, *J* = 8.1, 6.9 Hz, 2H), 2.11 (dt, *J* = 7.8, 7.2 Hz, 2H), 3.34 (s, 3 H), 3.35 (s, 3H), 3.38 (t, *J* = 6.4 Hz, 2H), 3.39 (t, *J* = 6.2 Hz, 2H), 4.42 - 4.50 (m, 2H), 4.80 (dt, *J* = 10.5, 2.0 Hz, 1H), 5.62 (dt, *J* = 7.8, 1.6 Hz, 1H), 5.67 (tt, *J* = 7.6, 2.5 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ ppm 21.5, 23.8, 24.9, 25.7, 26.1, 29.2, 29.5, 42.9, 58.6, 58.6, 68.3, 71.9, 72.0, 79.1, 116.7, 116.7, 137.2, 140.8; HR-MS (ESI) calculated for $C_{18}H_{32}O_3Na$ [*M*+Na]$^+$: 319.2249, found: 319.2258.

(3*Z*, 4*Z*)-2-isobutyl-3-(3-(4-methoxybenzyloxy)butylidene)-4-(4-methoxybutylidene)-tetrahydrofuran (6e)



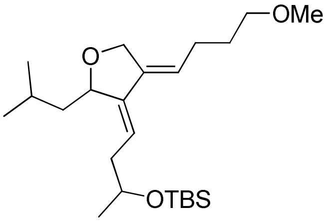
Chemical Formula: $C_{25}H_{38}O_4$
Exact Mass: 402,2770
Molecular Weight: 402,5668

Yield 82 % (17.7 mg, 44.0 µmol). R_f = 0.18 (*n*-hexane/ethyl acetate 10:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.93 (d, *J* = 6.6 Hz, 3 H)/0.94 (d, *J* = 6.6 Hz, 3 H)*, 0.98 (d, *J* = 6.6 Hz, 3 H), 1.09 - 1.26 (m, 1 H), 1.22 (d, *J* = 6.2 Hz, 3 H), 1.41 - 1.56 (m, 1 H), 1.69 (tt, *J* = 6.9, 6.9 Hz, 1 H), 1.79 - 1.93 (m, 1 H), 2.07 (dt, *J* = 8.2, 7.3 Hz, 2 H), 2.14 - 2.27 (m, 1 H), 2.28 - 2.42 (m, 1 H), 3.34 (s, 3 H), 3.38 (t, *J* = 6.4 Hz, 2 H), 3.57 (tq, *J* = 6.5, 5.8 Hz, 1 H), 3.81 (s, 3 H), 4.40 - 4.54 (m, 2 H), 4.46 (s, 2 H), 4.78 (td, *J* = 10.6, 2.4 Hz, 2 H), 5.61 - 5.74 (m, 2 H), 6.88 (d, *J* = 8.8 Hz, 2 H), 7.27 (d, *J* = 8.8 Hz, 2 H)/7.28 (d, *J* = 8.8 Hz, 2 H)*; ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 19.7, 21.5/21.6**, 23.8/23.8**, 24.9/24.9**, 26.1, 29.2, 36.0/36.3**, 42.8/42.8**, 55.3, 58.6, 68.3, 70.1/70.1**, 72.0, 74.1/74.3**, 79.2/79.2**, 113.3, 113.8, 116.9/117.0**, 129.2, 130.9/130.9**, 137.2, 141.8/141.9**, 159.1; HR-MS (ESI) calculated for $C_{25}H_{38}O_4Na$ [*M*+Na]$^+$: 402.2770, found: 402.2771.

*Diastereomers slightly differ in ^{1}H – chemical shifts.

**Diastereomers slightly differ in ^{13}C – chemical shifts.

tert-Butyl((*Z*)-4-((*Z*)-2-isobutyl-4-(4-methoxybutylidene)dihydrofuran-3(2*H*)-ylidene)butan-2-yloxy)dimethylsilane (6f)



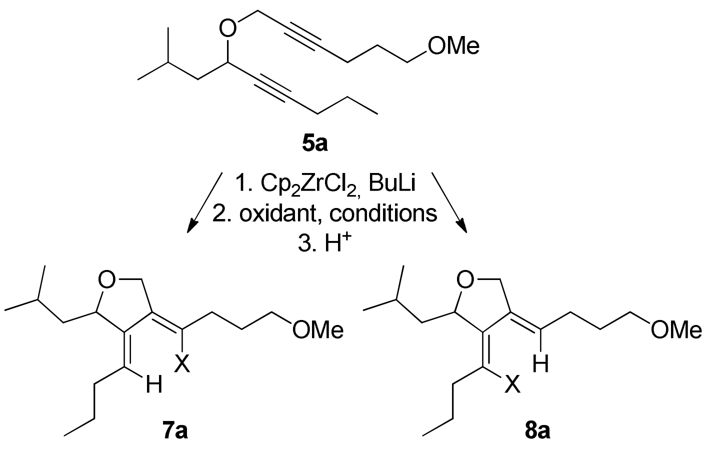
Chemical Formula: $C_{23}H_{44}O_3Si$
Exact Mass: 396,3060
Molecular Weight: 396,6792

Yield 47 % (10.1 mg, 25.0 µmol). R_f = 0.31 (*n*-hexane/ethyl acetate 10:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ ppm 0.05 (s, 3H)/0.06 (s, 3H)*, 0.06 (s, 3H)/0.06 (s, 3H)*, 0.89 (s, 9H)/0.90 (s, 9H)*, 0.94 (d, *J* = 6.8 Hz, 3H), 0.98 (d, *J* = 6.7 Hz, 3H), 1.13 (ddd, *J* = 14.0, 9.6, 2.8 Hz, 1H)/1.19 (ddd, *J* = 14.2, 9.6, 2.8 Hz, 1H)*, 1.16 (d, *J* = 6.1 Hz, 3H), 1.17 (d, *J* = 6.1 Hz, 3H), 1.48 (ddd, *J* = 14.3, 10.5, 4.2 Hz, 1H)/1.49 (ddd, *J* = 14.3, 10.5, 4.2 Hz, 1H)*, 1.69 (quin, *J* = 7.1 Hz, 2H), 1.82 - 1.90 (m, 1 H), 2.07 (dt, *J* = 8.1, 7.2 Hz, 2H), 2.12 (ddd, *J* = 14.6, 8.4, 6.6 Hz, 1H), 2.19 (ddd, *J* = 14.8, 8.3, 6.4 Hz, 1H), 3.34 (s, 3H), 3.37 (t, *J* = 6.5 Hz, 2H), 3.83 - 3.89 (m, 1H), 4.41 - 4.50 (m, 2H), 4.74 - 4.80 (m, 1H), 5.63 - 5.70 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ ppm -4.8/-4.7**, -4.6/-4.5**, 18.1/18.2**, 21.5/21.5**, 23.8/23.8**, 23.8/23.9**, 24.8/24.9**, 25.8/25.9**, 26.1, 29.3, 39.3/39.5**, 42.9/43.0**, 58.6, 68.3/68.4**, 68.6/68.6**, 71.9, 79.1/79.2**, 114.1, 116.7/116.7**, 137.2/137.3**, 141.3/141.5**; HR-MS (ESI) calculated for $C_{23}H_{44}O_3SiNa$ [*M*+Na]$^+$: 419.2957, found: 419.2961.

*Diastereomers slightly differ in ^{1}H – chemical shifts.

**Diastereomers slightly differ in ^{13}C – chemical shifts.

Table S1. Zirconocene-mediated cyclisation of 1, 6-diyne **5a** and oxidative ring-opening.



entry	oxidant	conditions[a]	**7a** : **8a**	yield [%]
1	NIS (X=I)	0 °C, 2 h	-	0%[b]
2	NBS (X=Br)	0 °C, 2 h	-	dec.[c]
3	NCS (X=Cl)	0 °C, 3 h	-	0%[b]
4	I_2 (1.0 eq.) (X=I)	0 °C, 3 h	-	dec.[c]
5	*n*-BuLi, $CBrCl_3$ (X=Br)	-78 °C to rt, 2 h	-	dec.[c]
6	$AlMe_3$ (X=Me)	rt to 50 °C, 2 h	-	0%[b]
7	I_2 (1.0 eq.) (X=I)	-78 °C, 2 h	-	56%[d]
8	NBS (X=Br)	-78 °C, 2 h	> 20:1	65%

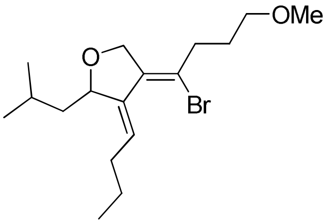
[a] All reactions were initiated in the same manner by zirconocene-mediated cyclization (step 1) and hydrolysed by addition of 3N HCl. [b] No conversion was detected and **6** was reisolated by column chromatography. [c] dec.: decomposition. [d] A 3:1 mixture of the diiodide and a monoiodide was obtained.

General Procedure for the Preparation of 3-Bromoalkylidene-4-alkylidene-substituted Tetrahydrofurans from 1,6-Diynes 5a-f:

1.00 eq. of Cp_2ZrCl_2 was dissolved in extra dry THF and cooled under argon to -78 °C. Then, 2.00 eq. of *n*-butyllithium (2.0 M in cyclohexane) were added via syringe and the resulting yellow solution was stirred at -78 °C. After 30 min of stirring, 1.00 eq. of the pre-dried 1,6-diyne in extra dry THF was successively added and the solution was allowed to warm to room temperature. After 2 h of stirring, the reaction mixture was again cooled to -78 °C, 1.20 eq. of NBS were added and stirring was continued at this temperature for additional 2 h. The solution was then allowed to warm to room temperature and immediately quenched with 1N HCl. Phases were separated and the aqueous layer was extracted with diethyl ether. The combined organic layers were dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by flash chromatography afforded the corresponding bromides **7a-d, 7f, 8d-e** in variable yields given below.

1,6-Diyne	Cp_2ZrCl_2	*n*-BuLi	THF	NBS	Product	Purification
5a 14.0 mg (54.0 μmol)	16.0 mg (54.0 μmol)	54.0 μl (108 μmol)	0.2 + 0.2 ml	12.0 mg 65.0 μmol	**7a**	10.0 g SiO_2, *n*-hexane/ethyl acetate (40:1)
5b 15.0 mg (54.0 μmol)	16.0 mg (54.0 μmol)	54.0 μl (108 μmol)	0.2 + 0.2 ml	12.0 mg 65.0 μmol	**7b**	10.0 g SiO_2, *n*-hexane/ethyl acetate (40:1)
5c 13.0 mg (54.0 μmol)	16.0 mg (54.0 μmol)	54.0 μl (108 μmol)	0.2 + 0.2 ml	12.0 mg 65.0 μmol	**7c**	10.0 g SiO_2, *n*-hexane/ethyl acetate (40:1)
5d 3.90 mg (13.0 μmol)	4.00 mg (13.0 μmol)	13.0 μl (26.0 μmol)	0.1 + 0.1 ml	2.80 mg 15.6 μmol	**7d/8d**	5.00 g SiO_2, *n*-hexane/ethyl acetate (40:1)
5e 44.0 mg (108 μmol)	32.0 mg (108 μmol)	108 μl (216 μmol)	0.4 + 0.4 ml	24.0 mg 130 μmol	**8e**	10.0 g SiO_2, *n*-hexane/ethyl acetate (20:1)
5f 21.0 mg (54.0 μmol)	16.0 mg (54.0 μmol)	54.0 μl (108 μmol)	0.2 + 0.2 ml	12.0 mg 65.0 μmol	**7f**	10.0 g SiO_2, *n*-hexane/ethyl acetate (40:1)

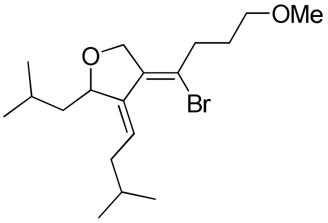
(3*Z*, 4*E*)-4-(1-Bromo-4-methoxybutylidene)-3-butylidene-2-isobutyltetrahydrofuran (7a)



Chemical Formula: $C_{17}H_{29}BrO_2$
Exact Mass: 344,1351
Molecular Weight: 345,3150

Yield 65 % (12.2 mg, 35.0 µmol). R_f = 0.36 (*n*-hexane/ethyl acetate 10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 0.95 (d, *J* = 6.9 Hz, 3H), 0.98 (d, *J* = 7.3 Hz, 3H), 0.98 (d, *J* = 6.6 Hz, 3H), 1.15 (ddd, *J* = 14.3, 9.6, 2.6 Hz, 1H), 1.49 (tq, *J* = 8.6, 6.8 Hz, 2H), 1.51 (ddd, *J* = 14.3, 10.4, 4.0 Hz, 1H), 1.79 - 1.88 (m, 1H), 1.87 (quin, *J* = 6.8 Hz, 2H), 1.99 - 2.12 (m, 2H), 2.45 - 2.54 (m, 2H), 3.33 (s, 3H), 3.37 (t, *J* = 6.0 Hz, 2H), 4.46 - 4.55 (m, 2H), 4.87 (dt, *J* = 10.4, 2.2 Hz, 1H), 6.68 (dt, *J* = 7.4, 1.8 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 13.9, 21.6, 22.7, 23.8, 24.9, 27.9, 31.8, 37.0, 42.7, 58.5, 70.7, 70.8, 80.0, 116.0, 127.3, 134.0, 139.3; HR-MS (ESI) calculated for $C_{17}H_{29}BrO_2Na$ $[M+Na]^+$: 367.1249, found: 367.1251.

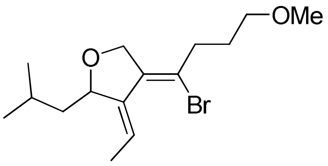
(3*Z*, 4*E*)-4-(1-Bromo-4-methoxybutylidene)-2-isobutyl-3-(3-methylbutylidene)tetrahydrofuran (7b)



Chemical Formula: $C_{18}H_{31}BrO_2$
Exact Mass: 358,1507
Molecular Weight: 359,3415

Yield 65 % (12.4 mg, 34.0 µmol).[7] R_f = 0.36 (*n*-hexane/ethyl acetate 10:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.94 (d, *J* = 6.9 Hz, 3H), 0.95 (d, *J* = 6.6 Hz, 3H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.97 (d, *J* = 6.6 Hz, 3H), 1.15 (ddd, *J* = 14.2, 9.6, 2.6 Hz, 1H), 1.51 (ddd, *J* = 14.3, 10.4, 4.0 Hz, 1H), 1.63 - 1.78 (m, 1H), 1.79 - 1.88 (m, 1H), 1.87 (quin, *J* = 6.2 Hz, 2H), 1.92 (ddd, *J* = 14.2, 7.6, 7.2 Hz, 1H), 2.00 (ddd, *J* = 14.3, 7.4, 7.2 Hz, 1H), 2.50 (dt, *J* = 7.1, 2.2 Hz, 1H), 3.33 (s, 3H), 3.37 (t, *J* = 6.0 Hz, 2H), 4.51 (br. s., 2H), 4.85 (dt, *J* = 10.4, 2.1 Hz, 1H), 6.71 (dt, *J* = 7.4, 1.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 21.6, 22.3, 22.7, 23.8, 24.9, 27.8, 28.8, 36.9, 38.8, 42.6, 58.5, 70.7, 70.7, 79.9, 116.0, 126.4, 134.0, 139.6; HR-MS (ESI) calculated for $C_{18}H_{31}BrO_2Na$ [*M*+Na]$^+$: 381.1405, found: 381.1401.

(3*Z*, 4*E*)-4-(1-bromo-4-methoxybutylidene)-3-ethylidene-2-isobutyltetrahydrofuran (7c)



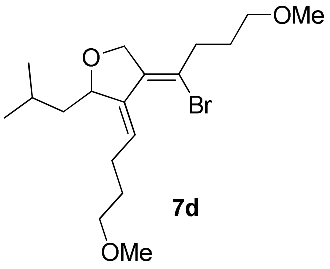
Chemical Formula: $C_{15}H_{25}BrO_2$
Exact Mass: 316,1038
Molecular Weight: 317,2618

Yield 64 % (10.9 mg, 34.0 µmol). R_f = 0.35 (*n*-hexane/ethyl acetate 10:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 0.95 (d, *J* = 7.0 Hz, 3H), 0.99 (d, *J* = 6.6 Hz, 3H), 1.18 (ddd, *J* = 14.1, 9.5, 2.6 Hz, 1H), 1.51 (ddd, *J* = 14.4, 10.6, 4.2 Hz, 1H), 1.74 (d, *J* = 7.0 Hz, 3H), 1.79 - 1.86 (m, 1H), 1.87 (quin, *J* = 6.6 Hz, 2H), 2.49 (t, *J* = 6.9 Hz, 1H), 2.50 (t, *J* = 7.3 Hz, 1H), 3.33 (s, 3 H), 3.37 (t, *J* = 6.0 Hz, 2H), 4.46 - 4.58 (m, 2H), 4.87 - 4.94 (m, 1H), 6.77 (dq, *J* = 7.3, 1.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm 15.1, 21.5, 23.7, 24.9, 27.8, 36.9, 42.2, 58.5, 70.7, 70.9, 79.9, 115.9, 121.5, 133.9, 140.3; HR-MS (ESI) calculated for $C_{15}H_{26}O_2Na$ [*M*+Na]$^+$: 339.0936, found: 339.0940.

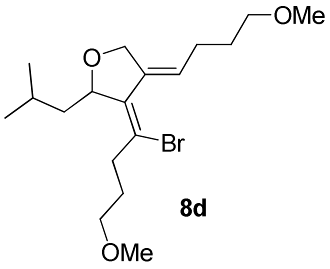
---

[7] Product could only be obtained as a 3:1 mixture of product and the corresponding 1,6-diyne which could not be separated by column chromatography. Yield calculations were based on ^{1}H-NMR integral measurements.

(3*Z*, 4*E*)-4-(1-bromo-4-methoxybutylidene)-2-isobutyl-3-(4-methoxybutylidene)tetrahydrofuran (7d) / (3E,4Z)-3-(1-bromo-4-methoxybutylidene)-2-isobutyl-4-(4-methoxybutylidene)tetrahydrofuran (8d)



7d



8d

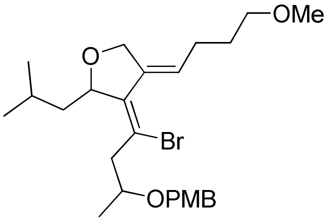
Chemical Formula: $C_{18}H_{31}BrO_3$
Exact Mass: 374,1457
Molecular Weight: 375,3409

Yield 46 % (2.20 mg, 6.00 μmol). R$_f$ = 0.37 (*n*-hexane/ethyl acetate 10:1); **7d**: ^{1}H NMR (500 MHz, CDCl$_3$) δ ppm 0.87 (d, *J* = 6.9 Hz, 3H)*, 0.91 (d, *J* = 6.6 Hz, 3H)*, 1.01 - 1.12 (m, 1H)*, 1.40 - 1.51 (m, 1H)*, 1.62 - 1.70 (m, 2H)*, 1.72 - 1.79 (m, 1H)*, 1.80 (quin, *J* = 6.6 Hz, 2H), 2.09 (dq, *J* = 10.8, 7.5, 7.2 Hz, 1H), 2.07 (dq, *J* = 10.8, 7.5, 7.2 Hz, 1H), 2.43 (t, *J* = 7.2 Hz, 2H), 3.25 - 3.28 (s, 3H)*, 3.25 - 3.28 (s, 3H)*, 3.28 - 3.37 (m, 4H)*, 4.42 - 4.45 (m, 2H), 4.78 - 4.83 (m, 1H)*, 6.56 - 6.65 (m, 1H)*; ^{13}C NMR (126 MHz, CDCl$_3$) δ ppm 20.3/20.5**, 22.7/22.7**, 23.8/23.9**, 25.2, 26.8/27.3**, 28.0/28.3**, 36.0, 41.3/41.6**, 57.5/57.5**, 57.6/57.6**, 69.7, 69.7/69.8**, 70.8/70.9**, 78.9, 115.3, 125.4, 132.9, 138.8; **8d**: ^{1}H NMR (500 MHz, CDCl$_3$) δ ppm 0.87 (d, *J* = 6.9 Hz, 3H)*, 0.91 (d, *J* = 6.6 Hz, 3H)*, 1.01 - 1.12 (m, 1H)*, 1.40 - 1.51 (m, 1H)*, 1.62 - 1.70 (m, 2H)*, 1.72 - 1.79 (m, 1H)*, 1.77 - 1.82 (m, 1H), 1.83 - 1.91 (m, 1H), 1.99 - 2.06 (m, 2H), 2.36 - 2.46 (m, 1H), 2.48 - 2.57 (m, 1H), 3.25 - 3.28 (s, 3H)*, 3.25 - 3.28 (s, 3H)*, 3.28 - 3.37 (m, 4H), 4.45 - 4.47 (m, 2H), 4.78 - 4.83 (m, 1H)*, 6.56 - 6.65 (m, 1H)*; ^{13}C NMR (126 MHz, CDCl$_3$) δ ppm 20.3 (s), 20.5 (s), 22.7 (s), 22.7 (s), 23.8 (s), 23.9 (s), 25.5 (s), 26.8 (s), 27.3 (s), 28.0 (s), 28.3 (s), 35.6 (s), 41.3 (s), 41.6 (s), 57.5 (s), 57.5 (s), 57.6 (s), 57.6 (s), 68.1 (s), 69.7 (s), 69.8 (s), 70.8 (s), 70.9 (s), 80.6 (s), 117.0 (s), 126.3 (s), 134.6 (s), 137.0 (s) ^{13}C NMR (126 MHz, CDCl$_3$) δ ppm 20.3/20.5**, 22.7/22.7**, 23.8/23.9**, 25.5, 26.8/27.3**, 28.0/28.3**, 35.6, 41.3/41.6**, 57.5/57.5**, 57.6/57.6**, 68.1, 69.7/69.8**, 70.8/70.9**, 80.6, 117.0, 126.3, 134.6, 137.0; HR-MS (ESI) calculated for $C_{18}H_{31}BrO_3Na$ [*M*+Na]$^+$: 397.1354, found: 397.1350.

^{*1}H-signals could not be clearly assigned to one of the regioisomers.

^{**13}C-signals could not be clearly assigned to one of the regioisomers.

(3*Z*, 4*E*)-4-(1-bromo-4-methoxybutylidene)-2-isobutyl-3-(3-(4-methoxybenzyloxy)-butylidene)tetrahydrofuran (8e)



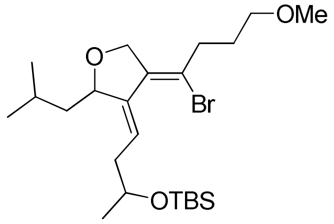
Chemical Formula: $C_{25}H_{37}BrO_4$
Exact Mass: 480,1875
Molecular Weight: 481,4629

Yield 69 % (36.1 mg, 75.0 µmol).[8] R_f = 0.18 (*n*-hexane/ethyl acetate 10:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ ppm 0.88 (d, *J* = 6.8 Hz, 3 H), 0.94 (d, *J* = 6.6 Hz, 3 H), 1.24 (d, *J* = 6.1 Hz, 3 H), 1.29 (ddd, *J* = 14.6, 9.8, 2.4 Hz, 2 H), 1.47 (ddd, *J* = 14.8, 10.6, 3.8 Hz, 1 H), 1.76 (tt, *J* = 6.9, 6.7 Hz, 2 H), 1.78 - 1.83 (m, 1 H), 2.12 (td, *J* = 8.1, 7.2 Hz, 2 H), 2.51 (dd, *J* = 14.2, 7.1 Hz, 1 H), 2.80 (dd, *J* = 14.2, 6.6 Hz, 1 H), 3.35 (s, 3 H), 3.42 (t, *J* = 6.4 Hz, 2 H), 3.81 (s, 3 H), 4.00 (qt, *J* = 6.2, 6.0 Hz, 1 H), 4.45 (d, *J* = 11.3 Hz, 1 H), 4.52 (d, *J* = 11.3 Hz, 1 H), 4.53 (s, 2 H), 4.85 (dd, *J* = 11.2, 2.4 Hz, 1 H), 6.70 (tt, *J* = 7.5, 2.4 Hz, 1 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 7.26 (d, *J* = 8.4 Hz, 2 H); ^{13}C NMR (151 MHz, $CDCl_3$) δ ppm 19.5, 21.3, 23.6, 24.8, 26.5, 29.0, 41.8, 47.3, 55.3, 58.6, 68.9, 70.7, 71.9, 73.5, 82.0, 113.7, 115.1, 127.7, 129.2, 130.8, 135.7, 139.0, 159.0; HR-MS (ESI) calculated for $C_{25}H_{37}BrO_4Na$ $[M+Na]^+$: 503.1773, found: 503.1773.

---

[8] The diastereomeric mixture could be separated by column chromatography. One of the diastereomers was obtained in pure form, the other diastereomer could only be afforded in an approximately 1:1 mixture of the diastereomers. NMR-data were received from pure diastereomer.

((*Z*)-4-((*E*)-4-(1-bromo-4-methoxybutylidene)-2-isobutyldihydrofuran-3(2*H*)-ylidene)butan-2-yloxy)(*tert*-butyl)dimethylsilane (7f)



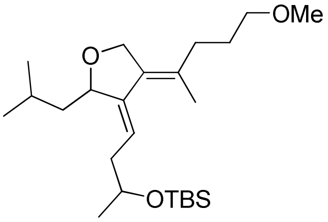
Chemical Formula: $C_{23}H_{43}BrO_3Si$
Exact Mass: 474,2165
Molecular Weight: 475,5752

Yield 80 % (20.4 mg, 43.0 μmol). R$_f$ = 0.31 (*n*-hexane/ethyl acetate 10:1); ^{1}H NMR (500 MHz, CDCl$_3$) δ ppm 0.06 (s, 3H)/0.07 (s, 3H)*, 0.08 (s, 6H), 0.89 (s, 9H)/0.90 (s, 9H)*, 0.94 (d, *J* = 6.6 Hz, 3H), 0.98 (d, *J* = 6.6 Hz, 3H), 1.15 (ddd, *J* = 14.5, 9.7, 2.6 Hz, 1H)/1.21 (ddd, *J* = 14.8, 8.8, 2.8 Hz, 1H)*, 1.19 (d, *J* = 6.0 Hz, 3 H), 1.50 (ddd, *J* = 14.8, 10.4, 4.2 Hz, 1H)/1.51 (ddd, *J* = 14.7, 10.4, 4.2 Hz, 1H)*, 1.78 - 1.85 (m, 1H), 1.87 (quin, *J* = 6.6 Hz, 2H), 2.16 (ddd, *J* = 15.0, 8.2, 6.1 Hz, 1H), 2.25 (ddd, *J* = 14.6, 7.5, 7.0 Hz, 1H), 2.43 - 2.57 (m, 2H), 3.33 (s, 3H), 3.37 (t, *J* = 5.9 Hz, 2H), 3.88 - 3.96 (m, 1H), 4.48 - 4.55 (m, 2H), 4.87 (tt, *J* = 10.4, 1.8 Hz, 1H), 6.69 - 6.75 (m, 1H); ^{13}C NMR (126 MHz, CDCl$_3$) δ ppm -4.7/-4.6**, -4.5/-4.5**, 18.1/18.1**, 21.5/21.6**, 23.7/23.8**, 23.9/23.9**, 24.9/24.9**, 25.9/25.9**, 27.8/27.9**, 36.9, 39.9/40.1**, 42.5/42.6**, 58.5, 68.2/68.3**, 70.6/70.6**, 70.7/70.8**, 80.0/80.0**, 116.2/116.3**, 123.7123.8**, 133.9/134.0**, 140.2/140.5**; HR-MS (ESI) calculated for $C_{23}H_{43}BrO_3SiNa$ [*M*+Na]$^{+}$: 497.2063, found: 497.2073.

*Diastereomers slightly differ in ^{1}H – chemical shifts.

**Diastereomers slightly differ in ^{13}C – chemical shifts.

***tert*-butyl((*Z*)-4-((*Z*)-2-isobutyl-4-(5-methoxypentan-2-ylidene)dihydrofuran-3(2*H*)-ylidene)butan-2-yloxy)dimethylsilane (10)**



Chemical Formula: $C_{24}H_{46}O_3Si$
Exact Mass: 410,3216
Molecular Weight: 410,7057

To a stirring solution of bromide **7f** (11.5 mg, 24.0 µmol, 1.00 eq.) in dry THF (0.60 ml) at -78 °C was added *tert*-butyllithium (1.7 M in pentane, 34.0 µl, 48.0 µmol, 2.00 eq.). After stirring at that temperature for 15 min, Me_2SO_4 (3.50 µl, 35 µmol, 1.20 eq.) was subsequently added. The reaction mixture was allowed to warm to room temperature, stirred for additional 15 min and quenched with water (0.50 ml). Phases were separated and the aqueous layer was extracted with diethyl ether (3 x 2.00 ml). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (10.0 g SiO_2, *n*-hexane/ethyl acetate 40:1) afforded a 5:1 mixture of **9** and diene **7f** (7.80 mg, 19.0 µmol, 80 % of pure **9**).[9] R_f = 0.31 (*n*-hexane/ethyl acetate 10:1); ^1H NMR (400 MHz, $CDCl_3$) δ ppm 0.05 (s, 3 H)/0.07 (s, 3 H)*, 0.06 (s, 6 H), 0.89 (s, 9 H)/0.90 (s, 9 H)*, 0.94 (d, *J* = 6.7 Hz, 3 H), 0.98 (d, *J* = 6.7 Hz, 3 H), 1.12 - 1.16 (m, 1 H), 1.18 (d, *J* = 6.0 Hz, 3 H), 1.45 - 1.51 (m, 1 H), 1.61 - 1.76 (m, 2 H), 1.81 - 1.88 (m, 1 H), 1.90 (s, 3 H), 1.96 - 2.10 (m, 2 H), 2.13 - 2.28 (m, 2 H), 3.32 - 3.35 (m, 2 H), 3.33 (s, 3 H), 3.88 (tq, *J* = 6.4, 6.2 Hz, 1 H), 4.43 (d, *J* = 12.4 Hz, 1 H), 4.50 (d, *J* = 12.1 Hz, 1 H), 4.75 - 4.82 (m, 1 H), 5.55 - 5.63 (m, 1 H); ^{13}C NMR (151 MHz, $CDCL_3$) δ ppm -4.7/-4.7**, -4.5/-4.4**, 18.1/18.1**, 19.8/19.8**, 21.6/21.6**, 23.7/23.8**, 23.8/23.9**, 24.8/24.8**, 25.8/25.9**, 27.5/27.5**, 33.8/33.8**, 40.0/40.2**, 43.0/43.1**, 58.6, 68.4, 68.6, 69.5/69.6**, 72.0/72.0**, 79.2/79.3**, 120.2/120.3**, 128.9/128.9**, 130.8/130.8**, 142.0/142.3**; HR-MS (ESI) calculated for $C_{24}H_{46}O_3SiNa$ $[M+Na]^+$: 433.3114, found: 433.3118.

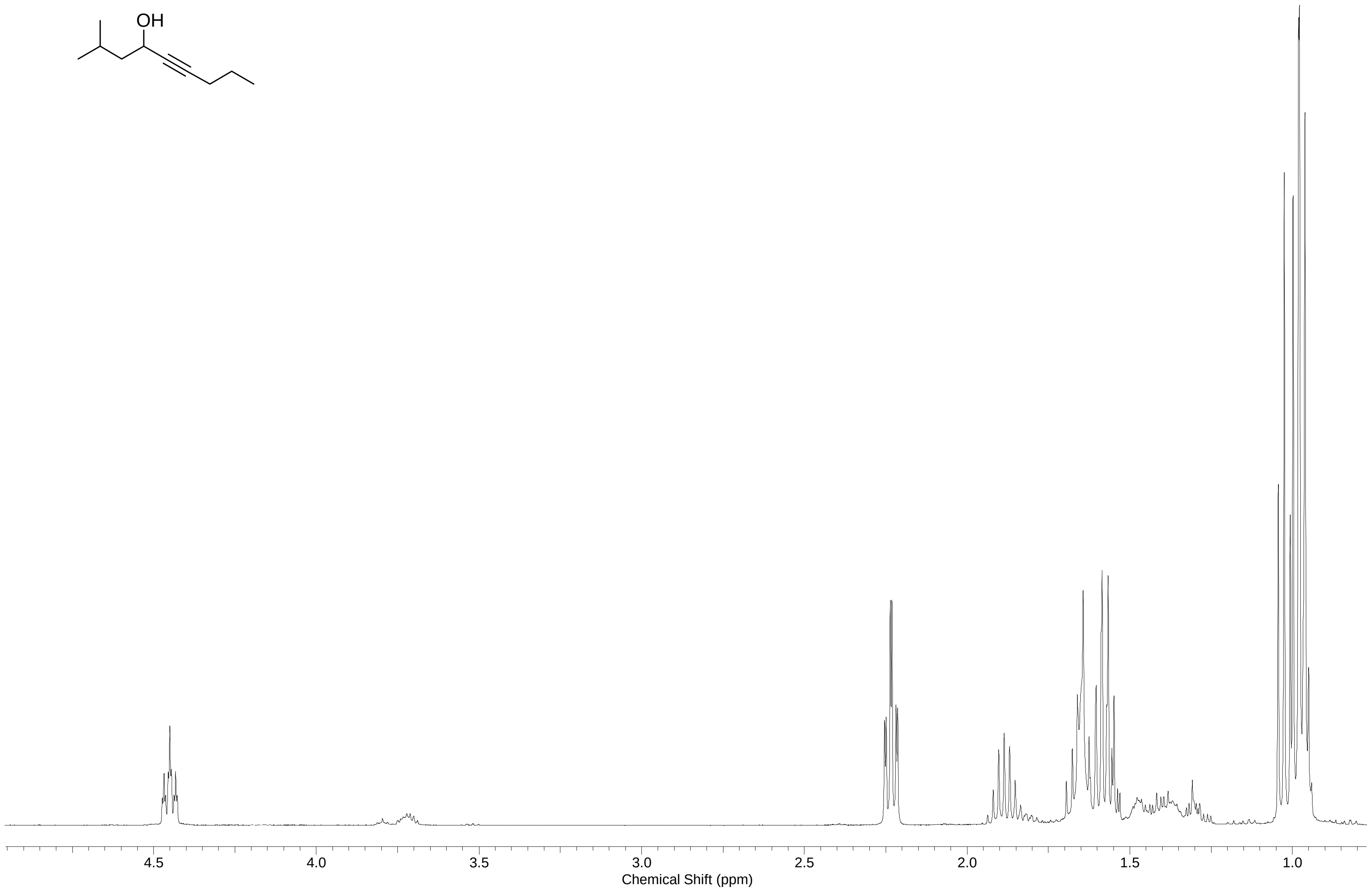
*Diastereomers slightly differ in ^1H – chemical shifts.

