

Electronic Supplementary Information

Strategy Towards the Enantioselective Synthesis of Schiglautone A

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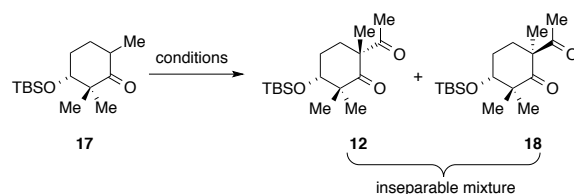
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1. Supplementary Tables

Table S1. Screening of acetylation conditions.

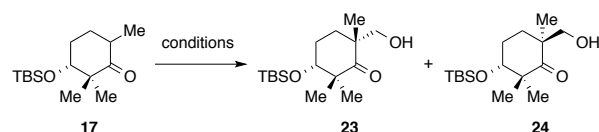


Entry	Conditions	Yield (%) ^a	Ratio ^b 12:18
1	LDA, MeC(O)CN, THF, -78 °C to rt, 1.25 h	78	0:1
2	LDA, MeC(O)CN, HMPA, THF, -78 °C to rt, 12 h	70	0:1
3	LDA, MeC(O)CN, TMEDA, THF, -78 °C to rt, 12 h	60	0:1
4	a) LiHMDS, ZnCl ₂ , MeCHO, THF, -78 °C to rt, 12 h; b) PCC, DCM, rt, 12 h	58	1:2
5	a) LDA, MeCHO, THF, -78 °C to -30 °C, 4 h; b) PCC, DCM, rt, 12 h	62	1:1.5
6	a) LDA, HMPA, MeCHO, THF, -78 °C to -30 °C, 5 h; b) PCC, DCM, rt, 12 h	65	1:1.25
7	a) LDA, TMEDA, MeCHO, THF, -78 °C to -20 °C, 4 h; b) PCC, DCM, rt, 12 h	71	1:1
8	a) TiCl ₄ (0.2 equiv), MeCHO, benzene, rt, 1 h; b) PCC, DCM, rt, 12 h	55	1:1

^a Combined yield of 12 and 18.

^b Ratio determined on ¹H-NMR of crude mixture.

Table S2. Screening of hydroxymethylation conditions.



Entry	Conditions	Yield (%) ^a	Ratio ^b 23:24
1	10% KOH in MeOH, formalin, MeOH, 0 °C to rt	0	/
2	DBU, formalin, THF, 0 °C, 48 h	68	1:1
3	DBN, formalin, THF, 0 °C, 12 h	44	1:1
4	Hunig's base, formalin, THF, 0 °C to rt, 12 h	0	/
5	LDA, CH ₂ O (g), -78 °C to -40 °C, 20 min	Complex mixture	/
6	a) LDA, TMSCl, THF, -20 °C to rt, 4.5 h; b) TBAF·3H ₂ O, formalin, THF	57	1.2:1
7 ¹	a) LDA, TMSCl, THF, -20 °C to rt, 4.5 h; b) Sc(OTf) ₃ , formalin, THF, rt, 1 h	64	1.3:1
8 ²	a) LDA, TMSCl, THF, -20 °C to rt, 4.5 h; b) Sc(SDS) ₃ , formalin, H ₂ O, rt, 12 h	0	/

^a Combined yield of 12 and 18.

^b Ratio determined on ¹H-NMR of crude mixture.

¹ S. Ishikawa, T. Hamada, K. Manabe, and S. Kobayashi, *J. Am. Chem. Soc.*, 2004, **126**, 12236.

² K. Manabe, Y. Mori, T. Wakabayashi, S. Nagayama and S. Kobayashi, *J. Am. Chem. Soc.*, 2004, **126**, 12236.

2. Supplementary Chart

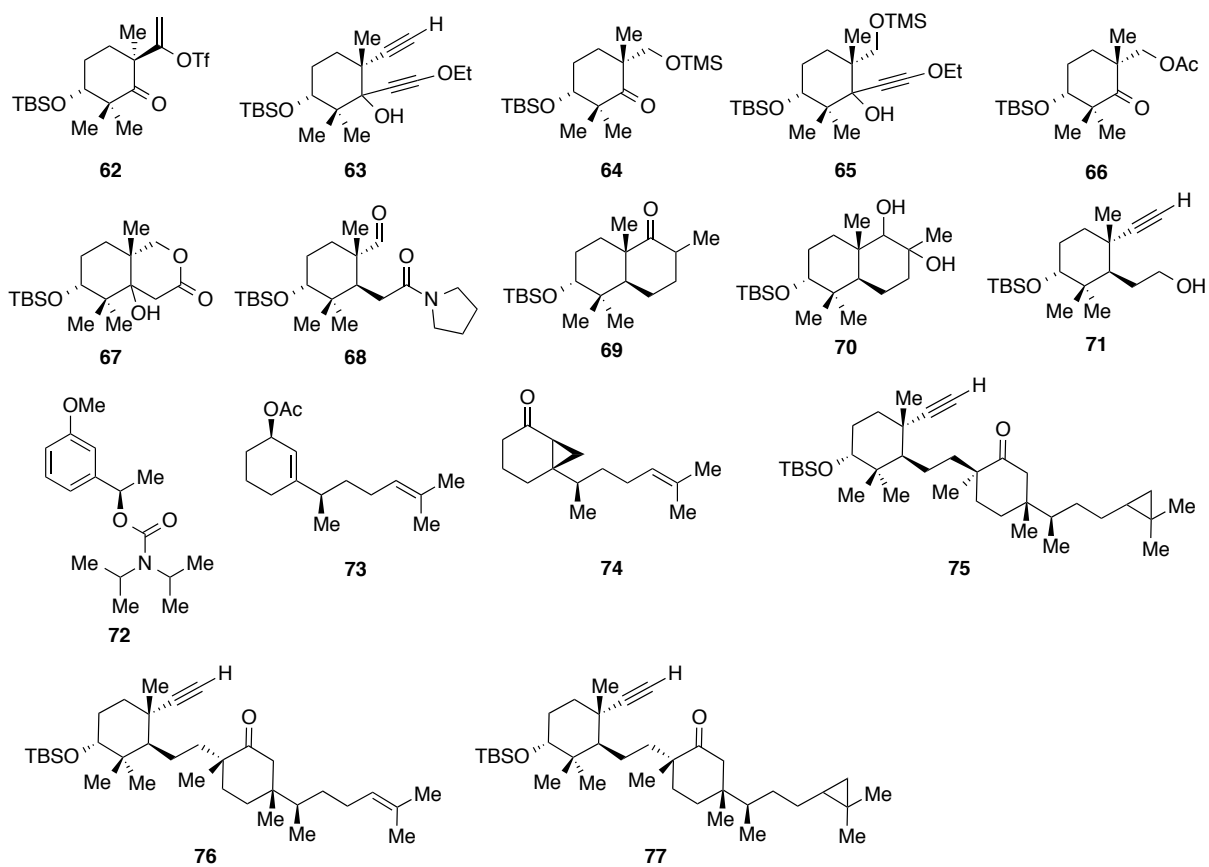
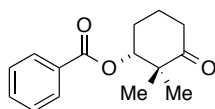


Chart S1. Structures of compounds **62** to **77**.

3. Experimental

General Methods: All non-aqueous reactions were performed in flame-dried glassware under a positive pressure of dry Ar unless otherwise stated. For reactions Et₂O, THF, MeCN, DCM, and toluene were dried using a solvent purification system under an atmosphere of dry N₂. Under an atmosphere of dry N₂, MeOH was distilled from magnesium turnings, benzene was distilled over sodium/benzophenone, (iPr)₂NH and pyridine were distilled from KOH, (iPr)₂NEt and Et₃N were distilled from CaH₂. TMSCl was distilled from CaH₂ and stored under an atmosphere of dry Ar. *m*-CPBA was purified according to a known method.³ Reactions were magnetically stirred and monitored by thin layer chromatography (TLC). TLC was performed on silica gel 60 F254 TLC glass plates and visualized with UV fluorescence quenching at 254 nm and 366 nm and stained in Seebach's stain.⁴ Solvent evaporation under reduced pressure was performed by rotary evaporation at 40 °C at the appropriate pressure. Column chromatographic purification was performed as flash column chromatography using silica gel (230–400 mesh, 60 Å) as stationary phase.⁵ The yields refer to chromatographically purified compounds, unless stated otherwise. Chemical shifts (δ) are reported in ppm with the residual solvent signal as internal standard (chloroform at 7.26 and 77.16 for ¹H and ¹³C spectroscopy, respectively), unless otherwise noted. Coupling constants (J) are reported in hertz (Hz). The following abbreviations were used: s = singlet, d = doublet, t = triplet, q = quadruplet, m = multiplet, br = broad, app = apparent. Infrared spectra were recorded as thin films. Absorptions are given in wavenumbers (cm⁻¹). High-resolution mass spectra (HRMS) were measured on a mass spectrometer equipped with a positive ion electrospray ionization (ESI) or electron ionization (EI) source, and analyzed using a quadrupole time-of-flight (Q-TOF) system. Optical rotations were measured at the indicated wavelength with 100 mm path length cell. Concentrations are given in g/100 mL in the indicated solvent. Melting points were determined in an open capillary and are uncorrected. Enantiomeric excesses were determined by chiral analytical supercritical fluid chromatography (SFC) apparatus. Utilized columns and conditions are specified, retention times (t_R) are given in minutes. The carbon numbering for NOESY analysis of synthetic intermediates follows schiglautone A carbon numbering and corresponds to the numbering in the schemes.

(*R*)-2,2-Dimethyl-3-oxocyclohexyl benzoate (**10**)



Et₃N (31.0 μL, 0.225 mmol), DMAP (27.5 mg, 0.225 mmol) and BzCl (19.6 μL, 0.169 mmol) were successively added to a solution of **9** (8.0 mg, 56 μmol)⁶ in DCM (0.560 mL) at 0 °C. The solution was let to warm up to rt and stirred for 24 h. Sat. aq. NaHCO₃ was added and the aqueous layer was extracted three times with DCM. The organic phase was washed with sat. aq. NaHCO₃ and brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂; hexane/EtOAc, 4:1) to give **10** (10 mg, 72%) as a colorless oil.

R_f=0.44 (hexane/EtOAc, 4:1); ¹H-NMR (CDCl₃, 300 MHz): δ 8.03–8.01 (m, 1H), 8.01–7.99 (m, 1H), 7.60–7.54 (m, 1H), 7.47–7.41 (m, 2H), 5.20 (dd, *J* = 6.1, 2.7 Hz, 1H), 2.63–2.42 (m, 2H), 2.26–2.16 (m,

³ T. E. Mlsna, J. A. Young and D. D. Z. DesMarteau, *Anorg. Allg. Chem.*, 2002, **628**, 1789.

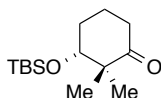
⁴ Composition is given in the supporting information of: D. Seebach, R. Imwinkelried, and G. Stucky, *Helv. Chim. Acta*, 1987, **70**, 448.

⁵ W. C. Still, M. Kahn, A. Mitra, *J. Org. Chem.* 1978, **43**, 2923.

⁶ Keto-alcohol **9** was prepared by a known method: Chênevert, C. Lévesque and P. Morin, *J. Org. Chem.*, 2008, **73**, 9501.

1H), 2.11–1.97 (m, 2H), 1.91–1.81 (m, 1H), 1.26 (s, 3H), 1.20 (s, 3H) ppm; ^{13}C -NMR (CDCl_3 , 75 MHz): δ 213.4, 165.7, 133.3, 130.2, 129.7 (2C), 128.6 (2C), 80.1, 49.8, 37.4, 26.0, 23.6, 21.1, 20.7 ppm; IR (thin film): ν 2949, 2876, 1711, 1451, 1262, 1108, 710 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{Na}]^+$ Calcd for $\text{C}_{15}\text{H}_{18}\text{NaO}_3$ 269.1148, found 269.1142; $[\alpha]_{\text{D}}^{22}$ -49.6 (c 0.455, CHCl_3); SFC (column IA; CO_2/iPrOH , 98:2; 2.00 $\text{mL}\cdot\text{min}^{-1}$; 100 bar; 25 $^\circ\text{C}$): major enantiomer t_{R} = 6.542, minor enantiomer t_{R} = 7.683, 93.9% ee.

(*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-2,2-dimethylcyclohexanone (14**)**

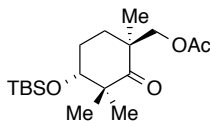


The TBS protection of the enantiomer of **9** has been reported via a different method.⁷

2,6-lutidine (3.32 mL, 28.5 mmol) and TBSOTf (5.23 mL, 22.8 mmol) were added dropwise to a solution of **9** (2.70 g, 19.0 mmol) in DCM (95 mL) at 0 $^\circ\text{C}$. The solution was stirred for 20 min, before sat. aq. NH_4Cl was added. The aqueous layer was extracted three times with DCM. The organic phase was washed successively with 5% HCl, sat. aq. NaHCO_3 and brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2 ; pentane/ Et_2O , 25:1) to give **14** (4.21 g, 86%) as an oil. The analytical data were found to be consistent with the one reported in the literature.⁷

R_f =0.30 (hexane/ EtOAc , 18:1); ^1H -NMR (CDCl_3 , 300 MHz): δ 3.67 (dd, J = 7.2, 2.8 Hz, 1H), 2.06–1.91 (m, 2H), 1.78–1.58 (m, 2H), 1.12 (s, 3H), 1.08 (s, 3H), 0.88 (s, 9H), 0.04 (s, 3H), 0.04 (s, 3H) ppm; ^{13}C -NMR (CDCl_3 , 75 MHz): δ 215.2, 78.5, 51.8, 37.4, 29.5, 25.9 (3C), 23.3, 20.6, 18.2, -4.1 , -4.9 ppm; IR (thin film): ν 2951, 2858, 1710, 1464, 1253, 1080, 831, 773 cm^{-1} ; HRMS (EI) m/z : $[\text{M}-\text{CH}_3]^+$ Calcd for $\text{C}_{13}\text{H}_{25}\text{O}_2\text{Si}$ 241.1619, found 241.1623; $[\alpha]_{\text{D}}^{22}$ -25.7 (c 0.270, CHCl_3).

((1*S*,4*R*)-4-((*tert*-Butyldimethylsilyl)oxy)-1,3,3-trimethyl-2-oxocyclohexyl)methyl acetate (16**)**



NaH (60% in oil, 46.8 mg, 1.17 mmol) was added to a solution of **14** (100 mg, 0.390 mmol) and dimethyl carbonate (329 μL , 3.90 mmol) in THF (0.98 mL). The mixture was heated at reflux at 70 $^\circ\text{C}$ for 12 h, cooled to rt, and poured slowly into a stirred solution of 1 M HCl at 0 $^\circ\text{C}$. The aqueous layer was extracted three times with Et_2O . The organic phase was washed with brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure to give carboxylate **13** as a yellow oil that was used into the next step without any purification.

^1H -NMR (CDCl_3 , 300 MHz): δ 12.36 (s, 1H), 3.74 (s, 3H), 3.55 (dd, J = 9.0, 3.3 Hz, 1H), 2.36 (dt, J = 16.0, 5.7 Hz, 1H), 2.15 (ddd, J = 16.0, 8.6, 6.0 Hz, 1H), 1.75–1.69 (m, 1H), 1.67–1.59 (m, 1H), 1.18 (s, 3H), 1.13 (s, 3H), 0.09 (s, 9H), 0.06 (s, 3H), 0.06 (s, 3H) ppm.

A solution of **13** (118 mg, 0.375 mmol) in THF (1.3 mL)/ HMPA (0.26 mL) was added dropwise to a suspension of NaH (23.7 mg, 0.938 mmol) in THF (0.3 mL) at rt. The mixture was stirred at rt for 15 min before MeI (0.235 mL, 3.75 mmol) was added dropwise. The mixture was stirred at rt for 1 h, and sat. aq. NH_4Cl and Et_2O were added. The aqueous layer was extracted three times with Et_2O . The organic phase was washed with brine, dried

⁷ K. Mori and H. Watanabe, *Tetrahedron*, 1986, **42**, 273.

over Na₂SO₄, filtered and concentrated under reduced pressure to give **15** as a mixture of diastereoisomers that was used into the next step without any purification.

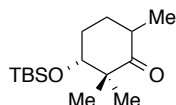
A solution of **15** (98 mg, 0.32 mmol) in THF (1.5 mL) was added dropwise to a suspension of LiAlH₄ (41.6 mg, 1.10 mmol) in THF (0.3 mL) at 0 °C. The grey suspension was stirred at 0 °C for 3 h. Rochelle's salt was added, the aqueous layer was extracted three times with Et₂O. The organic phase was washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure to give the diol as a mixture of diastereoisomers that was used into the next step without any purification.

A solution of diol (98 mg, 0.32 mmol) in pyridine (3.2 mL) and Ac₂O (6.48 mL) was stirred at rt for 30 min. Ice was added and the mixture was stirred for 30 min. The aqueous layer was extracted three times with Et₂O. The organic phase was washed with 1 M HCl, water and brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure to give ((4*R*)-4-((*tert*-butyldimethylsilyl)oxy)-2-hydroxy-1,3,3-trimethylcyclohexyl)methyl acetate as a mixture of diastereoisomers that was used into the next step without any purification.

PCC (344 mg, 0.319 mmol) was added portionwise to a solution of the crude product obtained in the previous step (110 mg, 0.319 mmol) dissolved in DCM (3.2 mL) at rt. The slurry was stirred at rt for 6 h, before SiO₂ (400 mg) was added. The slurry was stirred for 1 h, then passed on a pad of celite, washing DCM, and the filtrate was concentrated. The residue was purified by column chromatography (SiO₂; pentane/Et₂O, 5:1) to give **16** (48 mg, 44 % over 5 steps) and **66** (14 mg, 13% over 5 steps). The relative stereochemistry was determined by comparison with **66** obtained as a single diastereoisomer (*vide infra*).

Data for **16**: *R*_f=0.33 (pentane/Et₂O, 6:1); ¹H-NMR (CDCl₃, 400 MHz): δ 4.22 (d, *J* = 10.7 Hz, 1H), 3.87 (d, *J* = 10.7 Hz, 1H), 3.62 (dd, *J* = 8.2, 4.2 Hz, 1H), 2.02 (s, 3H), 1.92–1.83 (m, 2H), 1.75–1.70 (m, 2H), 1.13 (s, 3H), 1.11 (s, 3H), 1.09 (s, 3H), 0.89 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H) ppm; ¹³C-NMR (CDCl₃, 101 MHz): δ 217.0, 171.0, 77.0, 70.2, 51.4, 46.9, 29.1, 26.5, 25.9 (3C), 23.9, 23.2, 22.0, 21.0, 18.2, –4.0, –4.9 ppm; HRMS (ESI) *m/z*: [M+NH₄]⁺ Calcd for C₁₈H₃₈NO₄Si 360.2564, found 360.2564; [α]_D²³ –12.4 (*c* 0.850, CHCl₃).

(3*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-2,2,6-trimethylcyclohexanone (**17**)



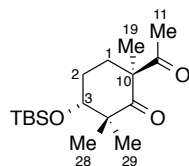
The synthesis of the enantiomer of **17** has been reported.⁷

n-BuLi (1.6 M in hexane, 3.22 mL, 5.15 mmol) was added dropwise to a solution of (iPr)₂NH (0.767 mL, 5.38 mmol) in THF (17 mL) at 0 °C. The pale yellow solution was stirred at 0 °C for 10 min, then cooled to –78 °C. HMPA (0.814 mL, 4.68 mmol) was added dropwise followed by a solution of **14** (1.20 g, 4.68 mmol) in THF (6 mL). The mixture was stirred at –78 °C for 30 min, then at 0 °C for 20 min and cooled again to –78 °C. MeI (0.439 mL, 7.02 mmol) was then added dropwise and the mixture was let to warm up to rt over 12 h. Sat. aq. NH₄Cl and Et₂O were added. The aqueous layer was extracted three times with Et₂O, the organic phase was washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂; pentane/Et₂O, 25:1) to give **17** (1.21 g, 96%) as a 7:3 mixture of diastereoisomers.

The analytical data were found to be consistent with the one reported in the literature.⁷ *R*_f=0.38 (major) and 0.44 (minor) (hexane/EtOAc, 18:1); ¹H-NMR (CDCl₃, 400 MHz): δ 3.84–3.82 (m, 0.7H), 3.46–3.42 (m, 0.3H), 2.68–2.56 (m, 1H), 2.20–2.12 (m, 0.7H), 1.93–1.78 (m, 2.3H), 1.65 (dq, *J* = 14.0, 3.5 Hz, 0.7H), 1.16 (s, 2.1H), 1.15–1.11 (m, 0.3H), 1.08 (s, 0.9H), 1.07 (s, 0.9H), 1.04 (s, 2.1H), 0.99 (d, *J* = 6.5 Hz, 2.1H), 0.97 (d, *J* = 6.5 Hz, 0.9H), 0.89 (s, 2.7H), 0.84 (s, 6.3H), 0.04 (s, 1H), 0.03 (s, 1H), 0.01 (s, 4H) ppm; ¹³C-NMR (CDCl₃, 101 MHz, the asterisk denotes the minor diastereoisomer signals): δ 216.1, 215.5*, 80.0, 77.8*, 52.3*, 50.8, 40.2, 39.6*,

30.8*, 30.1, 29.3*, 28.9, 26.0* (3C), 25.9 (3C), 25.2, 22.2, 22.1*, 19.4*, 18.2*, 18.2, 15.2, 14.9*, -3.9*, -4.3, -4.9*, -4.9 ppm; IR (thin film): ν 2931, 2858, 1709, 1473, 1254, 1076, 1027, 833, 773 cm^{-1} ; HRMS (EI) m/z : $[\text{M}-\text{C}_4\text{H}_9]^+$ Calcd for $\text{C}_{11}\text{H}_{21}\text{O}_2\text{Si}$ 213.1306, found 213.1304.

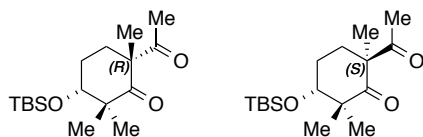
(3*R*,6*S*)-6-Acetyl-3-((*tert*-butyldimethylsilyl)oxy)-2,2,6-trimethylcyclohexanone (18)



A solution of **17** (50.0 mg, 0.185 mmol) in THF (0.90 mL) was added dropwise to a solution of LDA (1 M in THF, 0.203 mL, 0.203 mmol) in THF (0.90 mL) at -78°C . The mixture was stirred at -78°C for 10 min, then warmed up to 0°C and stirred at 0°C for 50 min. The mixture was then cooled again to -78°C and acetyl cyanide (15.7 μL , 0.222 mmol) was added dropwise. The mixture was stirred at -78°C for 20 min. Water and Et_2O were added and the solution was warmed up to rt. The aqueous layer was extracted three times with Et_2O . The organic phase was washed with brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2 ; pentane/ Et_2O , 20:1) to give **18** (45 mg, 78%) as a single diastereoisomer. The stereochemistry was determined by NOESY analysis.

R_f =0.35 (hexane/ EtOAc , 16:1); ^1H -NMR (CDCl_3 , 600 MHz): δ 3.77–3.75 (m, 1H), 2.36 (app. dddd, J = 13.5, 4.3, 3.1, 1.2 Hz, 1H), 2.17 (app. dddd, J = 14.4, 13.3, 4.3, 2.0 Hz, 1H), 2.04 (s, 3H), 1.81 (td, J = 13.4, 4.4 Hz, 1H), 1.62–1.57 (m, 1H), 1.25 (s, 3H), 1.08 (s, 3H), 0.95 (s, 3H), 0.85 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H) ppm; ^{13}C -NMR (CDCl_3 , 150 MHz): δ 212.9, 206.0, 79.3, 63.2, 52.6, 28.7, 26.4, 25.9 (3C), 25.3, 23.9, 23.7, 23.0, 18.2, -4.3, -4.9 ppm; ^1H - ^1H -NOESY (CDCl_3 , 500 MHz, relevant cross-peaks): δ 3.76 and 2.18 [$\text{H}(3)-\text{H}_\beta(2)$], 1.59 and 1.25 [$\text{H}_\alpha(2)-\text{C}(19)\text{H}_3$] ppm; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{17}\text{H}_{33}\text{O}_3\text{Si}$ 313.2193, found 313.2196; $[\alpha]_D^{22}$ -56.6 (c 0.210, CHCl_3).

(3*R*,6*R*)-6-Acetyl-3-((*tert*-butyldimethylsilyl)oxy)-2,2,6-trimethylcyclohexan-1-one (12) and (3*R*,6*S*)-6-acetyl-3-((*tert*-butyldimethylsilyl)oxy)-2,2,6-trimethylcyclo hexanone (18)



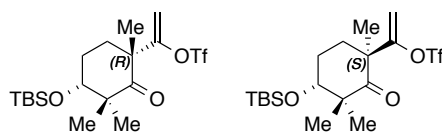
$n\text{-BuLi}$ (1.6 M in hexane, 8.46 mL, 13.5 mmol) was added dropwise to a solution of $(i\text{Pr})_2\text{NH}$ (1.94 mL, 13.6 mmol) in THF (30 mL) at 0°C . The pale yellow solution was stirred at 0°C for 10 min, then cooled to -78°C . TMEDA (8.03 mL, 53.2 mmol) was added dropwise followed by the dropwise addition of a solution of **17** (1.20 g, 4.44 mmol) in THF (14 mL). The resulting solution was stirred at -78°C for 1 h, then warmed to -20°C and stirred at -20°C for 1 h, before being cooled again to -78°C . Acetaldehyde (5.01 mL, 89.0 mmol) was added dropwise and the solution was stirred for 1 h at -78°C . Sat. aq. NH_4Cl and Et_2O were added, and the mixture was warmed up to rt. The aq. layer was extracted three times with Et_2O . The organic phase was washed with sat. aq. NaHCO_3 and brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by passed through a pad of silica gel, washing pentane/ Et_2O (4:1), and concentrated under reduced

pressure to give the ketoalcohols as a mixture of diastereoisomers. It was used in the next step without further purification.

PCC (2.76 g, 12.8 mmol) was added portionwise to a solution of the product obtained in the previous step (1.15 g, 3.66 mmol) in DCM (18 mL). The brown slurry was stirred at rt for 12 h. SiO₂ (3 g) was added, and the mixture was stirred for 1 h, then filtered on a pad of celite, washing DCM. The filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂; hexane/EtOAc, 25:1) to give a mixture of **12** and **18** (1.13 g, 82% over 2 steps, 1:1), which could not be separated by column chromatography.

R_f=0.55 (hexane/EtOAc, 10:1); ¹H-NMR (CDCl₃, 400 MHz): δ 3.78–3.75 (m, 1H), 3.57 (dd, *J* = 9.5, 4.2 Hz, 1H), 2.50 (dt, *J* = 13.9, 4.8 Hz, 1H), 2.36 (dt, *J* = 13.4, 3.8 Hz, 1H), 2.21–2.14 (m, 1H), 2.05 (s, 6H), 1.95–1.78 (m, 2H), 1.63–1.57 (m, 1H), 1.26 (s, 3H), 1.25 (s, 3H), 1.22–1.16 (m, 1H), 1.13 (s, 3H), 1.09 (s, 3H), 0.96 (br s, 6H), 0.88 (s, 9H), 0.86 (s, 9H), 0.06–0.03 (m, 12H) ppm; ¹³C-NMR (CDCl₃, 101 MHz, asterisk denotes the signals for **18**): δ 213.3, 212.9*, 206.0*, 205.1, 79.3*, 77.1, 63.3*, 62.2, 53.3, 52.6*, 28.9, 28.7*, 27.4, 26.4*, 25.9 (6C), 25.8, 25.3*, 24.0*, 23.7*, 23.5, 23.3, 23.1*, 19.8, 18.2*, 18.2, –4.0, –4.3*, –4.9, –4.9* ppm; IR (thin film): ν 2954, 2858, 1719, 1695, 1466, 1360, 1254, 1083, 837, 775 cm^{–1}; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₇H₃₂NaO₃Si 335.2013, found 335.2019.

1-((1*R*,4*R*)-4-((*tert*-Butyldimethylsilyl)oxy)-1,3,3-trimethyl-2-oxocyclohexyl)vinyltrifluoromethane sulfonate (19**) and 1-((1*S*,4*R*)-4-((*tert*-butyldimethylsilyl)oxy)-1,3,3-trimethyl-2-oxocyclohexyl)vinyl trifluoromethanesulfonate (**62**)**

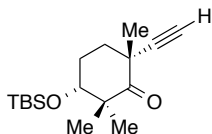


PhNTf₂ (2.51 g, 7.04 mmol) was added to the mixture of **12** and **18** (1.10 g, 3.52 mmol) in THF (35 mL) at –78 °C. Then KHMDS (0.5 M in THF, 7.74 mL, 3.87 mmol) was added over 20 min. The reaction mixture was then stirred at –78 °C for 2 h. Sat. aq. NaHCO₃ and H₂O were added, and the mixture was warmed up to rt. The aqueous layer was extracted three times with Et₂O. The organic phase was washed with brine, dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂; hexane/DCM, 4:1 to 3:1) to give **19** (730 mg, 47%) and **62** (721 mg, 46%) as white solids. The relative stereochemistry of **19** and **62** was determined by comparison with the enol triflate obtained by the same procedure from **18**.

Data for **19**: *R_f*=0.25 (hexane/DCM, 2:1); ¹H-NMR (CDCl₃, 400 MHz): δ 5.28 (d, *J* = 4.8 Hz, 1H), 5.11 (d, *J* = 4.8 Hz, 1H), 3.63–3.60 (m, 1H), 2.43–2.37 (m, 1H), 1.95–1.90 (m, 2H), 1.53–1.43 (m, 1H), 1.32 (s, 3H), 1.14 (s, 3H), 1.12 (s, 3H), 0.89 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H) ppm; ¹³C-NMR (CDCl₃, 101 MHz): δ 211.5, 158.4, 102.2, 77.1, 52.8, 52.6, 34.8, 30.6, 26.7, 25.9 (3C), 24.8, 24.7, 21.3, 18.2, –4.1, –4.9 ppm; ³¹F-NMR (CDCl₃, 282 MHz): δ –74.70 ppm; IR (thin film): ν 2954, 2859, 1710, 1654, 1419, 1208, 1141, 1079, 931, 836, 775 cm^{–1}; HRMS (ESI) *m/z*: [M+NH₄]⁺ Calcd for C₁₈H₃₅F₃NO₅SSi 462.1952, found 462.1950; [α]_D²² +15.6 (*c* 0.920, CHCl₃).

Data for **62**: *R_f*=0.39 (hexane/DCM, 2:1); ¹H-NMR (CDCl₃, 400 MHz): δ 5.27 (d, *J* = 4.7 Hz, 1H), 5.14 (d, *J* = 4.7 Hz, 1H), 3.77 (dd, *J* = 5.9, 2.5 Hz, 1H), 2.21–2.13 (m, 1H), 2.08–2.04 (m, 2H), 1.76–1.69 (m, 1H), 1.32 (s, 3H), 1.17 (s, 3H), 1.10 (s, 3H), 0.87 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H) ppm; ¹³C-NMR (CDCl₃, 101 MHz): δ 211.5, 158.6, 102.3, 77.9, 52.7, 52.2, 30.3, 26.1, 25.9 (3C), 25.2, 25.0, 23.0, 18.2, –4.3, –4.9 ppm; ³¹F-NMR (CDCl₃, 282 MHz): δ –74.61 ppm; IR (thin film): ν 2956, 2860, 1709, 1418, 1209, 1078, 934 cm^{–1}; HRMS (ESI) *m/z*: [M+NH₄]⁺ Calcd for C₁₈H₃₅F₃NO₅SSi 462.1952, found 462.1950; [α]_D²² –46.2 (*c* 1.01, CHCl₃).

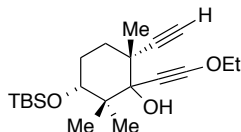
(3*R*,6*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-6-ethynyl-2,2,6-trimethylcyclohexanone (20)



A solution of **19** (700 mg, 1.58 mmol) in pyridine (16 mL) was heated at 60 °C for 36 h. The mixture was then cooled to rt and treated with 5% citric acid and Et₂O. The aqueous layer was extracted three times with Et₂O. The organic phase was washed with aq. CuSO₄, sat. aq. NaHCO₃ and brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂; pentane/Et₂O, 25:1) to give **20** (422 mg, 91%) as a colorless oil.

R_f=0.50 (hexane/EtOAc, 16:1); ¹H-NMR (CDCl₃, 400 MHz): δ 3.47 (dd, *J* = 11.4, 4.0 Hz, 1H), 2.28 (s, 1H), 2.30–2.19 (m, 1H), 2.07 (dt, *J* = 13.8, 3.7 Hz, 1H), 1.82–1.75 (m, 1H), 1.43–1.39 (m, 1H), 1.33 (s, 3H), 1.32 (s, 3H), 1.11 (s, 3H), 0.91 (s, 9H), 0.08 (s, 3H), 0.05 (s, 3H) ppm; ¹³C-NMR (CDCl₃, 101 MHz): δ 210.4, 86.9, 77.6, 71.9, 53.9, 42.5, 35.2, 28.2, 25.9 (3C), 25.8, 23.7, 22.5, 22.1, –3.9, –4.9 ppm; IR (thin film): ν 3311, 2933, 2858, 1712, 1464, 1254, 1090, 835, 773, 633 cm^{–1}; HRMS (ESI) *m/z*: [M+H]⁺ Calcd for C₁₇H₃₁O₂Si 295.2088, found 295.2087; [α]_D²¹ +47.1 (*c* 0.475, CHCl₃).

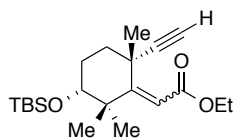
(3*R*,6*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-1-(ethoxyethynyl)-6-ethynyl-2,2,6-trimethyl cyclohexanol (63)



A solution of ethoxyethyne (0.407 mL, 2.04 mmol) in Et₂O (8.0 mL) was slowly treated at –78 °C with *n*-BuLi (1.6 M in hexane, 1.10 mL, 1.77 mmol). The solution was stirred at –78 °C for 30 min, then warmed up to 0 °C and stirred at 0 °C for 1 h. It was then cooled again to –78 °C and a solution of **20** (400 mg, 1.36 mmol) in Et₂O (5.6 mL) was added slowly. The solution was stirred at –78 °C for 30 min and allowed to warm up to rt over 12 h. Sat. aq. NH₄Cl and Et₂O were added, the aqueous layer was extracted three times with Et₂O. The organic phase was washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂; pentane/Et₂O, 25:1) to give **63** (395 mg, 80%) as a mixture of epimers (4:1).

R_f=0.22 (major) and 0.38 (minor) (hexane/EtOAc, 12:1); ¹H-NMR (CDCl₃, 400 MHz): δ 4.11 (q, *J* = 7.3 Hz, 1H), 3.70–3.67 (m, 0.2H), 3.64 (dd, *J* = 10.4, 3.7 Hz, 0.8H), 2.28 (s, 0.8H), 2.18 (s, 0.2H), 1.83–1.78 (m, 1H), 1.64–1.57 (m, 2H), 1.45 (s, 2.4H), 1.43–1.41 (m, 0.6H), 1.41–1.39 (m, 3H), 1.28–1.26 (m, 2H), 1.21 (br s, 3H), 1.13 (s, 2.4H), 1.11 (s, 0.6H), 0.90 (s, 9H), 0.05–0.03 (m, 6H) ppm; ¹³C-NMR (CDCl₃, 101 MHz, the asterisk denotes the minor diastereoisomer signals): δ 78.1*, 75.8, 74.7*, 74.6, 73.9*, 71.0, 46.2*, 38.4, 34.3, 33.7*, 28.8, 28.4*, 28.1, 27.3, 26.0, 25.3, 24.5*, 22.5, 19.5*, 18.2, 15.4, 14.7*, 14.2, –3.8*, –3.9, –4.7*, –4.8 ppm; IR (thin film): ν 3311, 2930, 2857, 2264, 1472, 1387, 1252, 1087, 1034, 834, 773, 627 cm^{–1}; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₂₁H₃₆NaO₃Si 387.2326, found 387.2328.

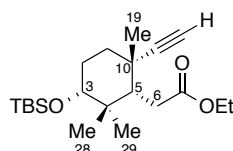
Ethyl-2-((3*R*,6*R*)-3-((*tert*-butyldimethylsilyl)oxy)-6-ethynyl-2,2,6-trimethylcyclo-hexylidene)acetate (21**)**



Sc(OTf)₃ (10.8 mg, 22.0 μmol) was added to a mixture of **63** (800 mg, 2.19 mmol) in DCM/EtOH (4:1, 13.2:3.3 mL). The mixture was stirred at rt for 6 h and then concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂; pentane/Et₂O, 40:1 to 20:1) to give **21** (550 mg, 69%) as a mixture of (*E*) and (*Z*) isomers (5:4).

R_f=0.63 and 0.69 (hexane/EtOAc, 10:1); ¹H-NMR (CDCl₃, 400 MHz): δ 6.05 (s, 0.4H), 5.89 (s, 0.6H), 4.22–4.14 (m, 2H), 3.49–3.45 (m, 0.6H), 3.35 (dd, *J* = 9.7, 4.0 Hz, 0.4H), 2.23 (s, 0.3H), 2.28–2.21 (m, 0.6H), 2.20 (s, 0.3H), 2.06–1.69 (m, 2.55H), 1.61 (s, 1.65H), 1.59–1.56 (m, 0.55H), 1.51–1.47 (m, 0.55H), 1.45 (s, 1.35H), 1.34 (s, 1.35H), 1.31 (app td, *J* = 7.2, 1.1 Hz, 3H), 1.22–1.21 (m, 3H), 1.13 (s, 1.5H), 0.89 (s, 9H), 0.05–0.03 (m, 6H) ppm; ¹³C-NMR (CDCl₃, 101 MHz, the asterisk denotes the signals for one of the two isomers): δ 170.2, 169.2*, 157.5, 154.8*, 118.8, 118.7*, 91.3, 91.0*, 77.2*, 75.6, 70.2*, 69.0, 60.8*, 60.6, 44.1*, 43.5, 37.2*, 36.9, 36.8*, 35.6, 31.1, 29.2 (2C), 27.8*, 26.7, 26.5 (2C), 26.0 (3C), 26.0* (3C), 23.5*, 18.3, 18.3*, 14.2, 14.2*, –3.8*, –4.0, –4.8, –4.8* ppm; IR (thin film): ν 3310, 2931, 2857, 1724, 1463, 1251, 1212, 1105, 1028, 834, 773, 629 cm^{–1}; HRMS (ESI) *m/z*: [M+H]⁺ Calcd for C₂₁H₃₇O₃Si 365.2506, found 365.2503.

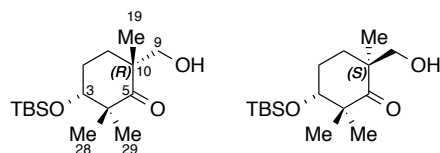
Ethyl 2-((1*S*,3*R*,6*S*)-3-((*tert*-butyldimethylsilyl)oxy)-6-ethynyl-2,2,6-trimethylcyclo hexyl) acetate (22**)**



Mg turnings were predried in the oven at 120 °C for 1 h before use. Mg turnings (8.3 mg, 0.34 mmol) were added to a stirred solution of **21** (12.5 mg, 34.0 μmol) in MeOH (0.34 mL) at rt. The suspension was stirred at rt for 4 h. 3 N aq. HCl solution was added until Mg dissolved, and Et₂O was added. The aqueous layer was extracted three times with Et₂O. The organic phase was washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure to afford **22** (10 mg, 80%) as a yellow oil along some unidentified impurities. The stereochemistry of was determined by NOESY analysis.

R_f=0.50 (hexane/EtOAc, 14:1); ¹H-NMR (CDCl₃, 500 MHz): δ 4.14 (q, *J* = 7.1 Hz, 2H), 3.26 (dd, *J* = 11.3, 4.0 Hz, 1H), 2.55 (dd, *J* = 17.6, 5.7 Hz, 1H), 2.48 (dd, *J* = 17.7, 3.7 Hz, 1H), 2.11 (s, 1H), 1.87–1.81 (m, 2H), 1.67 (dd, *J* = 5.8, 3.6 Hz, 1H), 1.55–1.52 (m, 1H), 1.40–1.37 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.13 (s, 3H), 0.98 (s, 3H), 0.89 (s, 9H), 0.88 (m, 3H), 0.88 (m, 3H), 0.04 (s, 3H), 0.03 (s, 3H) ppm; ¹³C-NMR (CDCl₃, 125 MHz): δ 174.7, 89.8, 78.7, 71.3, 60.7, 49.5, 41.0, 38.8, 35.9, 33.3, 30.6, 30.5, 28.9, 27.6, 26.0 (3C), 14.7, 14.4, –3.7, –4.8 ppm; ¹H-¹H-NOESY (CDCl₃, 500 MHz, relevant cross-peaks): δ 1.67 and 1.13 [H(5)–H(19)], 1.67 and 0.88 [H(5)–C(28)H₃], 3.26 and 1.67 [H(3) and H(5)] ppm; HRMS (ESI) *m/z*: [M+H]⁺ Calcd for C₂₁H₃₉O₃Si 367.2663, found 367.2657.

(3*R*,6*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-6-(hydroxymethyl)-2,2,6-trimethylcyclohexanone (23) and **(3*R*,6*S*)-3-((*tert*-butyldimethylsilyl)oxy)-6-(hydroxymethyl)-2,2,6-trimethylcyclohexanone (24)**



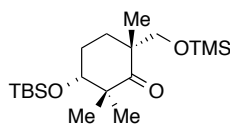
n-BuLi (1.6 M in hexane, 14.4 mL, 23.1 mmol) was added to a solution of (iPr)₂NH (3.29 mL, 23.1 mmol) in THF (250 mL) at 0 °C. The pale yellow solution was stirred at 0 °C for 10 min before a solution of **17** (2.50 g, 9.24 mmol) in THF (50 mL) was added dropwise. The mixture was stirred at 0 °C for 15 min, cooled to –20 °C, and TMSCl (4.73 mL, 37.0 mmol) was added dropwise. The resulting solution was let to warm up to rt over 4 h. Et₃N was added, followed by sat. aq. NaHCO₃. The aqueous layer was extracted three times with Et₂O. The organic phase was washed with water and brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was passed on a small pad of silica gel, washing pentane/Et₂O, (20:1) to give a residue, which was used directly in the next step.

Sc(OTf)₃ (407 mg, 0.827 mmol) was added in one portion to a solution of enol silyl ether (3.15 g, 9.19 mmol) and formaldehyde (37% in water, 28 mL) in THF (66 mL). The mixture was stirred at rt for 1 h. EtOAc and water were added, and the aqueous layer was extracted three times with EtOAc. The organic phase was washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂; pentane/Et₂O, 4:1 to 3:1) to give **23** (1.01 g, 36%), **24** (767 mg, 28%) and **17** (425 mg, 17%).

Data for **23**: *R*_f=0.28 (pentane/Et₂O, 3:1); ¹H-NMR (CDCl₃, 600 MHz): δ 3.78–3.76 (m, 1H), 3.46 (dd, *J* = 11.1, 4.9 Hz, 1H), 3.37 (dd, *J* = 11.1, 8.2 Hz, 1H), 2.78 (dd, *J* = 8.3, 5.2 Hz, 1H), 2.23–2.17 (m, 2H), 1.75–1.68 (m, 1H), 1.33–1.31 (m, 1H), 1.21 (s, 3H), 1.16 (s, 3H), 1.06 (s, 3H), 0.87 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H) ppm; ¹³C-NMR (CDCl₃, 151 MHz): δ 222.9, 77.7, 70.7, 50.9, 48.3, 28.6, 25.9 (3C), 25.5, 25.2, 23.3, 23.1, 18.2, –4.3, –4.9 ppm; ¹H-¹H-NOESY (CDCl₃, 600 MHz, relevant cross-peaks): δ 3.77 and 1.15 [H(3)–C(19)H₃], 3.77 and 1.06 [H(3)–C(28)H₃], 3.46 and 1.21 [H(9)–C(29)H₃], 3.37 and 1.21 [H(9)–C(29)H₃] ppm; IR (thin film): ν 3449, 2931, 2858, 1693, 1464, 1380, 1254, 1086, 836, 774 cm^{–1}; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₆H₃₂NaO₃Si 323.2013, found 323.2013; [α]_D²² –24.7 (*c* 0.720, CHCl₃).

Data for **24**: *R*_f=0.20 (pentane/Et₂O, 3:1); ¹H-NMR (CDCl₃, 600 MHz): δ 3.59–3.53 (m, 2H), 3.32 (dd, *J* = 11.1, 6.2 Hz, 1H), 2.44 (dd, *J* = 7.4, 6.3 Hz, 1H), 2.02–1.79 (m, 2H), 1.72 (td, *J* = 13.0, 12.4, 4.0 Hz, 1H), 1.52 (dt, *J* = 13.8, 4.3 Hz, 1H), 1.15 (s, 3H), 1.09 (s, 6H), 0.90 (s, 9H), 0.08 (s, 3H), 0.05 (s, 3H) ppm; ¹³C-NMR (CDCl₃, 151 MHz): δ 221.5, 77.0, 70.2, 52.0, 48.7, 29.1, 26.7, 26.0 (3C), 23.5, 22.6, 21.0, 18.2, –3.9, –4.8 ppm; HRMS (ESI) *m/z*: [M+Na]⁺ Calcd for C₁₆H₃₂NaO₃Si 323.2013, found 323.2013; [α]_D²² –11.7 (*c* 0.550, CHCl₃).

(3*R*,6*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-2,2,6-trimethyl-6-(((trimethylsilyl)oxy)methyl)cyclohexanone (64)

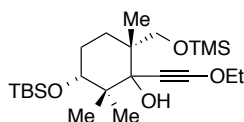


Et₃N (2.51 mL, 18.0 mmol) and TMSCl (1.53 mL, 12.0 mmol) were added successively to a solution of **23** (1.80 g, 5.99 mmol) in DCM (30 mL) at 0 °C. The solution was stirred at 0 °C for 2 h. Et₃N (3.6 mL) and water were added. The aqueous layer was extracted three times with DCM. The organic phase was washed with brine, dried

over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂; pentane/Et₂O, 10:1) to give **64** (2.10 g, 94%) as a colorless oil.

R_f =0.92 (pentane/Et₂O, 10:1); ¹H-NMR (CDCl₃, 400 MHz): δ 3.71–3.69 (m, 1H), 3.68 (d, J = 9.5 Hz, 1H), 3.34 (d, J = 9.6 Hz, 1H), 2.34–2.27 (m, 1H), 2.06–1.98 (m, 1H), 1.79–1.72 (m, 1H), 1.40–1.34 (m, 1H), 1.12 (s, 3H), 1.04 (s, 3H), 1.03 (s, 3H), 0.88 (s, 9H), 0.07 (s, 9H), 0.06 (s, 3H), 0.03 (s, 3H) ppm; ¹³C-NMR (CDCl₃, 101 MHz): δ 218.9, 77.2, 68.7, 50.8, 49.0, 28.2, 26.1, 26.0 (3C), 25.8, 23.2, 22.0, 18.2, –0.4 (3C), –4.2, –4.9 ppm; HRMS (ESI) m/z : [M+H]⁺ Calcd for C₁₉H₄₁O₃Si₂ 373.2589, found 373.2586; [α]_D²² –4.4 (c 0.660, CHCl₃).

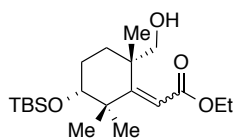
(3*R*,6*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-1-(ethoxyethynyl)-2,2,6-trimethyl-6-(((trimethylsilyl)oxy)methyl)cyclohexanol (65)



A solution of ethoxyethyne (40% w/w in hexanes, 1.05 mL, 5.80 mmol) in Et₂O (22 mL) was slowly treated at –78 °C with *n*-BuLi (1.6 M in hexane, 3.22 mL, 5.15 mmol). The solution was stirred at –78 °C for 30 min, then warmed up to 0 °C and stirred at 0 °C for 30 min. It was then cooled to –78 °C, and a solution of **64** (1.20 g, 3.22 mmol) in Et₂O (8 mL) was added dropwise. The solution was then let to warm up to rt over 12 h. NH₄Cl was added, the aqueous layer was extracted three times with Et₂O. The organic phase was washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂; pentane/Et₂O, 15:1) to give **65** (1.02 g, 71%) as a single diastereoisomer (stereochemistry not established).

R_f =0.46 (pentane/Et₂O, 10:1); ¹H-NMR (CDCl₃, 400 MHz): δ 4.69 (br s, 1H), 4.09 (q, J = 7.1 Hz, 2H), 3.82 (d, J = 9.5 Hz, 1H), 3.74 (d, J = 9.6 Hz, 1H), 3.68 (dd, J = 4.1, 2.4 Hz, 1H), 1.89–1.82 (m, 1H), 1.69–1.62 (m, 1H), 1.54–1.43 (m, 1H), 1.38 (t, J = 7.1 Hz, 3H), 1.36–1.28 (m, 1H), 1.15 (s, 3H), 1.14 (s, 3H), 1.12 (s, 3H), 0.90 (s, 9H), 0.10 (s, 9H), 0.08 (s, 6H) ppm; ¹³C-NMR (CDCl₃, 101 MHz): δ 94.5, 79.7, 77.5, 74.4, 70.0, 25.9 (3C), 25.7, 25.6, 18.1, 14.7, –0.3 (3C), –4.4, –5.0 ppm; HRMS (ESI) m/z : [M+H]⁺ Calcd for C₂₃H₄₇O₄Si₂ 443.3007, found 443.3001.

Ethyl 2-((3*R*,6*S*)-3-((*tert*-butyldimethylsilyl)oxy)-2,2,6-trimethyl-6-(((trimethylsilyl)oxy)methyl)cyclohexylidene)acetate (25)

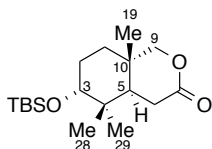


Sc(OTf)₃ (111 mg, 0.226 mmol) was added in one portion to a mixture of **65** (1.00 g, 2.26 mmol) in DCM/EtOH (4:1, 18:4.5 mL) at rt. The mixture was stirred at rt for 20 min, then concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂; pentane/Et₂O, 3:1) to give **25** (782 mg, 93%) as a single isomer.

R_f =0.27 (pentane/Et₂O, 8:1); ¹H-NMR (CDCl₃, 400 MHz): δ 5.77 (s, 1H), 4.17 (q, J = 7.1 Hz, 2H), 3.52–3.49 (m, 1H), 3.44–3.39 (m, 2H), 2.89 (app ddd, J = 13.8, 6.7, 4.6 Hz, 1H), 1.75–1.70 (m, 1H), 1.68–1.60 (m, 1H), 1.39–1.34 (m, 1H), 1.32–1.27 (m, 1H), 1.30 (t, J = 7.2 Hz, 3H), 1.24 (s, 3H), 1.18 (s, 3H), 1.09 (s, 3H), 0.88 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H) ppm; ¹³C-NMR (CDCl₃, 101 MHz): δ 170.1, 157.8, 120.1, 77.3, 70.1, 60.8, 42.9,

42.3, 31.2, 28.0, 26.8, 26.7, 26.0 (3C), 23.2, 18.2, 14.2, -3.8, -4.9 ppm; IR (thin film): ν 3471, 2930, 2857, 1714, 1466, 1248, 1066, 834, 774 cm^{-1} ; HRMS (ESI) m/z : $[M+H]^+$ Calcd for $\text{C}_{20}\text{H}_{39}\text{O}_4\text{Si}$ 371.2612, found 371.2611; $[\alpha]_{\text{D}}^{22}$ -88.2 (c 0.950, CHCl_3).

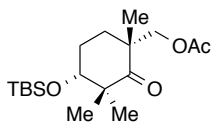
(4*aR*,6*R*,8*aS*)-6-((*tert*-Butyldimethylsilyl)oxy)-5,5,8*a*-trimethylhexahydro-1*H*-isochromen-3(4*H*)-one (26)



$\text{B}(\text{OiPr})_3$ (125 μL , 0.540 mmol) was added dropwise to a mixture of **25** (200 mg, 0.540 mmol), Crabtree's catalyst (43.4 mg, 54.0 μmol) and powdered 4 \AA m.s. (1.0 g) in DCE (6.8 mL) at rt under Ar. H_2 was bubbled into the mixture for 10 min. The mixture was then heated up to 80 $^\circ\text{C}$ under H_2 (balloon) and stirred at 80 $^\circ\text{C}$ for 24 h. The brown mixture was then cooled to rt, filtered through a plug of cotton, and partitioned between 1 M HCl and DCM. The aqueous layer was extracted three times with DCM. The organic phase was washed with brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2 ; pentane/ Et_2O , 4:1) to give **26** (62 mg, 35%) as a colorless oil. The relative stereochemistry was determined by NOESY analysis.

R_f =0.52 (pentane/ Et_2O , 2:1); ^1H -NMR (CDCl_3 , 600 MHz): δ 3.89 (d, J = 10.4 Hz, 1H), 3.83 (d, J = 10.3 Hz, 1H), 3.46 (dd, J = 3.2, 1.8 Hz, 1H), 2.55 (ddd, J = 18.6, 6.0, 0.6 Hz, 1H), 2.40 (dd, J = 18.6, 13.9 Hz, 1H), 2.06 (dd, J = 13.9, 6.0 Hz, 1H), 1.95–1.90 (m, 1H), 1.59–1.52 (m, 2H), 1.16–1.12 (m, 1H), 1.08 (s, 3H), 0.90 (s, 9H), 0.86 (s, 3H), 0.83 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H) ppm; ^{13}C -NMR (CDCl_3 , 150 MHz): δ 171.8, 83.9, 75.6, 40.2, 37.3, 32.9, 28.8, 27.7, 27.5, 26.1 (3C), 25.0, 20.5, 18.3, 17.4, -4.3, -4.7 ppm; IR (thin film): ν 2929, 2855, 1731, 1473, 1462, 1390, 1246, 1190, 1052, 833, 770, 671 cm^{-1} ; ^1H - ^1H -NOESY (CDCl_3 , 600 MHz, relevant cross-peaks): δ 3.84 and 1.08 [$\text{H}_\beta(9)$ -C(19) H_3], 3.89 and 2.06 [$\text{H}_\alpha(9)$ -H(5)] ppm; HRMS (ESI) m/z : $[M+H]^+$ Calcd for $\text{C}_{18}\text{H}_{35}\text{O}_3\text{Si}_2$ 327.2350, found 327.2348; $[\alpha]_{\text{D}}^{23}$ -25.3 (c 0.340, CHCl_3).

((1*R*,4*R*)-4-((*tert*-Butyldimethylsilyl)oxy)-1,3,3-trimethyl-2-oxocyclohexyl)methyl acetate (66)

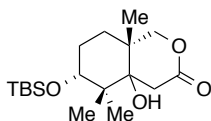


Et_3N (2.33 mL, 16.7 mmol), DMAP (40.9 mg, 0.335 mmol) and Ac_2O (0.632 mL, 6.70 mmol) were successively added to a solution of **23** (1.01 g, 3.35 mmol) in DCM (25 mL) at rt. The mixture was stirred at rt for 2 h. Sat. aq. NH_4Cl was added. The aqueous layer was extracted three times with DCM. The organic phase was washed with brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2 ; pentane/ Et_2O , 5:1) to give **66** (1.10 g, 96%) as a pale yellow oil.

R_f =0.41 (pentane/ Et_2O , 6:1); ^1H -NMR (CDCl_3 , 400 MHz): δ 4.29 (d, J = 10.7 Hz, 1H), 3.81 (d, J = 10.7 Hz, 1H), 3.75 (dd, J = 5.5, 2.3 Hz, 1H), 2.39 (td, J = 13.0, 4.2 Hz, 1H), 2.14 (dddd, J = 14.4, 12.1, 4.1, 2.3 Hz, 1H), 2.01 (s, 3H), 1.74 (app dq, J = 14.3, 4.7 Hz, 1H), 1.40 (dt, J = 13.5, 4.2 Hz, 1H), 1.15 (s, 3H), 1.13 (s, 3H), 1.08 (s, 3H), 0.89 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H) ppm; ^{13}C -NMR (CDCl_3 , 101 MHz): δ 217.1, 171.3, 77.2, 69.8, 50.7, 47.2, 28.2, 26.1, 26.0 (3C), 25.5, 23.4, 22.8, 21.1, 18.2, -4.3, -4.9 ppm; IR (thin film): ν 2931, 2858, 1745, 1702, 1463, 1372, 1235, 1079, 1030, 833, 774, 679 cm^{-1} ; HRMS (ESI) m/z : $[M+H]^+$ Calcd for $\text{C}_{18}\text{H}_{35}\text{O}_4\text{Si}$

343.2299, found 343.2297; $[\alpha]_D^{22} -18.4$ (c 0.445, CHCl_3).

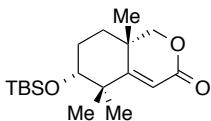
(6*R*,8*aR*)-6-((*tert*-Butyldimethylsilyl)oxy)-4*a*-hydroxy-5,5,8*a*-trimethylhexahydro-1*H*-isochromen-3(4*H*)-one (67)



To a solution of $(i\text{Pr})_2\text{NH}$ (0.917 mL, 6.43 mmol) in THF (45 mL) at 0 °C was added $n\text{-BuLi}$ (1.6 M in hexane, 3.82 mL, 6.11 mmol). The pale yellow solution was stirred at 0 °C for 10 min then cooled to -78 °C. **66** (1.10 g, 3.22 mmol) in THF (17 mL) was added dropwise and the resulting solution let to stir at -78 °C for 2 h. Sat. aq. NH_4Cl and Et_2O were added and the solution let to warm up to rt. The aqueous layer was extracted three times with Et_2O . The organic phase was washed with brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was passed on a pad of silica gel, washing pentane/ Et_2O (1:1) to give **67** (1.03 g, 94%) as a pale yellow oil.

$R_f=0.13$ (pentane/ Et_2O , 2:1); $^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ 4.28 (d, $J = 11.6$ Hz, 1H), 3.82–3.73 (m, 2H), 3.67–3.64 (m, 1H), 2.38 (d, $J = 18.8$ Hz, 1H), 1.99–1.92 (m, 2H), 1.56–1.54 (m, 1H), 1.35–1.29 (m, 2H), 1.06 (s, 3H), 1.03 (s, 3H), 0.94 (s, 3H), 0.89 (s, 9H), 0.06 (s, 6H) ppm; $^{13}\text{C-NMR}$ (CDCl_3 , 101 MHz): δ 171.4, 76.2, 75.5, 74.8, 43.9, 39.9, 39.9, 37.4, 27.4, 26.0 (3C), 25.9, 24.1, 21.3, 19.6, -4.4, -4.8 ppm; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{18}\text{H}_{35}\text{O}_4\text{Si}$ 343.2299, found 343.2296.

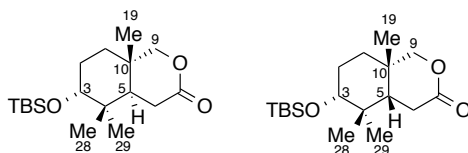
(6*R*,8*aS*)-6-((*tert*-Butyldimethylsilyl)oxy)-5,5,8*a*-trimethyl-6,7,8,8*a*-tetrahydro-1*H*-isochromen-3(5*H*)-one (28)



To a solution of **67** (1.03 g, 3.01 mmol) in DCM (30 mL) at 0 °C were added pyridine (12.2 mL, 150 mmol) and SOCl_2 (5.49 mL, 75.0 mmol). The mixture was stirred at 0 °C for 45 min. Sat. aq. NaHCO_3 and DCM were added. The aqueous layer was extracted three times with DCM. The organic phase was washed with NaHCO_3 , aq. CuSO_4 and brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2 ; pentane/ Et_2O , 3:1) to give **28** (750 mg, 77%) as a pale yellow oil.

$R_f=0.39$ (pentane/ Et_2O , 2:1); $^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ 5.84 (s, 1H), 3.97 (d, $J = 10.5$ Hz, 1H), 3.87 (d, $J = 10.6$ Hz, 1H), 3.60 (dd, $J = 4.0$, 1.7 Hz, 1H), 2.09 (tdd, $J = 14.1$, 4.1, 1.7 Hz, 1H), 1.75 (td, $J = 13.4$, 4.3 Hz, 1H), 2.14 (dtd, $J = 14.2$, 4.1, 2.7 Hz, 1H), 1.35 (s, 3H), 1.29–1.24 (m, 1H), 1.16 (s, 3H), 1.16 (s, 3H), 0.86 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H) ppm; $^{13}\text{C-NMR}$ (CDCl_3 , 101 MHz): δ 173.4, 165.9, 114.9, 78.9, 76.3, 41.6, 34.7, 28.4, 27.5, 26.6, 26.0 (3C), 25.2, 24.5, 18.2, -4.2, -4.9 ppm; IR (thin film): ν 2954, 2860, 1712, 1459, 1246, 1064, 832, 774 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{18}\text{H}_{33}\text{O}_3\text{Si}$ 325.2193, found 325.2193; $[\alpha]_D^{22} -108.9$ (c 0.535, CHCl_3).

(4a*R*,6*R*,8a*S*)-6-((*tert*-Butyldimethylsilyl)oxy)-5,5,8a-trimethylhexahydro-1*H*-isochromen-3(4*H*)-one (26)
and (4a*S*,6*R*,8a*S*)-6-((*tert*-Butyldimethylsilyl)oxy)-5,5,8a-trimethylhexahydro-1*H*-isochromen-3(4*H*)-one (27)



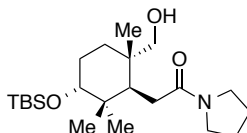
Lithium wire (457 mg, 28.2 mmol) was dissolved in ammonia (ca. 24 mL) at -78°C under N_2 . A solution of **28** (457 mg, 1.41 mmol) in *t*BuOH / THF (1.2 mL/3.0 mL) was added dropwise. The dark blue mixture was stirred at -78°C for 1 h and at -33°C for 2 h. Isoprene was then added dropwise until the blue color disappeared, then solid NH_4Cl (1.3 g) was added portionwise. Ammonia was removed under a stream of N_2 while the mixture was let to warm up to rt. Et_2O was added, followed by sat. aq. NH_4Cl . The aqueous layer was extracted three times with Et_2O . The organic phase was washed with brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure to give a mixture of lactols that were oxidized directly.

Fetizon reagent (2.27 g, 4.11 mmol) was added in 5 portions over 1 h to a refluxing solution of the crude from the previous step in toluene (14 mL) at 115°C . The slurry was stirred at 115°C for 3 h, then cooled to rt. It was then filtered on a pad of celite, washing EtOAc , and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2 ; pentane/ Et_2O , 4:1) to give **26** (243 mg, 54%) and **27** (100 mg, 22 %). The relative stereochemistry of **27** was determined by NOESY analysis.

Data for **26**: For full characterization, *vide supra*. ^1H -NMR (CDCl_3 , 600 MHz): δ 3.90 (dd, $J = 10.4, 0.9$ Hz, 1H), 3.83 (d, $J = 10.4$ Hz, 1H), 3.46 (dd, $J = 3.5, 1.9$ Hz, 1H), 2.56 (dd, $J = 18.6, 6.1$ Hz, 1H), 2.40 (dd, $J = 18.6, 13.8$ Hz, 1H), 2.06 (dd, $J = 13.7, 6.1$ Hz, 1H), 1.97–1.89 (m, 1H), 1.61–1.57 (m, 2H), 1.16–1.12 (m, 1H), 1.09 (s, 3H), 0.90 (s, 9H), 0.86 (s, 3H), 0.83 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H) ppm; ^{13}C -NMR (CDCl_3 , 150 MHz): δ 171.8, 83.9, 75.6, 40.2, 37.3, 32.9, 28.8, 27.7, 27.5, 26.1 (3C), 25.0, 20.5, 18.3, 17.4, -4.3 , -4.7 ppm.

