Supplementary Information

Low-valent titanium(II) mediated intramolecular and regioselective alkyne/alkoxyallene reductive coupling reactions

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Abstract: Low-valent titanium(II) complexes turned out to be suitable reagents in the promotion of alkyne/alkoxyallene coupling reactions in intramolecular fashion. The conditions developed herein led to a broad range of highly functionalized cyclic adducts with excellent regioselectivities toward the central carbon of the alkoxyallene moiety. Good yields (up to 76%) were obtained over 19 examples. One-pot late functionalization by electrophile trapping was also possible and led to excellent diastereoselectivities (up to 95/5 d.r.).

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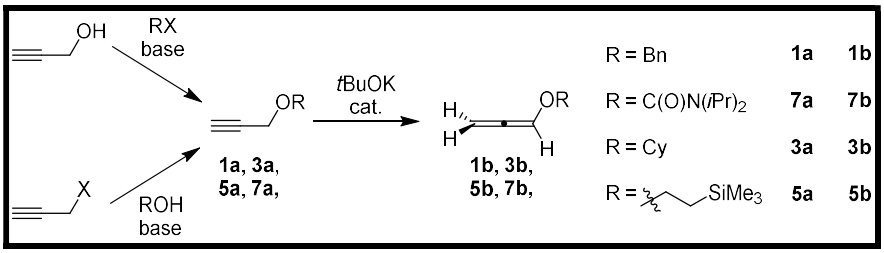
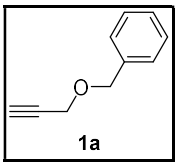
1. General information

All reactions sensitive to moisture and/or air were carried out under argon atmosphere in dry, freshly distilled solvents under anhydrous conditions using oven-dried glassware, unless otherwise noted. THF and toluene were distilled over sodium/benzophenone system, DCM, DMSO and DMF were distilled over calcium hydride. Reactions were monitored by TLC (silica gel 60 F254plates) and visualization was accomplished with UV light (254 nm & 366 nm) and subsequent use of phosphomolybdic acid solution in EtOH (5%), $KMnO_4$ solution or vanillin/sulphuric acid solution in EtOH, followed by heating at 100-110 °C. Flash chromatography was performed on silica gel 60 (particle size 0.040-0.063 µm). Yield refers to chromatographically and spectroscopically pure compounds, unless otherwise noted. ^{1}H NMR spectra were recorded at 300 and 400 MHz. Chemical shifts are expressed in ppm, relative to the residual ^{1}H solvent signal ($CDCl_3$: δ = 7.26 ppm) as the internal reference. Coupling constants (*J*) are reported in hertz (Hz). The following abbreviations are used to designate the multiplicities: s = singlet; d = doublet; t = triplet; q = quartet; quint. = quintet, sext. = sextet, sept. = septet, m = multiplet; br = broad. ^{1}H NMR assignments were confirmed by 2D COSY spectra. The given multiplicities reflect apparent signal patterns. Diastereomer ratio (*dr*) was estimated by ^{1}H NMR spectroscopic analysis (300 and 400 MHz), unless otherwise noted. ^{13}C NMR spectra were recorded at 75 MHz and 100 MHz. Chemical shifts are given in ppm relative to the residual ^{13}C solvent signal ($CDCl_3$: δ = 77.16 ppm). ^{13}C NMR assignments were confirmed by 2D HSQC and HMBC spectra. Coupling constants (*J*) are given in Hz for all NMR spectroscopic data. IR spectra were recorded with a FT-IR spectrometer. High-resolution mass spectra (HRMS) were measured on a mass spectrometer equipped with a TOF system and an electrospray ionization (ESI) ion source. Deuterated solvents were used as supplied.

2. Preparation of cyclization precursors



((prop-2-yn-1-yloxy)methyl)benzene **1a**

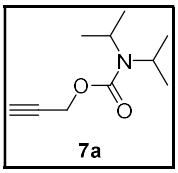


To a suspension of KOH (15.0 g, 267 mmol, 3 equiv) in DMSO (100 mL, 2.7 M), were successively added propargylic alcohol (5.15 mL, 89 mmol, 1 equiv) and benzyl bromide (10.6 mL, 89 mmol, 1 equiv) at 0°C. The brown solution was warmed to room temperature and stirred for 2h. After total completion, monitored by TLC, water (100 mL) was added and the aqueous layer was extracted with ethyl acetate (3 × 40 mL). Combined organic layers were washed with water (3 × 75 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over silica gel (cyclohexane/ethyl acetate 50/50) afforded pure **1a** (11.35 g, 77 mmol, 87 %) as a yellow liquid.

Spectroscopic data were in accordance with those reported in literature.[1]

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37 – 7.29 (m, 5H), 4.62 (s, 2H), 4.18 (d, J = 2.4 Hz, 2H), 2.47 (t, J = 2.4 Hz, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 137.4, 128.6, 128.3, 128.0, 79.8, 74.7, 71.6, 51.2.

prop-2-yn-1-yl diisopropylcarbamate **7a**



To a solution of sodium hydride (1.32 g, 33 mmol, 60% in mineral oil, 1.1 equiv) under argon atmosphere in dry THF (75 mL, 0.44 M), was added dropwise, at 0°C, propargyl alcohol (1.73 mL, 30 mmol, 1 equiv). The grey solution was stirred for 30 minutes at this temperature before the addition of diisopropyl carbamoyl chloride (4.91 g, 30 mmol, 1 equiv). The brown solution was warmed to room temperature and stirred overnight. After total completion, monitored by TLC, water (50 mL) was added and the aqueous layer was extracted with ethyl acetate (2 × 40 mL). Combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Distillation of the crude under reduced pressure afforded pure **7a** (4.46 g, 24.3 mmol, 81 %) as a colourless liquid.

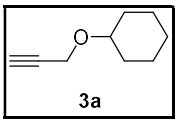
Spectroscopic data were in accordance with those reported in literature.[2]

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.70 (d, J = 2.5 Hz, 2H), 4.00 – 3.82 (m, 2H), 2.47 (t, J = 2.5 Hz, 1H), 1.22 (d, J = 6.8 Hz, 12H).

[1] B. M. Trost and J. Xie, *J. Am. Chem. Soc.*, **2006**, *128*, 6044–6045.
[2] D. Hoppe, C. Gonschorrer, D. Schmidt, E. Egert, *Tetrahedron*. **1987**, *43*, 2457–2466.

^{13}C NMR (75 MHz, $CDCl_3$): δ 154.7, 79.0, 74.1, 52.2, 46.2, 21.1.

(prop-2-yn-1-yloxy)cyclohexane **3a**



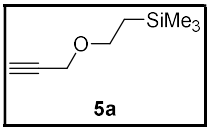
3a

To a solution of sodium hydride (1.20 g, 30 mmol, 60% in mineral oil, 1.25 equiv) under argon atmosphere in dry THF (100 mL, 0.3 M), was added dropwise, at 0°C, cyclohexanol (2.50 mL, 24 mmol, 1 equiv). The grey solution was stirred for 30 minutes at this temperature before the addition of propargyl bromide (2.90 mL, 26.4 mmol, 1.1 equiv). The brown solution was warmed to room temperature and stirred overnight. After total completion, monitored by TLC, a satured NH_4Cl solution (30 mL) was added and the aqueous layer was extracted with diethyl ether (2 × 30 mL). Combined organic layers were washed with brine (25 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over silica gel (cyclohexane/ethyl acetate 100/0 to 95/5) afforded pure **3a** (2.32 g, 16.8 mmol, 70 %) as a yellow liquid.

Spectroscopic data were in accordance with those reported in literature.[3]

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.18 (d, J = 2.4 Hz, 2H), 3.47 (tt, J = 8.9, 4.2 Hz, 1H), 2.39 (t, J = 2.4 Hz, 1H), 2.00 – 1.85 (m, 2H), 1.80 – 1.67 (m, 2H), 1.58-1.48 (m, 1H), 1.38 – 1.16 (m, 5H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 80.7, 76.7, 73.7, 55.0, 32.0, 25.8, 24.2.

trimethyl(2-(prop-2-yn-1-yloxy)ethyl)silane **5a**



5a

To a solution of sodium hydride (1.20 g, 30.0 mmol, 60% in mineral oil, 1.0 equiv) under argon atmosphere in dry THF (15 mL, 2 M), was added dropwise, at 0°C, trimetylsilylethanol (4.30 mL, 30 mmol, 1 equiv). The grey solution was warmed to room temperature and stirred for 30 minutes before the addition at 0°C of propargyl bromide (3.60 mL, 33 mmol, 1.1 equiv). The brown solution was warmed to room temperature and stirred overnight. After total completion, monitored by TLC, a satured NH_4Cl solution (30 mL) was added and the aqueous layer was extracted with diethyl ether (2 × 30 mL). Combined organic layers were washed with brine (25 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over silica gel (cyclohexane/ethyl acetate 100/0 to 90/10) afforded pure **5a** (2.97 g, 18.9 mmol, 63 %) as an orange liquid.

Spectroscopic data were in accordance with those reported in literature.[4]

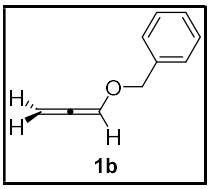
^{1}H NMR (300 MHz, $CDCl_3$): δ 4.12 (d, J = 2.4 Hz, 2H), 3.65 – 3.54 (m, 2H), 2.41 (t, J = 2.4 Hz, 1H), 1.03 – 0.89 (m, ~~1H~~ 2H ? sinon, il manque 1H), 0.02 (s, 9H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 80.2, 74.1, 67.5, 57.5, 18.1, -1.3.

[3] D. J. Wardrop and J. Fritz, *Org. Lett.*, **2006**, *8*, 3659–3662.
[4] R. W. Hoffmann, B. Kemper, R. Metternich and T. Lehmeier, *Liebigs Ann. Chem.*, **1985**, 2246–2260.

General procedure for the isomerization of the alkyne (GP1)

To a solution of the corresponding propargylic ether (1 equiv), under argon atmosphere, in dry THF (0.66 M), was added potassium *tert*-butoxide (0.33 equiv). After total completion, monitored by TLC, the black solution was filtered through a Celite® pad and the filtrate was concentrated under reduced pressure.

((propa-1,2-dien-1-yloxy)methyl)benzene **1b**



1b

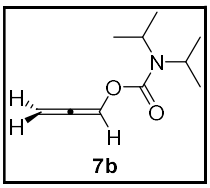
Crude compound **1b** was obtained from the corresponding propargylic ether **1a** following **GP1** on 20 mmol scale (2.92 g).

Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0) afforded pure **1b** (2.62 g, 18 mmol, 90 %) as a yellow liquid.

Spectroscopic data were in accordance with those reported in literature.[5]

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40 – 7.27 (m, 5H), 6.85 (t, J = 5.9 Hz, 1H), 5.49 (d, J = 5.9 Hz, 2H), 4.62 (s, 2H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 201.4, 137.4, 128.6, 128.0, 128.0, 121.7, 91.3, 70.7.

propa-1,2-dien-1-yl diisopropylcarbamate **7b**



7b

Crude compound **7b** was obtained from the corresponding propargylic ether **7a** following **GP1** on 20 mmol scale (3.66 g).

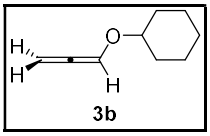
Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 98/2) afforded clean **7b** (2.05 g, 11.2 mmol, 56 %) as a colourless liquid.

Spectroscopic data were in accordance with those reported in literature.[5]

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48 (t, J = 6.0 Hz, 1H), 5.42 (d, J = 6.0 Hz), 3.99 (s, 1H), 3.89 (s,1H), 1.24 (s, 6H), 1.23 (s, 6H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 200.9, 152.7, 112.3, 88.8, 46.6, 46.0, 21.3, 20.4.

[5] A. Tap, C. Lecourt, S. Dhambri, M. Arnould, G. Galvani, O. Nguyen Van Buu, M. Jouanneau, J.-P. Férézou, J. Ardisson, M.-I. Lannou and G. Sorin, *Chem. Eur. J.*, **2016**, *22*, 4938–4944.

(propa-1,2-dien-1-yloxy)cyclohexane **3b**



3b

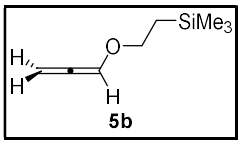
Crude compound **3b** was obtained from the corresponding propargylic ether **3a** following **GP1** on 16.7 mmol scale (2.319 g).

Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0) afforded pure **3b** (1.70 g, 12.2 mmol, 73 %) as a yellow liquid.

Spectroscopic data were in accordance with those reported in literature.[6]

^{1}H NMR (300 MHz, $CDCl_3$): δ 6.62 (t, J = 6.0 Hz, 1H), 5.37 (d, J = 6.0 Hz, 2H), 3.72 – 3.59 (m, 1H), 1.96 – 1.82 (m, 2H), 1.81 – 1.65 (m, 2H), 1.62 – 1.47 (m, 1H), 1.47 – 1.17 (m, 5H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 201.9, 120.0, 89.6, 76.7, 31.9, 25.7, 23.9.

trimethyl(2-(propa-1,2-dien-1-yloxy)ethyl)silane **5b**



5b

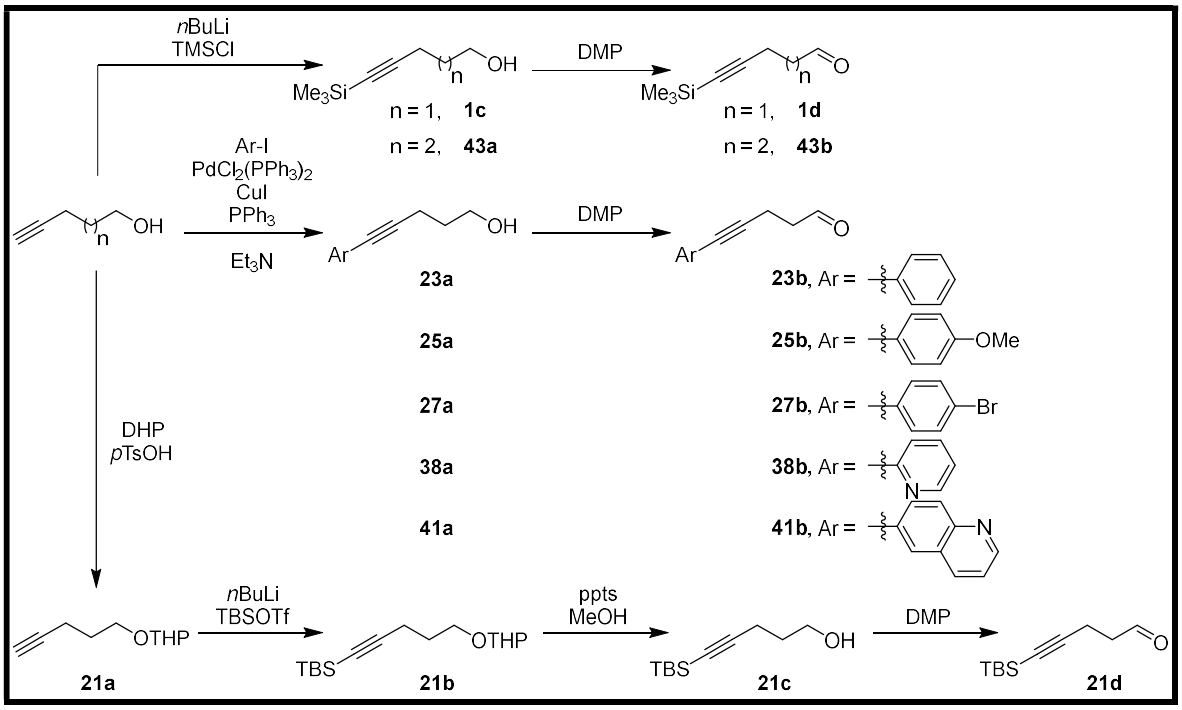
Crude compound **5b** was obtained from the corresponding propargylic ether **5a** following **GP1** on 19.0 mmol scale (2.97 g).

Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0) afforded pure **5b** (1.07 g, 6.80 mmol, 36 %) as a colourless liquid.

Spectroscopic data were in accordance with those reported in literature.[7]

^{1}H NMR (300 MHz, $CDCl_3$): δ 6.70 (t, J = 5.9 Hz, 1H), 5.41 (d, J = 5.9 Hz, 2H), 4.26 – 2.87 (m, 2H), 1.18 – 0.43 (m, 2H), 0.02 (s, 9H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 201.6, 121.3, 90.2, 66.5, 17.9, -1.2.

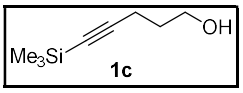
[6] Y. Wang, M. Jiang and J.-T. Liu, *Adv. Synth. Catal.*, **2014**, *356*, 2907–2912.
[7] M. Helms, W. Schade, R. Pulz, T. Watanabe, A. Al-Harrasi, L. Fišera, I. Hlobilová, G. Zahn and H.-U. Reißig, *Eur. J. Org. Chem.*, **2005**, 1003–1019.



General procedure for the silylation of the alkyne (GP2)

To a solution of the corresponding yn-ol (1 equiv), at -78°C under argon atmosphere, in dry THF (0.5 M), was added dropwise a solution of *n*-butyllithium (2.1 equiv). The bright yellow solution was stirred for 1 hour and freshly distilled TMSCl (2 equiv) was added dropwise at the same temperature. Stirring was maintained one further hour before addition of HCl (6 M, 25 mL) and the solution was vigorously stirred for 10 minutes. The aqueous layer was extracted with ethyl acetate (2 × 30 mL). Combined organic layers were washed with a satured $NaHCO_3$ solution (50 mL), dried over $MgSO_4$ and concentrated under reduced pressure.

5-(trimethylsilyl)pent-4-yn-1-ol **1c**

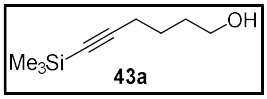


Clean crude compound **1c** (3.72 g, 23.8 mmol, quant.) was obtained from 4-pentyn-1-ol following **GP2** on 23.8 mmol scale (2.21 mL) as a clear oil and was directly used without purification.

Spectroscopic data were in accordance with those reported in literature.[8]

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.76 (t, J = 6.1 Hz, 2H), 2.35 (t, J = 6.9 Hz, 2H), 1.77 (tt, J = 6.9, 6.1 Hz, 2H), 0.15 (s, 9H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 106.8, 85.4, 62.0, 31.3, 16.7, 0.2.

6-(trimethylsilyl)hex-5-yn-1-ol **43a**



[8] C. Tresse, C. Guissart, S. Schweizer, Y. Bouhoute, A.-C. Chany, M.-L. Goddard, N. Blanchard and G. Evano, *Adv. Synth. Catal.*, **2014**, *356*, 2051–2060.

Clean crude compound **43a** (3.41 g, 20.0 mmol, quant.) was obtained from 5-hexyn-1-ol following **GP2** on 23.8 mmol scale (2.21 mL) as a clear oil and was directly used without purification.

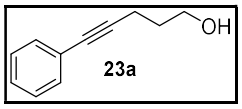
Spectroscopic data were in accordance with those reported in literature.[9]

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.67 (t, J = 6.0 Hz, 2H), 2.27 (t, J = 6.6 Hz, 2H), 1.73 – 1.54 (m, 4H), 1.42 (br s, 1H), 0.14 (s, 9H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 107.3, 84.9, 62.5, 31.9, 25.0, 19.7, 0.3.

General procedure for Sonogashira coupling reactions (GP3)

To a solution of the corresponding aryl halide derivative (1.1 equiv), under argon atmosphere, in freshly distilled triethylamine (0.5 M), were successively added $Pd(PPh_3)Cl_2$ (2 mol%), CuI (4 mol%) and PPh_3 (4 mol%). The yellow solution was stirred for 5 minutes at room temperature and 4-pentyn-1-ol was added dropwise. The resulting heterogeneous mixture was vigorously stirred overnight at room temperature. After total completion, monitored by TLC, triethylamine was removed under reduced pressure. Purification of the crude by flash chromatography over silica gel afforded the pure corresponding coupling product.

5-phenylpent-4-yn-1-ol **23a**

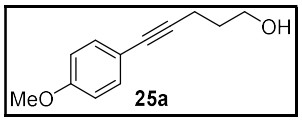


Compound **23a** was obtained by coupling reaction between 4-pentyn-1-ol and iodobenzene following **GP3** on 20.0 mmol scale. Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 100/0 to 80/20) afforded pure **23a** as an orange liquid (2.88 g, 18.0 mmol, 90 %).

Spectroscopic data were in accordance with those reported in literature.[10]

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44 – 7.35 (m, 2H), 7.33 – 7.24 (m, 3H), 3.83 (dt, J = 6.0, 5.2 Hz, 2H), 2.55 (t, J = 6.9 Hz, 2H), 1.94 – 1.78 (m, 2H), 1.55 (t, J = 5.2 Hz, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 131.7, 128.3, 127.8, 123.9, 89.4, 81.3, 61.9, 31.5, 16.1.

5-(4-methoxyphenyl)pent-4-yn-1-ol **25a**



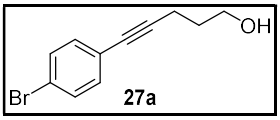
Compound **25a** was obtained by coupling reaction between 4-pentyn-1-ol and 1-iodo-4-methoxybenzene following **GP3** on 20.0 mmol scale. Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 100/0 to 80/20) afforded pure **25a** as an orange solid (3.40 mg, 17.8 mmol, 89 %).

Spectroscopic data were in accordance with those reported in literature.[11]

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36 – 7.29 (m, 2H), 6.84 – 6.78 (m, 2H), 3.82 (dt, J = 5.5, 5.3 Hz, 2H), 3.80 (s, 3H), 2.53 (t, J = 6.9 Hz, 2H), 1.86 (m, 2H), 1.51 (d, J = 5.3 Hz, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 159.3, 133.0, 116.0, 114.0, 87.8, 81.1, 62.1, 55.4, 31.6, 16.2.

[9] B. Rubial, A. Ballesteros and J. M. González, *Eur. J. Org. Chem.*, **2018**, 6194–6198.
[10] H. Lu, C. Li, H. Jiang, C. L. Lizardi and X. P. Zhang, *Angew. Chem.*, **2014**, *126*, 7148–7152.
[11] N. Okamoto, Y. Miwa, H. Minami, K. Takeda and R. Yanada, *J. Org. Chem.*, **2011**, *76*, 9133–9138.

5-(4-bromophenyl)pent-4-yn-1-ol **27a**



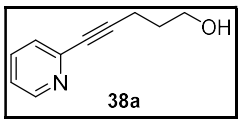
27a

Compound **27a** was obtained by coupling reaction between 4-pentyn-1-ol and 1-bromo-4-iodobenzene following **GP3** on 15.0 mmol scale. Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 100/0 to 80/20) afforded pure **27a** as a yellow crystal (2.73 g, 11.4 mmol, 76 %).

Spectroscopic data were in accordance with those reported in literature.[12]

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.44 – 7.37 (m, 2H), 7.27 – 7.21 (m, 2H), 3.81 (dt, *J* = 5.9, 5.7 Hz, 2H), 2.53 (t, *J* = 6.9 Hz, 2H), 1.86 (tt, *J* = 6.9, 5.9 Hz, 2H), 1.46 (t, *J* = 5.7 Hz, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 133.1, 131.6, 122.8, 121.9, 90.8, 80.3, 61.9, 31.4, 16.1.

5-(pyridin-2-yl)pent-4-yn-1-ol **38a**



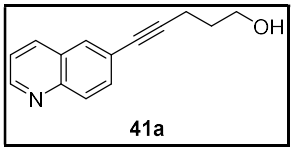
38a

Compound **38a** was obtained by coupling reaction between 4-pentyn-1-ol and 2-bromopyridine following **GP3** on 15.0 mmol scale. Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 0/100) afforded pure **38a** as a yellow oil (1.74 g, 10.8 mmol, 72%).

Spectroscopic data were in accordance with those reported in literature.[13]

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.49 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H), 7.58 (tdd, *J* = 7.8, 1.8, 1.0 Hz, 1H), 7.33 (dq, *J* = 7.8, 1.0 Hz, 1H), 7.15 (ddt, *J* = 7.3, 4.9, 1.0 Hz, 1H), 3.78 (dt, *J* = 6.0 Hz, 2H), 3.06 (br s, 1H), 2.55 (t, *J* = 7.0 Hz, 1H), 1.86 (tt, *J* = 7.0, 6.0 Hz, 2H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 149.7, 143.7, 136.3, 126.9, 122.5, 90.6, 80.7, 61.3, 31.2, 16.0.

5-(quinolin-6-yl)pent-4-yn-1-ol **41a**



41a

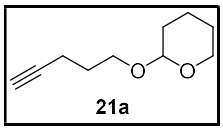
Compound **41a** was obtained by coupling reaction between 4-pentyn-1-ol and 5-bromoquinoline following **GP3** on 10.0 mmol scale. Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 90/10 to 25/75) afforded pure **41a** as a yellow-orange solid (1.90 g, 9.0 mmol, 90%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.89 (dd, *J* = 4.3, 1.8 Hz, 1H), 8.13 – 8.03 (m, 1H), 8.01 (d, *J* = 8.7 Hz, 1H), 7.87 (s, 1H), 7.68 (dd, *J* = 8.8, 1.9 Hz, 1H), 7.40 (dd, *J* = 8.3, 4.3 Hz, 1H), 3.91 – 3.80 (m, 2H), 2.61 (t, *J* = 7.0 Hz, 2H), 1.97 – 1.85 (m, 2H), 1.59 (s, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 150.5, 147.2, 135.8, 132.6, 130.8, 129.2, 128.1, 122.3, 121.7, 91.3, 80.7, 61.4, 31.5, 16.1.

[12] T. Ueda, N. Kanomata and H. Machida, *Org. Lett.*, **2005**, *7*, 2365–2368.
[13] Z.-Y. Sun, S. Zhou, K. Yang, M. Guo, W. Zhao, X. Tang and G. Wang, *Org. Lett.*, **2020**, *22*, 6214–6219.

HRMS (ESI): m/z calculated for $[M+H]^+$ 212.1070 g.mol^{-1}, found 212.1072 g.mol^{-1}.
FTIR (film cm^{-1}): 3284, 3017, 2949, 2888, 2220, 1918, 1494, 1325, 1288, 1276, 1261, 1067, 905, 884, 831, 805, 764, 750, 722, 693, 662.

2-(pent-4-yn-1-yloxy)tetrahydro-2*H*-pyran **21a**

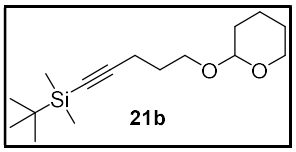


To a solution of 4-pentyn-1-ol (5.33 mL, 57.3 mmol, 1 equiv) in THF (57 mL, 1M) were added *para*-toluenesulfonic acid monohydrate (272 mg, 1.4 mmol, 0.025 equiv) and 3,4-dihydro-2*H*-pyrane (6.25 mL, 68.8 mmol, 1.2 equiv) and the solution was stirred overnight at room temperature. After total completion, monitored by TLC, a satured $NaHCO_3$ solution (50 mL) was added and the mixture was stirred for 15 minutes. The aqueous layer was extracted with diethyl ether (2 × 25 mL). Combined organic layers were washed with brine (50 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over silica gel (cyclohexane/ethyl acetate 100/0 to 75/25) afforded pure **21a** (8.10 g, 48.1 mmol, 84%) as a yellow liquid.

Spectroscopic data were in accordance with those reported in literature.[14]

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.65 (dd, J = 4.3, 2.7 Hz, 1H), 3.99-3.82 (m, 2H), 3.63-3.47 (m, 2H), 2.37 (td, J = 7.3, 2.6 Hz, 2H), 2.00 (t, J = 2.6 Hz, 1H), 1.94 – 1.82 (m, 3H), 1.82-1.70 (m, 1H), 1.94 – 1.82 (m, 3H), 1.69-1.51 (m, 4H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 98.9, 84.1, 68.5, 65.9, 62.3, 30.8, 28.8, 25.6, 19.6, 15.4.

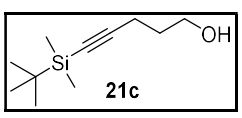
tert-butyldimethyl(5-((tetrahydro-2*H*-pyran-2-yl)oxy)pent-1-yn-1-yl)silane **21b**



To a solution of **21a** (2.52 g, 15 mmol, 1 equiv), at -78°C under argon atmosphere, in dry THF (35 mL, 0.45 M), was added dropwise a solution of *n*-butyllithium (16.5 mmol, 1.1 equiv). The yellow solution was stirred for 30 minutes and *tert*-butyldimethylsilyl trifluoromethanesulfonate (6.8 mL, 16.5 mmol, 1.1 equiv) was added dropwise at the same temperature. Stirring was kept further 1 hour before addition of a satured NH_4Cl solution (30 mL). The aqueous layer was extracted with ethyl acetate (2 × 25 mL). Combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Crude compound **21b** was quantitatively obtained as a colourless liquid and directly used without purification.

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.59 (t, J = 3.4 Hz, 1H), 3.92 – 3.76 (m, 2H), 3.54 – 3.43 (m, 2H), 2.35 (t, J = 7.2 Hz, 2H), 1.87 – 1.75 (m, 2H), 1.63 – 1.46 (m, 6H), 0.92 (s, 9H), 0.07 (s, 6H).

5-(*tert*-butyldimethylsilyl)pent-4-yn-1-ol **21c**



[14] M. P. Heitz, A. Wagner, C. Mioskowski, J. P. Noel and J. P. Beaucourt, *J. Org. Chem.*, **1989**, *54*, 500–503.

To a solution of crude **21b** (4.24 g, 15.0 mmol, 1 equiv), in MeOH (20 mL, 0.75 M), was added pyridinium *p*-toluenesulfonate (380 mg, 1.50 mmol, 0.1 equiv) in one portion and the solution was stirred overnight at room temperature. After total completion, monitored by TLC, water (10 mL) was added. The aqueous layer was extracted with ethyl acetate (2 × 20 mL). Combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 1/0 to 8/2) afforded pure **21c** (1.98 g, 10.1 mmol, 67 % over 2 steps) as a colourless liquid.

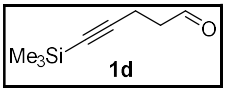
Spectroscopic data were in accordance with those reported in literature.[15]

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.77 (dt, J = 5.9, 5.6 Hz, 2H), 2.36 (t, J = 6.9 Hz, 2H), 1.78 (tt, J = 6.9, 5.9 Hz, 2H), 1.61 (br s, 1H), 0.92 (s, 9H), 0.08 (s, 6H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 107.3, 83.5, 62.1, 31.4, 27.0, 26.2, 16.7, -4.3.

General procedure for the Dess-Martin oxidation (GP4)

To a solution of the corresponding alcohol (1 equiv) in dichloromethane (0.16 M), was added Dess-Martin Periodinane (1.1 equiv). After total completion, monitored by TLC, a satured $NaHCO_3$ solution (20 mL) was added and the mixture was vigorously stirred for 5 minutes. The aqueous was extracted with dichloromethane (2 × 20 mL). Combined organic layers were washed with water (20 mL), dried over $MgSO_4$ and carefully concentrated under reduced pressure.

5-(trimethylsilyl)pent-4-ynal **1d**



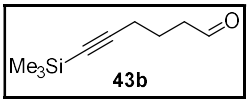
Crude compound **1d** was obtained from the corresponding alcohol **1c** following **GP4** on 10.0 mmol scale (1.56 g).

After evaporation of the solvent, pentane (≈ 25 mL) was added. The white insoluble solid was filtrated and the filtrate was concentrated under reduced pressure. Product **1d** (1.54 g, 10.0 mmol, quant.) was obtained as a clean bright yellow oil and directly used without further purification.

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.79 (t, J = 1.2 Hz, 1H), 2.68 (dt, J = 6.6, 1.2 Hz, 2H), 2.54 (t, J = 6.6 Hz, 2H), 0.14 (s, 9H).

Spectroscopic data were in accordance with those reported in literature.[16]

6-(trimethylsilyl)hex-5-ynal **43b**



Crude compound **43b** was obtained from the corresponding alcohol **43a** following **GP4** on 5.00 mmol scale (851 mg).

After evaporation of the solvent, pentane (≈ 25 mL) was added. The white insoluble solid was filtrated and the filtrate was concentrated under reduced pressure. Product **43b** (1.54 g, 10.0 mmol, quant.) was obtained as a clean bright yellow liquid and directly used without further purification.

[15] R. D. Kavthe, Y. Ishikawa, I. Kusuma and N. Asao, *Chem. Eur. J.*, **2018**, *24*, 15777–15780.
[16] F. Beaufils, F. Denes, B. Becattini, P. Renaud and K. Schenk, *Adv. Synth. Cat.*, **2005**, *347*, 1587 – 1594.

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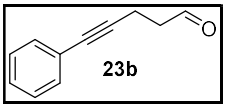
^{1}H NMR (300 MHz, $CDCl_3$): δ 9.81 (t, J = 1.4 Hz, 1H), 2.58 (td, J = 7.2, 1.4 Hz, 2H), 2.30 (t, J = 6.9 Hz, 2H), 1.84 (tt, J = 7.2, 6.9 Hz, 2H), 0.15 (s, 9H).

Spectroscopic data were in accordance with those reported in literature.[17]

5-phenylpent-4-ynal **23b**



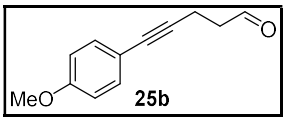
Crude compound **23b** was obtained from the corresponding alcohol **23a** following **GP4** on 5.00 mmol scale (801 mg).

After evaporation of the solvent, pentane (≈ 25 mL) was added. The white insoluble solid was filtrated and the filtrate was concentrated under reduced pressure. Product **23b** (759 mg, 4.80 mmol, 96 %) was obtained as a clean yellow liquid and directly used without further purification.

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.86 (t, J = 0.8 Hz, 1H), 7.41 – 7.34 (m, 2H), 7.31 – 7.24 (m, 3H), 2.84 – 2.68 (m, 4H).

Spectroscopic data were in accordance with those reported in literature.[18]

5-(4-methoxyphenyl)pent-4-ynal **25b**



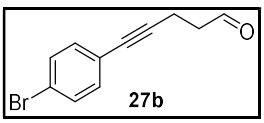
Compound **25b** was obtained from the corresponding alcohol **25a** following **GP4** on 5.00 mmol scale (801 mg).

After evaporation of the solvent, a pentane/Et_2O mixture (90/10, ≈ 25 mL) was added. The white insoluble solid was filtrated and the filtrate was concentrated under reduced pressure. Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 85/15) afforded clean **25b** (859 mg, 4.55 mmol, 91 %) as a yellow liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.85 (t, J = 1.1 Hz, 1H), 7.35 – 7.27 (m, 2H), 6.85 – 6.76 (m, 2H), 3.80 (s, 3H), 2.81 – 2.66 (m, 4H).

Spectroscopic data were in accordance with those reported in literature.[19]

5-(4-bromophenyl)pent-4-ynal **27b**



Crude compound **27b** was obtained from the corresponding alcohol **27a** following **GP4** on 5.00 mmol scale (1.19 g).

After evaporation of the solvent, a pentane/Et_2O mixture (80/20, ≈ 25 mL) was added. The white insoluble solid was filtrated and the filtrate was concentrated under reduced pressure. Product **27b**

[17] G. D. Harris, R. J. Herr and S. M. Weinreb, *J. Org. Chem*., **1993**, *58*, 5452 – 5464.

[18] R. Jana and J. A. Tunge, *Org. Lett.,* **2009**, *11*, 971 – 974.

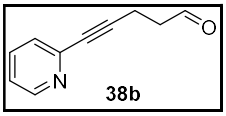
[19] Z. Hearne and C.J. Li, *Chem. Commun*., **2017**, *53*, 6136 – 6139.

(1.185 g, 5.00 mmol, quant.) was obtained as a clean yellow liquid and directly used without further purification.

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.84 (t, J = 1.2 Hz, 1H), 7.46 – 7.36 (m, 2H), 7.26 – 7.20 (m, 2H), 2.81 – 2.66 (m, 4H).

Spectroscopic data were in accordance with those reported in literature.[20]

5-(pyridin-2-yl)pent-4-ynal **38b**



38b

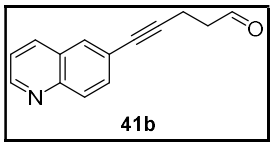
Clean compound **38b** was obtained from the corresponding alcohol **38a** following **GP4** on 5.00 mmol scale (806 mg).

After evaporation of the solvent, a pentane/Et_2O mixture (50/50, ≈ 25 mL) was added. The white insoluble solid was filtrated and the filtrate was concentrated under reduced pressure. Purification of the crude by flash chromatography over silica gel (Et_2O) afforded clean **38b** (593 mg, 3.70 mmol, 74 %) as a brown oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.85 (t, J = 0.9 Hz, 1H), 8.54 (ddd, J = 4.9, 1.8, 0.9 Hz, 1H), 7.62 (tdd, J = 7.8, 1.8, 0.7 Hz, 1H), 7.37 (dt, J = 7.8, 1.1 Hz, 1H), 7.20 (ddt, J = 6.8, 4.9, 0.9 Hz, 1H), 2.86 – 2.72 (m, 4H).

Spectroscopic data were in accordance with those reported in literature.[21]

5-(quinolin-6-yl)pent-4-ynal **41b**



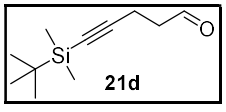
41b

Clean compound **41b** was obtained from the corresponding alcohol **41a** following **GP4** on 5.00 mmol scale (1.05 g).

After evaporation of the solvent, pentane was added. Dichloromethane was added dropwise until the white solid starts to be solubilized. The solid was filtrated and the filtrate was concentrated under reduced pressure. This step was repeated three times to give clean **41b** (982 mg, 4.69 mmol, 93 %) as a yellow oil and the product was directly used in the next step.

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.88 (t, J = 1.0 Hz, 1H), 8.89 (dd, J = 4.3, 1.4 Hz, 1H), 8.11 – 8.05 (m, 1H), 8.04 – 7.99 (m, 1H), 7.87 (d, J = 1.9 Hz, 1H), 7.66 (dd, J = 8.8, 1.9, 1.0 Hz, 1H), 7.40 (dd, J = 8.3, 4.3 Hz, 1H), 2.85 – 2.75 (m, 4H).

5-(*tert*-butyldimethylsilyl)pent-4-ynal **21d**



21d

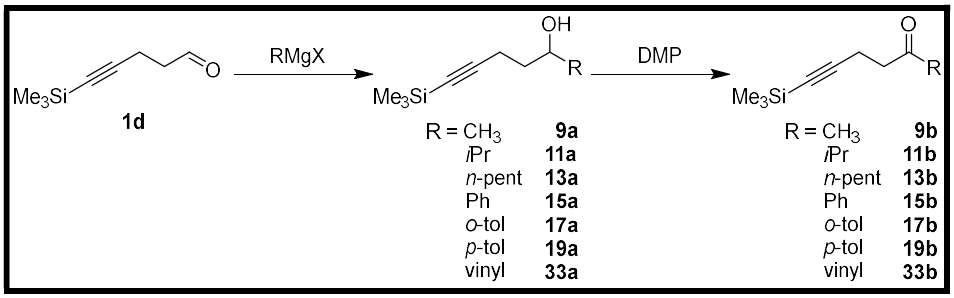
[20] F. Erver and G. Hilt, *Org. Lett.* **2012**, *14*, 1884 – 1887.
[21] A. Jean, J. Blanchet, J. Rouden, J. Maddaluno and M. De Paolis, *Chem. Commun*., **2013**, *49*, 1651 – 1653.

Crude compound **21d** was obtained from the corresponding alcohol **21c** following **GP4** on 5.00 mmol scale (992 mg).

After evaporation of the solvent, pentane (≈ 25 mL) was added. The white insoluble solid was filtrated and the filtrate was concentrated under reduced pressure. Product **21d** (803 mg, 4.10 mmol, 82 %) was obtained as a clean colourless liquid and directly used without further purification.

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.79 (t, J = 1.2 Hz, 1H), 2.70 – 2.63 (m, 2H), 2.59 – 2.51 (m, 2H), 0.90 (s, 9H), 0.06 (s, 6H).

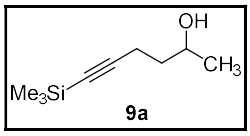
Spectroscopic data were in accordance with those reported in literature.[22]



General procedure for the addition of Grignard reagents on the aldehyde 1d (GP5)

To a stirred solution of **1d** (1 equiv), under argon atmosphere, in dry THF (0.5 M), was added dropwise the corresponding Grignard reagent (2 equiv) at 0°C. The brown solution was warmed to room temperature and stirred overnight. After total completion, monitored by TLC, a satured NH_4Cl (15 mL) was slowly added and the aqueous layer was extracted with Et_2O (2 × 15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The crude corresponding alcohol was directly used without purification.

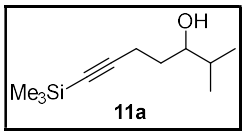
6-(trimethylsilyl)hex-5-yn-2-ol **9a**



Compound **9a** was obtained by addition of methylmagnesium bromide on the aldehyde **1d** following **GP5** on 4.50 mmol scale (694 mg). Crude alcohol **9a** was obtained as a light-yellow liquid and used without purification.

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.94 (dq, J = 6.2, 1.6 Hz, 1H), 2.35 (td, J = 7.1, 1.6 Hz, 2H), 1.69 – 1.62 (m, 2H), 1.22 (d, J = 6.2 Hz, 3H), 0.15 (s, 9H).

2-methyl-7-(trimethylsilyl)hept-6-yn-3-ol **11a**

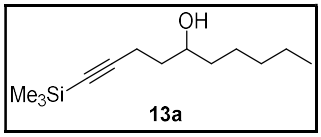


[22] T. M. Bertolini, Q. H. Nguyen, D. F. Harvey, *J. Org. Chem.*, **2002**, *67*, 8675 – 8678.

Compound **11a** was obtained by addition of isopropylmagnesium chloride on the aldehyde **1d** following **GP5** on 5.00 mmol scale (771 mg). Crude alcohol **11a** was obtained as a yellow liquid and used without purification.

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.56 – 3.40 (m, 1H), 2.41 – 2.30 (m, 2H), 1.91 – 1.50 (m, 3H), 0.92 (d, J = 6.7 Hz, 6H), 0.15 (s, 9H).

1-(trimethylsilyl)dec-1-yn-5-ol **13a**

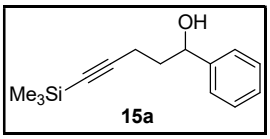


13a

Compound **13a** was obtained by addition of *n*-pentylmagnesium chloride on the aldehyde **1d** following **GP5** on 4.20 mmol scale (648 mg). Crude alcohol **13a** was obtained as a yellow liquid and used without purification.

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.84 – 3.74 (m, 1H), 2.42 (t, J = 7.1 Hz, 2H), 1.87 – 1.69 (m, 2H), 1.69 – 1.58 (m, 2H), 1.55 – 1.45 (m, 2H), 1.44 – 1.28 (m, 4H), 1.03 – 0.89 (m, 3H), 0.20 (s, 9H).

1-phenyl-5-(trimethylsilyl)pent-4-yn-1-ol **15a**

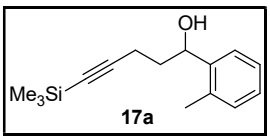


15a

Compound **15a** was obtained by addition of phenylmagnesium bromide on the aldehyde **1d** following **GP5** on 4.80 mmol scale (740 mg). Crude alcohol **15a** was obtained as a yellow liquid and used without purification.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47 – 7.27 (m, 5H), 4.90 – 4.80 (m, 1H), 2.45 – 2.22 (m, 2H), 2.14 (s, 1H), 2.07 – 1.82 (m, 2H), 0.17 (s, 9H).

1-(*o*-tolyl)-5-(trimethylsilyl)pent-4-yn-1-ol **17a**

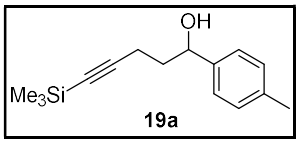


17a

Compound **17a** was obtained by addition of *o*-tolylmagnesium chloride on the aldehyde **1d** following **GP5** on 4.20 mmol scale (648 mg). Crude alcohol **17a** was obtained as a yellow liquid and used without purification.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49 (d, 1H), 7.26 – 7.10 (m, 3H), 5.14 (s, 1H), 2.61 – 2.29 (m, 5H), 1.99 (d, J = 3.4 Hz, 1H), 1.95 – 1.83 (m, 2H).

1-(*p*-tolyl)-5-(trimethylsilyl)pent-4-yn-1-ol **19a**

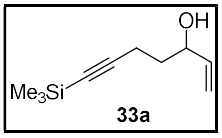


19a

Compound **19a** was obtained by addition of *p*-tolylmagnesium bromide on the aldehyde **1d** following **GP5** on 5.00 mmol scale (771 mg). Crude alcohol **19a** was obtained as an orange liquid and used without purification.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50 – 7.44 (m, 2H), 7.20 – 7.13 (m, 2H), 4.85 – 4.76 (m, 1H), 2.42 – 2.24 (m, 5H), 2.07 – 1.90 (m, 2H), 0.16 (s, 9H).

7-(trimethylsilyl)hept-1-en-6-yn-3-ol **33a**

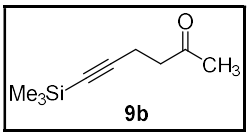


33a

Compound **33a** was obtained by addition of vinylmagnesium bromide on the aldehyde **1d** following **GP5** on 5.00 mmol scale (771 mg). Crude alcohol **33a** was obtained as a yellow liquid and used without purification.

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.87 (ddd, J = 17.1, 10.5, 6.0 Hz, 1H), 5.27 (dd, J = 17.1, 1.4 Hz, 1H), 5.14 (dd, J = 10.5, 1.4 Hz, 1H), 4.31 – 4.23 (m, 1H), 2.42 – 2.26 (m, 2H), 1.79 – 1.70 (m, 2H), 0.15 (s, 9H).

6-(trimethylsilyl)hex-5-yn-2-one **9b**



9b

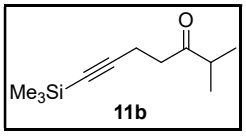
Pure compound **9b** was obtained from the corresponding crude alcohol **9a** following **GP4** on 4.50 mmol scale (766 mg).

After evaporation of the solvent, pentane (≈ 25 mL) was added. The white insoluble solid was filtrated and the filtrate was concentrated under reduced pressure. Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 50/50) afforded pure ketone **9b** (632 mg, 3.75 mmol, 83 % over 2 steps) as a yellow liquid.

Spectroscopic data were in accordance with those reported in literature.[23]

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.73 – 2.62 (m, 2H), 2.50 – 2.44 (m, 2H), 2.17 (s, 3H), 0.13 (s, 9H).

2-methyl-7-(trimethylsilyl)hept-6-yn-3-one **11b**



11b

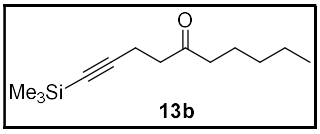
Pure compound **11b** was obtained from the corresponding crude alcohol **11a** following **GP4** on 5.00 mmol scale (992 mg).

After evaporation of the solvent, pentane (≈ 25 mL) was added. The white insoluble solid was filtrated and the filtrate was concentrated under reduced pressure. Purification by flash chromatography over silica gel (Et_2O) afforded pure ketone **11b** (631 mg, 3.21 mmol, 64 % over 2 steps) as an orange liquid.

[23] G. A. Suárez-Ortiz, P. Sharma, M. Amézquita-Valencia, I. Arellano, A. Cabrera and N. Rosas, *Tetrahedron Letters*, **2011**, *52*, 1641–1643.

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.72 – 2.65 (m, 2H), 2.65 – 2.51 (m, 1H), 2.50 – 2.43 (m, 2H), 1.10 (d, J = 6.9 Hz, 6H), 0.12 (s, 9H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 212.6, 106.1, 85.0, 41.0, 39.4, 18.2, 14.7, 0.2.
HRMS (ESI): m/z calculated for $[M+H]^+$ 197.1356 g.mol^{-1}, found 197.1360 g.mol^{-1}, calculated for $[M+Na]^+$ 219.1176 g.mol^{-1}, found 219.1176 g.mol^{-1}.
FTIR (film cm^{-1}): 2962, 2176, 1714, 1467, 1409, 1384, 1362, 1275, 1249, 1075, 1035, 985, 836, 757, 698.

1-(trimethylsilyl)dec-1-yn-5-one **13b**



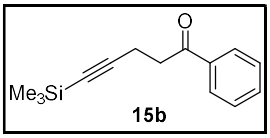
13b

Pure compound **13b** was obtained from the corresponding crude alcohol **13a** following **GP4** on 4.20 mmol scale (953 mg).

After evaporation of the solvent, pentane (≈ 25 mL) was added. The white insoluble solid was filtrated and the filtrate was concentrated under reduced pressure. Purification by flash chromatography over silica gel (Et_2O) afforded pure ketone **13b** (852 mg, 3.80 mmol, 90 % over 2 steps) as a yellow liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ 2.67 – 2.60 (m, 2H), 2.50 – 2.44 (m, 2H), 2.41 (t, J = 7.4 Hz, 2H), 1.58 (p, J = 7.4 Hz, 2H), 1.37 – 1.20 (m, 4H), 0.89 (t, J = 6.8 Hz, 3H), 0.13 (s, 9H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 209.2, 106.0, 85.2, 43.1, 41.6, 31.5, 23.6, 22.6, 14.6, 14.0, 0.2.
HRMS (ESI): m/z calculated for $[M+H]^+$ 225.1669 g.mol^{-1}, found 225.1672 g.mol^{-1}, calculated for $[M+Na]^+$ 247.1489 g.mol^{-1}, found 247.1495 g.mol^{-1}.
FTIR (film cm^{-1}): 3005, 2957, 2930, 2860, 2176, 1716, 1629, 1406, 1370, 1275, 1259, 1250, 1127, 1078, 1044, 1008, 982, 839, 758, 750, 701.

1-phenyl-5-(trimethylsilyl)pent-4-yn-1-one **15b**



15b

Pure compound **15b** was obtained from the corresponding crude alcohol **15a** following **GP4** on 4.80 mmol scale (1.12 g).

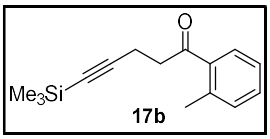
After evaporation of the solvent, pentane (≈ 25 mL) was added. The white insoluble solid was filtrated and the filtrate was concentrated under reduced pressure. Purification by flash chromatography over silica gel (Et_2O) afforded pure ketone **15b** (1.02 g, 4.42 mmol, 92 % over 2 steps) as a yellow liquid.

Spectroscopic data were in accordance with those reported in literature.[24]

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.01 – 7.93 (m, 2H), 7.63 – 7.53 (m, 1H), 7.52 – 7.42 (m, 2H), 3.29 – 3.19 (m, 2H), 2.71 – 2.62 (m, 2H), 0.14 (s, 9H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 198.1, 136.7, 133.4, 128.8, 128.2, 106.1, 85.3, 37.9, 14.9, 0.2.

1-(*o*-tolyl)-5-(trimethylsilyl)pent-4-yn-1-one **17b**

[24] H. Wu, W. Zi, G. Li, H. Lu and F. D. Toste, *Angew. Chem. Int. Ed.*, **2015**, *54*, 8529–8532.



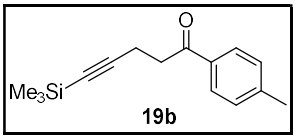
17b

Pure compound **17b** was obtained from the corresponding crude alcohol **17a** following **GP4** on 4.20 mmol scale (1.04 g).

After evaporation of the solvent, a pentane/Et_2O mixture (90/10, ≈ 25 mL) was added. The white insoluble solid was filtrated and the filtrate was concentrated under reduced pressure. Purification by flash chromatography over silica gel (Et_2O 100%) afforded pure ketone **17b** (912 mg, 3.73 mmol, 89 % over 2 steps) as a brown liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65 (d, J = 7.6 Hz, 1H), 7.42 – 7.34 (m, 1H), 7.31 – 7.20 (m, 2H), 3.18 – 3.10 (m, 2H), 2.68 – 2.60 (m, 2H), 2.50 (s, 3H), 0.13 (s, 9H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 202.1, 138.3, 137.7, 132.1, 131.5, 128.6, 125.8, 106.0, 85.3, 40.6, 21.4, 15.2, 0.2.
HRMS (ESI): m/z calculated for $[M+H]^+$ 245.1356 g.mol^{-1}, found 245.1362 g.mol^{-1}, calculated for $[M+Na]^+$ 267.1176 g.mol^{-1}, found 267.1184 g.mol^{-1}.
FTIR (film cm^{-1}): 3006, 2960, 2176, 1686, 1486, 1381, 1353, 1275, 1259, 1250, 1054, 965, 841, 750.

1-(*p*-tolyl)-5-(trimethylsilyl)pent-4-yn-1-one **19b**



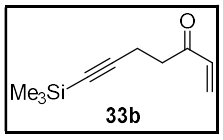
19b

Pure compound **19b** was obtained from the corresponding crude alcohol **19a** following **GP4** on 5.00 mmol scale (1.23 g).

After evaporation of the solvent, a pentane/Et_2O mixture (90/10, ≈ 25 mL) was added. The white insoluble solid was filtrated and the filtrate was concentrated under reduced pressure. Purification by flash chromatography over silica gel (cyclohexane/ethyl acetate 100/0 to 95/5) afforded pure ketone **19b** (903 mg, 3.69 mmol, 74 % over 2 steps) as a white solid.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.90 – 7.84 (m, 2H), 7.30 – 7.22 (m, 2H), 3.25 – 3.14 (m, 2H), 2.70 – 2.60 (m, 1H), 2.41 (s, 3H), 0.14 (s, 9H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 197.7, 144.2, 134.3, 129.4, 128.3, 106.2, 85.2, 37.8, 21.8, 14.9, 0.2.
HRMS (ESI): m/z calculated for $[M+H]^+$ 245.1356 g.mol^{-1}, found 245.1358 g.mol^{-1}, calculated for $[M+Na]^+$ 267.1176 g.mol^{-1}, found 267.1182 g.mol^{-1}.
FTIR (film cm^{-1}): 2958, 2922, 2175, 1677, 1606, 1413, 1364, 1284, 1249, 1183, 1060, 1033, 968, 840, 761, 699.

7-(trimethylsilyl)hept-1-en-6-yn-3-one **33b**



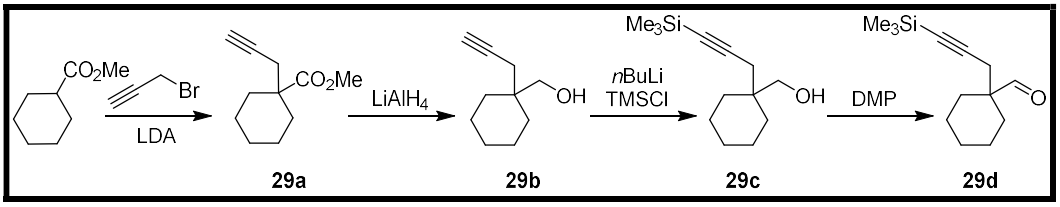
33b

Pure compound **33b** was obtained from the corresponding crude alcohol **33a** following **GP4** on 5.00 mmol scale (912 mg).

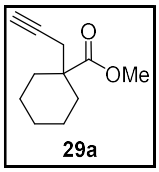
After evaporation of the solvent, pentane (≈ 25 mL) was added. The white insoluble solid was filtrated and the filtrate was concentrated under reduced pressure. Purification by flash chromatography over silica gel (Et_2O) afforded pure ketone **33b** (856 mg, 5.00 mmol, quant. over 2 steps) as a brown oil.

Spectroscopic data were in accordance with those reported in literature.[25]

^{1}H NMR (300 MHz, $CDCl_3$): δ 6.37 (dd, J = 17.7, 10.2 Hz, 1H), 6.25 (dd, J = 17.7, 1.5 Hz, 1H), 5.87 (dd, J = 10.2, 1.5 Hz, 1H), 2.89 – 2.81 (m, 2H), 2.59 – 2.50 (m, 2H), 0.14 (s, 9H).



methyl 1-(prop-2-yn-1-yl)cyclohexanecarboxylate **29a**

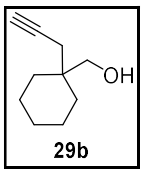


To a solution of freshly distilled diisopropylamine (8.40 mL, 60 mmol, 1.2 equiv) under argon atmosphere in dry THF (25 mL, 2.4 M), was added dropwise at -78 °C a solution of *n*-butyllithium (60 mmol, 1.2 equiv). The bright yellow solution was stirred for 30 min at -78 °C before the dropwise addition of methyl cyclohexanecarboxylate (7.15 mL, 50 mmol, 1 equiv). Stirring was maintained for 30 min at -78 °C before the dropwise addition of propargyl bromide (6.55 mL, 60 mmol, 80% in toluene, 1.2 equiv). The brown solution was warmed to room temperature and stirred overnight. After total completion, monitored by TLC, a satured NH_4Cl solution (100 mL) was added and the aqueous layer was extracted with ethyl acetate (2 × 50 mL). The combined organic layers were washed with HCl (100 mL, 2 M), a satured $NaHCO_3$ solution (50 mL), dried over $MgSO_4$ and concentrated under reduced pressure, affording clean crude **29a**, which was directly used without purification.

Spectroscopic data were in accordance with those reported in literature.[26]

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.71 (s, 3H), 2.41 (d, J = 2.4 Hz, 2H), 2.13 – 2.00 (m, 3H), (m, 8H).

(1-(prop-2-yn-1-yl)cyclohexyl)methanol **29b**



To a stirred solution of lithium aluminium hydride (4.17 g, 110 mmol, 2.2 equiv) in dry THF (110 mL, 1 M) was added dropwise, at 0 °C, a solution of **29a** (9.00 g, 50 mmol, 1 equiv) in dry THF (50 mL, 1 M). The green-grey solution was then stirred for 30 min at 0°C and 2h at room temperature. Reaction was quenched by a slow addition at 0 °C of water (14 mL), NaOH 15% (14 mL) and water (25 mL). The white

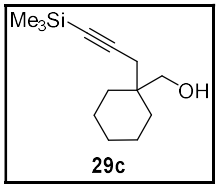
[25] S. Chattexjee and E.-I. Negishi, *J. Org. Chem.*, **1985**, *285*, C1–C4.
[26] A. P. Häring, P. Klahn, M. Jübermann, F. Mohr and S. F. Kirsch, *Monatsh Chem*, **2015**, *146*, 119–134.

precipitate was filtered through a Celite® pad and washed with ethyl acetate (100 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over silica gel (cyclohexane/ethyl acetate 100/0 to 80/20) afforded pure **29b** (6.43 g, 42 mmol, 84 %) as a colourless liquid.

Spectroscopic data were in accordance with those reported in literature.[27]

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.55 (d, J = 5.5 Hz, 2H), 2.26 (d, J = 2.7 Hz, 2H), 2.00 (t, J = 2.7 Hz, 2H), 1.62-1.55 (m, 2H), 1.48 – 1.37 (m, 8H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 82.1, 70.5, 68.7, 37.7, 32.0, 26.3, 25.2, 21.6.

(1-(3-(trimethylsilyl)prop-2-yn-1-yl)cyclohexyl)methanol **29c**



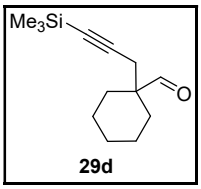
29c

Crude compound **29c** was obtained from the corresponding alcohol **29b** following **GP2** on 11.8 mmol scale (1.81 g).

Purification of the crude by flash chromatography over silica gel (cyclohexane/ethyl acetate 50/50) afforded pure **29c** (2.35 g, 10.4 mmol, 88 %) as a yellow liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ 3.54 (d, J = 6.3 Hz, 2H), 2.26 (s, 2H), 1.73 (t, J = 6.3 Hz, 1H), 1.55 – 1.26 (m, 10H), 0.15 (s, 9H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 105.1, 87.3, 69.1, 38.0, 32.1, 27.2, 26.3, 21.7, 0.3.
HRMS (ESI): m/z calculated for $[M+H]^+$ 225.1669 g.mol^{-1}, found 225.1673 g.mol^{-1}, calculated for $[M+Na]^+$ 247.1489 g.mol^{-1}, found 247.1492 g.mol^{-1}.
FTIR (film cm^{-1}): 3344, 2926, 2853, 2171, 1453, 1422, 1275, 1248, 1036, 838, 757, 697.

1-(3-(trimethylsilyl)prop-2-yn-1-yl)cyclohexanecarbaldehyde **29d**



29d

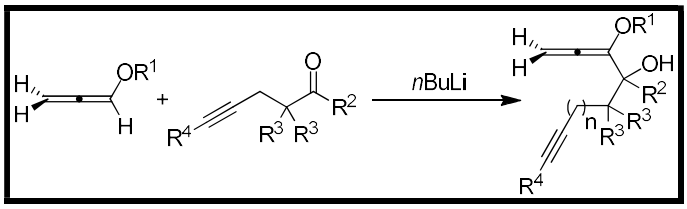
Pure compound **29d** was obtained from the corresponding crude alcohol **29c** following **GP4** on 5.00 mmol scale (1.11 g).

After evaporation of the solvent, pentane (≈ 25 mL) was added. The white insoluble solid was filtrated and the filtrate was concentrated under reduced pressure. Purification by flash chromatography over silica gel (cyclohexane/AcOEt 100/0 to 95/5) afforded pure aldehyde **29d** (611 mg, 2.75 mmol, 55 %) as a yellow liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.55 (s, 1H), 2.33 (s, 2H), 1.98 – 1.84 (m, 2H), 1.66 – 1.22 (m, 8H), 0.14 (s, 9H).

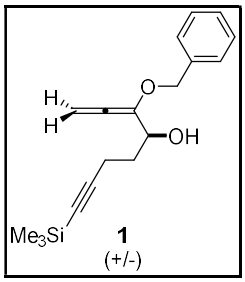
General procedure to access the cyclization precursors (GP6)

[27] M. Ochiai, Y. Nishi, T. Mori, N. Tada, T. Suefuji and H. J. Frohn, *J. Am. Chem. Soc.*, **2005**, *127*, 10460–10461.



To a solution of the corresponding alkoxyallene (1.1 equiv), under argon atmosphere, in dry THF (0.37 M), was added dropwise at -78°C a solution of butyllithium (1.1 equiv, in hexane). The yellow solution was allowed to warm to -50°C over 30 minutes. The corresponding aldehyde/ketone, in solution in dry THF (0.5 M) was thus added dropwise by cannula and the mixture was allowed to warm to -50°C over 30 minutes. After total completion, monitored by TLC, water (25 mL) was added. The aqueous layer was extracted with Et_2O (2 × 20 mL). The combined organic layer were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) afforded the pure corresponding alkoxyallene-yne precursor.

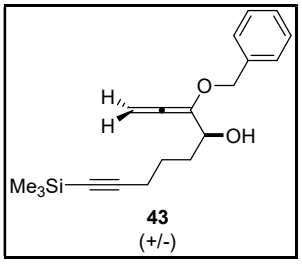
(+/-)-3-(benzyloxy)-8-(trimethylsilyl)octa-1,2-dien-7-yn-4-ol **1**



Compound **1** was obtained from the alkoxyallene **1b** (2.41 g, 16.5 mmol, 1.1 equiv) and the aldehyde **1d** (2.31 g, 15 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 90/10) afforded pure **1** (2.65 g, 8.85 mmol, 59 %) as a yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.28 (m, 5H), 5.56 (d, J = 1.9 Hz, 2H), 4.65 (s, 2H), 4.35 (t, J = 5.4 Hz, 1H), 2.41 – 2.30 (m, 2H), 2.22 (s, 1H), 2.00 – 1.79 (m, 2H), 0.14 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1, 137.3, 134.2, 128.5, 128.0, 127.9, 106.9, 92.7, 85.1, 71.0, 70.1, 33.4, 16.3, 0.3.
HRMS (ESI): m/z calculated for $[M+H]^+$ 301.1618 g.mol^{-1}, found 301.1619 g.mol^{-1}.
FTIR (film cm^{-1}): 3448, 3005, 2958, 2899, 2173, 1725, 1454, 1259, 1275, 1249, 1161, 1048, 1027, 899, 837, 750, 695.

(+/-)-3-(benzyloxy)-9-(trimethylsilyl)nona-1,2-dien-8-yn-4-ol **43**

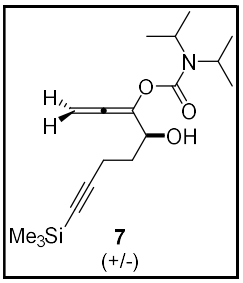


Compound **43** was obtained from the alkoxyallene **1b** (804 mg, 5.50 mmol, 1.1 equiv) and the aldehyde **43b** (841 mg, 5.00 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography

over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 95/5) afforded pure **43** (733 mg, 2.35 mmol, 47 %) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.28 (m, 5H), 5.55 (dd, J = 1.9, 1.0 Hz, 2H), 4.65 (s, 2H), 4.27 – 4.20 (m, 1H), 2.26 (t, J = 7.0 Hz, 2H), 2.02 (d, J = 5.8 Hz, 1H), 1.87 – 1.53 (m, 4H), 0.14 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1, 137.4, 134.6, 128.5, 128.0, 127.9, 107.3, 92.6, 84.9, 70.9, 70.8, 33.7, 24.7, 19.8, 0.3.
HRMS (ESI): m/z calculated for $[M+H]^+$ 315.1775 g.mol^{-1}, found 315.1781 g.mol^{-1}.
FTIR (film cm^{-1}): 3446, 3032, 2957, 2899, 2173, 1727, 1454, 1407, 1379, 1248, 1204, 1166, 1042, 1025, 837, 757, 696.