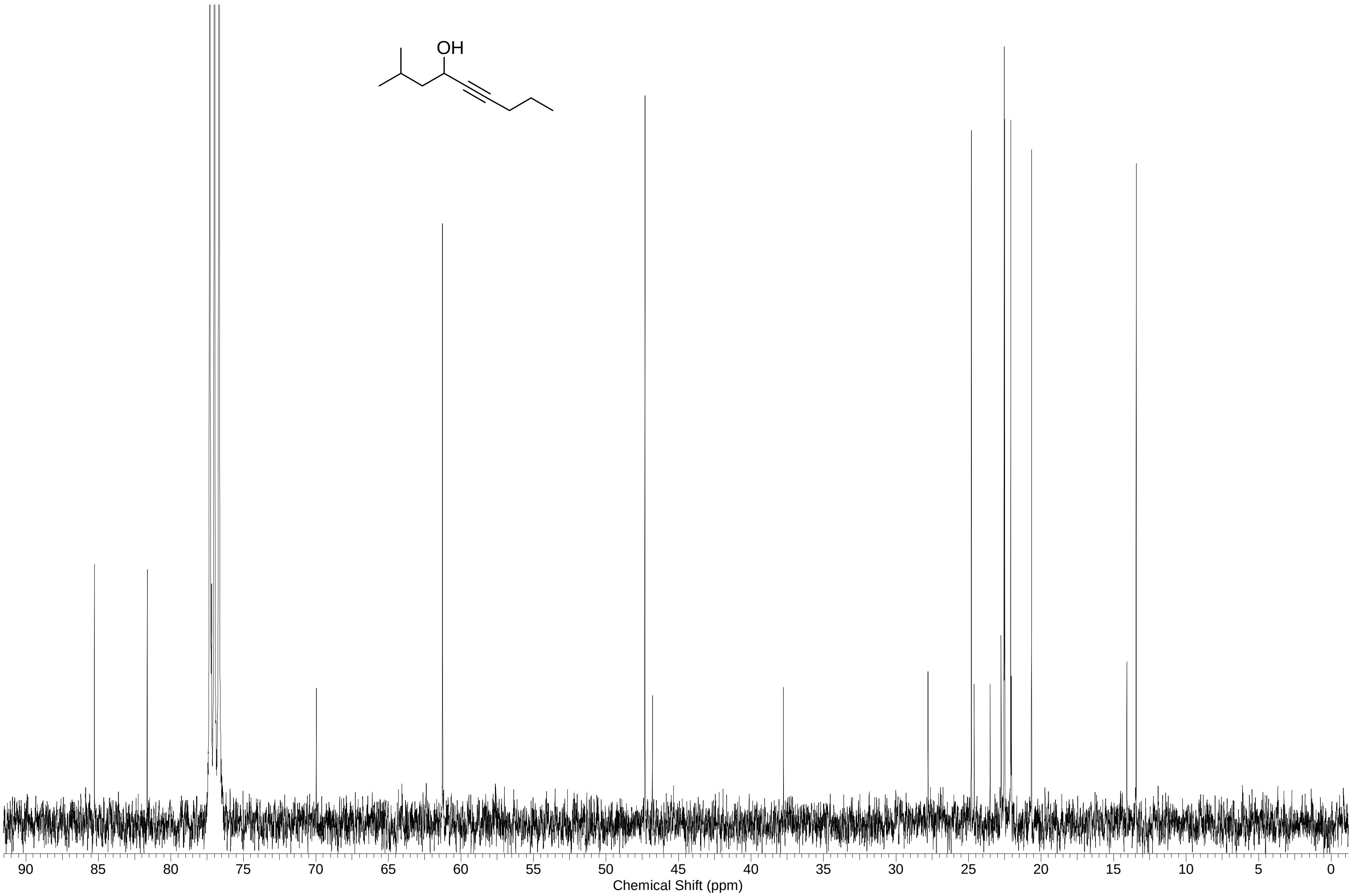
**Diastereomers slightly differ in ^{13}C – chemical shifts.

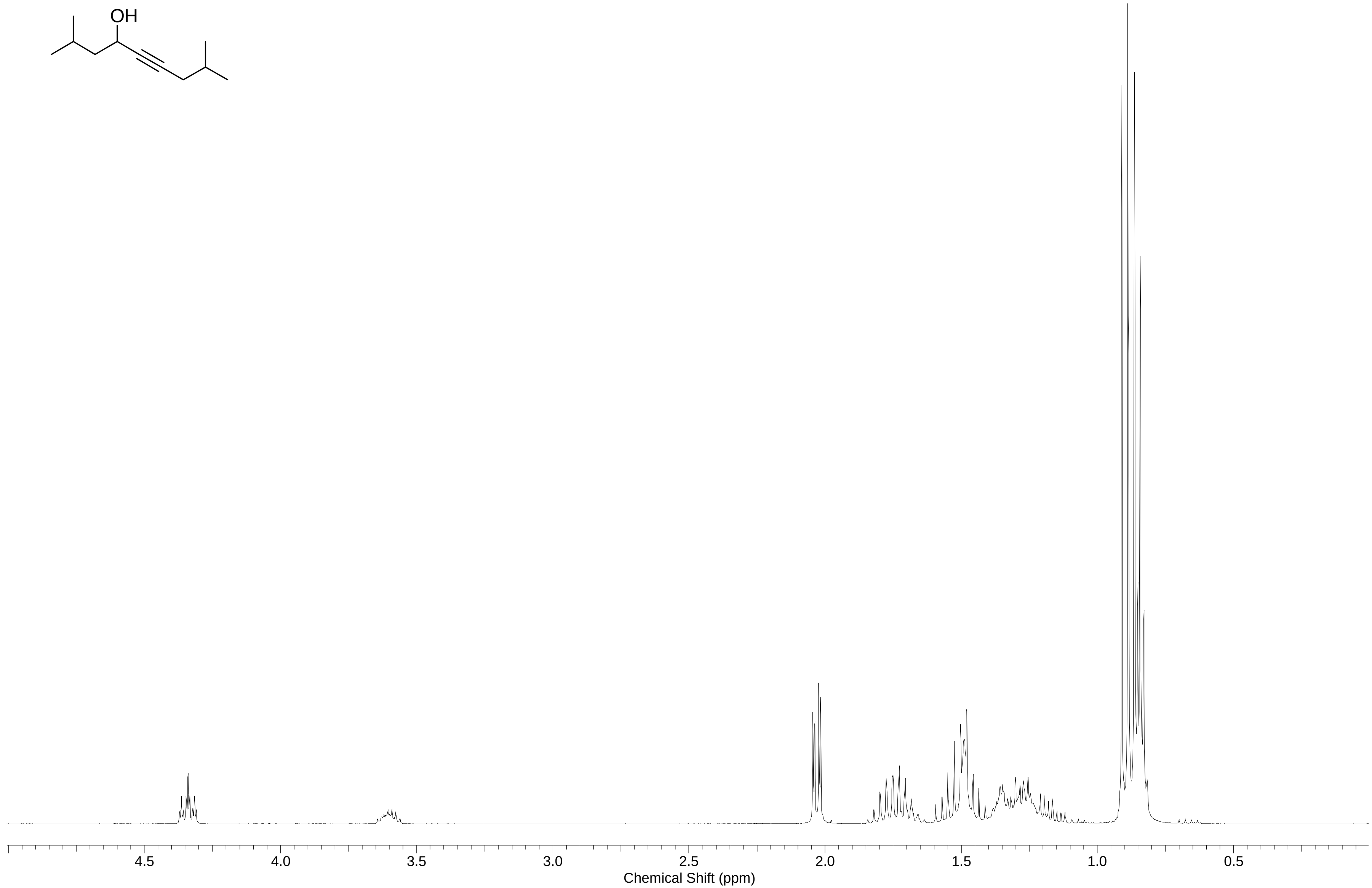
---

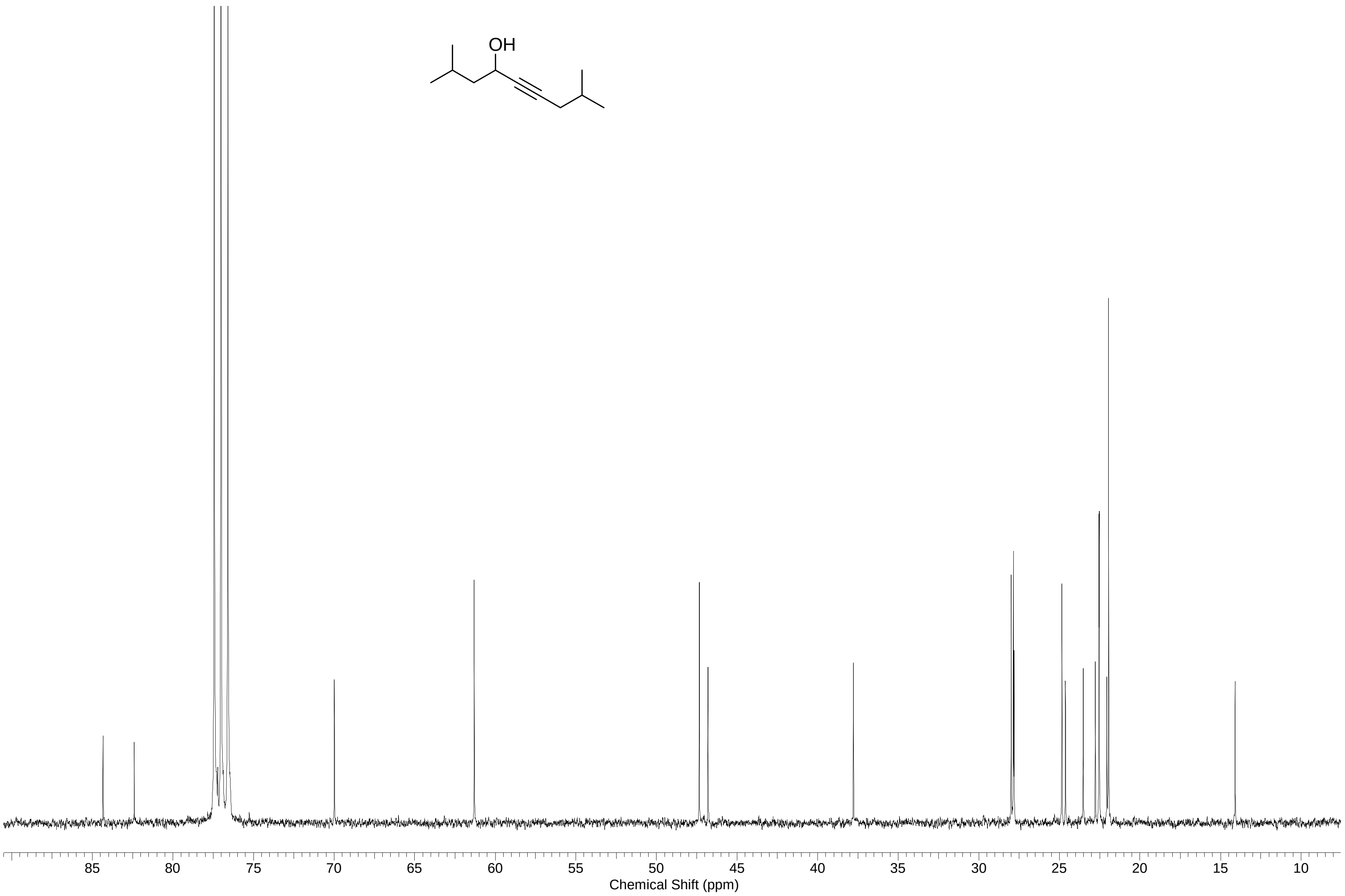
[9] Yield calculations were based on ^1H-NMR integral measurements.

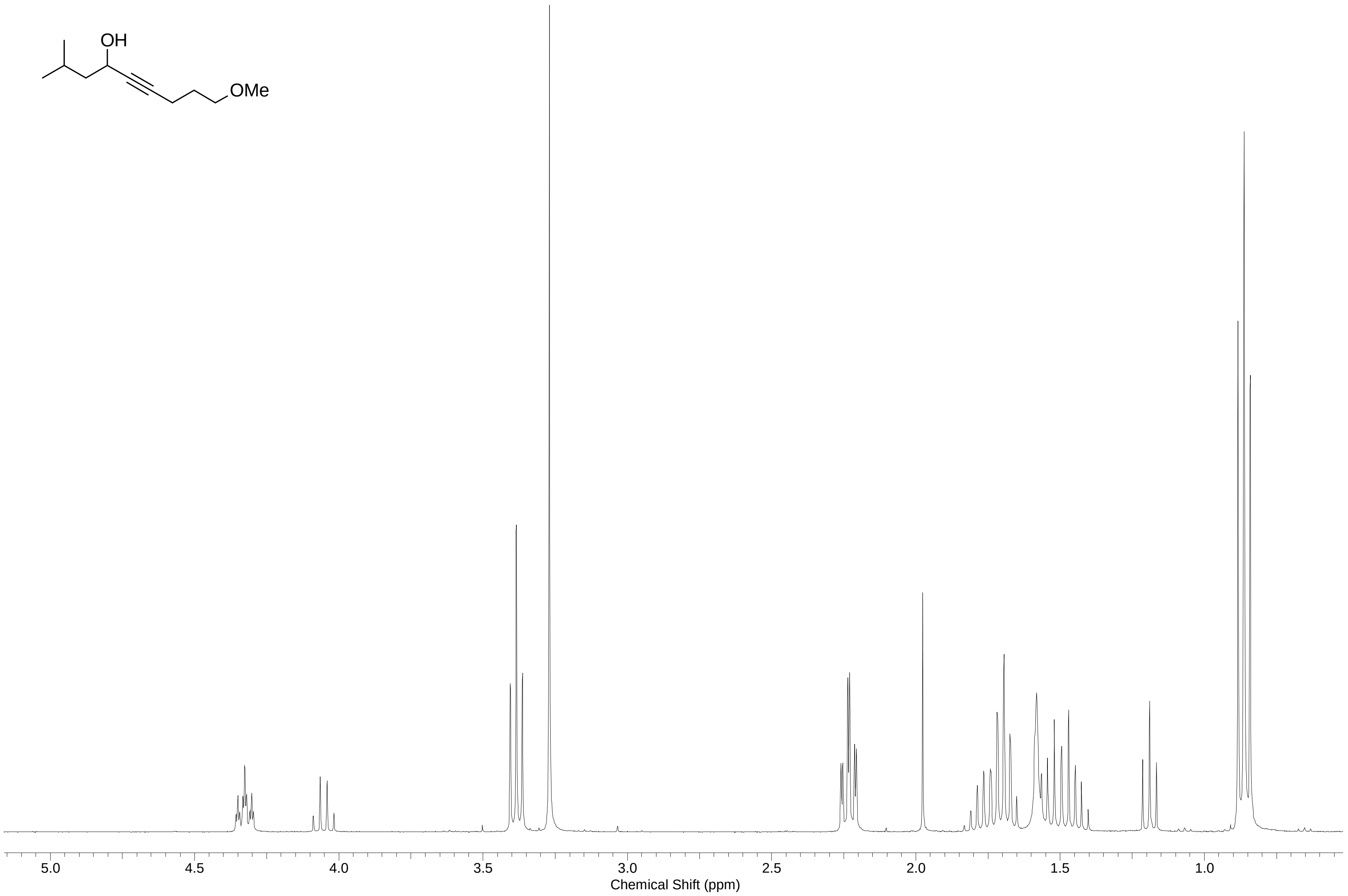
II. COPIES OF ^{1}H AND ^{13}C NMR SPECTRA.

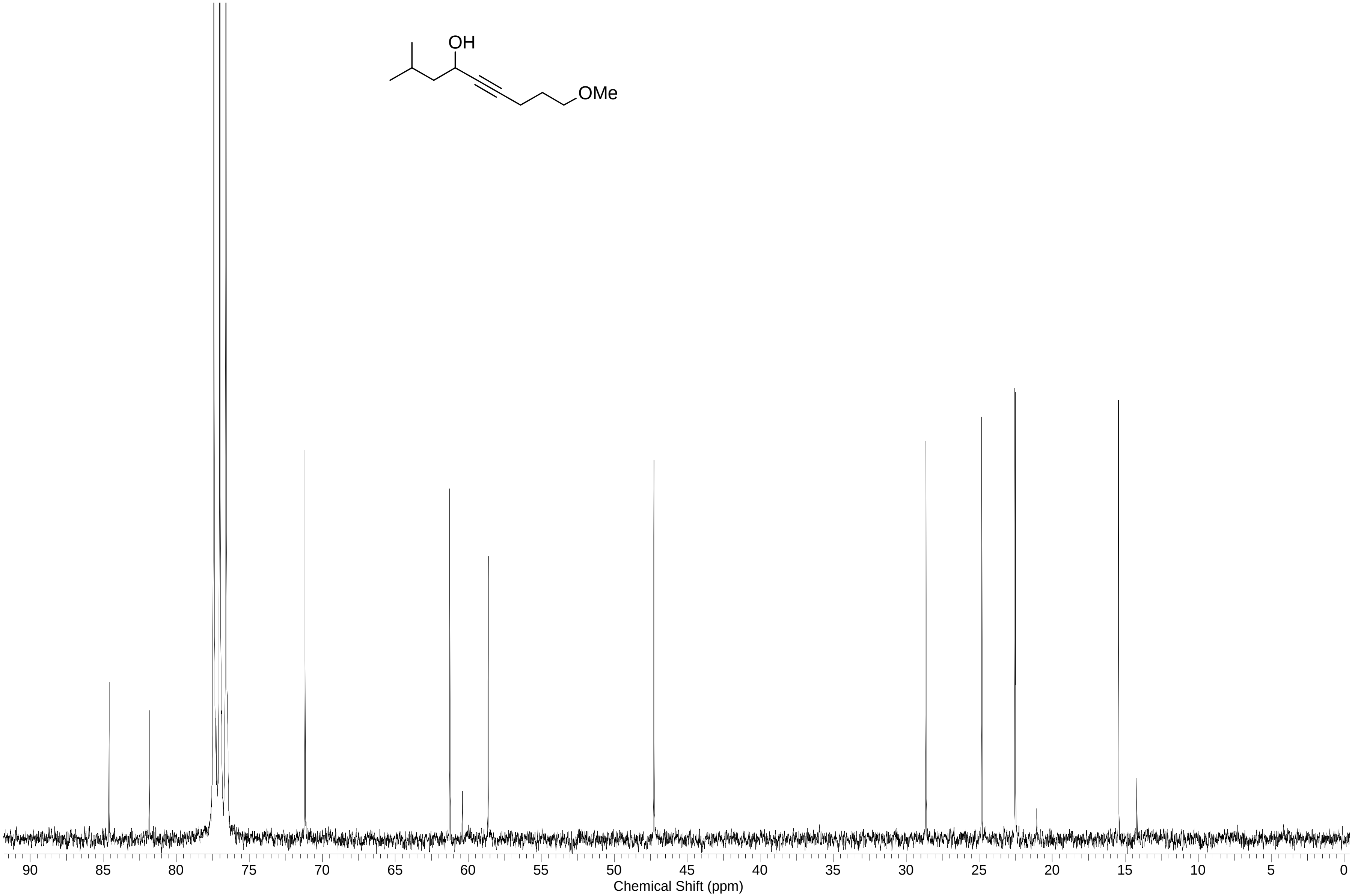

OH
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

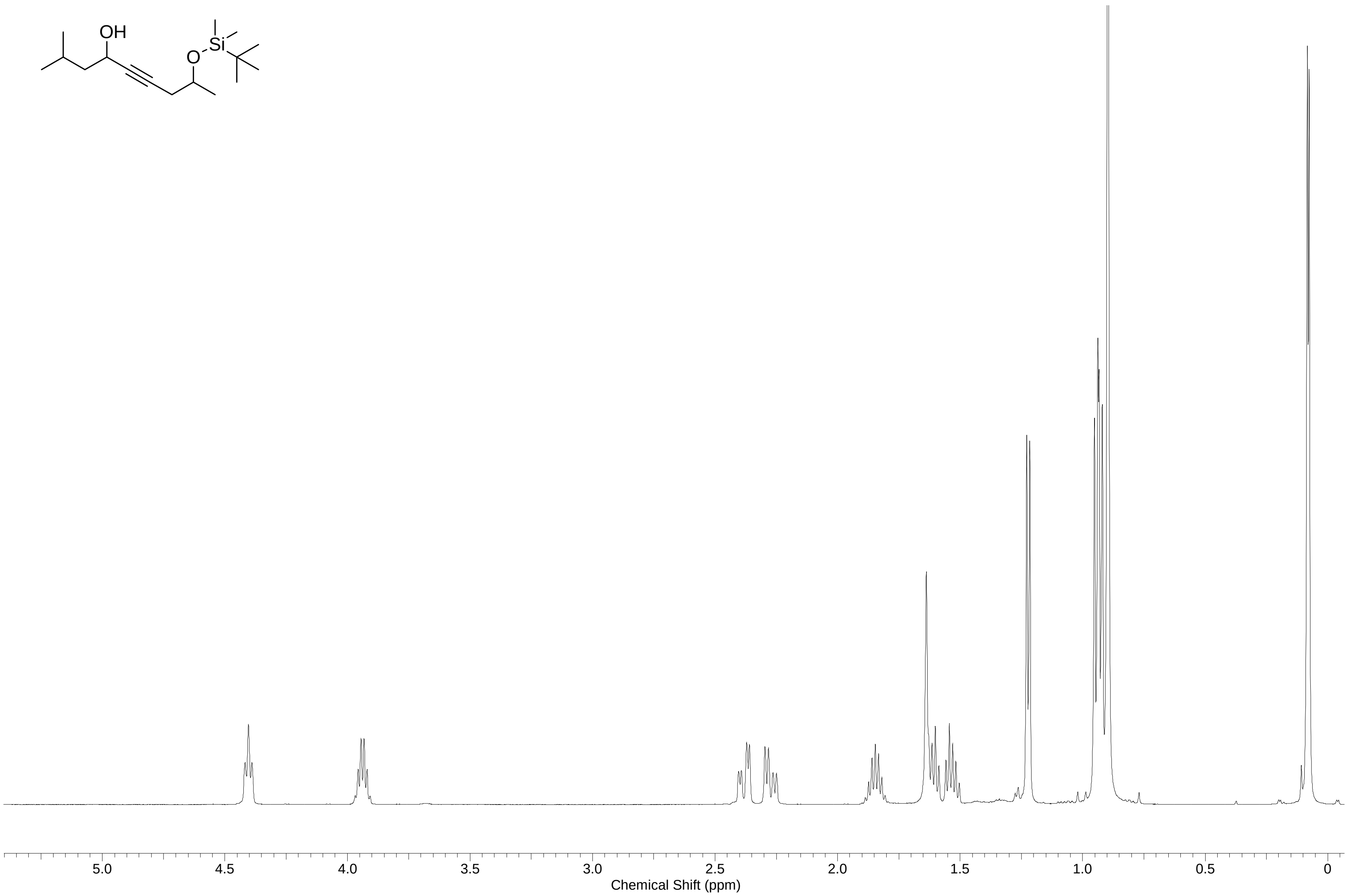

OH
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
Chemical Shift (ppm)

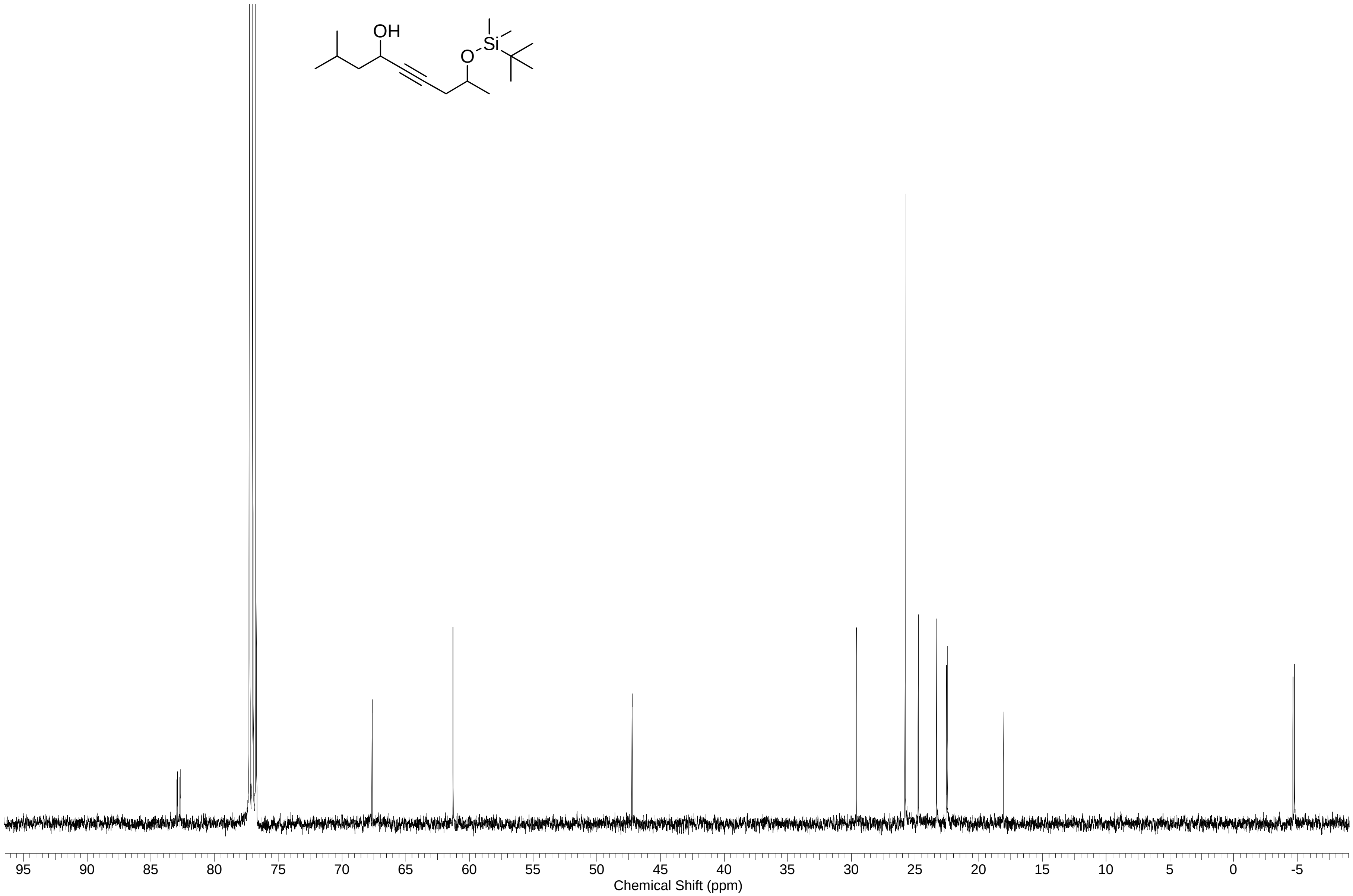

OH
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

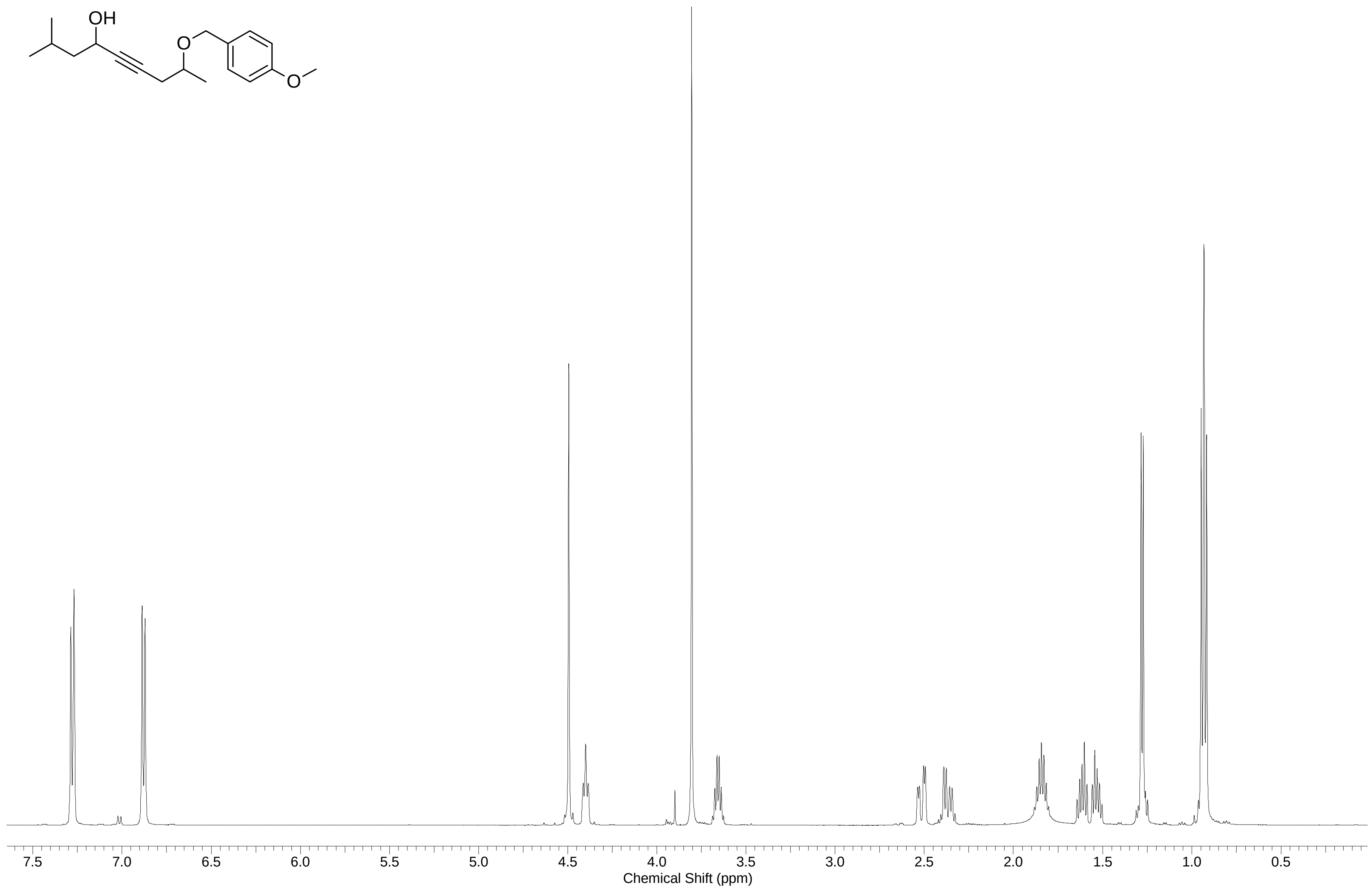

OH
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
Chemical Shift (ppm)

