Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Carboxylate-Assisted Ruthenium(II)-Catalyzed C–H Activations of Monodentate Amides with Alkenes

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Contents

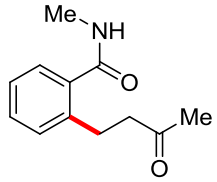
General Remarks

Catalytic reactions were carried out in Schlenk tubes under an argon atmosphere using pre-dried glassware. 1,4-Dioxane was dried and distilled over Na under nitrogen. The following starting materials were synthesized according to previously described methods: Aryl amides **1a-1r**, [D_5]-**1a**,[1] acetanilides **4**,[2] alkenes **2b**.[3] Other chemicals were obtained from commercial sources and were used without further purification. Yields refer to isolated compounds, estimated to be > 95% pure as determined by ^{1}H-NMR and GC-analysis. Chromatography: Merck silica gel 60 (40-63 µm). NMR: Spectra were recorded on Varian Unity 300, Mercury 300 or Inova 500 in the solvent indicated; chemical shifts (δ) are given in ppm. All IR spectra were recorded on a Bruker FT-IR Alpha device. MS: EI-MS-spectra were recorded with Finnigan MAT 95, 70 eV; High resolution mass spectrometry (HRMS) with APEX IV 7T FTICR, Bruker Daltonic. M. p.: Stuart melting point apparatus SMP3, Barlworld Scientific, values are uncorrected.

Representative Procedure

Representative Procedure A: A suspension of aryl amide **1** or acetanilide **4** (0.5 mmol, 1.0 equiv), *α,β*-unsaturated ketone **2** (1.0 mmol, 2.0 equiv), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), KO_2CMes (30.3 mg, 30 mol %) and $MesCO_2H$ (82 mg, 0.5 mmol, 1.0 equiv) in degassed H_2O (2.0 mL) was stirred at 120 °C for 20 h under an atmosphere of N_2. At ambient temperature, aq. NaCl (15 mL) was added. The reaction mixture was extracted with EtOAc (3×20 mL), and the combined organic layers were dried over Na_2SO_4. Evaporation of the solvents *in vacuo* and purification of the remaining residue by column chromatography on silica gel (*n*-hexane/EtOAc) yielded products **3**.

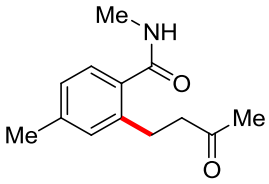
Representative Procedure B: A suspension of acetanilides **4** (0.5 mmol, 1.0 equiv), *α,β*-unsaturated ketone **2** (1.0 mmol, 2.0 equiv), $[RuCl_2(p\text{-cymene})]_2$ (7.7 mg, 2.5 mol %), $AgSbF_6$ (17.2 mg, 20 mol %) and $Cu(OAc)_2$ (190 mg, 2.1 equiv) in 1,4-dioxane (2.0 mL) was stirred at 140 °C for 20 h under an atmosphere of N_2. At ambient temperature, H_2O (15 mL) was added. The reaction mixture was extracted with EtOAc (3×20 mL) and the combined organic phase was washed with brine (20 mL) and dried over Na_2SO_4. Evaporation of the solvents *in vacuo* and purification of the remaining residue by column chromatography on silica gel (*n*-hexane/EtOAc) yielded products **6**.



***N*-Methyl-2-(3-oxobutyl)benzamide** (**3aa**)

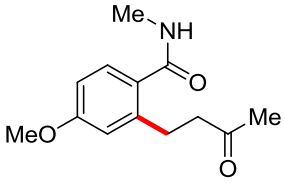
The general procedure **A** was followed using **1a** (68 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **3aa** (82 mg, 80%) as a colorless solid. M. p. = 117−119 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.36 – 7.27 (m, 2H), 7.21 – 7.13 (m, 2H), 6.36 (br s, 1H), 2.96 (d, J = 4.9 Hz, 3H), 2.93 (t, J = 6.0 Hz, 2H), 2.87 (t, J = 6.0 Hz, 2H), 2.10 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75MHz): δ = 208.6 (C_q), 170.6 (C_q), 138.9 (C_q), 136.7 (C_q), 129.9 (CH), 129.7 (CH), 127.2 (CH), 126.2 (CH), 45.2 (CH_2), 30.0 (CH_3), 27.2 (CH_2), 26.6 (CH_3). IR (ATR): 3290, 1707,

1631, 1368, 1166, 661 cm^{-1}. MS (EI) m/z (relative intensity) 205 (10) [M^+], 175 (10), 162 (100), 144 (10), 131 (45), 103 (5). HR-MS (ESI) m/z calcd for $C_{12}H_{16}NO_2$ [M+H^+] 206.1181, found 206.1177.



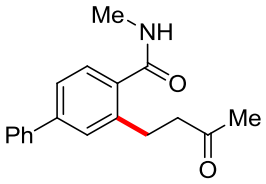
***N*,4-Dimethyl-2-(3-oxobutyl)benzamide** (**3ba**)

The general procedure **A** was followed using **1b** (75 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1→1:1) yielded **3ba** (77 mg, 70%) as a colorless solid. M. p. = 108−109 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.24 (dd, *J* = 7.1, 1.4 Hz, 1H), 7.00 (s, 1H), 6.99 (d, *J* = 7.1 Hz, 1H), 6.26 (br s, 1H), 2.96 (d, *J* = 4.9 Hz, 3H), 2.90 (t, *J* = 6.0 Hz, 2H), 2.89 (t, *J* = 6.0 Hz, 2H), 2.30 (s, 3H), 2.11 (s, 3H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 208.5 (C_q), 170.5 (C_q), 139.9 (C_q), 139.0 (C_q), 133.6 (C_q), 130.5 (CH), 127.1 (CH), 126.8 (CH), 45.4 (CH_2), 30.0 (CH_3), 27.3 (CH_2), 26.7 (CH_3), 21.3 (CH_3). IR (ATR): 3287, 1710, 1632, 1542, 1164, 693 cm^{-1}. MS (EI) m/z (relative intensity) 219 (10) [M^+], 189 (5), 176 (100), 161 (10), 145 (45), 115 (15). HR-MS (EI) m/z calcd for $C_{13}H_{17}NO_2$ [M^+] 219.1259, found 219.1256.



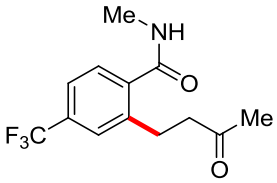
4-Methoxy-*N*-methyl-2-(3-oxobutyl)benzamide (**3ca**)

The general procedure **A** was followed using **1c** (83 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **3ca** (94 mg, 80%) as a colorless solid. M. p. = 107−109 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.29 (dd, *J* = 8.1, 0.8 Hz, 1H), 6.70 (s, 1H), 6.66 (d, *J* = 8.1 Hz, 1H), 6.34 (br s, 1H), 3.76 (s, 3H), 2.93 (d, *J* = 5.1 Hz, 3H), 2.93 (t, *J* = 6.4 Hz, 2H), 2.86 (t, *J* = 6.4 Hz, 2H), 2.10 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 208.6 (C_q), 170.3 (C_q), 160.6 (C_q), 141.4 (C_q), 128.9 (C_q), 128.9 (CH), 115.4 (CH), 111.2 (CH), 55.2 (CH_3), 45.2 (CH_2), 29.9 (CH_3), 27.5 (CH_2), 26.6 (CH_3). IR (ATR): 3288, 1705, 1543, 1247, 1157, 696 cm^{-1}. MS (EI) m/z (relative intensity) 235 (15) [M^+], 205 (10), 192 (100), 177 (5), 161 (60), 135 (10). HR-MS (EI) m/z calcd for $C_{13}H_{17}NO_3$ [M^+] 235.1208, found 235.1206.



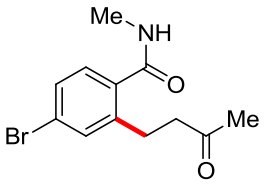
***N*-Methyl-3-(3-oxobutyl)-[1,1'-biphenyl]-4-carboxamide** (**3da**)

The general procedure **A** was followed using **1d** (106 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **3da** (111 mg, 79%) as a colorless solid. M. p. = 153−155 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.60 – 7.48 (m, 2H), 7.48 – 7.38 (m, 5H), 7.38 – 7.28 (m, 1H), 6.42 (br s, 1H), 3.10 – 3.00 (m, 2H), 2.98 (d, J = 4.9 Hz, 3H), 2.96 – 2.83 (m, 2H), 2.12 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 208.5 (C_q), 170.4 (C_q), 142.8 (C_q), 140.1 (C_q), 139.6 (C_q), 135.3 (C_q), 128.8 (CH), 128.6 (CH), 127.7 (CH), 127.7 (CH), 127.1 (CH), 124.9 (CH), 45.3 (CH_2), 29.9 (CH_3), 27.4 (CH_2), 26.6 (CH_3). IR (ATR): 3287, 1709, 1630, 1543, 1160, 697 cm^{-1}. MS (EI) m/z (relative intensity) 281 (15) [M^+], 250 (5), 238 (100), 207 (40), 178 (20), 165 (15). HR-MS (EI) m/z calcd for $C_{18}H_{19}NO_2$ [M^+] 281.1416, found 281.1417.



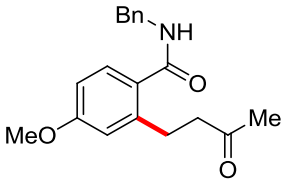
***N*-Methyl-2-(3-oxobutyl)-4-(trifluoromethyl)benzamide** (**3ea**)

The general procedure **A** was followed using **1e** (102 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **3ea** (99 mg, 73%) as a colorless solid. M. p. = 117−119 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.46 – 7.43 (m, 3H), 6.58 (br s, 1H), 2.99 (d, J = 4.9 Hz, 3H), 2.96 (t, J = 5.0 Hz, 2H), 2.94 (t, J = 5.0 Hz, 2H), 2.13 (s, 3H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 207.9 (C_q), 169.2 (C_q), 140.1 (C_q), 139.6 (C_q), 131.8 (C_q, J_{C-F} = 32.4 Hz), 127.8 (CH), 126.2 (CH, J_{C-F} = 3.7 Hz), 124.0 (C_q, J_{C-F} = 271.5 Hz), 123.1 (CH, J_{C-F} = 3.7 Hz), 44.7 (CH_2), 30.02 (CH_3), 26.8 (CH_2), 26.8 (CH_3). ^{19}F-NMR ($CDCl_3$, 282 MHz): δ = -62.9 (s). IR (ATR): 3294, 1713, 1550, 1333, 1114, 696 cm^{-1}. MS (EI) m/z (relative intensity) 273 (5) [M^+], 254 (5), 230 (60), 199 (20), 151 (10), 43 (100). HR-MS (EI) m/z calcd for $C_{13}H_{14}F_3NO_2$ [M^+] 273.0977, found 273.0973.



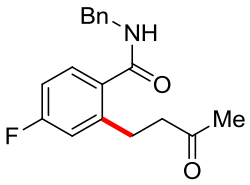
4-Bromo-*N*-methyl-2-(3-oxobutyl)benzamide (**3fa**)

The general procedure **A** was followed using **1f** (107 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1→1:1) yielded **3fa** (113 mg, 81%) as a colorless solid. M. p. = 132−134 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.40 – 7.29 (m, 2H), 7.27 – 7.21 (m, 1H), 6.52 (br s, 1H), 2.99 – 2.92 (m, 4H), 2.92 (d, J = 1.6 Hz, 3H), 2.15 (s, 3H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 208.0 (C_q), 169.5 (C_q), 141.1 (C_q), 135.6 (C_q), 132.4 (CH), 129.3 (CH), 128.8 (CH), 124.0 (C_q), 44.8 (CH_2), 30.0 (CH_3), 26.8 (CH_2), 26.7 (CH_3) IR (ATR): 3287, 1705, 1639, 1543, 1167, 686 cm^{-1}. MS (EI) m/z (relative intensity) 283 (5) [M^+], 240 (100), 225 (10), 211 (35), 183 (10), 102 (20). HR-MS (ESI) m/z calcd for $C_{12}H_{14}NO_2{}^{79}Br$ [M^+] 283.0208, found 283.0210.



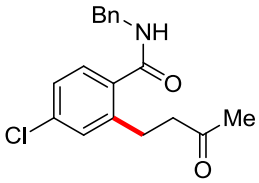
***N*-Benzyl-4-methoxy-2-(3-oxobutyl)benzamide** (**3ga**)

The general procedure **A** was followed using **1g** (121 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **3ga** (106 mg, 68%) as a colorless solid. M. p. = 131−133 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.37 – 7.31 (m, 5H), 7.32 – 7.25 (m, 1H), 6.74 (d, J = 2.6 Hz, 1H), 6.70 (dd, J = 8.4, 2.6 Hz, 1H), 6.44 (br s, 1H), 4.59 (d, J = 5.8 Hz, 2H), 3.78 (s, 3H), 2.99 (t, J = 7.1 Hz, 2H), 2.86 (t, J = 7.1 Hz, 2H), 2.09 (s, 3H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 208.3 (C_q), 169.4 (C_q), 160.8 (C_q), 141.9 (C_q), 138.3 (C_q), 128.8 (CH), 128.8 (CH), 128.6 (C_q), 127.8 (CH), 127.5 (CH), 115.7 (CH), 111.3 (CH), 55.3 (CH_3), 45.3 (CH_2), 44.0 (CH_2), 29.9 (CH_3), 27.7 (CH_2). IR (ATR): 3280, 1706, 1628, 1268, 1025, 694 cm^{-1}. MS (EI) m/z (relative intensity) 311 (15) [M^+], 268 (45), 205 (20), 161 (30), 106 (25), 91 (100). HR-MS (ESI) m/z calcd for $C_{19}H_{22}NO_3$ [M+H^+] 312.1600, found 312.1600.



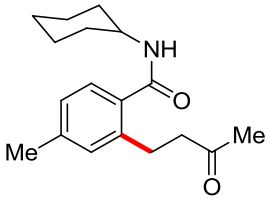
***N*-Benzyl-4-fluoro-2-(3-oxobutyl)benzamide** (**3ha**)

The general procedure **A** was followed using **1h** (115 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 5:1→2:1) yielded **3ha** (109 mg, 73%) as a colorless solid. M. p. = 112−114 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.40 – 7.25 (m, 6H), 6.93 – 6.81 (m, 2H), 6.74 (t, J = 5.8 Hz, 1H), 4.57 (d, J = 5.8 Hz, 2H), 2.94 (t, J = 6.6 Hz, 2H), 2.83 (t, J = 6.6 Hz, 2H), 2.07 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 208.0 (C_q), 168.9 (C_q), 163.4 (C_q, $J_{C\text{-}F}$ = 249.7 Hz), 142.3 (C_q, $J_{C\text{-}F}$ = 7.8 Hz), 138.1 (C_q), 132.5 (C_q, $J_{C\text{-}F}$ = 3.1 Hz), 129.3 (CH, $J_{C\text{-}F}$ = 8.8 Hz), 128.8 (CH), 127.8 (CH), 127.6 (CH), 116.6 (CH, $J_{C\text{-}F}$ = 21.4 Hz), 113.2 (CH, $J_{C\text{-}F}$ = 21.6 Hz), 44.7 (CH_2), 44.0 (CH_2), 29.9 (CH_3), 27.1 (CH_2, $J_{C\text{-}F}$ = 1.6 Hz). ^{19}F-NMR ($CDCl_3$, 282 MHz): δ = -110.4 (ddd, J = 9.8, 8.1, 5.8 Hz). IR (ATR): 3281, 1709, 1635, 1234, 1168, 694 cm^{-1}. MS (EI) m/z (relative intensity) 299 (10) [M^+], 256 (30), 193 (10), 149 (25), 106 (65), 91 (100). HR-MS (EI) m/z calcd for $C_{18}H_{18}FNO_2$ [M^+] 299.1322, found 299.1323.



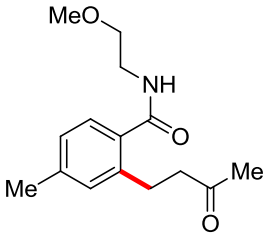
***N*-benzyl-4-chloro-2-(3-oxobutyl)benzamide** (**3ia**)

The general procedure **A** was followed using **1i** (123 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **3ia** (97 mg, 62%) as a colorless solid. M. p. = 125−126 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.37 – 7.25 (m, 6H), 7.20 – 7.18 (m, 1H), 7.16 (dd, J = 8.1, 2.1 Hz, 1H), 6.67 (d, J = 6.4 Hz, 1H), 4.59 (d, J = 5.8 Hz, 2H), 2.93 (t, J = 6.6 Hz, 2H), 2.85 (t, J = 6.6 Hz, 2H), 2.09 (s, 3H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 207.7 (C_q), 168.6 (C_q), 141.2 (C_q), 137.9 (C_q), 135.8 (C_q), 134.7 (C_q), 129.8 (CH), 128.7 (CH), 128.6 (CH), 127.8 (CH), 127.6 (CH), 126.4 (CH), 44.8 (CH_2), 44.1 (CH_2), 30.0 (CH_3), 27.0 (CH_2). IR (ATR): 3279, 1708, 1637, 1541, 1163, 692 cm^{-1}. MS (EI) m/z (relative intensity) 315 (10) [M^+], 272 (30), 209 (5), 165 (15), 106 (75), 91 (100). HR-MS (EI) m/z calcd for $C_{18}H_{18}NClO_2$ [M^+] 315.1026, found 315.1030.



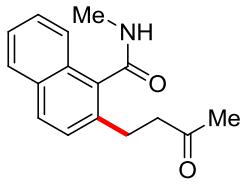
***N*-Cyclohexyl-4-methyl-2-(3-oxobutyl)benzamide (3ja)**

The general procedure **A** was followed using **1j** (109 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **3ja** (100 mg, 70%) as a colorless solid. M. p. = 143−145 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.30 – 7.20 (m, 1H), 7.02 (s, 1H), 7.01 (d, J = 6.8 Hz, 1H), 6.04 (d, J = 8.2 Hz, 1H), 4.13 – 3.82 (m, 1H), 2.96 (t, J = 6.2 Hz, 2H), 2.87 (t, J = 6.2 Hz, 2H), 2.32 (s, 3H), 2.12 (s, 3H), 2.05 – 1.95 (m, 2H), 1.78 – 1.59 (m, 3H), 1.54 – 1.32 (m, 2H), 1.31 – 1.09 (m, 3H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 208.2 (C_q), 169.0 (C_q), 139.8 (C_q), 138.9 (C_q), 134.1 (C_q), 130.5 (CH), 127.0 (CH), 126.8 (CH), 48.6 (CH), 45.4 (CH_2), 33.2 (CH_2), 30.0 (CH_3), 27.4 (CH_2), 25.6 (CH_2), 25.0 (CH_2), 21.3 (CH_3). IR (ATR): 3278, 2923, 1712, 1631, 1537, 699 cm^{-1}. MS (EI) m/z (relative intensity) 287 (35) [M^+], 244 (100), 189 (70), 162 (70), 145 (60). HR-MS (EI) m/z calcd for $C_{18}H_{25}NO_2$ [M^+] 287.1885, found 287.1879.



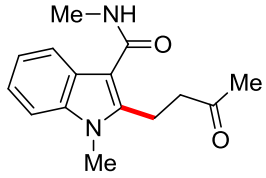
***N*-(2-Methoxyethyl)-4-methyl-2-(3-oxobutyl)benzamide (3ka)**

The general procedure **A** was followed using **1k** (97 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **3ka** (76 mg, 58%) as an oil. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.25 (d, J = 7.7 Hz, 1H), 7.01 (s, 1H), 7.00 (d, J = 7.7 Hz, 1H), 6.40 (br s, 1H), 3.60 (dt, J = 6.2, 1.4 Hz 2H), 3.53 (dt, J = 6.2, 1.4 Hz, 2H), 3.35 (s, 3H), 2.95 (dt, J = 6.8, 2.1 Hz, 2H), 2.83 (dt, J = 6.8, 2.1 Hz, 2H), 2.31 (s, 3H), 2.11 (s, 3H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 208.1 (C_q), 169.8 (C_q), 140.1 (C_q), 139.3 (C_q), 133.4 (C_q), 130.8 (CH), 127.1 (CH), 126.8 (CH), 71.2 (CH_2), 58.8 (CH_3), 45.6 (CH_2), 39.6 (CH_2), 30.0 (CH_3), 27.6 (CH_2), 21.3 (CH_3). IR (ATR): 3313, 2928, 1640, 1530, 1302, 1121 cm^{-1}. MS (EI) m/z (relative intensity) 263 (5) [M^+], 248 (10), 231 (10), 220 (30), 189 (75), 145 (100). HR-MS (EI) m/z calcd for $C_{15}H_{21}NO_3$ [M^+] 263.1521, found 263.1524.



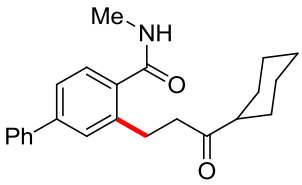
***N*-Methyl-2-(3-oxobutyl)-1-naphthamide** (**3la**)

The general procedure **A** was followed using **1l** (93 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **3la** (57 mg, 45%) as a colorless solid. M. p. = 153−155 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.91 – 7.62 (m, 3H), 7.54 – 7.35 (m, 2H), 7.25 (d, *J* = 8.3 Hz, 1H), 6.46 (br s, 1H), 3.08 (d, *J* = 5.4 Hz, 3H), 3.01 – 2.78 (m, 4H), 2.09 (s, 3H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 208.0 (C_q), 170.1 (C_q), 134.6 (C_q), 134.1 (C_q), 131.8 (C_q), 130.2 (C_q), 129.1 (CH), 127.8 (CH), 126.8 (CH), 126.3 (CH), 125.6 (CH), 124.8 (CH), 44.7 (CH_2), 30.1 (CH_3), 27.4 (CH_2), 26.6 (CH_3). IR (ATR): 3261, 1704, 1627, 1260, 745, 448 cm^{-1}. MS (EI) m/z (relative intensity) 255 (20) [M^+], 224 (10), 212 (100), 197 (20), 181 (50), 155 (25). HR-MS (EI) m/z calcd for $C_{16}H_{17}NO_2$ [M^+] 255.1259, found 255.1261.



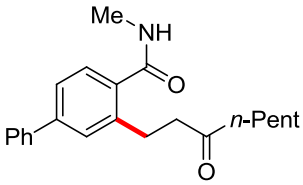
***N*,1-Dimethyl-2-(3-oxobutyl)-1*H*-indole-3-carboxamide** (**3ma**)

The general procedure **A** was followed using **1m** (94 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1→1:1) yielded **3ma** (65 mg, 50%) as a colorless solid. M. p. = 151−153 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.67 (dd, *J* = 7.0, 2.0 Hz, 1H), 7.35 – 7.29 (m, 1H), 7.26 – 7.15 (m, 2H), 6.08 (br s, 1H), 3.74 (s, 3H), 3.35 (t, *J* = 7.5 Hz, 2H), 3.04 (d, *J* = 4.9 Hz, 3H), 2.93 (t, *J* = 7.5 Hz, 2H), 2.15 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): = δ 207.8 (C_q), 166.6 (C_q), 144.9 (C_q), 136.6 (C_q), 124.8 (C_q), 121.8 (CH), 121.2 (CH), 118.4 (CH), 110.0 (CH), 107.6 (C_q), 43.3 (CH_2), 29.9 (CH_3), 29.6 (CH_3), 26.3 (CH_3), 19.8 (CH_2). IR (ATR): 3293, 1711, 1619, 1539, 1167, 734 cm^{-1}. MS (EI) m/z (relative intensity) 258 (55) [M^+], 227 (15), 215 (80), 200 (10), 184 (100), 172 (15), 158 (85). HR-MS (EI) m/z calcd for $C_{15}H_{18}N_2O_2$ [M^+] 258.1368, found 258.1363.



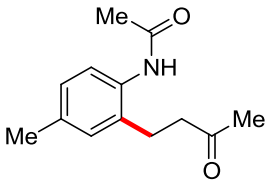
3-(3-Cyclohexyl-3-oxopropyl)-*N*-methyl-[1,1'-biphenyl]-4-carboxamide (**3db**)

The general procedure **A** was followed using **1d** (106 mg, 0.5 mmol) and **2b** (138 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **3db** (79 mg, 45%) as a colorless solid. M. p. = 155−157 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.55 (d, J = 7.4 Hz, 2H), 7.50 – 7.30 (m, 6H), 6.56 (br s, 1H), 3.00 (d, J = 4.9 Hz, 3H), 2.99 (t, J = 5.7 Hz, 2H), 2.94 (t, J = 5.7 Hz, 2H), 2.34 – 2.25 (m, 1H), 1.82 – 1.70 (m, 4H), 1.34 – 1.11 (m, 6H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 213.7 (C_q), 170.3 (C_q), 142.6 (C_q), 140.2 (C_q), 139.6 (C_q), 135.4 (C_q), 128.7 (CH), 128.3 (CH), 127.8 (CH), 127.6 (CH), 127.0 (CH), 124.8 (CH), 50.9 (CH), 42.2 (CH_2), 28.5 (CH_2), 27.3 (CH_2), 26.8 (CH_3), 25.9 (CH_2), 25.7 (CH_2). IR (ATR): 3289, 2927, 1699, 1630, 1538, 1312, 697 cm^{-1}. MS (EI) m/z (relative intensity) 349 (20) [M^+], 318 (5), 238 (100), 209 (40), 178 (15), 165 (15). HR-MS (EI) m/z calcd for $C_{23}H_{27}NO_2$ [M^+] 349.2042, found 249.2039.



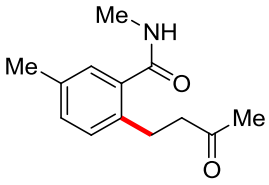
***N*-Methyl-3-(3-oxooct-1-yl)-[1,1'-biphenyl]-4-carboxamide** (**3dc**)

The general procedure **A** was followed using **1d** (106 mg, 0.5 mmol) and **2c** (126 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1) yielded **3dc** (84 mg, 50%) as a colorless solid. M. p. = 128−130 °C. ^{1}H-NMR ($CDCl_3$, 500 MHz): δ = 7.57 – 7.50 (m, 2H), 7.46 – 7.38 (m, 5H), 7.37 – 7.32 (m, 1H), 6.46 (br s, J = 4.9 Hz, 1H), 3.03 (t, J = 7.2 Hz, 2H), 3.00 (d, J = 4.9 Hz, 3H), 2.90 (t, J = 7.2 Hz, 2H), 2.36 (t, J = 7.5 Hz, 2H), 1.52 (p, J = 7.5 Hz, 2H), 1.31 – 1.13 (m, 4H), 0.83 (t, J = 7.1 Hz, 3H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 211.1 (C_q), 170.4 (C_q), 142.8 (C_q), 140.2 (C_q), 139.6 (C_q), 135.5 (C_q), 128.8 (CH), 128.5 (CH), 127.9 (CH), 127.7 (CH), 127.1 (CH), 124.9 (CH), 44.2 (CH_2), 43.0 (CH_2), 31.4 (CH_2), 27.3 (CH_2), 26.7 (CH_3), 23.5 (CH_2), 22.4 (CH_2), 13.9 (CH_3). IR (ATR): 3287, 1710, 1632, 1542, 1164, 693 cm^{-1}. MS (EI) m/z (relative intensity) 337 (5) [M^+], 281 (25), 238 (100), 223 (5), 207 (35), 178 (15). HR-MS (EI) m/z calcd for $C_{22}H_{27}NO_2$ [M^+] 337.2042, found 337.2048.



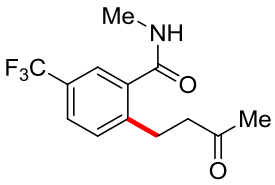
***N*-(4-Methyl-2-(3-oxobutyl)phenyl)acetamide** (**5aa**)

The general procedure **A** was followed using **4a** (75 mg, 0.5 mmol), methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) and KO_2CMes (51 mg, 50 mol %) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1→1:1) yielded **5aa** (51 mg, 47%) as a colorless solid. M. p. = 124−126 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.84 (br s, 1H), 7.62 (d, J = 8.2 Hz, 1H), 6.99 (dd, J = 8.2, 2.1 Hz, 1H), 6.89 (d, J = 2.1 Hz, 1H), 2.87 (dt, J = 6.2, 2.0 Hz, 2H), 2.75 (dt, J = 6.2, 2.0 Hz, 2H), 2.26 (s, 3H), 2.24 (s, 3H), 2.12 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 210.3 (C_q), 168.8 (C_q), 134.7 (C_q), 133.0 (C_q), 132.6 (C_q), 130.3 (CH), 127.7 (CH), 124.4 (CH), 45.3 (CH_2), 29.9 (CH_3), 24.2 (CH_3), 23.8 (CH_2), 20.8 (CH_3). IR (ATR): 3282, 1709, 1641, 1522, 1287, 811 cm^{-1}. MS (EI) m/z (relative intensity) 219 (60) [M^+], 176 (75), 162 (40), 134 (100), 120 (85), 107 (10). HR-MS (EI) m/z calcd for $C_{13}H_{17}NO_2$ [M^+] 219.1259, found 219.1259.



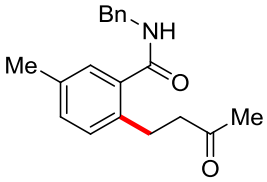
***N*,5-Dimethyl-2-(3-oxobutyl)benzamide** (**3na**)

The general procedure **A** was followed using **1n** (75 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1→1:1) yielded **3na** (68 mg, 62%) as a colorless solid. M. p. = 112−114 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.15 (d, J = 1.8 Hz, 1H), 7.10 (dd, J = 7.9, 1.8 Hz, 1H), 7.07 (d, J = 7.9 Hz, 1H), 6.39 (br s, 1H), 2.96 (d, J = 4.9 Hz, 3H), 2.89 (t, J = 5.0 Hz, 2H), 2.87 (t, J = 5.0 Hz, 2H), 2.28 (s, 3H), 2.10 (s, 3H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 208.6 (C_q), 170.6 (C_q), 136.4 (C_q), 135.8 (C_q), 135.6 (C_q), 130.6 (CH), 129.5 (CH), 127.8 (CH), 45.3 (CH_2), 30.1 (CH_3), 26.7 (CH_2), 26.7 (CH_3), 20.9 (CH_3). IR (ATR): 3285, 1709, 1541, 1319, 1160, 697 cm^{-1}. MS (EI) m/z (relative intensity) 219 (15) [M^+], 189 (5), 176 (100), 161 (10), 145 (60), 117 (15). HR-MS (EI) m/z calcd for $C_{13}H_{17}NO_2$ [M^+] 219.1259, found 219.1252.



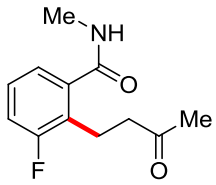
***N*-Methyl-2-(3-oxobutyl)-5-(trifluoromethyl)benzamide (3oa)**

The general procedure **A** was followed using **1o** (102 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **3oa** (85 mg, 62%) as a colorless solid. M. p. = 96−98 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.60 (dt, J = 1.6, 0.7 Hz, 1H), 7.56 – 7.49 (m, 1H), 7.32 (dt, J = 8.3, 0.8 Hz, 1H), 6.61 (br s, 1H), 2.97 (t, J = 5.8 Hz, 2H), 2.98 (d, J = 5.2 Hz, 3H), 2.89 (t, J = 5.8 Hz, 2H), 2.11 (s, 3H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 207.9 (C_q), 169.0 (C_q), 142.9 (C_q, J_{C-F} = 1.7 Hz), 137.2 (C_q), 130.1 (CH), 128.6 (C_q, J_{C-F} = 32.8 Hz), 126.4 (CH, J_{C-F} = 3.7 Hz), 124.3 (CH, J_{C-F} = 3.8 Hz), 123.2 (C_q, J_{C-F} = 271.5 Hz), 44.7 (CH_2), 30.0 (CH_3), 26.9 (CH_2), 26.8 (CH_3). ^{19}F-NMR ($CDCl_3$, 282 MHz): δ = -62.6 (s). IR (ATR): 3286, 1705, 1552, 1311, 1115, 641 cm^{-1}. MS (EI) m/z (relative intensity) 273 (5) [M^+], 243 (5), 230 (100), 215 (10), 199 (35), 189 (10). HR-MS (EI) m/z calcd for $C_{13}H_{14}NO_2F_3$ [M^+] 273.0977, found 273.0979.