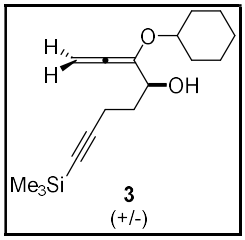
(+/-)-4-hydroxy-8-(trimethylsilyl)octa-1,2-dien-7-yn-3-yl diisopropylcarbamate **7**



Compound **7** was obtained from the alkoxyallene **7b** (1.05 g, 5.50 mmol, 1.1 equiv) and the aldehyde **1d** (771 mg, 5.0 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 70/30) afforded pure **7** (811 mg, 2.40 mmol, 48%) as a yellow-orange oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.45 – 5.38 (m, 2H), 4.40 – 4.32 (m, 1H), 4.07 (s, 1H), 3.85 (d, J = 4.5 Hz, 1H), 2.39 (t, J = 7.2 Hz, 2H), 1.92 – 1.76 (m, 2H), 1.26 (d, J = 6.8 Hz, 12H), 0.15 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 201.9, 155.1, 125.7, 106.7, 87.5, 85.1, 70.4, 47.3, 46.3, 33.5, 21.6, 20.5, 16.4, 0.3.
HRMS (ESI): m/z calculated for $[M+H]^+$ 338.2146 g.mol^{-1}, found 338.2153 g.mol^{-1}, calculated for $[M+Na]^+$ 360.1965 g.mol^{-1}, found 360.1972 g.mol^{-1}, calculated for $[M+K]^+$ 376.1730 g.mol^{-1}, found 376.1721 g.mol^{-1}.
FTIR (film cm^{-1}): 3420, 2964, 2936, 2174, 2686, 1431, 1370, 1300, 1277, 1249, 1211, 1186, 1133, 1091, 1042, 838, 758.

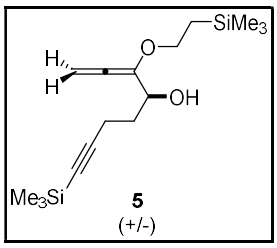
(+/-)-3-(cyclohexyloxy)-8-(trimethylsilyl)octa-1,2-dien-7-yn-4-ol **3**



Compound **3** was obtained from the alkoxyallene **3b** (304 mg, 2.20 mmol, 1.1 equiv) and the aldehyde **1d** (308 mg, 2.00 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 97.5/2.5) afforded clean **3** (152 mg, 0.52 mmol, 26 %) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.46 (d, J = 1.8 Hz, 2H), 4.23 (dddd, J = 7.8, 6.9, 3.7, 1.8 Hz, 1H), 3.70 (ddd, J = 12.6, 8.5, 3.7 Hz, 1H), 2.34 (t, J = 7.5 Hz, 2H), 2.18 – 2.13 (m, 1H), 1.94 – 1.76 (m, 2H), 1.75 – 1.65 (m, 2H), 1.55 – 1.46 (m, 1H), 1.44 – 1.36 (m, 3H), 1.34 – 1.20 (m, 4H), 0.13 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 197.2, 132.4, 107.6, 91.5, 84.9, 76.0, 70.2, 33.6, 31.8, 31.7, 25.8, 23.8, 23.8, 16.3, 0.3.
HRMS (ESI): m/z calculated for $[M+H]^+$ 293.1931 g.mol^{-1}, found 293.1935 g.mol^{-1}, calculated for $[M+Na]^+$ 315.1751 g.mol^{-1}, found 315.1751 g.mol^{-1}.
FTIR (film cm^{-1}): 3427, 2934, 2858, 2175, 1728, 1450, 1408, 1359, 1275, 1248, 1162, 1051, 838, 758, 697.

(+/-)-8-(trimethylsilyl)-3-(2-(trimethylsilyl)ethoxy)octa-1,2-dien-7-yn-4-ol **5**

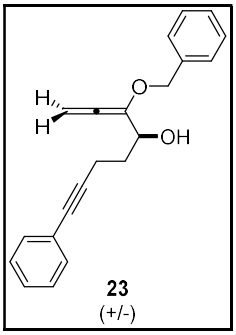


Compound **5** was obtained from the alkoxyallene **5b** (1.39 g, 8.93 mmol, 1.1 equiv) and the aldehyde **1d** (1.25 g, 8.12 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 95/5) afforded pure **5** (973 mg, 3.17 mmol, 39%) as a bright yellow liquid.

Only ^{1}H and ^{13}C NMR are available due to the high instability of the product and its rapid decomposition occurring even neat at -20°C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.50 (d, J = 1.8 Hz, 2H), 4.29 – 4.22 (m, 1H), 3.75 – 3.63 (m, 2H), 2.41 – 2.31 (m, 2H), 2.12 (d, J = 5.8 Hz, 1H), 1.95 – 1.75 (m, 2H), 1.06 – 0.96 (m, 2H), 0.13 (s, 9H), 0.02 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1, 133.8, 106.9, 91.8, 85.0, 70.1, 66.7, 33.5, 17.9, 16.3, 0.3, -1.2.

(+/-)-3-(benzyloxy)-8-phenylocta-1,2-dien-7-yn-4-ol **23**

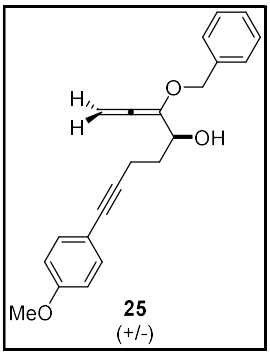


Compound **23** was obtained from the alkoxyallene **1b** (772 mg, 5.28 mmol, 1.1 equiv) and the aldehyde **23b** (759 mg, 4.80 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 90/10) afforded pure **23** (595 mg, 1.97 mmol, 41%) as an orange oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.23 (m, 10H), 5.58 (d, J = 1.9 Hz, 2H), 4.66 (s, 2H), 4.47 – 4.40 (m, 1H), 2.60 – 2.51 (m, 2H), 2.18 – 2.12 (m, 1H), 2.08 – 1.88 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1, 137.3, 134.2, 131.7, 128.6, 128.3, 128.1, 127.9, 127.7, 124.0, 92.8, 89.6, 81.1, 70.9, 70.0, 33.5, 15.8.

HRMS (ESI): m/z calculated for $[M+H]^+$ 305.1536 g.mol^{-1}, found 305.1537 g.mol^{-1}, calculated for $[M+Na]^+$ 327.1355 g.mol^{-1}, found 327.1361 g.mol^{-1}.
FTIR (film cm^{-1}): 3420, 3031, 3006, 2973, 2929, 2868, 1956, 1724, 1598, 1490, 1453, 1442, 1275, 1260, 1155, 1091, 1069, 1045, 1026, 891, 751, 690.

(+/-)-3-(benzyloxy)-8-(4-methoxyphenyl)octa-1,2-dien-7-yn-4-ol **25**

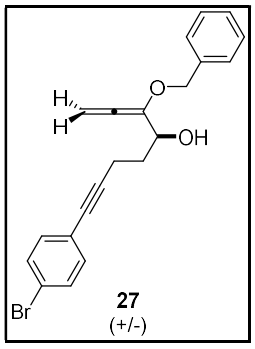


25
(+/-)

Compound **25** was obtained from the alkoxyallene **1b** (732 mg, 5.00 mmol, 1.1 equiv) and the aldehyde **25b** (859 mg, 4.55 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 95/5 to 85/15) afforded clean **25** (812 mg, 2.41 mmol, 53%) as an orange oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.28 (m, 7H), 6.83 – 6.79 (m, 2H), 5.58 (d, J = 1.8 Hz, 2H), 4.66 (s, 2H), 4.47 – 4.38 (m, 1H), 3.79 (s, 3H), 2.56 – 2.50 (m, 2H), 2.17 (d, J = 5.8 Hz, 1H), 2.04 – 1.87 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1, 159.2, 137.4, 134.3, 133.1, 133.0, 128.6, 128.0, 127.9, 113.9, 92.8, 87.9, 80.8, 70.9, 70.1, 55.4, 33.6, 15.8.
HRMS (ESI): m/z calculated for $[M+H]^+$ 335.1642 g.mol^{-1}, found 335.1637 g.mol^{-1}, calculated for $[M+Na]^+$ 357.1461 g.mol^{-1}, found 357.1462 g.mol^{-1}.
FTIR (film cm^{-1}): 3447, 2934, 2837, 1722, 1659, 1605, 1508, , 1454, 1442, 1288, 1244, 1171, 1104, 1068, 1026, 830, 737, 697.

(+/-)-3-(benzyloxy)-8-(4-bromophenyl)octa-1,2-dien-7-yn-4-ol **27**



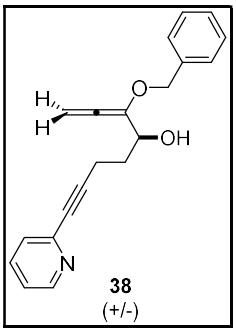
27
(+/-)

Compound **27** was obtained from the alkoxyallene **1b** (804 mg, 5.50 mmol, 1.1 equiv) and the aldehyde **27b** (1.18 g, 5.00 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 85/15) afforded pure **27** (1.13 g, 2.95 mmol, 59%) as a brown oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.37 (m, 2H), 7.37 – 7.28 (m, 5H), 7.25 – 7.21 (m, 2H), 5.58 (s, 2H), 4.66 (s, 2H), 4.45 – 4.36 (m, 1H), 2.53 (t, J = 7.2 Hz, 2H), 2.14 (d, J = 5.7 Hz, 1H), 2.04 – 1.87 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 197.0, 137.3, 134.2, 133.2, 131.5, 128.6, 128.1, 127.9, 123.0, 121.8, 92.9, 90.9, 80.1, 71.0, 69.9, 33.4, 15.8.
HRMS (ESI): m/z calculated for $[M+H]^+$ 383.0641 g.mol^{-1}, found 383.0648 g.mol^{-1}.

FTIR (film cm^{-1}): 3426, 3030, 3006, 2935, 2233, 1903, 1722, 1485, 1454, 1428, 1393, 1275, 1260, 1205, 1157, 1069, 1009, 823, 764, 749, 697.

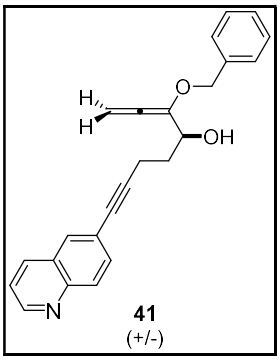
(+/-)-3-(benzyloxy)-8-(pyridin-2-yl)octa-1,2-dien-7-yn-4-ol **38**



Compound **38** was obtained from the alkoxyallene **1b** (597 mg, 4.09 mmol, 1.1 equiv) and the aldehyde **38b** (593 mg, 3.72 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 50/50) afforded pure **38** (392 mg, 1.26 mmol, 34%) as a brown oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.53 (ddd, J = 4.9, 1.8, 0.9 Hz, 1H), 7.64 – 7.54 (m, 1H), 7.40 – 7.27 (m, 6H), 7.17 (ddd, J = 7.7, 4.9, 1.2 Hz, 1H), 5.57 (d, J = 1.9 Hz, 2H), 4.65 (s, 2H), 4.46 – 4.37 (m, 1H), 2.59 (t, J = 7.3 Hz, 2H), 2.23 (d, J = 5.6 Hz, 1H), 2.10 – 1.90 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 197.0, 150.0, 144.0, 137.3, 136.1, 134.2, 128.6, 128.1, 128.0, 127.0, 122.4, 92.9, 90.4, 80.7, 70.9, 70.0, 33.1, 15.8.
HRMS (ESI): m/z calculated for $[M+H]^+$ 306.1488 $g.mol^{-1}$, found 306.1491 $g.mol^{-1}$, calculated for $[M+Na]^+$ 328.1308 $g.mol^{-1}$, found 328.1308 $g.mol^{-1}$.
FTIR (film cm^{-1}): 3223, 3063, 3032, 2930, 2227, 1956, 1723, 1584, 1561, 1464, 1454, 1427, 1273, 1152, 1092, 1049, 1026, 996, 907, 776, 728, 695.

(+/-)-3-(benzyloxy)-8-(quinolin-6-yl)octa-1,2-dien-7-yn-4-ol **41**



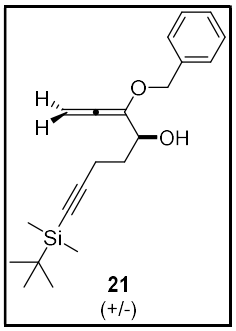
Compound **41** was obtained from the alkoxyallene **1b** (755 mg, 5.16 mmol, 1.1 equiv) and the aldehyde **41b** (982 mg, 4.65 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 50/50) afforded pure **41** (609 mg, 1.71 mmol, 37%) as an orange oil.

Only ^{1}H and ^{13}C NMR are available due to the high instability of the product and its rapid decomposition occurring even neat at -20°C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.86 (dd, J = 4.3, 1.7 Hz, 1H), 8.05 (dd, J = 8.4, 1.7 Hz, 1H), 8.00 (dd, J = 8.7, 0.8 Hz, 1H), 7.84 (d, J = 1.8 Hz, 1H), 7.65 (dd, J = 8.7, 1.9 Hz, 1H), 7.41 – 7.27 (m, 6H), 5.58 (d, J = 1.8 Hz, 2H), 4.67 (s, 2H), 4.52 – 4.44 (m, 1H), 2.65 – 2.57 (m, 2H), 2.11 – 1.93 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1, 150.7, 147.5, 137.3, 135.7, 134.3, 132.6, 130.9, 129.4, 128.5, 128.1, 128.0, 127.9, 122.4, 121.7, 92.8, 91.2, 80.7, 70.9, 69.9, 33.4, 15.9.

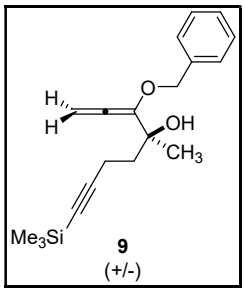
(+/-)-3-(benzyloxy)-8-(*tert*-butyldimethylsilyl)octa-1,2-dien-7-yn-4-ol **21**



Compound **21** was obtained from the alkoxyallene **1b** (651 mg, 4.45 mmol, 1.1 equiv) and the aldehyde **21d** (795 mg, 4.05 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 95/5 to 90/10) afforded pure **21** (732 mg, 2.15 mmol, 53 %) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.28 (m, 5H), 5.58 – 5.52 (m, 2H), 4.65 (s, 2H), 4.42 – 4.31 (m, 1H), 2.44 – 2.29 (m, 2H), 2.14 (d, J = 6.0 Hz, 1H), 2.01 – 1.79 (m, 2H), 0.92 (s, 9H), 0.08 (s, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1, 137.4, 134.1, 128.5, 128.0, 127.9, 107.4, 92.7, 83.2, 70.9, 70.1, 33.6, 27.1, 26.2, 16.3, -4.3.
HRMS (ESI): m/z calculated for $[M+H]^+$ 343.2088 g.mol^{-1}, found 343.2089 g.mol^{-1}, calculated for $[M+Na]^+$ 365.1907 g.mol^{-1}, found 365.1906 g.mol^{-1}.
FTIR (film cm^{-1}): 3449, 3005, 2953, 2929, 2885, 2856, 2173, 1728, 1470, 1462, 1275, 1259, 1204, 1166, 1046, 1026, 1007, 836, 809, 765, 749, 696, 679.

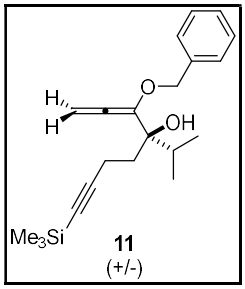
(+/-)-3-(benzyloxy)-4-methyl-8-(trimethylsilyl)octa-1,2-dien-7-yn-4-ol **9**



Compound **9** was obtained from the alkoxyallene **1b** (603 mg, 4.12 mmol, 1.1 equiv) and the ketone **9b** (632 mg, 3.75 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 90/10) afforded pure **9** (834 mg, 2.66 mmol, 71 %) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.28 (m, 5H), 5.60 (s, 2H), 4.63 (s, 2H), 2.52 (s, 1H), 2.37 – 2.20 (m, 2H), 2.03 – 1.85 (m, 2H), 1.36 (s, 3H), 0.14 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 196.7, 137.4, 137.1, 128.5, 128.0, 127.8, 107.7, 93.6, 84.9, 72.4, 71.0, 39.0, 26.1, 15.2, 0.2.
HRMS (ESI): m/z calculated for $[M+Na]^+$ 337.1594 g.mol^{-1}, found 337.1596 g.mol^{-1}.
FTIR (film cm^{-1}): 3448, 3032, 2958, 2173, 1954, 1721, 1497, 1454, 1378, 1249, 1168, 1107, 1089, 837, 757, 732, 695.

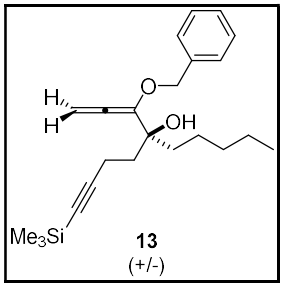
(+/-)-3-(benzyloxy)-4-isopropyl-8-(trimethylsilyl)octa-1,2-dien-7-yn-4-ol **11**



Compound **11** was obtained from the alkoxyallene **1b** (491 mg, 3.36 mmol, 1.1 equiv) and the ketone **11b** (600 mg, 3.05 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 95/5) afforded pure **11** (772 mg, 2.26 mmol, 74 %) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.28 (m, 5H), 5.64 (d, J = 0.8 Hz, 2H), 4.62 (s, 2H), 2.42 – 2.32 (m, 1H), 2.23 (ddd, J = 16.9, 9.3, 5.2 Hz, 1H), 2.17 (s, 1H), 2.02 – 1.93 (m, 2H), 1.93 – 1.84 (m, 1H), 0.97 (d, J = 6.8 Hz, 3H), 0.91 (d, J = 6.9 Hz, 3H), 0.16 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 198.0, 137.4, 136.0, 128.5, 127.9, 127.7, 108.2, 94.0, 84.5, 76.4, 71.0, 35.3, 35.0, 17.4, 16.4, 15.1, 0.3.
HRMS (ESI): m/z calculated for $[M+Na]^+$ 365.1907 g.mol^{-1}, found 365.1904 g.mol^{-1}.
FTIR (film cm^{-1}): 3536, 2962, 2877, 2173, 1953, 1725, 1454, 1383, 1248, 1164, 1122, 1046, 1029, 837, 758, 732, 695.

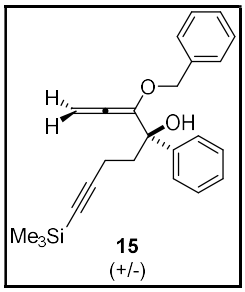
(+/-)-5-(1-(benzyloxy)propa-1,2-dien-1-yl)-1-(trimethylsilyl)dec-1-yn-5-ol **13**



Compound **13** was obtained from the alkoxyallene **1b** (592 mg, 4.05 mmol, 1.1 equiv) and the ketone **13b** (825 mg, 3.68 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 98/2) afforded pure **13** (730 mg, 1.95 mmol, 53 %) as a yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.27 (m, 5H), 5.62 (s, 2H), 4.62 (s, 2H), 2.36 (s, 1H), 2.34 – 2.17 (m, 2H), 1.98 – 1.80 (m, 2H), 1.71 – 1.54 (m, 2H), 1.39 – 1.19 (m, 6H), 0.87 (t, J = 6.8 Hz, 3H), 0.14 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 197.5, 137.5, 136.2, 128.5, 128.0, 127.8, 108.0, 93.9, 84.7, 74.6, 71.0, 39.0, 37.6, 32.3, 23.2, 22.8, 14.9, 14.2, 0.3.
HRMS (ESI): m/z calculated for $[M+H]^+$ 371.2401 g.mol^{-1}, found 371.2405 g.mol^{-1}, calculated for $[M+Na]^+$ 393.2220 g.mol^{-1}, found 393.2229 g.mol^{-1}.
FTIR (film cm^{-1}): 3449, 3005, 2956, 2930, 2870, 2174, 1722, 1642, 1454, 1275, 1259, 1249, 1173, 1122, 1050, 1027, 838, 750, 696.

(+/-)-3-(benzyloxy)-4-phenyl-8-(trimethylsilyl)octa-1,2-dien-7-yn-4-ol **15**

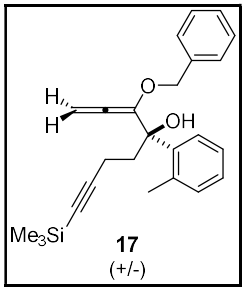


15
(+/-)

Compound **15** was obtained from the alkoxyallene **1b** (713 mg, 4.87 mmol, 1.1 equiv) and the ketone **15b** (1.02 g, 4.43 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 97.5/2.5) afforded pure **15** (353 mg, 0.93 mmol, 21 %) as an orange oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.31 (m, 2H), 7.22 – 7.15 (m, 2H), 7.15 – 7.09 (m, 4H), 7.05 – 6.99 (m, 2H), 5.53 (s, 2H), 4.51 (d, *J* = 12.0 Hz, 1H), 4.46 (d, *J* = 12.0 Hz, 1H), 2.83 (s, 1H), 2.25 – 2.14 (m, 1H), 2.14 – 1.91 (m, 3H), -0.02 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 197.2, 144.3, 137.2, 136.3, 128.4, 128.1, 127.9, 127.7, 127.3, 125.7, 107.7, 94.1, 84.5, 76.3, 71.1, 39.1, 14.8, 0.3.
HRMS (ESI): m/z calculated for $[M+H]^+$ 377.1931 g.mol^{-1}, found 377.1933 g.mol^{-1}, calculated for $[M+Na]^+$ 399.1751 g.mol^{-1}, found 399.1752 g.mol^{-1}.
FTIR (film cm^{-1}): 3551, 3063, 3030, 2959, 2173, 1956, 1725, 1494, 1446, 1275, 1249, 1158, 1096, 1058, 891, 837, 757, 732, 695.

(+/-)-3-(benzyloxy)-4-(*o*-tolyl)-8-(trimethylsilyl)octa-1,2-dien-7-yn-4-ol **17**

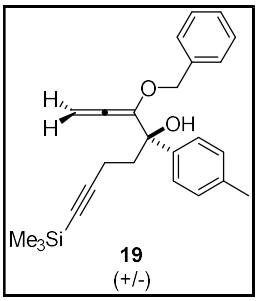


17
(+/-)

Compound **17** was obtained from the alkoxyallene **1b** (592 mg, 4.05 mmol, 1.1 equiv) and the ketone **17b** (900 mg, 3.68 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 95/5) afforded pure **17** (1.07 g, 2.72 mmol, 74 %) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 – 7.53 (m, 1H), 7.31 – 7.26 (m, 3H), 7.21 – 7.17 (m, 2H), 7.17 – 7.11 (m, 3H), 5.66 (d, *J* = 8.2 Hz, 1H), 5.62 (d, *J* = 8.2 Hz, 1H), 4.69 (d, *J* = 12.2 Hz, 1H), 4.65 (d, *J* = 12.2 Hz, 1H), 2.96 (s, 1H), 2.38 (s, 3H), 2.38 – 2.30 (m, 1H), 2.29 – 2.24 (m, 2H), 2.19 – 2.10 (m, 1H), 0.14 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 197.8, 140.7, 137.3, 136.1, 135.9, 132.4, 128.4, 127.9, 127.7, 127.5, 127.3, 125.6, 107.7, 93.7, 84.4, 77.6, 70.8, 36.9, 21.5, 14.9, 0.3.
HRMS (ESI): m/z calculated for $[M+H]^+$ 391.2088 g.mol^{-1}, found 391.2093 g.mol^{-1}, calculated for $[M+Na]^+$ 413.1907 g.mol^{-1}, found 413.1920 g.mol^{-1}.
FTIR (film cm^{-1}): 3552, 3063, 3006, 2959, 2173, 1956, 1453, 1275, 1259, 1249, 1175, 1157, 1088, 1050, 1025, 997, 888, 837, 751, 694.

(+/-)-3-(benzyloxy)-4-(*p*-tolyl)-8-(trimethylsilyl)octa-1,2-dien-7-yn-4-ol **19**

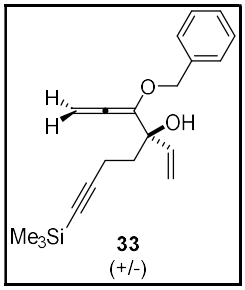


19
(+/-)

Compound **19** was obtained from the alkoxyallene **1** (591 mg, 4.05 mmol, 1.1 equiv) and the ketone **75b** (900 mg, 3.68 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 95/5) afforded pure **75** (1.115 g, 2.83 mmol, 77 %) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.33 (m, 2H), 7.31 – 7.25 (m, 3H), 7.21 – 7.15 (m, 2H), 7.15 – 7.10 (m, 2H), 5.67 (s, 2H), 4.65 (d, *J* = 12.1 Hz, 1H), 4.61 (d, *J* = 12.1 Hz, 1H), 2.93 (s, 1H), 2.35 (s, 3H), 2.34 – 2.06 (m, 4H), 0.12 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 197.2, 141.4, 137.3, 136.9, 136.4, 128.8, 128.4, 127.9, 127.7, 125.6, 107.8, 94.0, 84.4, 76.2, 71.0, 39.1, 21.2, 14.8, 0.3.
HRMS (ESI): m/z calculated for $[M+Na]^+$ 413.1907 g.mol^{-1}, found 413.1910 g.mol^{-1}.
FTIR (film cm^{-1}): 3552, 3030, 2960, 2866, 2174, 1956, 1453, 1275, 1249, 1178, 1158, 1093, 1059, 1028, 1018, 838, 817, 757, 695.

(+/-)-3-(benzyloxy)-8-(trimethylsilyl)-4-vinylocta-1,2-dien-7-yn-4-ol **33**

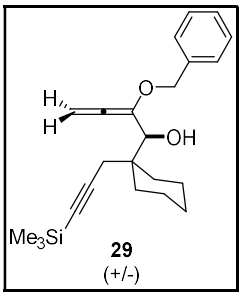


33
(+/-)

Compound **33** was obtained from the alkoxyallene **1b** (764 mg, 5.22 mmol, 1.1 equiv) and the ketone **33b** (856 mg, 4.75 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 95/5) afforded pure **33** (403 mg, 1.23 mmol, 26 %) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.27 (m, 5H), 5.98 (dd, *J* = 17.2, 10.7 Hz, 1H), 5.62 (s, 2H), 5.39 (dd, *J* = 17.2, 1.4 Hz, 1H), 5.16 (dd, *J* = 10.7, 1.4 Hz, 1H), 4.63 (s, 2H), 2.49 (s, 1H), 2.34 – 2.25 (m, 2H), 2.11 – 2.00 (m, 1H), 1.90 (dt, *J* = 13.8, 7.8 Hz, 1H), 0.14 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 196.7, 140.6, 137.3, 136.1, 128.5, 128.0, 127.8, 113.9, 107.7, 94.2, 84.8, 74.5, 71.1, 37.4, 14.7, 0.3.
HRMS (ESI): m/z calculated for $[M+Na]^+$ 349.1594 g.mol^{-1}, found 349.1596 g.mol^{-1}.
FTIR (film cm^{-1}): 3472, 3031, 2958, 2174, 1722, 1454, 1407, 1356, 1275, 1249, 1205, 1175, 1048, 1025, 994, 933, 838, 757, 696.

(+/-)-2-(benzyloxy)-1-(1-(3-(trimethylsilyl)prop-2-yn-1-yl)cyclohexyl)buta-2,3-dien-1-ol **29**



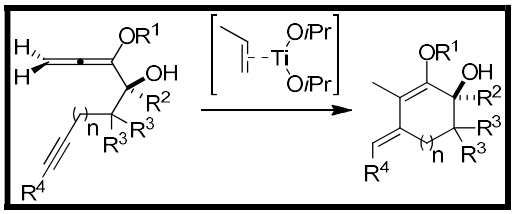
29
(+/-)

Compound **29** was obtained from the alkoxyallene **1b** (433 mg, 3.00 mmol, 1.1 equiv) and the aldehyde **29d** (600 mg, 2.70 mmol, 1 equiv) following **GP6**. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 90/10) afforded pure **29** (662 mg, 1.78 mmol, 66 %) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.27 (m, 5H), 5.58 – 5.49 (m, 2H), 4.63 (s, 2H), 4.25 (d, *J* = 9.3 Hz, 1H), 2.72 (d, *J* = 9.3 Hz, 1H), 2.48 (d, *J* = 17.1 Hz, 1H), 2.33 (d, *J* = 17.1 Hz, 1H), 1.72 – 1.60 (m, 2H), 1.60 – 1.39 (m, 6H), 1.39 – 1.24 (m, 2H), 0.13 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 198.8, 137.4, 132.5, 128.5, 127.8, 127.7, 106.1, 91.7, 87.5, 70.8, 41.5, 32.5, 31.3, 26.1, 25.1, 22.4, 21.6, 0.2.
HRMS (ESI): m/z calculated for $[M+H]^+$ 369.2244 g.mol^{-1}, found 369.2246 g.mol^{-1}, calculated for $[M+Na]^+$ 391.2064 g.mol^{-1}, found 391.2068 g.mol^{-1}.
FTIR (film cm^{-1}): 3472, 2929, 2860, 2171, 1723, 1657, 1454, 1275, 1248, 1026, 910, 838, 757, 696.

3. Cyclization reactions

General procedures for the low-valent titanium mediated cyclization



- ✓ **Conditions A : Preliminary deprotonation step + hydrolysis (H_2O)**

To a solution of the corresponding alkoxyallene-yne (1.0 equiv), under argon atmosphere, in dry Et_2O (0.05 M) at 0°C was slowly added a solution of *i*PrMgCl (1.0 equiv, in Et_2O). The yellow solution was stirred for 3 min before the slow addition of $Ti(OiPr)_4$ (2.0 equiv) at 0°C and further stirring at this temperature for 2 min. After cooling down to -40°C, *i*PrMgCl (4.0 equiv, in Et_2O) was slowly added and the resulting brown/black solution was allowed to warm to -30°C over 10 min. After total completion, monitored by TLC, water (15 mL) and Et_2O (15 mL) were added. The white precipitate was filtered through a Celite® pad and washed with Et_2O (15 mL). The aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic layer were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) afforded the pure corresponding cyclized product.

- ✓ **Conditions AE : Preliminary deprotonation step + Electrophile + hydrolysis (H_2O)**

To a solution of the corresponding alkoxyallene-yne (1.0 equiv), under argon atmosphere, in dry Et_2O (0.05 M) at 0°C was slowly added a solution of *i*PrMgCl (1.0 equiv, in Et_2O). The yellow solution was stirred for 3 min before the slow addition of $Ti(OiPr)_4$ (2.0 equiv) at 0°C and further stirring at this temperature for 2 min. After cooling down to -40°C, *i*PrMgCl (4.0 equiv, in Et_2O) was slowly added and

the resulting brown/black solution was allowed to warm to -30°C over 10 min. The corresponding electrophile (1.1 equiv) was slowly added at -30°C. The solution was stirred for 5 min at -30°C and further 25 min at 0°C. After total completion, monitored by TLC, water (15 mL) and Et_2O (15 mL) were added. The white precipitate was filtered through a Celite® pad and washed with Et_2O (15 mL). The aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic layer were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) afforded the pure corresponding cyclized product.

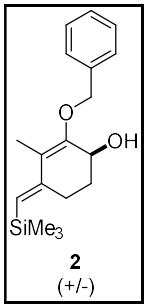
- ✓ **Conditions B : No preliminary deprotonation step + hydrolysis (H_2O)**

To a solution of the corresponding alkoxyallene-yne (1.0 equiv), under argon atmosphere, in dry Et_2O (0.05 M) at 0°C was slowly added Ti(O*i*Pr)$_4$ (2.0 equiv) and the solution was stirred for 2 min. After cooling down to -40°C, *i*PrMgCl (4.0 equiv, in Et_2O) was slowly added and the resulting brown/black solution was allowed to warm to -30°C over 10 min. After total completion, monitored by TLC, water (15 mL) and Et_2O (15 mL) were added. The white precipitate was filtered through a Celite® pad and washed with Et_2O (15 mL). The aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic layer were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) afforded the pure corresponding cyclized product.

- ✓ **Conditions BE : No preliminary deprotonation step + Electrophile + hydrolysis (H_2O)**

To a solution of the corresponding alkoxyallene-yne (1.0 equiv), under argon atmosphere, in dry Et_2O (0.05 M) at 0°C was slowly added Ti(O*i*Pr)$_4$ (2.0 equiv) and the solution was stirred for 2 min. After cooling down to -40°C, *i*PrMgCl (4.0 equiv, in Et_2O) was slowly added and the resulting brown/black solution was allowed to warm to -30°C over 10 min. The corresponding electrophile (1.1 equiv) was slowly added at -30°C. The solution was stirred for 5 min at -30°C and further 25 min at 0°C. After total completion, monitored by TLC, water (15 mL) and Et_2O (15 mL) were added. The white precipitate was filtered through a Celite® pad and washed with Et_2O (15 mL). The aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic layer were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) afforded the pure corresponding cyclized product.

(+/-)-(*E*)-2-(benzyloxy)-3-methyl-4-((trimethylsilyl)methylene)cyclohex-2-enol **2**



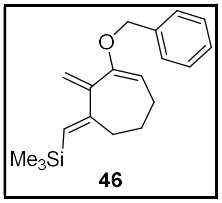
2
(+/-)

Cyclization was performed following **Conditions A** starting from the alkoxyallene-yne **1** (150 mg, 0.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 1/0 to 85/15) afforded pure cyclized product **2** (102 mg, 0.34 mmol, 68 %) as a white solid.

Cyclization was performed following **Conditions A** starting from the alkoxyallene-yne **1** (1.00 g, 3.33 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 85/15) afforded pure cyclized product **2** (493 mg, 1.63 mmol, 49 %) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.29 (m, 5H), 5.45 (s, 1H), 5.00 (d, J = 11.8 Hz, 1H), 4.89 (d, J = 11.8 Hz, 1H), 4.49 – 4.41 (m, 1H), 2.59 – 2.48 (m, 1H), 2.38 (ddd, J = 14.9, 6.8, 3.9 Hz, 1H), 2.04 (d, J = 5.0 Hz, 1H), 1.98 – 1.89 (m, 1H), 1.88 – 1.79 (m, 4H), 0.20 – 0.11 (m, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 153.0, 151.9, 137.8, 128.7, 128.1, 127.7, 122.1, 121.0, 71.6, 64.7, 31.6, 26.6, 11.5, 0.4.
HRMS (ESI): m/z calculated for $[M+H]^+$ 303.1775 g.mol^{-1}, found 303.1778 g.mol^{-1}, calculated for $[M+Na]^+$ 325.1594 g.mol^{-1}, found 325.1596 g.mol^{-1}.
FTIR (film cm^{-1}): 3388, 3005, 2988, 2951, 2895, 2706, 2319, 1656, 1620, 1570, 1497, 1454, 1377, 1354, 1275, 1260, 1188, 1173, 1081, 834, 764, 750.

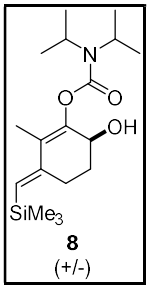
(*E*)-((3-(benzyloxy)-2-methylenecyclohept-3-en-1-ylidene)methyl)trimethylsilane **46**



To a solution of **43** (157 mg, 0.5 mmol, 1.0 equiv), under argon atmosphere, in dry Et_2O (10 mL, 0.05 M), was added slowly at 0°C a solution of *i*PrMgCl (1.0 equiv, in Et_2O). The yellow solution was stirred for 3 min before the slow addition of $Ti(OiPr)_4$ (0.30 mL, 1.0 mmol 2.0 equiv) at 0°C and further stirring at this temperature for 2 min. After cooling down to -40°C, *i*PrMgCl (4.0 equiv, in Et_2O) was slowly added and the resulting brown/black solution was allowed to warm to room temperature over 10 min. After total completion, monitored by TLC, water (15 mL) and Et_2O (15 mL) were added. The white precipitate was filtered through a Celite® pad and washed with Et_2O (15 mL). The aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic layer were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 90/10) afforded clean **46** as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 – 7.07 (m, 5H), 5.64 (s, 1H), 5.25 (d, J = 2.3 Hz, 1H), 5.09 (s, 1H), 4.87 (t, J = 7.3 Hz, 1H), 4.61 (s, 2H), 2.24 (t, J = 7.1 Hz, 2H), 1.95 (dt, J = 7.3, 6.8 Hz, 2H), 1.64 – 1.55 (m, 2H), -0.02 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 157.1, 153.7, 150.5, 137.9, 128.5, 127.7, 127.4, 126.5, 112.4, 102.3, 69.7, 31.1, 27.9, 22.1, 0.5.
HRMS (ESI): m/z calculated for $[M+H]^+$ 299.1826 g.mol^{-1}, found 299.1826 g.mol^{-1}.
FTIR (film cm^{-1}): 2949, 2851, 1630, 1454, 1367, 1275, 1260, 1217, 1175, 1156, 1111, 838, 764, 750, 695.

(+/-)-(*E*)-6-hydroxy-2-methyl-3-((trimethylsilyl)methylene)cyclohex-1-en-1-yl diisopropylcarbamate **8**

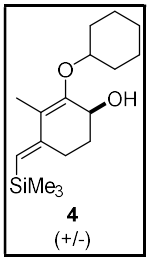


Cyclization was performed following **Conditions B** starting from the alkoxyallene-yne **7** (169 mg, 0.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with

pure cyclohexane) (cyclohexane/ethyl acetate 95/5 to 90/10) afforded pure cyclized product **8** (34 mg, 0.09 mmol, 17 %) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.60 (s, 1H), 4.25 (s, 1H), 4.11 (s, 1H), 4.08 – 3.92 (m, 2H), 2.74 (dddd, *J* = 14.8, 12.5, 4.1, 2.0 Hz, 1H), 2.46 (dt, *J* = 15.0, 4.3 Hz, 1H), 2.01 – 1.91 (m, 1H), 1.88 – 1.79 (m, 1H), 1.77 (s, 3H), 1.36 – 1.22 (m, 12H), 0.16 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 155.1, 151.0, 147.6, 125.9, 124.8, 66.7, 46.8, 31.3, 26.0, 21.5, 20.6, 11.6, 0.2.
HRMS (ESI): m/z calculated for $[M+H]^+$ 340.2302 g.mol^{-1}, found 340.2303 g.mol^{-1}, calculated for $[M+Na]^+$ 362.2122 g.mol^{-1}, found 362.2125 g.mol^{-1}.
FTIR (film cm^{-1}): 3434, 3004, 2967, 2706, 2319, 1685, 1575, 1436, 1370, 1320, 1275, 1260, 1149, 1101, 1078, 1044, 842, 764, 750, 692.

(+/-)-(*E*)-2-(cyclohexyloxy)-3-methyl-4-((trimethylsilyl)methylene)cyclohex-2-enol **4**

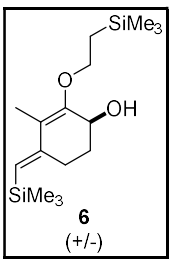


4
(+/-)

Cyclization was performed following **Conditions A** starting from the alkoxyallene-yne **3** (146 mg, 0.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 95/5) afforded clean cyclized product **4** (48 mg, 0.17 mmol, 33 %) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.39 (s, 1H), 4.38 (s, 1H), 4.04 – 3.94 (m, 1H), 2.57 – 2.49 (m, 1H), 2.39 – 2.30 (m, 1H), 2.12 (s, 1H), 2.01 – 1.91 (m, 2H), 1.84 – 1.69 (m, 6H), 1.58 – 1.46 (m, 2H), 1.42 – 1.20 (m, 5H), 0.13 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 152.3, 151.9, 121.5, 121.4, 76.7, 64.9, 33.2, 32.8, 31.6, 26.8, 25.7, 24.2, 24.1, 11.8, 0.4.
HRMS (ESI): m/z calculated for $[M+H]^+$ 295.2088 g.mol^{-1}, found 295.2091 g.mol^{-1}, calculated for $[M+Na]^+$ 317.1907 g.mol^{-1}, found 317.1909 g.mol^{-1}.
FTIR (film cm^{-1}): 3451, 2931, 2856, 1720, 1665, 1451, 1377, 1275, 1259, 1205, 1173, 1074, 1056, 1021, 839, 764, 750, 692.

(+/-)-(*E*)-3-methyl-2-(2-(trimethylsilyl)ethoxy)-4-((trimethylsilyl)methylene)cyclohex-2-enol **6**



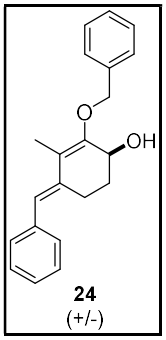
6
(+/-)

Cyclization was performed following **Conditions A** starting from the alkoxyallene-yne **5** (156 mg, 0.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 85/15) afforded clean cyclized product **6** (36 mg, 0.12 mmol, 23 %) as a yellow oil.

Only ^{1}H and ^{13}C NMR are available due to the high instability of the product and its rapid decomposition occurring even neat at -20°C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.41 (s, 1H), 4.40 (s, 1H), 4.06 – 3.96 (m, 1H), 3.89 – 3.80 (m, 1H), 2.58 – 2.47 (m, 1H), 2.36 (ddd, *J* = 14.8, 7.4, 3.7 Hz, 1H), 2.08 (s, 1H), 2.01 – 1.89 (m, 1H), 1.86 – 1.76 (m, 4H), 1.12 – 0.98 (m, 2H), 0.13 (s, 9H), 0.04 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 153.2, 152.2, 121.7, 120.6, 67.6, 64.6, 31.6, 26.7, 19.0, 11.5, 0.4, -1.2.

(+/-)-(*E*)-4-benzylidene-2-(benzyloxy)-3-methylcyclohex-2-enol **24**

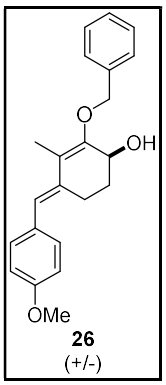


24
(+/-)

Cyclization was performed following **Conditions B** starting from the alkoxyallene-yne **23** (152 mg, 0.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 90/10) afforded clean cyclized product **24** (94 mg, 0.31 mmol, 62 %) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 – 7.18 (m, 10H), 6.47 (s, 1H), 5.04 (d, *J* = 11.7 Hz, 1H), 4.93 (d, *J* = 11.7 Hz, 1H), 4.48 (s, 1H), 2.73 – 2.58 (m, 2H), 2.01 (s, 1H), 1.97 (d, *J* = 1.1 Hz, 3H), 1.93 – 1.78 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 152.9, 138.5, 137.8, 137.8, 129.3, 128.7, 128.2, 128.1, 127.8, 126.3, 123.3, 120.2, 71.8, 64.6, 31.6, 22.5, 11.6.
HRMS (ESI): m/z calculated for $[M+Na]^+$ 329.1512 g.mol^{-1}, found 329.1515 g.mol^{-1}.
FTIR (film cm^{-1}): 3408, 3028, 2927, 1723, 1671, 1623, 1597, 1495, 1453, 1377, 1275, 1260, 1190, 1110, 1078, 1026, 749, 697.

(+/-)-(*E*)-2-(benzyloxy)-4-(4-methoxybenzylidene)-3-methylcyclohex-2-enol **26**

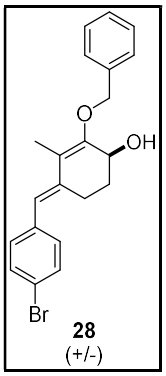


26
(+/-)

Cyclization was performed following **Conditions B** starting from the alkoxyallene-yne **25** (168 mg, 0.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 85/15) afforded clean cyclized product **26** (73 mg, 0.22 mmol, 43 %) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 – 7.37 (m, 4H), 7.37 – 7.30 (m, 1H), 7.25 – 7.19 (m, 2H), 6.93 – 6.85 (m, 2H), 6.41 (s, 1H), 5.02 (d, *J* = 11.7 Hz, 1H), 4.92 (d, *J* = 11.7 Hz, 1H), 4.48 (s, 1H), 3.82 (s, 3H), 2.70 – 2.57 (m, 2H), 2.06 – 2.00 (m, 1H), 1.96 (s, 3H), 1.92 – 1.79 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 158.1, 152.4, 137.9, 136.4, 130.4, 128.7, 128.1, 128.0, 127.8, 122.9, 120.4, 113.7, 71.8, 64.7, 55.4, 31.5, 22.5, 11.6.
HRMS (ESI): m/z calculated for $[M+Na]^+$ 359.1618 g.mol^{-1}, found 359.1623 g.mol^{-1}.
FTIR (film cm^{-1}): 3406, 3030, 3001, 2929, 2835, 1620, 1605, 1507, 1453, 1441, 1377, 1299, 1275, 1246, 1217, 1173, 1108, 1087, 1032, 909, 828, 817, 736, 698.

(+/-)-(*E*)-2-(benzyloxy)-4-(4-bromobenzylidene)-3-methylcyclohex-2-enol **28**

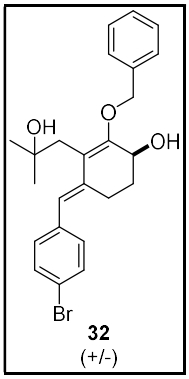


28
(+/-)

Cyclization was performed following **Conditions B** starting from the alkoxyallene-yne **27** (191 mg, 0.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 90/10) afforded pure cyclized product **28** (107 mg, 0.28 mmol, 56 %) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 – 7.37 (m, 6H), 7.36 – 7.31 (m, 1H), 7.15 – 7.11 (m, 2H), 6.37 (s, 1H), 5.04 (d, *J* = 11.8 Hz, 1H), 4.94 (d, *J* = 11.8 Hz, 1H), 4.48 (s, 1H), 2.69 – 2.52 (m, 2H), 2.09 (s, 1H), 1.96 (s, 3H), 1.92 – 1.78 (m, 2H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 153.2, 138.6, 137.7, 137.4, 131.3, 130.8, 128.7, 128.1, 127.7, 122.0, 120.0, 119.8, 71.6, 64.4, 31.4, 22.4, 11.5.
HRMS (ESI): m/z calculated for $[M+Na]^+$ 407.0617 g.mol^{-1}, found 407.0619 g.mol^{-1}.
FTIR (film cm^{-1}): 3373, 3029, 3005, 2922, 2864, 2320, 1903, 1621, 1485, 1453, 1390, 1377, 1275, 1260, 1190, 1072, 1008, 764, 749, 697.

(+/-)-(*E*)-2-(benzyloxy)-4-(4-bromobenzylidene)-3-(2-hydroxy-2-methylpropyl)cyclohex-2-enol **32**



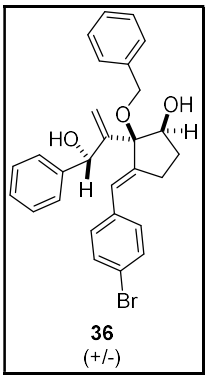
32
(+/-)

Cyclization was performed following **Conditions BE** starting from the alkoxyallene-yne **27** (191 mg, 0.50 mmol) and acetone (40 μL, 0.55 mmol) as the electrophile of the reaction. Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane)

(cyclohexane/ethyl acetate 100/0 to 60/40) afforded pure cyclized and trapped product **32** (139 mg, 0.32 mmol, 63 %) as a bright yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 – 7.39 (m, 2H), 7.39 – 7.35 (m, 4H), 7.35 – 7.30 (m, 1H), 7.10 – 7.04 (m, 2H), 6.43 (s, 1H), 5.15 (d, *J* = 11.8 Hz, 1H), 4.99 (d, *J* = 11.8 Hz, 1H), 4.51 (s, 1H), 3.91 (d, *J* = 6.5 Hz, 1H), 3.27 (s, 1H), 2.83 (d, *J* = 14.6 Hz, 1H), 2.66 – 2.50 (m, 3H), 1.91 (dq, *J* = 13.2, 4.4 Hz, 1H), 1.83 – 1.72 (m, 1H), 1.29 (s, 3H), 1.18 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 154.1, 138.4, 137.3, 137.3, 131.3, 130.8, 128.7, 128.1, 127.5, 122.6, 120.0, 118.9, 72.9, 70.0, 63.0, 37.4, 31.7, 31.5, 29.5, 22.1.
HRMS (ESI): m/z calculated for $[M+Na]^+$ 465.1036 and 467.1019 g.mol^{-1}, found 465.1033 and 467.1018 g.mol^{-1}
FTIR (film cm^{-1}): 3418, 2971, 2927, 2248, 1731, 1669, 1590, 1486, 1453, 1383, 1369, 1275, 1261, 1069, 1009, 975, 907, 822, 763, 749, 729, 697.
$C_{24}H_{27}BrNaO_3$

(+/-)-(1*S*,2*S*,*E*)-2-(benzyloxy)-3-(4-bromobenzylidene)-2-((*R*)-3-hydroxy-3-phenylprop-1-en-2-yl) cyclopentanol **36**

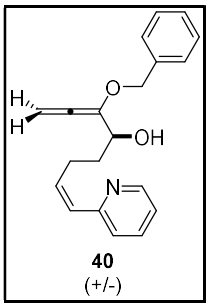


36
(+/-)

Cyclization was performed following **Conditions BE** starting from the alkoxyallene-yne **27** (191 mg, 0.50 mmol) and benzaldehyde (56 μL, 0.55 mmol) as the electrophile of the reaction. Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 90/10) afforded pure cyclized and trapped product **36** (59 mg, 0.12 mmol, 24 %) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 – 7.50 (m, 2H), 7.46 – 7.27 (m, 10H), 7.04 – 6.99 (m, 2H), 6.35 (s, 1H), 5.67 (s, 1H), 5.51 (s, 1H), 5.11 (s, 1H), 4.77 (s, 2H), 4.09 (dd, *J* = 10.9, 3.9 Hz, 1H), 3.75 (s, 1H), 2.88 (s, 1H), 2.76 – 2.64 (m, 1H), 2.23 – 2.13 (m, 1H), 2.02 – 1.90 (m, 1H), 1.89 – 1.81 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 147.5, 140.7, 139.7, 139.0, 136.3, 131.4, 130.9, 128.6, 128.5, 128.5, 128.2, 127.8, 127.1, 126.5, 120.8, 116.6, 82.3, 78.2, 70.6, 65.5, 28.8, 25.4.
HRMS (ESI): m/z calculated for $[M+NH_4]^+$ 508.1482 g.mol^{-1}, found 508.1479 g.mol^{-1}, calculated for $[M+Na]^+$ 513.1036 g.mol^{-1}, found 513.1035 g.mol^{-1}.
FTIR (film cm^{-1}): 3371, 3086, 3061, 3029, 2926, 1952, 1603, 1595, 1495, 1452, 1385, 1275, 1264, 1192, 1070, 1026, 1007, 915, 875, 823, 784, 748, 732, 696.

(+/-)-(*Z*)-3-(benzyloxy)-8-(pyridin-2-yl)octa-1,2,7-trien-4-ol **40**

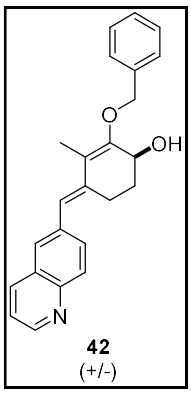


40
(+/-)

Reaction was performed following **Conditions B** starting from the alkoxyallene-yne **38** (153 mg, 0.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 80/20 to 50/50) afforded pure reduced product **40** (65 mg, 0.21 mmol, 42 %) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54 (ddd, *J* = 5.0, 1.9, 0.9 Hz, 1H), 7.67 (td, *J* = 7.7, 1.9 Hz, 1H), 7.41 – 7.32 (m, 4H), 7.32 – 7.26 (m, 1H), 7.17 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.14 (ddd, *J* = 7.6, 5.0, 1.2 Hz, 1H), 6.76 (d, *J* = 3.6 Hz, 1H), 6.51 (d, *J* = 11.6 Hz, 1H), 5.87 (td, *J* = 11.6, 6.2 Hz, 1H), 5.59 – 5.50 (m, 2H), 4.70 (s, 2H), 4.46 – 4.38 (m, 1H), 3.27 (dtdd, *J* = 13.7, 11.4, 4.8, 1.0 Hz, 1H), 2.39 – 2.28 (m, 1H), 2.01 (ddd, *J* = 13.7, 10.0, 4.9 Hz, 1H), 1.96 – 1.88 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 198.1, 155.8, 148.3, 137.8, 137.1, 136.7, 135.9, 128.8, 128.3, 127.8, 127.6, 124.5, 121.7, 91.8, 70.6, 68.4, 33.4, 24.6.
HRMS (ESI): m/z calculated for $[M+H]^+$ 308.1645 g.mol^{-1}, found 308.1650 g.mol^{-1}.
FTIR (film cm^{-1}): 3188, 3064, 3014, 2919, 2865, 2238, 1956, 1723, 1645, 1588, 1583, 1496, 1453, 1275, 1261, 1151, 1077, 1048, 1025, 1001, 909, 763, 747, 729.

(+/-)-(*E*)-2-(benzyloxy)-3-methyl-4-(quinolin-6-ylmethylene)cyclohex-2-enol **42**



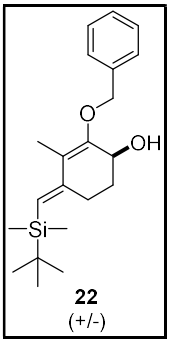
42
(+/-)

Reaction was performed following **Conditions 1.5 × B** starting from the alkoxyallene-yne **41** (89 mg, 0.25 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 60/40) afforded product **42** (16 mg, 0.04 mmol, 18 %) as an orange oil.

Only ^{1}H and ^{13}C NMR are available due to the high instability of the product and its rapid decomposition occurring even neat at -20°C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.86 (dd, *J* = 4.3, 1.7 Hz, 1H), 8.10 (dd, *J* = 8.3, 1.7 Hz, 1H), 8.05 (d, *J* = 8.7 Hz, 1H), 7.67 (s, 1H), 7.63 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.47 – 7.31 (m, 6H), 6.59 (s, 1H), 5.07 (d, *J* = 11.8 Hz, 1H), 4.97 (d, *J* = 11.8 Hz, 1H), 4.52 (t, *J* = 4.1 Hz, 1H), 2.83 – 2.64 (m, 2H), 2.01 (s, 3H), 1.97 – 1.82 (m, 2H), 1.72 (s, 1H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 153.3, 150.0, 146.9, 139.1, 137.6, 136.7, 135.9, 131.5, 128.9, 128.6, 128.2, 128.0, 127.6, 127.2, 122.3, 121.3, 119.7, 71.6, 64.3, 31.4, 22.5, 11.5.

(+/-)-(*E*)-2-(benzyloxy)-4-((*tert*-butyldimethylsilyl)methylene)-3-methylcyclohex-2-enol **22**

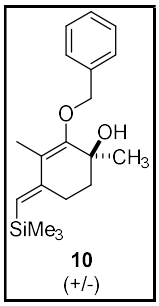


22
(+/-)

Cyclization was performed following **Conditions A** starting from the alkoxyallene-yne **21** (171 mg, 0.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 95/5 to 85/15) afforded pure cyclized product **22** (100 mg, 0.29 mmol, 58 %) as a white crystal.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.35 (m, 4H), 7.34 – 7.30 (m, 1H), 5.47 (s, 1H), 5.01 (d, *J* = 11.8 Hz, 1H), 4.89 (d, *J* = 11.8 Hz, 1H), 4.49 – 4.42 (m, 1H), 2.53 (dddd, *J* = 14.7, 10.5, 4.1, 1.5 Hz, 1H), 2.39 (ddd, *J* = 14.8, 6.9, 3.9 Hz, 2H), 2.10 (s, 1H), 1.98 – 1.89 (m, 1H), 1.89 – 1.78 (m, 3H), 0.92 (s, 9H), 0.13 (s, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 152.9, 152.6, 137.9, 128.7, 128.1, 127.7, 121.2, 119.5, 71.6, 64.6, 31.7, 26.8, 26.7, 17.4, 11.6, -3.8, -3.9.
HRMS (ESI): m/z calculated for $[M+H]^+$ 345.2244 g.mol^{-1}, found 345.2244 g.mol^{-1}, calculated for $[M+Na]^+$ 367.2064 g.mol^{-1}, found 367.2068 g.mol^{-1}.
FTIR (film cm^{-1}): 3339, 2950, 2925, 2854, 1621, 1571, 1469, 1462, 1454, 1384, 1360, 1255, 1247, 1187, 1172, 1113, 1083, 1050, 1006, 908, 823, 805, 776, 749, 696, 582.

(+/-)-(*E*)-2-(benzyloxy)-1,3-dimethyl-4-((trimethylsilyl)methylene)cyclohex-2-enol **10**

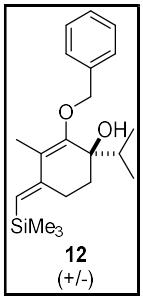


10
(+/-)

Cyclization was performed following **Conditions A** starting from the alkoxyallene-yne **9** (157 mg, 0.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 90/10) afforded clean cyclized product **10** (83 mg, 0.26 mmol, 52 %) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 – 7.28 (m, 5H), 5.50 (s, 1H), 4.99 (d, *J* = 11.4 Hz, 1H), 4.87 (d, *J* = 11.4 Hz, 1H), 2.60 (dddd, *J* = 14.8, 8.8, 4.6, 1.3 Hz, 1H), 2.50 – 2.40 (m, 1H), 2.07 (s, 1H), 1.91 – 1.83 (m, 5H), 1.44 (s, 3H), 0.18 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 156.7, 152.2, 137.9, 128.6, 128.0, 127.6, 122.3, 122.1, 75.8, 71.3, 38.2, 27.8, 26.9, 12.3, 0.3.
HRMS (ESI): m/z calculated for $[M+Na]^+$ 339.1751 g.mol^{-1}, found 339.1756 g.mol^{-1}.
FTIR (film cm^{-1}): 3447, 3065, 3031, 2952, 1616, 1578, 1497, 1453, 1370, 1328, 1275, 1259, 1246, 1149, 1092, 1070, 1016, 858, 834, 764, 749, 694.

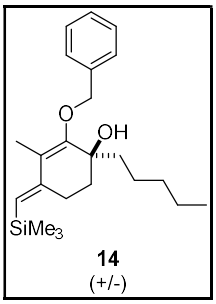
(+/-)-(*E*)-2-(benzyloxy)-1-isopropyl-3-methyl-4-((trimethylsilyl)methylene)cyclohex-2-enol **12**



Cyclization was performed following **Conditions A** starting from the alkoxyallene-yne **11** (171 mg, 0.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 95/5) afforded pure cyclized product **12** (41 mg, 0.12 mmol, 24 %) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 – 7.26 (m, 5H), 5.49 (s, 1H), 4.92 (s, 2H), 2.58 – 2.37 (m, 2H), 2.48 (hept, *J* = 6.9 Hz, 1H), 1.87 (s, 3H), 1.72 – 1.64 (m, 2H), 1.56 (s, 1H), 0.94 (d, *J* = 6.9 Hz, 3H), 0.82 (d, *J* = 6.9 Hz, 3H), 0.16 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 156.8, 152.5, 138.3, 128.7, 128.0, 127.6, 123.6, 121.9, 76.4, 76.0, 34.7, 29.5, 26.9, 18.5, 15.9, 12.3, 0.4.
HRMS (ESI): m/z calculated for $[M+Na]^+$ 367.2064 g.mol^{-1}, found 367.2062 g.mol^{-1}.
FTIR (film cm^{-1}): 3481, 3005, 2956, 2173, 1614, 1575, 1497, 1454, 1393, 1275, 1260, 1172, 1147, 1125, 1011, 857, 839, 764, 750, 696.

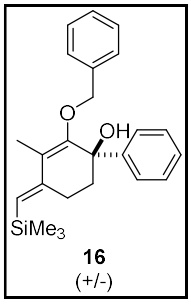
(+/-)-(*E*)-2-(benzyloxy)-3-methyl-1-pentyl-4-((trimethylsilyl)methylene)cyclohex-2-enol **14**



Cyclization was performed following **Conditions A** starting from the alkoxyallene-yne **13** (185 mg, 0.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 95/5) afforded pure cyclized product **14** (55 mg, 0.14 mmol, 29 %) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 – 7.29 (m, 5H), 5.48 (s, 1H), 4.96 (d, *J* = 11.5 Hz, 1H), 4.86 (d, *J* = 11.5 Hz, 1H), 2.58 – 2.48 (m, 1H), 2.43 (ddd, *J* = 14.9, 7.3, 4.1 Hz, 1H), 1.86 (s, 3H), 1.82 – 1.63 (m, 4H), 1.38 – 1.19 (m, 6H), 0.87 (t, *J* = 6.9 Hz, 3H), 0.15 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 157.1, 152.4, 138.1, 128.7, 128.0, 127.7, 122.7, 122.2, 76.0, 73.8, 39.3, 34.4, 32.5, 27.5, 23.6, 22.7, 14.2, 12.4, 0.4.
HRMS (ESI): m/z calculated for $[M+H]^+$ 373.2557 g.mol^{-1}, found 373.2547 g.mol^{-1}, calculated for $[M+Na]^+$ 395.2377 g.mol^{-1}, found 395.2384 g.mol^{-1}.
FTIR (film cm^{-1}): 3452, 2952, 2928, 2859, 1613, 1574, 1454, 1376, 1303, 1246, 1173, 1145, 1084, 1013, 937, 913, 861, 837, 749, 732, 695.

(+/-)-(*E*)-6-(benzyloxy)-5-methyl-4-((trimethylsilyl)methylene)-1,2,3,4-tetrahydro-[1,1'-biphenyl]-1-ol **16**

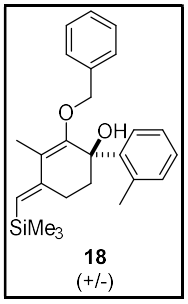


16
(+/-)

Cyclization was performed following **Conditions A** starting from the alkoxyallene-yne **15** (188 mg, 0.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 97.5/2.5) afforded pure cyclized product **16** (67 mg, 0.18 mmol, 35 %) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 – 7.51 (m, 2H), 7.39 – 7.25 (m, 6H), 7.19 – 7.14 (m, 2H), 5.61 (s, 1H), 4.76 (d, *J* = 11.4 Hz, 1H), 4.70 (d, *J* = 11.4 Hz, 1H), 2.75 (s, 1H), 2.57 (ddd, *J* = 15.3, 6.6, 4.1 Hz, 1H), 2.39 – 2.25 (m, 1H), 2.17 – 2.04 (m, 2H), 2.03 (s, 3H), 0.16 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 154.8, 151.9, 145.5, 137.6, 128.6, 128.2, 128.0, 127.7, 127.3, 126.2, 123.7, 123.0, 75.8, 75.3, 40.2, 27.5, 12.5, 0.3.
HRMS (ESI): m/z calculated for $[M+Na]^+$ 401.1907 g.mol^{-1}, found 401.1907 g.mol^{-1}.
FTIR (film cm^{-1}): 3451, 3061, 3005, 2952, 2319, 2174, 1958, 1656, 1606, 1571, 1495, 1448, 1372, 1328, 1280, 1275, 1172, 1091, 1018, 838, 764, 750, 697.

(+/-)-(*E*)-6-(benzyloxy)-2',5-dimethyl-4-((trimethylsilyl)methylene)-1,2,3,4-tetrahydro-[1,1'-biphenyl]-1-ol **18**

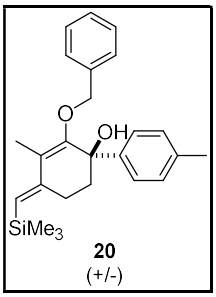


18
(+/-)

Cyclization was performed following **Conditions A** starting from the alkoxyallene-yne **17** (195 mg, 0.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 98/2) afforded clean cyclized product **18** (54 mg, 0.14 mmol, 27 %) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 – 7.53 (m, 1H), 7.31 – 7.07 (m, 8H), 5.57 (s, 1H), 4.77 (d, *J* = 2.0 Hz, 2H), 2.65 – 2.54 (m, 1H), 2.52 (s, 1H), 2.43 (s, 3H), 2.41 – 2.32 (m, 1H), 2.30 – 2.20 (m, 1H), 1.98 (s, 3H), 1.96 – 1.89 (m, 1H), 0.15 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 154.8, 151.7, 143.9, 137.7, 132.3, 132.3, 128.4, 127.8, 127.6, 127.2, 127.1, 125.3, 125.3, 76.3, 74.7, 37.7, 28.1, 21.1, 12.3, 0.2.
HRMS (ESI): m/z calculated for $[M+H]^+$ 393.2244 g.mol^{-1}, found 393.2249 g.mol^{-1}, calculated for $[M+Na]^+$ 415.2064 g.mol^{-1}, found 415.2072 g.mol^{-1}.
FTIR (film cm^{-1}): 3449, 3006, 2989, 2319, 1656, 1607, 1454, 1379, 1275, 1260, 1090, 1021, 842, 764, 750, 699.

(+/-)-(*E*)-6-(benzyloxy)-4',5-dimethyl-4-((trimethylsilyl)methylene)-1,2,3,4-tetrahydro-[1,1'-biphenyl]-1-ol **20**

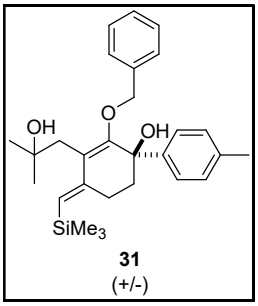


Cyclization was performed following **Conditions A** starting from the alkoxyallene-yne **19** (195 mg, 0.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 95/5) afforded pure cyclized product **20** (147 mg, 0.38 mmol, 75 %) as a yellow oil.