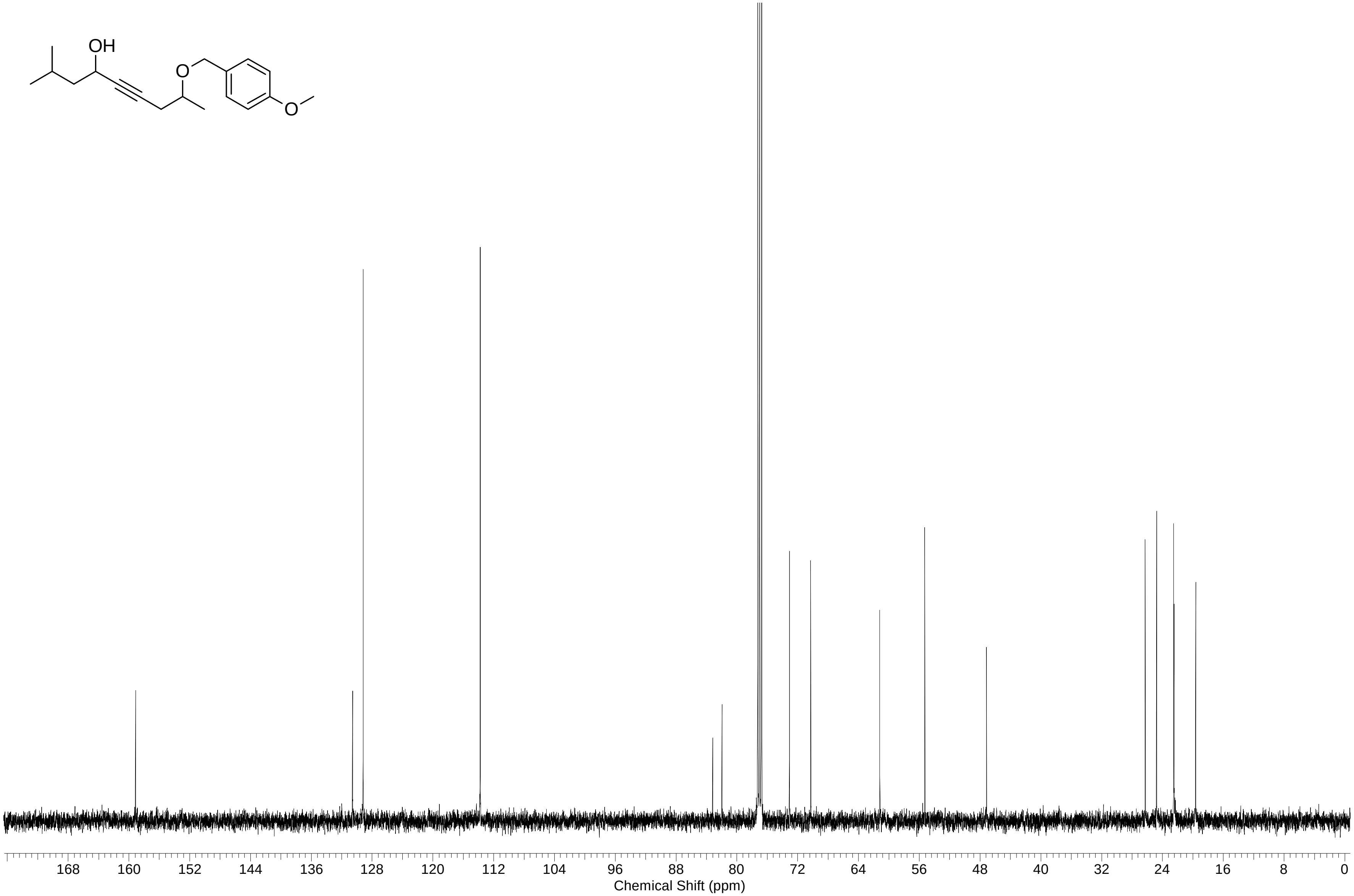

OH
OMe
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

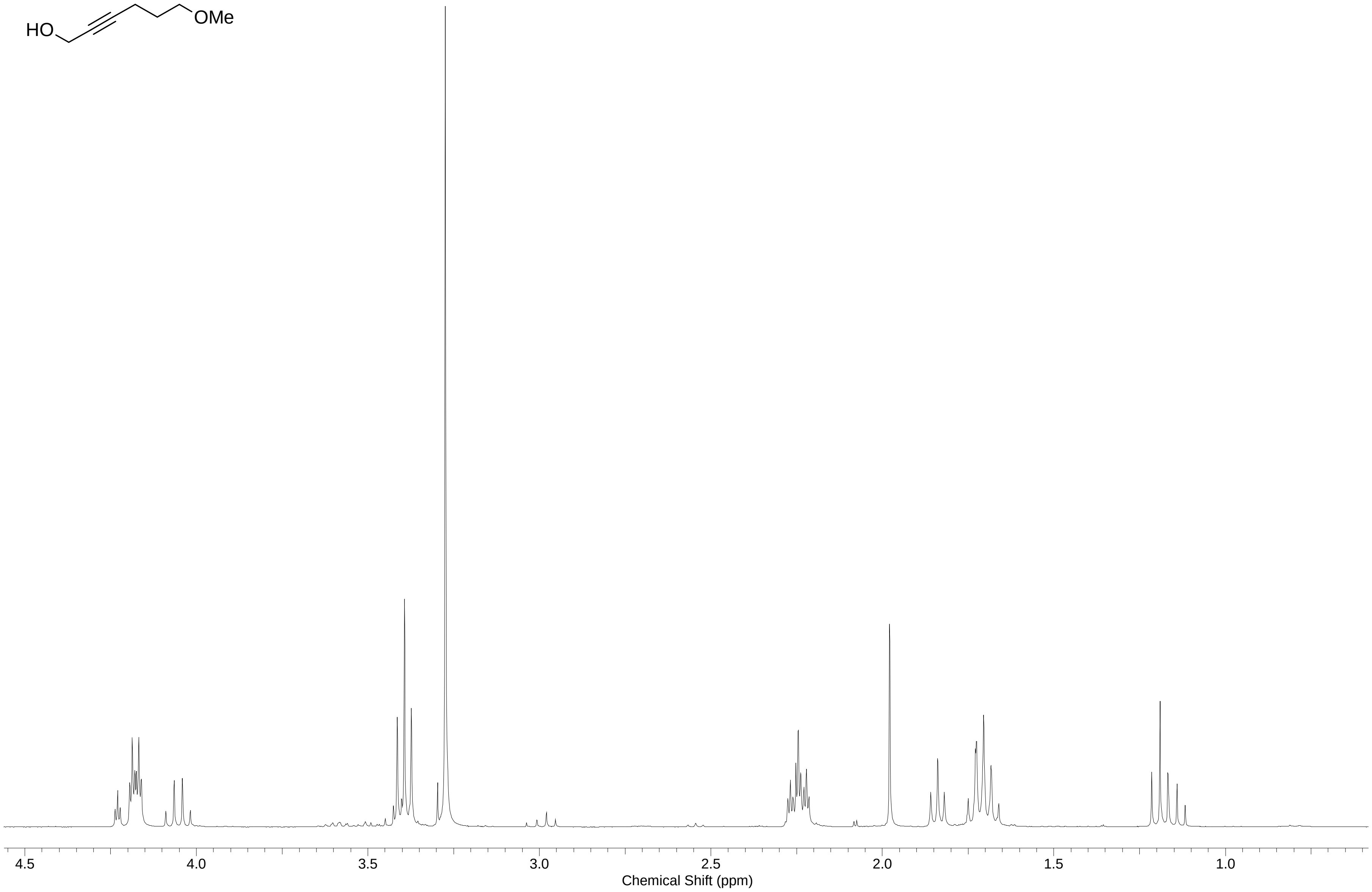

OH
OMe
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
Chemical Shift (ppm)

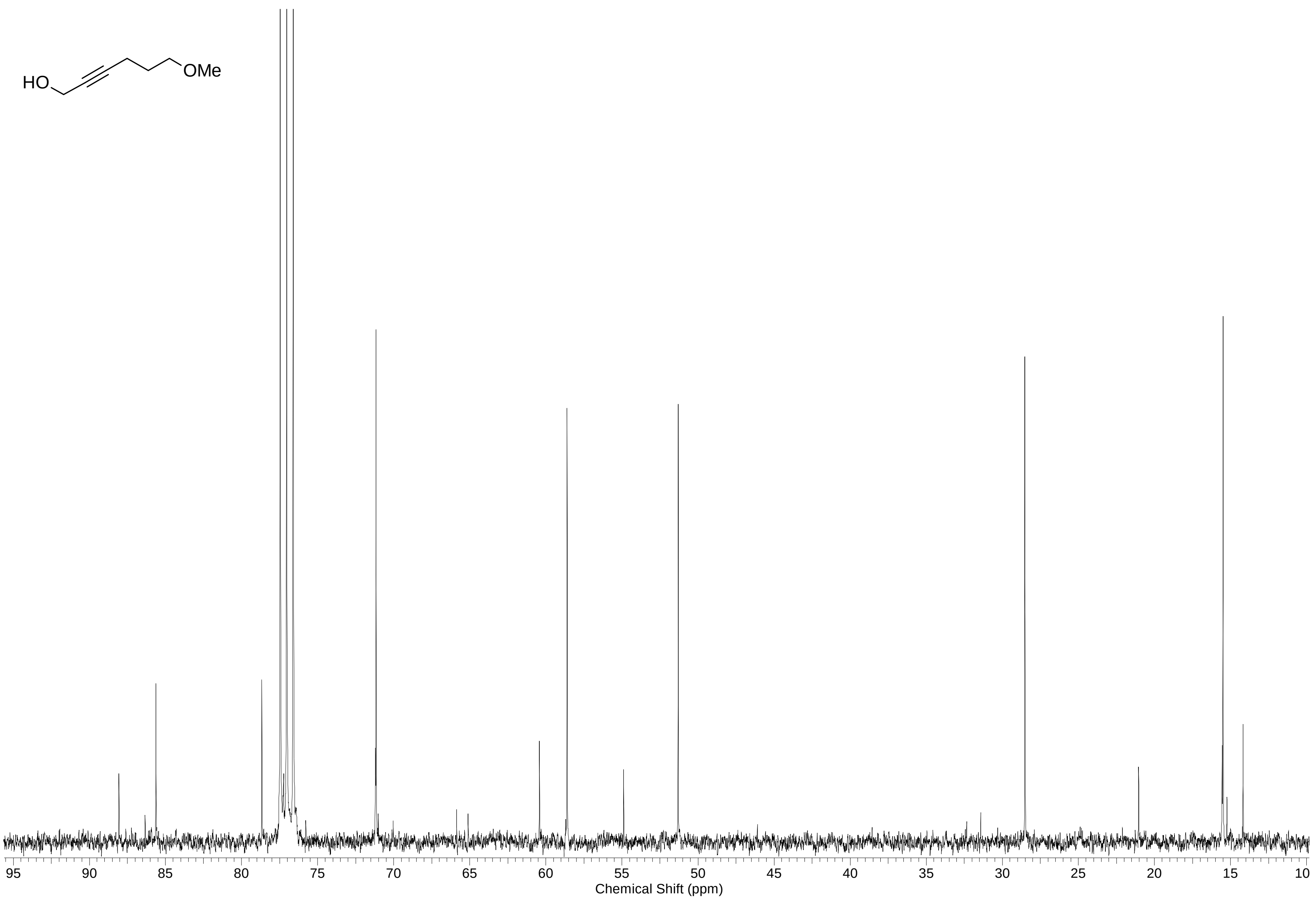

OH
O
Si
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

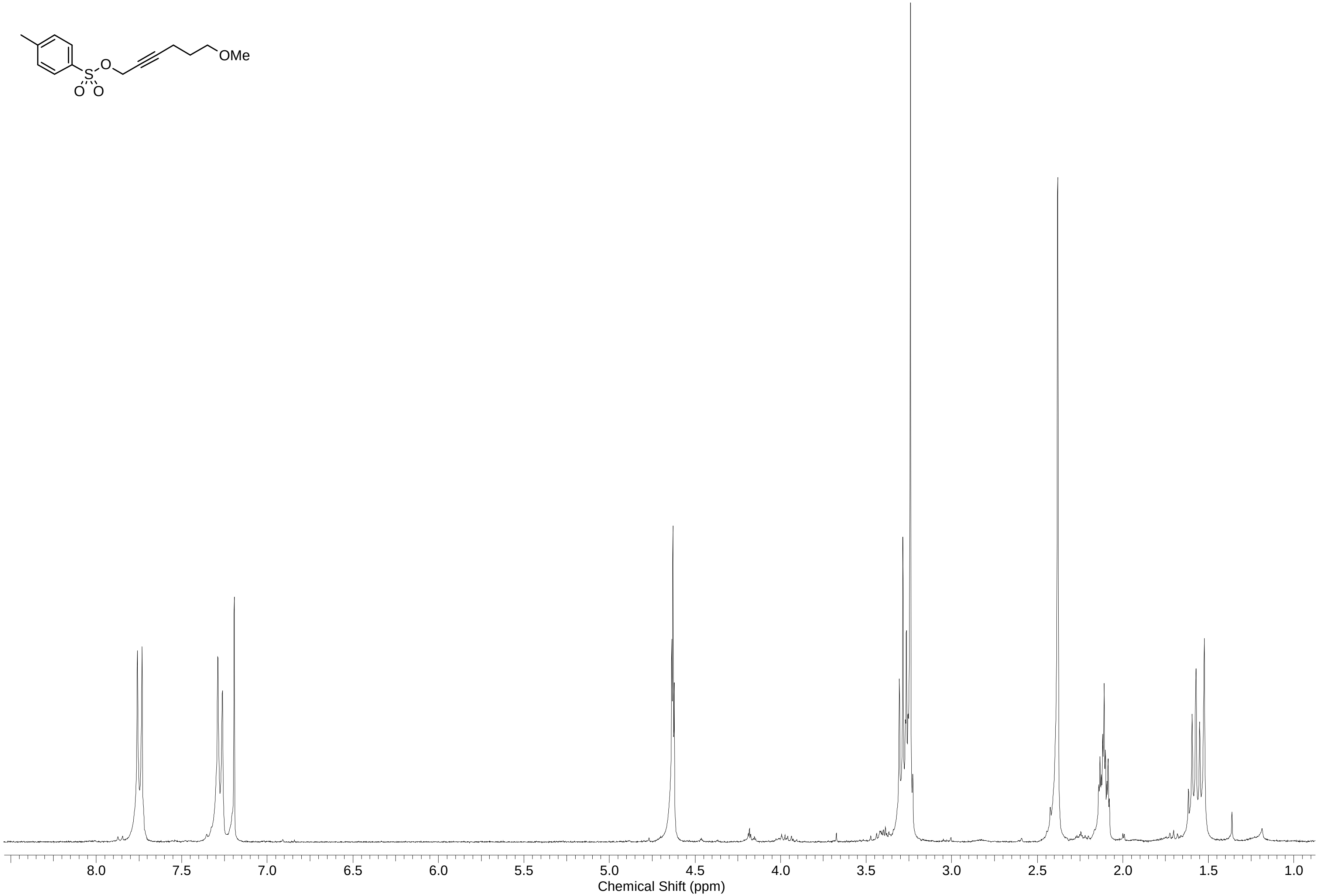

OH
O
Si
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
Chemical Shift (ppm)

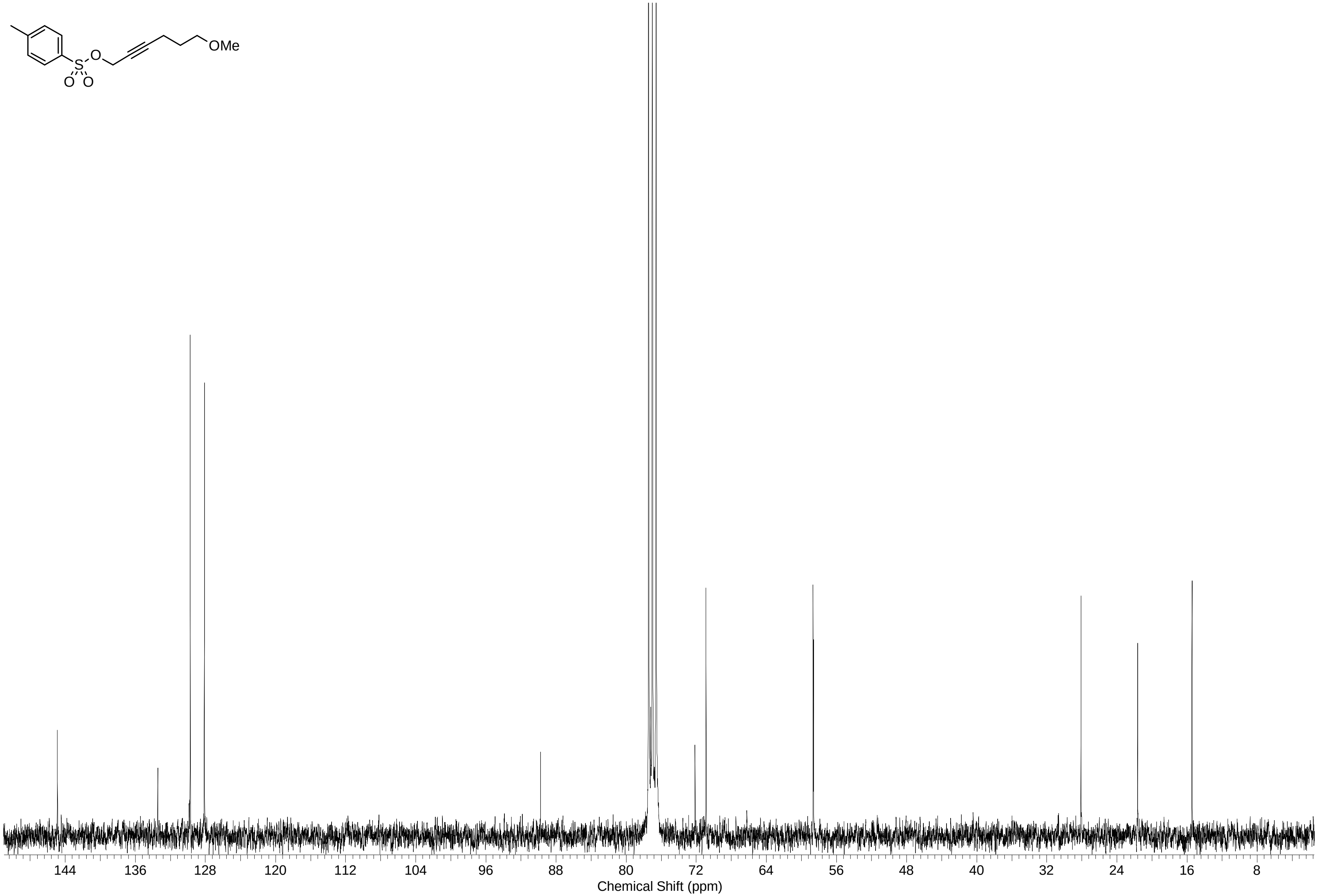

OH
O
O
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)


OH
O
O
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

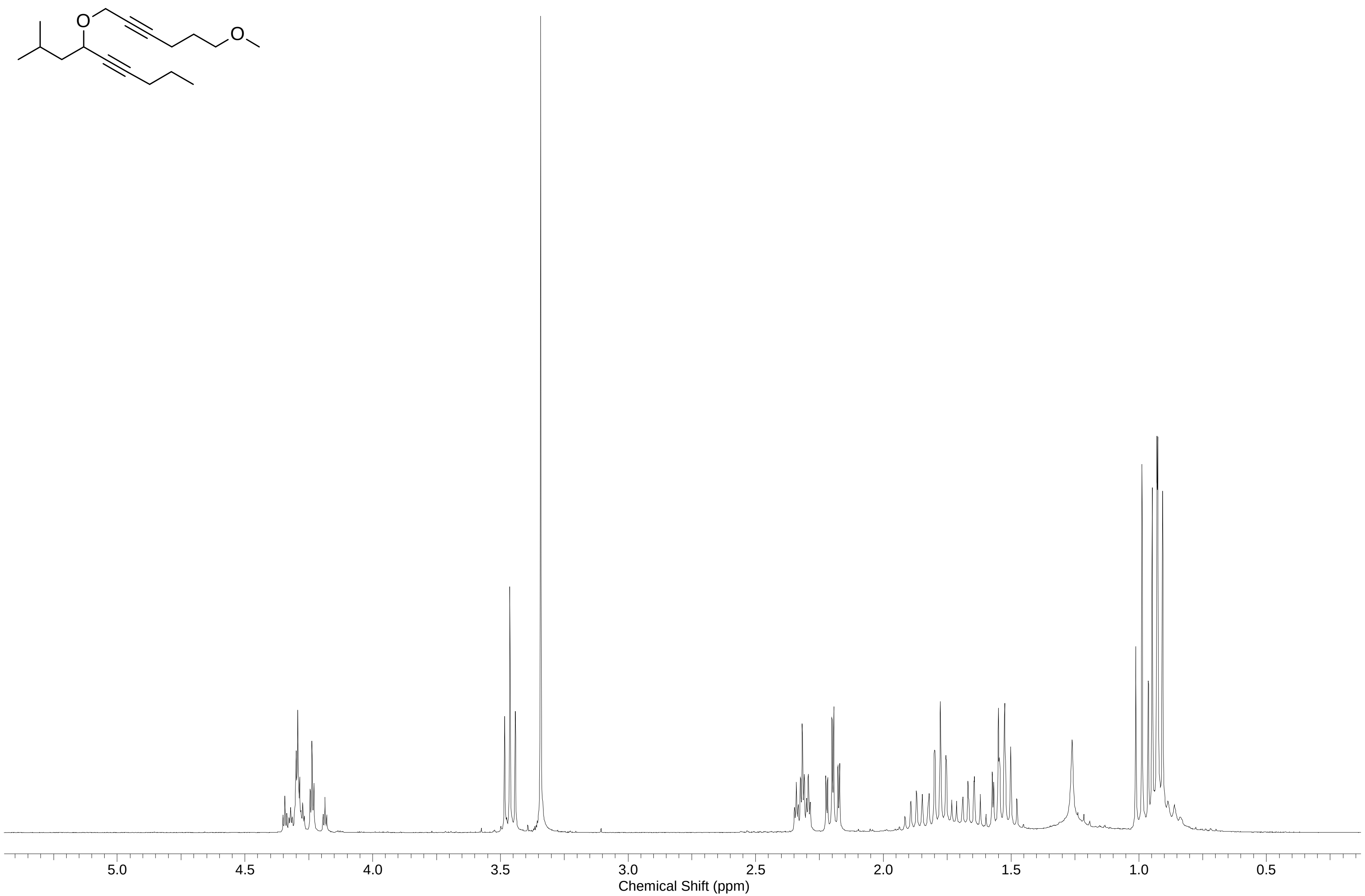

HO
OMe
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

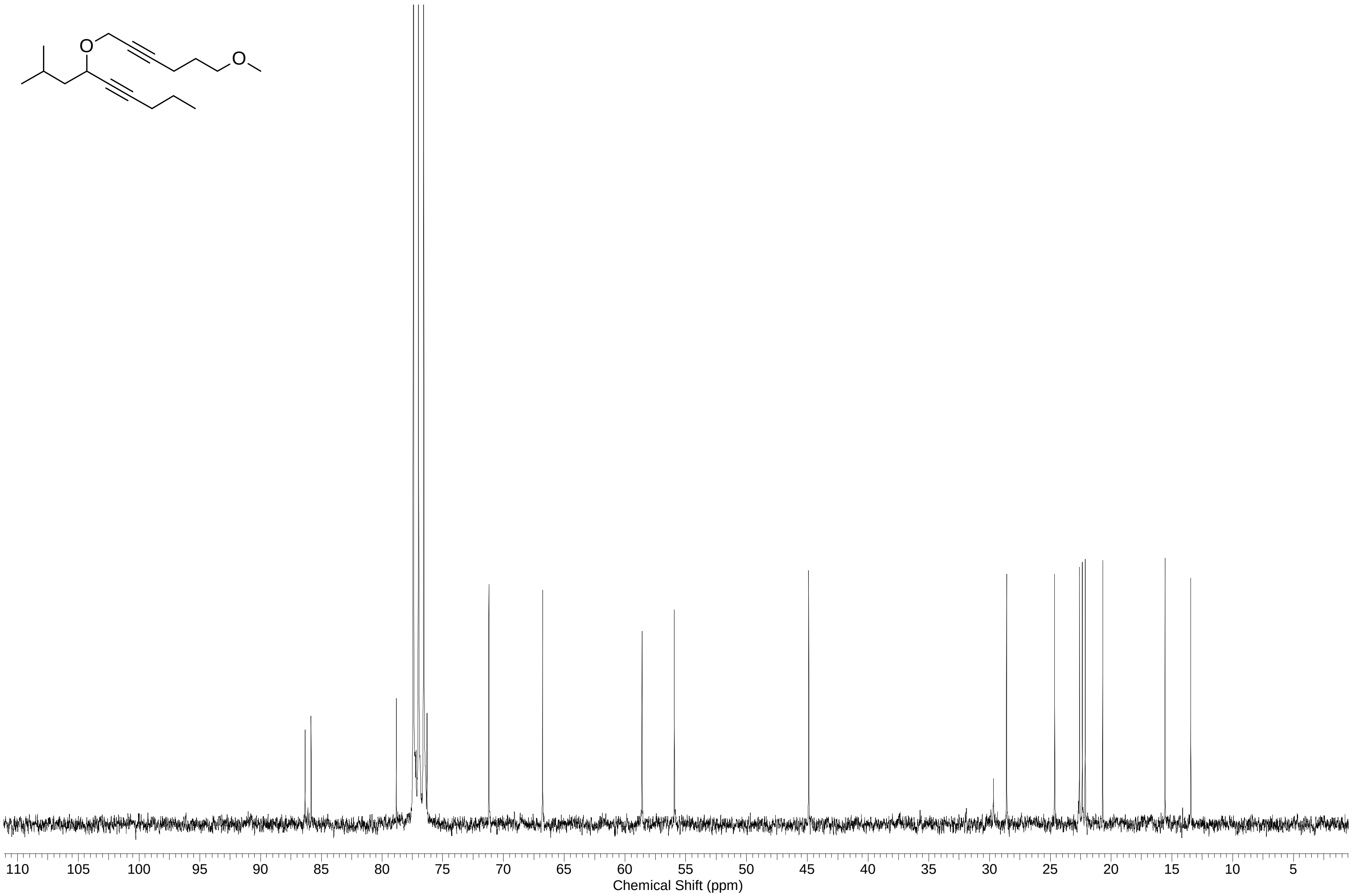

HO
OMe
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
Chemical Shift (ppm)

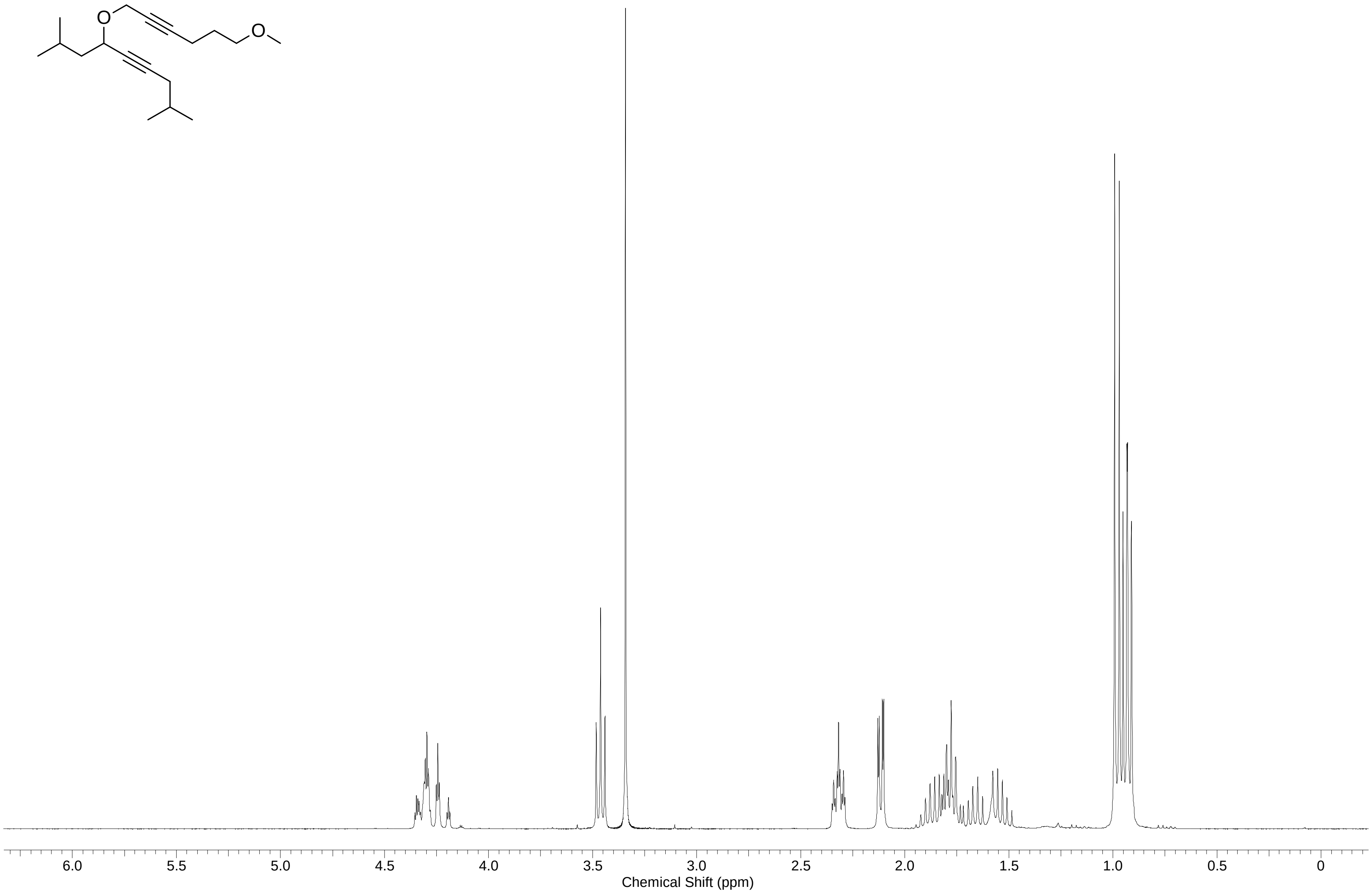

S
O
O O
OMe
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

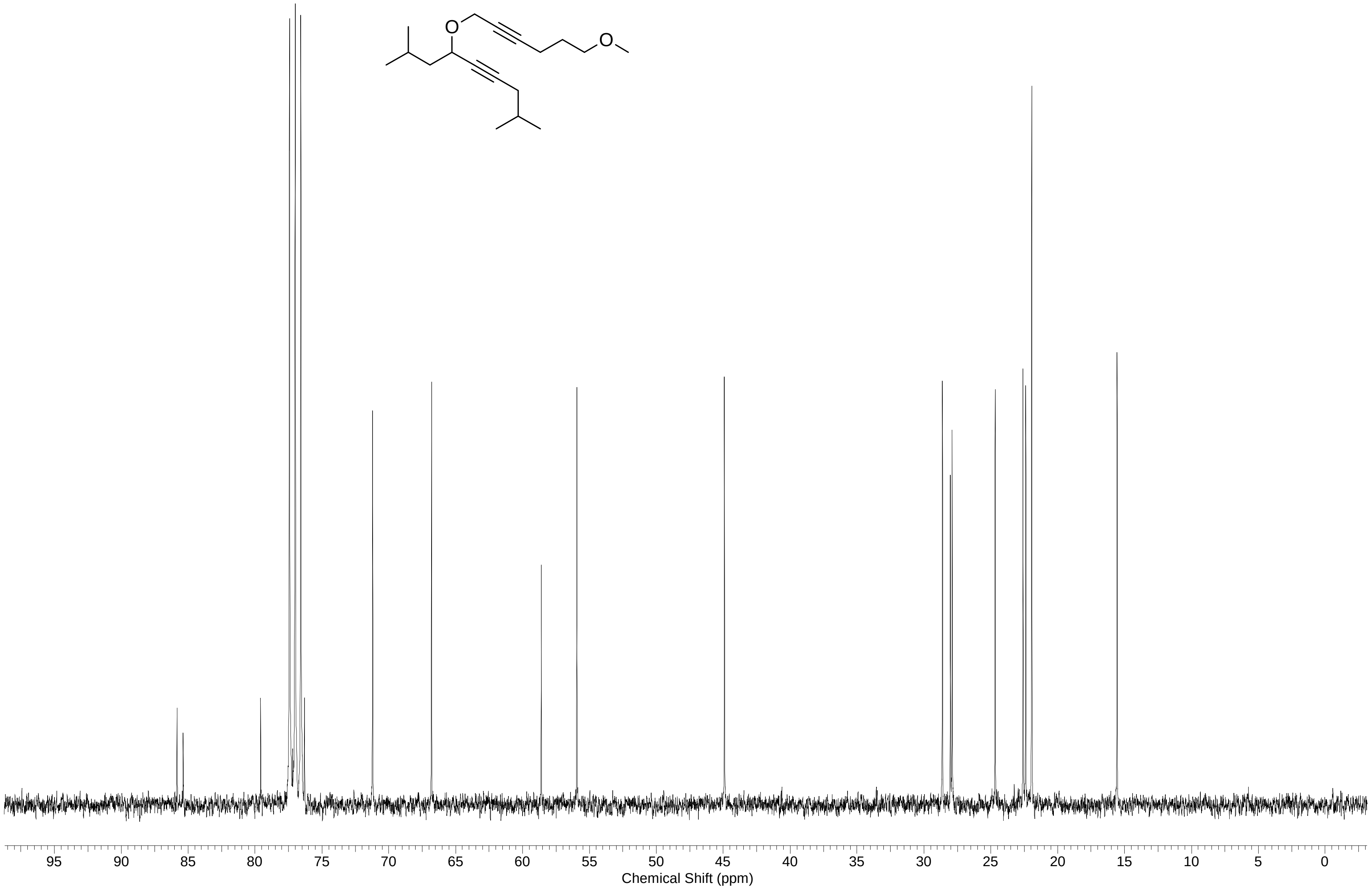

OMe
S
O
O
O
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)

