

# Electronic Supplementary Information:

## **SmI<sub>2</sub>-induced nitron tandem**

### **β-elimination/alkylation**

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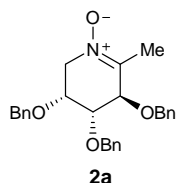
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## 1- General experimental methods

Reactions were performed under Schlenk conditions, with a positive pressure of dry argon in oven-dried, or flame-dried glassware equipped with a magnetic stir bar. Standard inert atmosphere techniques were used in handling all air- and moisture-sensitive reagents. Toluene was freshly distilled from sodium. Dry THF was obtained by filtration through activated molecular sieves. H<sub>2</sub>O and D<sub>2</sub>O (99.97% D) were deoxygenated by refluxing under a current of argon during 30 min. Cyclohexanone and benzaldehyde were distilled over MgSO<sub>4</sub>. Cyclopentanone was distilled over 4 Å MS. 3-pentanone was refluxed during 2 hours over CaCl<sub>2</sub>, stirred with fresh CaCl<sub>2</sub> during 15 h and distilled. Ethyl glyoxylate in toluene was distilled prior to use then its concentration was measured by <sup>1</sup>H NMR. Cyclohexanecarboxaldehyde, ethyl 3,3,3-trifluoropyruvate and ethyl acrylate were also freshly distilled prior to use. Reactions were monitored by thin layer chromatography (TLC) using commercial aluminum-backed silica gel plates. TLC spots were viewed under ultraviolet light and by heating the plate after treatment with a 3% solution of potassium permanganate in 10% aqueous potassium hydroxyde (w/v). Product purification by gravity column chromatography was performed using Silica Gel 60 (70-230 mesh). Infrared (IR) spectra were recorded on a Fourier Transform spectrometer as neat films. The data are reported in reciprocal centimeters (cm<sup>-1</sup>) and are assigned as following: br (broad), s (strong), m (medium), w (weak). <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded in CDCl<sub>3</sub> (unless otherwise stated). Chemical shifts for <sup>1</sup>H spectra are values from tetramethylsilane in CDCl<sub>3</sub> (δ 0.00). Chemical shifts for <sup>13</sup>C spectra are values from CDCl<sub>3</sub> (δ 77.16). <sup>1</sup>H NMR spectra are reported as follows: chemical shift (ppm), multiplicity (br: broad; s: singlet; d: doublet; t: triplet; q: quadruplet; m: multiplet), coupling constants (Hz) and integration. Mass spectra (MS) were recorded using the ESI technique. High resolution mass spectra (HRMS) were recorded at the LCOSB, UMR 7613, Université Pierre et Marie Curie, Paris. Elemental analyses were performed at the Service d'Analyse Elementaire du Département de Chimie Moléculaire, Grenoble.

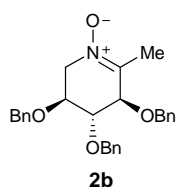
## 2- Typical procedures:



### Preparation of nitrone **2a**:

To a solution of carefully deoxygenated nitrone **1a** (50 mg, 0.09 mmol) in THF/H<sub>2</sub>O (1:1, 0.6 mL) a 0.1 M solution of SmI<sub>2</sub> (2.0 mL, 0.20 mmol) was added at 0 °C under argon. The temperature was allowed to reach the room temperature in a period of 3.5 h. A saturated aqueous solution of Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> (2 mL), a saturated aqueous solution of NaHCO<sub>3</sub> (2 mL) and AcOEt (2 mL) were then added. The phases were separated then the aqueous phase was extracted twice with AcOEt (20 mL). The organic phase was dried over MgSO<sub>4</sub> and concentrated under vacuum to give a residue, which upon column chromatography over silica gel (pentane/AcOEt: 3:1, 1:1 then AcOEt/MeOH: 1:0 then 8:1) yielded **2a** (34 mg, 81%) as a pale yellow oil.

**(3R,4R,5R)-3,4,5-tris(benzyloxy)-2-methyl-piperidine 1-oxide (2a)**:  $[\alpha]_D^{20} = -54$  (*c* 1.00, CHCl<sub>3</sub>); MS (ESI) *m/z* 432 [M+H]<sup>+</sup>; IR  $\nu$  (neat, cm<sup>-1</sup>) 3029 (m), 2869 (m), 1612 (m), 1446 (s), 1198 (s), 1071 (s); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  2.02 (s, 3H), 3.86 (dd, *J* = 1.9 and 4.6 Hz, 1H), 3.94 (br d, *J* = 17 Hz, 1H), 4.03-4.16 (m, 3H), 4.50 (d, *J* = 11.5 Hz, 1H), 4.52-4.66 (m, 4H), 4.73 (d, *J* = 12.0 Hz, 1H), 7.21-7.23 (m, 2H), 7.28-7.38 (m, 13H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  16.0, 58.8, 71.0, 71.9, 72.7, 73.9, 74.1, 76.8, 127.9-128.7, 137.2, 137.5, 137.8, 143.5; Anal. Calcd for C<sub>27</sub>H<sub>29</sub>NO<sub>4</sub>: C, 75.16; H, 6.78; N, 3.25; Found: C, 74.89; H, 6.80; N, 3.14.

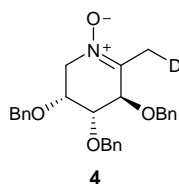


### Preparation of nitrone **2b**:

To a solution of carefully deoxygenated nitrone **1b** (20 mg, 0.04 mmol) in THF (0.5 mL) a 0.1 M solution of SmI<sub>2</sub> (0.8 mL, 0.08 mmol) was added at -40 °C under argon. The temperature was

allowed to reach  $-5\text{ }^{\circ}\text{C}$  over a period of 1.5 h. A saturated aqueous solution of  $\text{Na}_2\text{S}_2\text{O}_3$  (2 mL), a saturated aqueous solution of  $\text{NaHCO}_3$  (2 mL) and AcOEt (2 mL) were then added. The phases were separated then the aqueous phase was extracted twice with AcOEt (20 mL). The organic phase was dried over  $\text{MgSO}_4$  and concentrated under vacuum to give a residue, which upon column chromatography over silica gel (AcOEt/MeOH: 1:0 then 8:1), yielded **2b** (12 mg, 80%) as a pale yellow oil.

**(3R,4R,5S)-3,4,5-tris(benzyloxy)-2-methyl-piperidine 1-oxide (2b)**:  $[\alpha]_{\text{D}}^{20} = -4$  ( $c$  0.80,  $\text{CHCl}_3$ ); MS (ESI)  $m/z$  432  $[\text{M}+\text{H}]^+$ ; IR  $\nu$  (neat,  $\text{cm}^{-1}$ ) 3058 (m), 3033 (m), 2926 (m), 2859 (m), 1606 (m), 1495 (m), 1455 (s), 1094 (s), 1062 (s);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  2.10 (s, 3H), 3.88-4.13 (m, 5H), 4.56 (d,  $J = 11.4$  Hz, 1H), 4.61-4.69 (m, 4H), 4.73 (d,  $J = 11.4$  Hz, 1H), 7.26-7.38 (m, 15H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  15.5, 59.9, 72.3, 73.0, 73.4, 73.6, 77.1, 78.2, 128.0-129.0, 131.0, 137.2, 137.3, 137.6, 143.8.



#### Preparation of deuterated nitrone **4**:

Nitronone **1** (50 mg, 0.09 mmol) was co-evaporated three times with toluene (1 mL) at  $35\text{ }^{\circ}\text{C}$  and was carefully deoxygenated. To a dry solution of deoxygenated nitronone **1** in THF/ $\text{D}_2\text{O}$  (1:1, 0.6 mL) a 0.1 M solution of  $\text{SmI}_2$  (2.0 mL, 0.20 mmol) was added at  $0\text{ }^{\circ}\text{C}$  under argon. The temperature was allowed to reach the room temperature in a period of 3.5 h. A saturated aqueous solution of  $\text{Na}_2\text{S}_2\text{O}_3$  (2 mL), a saturated aqueous solution of  $\text{NaHCO}_3$  (2 mL) and AcOEt (2 mL) were then added. The phases were separated then the aqueous phase was extracted twice with AcOEt (20 mL). The organic phase was dried over  $\text{MgSO}_4$  and concentrated under vacuum to give a residue, which upon column chromatography over silica gel (AcOEt/MeOH: 1:0 then 8:1) yielded **4** (34 mg, 81%) as a beige oil.

**(3R,4R,5R)-3,4,5-tris(benzyloxy)-2-monodeuteriomethyl-piperidine 1-oxide (4)**:  $[\alpha]_{\text{D}}^{20} = -55$  ( $c$  0.74,  $\text{CHCl}_3$ ); MS (ESI)  $m/z$  455  $[\text{M}+\text{Na}]^+$ ; IR  $\nu$  (neat,  $\text{cm}^{-1}$ ) 3033 (m), 2894 (m), 2868 (m), 1606 (m), 1497 (m), 1454 (s), 1194 (m), 1120 (s), 1090 (s);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  2.00 (s, 2H), 3.86 (dd,  $J = 1.9$  and  $4.6$  Hz, 1H), 3.94 (br d,  $J = 19$  Hz, 1H), 4.02-4.16 (m, 3H), 4.50 (d,  $J = 11.5$  Hz,

1H), 4.55-4.64 (m, 4H), 4.73 (d,  $J = 12.0$  Hz, 1H), 7.21-7.23 (m, 2H), 7.27-7.38 (m, 13H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  15.7 (t), 58.9, 71.1, 72.0, 72.7, 73.9, 74.1, 76.9, 127.9-128.7, 137.3, 137.5, 137.8, 143.0.

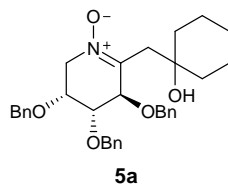
**General procedure for the preparation of  $\beta$ -functionalized nitrones using Grignard-type conditions (method A):**

Nitron **1** (50 mg, 0.09 mmol) was co-evaporated three times with toluene (1 mL) at 35 °C then was carefully deoxygenated. To the solution of deoxygenated nitron **1** in dry THF (0.5 mL) a 0.1 M solution of  $\text{SmI}_2$  (2.0 mL, 0.20 mmol) was added at -60 °C under argon. After disappearance of the typical blue color, the carbonyl compound (0.20 mmol) was added and the temperature was raised until room temperature during 5 h. A saturated aqueous solution of  $\text{Na}_2\text{S}_2\text{O}_3$  (2 mL), a saturated aqueous solution of  $\text{NaHCO}_3$  (2 mL) and AcOEt (2 mL) were added. The phases were separated then the aqueous phase was extracted twice with AcOEt (20 mL). The organic phase was dried over  $\text{MgSO}_4$  and concentrated to afford crude oil which upon column chromatography (pentane/AcOEt : 6:1 to 0:1 then AcOEt/MeOH : 8:1) afforded the pure  $\beta$ -functionalized nitron (**5-11**) and nitron **2**.

**General procedure for the preparation of  $\beta$ -functionalized nitrones using Barbier-type conditions (method B):**

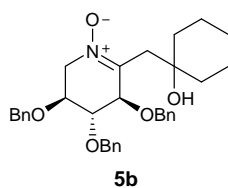
Nitron **1** (50 mg, 0.09 mmol) was coevaporated three times with toluene (1 mL) at 35 °C then was carefully deoxygenated. To a solution of deoxygenated nitron **1** and carbonyl compound (0.20 mmol) in dry THF (0.5 mL), a 0.1 M solution of  $\text{SmI}_2$  (2.0 mL, 0.20 mmol) was added at -60 °C under argon. The temperature was raised until room temperature during 5 h. A saturated aqueous solution of  $\text{Na}_2\text{S}_2\text{O}_3$  (2 mL), a saturated aqueous solution of  $\text{NaHCO}_3$  (2 mL) and AcOEt (2 mL) were added. The phases were separated then the aqueous phase was extracted twice with AcOEt (20 mL). The organic phase was dried over  $\text{MgSO}_4$  and concentrated to afford crude oil which upon column chromatography (pentane/AcOEt : 6:1 to 0:1 then AcOEt/MeOH : 8:1) afforded the pure  $\beta$ -functionalized nitron (**5-11**) and nitron **2**.

