

Diastereoselective Synthesis of Substituted Diaziridines from Simple Ketones and Aldehydes

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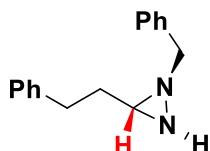
A. MATERIALS AND METHODS

Reagents were obtained from Aldrich Chemical (www.sigma-aldrich.com), Acros Organics (www.us.vwr.com) or Alfa Aesar (www.us.vwr.com) and used without further purification. Solvents were obtained from EMD Miliphore DrySol (www.us.vwr.com) and degassed with N₂. Solution phase reactions were performed in glass vials or round bottom flasks without inert atmosphere and magnetic stirring. Cold baths were generated as follows: 0 °C, wet ice/water; –10 °C, ice/acetone; –20 °C, dry ice/isopropanol monitored with a thermometer; –44 °C, dry ice/CH₃CN; –63 °C, dry ice/chloroform; –78 °C, dry ice/acetone; –100 °C, dry ice/Et₂O.

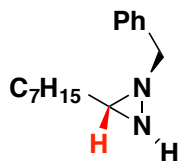
TLC was performed on 0.25 mm E. Merck silica gel 60 F254 plates and visualized under UV light (254 nm) or by staining with potassium permanganate (KMnO₄), cerium ammonium molybdenate (CAM), phosphomolybdic acid (PMA), iodine (I₂), or *p*-anisaldehyde. Silica flash chromatography was performed on E. Merck 230–400 mesh silica gel 60. Automated chromatography was performed on a ISOLERA Prime instrument with 10 g. SNAP silica gel normal phase cartridges using a flow rate of 12.0 mL/min and a gradient of 0–100% EtOAc in heptanes over 20 min with UV detection at 254 nm. UPLC was carried out on a Agilent 1100 UPLC with a Phenomenex 5 cm × 4.6 mm, 3 μm, 120 Å, C18 reverse phase column using a flow rate of 0.1 mL/min and a gradient of 80–95% CH₃CN in 0.1% aq TFA over 5 min with UV detection at 254 nm. Analytical LC–MS was carried out on a Agilent 1100 UPLC System with Ion Trap MS Detector with a Phenomenex 5 cm × 4.6 mm, 3 μm, 120 Å, C18 reverse phase column using a flow rate of 0.1 mL/min and a gradient of 80–100% CH₃CN in 0.1% aq TFA over 5 min with UV detection at 254 nm. NMR spectra were recorded on Varian Mercury II 400 MHz Spectrometer at 24 °C in CDCl₃ unless otherwise indicated. Chemical shifts are expressed in ppm relative to TMS (¹H, 0 ppm) or solvent signals: CDCl₃ (¹H, 7.23 ppm; ¹³C, 77.0 ppm; coupling constants are expressed in Hz.

B. REACTION SCOPE FOR ALDEHYDES AND KETONES:

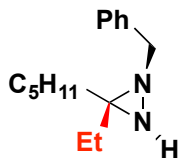
General method for the synthesis of *trans*-1,3-disubstituted-diaziridine. In a 10 mL round bottom flask at 0 °C, aldehyde/ketone (1.0 mmol, 1.0 equiv) and amine (1.0 mmol, 1.0 equiv) were dissolved in 4 mL of CHCl₃. At 0 °C, NaHCO₃ (1.5 mmol, 1.5 equiv) was added and the reaction was allowed to stir for 10 min. Then, HOSA (1 mmol, 1 equiv) was added in two portions, and the mixture was stirred until complete conversion had occurred as judged by TLC (approximately 6 h). The mixture was then cooled to 0 °C and quenched with satd aq NH₄Cl. The mixture was extracted with EtOAc (3 × 25 mL), dried (Na₂SO₄), filtered, and concentrated by rotary evaporation to afford the crude product. Purification by automated silica gel flash chromatography (heptanes/EtOAc) yielded the corresponding *trans*-1,3-disubstituted-diaziridine.



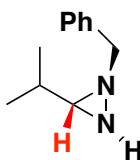
***trans*-1-Benzyl-3-phenethyldiaziridine (1a).** Purification by automated silica gel flash chromatography (10 g cartridge, 14 ml/min. 20:1 heptanes/EtOAc to 1:4 heptanes/EtOAc over 12 min) yielded the diaziridine **1a** (209 mg, 88%) as a light yellow oil. **TLC:** R_f 0.48 (1:1 heptanes/EtOAc). **UPLC:** t_{ret} = 0.92 min. **¹H-NMR** (400 MHz, CDCl₃): δ 7.40–7.05 (m, 9H), 3.63 (d, J = 7 Hz, 1H), 3.35 (d, J = 7 Hz, 1H), 2.67 (dd, J = 16.8, 5.9 Hz, 2H), 2.59–2.57 (m, 1H), 1.89–1.83 (m, 2H), 1.79 (bs, 1H). **¹³C-NMR** (125 MHz, CDCl₃): δ 140.6, 137.6, 128.5 (2C), 128.3 (2C), 128.2 (2C), 128.1 (2C), 127.2, 125.9, 64.5, 59.3, 36.0, 31.9 ppm. **ESI-MS** m/z (rel int): (pos) 239.2 ([M+H]⁺, 100); (neg) 237.2 ([M-H]⁻, 100).



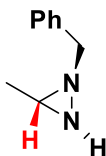
***trans*-1-benzyl-3-heptyldiaziridine (2).** Purification by automated silica gel flash chromatography (10 g cartridge, 14 ml/min. 20:1 heptanes/EtOAc to 1:4 heptanes/EtOAc over 12 min) yielded the diaziridine **2** (195 mg, 89%) as a colorless oil. **TLC:** R_f 0.64 (1:1 heptanes/EtOAc). **UPLC:** t_{ret} = 1.15 min. **¹H-NMR** (400 MHz, CDCl₃): δ 7.35–7.21 (m, 5H), 3.52 (d, J = 7 Hz, 1H), 3.43 (d, J = 7 Hz, 1H), 2.59–2.56 (m, 1H), 1.69 (bs, 1H), 1.50–1.40 (m, 2H), 1.29–1.25 (m, 2H), 1.24–1.19 (m, 8H), 0.75 (t, J = 7.5 Hz, 3H). **¹³C-NMR** (125 MHz, CDCl₃): δ 137.7, 128.6 (2C), 128.3 (2C), 127.3, 64.6, 59.8, 34.6, 31.3, 29.2, 28.5, 25.9, 22.6, 13.8 ppm. **ESI-MS** m/z (rel int): (pos) 233.2 ([M+H]⁺, 100); (neg) 231.2 ([M-H]⁻, 100).



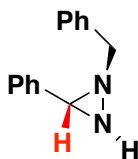
trans-1-benzyl-3-hexyl-3-methyldiaziridine (3). Purification by automated silica gel flash chromatography (10 g cartridge, 14 ml/min. 20:1 heptanes/EtOAc to 1:4 heptanes/EtOAc over 12 min) yielded the diaziridine **3** (183 mg, 84%). **TLC:** R_f 0.62 (1:1 heptanes/EtOAc). **UPLC:** t_{ret} major = 1.25 min, t_{ret} minor = 1.18 min. **$^1\text{H-NMR}$** (400 MHz, minor isomer resonances are underlined, CDCl_3): δ 7.38–7.22 (m, 5H), 3.74 (dd, $J = 13.7, 7.5$ Hz, 1H), 3.65 (dd, $J = 13.7, 5.9$ Hz, 1H), 1.98 (s, 0.66H), 1.95 (s, 0.33H), 1.78–1.58 (m, 3H), 1.49–1.40 (m, 2H), 1.38–1.20 (m, 5H), 1.16 (t, $J = 7.3$ Hz, 1.1 H), 0.93–0.82 (m, 4.9H). **$^{13}\text{C-NMR}$** (125 MHz, CDCl_3): δ 139.1, 128.4 (2C), 128.2 (2C), 126.9, 64.4, 56.9, 56.8, 37.9, 32.2, 31.9, 31.2, 28.2, 25.3, 24.5, 22.6, 21.6, 14.0, 9.9, 9.0 ppm. **ESI-MS** m/z (rel int): (pos) 233.3 ($[\text{M}+\text{H}]^+$, 100); (neg) 231.3 ($[\text{M}-\text{H}]^-$, 100).



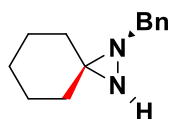
trans-1-benzyl-3-isopropylidiaziridine (4). Purification by automated silica gel flash chromatography (10 g cartridge, 14 ml/min. 20:1 heptanes/EtOAc to 1:4 heptanes/EtOAc over 12 min) yielded the diaziridine **4** (132 mg, 80%) as light yellow oil. **TLC:** R_f 0.57 (1:1 heptanes/EtOAc). **UPLC:** $t_{ret} = 1.00$ min. **$^1\text{H-NMR}$** (400 MHz, CDCl_3): δ 7.45–7.25 (m, 5H), 3.66 (d, $J = 7$ Hz, 1H), 3.44 (d, $J = 7$ Hz, 1H), 2.44 (d, $J = 8$ Hz, 1H), 1.82 (bs, 1H), 1.33 (septet, $J = 7.5$ Hz, 2H), 0.98 (d, $J = 7.5$ Hz, 3H), 0.95 (d, $J = 7.5$ Hz, 3H). **$^{13}\text{C-NMR}$** (125 MHz, CDCl_3): δ 137.7, 129.1 (2C), 128.6 (2C), 127.3, 65.9, 65.1, 33.1, 18.8, 18.1 ppm. **ESI-MS** m/z (rel int): (pos) 177.3 ($[\text{M}+\text{H}]^+$, 100); (neg) 175.3 ($[\text{M}-\text{H}]^-$, 100).



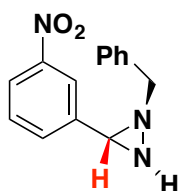
trans-1-benzyl-3-methyldiaziridine (5). Purification by automated silica gel flash chromatography (10 g cartridge, 14 ml/min. 20:1 heptanes/EtOAc to 1:4 heptanes/EtOAc over 12 min) yielded the diaziridine **5** (118 mg, 85%) as a colorless oil. **TLC:** R_f 0.53 (1:1 heptanes/EtOAc). **UPLC:** $t_{ret} = 1.06$ min. **$^1\text{H-NMR}$** (400 MHz, CDCl_3): δ 7.42–7.24 (m, 5H), 3.59 (d, $J = 6.9$ Hz, 1H), 3.52 (d, $J = 6.9$ Hz, 1H), 3.59 (d, $J = 6.9$ Hz, 1H), 2.71 (dq, $J = 7.3, 4.9$ Hz, 1H), 1.66 (bs, 1H), 1.38 (d, $J = 4.9$ Hz, 3H). **$^{13}\text{C-NMR}$** (100 MHz, CDCl_3): δ 138.2, 128.7 (2C), 128.4 (2C), 127.5, 64.8, 56.2, 20.3 ppm. **ESI-MS** m/z (rel int): (pos) 149.2 ($[\text{M}+\text{H}]^+$, 100); (neg) 147.2 ($[\text{M}-\text{H}]^-$, 100).



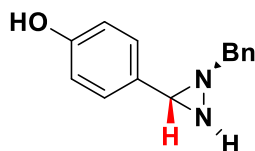
trans-1-benzyl-3-phenyldiaziridine (6). Purification by automated silica gel flash chromatography (10 g cartridge, 14 ml/min. 20:1 heptanes/EtOAc to 1:4 heptanes/EtOAc over 12 min) yielded the diaziridine **6** (172 mg, 87%) as a light yellow oil. **TLC:** R_f 0.51 (1:1 heptanes/EtOAc). **UPLC:** $t_{ret} = 1.03$ min. **$^1\text{H-NMR}$** (400 MHz, CDCl_3): δ 7.54–7.25 (m, 10H), 3.82 (d, $J = 7.1$ Hz, 1H), 3.74 (d, $J = 7.1$ Hz, 1H), 3.59 (d, $J = 3.5$ Hz, 1H), 2.09 (d, $J = 3.1$ Hz, 1H). **$^{13}\text{C-NMR}$** (100 MHz, CDCl_3): δ 137.6, 137.5, 129.9 (2C), 128.8 (2C), 128.7 (2C), 127.3 (2C), 127.0, 126.3, 64.7, 60.0 ppm. **ESI-MS** m/z (rel int): (pos) 211.2 ($[\text{M}+\text{H}]^+$, 100); (neg) 209.2 ($[\text{M}-\text{H}]^-$, 100).