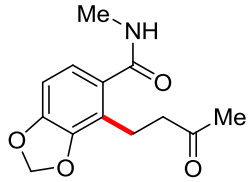
***N*-Benzyl-5-methyl-2-(3-oxobutyl)benzamide (3pa)**

The general procedure **A** was followed using **1p** (113 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 2:1) yielded **3pa** (94 mg, 64%) as a colorless solid. M. p. = 130−132 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.43 – 7.25 (m, 5H), 7.17 (d, J = 0.9 Hz, 1H), 7.14 – 7.06 (m, 2H), 6.52 (br s, 1H), 4.60 (d, J = 5.8 Hz, 2H), 3.01 (t, J = 6.8 Hz, 2H), 2.82 (t, J = 6.8 Hz, 2H), 2.29 (s, 3H), 2.07 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 208.5 (C_q), 169.9 (C_q), 138.2 (C_q), 136.2 (C_q), 136.0 (C_q), 136.0 (C_q), 130.8 (CH), 129.9 (CH), 128.8 (CH), 127.9 (CH), 127.7 (CH), 127.6 (CH), 45.4 (CH_2), 44.0 (CH_2), 29.9 (CH_3), 26.9 (CH_2), 20.8 (CH_3). IR (ATR): 3242, 1707, 1634, 1311, 821, 702 cm^{-1}. MS (EI) m/z (relative intensity) 295 (20) [M^+], 252 (40), 189 (5), 145 (20), 106 (30), 91 (100). HR-MS (EI) m/z calcd for $C_{19}H_{21}NO_2$ [M^+] 295.1572, found 295.1580.



3-Fluoro-*N*-methyl-2-(3-oxobutyl)benzamide (**3qa**)

The general procedure **A** was followed using **1q** (77 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1) yielded **3qa** (86 mg, 77%) as a colorless solid. M. p. = 123−125 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.21 – 7.12 (m, 2H), 7.09 – 6.93 (m, 1H), 6.55 (br s, 1H), 2.96 (d, J = 4.9 Hz, 3H), 2.94 (t, J = 5.4 Hz, 2H), 2.89 (t, J = 5.4 Hz, 2H), 2.12 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 208.7 (C_q), 169.3 (C_q, J = 3.2 Hz), 161.4 (C_q, J = 246.1 Hz), 139.1 (C_q, J = 4.3 Hz), 127.8 (CH, J = 8.9 Hz), 126.1 (C_q, J = 16.7 Hz), 122.9 (CH, J = 3.4 Hz), 116.7 (CH, J = 23.0 Hz), 43.5 (CH_2, J = 2.4 Hz), 29.8 (CH_3), 26.7 (CH_3), 21.1 (CH_2, J = 2.9 Hz). ^{19}F-NMR ($CDCl_3$, 282 MHz): δ = -116.1 (dd, J = 10.2, 4.4 Hz). IR (ATR): 3291, 1703, 1547, 1319, 1163, 710 cm^{-1}. MS (EI) m/z (relative intensity) 223 (10) [M^+], 180 (100), 165 (15), 149 (60), 121 (15), 101 (15). HR-MS (EI) m/z calcd for $C_{12}H_{14}NO_2F$ [M^+] 223.1009, found 223.1006.

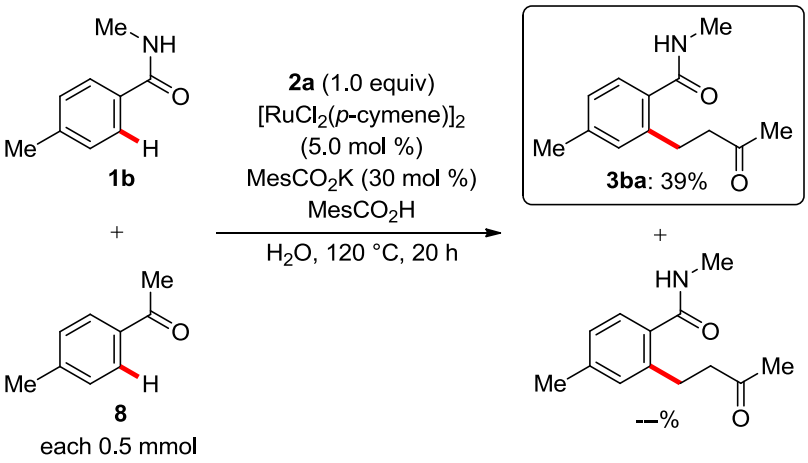


***N*-Methyl-4-(3-oxobutyl)benzo[*d*][1,3]dioxole-5-carboxamide** (**3ra**)

The general procedure **A** was followed using **1r** (90 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 1:1→1:2) yielded **3ra** (100 mg, 80%) as a colorless solid. M. p. = 139−141 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 6.93 (d, J = 8.0 Hz, 1H), 6.64 (d, J = 8.0 Hz, 1H), 6.47 (br s, 1H), 5.95 (s, 2H), 2.94 (d, J = 4.9 Hz, 3H), 2.95 – 2.88 (m, 4H), 2.13 (s, 3H). ^{13}C-NMR ($CDCl_3$, 125 MHz): δ = 208.7 (C_q), 169.5 (C_q), 148.1 (C_q), 146.2 (C_q), 131.0 (C_q), 121.5 (CH), 121.1 (C_q), 106.2 (CH), 101.1 (CH_2), 43.0 (CH_2), 29.9 (CH_3), 26.7 (CH_3), 21.7 (CH_2). IR (ATR): 3301, 1706, 1543, 1251, 1040, 705 cm^{-1}. MS (EI) m/z (relative intensity) 249 (25) [M^+], 218 (15), 206 (100), 188 (5), 175 (65), 149 (15). HR-MS (EI) m/z calcd for $C_{13}H_{15}NO_4$ [M^+] 249.1001, found 249.1006.

Competition Experiment:

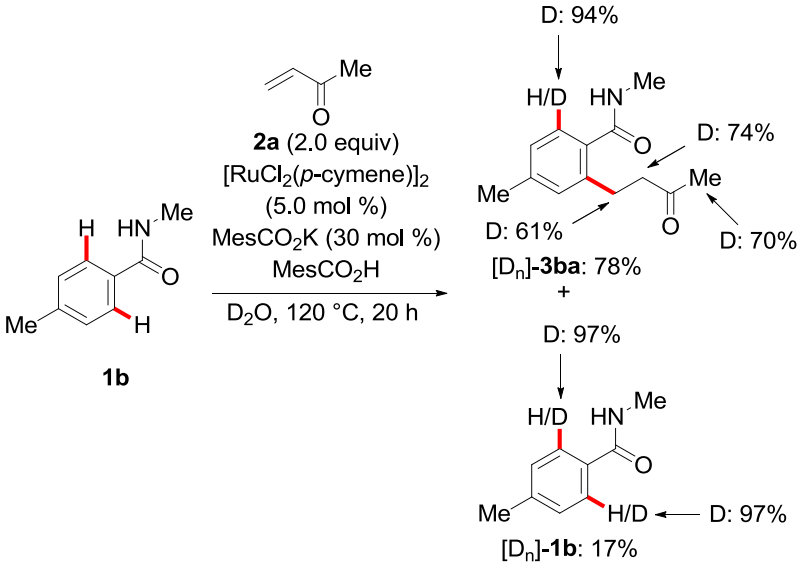
Intermolecular Competition Experiments Between Arenes with Different Directing Groups:



A suspension of MVK (**2a**) (35 mg, 0.5 mmol), *N*,4-dimethylbenzamide (**1b**) (75 mg, 0.5 mmol), 1-(*p*-tolyl)ethanone (**8**) (67 mg, 0.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), $MesCO_2K$ (30.3 mg, 30.0 mol %) and $MesCO_2H$ (82 mg, 1.0 equiv) in H_2O (2.0 mL) was stirred at 120 ℃ for 20 h under an atmosphere of argon. At ambient temperature, aq. NaCl (15 mL) was added. The reaction mixture was extracted with EtOAc (3×20 mL). The combined organic layers were dried over Na_2SO_4. Evaporation of the solvents *in vacuo* and purification of the remaining residue by column chromatography on silica gel (*n*-hexane/EtOAc 1:1) yielded product **3ba** (43 mg, 39%) as the sole product.

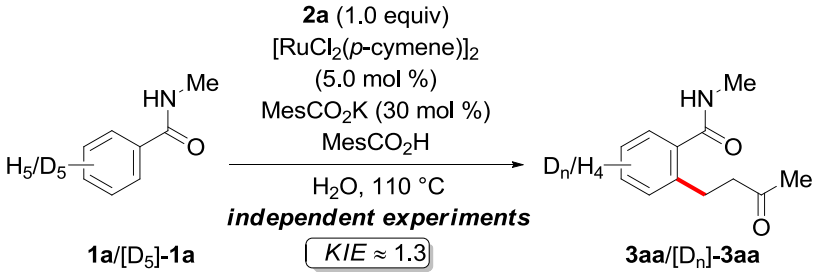
H/D Exchange Experiment:

Ruthenium(II)-Catalyzed H/D Exchange on Substrate 1b with D_2O as the solvent:

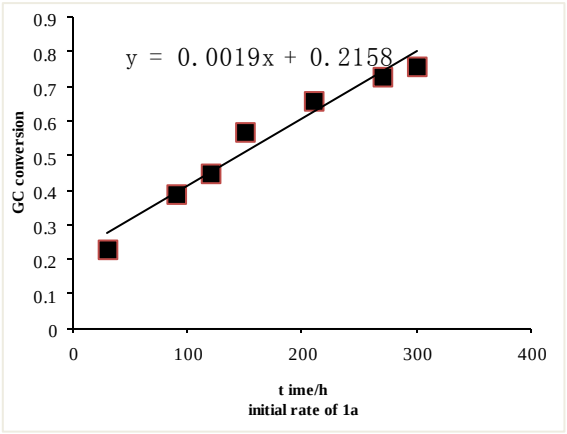


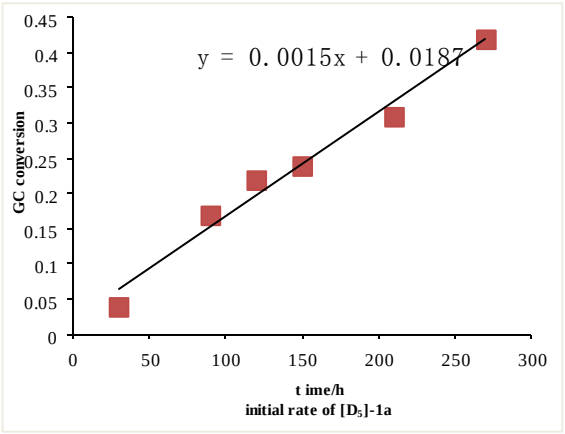
A suspension of MVK (**2a**) (70 mg, 1.0 mmol), *N*,4-dimethylbenzamide (**1b**) (75 mg, 0.5 mmol), $[RuCl_2(p\text{-cymene})]_2$ (15.3 mg, 5.0 mol %), $MesCO_2K$ (30.3 mg, 30.0 mol %) and $MesCO_2H$ (82 mg, 1.0 equiv) in a solvent of D_2O (2.0 mL) was stirred at 120 ℃ for 20 h under an atmosphere of argon. At ambient temperature, aq. NaCl (15 mL) was added. The reaction mixture was extracted with EtOAc (3×20 mL). The combined organic layers were dried over Na_2SO_4. Evaporation of the solvents *in vacuo* and purification of the remaining residue by column chromatography on silica gel (*n*-hexane/EtOAc 1:1→1:2) yielded product $[D_n]$-**3ba** (85 mg, 78%) as a white solid, and reisolated starting material $[D_n]$-**1b** (13 mg, 17%) as a white solid. The deuterium-incorporation in $[D_n]$-**3ba** and $[D_n]$-**1b** was estimated by ^{1}H-NMR spectroscopy.

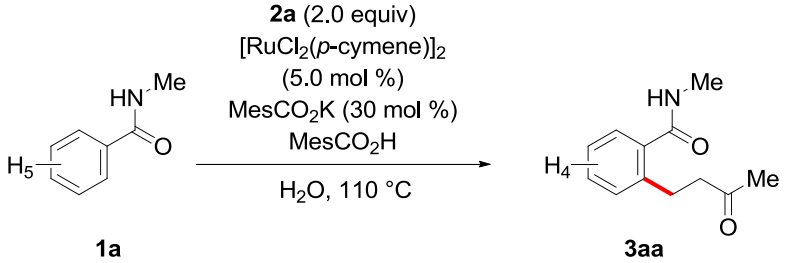
Kinetic Isotope Effect



Two independent reactions with **1a** or deuterated substrate [D_5]-**1a** under the standard conditions were performed: Suspensions of MVK (**2a**) (70 mg, 1.0 mmol), substrates **1a** (68 mg, 0.5 mmol) or [D_5]-**1a** (70 mg, 0.5 mmol), [$RuCl_2$(*p*-cymene)]$_2$ (15.3 mg, 5.0 mol %), $MesCO_2K$ (30.3 mg, 30.0 mol %) and $MesCO_2H$ (82 mg, 0.5 mmol) in H_2O (2.0 mL) were stirred at 110 ℃ for 0.5 h, 1.5 h, 2.0 h, 2.5 h, 3.5 h, 4.5 h, 5.0 h under an atmosphere of argon, respectively. The consumption of substrate **1a** or [D_5]-**1a** and the appearance of the products **3aa** or [D_n]-**3aa** were monitored by GC analysis. These experiments indicated that the C–H bond activation is not the turnover-limiting step of the ruthenium(II)-catalyzed C–H alkylation reaction.

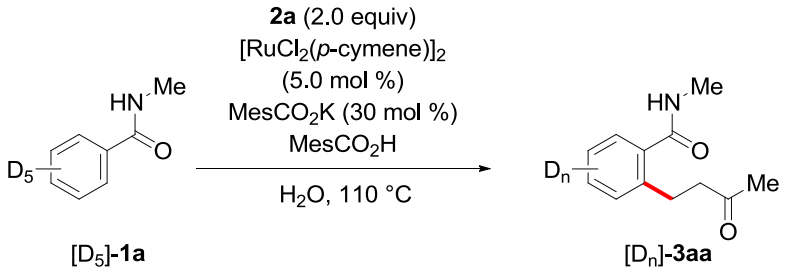




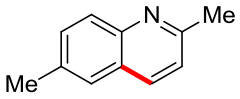


t/(h)	0.5	1.5	2.0	2.5	3.5	4.5	5.0
3aa	0.23	0.39	0.57	0.45	0.66	0.73	0.76

1a	0.77	0.61	0.43	0.55	0.34	0.27	0.24

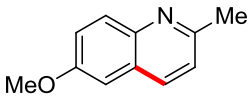


t/(h)	0.5	1.5	2.0	2.5	3.5	4.5
[D_n]-**3aa**	0.04	0.17	0.22	0.24	0.31	0.42
[D_5]-**1a**	0.96	0.83	0.78	0.76	0.69	0.58



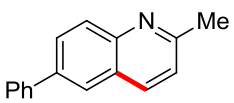
2,6-Dimethylquinoline (**6aa**)

The general procedure **B** was followed using **4a** (75 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 6:1) yielded **6aa** (52 mg, 66%) as a yellow oil. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.91 (d, J = 8.7 Hz, 1H), 7.89 (d, J = 9.0 Hz, 1H), 7.49 (s, 1H), 7.48 (dd, J = 7.6, 1.8 Hz, 1H), 7.20 (d, J = 8.3 Hz, 1H), 2.69 (s, 3H), 2.48 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 157.9 (C_q), 146.4 (C_q), 135.5 (CH), 135.3 (C_q), 131.6 (CH), 128.2 (CH), 126.4 (C_q), 126.3 (CH), 121.9 (CH), 25.2 (CH_3), 21.4 (CH_3). IR (ATR): 2917, 1601, 1495, 1119, 825, 592 cm^{-1}. MS (EI) m/z (relative intensity) 157 (100) [M^+], 142 (20), 128 (10), 115 (20), 89 (10), 77 (10). HR-MS (EI) m/z calcd for $C_{11}H_{11}N$ [M^+] 157.0891, found 157.0884. The spectral data were in accordance with those reported in the literature.[4,5]



6-Methoxy-2-methylquinoline (**6ba**)

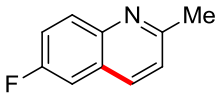
The general procedure **B** was followed using **4b** (83 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **6ba** (60 mg, 69%) as a yellow oil. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.94 – 7.90 (m, 1H), 7.89 – 7.85 (m, 1H), 7.30 (dd, J = 9.2, 2.8 Hz, 1H), 7.20 (d, J = 8.4 Hz, 1H), 7.01 (d, J = 2.8 Hz, 1H), 3.88 (s, 3H), 2.67 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 157.1 (C_q), 156.3 (C_q), 143.9 (C_q), 135.0 (CH), 130.0 (CH), 127.3 (C_q), 122.2 (CH), 121.8 (CH), 105.2 (CH), 55.4 (CH_3), 25.0 (CH_3). IR (ATR): 2937, 1602, 1498, 1229, 1029, 830 cm^{-1}. MS (EI) m/z (relative intensity) 173 (100) [M^+], 158 (50), 143 (5), 130 (80), 115 (5), 103 (20). HR-MS (ESI) m/z calcd for $C_{11}H_{12}NO$ [$M+H^+$] 174.0919, found 174.0921. The spectral data were in accordance with those reported in the literature.[4,5]



2-Methyl-6-phenylquinoline (**6ca**)

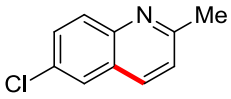
The general procedure **B** was followed using **4c** (106 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc

5:1) yielded **6ca** (57 mg, 52%) as an off white solid. M. p. = 92−93 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.09 (dd, J = 8.9, 2.1 Hz, 2H), 7.99 – 7.91 (m, 2H), 7.76 – 7.65 (m, 2H), 7.5 (d, J = 7.5 Hz, 1H), 7.48 (d, J = 6.6 Hz, 1H), 7.43 – 7.35 (m, 1H), 7.31 (d, J = 8.4 Hz, 1H), 2.77 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 159.0 (C_q), 147.3 (C_q), 140.5 (C_q), 138.4 (C_q), 136.3 (CH), 129.1 (CH), 129.0 (CH), 128.9 (CH), 127.5 (CH), 127.4 (CH), 126.6 (C_q), 125.2 (CH), 122.4 (CH), 25.4 (CH_3). IR (ATR): 2998, 1595, 1488, 1314, 892, 764 cm^{-1}. MS (EI) m/z (relative intensity) 219 (100) [M^+], 204 (5), 191 (5), 176 (5), 152 (5). HR-MS (EI) m/z calcd for $C_{16}H_{13}N$ [M^+] 219.1048, found 219.1049. The spectral data were in accordance with those reported in the literature.[6]



6-Fluoro-2-methylquinoline (**6da**)

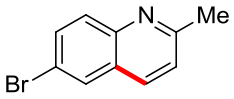
The general procedure **B** was followed using **4d** (77 mg, 0.5 mmol), methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) and [$RuCl_2$(*p*-cymene)]$_2$ (15.3 mg, 5.0 mol %) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **6da** (47 mg, 58%) as an off white solid. M. p. = 51−53 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.05 – 7.91 (m, 2H), 7.42 (ddd, J = 9.1, 8.4, 2.8 Hz, 1H), 7.36 (dd, J = 8.9, 2.8 Hz, 1H), 7.27 (dd, J = 8.4, 0.8 Hz, 1H), 2.71 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 159.9 (C_q, $J_{C\text{-}F}$ = 250.1 Hz), 158.3 (C_q), 144.9 (C_q), 135.5 (CH, $J_{C\text{-}F}$ = 5.1 Hz), 131.0 (CH, $J_{C\text{-}F}$ = 9.0 Hz), 126.9 (C_q, $J_{C\text{-}F}$ = 10.1 Hz), 122.7 (CH), 119.4 (CH, $J_{C\text{-}F}$ = 25.6 Hz), 110.5 (CH, $J_{C\text{-}F}$ = 21.8 Hz), 25.2 (CH_3). ^{19}F-NMR ($CDCl_3$, 282 MHz): δ = -115.0 (td, J = 8.6, 5.3 Hz). IR (ATR): 3058, 1652, 1439, 1329, 749, 509 cm^{-1}. MS (EI) m/z (relative intensity) 161 (100) [M^+], 146 (5), 133 (10). HR-MS (EI) m/z calcd for $C_{10}H_8NF$ [M^+] 161.0641, found 161.0638. The spectral data were in accordance with those reported in the literature.[4,7]



6-Chloro-2-methylquinoline (**6ea**)

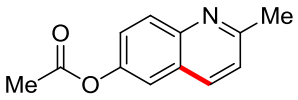
The general procedure **B** was followed using **4e** (85 mg, 0.5 mmol), methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) and [$RuCl_2$(*p*-cymene)]$_2$ (15.3 mg, 5.0 mol %) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **6ea** (53 mg, 60%) as an off white solid. M. p. = 95−97 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.9 (d, J = 8.6 Hz, 2H), 7.7 (d, J = 2.4 Hz, 1H), 7.57 (dd, J = 9.0, 2.3 Hz, 1H), 7.26 (d, J = 8.4 Hz, 1H), 2.70 (s, 3H). ^{13}C-NMR

($CDCl_3$, 75 MHz): δ = 159.3 (C_q), 146.2 (C_q), 135.2 (CH), 131.2 (C_q), 130.2 (CH), 130.2 (CH), 127.0 (C_q), 126.1 (CH), 122.8 (CH), 25.3 (CH_3). IR (ATR): 3050, 1597, 1468, 1067, 830, 641 cm^{-1}. MS (EI) m/z (relative intensity) 177 (100) [M^+], 162 (10), 142 (15), 133 (15), 115 (15), 105 (5). HR-MS (EI) m/z calcd for $C_{10}H_8NCl$ [M^+] 177.0345, found 177.0341. The spectral data were in accordance with those reported in the literature.[4,7]



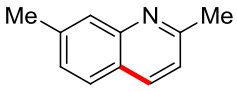
6-Bromo-2-methylquinoline (**6fa**)

The general procedure **B** was followed using **4f** (107 mg, 0.5 mmol), methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) and [$RuCl_2$(*p*-cymene)]$_2$ (15.3 mg, 5.0 mol %) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **6fa** (56 mg, 51%) as an off white solid. M. p. = 98−100 °C. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.95 – 7.90 (m, 1H), 7.89 (d, *J* = 2.3 Hz, 1H), 7.87 – 7.82 (m, 1H), 7.71 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.27 (d, *J* = 8.5 Hz, 1H), 2.70 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 159.5 (C_q), 146.4 (C_q), 135.1 (CH), 132.8 (CH), 130.4 (CH), 129.5 (CH), 127.6 (C_q), 122.8 (CH), 119.3 (C_q), 25.4 (CH_3). IR (ATR): 3048, 1594, 1488, 1300, 1071, 828 cm^{-1}. MS (EI) m/z (relative intensity) 221 (100) [M^+], 205 (5), 142 (20), 115 (30). HR-MS (EI) m/z calcd for $C_{10}H_8N^{79}Br$ [M^+] 220.9840, found 220.9838. The spectral data were in accordance with those reported in the literature.[4,7,8]



2-Methylquinolin-6-yl acetate (**6ga**)

The general procedure **B** was followed using **4g** (97 mg, 0.5 mmol), methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) and [$RuCl_2$(*p*-cymene)]$_2$ (15.3 mg, 5.0 mol %) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 3:1) yielded **6ga** (51 mg, 51%) as an oil. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.99 (d, *J* = 8.8 Hz, 1H), 7.96 (d, *J* = 8.5 Hz, 1H), 7.48 (d, *J* = 2.5 Hz, 1H), 7.38 (dd, *J* = 9.0, 2.6 Hz, 1H), 7.28 – 7.22 (m, 1H), 2.71 (s, 3H), 2.32 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 169.4 (C_q), 158.8 (C_q), 147.8 (C_q), 145.8 (C_q), 135.8 (CH), 130.1 (CH), 126.6 (C_q), 124.4 (CH), 122.5 (CH), 118.1 (CH), 25.2 (CH_3), 21.1 (CH_3). IR (ATR): 1713, 1598, 1504, 1429, 1234, 832 cm^{-1}. MS (EI) m/z (relative intensity) 201 (5) [M^+], 159 (100), 130 (10), 103 (5). HR-MS (EI) m/z calcd for $C_{12}H_{11}NO_2$ [M^+] 201.0790, found 201.0789. The spectral data were in accordance with those reported in the literature.[9]



2,7-Dimethylquinoline (**6ha**)

The general procedure **B** was followed using **4h** (75 mg, 0.5 mmol) and methyl vinyl ketone (**2a**) (70 mg, 1.0 mmol) for 20 h. Purification by column chromatography (*n*-hexane/EtOAc 5:1) yielded **6ha** (49 mg, 62%) as an oil. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.96 (d, J = 8.4 Hz, 1H), 7.78 (d, J = 0.8 Hz, 1H), 7.63 (d, J = 8.3 Hz, 1H), 7.29 (dd, J = 8.3, 1.7 Hz, 1H), 7.19 (d, J = 8.4 Hz, 1H), 2.70 (s, 3H), 2.52 (s, 3H). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 158.9 (C_q), 148.1 (C_q), 139.6 (C_q), 135.8 (CH), 127.8 (CH), 127.7 (CH), 127.1 (CH), 124.5 (C_q), 121.1 (CH), 25.3 (CH_3), 21.9 (CH_3). IR (ATR): 2916, 1601, 1505, 1305, 835, 776 cm^{-1}. MS (EI) m/z (relative intensity) 157 (100) [M^+], 142 (20), 128 (5), 115 (15), 89 (5). HR-MS (EI) m/z calcd for $C_{11}H_{11}N$ [M^+] 157.0891, found 157.0889. The spectral data were in accordance with those reported in the literature.[4,10]

References:

[1] Q. Tang, D. Xia, X. Jin, Q. Zhang, X.-Q. Sun and C. Wang, *J. Am. Chem. Soc.* 2013, **135**, 4628–4631.

[2] L. Ackermann, L. Wang, R. Wolfram and A. V. Lygin, *Org. Lett.*, 2012, **14**, 728–731.

[3] G. Rouquet and N. Chatani, *Chem. Sci.*, 2013, **4**, 10737–10742.

[4] Y. Matsubara, S. Hirakawa, Y. Yamaguchi and Z.-I. Yoshida, *Angew. Chem. Int. Ed.*, 2011, **50**, 7670–7673.

[5] V. Sridharan, C. Avendaño and J. C. Menéndez, *Tetrahedron*, 2007, **63**, 673–681.

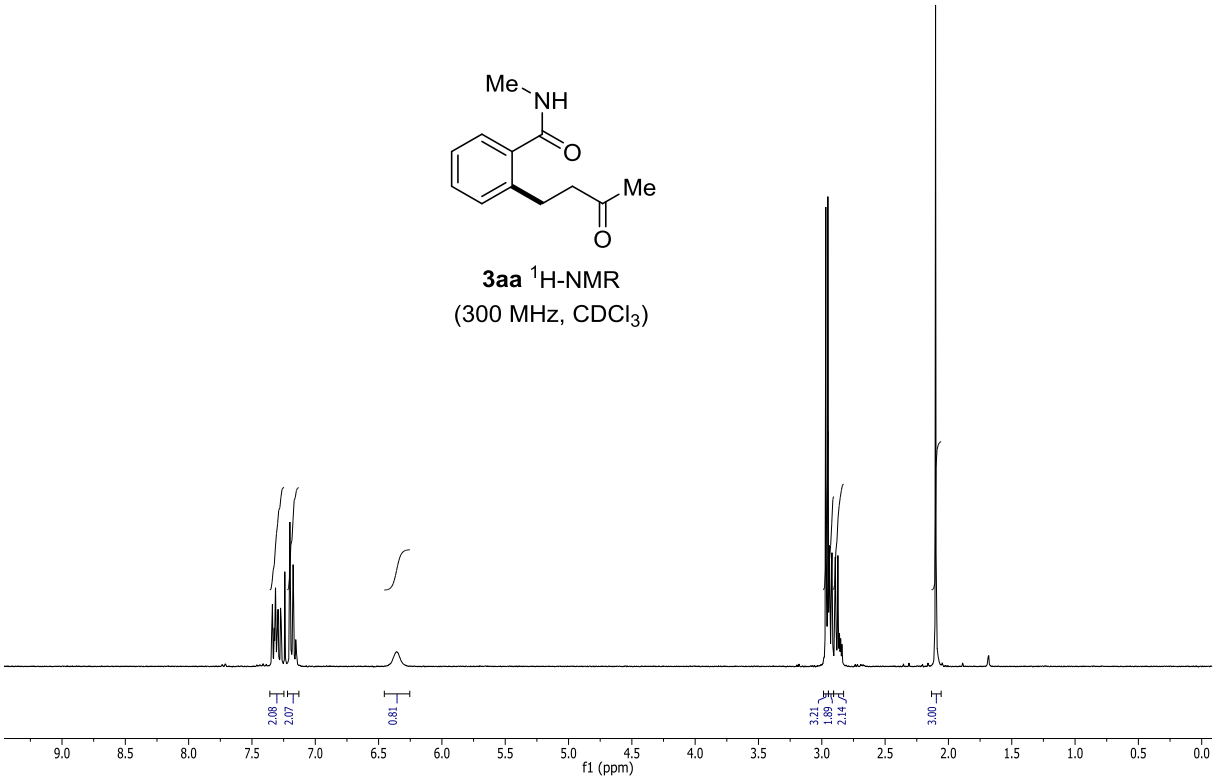
[6] F. Mongin, L. Mojovic, B. Guillamet, F. Trécourt and G. Quéguiner, *J. Org. Chem.*, 2002, **67**, 8991–8994.

[7] C. Ramesh, V. Kavala, C.-W. Kuo and C.-F. Yao, *Tetrahedron Lett.*, 2010, **51**, 5234-5237.

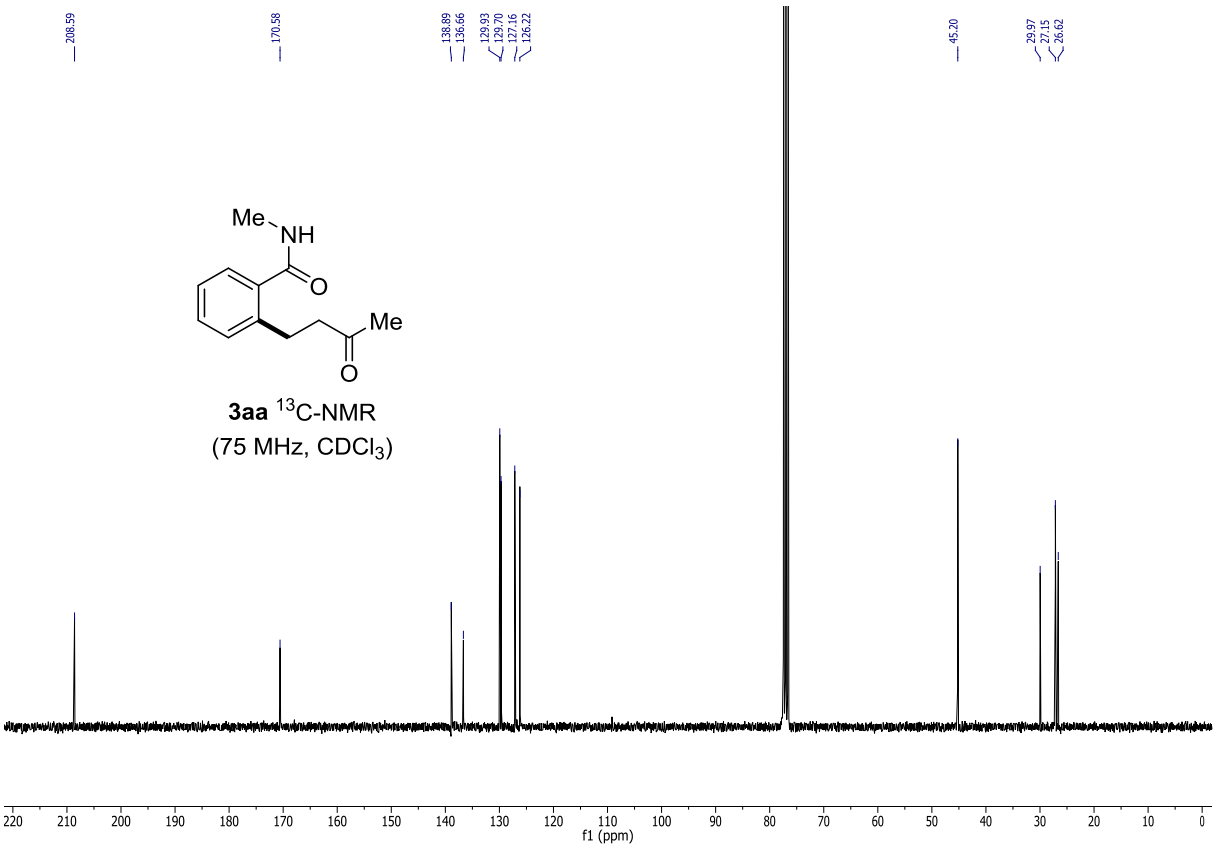
[8] K. A. Reynolds, D. J. Young and W. A. Loughlin, *Synthesis*, 2010, 3645–3648.

[9] K. Jyothish, R. R. Avirah and D. Ramaiah, *Org. Lett.*, 2006, **8**, 111–114.