### 3- Characterization of adducts 5-11



#### **1-((3R,4R,5R)-3,4,5-tris(benzyloxy)-1-oxy-3,4,5,6-tetrahydro-pyridin-2-ylmethyl)-cyclohexanol**

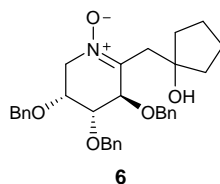
**(5a)** was obtained by method A from cyclohexanone (21  $\mu$ L, 0.20 mmol) and nitrone **1a** (50 mg, 0.09 mmol) as a pale yellow oil (26 mg, 53%) or by method B from cyclohexanone (21  $\mu$ L, 0.20 mmol) and nitrone **1a** (50 mg, 0.09 mmol) as a pale yellow oil (30 mg, 61%):  $[\alpha]_D^{20} = -87$  (*c* 1.00,  $\text{CHCl}_3$ ); MS (ESI)  $m/z$  530  $[\text{M}+\text{H}]^+$ ; IR  $\nu$  (neat,  $\text{cm}^{-1}$ ) 3402 (br), 3254 (br), 3021 (m), 2926 (s), 2849 (s), 1603 (m), 1493 (m), 1456 (s), 1349 (m), 1210 (m), 1063 (s);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  1.02-1.76 (m, 10H), 2.23 (d,  $J = 13.7$  Hz, 1H), 2.88 (d,  $J = 13.7$  Hz, 1H), 3.86 (dd,  $J = 1.8$  and 4.1 Hz, 1H), 3.92 (dd,  $J = 4.1$  and 14.1 Hz, 1H), 4.03-4.18 (m, 3H), 4.34 (d,  $J = 11.7$  Hz, 1H), 4.53-4.64 (m, 4H), 4.74 (d,  $J = 12.2$  Hz, 1H), 6.26 (s, 1H), 7.10-7.20 (m, 2H), 7.27-7.40 (m, 13H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  22.4, 25.9, 38.1, 39.9, 41.6, 58.4, 71.1, 72.1, 72.7, 72.9, 73.7, 74.2, 76.3, 127.9-128.8, 136.8, 137.5, 137.8, 146.2; HRMS (ESI) Calcd for  $\text{C}_{33}\text{H}_{40}\text{N}_1\text{O}_5$ :  $m/z = 530.29010$   $[\text{M}+\text{H}]^+$ ; Found  $m/z = 530.28998$ .



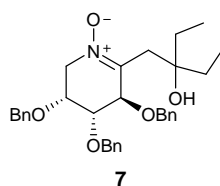
#### **1-((3R,4R,5S)-3,4,5-tris(benzyloxy)-1-oxy-3,4,5,6-tetrahydro-pyridin-2-ylmethyl)-cyclohexanol**

**(5b)** was obtained by method A from cyclohexanone (21  $\mu$ L, 0.20 mmol) and nitrone **1b** (50 mg, 0.09 mmol) as a pale yellow oil (29 mg, 60%):  $[\alpha]_D^{20} = -22$  (*c* 0.50,  $\text{CHCl}_3$ ); MS (ESI)  $m/z$  530  $[\text{M}+\text{H}]^+$ ; IR  $\nu$  (neat,  $\text{cm}^{-1}$ ) 3242 (br), 3057 (m), 3021 (m), 2922 (s), 2853 (s), 1607 (m), 1493 (m), 1448 (s), 1210 (m), 1071 (s);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.00-1.15 (m, 2H), 1.24-1.38 (m, 3H), 1.46-1.66 (m, 5H), 2.46 (d,  $J = 13.6$  Hz, 1H), 2.94 (d,  $J = 13.6$  Hz, 1H), 3.82-3.92 (m, 2H), 3.93-4.02 (m, 1H), 4.05-4.15 (m, 2H), 4.45 (d,  $J = 11.6$  Hz, 1H), 4.52-4.63 (m, 4H), 4.65-4.69 (m, 2H), 6.25 (s, 1H),

7.25-7.39 (m, 15H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  22.2, 22.3, 25.9, 38.3, 39.7, 41.3, 59.5, 72.0, 72.7, 73.1, 73.2, 74.1, 75.0, 77.2, 127.9-128.8, 136.8, 137.2, 146.5; HRMS (ESI) Calcd for  $\text{C}_{33}\text{H}_{40}\text{N}_1\text{O}_5$ :  $m/z = 530.29010$  [ $\text{M}+\text{H}^+$ ]; Found  $m/z = 530.29017$ .

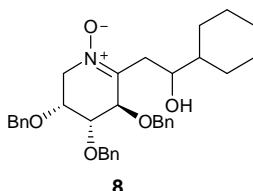


**1-((3R,4R,5R)-3,4,5-tris(benzyloxy)-1-oxy-3,4,5,6-tetrahydro-pyridin-2-ylmethyl)-cyclopentanol (6)** was obtained by method A from cyclopentanone (18  $\mu\text{L}$ , 0.20 mmol) and nitrone **1a** (50 mg, 0.09 mmol) as a pale yellow oil (30 mg, 63%) or by method B from cyclopentanone (18  $\mu\text{L}$ , 0.20 mmol) and nitrone **1a** (50 mg, 0.09 mmol) as a pale yellow oil (28 mg, 58%):  $[\alpha]_{\text{D}}^{20} = -77$  ( $c$  0.36,  $\text{CHCl}_3$ ); MS (ESI)  $m/z$  516 [ $\text{M}+\text{H}^+$ ]; IR  $\nu$  (neat,  $\text{cm}^{-1}$ ) 3254 (br), 3062 (m), 3029 (m), 2951 (s), 2869 (s), 1599 (m), 1493 (m), 1448 (s), 1198 (m), 1050 (s);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.13-1.76 (m, 8H), 2.29 (d,  $J = 13.7$  Hz, 1H), 3.09 (d,  $J = 13.7$  Hz, 1H), 3.86 (dd,  $J = 1.9$  and 4.0 Hz, 1H), 3.92 (dd,  $J = 4.5$  and 14.6 Hz, 1H), 4.02-4.18 (m, 3H), 4.34 (d,  $J = 11.7$  Hz, 1H), 4.53-4.64 (m, 4H), 4.74 (d,  $J = 12.2$  Hz, 1H), 6.27 (s, 1H), 7.15-7.17 (m, 2H), 7.30-7.37 (m, 13H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  23.0, 23.6, 39.7, 40.4, 41.1, 58.4, 71.0, 72.1, 72.7, 72.9, 73.7, 76.3, 83.5, 128.0-129.7, 136.8, 137.5, 137.8, 146.4; HRMS (ESI) Calcd for  $\text{C}_{32}\text{H}_{38}\text{N}_1\text{O}_5$ :  $m/z = 516.27445$  [ $\text{M}+\text{H}^+$ ]; Found  $m/z = 516.27433$ .

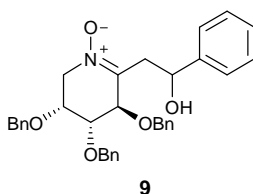


**3-((3R,4R,5R)-3,4,5-Tris-benzyloxy-1-oxy-3,4,5,6-tetrahydro-pyridin-2-ylmethyl)-pentan-3-ol (7)** was obtained by method A from 3-pentanone (21  $\mu\text{L}$ , 0.20 mmol) and nitrone **1a** (50 mg, 0.09 mmol) as a pale yellow oil (15 mg, 31%):  $[\alpha]_{\text{D}}^{20} = -39$  ( $c$  0.70,  $\text{CHCl}_3$ ); MS (ESI)  $m/z$  518 [ $\text{M}+\text{H}^+$ ]; IR  $\nu$  (neat,  $\text{cm}^{-1}$ ) 3234 (br), 3066 (m), 3028 (m), 2961 (s), 2935 (s), 2875 (s), 1605 (m), 1452 (s), 1366 (m), 1089 (s);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.75 (t,  $J = 7.4$ , 3H), 0.81 (t,  $J = 7.4$ , 3H), 1.19-1.51 (m, 4H), 2.19 (d,  $J = 13.7$  Hz, 1H), 2.92 (d,  $J = 13.7$  Hz, 1H), 3.86 (dd,  $J = 1.9$  and 4.1 Hz, 1H), 3.92 (dd,  $J = 4.4$  and 14.4 Hz, 1H), 4.04-4.16 (m, 3H), 4.36 (d,  $J = 11.7$  Hz, 1H), 4.52-4.63 (m, 4H),

4.75 (d,  $J = 12.2$  Hz, 1H), 6.27 (s, 1H), 7.15-7.18 (m, 2H), 7.28-7.38 (m, 13H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  8.1, 31.9, 32.3, 39.4, 58.4, 71.1, 72.1, 72.7, 72.9, 73.8, 76.5, 77.4, 127.6-128.9, 136.8, 137.5, 137.8, 146.6.



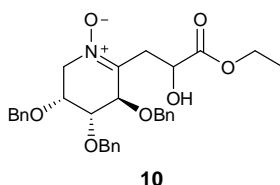
**1-cyclohexyl-2-((3R,4R,5R)-3,4,5-tris-benzyloxy-1-oxy-3,4,5,6-tetrahydro-pyridin-2-yl)-ethanol (8)** was obtained by method A from cyclohexanecarboxaldehyde (25  $\mu\text{L}$ , 0.20 mmol) and nitrone **1a** (50 mg, 0.09 mmol) as a mixture of diastereoisomers (39 mg, 77%, 70:30, pale yellow oil) or by method B from cyclohexanecarboxaldehyde (25  $\mu\text{L}$ , 0.20 mmol) as a mixture of diastereoisomers (39 mg, 77%, 80:20, pale yellow oil). The major diastereoisomer crystallized in pentane/ether (15 mg, 30%): mp 89-90  $^{\circ}\text{C}$ ;  $[\alpha]_{\text{D}}^{20} = -11$  ( $c$  0.40,  $\text{CHCl}_3$ ); MS (ESI)  $m/z$  544  $[\text{M}+\text{H}]^+$ ; IR  $\nu$  (neat,  $\text{cm}^{-1}$ ) 3462 (br), 3063 (w), 3024 (w), 2916 (s), 2846 (s), 1718 (m), 1450 (s), 1254 (m), 1116 (s), 1085 (s), 1025 (m);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.85-1.30 (m, 6H), 1.49-1.80 (m, 5H), 2.35 (dd,  $J = 1.6$  and 13.2 Hz, 1H), 2.87 (dd,  $J = 9.6$  and 13.0 Hz, 1H), 3.71-3.75 (m, 1H), 3.85 (d,  $J = 5.0$  Hz, 1H), 3.92-4.14 (m, 3H), 4.23 (d,  $J = 4.9$  Hz, 1H), 4.49 (d,  $J = 11.5$  Hz, 1H), 4.52-4.73 (m, 5H), 5.29 (d,  $J = 3.7$  Hz, 1H), 7.18-7.23 (m, 2H), 7.27-7.40 (m, 13H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  26.3, 26.4, 26.7, 28.0, 29.0, 35.4, 44.9, 59.1, 70.9, 72.1, 72.7, 74.3, 76.6, 77.6, 128.0-128.8, 137.2, 137.4, 137.7, 147.4.



