

Controlling Regiochemistry in the Gold-Catalyzed Synthesis of Unsaturated Spiroketal.

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Supporting Information

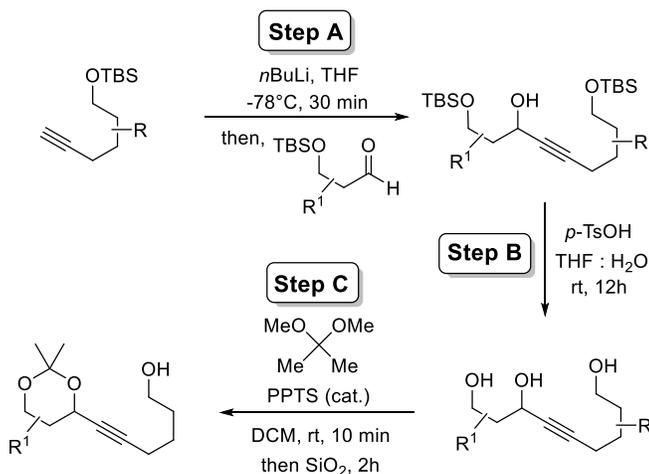
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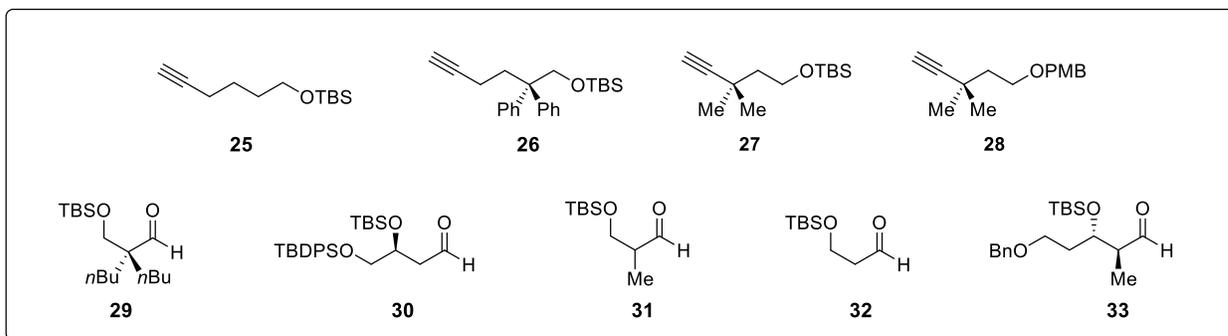
1. General considerations

All reactions were carried out under an atmosphere of nitrogen unless otherwise specified. Anhydrous solvents were transferred via syringe to flame-dried glassware, which had been cooled under a stream of dry nitrogen. Anhydrous tetrahydrofuran (THF), acetonitrile, diethyl ether, dichloromethane, and pentane were dried using an mBraun solvent purification system. Analytical thin layer chromatography (TLC) was performed using 250 μm Silica Gel 60 F254 pre-coated plates (EMD Chemicals Inc.). Flash column chromatography was performed using 230-400 Mesh 60A Silica Gel (Whatman Inc.). Proton nuclear magnetic resonance (^1H NMR) spectra were recorded using Varian Unity Inova 500 MHz and Varian Mercury 300 MHz spectrometers. Chemical shifts (δ) are reported in parts per million (ppm) downfield relative to tetramethylsilane (TMS, 0.0 ppm) or CDCl_3 (7.27 ppm). Coupling constants (J) are reported in Hz. Multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; m, multiplet; b, broad; Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded using a Varian Unity Mercury 300 spectrometer at 75 MHz and a Varian Unity Inova 500 MHz at 125 MHz. Chemical shifts are reported in ppm relative to the carbon resonance of CDCl_3 (77.23 ppm). High resolution mass spectra (HRMS) were obtained by Mass Spectrometry Core Laboratory of University of Florida, and are reported as m/z (relative ratio). A Agilent 6200 ESI-TOF instrument was used. A IonSense DART ET-100 ionization source was coupled to the instrument for DART-TOF analysis. Accurate m/z are reported for the molecular ion $[\text{M}+\text{H}]^+$, $[\text{M}+\text{NH}_4]^+$ or $[\text{M}+\text{Na}]^+$. The reagents 1,3-propanediol, 2,2-di-*n*-butyl-1,3-propanediol, and 2-methyl-1,3-propanediol were purchased from Sigma-Aldrich and used without further purification.

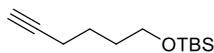
2. General scheme for the synthesis of triols and acetonides



3. Preparation of alkynes and aldehydes employed in the alkynylations

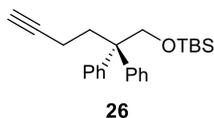


Procedure for the preparation of alkynes **25**¹, **26**²



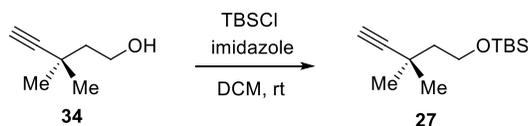
25

tert-butyl(hex-5-yn-1-yloxy)dimethylsilane (**25**). Synthesis of alkyne **25**¹ was accomplished according to previous reported literature procedure, and the spectroscopic data matched the reported data for this compound. Obtained as a colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 3.63 (t, 2H, $J = 6.0$ Hz), 2.24-2.18 (m, 2H), 1.94 (t, 1H, $J = 2.7$ Hz), 1.56-1.65 (m, 4H), 0.89 (s, 9H), 0.04 (s, 6H). ¹³C NMR (75 MHz, CDCl₃): δ 84.5, 68.2, 62.6, 31.8, 26.0, 24.9, 18.3, 18.2, -5.3.



tert-butyl((2,2-diphenylhex-5-yn-1-yl)oxy)dimethylsilane (**26**). Synthesis of alkyne **26**² was accomplished according to previous reported literature procedure, and the spectroscopic data matched the reported data for this compound. Obtained as a colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 7.27-7.11 (m, 10H), 4.10 (s, 2H), 2.51-2.44 (m, 2H), 1.98-1.88 (m, 3H), 0.81 (s, 9H), -0.15 (s, 6H). ¹³C NMR (75 MHz, CDCl₃): δ 145.8, 128.2, 127.8, 126.0, 85.0, 68.4, 68.0, 51.4, 35.6, 25.8, 18.1, 14.3, -5.9.

Procedure for the preparation of alkyne 27

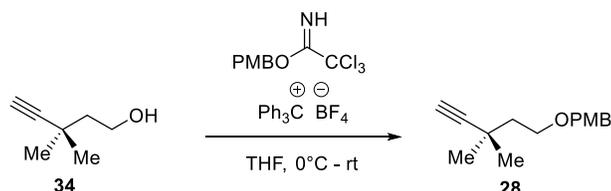


3,3-dimethylpent-4-yn-1-ol (**34**): Synthesis of the alkyne **34**³ was accomplished according to previously reported experimental procedures, and the spectroscopic data matched the reported data for this compound. Obtained as a colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 3.87 (t, *J* = 6.6 Hz, 2H), 2.17 (s, 1H), 1.78 (bs, 1H), 1.73 (t, *J* = 6.8 Hz, 2H), 1.26 (s, 6H). ¹³C NMR (75 MHz, CDCl₃): δ 91.4, 68.8, 60.3, 45.2, 29.5, 29.3.

tert-butyl((3,3-dimethylpent-4-yn-1-yl)oxy)dimethylsilane (**27**). TBSCl (0.580 g, 3.85 mmol, 1.1 equiv) was added in one portion to a solution of **34** (0.393 g, 3.50 mmol, 1.0 equiv) and imidazole (0.524 g, 7.70 mmol, 2.2 equiv) in dry CH₂Cl₂ (15 mL) at room temperature. The reaction was stirred for 12 h and quenched by the addition of water (10 mL). The mixture was diluted with CH₂Cl₂ (10 mL), and the organic layer was washed with brine (10 mL). The aqueous layer was washed with CH₂Cl₂ (10 mL). The organic layers were combined, dried over MgSO₄, concentrated, and purified by flash chromatography (5% EtOAc/Hexanes) to give **27** as a

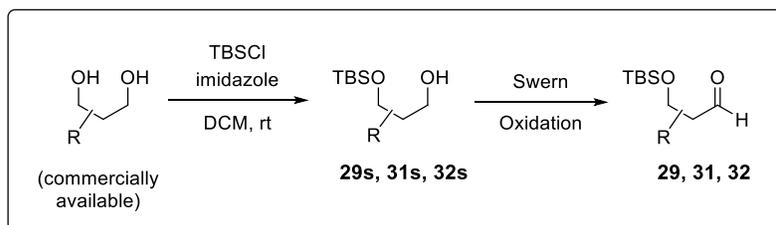
colorless oil (0.547 g, 69%). $R_f = 0.73$ (10% EtOAc/hexanes, KMnO_4 stain). ^1H NMR (300 MHz, CDCl_3): δ 3.83 (dd, $J = 7.7$ Hz, $J = 7.0$ Hz, 2H), 2.09 (s, 1H), 1.69 (t, $J = 7.4$ Hz, 2H), 1.24 (s, 6H), 0.91 (s, 9H), 0.07 (s, 6H). ^{13}C NMR (75 MHz, CDCl_3): δ 91.4, 68.3, 60.9, 45.5, 29.9, 26.2, 26.2, 18.5, -5.0, -5.1.

Procedure for the preparation of alkyne **28**



1-(((3,3-dimethylpent-4-yn-1-yl)oxy)methyl)-4-methoxybenzene (**28**). To a flask containing triphenylcarbenium tetrafluoroborate (0.151 g, 0.5 mmol, 0.1 equiv) was added, at room temperature, a solution of **34** (0.561 g, 5.0 mmol, 1.0 equiv) and 4-methoxybenzyl 2,2,2-trichloroacetimidate (1.413 g, 5.0 mmol, 1.0 equiv) in dry THF (10.0 mL). The mixture was stirred at room temperature for 3 h. Then EtOAc was added (20 mL) and the mixture was washed with 3M NaOH solution (2 x 10 mL). The organic layer was separated, dried over MgSO_4 and evaporated under reduced pressure. The residue was subjected to flash chromatography (0-5% EtOAc/ Hexanes) to furnish the product **28** as a colorless oil (0.651 g, 56%). $R_f = 0.71$ (20% EtOAc/hexanes, KMnO_4 stain) ^1H NMR (300 MHz, CDCl_3): δ 7.33 – 7.25 (m, 2H), 6.93 – 6.87 (m, 2H), 4.48 (s, 2H), 3.82 (s, 3H), 3.71 (t, $J = 7.0$ Hz, 2H), 2.13 (d, 1H), 1.80 (t, $J = 7.2$, 2H), 1.28 (s, 6H). ^{13}C NMR (75 MHz, CDCl_3): δ 159.3, 130.8, 129.4, 129.3, 113.9, 91.3, 72.8, 68.3, 55.4, 42.3, 29.9, 29.7.

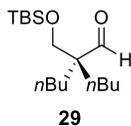
General procedure for the preparation of aldehydes **29**, **31**⁴ and **32**⁵



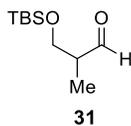
TBSCl (1.506 g, 10 mmol, 1.0 equiv) was added in one portion to a solution of the corresponding commercially available 1,3-propanediol derivative (10 mmol, 1.0 equiv), Et₃N (2.79 mL, 20.0 mmol, 2.0 equiv) in dry CH₂Cl₂ (50 mL) at room temperature. The reaction was stirred for 14 h and quenched by the addition of water (20 mL). The mixture was diluted with CH₂Cl₂ (20 mL), and the organic layer was washed with brine (30 mL). The aqueous layer was extracted with CH₂Cl₂ (30 mL). The organic layers were combined, dried over MgSO₄, concentrated, and purified by flash chromatography (5-10% EtOAc/Hexanes) to give the alcohol in 80-95% yield.

A solution of oxalyl chloride (3.75 mL, 2M in CH₂Cl₂, 7.5 mmol, 1.5 equiv) was added in a dropwise fashion to a -78°C solution of anhydrous DMSO (0.71 mL, 10 mmol, 2.0 equiv) in CH₂Cl₂ (20 mL). The mixture was stirred for 30 min and the monoprotected alcohol **29s**, **31s** or **32s** (5 mmol, 1.0 equiv) was added in a dropwise fashion. The mixture was stirred for 30 min before the addition of Et₃N (2.09 mL, 15.0 mmol, 3.0 equiv). The reaction was then slowly warmed up to room temperature and stirred for 2 h. If stirring became difficult, CH₂Cl₂ (20 mL) was added to the reaction mixture. After 2 h, the reaction was quenched with the addition of water (20 mL). The organic layer was successively washed with 5 portions of 10 mL of water and the combined extract was dried over MgSO₄, and concentrated to furnish an oil. The crude residue was then dissolved in Et₂O (10 mL) and a white precipitate was formed, which was then

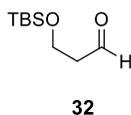
filtered and the residual ether was evaporated under reduced pressure to yield the title aldehydes **29**, **31** or **32**, which were used in the next step without further purification.



2-butyl-2-(((*tert*-butyldimethylsilyloxy)methyl)hexanal (**29**). The following compound was obtained according to the aforementioned general procedure in 78% yield as a slightly yellowish oil. $R_f = 0.68$ (10% EtOAc/hexanes, KMnO_4 stain). ^1H NMR (300 MHz, CDCl_3): δ 9.52 (s, 1H), 3.65 (s, 2H), 1.50 (q, $J = 7.5$ Hz, 4H), 1.30 (p, $J = 7.2$ Hz, 4H), 1.20 – 1.11 (m, 4H), 0.90 (t, $J = 7.5$ Hz, 6H), 0.87 (s, 9H), 0.03 (s, 6H). ^{13}C NMR (75 MHz, CDCl_3): δ 207.2, 63.9, 54.4, 29.4, 25.9, 25.6, 23.6, 14.2, -5.9.



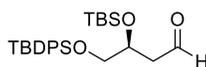
3-(((*tert*-butyldimethylsilyloxy)-2-methylpropanal (**31**). The spectroscopic data of **31**⁴ matched the reported data for this compound. The aldehyde **31** was synthesized in its racemic form in 76% yield as a slightly yellowish oil. $R_f = 0.71$ (20% EtOAc/hexanes, KMnO_4 stain). ^1H NMR (300 MHz, CDCl_3): δ 9.72 (d, $J = 1.6$ Hz, 1H), 3.83 (dd, $J = 10.2$ Hz, $J = 5.2$ Hz, 1H), 3.79 (dd, $J = 10.2$ Hz, 6.3 Hz, 1H), 2.54-2.49 (m, 1H), 1.07 (d, $J = 7.1$ Hz, 3H), 0.86 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (75 MHz, CDCl_3): δ 204.7, 63.4, 48.8, 25.8, 18.2, 10.2, -5.6, -5.6.



3-(((*tert*-butyldimethylsilyloxy)propanal (**32**). The spectroscopic data of **32**⁵ matched the reported data for this compound. Obtained in 83% yield, as a slightly yellowish oil. $R_f = 0.43$

(10% EtOAc/hexanes, KMnO₄ stain). ¹H NMR (300 MHz, CDCl₃): δ 9.77 (t, *J*=2.1 Hz, 1H, H), 3.96 (t, *J*=6.0 Hz, 2H), 2.57 (td, *J*=6.0, 2.1 Hz, 2H), 0.85 (s, 9H), 0.04 (s, 6H). ¹³C NMR (75 MHz, CDCl₃): δ 202.0, 57.3, 46.5, 25.7, 18.2, -5.5.

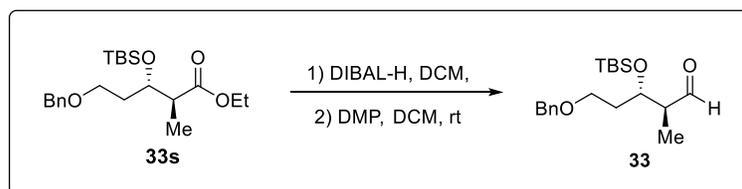
Procedure for the preparation of aldehyde **30**²



30

(*S*)-3-((*tert*-butyldimethylsilyloxy)-4-((*tert*-butyldiphenylsilyloxy)butanal (**30**). Synthesis of the non-racemic **30**² was accomplished according to previously reported experimental procedures and the spectroscopic data matched with the reported data for this compound. Obtained as a slightly yellowish oil. *R_f* = 0.54 (10% EtOAc/hexanes, KMnO₄ stain). ¹H NMR (300 MHz, CDCl₃): δ 9.86 (t, *J* = 2.7 Hz, 1H), 7.70 -7.65 (m, 4H), 7.48 -7.36 (m, 6H), 4.28 - 4.19 (m, 1H), 3.67 (dd, *J* = 10.2 Hz, *J* = 4.5 Hz, 1H), 3.53 (dd, *J* = 10.2 Hz, *J* = 7.5 Hz, 1H), 2.78 (ddd, *J* = 16.2 Hz, *J* = 4.5 Hz, *J* = 2.1 Hz, 1H), 2.61 (ddd, *J* = 16.2 Hz, *J* = 6.6 Hz, *J* = 3.0 Hz, 1H). 1.06 (s, 9H), 0.01 (s, 3H), -0.06 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 201.8, 135.6, 135.5, 133.1, 133.0, 129.8, 129.7, 127.8, 127.7, 68.7, 67.4, 48.8, 26.8, 25.7, 19.1, 17.9, -5.5.

Procedure for the preparation of aldehyde **33**



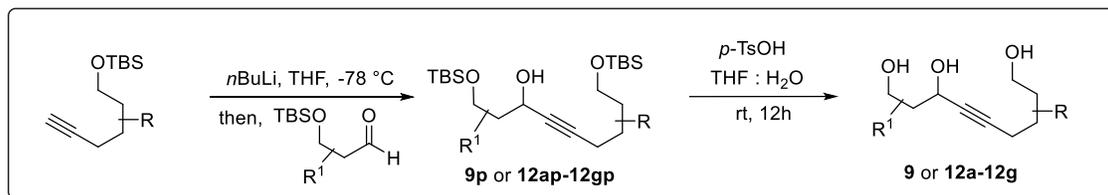
tert-butyl-((3,3-dimethylpent-4-yn-1-yl)oxy)dimethylsilane (**33**). Synthesis of the ester **33s**⁶ was accomplished according to previously reported experimental procedures, and the spectroscopic data matched with the reported data for this compound. The ester **33s** was

synthesized in its racemic form and obtained as a colorless oil. ^1H NMR (500 MHz, CDCl_3): δ 7.34 - 7.27 (m, 5H), 4.48 (s, 2H), 4.18 - 4.07 (m, 3H), 3.54 (t, $J=6.8$ Hz, 2H), 2.64 (ddd, $J=13.3$ Hz, $J=7.0$ Hz, $J=7.0$ Hz, 1H), 1.83 - 1.77 (m, 2H), 1.24 (t, $J=7.2$ Hz, 3H), 0.86 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3): δ 174.5, 138.6, 128.3, 127.5, 127.4, 72.8, 70.7, 66.5, 60.2, 45.7, 33.1, 25.8, 18.0, 14.2, 11.6, 24.7, 24.9.

A solution of DIBAL-H in hexanes (9.81 mmol, 1.0 M in hexanes, 3.0 equiv) was added to a solution of the ester **33s** (1.244 g, 3.27 mmol, 1.0 equiv) in CH_2Cl_2 (15 mL) at -25 °C, and the reaction was stirred for 45 min. The reaction was then quenched with Rochelle's Salt (10 mL) and NH_4Cl (saturated solution, 20 mL) and Et_2O (150 mL) was added to the mixture. After 30 min, the aqueous layer was extracted, and the combined extracts dried over MgSO_4 and concentrated to furnish an oil. The residue was subjected to flash chromatography (10% EtOAc/Hexanes) to provide the primary alcohol as a colorless oil (0.907 g, 82%), which was directly taken to the oxidation step.

Dess-Martin periodinane (1.14 g, 2.69 mmol, 1.2 equiv) was added to a solution of the alcohol obtained above (0.760 g, 2.25 mmol, 1 equiv) in CH_2Cl_2 (15 mL) at 0°C . After 1h, CH_2Cl_2 (30 mL) was added, followed by NaHCO_3 (saturated solution, 20 mL). The aqueous layer was extracted and the combined extracts dried over MgSO_4 and concentrated to furnish an oil. The residue was subjected to flash chromatography (10% EtOAc/Hexanes) to furnish the aldehyde **33** as a colorless oil (0.673 g, 89%). $R_f = 0.65$ (20% EtOAc/hexanes, KMnO_4 stain). ^1H NMR (500 MHz, CDCl_3): δ 9.73 (d, $J=2.1$ Hz, 1H), 7.39 - 7.25 (m, 5H), 5.31 (s, 2H), 4.53 - 4.49 (m, 2H), 4.17 (dt, $J=6.7$ Hz, $J=4.9$ Hz, 1H), 2.54 (qdd, $J=7.0$ Hz, $J=4.7$ Hz, $J=2.1$ Hz, 1H), 1.92 - 1.72 (m, 2H), 1.12 (d, $J=7.1$ Hz, 3H), 0.88 (s, 9H), 0.07 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3): δ 204.9, 138.50, 128.6, 127.8, 73.2, 70.7, 66.5, 53.6, 51.9, 34.9, 26.0, 18.2, 10.3, -4.3, -4.5.

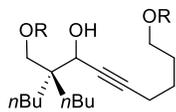
4. General procedure for the preparation of triols (Step A + B)



To a solution of the protected alkyne **25**, **26**, **27** or **28** (5-30 mmol, 1.0 equiv) in dry THF (15-100.0 mL) was added *n*-BuLi (2.1 mL per 5 mmol of substrate, 2.5 M in hexanes, 1.05 equiv) dropwise at -78 °C. The mixture was kept at this temperature for 30 min, and then stirred at room temperature for 15 min (this was performed by taking the flask out of the acetone/dry ice bath). The reaction mixture was then cooled to -78 °C and a solution of the aldehyde **29**, **30**, **31**, **32** or **33** (5.5-33 mmol, 1.1 equiv) in dry THF (5-20 mL) was added. The mixture was stirred for 1 h at -78 °C, then warmed to room temperature and stirred for an additional 1 h. The reaction was diluted with EtOAc (30-150.0 mL) and quenched with saturated NH₄Cl (10-50.0 mL). The aqueous layer was extracted with EtOAc (2x5-30 mL) and the combined organic extracts were dried over MgSO₄ and evaporated under reduced pressure. The residue was subjected to flash chromatography (0-5% EtOAc/ Hexanes) to furnish the desired silyl protected monopropargylic triols **9p** or **12ap-12gp**. The diastereomeric pairs **12ap/12bp** and **12cp/12dp** were separated by flash column chromatography without major problems.

To a solution of silyl protected monopropargylic triols **9p** or **12ap-12gp** (0.5-2.0 mmol, 1.0 equiv) in a mixture of THF: H₂O (10 : 1, 10.0 mL per mmol of substrate) at room temperature was added TsOH (0.188 g per mmol of substrate, 0.5-2.0 mmol, 1.0 equiv). The mixture was stirred for 15 h, and quenched with Et₃N (0.191 mL per mmol of substrate, 0.5-2.0 mmol, 1.0 equiv). The solvent was removed under reduced pressure, and the residue was subjected to flash

chromatography (40-90% EtOAc/ Hexanes) to furnish the desired monopropargylic triols **9** or **12a-12g**.



9p, R= TBS; **9**, R= H

6,6-dibutyl-2,2,3,3,15,15,16,16-octamethyl-4,14-dioxa-3,15-disilaheptadec-8-yn-7-ol (**9p**).

The following compound was obtained according to the aforementioned general procedure.

Obtained in 59% yield as a colorless oil. $R_f = 0.61$ (10% EtOAc/hexanes, KMnO_4 stain). ^1H

NMR (300 MHz, CDCl_3): δ 4.21 (d, $J = 10.0$ Hz, 1H), 4.10 (d, $J = 8.8$ Hz, 1H), 3.88 (d, $J = 9.7$

Hz, 1H), 3.61 (t, $J = 6.0$ Hz, 2H), 3.45 (d, $J = 9.7$ Hz, 1H), 2.25 (td, $J = 6.8$ Hz, $J = 1.9$ Hz, 2H),

1.67-1.07 (m, 16H), 0.93 - 0.85 (m, 6H), 0.89 (s, 9H), 0.88 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H),

0.03 (s, 6H). ^{13}C NMR (75MHz, CDCl_3): δ 86.0, 80.2, 70.2, 68.8, 62.7, 43.3, 32.2, 31.2, 29.6,

26.3, 26.1, 26.0, 25.5, 25.2, 23.8, 18.8, 18.5, 18.3, 14.3, 14.2, -5.2, -5.6.