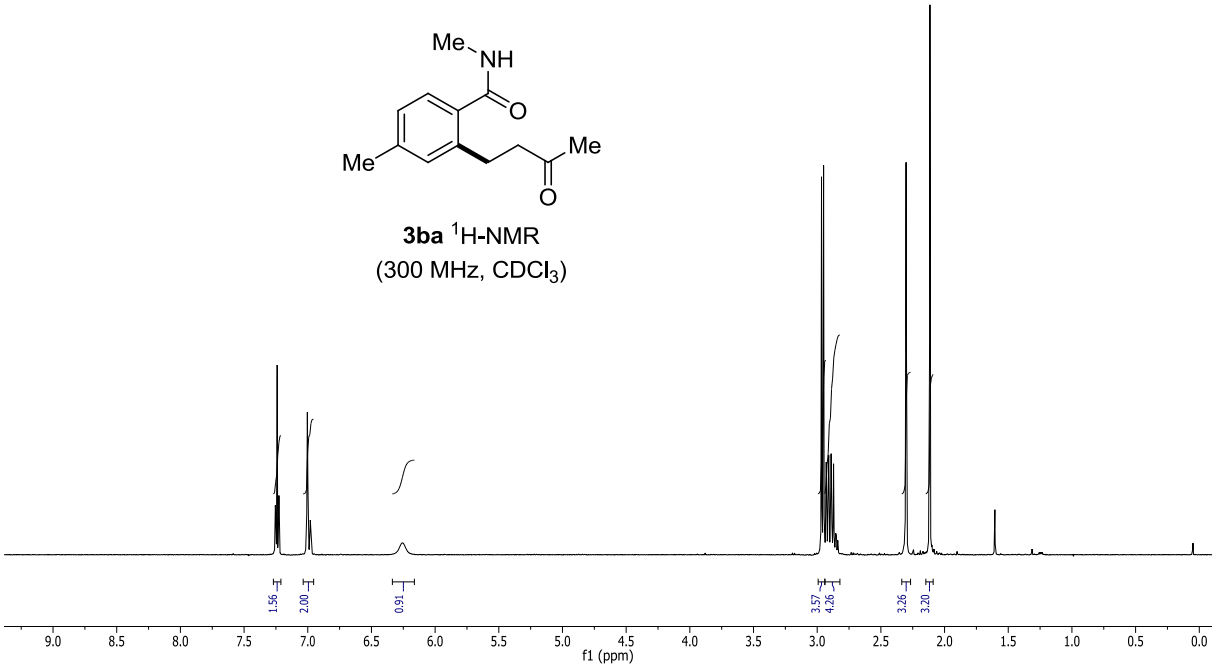
[10] J. Jaroszewska, I. Wawer and J. Oszczapowicz, *Org. Magn. Res.*, 1984, **22**, 323–327.



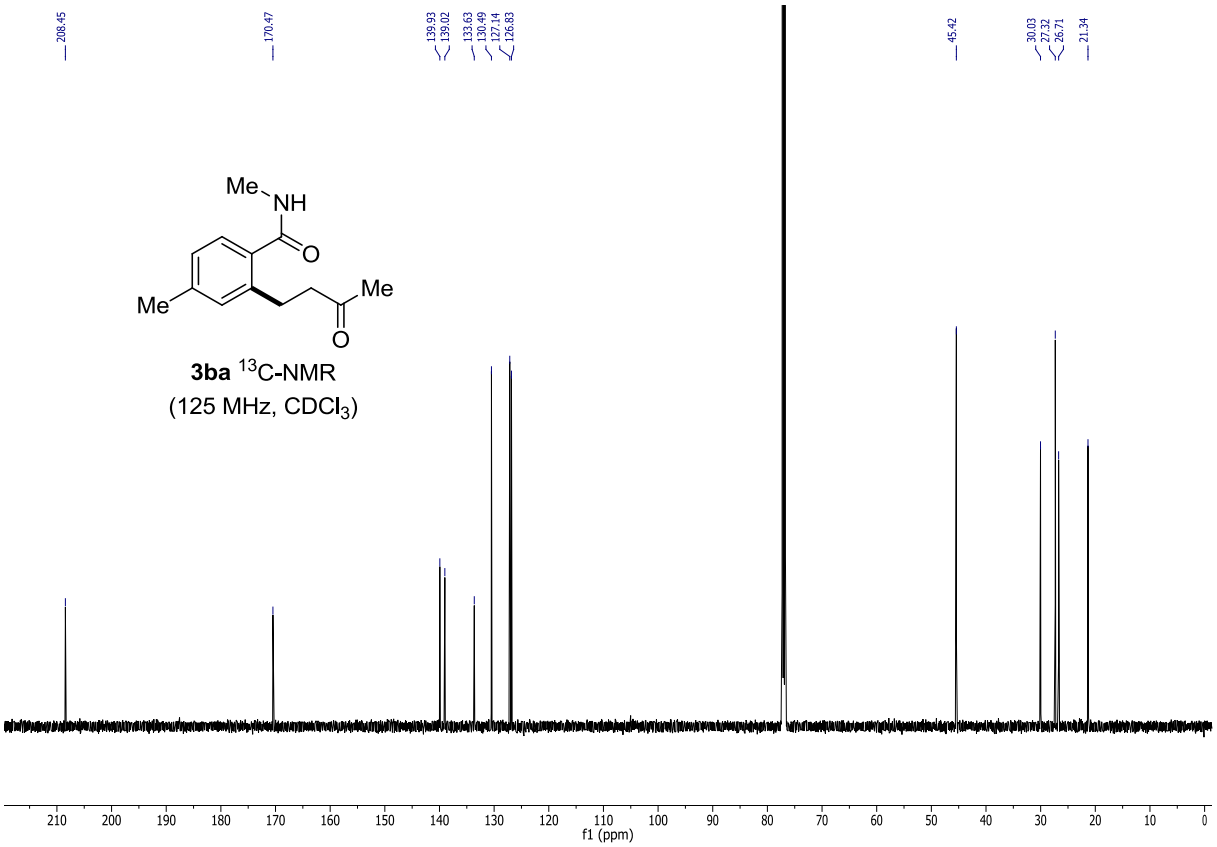
3aa ^{1}H-NMR
(300 MHz, $CDCl_3$)



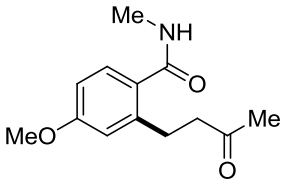
3aa ^{13}C-NMR
(75 MHz, $CDCl_3$)



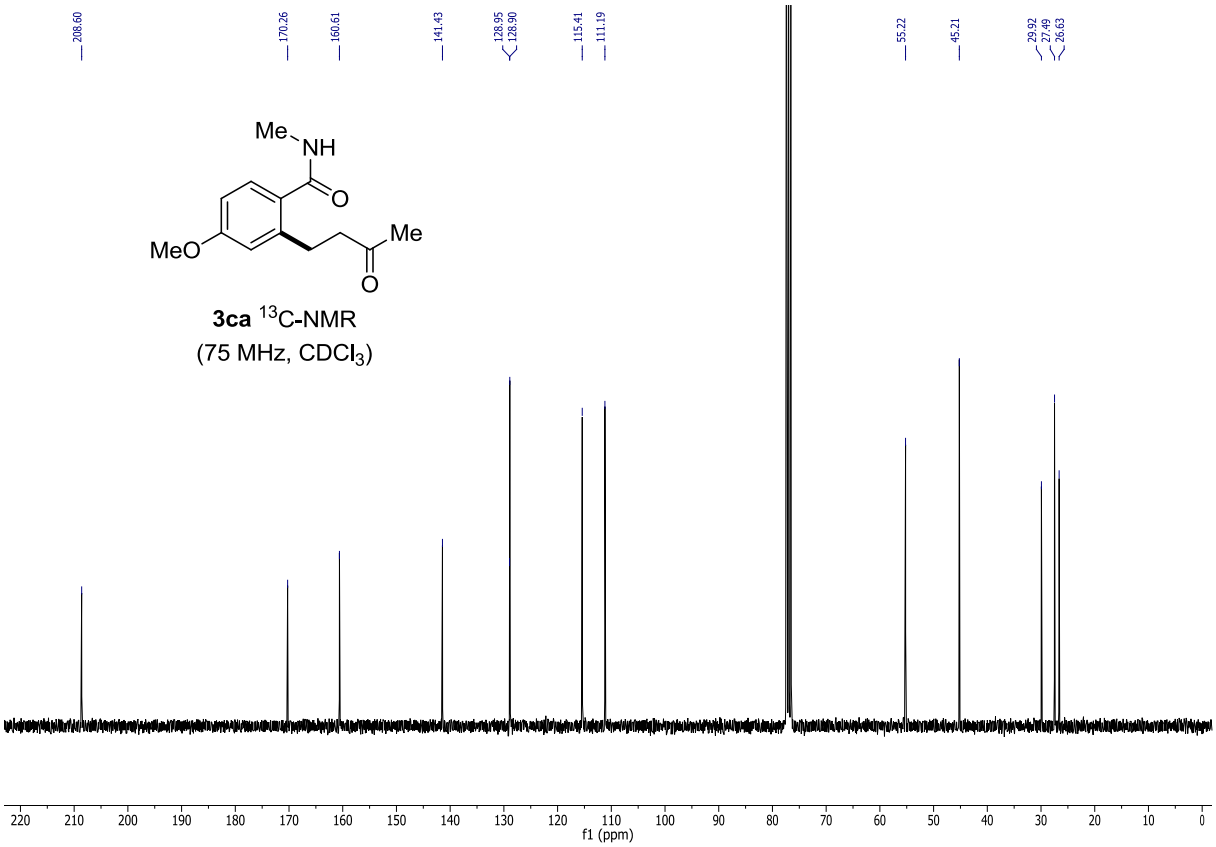
3ba ^{1}H-NMR
(300 MHz, $CDCl_3$)



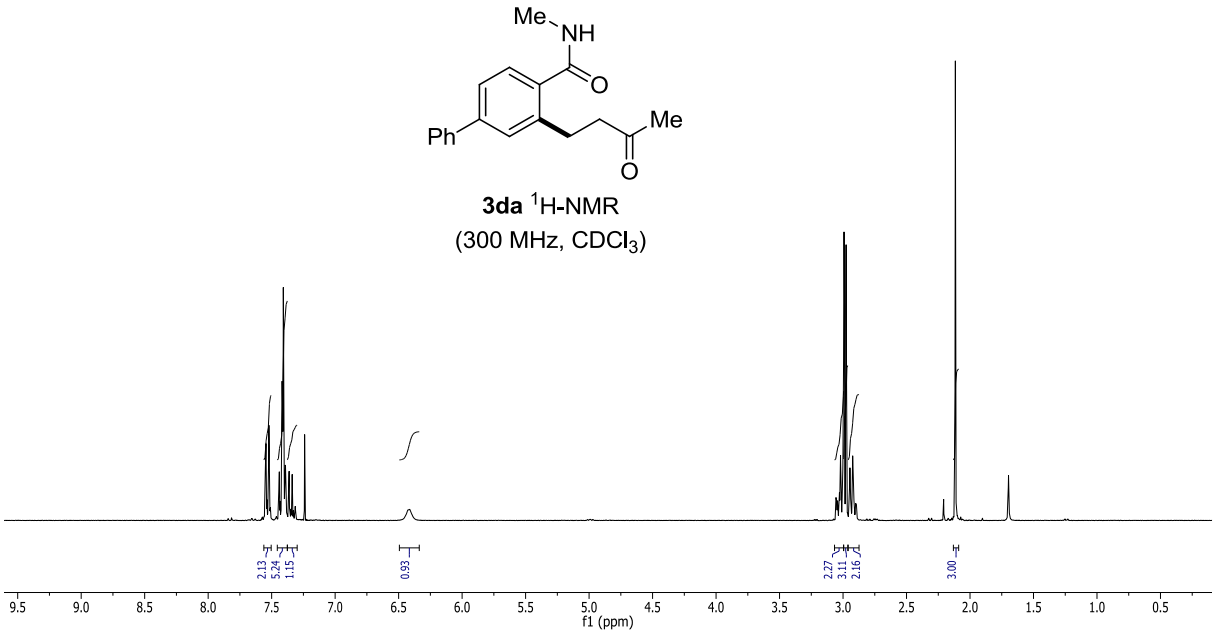
3ba ^{13}C-NMR
(125 MHz, $CDCl_3$)



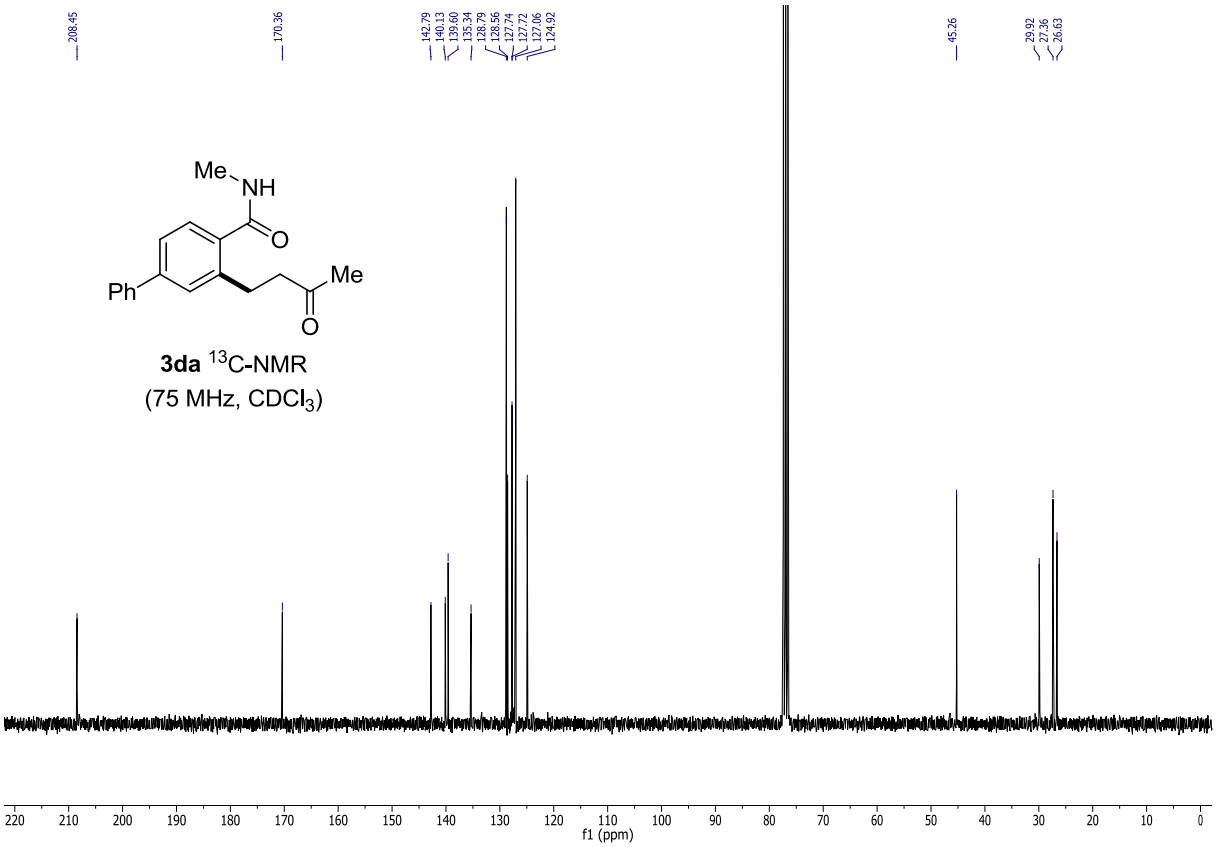
3ca ^{1}H-NMR
(300 MHz, $CDCl_3$)



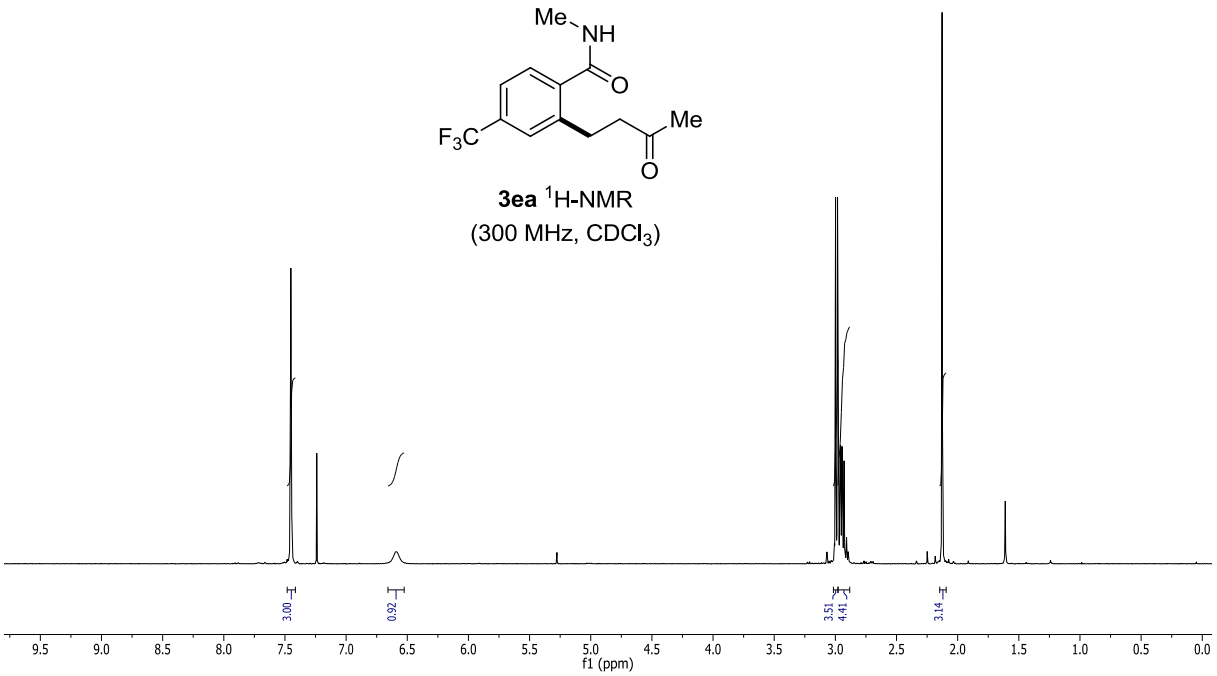
3ca ^{13}C-NMR
(75 MHz, $CDCl_3$)

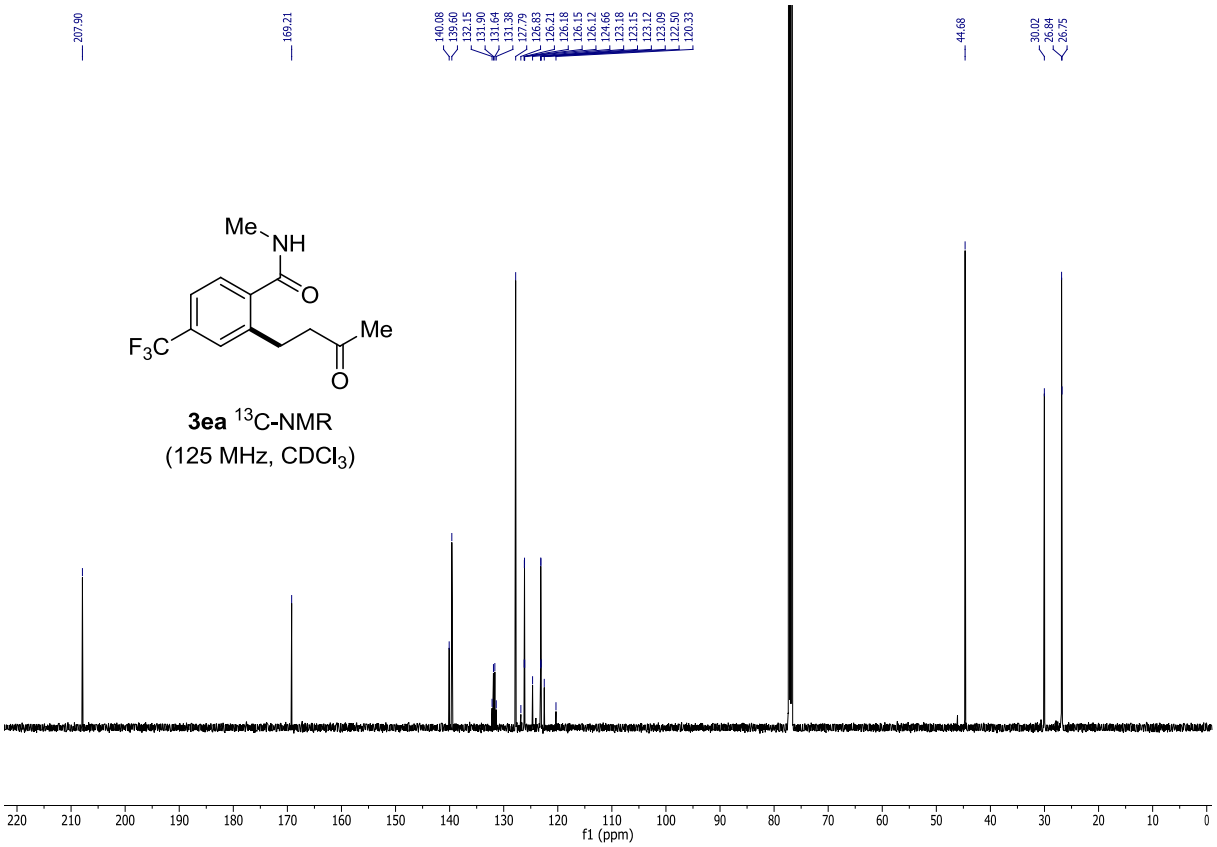


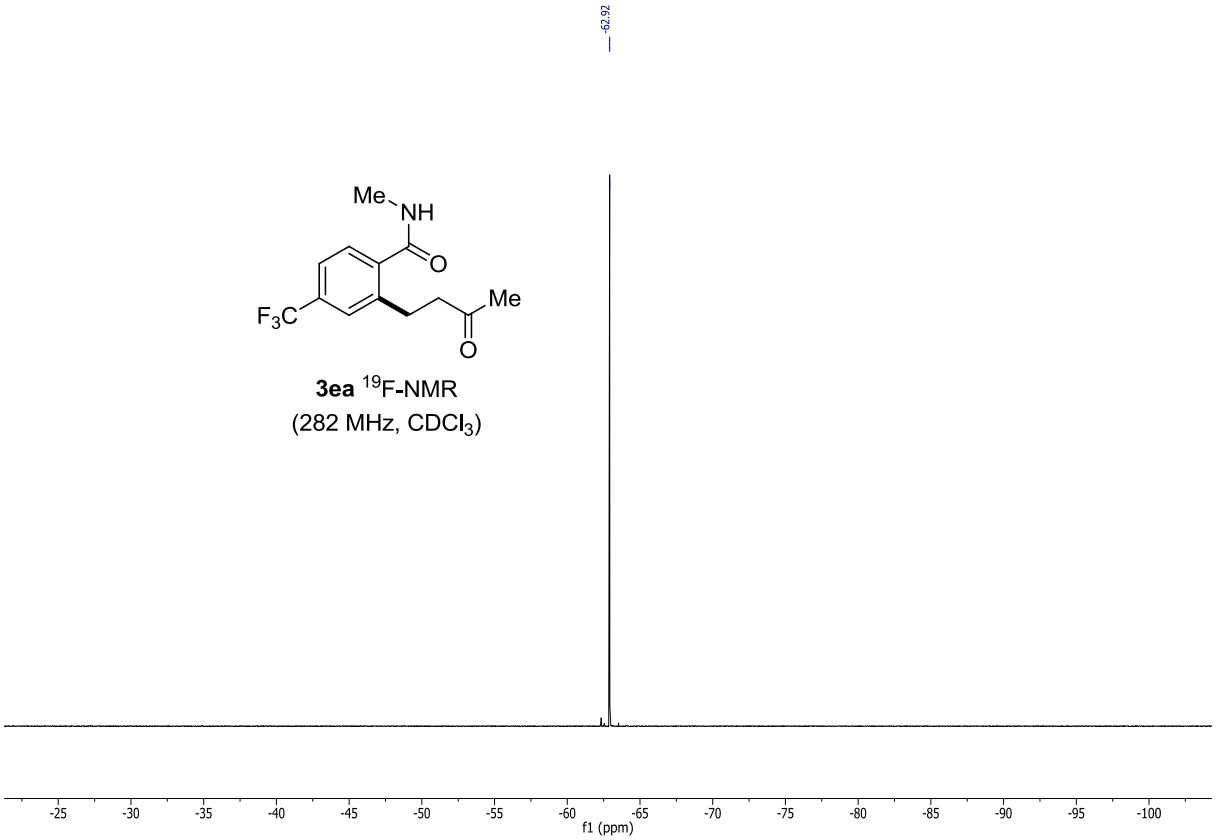
3da ^{1}H-NMR
(300 MHz, $CDCl_3$)



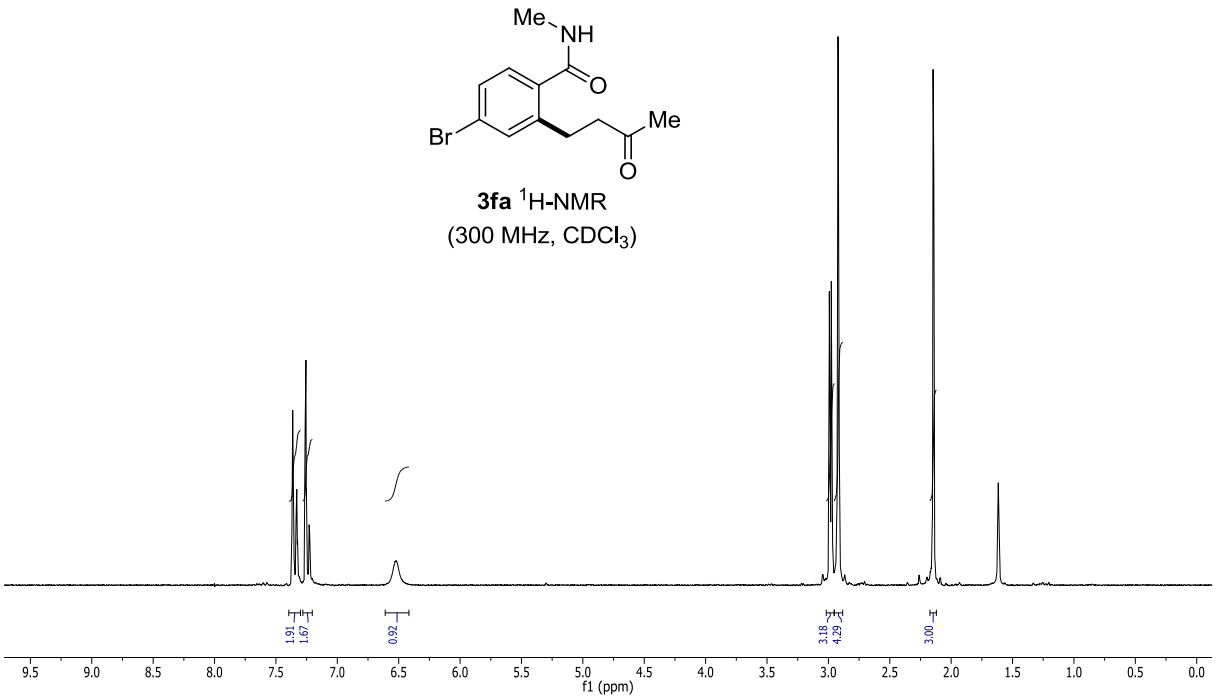
3da ^{13}C-NMR
(75 MHz, $CDCl_3$)


Me
NH
O
F3C
Me
O
3ea 1H-NMR
(300 MHz, CDCl3)
3.00
0.92
3.51
4.41
3.14
f1 (ppm)

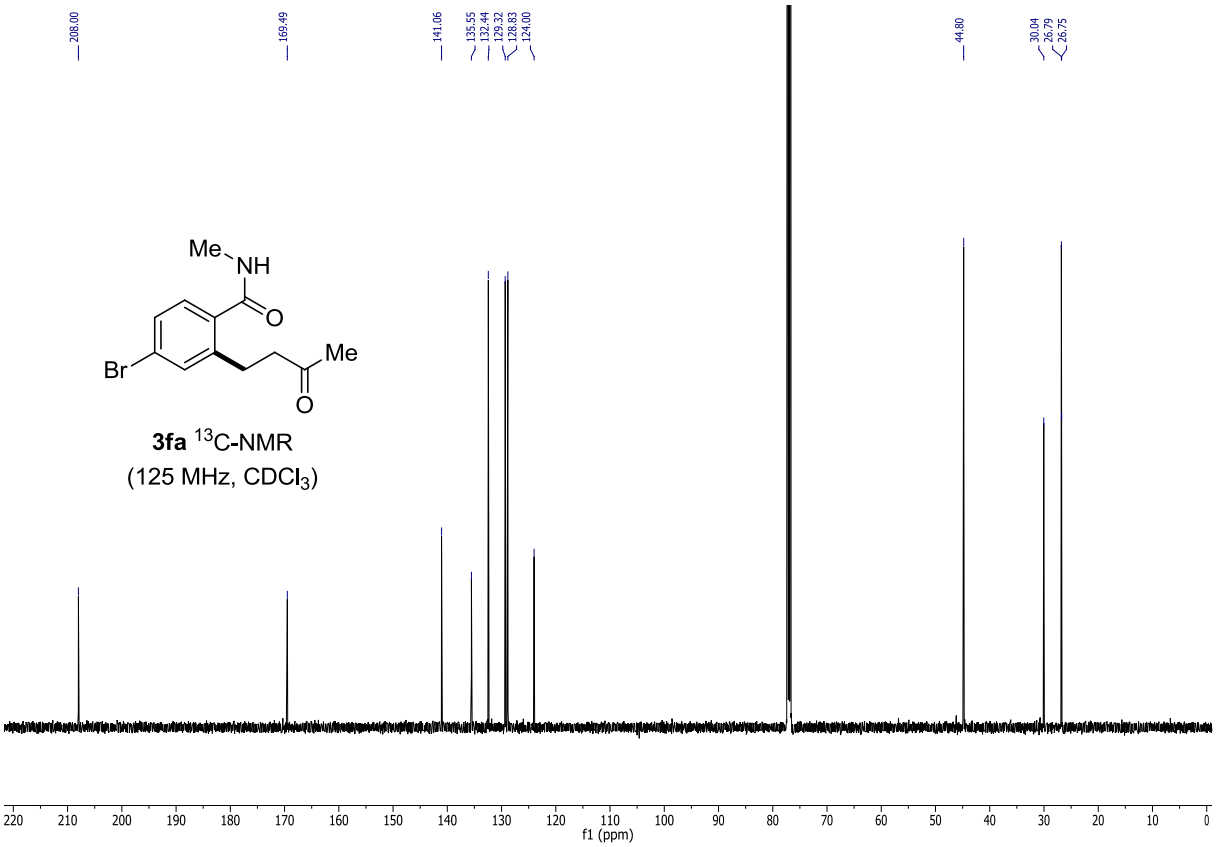

207.90
169.21
140.08
139.60
132.15
131.90
131.64
131.38
127.79
126.83
126.21
126.18
126.15
126.12
124.66
123.18
123.15
123.12
123.09
122.50
120.33
44.68
30.02
26.84
26.75
Me
NH
O
F3C
Me
O
3ea 13C-NMR
(125 MHz, CDCl3)
f1 (ppm)