Cyclization was performed following **Conditions A** starting from the alkoxyallene-yne **19** (585 mg, 1.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 95/5) afforded pure cyclized product **20** (420 mg, 1.07 mmol, 71 %) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 – 7.39 (m, 2H), 7.32 – 7.25 (m, 3H), 7.22 – 7.15 (m, 4H), 5.60 (s, 1H), 4.77 (d, J = 11.1 Hz, 1H), 4.72 (d, J = 11.1 Hz, 1H), 2.73 (s, 1H), 2.57 (ddd, J = 15.1, 6.2, 4.0 Hz, 1H), 2.37 (s, 3H), 2.33 – 2.25 (m, 1H), 2.17 – 2.04 (m, 2H), 2.03 (s, 3H), 0.17 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 155.0, 152.0, 142.5, 137.7, 137.0, 128.9, 128.5, 128.0, 127.7, 126.2, 123.5, 122.8, 75.7, 75.3, 40.1, 27.6, 21.2, 12.5, 0.3.
HRMS (ESI): m/z calculated for $[M+Na]^+$ 415.2064 g.mol^{-1}, found 415.2064 g.mol^{-1}, calculated for $[M+K]^+$ 431.1803 g.mol^{-1}, found 431.1810 g.mol^{-1}.
FTIR (film cm^{-1}): 3552, 3030, 2951, 2924, 2246, 2175, 1609, 1570, 1510, 1453, 1406, 1260, 1246, 1169, 1086, 1018, 908, 857, 835, 818, 764, 748, 694.

(+/-)-(*E*)-6-(benzyloxy)-5-(2-hydroxy-2-methylpropyl)-4'-methyl-4-((trimethylsilyl)methylene)-1,2,3,4-tetrahydro-[1,1'-biphenyl]-1-ol **31**

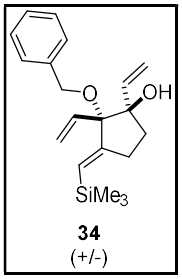


Cyclization was performed following **Conditions AE** starting from the alkoxyallene-yne **19** (195 mg, 0.50 mmol) and acetone (40 μL, 0.55 mmol) as the electrophile of the reaction. Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 95/5) afforded pure cyclized and trapped product **31** (171 mg, 0.38 mmol, 76 %) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 – 7.43 (m, 2H), 7.28 – 7.22 (m, 3H), 7.20 – 7.15 (m, 2H), 7.11 – 7.07 (m, 2H), 5.63 (s, 1H), 4.68 (d, J = 11.3 Hz, 1H), 4.64 (d, J = 11.3 Hz, 1H), 3.14 (s, 1H), 2.74 (s, 1H), 2.71 (d, J = 2.2 Hz, 2H), 2.63 – 2.53 (m, 1H), 2.44 – 2.31 (m, 4H), 2.15 – 1.99 (m, 2H), 1.20 (s, 6H), 0.13 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 155.3, 151.3, 142.0, 137.2, 137.0, 129.0, 128.6, 128.1, 127.8, 125.9, 124.6, 75.6, 73.8, 72.6, 42.0, 38.0, 30.9, 30.4, 27.9, 21.2, 0.3.
HRMS (ESI): m/z calculated for $[M+H]^+$ 451.2663 g.mol^{-1}, found 451.2664 g.mol^{-1}, calculated for $[M+Na]^+$ 473.2482 g.mol^{-1}, found 473.2481 g.mol^{-1}.
FTIR (film cm^{-1}): 3389, 2954, 1598, 1511, 1454, 1377, 1247, 1181, 1134, 1103, 1022, 945, 904, 845, 819, 749, 697.

(+/-)-(1*R*,2*S*,*E*)-2-(benzyloxy)-3-((trimethylsilyl)methylene)-1,2-divinylcyclopentanol **34**

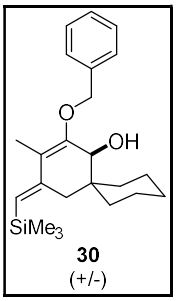


34
(+/-)

Cyclization was performed following **Conditions A** starting from the alkoxyallene-yne **33** (163 mg, 0.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 95/5) afforded pure cyclized product **34** (36 mg, 0.11 mmol, 22 %) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.22 (m, 5H), 6.36 (dd, *J* = 17.5, 10.9 Hz, 1H), 5.82 (dd, *J* = 17.9, 11.2 Hz, 1H), 5.60 (t, *J* = 2.6 Hz, 1H), 5.54 (dd, *J* = 11.2, 1.8 Hz, 1H), 5.32 (dd, *J* = 17.9, 1.8 Hz, 1H), 5.27 (dd, *J* = 17.5, 1.0 Hz, 1H), 5.18 (dd, *J* = 10.9, 1.0 Hz, 1H), 4.27 (s, 2H), 2.71 – 2.58 (m, 1H), 2.47 (ddd, *J* = 15.3, 10.2, 3.8 Hz, 1H), 2.36 – 2.25 (m, 1H), 1.77 – 1.68 (m, 1H), 1.51 (s, 1H), 0.14 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 157.2, 140.0, 139.7, 135.0, 128.3, 127.7, 127.1, 127.0, 121.4, 114.1, 92.1, 84.2, 65.4, 35.3, 29.0, -0.3.
HRMS (ESI): m/z calculated for $[M+Na]^+$ 351.1751 g.mol^{-1}, found 351.1747 g.mol^{-1}.
FTIR (film cm^{-1}): 3480, 3088, 3030, 2952, 1731, 1620, 1453, 1407, 1375, 1275, 1259, 1248, 1119, 1055, 1028, 999, 919, 846, 764, 749, 696.

(+/-)-(*E*)-2-(benzyloxy)-3-methyl-4-((trimethylsilyl)methylene)spiro[5.5]undec-2-en-1-ol **30**



30
(+/-)

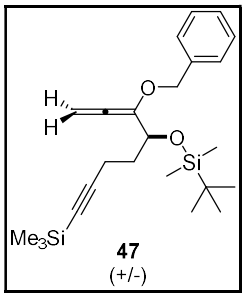
Cyclization was performed following **Conditions A** starting from the alkoxyallene-yne **29** (184 mg, 0.50 mmol). Purification by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) (cyclohexane/ethyl acetate 100/0 to 95/5) afforded clean cyclized product **30** (68 mg, 0.19 mmol, 37 %) as a colourless oil.

Only ^{1}H and ^{13}C NMR are available due to the high instability of the product and its rapid decomposition occurring even neat at -20°C.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 – 7.29 (m, 5H), 5.52 (s, 1H), 5.03 (d, *J* = 11.9 Hz, 1H), 4.94 (d, *J* = 11.9 Hz, 1H), 4.08 (s, 1H), 2.43 (d, *J* = 15.0 Hz, 1H), 2.30 (d, *J* = 15.0 Hz, 1H), 1.86 (s, 3H), 1.67 – 1.19 (m, 10H), 0.20 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1, 150.1, 138.0, 128.6, 127.6, 127.5, 123.2, 119.5, 71.3, 71.2, 37.6, 32.8, 27.0, 22.2, 22.0, 21.7, 11.0, 0.6.

Synthesis of the protected alcohol cyclization precursors

(+/-)-(6-(benzyloxy)-5-((*tert*-butyldimethylsilyl)oxy)octa-6,7-dien-1-yn-1-yl)trimethylsilane **47**

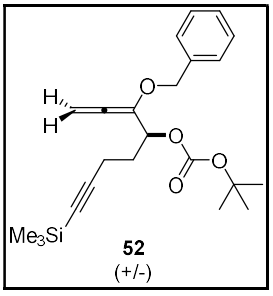


47
(+/-)

To a solution of **1** (2.55 g, 8.48 mmol, 1 equiv) under argon atmosphere in dry dichloromethane at room temperature (85 mL, 0.1 M) was added 2.6-lutidine (3.93 mL, 34.0 mmol, 4 equiv) and the mixture was stirred for 10 min. *Tert*-butyldimethylsilyl trifluoromethanesulfonate (5.85 mL, 25.4 mmol, 3 equiv) was then added dropwise and the solution was stirred at room temperature for 2 hours. After total completion, monitored by TLC, water (50 mL) was added and the aqueous layer was extracted with dichloromethane (2 × 40 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over deactivated silica gel (cyclohexane/ethyl acetate 100/0 to 98/2) afforded pure **47** (2.74 g, 6.61 mmol, 78 %) as a yellow liquid.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.26 (m, 5H), 5.47 (dd, *J* = 7.7, 1.2 Hz, 1H), 5.43 (dd, *J* = 7.7, 1.2 Hz, 1H), 4.63 (d, *J* = 12.2 Hz, 1H), 4.60 (d, *J* = 12.1 Hz, 1H), 4.34 (ddt, *J* = 7.1, 5.7, 1.3 Hz, 1H), 2.33 – 2.26 (m, 2H), 1.96 – 1.86 (m, 2H), 0.89 (s, 9H), 0.14 (s, 9H), 0.08 (s, 3H), 0.04 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 198.7, 137.8, 134.6, 128.4, 127.8, 127.7, 107.3, 91.3, 84.8, 71.2, 70.6, 34.3, 26.1, 18.4, 16.3, 0.3, -4.4, -4.9.
HRMS and UV analysis not available due to quick and intensive degradation

(+/-)-3-(benzyloxy)-8-(trimethylsilyl)octa-1,2-dien-7-yn-4-yl *tert*-butyl carbonate **52**



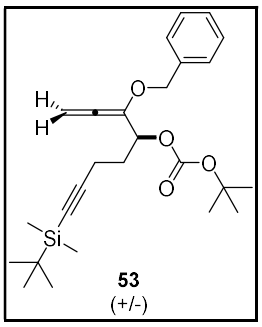
52
(+/-)

To a solution of **1** (1.50 g, 5.00 mmol, 1 equiv) under argon atmosphere in dry dichloromethane at 0°C (15 mL, 0.1 M), was added DMAP (61 mg, 0.50 mmol, 0.1 equiv), followed by Boc_2O (1.31 g, 6.00 mmol, 1.2 equiv) and the solution was stirred at 0°C for 3 hours. After total completion, monitored by TLC, water (10 mL) was added and the aqueous layer was extracted with dichloromethane (2 × 15 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure.

Purification of the crude by flash chromatography over deactivated silica gel (cyclohexane/ethyl acetate 100/0 to 90/10) afforded clean **52** (1.59 g, 3.95 mmol, 79 %) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.27 (m, 5H), 5.56 (dd, *J* = 8.2, 1.7 Hz, 1H), 5.52 (dd, *J* = 8.2, 1.7 Hz, 1H), 5.25 – 5.21 (m, 1H), 4.64 (s, 2H), 2.33 – 2.27 (m, 2H), 2.07 – 1.99 (m, 2H), 1.47 (s, 9H), 0.14 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 198.2, 152.9, 137.4, 131.2, 128.4, 127.8, 127.6, 106.0, 92.6, 85.2, 82.3, 74.4, 70.7, 30.9, 27.9, 16.2, 0.2.
HRMS (ESI): m/z calculated for $[M+Na]^+$ 423.1962 g.mol^{-1}, found 423.1960 g.mol^{-1}.

(+/-)-3-(benzyloxy)-8-(*tert*-butyldimethylsilyl)octa-1,2-dien-7-yn-4-yl tert-butyl carbonate **53**



To a solution of **21** (315 mg, 0.91 mmol, 1 equiv) under argon atmosphere in dry dichloromethane (9 mL, 0.1 M), was added at 0°C DMAP (11 mg, 0.09 mmol, 0.1 equiv), followed by Boc_2O (241 mg, 1.09 mmol, 1.2 equiv) and the solution was stirred at 0°C for 3 hours. After total completion, monitored by TLC, water (2 mL) was added and the aqueous layer was extracted with dichloromethane (2 × 5 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over deactivated silica gel (cyclohexane/ethyl acetate 100/0 to 90/10) afforded clean **53** (256 mg, 0.60 mmol, 66 %) as an orange oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.27 (m, 5H), 5.56 (dd, *J* = 8.2, 1.6 Hz, 1H), 5.51 (dd, *J* = 8.2, 1.6 Hz, 1H), 5.23 (ddt, *J* = 7.5, 6.0, 1.5 Hz, 1H), 4.64 (s, 2H), 2.35 – 2.28 (m, 2H), 2.09 – 1.97 (m, 2H), 1.47 (s, 9H), 0.92 (s, 9H), 0.07 (s, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 198.1, 152.8, 137.5, 131.2, 128.4, 127.8, 127.6, 106.5, 92.7, 83.4, 82.3, 74.4, 70.7, 31.2, 27.9, 26.2, 16.6, 16.3, -4.3.
HRMS and UV analysis not available due to quick and intensive degradation

General procedures for the low-valent titanium mediated cyclization

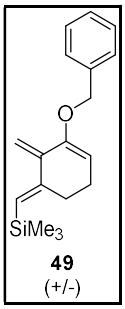
- ✓ **Conditions C1 :**

To a solution of $Ti(O\textit{i}Pr)_4$ (2.5 equiv), under argon atmosphere in dry Et_2O (0.05 M) at -40°C was slowly added a solution of *i*PrMgCl (5.0 equiv, in Et_2O). The resulting brown/black solution was kept at this temperature for 10 minutes before putting it in an ice bath and immediate addition of a solution of the corresponding alkoxyallen-yne (1.0 equiv) in dry Et_2O (0.05 M) by cannula. After total completion, monitored by TLC, water (15 mL) and Et_2O (15 mL) were added. The white precipitate was filtered through a Celite® pad and washed with Et_2O (15 mL). The aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) afforded the corresponding cyclized product.

- ✓ **Conditions C2 :**

To a solution of Ti(O*i*Pr)$_4$ (2.5 equiv), under argon atmosphere in dry toluene (0.05 M), at -40°C was slowly added a solution of *i*PrMgCl (5.0 equiv, in Et_2O). The resulting brown/black solution was kept at this temperature for 10 minutes before putting it in an ice bath and immediate addition of a solution of the corresponding alkoxyallen-yne (1.0 equiv) in dry toluene (0.05 M) by cannula. After total completion, monitored by TLC, water (15 mL) and Et_2O (15 mL) were added. The white precipitate was filtered through a Celite® pad and washed with Et_2O (15 mL). The aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the crude by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure cyclohexane) afforded the corresponding cyclized product.

(*E*)-((3-(benzyloxy)-2-methylenecyclohex-3-en-1-ylidene)methyl)trimethylsilane **49**

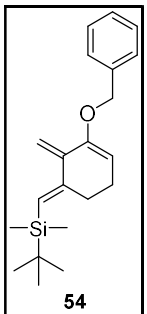


49
(+/-)

Cyclization was performed following **Conditions C2** starting from the alkoxyallene-yne **52** (80 mg, 0.20 mmol). Compound **49** was not stable over deactivated silica gel and could not be isolated in a pure form. Only ^{1}H NMR data of the crude **49** are available (44% by ^{1}H NMR integration).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.26 (m, 5H), 5.84 (s, 1H), 5.44 (s, 1H), 5.30 (s, 1H), 5.10 (t, *J* = 4.4 Hz, 1H), 4.83 (s, 2H), 2.48 (t, *J* = 6.2 Hz, 2H), 2.29 (dt, *J* = 6.2, 4.4 Hz, 1H), 0.17 (s, 9H).
HRMS (ESI): m/z calculated for $[M+H]^+$ 285.1664 g.mol^{-1}, found 285.1669 g.mol^{-1}.

(*E*)-((3-(benzyloxy)-2-methylenecyclohex-3-en-1-ylidene)methyl)(*tert*-butyl)dimethylsilane **54**

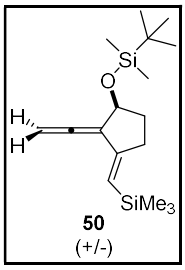


54
(+/-)

Cyclization was performed following **Conditions C2** starting from the alkoxyallene-yne **53** (85 mg, 0.20 mmol). Purifications by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure pentane) (pentane) afforded **54** (19 mg, 0.06 mmol, 29%) as a colourless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.29 (m, 5H), 5.84 (s, 1H), 5.44 (dd, *J* = 1.8, 0.8 Hz, 1H), 5.30 – 5.26 (m, 1H), 5.13 – 5.07 (m, 1H), 4.83 (s, 2H), 2.47 (t, *J* = 6.3 Hz, 2H), 2.32 – 2.23 (m, 2H), 0.92 (s, 9H), 0.13 (s, 6H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 154.5, 151.3, 143.2, 137.8, 128.5, 127.7, 127.4, 120.3, 107.2, 100.6, 69.2, 31.6, 26.6, 25.0, 17.2, -3.8.
HRMS and UV analysis not available due to quick and intensive degradation

(+/-)-(*E*)-*tert*-butyldimethyl((3-((trimethylsilyl)methylene)-2-vinylidenecyclopentyl)oxy)silane **50**

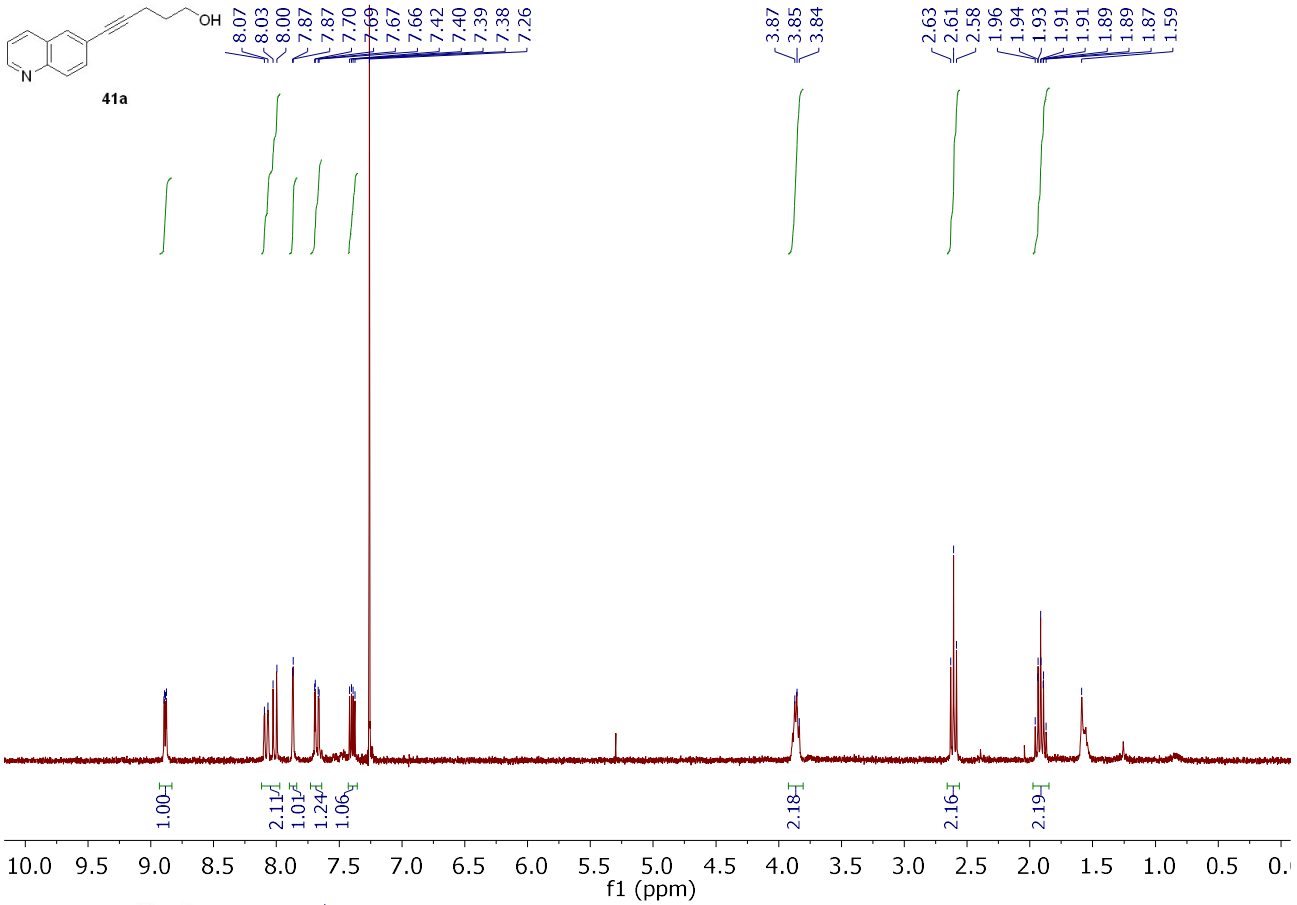


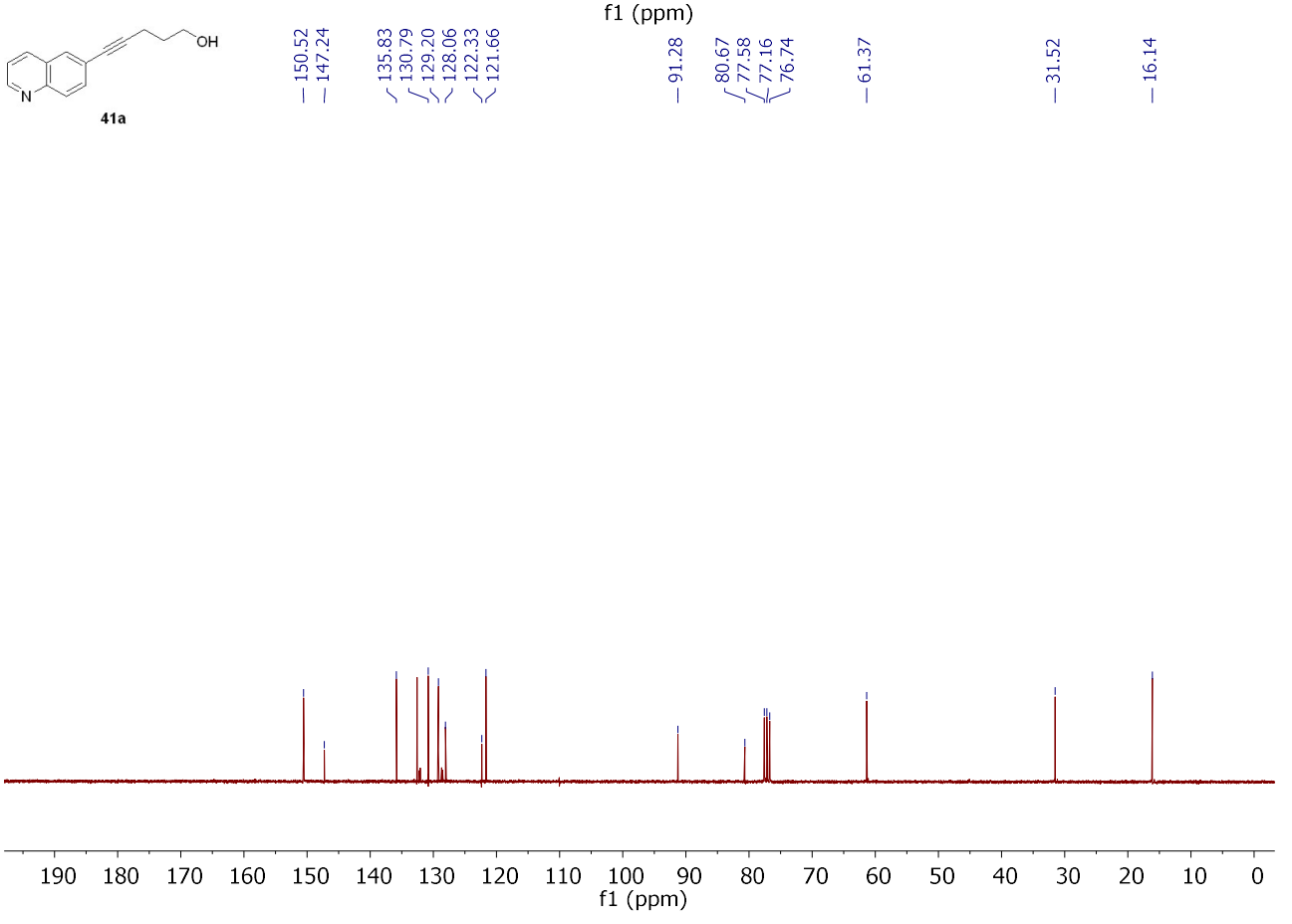
50
(+/-)

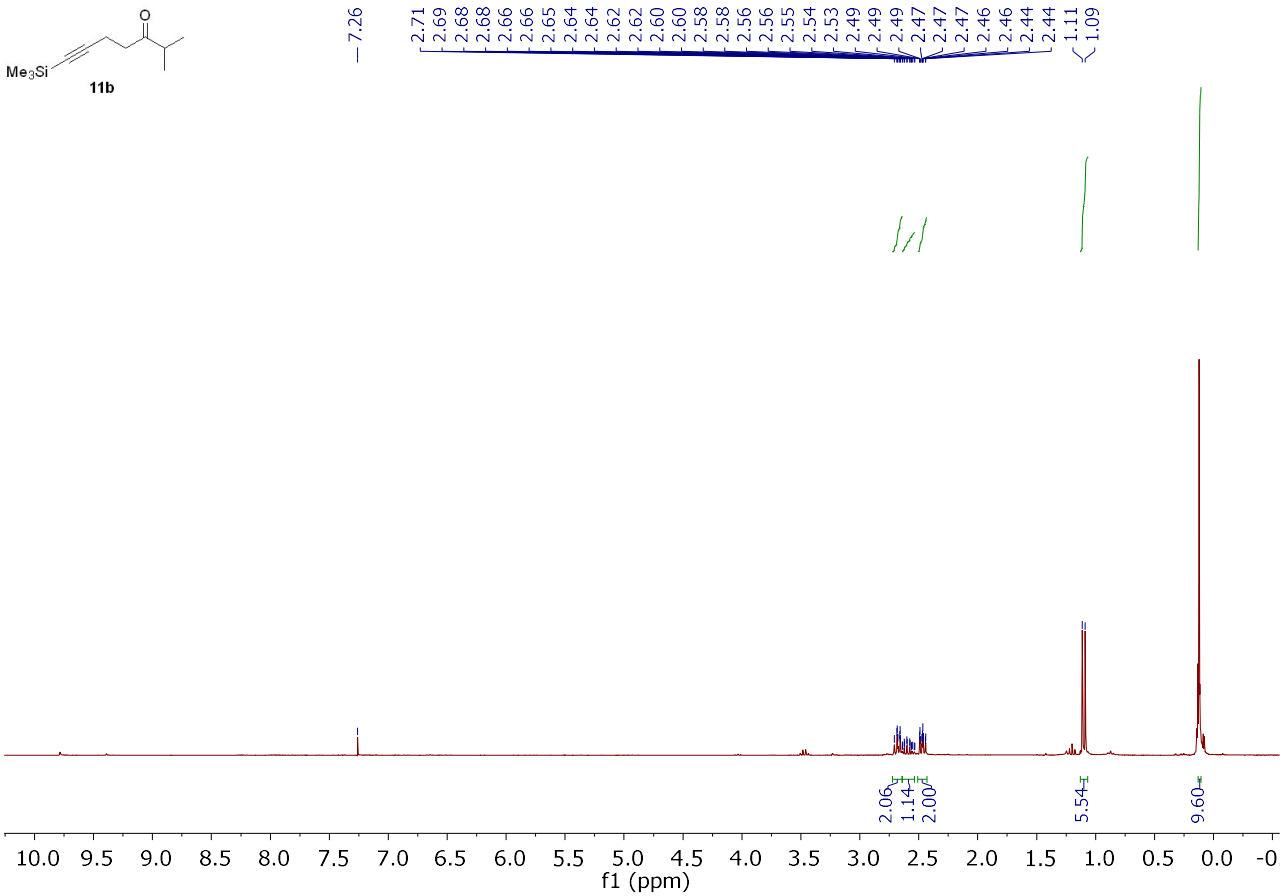
Cyclization was performed following **Conditions C1** starting from the alkoxyallene-yne **47** (83 mg, 0.20 mmol). Several purifications by flash chromatography over deactivated silica gel (by 5% Et_3N and washed with pure pentane) (pentane) afforded cyclized product **50** as traces (46 % by NMR integration of the crude).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.71 (s, 1H), 5.24 – 5.17 (m, 1H), 5.16 – 5.09 (m, 1H), 4.76 (tt, J = 6.2, 3.4 Hz, 1H), 2.65 – 2.53 (m, 1H), 2.37 – 2.28 (m, 1H), 1.95 (ddt, J = 12.2, 7.7, 6.2 Hz, 1H), 1.80 – 1.68 (m, 1H), 0.89 (s, 9H), 0.11 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$): δ 205.6, 152.9, 121.4, 112.4, 81.4, 75.0, 35.4, 30.3, 26.0, 18.4, -0.2, -4.2, -4.6.
HRMS (ESI): m/z calculated for $[M+H]^+$ 309.2064 g.mol^{-1}, found 309.2058 g.mol^{-1}.

4. NMR spectra



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2.68
2.68
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2.65
2.64
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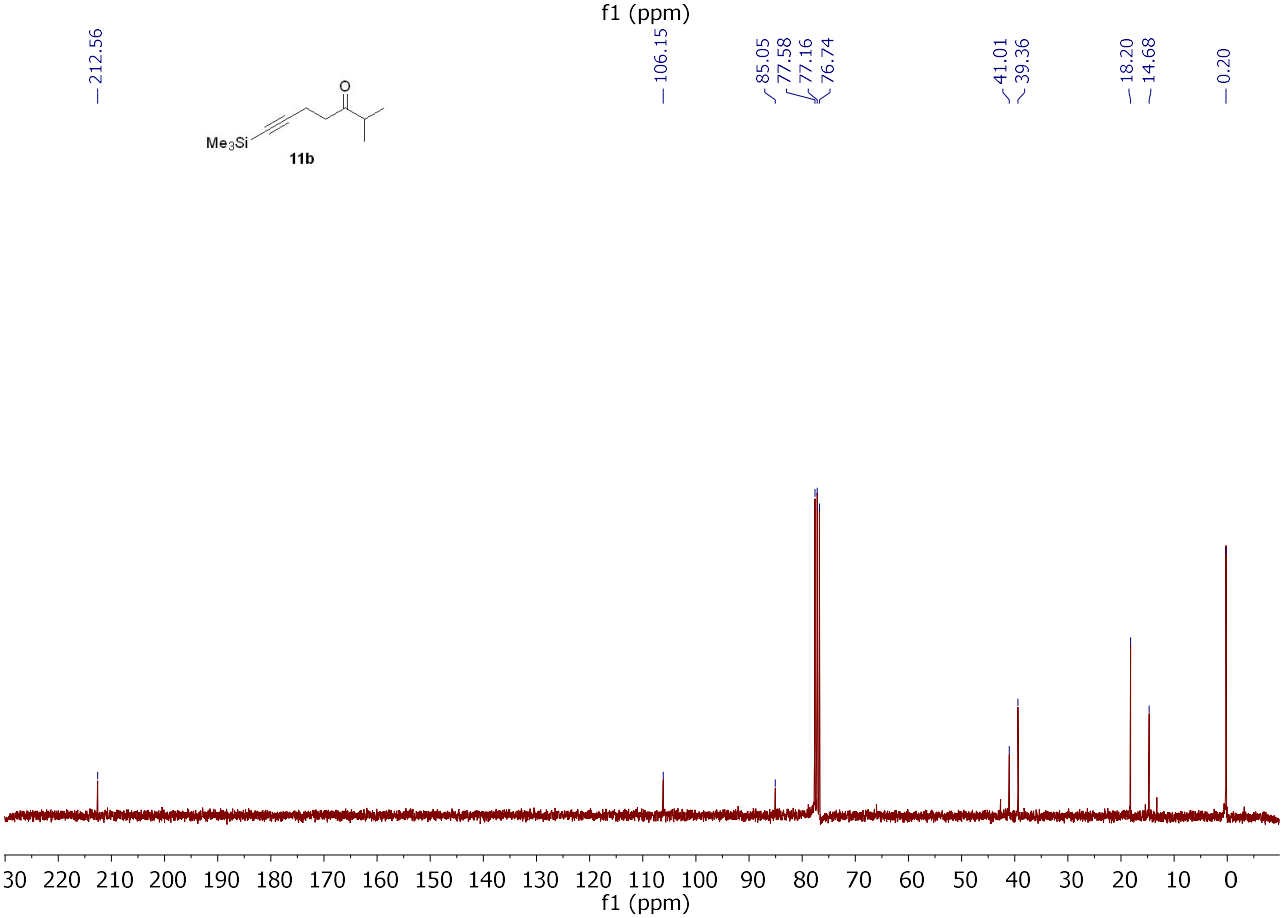
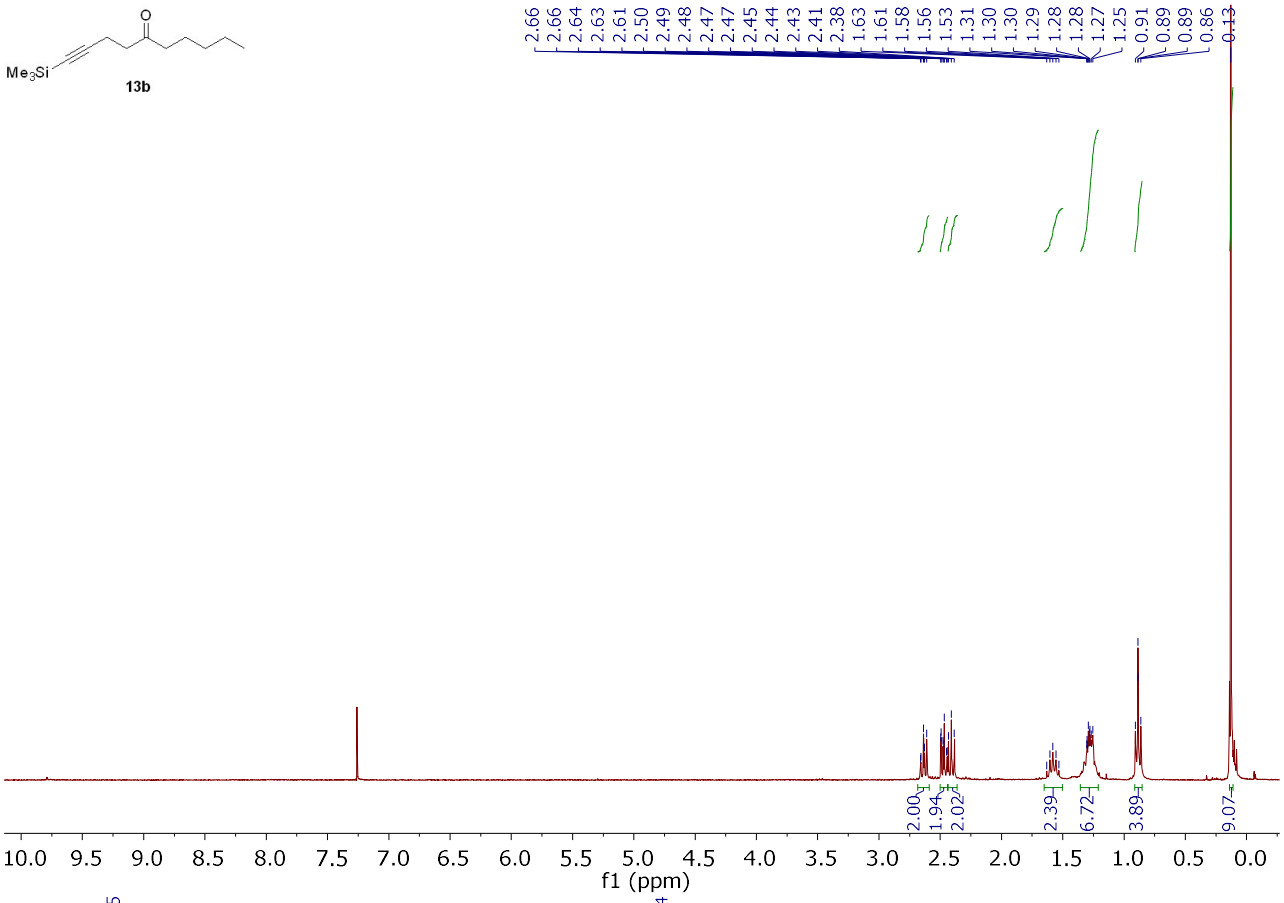
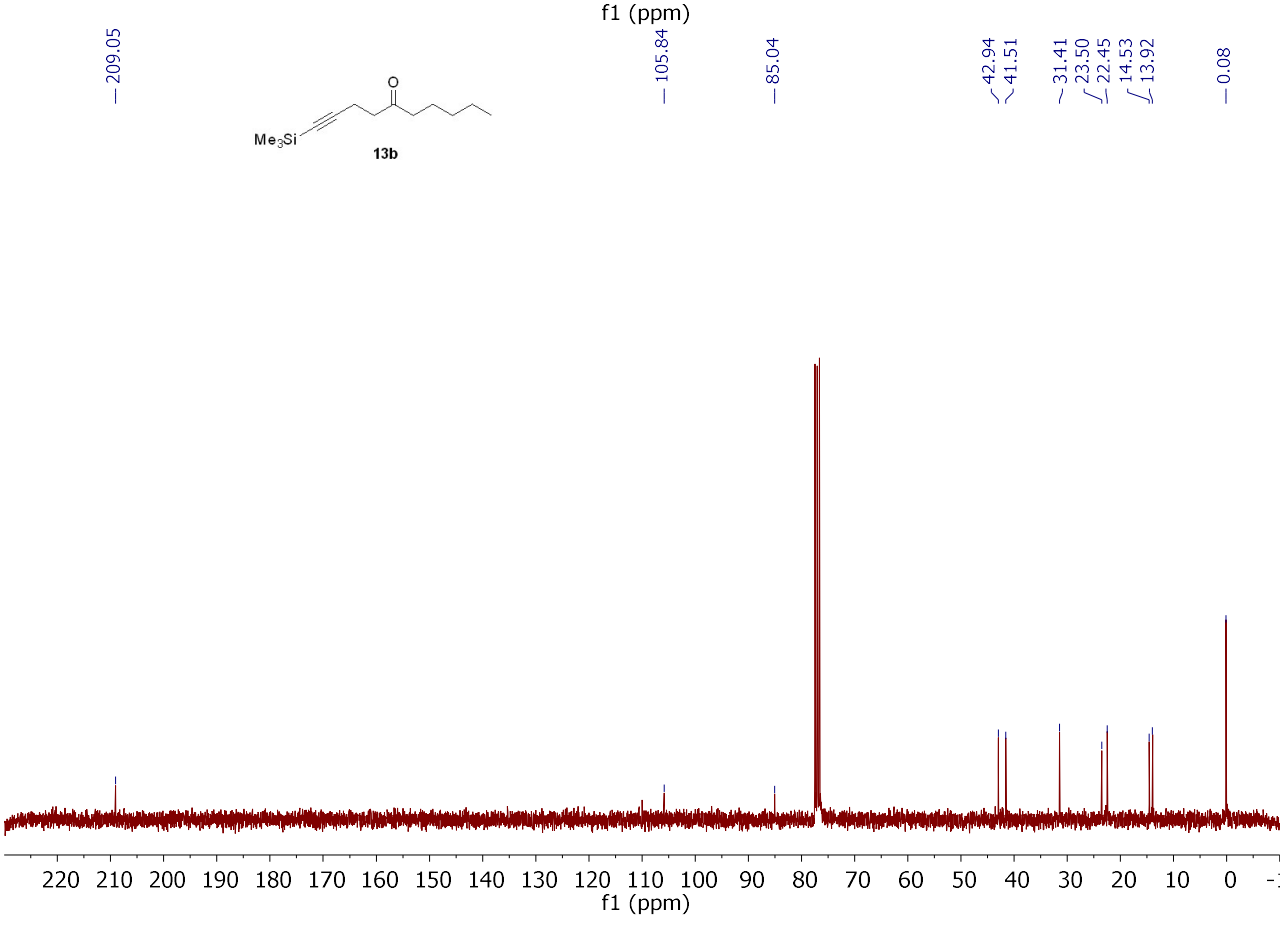
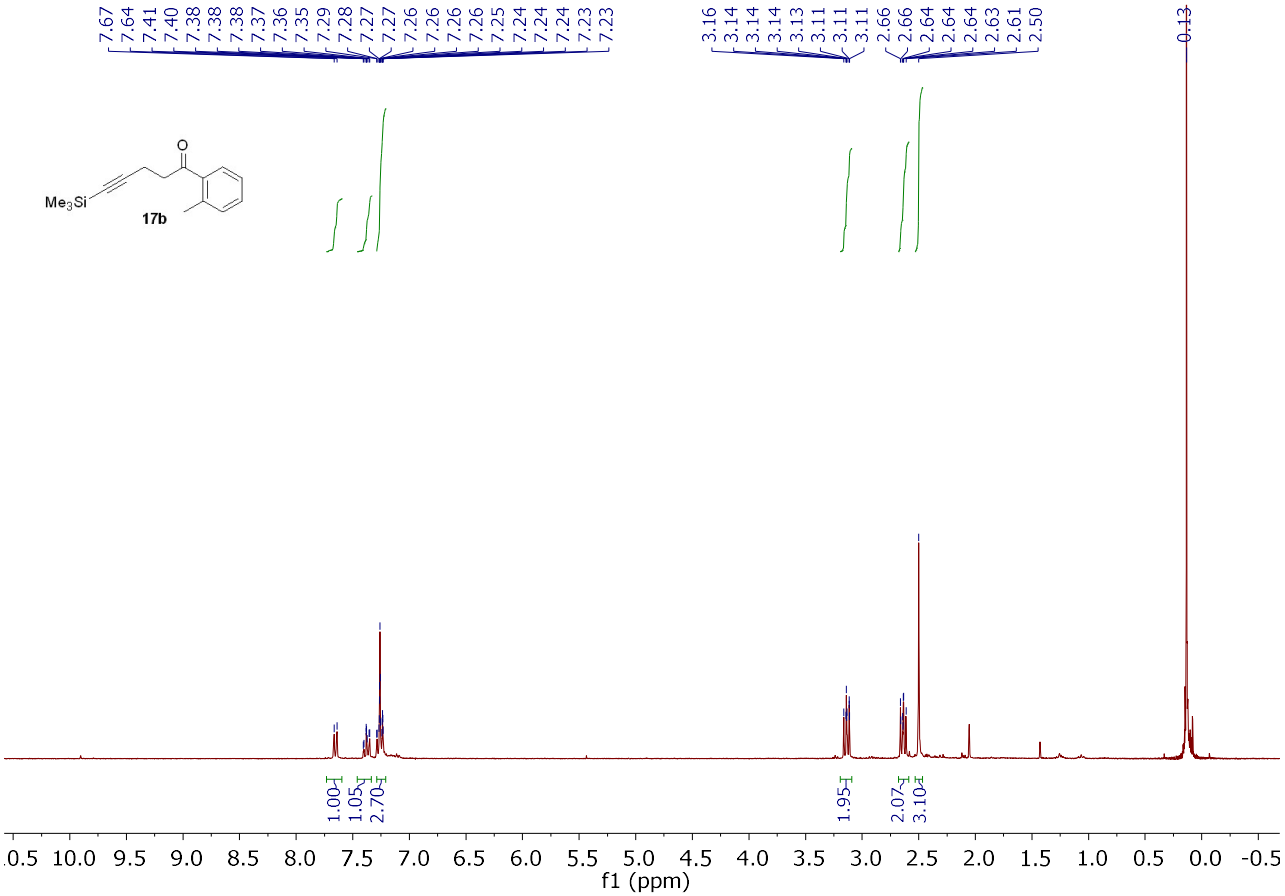
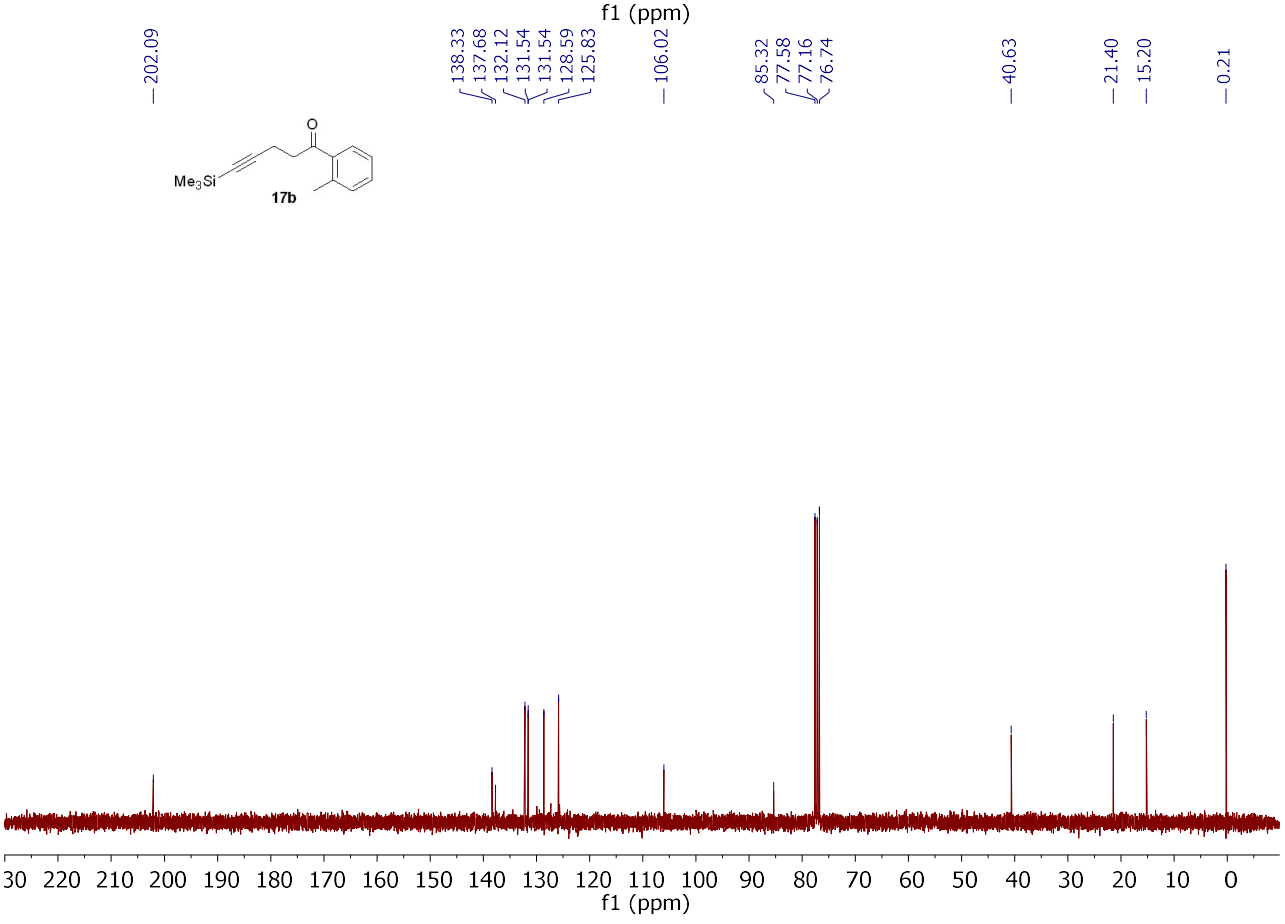
2.62
2.62
2.60
2.60
2.58
2.58
2.56
2.56
2.55
2.54
2.53
2.49
2.49
2.49
2.47
2.47
2.47
2.46
2.46
2.44
2.44
1.11
1.09
2.06
1.14
2.00
5.54
9.60
f1 (ppm)


212.56
106.15
85.05
77.58
77.16
76.74
41.01
39.36
18.20
14.68
0.20
Me3Si
11b
f1 (ppm)


Me3Si
13b
2.66
2.66
2.64
2.63
2.61
2.50
2.49
2.48
2.47
2.47
2.45
2.44
2.43
2.41
2.38
1.63
1.61
1.58
1.56
1.53
1.31
1.30
1.30
1.29
1.28
1.28
1.27
1.25
0.91
0.89
0.89
0.86
0.13
2.00
1.94
2.02
2.39
6.72
3.89
9.07
10.0 9.5 9.0 8.5 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 0.5 0.0
f1 (ppm)


209.05
105.84
85.04
42.94
41.51
31.41
23.50
22.45
14.53
13.92
0.08
Me3Si
13b
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.67 7.64 7.41 7.40 7.38 7.38 7.38 7.37 7.36 7.35 7.29 7.28 7.27 7.27 7.26 7.26 7.26 7.25 7.24 7.24 7.24 7.23 7.23
3.16 3.14 3.14 3.14 3.13 3.11 3.11 3.11 2.66 2.66 2.64 2.64 2.64 2.63 2.61 2.50
0.13
O
Me3Si
17b
1.00 1.05 2.70 1.95 2.07 3.10
f1 (ppm)


