

## Supporting Information

### **Oxidative Bridgehead functionalization of (4+3) Cycloadducts Obtained from Oxidopyridinium Ions**

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## 1. General Information

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on either an AVIII-500 ( $^1\text{H}$  NMR: 500 MHz;  $^{13}\text{C}$  NMR: 100 MHz) or an AVIII-600 ( $^1\text{H}$  NMR: 600 MHz;  $^{13}\text{C}$  NMR: 125 MHz) spectrometer. Chemical shifts are reported in ppm ( $\delta$ ) relative to tetramethylsilane (TMS) as an internal standard [ $\text{CDCl}_3$ :  $^1\text{H}$  NMR (0.00 ppm),  $^{13}\text{C}$  NMR (77.16 ppm)]. When  $\text{CDCl}_3$  does not contain tetramethylsilane, residual traces of the hydrogenated solvent were used as an internal reference (7.26 ppm). Signal splitting patterns are indicated as such: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sex = sextet, hept = heptet, m = multiplet, dd = doublet, ddd = doublet of doublet, dddd = doublet of doublet of doublet of doublet, td = triplet of doublet, etc. Melting points of crystalline compound were determined with a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were recorded on a Thermo Nicolet Summit Pro FT-IR spectrometer and characteristic peaks were highlighted. High-Resolution Mass Spectrometry (HR-MS) was recorded on a Bruker 12 Tesla APEX-Qe FTICR-MS with an Apollo II ion source (performed by College of Science Major Instrumentation Center, Old Dominion University).

All reactions were carried out in oven-dried glassware, with a magnetic stir bar, and under an atmosphere of argon (balloon) unless otherwise noted. *N*-iodosuccinimide was purchased from Ambeed and was used as received. ACS reagent grade hexanes and ethyl acetate were purchased from Fisher and were used as received. ACS reagent grade dichloromethane was purchased from Fisher and dried over 4 Å molecular sieves. ACS grade acetonitrile was purchased from Fisher and was distilled under an atmosphere of nitrogen over calcium hydride. ACS reagent grade triethylamine was purchased from Sigma Aldrich and was distilled under an atmosphere of nitrogen over calcium hydride. ACS grade hexafluoroisopropanol was purchased from Halocarbon

and dried over 4 Å molecular sieves. Analytical thin layer chromatography (TLC) was performed on TLC Silica gel 60 F<sub>254</sub> plates and visualized with a handheld UV lamp (254 nm). The plates were stained with iodine or vanillin for further evaluation. Flash chromatography was performed using 40 – 63 micron silica gel purchased from ZeoChem.

Single crystal X-ray diffraction data was collected on a Bruker X8 Prospector diffractometer equipped with an Apex II CCD area detector (Bruker AXS, Madison, WI, USA) using Cu-K $\alpha$  radiation from a microfocus source ( $\lambda = 1.54178$  Å; beam power: 45 kV, 0.65 mA). A full sphere of unique data was collected to greatest completeness possible with a 3-circle goniometer using strategies of scans about the omega and phi axes. The Bruker Apex3 software suite was used for unit cell determination, data collection, data reduction, absorption correction and scaling, and space group determination.<sup>1</sup>

The crystal structure was solved by direct methods as implemented in SHELXS<sup>2</sup> and refined by full-matrix least squares refinement against  $|F^2|$  using SHELXL v.2017.<sup>3</sup> Olex2 was used as an interface for model building and refinement programs.<sup>4</sup> Non-hydrogen atoms were located from the difference map and refined anisotropically. Hydrogen atoms were placed in calculated positions, and their thermal parameters and coordinates were constrained to ride on the carrier atoms. Hydrogen atoms on methyl groups were refined using a riding-rotating model.

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<sup>1</sup> Apex3, AXScale, and SAINT, version 2017.3-0, Bruker AXS, Inc., Madison, WI, 2017.

<sup>2</sup> G. M. Sheldrick, SHELXS, v.2013-1, 2013.

<sup>3</sup> G. M. Sheldrick, *Acta Cryst. Sect. C. Struct. Chem.* 2015, **71**, 3.

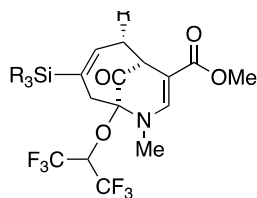
<sup>4</sup> O.V. Dolomanov, L.J. Bourhis, R.J. Gildea, J.A.K. Howard, H. Puschmann, *J. Appl. Cryst.*, 2009, **42**, 339.

## 2. Experimental Procedures

### 2.1 General Procedure for Preparation of Starting Materials

The starting materials were synthesized according to the known literature procedure.<sup>5</sup> To an oven-dried 15 mL seal tube (CG-1880-21 pressure vessel) equipped with a magnetic stir bar was added *N*-methyloxidopyridinium ion (0.63 mmol, 1.0 equiv) and diene (1.9 mmol, 3.0 equiv) in acetonitrile (6.3 mL, 0.1 M) at room temperature. The mixture was then degassed with an argon balloon for 5 min followed by addition of triethylamine (1.9 mmol, 3.0 equiv), sealed with screw cap, and heated for 24 h at 85 °C in an oil bath. Upon heating for 1 h, the reaction solution changed in color from pale-yellow to brown. After 24 h, the reaction mixture was cooled to room temperature, quenched with 16 drops of 10% HCl, and extracted with dichloromethane (3 x 15 mL). The combined organic layers were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, concentrated under reduced pressure, and purified by flash chromatography on silica gel (20 - 30% EtOAc:Hexanes) to obtain the respective cycloadduct starting material as an isomeric mixture.

### 2.2 General Procedure for Synthesis of Products

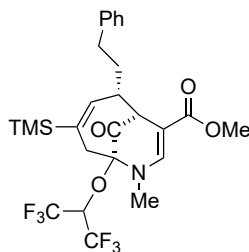


To an oven-dried 10 mL RBF equipped with a magnetic stir bar was added an isomeric mixture of cycloadduct (100 mg, 0.25 mmol, 1.0 equiv) in hexafluoroisopropanol (4.0 mL, 0.06 M) at room temperature. The solution was cooled to 0 °C, and upon addition of *N*-Iodosuccinimide (85.5 mg, 0.38 mmol, 1.5 equiv), the mixture changed in color from pale-yellow to orange/brown. The mixture was allowed to warm to room temperature and stir for the indicated time (1 - 23 h).

<sup>5</sup> W. Sungnoi, A. B. Keto, R. B. Roseli, J. Liu, H. Wang, C. Fu, E. L. Regalado, E. H. Krenske, M. Harmata, *Org. Lett.*, 2021, **23**, 8302.

Reactions were monitored by TLC (20 - 30% EtOAc:Hexanes) until all starting material was consumed. Upon completion, the reaction was quenched with water to give a dark red solution, and the resulting mixture was extracted with dichloromethane (3 x 5 mL). The combined organic layers were washed with NaHCO<sub>3</sub>, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, concentrated under reduced pressure, and purified by flash chromatography on silica gel (20 - 30% EtOAc:Hexanes) to obtain the product.

**Methyl (1*R*,2*R*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-2-phenethyl-4-(trimethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (4a, known compound<sup>5</sup>)**



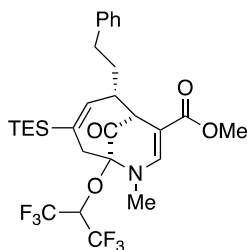
**1 mmol scale**

To an oven-dried 25 mL RBF equipped with a magnetic stir bar was added cycloadduct (400 mg, 1.0 mmol, 1.0 equiv, isomeric ratio of 81:13:6) in hexafluoroisopropanol (11.1 mL, 0.09 M) at room temperature. The solution was cooled to 0 °C, and upon addition of *N*-Iodosuccinimide (337.5 mg, 1.5 mmol, 1.5 equiv), the mixture changed in color from pale-yellow to orange/brown. The mixture was allowed to warm to room temperature and stirred for 21 h. The reaction was monitored by TLC (30% EtOAc:Hexanes) until all starting material was consumed. Upon completion, the reaction was quenched with water to give a dark red solution, and the resulting mixture was extracted with dichloromethane (3 x 15 mL). The combined organic layers were washed with NaHCO<sub>3</sub>, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, concentrated under reduced pressure, and

purified by flash chromatography on silica gel (30% EtOAc:Hexanes,  $R_f = 0.72$ ) to obtain the product as a pale-yellow solid (300 mg, 0.53 mmol, 53%). Recrystallization (70% EtOH:H<sub>2</sub>O) gave a white solid, mp = 150 - 151°C.

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>): δ 7.30 – 7.27 (2H, m), 7.21 (1H, s), 7.20 – 7.17 (3H, m), 6.19 (1H, dd,  $J = 7.5, 3.0$  Hz), 4.86 (1H, hept,  $J = 6.0$  Hz), 3.68 (1H, s), 3.67 (3H, s), 2.90 – 2.86 (2H, m), 2.82 – 2.76 (4H, m), 2.63 (1H, ddd,  $J = 13.0, 10.5, 6.0$  Hz), 2.29 (1H, dd,  $J = 17.0, 3.5$  Hz), 1.70 (1H, dddd,  $J = 13.5, 10.0, 7.5, 6.0$  Hz), 1.50 (1H, dddd,  $J = 13.5, 10.0, 8.0, 6.0$  Hz), 0.11 (9H, s); **<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>): 199.8, 166.8, 146.4, 143.8, 141.7, 134.0, 128.5, 128.5, 126.1, 121.5 (q,  $J = 286.9$  Hz), 121.2 (q,  $J = 288.4$  Hz), 97.4, 93.8, 71.5 (hept,  $J = 33.2$  Hz), 51.2, 49.4, 43.3, 36.6, 34.8, 34.6, 34.1, -1.2; **IR** (CHCl<sub>3</sub>)  $\nu_{\max}$ : 3030, 2954, 2918, 1739, 1695, 1628, 1365, 1247, 1245, 1187, 1103, 1058, 998, 837, 737, 691 cm<sup>-1</sup>; **HRMS (m/z)**: (ESI-FTICR) calcd for (C<sub>26</sub>H<sub>31</sub>F<sub>6</sub>NO<sub>4</sub>Si)Na [M+Na]<sup>+</sup>: 586.1819, found: 586.1813.

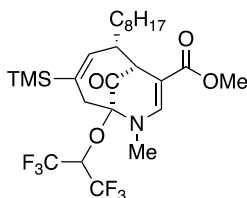
**Methyl (1*R*,2*R*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-2-phenethyl-4-(triethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (6a)**



According to the general procedure, the respective cycloadduct (isomeric ratio of 81:15:4) yielded **6a** as a white solid (66 mg, 0.11 mmol, 54%) after purification by flash chromatography (30% EtOAc:Hexanes,  $R_f = 0.68$ ). Recrystallization (20% EtOH:H<sub>2</sub>O) gave white solid, mp = 93 - 94°C.

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>): δ 7.30 – 7.27 (2H, m), 7.22 (1H, s), 7.20 – 7.17 (3H, m), 6.17 (1H, dd, *J* = 7.6, 3.0 Hz), 4.89 (1H, hept, *J* = 6.0 Hz), 3.68 (1H, d, *J* = 5.0 Hz), 3.67 (3H, s), 2.91 (1H, qd, *J* = 7.5, 3.9 Hz), 2.85 (1H, d, *J* = 16.5 Hz), 2.80 (3H, s), 2.77 (1H, dd, *J* = 8.0, 3.5 Hz), 2.66 (1H, ddd, *J* = 14.0, 10.5, 6.0 Hz), 2.26 (1H, dd, *J* = 16.5, 3.0 Hz), 1.72 (1H, dddd, *J* = 13.1, 10.3, 7.0, 5.9 Hz), 1.51 (1H, dddd, *J* = 13.6, 10.2, 7.8, 5.8 Hz), 0.92 (9H, t, *J* = 7.9 Hz), 0.63 (6H, tdd, *J* = 22.5, 15.1, 7.5 Hz); **<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>) δ 199.9, 166.8, 146.3, 145.0, 141.7, 131.0, 128.6, 128.6, 126.1, 121.6 (q, *J* = 288.4 Hz), 121.2 (q, *J* = 285.4 Hz), 97.3, 93.6, 71.5 (hept, *J* = 32.2 Hz), 51.3, 49.5, 43.6, 37.0, 34.9, 34.8, 34.2, 7.6, 3.2; **IR** (MeOH)  $\nu_{\max}$  = 3194, 2969, 2842, 1734, 1693, 1639, 1344, 1287, 1186, 1098, 938, 877, 737, 696 cm<sup>-1</sup>; **HRMS (m/z)**: (ESI-FTICR) calcd for (C<sub>29</sub>H<sub>37</sub>F<sub>6</sub>NO<sub>4</sub>Si)Na [M+Na]<sup>+</sup>: 628.2288, found 628.2280.

**Methyl (1*R*,2*R*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-2-octyl-10-oxo-4-(trimethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (8a)**

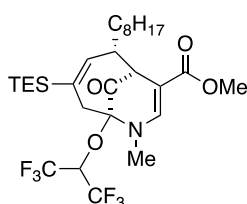


According to the general procedure, the respective cycloadduct (isomeric ratio of 82:14:4) yielded **8a** as a white solid (66 mg, 0.12 mmol, 46%) after purification by flash chromatography (20% EtOAc:Hexanes, *R<sub>f</sub>* = 0.65). Recrystallization (80% EtOH:H<sub>2</sub>O) gave long, white needles, mp = 78 - 79°C.

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>) δ 7.20 (1H, s), 6.18 (1H, dd, *J* = 7.6, 3.0 Hz), 4.84 (1H, hept, *J* = 6.0 Hz), 3.69 (3H, s), 3.58 (1H, d, *J* = 3.7 Hz), 2.85 (1H, d, *J* = 16.5 Hz), 2.81 (1H, td, *J* = 7.0, 3.5 Hz), 2.78 (3H, s), 2.27 (1H, dd, *J* = 16.5, 3.0 Hz), 1.44 - 1.16 (14H, m), 0.88 (3H, t, *J* = 6.8 Hz), 0.10 (9H, s); **<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>): 199.9, 166.9, 146.3, 144.4, 133.3, 121.6 (q, *J* = 288.4

Hz), 121.2 (q,  $J = 280.9$  Hz), 97.6, 93.9, 71.6 (hept,  $J = 34.7$  Hz), 51.3, 49.6, 43.9, 36.6, 34.8, 32.8, 32.0, 29.6, 29.4, 27.8, 22.8, 14.2, -1.1; **IR** ( $\text{CHCl}_3$ )  $\nu_{\text{max}}$ : 2931, 2922, 2853, 1734, 1676, 1641, 1361, 1279, 1234, 1188, 1102, 1070, 829, 763, 687  $\text{cm}^{-1}$ ; **HRMS** ( $m/z$ ): calcd for  $(\text{C}_{26}\text{H}_{39}\text{F}_6\text{NO}_4\text{Si})\text{H} [\text{M}+\text{H}]^+$ : 572.2625, found: 572.2623.

**Methyl (1*R*,2*R*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-2-octyl-10-oxo-4-(triethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (10a)**

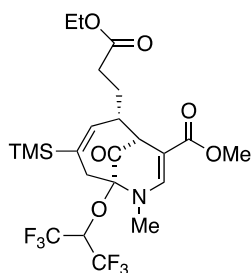


According to the general procedure, the respective cycloadduct (isomeric ratio of 89:9:2) yielded **10a** as a white solid (72 mg, 0.12 mmol, 52%) after purification by flash chromatography (20% EtOAc:Hexanes,  $R_f = 0.60$ ). Recrystallization (70% EtOH:H<sub>2</sub>O) gave long, white needles, mp = 66 - 67°C.

**<sup>1</sup>H NMR** (600 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.21 (1H, s), 6.15 (1H, dd,  $J = 7.6, 3.0$  Hz), 4.88 (1H, hept,  $J = 5.9$  Hz), 3.69 (3H, s), 3.59 (1H, d,  $J = 3.8$  Hz), 2.87 – 2.81 (2H, m), 2.79 (3H, s), 2.24 (1H, dd,  $J = 16.5, 3.0$  Hz), 1.48 – 1.17 (14H, m), 0.91 (9H, t,  $J = 8.0$  Hz), 0.88 (3H, t,  $J = 6.6$  Hz), 0.68 – 0.56 (6H, m); **<sup>13</sup>C NMR** (151 MHz,  $\text{CDCl}_3$ )  $\delta$  199.9, 166.8, 146.1, 145.6, 130.2, 121.5 (q,  $J = 285.4$  Hz), 121.2 (q,  $J = 285.4$  Hz), 97.6, 93.7, 71.5 (hept,  $J = 33.2$  Hz), 51.2, 49.6, 44.1, 36.9, 34.7, 33.1, 32.0, 29.6, 29.4, 27.9, 22.8, 14.2, 7.5; **IR** (neat)  $\nu_{\text{max}}$  = 2928, 2919, 2853, 1731, 1677, 1642, 1358, 1278, 1234, 1189, 1101, 1069, 1004, 872, 688  $\text{cm}^{-1}$ ; **HRMS** ( $m/z$ ): (ESI-FTICR) calcd for  $(\text{C}_{29}\text{H}_{45}\text{F}_6\text{NO}_4\text{Si})\text{H} [\text{M}+\text{H}]^+$ : 614.3095, found 614.3096.