2,2-dibutylnon-4-yne-1,3,9-triol (**9**). The following compound was obtained according to the aforementioned general procedure. Obtained in 85% yield as a colorless oil. $R_f = 0.14$ (40% EtOAc/hexanes, KMnO_4 stain). ^1H NMR (500 MHz, CDCl_3): δ 4.34 (s, 1H), 3.87 (d, $J = 10.8$

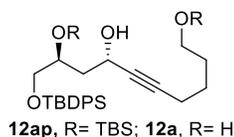
Hz, 1H), 3.70 (t, $J = 6.2$ Hz, 2H), 3.56 (d, $J = 11.1$ Hz, 1H), 2.97 (bs, 1H), 2.42 (bs, 1H), 2.31 (t,

$J = 7.6$ Hz, 2H), 1.77 - 1.42 (m, 8H), 1.41 - 1.14 (m, 8H), 0.98 - 0.87 (q, $J = 8.8$ Hz, 6H). ^{13}C

NMR (75 MHz, CDCl_3): δ 86.9, 80.1, 70.0, 67.9, 62.4, 43.6, 31.9, 31.1, 29.9, 25.5, 25.2, 25.1,

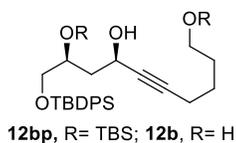
23.8, 18.8, 14.3, 14.2. HRMS (DART-TOF) m/z : $[\text{M}+\text{NH}_4]^+$ Calcd for $\text{C}_{17}\text{H}_{36}\text{NO}_3^+$ 302.2690;

Found 302.2698.



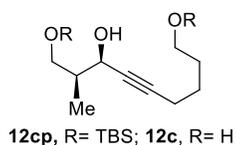
(6*S*,8*R*)-6-((*tert*-butyldimethylsilyl)oxy)-2,2,16,16,17,17-hexamethyl-3,3-diphenyl-4,15-dioxa-3,16-disilaoctadec-9-yn-8-ol (**12ap**). Synthesis of compound **12ap**² was accomplished according to previously reported experimental procedures, and the spectroscopic data matched with the reported data for this compound. Obtained as a colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 7.71-7.65 (m, 4H), 7.48-7.35 (m, 6H), 4.69-4.58 (m, 1H), 4.12-4.01 (m, 1H), 3.64 (t, *J* = 5.4 Hz, 1H), 3.62 (dd, *J* = 10.2, 5.4 Hz, 1H), 3.55 (dd, *J* = 10.2, 7.2 Hz, 1H), 3.04 (d, *J* = 5.1 Hz, 1H), 2.26 (dt, *J* = 6.9, 2.1 Hz, 2H), 2.08 (ddd, *J* = 15.2, 8.4, 3.6 Hz, 1H), 1.96 (ddd, *J* = 15.2, 6.9, 3.6 Hz, 1H), 1.67-1.55 (m, 4H), 1.06 (s, 9H), 0.90 (s, 9H), 0.84 (s, 9H), 0.06 (s, 6H), 0.04 (s, 3H), -0.08 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 135.6, 135.5, 133.3, 133.2, 129.8, 129.7, 127.7, 84.8, 81.4, 70.9, 66.9, 62.6, 59.9, 41.6, 32.0, 26.8, 26.0, 25.8, 25.1, 19.2, 18.6, 18.3, 17.9, -5.2, -5.5.

(7*R*,9*S*)-10-((*tert*-butyldiphenylsilyl)oxy)dec-5-yne-1,7,9-triol (**12a**). Synthesis of compound **12a**² was accomplished according to previously reported experimental procedures, and the spectroscopic data matched with the reported data for this compound. Obtained as a colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 7.68-7.64 (m, 4H), 7.44-7.35 (m, 6H), 4.68-4.57 (m, 1H), 4.28-4.19 (m, 1H), 3.68-3.62 (m, 3H), 3.57 (dd, *J* = 10.2 Hz, *J* = 3.6 Hz, 1H), 2.77 (bs, 3H), 2.25 (dt, *J* = 6.6 Hz, *J* = 1.8 Hz, 2H), 1.91-1.80 (m, 1H), 1.70-1.53 (m, 5H), 1.07 (s, 9H). ¹³C NMR (75 MHz, CDCl₃): δ 135.5, 135.5, 133.0, 133.0, 129.8, 127.8, 85.3, 81.2, 69.7, 67.7, 62.2, 60.6, 39.4, 31.7, 26.8, 24.8, 19.2, 18.4.



(6*S*,8*S*)-6-((*tert*-butyldimethylsilyl)oxy)-2,2,16,16,17,17-hexamethyl-3,3-diphenyl-4,15-dioxa-3,16-disilaoctadec-9-yn-8-ol (**12bp**). Synthesis of compound **12bp**² was accomplished according to previously reported experimental procedures, and the spectroscopic data matched with the reported data for this compound. Obtained as a colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 7.71-7.66 (m, 4H), 7.47-7.35 (m, 6H), 4.62-4.54 (m, 1H), 4.02-3.93 (m, 1H), 3.63 (t, *J* = 5.7 Hz, 1H), 3.62 (dd, *J* = 9.9, 4.8 Hz, 1H), 3.53 (dd, *J* = 9.9, 7.2 Hz, 1H), 2.83 (d, *J* = 5.1 Hz, 1H), 2.26 (dt, *J* = 6.9, 1.8 Hz, 2H), 2.10 (ddd, *J* = 13.8, 6.6, 4.5 Hz, 1H), 2.00-1.90 (m, 1H), 1.66-1.56 (m, 4H), 1.07 (s, 9H), 0.90 (s, 9H), 0.82 (s, 9H), 0.05 (s, 6H), 0.01 (s, 3H), -0.12 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): δ 135.6, 135.5, 133.2, 133.1, 129.8, 129.7, 127.7, 127.7, 85.5, 81.2, 71.0, 68.0, 62.6, 60.8, 43.4, 32.0, 26.8, 25.9, 25.8, 25.2, 19.2, 18.6, 18.3, 17.9, -5.2, -5.6.

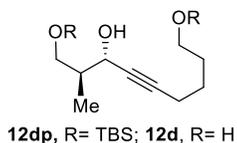
(7*S*,9*S*)-10-((*tert*-butyldiphenylsilyl)oxy)dec-5-yne-1,7,9-triol (**12b**). Synthesis of compound **12b**² was accomplished according to previously reported experimental procedures, and the spectroscopic data matched with the reported data for this compound. Obtained as a colorless oil. ¹H NMR (300 MHz, CDCl₃): δ 7.68-7.64 (m, 4H), 7.44-7.35 (m, 6H), 4.64-4.59 (m, 1H), 4.02-3.93 (m, 1H), 3.67-3.61 (m, 3H), 3.57 (dd, *J* = 10.2 Hz, *J* = 6.9 Hz, 1H), 3.35 (bs, 1H), 3.03 (bs, 2H), 2.23 (dt, *J* = 6.3 Hz, *J* = 1.8 Hz, 2H), 1.92-1.81 (m, 2H), 1.74-1.51 (m, 4H), 1.07 (s, 9H). ¹³C NMR (75 MHz, CDCl₃): δ 135.5, 133.0, 132.9, 129.8, 127.8, 85.1, 81.1, 71.2, 67.7, 62.2, 61.6, 40.8, 31.6, 26.8, 24.7, 19.2, 18.4.



(6*S**,7*R**)-2,2,3,3,6,15,15,16,16-nonamethyl-4,14-dioxa-3,15-disilaheptadec-8-yn-7-ol (**12cp**).

The following compound was obtained according to the aforementioned general procedure in 22% yield as a colorless oil. $R_f = 0.54$ (10% EtOAc/hexanes, KMnO_4 stain). $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 4.43 (ddd, $J = 7.8$ Hz, $J = 3.4$ Hz, $J = 1.9$ Hz, 1H), 3.85 (dd, $J = 9.8$ Hz, $J = 9.1$ Hz, 1H), 3.77 (d, $J = 7.9$ Hz, 1H), 3.66 (ddd, $J = 9.8$ Hz, $J = 4.4$ Hz, $J = 0.7$ Hz, 1H), 3.63 (t, $J = 6.0$ Hz, 2H), 2.27 (td, $J = 6.9$, 2.1 Hz, 2H), 2.12 (m, 1H), 1.67 – 1.55 (m, 4H), 0.91 (s, 9H), 0.90 (s, 9H), 0.92 – 0.86 (m, 3H), 0.10 (s, 3H), 0.09 (s, 3H), 0.05 (s, 6H). $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 86.1, 79.6, 67.4, 66.9, 62.8, 40.2, 32.2, 26.1, 26.0, 25.4, 18.8, 18.5, 18.3, 12.7, -5.1, -5.4, -5.5.

(2*S**,3*R**)-2-methylnon-4-yne-1,3,9-triol (**12c**). The following compound was obtained according to the aforementioned general procedure in 47% yield as a colorless oil. $R_f = 0.40$ (pure EtOAc, KMnO_4 stain). $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 4.48 (dt, $J = 4.0$ Hz, $J = 2.0$ Hz, 1H), 3.85 (dd, $J = 10.7$ Hz, $J = 8.6$ Hz, 1H), 3.70 – 3.65 (m, 3H), 2.83 (bs, 3H), 2.29 (td, $J = 6.8$ Hz, $J = 2.0$ Hz, 2H), 2.13 – 2.04 (m, 1H), 1.74 – 1.57 (m, 4H), 0.93 (d, $J = 7.0$ Hz, 3H). $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 86.8, 79.7, 67.1, 66.0, 62.5, 40.5, 31.9, 25.1, 18.7, 12.7. HRMS (DART-TOF) m/z : $[\text{M}+\text{NH}_4]^+$ Calcd for $\text{C}_{10}\text{H}_{22}\text{NO}_3^+$ 204.1594; Found 204.1602.

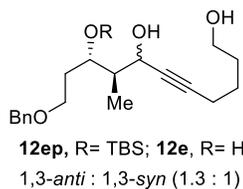


(6*S**,7*S**)-2,2,3,3,6,15,15,16,16-nonamethyl-4,14-dioxa-3,15-disilaheptadec-8-yn-7-ol (**12dp**).

The following compound was obtained according to the aforementioned general procedure in 20% yield as a colorless oil. $R_f = 0.42$ (10% EtOAc/hexanes, KMnO_4 stain). $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 4.38 (ddt, $J = 6.8$ Hz, $J = 4.9$ Hz, $J = 2.0$ Hz, 1H), 3.89 (dd, $J = 10.0$ Hz, $J = 4.1$ Hz, 1H), 3.63 (t, $J = 6.0$ Hz, 2H), 3.57 (dd, $J = 10.0$ Hz, $J = 6.9$ Hz, 1H), 3.37 (d, $J = 5.0$ Hz, 1H),

2.26 (td, $J = 6.9$ Hz, $J = 2.0$ Hz, 2H), 1.90 (qd, $J = 6.7$ Hz, $J = 4.1$ Hz, 1H), 1.66 – 1.54 (m, 4H), 1.00 (d, $J = 6.9$ Hz, 3H), 0.90 (s, 9H), 0.90 (s, 9H), 0.08 (s, 3H), 0.08 (s, 3H), 0.05 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3): δ 85.9, 80.4, 67.2, 67.1, 62.8, 41.2, 32.2, 26.2, 26.0, 25.4, 18.8, 18.5, 18.4, 13.2, -5.1, -5.4, -5.4.

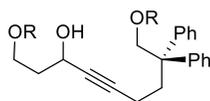
(2*S**,3*S**)-2-methylnon-4-yne-1,3,9-triol (**12d**). The following compound was obtained according to the aforementioned general procedure in 52% yield as a colorless oil. $R_f = 0.40$ (pure EtOAc, KMnO_4 stain). ^1H NMR (500 MHz, CDCl_3): δ 4.37 (dt, $J = 7.0$ Hz, $J = 2.2$ Hz, 1H), 3.80 (dd, $J = 11.0$ Hz, $J = 3.9$ Hz, 1H), 3.68 (t, $J = 6.3$ Hz, 2H), 3.64 (dd, $J = 11.0$ Hz, $J = 7.2$ Hz, 1H), 2.64 (bs, 3H), 2.28 (td, $J = 6.8$ Hz, $J = 2.0$ Hz, 2H), 1.95 (ddt, $J = 10.9$ Hz, $J = 7.0$ Hz, $J = 3.9$ Hz, 1H), 1.74 – 1.54 (m, 4H), 1.00 (dd, $J = 7.0$ Hz, $J = 0.7$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 86.4, 80.7, 67.3, 66.7, 62.5, 41.6, 31.9, 25.1, 18.7, 13.3. HRMS (DART-TOF) m/z : $[\text{M}+\text{NH}_4]^+$ Calcd for $\text{C}_{10}\text{H}_{22}\text{NO}_3^+$ 204.1594; Found 204.1597.



(5*S**,6*R**)-5-(2-(benzyloxy)ethyl)-2,2,3,3,6,15,15,16,16-nonamethyl-4,14-dioxa-3,15-disilaheptadec-8-yn-7-ol (**12ep**). The following compound was obtained according to the aforementioned general procedure in 68% yield as a colorless oil. $R_f = 0.63$ and 0.57 for each of the two diastereomers (20% EtOAc/ Hexanes, KMnO_4 stain). ^1H NMR (500 MHz, CDCl_3): δ (mixture of diastereomers) 7.38 – 7.25 (m, 10H), 4.61 (dd, $J = 2.3$ Hz, $J = 1.3$ Hz, 1H), 4.50 (s, 2H), 4.49 (s, 2H), 4.43 – 4.37 (m, 1H), 4.04 (q, $J = 5.5$ Hz, 1H), 3.92 (td, $J = 6.1$ Hz, $J = 4.2$ Hz, 1H), 3.68 – 3.49 (m, 5H), 3.37 (d, $J = 4.3$ Hz, 1H), 2.45 (d, $J = 4.7$ Hz, 1H), 2.25 (tdd, $J = 6.8$ Hz, $J = 3.7$ Hz, $J = 2.0$ Hz, 4H), 1.97 – 1.77 (m, 8H), 1.69 – 1.52 (m, 5H), 1.08 (d, $J = 7.0$ Hz, 3H),

0.98 (d, $J = 6.9$ Hz, 3H), 0.93 – 0.86 (m, 36H), 0.13 – 0.04 (m, 24H). ^{13}C NMR (125 MHz, CDCl_3): δ (mixture of diastereomers) 138.6, 138.6, 128.6, 127.9, 127.8, 127.8, 127.7, 86.6, 85.7, 80.4, 80.2, 74.0, 73.3, 73.2, 72.0, 66.8, 66.5, 65.4, 64.5, 62.8, 62.8, 44.7, 42.4, 34.6, 33.7, 32.2, 26.2, 26.1, 26.1, 25.4, 18.8, 18.6, 18.2, 18.2, 12.4, 11.8, -4.2, -4.5, -5.1.

(8*S**,9*S**)-11-(benzyloxy)-8-methylundec-5-yne-1,7,9-triol (**12e**). The following compound was obtained according to the aforementioned general procedure in 52% yield as a colorless oil. $R_f = 0.62$ and 0.54 for each of the 2 diastereomers (pure EtOAc, KMnO_4 stain). ^1H NMR (500 MHz, CDCl_3): δ (mixture of diastereomers) δ 7.38 – 7.24 (m, 10H), 4.54 – 4.48. (m, 6H), 4.14 (bs, 1H), 4.01 (td, $J = 8.9$ Hz, $J = 2.4$ Hz, 2H), 3.80 – 3.57 (m, 6H), 3.61 (t, $J = 6.5$ Hz, 4H), 2.50 (bs, 2H), 2.30 – 2.21 (m, 4H), 1.97 – 1.69 (m, 6H), 1.71 – 1.53 (m, 8H), 0.93 (dd, $J = 10.6$, 6.9 Hz, 6H). ^{13}C NMR (125 MHz, CDCl_3): δ (mixture of diastereomers) 137.9, 137.8, 128.6, 128.6, 128.0, 127.9, 127.9, 86.0, 80.4, 80.0, 75.2, 74.5, 73.5, 69.1, 66.8, 66.5, 62.2, 44.8, 43.4, 34.3, 34.0, 31.8, 25.1, 25.0, 18.7, 13.4, 12.8. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{19}\text{H}_{29}\text{O}_4^+$ 321.2060; Found 321.2051.



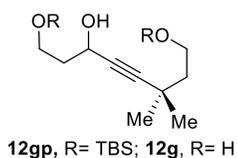
12fp, R= TBS; **12f**, R= H

2,2,3,3,15,15,16,16-octamethyl-12,12-diphenyl-4,14-dioxa-3,15-disilaheptadec-8-yn-7-ol

(**12fp**). Synthesis of compound **12fp**² was accomplished according to previously reported experimental procedures, and the spectroscopic data matched with the reported data for this compound. Obtained as a colorless oil. ^1H NMR (300 MHz, CDCl_3): δ 7.28-7.13 (m, 10H), 4.60-4.52 (m, 1H), 4.07 (s, 2H), 4.04-3.96 (m, 1H), 3.84-3.76 (m, 1H), 3.24 (d, $J = 5.7$ Hz, 1H), 2.50-2.43 (m, 2H), 2.05-1.76 (m, 4H), 0.90 (s, 9H), 0.78 (s, 9H), 0.08 (d, $J = 2.1$ Hz, 6H), -0.18 (s, 6H).

^{13}C NMR (75MHz, CDCl_3): δ 145.9, 128.3, 127.8, 126.0, 85.6, 80.5, 68.4, 62.0, 61.2, 51.4, 39.0, 35.8, 25.8, 25.7, 18.2, 18.1, 14.5, -5.5, -5.5, -5.9.

8,8-diphenylnon-4-yne-1,3,9-triol (**12f**). Synthesis of compound **12f**² was accomplished according to previously reported experimental procedures, and the spectroscopic data matched with the reported data for this compound. Obtained as a colorless oil. $R_f = 0.05$ (20% EtOAc/hexanes, KMnO_4 stain). ^1H NMR (300 MHz, CDCl_3): δ 7.30 - 7.11(m, 10H), 4.55-4.51 (m, 1H), 4.16 (s, 2H), 3.92-3.84 (m, 1H), 3.79-3.71 (m, 1H), 2.43 (t, $J = 7.5$ Hz, 2H), 2.04-1.79 (m, 4H). ^{13}C NMR (75 MHz, CDCl_3): δ 145.0, 128.3, 128.0, 126.4, 85.8, 80.8, 67.4, 61.4, 60.2, 51.6, 39.1, 34.8, 14.2.

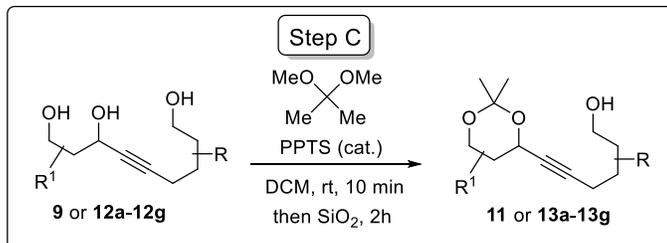


2,2,3,3,10,10,14,14,15,15-decamethyl-4,13-dioxa-3,14-disilaheptadec-8-yn-7-ol (**12gp**). The following compound was obtained according to the aforementioned general procedure in 51% as a colorless oil. $R_f = 0.36$ (10% EtOAc/ Hexanes, KMnO_4 stain). ^1H NMR (500 MHz, CDCl_3): δ 4.60 (t, $J = 5.5$ Hz, 1H), 4.07 - 3.96 (m, 1H), 3.81 (t, $J = 7.5$ Hz, 2H), 3.84 - 3.78 (m, 1H), 2.02 - 1.90 (m, 1H), 1.89 - 1.79 (m, 1H), 1.67 (t, $J = 7.5$ Hz, 2H), 1.22 (s, 6H), 0.91 (s, 9H), 0.90 (s, 9H), 0.10 (s, 3H), 0.09 (s, 3H), 0.07 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3): δ 92.0, 80.9, 62.2, 61.4, 61.1, 45.7, 39.4, 30.0, 29.9, 26.2, 26.1, 18.5, 18.4, -5.0, -5.3.

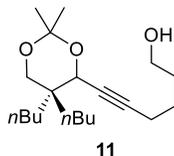
6,6-dimethyloct-4-yne-1,3,8-triol (**12g**): The following compound was obtained according to the aforementioned general procedure in 78% yield a colorless oil. $R_f = 0.31$ (pure EtOAc, KMnO_4 stain). ^1H NMR (500 MHz, CDCl_3): δ 4.60 (dd, $J = 6.7$ Hz, $J = 5.0$ Hz, 1H), 3.93 (ddd, $J = 11.3$ Hz, $J = 7.3$ Hz, $J = 4.3$ Hz, 1H), 3.83 (t, $J = 6.7$ Hz, 2H), 3.84 - 3.78 (m, 1H), 3.30 (bs,

3H), 1.99 – 1.85 (m, 2H), 1.71 (t, $J = 6.7$ Hz, 2H), 1.23 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3): δ 92.6, 81.5, 61.5, 60.4, 60.3, 45.4, 39.5, 29.9, 29.8, 29.7. HRMS (DART-TOF) m/z : $[\text{M}+\text{NH}_4]^+$ Calcd for $\text{C}_{10}\text{H}_{22}\text{NO}_3^+$ 204.1594; Found 204.1603.

5. General procedure for the preparation of acetonides (Step C)

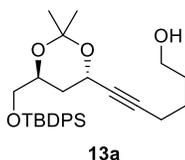


To a solution of the monopropargylic triols **9** or **12a-12g** (0.2-1.0 mmol, 1.0 equiv) and 2,2-dimethoxypropane (1.23 mL per mmol of substrate, 2.0-10.0 mmol, 10 equiv) in CH_2Cl_2 (1.0-5.0 mL) was added PPTS (25.1 mg per mmol of substrate, 0.02 mmol-0.1 mmol, 0.1 equiv). The mixture was stirred for 10 min, and then diluted with NaHCO_3 saturated solution (1-5 mL) and EtOAc (5-20 mL). The organic layer was washed with water (1-3 mL) and brine (1-3 mL), dried over MgSO_4 and concentrated under reduced pressure. The residue was then dissolved in wet CH_2Cl_2 (2-10 mL), and silica gel (1.0 g per mmol of substrate) was added, the mixture was then stirred for 2h and subjected to flash chromatography (5-10% EtOAc/Hexanes) to furnish the desired acetonides **11** or **13a-13g**.

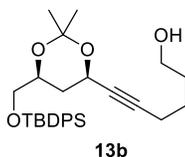


6-(5,5-dibutyl-2,2-dimethyl-1,3-dioxan-4-yl)hex-5-yn-1-ol (**11**). The following compound was obtained according to the aforementioned general procedure in 52% as a colorless oil. $R_f = 0.29$ (20% EtOAc/hexanes, KMnO_4 stain). ^1H NMR (300 MHz, CDCl_3): δ 4.52 (s, 1H), 3.63 (t, $J = 6.2$ Hz, 2H), 3.56 (s, 2H), 2.26 (t, $J = 5.7$ Hz, 2H), 1.87 – 1.77 (m, 1H), 1.71 – 1.53 (m, 3H), 1.41 (s,

6H), 1.37 – 1.16 (m, 12H), 0.90 (q, $J = 6.4$ Hz, 6H). ^{13}C NMR (75 MHz, CDCl_3): δ 99.1, 87.1, 69.2, 65.9, 62.42, 38.5, 33.8, 32.0, 30.2, 28.8, 25.8, 25.6, 24.9, 23.9, 23.9, 20.2, 18.9, 14.3, 14.1. HRMS (ESI-TOF) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{20}\text{H}_{36}\text{NaO}_3^+$ 347.2557; Found 342.2472.

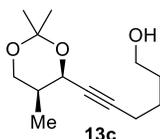


6-((4*S*,6*S*)-6-(((*tert*-butyldiphenylsilyl)oxy)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)hex-5-yn-1-ol (**13a**). Synthesis of compounds **13a**² was accomplished according to aforementioned general procedure, and the spectroscopic data matched with the reported data for this compound. Obtained in 47% yield as a colorless oil. ^1H NMR (500 MHz, CDCl_3): δ 7.71-7.67 (m, 4H), 7.45-7.33 (m, 6H), 4.69 (tt, $J = 5.7$ Hz, $J = 2.1$ Hz, 1H), 4.12 (ddd, $J = 10.2$ Hz, $J = 6.0$ Hz, $J = 5.1$ Hz, 1H), 3.72 (dd, $J = 10.5$ Hz, $J = 6.0$ Hz, 1H), 3.67 (t, $J = 6.3$ Hz, 2H), 3.61 (dd, $J = 10.5$ Hz, $J = 5.1$ Hz, 1H), 2.28 (dt, $J = 6.6$ Hz, $J = 2.1$ Hz, 2H), 1.89-1.79 (m, 2H), 1.71-1.58 (m, 4H), 1.54 (s, 3H), 1.36 (s, 3H), 1.06 (s, 9H). ^{13}C NMR (125 MHz, CDCl_3): δ 135.7, 135.6, 133.6, 133.6, 129.6, 129.6, 127.6, 127.6, 100.2, 85.9, 80.5, 66.8, 66.7, 62.4, 59.3, 34.2, 31.9, 28.0, 26.8, 24.8, 23.8, 19.3, 18.6.