202.09
138.33 137.68 132.12 131.54 131.54 128.59 125.83
106.02
85.32 77.58 77.16 76.74
40.63
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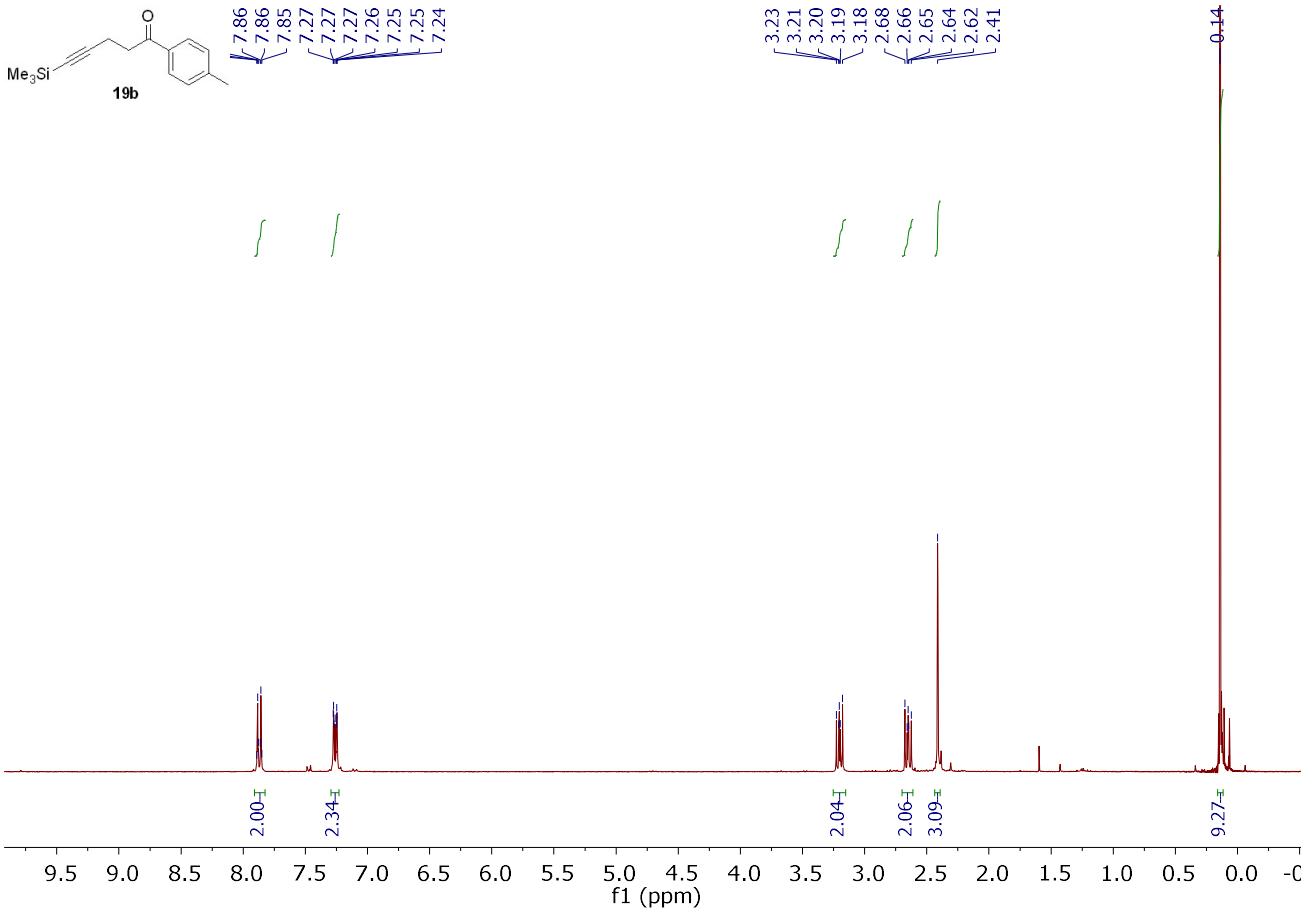
0.21
O
Me3Si
17b
f1 (ppm)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19b
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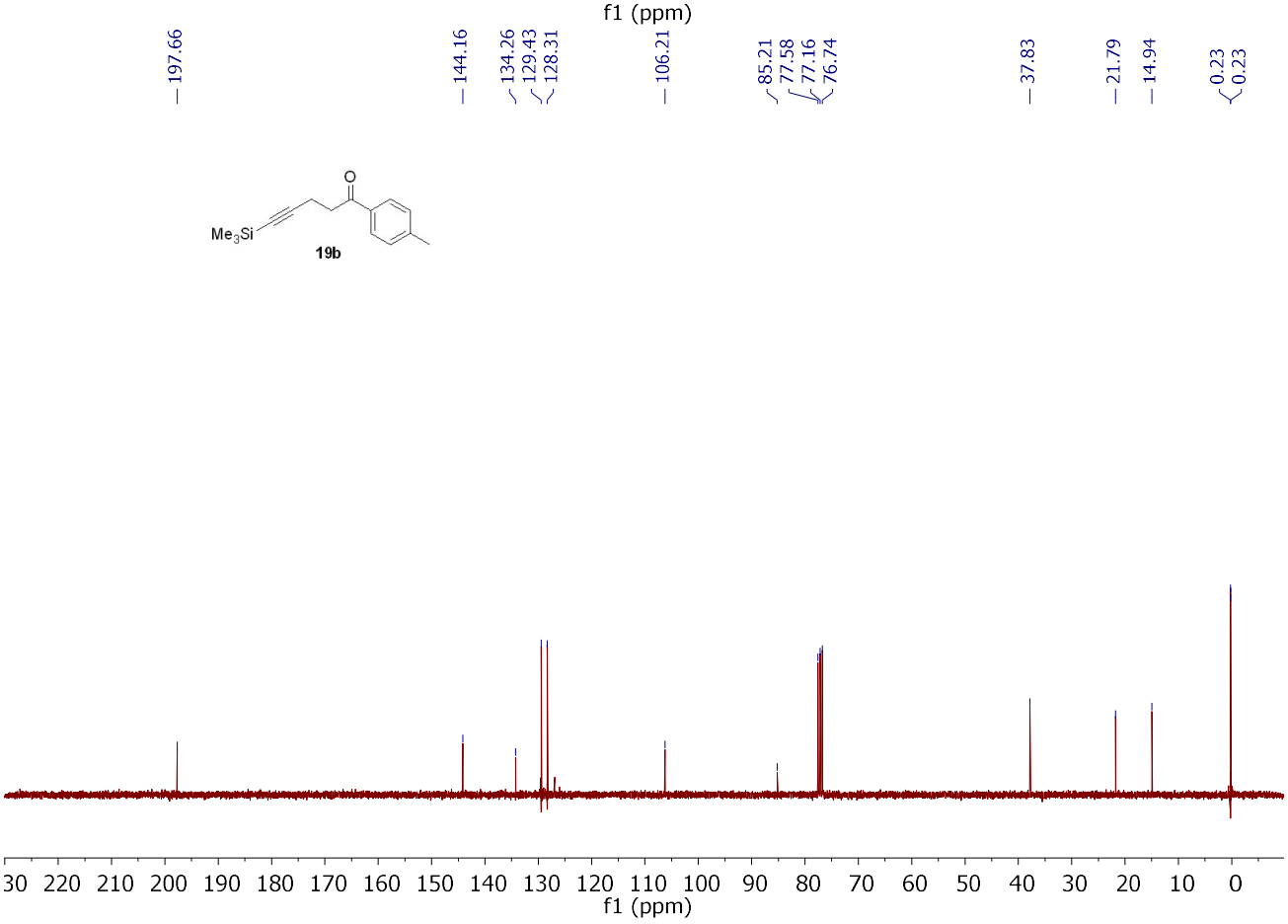
7.86
7.85
7.27
7.27
7.27
7.26
7.25
7.25
7.24
3.23
3.21
3.20
3.19
3.18
2.68
2.66
2.65
2.64
2.62
2.41
0.14
2.00
2.34
2.04
2.06
3.09
9.27
f1 (ppm)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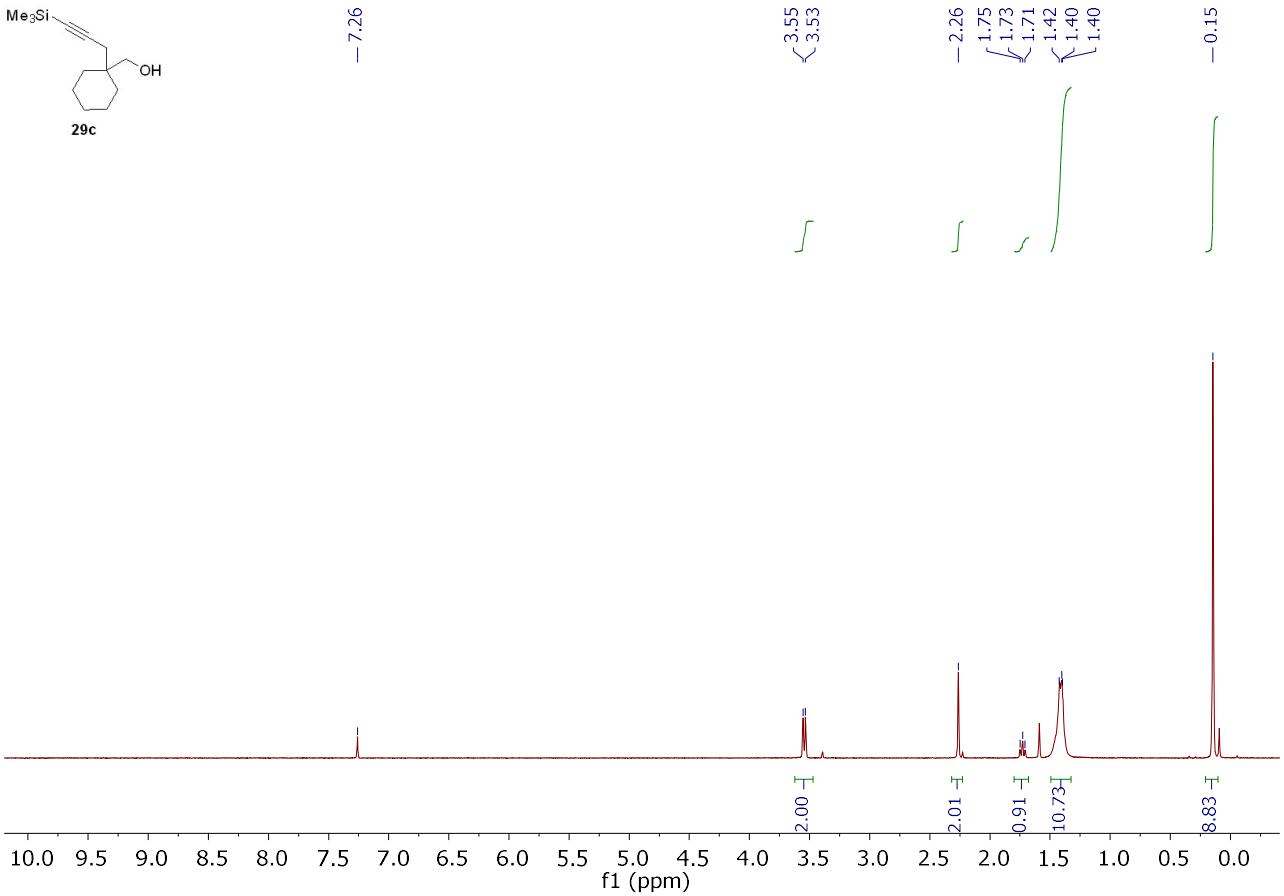
144.16
134.26
129.43
128.31
106.21
85.21
77.58
77.16
76.74
37.83
21.79
14.94
0.23
0.23
Me3Si
19b
f1 (ppm)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OH
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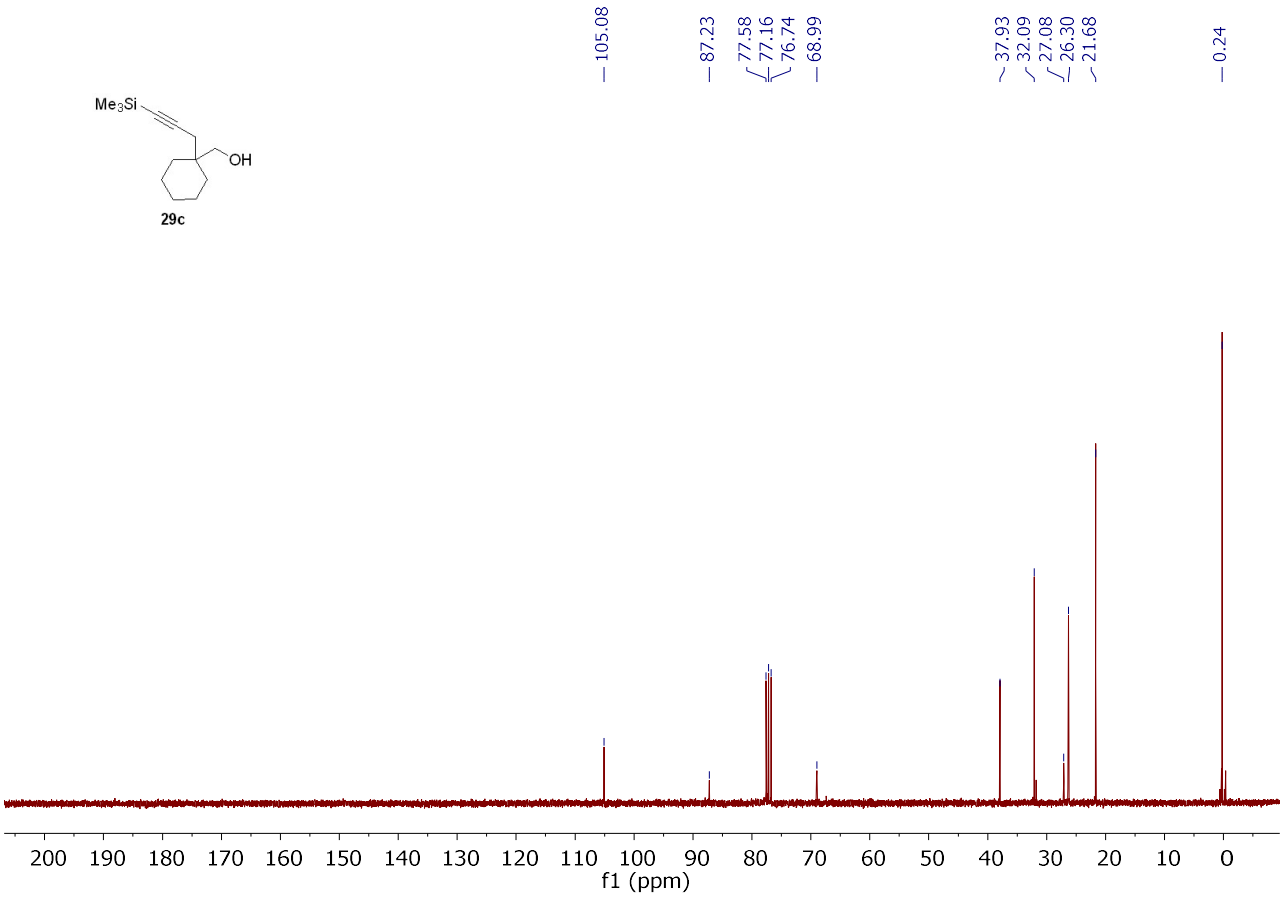
3.55
3.53
2.26
1.75
1.73
1.71
1.42
1.40
1.40
0.15
2.00
2.01
0.91
10.73
8.83
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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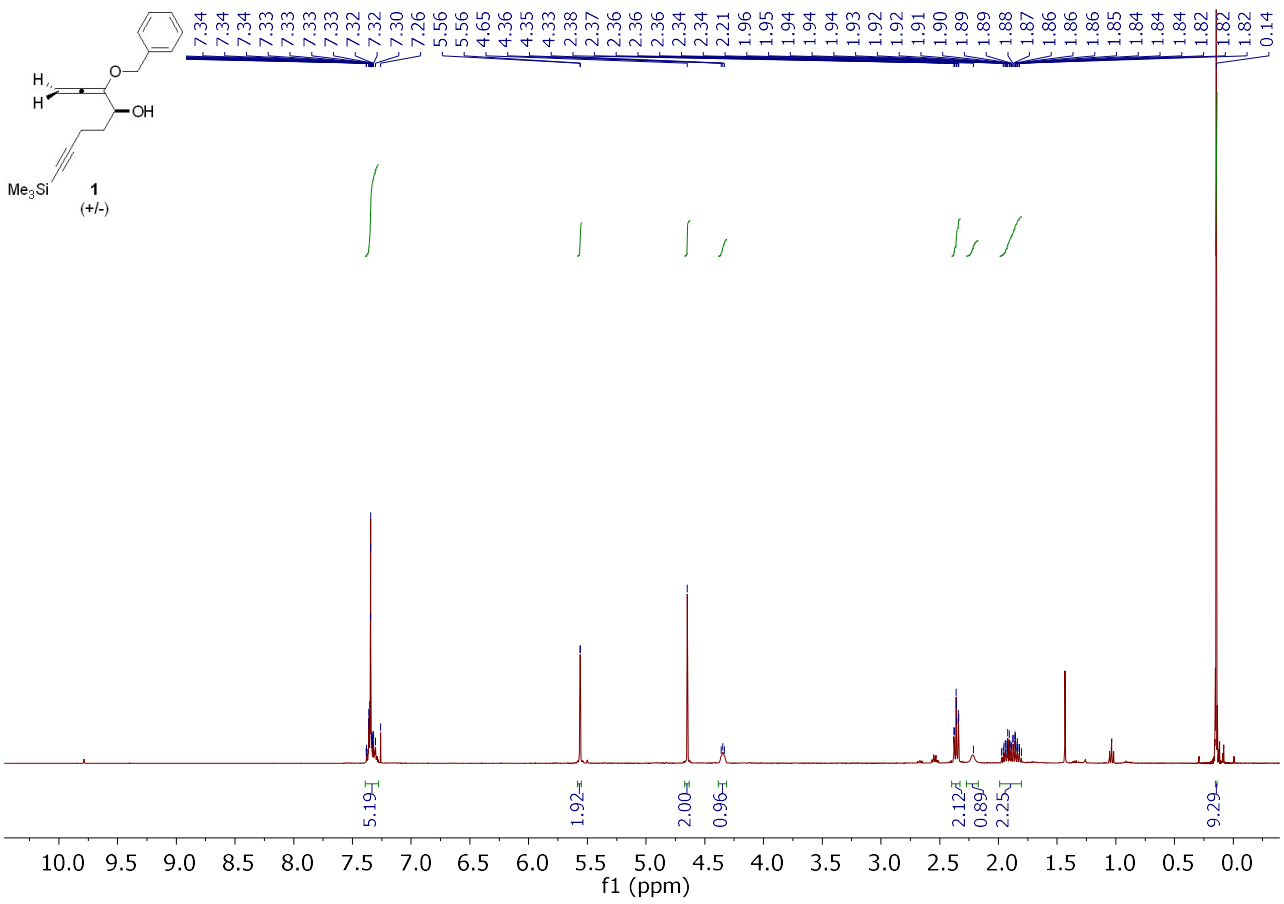
OH
29c
105.08
87.23
77.58
77.16
76.74
68.99
37.93
32.09
27.08
26.30
21.68
0.24
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.34
7.33
7.33
7.33
7.33
7.32
7.32
7.30
7.26
5.56
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4.65
4.36
4.35
4.33
2.38
2.37
2.36
2.36
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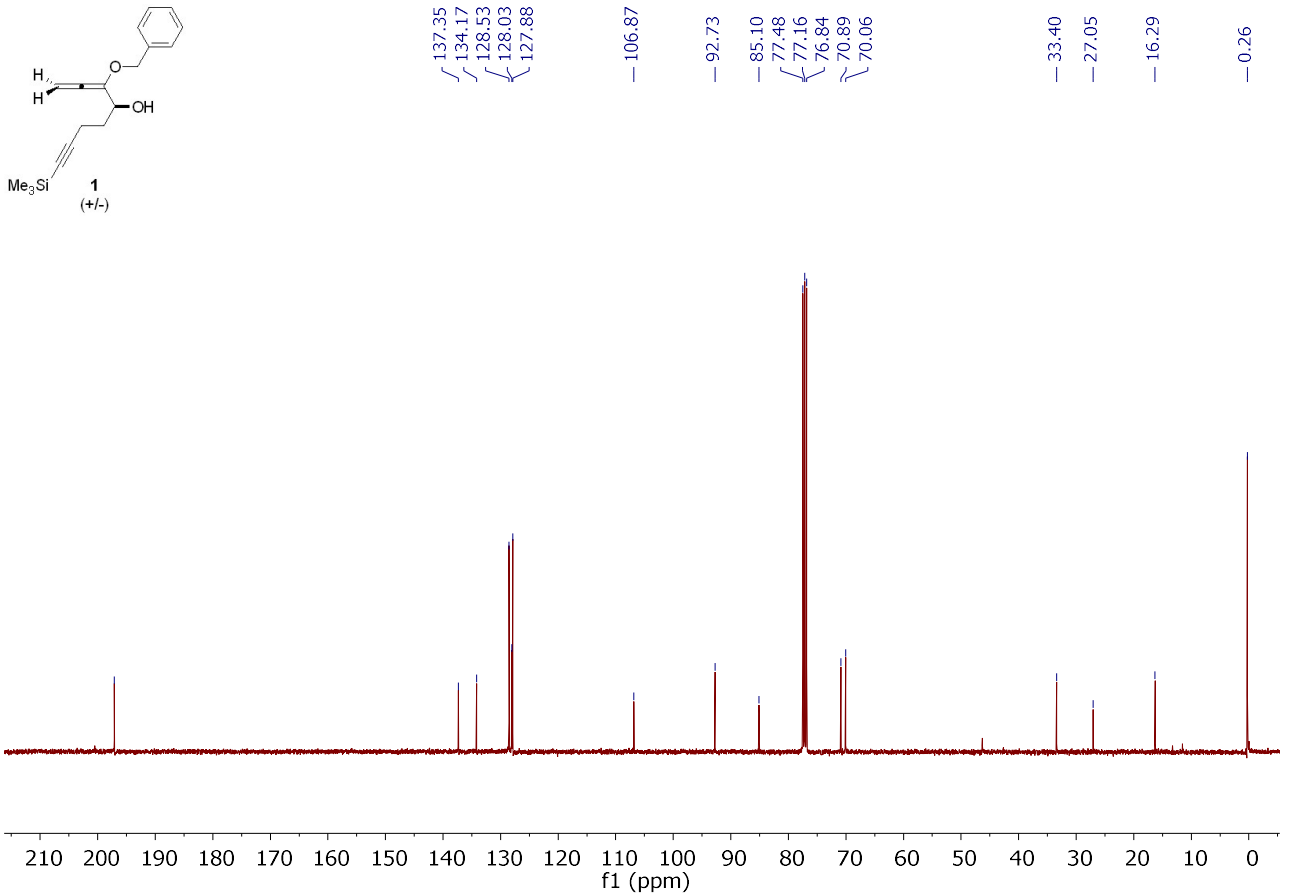
2.34
2.34
2.21
1.96
1.95
1.94
1.94
1.94
1.93
1.92
1.92
1.91
1.90
1.89
1.89
1.88
1.87
1.86
1.86
1.86
1.85
1.84
1.84
1.84
1.82
1.82
1.82
0.14
H
H
O
OH
Me3Si
1
(+/-)
5.19
1.92
2.00
0.96
2.12
0.89
2.25
9.29
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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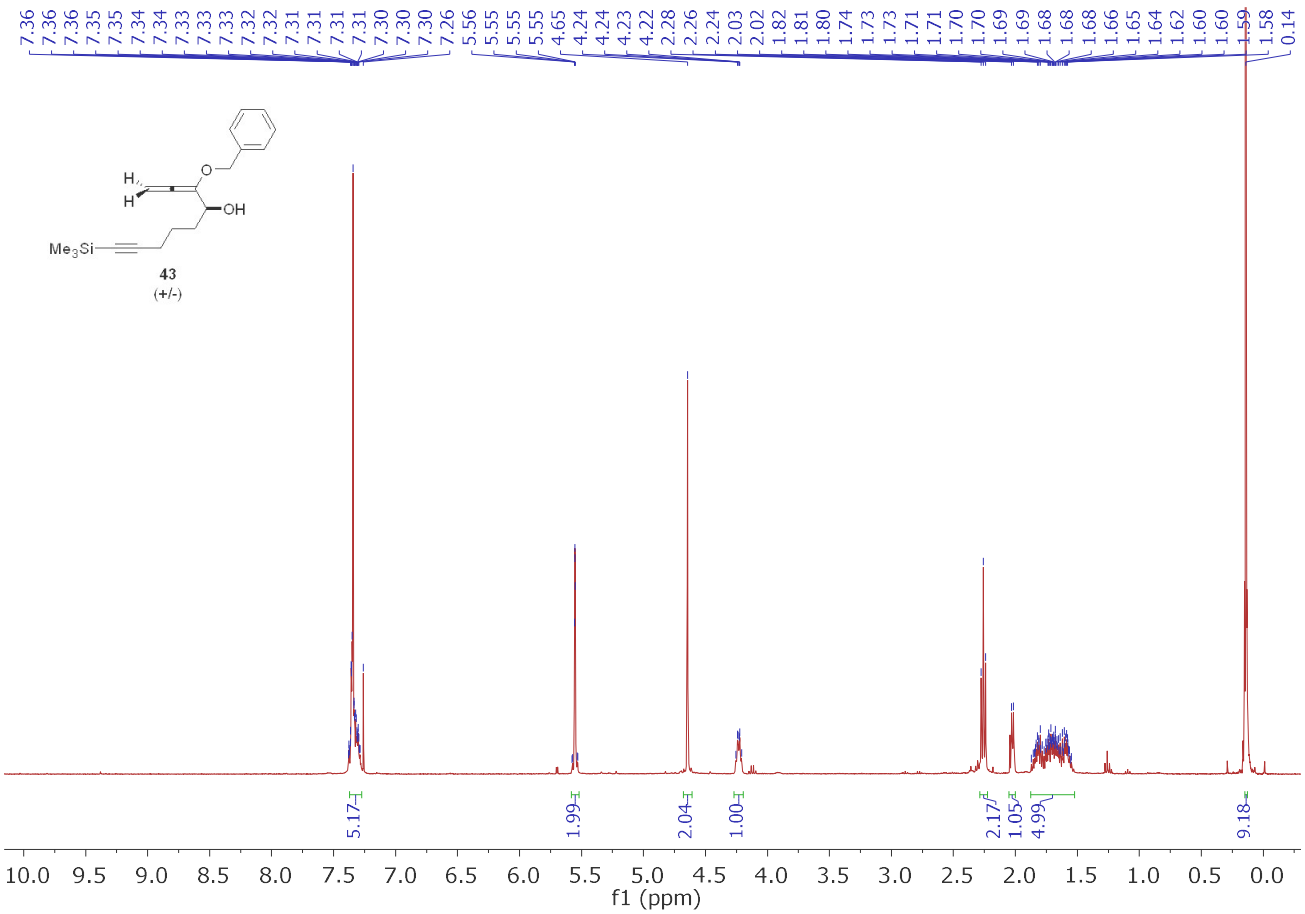
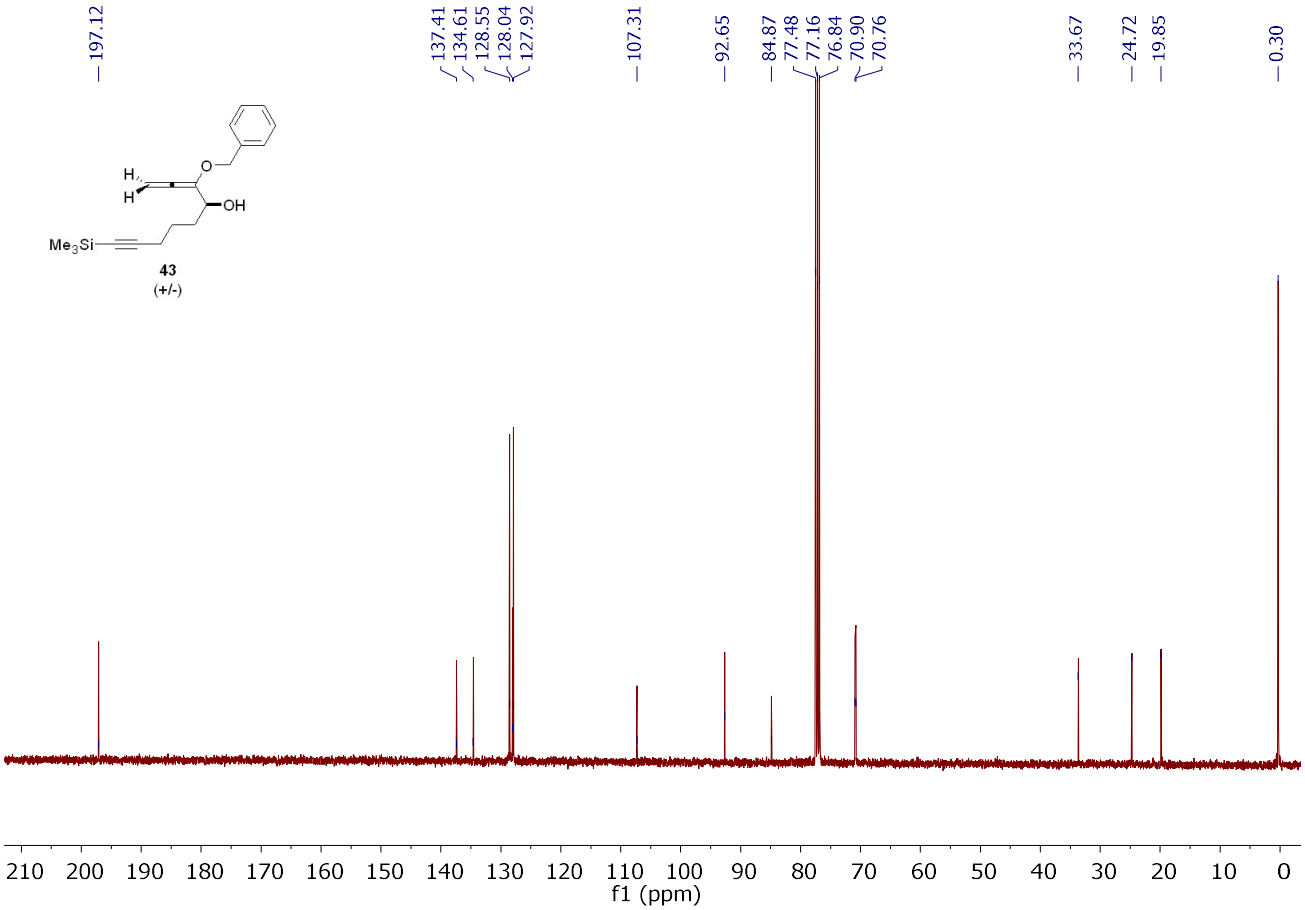
134.17
128.53
128.03
127.88
106.87
92.73
85.10
77.48
77.16
76.84
70.89
70.06
33.40
27.05
16.29
0.26
H
H
O
OH
Me3Si
1
(+/-)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.36 7.36 7.36 7.35 7.35 7.34 7.34 7.33 7.33 7.33 7.32 7.32 7.31 7.31 7.31 7.31 7.30 7.30 7.30 7.26
5.56 5.55 5.55 5.55 4.65 4.24 4.24 4.23 4.22 2.28 2.26 2.24 2.03 2.02 1.82 1.81 1.80 1.74 1.73 1.73 1.71 1.71 1.70 1.70 1.69 1.69 1.68 1.68 1.68 1.66 1.65 1.64 1.62 1.60 1.60 1.59 1.58 0.14
H
H
O
OH
Me3Si
43
(+/-)
5.17
1.99
2.04
1.00
2.17
1.05
4.99
9.18
10.0 9.5 9.0 8.5 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 0.5 0.0
f1 (ppm)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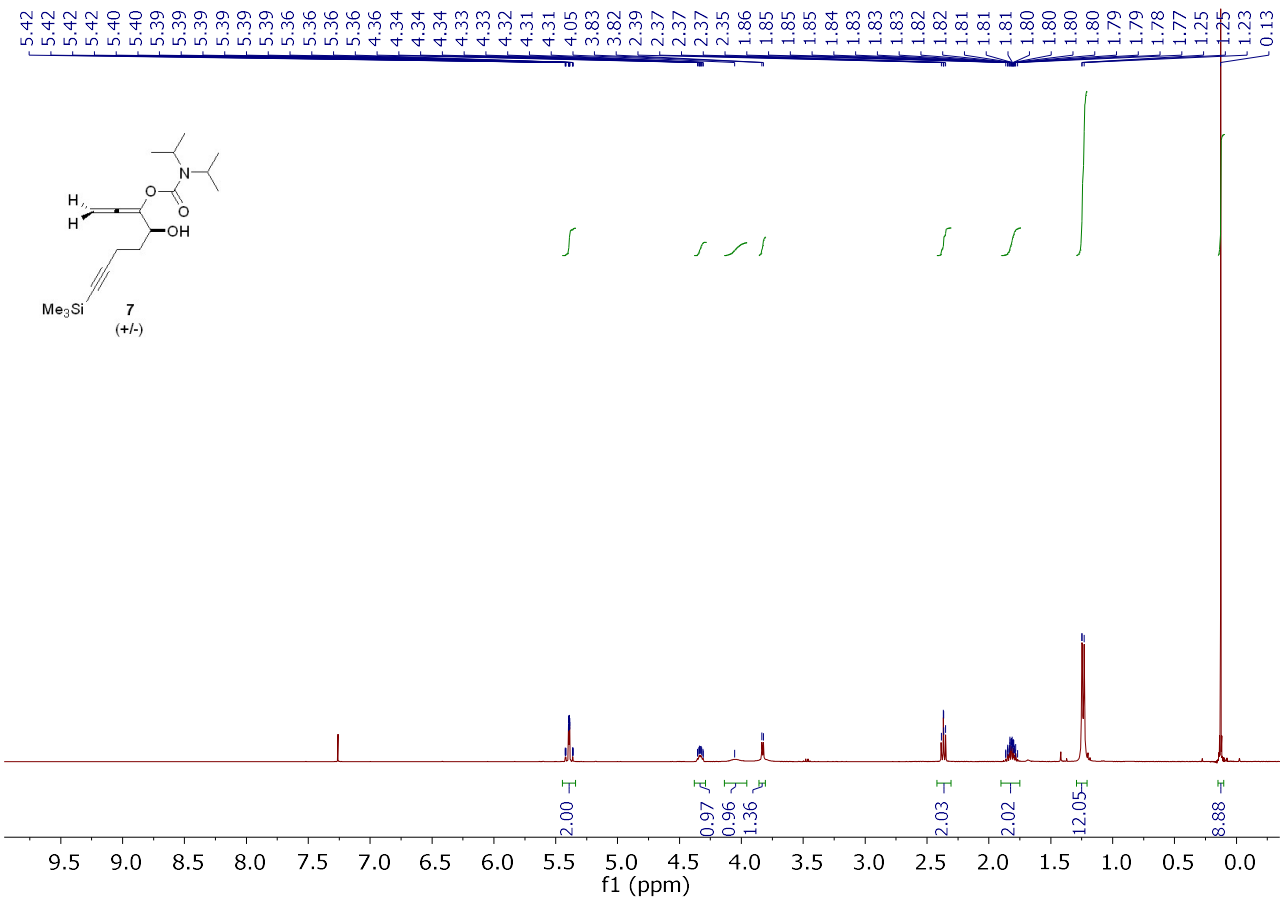
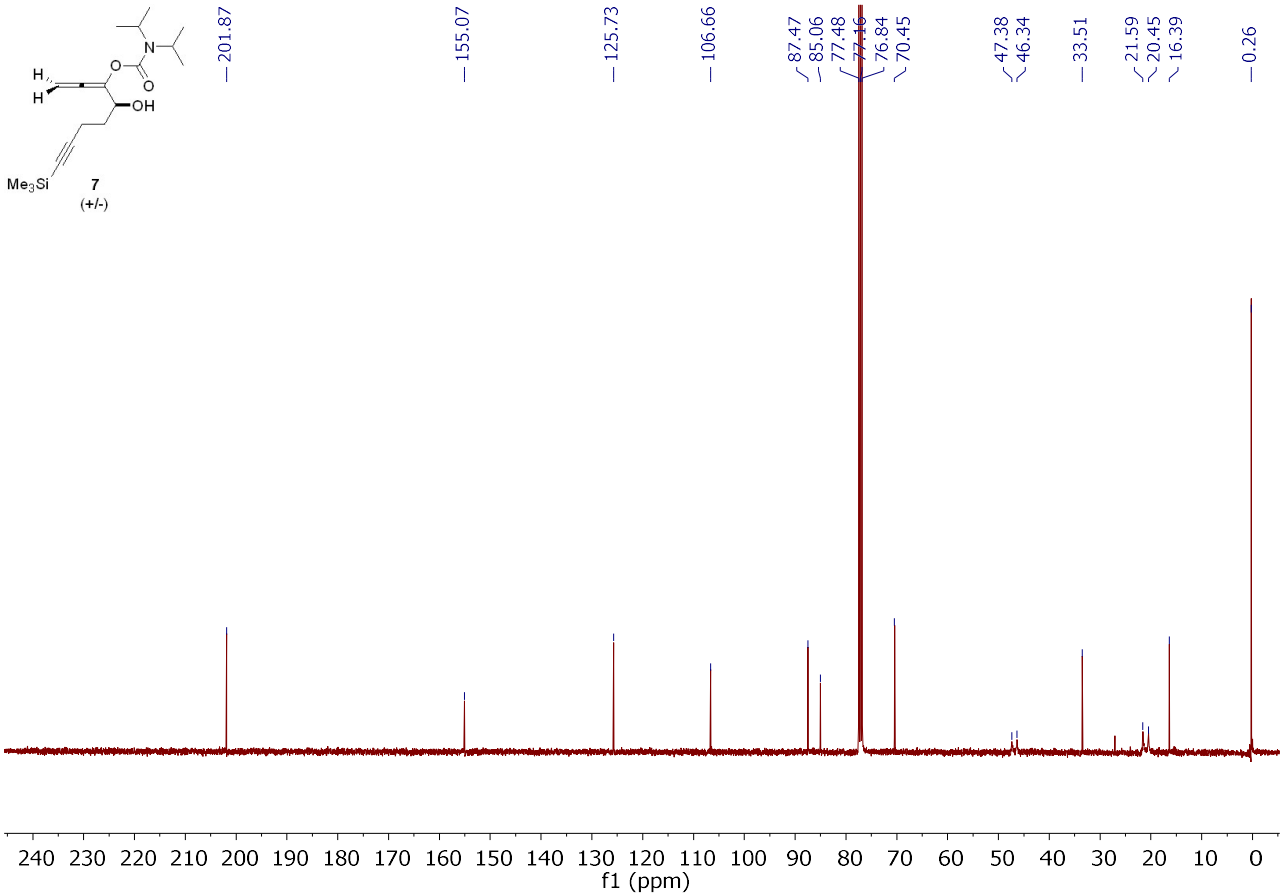
137.41
134.61
128.55
128.04
127.92
107.31
92.65
84.87
77.48
77.16
76.84
70.90
70.76
33.67
24.72
19.85
0.30
H
H
O
OH
Me3Si
43
(+/-)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


5.42 5.42 5.42 5.42 5.40 5.40 5.39 5.39 5.39 5.39 5.39 5.39 5.36 5.36 5.36 5.36 4.36 4.34 4.34 4.34 4.33 4.33 4.32 4.31 4.31 4.05 3.83 3.82 2.39 2.37 2.37 2.37 2.35 1.86 1.85 1.85 1.85 1.84 1.83 1.83 1.83 1.82 1.82 1.81 1.81 1.81 1.80 1.80 1.80 1.80 1.79 1.79 1.78 1.77 1.25 1.25 1.23 0.13
H
H
O
N
O
OH
Me3Si
7
(+/-)
2.00
0.97
0.96
1.36
2.03
2.02
12.05
8.88
9.5 9.0 8.5 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 0.5 0.0
f1 (ppm)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77.16
76.84
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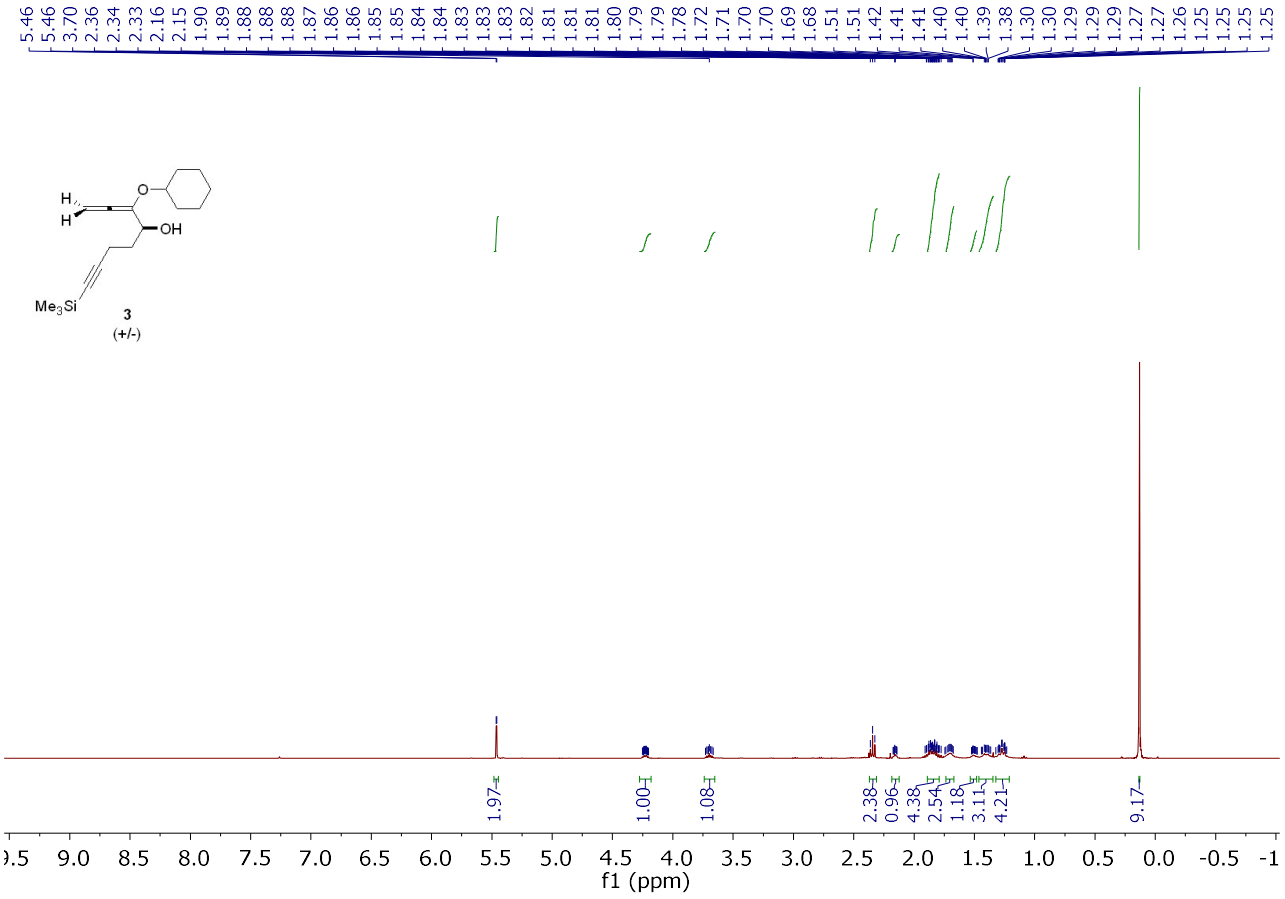
21.59
20.45
16.39
0.26
Me3Si
7
(+/-)
f1 (ppm)


Me3Si
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(+/-)
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4.38
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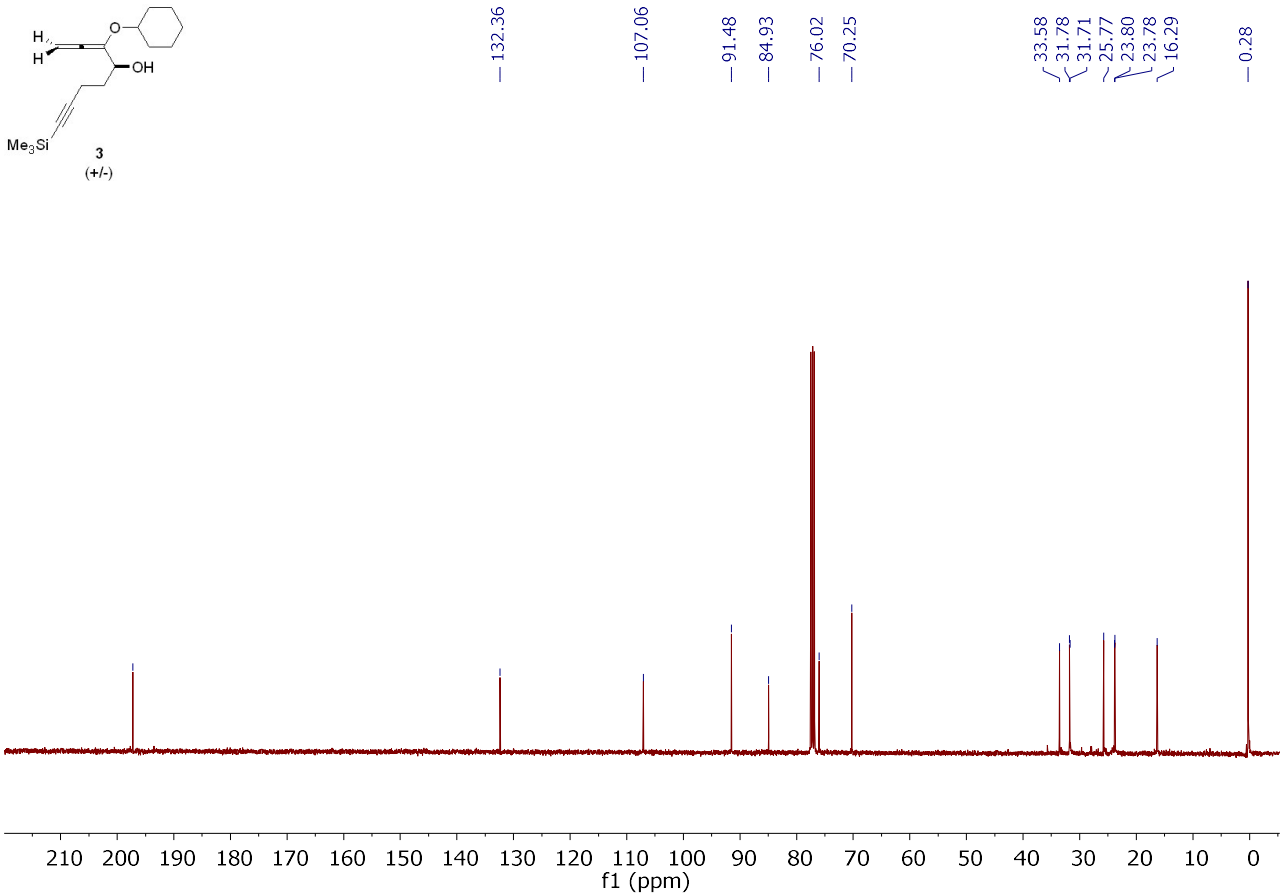
3.11
4.21
9.17
f1 (ppm)


H
H
O
OH
Me3Si
3
(+/-)
132.36
107.06
91.48
84.93
76.02
70.25
33.58
31.78
31.71
25.77
23.80
23.78
16.29
0.28
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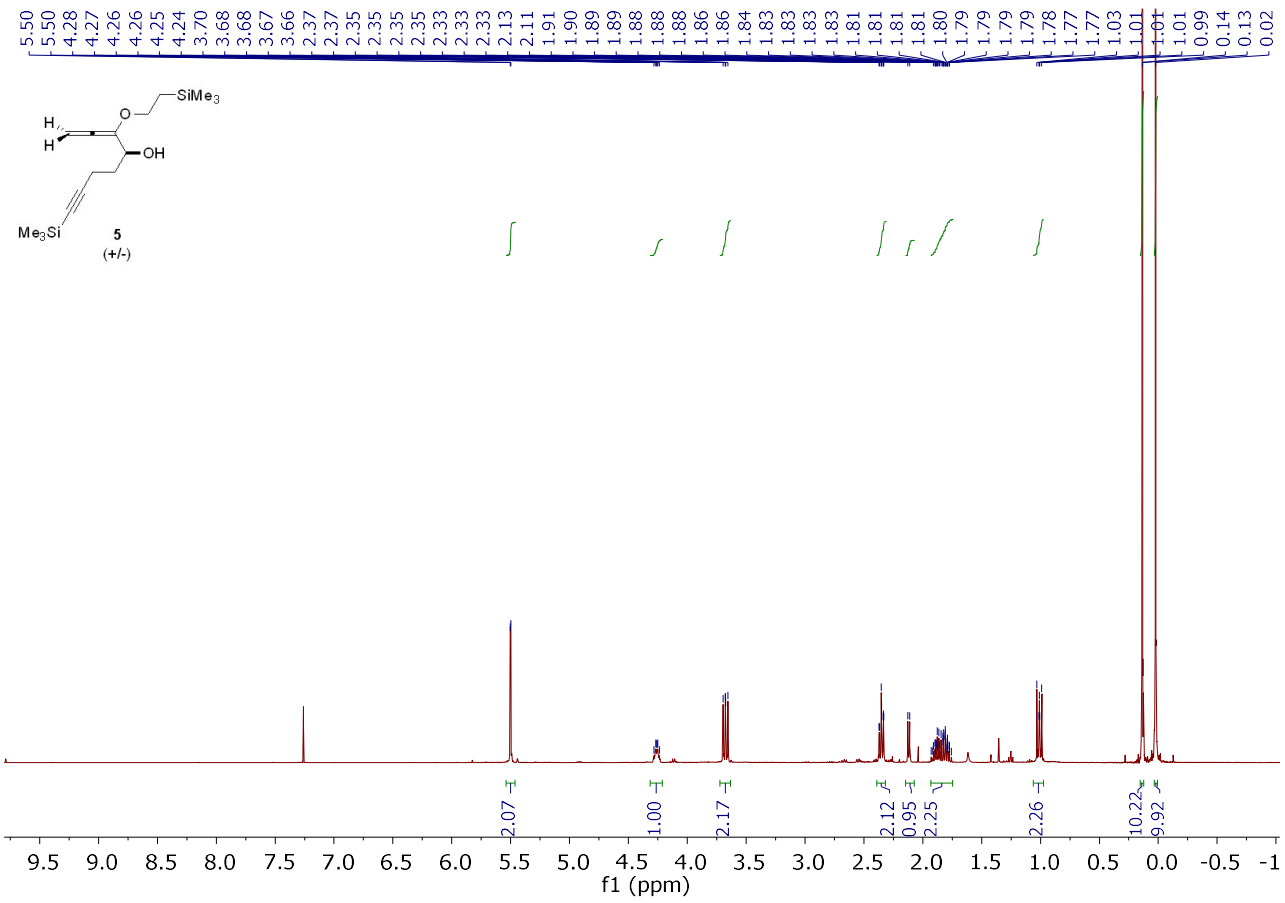
f1 (ppm)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4.25
4.24
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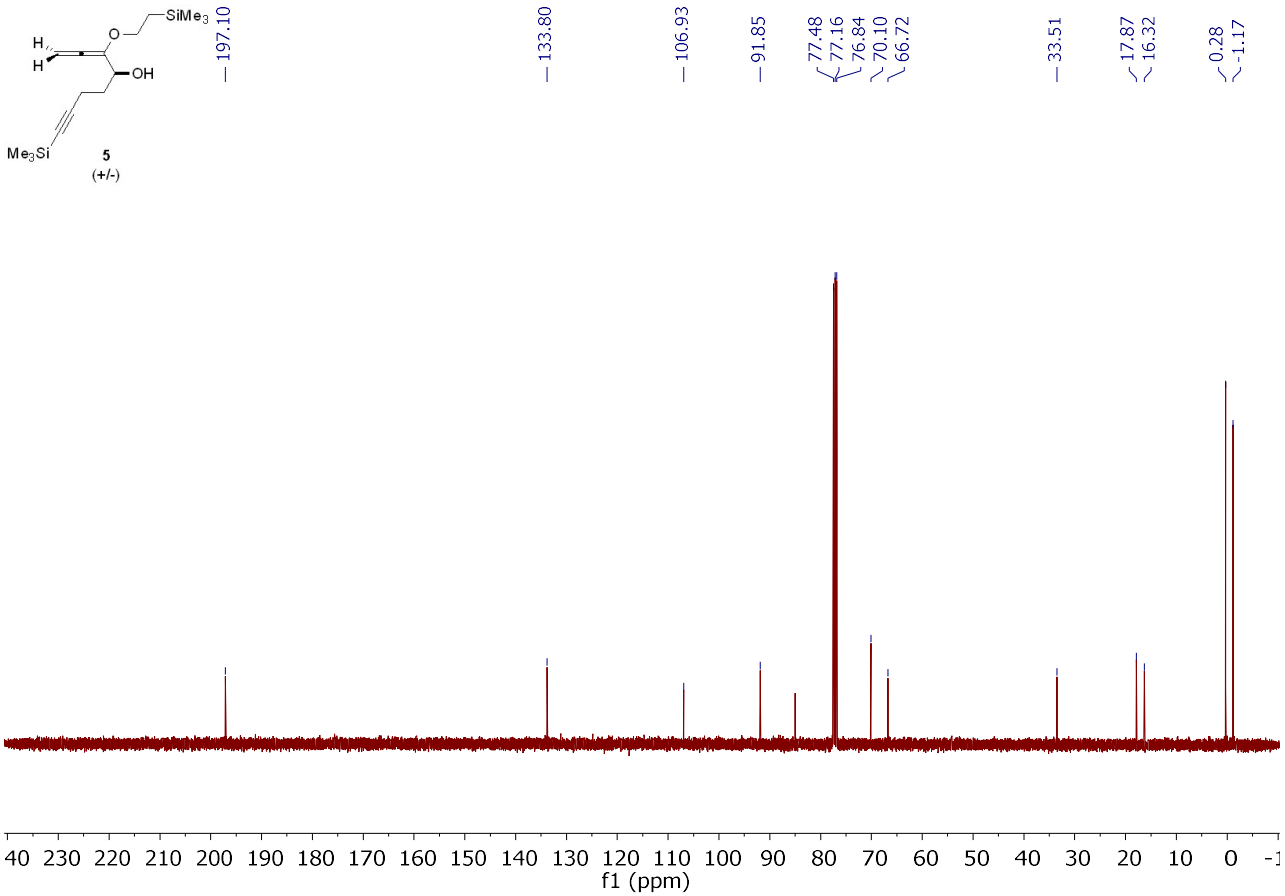
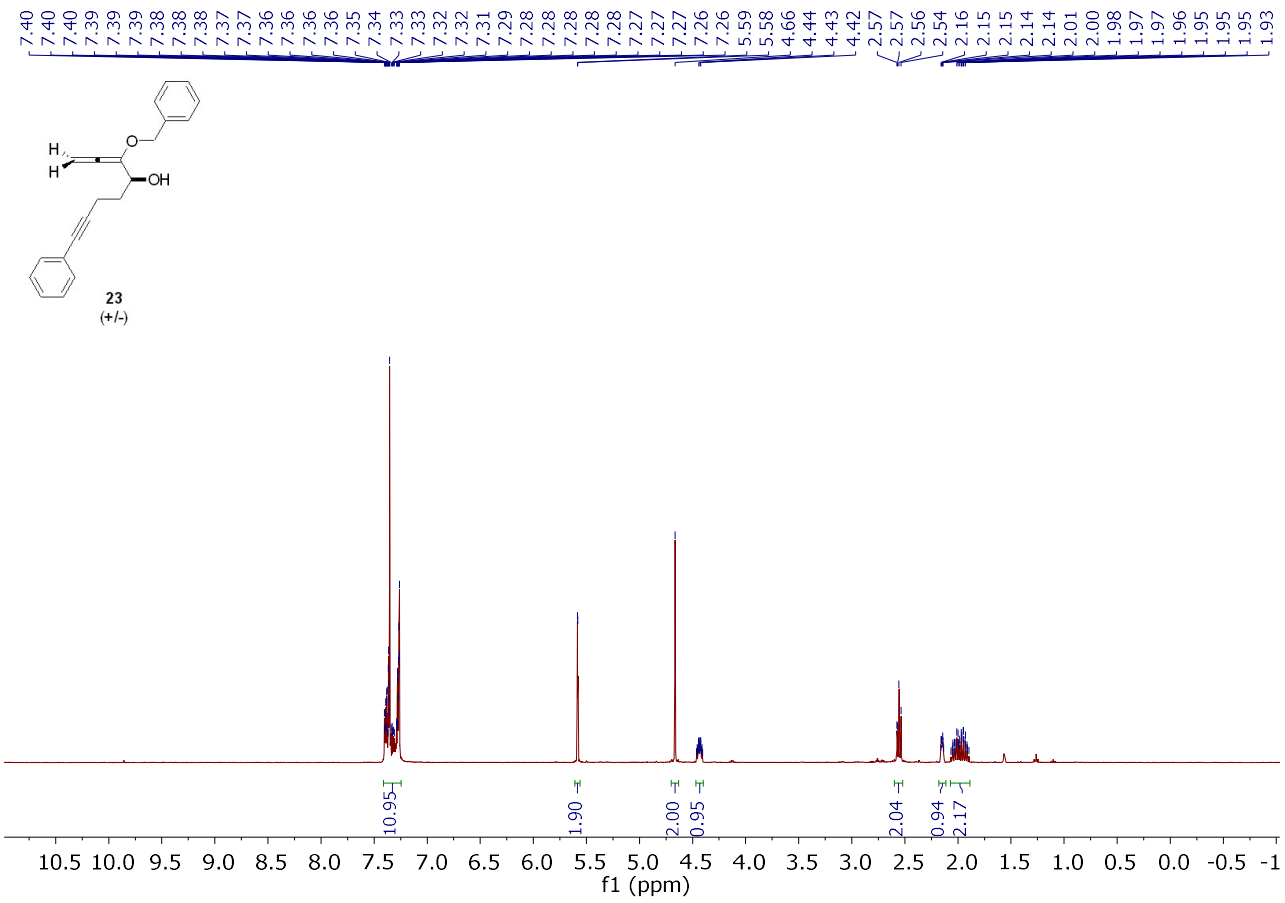
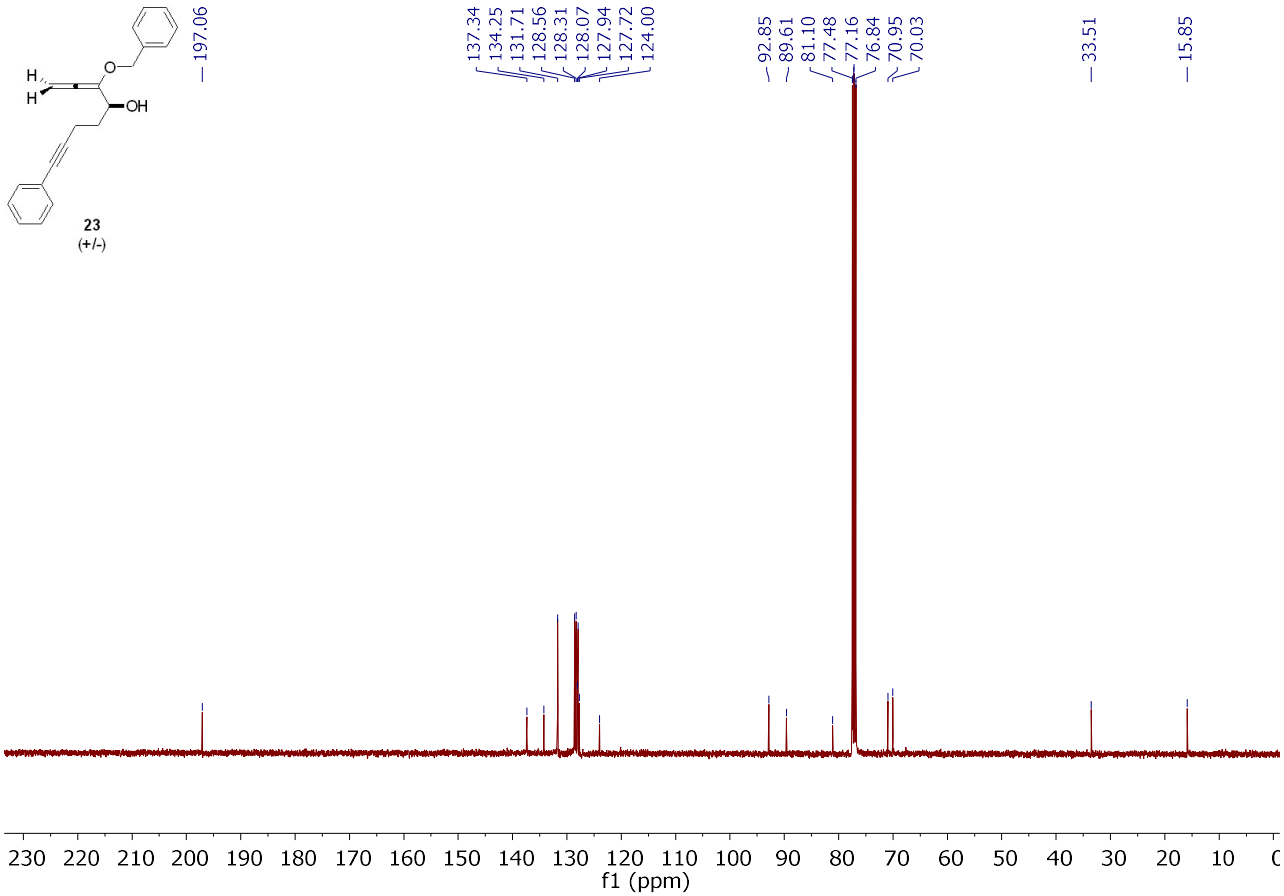
3.68
3.68
3.67
3.66
2.37
2.37
2.35
2.35
2.35
2.35
2.33
2.33
2.33
2.13
2.11
1.91
1.90
1.89
1.89
1.88
1.88
1.88
1.86
1.86
1.84
1.83
1.83
1.83
1.83
1.81
1.81
1.81
1.81
1.80
1.79
1.79
1.79
1.79
1.78
1.77
1.77
1.03
1.01
1.01
0.99
0.14
0.13
0.02
SiMe3
H
H
O
OH
Me3Si
5
(+/-)
2.07
1.00
2.17
2.12
0.95
2.25
2.26
10.22
9.92
9.5 9.0 8.5 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 0.5 0.0 -0.5 -1
f1 (ppm)


SiMe3
O
H
H
OH
Me3Si
5
(+/-)
197.10
133.80
106.93
91.85
77.48
77.16
76.84
70.10
66.72
33.51
17.87
16.32
0.28
-1.17
f1 (ppm)