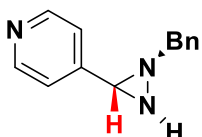
1-benzyl-1,2-diazaspiro[2.5]octane (7). Purification by automated silica gel flash chromatography (10 g cartridge, 14 ml/min. 20:1 heptanes/EtOAc to 1:4 heptanes/EtOAc over 12 min) yielded the diaziridine **7** (181 mg, 91%) as a colorless oil. **TLC:** R_f 0.60 (1:1 heptanes/EtOAc). **UPLC:** $t_{ret} = 1.12$ min. **$^1\text{H-NMR}$** (400 MHz, CDCl_3): δ 7.41–7.22 (m, 5H), 3.78 (d, $J = 13.8$ Hz, 1H), 3.69 (d, $J = 13.8$ Hz, 1H), 2.01 (s, 1H), 1.85–1.72 (m, 2H), 1.72–1.56 (m, 5H), 1.56–1.41 (m, 3H). **$^{13}\text{C-NMR}$** (100 MHz, CDCl_3): δ 139.3, 128.6 (2C), 128.5 (2C), 127.1, 62.0, 56.6, 39.4, 28.5, 25.7, 25.3, 25.2 ppm. **ESI-MS** m/z (rel int): (pos) 211.2 ($[\text{M}+\text{H}]^+$, 100); (neg) 209.2 ($[\text{M}-\text{H}]^-$, 100).



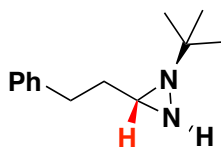
trans-1-benzyl-3-(3-nitrophenyl)diaziridine (8). Purification by automated silica gel flash chromatography (10 g cartridge, 14 ml/min. 20:1 heptanes/EtOAc to 1:4 heptanes/EtOAc over 12 min) yielded the diaziridine **8** (187 mg, 78%) as a colorless oil. **TLC:** R_f 0.48 (1:1 heptanes/EtOAc). **UPLC:** $t_{ret} = 1.10$ min. **$^1\text{H-NMR}$** (400 MHz, CDCl_3): δ 8.28–8.22 (m, 1H), 8.16–8.09 (m, 1H), 7.72–7.68 (m, 1H), 7.53–7.49 (m, 1H), 7.38–7.33 (m, 4H), 7.29–7.24 (m, 1H), 4.82 (s, 1H), 3.92 (d, $J = 2.4$ Hz, 1H), 3.83 (d, $J = 2.2$ Hz, 1H), 1.76 (bs, 1H). **$^{13}\text{C-NMR}$** (100 MHz, CDCl_3): δ 142.8, 139.9, 134.4, 129.6 (2C), 129.4 (2C), 128.7 (2C), 128.4 (2C), 123.3, 122.2, 53.5, 52.4 ppm. **ESI-MS** m/z (rel int): (pos) 256.2 ($[\text{M}+\text{H}]^+$, 100); (neg) 254.2 ($[\text{M}-\text{H}]^-$, 100).



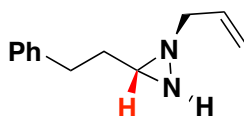
trans-4-(1-benzylidiaziridin-3-yl)phenol (9). Purification by automated silica gel flash chromatography (10 g cartridge, 14 ml/min. 20:1 heptanes/EtOAc to 1:4 heptanes/EtOAc over 12 min) yielded the diaziridine **9** (170 mg, 80%) as a yellow oil. **TLC:** R_f 0.35 (1:1 heptanes/EtOAc). **UPLC:** t_{ret} = 1.08 min. **$^1\text{H-NMR}$** (400 MHz, CDCl_3): δ 8.59 (bs, 1H), 8.07 (s, 1H), 7.43–7.21 (m, 6H), 7.12–7.07 (m, 3H), 6.88 (d, J = 7.1 Hz, 1H), 3.82 (d, J = 8.4 Hz, 1H), 3.76 (d, J = 8.2 Hz, 1H), 3.57 (d, J = 2.6 Hz, 1H), 2.19 (bs, 1H). **$^{13}\text{C-NMR}$** (100 MHz, CDCl_3): δ 137.6, 137.5, 129.9 (2C), 128.8 (2C), 128.7 (2C), 127.3 (2C), 127.0, 126.3, 64.7, 60.0 ppm. **ESI-MS** m/z (rel int): (pos) 227.2 ($[\text{M}+\text{H}]^+$, 100); (neg) 225.2 ($[\text{M}-\text{H}]^-$, 100).



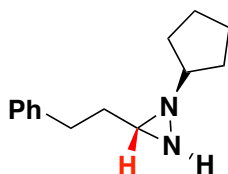
trans-4-(1-benzylidiaziridin-3-yl)pyridine (10). Purification by automated silica gel flash chromatography (10 g cartridge, 14 ml/min. 20:1 heptanes/EtOAc to 1:4 heptanes/EtOAc over 12 min) yielded the diaziridine **10** (169 mg, 85%) as a colorless oil. **TLC:** R_f 0.32 (1:1 heptanes/EtOAc). **UPLC:** t_{ret} = 0.95 min. **$^1\text{H-NMR}$** (400 MHz, CDCl_3): δ 8.55–8.51 (m, 2H), 7.44–7.23 (m, 7H), 3.78 (d, J = 7.1 Hz, 1H), 3.68 (d, J = 7.1 Hz, 1H), 3.48 (d, J = 2.2 Hz, 1H), 2.22 (d, J = 2.4 Hz, 1H). **$^{13}\text{C-NMR}$** (125 MHz, CDCl_3): δ 149.9, 146.2, 137.0, 128.1 (2C), 128.0 (2C), 127.3, 121.1, 64.3, 58.2 ppm. **ESI-MS** m/z (rel int): (pos) 212.1 ($[\text{M}+\text{H}]^+$, 100); (neg) 210.2 ($[\text{M}-\text{H}]^-$, 100).

C. REACTION SCOPE FOR AMINES:

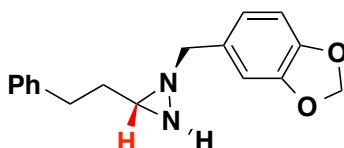
trans-1-(tert-butyl)-3-phenethylidiaziridine (11). Purification by automated silica gel flash chromatography (10 g cartridge, 14 ml/min. 20:1 heptanes/EtOAc to 1:4 heptanes/EtOAc over 12 min) yielded the diaziridine **11** (171 mg, 89%) as a colorless oil. **TLC:** R_f 0.31 (1:1 hexanes/EtOAc). **UPLC:** t_{ret} = 0.91 min. **$^1\text{H-NMR}$** (400 MHz, CDCl_3): δ 7.31–7.19 (m, 5H), 2.92–2.59 (m, 3H), 1.95 (ddd, J = 8.5, 4.3, 1.6 Hz, 1H), 1.73 (td, J = 6.7, 2.9 Hz, 1H), 1.39 (d, J = 7.3 Hz, 1H), 4.01 (s, 9H). **$^{13}\text{C-NMR}$** (100 MHz, CDCl_3): δ 140.9, 128.4 (2C), 128.1 (2C), 125.6, 54.8, 52.5, 36.8, 32.4, 25.7 (3C) ppm. **ESI-MS** m/z (rel int): (pos) 205.1 ($[\text{M}+\text{H}]^+$, 100); (neg) 203.1 ($[\text{M}-\text{H}]^-$, 100).



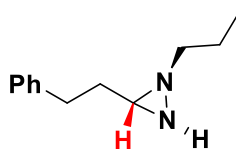
trans-1-allyl-3-phenethylidiaziridine (12). Purification by automated silica gel flash chromatography (10 g cartridge, 14 ml/min. 20:1 heptanes/EtOAc to 1:4 heptanes/EtOAc over 12 min) yielded the diaziridine **12** (138 mg, 78%) as a colorless oil. **TLC:** R_f 0.31 (1:1 hexanes/EtOAc). **UPLC:** t_{ret} = 0.98 min. **$^1\text{H-NMR}$** (400 MHz, CDCl_3): δ 7.32–7.20 (m, 5H), 5.88 (dddd, J = 16, 10, 8, 6.5 Hz, 1H), 5.25 (d, J = 16 Hz), 5.21 (d, J = 10 Hz), 3.00 (td, J = 6.2, 5.3 Hz, 2H), 3.00 (dt, J = 6.2, 1.3 Hz, 2H), 2.81 (t, J = 7.3 Hz, 2H), 2.54 (dd, J = 7.2, 5.4 Hz, 1H), 1.88 (td, J = 7.6, 5.4 Hz, 2H), 1.67 (d, J = 7.3 Hz, 1H). **$^{13}\text{C-NMR}$** (100 MHz, CDCl_3): δ 140.7, 133.8, 128.4 (2C), 128.2 (2C), 126.1, 117.4, 63.2, 59.3, 36.2, 32.1 ppm. **ESI-MS** m/z (rel int): (pos) 189.1 ($[\text{M}+\text{H}]^+$, 100); (neg) 187.1 ($[\text{M}-\text{H}]^-$, 100).



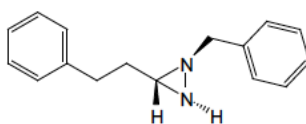
trans-1-cyclopentyl-3-phenethylidiaziridine (13). Purification by automated silica gel flash chromatography (10 g cartridge, 14 ml/min. 20:1 heptanes/EtOAc to 1:4 heptanes/EtOAc over 12 min) yielded the diaziridine **13** (154 mg, 76%) as a colorless oil. **TLC:** R_f 0.31 (1:1 hexanes/EtOAc). **UPLC:** t_{ret} = 0.93 min. **$^1\text{H-NMR}$** (400 MHz, CDCl_3): δ 7.40–7.12 (m, 5H), 2.81 (dt, J = 7.1, 6.7 Hz, 2H), 2.58–2.43 (m, 1H), 2.16 (d, J = 6.3 Hz, 1H), 1.92 (dt, J = 9.0, 6.8 Hz, 1H), 1.87–1.84 (m, 6H), 1.62–1.39 (m, 3H). **$^{13}\text{C-NMR}$** (100 MHz, CDCl_3): δ 140.7, 128.4 (2C), 128.2 (2C), 126.0, 71.0, 59.2, 36.2, 32.3, 32.1, 30.6, 24.7, 24.4 ppm. **ESI-MS** m/z (rel int): (pos) 217.1 ($[\text{M}+\text{H}]^+$, 100); (neg) 215.1 ($[\text{M}-\text{H}]^-$, 100).



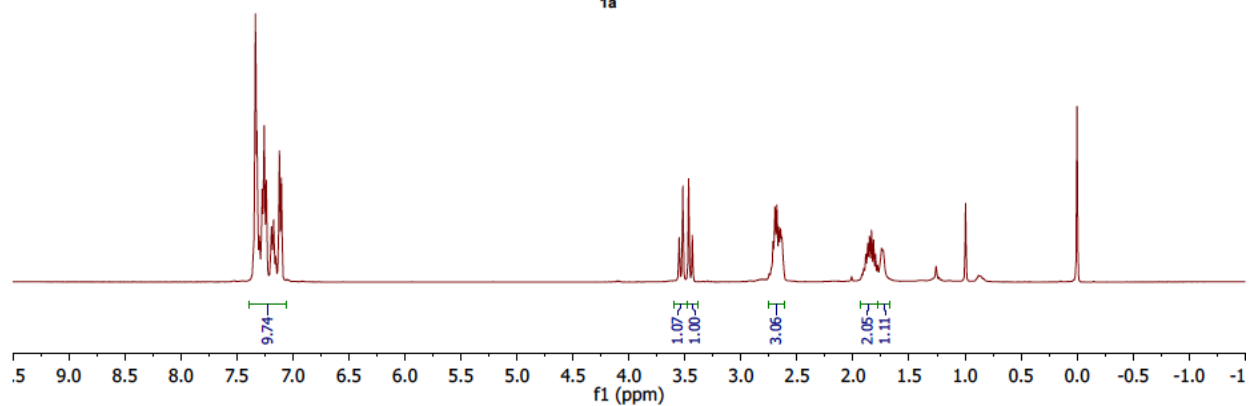
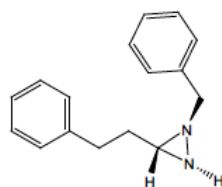
trans-1-(benzo[d][1,3]dioxol-5-ylmethyl)-3-phenethylidiaziridine (14). Purification by automated silica gel flash chromatography (10 g cartridge, 14 ml/min. 20:1 heptanes/EtOAc to 1:4 heptanes/EtOAc over 12 min) yielded the diaziridine **14** (226 mg, 85%) as a colorless oil. **TLC:** R_f 0.31 (1:1 hexanes/EtOAc). **UPLC:** t_{ret} = 1.29 min. **$^1\text{H-NMR}$** (400 MHz, CDCl_3): δ 7.37–7.06 (m, 5H), 6.87 (s, 1H), 6.76 (d, J = 7.3 Hz, 2H), 5.90 (s, 2H), 3.39 (s, 2H), 2.71 (t, J = 7.7 Hz, 1H), 2.60 (bs, 1H), 1.99–1.66 (m, 4H). **$^{13}\text{C-NMR}$** (100 MHz, CDCl_3): δ 147.4, 140.7, 140.6, 131.4, 128.3 (2C), 128.2 (2C), 126.0, 121.8, 109.1, 108.0, 100.7, 64.3, 59.2, 36.0, 31.9 ppm. **ESI-MS** m/z (rel int): (pos) 283.1 ($[\text{M}+\text{H}]^+$, 100); (neg) 281.0 ($[\text{M}-\text{H}]^-$, 100).