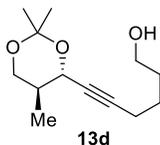


6-((4*R*,6*S*)-6-(((*tert*-butyldiphenylsilyl)oxy)methyl)-2,2-dimethyl-1,3-dioxan-4-yl)hex-5-yn-1-ol (**13b**). The following compound was obtained according to the aforementioned general procedure. Obtained in 45% yield as a colorless oil. $R_f = 0.41$ (40% EtOAc/hexanes, KMnO_4 stain). ^1H NMR (300 MHz, CDCl_3): δ 7.71-7.67 (m, 4H), 7.45-7.33 (m, 6H), 4.66 (dq, $J = 10.5$ Hz, $J = 3.2$ Hz, 1H), 4.02 – 3.90 (m, 1H), 3.70 (dd, $J = 10.5$ Hz, $J = 6.0$ Hz, 1H), 3.67 (t, $J = 6.3$

Hz, 2H), 3.55 (dd, $J = 10.5$ Hz, $J = 5.1$ Hz, 1H), 2.29 (td, $J = 9.5$ Hz, $J = 1.5$ Hz, 2H), 2.29 (dt, $J = 18.0$ Hz, $J = 2.5$ Hz, 1H), 1.69 - 1.52 (m, 5H), 1.44 (s, 3H), 1.42 (s, 3H), 1.06, (s, 9H). ^{13}C NMR (75 MHz, CDCl_3): δ 135.8, 133.7, 129.8, 127.9, 127.8, 127.8, 99.2, 85.2, 79.5, 69.6, 67.3, 62.5, 60.7, 35.0, 32.0, 30.1, 27.0, 24.9, 19.6, 19.5, 18.8. HRMS (DART-TOF) m/z : $[\text{M}+\text{NH}_4]^+$ Calcd for $\text{C}_{29}\text{H}_{44}\text{NO}_4\text{Si}^+$ 498.3034; Found 498.3029.

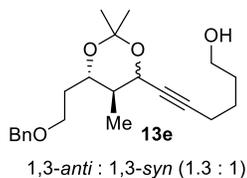


6-((4*R**,5*S**)-2,2,5-trimethyl-1,3-dioxan-4-yl)hex-5-yn-1-ol (**13c**). The following compound was obtained according to the aforementioned general procedure. Obtained in 52% yield as a colorless oil. $R_f = 0.29$ (20% EtOAc/hexanes, KMnO_4 stain). ^1H NMR (500 MHz, CDCl_3): δ 4.81 (dt, $J = 3.8$ Hz, $J = 2.0$ Hz, 1H), 4.02 (dd, $J = 11.7$ Hz, $J = 3.2$ Hz, 1H), 3.67 (t, $J = 6.4$ Hz, 2H), 3.63 (dd, $J = 11.7$ Hz, $J = 3.1$ Hz, 1H), 2.29 (td, $J = 6.9$ Hz, $J = 2.0$ Hz, 2H), 2.17 (s, 1H), 1.76 - 1.57 (m, 4H), 1.47 (s, 3H), 1.45 (s, 3H), 1.22 (d, $J = 7.0$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 99.3, 86.7, 78.5, 65.2, 64.7, 62.6, 33.2, 32.1, 28.9, 25.0, 20.6, 18.9, 12.3. HRMS (DART-TOF) m/z : $[\text{M}+\text{NH}_4]^+$ Calcd for $\text{C}_{13}\text{H}_{26}\text{NO}_3^+$ 244.1907; Found 244.1903.

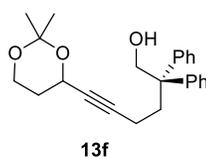


6-((4*S**,5*S**)-2,2,5-trimethyl-1,3-dioxan-4-yl)hex-5-yn-1-ol (**13d**). The following compound was obtained according to the aforementioned general procedure. Obtained in 53% yield as a colorless oil. $R_f = 0.30$ (40% EtOAc/hexanes, KMnO_4 stain). ^1H NMR (500 MHz, CDCl_3): δ 4.24 (dt, $J = 10.6$ Hz, $J = 2.0$ Hz, 1H), 3.75 (dd, $J = 11.9$ Hz, $J = 5.0$ Hz, 1H), 3.67 (t, $J = 6.2$ Hz,

2H), 3.52 (t, $J = 11.6$ Hz, 1H), 2.29 (td, $J = 6.7$ Hz, $J = 1.9$ Hz, 2H), 1.93 (m, 1H), 1.73 – 1.56 (m, 4H), 1.45 (s, 3H), 1.44 (s, 3H), 0.88 (d, $J = 6.8$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 99.0, 85.9, 78.4, 67.4, 66.0, 62.6, 35.8, 32.1, 29.9, 25.0, 19.0, 18.9, 13.2. HRMS (DART-TOF) m/z : $[\text{M}+\text{NH}_4]^+$ Calcd for $\text{C}_{13}\text{H}_{26}\text{NO}_3^+$ 244.1907; Found 244.1911.

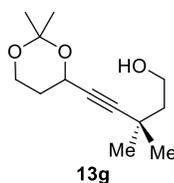


6-((5*S**,6*S**)-6-(2-(benzyloxy)ethyl)-2,2,5-trimethyl-1,3-dioxan-4-yl)hex-5-yn-1-ol (**13e**). The following compound was obtained according to the aforementioned general procedure. Obtained in 65% yield as a colorless oil. $R_f = 0.34$ and 0.26 for each of the 2 diastereomers (40% EtOAc/Hexanes, KMnO_4 stain). ^1H NMR (500 MHz, CDCl_3): δ (mixture of diastereomers) 7.38 – 7.24 (m, 10H), 4.65 (dt, $J = 5.7$ Hz, $J = 2.1$ Hz, 1H), 4.57 – 4.44 (m, 4H), 4.24 (dt, $J = 10.5$ Hz, $J = 1.9$ Hz, 1H), 3.76 (td, $J = 9.5$ Hz, $J = 2.7$ Hz, 1H), 3.70 – 3.52 (m, 9H), 2.28 (tt, $J = 6.8$ Hz, $J = 2.2$ Hz, 4H), 2.05 – 1.90 (m, 2H), 1.81 (ddt, $J = 12.0$ Hz, $J = 7.9$, $J = 6.0$ Hz, 1H), 1.72 – 1.53 (m, 11H), 1.52 (s, 3H), 1.43 (s, 3H), 1.41 (s, 3H), 1.35 (s, 3H), 0.95 (t, $J = 7.1$ Hz, 6H). ^{13}C NMR (125 MHz, CDCl_3): δ (mixture of diastereomers) 138.7, 128.5, 128.5, 127.8, 127.8, 100.5, 98.9, 88.1, 85.6, 78.7, 78.1, 73.2, 71.5, 69.6, 67.1, 66.7, 66.4, 64.7, 62.4, 40.4, 38.9, 33.8, 33.6, 32.1, 32.0, 30.2, 28.3, 25.0, 23.7, 19.5, 18.9, 18.8, 13.4, 13.0. HRMS (DART-TOF) m/z : $[\text{M}+\text{NH}_4]^+$ Calcd for $\text{C}_{22}\text{H}_{36}\text{NO}_4^+$ 378.2639; Found 378.2637.



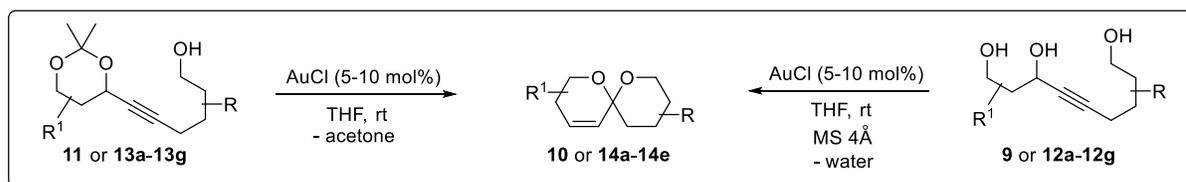
6-(2,2-dimethyl-1,3-dioxan-4-yl)-2,2-diphenylhex-5-yn-1-ol (**13f**). The following compound was obtained according to the aforementioned general procedure. Obtained in 50% yield as a

colorless oil. $R_f = 0.19$ (20% EtOAc/hexanes, KMnO_4 stain). $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.34 - 7.09 (m, 10H), 4.64 (dq, $J = 11.4$ Hz, $J = 3.5$ Hz, 1H), 4.14 (s, 2H), 3.93 (dt, $J = 11.6$ Hz, $J = 2.4$ Hz, 1H), 3.81 (ddd, $J = 11.6$ Hz, $J = 4.9$ Hz, $J = 2.1$ Hz, 1H), 2.49 – 2.39 (m, 2H), 2.05 – 1.87 (m, 2H), 4.64 (dq, $J = 16.2$ Hz, $J = 2.8$ Hz, 2H), 1.44 (s, 3H), 1.42 (s, 3H). $^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 144.9, 128.5, 128.3, 126.8, 99.1, 85.6, 79.3, 68.0, 60.7, 59.6, 52.0, 35.5, 32.4, 29.9, 19.5, 14.6. HRMS (DART-TOF) m/z : $[\text{M}+\text{NH}_4]^+$ Calcd for $\text{C}_{24}\text{H}_{32}\text{NO}_3^+$ 382.2377; Found 382.2395.

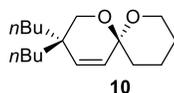


5-(2,2-dimethyl-1,3-dioxan-4-yl)-3,3-dimethylpent-4-yn-1-ol (**13g**). The following compound was obtained according to the aforementioned general procedure. Obtained in 60% yield as a colorless oil. $R_f = 0.32$ (40% EtOAc/ Hexanes, KMnO_4 stain). $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 4.67 (dd, $J = 11.2$ Hz, $J = 2.9$ Hz, 1H), 3.94 (td, $J = 11.8$ Hz, $J = 2.9$ Hz, 1H), 3.84 (t, $J = 6.4$ Hz, 1H), 3.86 – 3.82 (m, 1H), 1.95 (qd, $J = 11.9$, 4.8 Hz, 1H), 1.72 (t, $J = 6.6$ Hz, 1H), 1.67 (dq, $J = 13.2$ Hz, $J = 2.7$ Hz, 1H), 1.46 (s, 3H), 1.44 (s, 3H), 1.24 (s, 6H). $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ 99.1, 92.0, 80.1 60.6, 60.5, 59.5, 45.7, 32.5, 29.8, 29.7, 19.8. HRMS (DART-TOF) m/z : $[\text{M}+\text{NH}_4]^+$ Calcd for $\text{C}_{13}\text{H}_{26}\text{NO}_3^+$ 244.1907; Found 244.1911.

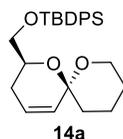
6. General procedure for the preparation of spiroketals



To a test tube (previously dried in the oven at 120° C overnight), under nitrogen atmosphere, was added AuCl (5 or 10 mol %). Then, a mixture containing the solvent of the reaction (THF or Et₂O) and the substrate (1.0 mL solvent/ mmol of substrate) was added into the test tube, and the mixture was stirred for 1h. After the reaction to be complete, it was filtered through a short plug of silica, which was flushed with CH₂Cl₂ and concentrated under reduced pressure to afford the crude mixture that was subjected to flash chromatography (0-2% EtOAc/ Hexanes) to deliver the desired spiroketals **10** and **14a-14e**. For the more volatile spiroketals **14b** and **14e** the plug of silica was flushed with Et₂O instead of CH₂Cl₂, and the concentration was performed at ambient pressure passing nitrogen through the sample, and flash chromatography was performed with 0-5% Et₂O/ pentanes. In the case triols were employed as substrates, molecular sieves 4Å (50 mg/ mmol of substrate) was added to the test tube along with the catalyst.

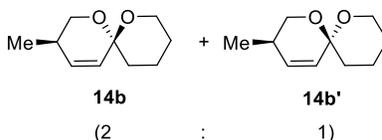


3,3-dibutyl-1,7-dioxaspiro[5.5]undec-4-ene (**10**). The following compound was obtained according to the aforementioned general procedure. Obtained in 67% (from **11**) and 20% (from **9**) yield as a colorless oil. $R_f = 0.86$ (20% EtOAc/ Hexanes, KMnO₄ stain). ¹H NMR (500 MHz, CDCl₃): δ 5.70 (d, $J = 10.1$ Hz, 1H), 5.54 (d, $J = 10.1$ Hz, 1H), 3.83 (td, $J = 11.6$ Hz, $J = 2.7$ Hz, 1H), 3.73 (d, $J = 11.1$ Hz, 1H), 3.66 – 3.60 (m, 1H), 3.43 (d, $J = 11.5$ Hz, 1H), 1.87 (dt, $J = 14.2$, 4.1 Hz, 1H), 1.71 – 1.06 (m, 17H), 0.90 (q, $J = 6.7$ Hz, 6H). ¹³C NMR (75 MHz, CDCl₃): δ 137.0, 128.9, 93.2, 67.0, 61.2, 37.1, 36.8, 35.6, 35.6, 35.1, 26.5, 25.8, 25.3, 23.8, 18.9, 14.4. HRMS (DART-TOF) m/z: [M+H]⁺ Calcd for C₁₇H₃₁O₂⁺ 267.2319; Found 267.2320.



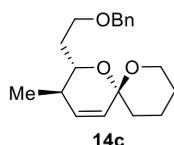
((2*S*,6*S*)-1,7-dioxaspiro[5.5]undec-4-en-2-ylmethoxy)(tert-butyl)diphenylsilane (**14a**).

Synthesis of compounds **14a**² was accomplished according to the aforementioned general procedure, and the spectroscopic data matched with the reported data for this compound. Obtained in 72% (from **13a**), 74% (from **13b**), 95% (from **12a**) and 30% (from **12b**) yield as a colorless oil. $R_f = 0.89$ (40% EtOAc/ Hexanes, KMnO_4 stain). ^1H NMR (300 MHz, CDCl_3): δ 7.78-7.71 (m, 4H), 7.46-7.35 (m, 6H), 5.99 (dt, $J = 10.0$ Hz, $J = 5.0$ Hz, 1H), 5.67 (d, $J = 10.0$ Hz, 1H), 4.05 – 4.17-4.08 (m, 1H), 3.97 (dt, $J = 12.0$, 2.7 Hz, 1H), 3.79 (dd, $J = 10.2$, 6.6 Hz, 1H), 3.68 (dd, $J = 10.2$, 4.5 Hz, 1H), 3.63-3.57 (m, 1H), 2.35 (dddt, $J = 18.0$ Hz, $J = 9.0$ Hz, $J = 5.5$ Hz, $J = 2.5$ Hz, 1H), 2.01-1.93 (m, 3H), 1.73-1.45 (m, 5H), 1.06 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3): δ 135.8, 135.7, 133.9, 130.9, 129.5, 127.6, 93.4, 70.6, 67.7, 57.6, 34.7, 27.1, 26.8, 24.8, 19.3, 18.6.

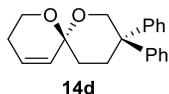


(3*R**,6*R**)-3-methyl-1,7-dioxaspiro[5.5]undec-4-ene (**14b**). The following compound was obtained according to the aforementioned general procedure. Obtained in 77% (from **13c**), 67% (from **13d**), 15% (from **12c**) and 15% (from **12d**) yield as a colorless oil. $R_f = 0.59$ (20% EtOAc/ Hexanes, KMnO_4 stain). ^1H NMR (500 MHz, CDCl_3): δ (major diastereomer **14b**) 5.76 (d, $J = 10.1$ Hz, 1H), 5.62 – 5.55 (m, 1H), 3.89 – 3.82 (m, 1H), 3.70 (dd, $J = 11.1$ Hz, $J = 6.0$ Hz, 1H), 3.66 – 3.61 (m, 2H), 3.49 (t, $J = 10.8$ Hz, 1H), 2.47 – 2.35 (m, 1H), 1.86 (m, 1H), 1.73 – 1.45 (m, 6H), 0.96 – 0.87 (m, 3H). (minor diastereomer **14b'**) 5.90 (dd, $J = 10.2$ Hz, $J = 5.4$ Hz, 1H), 5.62

– 5.54 (m, 1H), 4.07 (dd, $J = 11.1$ Hz, $J = 3.8$ Hz, 1H), 3.89 – 3.81 (m, 1H), 3.66 – 3.61 (m, 1H), 3.49 (d, $J = 11.1$ Hz, $J = 1.1$ Hz, 1H), 2.08 – 2.01 (m, 1H), 1.86 (m, 1H), 1.74 – 1.46 (m, 6H), 1.10 (d, $J = 7.1$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ (mixture of diastereomers) 134.6, 133.5, 129.8, 129.6, 93.1, 64.8, 63.9, 61.2, 61.2, 35.0, 29.5, 29.3, 25.2, 18.9, 18.8, 18.3, 16.1. HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{10}\text{H}_{17}\text{O}_2^+$ 169.1223; Found 169.1227.

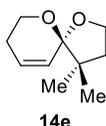


(2R*,3S*,6S*)-2-(2-(benzyloxy)ethyl)-3-methyl-1,7-dioxaspiro[5.5]undec-4-ene (**14c**). The following compound was obtained according to the aforementioned general procedure. Obtained in 52% (from **13f**), and 10% (from **12f**) yield as a colorless oil. $R_f = 0.65$ (20% EtOAc/ Hexanes, KMnO_4 stain). ^1H NMR (500 MHz, CDCl_3): δ 7.40 – 7.25 (m, 5H), 5.67 (dd, $J = 10.0$ Hz, $J = 1.8$ Hz, 1H), 5.58 (dd, $J = 10.0$ Hz, $J = 2.5$ Hz, 1H), 4.55 (s, 2H), 3.81 – 3.68 (m, 3H), 3.68 – 3.55 (m, 2H), 2.16 – 2.01 (m, 2H), 1.90 – 1.79 (m, 1H), 1.79 – 1.69 (m, 1H), 1.68 – 1.53 (m, 4H), 1.51 – 1.44 (m, 1H), 0.97 (d, $J = 7.2$ Hz, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 138.8, 134.6, 129.6, 128.5, 127.9, 127.7, 93.5, 73.3, 70.5, 67.6, 61.3, 35.2, 34.9, 33.6, 25.3, 18.8, 17.0. HRMS (DART-TOF) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{19}\text{H}_{27}\text{O}_3^+$ 303.1955; Found 303.1955.



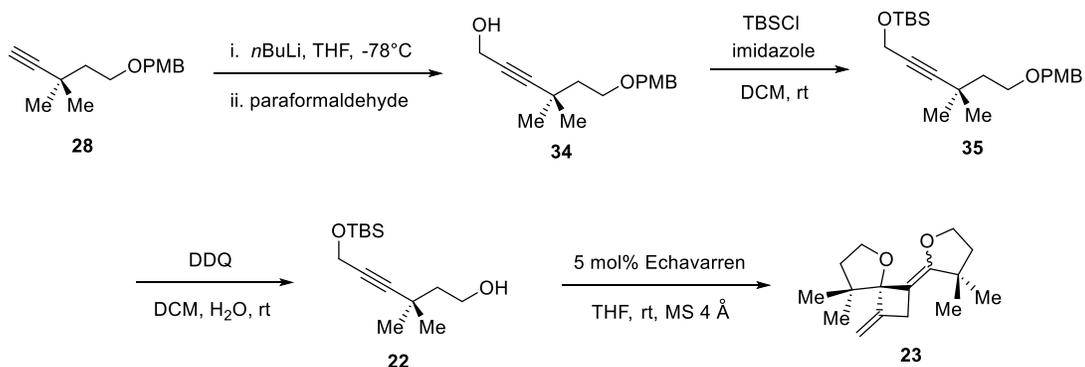
9,9-diphenyl-1,7-dioxaspiro[5.5]undec-4-ene (**14d**²). Synthesis of compounds **14d**² was accomplished according to the aforementioned general procedure, and the spectroscopic data matched with the reported data for this compound. Obtained in 74% (from **11**), and 81% (from **10**) yield as a colorless oil. $R_f = 0.70$ (20% EtOAc/ Hexanes, KMnO_4 stain). ^1H NMR (300 MHz,

CDCl₃): δ 7.48-7.31(m, 2H), 7.30-7.15 (m, 8H), 5.99-5.93 (m, 1H), 5.53 (ddd, $J = 10.2$ Hz , $J = 2.7$ Hz , $J = 1.5$ Hz, 1H), 4.32 (dd, $J = 11.7$ Hz, $J = 3.0$ Hz, 1H), 4.00-3.90 (m, 2H), 3.80-3.74 (dd, $J = 11.1$ Hz, $J = 6.3$ Hz, 1H), 2.88 (dt, $J = 13.2$ Hz, $J = 3.9$ Hz, 1H), 2.38-2.20 (m, 2H), 1.89 (dt, $J = 18.0$ Hz, $J = 4.5$ Hz, 1H), 1.66 (dt, $J = 13.5$ Hz, $J = 3.6$ Hz, 1H), 1.48 (dt, $J = 13.5$, $J = 3.6$ Hz, 1H). ¹³C NMR (75 MHz, CDCl₃): δ 146.6, 145.3, 130.1, 128.5, 128.3, 128.2, 128.0, 127.0, 126.3, 125.8, 92.5, 67.5, 57.8, 45.4, 31.2, 29.3, 24.7.

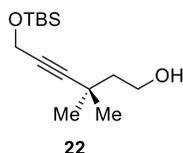


1,1-dimethyl-6-oxaspiro[4.5]dec-9-ene (**14e**). The following compound was obtained according to the aforementioned general procedure. Obtained in 47% (from **13g**), and 45% (from **12g**) yield as a colorless oil. $R_f = 0.55$ (20% EtOAc/ Hexanes, KMnO₄ stain). ¹H NMR (500 MHz, CDCl₃): δ 6.14 (dd, $J = 11.1$ Hz, $J = 7.4$ Hz, 1H), 5.68 (d, $J = 10.2$ Hz, 1H), 3.90 (m, dd, $J = 19.9$ Hz, $J = 9.8$ Hz, 2H), 3.93 – 3.86 (m, 1H), 3.75 (dd, $J = 12.1$ Hz, $J = 5.6$ Hz, 1H), 2.24 (t, $J = 15.1$ Hz, 1H), 2.16 (q, $J = 10.4$ Hz, 1H), 1.84 (d, $J = 18.0$ Hz, 1H), 1.70 – 1.61 (m, 1H), 1.03 (s, 3H), 1.02 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 131.8, 124.8, 104.7, 65.1, 58.8, 45.4, 38.9, 25.2, 25.1, 22.2. HRMS (ESI-TOF) m/z : $[M+H]^+$ Calcd for C₁₀H₁₇O₂⁺ 169.1223; Found 169.1228.

7. Preparation of cyclobutane **23**



Procedure for the preparation of **22**:



6-((*tert*-butyldimethylsilyl)oxy)-3,3-dimethylhex-4-yn-1-ol (**22**). To a solution of **28** (0.232 g, 1.0 mmol, 1.0 equiv) in dry THF (5.0 mL) was added *n*-BuLi (0.48 mL, 2.5 M in hexanes, 1.2 mmol, 1.2 equiv) dropwise at -78°C. The mixture was kept at this temperature for 30 min, and then stirred at room temperature for 15 min (this was performed by taking the flask out of the acetone/dry ice bath). After the reaction mixture was cooled to -78 °C, the flask was quickly opened and paraformaldehyde (0.600 g, 20.0 mmol, 20.0 equiv) was added. The mixture was stirred for 30 min at -78 °C, then warmed to room temperature and stirred for an additional 1 h. The reaction was diluted with EtOAc (15.0 mL) and quenched with saturated NH₄Cl (10.0 mL). The aqueous layer was extracted with EtOAc (2x10 mL) and the combined organic extracts were dried over MgSO₄ and evaporated under reduced pressure. The residue was subjected to flash chromatography (5% EtOAc/ Hexanes) to furnish the product **34** (0.126 g, 48%) as a colorless oil. *R_f* = 0.15 (20% EtOAc/ Hexanes, KMnO₄ stain). ¹H NMR (500 MHz, CDCl₃): δ 7.26 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.6 Hz, 2H), 4.45 (s, 2H), 4.23 (s, 2H), 3.81 (s, 3H), 3.65 (t, *J* = 7.2 Hz,

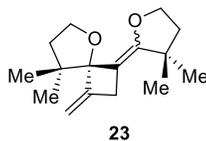
2H), 1.76 (t, $J = 7.2$ Hz, 2H), 1.23 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3): δ 159.3, 130.8, 129.5, 114.0, 93.1, 78.6, 72.8, 67.9, 55.5, 51.6, 42.4, 30.1, 29.8.

TBSCl (0.068 g, 0.45 mmol, 1.5 equiv) was added in one portion to a solution of **34** (0.079 g, 0.3 mmol, 1.0 equiv) and imidazole (0.061 g, 0.9 mmol, 3.0 equiv) in dry CH_2Cl_2 (5 mL) at room temperature. The reaction was stirred for 13 h and quenched by the addition of water (2 mL). The mixture was diluted with CH_2Cl_2 (10 mL), and the organic layer was washed with brine (4 mL). The aqueous layer was washed with CH_2Cl_2 (2 mL). The organic layers were combined, dried over MgSO_4 , concentrated, and the compound **35** (0.107 g, 95%) as a colorless oil was taken to the next step without further purification. $R_f = 0.67$ (20% EtOAc/ Hexanes, KMnO_4 stain). ^1H NMR (500 MHz, CDCl_3): δ 7.27 (d, $J = 8.6$ Hz, 2H), 6.88 (d, $J = 8.6$ Hz, 2H), 4.44 (s, 2H), 4.30 (s, 2H), 3.81 (s, 3H), 3.66 (t, $J = 7.7$ Hz, 2H), 1.76 (t, $J = 7.4$ Hz, 2H), 1.22 (s, 6H), 0.92 (s, 9H), 0.12 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3): δ 159.3, 130.9, 129.4, 127.7, 114.0, 91.8, 79.1, 72.9, 68.1, 64.9, 55.5, 52.2, 42.5, 30.1, 29.8, 26.2, 26.1, 18.5, -4.8.