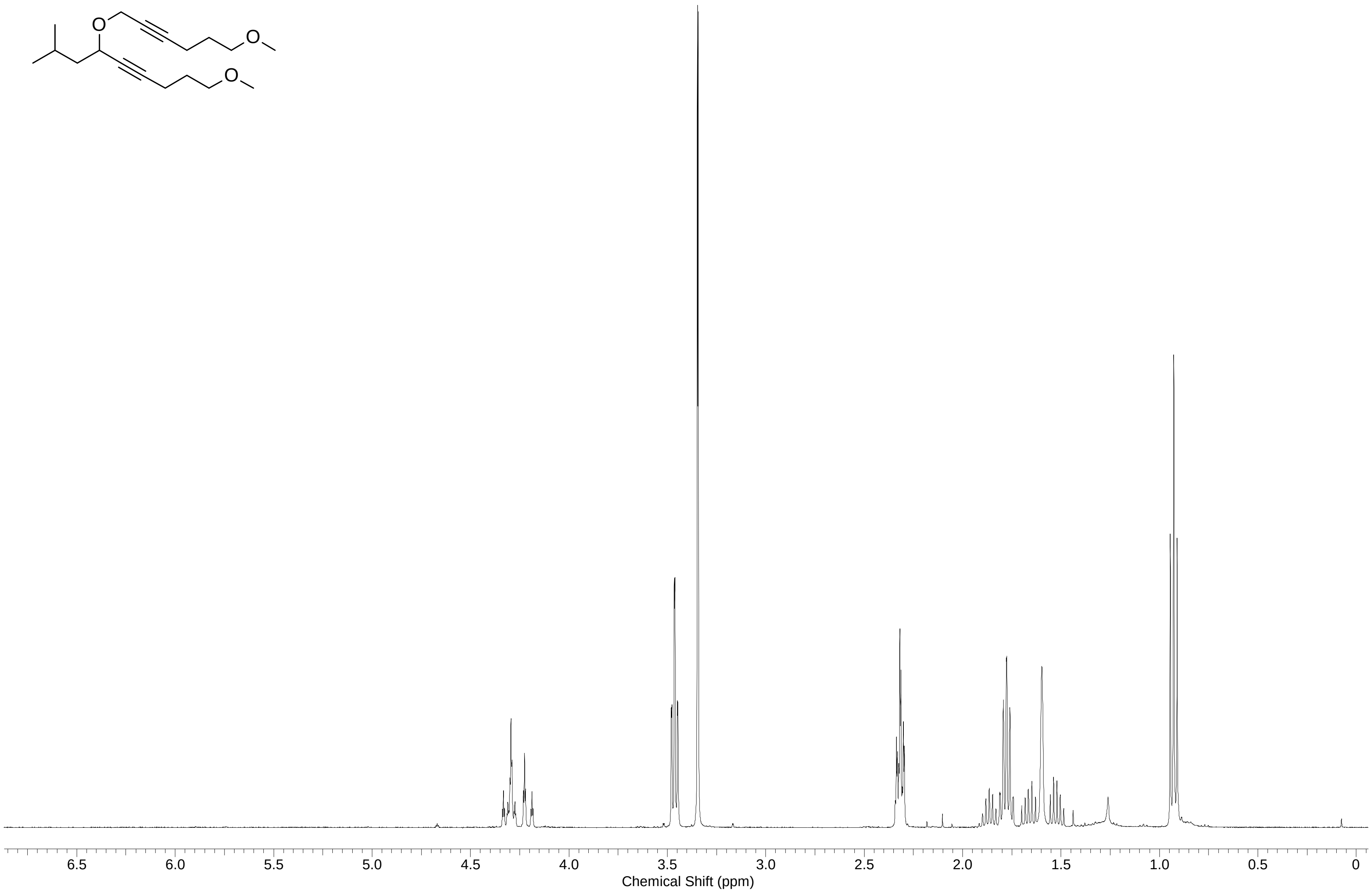
Electronic Supplementary Material (ESI) for Chemical Communications

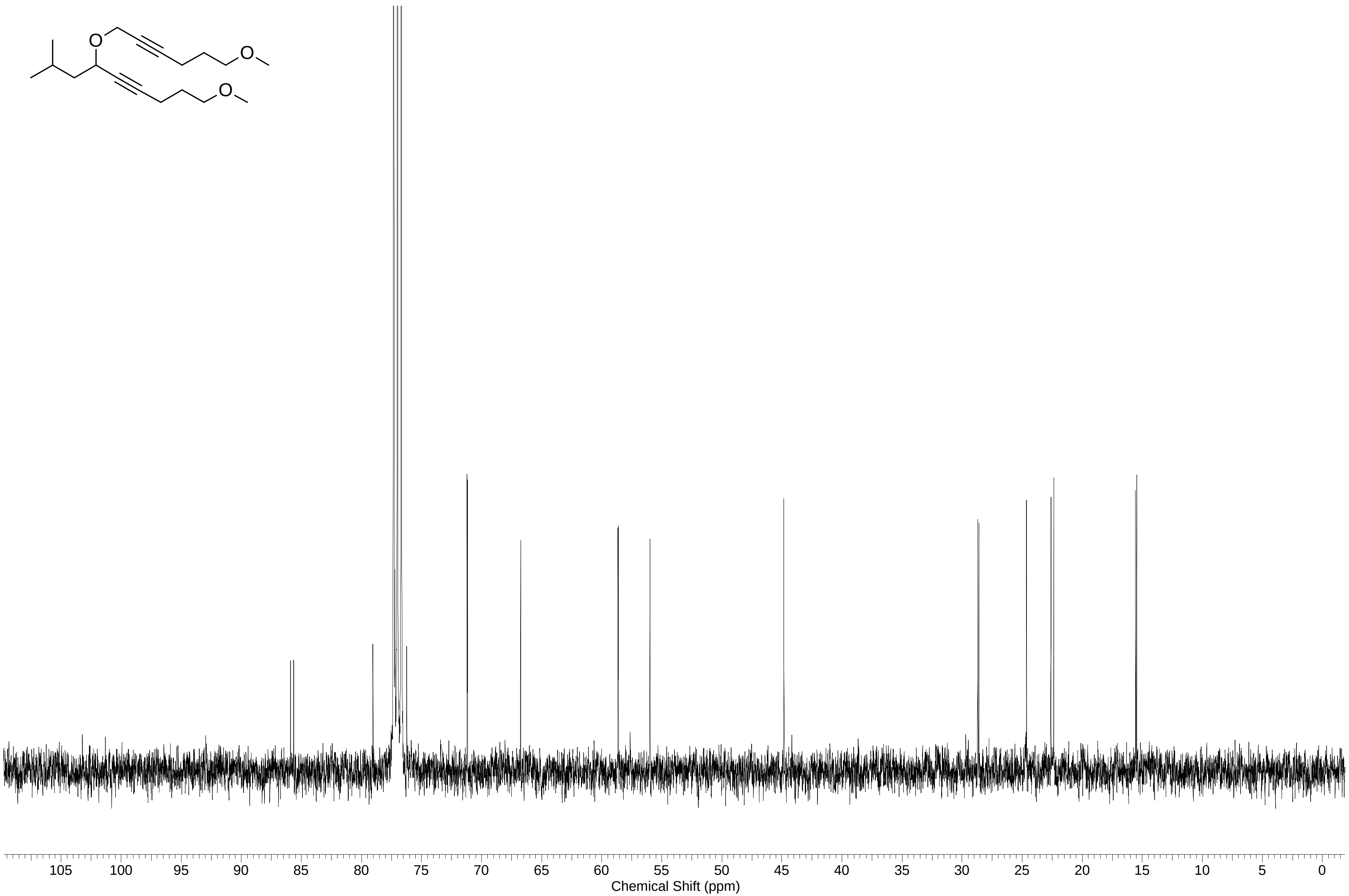


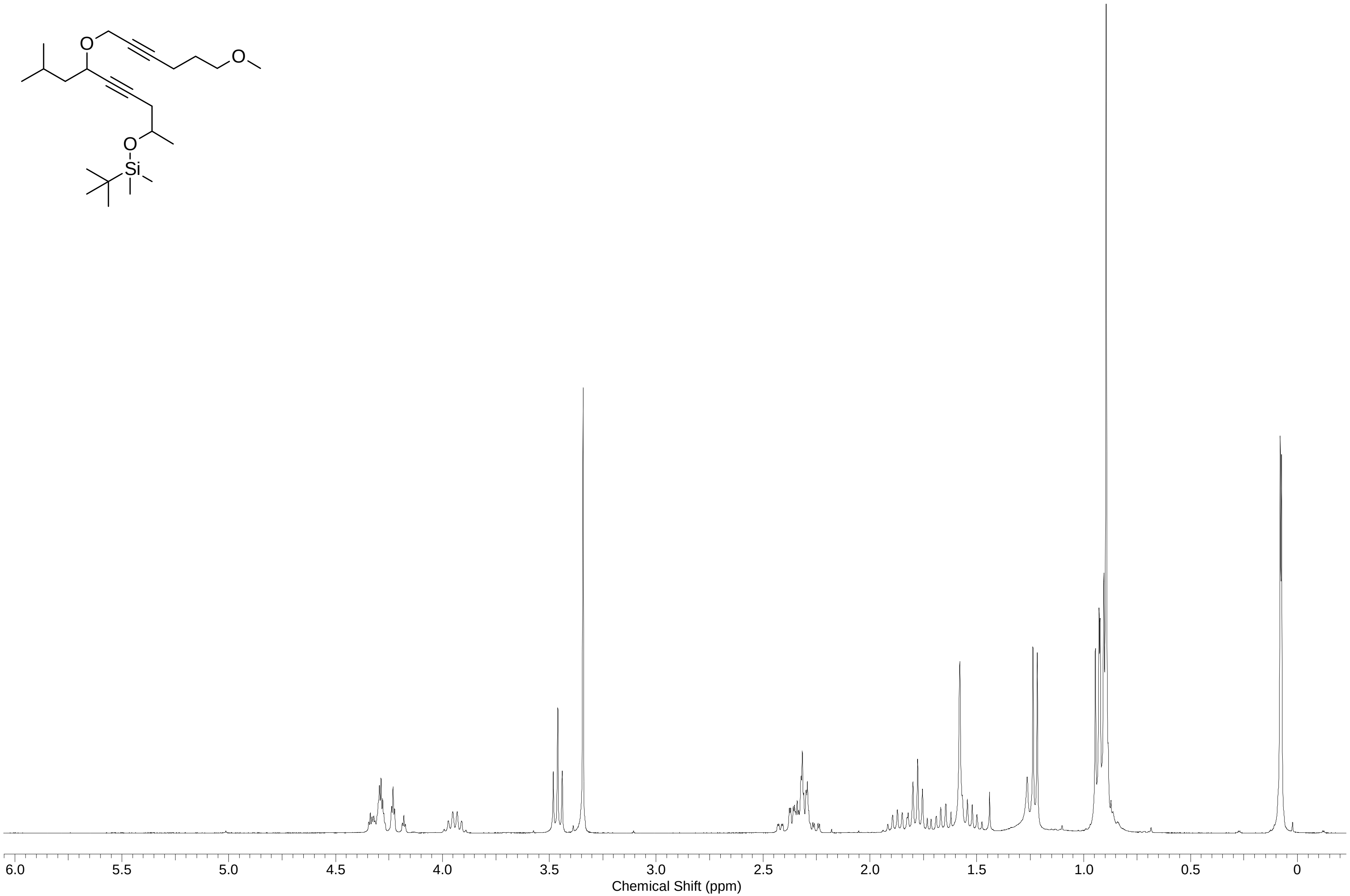

O
O
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
Chemical Shift (ppm)


O
O
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

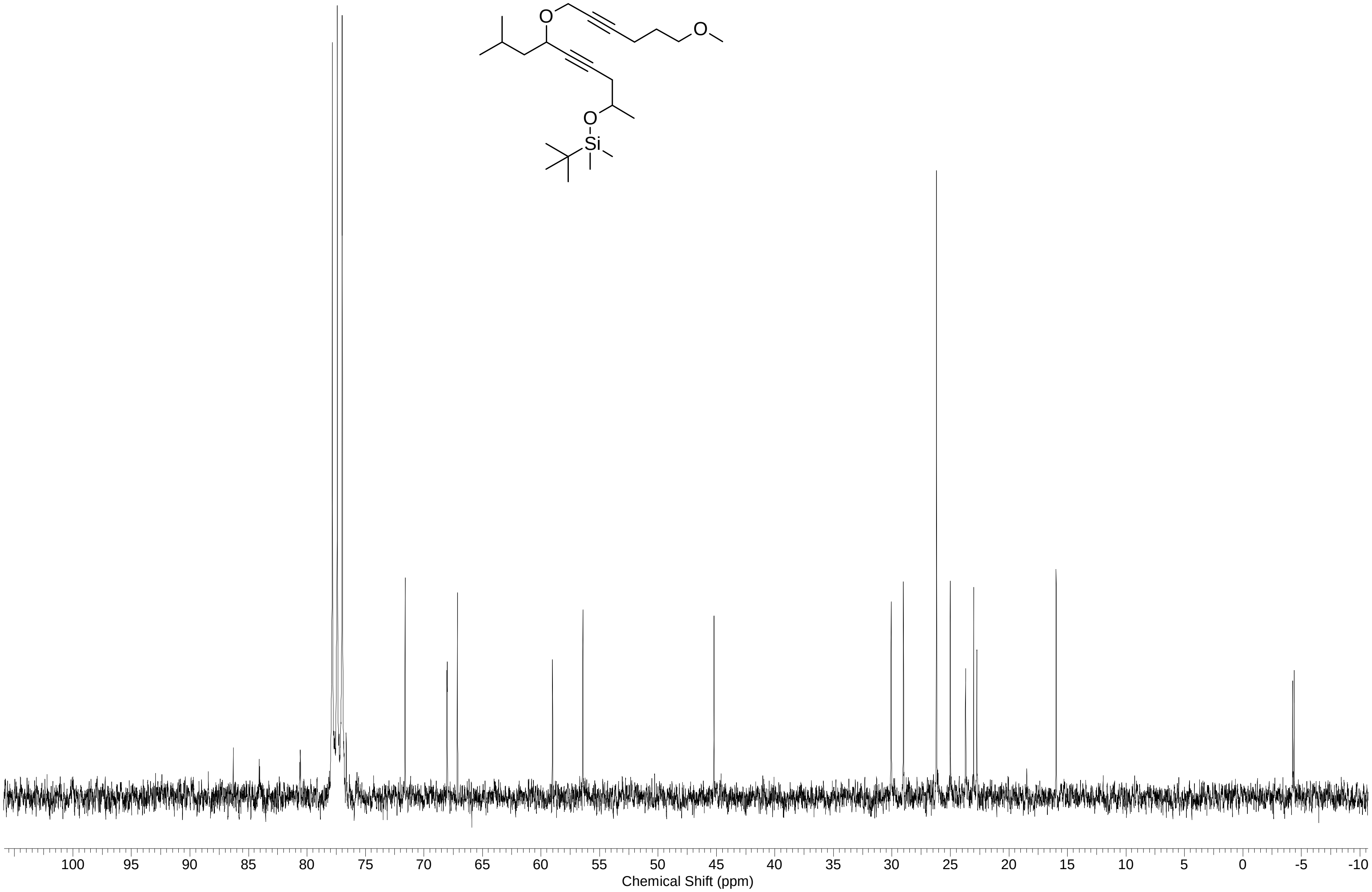

O
O
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
Chemical Shift (ppm)

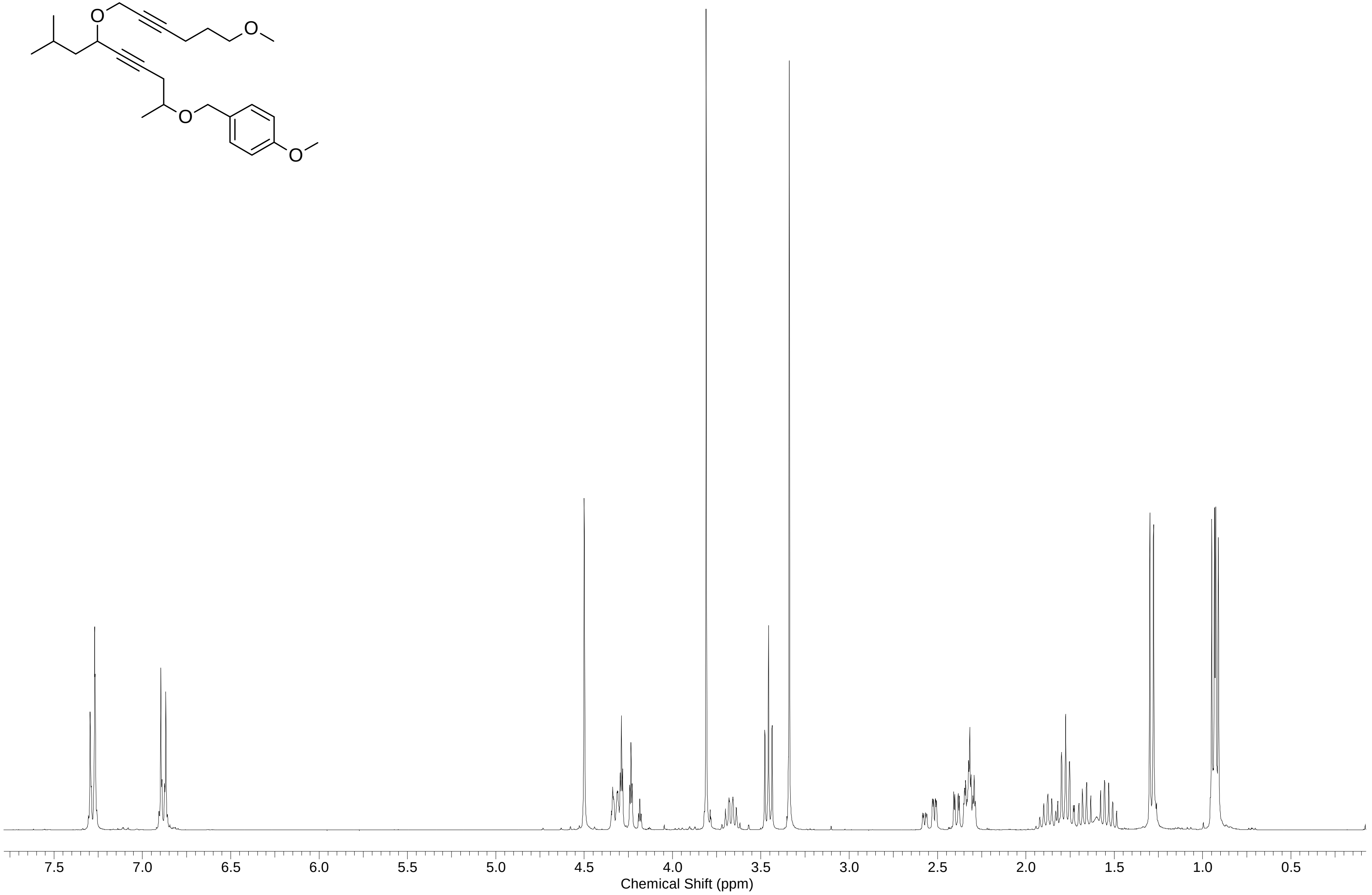

O
O
O
O
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

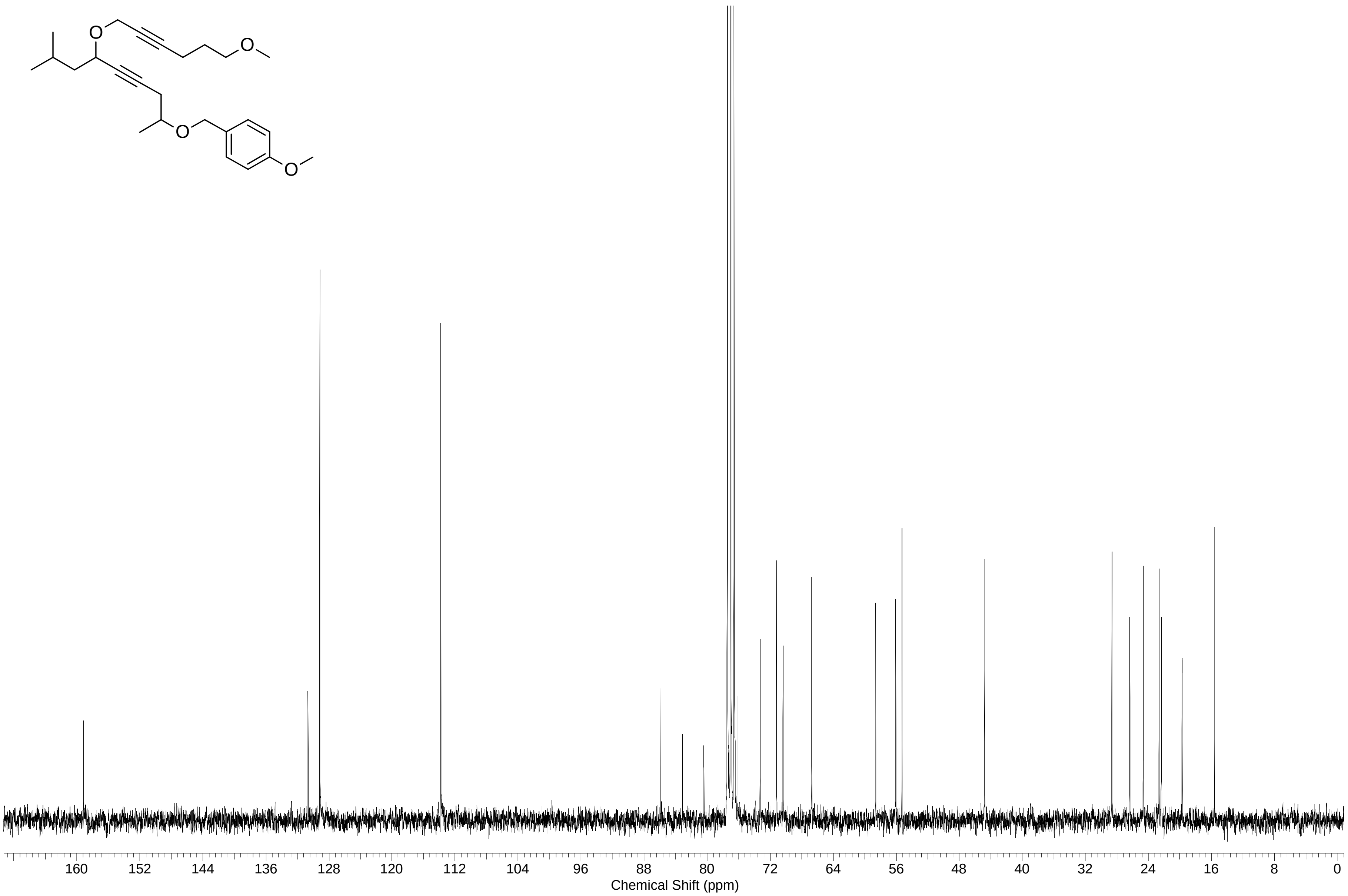

O
O
O
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
Chemical Shift (ppm)

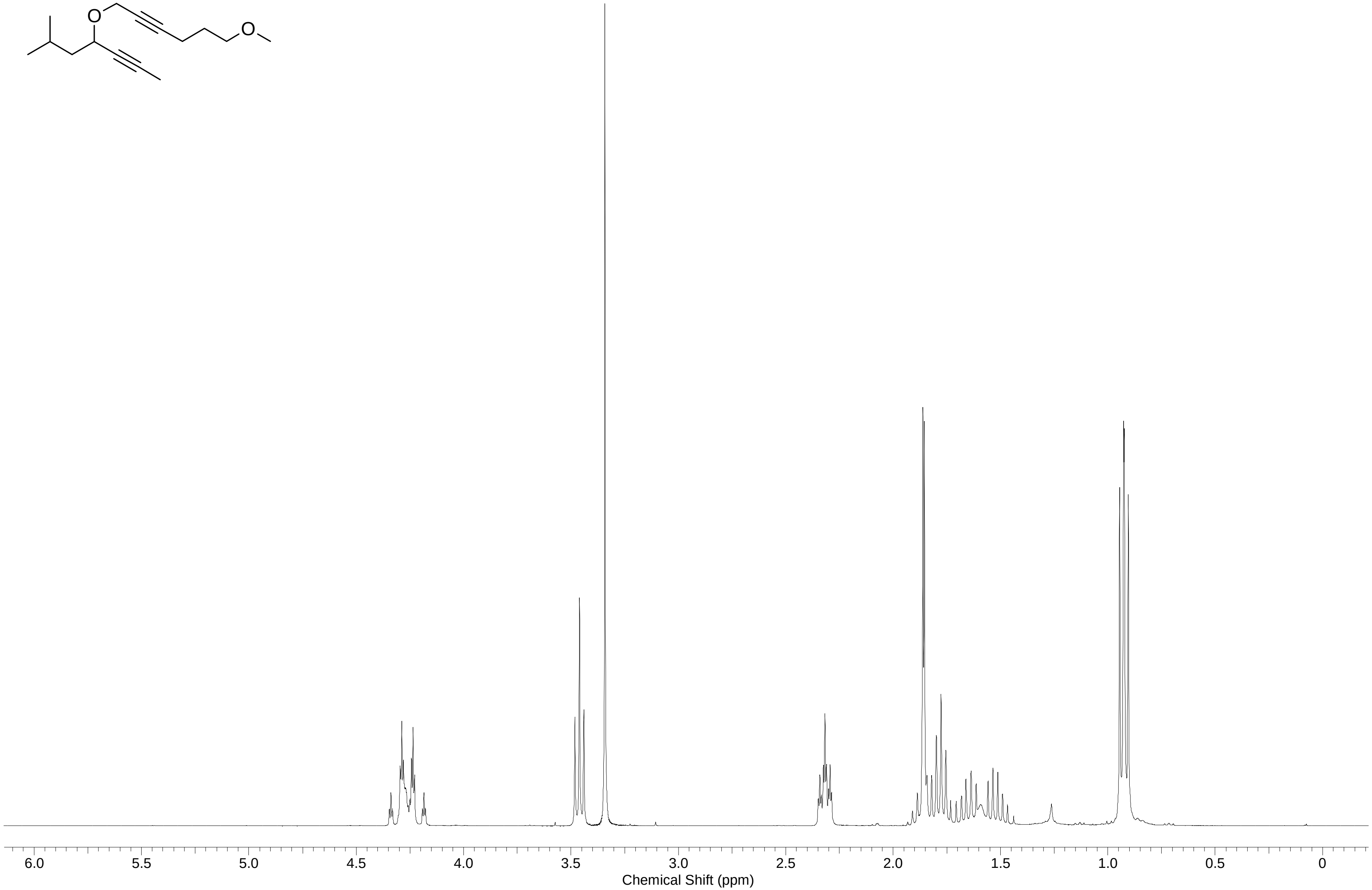

O
O
O
Si

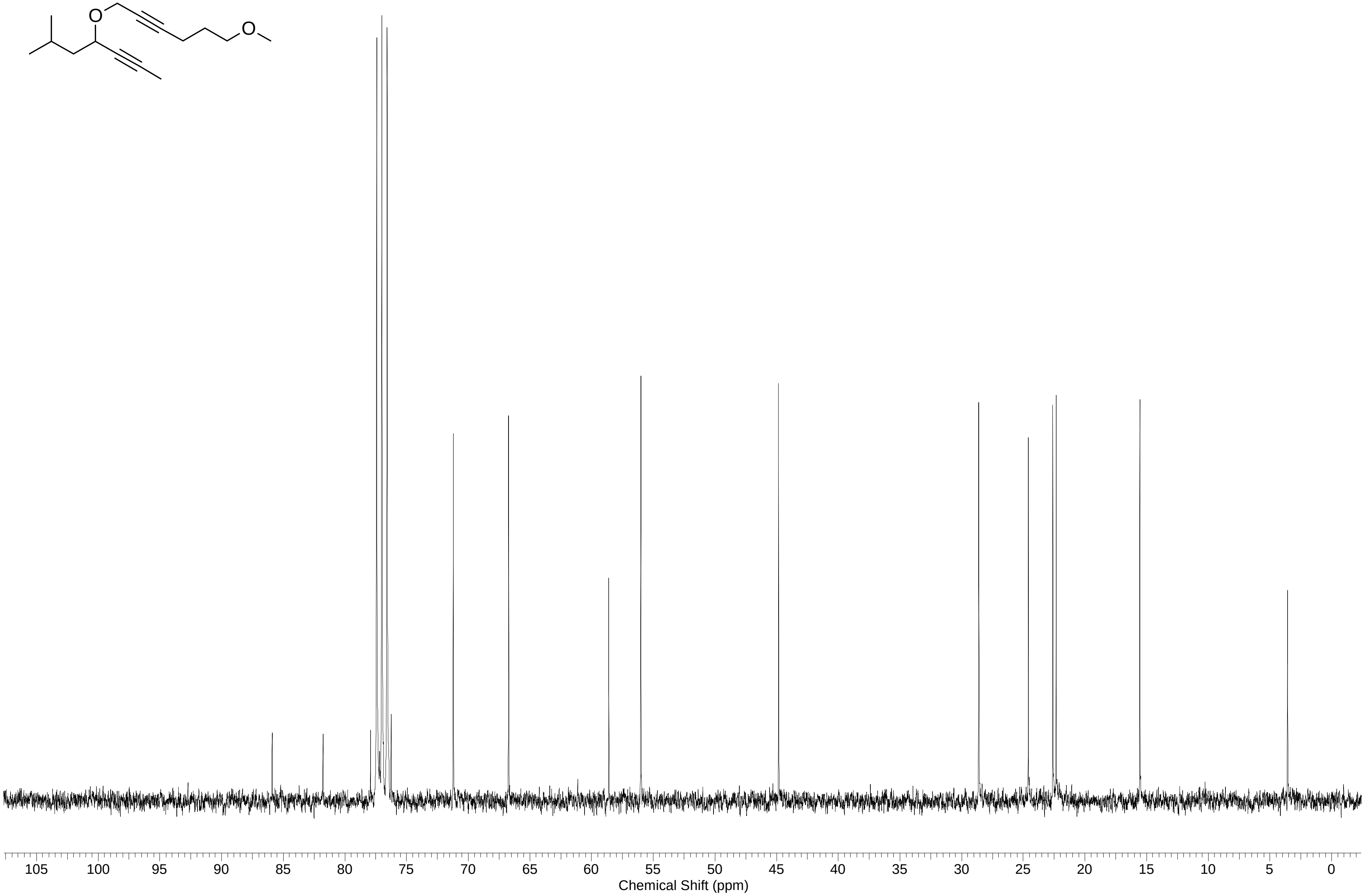
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

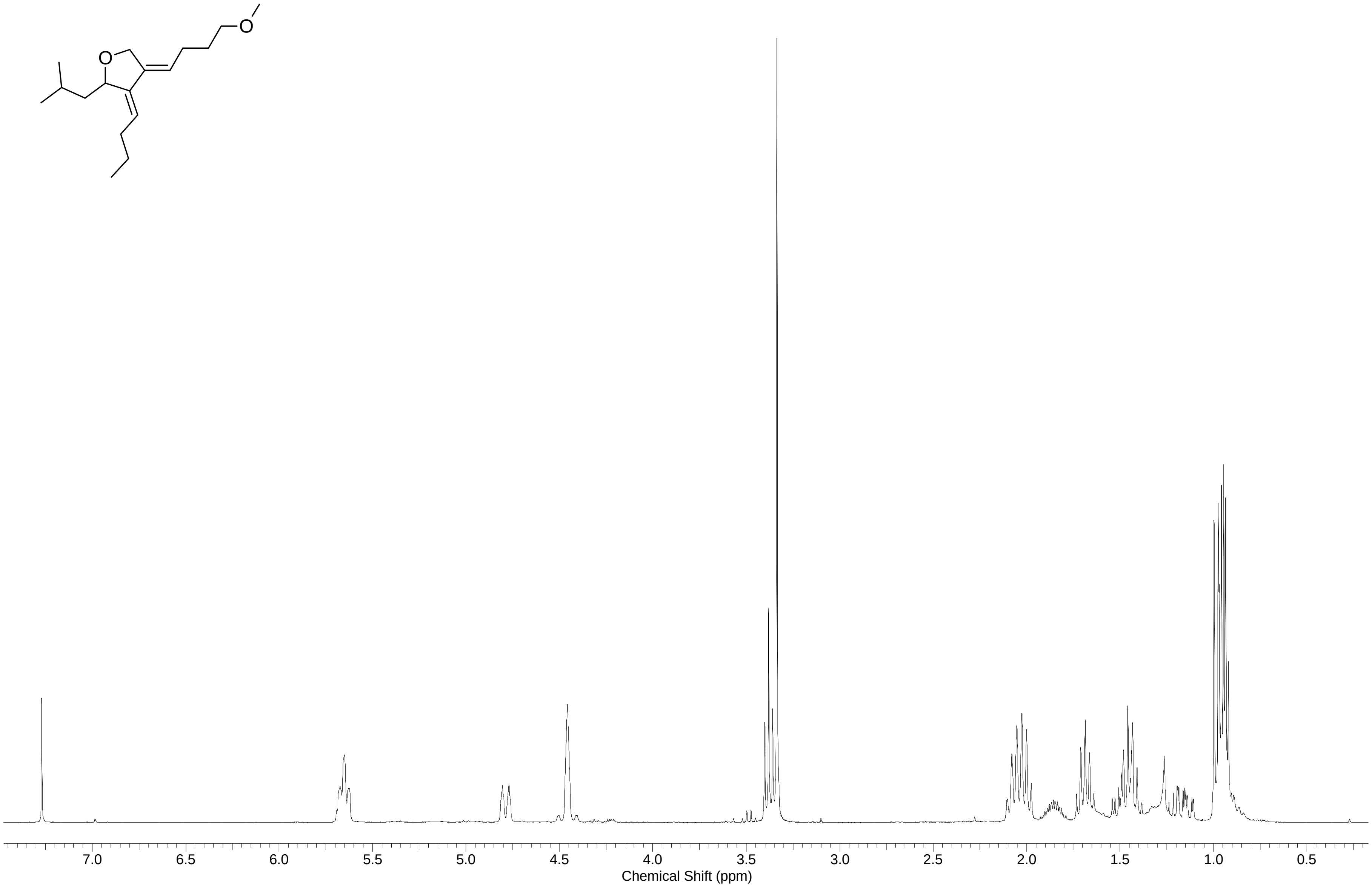

O
O
O
Si
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
Chemical Shift (ppm)