**methyl (1*R*,2*R*,6*R*)-2-(3-ethoxy-3-oxopropyl)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-4-(trimethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (12a)**



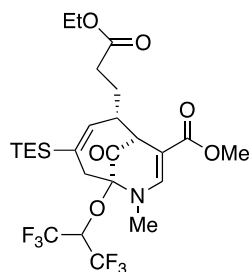


According to the general procedure, the respective cycloadduct (isomeric ratio of 80:16:4) yielded **12a** as a pale-yellow oil (56 mg, 0.10 mmol, 44%) after purification by flash chromatography (30% EtOAc:Hexanes,  $R_f = 0.63$ ).

$^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.22 (1H, s), 6.16 (1H, dd,  $J = 7.6, 3.1$  Hz), 4.84 (1H, hept,  $J = 6.0$  Hz), 4.14 (2H, q,  $J = 7.5$  Hz), 3.69 (3H, s), 3.56 (1H, d,  $J = 3.6$  Hz), 2.90 – 2.83 (2H, m), 2.79 (3H, s), 2.45 (1H, ddt,  $J = 15.5, 9.0, 6.5$  Hz), 2.35 (1H, dddd,  $J = 21.3, 15.4, 9.1, 6.1$  Hz), 2.29 (1H, dd,  $J = 16.5, 3.0$  Hz), 1.70 – 1.55 (2H, m), 1.26 (3H, t,  $J = 7.1$  Hz), 0.11 (9H, s);  $^{13}\text{C NMR}$  (151 MHz,  $\text{CDCl}_3$ )  $\delta$  199.7, 173.0, 166.7, 146.4, 142.8, 134.8, 121.5 (q,  $J = 286.9$  Hz), 121.2 (q,  $J = 286.9$  Hz), 97.2, 93.7, 71.5 (hept,  $J = 33.2$  Hz), 60.6, 51.3, 49.1, 43.0, 36.7, 34.8, 32.4, 27.6, 14.3, -1.2; **IR (neat)**  $\nu_{\text{max}} = 2951, 2865, 1731, 1646, 1637, 1196, 1188, 1067, 1059, 1010, 835, 750, 687$   $\text{cm}^{-1}$ ;

**HRMS (m/z):** (ESI-FTICR) calcd for  $(\text{C}_{23}\text{H}_{31}\text{F}_6\text{NO}_6\text{Si})\text{H M}+\text{H}]^+$ : 560.1898, found. 560.1894.

**Methyl (1*R*,2*R*,6*R*)-2-(3-ethoxy-3-oxopropyl)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-4-(triethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (14a)**

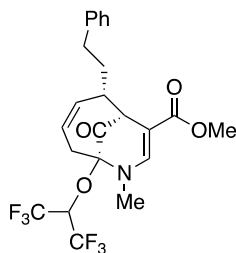


According to the general procedure, the respective cycloadduct (isomeric ratio of 83:16:1) yielded **14a** as a white solid (62 mg, 0.10 mmol, 38%) after purification by flash chromatography (30%

EtOAc:Hexanes,  $R_f = 0.66$ ). Recrystallization (70% EtOH:H<sub>2</sub>O) gave short, white needles, mp = 87 - 88°C.

**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.22 (1H, s), 6.13 (1H, dd,  $J = 7.5, 3.0$  Hz), 4.87 (1H, hept,  $J = 5.9$  Hz), 4.14 (2H, q,  $J = 7.2$  Hz), 3.68 (3H, s), 3.57 (1H, d,  $J = 3.7$  Hz), 2.89 (1H, dd,  $J = 7.8, 3.6$  Hz), 2.86 (1H, d,  $J = 16.2$  Hz), 2.81 (3H, s), 2.47 (1H, ddd,  $J = 16.2, 9.6, 6.6$  Hz), 2.37 (1H, ddd,  $J = 15.0, 9.0, 6.0$  Hz), 2.25 (1H, dd,  $J = 16.6, 3.0$  Hz), 1.70 – 1.56 (2H, m), 1.26 (3H, t,  $J = 7.2$  Hz), 0.92 (9H, t,  $J = 7.9$  Hz), 0.69 – 0.59 (6H, m); **<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>):  $\delta$  199.7, 173.0, 166.7, 146.3, 144.1, 131.7, 121.5 (q,  $J = 286.9$  Hz), 121.2 (q,  $J = 286.9$  Hz), 97.1, 93.6, 71.5 (hept,  $J = 33.2$  Hz), 60.6, 51.3, 49.1, 43.2, 37.0, 34.8, 32.4, 27.9, 14.3, 7.5, 3.1; **IR (neat)**  $\nu_{\max} = 2965, 2865, 1732, 1681, 1640, 1345, 1236, 1189, 1074, 1057, 1008, 877, 688$  cm<sup>-1</sup>; **HRMS (m/z):** (ESI-FTICR) calcd for (C<sub>26</sub>H<sub>37</sub>F<sub>6</sub>NO<sub>6</sub>Si)H [M+H]<sup>+</sup>: 602.2367, found: 602.2366.

**Methyl (1*R*,2*S*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-2-phenethyl-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (16a)**

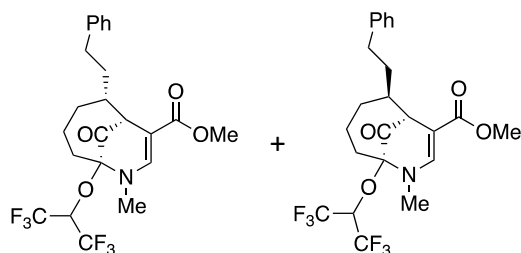


According to the general procedure, the respective cycloadduct (isomeric ratio of 46:54) yielded **16a** as a white cotton (16 mg, 0.03 mmol, 16%) after purification by flash chromatography (30% EtOAc:Hexanes,  $R_f = 0.63$ ). Recrystallization (70 % EtOH:H<sub>2</sub>O) gave a white cotton, mp = 129 - 130°C.

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.28 (2H, t,  $J = 7.5$  Hz), 7.24 (1H, s), 7.21 – 7.16 (3H, m), 5.92 (1H, ddd,  $J = 11.7, 8.2, 2.9$  Hz), 5.70 (1H, ddd,  $J = 12.4, 9.3, 3.4$  Hz), 4.80 (1H, hept,  $J = 6.0$  Hz),

3.70 (1H, d,  $J = 4.0$  Hz), 3.67 (3H, s), 2.84 (1H, td,  $J = 7.7, 4.0$  Hz), 2.81 (3H, s), 2.80 – 2.75 (2H, m), 2.66 (1H, ddd,  $J = 13.8, 10.0, 5.9$  Hz), 2.31 (1H, dt,  $J = 16.3, 3.2$  Hz), 1.76 (1H, dddd,  $J = 13.4, 10.1, 7.0, 5.9$  Hz), 1.57 (1H, dddd,  $J = 13.9, 10.1, 8.1, 5.9$  Hz);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  199.7, 166.8, 147.0, 141.7, 136.8, 128.5, 126.1, 121.6 (q,  $J = 289.9$  Hz), 121.2 (q,  $J = 285.4$  Hz), 98.1, 93.5, 71.5 (hept,  $J = 34.7$  Hz), 51.3, 50.2, 42.0, 34.9, 34.6, 34.3, 34.1; IR ( $\text{CHCl}_3$ )  $\nu_{\text{max}} = 2953, 2864, 1702, 1685, 1635, 1439, 1334, 1232, 1187, 1096, 1058, 1009, 876, 753, 688$   $\text{cm}^{-1}$ ; HRMS ( $m/z$ ): (ESI-FTICR) calcd for  $(\text{C}_{23}\text{H}_{23}\text{F}_6\text{NO}_4)\text{Na}$   $[\text{M}+\text{Na}]^+$ : 514.1423, found: 514.1424.

**Methyl (1*R*,2*R*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-2-phenethyl-7-azabicyclo[4.3.1]dec-8-ene-9-carboxylate (18a-b)**

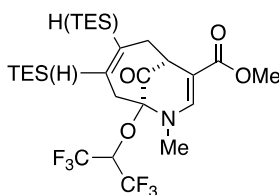


According to the general procedure, the respective cycloadduct (isomeric ratio of 45:55) yielded **18a-b** as a white solid (10 mg, 0.02 mmol, 33%, isomeric ratio of 63:37) after purification by flash chromatography (30% EtOAc:Hexanes,  $R_f = 0.84$ ).

$^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.46 (1H, s) minor isomer, 7.33 (1H, s) major isomer, 7.28 – 7.24 (4H, m), 7.20 – 7.14 (6H, m), 4.60 (1H, hept,  $J = 5.9$  Hz) major isomer, 4.46 (1H, hept,  $J = 5.9$  Hz) minor isomer, 3.81 (1H, s), 3.76 (1H, s), 3.70 (3H, s) major isomer, 3.69 (3H, s) minor isomer, 3.38 (1H, d,  $J = 2.5$  Hz), 2.96 (3H, s) major isomer, 2.93 (3H, s) minor isomer, 2.86 – 2.59 (4H, m), 2.29 (1H, dt,  $J = 14.8, 3.8$  Hz), 2.18 – 2.11 (1H, m), 2.05 – 1.91 (3H, m), 1.89 – 1.73 (4H, m), 1.68 – 1.58 (3H, m), 1.53 – 1.47 (1H, m), 1.38 (1H, dddd,  $J = 13.5, 9.8, 7.1, 6.0$  Hz), 1.29 – 1.22 (2H, m), 1.05 (1H, dt,  $J = 14.3, 11.2$  Hz);  $^{13}\text{C}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  201.6, 200.9, 195.0,

167.5, 167.0, 164.8, 146.7, 145.4, 142.7, 142.2, 142.1, 139.9, 134.1, 130.9, 128.5, 128.5, 128.5, 128.4, 126.0, 125.9, 125.8, 121.6 (q,  $J = 284.8$  Hz), 121.2 (q,  $J = 284.9$  Hz), 112.6, 101.3, 96.1, 94.5, 94.4, 71.1 (hept,  $J = 32.6$  Hz), 51.5, 51.3, 51.1, 50.3, 48.6, 44.6, 44.6, 42.4, 38.7, 38.3, 38.3, 36.2, 35.2, 35.0, 34.9, 34.8, 34.6, 33.9, 33.0, 31.6, 30.9, 29.6, 26.6, 21.2, 20.8, 19.4; **IR** ( $\text{CHCl}_3$ )  $\nu_{\text{max}} = 3023, 2858, 1708, 1637, 1630, 1537, 1439, 1252, 1196, 1188, 1097, 871, 749, 687$   $\text{cm}^{-1}$ ; **HRMS** ( $m/z$ ): (ESI-FTICR) calcd for  $(\text{C}_{23}\text{H}_{25}\text{F}_6\text{NO}_4\text{Si})\text{Na}$   $[\text{M}+\text{Na}]^+$ : 516.1580, found: 516.1575.

**Methyl (1*R*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-3-(triethylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (20a/20c)**

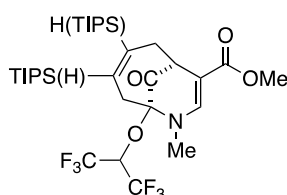


According to the general procedure, the respective cycloadduct (isomeric ratio of 41:59) yielded **20a/c** as a white solid (53 mg, 0.11 mmol, 35%, isomeric ratio of 41:59) after purification by flash chromatography (30% EtOAc:Hexanes,  $R_f = 0.70$ ). Recrystallization (70% EtOH:H<sub>2</sub>O) gave short, white needles.

**<sup>1</sup>H NMR** (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.20 (1H, s) minor isomer, 7.14 (1H, s) major isomer, 6.14 (1H, dt,  $J = 8.6, 3.4$  Hz) major isomer, 6.09 (1H, dt,  $J = 8.3, 2.8$  Hz) minor isomer, 4.91 (2H, hept,  $J = 6.5$  Hz) major and minor isomers, 3.76 (1H, dd,  $J = 5.6, 2.7$  Hz), 3.71 (1H, t,  $J = 4.2$  Hz), 3.69 (3H, s) minor isomer, 3.68 (3H, s) major isomer, 3.01 – 2.88 (4H, m) major and minor isomers, 2.80 (3H, s) minor isomer, 2.79 (3H, s) major isomer, 2.26 (1H, ddd,  $J = 15.7, 3.7, 1.8$  Hz), 2.23 – 2.16 (2H, m) major and minor isomers, 2.11 (1H, dq,  $J = 15.4, 2.7$  Hz), 0.91 (9H, t,  $J = 7.9$  Hz) minor isomer, 0.87 (9H, t,  $J = 7.9$  Hz) major isomer, 0.69 – 0.46 (12H, m) major and minor isomers; **<sup>13</sup>C NMR** (151 MHz,  $\text{CDCl}_3$ )  $\delta$  201.6, 201.1, 166.8, 166.6, 146.9, 146.2, 144.9, 140.4, 133.5, 131.5, 121.6

(q,  $J = 283.9$  Hz), 121.2 (q,  $J = 285.4$  Hz), 97.5, 96.6, 94.7, 94.5, 71.8 (hept,  $J = 33.2$  Hz), 51.3, 51.3, 47.2, 46.0, 38.4, 37.2, 35.0, 34.9, 33.4, 33.2, 7.5, 7.4, 3.2, 2.2; **IR** (neat)  $\nu_{\max} = 2966, 2875, 1733, 1674, 1642, 1364, 1247, 1242, 1187, 1102, 1062, 1016, 872, 690$  cm<sup>-1</sup>; **HRMS** (m/z): (ESI-FTICR) calcd for (C<sub>21</sub>H<sub>29</sub>F<sub>6</sub>NO<sub>4</sub>Si)H [M+H]<sup>+</sup>: 502.1843, found: 502.1847.

**Methyl (1*R*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-3-(triisopropylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (22a/22c)**

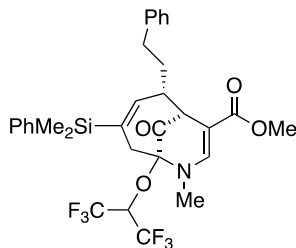


According to the general procedure, the respective cycloadduct (isomeric ratio of 46:54) yielded **22a/c** as a white solid (80 mg, 0.15 mmol, 59%, isomeric ratio of 17:83) after purification by flash chromatography (30% EtOAc:Hexanes,  $R_f = 0.55$ ). Recrystallization (70% EtOH:H<sub>2</sub>O) gave short, white needles.

**<sup>1</sup>H NMR** (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.23 (1H, s) major isomer, 7.18 (1H, s) minor isomer, 6.15 (1H, dt, = 8.8, 3.3 Hz) minor isomer, 6.09 (1H, dt,  $J = 8.1, 2.8$  Hz) major isomer, 4.99 (1H, hept,  $J = 6.0$  Hz) major isomer, 4.88 (1H, hept, = 6.1 Hz) minor isomer, 3.76 (1H, dd, = 5.2, 3.1 Hz), 3.71 (1H, t,  $J = 4.3$  Hz), 3.69 (3H, s) major isomer, 3.66 (3H, s) minor isomer, 3.03 – 2.97 (3H, m) major and minor isomers, 2.92 (1H, ddd, = 16.1, 8.3, 4.6 Hz), 2.87 (3H, s) major isomer, 2.81 (3H, s) minor isomer, 2.32 – 2.28 (1H, m), 2.28 – 2.21 (2H, m), 2.16 (1H, dq,  $J = 15.5, 3.0$  Hz) 1.20 – 1.11 (6H, m) major and minor isomers, 1.06 (18H, dd,  $J = 9.5, 7.2$  Hz) major isomer, 1.00 (18H, dd, = 23.6, 7.4 Hz) minor isomer; **<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>)  $\delta$  201.7, 201.1, 166.8, 166.6, 146.9, 146.1, 142.8, 140.7, 132.6, 132.5, 121.5 (q,  $J = 288.4$  Hz), 121.2 (q,  $J = 283.9$  Hz), 97.6, 96.5, 94.5, 94.4, 71.6 (hept,  $J = 33.2$  Hz), 51.3, 46.9, 45.7, 39.4, 37.3, 35.4, 34.9, 34.3, 33.7, 19.1,

19.0, 18.8, 18.5, 11.6, 10.8; **IR** (neat)  $\nu_{\max}$  = 2955, 2866, 1734, 1675, 1641, 1362, 1340, 1284, 1242, 1188, 1101, 877, 659, 656  $\text{cm}^{-1}$ ; **HRMS** ( $m/z$ ): (ESI-FTICR) calcd for  $(\text{C}_{24}\text{H}_{35}\text{F}_6\text{NO}_4\text{Si})\text{Na}$   $[\text{M}+\text{Na}]^+$ : 566.2132, found: 566.2128.