DDQ (0.055 g, 0.24 mmol, 1.2 equiv) was added in one portion to a solution of **35** (0.079 g, 0.2 mmol, 1.0 equiv) in dry CH_2Cl_2 : H_2O (9 : 1, 10 mL) at room temperature. The reaction was stirred for 2 h and the precipitated formed was filtered off over a plug of celite. Celite was washed with CH_2Cl_2 (20 mL). The crude mixture was then washed with NaHCO_3 saturated solution (5 mL) The organic layer was washed with water (2x5 mL), combined, dried over MgSO_4 , and concentrated. Flash chromatography (1-10% EtOAc/ Hexanes) gave the title compound **22** (0.024 g, 45%) as a colorless oil. $R_f = 0.33$ (20% EtOAc/ Hexanes, KMnO_4 stain). ^1H NMR (500 MHz, CDCl_3): δ 4.29 (s, 2H), 3.84 (t, $J = 6.6$ Hz, 2H), 1.71 (t, $J = 6.6$ Hz, 2H), 1.24 (s, 6H), 0.91 (s, 9H), 0.12 (s, 6H). ^{13}C NMR (125 MHz, CDCl_3): δ 92.0, 79.8, 60.7, 52.1,

45.6, 29.8, 29.7, 26.0, 26.0, 18.5, -4.8. HRMS (ESI-TOF) m/z : $[M+H]^+$ Calcd for $C_{14}H_{29}O_2Si^+$ 257.1931; Found 257.1942.

Procedure for the preparation of **23**

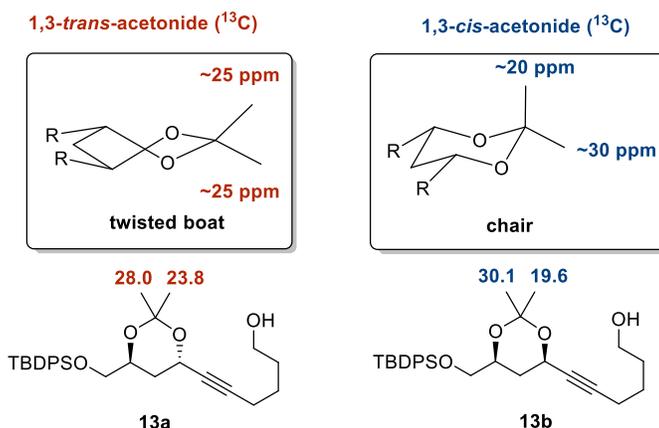


1-(3,3-dimethyldihydrofuran-2(3H)-ylidene)-8,8-dimethyl-3-methylene-5-oxaspiro[3.4]octane (**23**). To a test tube (previously dried in the oven at 120°C overnight), under nitrogen atmosphere, was added $[(t\text{-Bu})_2(o\text{-biphenyl})P]AuMeCN \cdot SbF_6^-$ (5 mol %) and molecular sieves 4Å (100 mg/mmol of substrate). Then, a mixture containing THF (2.1 mL) and the compound **22** (0.0532 g, 0.21 mmol, 1.0 equiv) was added into the test tube, and the mixture was stirred for 20 min. After TLC showed that the reaction was complete, the mixture was filtered through a short plug of silica, which was flushed with CH_2Cl_2 : Et_3N (99 : 1) and concentrated under reduced pressure to afford the crude mixture that was subjected to flash chromatography (1% Et_3N / 20-50% CH_2Cl_2 / Hexanes) to deliver the title compound **23** (0.0100 g, 39%) as a colorless oil. $R_f = 0.69$ (20% $EtOAc$ / Hexanes, $KMnO_4$ stain). 1H NMR (500 MHz, $CDCl_3$): δ 4.99 (dt, $J = 2.3$ Hz, $J = 1.1$ Hz, 1H), 4.83 (dt, $J = 2.2$ Hz, $J = 1.1$ Hz, 1H), 4.18 – 4.06 (m, 2H), 4.04 – 3.99 (m, 2H), 2.92 (dt, $J = 17.7$ Hz, $J = 2.4$ Hz, 1H), 2.65 (dt, $J = 17.7$ Hz, $J = 1.0$ Hz, 1H), 2.11 (dt, $J = 12.1$ Hz, $J = 9.1$ Hz, 1H), 1.79 (ddd, $J = 12.1$ Hz, $J = 5.4$ Hz, $J = 4.1$ Hz, 1H), 1.72 (ddd, $J = 15.0$ Hz, $J = 11.2$ Hz, $J = 4.3$ Hz, 1H), 1.51 (ddd, $J = 13.6$ Hz, $J = 3.9$ Hz, $J = 2.6$ Hz, 1H), 1.26 (s, 3H), 1.19 (s, 3H), 1.05 (s, 3H), 1.01 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 152.5, 151.8, 117.3, 105.3, 99.4, 66.2, 64.0, 43.6, 41.3, 40.4, 36.7, 30.7, 30.5, 29.4, 28.4, 25.2. HRMS (ESI-TOF) m/z : $[M+H]^+$ Calcd for $C_{16}H_{25}O_2^+$ 249.1849; Found 249.1851.

8. Determination of relative stereochemistry of acetonides and triols

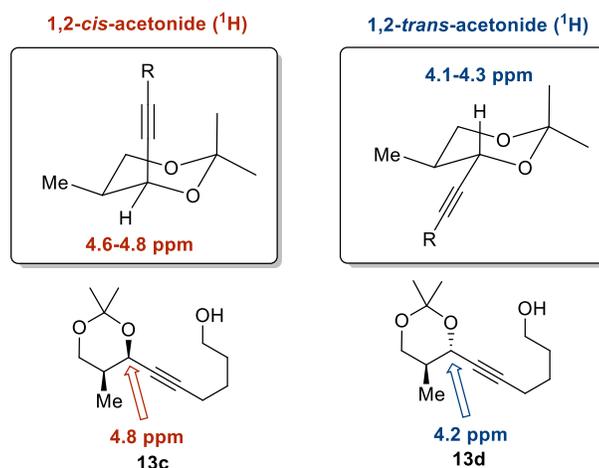
Regarding the relative stereochemistries of the diastereomeric pair of acetonides **13a/13b** and **13c/13d**, it is important to mention that these were directly determined, while stereochemistry of the precursors were indirectly determined, based on the assignment of the acetonides. Thus, relative stereochemistries of the acetonides were extrapolated to the triols.

According to Rychnovsky and coworkers,⁶ 1,3-*cis*-acetonides and 1,3-*trans*-acetonides present different ¹³C NMR chemical shifts for the 2 diastereotopic *gem*-dimethyl groups of the acetonide. 1,3-*cis*-acetonides are most likely in the most stable chair conformation, the chemical shifts of the axial and equatorial methyl groups are different, with values around 20 and 30 ppm, respectively. Differently, 1,3-*trans*-acetonides can be distorted to a twisted boat conformation so that the methyl groups become pseudo axial and pseudo equatorial, and both methyl groups should have chemical shifts closer to 25 ppm. The diastereomers **13a** and **13b** were first analyzed,² and in the case of **13a** the signals corresponding to the methyl groups appear at 28.0 and 23.8 ppm, meaning that **13a** has a 1,3-*trans* relative stereochemistry. The signals for **13b** appear at 30.1 and 19.6 ppm, thus **13b** has a 1,3-*cis* relative stereochemistry.



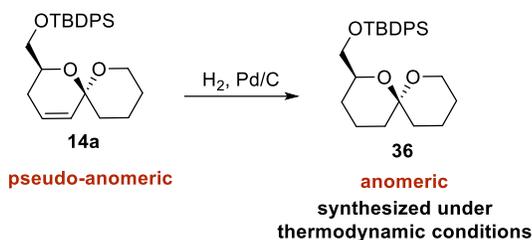
After determining the relative stereochemistry of **13a** and **13b**, the relative stereochemistry of the compounds **13c** and **13d** were assigned by analyzing the ¹H NMR chemical shift of the

propargylic proton. Considering the chair conformation as the most stable one, it is expected that axial protons should appear in more shielded regions. For **13c** the propargylic proton appears at 4.8 ppm, and in **13d** at 4.2 ppm.

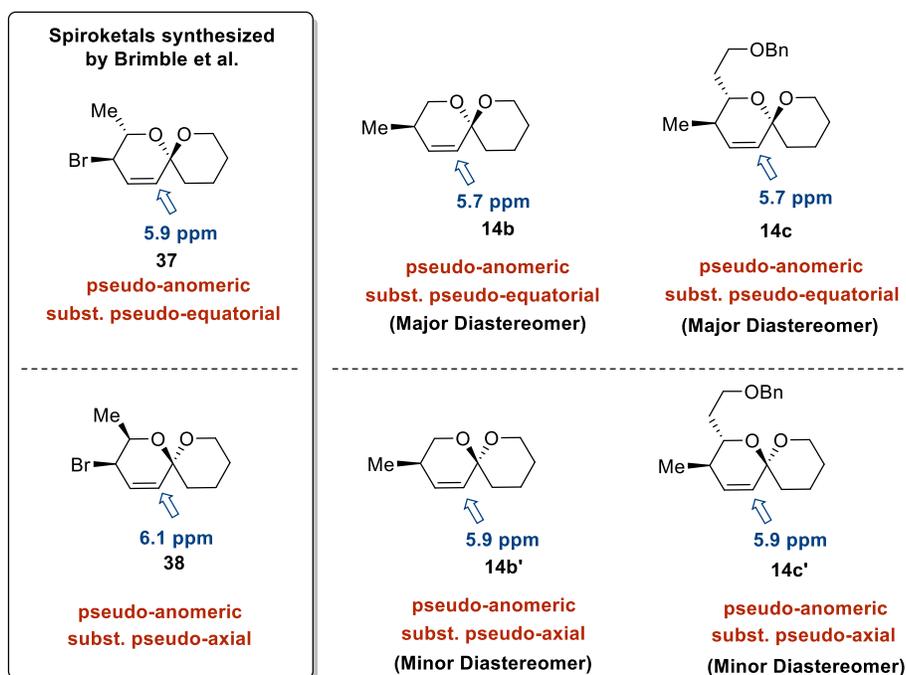


9. Determination of relative stereochemistry of the spiroketals

For the assignment of the relative stereochemistries of the spiroketals, it is important to note that all major diastereomers formed in the gold-catalyzed reactions are thermodynamic spiroketals. In other words, the major diastereomers synthesized in this project are pseudoanomeric spiroketals containing the maximum number of substituents in the pseudoequatorial position. Previously, it was demonstrated that compound **14a** could be hydrogenated to form the anomeric saturated spiroketal **36**,^{2,7} which was synthesized under thermodynamic conditions. As a consequence, the stereochemistry at the spirocarbon could easily be extrapolated, since **36** has a doubly anomeric spirocarbon, and the substituent in the equatorial position.



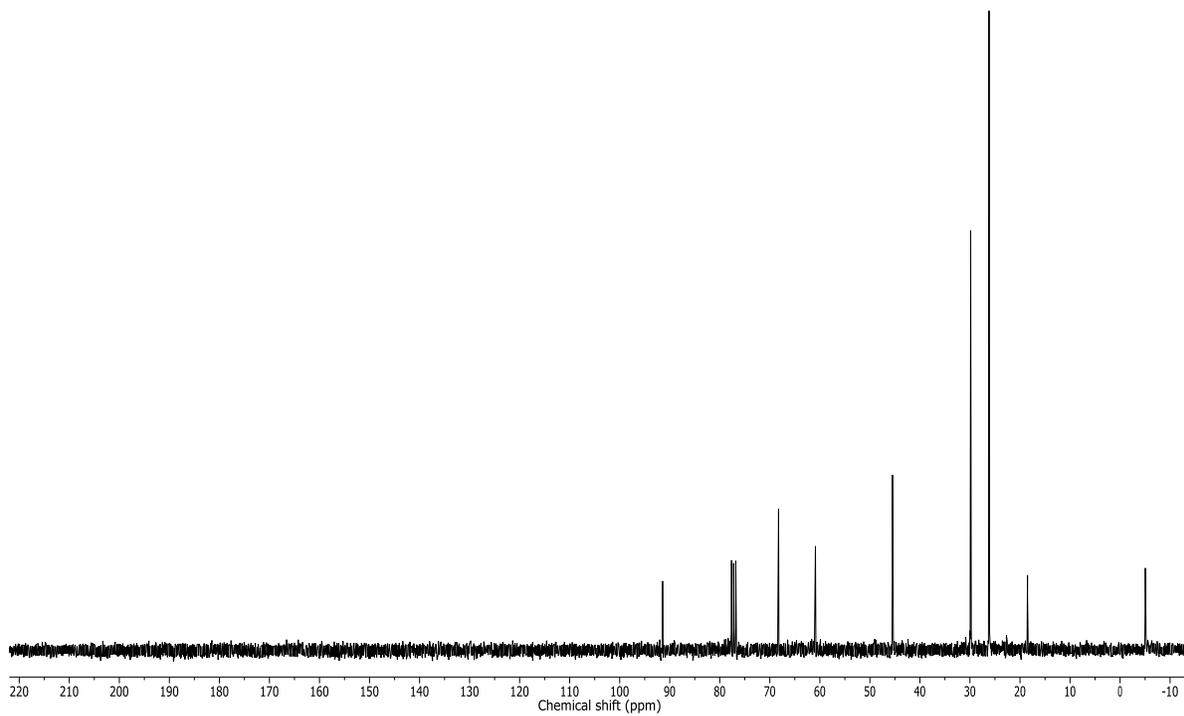
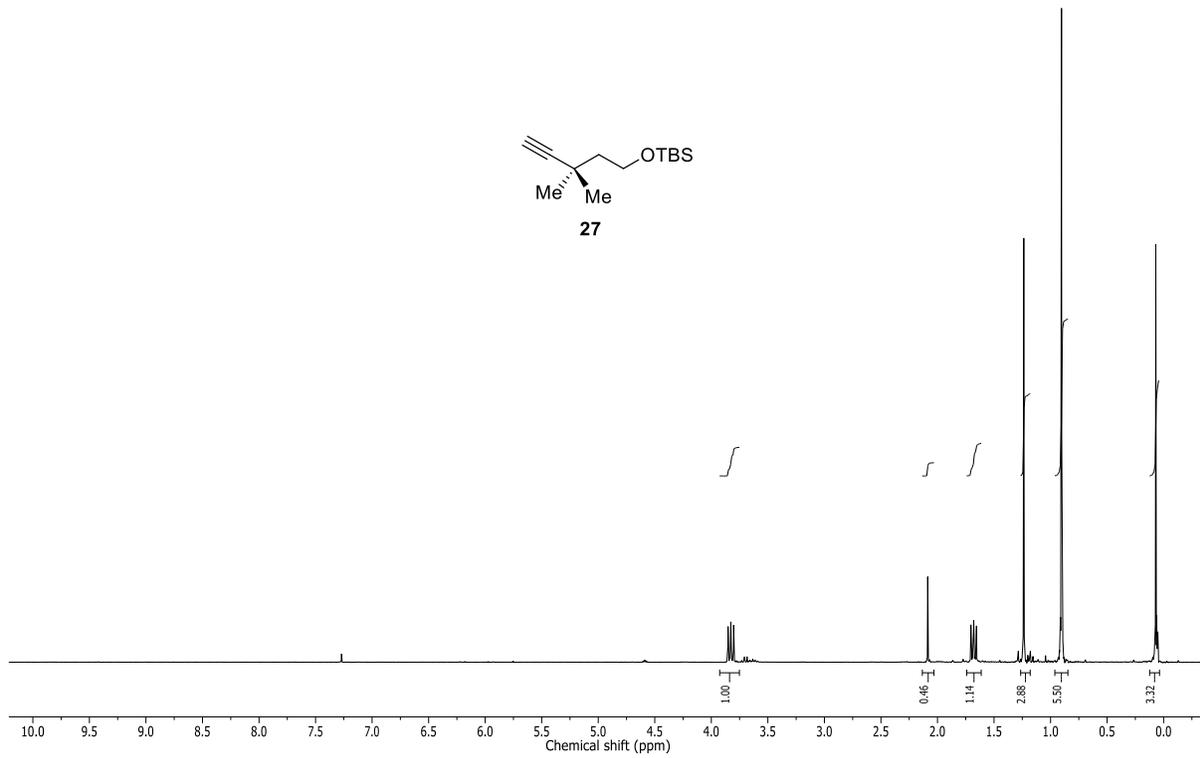
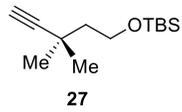
The stereochemistry of the other spiroketals were assigned by comparison with the spiroketal **14a**, and with the unsaturated spiroketals **37** and **38** synthesized by Brimble and coworkers.⁸ In this report, the chemical shifts of the olefinic protons (in the α -position with relation to the spirocarbon) for the diastereomers **37** and **38** were 5.9 and 6.1 ppm, respectively. A direct comparison with other spiroketals synthesized in the project showed that the major spiroketals show, in all cases, the presence of a more shielded signal for the same type of proton, in comparison with the minor diastereomer. Note that the major diastereomer **14b** shows, in the ^1H NMR spectrum, a signal at 5.7 ppm, while the minor **14b'** presents a more deshielded signal at 5.9 ppm. The same occurs with the pair of diastereomers **14c** and **14c'**.

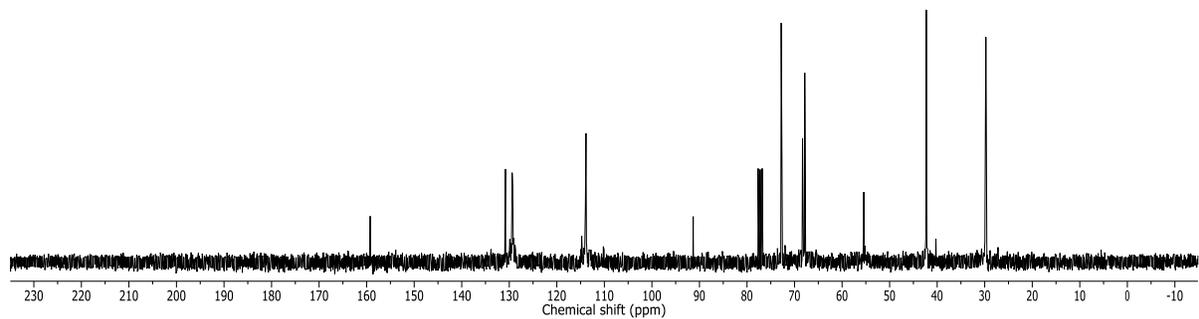
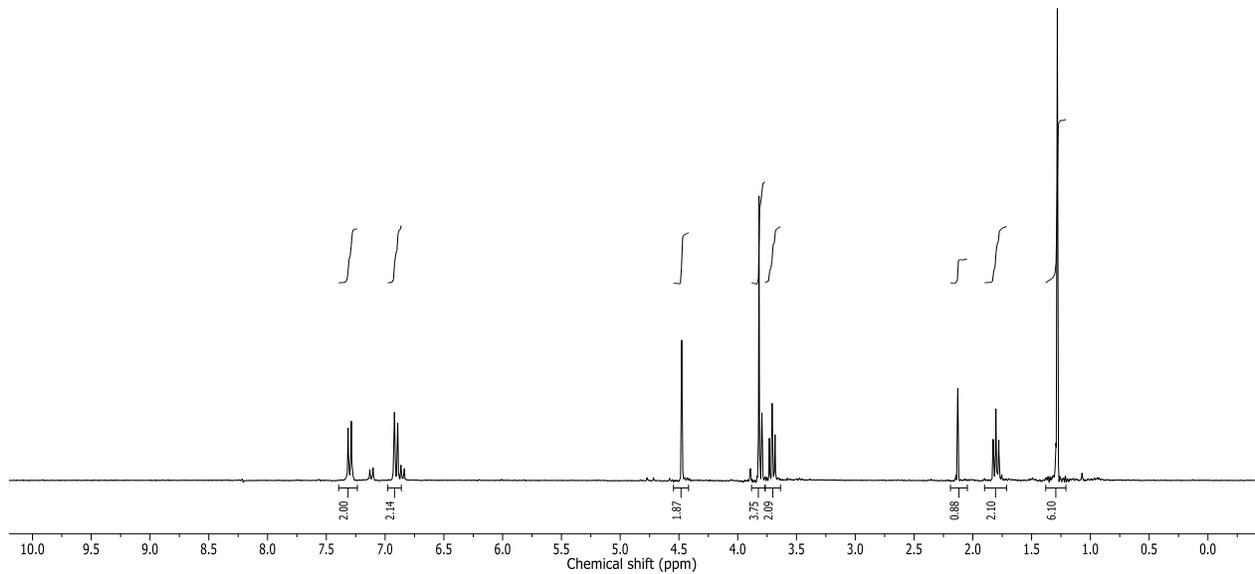
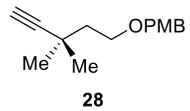


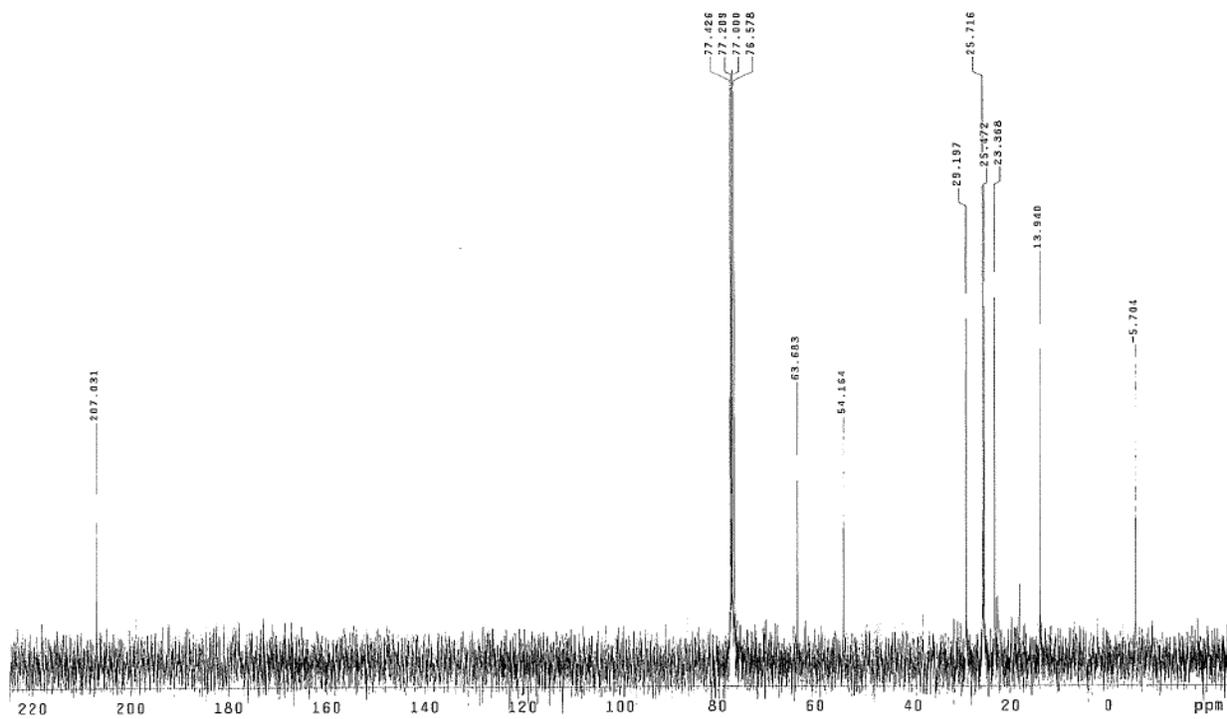
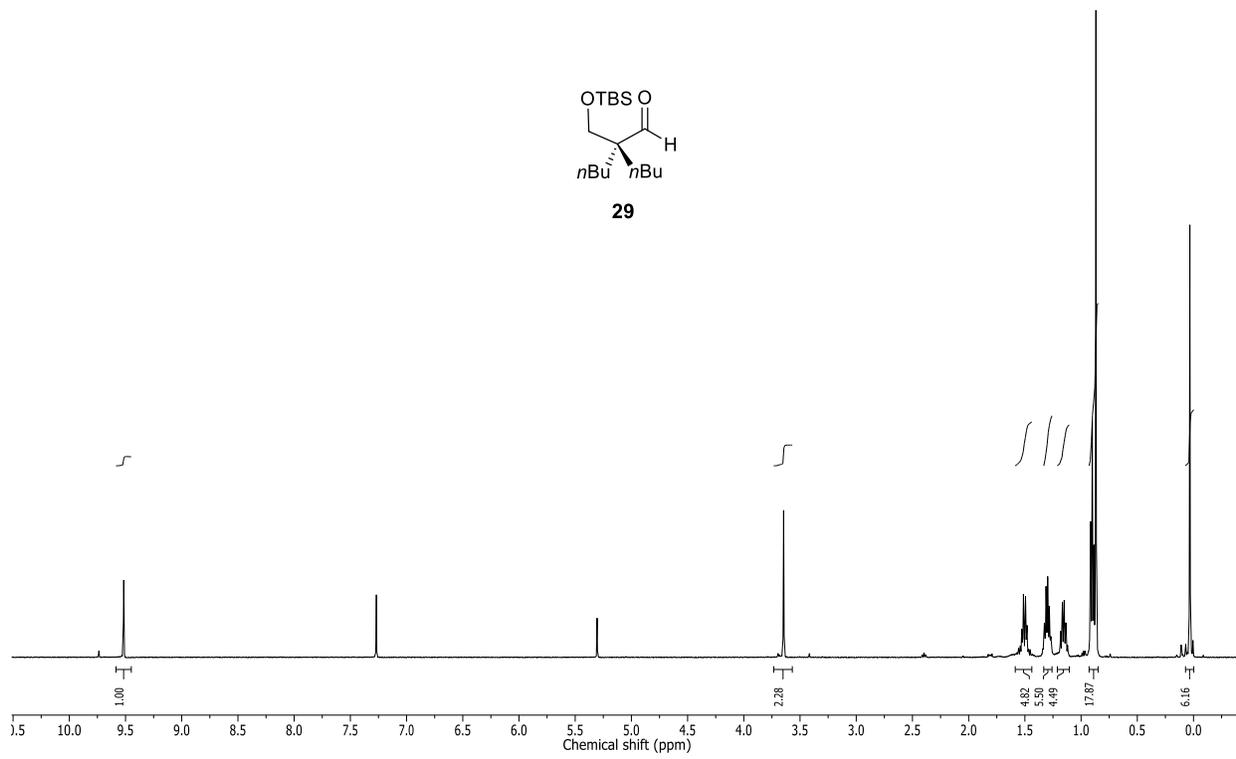
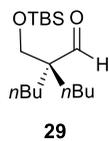
10. References