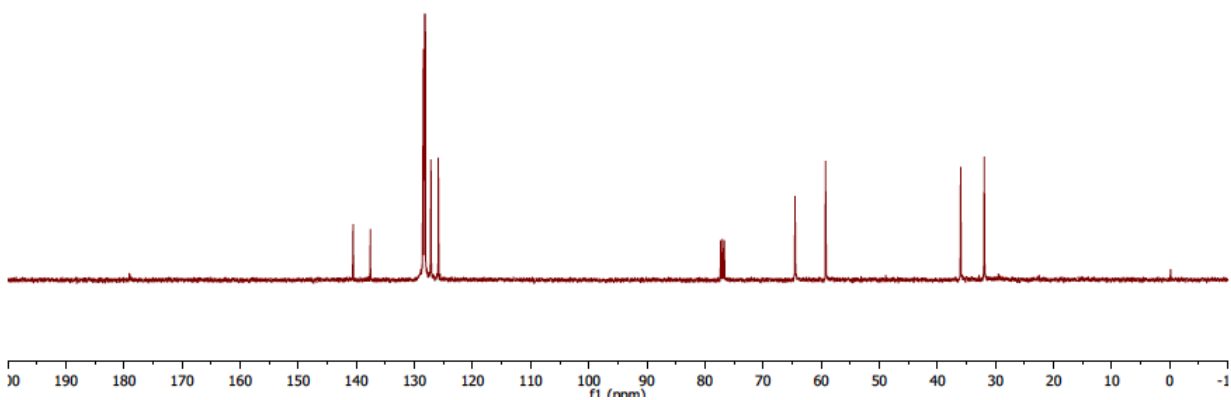
trans-3-phenethyl-1-propyldiaziridine (15). Purification by automated silica gel flash chromatography (10 g cartridge, 14 ml/min. 20:1 heptanes/EtOAc to 1:4 heptanes/EtOAc over 12 min) yielded the diaziridine **15** (170 mg, 94%) as a colorless oil. **TLC:** R_f 0.31 (1:1 hexanes/EtOAc). **UPLC:** t_{ret} = 1.01 min. **$^1\text{H-NMR}$** (400 MHz, CDCl_3): δ 7.26–7.15 (m, 5H), 2.75 (td, J = 7.5, 4.9 Hz, 2H), 2.42 (q, J = 6.0 Hz, 1H), 2.38 – 2.29 (m, 1H), 2.30 – 2.17 (m, 1H), 1.88 – 1.72 (m, 2H), 1.64 – 1.50 (m, 3H), 0.91 (t, J = 7.4 Hz, 3H). **$^{13}\text{C-NMR}$** (100 MHz, CDCl_3): δ 140.5, 128.2 (2C), 128.0 (2C), 125.8, 62.5, 59.2, 36.0, 31.9, 21.5, 11.6 ppm. **ESI-MS** m/z (rel int): (pos) 191.1 ($[\text{M}+\text{H}]^+$, 100); (neg) 189.1 ($[\text{M}-\text{H}]^-$, 100).

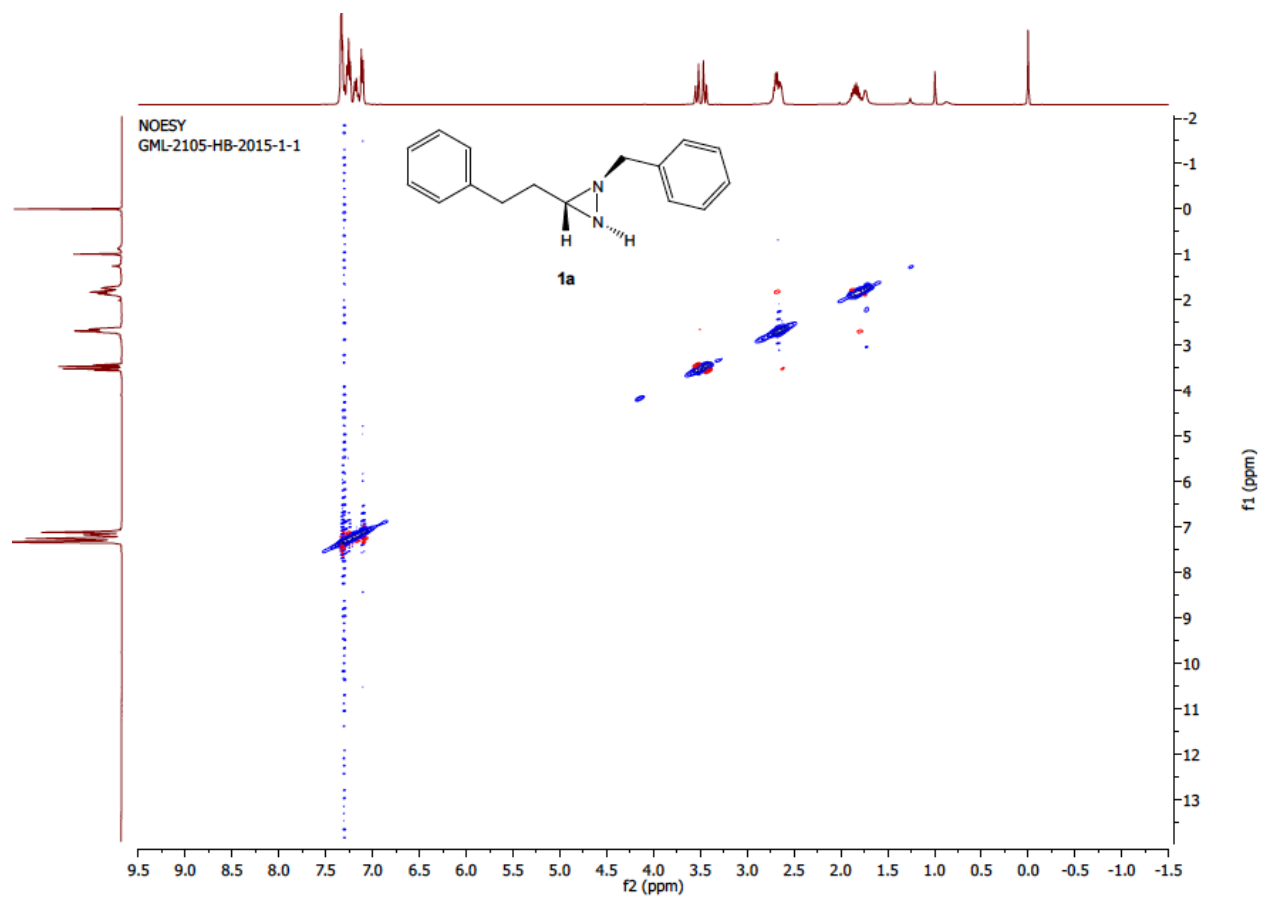
PROTON
HB

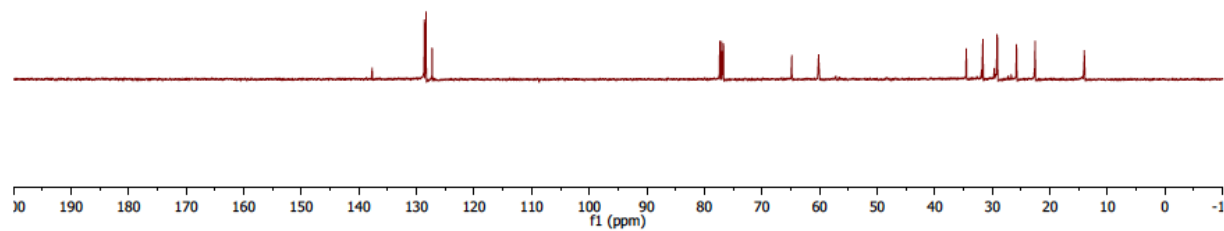
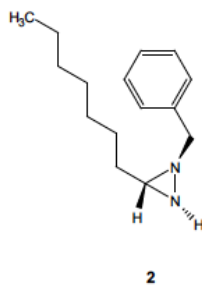
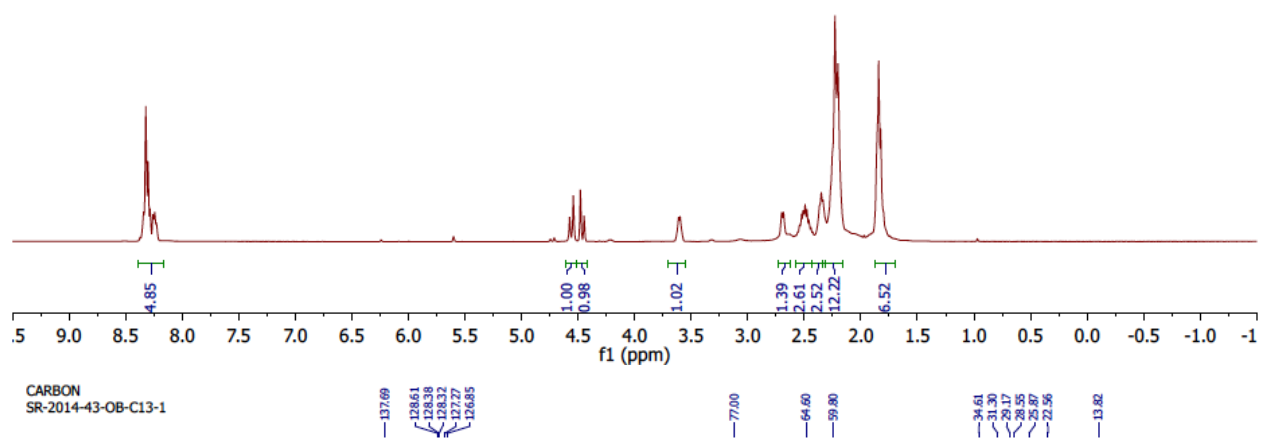
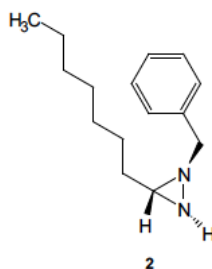
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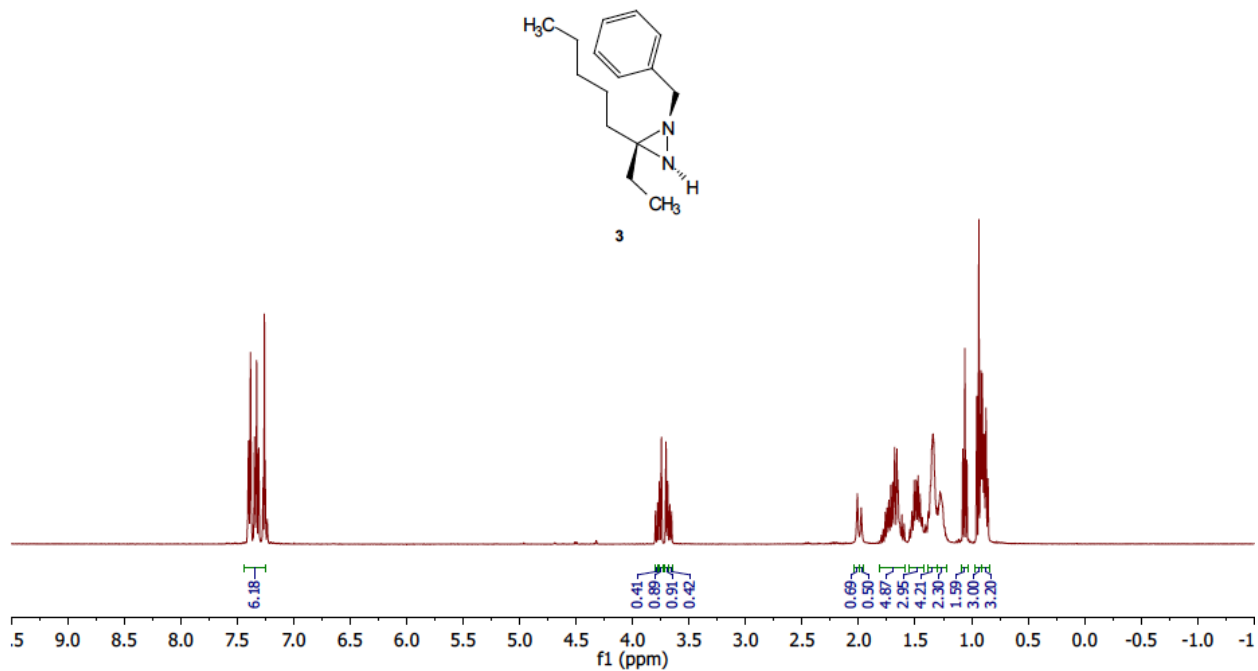
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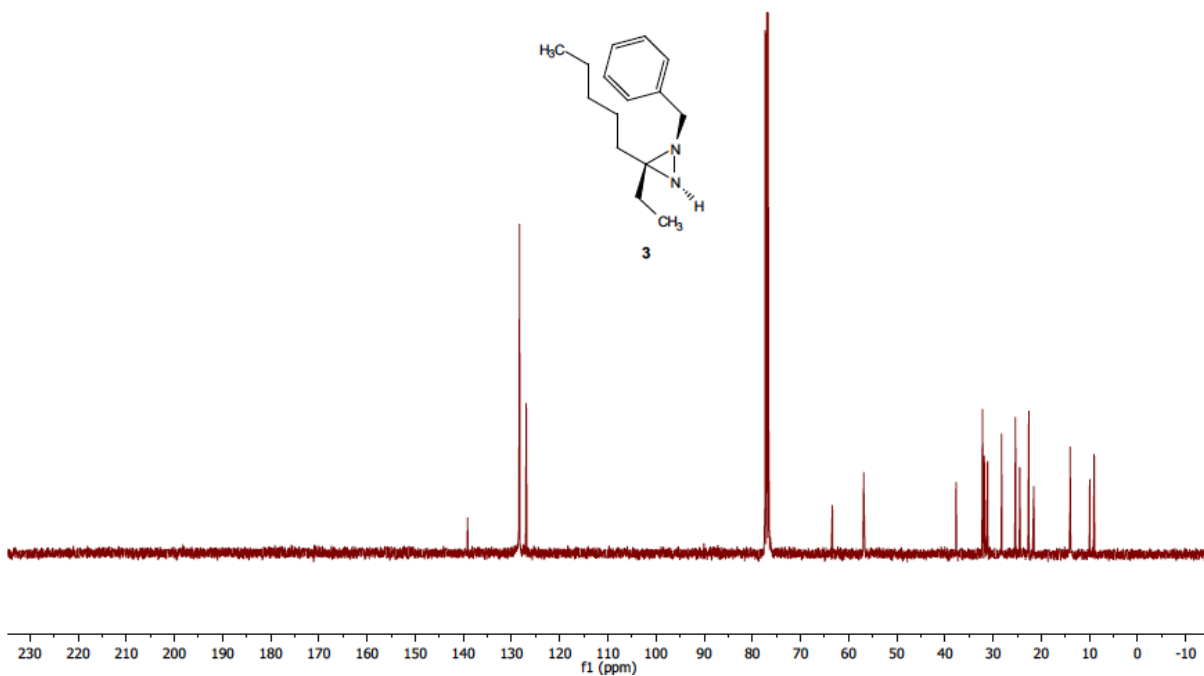