Data for **27**: $R_f=0.28$ (pentane/ Et_2O , 2:1); ^1H -NMR (CDCl_3 , 600 MHz): δ 4.47 (d, $J = 11.7$ Hz, 1H), 3.84 (dd, $J = 11.7, 1.5$ Hz, 1H), 3.31–3.29 (m, 1H), 2.68–2.62 (m, 2H), 1.60–1.57 (m, 2H), 1.55–1.52 (m, 1H), 1.44–1.42 (m, 1H), 1.41–1.38 (m, 1H), 1.13 (s, 3H), 0.96 (s, 3H), 0.89 (s, 9H), 0.87 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H) ppm; ^{13}C -NMR (CDCl_3 , 101 MHz): δ 171.4, 77.9, 76.0, 46.7, 39.8, 32.9, 31.3, 29.1, 28.7, 28.7, 27.5, 26.0 (3C), 18.2, 16.0, -3.8 , -4.8 ppm; ^1H - ^1H -NOESY (CDCl_3 , 600 MHz, relevant cross-peaks): δ 1.43 and 1.16 [H(5)–C(19) H_3], 1.43 and 0.96 [H(5)–C(28) H_3] ppm; IR (thin film): ν 2928, 2856, 1729, 1470, 1254, 1073, 1054, 833, 772, 670 cm^{-1} ; HRMS (ESI) m/z : $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{18}\text{H}_{35}\text{O}_3\text{Si}$ 327.2350, found 327.2353; $[\alpha]_{\text{D}}^{23} -1.4$ (c 0.330, CHCl_3).

2-((1*R*,3*R*,6*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-6-(hydroxymethyl)-2,2,6-trimethylcyclohexyl)-1-(pyrrolidin-1-yl)ethanone (29)

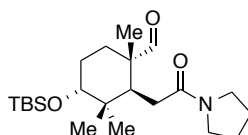


A solution of **26** (243 mg, 0.744 mmol), pyrrolidine (308 μL , 3.72 mmol) and Et_3N (2.07 mL, 14.9 mmol) was stirred at reflux at 80°C for 12 h. The solution was then cooled to rt. Water and Et_2O were added. The aqueous layer was extracted three times with Et_2O . The organic phase was washed with water and brine, dried over

Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂; Et₂O) to give **29** (208 mg, 70%) as a white solid.

R_f =0.28 (pentane/Et₂O, 1:2); ¹H-NMR (CDCl₃, 400 MHz): δ 4.73 (d, J = 9.9 Hz, 1H), 3.54–3.44 (m, 4H), 3.41 (dd, J = 3.3, 1.6 Hz, 1H), 3.17 (d, J = 12.1 Hz, 1H), 2.77 (t, J = 10.8 Hz, 1H), 2.66 (dd, J = 6.1, 3.2 Hz, 1H), 2.46 (dd, J = 13.8, 4.0 Hz, 1H), 2.18 (dd, J = 17.6, 3.2 Hz, 1H), 2.11 (dd, J = 17.6, 6.1 Hz, 1H), 2.02–1.95 (m, 2H), 1.92–1.83 (m, 3H), 1.50 (app. dq, J = 14.0, 3.5 Hz, 1H), 0.92 (s, 9H), 0.88 (s, 3H), 0.83 (s, 3H), 0.83–0.80 (m, 1H), 0.70 (s, 3H), 0.05 (s, 3H), 0.02 (s, 3H) ppm; ¹³C-NMR (CDCl₃, 101 MHz): δ 173.5, 76.2, 70.9, 46.8, 46.3, 39.4, 39.0, 36.1, 30.5, 29.1, 28.1, 26.2, 26.1 (3C), 25.7, 24.5, 22.9, 18.5, 18.4, –4.1, –4.7 ppm; IR (thin film): ν 3358, 2952, 2857, 1613, 1440, 1360, 1250, 1078, 832, 773 cm^{–1}; HRMS (ESI) m/z : [M+H]⁺ Calcd for C₂₂H₄₄NO₃Si 398.3085, found 398.3087; [α]_D²³ –50.9 (c 0.860, CHCl₃).

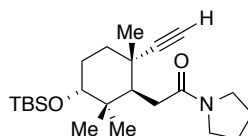
(1*S*,2*S*,4*R*)-4-((*tert*-Butyldimethylsilyl)oxy)-1,3,3-trimethyl-2-(2-oxo-2-(pyrrolidin-1-yl)ethyl)cyclohexane carbaldehyde (68**)**



Dess-Martin periodinane (266 mg, 0.628 mmol) was added portionwise to a solution of **29** (208 mg, 0.523 mmol) in DCM (5.2 mL) at 0 °C. The mixture was stirred at rt for 1 h. A mixture of NaHCO₃/Na₂S₂O₃ (1:1) was added to the mixture, which was stirred vigorously for 30 min at rt. The aqueous layer was extracted three times with DCM. The organic phase was washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure to afford **68** (200 mg, 97 %), which was used in the next step without further purification.

R_f =0.67 (Et₂O); ¹H-NMR (CDCl₃, 400 MHz): δ 9.30 (s, 1H), 3.45 (dd, J = 4.6, 2.1 Hz, 1H), 3.40 (q, J = 6.6 Hz, 4H), 2.91 (dd, J = 7.4, 4.3 Hz, 1H), 2.22 (dd, J = 16.3, 4.3 Hz, 1H), 2.13 (td, J = 12.9, 12.3, 3.4 Hz, 1H), 2.01 (dd, J = 16.3, 7.4 Hz, 1H), 1.78–1.95 (m, 5H), 1.56 (app. dq, J = 13.9, 4.2 Hz, 1H), 1.06 (s, 3H), 0.93 (s, 9H), 0.91 (s, 3H), 0.90 (s, 3H), 0.05 (s, 6H) ppm; ¹³C-NMR (CDCl₃, 101 MHz): δ 205.8, 170.6, 77.2, 75.8, 50.0, 46.6, 46.0, 38.2, 37.4, 31.5, 28.1, 26.3, 26.1 (3C), 26.1, 25.0, 24.4, 23.3, 18.3, 15.6, –4.2, –4.7 ppm; IR (thin film): ν 2952, 2858, 1981, 1722, 1646, 1430, 1339, 1254, 1079, 1010, 835, 773 cm^{–1}; HRMS (ESI) m/z : [M+H]⁺ Calcd for C₂₂H₄₂NO₃Si 396.2928, found 396.2933; [α]_D²⁴ –34.7 (c 0.580, CHCl₃).

2-((1*R*,3*R*,6*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-6-ethynyl-2,2,6-trimethylcyclohexyl)-1-(pyrrolidin-1-yl) ethanone (30**)**

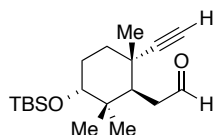


A solution of dimethyl (diazomethyl)phosphonate (152 mg, 1.01 mmol) in THF (3.2 mL) was added dropwise to a suspension of KO^tBu (111 mg, 0.986 mmol) in THF (3.2 mL) at –78 °C. The mixture was stirred for 10 min at –78 °C, then a solution of **68** (200 mg, 0.505 mmol) in THF (3.2 mL) was added dropwise. The mixture was stirred at –78 °C for 2 h then let to warm up to rt over 12 h. Water and Et₂O were added. The aqueous layer was extracted three times with Et₂O. The organic phase was washed with brine, dried over Na₂SO₄, filtered and

concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂; pentane/Et₂O, 1:1) to give **30** (180 mg, 91%) as a white solid.

R_f =0.34 (pentane/Et₂O, 1:2); ¹H-NMR (CDCl₃, 300 MHz): δ 3.52 (tt, J = 6.1, 3.3 Hz, 2H), 3.44 (t, J = 6.8 Hz, 2H), 3.38–3.36 (m, 1H), 2.78 (dd, J = 7.1, 4.5 Hz, 1H), 2.50 (dd, J = 15.7, 4.5 Hz, 1H), 2.34–2.21 (m, 2H), 2.05 (s, 1H), 1.99–1.90 (m, 2H), 1.86–1.77 (m, 3H), 1.53–1.50 (m, 1H), 1.47–1.44 (m, 1H), 1.23 (s, 3H), 0.92 (s, 9H), 0.89 (s, 3H), 0.87 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H) ppm; ¹³C-NMR (CDCl₃, 101 MHz): δ 172.0, 93.9, 76.1, 67.5, 46.8, 46.1, 42.3, 39.4, 35.5, 33.6, 33.3, 28.8, 26.4, 26.2 (3C), 25.7, 24.5, 23.0, 22.6, 18.4, –4.2, –4.7 ppm; IR (thin film): ν 2952, 2858, 1646, 1426, 1253, 1078, 1039, 1009, 835, 772, 626 cm^{–1}; HRMS (ESI) m/z : [M+H]⁺ Calcd for C₂₃H₄₂NO₂Si 392.2979, found 392.2975; [α]_D²² –32.7 (c 0.185, CHCl₃).

2-((1*R*,3*R*,6*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-6-ethynyl-2,2,6-trimethylcyclohexyl) acetaldehyde (**6**)

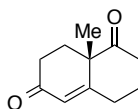


Ti(OiPr)₄ (123 μ L, 0.421 mmol) was added to a mixture of **30** (165 mg, 0.421 mmol) and diphenylsilane (118 μ L, 0.632 mmol) at rt. The mixture was stirred at rt for 12 h. The mixture was then diluted with THF (6 mL) and treated with sat. aq. NaHCO₃ (6 mL). It was then stirred vigorously for 3 h before being diluted with Et₂O. The aqueous layer was extracted three times with Et₂O. The organic phase was washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂; pentane/Et₂O, 1:1) to give **6** (83 mg, 61%) as a pale yellow oil.

For full characterization, see experimental section in manuscript (p.7).

¹H-NMR (CDCl₃, 400 MHz): δ 9.75 (dd, J = 3.3, 1.8 Hz, 1H), 3.42–3.41 (m, 1H), 2.64–2.58 (m, 2H), 2.39 (ddd, J = 17.9, 8.0, 3.3 Hz, 1H), 2.33–2.22 (m, 1H), 2.14 (s, 1H), 1.85–1.77 (m, 1H), 1.58–1.47 (m, 2H), 1.20 (s, 3H), 0.93 (s, 9H), 0.85 (s, 3H), 0.82 (s, 3H), 0.06 (s, 3H), 0.04 (s, 3H) ppm.

(*S*)-8a-Methyl-3,4,8,8a-tetrahydronaphthalene-1,6(2*H*,7*H*)-dione (**32**)⁸



A flask was charged with 2-methyl-2-(3-oxobutyl)cyclohexane-1,3-dione (30.1 g, 153 mmol)⁸, (*S*)-*N*-((*S*)-2'-(4-methylphenylsulfonamido)-[1,1'-binaphthalen]-2-yl)pyrrolidine-2-carboxamide⁹ (974 mg, 1.53 mmol), and benzoic acid (468 mg, 3.83 mol) and the slurry was stirred at rt for 5 days. It was then diluted with EtOAc, and activated charcoal (6 g) was added. The black slurry was stirred at rt for 15 h. Hexanes was added and the slurry was filtered through a pad of SiO₂, washing hexane/EtOAc (1:1). The filtrate was concentrated under reduced pressure. The residue was dissolved in *t*BuOMe (30 mL) at 45 °C, then let to cool down to rt and let to stand in the freezer for 12 h to crystallized. The supernatant liquid was removed and the crystals were dried under high vacuum to afford **32** (19.8 g, 72%).

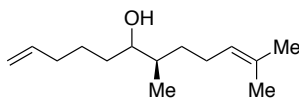
⁸ The compound was prepared according to: B. Bradshaw, G. Etxeberria-Jardí, J. Bonjoch, S. F. Vióquez, S. F.; G. Guillena and C. Nájera, *Org. Synth.*, 2011, **88**, 330.

⁹ The chiral catalyst was prepared according to: B. Bradshaw, G. Etxeberria-Jardí, J. Bonjoch, S. F. Vióquez, S. F.; G. Guillena and C. Nájera, *Org. Synth.*, 2011, **88**, 317.

The analytical data were found to be in accordance with the one reported in the literature.⁸

R_f =0.50 (EtOAc); Melting point: 49 °C; ¹H-NMR (CDCl₃, 400 MHz): δ 5.85 (s, 1H), 2.78–2.65 (m, 2H), 2.53–2.42 (m, 4H), 2.19–2.07 (m, 3H), 1.78–1.62 (m, 1H), 1.45 (s, 3H) ppm; HRMS (EI) m/z : [M]⁺ Calcd for C₁₁H₁₄O₂ 178.0989, found 178.0990; [α]_D²² +88.9 (*c* 1.00, CHCl₃); SFC (column IA; CO₂/*i*PrOH, 95:5; 2.00 mL.min⁻¹; 100 bar; 25 °C): minor enantiomer t_R = 3.850, major enantiomer t_R = 4.017, 98.2% *ee*.

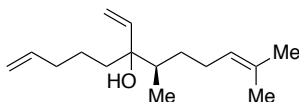
(7*R*)-7,11-Dimethyldodeca-1,10-dien-6-ol (40)



Magnesium turnings (2.01 g, 83.0 mmol) were added to THF (57 mL) at rt. 5-bromopent-1-ene (7.34 mL, 62.0 mmol) was added dropwise and the resulting brown mixture was stirred at rt for 2 h. Crude aldehyde **39**¹⁰ was dissolved in THF (54 mL) and cooled to –78 °C. The solution containing the Grignard reagent was added dropwise to the aldehyde solution *via* a cannula. The mixture was stirred at –78 °C for 20 min then warmed up to 0 °C and stirred at 0 °C for 30 min. NH₄Cl and Et₂O were added. The aqueous layer was extracted three times with Et₂O. The organic phase was washed with brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂; pentane/Et₂O, 15:1 to 5:1) to give **40** (2.62 g, 37% over 2 steps) as a mixture of diastereoisomers along some unidentified impurities.

R_f =0.29 (hexane/EtOAc, 8:1); ¹H-NMR (CDCl₃, 400 MHz): δ 5.82 (ddt, *J* = 16.9, 10.1, 6.7 Hz, 1H), 5.10 (tdt, *J* = 7.1, 2.9, 1.4 Hz, 1H), 5.01 (ddd, *J* = 17.1, 1.7 Hz, 1H), 4.95 (ddt, *J* = 10.2, 2.2, 1.2 Hz, 1H), 3.53–3.50 (m, 1H), 2.11–2.02 (m, 3H), 1.99–1.91 (m, 1H), 1.69 (d, *J* = 0.8 Hz, 3H), 1.61 (s, 3H), 1.58–1.53 (m, 1H), 1.50–1.37 (m, 4H), 1.24–1.16 (m, 2H), 0.90 (d, *J* = 6.8 Hz, 1H), 0.88 (d, *J* = 6.8 Hz, 2H) ppm; ¹³C-NMR (CDCl₃, 101 MHz, the asterisk denotes the signals for the minor diastereoisomer): δ 138.9, 131.6, 124.8*, 124.7, 114.7, 76.0*, 75.1, 38.6*, 37.9, 34.0, 33.9, 33.5, 32.9, 32.2, 31.0, 25.9, 25.9, 25.8*, 25.7, 25.6, 17.8, 17.8*, 15.3*, 13.7 ppm; IR (thin film): ν 3384, 2926, 2860, 1641, 1456, 1377, 1084, 991, 909, 634 cm⁻¹; HRMS (EI) m/z : [M–CH₃]⁺ Calcd for C₁₃H₂₃O 195.1744, found 195.1742.

(7*R*)-7,11-Dimethyl-6-vinyldodeca-1,10-dien-6-ol (41)



Pyridine (7.21 mL, 89.0 mmol) was added to a suspension of Dess-Martin periodinane (7.56 g, 17.8 mmol) in DCM (70 mL) at 0 °C and the solution was stirred at 0 °C for 10 min. A solution of **40** (2.52 g, 12.0 mmol) in DCM (49 mL) was then added dropwise and the mixture was stirred while warming up to rt over 2 h. The mixture was then poured into a stirred mixture of NaHCO₃/Et₂O (1:1). The aqueous layer was extracted three times with DCM. The organic phase was washed with Na₂S₂O₃ and brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure to give the ketone which was used in the next step without further purification.

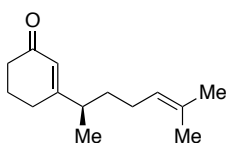
The crude product was dissolved in THF (50 mL), cooled to –78 °C and treated with a solution of vinyl magnesium bromide (1 M in THF, 20.2 mL, 20.2 mmol). The resulting solution was stirred at –78 °C for 1 h,

¹⁰ Aldehyde **39** was prepared from 5.12 g of 2,2-dimethyl-3-((*R*)-3-methylpent-4-en-1-yl)oxirane according to the procedure described in: B. V. Burger, W. G. B. Petersen, W. G. Weber and Z. M. Munro, *J. Chem. Ecol.*, 2002, **28**, 2527.

then let to warm up to rt over 2 h and stirred at rt for 2 h. NH_4Cl and Et_2O were added. The aqueous layer was extracted three times with Et_2O . The organic phase was washed with brine, dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2 ; pentane/ Et_2O , 15:1) to give **41** (2.01 g, 71% over 2 steps) as a mixture of diastereoisomers.

R_f =0.26 (pentane/ Et_2O , 15:1); $^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ 5.86–5.74 (m, 2H), 5.19 (ddd, J = 17.4, 4.8, 1.5 Hz, 1H), 5.13 (ddd, J = 10.9, 5.2, 1.5 Hz, 1H), 5.13–5.07 (m, 1H), 5.03–4.97 (m, 1H), 4.97–4.92 (m, 1H), 2.11–2.02 (m, 3H), 1.93–1.83 (m, 1H), 1.68 (s, 3H), 1.60 (s, 3H), 1.61–1.47 (m, 4H), 1.44–1.36 (m, 2H), 1.04–0.95 (m, 1H), 0.89 (t, J = 6.8 Hz, 3H) ppm; $^{13}\text{C-NMR}$ (CDCl_3 , 101 MHz): δ 142.9, 142.4, 138.9, 124.8, 124.7*, 114.7, 114.7*, 113.1, 113.0*, 78.0, 77.9*, 41.4, 41.2*, 37.9, 37.9*, 34.3, 34.3*, 31.7, 30.8*, 26.5, 26.5*, 25.9, 22.9, 22.7*, 17.8, 14.4, 13.2* ppm; IR (thin film): ν 3384, 2926, 2860, 1641, 1456, 1377, 1084, 991, 909, 634 cm^{-1} ; HRMS (EI) m/z : $[\text{M}-\text{C}_2\text{H}_5]^+$ Calcd for $\text{C}_{14}\text{H}_{25}\text{O}$ 209.1900, found 209.1906.

(*R*)-3-(6-Methylhept-5-en-2-yl)cyclohex-2-enone (**43**)



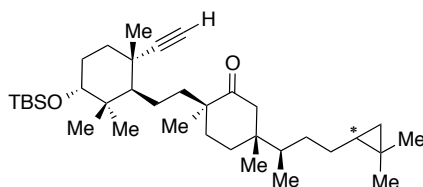
Grubbs I catalyst (139 mg, 0.169 mmol) was added portionwise to a solution of **41** (2.00 g, 8.46 mmol) in DCM (42 mL) at rt. The mixture was stirred at rt for 12 h, then concentrated carefully under reduced pressure. It was passed through a small pad of silica, washing pentane/ Et_2O (8:1). The volatile oil was subjected to the next step without further purification.

A solution of the above crude dissolved in DCM (30 mL) was added dropwise to a suspension of PCC (2.17 g, 10.1 mmol) and SiO_2 (2.17 g) in DCM (37 mL) at rt. The brown slurry was stirred at rt for 8 h. It was then filtered through a pad of silica, washing Et_2O , and the filtrate was carefully concentrated. The residue was purified by column chromatography (SiO_2 ; pentane/ Et_2O , 15:1 to 5:1) to give **43** (850 mg, 49% over 2 steps).

For full characterization, see experimental section in manuscript (p.10).

$^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ 5.87 (s, 1H), 5.06 (ddt, J = 8.4, 6.8, 1.4 Hz, 1H), 2.38–2.35 (m, 2H), 2.32–2.25 (m, 3H), 2.00–1.89 (m, 4H), 1.67 (s, 3H), 1.57 (s, 3H), 1.54–1.49 (m, 1H), 1.44–1.75 (m, 1H), 1.08 (d, J = 6.8 Hz, 3H) ppm; SFC (column AS-H; CO_2/iPrOH , 99:1; 2.00 $\text{mL}\cdot\text{min}^{-1}$; 100 bar; 25 $^\circ\text{C}$): minor enantiomer t_R = 8.600, major enantiomer t_R = 9.407, 69.1% *ee*.

(*2R,5R*)-2-(2-((*1R,3R,6S*)-3-((*tert*-Butyldimethylsilyl)oxy)-6-ethynyl-2,2,6-trimethylcyclohexyl)ethyl)-5-((*2R*)-4-(2,2-dimethylcyclopropyl)butan-2-yl)-2,5-dimethylcyclohexanone (**75**)

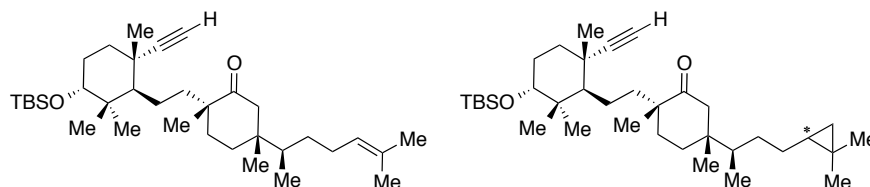


A solution of **58** (4.2 mg, 6.7 μmol) in EtOH (0.27 mL) was treated with aq. NaOH (0.5 M, 0.27 mL, 0.13 mmol), and the resulting mixture was refluxed at 100 $^\circ\text{C}$ for 12 h. The mixture was cooled to rt, EtOH was removed under reduced pressure and the residue was diluted with EtOAc. The aqueous layer was extracted three times with EtOAc. The organic phase was washed with 1 M HCl, water and brine, dried over Na_2SO_4 , filtered

and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂; hexane/EtOAc, 18:1) to afford **75** (2.5 mg, 67%) as a mixture of epimers along some minor unidentified impurities.

R_f =0.52 (hexane/EtOAc, 18:1); ¹H-NMR (CDCl₃, 600 MHz): δ 3.35–3.33 (m, 1H), 2.42 (app dd, J = 13.5, 4.5 Hz, 1H), 2.17–2.11 (m, 2H), 2.06 (s, 1H), 1.80–1.77 (m, 1H), 1.75–1.68 (m, 4H), 1.64–1.63 (m, 1H), 1.60–1.57 (m, 2H), 1.48–1.41 (m, 3H), 1.36–1.29 (m, 2H), 1.19 (s, 3H), 1.17–1.10 (m, 2H), 1.07 (s, 3H), 1.04 (s, 1.5H), 1.03 (s, 1.5H), 1.02 (s, 3H), 0.97–0.94 (m, 1H), 0.92 (s, 9H), 0.88 (br s, 3H), 0.81–0.79 (m, 9H), 0.42 (dddd, J = 12.1, 8.6, 5.2, 1.6 Hz, 1H), 0.35 (app dt, J = 8.3, 3.6 Hz, 1H), 0.04 (s, 3H), 0.04 (s, 3H), –0.12 (app t, J = 4.6 Hz, 0.5H), –0.16 (app t, J = 4.6 Hz, 0.5H) ppm; ¹³C-NMR (CDCl₃, 151 MHz): δ 216.7, 95.0, 75.9, 66.9, 49.1, 48.0, 47.1, 41.9, 41.4, 39.9, 38.6, 38.4, 35.8, 34.4, 34.4, 33.7, 31.4, 31.3, 31.3, 29.9, 29.2, 28.9, 27.8, 27.8, 26.2 (3C), 25.6, 25.1, 24.8, 22.7, 22.0, 21.9, 21.7, 20.0, 20.0, 19.8, 18.4, 15.7, 15.3, 14.3, 13.5, 13.4, –4.3, –4.7 ppm; HRMS (ESI) m/z : [M+NH₄]⁺ Calcd for C₃₆H₆₈NO₂Si 574.5014, found 574.5019.

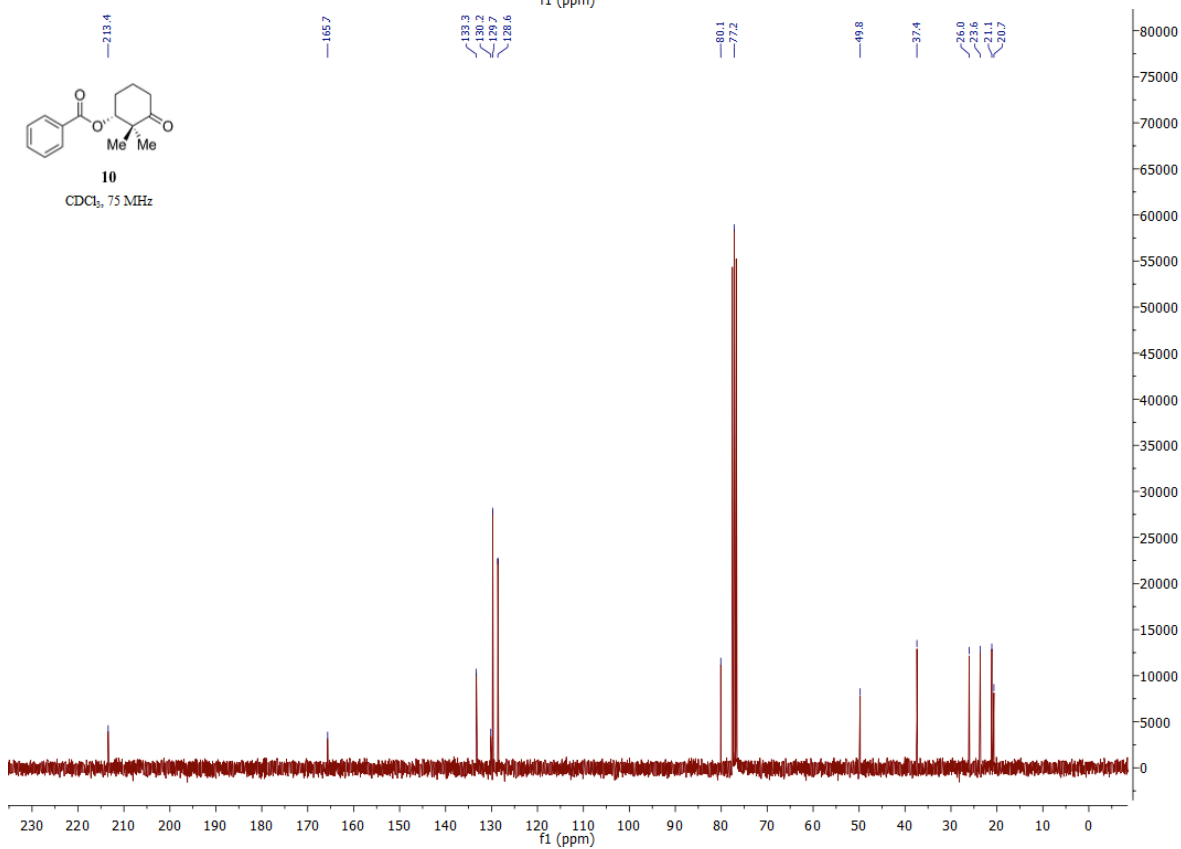
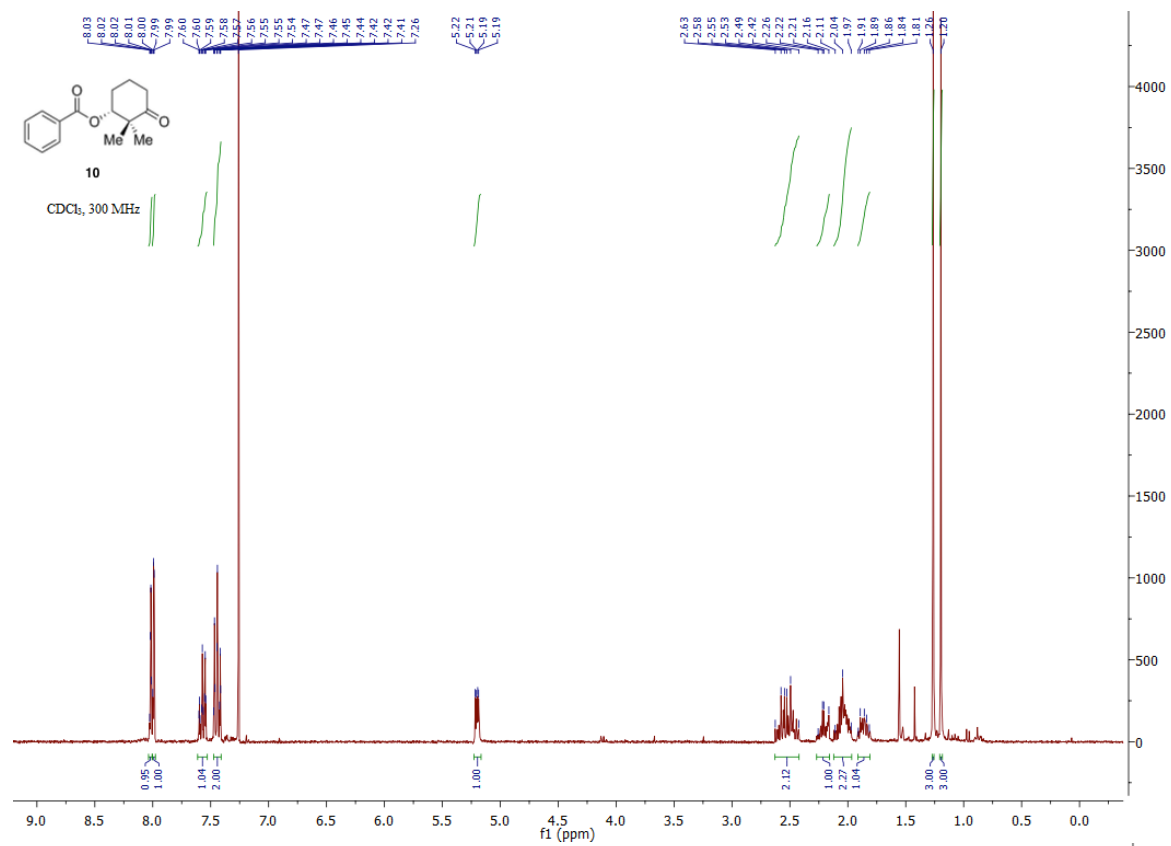
(2*S*,5*R*)-2-(2-((1*R*,3*R*,6*S*)-3-((*tert*-Butyldimethylsilyl)oxy)-6-ethynyl-2,2,6-trimethylcyclohexyl)ethyl)-2,5-dimethyl-5-((*R*)-6-methylhept-5-en-2-yl)cyclohexanone (76) and
(2*S*,5*R*)-2-(2-((1*R*,3*R*,6*S*)-3-((*tert*-butyldimethylsilyl)oxy)-6-ethynyl-2,2,6-trimethylcyclohexyl)ethyl)-5-((2*R*)-4-(2,2-dimethylcyclopropyl)butan-2-yl)-2,5-dimethylcyclohexanone (77)

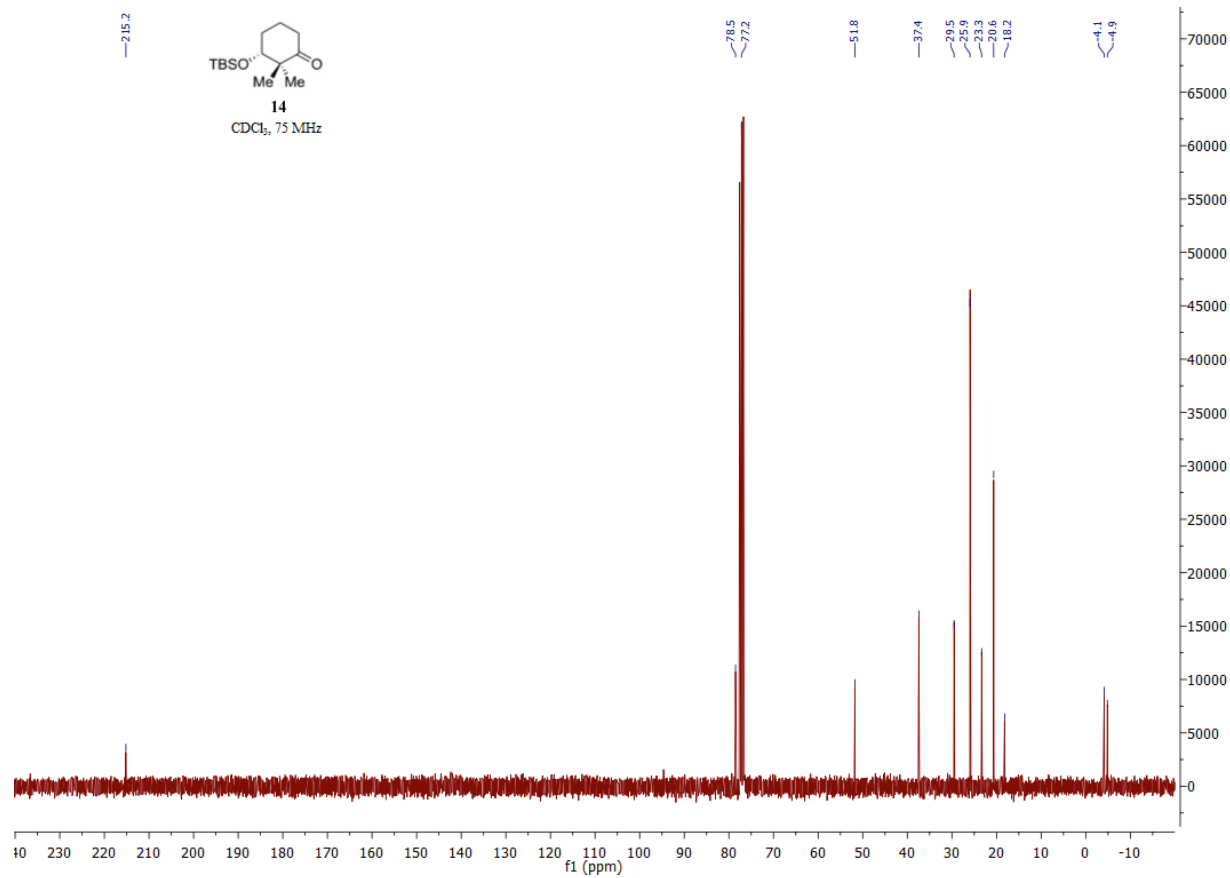
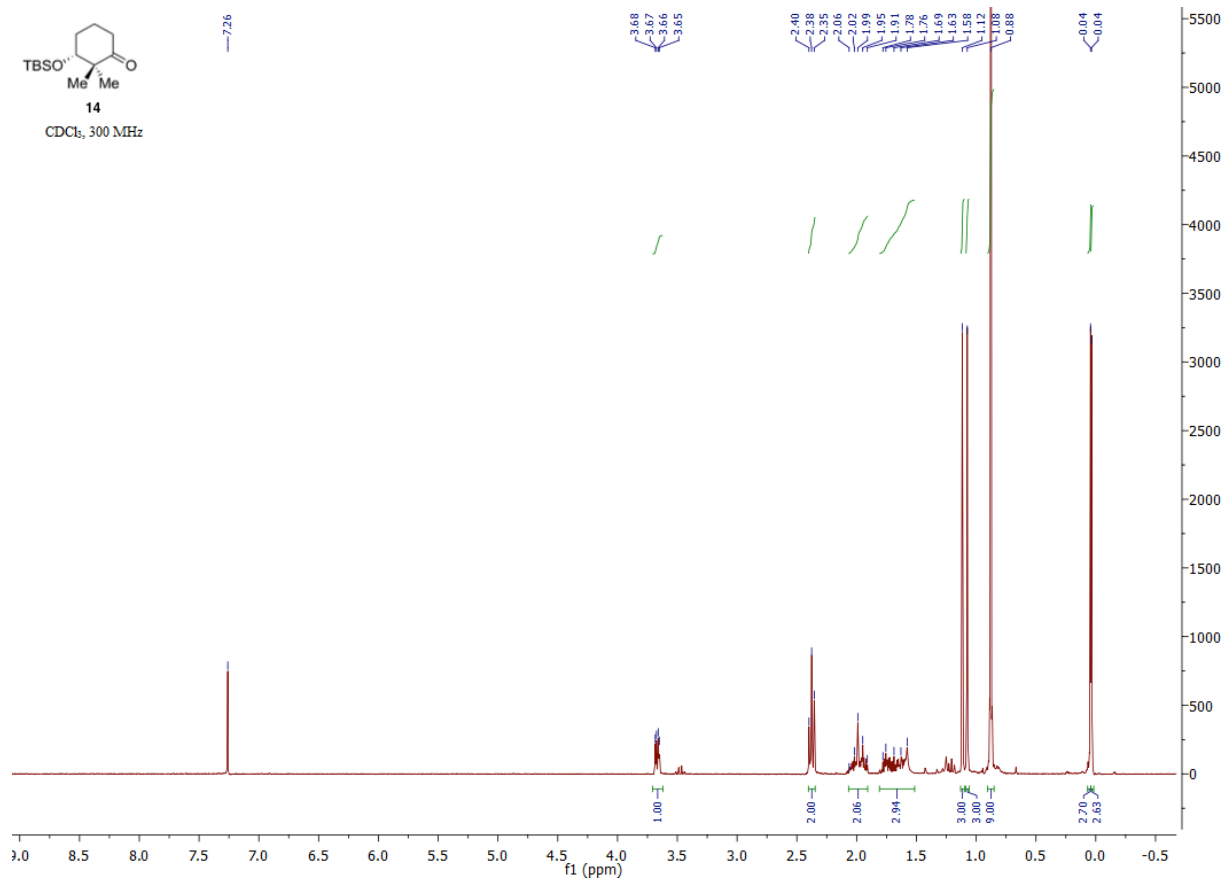


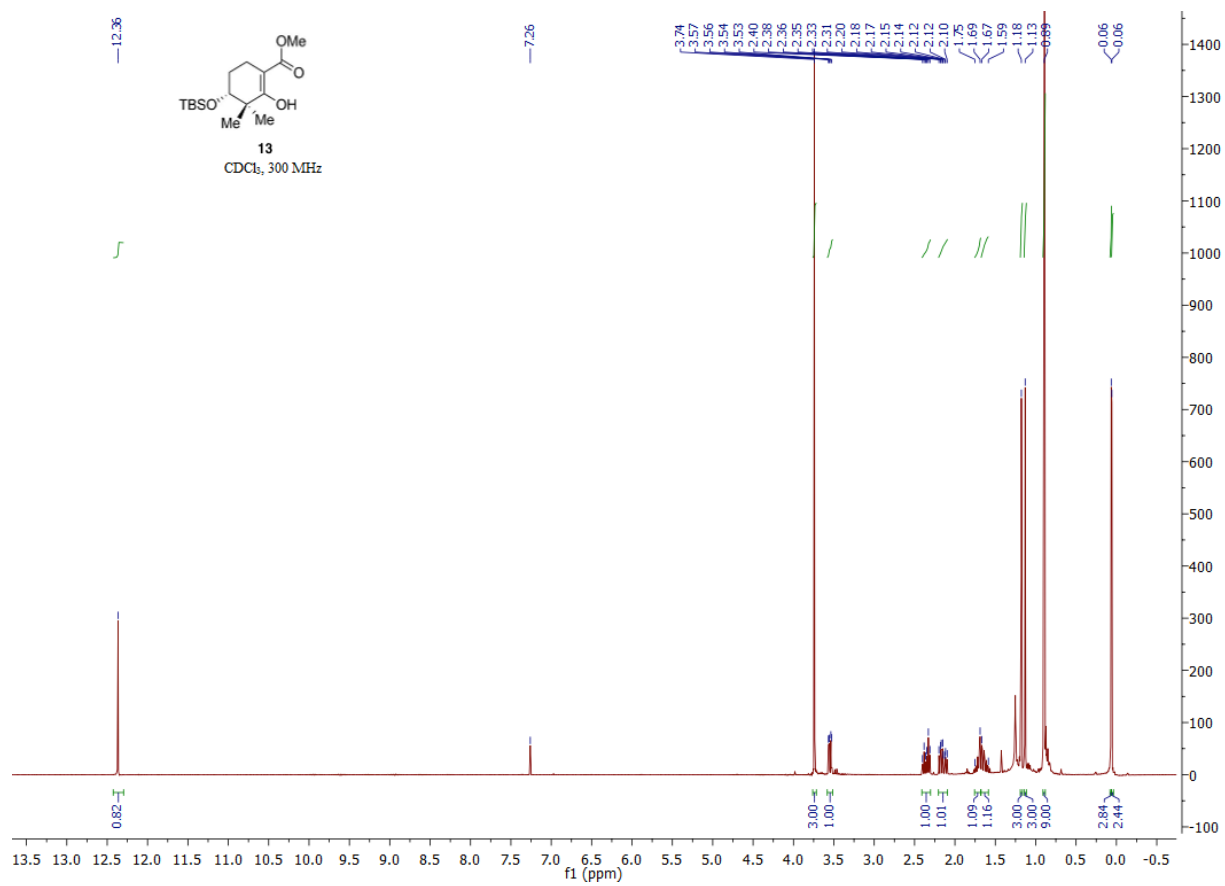
The mixture of **57** and **59** (1.7 mg) was dissolved in EtOH (0.11 mL) and treated with aq. NaOH (0.5 M, 0.11 mL, 55 μmol), and the resulting mixture was refluxed at 100 °C for 12 h. The mixture was cooled to rt, EtOH was removed under reduced pressure and the residue was diluted with EtOAc. The aqueous layer was extracted three times with EtOAc. The organic phase was washed with 1 M HCl, water and brine, dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (SiO₂; hexane/EtOAc, 18:1) to afford an inseparable mixture of **76** and **77** (1.1 mg, ca 2:3) along some minor unidentified impurities.

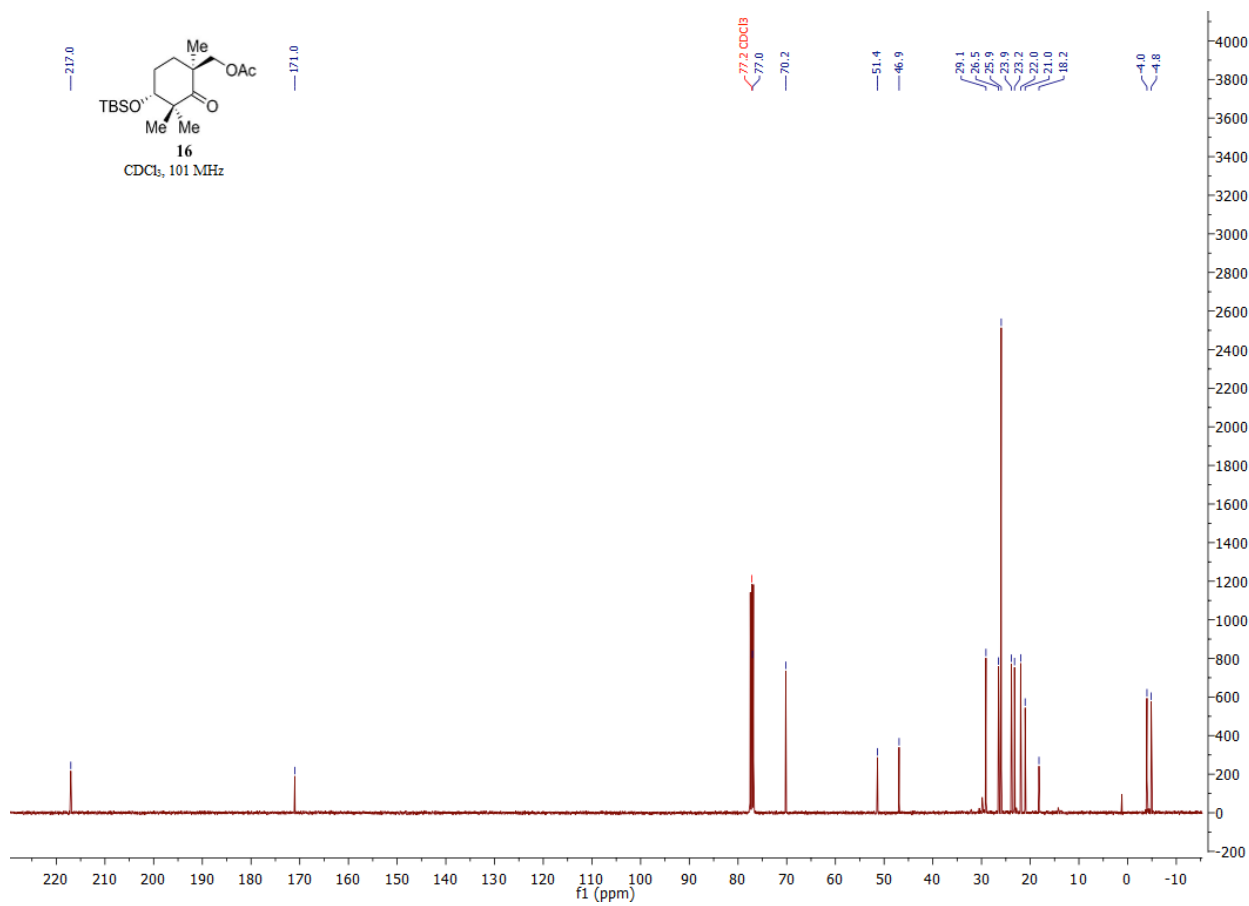
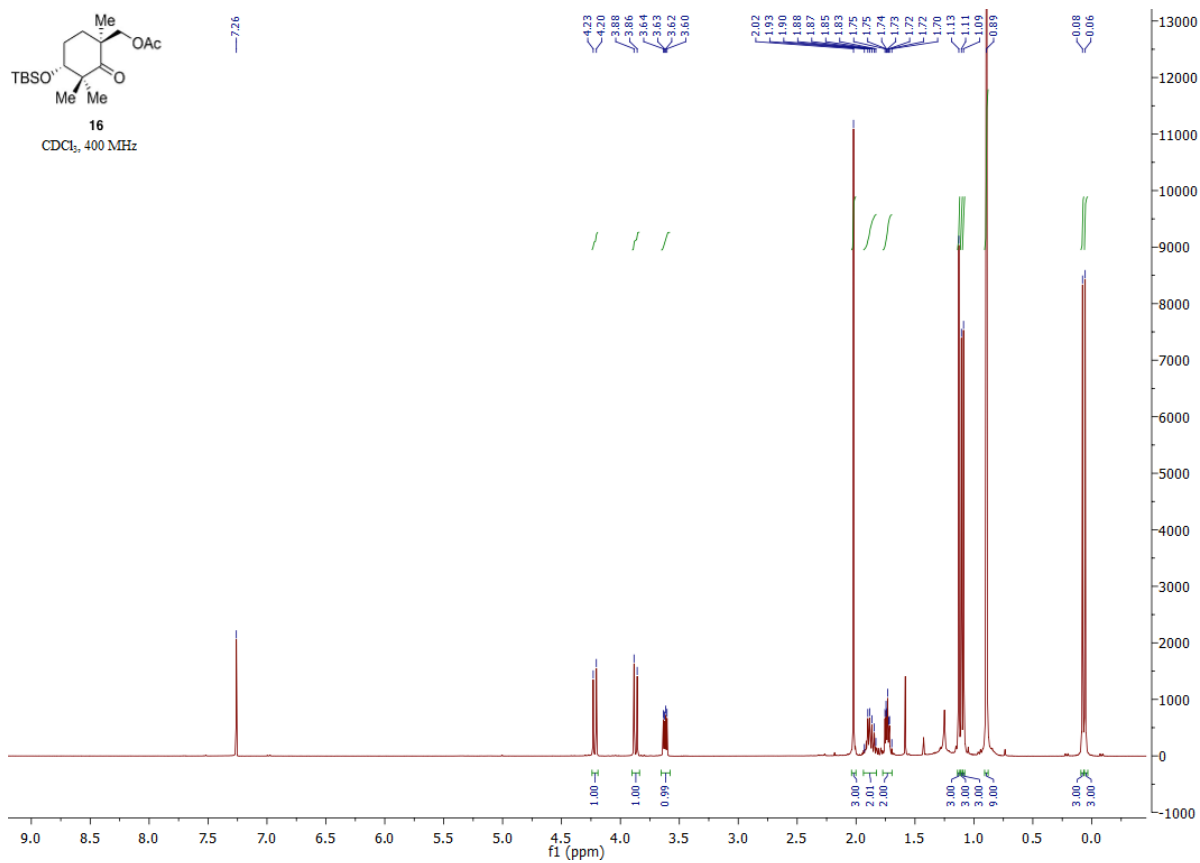
R_f =0.37 (hexane/EtOAc, 18:1); ¹H-NMR (CDCl₃, 600 MHz): δ 5.07 (app dtt, J = 8.0, 6.6, 1.5 Hz, 0.4H), 3.34 (br s, 1H), 2.53 (app t, J = 12.1 Hz, 1H), 2.36–2.25 (m, 2H), 2.13 (td, J = 13.0, 3.1 Hz, 1H), 2.08–2.04 (m, 2H), 2.03–2.02 (m, 1H), 1.91–1.83 (m, 2H), 1.80–1.74 (m, 1.6H), 1.73–1.69 (m, 1.4H), 1.68 (s, 1.2H), 1.66–1.61 (m, 3H), 1.60 (s, 1.8H), 1.47–1.40 (m, 3H), 1.36–1.29 (m, 3H), 1.14 (s, 3H), 1.04–1.01 (m, 6H), 0.98–0.95 (m, 2H), 0.93 (d, J = 1.0 Hz, 9H), 0.85–0.84 (m, 3H), 0.81 (m, 3H), 0.75 (app d, J = 10.6 Hz, 3H), 0.44–0.39 (m, 0.6H), 0.37–0.33 (m, 0.6H), 0.04 (app d, J = 3.7 Hz, 6H), –0.12––0.17 (m, 0.6H) ppm; ¹³C-NMR (CDCl₃, 151 MHz): δ 217.3, 217.2, 131.8, 124.7, 95.3, 75.8, 66.8, 48.9, 48.8, 48.7, 48.6, 48.5, 46.9, 44.1, 44.0, 43.5, 42.5, 42.5, 41.4, 41.4, 40.0, 36.4, 36.3, 35.8, 33.7, 32.1, 31.7, 31.6, 31.1, 30.3, 30.2, 30.1, 29.0, 27.8, 27.8, 26.8, 26.2, 25.9, 25.5, 25.1, 24.9, 22.9, 22.5, 22.3, 22.1, 22.1, 22.1, 21.8, 20.1, 20.0, 20.0, 19.9, 19.8, 19.8, 19.6, 18.4, 17.8, 14.0, 14.0, 13.7, 1.2, –4.2, –4.7 ppm; IR (thin film): ν 3311, 2926, 2855, 1705, 1462, 1377, 1258, 1096, 1076, 1009, 834, 773, 619 cm^{–1}; HRMS (ESI) m/z : [M+NH₄]⁺ Calcd for C₃₅H₆₆NO₂Si 560.4857, found 560.4853 and for C₃₆H₆₈NO₂Si 574.5014, found 574.5007.

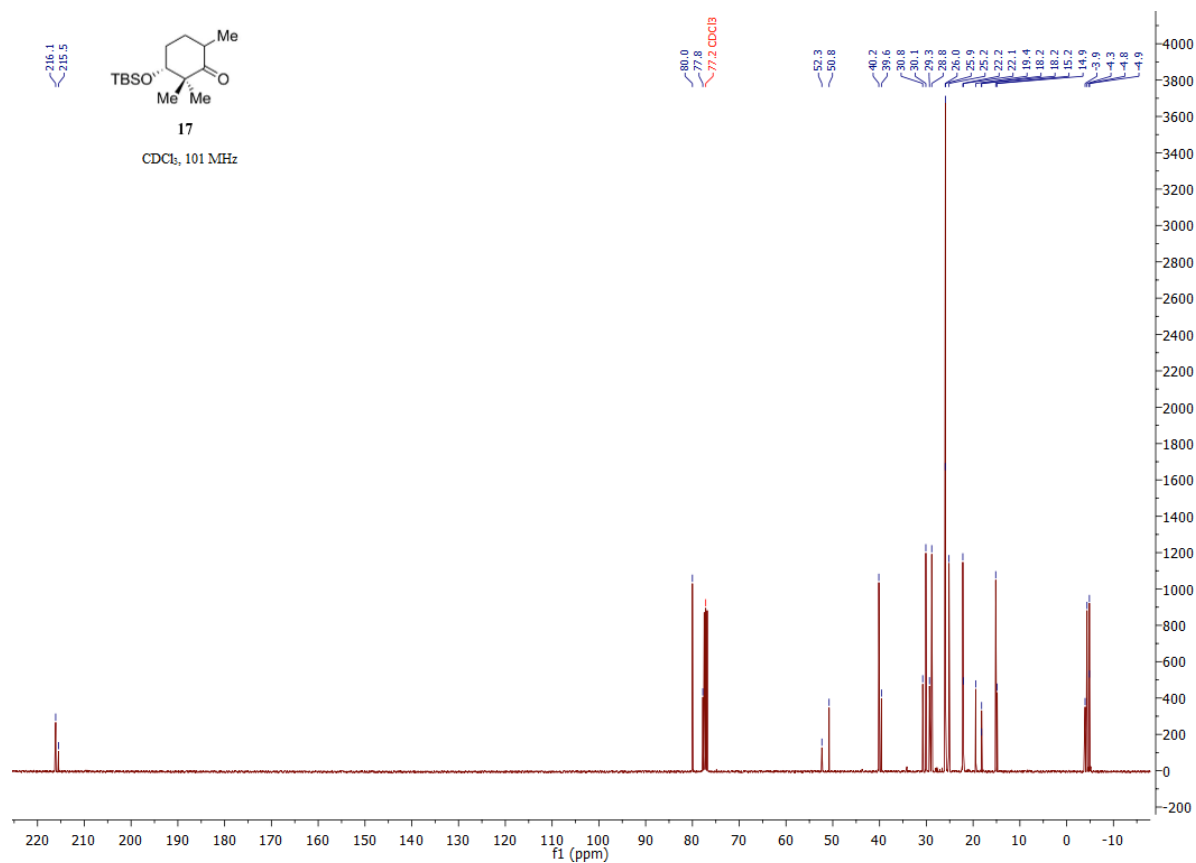
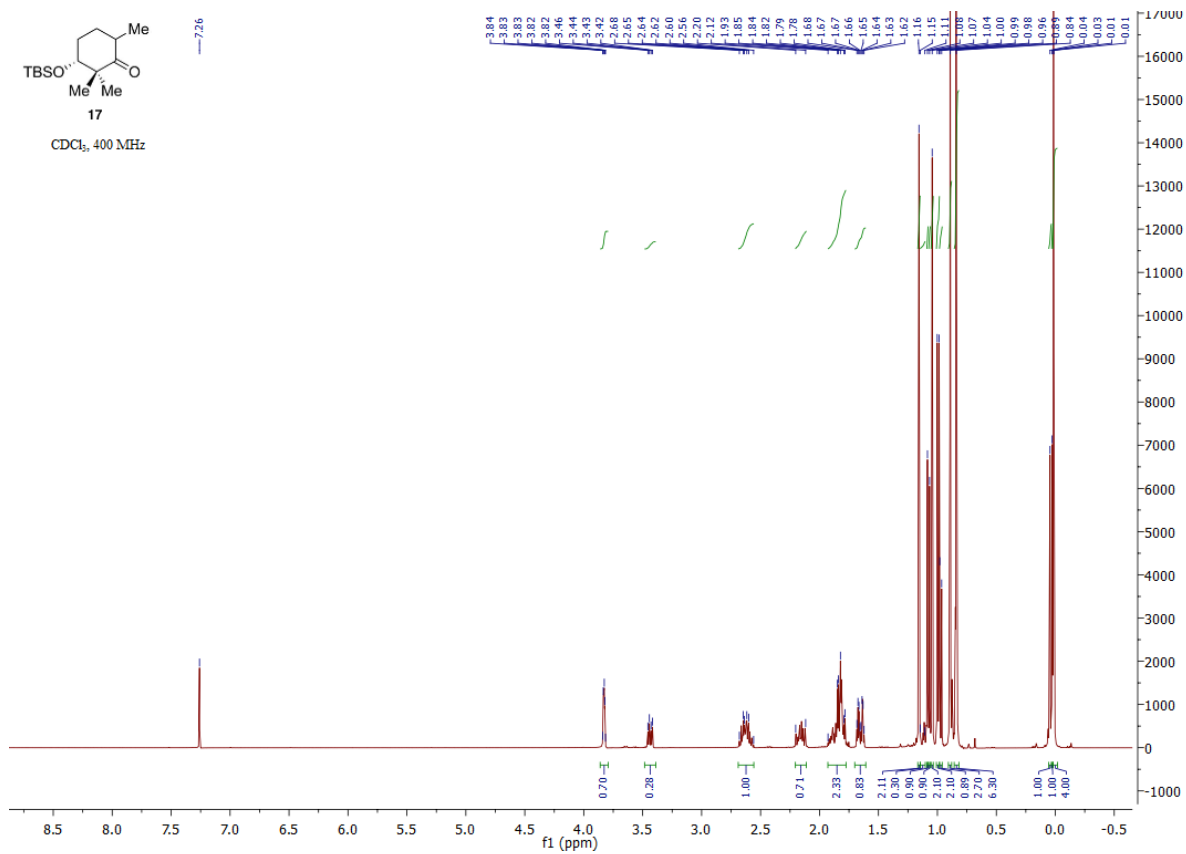
4. NMR spectra

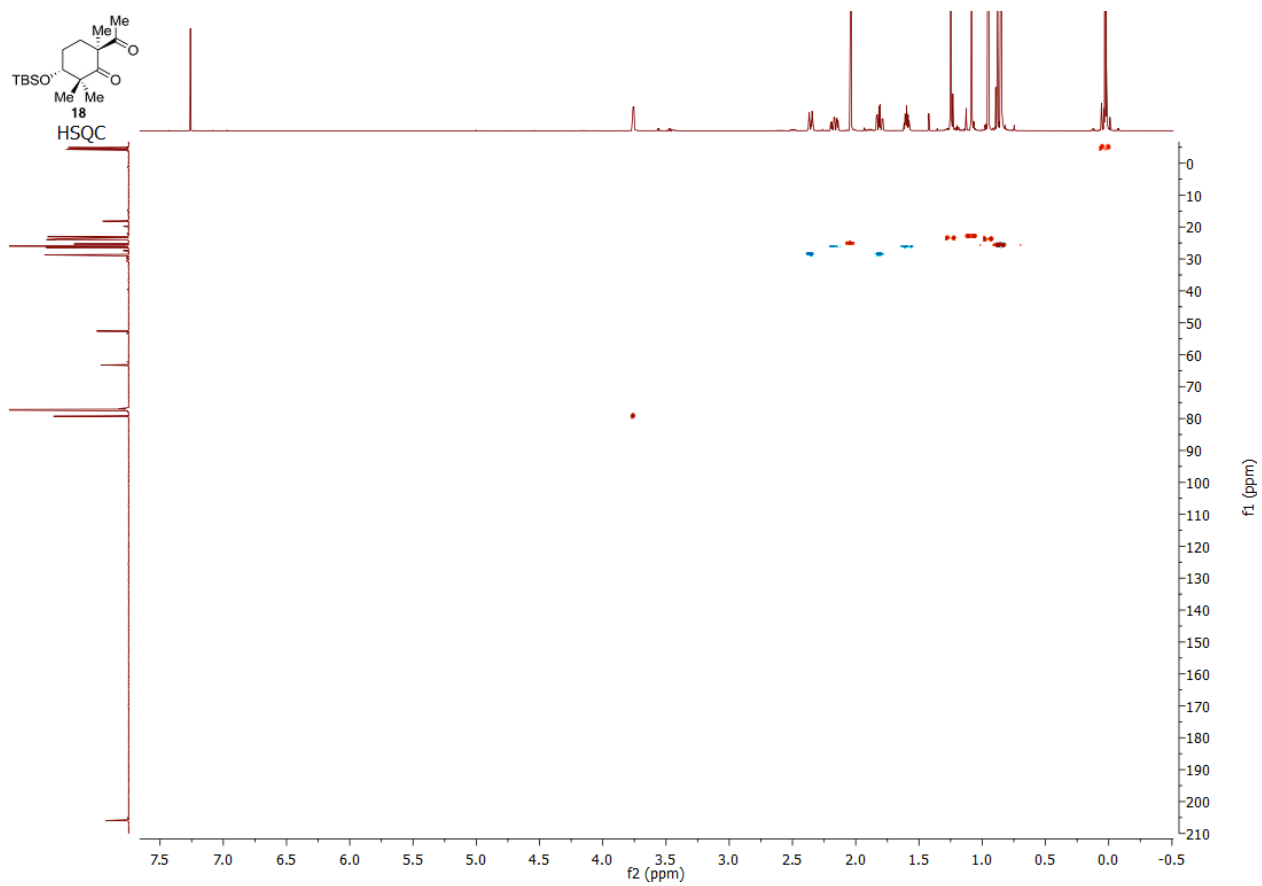
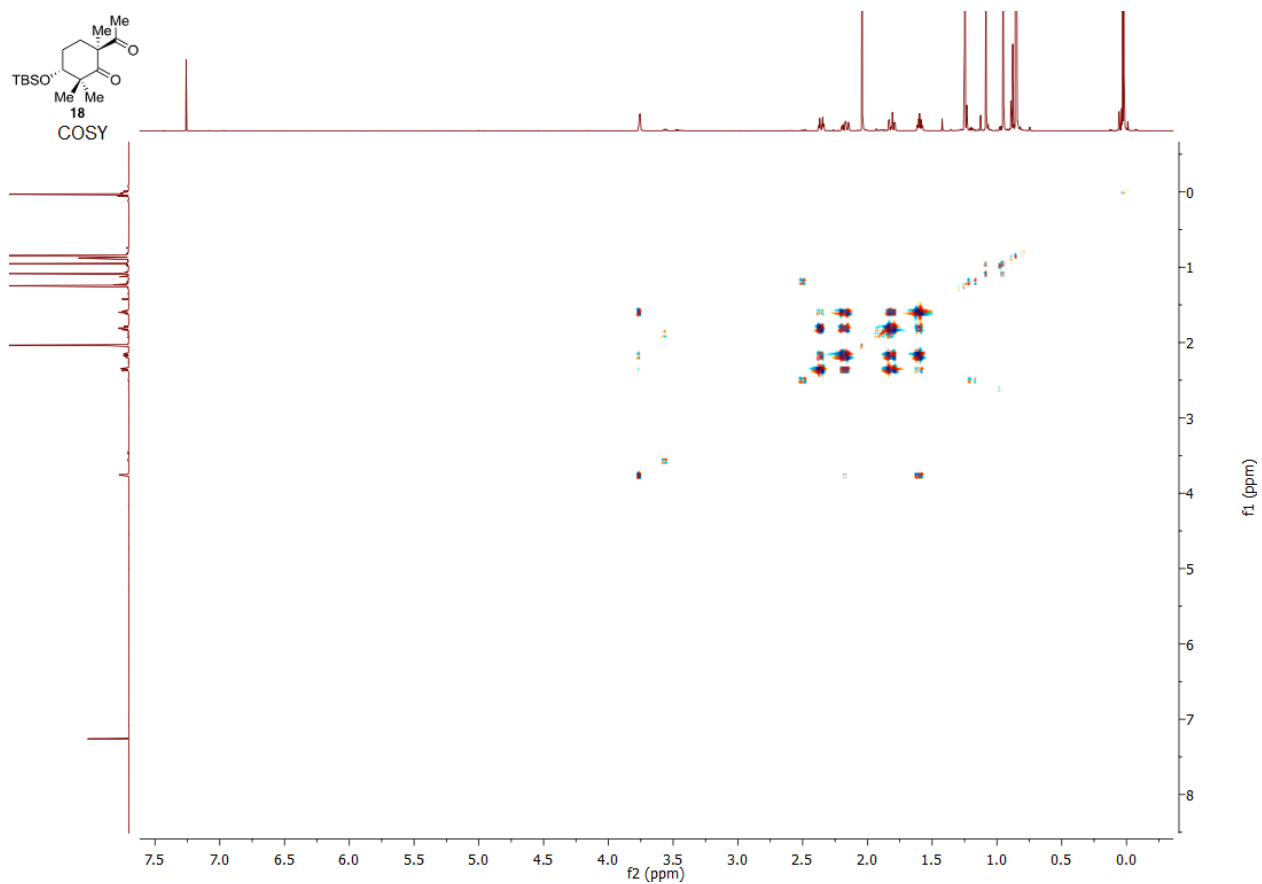