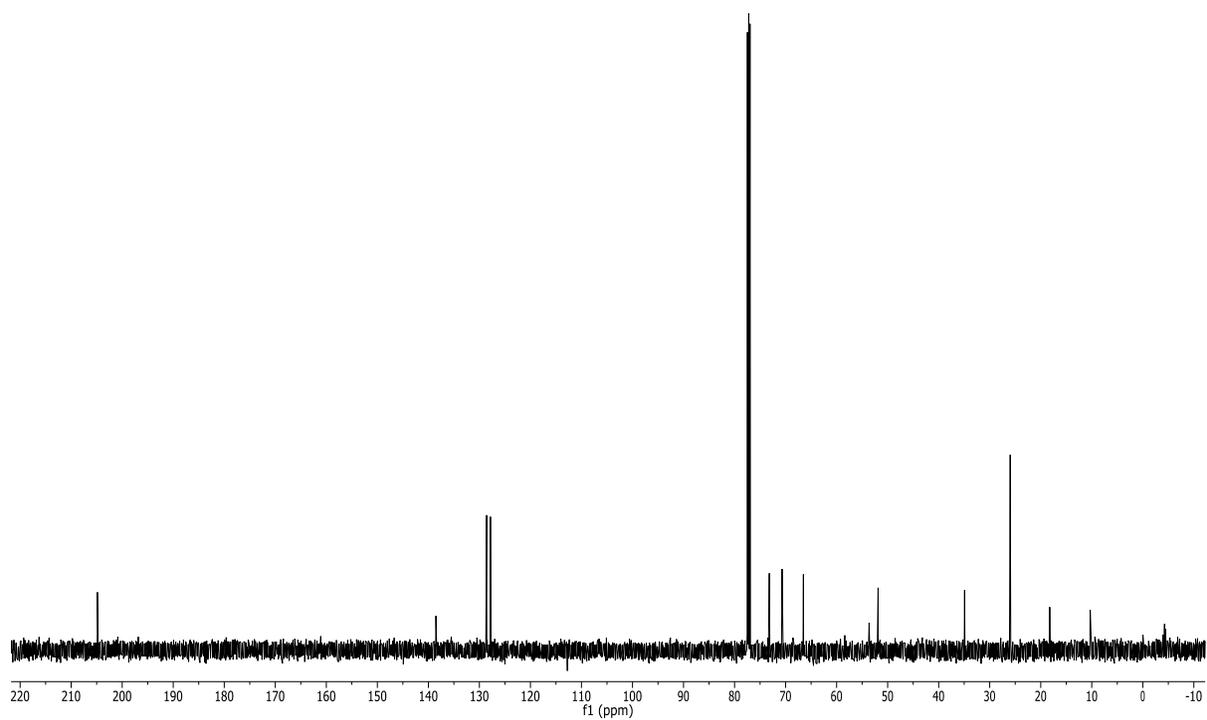
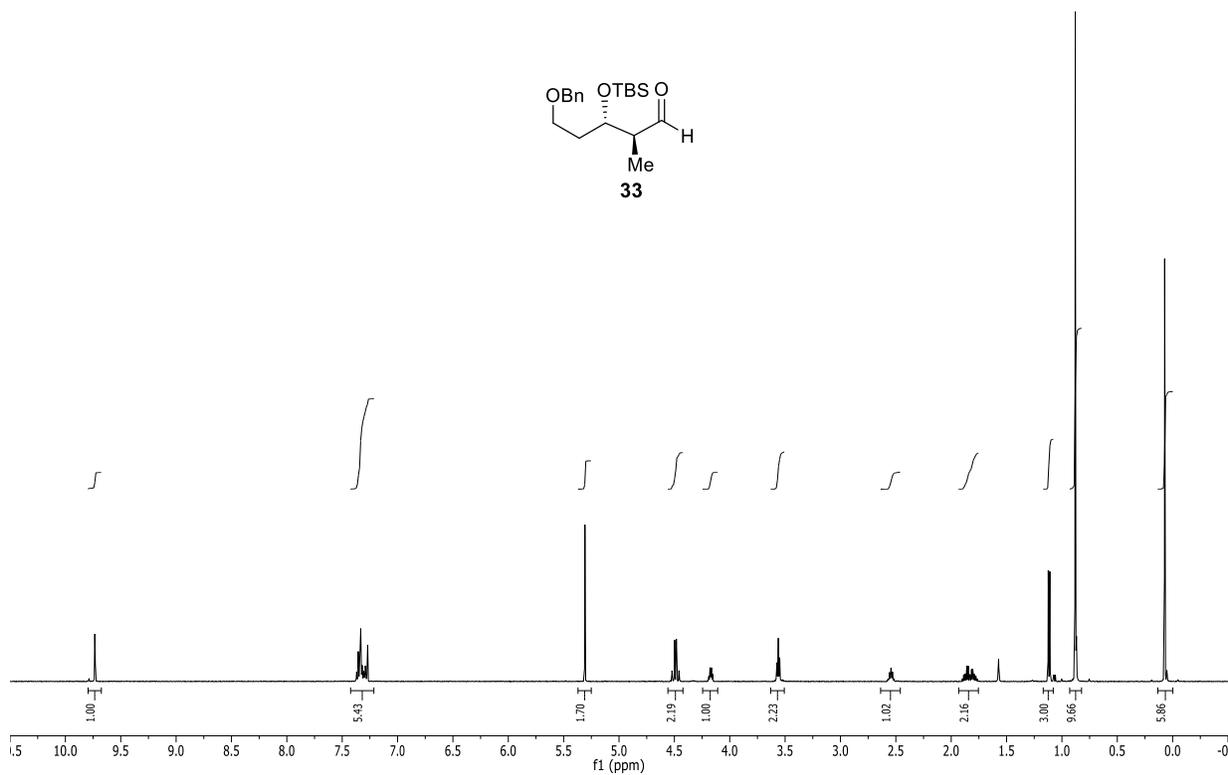
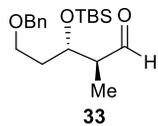
- 1) Guay, B.; Deslongchamps, P. *J. Org. Chem.* **2003**, *68*, 6140-6148.
- 2) Aponick, A.; Li, C. -Y.; Palmes, J. A. *Org. Lett.* **2009**, *11*, 121-124.
- 3) Rank, E.; Brückner, R. *Eur. J. Org. Chem.* **1998**, 1045-1053.
- 4) Ferrie, L., Reymond, S., Capdevielle, P., Cossy, J. *Org Lett.* **2007**, *9*, 2461-2464.
- 5) Gao, X.; Han, H.; Krische, M. J. *J. Am. Chem. Soc.* **2011**, *133*, 12795-12800.
- 6) Rychnovsky, S. D.; Rogers, B.; Yang, G. *J. Org. Chem.* **1993**, *58*, 3511-3515.
- 7) Conway, J. C.; Quayle, P.; Regan, A. C.; Urch, C. J. *Tetrahedron* **2005**, *61*, 11910-11923.
- 8) Brimble, M. A.; Edmonds, M. K.; Williams, G. M. *Tetrahedron* **1992**, *48*, 6455-6466.

11. NMR spectra of alkynes and aldehydes

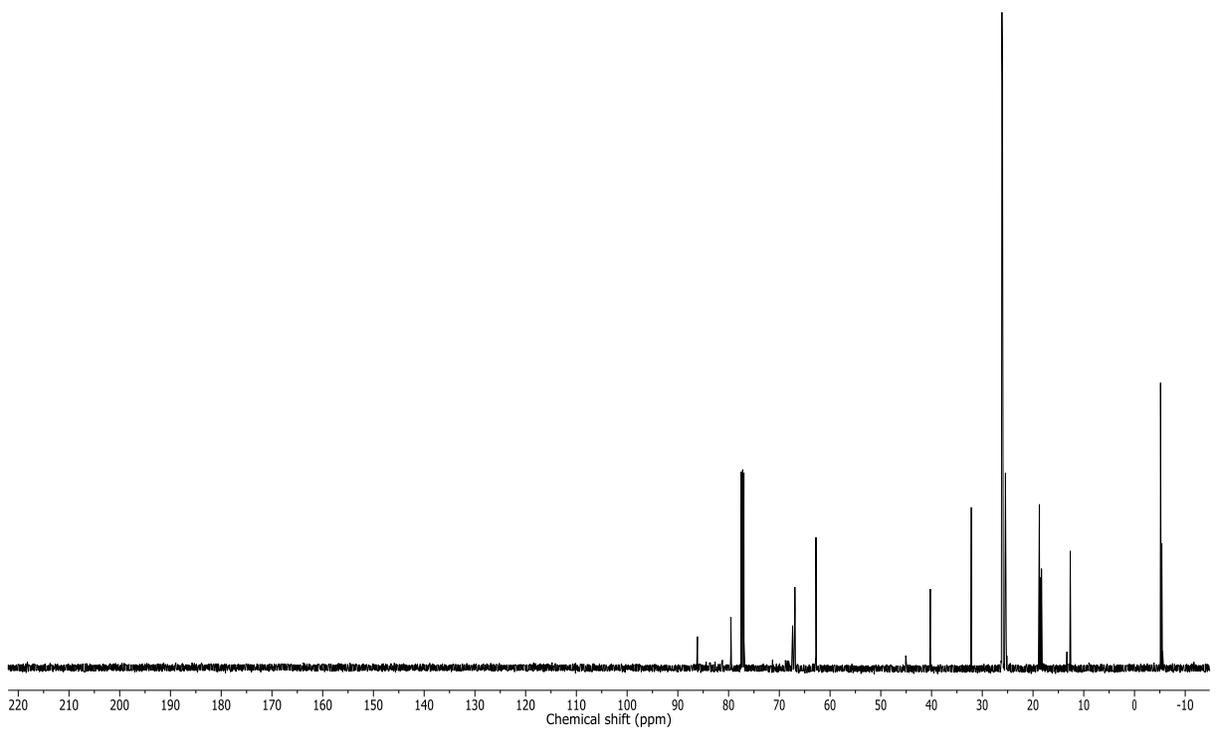
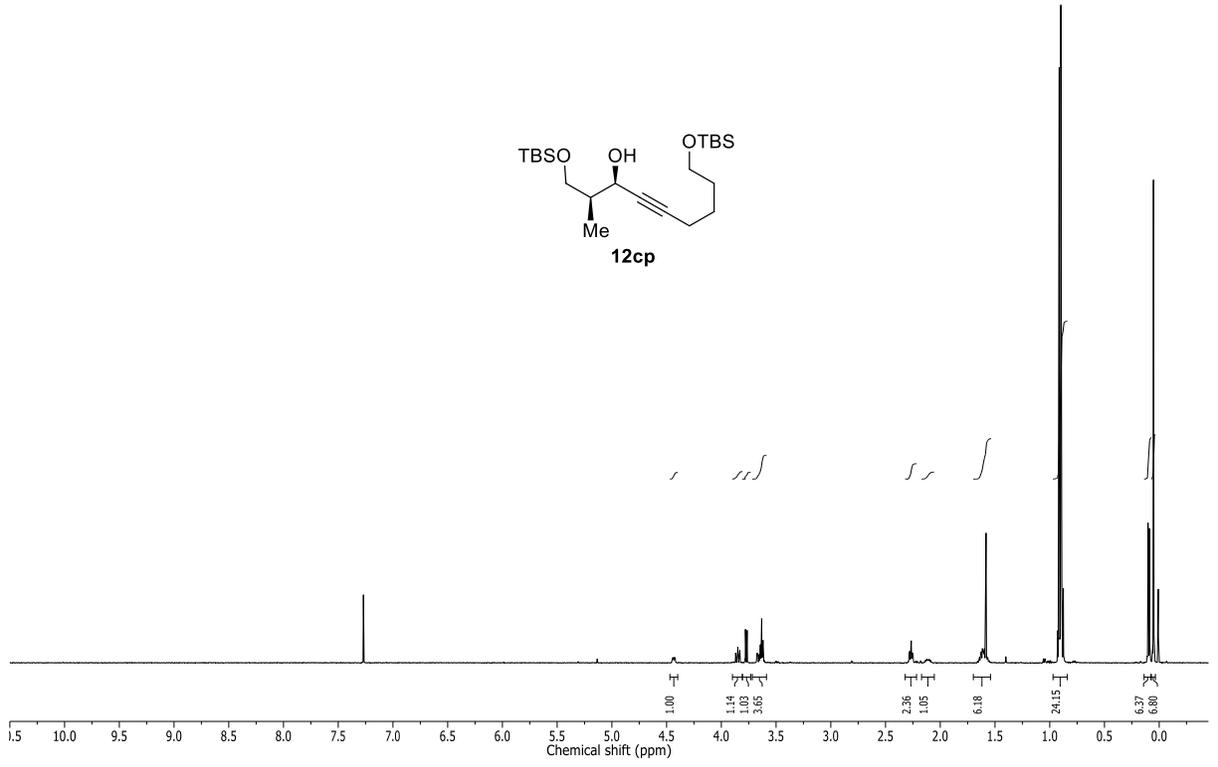


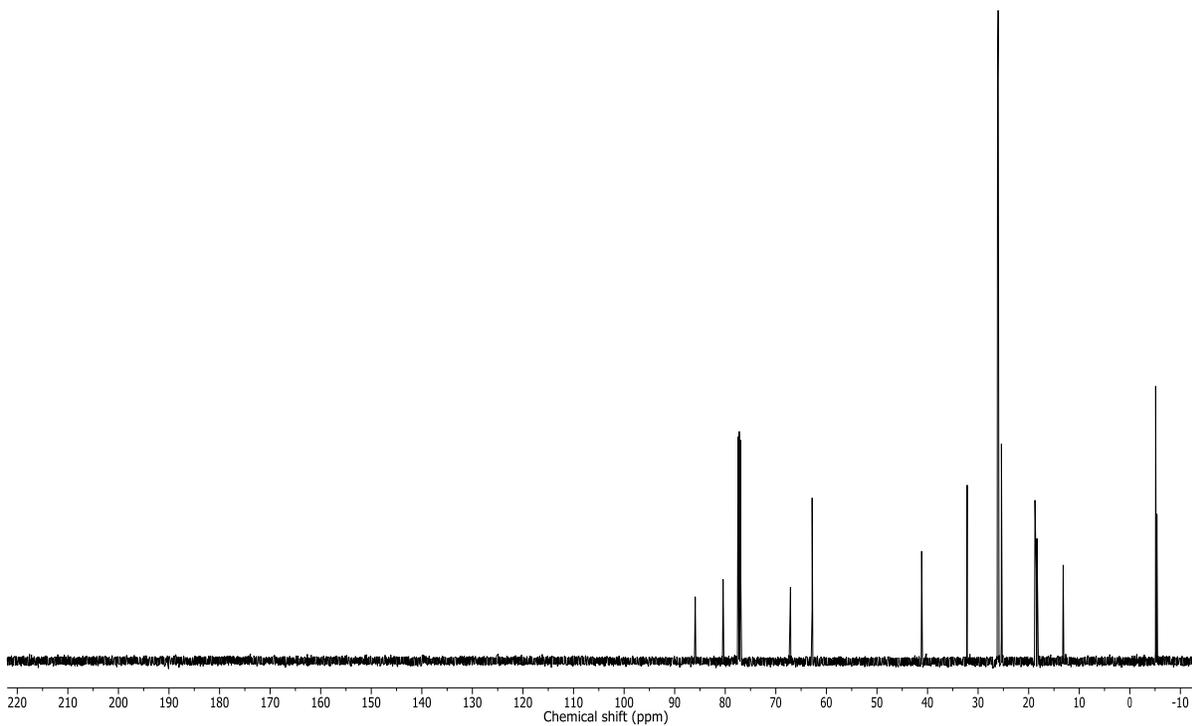
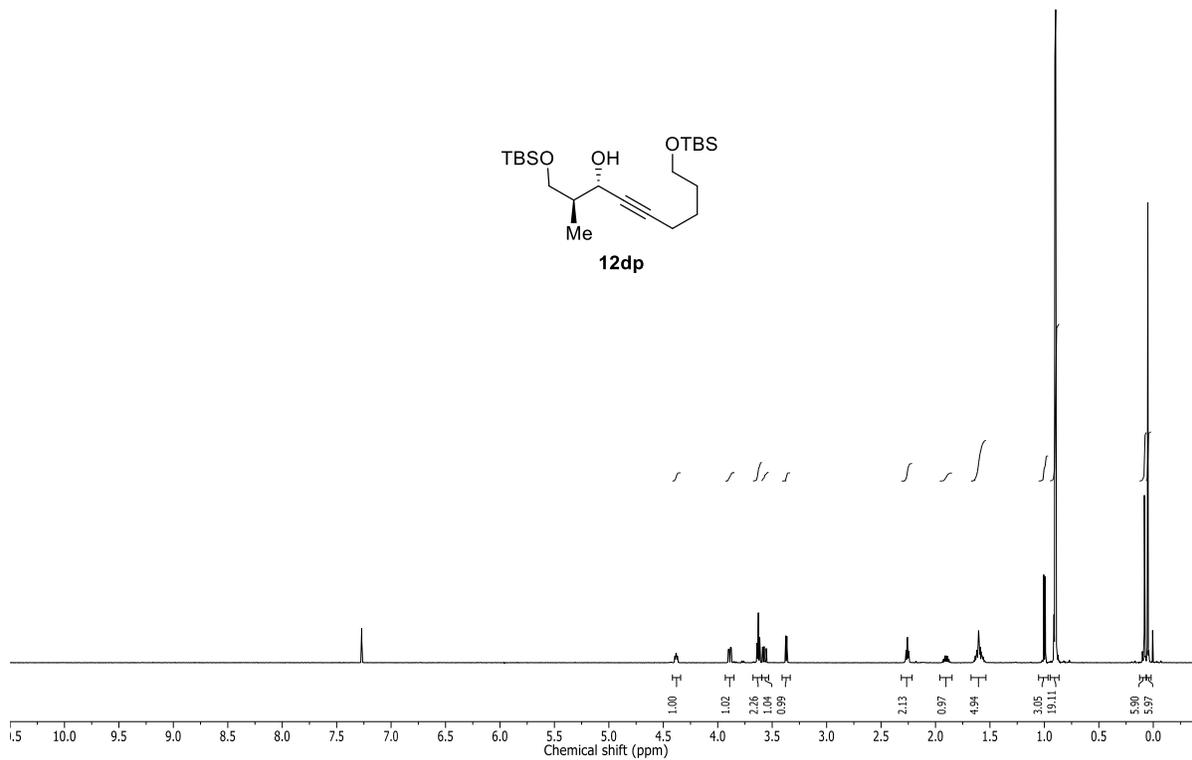
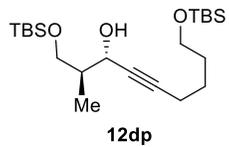


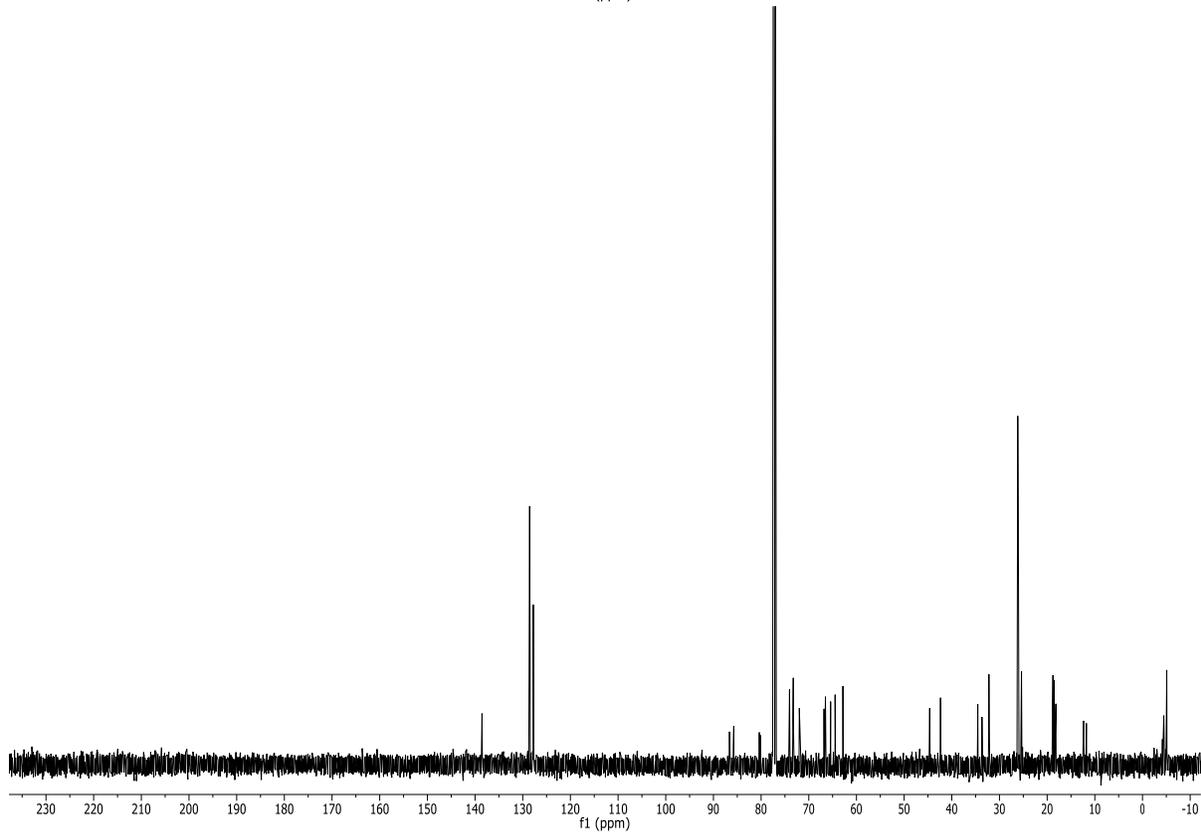
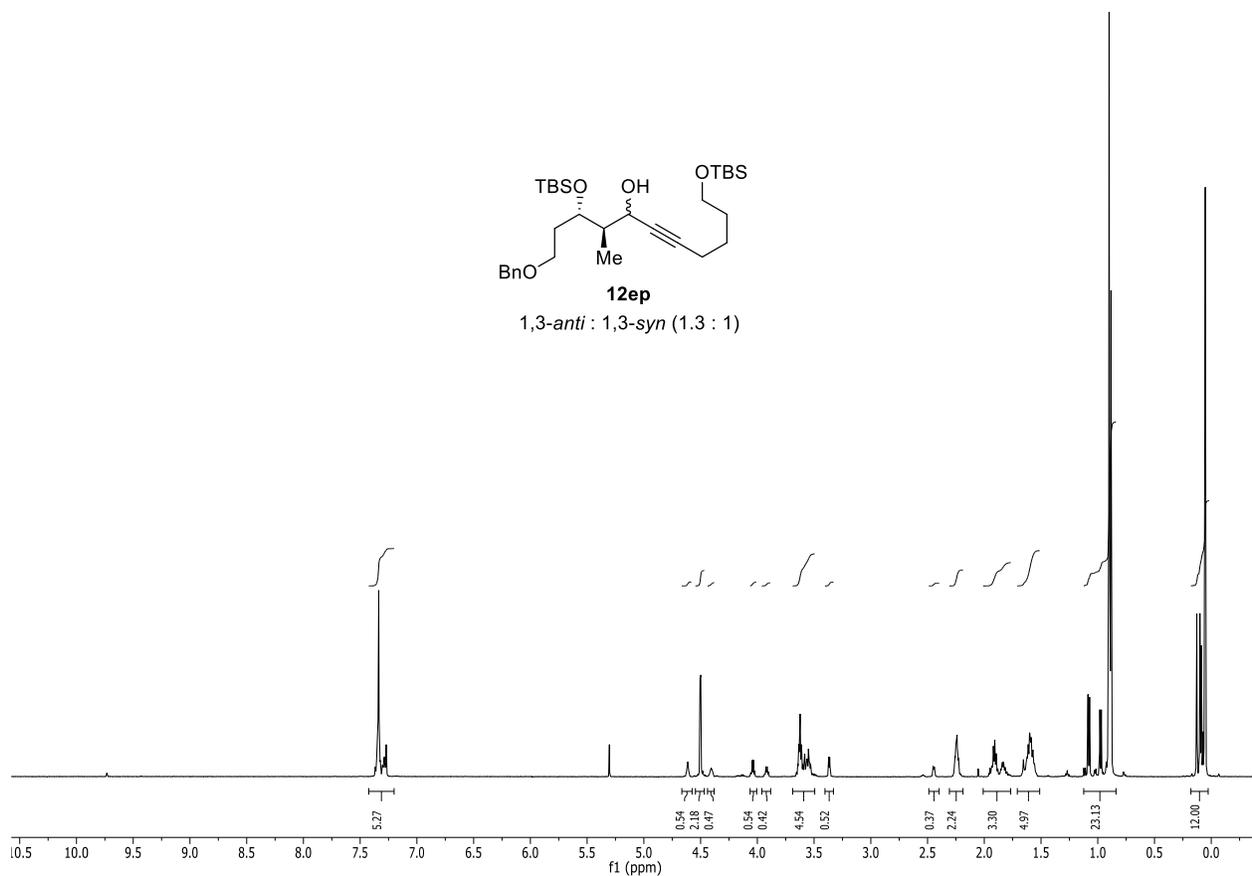
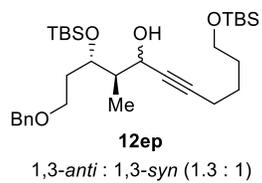




