

5-Bromo-norborn-2-en-7-one Derivatives as a Carbon Monoxide Source for Palladium Catalyzed Carbonylation Reactions

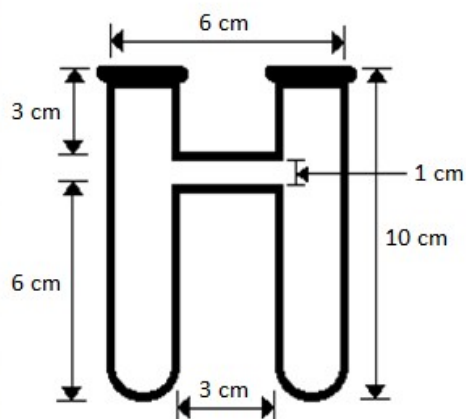
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Supporting Information

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Two-chamber glassware



Chamber A = CO generation chamber

Chamber B = Carbonylation reaction chamber

Conversion of starting material to Carbonylated product

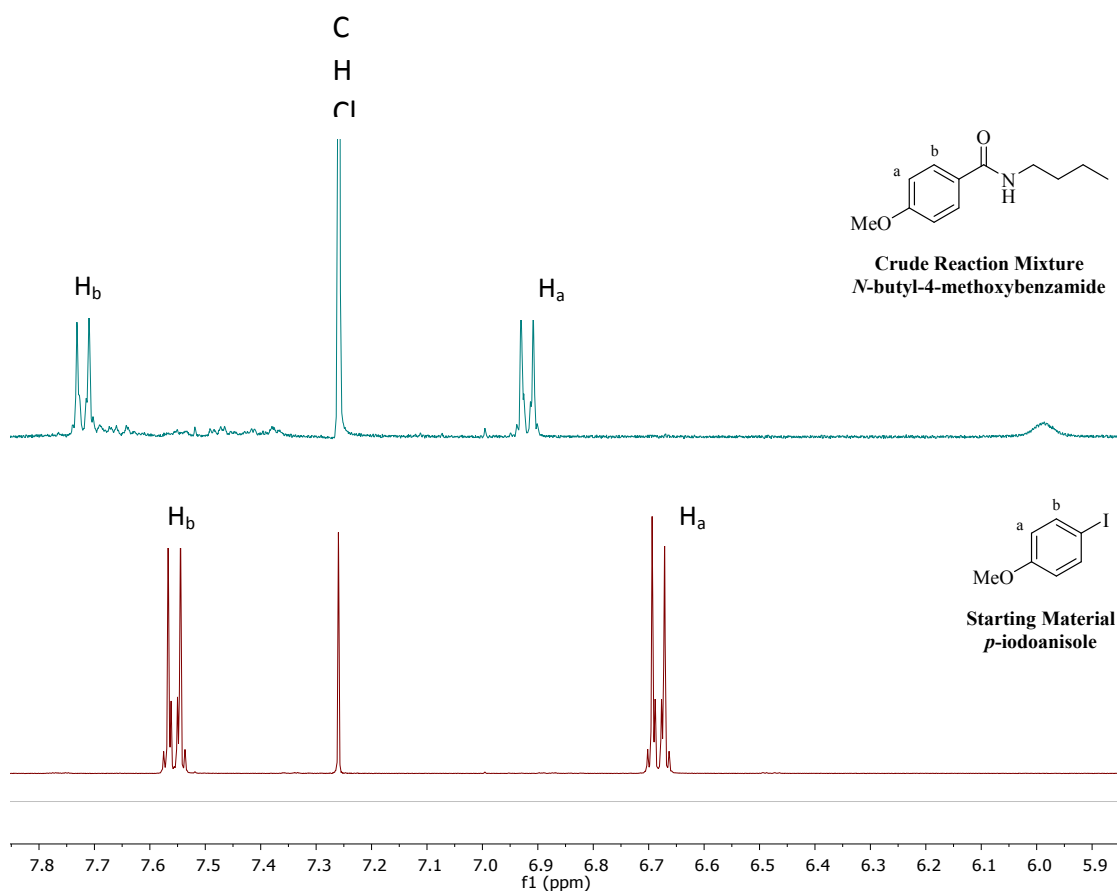
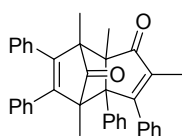


Figure S11: ^1H NMR spectrum (400 MHz, CDCl_3) of the aromatic region for the crude reaction mixture of **8a** with that of iodoanisole (Entry 1, Table 1).

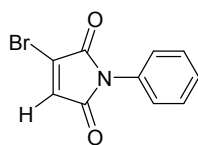
2,5-Dimethyl-3,4-diphenylcyclopentadien-1-one¹ (diene dimer) (**3**)



Benzil (10.0 g, 47.6 mmol) and pentan-3-one (7.59 mL, 71.4 mmol) in isopropanol (150 mL) were combined with KOH (3.47 g, 61.8 mmol) in isopropanol (100 mL) and the reaction mixture was stirred for 3 h at rt. Isopropanol was removed under reduced pressure, the residue was acidified with aqueous 5% HCl and extracted into EtOAc.

The organic layer was washed with water and brine, and dried over anhydrous MgSO₄. The filtrate was concentrated under reduced pressure. The residue was cooled to 0 °C, acetic anhydride (16 mL) and conc. H₂SO₄ (1.0 mL) were slowly added and the mixture stirred at rt o/n. The solution was added to cold water (100 mL) with stirring. The precipitate was collected, washed with H₂O, and dried under vacuum to afford the title compound **3** (8.98 g, 73%) as a white powder. ¹H NMR (400 MHz, CDCl₃) δ 0.58 (s, 3H), 1.25 (s, 3H), 1.64 (s, 3H), 2.25 (s, 3H), 6.70 (m, 2H), 6.89 - 7.00 (m, 8H), 7.04 - 7.12 (m, 5H), 7.20 - 7.29 (m, 5H); ¹³C NMR (101 MHz, CDCl₃) δ 10.0, 12.5, 12.6, 18.2, 58.6, 59.9, 61.2, 66.9, 127.00, 127.04, 127.2, 127.36, 127.43, 128.0, 129.0, 129.4, 130.3, 131.0, 132.0, 133.6, 134.1, 134.2, 140.2, 143.0, 143.3, 144.5, 166.0, 203.3, 209.6; HRMS-ESI *m/z* [M+Na]⁺ calc. for C₃₈H₃₂O₂Na⁺: 543.2295, found: 543.2278.

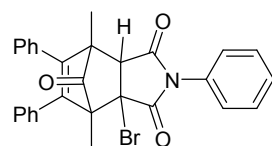
N-Phenyl-3-bromomaleimide² (**4a**)



A solution of *N*-phenylmaleimide (6.80 g, 39.3 mmol) in CCl₄ (60 ml) was added slowly to a solution of bromine (2.50 ml, 48.5 mmol) in CCl₄ (40 ml) at room temperature. The reaction mixture was refluxed for 1 hour, and then cooled to room temperature. The precipitate was filtered and washed with CCl₄ (ca. 20 ml) to give

2,3-dibromo-*N*-phenylmaleimide. The intermediate was dissolved in dry THF (120 ml) and added dropwise to a solution of triethylamine (5.63 ml, 40.4 mmol) in dry THF (20 ml) at 0 °C and the mixture was stirred for 2 hours. The solution was warmed to room temperature and concentrated *in vacuo*. Afterwards the residue was dissolved in EtOAc and washed with water and brine, and dried over anhydrous Na₂SO₄. The organic layer was concentrated *in vacuo* to give a pale brown residue which was purified by column chromatography (EtOAc/Pet. ether 1:9) to give the title compound **4a** (7.70 g, 78 %) as a pale brown solid. m.p. 159-161 °C (EtOAc/Pet. ether 1:9) (lit m.p. = 161-163 °C). ¹H NMR (500 MHz, CDCl₃) δ 7.02 (s, 1H), 7.33-7.35 (m, 2H), 7.38-7.41 (m, 1H), 7.46-7.49 (m, 2H). ¹³C NMR (125 MHz, CDCl₃) δ 126.2, 128.5, 129.4, 131.1, 131.96, 132.02, 164.3, 167.5; *v*_{max} (cm⁻¹) 1708 (C=O); Anal. calc. for C₁₀H₆BrNO₂: C, 47.65; H, 2.40; N, 5.56. Found: C, 47.89; H, 2.39; N, 5.54.

3a-Bromo-3a,4,7,7a-tetrahydro-4,7-dimethyl-2,5,6-triphenyl-4,7-methano-1H-isoindole-1,3,8(2H)-trione³ (**5a**)

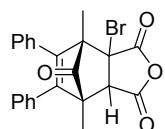


Diene dimer **3** (393 mg, 1.51 mmol) and *N*-phenyl-2-bromomaleimide (**4a**) (418 mg, 1.66 mmol) were refluxed in benzene (20 ml) for 6 h. The solution was concentrated *in vacuo* to afford a brown oil which was recrystallised in ether to afford the title compound **5a** (551 mg, 1.07 mmol, 71 %) as white

crystals. m.p. 173-177 °C (ether); ¹H NMR (500 MHz, CDCl₃) δ 1.68 (s, 3H), 1.71 (s, 3H), 3.71 (s, 1H),

6.97-7.00 (m, 4H), 7.16-7.29 (m, 8H), 7.43-7.51 (m, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 11.7, 12.6, 56.9, 59.0, 60.4, 61.1, 126.21, 128.3, 128.4, 128.4, 128.5, 129.2, 129.5, 129.6, 129.8, 131.3, 132.5, 132.6, 140.6, 144.8, 171.4, 172.0, 196.8 ν_{max} (cm^{-1}) 1780 (C=O), 1720 (C=O); HRMS-ESI $[\text{M}+\text{Na}]^+$ calc. for $\text{C}_{29}\text{H}_{22}^{79}\text{BrNO}_3\text{Na}^+$: 534.0699, Found: 534.0675.

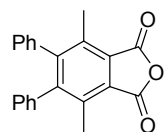
3a,4,7,7a-Tetrahydro-7a-bromo-4,7-dimethyl-5,6-diphenyl-4,7-methanoisobenzofuran-1,3,8-trione³ (**5b**)



Diene dimer (**3**) (999 mg, 0.192 mmol) and bromomaleic anhydride (1.295 mL, 3.84 mmol) were refluxed in toluene (60 mL) for 4 h. The orange solution was concentrated *in vacuo*. The product was triturated in ether and petrol to afford the title compound **5b** as an inseparable 6:1 mixture of the *endo* and *exo* isomers (808 mg, 96%) as a white solid. ν_{max} (cm^{-1}) 1775 (C=O), 1218 (C-O-C), 697 (C-Br); HRMS-ESI m/z $[\text{M}+\text{Na}]^+$ calc. for $\text{C}_{23}\text{H}_{17}^{79}\text{BrO}_4\text{Na}^+$: 459.0202, Found: 459.0171.

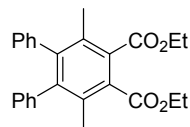
For the *endo* isomer; ^1H NMR (400 MHz, CDCl_3) δ *inter alia* 1.62 (s, 3H), 1.65 (s, 3H), 3.74 (s, 1H), 6.93 - 6.97 (m, 4H), 7.20 - 7.22 (dt, $J = 6.2, 2.1$ Hz, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ *inter alia* 11.3, 12.1, 56.7, 57.5, 61.1, 128.5, 128.6, 128.69, 128.71, 129.5, 129.8, 131.8, 131.9, 141.2, 145.6, 166.9, 167.0, 195.6. For the *exo* isomer; ^1H NMR (400 MHz, CDCl_3) δ *inter alia* 1.25 (s, 3H), 1.59 (s, 3H), 3.52 (s, 1H), 6.93 - 6.97 (m, 4H), 7.20 - 7.22 (dt, $J = 6.2, 2.1$ Hz, 6H).

4,7-Dimethyl-5,6-diphenyl-1,3-isobenzofurandione⁴ (**9**)



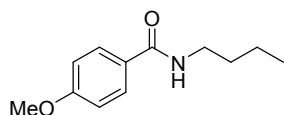
Et_3N (0.096 mL, 0.686 mmol) was added to cycloadduct **5b** (100 mg, 0.229 mmol) in toluene (4 mL) and heated at reflux for 3 h. The solvent was concentrated *in vacuo* and the residue extracted into EtOAc, then washed with 1M HCl and dried over MgSO_4 . The solvent was concentrated *in vacuo* to afford the title compound **9** (73.7 mg, 98%) as a pale solid. ^1H NMR (400 MHz, CDCl_3) δ 2.43 (s, 6H), 6.88 - 6.90 (m, 4H), 7.13 - 7.21 (m, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 16.1, 127.4, 127.8, 128.1, 129.4, 136.8, 138.0, 150.1, 163.6; ν_{max} (cm^{-1}) 1763 (C=O), 1685 (C=O), 1209 (C-O-C); HRMS-ESI m/z $[\text{M}+\text{Na}]^+$ calc. for: $\text{C}_{22}\text{H}_{16}\text{O}_3\text{Na}^+$: 351.0992, found: 351.0964.

Diethyl 3,6-dimethyl-4,5-diphenylphthalate⁵ (**12**)



Diethyl acetylenedicarboxylate (0.110 mL, 0.748 mmol) and diene dimer **3** (334 mg, 0.641 mmol) were added to a Kimax[®] tube, followed by 1,4-dioxane (6 mL). The Kimax[®] tube was sealed with a screwcap fitted with a silicon seal. The sealed system was heated to 80 °C for 20 h. The reaction mixture was cooled to rt and the solvent concentrated *in vacuo*. The crude product was purified by silica column chromatography (EtOAc/PE 1:4-1:1) to afford the title compound **12** (275 mg, 91%) as white crystals. ^1H NMR (400 MHz, CDCl_3) δ 1.39 (t, $J = 7.1$ Hz, 6H), 2.08 (s, 6H), 4.38 (q, $J = 7.1$ Hz, 4H), 6.88 (m, 4H), 7.11 (m, 6H); ^{13}C NMR (101 MHz, CDCl_3) δ 14.3, 18.5, 61.7, 126.6, 127.8, 129.8, 131.8, 132.1, 139.9, 144.4, 168.9; ν_{max} (cm^{-1}) 1723 (C=O); HRMS-ESI m/z $[\text{M}+\text{Na}]^+$ calc. for $\text{C}_{26}\text{H}_{26}\text{O}_4\text{Na}^+$: 425.1723, Found: 425.1736.

***N*-butyl-4-methoxybenzamide⁶ (8a)**



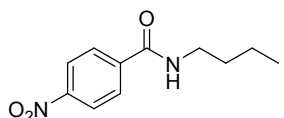
Diethyl acetylenedicarboxylate as CO source - two-chamber system

Following General Procedure A: Chamber A: diethyl acetylenedicarboxylate (0.110 mL, 0.748 mmol), diene dimer **3** (334 mg, 0.641 mmol) and 1,4-dioxane. Chamber B: Pd₂(dba)₃ (9.78 mg, 10.68 μmol), PPh₃ (11.21 mg, 0.043 mmol), *p*-iodoanisole (100 mg, 0.427 mmol), *n*-butylamine (0.097 mL, 0.983 mmol), 1,4-dioxane (4 mL) and Et₃N (0.137 mL, 0.983 mmol). The system was sealed and heated to 80 °C for 20 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated *in vacuo*. The crude product was purified by silica column chromatography (EtOAc/PE 1:4-1:1) to afford the title compound **10a** (84.5 mg, 95%) as white crystals. ¹H NMR (400 MHz, CDCl₃) δ 0.96 (t, *J* = 7.3 Hz, 3H), 1.39 - 1.44 (m, 2H), 1.56 - 1.63 (m, 2H), 3.42 - 3.47 (m, 2H), 3.85 (s, 3H), 5.98 (bs, 1H), 6.92 (d, *J* = 8.9 Hz, 2H), 7.72 (d, *J* = 8.9 Hz, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 13.8, 20.2, 31.8, 39.7, 55.4, 113.7, 127.1, 128.5, 162.0, 167.0; ν_{max} (cm⁻¹) 3319 (N-H stretch), 2963 (C-H stretch), 2839 (O-Me), 1627 (C=O), 1501 (N-H bend), 1237 (C-N stretch); HRMS-ESI *m/z* [M+Na]⁺ calc. for C₁₂H₁₇NO₂Na⁺: 230.1151, Found: 230.1129.

Using **5b** as CO source

Following General Procedure B: Chamber A: cycloadduct **5b** (280 mg, 0.641 mmol), 1,4-dioxane (5 mL) and Et₃N (0.137 mL, 0.983 mmol). Chamber B: Pd₂(dba)₃ (9.78 mg, 10.68 μmol), PPh₃ (11.21 mg, 0.043 mmol), *p*-iodoanisole (100 mg, 0.427 mmol), *n*-butylamine (0.097 mL, 0.983 mmol), 1,4-dioxane (4 mL) and Et₃N (0.089 mL, 0.641 mmol). The two-chamber system was sealed and heated to 80 °C for 20 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated *in vacuo*. The crude product was purified by silica column chromatography (EtOAc/PE 1:4-1:1) to afford the title compound **10a** (78.2 mg, 88%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 0.94 (t, *J* = 7.3 Hz, 3H), 1.35 - 1.38 (m, 2H), 1.54-1.61 (m, 2H) 3.40 - 3.45 (q, *J* = 7.1 Hz, 2H), 3.83 (s, 3H), 6.15 (bs, 1H), 6.89 (d, *J* = 8.9 Hz, 2H), 7.72 (d, *J* = 8.9 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 14.0, 20.3, 32.0, 39.9, 55.5, 113.8, 127.3, 128.7, 162.2, 167.1; ν_{max} (cm⁻¹) 3311 (N-H stretch), 2839 (C-H), 1623 (C=O), 1502 (N-H bend), 1296 (C-N stretch); HRMS-ESI *m/z* [M+Na]⁺ calc. for C₁₂H₁₇NO₂Na⁺: 230.1168, Found: 230.1164.

***N*-butyl-4-nitrobenzamide⁷ (8b)**



Diethyl acetylenedicarboxylate as CO source

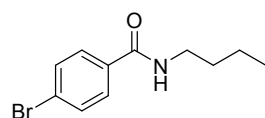
Following General Procedure A: Chamber A: Diethyl acetylenedicarboxylate (0.088 mL, 0.602 mmol), diene dimer **3** (157 mg, 0.301 mmol) and 1,4-dioxane (5 mL). Chamber B: Pd₂(dba)₃ (9.19 mg, 10.04 μmol), PPh₃ (10.53 mg, 0.040 mmol), 1-iodo-4-nitrobenzene (100 mg, 0.402 mmol), *n*-butylamine (0.091 mL, 0.924 mmol), 1,4-dioxane (4 mL) and Et₃N (0.129 mL, 0.924 mmol). The system was sealed and heated to 80 °C for 20 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated *in vacuo*. The crude product was purified by silica column chromatography (EtOAc/PE 1:4 - 1:1) to afford the title compound **10b** (73.1 mg, 82%) as a pale yellow solid. ¹H NMR (400 MHz, CDCl₃) δ 0.98 (t, *J* = 7.3 Hz, 3H), 1.38 - 1.48 (dq, *J* = 15.6, 7.3 Hz, 2H), 1.59 - 1.67 (m, 2H), 3.47 - 3.52 (td, *J* = 7.2, 5.3 Hz, 2H), 6.15 (bs, 1H), 7.92

(d, $J = 9.0$ Hz, 2H), 8.29 (d, $J = 8.3$ Hz, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 13.9, 20.3, 31.7, 40.3, 124.0, 128.2, 140.6, 149.6, 165.6. ν_{max} (cm^{-1}) 3302 (N-H stretch), 1634 (C=O), 1537 (N-H bend), 1510 (NO_2), 1346 (NO_2), 1295 (C-N stretch); HRMS-ESI m/z $[\text{M}+\text{Na}]^+$ calc. for $\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}_3\text{Na}^+$: 245.0897, Found: 245.0874

CORM as CO source

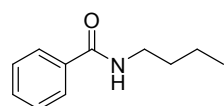
Following General Procedure B: Chamber A: cycloadduct **5b** (263 mg, 0.602 mmol), 1,4-dioxane (5 mL) and Et_3N (0.129 mL, 0.924 mmol). Chamber B: $\text{Pd}_2(\text{dba})_3$ (9.19 mg, 10.04 μmol), PPh_3 (10.53 mg, 0.040 mmol), 1-iodo-4-nitrobenzene (100 mg, 0.402 mmol), *n*-butylamine (0.091 mL, 0.924 mmol), 1,4-dioxane (4 mL) and Et_3N (0.129 mL, 0.924 mmol). The two-chamber system was sealed and heated to 80 °C for 20 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated *in vacuo*. The crude product was purified by silica column chromatography (EtOAc/PE 1:4 - 1:1) to afford the title compound **10b** (88.6 mg, 99%) as a pale yellow solid. ^1H NMR (400 MHz, CDCl_3) δ 0.98 (t, $J = 7.3$ Hz, 3H), 1.39 - 1.48 (m, 2H), 1.60 - 1.67 (m, 2H), 3.47 - 3.52 (m, 2H), 6.12 (bs, 1H), 7.92 (d, $J = 8.7$ Hz, 2H), 8.29 (d, $J = 8.7$ Hz, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 13.7, 20.1, 31.6, 40.1, 123.8, 128.0, 140.4, 149.5, 165.4; ν_{max} (cm^{-1}) 3302 (N-H stretch), 1634 (C=O), 1537 (N-H bend), 1510 (NO_2), 1346 (NO_2), 1295 (C-N stretch); HRMS-ESI m/z $[\text{M}+\text{Na}]^+$ calc. for $\text{C}_{12}\text{H}_{14}\text{N}_2\text{O}_3\text{Na}^+$: 245.0897, Found: 245.0899.

4-bromo-*N*-butylbenzamide⁸ (8c)



Following General Procedure B: Chamber A: cycloadduct **5b** (150 mg, 0.343 mmol), 1,4-dioxane (5 mL) and Et_3N (0.072 mL, 0.515 mmol). Chamber B: $\text{Pd}_2(\text{dba})_3$ (7.85 mg, 8.58 μmol), PPh_3 (9.00 mg, 0.034 mmol), 1-bromo-4-iodobenzene (97 mg, 0.343 mmol), *n*-butylamine (0.078 mL, 0.789 mmol), 1,4-dioxane (4 mL) and Et_3N (0.110 mL, 0.789 mmol). The two-chamber system was sealed and heated to 80 °C for 20 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated *in vacuo*. The crude product was purified by silica column chromatography (EtOAc/PE 1:6 - 2:1) to afford the title compound **10c** (73.1 mg, 81%) as an off white solid. ^1H NMR (400 MHz, CDCl_3) δ 0.96 (t, $J = 7.3$ Hz, 3H), 1.37 - 1.46 (m, 2H), 1.57 - 1.64 (m, 2H), 3.43 - 3.48 (m, 2H), 6.02 (bs, 1H), 7.63 (d, $J = 8.7$ Hz, 2H), 7.86 (d, $J = 8.7$ Hz, 2H); ^{13}C NMR (101 MHz, CDCl_3) 13.9, 31.0, 31.8, 40.0, 125.9, 128.6, 131.8, 133.8, 166.7; ν_{max} (cm^{-1}) 3321 (N-H stretch), 1631 (C=O), 1535 (N-H bend), 1297 (C-N stretch), 644 (C-Br); HRMS-ESI m/z $[\text{M}+\text{H}]^+$ calc. for $\text{C}_{11}\text{H}_{15}\text{NO}^{79}\text{Br}^+$: 256.0332, found: 256.0324.

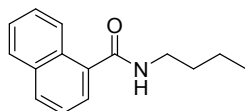
***N*-butylbenzamide⁹ (8d)**



Following General Procedure B: Chamber A: cycloadduct **5b** (322 mg, 0.735 mmol), 1,4-dioxane (5 mL) and Et_3N (0.157 mL, 1.127 mmol). Chamber B: $\text{Pd}_2(\text{dba})_3$ (11.22 mg, 0.012 mmol), PPh_3 (12.86 mg, 0.049 mmol), iodobenzene (0.055 mL, 0.490 mmol), *n*-butylamine (0.111 mL, 1.127 mmol), 1,4-dioxane (4 mL) and Et_3N (0.157 mL, 1.127 mmol). The two-chamber system was sealed and heated to 80 °C for 20 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated *in vacuo*. The crude product

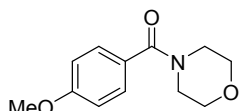
was purified by silica column chromatography (EtOAc/PE 0:1 - 1:4) to afford the title compound **10d** (84.1 mg, 97%) as an oil. ¹H NMR (400 MHz, CDCl₃) δ 0.96 (t, *J* = 7.3 Hz, 3H), 1.43 (m, 2H), 1.61 (m, 2H), 3.47 (td, *J* = 7.2, 5.7 Hz, 2H), 6.09 (bs, 1H), 7.43 (m, 2H), 7.48 (m, 1H), 7.75 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 13.8, 31.0, 31.8, 39.9, 127.0, 128.5, 131.3, 134.9, 167.7; *v*_{max} (cm⁻¹) 3317 (N-H stretch), 1634 (C=O), 1539 (N-H bend), 1307 (C-N stretch); HRMS-ESI *m/z* [M+Na]⁺ calc. for C₁₁H₁₅NONa⁺: 200.1046, Found: 200.1030.

***N*-butyl-1-naphthamide¹⁰ (8e)**



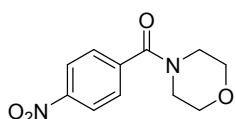
Following General Procedure B: Chamber A: cycloadduct **30** (367.5 mg, 0.840 mmol), 1,4-dioxane (5 mL) and Et₃N (0.137 mL, 0.984 mmol). Chamber B: Pd₂(dba)₃ (9.01 mg, 9.84 μmol), PPh₃ (10.32 mg, 0.039 mmol), 1-iodonaphthalene (0.057 mL, 0.394 mmol), *n*-butylamine (0.089 mL, 0.905 mmol), 1,4-dioxane (4 mL) and Et₃N (0.126 mL, 0.905 mmol). The two-chamber system was sealed and heated to 80 °C for 20 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated *in vacuo*. The crude ¹H NMR indicated that 90% of the starting material was converted to the title compound. The crude product was purified by silica column chromatography (EtOAc/PE 1:6 - 1:3) to give a pale orange solid. This was then triturated in DCM and petrol to afford the title compound **8e** (78 mg, 88%) as a white solid. ¹H NMR (400 MHz, CDCl₃) δ 0.99 (t, *J* = 7.35 Hz, 3H), 1.46 (m, 2H), 1.65 (m, 2H), 3.56 (m, 2H), 5.95 (bs, 1H), 7.45 (dd, *J* = 8.3, 7.0 Hz, 1H), 7.56 (m, 2H), 7.89 (m, 3H), 8.30 (ddd, *J* = 7.8, 1.9, 0.8 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 13.8, 20.2, 31.8, 39.8, 124.7, 124.7, 125.4, 126.4, 127.0, 128.3, 130.1, 130.4, 133.7, 134.9, 169.5; *v*_{max} (cm⁻¹) 3293 (N-H stretch), 3061 (C-H), 1653 (C=O), 1553 (N-H bend), 1298 (C-N stretch); HRMS-ESI *m/z* [M+Na]⁺ calc. for C₁₅H₁₇NONa⁺: 250.1194, Found: 250.1202.

Morpholino(4-methoxyphenyl)methanone¹¹ (10a)



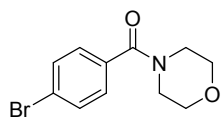
Following General Procedure B: Chamber A: cycloadduct **5b** (280 mg, 0.641 mmol), 1,4-dioxane (5 mL) and Et₃N (0.137 mL, 0.983 mmol). Chamber B: Pd₂(dba)₃ (9.78 mg, 10.68 μmol), PPh₃ (11.21 mg, 0.043 mmol), *p*-iodoanisole (100 mg, 0.427 mmol), morpholine (0.086 mL, 0.983 mmol), 1,4-dioxane (4 mL) and Et₃N (0.137 mL, 0.983 mmol). The two-chamber system was sealed and heated to 100 °C for 25 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated *in vacuo*. The crude product was purified by silica column chromatography (EtOAc/PE 2:1 - 6:1) to afford the title compound **10a** (70.8 mg, 75%) as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 3.64 - 3.70 (bm, 8H), 3.83 (s, 3H), 6.90 - 6.94 (m, 2H), 7.37 - 7.41 (m, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 43.7, 48.7, 55.5, 67.1, 113.9, 127.5, 129.3, 161.0, 170.5; *v*_{max} (cm⁻¹) 2857, 1627 (C=O), 1277 (C-N stretch), 1107 (C-O-C); HRMS-ESI *m/z* [M+Na]⁺ calc. for C₁₂H₁₅NO₃Na⁺: 244.0944, found: 244.0929.

Morpholino(4-nitrophenyl)methanone¹² (10b)



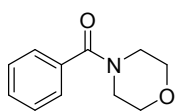
Following General Procedure B: Chamber A: cycloadduct **5b** (263 mg, 0.602 mmol), 1,4-dioxane (5 mL) and Et₃N (0.129 mL, 0.924 mmol). Chamber B: Pd₂(dba)₃ (9.19 mg, 10.04 μmol), PPh₃ (10.53 mg, 0.040 mmol), 1-iodo-4-nitrobenzene (100 mg, 0.402 mmol), morpholine (0.081 mL, 0.924 mmol), 1,4-dioxane (4 mL) and Et₃N (0.129 mL, 0.924 mmol). The two-chamber system was sealed and heated to 100 °C for 25 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated *in vacuo*. The crude product was purified by silica column chromatography (EtOAc/PE 1:1 - 6:1) to afford the title compound **10b** (83.1 mg, 88%) as an orange solid. ¹H NMR (400 MHz, CDCl₃) δ 3.39 - 3.81 (m, 8H), 7.57 - 7.60 (m, 2H), 8.28 - 8.31 (m, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 42.8, 48.2, 66.9, 124.1, 128.3, 141.6, 148.7, 168.2; ν_{max} (cm⁻¹) 2920 (C-H bend), 1631 (C=O), 1515 (NO₂), 1350 (NO₂), 1279 (C-N), 1105 (C-O-C); HRMS-ESI *m/z* [M+H]⁺ calc. for C₁₂H₁₃NO₃⁺: 237.0870, found: 237.0876.