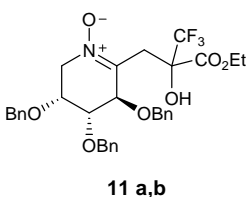
**1-phenyl-2-((3R,4R,5R)-3,4,5-tris-benzyloxy-1-oxy-3,4,5,6-tetrahydro-pyridin-2-yl)-ethanol (9)** was obtained by method A from benzaldehyde (20  $\mu\text{L}$ , 0.20 mmol) and nitrone **1a** (50 mg, 0.09 mmol) as a mixture of diastereoisomers (29 mg, 56%, 90:10, pale yellow oil). The major diastereoisomer was purified by column chromatography (18 mg, 36 %):  $[\alpha]_{\text{D}}^{20} = -101$  ( $c$  1.00,  $\text{CHCl}_3$ ); MS (ESI)  $m/z$  538  $[\text{M}+\text{H}]^+$ ; IR  $\nu$  (neat,  $\text{cm}^{-1}$ ) 3274 (br), 3062 (m), 3033 (m), 2922 (m), 2869 (m), 1608 (w), 1493 (m), 1452 (s), 1194 (m), 1084 (s);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  2.88 (dd,  $J =$



6.8 and 13.5 Hz, 1H), 3.05 (dd,  $J = 2.7$  and 13.5 Hz, 1H), 3.65 (d,  $J = 4.6$  Hz, 1H), 3.71 (dd,  $J = 1.8$  and 4.6 Hz, 1H), 3.90-4.02 (m, 2H), 4.13 (dd,  $J = 6.6$  and 14.1 Hz, 1H), 4.24 (d,  $J = 11.5$  Hz, 1H), 4.45 (s, 2H), 4.47-4.61 (m, 3H), 5.08-5.15 (m, 1H), 6.74 (d,  $J = 3.9$  Hz, 1H), 7.13-7.25 (m, 9H), 7.27-7.37 (m, 11H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  39.4, 58.8, 70.8, 72.1, 72.3, 73.5, 74.2, 74.8, 76.7, 125.4-128.8, 137.0, 137.4, 137.6, 144.5, 146.9; HRMS (ESI) Calcd for  $\text{C}_{34}\text{H}_{36}\text{N}_1\text{O}_5$ :  $m/z = 538.25880$   $[\text{M}+\text{H}^+]$ ; Found  $m/z = 538.25854$ .



**2-hydroxy-3-((3R,4R,5R)-3,4,5-tris-benzyloxy-1-oxy-3,4,5,6-tetrahydro-pyridin-2-yl)-propionic acid ethyl ester (10)** was obtained by method A from ethyl glyoxylate (68  $\mu\text{L}$ , 0.2 mmol) and nitrone **1a** (50 mg, 0.09 mmol) as a mixture of diastereoisomers (20 mg, 40%, 1:1, pale yellow oil): MS (ESI)  $m/z$  534  $[\text{M}+\text{H}]^+$ ; IR  $\nu$  (neat,  $\text{cm}^{-1}$ ) 3250 (br), 3062 (m), 3025 (m), 2926 (m), 2869 (m), 1734 (s), 1595 (m), 1493 (m), 1452 (s), 1366 (m), 1206 (s), 1087 (s);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.24 (t,  $J = 7.1$  Hz, 3H), 2.87-3.02 (m, 2H), 3.83-3.88 (m, 1H), 3.96 (dd,  $J = 4.2$  and 14.7 Hz, 1H), 4.02-4.05 (m, 1H), 4.07-4.21 (m, 3H), 4.22 (d,  $J = 4.8$  Hz, 0.55H), 4.32 (d,  $J = 4.8$  Hz, 0.45H), 4.46 (dd,  $J = 4.4$  and 8.0 Hz, 0.55H), 4.50-4.74 (m, 6.45H), 7.19-7.25 (m, 2H), 7.28-7.38 (m, 13H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  14.3, 34.6, 34.7, 58.9, 59.0, 61.5, 69.8, 70.7, 70.8, 71.1, 72.1, 72.2, 72.6, 72.8, 73.4, 73.8, 74.2, 74.5, 76.0, 77.1, 77.4, 127.9-128.8, 136.8, 137.1, 137.4, 137.6, 137.7, 143.9, 145.0, 173.4, 173.5.

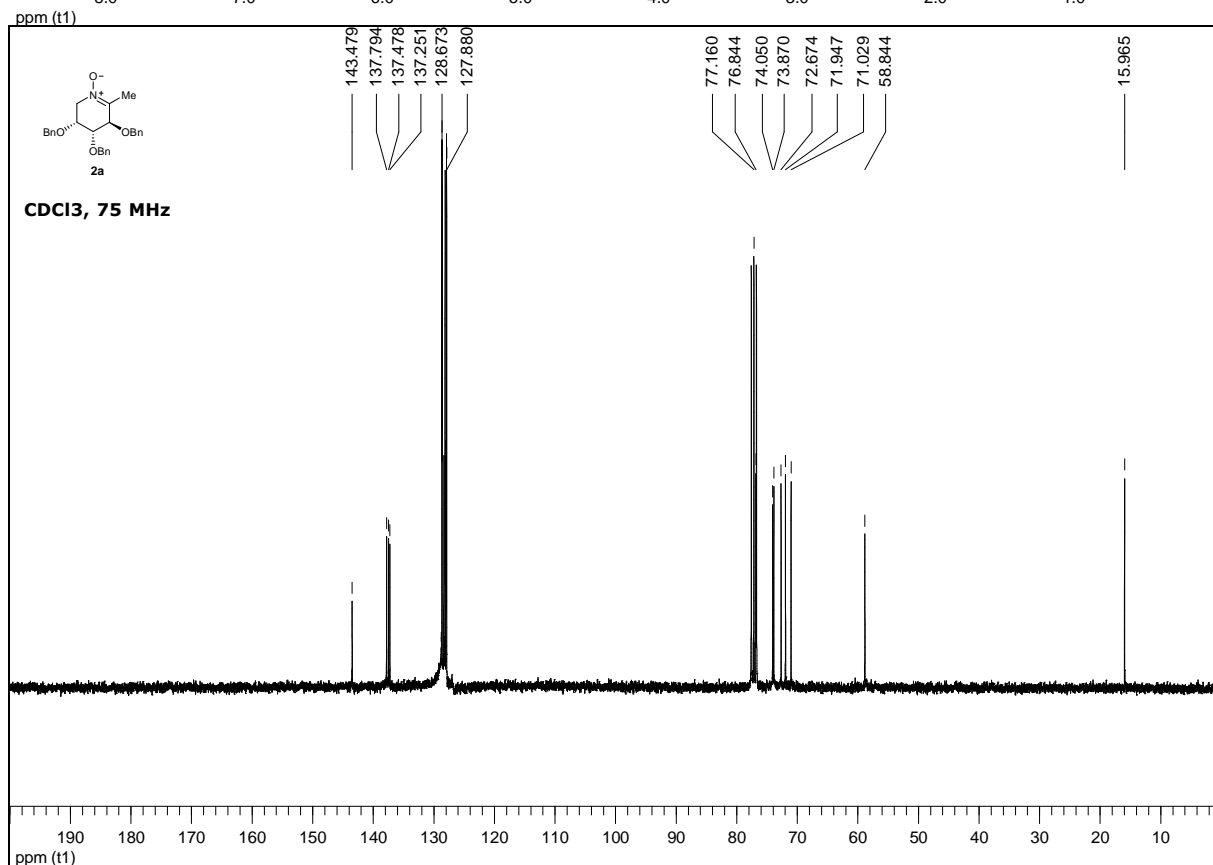
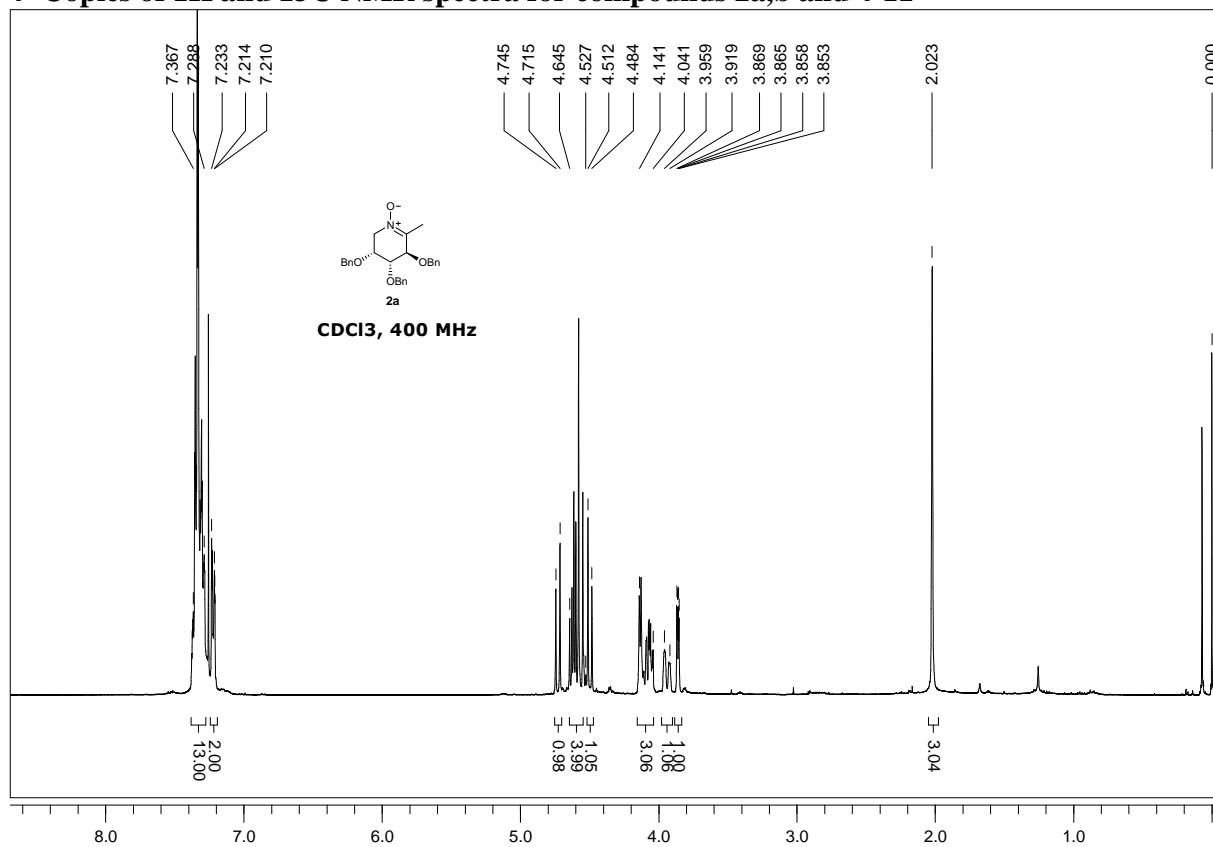


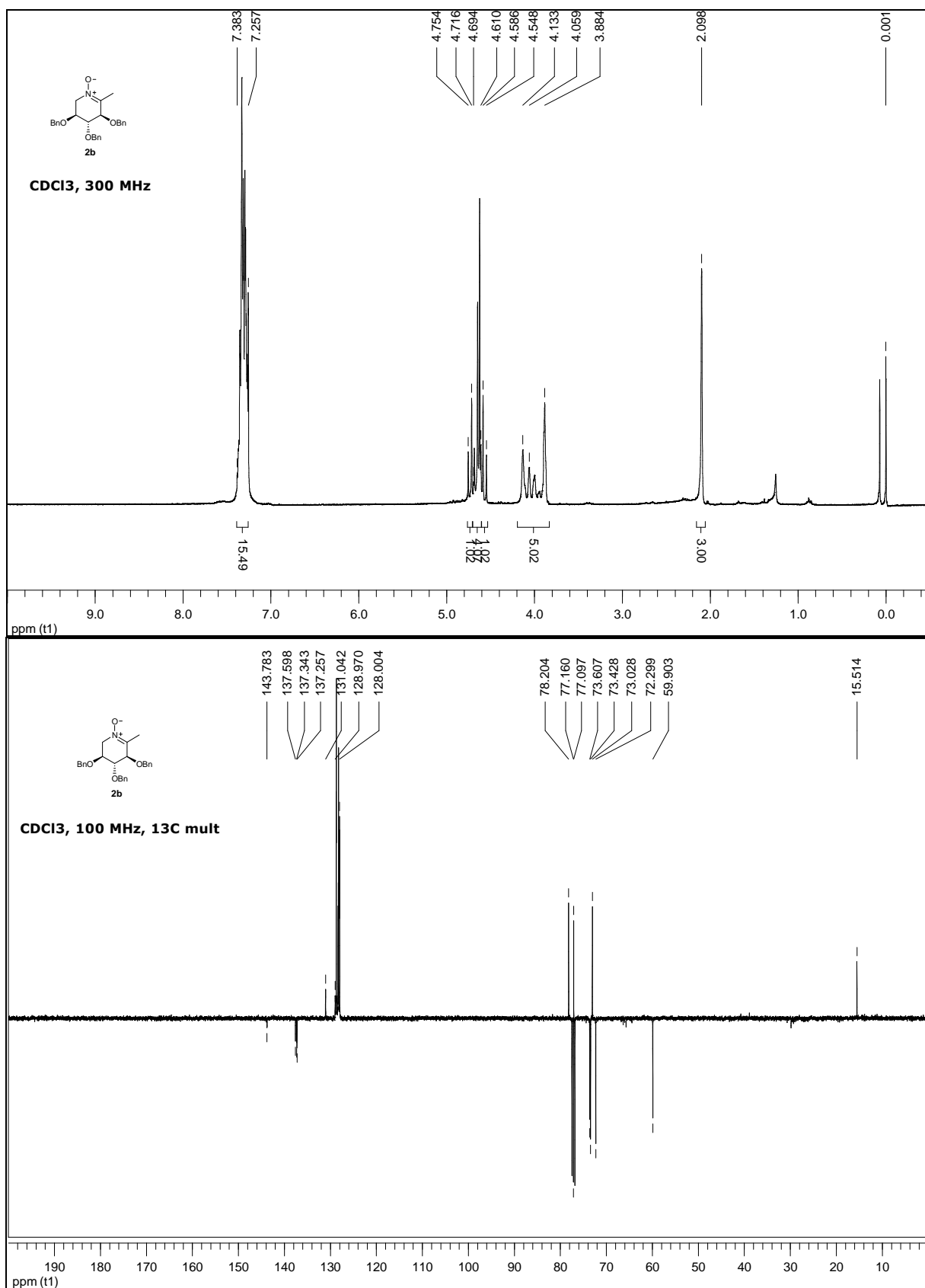
**3,3,3-Trifluoro-2-hydroxy-2-((3R,4R,5R)-3,4,5-tris-benzyloxy-1-oxy-3,4,5,6-tetrahydro-pyridin-2-ylmethyl)-propionic acid ethyl ester (11a,b)** were obtained by method A from 3,3,3-ethyltrifluoropyruvate (25  $\mu\text{L}$ , 0.2 mmol) and nitrone **1a** (50 mg, 0.09 mmol) as a mixture of diastereoisomers (15 mg, 27%, 1:1, pale yellow oil). The diastereoisomers were separated by column chromatography (pentane/AcOEt: 3:1 to 0:1).