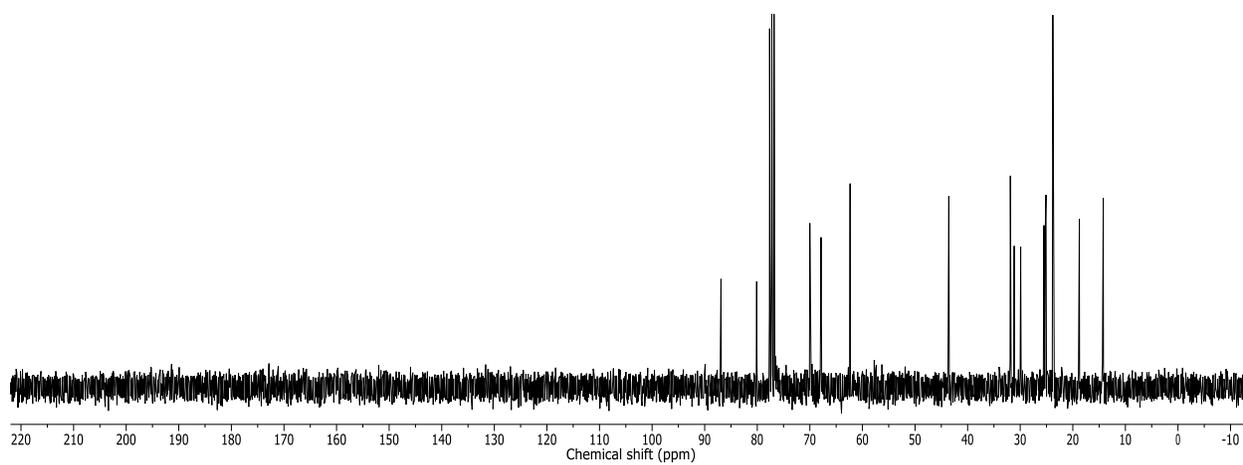
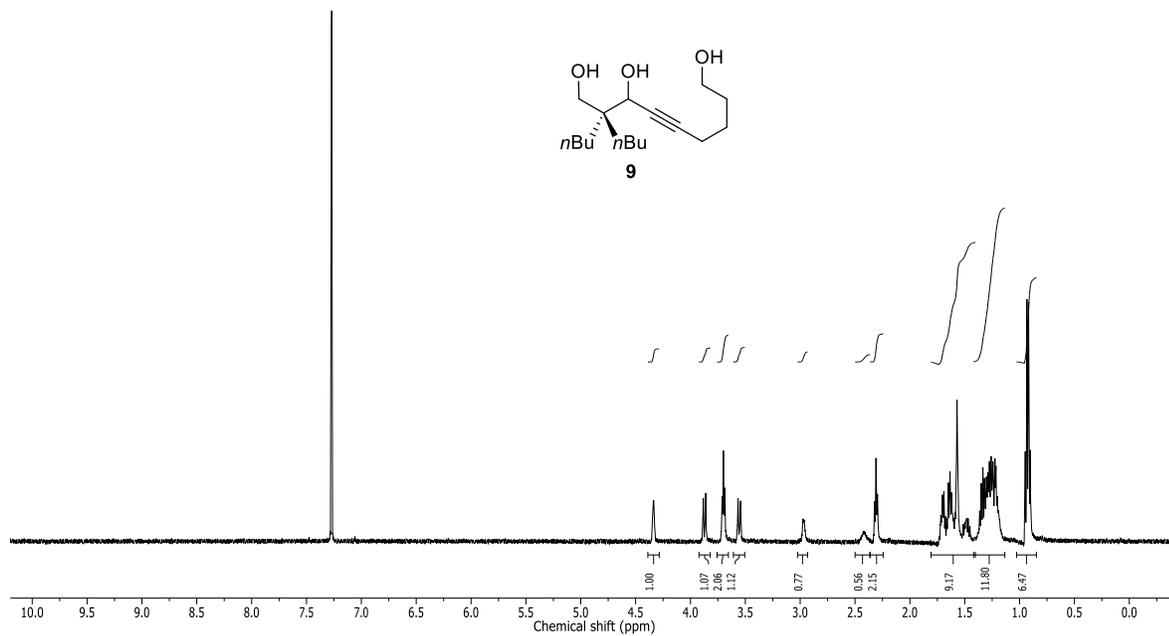
12. NMR spectra of protected triols

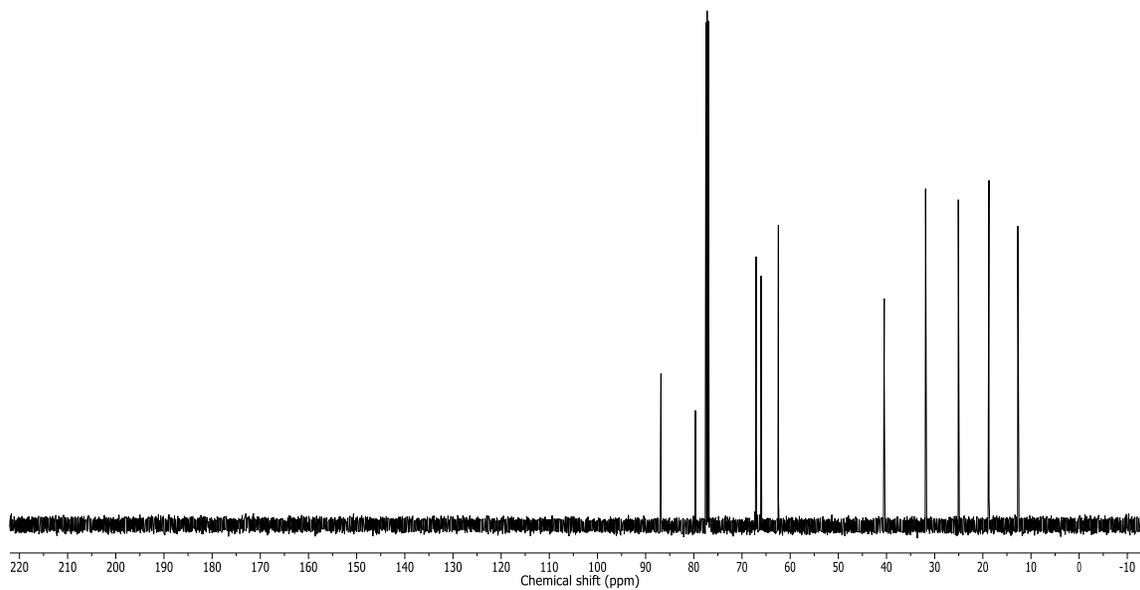
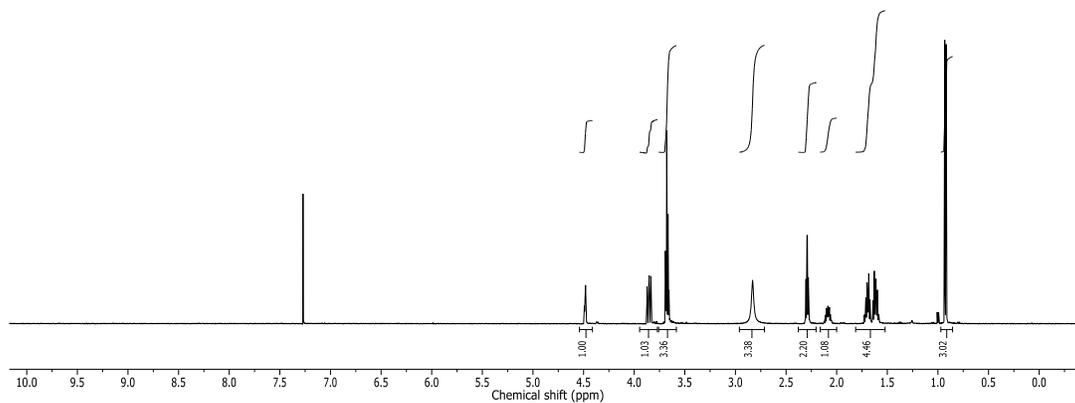
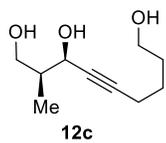


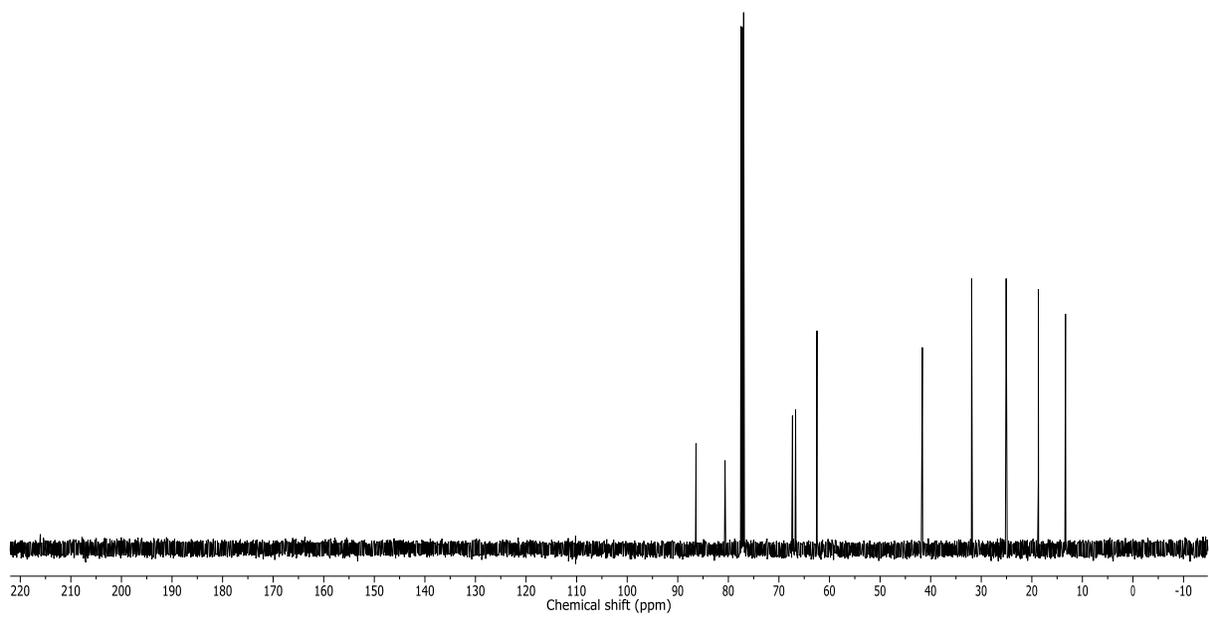
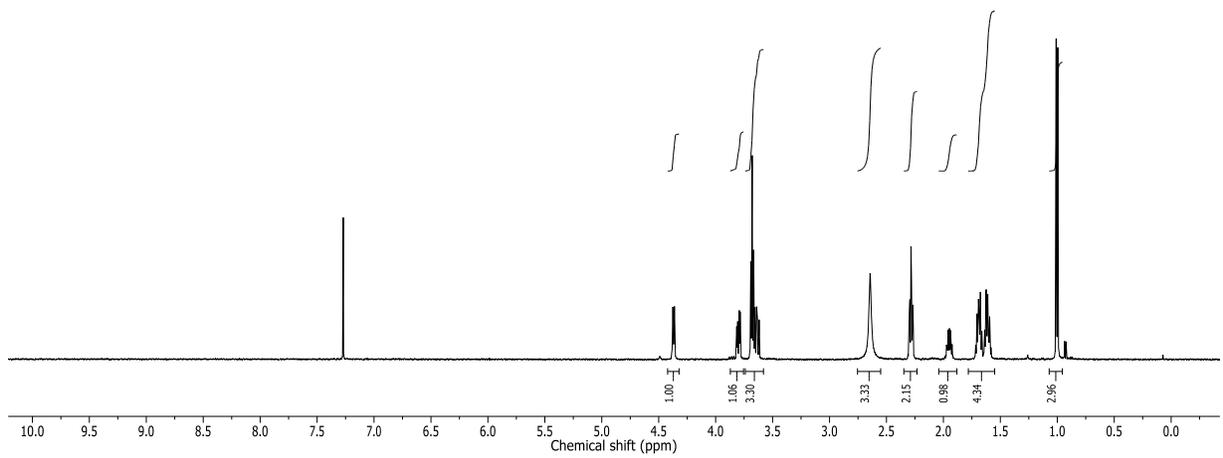
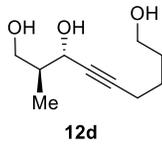


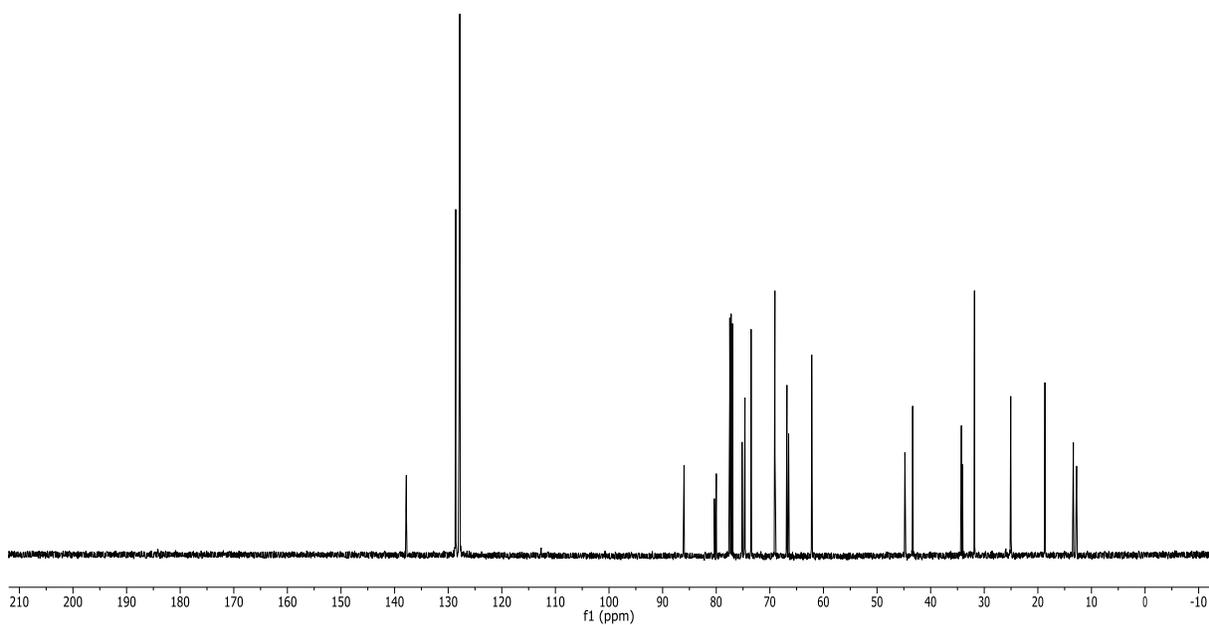
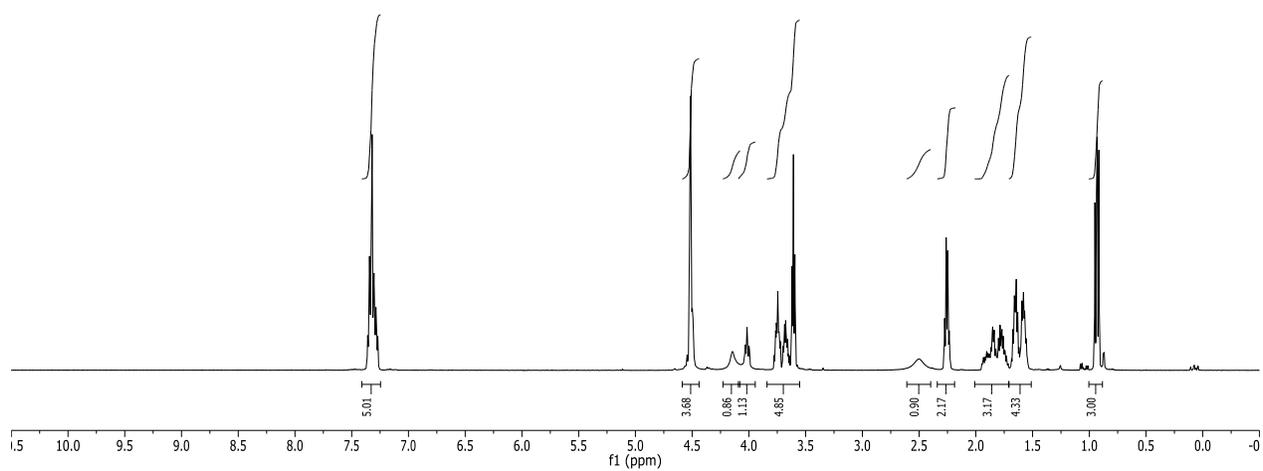
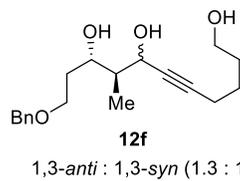


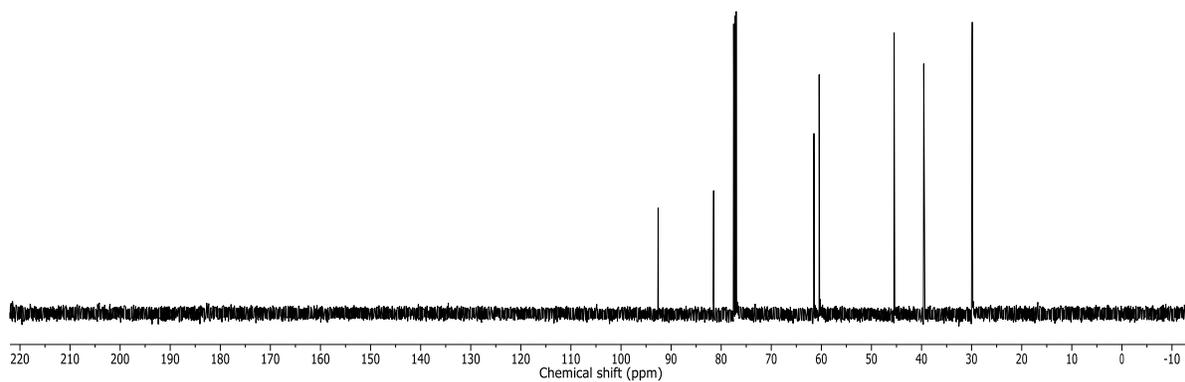
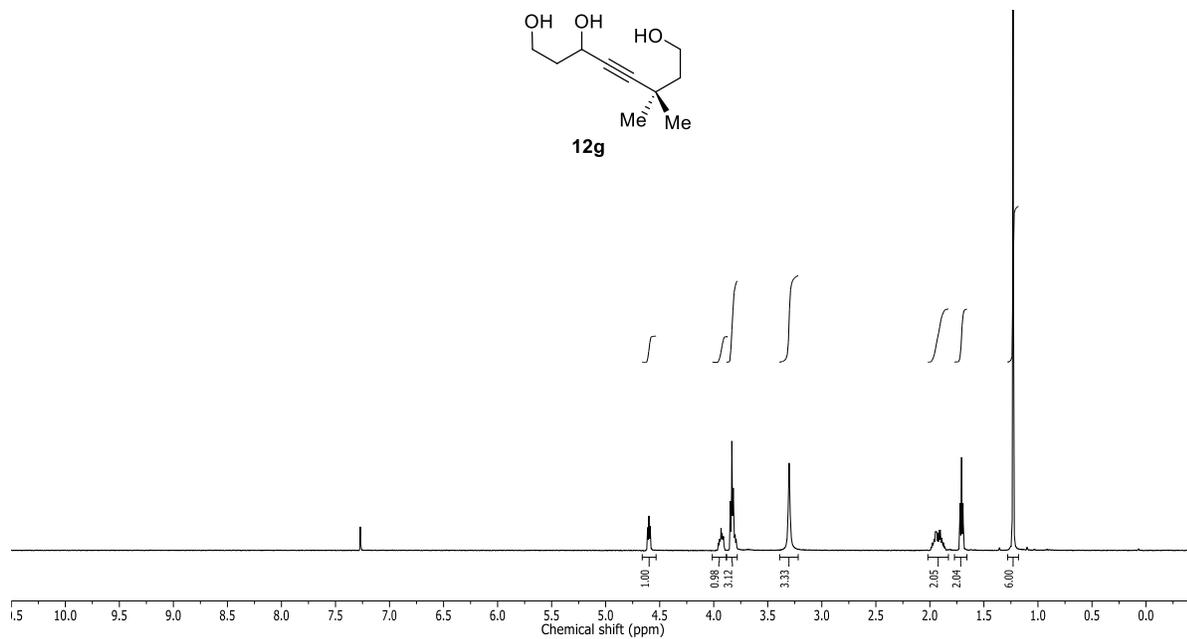
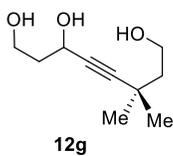
13. NMR spectra of triols



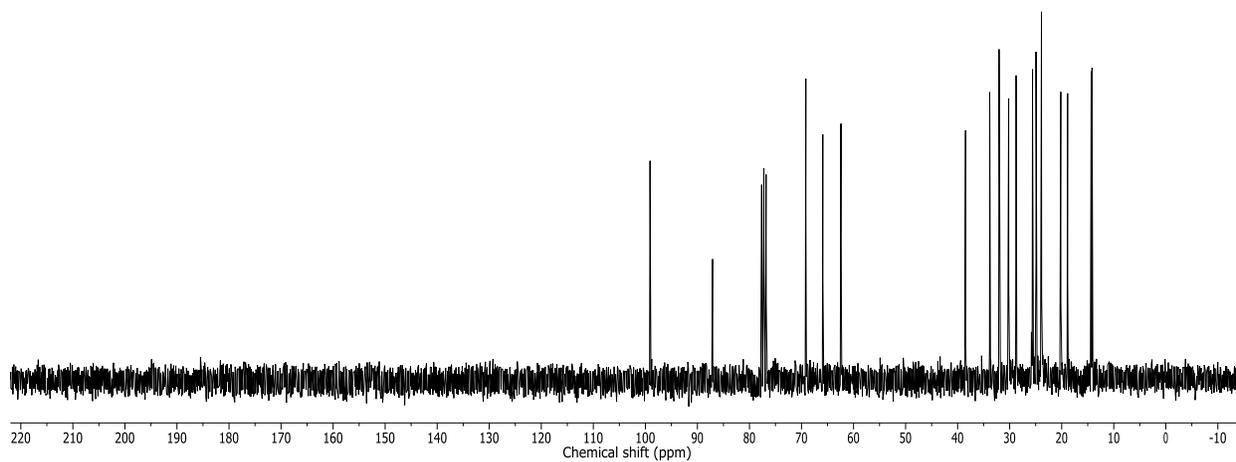
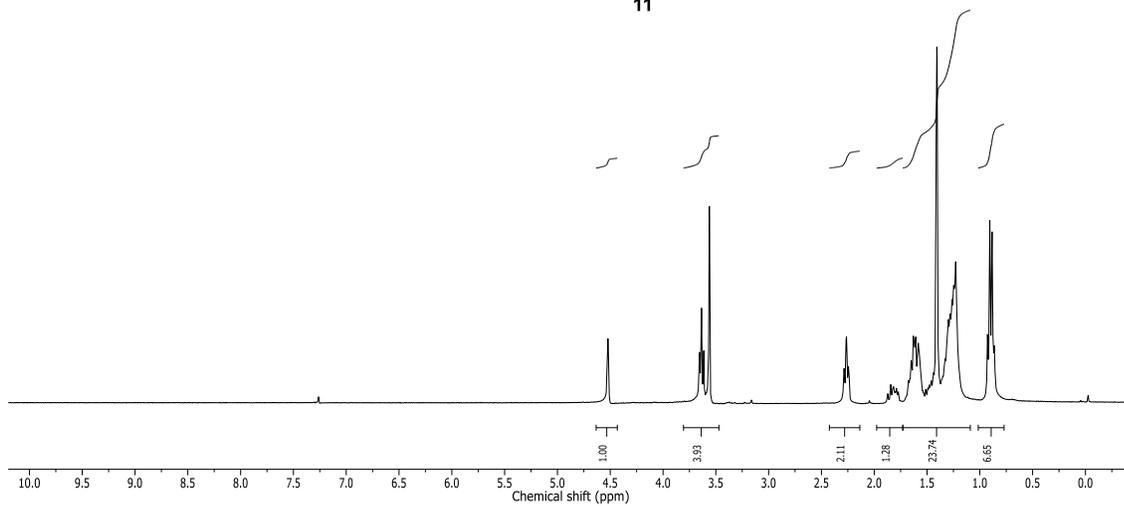
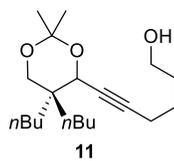