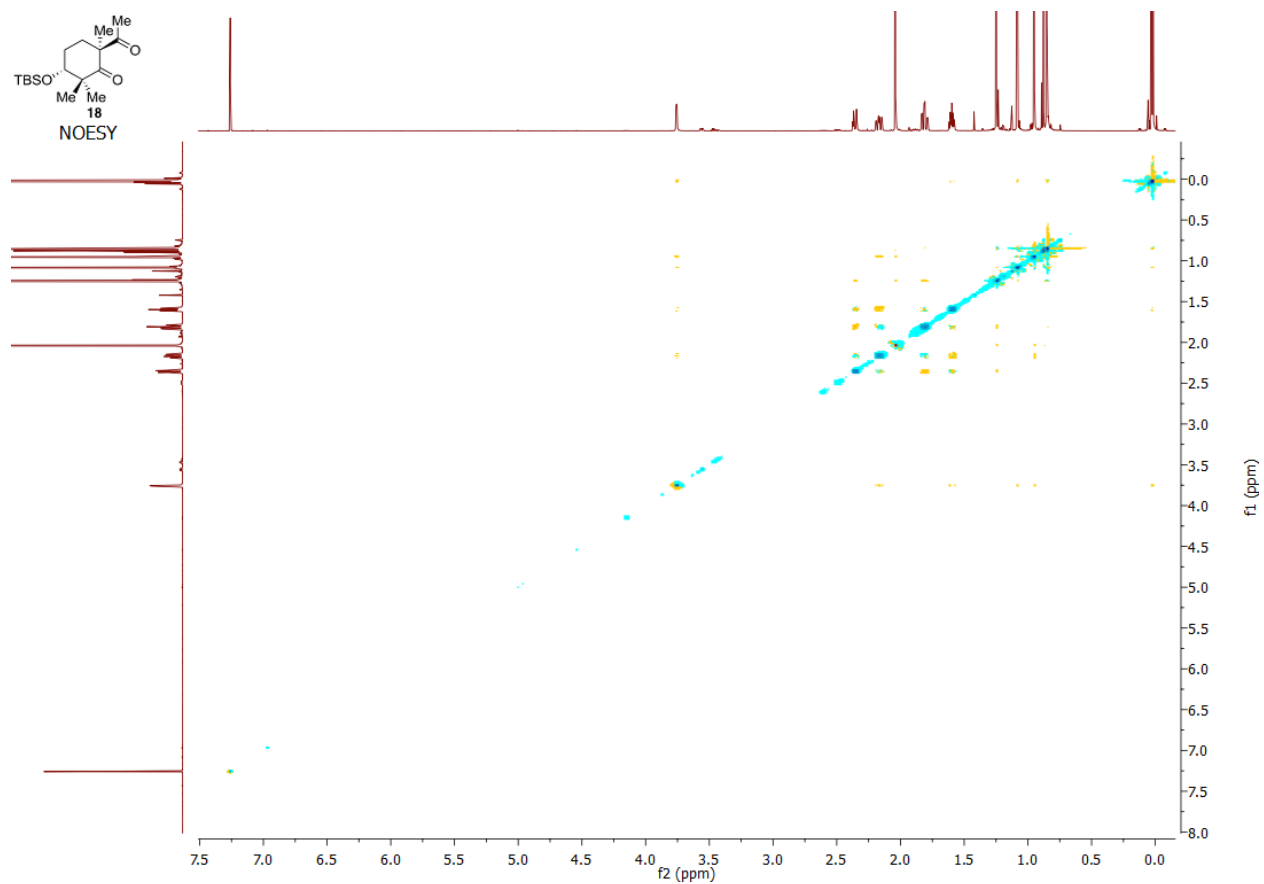


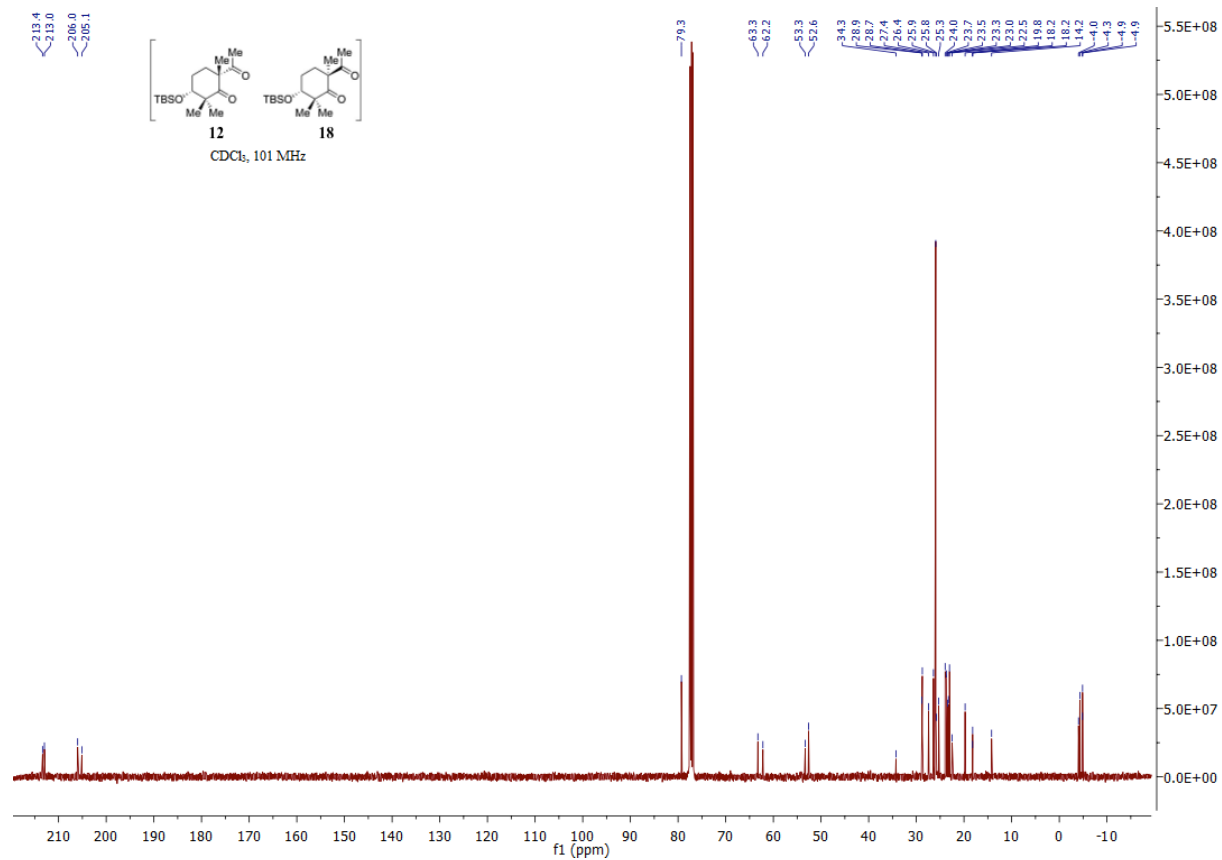
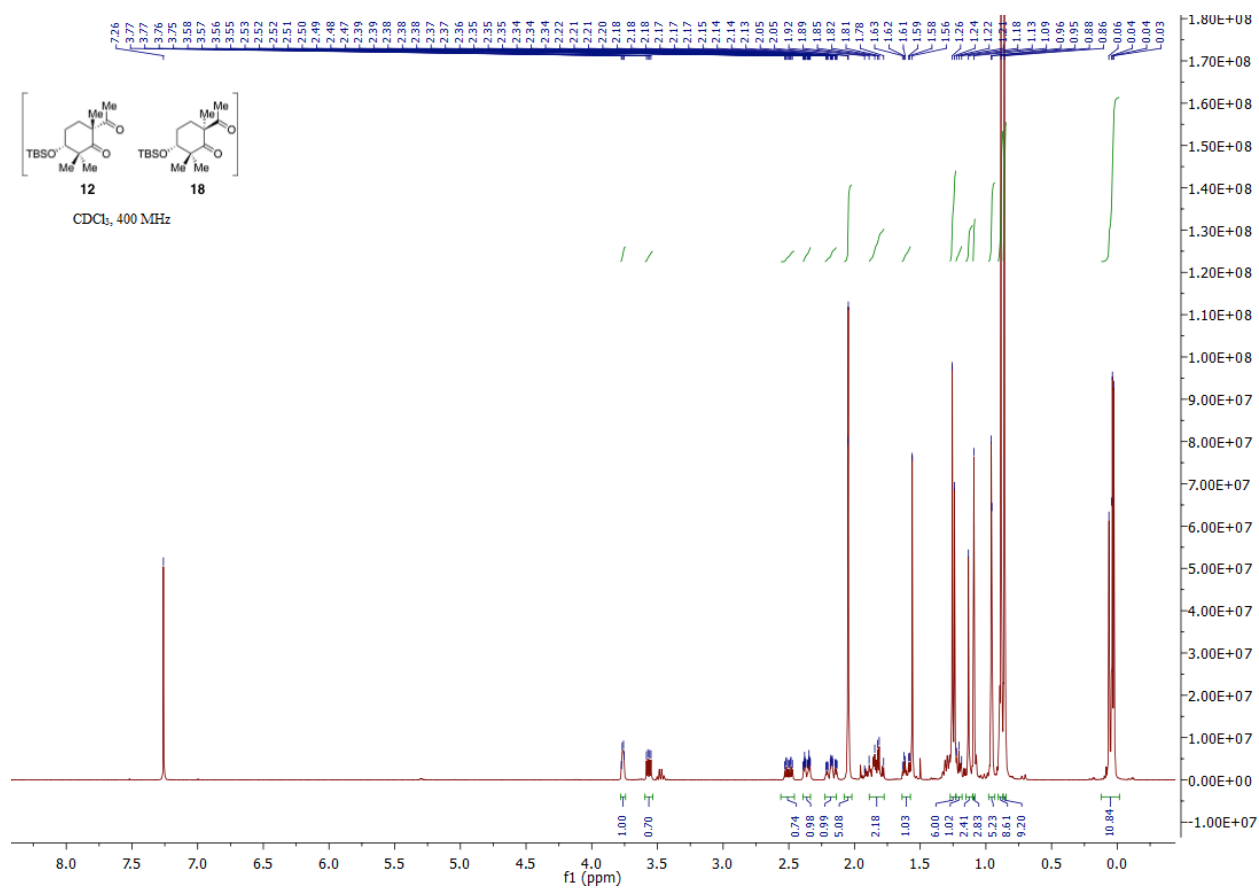


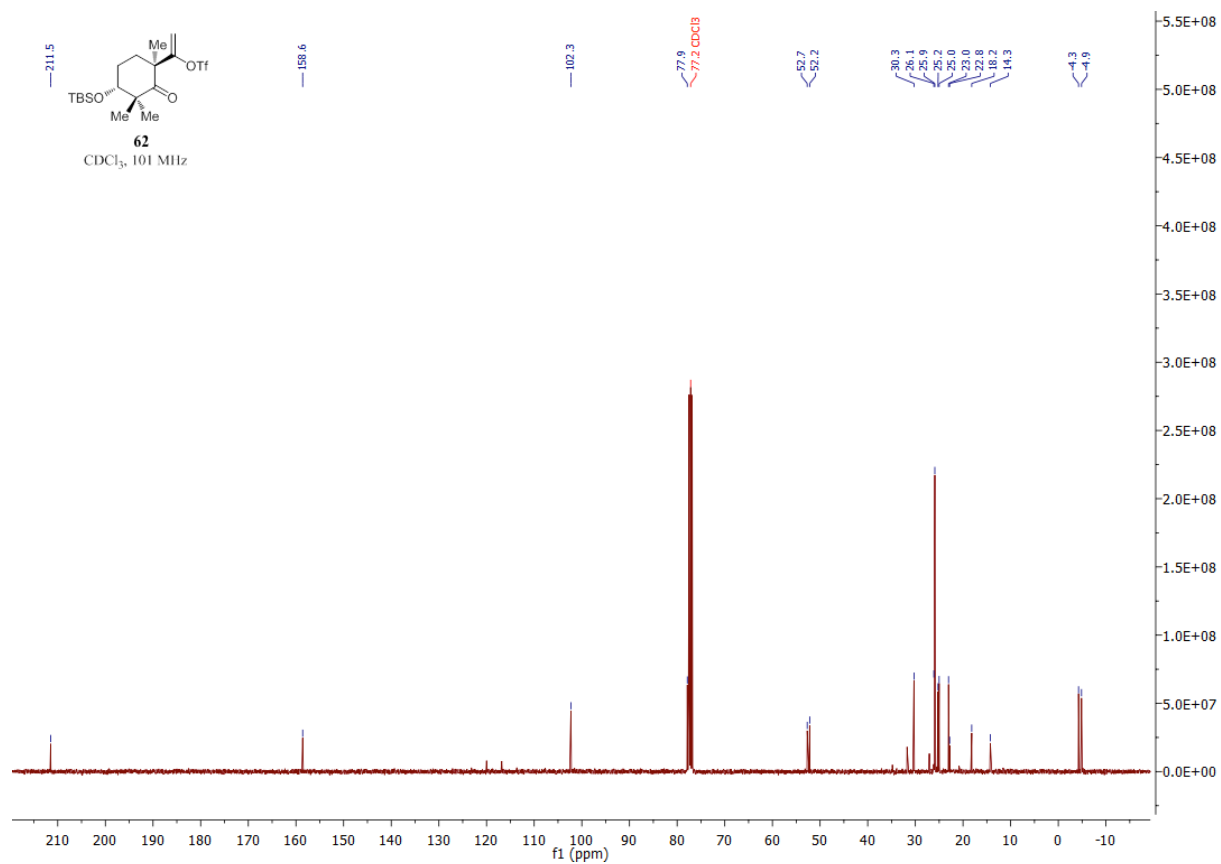
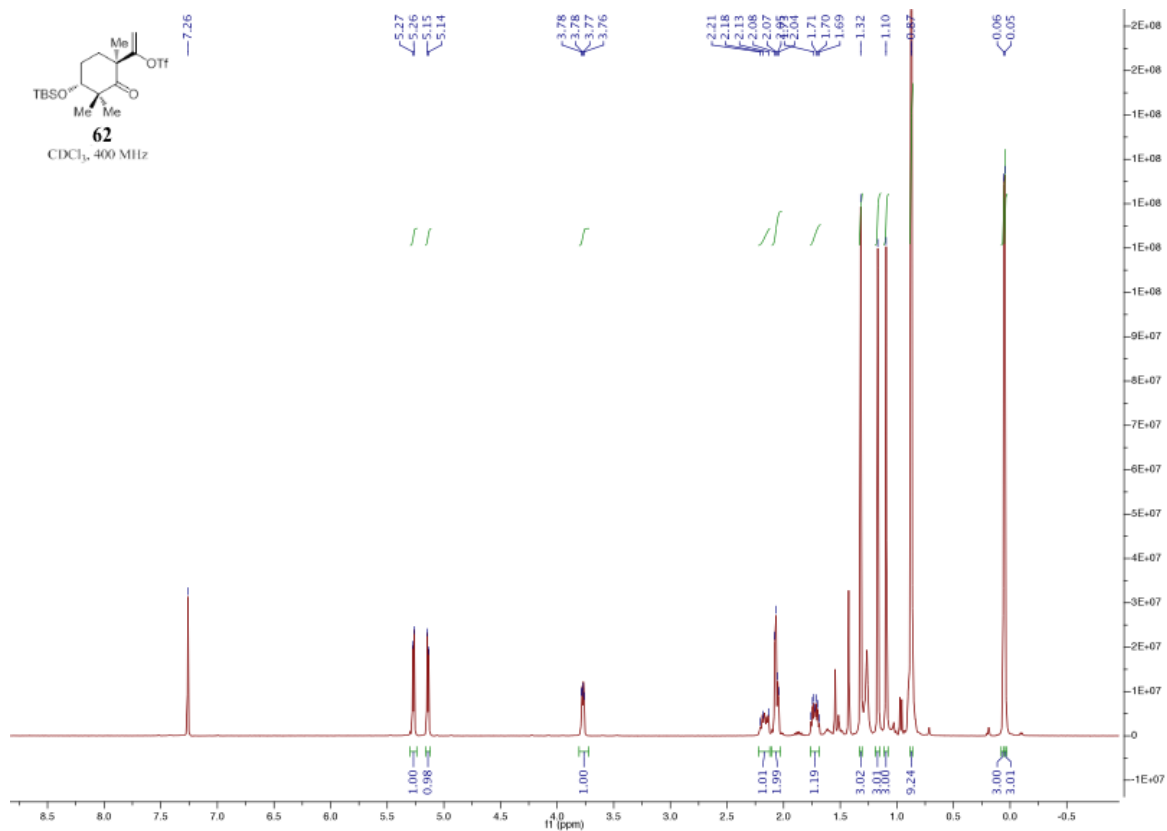


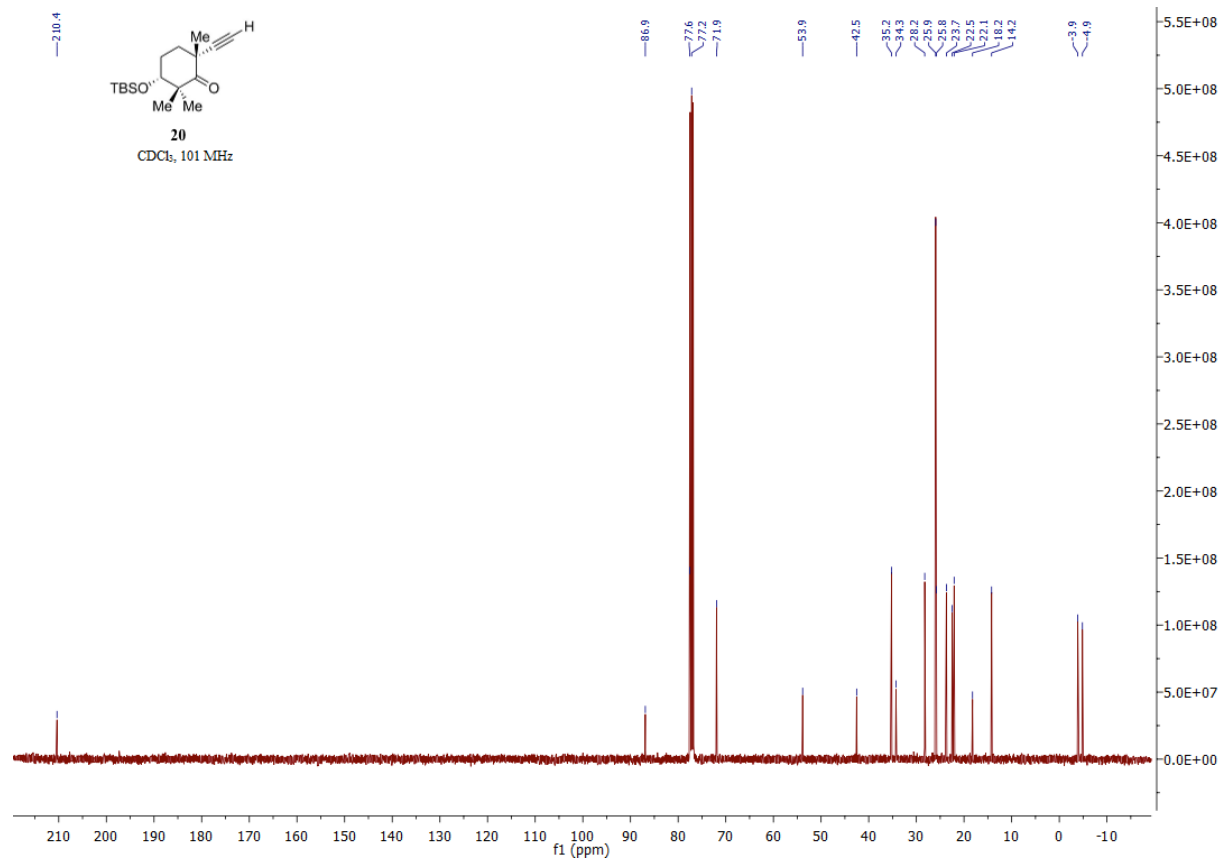
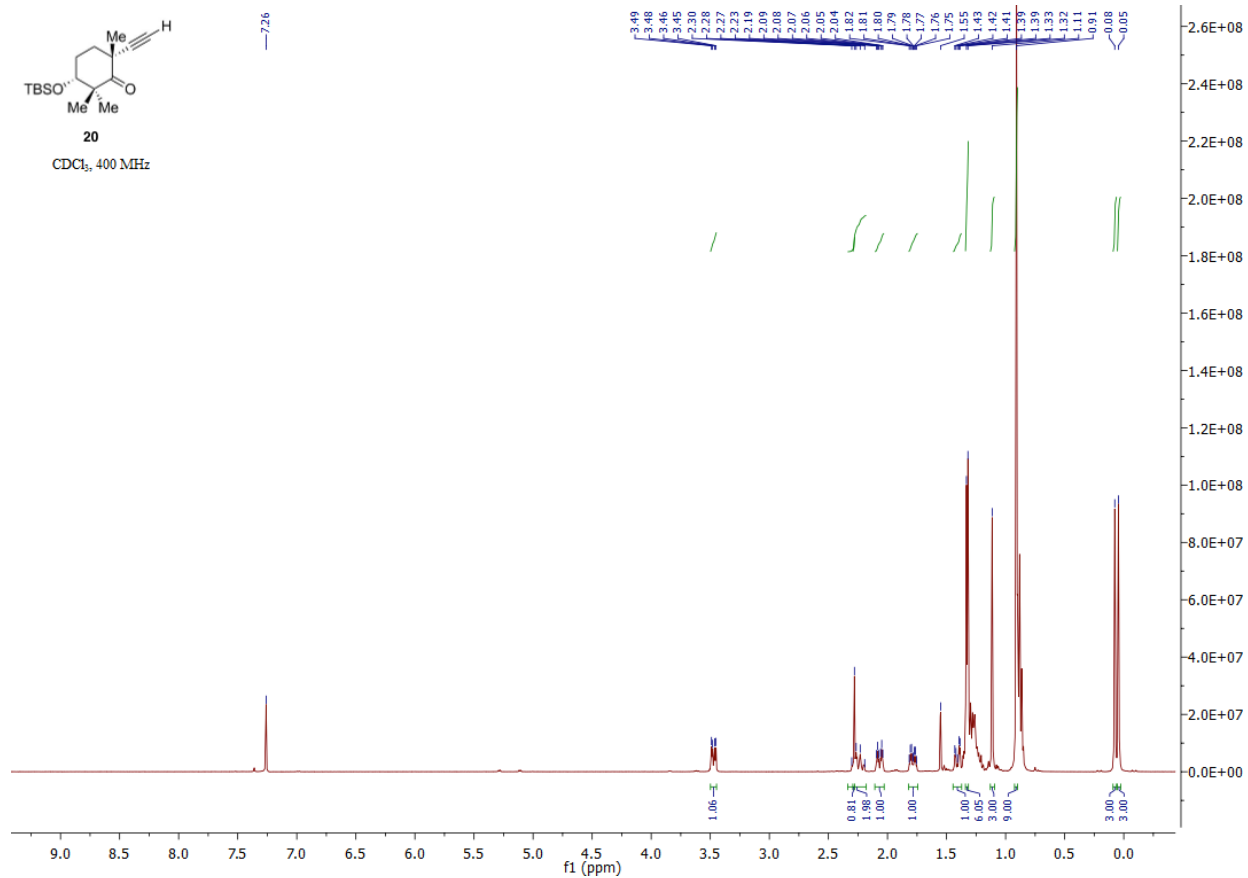


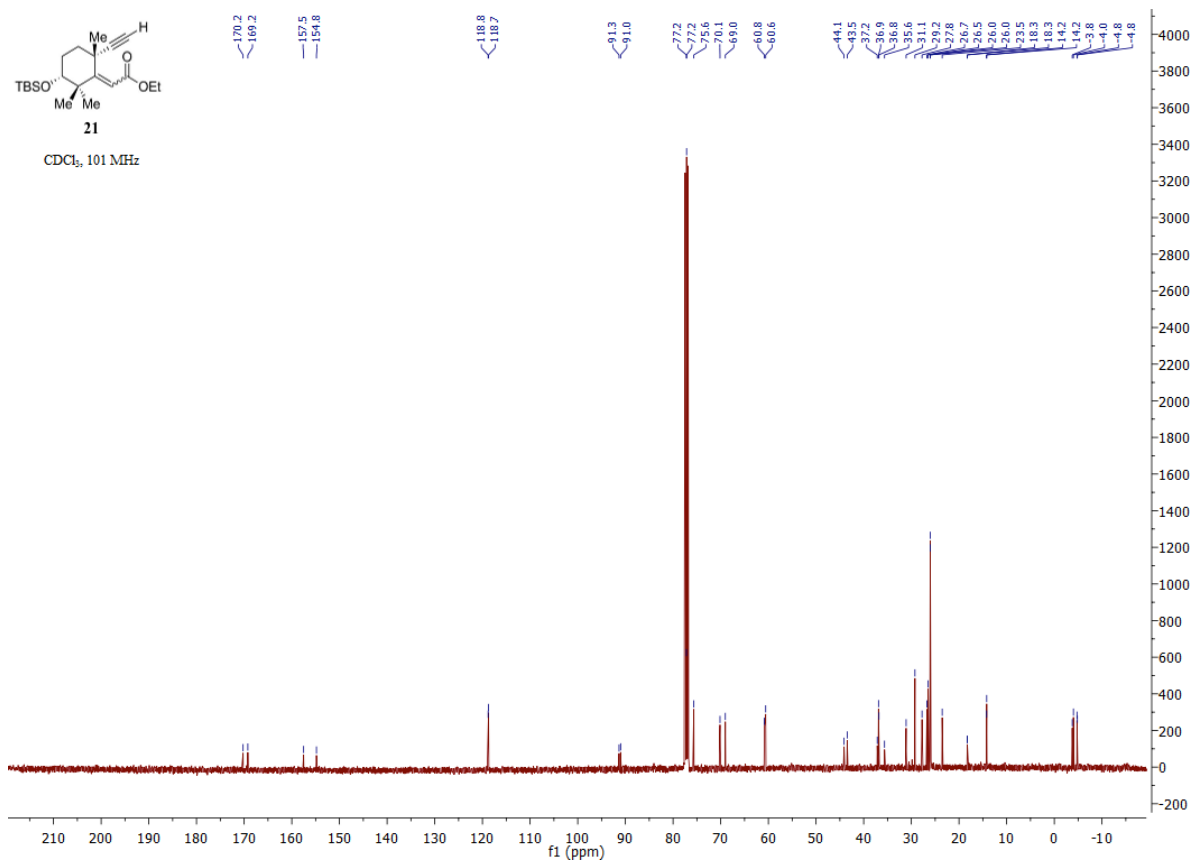
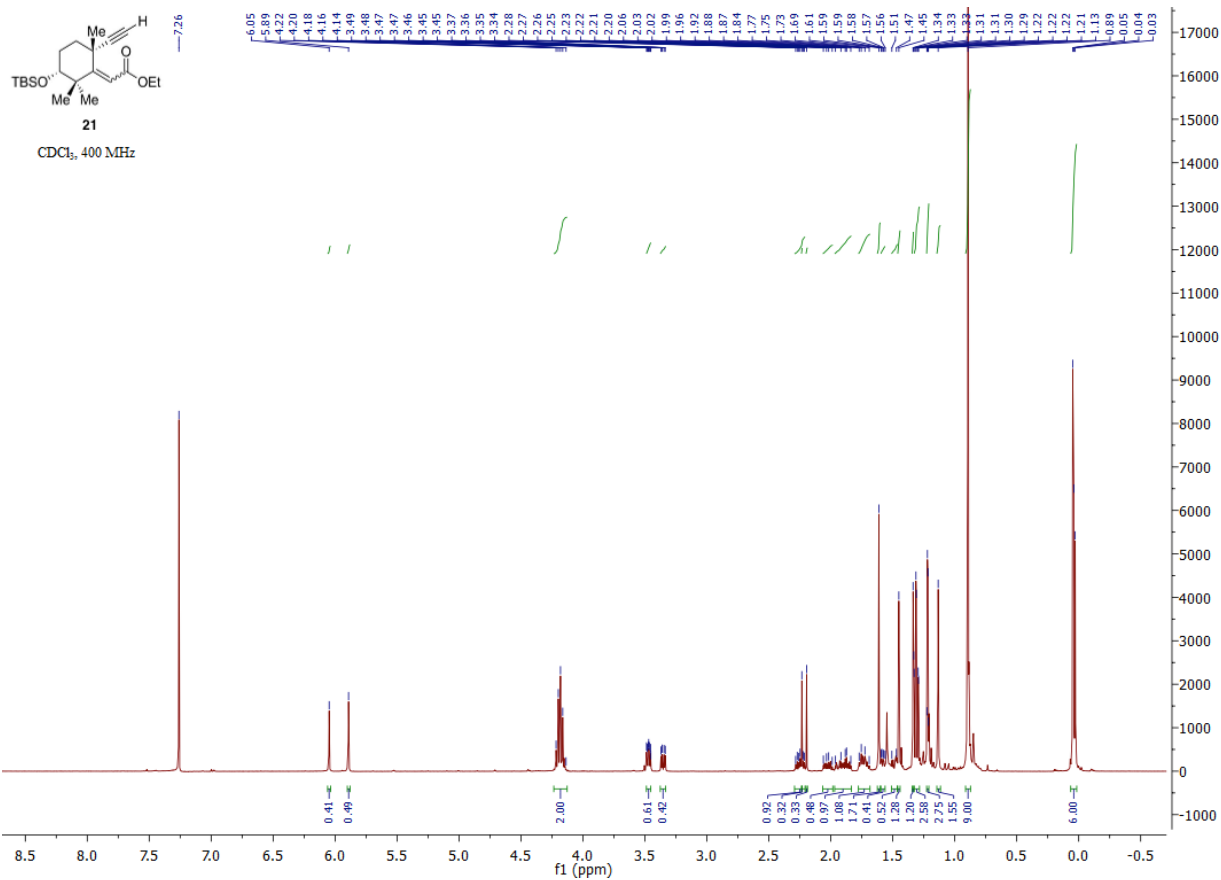


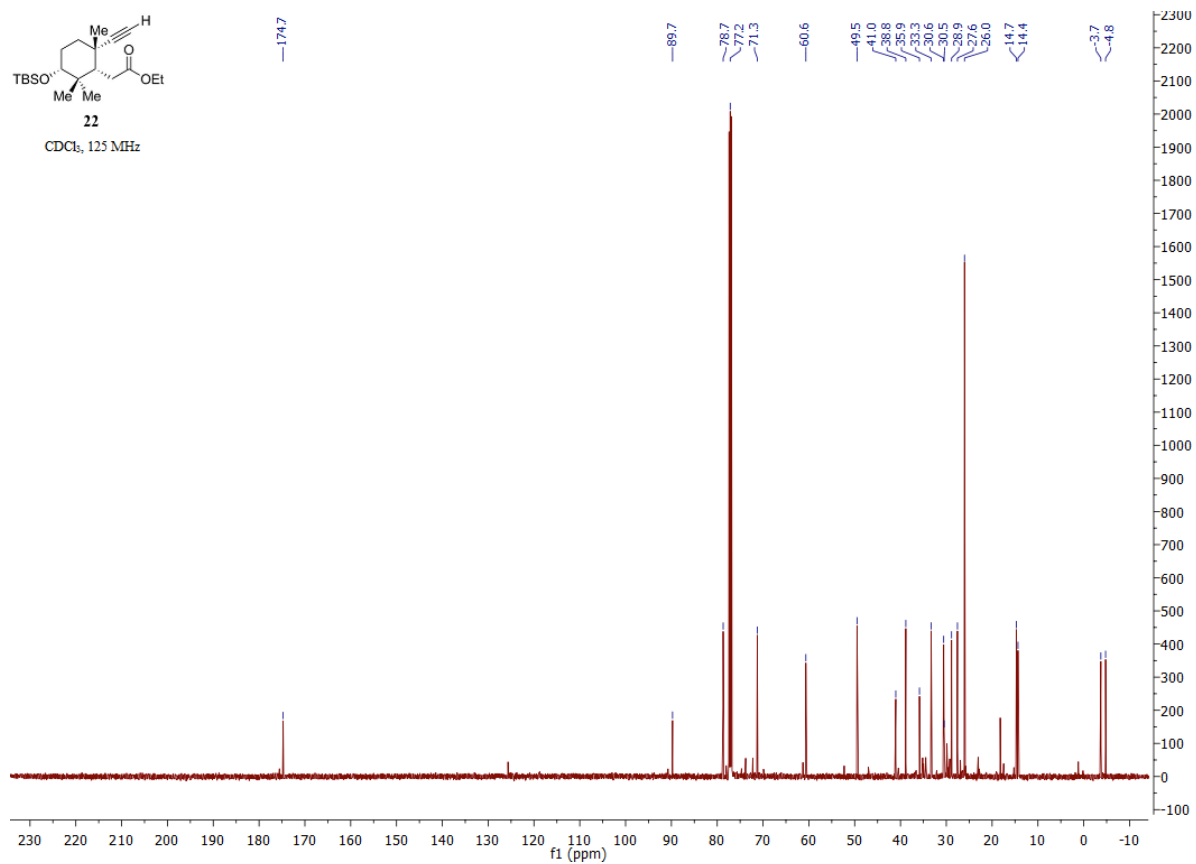
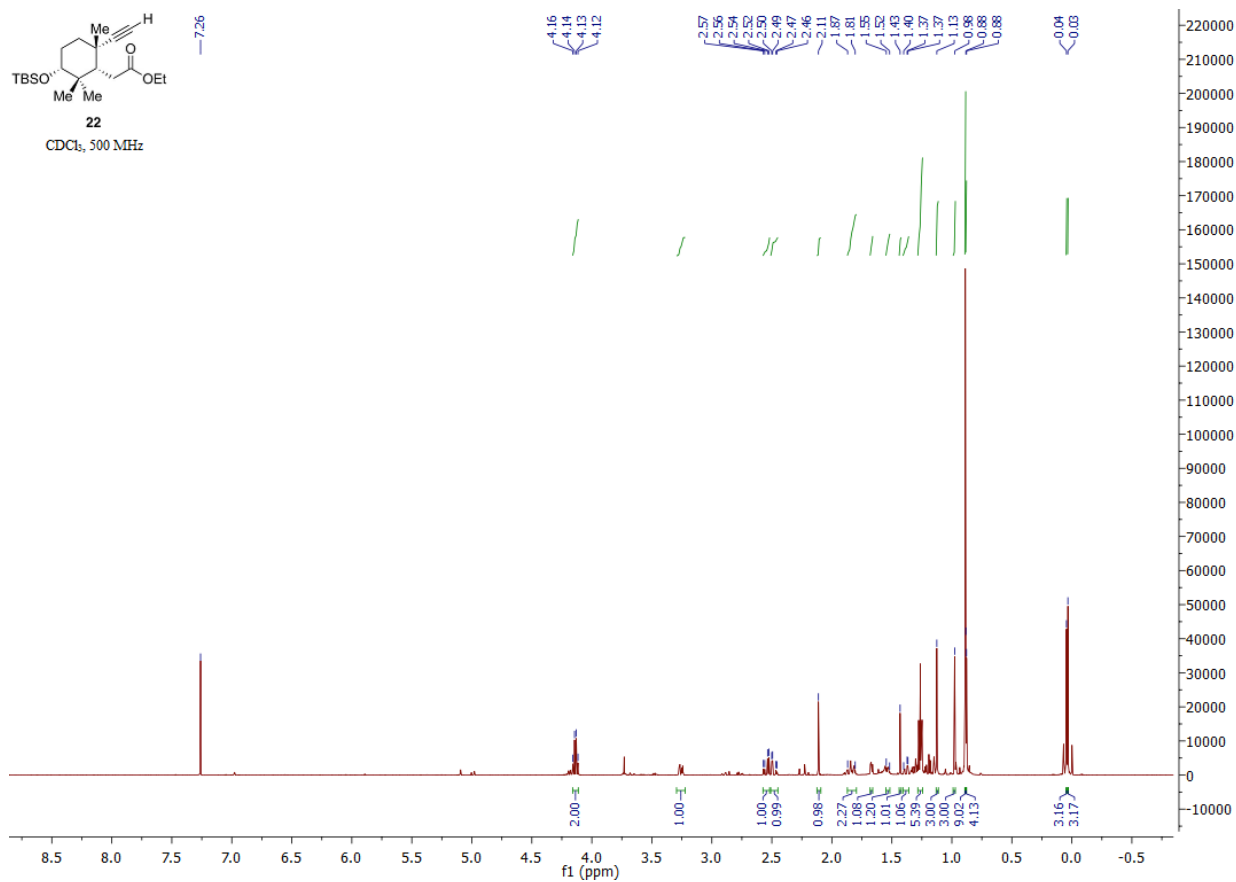


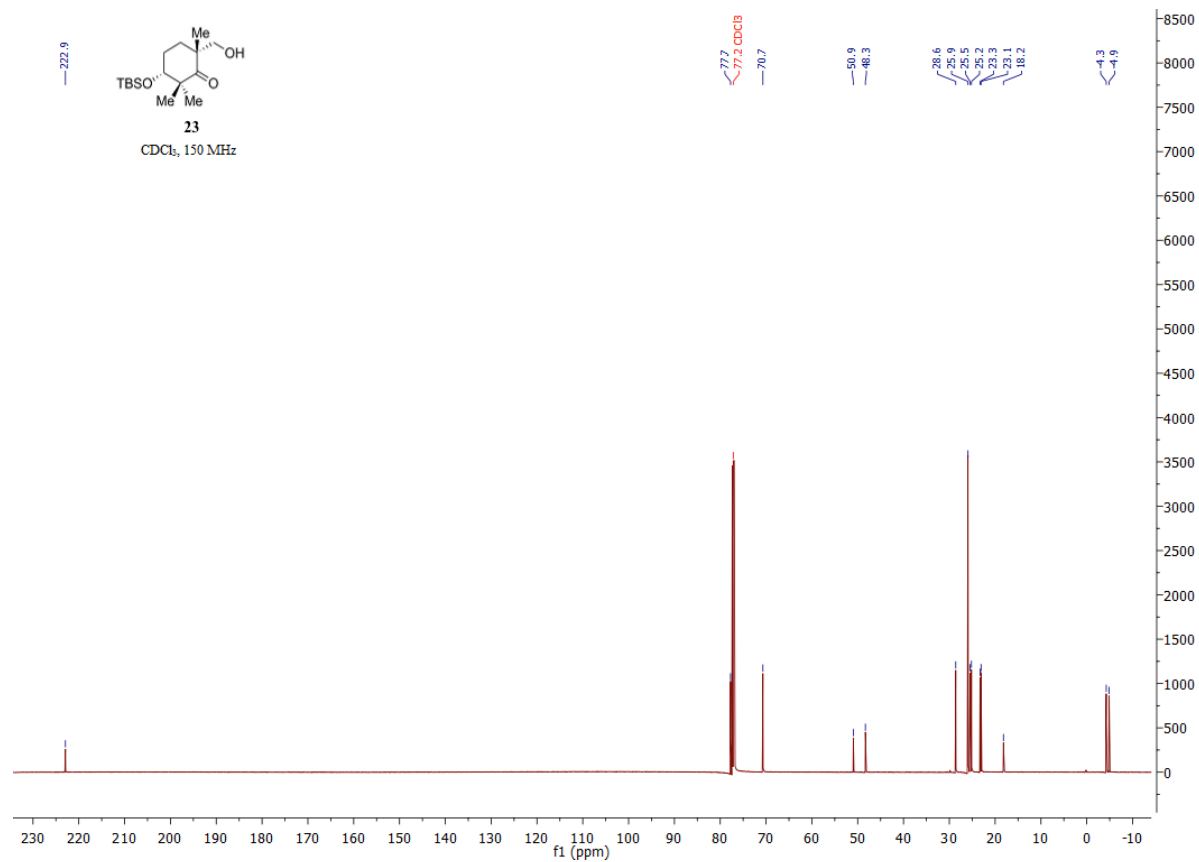
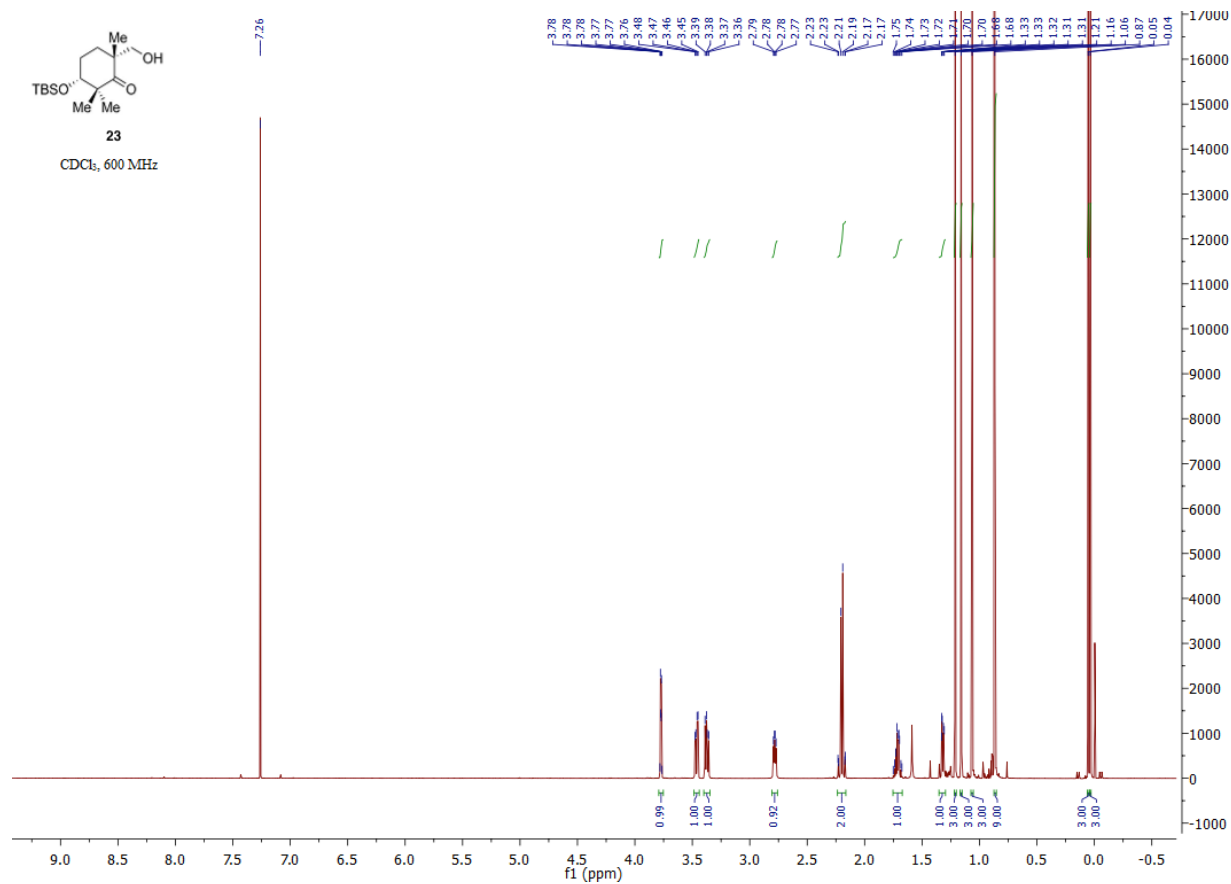


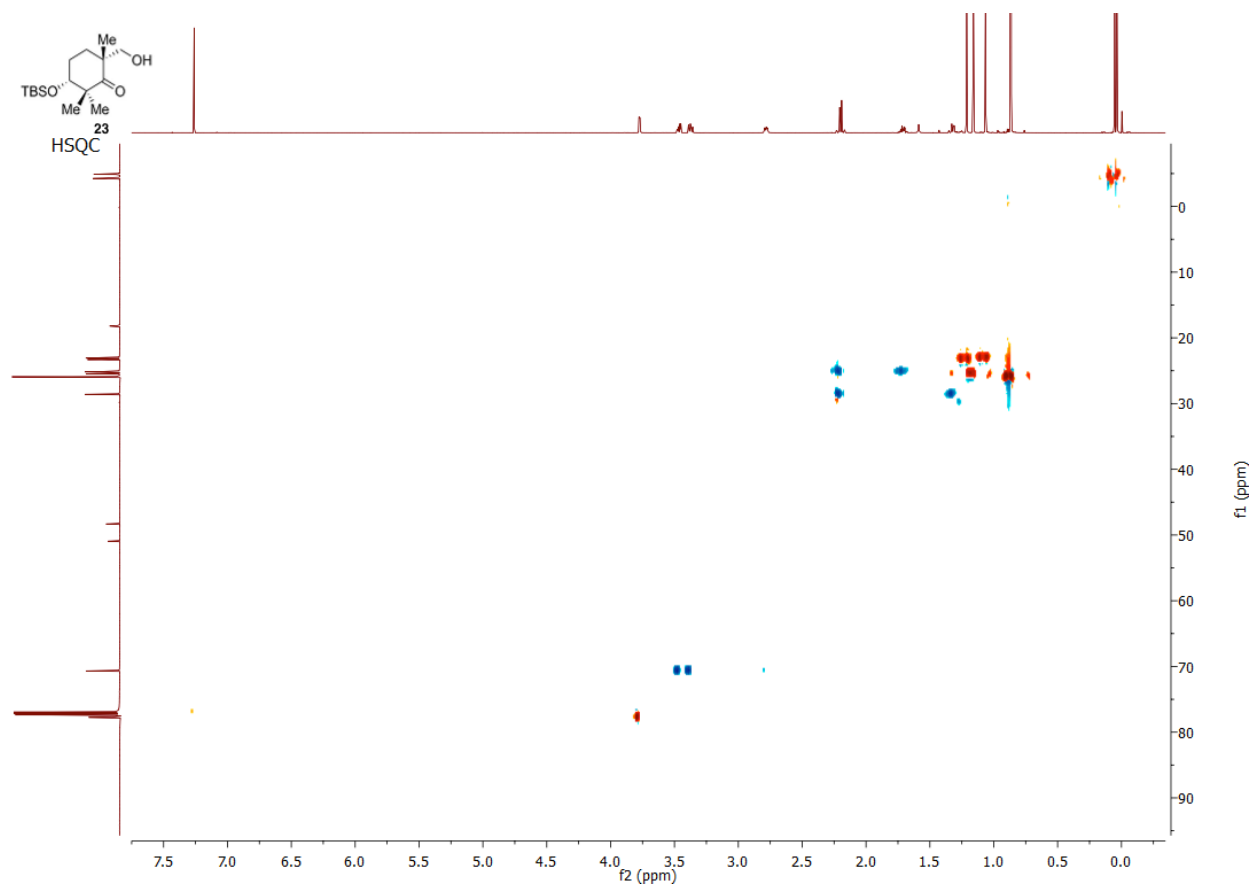
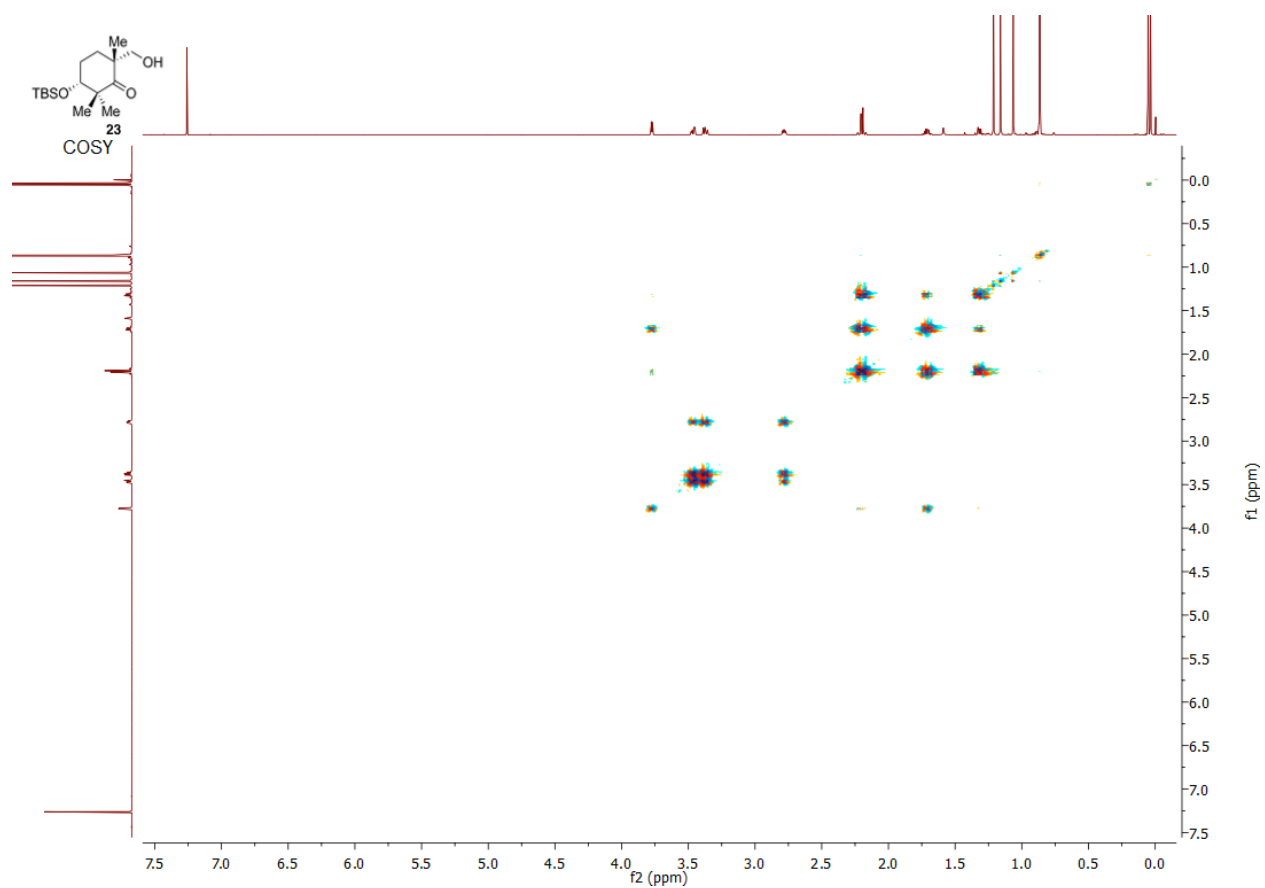


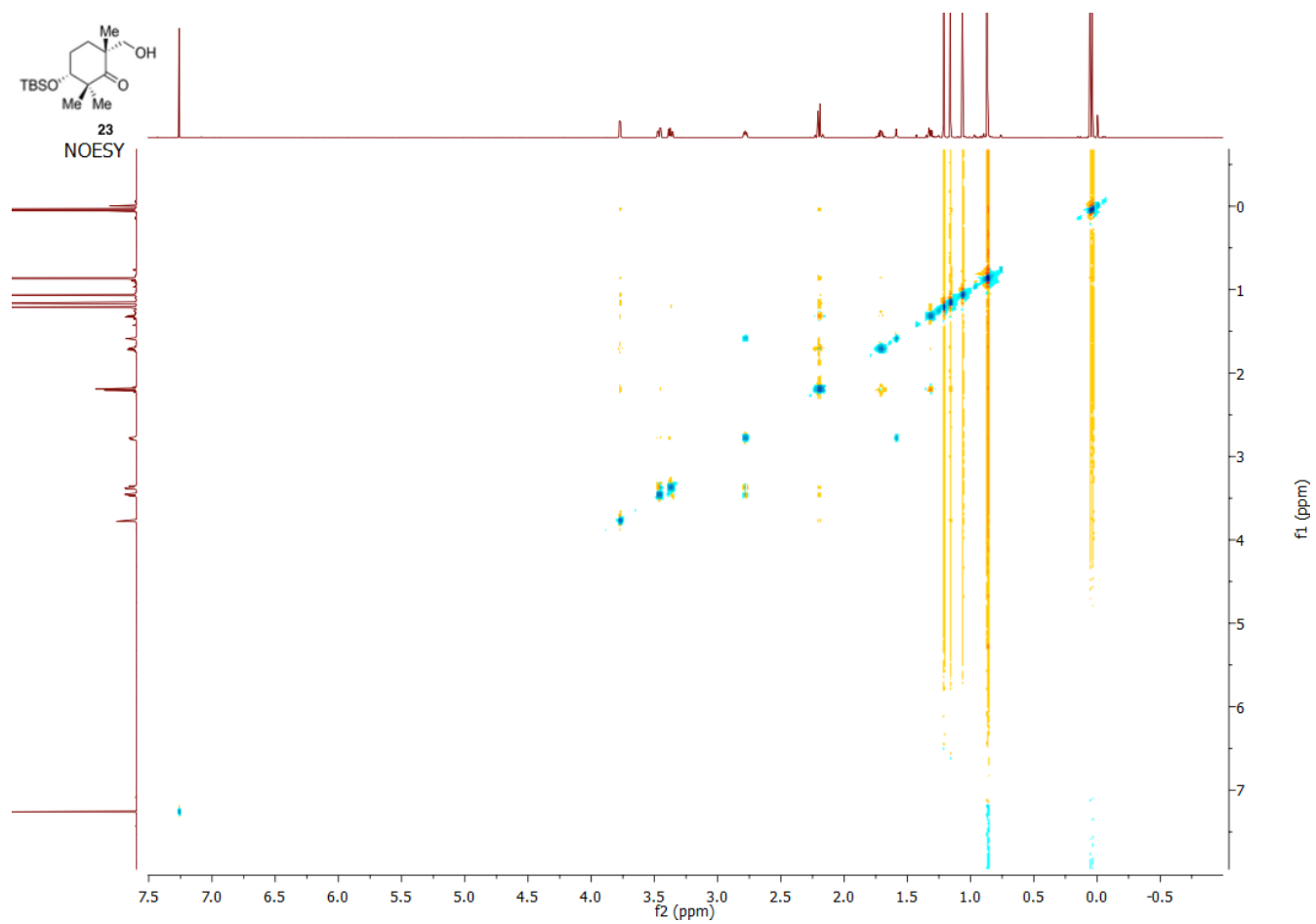


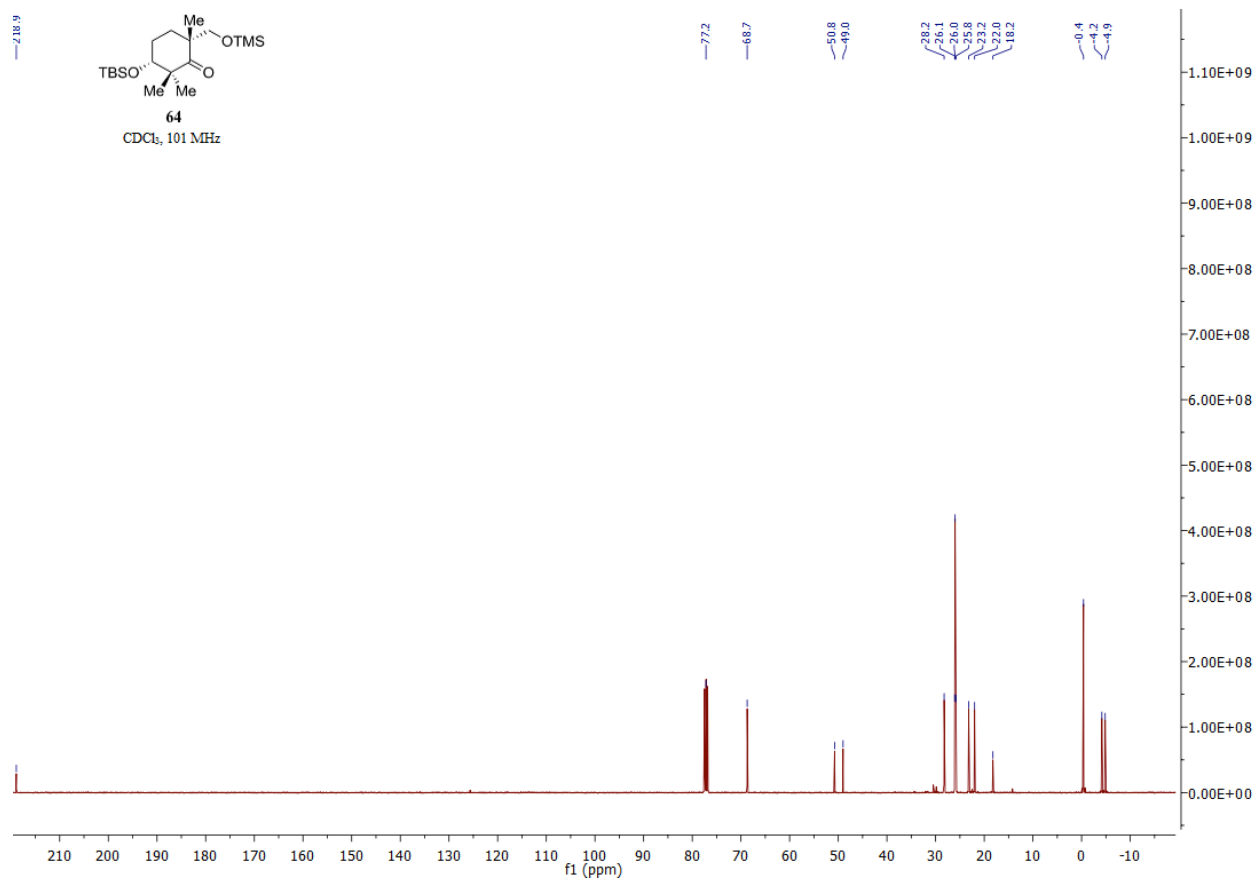
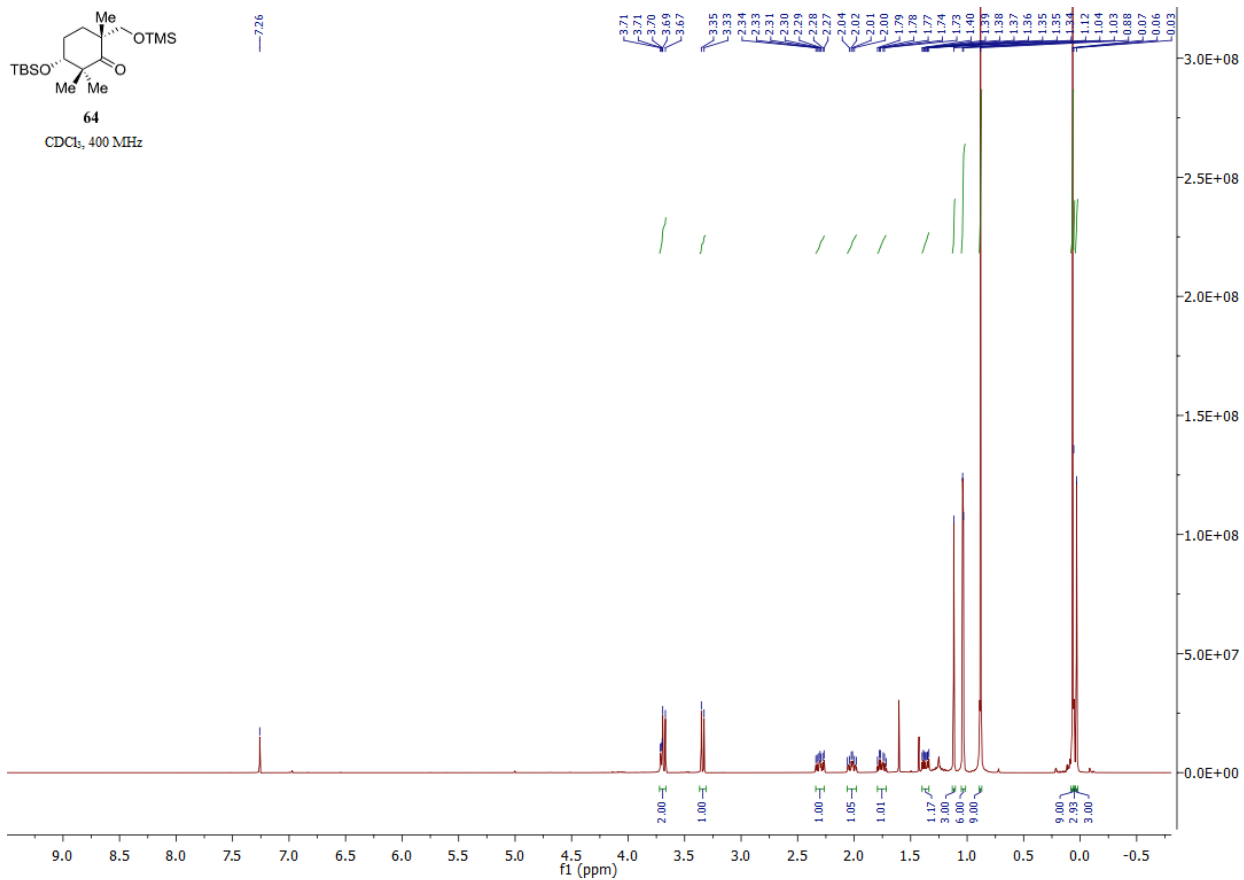