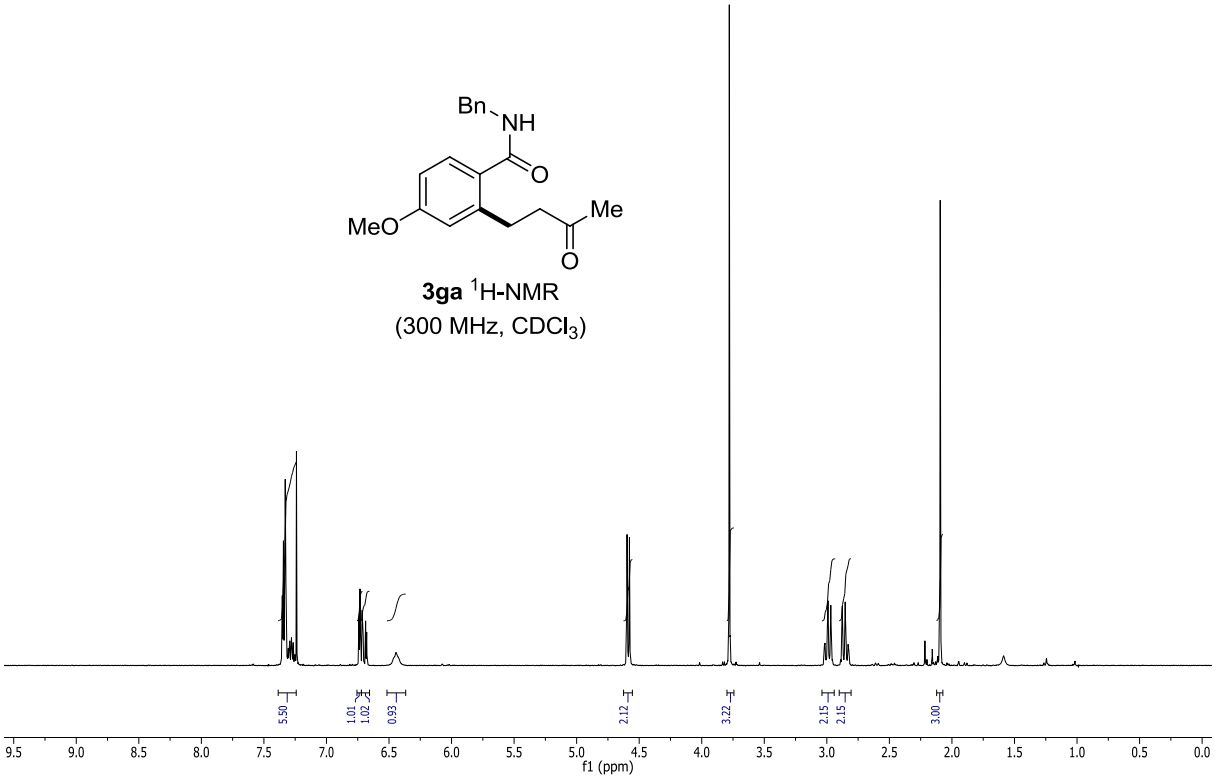
3ea ^{19}F-NMR
(282 MHz, $CDCl_3$)



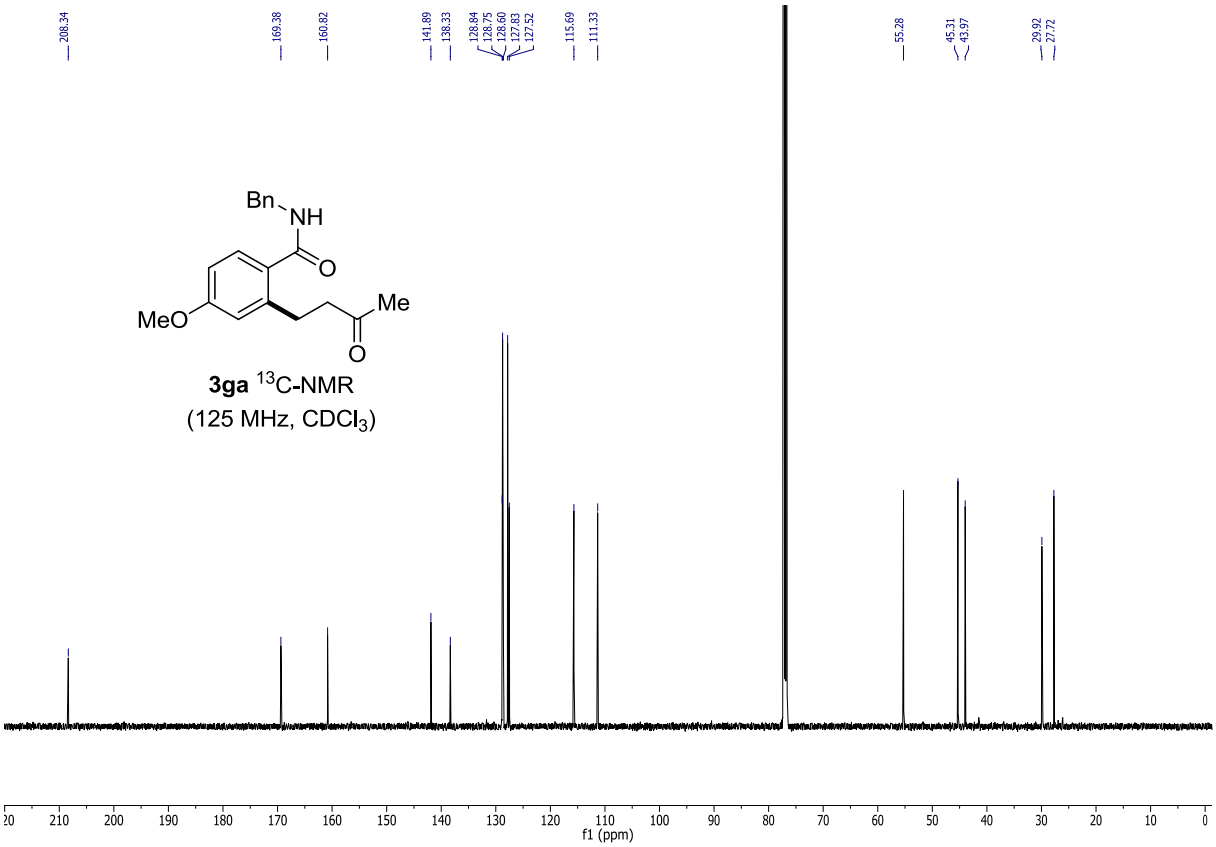
3fa ^{1}H-NMR
(300 MHz, $CDCl_3$)



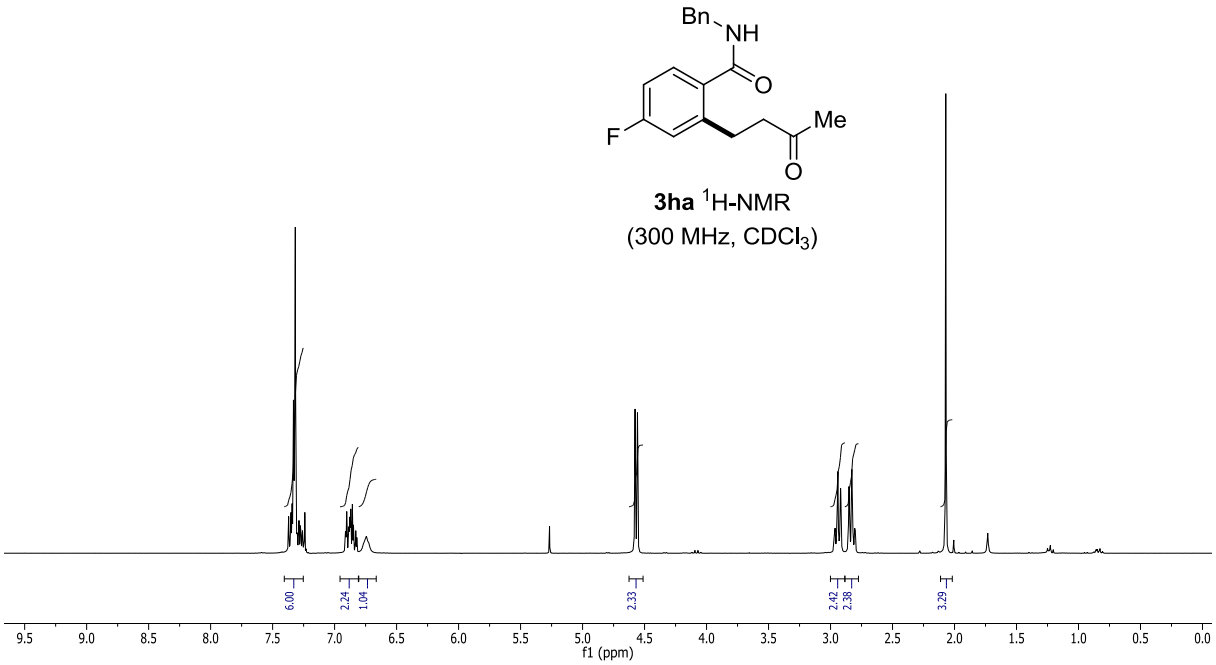
3fa ^{13}C-NMR
(125 MHz, $CDCl_3$)



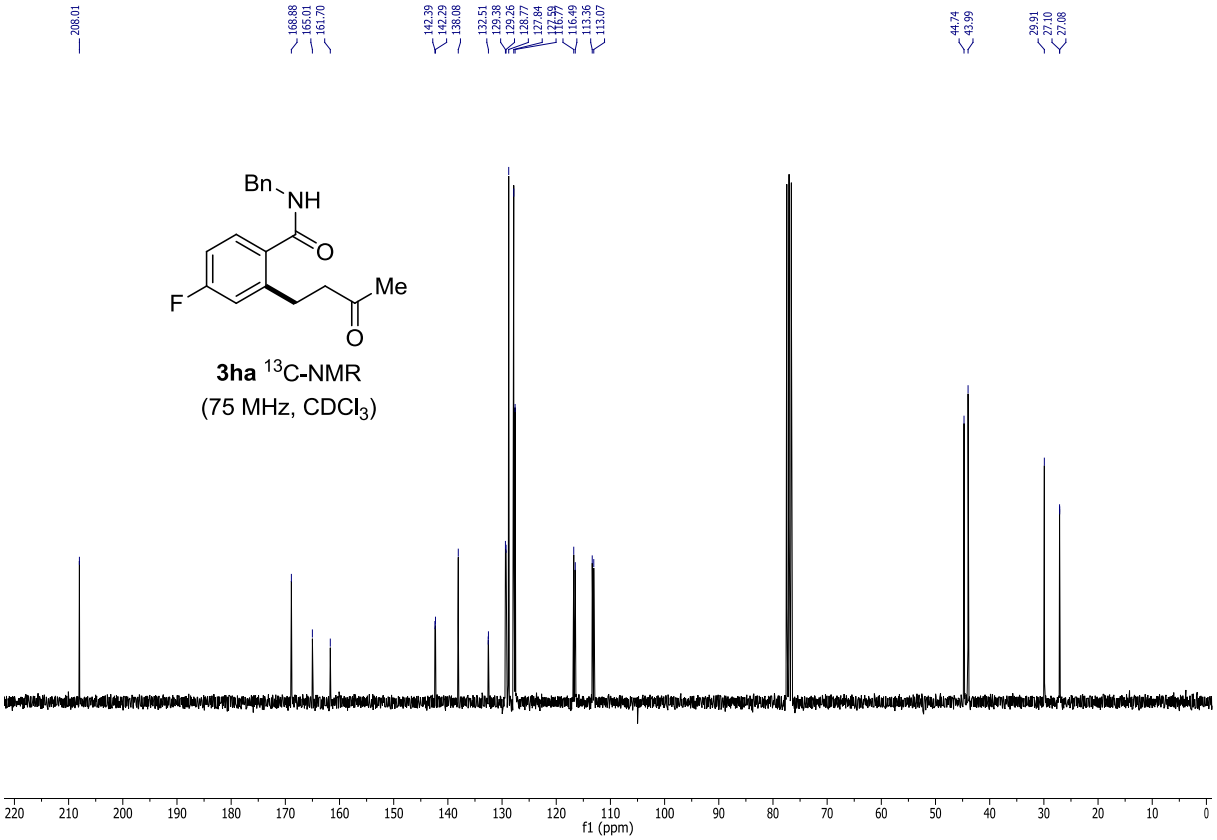
3ga ^{1}H-NMR
(300 MHz, $CDCl_3$)



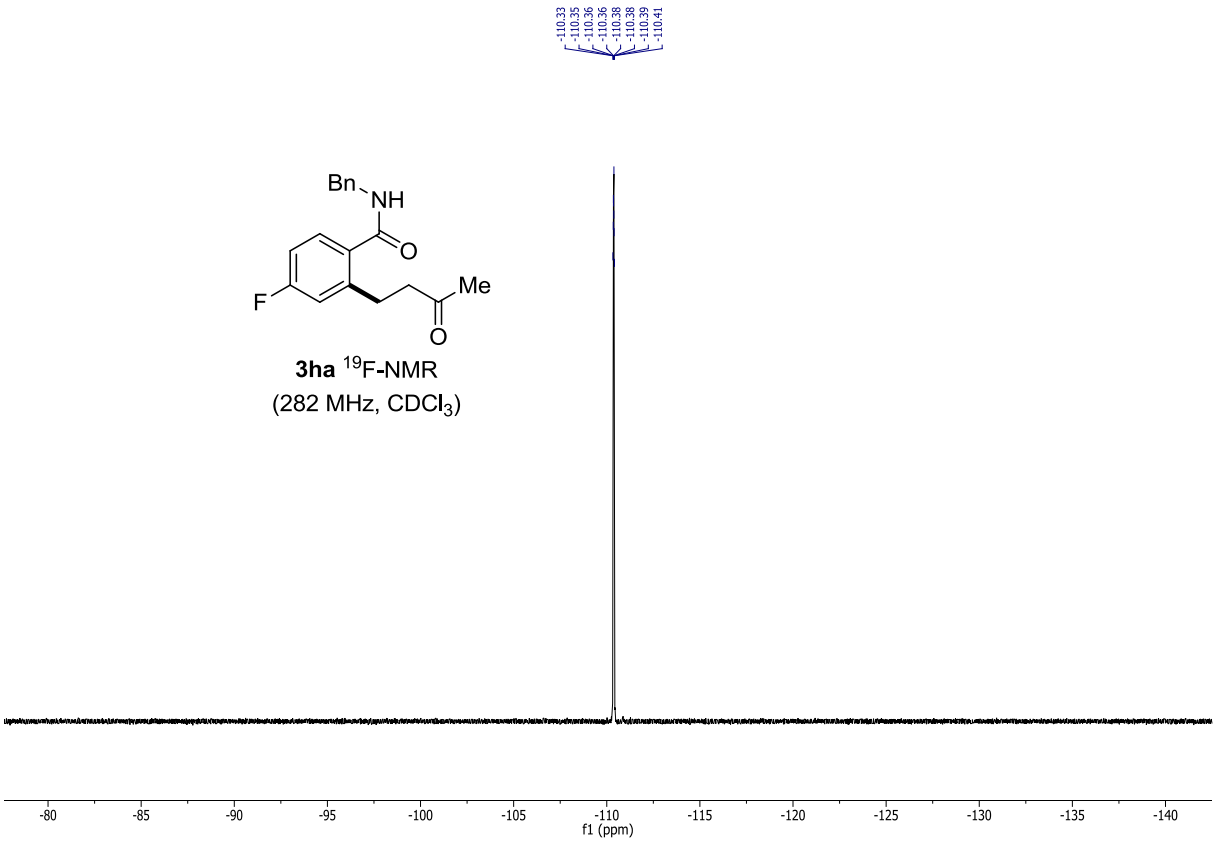
3ga ^{13}C-NMR
(125 MHz, $CDCl_3$)



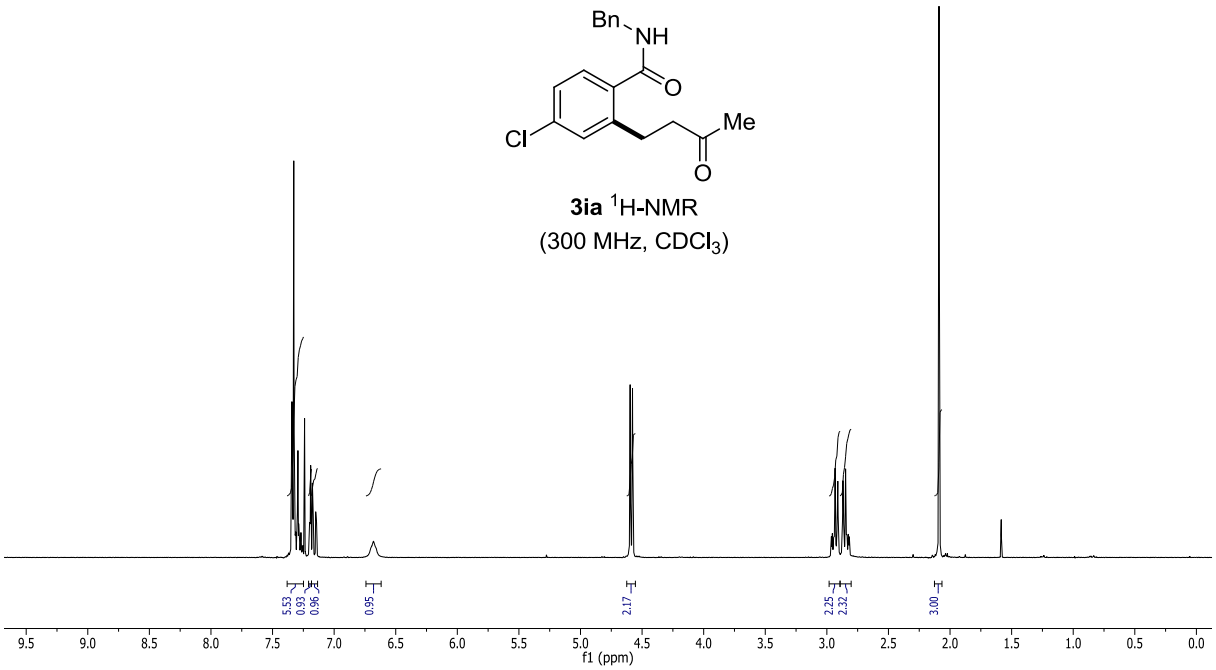
3ha ^{1}H-NMR
(300 MHz, $CDCl_3$)



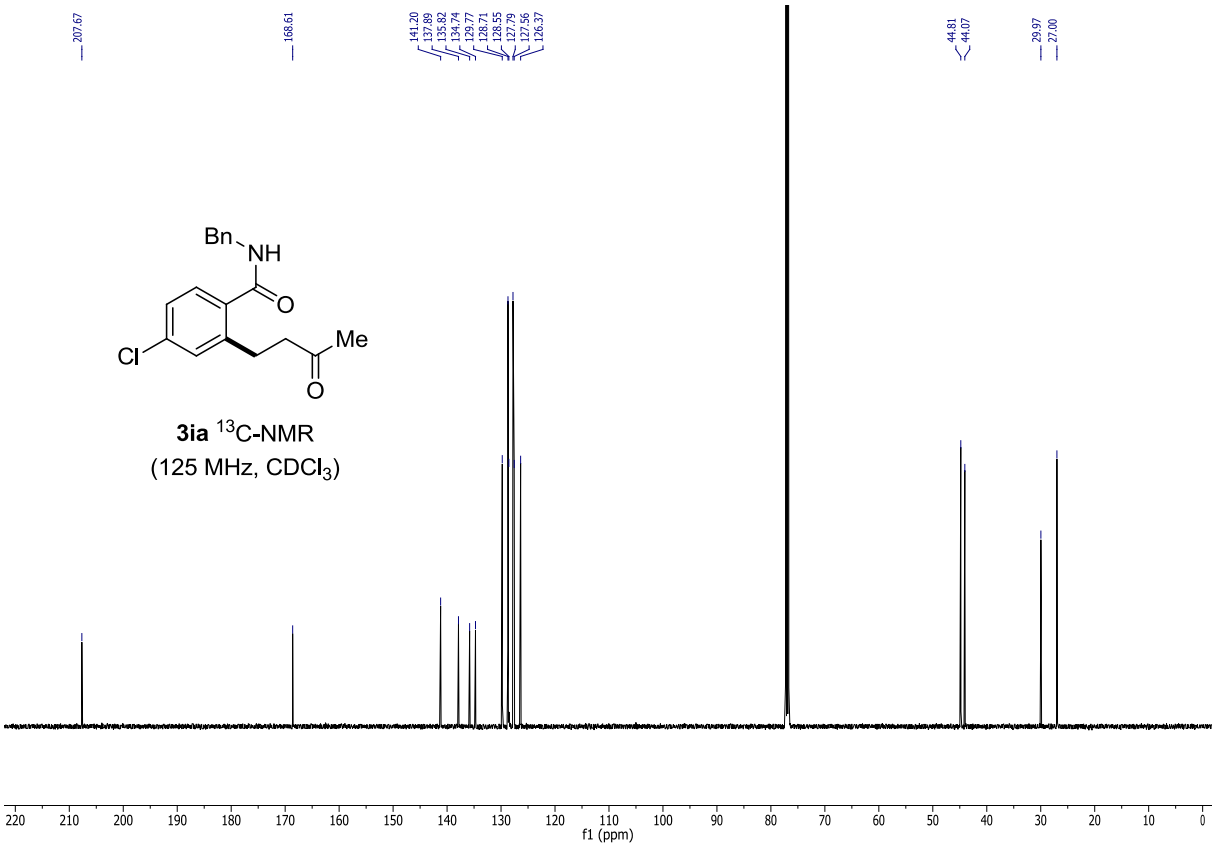
3ha ^{13}C-NMR
(75 MHz, $CDCl_3$)



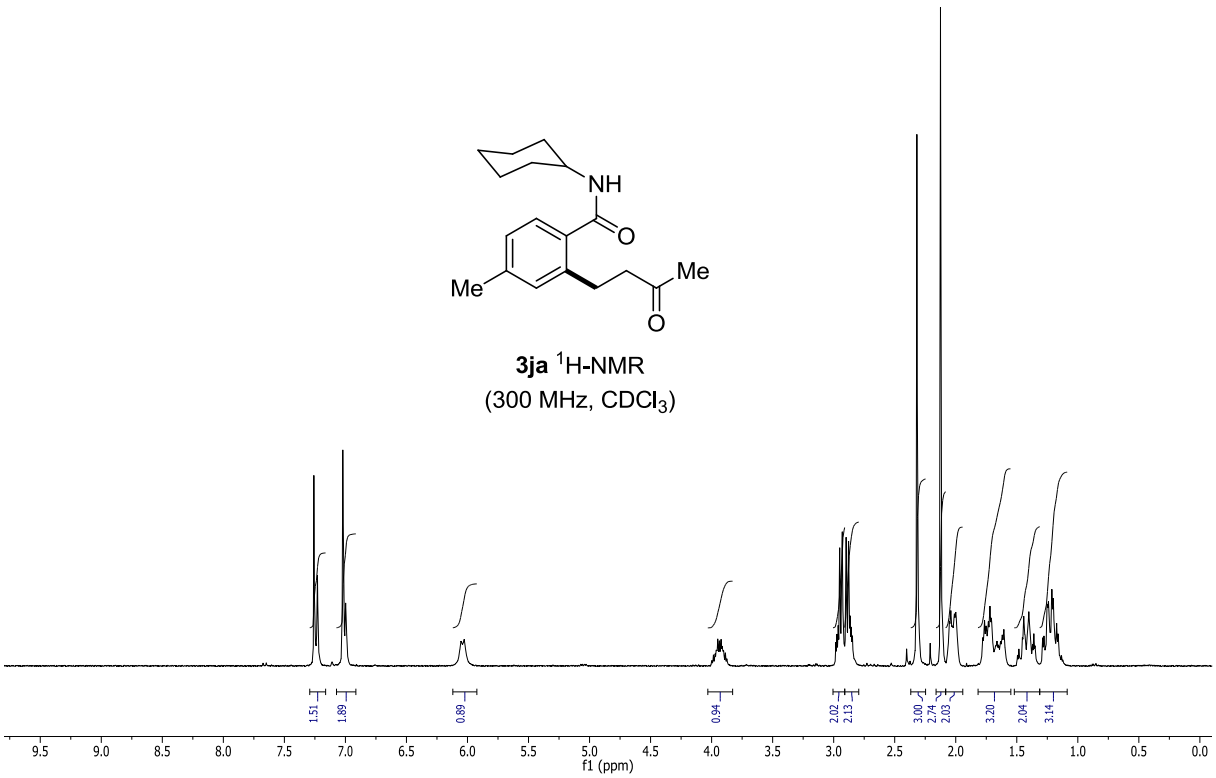
3ha ^{19}F-NMR
(282 MHz, $CDCl_3$)



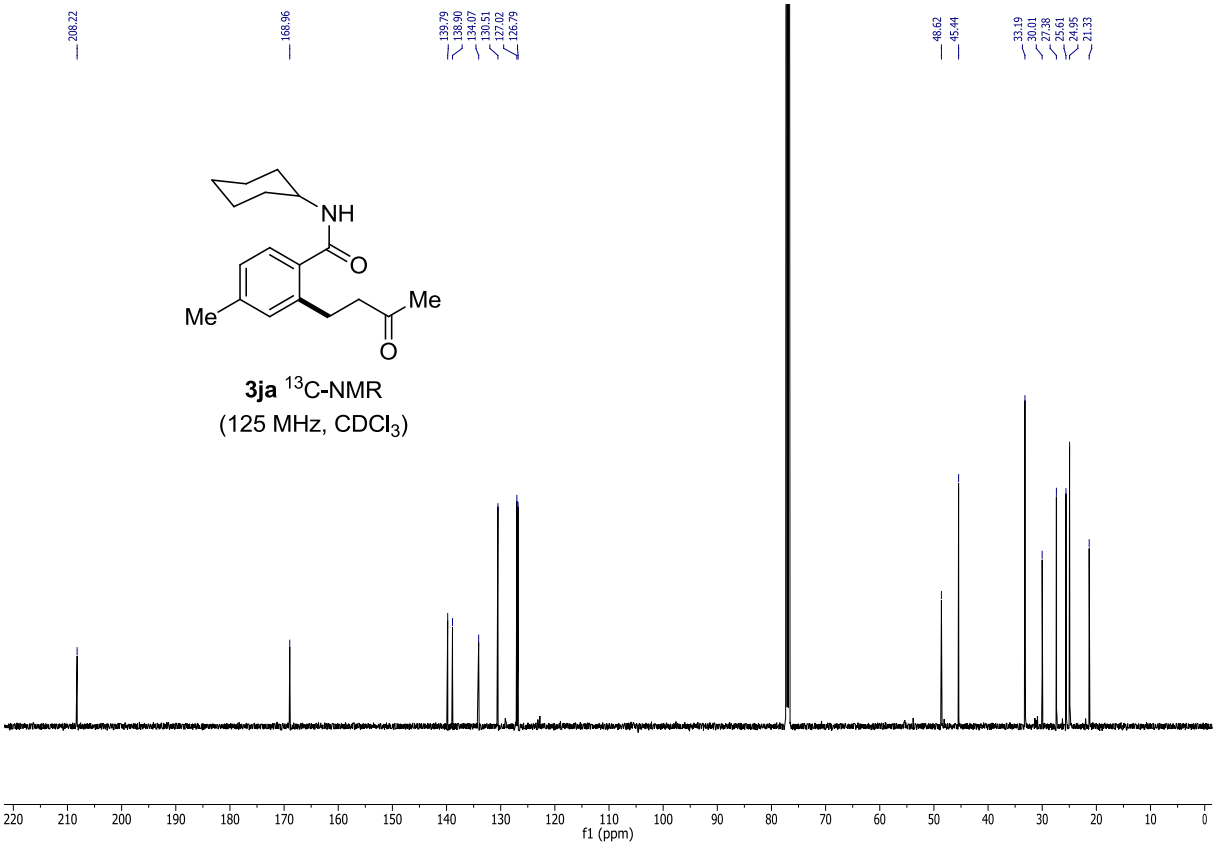
3ia ^{1}H-NMR
(300 MHz, $CDCl_3$)



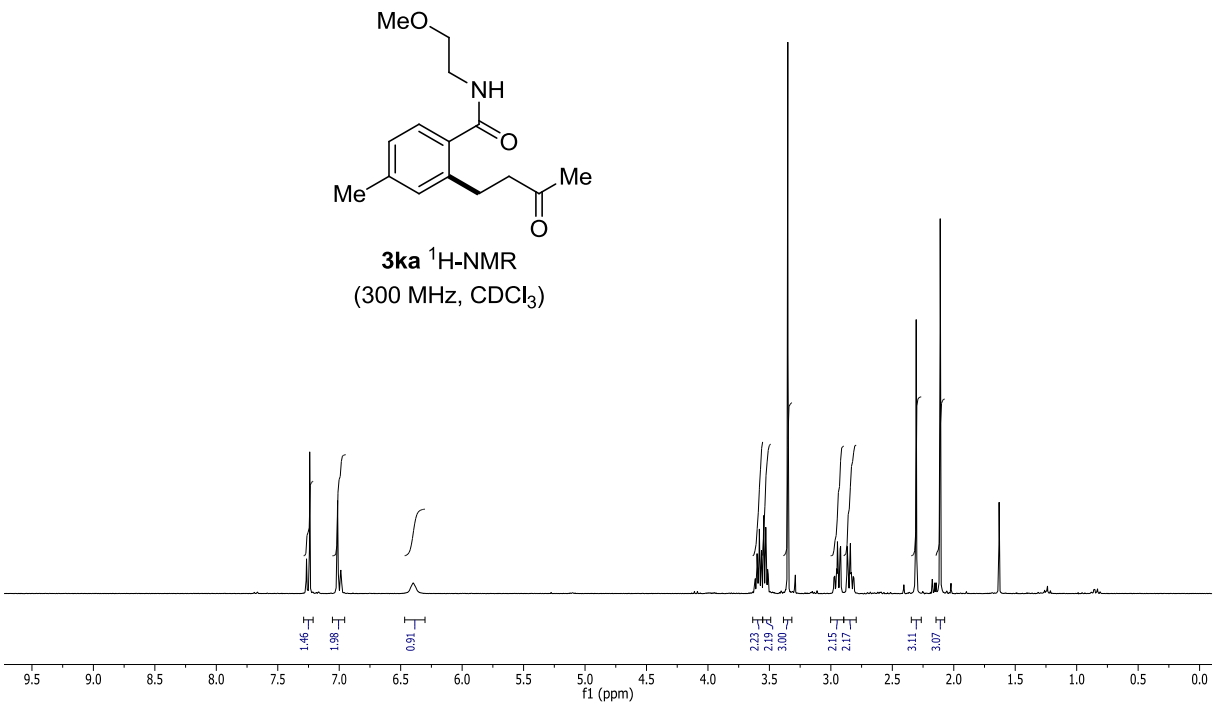
3ia ^{13}C-NMR
(125 MHz, $CDCl_3$)



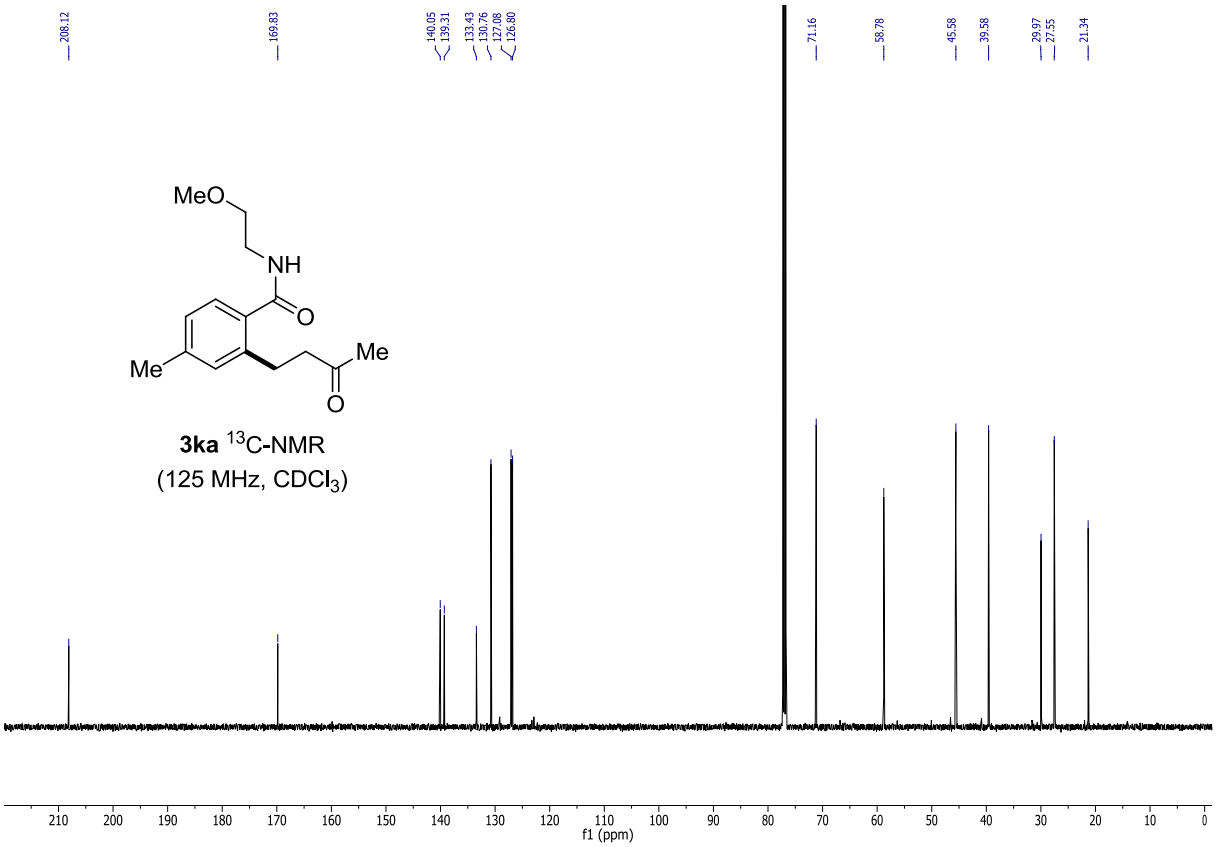
3ja ^{1}H-NMR
(300 MHz, $CDCl_3$)