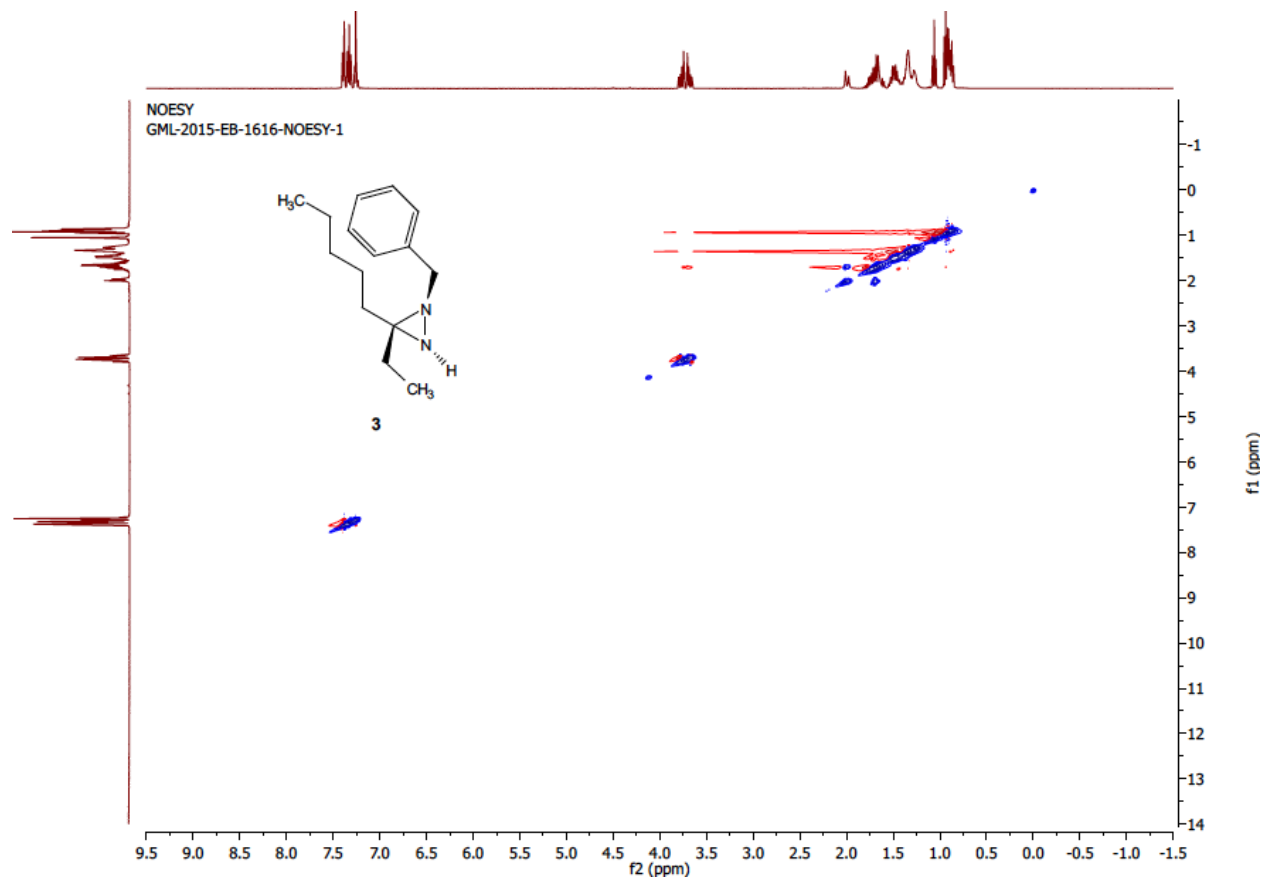
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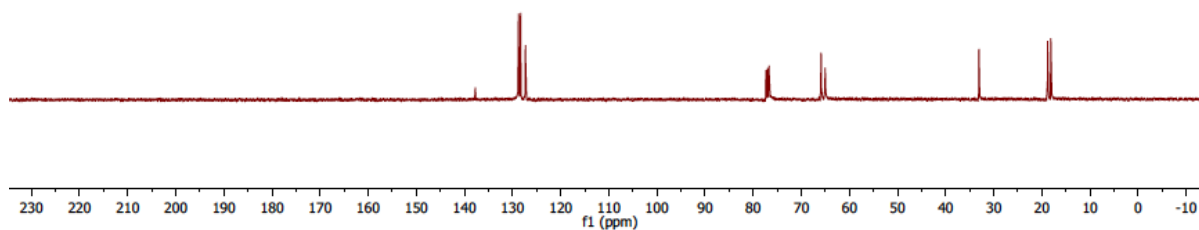
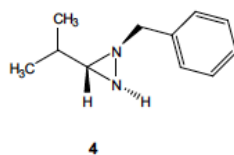
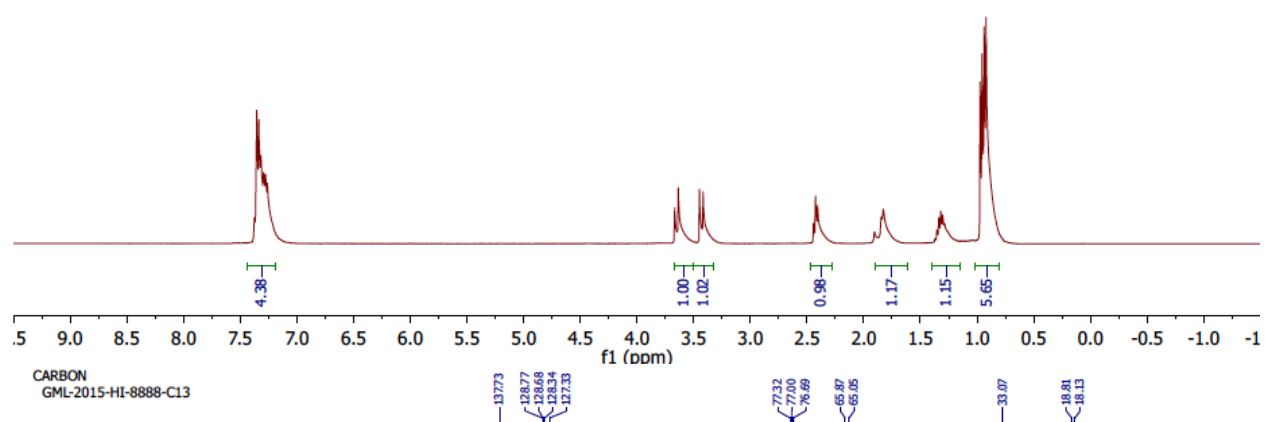
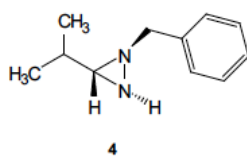


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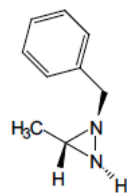