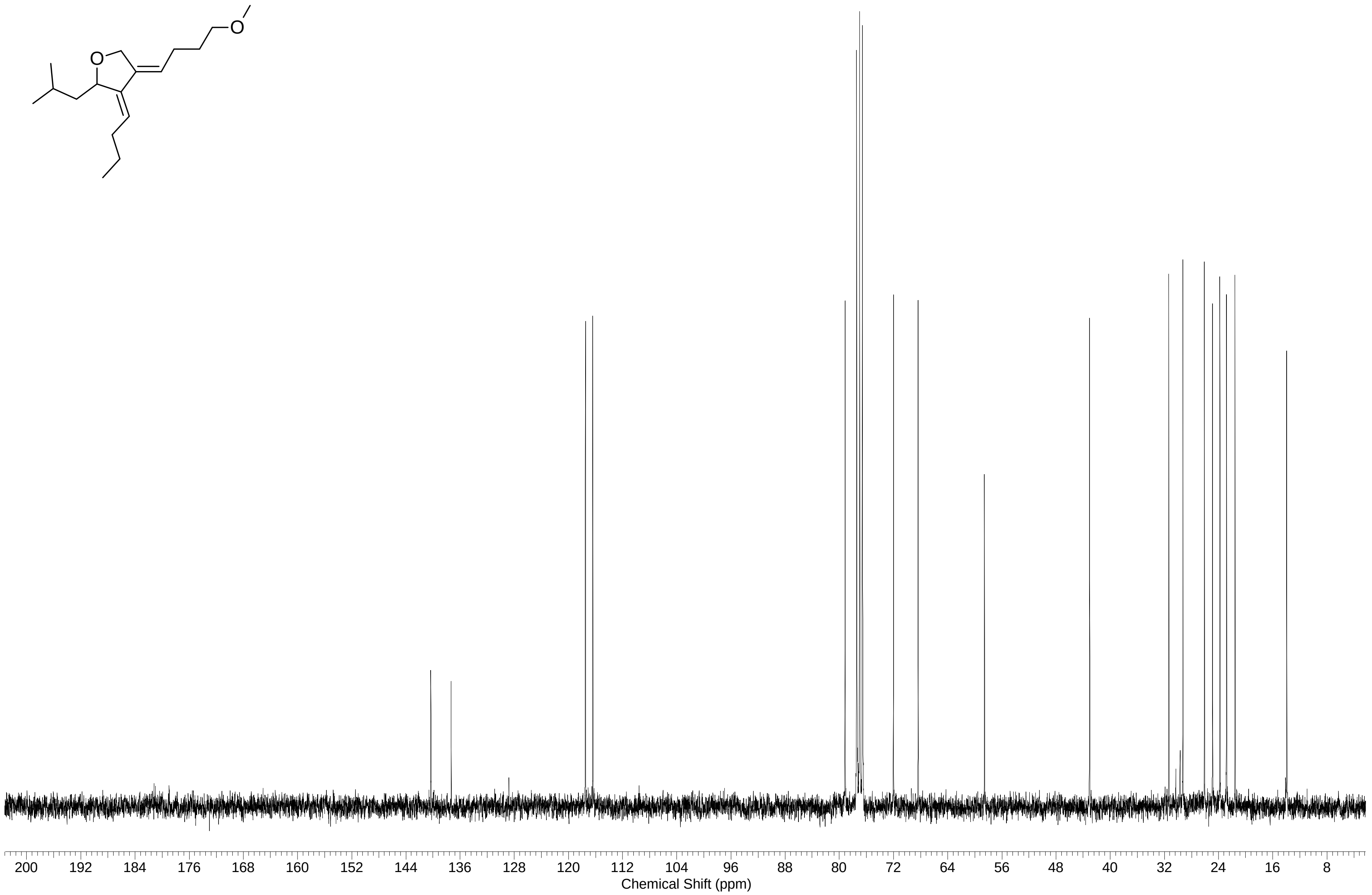

O
O
O
O
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

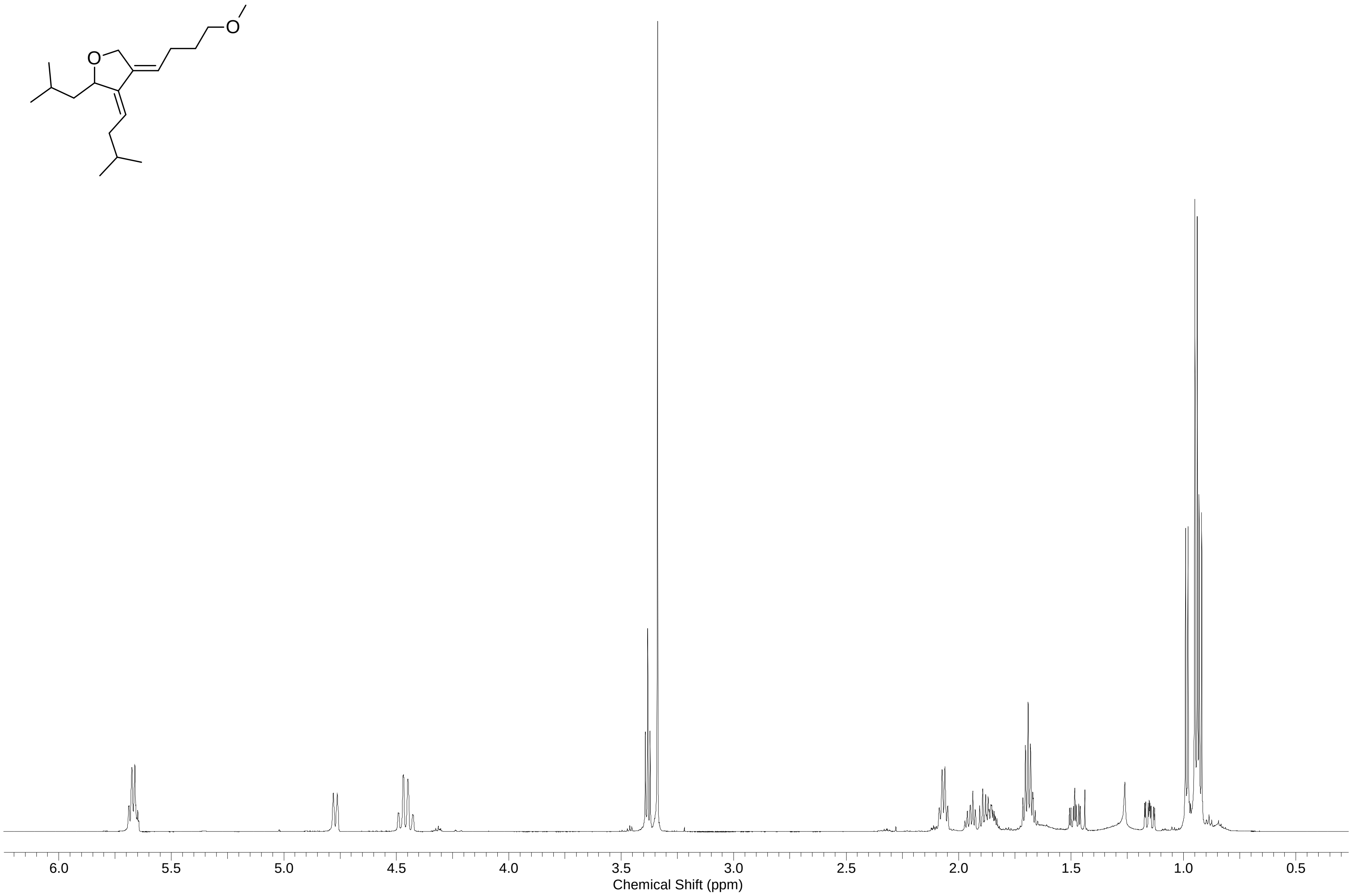

O
O
O
O
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


O
O
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

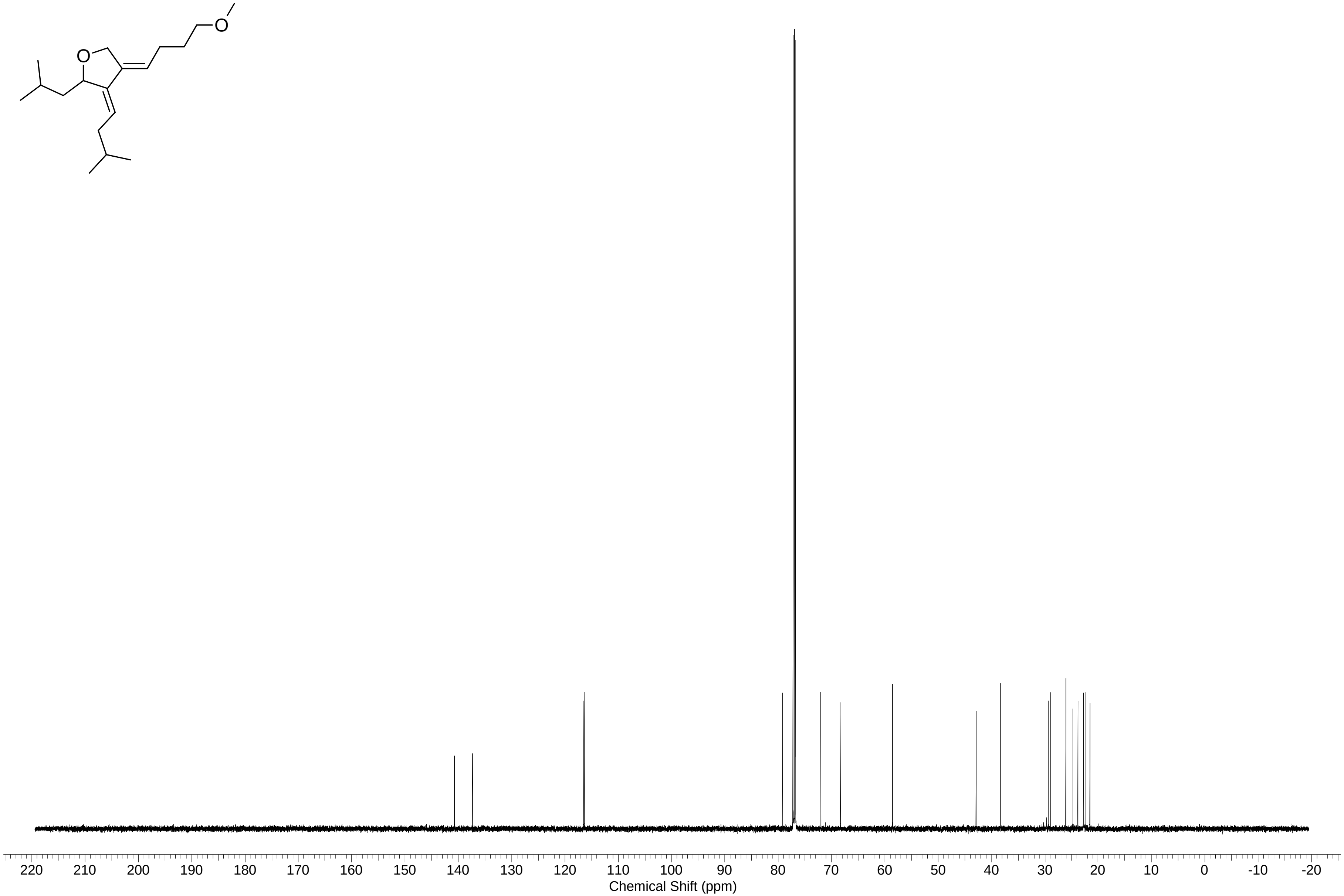

O
O
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
Chemical Shift (ppm)

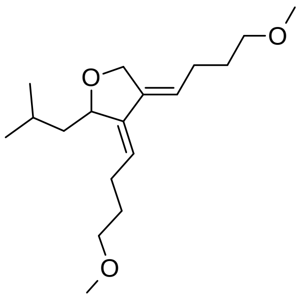

O
O
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

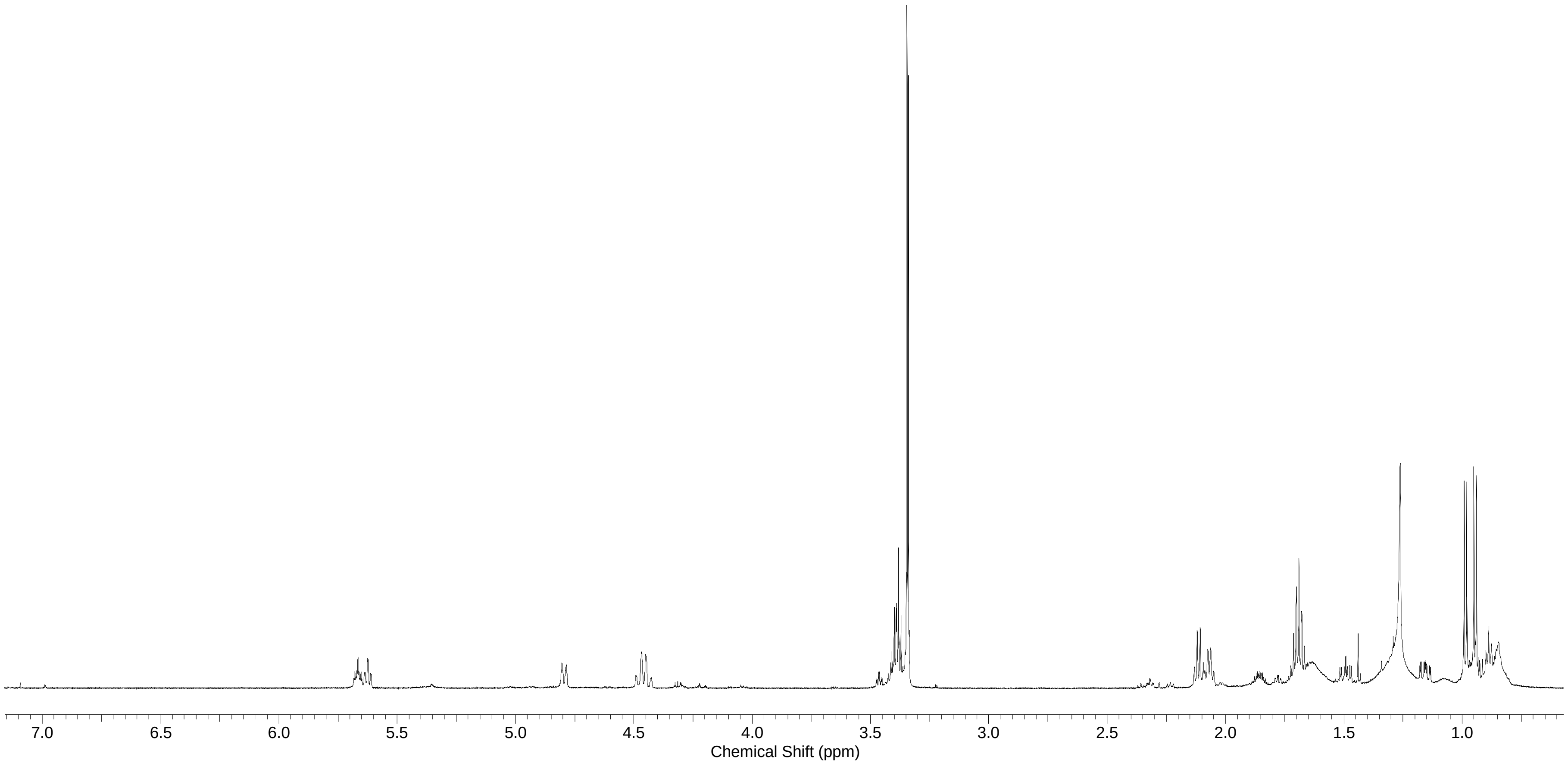

O
O
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)

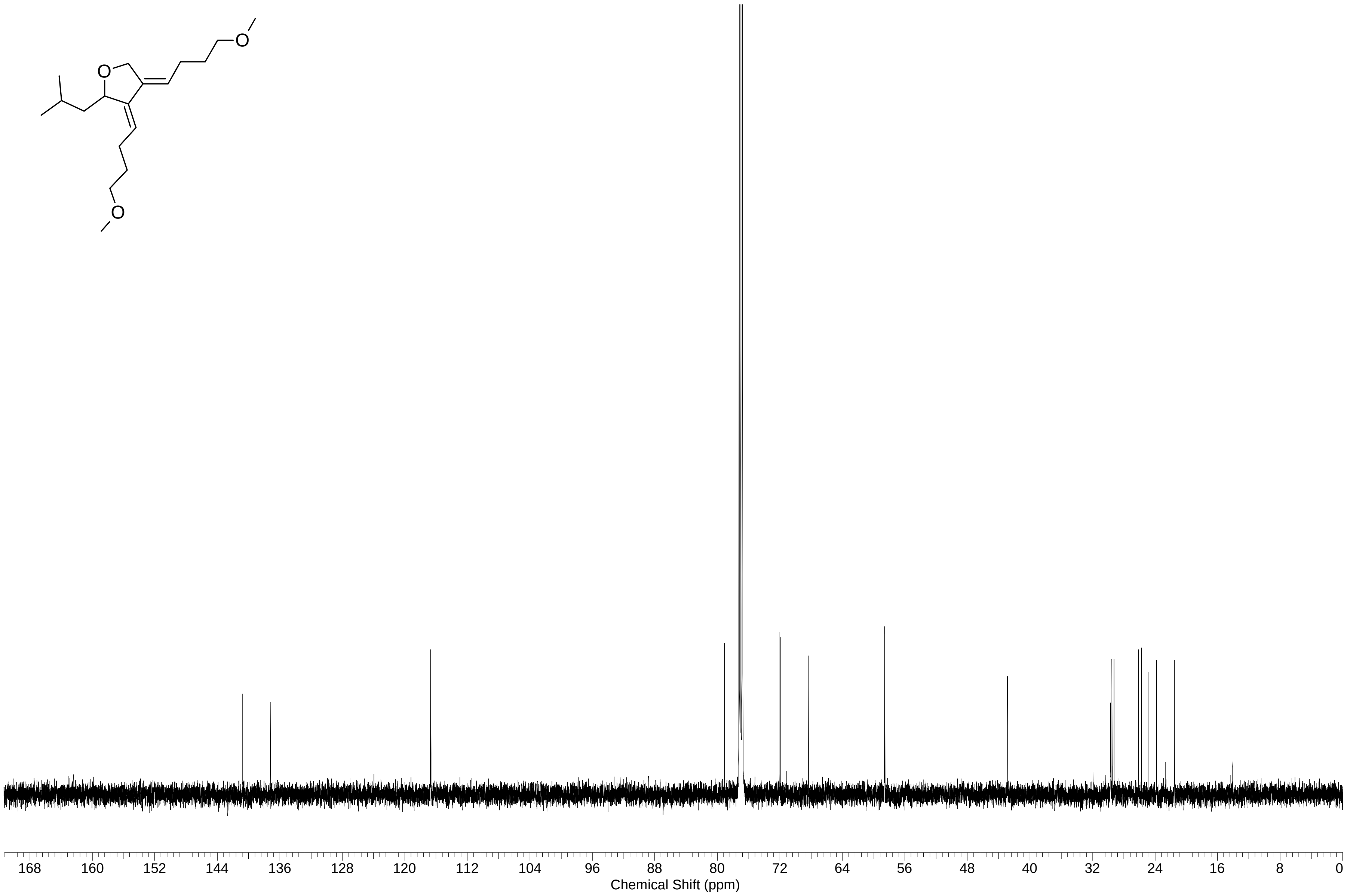

O
O
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

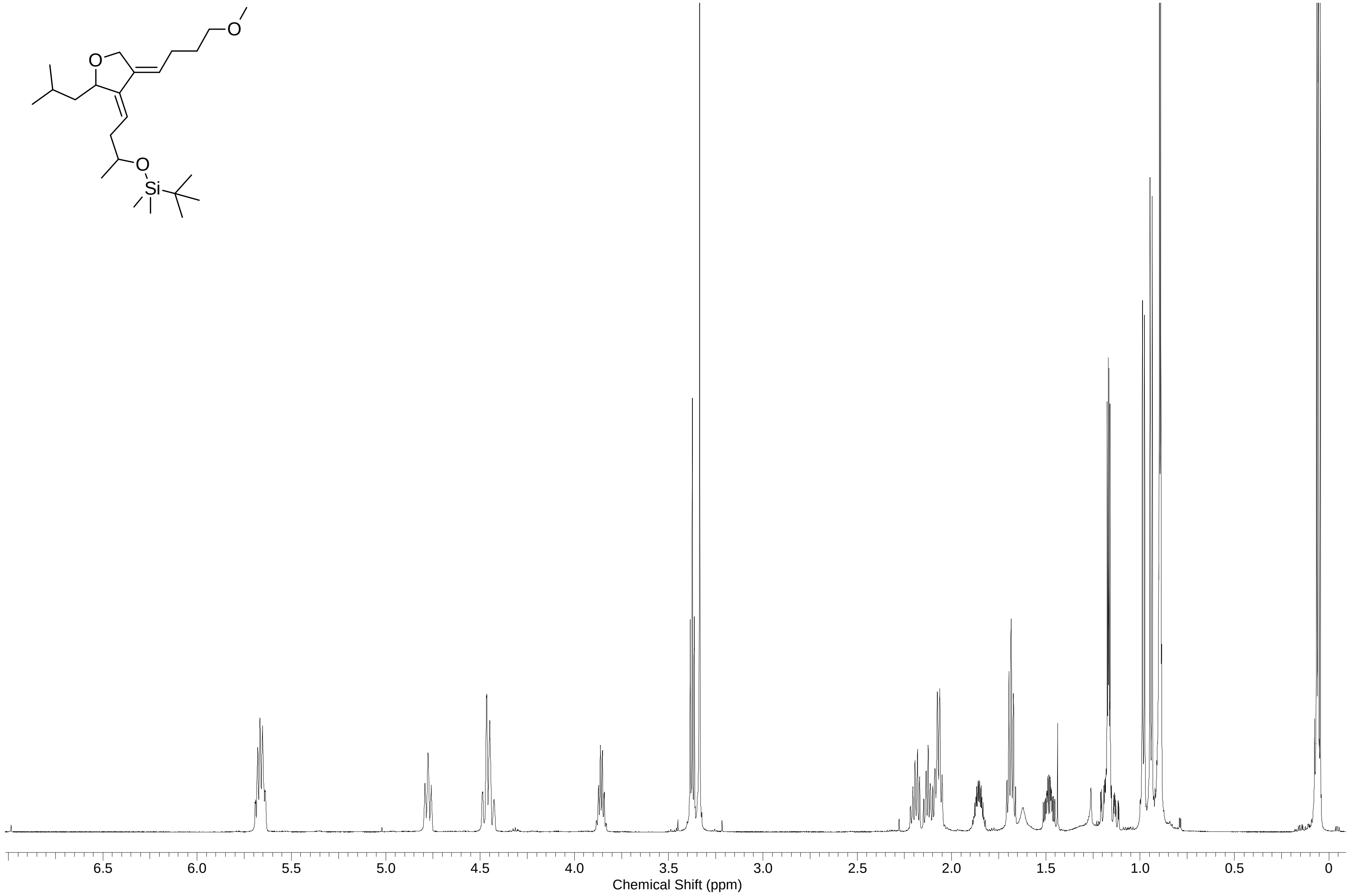
Electronic Supplementary Material (ESI) for Chemical Communications