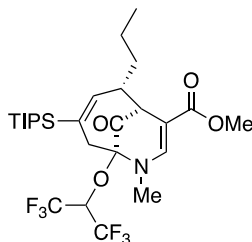
**Methyl (1*R*,2*R*,6*R*)-4-(dimethyl(phenyl)silyl)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-2-phenethyl-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (24a)**



According to the general procedure, the respective cycloadduct (isomeric ratio of 87:13) yielded **24a** as a pale-yellow oil (63 mg, 0.10 mmol, 31%) after purification by flash chromatography (30% EtOAc:Hexanes,  $R_f$  = 0.63).

**$^1\text{H}$  NMR** (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.49 – 7.48 (2H, m), 7.40 – 7.34 (3H, m), 7.28 (2H, t,  $J$  = 7.4 Hz), 7.21 – 7.13 (3H, m), 7.13 (1H, s), 6.29 (1H, dd,  $J$  = 7.6, 3.0 Hz), 4.83 (1H, hept,  $J$  = 5.9 Hz), 3.67 (3H, s), 3.66 (1H, d,  $J$  = 3.7 Hz), 2.91 (1H, qd,  $J$  = 7.5, 3.8 Hz), 2.84 (1H, d,  $J$  = 16.6 Hz), 2.78 (1H, ddd,  $J$  = 14.1, 10.3, 6.4 Hz), 2.63 (1H, ddd,  $J$  = 13.9, 10.1, 5.8 Hz), 2.36 (3H, s), 2.25 (1H, dd,  $J$  = 16.5, 3.0 Hz), 1.72 (1H, dddd,  $J$  = 13.5, 10.1, 7.0, 6.2 Hz), 1.52 (1H, dddd,  $J$  = 13.6, 10.0, 7.7, 5.8 Hz), 0.40 (6H, d,  $J$  = 9.9 Hz);  **$^{13}\text{C}$  NMR** (151 MHz,  $\text{CDCl}_3$ )  $\delta$  199.8, 166.9, 146.5, 145.4, 141.6, 137.2, 134.2, 132.6, 129.8, 128.6, 128.6, 128.3, 126.2, 121.5 (q,  $J$  = 286.9 Hz), 121.2 (q,  $J$  = 288.4 Hz), 96.9, 93.6, 71.5 (hept,  $J$  = 33.2 Hz), 51.3, 49.3, 43.4, 36.7, 34.7, 34.3, 34.1, -2.8, -3.0; **IR** (neat)  $\nu_{\max}$  = 3023, 2951, 1704, 1643, 1631, 1428, 1296, 1241, 1199, 1188, 1098, 1061, 765, 735, 687  $\text{cm}^{-1}$ ; **HRMS** ( $m/z$ ): (ESI-FTICR) calcd for  $(\text{C}_{31}\text{H}_{33}\text{F}_6\text{NO}_4\text{Si})\text{Na}$   $[\text{M}+\text{Na}]^+$ : 648.1975, found: 648.1982.

**Methyl (1*R*,2*R*,6*R*)-6-((1,1,1,3,3,3-hexafluoropropan-2-yl)oxy)-7-methyl-10-oxo-2-propyl-4-(triisopropylsilyl)-7-azabicyclo[4.3.1]deca-3,8-diene-9-carboxylate (26a)**



According to the general procedure, the respective cycloadduct (isomeric ratio of 92:6:2) yielded **26a** as a white solid (90 mg, 0.15 mmol, 64%) after purification by flash chromatography (20% EtOAc:Hexanes,  $R_f = 0.64$ ). Recrystallization (70% EtOH:H<sub>2</sub>O) gave short, white needles, mp = 126 - 127°C.

**<sup>1</sup>H NMR** (600 MHz, CDCl<sub>3</sub>)  $\delta$  7.25 (1H, s), 6.14 (1H, dd,  $J = 7.4, 2.7$  Hz), 4.94 (1H, hept,  $J = 6.0$  Hz), 3.69 (3H, s), 3.39 (1H, d,  $J = 4.1$  Hz), 2.90 (1H, d,  $J = 16.5$  Hz), 2.87 (3H, s), 2.83 (1H, qd,  $J = 7.4, 4.1$  Hz), 2.29 (1H, dd,  $J = 16.5, 2.8$  Hz), 1.52 (1H, dddd,  $J = 13.0, 10.5, 7.5, 5.5$  Hz), 1.47 – 1.33 (2H, m), 1.29 – 1.22 (1H, m), 1.16 (3H, hept,  $J = 7.8$  Hz), 1.07 (18H, dd,  $J = 10.1, 7.3$  Hz), 0.93 (3H, t,  $J = 7.2$  Hz); **<sup>13</sup>C NMR** (151 MHz, CDCl<sub>3</sub>)  $\delta$  199.9, 166.8, 146.0, 129.9, 121.5 (q,  $J = 285.7$  Hz), 121.2 (q,  $J = 283.9$  Hz), 97.5, 93.6, 71.5 (hept,  $J = 33.4$  Hz), 51.2, 49.0, 44.2, 38.1, 35.2, 35.0, 20.9, 19.0, 18.9, 13.8, 11.6; **IR** (CHCl<sub>3</sub>)  $\nu_{\max} = 2948, 2868, 1701, 1648, 1641, 1440, 1340, 1264, 1198, 1192, 1101, 1062, 1001, 880, 734$  cm<sup>-1</sup>; **HRMS** ( $m/z$ ): (ESI-FTICR) calcd for (C<sub>27</sub>H<sub>41</sub>F<sub>6</sub>NO<sub>4</sub>Si)Na [M+Na]<sup>+</sup>: 608.2601, found: 608.2590.

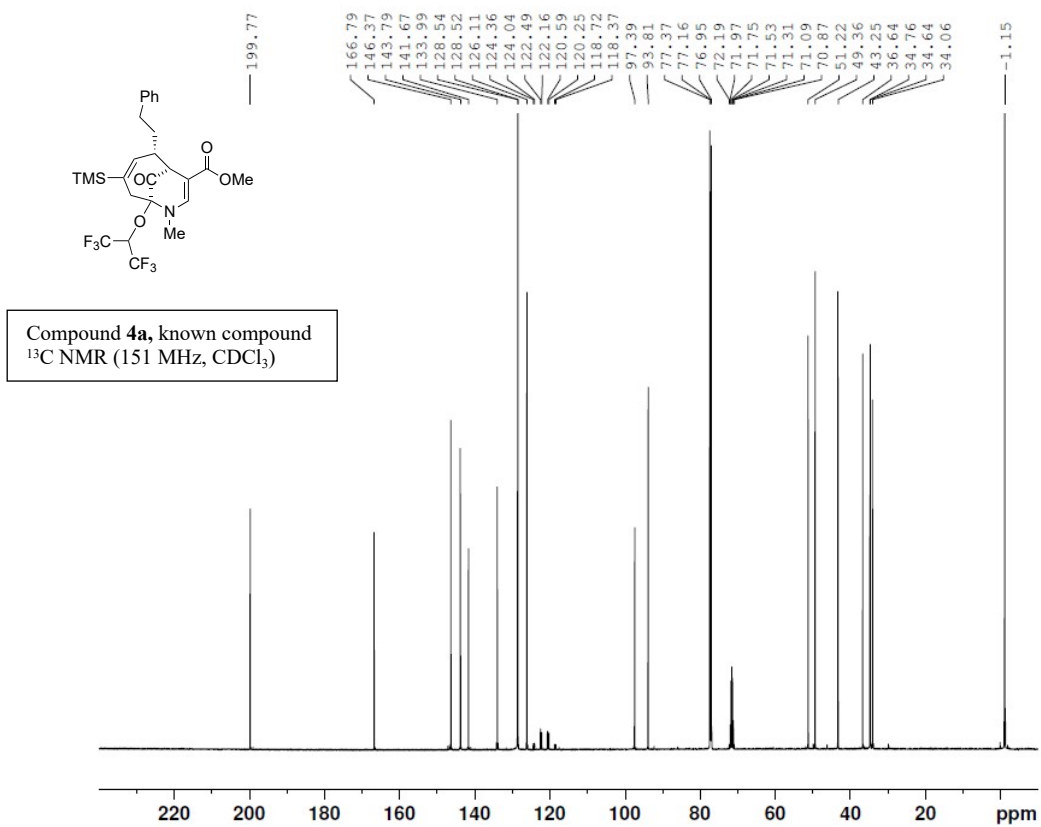
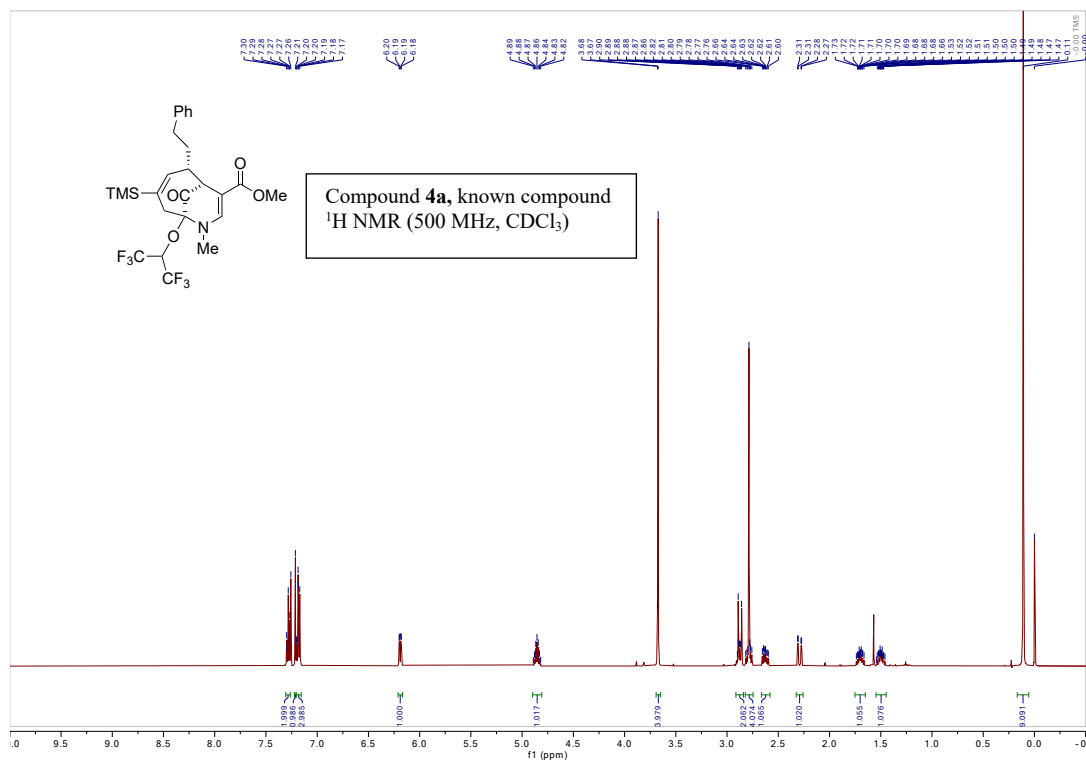
### 3. Table of trapping studies