O
H
H
OH
23
(+/-)
10.95
1.90
2.00
0.95
2.04
0.94
2.17
f1 (ppm)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128.07
127.94
127.72
124.00
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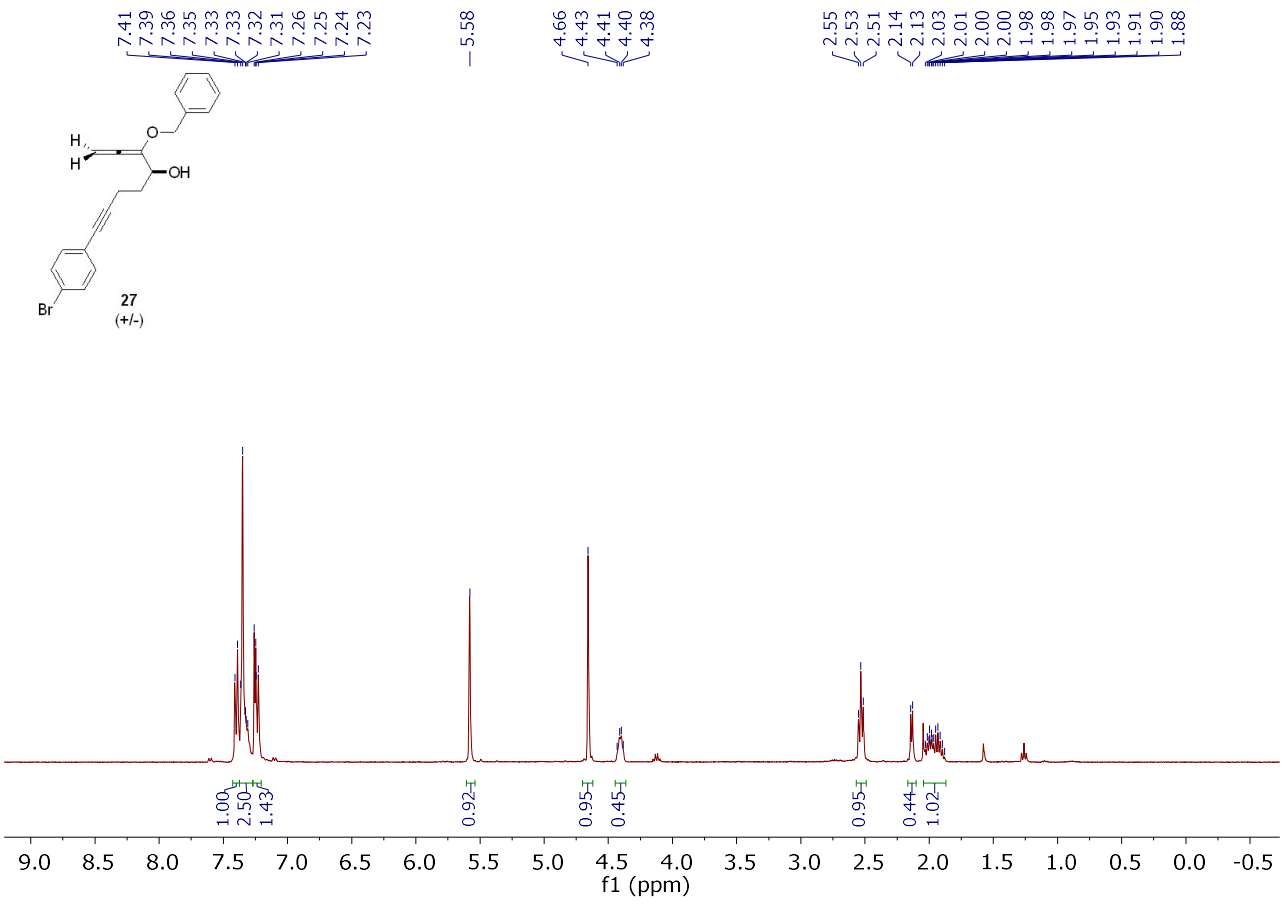
77.48
77.16
76.84
70.95
70.03
33.51
15.85
H
H
O
OH
23
(+/-)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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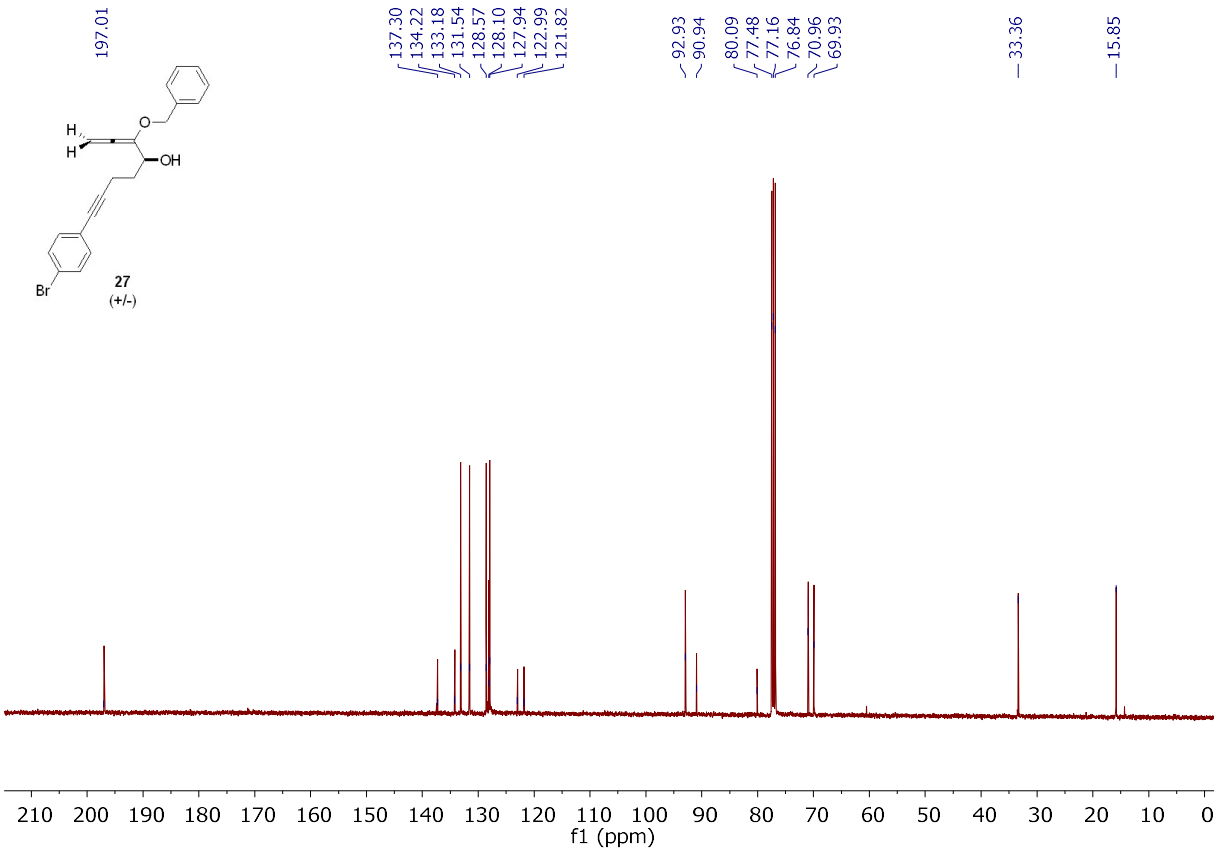
7.33
7.32
7.31
7.26
7.25
7.24
7.23
5.58
4.66
4.43
4.41
4.40
4.38
2.55
2.53
2.51
2.14
2.13
2.03
2.01
2.00
2.00
1.98
1.98
1.97
1.95
1.93
1.91
1.90
1.88
H
H
O
OH
Br
27
(+/-)
1.00
2.50
1.43
0.92
0.95
0.45
0.95
0.44
1.02
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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128.10
127.94
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121.82
92.93
90.94
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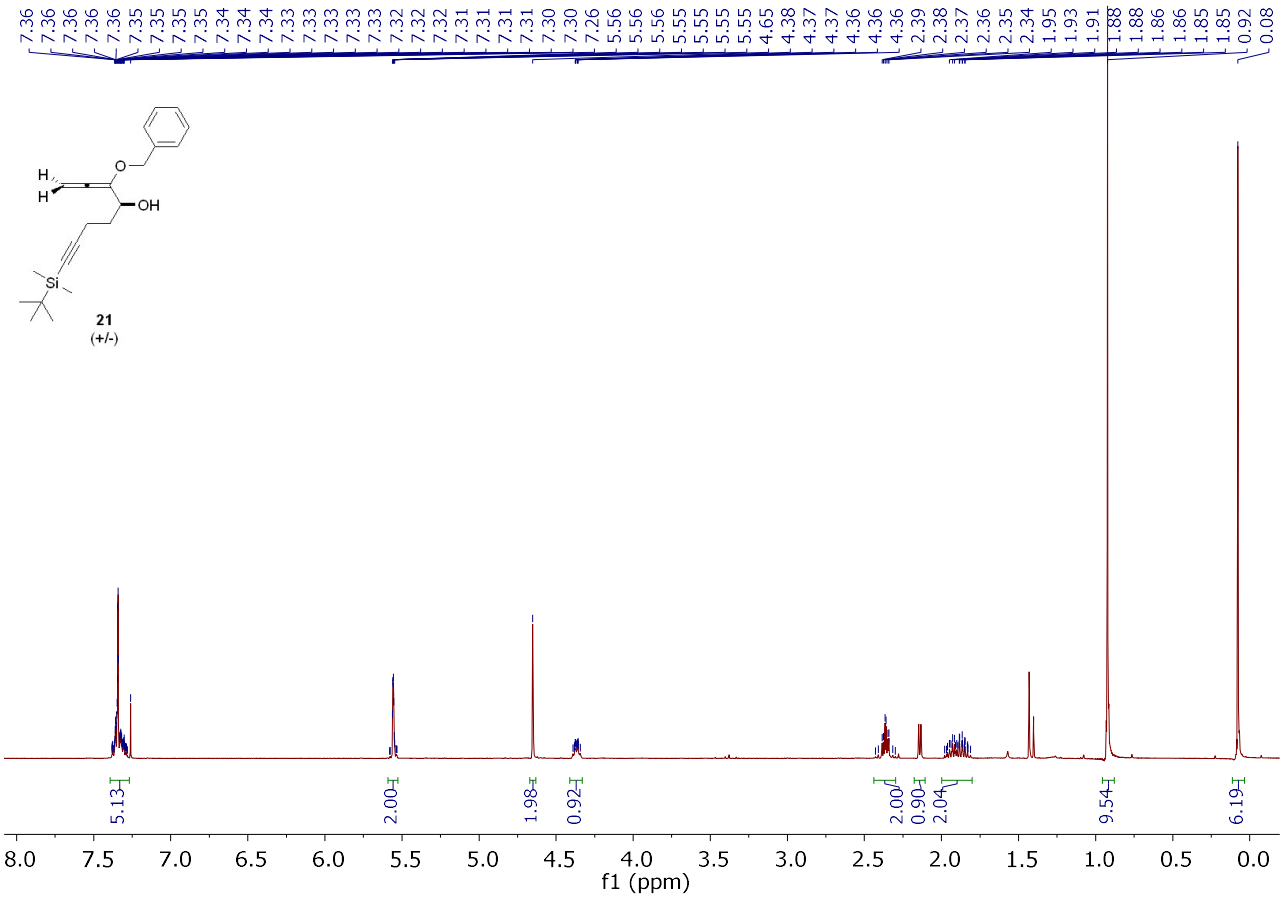
77.48
77.16
76.84
70.96
69.93
33.36
15.85
H
H
O
OH
Br
27
(+/-)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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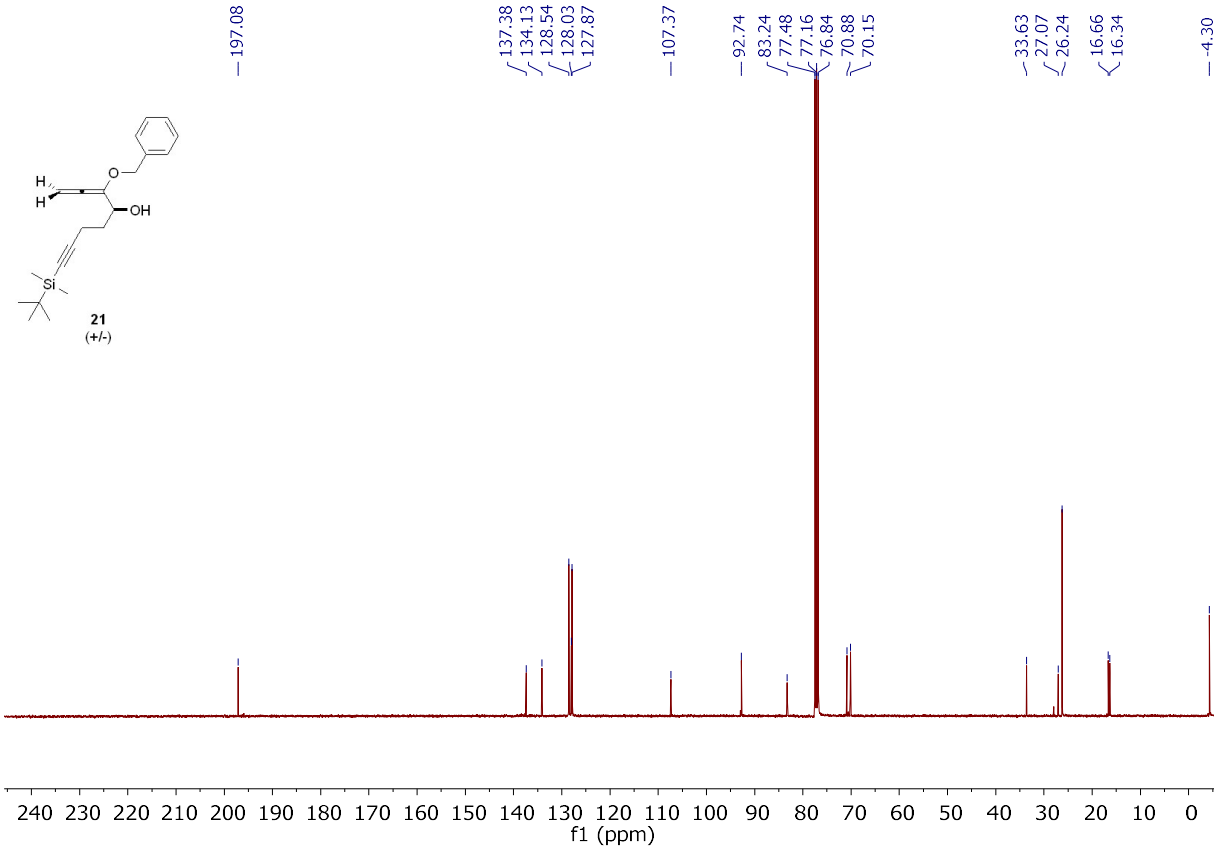
H
H
O
OH
Si
21
(+/-)
5.13
2.00
1.98
0.92
2.00
0.90
2.04
9.54
6.19
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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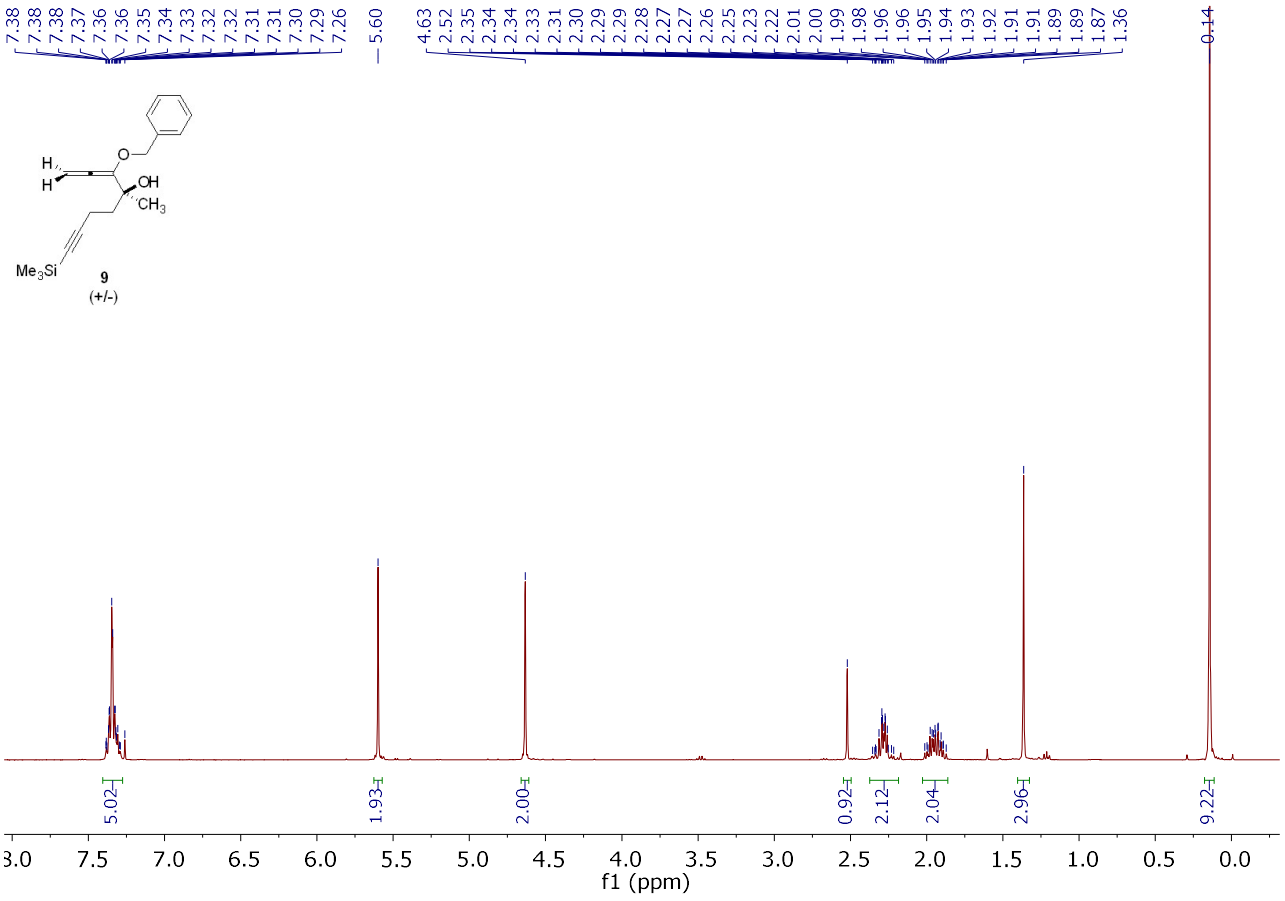
137.38
134.13
128.54
128.03
127.87
107.37
92.74
83.24
77.48
77.16
76.84
70.88
70.15
33.63
27.07
26.24
16.66
16.34
-4.30
O
H
H
OH
Si
21
(+/-)
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.38
7.38
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7.34
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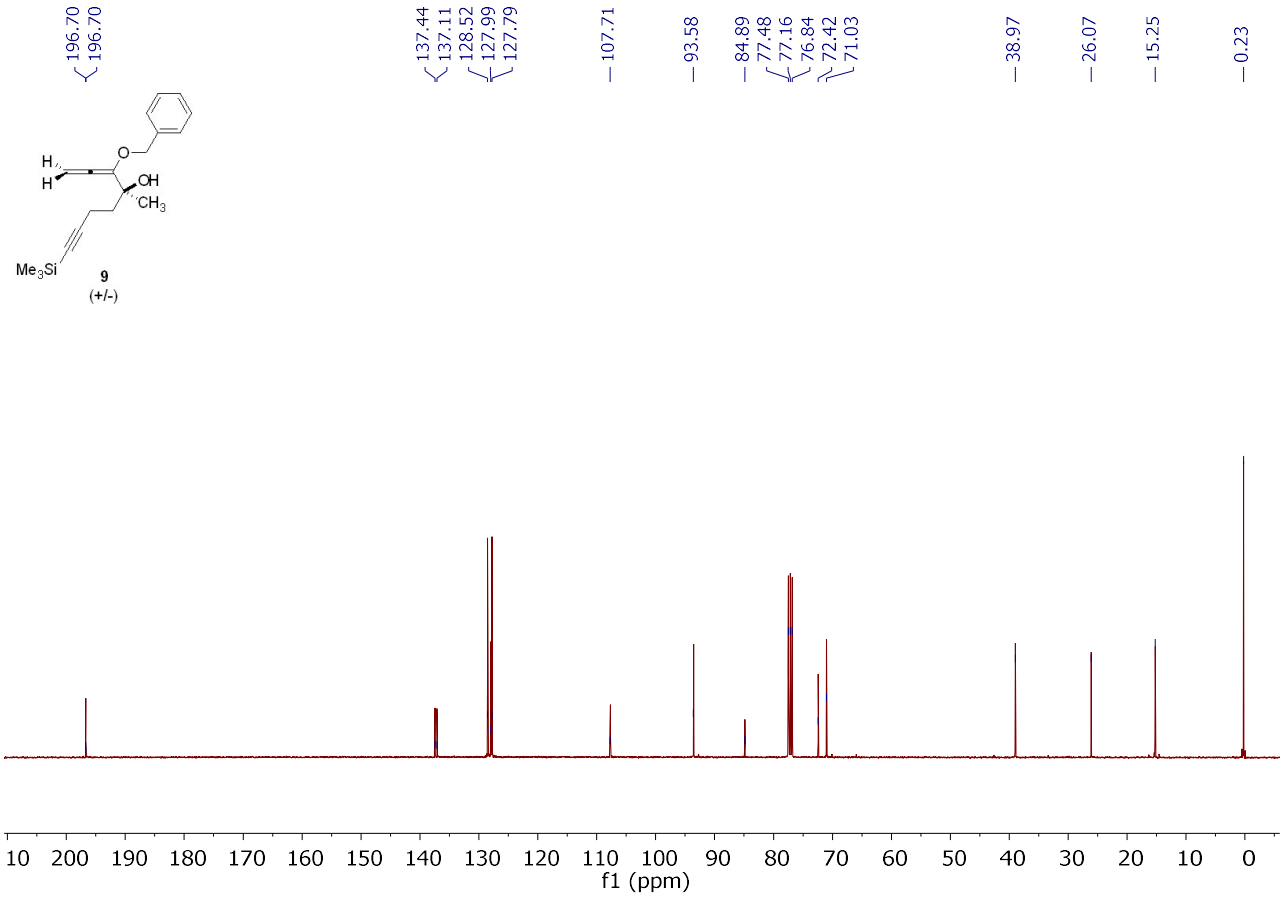
7.31
7.31
7.30
7.29
7.26
5.60
4.63
2.52
2.35
2.34
2.34
2.33
2.31
2.30
2.29
2.29
2.28
2.27
2.27
2.26
2.25
2.23
2.22
2.01
2.00
1.99
1.98
1.96
1.96
1.95
1.94
1.93
1.92
1.91
1.91
1.89
1.89
1.87
1.36
0.14
O
H
H
OH
CH3
Me3Si
9
(+/-)
5.02
1.93
2.00
0.92
2.12
2.04
2.96
9.22
3.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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127.79
107.71
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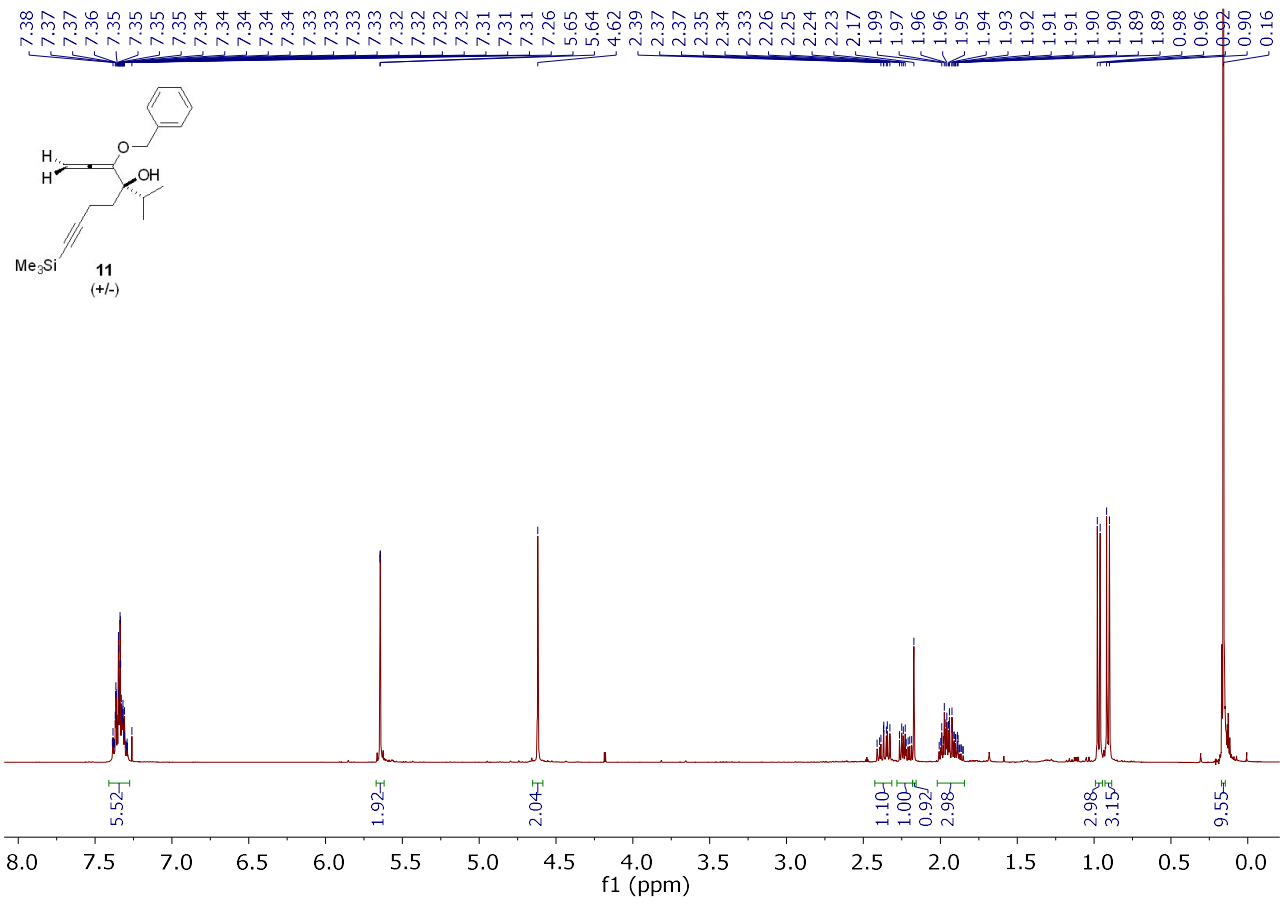
84.89
77.48
77.16
76.84
72.42
71.03
38.97
26.07
15.25
0.23
H
H
O
OH
CH3
Me3Si
9
(+/-)
f1 (ppm)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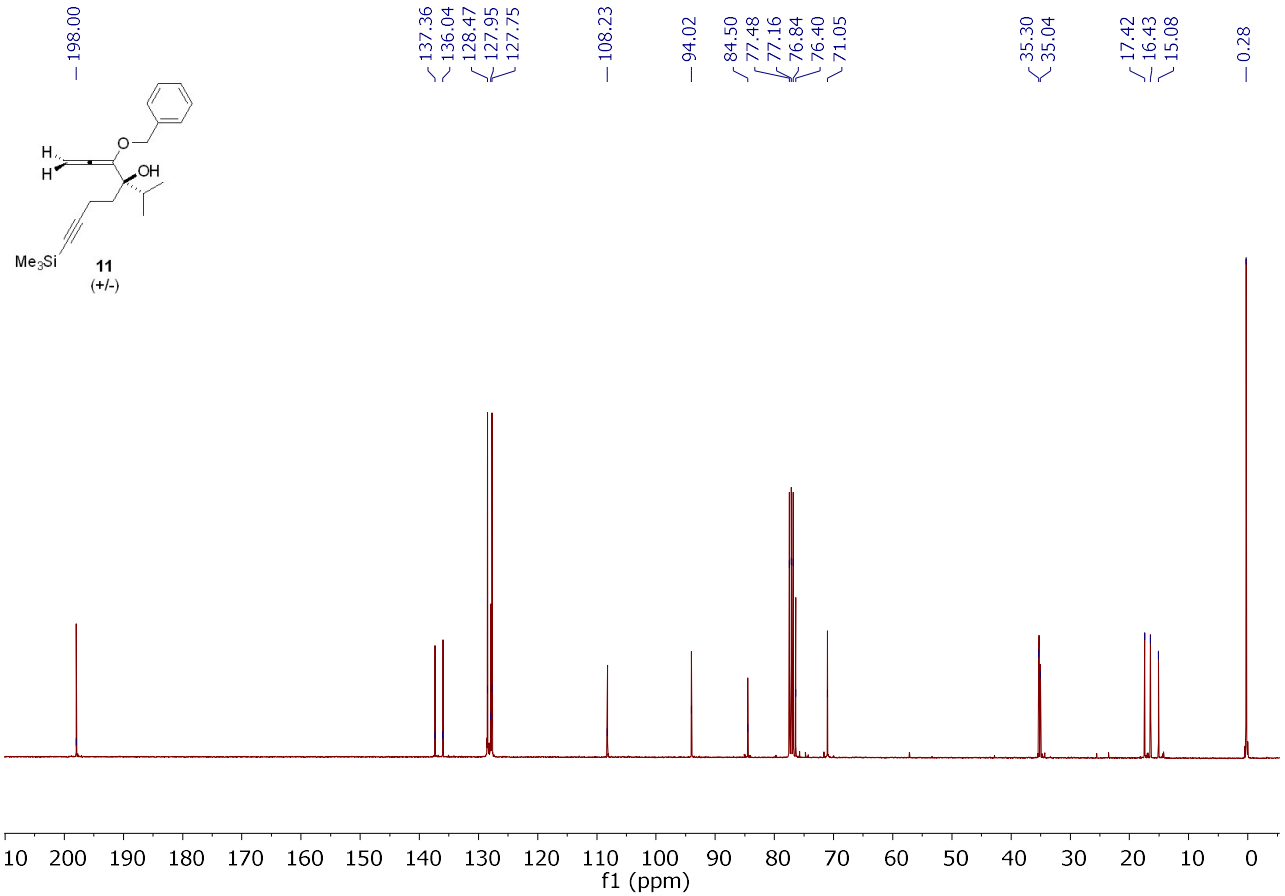
7.33
7.33
7.33
7.32
7.32
7.32
7.32
7.31
7.31
7.31
7.26
5.65
5.64
4.62
2.39
2.37
2.37
2.35
2.34
2.33
2.26
2.25
2.24
2.23
2.17
1.99
1.97
1.96
1.96
1.95
1.94
1.93
1.92
1.91
1.91
1.90
1.90
1.89
1.89
0.98
0.96
0.92
0.90
0.16
H
H
O
OH
Me3Si
11
(+/-)
5.52
1.92
2.04
1.10
1.00
0.92
2.98
2.98
3.15
9.55
f1 (ppm)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137.36
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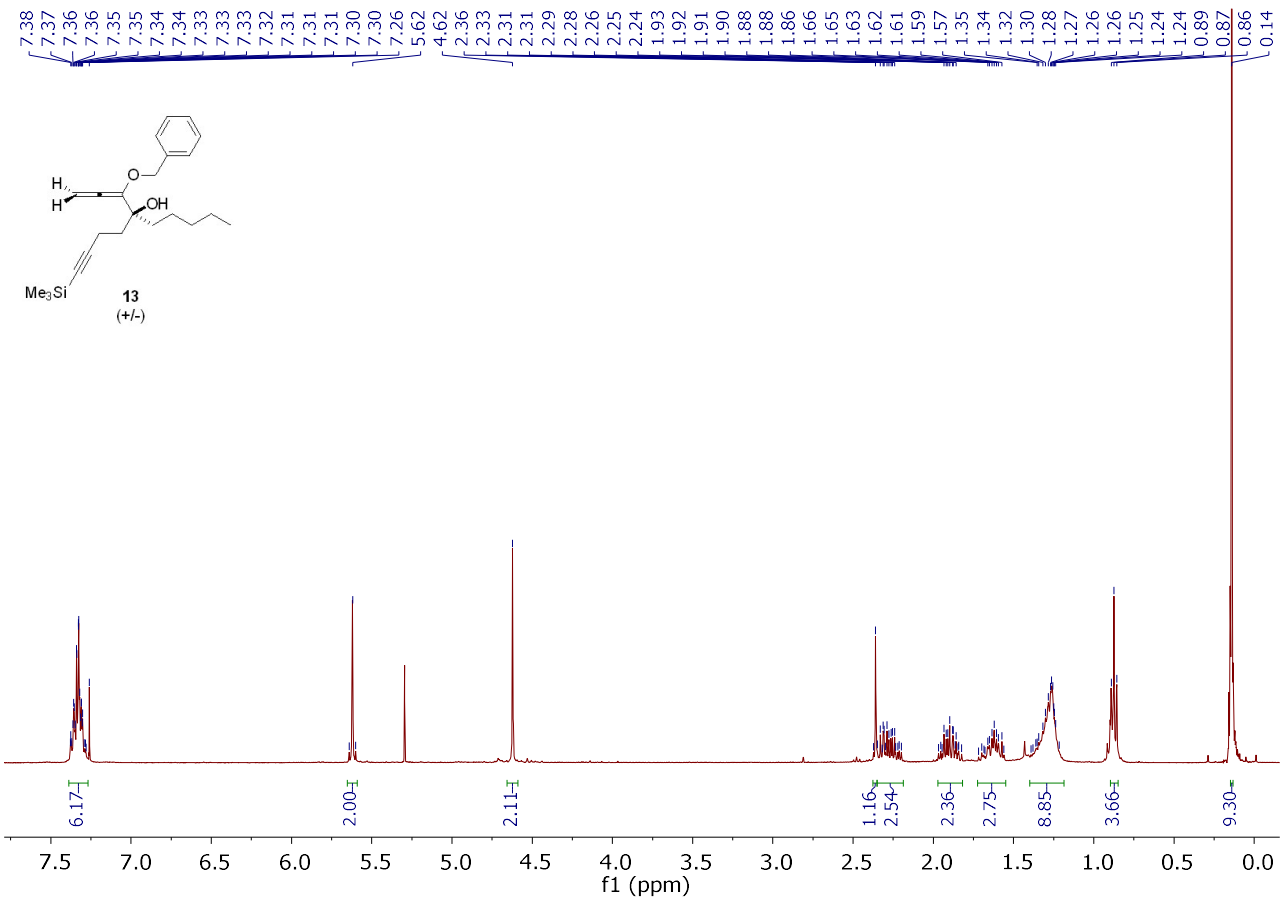
128.47
127.95
127.75
108.23
94.02
84.50
77.48
77.16
76.84
76.40
71.05
35.30
35.04
17.42
16.43
15.08
0.28
H
H
O
OH
Me3Si
11
(+/-)
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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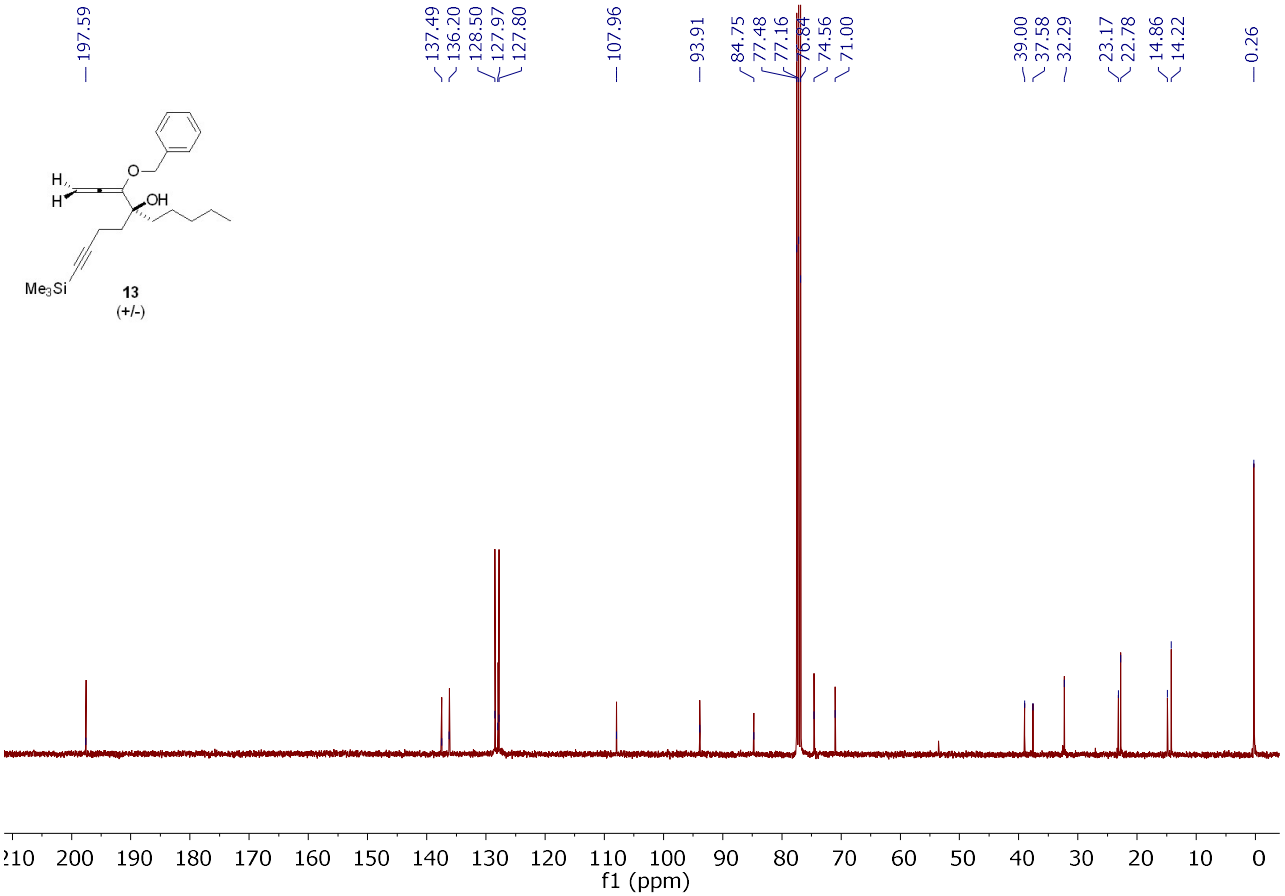
7.32
7.31
7.31
7.31
7.30
7.30
7.26
5.62
4.62
2.36
2.33
2.31
2.31
2.29
2.28
2.26
2.25
2.24
1.93
1.92
1.91
1.90
1.88
1.88
1.86
1.66
1.65
1.63
1.62
1.61
1.59
1.57
1.35
1.34
1.32
1.30
1.28
1.27
1.26
1.26
1.25
1.24
1.24
0.89
0.87
0.86
0.14
H
H
O
OH
Me3Si
13
(+/-)
6.17
2.00
2.11
1.16
2.54
2.36
2.75
8.85
3.66
9.30
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 0.0
f1 (ppm)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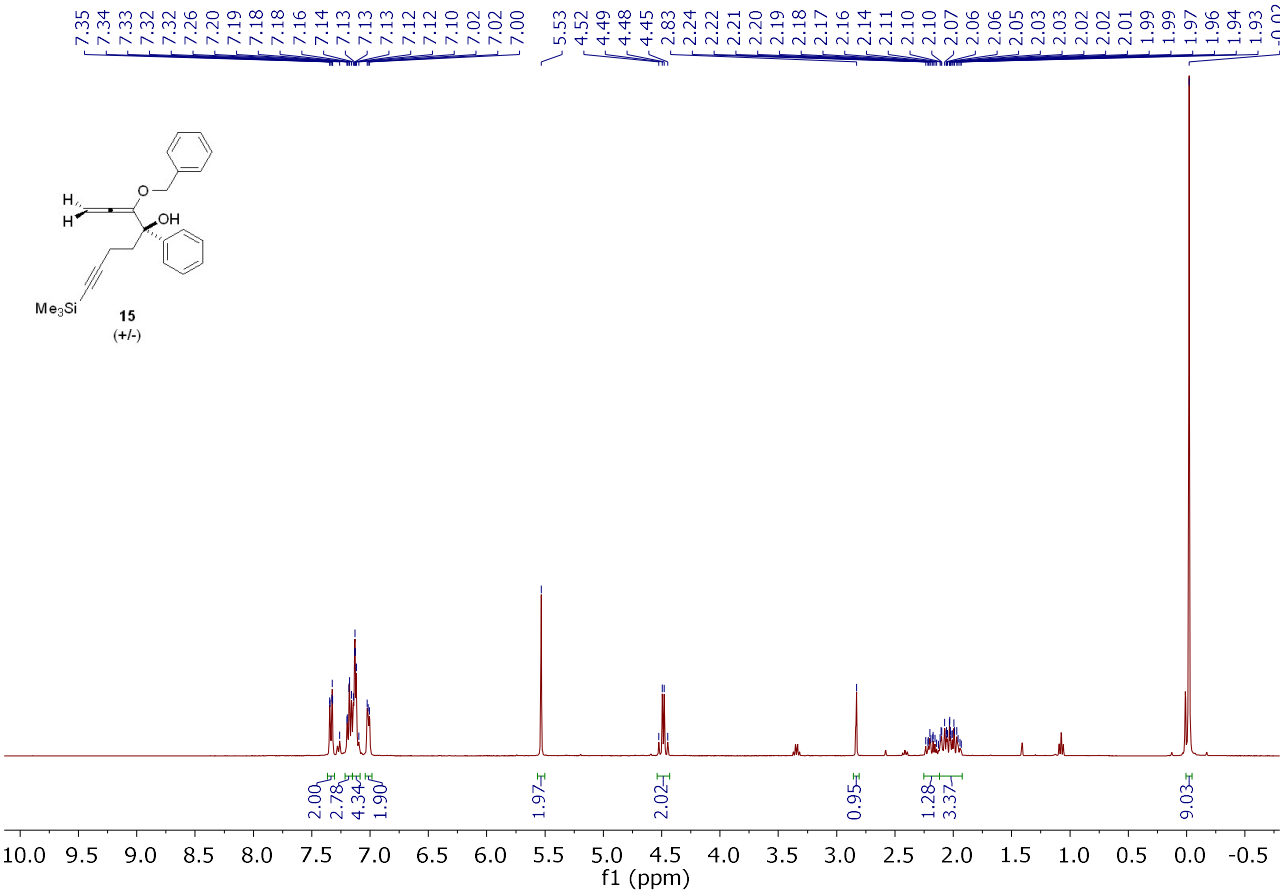
137.49
136.20
128.50
127.97
127.80
107.96
93.91
84.75
77.48
77.16
76.84
74.56
71.00
39.00
37.58
32.29
23.17
22.78
14.86
14.22
0.26
O
OH
H
H
Me3Si
13
(+/-)
f1 (ppm)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7.34
7.33
7.32
7.32
7.26
7.20
7.19
7.18
7.18
7.16
7.14
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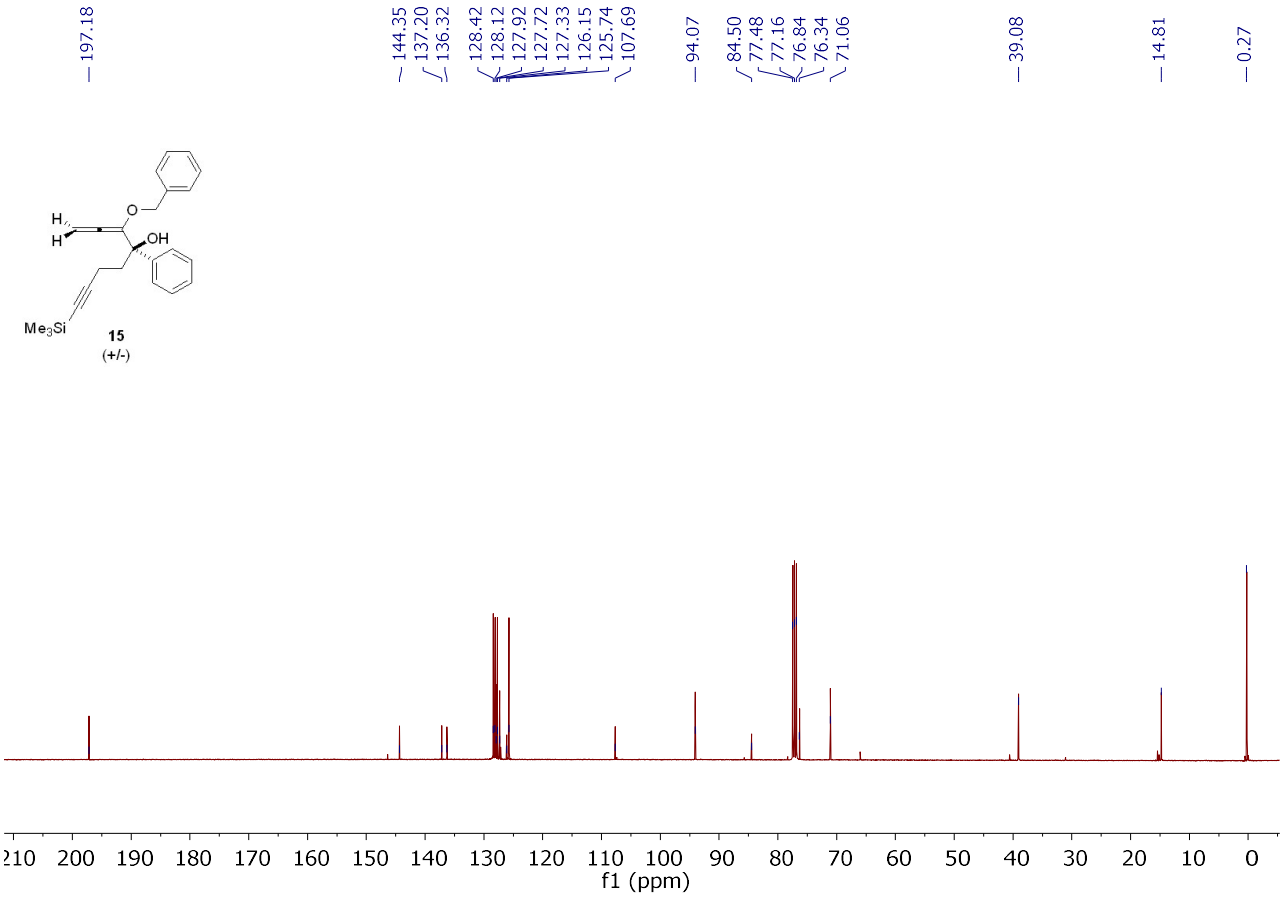
7.13
7.13
7.12
7.12
7.10
7.02
7.02
7.00
5.53
4.52
4.49
4.48
4.45
2.83
2.24
2.22
2.21
2.20
2.19
2.18
2.17
2.16
2.14
2.11
2.10
2.10
2.07
2.06
2.06
2.05
2.03
2.03
2.02
2.02
2.01
1.99
1.99
1.97
1.96
1.94
1.93
O
OH
H
H
Me3Si
15
(+/-)
2.00
2.78
4.34
1.90
1.97
2.02
0.95
1.28
3.37
9.03
f1 (ppm)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144.35
137.20
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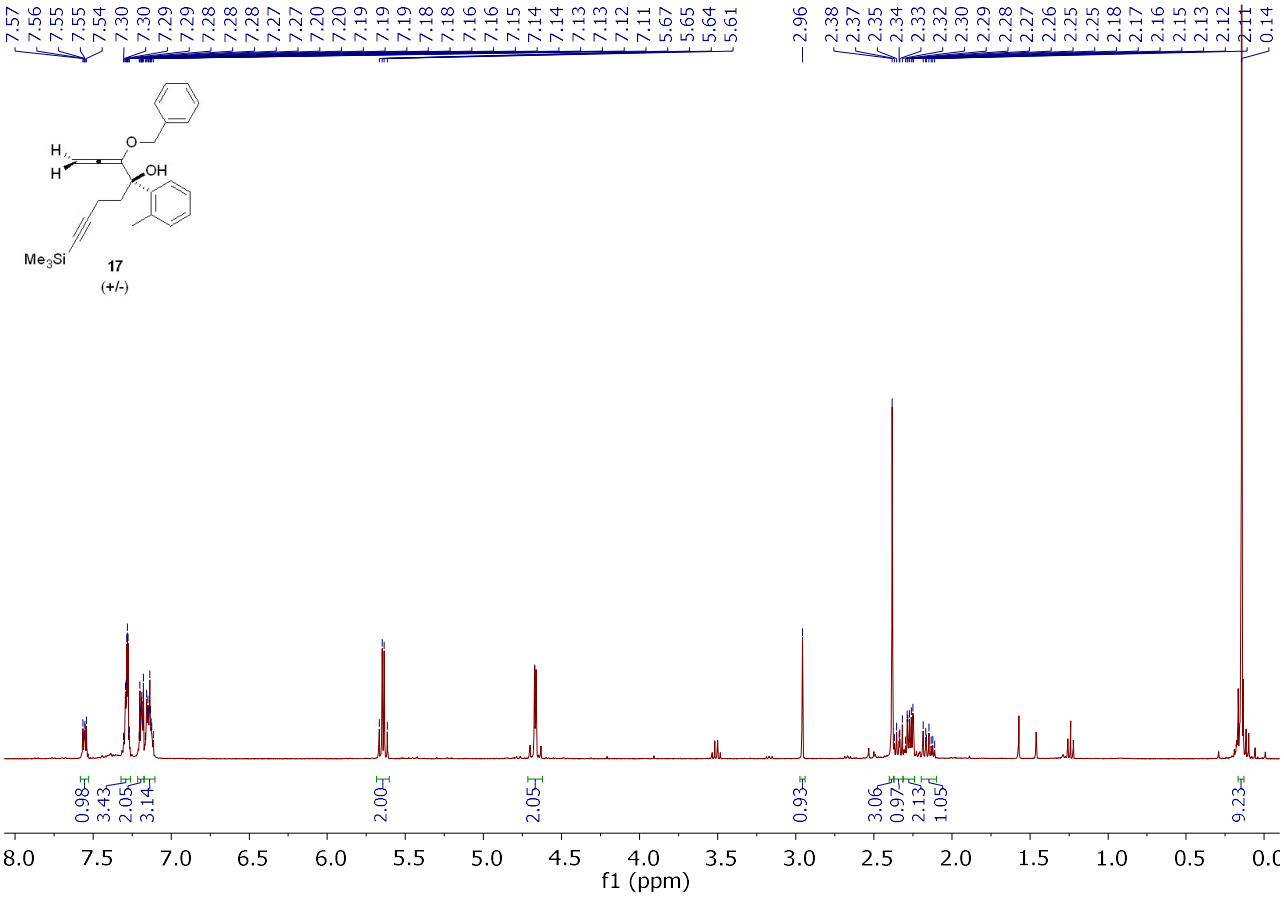
128.42
128.12
127.92
127.72
127.33
126.15
125.74
107.69
94.07
84.50
77.48
77.16
76.84
76.34
71.06
39.08
14.81
0.27
H
H
O
OH
Me3Si
15
(+/-)
f1 (ppm)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7.56
7.55
7.55
7.54
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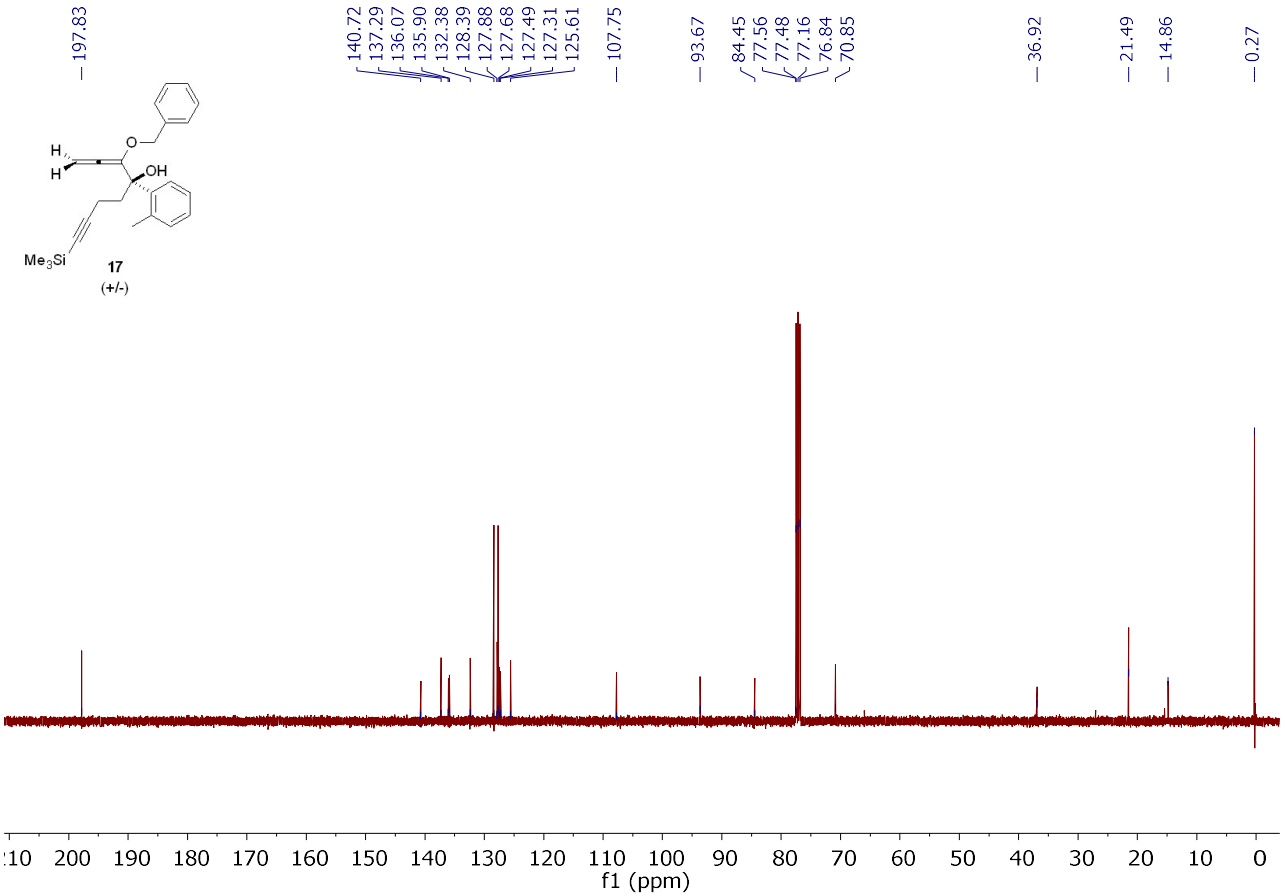
7.30
7.29
7.29
7.28
7.28
7.28
7.27
7.27
7.20
7.20
7.19
7.19
7.19
7.18
7.18
7.16
7.16
7.15
7.14
7.14
7.13
7.13
7.12
7.11
5.67
5.65
5.64
5.61
2.96
2.38
2.37
2.35
2.34
2.33
2.32
2.30
2.29
2.28
2.27
2.26
2.25
2.25
2.18
2.17
2.16
2.15
2.13
2.12
2.11
0.14
H
H
O
OH
Me3Si
17
(+/-)
0.98
3.43
2.05
3.14
2.00
2.05
0.93
3.06
0.97
2.13
1.05
9.23
f1 (ppm)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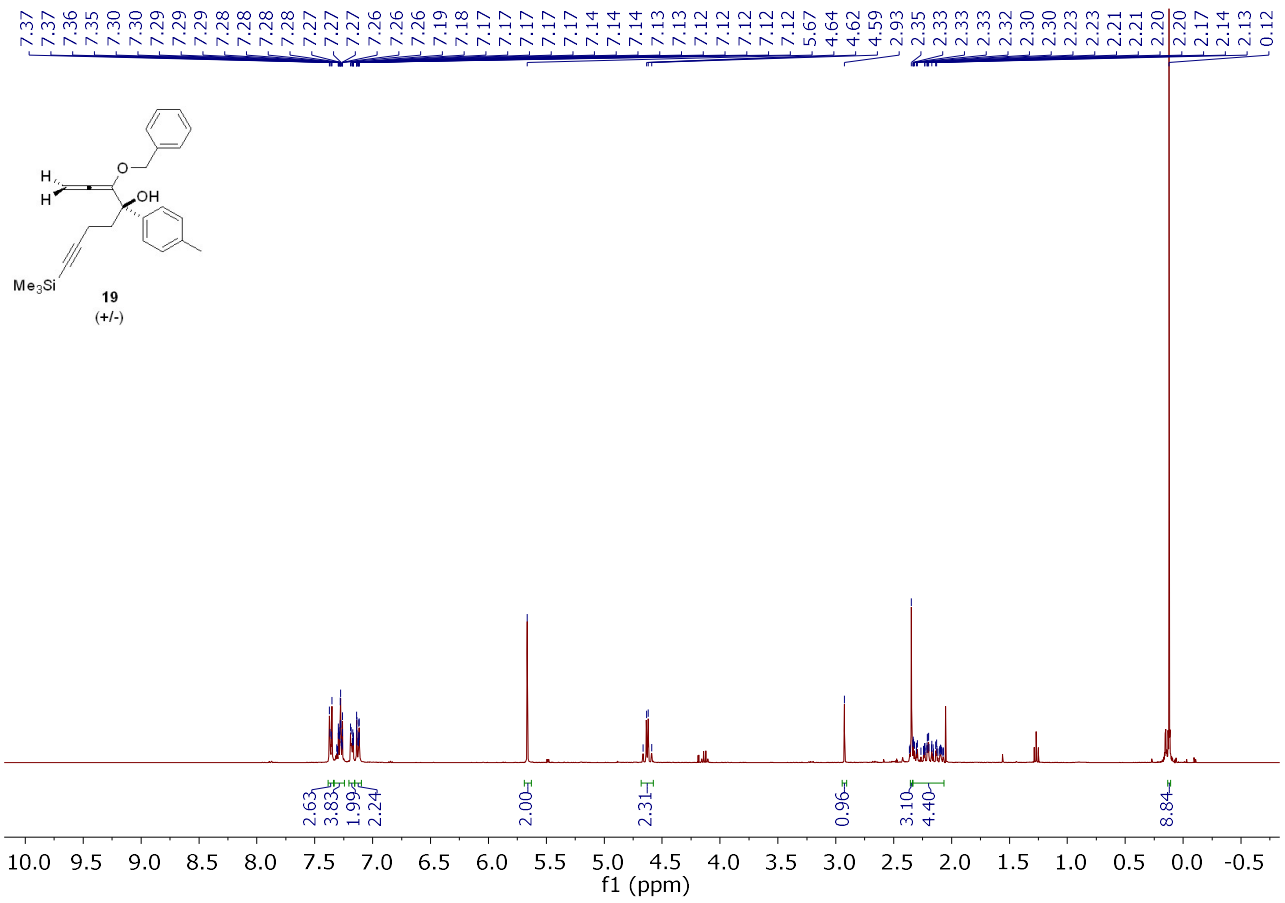
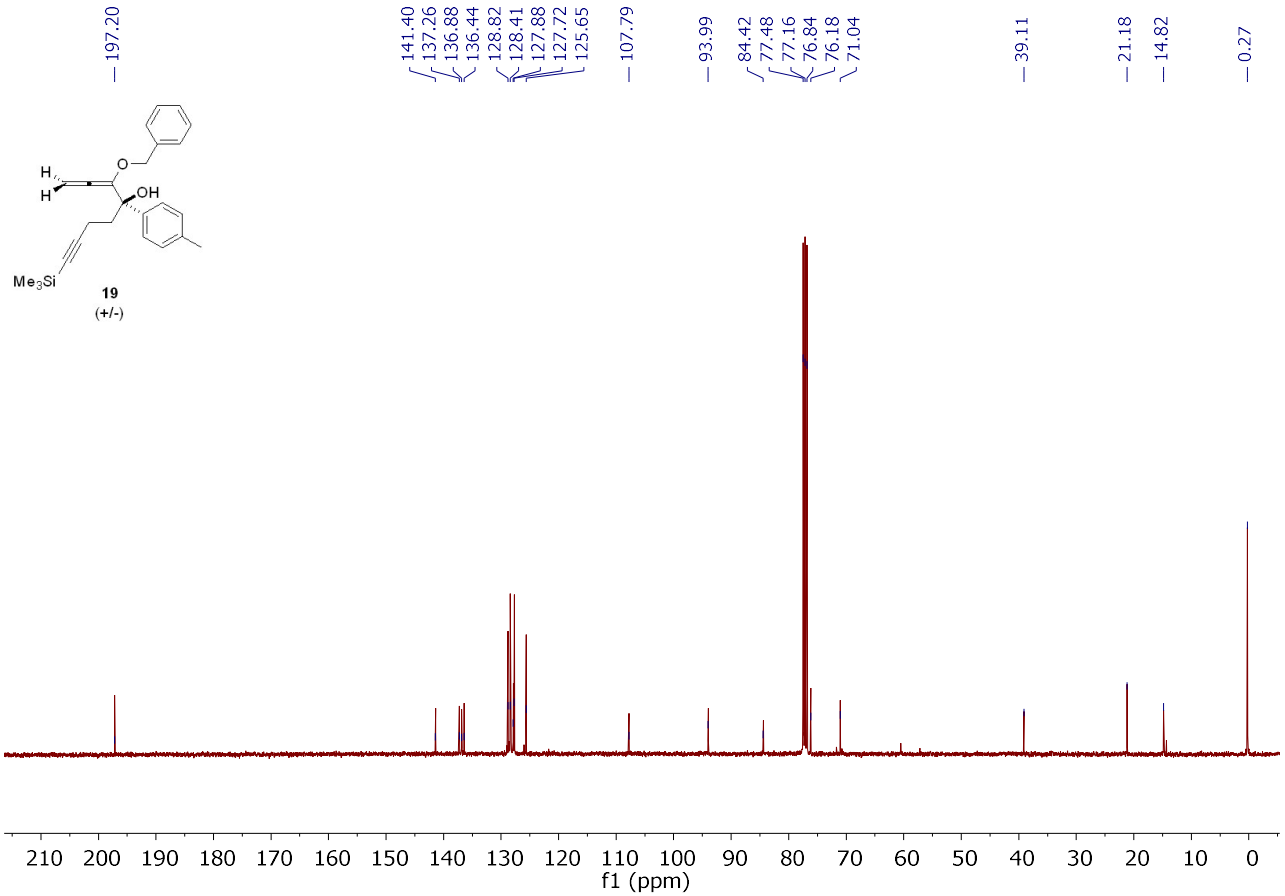
140.72
137.29
136.07
135.90
132.38
128.39
127.88
127.68
127.49
127.31
125.61
107.75
93.67
84.45
77.56
77.48
77.16
76.84
70.85
36.92
21.49
14.86
0.27
Me3Si
17
(+/-)
f1 (ppm)


Me3Si
19
(+/-)
2.63
3.83
1.99
2.24
2.00
2.31
0.96
3.10
4.40
8.84
f1 (ppm)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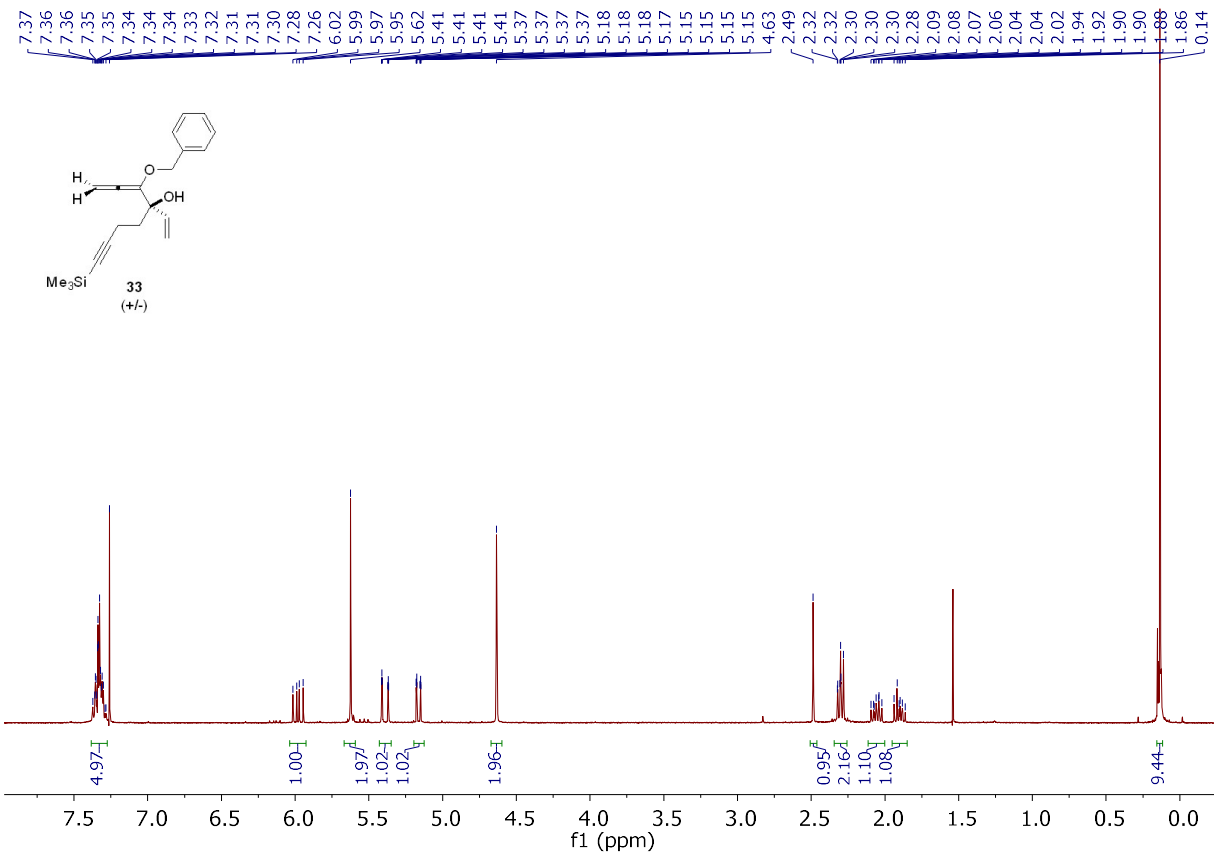
141.40
137.26
136.88
136.44
128.82
128.41
127.88
127.72
125.65
107.79
93.99
84.42
77.48
77.16
76.84
76.18
71.04
39.11
21.18
14.82
0.27
H
H
O
OH
Me3Si
19
(+/-)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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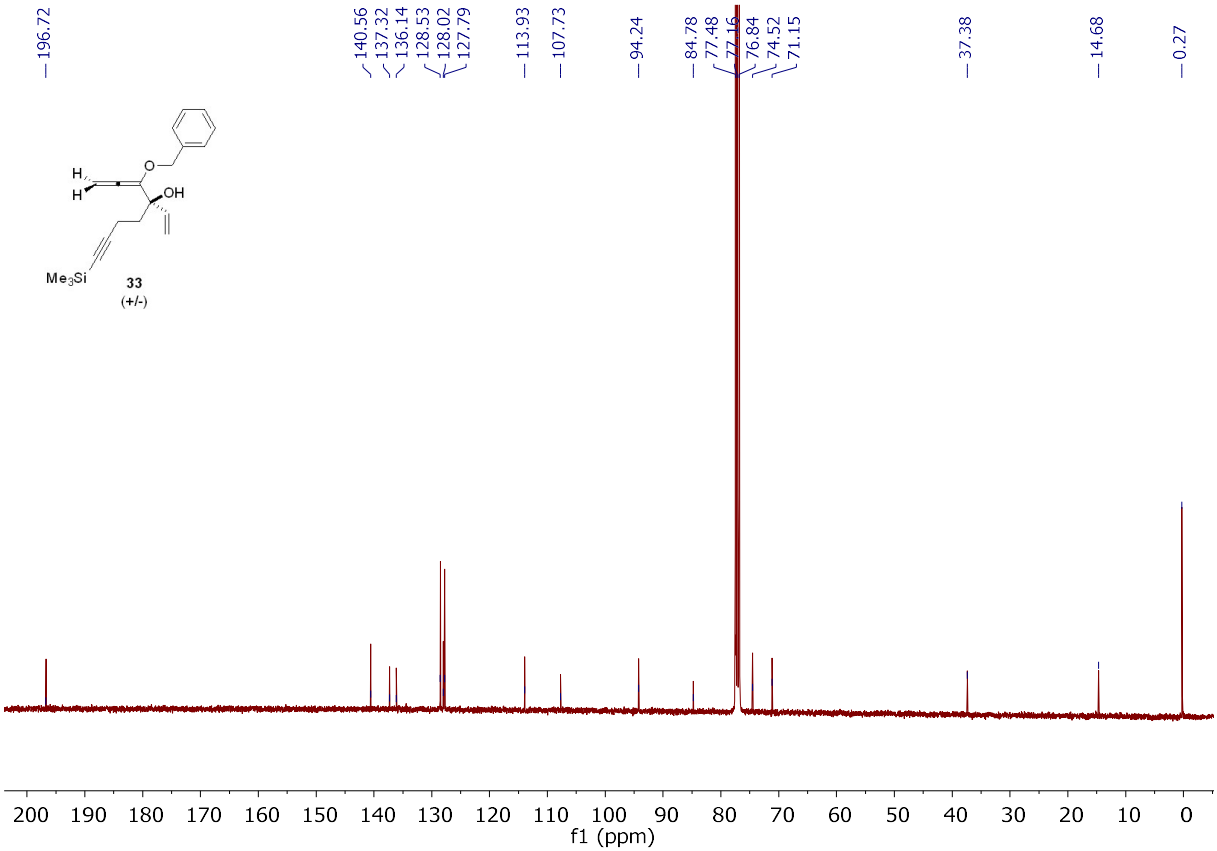
7.34
7.34
7.34
7.33
7.32
7.31
7.31
7.30
7.28
7.26
6.02
5.99
5.97
5.95
5.62
5.41
5.41
5.41
5.41
5.37
5.37
5.37
5.37
5.18
5.18
5.17
5.15
5.15
5.15
5.15
4.63
2.49
2.32
2.32
2.30
2.30
2.30
2.28
2.09
2.08
2.07
2.06
2.04
2.04
2.02
1.94
1.92
1.90
1.90
1.88
1.86
0.14
H
H
O
OH
Me3Si
33
(+/-)
4.97
1.00
1.97
1.02
1.02
1.96
0.95
2.16
1.10
1.08
9.44
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 0.0
f1 (ppm)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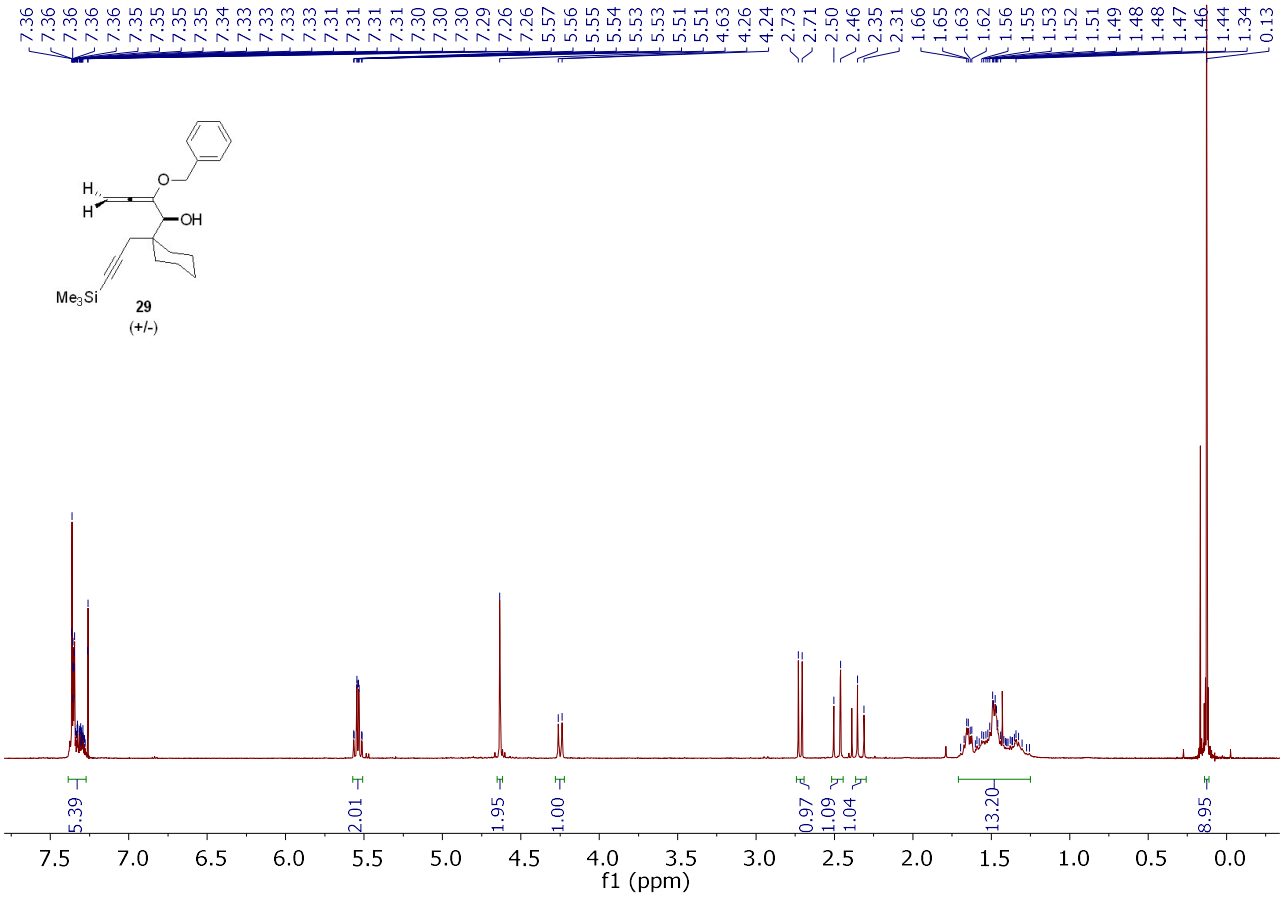
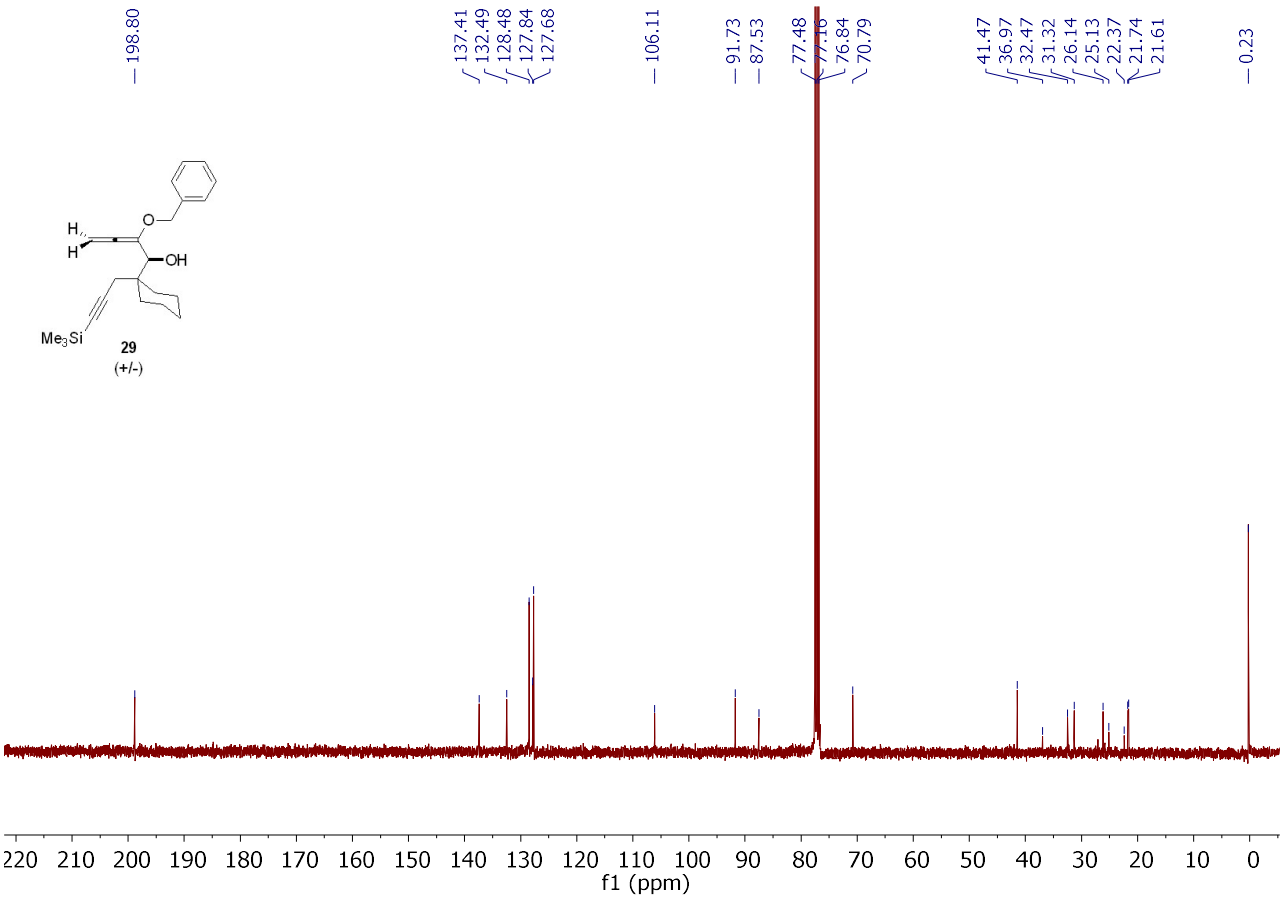
136.14
128.53
128.02
127.79
113.93
107.73
94.24
84.78
77.48
77.16
76.84
74.52
71.15
37.38
14.68
0.27
H
H
O
OH
Me3Si
33
(+/-)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.36 7.36 7.36 7.36 7.35 7.35 7.35 7.34 7.33 7.33 7.33 7.31 7.31 7.31 7.31 7.30 7.30 7.30 7.29 7.26 7.26 5.57 5.56 5.55 5.54 5.53 5.53 5.51 5.51 4.63 4.26 4.24 2.73 2.71 2.50 2.46 2.35 2.31 1.66 1.65 1.63 1.62 1.56 1.55 1.53 1.52 1.51 1.49 1.48 1.48 1.47 1.46 1.44 1.34 0.13
H
H
O
OH
Me3Si
29
(+/-)
5.39
2.01
1.95
1.00
0.97
1.09
1.04
13.20
8.95
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 0.0
f1 (ppm)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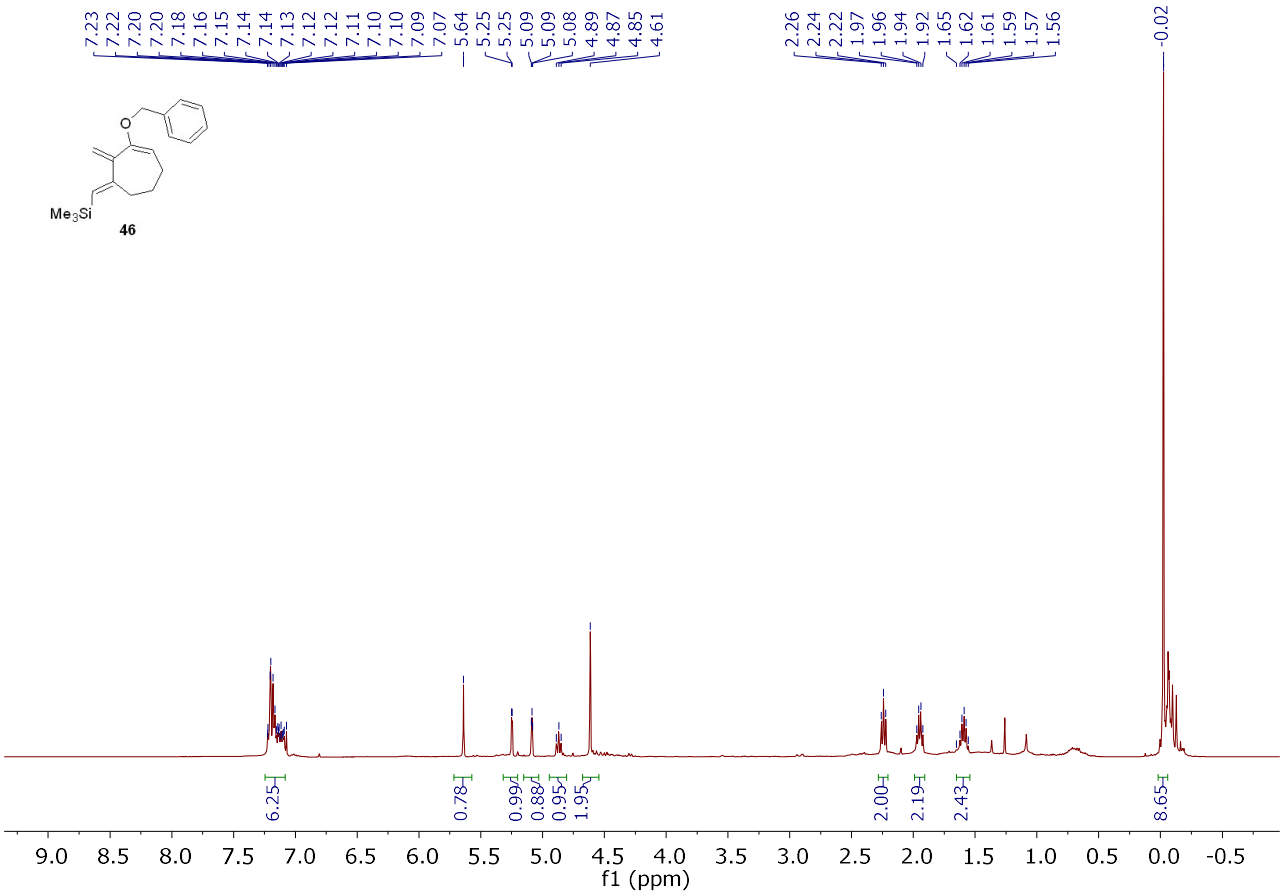
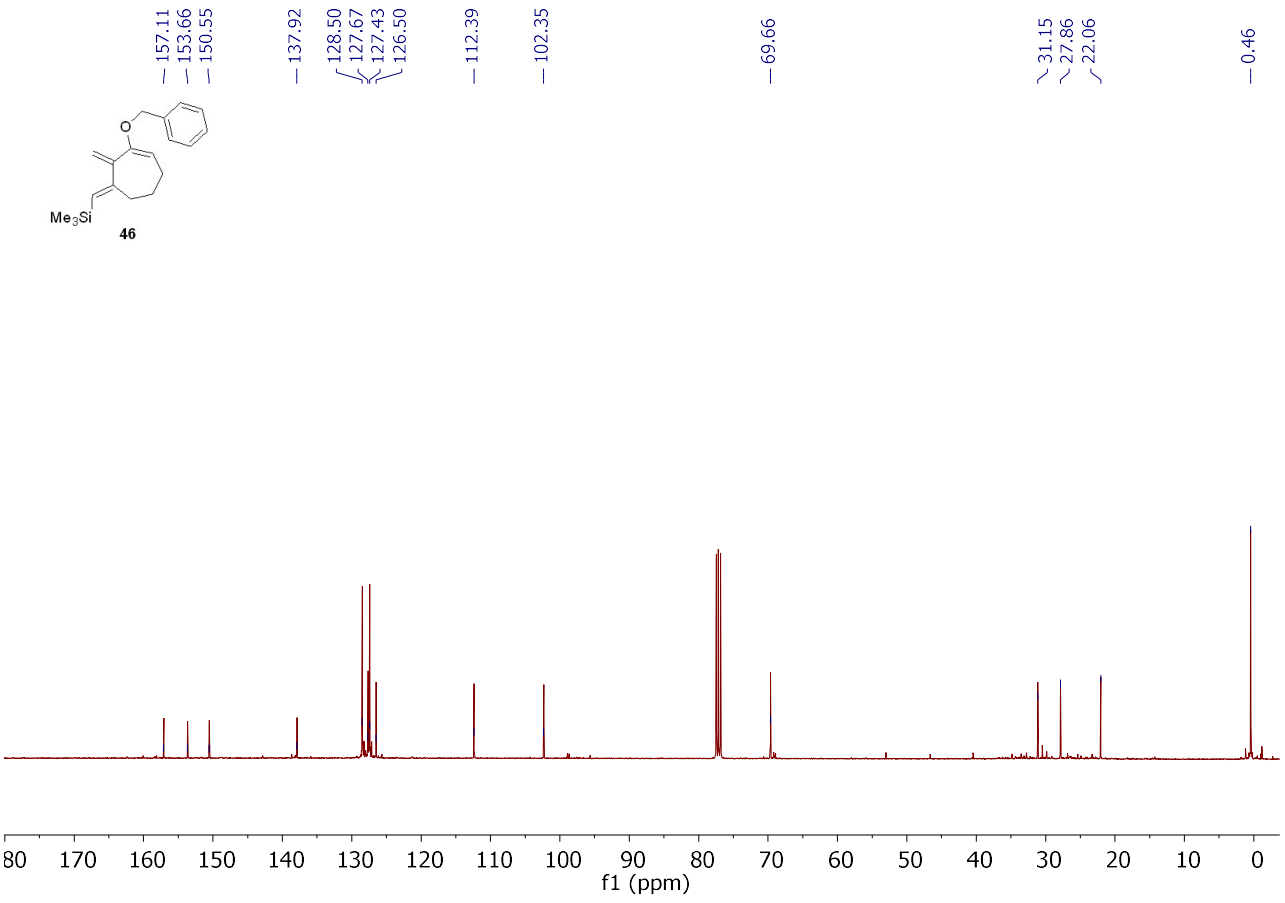
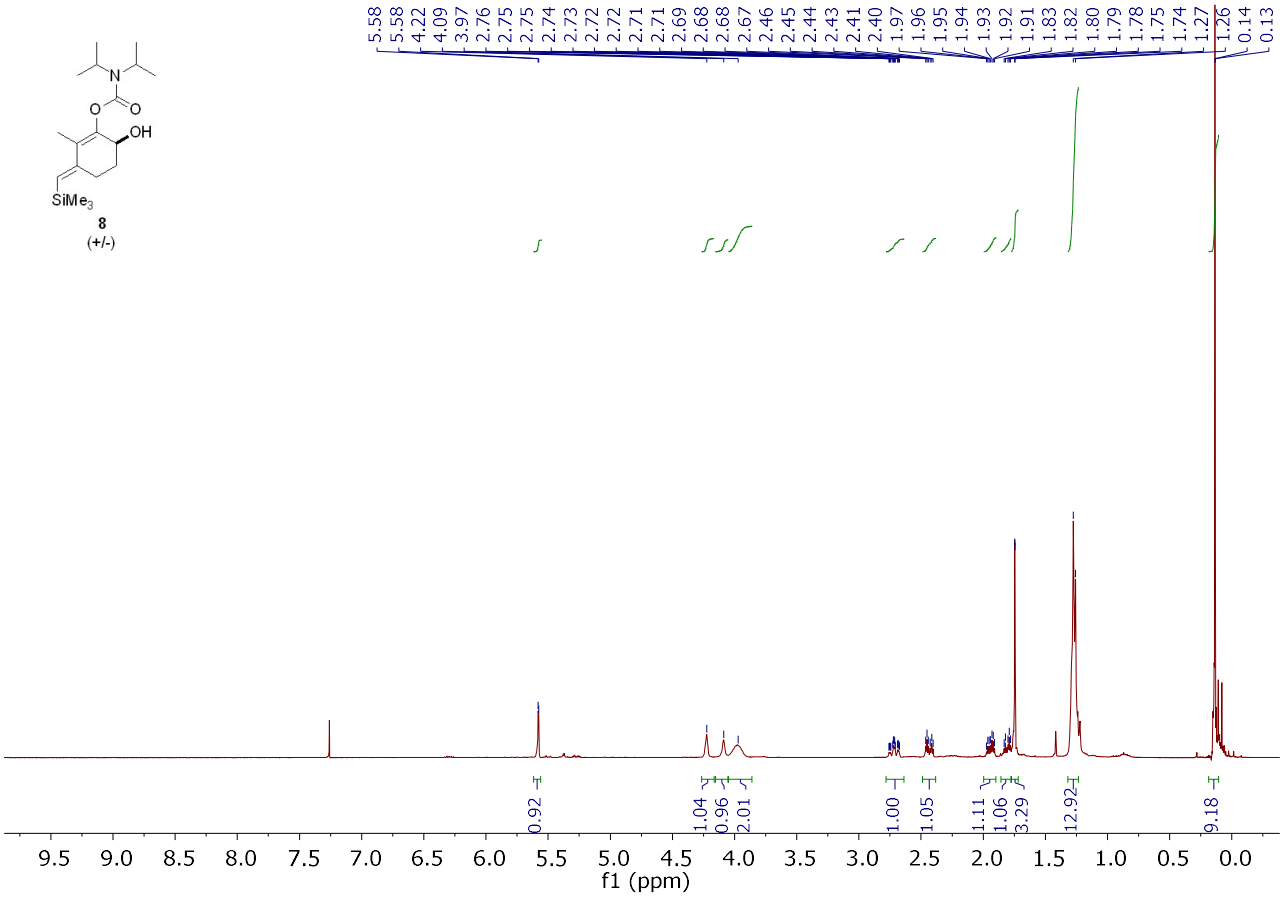
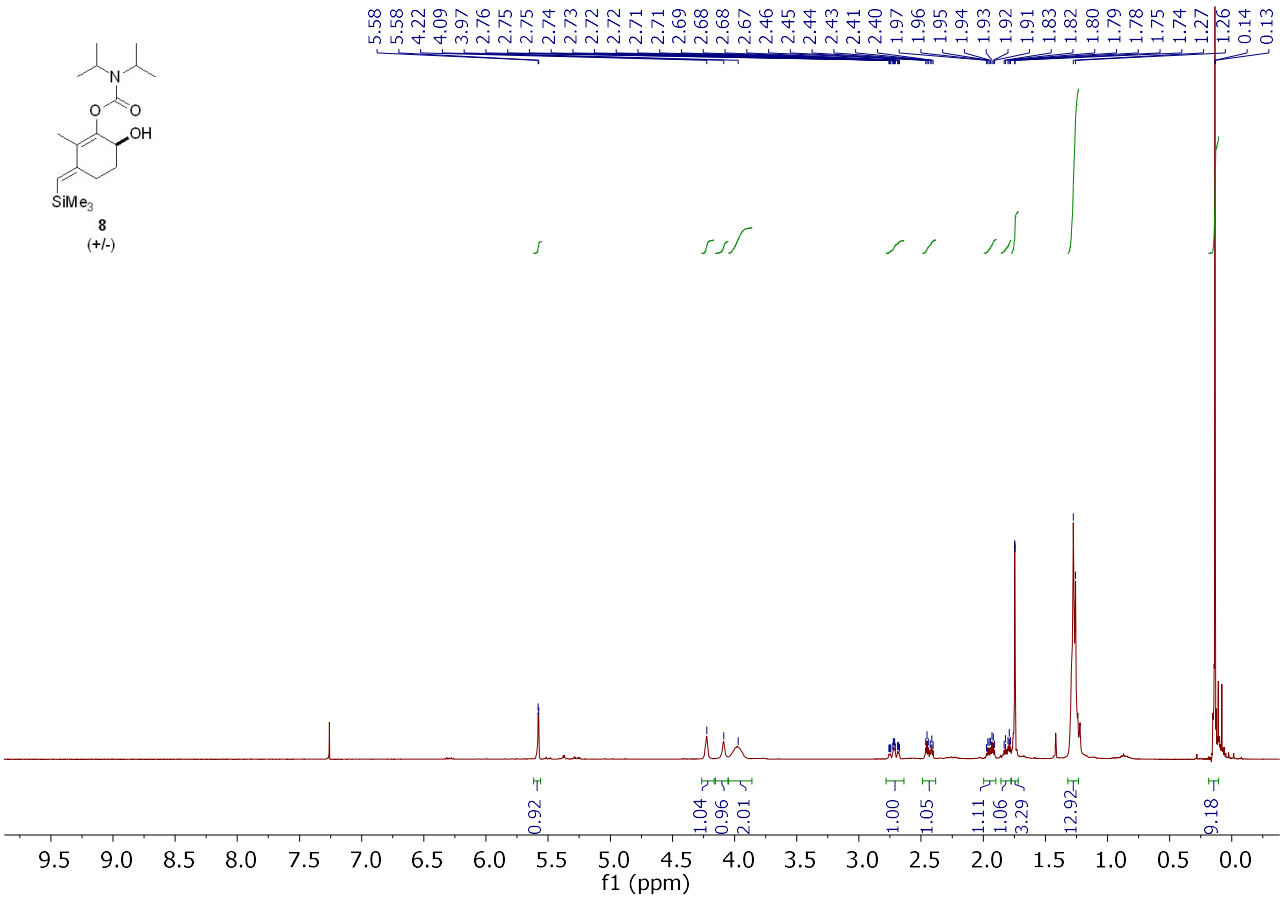
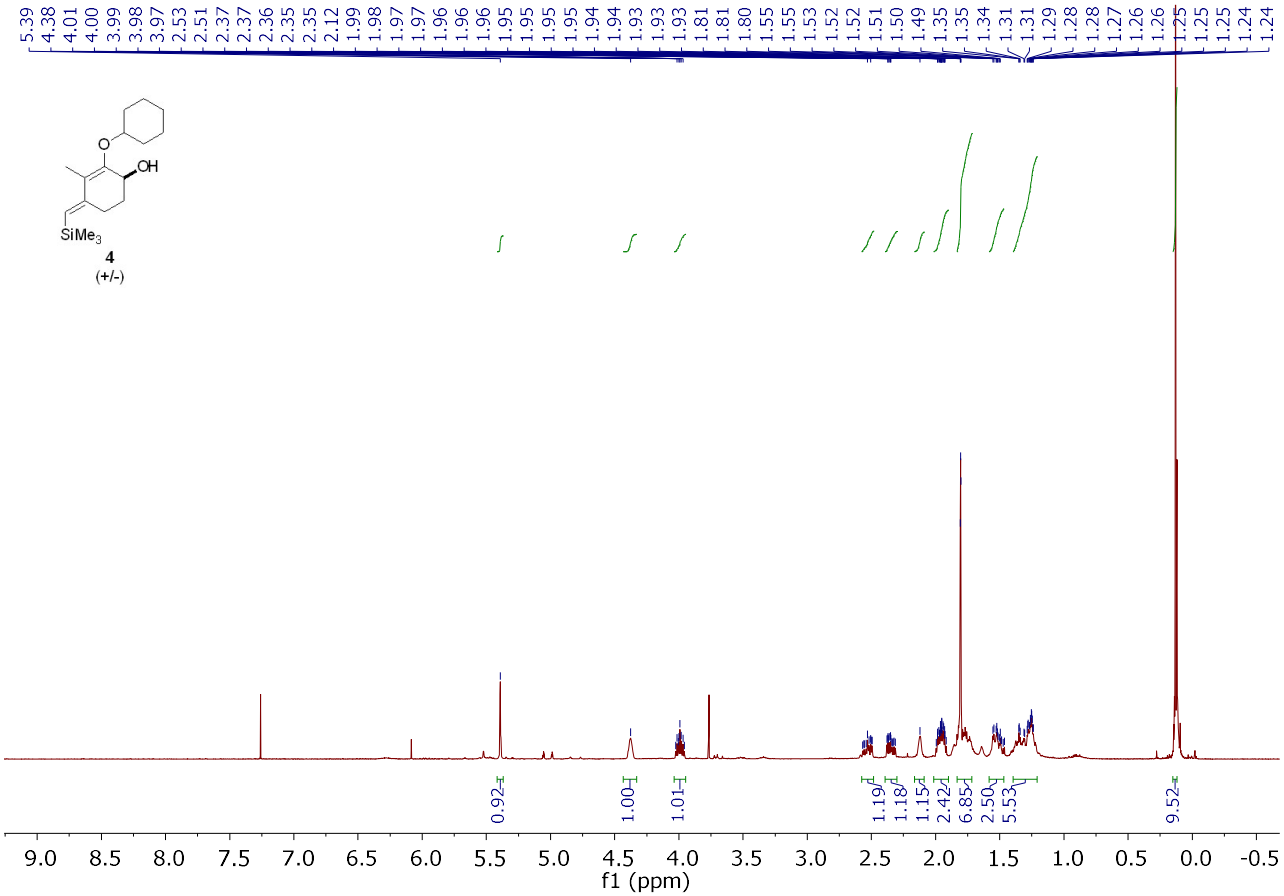
127.68
106.11
91.73
87.53
77.48
77.16
76.84
70.79
41.47
36.97
32.47
31.32
26.14
25.13
22.37
21.74
21.61
0.23
H
H
O
OH
Me3Si
29
(+/-)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