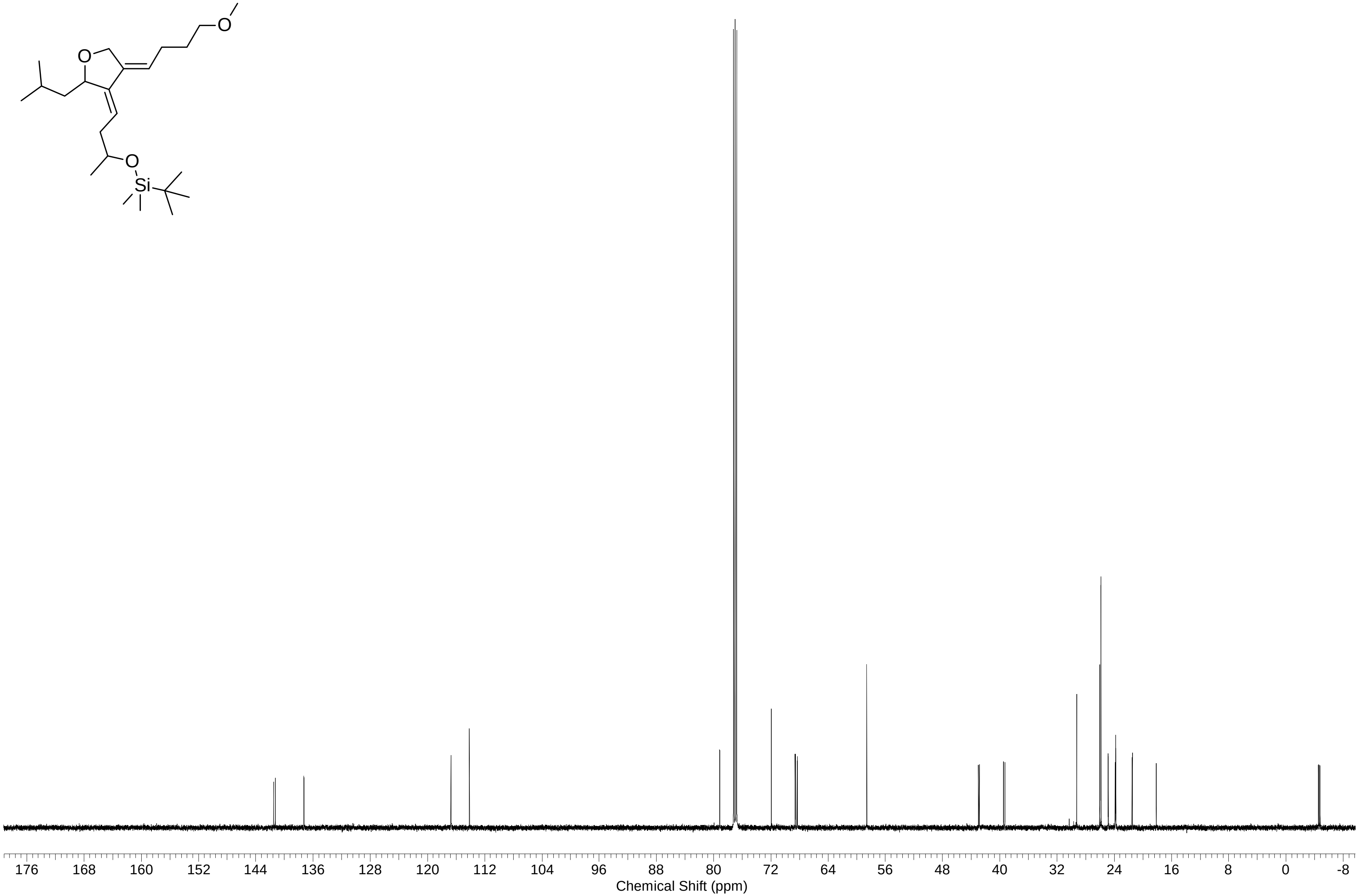


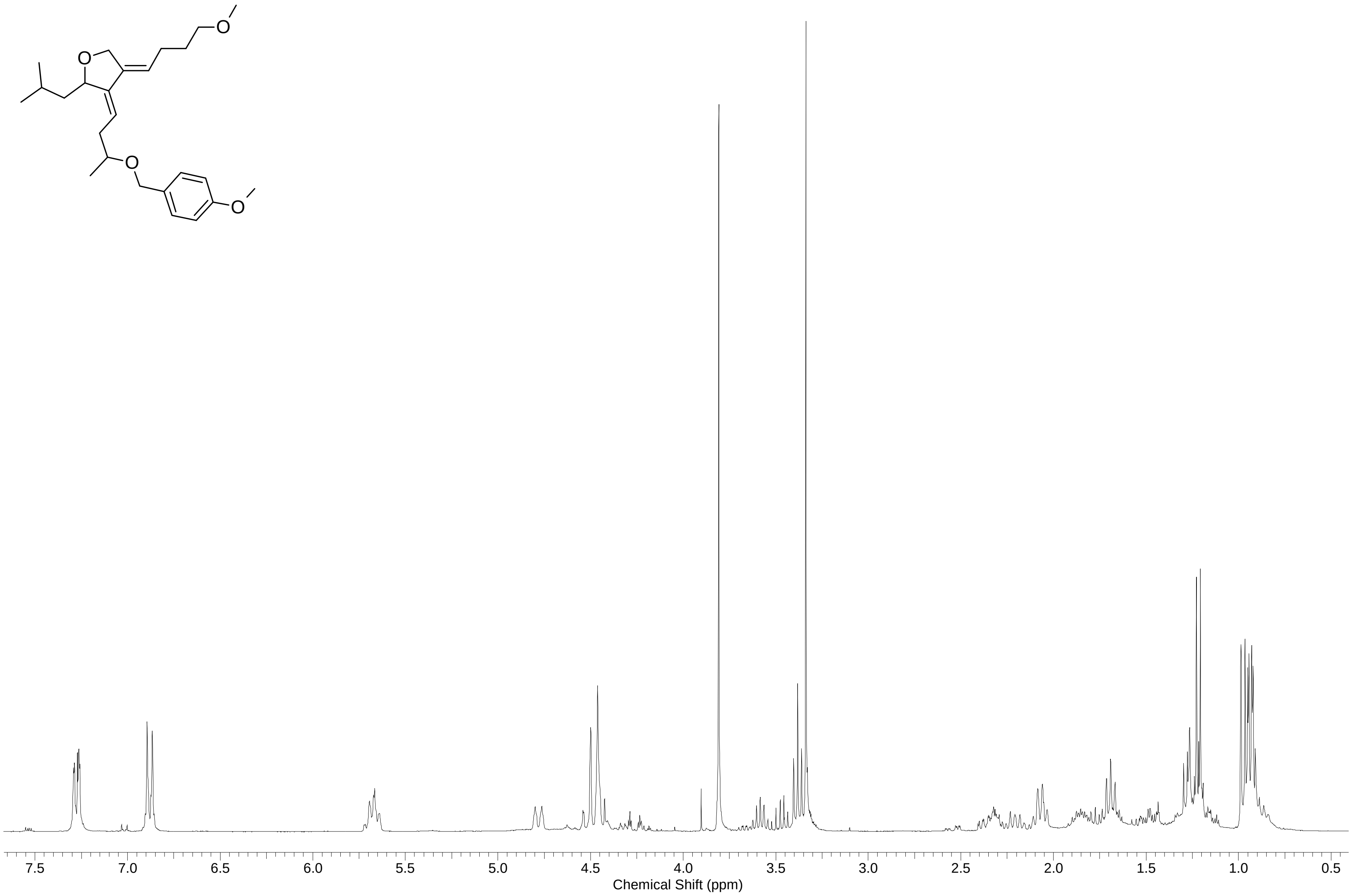

O
O
O

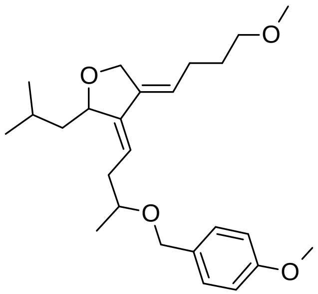

7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

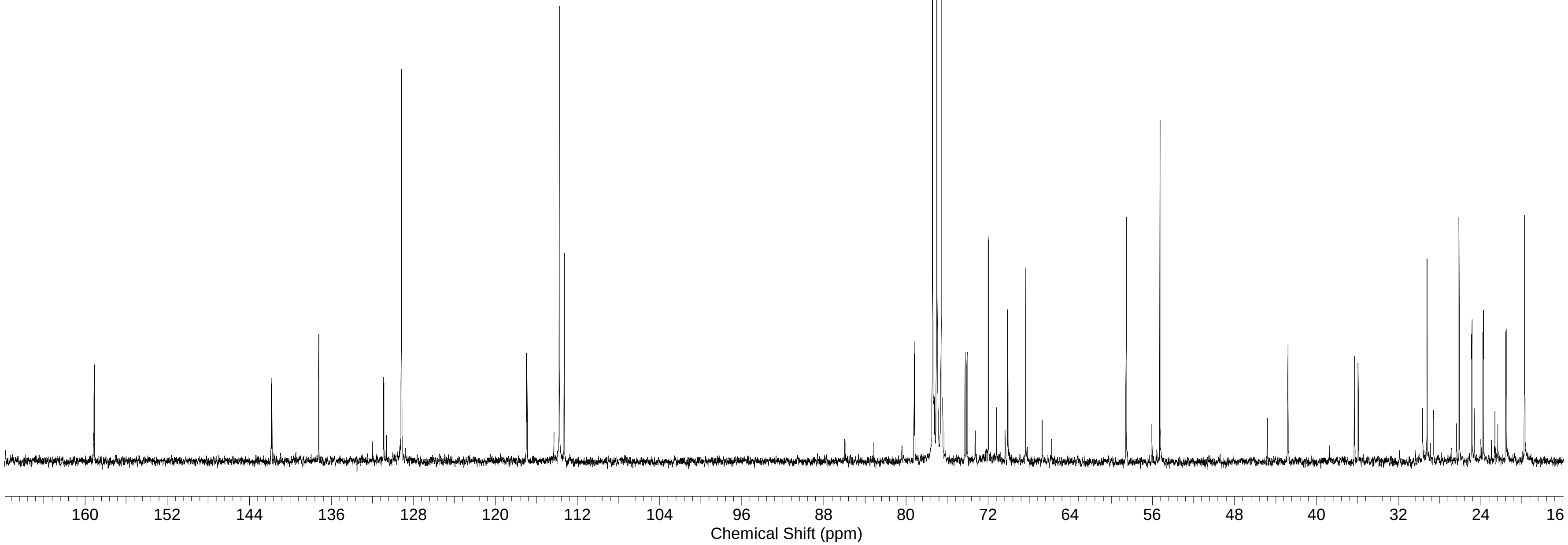

O
O
O
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

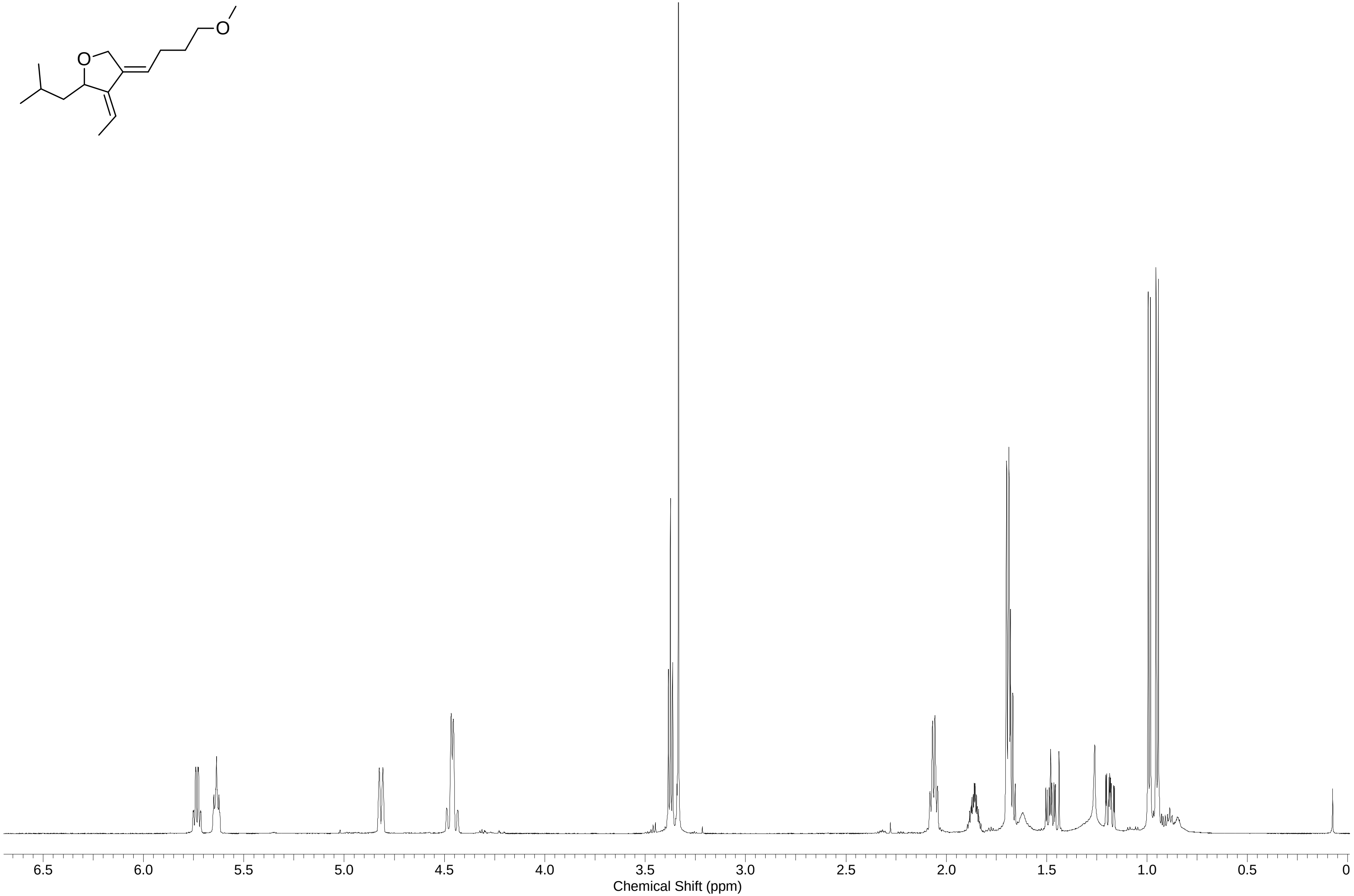

O
O
O
Si
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

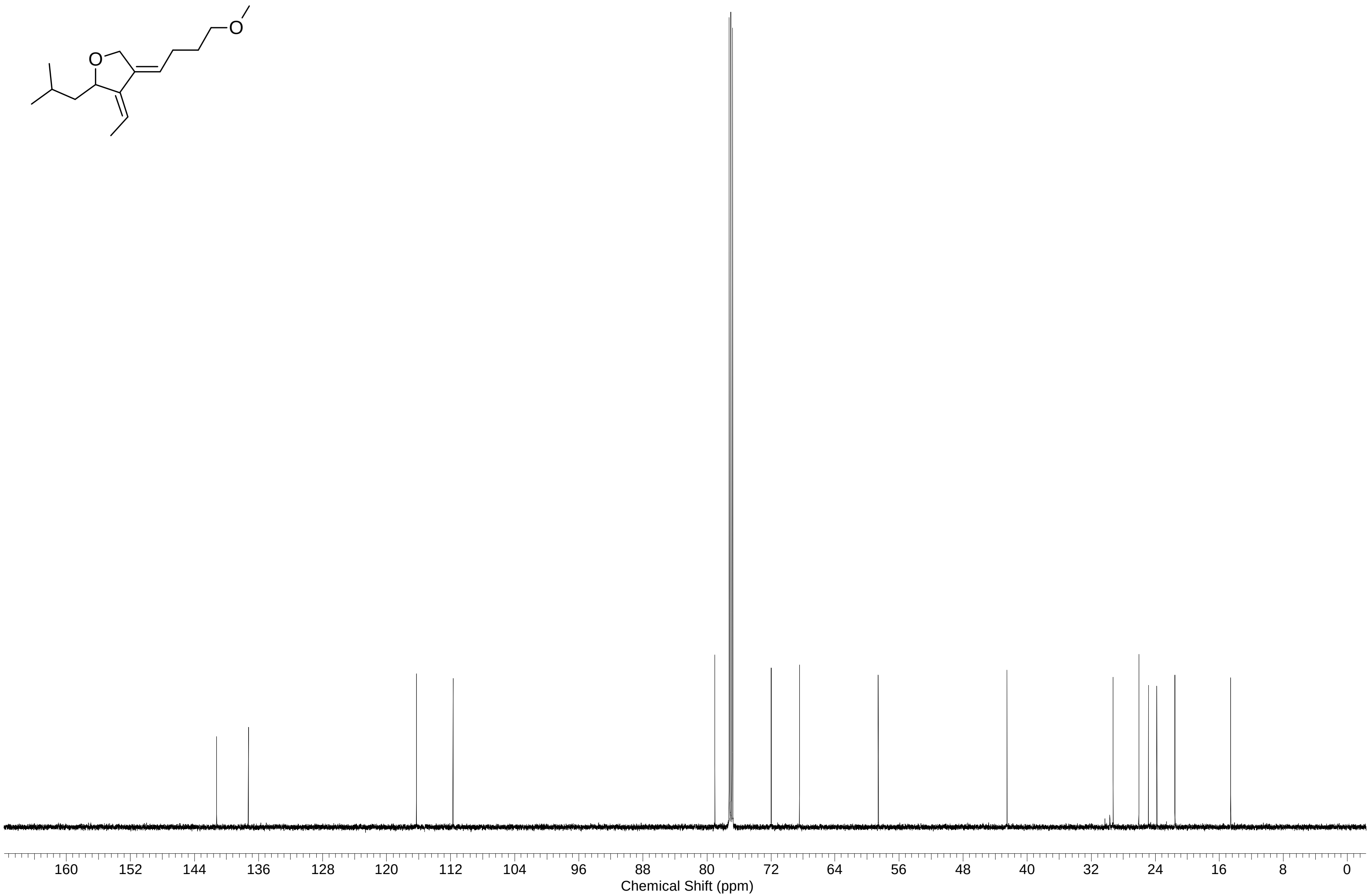

O
O
O
Si
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
-8
Chemical Shift (ppm)

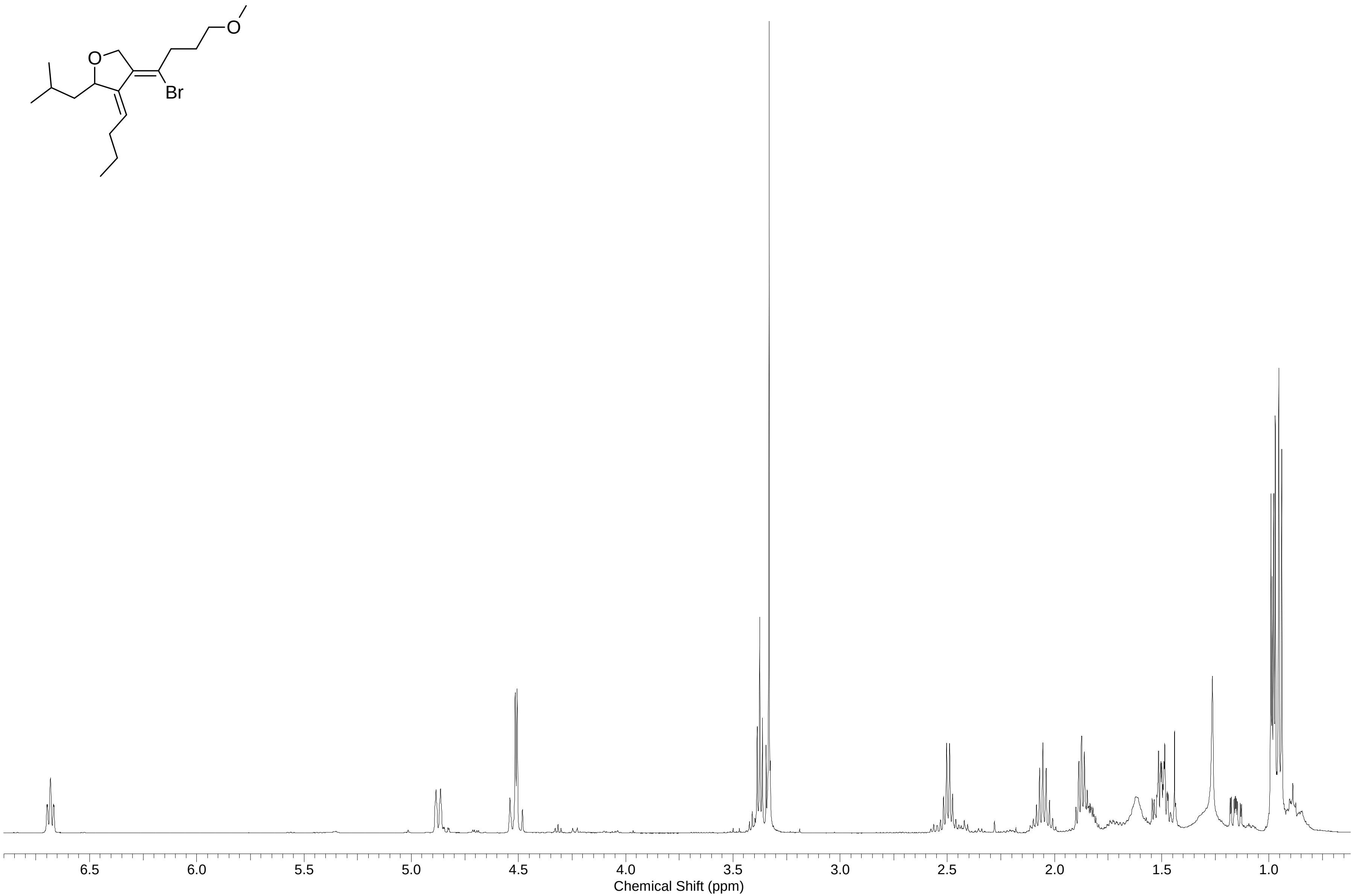

O
O
O
O
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

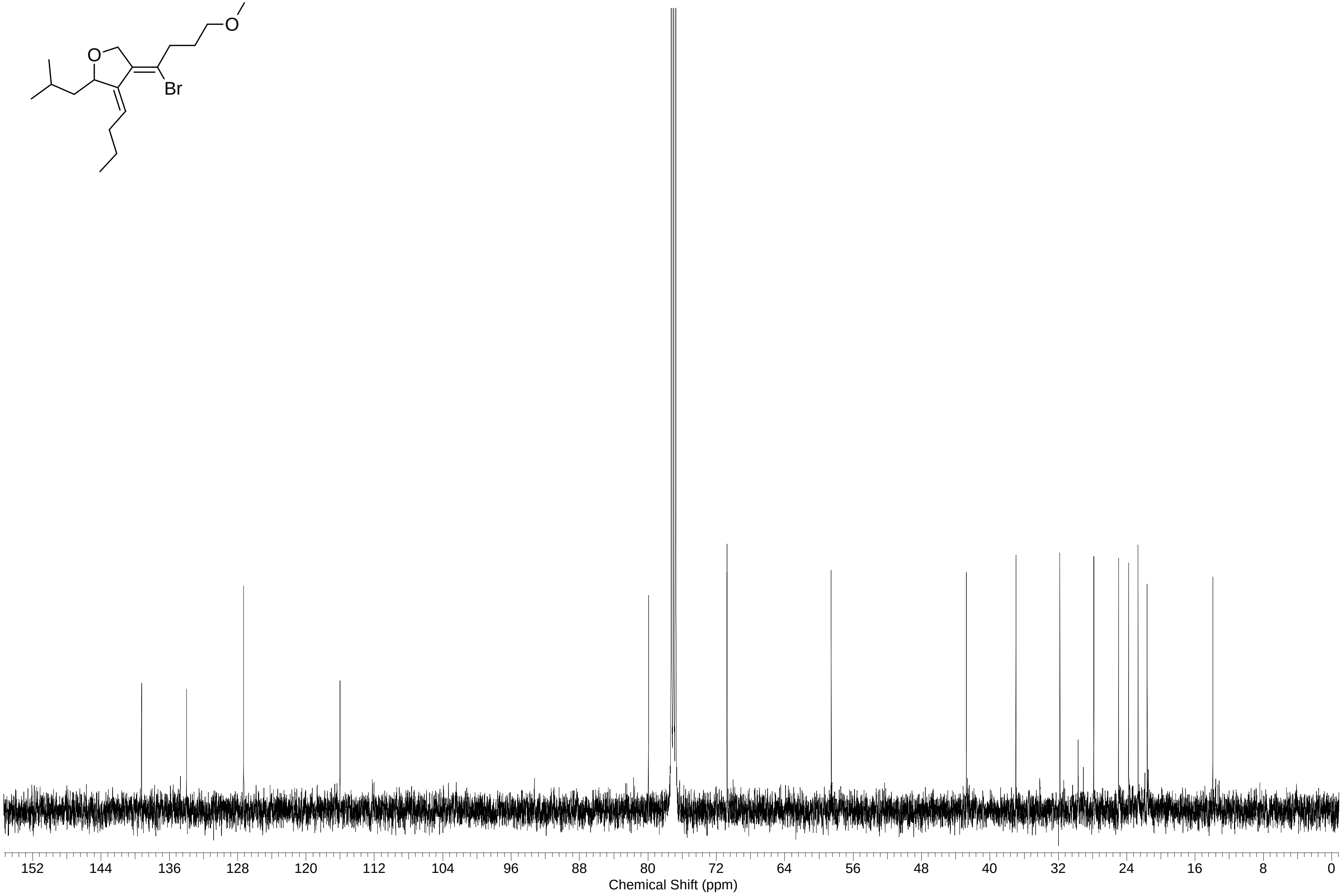

O
O
O
O

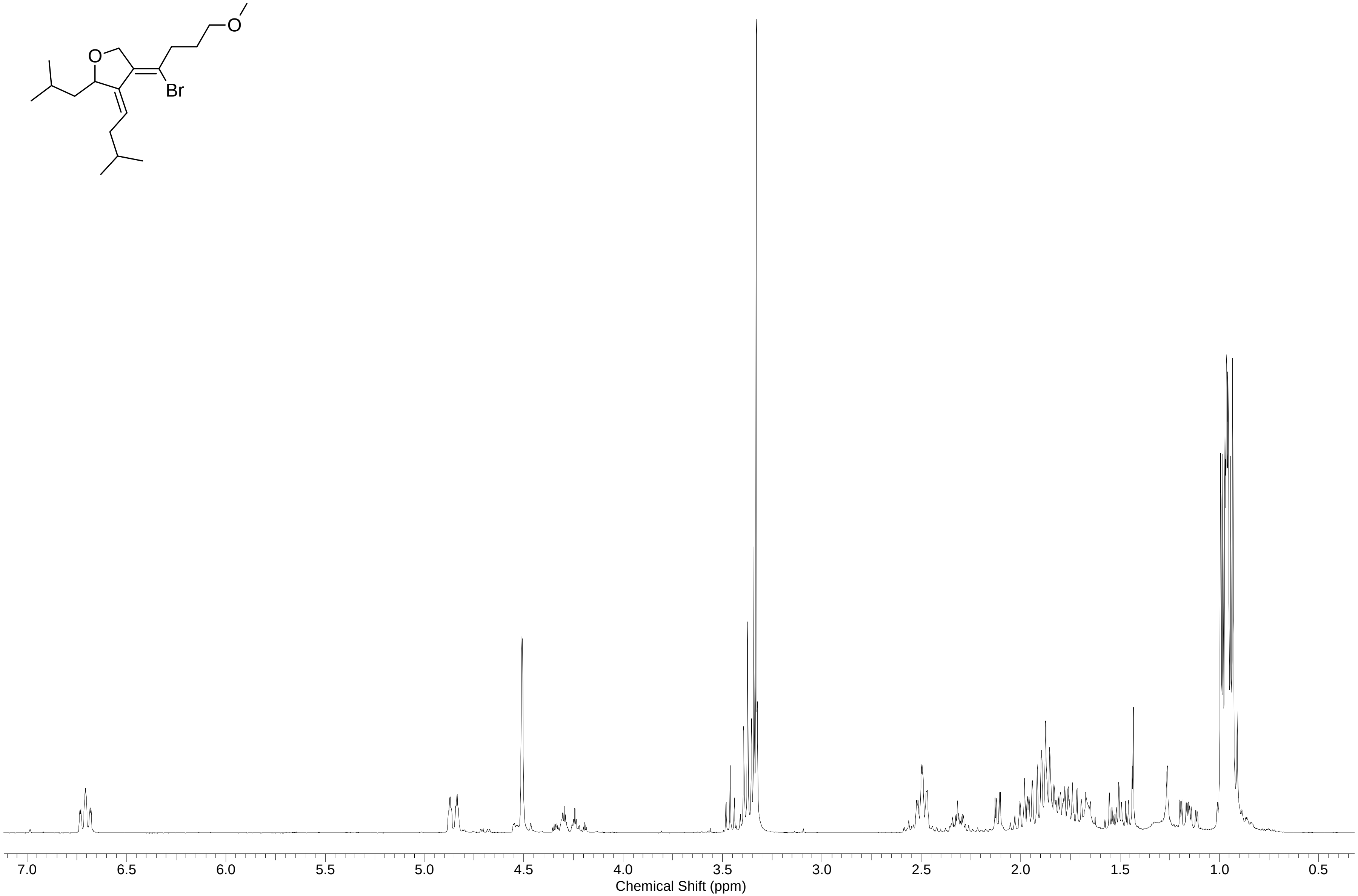

160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)


O
O
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

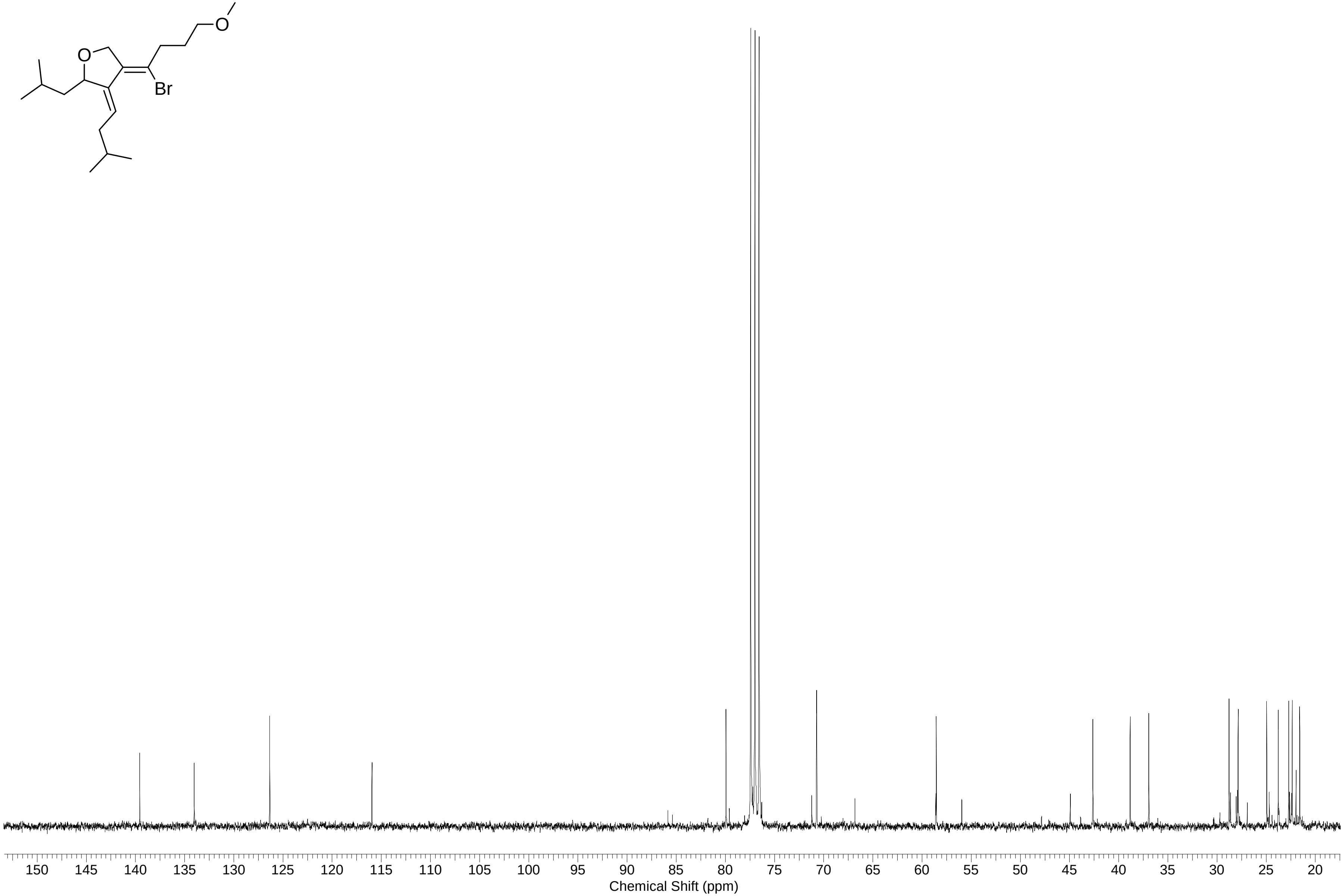

O
O
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)


O
O
Br
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)

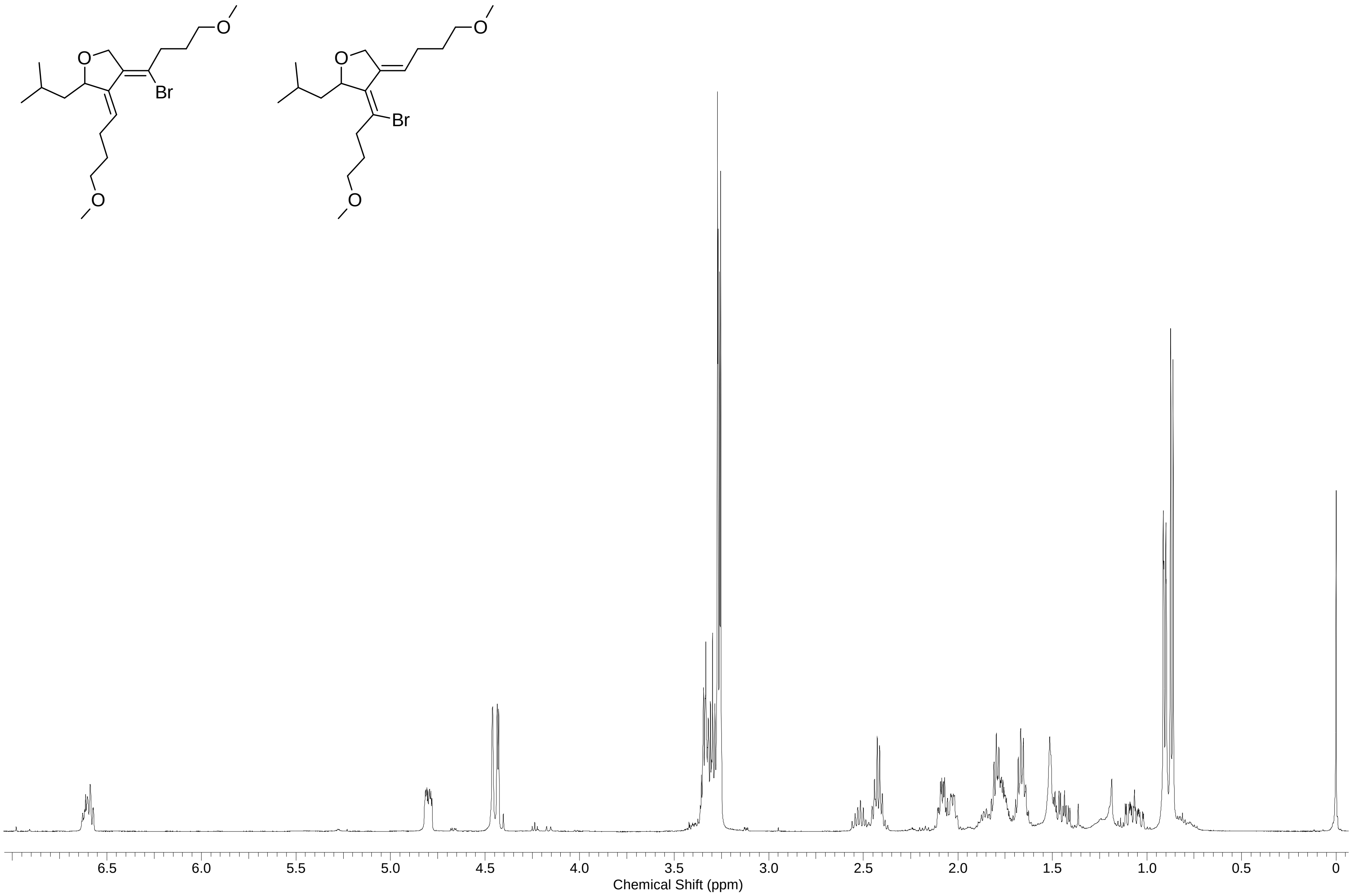

O
O
Br
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

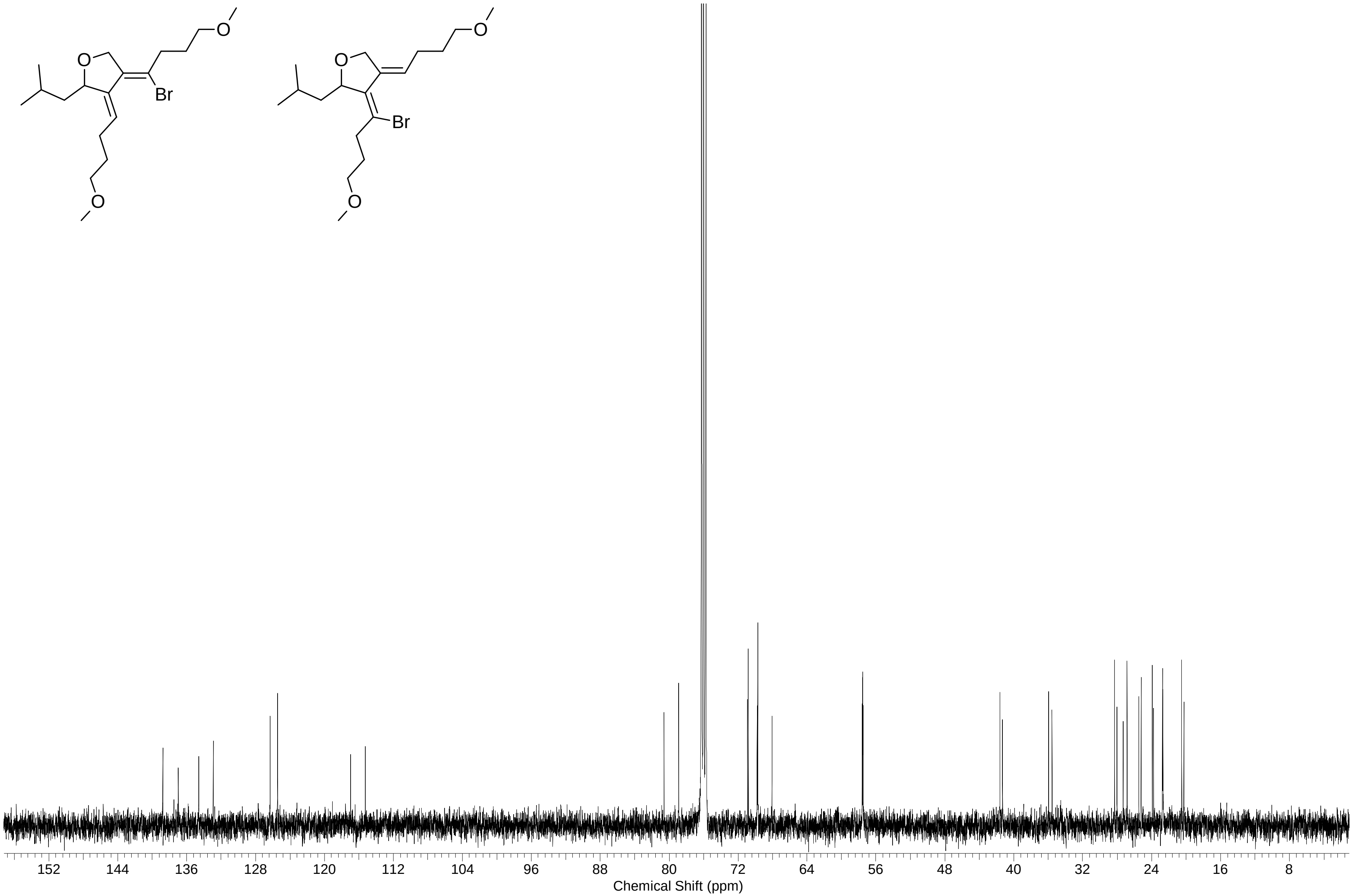

O
O
Br

7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

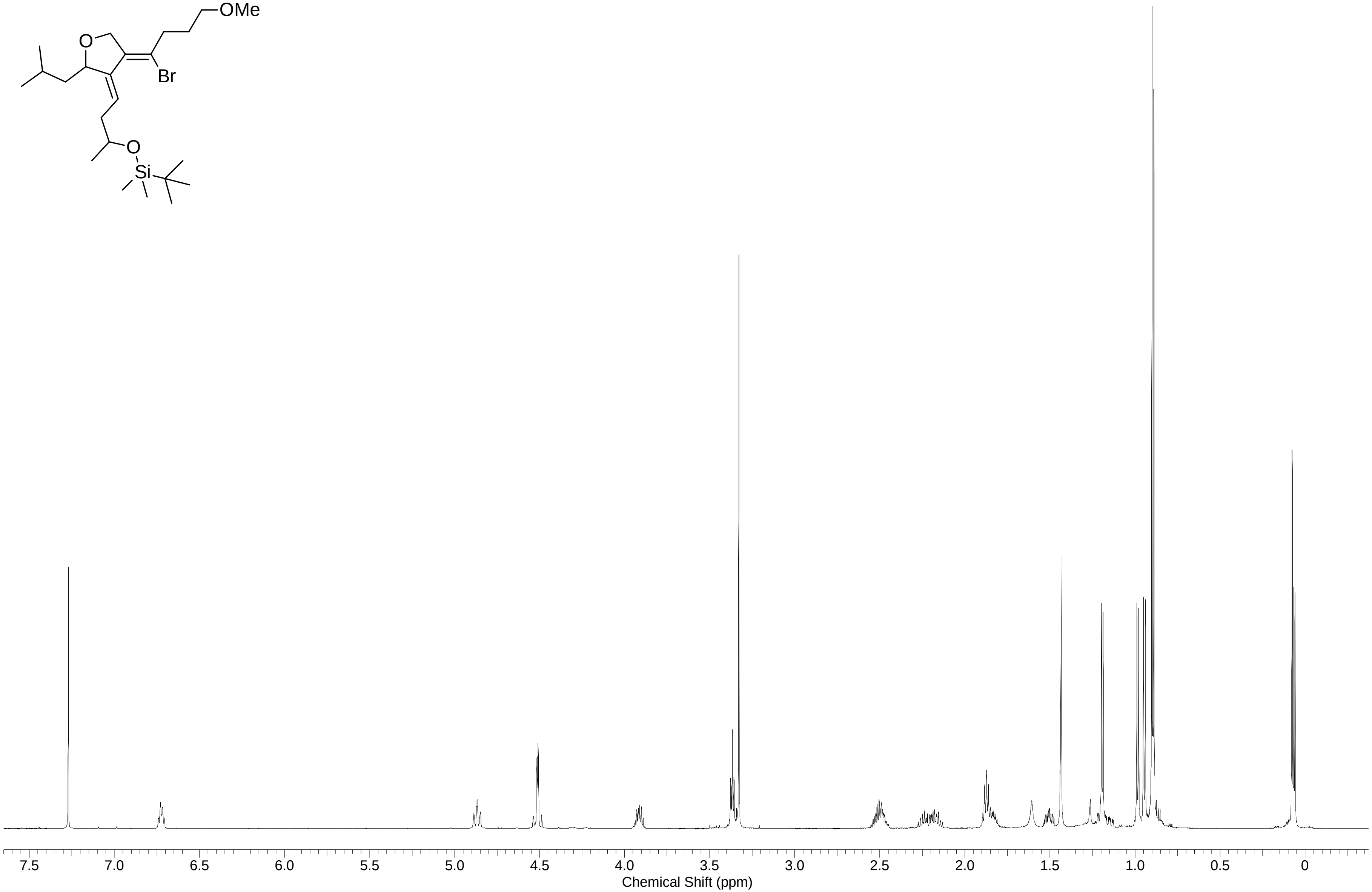

O
O
Br

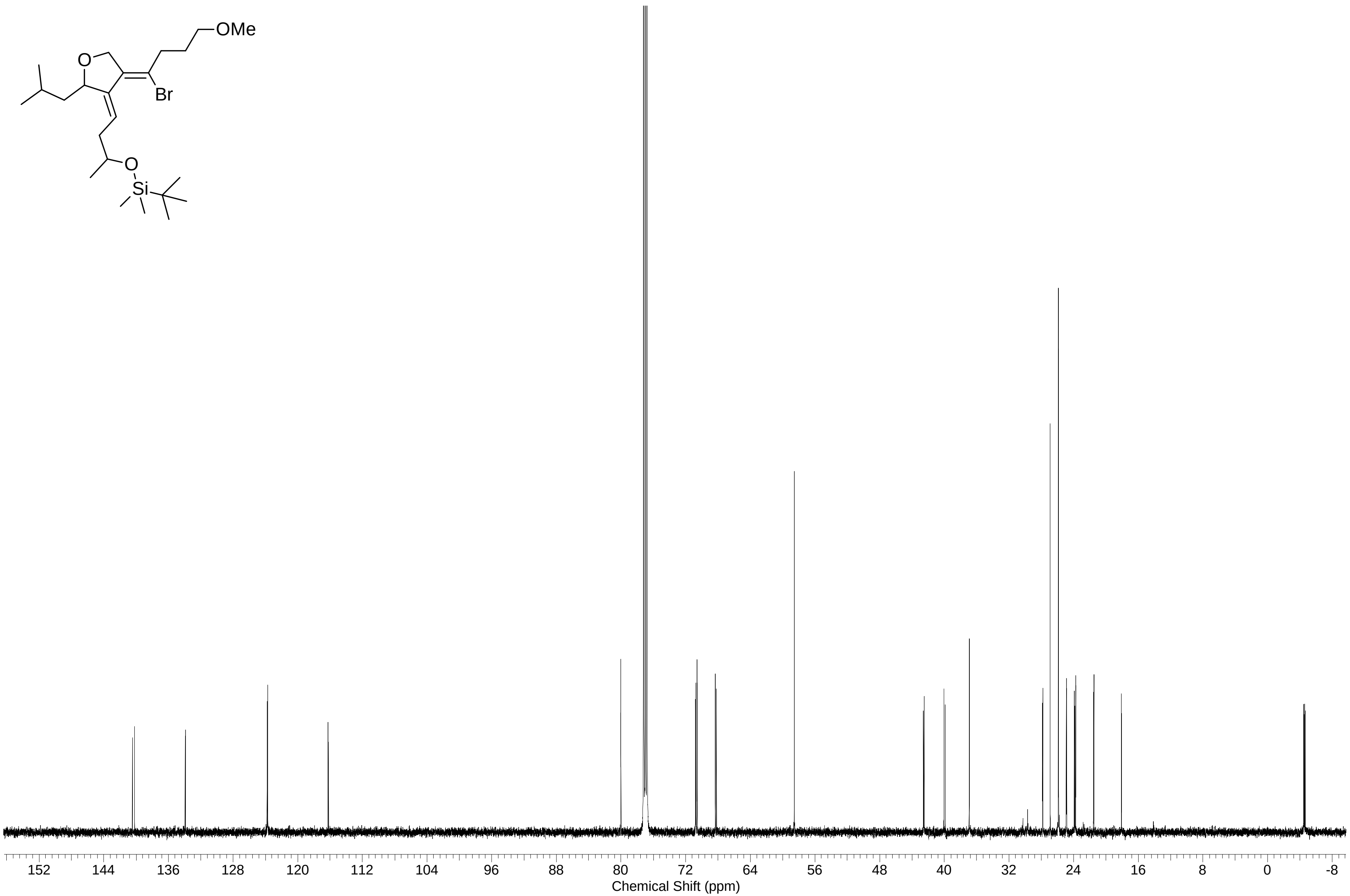
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
Chemical Shift (ppm)