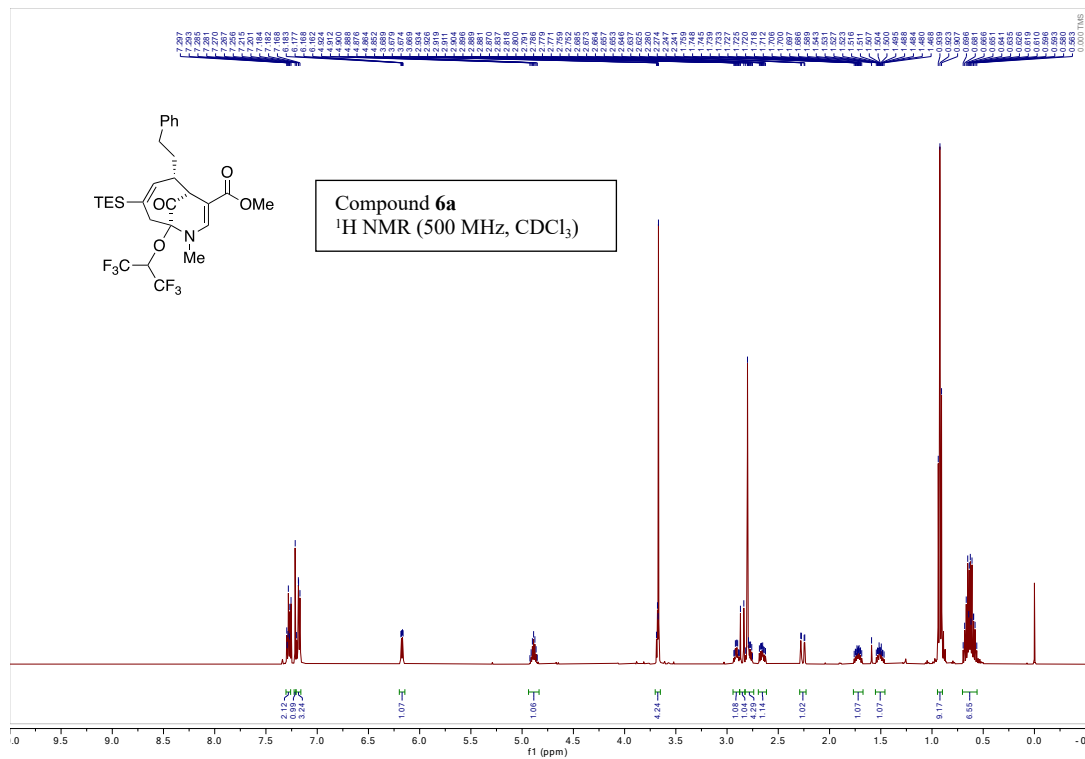


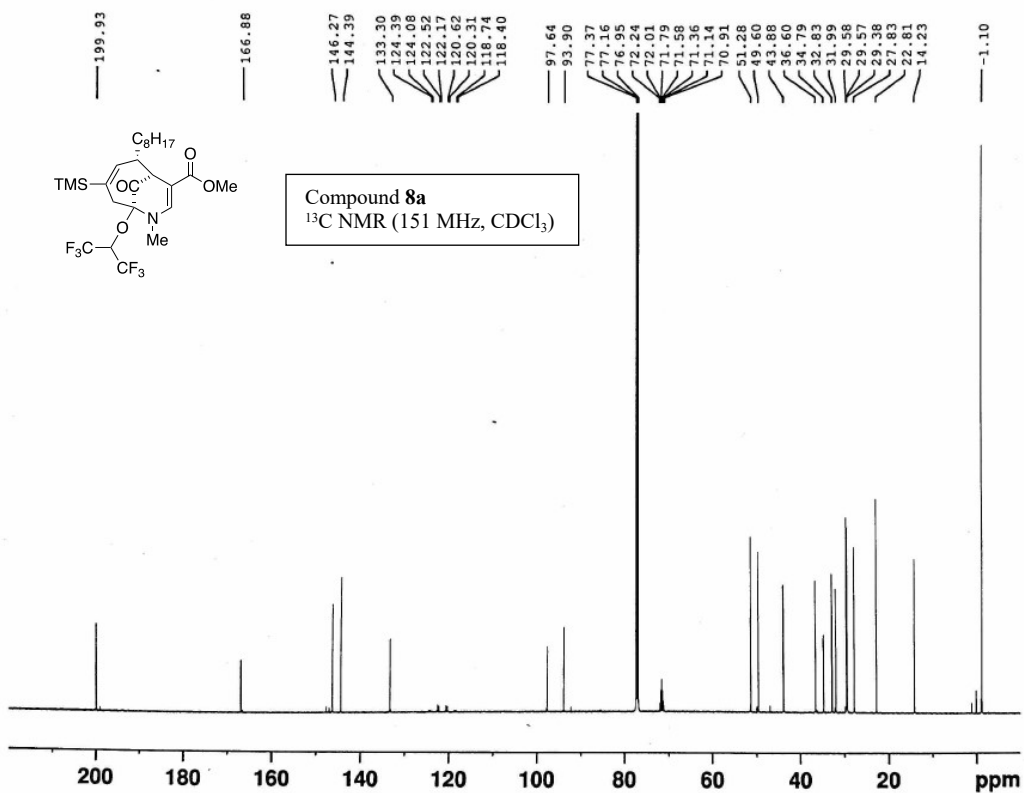
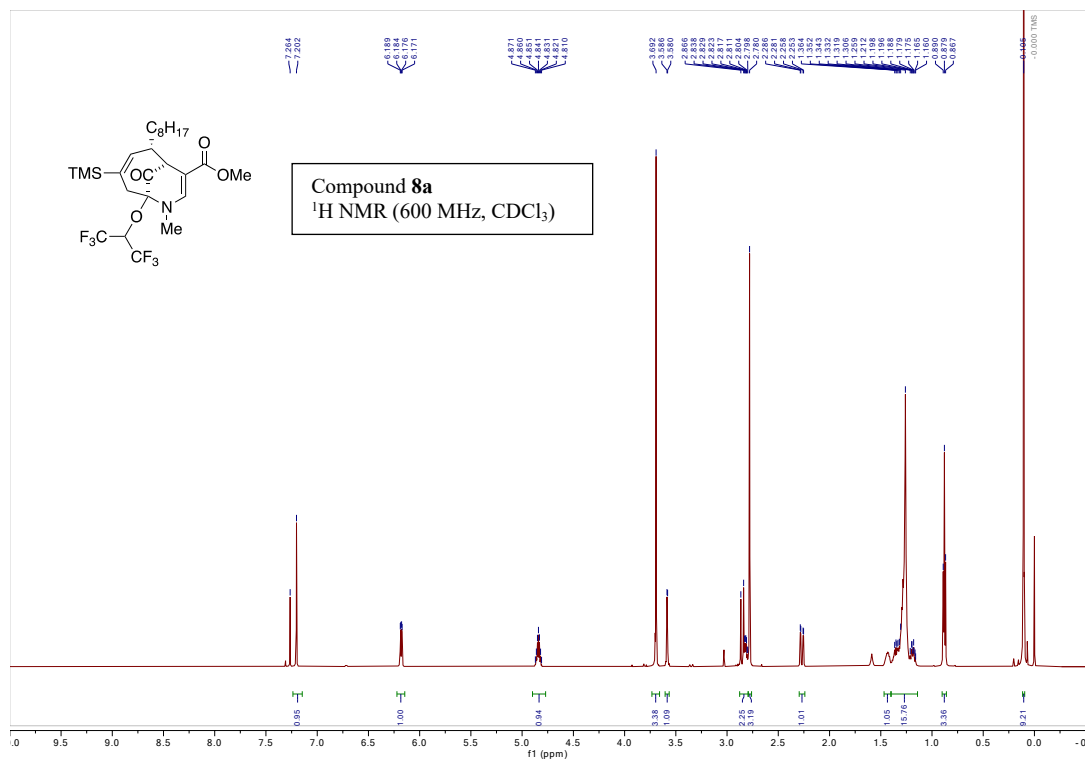
Substrate	NIS (eq.)	Reagents (eq.)	Solvent (M)	Time (h)	Temp. (°C)	Product
	1.5	LiI (5.0)	HFIP (0.09)	5	0 to rt	SM recovered 60% HFIP substituted (5%)
	1.5	LiI (5.0)	HFIP (400 eq.), CH <sub>3</sub> CN (0.09)	7	0 to rt	SM recovered 60%
	1.5	NaI (5.0)	HFIP (0.09)	5	0 to rt	SM recovered 64% HFIP substituted 11%
	1.5	TFA (0.6)	TFE (0.08)	6	0 to rt	Decomposed
	-	NBS (1.5)	TFE (0.09)	8	0 to 80	Decomposed
	1.5	NaBr (5.0)	HFIP (0.09)	1	0 to rt	HFIP substituted 46%
	1.5	NaBr (5.0)	HFIP (2.0 eq.), CH <sub>3</sub> CN (0.09)	21	0 to 85	SM recovered 29%
	1.5	NaBr (5.0)	HFIP (30.0 eq.), CH <sub>3</sub> CN (0.09)	4	0 to rt	SM recovered 50%

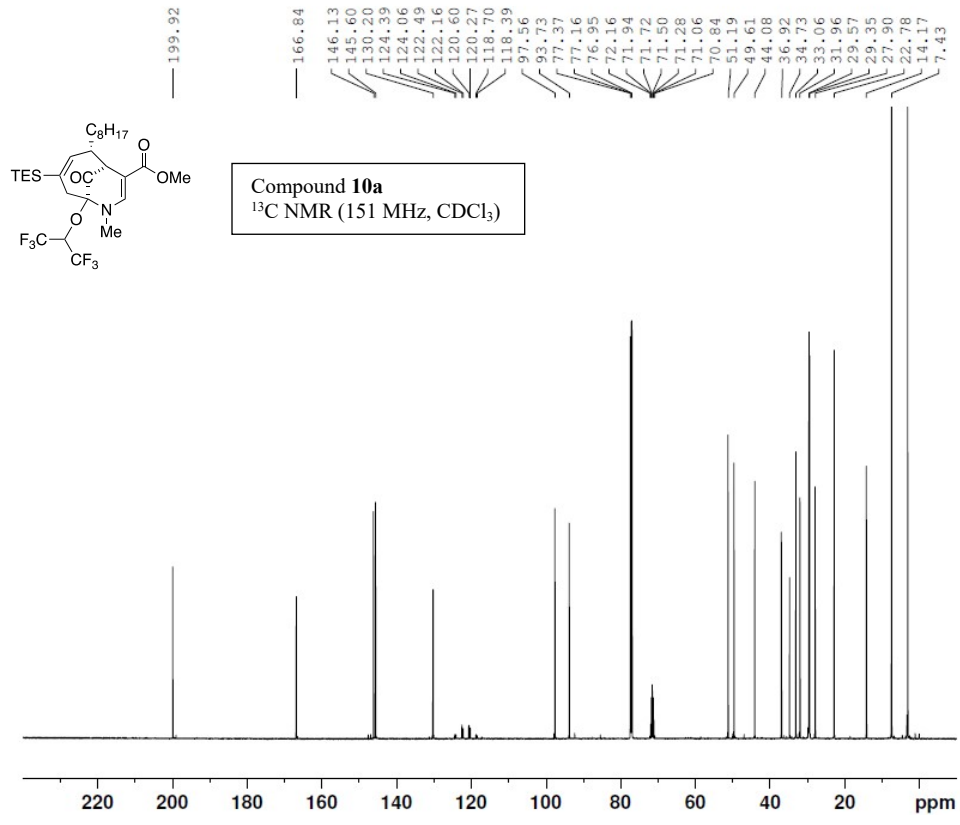
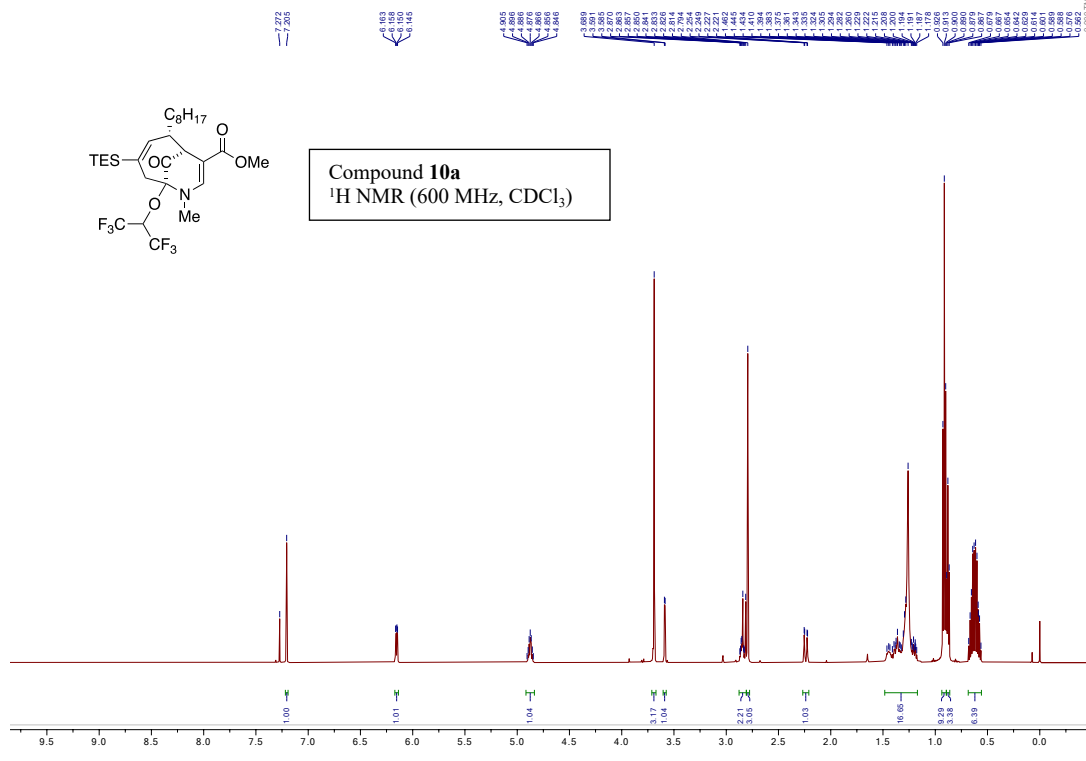


#### 4. Spectral data $^1\text{H}$ NMR, $^{13}\text{C}$ NMR of compound 4a-26a

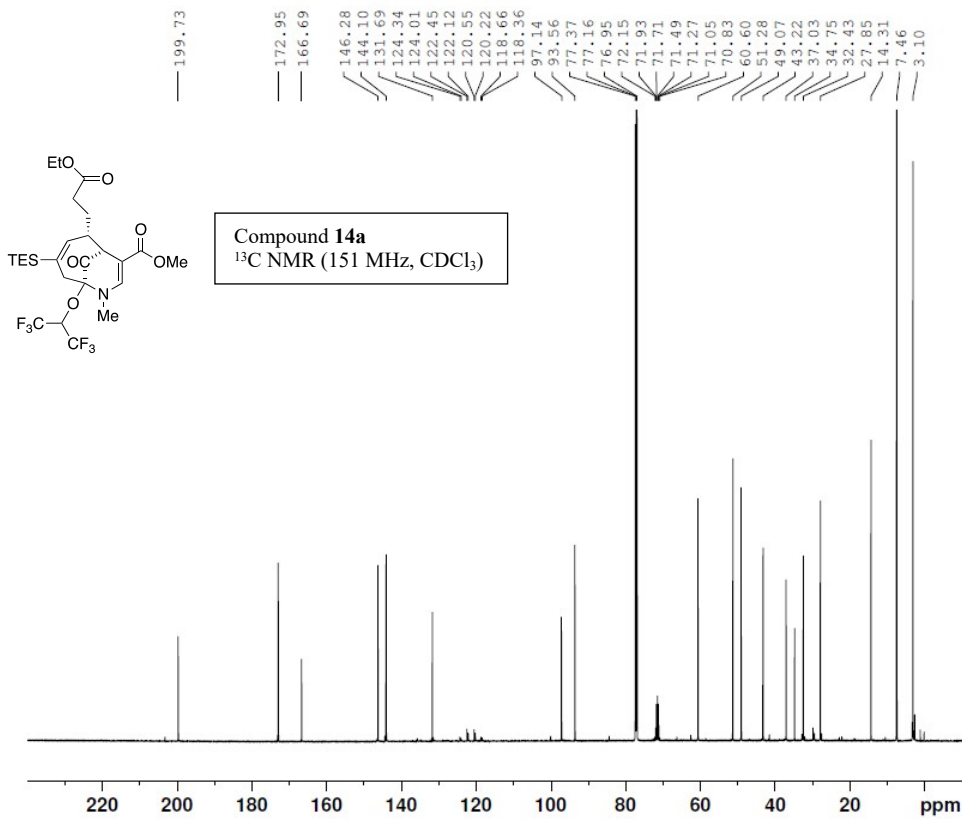
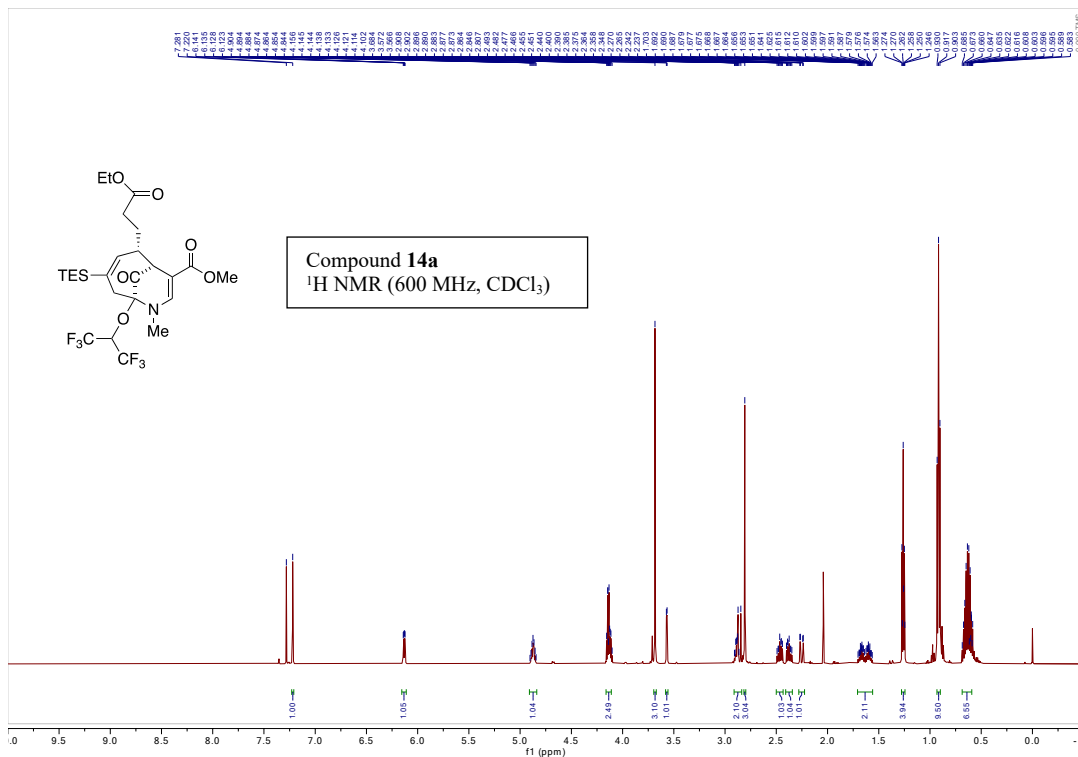


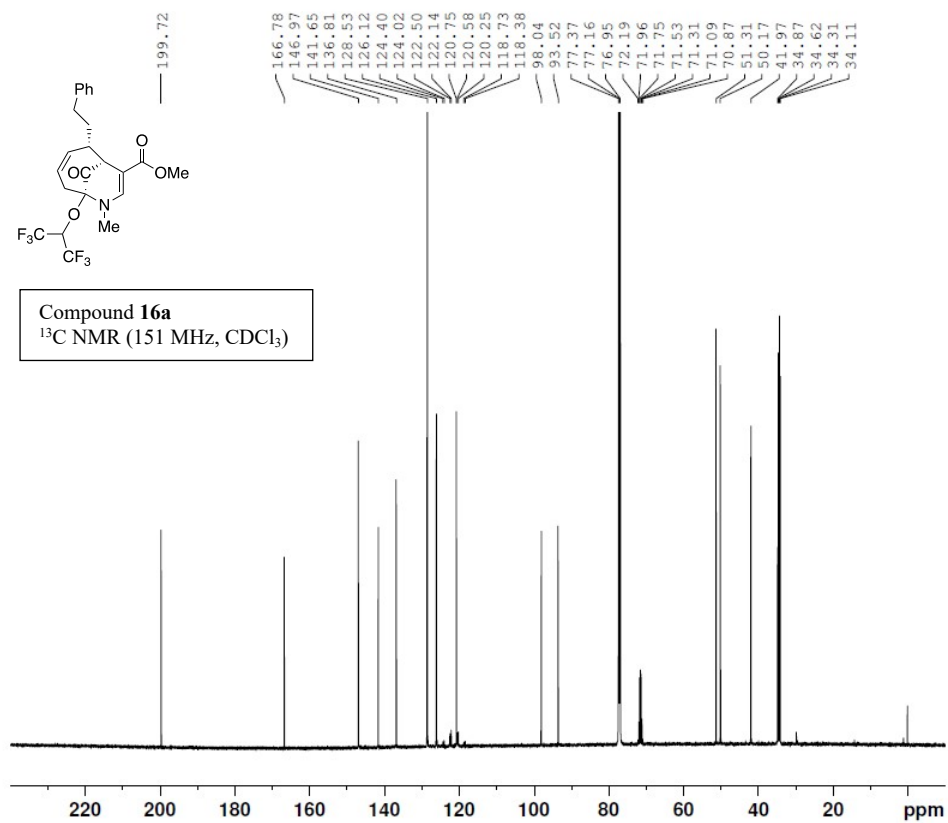
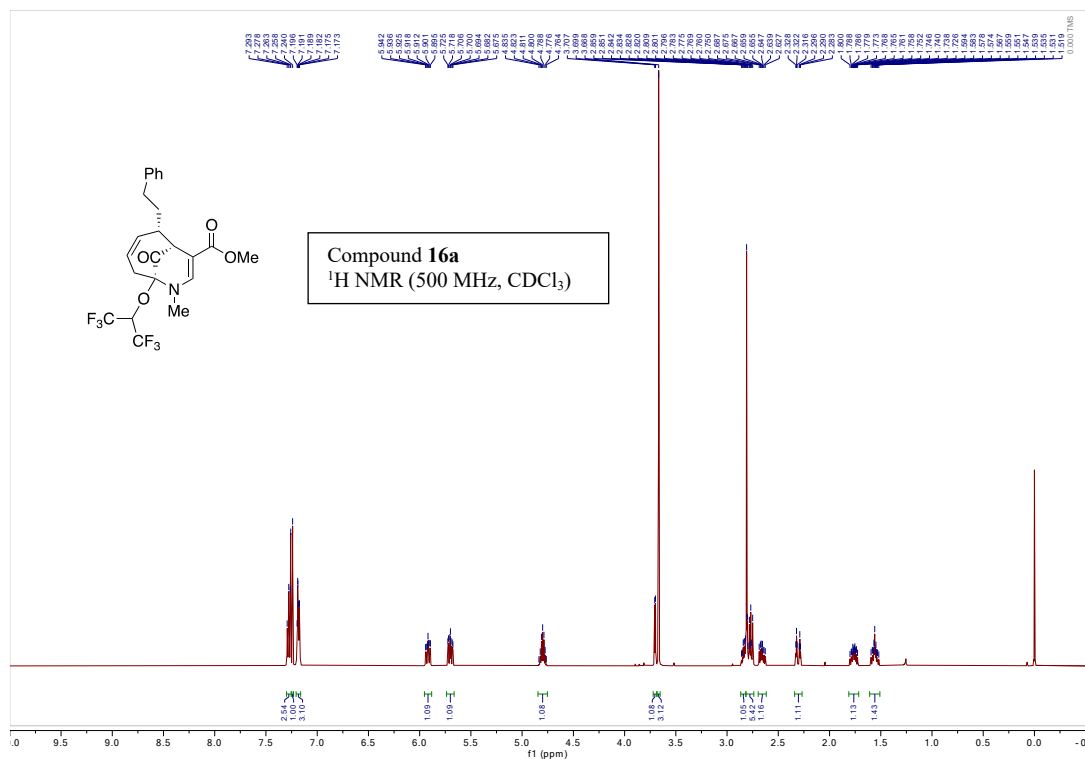