Morpholino(4-bromophenyl)methanone¹³ (10c)



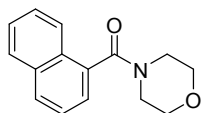
Following General Procedure B: Chamber A: cycloadduct **5b** (232 mg, 0.530 mmol), 1,4-dioxane (5 mL) and Et₃N (0.113 mL, 0.813 mmol). Chamber B: Pd₂(dba)₃ (8.09 mg, 8.84 μmol), PPh₃ (9.27 mg, 0.035 mmol), 1-bromo-4-iodobenzene (100 mg, 0.353 mmol), morpholine (0.071 mL, 0.813 mmol), 1,4-dioxane (4 mL) and Et₃N (0.113 mL, 0.813 mmol). The two-chamber system was sealed and heated to 100 °C for 25 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated *in vacuo*. The crude product was purified by silica column chromatography (EtOAc/PE 1:1 - 4:1) to afford the title compound **10c** as a pale orange oil (67.5 mg, 72%); ¹H NMR (400 MHz, CDCl₃) δ 3.46 - 3.70 (m, 8H), 7.28 - 7.30 (m, 2H), 7.55 - 7.57 (m, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 42.8, 48.2, 67.0, 124.4, 129.0, 132.0, 134.2, 169.5; ν_{max} (cm⁻¹) 1628 (C=O), 1276 (C-N stretch), 1111 (C-O-C); HRMS-ESI *m/z* [M+H]⁺ calc. for C₁₁H₁₃NO₂⁷⁹Br⁺: 270.0124, found: 270.0122.

Morpholino(phenyl)methanone¹² (10d)



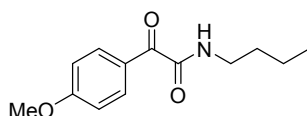
Following General Procedure B: Chamber A: cycloadduct **30** (322 mg, 0.735 mmol), 1,4-dioxane (5 mL) and Et₃N (0.157 mL, 1.127 mmol). Chamber B: Pd₂(dba)₃ (11.22 mg, 0.012 mmol), PPh₃ (12.86 mg, 0.049 mmol), iodobenzene (0.055 mL, 0.490 mmol), morpholine (0.099 mL, 1.127 mmol), 1,4-dioxane (4 mL) and Et₃N (0.157 mL, 1.127 mmol). The two-chamber system was sealed and heated to 100 °C for 25 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated *in vacuo*. The crude product was purified by silica column chromatography (EtOAc/PE 1:1 - 4:1) to afford the title compound **10d** (93 mg, 99%). ¹H NMR (400 MHz, CDCl₃) δ 3.46 - 3.75 (m, 8H), 7.39 - 7.43 (m, 5H); ¹³C NMR (101 MHz, CDCl₃) δ: 42.7, 48.3, 67.0, 127.2, 128.7, 130.0, 135.5, 170.6; ν_{max} (cm⁻¹); 1625 (C=O), 1275 (C-N stretch), 1110 (C-O-C); 544 (C-Br); HRMS-ESI *m/z* [M+Na]⁺ calc. for C₁₁H₁₃NO₂Na⁺: 214.0838, found: 214.0839.

Morpholino(naphthalen-1-yl)methanone¹³ (**10e**)



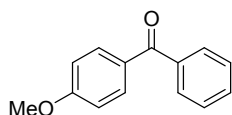
Following General Procedure B: Chamber A: cycloadduct **5b** (258 mg, 0.590 mmol), 1,4-dioxane (5 mL) and Et₃N (0.126 mL, 0.905 mmol). Chamber B: Pd₂(dba)₃ (9.01 mg, 9.84 μmol), PPh₃ (10.32 mg, 0.039 mmol), 1-iodonaphthalene (0.057 mL, 0.394 mmol), morpholine (0.079 mL, 0.905 mmol), 1,4-dioxane (4 mL) and Et₃N (0.126 mL, 0.905 mmol). The two-chamber system was sealed and heated to 100 °C for 25 h. The reaction mixture was cooled to rt, and the solvent in Chamber B was concentrated *in vacuo*. The crude ¹H NMR indicated that only 80% of the starting material was converted into the title compound. The crude product was purified by silica column chromatography (EtOAc/PE 1:2 - 4:1) to afford the title compound **10e** (71.2 mg, 75%). ¹H NMR (400 MHz, CDCl₃) δ 3.16 - 3.25 (m, 2H), 3.47 - 3.56 (m, 2H), 3.83 - 4.04 (m, 4H), 7.41 - 7.43 (dd, *J* = 7.0, 1.3 Hz, 1H), 7.47 - 7.57 (m, 4H), 7.84 - 7.90 (m, 3H); ¹³C NMR (101 MHz, CDCl₃) δ; 42.3, 47.8, 67.1, 67.2, 124.1, 124.7, 125.3, 126.7, 127.3, 128.6, 129.5, 129.7, 133.6, 133.8, 169.6; *v*_{max} (cm⁻¹) 1629 (C=O), 1247 (C-N stretch), 1111 (C-O-C); HRMS-ESI *m/z* [M+Na]⁺ calc. for C₁₅H₁₅NO₂Na⁺: 264.0995, found: 264.0994.

N-butyl-2-(4-methoxyphenyl)-2-oxoacetamide (**13**)



Chamber A: Cycloadduct **5b** (654 mg, 1.496 mmol) was added followed by Toluene (6 mL). Chamber B: Pd₂(dba)₃ (19.56 mg, 0.021 mmol), tri-*tert*-butylphosphonium tetrafluoroborate (12.40 mg, 0.043 mmol), *p*-iodoanisole (100 mg, 0.427 mmol) were added followed by toluene (5 mL), butylamine (0.063 mL, 0.641 mmol) and DBU (0.128 mL, 0.855 mmol). The system was flushed with argon then DBU (0.256 mL, 1.709 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The sealed system was left to stir for 25 h. The solvent in Chamber B was concentrated *in vacuo*. The crude product was purified by silica column chromatography (EtOAc/PE 1:9 - 2:3) to afford the title compound **13** (64.7 mg, 64%) as a pale yellow solid. ¹H NMR (400 MHz, CDCl₃) δ 0.94 (t, *J* = 7.3 Hz, 3H), 1.34 - 1.44 (m, 2H), 1.54 - 1.61 (m, 2H), 3.34 - 3.40 (m, 2H), 3.87 - 3.88 (m, 3H), 6.93 (dt, *J* = 9.0, 1.3 Hz, 2H), 7.15 (bs, 1H), 8.40 (dt, *J* = 9.2, 1.8 Hz, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 13.8, 20.2, 31.5, 39.2, 55.7, 113.9, 126.6, 134.0, 162.4, 164.8, 186.0; *v*_{max} (cm⁻¹) 3242 (NH), 2933 (OMe), 1667, 1630 (C=O); HRMS-ESI *m/z* [M+Na]⁺ calc. for C₁₃H₁₇NO₃Na⁺: 258.1101, Found: 258.1118.

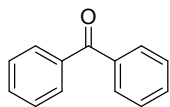
(4-methoxyphenyl)(phenyl)methanone¹⁴ (**15a**)



Following General Procedure C: Chamber A: Cycloadduct **5b** (561 mg, 1.282 mmol) was added, followed by 1,4-dioxane (5 mL). Chamber B: Pd₂(dba)₃ (7.83 mg, 8.55 μmol), phenylboronic acid (78 mg, 0.641 mmol), *p*-iodoanisole (100 mg, 0.427 mmol) and K₂CO₃ (177 mg, 1.282 mmol) were added, followed by anisole (4 mL). The system was flushed with argon then Et₃N (0.208 mL, 1.496 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to sit for 30 min to release CO before being heated to 80 °C for 25 h. The reaction mixtures were cooled to rt and the solvent in Chamber B concentrated *in vacuo*. The crude product was purified by silica column chromatography (EtOAc/PE) to afford the title compound **15a** (67.5 mg, 74%) as a yellow oil. ¹H NMR (400 MHz, CDCl₃)

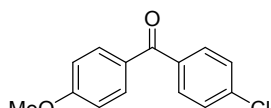
δ 3.89 (s, 3H), 6.97 (d, J = 8.6 Hz, 2H), 7.47 (t, J = 7.6 Hz, 2H), 7.57 (t, J = 7.5 Hz, 1H), 7.76 (d, J = 8.1 Hz, 2H), 7.83 (d, J = 8.5 Hz, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 55.6, 113.7, 128.3, 129.9, 130.3, 132.0, 132.7, 138.4, 163.3, 195.8; ν_{max} (cm^{-1}) 2841 (OMe), 1649 (C=O); HRMS-ESI m/z $[\text{M}+\text{Na}]^+$ calc. for $\text{C}_{14}\text{H}_{12}\text{O}_2\text{Na}^+$: 235.0729, Found: 235.0730.

Benzophenone (15b)



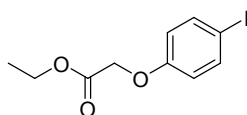
Following General Procedure C: Chamber A: Cycloadduct **5b** (643 mg, 1.471 mmol) was added, followed by 1,4-dioxane (5 mL). Chamber B: $\text{Pd}_2(\text{dba})_3$ (8.98 mg, 9.80 μmol), phenylboronic acid (90 mg, 0.735 mmol) and K_2CO_3 (203 mg, 1.471 mmol) were added, followed by anisole (5 mL) and iodobenzene (0.055 mL, 0.490 mmol). The system was flushed with argon then Et_3N (0.239 mL, 1.716 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to sit for 30 min to release CO before being heated to 80 $^\circ\text{C}$ for 24 h. The reaction mixtures were cooled to rt and the solvent in Chamber B concentrated *in vacuo*. The crude product was purified by silica column chromatography to afford the title compound **15b** (69.3 mg, 78%) as a yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 7.49 (m, 4H), 7.59 (m, 2H), 7.81 (m, 4H). ^{13}C NMR (101 MHz, CDCl_3) δ 128.4, 130.2, 132.5, 137.7, 196.9; ν_{max} (cm^{-1}) 1655 (C=O); HRMS-ESI m/z $[\text{M}+\text{Na}]^+$ calc. for $\text{C}_{13}\text{H}_{10}\text{ONa}^+$: 205.0622, Found: 205.0624.

(4'-chlorophenyl)-(4-methoxyphenyl)methanone¹⁵ (15c)



Following General Procedure C: Chamber A: Cycloadduct **5b** (561 mg, 1.282 mmol) was added, followed by 1,4-dioxane (5 mL). Chamber B: $\text{Pd}_2(\text{dba})_3$ (7.83 mg, 8.55 μmol), 4-chlorophenylboronic acid (100 mg, 0.641 mmol), *p*-iodoanisole (100 mg, 0.427 mmol) and K_2CO_3 (177 mg, 1.282 mmol) were added, followed by anisole (4 mL). The system was flushed with argon then Et_3N (0.208 mL, 1.496 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to sit for 30 min to release CO before being heated to 80 $^\circ\text{C}$ for 24 h. The reaction mixtures were cooled to rt and the solvent in Chamber B concentrated *in vacuo*. The crude product was purified by silica column chromatography (EtOAc/PE) to afford the title compound **15c** (98.8 mg, 94%) as a yellow solid. ^1H NMR (400 MHz, CDCl_3) δ 3.90 (s, 3H), 6.97 (d, J = 8.9 Hz, 2H), 7.45 (d, J = 8.6 Hz, 2H), 7.71 (d, J = 8.5 Hz, 2H), 7.80 (d, J = 8.9 Hz, 2H); ^{13}C NMR (101 MHz, CDCl_3) δ 55.7, 113.8, 128.7, 129.9, 131.3, 132.6, 136.7, 138.4, 163.5, 194.5; ν_{max} (cm^{-1}) 2842 (OMe), 1639 (C=O), 759 (Ar-Cl); HRMS-ESI m/z $[\text{M}+\text{Na}]^+$ calc. for $\text{C}_{14}\text{H}_{11}^{35}\text{ClO}_2\text{Na}^+$: 269.0335, Found: 269.0340.

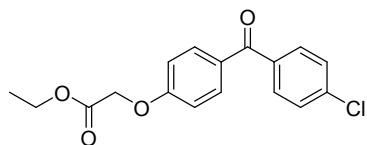
Ethyl 2-(4-iodophenoxy)acetate¹⁶ (6f)



To a solution of 4-iodophenol (1 g, 4.55 mmol) in acetone (100 mL), K_2CO_3 (1.885 g, 13.64 mmol) and ethyl 2-bromoacetate (0.553 mL, 5.00 mmol) were added. The mixture was heated at reflux o/n. The reaction progress was monitored by TLC until no starting material was observed. The reaction was allowed to cool to rt and the solution was concentrated *in vacuo*. The residue was dissolved in DCM and washed with water (2 x 40 mL). The organic layer was dried with MgSO_4 , filtered and concentrated *in vacuo*. The crude

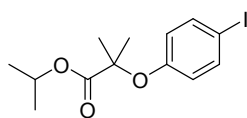
product was purified by silica column chromatography (DCM 100%) to afford the title compound **6f** (1.390 g, 99%) as a white crystalline solid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 1.29 (t, $J = 7.1$ Hz, 3H), 4.27 (q, $J = 7.1$ Hz, 2H), 4.58 (s, 2H), 6.69 (d, $J = 8.9$ Hz, 2H), 7.57 (d, $J = 8.9$ Hz, 2H); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 14.3, 61.6, 65.6, 84.2, 117.2, 138.5, 157.9, 168.7; ν_{max} (cm^{-1}) 1754 (C=O), 1198 (C-O-C); HRMS-ESI m/z $[\text{M}+\text{Na}]^+$ calc. for $\text{C}_{10}\text{H}_{11}\text{IO}_3\text{Na}^+$: 328.9645, found: 328.9645.

Ethyl 2-(4-(4-chlorobenzoyl)phenoxy)acetate (**15d**)



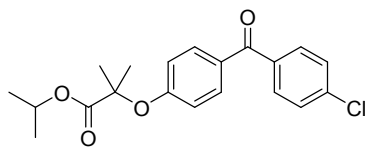
Following General Procedure C: Chamber A: Cycloadduct **5b** (643 mg, 1.470 mmol) was added, followed by 1,4-dioxane (4 mL). Chamber B: Ethyl 2-(4-iodophenoxy)acetate (150 mg, 0.490 mmol), (4-chlorophenyl)boronic acid (115 mg, 0.735 mmol), K_2CO_3 (203 mg, 1.470 mmol) and $\text{Pd}_2(\text{dba})_3$ (8.97 mg, 9.80 μmol) were added, followed by anisole (4 mL). The system was flushed with argon then Et_3N (0.239 mL, 1.715 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to sit for 30 min to release CO before being heated to 80 $^\circ\text{C}$ for 30 h. The reaction mixtures were cooled to rt and the solvent in Chamber B concentrated *in vacuo*. The crude product was purified by silica column chromatography (EtOAc/PE 1:15 - 1:5) to afford the title compound **15d** (117.6 mg, 75%). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 1.31 (t, $J = 7.1$ Hz, 3H), 4.29 (q, $J = 7.1$ Hz, 2H), 4.71 (s, 2H), 6.98 (d, $J = 8.6$ Hz, 2H), 7.45 (d, $J = 8.3$ Hz, 2H), 7.71 (d, $J = 8.4$ Hz, 2H), 7.80 (d, $J = 8.6$ Hz, 2H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 14.3, 61.8, 65.3, 114.4, 128.7, 130.9, 131.3, 132.6, 136.4, 138.6, 161.5, 168.4, 194.4; ν_{max} (cm^{-1}) 1755 (C=O), 1651 (C=O aryl), 1201 (C-O-C), 760 (Ar-Cl); HRMS-ESI m/z $[\text{M}+\text{Na}]^+$ calc. for $\text{C}_{17}\text{H}_{15}^{35}\text{ClO}_4\text{Na}^+$: 341.0551, found: 341.0549

Isopropyl 2-(4-iodophenoxy)-2-methylpropanoate (**6g**)



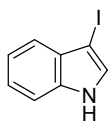
4-iodophenol (200 mg, 0.909 mmol) and anhydrous K_2CO_3 (377 mg, 2.73 mmol) were mixed in dry acetonitrile (20 mL). Isopropyl 2-bromo-2-methylpropanoate (0.184 mL, 1.091 mmol) was introduced to the suspension, and the reaction mixture was heated at reflux for 18 h. The reaction progress was monitored by TLC. After the mixture was cooled to rt, the reaction was terminated by addition of 1 M HCl (30 mL), and the product was extracted with ethyl acetate (50 mL). The organic layer was washed with water and brine and dried over MgSO_4 filtered and concentrated *in vacuo*. The crude product was purified by silica column chromatography to afford the title compound **6g** (172.6 mg, 54.5%). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 1.21 (d, $J = 6.3$ Hz, 6H), 1.57 (s, 6H), 5.07 (hept, $J = 6.3$ Hz, 1H), 6.59 - 6.63 (m, 2H), 7.49 - 7.53 (m, 2H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 21.7, 25.4, 69.3, 79.4, 84.6, 121.2, 138.1, 155.6, 173.6; ν_{max} (cm^{-1}) 1724 (C=O), 1100 (C-O-C); HRMS-ESI m/z $[\text{M}+\text{Na}]^+$ calc. for $\text{C}_{13}\text{H}_{17}\text{IO}_3\text{Na}^+$: 371.0115, found: 371.0111.

Isopropyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate¹⁷ (**15e**)



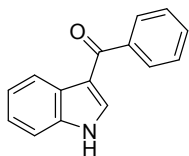
Following General Procedure C: Chamber A: Cycloadduct **5b** (565 mg, 1.292 mmol) was added, followed by 1,4-dioxane (4 mL). Chamber B: isopropyl 2-(4-iodophenoxy)-2-methylpropanoate (150 mg, 0.431 mmol), (4-chlorophenyl)boronic acid (81 mg, 0.517 mmol), K₂CO₃ (179 mg, 1.292 mmol) and Pd₂(dba)₃ (7.89 mg, 8.62 μmol) were added, followed by anisole (4 mL). The system was flushed with argon then Et₃N (0.210 mL, 1.508 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to sit for 30 min to release CO before being heated to 80 °C for 65 h. The reaction mixtures were cooled to rt and the solvent in Chamber B concentrated *in vacuo*. The crude product was purified by silica column chromatography (DCM/PE 10% - 100%) to afford the title compound **15e** (124.9 mg, 80%). ¹H NMR (400 MHz, CDCl₃) δ 1.20 (d, *J* = 6.3 Hz, 6H), 1.66 (s, 6H), 5.09 (sept, *J* = 6.1 Hz, 1H), 6.86 (d, *J* = 8.3 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.70 (d, *J* = 8.7 Hz, 2H), 7.73 (d, *J* = 8.7 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 21.7, 25.5, 69.5, 76.8, 117.4, 128.7, 130.4, 131.3, 132.1, 136.6, 138.5, 159.9, 173.2, 194.4; ν_{max} (cm⁻¹) 1727 (C=O), 1653 (C=O aryl), 1144 (C-O-C), 762 (C-Cl); HRMS-ESI *m/z* [M+Na]⁺ calc. for C₂₀H₂₁ClO₄Na: 383.1021, found: 383.0997.

3-iodo-1*H*-indole¹⁸ (**16**)



A solution of iodine (4.38 g, 17.24 mmol) in DMF (30 mL) was added dropwise to a solution of 1*H*-indole (2 g, 17.07 mmol) and KOH (2.395 g, 42.7 mmol) in DMF (30 mL) and stirred at rt for one hour. The reaction mixture was poured into ice and water (400 mL) containing ammonia (0.5%) and sodium metabisulfite (0.1% aqueous solution). The resulting precipitate was filtered and washed with water to give the title compound **16b** (3.2 g, 77%) as a crystalline solid which was used without further purification. Warning: strong unpleasant odour associated with this compound (similar to that of skatole). ¹H NMR (400 MHz, CDCl₃) δ 7.18 - 7.24 (m, 2H), 7.30 (d, *J* = 2.5 Hz, 1H), 7.37 (d, *J* = 7.9, 1H), 7.47 (d, *J* = 7.7, 1H), 8.34 (bs, 1H).

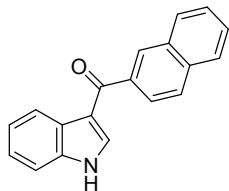
1*H*-indol-3-ylphenylmethanone¹⁹ (**17**)



Following General Procedure C: Chamber A: Cycloadduct **5b** (0.656 g, 1.500 mmol) was added, followed by 1,4-dioxane (4 mL). Chamber B: 3-iodo-1*H*-indole (0.122 g, 0.5 mmol), phenylboronic acid (0.073 g, 0.600 mmol), K₂CO₃ (0.207 g, 1.500 mmol) and Pd₂(dba)₃ (9.16 mg, 10.00 μmol) were added, followed by anisole (4 mL). The system was flushed with argon then Et₃N (0.244 mL, 1.750 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to sit for 30 min to release CO before being heated to 80 °C for 25 h. The reaction mixtures were cooled to rt and the solvent in Chamber B concentrated *in vacuo*. The crude product was purified by silica column chromatography (PE: EtOAc 9:1 - 1:1) to afford the title compound **17** (55.4 mg, 50%) ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.22 - 7.29 (m, 2H), 7.51 - 7.57 (m, 3H), 7.59 - 7.64 (m, 1H), 7.79 (d, *J* = 6.8 Hz, 2H), 7.93 (s, 1H), 8.26 (d, *J* = 6.9 Hz, 1H), 12.06 (s, 1H); ¹³C NMR (101 MHz, DMSO) δ 112.2, 115.0, 121.4,

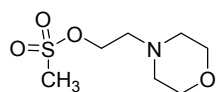
121.9, 123.1, 126.2, 128.36, 128.38, 131.0, 135.8, 136.7, 140.5, 189.9; ν_{\max} (cm⁻¹) 3142 (N-H), 2922 (C-H), 1596 (C=O), 1427.

(1*H*-indol-3-yl)(naphthalen-2-yl)methanone (18)



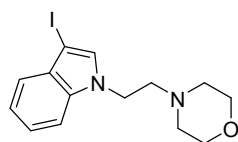
Following General Procedure C: Cycloadduct **5b** (656 mg, 1.5 mmol) was added, followed by 1,4-dioxane (4 mL). In Chamber B: 3-iodo-1*H*-indole (122 mg, 0.50 mmol), 2-naphthylboronic acid (103 mg, 0.600 mmol), K₂CO₃ (207 mg, 1.50 mmol) and Pd₂(dba)₃ (9.16 mg, 10.00 μmol) were added, followed by anisole (4 mL). The system was flushed with argon then Et₃N (0.244 mL, 1.750 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to sit for 30 min to release CO before being heated to 80 °C for 25 h. The reaction mixtures were cooled to rt and the solvent in Chamber B concentrated *in vacuo*. The crude product was purified by silica column chromatography (PE: EtOAc 9:1 - 1:1) to afford the title compound **18** (59.9 mg, 44%). ¹H NMR (400 MHz, CDCl₃) δ 7.38 - 7.33 (m, 2H), 7.50 - 7.46 (m, 1H), 7.63 - 7.54 (m, 2H), 7.77 (d, *J* = 3.0 Hz, 1H), 7.98 - 7.90 (m, 4H), 8.34 (s, 1H), 8.48 - 8.41 (m, 1H), 8.62 (s, 1H); ¹³C NMR (101 MHz, DMSO) δ 112.3, 115.2, 121.5, 121.9, 123.2, 125.3, 126.3, 126.7, 127.64, 127.64, 128.1, 129.2, 132.2, 134.2, 136.0, 136.7, 137.7, 189.90; ν_{\max} (cm⁻¹) 3147 (N-H stretch), 1596 (C=O); HRMS-ESI *m/z* [M+Na]⁺ calc. for C₁₉H₁₃NONa⁺: 294.0889, found: 294.0868.

2-morpholinoethyl methanesulfonate (19)



A solution of 2-morpholinoethanol (1 mL, 8.26 mmol) and Et₃N (3.45 mL, 24.77 mmol) in THF (50 mL) was cooled to 0 °C. Methanesulfonyl chloride (0.959 mL, 12.38 mmol) was added dropwise over 5 min to the mixture which was then stirred at 0 °C for 10 min. The ice bath was then removed and the reaction mixture stirred at rt for an additional 2 h. The reaction mixture was filtered through Celite® 545 with THF and concentrated under reduced pressure. The crude 2-morpholinoethyl methanesulfonate **19** was used without further purification. ¹H NMR (400 MHz, CDCl₃) *inter alia* δ 2.55 (t, *J* = 4.6 Hz, 4H), 2.74 (t, *J* = 5.5 Hz, 2H), 3.09 (s, 3H), 3.74 - 3.70 (m, 4H), 4.35 (t, *J* = 5.5 Hz, 2H).

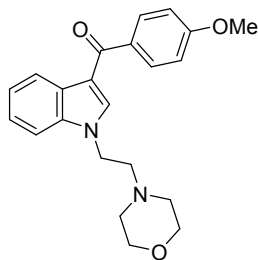
4-(2-(3-iodo-1*H*-indol-1-yl)ethyl)morpholine²⁰ (20)



To 3-iodo-1*H*-indole (0.610 g, 2.510 mmol) in DMF (30 mL) at 0 °C was added NaH (60% dispersion in mineral oil, 0.502 g, 12.55 mmol) portion wise over 5 min. The mixture was stirred for 10 min at 0 °C and then was allowed to warm to ambient temperature. The mixture was stirred for 1 h at ambient temperature and then was cooled to 0 °C. The 2-morpholinoethyl methanesulfonate (1.0 g, 4.78 mmol) in 2 mL of THF was added rapidly *via* cannula. After the addition was complete, the ice bath was removed and the mixture was stirred for 4 h at ambient temperature. The mixture was then cooled to 0 °C, was quenched with 30 mL of saturated, aqueous NH₄Cl and was diluted with 30 mL of EtOAc. The layers were separated, and the aqueous layer was extracted EtOAc (3 x 15 mL). The combined organic extracts were washed with water (4 x 10 mL) and brine (4 x 10 mL) and then were dried over anhydrous MgSO₄,

filtered, concentrated under reduced pressure, and purified by silica column chromatography (CHCl₃ : EtOAc 1:0 - 1:1) to afford the title compound **20** (808.4 mg, 90%) as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 2.55 - 2.45 (m, 4H), 2.74 (t, *J* = 6.8 Hz, 2H), 3.77 - 3.67 (m, 4H), 4.25 (t, *J* = 6.8 Hz, 2H), 7.20 (ddd, *J* = 8.0, 6.9, 1.2 Hz, 1H), 7.24 - 7.30 (m, 2H), 7.33 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.45 (dt, *J* = 7.8, 1.0 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 44.3, 54.0, 58.3, 67.0, 109.5, 120.5, 121.5, 122.8, 130.6, 132.1, 136.2; *v*_{max} (cm⁻¹) 1141 (C-O-C), 726 (C-I); HRMS-ESI *m/z* [M+H]⁺ calc. for C₁₄H₁₈N₂OI⁺: 357.0458, found: 357.0458.

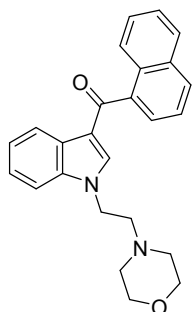
(4-methoxyphenyl)(1-(2-morpholinoethyl)-1*H*-indol-3-yl)methanone (**21**)



Following General Procedure C: Chamber A: Cycloadduct **5b** (552 mg, 1.263 mmol) was added, followed by 1,4-dioxane (4 mL). In Chamber B: 4-(2-(3-iodo-1*H*-indol-1-yl)ethyl)morpholine (150 mg, 0.421 mmol) in 0.2 mL anisole, (4-methoxyphenyl)boronic acid (77 mg, 0.505 mmol), K₂CO₃ (175 mg, 1.263 mmol) and Pd₂(dba)₃ (7.71 mg, 8.42 μmol) were added, followed by anisole (3.8 mL). The system was flushed with argon then Et₃N (0.205 mL, 1.474 mmol)

was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to stir for 30 min to release CO before being heated to 80 °C for 25 h. The reaction mixtures were cooled to rt and the solvent in Chamber B concentrated *in vacuo*. The crude product was purified by silica column chromatography (CHCl₃: EtOAc 2:1 - 1:2) to afford the title compound **21** (65.4 mg, 43%) as a pale yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 2.51 (t, *J* = 4.4 Hz, 4H), 2.79 (d, *J* = 6.3 Hz, 2H), 3.71 (t, *J* = 4.8 Hz, 4H), 3.90 (s, 3H), 4.27 (d, *J* = 6.6 Hz, 2H), 6.99 (d, *J* = 8.7 Hz, 2H), 7.29 - 7.37 (m, 2H), 7.40 (m, 1H), 7.70 (s, 1H), 7.85 (d, *J* = 8.7 Hz, 2H), 8.35 - 8.43 (m, 1H); ¹³C NMR (101 MHz, CDCl₃) δ 44.2, 53.8, 55.6, 57.8, 66.9, 109.6, 113.6, 115.9, 122.6, 122.9, 123.6, 127.5, 131.1, 133.5, 136.8, 137.0, 162.4, 189.9; *v*_{max} (cm⁻¹) 2850 (C-H), 1598 (C=O), 1252 (C-N), 1114 (C-O-C); HRMS-ESI *m/z* [M+H]⁺ calc. for C₂₂H₂₅N₂O₃⁺: 365.1860; found: 365.1837.