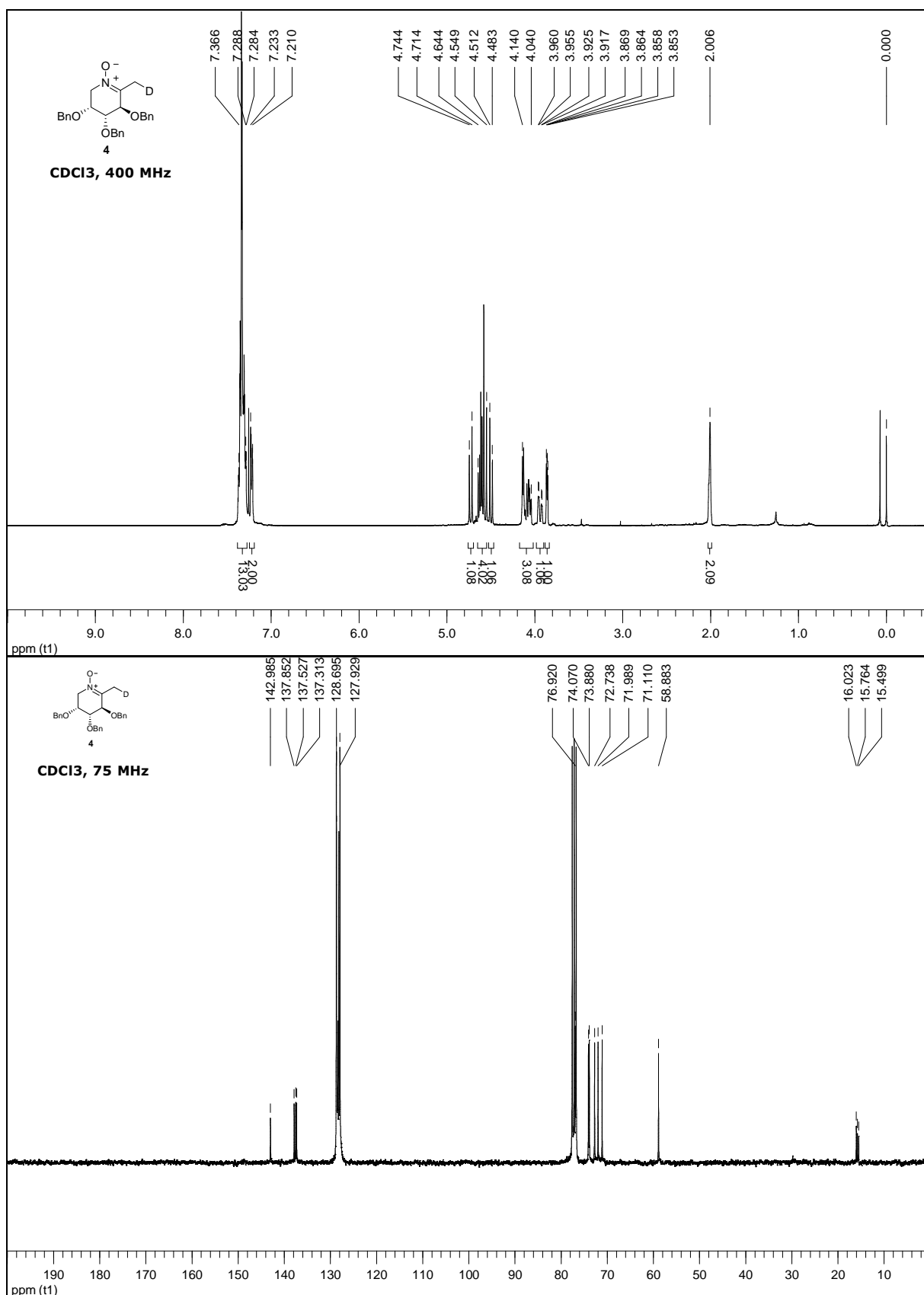
Diastereoisomer **11a** (7 mg, 14 %, pale yellow oil):  $[\alpha]_D^{20} = -95$  (*c* 0.50, CHCl<sub>3</sub>); MS (ESI) *m/z* 624 [M+Na]<sup>+</sup>; IR  $\nu$  (neat, cm<sup>-1</sup>) 3341 (br), 3024 (m), 2924 (m), 2869 (m), 1745 (s), 1606 (m), 1454 (s), 1263 (s), 1185 (s), 1072 (s); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  1.18 (t, *J* = 7.1 Hz, 3H), 2.98 (d, *J* = 13.9 Hz, 1H), 3.32 (d, *J* = 13.9 Hz, 1H), 3.80 (dd, *J* = 1.7 and 4.2 Hz, 1H), 3.88 (dd, *J* = 3.8 and 13.8 Hz, 1H), 3.97-4.21 (m, 4H), 4.38 (d, *J* = 4.3 Hz, 1H), 4.54 (s, 2H), 4.56-4.62 (m, 3H), 4.66 (d, *J* = 12.0 Hz, 1H), 7.21-7.24 (m, 2H), 7.27-7.40 (m, 13H), 8.70 (s, 1H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  0.6 (q), 14.0, 33.3, 58.6, 62.8, 70.9, 72.2, 72.6, 72.8, 74.7, 76.3, 77.3, 127.9-128.9, 136.8, 137.3, 137.5, 144.0, 168.7.

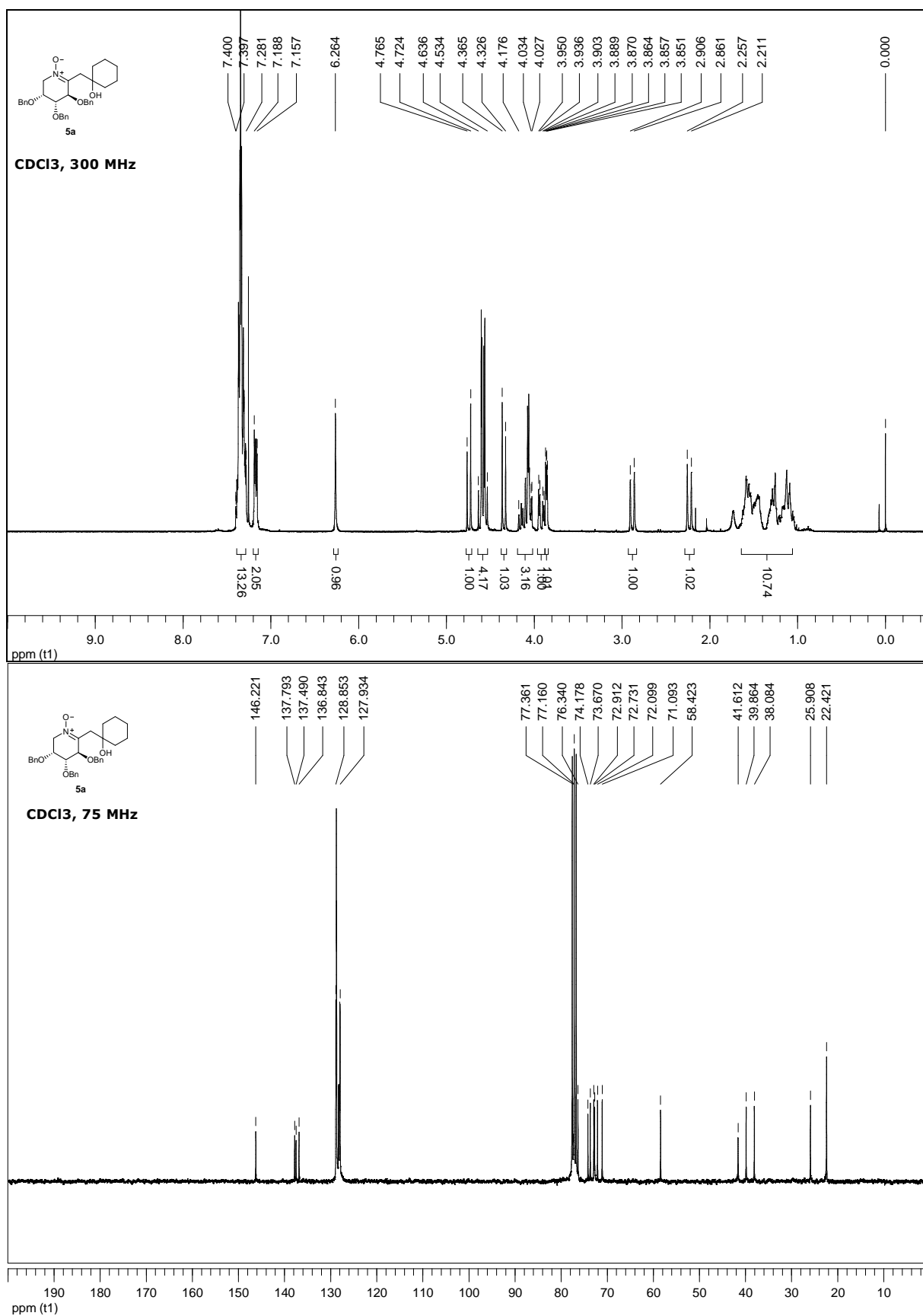
Diastereoisomer **11b** (6 mg, 13 %, pale yellow oil):  $[\alpha]_D^{20} = -48$  (*c* 0.50, CHCl<sub>3</sub>); MS (ESI) *m/z* 624 [M+Na]<sup>+</sup>; IR  $\nu$  (neat, cm<sup>-1</sup>) 3341 (br), 3024 (m), 2924 (m), 2868 (m), 1745 (m), 1454 (s), 1263 (s), 1185 (s), 1072 (s); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  1.26 (t, *J* = 7.1 Hz, 3H), 3.08 (d, *J* = 14.2 Hz, 1H), 3.26 (d, *J* = 14.0 Hz, 1H), 3.81 (dd, *J* = 2.0 and 4.5 Hz, 1H), 3.89 (dd, *J* = 4.1 and 14.6 Hz, 1H), 3.98-4.04 (m, 1H), 4.06-4.25 (m, 4H), 4.45-4.61 (m, 5H), 4.66 (d, *J* = 12.1 Hz, 1H), 7.17-7.23 (m, 2H), 7.28-7.41 (m, 13H), 8.12 (s, 1H); <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>)  $\delta$  0.7 (q), 14.0, 33.4, 58.8, 62.9, 70.6, 72.1, 72.7, 73.1, 74.5, 76.0, 77.4, 127.9-128.9, 136.8, 137.4, 137.6, 143.5, 168.5.