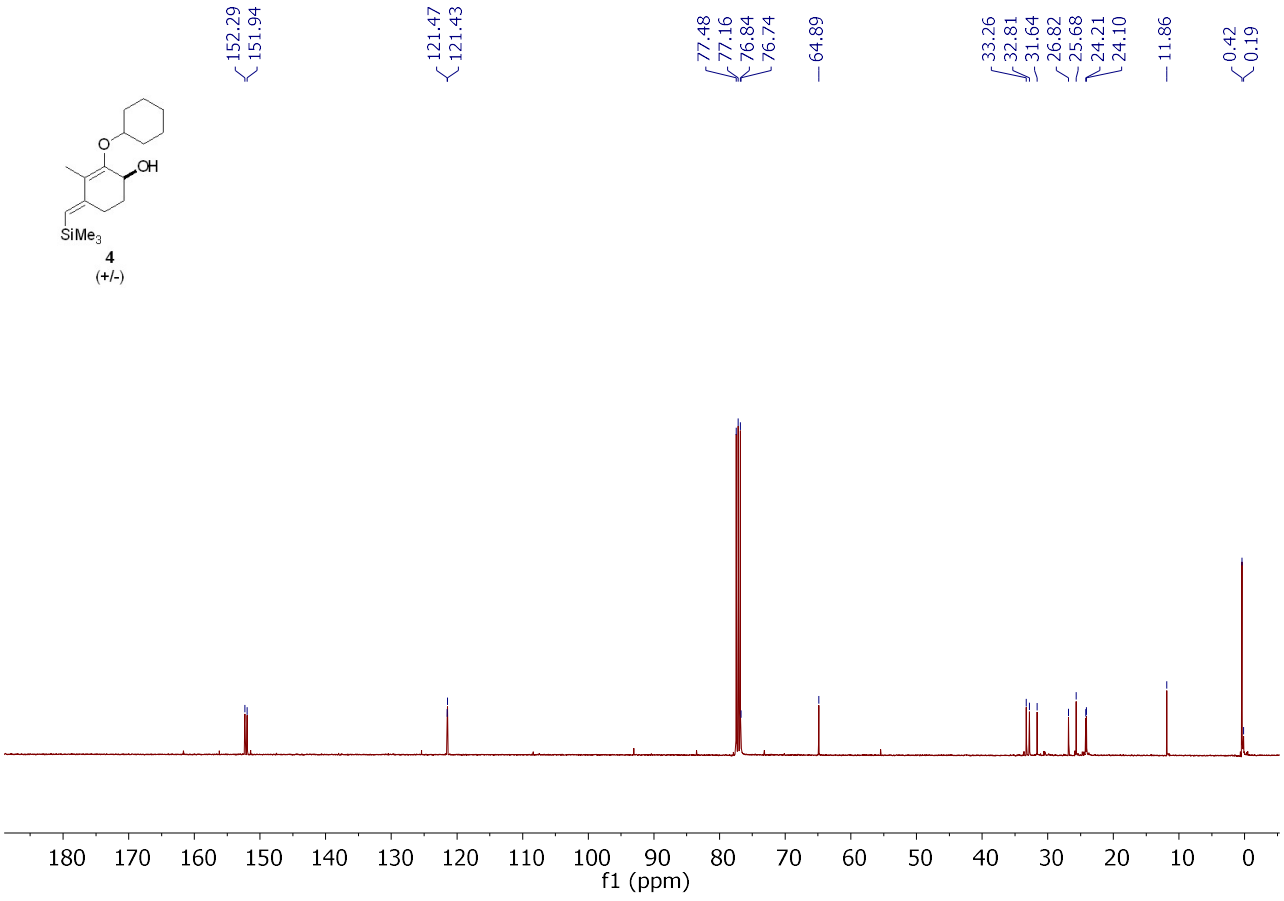

7.23
7.22
7.20
7.20
7.18
7.16
7.15
7.14
7.14
7.13
7.12
7.12
7.11
7.10
7.10
7.09
7.07
5.64
5.25
5.25
5.09
5.09
5.08
4.89
4.87
4.85
4.61
2.26
2.24
2.22
1.97
1.96
1.94
1.92
1.65
1.62
1.61
1.59
1.57
1.56
-0.02
O
Me3Si
46
6.25
0.78
0.99
0.88
0.95
1.95
2.00
2.19
2.43
8.65
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

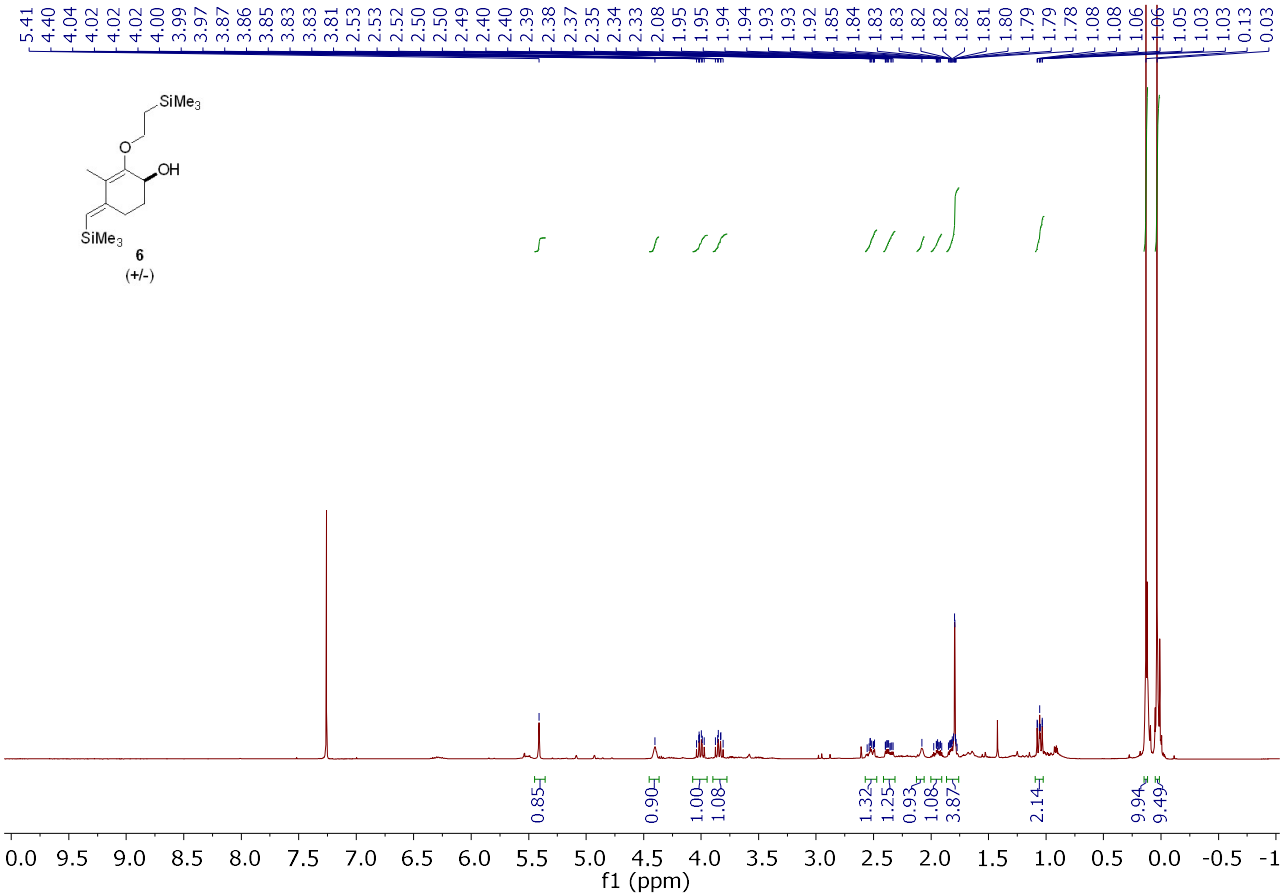

157.11
153.66
150.55
137.92
128.50
127.67
127.43
126.50
112.39
102.35
69.66
31.15
27.86
22.06
0.46
O
Me3Si
46
80 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

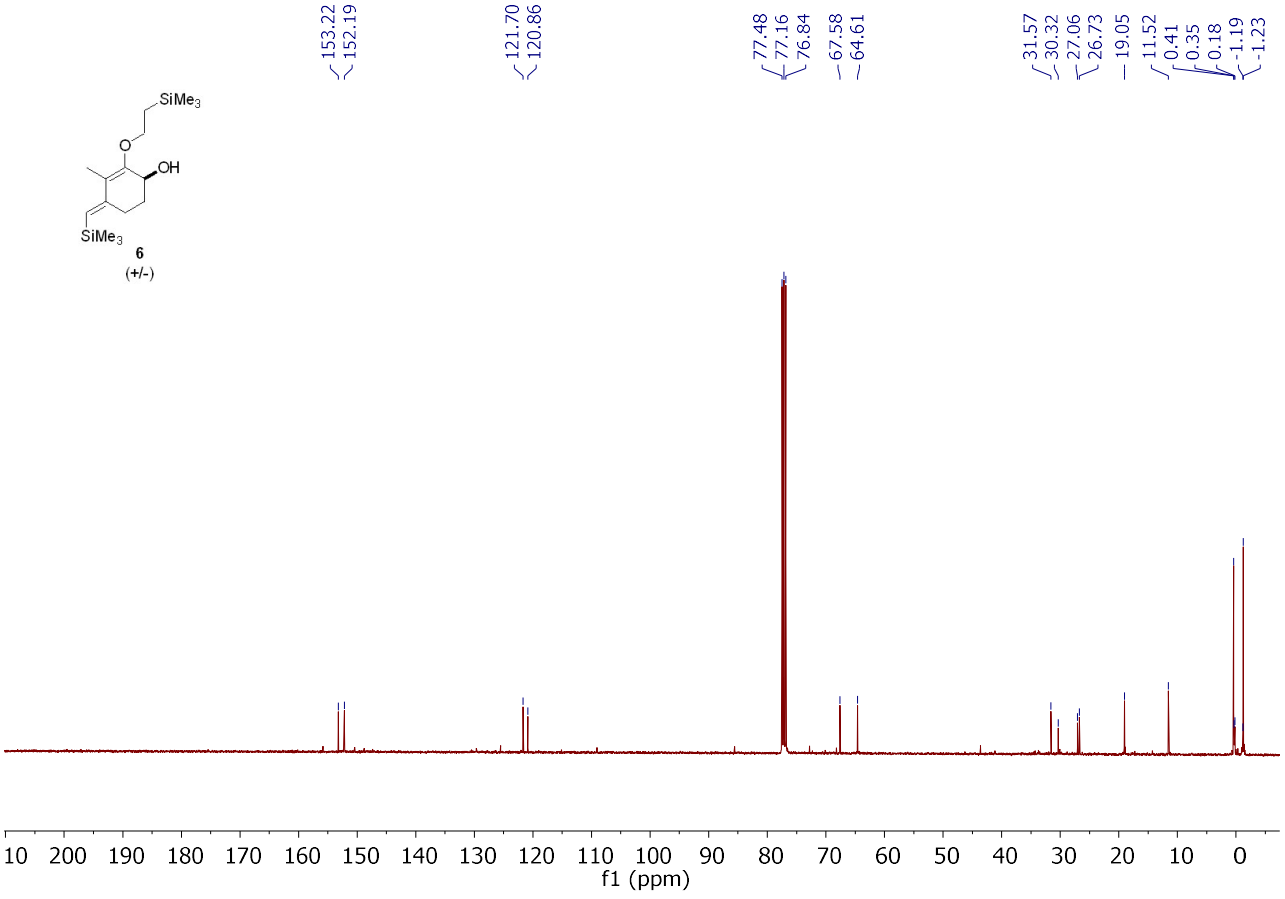

5.58 5.58 4.22 4.09 3.97 2.76 2.75 2.75 2.74 2.73 2.72 2.72 2.71 2.71 2.69 2.68 2.68 2.67 2.46 2.45 2.44 2.43 2.41 2.40 1.97 1.96 1.95 1.94 1.93 1.92 1.91 1.83 1.82 1.80 1.79 1.78 1.75 1.74 1.27 1.26 0.14 0.13
N
O
O
OH
SiMe3
8
(+/-)
0.92
1.04
0.96
2.01
1.00
1.05
1.11
1.06
3.29
12.92
9.18
9.5 9.0 8.5 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 0.5 0.0
f1 (ppm)

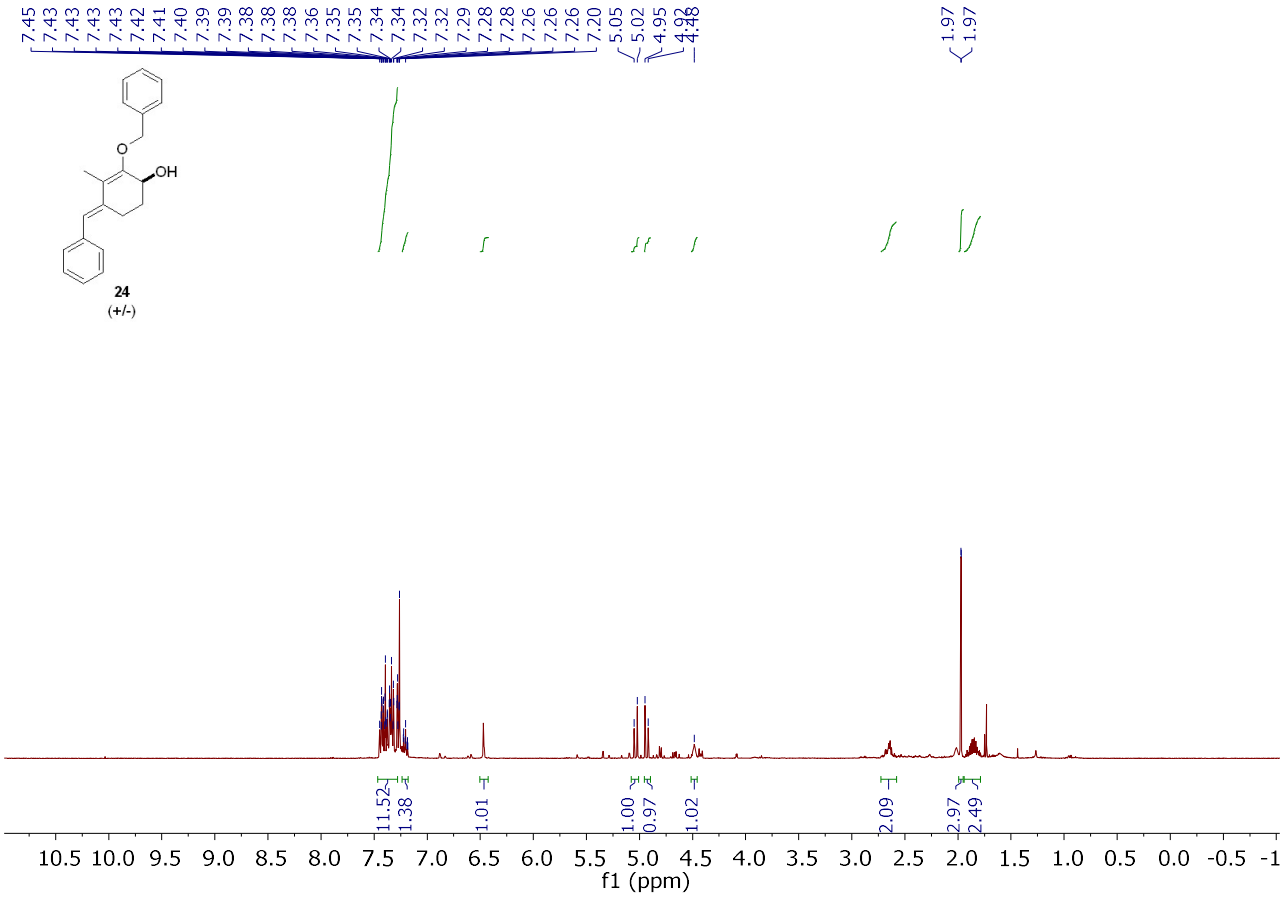

5.58 5.58 4.22 4.09 3.97 2.76 2.75 2.75 2.74 2.73 2.72 2.72 2.71 2.71 2.69 2.68 2.68 2.67 2.46 2.45 2.44 2.43 2.41 2.40 1.97 1.96 1.95 1.94 1.93 1.92 1.91 1.83 1.82 1.80 1.79 1.78 1.75 1.74 1.27 1.26 0.14 0.13
N
O
O
OH
SiMe3
8
(+/-)
0.92
1.04
0.96
2.01
1.00
1.05
1.11
1.06
3.29
12.92
9.18
9.5 9.0 8.5 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 0.5 0.0
f1 (ppm)

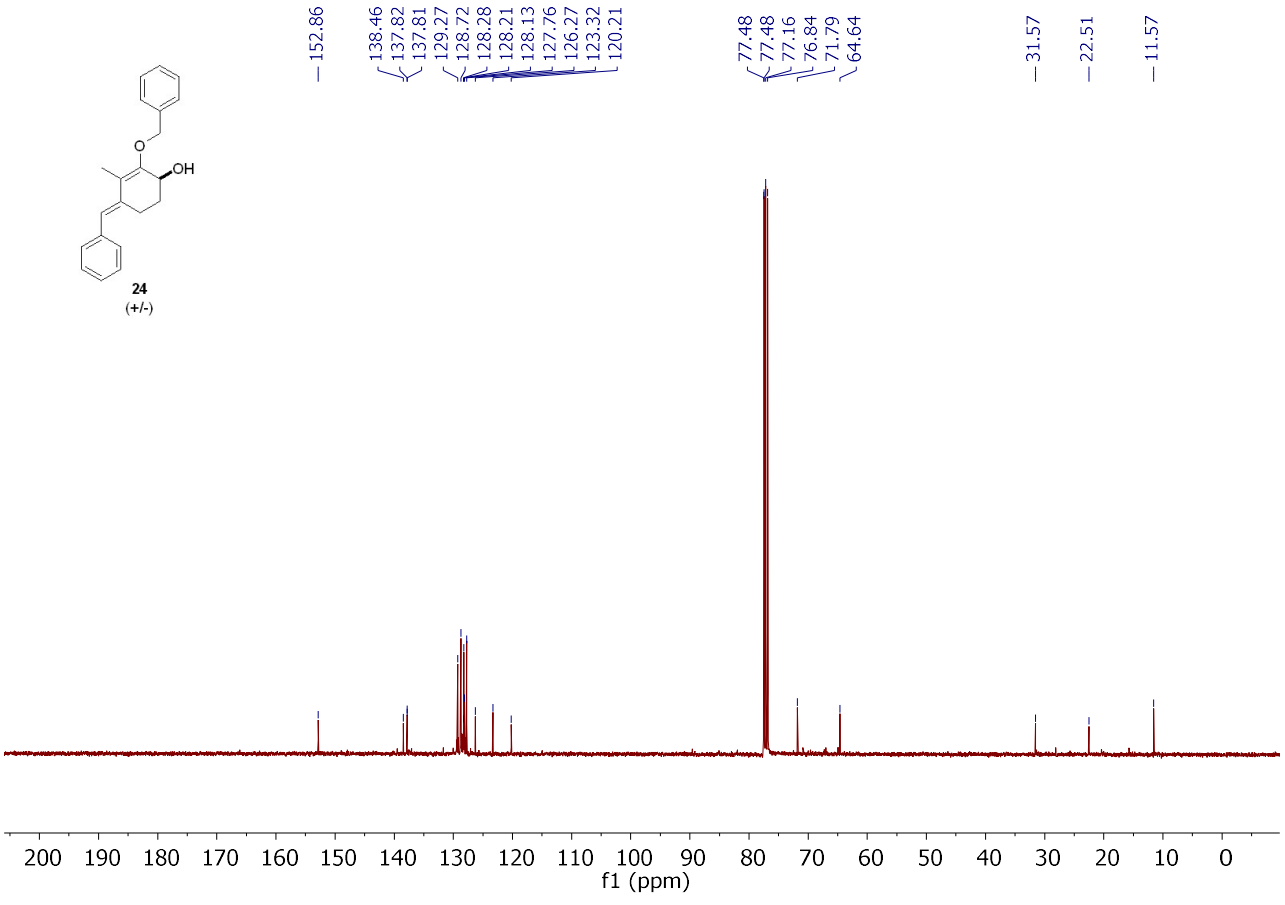

5.39 4.38 4.01 4.00 3.99 3.98 3.97 2.53 2.51 2.37 2.37 2.36 2.35 2.35 2.12 1.99 1.98 1.97 1.97 1.96 1.96 1.96 1.95 1.95 1.95 1.95 1.94 1.94 1.93 1.93 1.93 1.81 1.81 1.80 1.55 1.55 1.53 1.52 1.52 1.51 1.50 1.49 1.35 1.35 1.34 1.31 1.31 1.29 1.28 1.28 1.27 1.26 1.26 1.25 1.25 1.25 1.24 1.24
O
OH
SiMe3
4
(+/-)
0.92 1.00 1.01 1.19 1.18 1.15 2.42 6.85 2.50 5.53 9.52
9.0 8.5 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 0.5 0.0 -0.5
f1 (ppm)

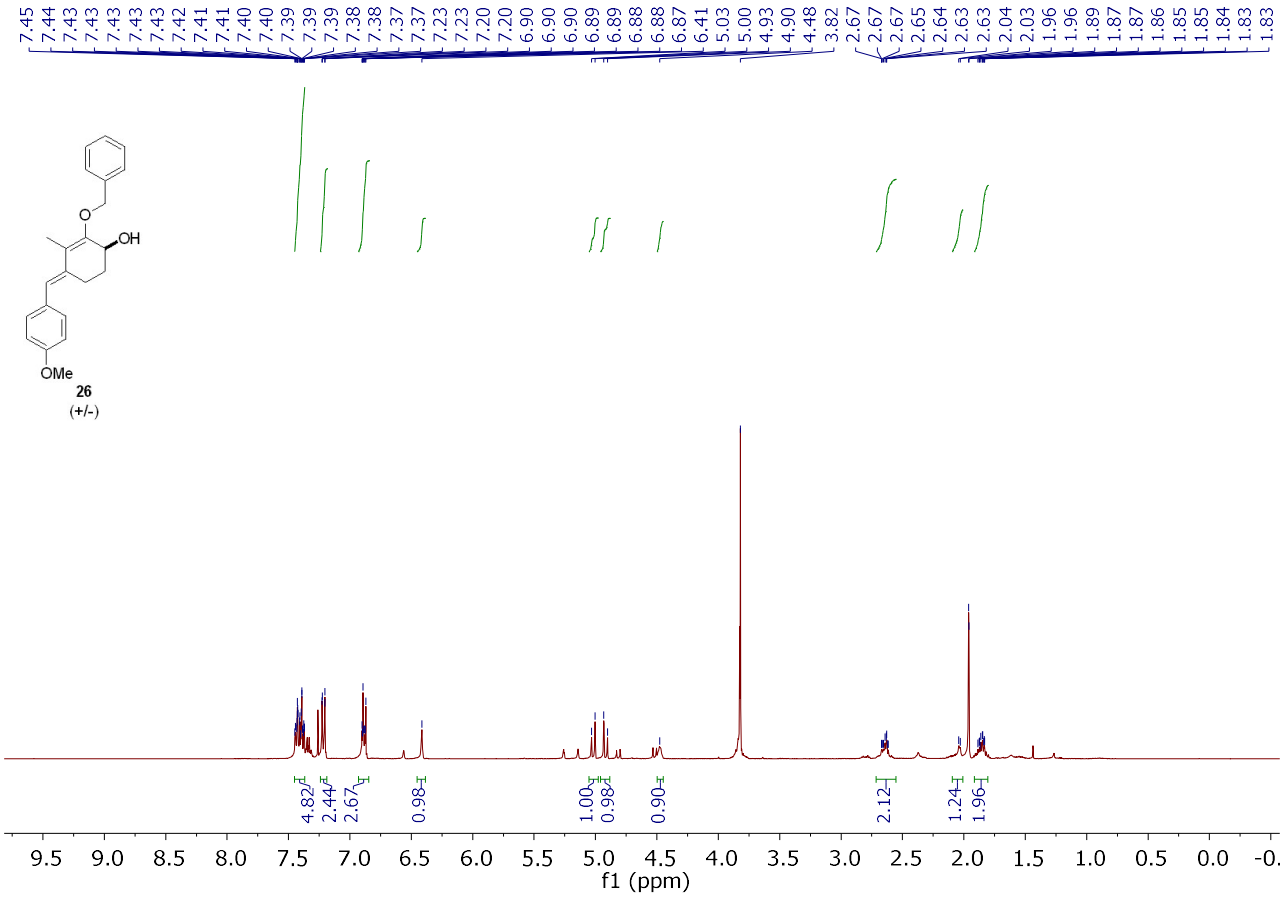

152.29 151.94 121.47 121.43 77.48 77.16 76.84 76.74 64.89 33.26 32.81 31.64 26.82 25.68 24.21 24.10 11.86 0.42 0.19
O
OH
SiMe3
4
(+/-)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

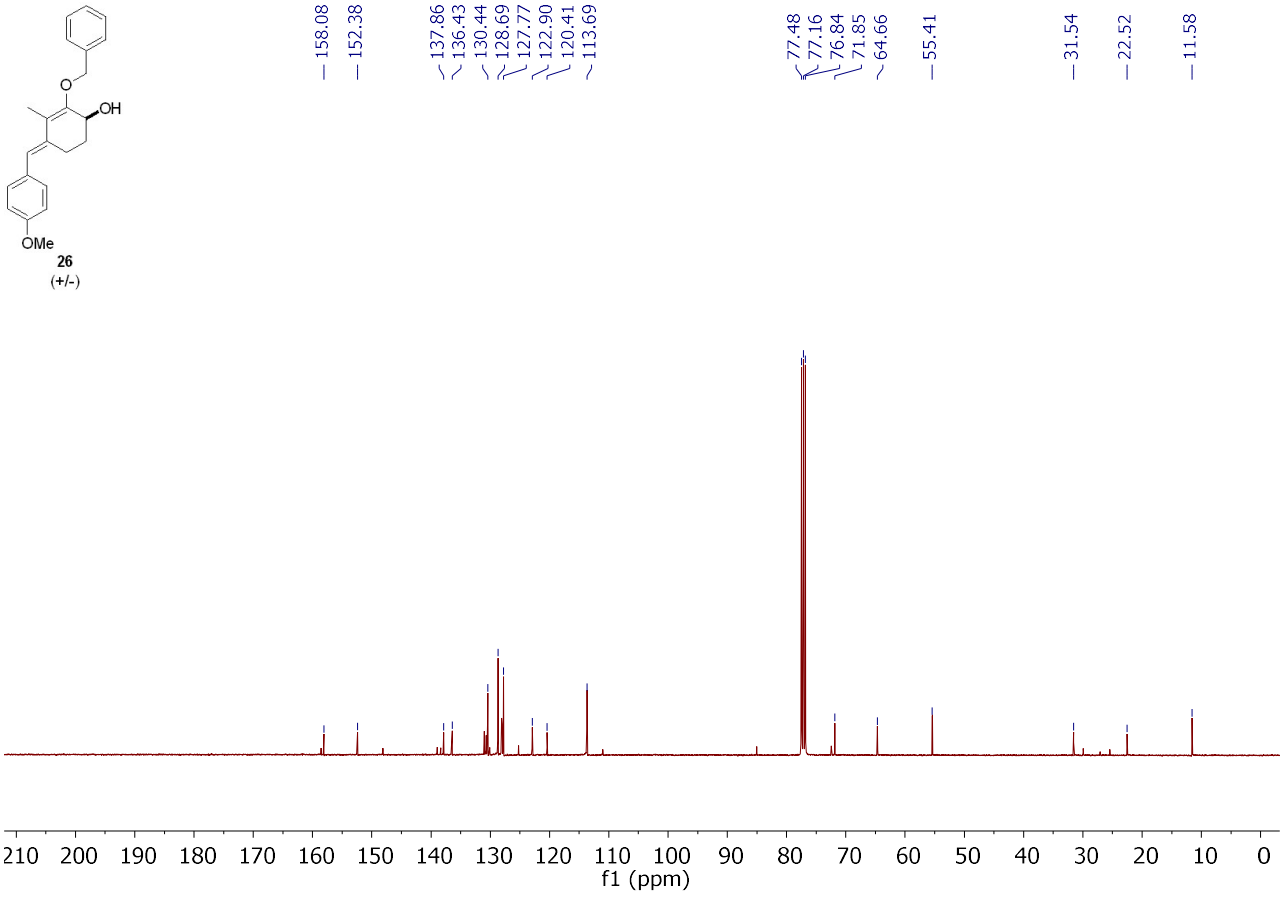

SiMe3
O
OH
SiMe3
6
(+/-)
f1 (ppm)

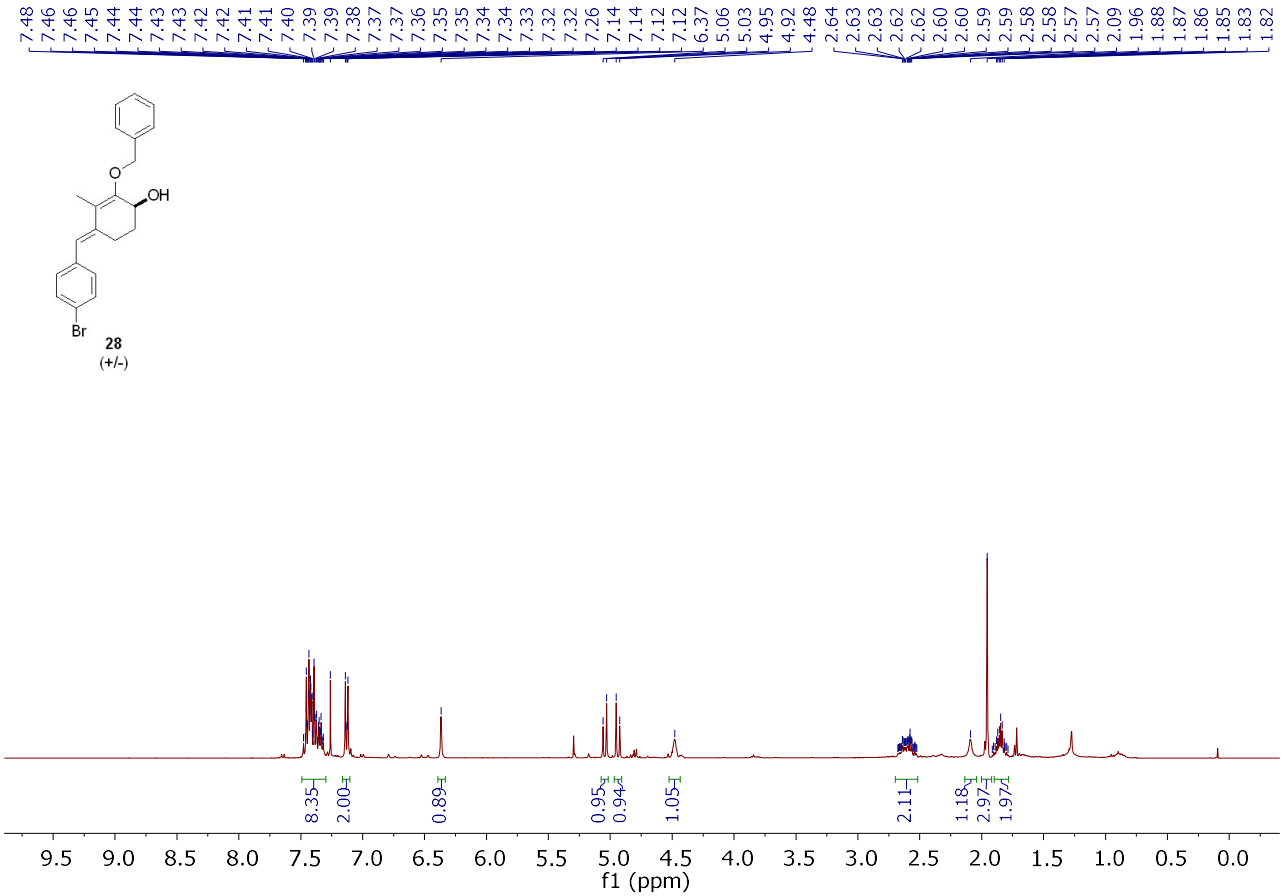

SiMe3
O
OH
SiMe3
6
(+/-)
f1 (ppm)

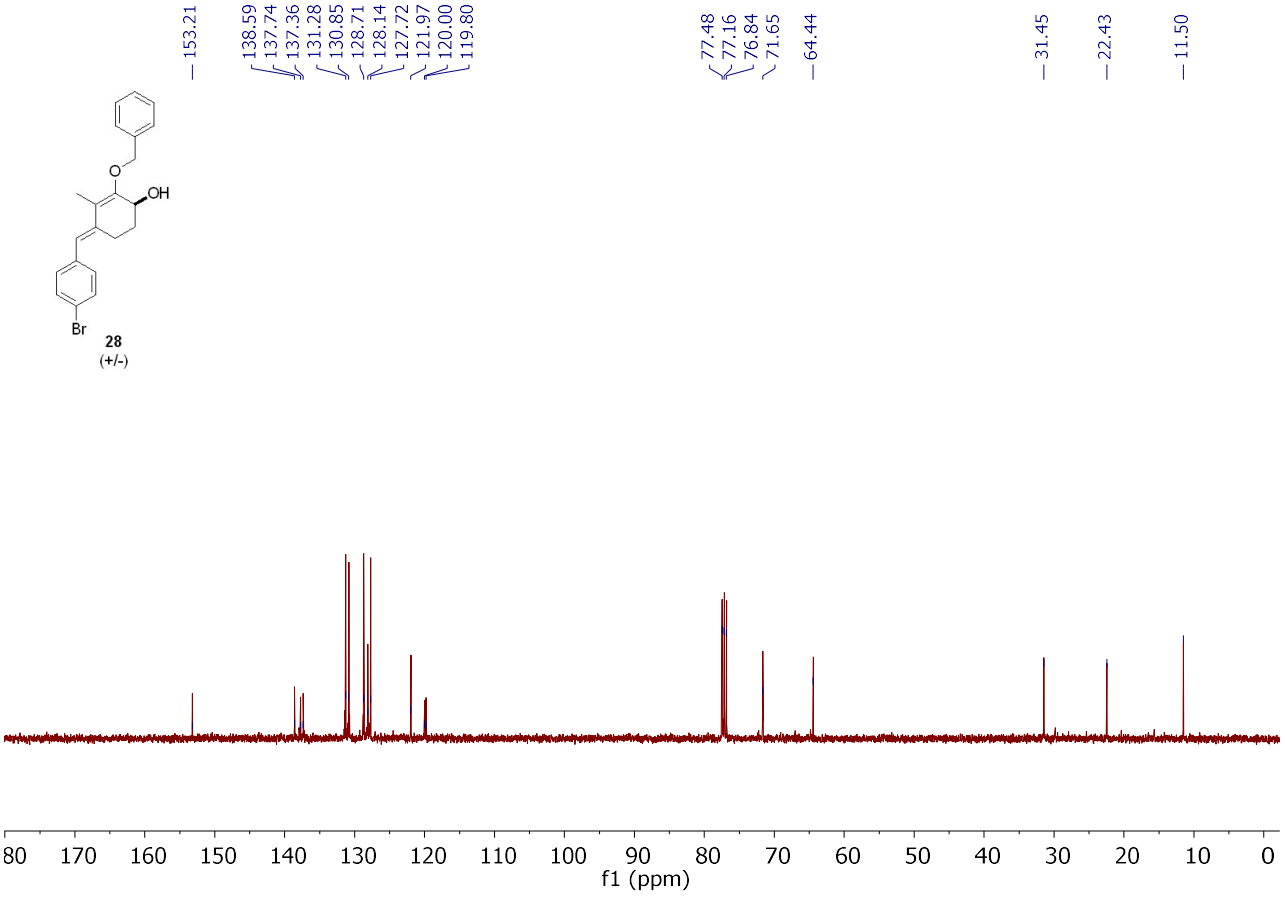

7.45 7.43 7.43 7.43 7.43 7.42 7.41 7.40 7.39 7.39 7.38 7.38 7.38 7.36 7.35 7.35 7.34 7.34 7.32 7.32 7.29 7.28 7.28 7.26 7.26 7.20 5.05 5.02 4.95 4.92 4.48
1.97 1.97
O
OH
24
(+/-)
11.52 1.38 1.01 1.00 0.97 1.02 2.09 2.97 2.49
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

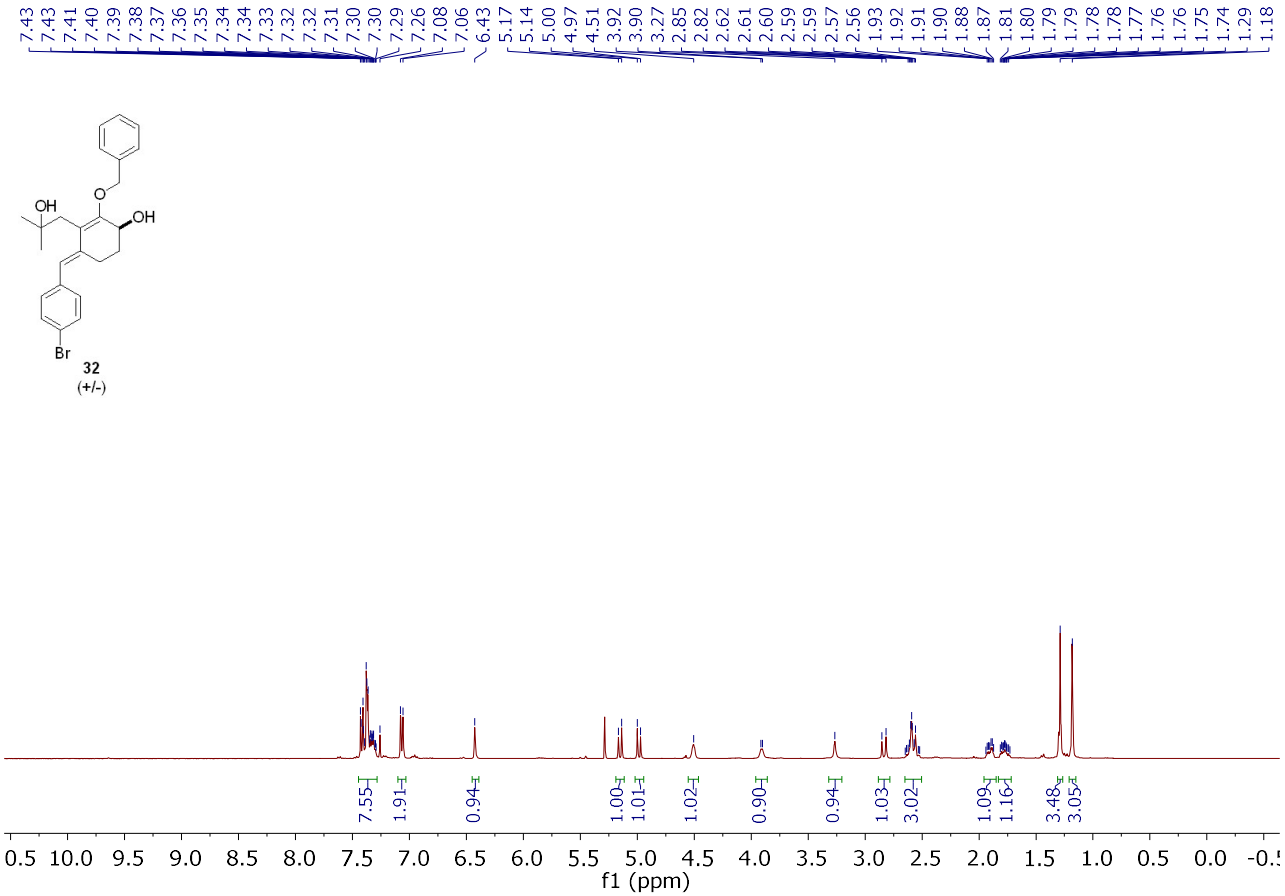

152.86 138.46 137.82 137.81 129.27 128.72 128.28 128.21 128.13 127.76 126.27 123.32 120.21
77.48 77.48 77.16 76.84 71.79 64.64
31.57 22.51 11.57
O
OH
24
(+/-)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

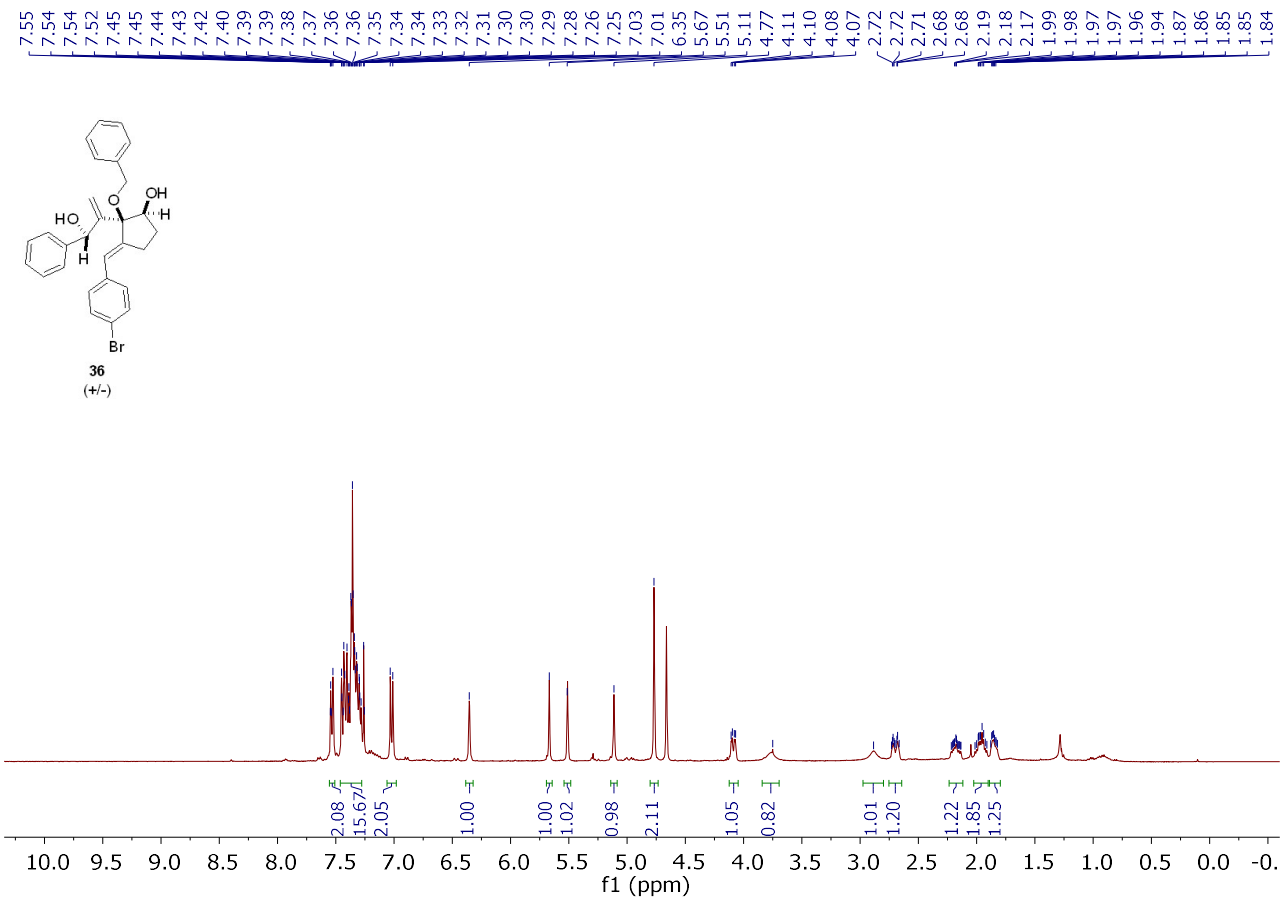

7.45 7.44 7.43 7.43 7.43 7.43 7.43 7.42 7.41 7.41 7.40 7.40 7.39 7.39 7.39 7.38 7.38 7.37 7.37 7.23 7.20 7.20 6.90 6.90 6.89 6.89 6.88 6.88 6.87 6.41 5.03 5.00 4.93 4.90 4.48 3.82 2.67 2.67 2.67 2.65 2.64 2.63 2.63 2.04 2.03 1.96 1.96 1.89 1.87 1.87 1.86 1.85 1.85 1.84 1.83 1.83
O
OH
OMe
26
(+/-)
4.82 2.44 2.67 0.98 1.00 0.98 0.90 2.12 1.24 1.96
9.5 9.0 8.5 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 0.5 0.0 -0.
f1 (ppm)

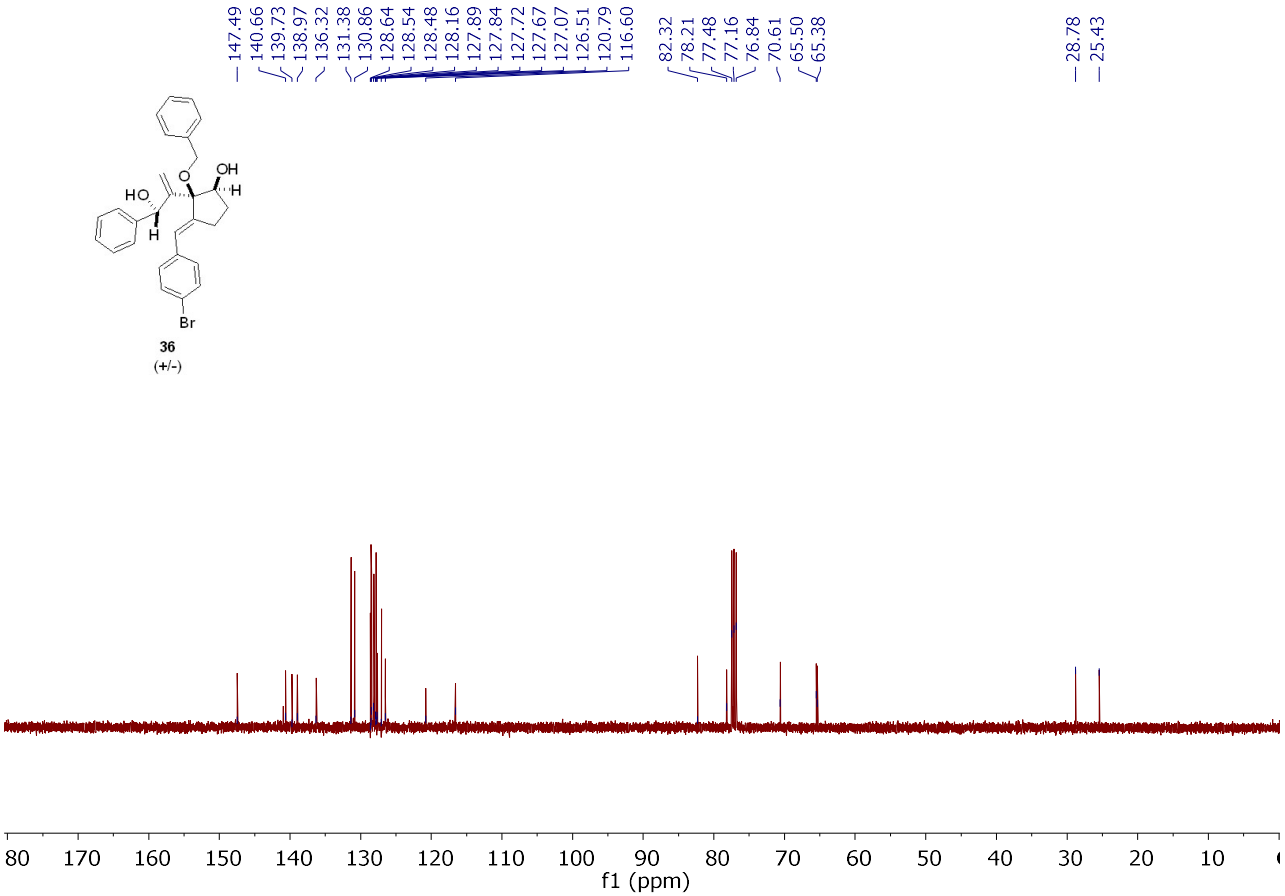

158.08 152.38 137.86 136.43 130.44 128.69 127.77 122.90 120.41 113.69 77.48 77.16 76.84 71.85 64.66 55.41 31.54 22.52 11.58
O
OH
OMe
26
(+/-)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

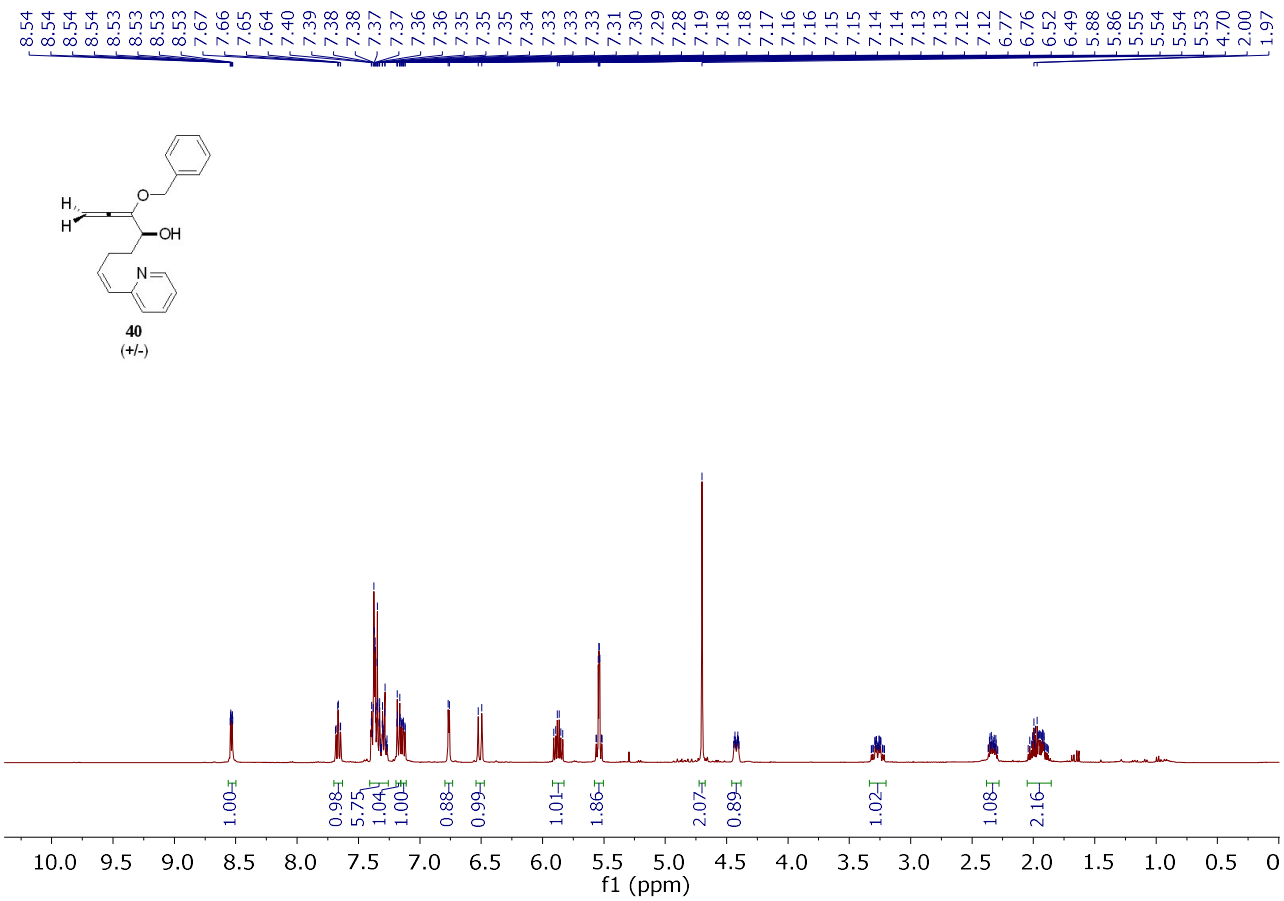

7.48 7.46 7.46 7.45 7.44 7.44 7.43 7.43 7.42 7.42 7.41 7.41 7.40 7.39 7.39 7.38 7.37 7.37 7.36 7.35 7.35 7.34 7.34 7.33 7.32 7.32 7.26 7.14 7.14 7.12 7.12 6.37 5.06 5.03 4.95 4.92 4.48 2.64 2.63 2.63 2.62 2.62 2.60 2.60 2.59 2.59 2.58 2.58 2.57 2.57 2.09 1.96 1.88 1.87 1.86 1.85 1.83 1.82
OH
Br
28
(+/-)
8.35 2.00 0.89 0.95 0.94 1.05 2.11 1.18 2.97 1.97
9.5 9.0 8.5 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 0.5 0.0
f1 (ppm)

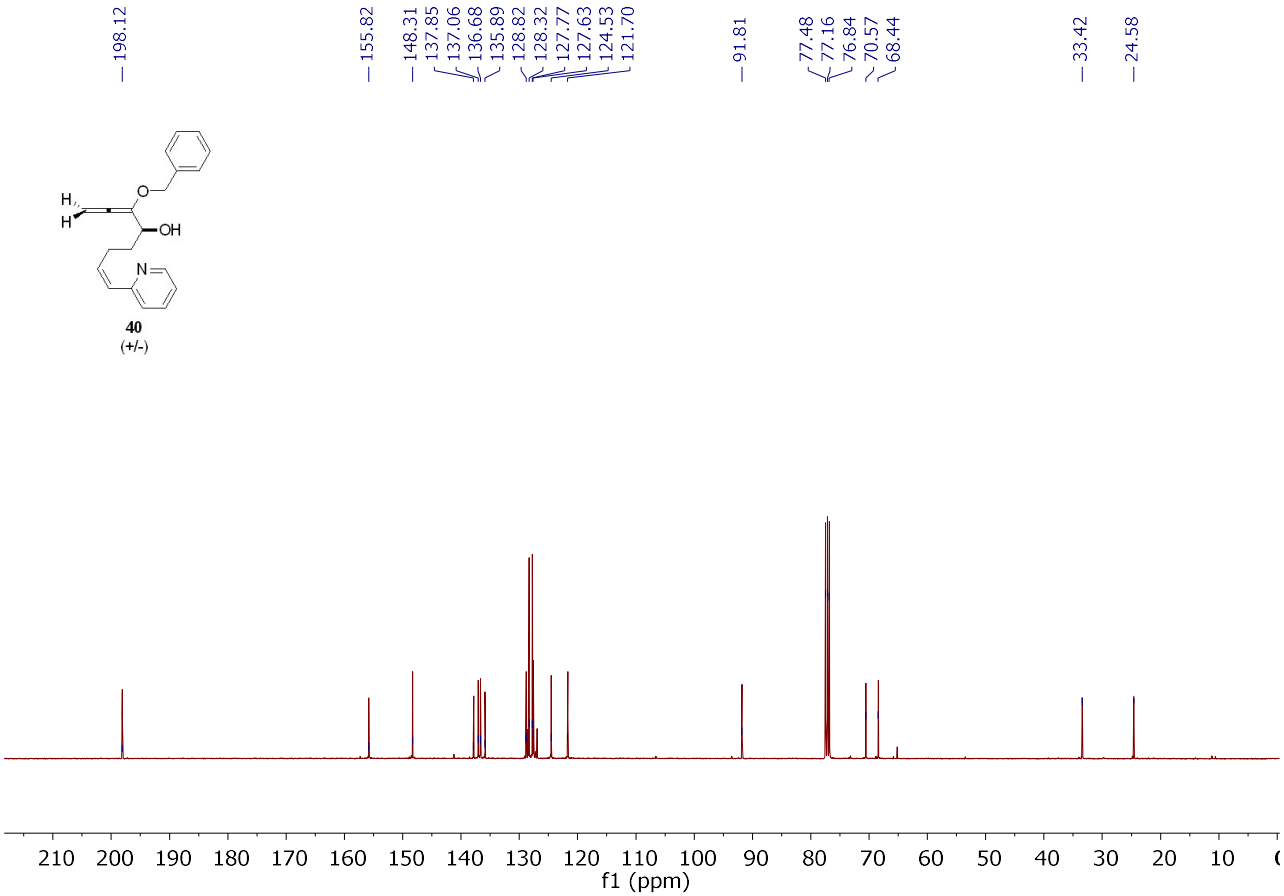

153.21
138.59 137.74 137.36 131.28 130.85 128.71 128.14 127.72 121.97 120.00 119.80
77.48 77.16 76.84 71.65
64.44
31.45
22.43
11.50
OH
Br
28
(+/-)
80 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