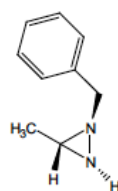
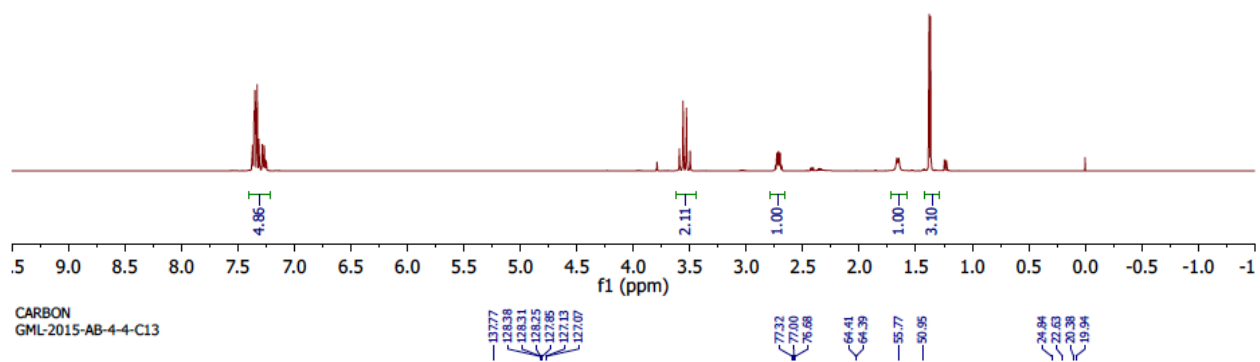
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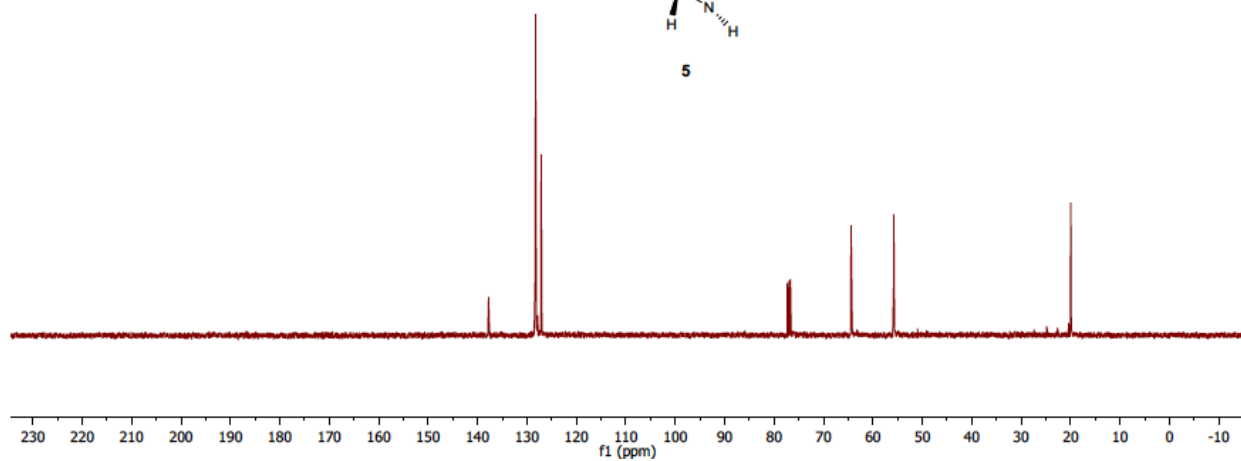
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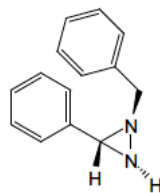
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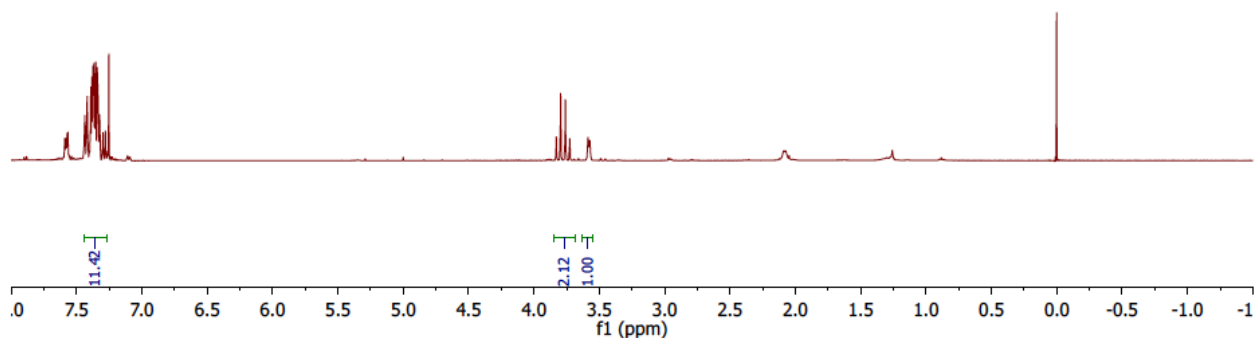
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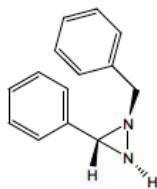


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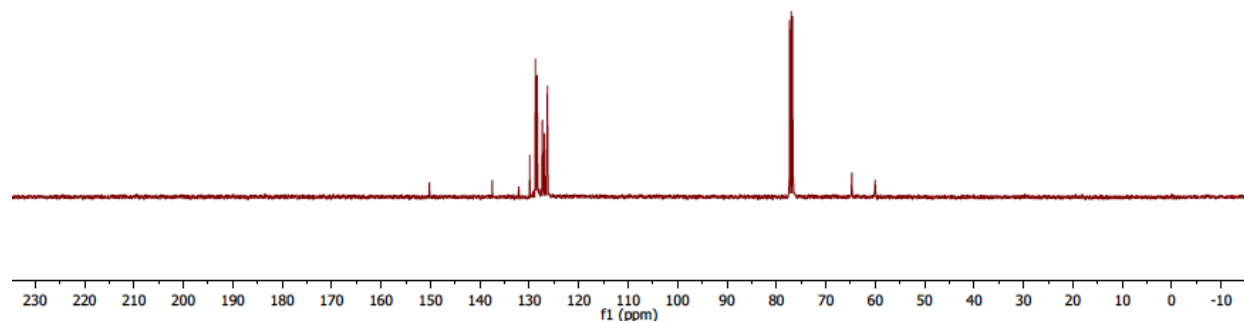


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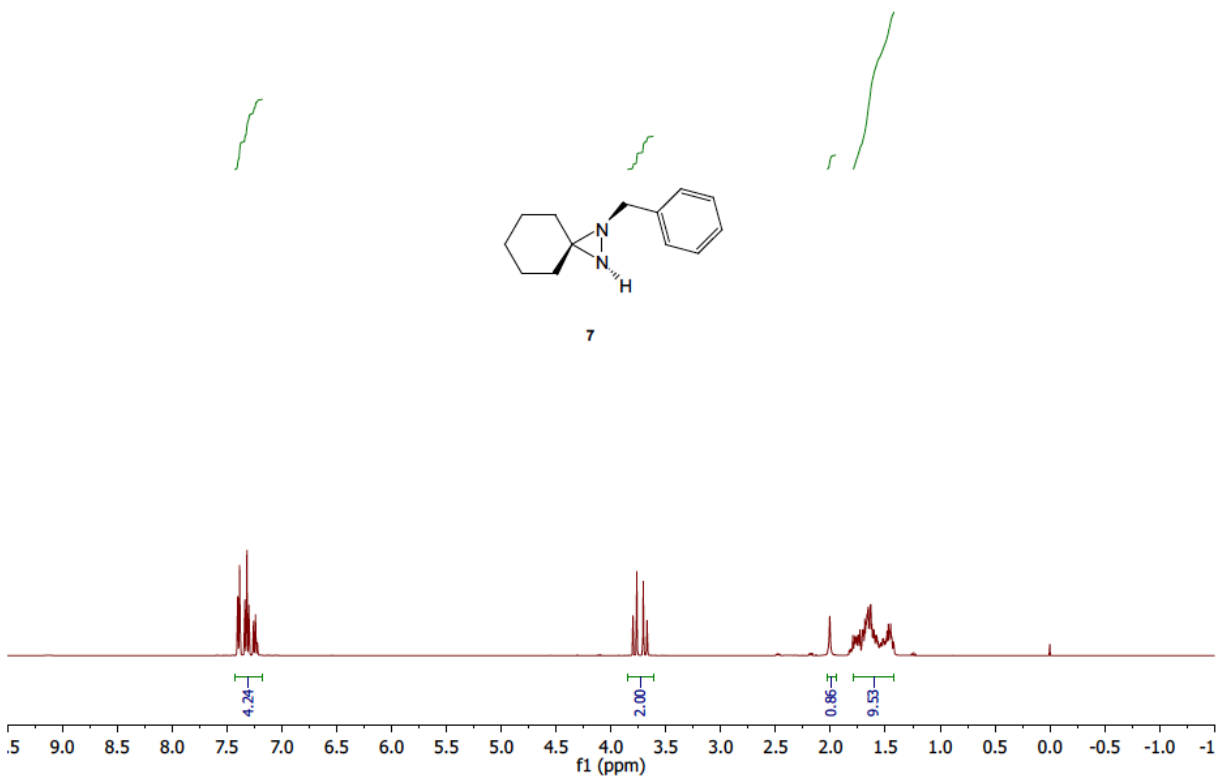
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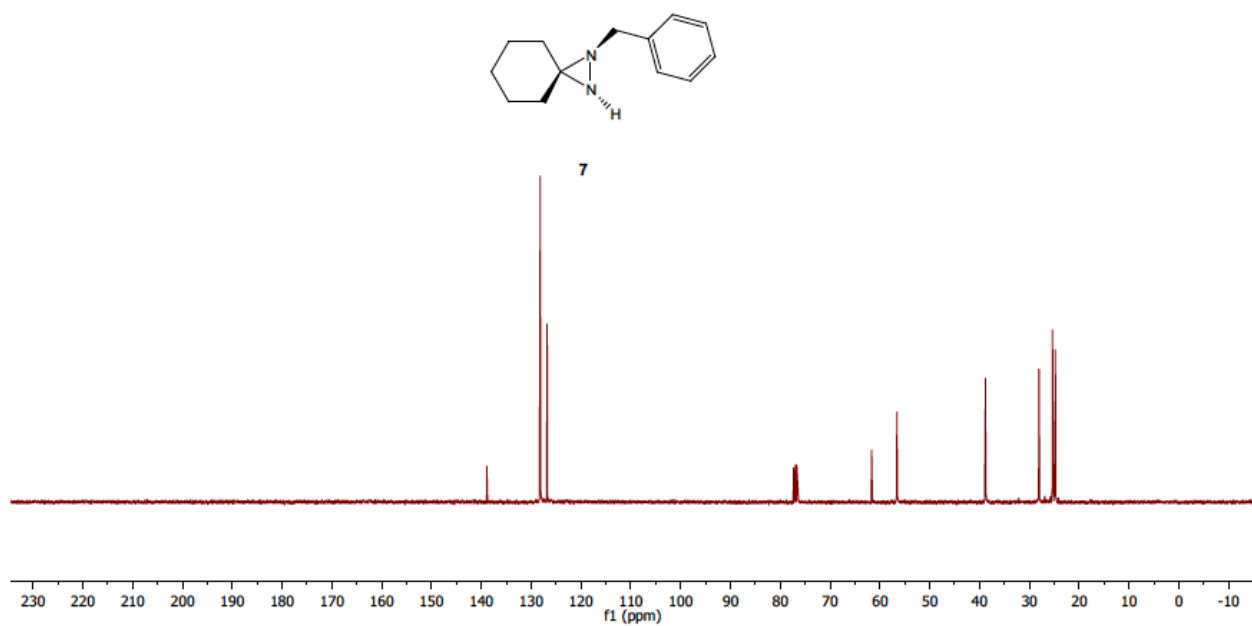
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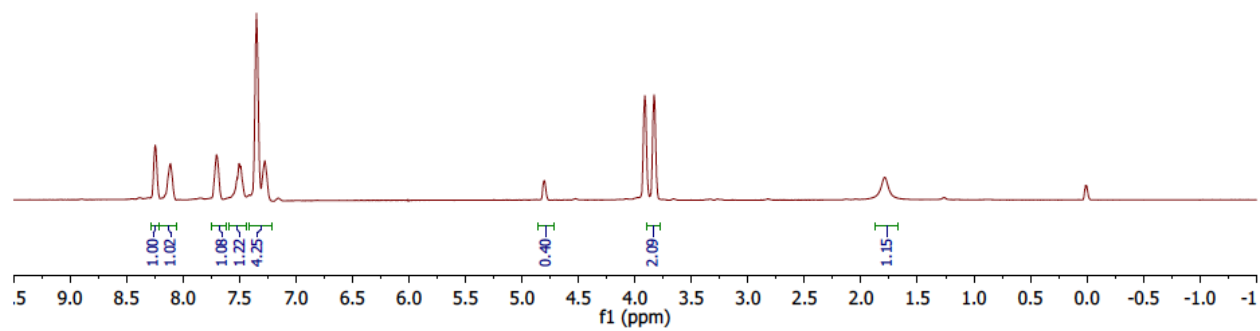
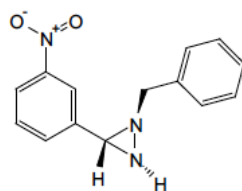
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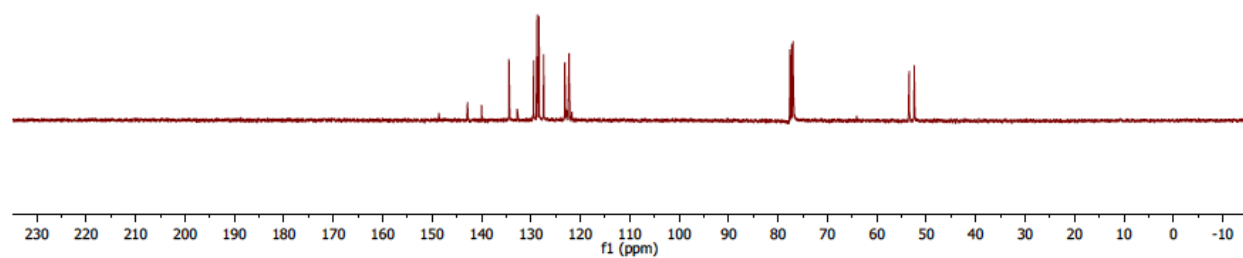
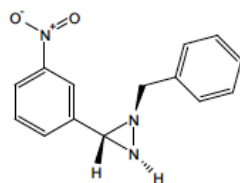
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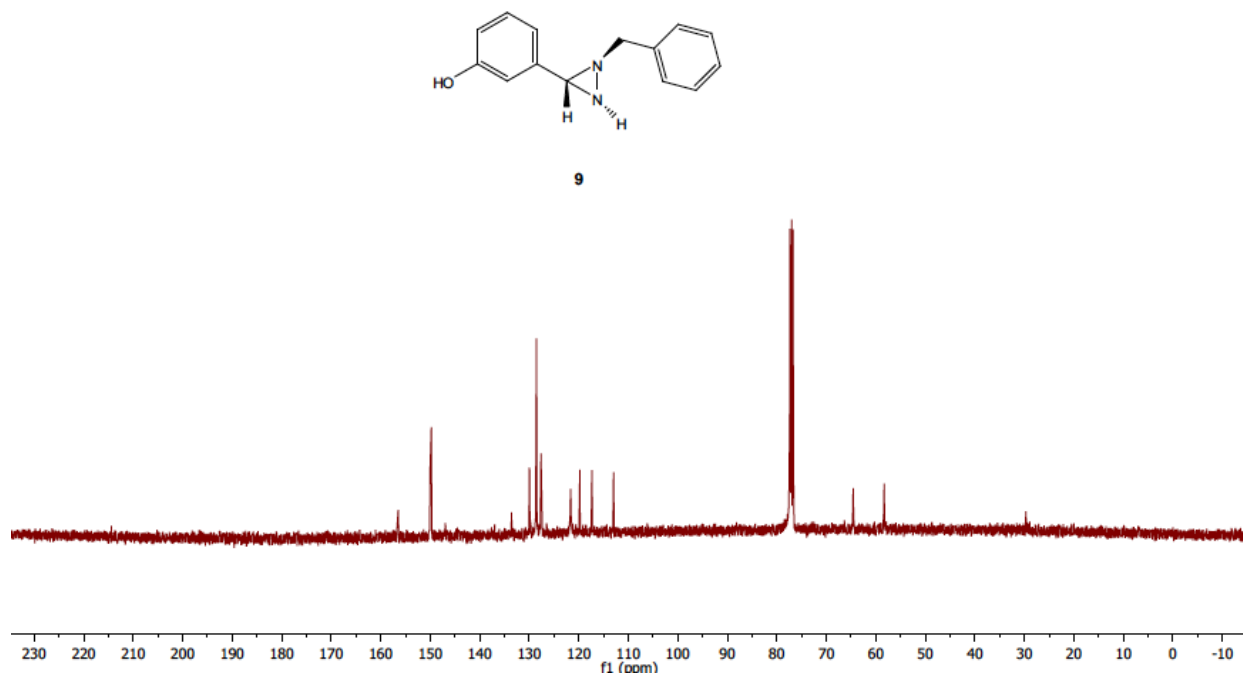
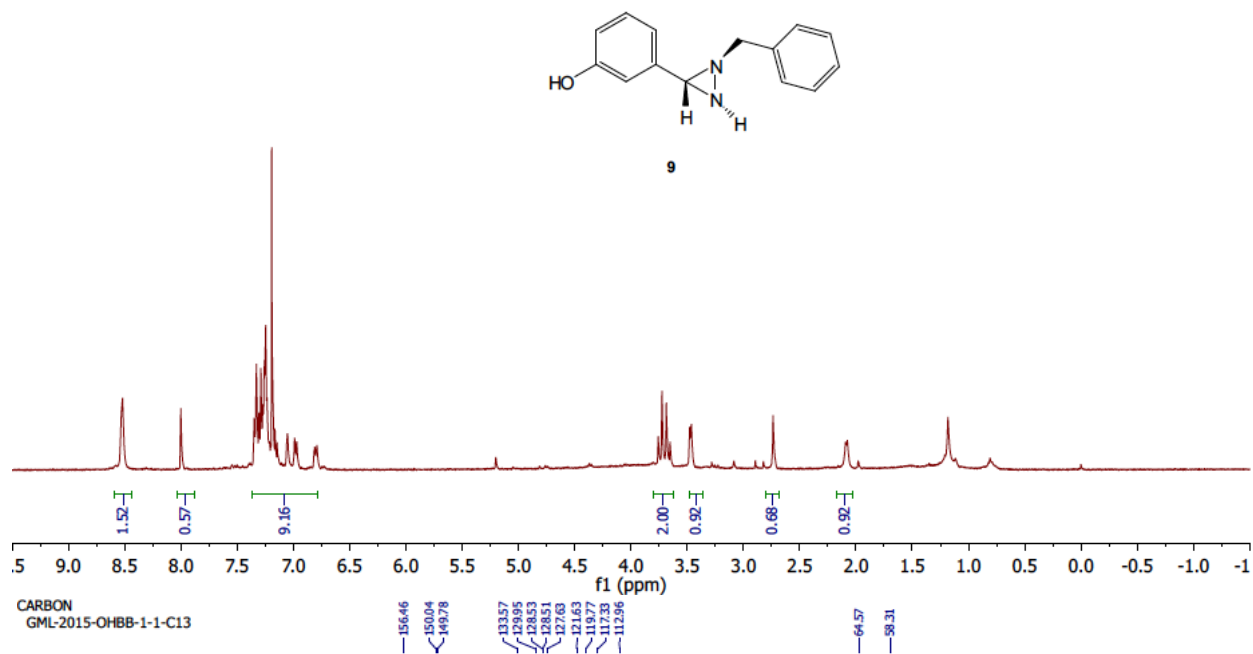