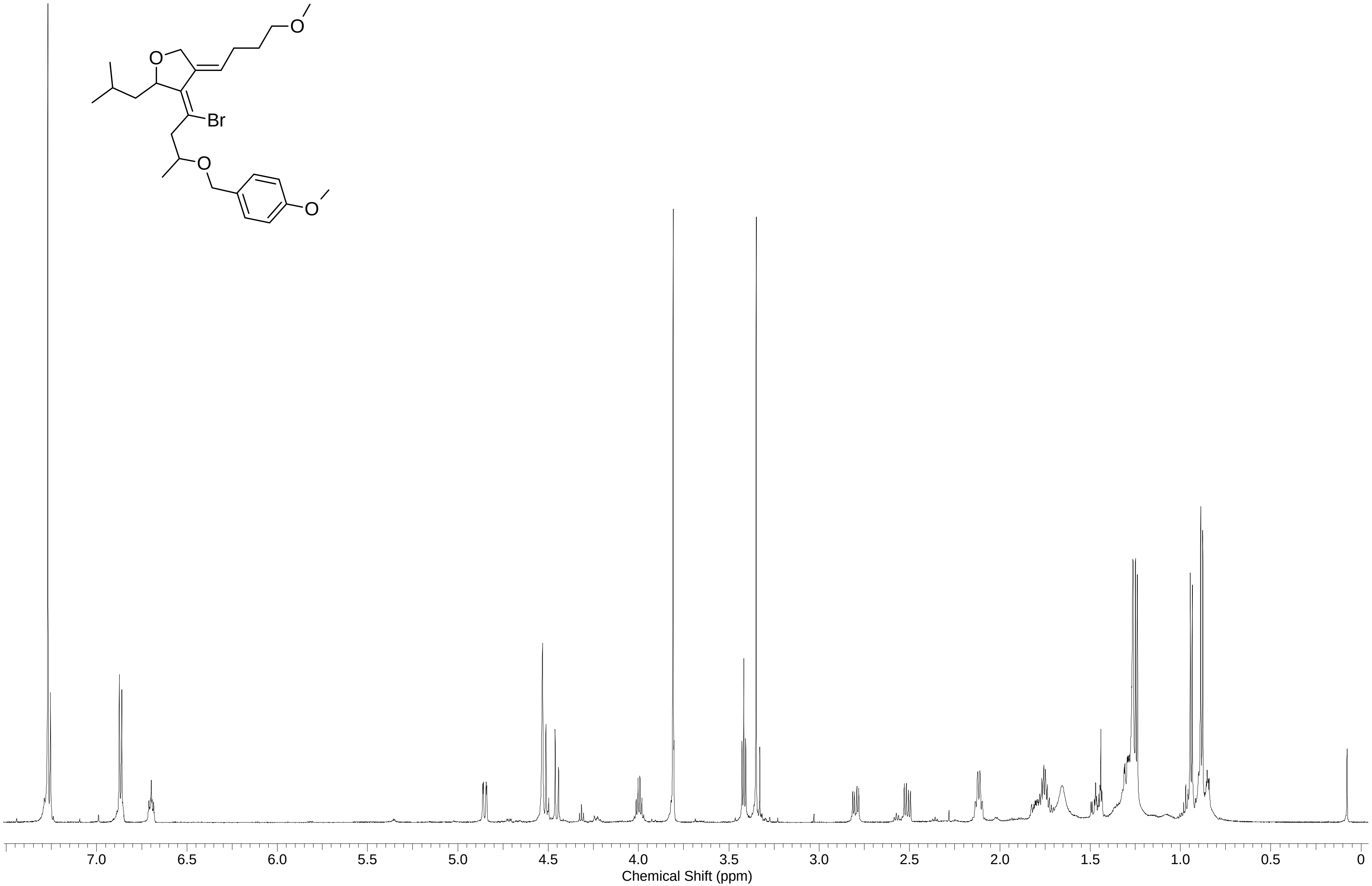

O
Br
O
O
O
Br
O
O
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

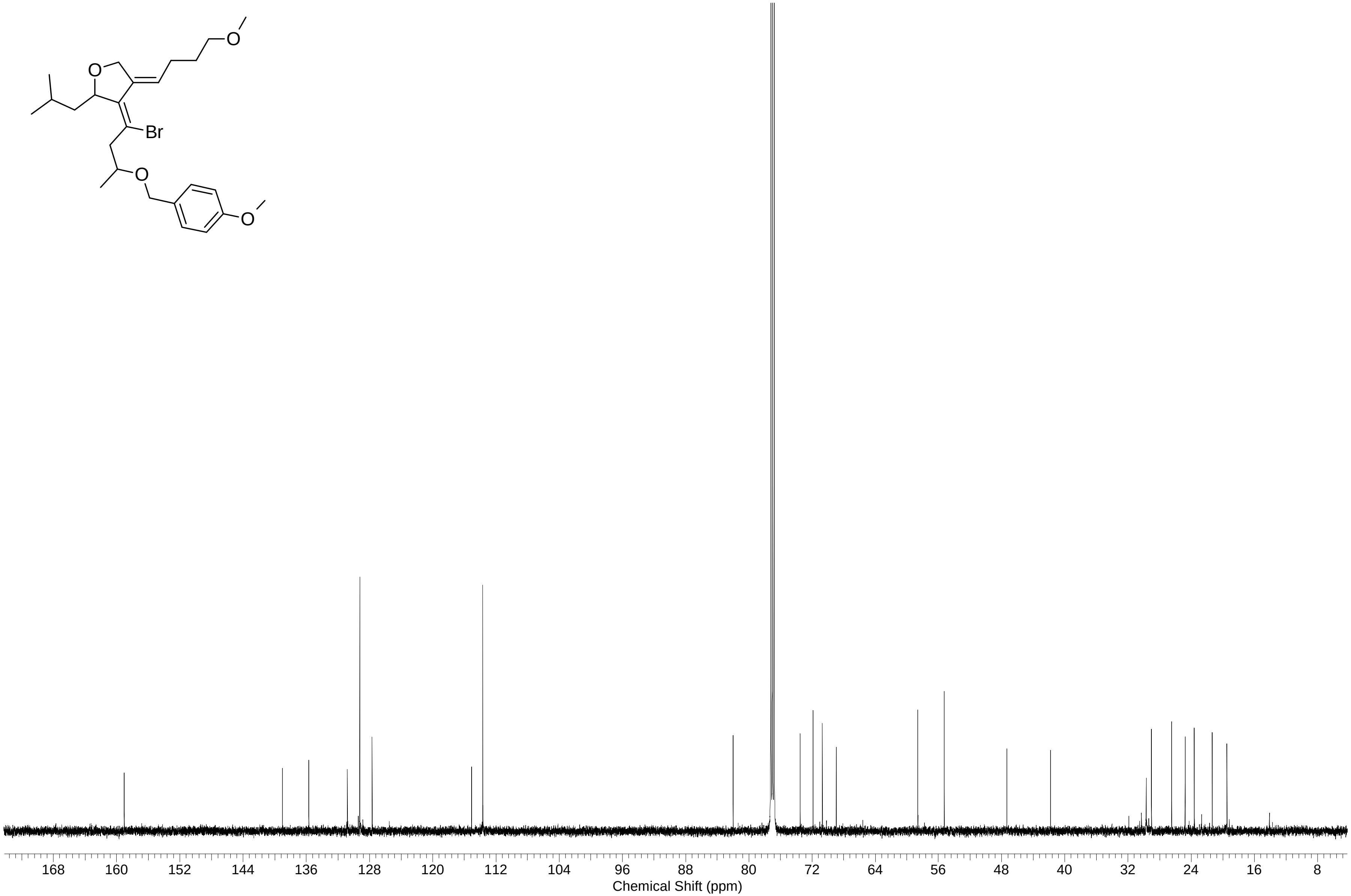

O
O
O
Br
O
O
O
Br

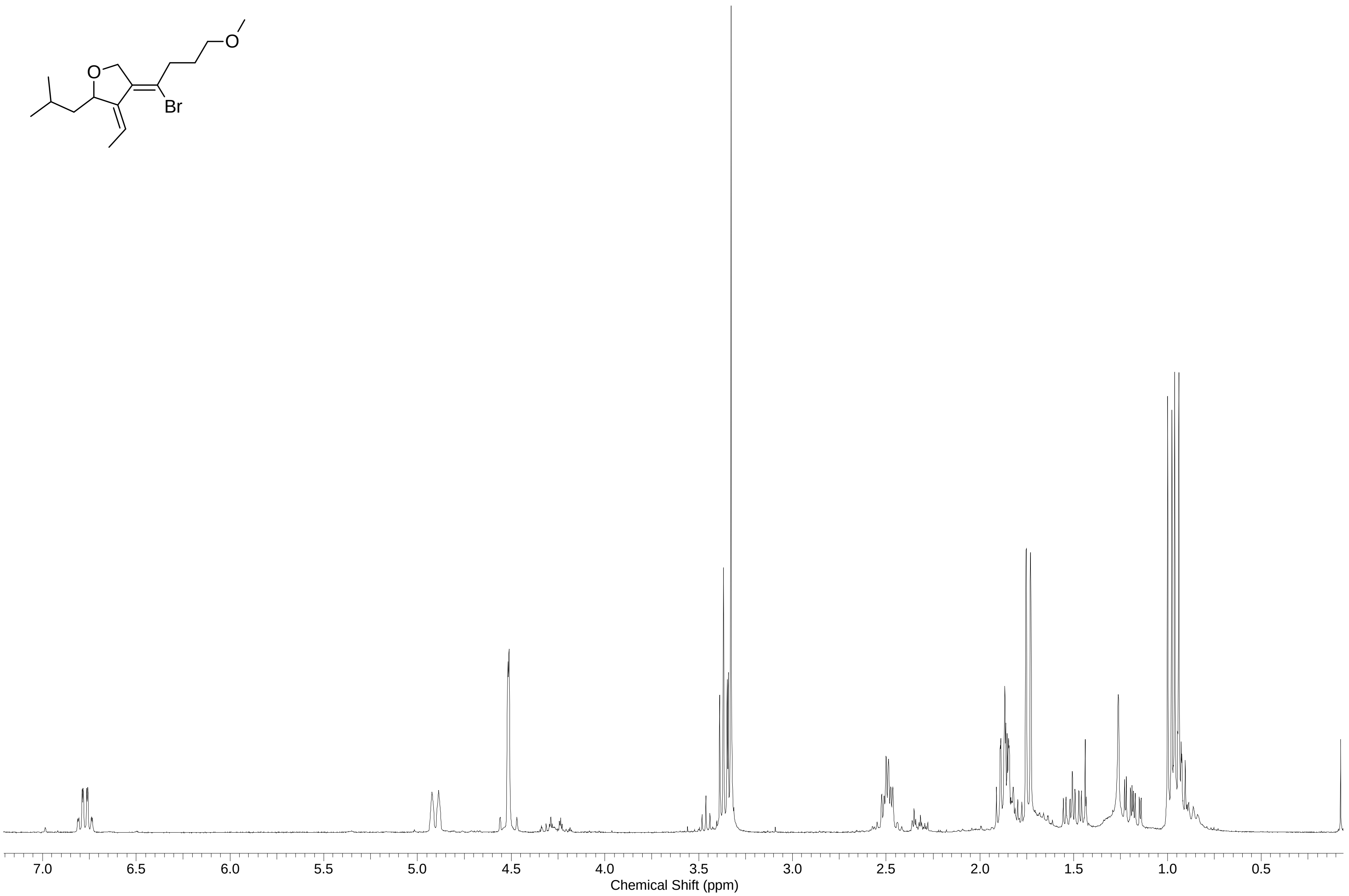
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)

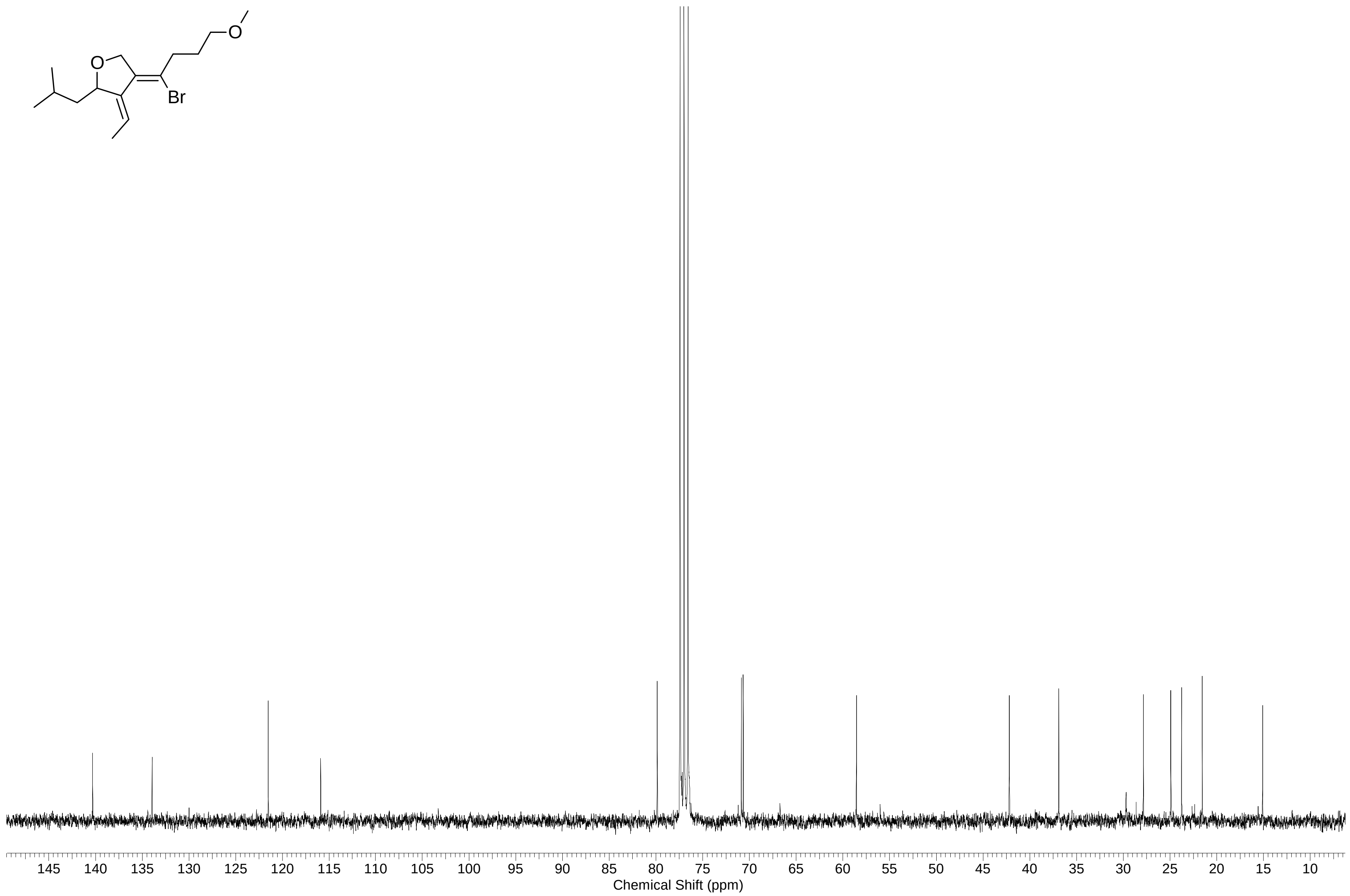

OMe
O
Br
O
Si
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)

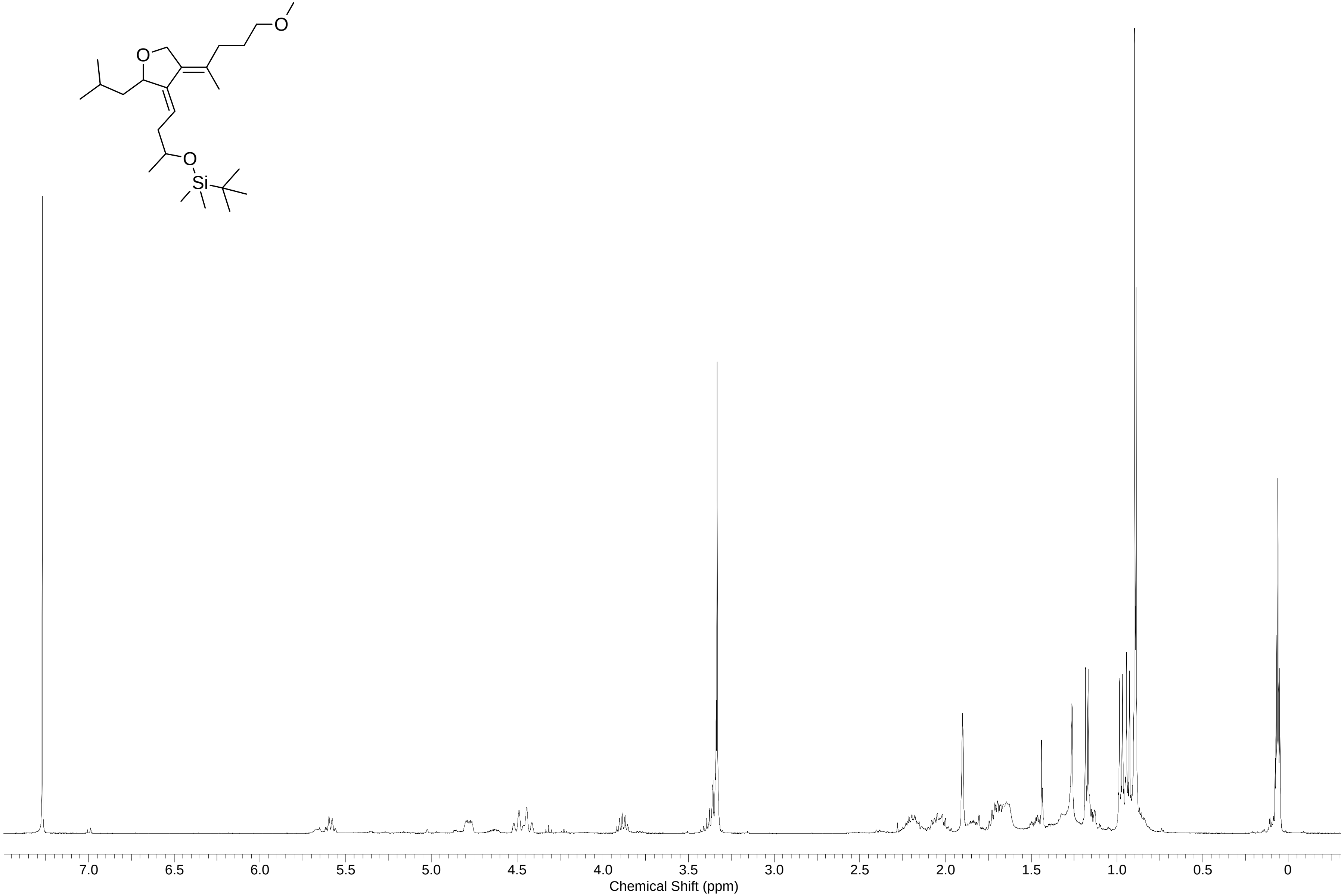

OMe
O
Br
O
Si
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
-8
Chemical Shift (ppm)

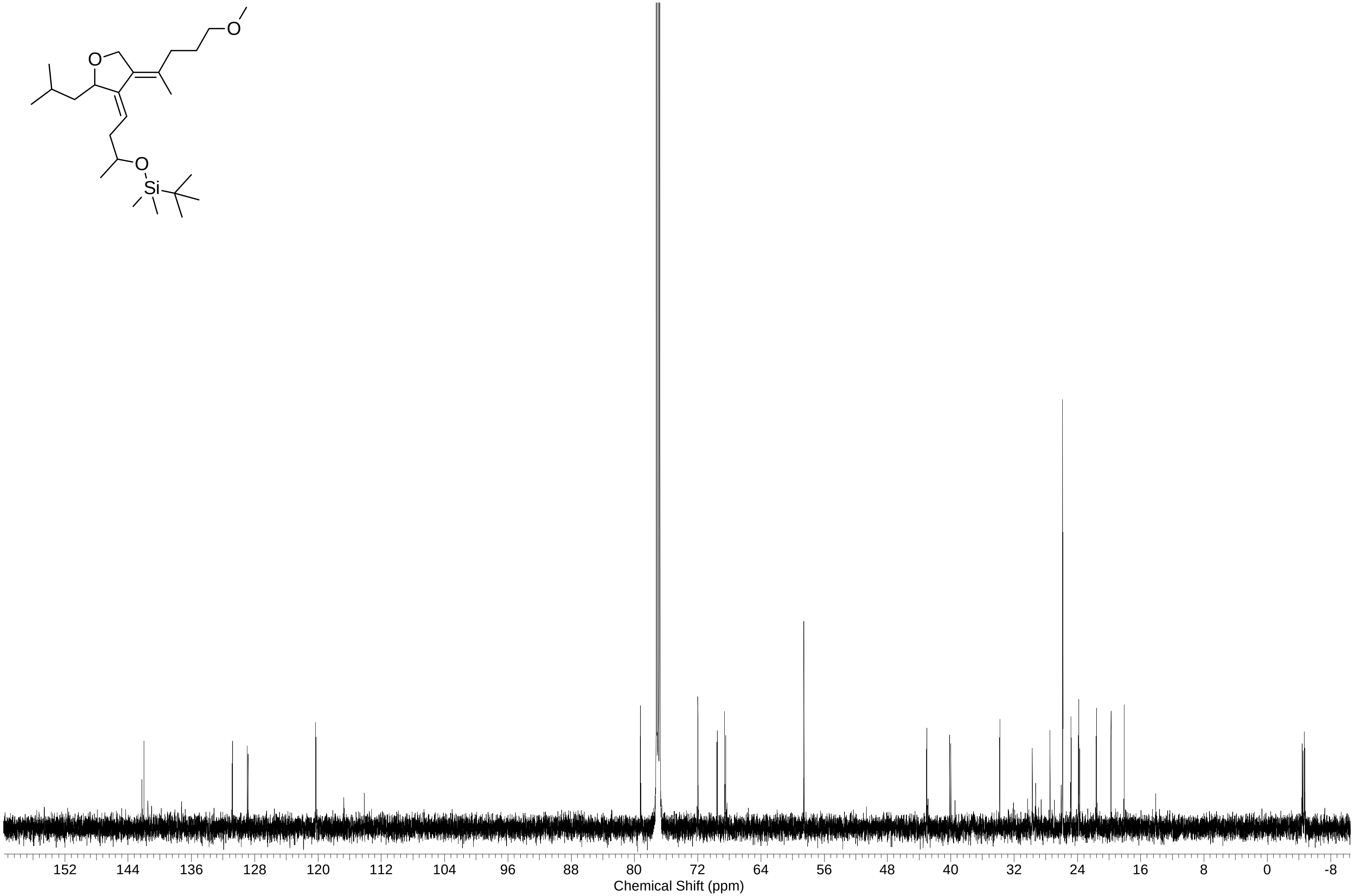

O
O
Br
O
O
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


O
O
Br
O
O
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)


O
O
Br
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)


O
O
Br
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
Chemical Shift (ppm)


O
O
O
Si
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
Chemical Shift (ppm)


O
O
O
Si
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
-8
Chemical Shift (ppm)

III. COMPUTATIONAL DETAILS

3.1 General procedures

All stationary points on the potential energy surface (PES) presented herein were calculated with density functional theory (DFT), with the hybrid B3LYP[10] functional (with Becke's three parameter exchange functional and the correlation functional from Lee, Yang and Parr). Unless otherwise stated, the LANL2DZ[11] basis set, which employs effective core potentials (ECPs) for transition metals, in combination with a solvent model as indicated in THF as solvent was used. DFT calculations were performed with the Gaussian09[12] (G09) software package. Minima were found using the standard optimization technique implemented in G09. The nature of each stationary point was determined by vibrational analysis using the same method and basis set. All of the minima presented in this study have all-real vibrational frequencies and do not show any imaginary value. Since the mechanism of the electrophilic NBS bromination for our substrate is not clear,[13] transition states were not calculated.

Instead, we focused on the calculation of the brominated intermediates **S12-S15**, with either the bromine positioned at C15 or C18 (Figure S1). These structures were chosen as representatives for the experimentally observed selectivities. We focused on the electrophilic attack from the top face (*vide infra*) of the zirconacyclopentadiene and compared the free enthalpies of both resulting regioisomers (15*R*-bromo and 18*S*-bromo) in different geometries (a-c).

---

[10] a) A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648-5652; b) A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 1372-1377; c) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785-789.

[11] a) T. H. Dunning, P. J. Hay, in Modern Theoretical Chemistry, Vol. 3 (Ed.: H. F. Schaefer), Plenum, New York, **1976**, pp. 1971-1928; b) P. J. Hay, W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 270-283; c) W. R. Wadt, P. J. Hay, *J. Chem. Phys.* **1985**, *82*, 284-298; d) P. J. Hay, W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 299-310.

[12] M. J. F. Gaussian 09 (Revision A.02), G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, **2009**.

[13] It's not clear if molecular NBS or remaining Br_2 from NBS synthesis induces the bromination, or if NBS dissociates before bromination;

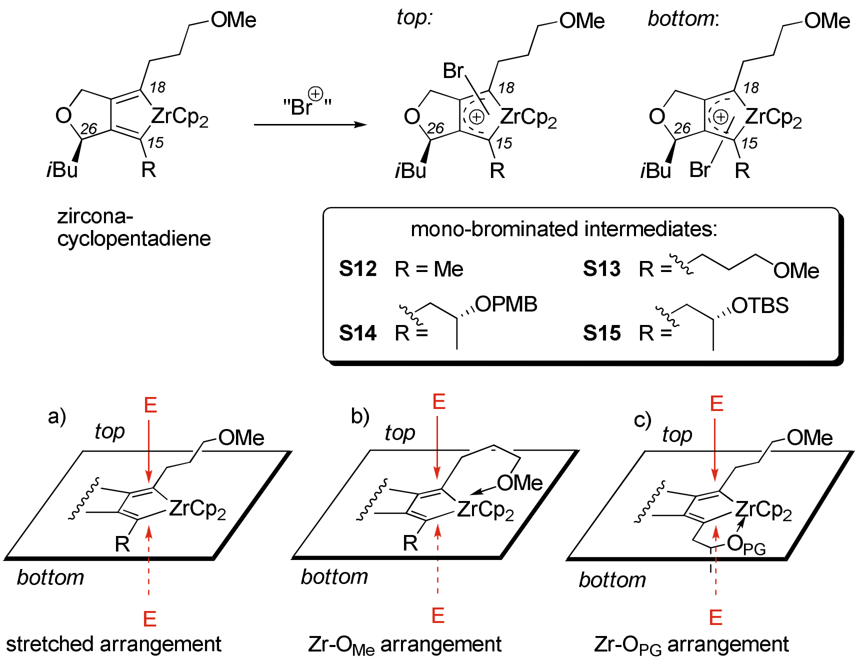


Figure S1. Bromination of the zirconacyclopentadiene precursor, either from the top or bottom face and the possible geometries a) – c) for the mono-brominated intermediates **S12-S15**.

3.2 Generation of the input structures

Zirconacyclopentadiene precursors were optimized at DFT/B3LYP level of theory with basis set and solvent model as indicated, followed by frequency calculations. The mono-brominated intermediates in the stretched arrangement for the top face attack (15*R*- and 18*S*-bromo-species) as well as for the bottom face attack (15*S*- and 18*R*-bromo-species) were obtained by adding a hydrogen atom at the corresponding carbon atoms C15 and C18 in the pre-optimized neutral structures, followed by subsequent substitution with bromine. The C-Br bond length was adjusted automatically. The over-all charge was set to +1. The four structures were again optimized at DFT/B3LYP level of theory with basis set and solvent model as indicated, followed by frequency analysis. The resulting free enthalpies for 15*R*- and 15*S*-bomo-species as well as for 18*S*- and 18*R*-bromo-species were finally compared. For the mono-brominated species with Zr-O_{Me}- and Zr-O_{PG}-arrangement the side chain containing the electron donor function was additionally arranged close to the metal center before geometry optimization.

3.3 Basis sets and solvent models

Concerning a possible solvent model dependency and the accuracy of the relative energies derived from smaller basis sets, a benchmark study was carried out. As model structure we took the neutral structure **S16** (Table S2), which misses the *i*-butyl group at C26 and bears two identical residues at the pentacyclic Zr-system. We calculated the positively charged bromonium intermediates 15*R*-bromo-**S16** and 18*S*-bromo-**S16**. Due to the symmetric nature of the substitution pattern at the metallacycle, the energy values for both mono-brominated intermediates should be similar, independent from the choice of the basis set or solvent model. As shown in Table S2, employing the LANL2DZ basis set with either the polarizable continuum model (PCM)[14] or the polarizable conductor calculation model (CPCM)[15] and THF (ε = 7.4257) as solvent showed almost the same energies for the mono-brominated species of **S16** ($\Delta\Delta G < 1$ kJ mol^{-1}). The larger Def2-TZVP[16] basis set delivered the same tendencies, with an energy deviation of about 2-4 kJ mol^{-1}. This revealed that the LANL2DZ basis set should be accurate enough for our molecular system. Based on these results, further calculations were performed using a combination of LANL2DZ basis set and PCM solvent model for the uncharged Zr-precursors as well as for the charged mono-brominated intermediates.