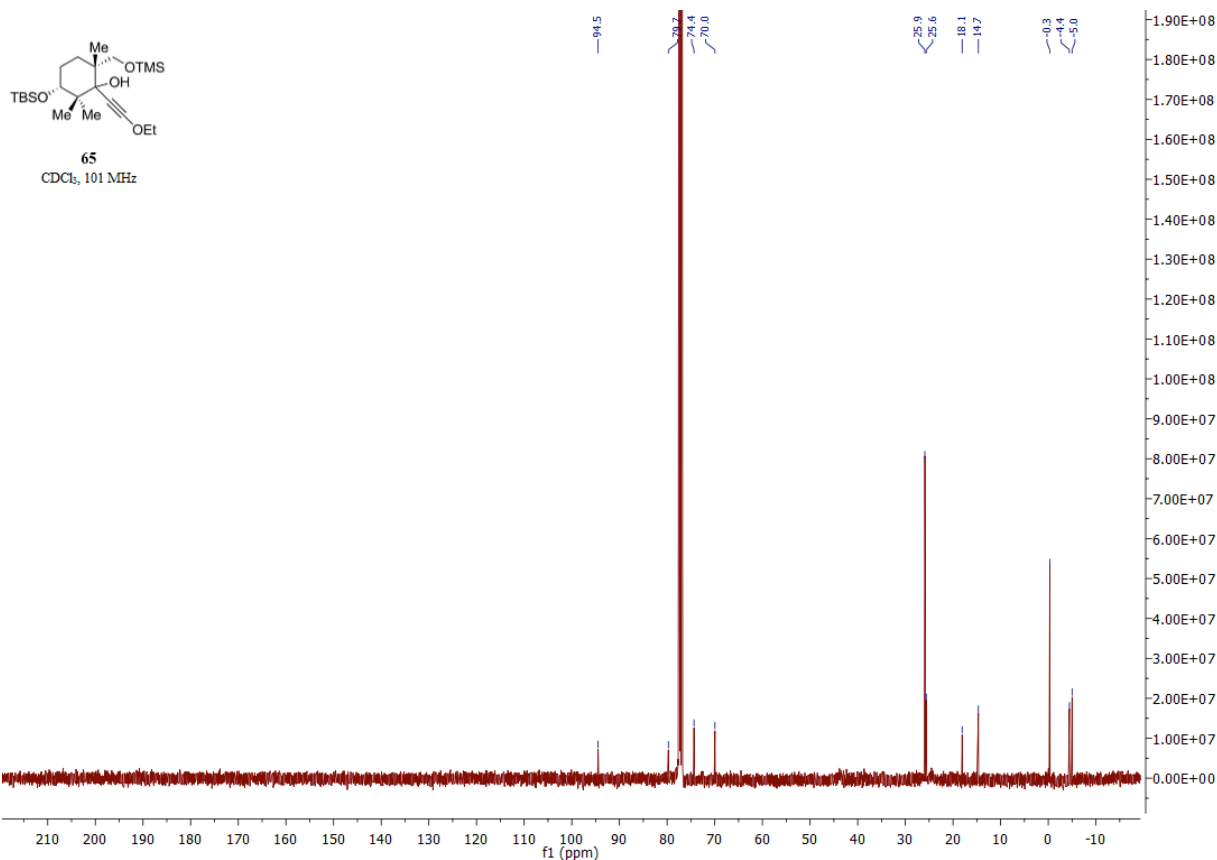


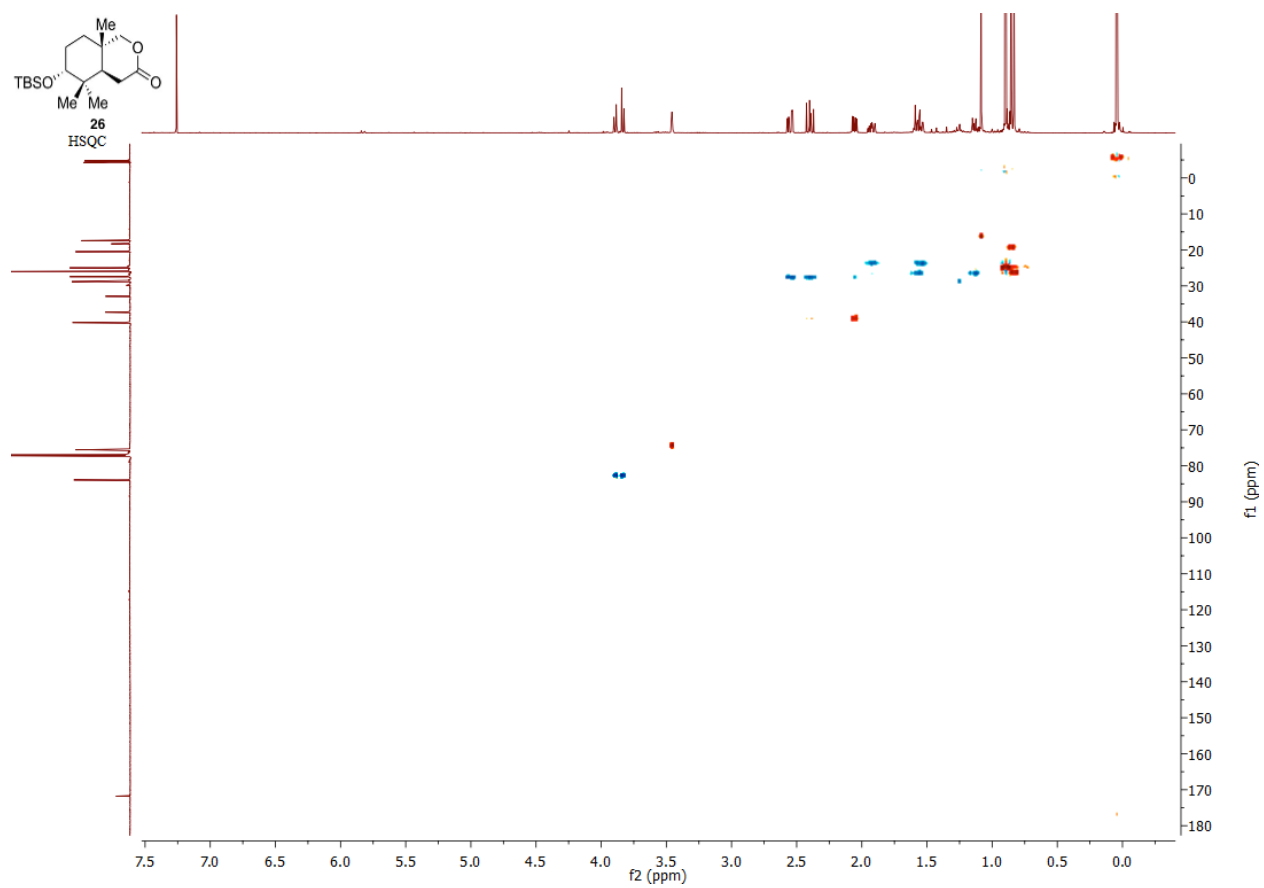
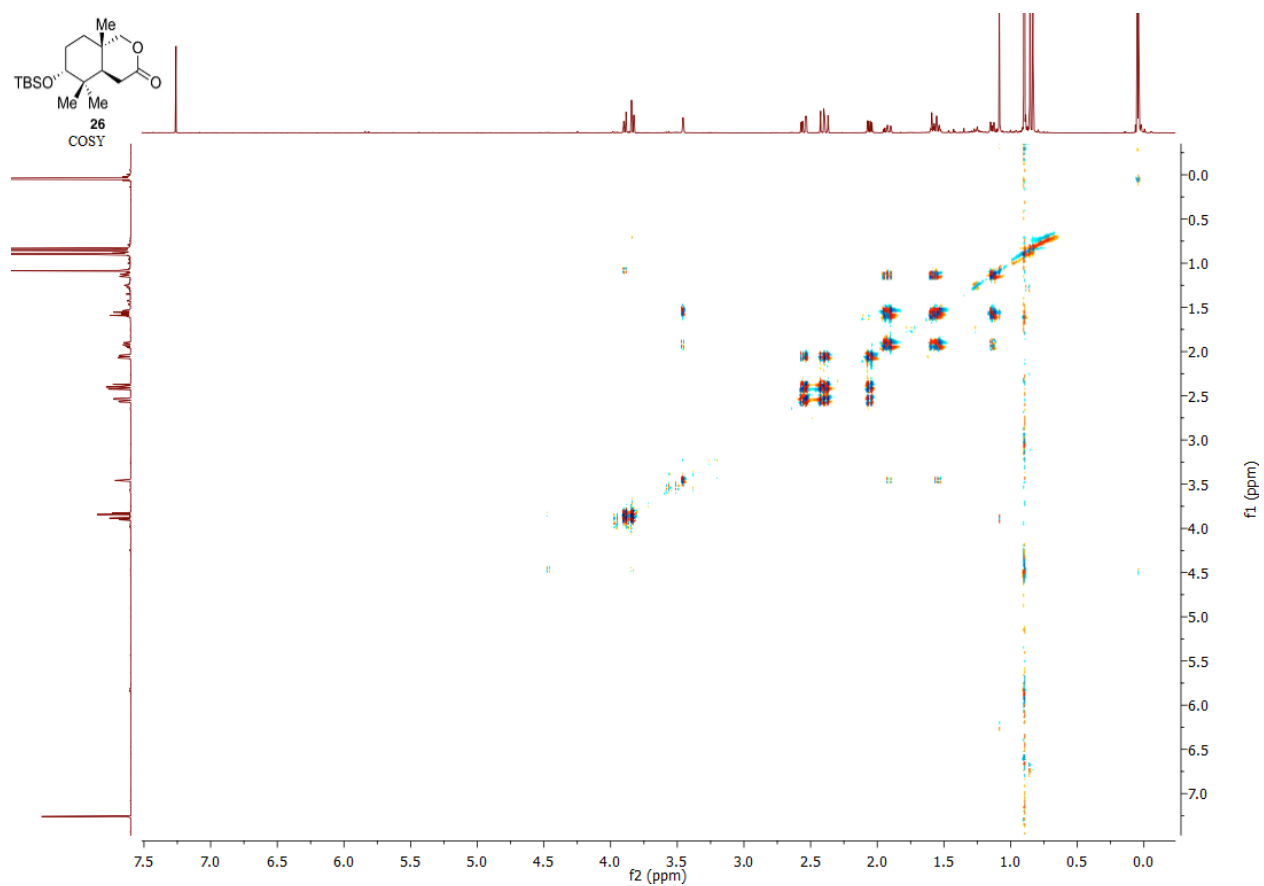


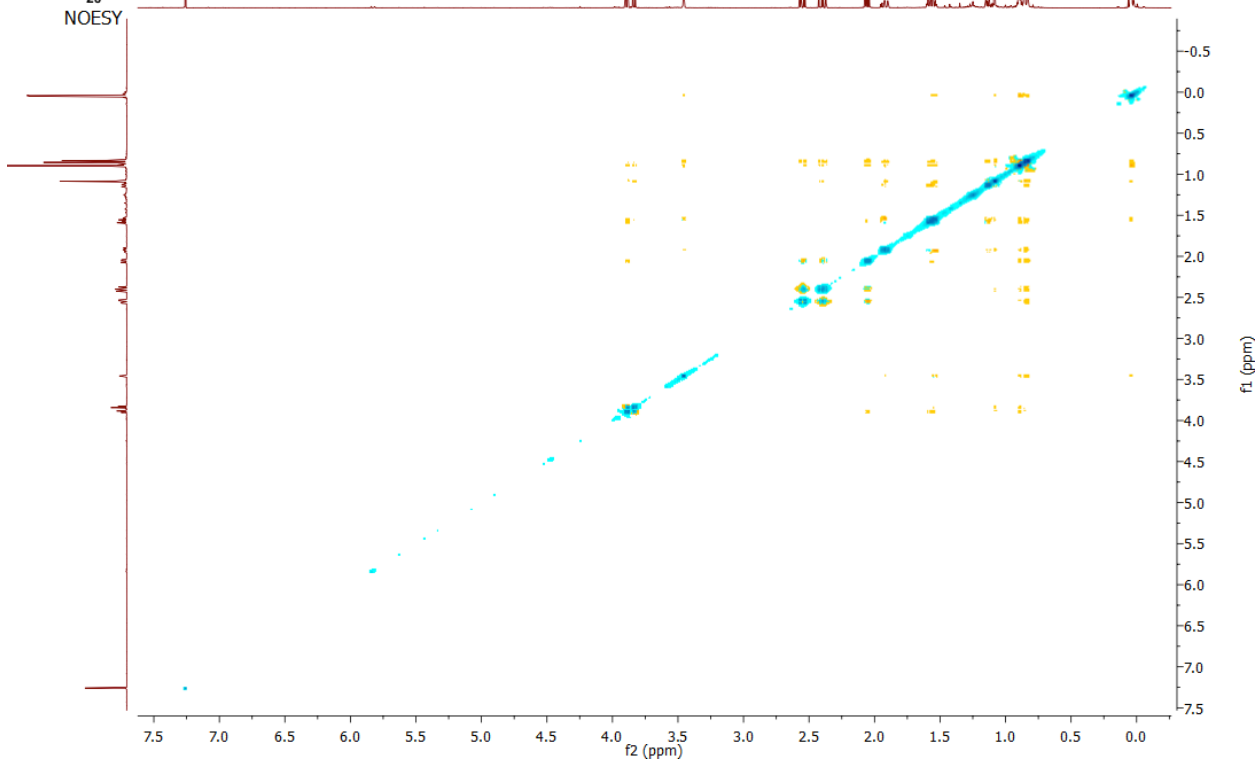
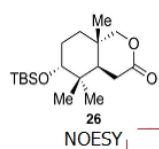


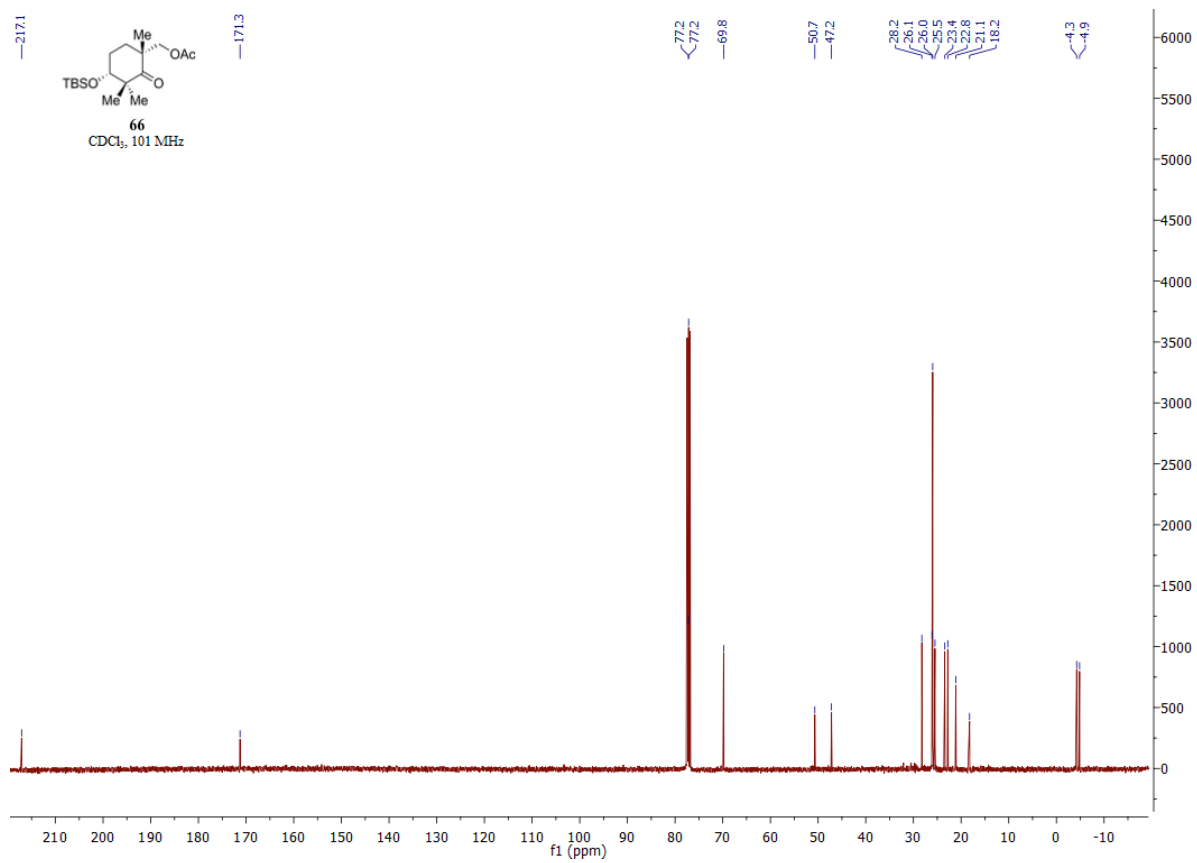
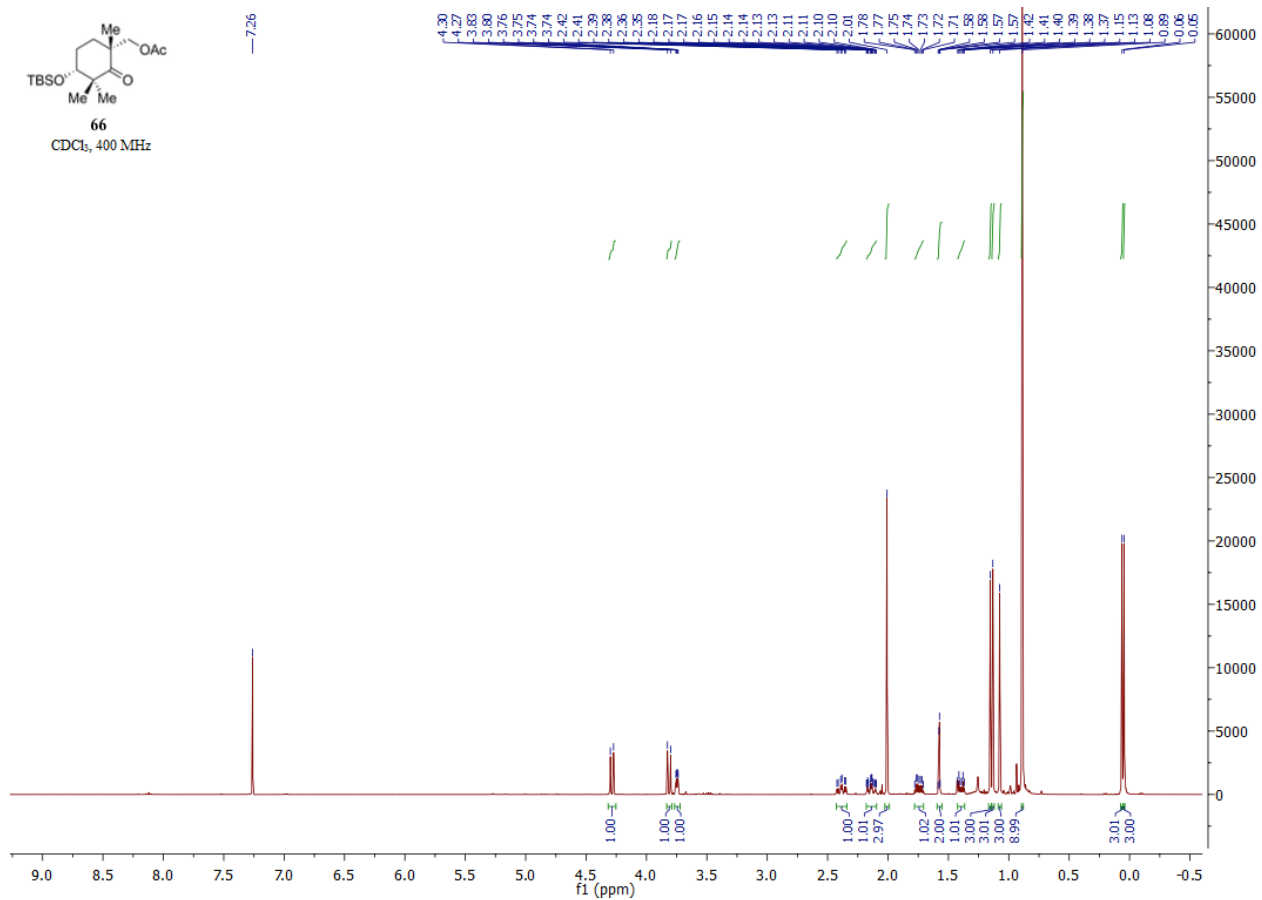


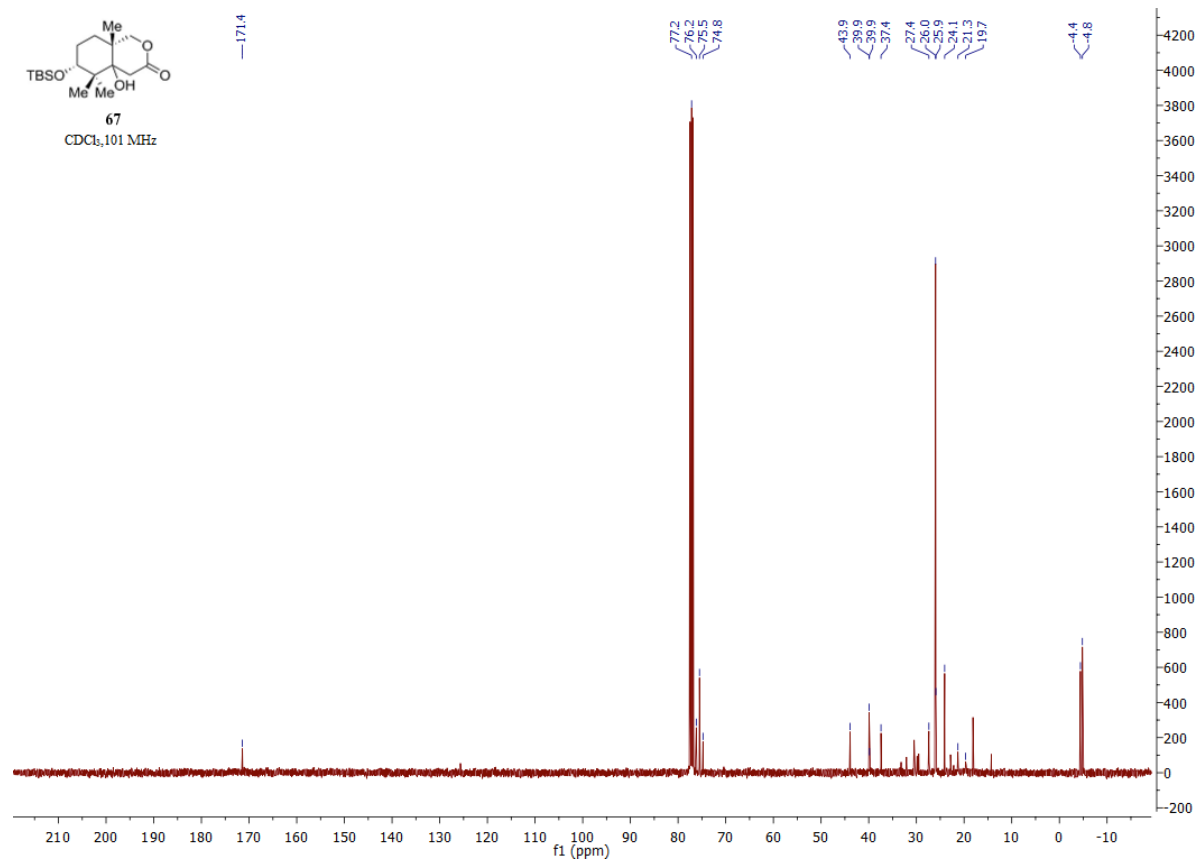
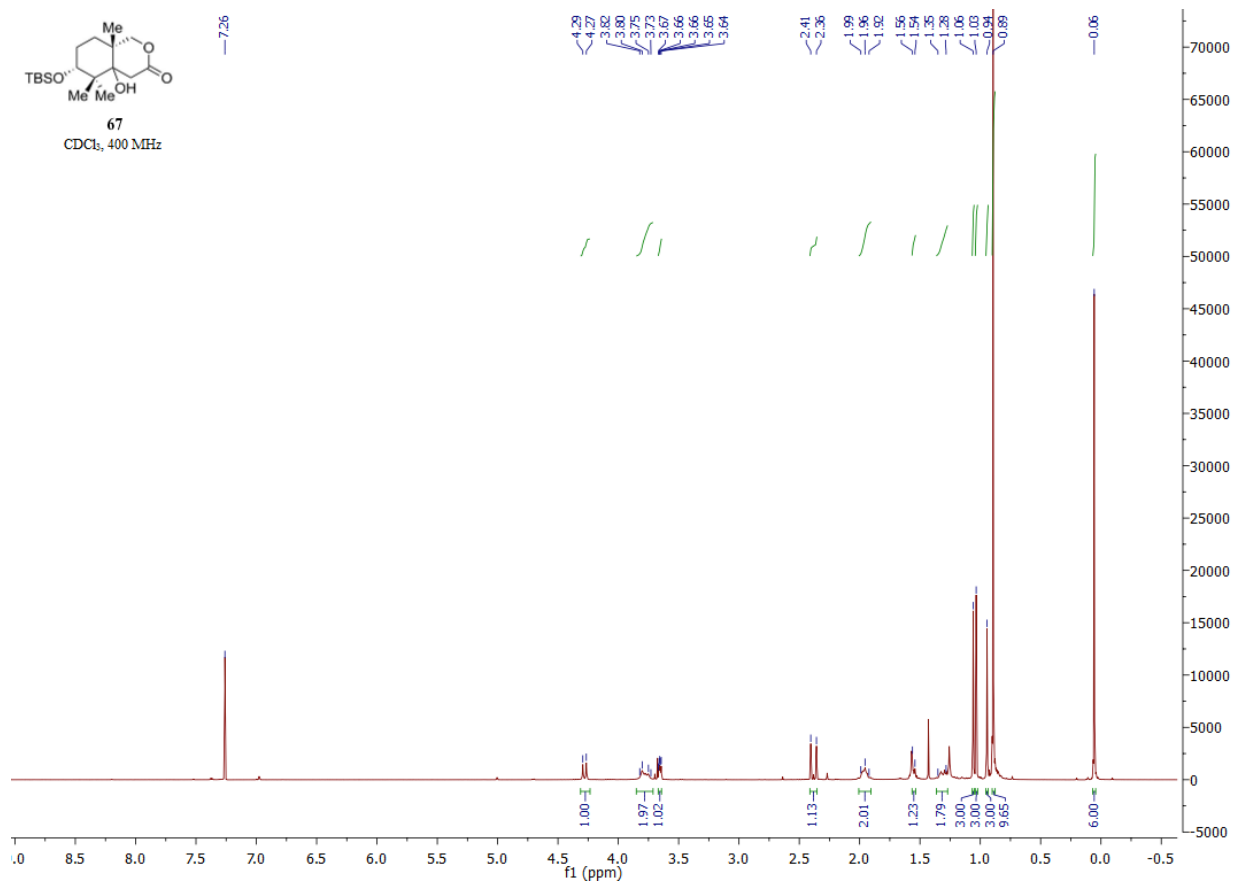


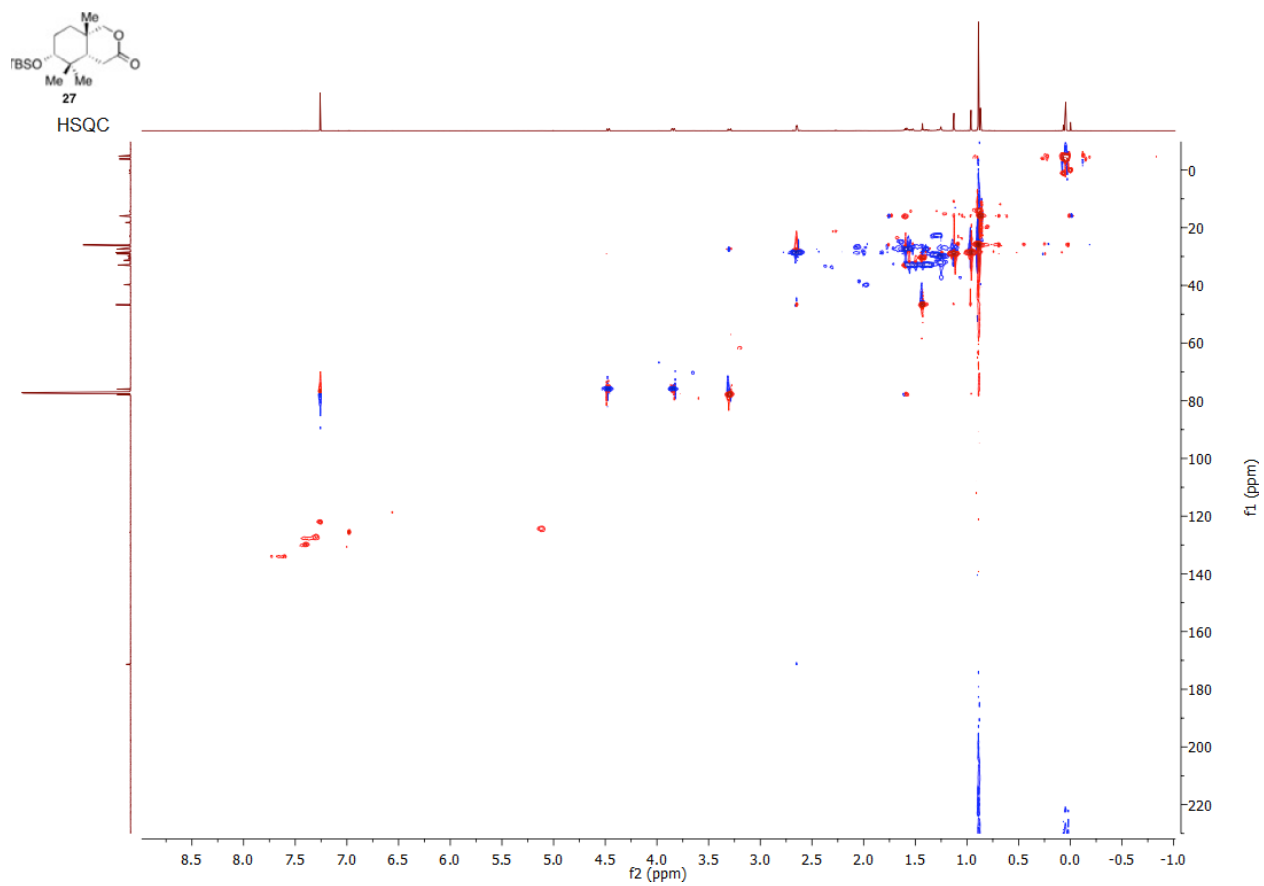
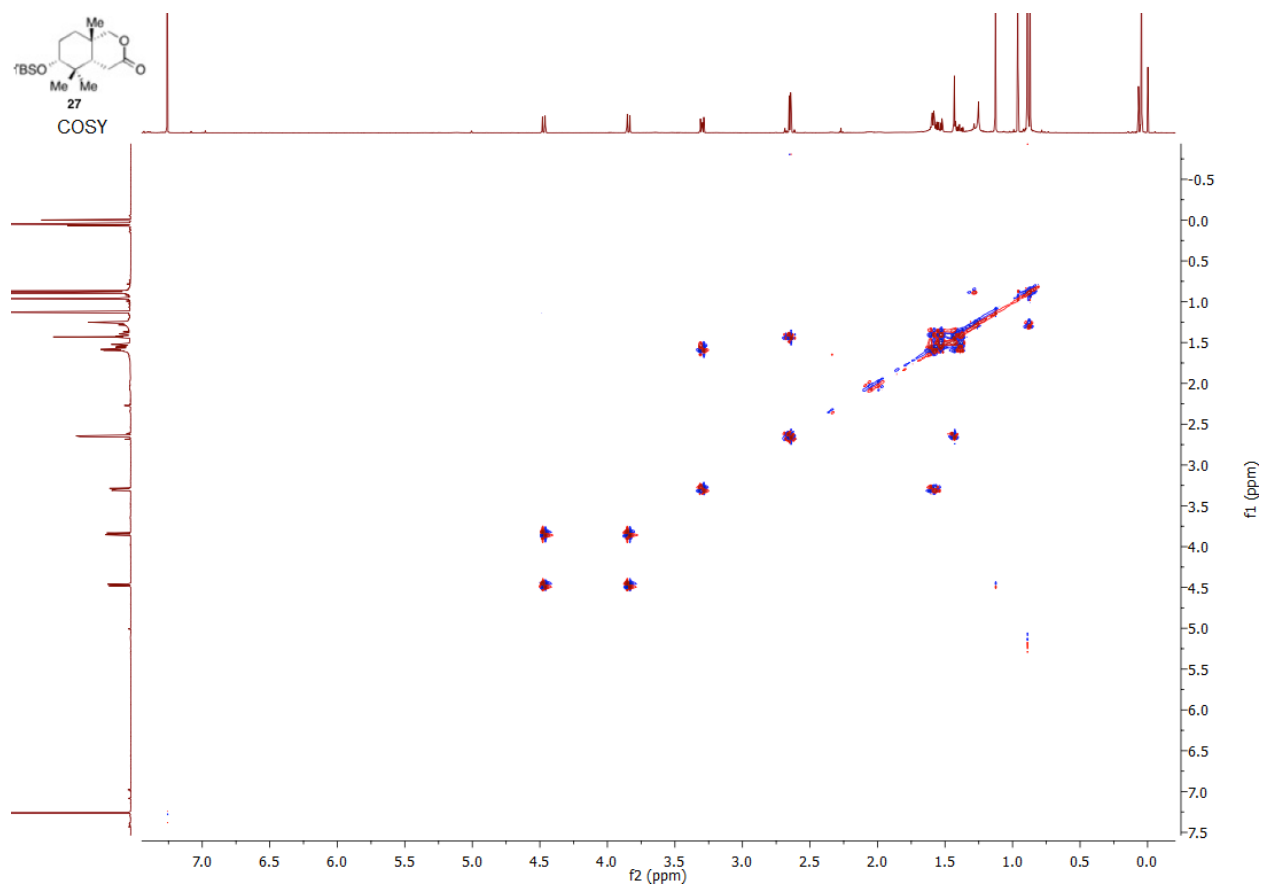


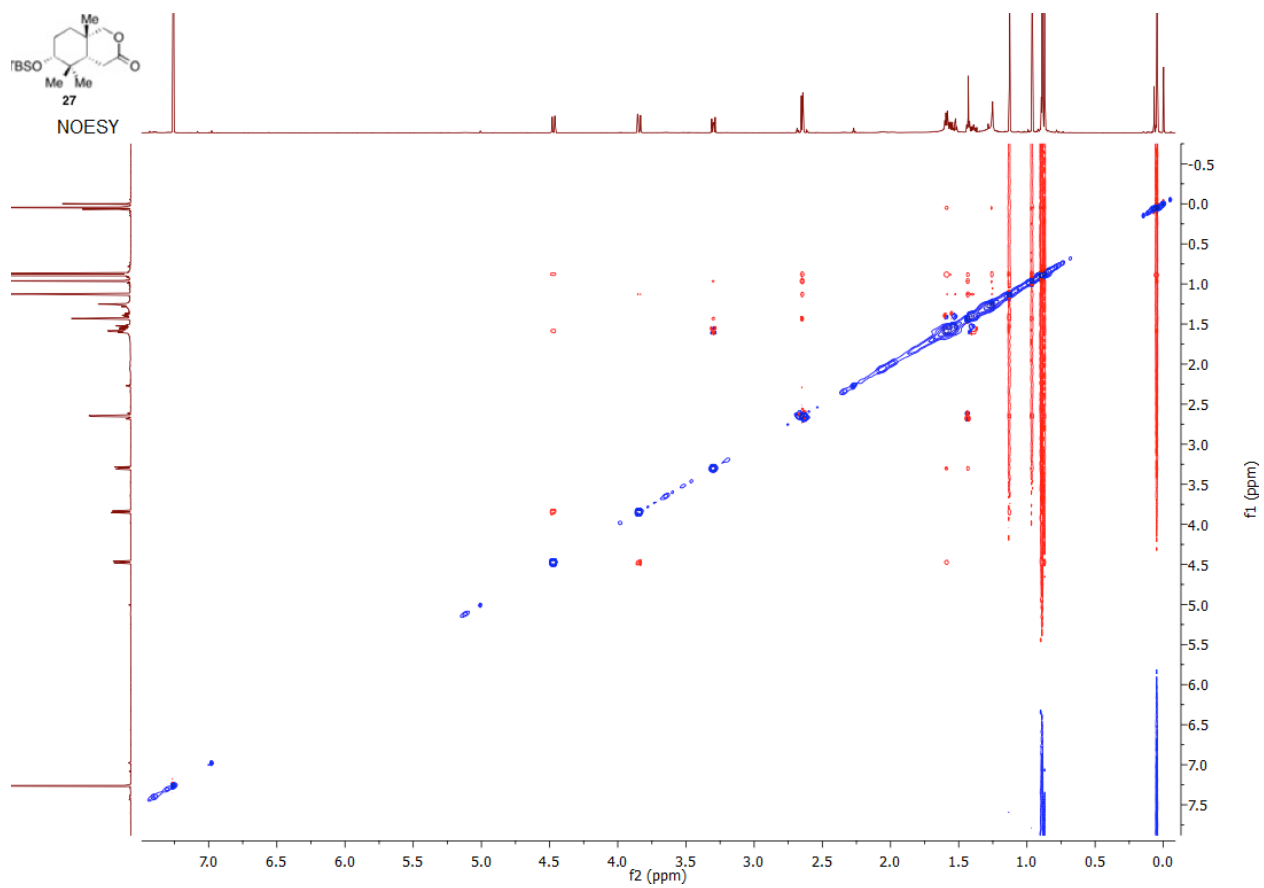


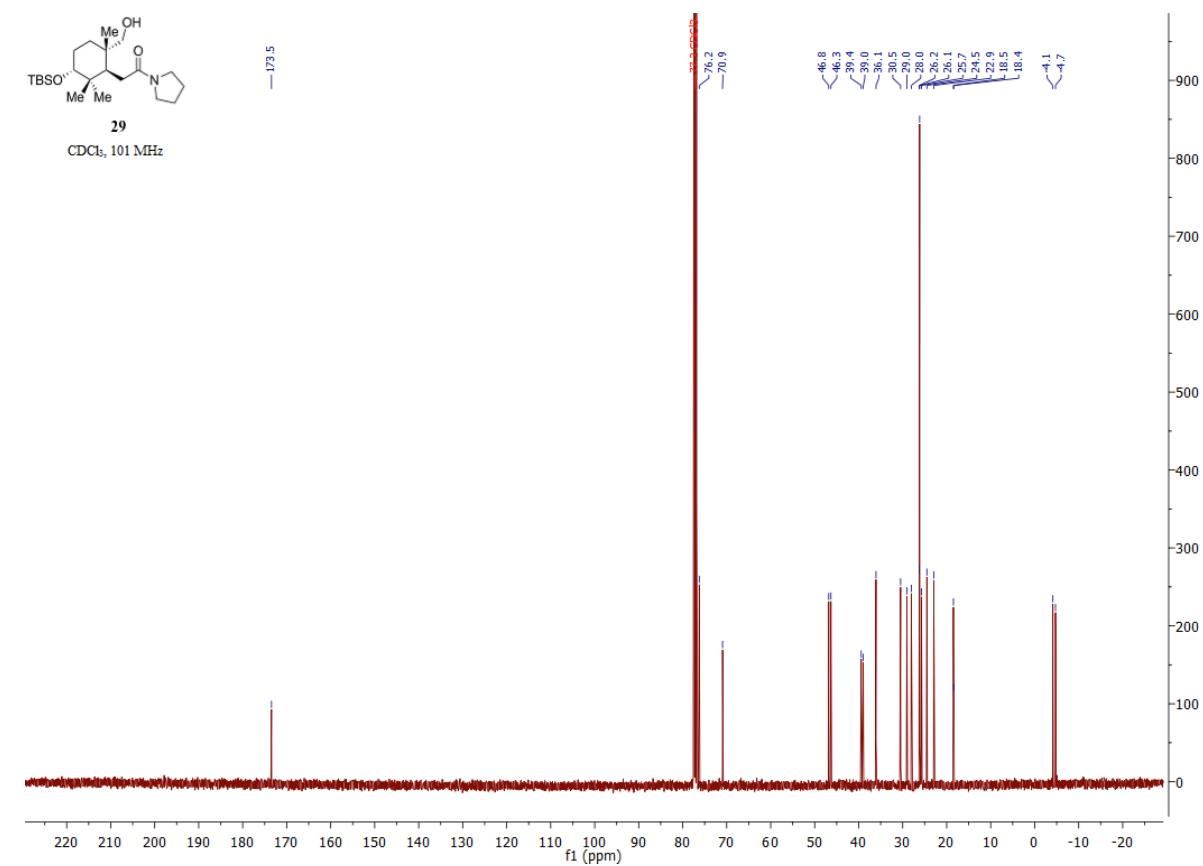


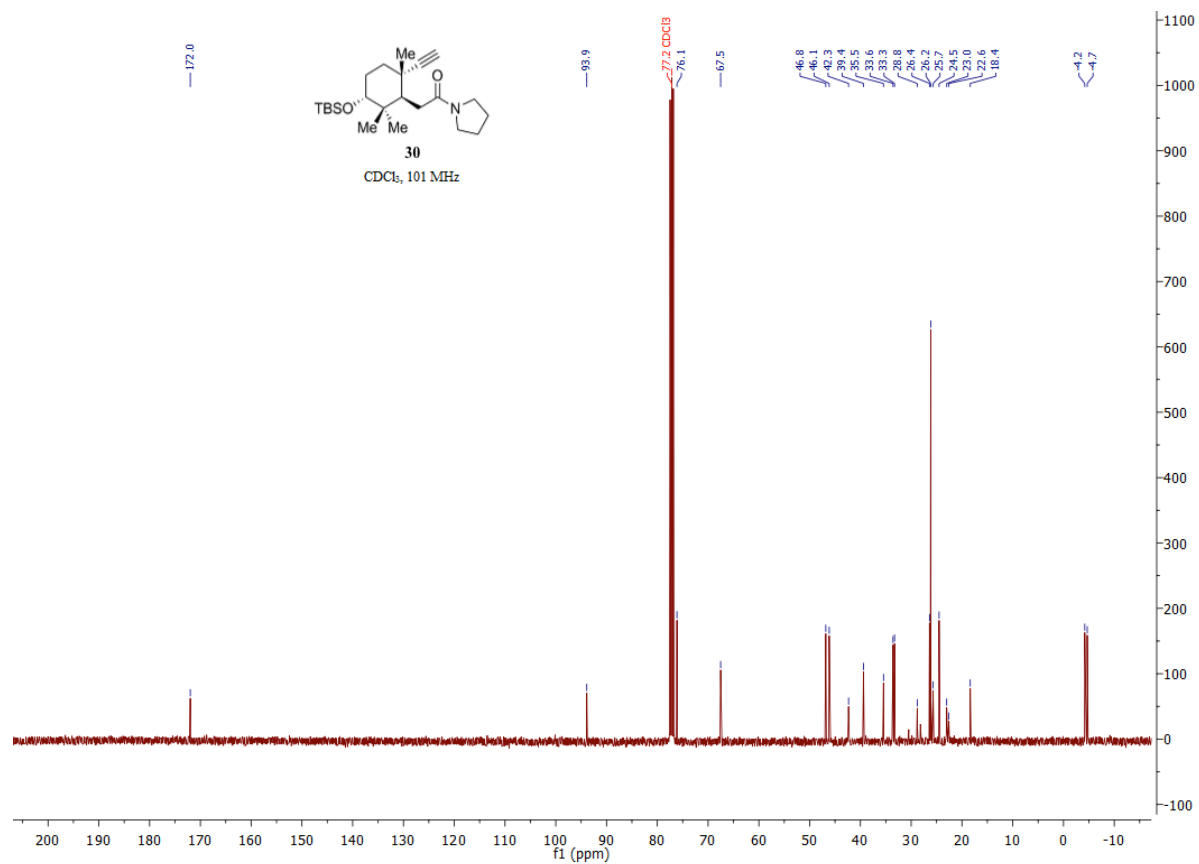
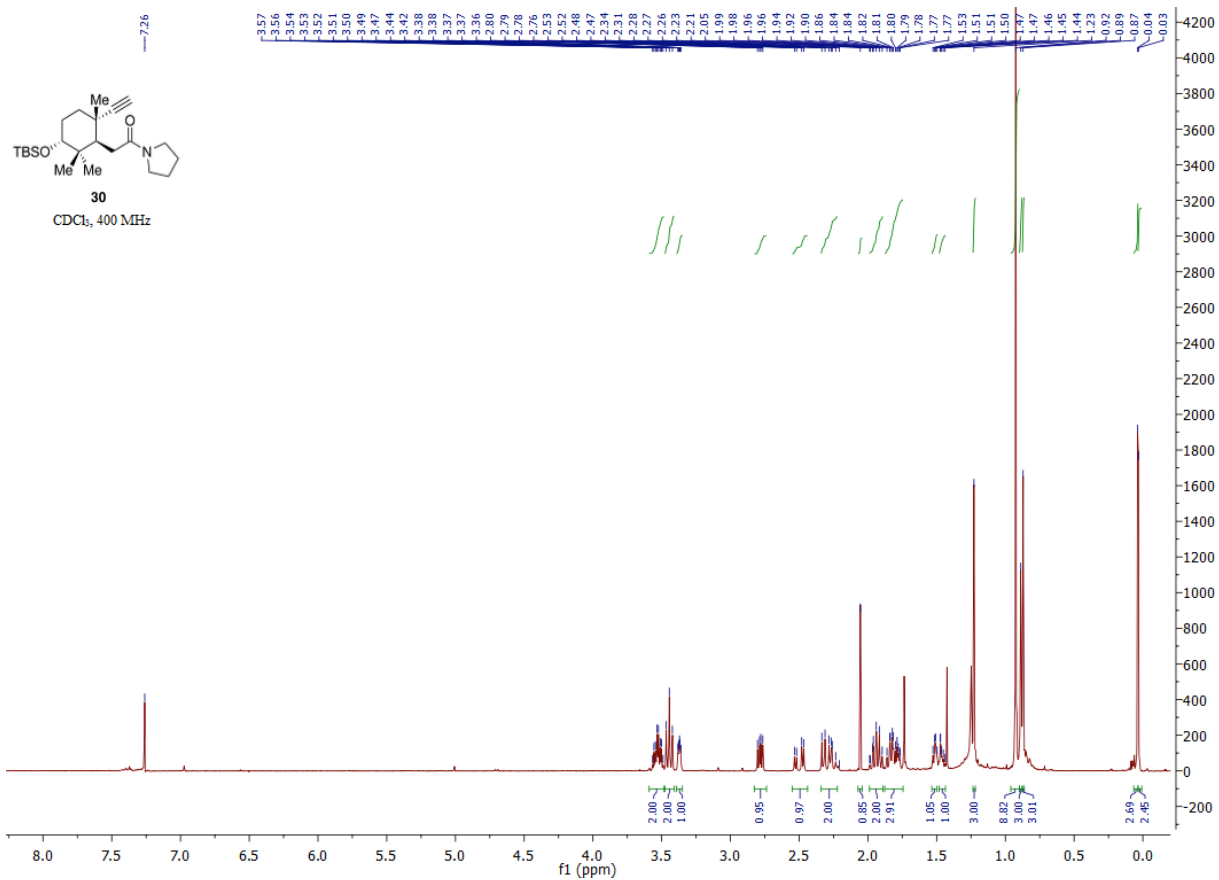


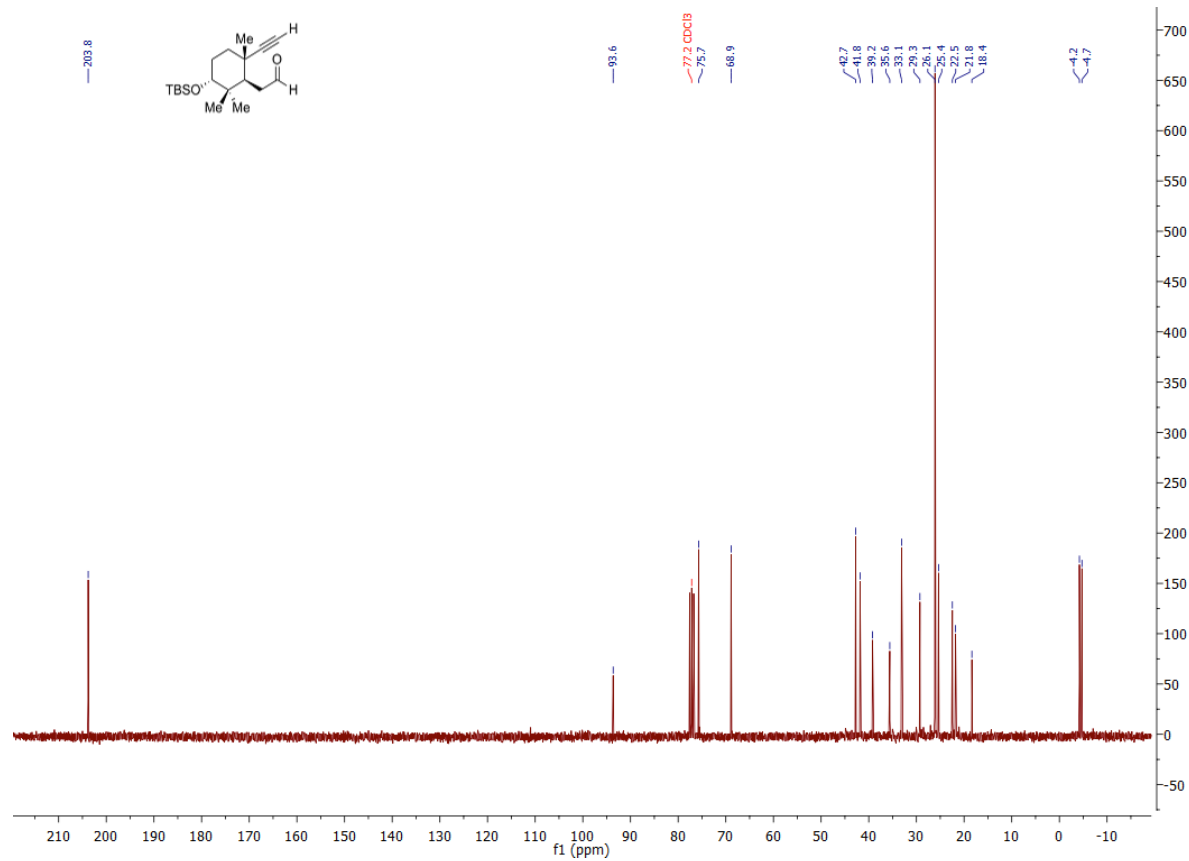
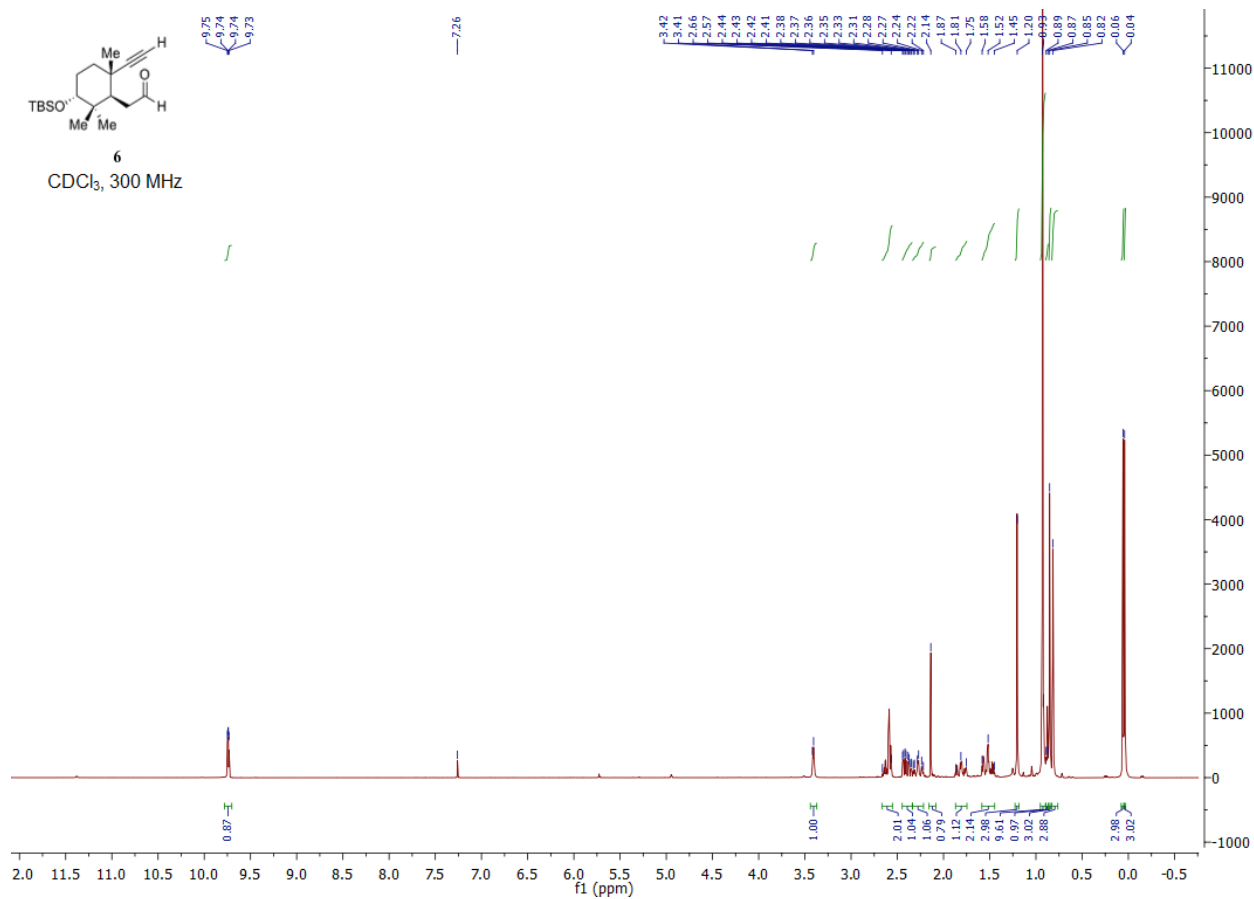


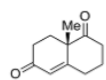






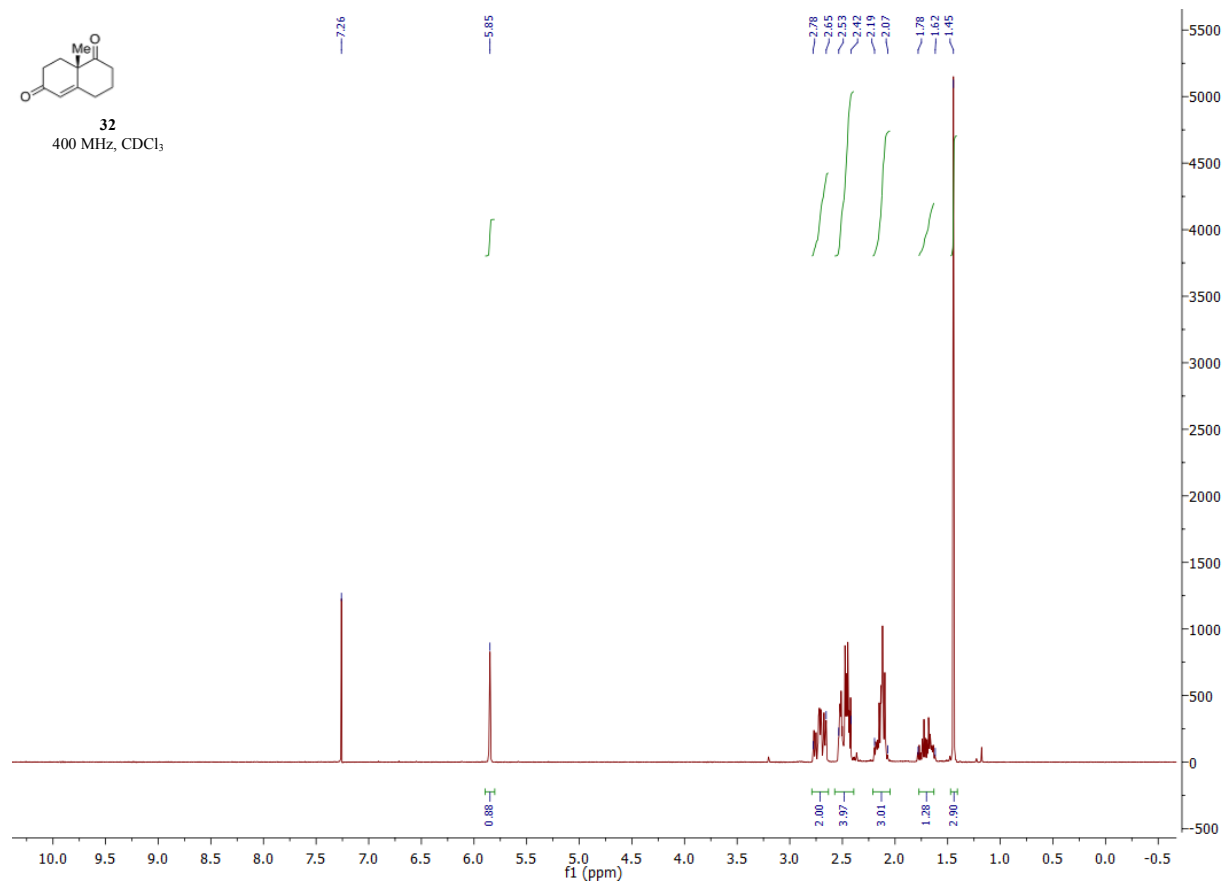


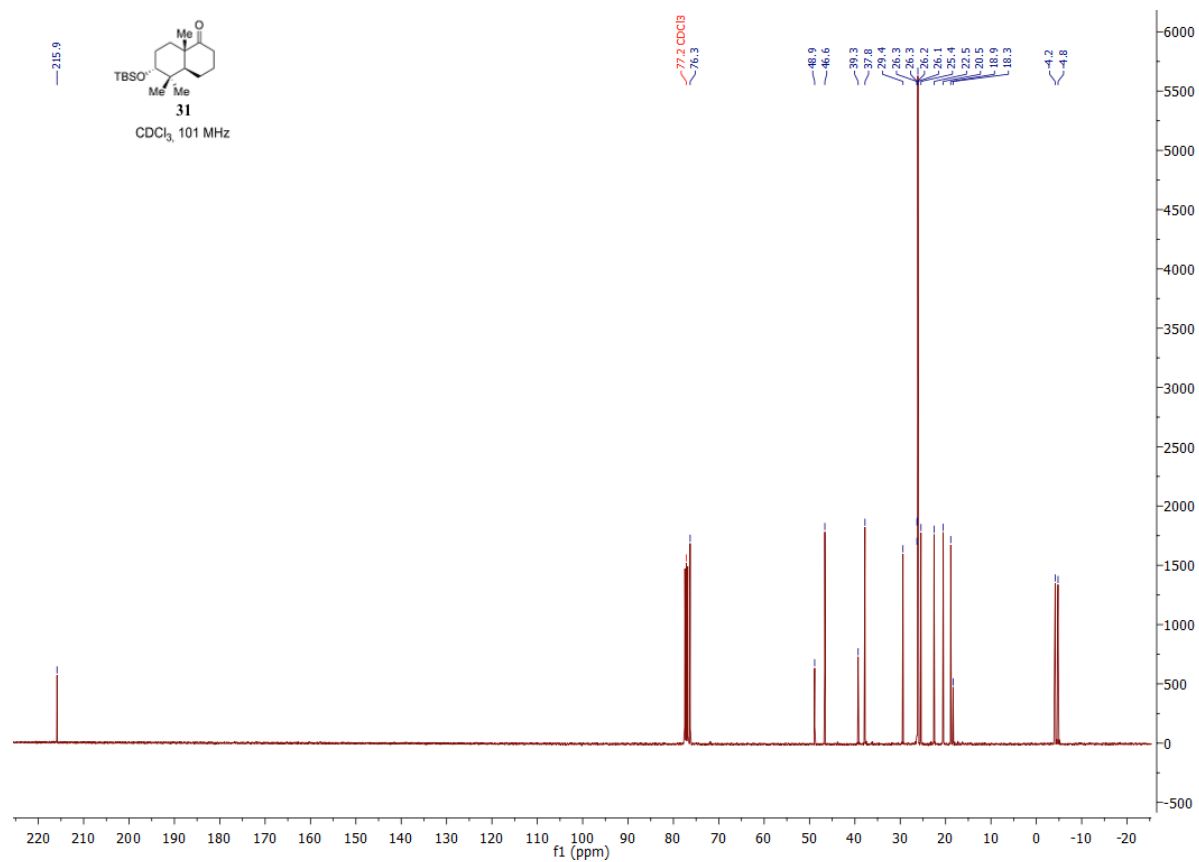
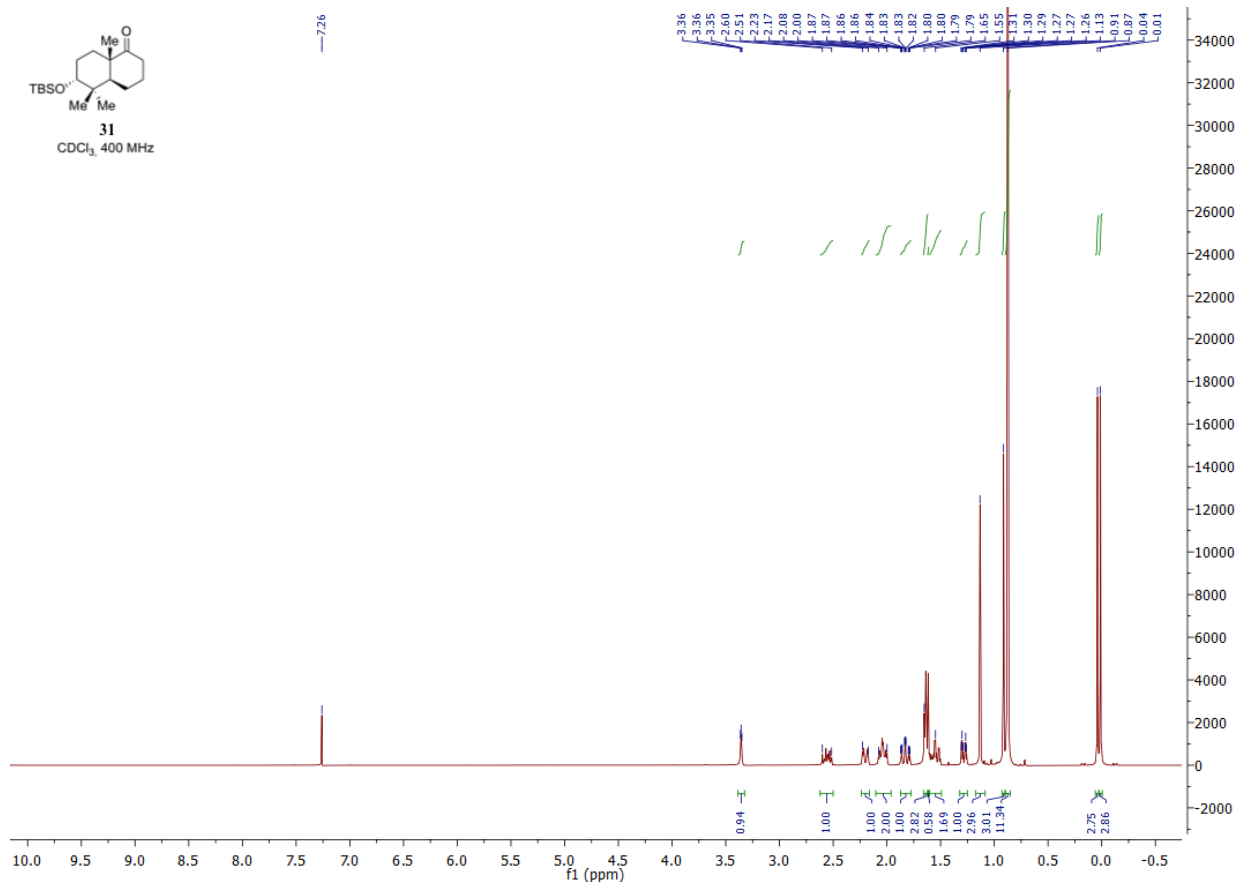