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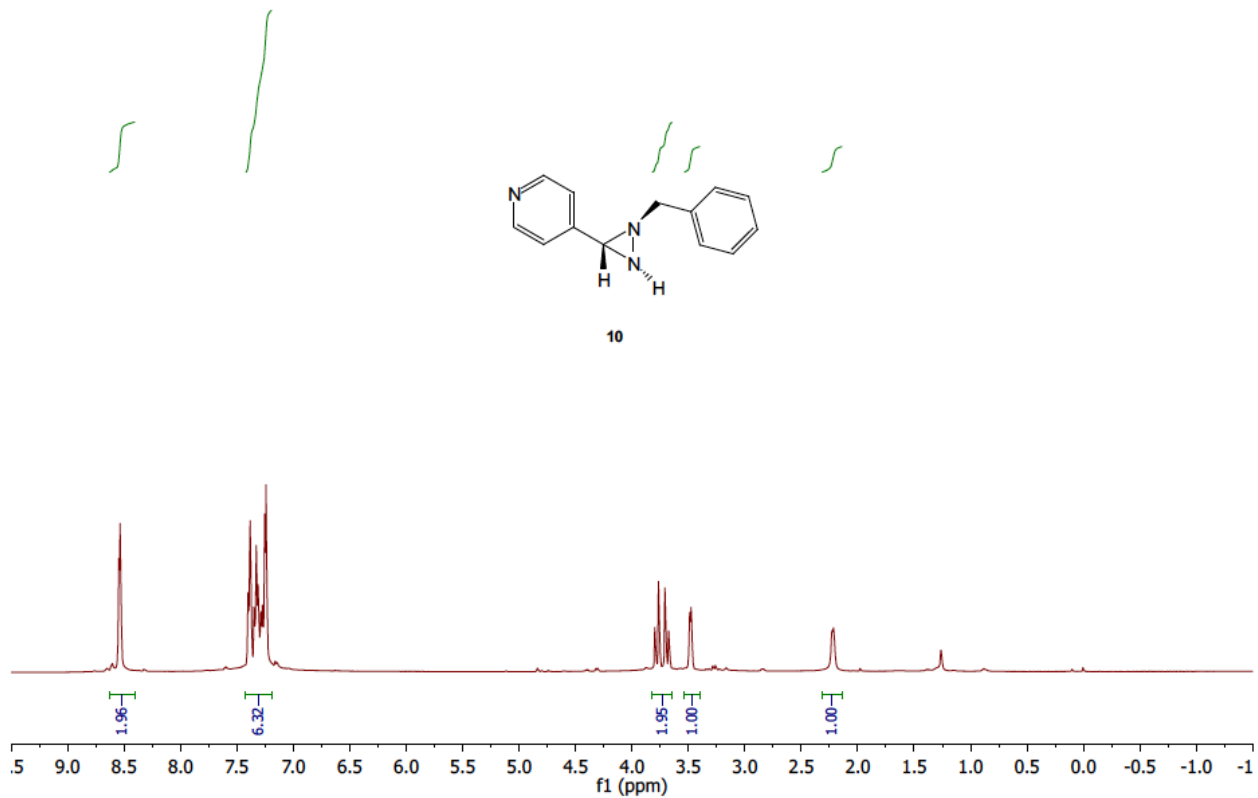


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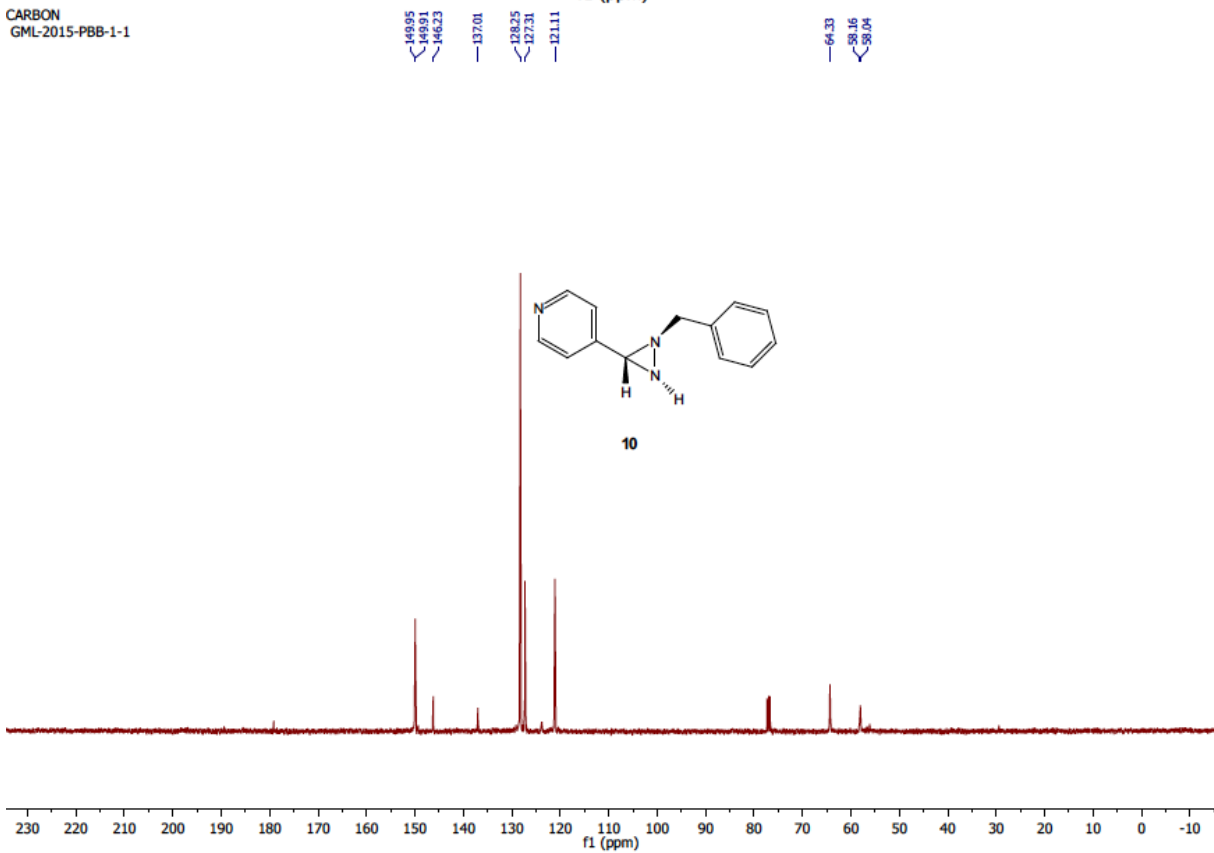