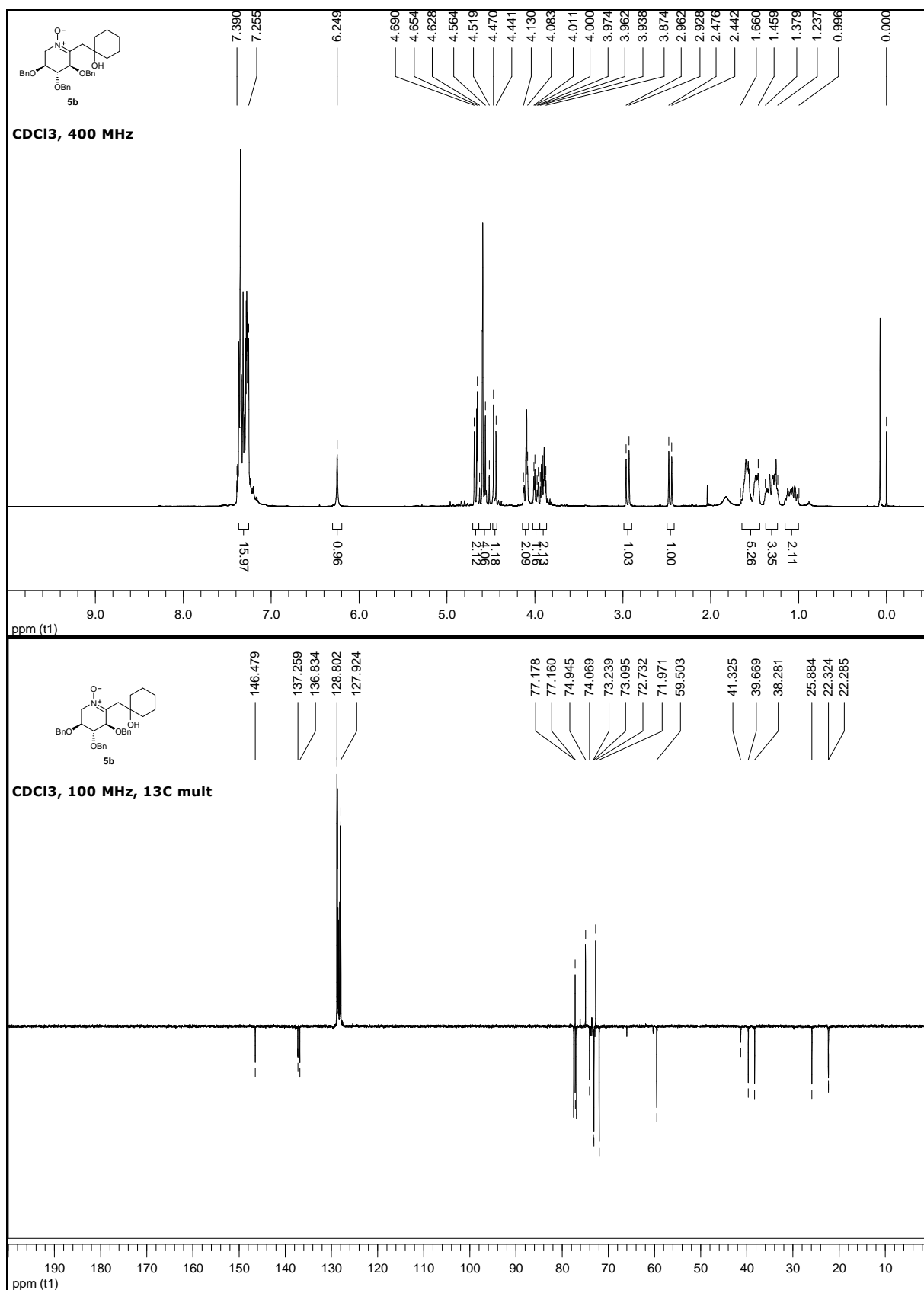
#### 4- Copies of <sup>1</sup>H and <sup>13</sup>C NMR spectra for compounds 2a,b and 4-11

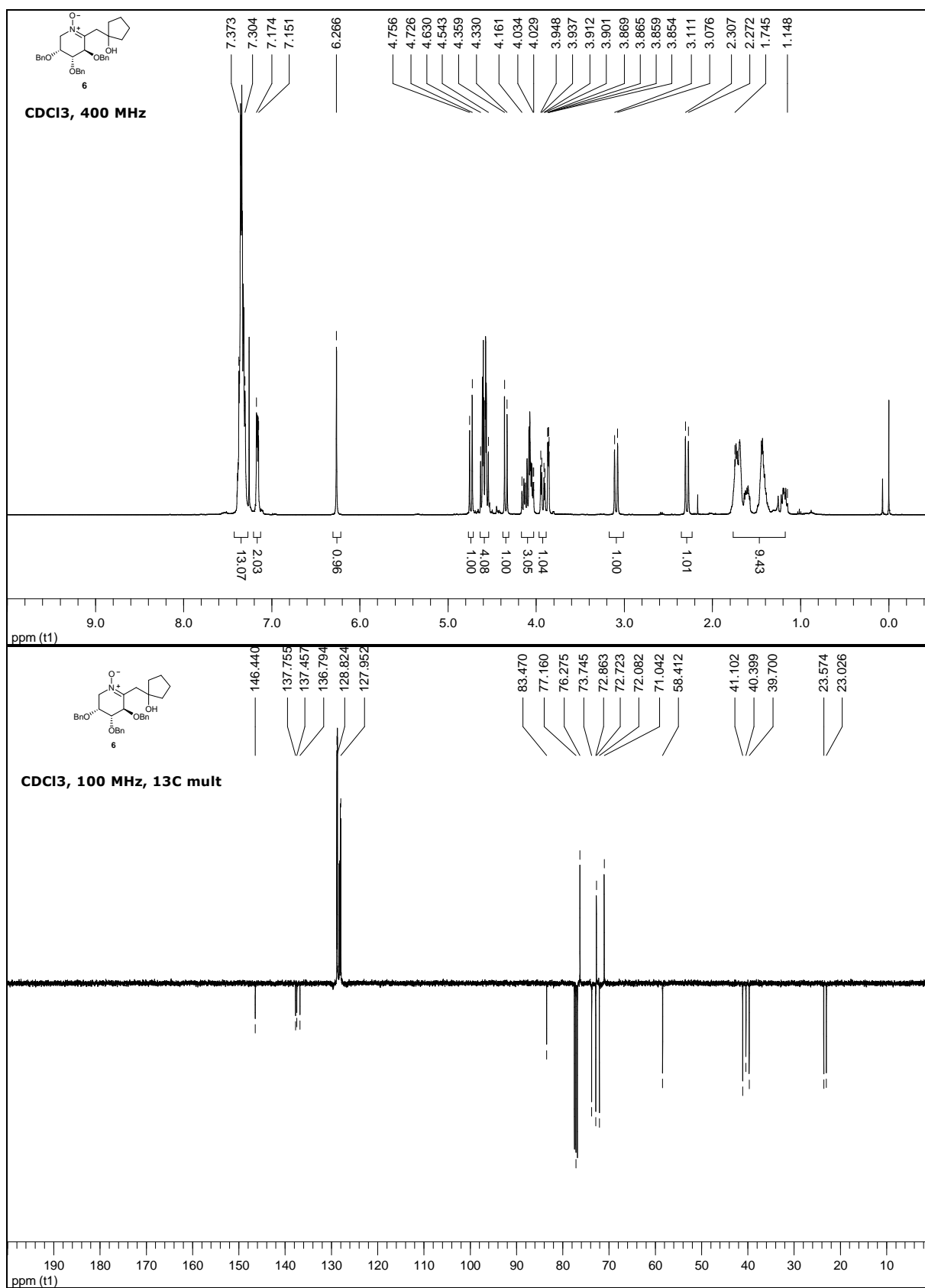




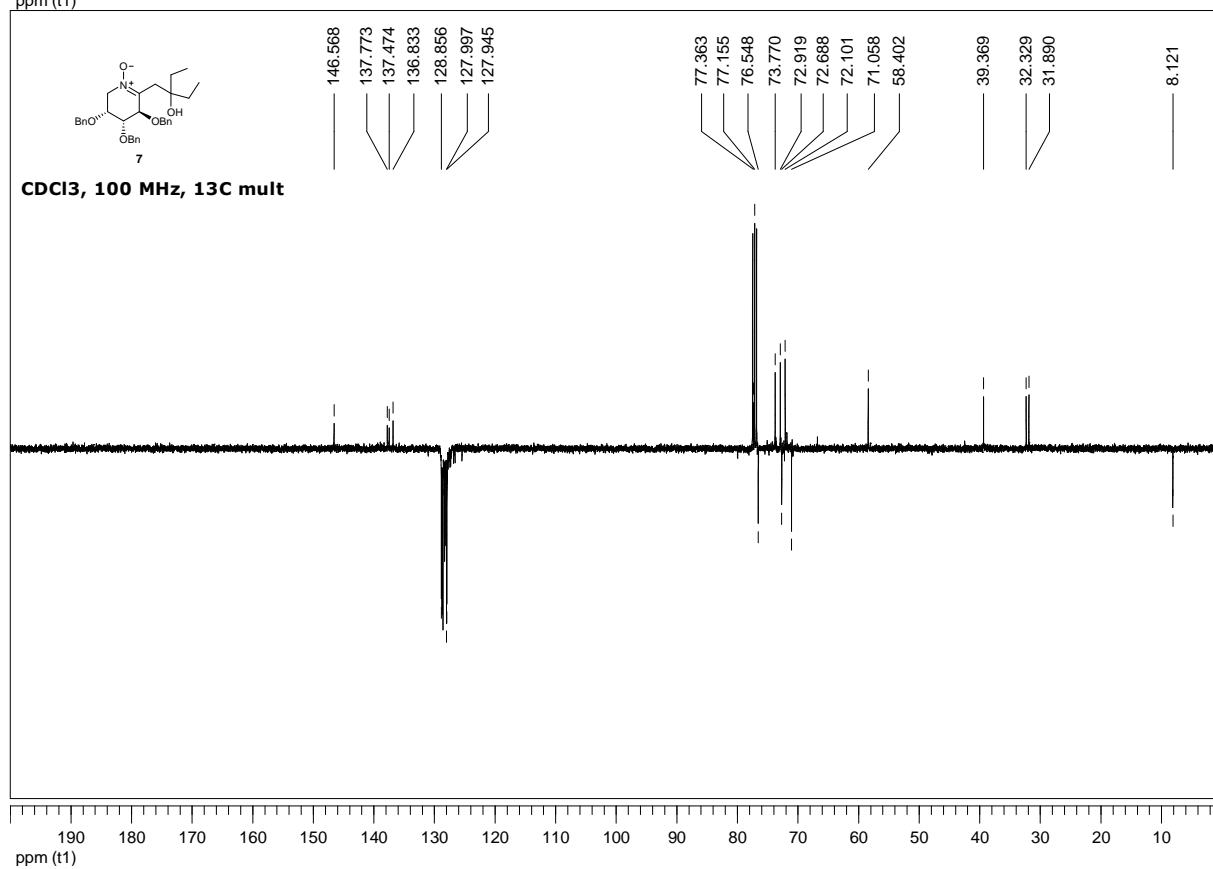
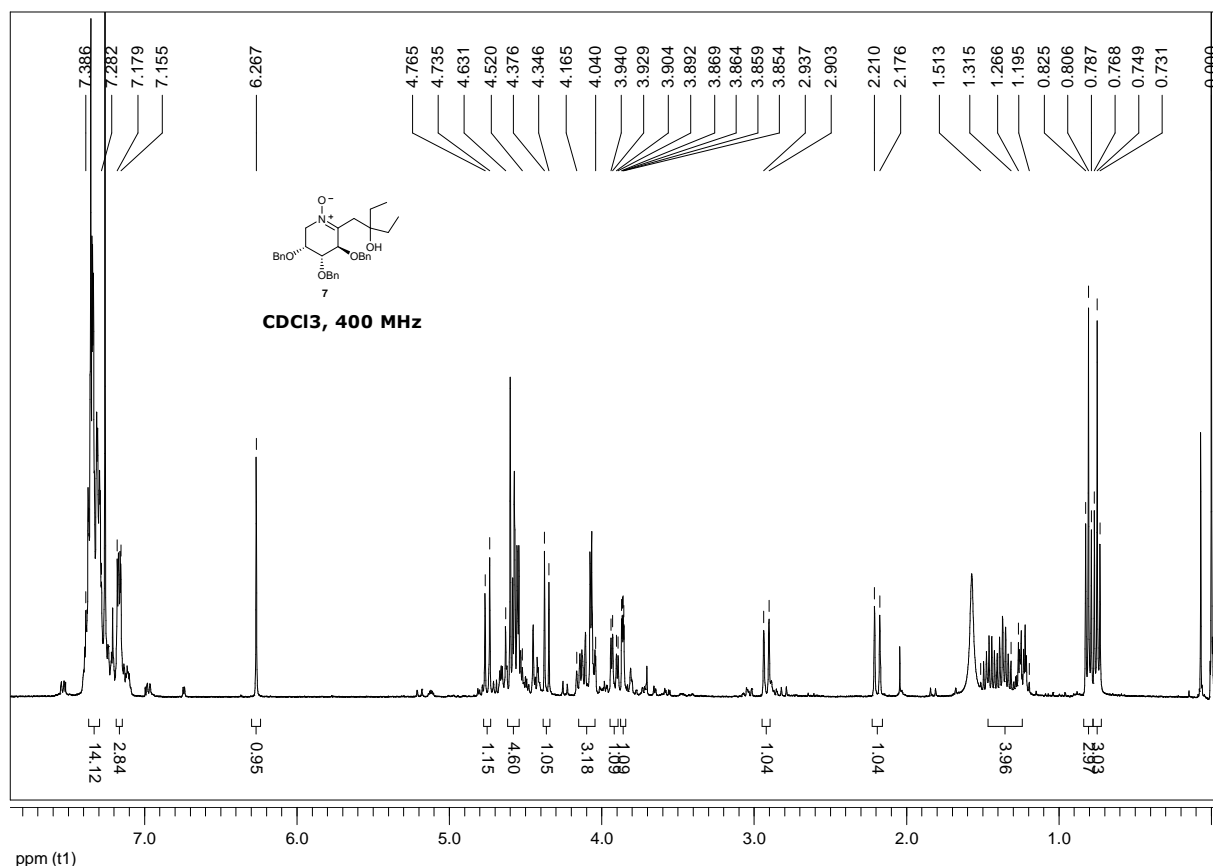