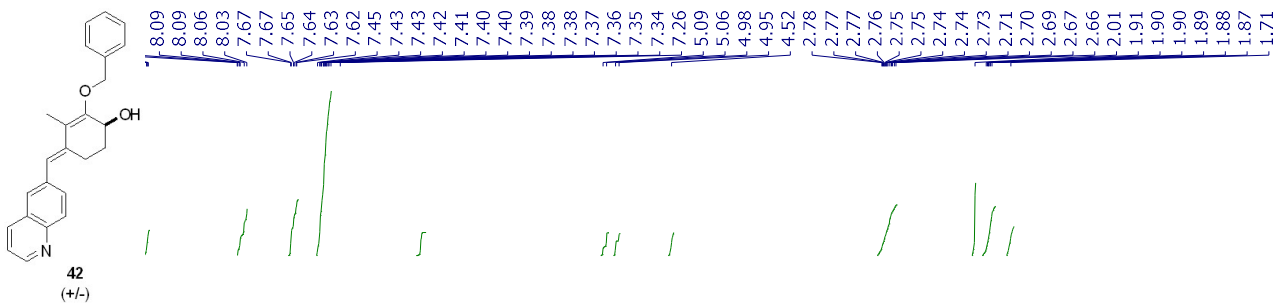

7.43 7.43 7.41 7.40 7.39 7.38 7.37 7.36 7.35 7.34 7.34 7.33 7.32 7.32 7.31 7.30 7.30 7.29 7.26 7.08 7.06 6.43 5.17 5.14 5.00 4.97 4.51 3.92 3.90 3.27 2.85 2.82 2.62 2.61 2.60 2.59 2.59 2.57 2.56 1.93 1.92 1.91 1.90 1.88 1.87 1.81 1.80 1.79 1.79 1.78 1.78 1.77 1.76 1.76 1.75 1.74 1.29 1.18
OH
O
OH
Br
32
(+/-)
7.55 1.91 0.94 1.00 1.01 1.02 0.90 0.94 1.03 3.02 1.09 1.16 3.48 3.05
0.5 10.0 9.5 9.0 8.5 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 0.5 0.0 -0.5
f1 (ppm)
154.14 138.42 137.34 137.31 131.26 130.81 128.75 128.15 127.52 122.63 120.02 118.94 77.48 77.16 76.84 72.90 70.03 63.03 37.39 31.73 31.48 29.54 22.06
OH
O
OH
Br
32
(+/-)
80 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

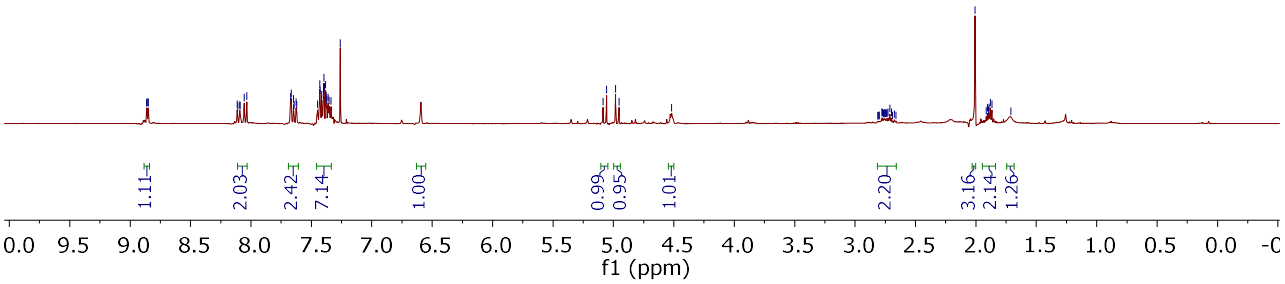

7.55 7.54 7.54 7.52 7.45 7.45 7.44 7.43 7.42 7.40 7.39 7.39 7.38 7.37 7.36 7.36 7.35 7.34 7.34 7.33 7.32 7.31 7.30 7.30 7.29 7.28 7.26 7.25 7.03 7.01 6.35 5.67 5.51 5.11 4.77 4.11 4.10 4.08 4.07 2.72 2.72 2.71 2.68 2.19 2.18 2.17 1.99 1.98 1.97 1.97 1.96 1.94 1.87 1.86 1.85 1.85 1.84
OH
HO
H
O
H
Br
36
(+/-)
2.08 15.67 2.05 1.00 1.00 1.02 0.98 2.11 1.05 0.82 1.01 1.20 1.22 1.85 1.25
10.0 9.5 9.0 8.5 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 0.5 0.0 -0.
f1 (ppm)

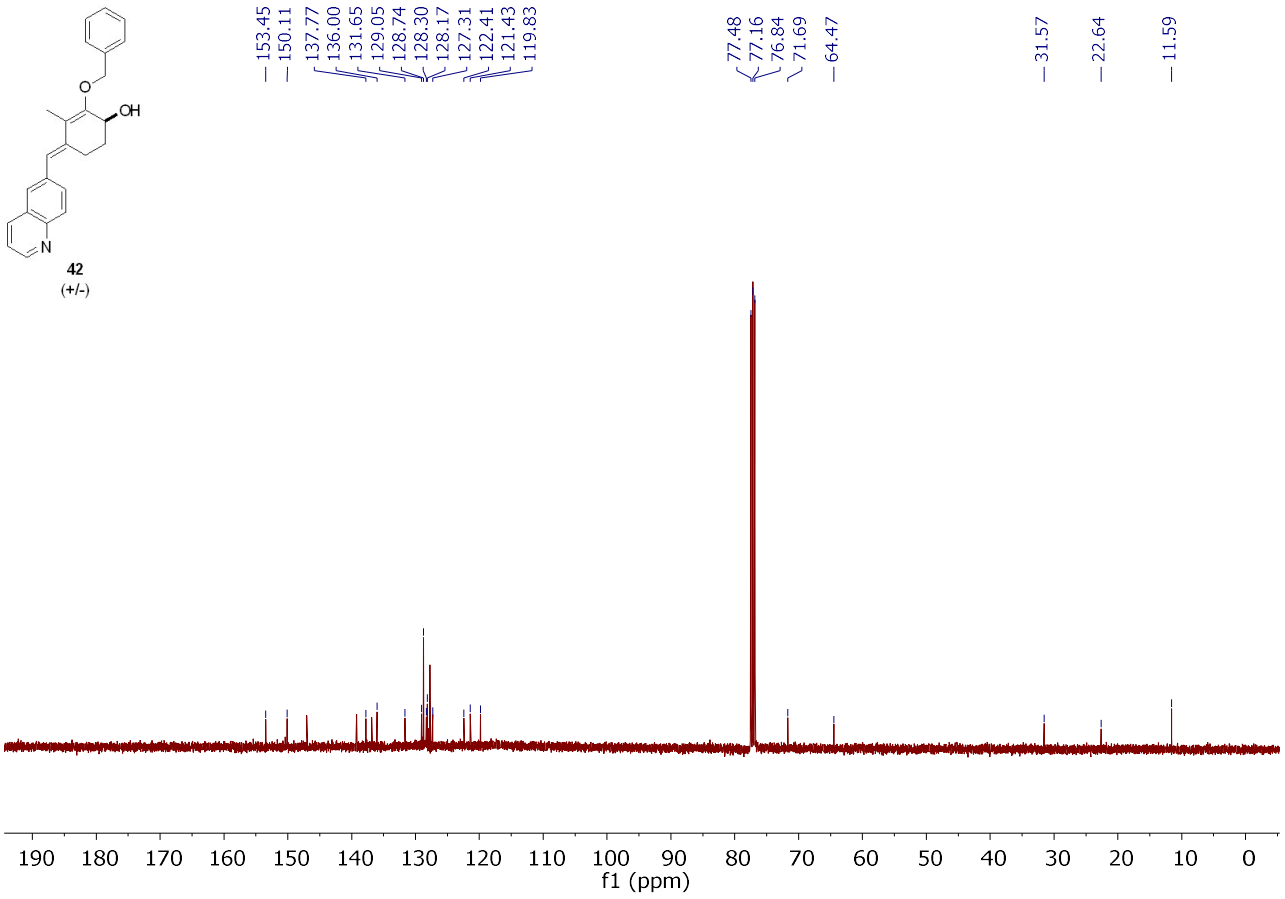

147.49 140.66 139.73 138.97 136.32 131.38 130.86 128.64 128.54 128.48 128.16 127.89 127.84 127.72 127.67 127.07 126.51 120.79 116.60 82.32 78.21 77.48 77.16 76.84 70.61 65.50 65.38 28.78 25.43
OH
HO
H
O
H
Br
36
(+/-)
80 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

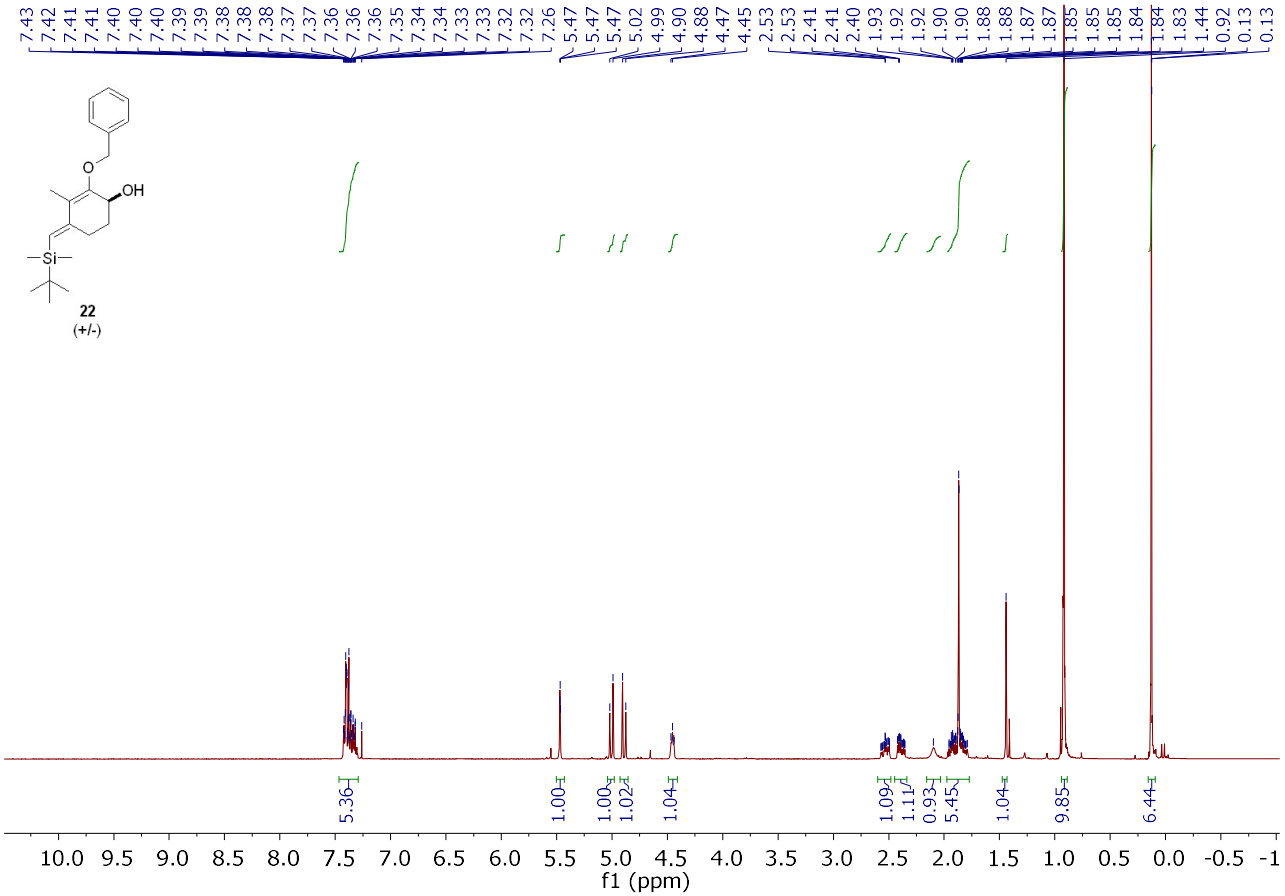

8.54 8.54 8.54 8.54 8.53 8.53 8.53 8.53 7.67 7.66 7.65 7.64 7.40 7.39 7.38 7.38 7.37 7.37 7.36 7.36 7.35 7.35 7.35 7.34 7.33 7.33 7.31 7.30 7.29 7.28 7.19 7.18 7.18 7.17 7.16 7.16 7.15 7.15 7.14 7.14 7.13 7.13 7.12 7.12 6.77 6.76 6.52 6.49 5.88 5.86 5.55 5.54 5.54 5.53 4.70 2.00 1.97
H
H
O
OH
N
40
(+/-)
1.00 0.98 5.75 1.04 1.00 0.88 0.99 1.01 1.86 2.07 0.89 1.02 1.08 2.16
10.0 9.5 9.0 8.5 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 0.5 0
f1 (ppm)

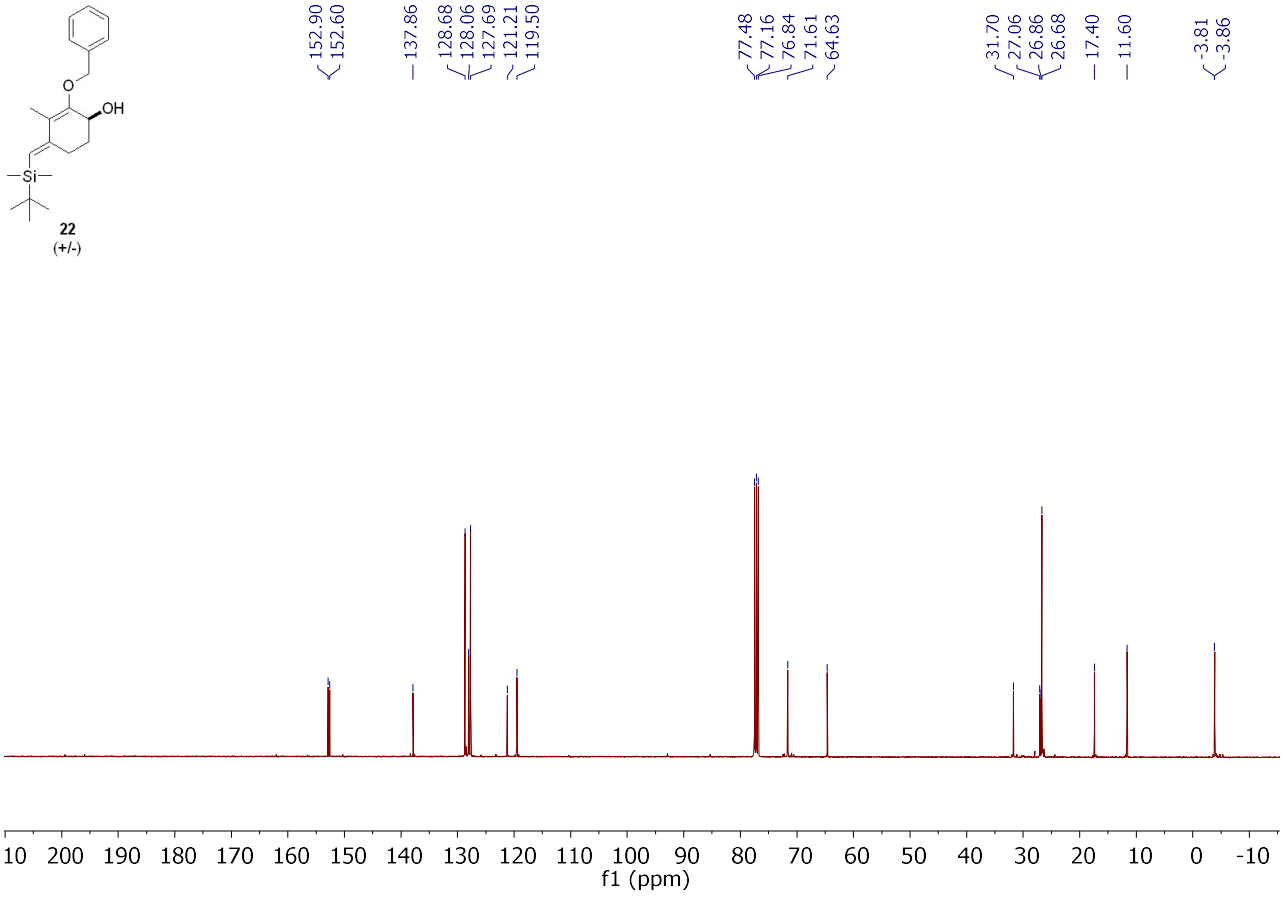

198.12 155.82 148.31 137.85 137.06 136.68 135.89 128.82 128.32 127.77 127.63 124.53 121.70 91.81 77.48 77.16 76.84 70.57 68.44 33.42 24.58
H
H
O
OH
N
40
(+/-)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

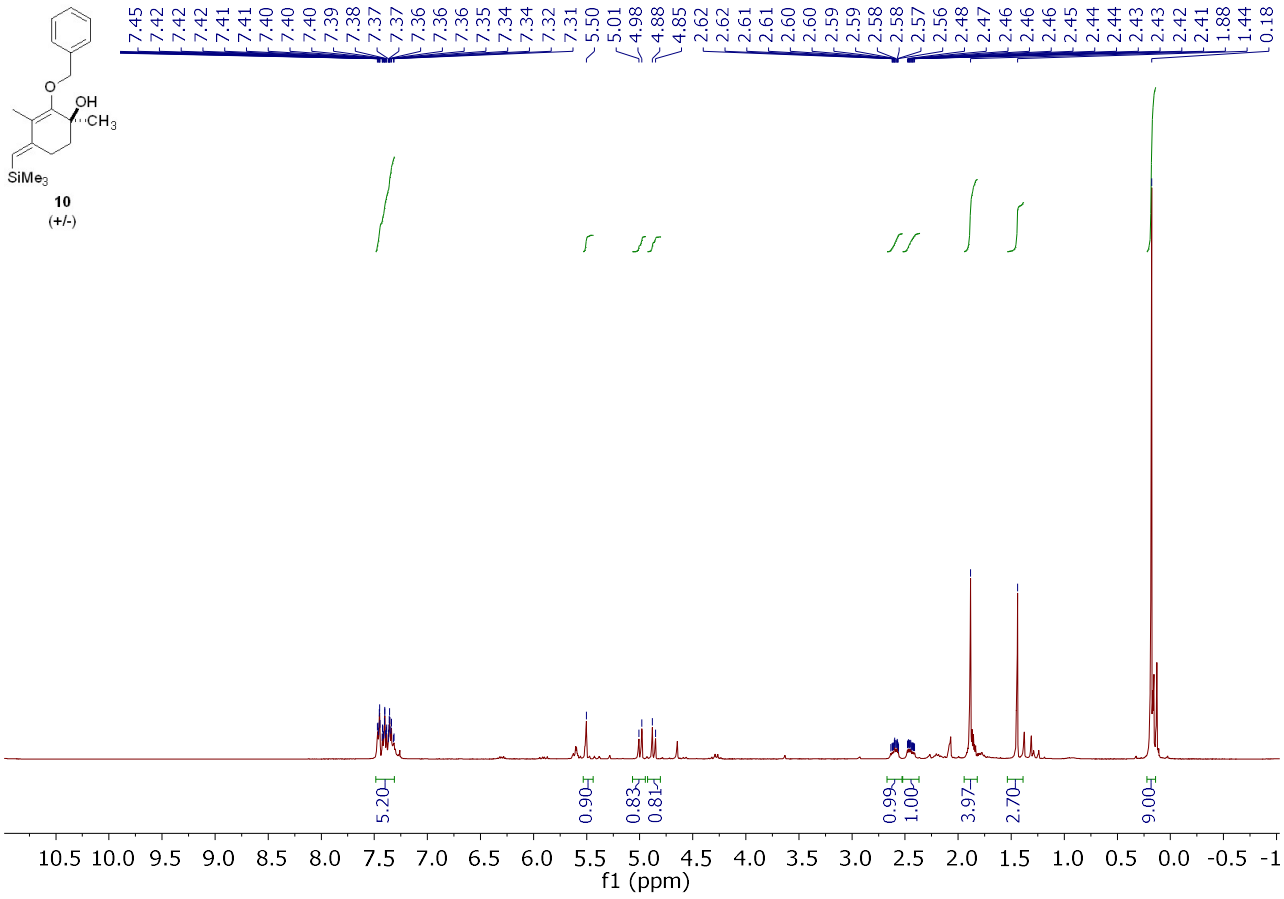

8.09
8.09
8.06
8.03
7.67
7.67
7.65
7.64
7.63
7.62
7.45
7.43
7.43
7.42
7.41
7.40
7.40
7.39
7.38
7.38
7.37
7.36
7.35
7.34
7.26
5.09
5.06
4.98
4.95
4.52
2.78
2.77
2.77
2.76
2.75
2.75
2.74
2.74
2.73
2.71
2.70
2.69
2.67
2.66
2.01
1.91
1.90
1.90
1.89
1.88
1.87
1.71
OH
O
N
42
(+/-)

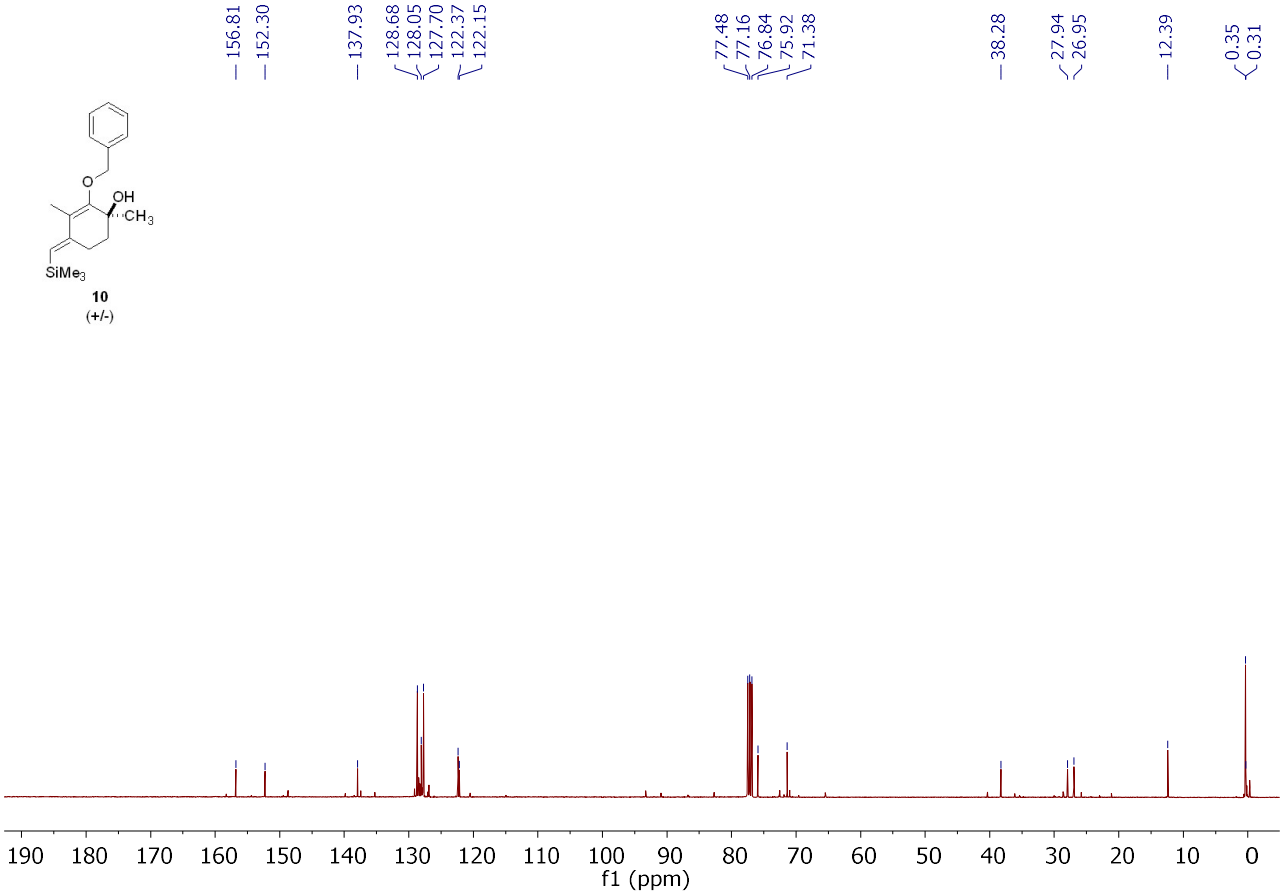

1.11
2.03
2.42
7.14
1.00
0.99
0.95
1.01
2.20
3.16
2.14
1.26
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

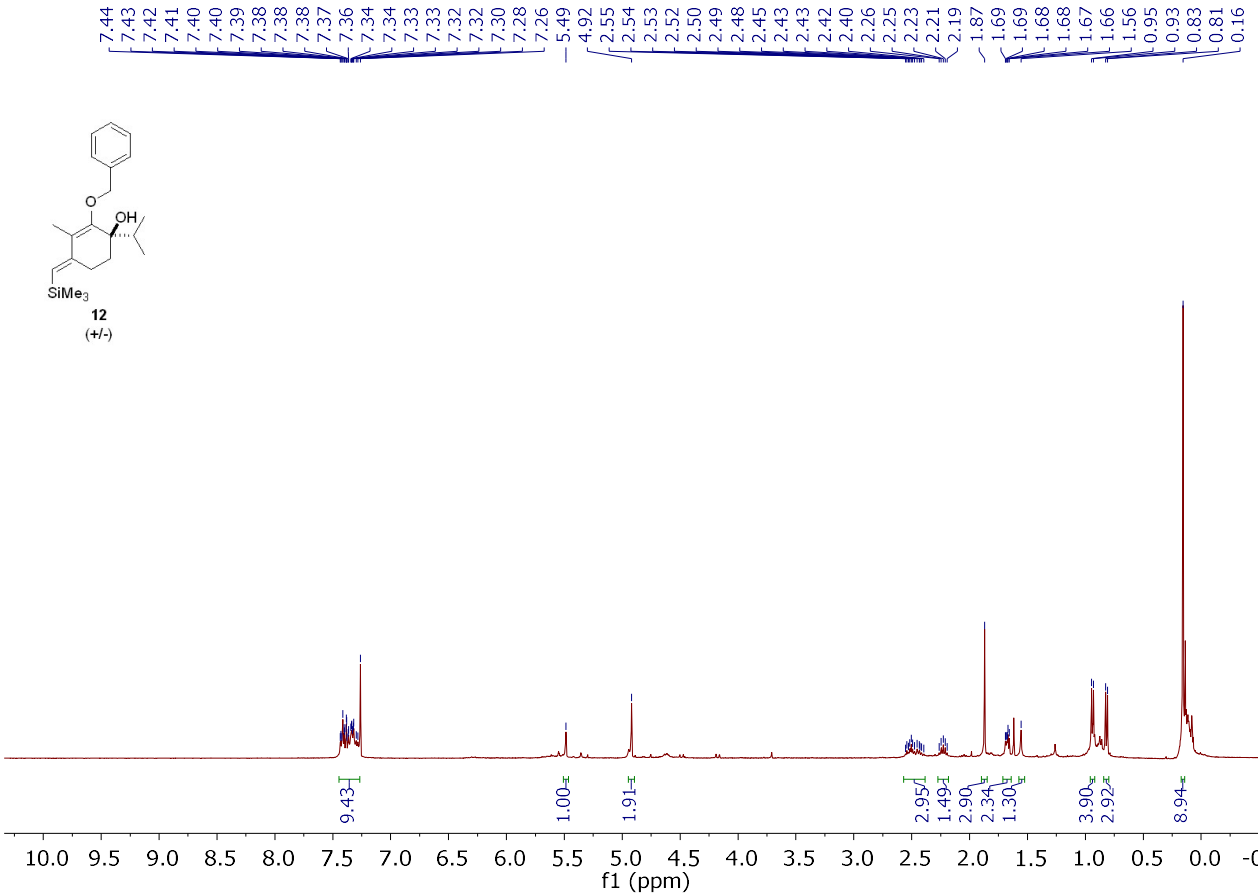

153.45
150.11
137.77
136.00
131.65
129.05
128.74
128.30
128.17
127.31
122.41
121.43
119.83
77.48
77.16
76.84
71.69
64.47
31.57
22.64
11.59
OH
O
N
42
(+/-)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

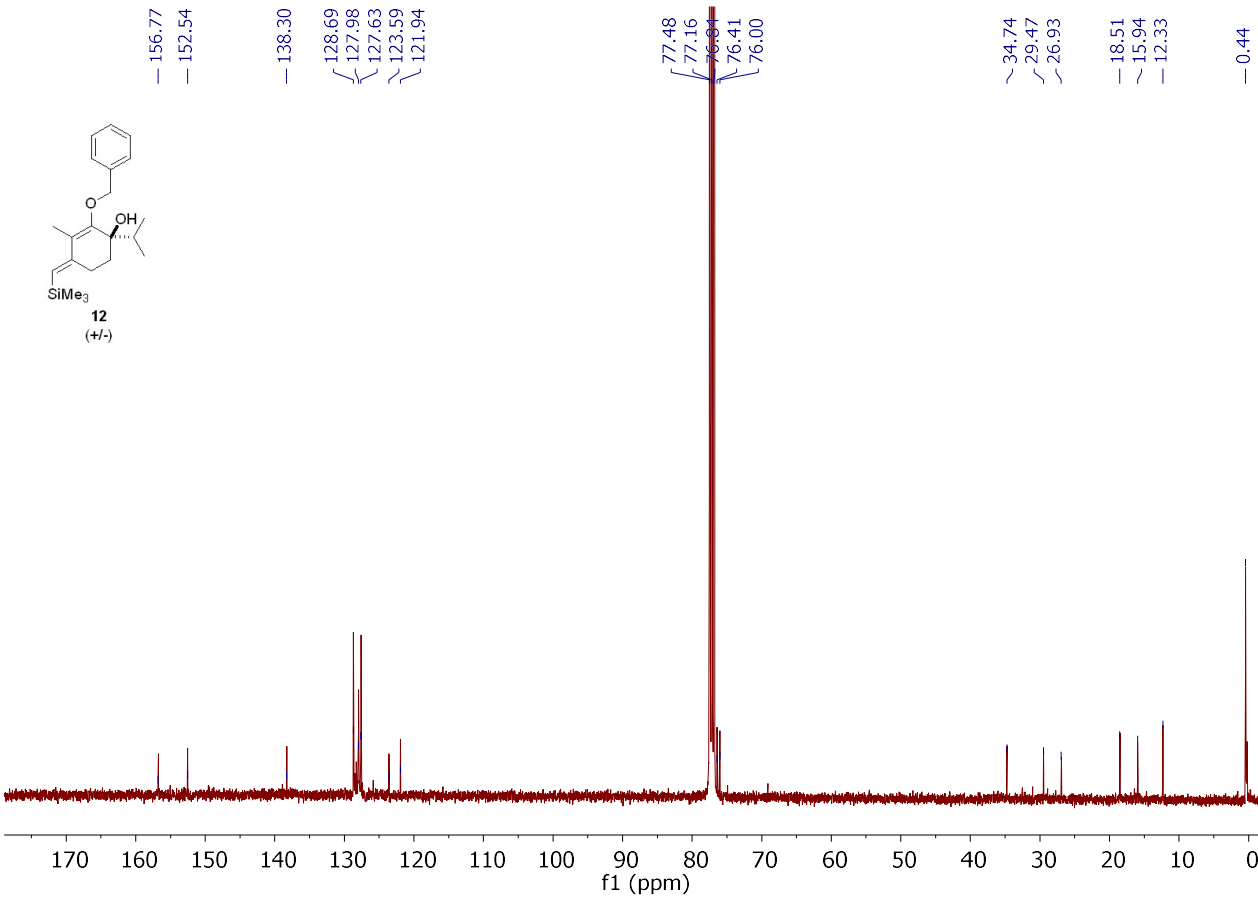

22
(+/-)
f1 (ppm)

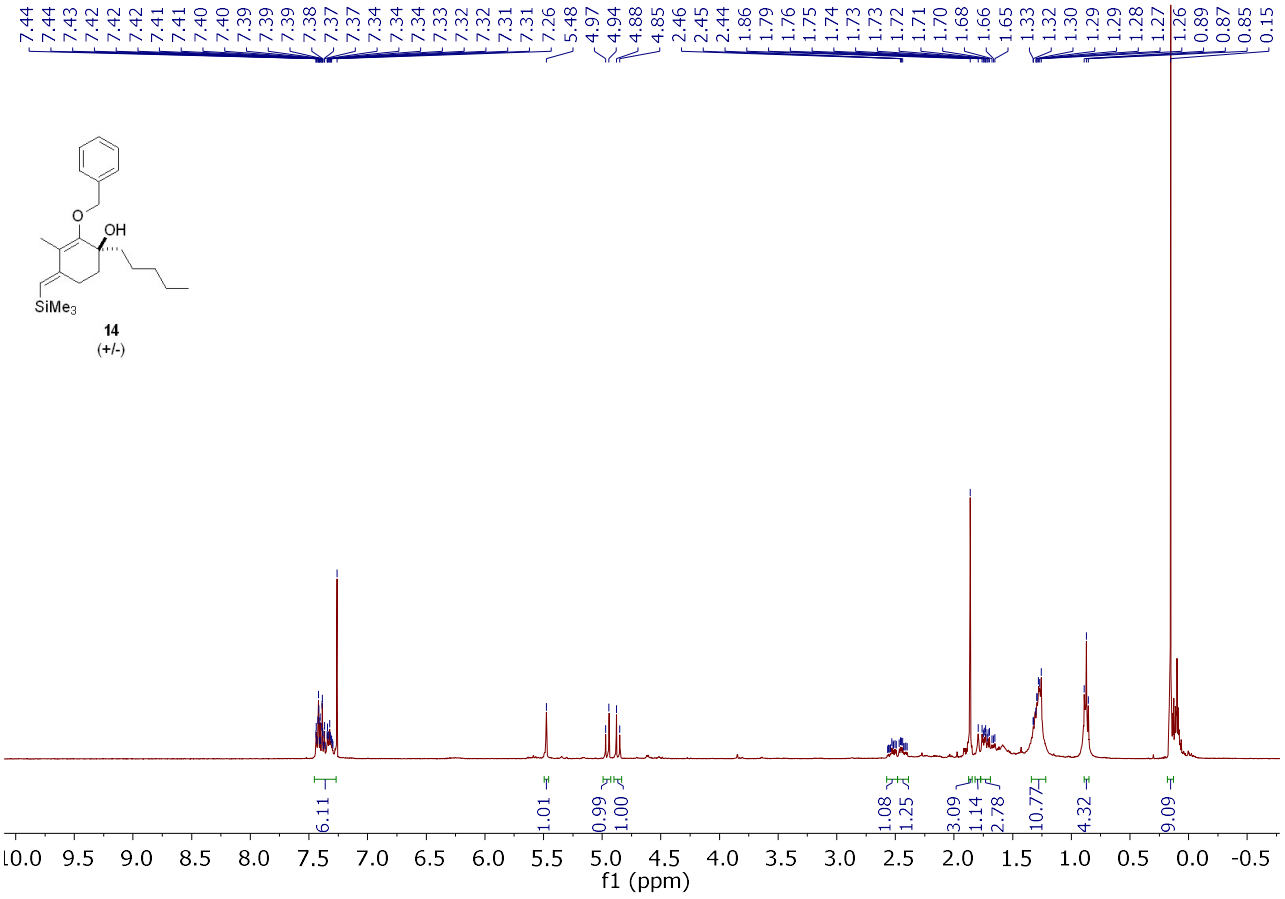

22
(+/-)
f1 (ppm)

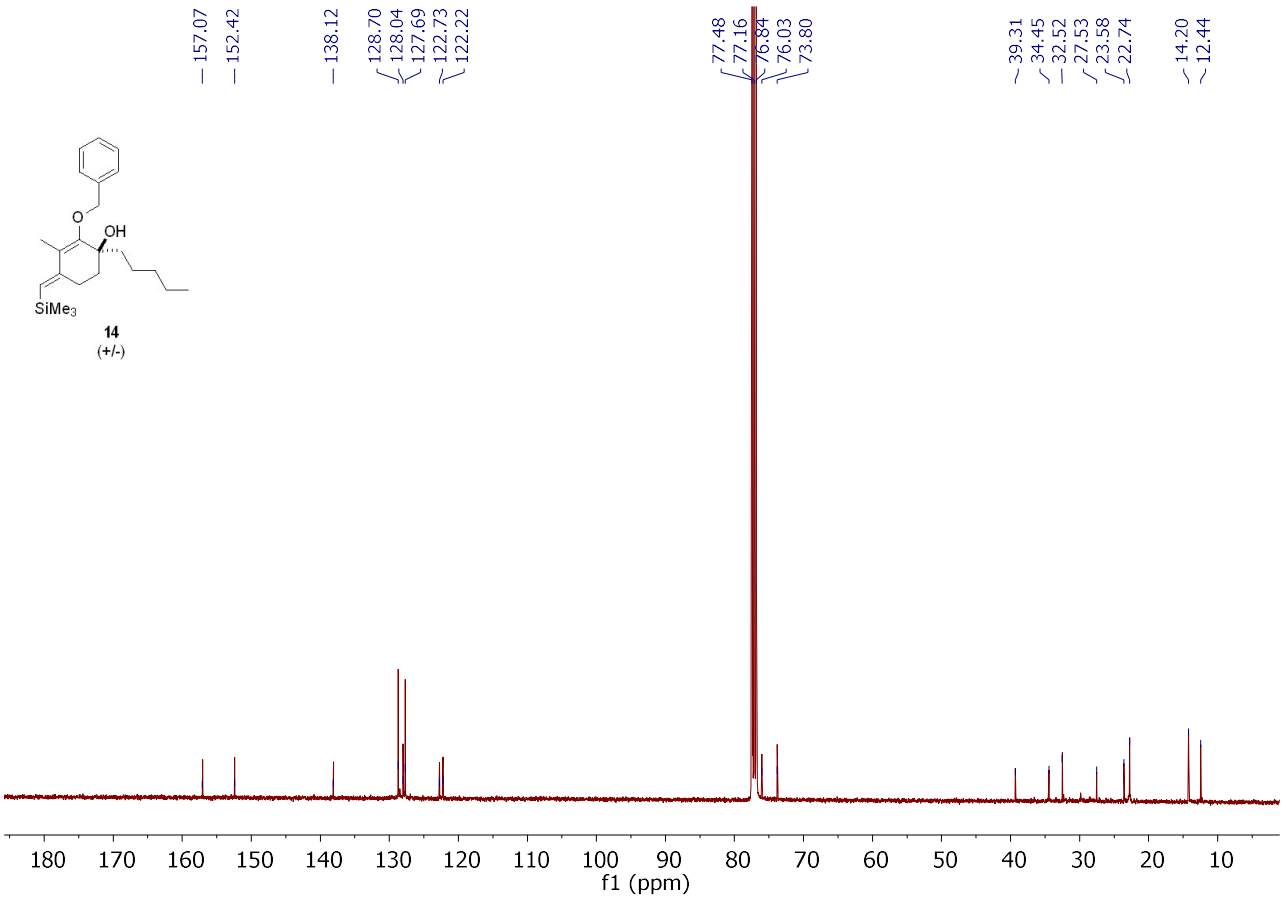

OH
CH3
SiMe3
10
(+/-)
f1 (ppm)

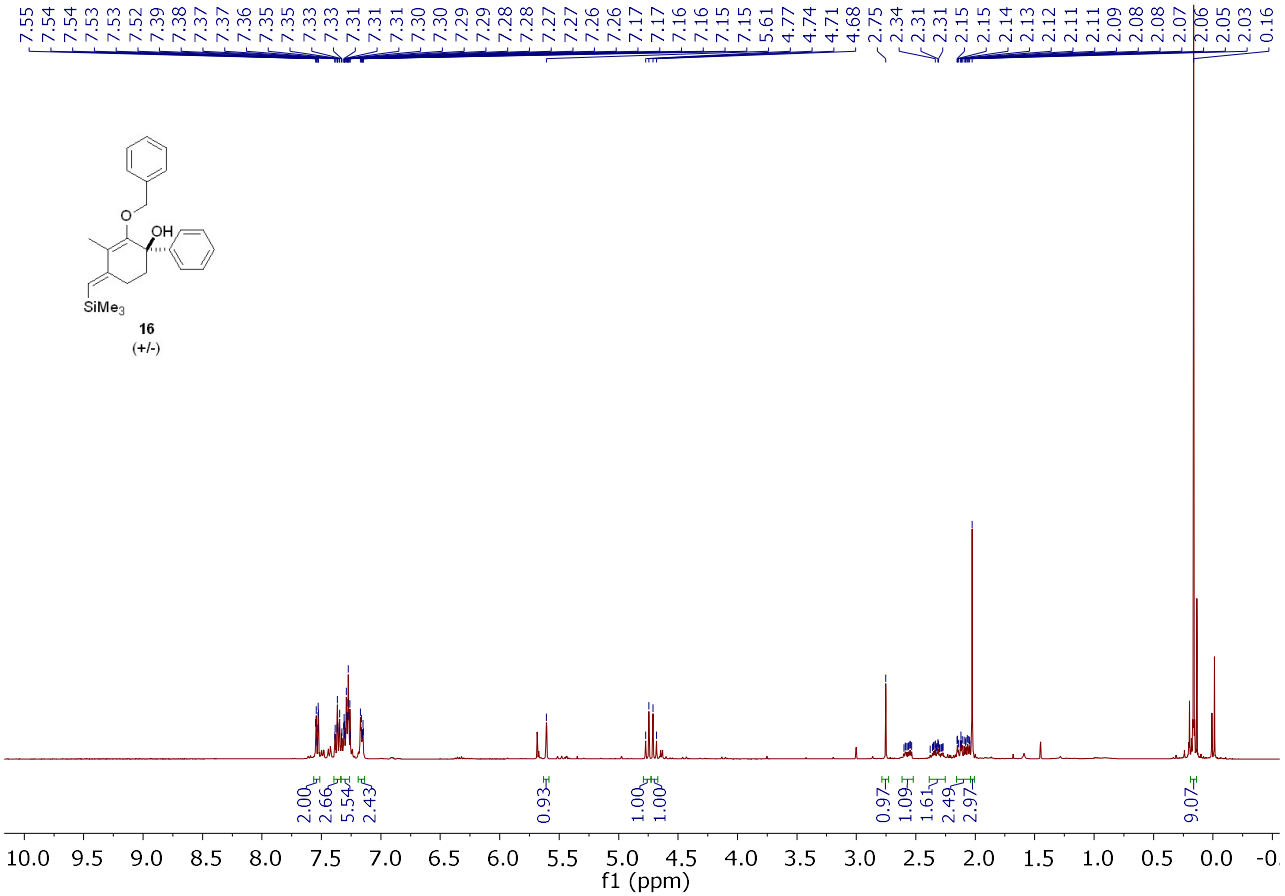

OH
CH3
SiMe3
10
(+/-)
f1 (ppm)

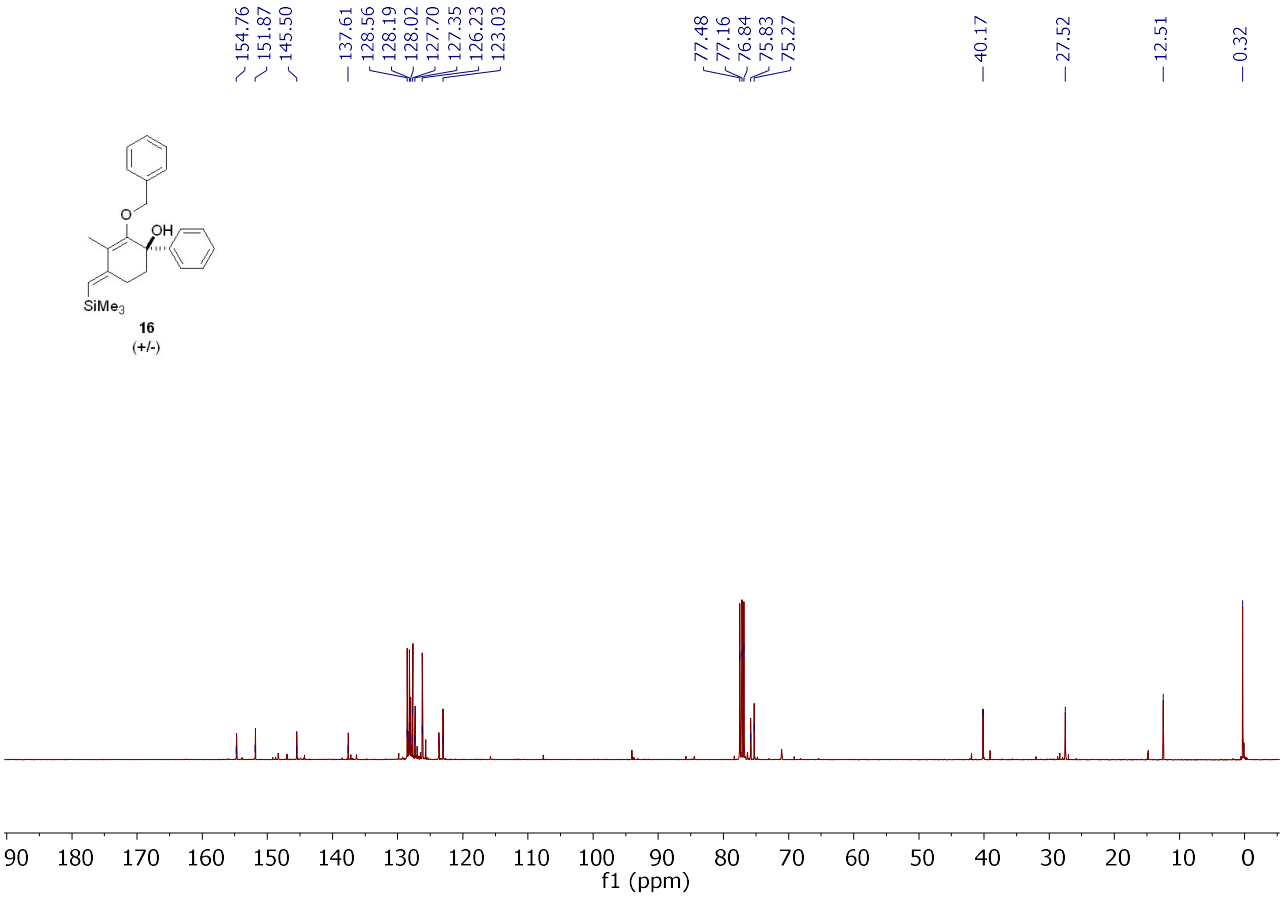

7.44 7.43 7.42 7.41 7.40 7.40 7.39 7.38 7.38 7.38 7.37 7.36 7.34 7.34 7.33 7.33 7.32 7.32 7.30 7.28 7.26 5.49 4.92 2.55 2.54 2.53 2.52 2.50 2.49 2.48 2.45 2.43 2.43 2.42 2.40 2.26 2.25 2.23 2.21 2.19 1.87 1.69 1.69 1.68 1.68 1.67 1.66 1.56 0.95 0.93 0.83 0.81 0.16
O
OH
SiMe3
12
(+/-)
9.43 1.00 1.91 2.95 1.49 2.90 2.34 1.30 3.90 2.92 8.94
10.0 9.5 9.0 8.5 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 0.5 0.0 -0.5
f1 (ppm)


156.77 152.54 138.30 128.69 127.98 127.63 123.59 121.94 77.48 77.16 76.84 76.41 76.00 34.74 29.47 26.93 18.51 15.94 12.33 0.44
O
OH
SiMe3
12
(+/-)
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.44 7.44 7.43 7.42 7.42 7.42 7.41 7.41 7.40 7.40 7.39 7.39 7.39 7.38 7.37 7.37 7.34 7.34 7.34 7.33 7.32 7.32 7.31 7.31 7.26 5.48 4.97 4.94 4.88 4.85 2.46 2.45 2.44 1.86 1.79 1.76 1.75 1.74 1.73 1.73 1.72 1.71 1.70 1.68 1.66 1.65 1.33 1.32 1.30 1.29 1.29 1.28 1.27 1.26 0.89 0.87 0.85 0.15
O
OH
SiMe3
14
(+/-)
6.11 1.01 0.99 1.00 1.08 1.25 3.09 1.14 2.78 10.77 4.32 9.09
f1 (ppm)


157.07 152.42 138.12 128.70 128.04 127.69 122.73 122.22 77.48 77.16 76.84 76.03 73.80 39.31 34.45 32.52 27.53 23.58 22.74 14.20 12.44
O
OH
SiMe3
14
(+/-)
f1 (ppm)


7.55 7.54 7.54 7.53 7.53 7.52 7.39 7.38 7.37 7.37 7.36 7.35 7.35 7.33 7.33 7.31 7.31 7.31 7.30 7.30 7.29 7.29 7.28 7.28 7.27 7.27 7.26 7.26 7.17 7.17 7.16 7.16 7.15 7.15 5.61 4.77 4.74 4.71 4.68 2.75 2.34 2.31 2.31 2.15 2.15 2.14 2.13 2.12 2.11 2.11 2.09 2.08 2.08 2.07 2.06 2.05 2.03 0.16
O
OH
SiMe3
16
(+/-)
2.00 2.66 5.54 2.43 0.93 1.00 1.00 0.97 1.09 1.61 2.49 2.97 9.07
10.0 9.5 9.0 8.5 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 0.5 0.0 -0
f1 (ppm)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O
OH
SiMe3
16
(+/-)
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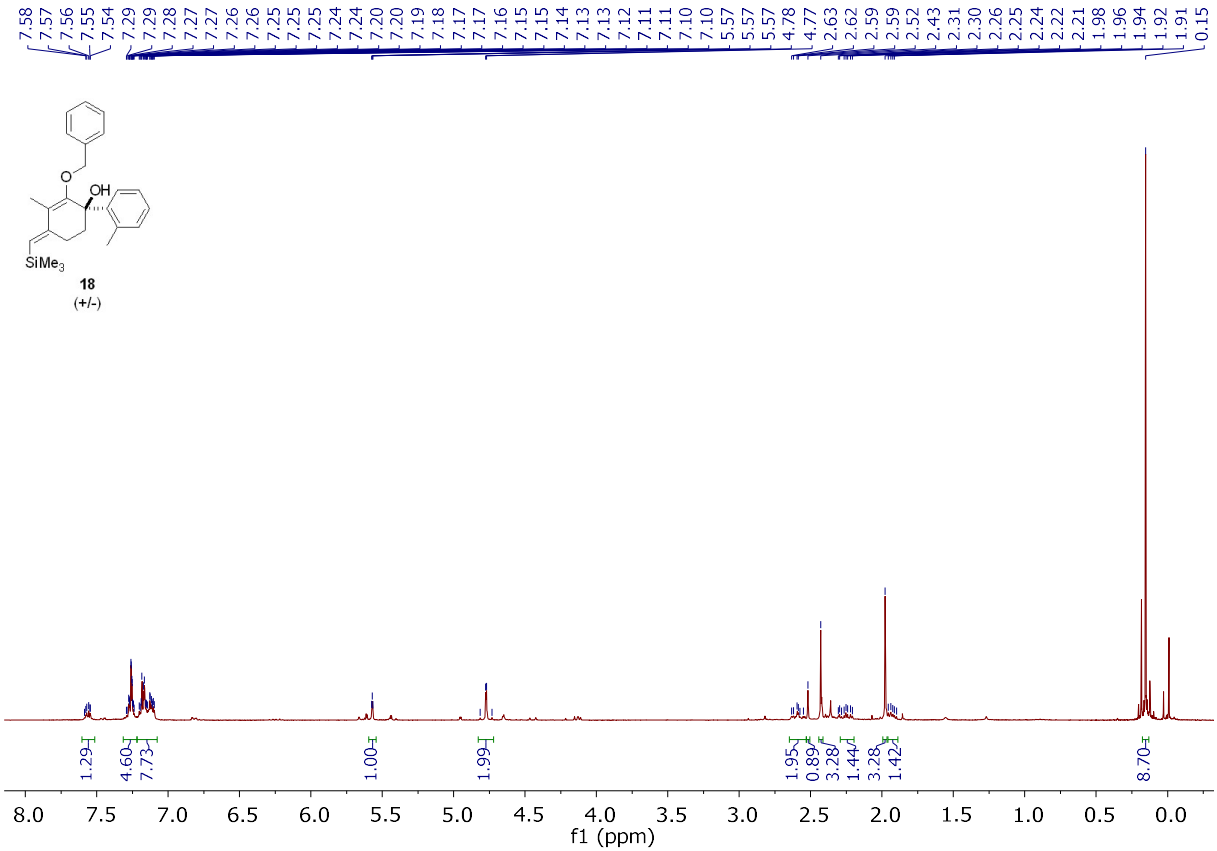
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O
OH
SiMe3
18
(+/-)
1.29 4.60 7.73 1.00 1.99 1.95 0.89 3.28 1.44 3.28 1.42 8.70
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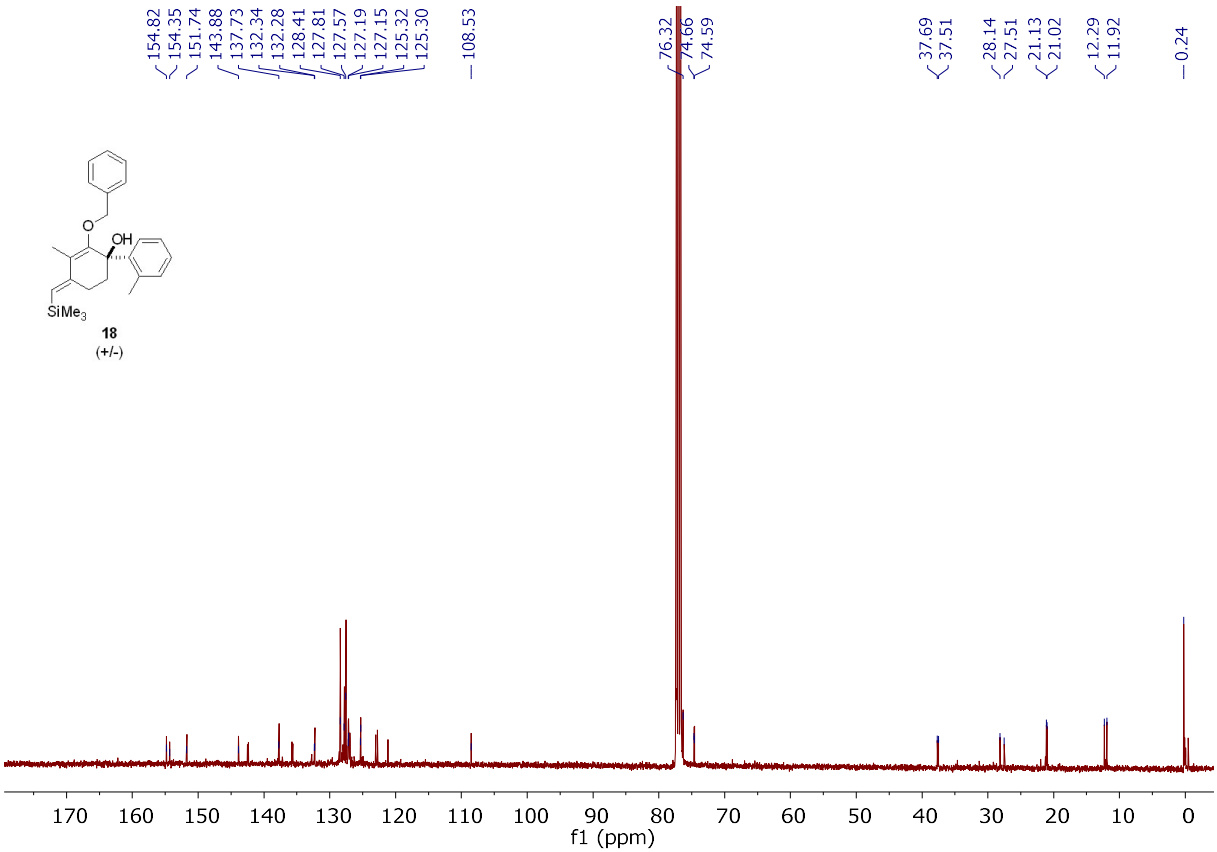
f1 (ppm)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O
OH
SiMe3
18
(+/-)
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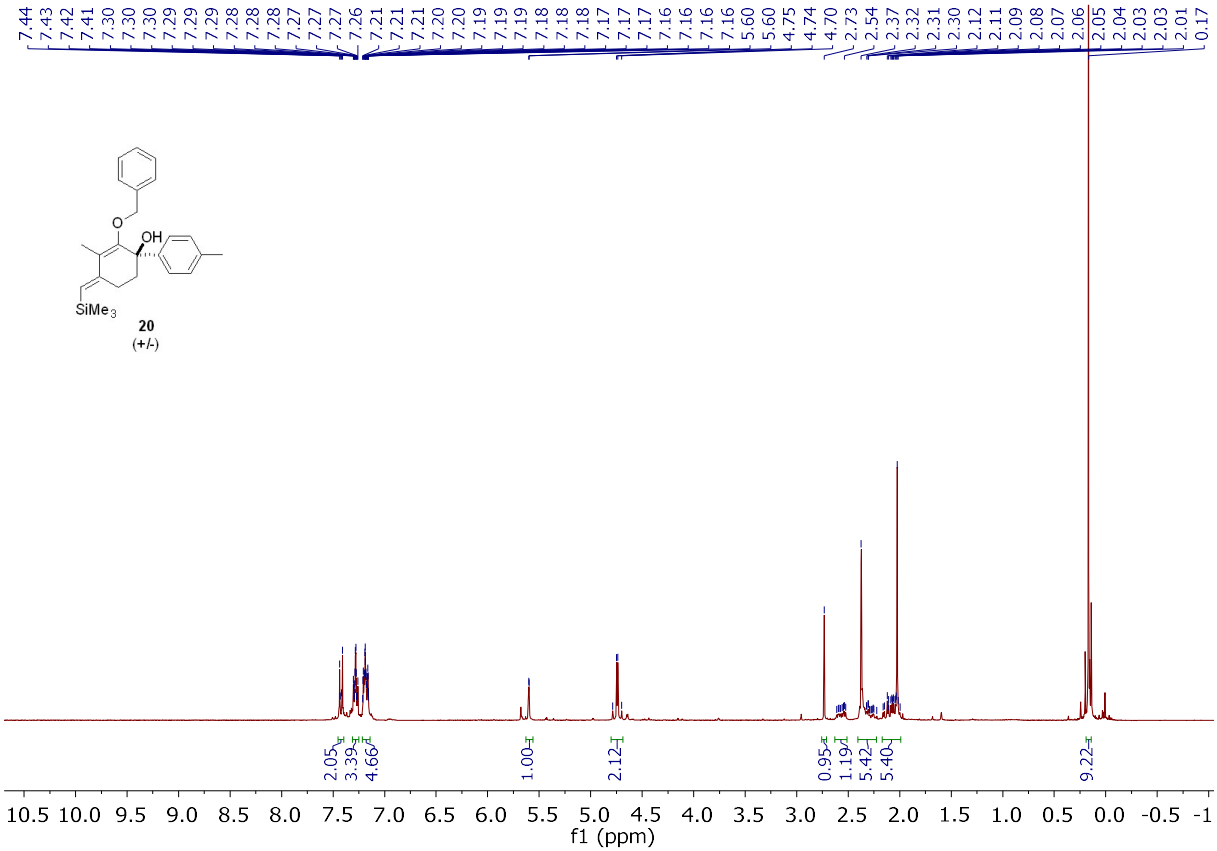
f1 (ppm)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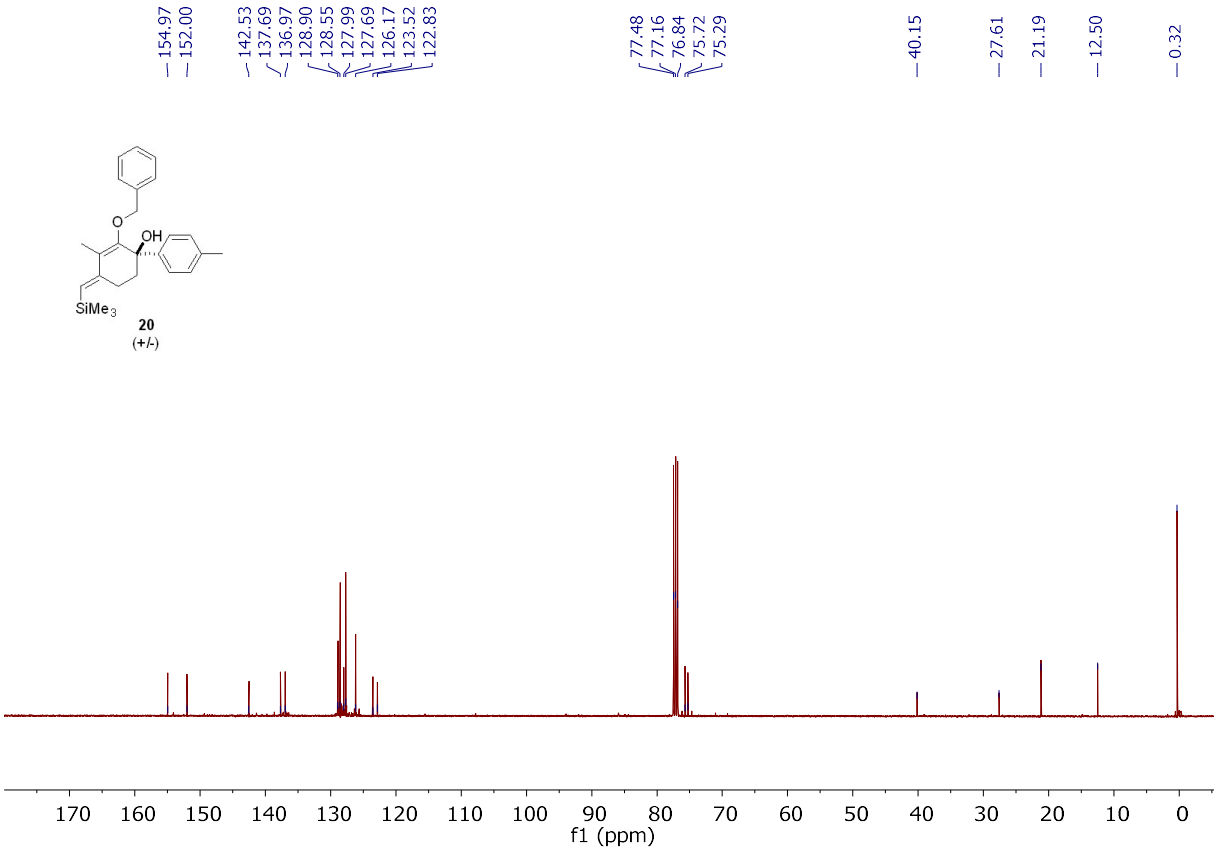
O
OH
SiMe3
20
(+/-)
2.05
3.39
4.66
1.00
2.12
0.95
1.19
5.42
5.40
9.22
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)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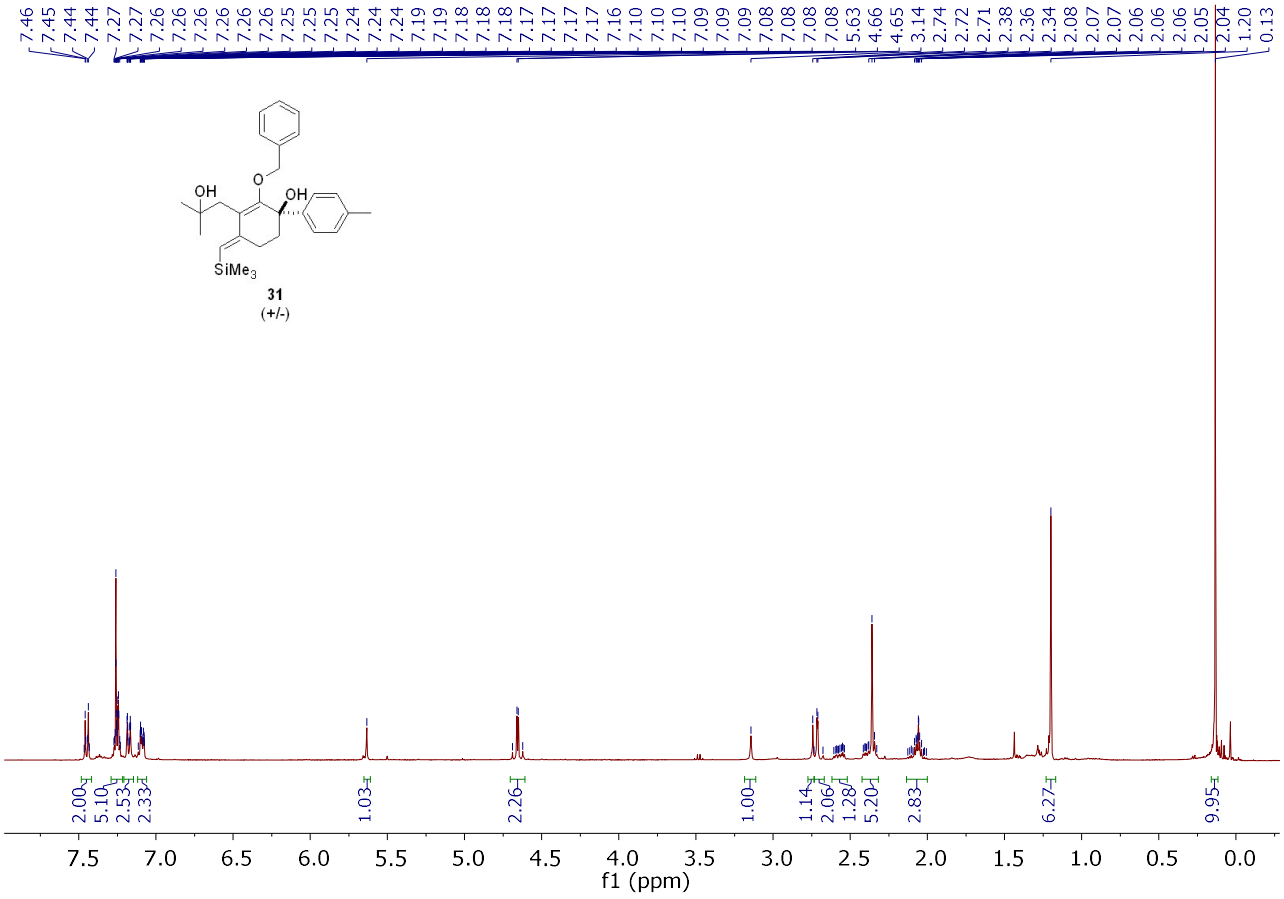
142.53
137.69
136.97
128.90
128.55
127.99
127.69
126.17
123.52
122.83
77.48
77.16
76.84
75.72
75.29
40.15
27.61
21.19
12.50
0.32
O
OH
SiMe3
20
(+/-)
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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OH
O
OH
SiMe3
31
(+/-)
2.00 5.10 2.53 2.33 1.03 2.26 1.00 1.14 2.06 1.28 5.20 2.83 6.27 9.95
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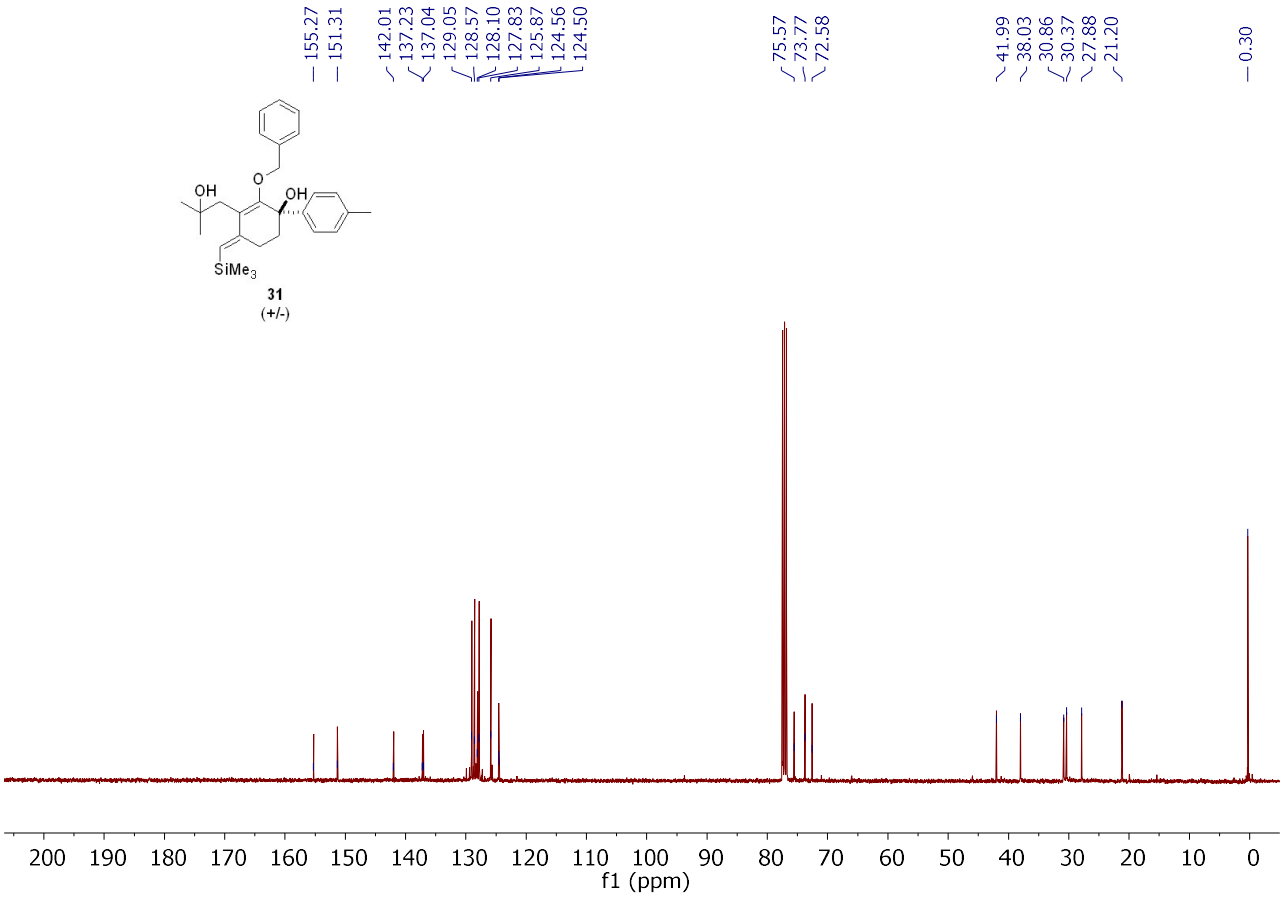
f1 (ppm)