(1-(2-morpholinoethyl)-1*H*-indol-3-yl)(naphthalen-1-yl)methanone²¹ (**22**)

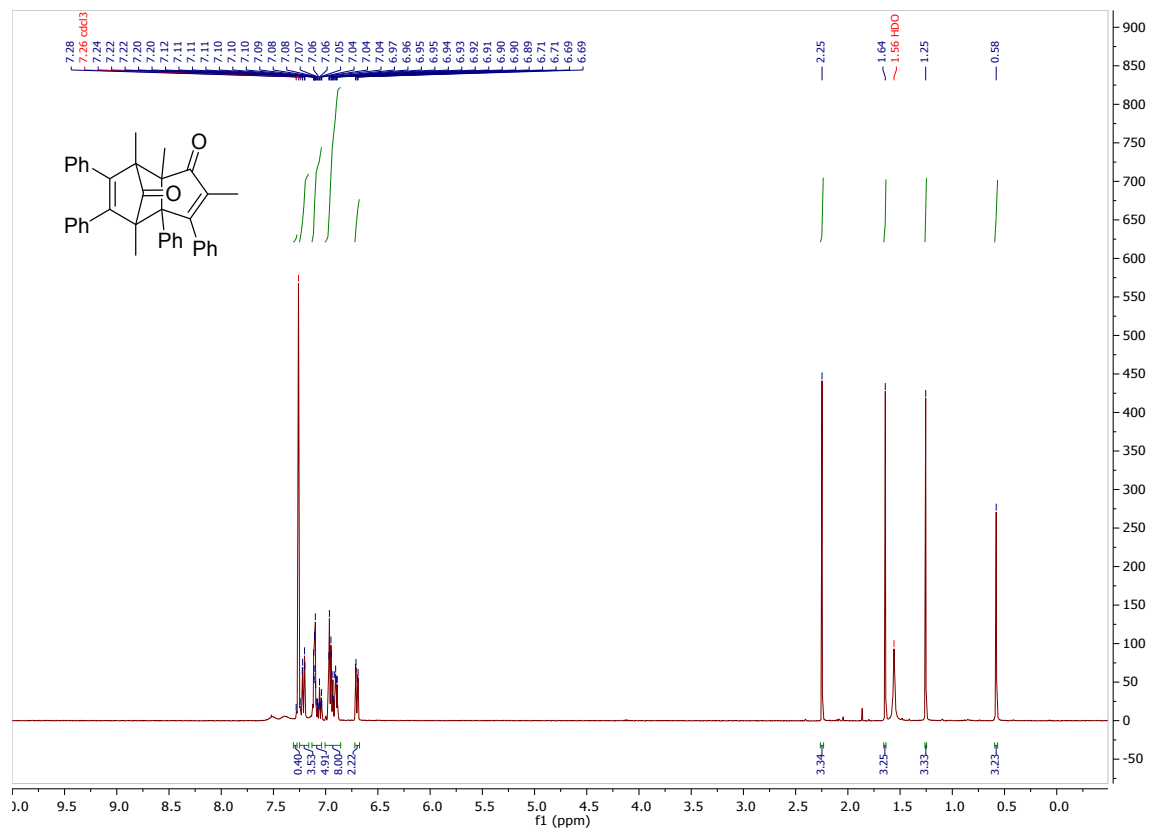


Following General Procedure C: Chamber A: Cycloadduct **5b** (552 mg, 1.263 mmol) was added, followed by 1,4-dioxane (4 mL). In Chamber B: 4-(2-(3-iodo-1*H*-indol-1-yl)ethyl)morpholine (150 mg, 0.421 mmol), naphthalen-1-ylboronic acid (87 mg, 0.505 mmol), K₂CO₃ (175 mg, 1.263 mmol) and Pd₂(dba)₃ (7.71 mg, 8.42 μmol) were added, followed by anisole (4 mL). The system was flushed with argon then Et₃N (0.205 mL, 1.474 mmol) was added to Chamber A, the system was then sealed with screwcaps fitted with silicon seals. The system was allowed to stir for 30 min to

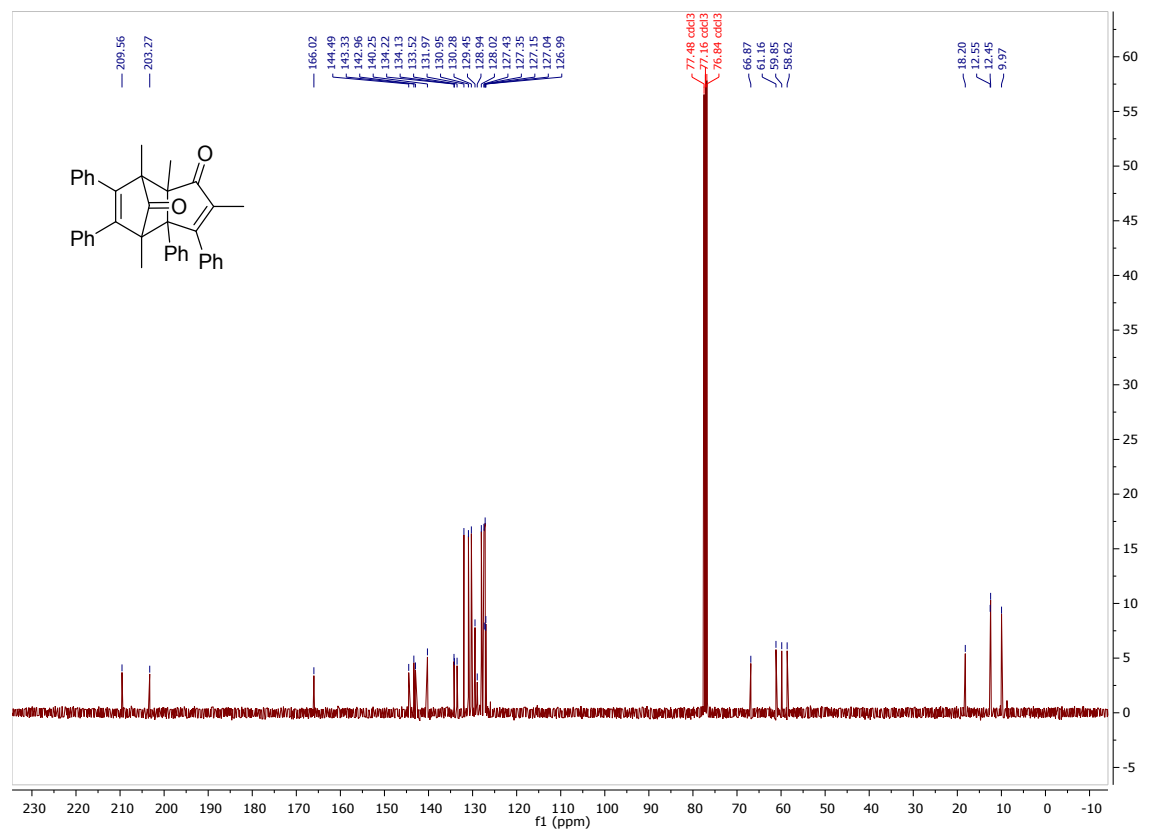
release CO before being heated to 80 °C for 30 h. The reaction mixtures were cooled to rt and the anisole in Chamber B concentrated *in vacuo*. The crude product was purified by silica column chromatography (CHCl₃: EtOAc 2:1 - 1:2) to afford the title compound **22** as a 3:1 mixture of product to the non-carbonylative Suzuki side product (101.5 mg, 63%). ¹H NMR (400 MHz, CDCl₃) δ 3.04 (s, 4H), 3.29 (t, *J* = 7.1 Hz, 2H), 3.90 (t, *J* = 4.7 Hz, 4H), 4.57 - 4.66 (m, 2H), 7.36 - 7.57 (m, 6H), 7.64 (d, *J* = 7.5 Hz, 1H), 7.91 (d, *J* = 7.5 Hz, 1H), 7.98 (d, *J* = 8.2 Hz, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 8.45 - 8.52 (m,

¹H), ¹³C NMR (101 MHz, CDCl₃) δ 41.5, 52.7, 56.1, 64.1, 109.5, 119.2, 123.5, 123.8, 124.7, 124.8, 125.8, 126.1, 126.5, 127.07, 127.11, 128.5, 130.6, 130.7, 133.9, 135.6, 137.3, 138.5, 192.3; ν_{max} (cm⁻¹) 1672 (C=O), 1196 (C-N stretch), 1133 (C-O-C); HRMS-ESI *m/z* [M+H]⁺ calc. for C₂₁H₂₅N₂O₂⁺:385.1911, found: 358.1882.

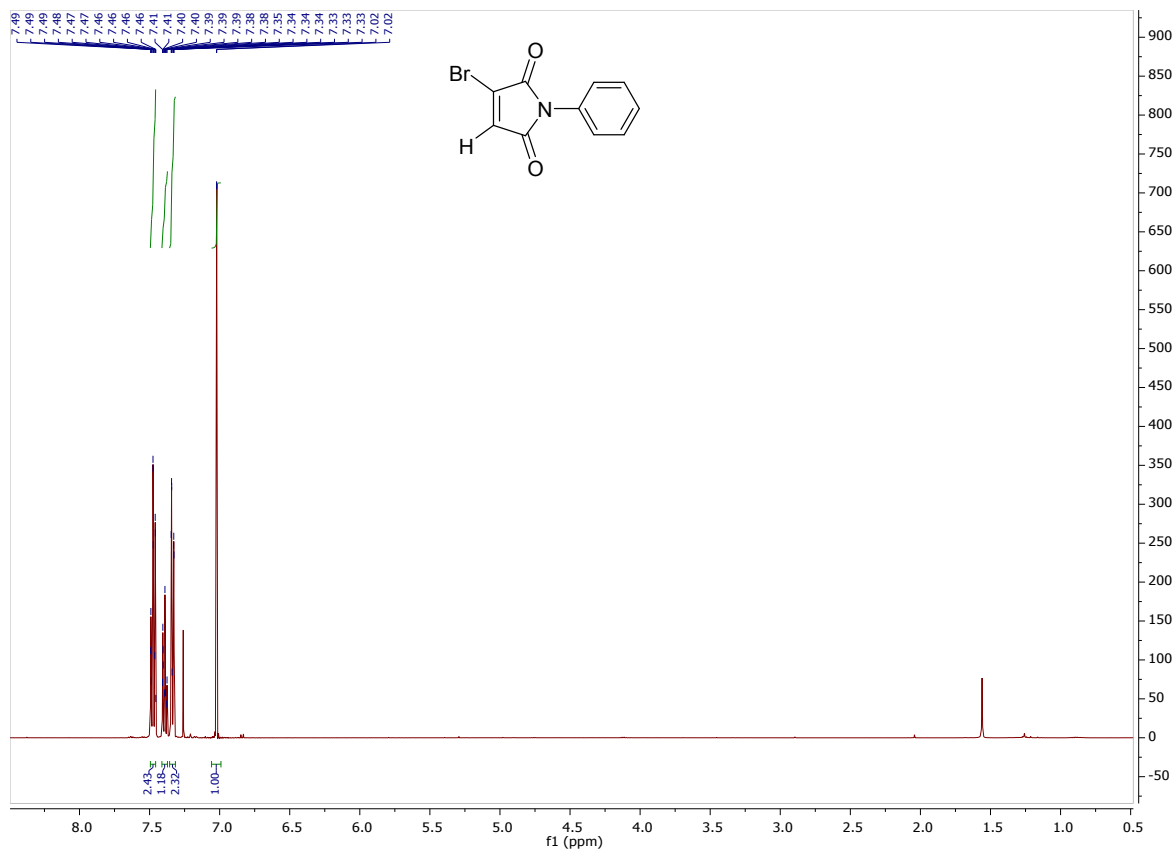
2,5-Dimethyl-3,4-diphenylcyclopentadien-1-one (diene dimer) (3) (400 MHz, CDCl₃)



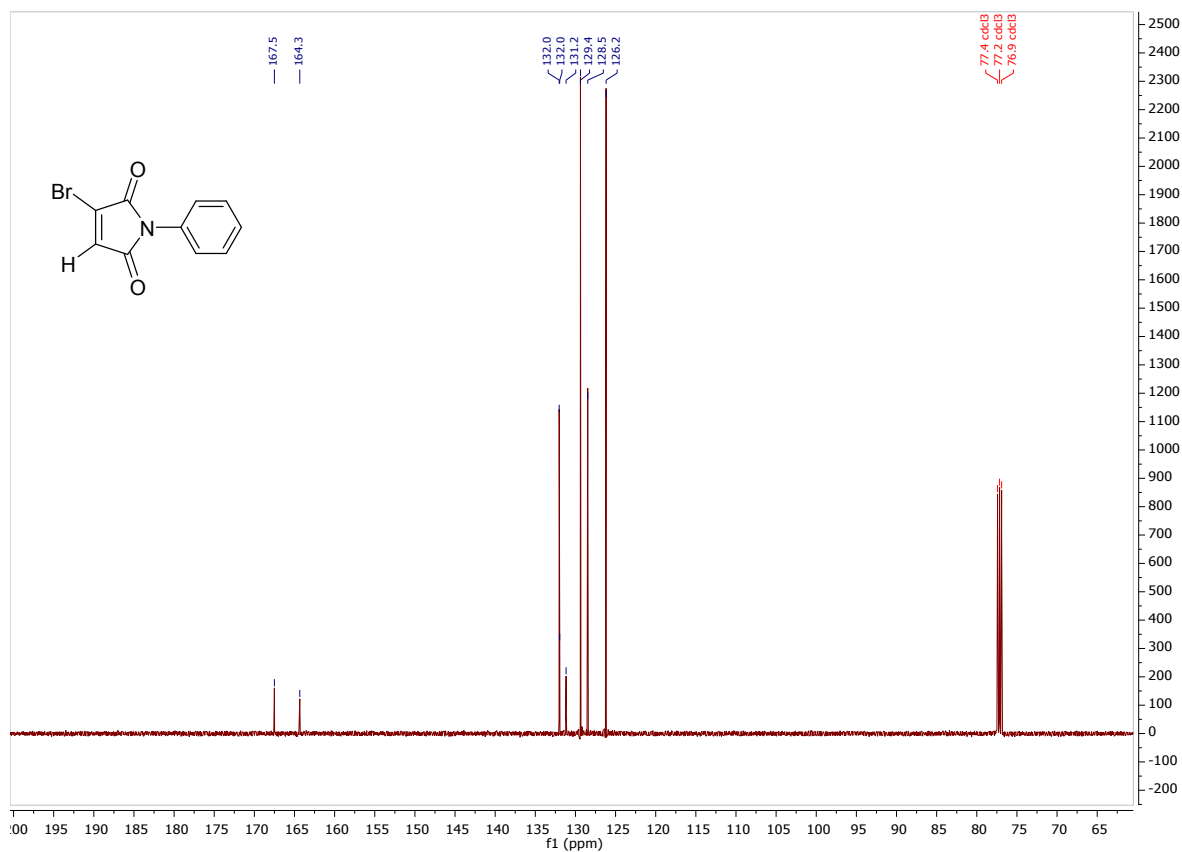
(100 MHz, CDCl₃)



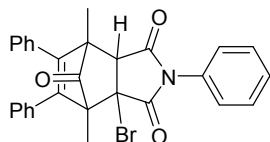
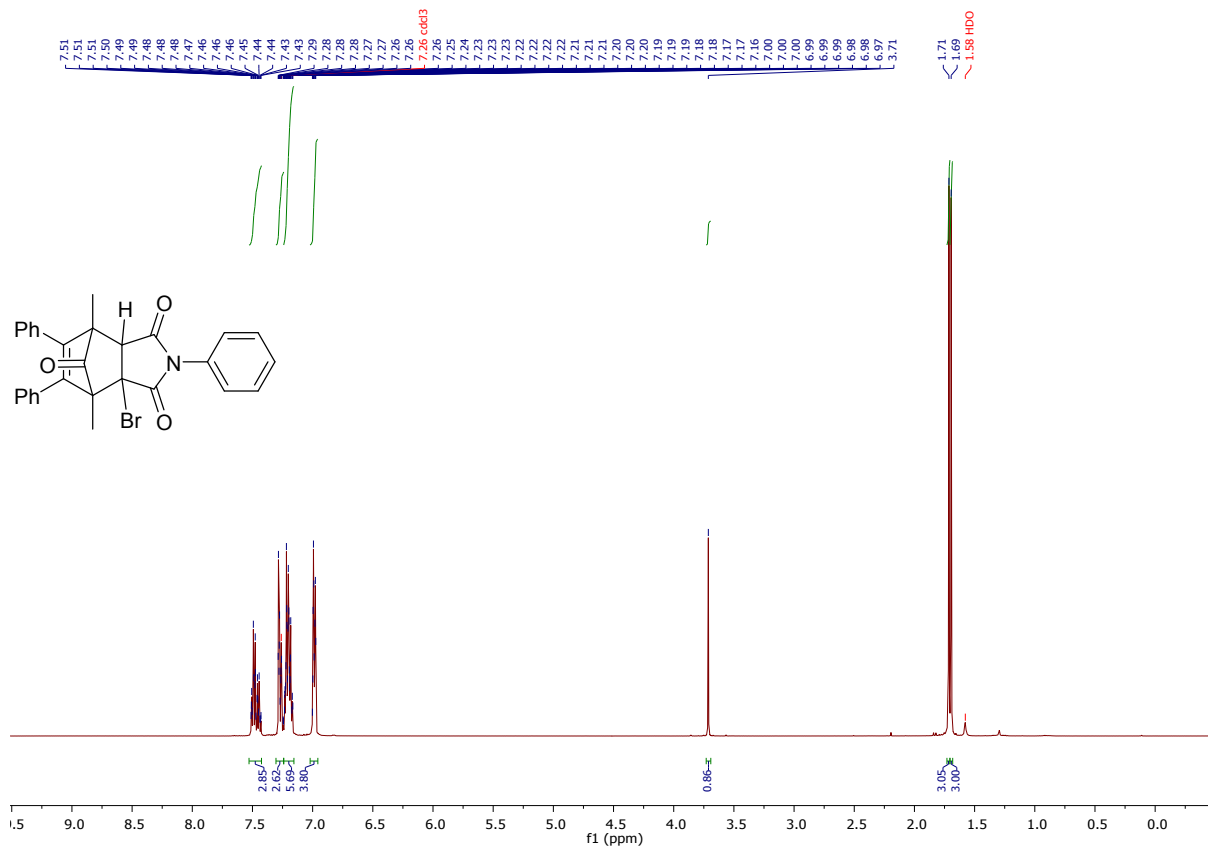
N-Phenyl-3-bromomaleimide (4a) (400 MHz, CDCl₃)



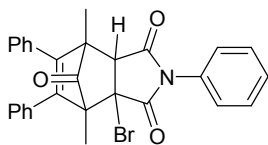
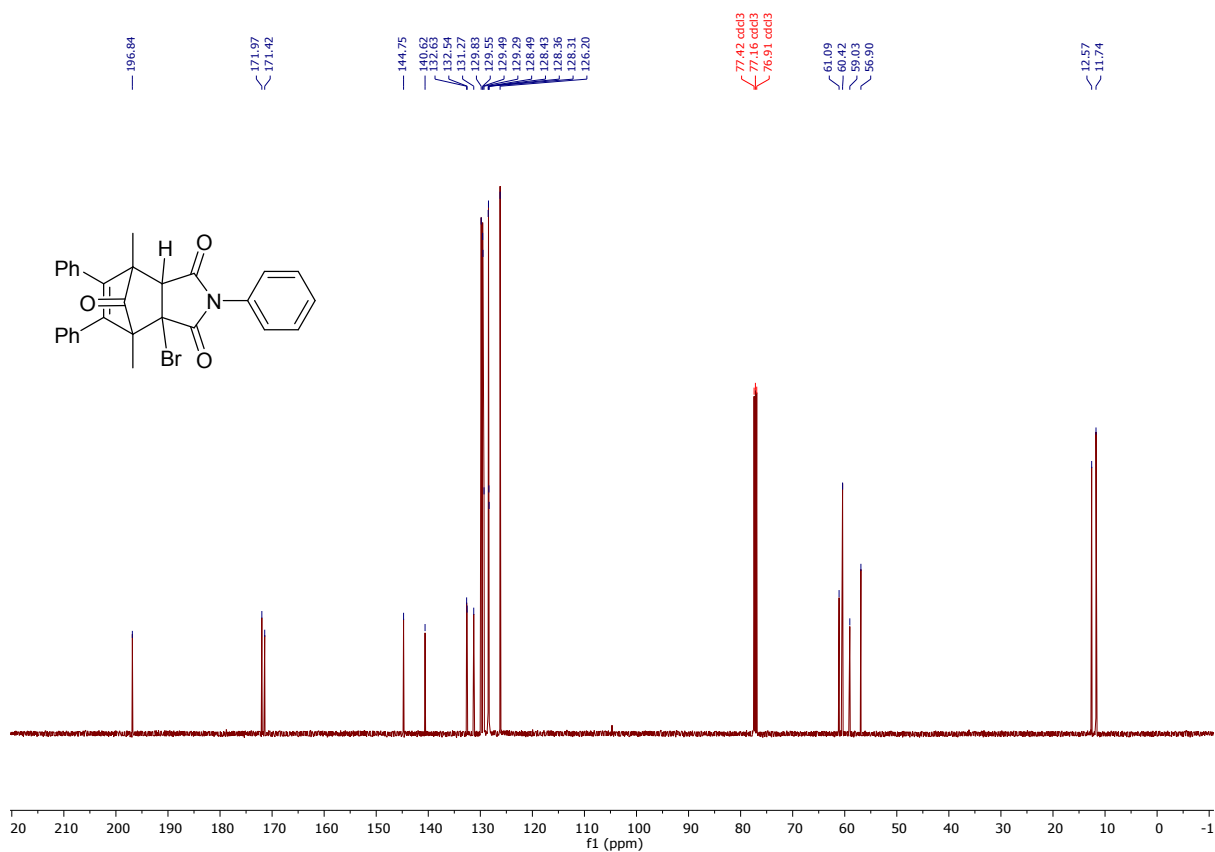
(100 MHz, CDCl₃)



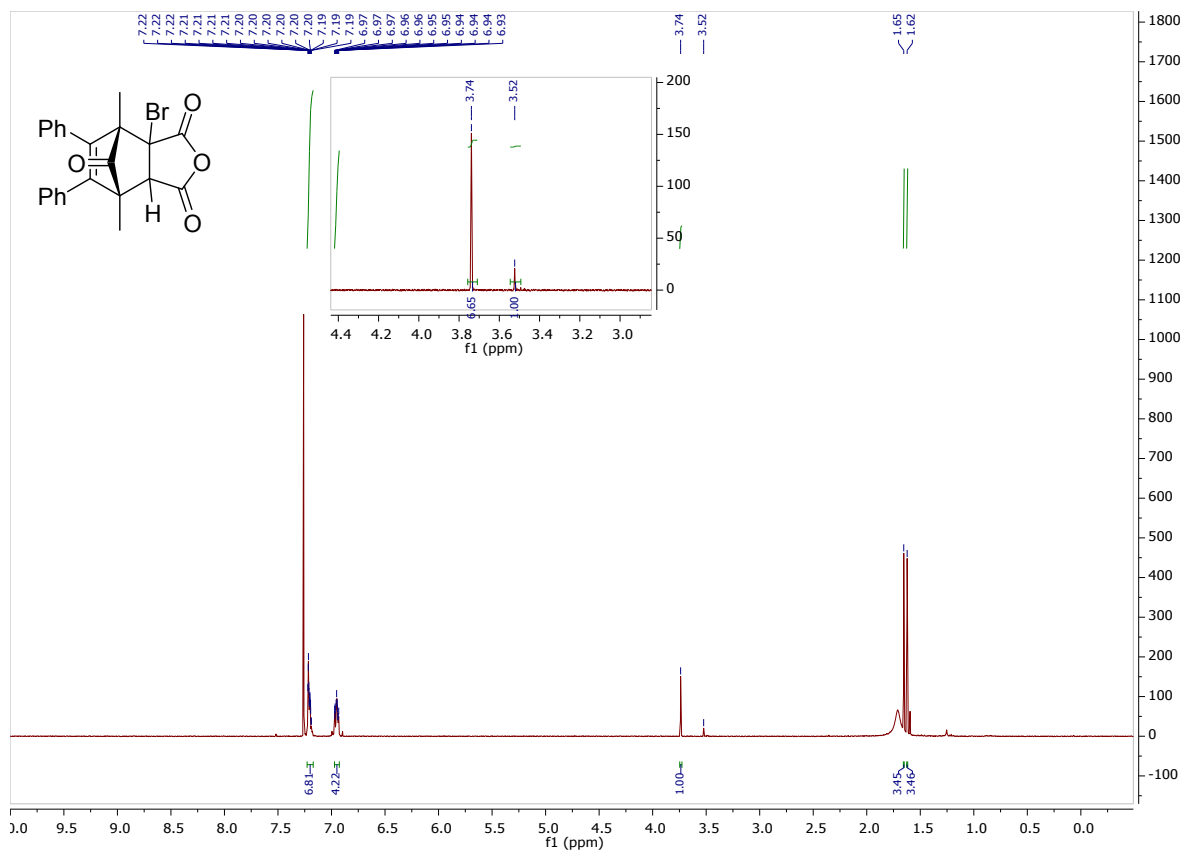
3a-Bromo-3a,4,7,7a-tetrahydro-4,7-dimethyl-2,5,6-triphenyl-4,7-methano-1H-isoindole-1,3,8(2H)-trione *endo* (5a) (500 MHz, CDCl₃)



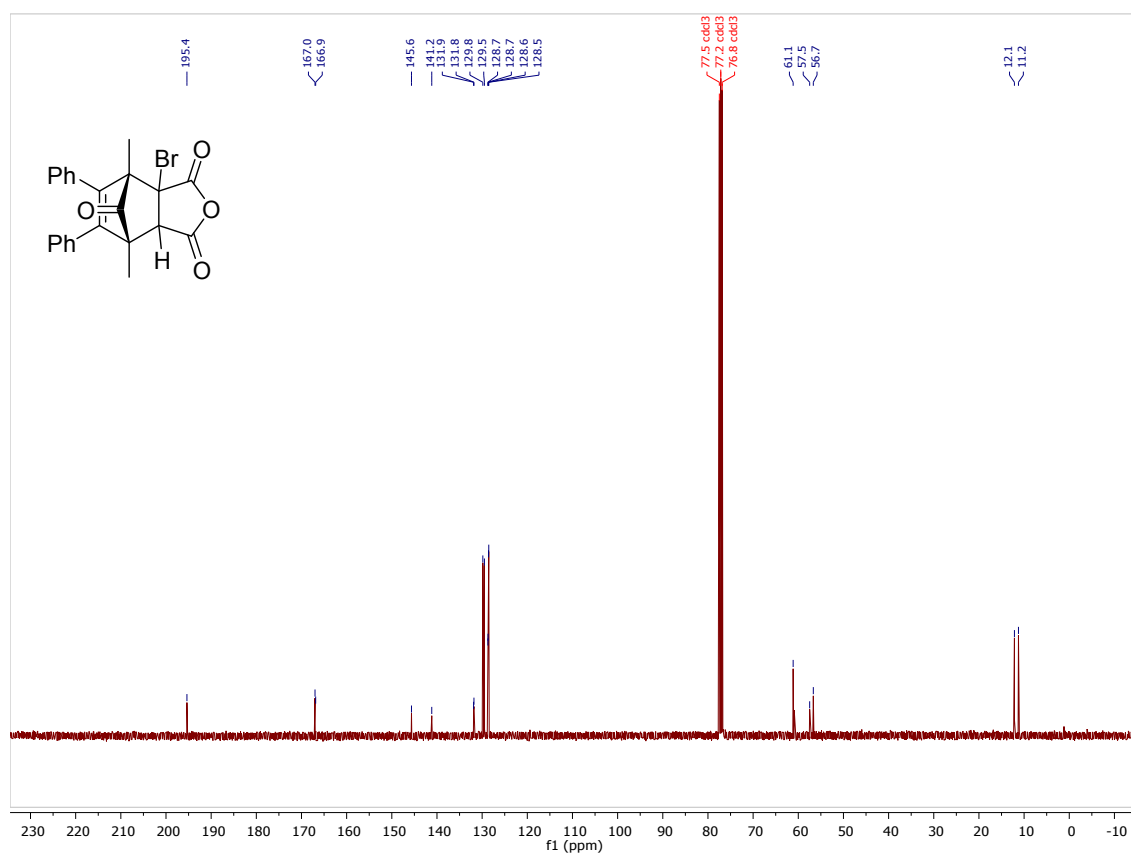
(125 MHz, CDCl₃)



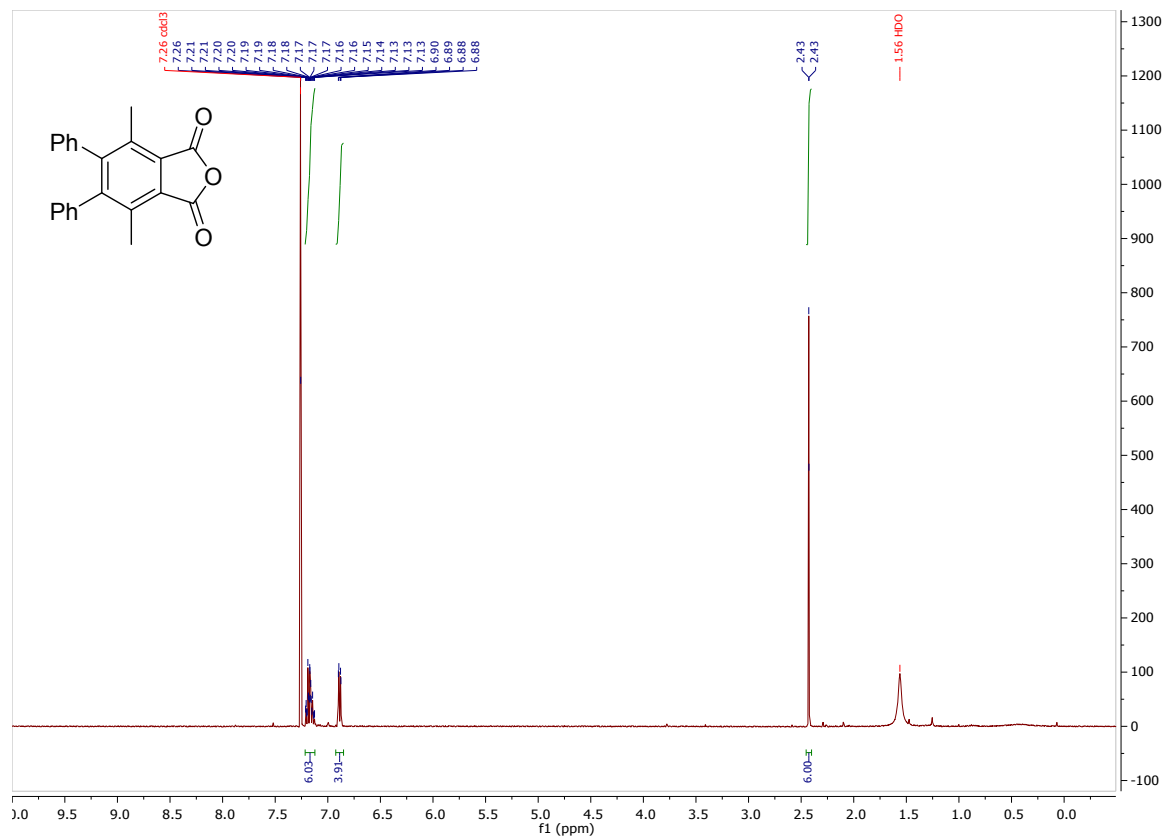
3a,4,7,7a-Tetrahydro-7a-bromo-4,7-dimethyl-5,6-diphenyl-4,7-methanoisobenzofuran-1,3,8-trione (5b) (400 MHz, CDCl₃)