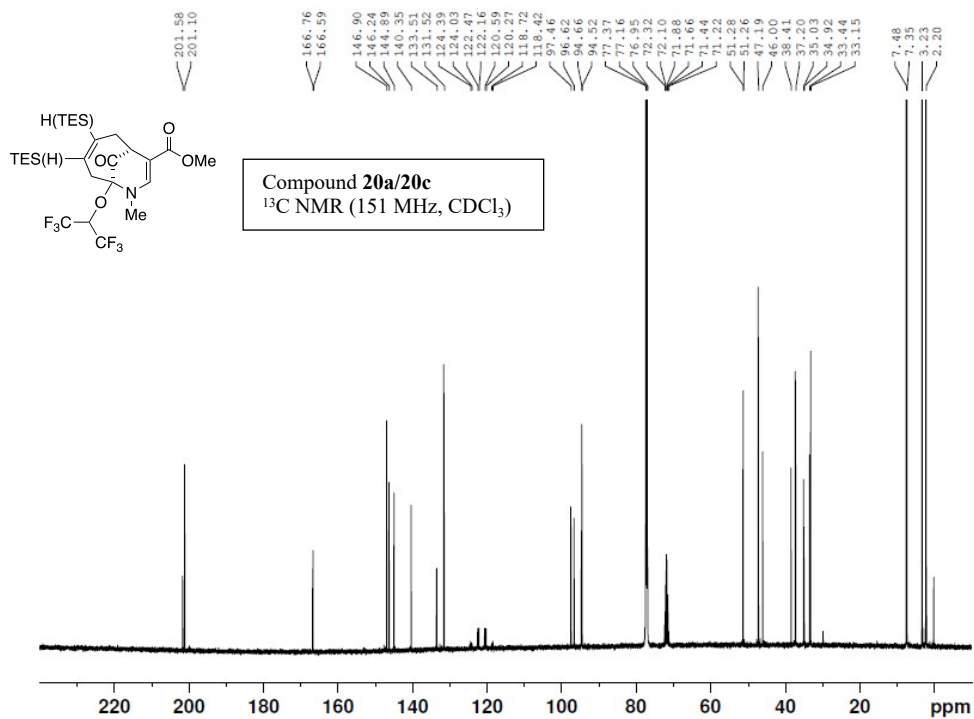
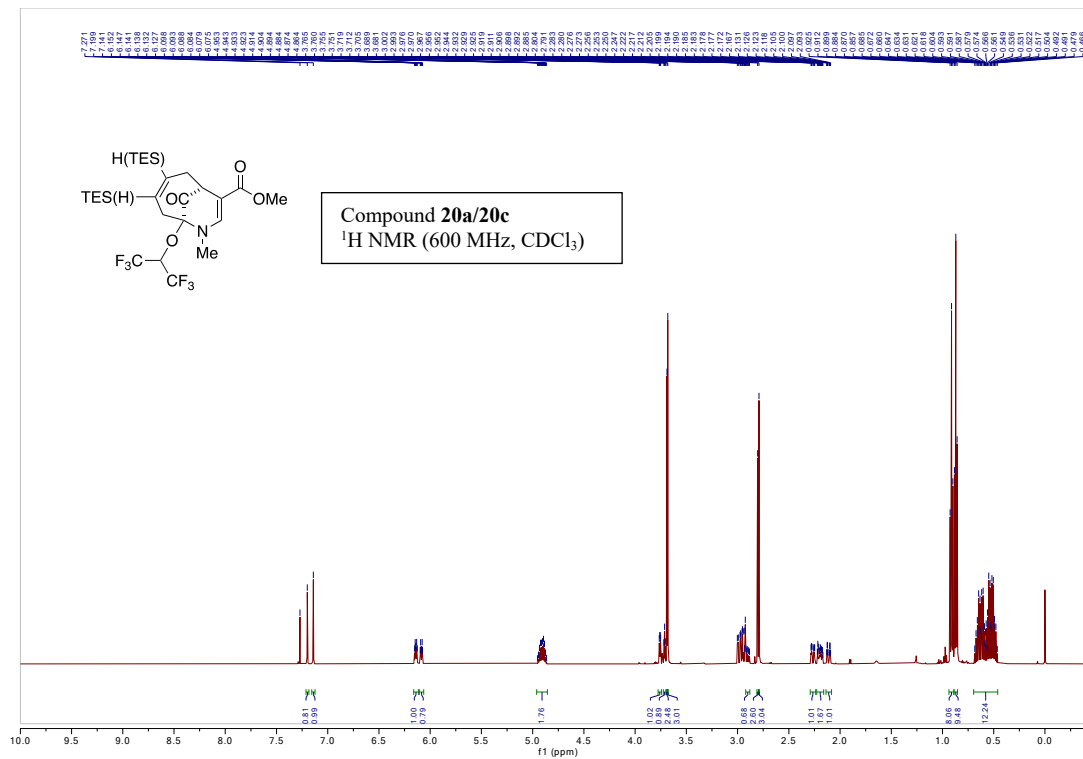




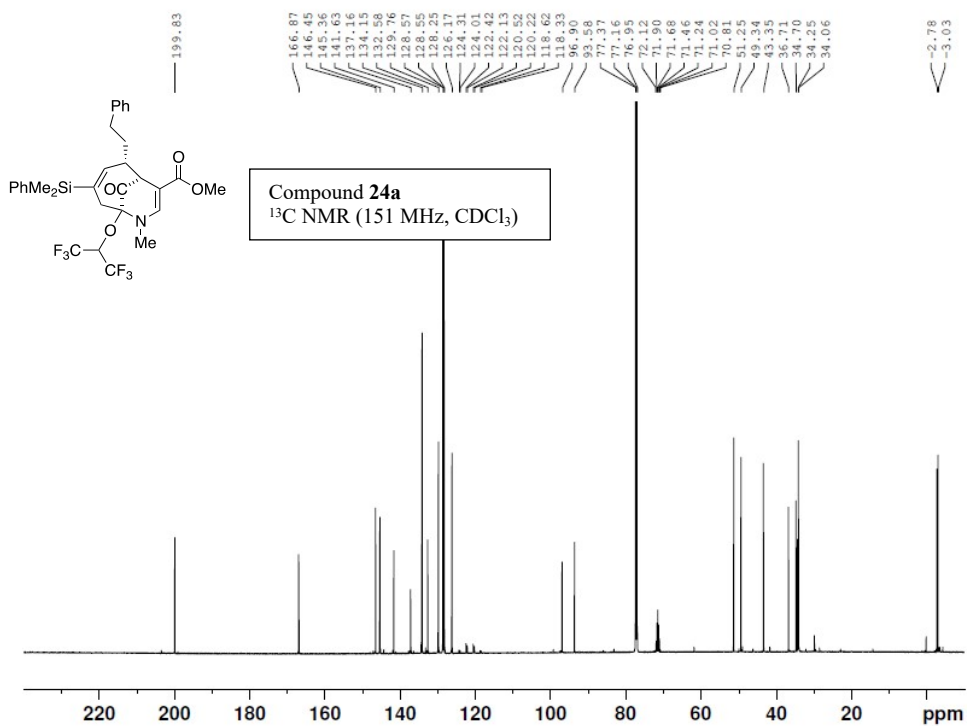
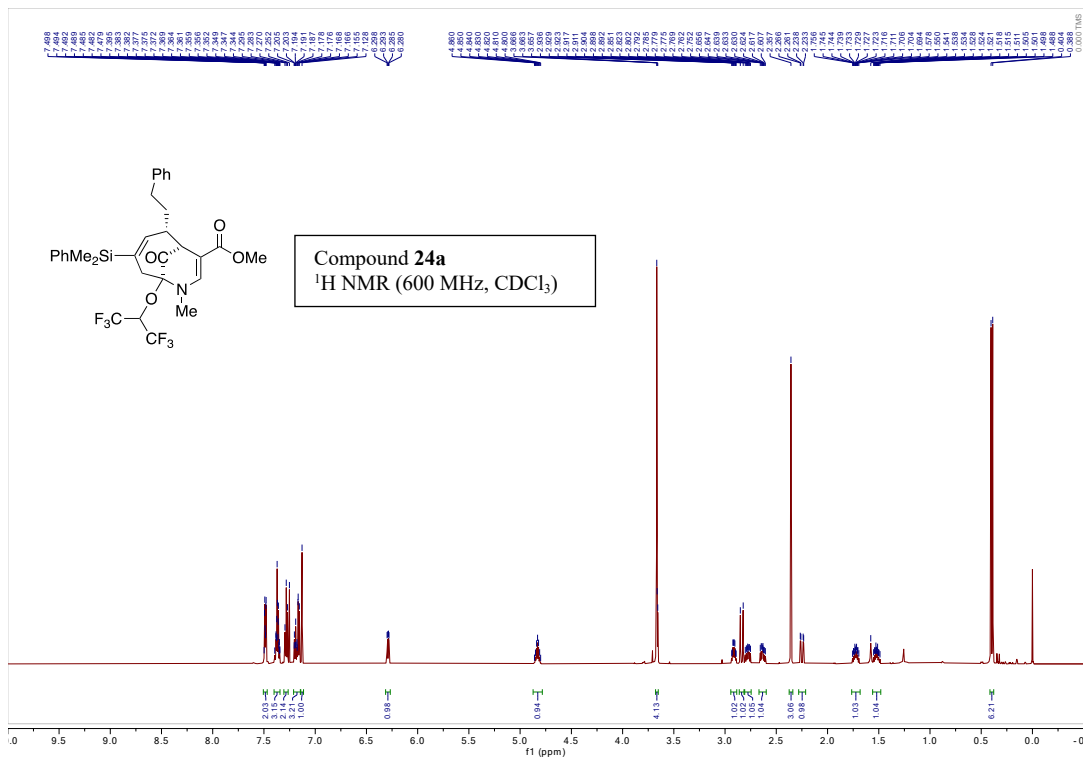






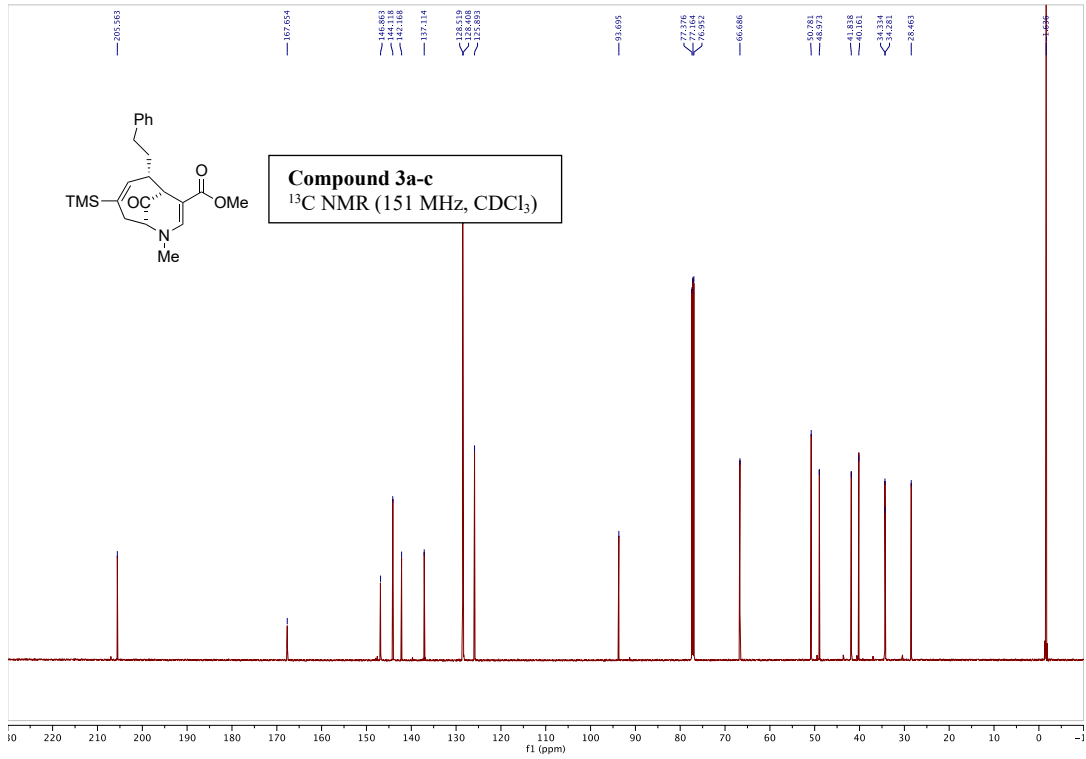
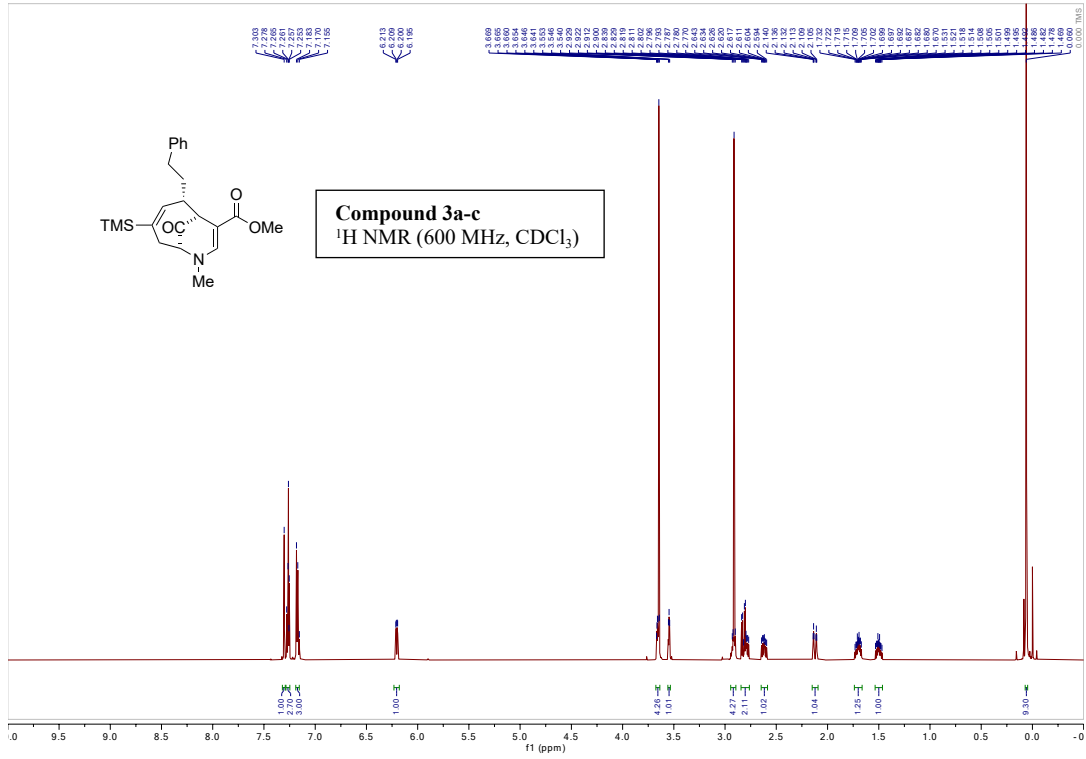