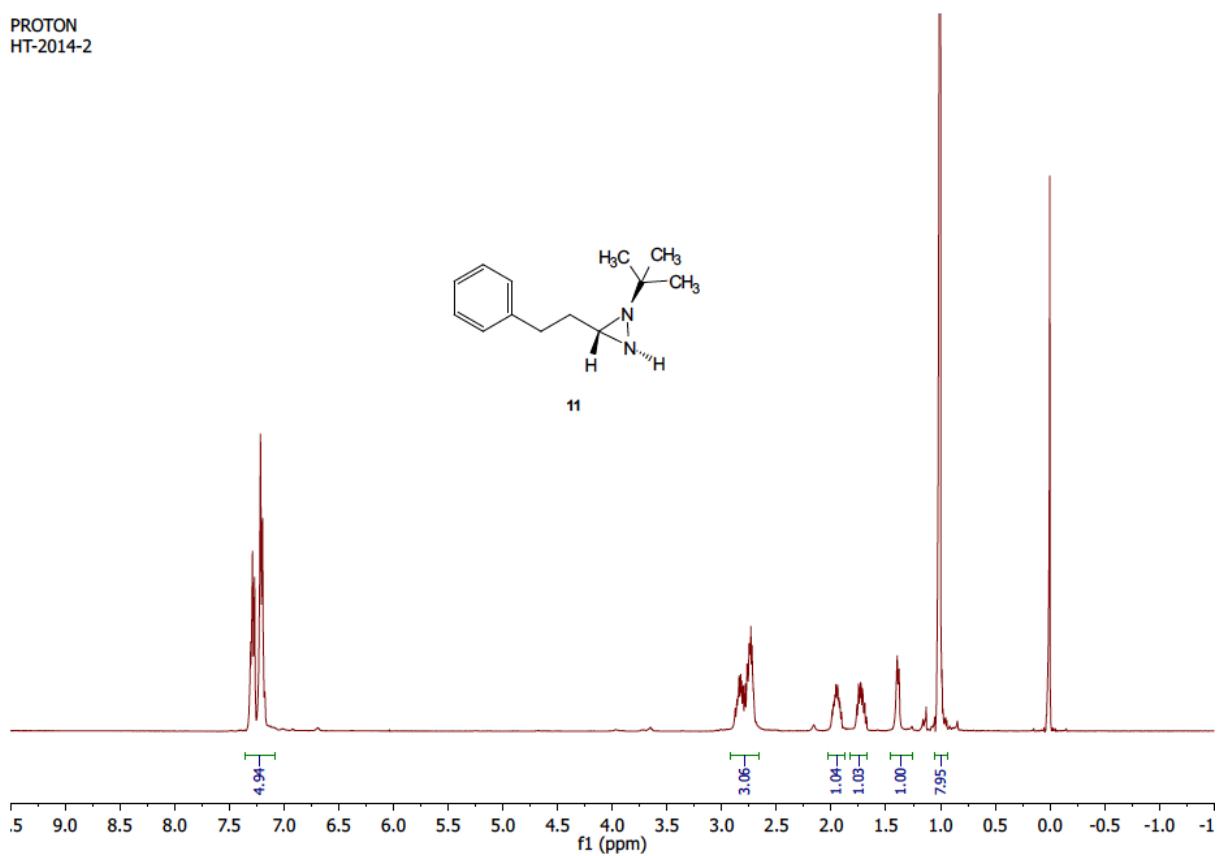
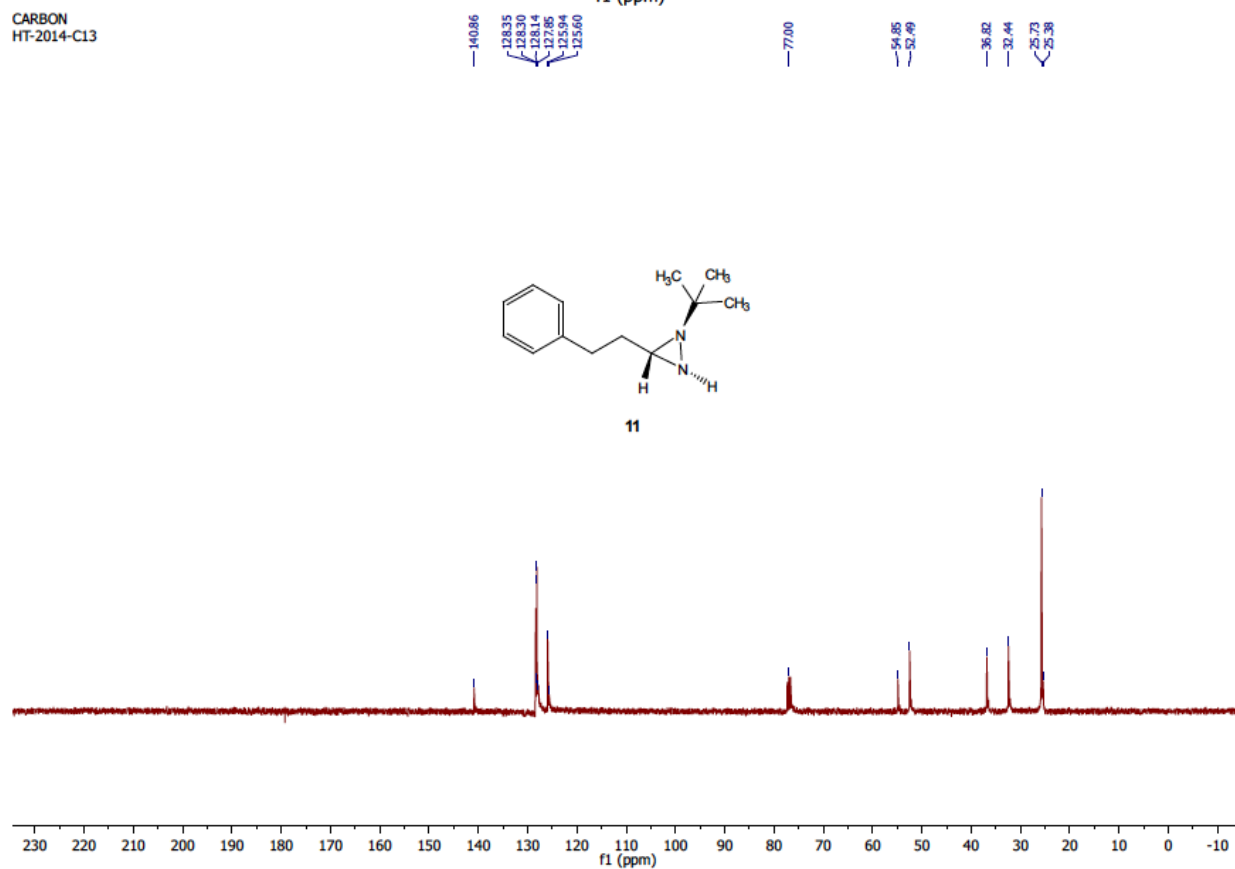
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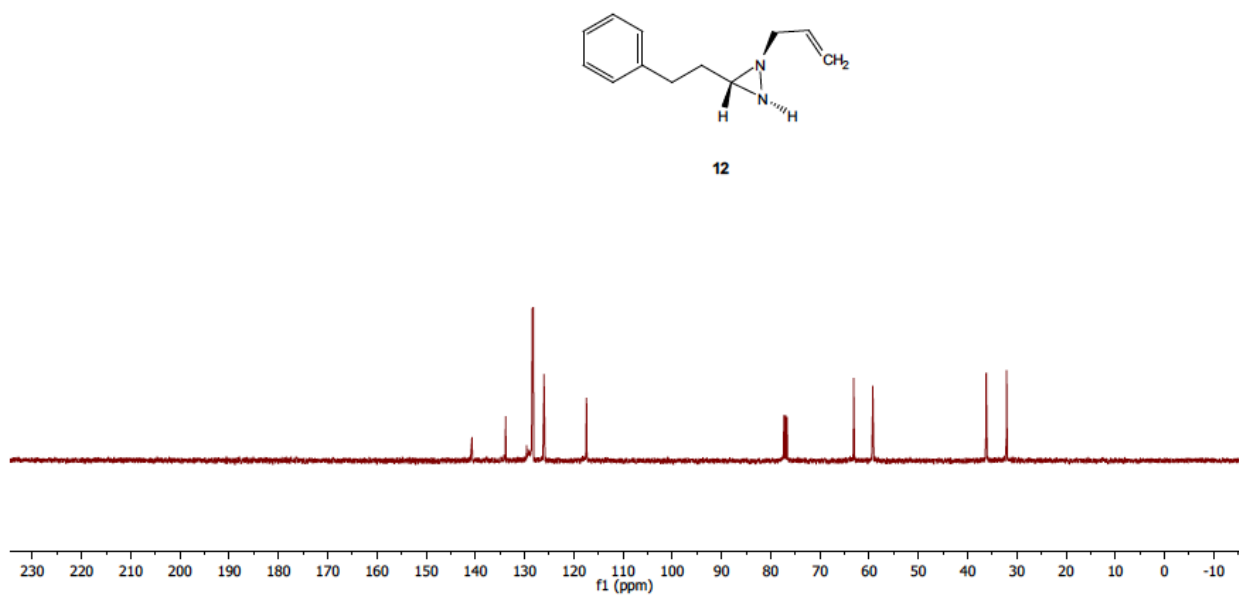
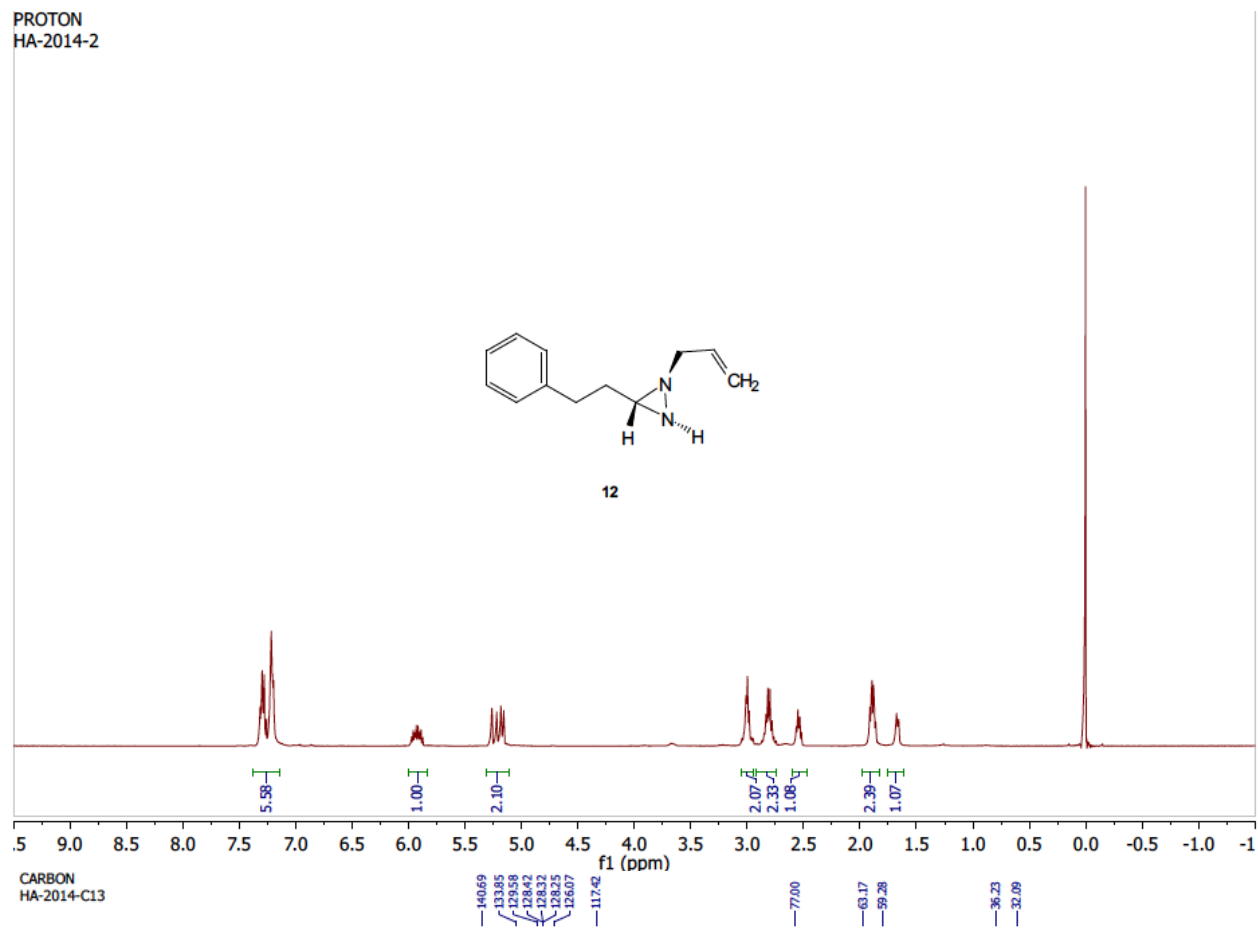
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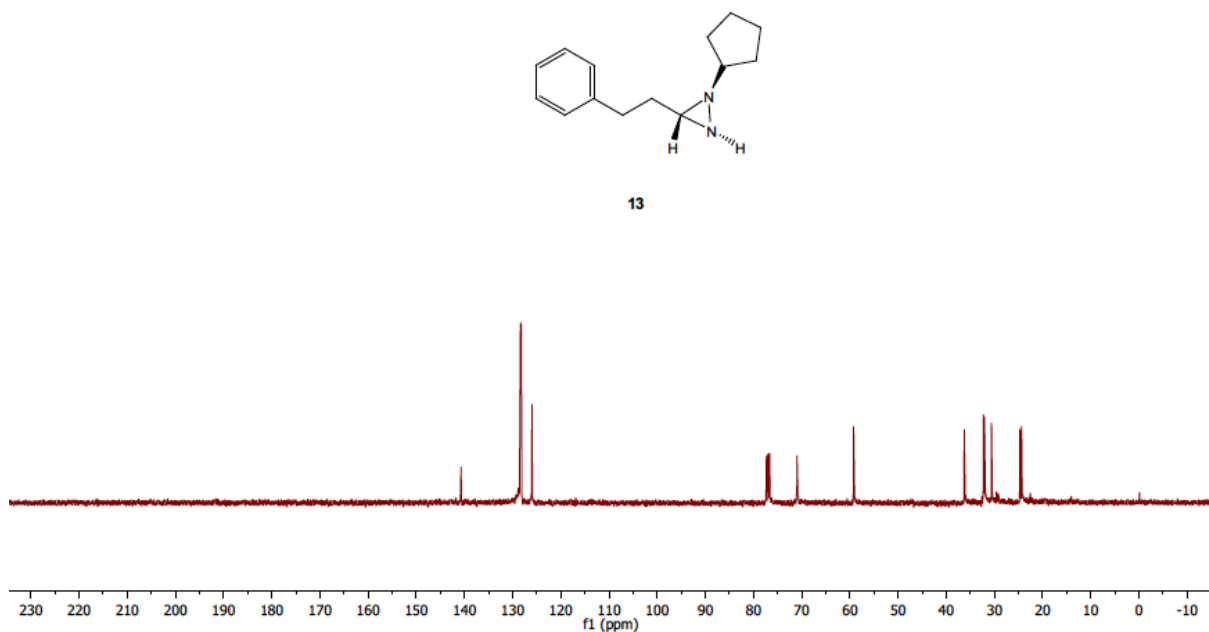
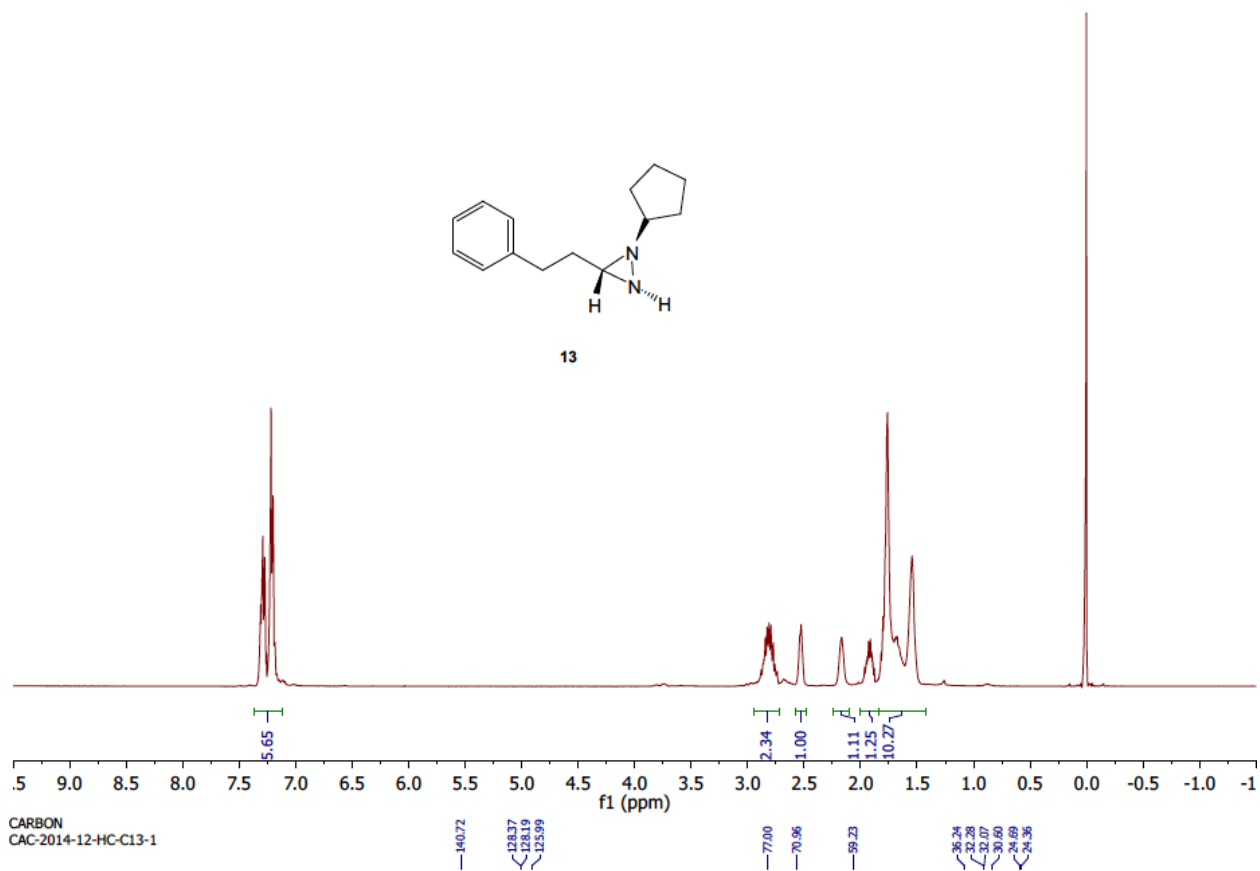