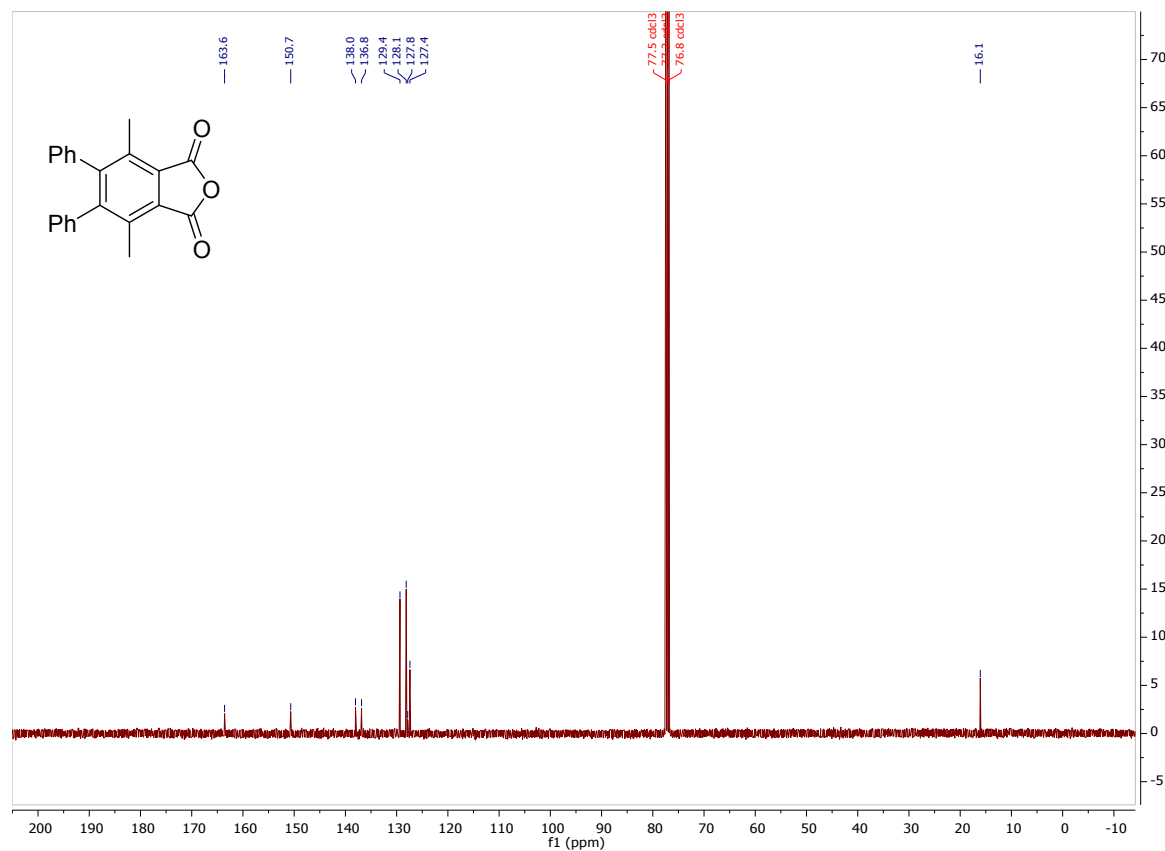
(100 MHz, CDCl₃)



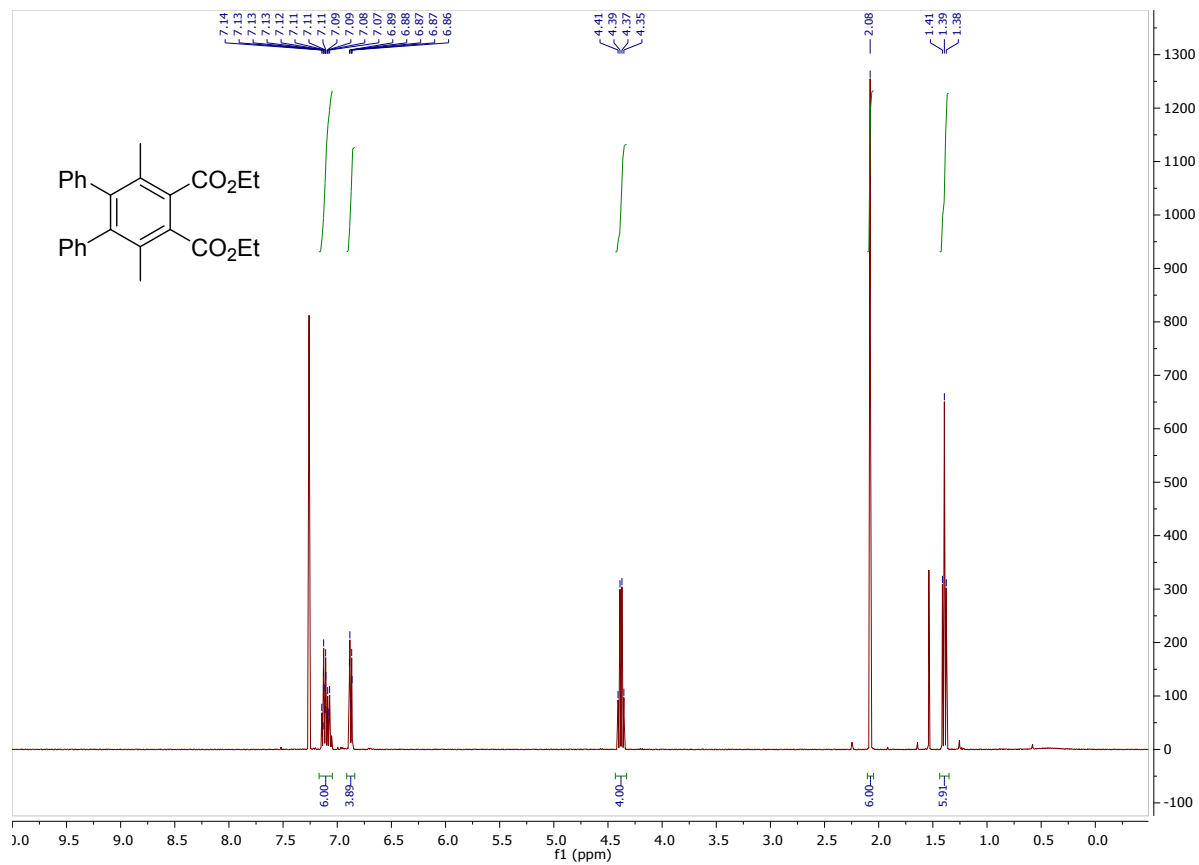
4,7-Dimethyl-5,6-diphenyl-1,3-isobenzofurandione (9) (400 MHz, CDCl₃)



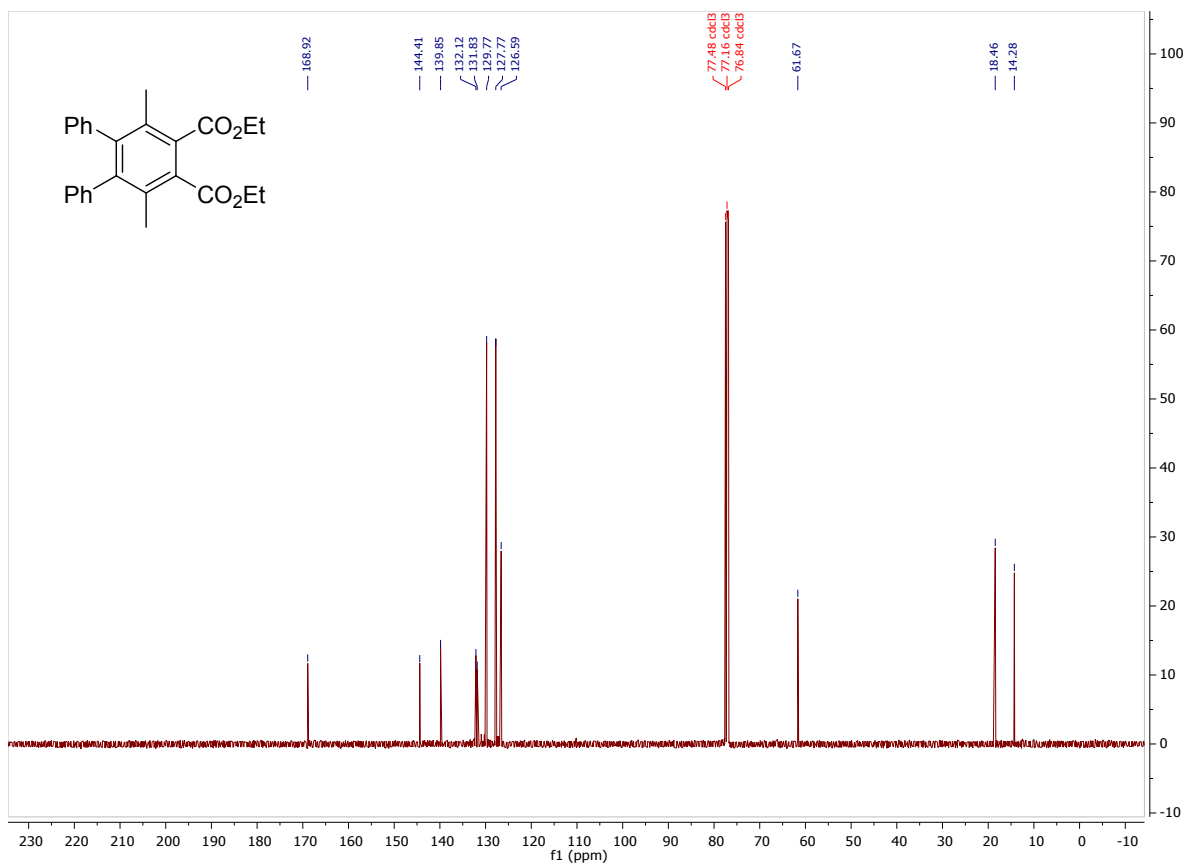
(100 MHz, CDCl₃)



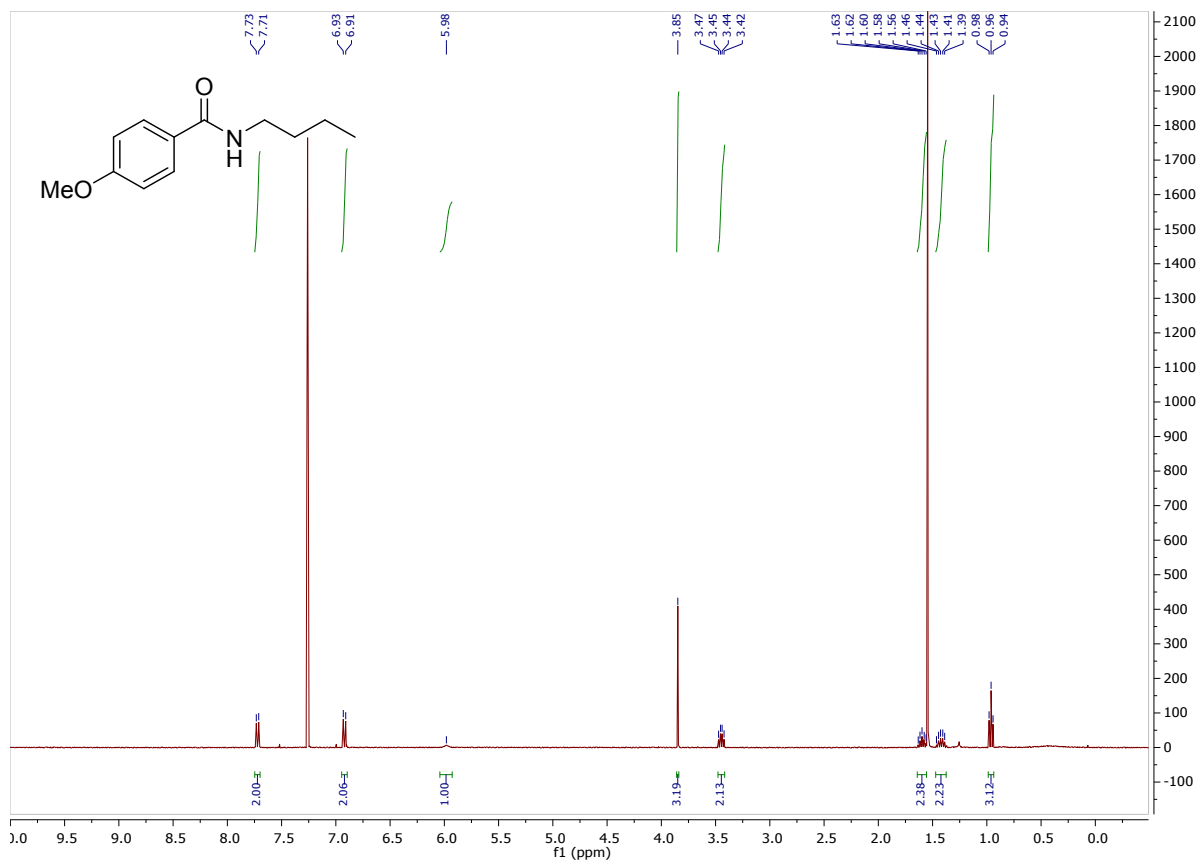
Diethyl 3,6-dimethyl-4,5-diphenylphthalate (12) (400 MHz, CDCl₃)



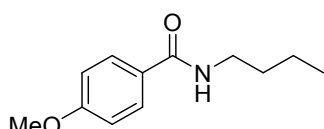
(100 MHz, CDCl₃)

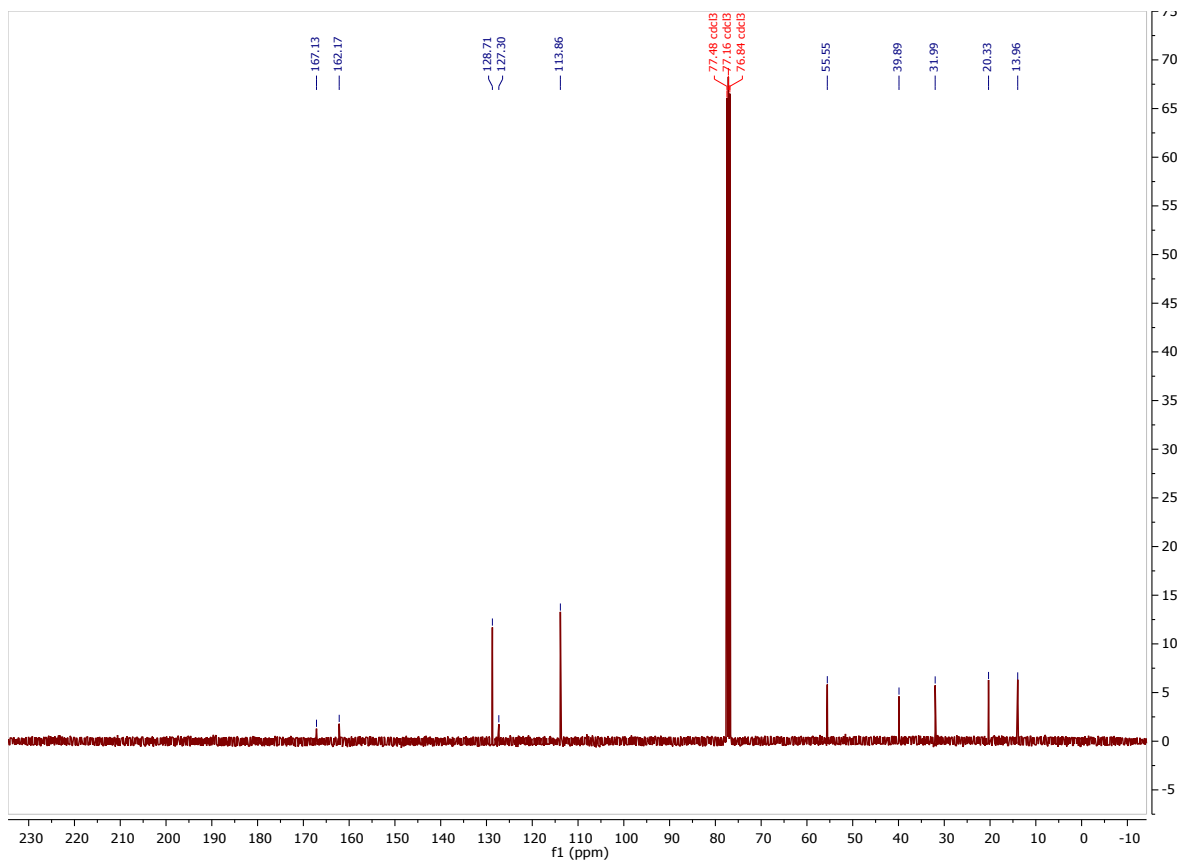


***N*-butyl-4-methoxybenzamide (8a)** (400 MHz, CDCl₃)

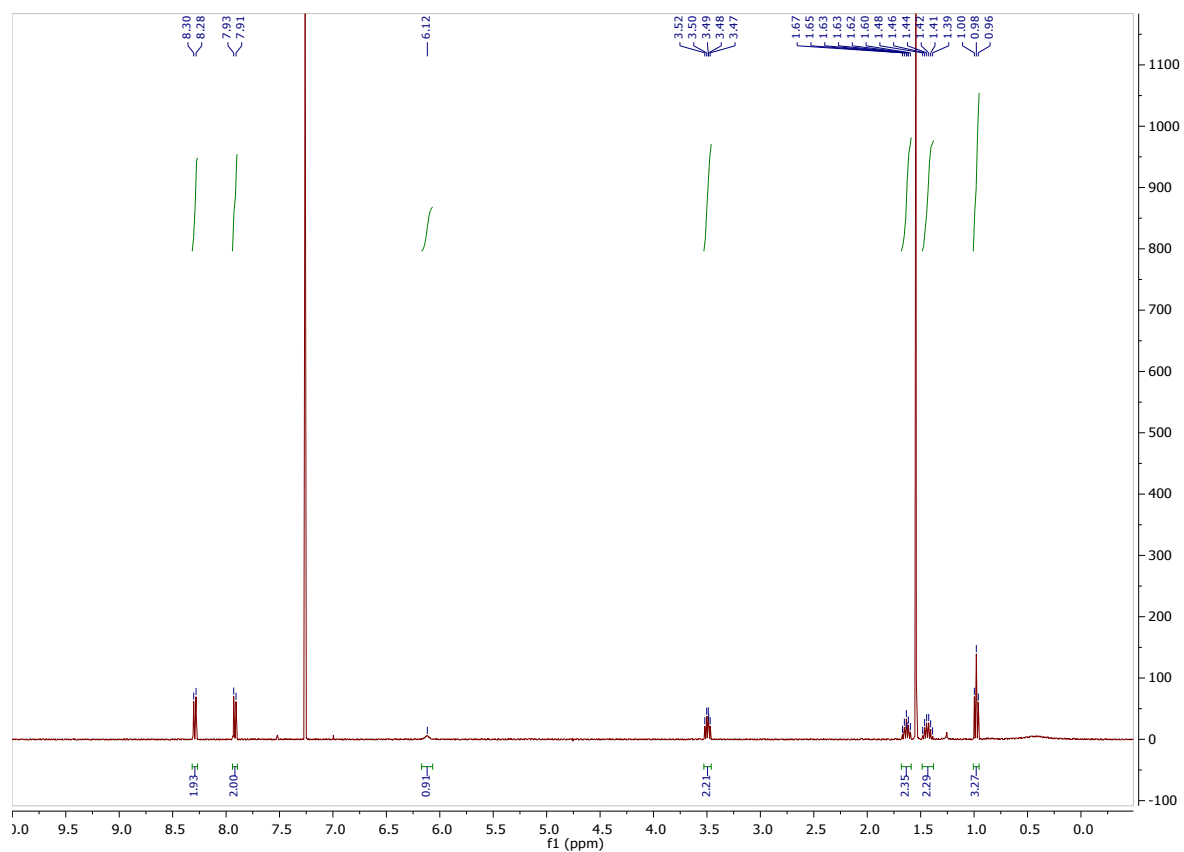


(100 MHz, CDCl₃)

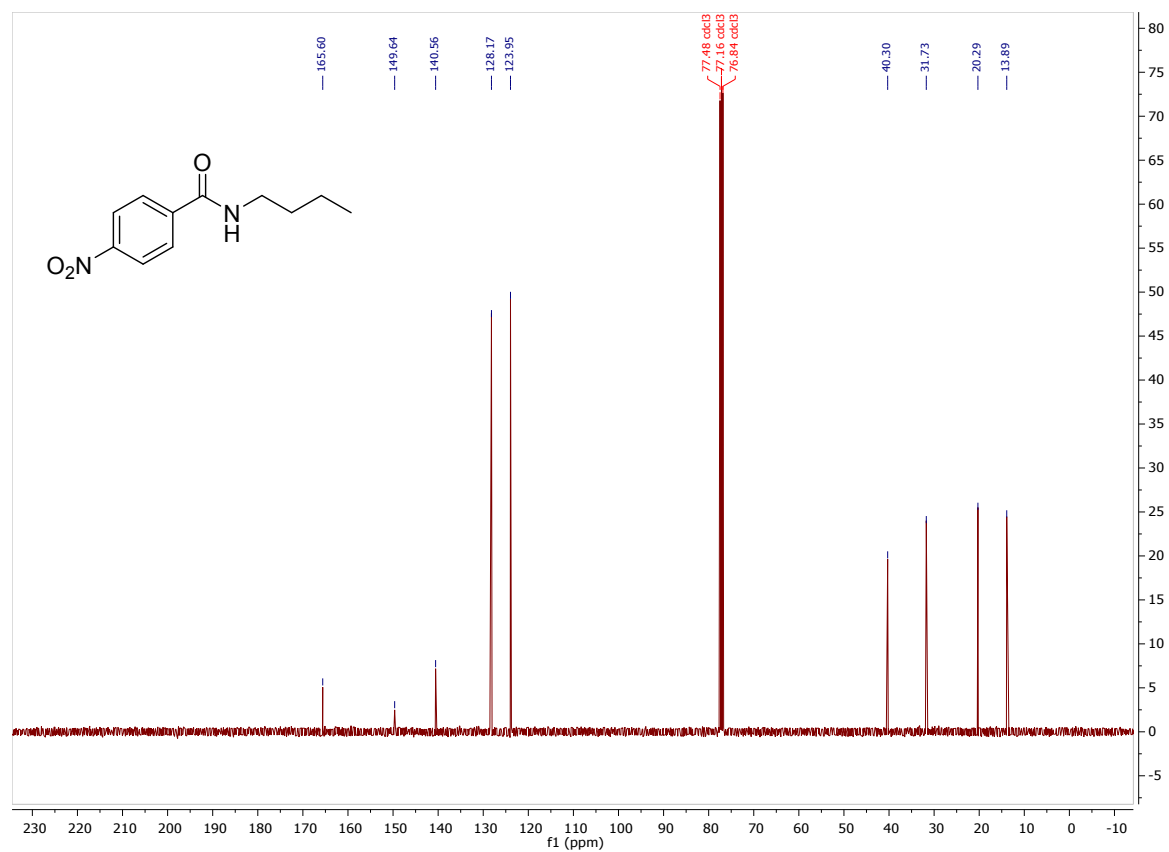




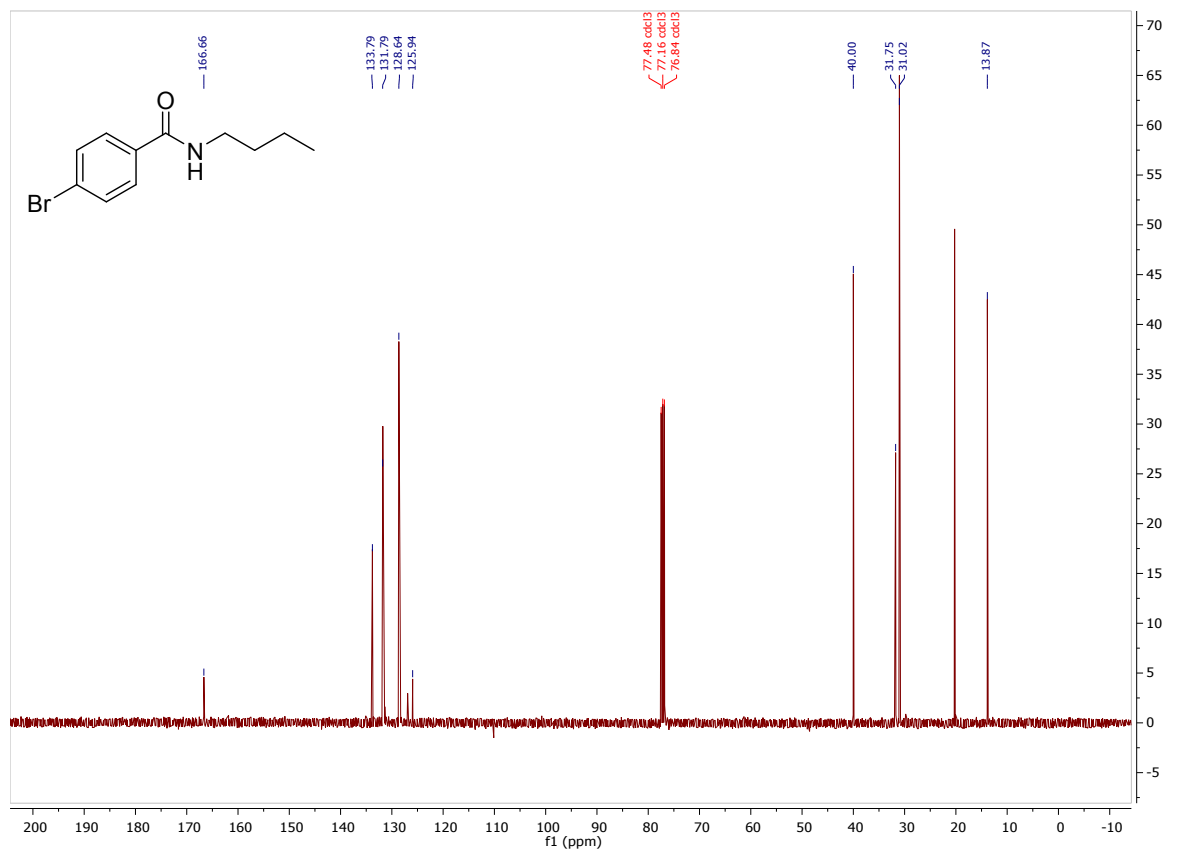
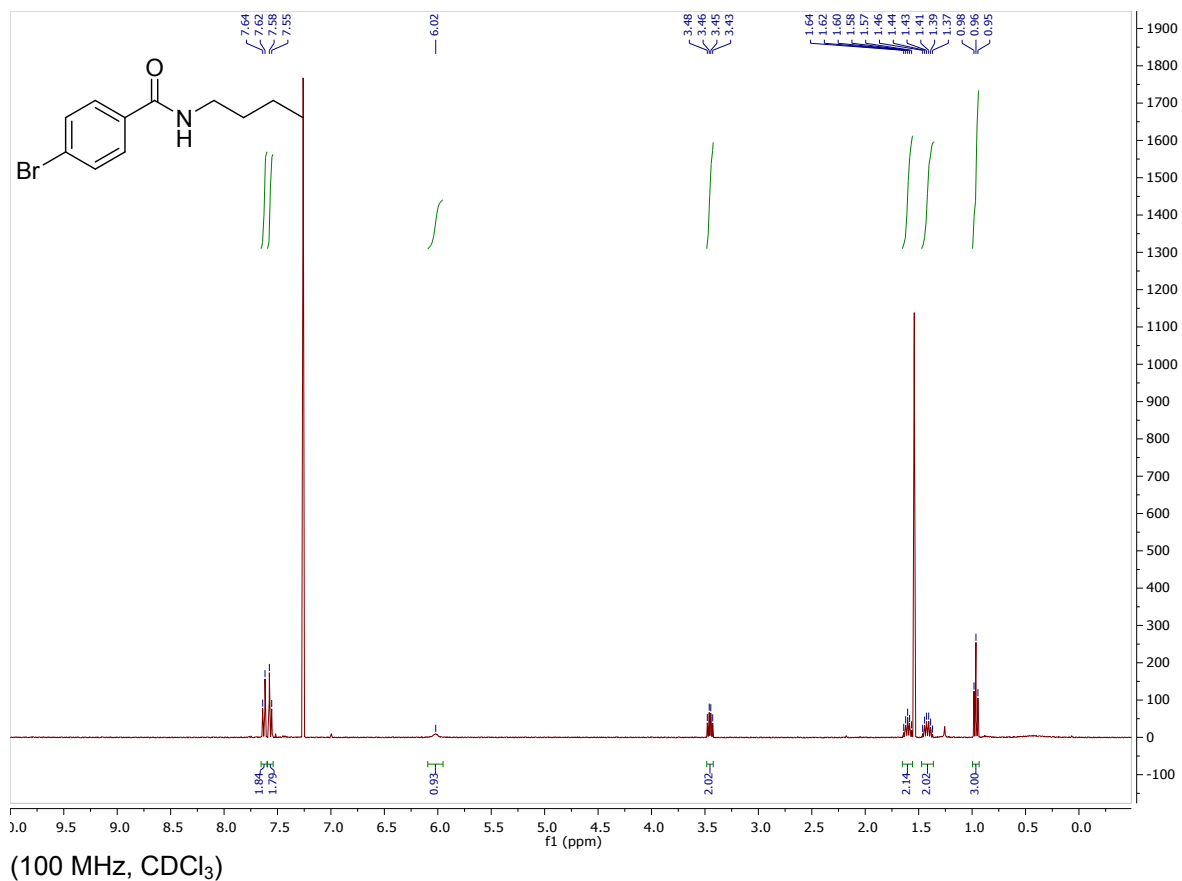
***N*-butyl-4-nitrobenzamide (8b)** (400 MHz, CDCl₃)