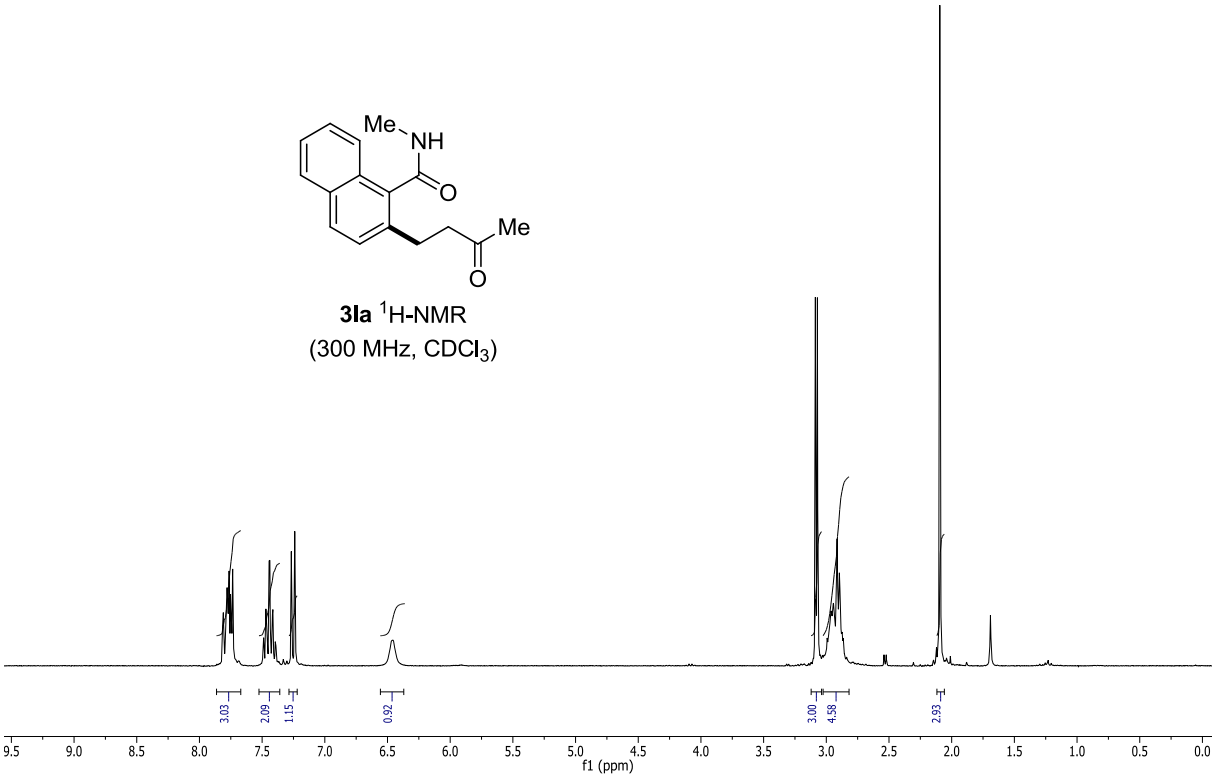
3ja ^{13}C-NMR
(125 MHz, $CDCl_3$)



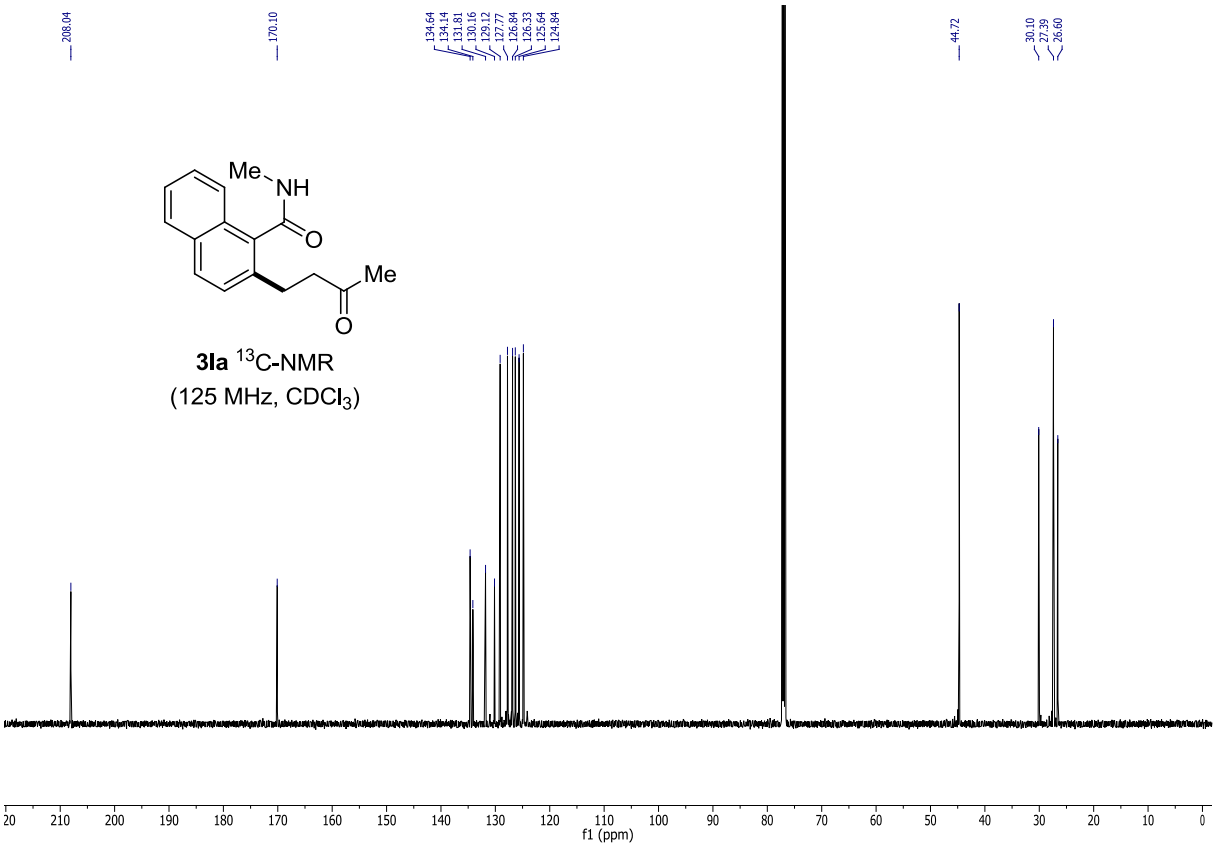
3ka ^{1}H-NMR
(300 MHz, $CDCl_3$)



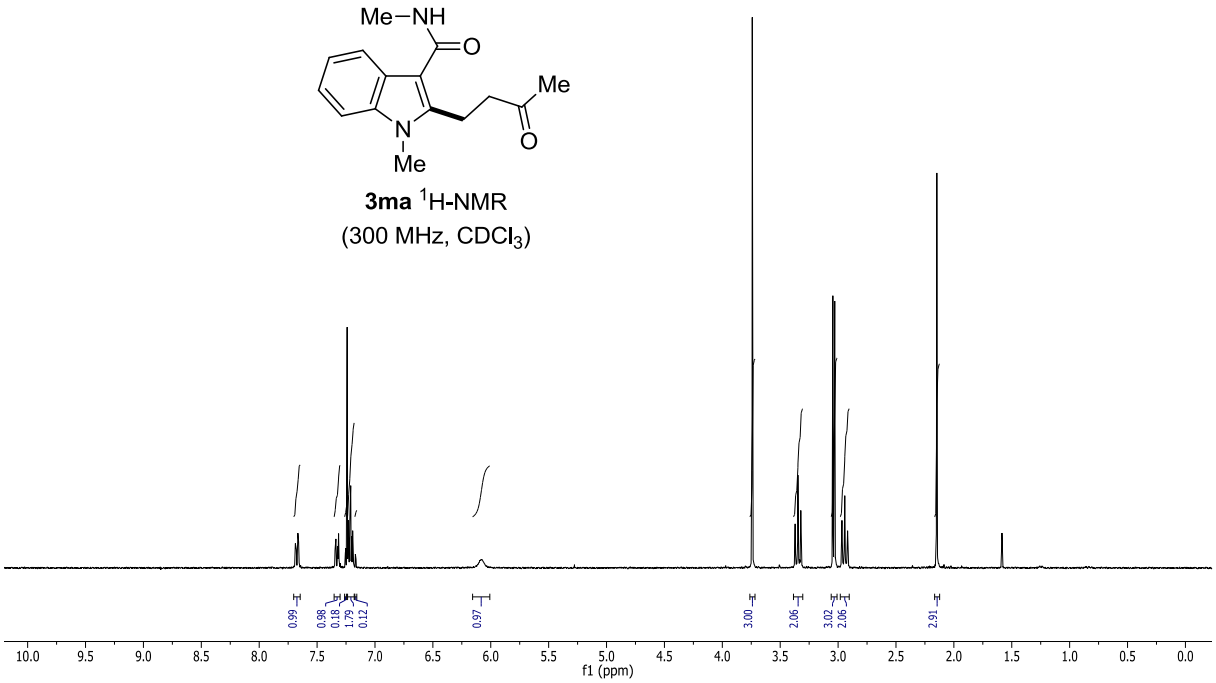
3ka ^{13}C-NMR
(125 MHz, $CDCl_3$)



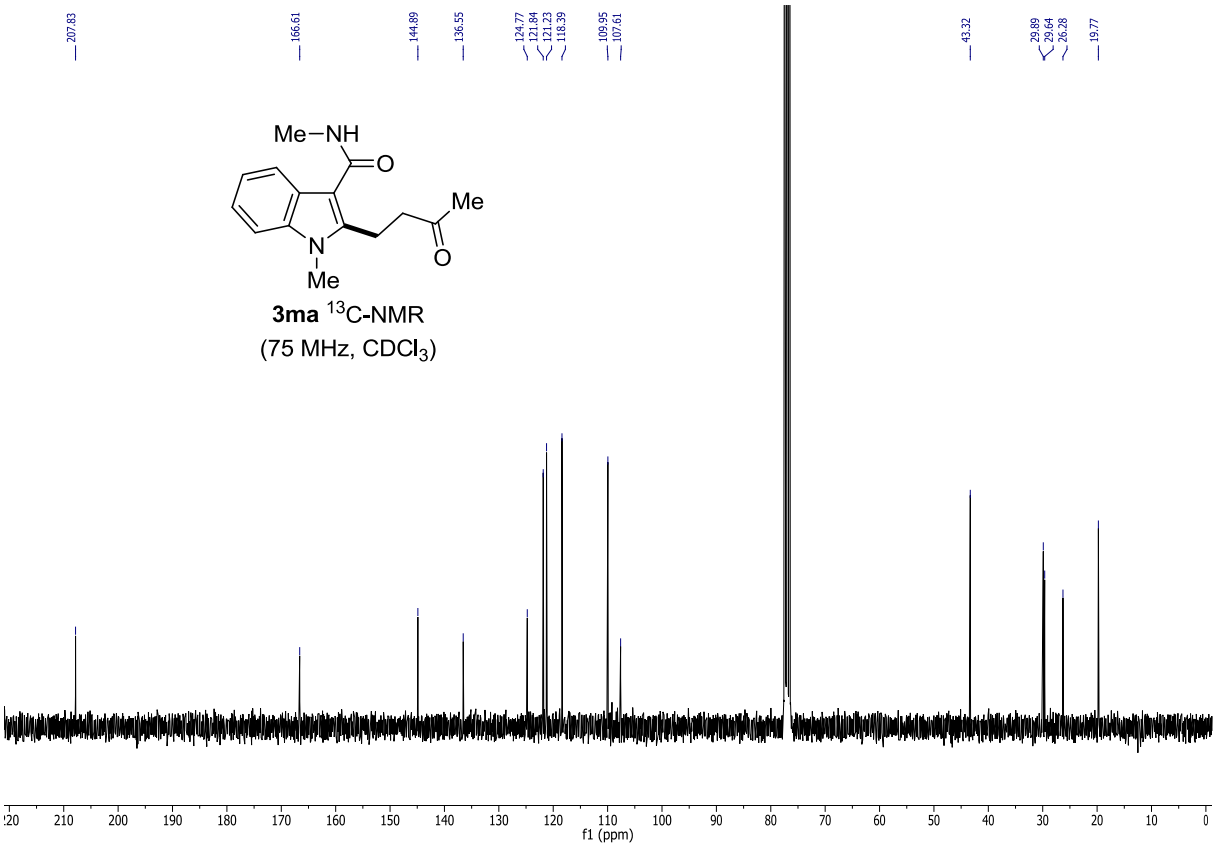
3la ^{1}H-NMR
(300 MHz, $CDCl_3$)



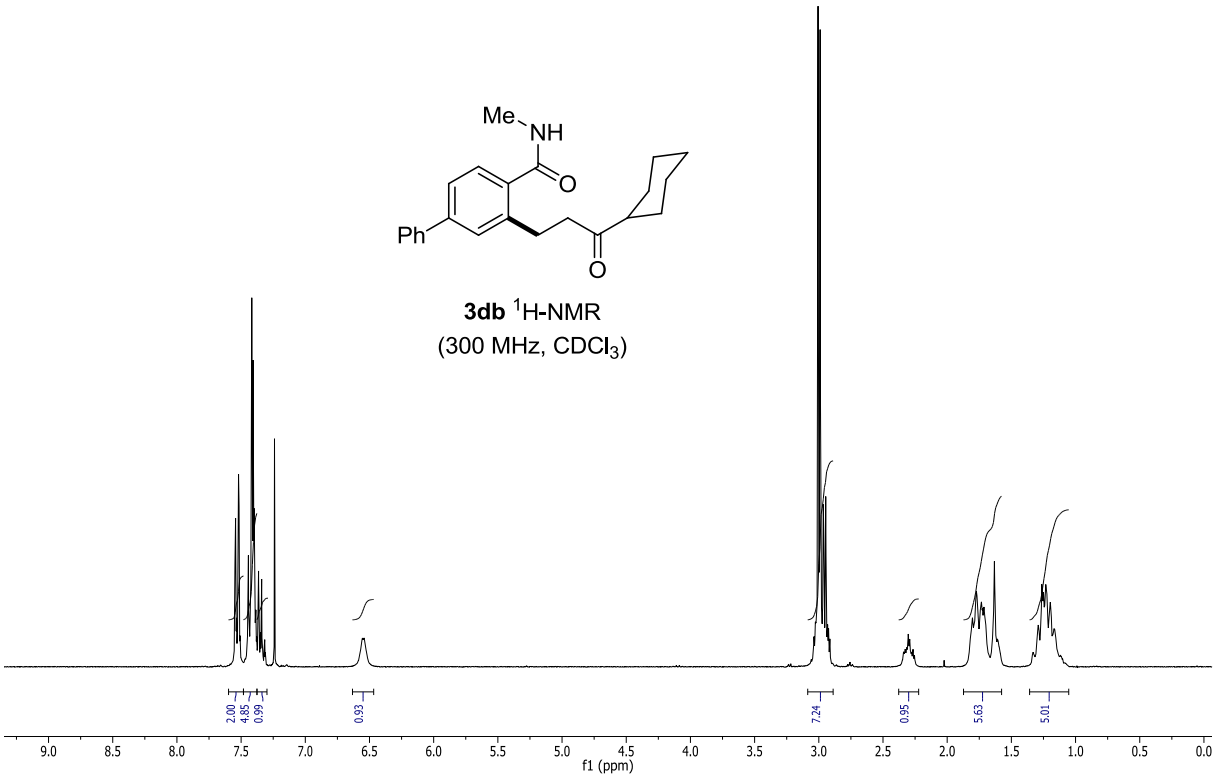
3la ^{13}C-NMR
(125 MHz, $CDCl_3$)



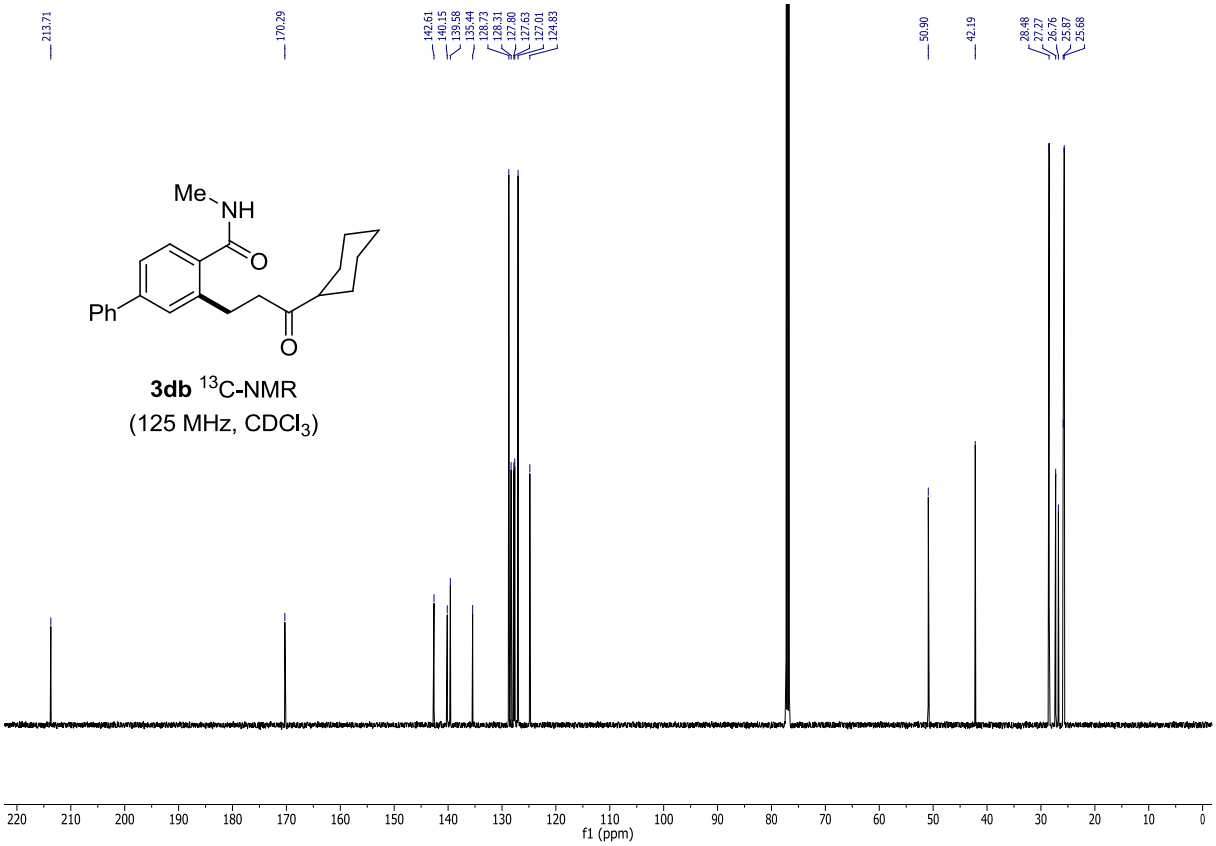
3ma ^{1}H-NMR
(300 MHz, $CDCl_3$)



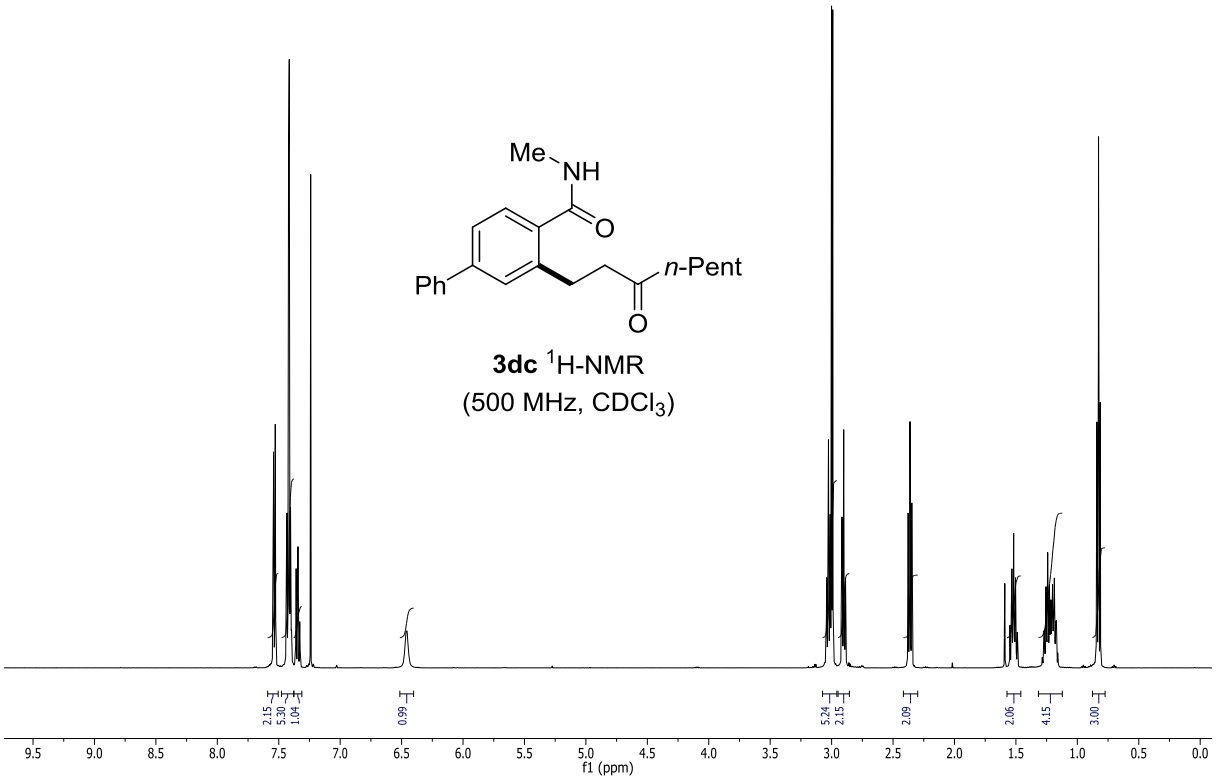
3ma ^{13}C-NMR
(75 MHz, $CDCl_3$)



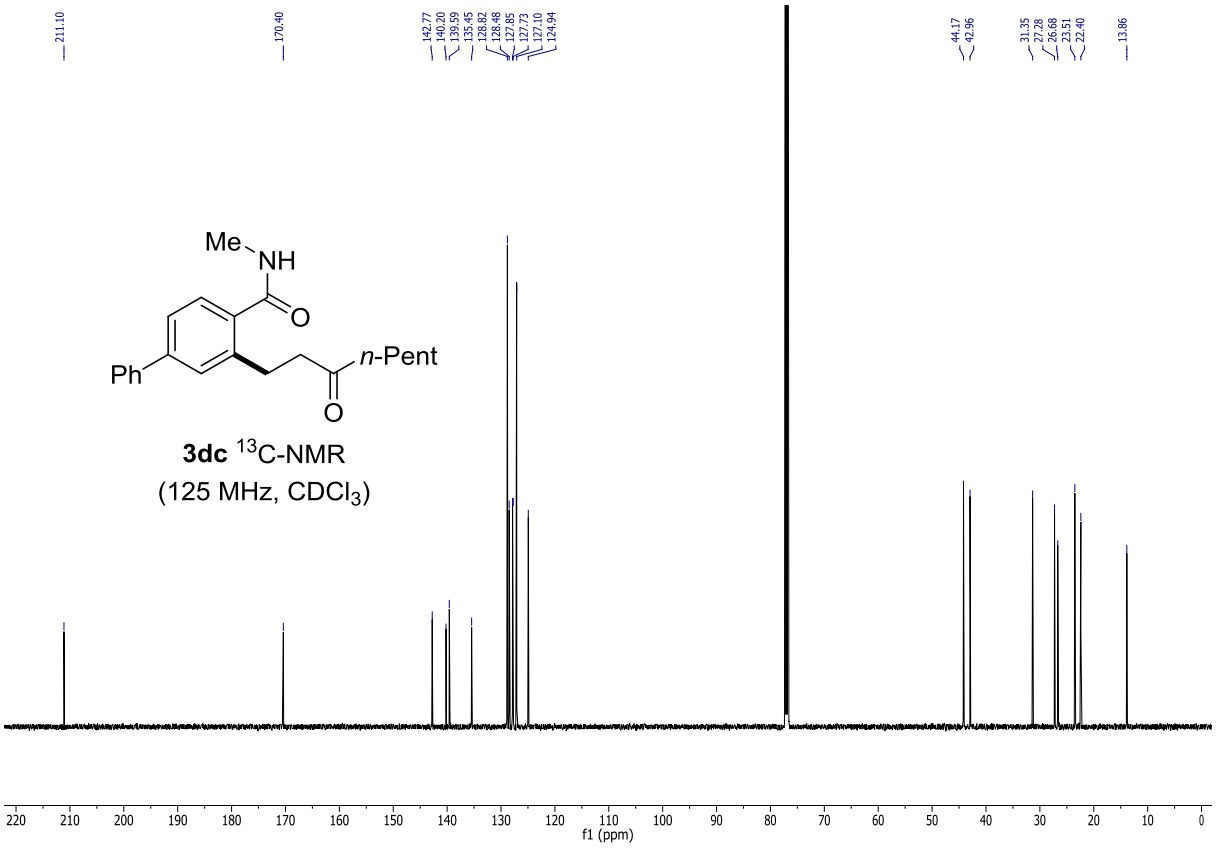
3db ^{1}H-NMR
(300 MHz, $CDCl_3$)



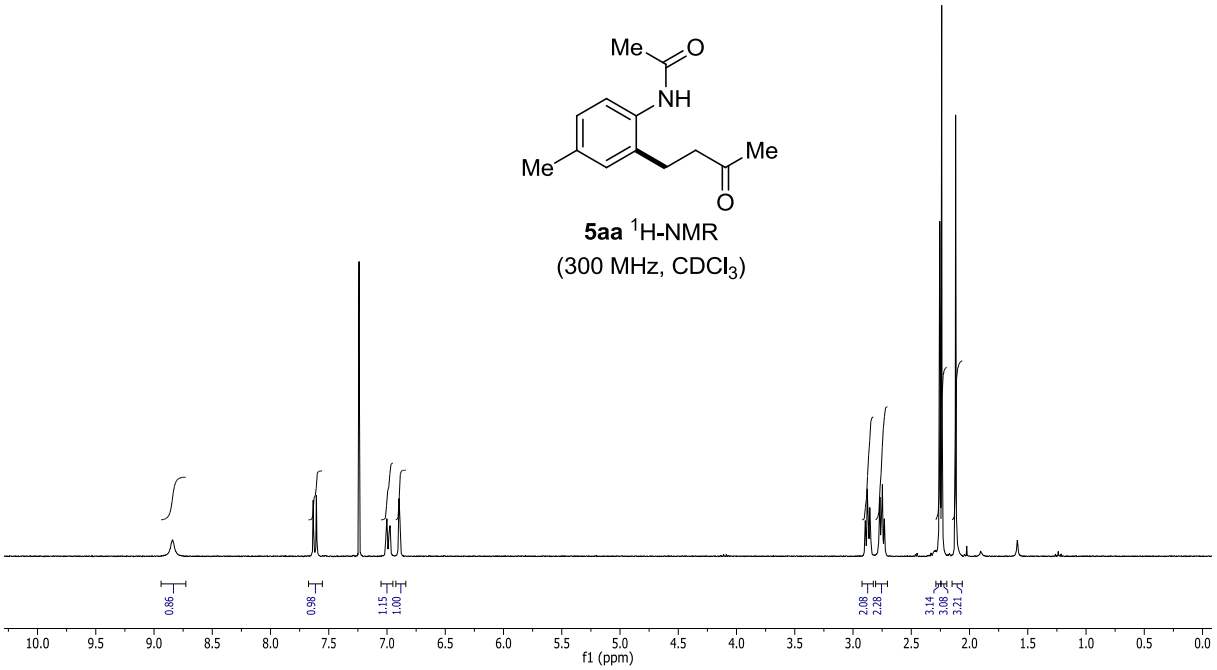
3db ^{13}C-NMR
(125 MHz, $CDCl_3$)



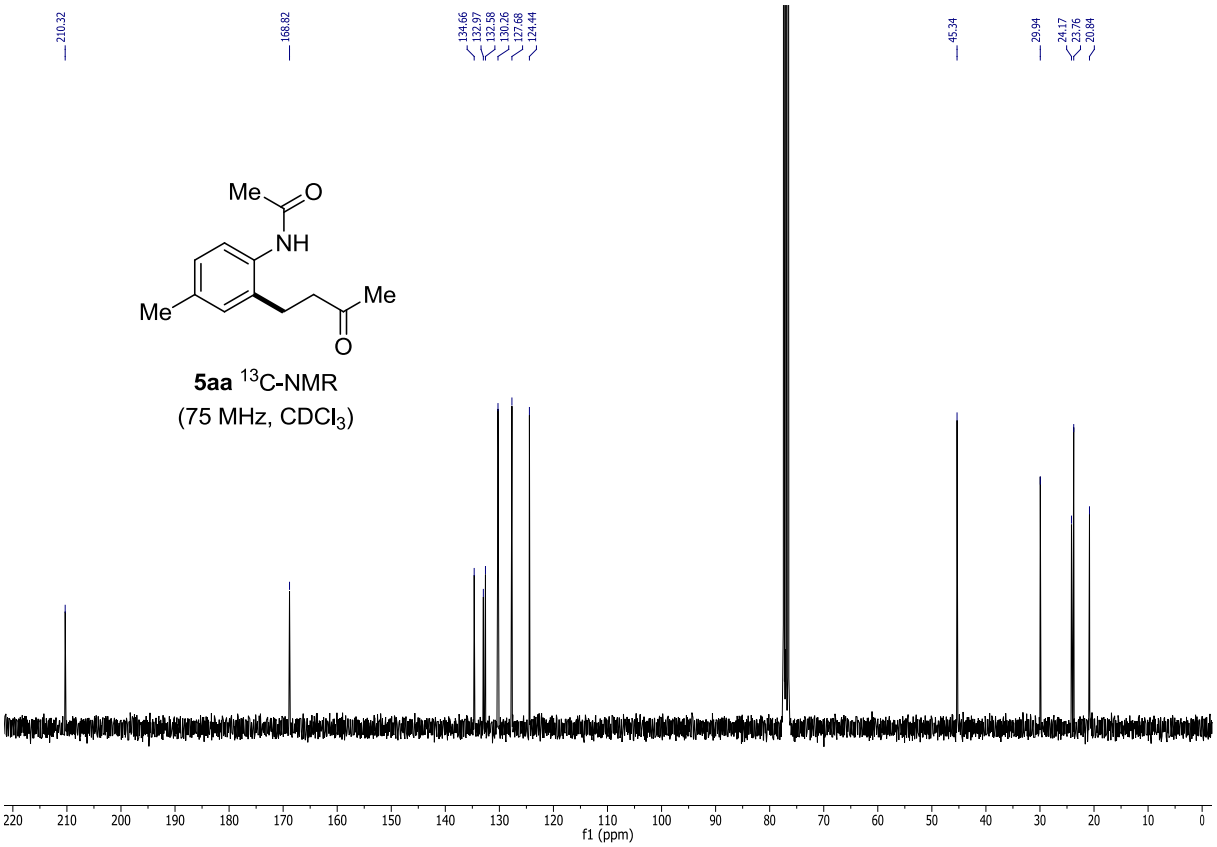
3dc ^{1}H-NMR
(500 MHz, $CDCl_3$)