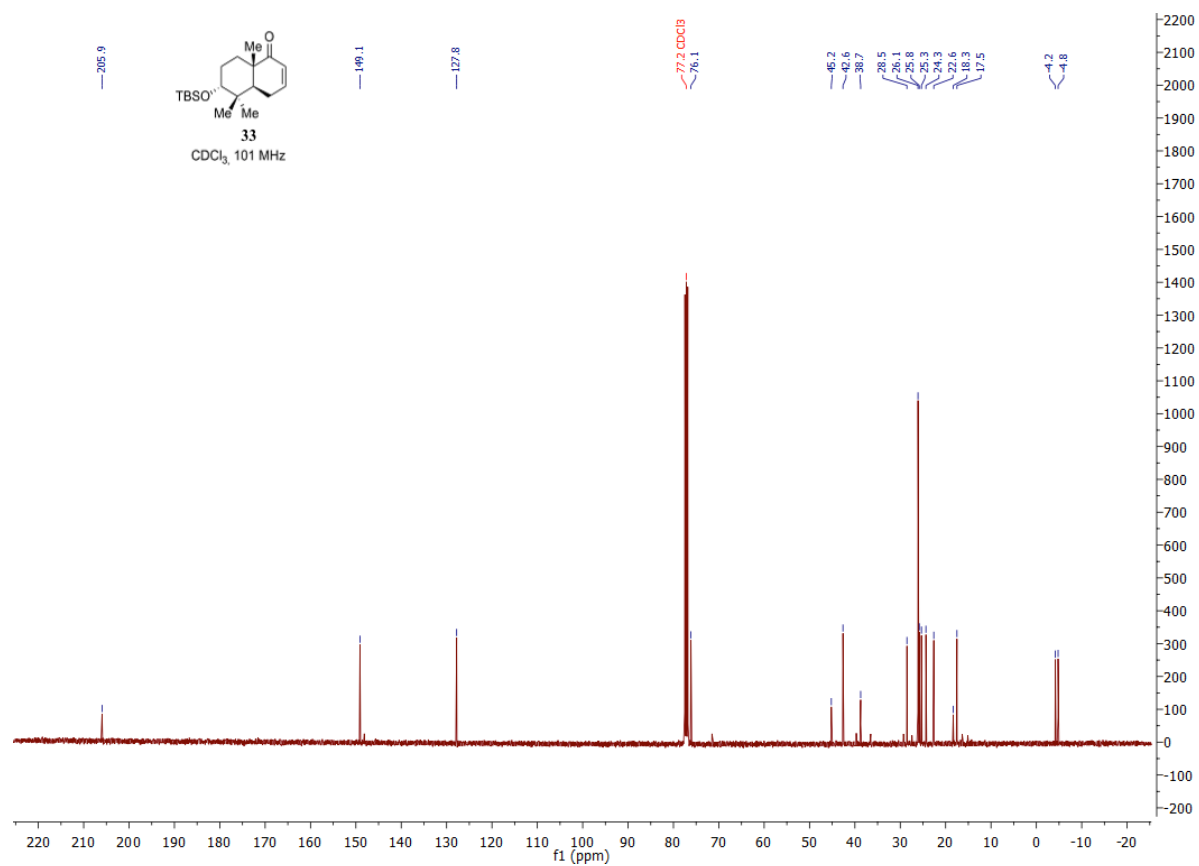
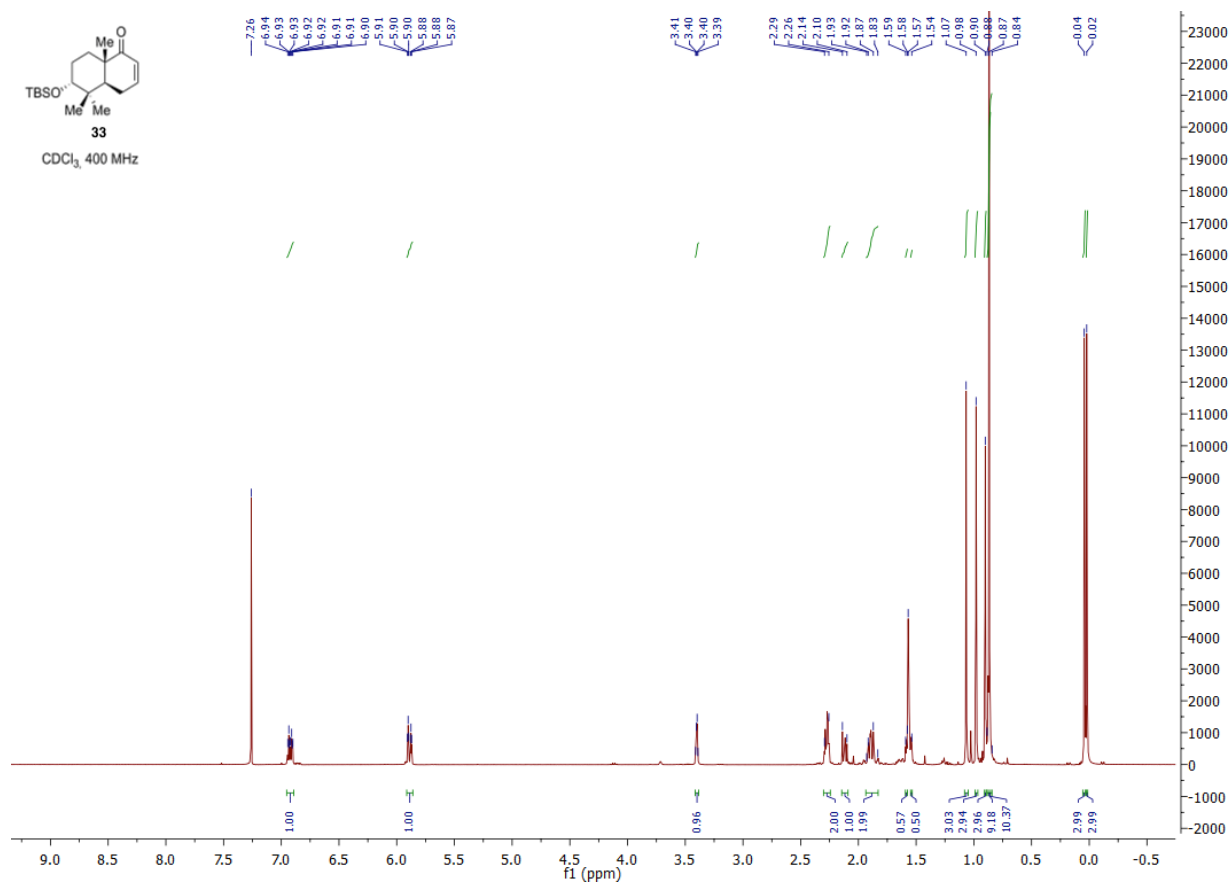


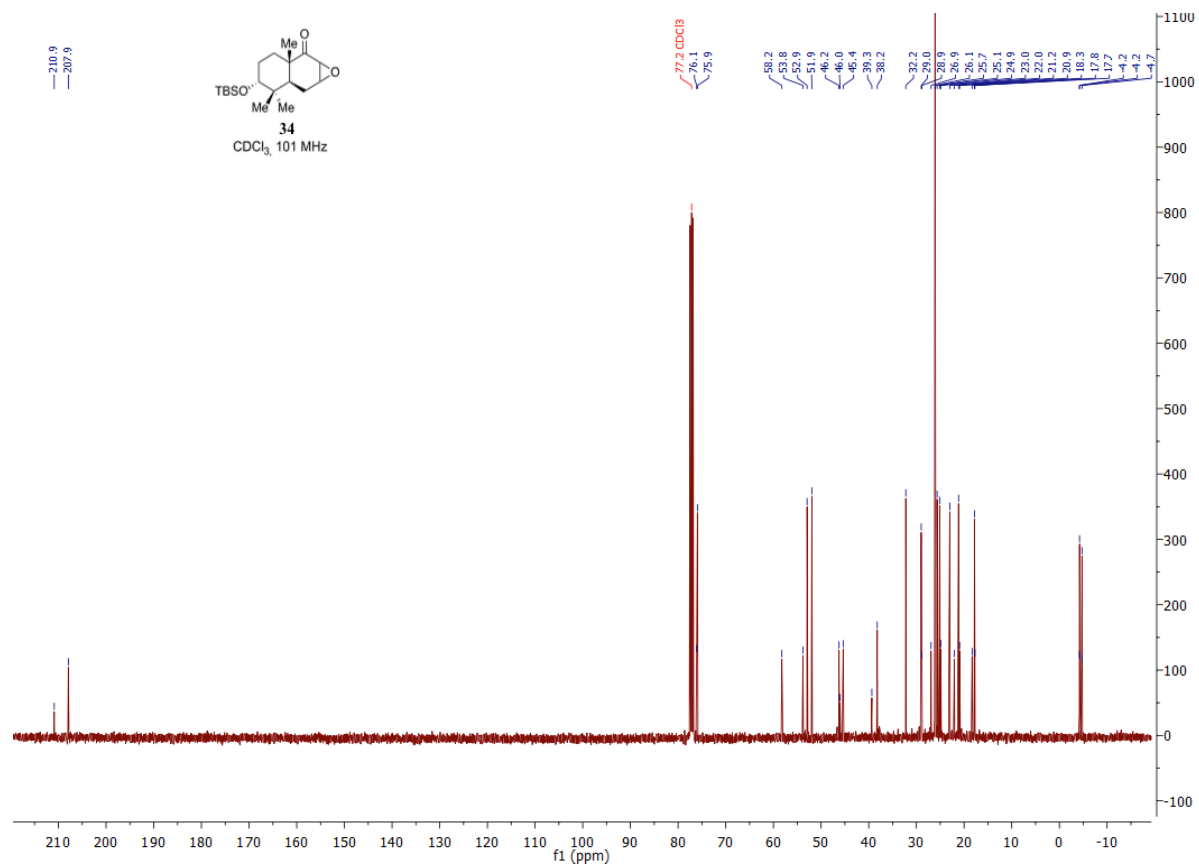
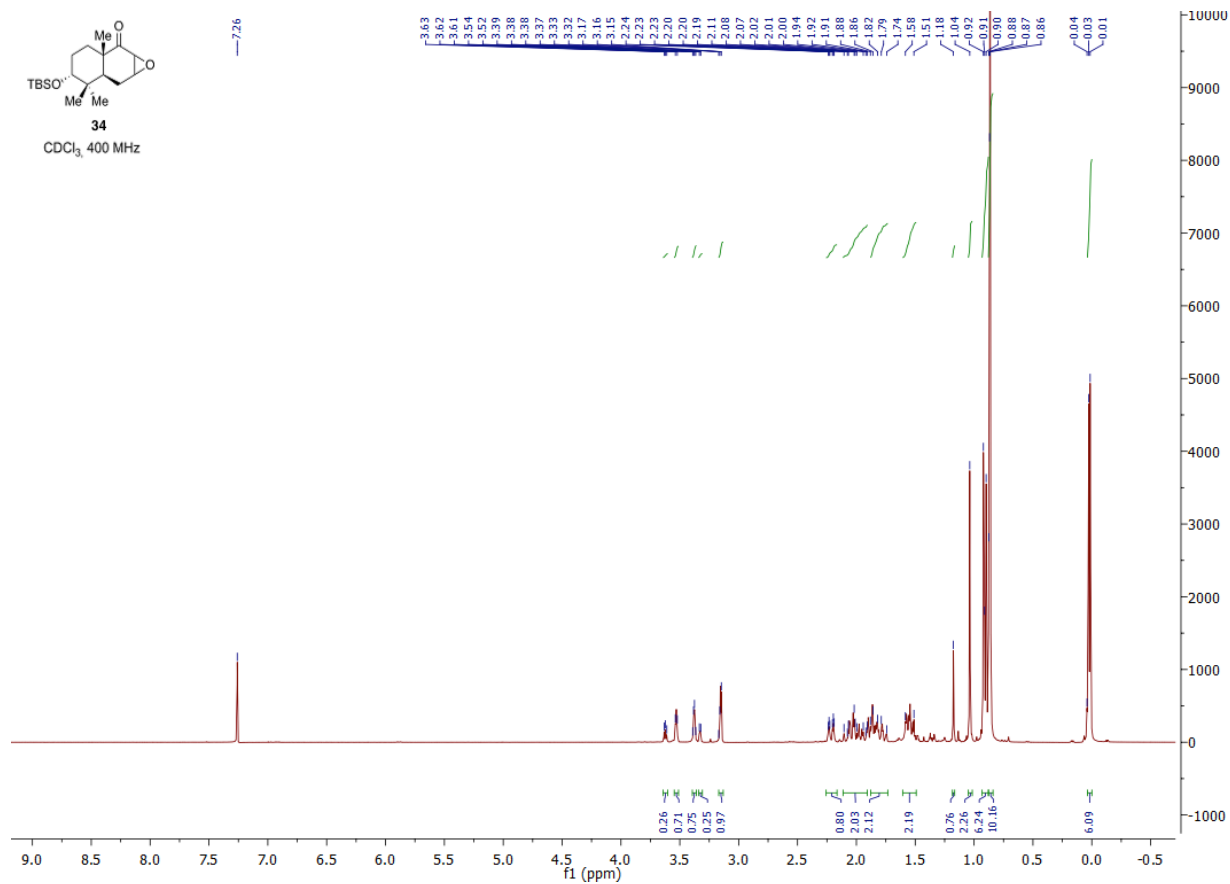
32

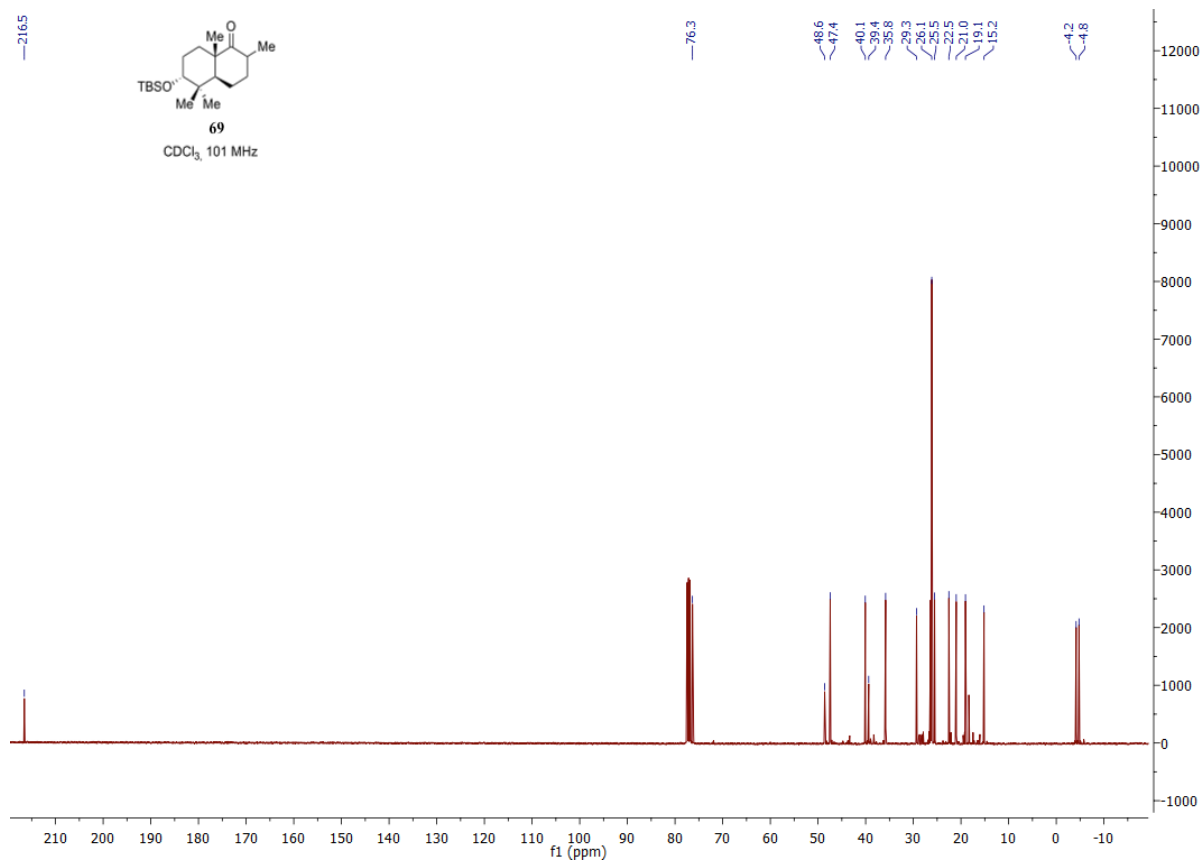
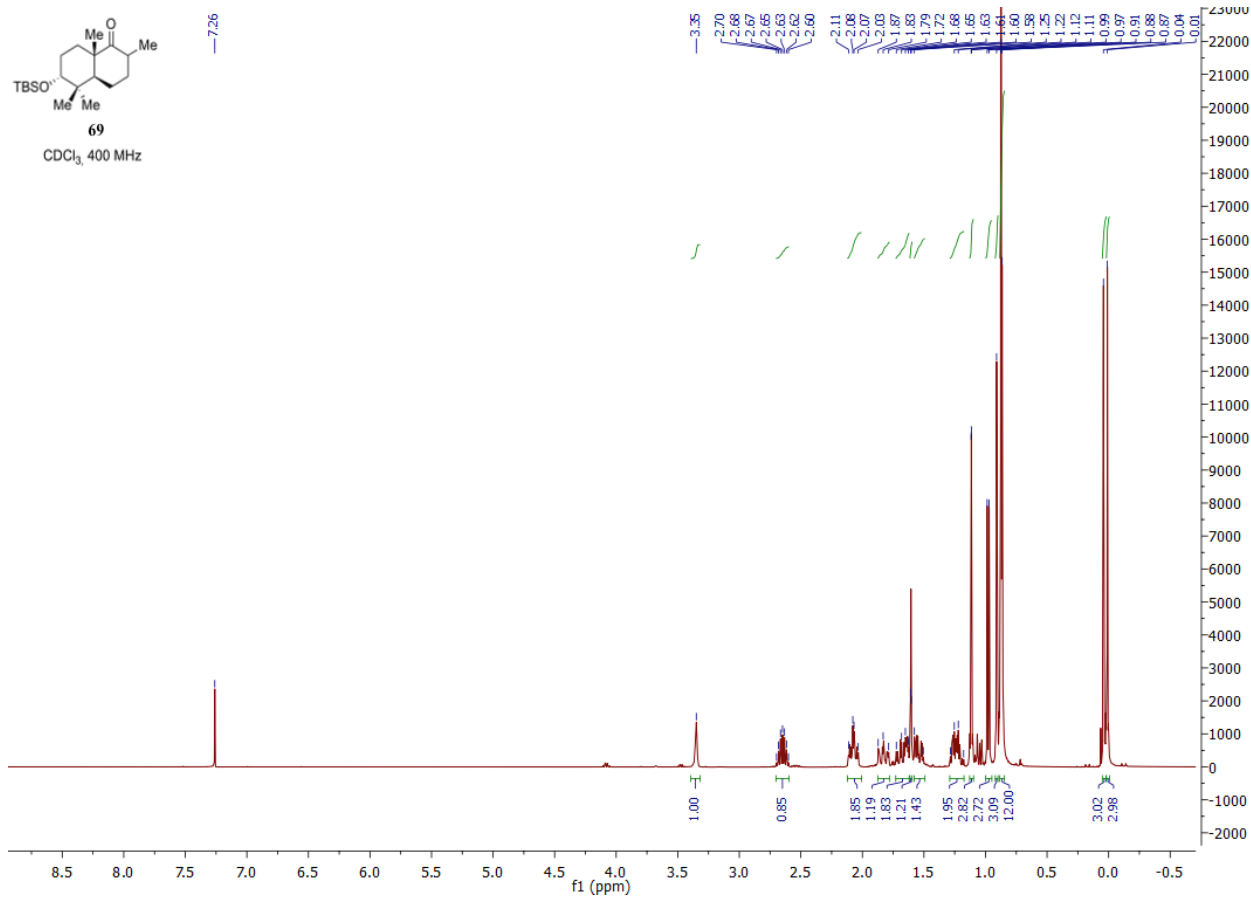
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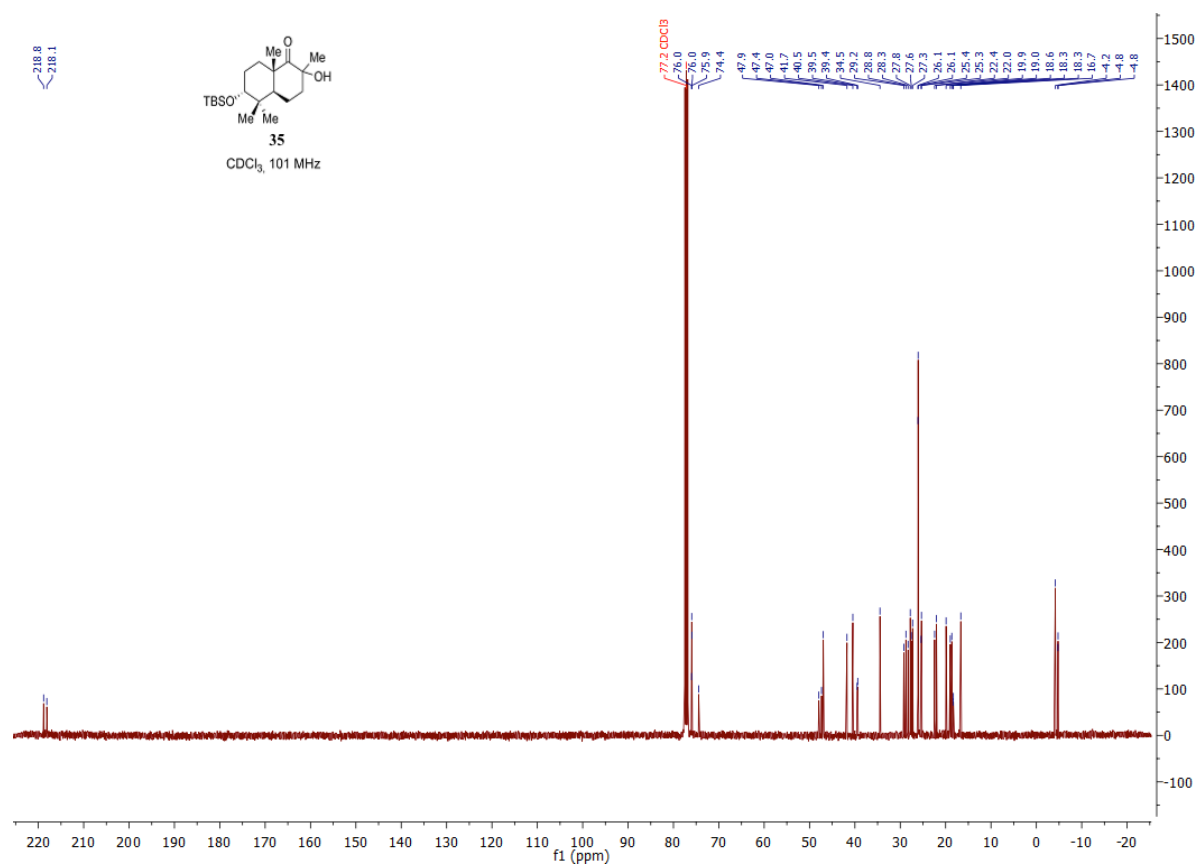
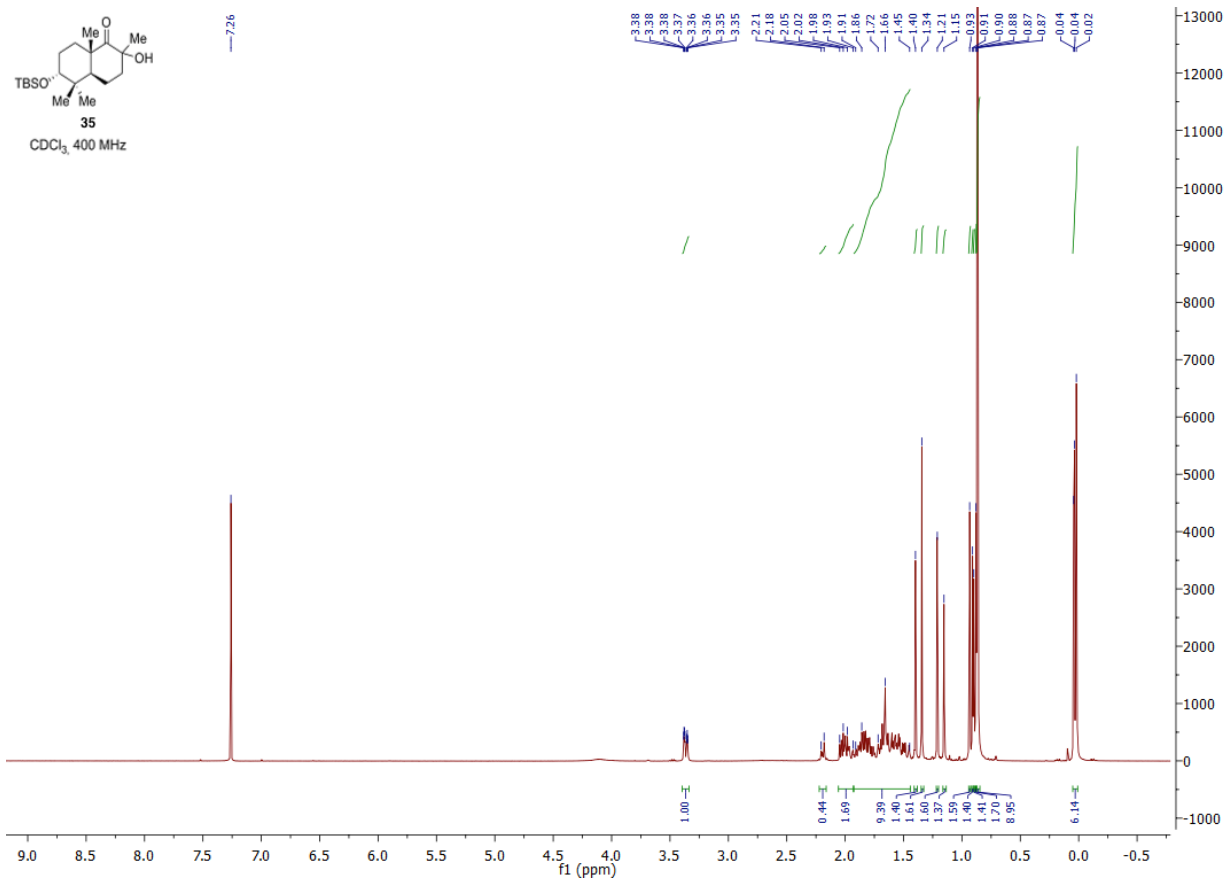


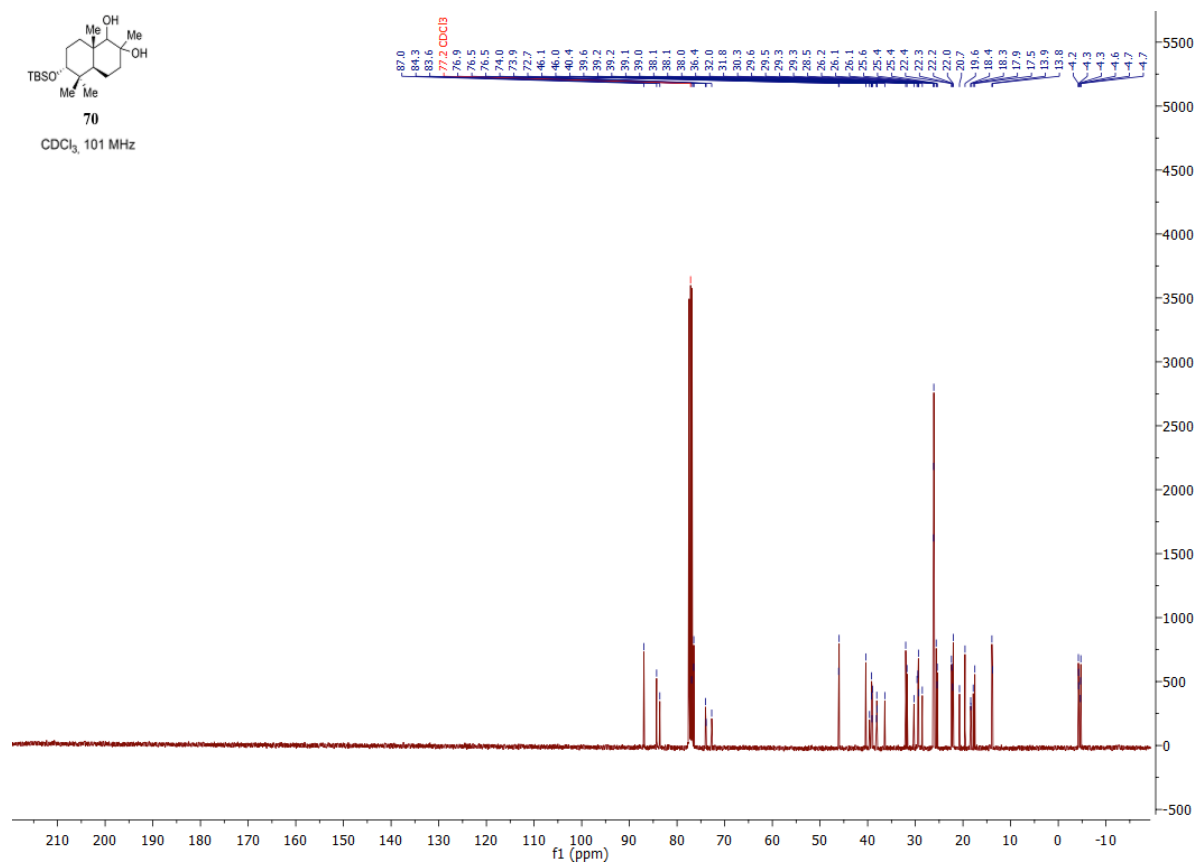
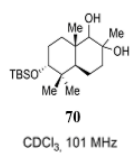
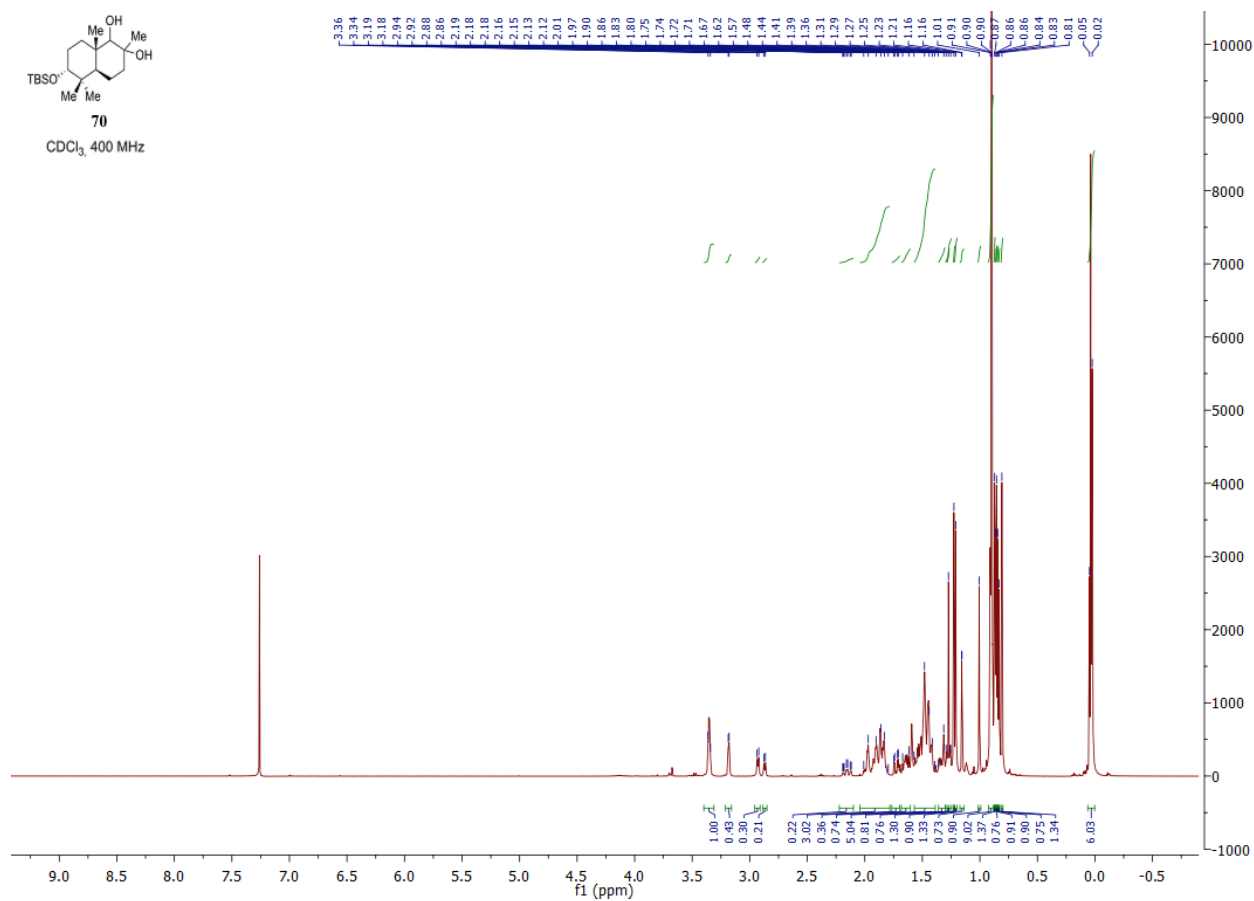
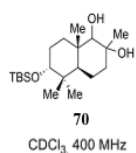


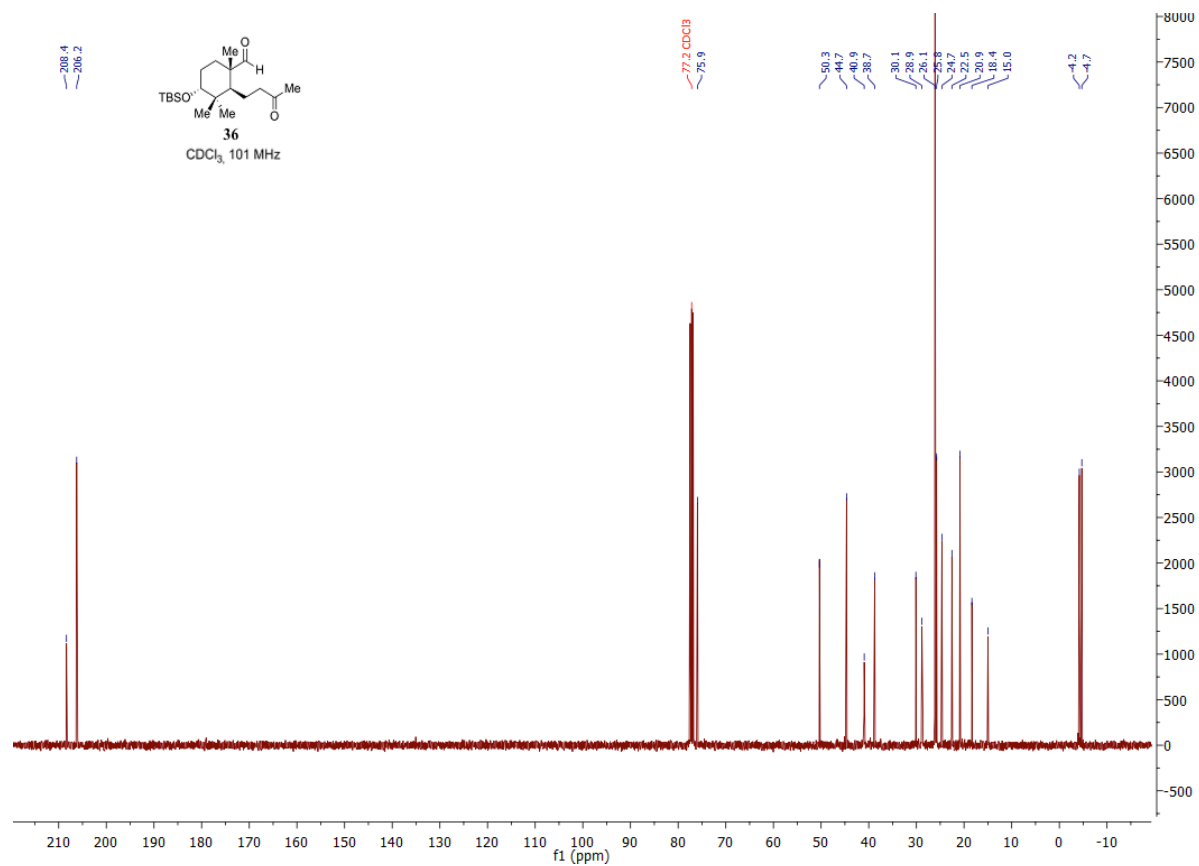
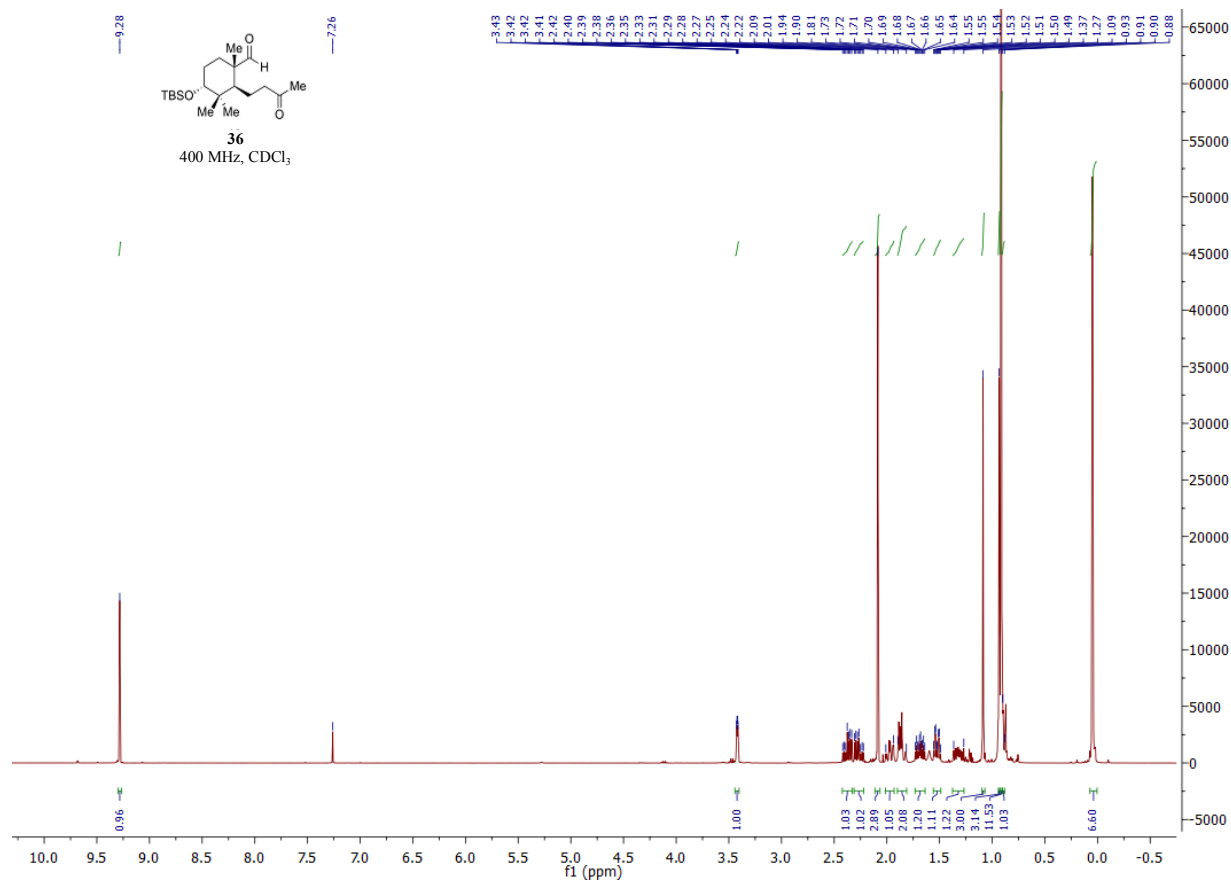


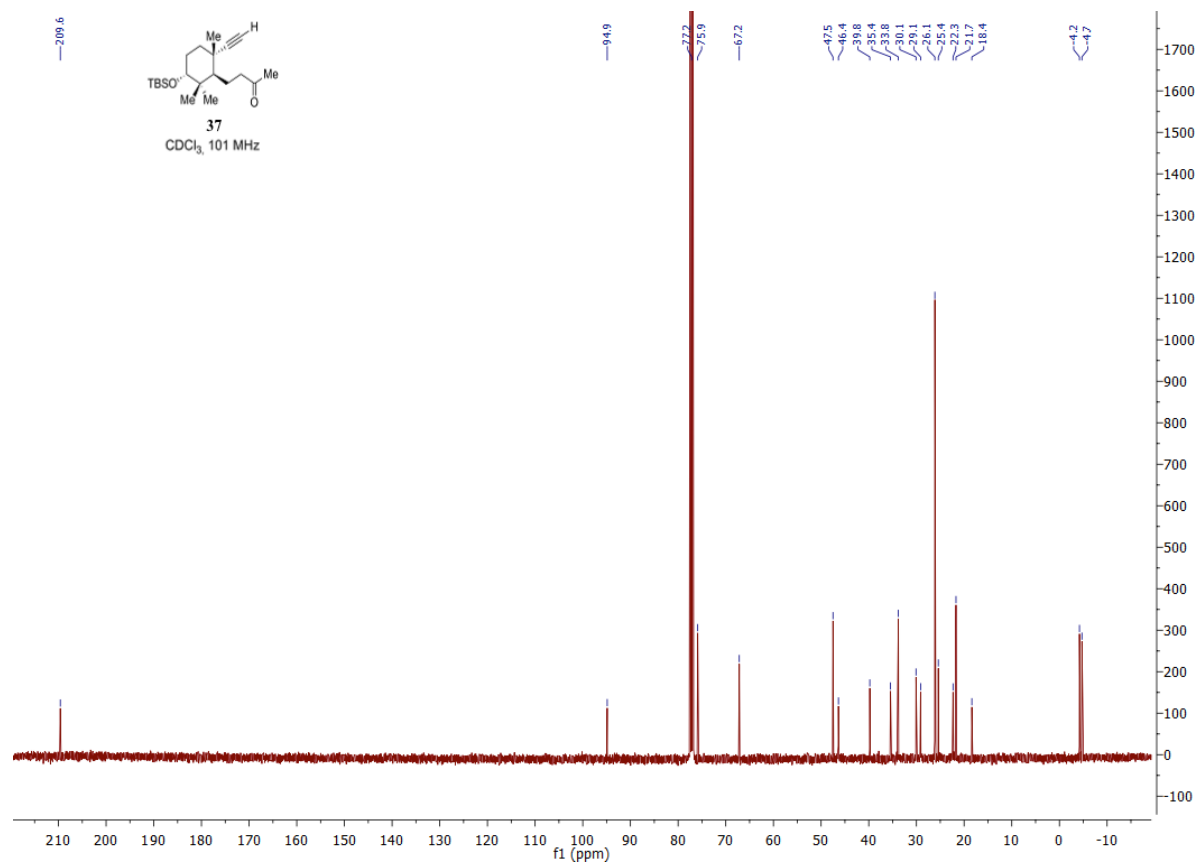
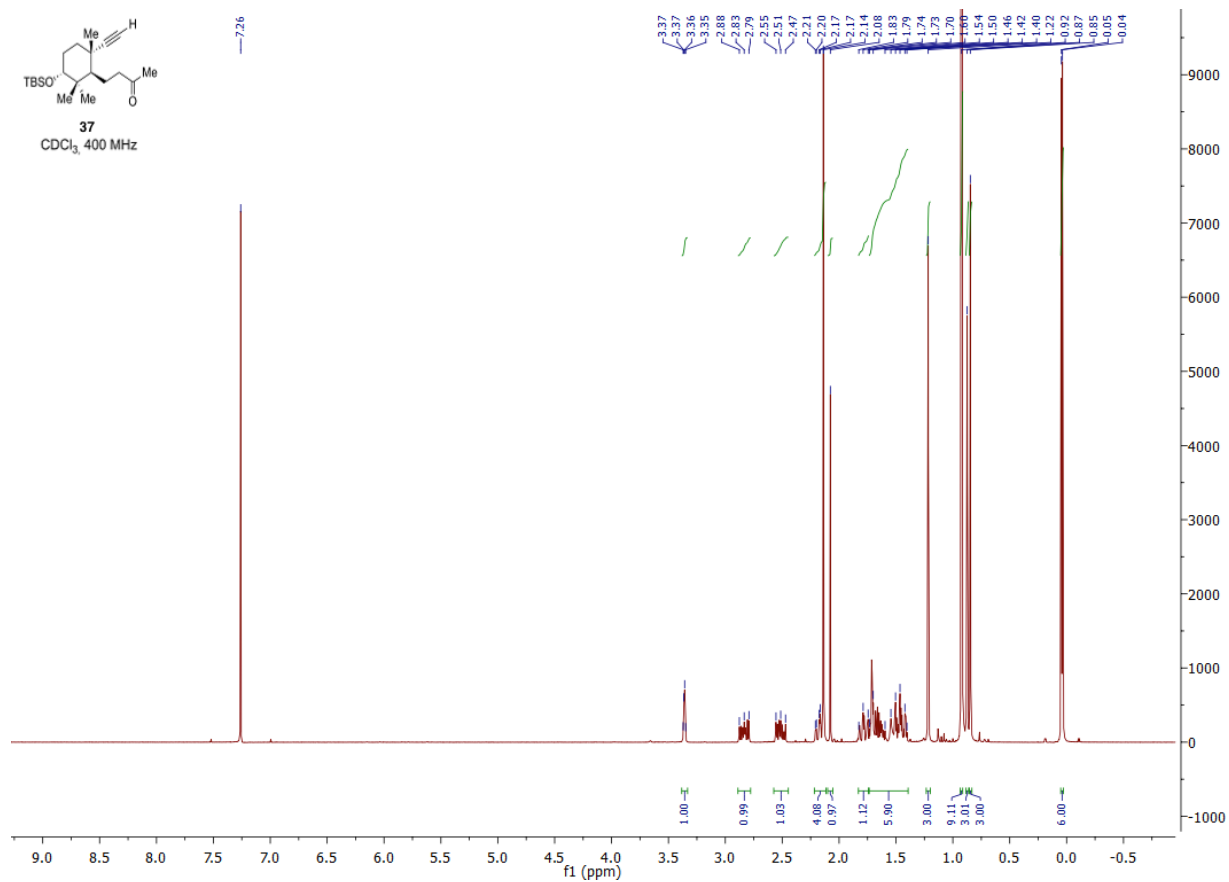


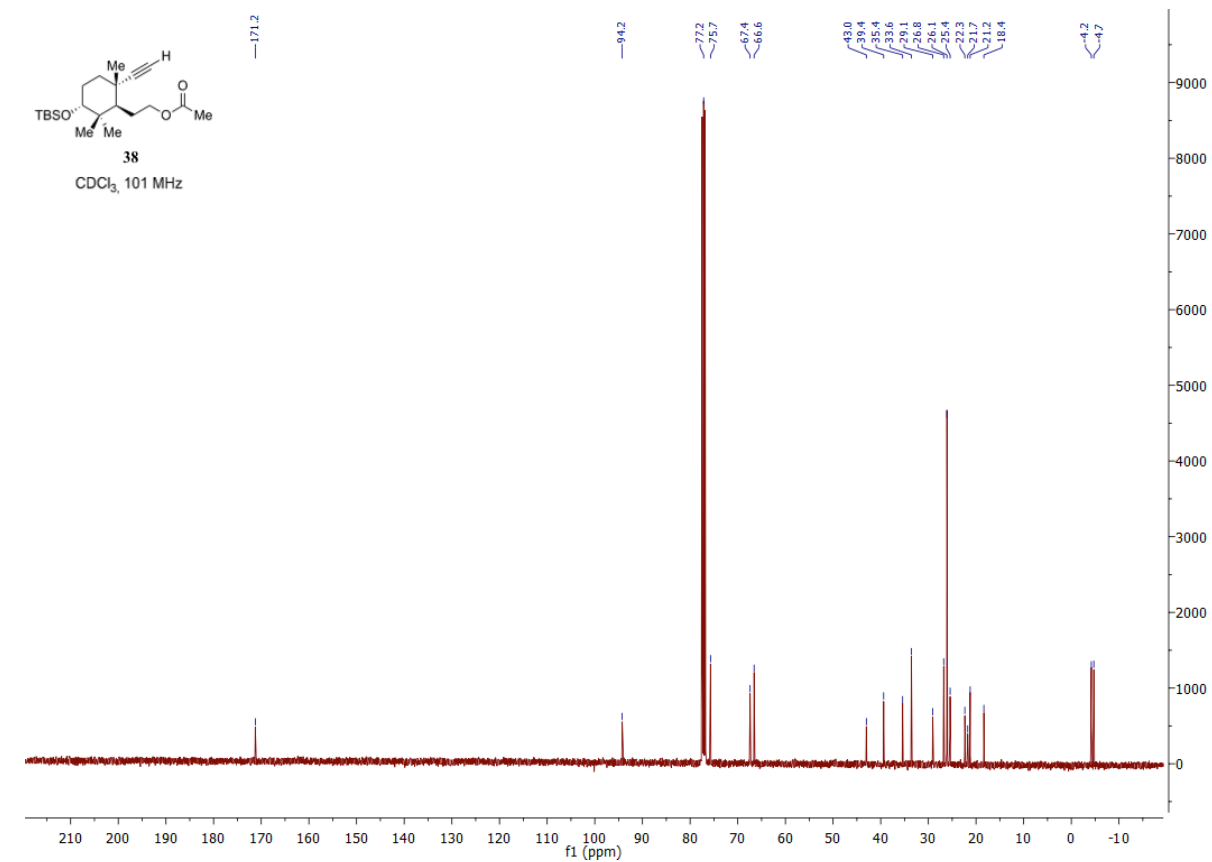


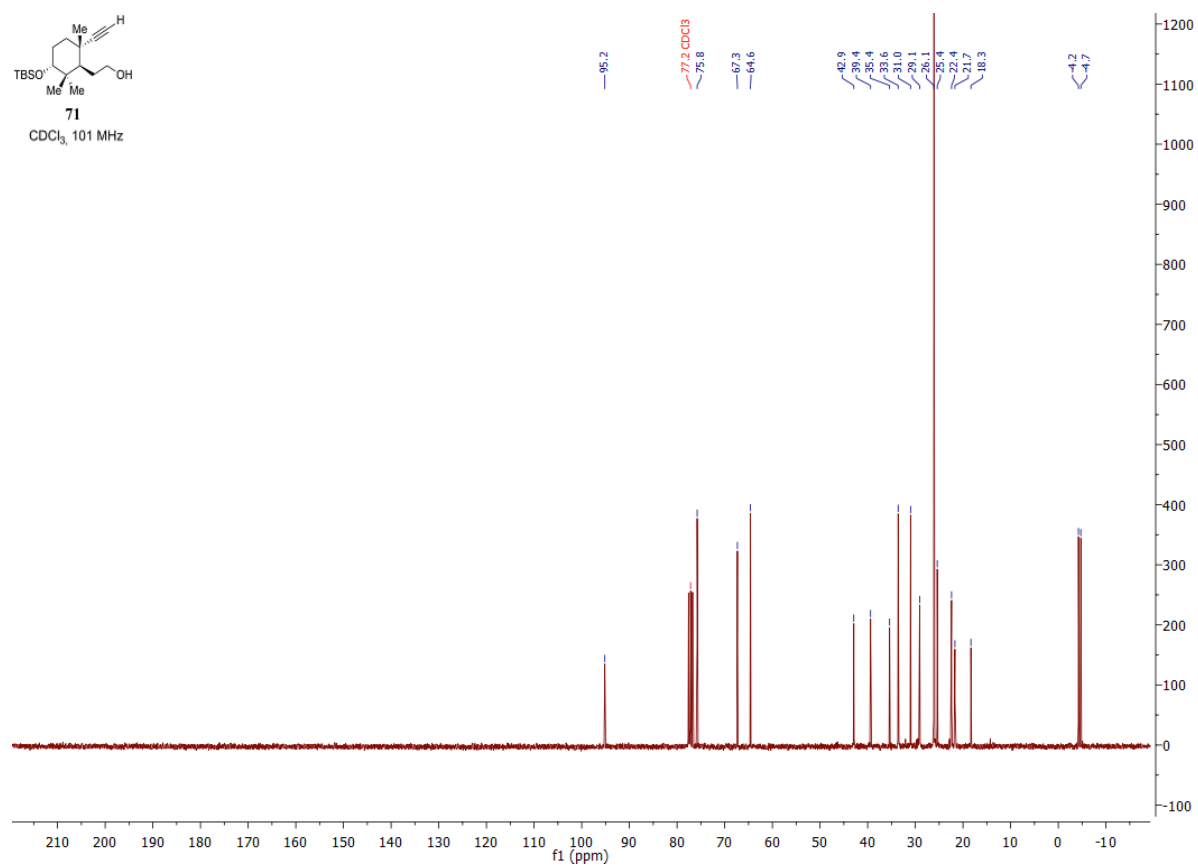
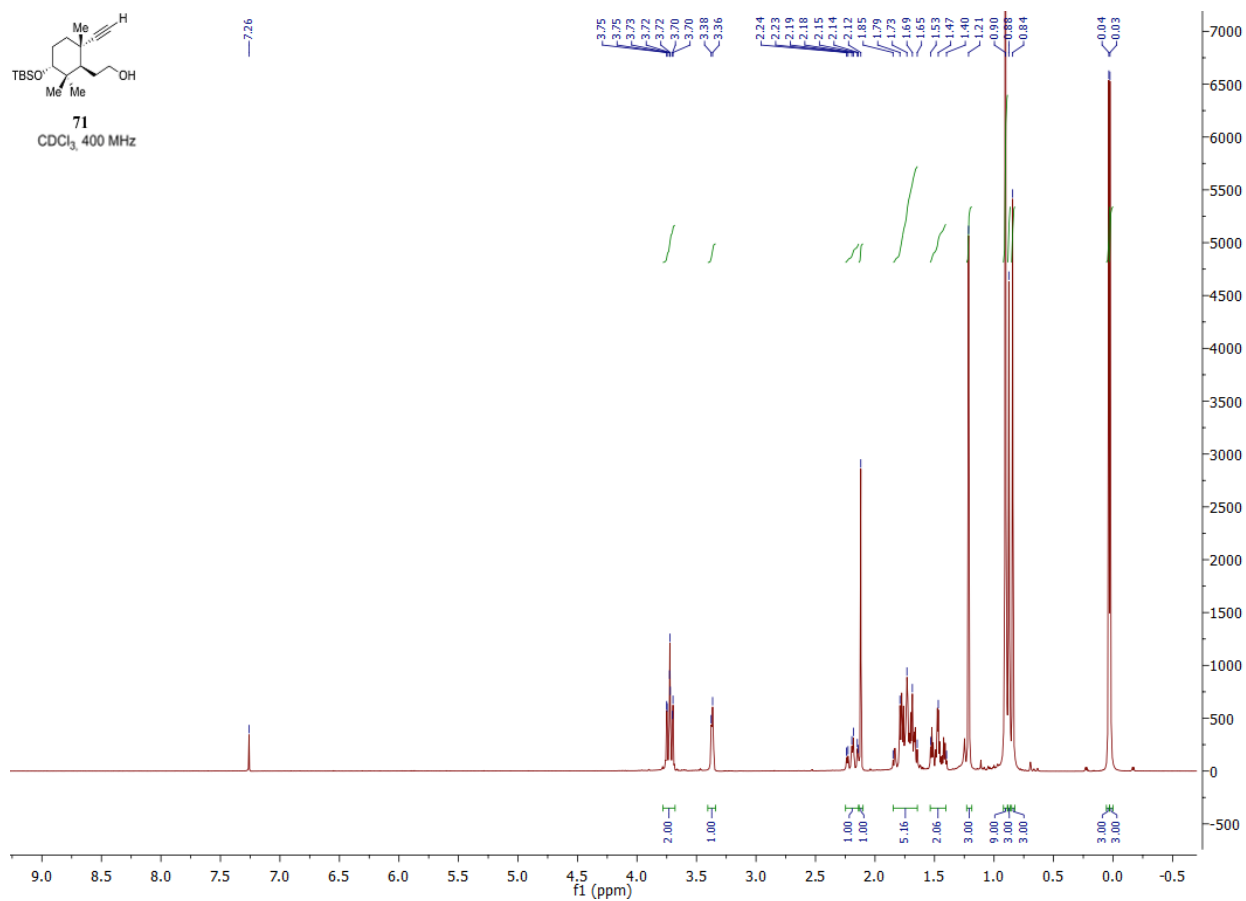


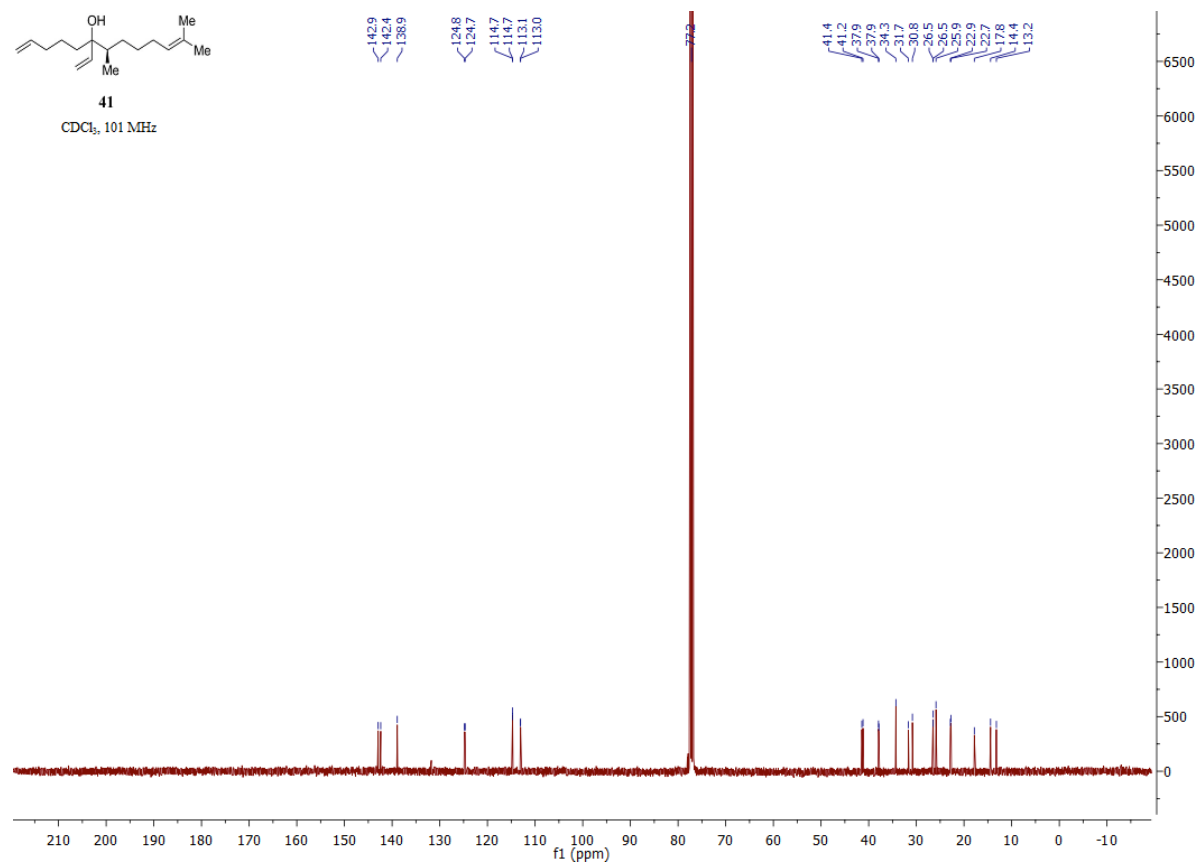
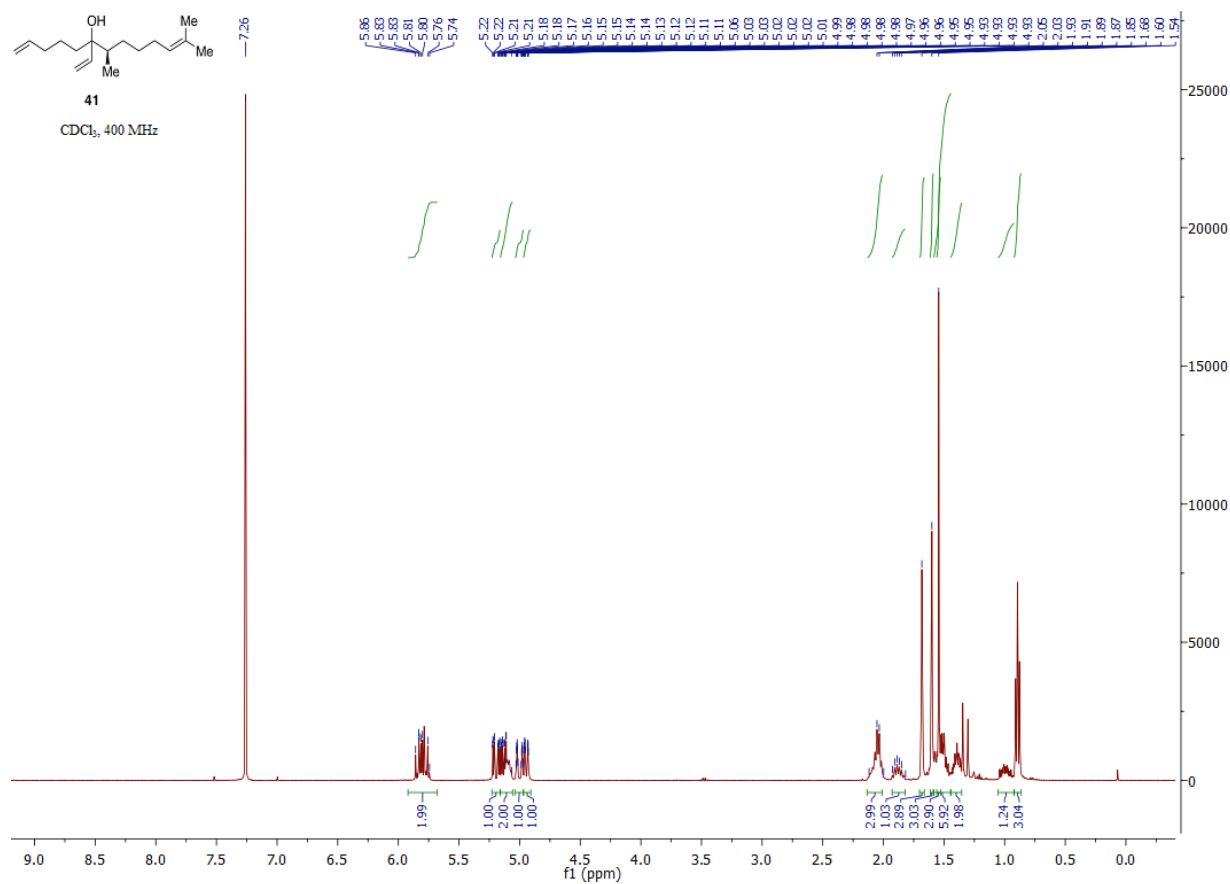