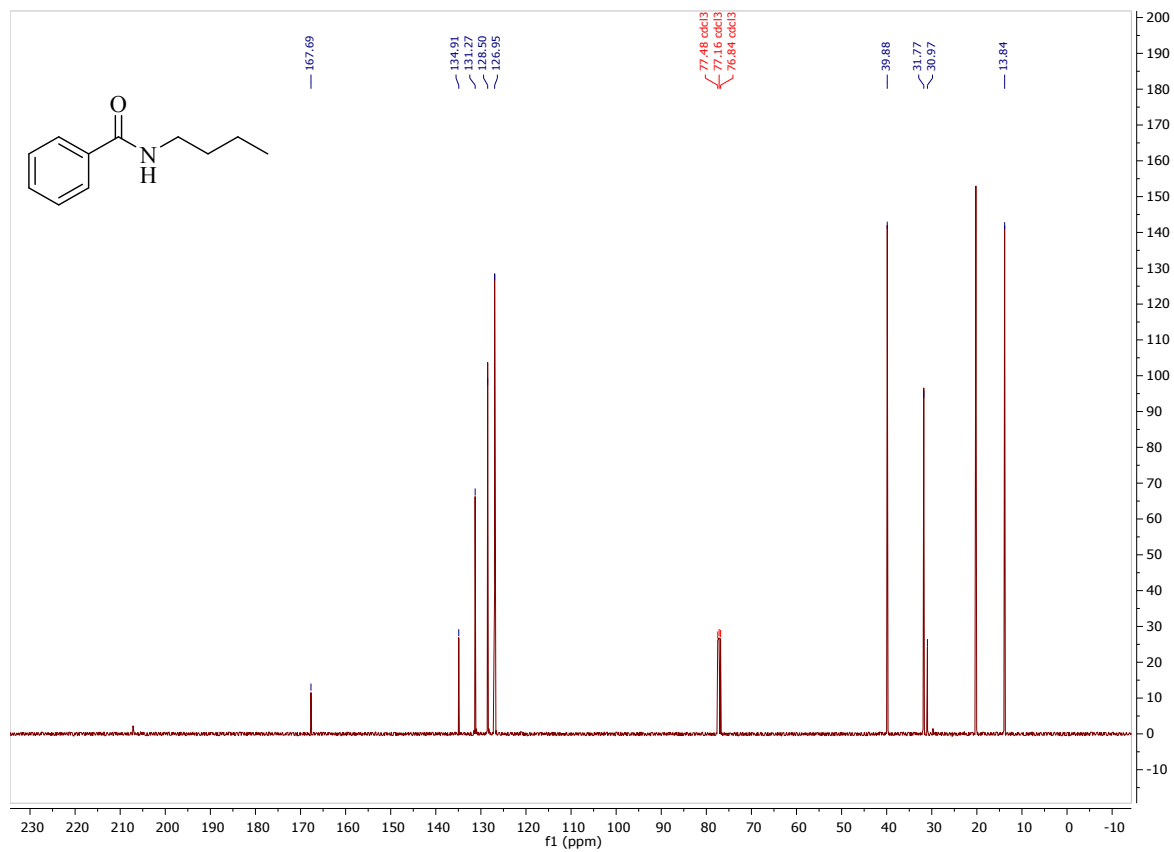
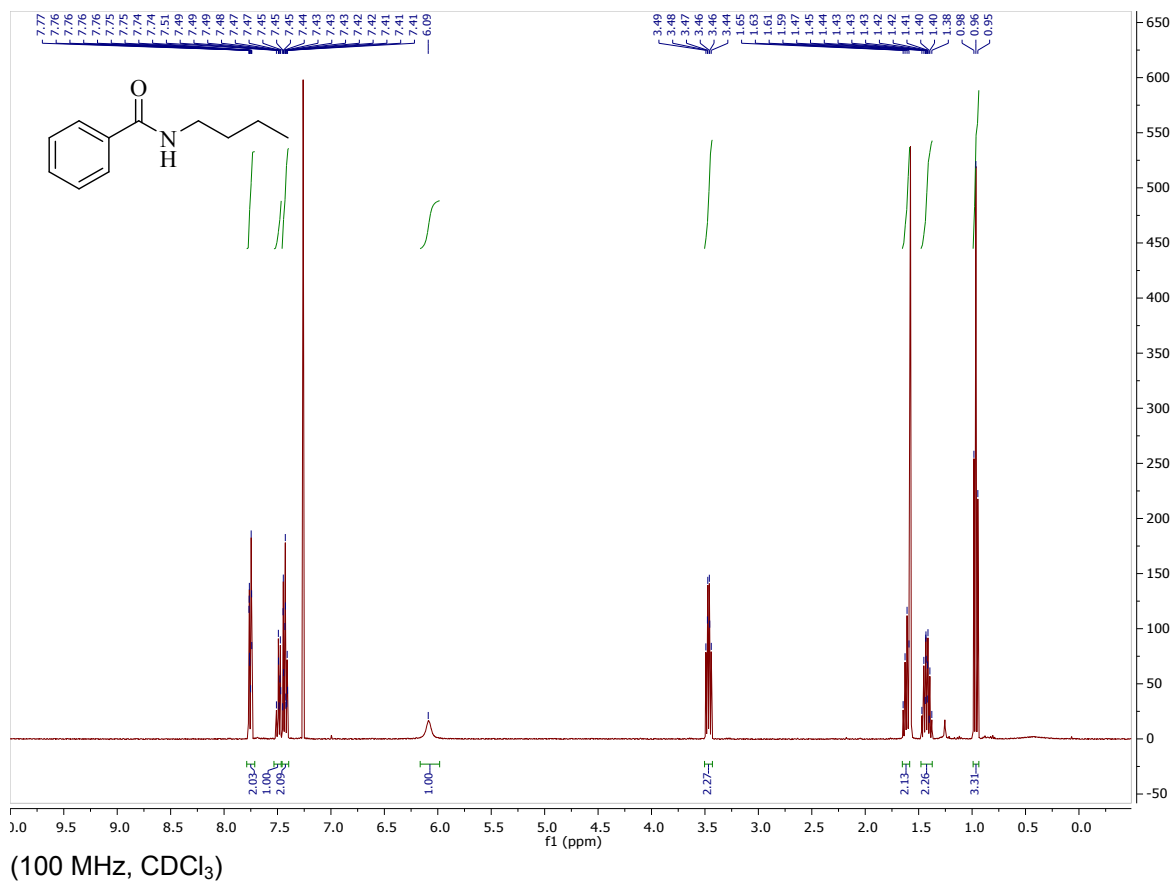
(100 MHz, CDCl₃)



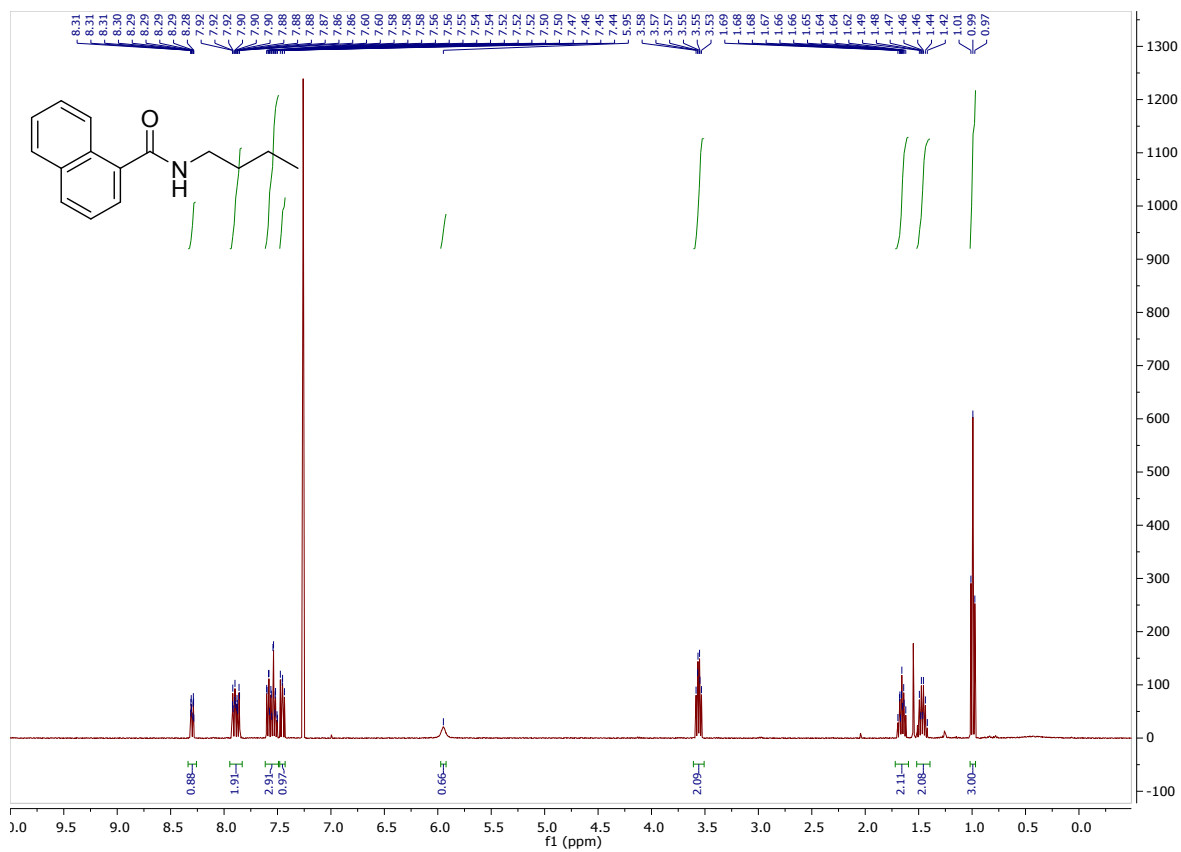
4-bromo-N-butylbenzamide (8c) (400 MHz, CDCl₃)



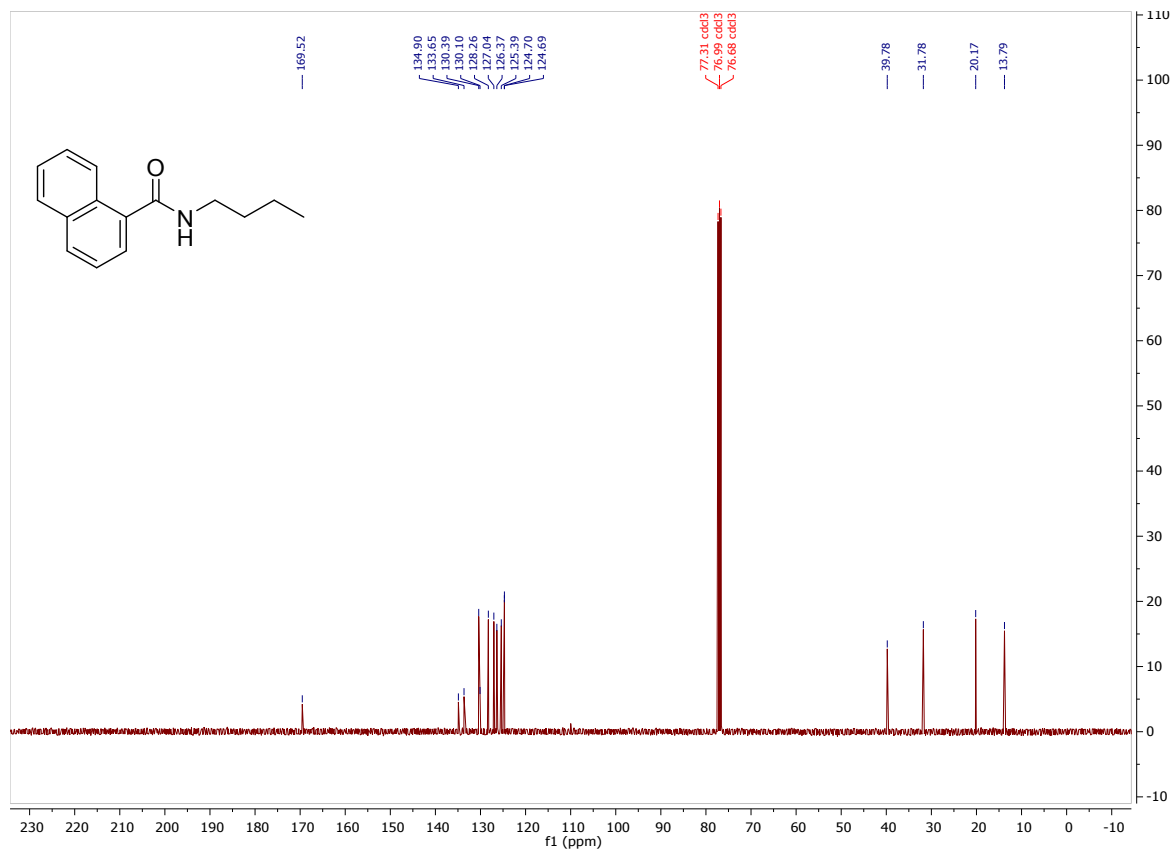
N-butylbenzamide (8d) (400 MHz, CDCl₃)



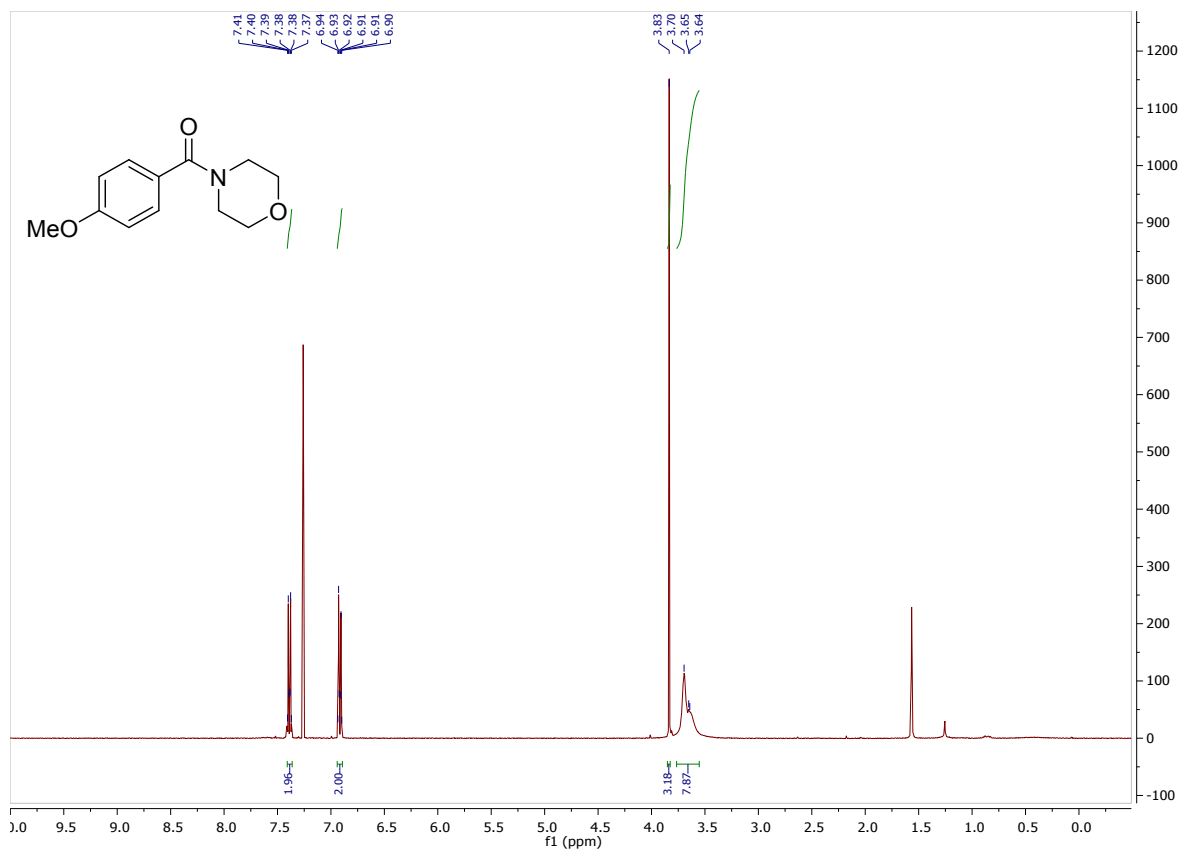
N-butyl-1-naphthamide (8e) (400 MHz, CDCl₃)



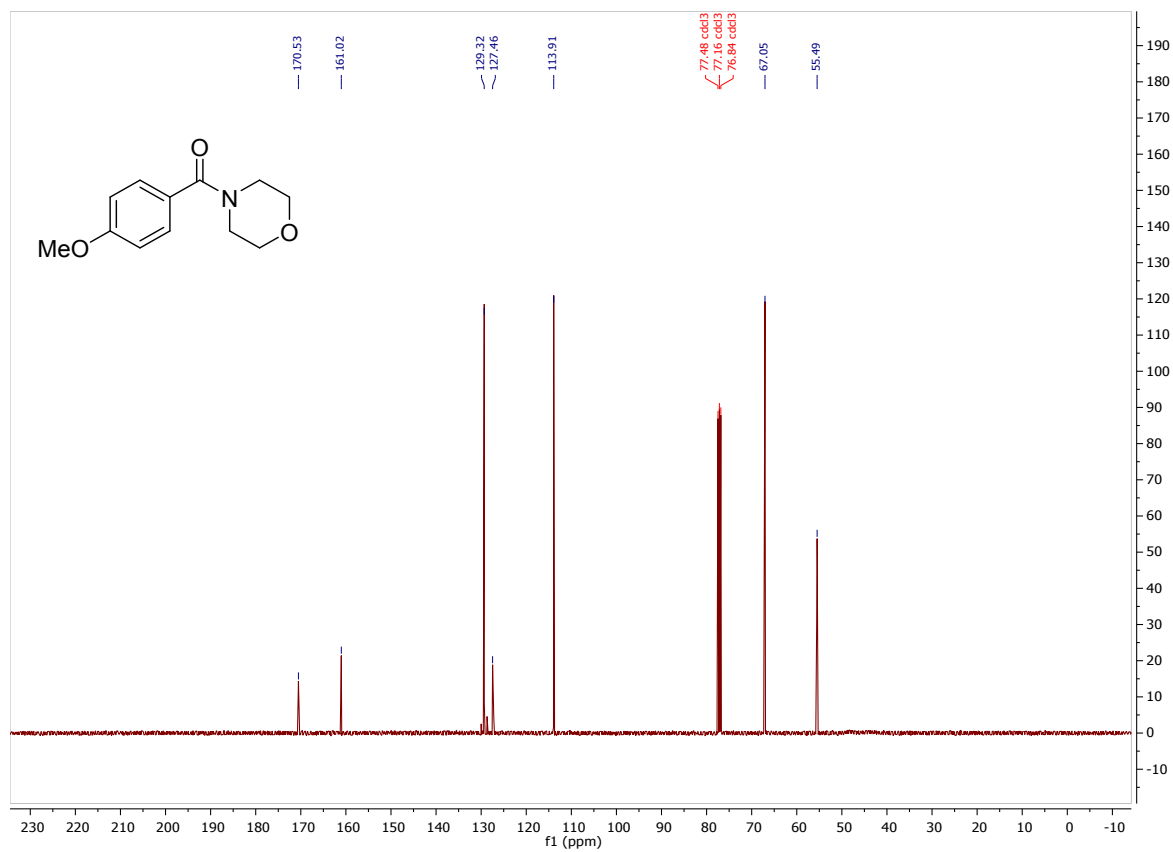
(100 MHz, CDCl₃)



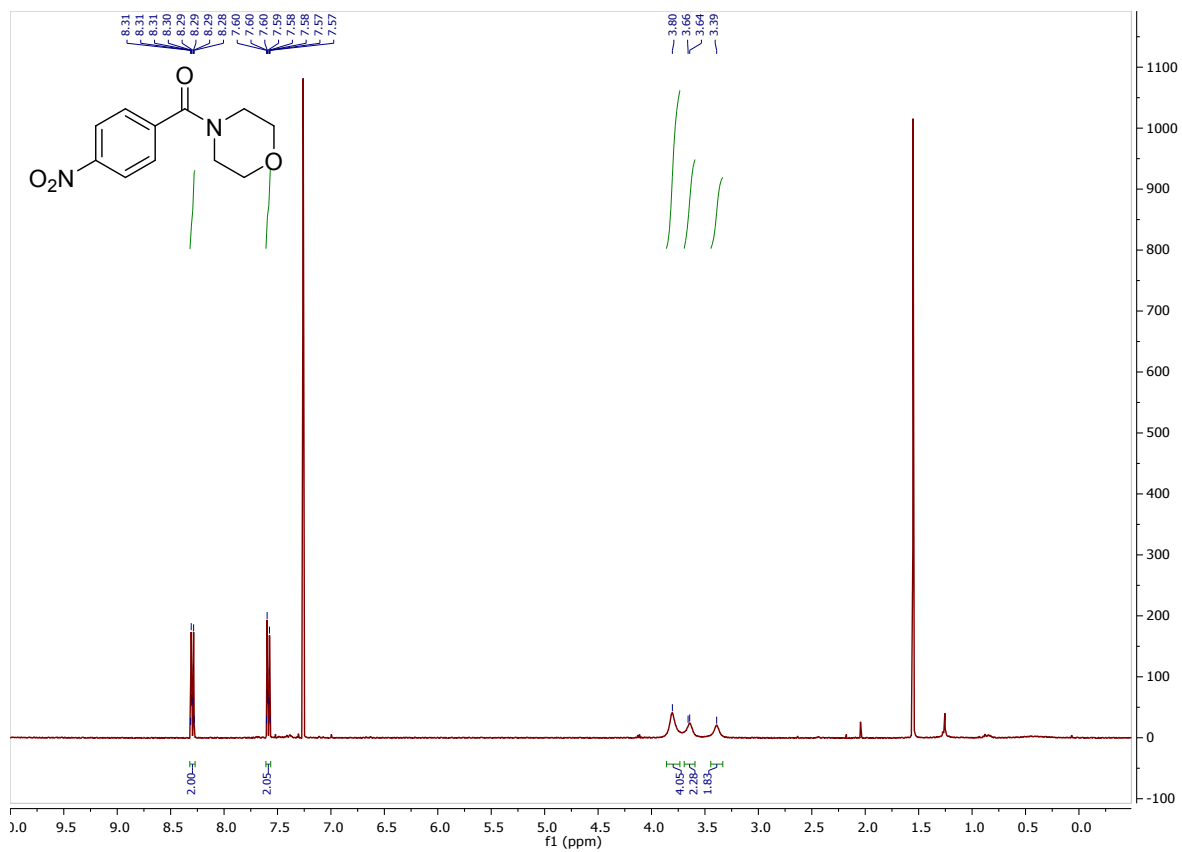
(4-methoxyphenyl)(morpholino)methanone (10a) (400 MHz, CDCl₃)



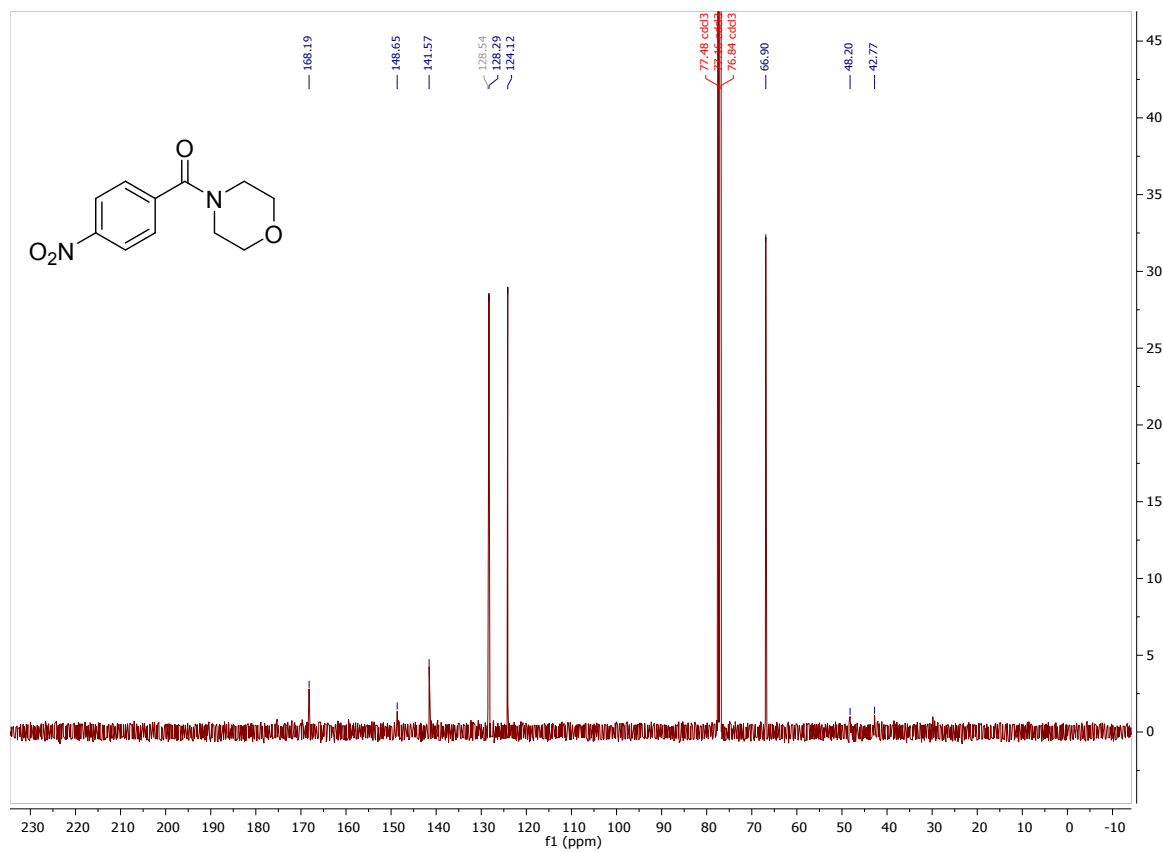
(100 MHz, CDCl₃)



Morpholino(4-nitrophenyl)methanone (10b) (400 MHz, CDCl₃)

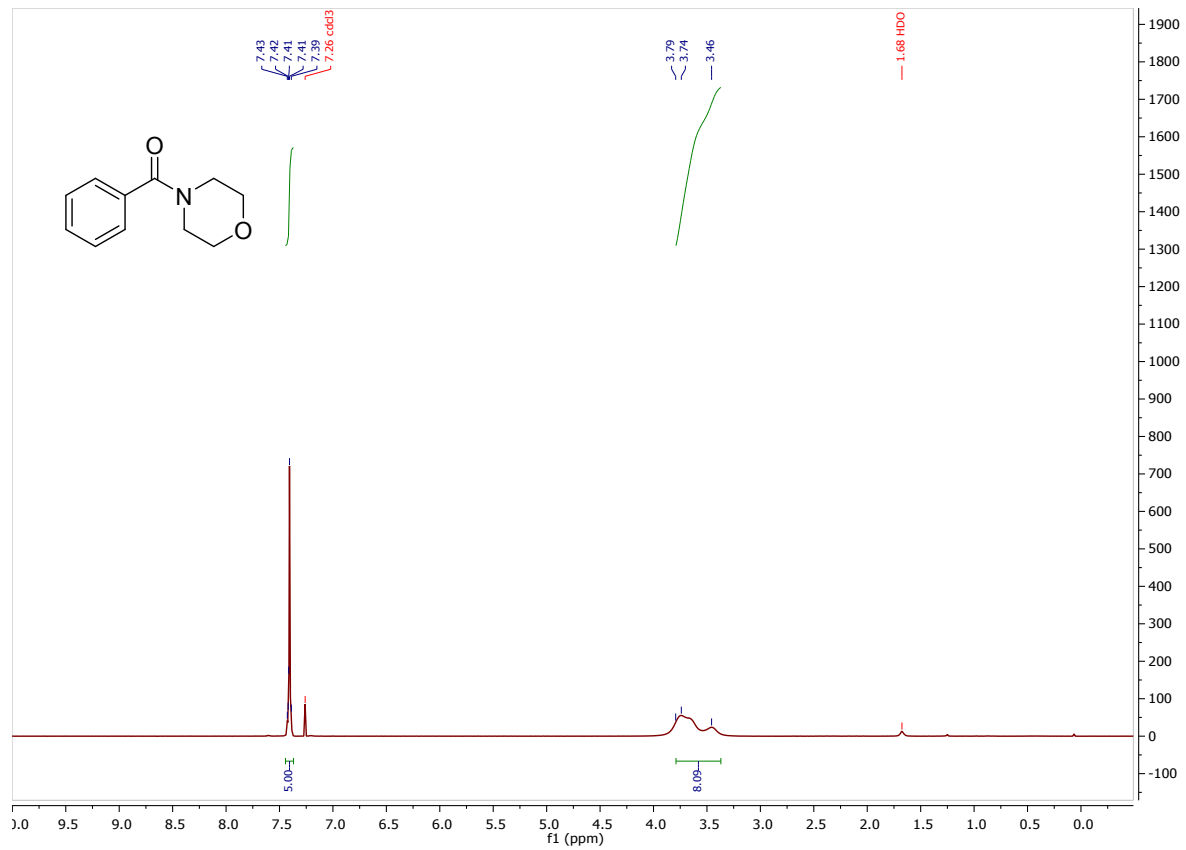


(100 MHz, CDCl₃)

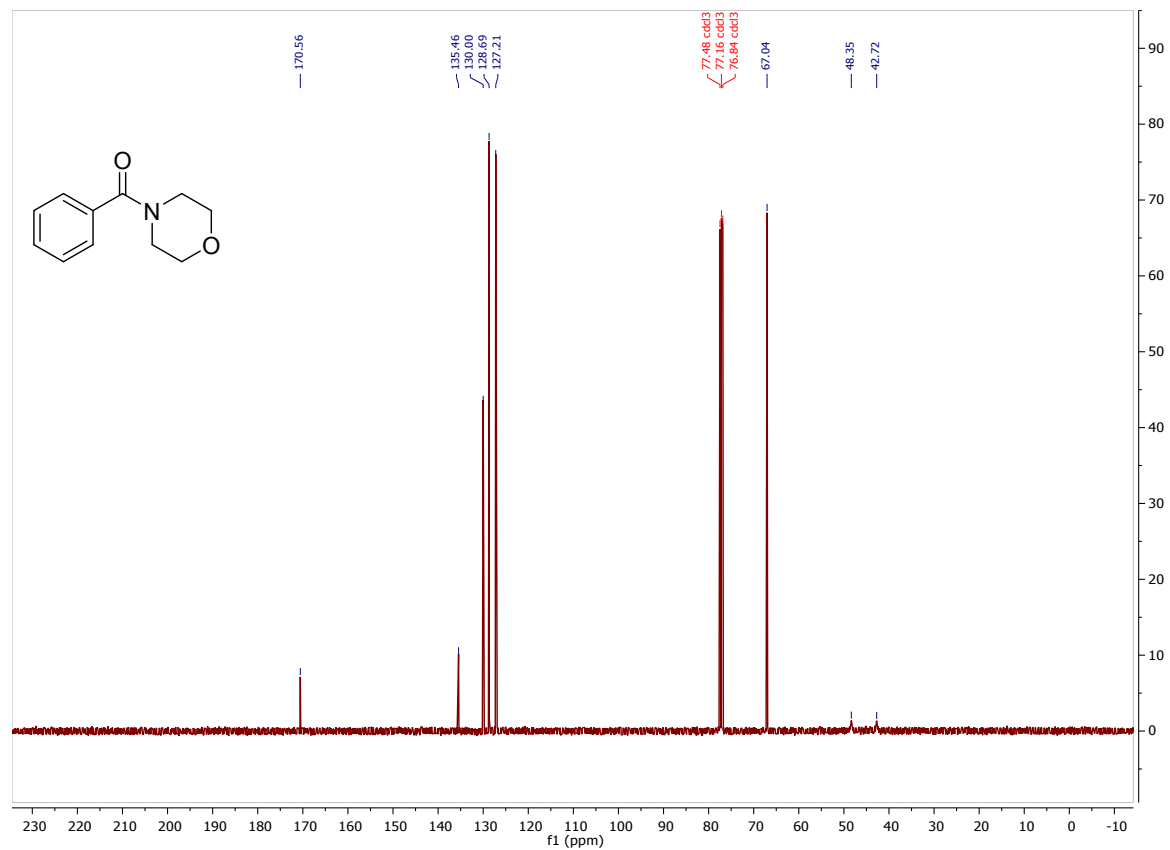


(4-bromophenyl)(morpholino)methanone (10c) (400 MHz, CDCl₃)