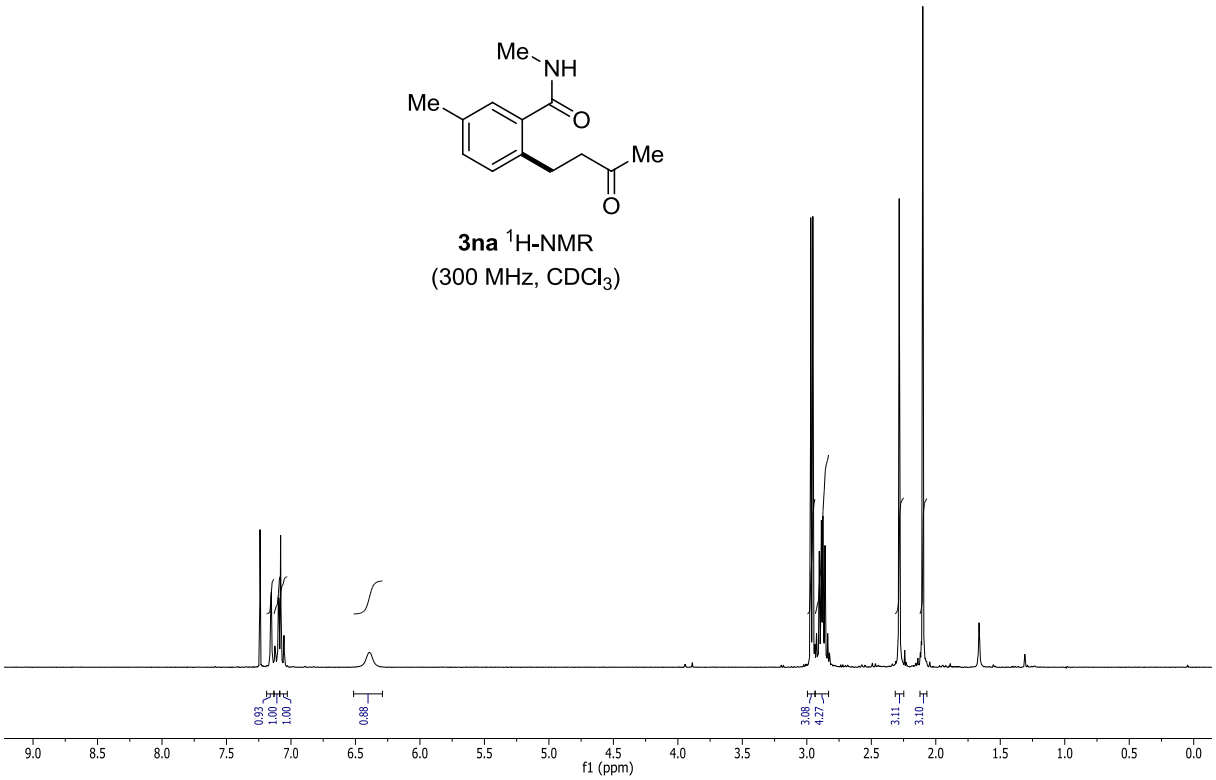
3dc ^{13}C-NMR
(125 MHz, $CDCl_3$)



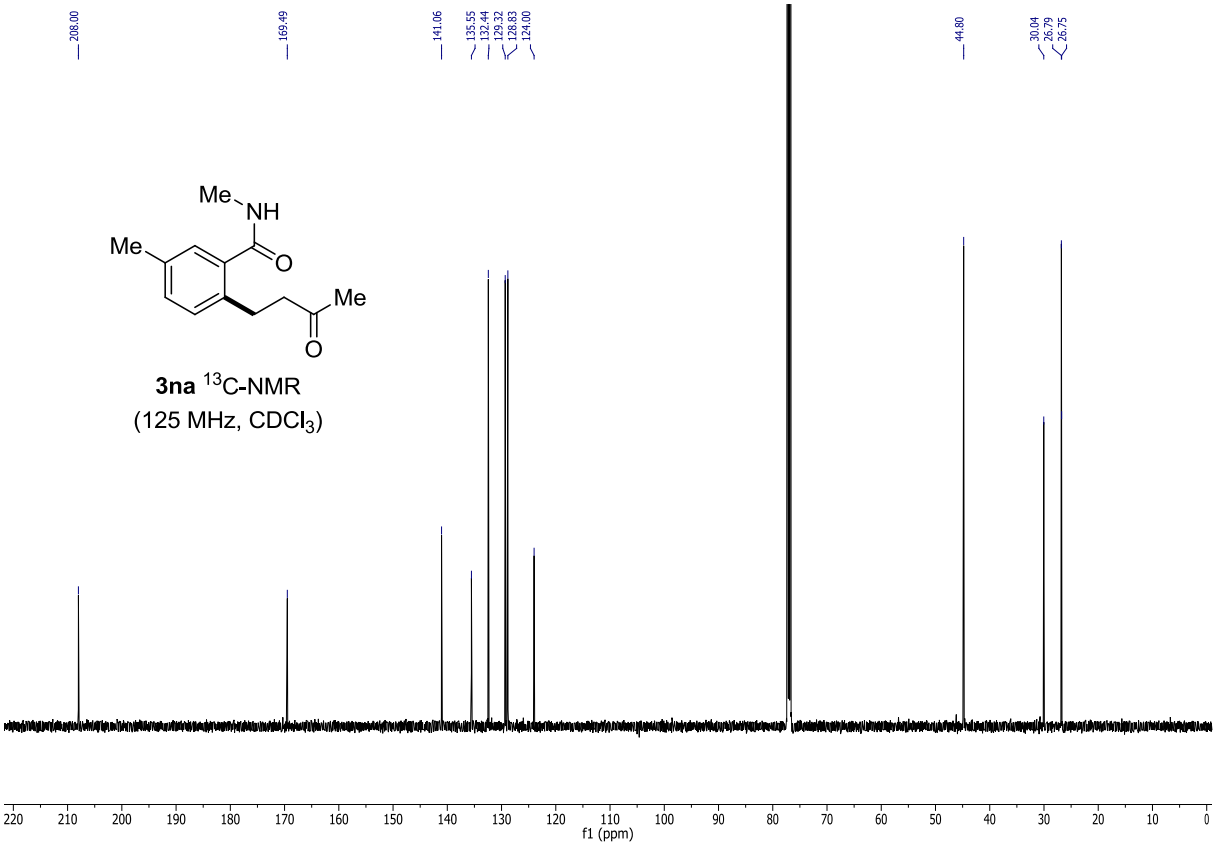
5aa ^{1}H-NMR
(300 MHz, $CDCl_3$)



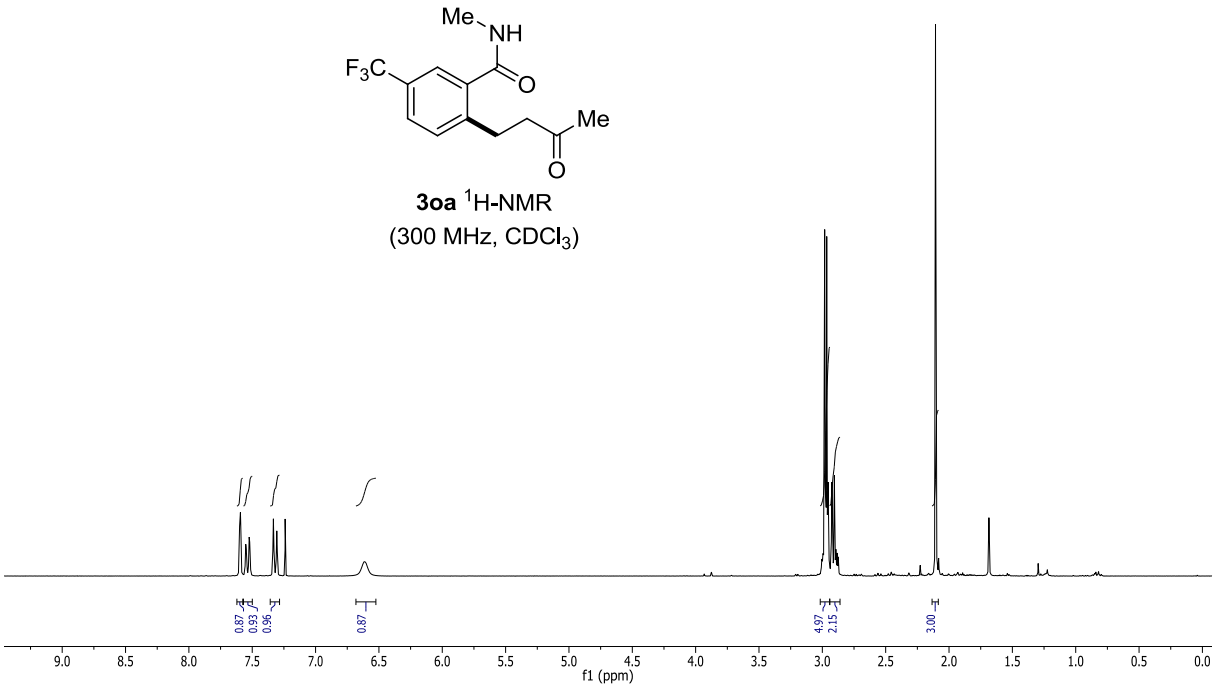
5aa ^{13}C-NMR
(75 MHz, $CDCl_3$)



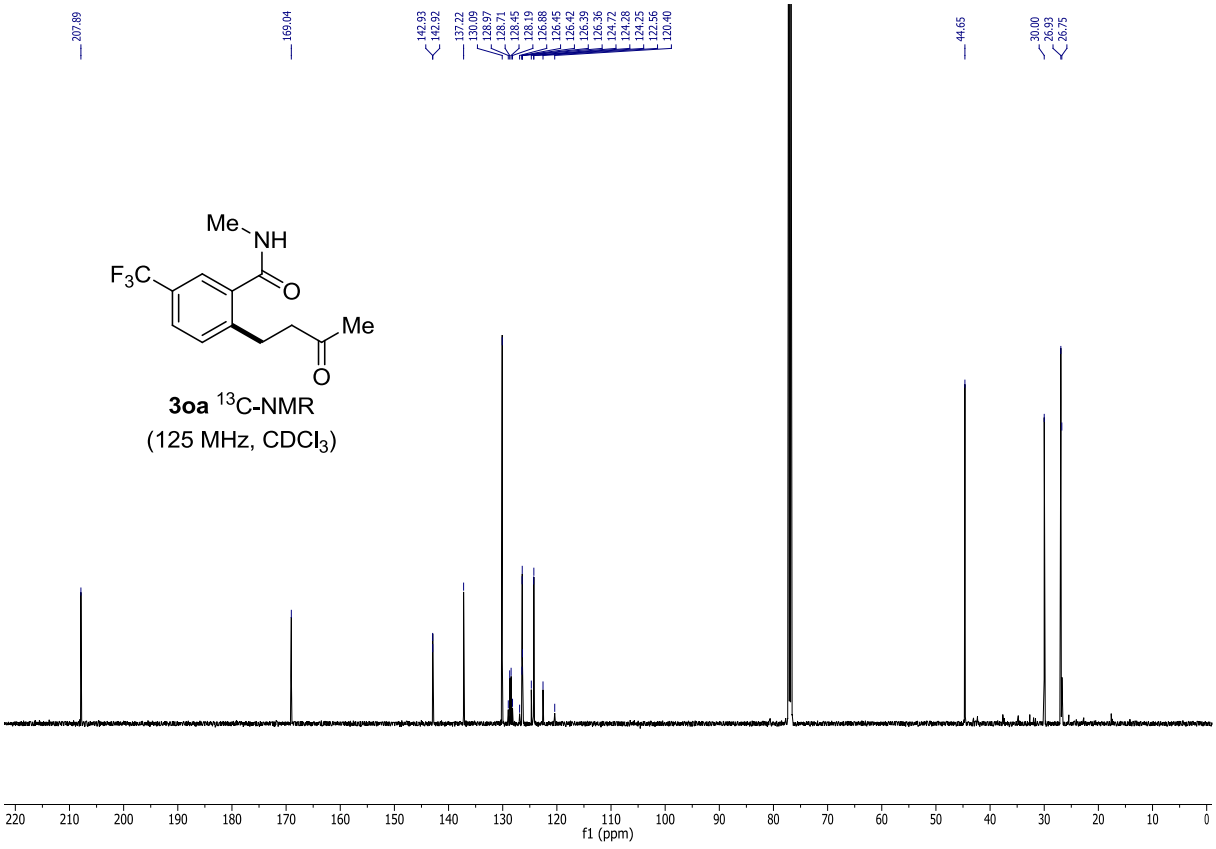
3na ^{1}H-NMR
(300 MHz, $CDCl_3$)



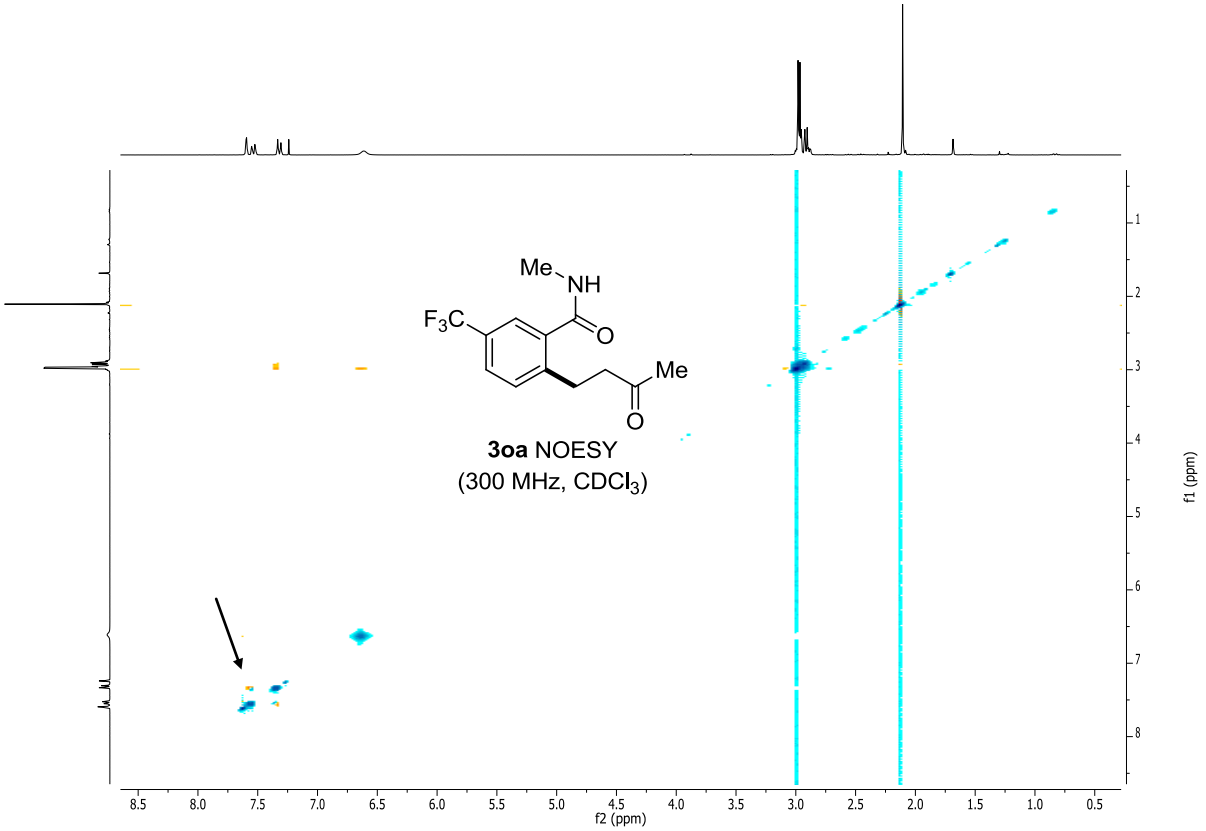
3na ^{13}C-NMR
(125 MHz, $CDCl_3$)



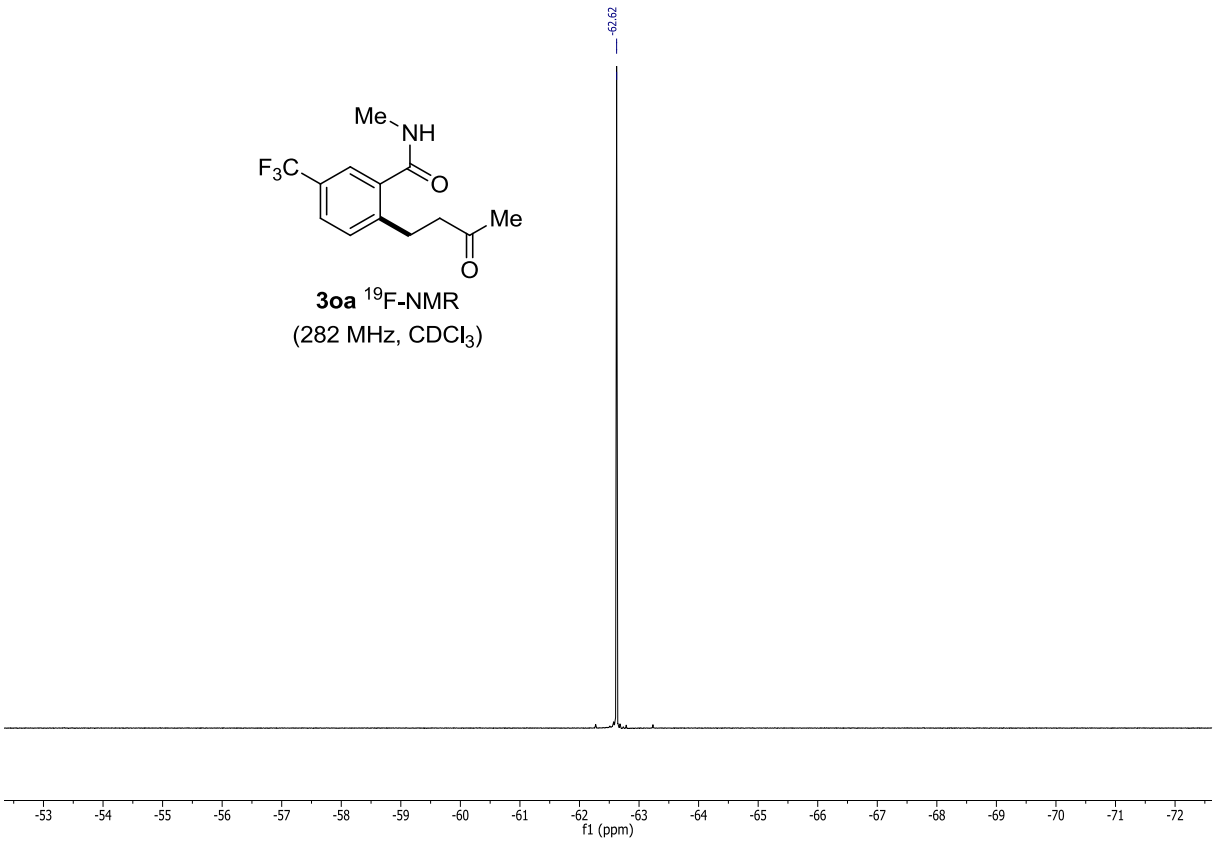
3oa ^{1}H-NMR
(300 MHz, $CDCl_3$)



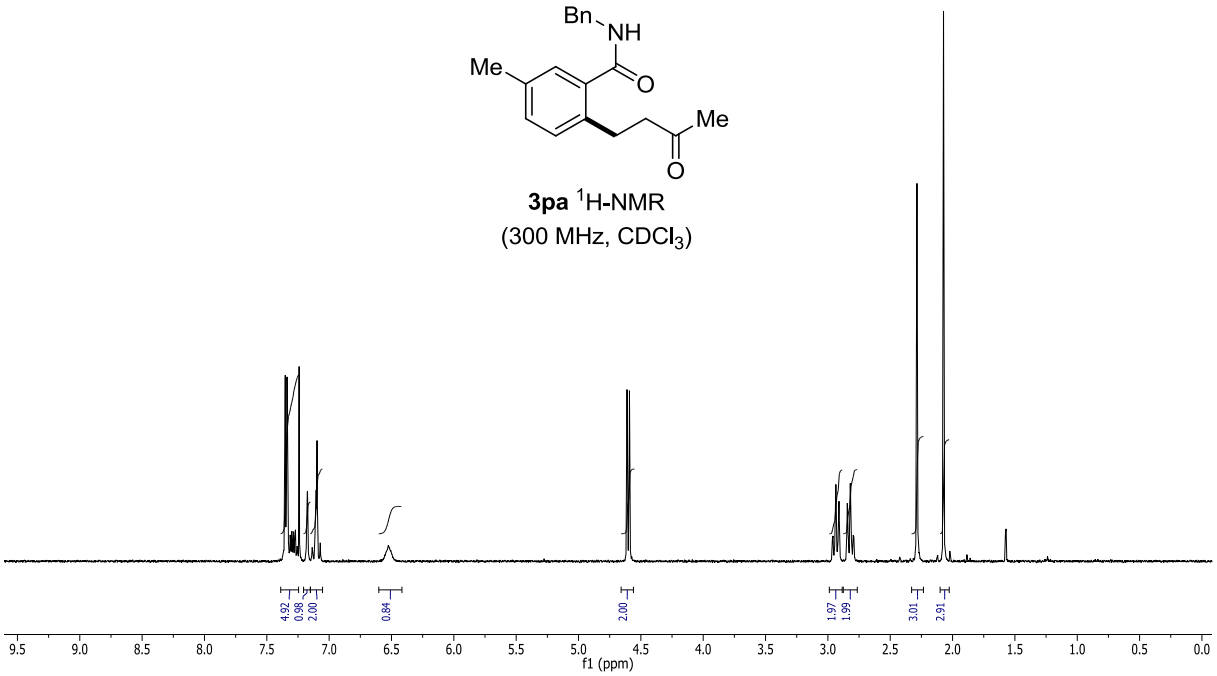
3oa ^{13}C-NMR
(125 MHz, $CDCl_3$)



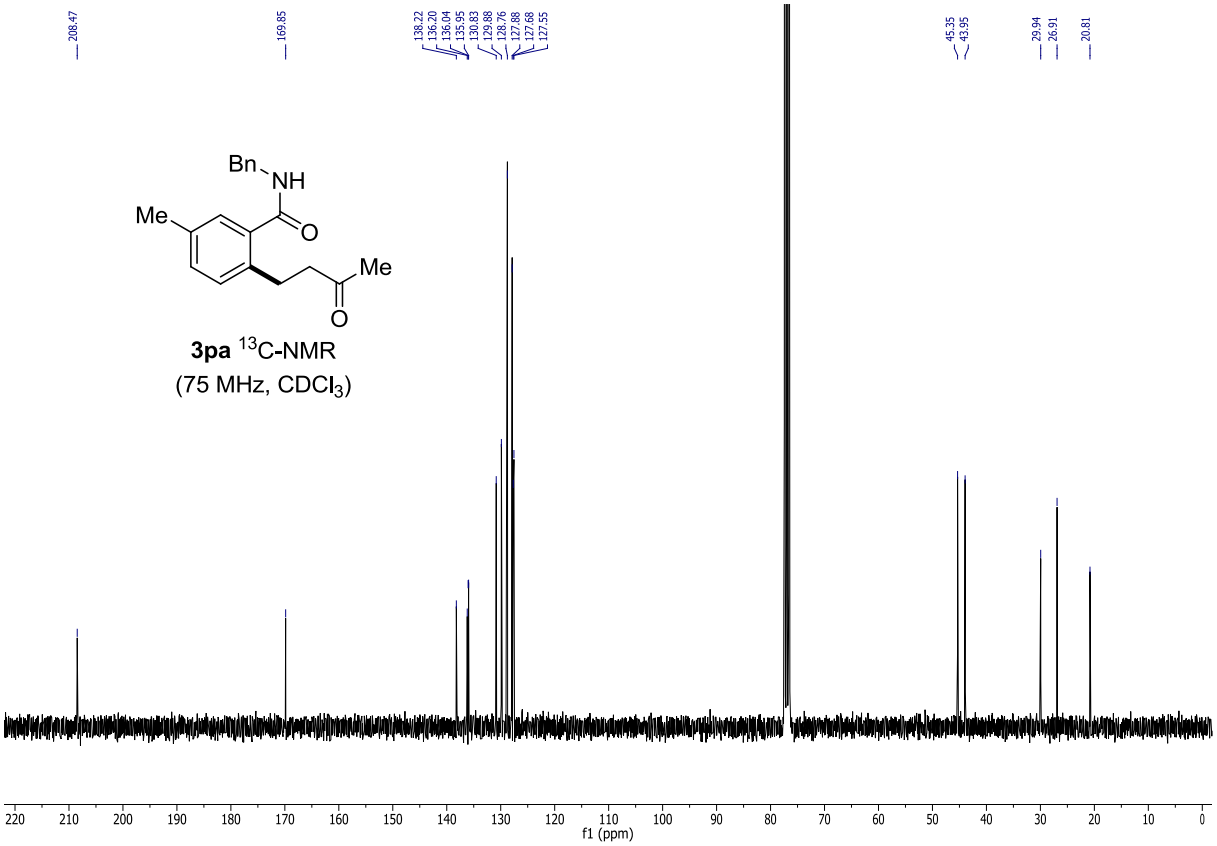
3oa NOESY
(300 MHz, $CDCl_3$)



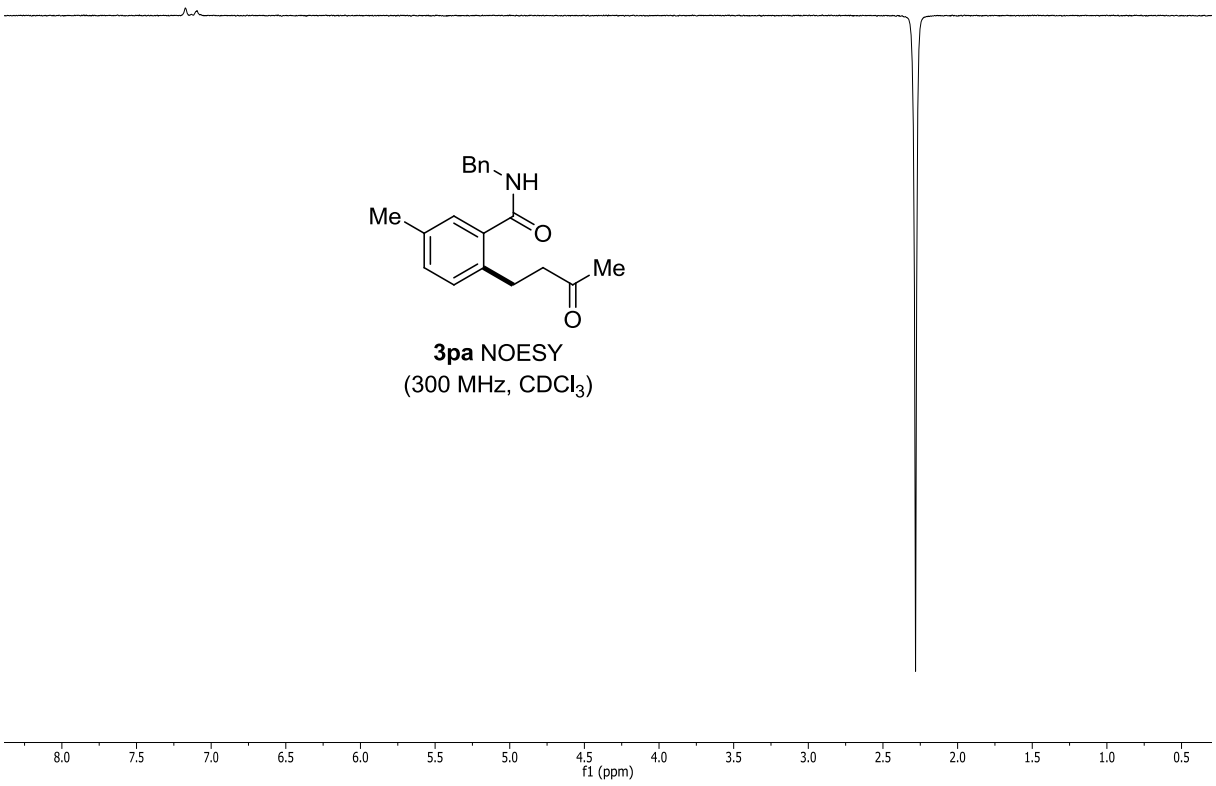
3oa ^{19}F-NMR
(282 MHz, $CDCl_3$)



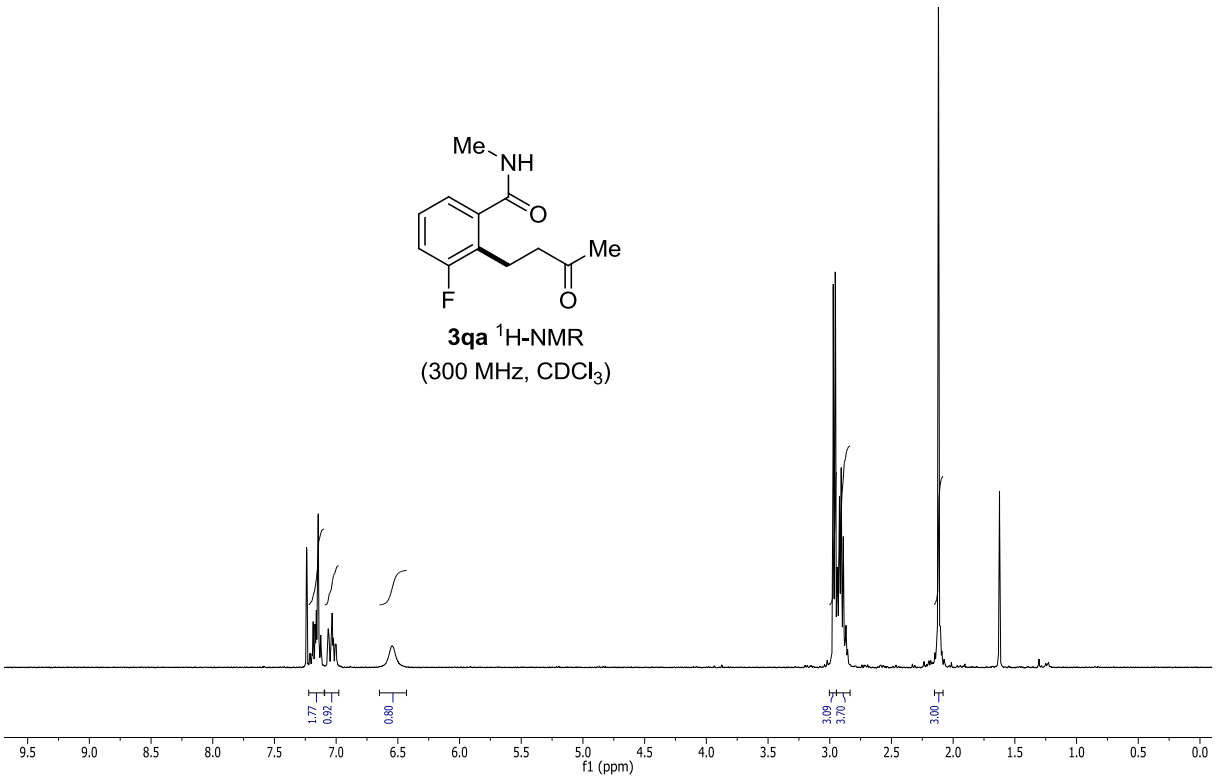
3pa ^{1}H-NMR
(300 MHz, $CDCl_3$)



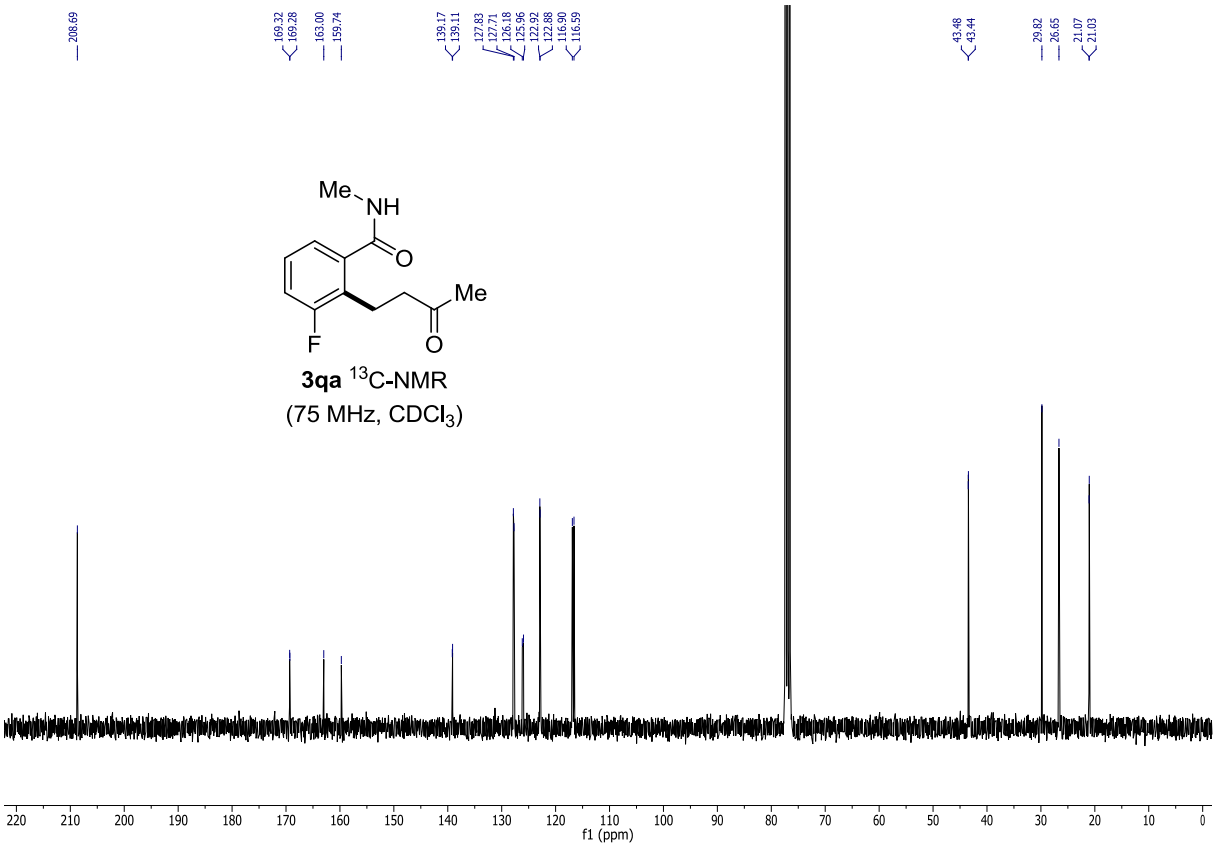
3pa ^{13}C-NMR
(75 MHz, $CDCl_3$)