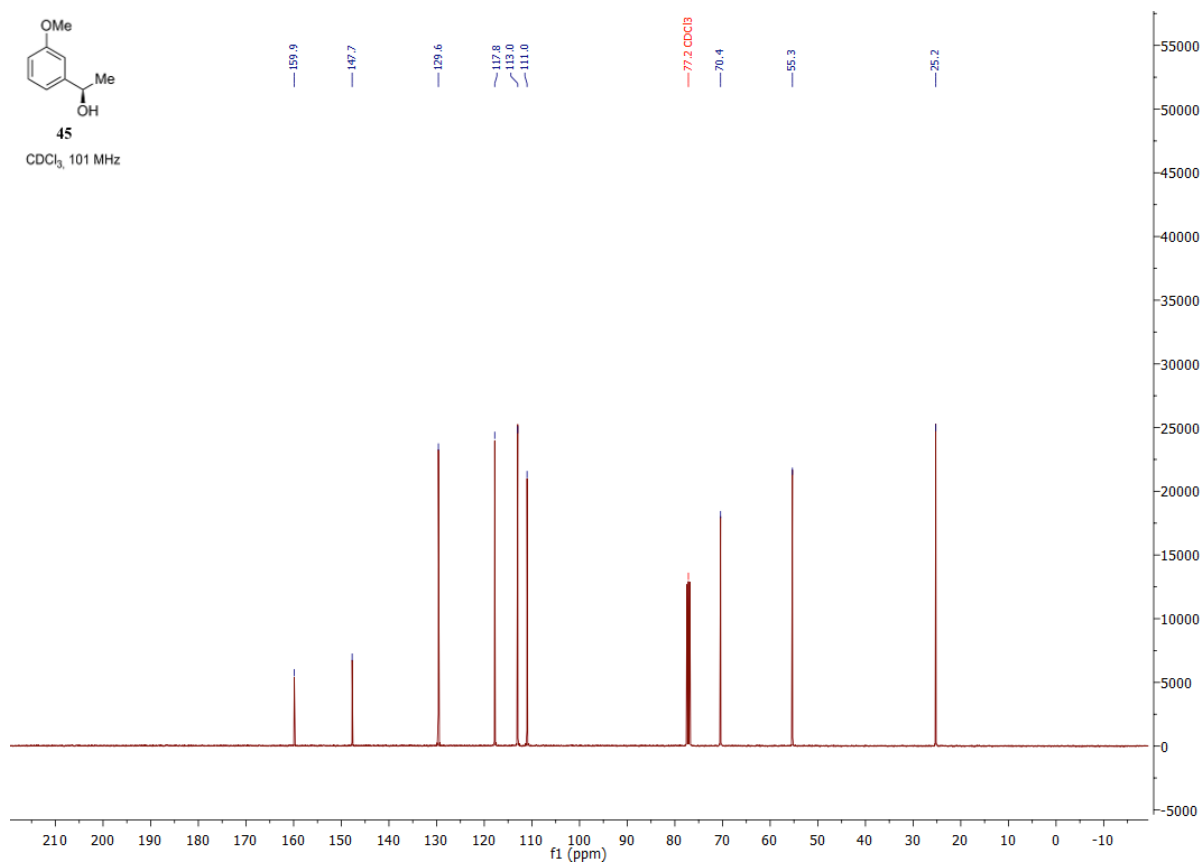
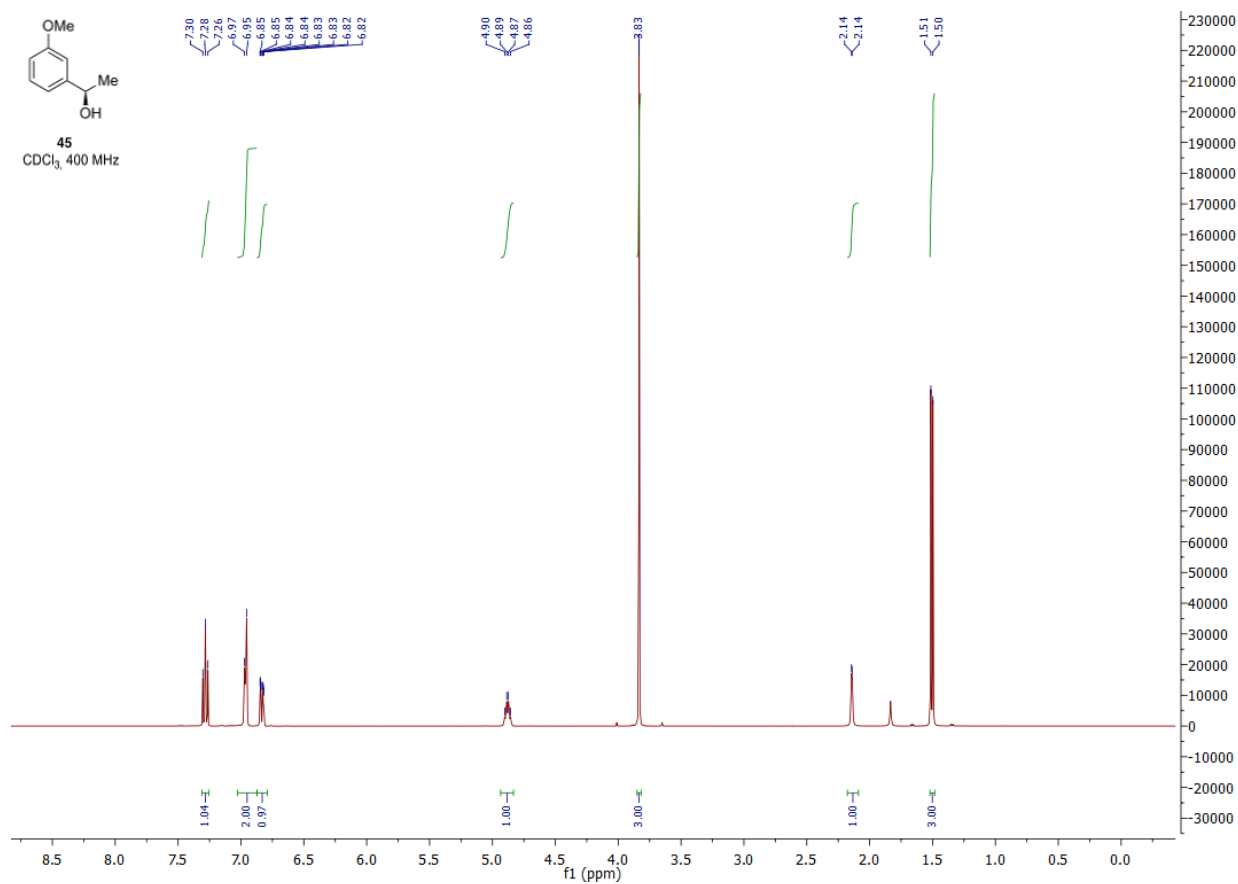


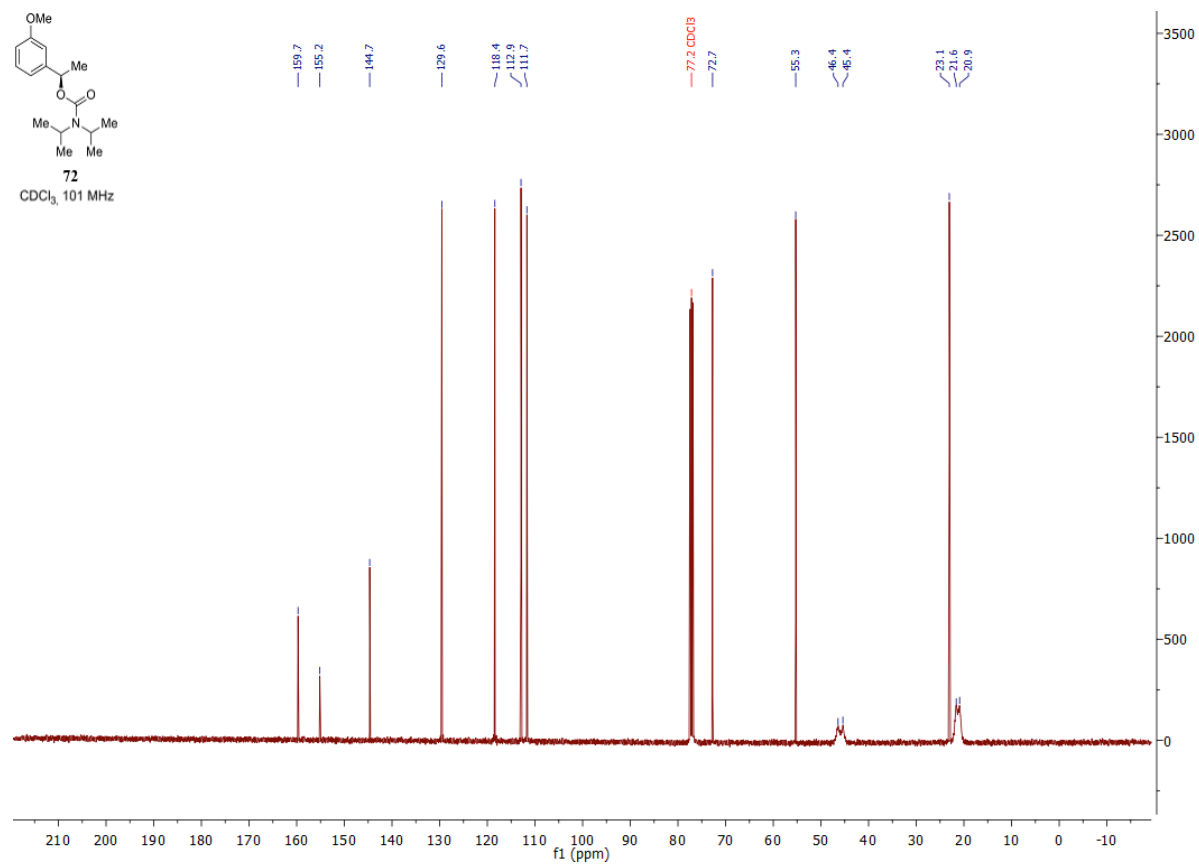
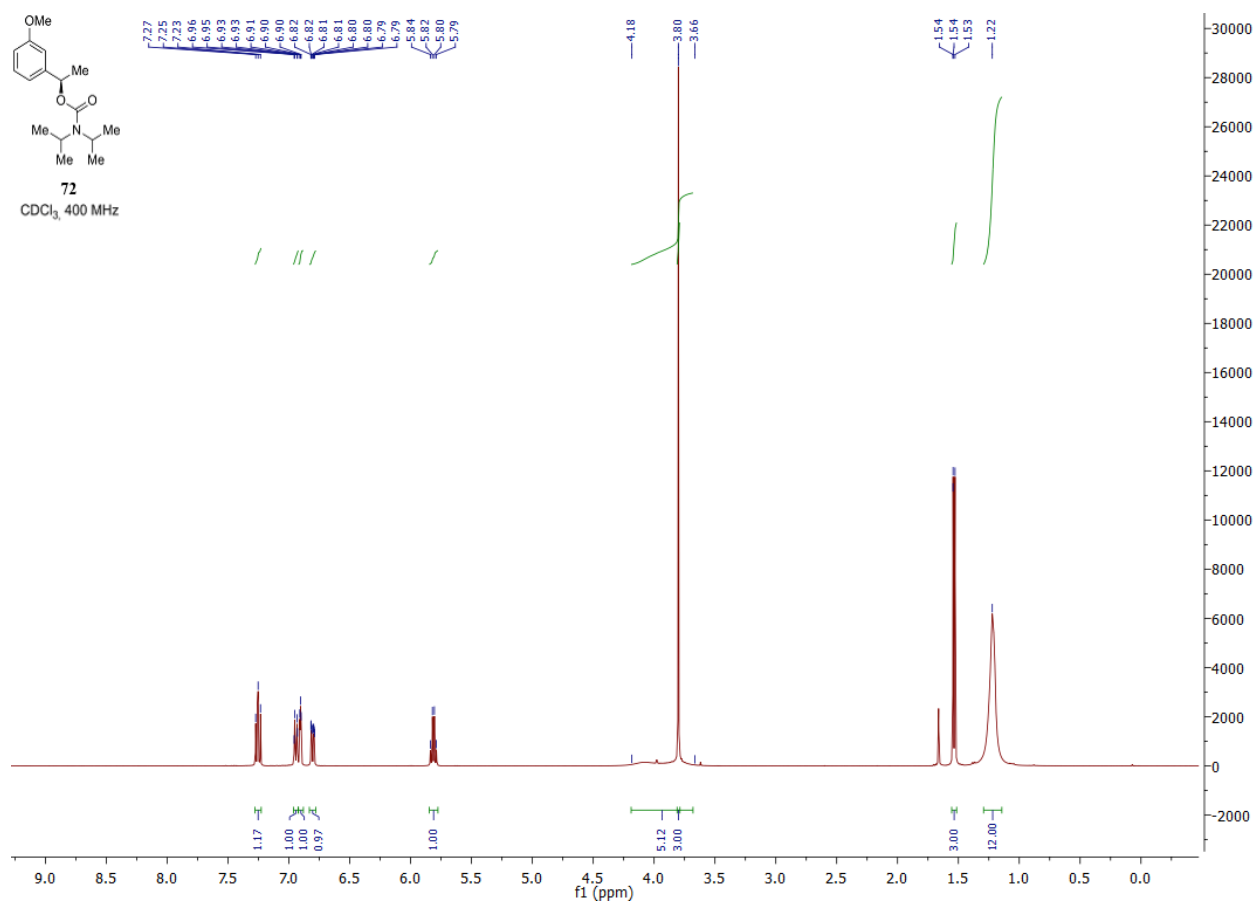


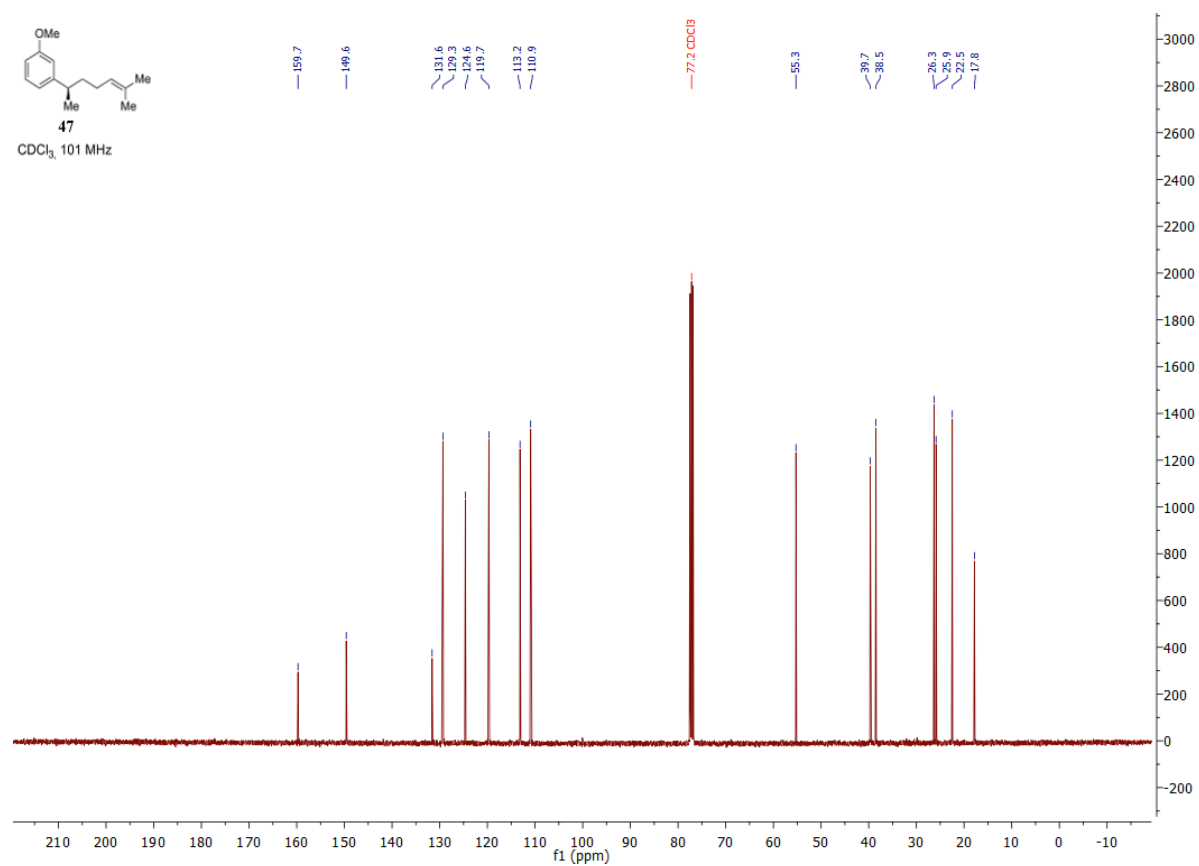
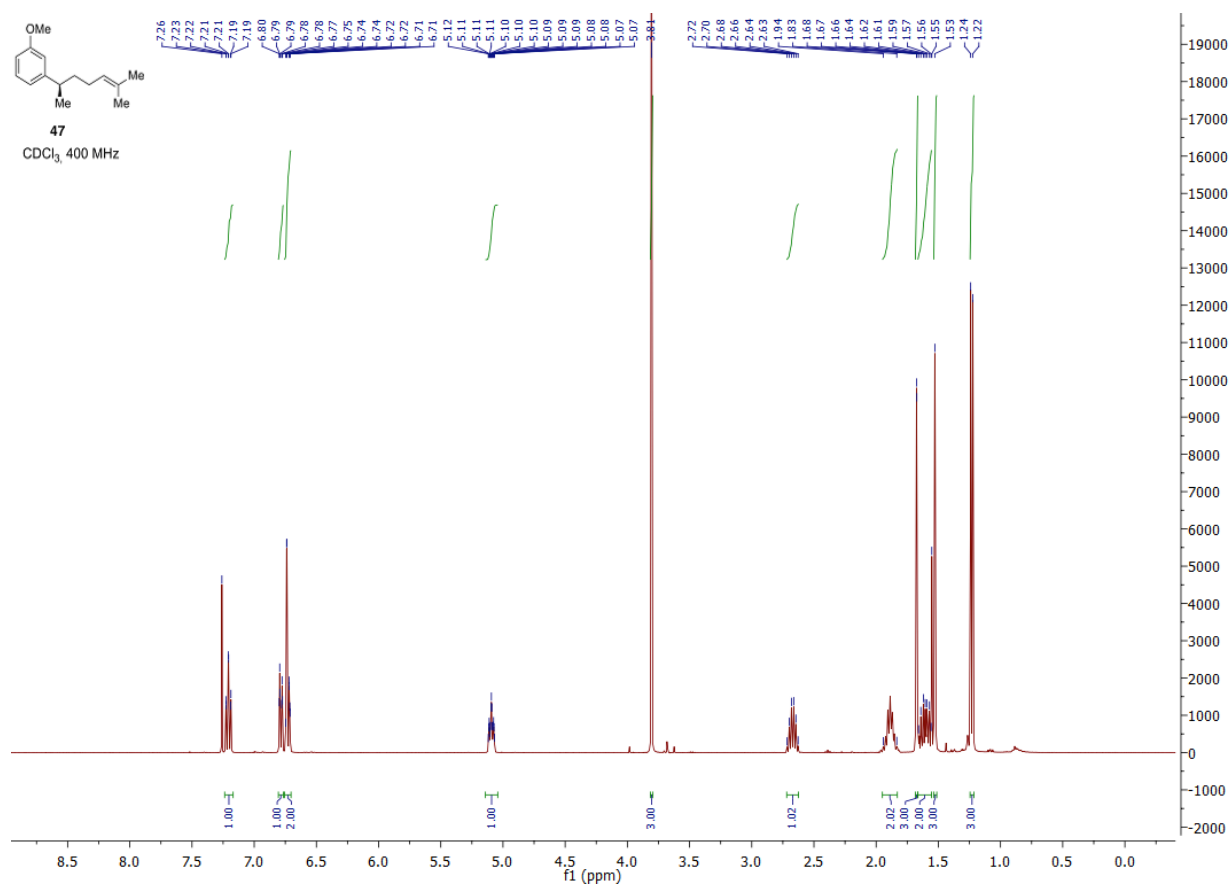


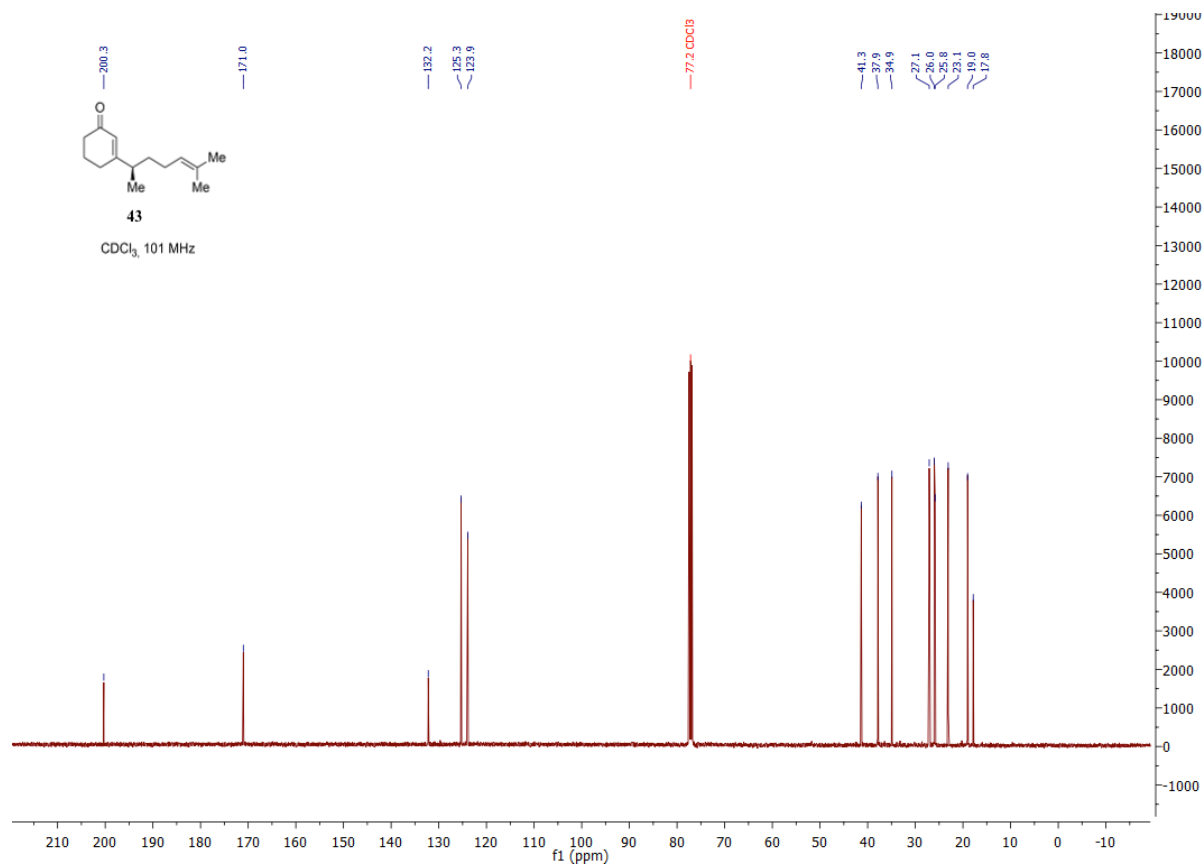
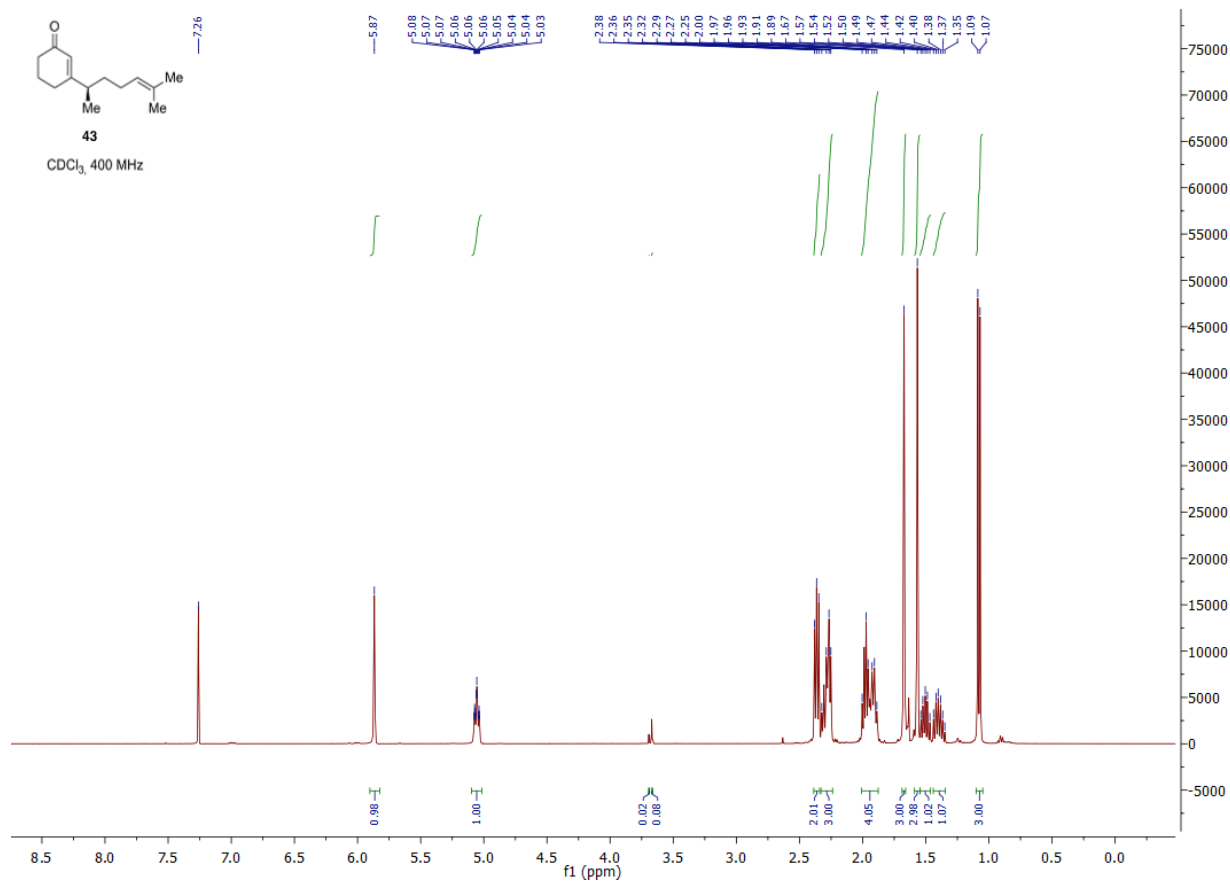


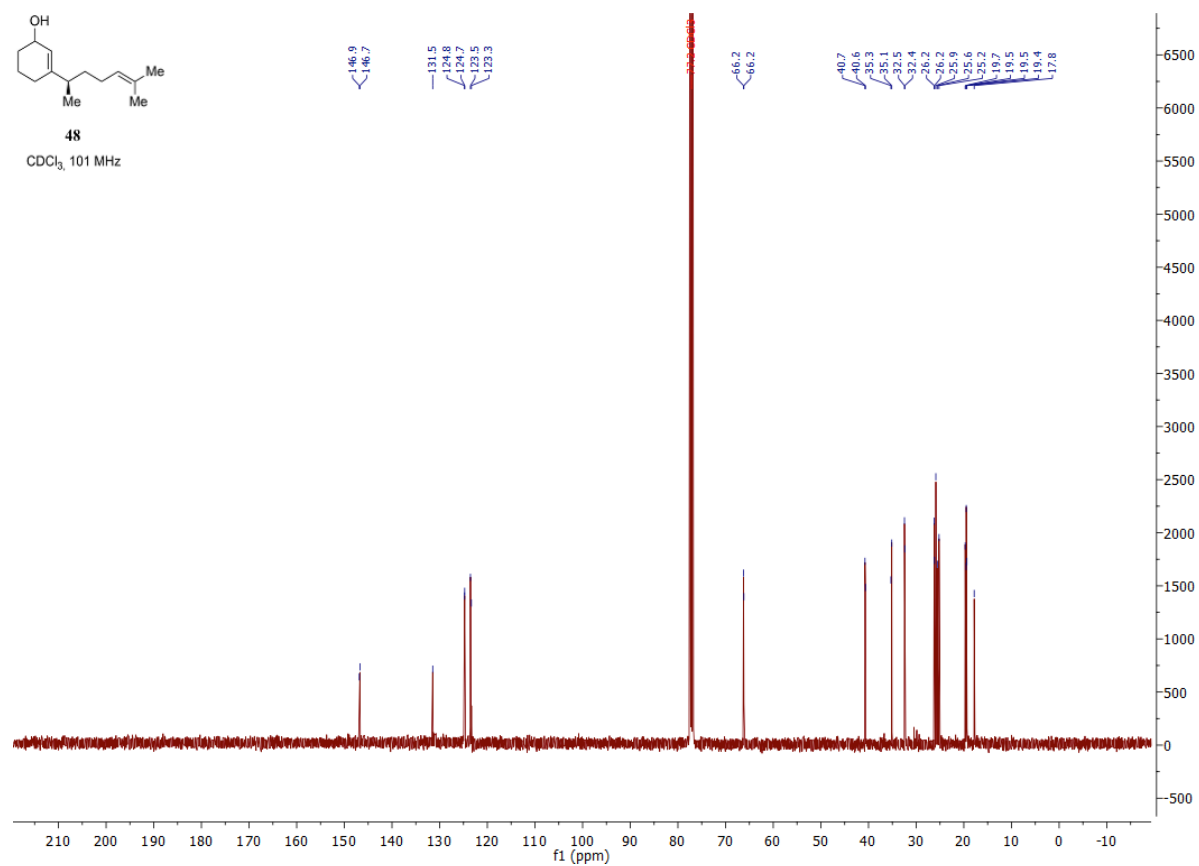
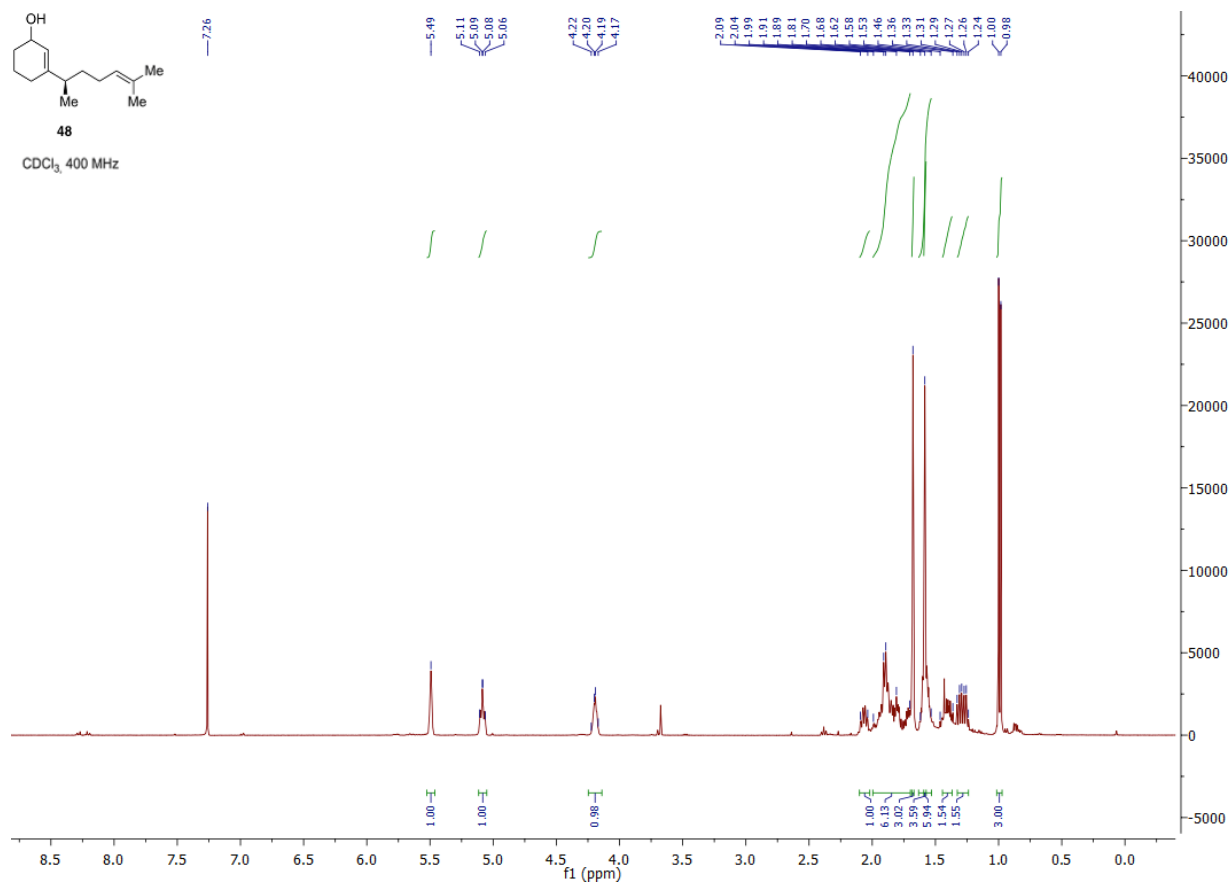


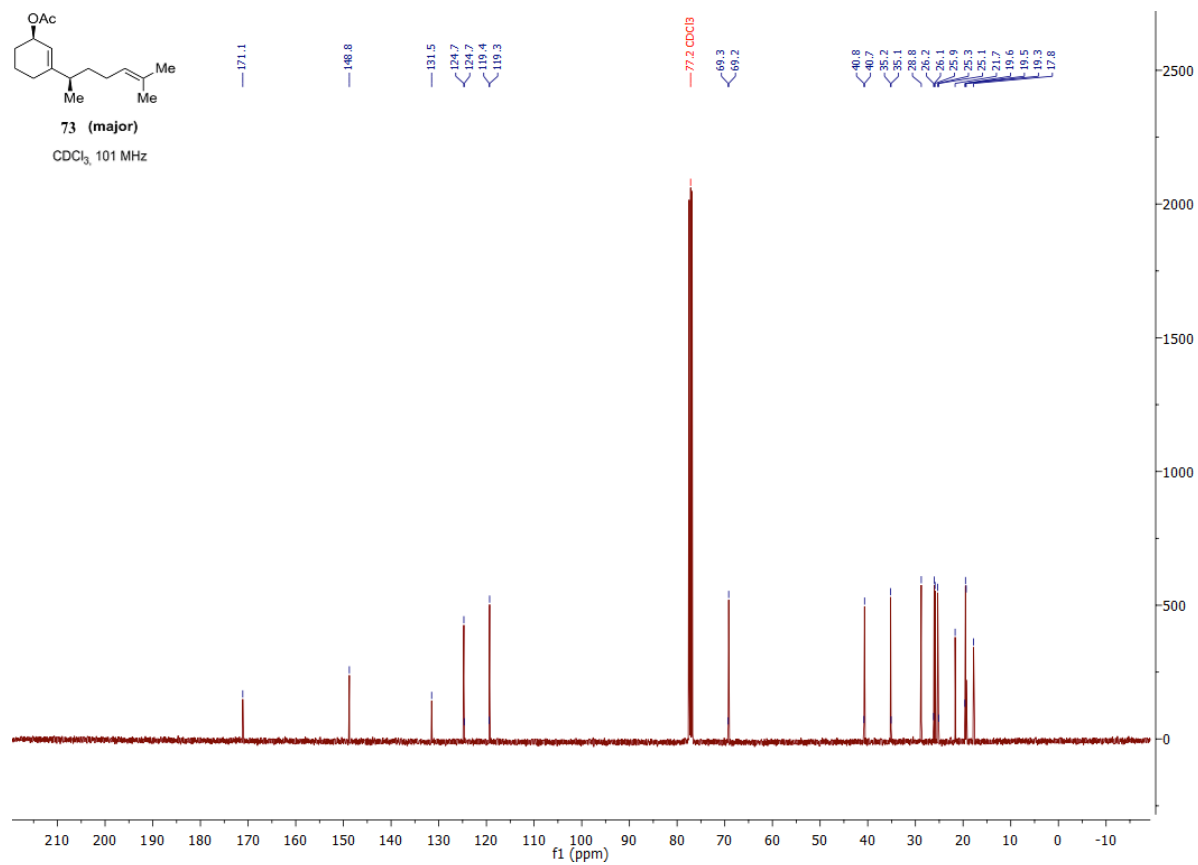
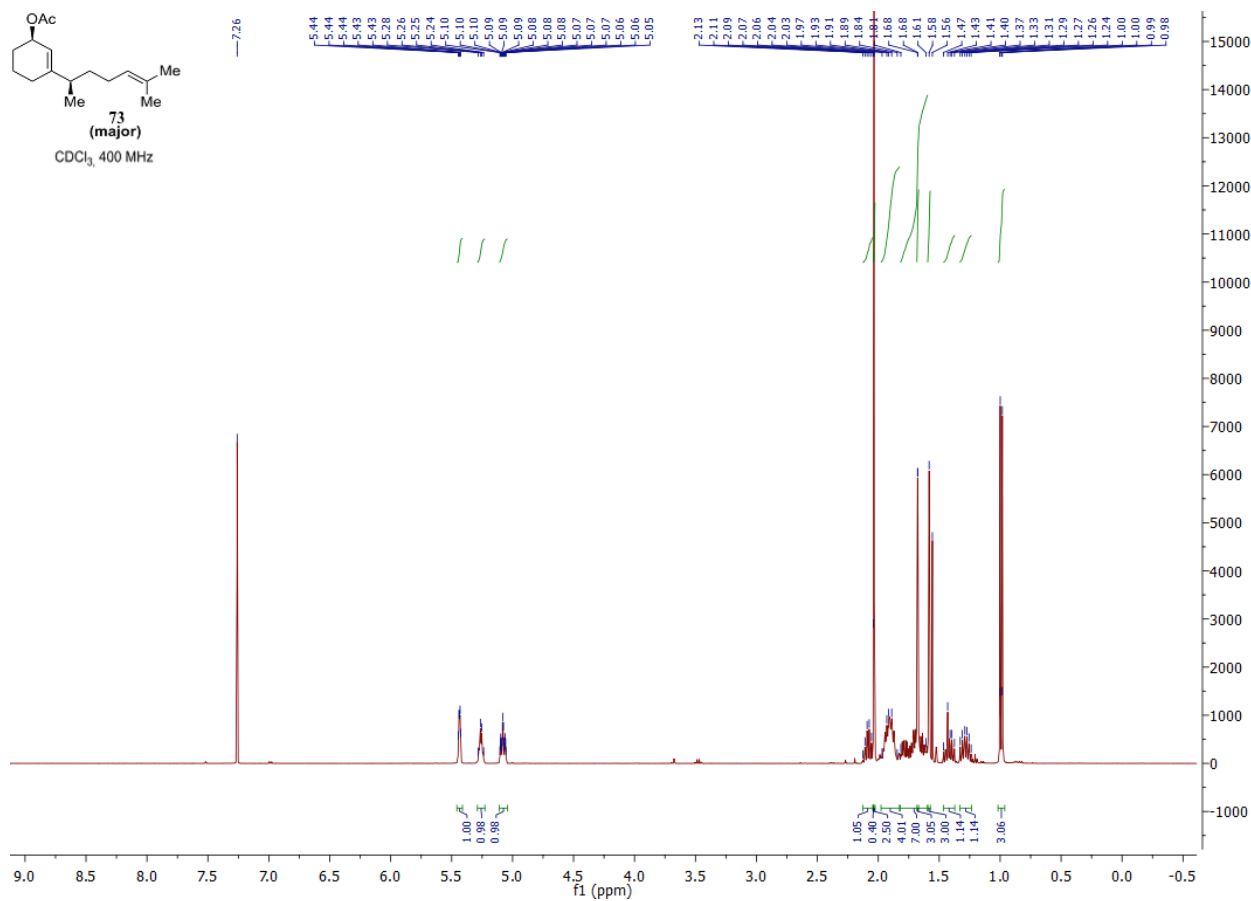


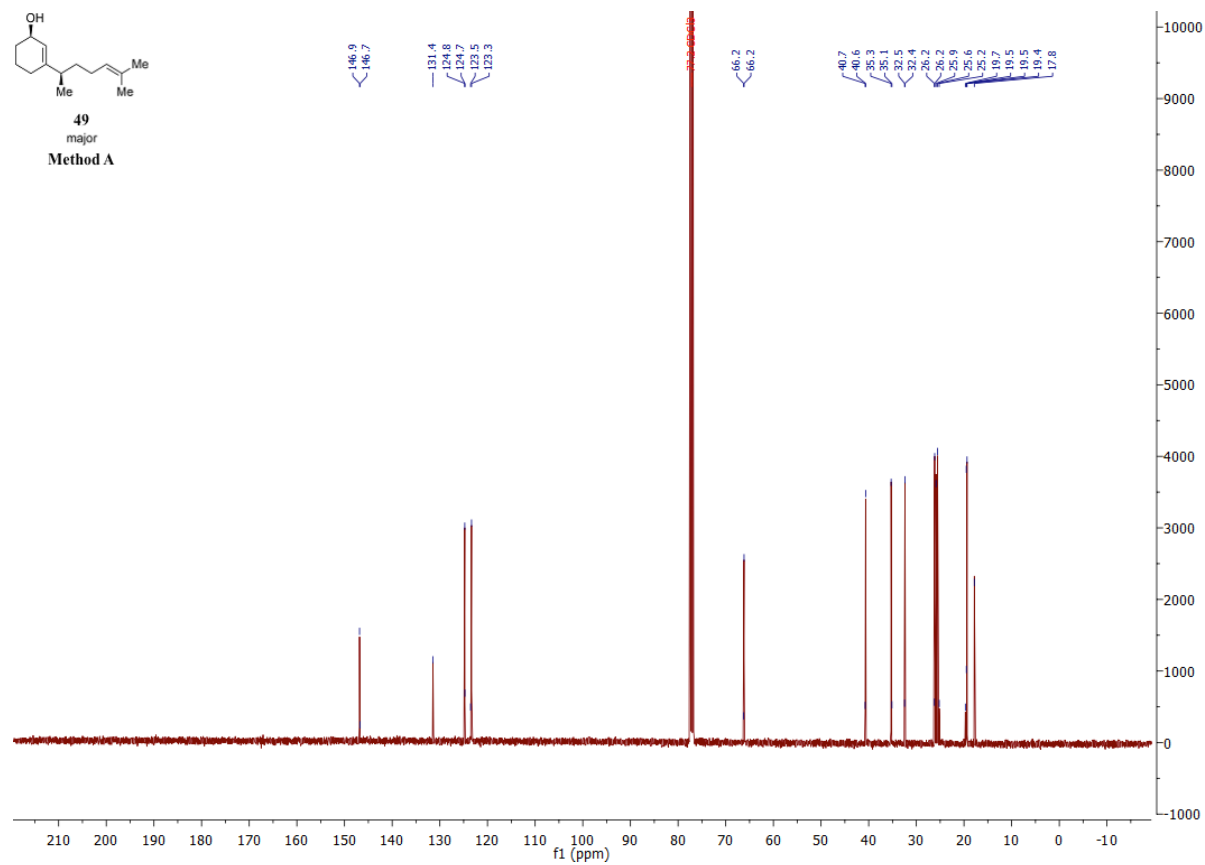
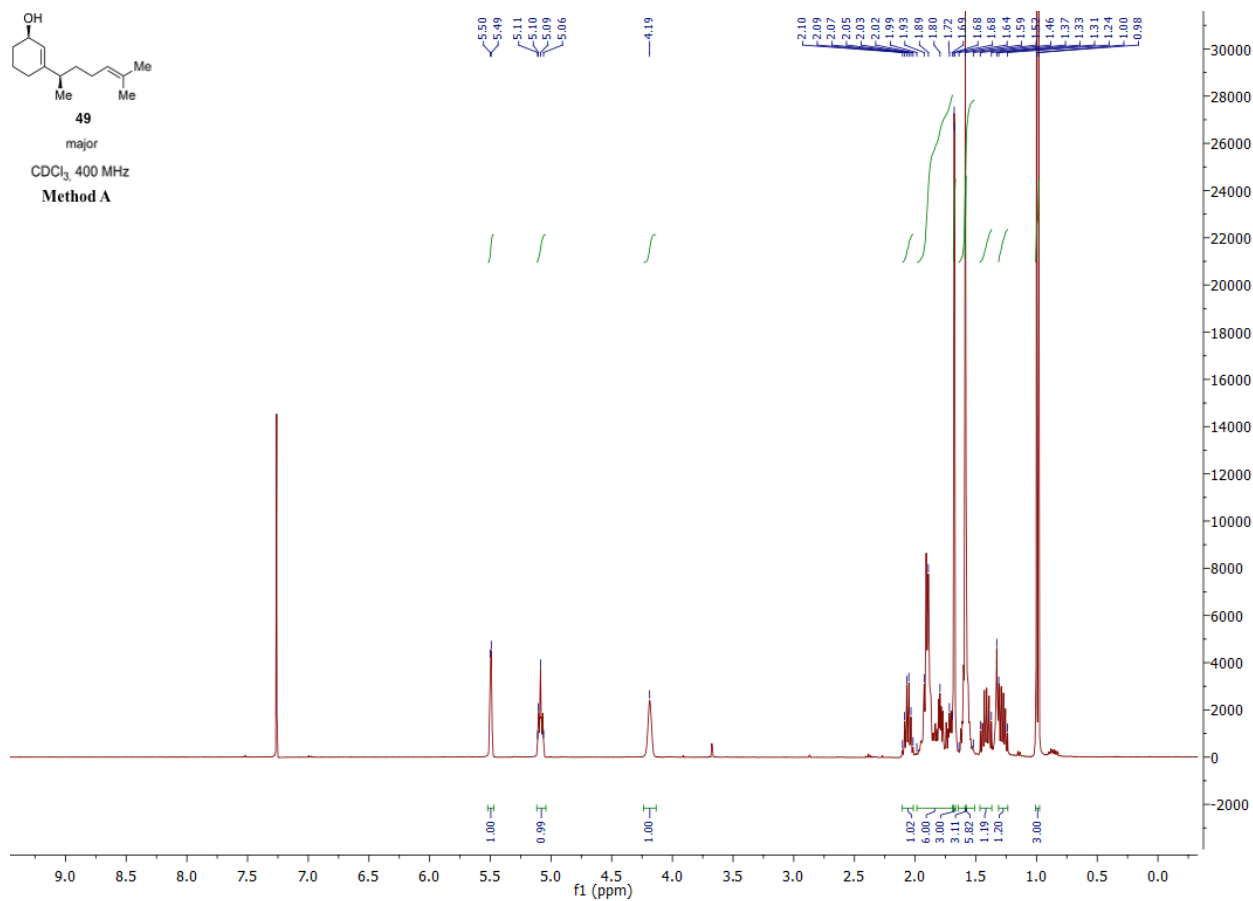


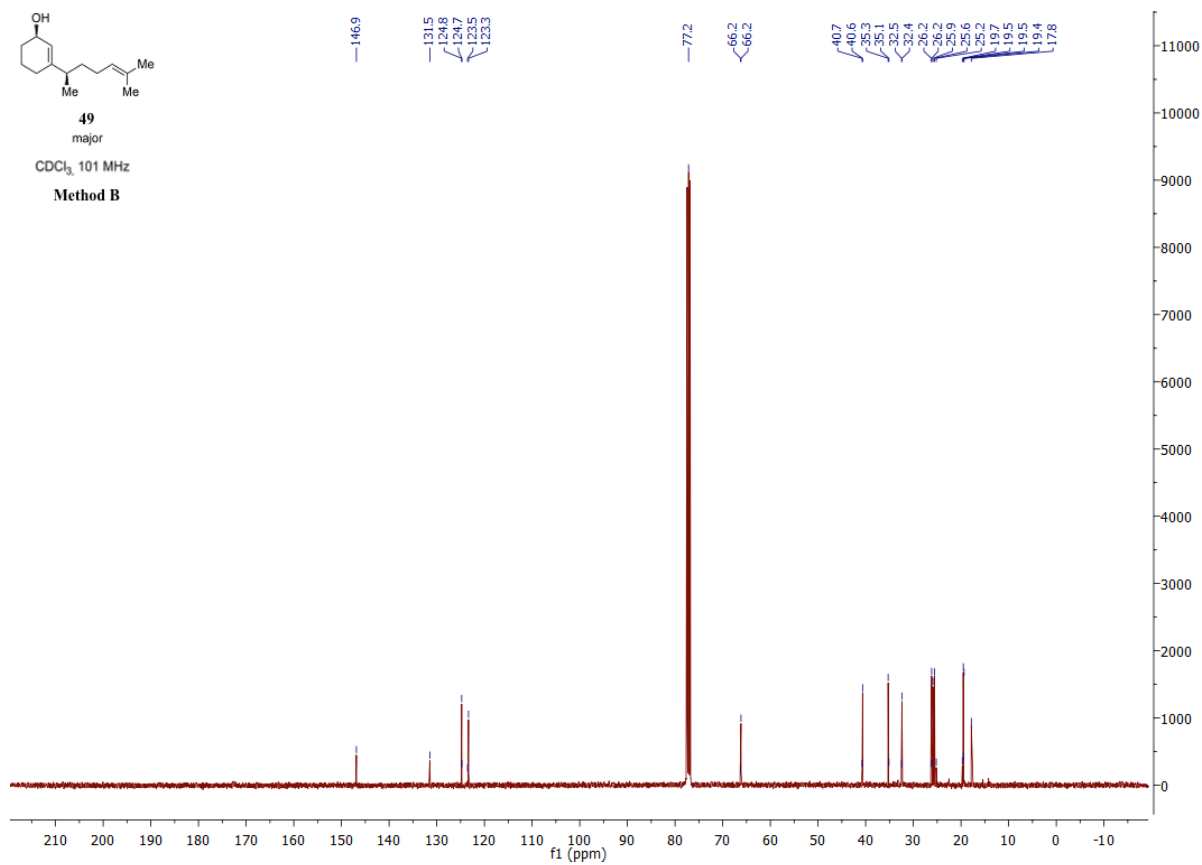
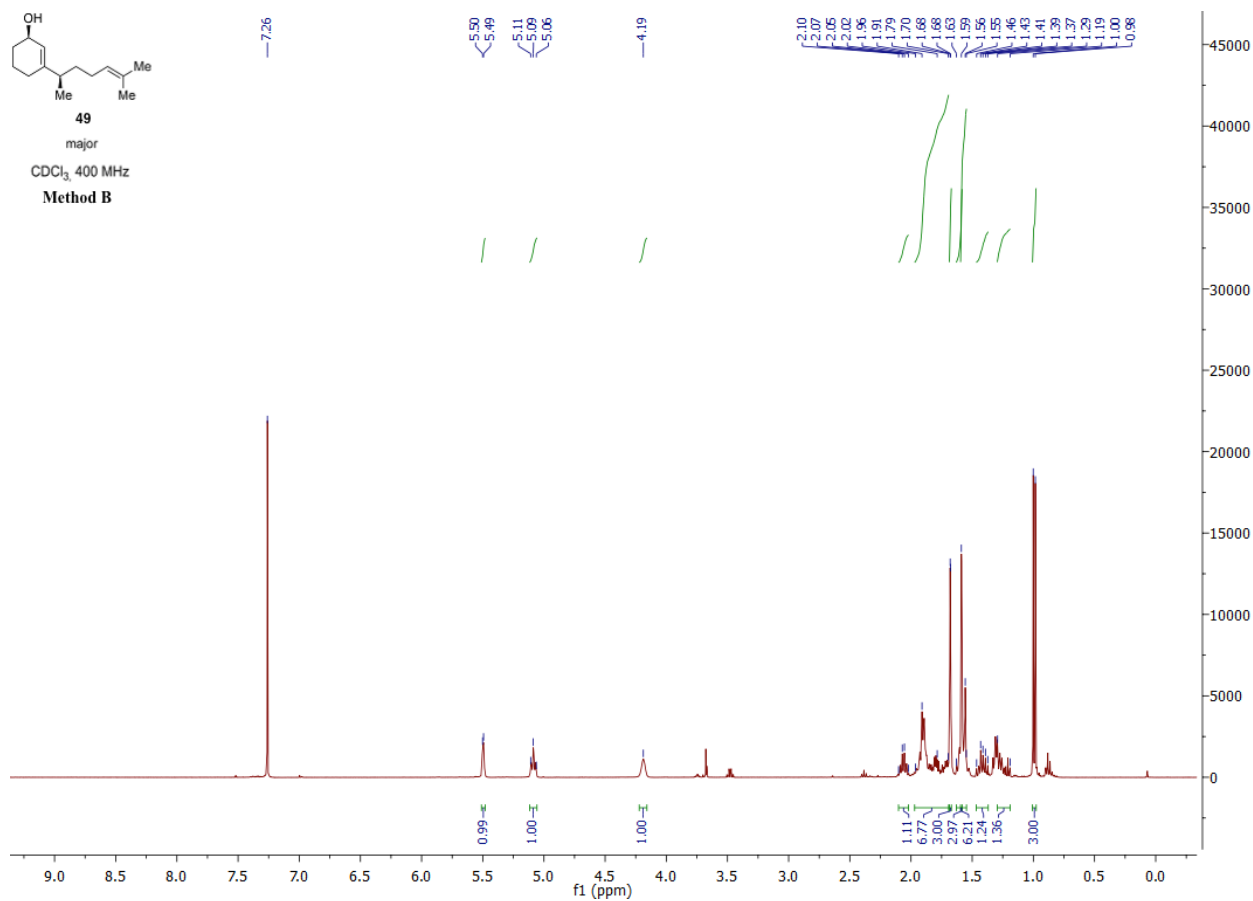


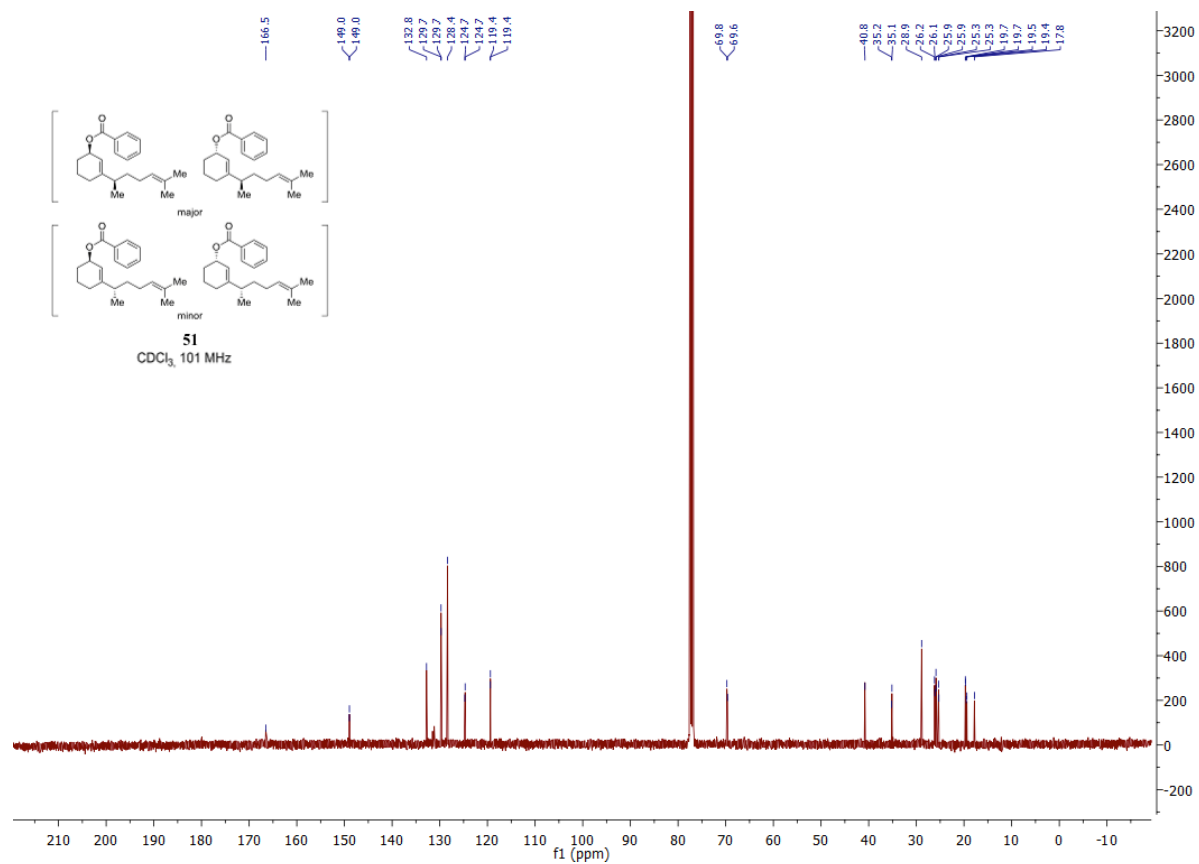
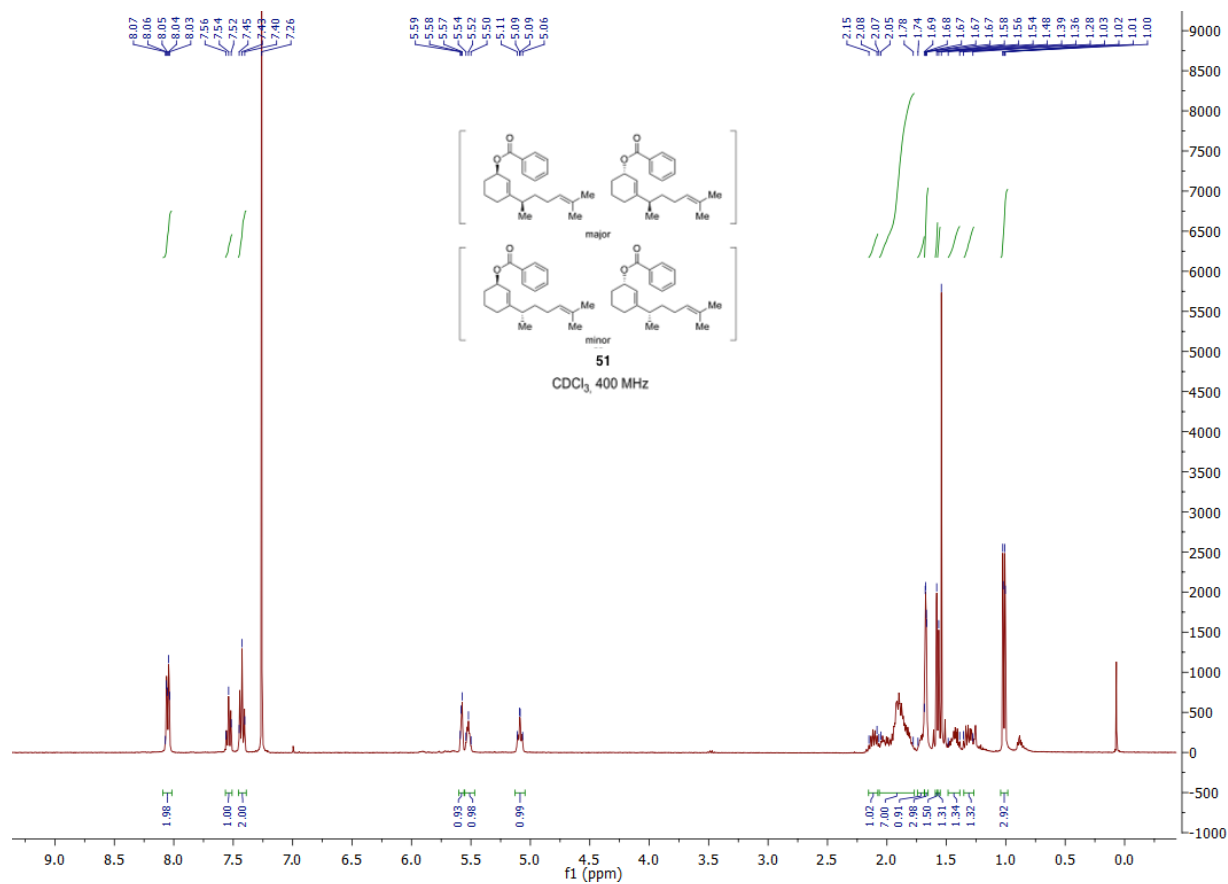