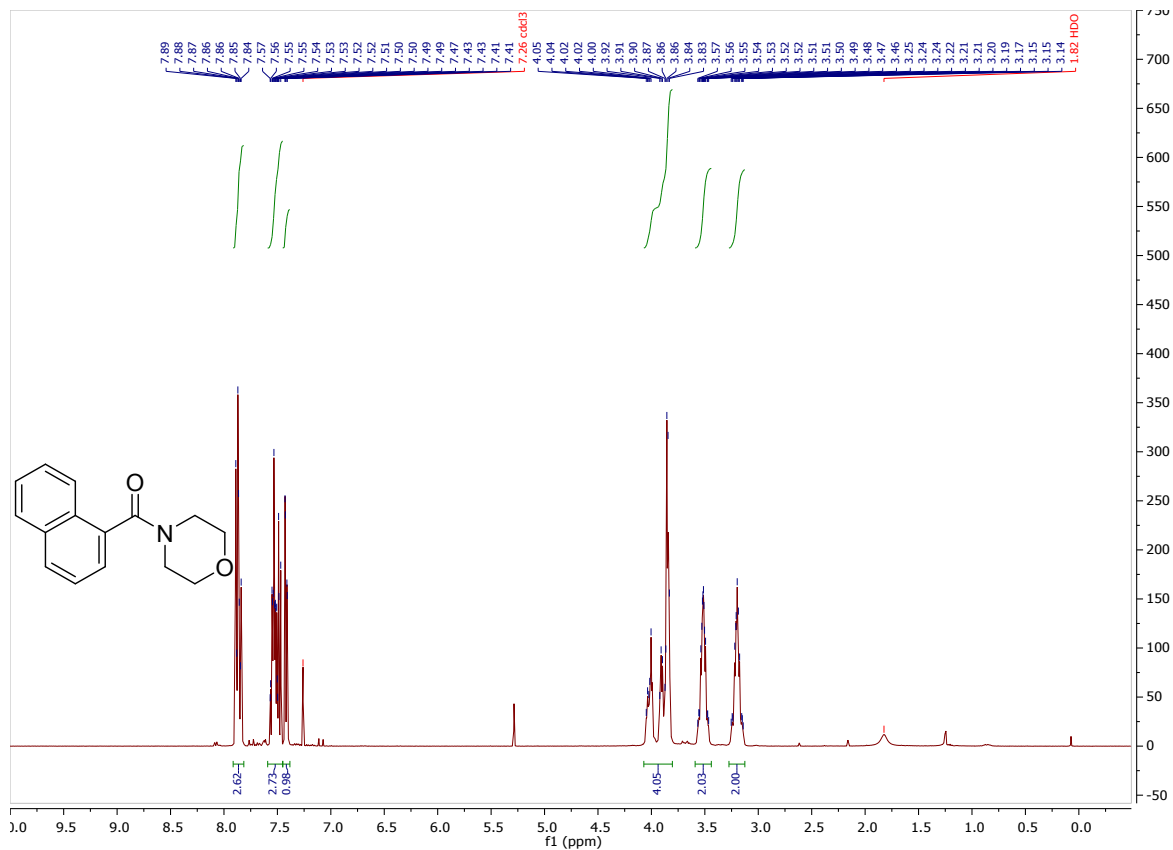
Morpholino(phenyl)methanone (10d) (400 MHz, CDCl₃)



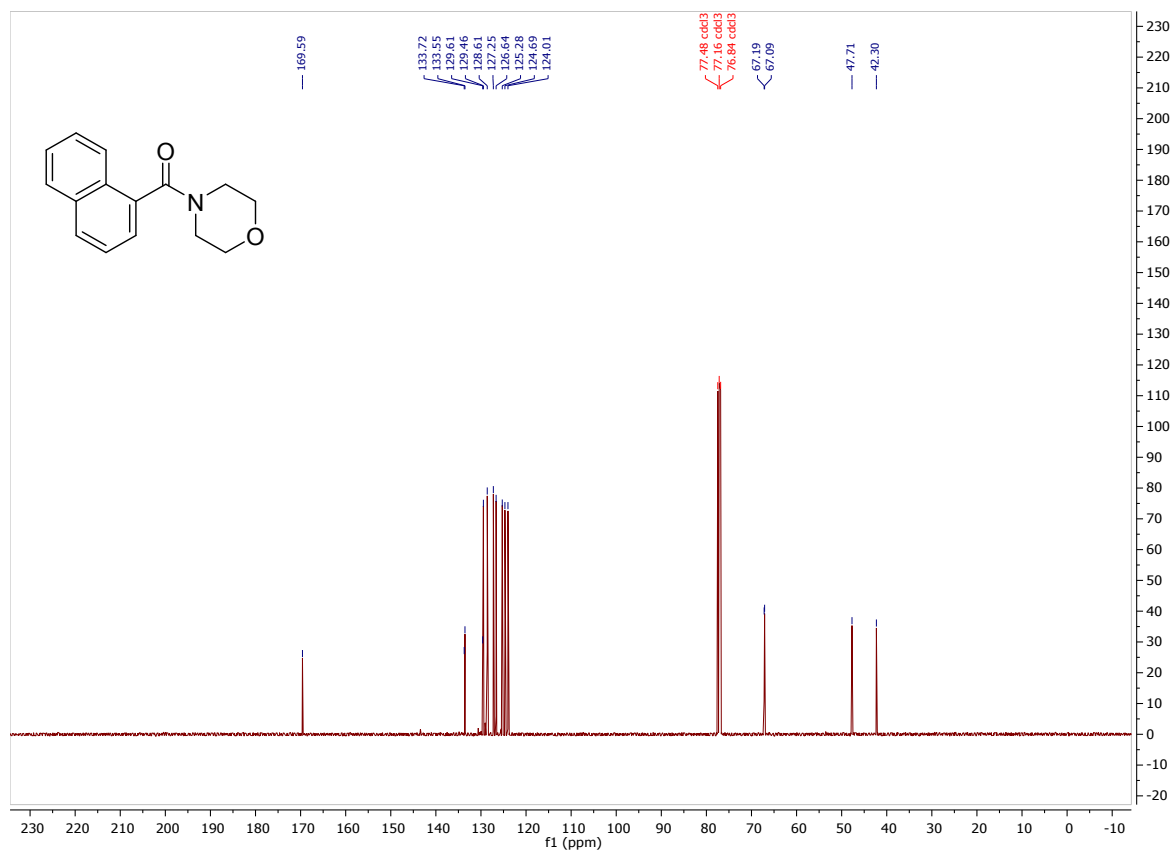
(100 MHz, CDCl₃)



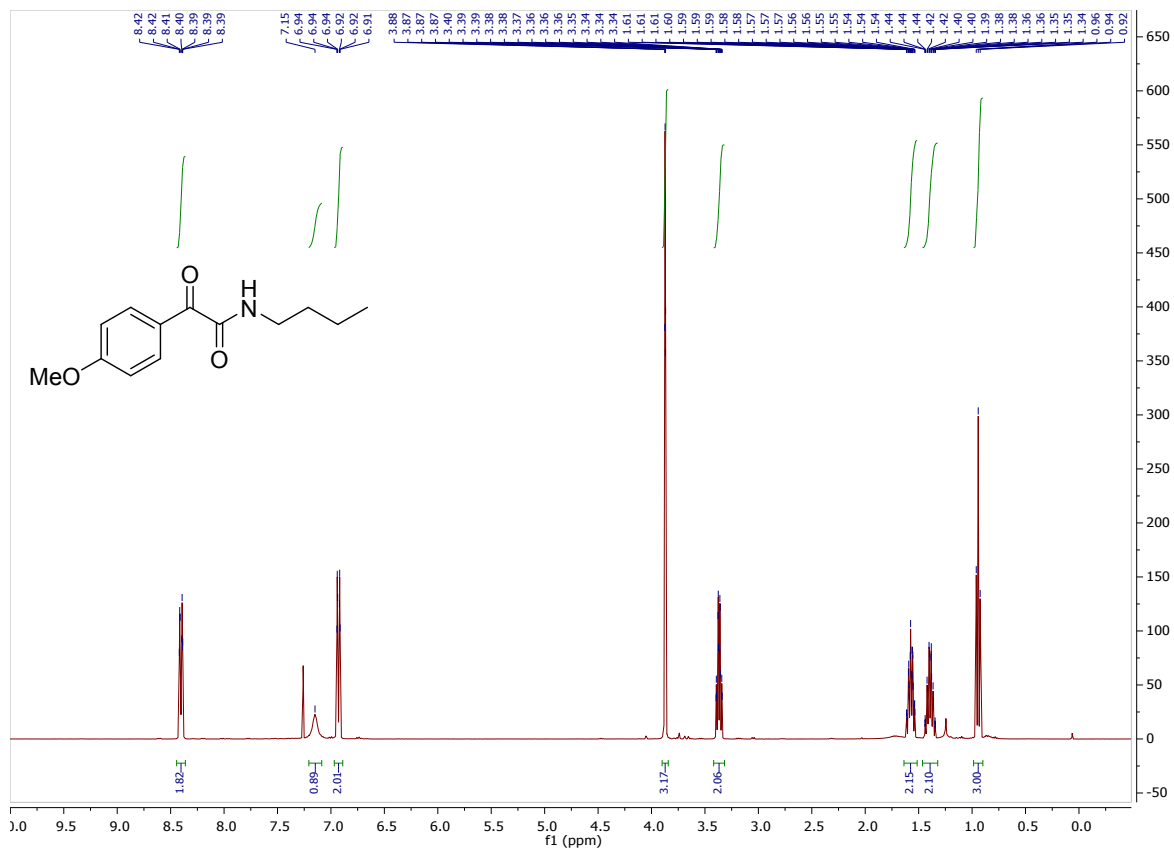
Morpholino(naphthalen-1-yl)methanone (10e) (400 MHz, CDCl₃)



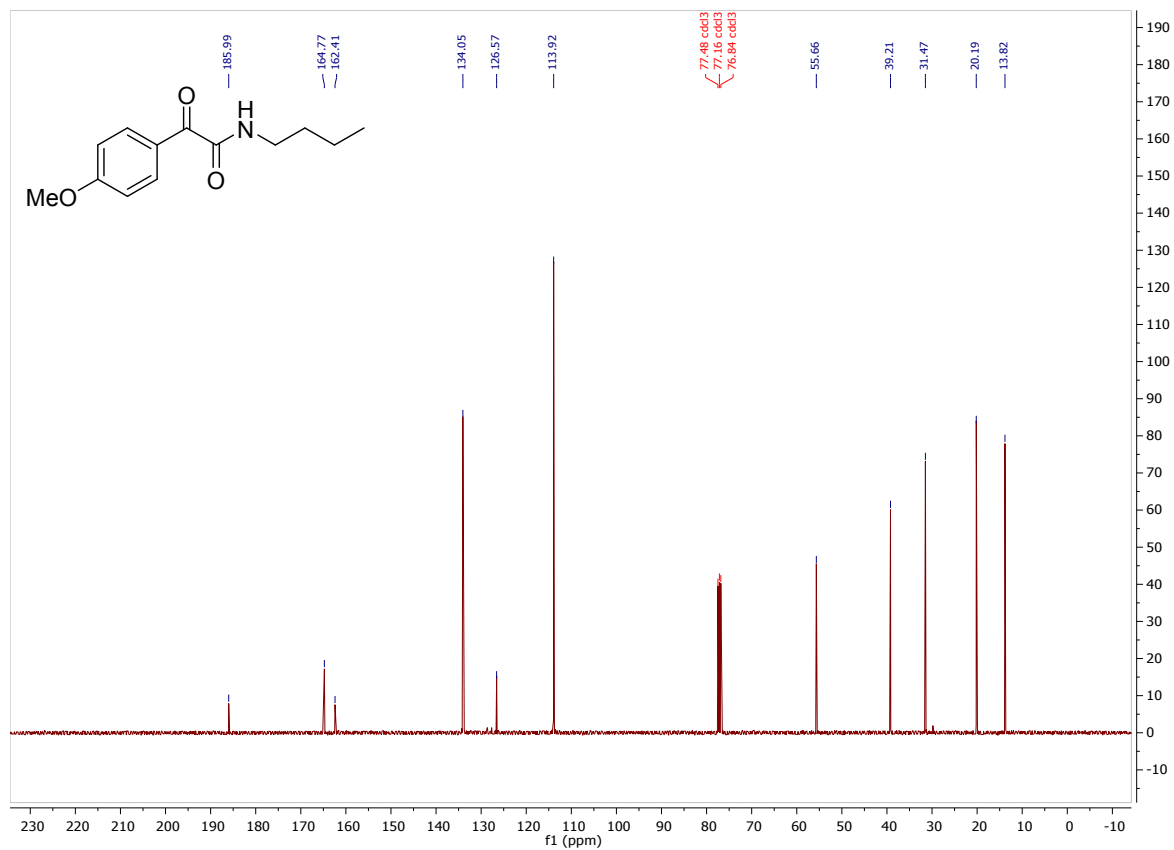
(100 MHz, CDCl₃)



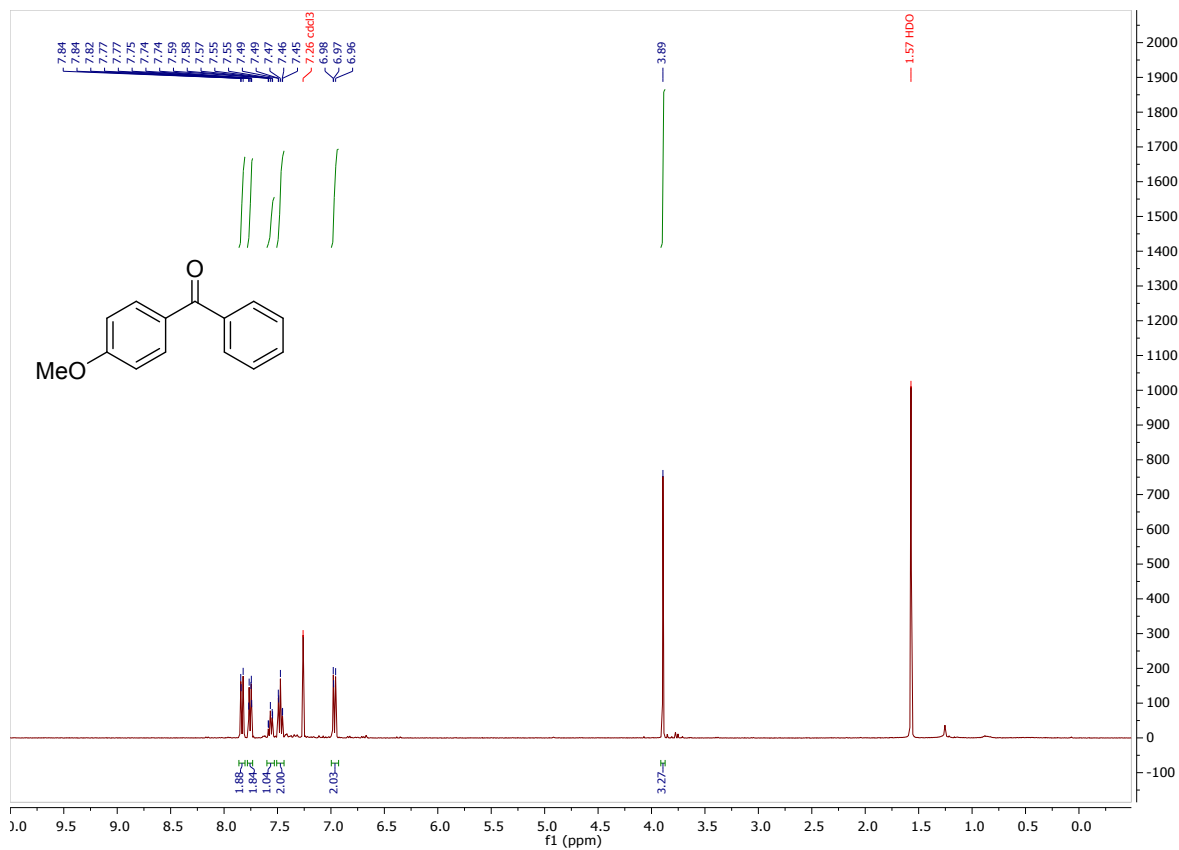
N-butyl-2-(4-methoxyphenyl)-2-oxoacetamide (13) (400 MHz, CDCl₃)



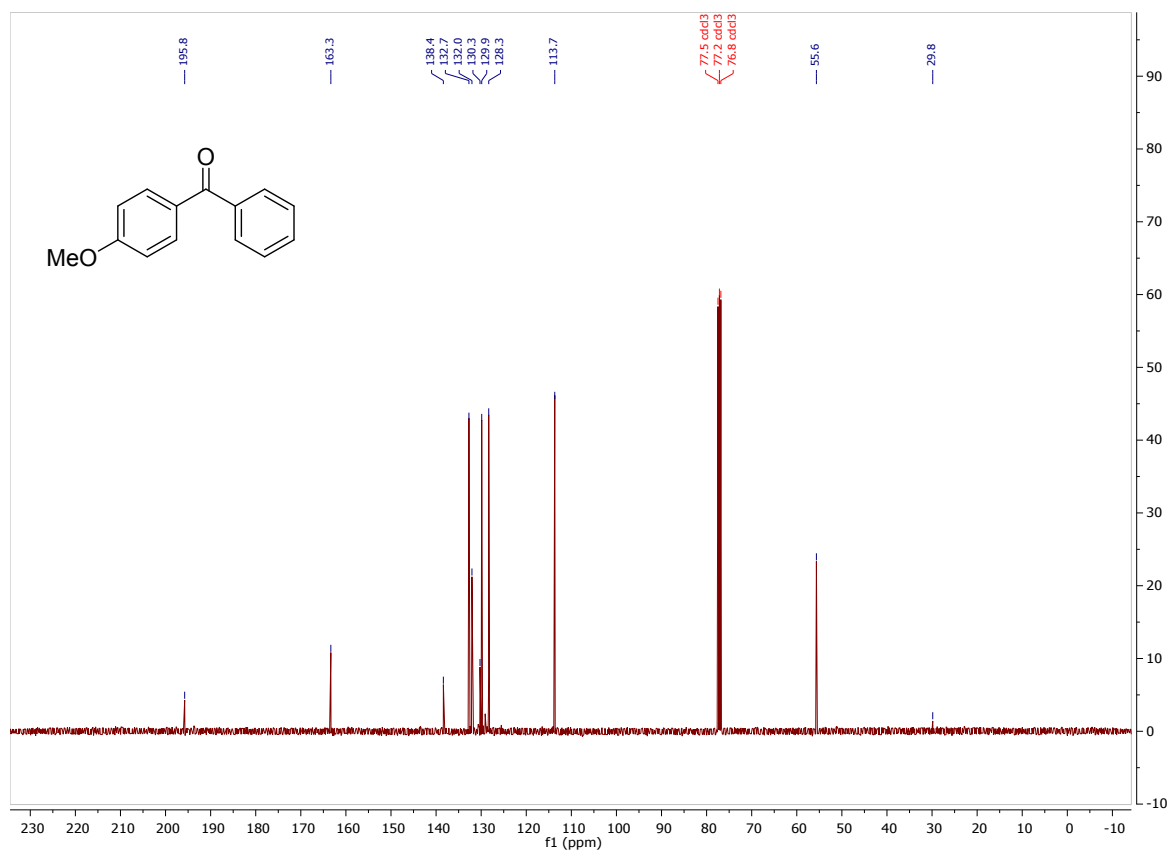
(100 MHz, CDCl₃)



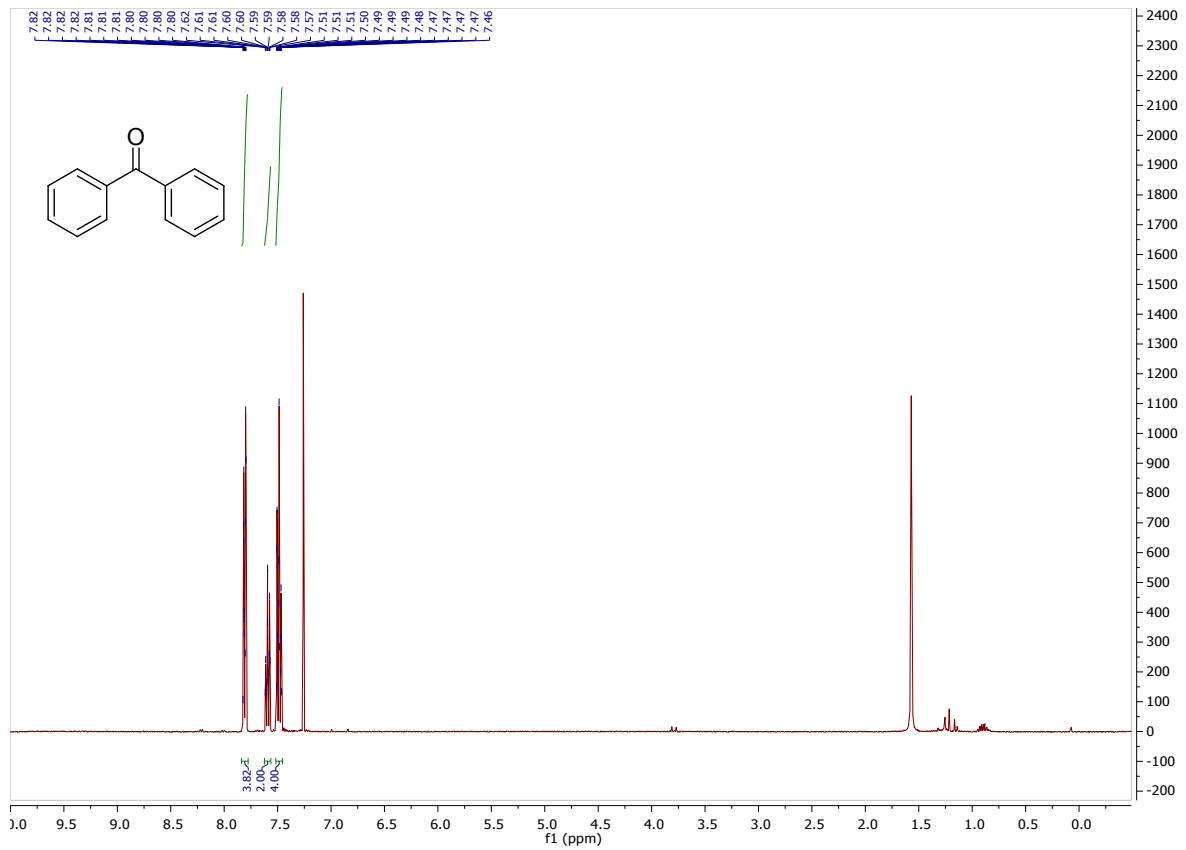
(4-methoxyphenyl)(phenyl)methanone (15a) (400 MHz, CDCl₃)



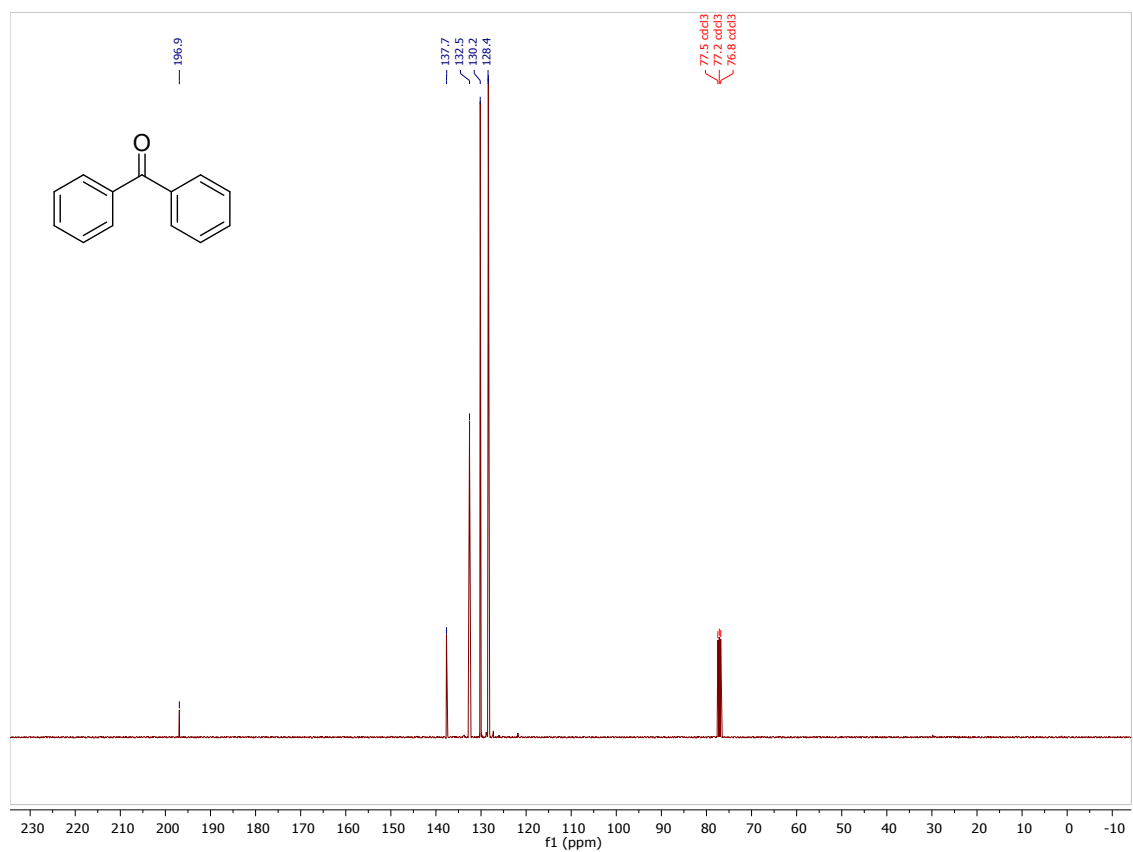
(100 MHz, CDCl₃)



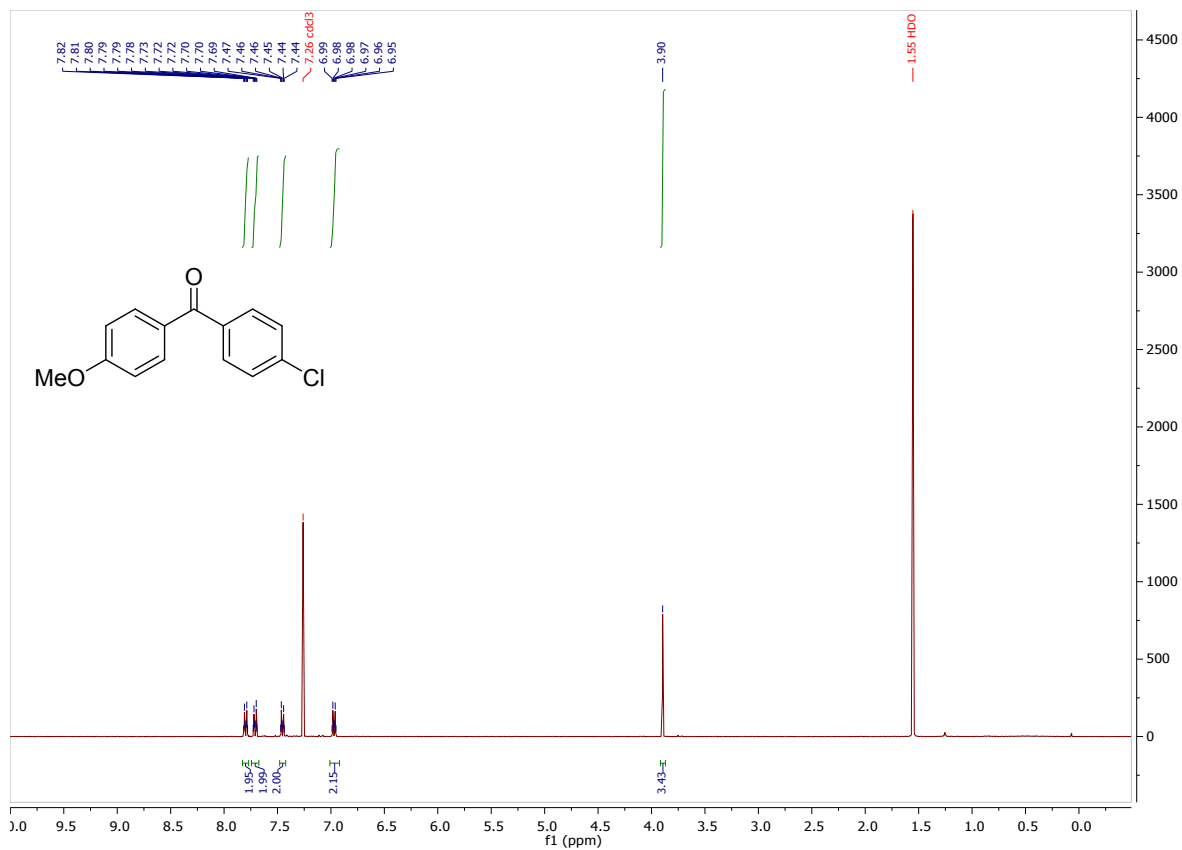
Benzophenone (15b) (400 MHz, CDCl₃)