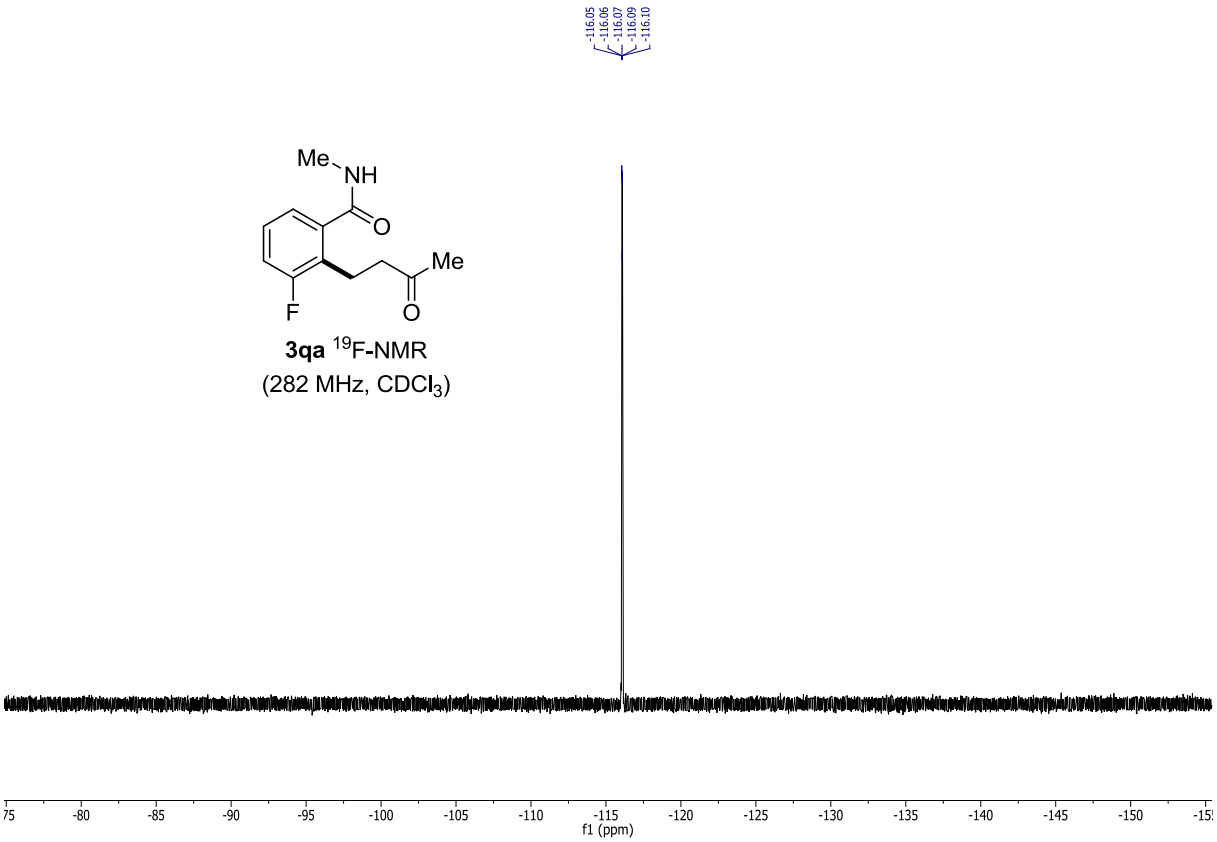
3pa NOESY
(300 MHz, $CDCl_3$)



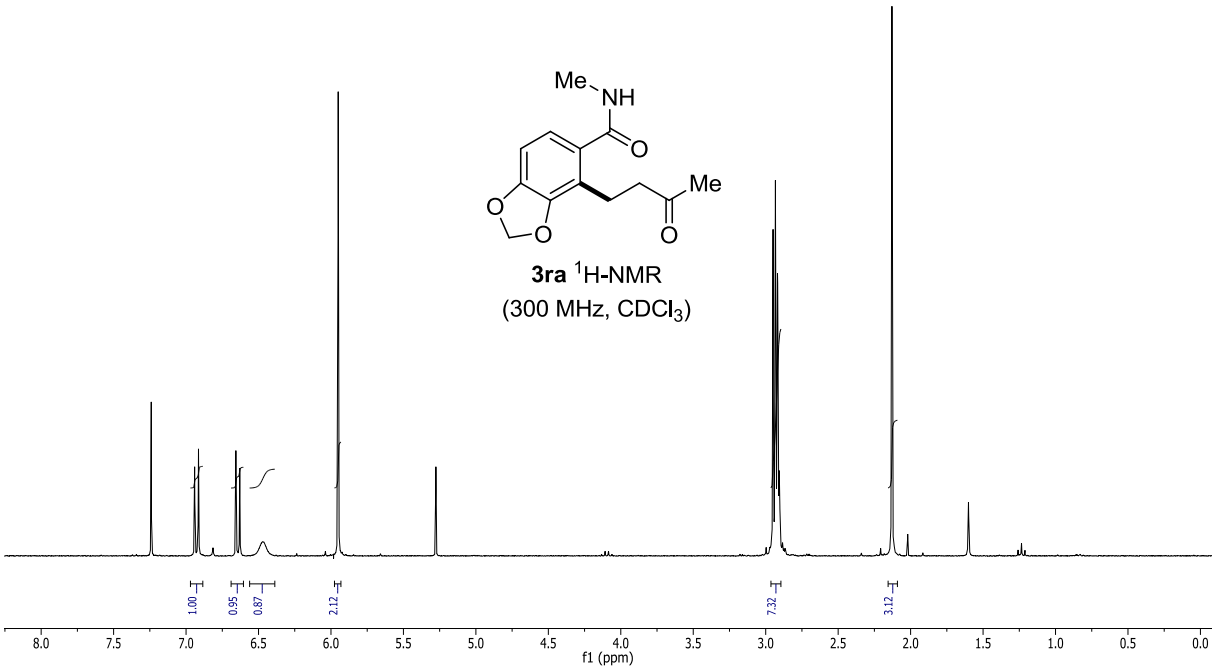
3qa ^{1}H-NMR
(300 MHz, $CDCl_3$)



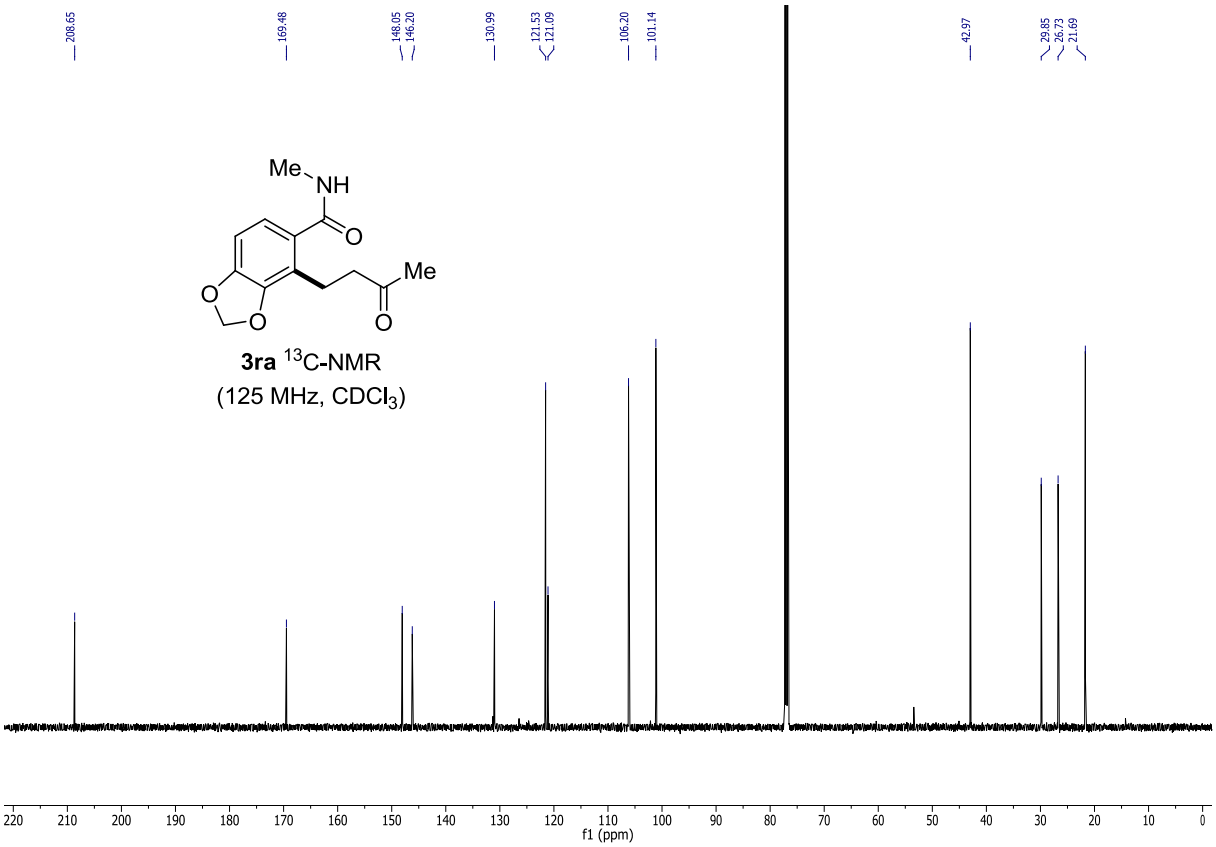
3qa ^{13}C-NMR
(75 MHz, $CDCl_3$)



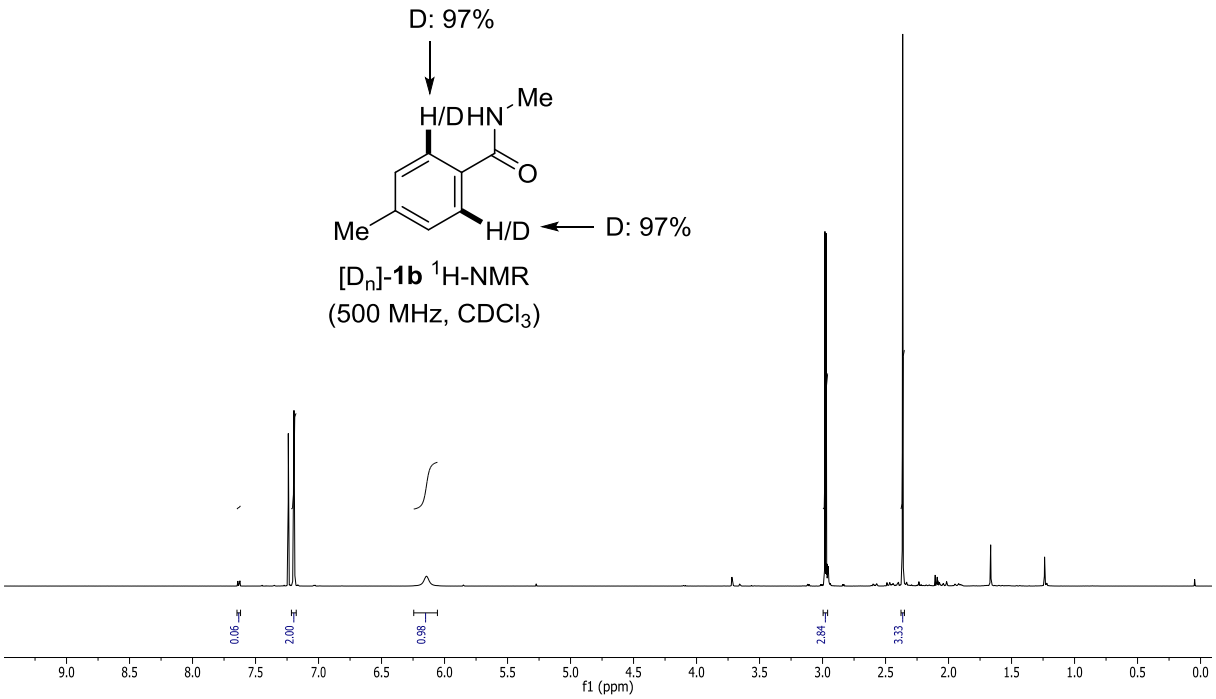
3qa ^{19}F-NMR
(282 MHz, $CDCl_3$)

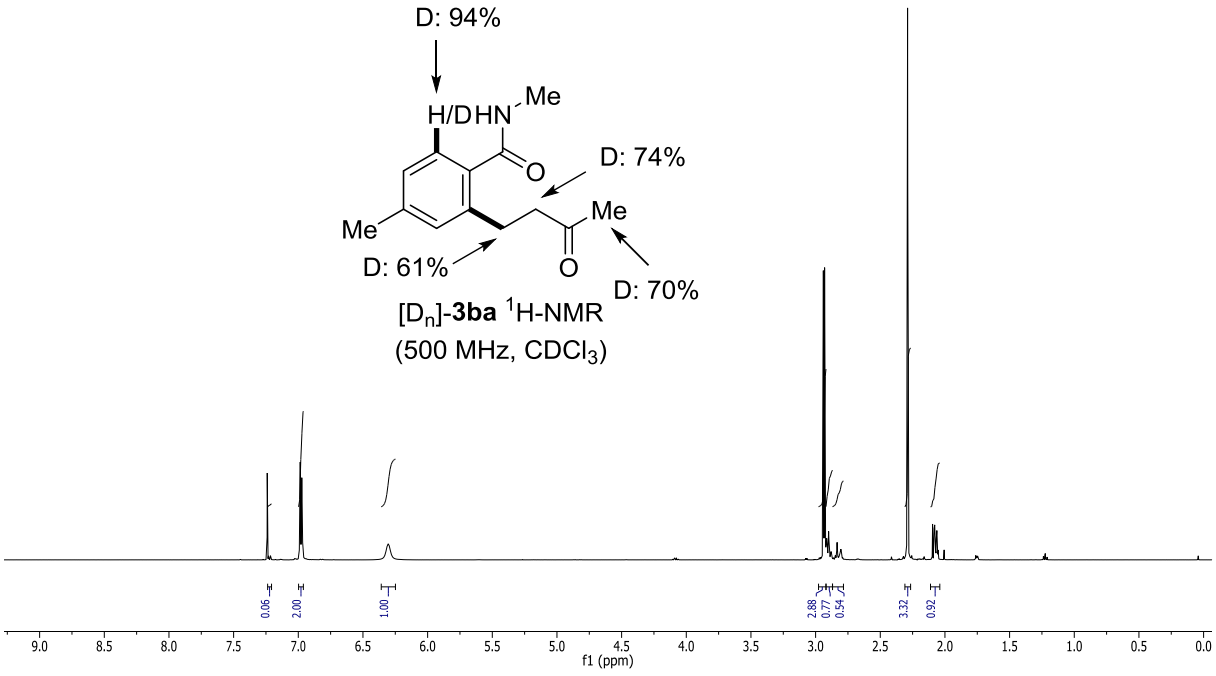


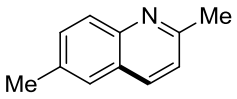
3ra ^{1}H-NMR
(300 MHz, $CDCl_3$)



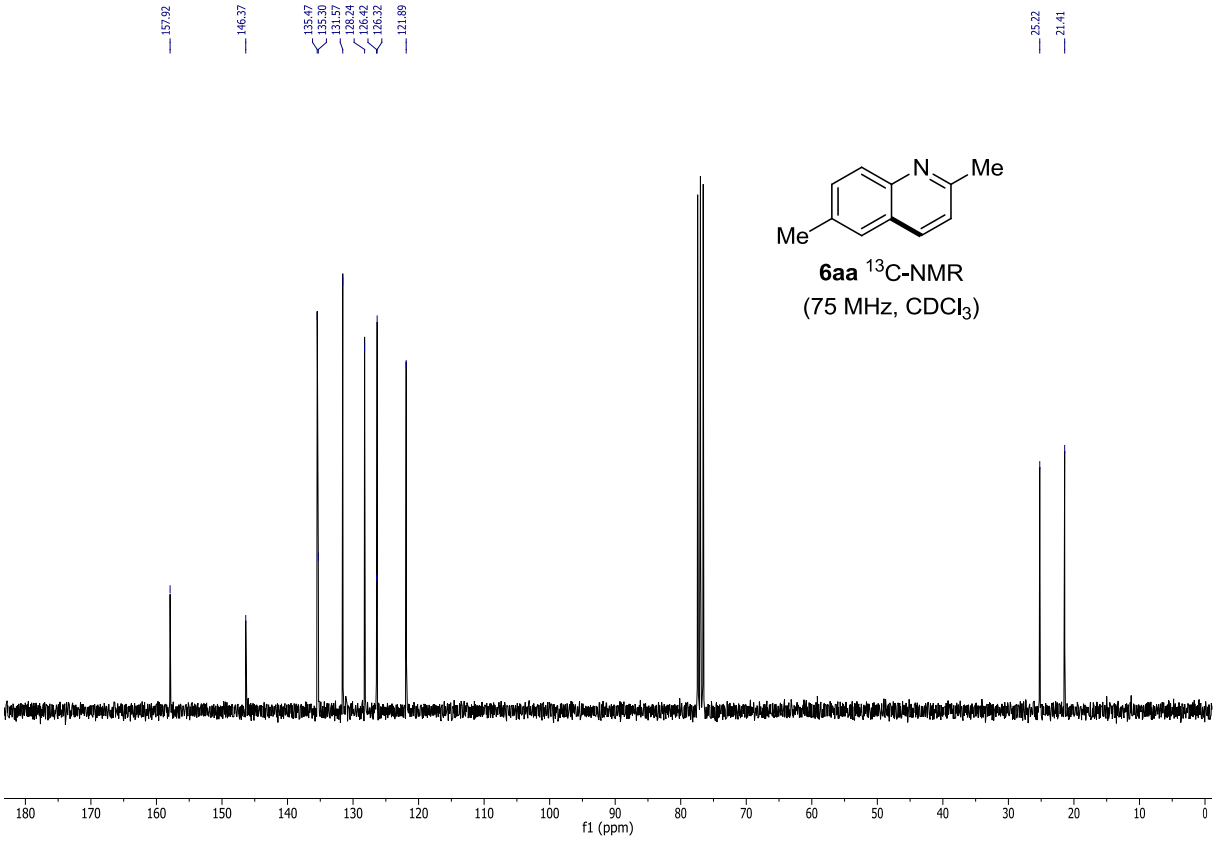
3ra ^{13}C-NMR
(125 MHz, $CDCl_3$)


D: 97%
H/D
HN
Me
O
Me
H/D
D: 97%
[Dn]-1b 1H-NMR
(500 MHz, CDCl3)
0.06
2.00
0.98
2.84
3.33
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

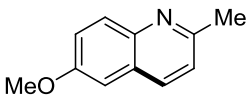

D: 94%
H/D
HN
Me
O
D: 74%
Me
Me
D: 61%
O
D: 70%
[Dn]-3ba 1H-NMR
(500 MHz, CDCl3)
0.06
2.00
1.00
2.88
0.77
0.54
3.32
0.92
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



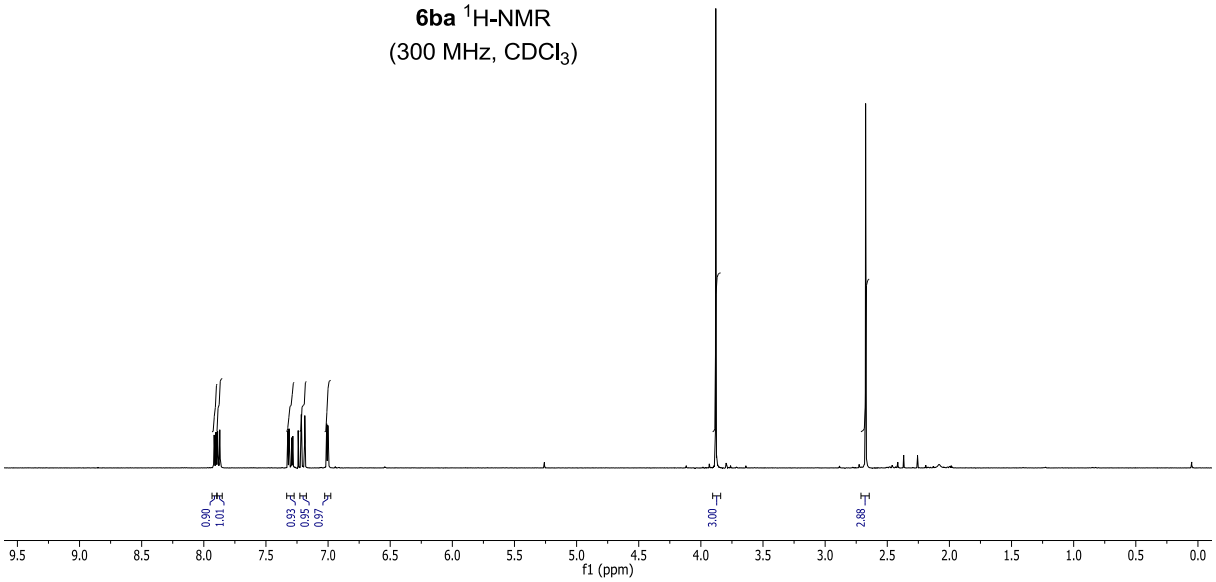
6aa ^{1}H-NMR
(300 MHz, $CDCl_3$)

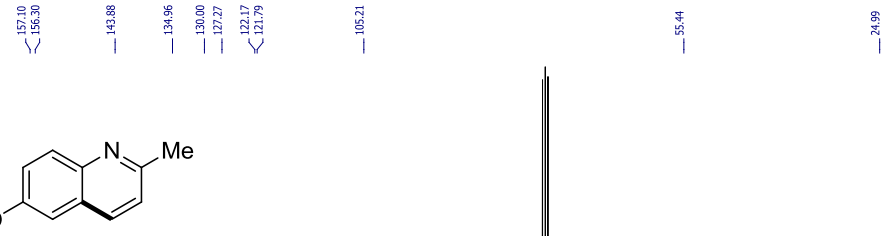


6aa ^{13}C-NMR
(75 MHz, $CDCl_3$)

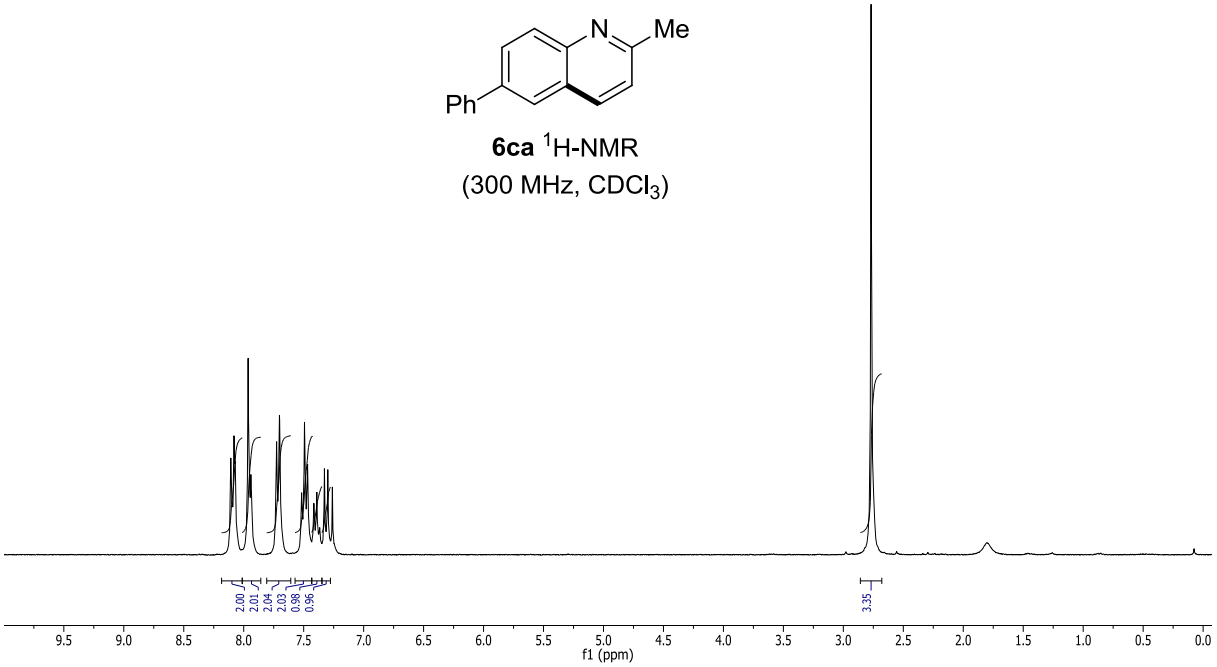


6ba ^{1}H-NMR
(300 MHz, $CDCl_3$)

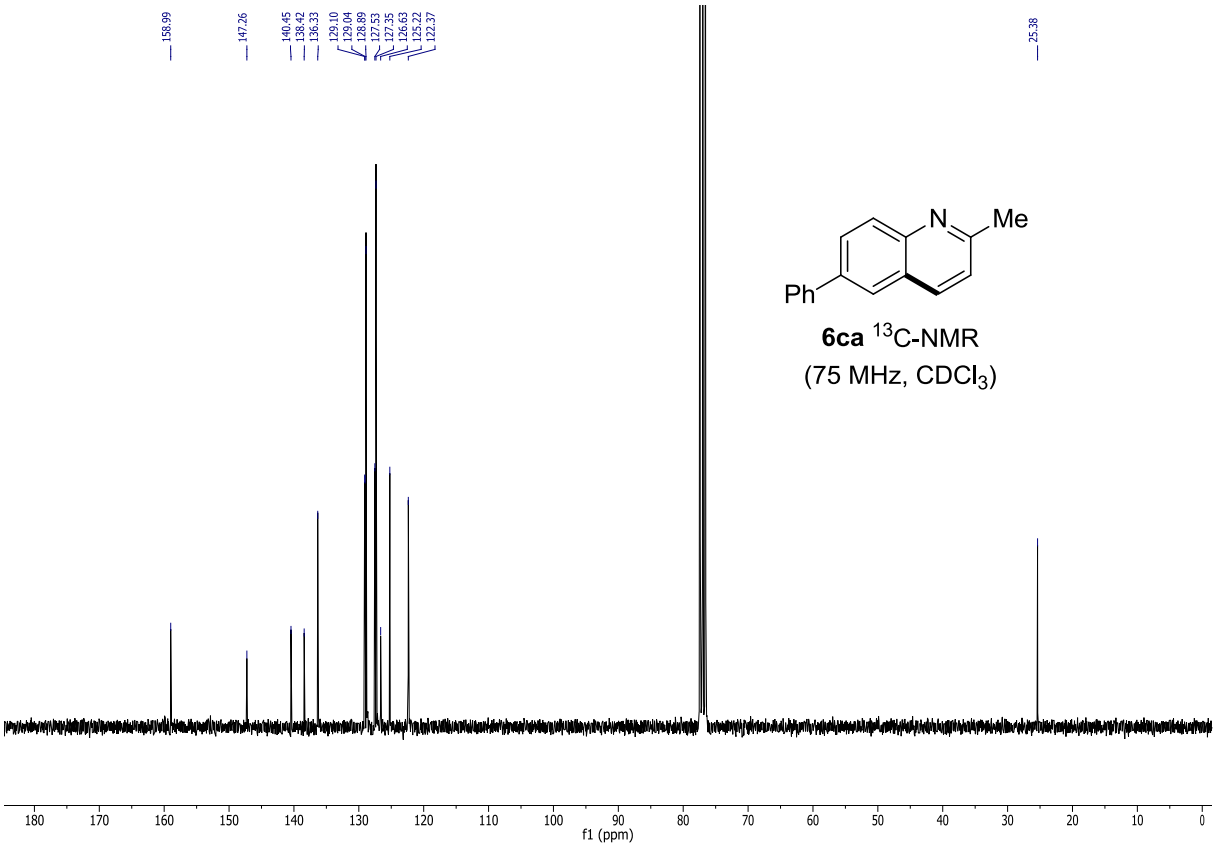




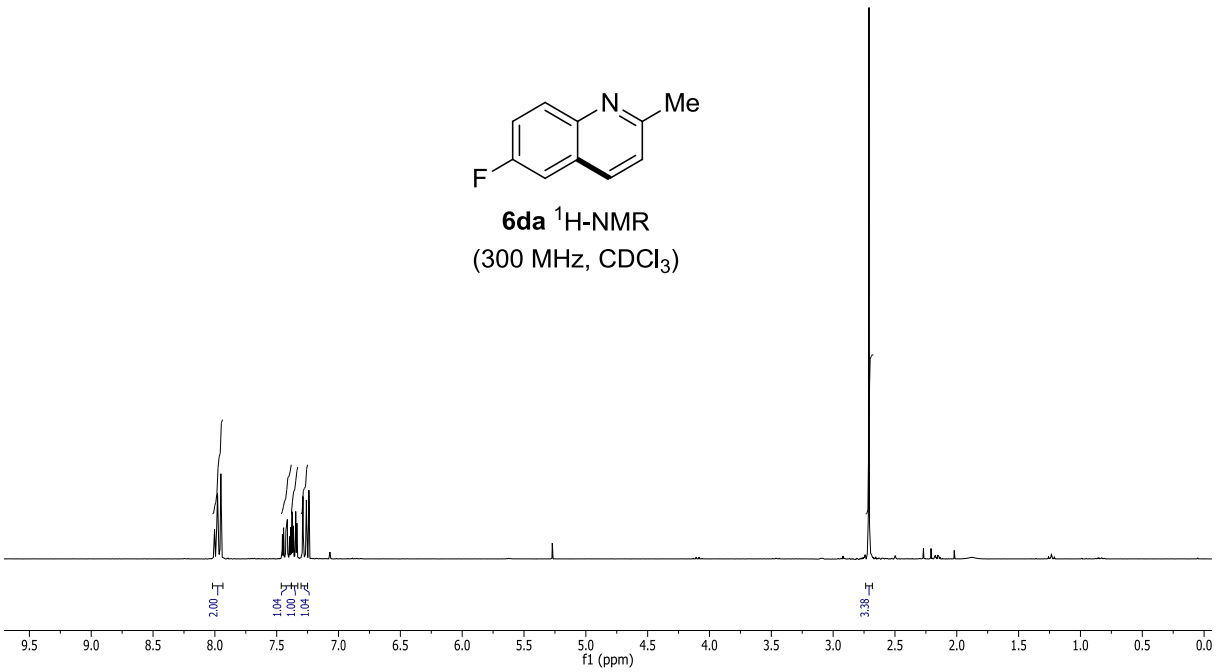
6ba ^{13}C-NMR
(75 MHz, $CDCl_3$)