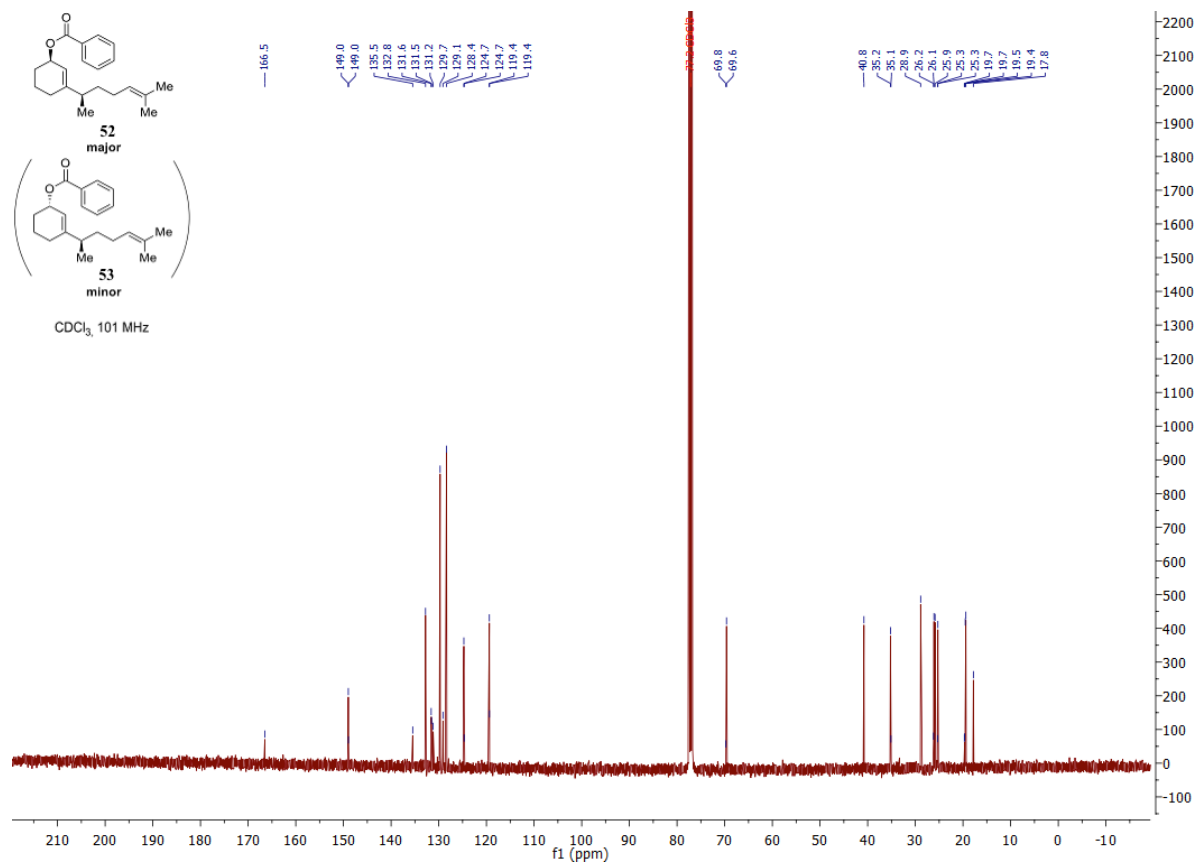
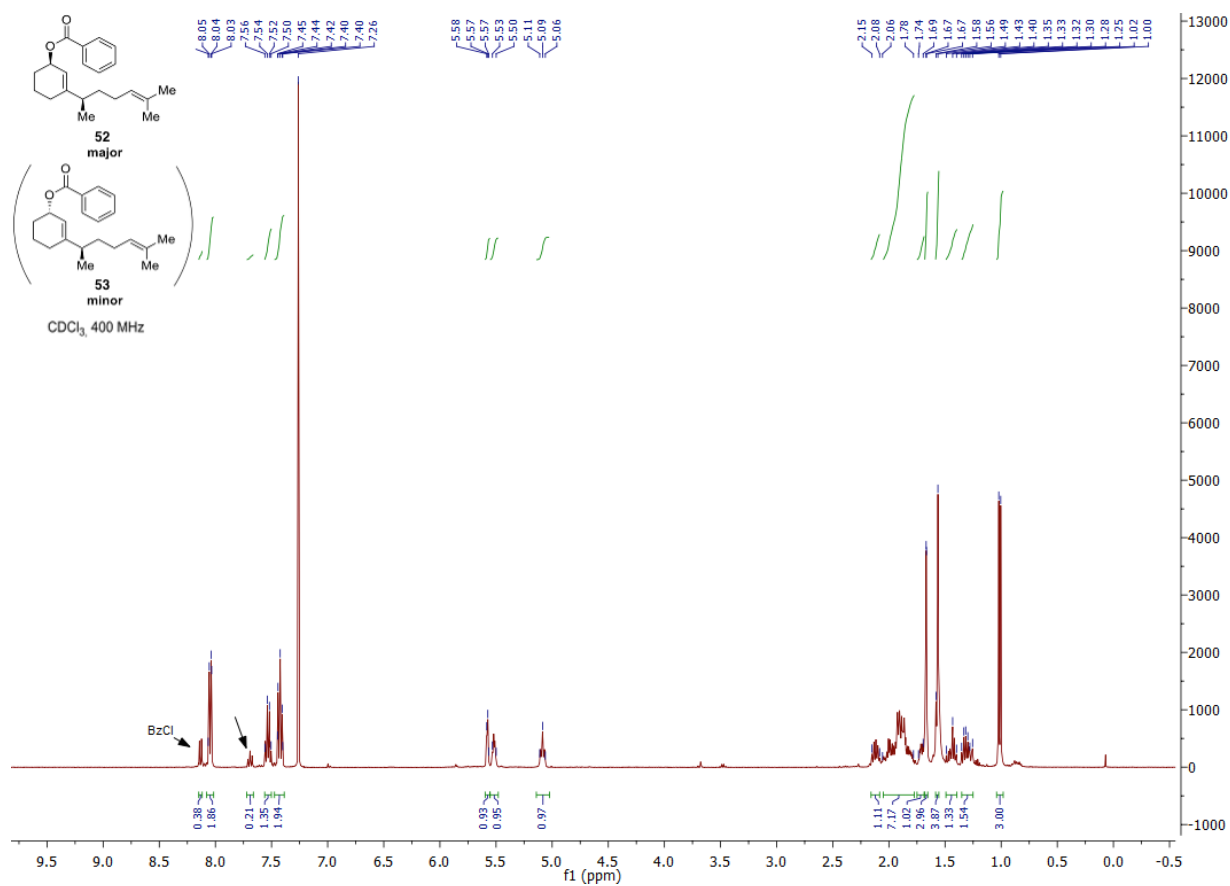


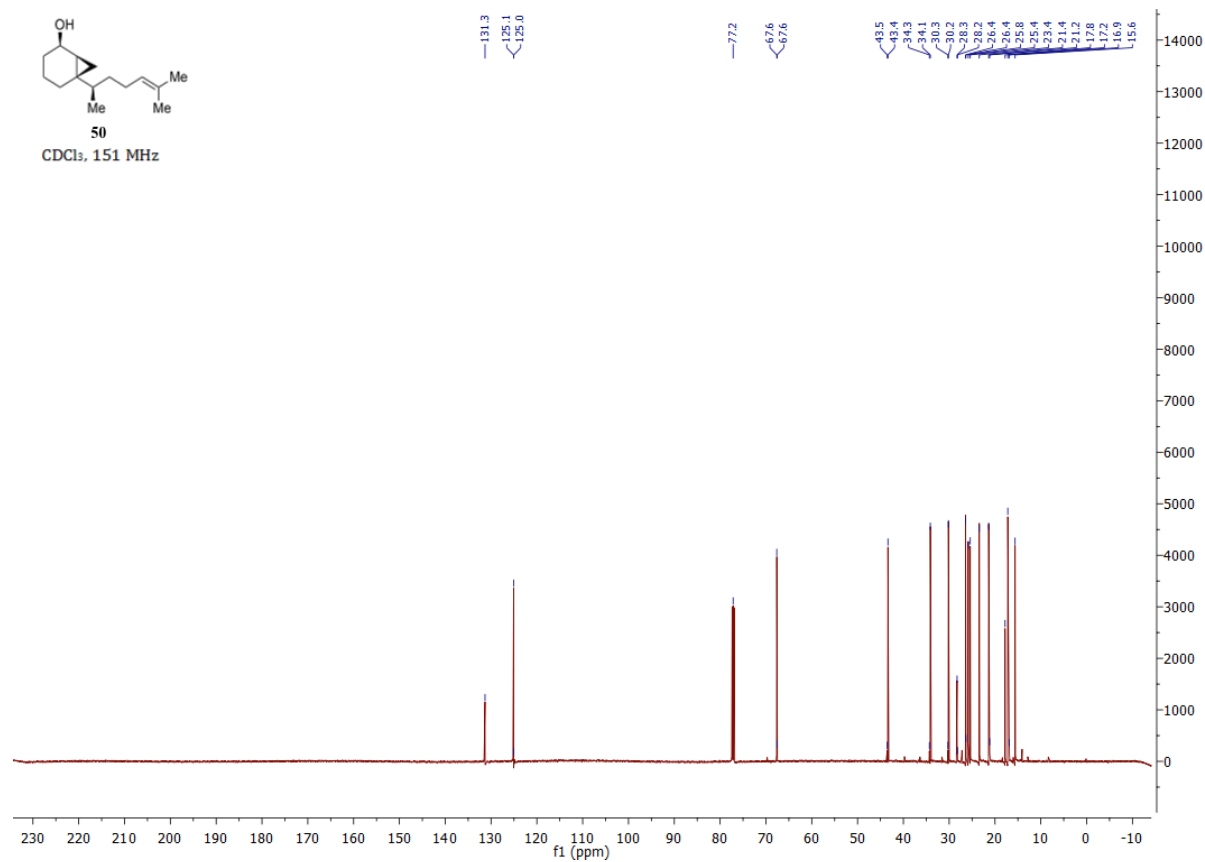
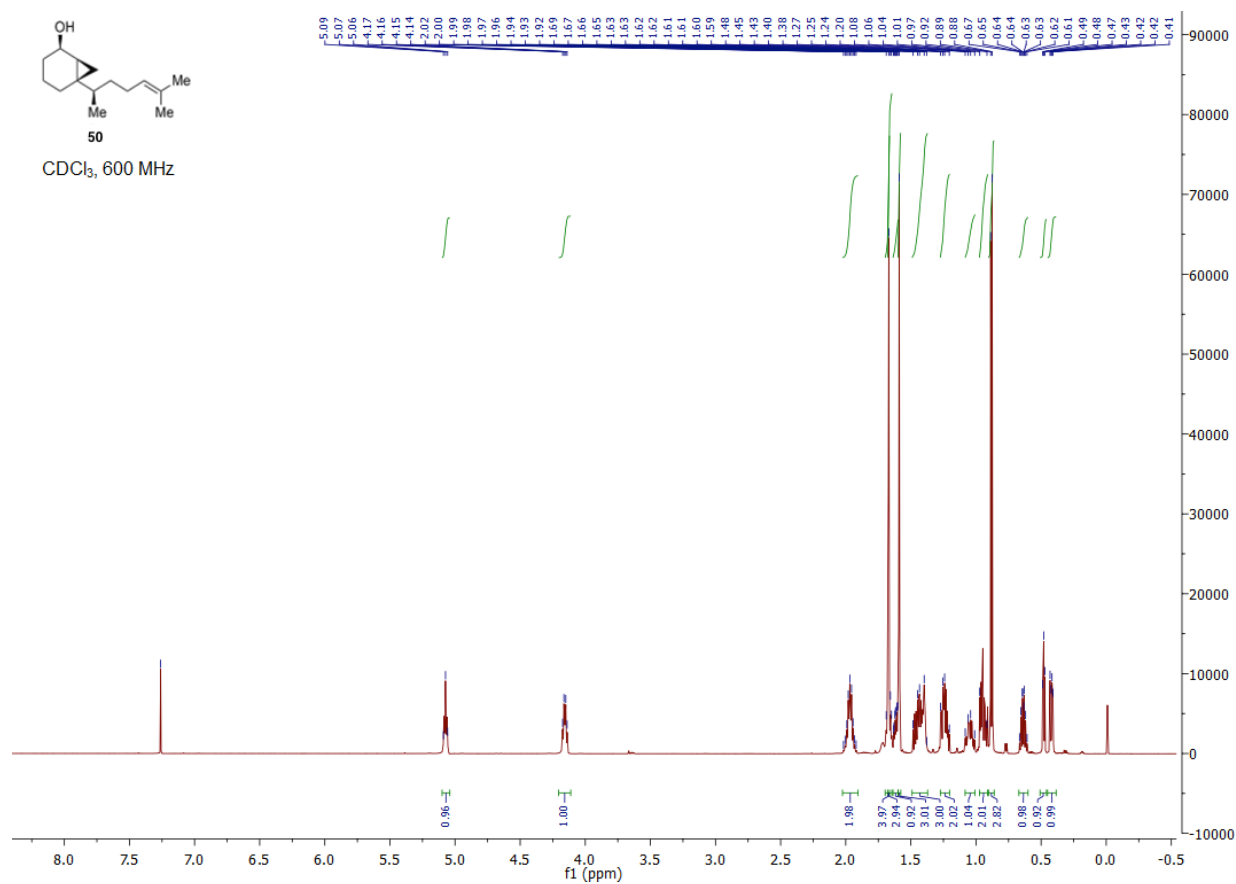


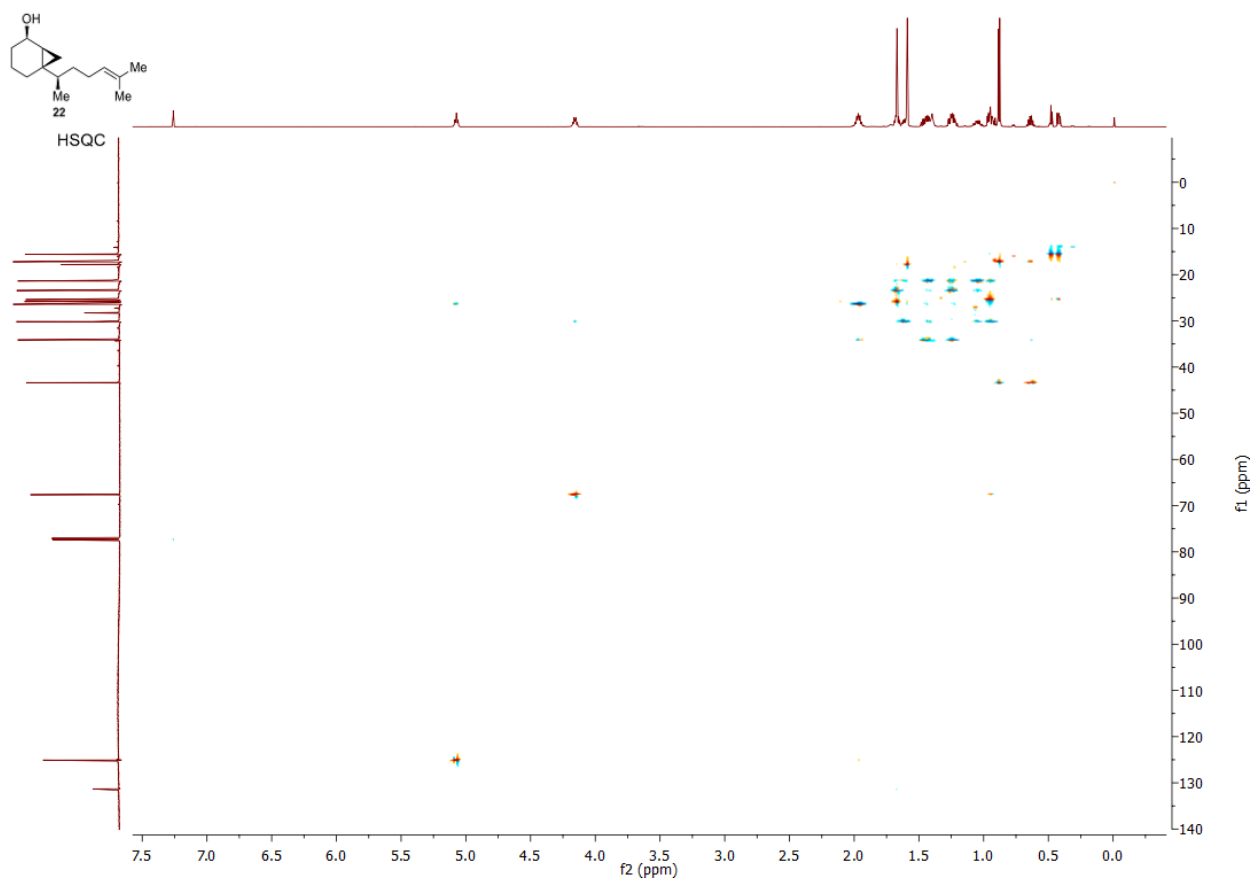
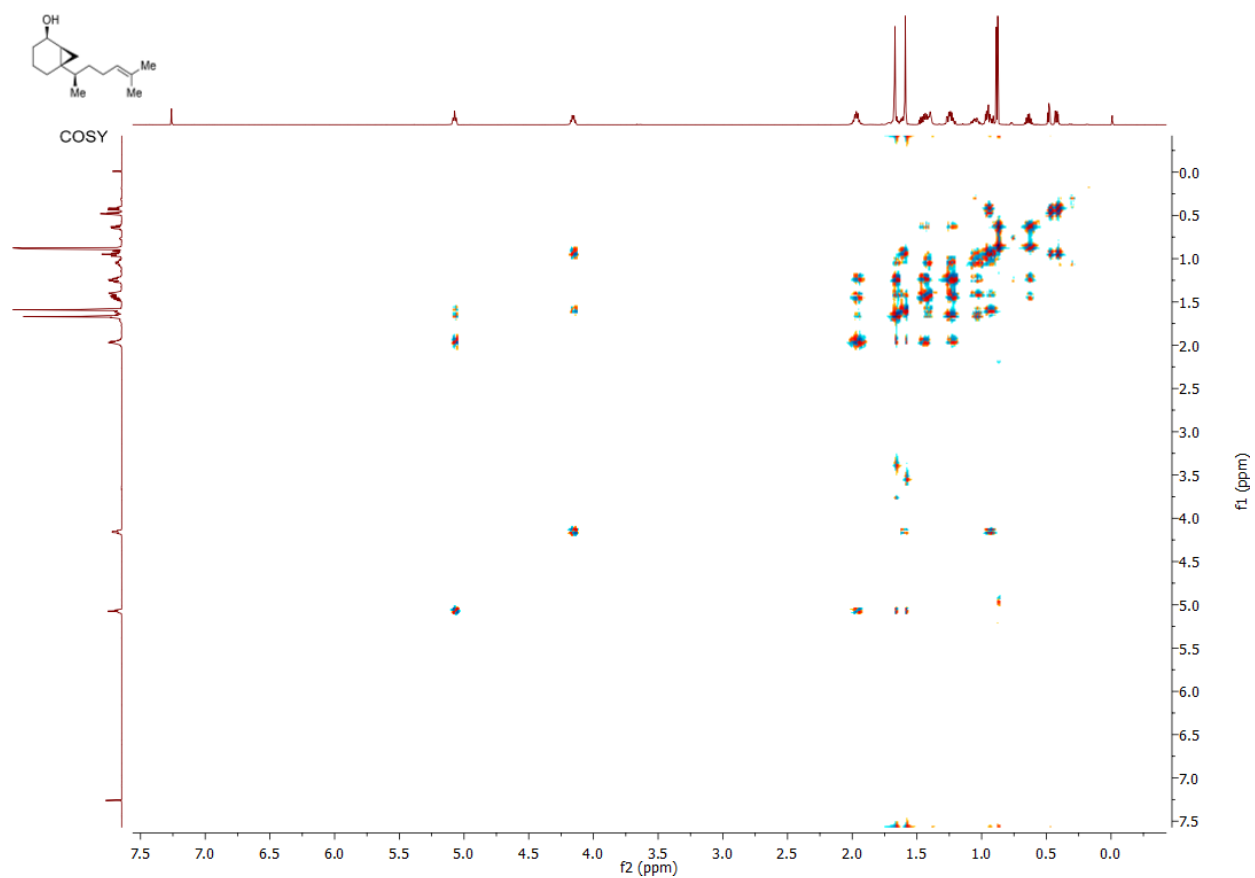


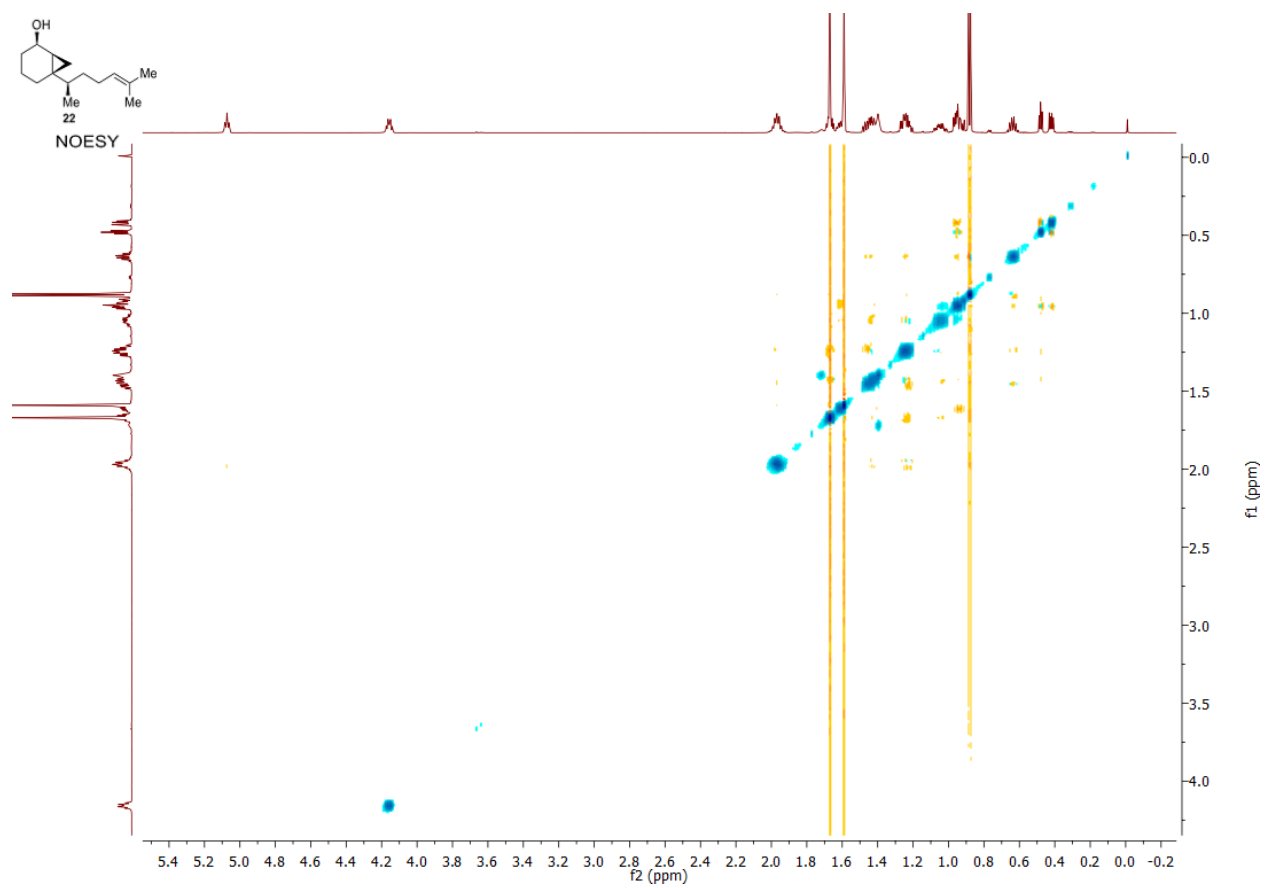
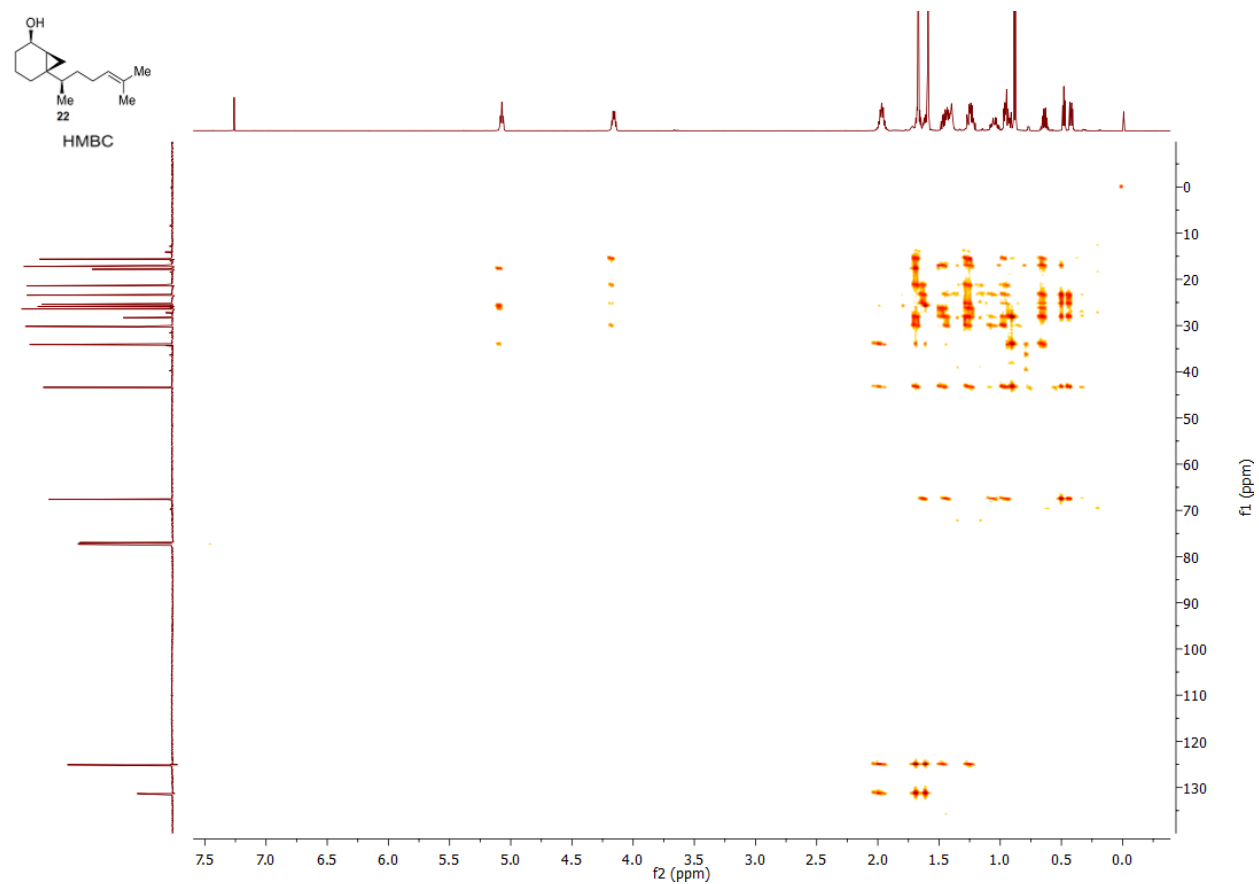


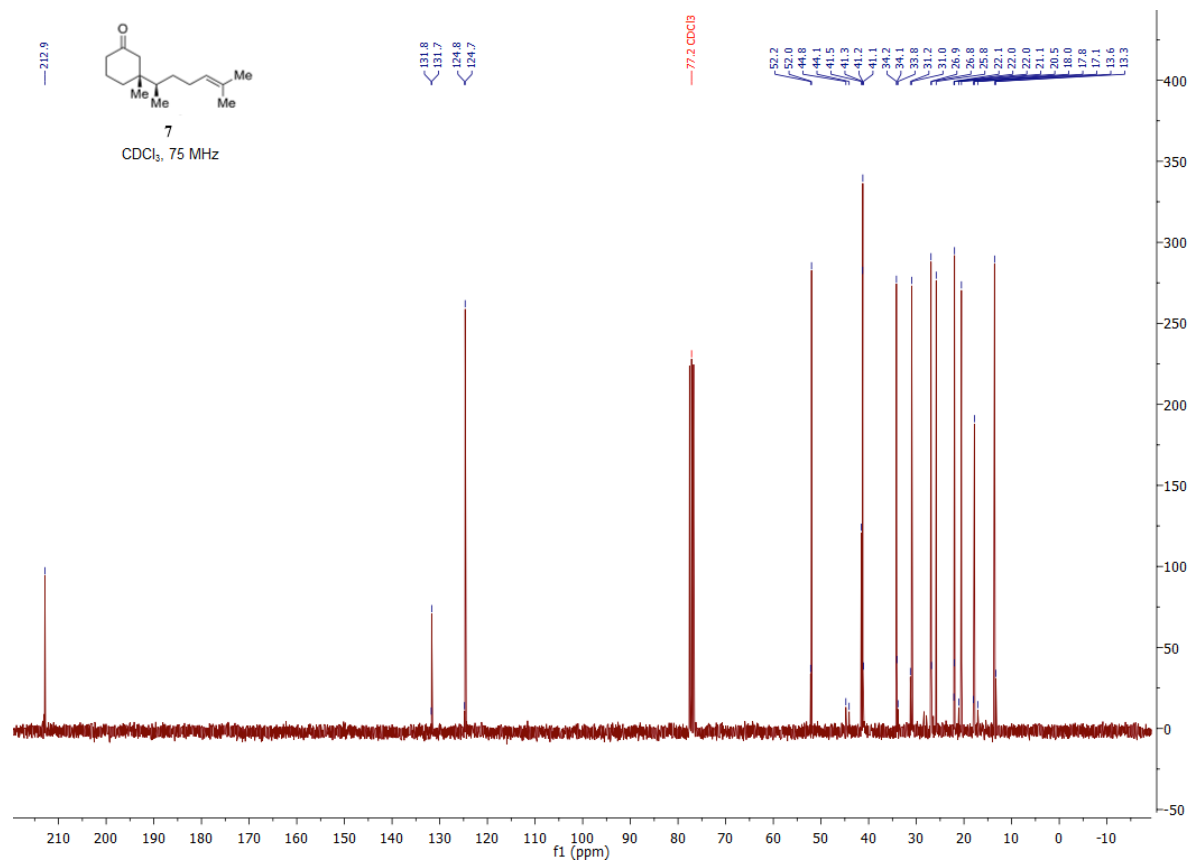
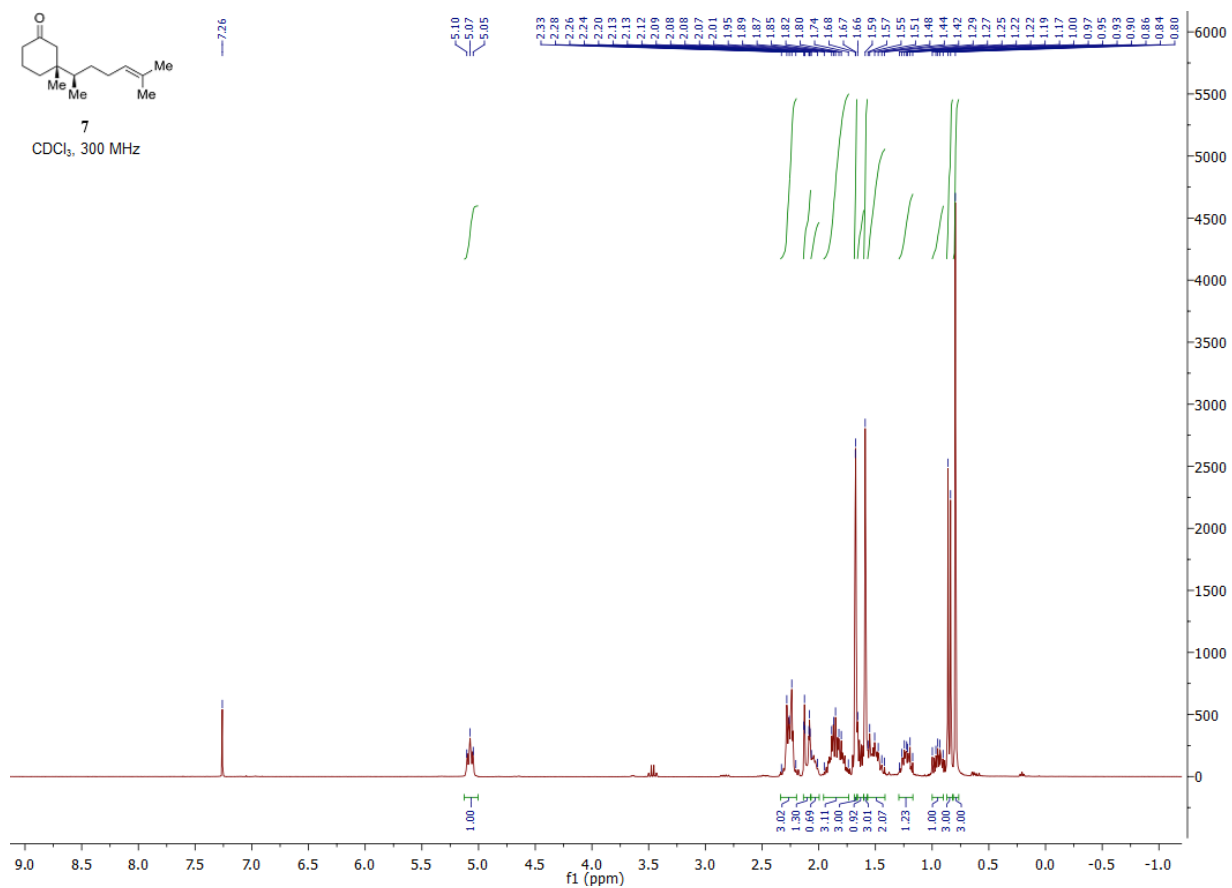


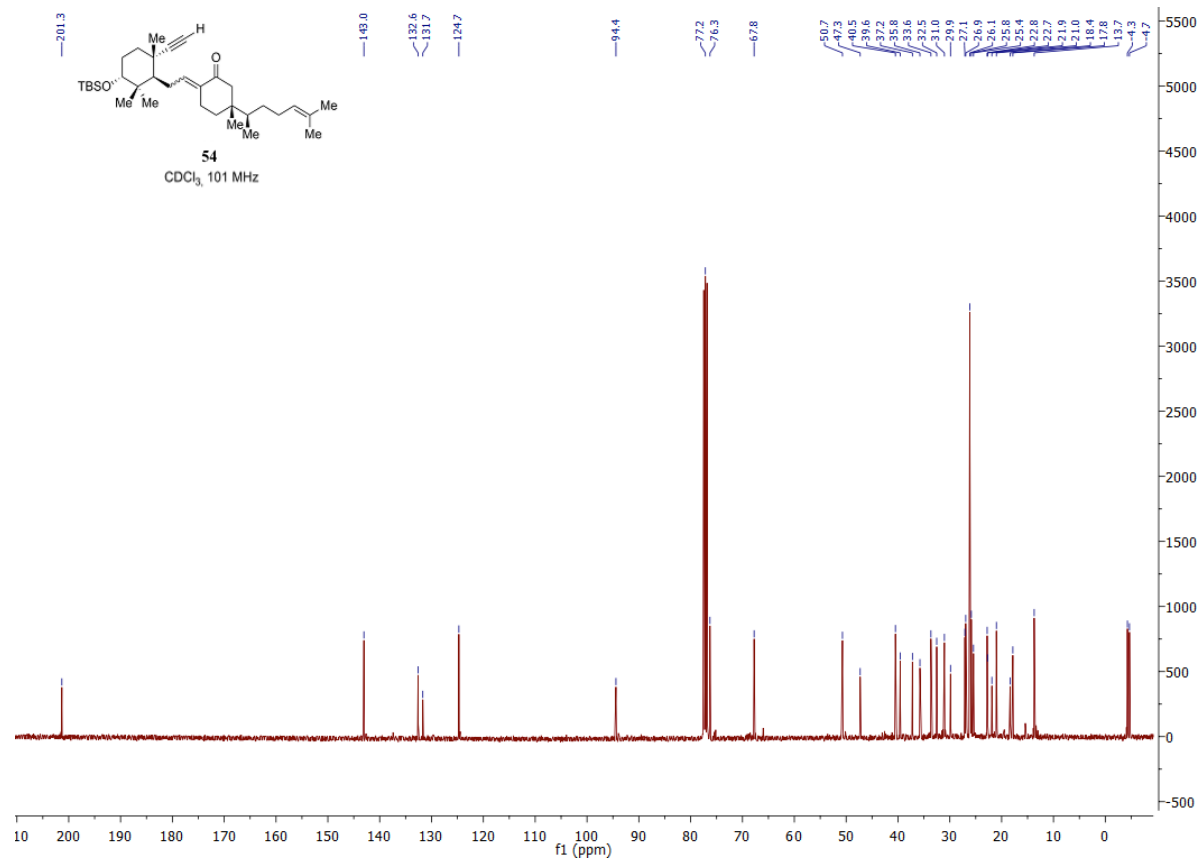
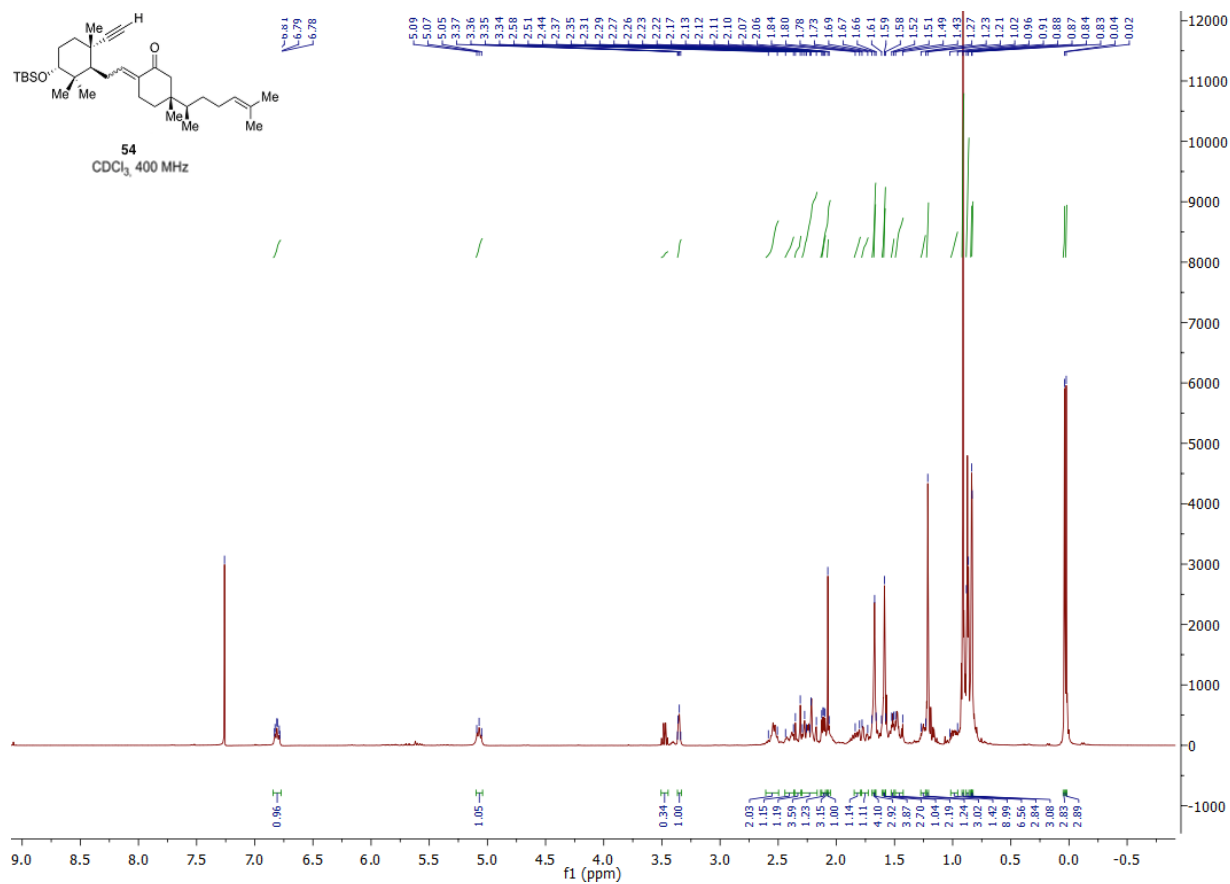


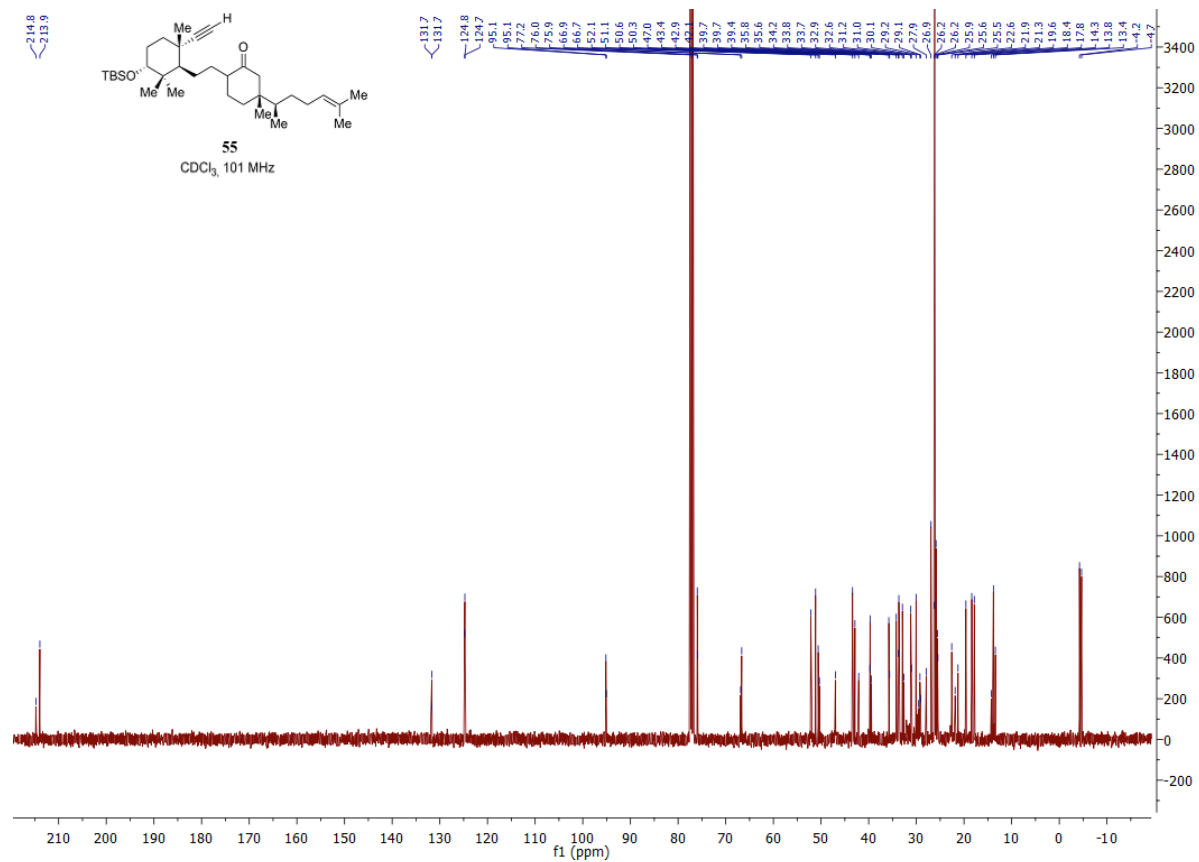
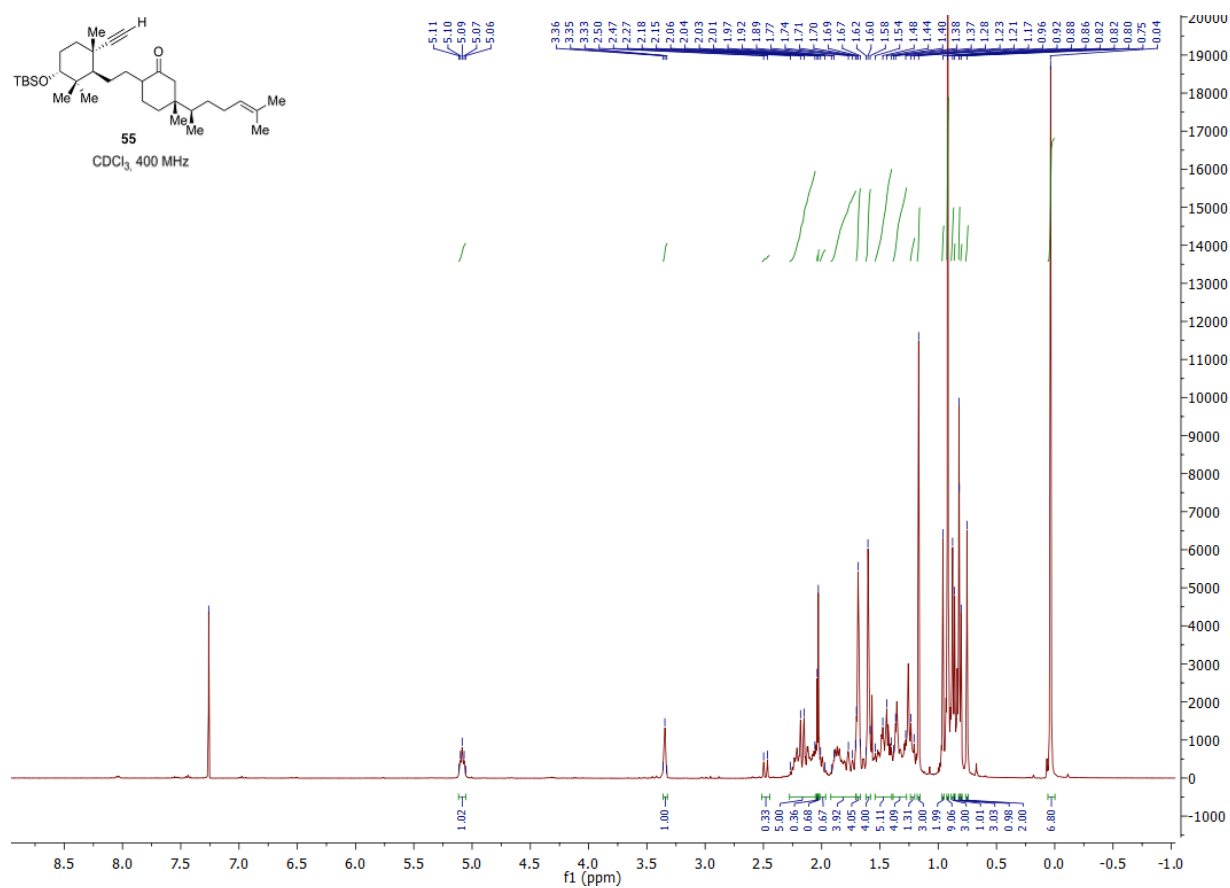


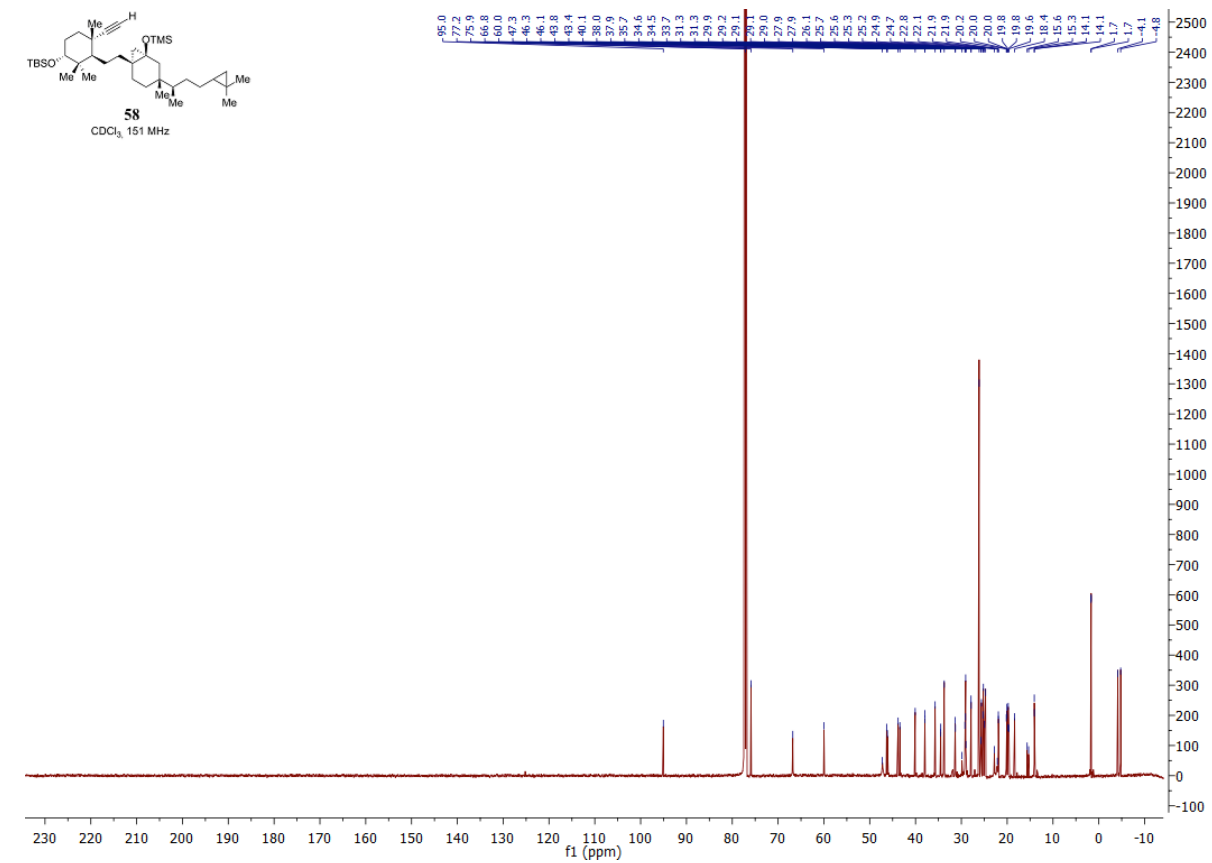




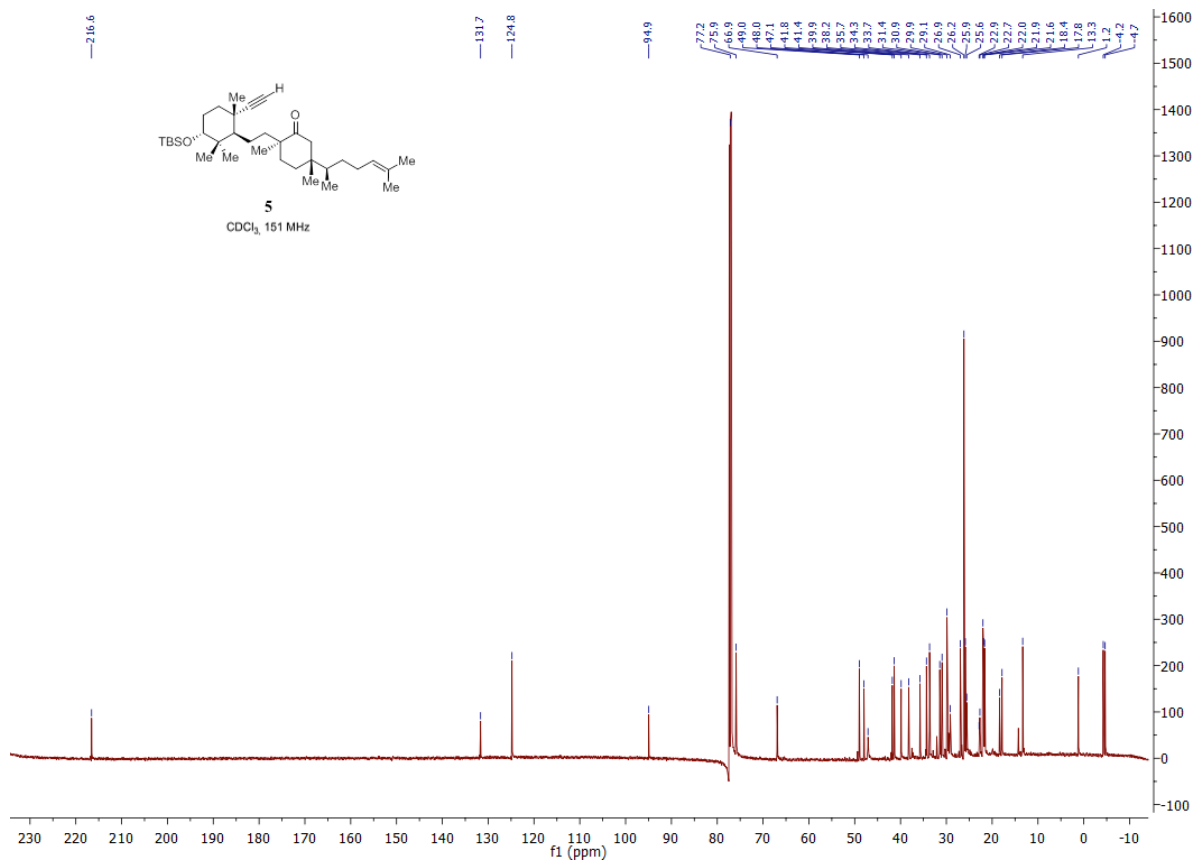
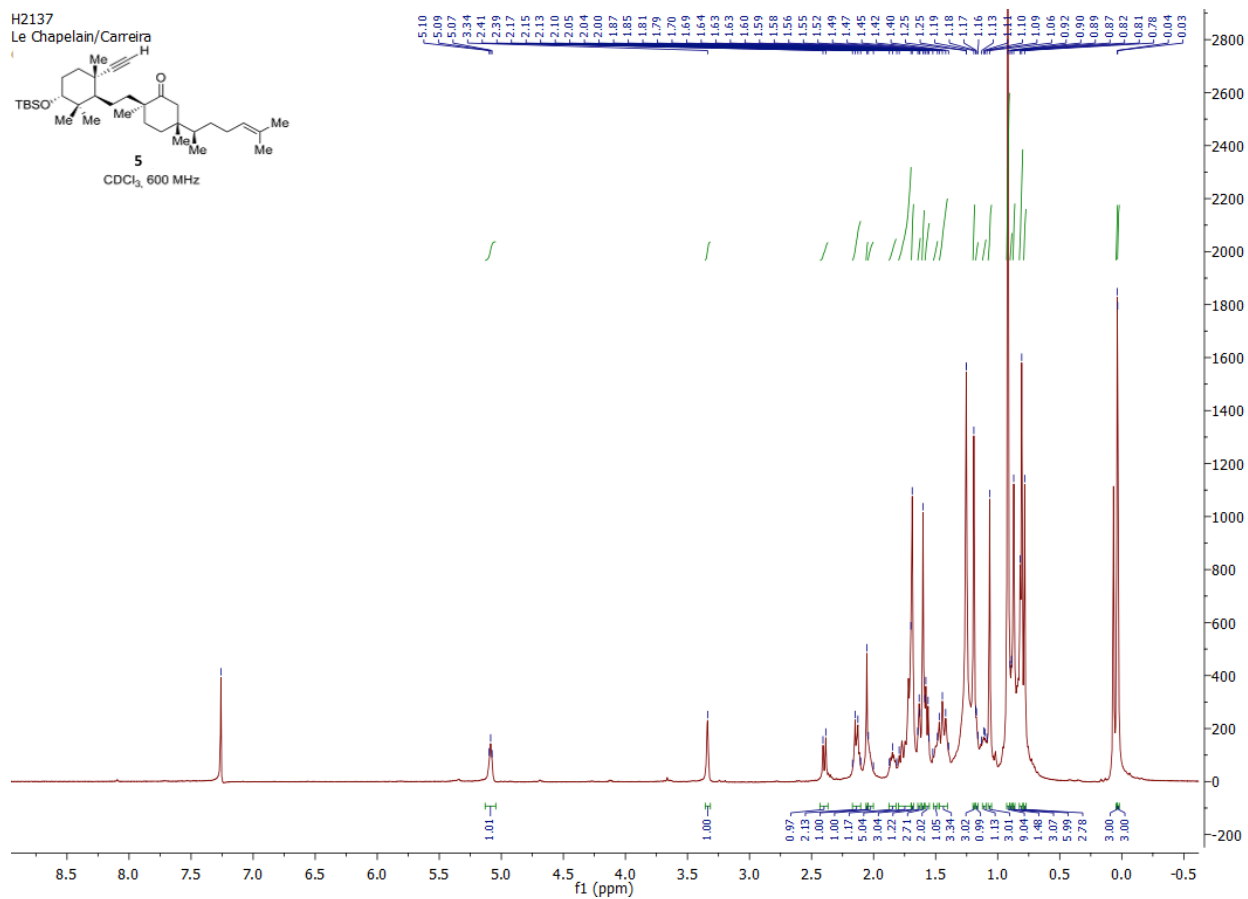


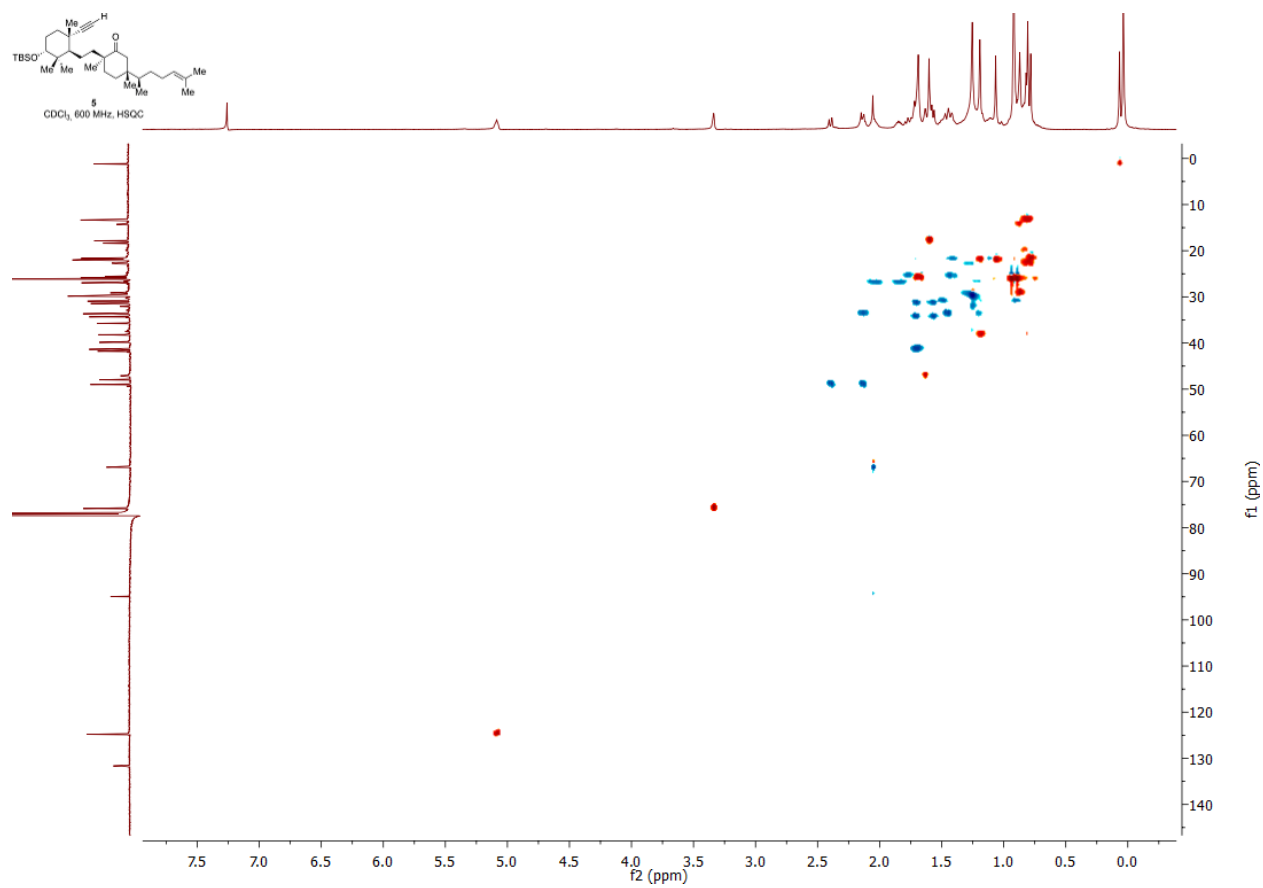
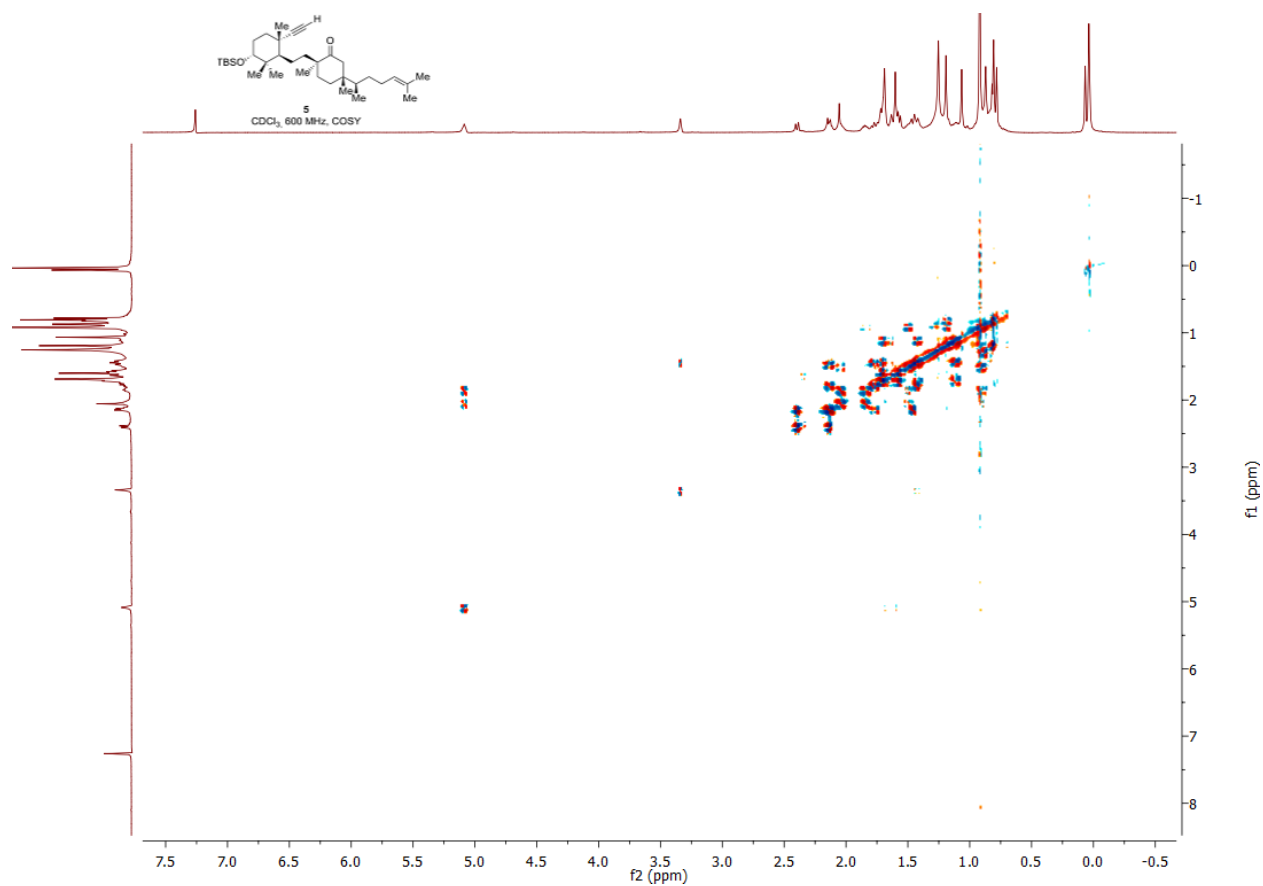