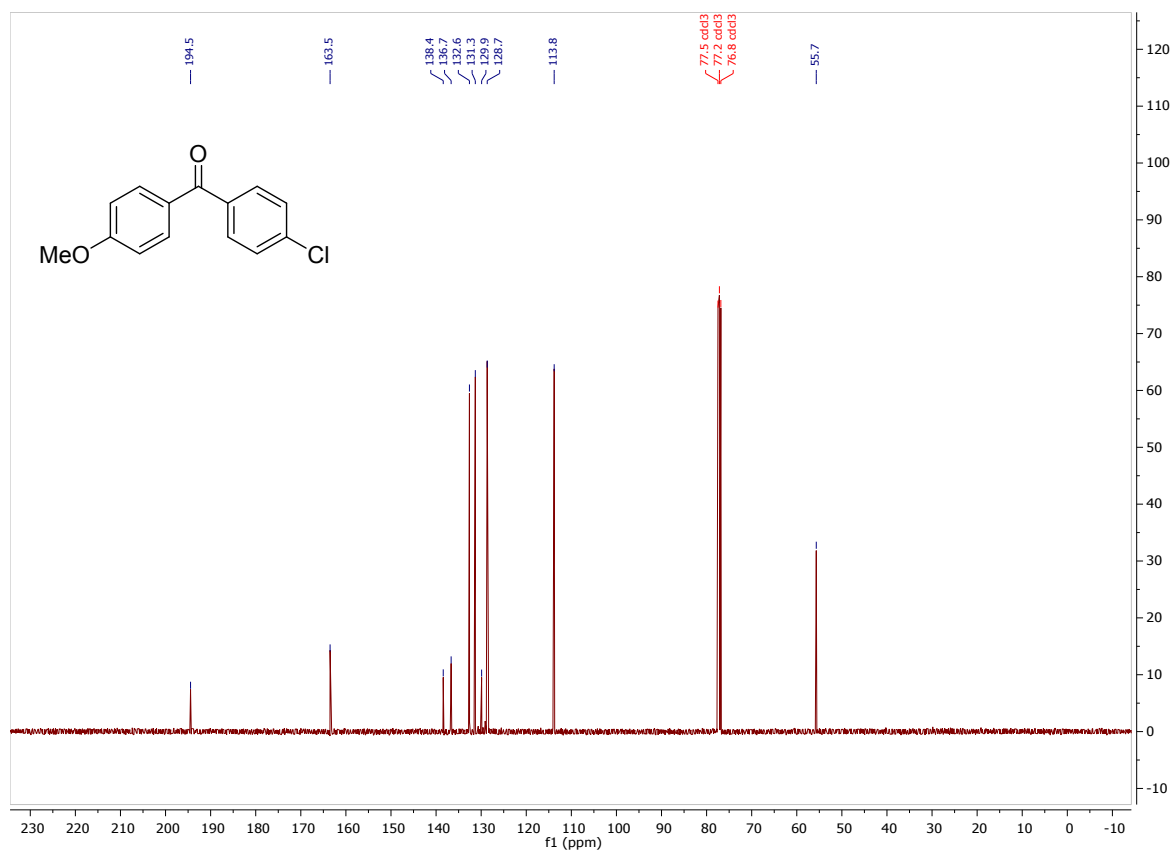
(100 MHz, CDCl₃)



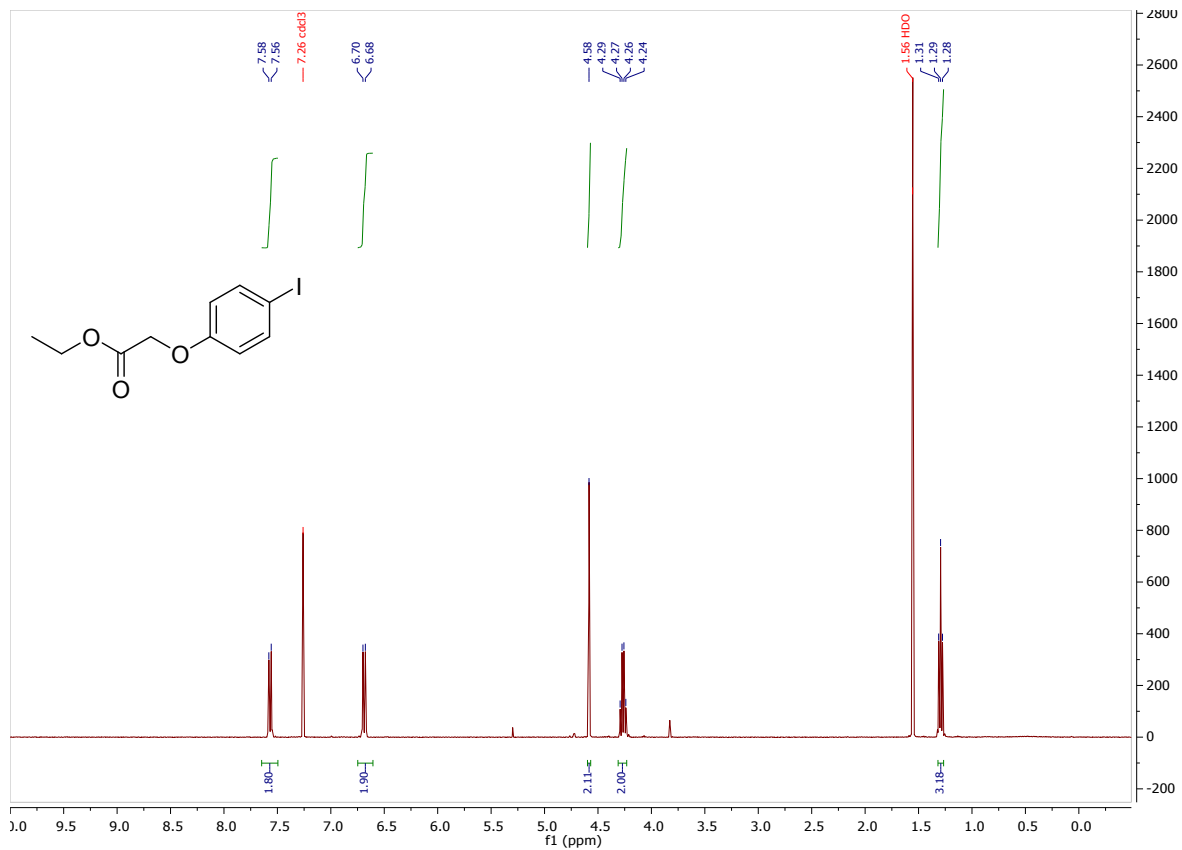
(4'-chlorophenyl)(4-methoxyphenyl)methanone (15c) (400 MHz, CDCl₃)



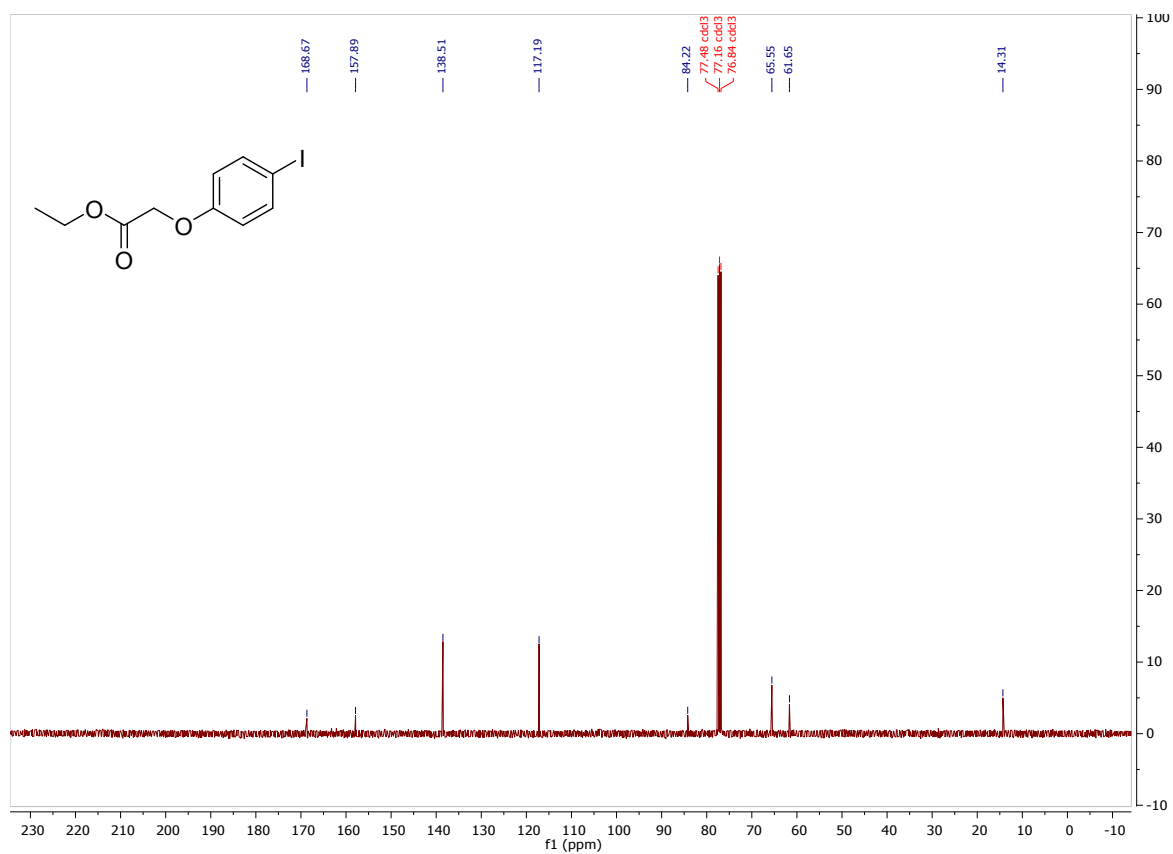
(100 MHz, CDCl₃)



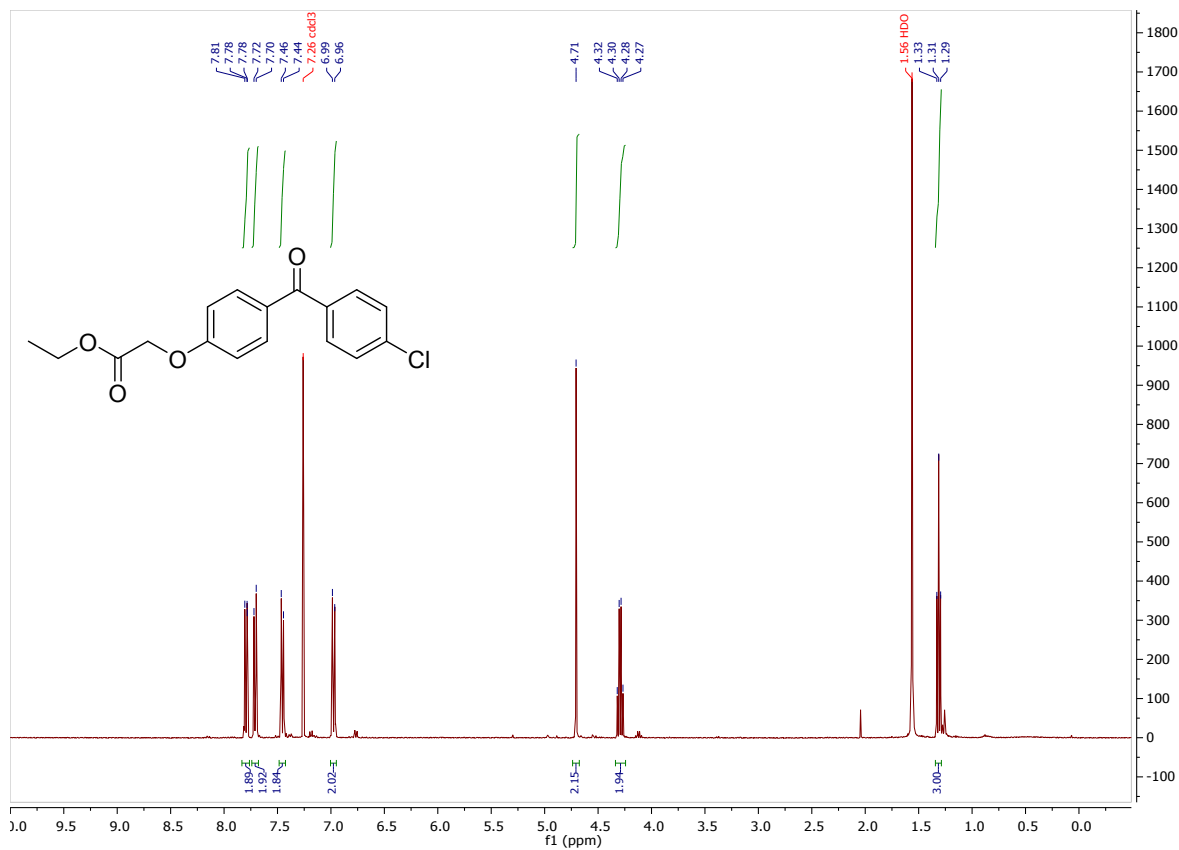
Ethyl 2-(4-iodophenoxy)acetate (**6f**) (400 MHz, CDCl₃)



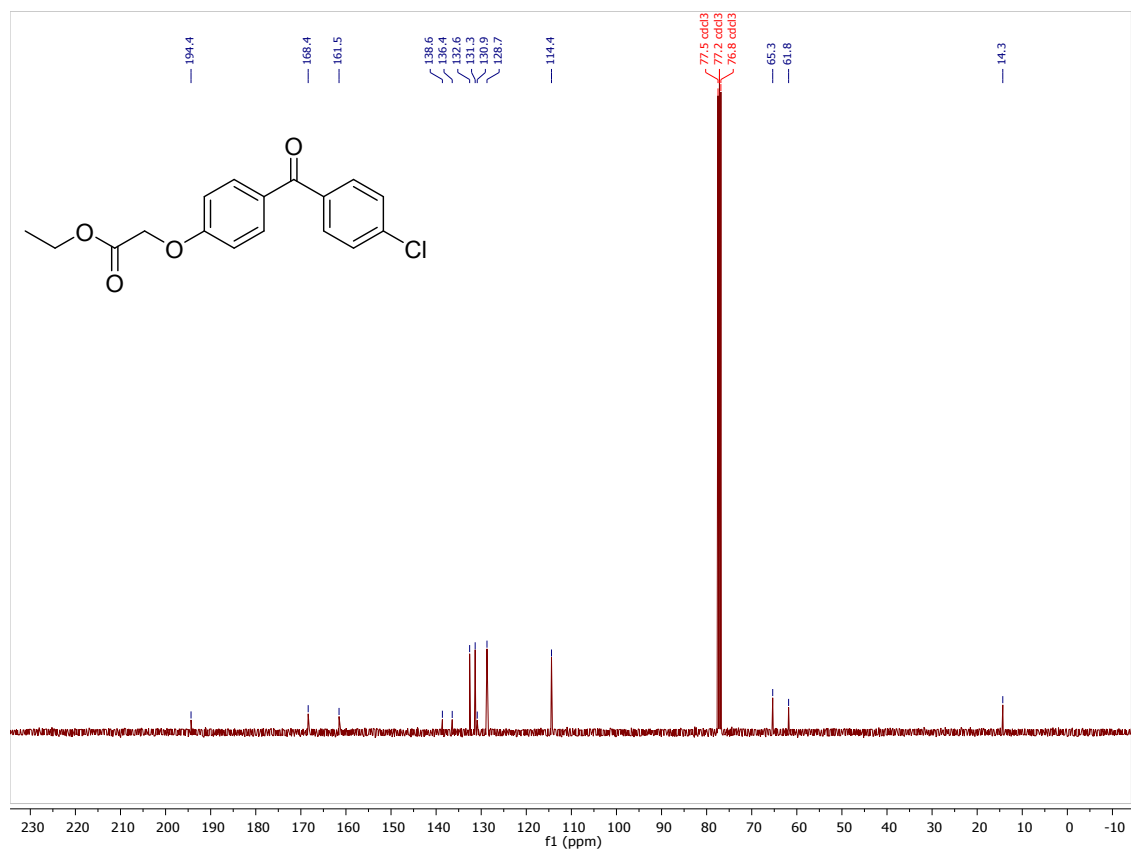
(100 MHz, CDCl₃)



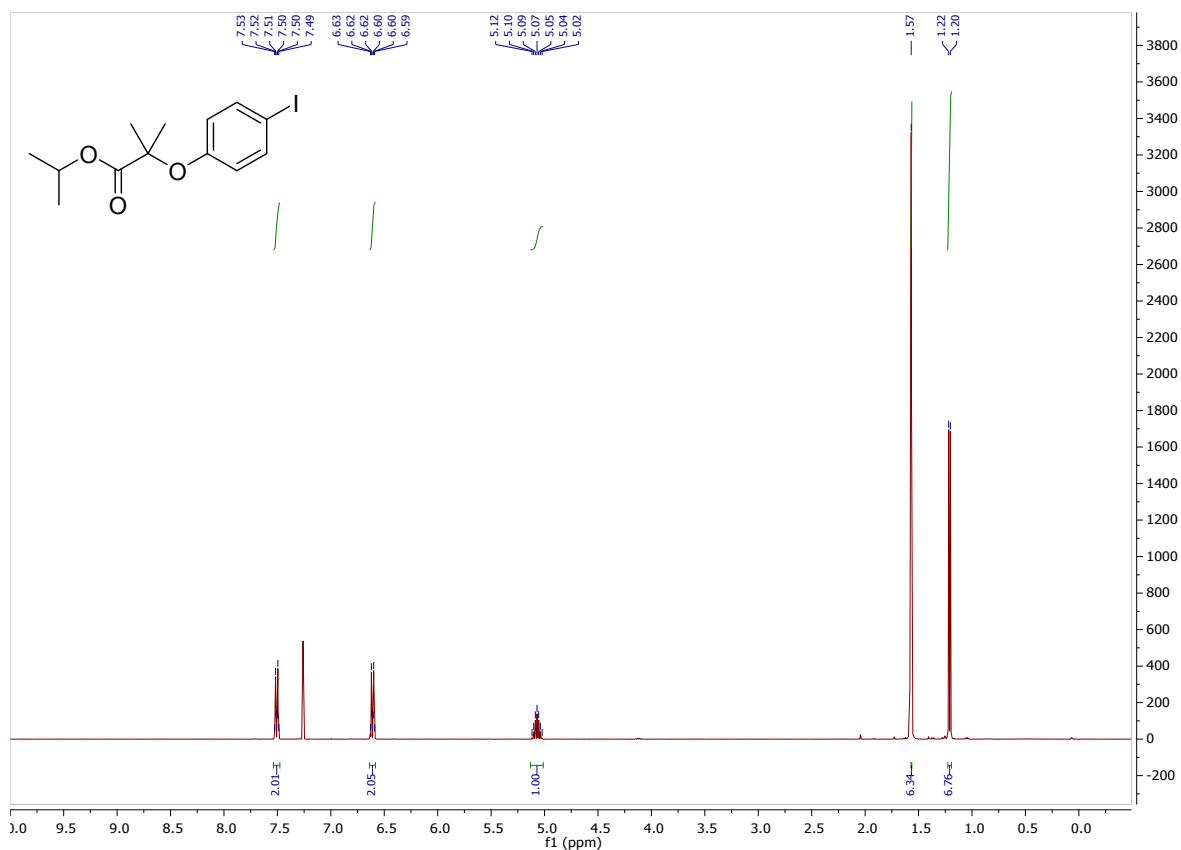
Ethyl 2-(4-(4-chlorobenzoyl)phenoxy)acetate (15d) (400 MHz, CDCl₃)



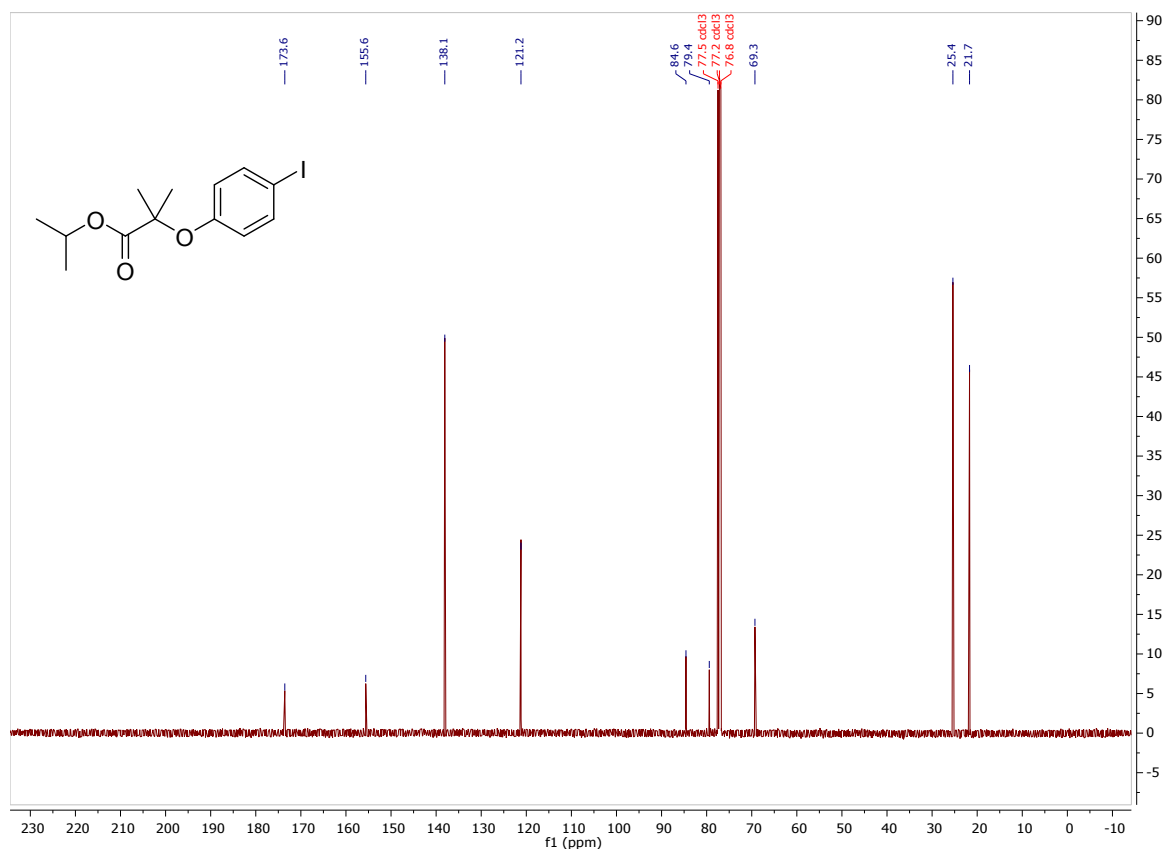
(100 MHz, CDCl₃)



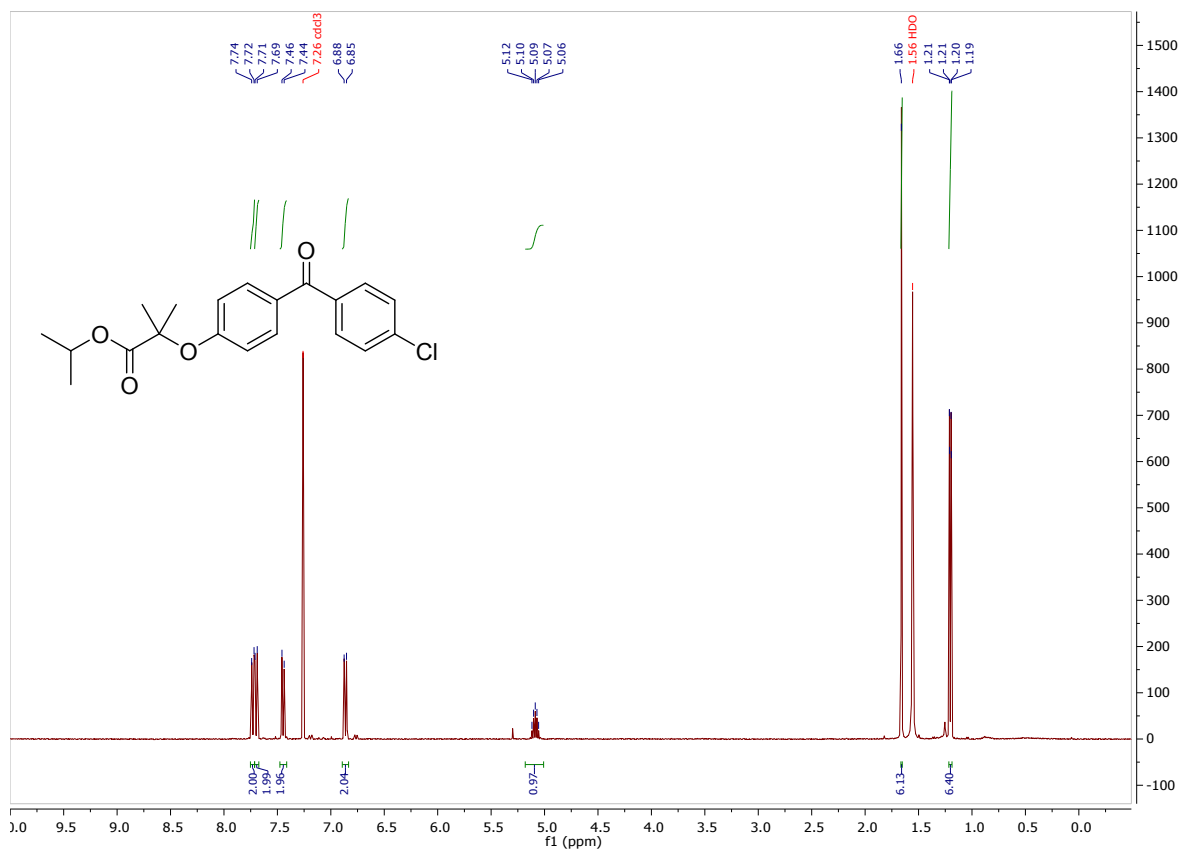
Isopropyl 2-(4-iodophenoxy)-2-methylpropanoate (6g) (400 MHz, CDCl₃)



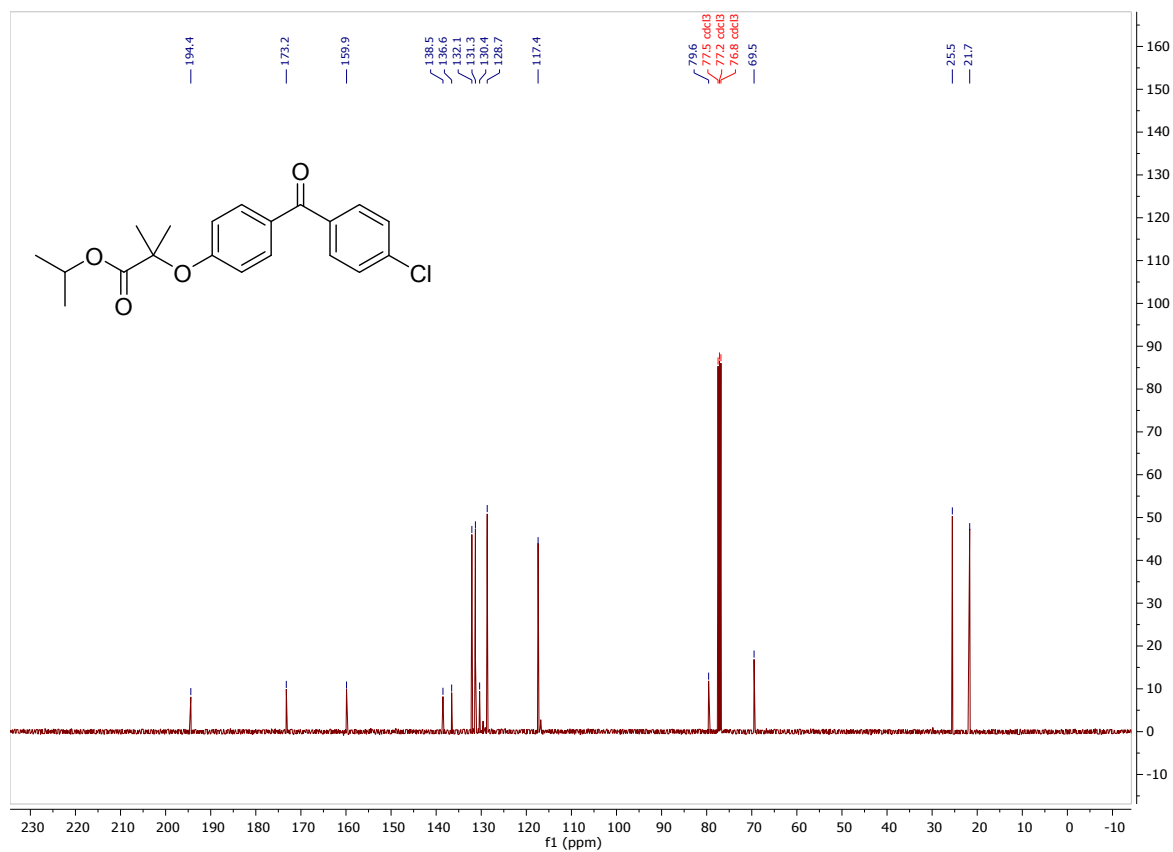
(100 MHz, CDCl₃)



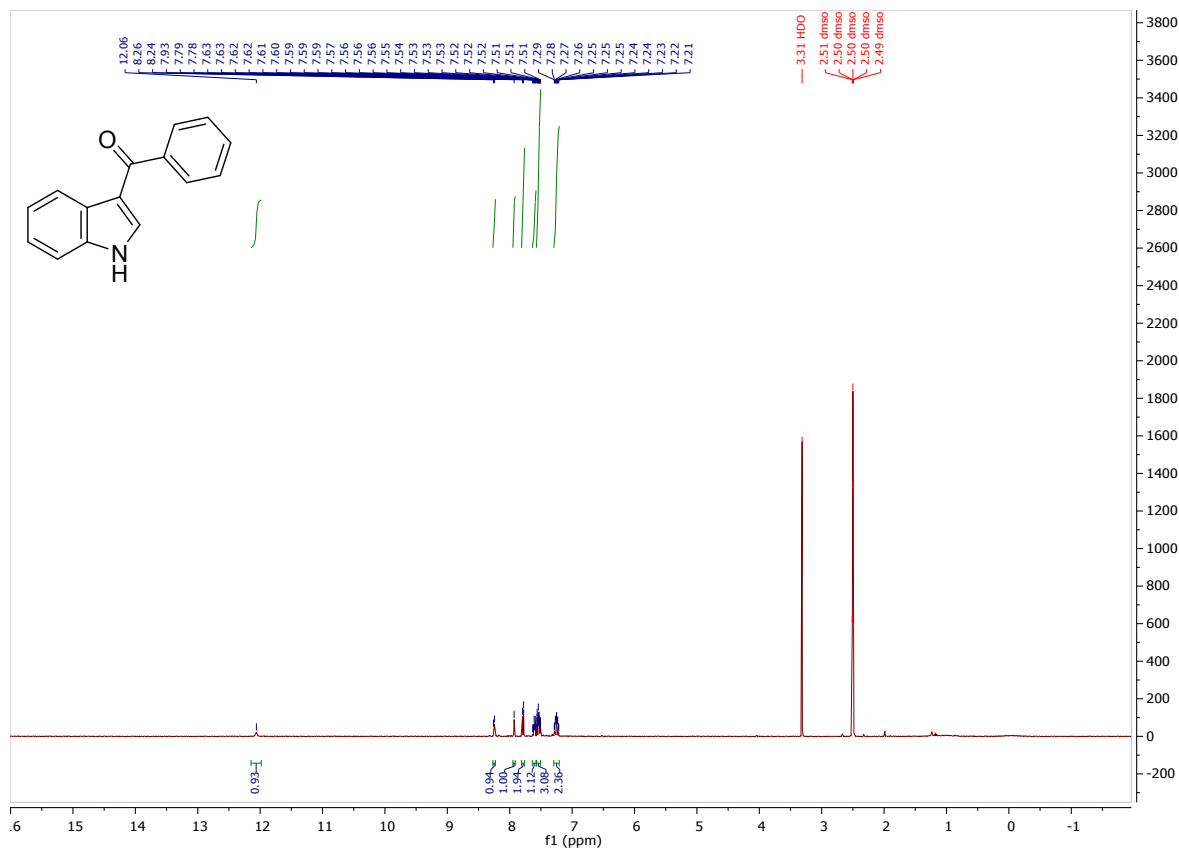
Isopropyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate (15e) (400 MHz, CDCl₃)