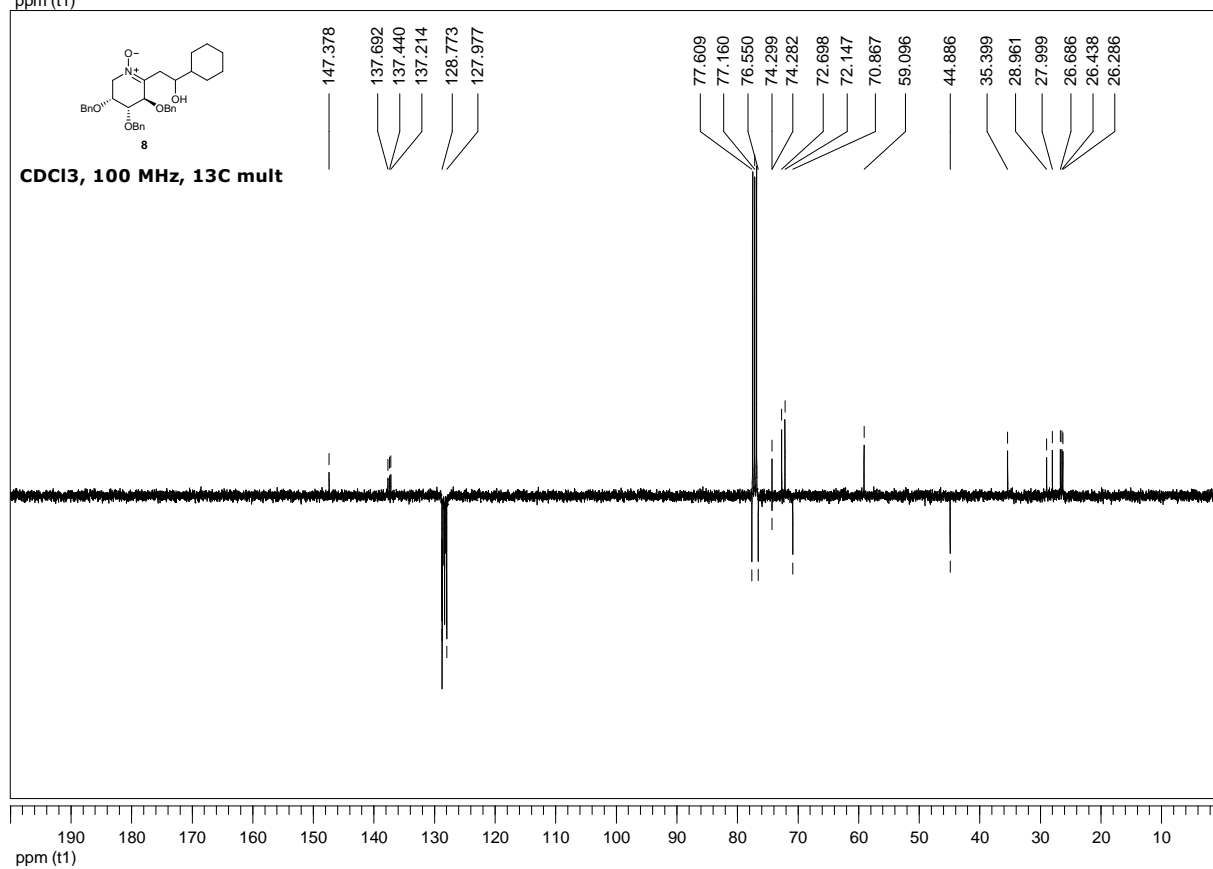
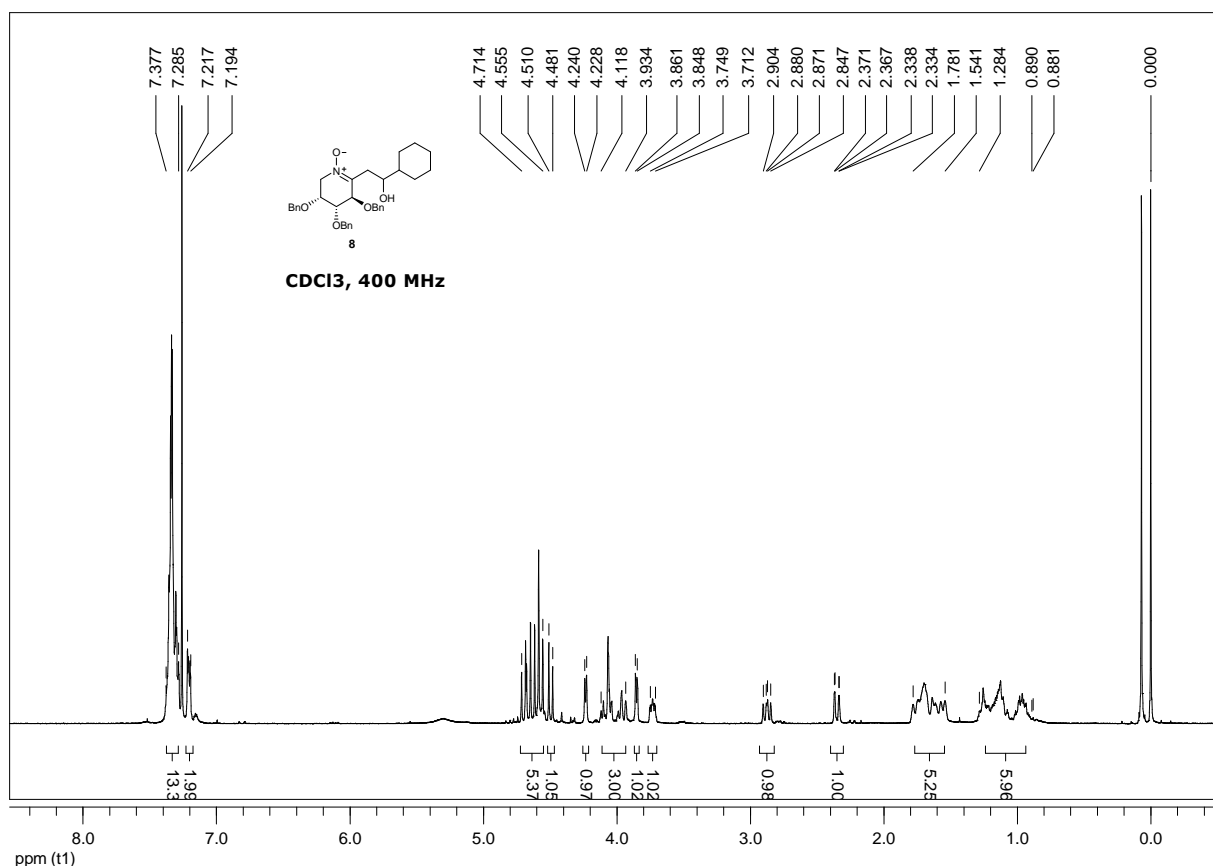