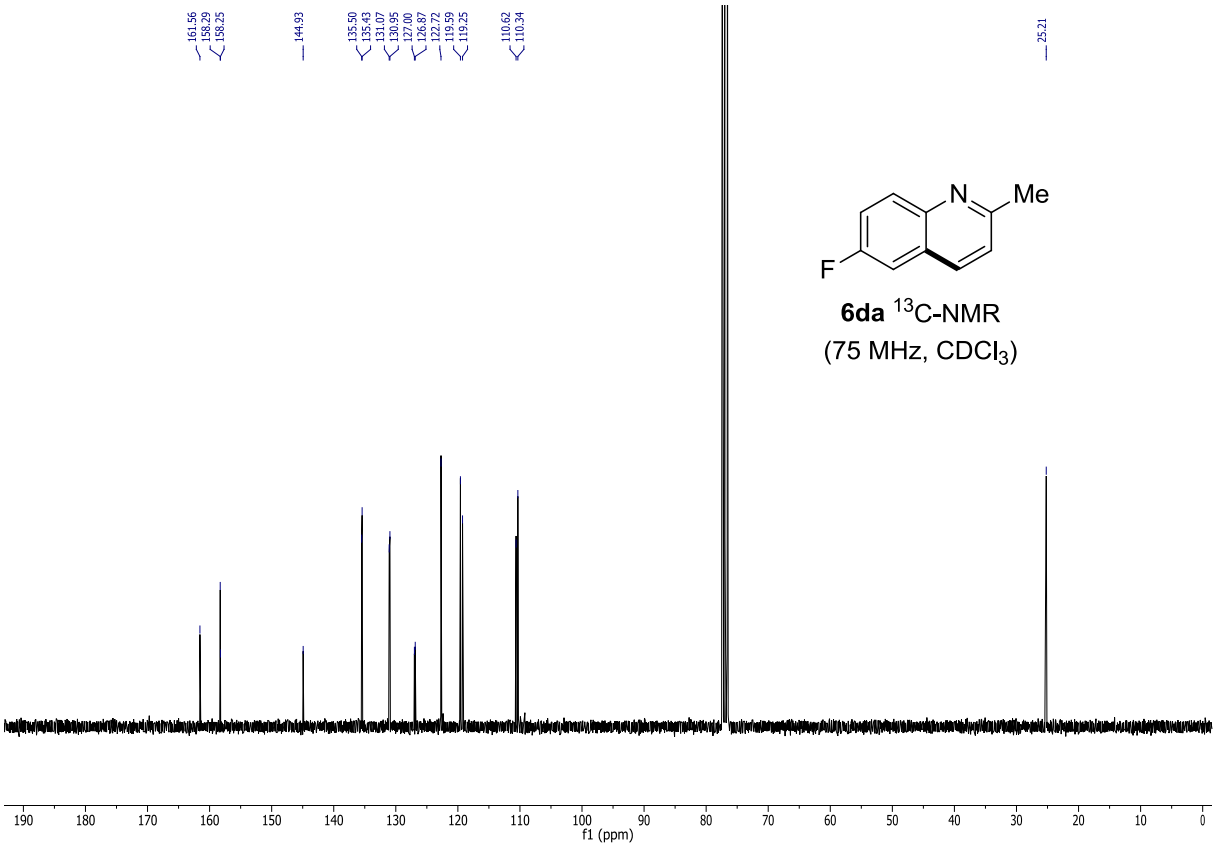
6ca ^{1}H-NMR
(300 MHz, $CDCl_3$)



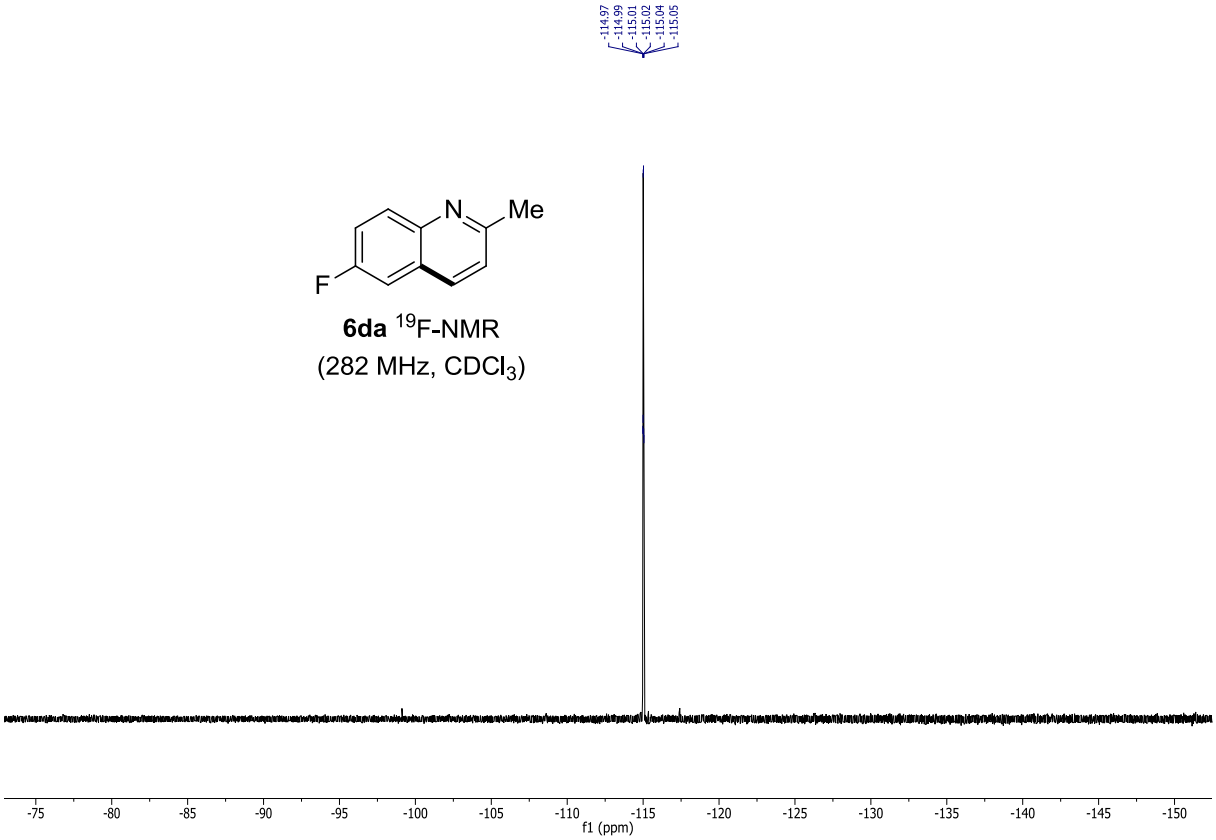
6ca ^{13}C-NMR
(75 MHz, $CDCl_3$)



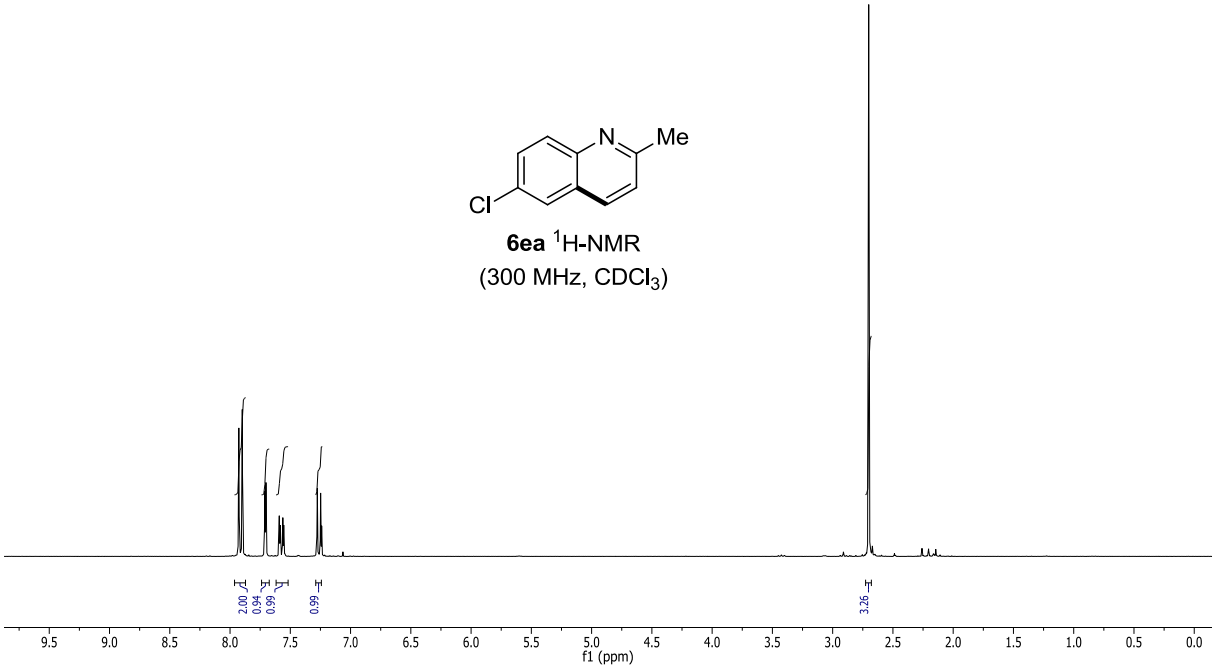
6da ^{1}H-NMR
(300 MHz, $CDCl_3$)



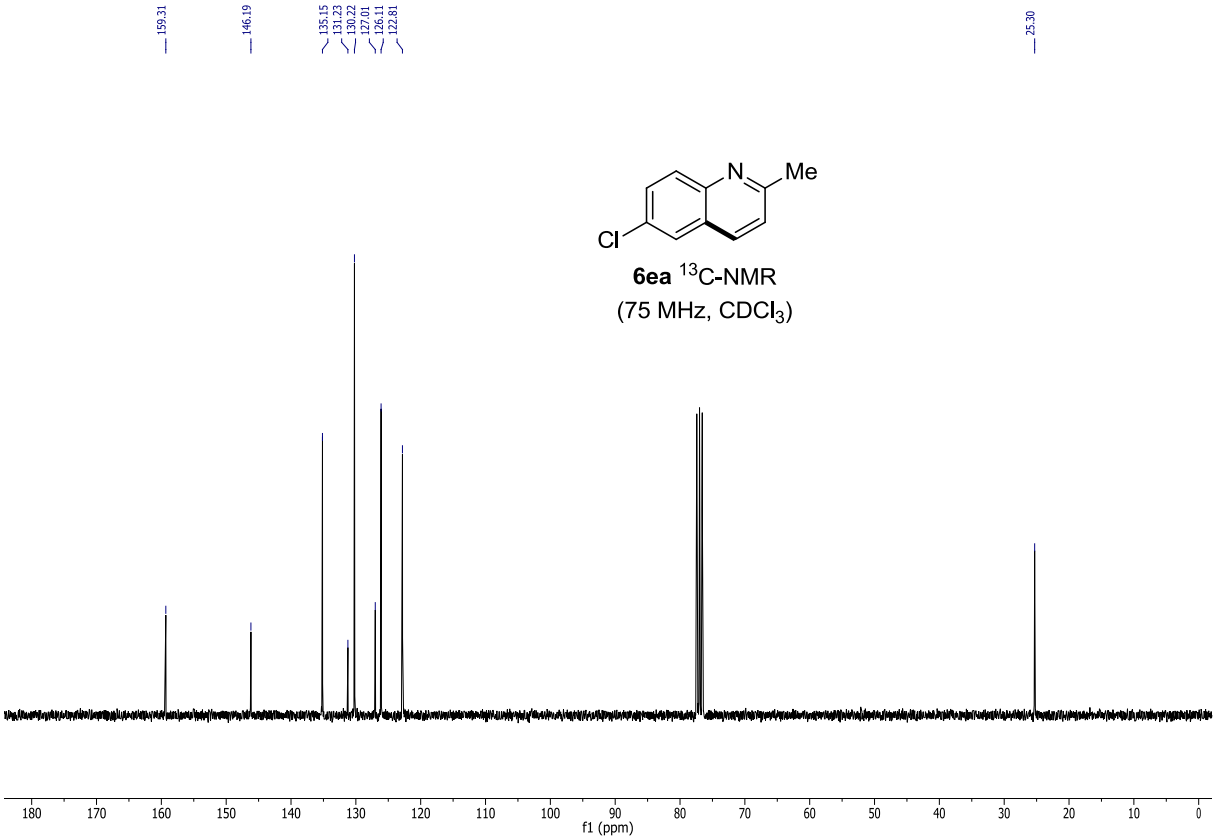
6da ^{13}C-NMR
(75 MHz, $CDCl_3$)



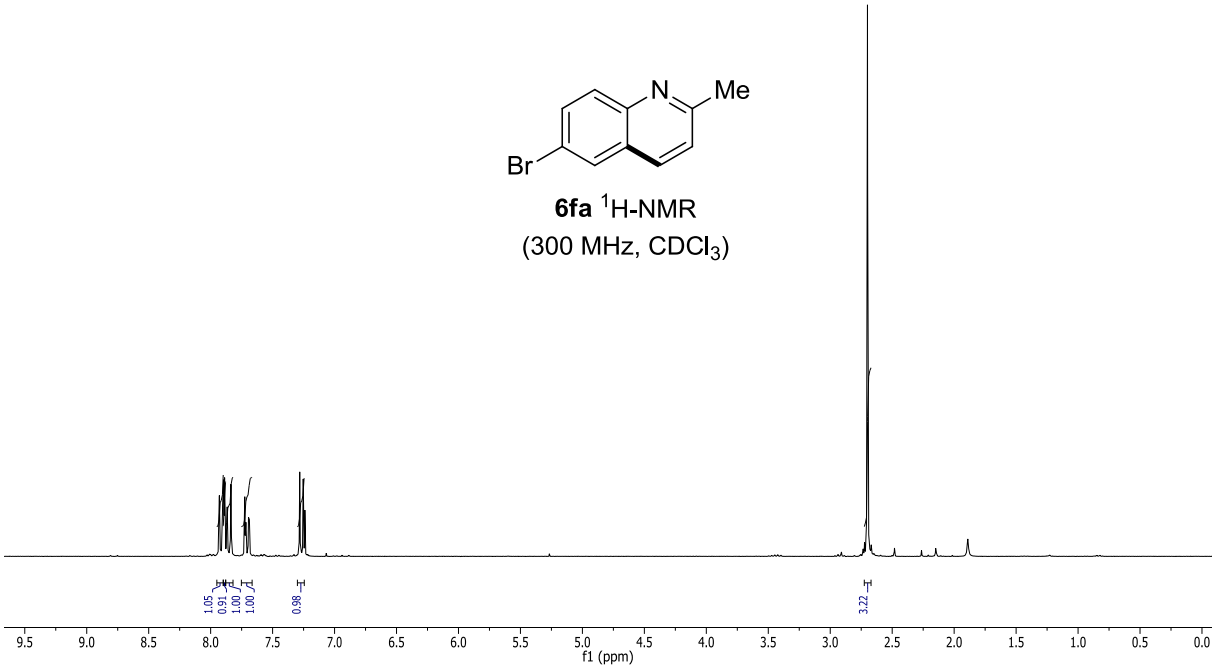
6da ^{19}F-NMR
(282 MHz, $CDCl_3$)



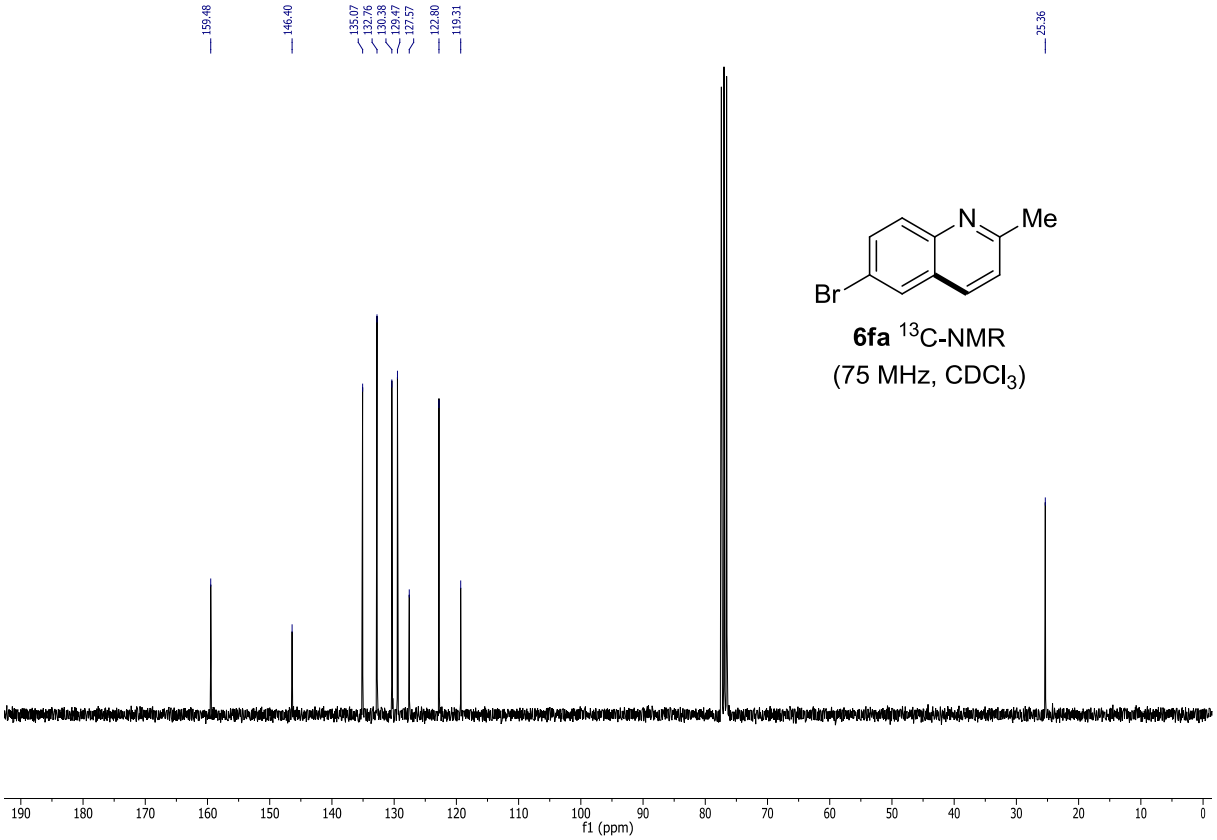
6ea ^{1}H-NMR
(300 MHz, $CDCl_3$)



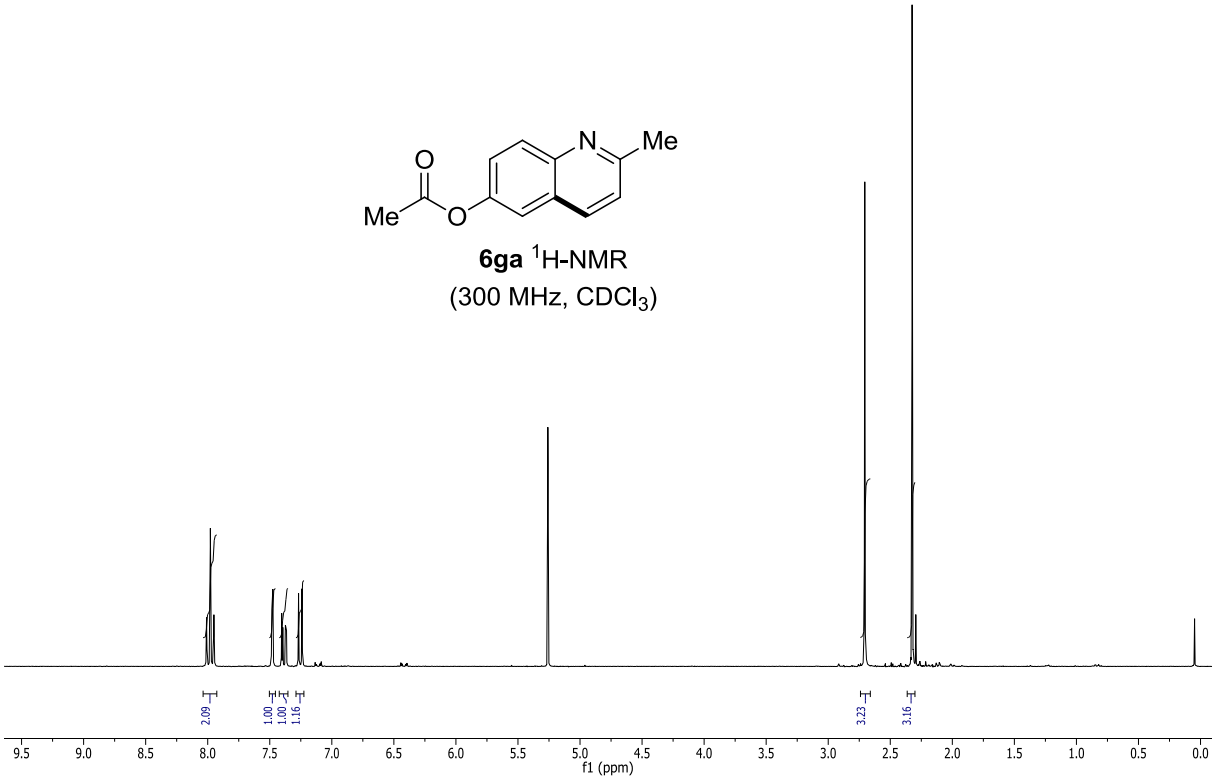
6ea ^{13}C-NMR
(75 MHz, $CDCl_3$)



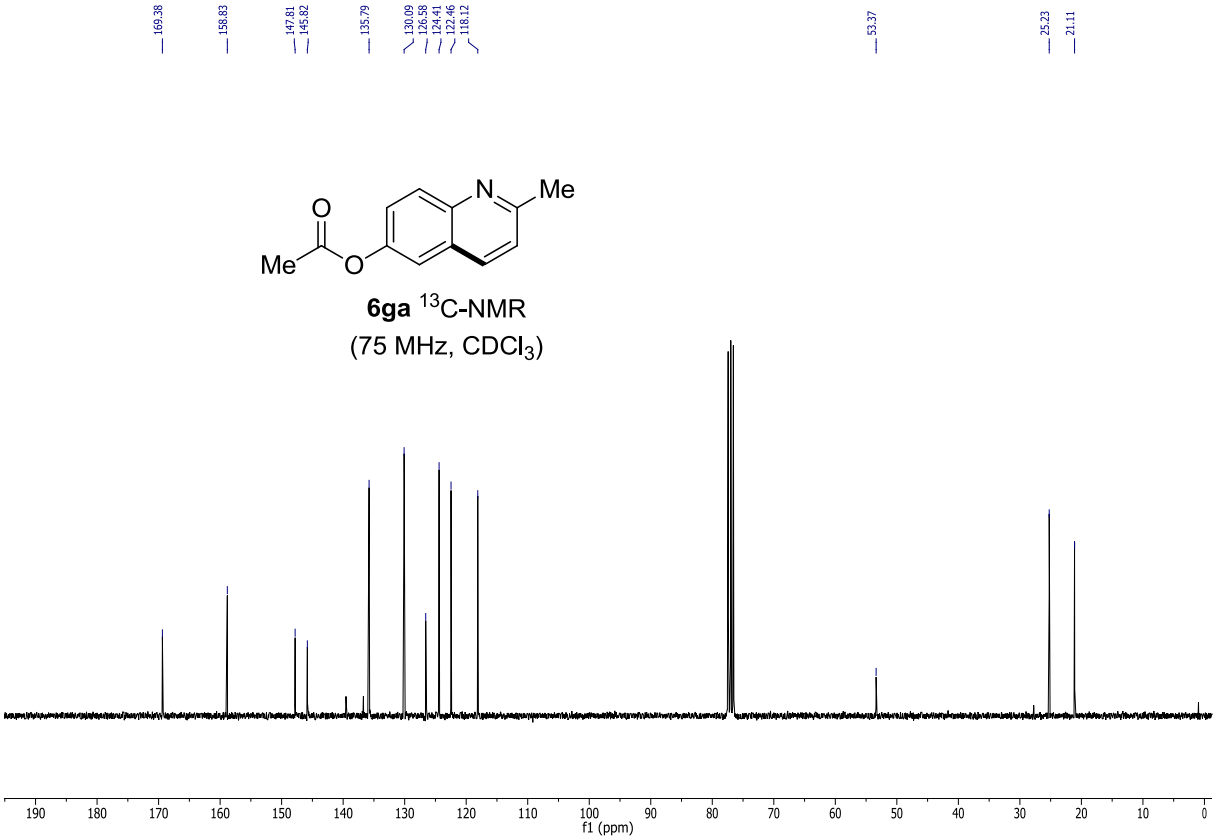
6fa ^{1}H-NMR
(300 MHz, $CDCl_3$)



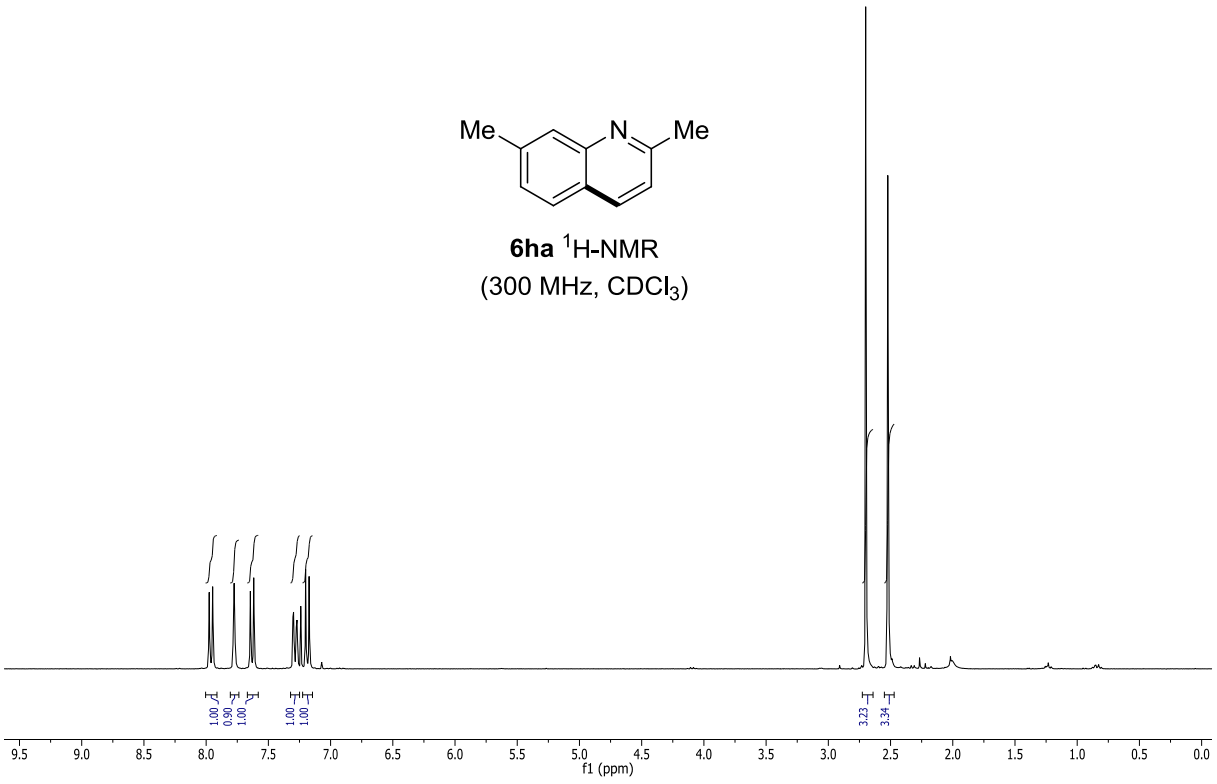
6fa ^{13}C-NMR
(75 MHz, $CDCl_3$)



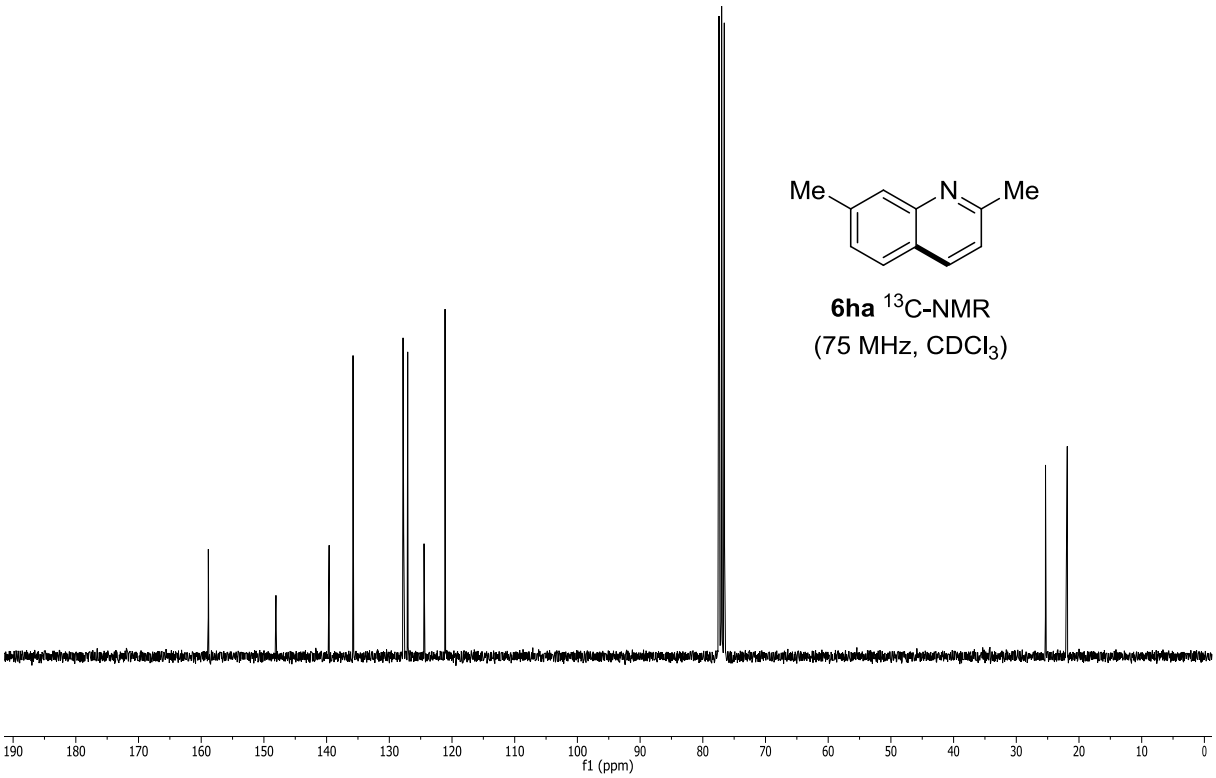
6ga ^{1}H-NMR
(300 MHz, $CDCl_3$)



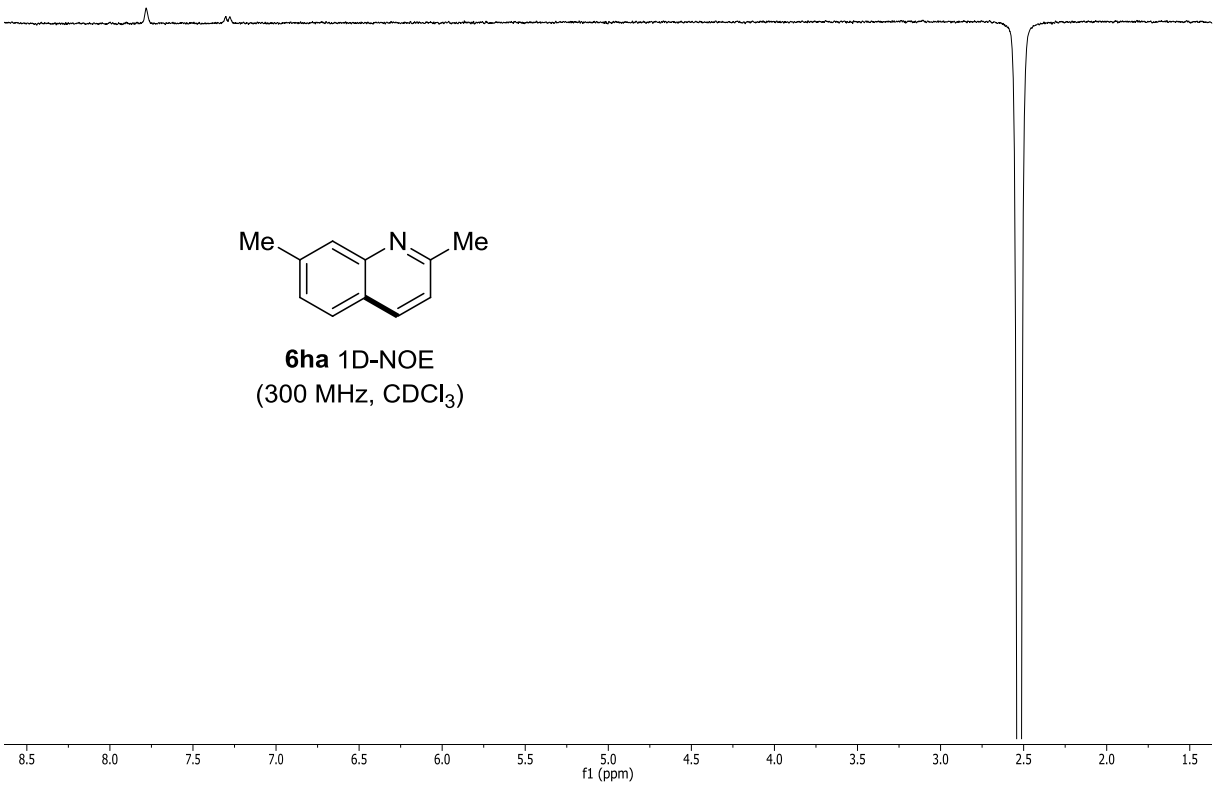
6ga ^{13}C-NMR
(75 MHz, $CDCl_3$)



6ha ^{1}H-NMR
(300 MHz, $CDCl_3$)



6ha ^{13}C-NMR
(75 MHz, $CDCl_3$)



6ha 1D-NOE
(300 MHz, $CDCl_3$)