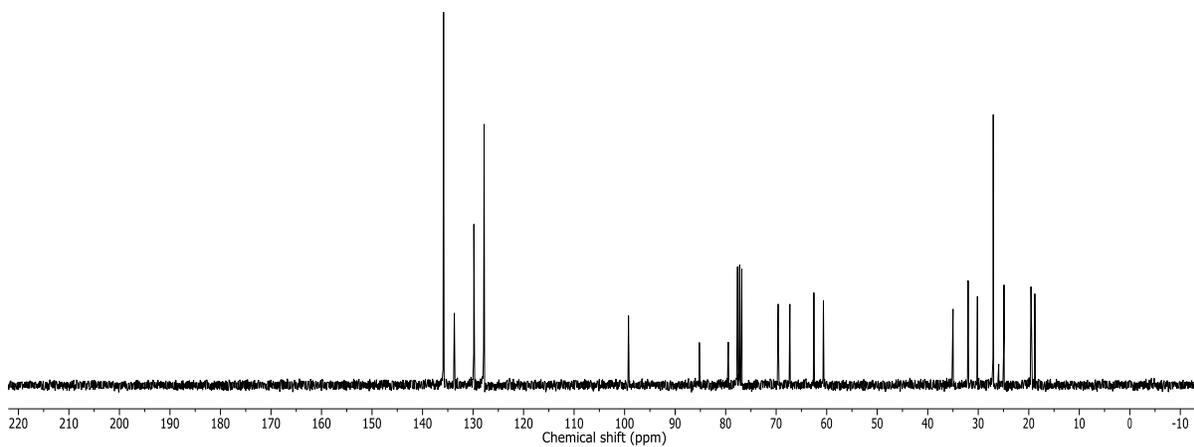
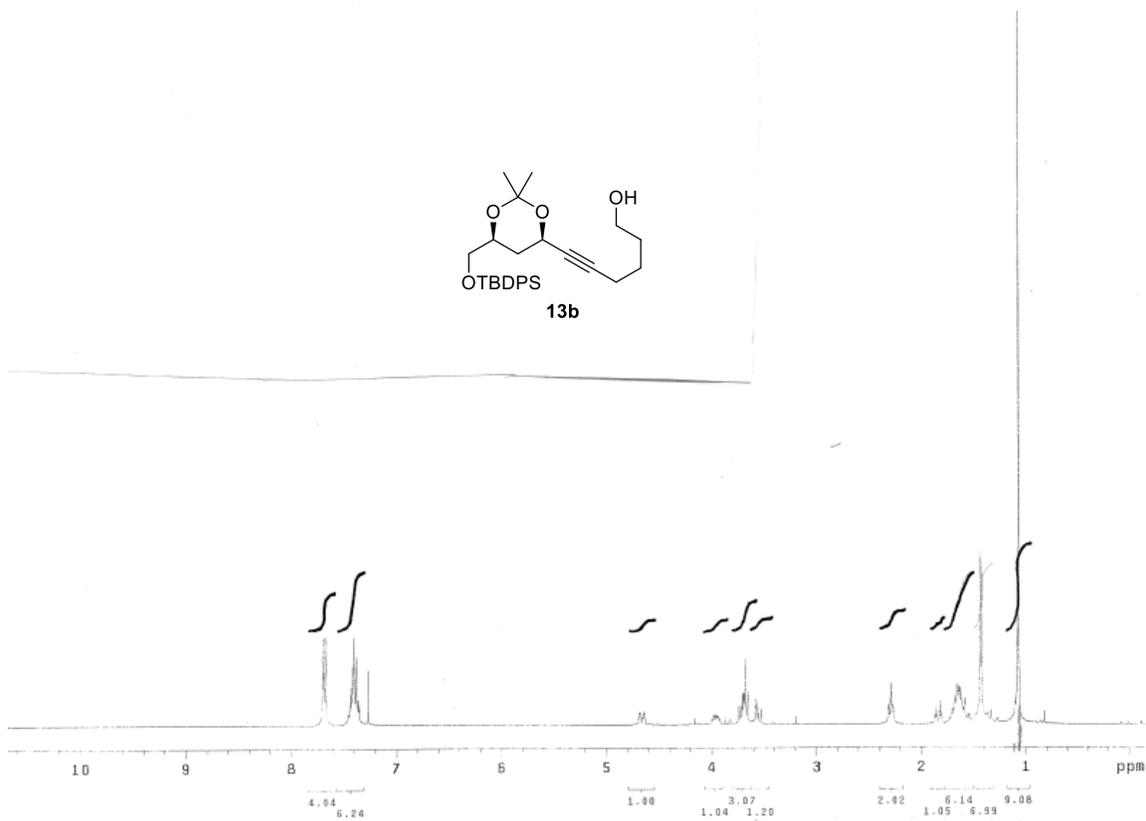
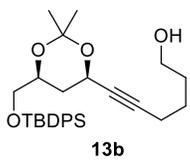


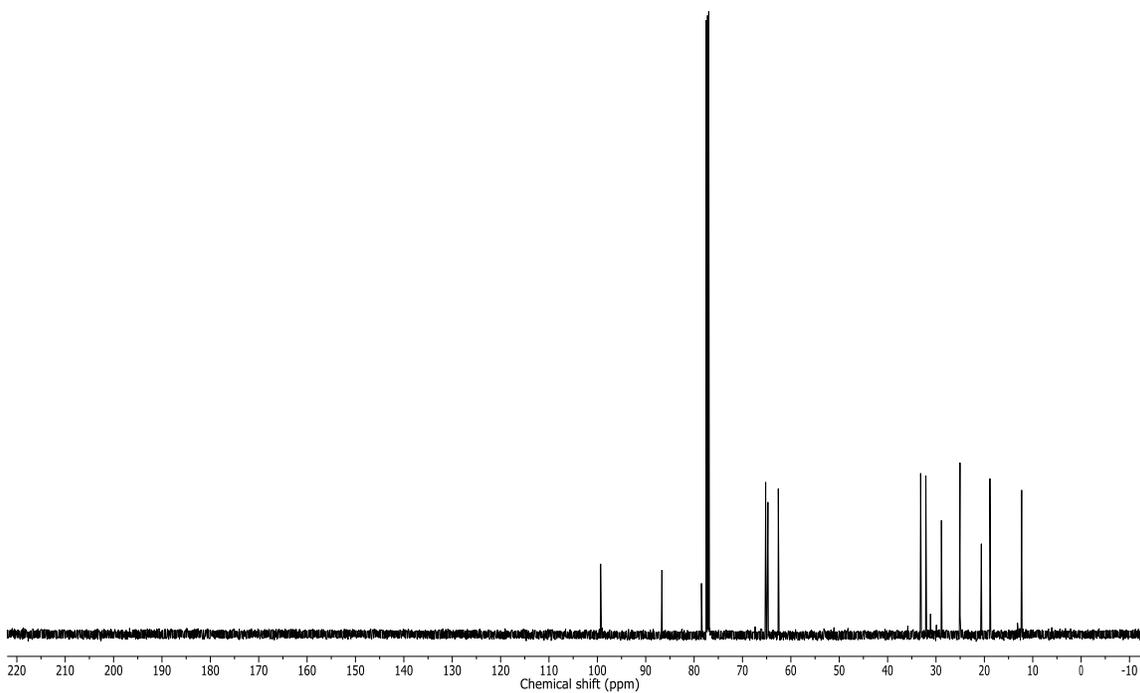
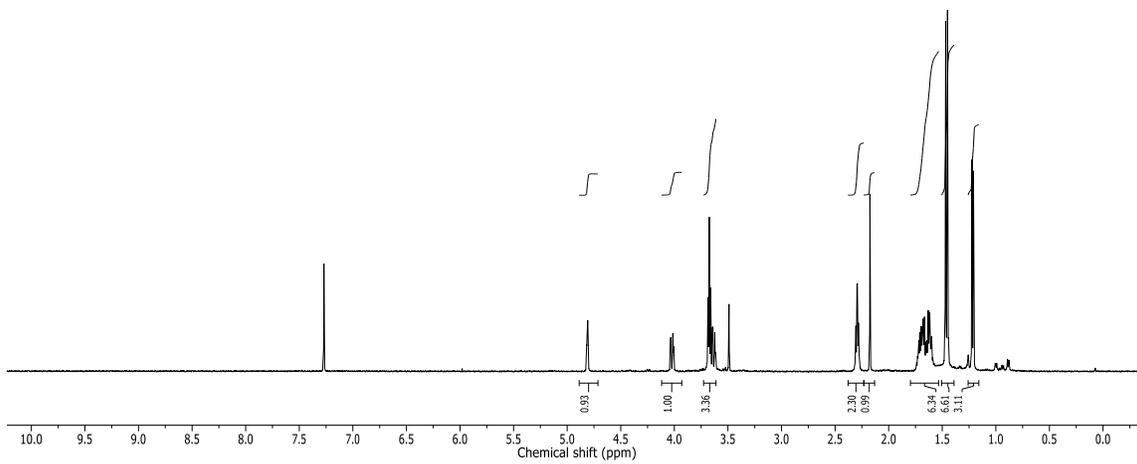
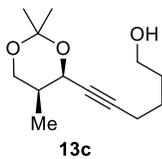


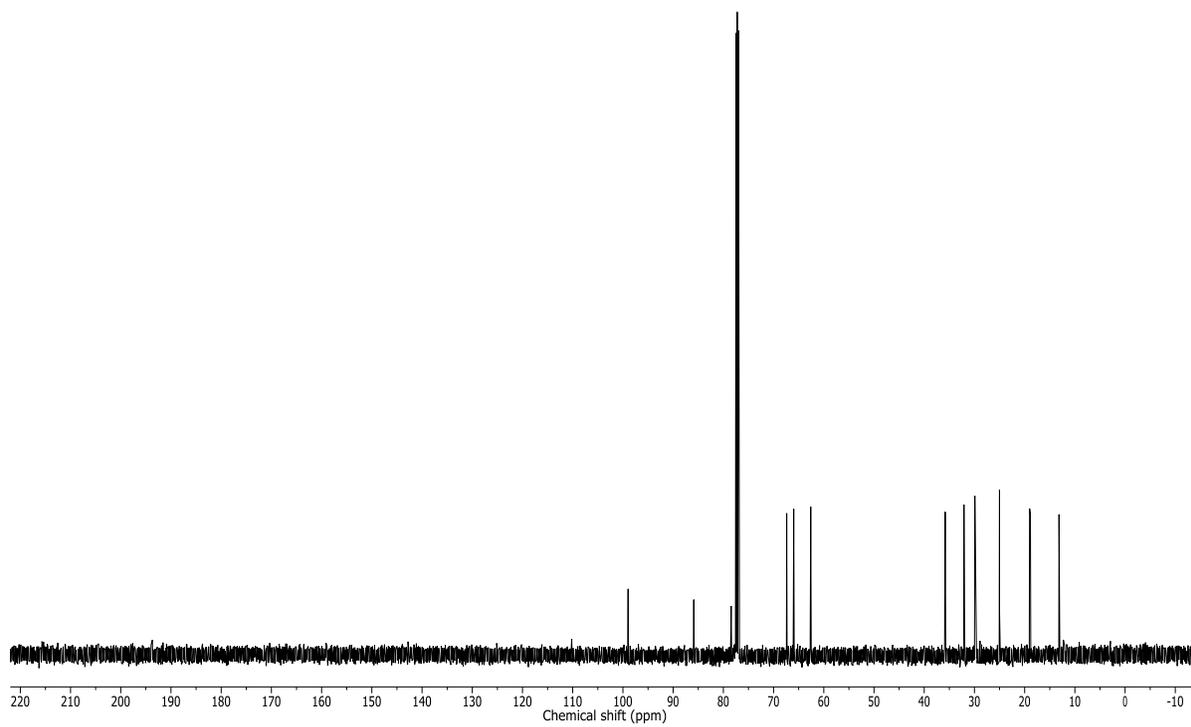
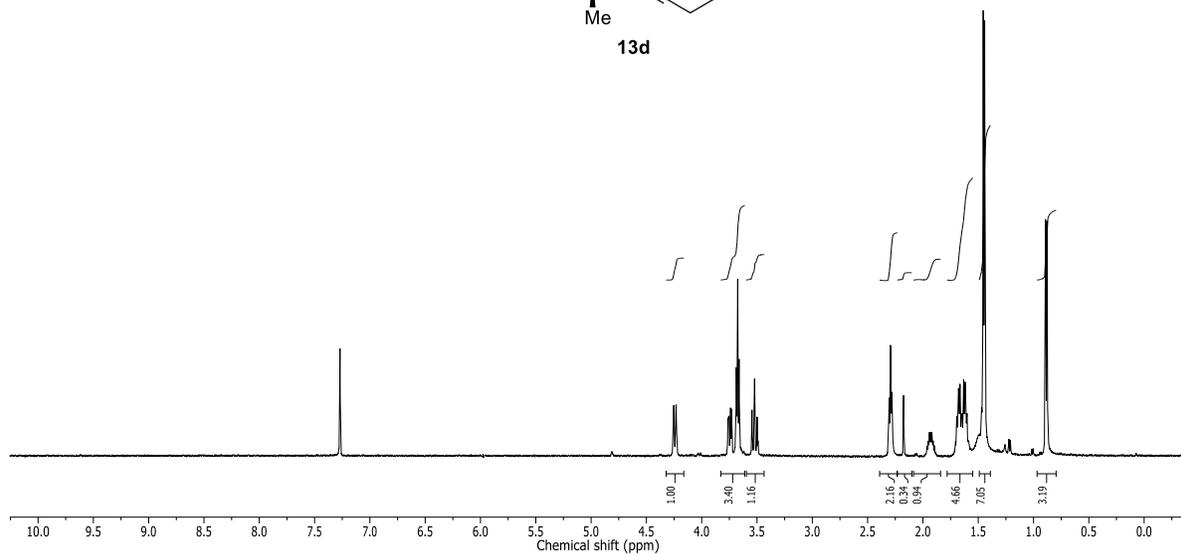
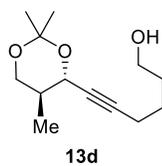


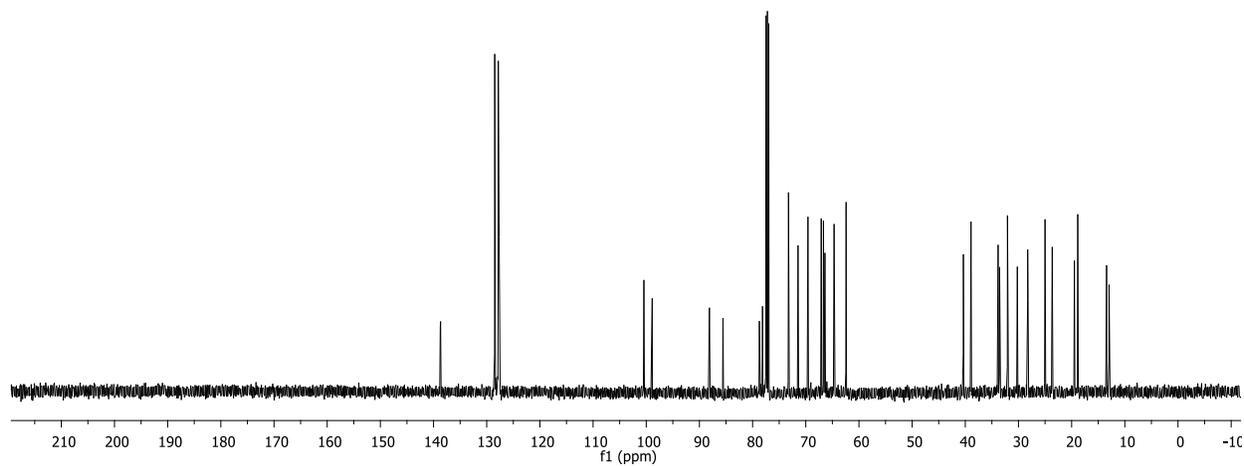
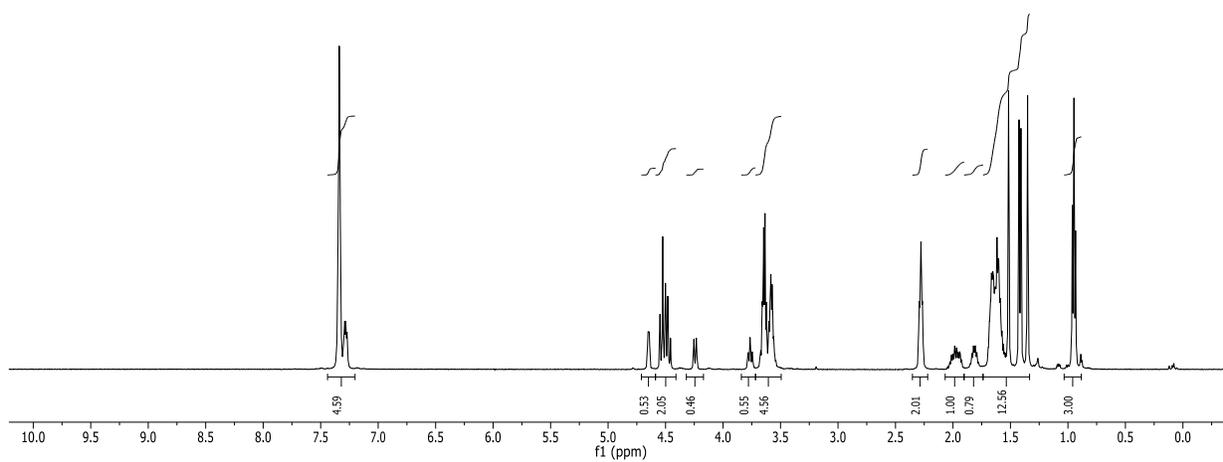
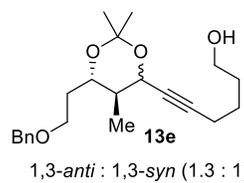
14. NMR spectra of acetonides

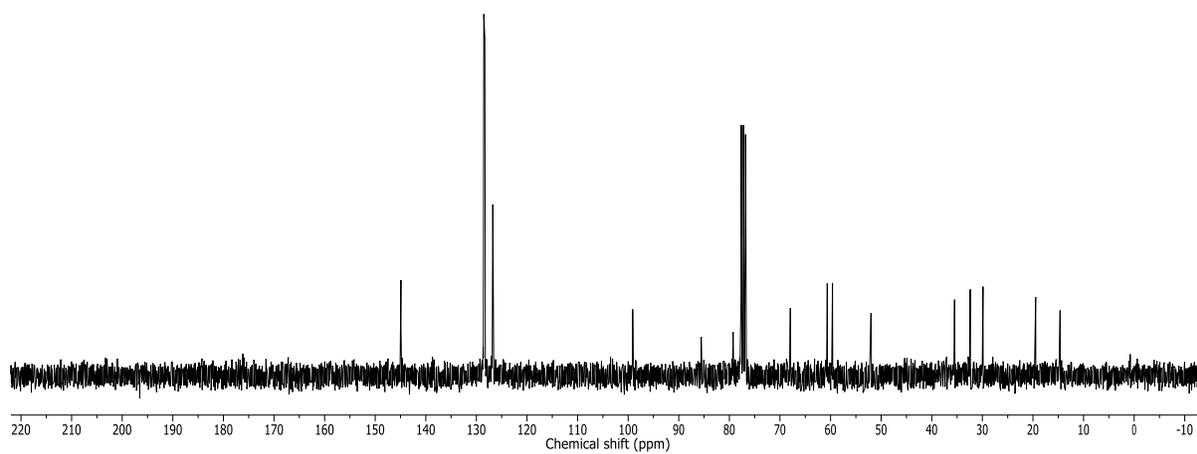
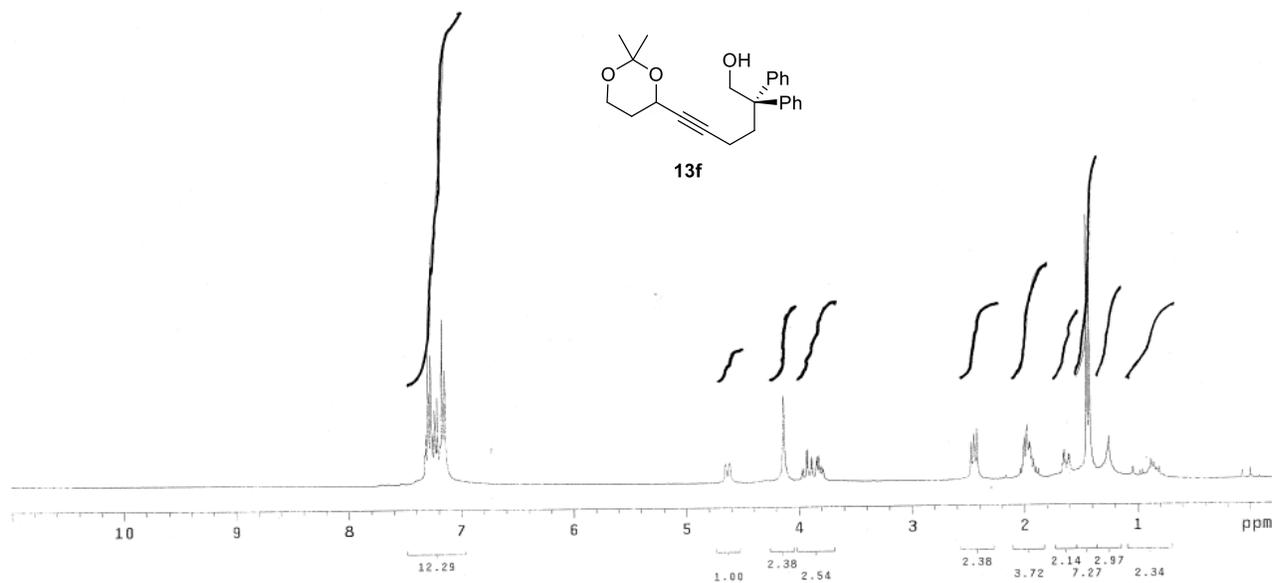