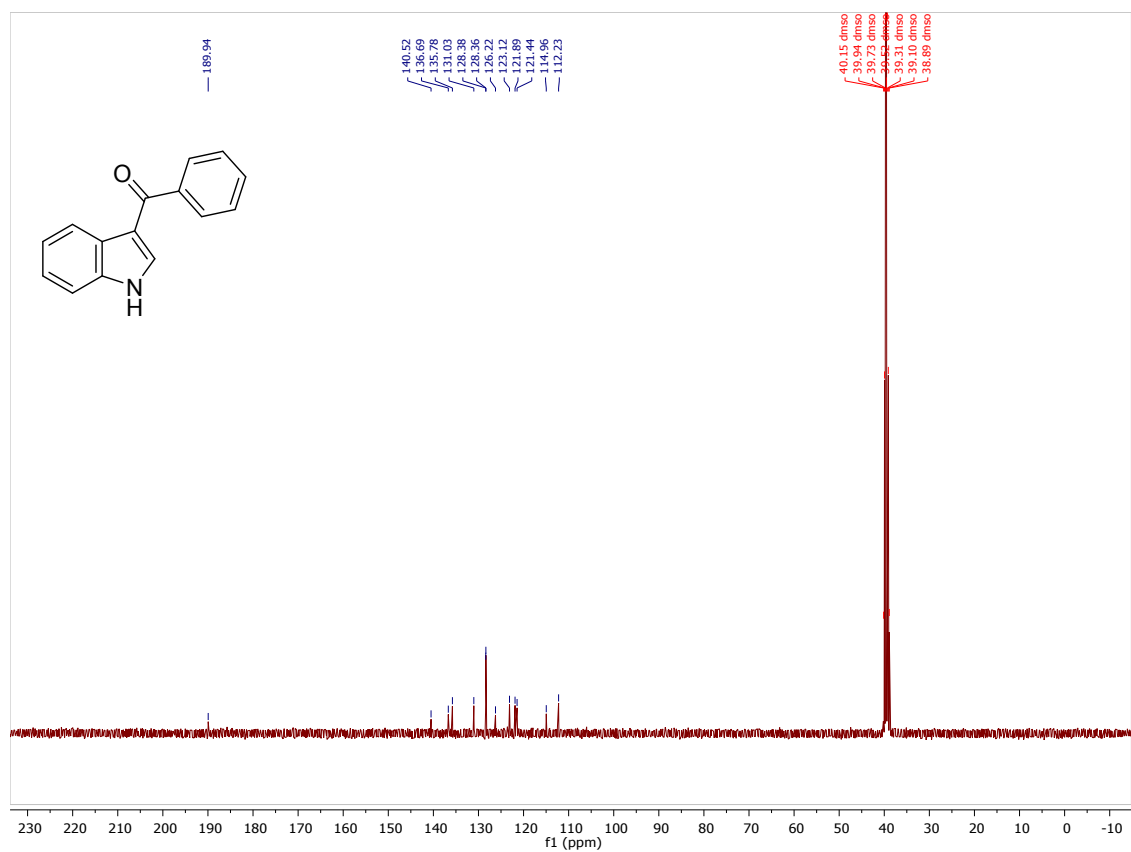
(100 MHz, CDCl₃)



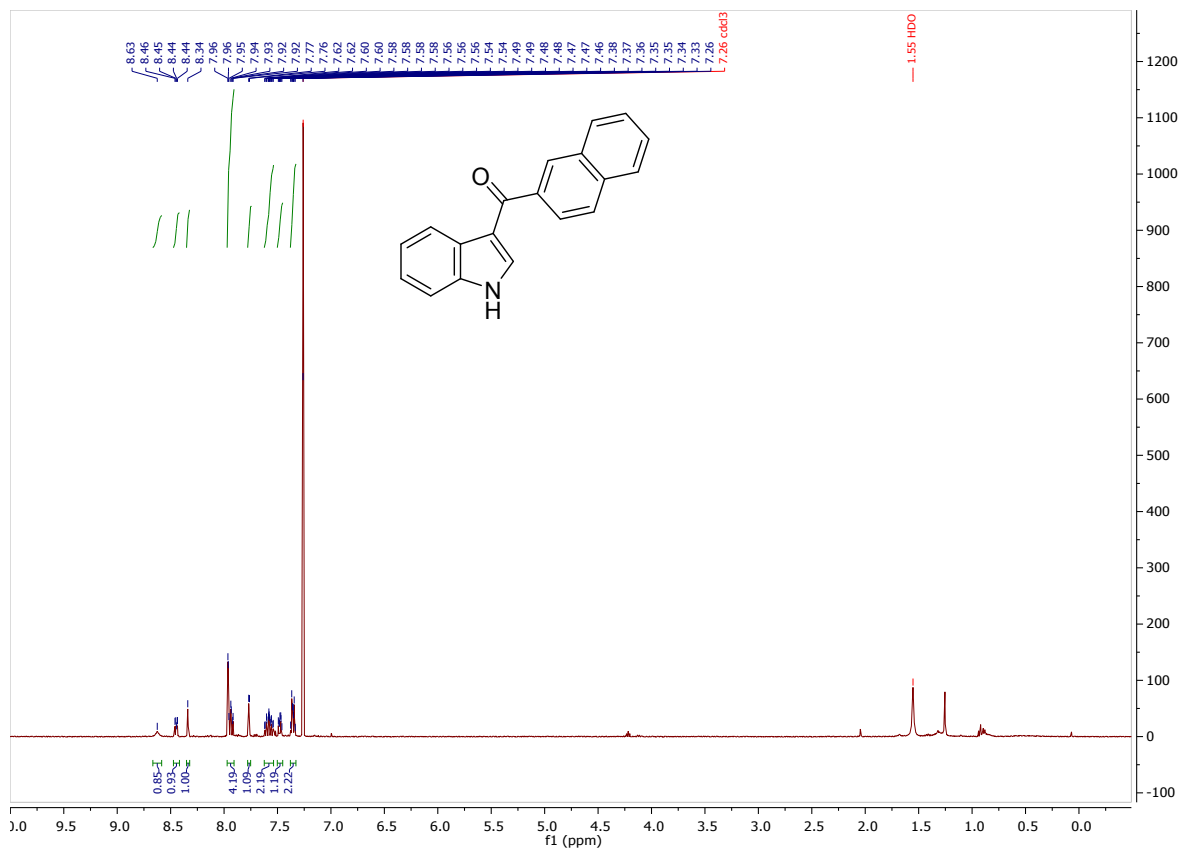
1H-indol-3-ylphenylmethanone (17) (400 MHz, CDCl₃)



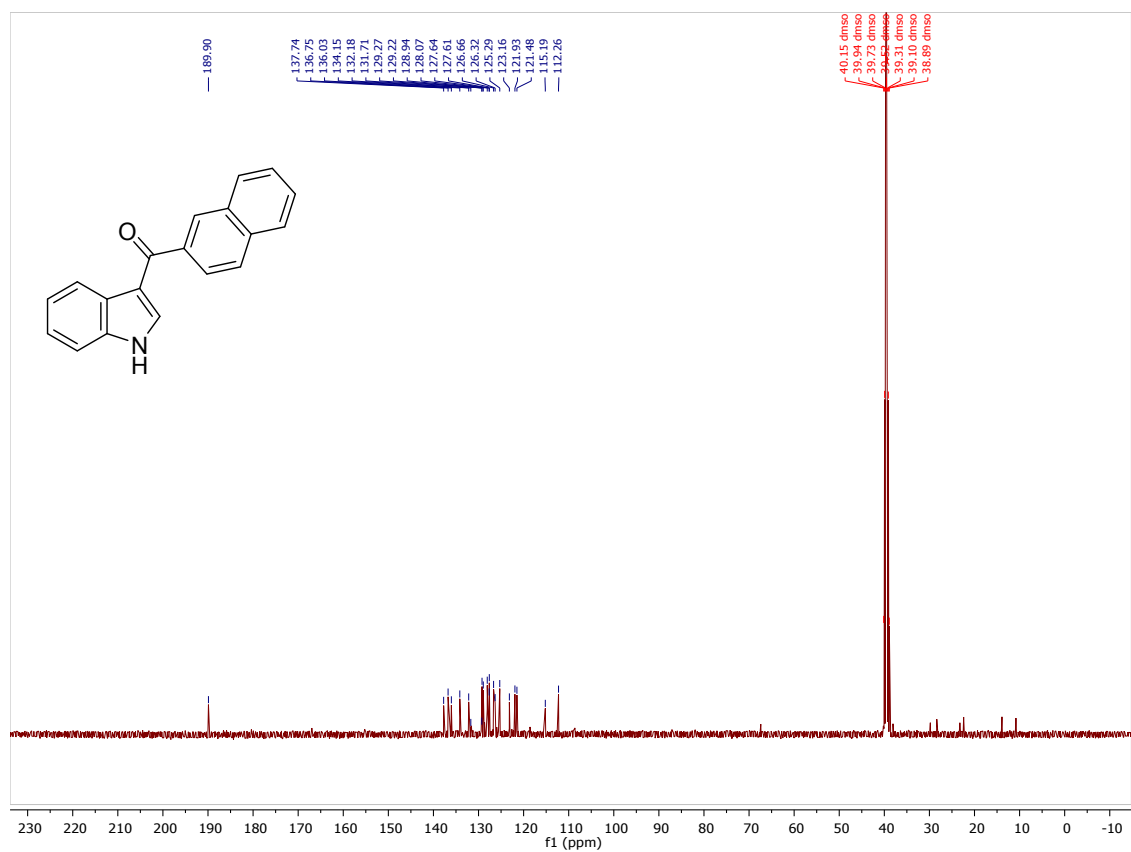
(100 MHz, CDCl₃)



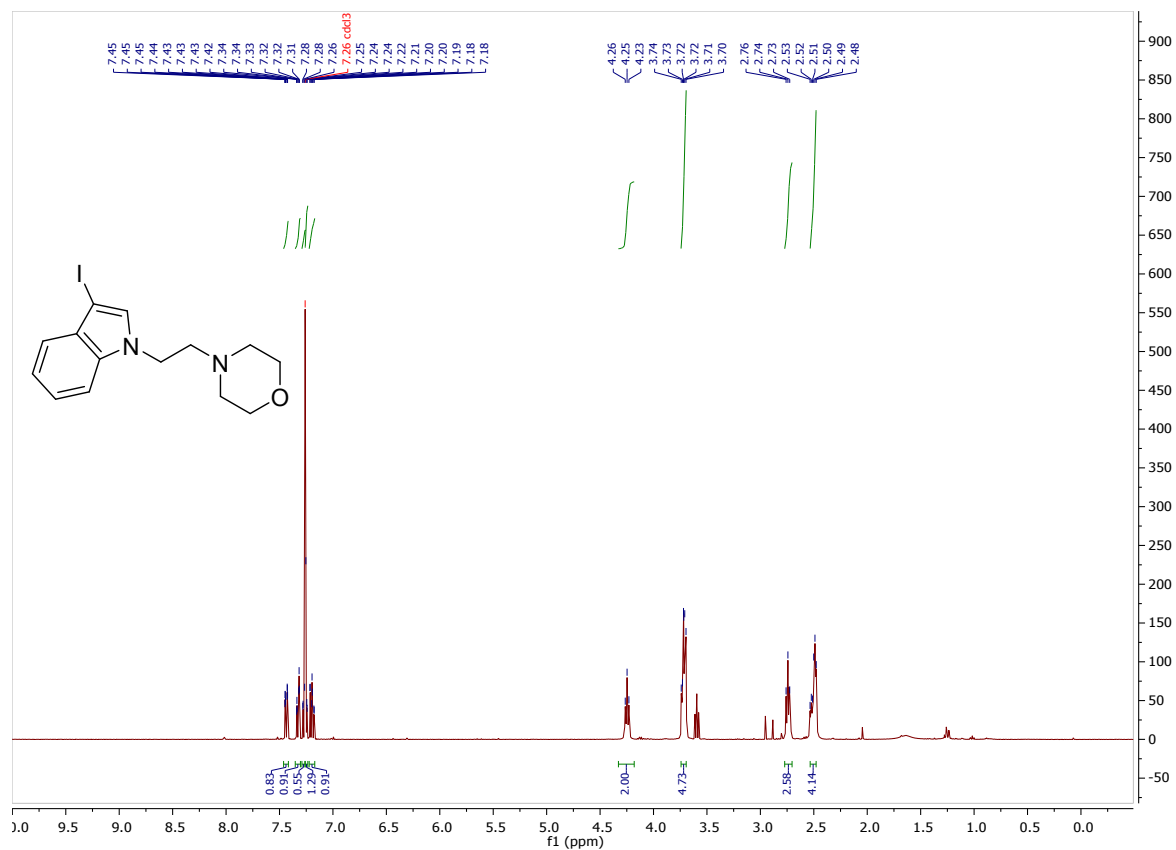
(1*H*-indol-3-yl)(naphthalen-2-yl)methanone (18) (400 MHz, CDCl₃)



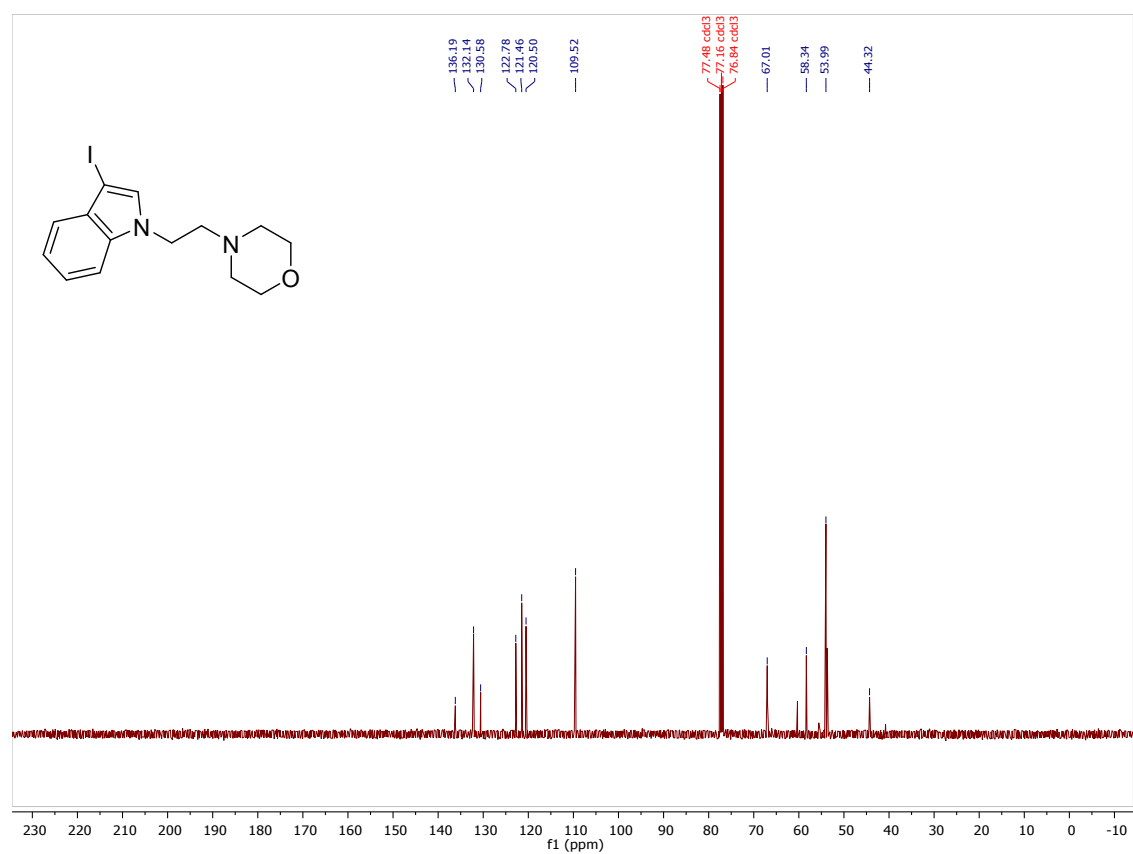
(100 MHz, CDCl₃)



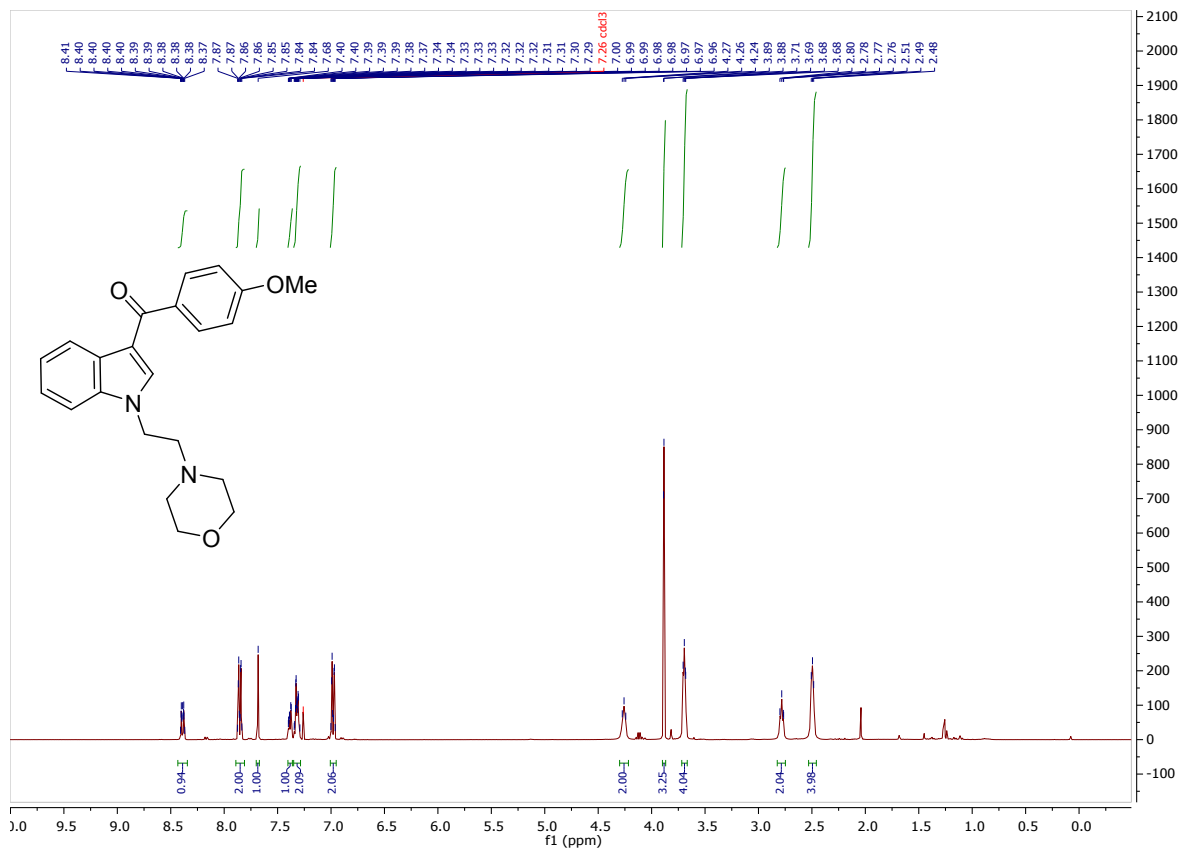
4-(2-(3-iodo-1*H*-indol-1-yl)ethyl)morpholine (20) (400 MHz, CDCl₃)



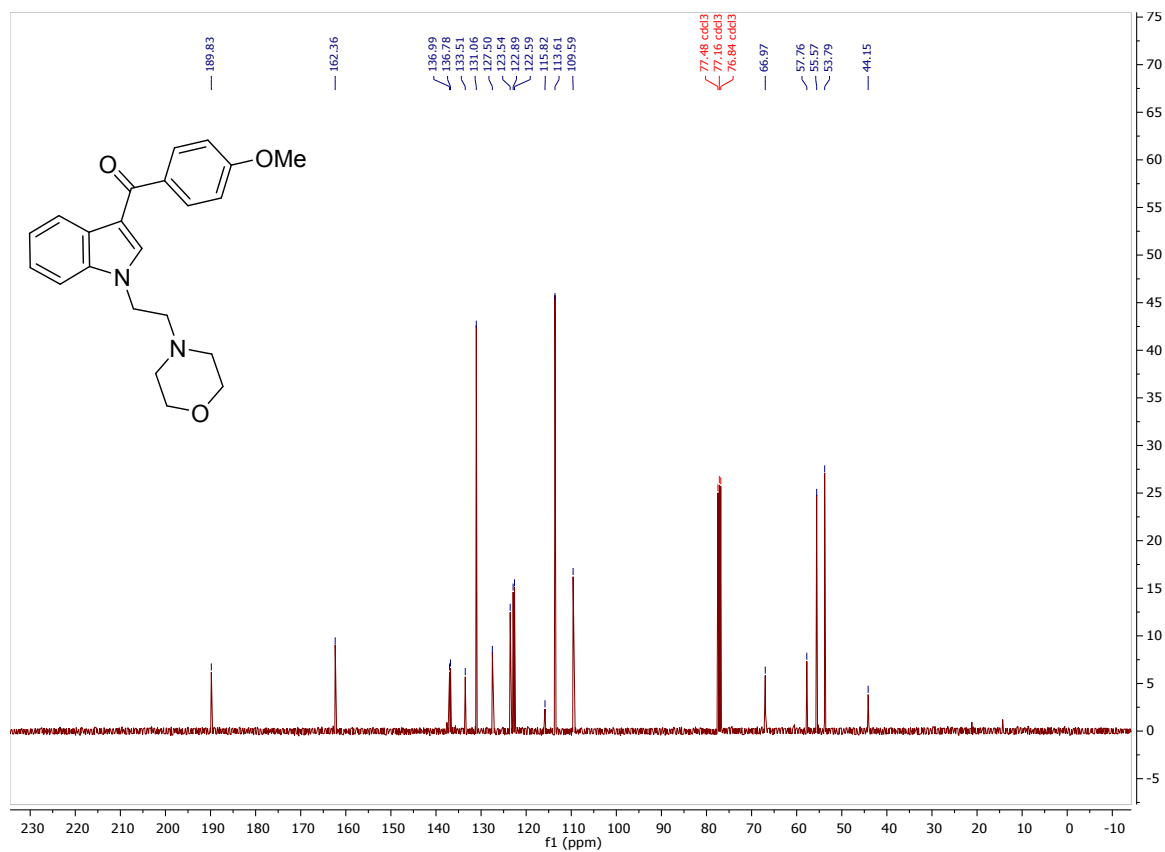
(100 MHz, CDCl₃)



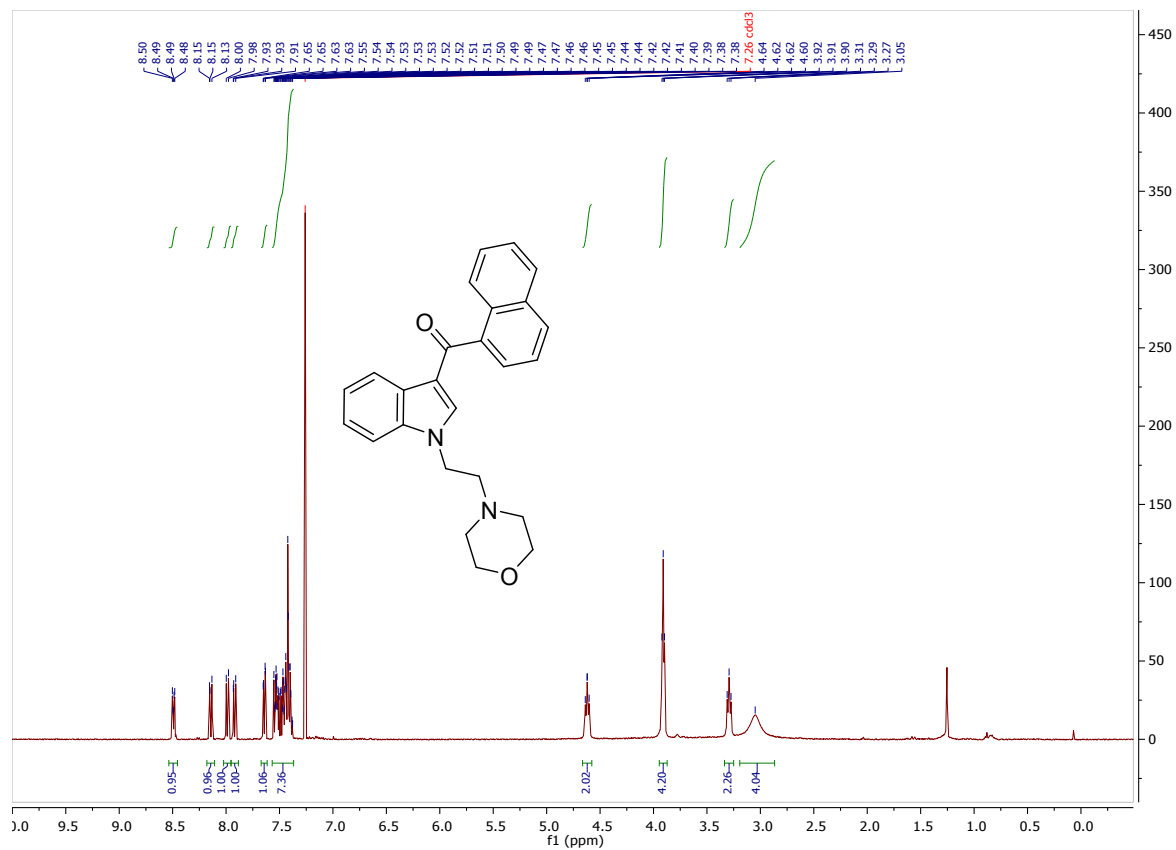
(4-methoxyphenyl)(1-(2-morpholinoethyl)-1H-indol-3-yl)methanone (21) (400 MHz, CDCl₃)



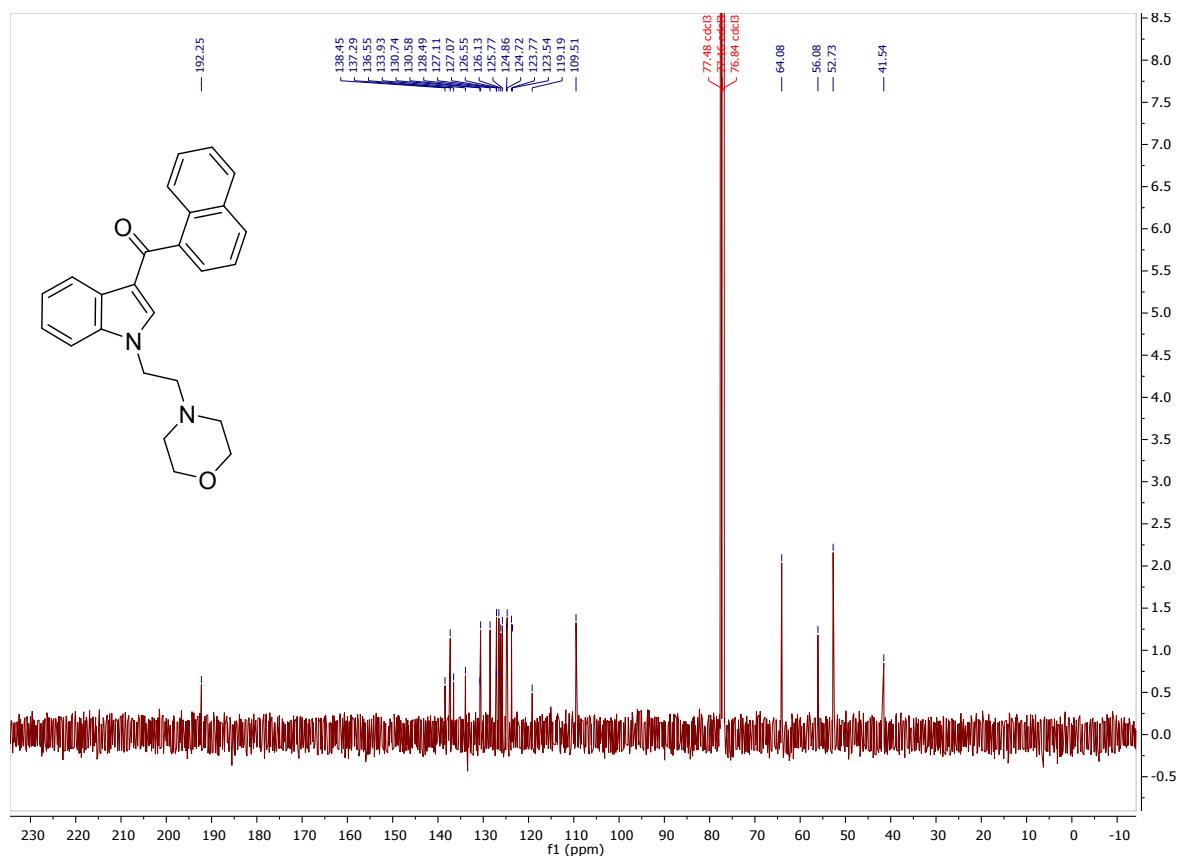
(100 MHz, CDCl₃)



(1-(2-morpholinoethyl)-1H-indol-3-yl)(naphthalen-1-yl)methanone (22) (400 MHz, CDCl₃)



(100 MHz, CDCl₃)



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