155.27 151.31 142.01 137.23 137.04 129.05 128.57 128.10 127.83 125.87 124.56 124.50 75.57 73.77 72.58 41.99 38.03 30.86 30.37 27.88 21.20 0.30
OH
O
OH
SiMe3
31
(+/-)
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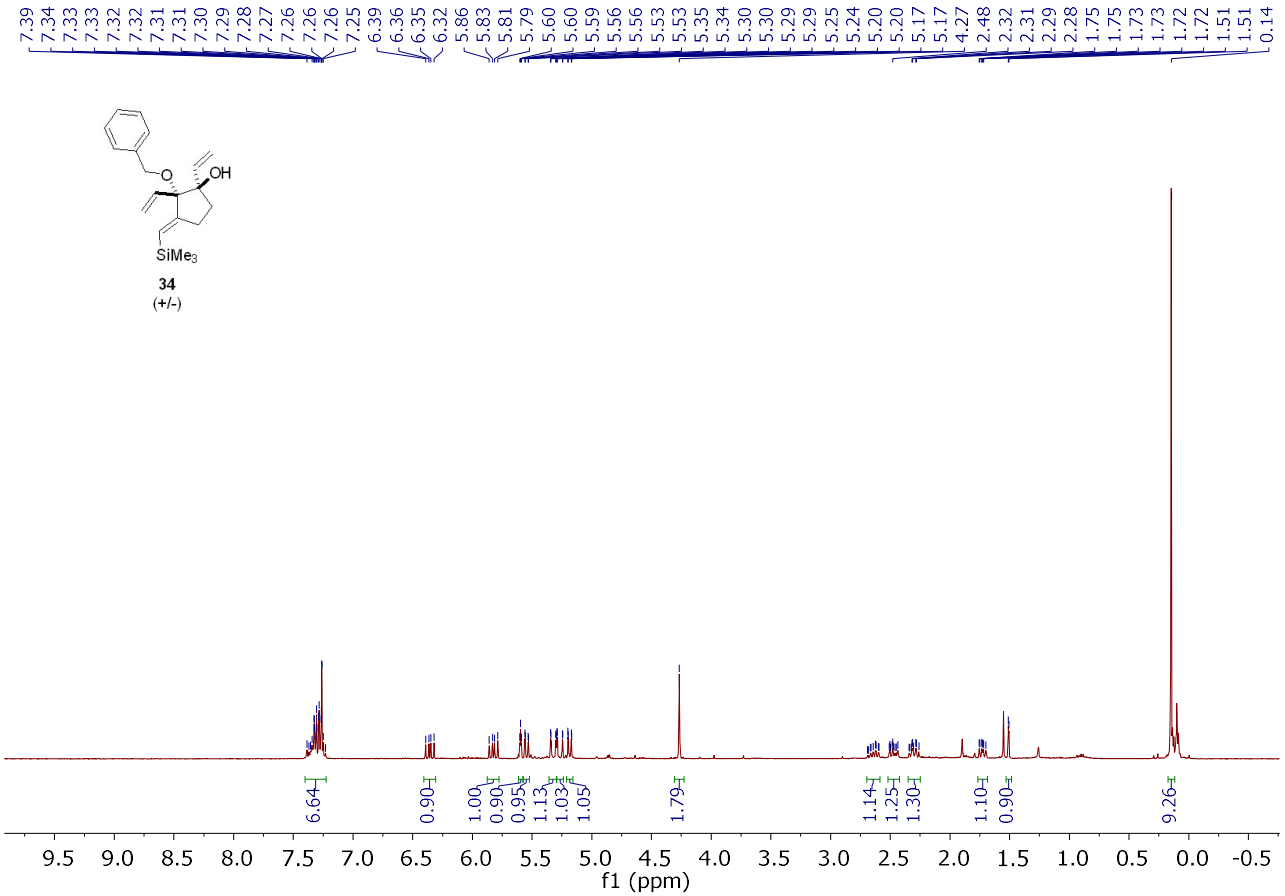
f1 (ppm)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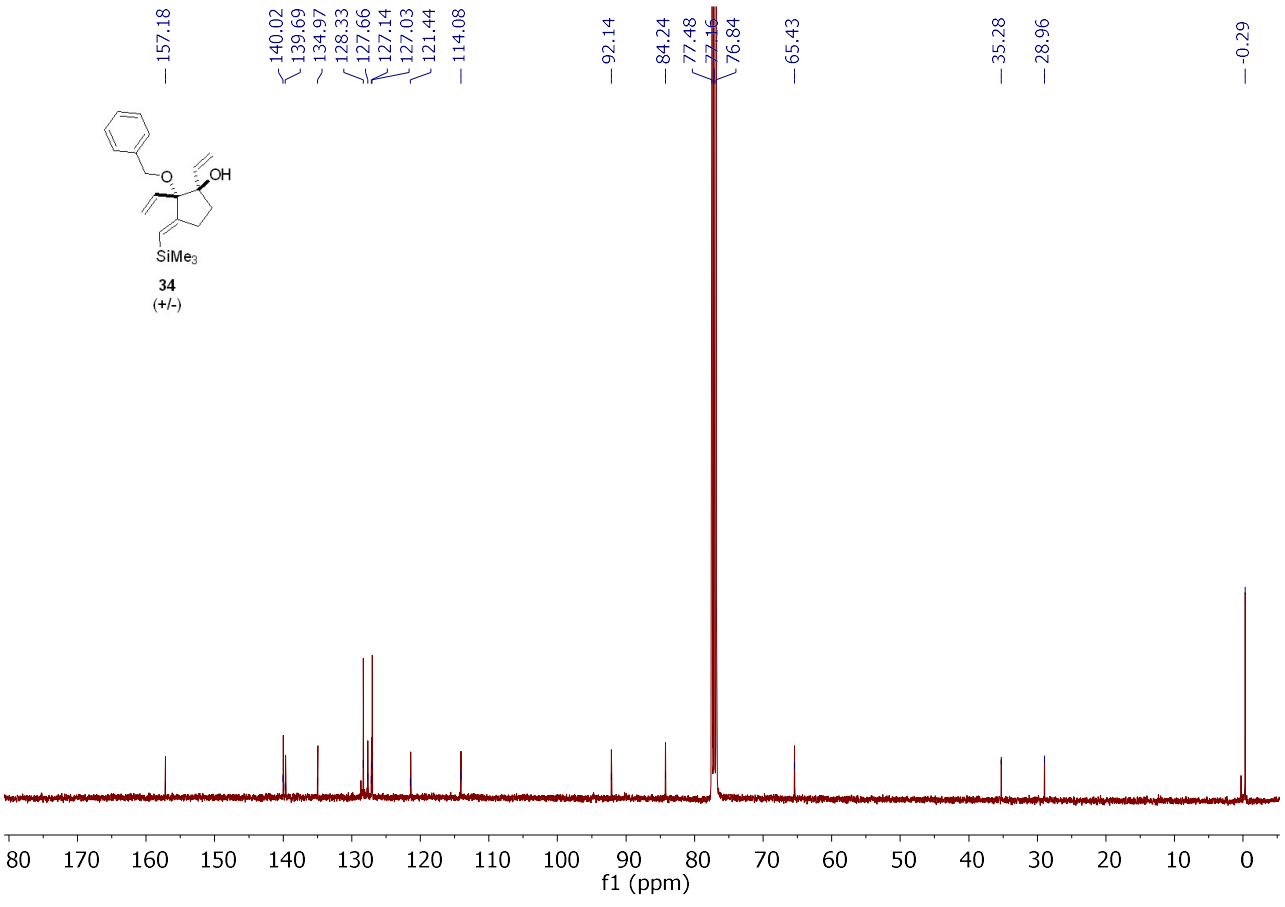
O
OH
SiMe3
34
(+/-)
6.64 0.90 1.00 0.90 0.95 1.13 1.03 1.05 1.79 1.14 1.25 1.30 1.10 0.90 9.26
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


157.18 140.02 139.69 134.97 128.33 127.66 127.14 127.03 121.44 114.08 92.14 84.24 77.48 77.16 76.84 65.43 35.28 28.96 -0.29
O
OH
SiMe3
34
(+/-)
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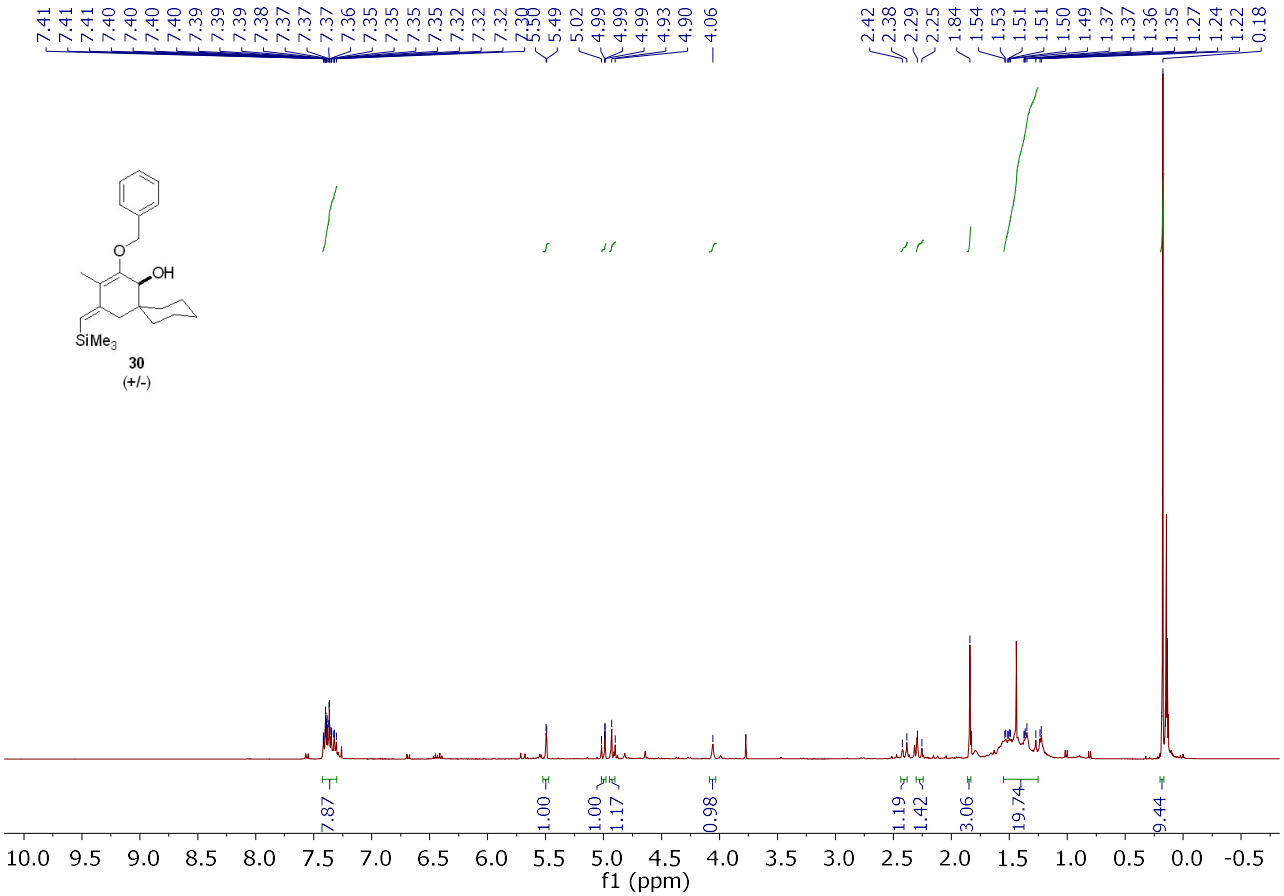
f1 (ppm)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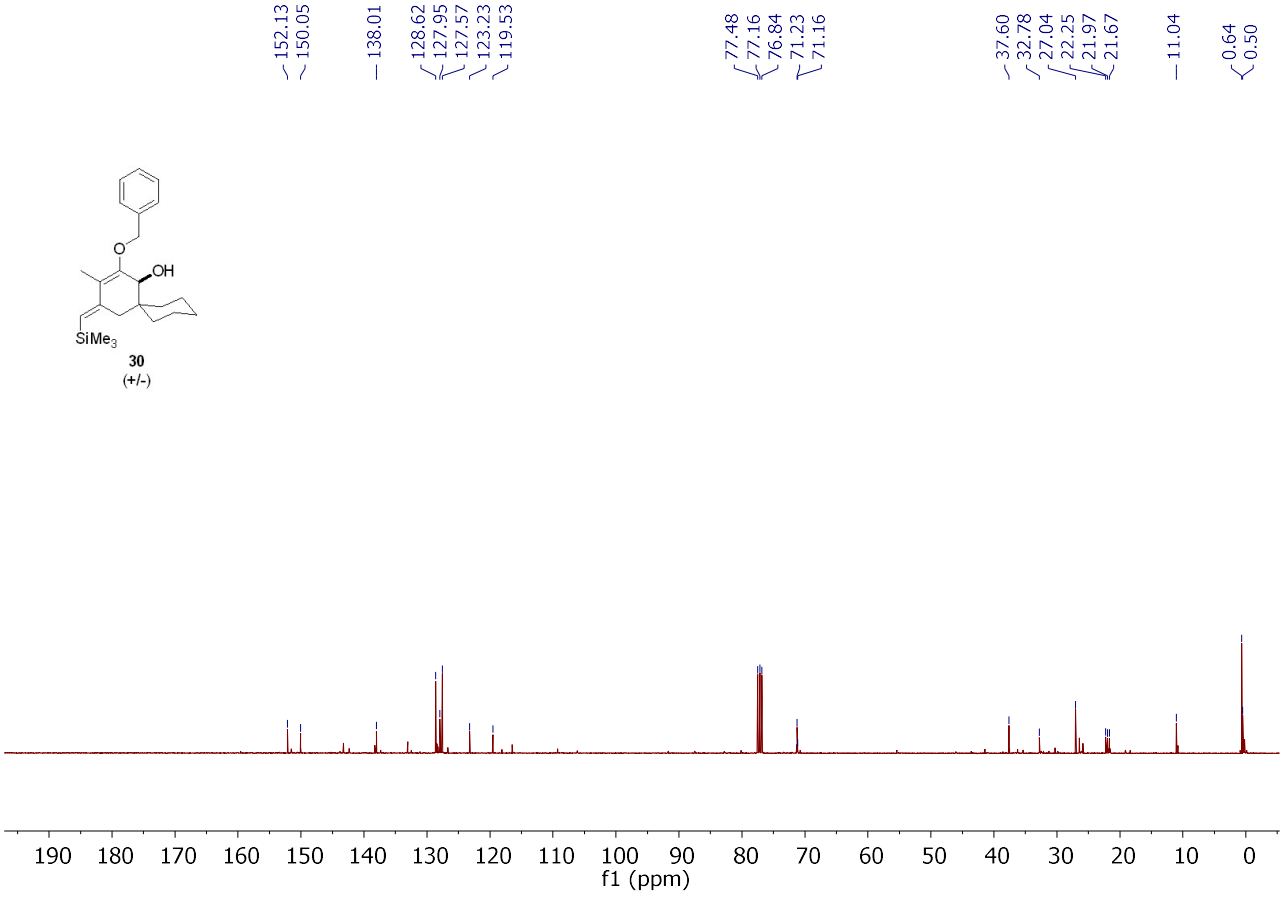
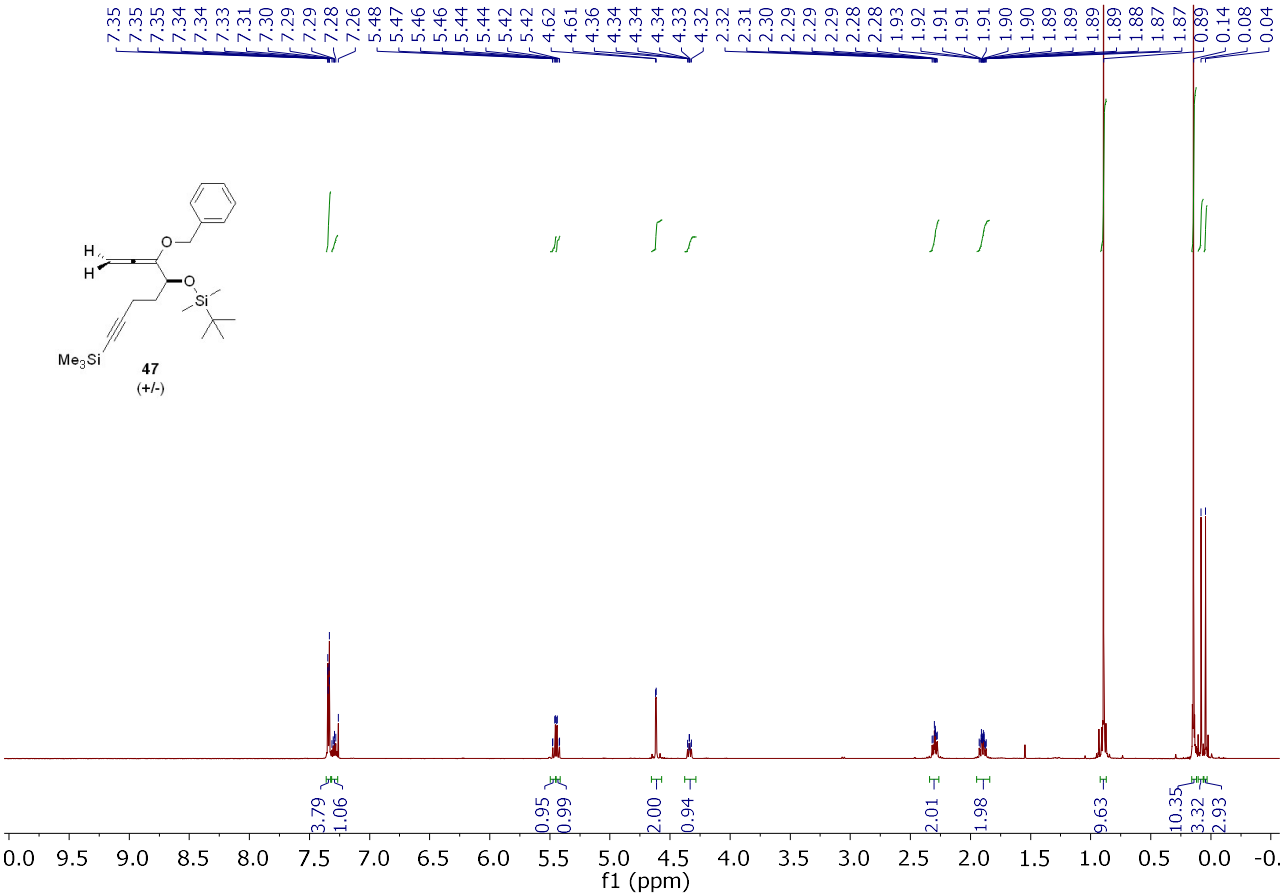
2.42 2.38 2.29 2.25 1.84 1.54 1.53 1.51 1.51 1.50 1.49 1.37 1.37 1.36 1.35 1.27 1.24 1.22 0.18
O
OH
SiMe3
30
(+/-)
7.87 1.00 1.00 1.17 0.98 1.19 1.42 3.06 19.74 9.44
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


152.13 150.05 138.01 128.62 127.95 127.57 123.23 119.53 77.48 77.16 76.84 71.23 71.16 37.60 32.78 27.04 22.25 21.97 21.67 11.04 0.64 0.50
O
OH
SiMe3
30
(+/-)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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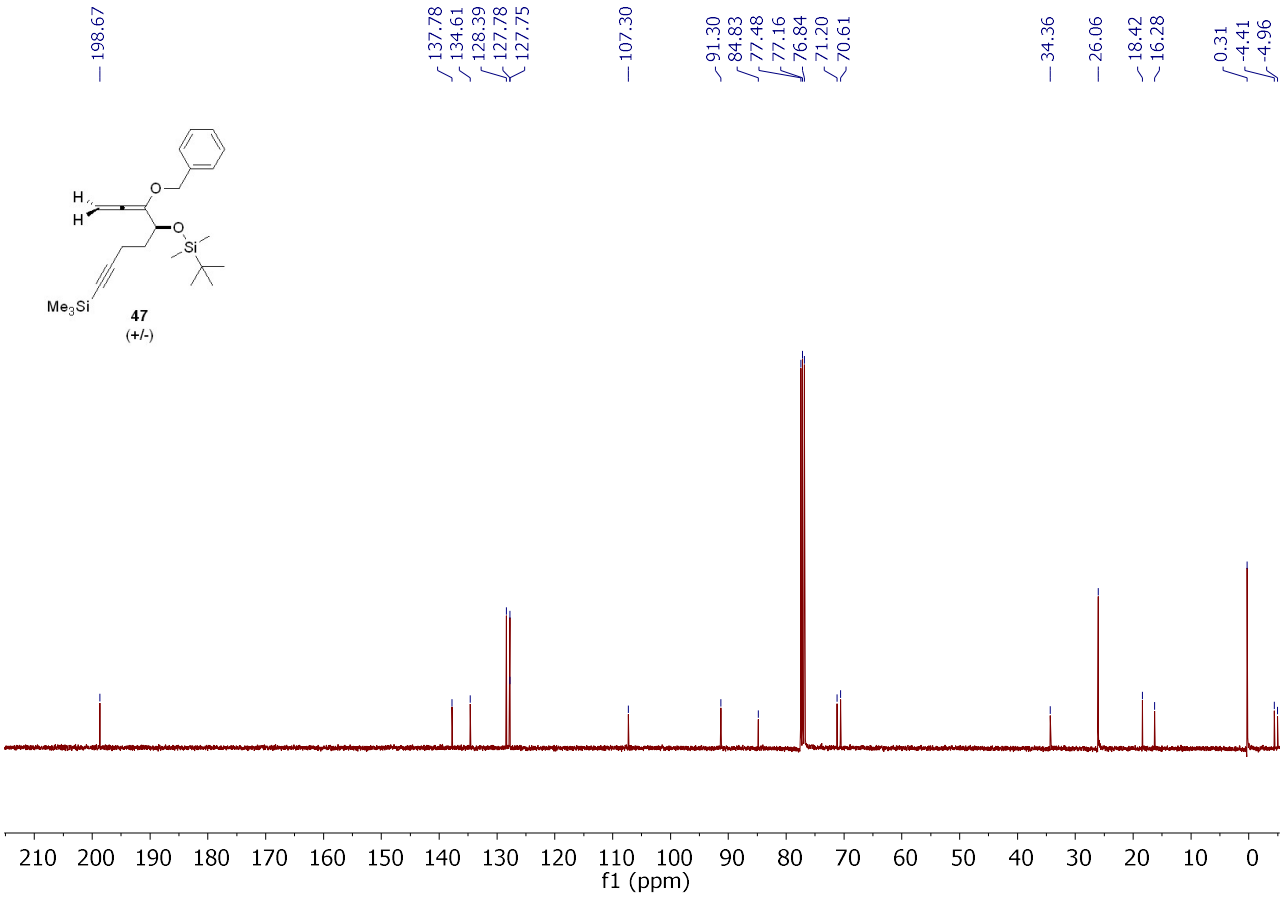
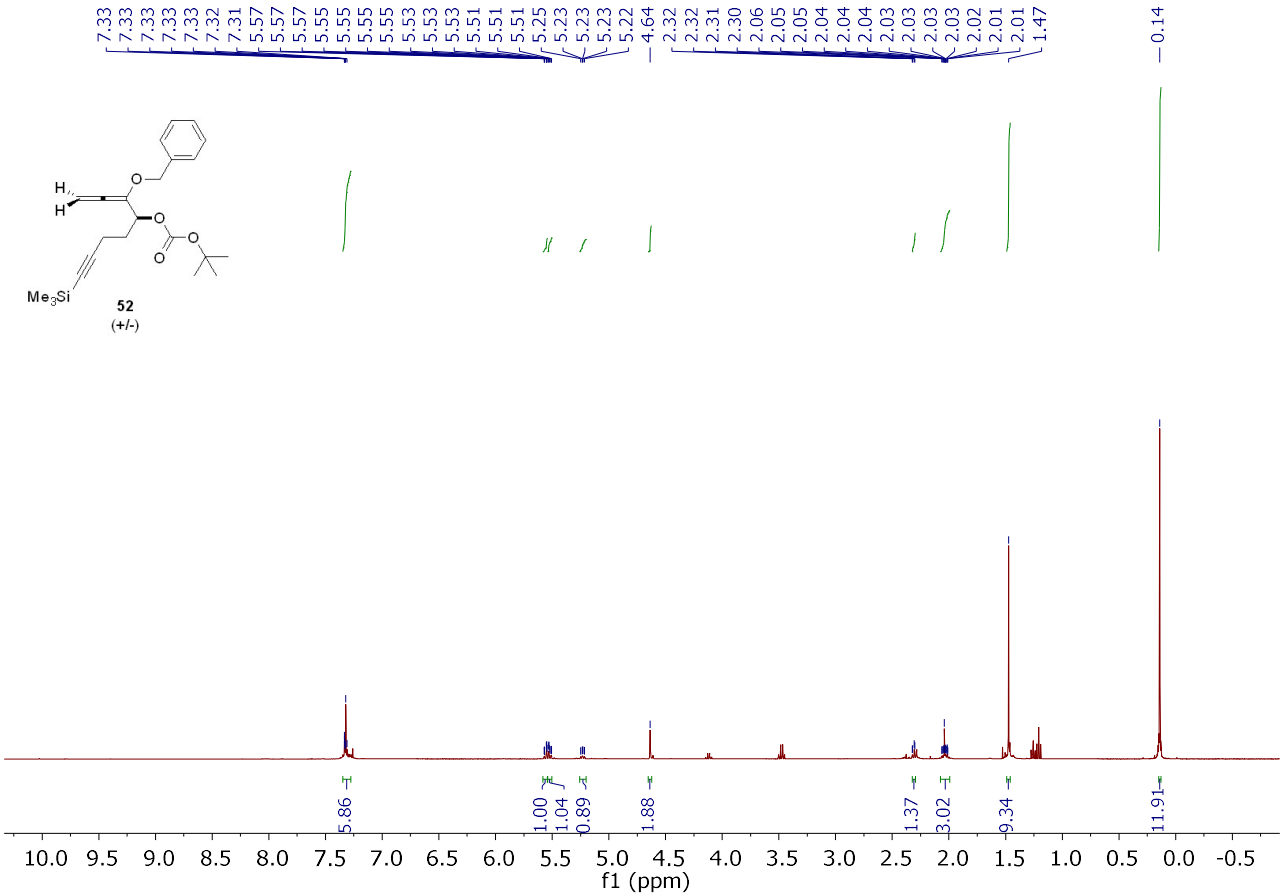
H
H
O
O
Si
Me3Si
47
(+/-)
3.79 1.06 0.95 0.99 2.00 0.94 2.01 1.98 9.63 10.35 3.32 2.93
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)


198.67
137.78 134.61 128.39 127.78 127.75
107.30
91.30 84.83 77.48 77.16 76.84 71.20 70.61
34.36
26.06
18.42 16.28
0.31 -4.41 -4.96
H
H
O
O
Si
Me3Si
47
(+/-)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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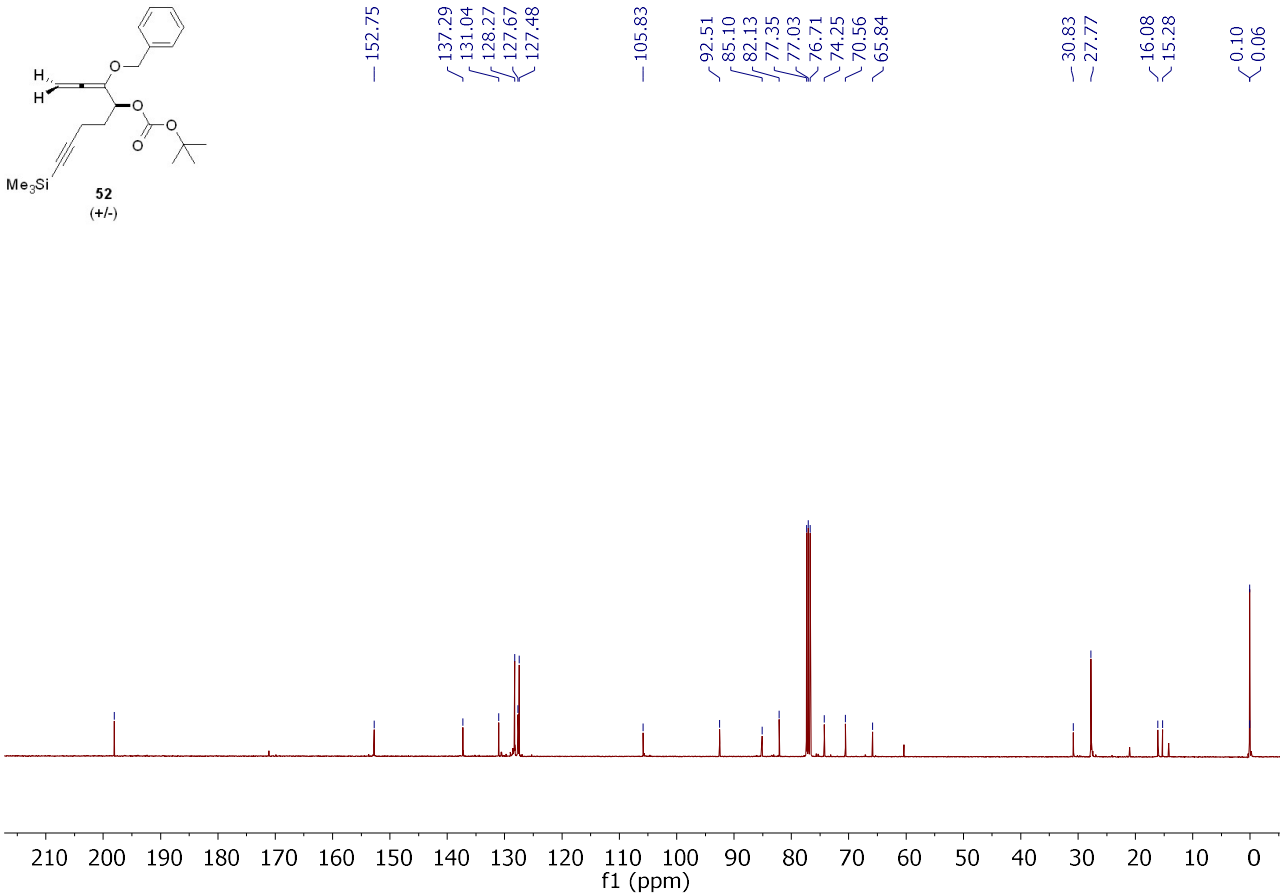
Me3Si
52
(+/-)
5.86 1.00 1.04 0.89 1.88 1.37 3.02 9.34 11.91
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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Me3Si
52
(+/-)
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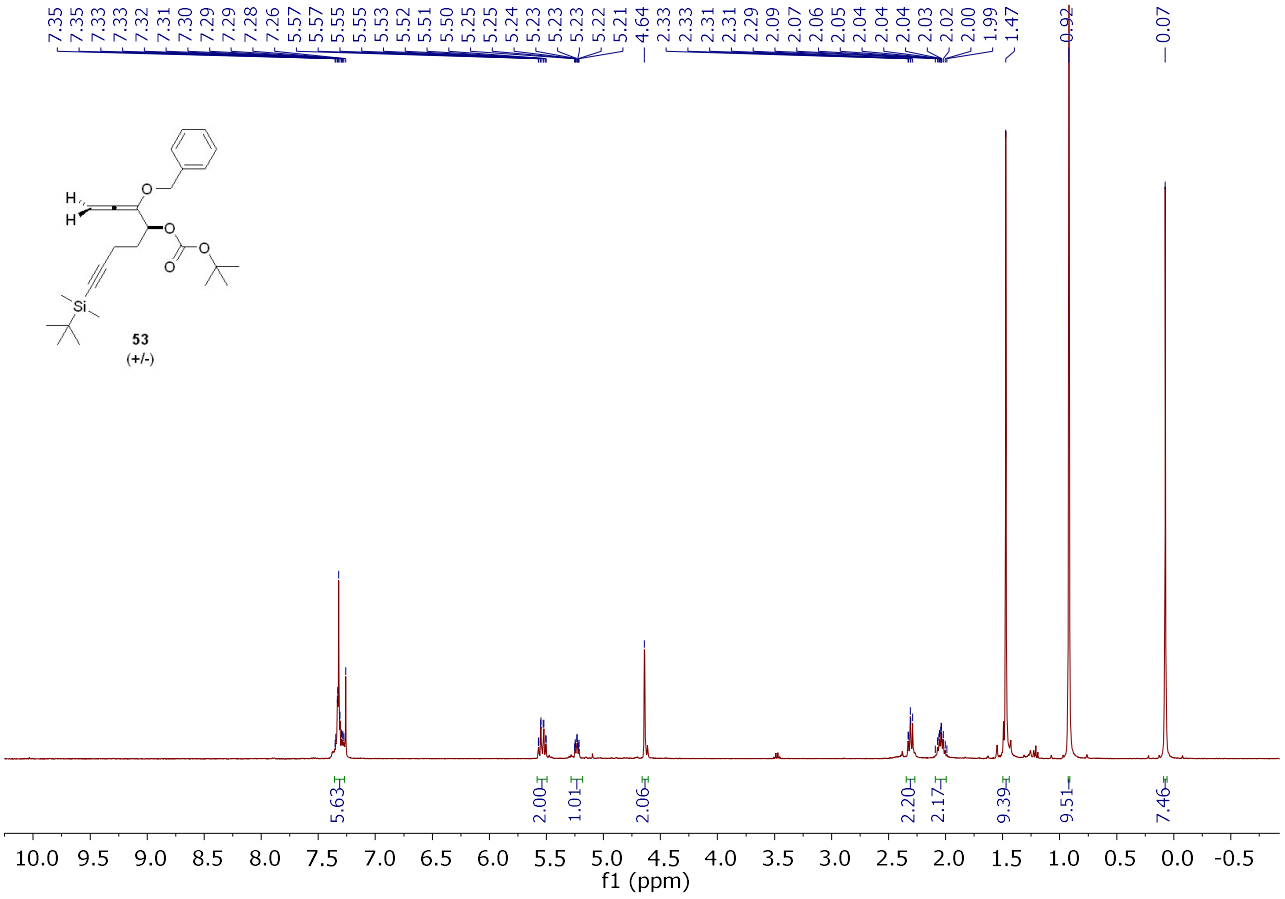
f1 (ppm)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7.33
7.33
7.32
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7.30
7.29
7.29
7.28
7.26
5.57
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5.55
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5.53
5.52
5.51
5.50
5.25
5.25
5.24
5.23
5.23
5.23
5.22
5.21
4.64
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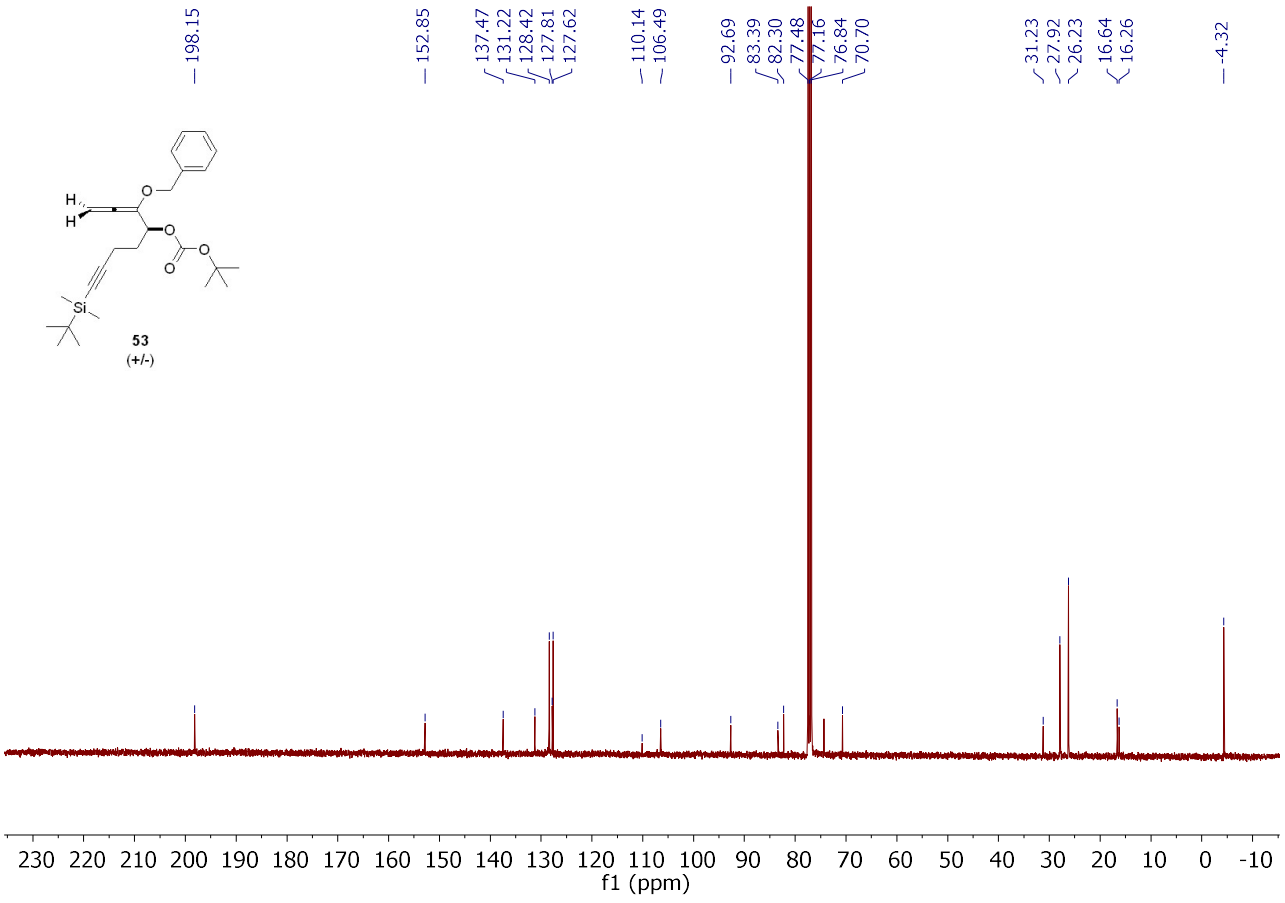
2.33
2.31
2.31
2.29
2.09
2.07
2.06
2.05
2.04
2.04
2.04
2.03
2.02
2.00
1.99
1.47
0.92
0.07
5.63
2.00
1.01
2.06
2.20
2.17
9.39
9.51
7.46
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
53
(+/-)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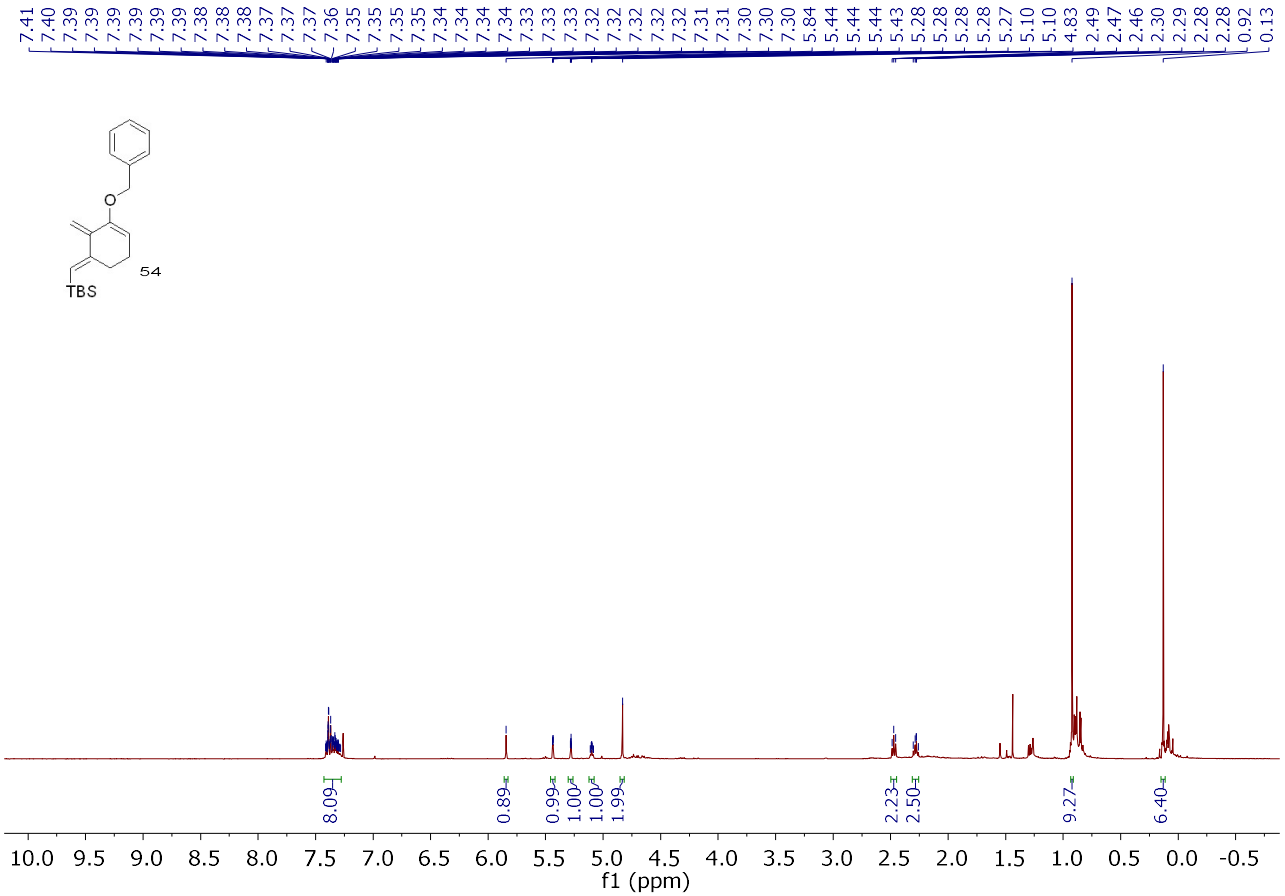
137.47
131.22
128.42
127.81
127.62
110.14
106.49
92.69
83.39
82.30
77.48
77.16
76.84
70.70
31.23
27.92
26.23
16.64
16.26
-4.32
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)
53
(+/-)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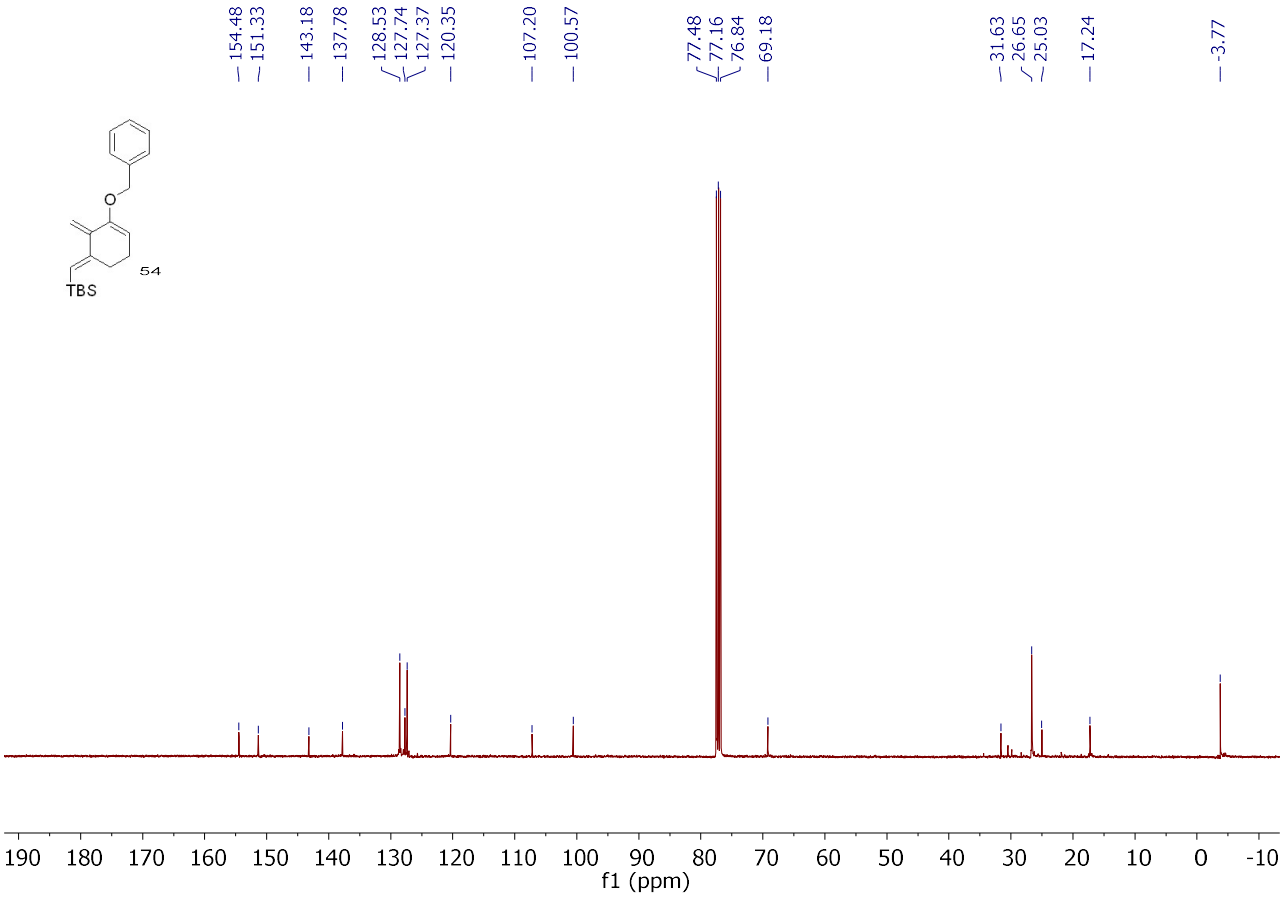
O
TBS
54
8.09 0.89 0.99 1.00 1.00 1.99 2.23 2.50 9.27 6.40
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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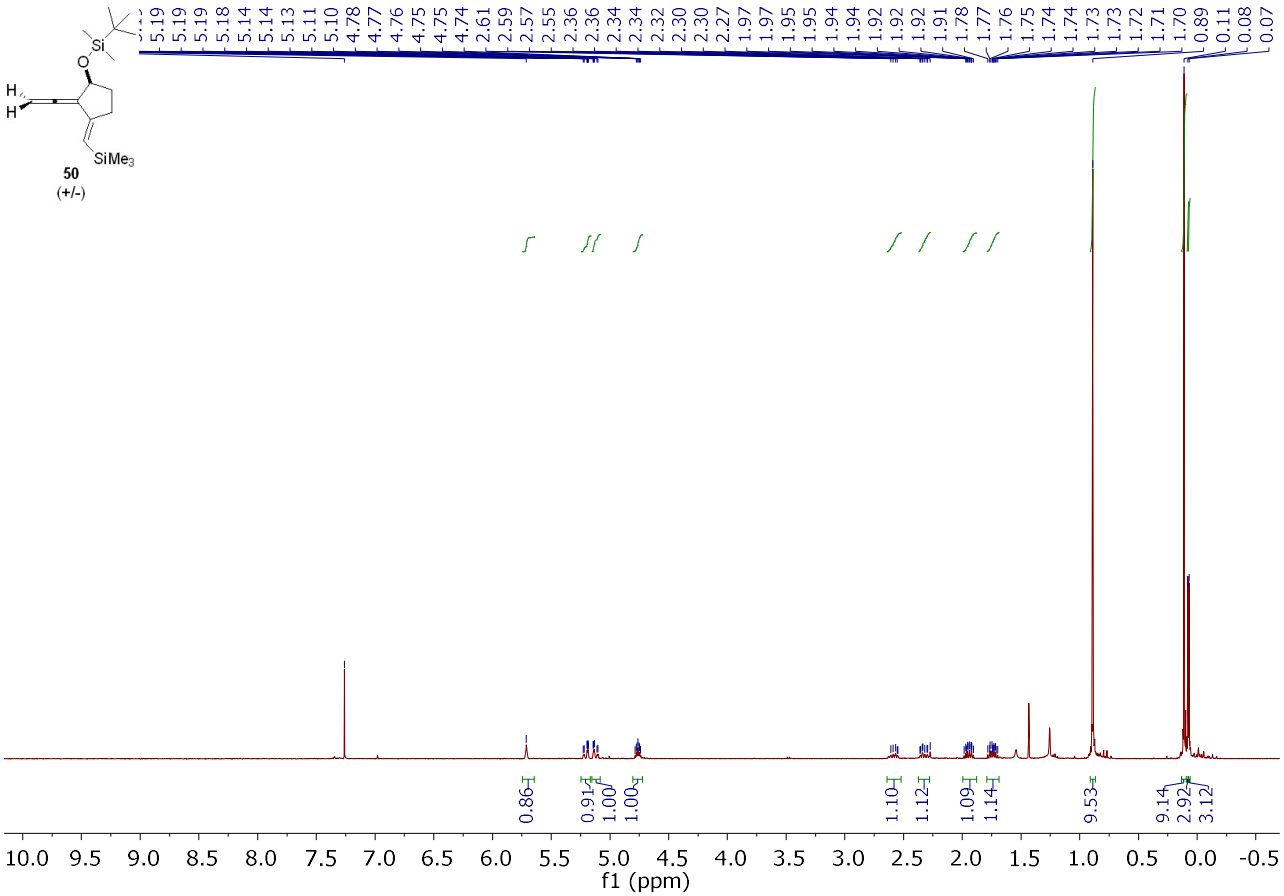
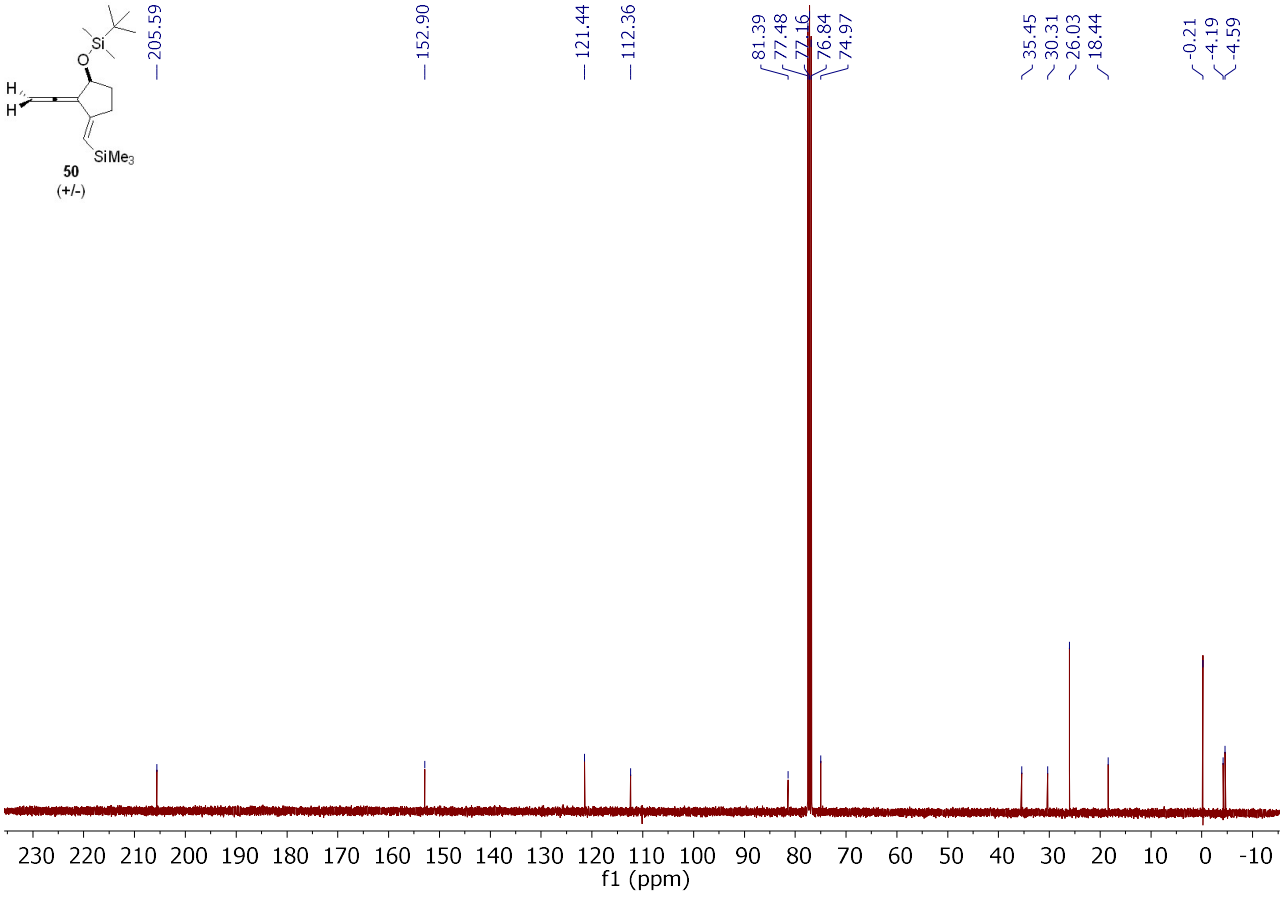
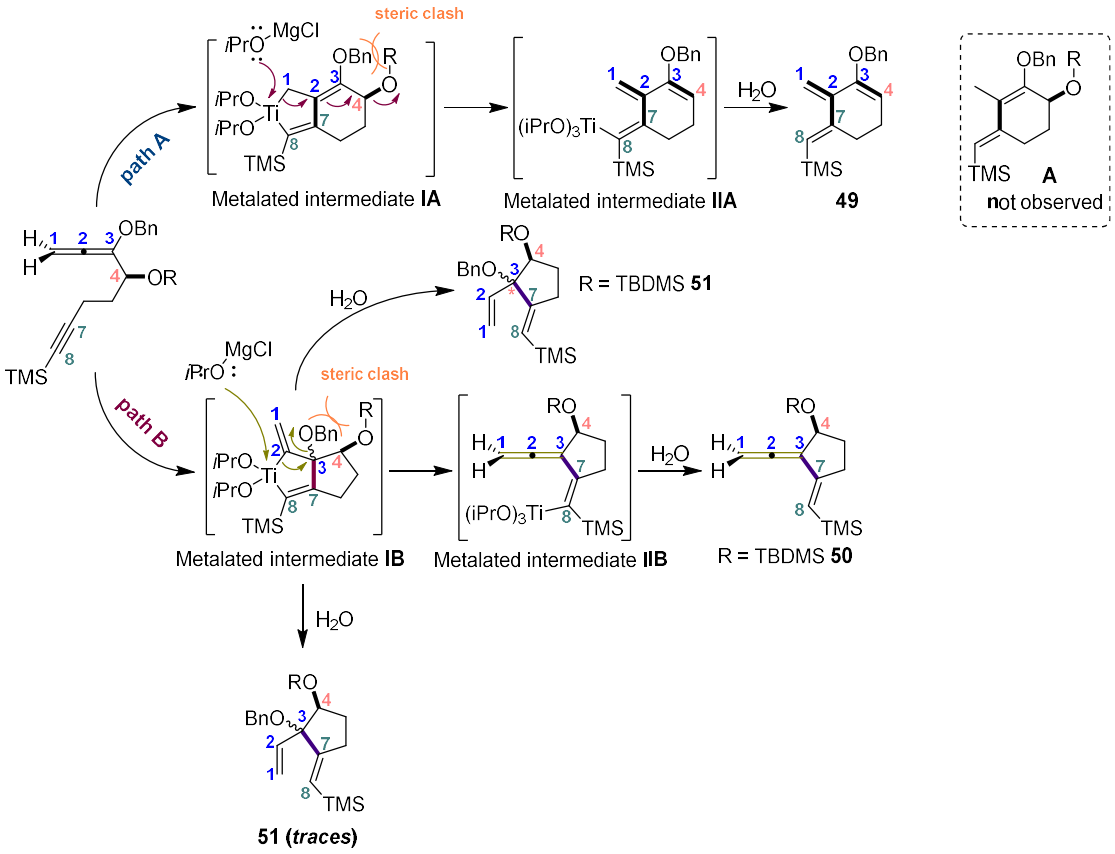
f1 (ppm)


SiMe3
50
(+/-)
f1 (ppm)


SiMe3
50
(+/-)
f1 (ppm)

5. Postulated Mechanisms

General scheme on postulated mechanism for the formation of compounds **34**, **49**, **50** and **51** depicted in scheme 3 and scheme 6 (main text)**.**



Scheme A

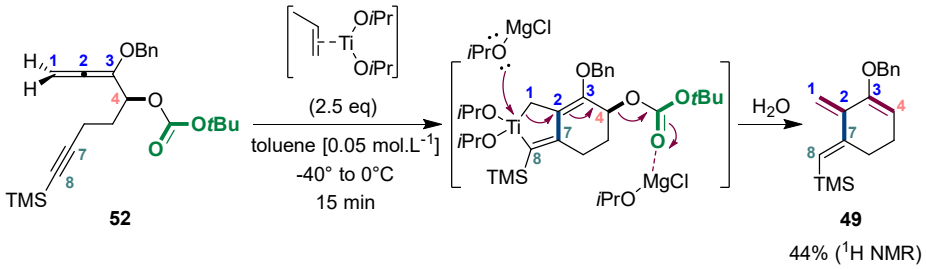
From a mechanistic point of view, the product **49** (Scheme A), results from an addition on the C_2 center leading to the metalated intermediate **IIA** (Path A). However, to date it has not been possible to rationalize the formation of this unique six-membered cycle. Indeed, product **A** was not observed at the end of the reaction, meaning that at the stage of hydrolysis of the reaction medium, the metalated intermediate **IA** had already been completely converted into metalated intermediate **IIA**. In the case where this behavior was the consequence of a steric hindrance between the benzyl and TBS groups, the experiment was repeated with a substrate which alcohol was previously protected by means of a less bulky trimethylsilyl group. Similarly, the only six-membered cyclized adduct observed was compound **49**.

Concerning the five-membered cyclized adducts **50** and **51** (Scheme A), their formation unambiguously results from an addition on the C3 center, leading to the metalated intermediate **IB**. The simple hydrolysis of **IB** thus led to the compound **51** which relative stereochemistry could not be elucidated due to the too small quantities of material recovered. This pathway also accounts for the formation of **34**.

In the case of silylated ether **47**, a rationale for the selective addition on the C3 center could be found in the comments made by Sato during his study devoted to the influence of homo-allylic alcohols on the stereoselectivity of its couplings. Indeed, Sato described free alcohols as more sterically demanding than OTBS-type silylated ethers, which subsequently led to the proposal for the formation of titanium

alkoxides. Thus, a plausible explanation could be that the C3 center is more accessible on the titanacyclopropene derived from free alcohol, than on its protected counterpart.

Detailed mechanism for the selective formation of compound **49** (main text - scheme 7)



Scheme B

It was undertaken to modulate the group onto the oxygen atom in order to facilitate the elimination process leading to metalated intermediate **IIA** (Scheme A). Thus, among the various tests carried out, it was established that carbonate **52** selectively provided product **49** (Scheme B), with a yield of 44%, determined by ^{1}H NMR.