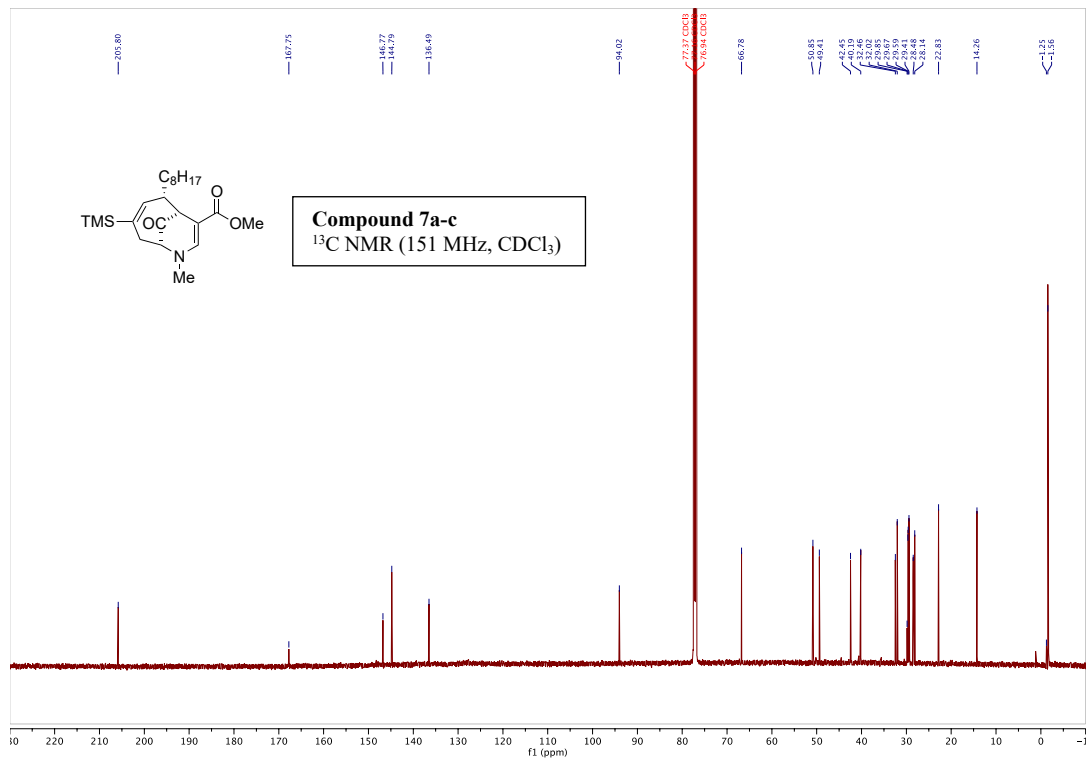
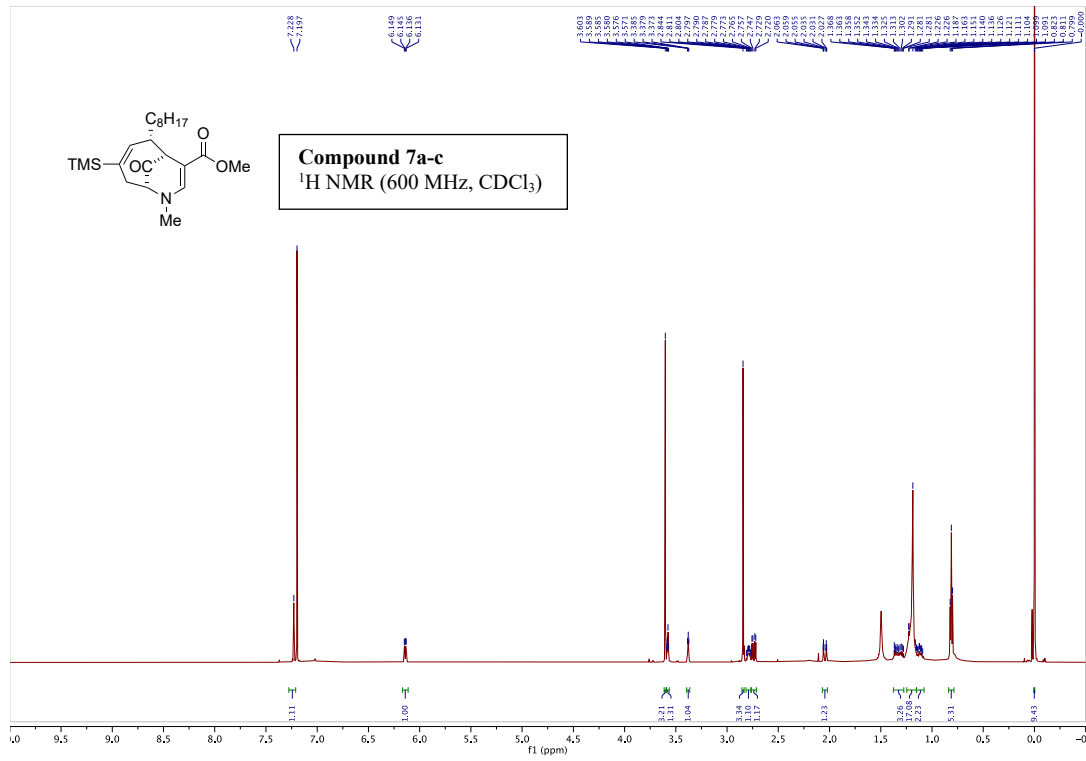


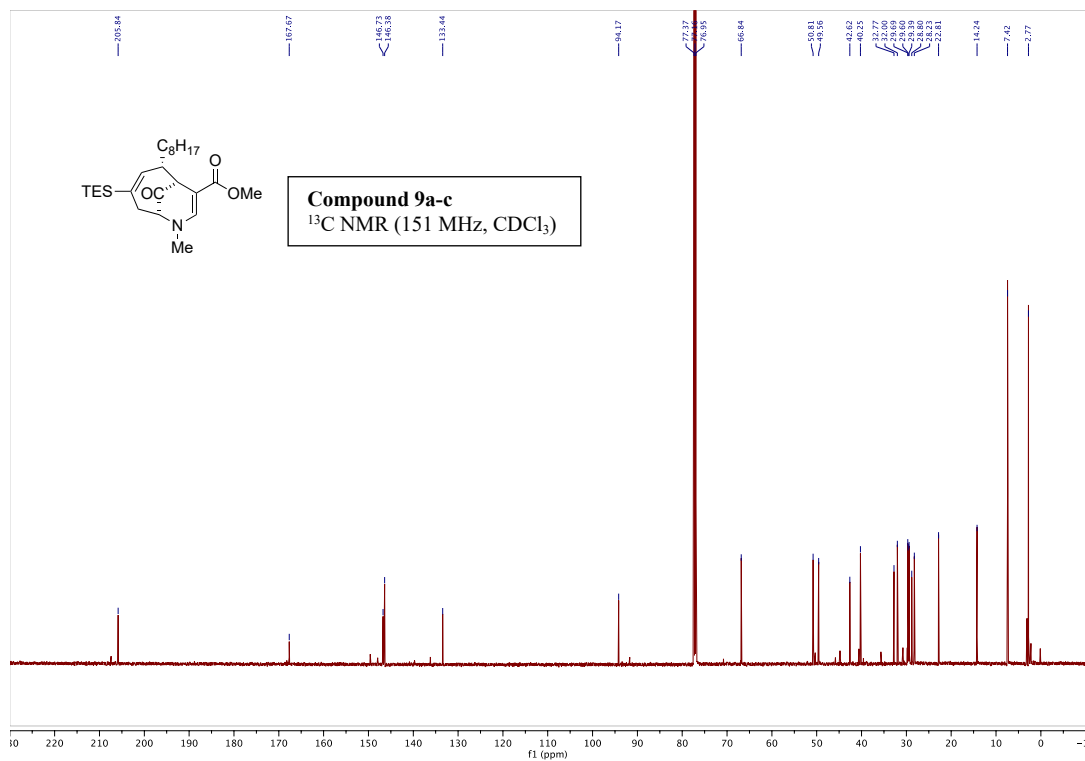
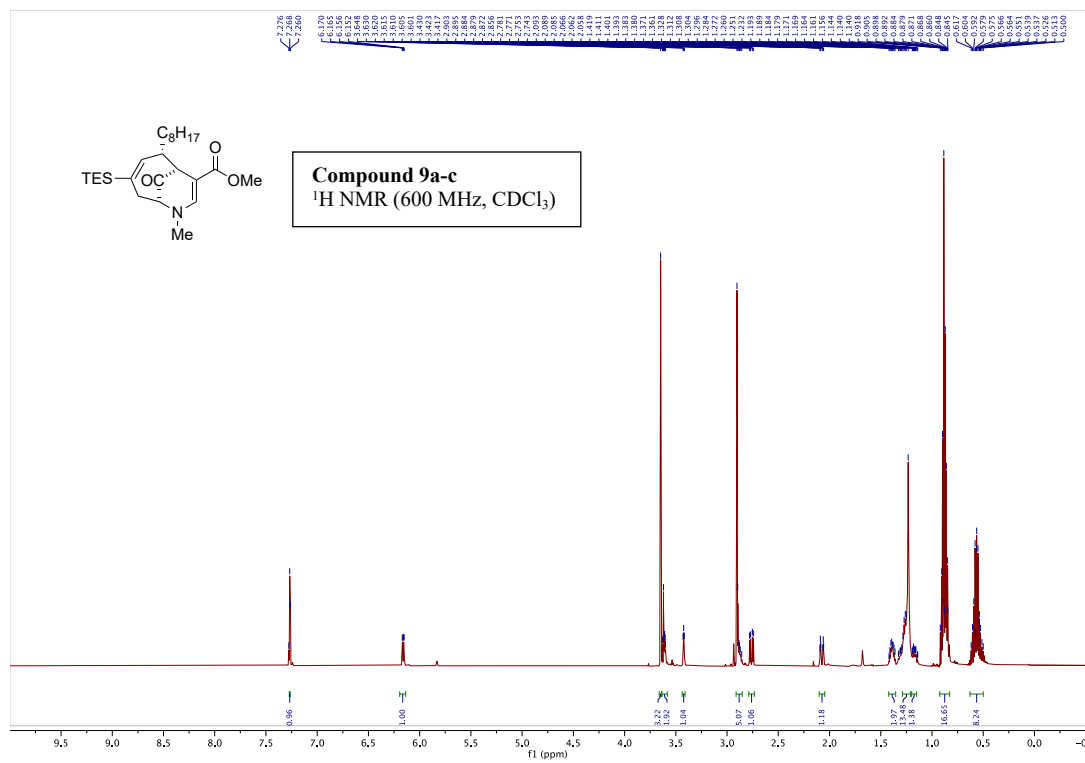


# 5. <sup>1</sup>H NMR, <sup>13</sup>C NMR of the known compounds

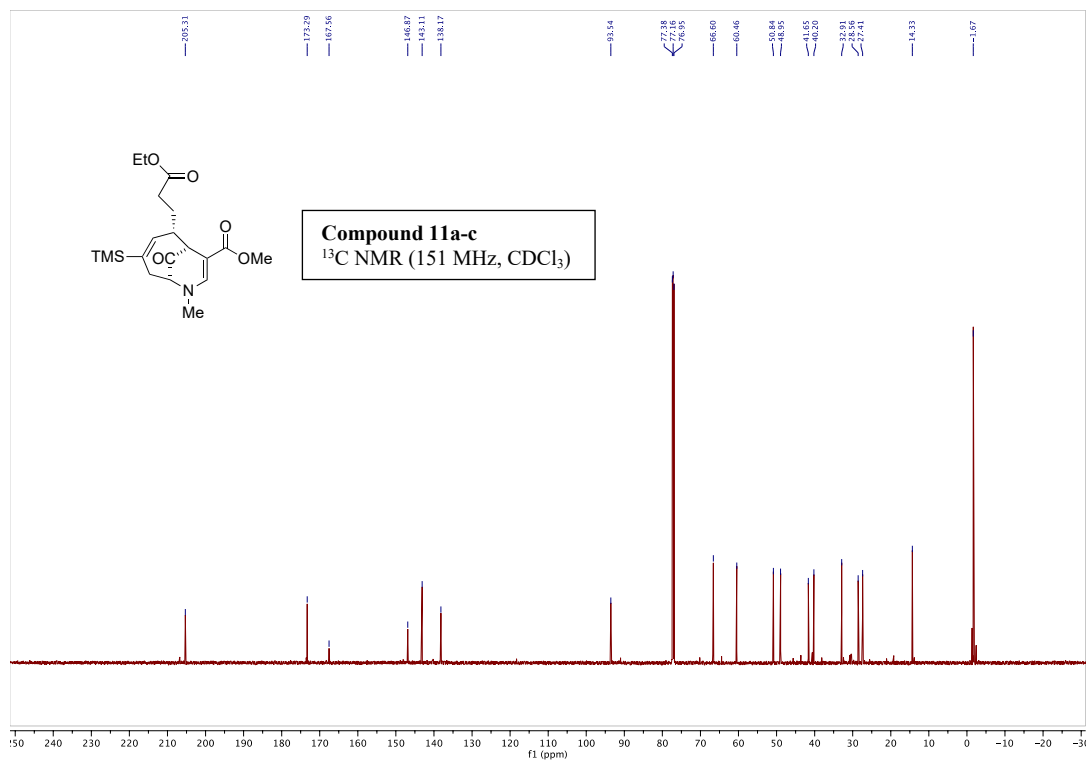
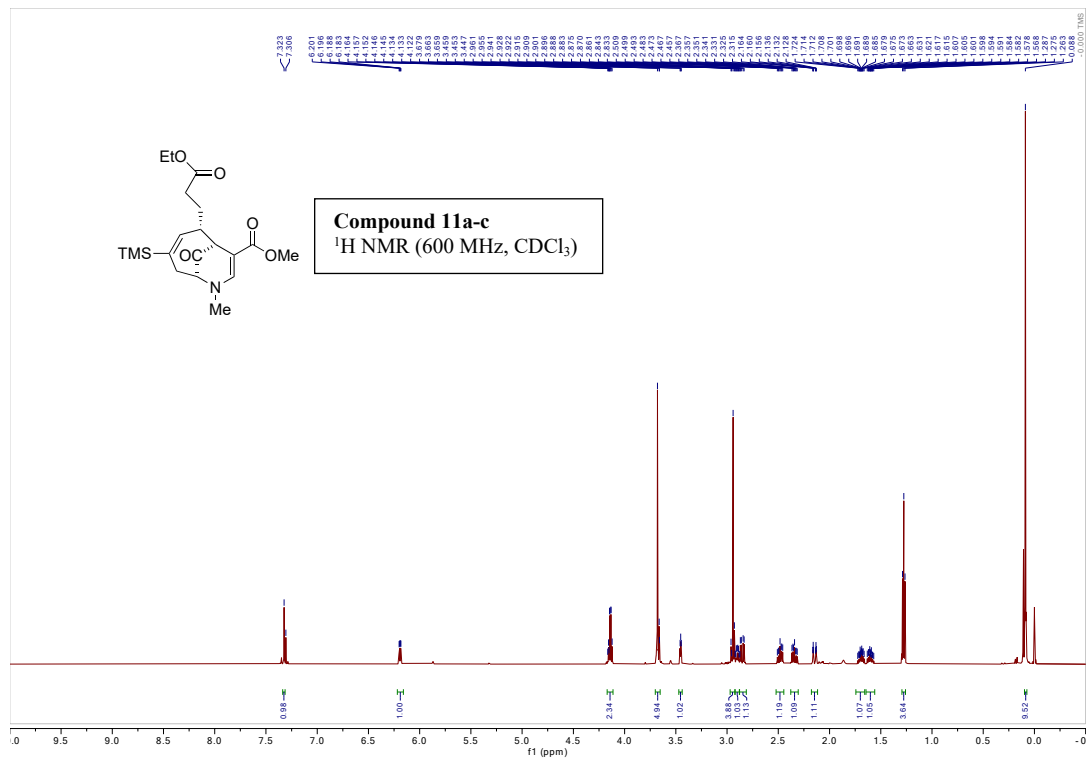