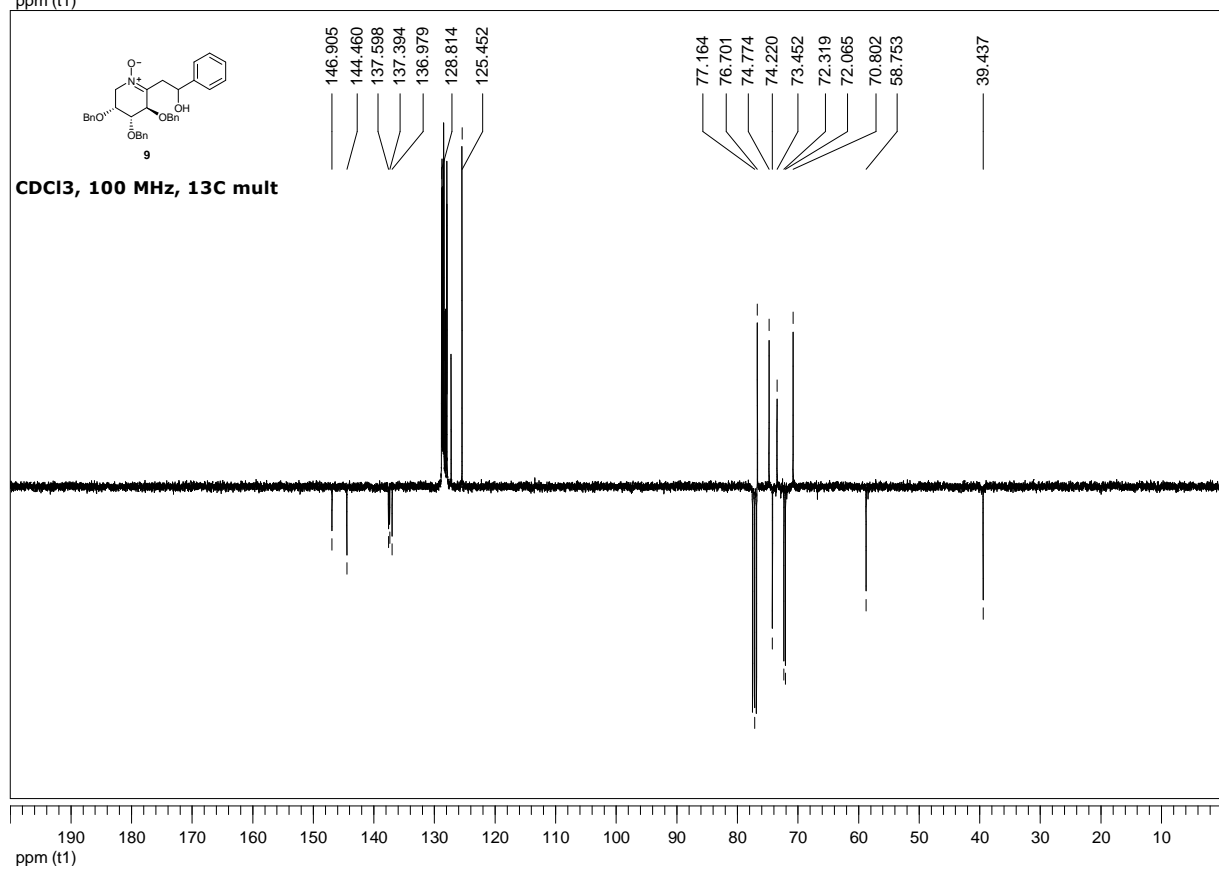
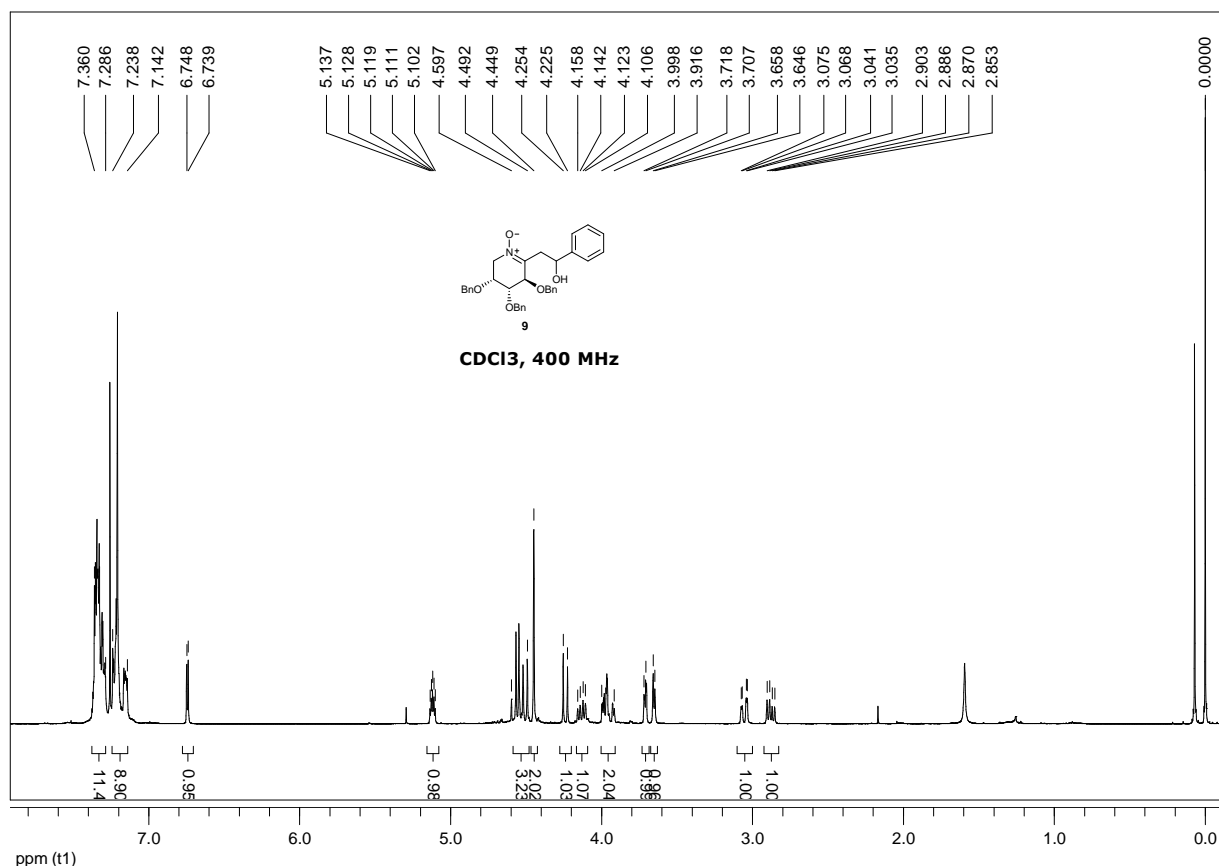


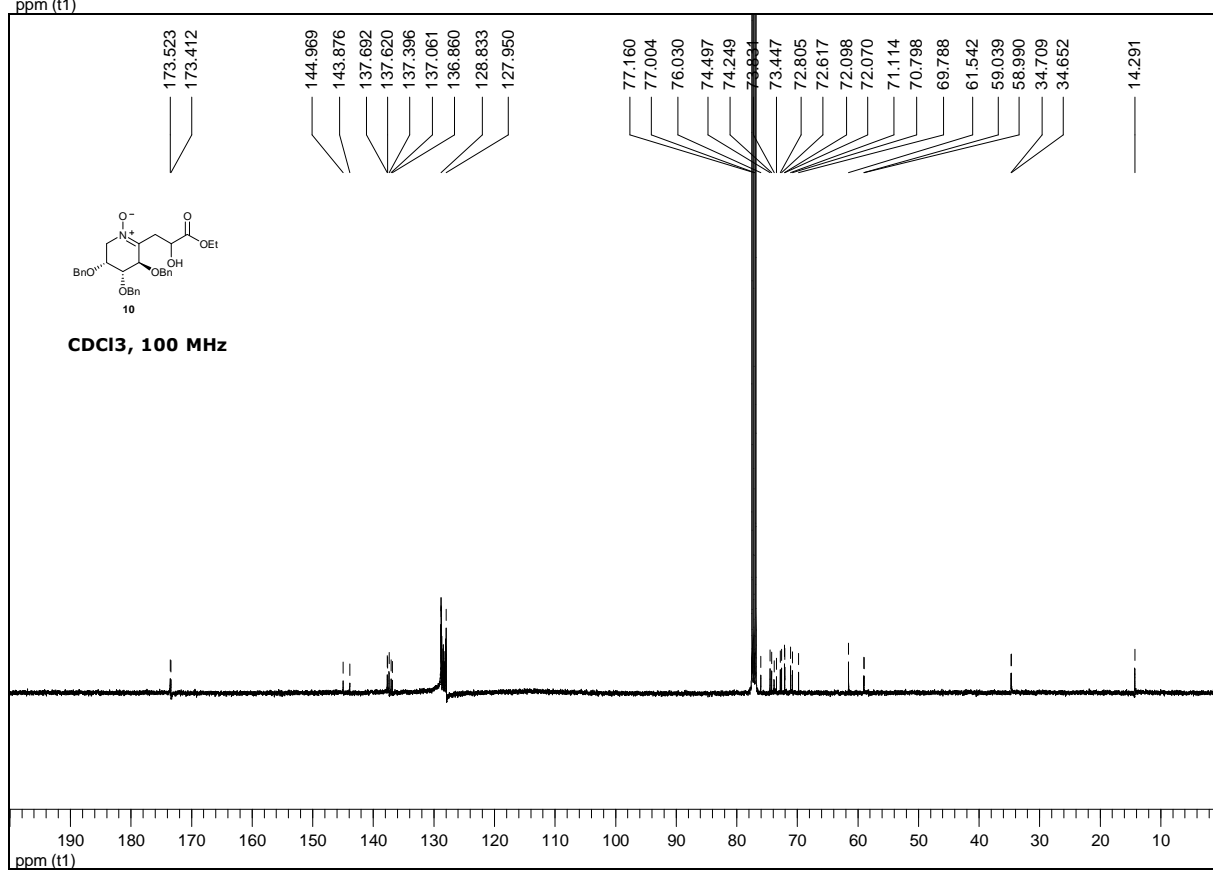
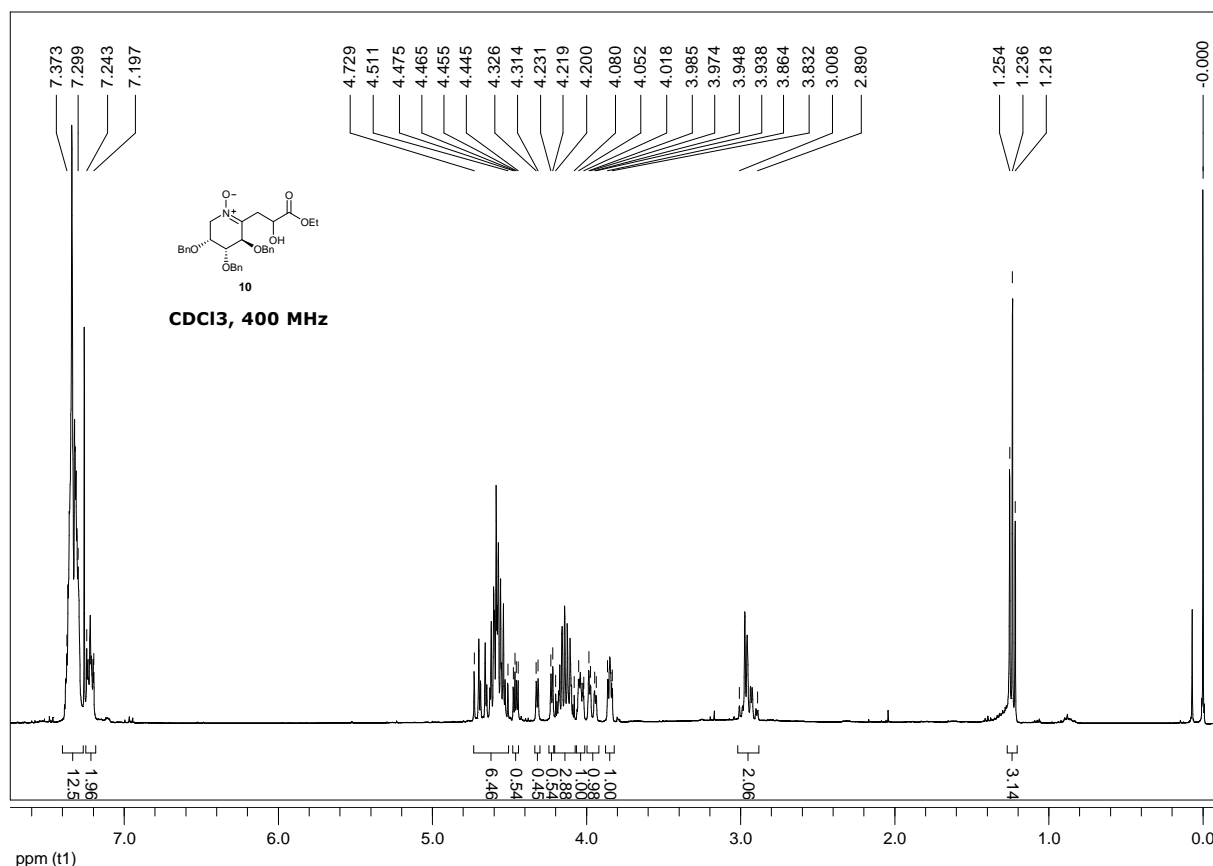