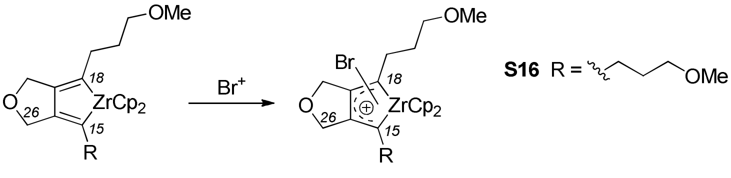
---

[14] a) S. Miertus, E. Scrocco, J. Tomasi, *Chem. Phys.* **1981**, *55*, 117-129 b) . Miertus , J. Tomasi, *Chem. Phys.* **1982**, *65*, 239-245; c) J. L. Pascual-ahuir, E. Silla, I. Tuñon, *J. Comput. Chem.* **1994**, *15*, 1127-1138; d) M. Cossi, V. Barone, R. Cammi, J. Tomasi, *Chem. Phys. Lett.* **1996**, *255*, 327-335; e) V. Barone, M. Cossi, J. Tomasi, *J. Chem. Phys.* **1997**, *107*, 3210-3221; f) E. Cances, B. Mennucci, J. Tomasi, *J. Chem. Phys.* **1997**, *107*, 3032-3041; g) B. Mennucci, E. Cancès, J. Tomasi, *J. Phys. Chem. B* **1997**, *101*, 10506-10517; h) V. Barone, M. Cossi, *J. Phys. Chem. A* **1998**, *102*, 1995-2001; i) M. Cossi, V. Barone, B. Mennucci, J. Tomasi, *Chem. Phys. Lett.* **1998**, *286*, 253-260; j) V. Barone, M. Cossi, J. Tomasi, *J. Comput. Chem.* **1998**, *19*, 404-417; k) R. Cammi, B. Mennucci, J. Tomasi, *J. Phys. Chem. A* **1999**, *103*, 9100-9108; l) M. Cossi, V. Barone, M. A. Robb, *J. Chem. Phys.* **1999**, *111*, 5295-5302; m) J. Tomasi, B. Mennucci, E. Cancès, *J. Mol. Struct.* **1999**, *464*, 211-226; n) R. Cammi, B. Mennucci, J. Tomasi, *J. Phys. Chem. A* **2000**, *104*, 5631-5637; o) M. Cossi, V. Barone, *J. Chem. Phys.* **2000**, *112*, 2427-2435; p) M. Cossi, V. Barone, *J. Chem. Phys.* **2001**, *115*, 4708-4717; q) M. Cossi, N. Rega, G. Scalmani, V. Barone, *J. Chem. Phys.* **2001**, *114*, 5691-5701; r) M. Cossi, G. Scalmani, N. Rega, V. Barone, *J. Chem. Phys.* **2002**, *117*, 43-54; s) M. Cossi, N. Rega, G. Scalmani, V. Barone, *J. Comput. Chem.* **2003**, *24*, 669-681; t) J. Tomasi, B. Mennucci, R. Cammi, *Chem. Rev.* **2005**, *105*, 2999-3094.

[15] a) V. Barone, M. Cossi, *J. Phys. Chem. A* **1998**, *102*, 1995-2001; b) M. Cossi, N. Rega, G. Scalmani, V. Barone, *J. Comput. Chem.* **2003**, *24*, 669-681.

[16] a) F. Weigend, R. Ahlrichs, *Phys. Chem. Chem. Phys.*, **2005,** *7*, 3297-3305; b) D. Andrae, U. Haeussermann, M.Dolg, H.Stoll, H.Preuss, *Theor. Chim. Acta* **1990**, *77*, 123-141.

Table S2. Solvent model dependency and accuracy of relative energies derived from small basis sets for structure **S16** and its mono-brominated intermediates either at position C15 or C18. Free enthalpies are calculated at DFT/B3LYP level of theory in combination with basis set and solvent model as indicated.



Zr-precursor-**S16** mono-brominated **S16**

substance[a]	basis set	solvent model[b]	ΔG [kJ mol^{-1}][c]
Zr-precursor-**S16**	LANL2DZ	PCM	0.0
15*R*-bromo-**S16**	LANL2DZ	PCM	89.1
18*S*-bromo-**S16**	LANL2DZ	PCM	88.6
Zr-precursor-**S16**	LANL2DZ	CPCM	0.0
15*R*-bromo-**S16**	LANL2DZ	CPCM	87.8
18*S*-bromo-**S16**	LANL2DZ	CPCM	87.7
Zr-precursor-**S16**	Def2_TZVP	PCM	0.0
15*R*-bromo-**S16**	Def2_TZVP	PCM	88.4
18*S*-bromo-**S16**	Def2_TZVP	PCM	92.8
Zr-precursor-**S16**	Def2_TZVP	CPCM	0.0
15*R*-bromo-**S16**	Def2_TZVP	CPCM	71.9
18*S*-bromo-**S16**	Def2_TZVP	CPCM	69.6

[a] For all mono-brominated structures the electrophilic attack from the top face is calculated, following the rational, that enantiomers produce the same energetic profile. [b] solvent=THF; [c] Free enthalpies for the Zr-precursors were set to zero. All other free enthalpies are relative values in relation to the corresponding Zr-precursor.

3.4 Top and bottom face attack

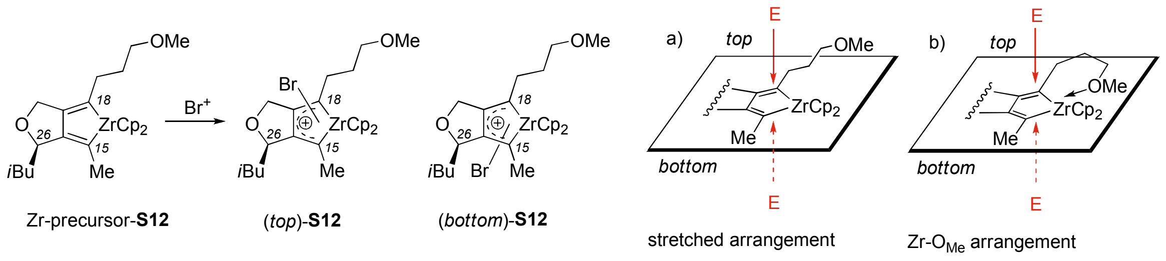
We wanted to investigate the steric influence of the *i*-butyl sidechain at C26. Structure **S12**, which displays a 20-fold enhanced selectivity for the bromination at C18 (cf. Table 2), was taken as representative for this study. We calculated all four possible regio- and diastereomers for the bromination reaction in the stretched arrangement and compared the relative energies for 15*R*- and 15*S*-bromo-**S12** as well as for 18*S*- and 18*R*-bromo-**S12** (Table S3). This revealed an energy difference of less than 8 kJ mol^{-1} for the top or bottom face attack at the same C-atom. The energy differences in the Zr-O$_{Me}$ arrangement indicate the same tendencies (< 6.5 kJ mol^{-1}). Considering the error range of DFT-calculations,[17] the observed energy difference indicates no significant influence of the *i*-butyl function on the selectivity for this

---

[17] M. C. Holthausen, *J. Comput. Chem.* **2005**, *26*, 1505-1518.

reaction. On this account, just the mono-brominated structures derived from top face attack on the Zr-precursors **S12-S15** (15*R*-bromo and 18*S*-bromo) were calculated.

Table S3. Bromination of the pentacyclic Zr-precursor **S12**, either from the top or bottom face of the diene system and the possible geometries a) and b) for the mono-brominated products of **S12**. Relative free enthalpies and bond lengths are shown in the table at the bottom. DFT-calculations were performed at the B3LYP/LANL2DZ level of theory with THF as solvent (PCM solvent model).



substance	electrophilic attack	ΔG^a [kJ mol^{-1}]	bond length [Å]					
			C15-Zr	C18-Zr	C15-Br	C18-Br	O$_{Me}$-Zr	O$_{PG}$-Zr
Zr-precursor-**S12**	-	0.0	2.25	2.25	-	-	-	-
15*R*-bromo-**S12**	top^b	91.4	2.43	2.35	2.16	-	-	-
18*S*-bromo-**S12**	top^b	86.2	2.32	2.44	-	2.15	-	-
15*S*-bromo-**S12**	bottom^b	97.8	2.40	2.35	2.18	-	-	-
18*R*-bromo-**S12**	bottom^b	89.3	2.32	2.42	-	2.18	-	-
15*R*-bromo-**S12**	top^c	107.9	2.60	2.39	2.15	-	2.47	-
18*S*-bromo-**S12**	top^c	74.8	2.36	2.47	-	2.19	2.49	-
15*S*-bromo-**S12**	bottom^c	104.1	2.50	2.39	2.21	-	2.49	-
18*R*-bromo-**S12**	bottom^c	81.3	2.36	2.46	-	2.21	2.48	-

[a] Free enthalpies for the Zr-precursors were set to zero. All other free enthalpies are relative values in relation to the corresponding Zr-precursor. [b] stretched arrangement; [c] Zr-O$_{Me}$ arrangement for methoxy side chain at C18 close to the Zr metal.

3.5 Free enthalpies and bond lengths for resulting mono-brominated intermediates

All structures in the stretched arrangement were obtained following the procedure described in section 3.2. For the Zr-O$_{Me}$ arrangement and Zr-O$_{PG}$ arrangement the "chelatization" between the metal and the side chain was sometimes removed during minimization. If so, the distance between the oxygen and the metal was frozen during optimization using the *opt=modredundant* keyword in Gaussian09. In a second optimization run, the Zr-O distance was again kept flexible to allow the side chain to adjust to the metal in a suitable manner. Additionally, sometimes the optimization process for the mono-brominated structures did not stop at the intermediate structure, but did minimize to the product structure with the metallacycle already opened. To prevent this outcome the bonds between the α-carbon atoms and the metal were frozen, the structure was minimized and the “frozen”-pre-optimized structure was again minimized with flexible treatment of all bond length.

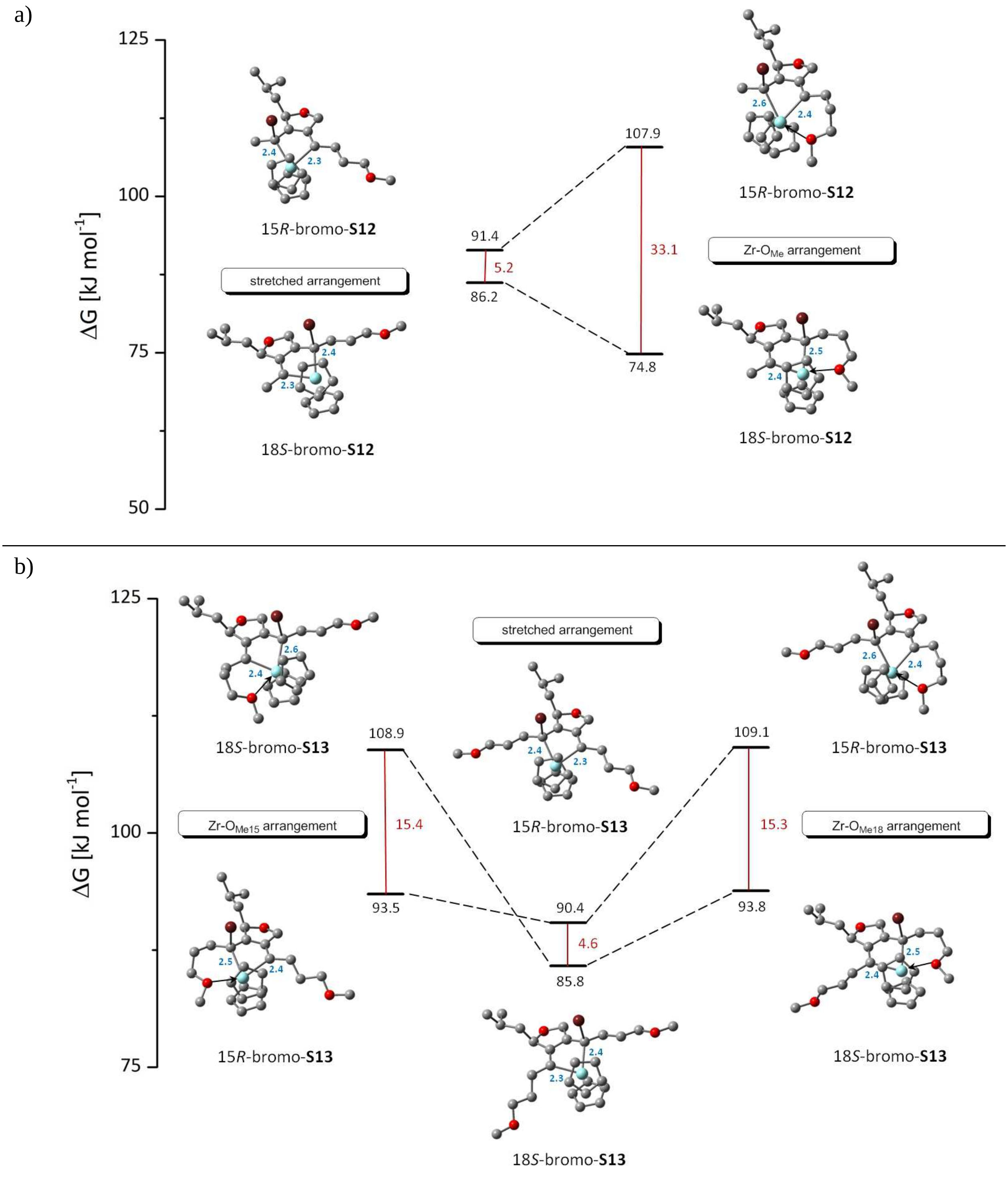
Table S4. Relative free enthalpies and bond lengths for the resulting mono-brominated intermediates **S12-S15** in different geometries. DFT-calculations were performed at the B3LYP level of theory, with the LANL2DZ basis set and THF as solvent (PCM solvent model).

substance	geometry[a]	ΔΔG [kJ mol^{-1}]	bond length [Å]					
			C15-Zr	C18-Zr	C15-Br	C18-Br	O_{Me}-Zr	O_{PG}-Zr
15*R*-bromo-**S12**	stretched	91.4	2.43	2.35	2.16	-	-	-
18*S*-bromo-**S12**	stretched	86.2	2.32	2.44	-	2.15	-	-
15*R*-bromo- **S12**	Zr-O_{Me}[b]	107.9	2.60	2.39	2.15	-	2.47	-
18*S*-bromo-**S12**	Zr-O_{Me}[b]	74.8	2.36	2.47	-	2.19	2.49	-
15*R*-bromo-**S13**	stretched	90.4	2.43	2.35	2.16	-	-	-
18*S*-bromo-**S13**	stretched	85.8	2.34	2.42	-	2.16	-	-
15*R*-bromo-**S13**	Zr-O_{Me}[b]	109.1	2.60	2.39	2.17	-	2.47	
18*S*-bromo-**S13**	Zr-O_{Me}[b]	93.8	2.35	2.44	-	2.17	2.59	-
15*R*-bromo-**S13**	Zr-O_{Me}[c]	93.5	2.51	2.40	2.17	-	2.55	-
18*S*-bromo-**S13**	Zr-O_{Me}[c]	108.9	2.34	2.42	-	2.22	2.63	-
15*R*-bromo-**S14**	stretched	90.6	2.44	2.31	2.16	-	-	-
18*S*-bromo-**S14**	stretched	92.9	2.36	2.43	-	2.16	-	-
15*R*-bromo-**S14**	Zr-O_{Me}[b]	136.3	2.56	2.38	2.22	-	2.47	-
18*S*-bromo-**S14**	Zr-O_{Me}[b]	95.8	2.38	2.46	-	2.20	2.51	-
15*R*-bromo-**S14**	Zr-O_{PG}	56.5	2.41	2.37	2.15	-	-	2.56
18*S*-bromo-**S14**	Zr-O_{PG}	97.4	2.34	2.55	-	2.14	-	3.15
15*R*-bromo-**S15**[d]	stretched	87.6	87.6	2.46	2.31	2.16	-	-
18*S*-bromo-**S15**[d]	stretched	90.0	90.0	2.34	2.43	-	2.16	-
15*R*-bromo-**S15**[d]	Zr-O_{Me}[b]	127.9	127.9	2.56	2.38	2.22	-	2.45
18*S*-bromo-**S15**[d]	Zr-O_{Me}[b]	90.6	90.6	2.40	2.48	-	2.18	2.51

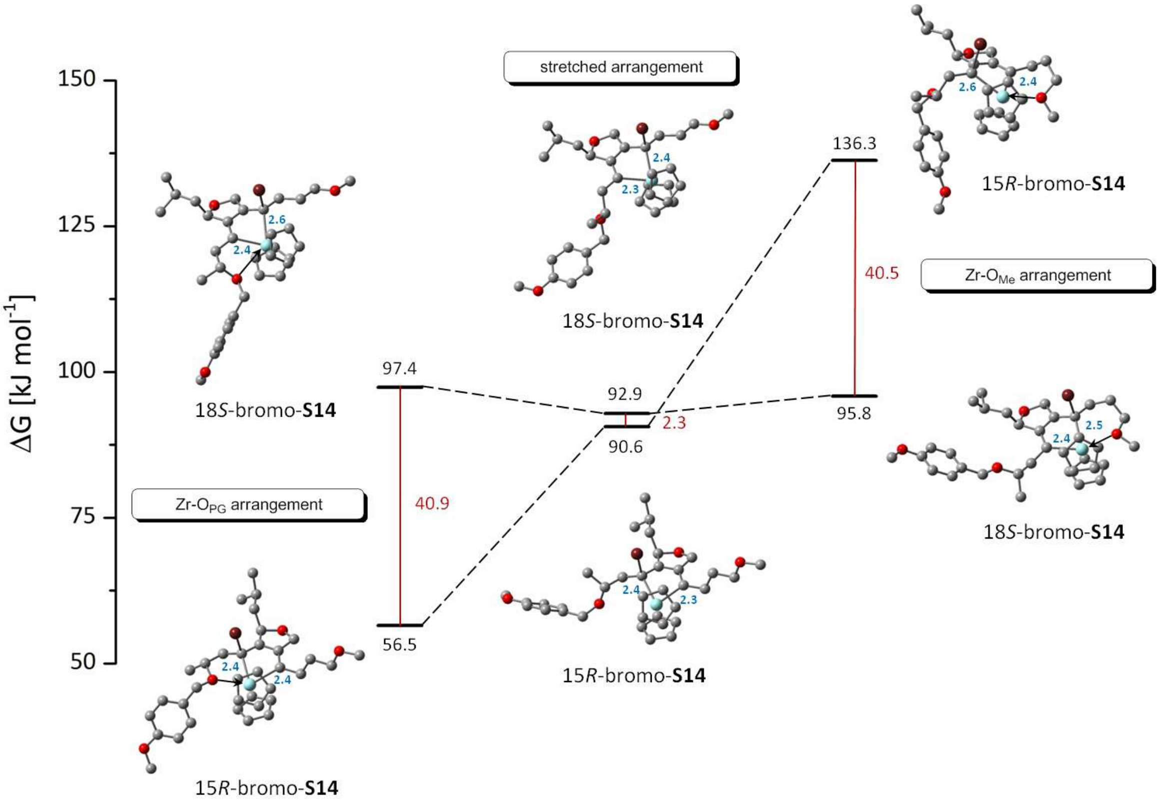
[a] resulting from the top face attack; [b] Zr-O_{Me} arrangement for methoxy side chain at C18 close to the Zr metal; [c] Zr-O_{Me} arrangement for methoxy side chain at C15 close to the Zr metal; [d] The corresponding Zr-O_{PG} arrangement was not found.

3.6 Energetic profiles and selected Cartesian coordinates for the B3LYP/LANL2DZ optimized structures of the mono-brominated intermediates in different geometries.

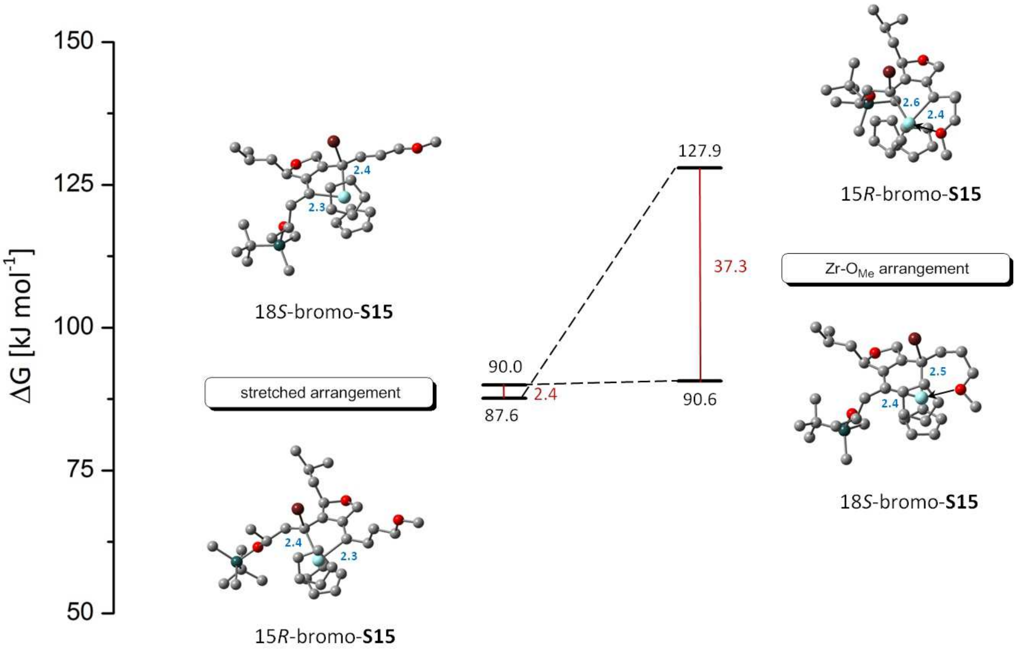
Table S5. Energy profiles a) - d) for the mono-brominated regioisomers **S12-S15** in different geometries. DFT-calculations were performed as full geometry optimization at B3LYP level of theory, with the LANL2DZ basis set and THF as solvent (PCM solvent model). Color code for the optimized structures: carbon (gray), oxygen (red), zirconium (cyan), bromine (dark red), silicium (deep teal). Hydrogens are not shown.



c)


ΔG [kJ mol^{-1}]
150
125
100
75
50
stretched arrangement
18S-bromo-**S14**
Zr-O$_{PG}$ arrangement
15R-bromo-**S14**
Zr-O$_{Me}$ arrangement
97.4
56.5
40.9
92.9
90.6
2.3
136.3
95.8
40.5
2.6
2.4
2.3
2.5

d)


ΔG [kJ mol^{-1}]
150
125
100
75
50
18S-bromo-**S15**
stretched arrangement
15R-bromo-**S15**
Zr-O$_{Me}$ arrangement
90.0
87.6
2.4
127.9
90.6
37.3
2.6
2.4
2.3
2.5

15*R*-bromo-**S12**, Zr-O_{Me} arrangement

atom	x	y	z
C	-2.969	-0.870	0.448
O	-2.979	-2.265	-0.071
C	-2.020	-2.357	-1.198
C	-1.023	-1.251	-0.882
C	-1.617	-0.344	0.000
C	-0.926	0.907	0.334
C	-1.501	1.746	1.481
C	0.330	-1.079	-1.230
Zr	1.546	0.122	0.438
C	2.294	-1.899	1.987
C	2.499	-0.687	2.713
C	0.890	-2.069	1.778
C	1.210	-0.106	2.973
C	0.221	-0.976	2.413
C	2.145	2.226	-0.978
C	1.547	2.709	0.240
C	3.414	1.667	-0.642
C	2.428	2.411	1.320
C	3.578	1.739	0.778
Br	-1.272	2.100	-1.419
C	0.824	-1.880	-2.405
C	2.235	-1.535	-2.895
C	3.339	-1.966	-1.943
O	3.322	-1.201	-0.662
C	4.658	-1.313	-0.032
H	-3.045	-0.941	1.542
H	-1.587	-3.362	-1.178
H	-2.539	-2.207	-2.155
H	-2.544	2.040	1.309
H	-1.464	1.183	2.422
H	-0.927	2.663	1.634
H	3.059	-2.586	1.659
H	3.446	-0.299	3.061
H	0.417	-2.909	1.288
H	1.018	0.782	3.559
H	-0.846	-0.872	2.523
H	1.731	2.331	-1.970
H	0.625	3.261	0.306
H	4.116	1.235	-1.340
H	2.282	2.684	2.355
H	4.454	1.441	1.336
H	0.773	-2.955	-2.146
H	0.110	-1.759	-3.237
H	2.424	-2.054	-3.844

atom	x	y	z
H	2.318	-0.460	-3.101
H	4.319	-1.788	-2.402
H	3.254	-3.031	-1.685
H	5.397	-0.811	-0.666
H	4.623	-0.837	0.943
H	4.918	-2.372	0.079
C	-4.174	-0.049	-0.100
H	-4.345	-0.353	-1.142
H	-3.909	1.015	-0.120
C	-5.476	-0.219	0.725
H	-5.244	0.062	1.767
C	-6.554	0.756	0.198
H	-6.811	0.525	-0.845
H	-7.472	0.680	0.794
H	-6.208	1.798	0.239
C	-6.008	-1.670	0.726
H	-6.914	-1.743	1.342
H	-6.264	-1.988	-0.294
H	-5.268	-2.377	1.117

18*S*-bromo-**S12**, Zr-O_{Me} arrangement

atom	x	y	z
C	-3.199	-0.459	-0.830
O	-3.364	0.663	-1.809
C	-2.238	1.602	-1.691
C	-1.227	0.900	-0.823
C	-1.732	-0.334	-0.425
C	-0.832	-1.270	0.137
C	-1.397	-2.601	0.571
C	0.122	1.353	-0.415
Zr	1.450	-0.680	0.045
C	0.649	2.528	-1.248
C	1.976	3.130	-0.761
C	3.210	2.306	-1.086
O	3.243	0.992	-0.375
C	4.644	0.506	-0.371
H	-3.397	-1.379	-1.395
H	-1.856	1.821	-2.696
H	-2.568	2.548	-1.236
H	-1.785	-2.497	1.598
H	-2.250	-2.923	-0.042
H	-0.655	-3.402	0.591
H	0.784	2.157	-2.278
H	-0.099	3.332	-1.301
H	2.126	4.099	-1.257

atom	x	y	z
H	1.931	3.332	0.315
H	4.109	2.850	-0.773
H	3.279	2.096	-2.163
H	4.655	-0.520	-0.013
H	5.051	0.543	-1.388
H	5.238	1.144	0.292
C	-4.188	-0.340	0.352
H	-4.226	0.712	0.670
H	-3.777	-0.910	1.199
C	-5.619	-0.863	0.065
H	-5.523	-1.899	-0.303
C	-6.437	-0.900	1.377
H	-6.549	0.111	1.794
H	-7.444	-1.302	1.198
H	-5.952	-1.528	2.136
C	-6.358	-0.038	-1.013
H	-7.352	-0.464	-1.205
H	-6.493	1.000	-0.678
H	-5.803	-0.013	-1.957
Br	-0.465	2.289	1.474
C	2.933	-1.956	1.799
C	3.050	-0.575	2.150
C	1.573	-2.350	2.017
H	3.735	-2.604	1.470
C	1.768	-0.109	2.578
H	3.951	0.017	2.129
C	0.855	-1.211	2.518
H	1.182	-3.351	1.904
H	1.538	0.888	2.919
H	-0.174	-1.189	2.843
C	1.152	-0.997	-2.546
C	2.565	-1.022	-2.347
C	0.603	-2.169	-1.918
H	0.604	-0.283	-3.145
C	2.892	-2.159	-1.544
H	3.266	-0.297	-2.735
C	1.675	-2.875	-1.279
H	-0.417	-2.511	-2.007
H	3.883	-2.473	-1.251
H	1.598	-3.822	-0.765

15*R*-bromo-**S14**, Zr-O$_{PG}$ arrangement

atom	x	y	z
C	2.560	2.629	-1.115
O	3.712	2.133	-1.911
C	4.034	0.748	-1.495
C	2.753	0.272	-0.822
C	1.947	1.371	-0.541
C	0.648	1.181	0.139
C	-0.401	2.247	-0.159
C	2.204	-1.028	-0.663
C	3.112	-2.180	-1.040
C	4.247	-2.375	0.016
C	5.171	-3.533	-0.375
O	6.180	-3.650	0.671
C	7.139	-4.724	0.428
H	1.877	3.124	-1.817
H	4.296	0.185	-2.396
H	4.896	0.755	-0.815
H	-0.073	3.261	0.111
H	2.556	-3.115	-1.155
H	3.599	-1.972	-2.008
H	4.845	-1.461	0.107
H	3.823	-2.580	1.005
H	4.605	-4.476	-0.458
H	5.656	-3.334	-1.346
H	7.838	-4.716	1.268
H	6.634	-5.701	0.380
H	7.689	-4.558	-0.510
H	-0.563	2.248	-1.246
Zr	-0.102	-1.095	-0.126
C	-0.297	-2.576	-2.218
C	-1.642	-2.207	-1.874
C	0.377	-1.399	-2.679
H	0.114	-3.576	-2.197
C	-1.790	-0.805	-2.118
H	-2.414	-2.884	-1.534
C	-0.539	-0.297	-2.589
H	1.369	-1.363	-3.105
H	-2.685	-0.225	-1.951
H	-0.340	0.714	-2.915
C	0.915	-2.084	2.073
C	-0.456	-1.790	2.330
C	0.962	-3.186	1.148
H	1.765	-1.590	2.521
C	-1.258	-2.699	1.551
H	-0.817	-1.026	3.003

atom	x	y	z
C	-0.371	-3.571	0.843
H	1.853	-3.685	0.801
H	-2.334	-2.796	1.564
H	-0.667	-4.384	0.195
C	-1.736	1.998	0.544
H	-1.660	2.321	1.591
C	-2.874	2.741	-0.167
H	-3.067	2.304	-1.154
H	-3.804	2.736	0.403
H	-2.575	3.788	-0.310
O	-1.961	0.509	0.604
C	-3.090	0.141	1.532
H	-2.818	-0.841	1.905
H	-3.053	0.846	2.370
C	-4.475	0.106	0.919
C	-5.484	0.978	1.392
C	-4.828	-0.842	-0.063
C	-6.790	0.922	0.889
H	-5.251	1.704	2.168
C	-6.130	-0.908	-0.590
H	-4.088	-1.554	-0.418
C	-7.116	-0.017	-0.114
H	-7.563	1.590	1.254
H	-6.363	-1.650	-1.347
C	-8.850	-0.933	-1.602
H	-9.904	-0.716	-1.782
H	-8.276	-0.776	-2.523
H	-8.738	-1.970	-1.262
O	-8.435	0.009	-0.559
C	3.038	3.648	-0.044
H	2.185	3.933	0.588
H	3.766	3.144	0.605
C	3.678	4.921	-0.654
H	4.453	4.599	-1.364
C	4.357	5.742	0.467
H	4.842	6.637	0.055
H	3.620	6.072	1.213
H	5.123	5.151	0.986
C	2.649	5.790	-1.415
H	2.193	5.256	-2.259
H	1.843	6.119	-0.743
H	3.133	6.687	-1.822
Br	1.161	1.426	2.210

18*S*-bromo-**S14**, Zr-O_{PG} arrangement

atom	x	y	z
C	1.020	3.354	-0.936
O	2.026	3.294	-2.044
C	2.930	2.159	-1.820
C	2.269	1.317	-0.760
C	1.063	1.936	-0.370
C	0.056	1.161	0.231
C	-1.262	1.848	0.496
C	2.747	0.053	-0.195
C	3.969	-0.562	-0.899
C	4.412	-1.945	-0.384
C	5.581	-2.501	-1.200
O	5.902	-3.823	-0.667
C	7.031	-4.454	-1.345
H	0.064	3.582	-1.417
H	3.076	1.631	-2.770
H	3.917	2.506	-1.471
H	-1.089	2.817	0.989
H	3.721	-0.652	-1.967
H	4.822	0.131	-0.841
H	4.722	-1.876	0.665
H	3.577	-2.657	-0.436
H	5.313	-2.588	-2.268
H	6.462	-1.842	-1.120
H	7.180	-5.427	-0.869
H	6.820	-4.596	-2.415
H	7.945	-3.849	-1.237
H	-1.718	2.093	-0.482
Zr	0.513	-1.130	0.108
C	-2.298	1.066	1.313
H	-1.893	0.839	2.312
C	-3.599	1.866	1.461
H	-4.048	2.072	0.482
H	-4.336	1.342	2.075
H	-3.378	2.824	1.950
O	-2.464	-0.218	0.593
C	-3.455	-1.176	1.140
H	-3.058	-2.150	0.834
H	-3.447	-1.132	2.238
C	-4.871	-0.995	0.622
C	-5.958	-1.019	1.526
C	-5.149	-0.865	-0.752
C	-7.281	-0.920	1.072
H	-5.773	-1.118	2.593
C	-6.470	-0.754	-1.227

atom	x	y	z
H	-4.335	-0.841	-1.471
C	-7.542	-0.786	-0.309
H	-8.117	-0.941	1.766
H	-6.647	-0.653	-2.292
C	-9.233	-0.548	-2.080
H	-10.323	-0.496	-2.106
H	-8.808	0.374	-2.498
H	-8.889	-1.414	-2.659
O	-8.887	-0.691	-0.665
C	1.399	4.446	0.085
H	0.697	4.396	0.932
H	2.396	4.211	0.486
C	1.399	5.886	-0.490
H	2.019	5.880	-1.399
C	2.041	6.856	0.528
H	2.077	7.877	0.127
H	1.461	6.882	1.462
H	3.067	6.553	0.775
C	-0.021	6.363	-0.873
H	-0.481	5.728	-1.641
H	-0.682	6.367	0.007
H	0.012	7.386	-1.271
Br	3.496	0.736	1.695
C	1.827	-2.161	2.068
C	0.890	-1.247	2.663
C	1.091	-3.242	1.491
H	2.901	-2.067	2.096
C	-0.421	-1.778	2.464
H	1.137	-0.346	3.203
C	-0.308	-2.996	1.721
H	1.509	-4.110	1.001
H	-1.335	-1.346	2.838
H	-1.120	-3.654	1.444
C	1.056	-1.511	-2.409
C	0.658	-2.776	-1.866
C	-0.083	-0.639	-2.391
H	2.019	-1.289	-2.841
C	-0.733	-2.689	-1.521
H	1.280	-3.657	-1.787
C	-1.187	-1.372	-1.852
H	-0.121	0.373	-2.769
H	-1.340	-3.493	-1.129
H	-2.179	-0.983	-1.695