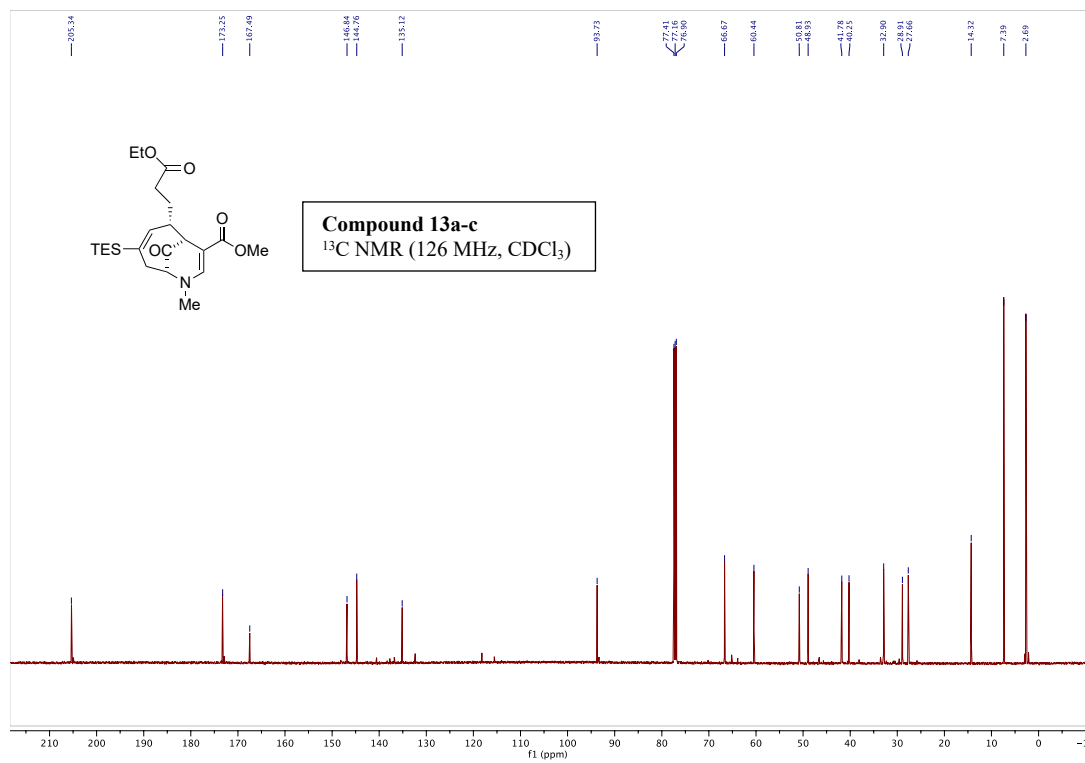
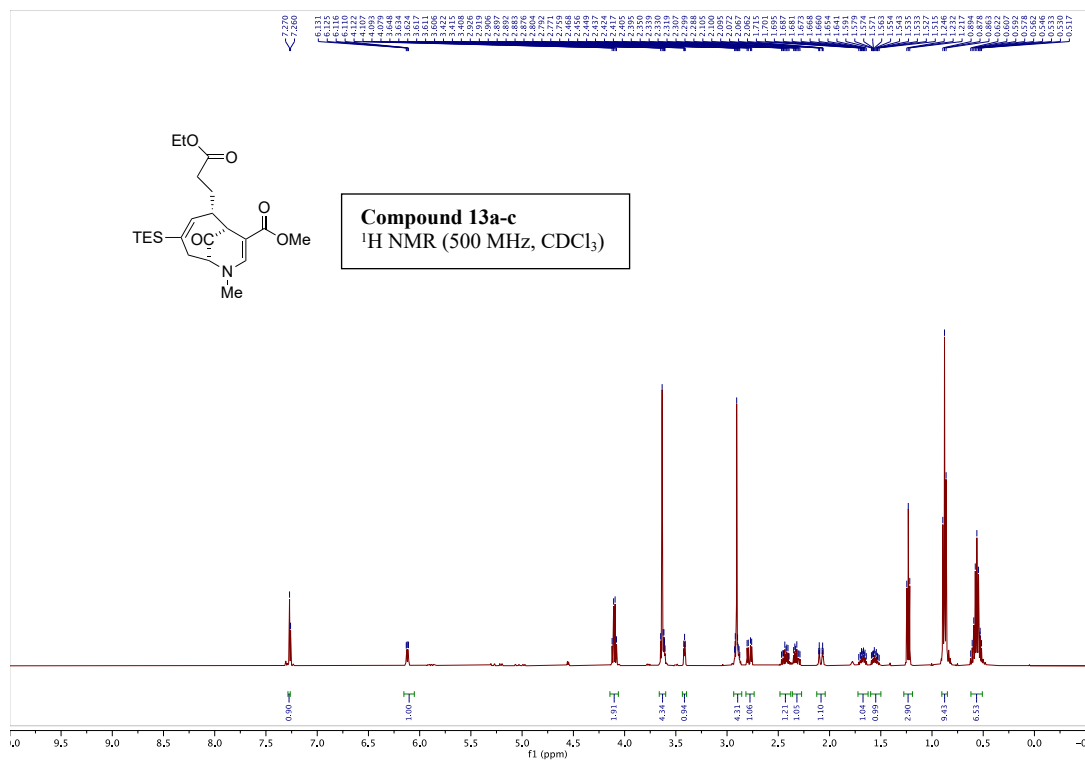




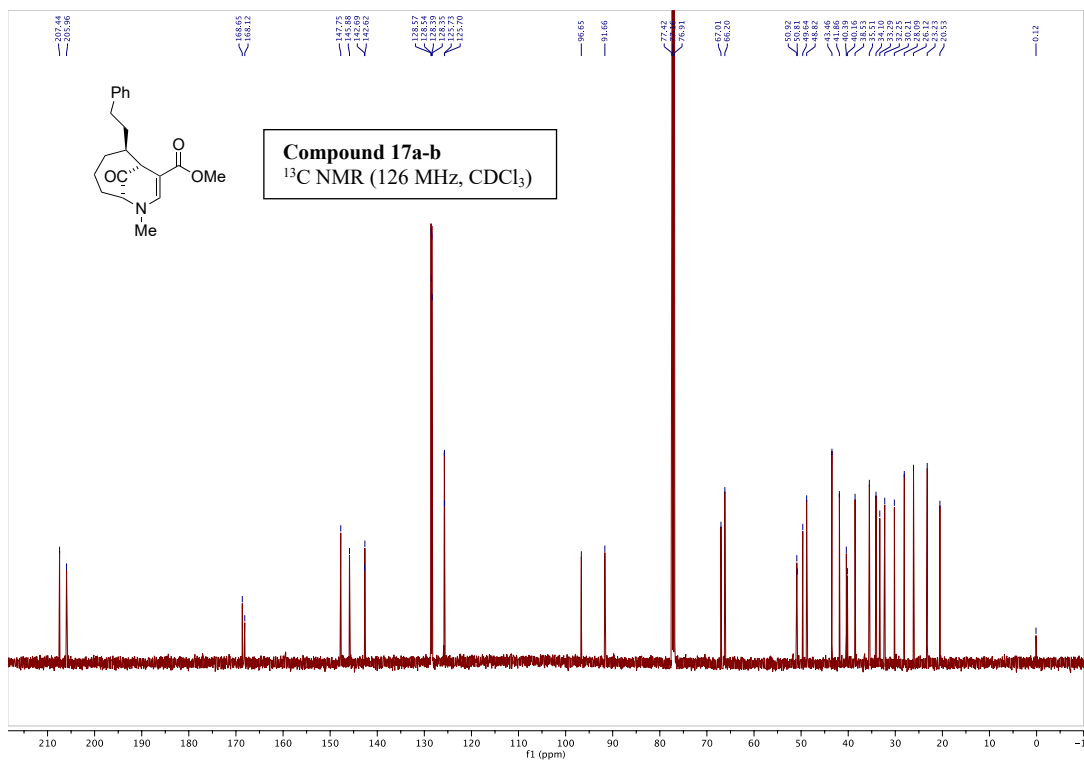
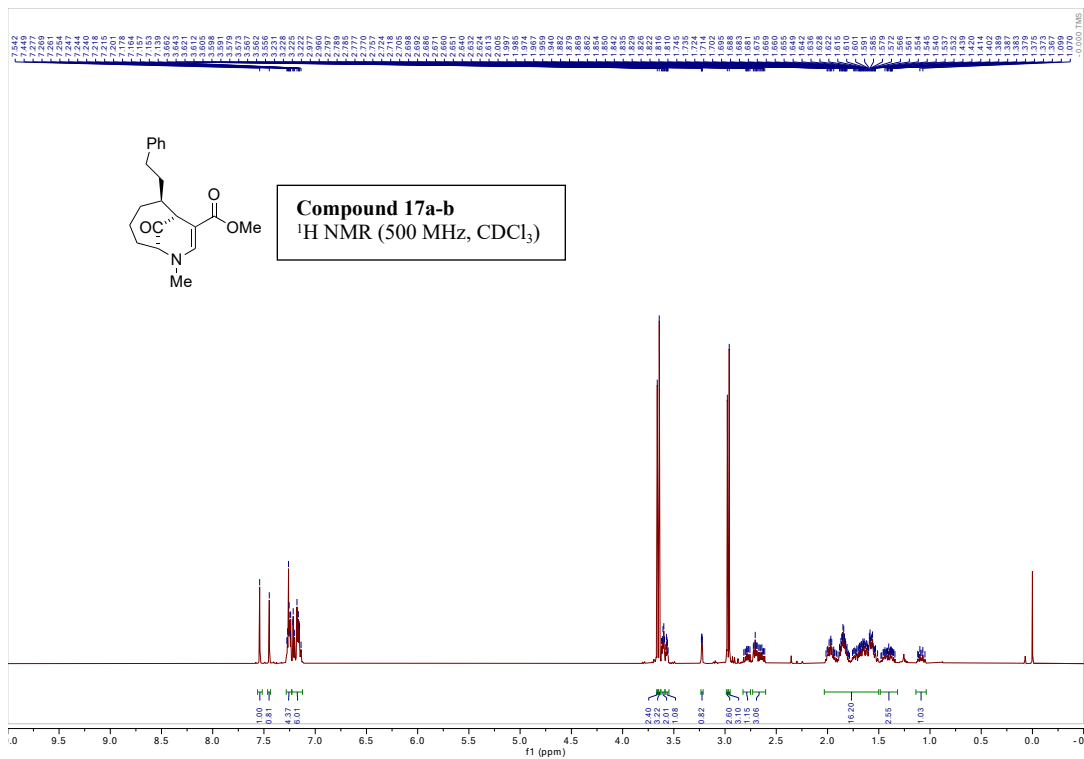


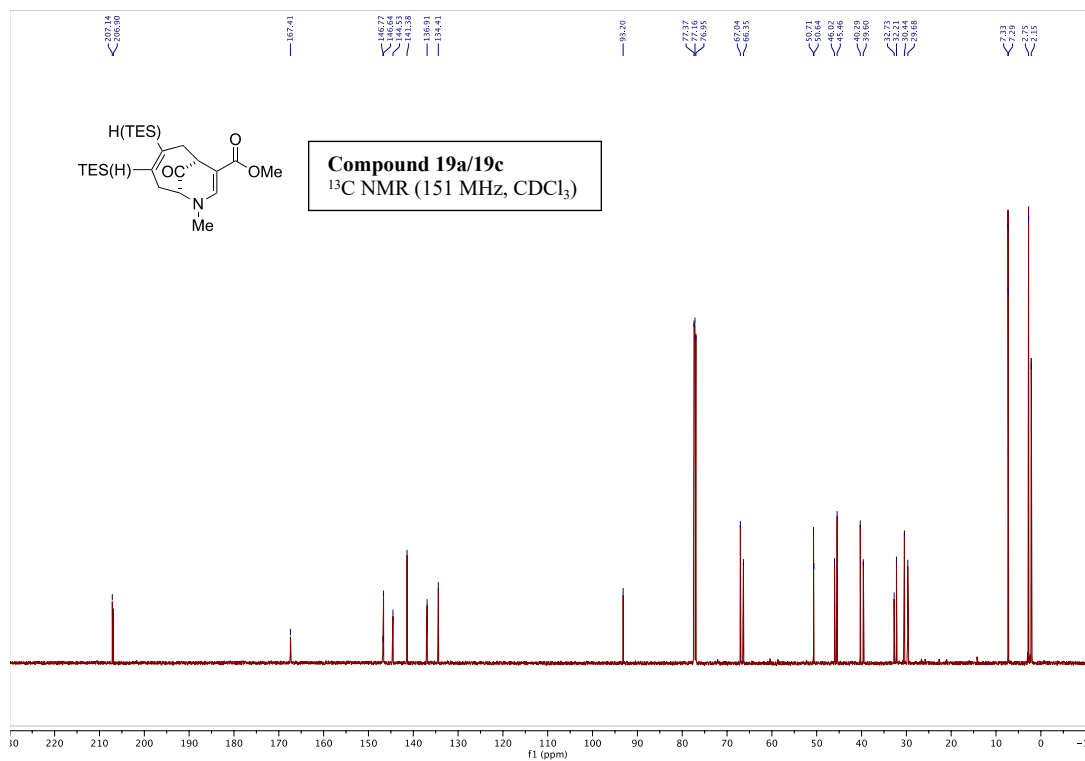
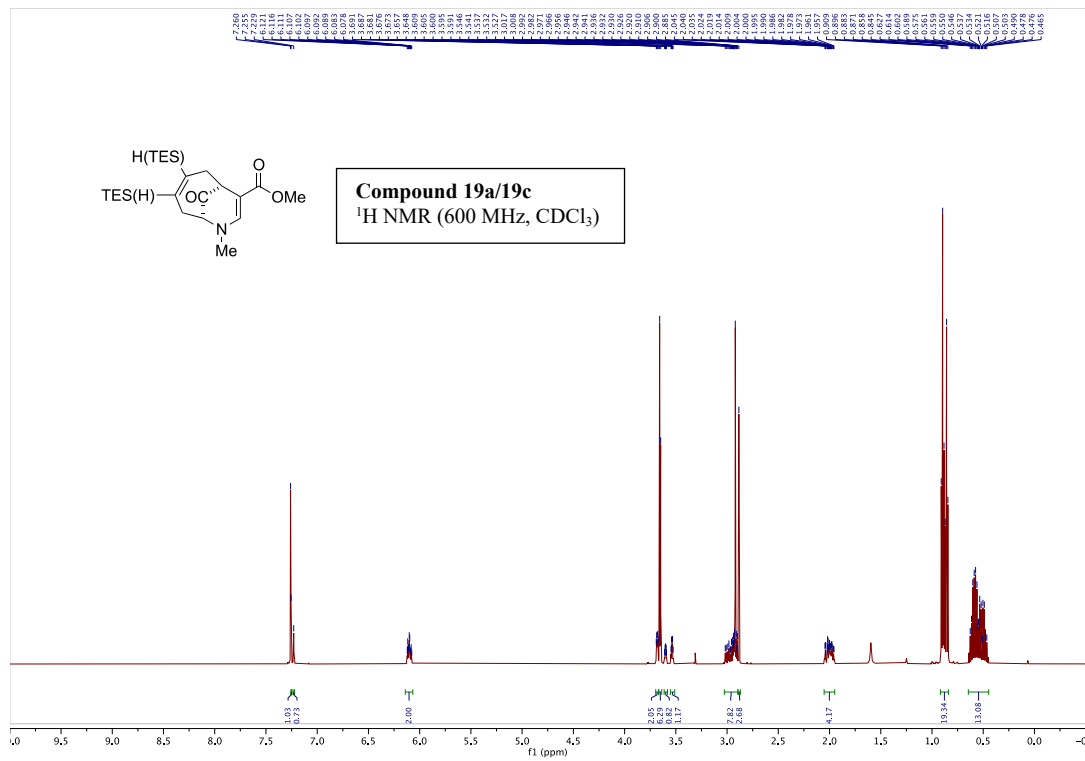