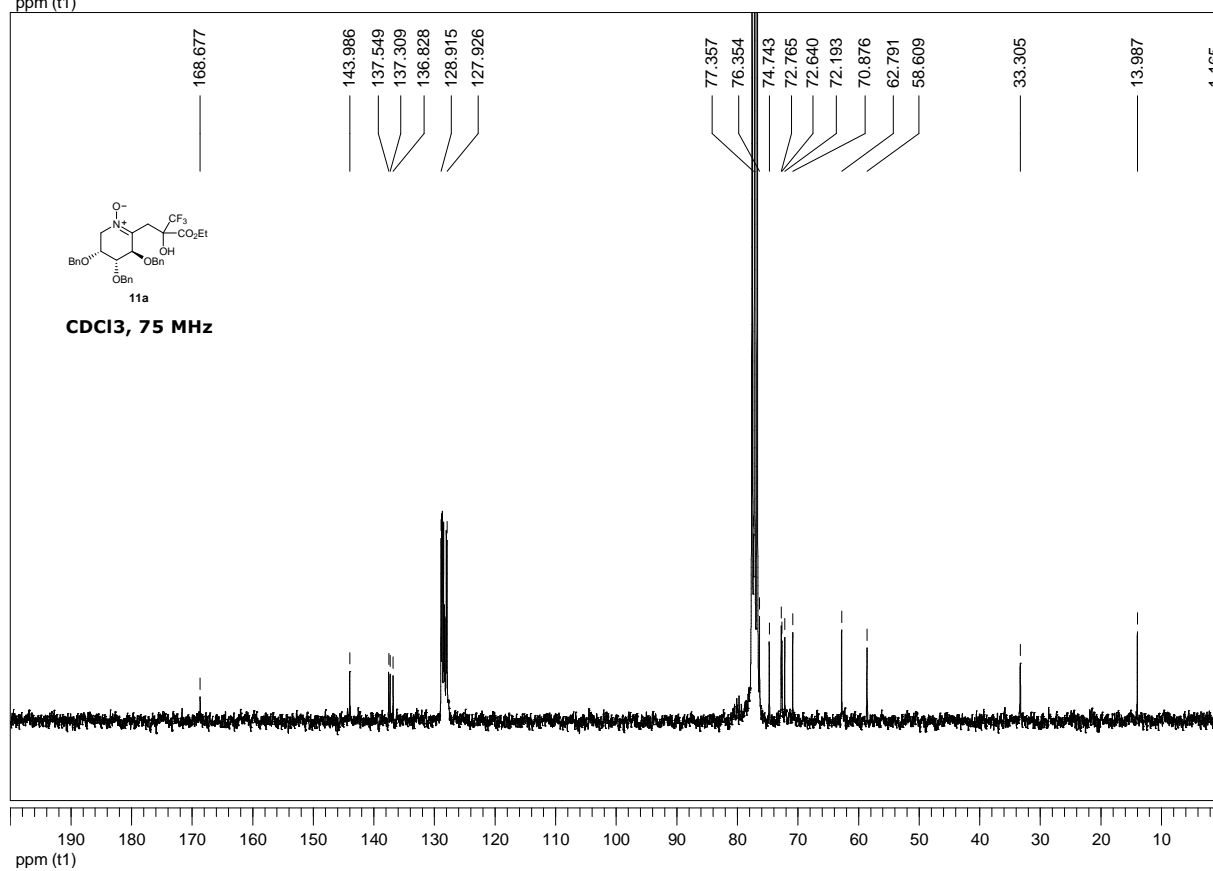
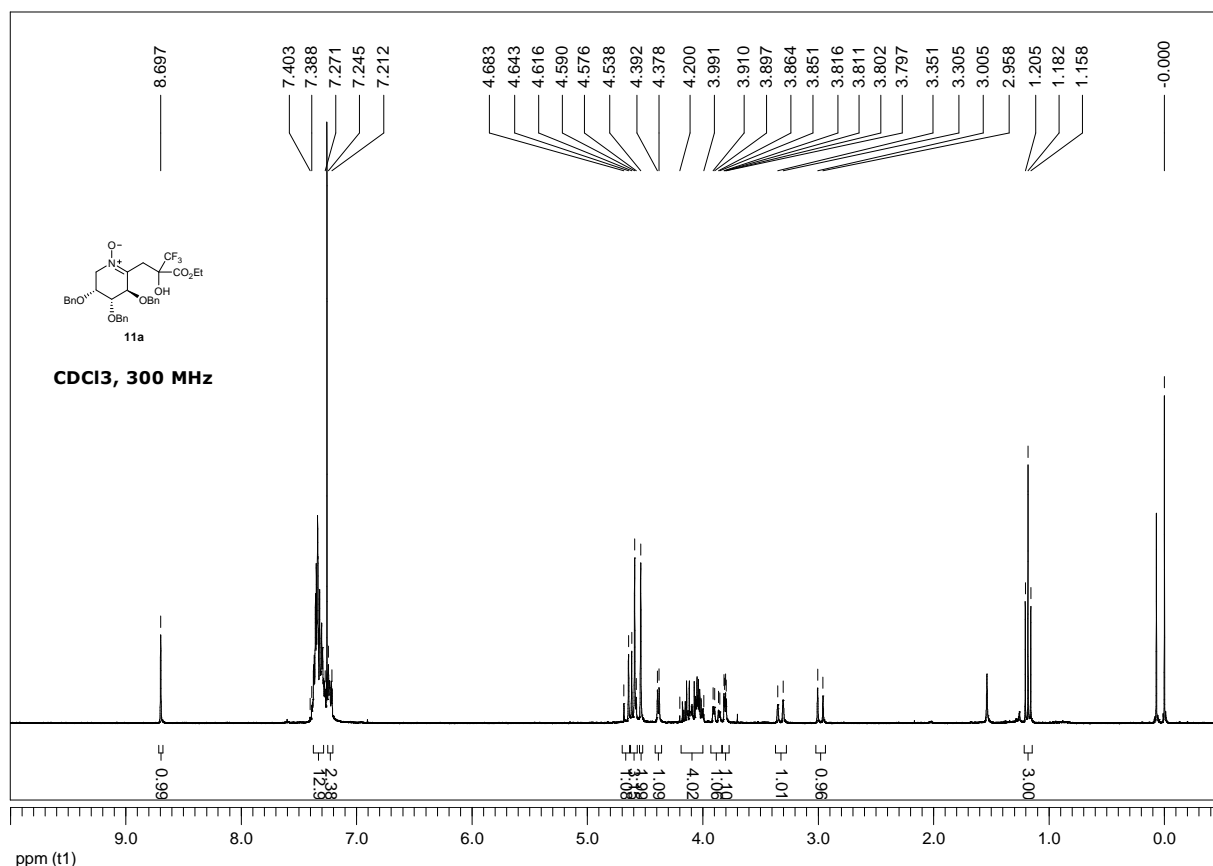


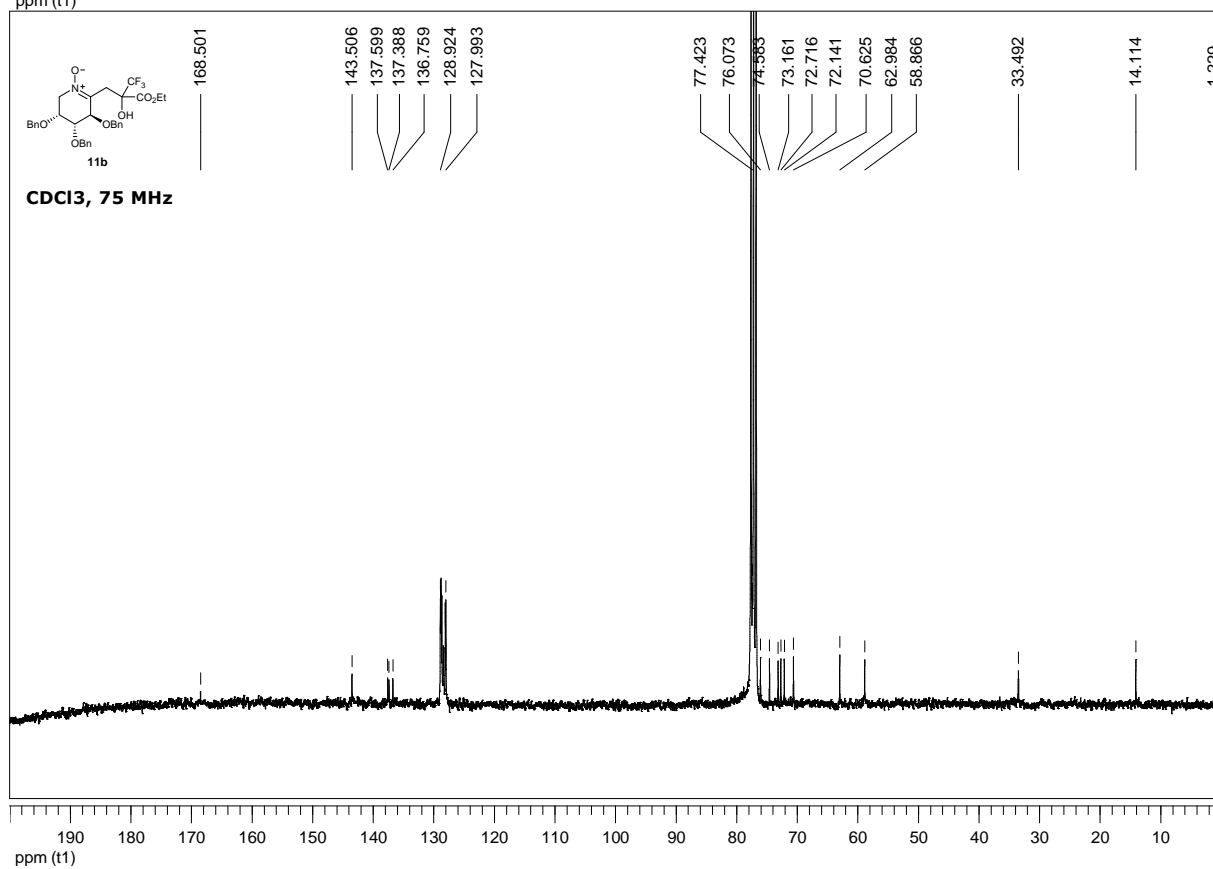
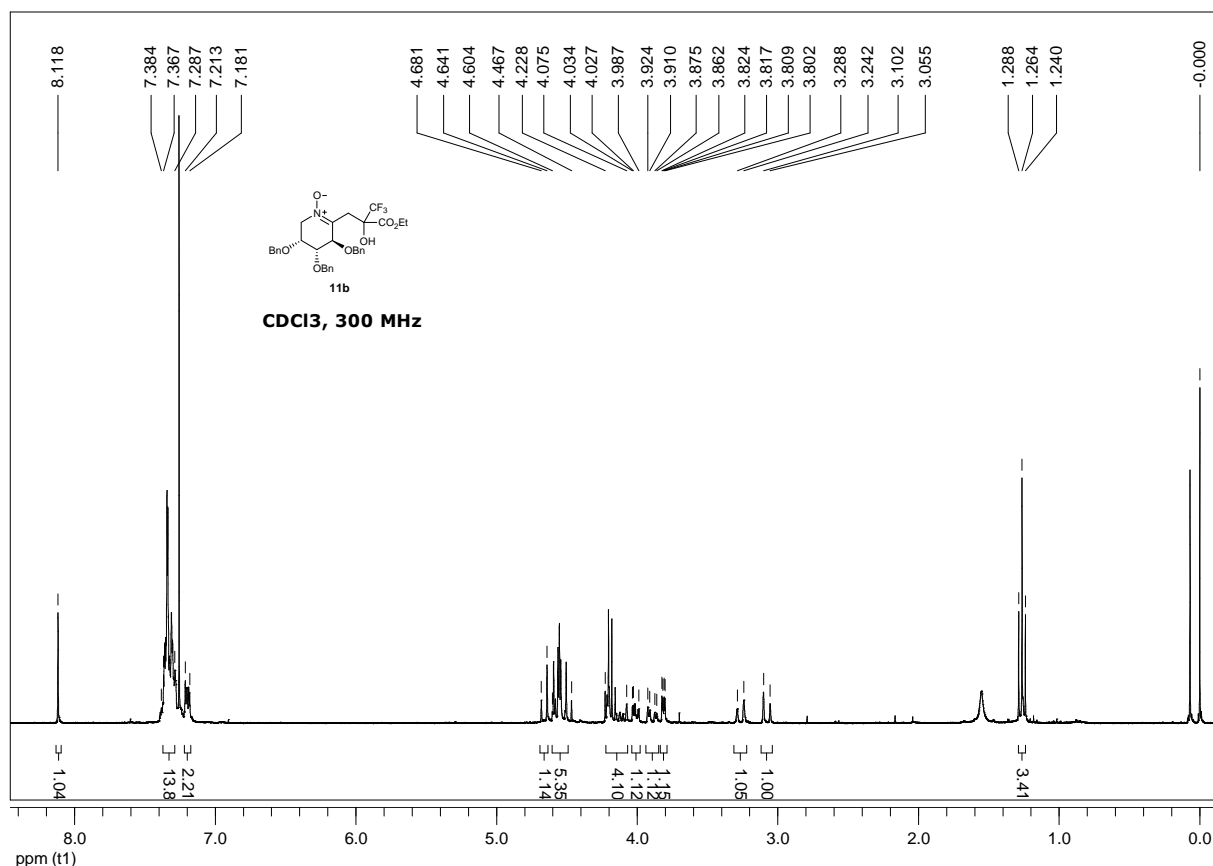












### 5 - Copie of mass spectrum (ESI) for compound 4

#### Generic Display Report (all)