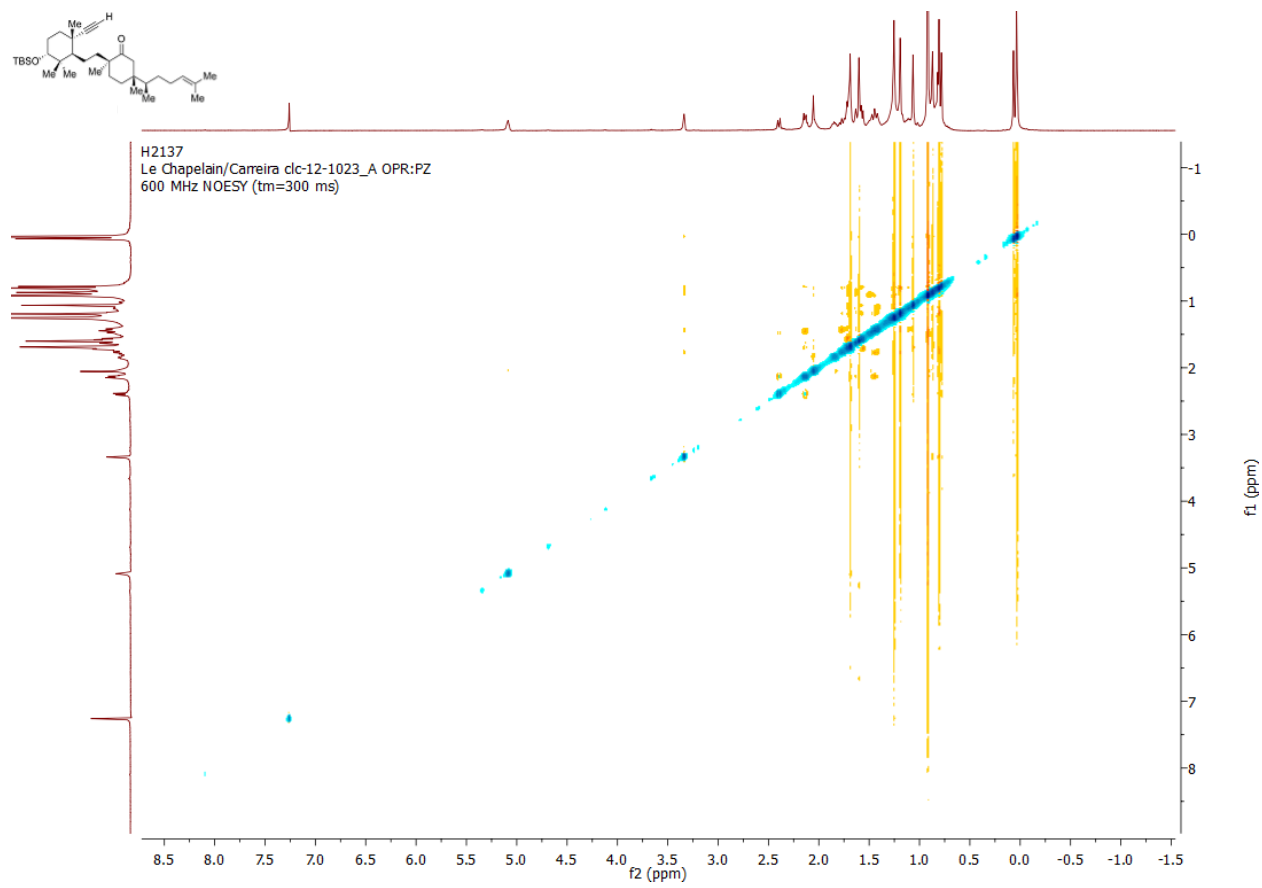
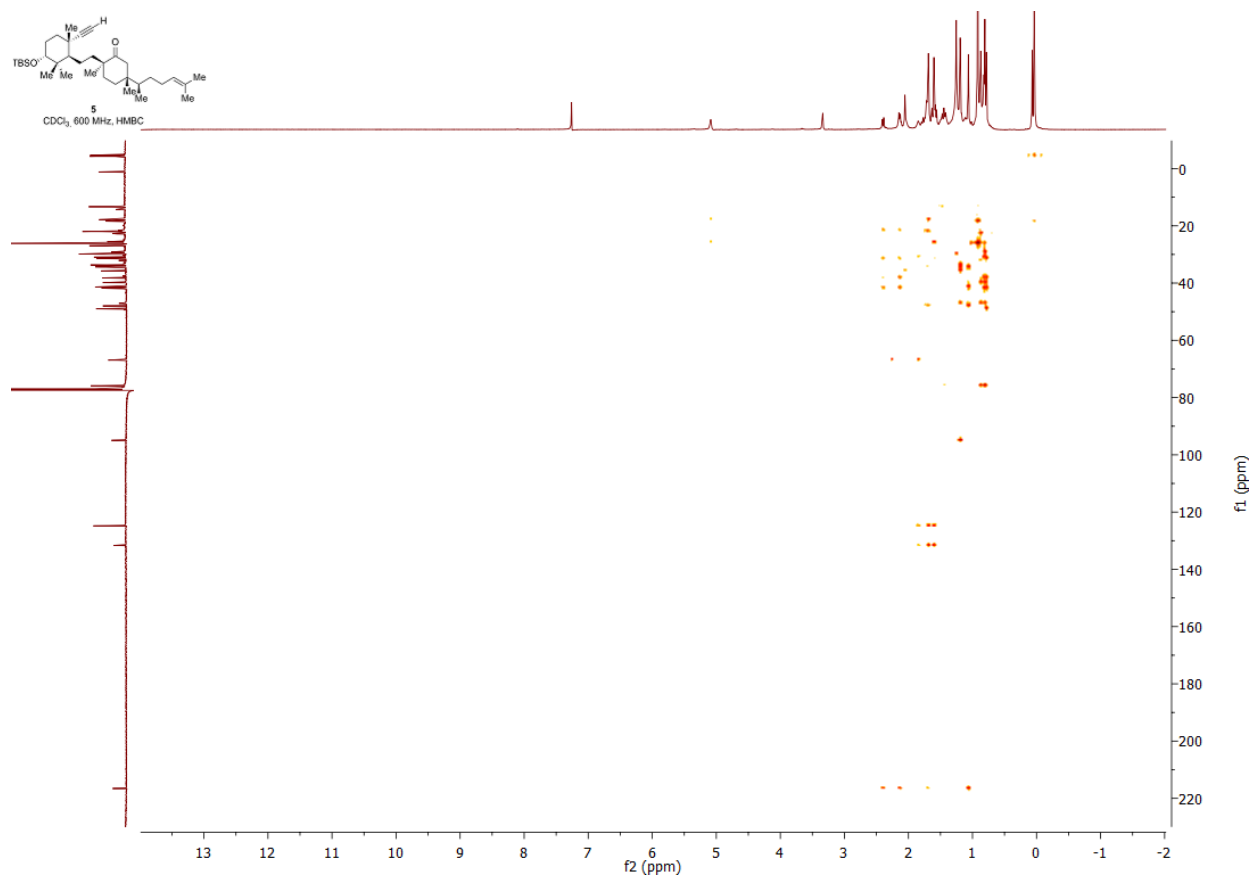


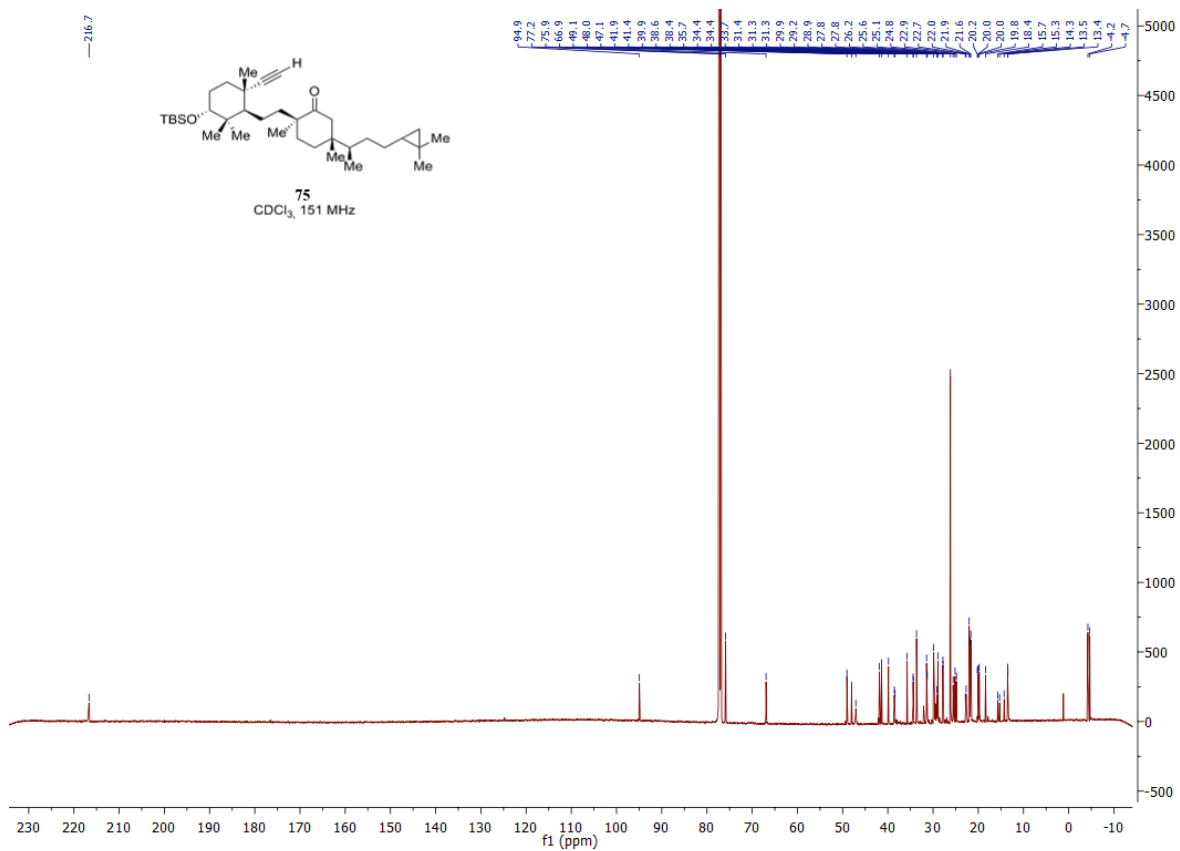
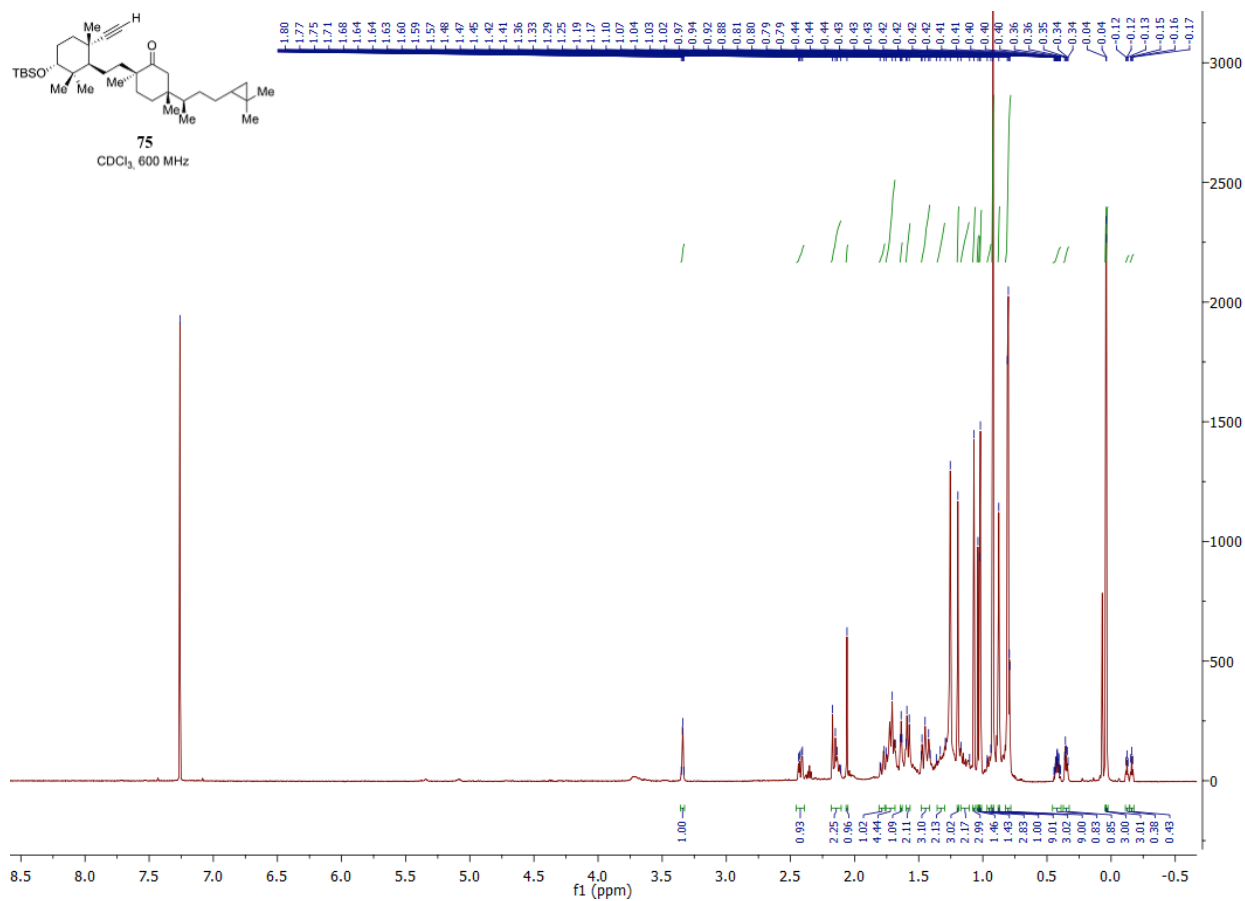


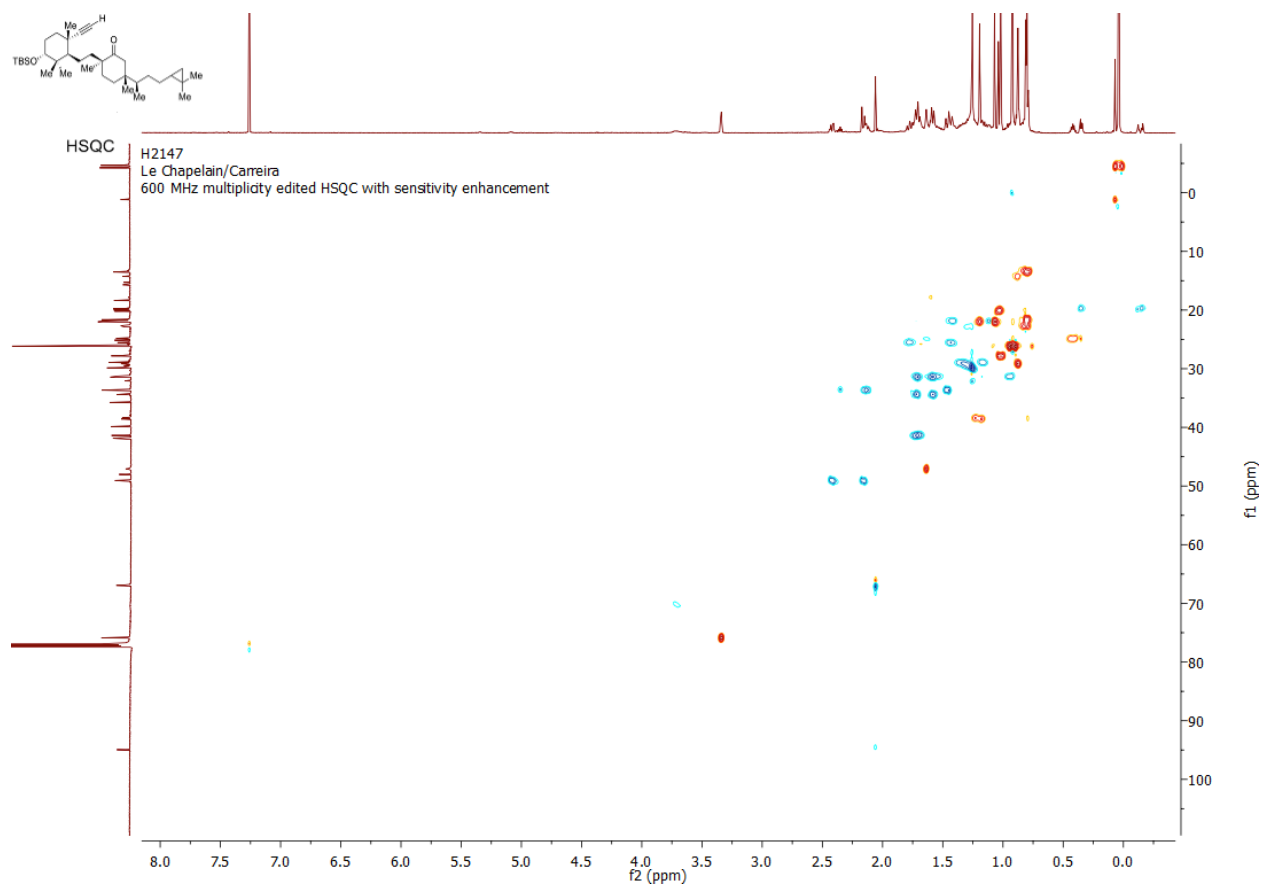
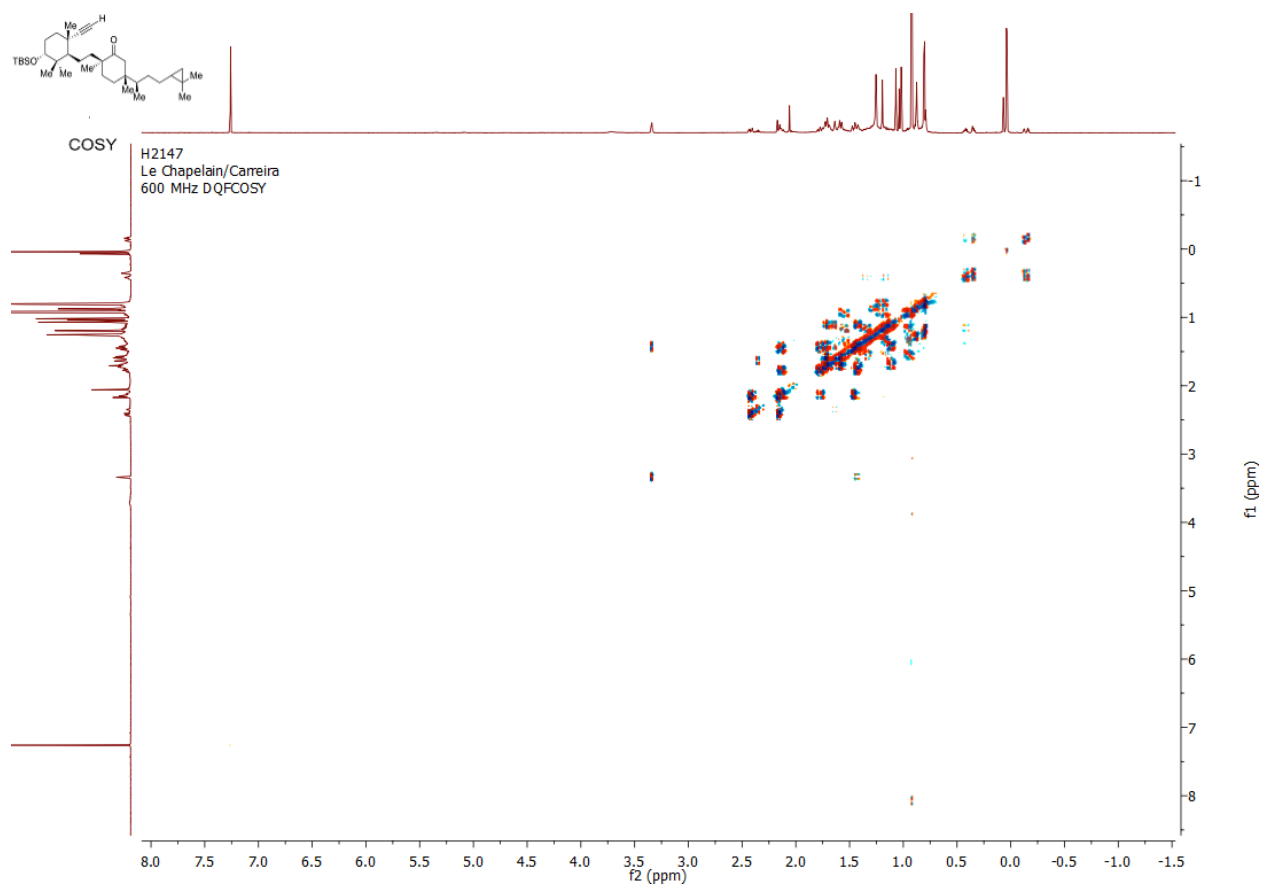
Le Chapelain/Carreira

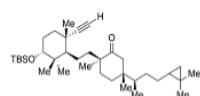






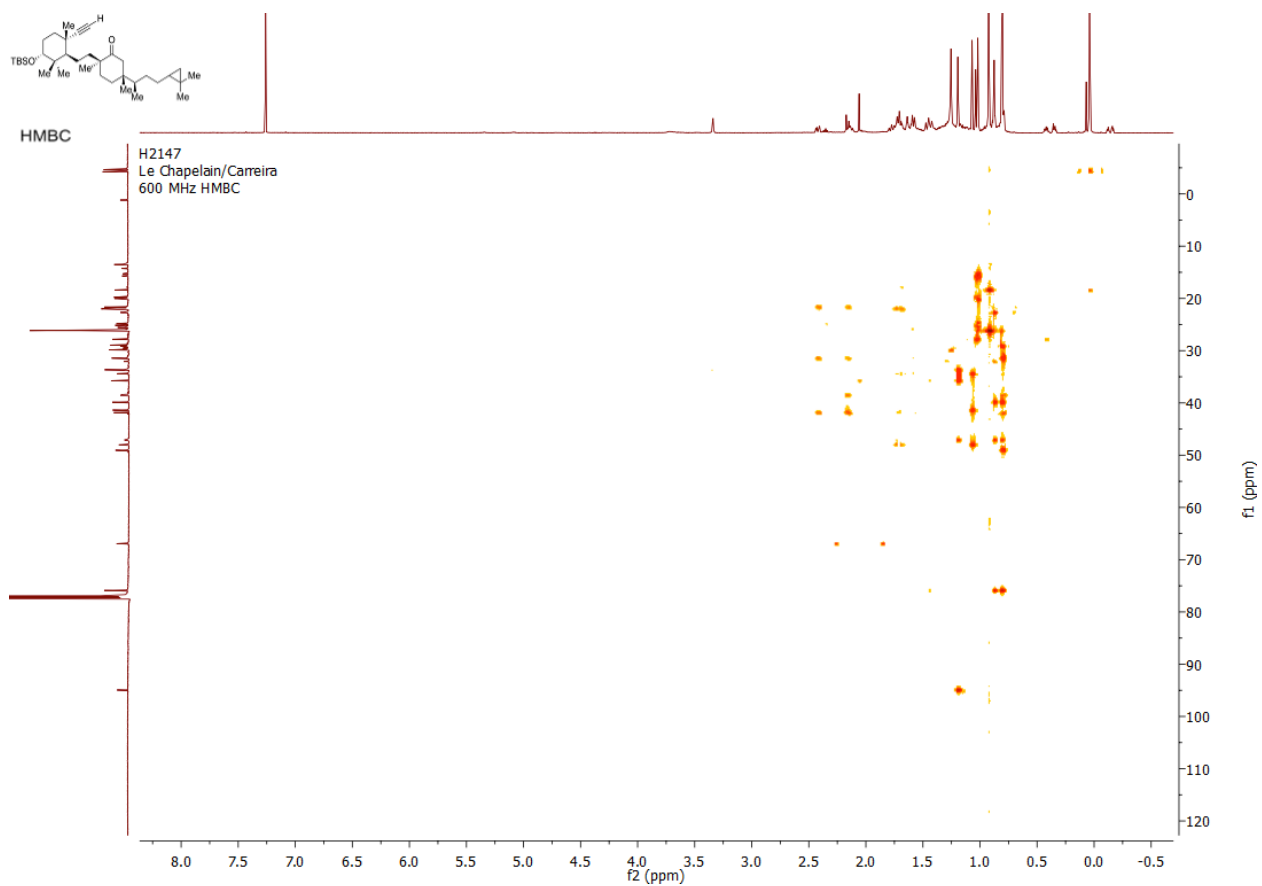


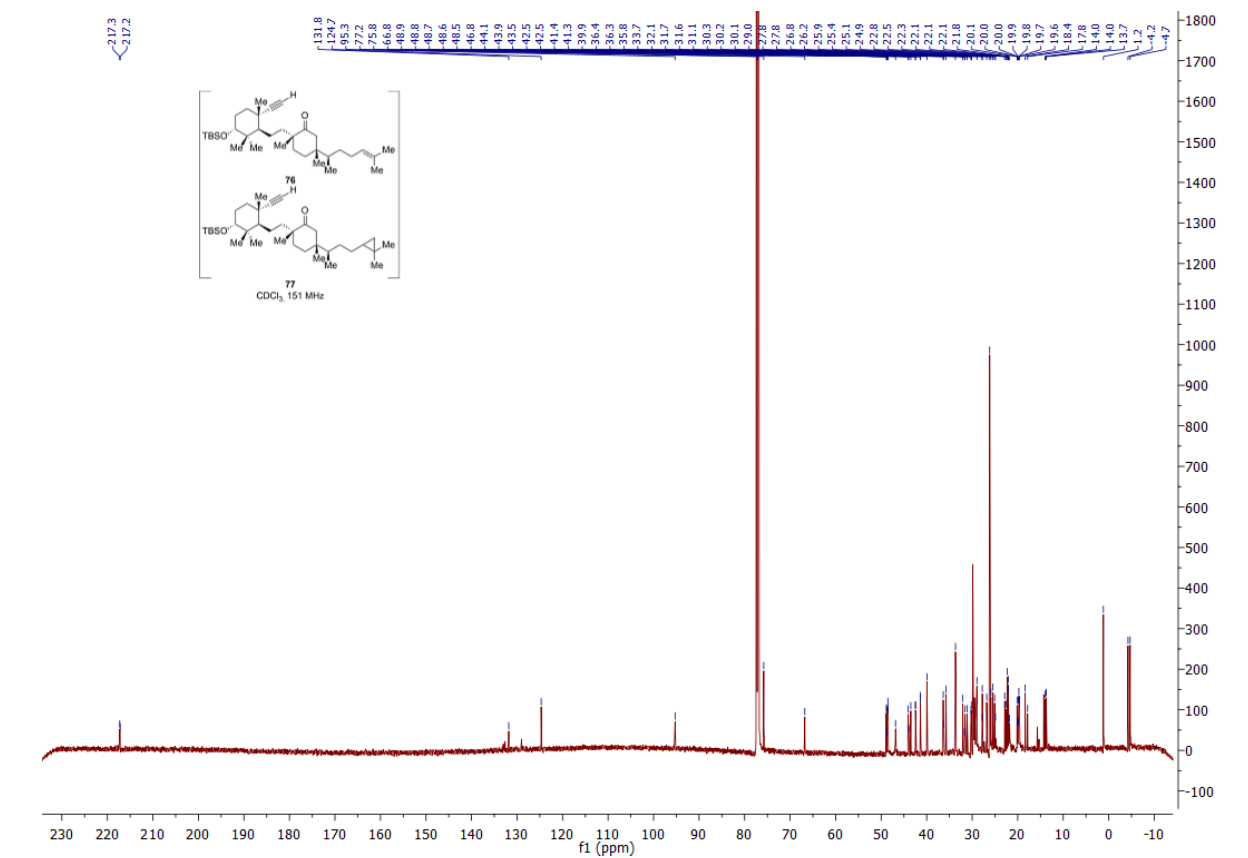


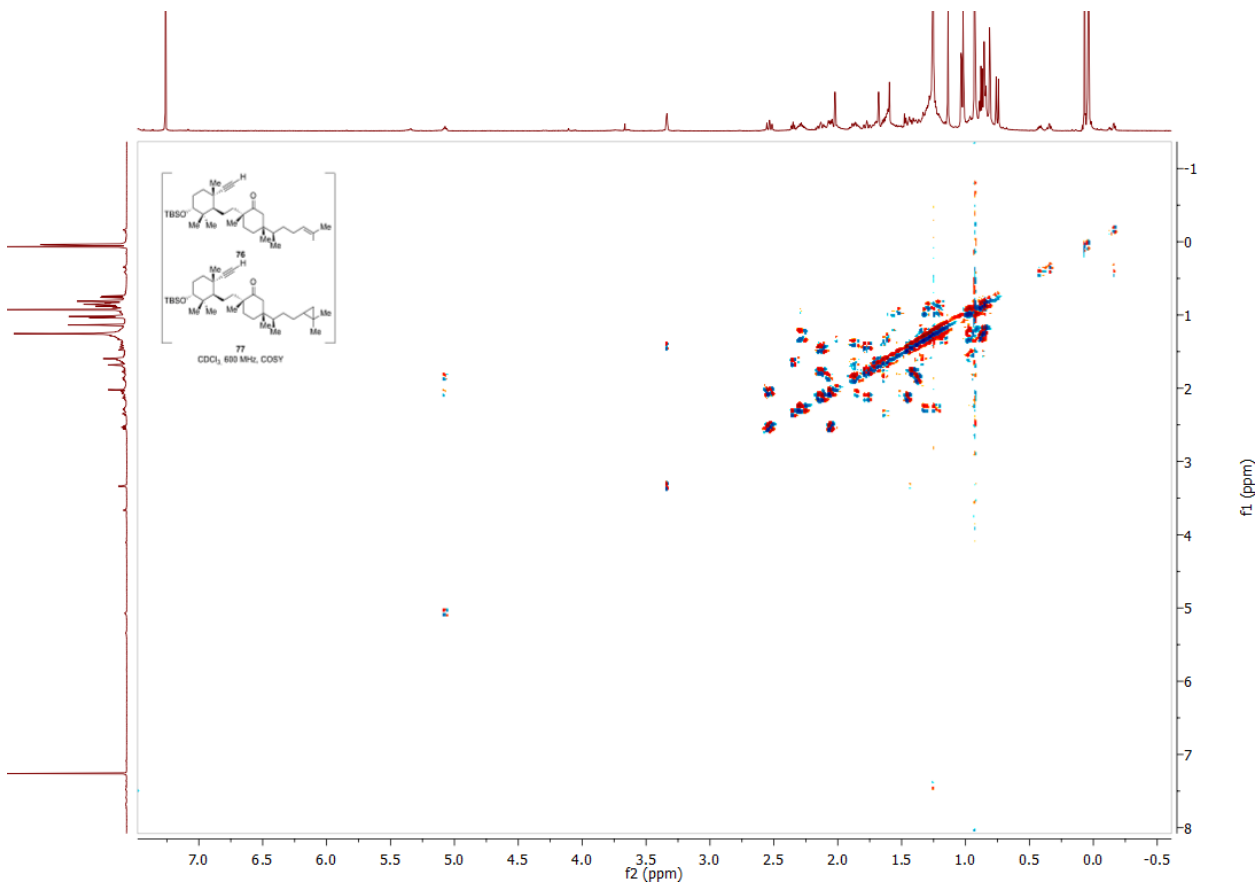
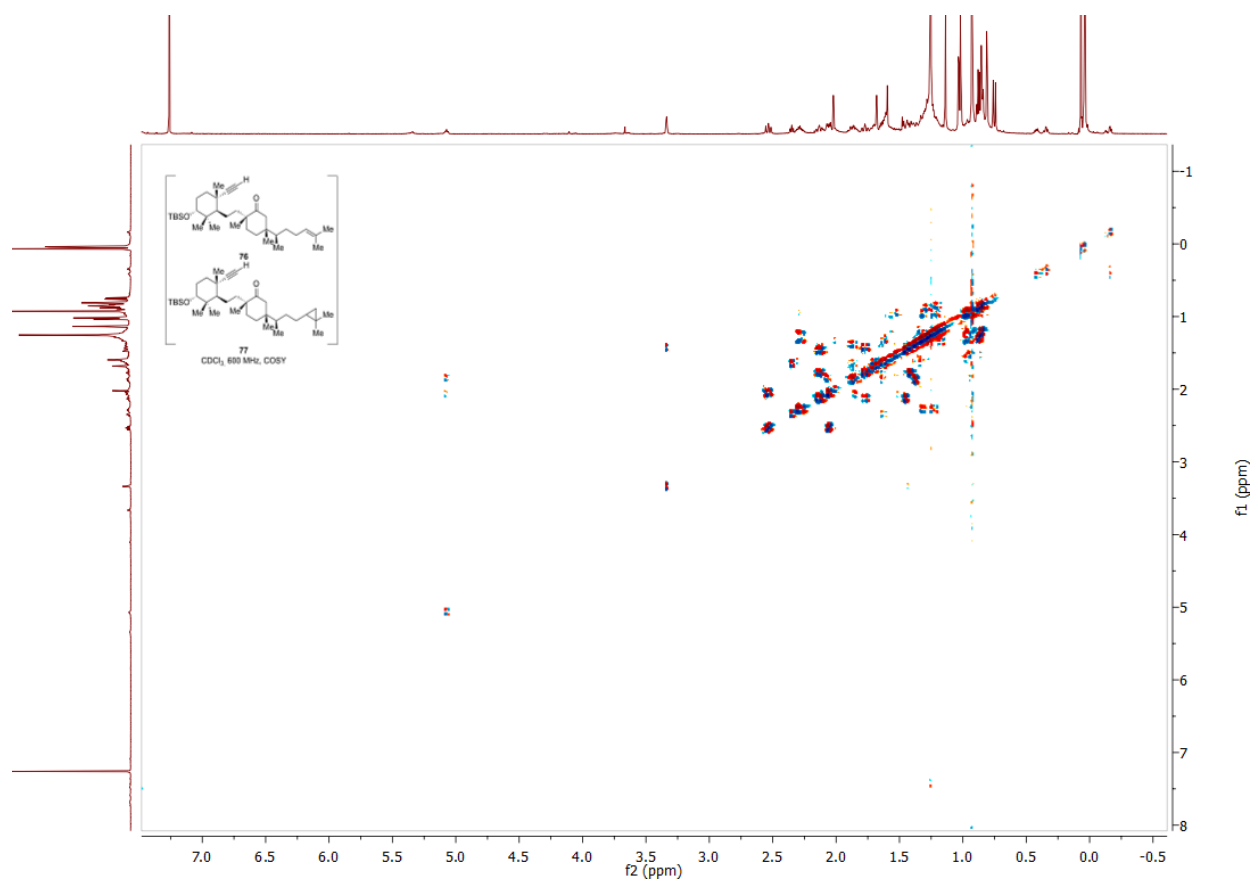


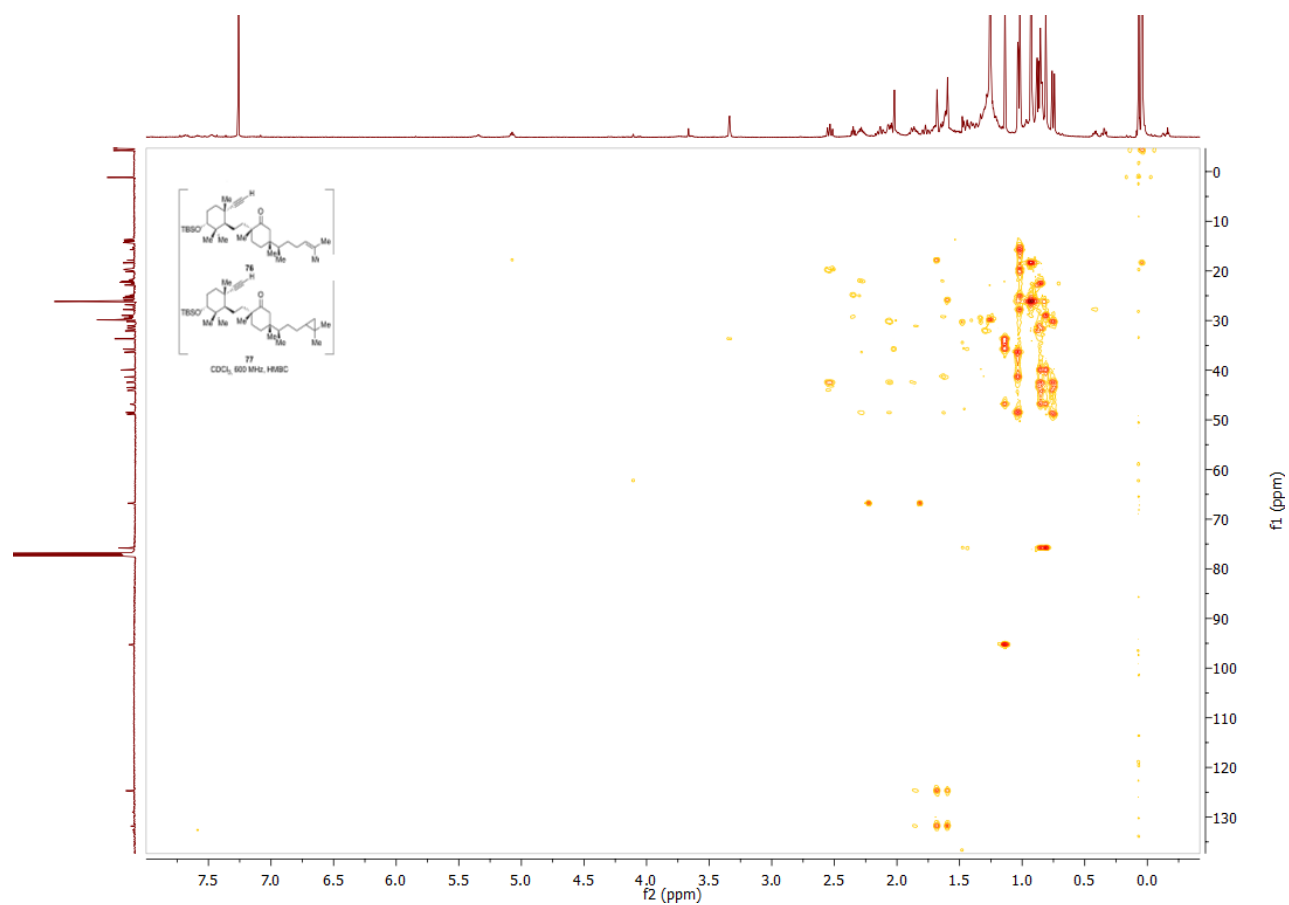
HMBC

H2147
Le Chapelain/Carreira
600 MHz HMBC



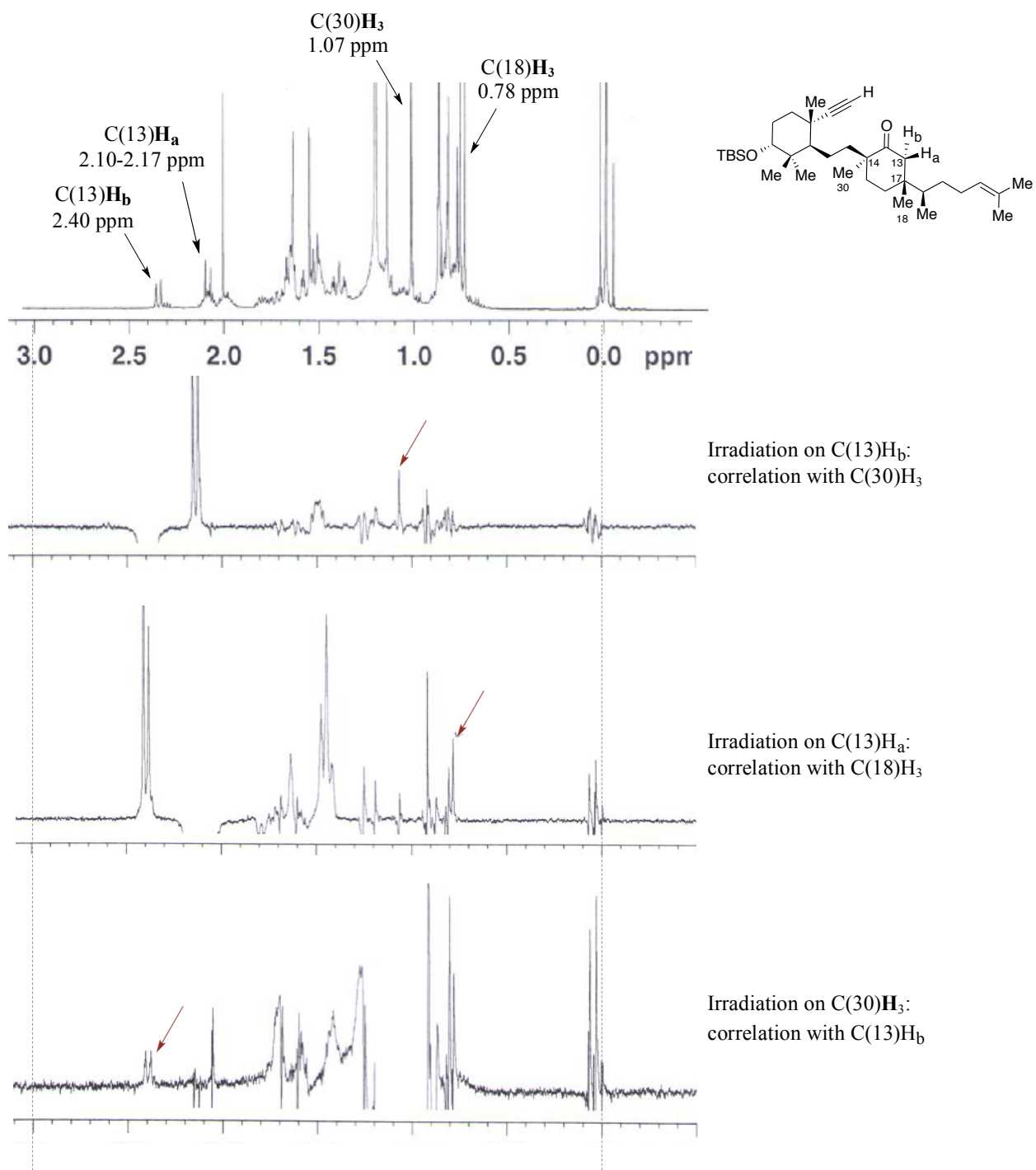




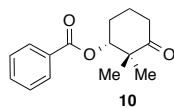


5. NOE spectra of ketone 5 for determination of stereochemistry at C(30)

Copies of the handouts with processing by the LOC NMR service.

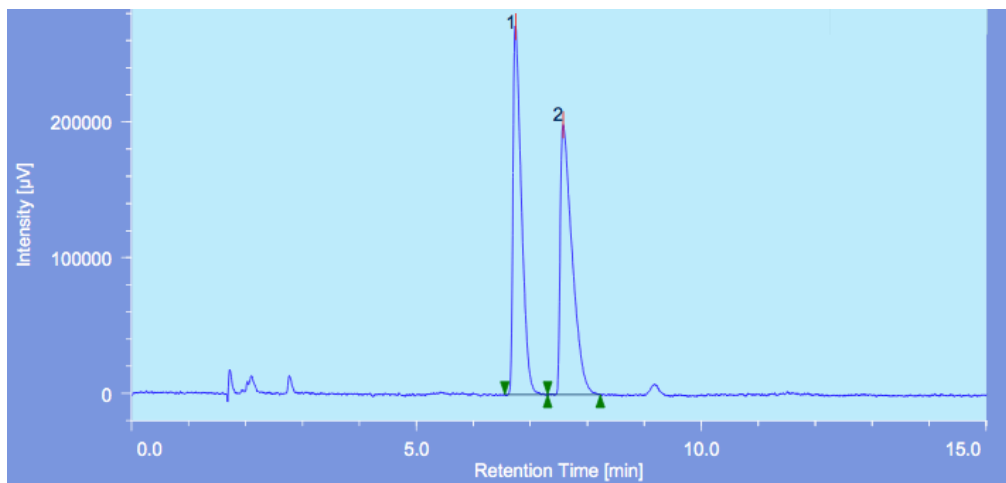


6. SFC chromatograms



- Racemate:

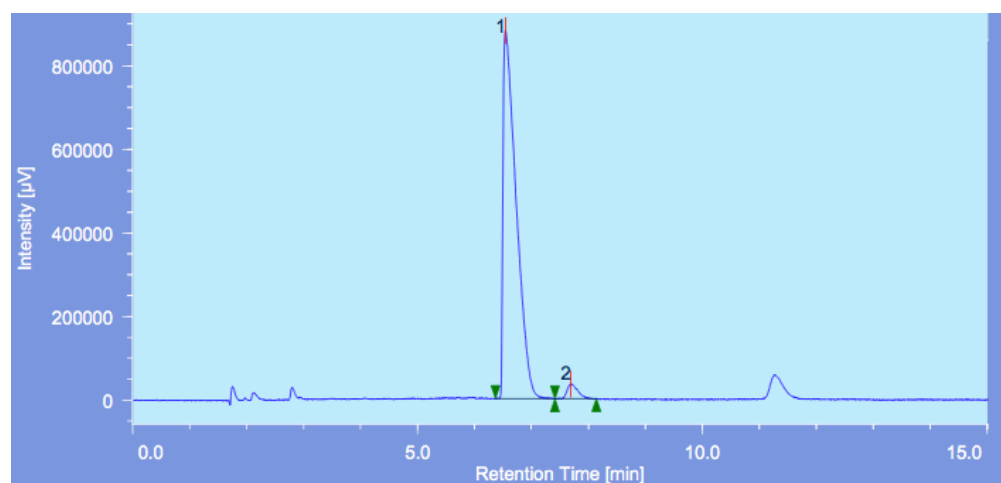
Column IA; CO₂/iPrOH, 98:2; 2.00 mL.min⁻¹; 100 bar; 25 °C



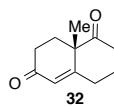
#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor
1	Unknown	1	6.742	2835413	271212	49.722	57.694	N/A	9572	2.560	1.902
2	Unknown	1	7.575	2867132	198874	50.278	42.306	N/A	6456	N/A	2.639

- Compound **10**:

Column IA; CO₂/iPrOH, 98:2; 2.00 mL.min⁻¹; 100 bar; 25 °C

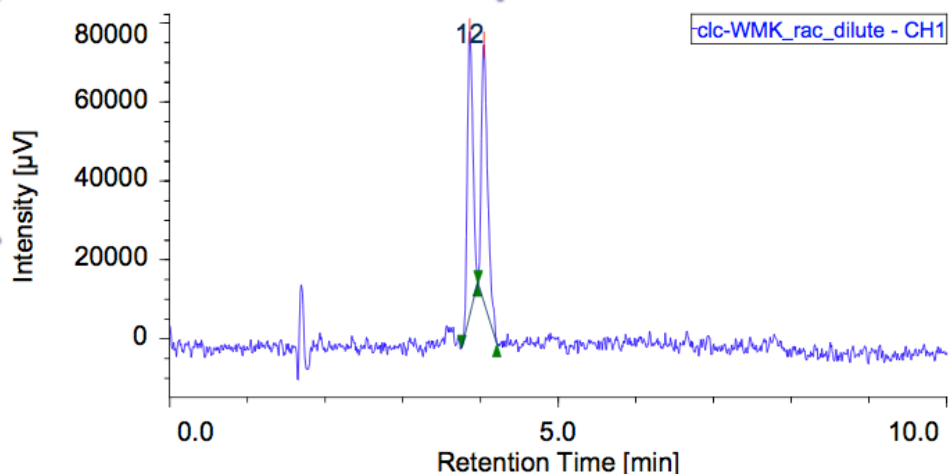


#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor
1	Unknown	1	6.542	14180529	880586	96.938	96.167	N/A	3644	2.947	3.454
2	Unknown	1	7.683	447896	35101	3.062	3.833	N/A	8018	N/A	1.638



- Racemate:

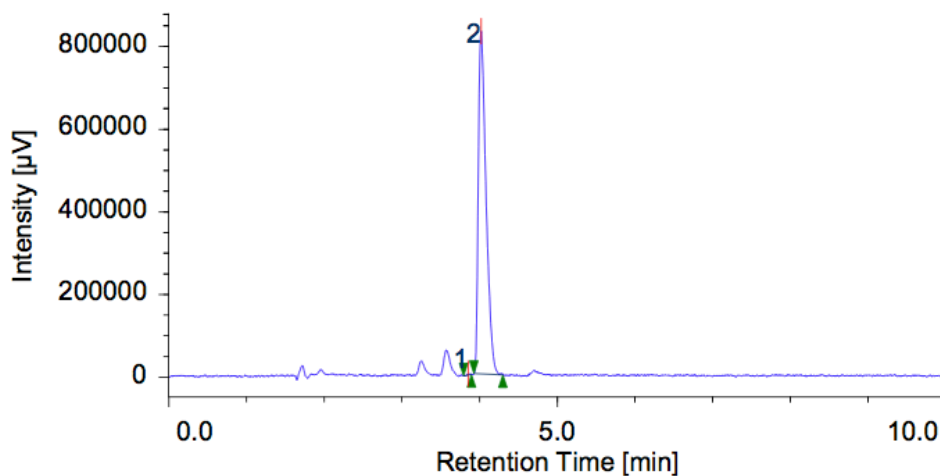
Column IA; CO₂/iPrOH, 95:5; 2.00 mL.min⁻¹; 100 bar; 25 °C



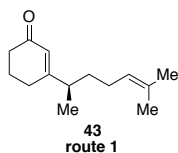
#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor
1	Unknown	1	3.858	355527	71992	48.874	52.491	N/A	13275	1.322	1.186
2	Unknown	1	4.042	371911	65160	51.126	47.509	N/A	12576	N/A	1.570

- Compound **32**:

Column IA; CO₂/iPrOH, 95:5; 2.00 mL.min⁻¹; 100 bar; 25 °C

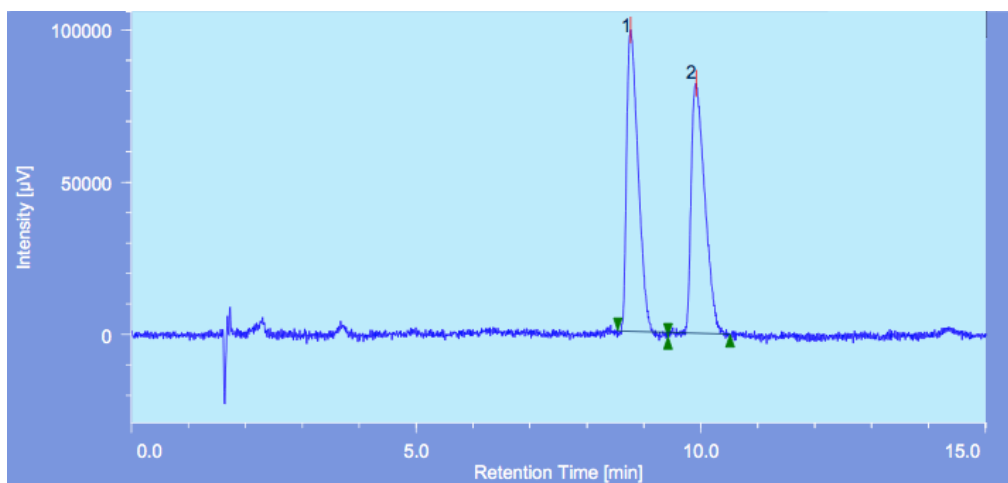


#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor
1	Unknown	1	3.850	7065	3525	0.124	0.424	N/A	93003	1.455	0.943
2	Unknown	1	4.017	5707688	828663	99.876	99.576	N/A	8031	N/A	1.653



- Racemate:

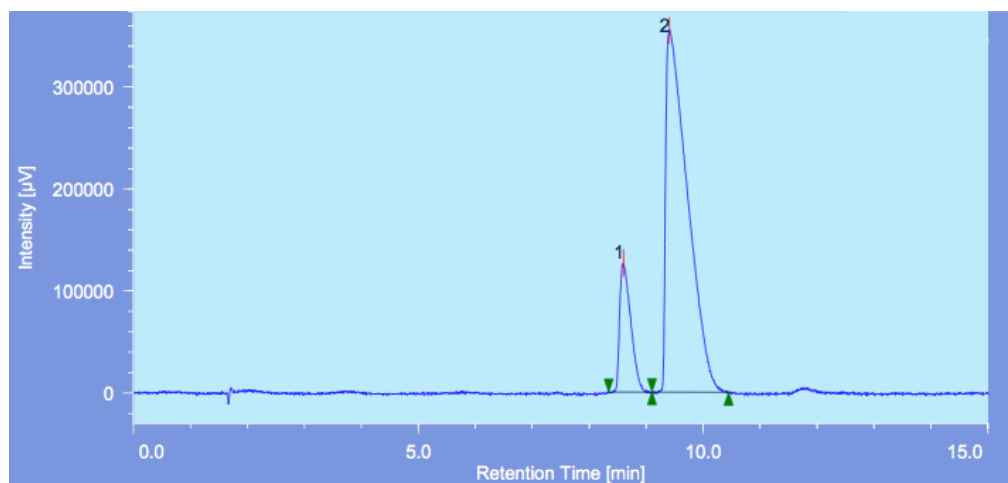
Column AS-H; CO₂/iPrOH, 99:1; 2.00 mL.min⁻¹; 100 bar; 25 °C



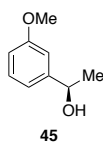
#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor
1	Unknown	9	8.767	1374305	99002	50.205	54.684	N/A	8762	2.817	1.694
2	Unknown	9	9.913	1363060	82041	49.795	45.316	N/A	8063	N/A	1.631

- Compound **43** (route 1):

Column AS-H; CO₂/iPrOH, 99:1; 2.00 mL.min⁻¹; 100 bar; 25 °C

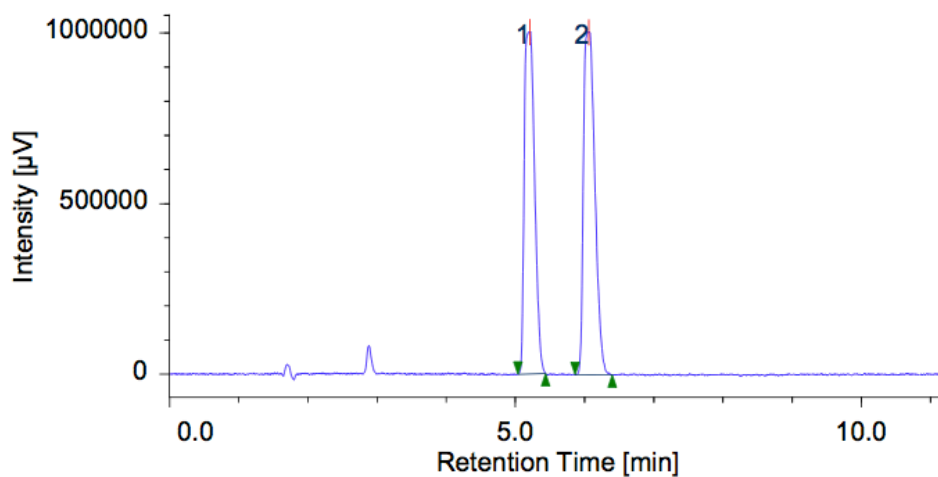


#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor
2	Unknown	9	8.600	1704346	126450	15.418	26.299	N/A	9065	1.504	1.776
1	Unknown	9	9.407	9349991	354369	84.582	73.701	N/A	2776	N/A	3.862



- Racemate:

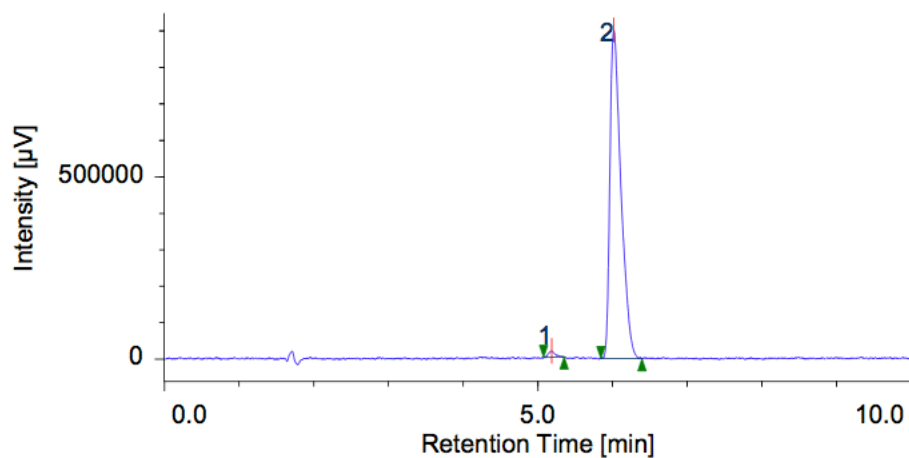
Column OJ-H; CO₂/iPrOH, 95:5; 2.00 mL.min⁻¹; 100 bar; 25 °C



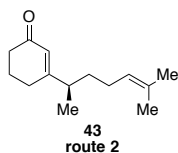
#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor
1	Unknown	1	5.208	10373520	1000660	47.322	49.936	N/A	5491	2.892	1.155
2	Unknown	1	6.058	11547439	1003207	52.678	50.064	N/A	6182	N/A	1.316

- Compound 45:

Column OJ-H; CO₂/iPrOH, 95:5; 2.00 mL.min⁻¹; 100 bar; 25 °C

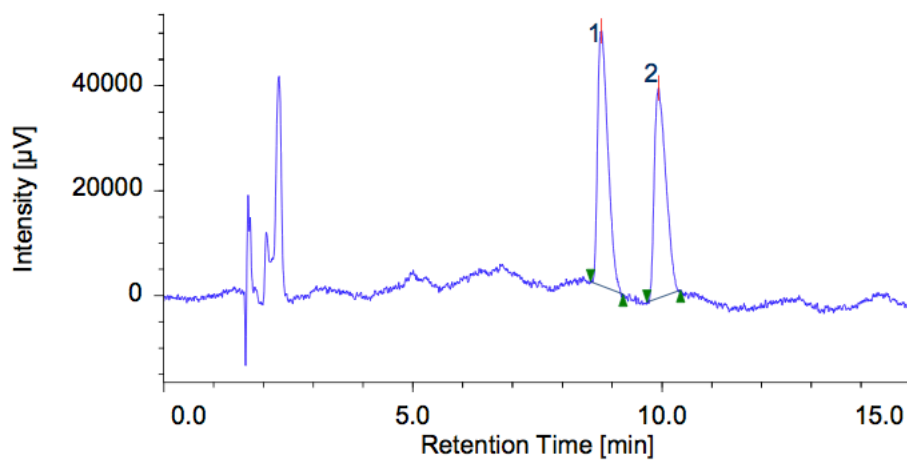


#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor
1	Unknown	1	5.183	105491	17424	1.131	1.899	N/A	17279	3.947	1.303
2	Unknown	1	6.017	9220723	900062	98.869	98.101	N/A	8204	N/A	1.626



- Racemate:

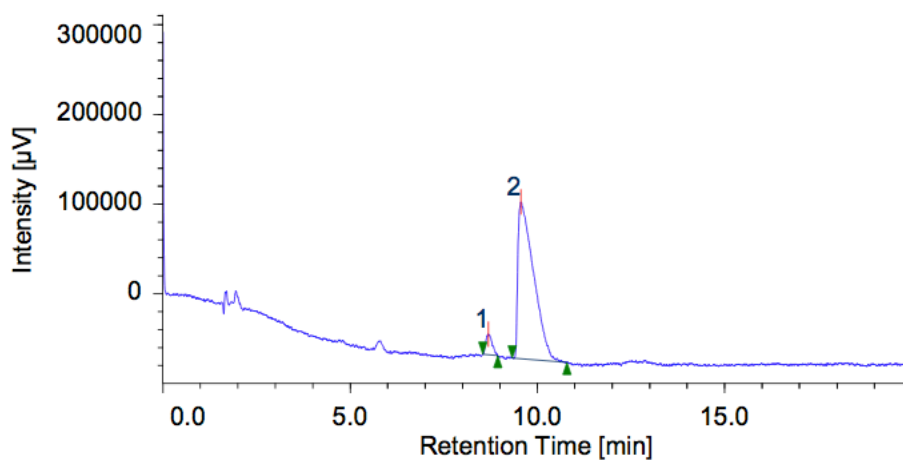
Column AS-H; CO₂/iPrOH, 99:1; 2.00 mL.min⁻¹; 100 bar; 25 °C



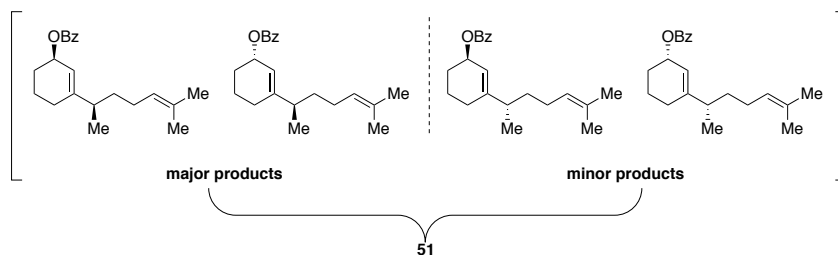
#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor
1	Unknown	1	8.783	694578	48531	51.818	54.820	N/A	8329	2.766	1.637
2	Unknown	1	9.925	645836	39998	48.182	45.180	N/A	8039	N/A	1.567

- Compound **43** (route 2):

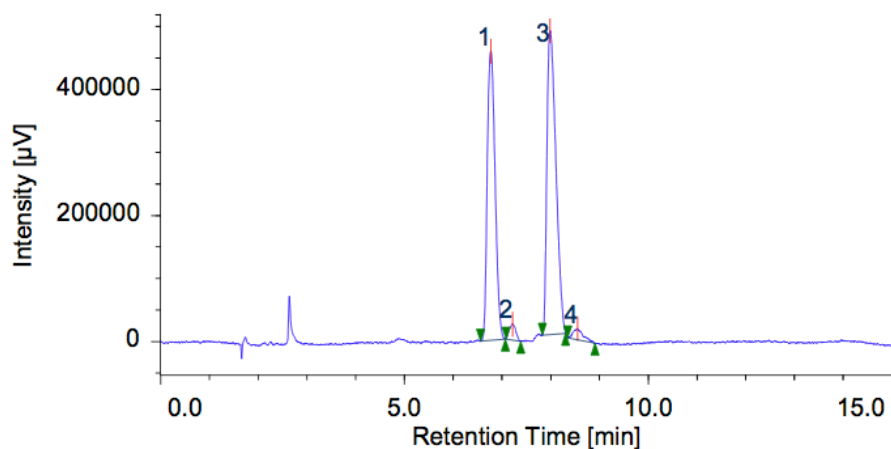
Column AS-H; CO₂/iPrOH, 99:1; 2.00 mL.min⁻¹; 100 bar; 25 °C



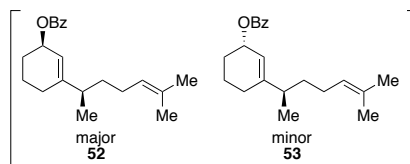
#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor
1	Unknown	1	8.692	268761	22984	5.031	11.611	N/A	13375	1.583	1.353
2	Unknown	1	9.558	5073279	174959	94.969	88.389	N/A	2302	N/A	3.295



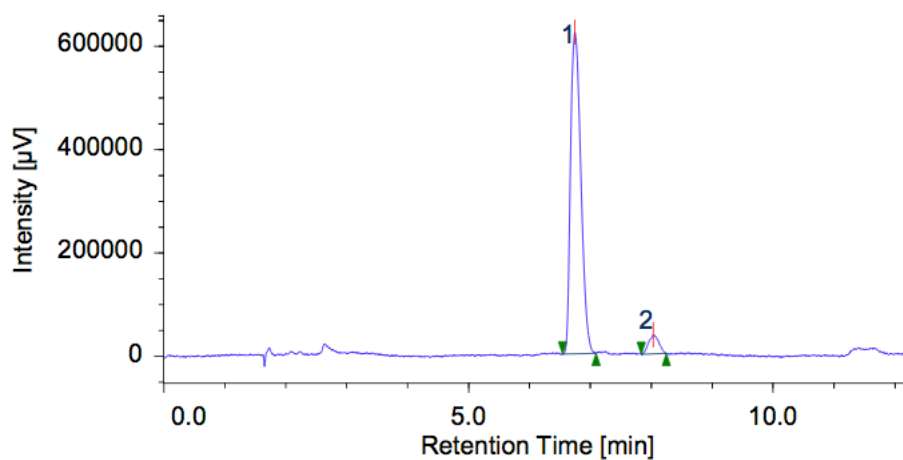
- Compounds **51**: column IB; CO₂/iPrOH, 99:1; 2.00 mL.min⁻¹; 100 bar; 25 °C



#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor
1	Unknown	1	6.767	5095390	458095	43.429	46.597	N/A	8004	1.578	1.272
2	Unknown	1	7.217	240263	25397	2.048	2.583	N/A	11487	2.490	1.046
3	Unknown	1	7.983	6144318	482004	52.369	49.029	N/A	8417	1.635	1.593
4	Unknown	1	8.550	252761	17604	2.154	1.791	N/A	9706	N/A	1.336



- Compounds **52-53**: column IB; CO₂/iPrOH, 99:1; 2.00 mL.min⁻¹; 100 bar; 25 °C



#	Peak Name	CH	tR [min]	Area [μV·sec]	Height [μV]	Area%	Height%	Quantity	NTP	Resolution	Symmetry Factor
1	Unknown	1	6.742	7319041	622217	94.577	94.427	N/A	7073	4.018	1.366
2	Unknown	1	8.025	419681	36720	5.423	5.573	N/A	10075	N/A	1.089