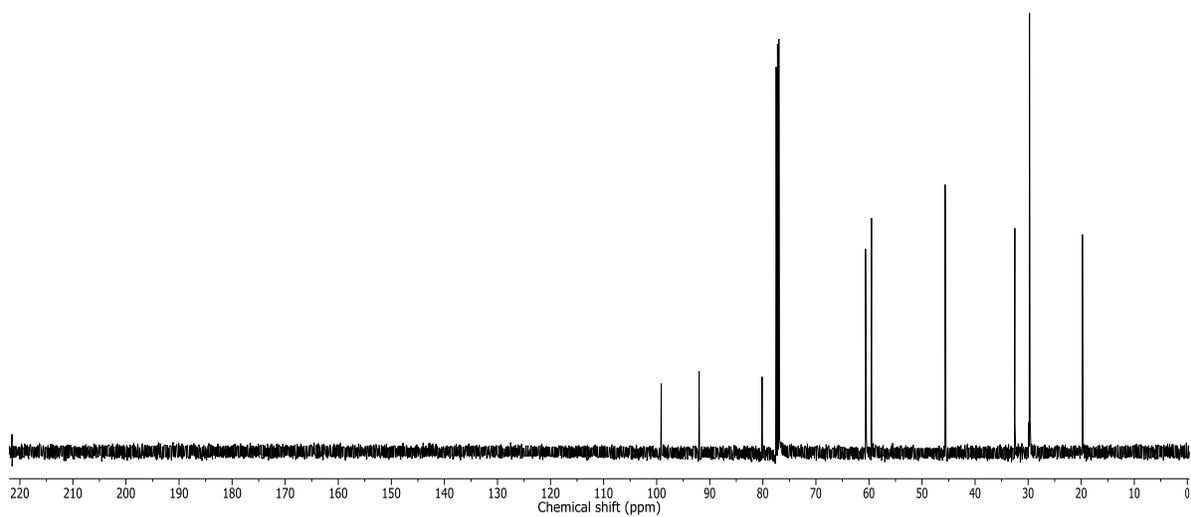
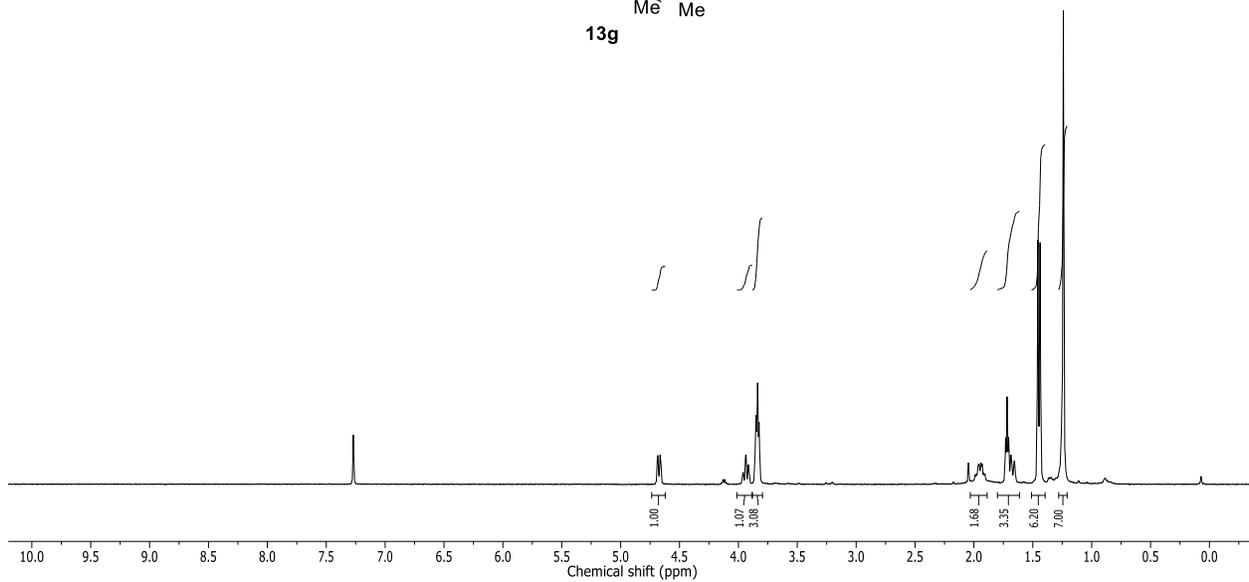
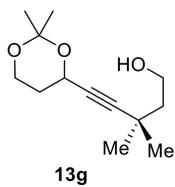




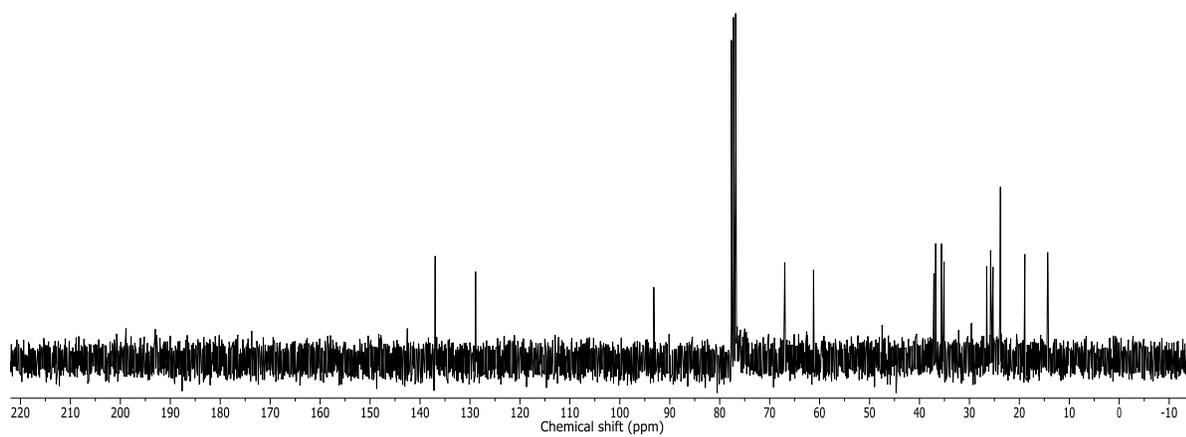
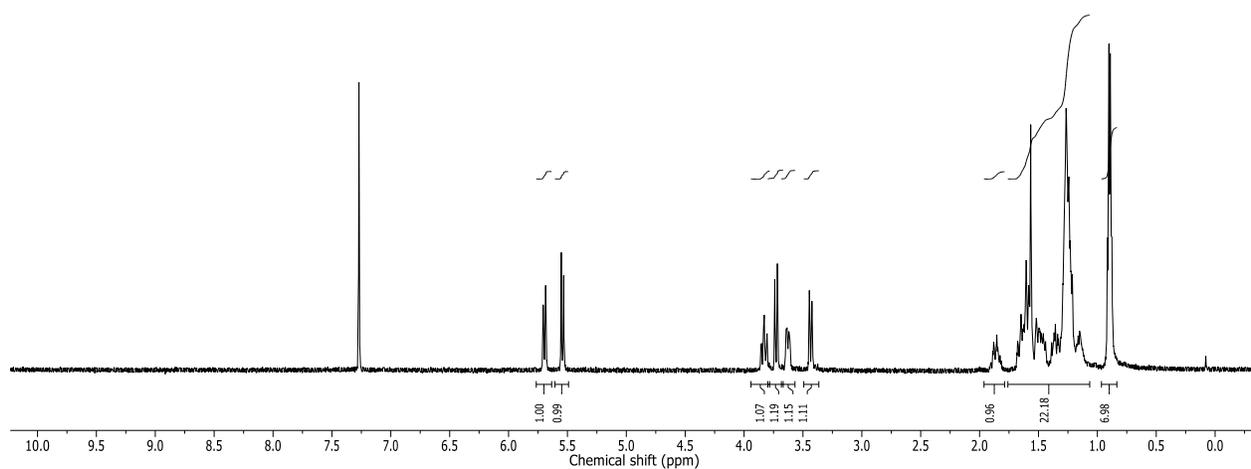
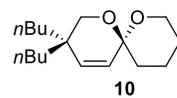


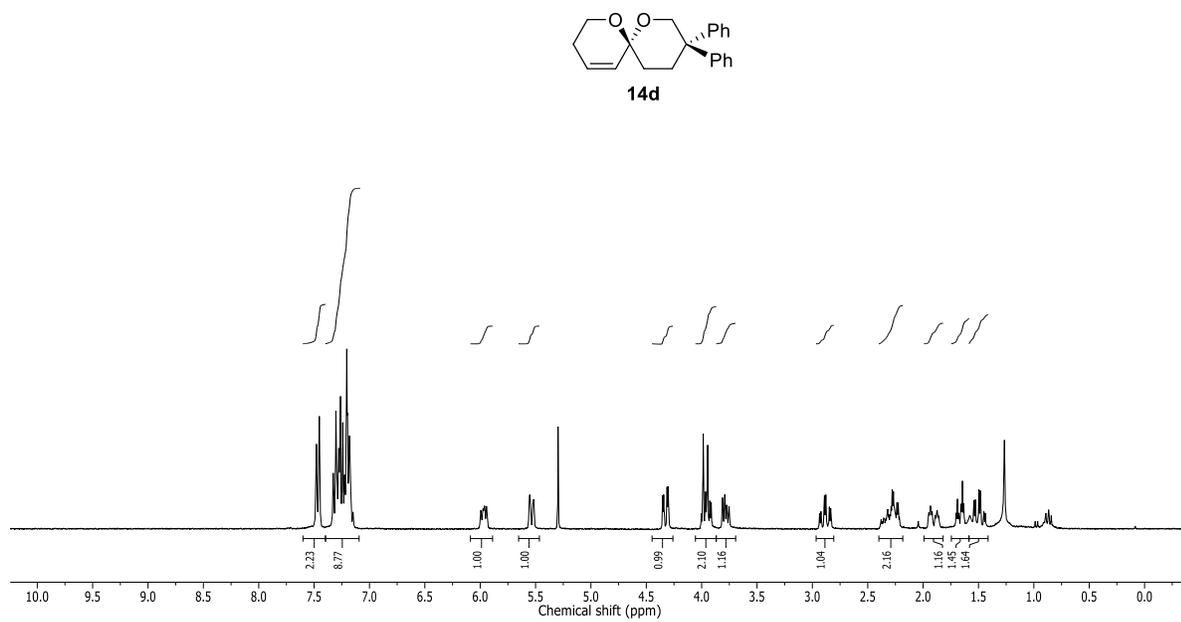
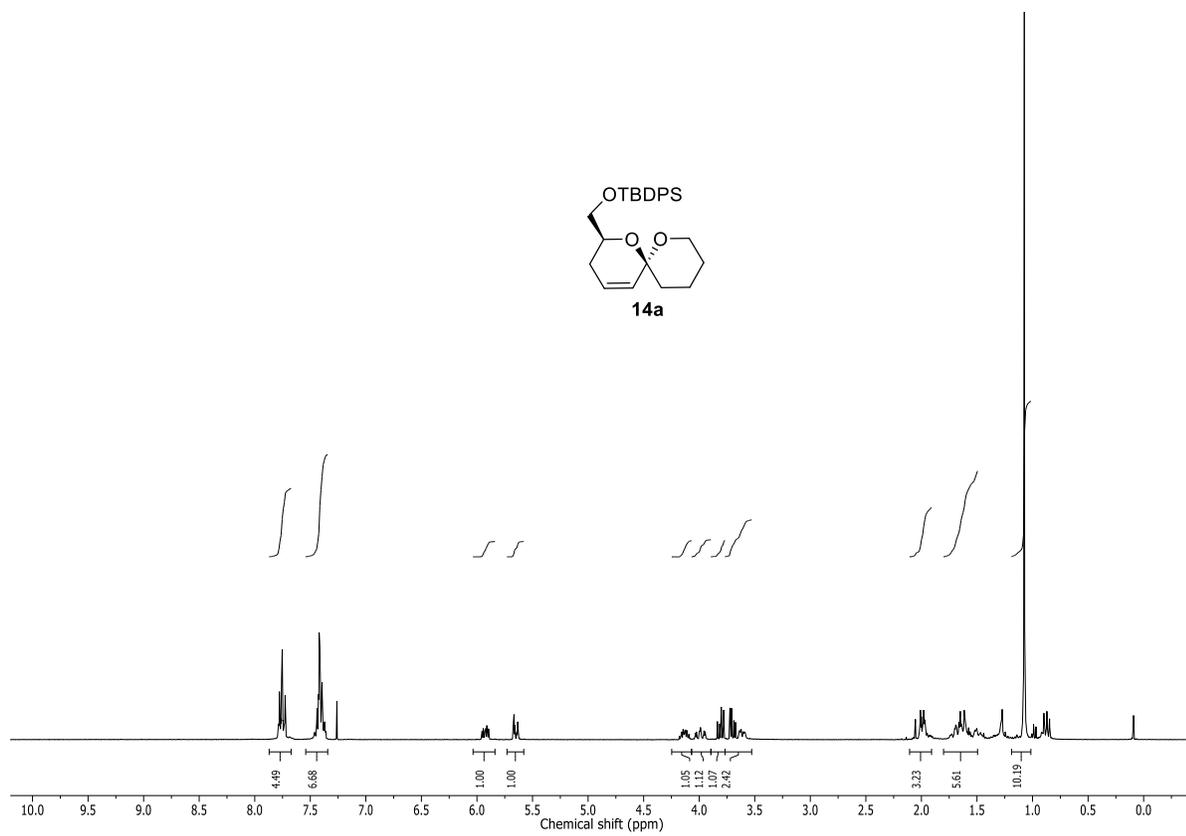


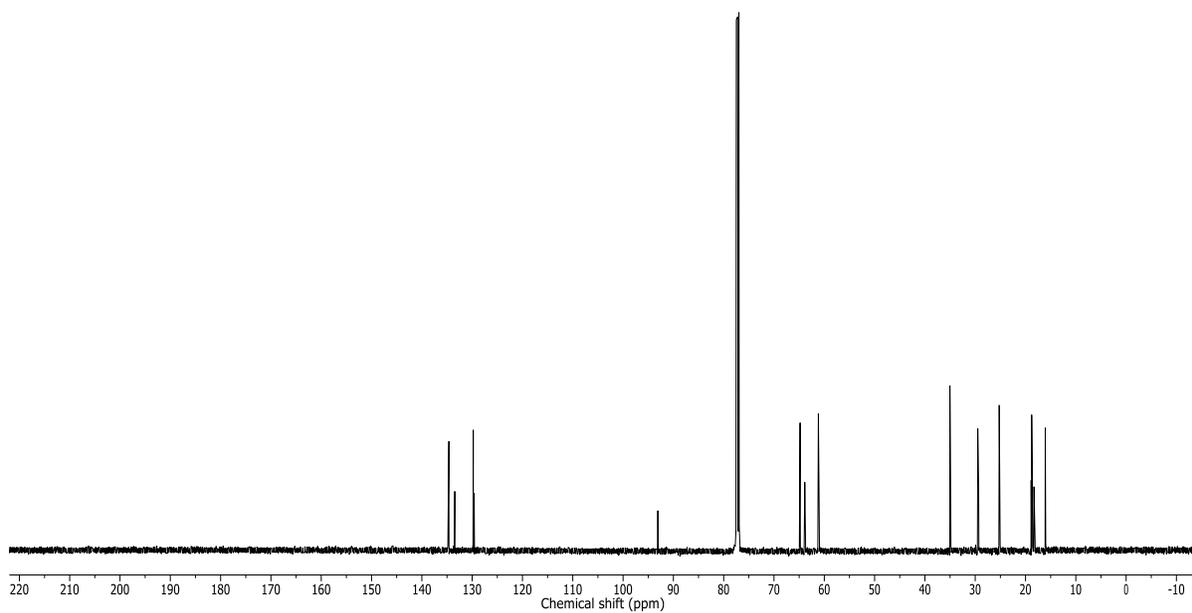
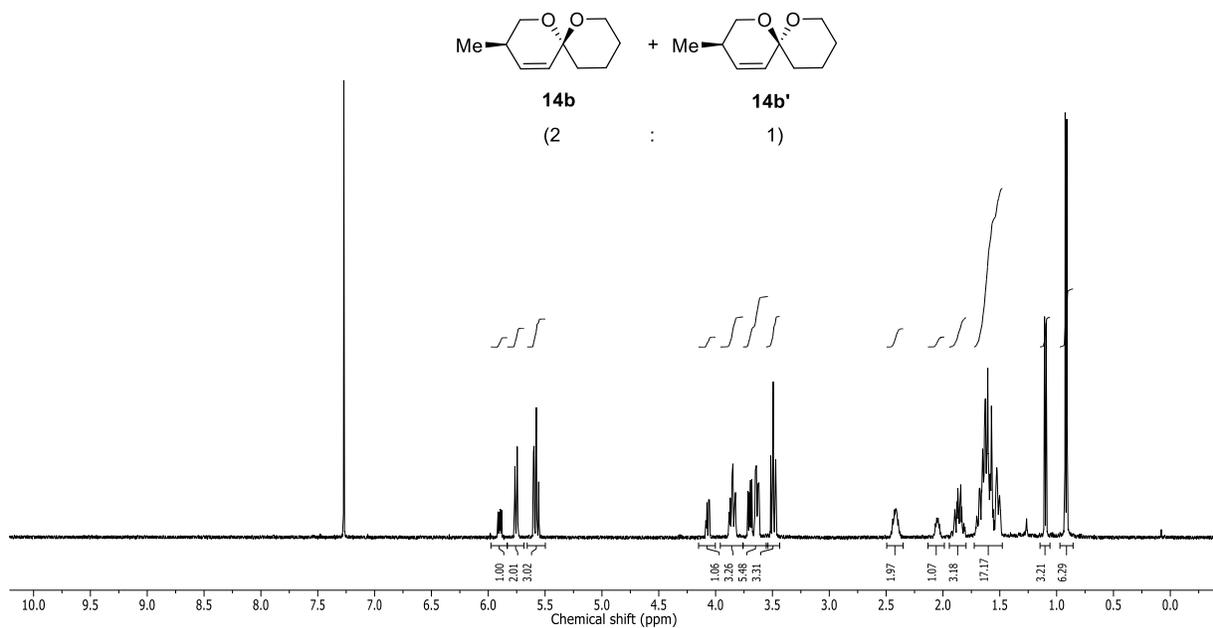


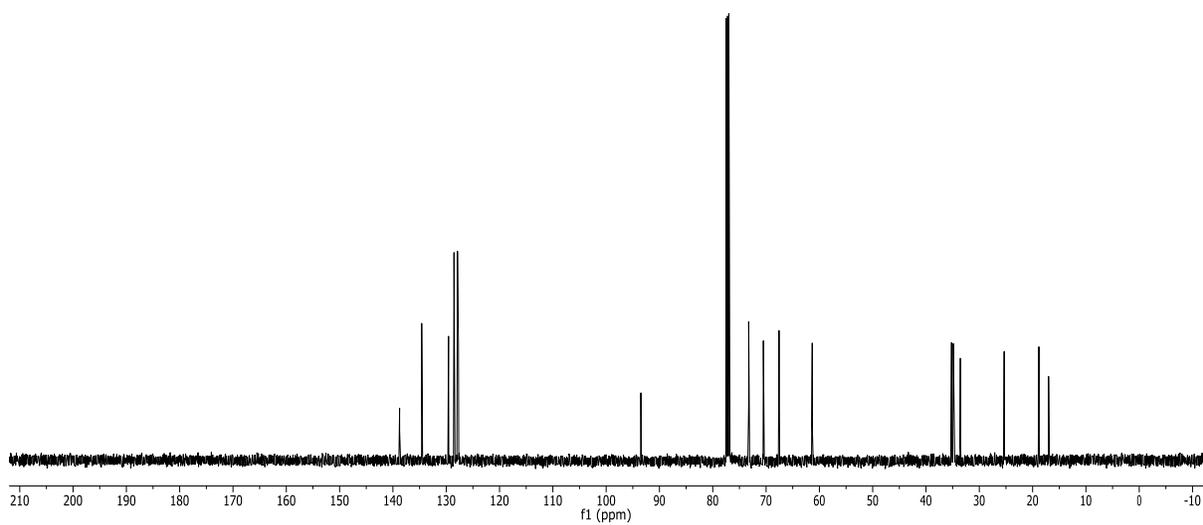
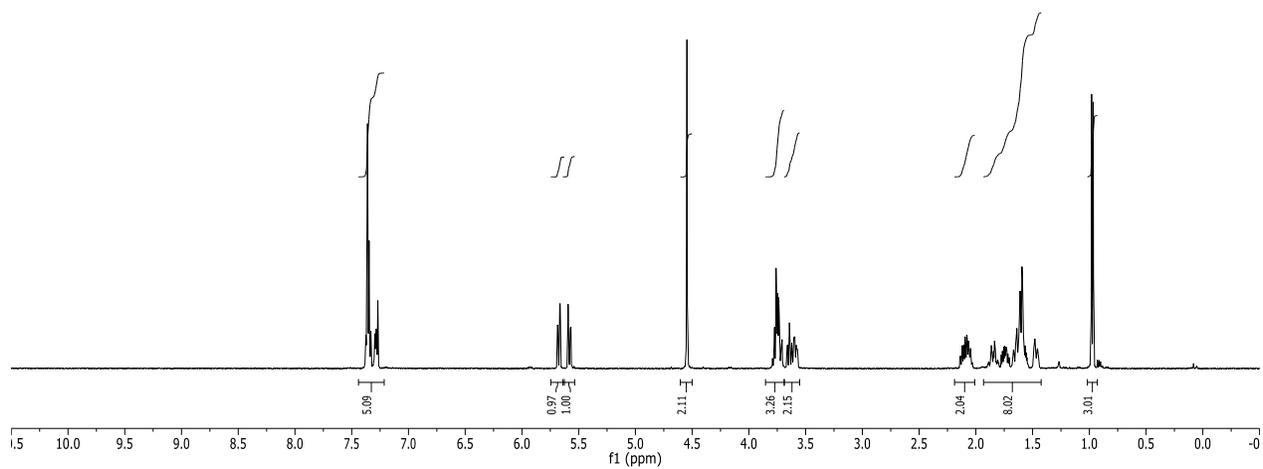
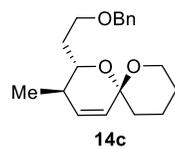


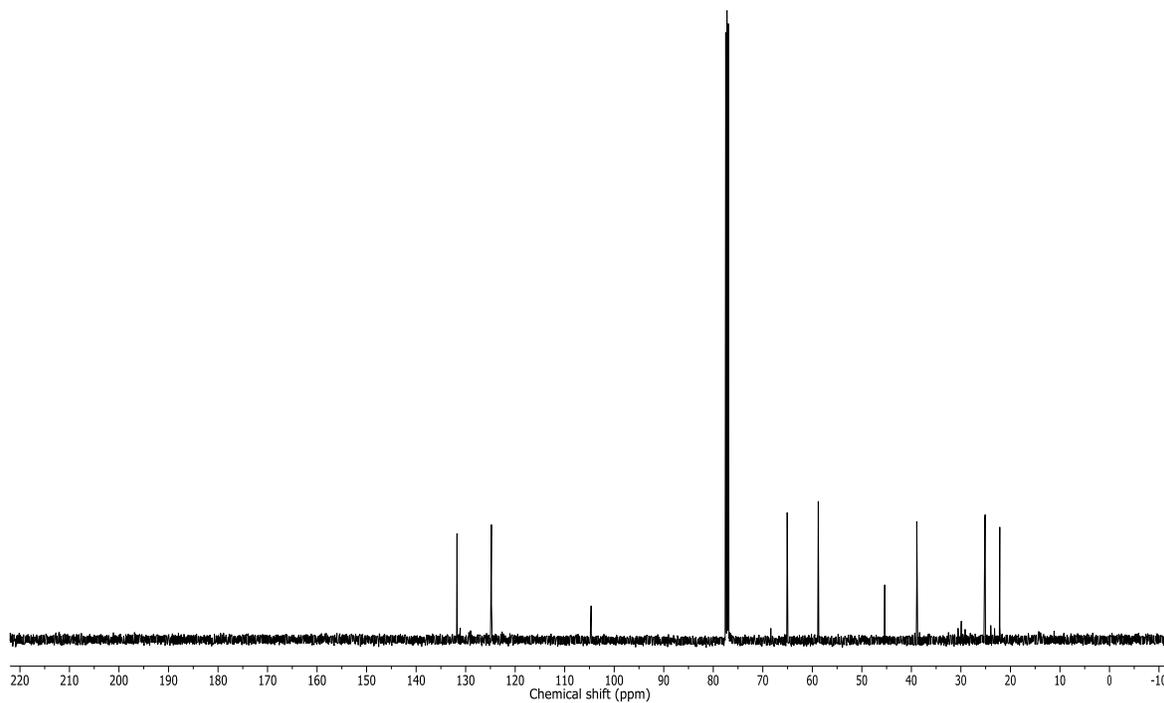
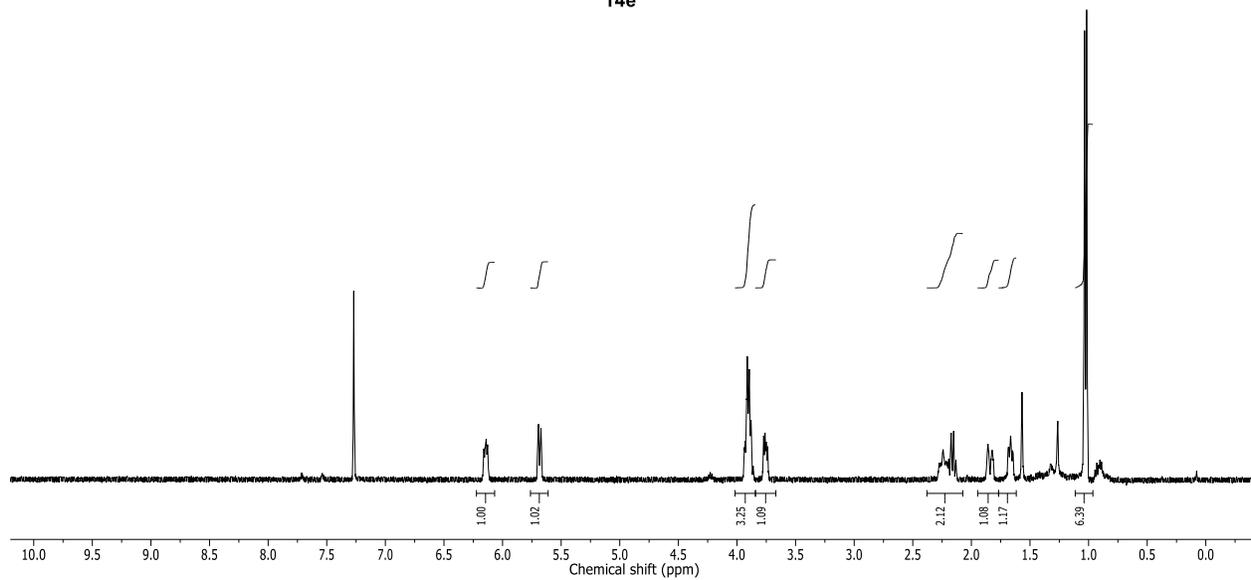
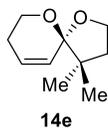
15. NMR spectra of spiroketals











16. NMR spectra of cyclobutane 23 and its precursors