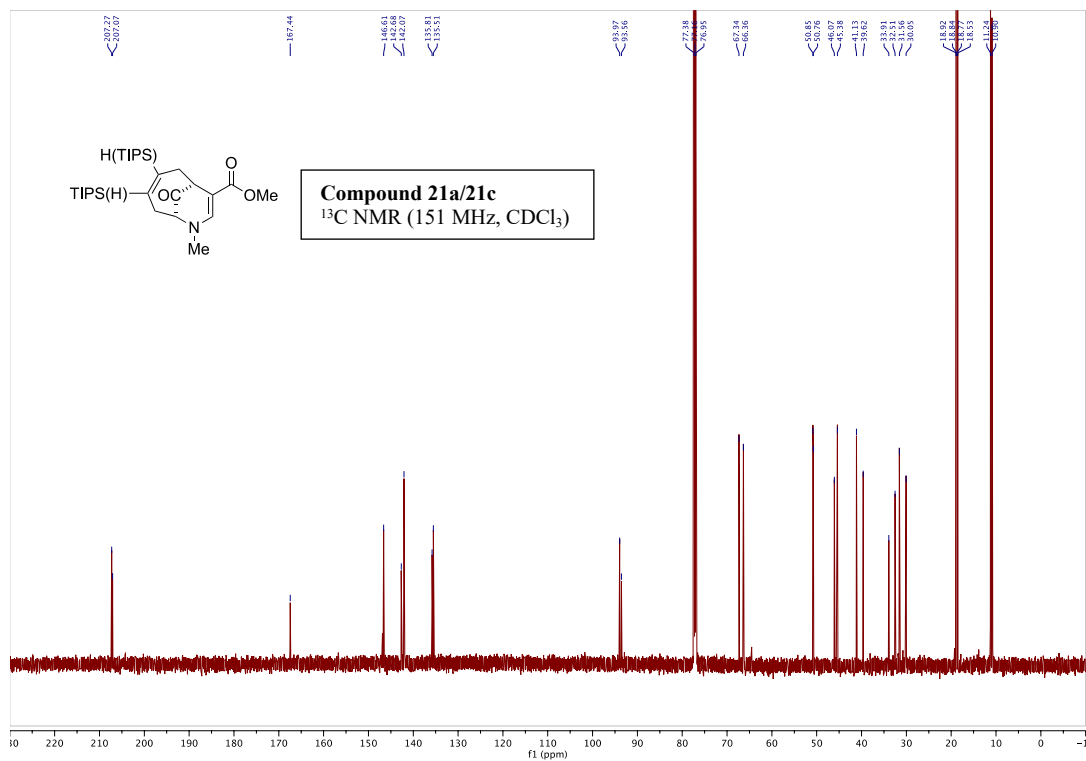
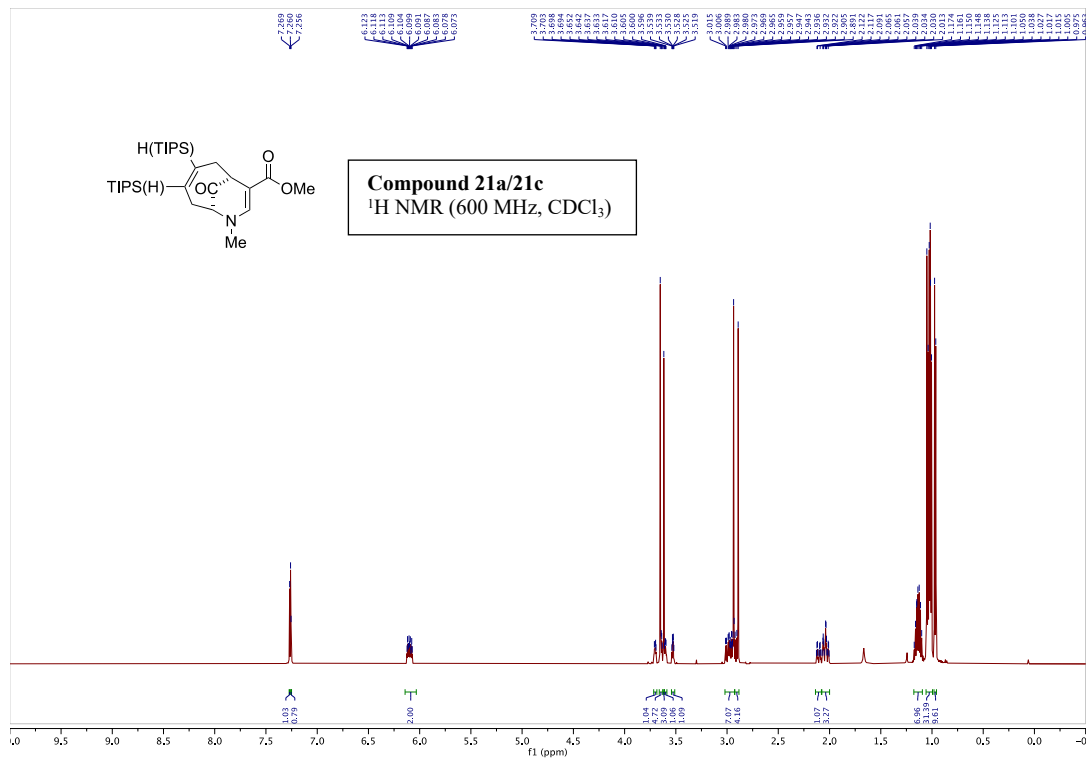


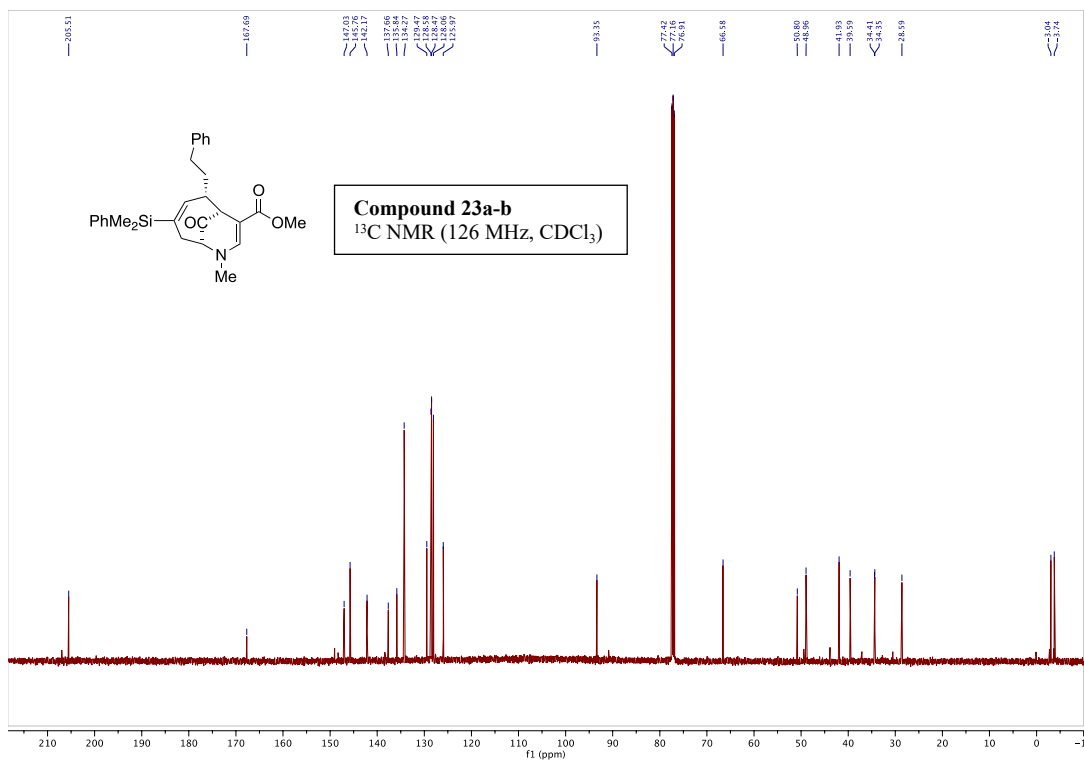
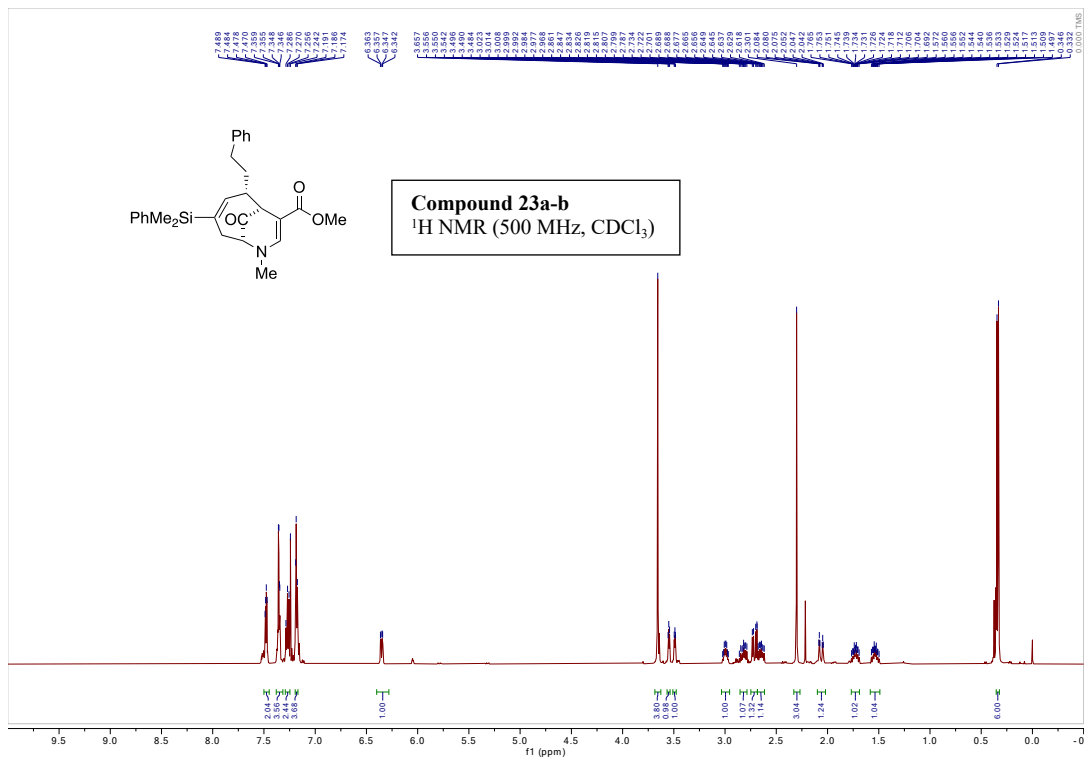


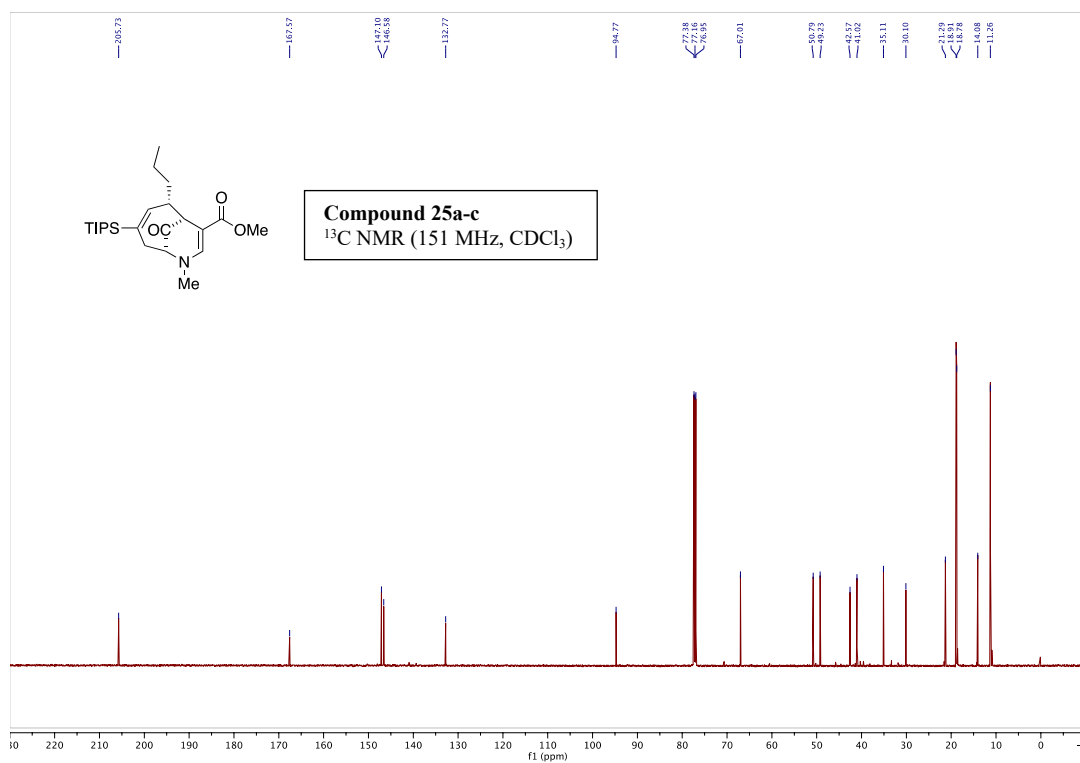
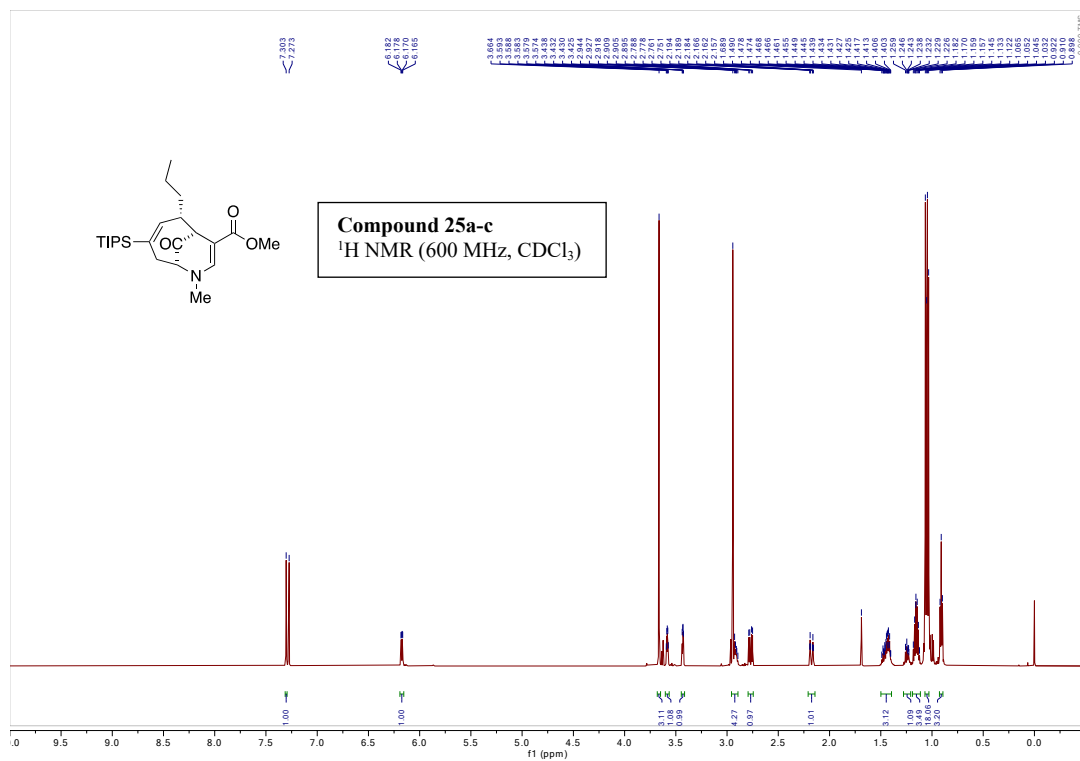






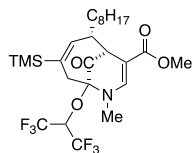








## 6. X-Ray Crystallographic Data of Compound 8a



Bond precision: C-C = 0.0019 Å

Wavelength=1.54178

Cell: a=7.2552(2) b=13.8552(4) c=15.7314(5)  
 alpha=105.3326(16) beta=99.3403(19) gamma=101.6075(17)

Temperature: 150 K

	Calculated	Reported
Volume	1454.49 (8)	1454.49(8)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C <sub>26</sub> H <sub>39</sub> F <sub>6</sub> N O <sub>4</sub> Si	C <sub>26</sub> H <sub>39</sub> F <sub>6</sub> N O <sub>4</sub> Si
Sum formula	C <sub>26</sub> H <sub>39</sub> F <sub>6</sub> N O <sub>4</sub> Si	C <sub>26</sub> H <sub>39</sub> F <sub>6</sub> N O <sub>4</sub> Si
Mr	571.67	571.67
Dx, g cm <sup>-3</sup>	1.305	1.305
Z	2	2
Mu (mm <sup>-1</sup> )	1.335	1.335
F000	604.0	604.0
F000'	606.71	
h, k, lmax	9, 17, 19	9, 17, 19
Nref	5928	5717
Tmin, Tmax	0.880, 0.961	0.661, 0.754
Tmin'	0.563	

Correction method= # Reported T Limits: Tmin=0.661 Tmax=0.754  
 AbsCorr = NONE

Data completeness= 0.964

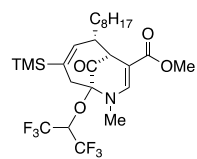
Theta(max)= 74.291

R(reflections)= 0.0340 (5225)

wR2(reflections)= 0.0899 (5717)

S = 1.020

Npar= 349



Thermal ellipsoids are set at the 50% probability level