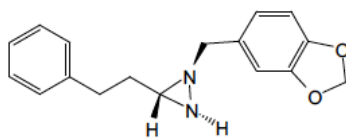
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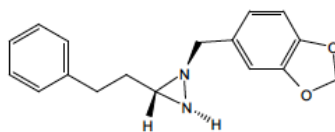
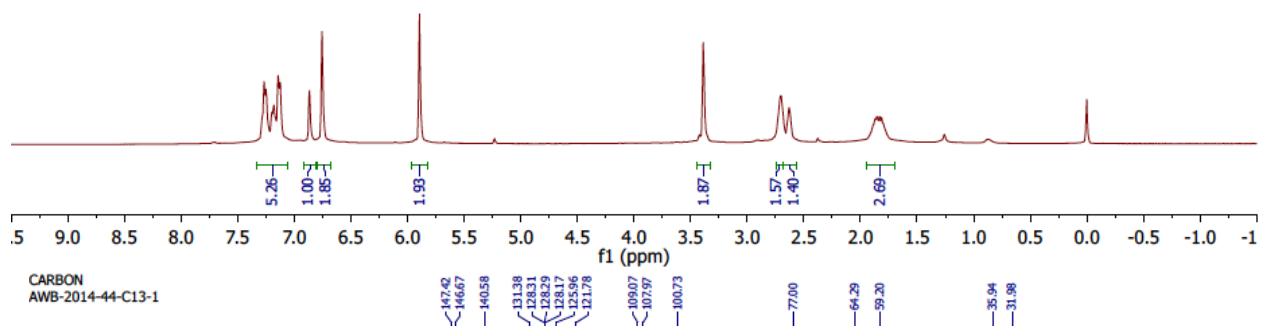
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HT-2014-2CARBON
HT-2014-C13



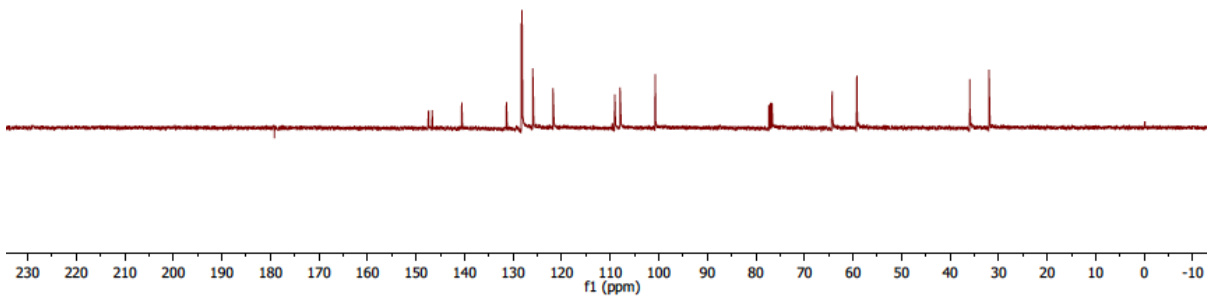
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HC-2014-2

PROTON
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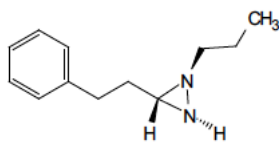
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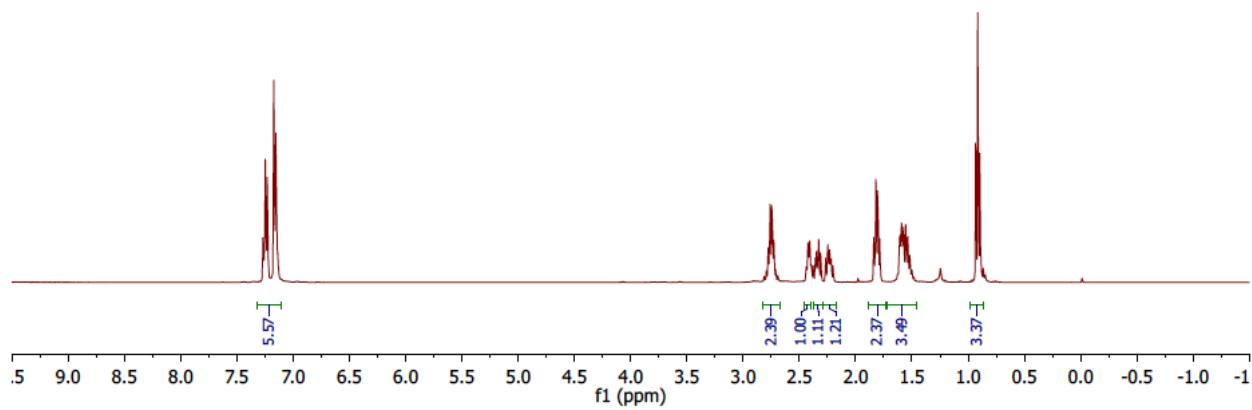
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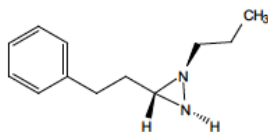
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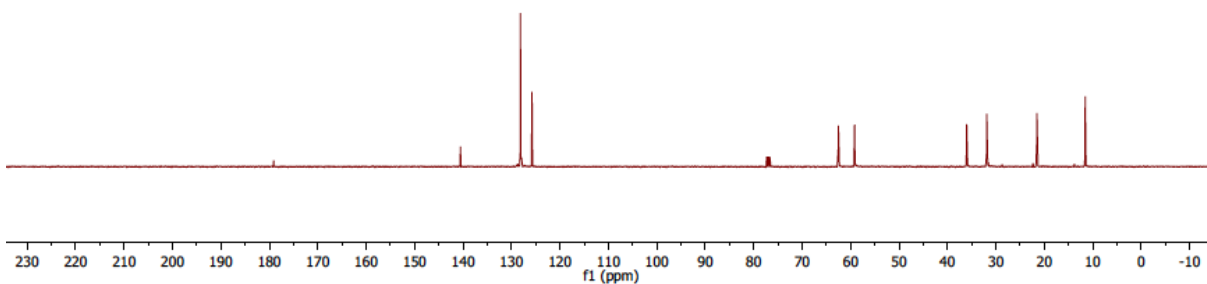
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CARBON
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15



E. UPLC TRACES: