Intramolecular oxidative C-H coupling for medium ring synthesis

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Supporting Information

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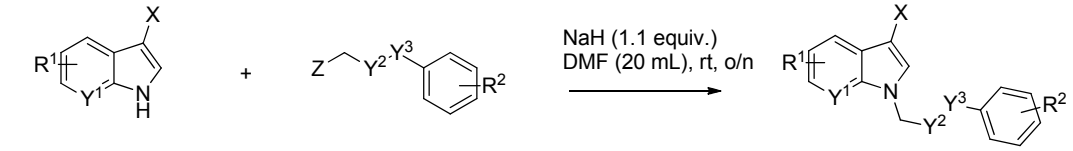
1: Experimental Procedures

General Methods

Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Brüker Ava500 (500 MHz) instrument and calibrated to residual solvent peaks: proton ($CDCl_3$ 7.26 ppm) and carbon ($CDCl_3$ 77.0 ppm). The ^{1}H data is presented as follows: chemical shift (in ppm on the δ scale), multiplicity (bs=broad singlet, s=singlet, d=doublet, t=triplet, q=quartet, p=pentet, m=multiplet), the coupling constant (J, in Hertz) and integration. The ^{13}C data is reported as the ppm on the δ scale followed by the interpretation. Electrospray and electron impact high resolution mass spectrometry was performed by the EPSRC National Mass Spectrometry Service Centre, Swansea, using a Finnigan MAT 900 XLT double focusing mass spectrometer. The data is recorded as the ionisation method followed by the calculated and measured masses. TLC was performed on Merck 60F254 silica plates and visualised by UV light and/or anisaldehyde or potassium permanganate stains. The compounds were purified by wet flash chromatography using Merck Kieselgel 60 (particle size 35-70) silica under a positive pressure. The eluent is quoted as a percentage. The temperature of the reaction mixture was monitored using a calibrated infrared temperature control under the reaction vessel. Solvents for starting material preparation were dried before use unless otherwise stated. Anhydrous solvents used for the coupling reaction were bought from Sigma-Aldrich and used as received. All other chemicals were purchased from a chemical supplier and used as received.

Preparation of starting materials

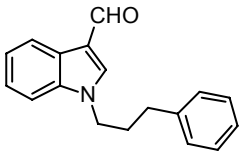


X= CHO, CN, CO_2Me, NO_2
Y1= C, N

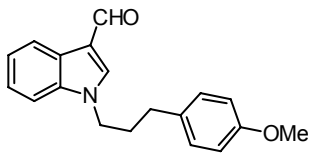
Z= Br, Cl
Y^2= C, O
Y^3= C, O, NMe, NMs

Scheme S1. Preparation of N-alkyl indole starting materials. All substrates for Charts 1 and 3 were prepared according to this scheme.

General procedure A for indole alkylation: Synthesis of 1-(3-Phenyl-propyl)-1H-indole-3-carbaldehyde, 1a.[1] To a solution of NaH (331 mg, 8.27 mmol, 60 wt% in mineral oil) in dry DMF (20 mL) at 0 ºC was added a solution of indole-3-carboxyaldehyde (1 g, 6.89 mmol) in dry DMF (2 mL), dropwise. The mixture was stirred at this temperature for 20 min. To the reaction mixture was added dropwise a solution of 1-bromo-3-phenylpropane (1.25 mL, 8.27 mmol) in DMF (2 mL) and the resulting solution was stirred at room temperature for 16 hr. Saturated aqueous $NaHCO_3$ was added and the mixture then extracted with EtOAc. The organic layer was washed with brine and dried over $MgSO_4$. Filtration, concentration in vacuo and purification by silica gel chromatography (*n*-hexane/Et_2O = 4/6) gave the desired product in a 92% yield as a white solid. Mp (Et_2O) = 48 °C. R_f (DCM) = 0.3. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.02 (s, 1H), 8.44 – 8.25 (m, 1H), 7.71 (s, 1H), 7.40 – 7.31 (m, 5H), 7.27 (ddd, *J* = 9.3, 4.7, 3.0 Hz, 1H), 7.23 – 7.14 (m, 2H), 4.21 (t, *J* = 7.2 Hz, 2H), 2.71 (t, *J* = 7.5 Hz, 2H), 2.35 – 2.22 (m, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 184.5 (quat), 140.1 (quat), 138.3 (CH), 137.2 (quat), 128.7 (2CH), 128.4 (2CH), 126.5 (CH), 125.5 (quat), 124.0 (CH), 123.0 (CH), 122.2 (CH), 118.1 (quat), 110.1 (CH), 46.5 (CH_2), 32.8 (CH_2), 30.9 (CH_2).



1-[3-(4-Methoxy-phenyl)-propyl]-1H-indole-3-carbaldehyde, 1b. Following general procedure A, using indole-3-carboxyaldehyde (697 mg, 4.80 mmol), NaH (209 mg, 5.23 mmol, 60 wt% in mineral oil) and 1-(3-bromopropyl)-4-methoxybenzene (1.0 g, 4.36 mmol). White solid; yield: 66%. Mp (Et_2O) = 83 °C. Rf [EtOAc/hexane (35:65)] = 0.34. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.50 – 8.24 (m, 1H), 7.70 (s, 1H), 7.40 – 7.30 (m, 3H), 7.16 – 7.04 (m, 2H), 6.96 – 6.83 (m, 2H), 4.19 (t, *J* = 7.2 Hz, 2H), 3.83 (s, 3H), 2.65 (t, *J* = 7.5 Hz, 2H), 2.33 – 2.18 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.5 (quat), 158.2 (quat), 138.2 (CH), 137.2 (quat), 132.1 (quat), 129.3 (2CH), 125.5 (quat), 124.0 (CH), 122.9 (CH), 122.2 (CH), 118.1 (quat), 114.1 (2CH), 110.1 (CH), 55.3 (CH_3), 46.4 (CH_2), 31.8 (CH_2), 31.1 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{19}H_{20}NO_2$: 294.1489; found 294.1487.



[1] Fiumana, A.; Jones, K. *Tetrahedron Lett.,* **2000**, *41*, 4209–4211.

1-[3-(4-Trifluoromethyl-phenyl)-propyl]-1H-indole-3-carbaldehyde, 1c. Following general procedure A, using indole-3-carboxyaldehyde (514 mg, 3.54 mmol), NaH (142 mg, 3.54 mmol, 60 wt% in mineral oil) and 1-(3-bromo-propyl)-4-trifluoromethyl-benzene (860 mg, 3.22 mmol). White solid; yield: 88%. Mp (Et_2O) = 53°C. Rf [Et_2O/hexane (7:3)] = 0.34. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.01 (s, 1H), 8.43 – 8.29 (m, 1H), 7.70 (s, 1H), 7.57 (d, *J* = 8.1 Hz, 2H), 7.39 – 7.30 (m, 3H), 7.28 (d, *J* = 8.0 Hz, 2H), 4.21 (t, *J* = 7.1 Hz, 2H), 2.79 – 2.67 (m, 2H), 2.35 – 2.20 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.5 (quat), 144.4 (d, *J* = 1.0 Hz, quat), 138.1 (CH), 137.1 (quat), 128.7 (2CH), 125.6 (q, *J* = 3.7 Hz, CH), 125.5 (quat), 124.2 (d, *J* = 271.9 Hz, quat), 124.1 (CH), 123.0 (CH), 122.2 (CH), 118.3 (quat), 110.0 (CH), 46.4 (CH_2), 32.6 (CH_2), 30.7 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{19}H_{17}NO_2F_3$: 332.1257; found 332.1256.

1-[3-(3-Fluoro-phenyl)-propyl]-1H-indole-3-carbaldehyde, 1d. Following general procedure A, using indole-3-carboxyaldehyde (280 mg, 1.93 mmol), NaH (78 mg, 1.93 mmol, 60 wt% in mineral oil) and 1-(3-bromo-propyl)-3-fluoro-benzene (350 mg, 1.60 mmol). White solid; yield: 72%. Mp (Et_2O) = 36 °C. Rf [Et_2O/hexane (7:3)] = 0.42. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.42 – 8.27 (m, 1H), 7.71 (s, 1H), 7.40 – 7.32 (m, 3H), 7.29 (td, *J* = 8.2, 6.1 Hz, 1H), 6.95 (td, *J* = 8.1, 2.6 Hz, 2H), 6.90 (dd, *J* = 9.8, 1.8 Hz, 1H), 4.22 (t, *J* = 7.2 Hz, 2H), 2.70 (t, *J* = 7.6 Hz, 2H), 2.38 – 2.19 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.5 (quat), 163.0 (d, *J* = 246.2 Hz, quat), 142.7 (d, *J* = 7.1 Hz, quat), 138.1 (CH), 137.1 (quat), 130.2 (d, *J* = 8.4 Hz, CH), 125.5 (quat), 124.1 (CH), 124.02 (d, *J* = 2.8 Hz, CH), 123.0 (CH), 122.2 (CH), 118.3 (quat), 115.19 (d, *J* = 21.1 Hz, CH), 113.4 (d, *J* = 21.0 Hz, CH), 110.0 (CH), 46.4 (CH_2), 32.5 (CH_2), 30.7 (CH_2).). HRMS (ES^+) cald. for $(M+H)^+$ $C_{18}H_{17}NO_2F$: 282.1289; found 282.1286.

1-Benzyloxymethyl-1H-indole-3-carbaldehyde, 1e. Following general procedure A using indole-3-carboxyaldehyde (1.0 g, 6.89 mmol), NaH (303 mg, 7.57 mmol, 60 wt% in mineral oil) and benzyl chloromethyl ether (1.15 mL, 8.26 mmol). White solid; yield: 78%. Mp (Et_2O) = 79 °C. R_f [hexane / Et_2O (1:1)] = 0.12. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.06 (s, 1H), 8.50 – 8.22 (m, 1H), 7.77 (s, 1H), 7.56 (dd, *J* = 6.0, 2.6 Hz, 1H), 7.43 – 7.34 (m, 5H), 7.32 – 7.27 (m, 2H), 5.60 (s, 2H), 4.49 (s, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 185.0 (quat), 138.3 (CH), 137.3 (quat), 136.2 (quat), 128.7 (2CH), 128.4 (2CH), 128.0 (CH), 125.6 (quat), 124.6 (CH), 123.5 (CH), 122.2 (CH), 119.1 (quat), 110.8 (CH), 75.8 (CH_2), 70.4 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{17}H_{16}NO_2$: 266.1176; found 266.1175.

1-Benzyloxymethyl-5-methoxy-1H-indole-3-carbaldehyde, 1f. Following general procedure A, using methyl 7-methoxy-indole-3-carboxylate (875 mg, 5.0 mmol), NaH (220 mg, 5.5 mmol, 60 wt% in mineral oil) and benzyl chloromethyl ether (1.3 mL, 9.16 mmol). White solid; yield: 92%. Mp (Et_2O) = 90 °C. Rf [hexane / Et_2O (2:8)] = 0.33. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.83 (d, *J* = 2.5 Hz, 1H), 7.72

(s, 1H), 7.43 (d, *J* = 8.9 Hz, 1H), 7.41 – 7.32 (m, 3H), 7.29 (dd, *J* = 5.4, 2.7 Hz, 2H), 7.02 (dd, *J* = 8.9, 2.5 Hz, 1H), 5.57 (s, 2H), 4.48 (s, 2H), 3.93 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.0 (quat), 157.0 (quat), 138.4 (CH), 136.1 (quat), 132.0 (quat), 128.7 (2CH), 128.4 (CH), 128.0 (2CH), 126.4 (quat), 118.9 (quat), 115.0 (CH), 111.7 (CH), 103.4 (CH), 75.9 (CH_2), 70.3 (CH_2), 55.8 (CH_3). HRMS (ES^+) cald. for $(M+H)^+$ $C_{18}H_{18}NO_3$: 296.1281; found 296.1284.

1-(2-Phenoxy-ethyl)-1H-indole-3-carbaldehyde, 1g. Following general procedure A, using indole-3-carboxyaldehyde (146.1 mg, 1.0 mmol), NaH (44 mg, 1.1 mmol, 60 wt% in mineral oil) and (2-bromo-ethoxy)-benzene (200 mg, 1.0 mmol). White solid; yield: 76%. Mp (Et_2O) = 117 °C. Rf [hexane/DCM (7:3)] = 0.59. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.04 (s, 1H), 8.36 (dd, *J* = 7.0, 1.1 Hz, 1H), 7.89 (s, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.37 (dtd, *J* = 16.0, 7.2, 1.2 Hz, 2H), 7.33 – 7.25 (m, 2H), 7.00 (t, *J* = 7.4 Hz, 1H), 6.87 (dd, *J* = 8.7, 0.9 Hz, 2H), 4.59 (t, *J* = 5.2 Hz, 2H), 4.35 (t, *J* = 5.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.7 (quat), 157.9 (quat), 139.2 (CH), 137.3 (quat), 129.7 (2CH), 125.4 (quat), 124.1 (CH), 123.1 (CH), 122.3 (CH), 121.7 (CH), 118.5 (quat), 114.5 (2CH), 109.8 (CH), 66.0 (CH_2), 46.5 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{17}H_{16}NO_2$: 266.1176; found 266.1172.

1-[2-(Methyl-phenyl-amino)-ethyl]-1H-indole-3-carbaldehyde, 1h. Following general procedure A, using indole-3-carboxyaldehyde (113 mg, 0.78 mmol), NaH (32 mg, 0.78 mmol, 60 wt% in mineral oil) and (2-bromo-ethyl)-methyl-phenyl-amine (167 mg, 0.78 mmol). White solid; yield: 83%. Mp (Et_2O) = 107 °C. Rf [DCM] = 0.34. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.97 (s, 1H), 8.42 – 8.29 (m, 1H), 7.60 (s, 1H), 7.45 – 7.33 (m, 3H), 7.30 (dd, *J* = 8.7, 7.3 Hz, 2H), 6.81 (t, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 8.2 Hz, 2H), 4.41 (t, *J* = 5.9 Hz, 2H), 3.81 (t, *J* = 5.9 Hz, 2H), 2.64 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.6 (quat), 147.9 (quat), 139.0 (CH), 137.0 (quat), 129.6 (2CH), 125.5 (quat), 124.2 (CH), 123.1 (CH), 122.4 (CH), 118.6 (quat), 117.3 (CH), 112.1 (CH), 109.8 (CH), 52.3 (CH_2), 44.8 (CH_2), 39.0 (CH_3). HRMS (ES^+) cald. for $(M+H)^+$ $C_{18}H_{19}N_2O$: 279.1492; found 279.1491.

N-(3,5-Dimethoxy-phenyl)-N-[2-(3-formyl-indol-1-yl)-ethyl]-methanesulfonamide, 1i. Following general procedure A, using indole-3-carboxyaldehyde (213 mg, 1.47 mmol), NaH (65 mg, 1.61 mmol, 60 wt% in mineral oil) and N-(2-Bromo-ethyl)-N-(3,5-dimethoxy-phenyl)-methanesulfonamide (505 mg, 1.50 mmol). White solid; yield: 60%. Mp (Et_2O) = 127 °C. Rf [DCM / EtOAc (9:1)] = 0.33. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.95 (s, 1H), 8.27 (dd, *J* = 6.5, 1.6 Hz, 1H), 7.69 (s, 1H), 7.43 – 7.21 (m, 3H), 6.37 (t, *J* = 2.2 Hz, 1H), 6.24 (d, *J* = 2.2 Hz, 2H), 4.42 (t, *J* = 6.5 Hz, 2H), 4.09 (t, *J* = 6.5 Hz, 2H), 3.67 (s, 6H), 2.85 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.6 (quat), 161.2 (quat), 140.9 (quat), 138.7 (CH), 137.1 (quat), 125.2 (quat), 124.3 (CH), 123.1 (CH), 122.2 (CH), 118.6 (quat), 110.0 (quat), 109.9 (CH), 106.1

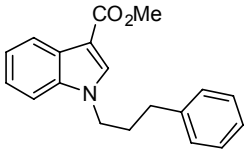
(2CH), 100.3 (CH), 55.5 ($2CH_3$), 50.5 (CH_2), 46.6 (CH_2), 37.1 (CH_3). HRMS (ES^+) cald. for $(M+H)^+$ $C_{20}H_{23}O_5N_2S$: 403.1322; found 403.1332.

1-(3-Phenyl-propyl)-1H-indole-3-carbonitrile, 1j. Following general procedure A, using 3-cyanoindole (300 mg, 2.11 mmol), NaH (93 mg, 2.32 mmol, 60 wt% in mineral oil) and bromo-3-phenylpropane (353 uL, 2.32 mmol). White solid; yield: 74%. Mp (Et_2O) = 50°C. Rf [hexane / Et_2O (1:1)] = 0.30. ^1H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 7.6 Hz, 1H), 7.60 (s, 1H), 7.40 – 7.30 (m, 5H), 7.30 – 7.24 (m, 1H), 7.19 (d, *J* = 7.2 Hz, 2H), 4.19 (t, *J* = 7.2 Hz, 2H), 2.69 (t, *J* = 7.5 Hz, 2H), 2.34 – 2.19 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.0 (quat), 135.3 (quat), 134.6 (CH), 128.7 (2CH), 128.3 (2CH), 128.0 (quat), 126.5 (CH), 123.8 (CH), 122.2 (CH), 120.0 (CH), 116.0 (quat), 110.5 (CH), 85.7 (quat), 46.4 (CH_2), 32.7 (CH_2), 31.0 (CH_2). HRMS (ES^+) cald. for $(M+NH_4)^+$ $C_{18}H_{20}N_3$: 278.1652; found 278.1649.

1-(3-Phenyl-propyl)-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile, 1k. Following general procedure A, using 7-azaindole-3-carbonitrile (300 mg, 2.1 mmol), NaH (92 mg, 2.30 mmol, 60 wt% in mineral oil) and bromo-3-phenylpropane (350 uL, 2.30 mmol). White solid; yield: 73%. Mp (Et_2O) = 65 °C. Rf [hexane / Et_2O (1:1)] = 0.23. ^1H NMR (500 MHz, $CDCl_3$) δ 8.48 (dd, *J* = 4.7, 1.4 Hz, 1H), 8.09 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.73 (s, 1H), 7.35 – 7.25 (m, 3H), 7.23 (t, *J* = 7.4 Hz, 1H), 7.18 (d, *J* = 7.2 Hz, 2H), 4.39 (t, *J* = 7.2 Hz, 2H), 2.69 (d, *J* = 7.9 Hz, 2H), 2.38 – 2.20 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.5 (quat), 145.2 (CH), 140.3 (quat), 135.0 (CH), 128.6 (2CH), 128.3 (2CH), 128.3 (CH), 126.3 (CH), 120.2 (quat), 118.2 (CH), 115.2 (quat), 84.3 (quat), 45.1 (CH_2), 32.8 (CH_2), 31.3 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{17}H_{16}N_3$: 262.1339; found 262.1335.

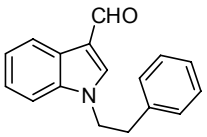
3-Nitro-1-(3-phenyl-propyl)-1H-pyrrolo[2,3-b]pyridine, 1l. Following general procedure A, using 3-nitro-7-azaindole (250 mg, 1.53 mmol), NaH (67.4 mg, 1.68 mmol, 60 wt% in mineral oil) and bromo-3-phenylpropane (255 uL, 1.68 mmol). White solid; yield: 56%. Mp (Et_2O) = 91 °C. Rf [DCM] = 0.42. ^1H NMR (500 MHz, $CDCl_3$) δ 8.57 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.49 (dd, *J* = 4.7, 1.6 Hz, 1H), 8.20 (s, 1H), 7.39 (dd, *J* = 8.0, 4.7 Hz, 1H), 7.35 – 7.27 (m, 2H), 7.25 – 7.21 (m, 1H), 7.19 (dd, *J* = 7.8, 0.9 Hz, 2H), 4.42 (t, *J* = 7.2 Hz, 2H), 2.73 (t, *J* = 7.8 Hz, 2H), 2.43 – 2.26 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.8 (quat), 145.6 (CH), 140.1 (quat), 130.0 (CH), 129.4 (CH), 128.6 (2CH), 128.3 (2CH), 127.0 (quat) 126.4 (CH), 120.0 (CH), 113.9 (quat), 45.3 (CH_2), 32.8 (CH_2), 31.1 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{16}H_{16}N_3O_2$: 282.1237; found 282.1236.

1-(3-Phenyl-propyl)-1H-indole-3-carboxylic acid methyl ester (1m, not shown in paper).[2] Following



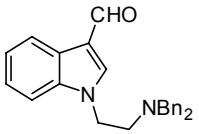
general procedure A, using methyl indole-3-carboxylate (2.0 g, 11.4 mmol), NaH (503 mg, 12.5 mmol, 60 wt% in mineral oil) and bromo-3-phenylpropane (2.0 mL, 13.11 mmol). White solid; yield: 81%. Mp (Et_2O) = 54°C. Rf [hexane / Et_2O (1:1)] = 0.38. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 – 8.15 (m, 1H), 7.85 (s, 1H), 7.36 – 7.29 (m, 5H), 7.25 (dd, *J* = 10.2, 4.5 Hz, 1H), 7.19 (dd, *J* = 7.9, 0.9 Hz, 2H), 4.18 (t, *J* = 7.2 Hz, 2H), 3.95 (s, 3H), 2.75 – 2.61 (m, 2H), 2.26 (dd, *J* = 7.9, 6.6 Hz, 2H).

1-Phenethyl-1H-indole-3-carbaldehyde (1n, not shown in paper). Following general procedure A, using



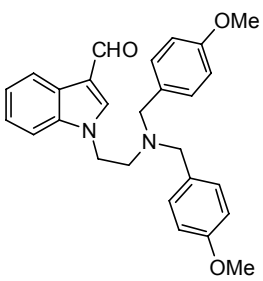
indole-3-carboxyaldehyde (520 mg, 3.58 mmol), NaH (158 mg, 3.95 mmol, 60 wt% in mineral oil) and (2-bromoethyl) benzene (533 uL, 3.94 mmol). White solid; yield: 88%. Mp (Et_2O) = 65 °C. Rf [Et_2O/hexane (8:2)] = 0.40. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.91 (s, 1H), 8.35 (dd, *J* = 6.3, 2.3 Hz, 1H), 7.44 – 7.40 (m, 2H), 7.40 – 7.33 (m, 2H), 7.33 – 7.24 (m, 3H), 7.08 – 7.02 (m, 2H), 4.43 (t, *J* = 7.1 Hz, 2H), 3.18 (t, *J* = 7.1 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.5 (quat), 138.7 (CH), 137.5 (quat), 136.9 (quat), 128.9 (2CH), 128.7 (2CH), 127.1 (CH), 125.5 (quat), 124.0 (CH), 123.0 (CH), 122.3 (CH), 118.0 (quat), 110.0 (CH), 49.0 (CH_2), 36.1 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{17}H_{16}NO$: 250.1226; found 250.1230.

1-(2-Dibenzylamino-ethyl)-1*H*-indole-3-carbaldehyde, 5b. Following general procedure A, using indole-



3-carboxyaldehyde (156 mg, 1.07 mmol), NaH (47 mg, 1.18 mmol, 60 wt% in mineral oil) and dibenzyl-(2-bromo-ethyl)-amine (295 mg, 0.97 mmol). White solid; yield: 77%. Mp (Et_2O) = 88 °C. Rf [Et_2O/hexane (7:3)] = 0.68. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.97 (s, 1H), 8.31 (d, *J* = 7.9 Hz, 1H), 7.54 (s, 1H), 7.37 – 7.14 (m, 12H), 7.01 (d, *J* = 8.2 Hz, 1H), 4.12 (t, *J* = 6.4 Hz, 2H), 3.68 (s, 4H), 2.93 (t, *J* = 6.4 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.6 (quat), 139.1 (CH), 138.6 (quat), 137.2 (quat), 128.7 (4CH), 128.4 (4CH), 127.3 (2CH), 125.3 (quat), 123.8 (CH), 122.8 (CH), 122.1 (CH), 118.0 (quat), 109.8 (CH), 59.4 ($2CH_2$), 52.4 (CH_2), 45.6(CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{25}H_{25}N_2O$: 369.1961; found 369.1964.

1-{2-[Bis-(4-methoxy-benzyl)-amino]-ethyl}-1*H*-indole-3-carbaldehyde, 5c. Following general procedure



A, using indole-3-carboxyaldehyde (223 mg, 1.53 mmol), NaH (63 mg, 1.55 mmol, 60 wt% in mineral oil) and (2-Bromo-ethyl)-bis-(4-methoxy-benzyl)-amine (508 mg, 1.40 mmol). Yellow oil; yield: 68%. Rf [DCM] = 0.37. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.99 (s, 1H), 8.31 (d, *J* = 7.9 Hz, 1H), 7.56 (s, 1H), 7.35 – 7.24 (m, 1H), 7.24 – 7.14 (m, 1H), 7.09 (d, *J* = 8.6 Hz, 4H), 7.02 (d, *J* = 8.2 Hz, 1H), 6.77 (d, *J* = 8.6 Hz, 4H), 4.08 (t, *J* = 6.3 Hz, 2H), 3.80 (s, 6H), 3.59 (s, 4H), 2.89 (t, *J* = 6.3 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.5 (quat), 158.8 (2 quat), 139.3 (CH), 137.2 (quat), 130.6 (2 quat),

[2] Vechorkin, O.; Proust, V.; Hu, X. *J. Am. Chem. Soc.* **2009**, *131*, 9756–976.

129.8 (4 CH), 125.3 (quat), 123.7 (CH), 122.7 (CH), 122.0 (CH), 117.9 (quat), 113.7 (4 CH), 109.9 (CH), 58.7 (2 CH_2), 55.3 (2 CH_3), 51.9 (CH_2), 45.7 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{27}H_{29}N_2O_3$: 429.2172; found 429.2172.

1-{(S)-2-[Bis-(4-methyl-benzyl)-amino]-propyl}-1*H*-indole-3-carbaldehyde, 5d. Following general procedure A, using indole-3-carboxyaldehyde (330 mg, 2.27 mmol), NaH (100 mg, 2.50 mmol, 60 wt% in mineral oil) and ((S)-2-Bromo-1-methyl-ethyl)-bis-(4-methyl-benzyl)-amine (692 mg, 2.00 mmol). Yellow oil; yield: 54%. Rf [Et2O/Hexane (1:1)] = 0.36. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.98 (s, 1H), 8.34 (d, *J* = 7.9 Hz, 1H), 7.54 (s, 1H), 7.29 (dd, *J* = 9.1, 5.9 Hz, 1H), 7.18 – 7.08 (m, 1H), 7.00 (q, *J* = 8.1 Hz, 8H), 6.93 (d, *J* = 8.3 Hz, 1H), 4.23 (dd, *J* = 14.3, 8.8 Hz, 1H), 3.97 (dd, *J* = 13.7, 6.7 Hz, 1H), 3.81 (d, *J* = 13.7 Hz, 2H), 3.51 – 3.28 (m, 3H), 2.31 (s, 6H), 1.14 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.6 (quat), 139.9 (CH), 137.3 (quat), 136.6 (2 quat), 136.0 (2 quat), 127.0 (4 CH), 128.3 (4 CH), 125.3 (quat), 123.7 (CH), 122.6 (CH), 122.1 (CH), 117.7 (quat), 110.0 (CH), 53.1 (2 CH_2), 51.5 (CH), 50.6 (CH_2), 21.0 (2 CH_3), 10.6 (CH_3). HRMS (ES^+) cald. for $(M+H)^+$ $C_{28}H_{31}N_2O$: 411.2431; found 411.2430.

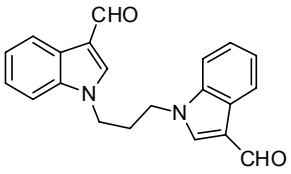
1-{2-[(4–Fluoro-benzyl)-(4-methoxy-benzyl)-amino]-ethyl}-1*H*-indole-3-carbaldehyde, 5e. Following general procedure A, using indole-3-carboxyaldehyde (130 mg, 0.89 mmol), NaH (36 mg, 0.89 mmol, 60 wt% in mineral oil) and (2-bromo-ethyl)-(4-fluoro-benzyl)-(4-methoxy-benzyl)-amine (283 mg, 0.81 mmol). Yellow oil; yield: 57%. Rf [EtOAc/hexane (7:3)] = 0.49. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.99 (s, 1H), 8.32 (d, *J* = 7.9 Hz, 1H), 7.56 (s, 1H), 7.29 (d, *J* = 6.7 Hz, 1H), 7.25 – 7.17 (m, 1H), 7.15 – 7.06 (m, 4H), 7.02 (d, *J* = 7.9 Hz, 1H), 6.89 (t, *J* = 8.7 Hz, 2H), 6.79 (d, *J* = 8.7 Hz, 2H), 4.11 (t, *J* = 6.3 Hz, 2H), 3.80 (s, 3H), 3.59 (s, 4H), 2.89 (t, *J* = 6.3 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.4 (quat), 161.9 (d, *J* = 245.4 Hz, quat), 158.9 (quat), 139.1 (CH), 137.1 (quat), 134.3 (quat), 134.3 (quat), 130.3 (quat), 130.0 (d, *J* = 7.9 Hz, 2CH), 129.8 (2CH), 125.3 (quat), 123.7 (CH), 122.8 (CH), 122.1 (CH), 118.0 (quat), 115.1 (d, *J* = 21.3 Hz, 2CH), 113.8 (2CH), 109.8 (CH), 58.5 (CH_2), 58.4 (CH_2), 55.2 (CH_3), 52.0 (CH_2), 45.6 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{26}H_{26}N_2O_2F$: 417.1973; found 417.1972.

1-[2-(Benzyl-methyl-amino)-ethyl]-1*H*-indole-3-carbaldehyde, 5f (not in paper). Following general procedure A, using indole-3-carboxyaldehyde (200 mg, 1.38 mmol), NaH (61 mg, 1.51 mmol, 60 wt% in mineral oil) and Benzyl-(2-bromo-ethyl)-methyl-amine (409 mg, 1.79 mmol). Yellow oil; yield: 78%. Rf [EtOAc/Hexane (1:1)] = 0.23. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.02 (s, 1H), 8.34 (dd, *J* = 6.5, 1.9 Hz, 1H), 7.76 (s, 1H), 7.37 – 7.25 (m, 3H), 7.25 – 7.19 (m, 3H), 7.14 (dd, *J* = 6.8, 2.6 Hz, 2H), 4.25 (t, *J* = 6.3 Hz, 2H), 3.56 (s, 2H), 2.84 (t, *J* = 6.3 Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.6 (quat), 139.2 (CH), 138.3 (quat), 137.3 (quat), 128.7 (2 CH), 128.3 (2CH), 127.2 (CH), 125.4 (quat), 123.8 (CH), 122.8 (CH), 122.1 (CH),

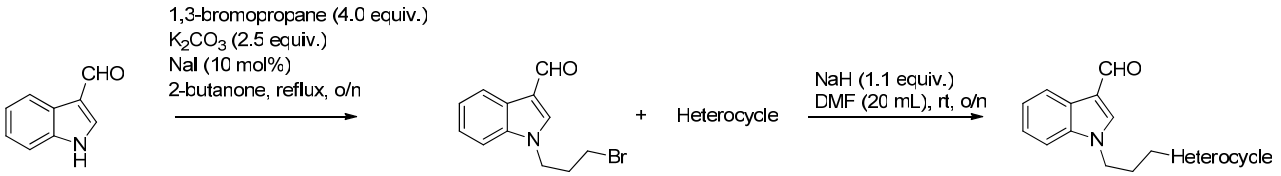
118.0 (quat), 109.8 (CH), 62.7 (CH_2), 55.6 (CH_2), 45.2 (CH_2), 42.6 (CH_3). HRMS (ES^+) cald. for $(M+H)^+$ $C_{19}H_{21}N_2O$: 293.1648; found 293.1649.

Synthesis of heteroaromatic-containing starting materials (Chart 2)

1,1'-(propane-1,3-diyl)bis(1H-indole-3-carbaldehyde), 3a. In a 100 mL round bottom flask was introduced

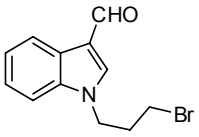


the indole-3-carboxyaldehyde (600 mg, 4.13 mmol, 2.2 equiv.), K_2CO_3 (656 mg, 4.74 mmol, 2.5 equiv.), 1,3-dibromopropane (222 uL, 1.9 mmol, 1.0 equiv.), a catalytic amount of NaI (29 mg, 10 mol%) and 40 mL of 2-butanone. The reaction mixture was refluxed for 16 hr and cooled down to room temperature. The inorganic salts were removed by filtration and the resulting filtrate was concentrated under vacuo. The crude mixture was purified by silica gel chromatography (ethyl acetate) and the final product was isolated in 81% yield as a white solid. Mp (Et_2O) = 157 °C. Rf [EtOAc/DCM (3:7)] = 0.30. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.01 (s, 2H), 8.36 (dd, *J* = 6.2, 2.8 Hz, 2H), 7.65 (s, 2H), 7.41 – 7.32 (m, 4H), 7.24 (dd, *J* = 6.2, 2.5 Hz, 2H), 4.25 (t, *J* = 6.9 Hz, 4H), 2.60 (p, *J* = 6.9 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.5 (2 quat), 137.5 (2 CH), 136.9 (2 quat), 125.5 (2 quat), 124.4 (2 CH), 123.3 (2 CH), 122.5 (2 CH), 118.7 (2 quat), 109.7 (2 CH), 44.0 ($2CH_2$), 29.5 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{21}H_{19}N_2O_2$: 331.1441; found 331.1438.



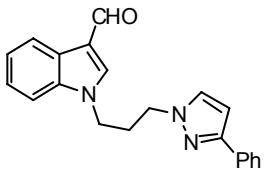
Scheme S2. Synthesis of N-alkyl indole substrates containing heteroaromatic groups.

1-**(3-Bromo-propyl)-1H-indole-3-carbaldehyde**[3] In a 500 mL round bottom flask was introduced the

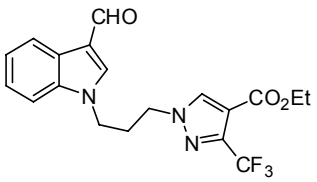


indole-3-carboxyaldehyde (5.0 g, 34.4 mmol, 1.0 equiv.), K_2CO_3 (12 g, 86.0 mmol, 2.5 equiv.), 1,3-dibromopropane (14 mL, 138 mmol, 4.0 equiv.), catalytic amount of NaI (516 mg, 10 mol%) and 250 mL of 2-butanone. The reaction mixture was refluxed for 16 hrs and cooled down to room temperature. The inorganic salts were removed by filtration and the resulting filtrate was concentrated under vacuo. The crude mixture was purified by silica gel chromatography (DCM) and the final product was obtained in 85% yield as yellow liquid. Rf [DCM] = 0.30. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.33 (dd, *J* = 6.6, 2.0 Hz, 1H), 7.77 (d, *J* = 3.2 Hz, 1H), 7.43 (dd, *J* = 6.8, 1.7 Hz, 1H), 7.39 – 7.31 (m, 2H), 4.40 (t, *J* = 6.6 Hz, 2H), 3.41 – 3.26 (m, 2H), 2.51 – 2.30 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.6 (quat), 138.6 (CH), 137.0 (quat), 125.5 (quat), 124.2 (CH), 123.1 (CH), 122.3 (CH), 118.3 (quat), 110.0 (CH), 44.9 (CH_2), 32.0 (CH_2), 29.9 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{12}H_{13}NOBr$: 266.0175; found 266.0170.

[3] Leigh, D. A.; Lusby, P. J.; McBurney, R. T.; Morelli, A.; Slawin, A. M. Z. Thomson, A. R.; Walker, D. B. *J. Am. Chem. Soc*., **2009**, *131*, 3762–3771.

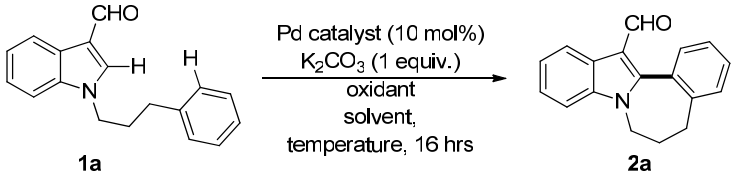
General procedure B for indole alkylation: Synthesis of 1-[3-(3-Phenyl-pyrazol-1-yl)-propyl]-1H-indole-3-carbaldehyde, 3b.  Following general procedure B, using 3-phenyl-1H-pyrazole (304 mg, 2.11 mmol), NaH (93 mg, 2.32 mmol, 60 wt% in mineral oil) and 1-(3-bromo-propyl)-1H-indole-3-carbaldehyde (673 mg, 2.53 mmol). White solid; yield: 51%. Mp (Et_2O) = 96 °C. Rf [Et_2O/hexane (8:2)] = 0.22. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.02 (s, 1H), 8.36 (d, *J* = 4.6 Hz, 1H), 8.06 – 7.72 (m, 3H), 7.57 – 7.30 (m, 7H), 6.63 (s, 1H), 4.28 (t, *J* = 6.5 Hz, 2H), 4.16 (t, *J* = 5.9 Hz, 2H), 2.64 – 2.38 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.6 (quat), 151.9 (quat), 139.0 (CH), 137.1 (quat), 133.4 (quat), 130.9 (CH), 128.8 (2CH), 127.9 (CH), 125.6 (2CH), 125.5 (quat), 124.1 (CH), 123.1 (CH), 122.3 (CH), 118.3 (quat), 110.1 (CH), 103.1 (CH), 48.6 (CH_2), 44.1 (CH_2), 30.2(CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{21}H_{20}N_3O$: 330.1601; found 330.1600.

1-[3-(1H-Benzoimidazol-2-yl)-propyl]-1H-indole-3-carbaldehyde, 3c. To a solution of NaH (93 mg, 2.32 mmol, 60 wt% in mineral oil) in dry DMF (20 mL) at 0 ºC was added dropwise a solution of benzimidazole (250 mg, 2.11 mmol) in dry DMF (2 mL). The mixture was stirred at this temperature for 20 min. To the reaction mixture was added dropwise a solution of 1-(3-bromo-propyl)-1H-indole-3-carbaldehyde (673 mg, 2.53 mmol) in DMF (2 mL) and the resulting solution was stirred at room temperature for 16 hr. Saturated aqueous $NaHCO_3$ was added and the mixture then extracted with ethyl acetate. The organic layer was washed with brine and dried over $MgSO_4$. Filtration, concentration in vacuo and purification by silica gel chromatography (EA/MeOH = 9/1) gave the desired product in 86% yield as a white solid. Mp (Et_2O) = 107 °C. Rf [EtOAc/MeOH (85:15)] = 0.22. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.02 (s, 1H), 8.42 – 8.27 (m, 1H), 8.01 (s, 1H), 7.87 (dd, *J* = 6.4, 2.5 Hz, 1H), 7.67 (s, 1H), 7.40 – 7.23 (m, 6H), 4.25 (m, 4H), 2.60 (p, *J* = 6.9 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.5 (quat), 143.6 (quat), 142.6 (CH), 137.7 (CH), 136.9 (quat), 133.3 (quat), 125.5 (quat), 124.4 (CH), 123.5 (CH), 123.3 (CH), 122.8 (CH), 122.5 (CH), 120.6 (CH), 118.7 (quat), 109.7 (CH), 109.4 (CH), 44.1 (CH_2), 42.0 (CH_2), 29.4 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{19}H_{18}N_3O$: 304.1444; found 304.1442.

1-[3-(3-Formyl-indol-1-yl)-propyl]-3-trifluoromethyl-1H-pyrazole-4-carboxylic acid ethyl ester, 3d.  Following general procedure B, using ethyl 3- (trifluoromethyl)-1H-pyrazole-4-carboxylate (439 mg, 2.11 mmol), NaH (93 mg, 2.32 mmol, 60 wt% in mineral oil) and 1-(3-bromo-propyl)-1H-indole-3-carbaldehyde (673 mg, 2.53 mmol). White solid; yield: 48%. Mp (Et_2O) = 75 °C. Rf [Et_2O/hexane (8:2)] = 0.23. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.94 (s, 1H), 8.28 (d, *J* = 7.1 Hz, 1H), 7.95 (s, 1H), 7.78 (s, 1H), 7.47 – 7.20 (m, 3H), 4.41 – 4.21 (m, 4H), 4.16 (t, *J* = 6.5 Hz, 2H), 2.63 – 2.39 (m, 2H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.6 (quat), 160.6 (quat), 141.9 (q, *J* = 38.5 Hz, quat), 138.6 (CH), 136.9 (quat), 135.9 (CH), 125.4 (quat), 124.3 (CH), 123.1 (CH), 122.2 (CH), 121.5 (quat) 118.4 (quat), 113.4 (quat), 109.9 (CH), 61.0 (CH_2), 49.6 (CH_2), 43.9 (CH_2), 29.7 (CH_2), 14.0 (CH_3). HRMS (ES^+) cald. for $(M+H)^+$ $C_{19}H_{19}N_3O_3F_3$: 394.1373; found 394.1371.

Optimisation of oxidative coupling

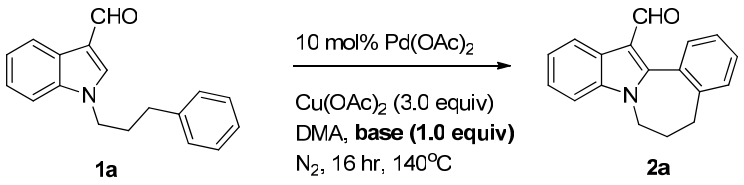
Initial screen:



entry	oxidant (equiv)	solvent (ratio)	temp.(°C)	yield[a] (%)
1	Ag_2CO_3 (2.0)	MeCN	80	10
2	$Cu(OAc)_2$ (2.0)	MeCN	80	12
3	$Cu(OAc)_2$ (3.0)	PhMe	110	-
4	$Cu(OAc)_2$ (3.0)	dioxane	110	trace
5	$Cu(OAc)_2$ (3.0)	DMA	140	73
6	**$Cu(OAc)_2$ (3.0)**	**DMA**	**85**	**77**
7	$Cu(OAc)_2$ (3.0)	Dioxane / DMA (1:1)	120	17
8	$Cu(OAc)_2$ (3.0)	Toluene / DMA (9:1)	120	trace
9	$Cu(OAc)_2$ (2.0)	DMA	85	55
10[b]	O_2 (1 atm)	DMA	140	-
11[c]	$FeCl_3$ (1.0)	DMA	140	-
12[b]	$Cu(OAc)_2$ (3.0)	DMA	140	70

Table S1. Reaction conditions: **1a** (0.2 mmol), $Pd(OAc)_2$ (0.02 mmol, 10 mol %), oxidant (0.2 -0.6 mmol), solvent (1.0 mL), N_2, 16 hr. [a] Isolated yield. [b] $PdCl_2$ used as catalyst. [c] No Pd catalyst.

Screening of bases



Entry	Base	Product	Entry	Base	Product
1	-	38% isol.	4	Cs_2CO_3	75% isol.
2	**K_2CO_3**	**73% isol.**	5	CsOPiv	<70%
3	KOAc	70% isol.	6	NaO*t*Bu	<70%

Table S2. The amount of base was varied in order to determine the optimal quantity for the reaction.

The following graph shows the observed ratio product / starting material determined by LCMS analysis by dividing the UV peak area of product formed by the UV peak area of starting material left after reaction.

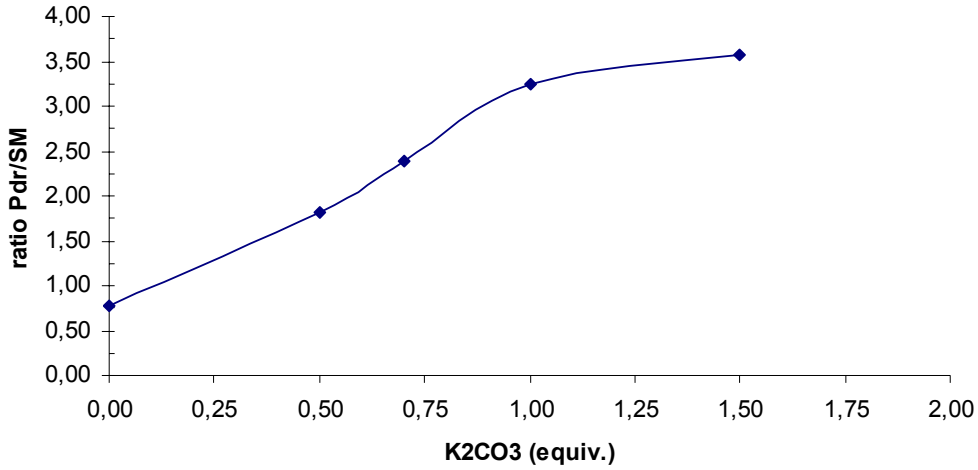
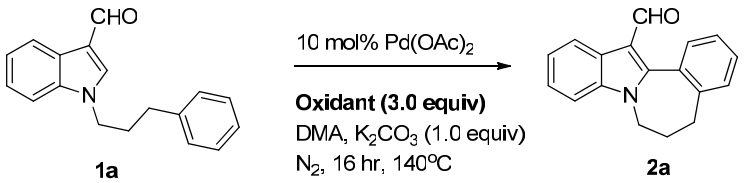


Figure S1. Product formation = f[$K_2CO_{3(equiv.)}$]

Screening of oxidants



Entry	Oxidant	Product	Entry	Oxidant	Product
1	**$Cu(OAc)_2$**	**73% isol.**	8	AgOAc	traces
2	$CuCO_3$	traces	9	AgF	traces
3	CuCl	S.M.	10	B.Q.	S.M.
4	CuCl + O_2	traces	11	$K_2S_2O_8$	decomp.
5	O_2 (1 atm)	traces	12	PIDA	decomp.
6	Ag_2CO_3	traces	13	TBHP	S.M.
7	AgTFA	S.M.	14	TBP	S.M.

Table S3

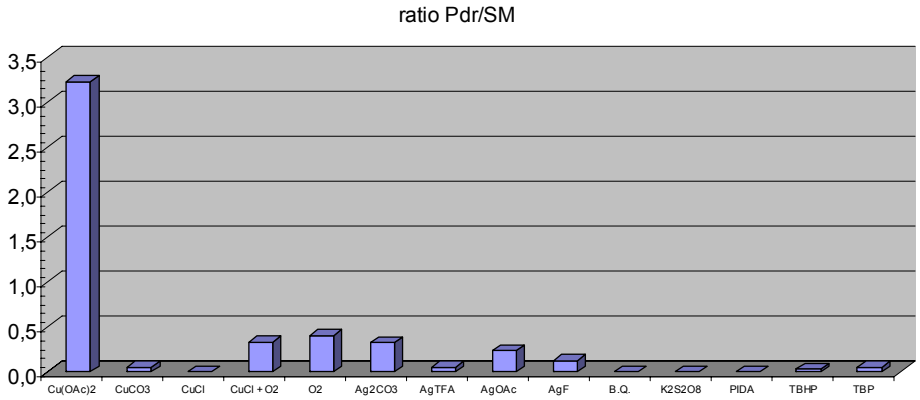
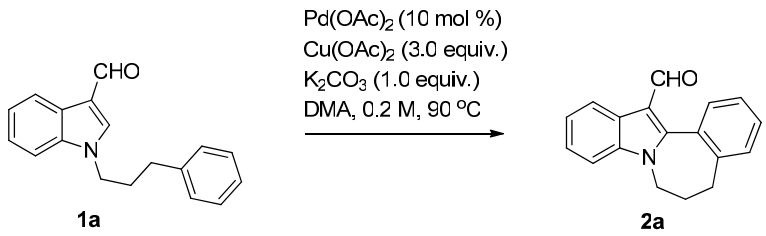


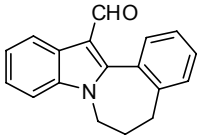
Figure S2. Screening of oxidants. The ratio of product formed / starting material remaining was determined by LCMS analysis. The chart shows the results obtained for each set of reaction conditions.

C-H/C-H coupling reaction

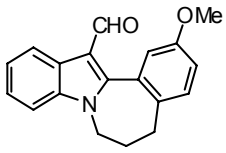


Scheme S4. Dehydrogenative coupling.

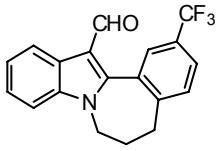
General procedure C for dehydrogenative coupling: Synthesis of 6,7-Dihydro-5H-benzo[3,4]azepino[1,2-a]indole-13-carbaldehyde, 2a. A screw cap test tube (100*11 mm) was loaded with finely crushed compound **1a** (53 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol) and $Cu(OAc)_2$ (109.0 mg, 0.6 mmol). Anhydrous DMA (1 mL) was then added and the tube was flushed with nitrogen before being sealed. The reaction mixture was allowed to stir at room temperature until the starting material completely dissolved before being placed into a pre-thermostated carrousel at 90 ºC for 16 hr. The mixture was allowed to cool down and directly poured on top of a long silica gel chromatography column. The product was eluted with a mixture hexane/Et_2O (50:50). Pure product was obtained in 77% yield as a white solid. Mp (Et_2O) = 126 °C. Rf [hexane / Et_2O (4:6)] = 0.40. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.07 (s, 1H), 8.52 (d, *J* = 6.9 Hz, 1H), 7.63 (d, *J* = 6.4 Hz, 1H), 7.56 – 7.31 (m, 6H), 4.46 (bs, 1H), 3.81 (bs, 1H), 2.79 - 2.70 (m, 2H), 2.52 (bs, 1H), 2.36 – 2.15 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.2 (quat), 150.7 (quat), 139.4 (quat), 136.1 (quat), 131.5 (CH), 130.4 (CH), 129.7 (CH), 129.5 (quat), 127.1 (CH), 125.6 (quat), 123.9 (CH), 123.0 (CH), 122.6 (CH), 114.1 (quat), 109.0 (CH), 41.0 (CH_2), 31.3 (CH_2), 30.6 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{18}H_{15}NO$: 262.1226; found 262.1233.



2-Methoxy-6,7- dihydro-5H- benzo [3,4] azepino [1,2-a] indole-13-carbaldehyde, 2b. Following general procedure C, using compound **1b** (58.6 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL). White solid; yield: 60%. Mp (Et_2O) = 144°C. Rf [Et_2O/hexane (7:3)] = 0.52. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.11 (s, 1H), 8.51 (dd, *J* = 6.7, 1.7 Hz, 1H), 7.44 (dd, *J* = 7.0, 1.5 Hz, 1H), 7.38 (dtd, *J* = 14.0, 7.0, 1.4 Hz, 2H), 7.31 (d, *J* = 8.3 Hz, 1H), 7.17 (d, *J* = 2.7 Hz, 1H), 7.03 (dd, *J* = 8.3, 2.7 Hz, 1H), 4.45 (bs, 1H), 3.89 (s, 3H), 3.82 (bs, 1H), 2.73 (bs, 1H), 2.60 (bs, 1H), 2.47 (bs, 1H), 2.22 (bs, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.2 (quat), 158.5 (quat), 150.6 (quat), 136.1 (quat), 131.3 (quat), 130.6 (CH), 130.3 (quat), 125.6 (quat), 123.9 (CH), 123.0 (CH), 122.6 (CH), 117.0 (CH), 115.7 (CH), 114.1 (quat), 109.0 (CH), 55.6 (CH_3), 41.1 (CH_2), 31.3 (CH_2), 29.6 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{19}H_{18}NO_2$: 292.1332; found 292.1331.

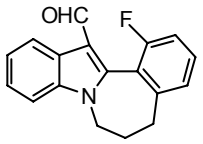


2-Trifluoromethyl-6,7-dihydro-5H-benzo[3,4]azepino[1,2-a]indole-13-carbaldehyde 2c. Following



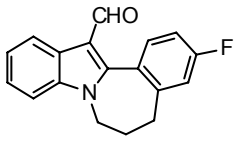
general procedure C, using compound **1c** (66.2 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL). White solid; yield: 80%. Mp (Et_2O) = 158°C. Rf [Et_2O/hexane (7:3)] = 0.50. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.06 (s, 1H), 8.51 (d, *J* = 7.4 Hz, 1H), 7.88 (s, 1H), 7.76 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.56 (d, *J* = 7.9 Hz, 1H), 7.50 – 7.34 (m, 3H), 4.51 (bs, 1H), 3.80 (bs, 1H), 2.88 (bs, 1H), 2.72 (bs, 1H), 2.57 (bs, 1H), 2.31 (bs, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.5 (quat), 148.4 (quat), 143.4 (d, *J* = 0.8 Hz, quat), 136.1 (quat), 130.3 (quat), 130.3 (CH), 129.8 (q, *J* = 33.0 Hz, quat), 127.9 (q, *J* = 3.7 Hz, CH), 127.0 (q, *J* = 3.6 Hz, CH), 125.5 (quat), 124.4 (CH), 123.8 (d, *J* = 272.3 Hz, quat), 123.3 (CH), 122.6 (CH), 114.5 (quat), 109.1 (CH), 40.9 (CH_2), 31.0 (CH_2), 30.6 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{19}H_{15}NOF_3$: 330.1100; found 330.1101.

1-Fluoro-6,7-dihydro-5H-benzo[3,4]azepino[1,2-a]indole-13-carbaldehyde 2d. Following general



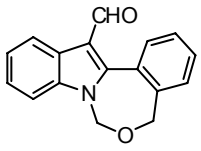
procedure C, using compound **1d** (56.2 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL). White solid; yield: 51%. Mp (Et_2O) = 139 °C. Rf [Et_2O/hexane (6:4)] = 0.39. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.02 (d, *J* = 5.4 Hz, 1H), 8.50 (dd, *J* = 6.1, 2.7 Hz, 1H), 7.50 – 7.46 (m, 1H), 7.44 (dd, *J* = 6.5, 2.5 Hz, 1H), 7.41 – 7.33 (m, 2H), 7.23 – 7.20 (m, 2H), 4.47 (dd, *J* = 14.6, 6.5 Hz, 1H), 3.81 (ddd, *J* = 14.3, 13.1, 5.7 Hz, 1H), 2.89 – 2.72 (m, 1H), 2.59 – 2.45 (m, 2H), 2.32 – 2.11 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.2 (d, *J* = 6.0 Hz, quat), 159.5 (d, *J* = 250.6 Hz, quat), 142.2 (quat), 141.9 (d, *J* = 0.8 Hz, quat), 136.4 (quat), 131.9 (d, *J* = 8.8 Hz, CH), 125.5 (quat), 125.2 (d, *J* = 3.2 Hz, CH), 123.9 (CH), 123.0 (CH), 122.6 (CH), 117.5 (d, *J* = 14.0 Hz, quat), 114.9 (d, *J* = 22.6 Hz, CH), 114.7 (d, *J* = 1.5 Hz, quat), 109.0 (CH), 40.8 (CH_2), 31.0 (CH_2), 30.4 (d, *J* = 2.2 Hz, CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{18}H_{15}NOF$: 280.1132; found 280.1132.

2-Fluoro-6,7-dihydro-5H-benzo[3,4]azepino[1,2-a]indole-13-carbaldehyde, 2d'. Following general procedure C, using compound **1d** (56.2 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02

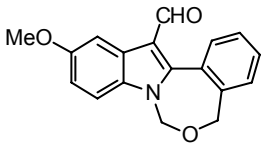


mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL). White solid; yield: 13%. Mp (Et_2O) = 179 °C. Rf [Et_2O/hexane (6:4)] = 0.48. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.50 (dd, *J* = 6.8, 1.7 Hz, 1H), 7.62 (dd, *J* = 8.3, 5.6 Hz, 1H), 7.44 (dd, *J* = 7.1, 1.6 Hz, 1H), 7.39 (dtd, *J* = 13.9, 6.9, 1.5 Hz, 2H), 7.22 – 7.11 (m, 2H), 4.47 (bs, 1H), 3.80 (bs, 1H), 2.77 – 2.71 (m, 2H), 2.53 (bs, 1H), 2.29 (bs, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.8 (quat), 163.8 (d, *J* = 251.3 Hz, quat), 149.5 (quat), 142.0 (d, *J* = 8.1 Hz, quat), 136.0 (quat), 133.3 (d, *J* = 8.8 Hz, CH), 125.6 – 125.5 (m, quat), 124.0 (CH), 123.1 (CH), 122.5 (CH), 116.9 (d, *J* = 21.8 Hz, CH), 114.2 (quat), 114.1 (d, *J* = 21.6 Hz, CH), 109.0 (CH), 40.9 (CH_2), 31.0 (CH_2), 30.7 (d, *J* = 1.2 Hz, CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{18}H_{15}NOF$: 280.1132; found 280.1132.

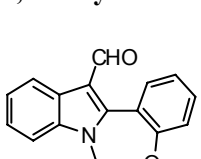
5H-6-Oxa-7a-aza-dibenzo[a,e]azulene-12-carbaldehyde, 2e. Following general procedure C, using compound **1e** (53 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL). White solid; yield: 70%. Mp (Et_2O) = 238 °C. Rf [hexane / Et_2O (1:1)] = 0.33. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.23 (s, 1H), 8.51 (dd, *J* = 6.9, 1.5 Hz, 1H), 7.85 – 7.77 (m, 1H), 7.68 – 7.61 (m, 2H), 7.61 – 7.56 (m, 1H), 7.57 – 7.51 (m, 1H), 7.49 – 7.37 (m, 2H), 5.52 (s, 2H), 4.65 (s, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 186.2 (quat), 149.4 (quat), 135.6 (quat), 134.3 (quat), 131.1 (CH), 130.9 (CH), 130.9 (CH), 130.4 (quat), 129.7 (CH), 125.8 (quat), 124.7 (CH), 123.7 (CH), 122.7 (CH), 114.5 (quat), 109.3 (CH), 69.6 (CH_2), 68.2 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{17}H_{14}NO_2$: 264.1019; found 264.1021.



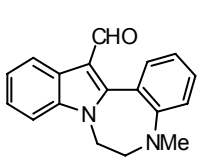
10-Methoxy-5H-6-oxa-7a-aza-dibenzo[a,e]azulene-12-carbaldehyde, 2f. Following general procedure C, using compound **1f** (59 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL). White solid; yield: 65%. Mp (Et_2O) = 148 °C. Rf [hexane / Et_2O (2:8)] = 0.46.^{1}H NMR (500 MHz, $CDCl_3$) δ 10.19 (s, 1H), 7.98 (d, *J* = 2.4 Hz, 1H), 7.84 – 7.72 (m, 1H), 7.68 – 7.58 (m, 2H), 7.56 (d, *J* = 6.8 Hz, 1H), 7.40 (d, *J* = 8.9 Hz, 1H), 7.04 (dd, *J* = 8.9, 2.5 Hz, 1H), 5.45 (s, 2H), 4.62 (s, 2H), 3.94 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.2 (quat), 157.1 (quat), 149.4 (quat), 134.2 (quat), 130.9 (CH), 130.9 (CH), 130.8 (CH), 130.5 (quat), 130.4 (quat), 129.7 (CH), 126.5 (quat), 115.1 (CH), 114.3 (quat), 110.1 (CH), 103.6 (CH), 69.7 (CH_2), 68.1 (CH_2), 55.9 (CH_3). HRMS (ES^+) cald. for $(M+H)^+$ $C_{18}H_{16}NO_3$: 294.1125; found 294.1126.



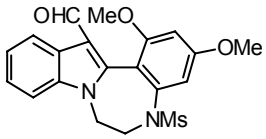
6,7-Dihydro-5-oxa-7a-aza-dibenzo[a,e]azulene-12-carbaldehyde, 2g. Following general procedure C, using compound **1g** (53 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL). White solid; yield: 63%. Mp (Et_2O) = 188 °C. Rf [DCM] = 0.29. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.14 (s, 1H), 8.65 – 8.42 (m, 1H), 7.66 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.55 (td, *J* = 7.8, 1.6 Hz, 1H), 7.46 – 7.33 (m, 4H), 7.33 – 7.26 (m, 1H), 4.67 (t, *J* = 5.7 Hz, 2H), 4.38 (t, *J* = 5.7 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.9 (quat), 154.1 (quat), 148.0 (quat), 135.7 (quat), 132.5 (CH), 132.1 (CH), 125.9 (quat), 124.9 (CH), 124.2 (CH), 123.4 (quat), 123.2 (CH), 123.2 (CH), 122.7 (CH), 108.6 (CH), 74.7 (CH_2), 41.5 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{17}H_{14}NO_2$: 264.1019; found 264.1022.



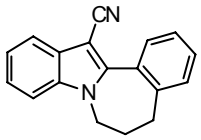
5-Methyl-6,7-dihydro-5H-benzo[5,6][1,4]diazepino[7,1-a]indole-13-carbaldehyde, 2h. Following general procedure C, using compound **1h** (56 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL). White solid; yield: 78%. Mp (Et_2O) = 186 °C. Rf [Et_2O/hexane (65:35)] = 0.24. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.01 (s, 1H), 8.52 (dd, *J* = 6.4, 2.3 Hz, 1H), 7.62 – 7.46 (m, 2H), 7.46 – 7.31 (m, 3H), 7.25 – 7.11 (m, 2H), 4.32 (bs, 2H), 3.62 (bs, 2H), 2.86 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.3 (quat), 150.3 (quat), 148.0 (quat), 135.5 (quat), 132.7 (CH), 131.5 (CH), 125.8 (quat), 123.7 (CH), 123.2



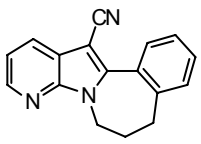
(quat), 123.0 (CH), 122.6 (CH), 122.1 (CH), 119.7 (CH), 114.0 (quat), 108.4 (CH), 60.4 (CH_2), 41.1 (CH_3), 41.1 (CH_2). HRMS (ES^+) cald. for $(2M+H)^+$ $C_{36}H_{33}N_4O_2$: 553.2598; found 553.2593.

5-Methanesulfonyl-1,3-dimethoxy-6,7-dihydro-5H-benzo[5,6][1,4]diazepino[7,1-a] indole-13-carbaldehyde, 2i. 

Following general procedure C, using compound **1i** (81 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL). White solid; yield: 87%. Mp (Et_2O) = 190 °C. Rf [DCM / EtOAc (9:1)] = 0.61. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.00 (s, 1H), 8.44 (dd, *J* = 6.6, 2.0 Hz, 1H), 7.45 – 7.32 (m, 3H), 6.89 (d, *J* = 2.3 Hz, 1H), 6.72 (d, *J* = 2.3 Hz, 1H), 4.50 (ddd, *J* = 28.4, 12.2, 8.6 Hz, 2H), 4.05 – 3.90 (m, 5H), 3.86 (s, 3H), 2.15 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.5 (quat), 163.0 (quat), 158.5 (quat), 142.3 (quat), 137.3 (quat), 135.6 (quat), 125.4 (quat), 124.1 (CH), 123.4 (CH), 122.7 (CH), 115.0 (quat), 110.6 (quat), 110.0 (CH), 108.6 (CH), 100.5 (CH), 56.1 (CH_3), 55.9 (CH_3), 53.1 (CH_2), 40.1 (CH_2), 38.6 (CH_3). HRMS (ES^+) cald. for $(M+H)^+$ $C_{20}H_{21}O_5N_2S_1$: 401.1166; found 401.1166.

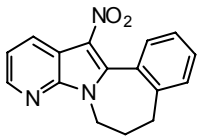
6,7-Dihydro-5H-benzo[3,4]azepino[1,2-a]indole-13-carbonitrile, 2j. 

Following general procedure C, using compound **1j** (52 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL). White solid; yield: 79%. Mp (Et_2O) = 119 °C. Rf [hexane / Et_2O (1:1)] = 0.37.^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 – 7.79 (m, 2H), 7.53 – 7.43 (m, 3H), 7.42 – 7.30 (m, 3H), 4.15 (t, *J* = 6.7 Hz, 2H), 2.73 (t, *J* = 7.1 Hz, 2H), 2.40 (p, *J* = 6.9 Hz, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 147.8 (quat), 138.6 (quat), 135.6 (quat), 130.4 (CH), 129.7 (CH), 129.7 (quat), 129.5 (CH), 127.9 (quat), 127.6 (CH), 123.7 (CH), 122.1 (CH), 119.8 (CH), 116.7 (quat), 109.7 (CH), 83.5 (quat), 41.7 (CH_2), 31.1 (CH_2), 30.6 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{18}H_{15}N_2$: 259.1230; found 259.1231.

6,7-Dihydro-5H-7a,8-diaza-dibenzo[a,e]azulene-12-carbonitrile, 2k. 

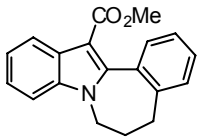
Following general procedure C, using compound **1k** (52 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL). White solid; yield: 87%. Mp (Et_2O) = 144 °C. Rf [hexane / Et_2O (3:7)] = 0.48.^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (s, 1H), 8.11 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.95 – 7.77 (m, 1H), 7.49 (dd, *J* = 5.2, 3.7 Hz, 2H), 7.40 (dd, *J* = 5.0, 3.8 Hz, 1H), 7.34 – 7.24 (m, 1H), 4.37 (t, *J* = 6.8 Hz, 2H), 2.73 (t, *J* = 7.1 Hz, 2H), 2.42 (p, *J* = 6.9 Hz, 2H).^{13}C NMR (126 MHz, $CDCl_3$) δ 148.6 (quat), 146.6 (quat), 144.7 (CH), 139.0 (quat), 130.8 (CH), 129.9 (CH), 129.5 (CH), 129.1 (quat), 127.9 (CH), 127.6 (CH), 120.7 (quat), 118.3 (CH), 81.4 (quat), 39.7 (CH_2), 30.9 (CH_2), 30.7 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{17}H_{14}N_3$: 260.1182; found 260.1185.

12-Nitro-6,7-dihydro-5H-7a,8-diaza-dibenzo[a,e]azulene, 2l. Following general procedure C, using



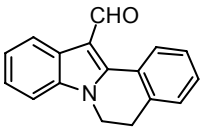
compound **1l** (56.2 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL). White solid; yield: 95%. Mp (Et_2O) = 168 °C. Rf [DCM] = 0.28. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66 (dd, *J* = 8.0, 1.3 Hz, 1H), 8.44 (d, *J* = 4.6 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.47 (tdd, *J* = 15.1, 10.7, 4.3 Hz, 2H), 7.37 (m, 2H), 5.13 (m, 1H), 3.48 (m, 1H), 2.77 (m, 1H), 2.60 (m, 1H), 2.49 (m, 1H), 2.22 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.4 (CH), 144.6 (quat), 142.3 (quat), 139.5 (quat), 132.1 (CH), 131.2 (CH), 130.0 (CH), 129.1 (CH), 127.9 (quat), 126.6 (CH), 122.9 (quat), 120.1 (CH), 115.0 (quat), 39.4 (CH_2), 31.4 (CH_2), 30.4 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{16}H_{14}N_3O_2$: 280.1081; found 280.1077.

6,7-Dihydro-5H-benzo[3,4]azepino[1,2-a]indole-13-carboxylic acid methyl ester (2m, not shown in paper). Following general procedure C, using compound **1m** (59 mg, 0.2 mmol), K_2CO_3



(28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL). White solid; yield: 24%. Mp (Et_2O) = 119 °C. Rf [hexane / Et_2O (1:1)] = 0.50. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 – 8.27 (m, 1H), 7.84 – 7.78 (m, 1H), 7.46 – 7.38 (m, 3H), 7.38 – 7.29 (m, 3H), 4.42 (m, 1H), 3.88 (s, 3H), 3.73 (m, 1H), 2.67 (m, 2H), 2.42 (m, 1H), 2.17 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.7 (quat), 145.9 (quat), 138.7 (quat), 135.5 (quat), 132.2 (CH), 130.9 (quat), 129.7 (CH), 128.6 (CH), 127.1 (quat), 126.1 (CH), 122.7 (CH), 122.4 (CH), 121.8 (CH), 109.0 (CH), 103.3 (quat), 50.8 (CH_3), 40.8 (CH_2), 31.2 (CH_2), 30.5 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{19}H_{18}NO_2$: 292.1332; found 292.1334.

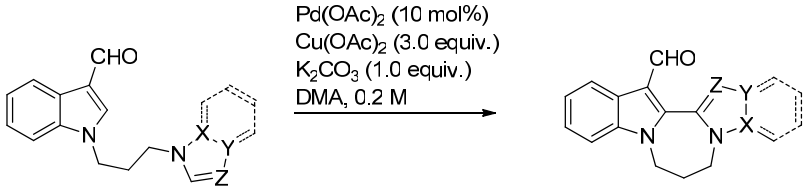
5,6-Dihydro-indolo[2,1-a]isoquinoline-12-carbaldehyde (2n, not shown in paper). Following general



procedure C, using compound **1n** (50 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL). White solid; yield: 87%. Mp (Et_2O) = 122 °C. Rf [Et_2O/hexane (1:1)] = 0.34. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.54 (s, 1H), 8.56 – 8.42 (m, 1H), 7.98 (dd, *J* = 5.4, 3.6 Hz, 1H), 7.48 – 7.43 (m, 2H), 7.43 – 7.39 (m, 2H), 7.35 (dtd, *J* = 14.0, 6.9, 1.5 Hz, 2H), 4.27 (t, *J* = 6.5 Hz, 2H), 3.20 (t, *J* = 6.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.6 (quat), 143.1 (quat), 135.8 (quat), 135.0 (quat), 130.0 (CH), 129.0 (CH), 128.5 (CH), 127.8 (CH), 127.1(quat), 126.7 (quat), 124.0 (CH), 123.3 (CH), 122.4 (CH), 113.4 (quat), 109.2 (CH), 40.1 (CH_2), 29.2 (CH_2).). HRMS (ES^+) cald. for $(M+H)^+$ $C_{17}H_{14}NO$: 248.1069; found 248.1067.

C-H/C-H coupling of indole-heterocycle derivatives (Chart 2)

General procedure C was employed, using alterations made to reaction temperature and time.



Scheme S5. Dehydrogenative coupling of heteroaromatic derivatives.

7,8-Dihydro-6H-[1,4]diazepino[1,2-a;4,3-a']diindole-14,15-dicarbaldehyde, 4a. Following general procedure C, using compound **3a** (66.0 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL) at 120 ºC for 8 hr. White solid; yield: 91%. Mp (Et_2O) = 276 °C. Rf [DCM/EtOAc (95:05)] = 0.54. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.06 (s, 2H), 8.52 (d, *J* = 8.0 Hz, 2H), 7.54 – 7.47 (m, 4H), 7.44 – 7.33 (m, 2H), 4.80 – 4.61 (m, 2H), 4.08 – 3.86 (m, 2H), 2.74 – 2.51 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.6 (2 quat), 136.9 (2 quat), 136.3 (2 quat), 125.7 (2 CH), 125.4 (2 quat), 123.8 (2 CH), 122.9 (2 CH), 118.4 (2 quat), 109.3 (2 CH), 40.8 ($2CH_2$), 29.6 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{21}H_{17}NO$: 329.1285; found 329.1282.

Compound 4b. Following general procedure C highlighted in Scheme S5, using compound **3b** (65.8 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL) at 120 ºC for 8 hr. White solid; yield: 84%. Mp (Et_2O) = 218 °C. Rf [Et_2O/hexane (8:2)] = 0.34. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.26 (s, 1H), 8.48 (d, *J* = 7.8 Hz, 1H), 7.95 – 7.84 (m, 2H), 7.52 – 7.35 (m, 6H), 7.04 (s, 1H), 4.48 (t, *J* = 6.7 Hz, 2H), 4.31 (t, *J* = 6.7 Hz, 2H), 2.64 (p, *J* = 6.7 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.1 (quat), 151.4 (quat), 138.9 (quat), 136.9 (quat), 133.3 (quat), 132.4 (quat), 128.9 (2CH), 128.3 (CH), 125.6 (2CH), 125.3 (quat), 124.8 (CH), 123.5 (CH), 122.7 (CH), 115.5 (quat), 109.2 (CH), 107.0 (CH), 47.9 (CH_2), 41.2 (CH_2), 30.0 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{21}H_{18}N_3O$: 328.1444; found 328.1445.

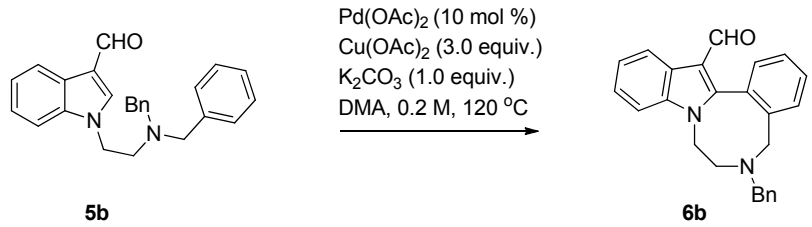
Compound 4c. Following general procedure C highlighted in Scheme S5, using compound **3c** (60.6 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL) at 140 ºC for 3 hr. White solid; yield: 62%. Mp (Et_2O) = 216 °C. Rf [DCM/EtOAc (1:1)] = 0.62. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.67 (s, 1H), 8.55 (d, *J* = 7.9 Hz, 1H), 7.95 (d, *J* = 7.2 Hz, 1H), 7.55 – 7.33 (m, 6H), 4.47 – 4.31 (m, 4H), 2.67 (p, *J* = 6.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 187.8 (quat), 143.6 (quat), 138.0 (quat), 137.0 (quat), 125.4 (quat), 125.2 (quat), 124.3 (CH), 123.6 (CH), 123.4 (CH), 123.2 (quat), 120.9 (CH), 118.1 (quat), 109.3 (CH), 109.3 (CH), 41.6 (CH_2), 41.0 (CH_2), 29.3 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{19}H_{16}N_3O$: 302.1288; found 302.1291.

Compound 4d. Following general procedure C highlighted in Scheme S5, using compound **3d** (78.6 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL) at 120 ºC for 24 hr. White solid; yield: 43%. Mp (Et_2O) = 120 °C. Rf [Et_2O/hexane (8:2)] = 0.45. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.03 (s, 1H), 8.47 (d, *J* = 8.0 Hz, 1H), 7.51 – 7.36 (m, 3H), 4.77 – 4.55 (m, 2H), 4.38 – 4.19 (m, 2H), 4.12 – 3.98 (m, 1H), 3.98 – 3.77 (m, 1H), 2.75 – 2.47 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz,

$CDCl_3$) δ 185.2 (quat), 160.2 (quat), 142.3 (q, *J* = 38.5 Hz, quat), 136.6 (quat), 136.5 (quat), 133.0 (quat), 125.4 (CH), 125.2 (quat), 123.7 (CH), 123.0 (CH), 120.3 (d, *J* = 270.0 Hz, quat), 116.9 (quat), 113.8 (quat), 109.2 (CH), 61.7 (CH_2), 48.5 (CH_2), 40.3 (CH_2), 29.9 (CH_2), 13.8 (CH_3). HRMS (ES^+) cald. for $(M+H)^+$ $C_{19}H_{17}N_3O_3F_3$: 392.1217; found 392.1215.

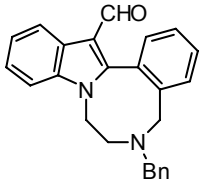
C-H/C-H coupling reaction for 8-membered ring synthesis (Chart 3)

General procedure C was employed at 120°C instead of 90°C

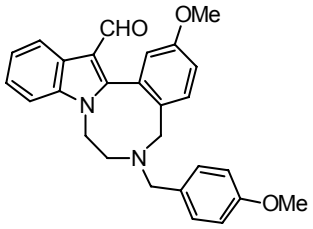


Scheme S6. Dehydrogenative coupling for 8-membered ring synthesis

Compound 6b. Following general procedure C highlighted in Scheme S6, using compound **5b** (73.6 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL) at 120 ºC for 16 hr. Whitish solid; yield: 60%. Mp (Et_2O) = 74 °C. Rf [Et_2O/hexane (7:3)] = 0.50. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.84 (s, 1H), 8.50 (dd, *J* = 5.7, 2.5 Hz, 1H), 7.52 – 7.48 (m, 2H), 7.45 – 7.28 (m, 9H), 7.18 (d, *J* = 7.6 Hz, 1H), 4.35 (dd, *J* = 15.3, 5.1 Hz, 1H), 3.97 – 3.76 (m, 3H), 3.57 (d, *J* = 13.2 Hz, 1H), 3.31 (dd, *J* = 13.2, 5.5 Hz, 1H), 3.06 (d, *J* = 14.1 Hz, 1H), 2.80 (dd, *J* = 13.0, 10.1 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.7 (quat), 151.0 (quat), 140.6 (quat), 138.6 (quat), 136.1 (quat), 132.2 (CH), 131.4 (CH), 130.6 (CH), 129.2 (2 CH), 128.5 (2 CH), 127.6 (quat), 127.6 (CH), 127.3 (CH), 125.7 (quat), 124.0 (CH), 123.4 (CH), 122.4 (CH), 114.8 (quat), 109.5 (CH), 61.8 (CH_2), 55.9 (CH_2), 54.9 (CH_2), 43.3 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{25}H_{23}N_2O$: 367.1805; found 367.1804.



Compound 6c. Following general procedure C highlighted in Scheme S6, using compound **5c** (85.6 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL) at 120 ºC for 16 hr. Yellowish oil; yield: 55%. Rf [DCM] = 0.23. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.91 (s, 1H), 8.51 (dd, *J* = 5.3, 3.1 Hz, 1H), 7.42 – 7.39 (m, 3H), 7.29 (d, *J* = 8.6 Hz, 2H), 7.18 – 6.99 (m, 3H), 6.93 (d, *J* = 8.6 Hz, 2H), 4.36 (dd, *J* = 15.3, 5.3 Hz, 1H), 3.92 (dd, *J* = 15.4, 9.9 Hz, 1H), 3.86 (bs, 6H), 3.81 (dd, *J* = 17.5, 7.8 Hz, 2H), 3.49 (d, *J* = 13.4 Hz, 1H), 3.32 (dd, *J* = 13.2, 5.5 Hz, 1H), 2.95 (d, *J* = 14.1 Hz, 1H), 2.77 (dd, *J* = 13.1, 10.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.6 (quat), 159.0 (quat), 158.3 (quat), 150.8 (quat), 136.0 (quat), 132.8 (quat), 132.7 (CH), 130.6 (quat), 130.4 (2 CH), 128.6 (quat), 125.6 (quat), 124.0 (CH),



123.4 (CH), 122.4 (CH), 116.7 (CH), 116.6(CH), 114.6 (quat), 113.8 (2 CH), 109.5 (CH), 60.9 (CH_2), 55.5 (CH_3), 55.3 (CH_3), 54.8 (CH_2), 54.8 (CH_2), 43.3 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{27}H_{27}N_2O_3$: 427.2016; found 427.2021.

Compound 6d. Following general procedure C highlighted in Scheme S6, using compound **5d** (82.1 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL) at 120 ºC for 16 hr. Yellowish oil; yield: 51%. Rf [DCM] = 0.32. ^{1}H NMR (500 MHz, $CDCl_3$, two diastereoisomers)[4] δ 9.92 (s, 1H), 9.78 (s, 1H), 8.57 – 8.50 (m, 2H), 7.45 – 7.23 (m, 12H), 7.21 (d, *J* = 7.8 Hz, 2H), 7.13 (d, *J* = 7.7 Hz, 1H), 7.06 (d, *J* = 7.7 Hz, 1H), 6.99 (d, *J* = 7.9 Hz, 2H), 6.90 (d, *J* = 7.9 Hz, 2H), 4.27 (dd, *J* = 15.1, 5.0 Hz, 1H), 4.16 (dd, *J* = 14.9, 3.4 Hz, 1H), 4.07 – 3.91 (m, 3H), 3.81 – 3.72 (m, 4H), 3.57 – 3.51 (m, 1H), 3.43 (d, *J* = 15.8 Hz, 1H), 3.36 (dd, *J* = 12.8, 8.7 Hz, 2H), 3.15 – 3.03 (m, 1H), 2.45 (s, 3H), 2.42 (s, 3H), 2.41 (s, 3H), 2.31 (s, 3H), 1.35 (d, *J* = 6.5 Hz, 3H), 1.05 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$, two diastereoisomers) δ 187.2 (quat), 186.9 (quat), 152.9 (quat), 152.0 (quat), 138.5 (quat), 138.0 (quat), 137.0 (quat), 136.9 (quat), 136.7 (quat), 136.5 (quat), 136.2 (quat), 136.1 (quat), 135.9 (quat), 135.7 (quat), 134.2 (CH), 133.7 (CH), 132.0 (CH), 130.9 (CH), 130.8 (CH), 129.5 (CH), 129.2 (2 CH), 128.9 (2 CH), 128.6 (2 CH), 128.5 (2 CH), 128.0 (quat), 126.8 (quat), 125.9 (quat), 125.6 (quat), 123.7 (CH), 123.7 (CH), 123.2 (CH), 123.1 (CH), 122.4 (CH), 122.3 (CH), 115.4 (quat), 114.5 (quat), 110.6 (CH), 109.4 (CH), 58.5 (CH_2), 57.0 (CH_2), 55.9 (CH), 53.8 (CH), 53.1 (CH_2), 48.9 (CH_2), 48.7 (CH_2), 45.6 (CH_2), 21.2 (CH_3), 21.1 (CH_3), 21.0 (CH_3), 20.9 (CH_3), 15.6 (CH_3), 15.3 (CH_3). HRMS (ES^+) cald. for $(M+H)^+$ $C_{28}H_{29}N_2O$: 409.2274; found 409.2277.

Compounds 6e and 6f. Following general procedure C highlighted in Scheme S6, using compound **5e** (51 mg, 0.122 mmol), K_2CO_3 (17.0 mg, 0.122 mmol), $Pd(OAc)_2$ (2.7 mg, 0.012 mmol), $Cu(OAc)_2$ (67.0 mg, 0.367 mmol) and anhydrous DMA (800 µL) at 120 ºC for 16 hr. Yellowish oil; yield: 62% as a 1.6 : 1 mixture of regioisomers (^{1}H NMR). Compounds **6e** and **6f** could not be completely separated by silica gel column chromatography - analytically pure samples for characterisation were isolated using preparative TLC.

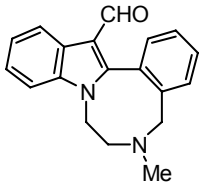
6e: Rf [Et_2O/Hexane (7:3)] = 0.47. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.89 (s, 1H), 8.59 – 8.41 (m, 1H), 7.47 – 7.37 (m, 3H), 7.28 (d, *J* = 7.0 Hz, 2H), 7.22 (ddd, *J* = 20.6, 8.5, 2.7 Hz, 2H), 7.12 (dd, *J* = 8.5, 5.6 Hz, 1H), 6.93 (d, *J* = 8.6 Hz, 2H), 4.40 (dd, *J* = 15.4, 5.1 Hz, 1H), 3.97 – 3.76 (m, 6H), 3.49 (d, *J* = 13.0 Hz, 1H), 3.33 (dd, *J* = 13.2, 5.6 Hz, 1H), 2.96 (d, *J* = 14.1 Hz, 1H), 2.79 (dd, *J* = 13.0, 9.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.1 (quat), 161.1 (d, *J* = 248.4 Hz, quat), 159.1 (quat), 149.1 (d, *J* = 2.0 Hz, quat), 136.8 (d, *J* =

[4] A ^{1}H NMR spectrum run at high temperature (400 MHz, 80 ºC, D_6-DMSO) did not produce any signal coalescence, suggesting a relatively high energy barrier to rotation around the biaryl axis. Studies on this stereoisomerism are ongoing.

3.5 Hz, quat), 136.0 (quat), 133.2 (d, *J* = 8.3 Hz, CH), 130.4 (2CH), 130.3 (quat), 129.3 (d, *J* = 8.4 Hz, quat), 125.6 (quat), 124.2 (CH), 123.6 (CH), 122.5 (CH), 118.5 (d, *J* = 22.5 Hz, CH), 117.6 (d, *J* = 20.9 Hz, CH), 114.9 (quat), 113.9 (2CH), 109.5 (CH), 61.2 (CH_2), 55.3 (CH_3), 54.8 (CH_2), 54.6 (CH_2), 43.5 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{26}H_{24}N_2O_2F$: 415.1816; found 415.1816.

6f: Rf [Et_2O/Hexane (7:3)] = 0.45. ^1H NMR (500 MHz, $CDCl_3$) δ 9.91 (s, 1H), 8.62 – 8.36 (m, 1H), 7.45 – 7.37 (m, 3H), 7.35 (dd, *J* = 8.5, 5.5 Hz, 2H), 7.12 – 7.02 (m, 5H), 4.37 (dd, *J* = 15.3, 5.1 Hz, 1H), 3.98 – 3.82 (m, 5H), 3.77 (d, *J* = 14.2 Hz, 1H), 3.54 (d, *J* = 13.3 Hz, 1H), 3.30 (dd, *J* = 13.3, 5.5 Hz, 1H), 3.02 (d, *J* = 14.2 Hz, 1H), 2.80 (dd, *J* = 13.1, 9.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.6 (quat), 162.2 (d, *J* = 245.6 Hz, quat), 158.4 (quat), 150.7 (quat), 136.0 (quat), 134.3 (d, *J* = 3.1 Hz, quat), 132.5 (quat), 132.5 (CH), 130.7 (d, *J* = 7.9 Hz, 2CH), 128.7 (quat), 125.6 (quat), 124.0 (CH), 123.5 (CH), 122.5 (CH), 116.9 (CH), 116.6 (CH), 115.3 (d, *J* = 21.3 Hz, 2CH), 114.7 (quat), 109.4 (CH), 60.6 (CH_2), 55.5 (CH_3), 55.1 (CH_2), 54.8 (CH_2), 43.2 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{26}H_{24}N_2O_2F$: 415.1816; found 415.1816.

Compound 6g (not in paper). Following general procedure C highlighted in Scheme S6, using compound

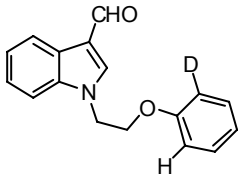


5f (58.4 mg, 0.2 mmol), K_2CO_3 (28.0 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL) at 120 ºC for 16 hr. Yellowish oil; yield: 37%. Rf [EtOAc/Hexane (1:1)] = 0.32. ^1H NMR (500 MHz, $CDCl_3$) δ 9.83 (s, 1H), 8.58 – 8.30 (m, 1H), 7.61 – 7.55 (m, 1H), 7.53 (d, *J* = 7.7 Hz, 2H), 7.45 (td, *J* = 7.4, 1.4 Hz, 1H), 7.42 – 7.35 (m, 3H), 4.31 (dd, *J* = 15.4, 5.3 Hz, 1H), 3.82 (dd, *J* = 15.5, 10.0 Hz, 1H), 3.73 (d, *J* = 13.9 Hz, 1H), 3.25 (dd, *J* = 13.5, 5.7 Hz, 1H), 3.14 (d, *J* = 13.9 Hz, 1H), 2.78 (dd, *J* = 13.5, 9.8 Hz, 1H), 2.53 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.6 (quat), 150.6 (quat), 139.8 (quat), 136.0 (quat), 132.2 (CH), 131.9 (CH), 130.7 (CH), 127.7 (quat), 127.5 (CH), 125.6 (quat), 124.0 (CH), 123.5 (CH), 122.4 (CH), 114.8 (quat), 109.4 (CH), 58.4 (CH_2), 56.7 (CH_2), 45.6 (CH_3), 42.7 (CH_2).). HRMS (ES^+) cald. for $(M+H)^+$ $C_{19}H_{19}N_2O$: 291.1492; found 291.1491.

II: Mechanistic studies: Kinetic Isotope Effects (KIEs)

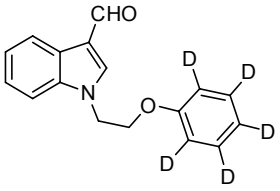
Synthesis of 1-(2-o-deuteriophenoxy-ethyl)-1*H*-indole-3-carbaldehyde, 1g-D.

1-(2-o-deuteriophenoxy-ethyl)-1*H*-indole-3-carbaldehyde, 1g-D. Following general procedure A, using



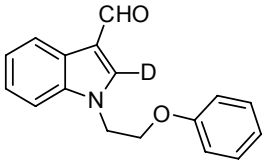
indole-3-carboxyaldehyde (174.0 mg, 1.2 mmol), NaH (48 mg, 1.2 mmol, 60 wt% in mineral oil) and (2-bromo-ethoxy)-2-deuteriobenzene[5] (197 mg, 1.0 mmol). White solid; yield: 75%. Mp (Et_2O) = 113 °C. Rf [hexane/Et_2O (3:7)] = 0.38. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.05 (s, 1H), 8.36 (dd, *J* = 7.0, 1.2 Hz, 1H), 7.89 (s, 1H), 7.49 – 7.43 (m, 1H), 7.43 – 7.33 (m, 2H), 7.33 – 7.26 (m, 2H), 7.00 (td, *J* = 7.4, 0.9 Hz, 1H), 6.87 (dd, *J* = 8.7, 0.8 Hz, 1H), 4.59 (t, *J* = 5.2 Hz, 2H), 4.35 (t, *J* = 5.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.7 (quat), 157.8 (quat), 139.2 (CH), 137.2 (quat), 129.7 (CH), 129.6 (CH), 125.4 (quat), 124.1 (CH), 123.0 (CH), 122.3 (CH), 121.6 (CH), 118.5 (quat), 114.5 (CH), 114.2 (t, *J* = 24.3 Hz, CD), 109.8 (CH), 66.0 (CH_2), 46.5 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{17}H_{15}(^2H_1)NO_2$: 267.1238; found 267.1238.

1-(2-d_5Phenoxy-ethyl)-1H-indole-3-carbaldehyde, 1g-D_5. Following general procedure A, using indole-3-



carboxyaldehyde (429 mg, 2.95 mmol), NaH (118 mg, 2.95 mmol, 60 wt% in mineral oil) and (2-bromo-ethoxy)-benzene-d_5 (610 mg, 2.96 mmol). Yellow solid; yield: 45%. Mp (Et_2O) = 122 °C. Rf [hexane/DCM (7:3)] = 0.61. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.05 (s, 1H), 8.36 (d, *J* = 7.7 Hz, 1H), 7.88 (s, 1H), 7.47 (d, *J* = 7.7 Hz, 1H), 7.43 – 7.32 (m, 2H), 4.59 (t, *J* = 5.2 Hz, 2H), 4.35 (t, *J* = 5.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.7 (quat), 157.8 (quat), 139.1 (CH), 137.3 (quat), 129.2 (t, *J* = 24.3 Hz, 2CD), 125.4 (quat), 124.1 (CH), 123.0 (CH), 122.3 (CH), 121.1 (t, *J* = 24.8 Hz, CD), 118.6 (quat), 114.0 (t, *J* = 24.3 Hz, 2CD), 109.8 (CH), 66.0 (CH_2), 46.5 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{17}H_{11}{}^2H_5NO_2$: 271.1489; found 271.1489.

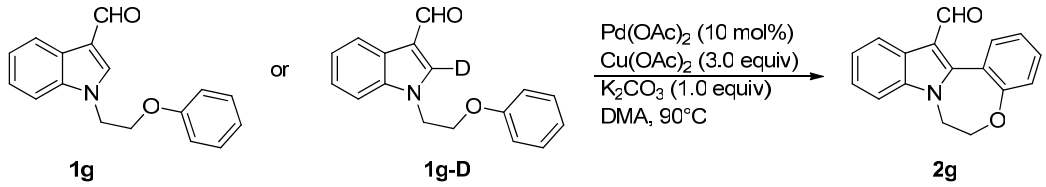
1-(2-Phenoxy-ethyl)-1H-(2-deutero)indole-3-carbaldehyde, 1g-(indole 2-D). Following general procedure



A, using 2-deuteroindole-3-carboxyaldehyde (226 mg, 1.55 mmol), NaH (68 mg, 1.70 mmol, 60 wt% in mineral oil) and (2-bromo-ethoxy)-benzene (374 mg, 1.90 mmol). Yellow solid; yield: 74%. Mp (Et_2O) = 115 °C. Rf [hexane/DCM (7:3)] = 0.60. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.06 (s, 1H), 8.36 (dd, *J* = 6.9, 1.2 Hz, 1H), 7.51 – 7.45 (m, 1H), 7.38 (ddt, *J* = 13.4, 7.2, 3.7 Hz, 2H), 7.32 – 7.26 (m, 2H), 7.03 – 6.96 (m, 1H), 6.93 – 6.82 (m, 2H), 4.61 (t, *J* = 5.2 Hz, 2H), 4.37 (t, *J* = 5.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 184.6 (quat), 157.8 (quat), 138.7 (t, *J* = 25.2 Hz, CD), 137.2 (quat), 129.7 (2CH), 125.4 (quat), 124.1 (CH), 123.0 (CH), 122.3 (CH), 121.7 (CH), 118.4 (quat), 114.5 (2CH), 109.8 (CH), 66.0 (CH_2), 46.5 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{17}H_{15}{}^2H_1NO_2$: 267.1238; found 267.1238.

[5] Wang, C.; Piel I.; Glorius, F. *J. Am. Chem. Soc.*, **2009**, *131*, 4194-4195.

Procedure for the determination of the intermolecular KIE at the indole C2 position.



1g **1g-D** **2g**

Method A:

General considerations. Reactions were run in 3 mL test tubes sealed with a screw cap. Each reaction in an individual vial represents a point within a kinetic run. Each reaction vial contained a constant concentration of oxidant, catalyst, base and substrate. The initial rate of the reaction was recorded by analysing the formation of the product over time at the beginning of the reaction. Duplicate experiments were performed in the same aluminium heating block pre-heated at 90 °C and at the desired time, reactions were stopped by freezing the reaction vials in an ice bath at 0 °C. A solution of methanol containing benzanilide as internal standard was used to quench the reactions and dilute the samples. Product formation was determined by LCMS using peak area of mass spectrometry response (Single Ion Monitoring (SIM)) for the product versus SIM of the internal standard (benzanilide).

Method A. For each experiment, a 3 mL screw vial was loaded with $Cu(OAc)_2$ (27.2 mg, 0.15 mmol) and K_2CO_3 (6.9 mg, 0.05 mmol). Then 200 µL of a DMA solution containing the starting material (0.1M) was added to the vial, followed by 200 µL of a DMA solution of $Pd(OAc)_2$ (0.1 M). Each vial was sealed and heated at the same time using a pre-thermostated carrousel at 90 °C. At the appropriate time, reactions were quenched by freezing them into an ice bath for 15 minutes. Then 5 µL aliquots were taken out and diluted into 1 mL using a solution of benzanilide (0.1 mM) in methanol. Samples were analysed by LCMS and mass spectroscopy response of the product formation was recorded ($SIM_{pdr}/SIM_{IS} = f(t)$).

Deutero indole		
Exp	**Time**	**SIM(Pdr)/SIM(IS)**
1	9	0,0119
2	12	0,0113
3	16	0,0114
4	20	0,0179
5	27	0,1050
6	35	0,1698
7	45	0,2618
8	55	0,3480
9	70	0,5279
10	90	0,6539

Proteo indole		
Exp	**Time**	**SIM(Pdr)/SIM(IS)**
1	9	0,0126
2	12	0,0366
3	16	0,0323
4	20	0,0677
5	27	0,2075
6	35	0,4198
7	45	0,6277
8	55	0,8244
9	70	1,0727
10	90	1,2070

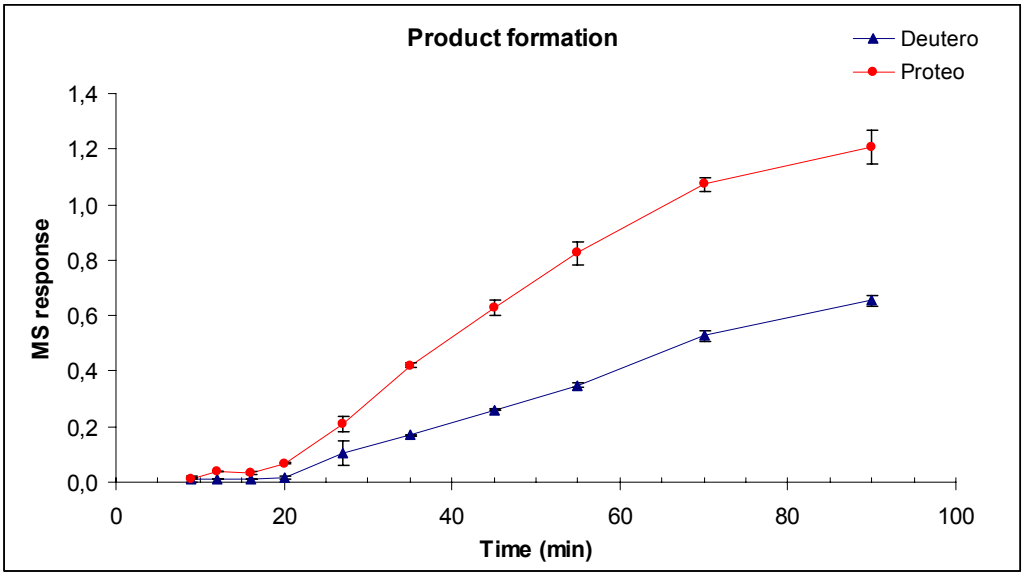


Figure S3. Method A: Product formation for proteo and deutero substrates versus time.

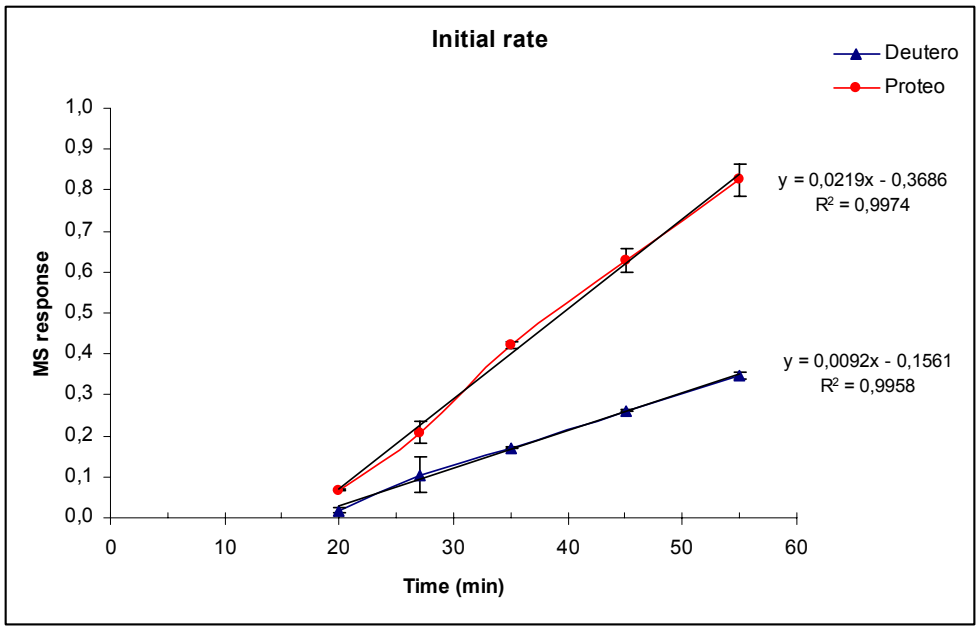


Figure S4. Method A: Initial rate of product formation for proteo and deutero substrates.

KIE: k_H / k_D = 0.0219 / 0.0092 = **2.38**

Method B:

General considerations. Method B is very similar to method A. The main difference is that the initial rates were determined by performing the reaction in a larger reaction vial and by taking aliquots from the same reaction mixture at desired amounts of time instead of having a reaction vial for each data point as in method A. Aliquots taken from the same reaction vessel were rapidly quenched by a methanolic solution of benzanilide used as internal standard. Method B afforded less standard deviation than method A. Experiments for both deuterated and non-deuterated substrates were conducted simultaneously in the same reaction block. The Initial rate for each substrate was determined from the average of two sets of trials.

Method B. A 5 mL microwave vial was charged with deuterated (or non-deuterated) indole (0.272 mmol), K_2CO_3 (41.5mg, 0.272 mmol), $Pd(OAc)_2$ (6.1 mg, 0.027 mmol), $Cu(OAc)_2$ (148.0 mg, 0.820 mmol) and anhydrous DMA (2 mL). The vial was then sealed with a serum cap and the reaction was flushed with nitrogen. The reaction mixture was allowed to stir at room temperature until the starting material completely dissolved before being placed into a pre-thermostated carrousel at 90 ºC. Aliquots (5 µL) were taken out at the desired time and diluted into 1 mL with a solution of benzanilide (0.1 mM) in methanol. Peak area of Single Ion Monitoring (SIM) for the product was recorded by LCMS versus SIM of the internal standard (benzanilide).

Deutero indole		
Exp	**Time**	**SIM(Pdr)/SIM(IS)**
1	5	0,0055
2	10	0,0144
3	15	0,1654
4	20	0,3846
5	25	0,5501
6	30	0,7414
7	35	0,8250
8	40	0,9041
9	45	0,9313
10	50	0,9764
11	65	0,9898

Proteo indole		
Exp	**Time**	**SIM(Pdr)/SIM(IS)**
1	5	0,0000
2	10	0,0220
3	15	0,2000
4	20	0,7552
5	25	1,2127
6	30	1,6432
7	35	1,8691
8	40	2,0775
9	45	2,1964
10	50	2,3340
11	65	2,5375

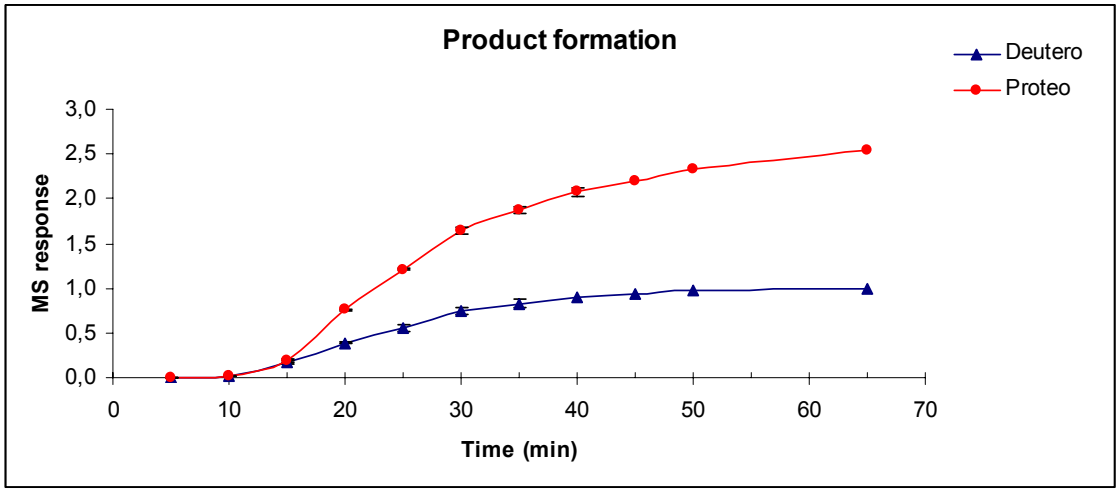


Figure S5. Method B: Product formation for proteo and deutero substrates versus time.

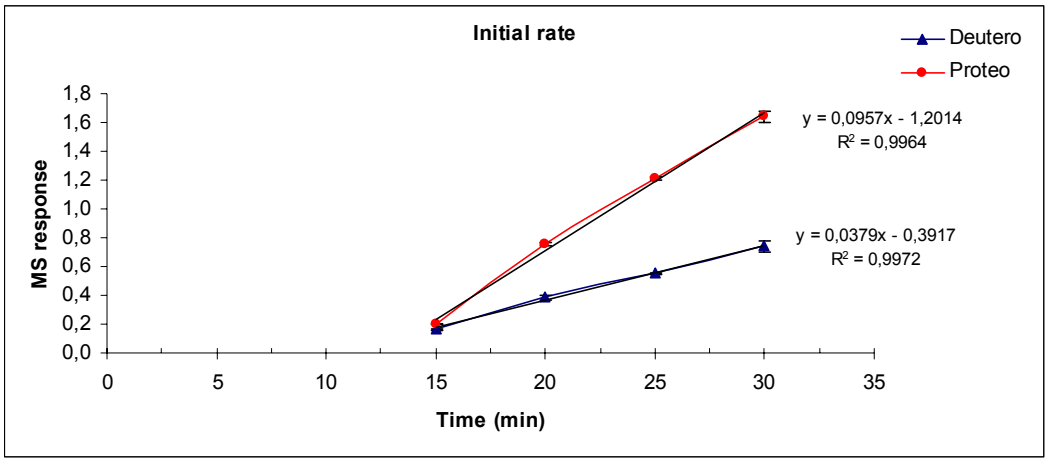
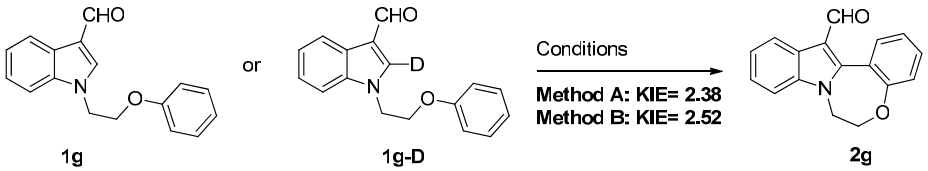


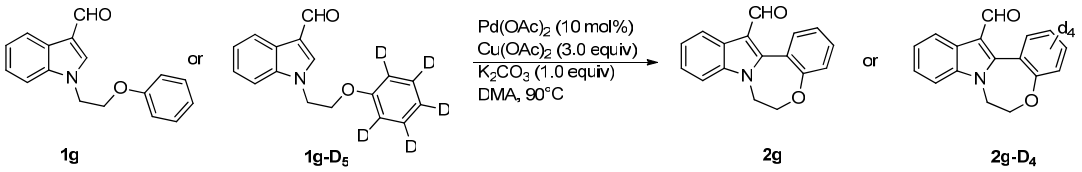
Figure S6. Method B: Initial rate of product formation for proteo and deutero substrates.

KIE: k_H / k_D = 0.0957 / 0.0379 = **2.52**

Summary:



Procedure for the determination of intermolecular KIE at the aryl position



Method A:

Method A as previously described was used to determine the initial rate of the reaction.

Deutero (d5) indole		
Exp	**Time**	**SIM(Pdr)/SIM(IS)**
1	9	0,0039
2	12	0,0123
3	16	0,0406
4	20	0,0828
5	27	0,1398
6	35	0,2127
7	45	0,3218
8	55	0,4585
9	70	0,5465
10	90	0,5873

Proteo indole		
Exp	**Time**	**SIM(Pdr)/SIM(IS)**
1	9	0,0126
2	12	0,0366
3	16	0,0323
4	20	0,0677
5	27	0,2075
6	35	0,4198
7	45	0,6277
8	55	0,8244
9	70	1,0727
10	90	1,2070

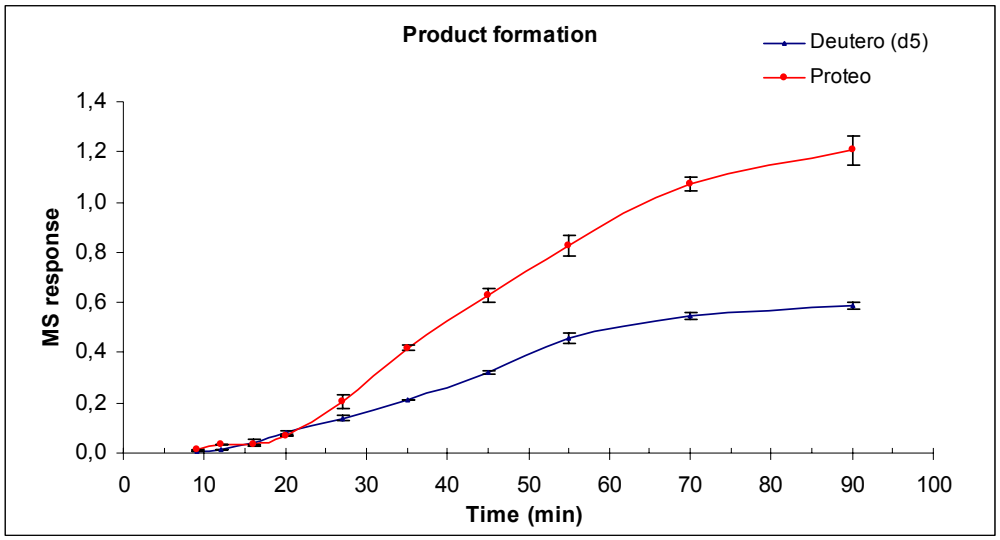


Figure S7. Method A: Product formation for proteo and deutero (d_5) substrates versus time.

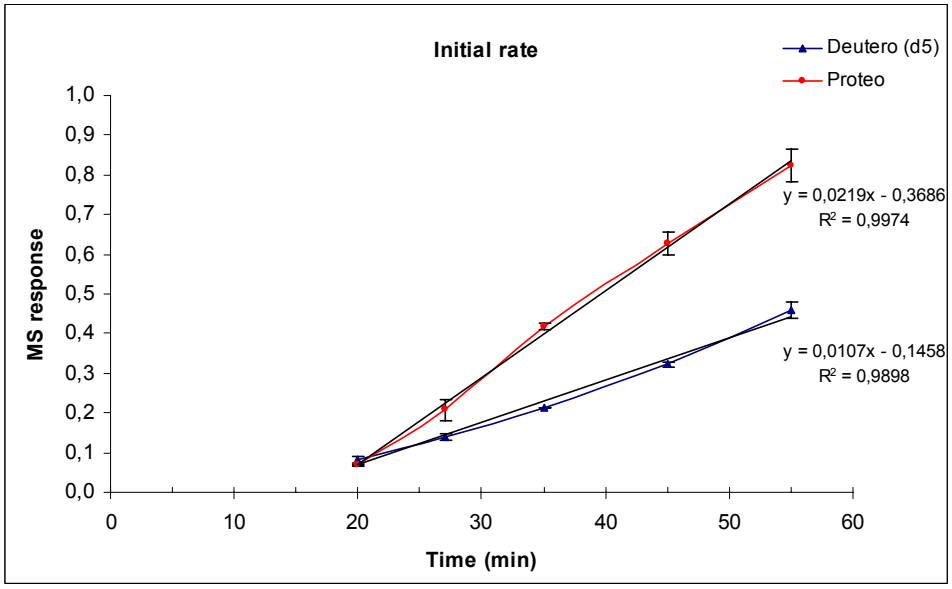


Figure S8. Method A: Initial rate of product formation for proteo and deutero (d_5) substrates.

KIE: k_H / k_D = 0.0219 / 0.0107 = **2.05**

Method B:

Method B was used to determine the initial rate of the reaction.

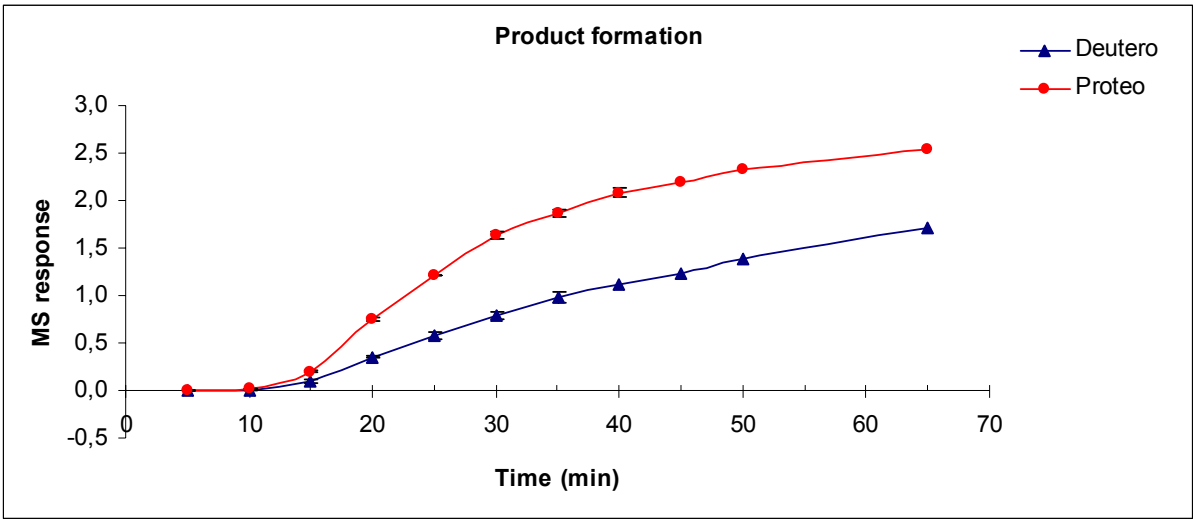


Figure S9. Method B: Product formation for proteo and deutero (d_5) substrates versus time.

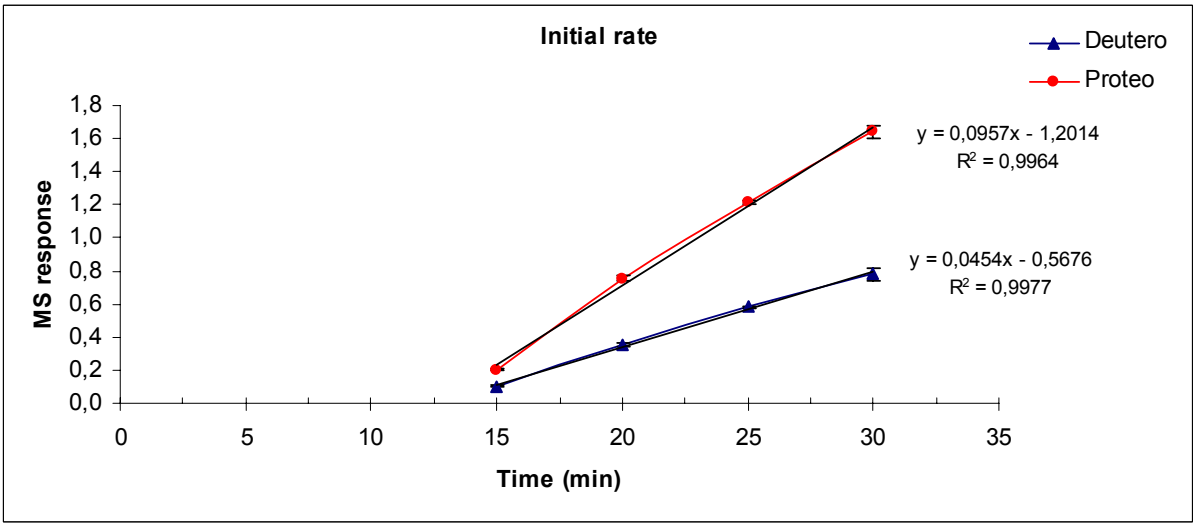
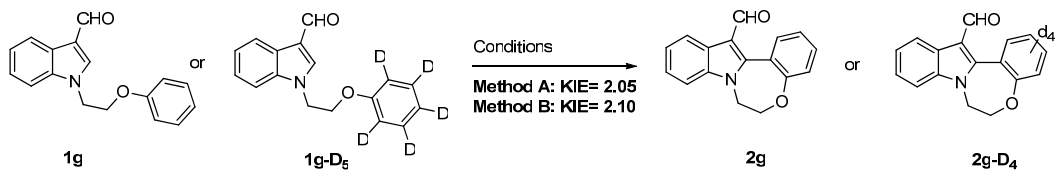


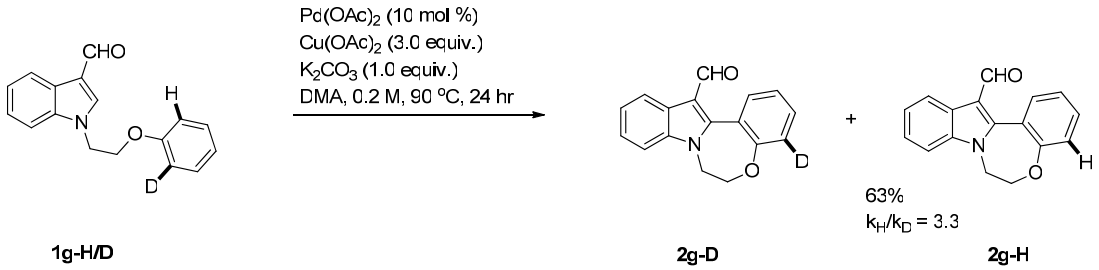
Figure S10. Method B: Initial rate of product formation for proteo and deutero (d_5) substrates.

$$\boxed{\textbf{KIE: } k_H / k_D = 0.0957 / 0.0454 = \textbf{2.10}}$$

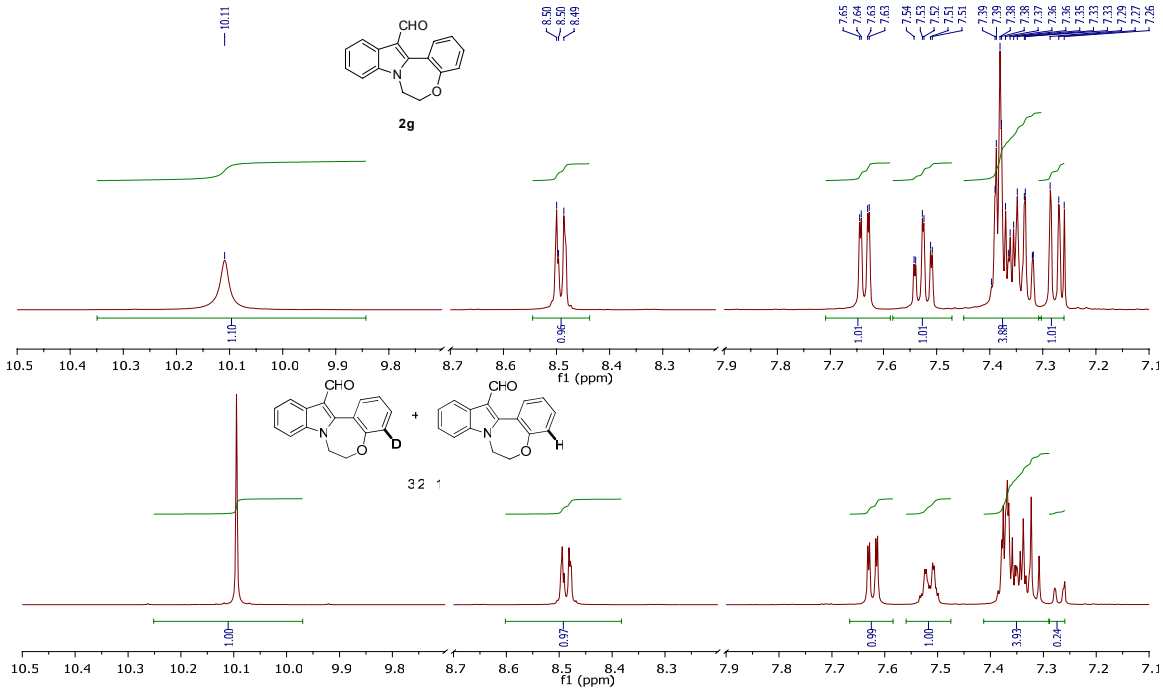
Summary:



Intramolecular KIE[5,6]



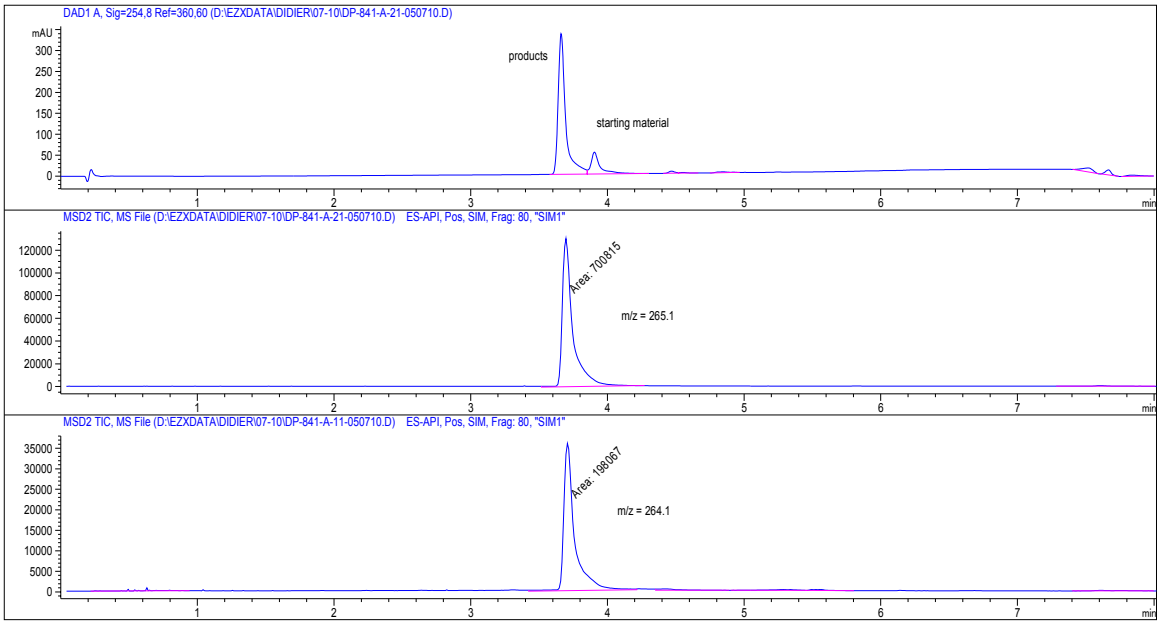
Following our general procedure C, 1-(2-o-deuteriophenoxy-ethyl)-1*H*-indole-3-carbaldehyde **1g-H/D** (60.0 mg, 0.225 mmol), K_2CO_3 (31.0 mg, 0.225 mmol), $Pd(OAc)_2$ (5.0 mg, 0.0225 mmol), $Cu(OAc)_2$ (123.0 mg, 0.675 mmol) were mixed in anhydrous DMA (1.5 mL). The tube was then sealed with a serum cap and the reaction was flushed with nitrogen. The reaction mixture was allowed to stir at room temperature until the starting material completely dissolved before being placed into a pre-heated carrousel at 90 ºC for 16 hr. The mixture was allowed to cool down and directly poured on top of a long silica gel column chromatography. The product was eluted with a mixture hexane/Et_2O (1:1). Pure product was obtained in 63% yield as a white solid. Rf [DCM] = 0.30. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.09 (s, 1H), 8.62 – 8.39 (m, 1H), 7.62 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.57 – 7.48 (m, 1H), 7.42 – 7.29 (m, 4H), 7.27 (dd, *J* = 8.4, 1.2 Hz, 0.24H), 4.62 (t, *J* = 5.7 Hz, 2H), 4.34 (t, *J* = 5.7 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.0 (quat), 154.1 (quat), 147.9 (quat), 135.7 (quat), 132.5 (CH), 132.0 (CH), 125.9 (quat), 124.9 (CH), 124.1 (CH), 123.4 (quat), 123.2 (CH), 122.9 (t, *J* = 24.9 Hz, CD), 122.7 (CH), 114.6 (quat), 108.6 (CH), 74.7 (CH_2), 41.5 (CH_2).



k_H/k_D = (1.00-0.24)/0.24 = **3.2**

Figure S11. Determination of intramolecular kinetic isotope effect by ^{1}H NMR

[6] Foresee, L. N.; Tunge, J. A. *Organometallics* **2005**, *24*, 6440-6444.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products
starting material
min
MSD2 TIC, MS File (D:\EZXDATA\DIDIER\07-10\DP-841-A-21-050710.D) ES-API, Pos, SIM, Frag: 80, "SIM1"
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m/z = 265.1
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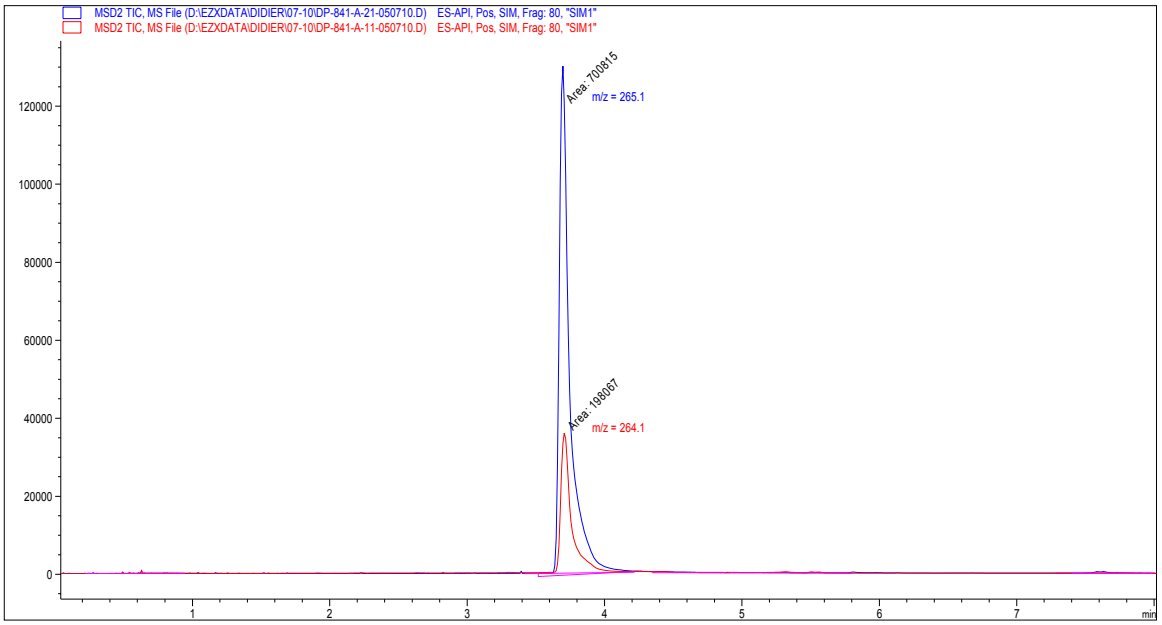
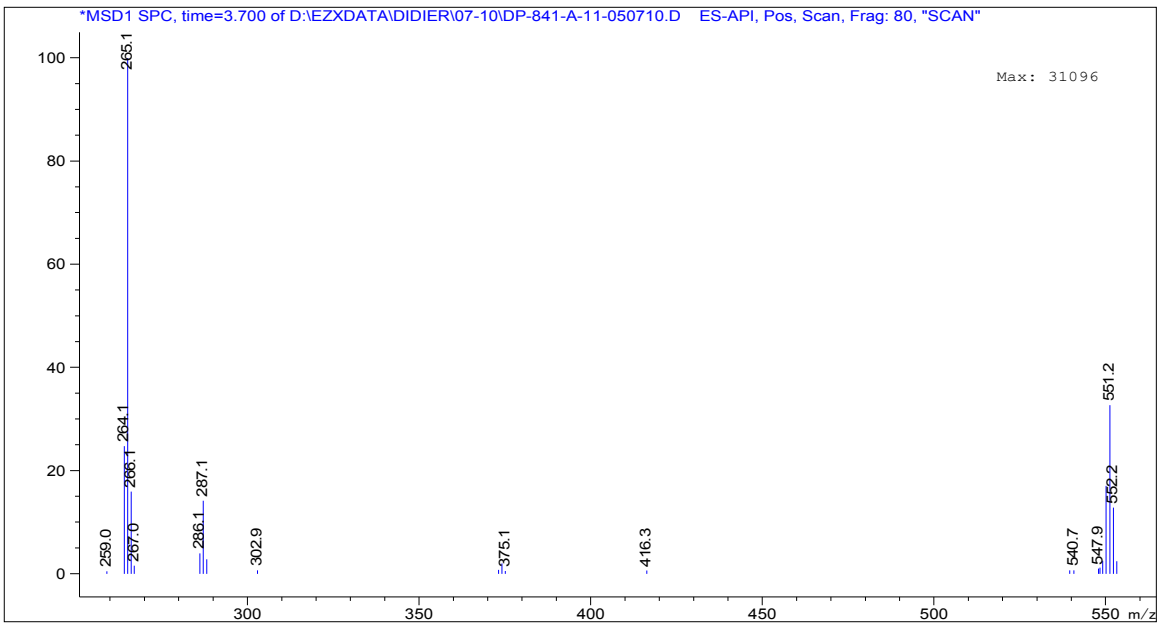
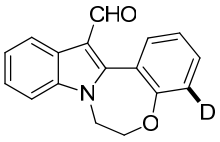
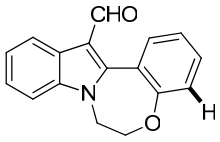
Area: 198067
m/z = 264.1


MSD2 TIC, MS File (D:\EZXDATA\DIDIER\07-10\DP-841-A-21-050710.D) ES-API, Pos, SIM, Frag: 80, "SIM1"
MSD2 TIC, MS File (D:\EZXDATA\DIDIER\07-10\DP-841-A-11-050710.D) ES-API, Pos, SIM, Frag: 80, "SIM1"
Area: 700815
m/z = 265.1
Area: 198067
m/z = 264.1
min





Chemical Formula: $C_{17}H_{12}DNO_2$
Exact Mass: 264.101
LRMS $(M+H)^+$= 265.1 (100%)



Chemical Formula: $C_{17}H_{13}NO_2$
Exact Mass: 263.095
LRMS $(M+H)^+$ = 264.1 (100%), 265.1 (18.8%)

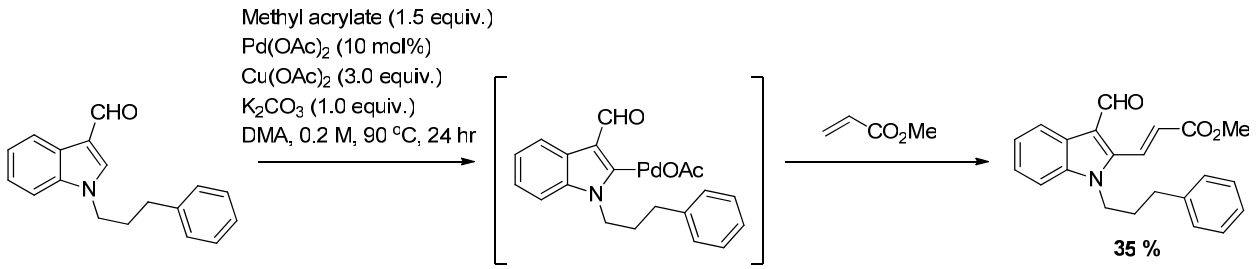
LRMS $(M+H)^+$	surface area	corrected surface area[a]
264.1	198067	198067
265.1	700815	663474[b]

[a]Carbon ^{13}C abundance: 1.109%, [b]reduced by carbon-isotope signal of [264.1]

ESI-MS ratio: [265.1]/[264.1] = k_H/k_D = 663474/198067 = **3.3**

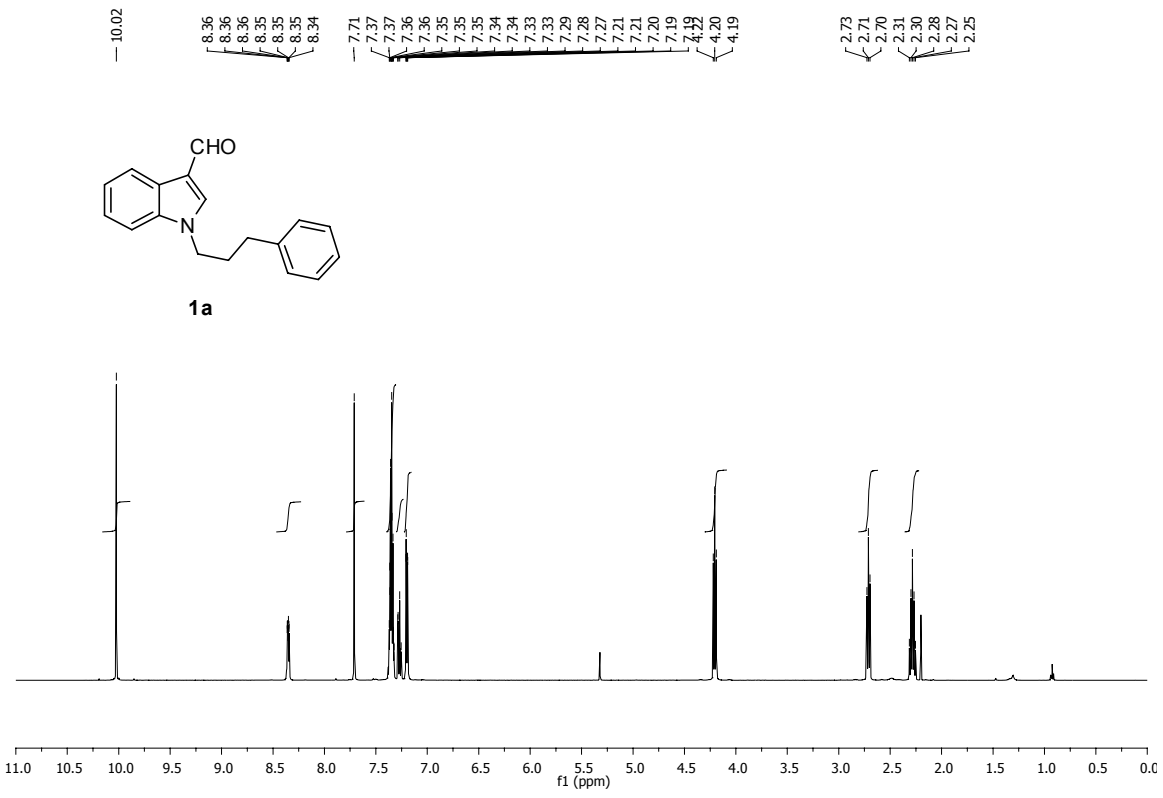
Figure S12. Determination of intramolecular kinetic isotope effect by LCMS analysis.

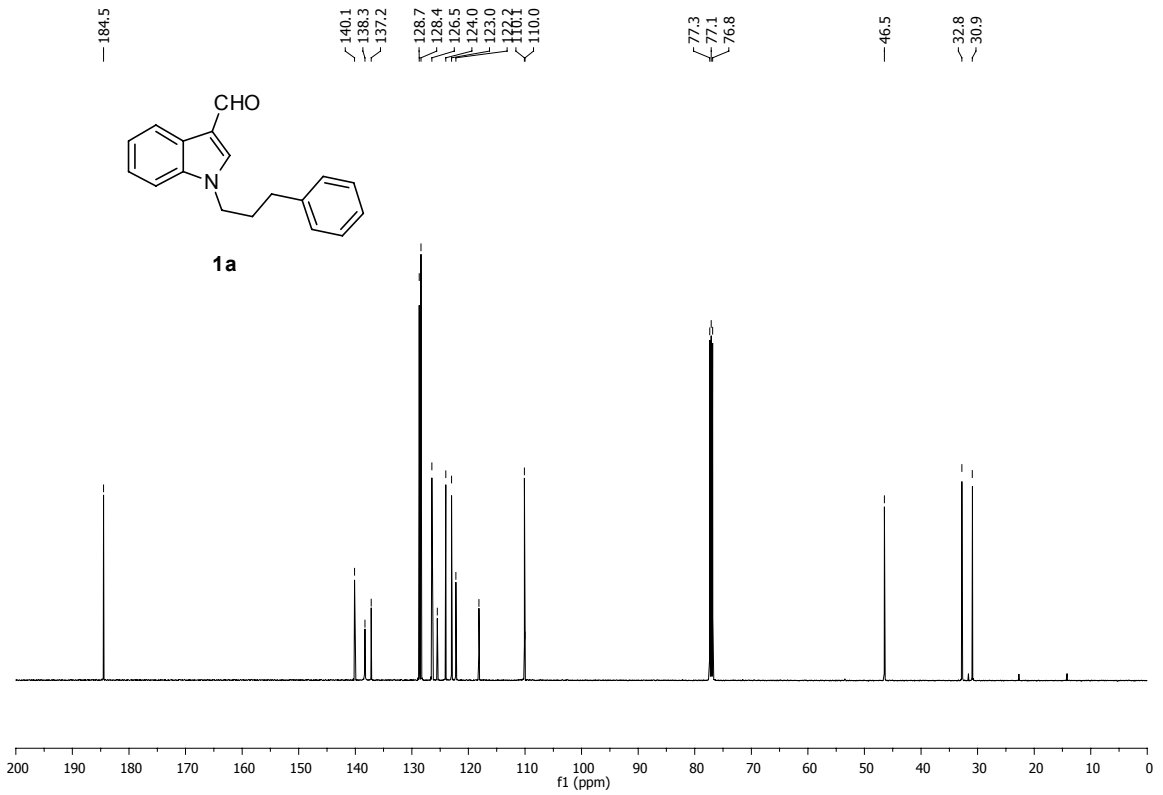
Trapping of palladated indole intermediate by oxidative Heck reaction (Scheme 1 in paper)

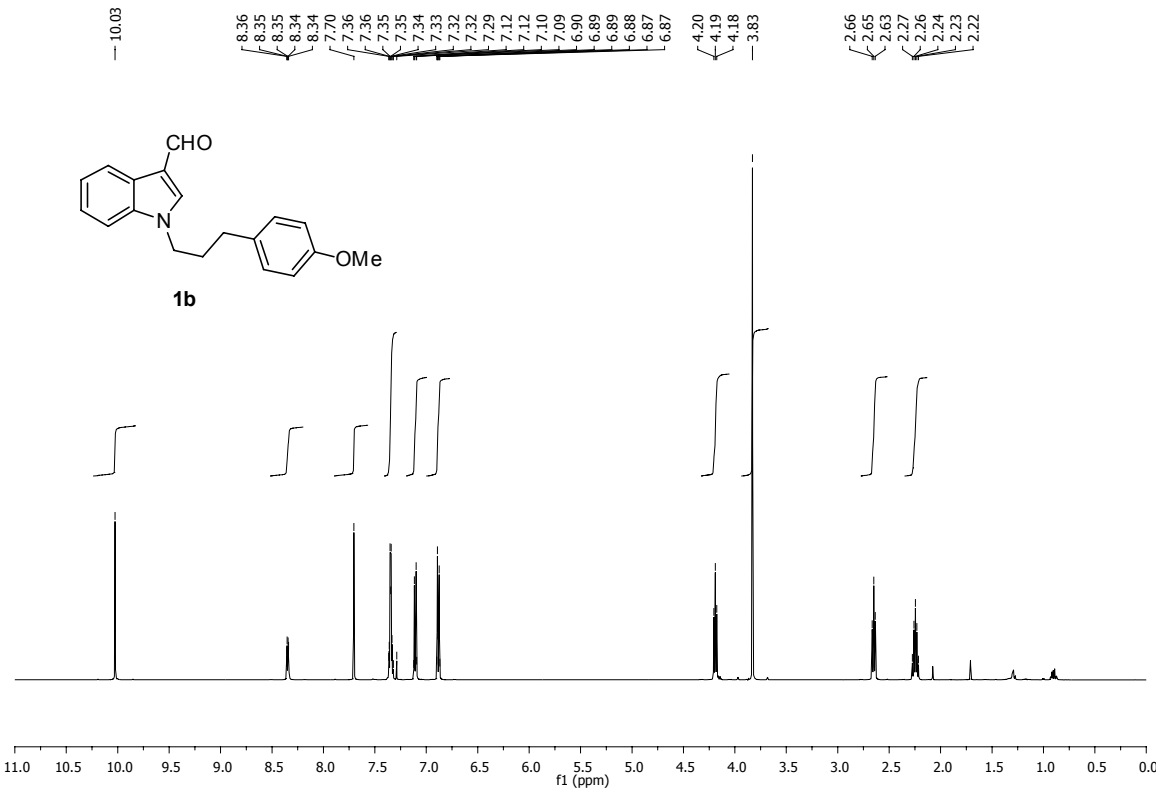


(E)-3-[3-Formyl-1-(3-phenyl-propyl)-1*H*-indol-2-yl]-acrylic acid methyl ester, 8. A 5 mL microwave vial was charged with 1-(3-Phenyl-propyl)-1H-indole-3-carbaldehyde **1a**. (53.0 mg, 0.20 mmol), methyl acrylate (27.0 uL, 0.30 mmol), K_2CO_3 (28.0 mg, 0.20 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), $Cu(OAc)_2$ (109.0 mg, 0.6 mmol) and anhydrous DMA (1 mL). The tube was then sealed with a serum cap and the reaction was flushed with nitrogen. The reaction mixture was allowed to stir at room temperature until the starting material completely dissolved before being placed into a pre-thermostated carrousel at 90 ºC for 16 hr. The mixture was allowed to cool down and directly poured on top of a long silica gel column chromatography. The product was eluted with a mixture hexane/Et_2O (75:35). Pure **8** was obtained in 35% yield as a yellow solid. Mp (Et_2O) = 93 °C. Rf [hexane / Et_2O (4:6)] = 0.50. ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.19 (s, 1H), 8.42 (dd, *J* = 6.8, 1.9 Hz, 1H), 7.85 (d, *J* = 15.9 Hz, 1H), 7.39 - 7.33 (m, 4H), 7.30 – 7.23 (m, 2H), 7.19 (d, *J* = 7.2 Hz, 2H), 6.53 (d, *J* = 15.9 Hz, 1H), 4.34 – 4.16 (m, 2H), 3.90 (s, 3H), 2.73 (t, *J* = 7.5 Hz, 2H), 2.28 – 2.11 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 185.0 (quat), 165.8 (quat), 142.2 (quat), 140.0 (quat), 137.1 (quat), 130.2 (CH), 128.7 (2 CH), 128.3 (2 CH), 127.9 (CH), 126.5 (CH), 125.9 (quat), 125.2 (CH), 123.6 (CH), 122.4 (CH), 117.0 (quat), 110.0 (CH), 52.3 (CH_3), 43.8 (CH_2), 32.9 (CH_2), 31.0 (CH_2). HRMS (ES^+) cald. for $(M+H)^+$ $C_{22}H_{22}NO_3$: 348.1594; found 348.1593.

III: NMR Spectra



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7.35
7.35
7.34
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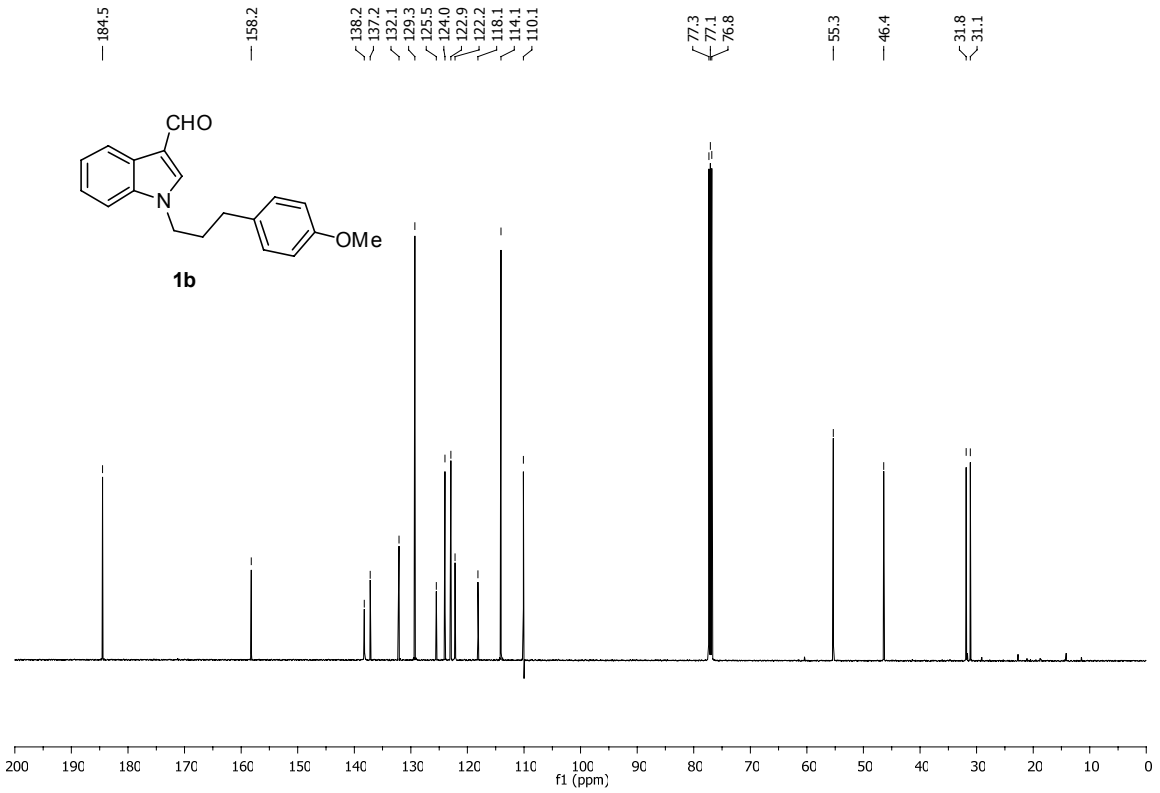
7.32
7.32
7.29
7.12
7.12
7.10
7.09
6.90
6.89
6.89
6.88
6.87
6.87
4.20
4.19
4.18
3.83
2.66
2.65
2.63
2.27
2.26
2.24
2.23
2.22
CHO
N
OMe
1b
f1 (ppm)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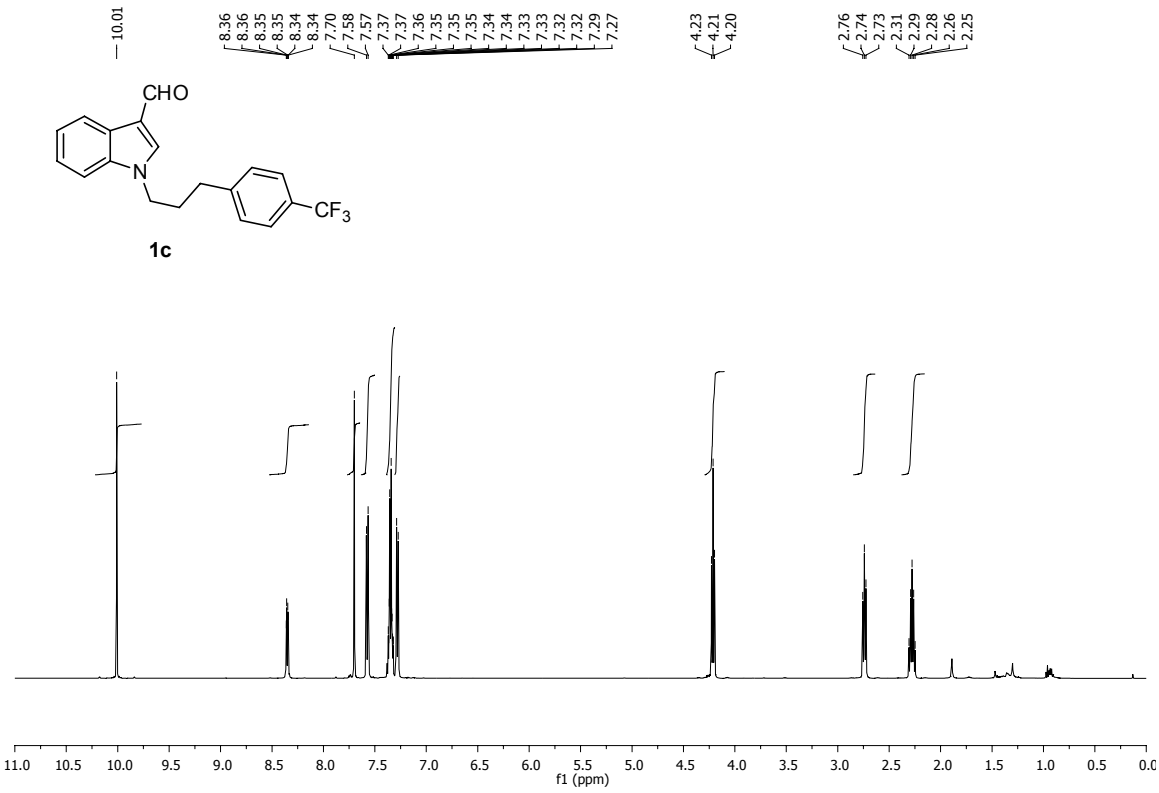
158.2
138.2
137.2
132.1
129.3
125.5
124.0
122.9
122.2
118.1
114.1
110.1
77.3
77.1
76.8
55.3
46.4
31.8
31.1
CHO
N
OMe
1b
f1 (ppm)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7.34
7.34
7.33
7.33
7.32
7.32
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4.23
4.21
4.20
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2.74
2.73
2.31
2.29
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2.25
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CF3
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9.5
9.0
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8.0
7.5
7.0
6.5
6.0
5.5
5.0
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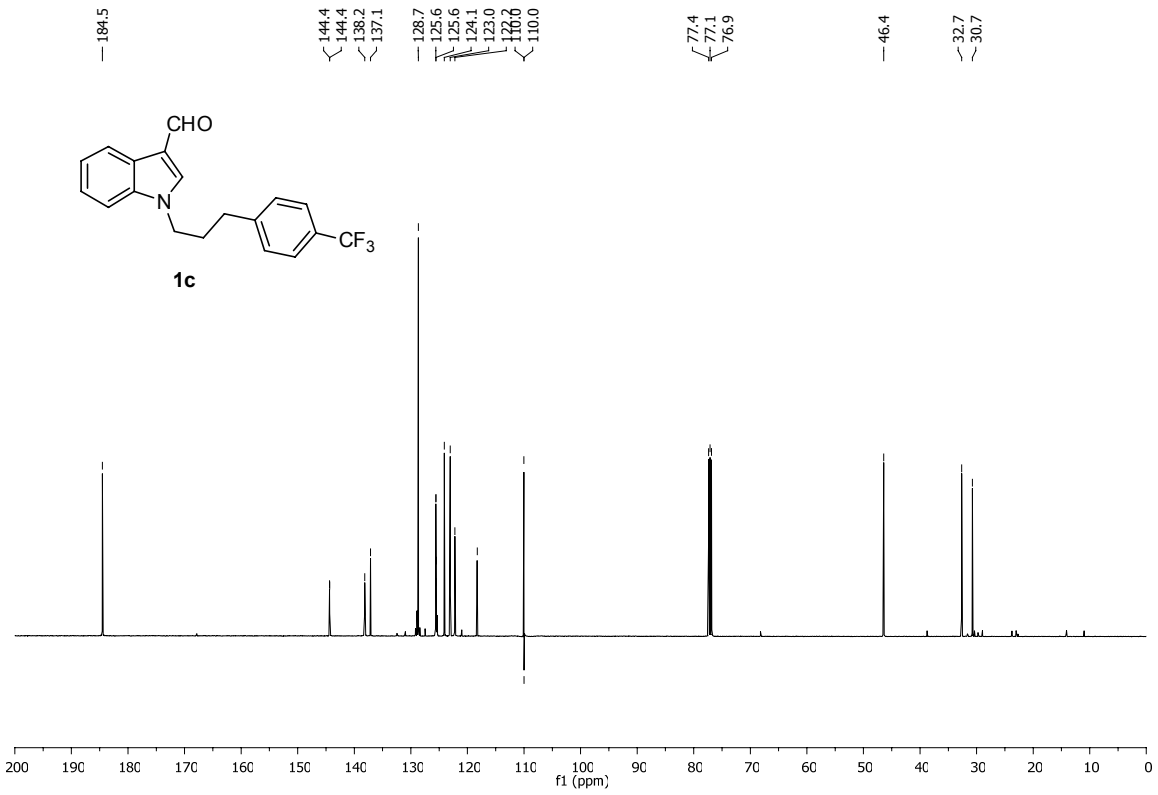
1.0
0.5
0.0
f1 (ppm)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144.4
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125.6
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123.0
122.2
110.0
110.0
77.4
77.1
76.9
46.4
32.7
30.7
CHO
N
CF3
1c
200
190
180
170
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150
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130
120
110
100
90
80
70
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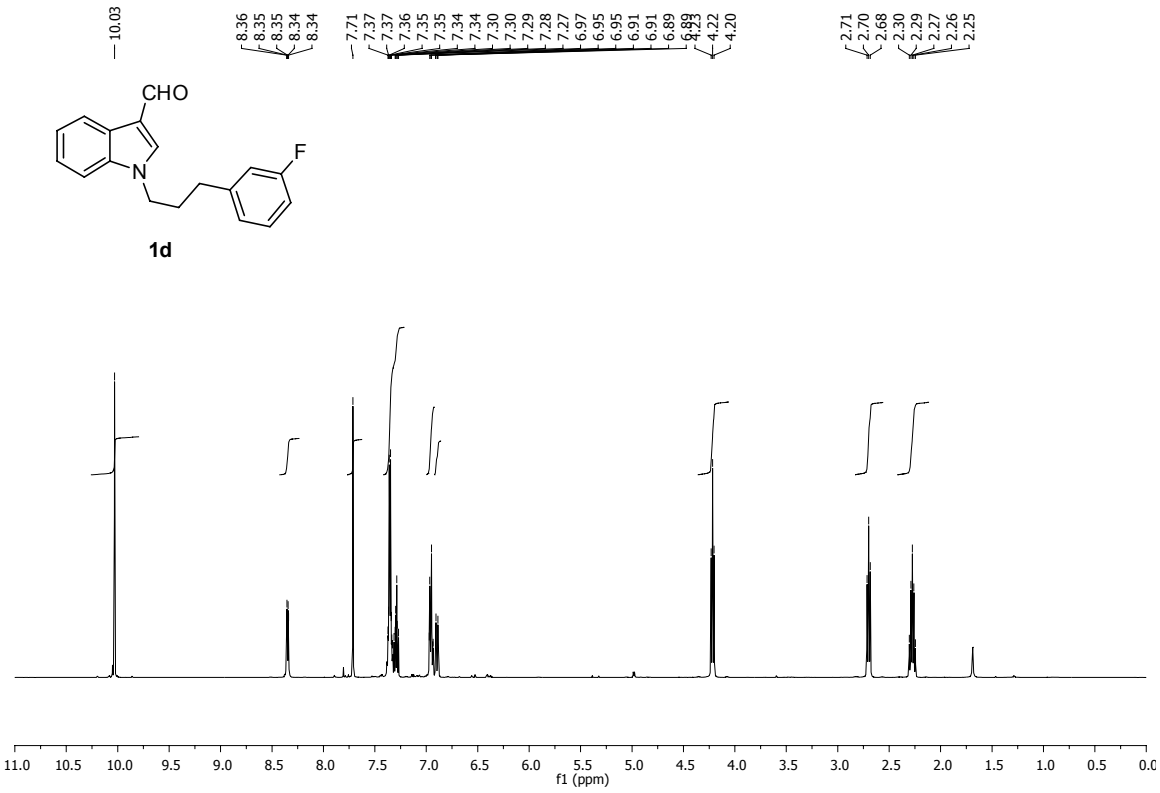
50
40
30
20
10
0
f1 (ppm)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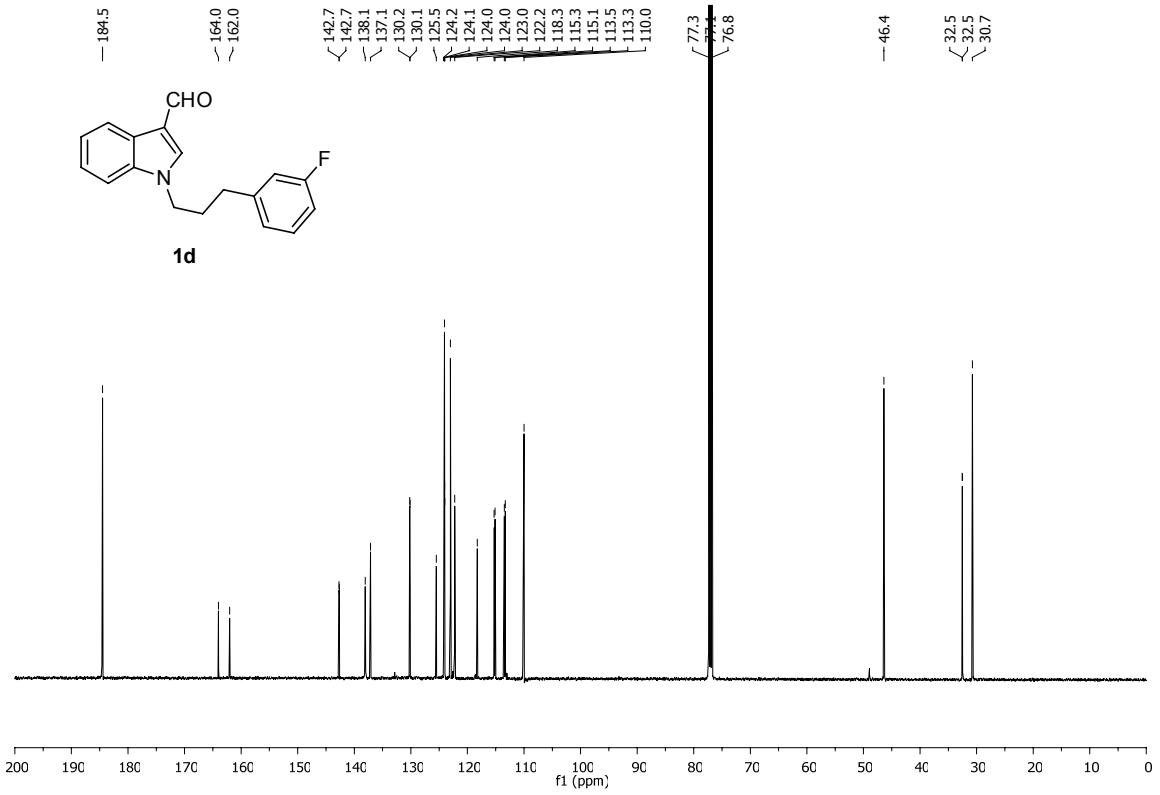
7.30
7.29
7.28
7.27
6.97
6.95
6.95
6.91
6.91
6.89
6.89
4.23
4.22
4.20
2.71
2.70
2.68
2.30
2.29
2.27
2.26
2.25
CHO
N
F
1d
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

.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130.2
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124.0
124.0
123.0
122.2
118.3
115.3
115.1
113.5
113.3
110.0
77.3
76.8
46.4
32.5
32.5
30.7
CHO
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F
1d
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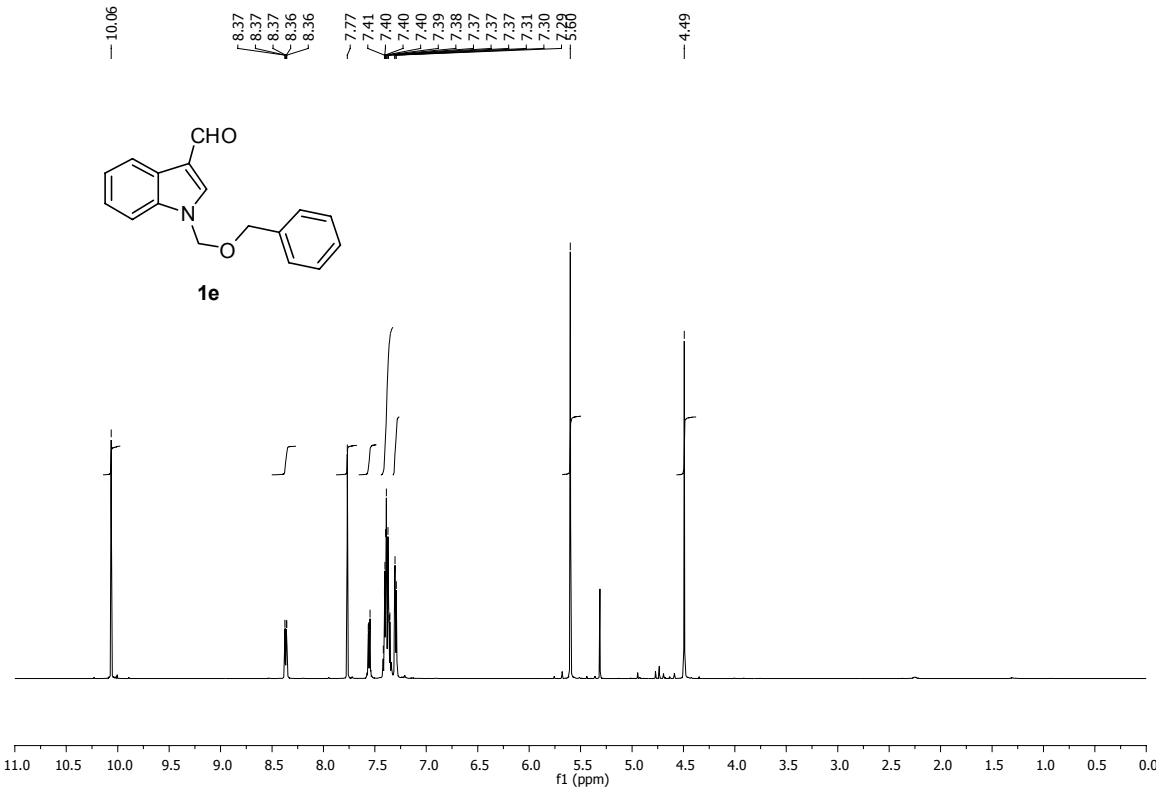
f1 (ppm)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7.38
7.37
7.37
7.37
7.31
7.30
7.28
5.60
4.49
CHO
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O
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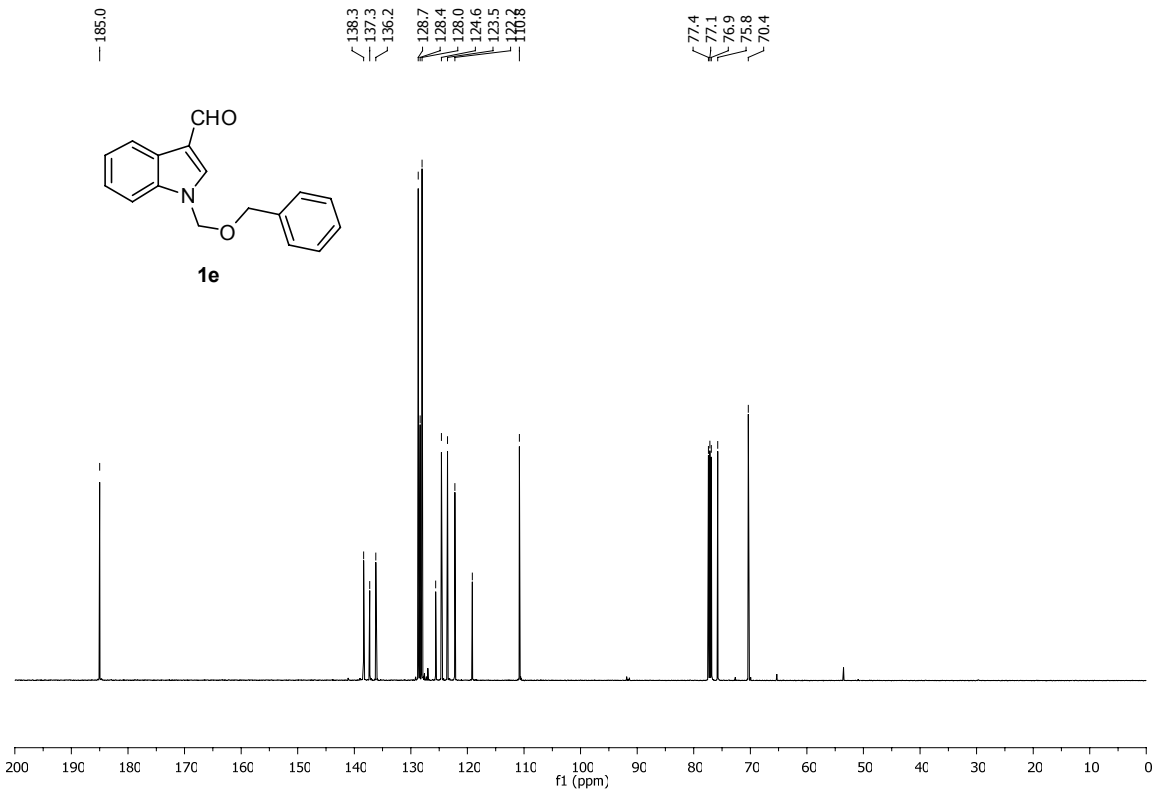
f1 (ppm)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137.3
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128.7
128.4
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124.6
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122.2
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O
1e
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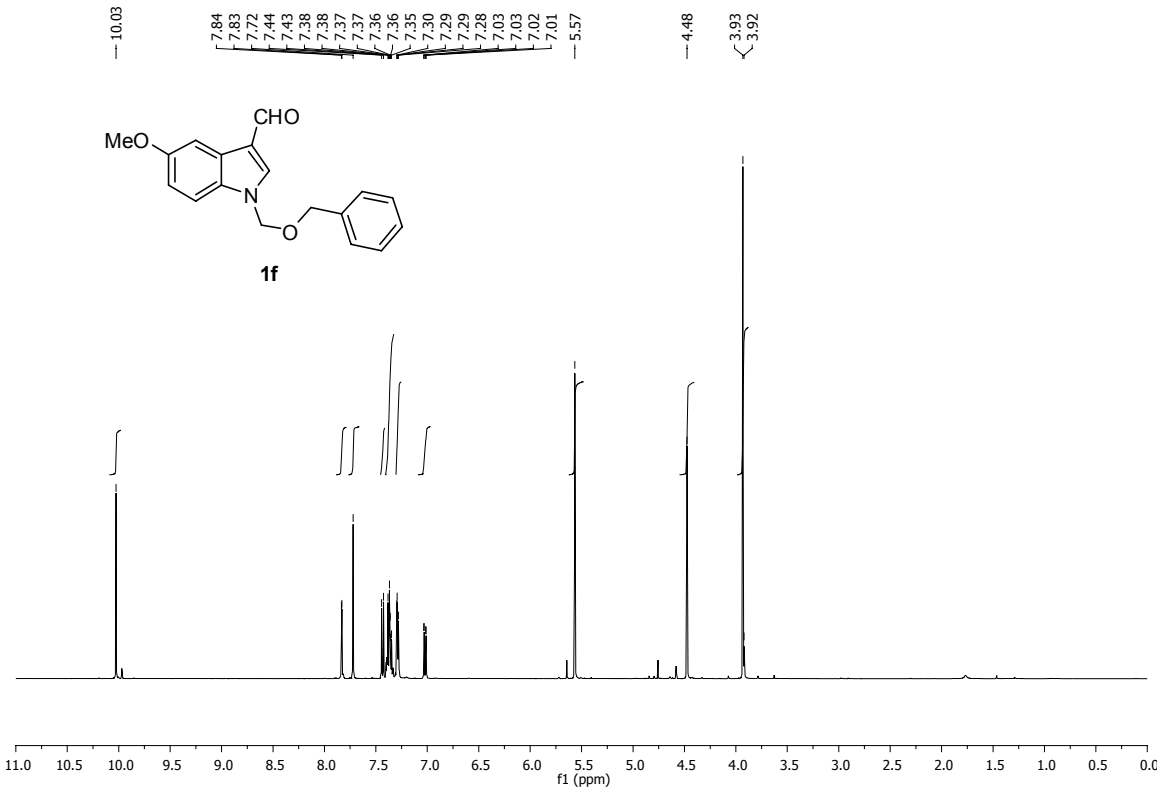
f1 (ppm)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7.30
7.29
7.29
7.28
7.03
7.03
7.02
7.01
5.57
4.48
3.93
3.92
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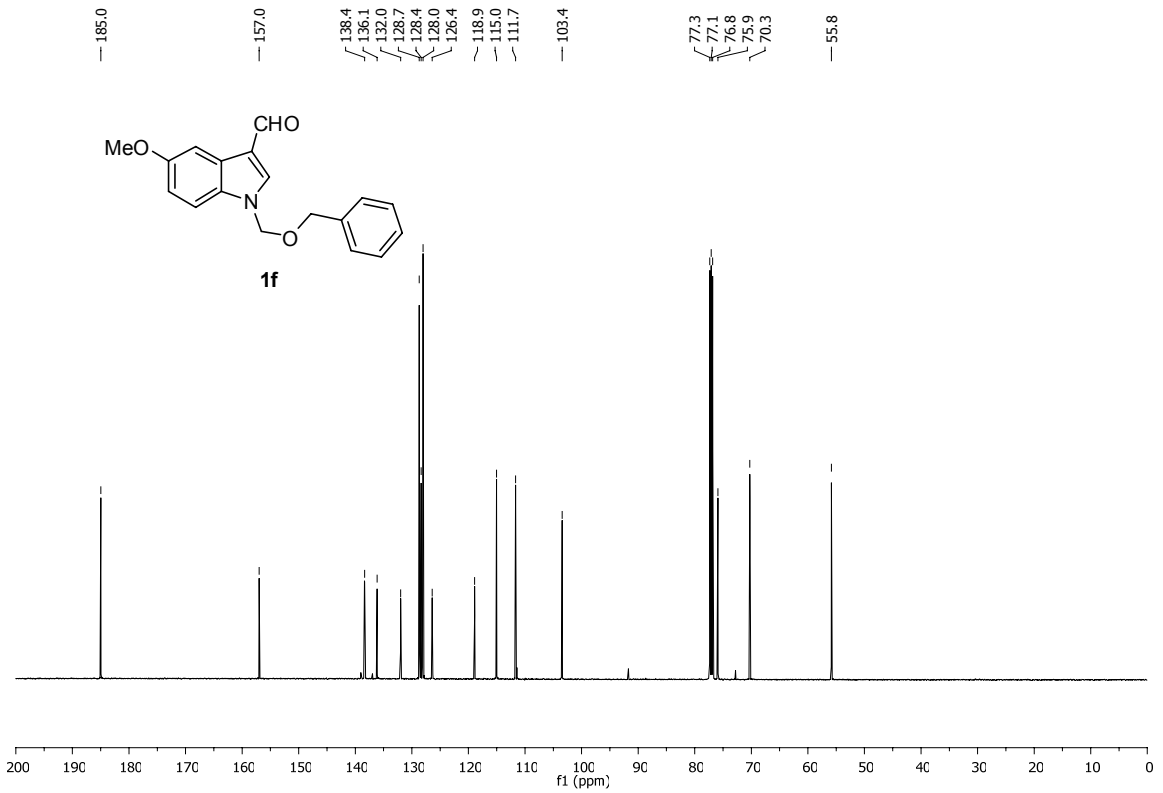
MeO
N
O
1f
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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132.0
128.7
128.4
128.0
126.4
118.9
115.0
111.7
103.4
77.3
77.1
76.8
75.9
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55.8
CHO
MeO
N
O
1f
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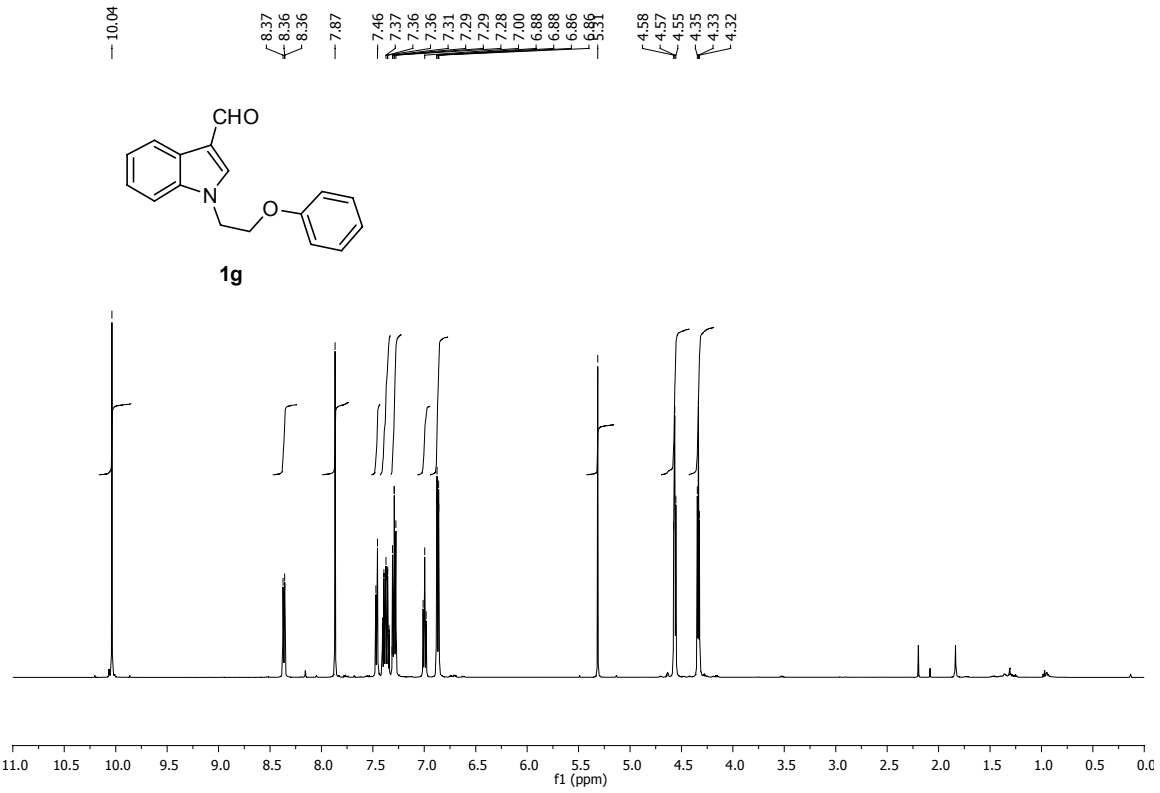
f1 (ppm)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4.57
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4.33
4.32
CHO
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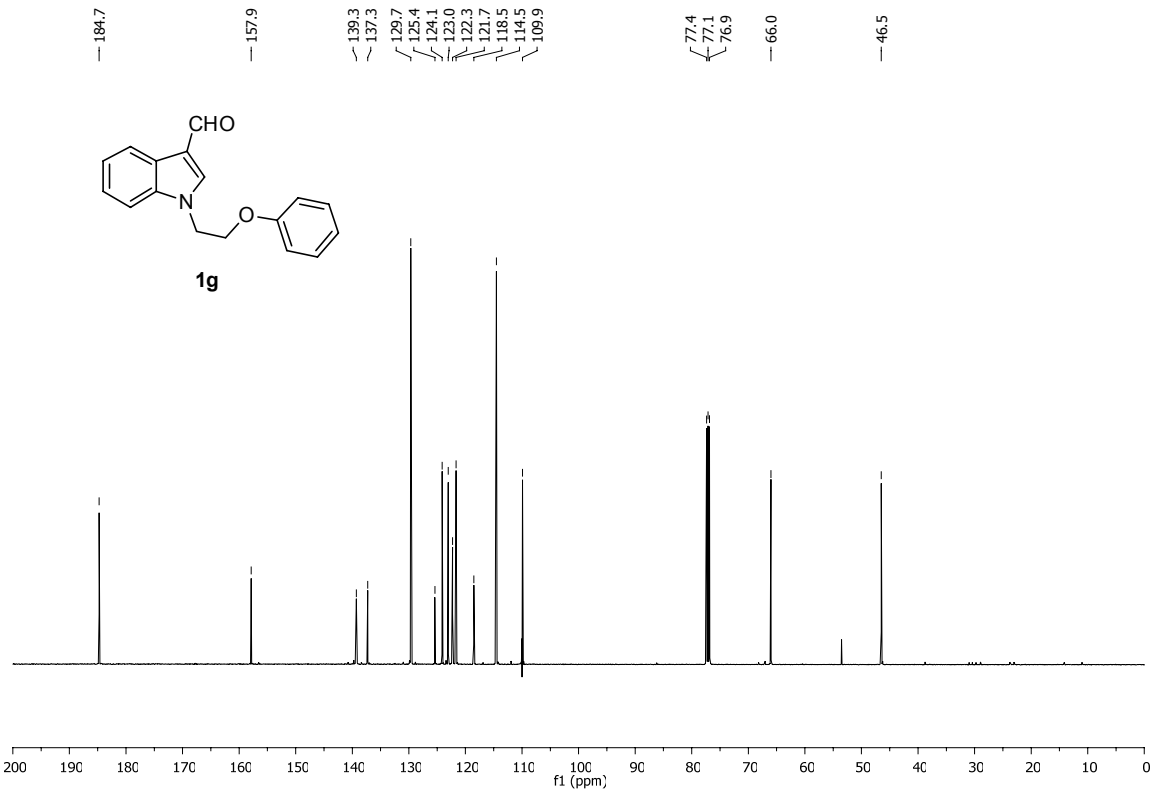
O
1g
f1 (ppm)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124.1
123.0
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121.7
118.5
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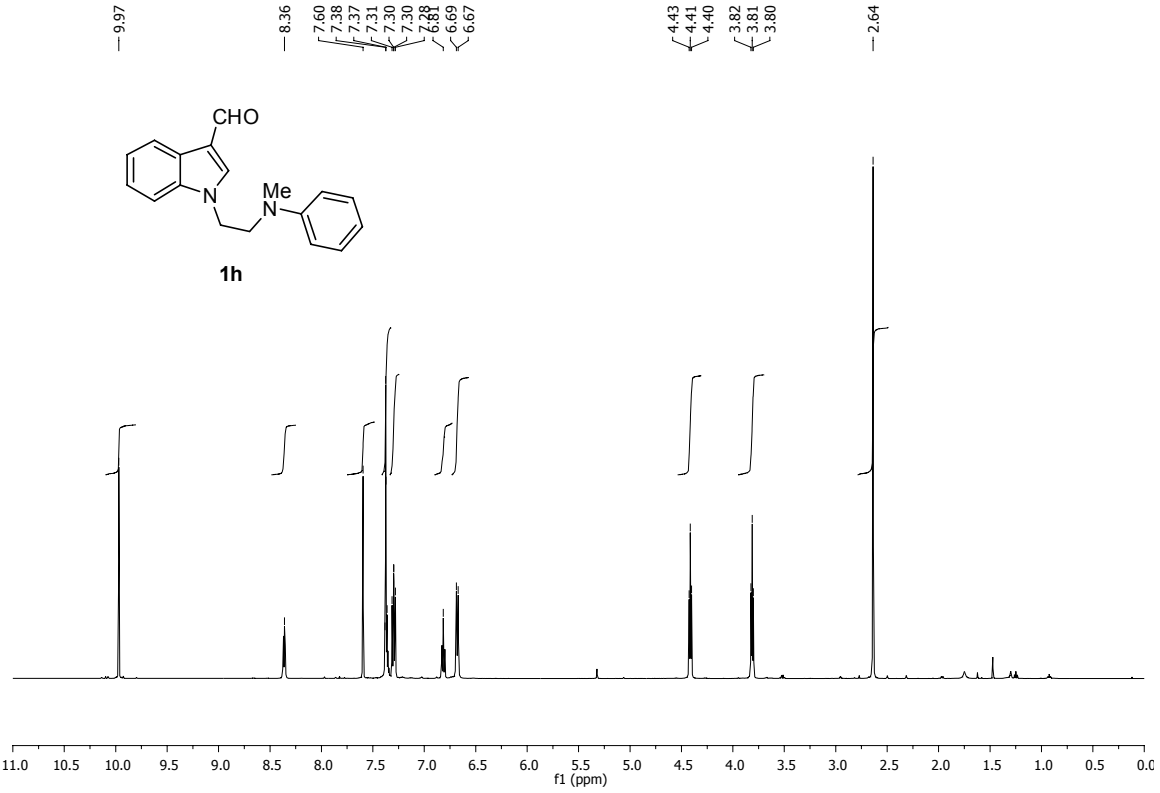
109.9
77.4
77.1
76.9
66.0
46.5
CHO
N
O
1g
f1 (ppm)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3.81
3.80
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Me
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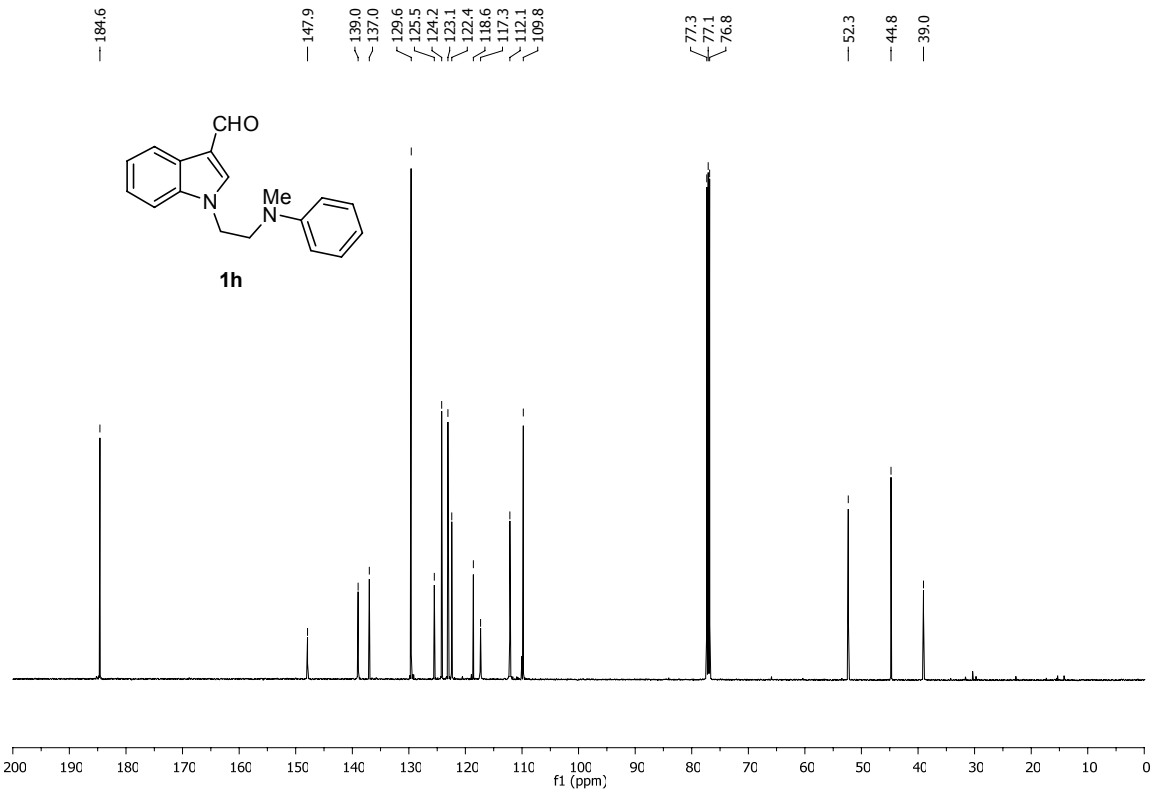
f1 (ppm)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123.1
122.4
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109.8
77.3
77.1
76.8
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Me
N
1h
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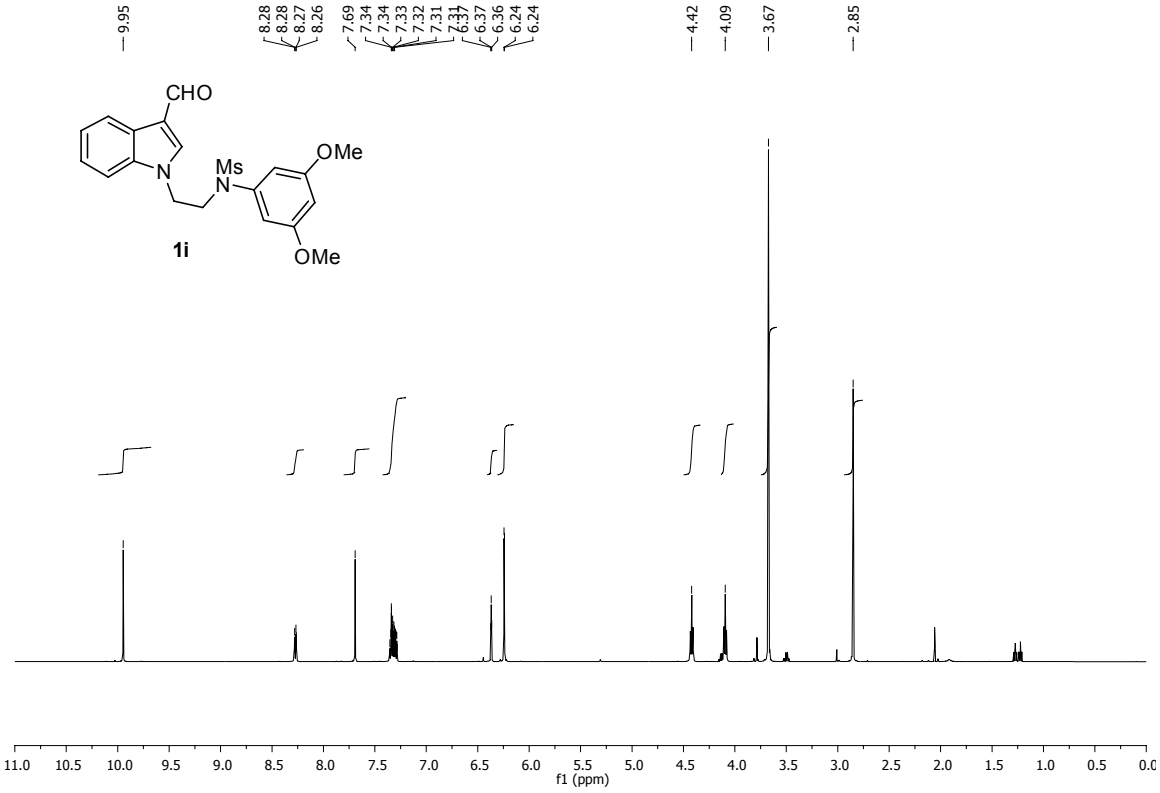
f1 (ppm)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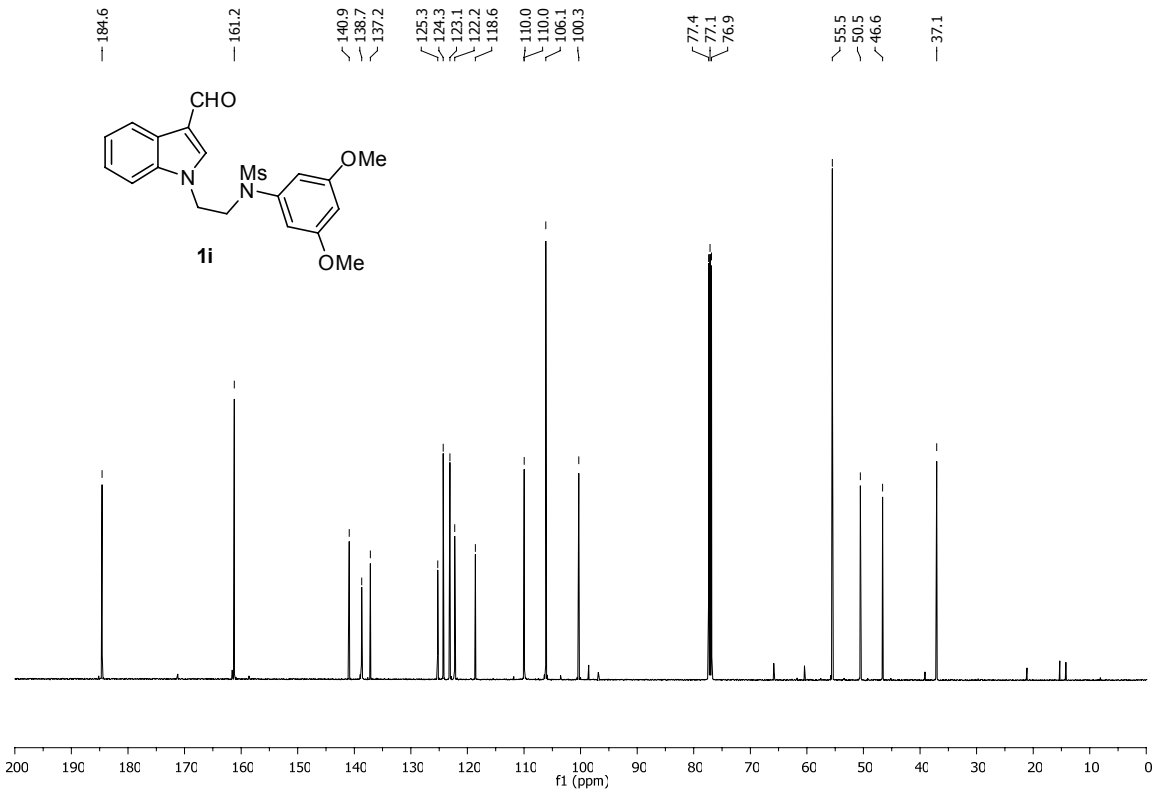
7.31
7.31
6.37
6.36
6.24
6.24
4.42
4.09
3.67
2.85
CHO
N
Ms
N
OMe
OMe
1i
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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77.4
77.1
76.9
55.5
50.5
46.6
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N
OMe
OMe
1i
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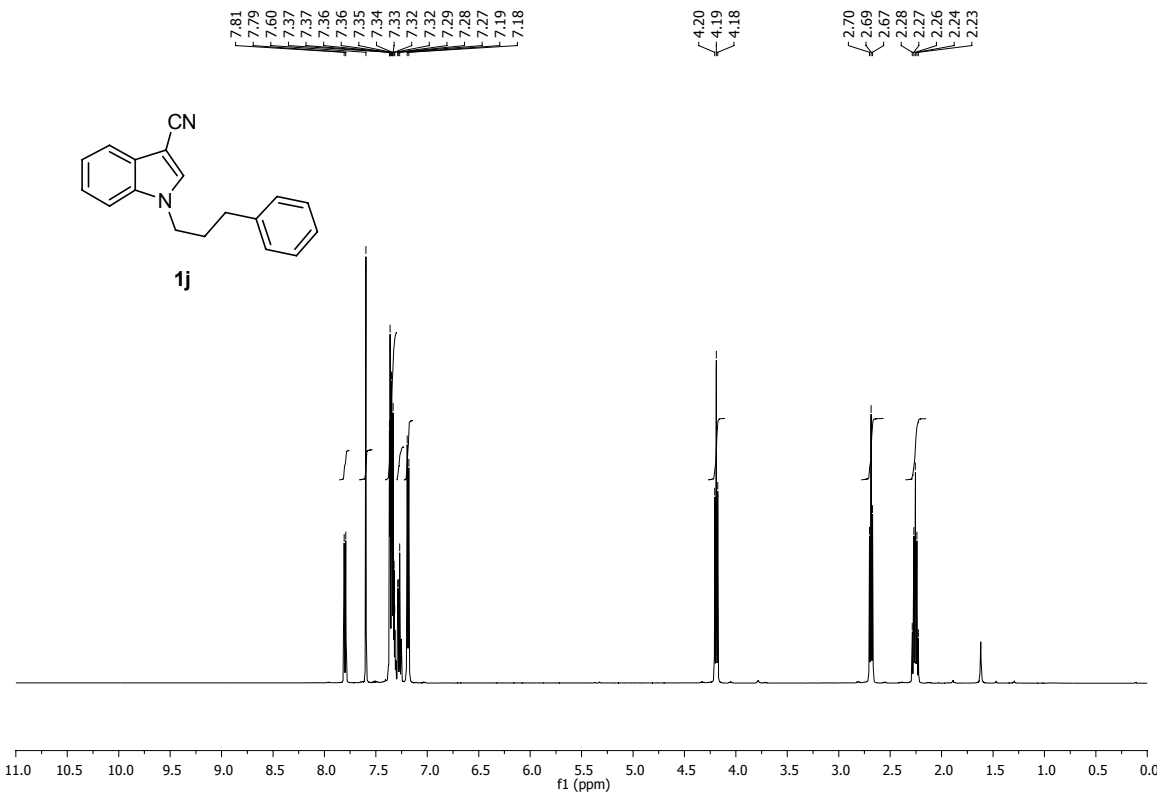
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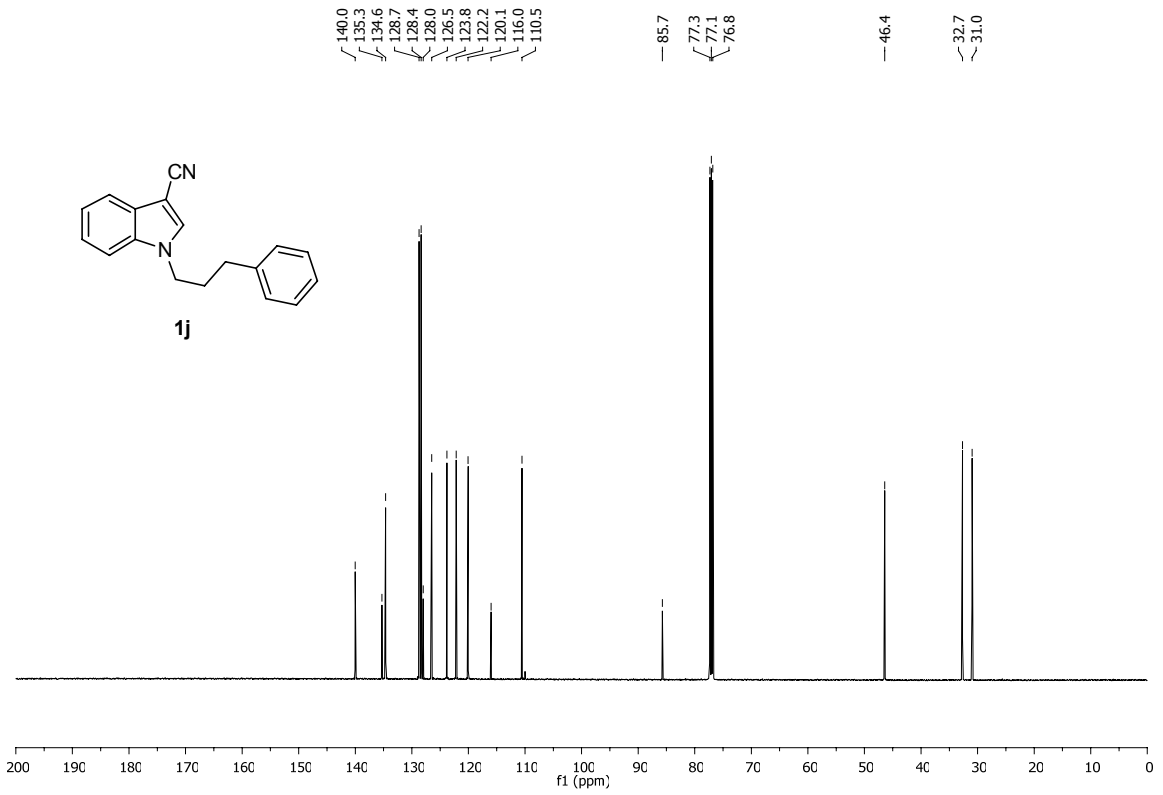
7.28
7.27
7.19
7.18
4.20
4.19
4.18
2.70
2.69
2.67
2.28
2.27
2.26
2.24
2.23
CN
N
1j
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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128.0
126.5
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116.0
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85.7
77.3
77.1
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32.7
31.0
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N
1j
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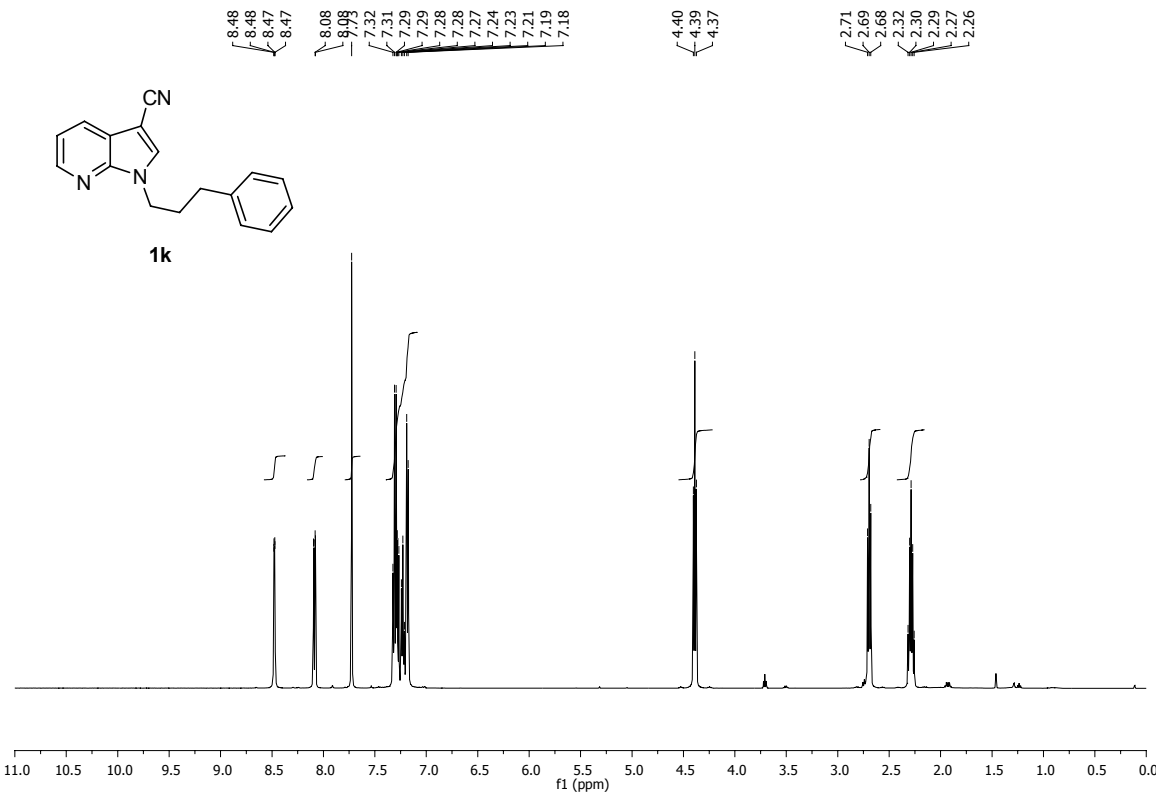
f1 (ppm)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4.37
2.71
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2.32
2.30
2.29
2.27
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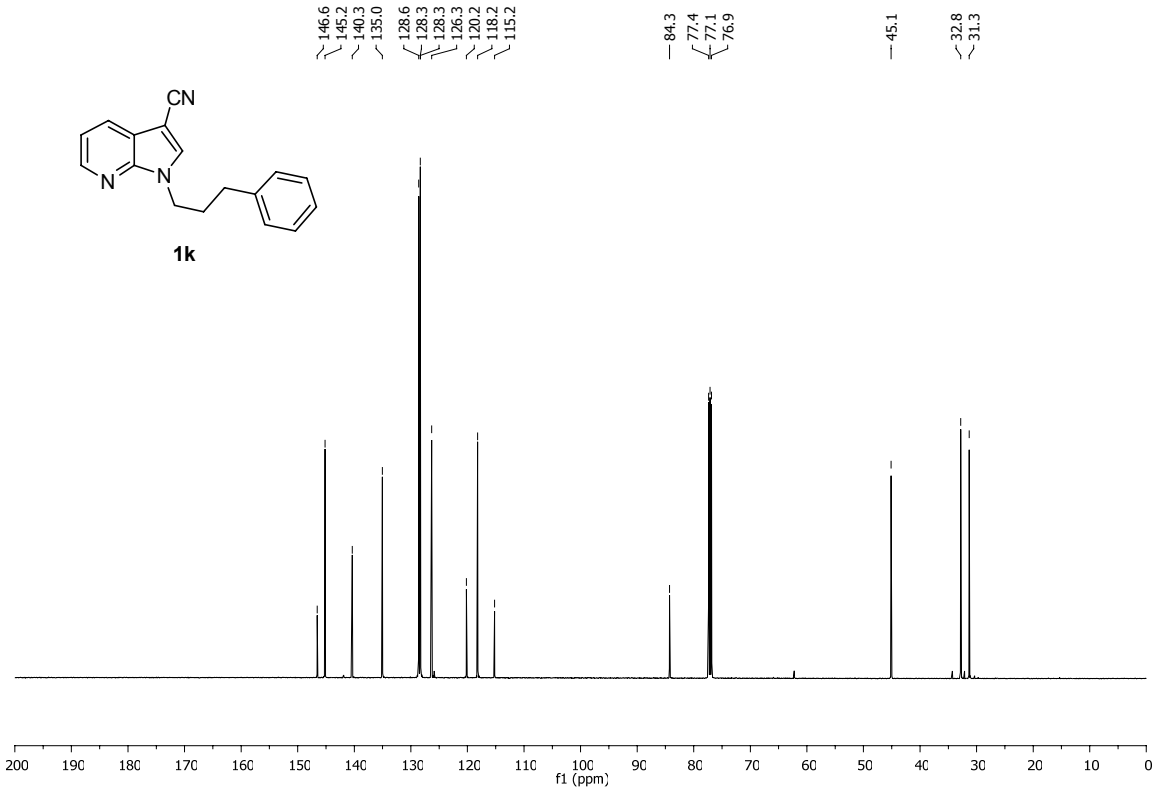
f1 (ppm)


146.6
145.2
140.3
135.0
128.6
128.3
128.3
126.3
120.2
118.2
115.2
84.3
77.4
77.1
76.9
45.1
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31.3
CN
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N
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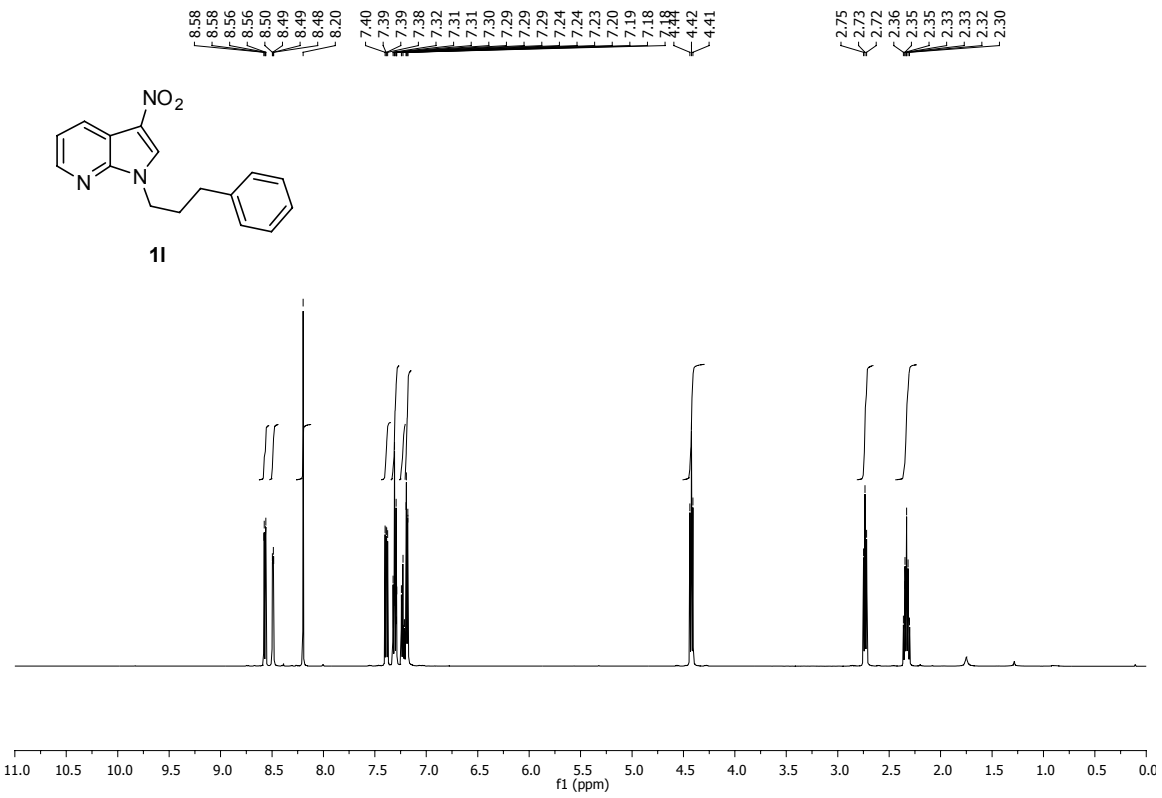
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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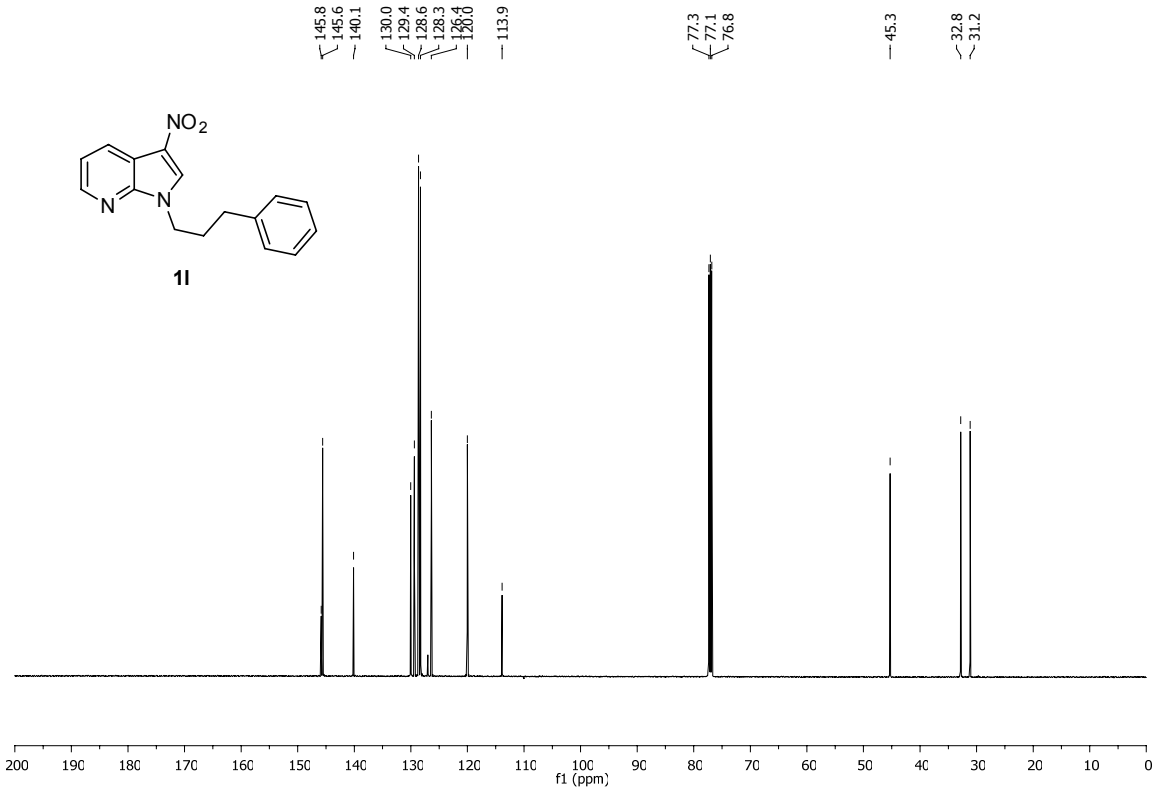
7.38
7.32
7.31
7.31
7.30
7.29
7.29
7.29
7.24
7.24
7.23
7.20
7.19
7.18
4.42
4.41
2.75
2.73
2.72
2.36
2.35
2.35
2.33
2.33
2.32
2.30
NO2
N
N
1l
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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129.4
128.6
128.3
126.4
120.0
113.9
77.3
77.1
76.8
45.3
32.8
31.2
NO2
N
N
1l
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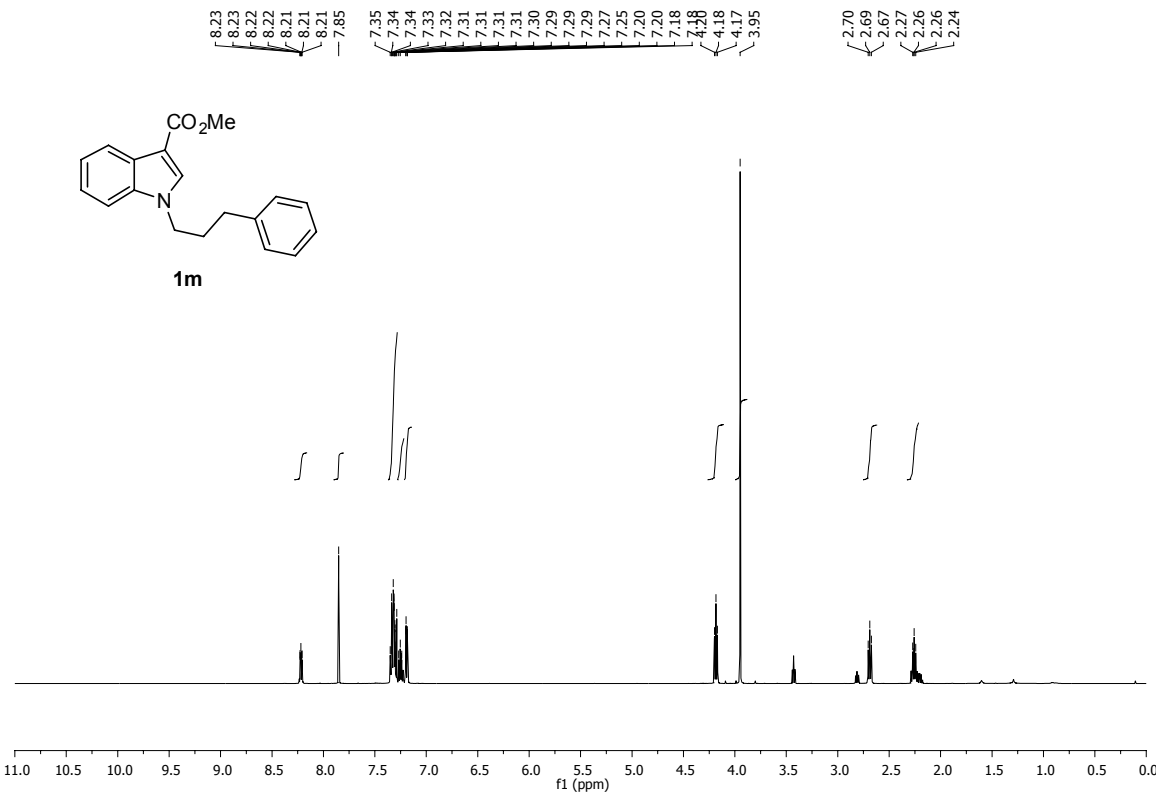
f1 (ppm)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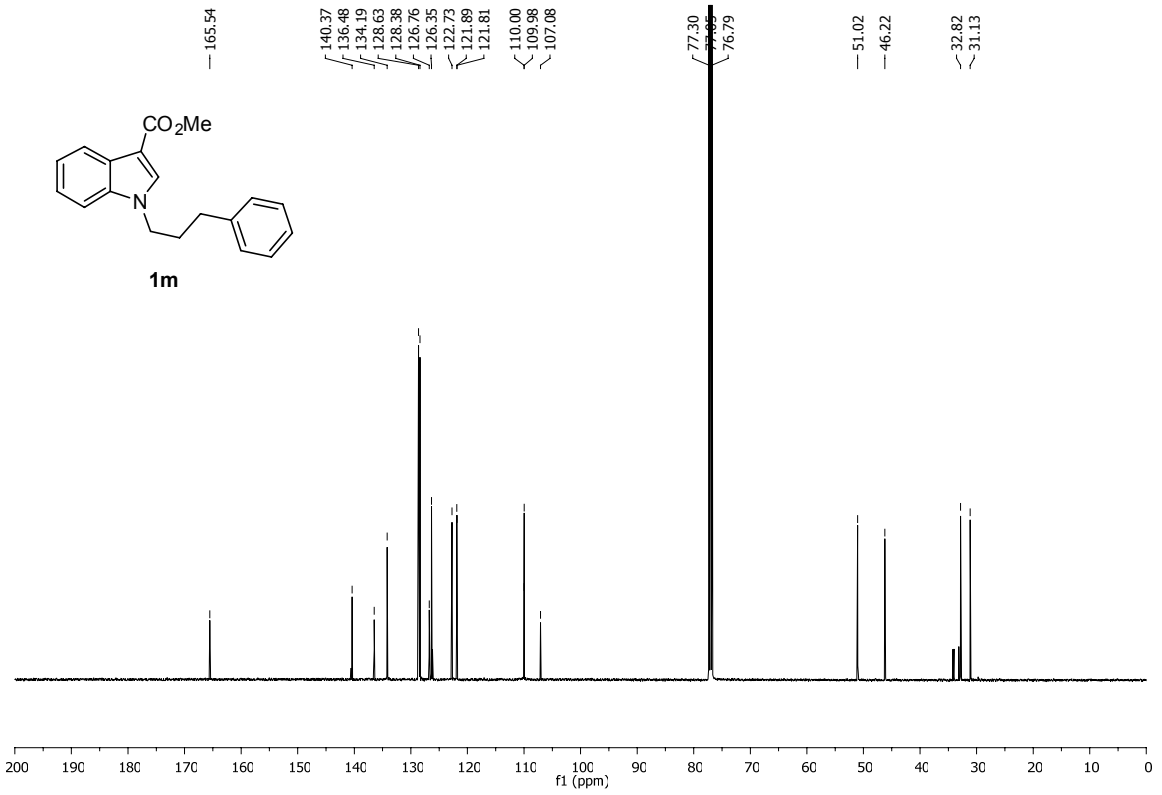
7.31
7.31
7.31
7.31
7.30
7.29
7.29
7.29
7.27
7.25
7.20
7.20
7.18
4.18
4.17
3.95
2.70
2.69
2.67
2.27
2.26
2.26
2.24
CO2Me
N
1m
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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136.48
134.19
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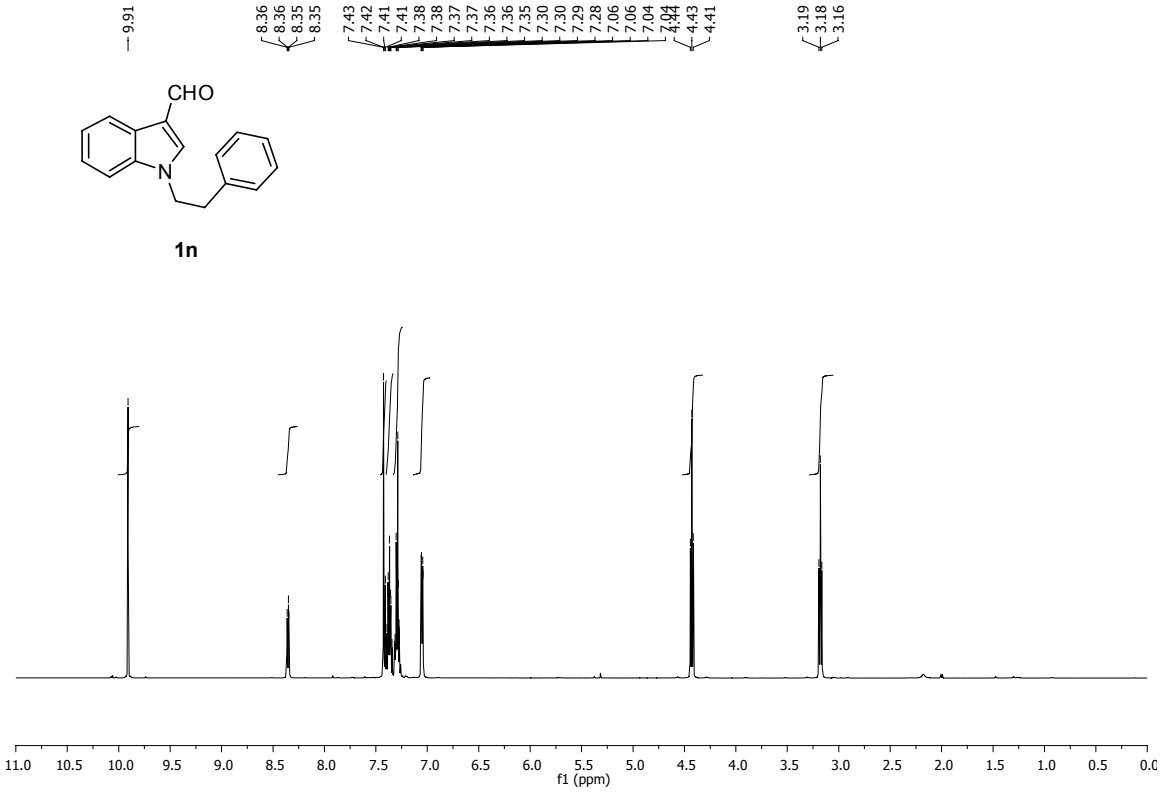
128.38
126.76
126.35
122.73
121.89
121.81
110.00
109.98
107.08
77.30
76.79
51.02
46.22
32.82
31.13
CO2Me
N
1m
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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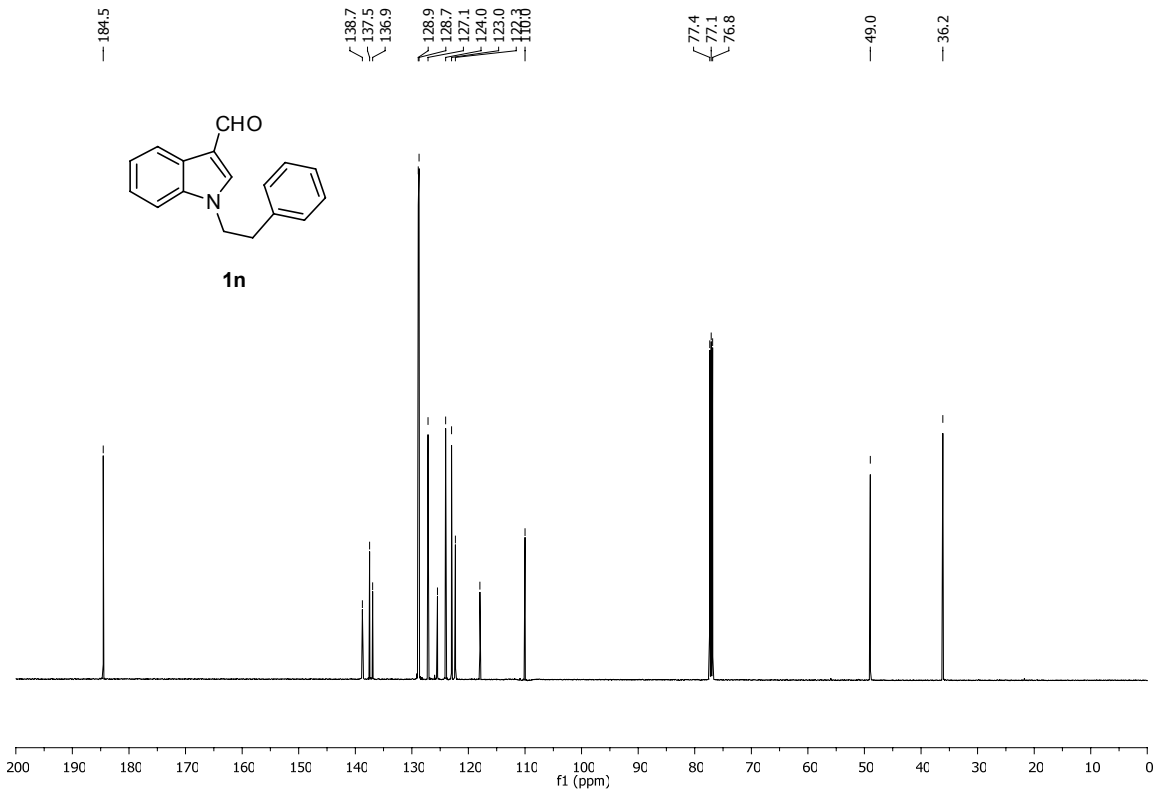
7.37
7.36
7.36
7.35
7.30
7.30
7.29
7.28
7.06
7.06
7.04
7.04
4.44
4.43
4.41
3.19
3.18
3.16
CHO
N
1n
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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138.7
137.5
136.9
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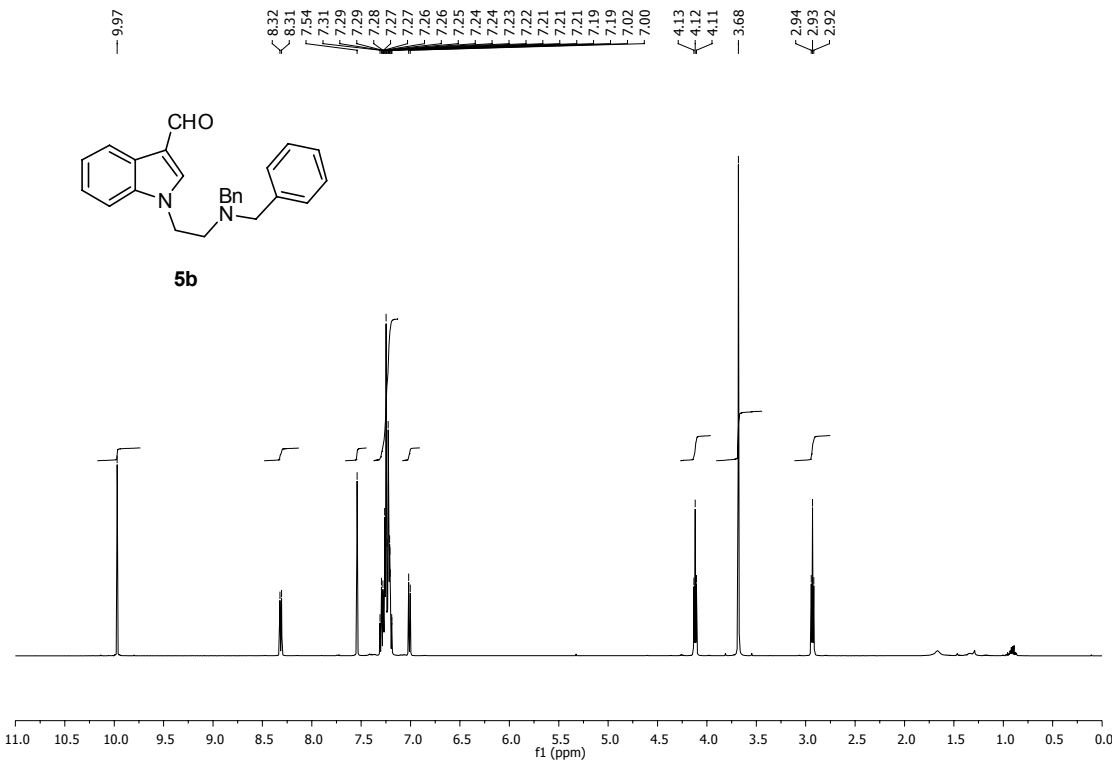
128.7
127.1
124.0
123.0
77.4
77.1
76.8
49.0
36.2
CHO
N
1n
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.54
7.31
7.29
7.29
7.29
7.28
7.27
7.27
7.26
7.26
7.25
7.24
7.24
7.23
7.22
7.21
7.21
7.21
7.19
7.19
7.02
7.00
4.13
4.12
4.11
3.68
2.94
2.93
2.92
CHO
N
Bn
N
5b
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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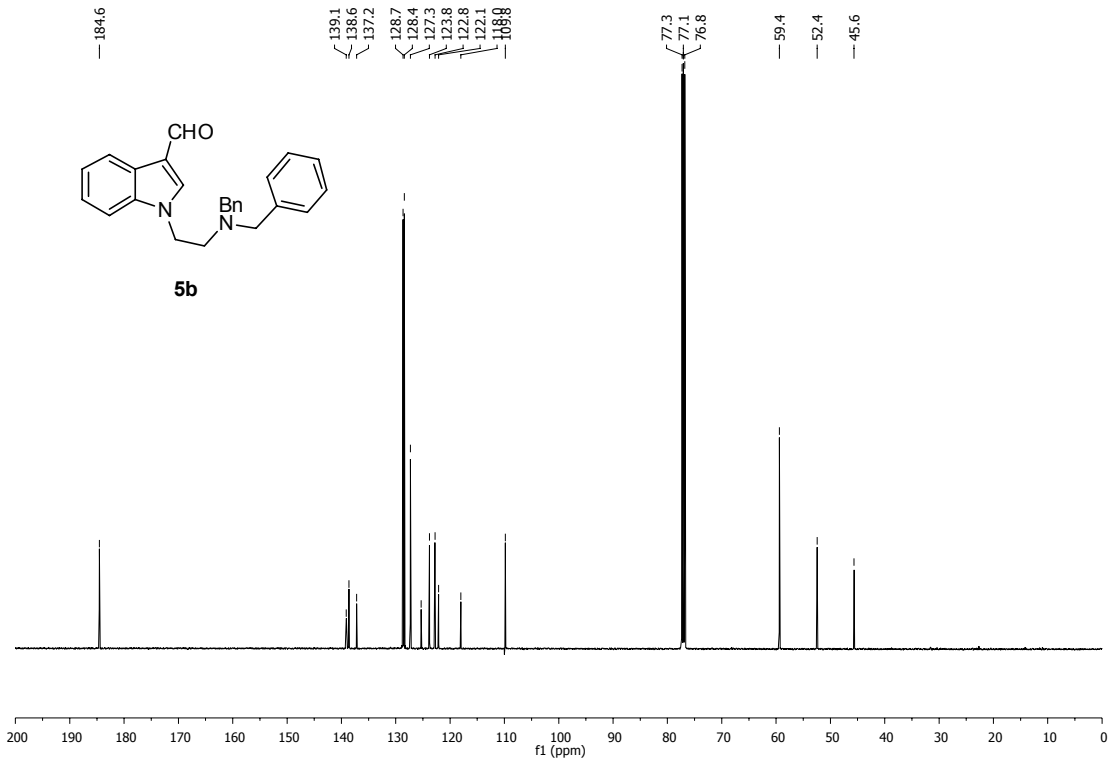
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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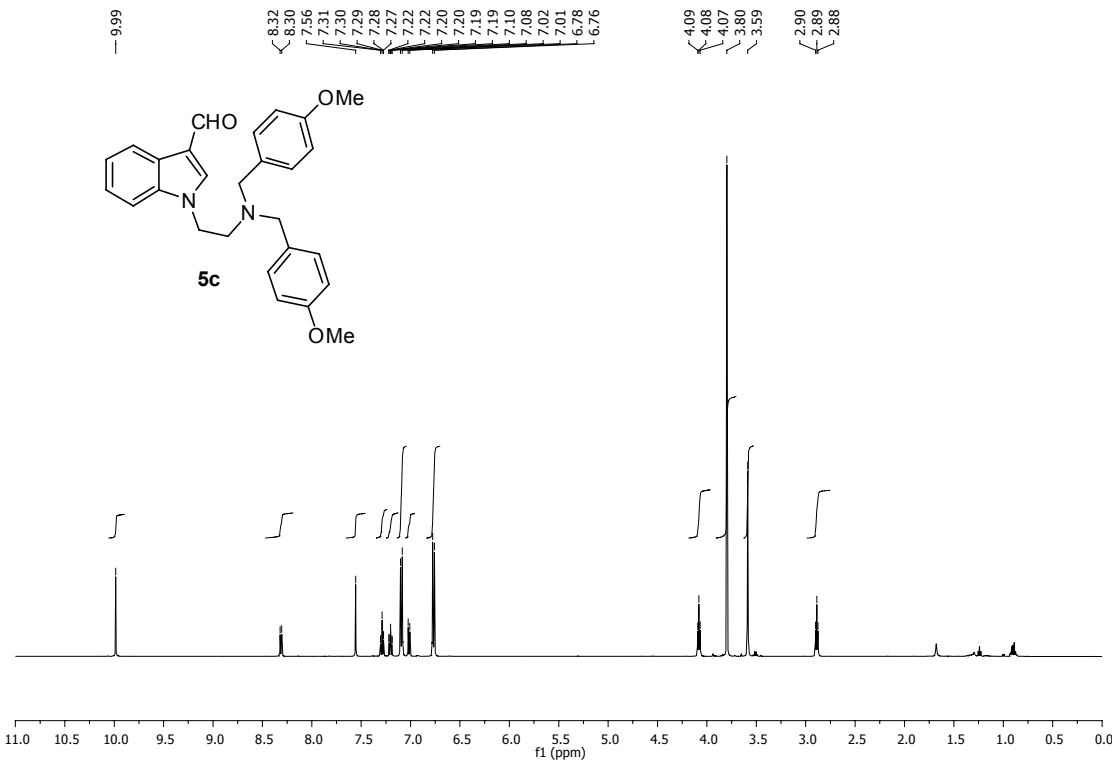
138.6
137.2
128.7
128.4
127.3
123.8
122.8
122.1
118.0
109.8
77.3
77.1
76.8
59.4
52.4
45.6
CHO
N
Bn
N
5b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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8.32
8.30
7.56
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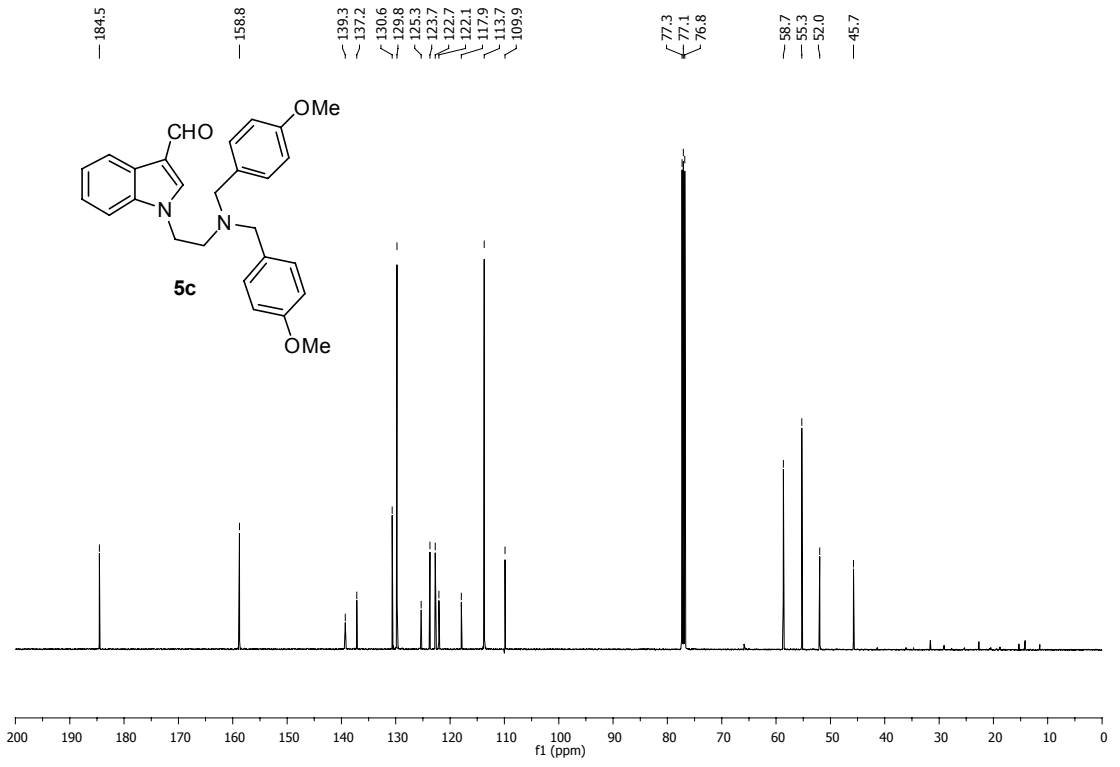
7.30
7.29
7.28
7.27
7.22
7.22
7.20
7.20
7.19
7.19
7.10
7.08
7.02
7.01
6.78
6.76
4.09
4.08
4.07
3.80
3.59
2.90
2.89
2.88
CHO
OMe
N
N
OMe
5c
f1 (ppm)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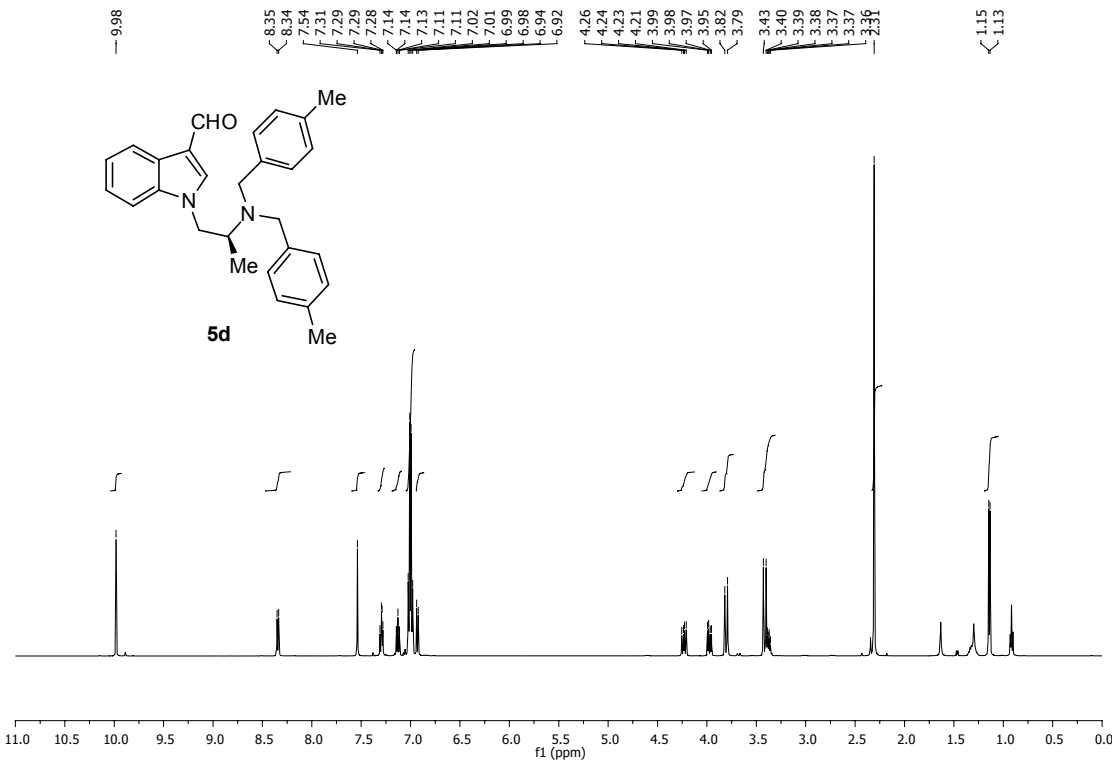
139.3
137.2
130.6
129.8
125.3
123.7
122.7
122.1
117.9
113.7
109.9
77.3
77.1
76.8
58.7
55.3
52.0
45.7
CHO
OMe
N
N
OMe
5c
f1 (ppm)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7.28
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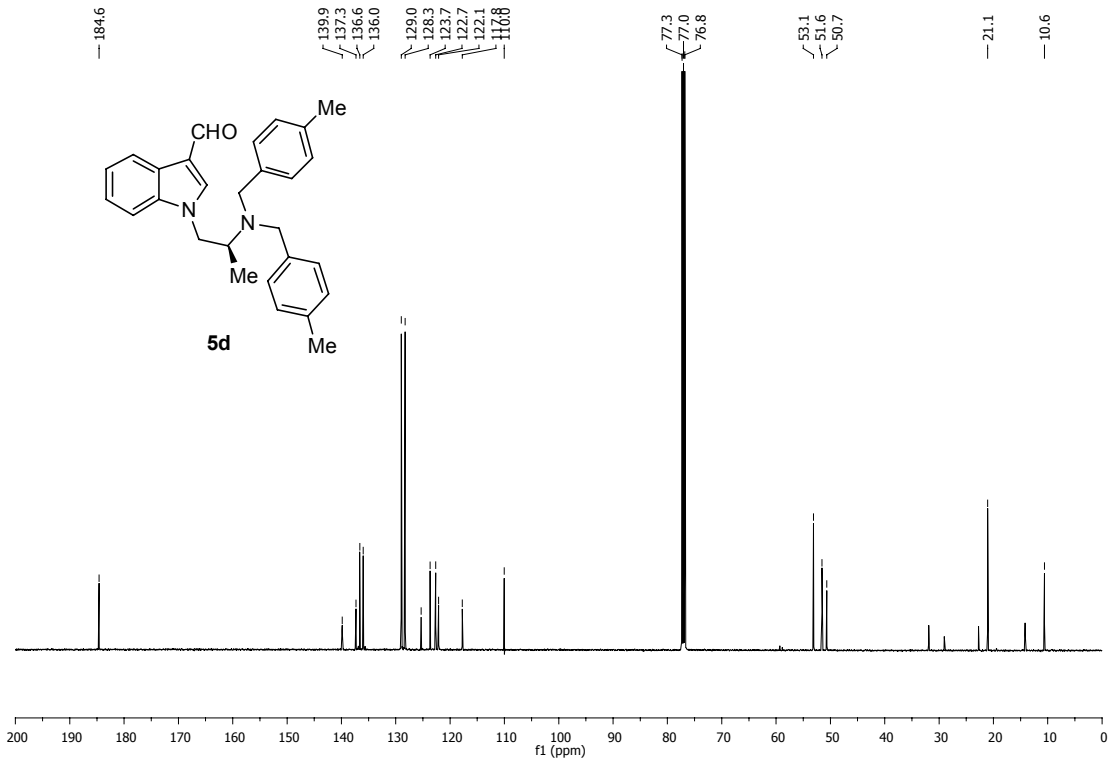
7.14
7.13
7.11
7.11
7.02
7.01
6.99
6.98
6.94
6.92
4.26
4.24
4.23
4.21
3.99
3.98
3.97
3.95
3.82
3.79
3.43
3.40
3.39
3.38
3.37
3.37
2.31
1.15
1.13
CHO
N
N
Me
Me
Me
Me
5d
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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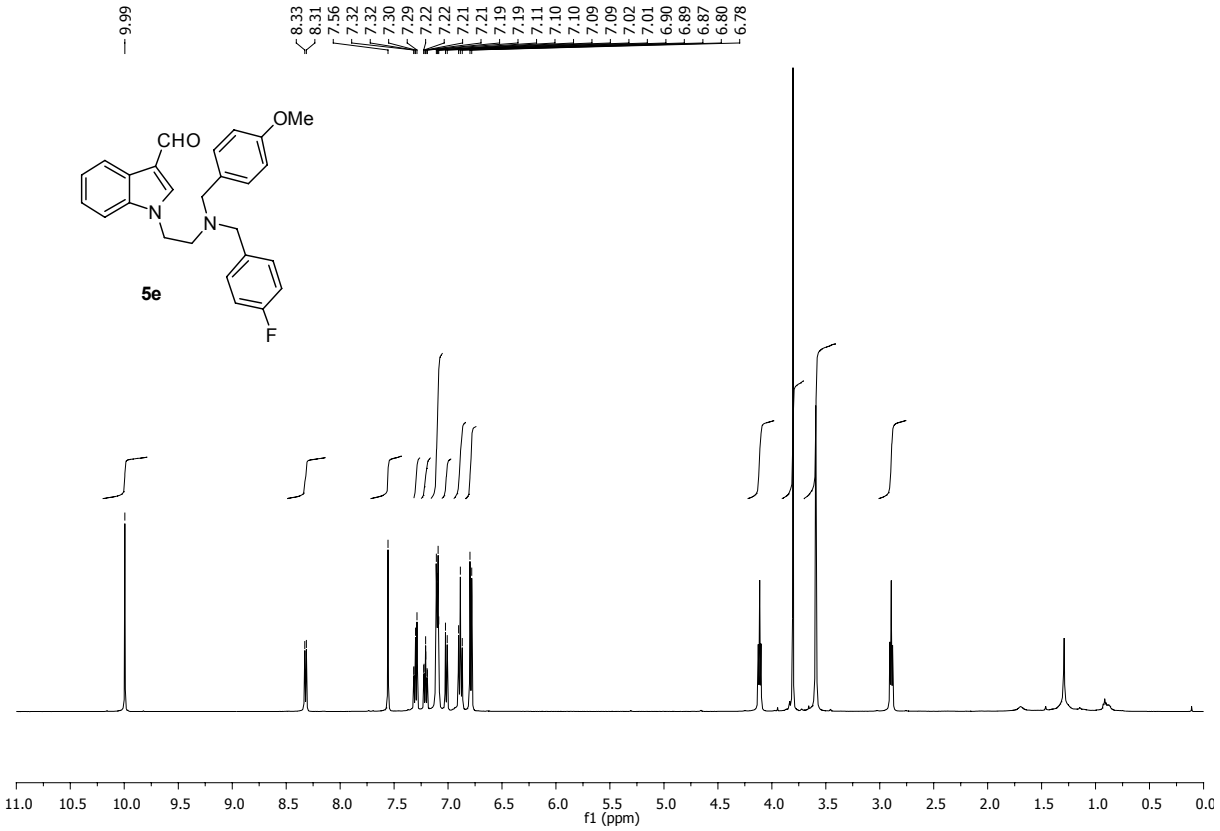
129.0
128.3
123.7
122.7
122.1
77.3
77.0
76.8
53.1
51.6
50.7
21.1
10.6
CHO
N
N
Me
Me
Me
Me
5d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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8.33
8.31
7.56
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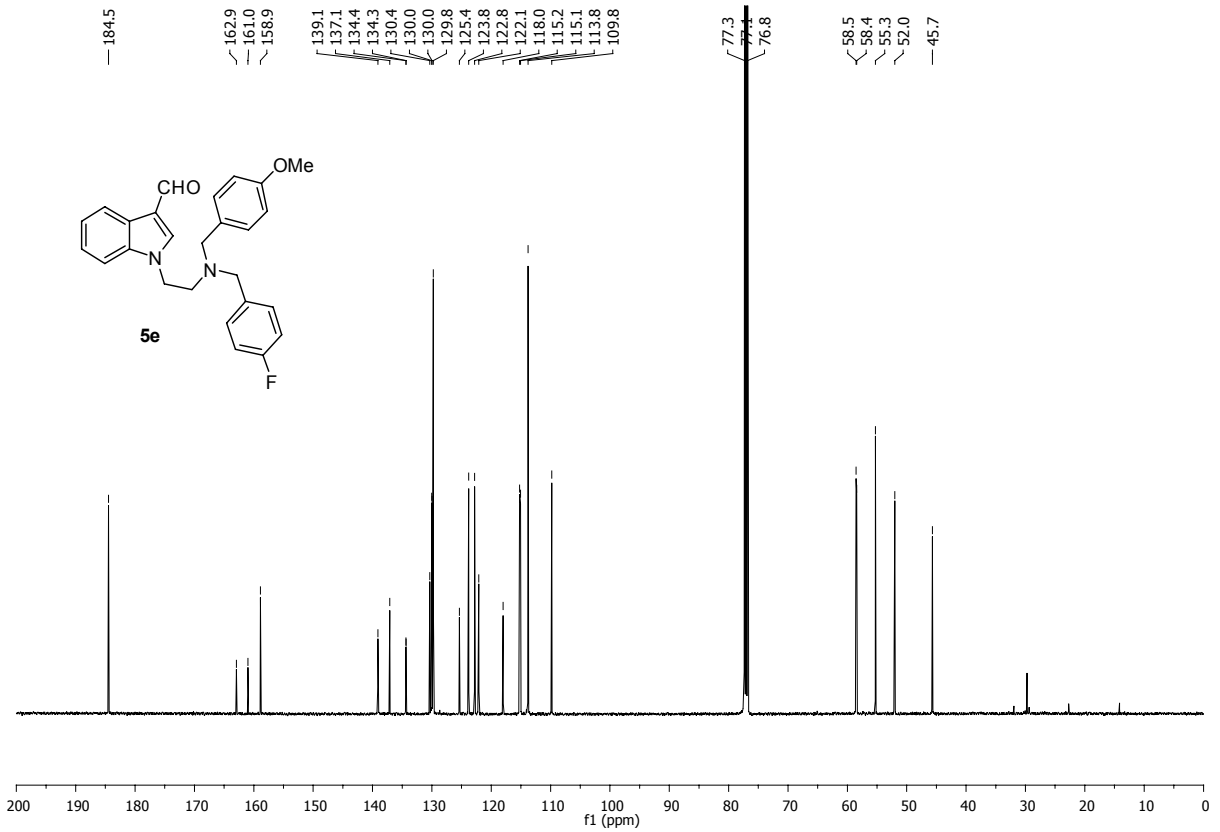
7.32
7.30
7.29
7.22
7.22
7.21
7.21
7.19
7.19
7.11
7.10
7.10
7.09
7.09
7.02
7.01
6.90
6.89
6.87
6.80
6.78
CHO
OMe
N
N
F
5e
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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158.9
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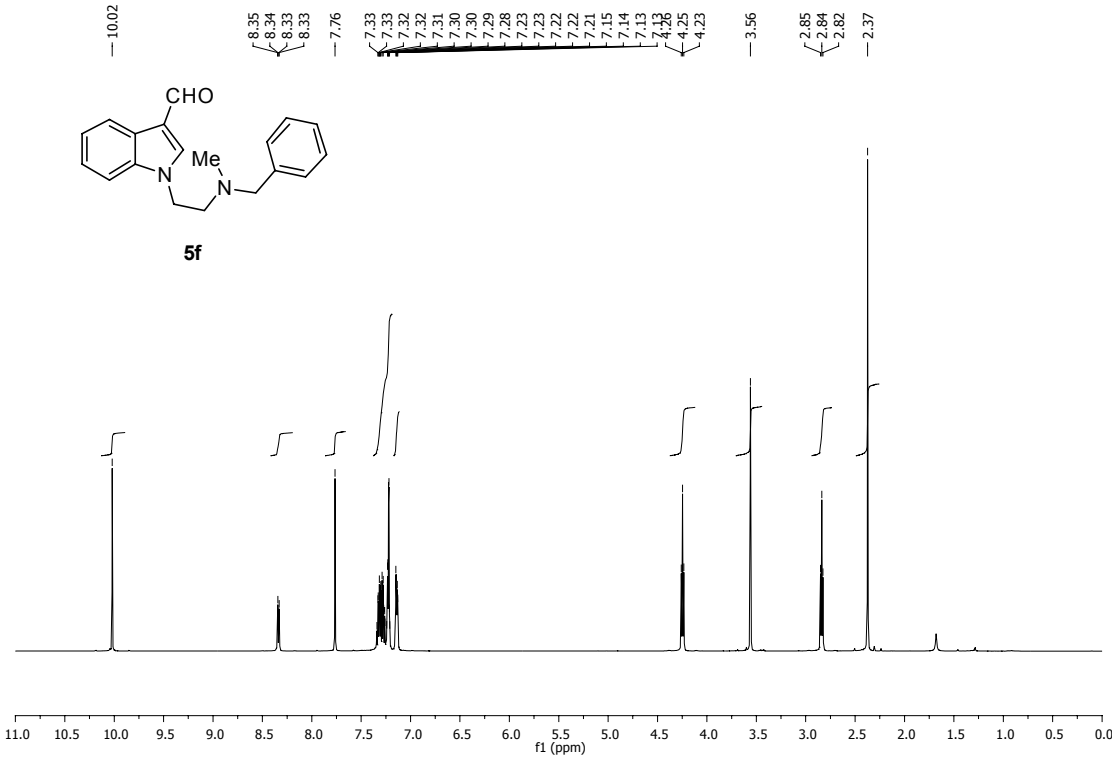
134.4
134.3
130.4
130.0
130.0
129.8
125.4
123.8
122.8
122.1
118.0
115.2
115.1
113.8
109.8
77.3
77.1
76.8
58.5
58.4
55.3
52.0
45.7
CHO
OMe
N
N
F
5e
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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8.33
7.76
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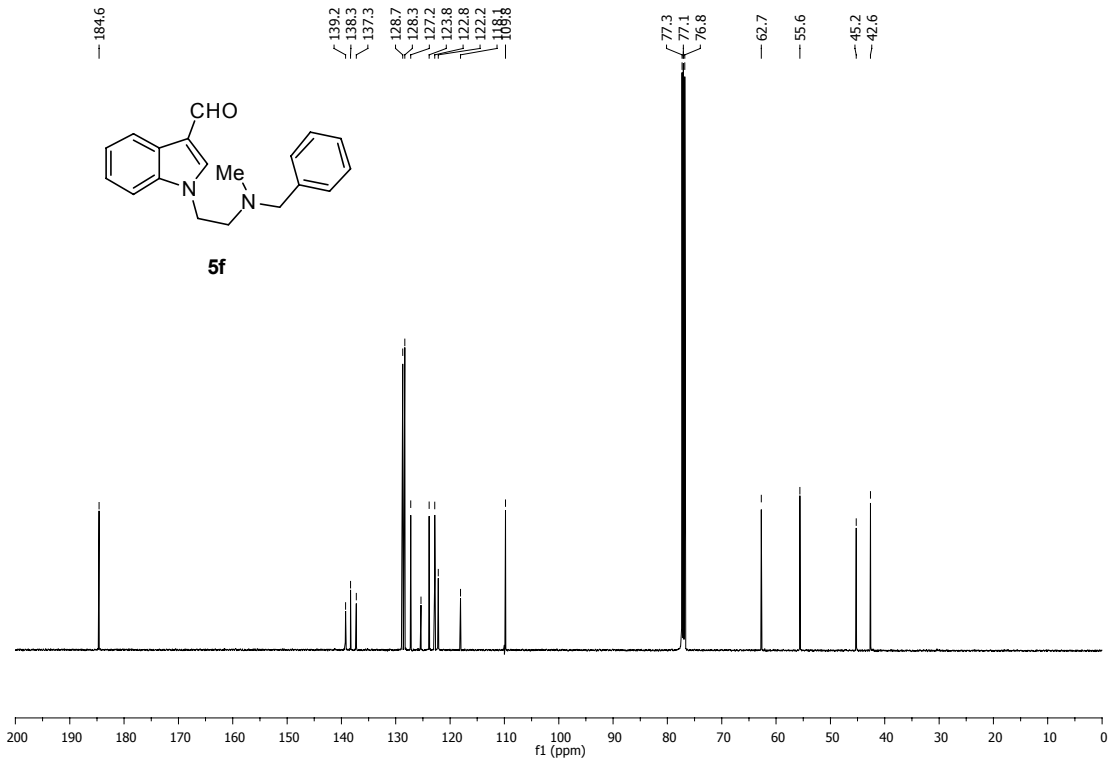
7.33
7.32
7.32
7.31
7.30
7.30
7.29
7.28
7.23
7.23
7.22
7.22
7.21
7.15
7.14
7.13
4.26
4.25
4.23
3.56
2.85
2.84
2.82
2.37
CHO
Me
N
N
5f
f1 (ppm)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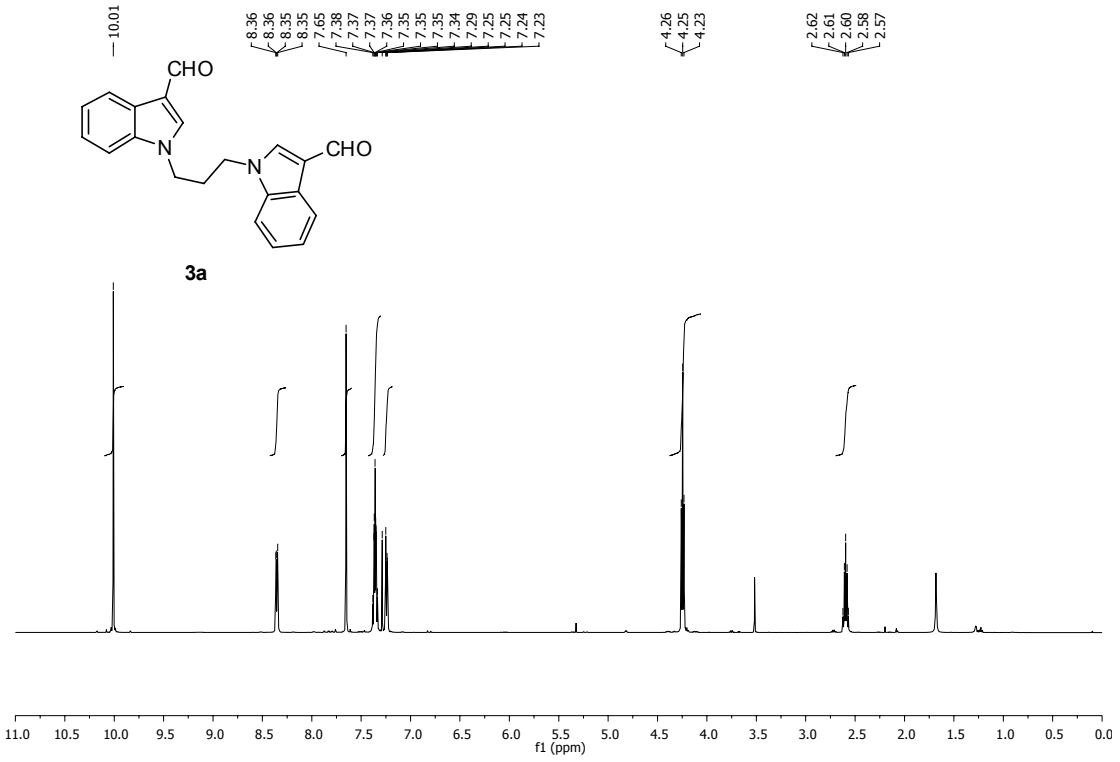
137.3
128.7
128.3
127.2
123.8
122.8
122.2
118.1
109.8
77.3
77.1
76.8
62.7
55.6
45.2
42.6
CHO
Me
N
N
5f
f1 (ppm)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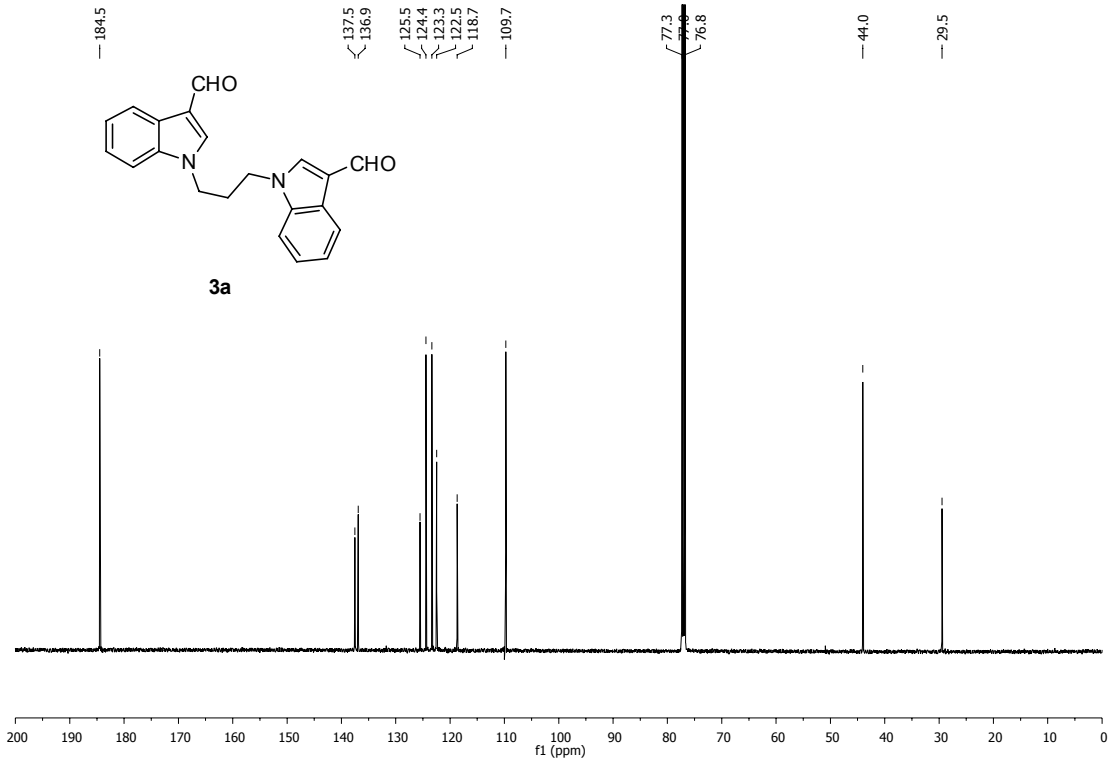
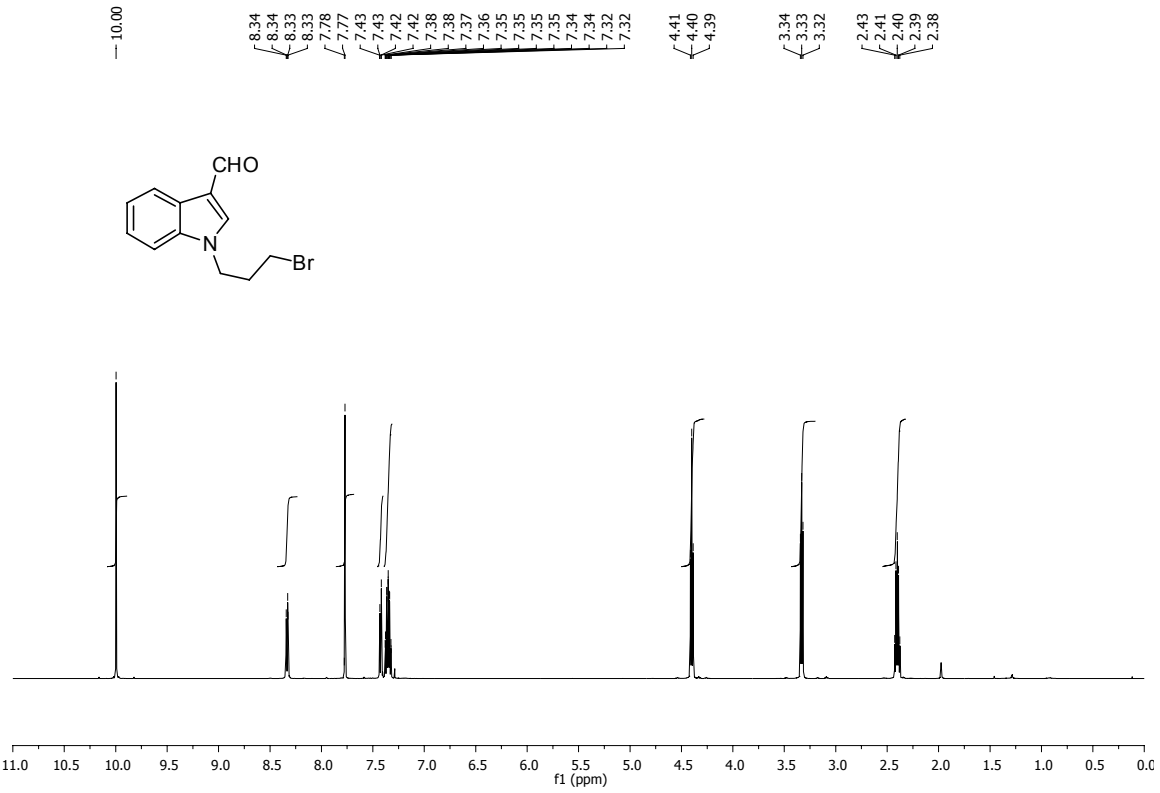
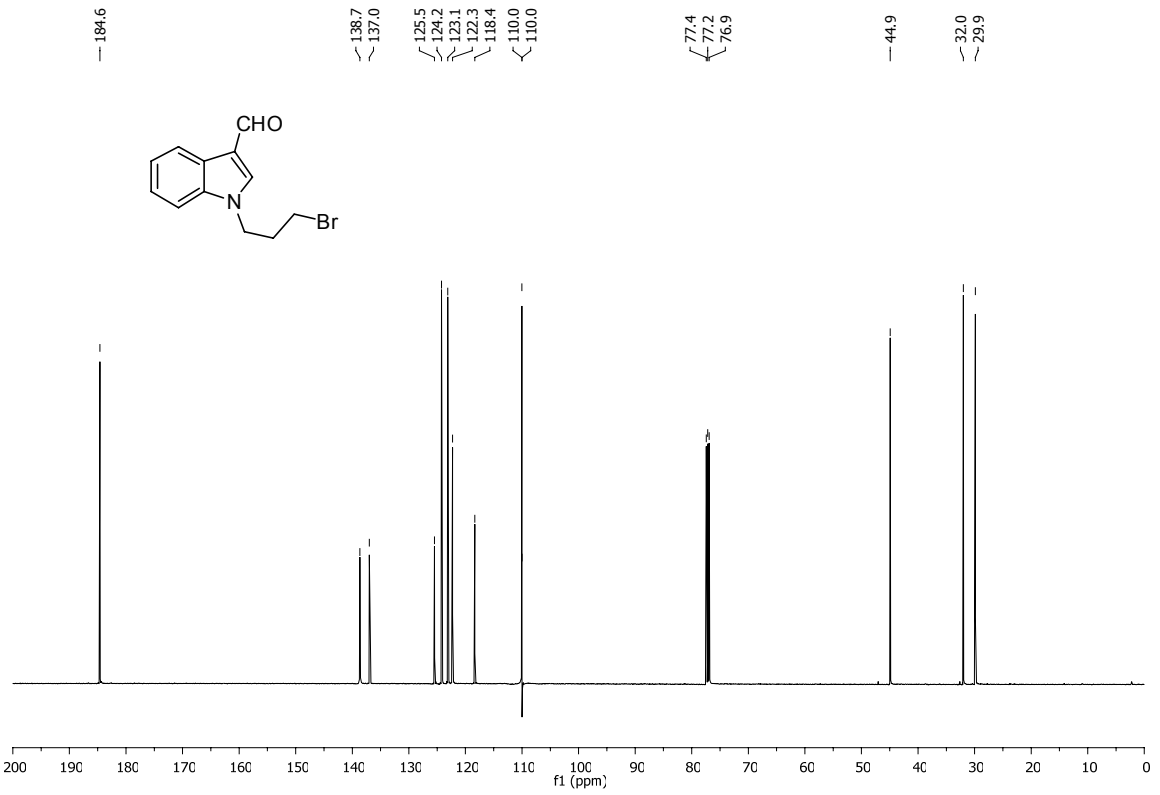
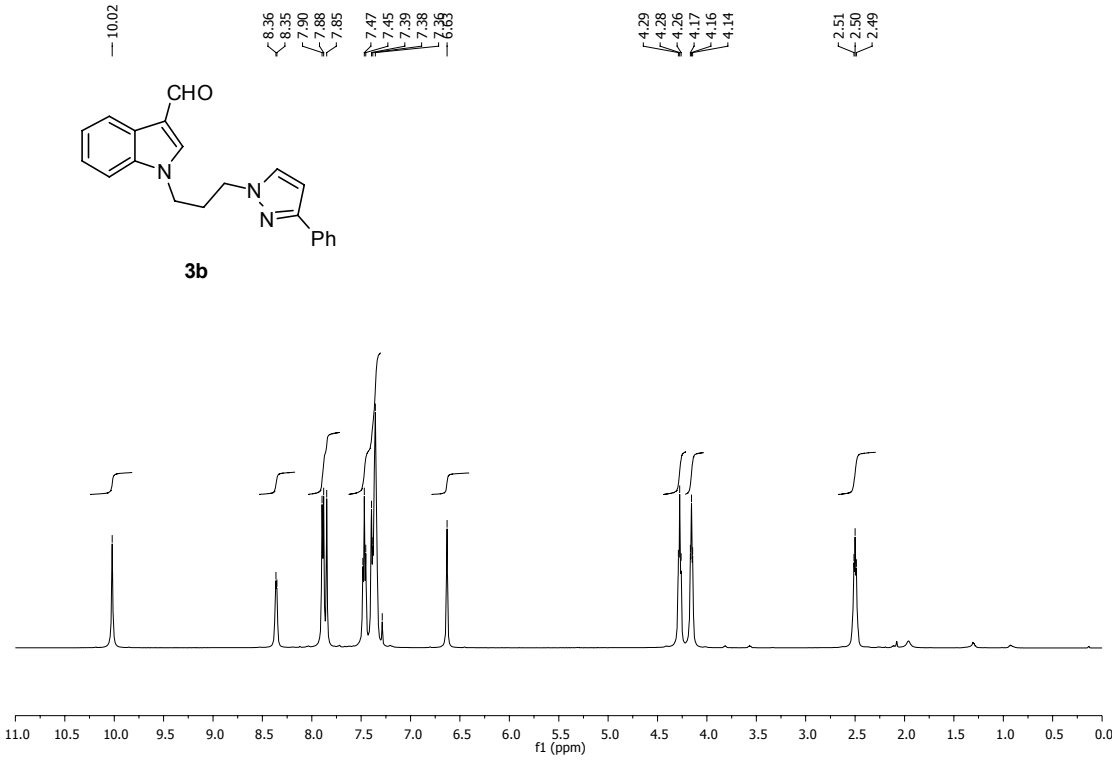
7.65
7.38
7.37
7.37
7.36
7.35
7.35
7.35
7.34
7.29
7.25
7.25
7.24
7.23
4.26
4.25
4.23
2.62
2.61
2.60
2.58
2.57
CHO
N
N
CHO
3a
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


184.5
137.5
136.9
125.5
124.4
123.3
122.5
118.7
109.7
77.3
76.8
44.0
29.5
CHO
N
N
CHO
3a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


10.00
8.34
8.34
8.33
8.33
7.78
7.77
7.43
7.43
7.42
7.42
7.38
7.38
7.37
7.36
7.35
7.35
7.35
7.35
7.34
7.34
7.32
7.32
4.41
4.40
4.39
3.34
3.33
3.32
2.43
2.41
2.40
2.39
2.38
CHO
N
Br
f1 (ppm)


184.6
138.7
137.0
125.5
124.2
123.1
122.3
118.4
110.0
110.0
77.4
77.2
76.9
44.9
32.0
29.9
CHO
N
Br
f1 (ppm)


10.02
8.36
8.35
7.90
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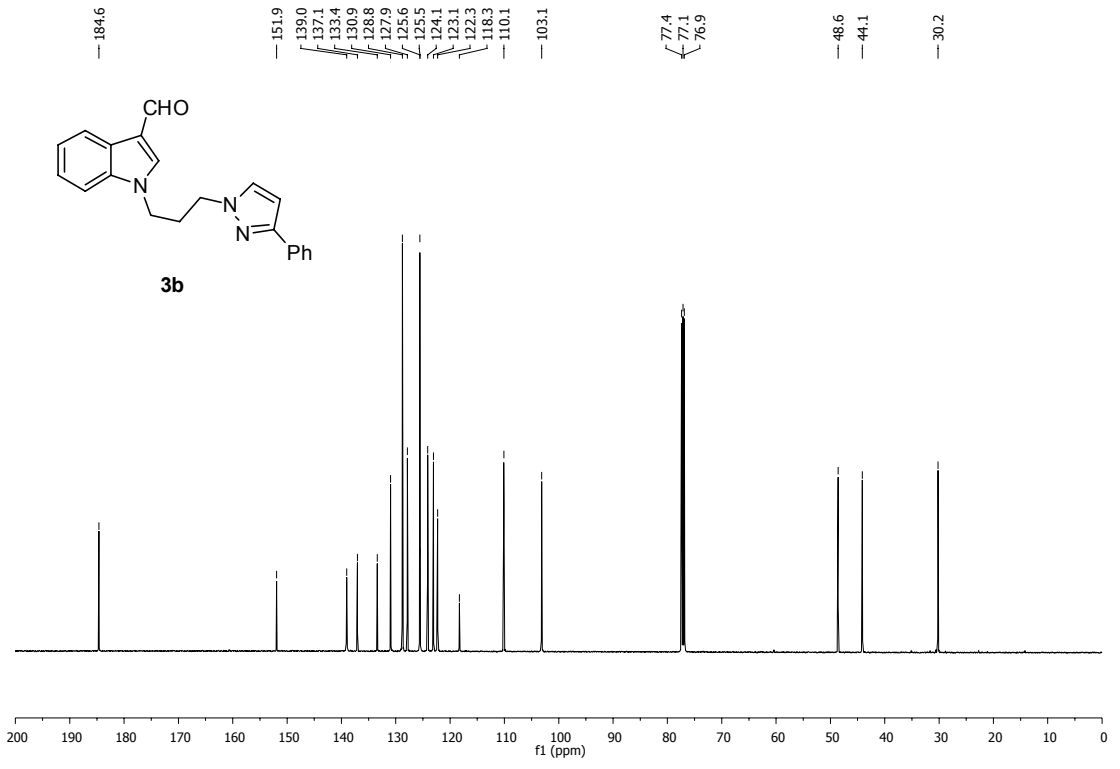
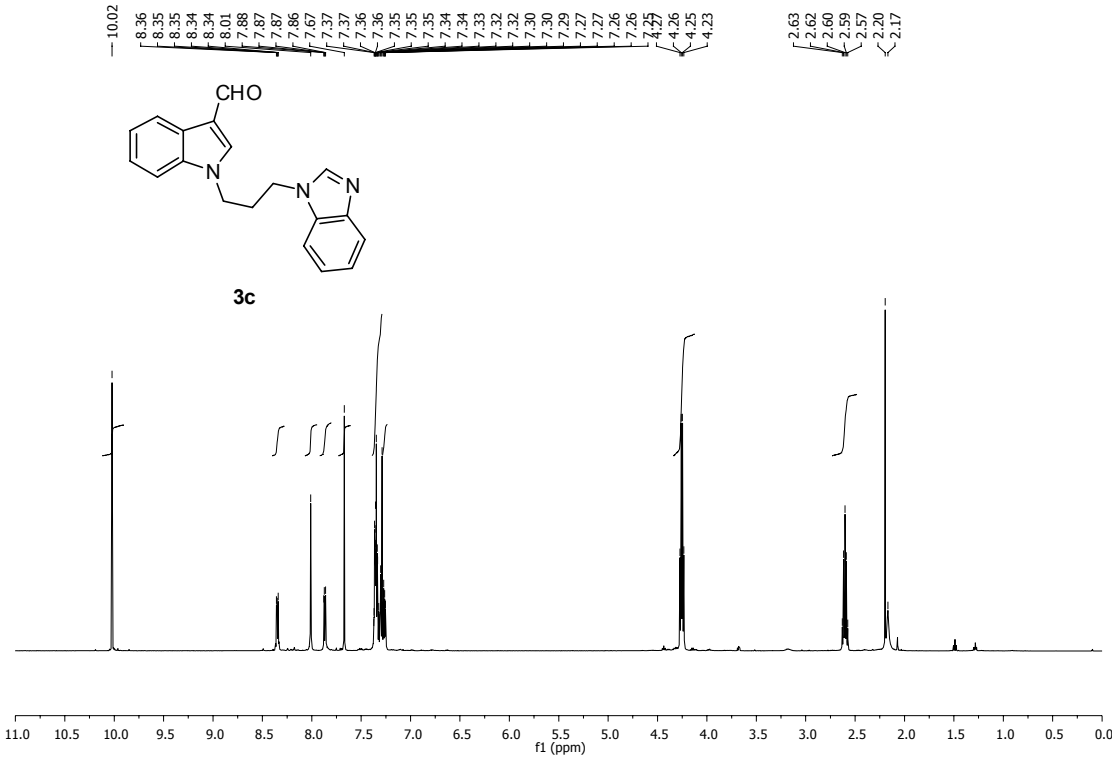
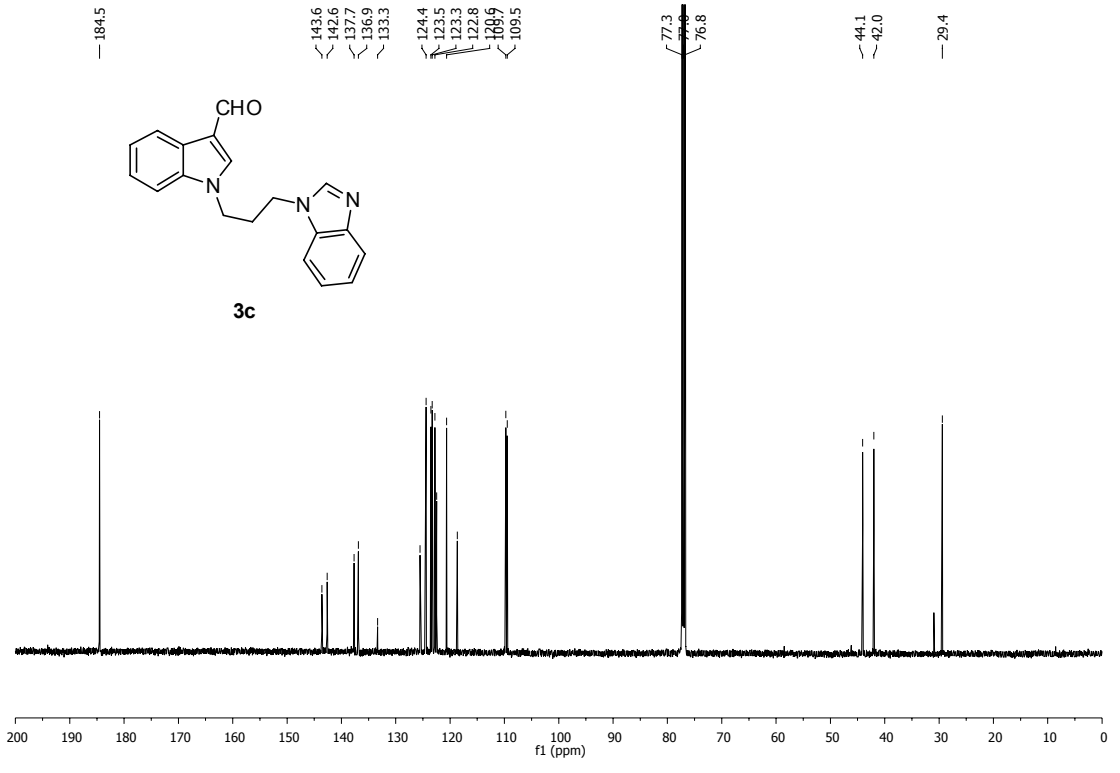
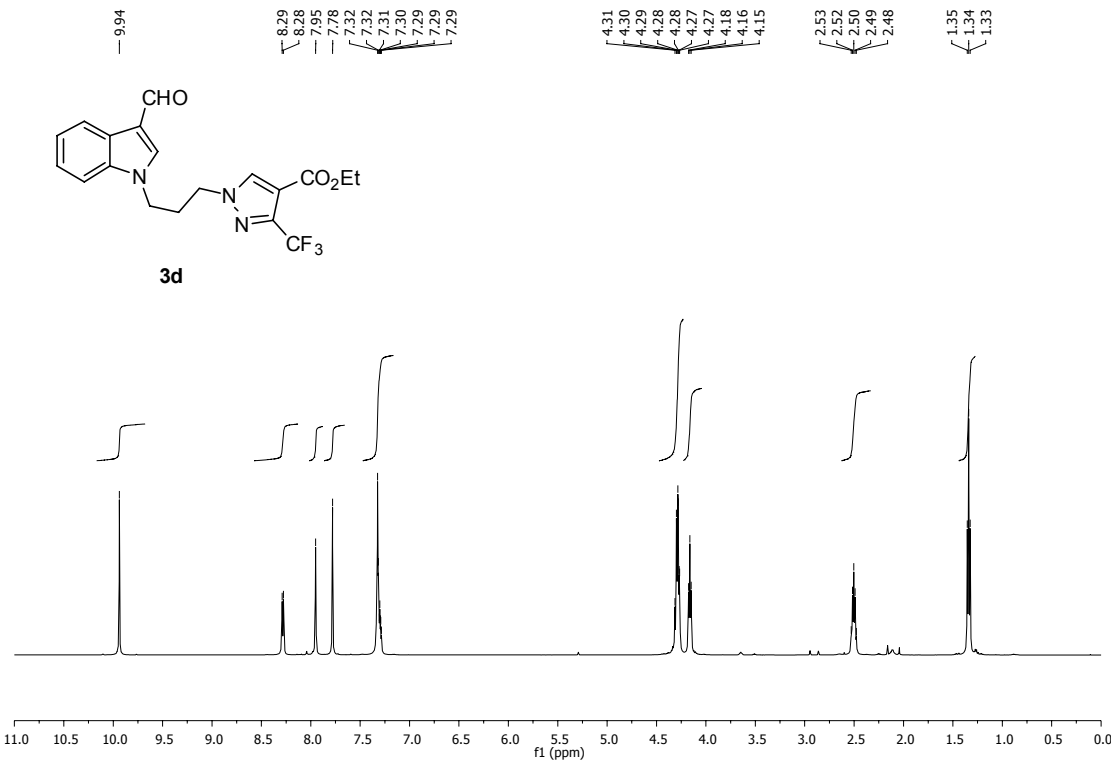
7.85
7.47
7.45
7.39
7.38
7.36
6.63
4.29
4.28
4.26
4.17
4.16
4.14
2.51
2.50
2.49
CHO
N
N
N
Ph
3b
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


184.6
151.9
139.0
137.1
133.4
130.9
128.8
127.9
125.6
125.5
124.1
123.1
122.3
118.3
110.1
103.1
77.4
77.1
76.9
48.6
44.1
30.2
CHO
N
N
N
Ph
3b
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


10.02
8.36
8.35
8.35
8.34
8.34
8.01
7.88
7.87
7.87
7.86
7.67
7.37
7.37
7.36
7.36
7.35
7.35
7.35
7.34
7.34
7.33
7.32
7.32
7.30
7.30
7.29
7.27
7.27
7.26
7.26
7.25
4.27
4.26
4.25
4.23
2.63
2.62
2.60
2.59
2.57
2.20
2.17
CHO
N
N
N
3c
11.0 10.5 10.0 9.5 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)


184.5
143.6
142.6
137.7
136.9
133.3
124.4
123.5
123.3
122.8
120.6
109.7
109.5
77.3
77.0
76.8
44.1
42.0
29.4
CHO
N
N
N
3c
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.32
7.31
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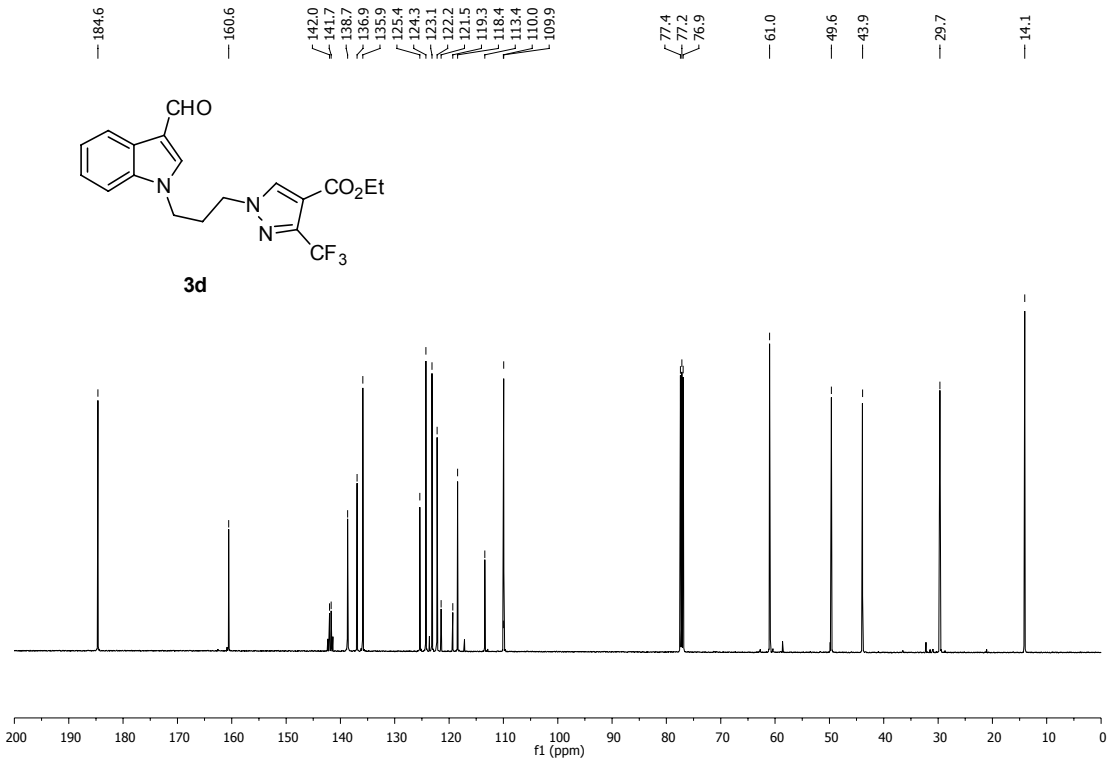
7.29
7.29
7.29
4.31
4.30
4.29
4.28
4.28
4.27
4.27
4.18
4.16
4.15
2.53
2.52
2.50
2.49
2.48
1.35
1.34
1.33
CHO
CO2Et
CF3
3d
f1 (ppm)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160.6
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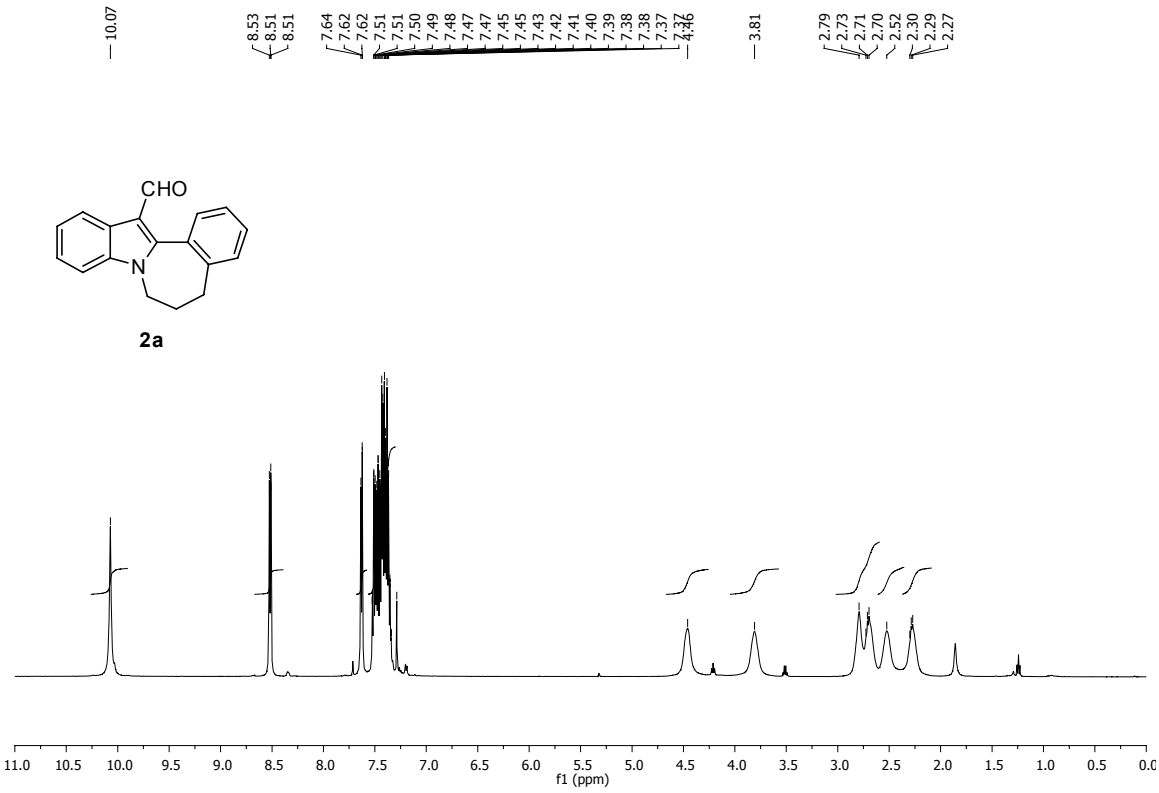
136.9
135.9
125.4
124.3
123.1
122.2
121.5
119.3
118.4
113.4
110.0
109.9
77.4
77.2
76.9
61.0
49.6
43.9
29.7
14.1
CHO
CO2Et
CF3
3d
f1 (ppm)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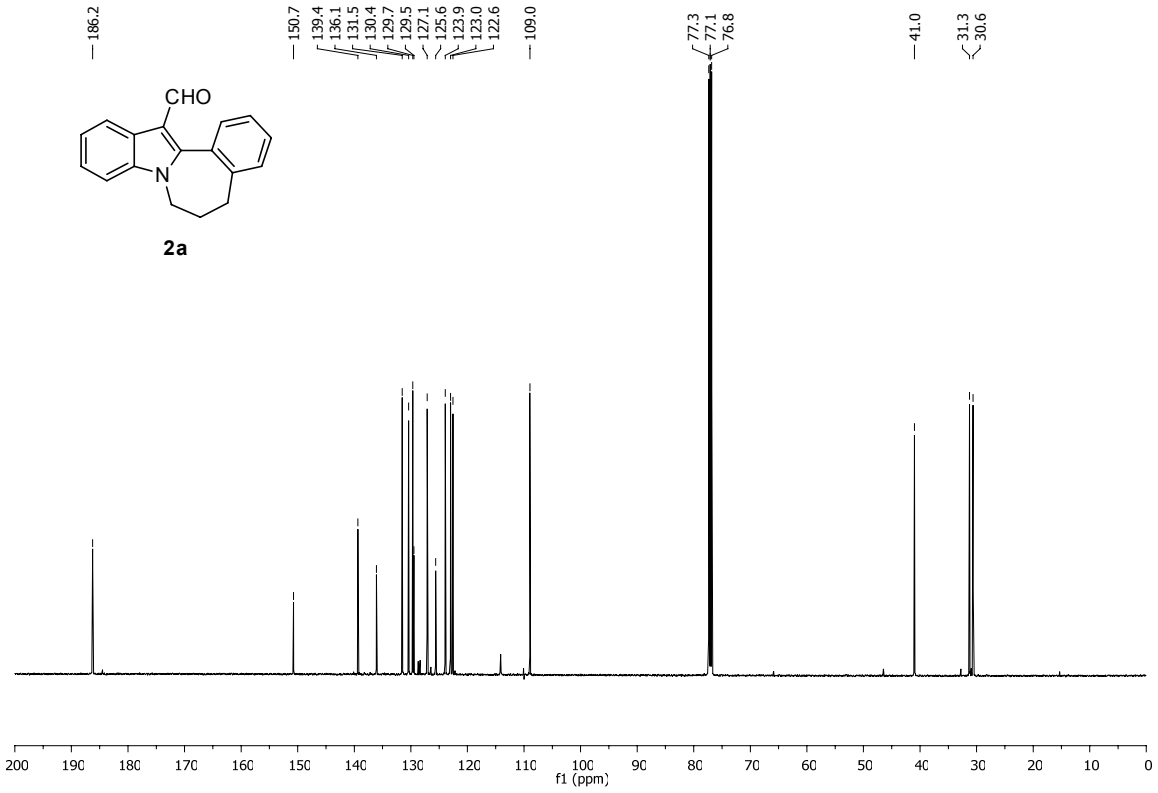
7.51
7.51
7.50
7.49
7.48
7.47
7.47
7.45
7.45
7.43
7.42
7.41
7.40
7.39
7.38
7.38
7.37
7.37
4.46
3.81
2.79
2.73
2.71
2.70
2.52
2.30
2.29
2.27
CHO
N
2a
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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139.4
136.1
131.5
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129.7
129.5
127.1
125.6
123.9
123.0
122.6
109.0
77.3
77.1
76.8
41.0
31.3
30.6
CHO
N
2a
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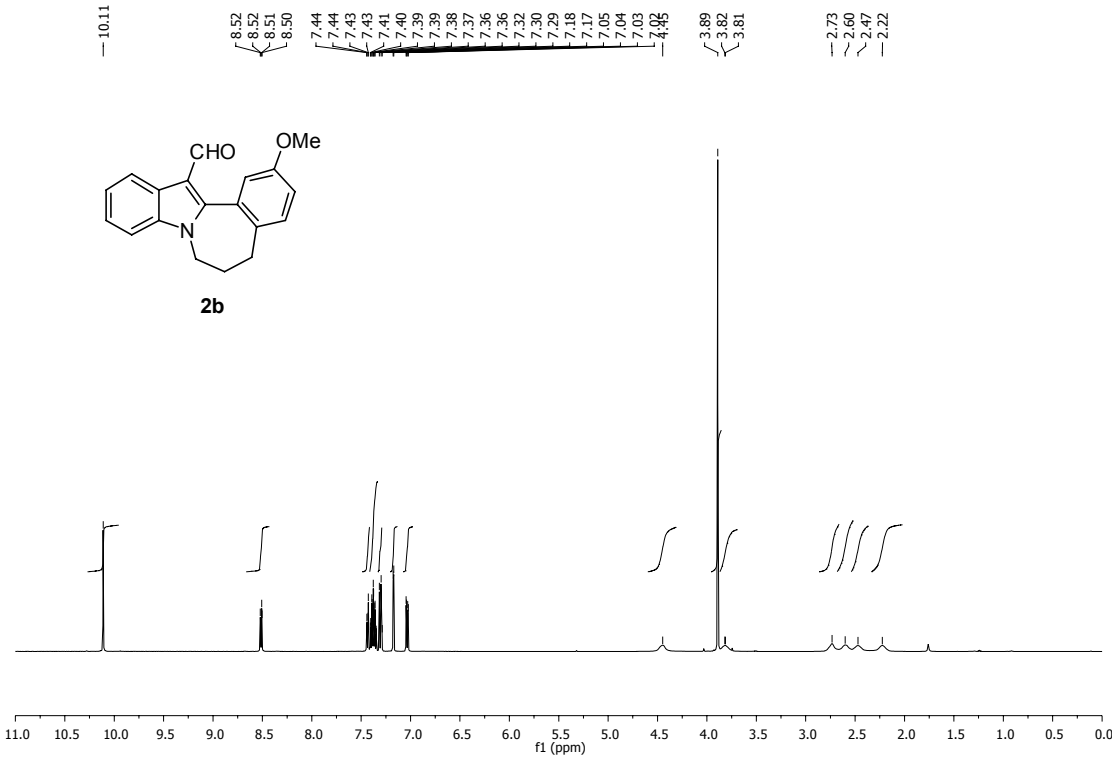
f1 (ppm)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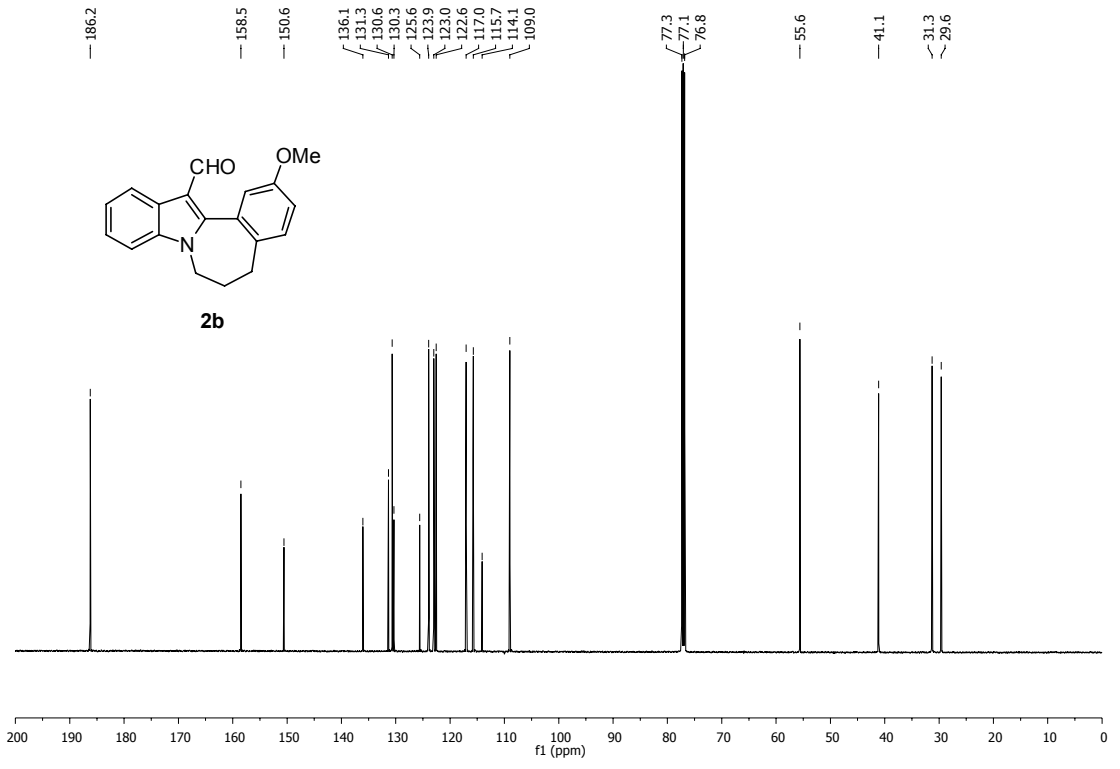
7.41
7.40
7.39
7.39
7.38
7.37
7.36
7.36
7.32
7.30
7.29
7.18
7.17
7.05
7.04
7.03
4.02
4.01
3.89
3.82
3.81
2.73
2.60
2.47
2.22
CHO
OMe
N
2b
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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158.5
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131.3
130.6
130.3
125.6
123.9
123.0
122.6
117.0
115.7
114.1
109.0
77.3
77.1
76.8
55.6
41.1
31.3
29.6
CHO
OMe
N
2b
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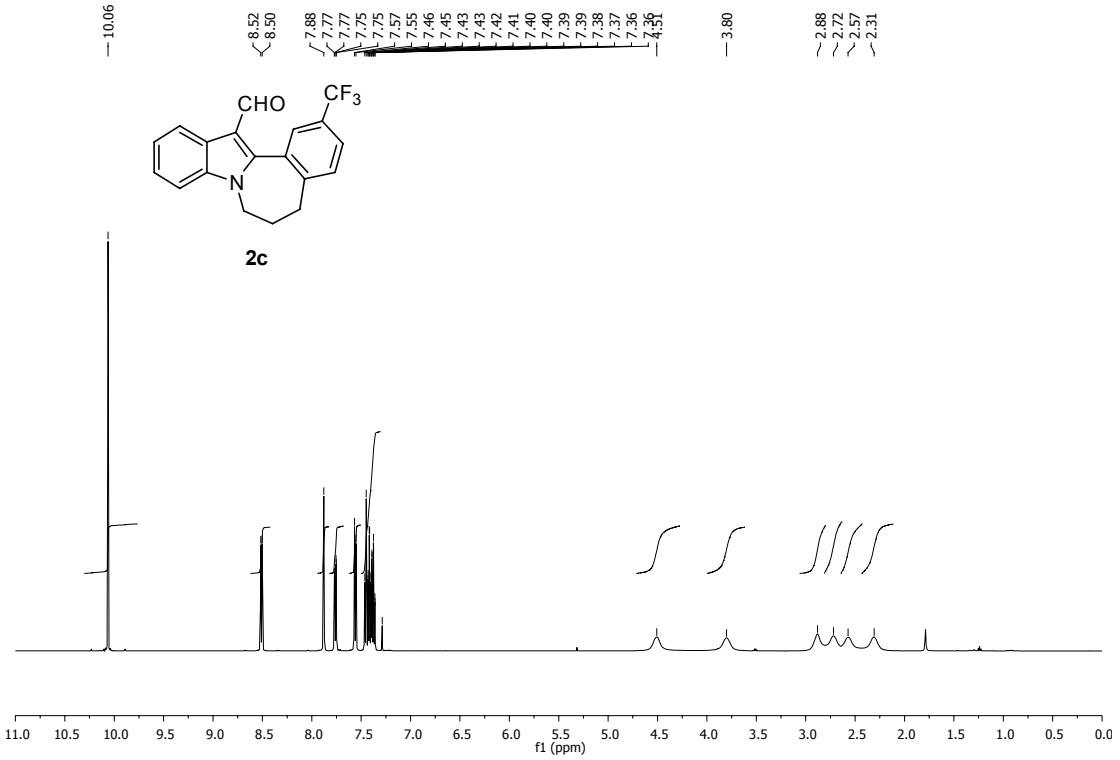
f1 (ppm)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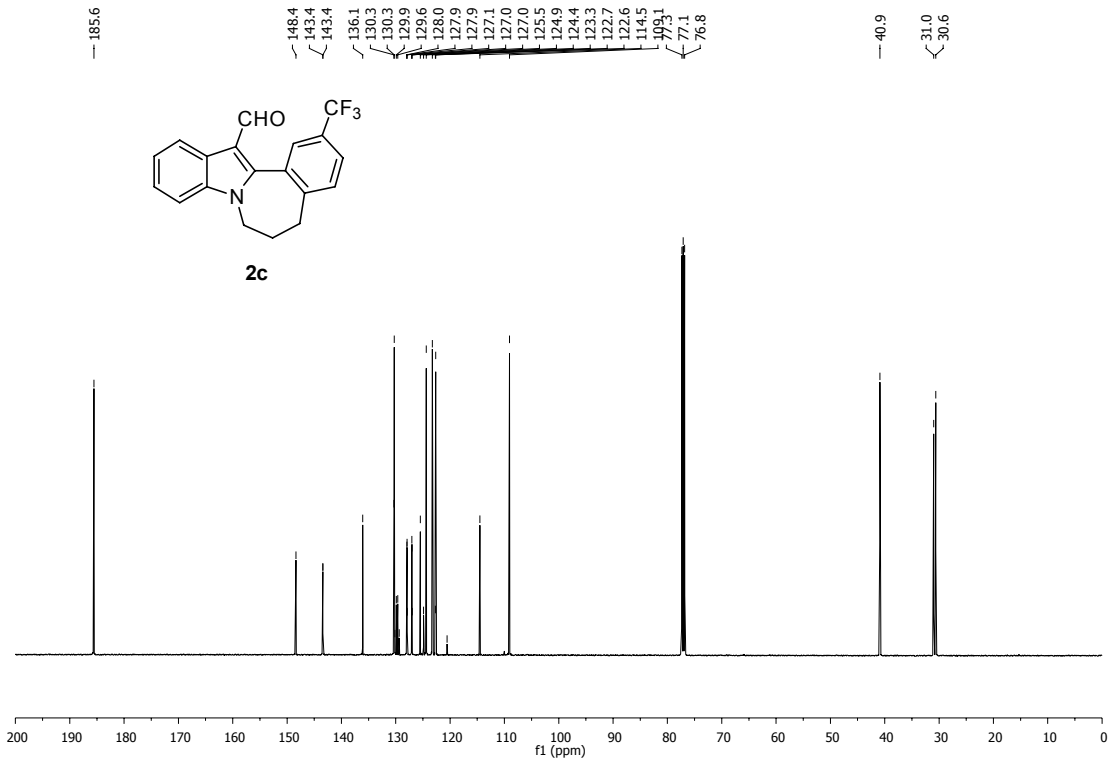
7.77
7.75
7.75
7.57
7.55
7.46
7.45
7.43
7.43
7.42
7.41
7.40
7.40
7.39
7.39
7.38
7.37
7.36
7.36
4.51
3.80
2.88
2.72
2.57
2.31
CHO
CF3
N
2c
f1 (ppm)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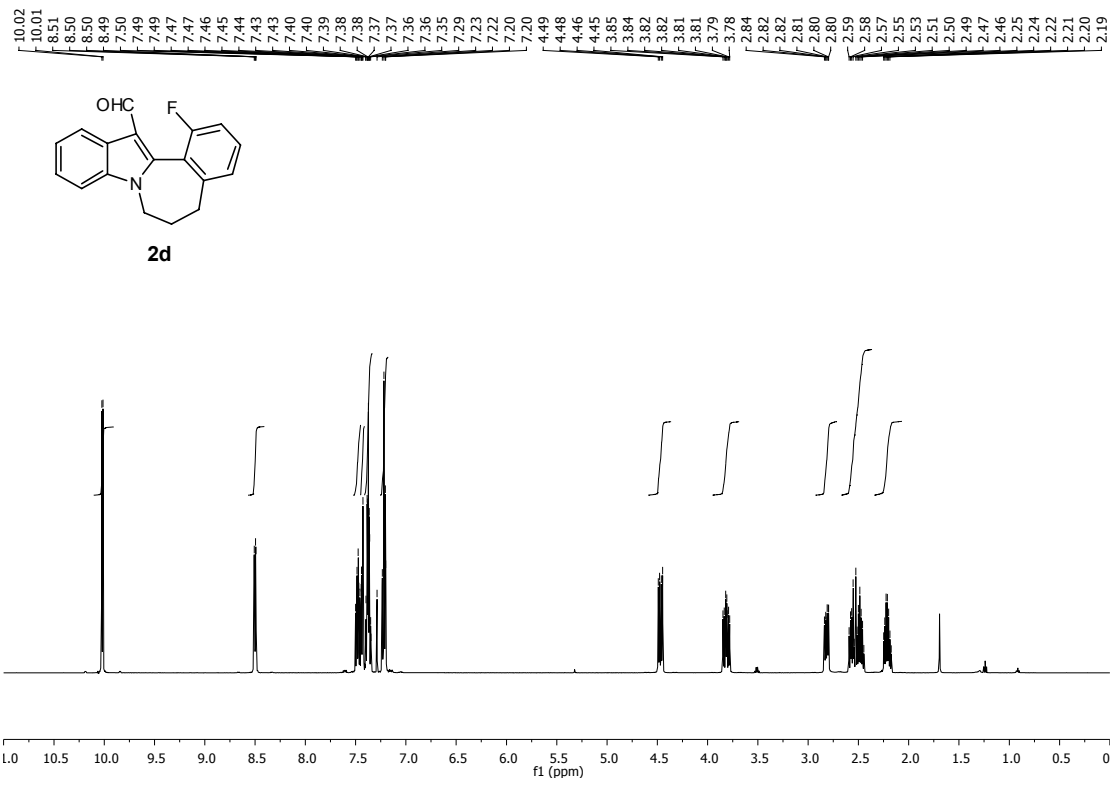
148.4
143.4
143.4
136.1
130.3
130.3
129.9
129.6
128.0
127.9
127.9
127.1
127.0
127.0
125.5
124.9
124.4
123.3
122.7
122.6
114.5
109.1
77.3
77.1
76.8
40.9
31.0
30.6
CHO
CF3
N
2c
f1 (ppm)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10.01
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7.49
7.49
7.47
7.47
7.46
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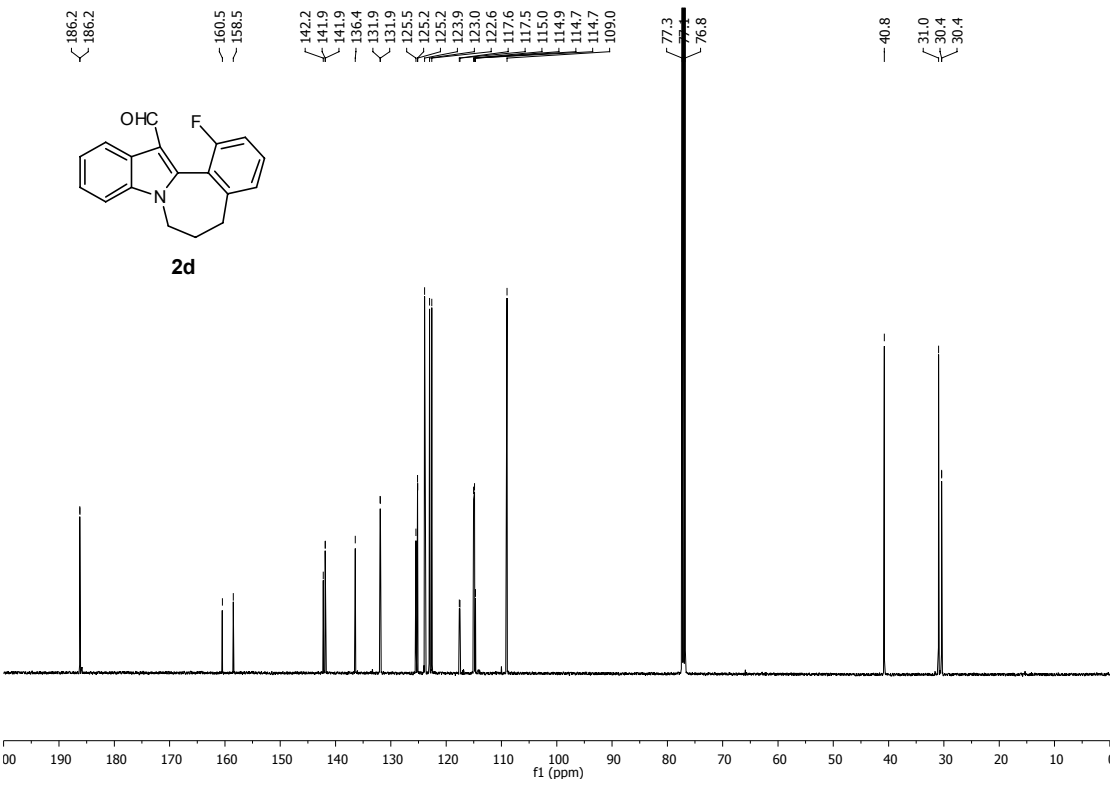
7.43
7.40
7.40
7.39
7.38
7.38
7.37
7.37
7.36
7.36
7.35
7.29
7.23
7.22
7.20
7.20
4.49
4.48
4.46
4.45
4.45
3.85
3.84
3.82
3.82
3.81
3.81
3.79
3.78
2.84
2.82
2.82
2.81
2.80
2.80
2.59
2.58
2.57
2.55
2.53
2.51
2.50
2.49
2.47
2.46
2.25
2.24
2.22
2.21
2.20
2.19
OHC
F
N
2d
1.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
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
f1 (ppm)


186.2
186.2
160.5
158.5
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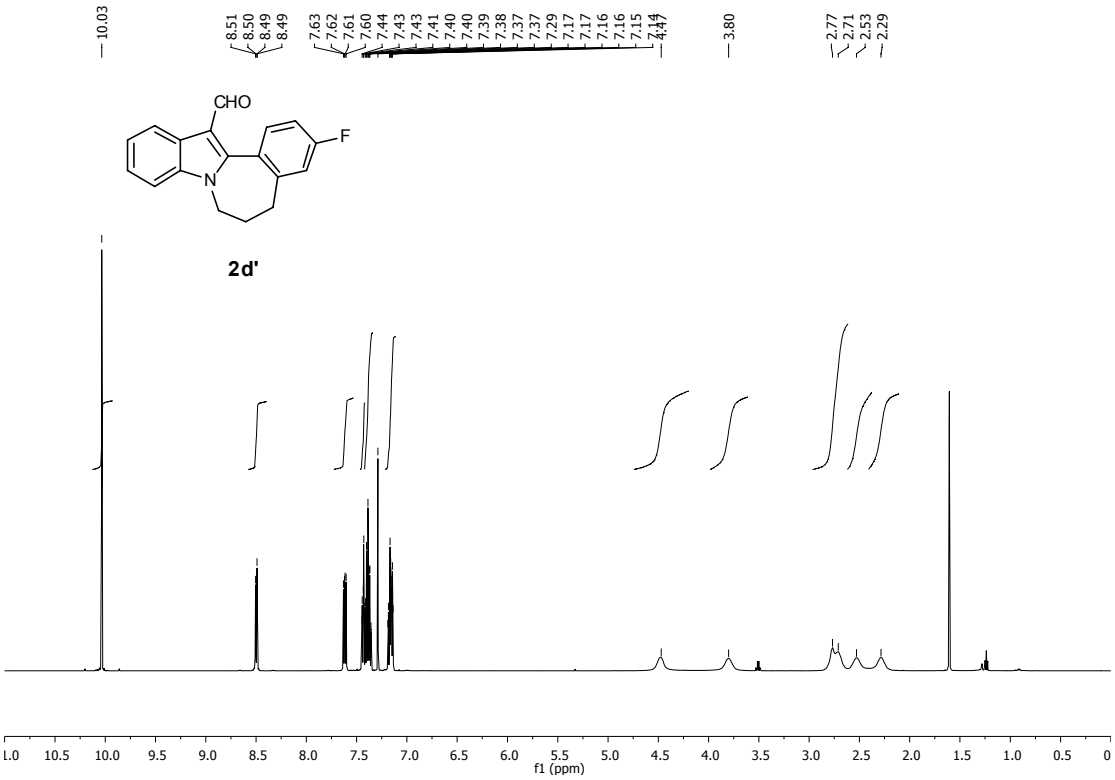
141.9
141.9
136.4
131.9
131.9
125.5
125.2
125.2
123.9
123.0
122.6
117.6
117.5
115.0
114.9
114.7
114.7
109.0
77.3
76.8
40.8
31.0
30.4
30.4
OHC
F
N
2d
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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7.61
7.60
7.44
7.43
7.43
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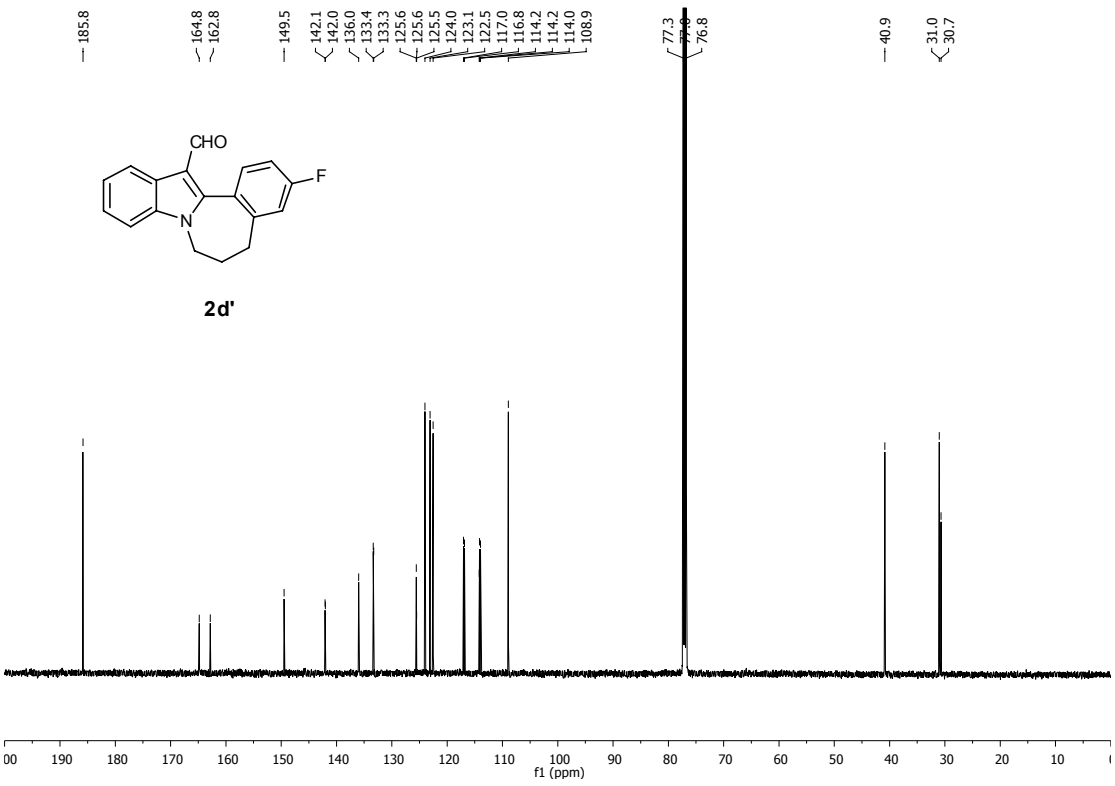
7.40
7.40
7.39
7.38
7.37
7.37
7.29
7.17
7.16
7.16
7.15
7.14
4.47
3.80
2.77
2.71
2.53
2.29
CHO
F
N
2d'
f1 (ppm)


185.8
164.8
162.8
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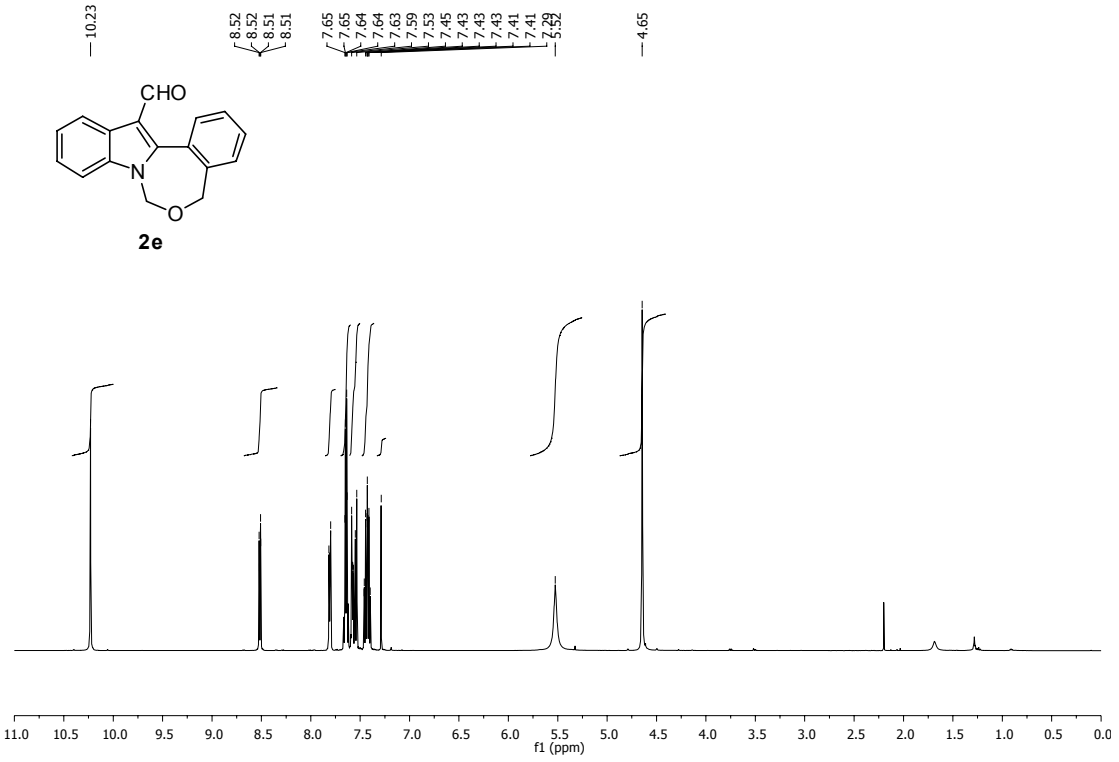
142.0
136.0
133.4
133.3
125.6
125.6
125.5
124.0
123.1
122.5
117.0
116.8
114.2
114.2
114.0
108.9
77.3
76.8
40.9
31.0
30.7
CHO
F
N
2d'
f1 (ppm)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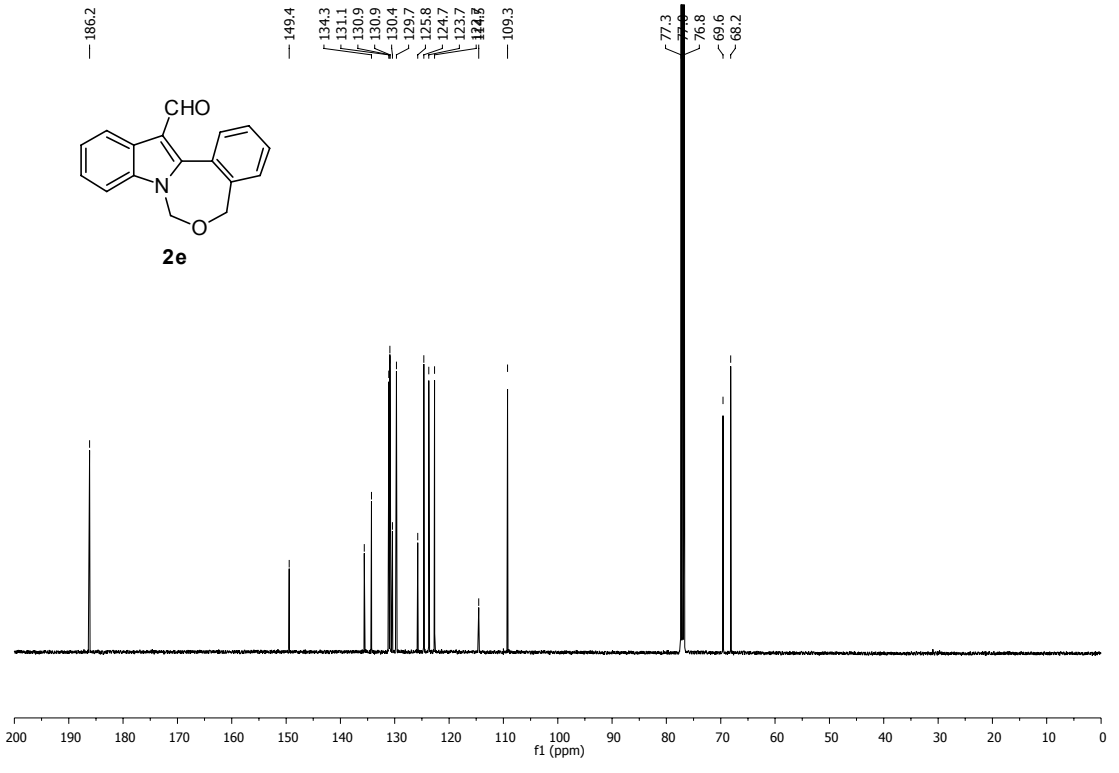
7.65
7.64
7.64
7.63
7.59
7.53
7.45
7.43
7.43
7.41
7.41
5.52
4.65
CHO
N
O
2e
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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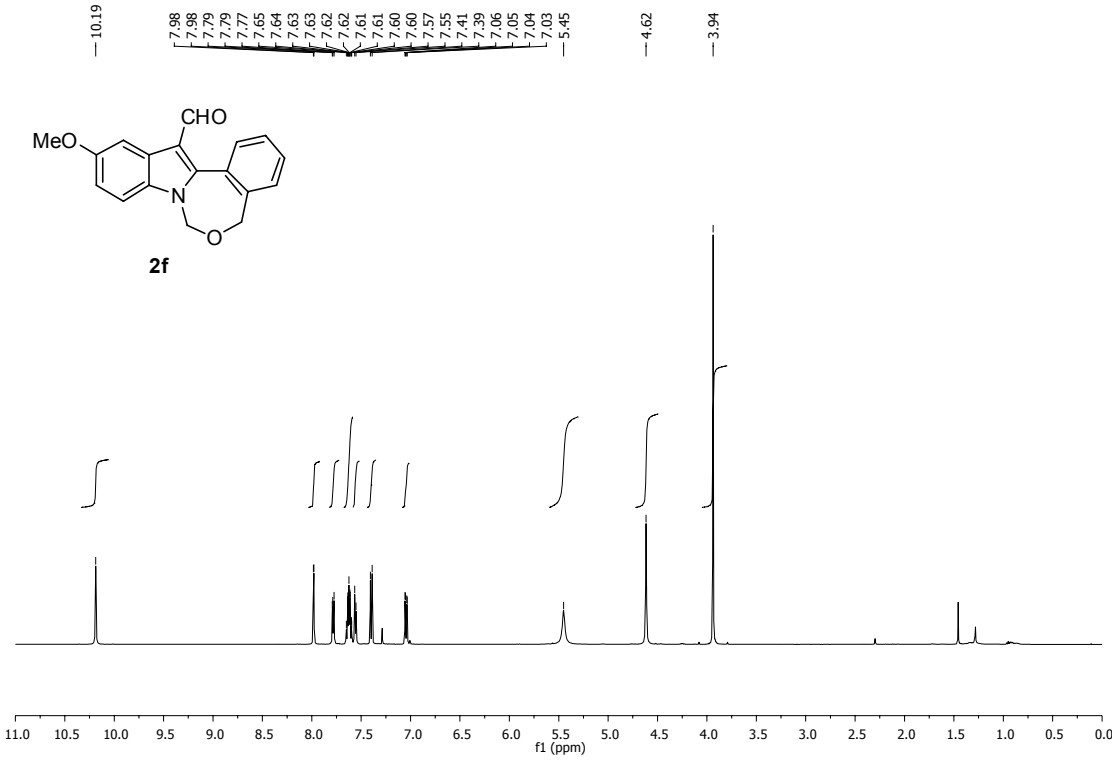
149.4
134.3
131.1
130.9
130.9
130.4
129.7
125.8
124.7
123.7
109.3
77.3
76.8
69.6
68.2
CHO
N
O
2e
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.63
7.63
7.62
7.62
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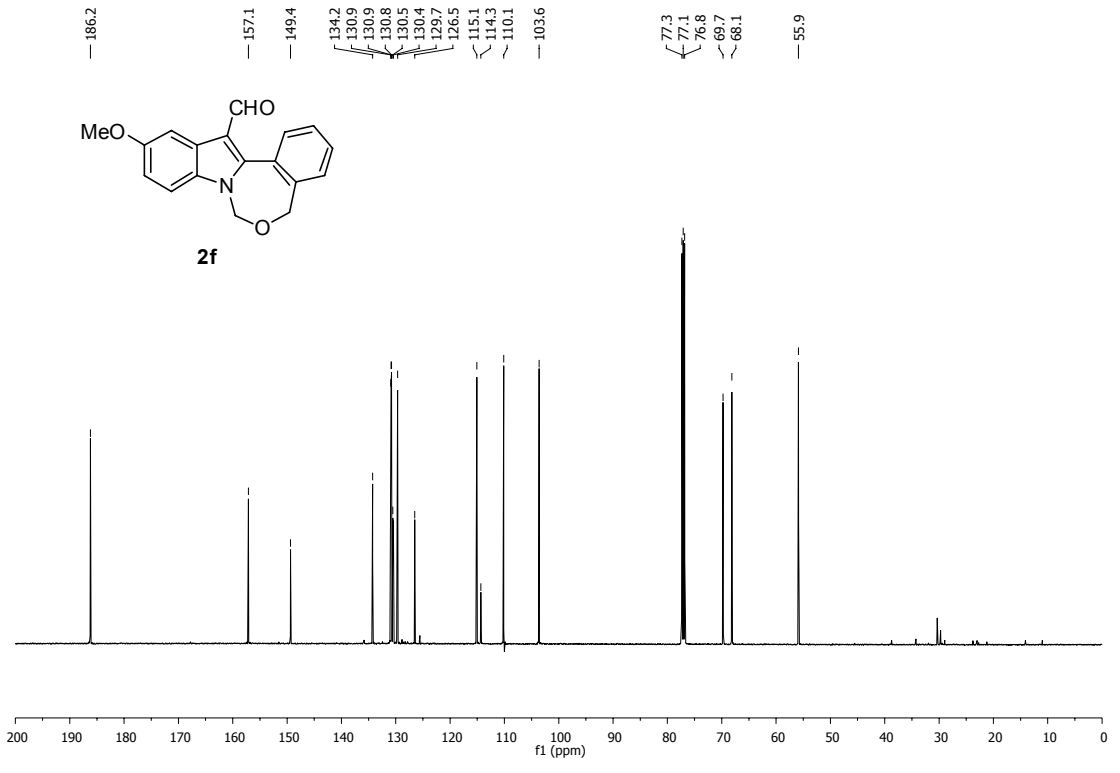
7.61
7.60
7.60
7.57
7.55
7.41
7.39
7.06
7.05
7.04
7.03
5.45
4.62
3.94
CHO
MeO
N
O
2f
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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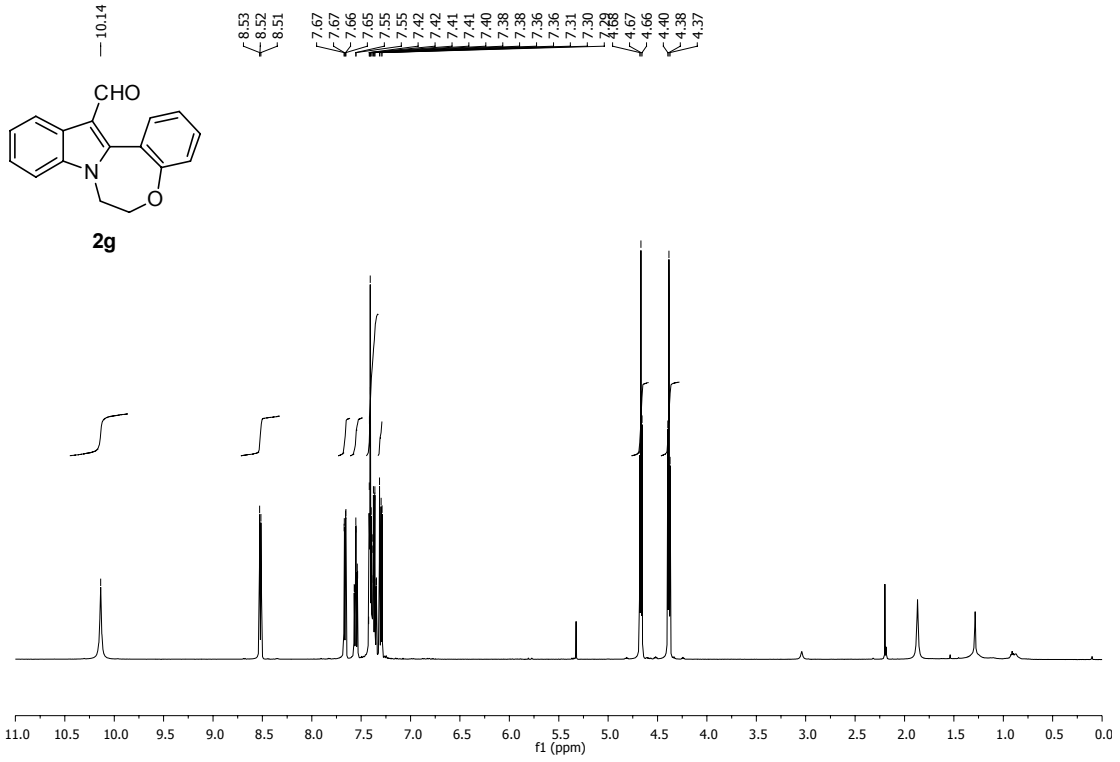
149.4
134.2
130.9
130.9
130.8
130.5
130.4
129.7
126.5
115.1
114.3
110.1
103.6
77.3
77.1
76.8
69.7
68.1
55.9
CHO
MeO
N
O
2f
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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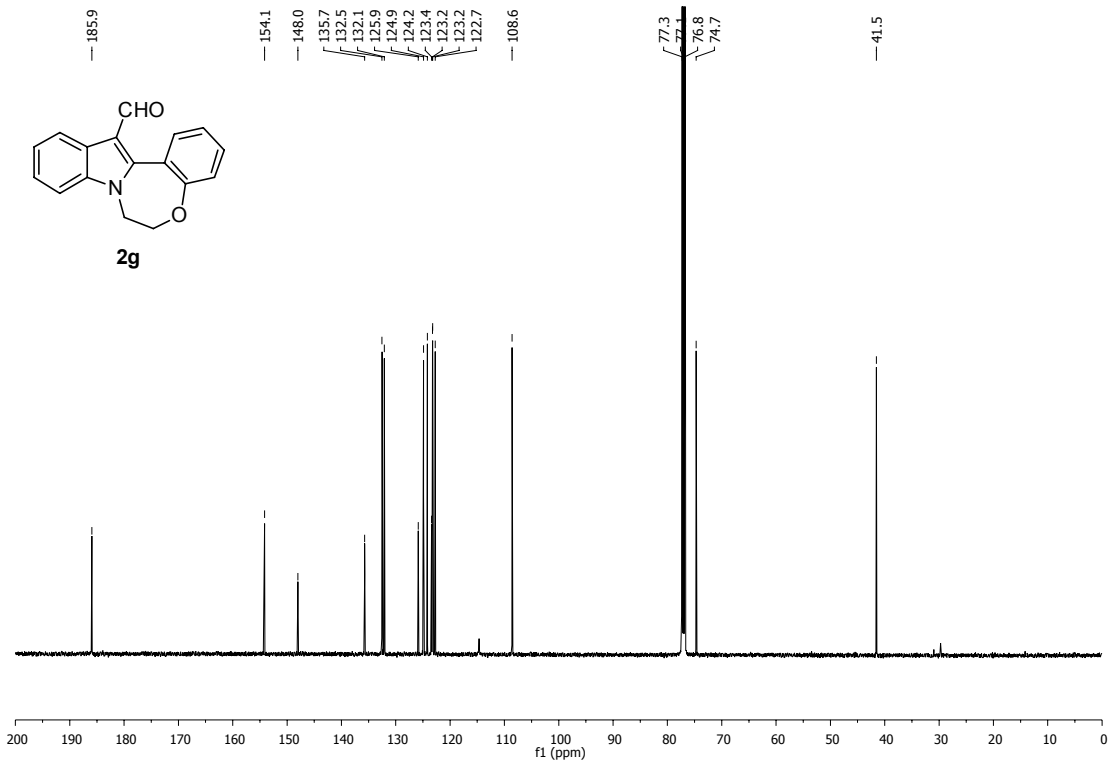
7.42
7.41
7.41
7.40
7.38
7.38
7.36
7.36
7.31
7.30
4.68
4.67
4.66
4.40
4.38
4.37
CHO
N
O
2g
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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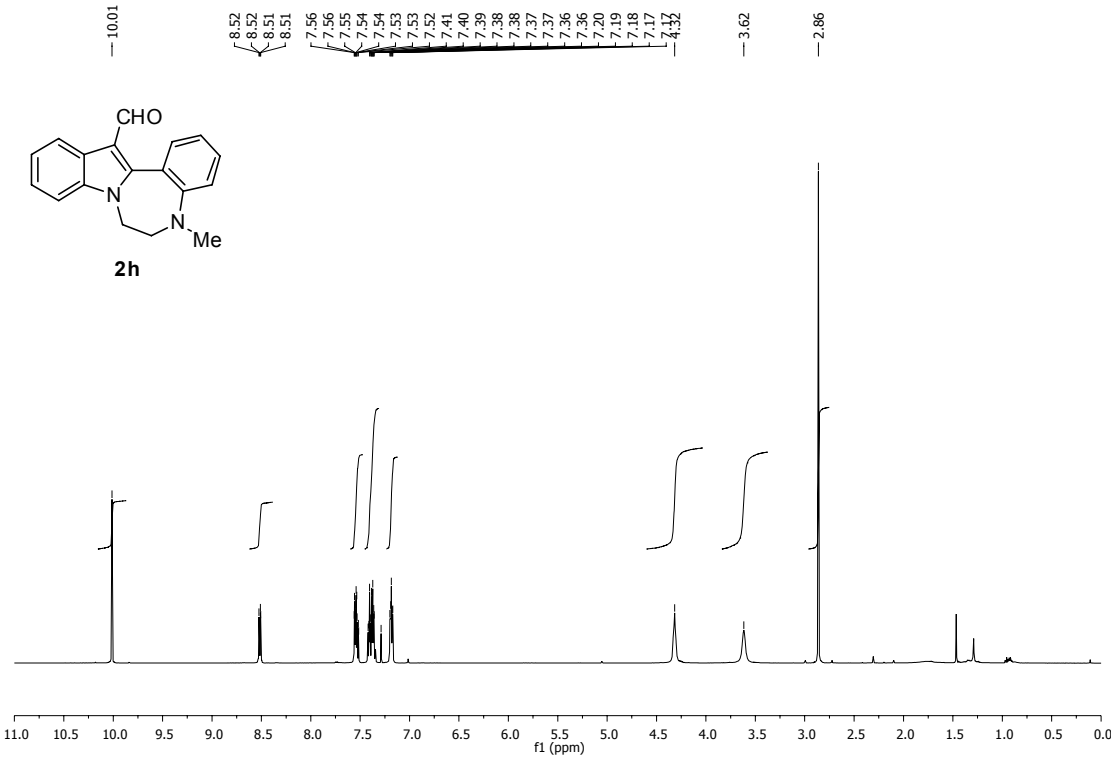
135.7
132.5
132.1
125.9
124.9
124.2
123.4
123.2
123.2
122.7
108.6
77.3
77.1
76.8
74.7
41.5
CHO
N
O
2g
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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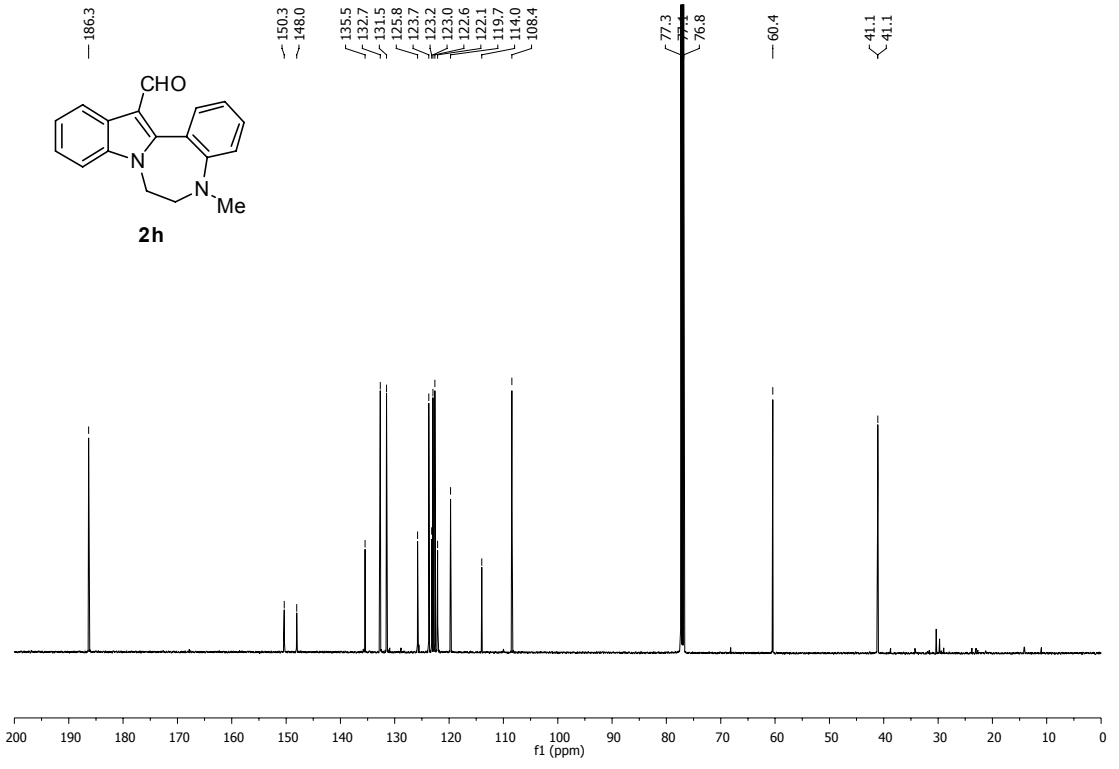
7.55
7.54
7.54
7.53
7.53
7.52
7.41
7.40
7.39
7.38
7.38
7.37
7.37
7.36
7.36
7.20
7.19
7.18
7.17
7.17
4.32
3.62
2.86
CHO
N
N
Me
2h
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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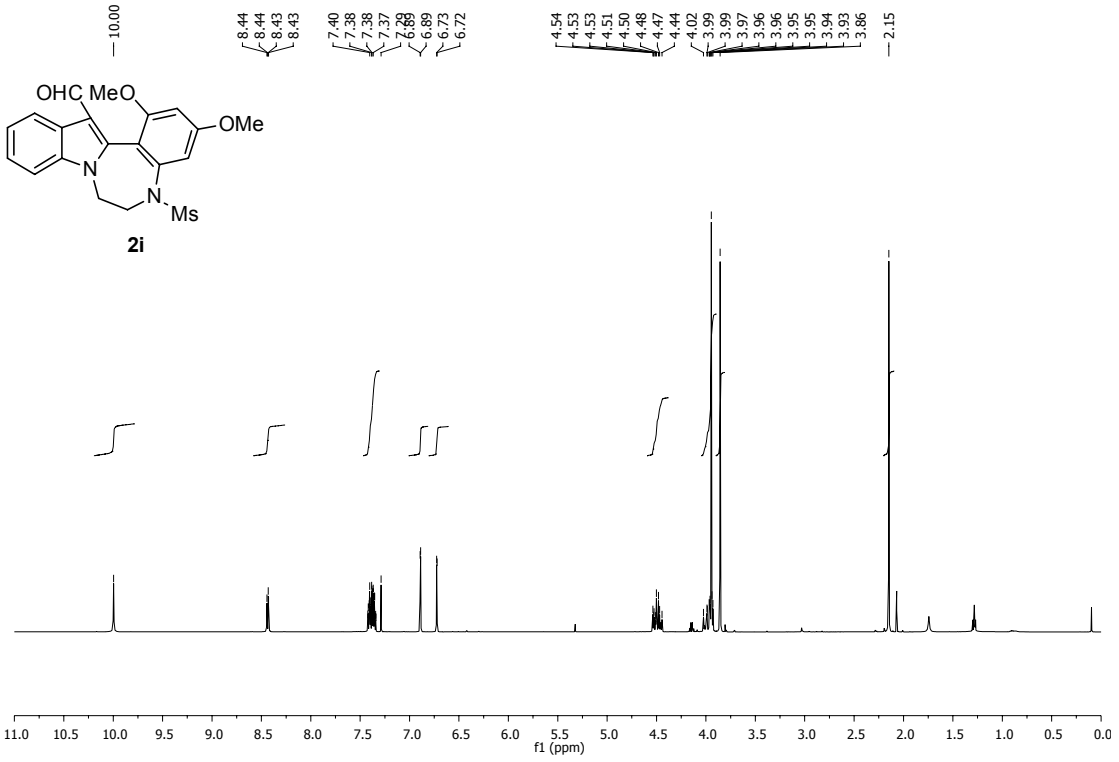
135.5
132.7
131.5
125.8
123.7
123.2
123.0
122.6
122.1
119.7
114.0
108.4
77.3
77.1
76.8
60.4
41.1
41.1
CHO
N
N
Me
2h
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.38
7.38
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6.89
6.89
6.73
6.72
4.54
4.53
4.53
4.51
4.50
4.48
4.47
4.44
4.02
3.99
3.99
3.97
3.96
3.96
3.95
3.95
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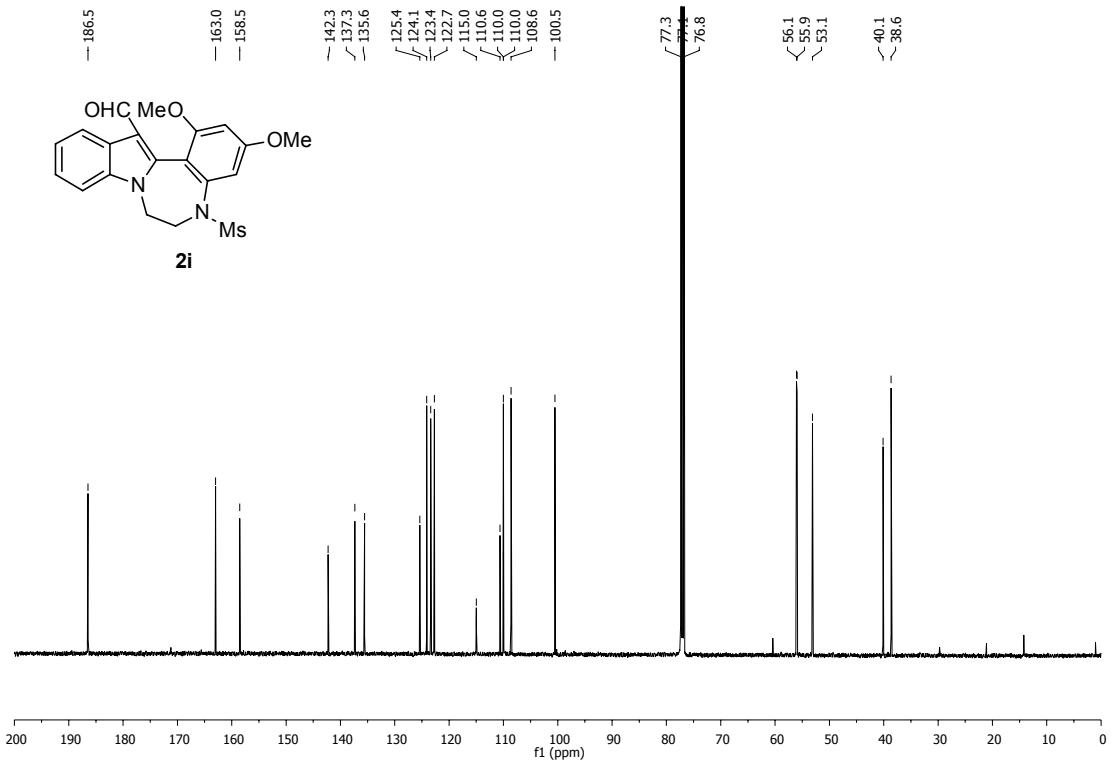
3.93
3.86
2.15
OHC
MeO
OMe
N
N
Ms
2i
f1 (ppm)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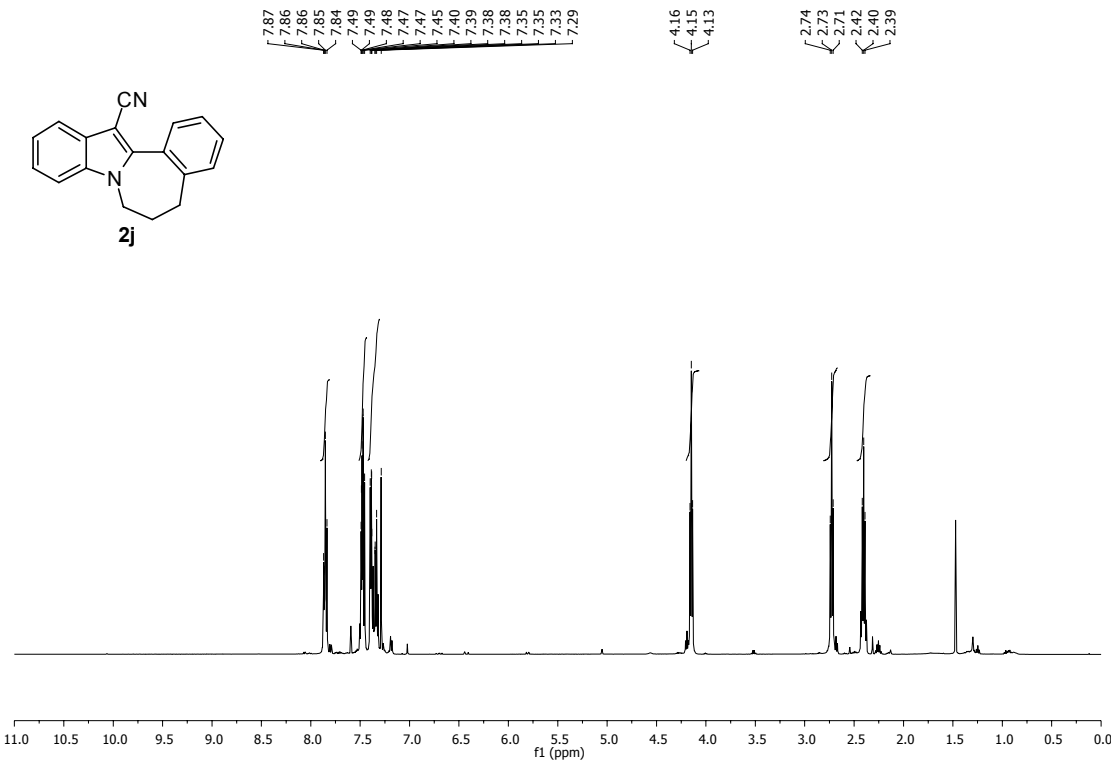
158.5
142.3
137.3
135.6
125.4
124.1
123.4
122.7
115.0
110.6
110.0
110.0
108.6
100.5
77.3
76.8
56.1
55.9
53.1
40.1
38.6
OHC
MeO
OMe
N
N
Ms
2i
f1 (ppm)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7.48
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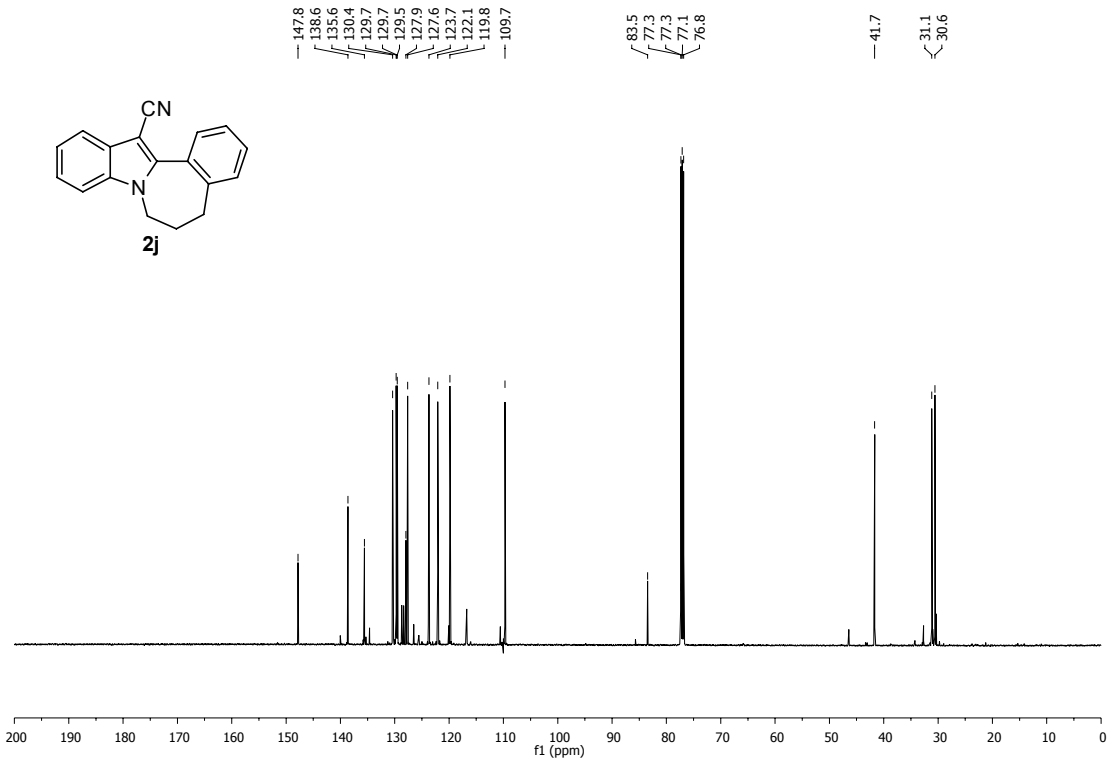
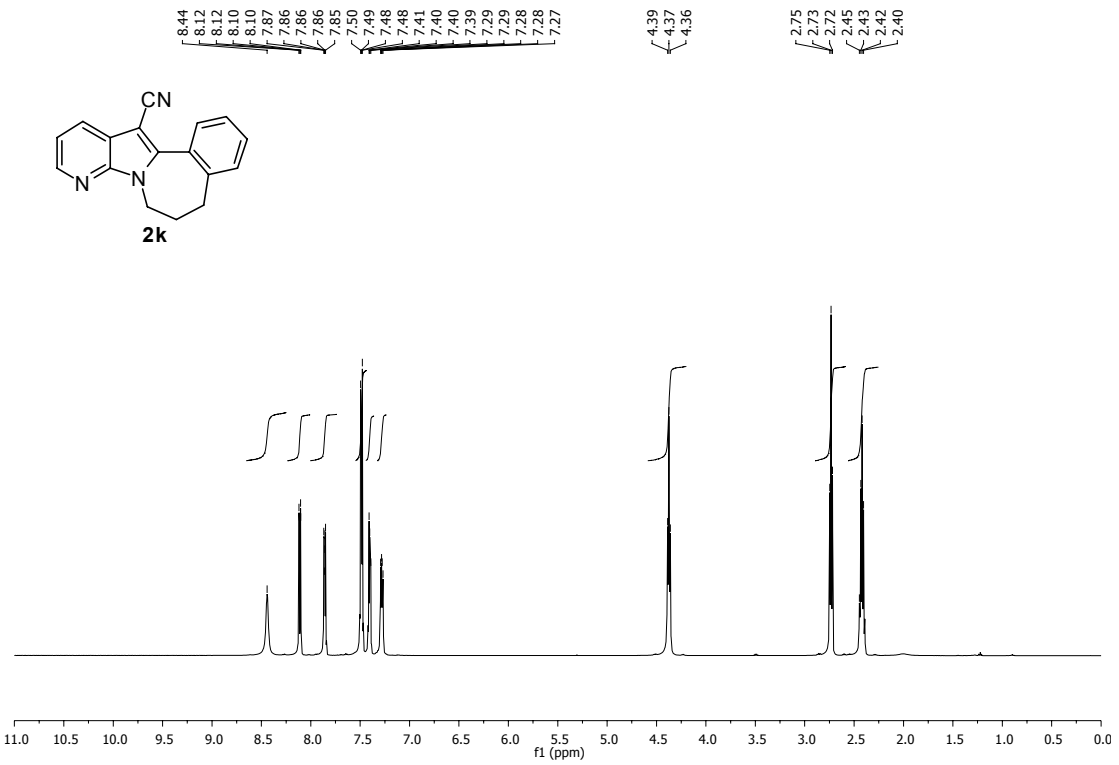
7.47
7.45
7.40
7.39
7.38
7.38
7.35
7.35
7.33
7.29
4.16
4.15
4.13
2.74
2.73
2.71
2.42
2.40
2.39
CN
N
2j
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


147.8
138.6
135.6
130.4
129.7
129.7
129.5
127.9
127.6
123.7
122.1
119.8
109.7
83.5
77.3
77.3
77.1
76.8
41.7
31.1
30.6
CN
N
2j
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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8.10
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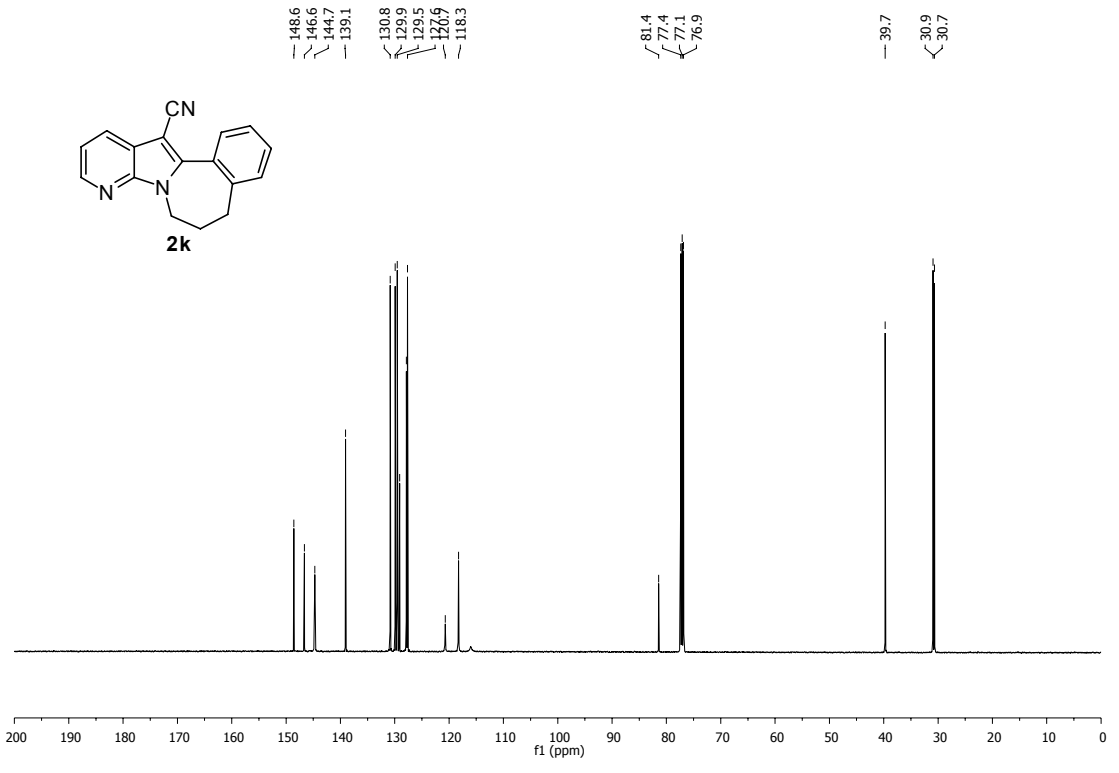
7.86
7.86
7.85
7.50
7.49
7.48
7.48
7.41
7.40
7.40
7.39
7.29
7.29
7.28
7.28
7.27
4.39
4.37
4.36
2.75
2.73
2.72
2.45
2.43
2.42
2.40
CN
N
N
2k
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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146.6
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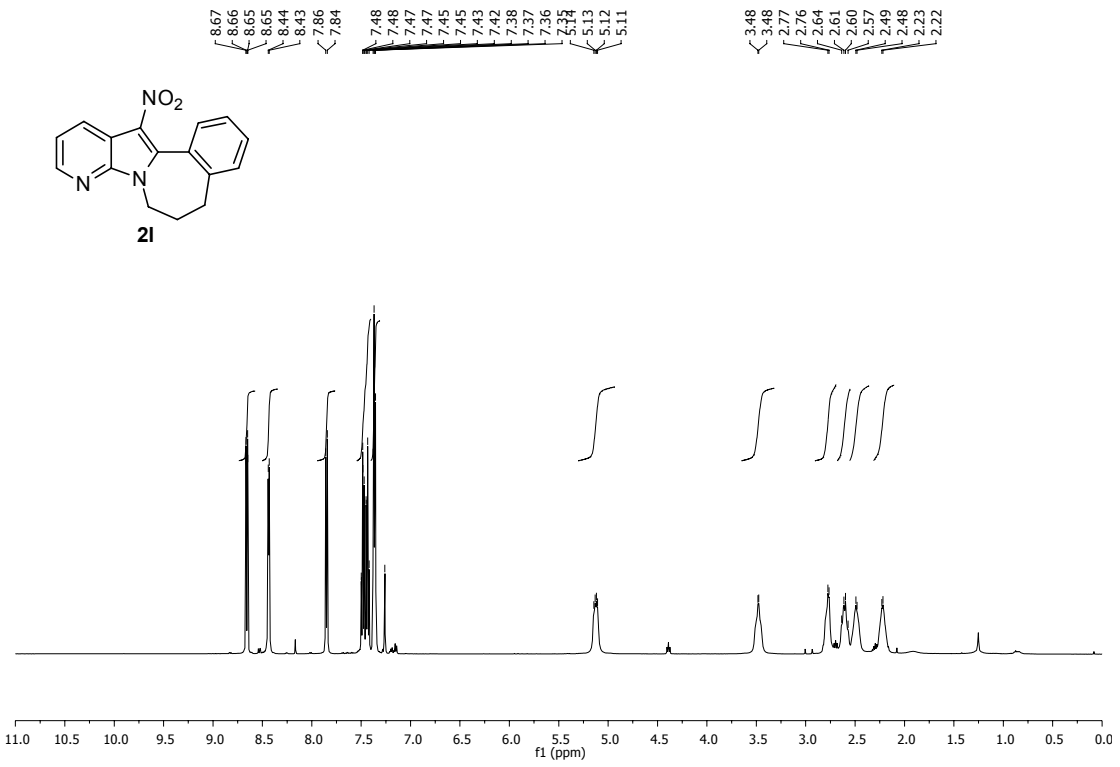
129.5
127.6
120.7
118.3
81.4
77.4
77.1
76.9
39.7
30.9
30.7
CN
N
N
2k
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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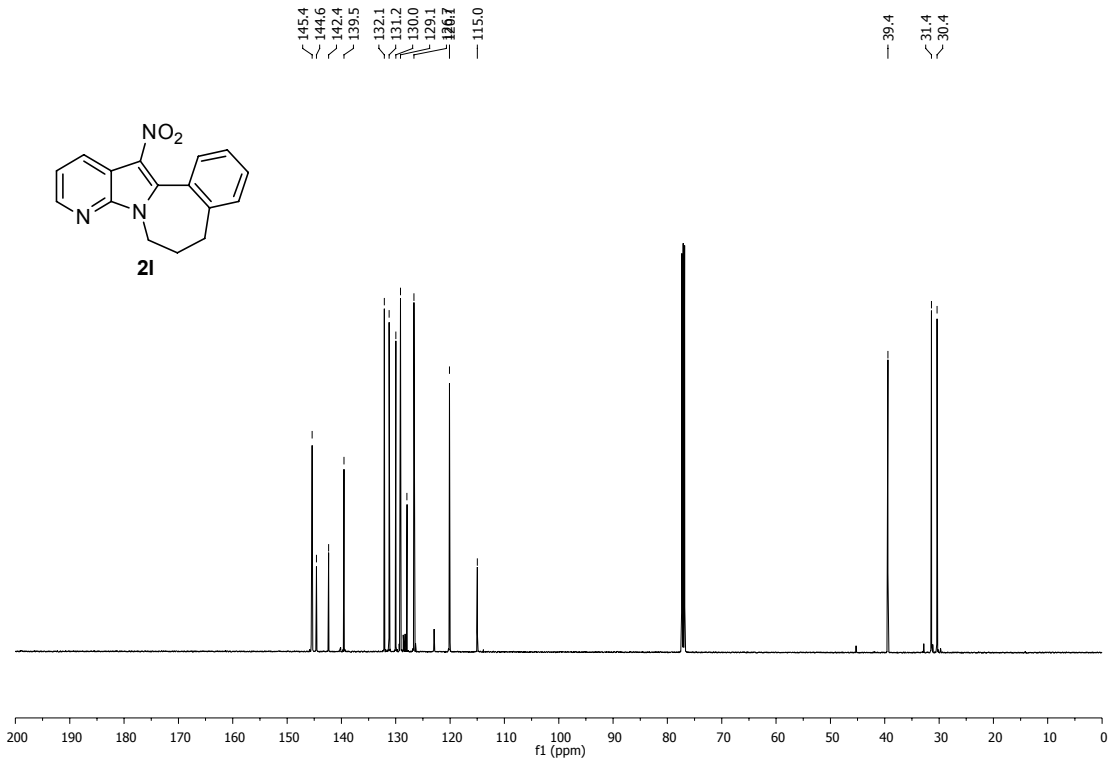
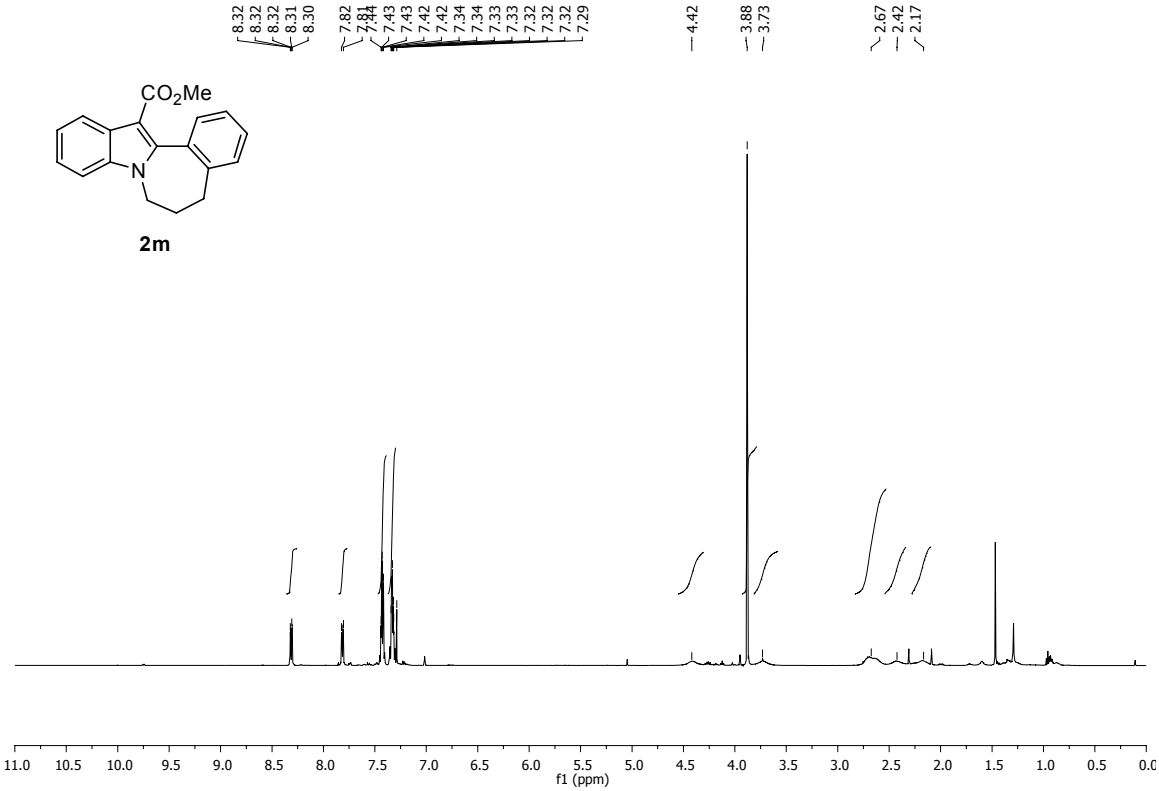
7.45
7.45
7.43
7.42
7.38
7.37
7.36
5.13
5.12
5.11
3.48
3.48
2.77
2.76
2.64
2.61
2.60
2.57
2.49
2.48
2.23
2.22
NO2
N
N
2l
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


145.4
144.6
142.4
139.5
132.1
131.2
130.0
129.1
115.0
39.4
31.4
30.4
NO2
N
N
2l
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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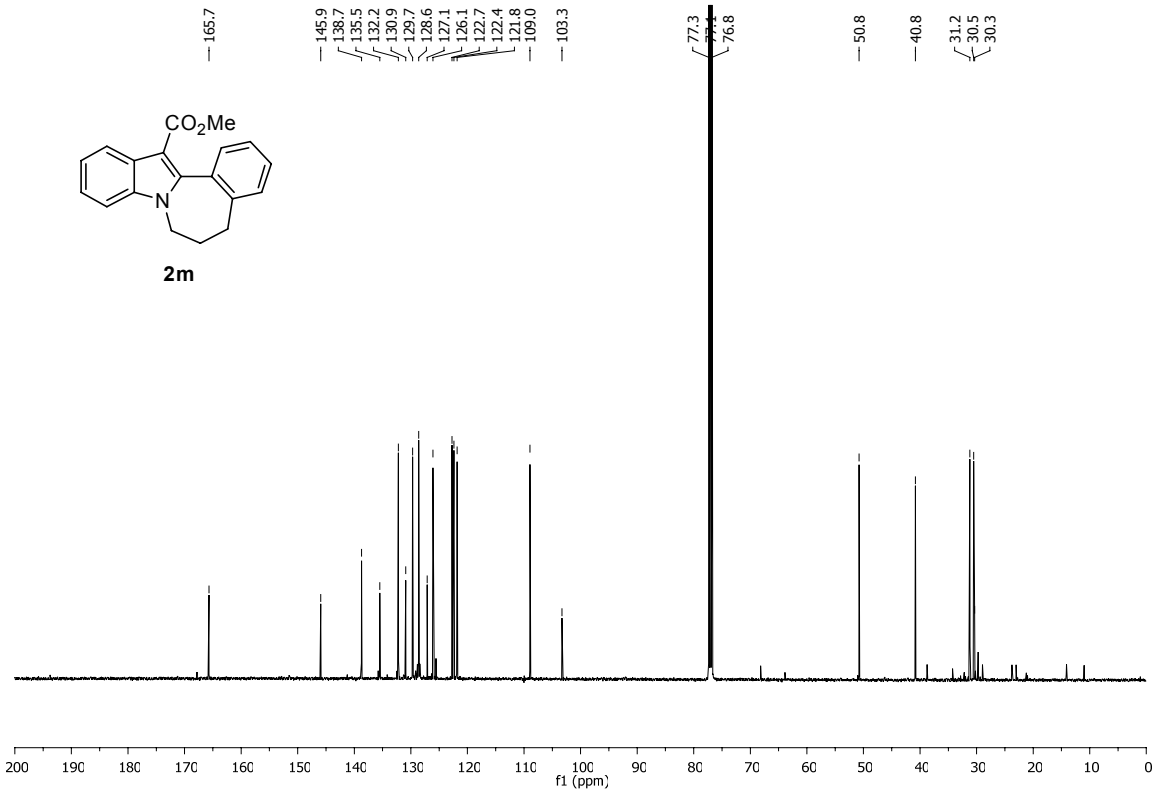
7.44
7.43
7.43
7.42
7.42
7.34
7.34
7.33
7.33
7.32
7.32
7.32
7.29
4.42
3.88
3.73
2.67
2.42
2.17
CO2Me
N
2m
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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145.9
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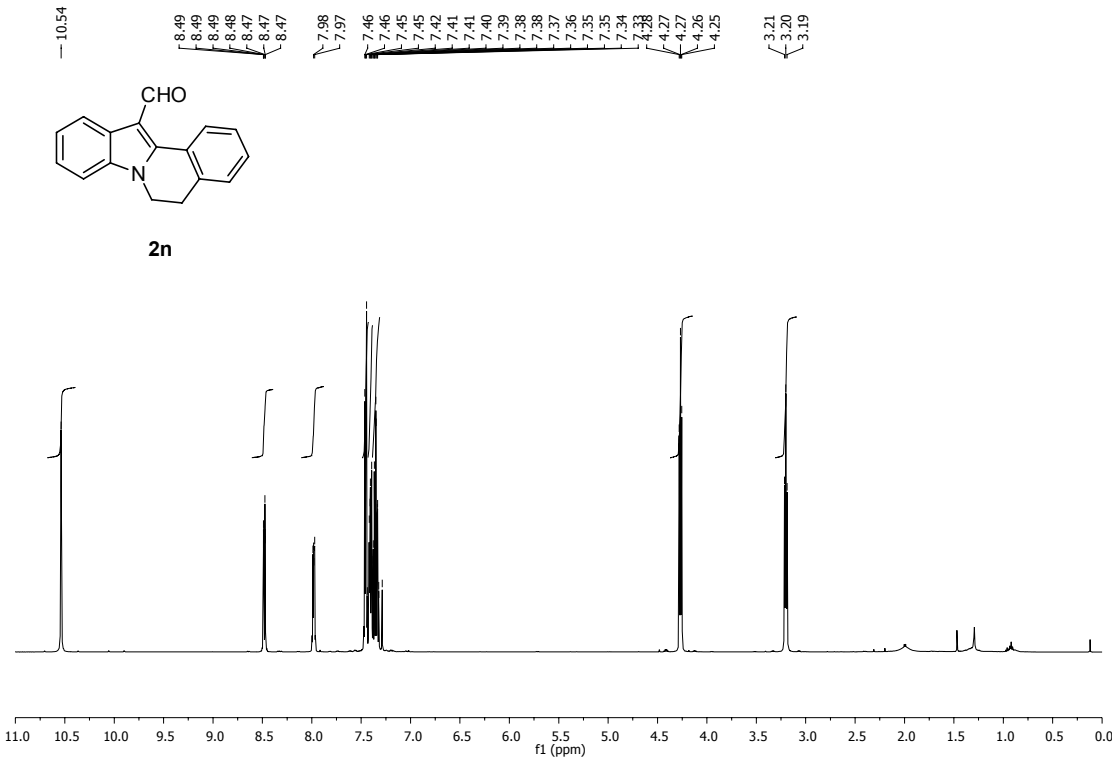
135.5
132.2
130.9
129.7
128.6
127.1
126.1
122.7
122.4
121.8
109.0
103.3
77.3
76.8
50.8
40.8
31.2
30.5
30.3
CO2Me
N
2m
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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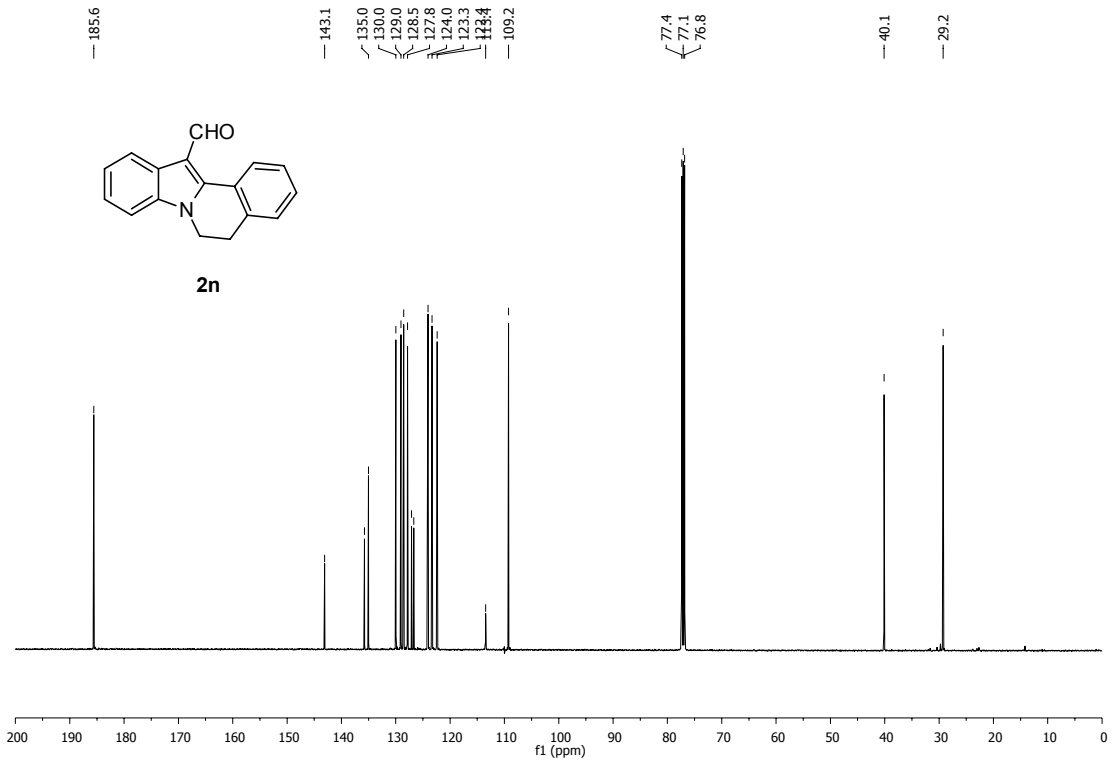
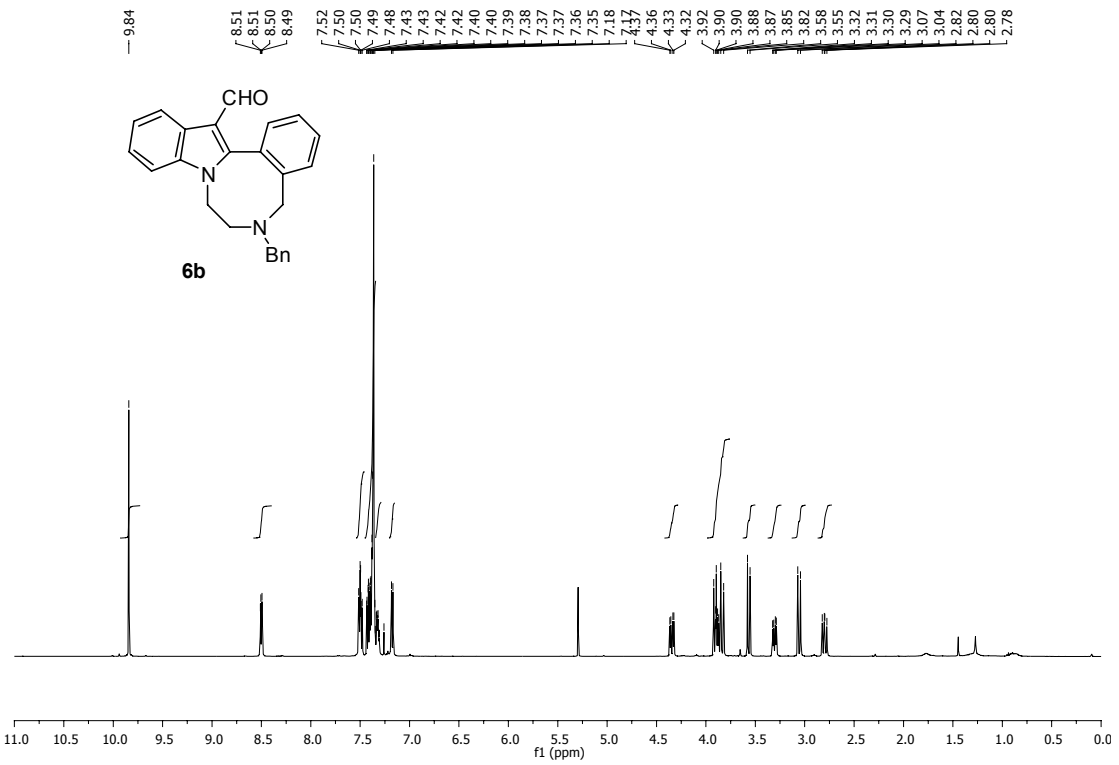
7.97
7.46
7.46
7.45
7.45
7.42
7.41
7.41
7.40
7.39
7.38
7.38
7.37
7.36
7.35
7.35
7.34
4.28
4.27
4.27
4.26
4.25
3.21
3.20
3.19
CHO
N
2n
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


185.6
143.1
135.0
130.0
129.0
128.5
127.8
124.0
123.3
109.2
77.4
77.1
76.8
40.1
29.2
CHO
N
2n
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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8.51
8.50
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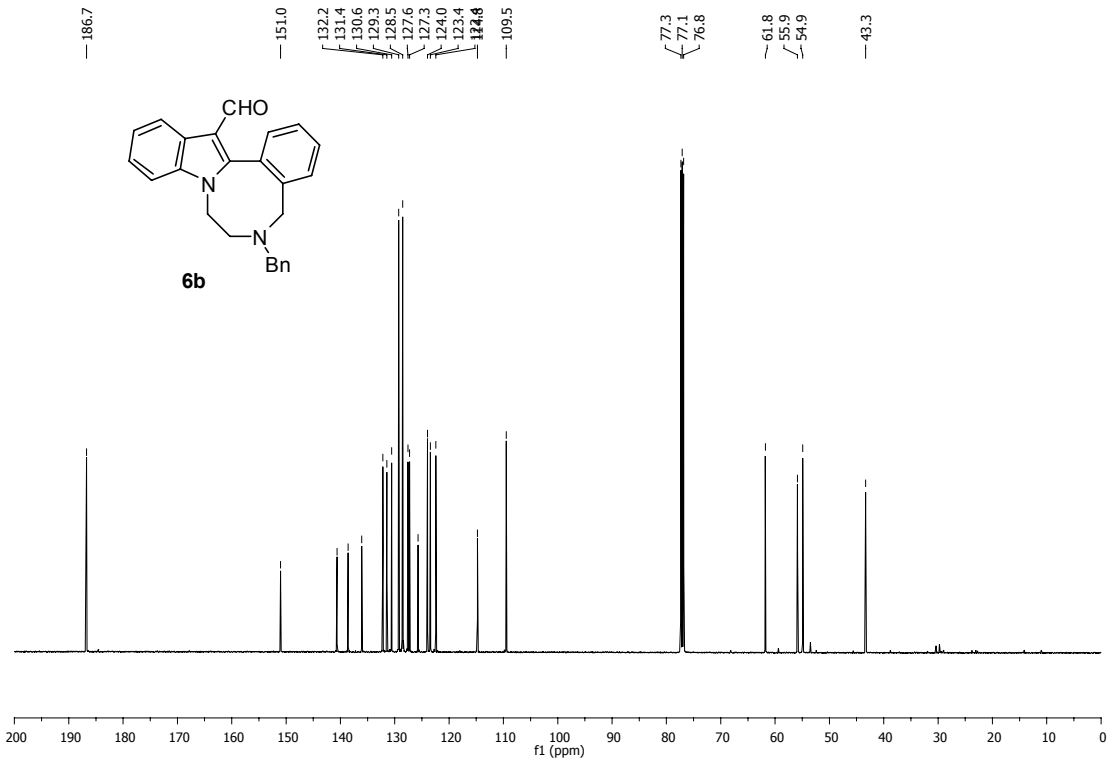
7.52
7.50
7.50
7.49
7.48
7.43
7.43
7.42
7.42
7.40
7.40
7.39
7.38
7.37
7.37
7.36
7.35
7.18
4.36
4.33
4.32
3.92
3.90
3.90
3.88
3.87
3.85
3.82
3.58
3.55
3.32
3.31
3.30
3.29
3.07
3.04
2.82
2.80
2.80
2.78
CHO
N
N
Bn
6b
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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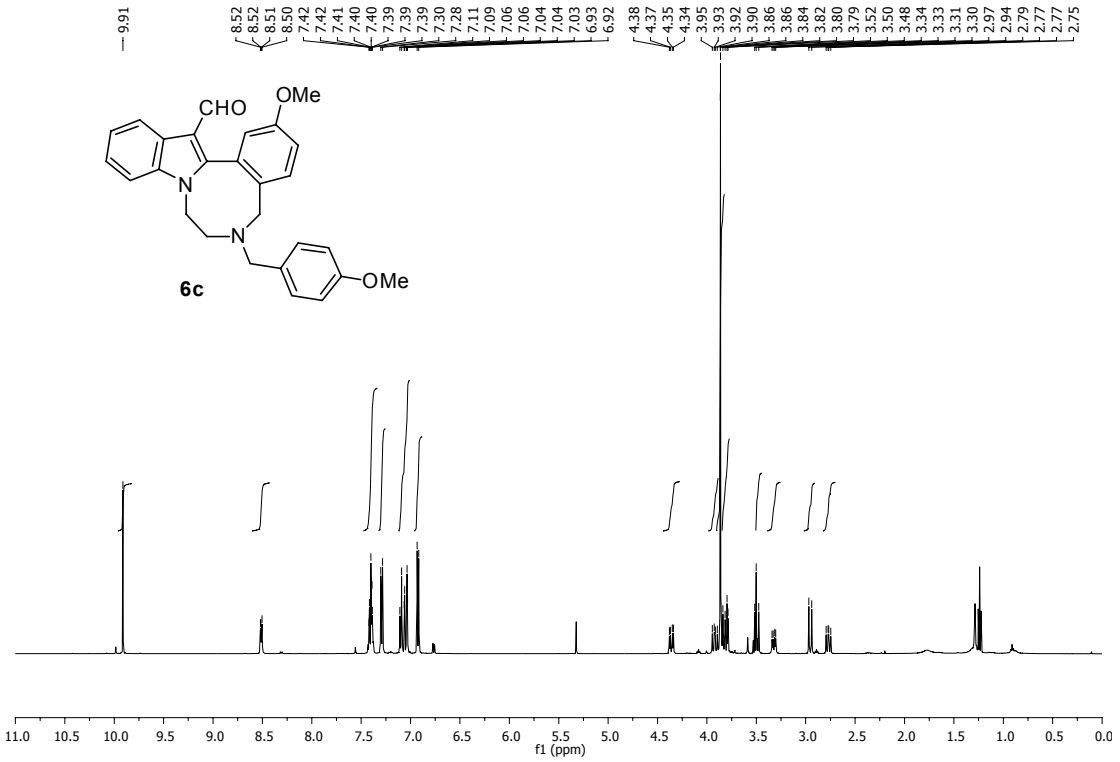
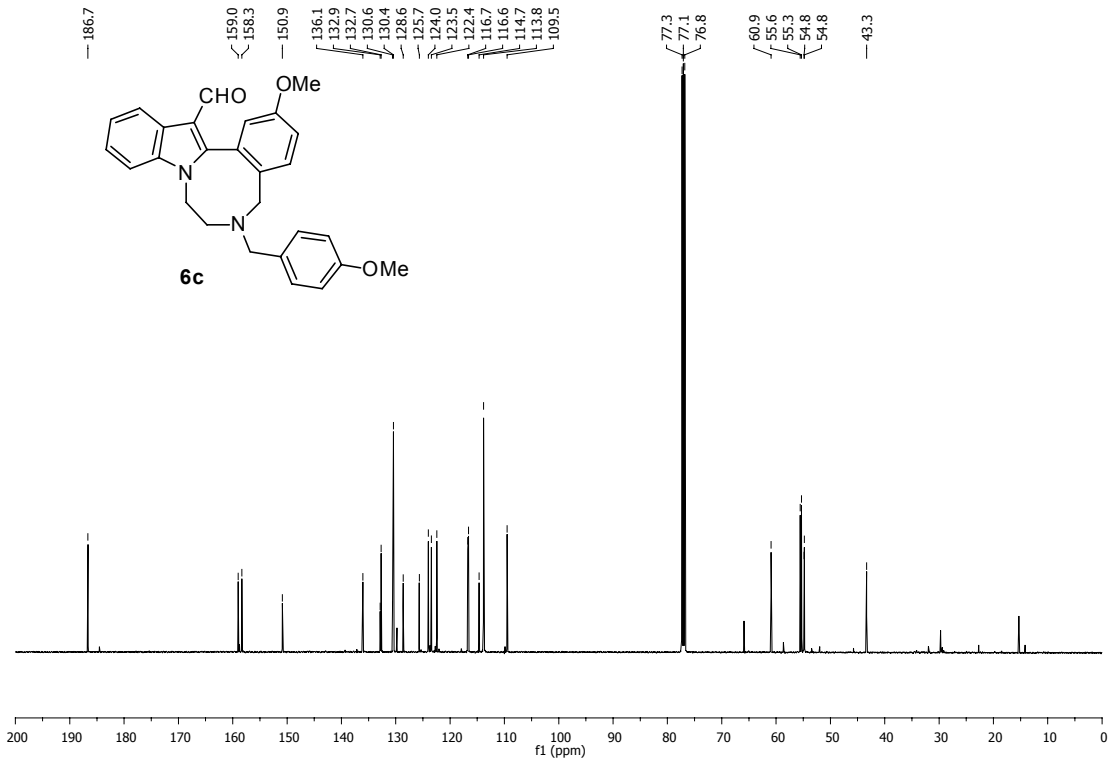
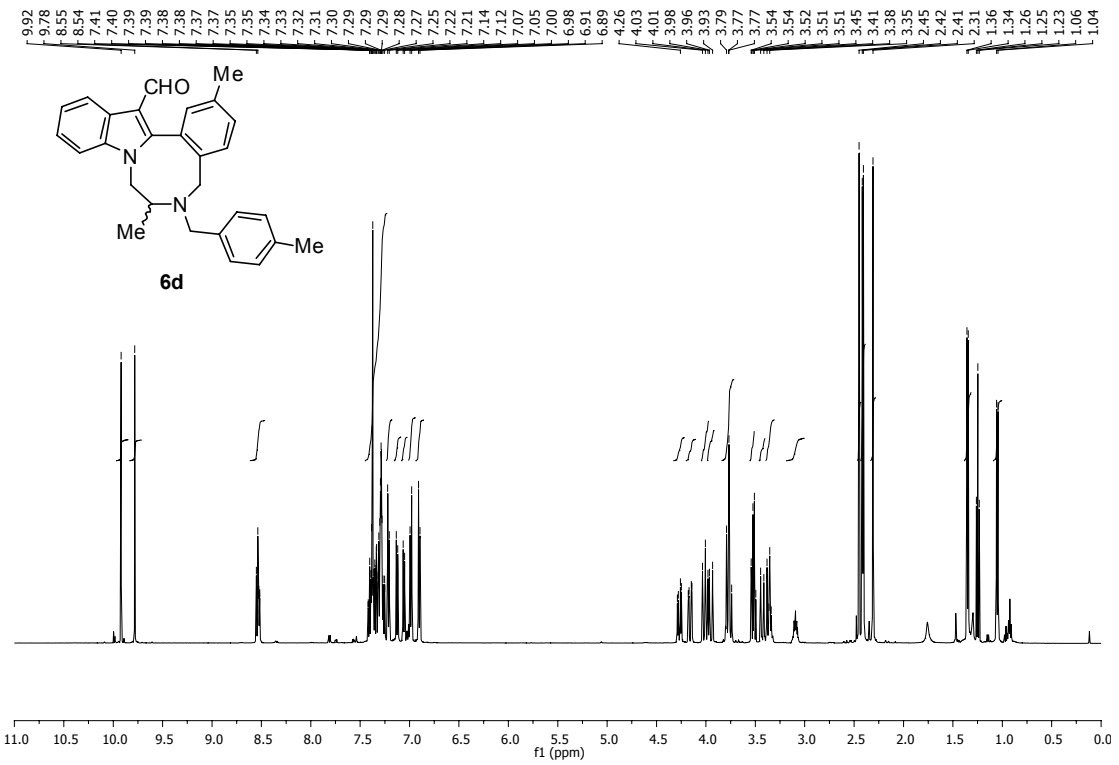
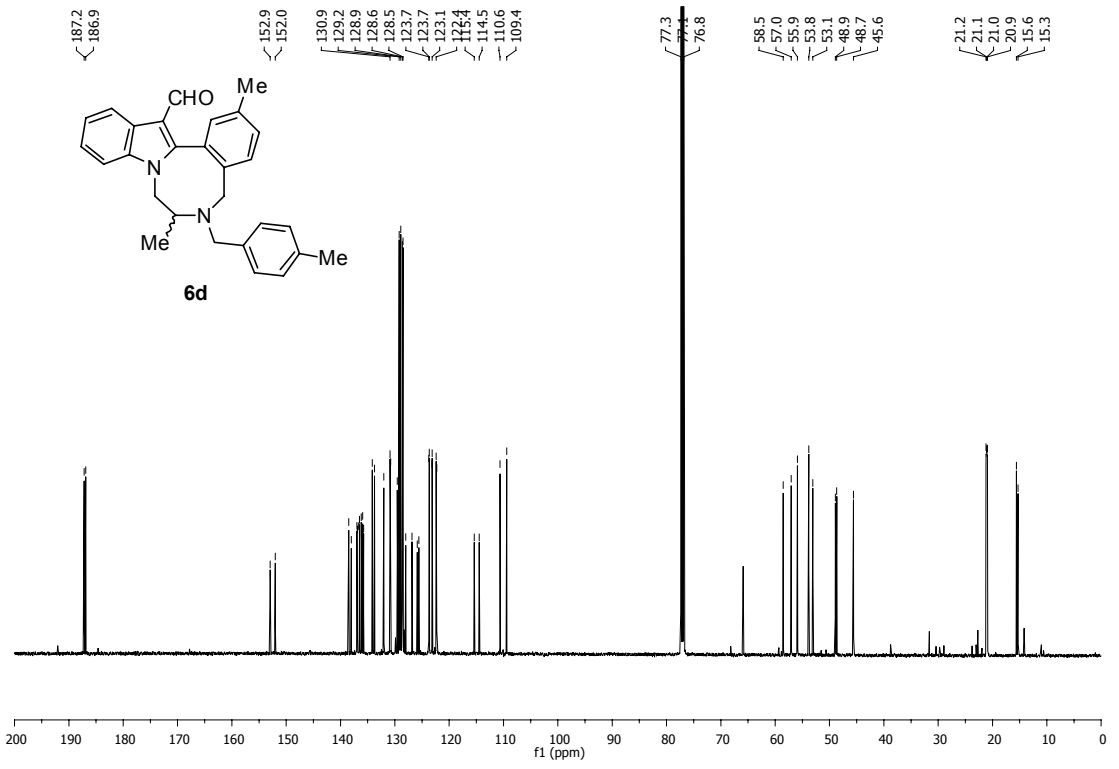
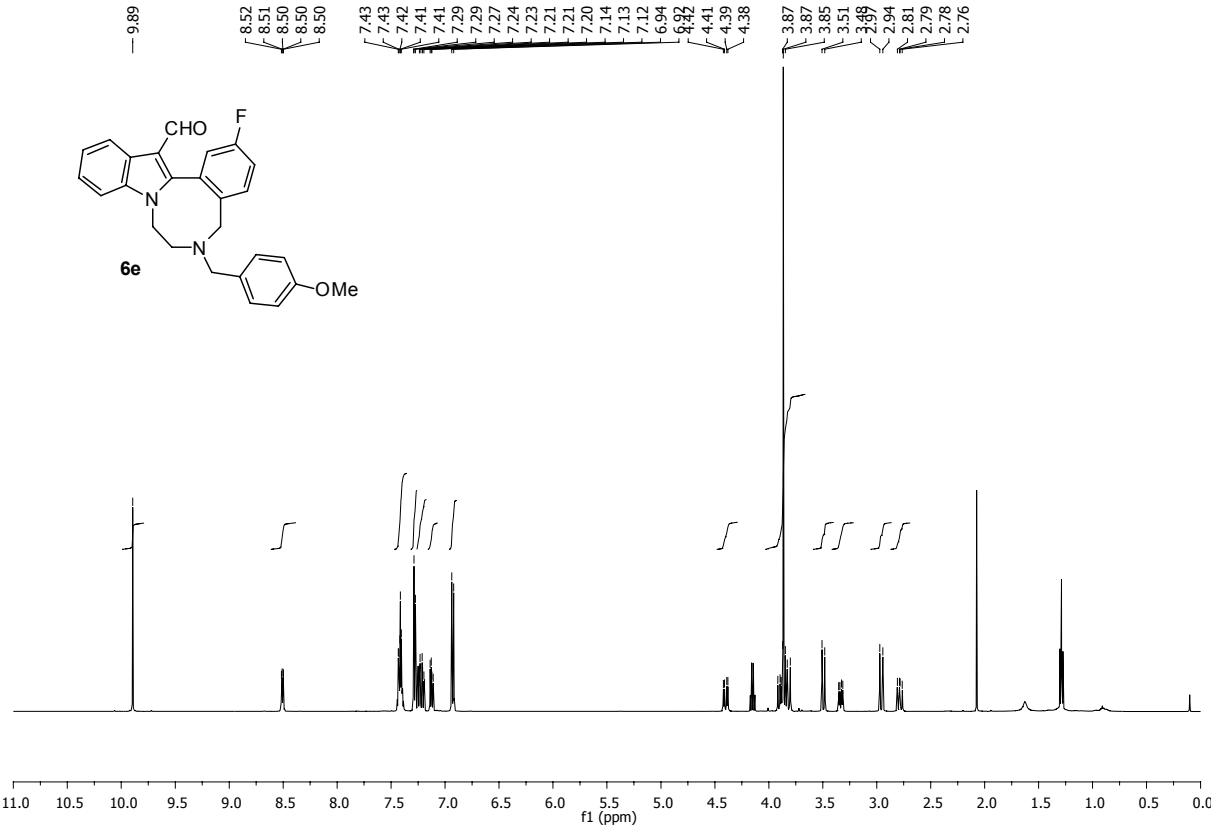
151.0
132.2
131.4
130.6
129.3
128.5
127.6
127.3
124.0
123.4
109.5
77.3
77.1
76.8
61.8
55.9
54.9
43.3
CHO
N
N
Bn
6b
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


9.91
8.52
8.52
8.51
8.50
7.42
7.42
7.41
7.40
7.40
7.39
7.39
7.39
7.30
7.28
7.11
7.09
7.06
7.06
7.04
7.04
7.03
6.93
6.92
4.38
4.37
4.35
4.34
3.95
3.93
3.92
3.90
3.86
3.86
3.84
3.82
3.80
3.79
3.52
3.50
3.48
3.34
3.33
3.31
3.30
2.97
2.94
2.79
2.77
2.77
2.75
CHO
OMe
N
N
OMe
6c
11.0
10.5
10.0
9.5
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)


186.7
159.0
158.3
150.9
136.1
132.9
132.7
130.6
130.4
128.6
125.7
124.0
123.5
122.4
116.7
116.6
114.7
113.8
109.5
77.3
77.1
76.8
60.9
55.6
55.3
54.8
54.8
43.3
CHO
OMe
N
N
OMe
6c
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.92 9.78 8.55 8.54 7.41 7.40 7.39 7.39 7.38 7.38 7.37 7.37 7.35 7.35 7.34 7.33 7.32 7.31 7.30 7.29 7.29 7.29 7.28 7.27 7.25 7.22 7.21 7.14 7.12 7.07 7.05 7.00 6.98 6.91 6.89 4.26 4.03 4.01 3.98 3.96 3.93 3.79 3.77 3.77 3.54 3.54 3.52 3.51 3.51 3.45 3.41 3.38 3.35 2.45 2.42 2.41 2.31 1.36 1.34 1.26 1.25 1.23 1.06 1.04
CHO
Me
N
N
Me
Me
6d
11.0 10.5 10.0 9.5 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)


187.2 186.9 152.9 152.0 130.9 129.2 128.9 128.6 128.5 123.7 123.7 123.1 114.5 110.6 109.4 77.3 76.8 58.5 57.0 55.9 53.8 53.1 48.9 48.7 45.6 21.2 21.1 21.0 20.9 15.6 15.3
CHO
Me
N
N
Me
Me
6d
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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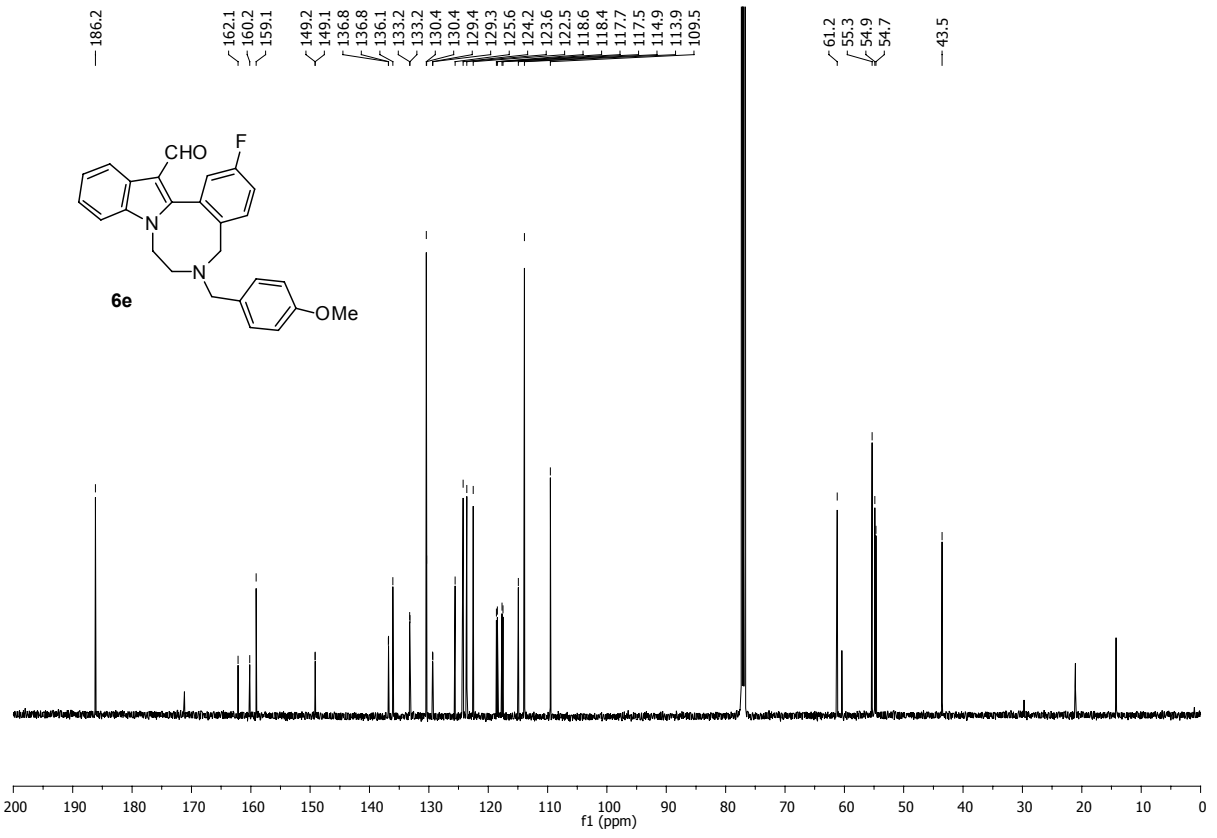
7.41
7.29
7.29
7.27
7.24
7.23
7.21
7.21
7.20
7.14
7.13
7.12
6.94
4.41
4.39
4.38
3.87
3.87
3.85
3.51
2.94
2.81
2.79
2.78
2.76
CHO
F
N
N
OMe
6e
f1 (ppm)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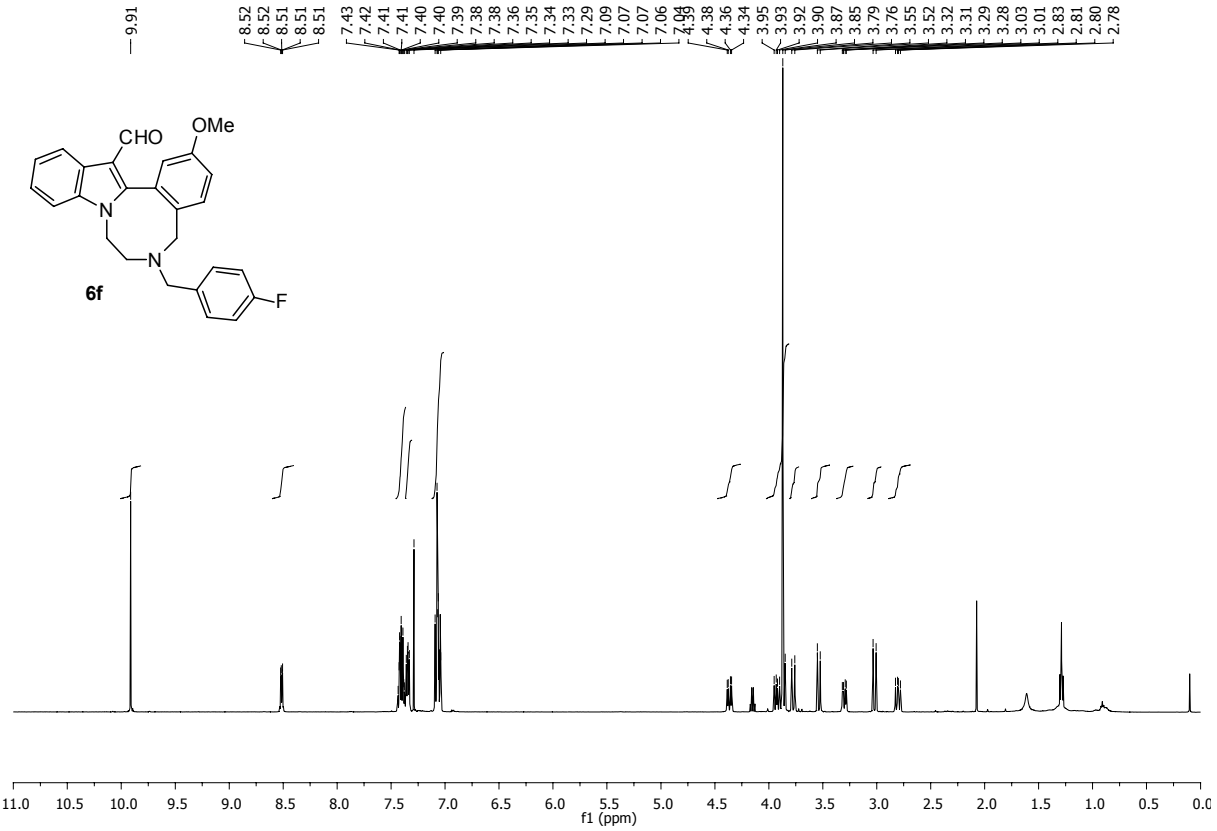
162.1
160.2
159.1
149.2
149.1
136.8
136.8
136.1
133.2
133.2
130.4
130.4
129.4
129.3
125.6
124.2
123.6
122.5
118.6
118.4
117.7
117.5
114.9
113.9
109.5
61.2
55.3
54.9
54.7
43.5
CHO
F
N
N
OMe
6e
f1 (ppm)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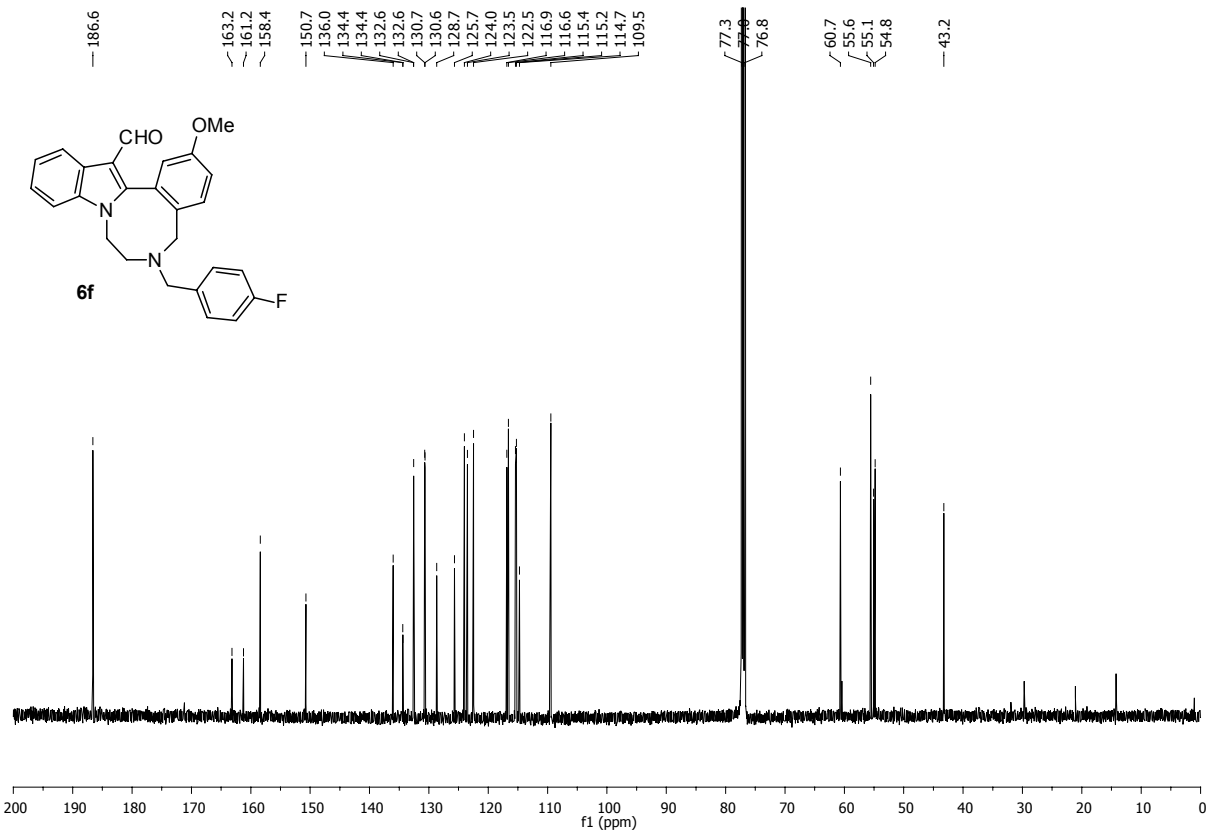
8.51
8.51
8.51
7.43
7.42
7.41
7.41
7.40
7.40
7.39
7.38
7.38
7.36
7.35
7.34
7.33
7.29
7.09
7.07
7.07
7.06
7.04
4.39
4.38
4.36
4.34
3.95
3.93
3.92
3.90
3.87
3.85
3.79
3.76
3.55
3.52
3.32
3.31
3.29
3.28
3.03
3.01
2.83
2.81
2.80
2.78
CHO
OMe
N
N
F
6f
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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163.2
161.2
158.4
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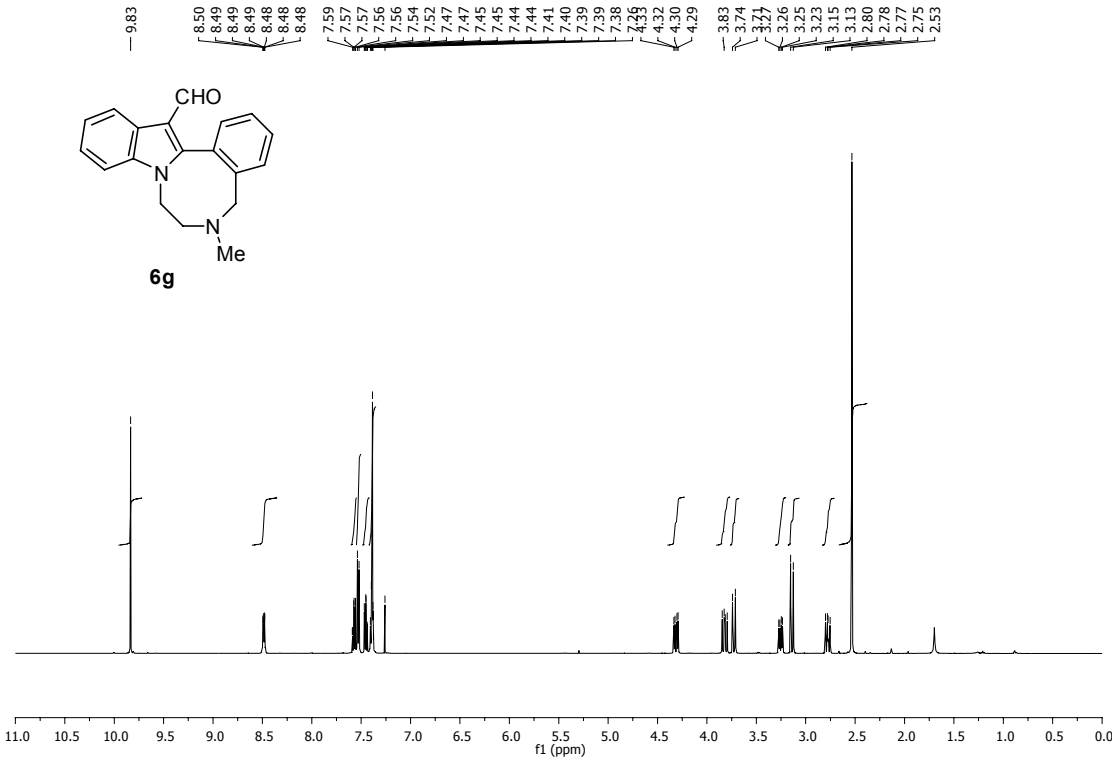
136.0
134.4
134.4
132.6
132.6
130.7
130.6
128.7
125.7
124.0
123.5
122.5
116.9
116.6
115.4
115.2
114.7
109.5
77.3
77.0
76.8
60.7
55.6
55.1
54.8
43.2
CHO
OMe
N
N
F
6f
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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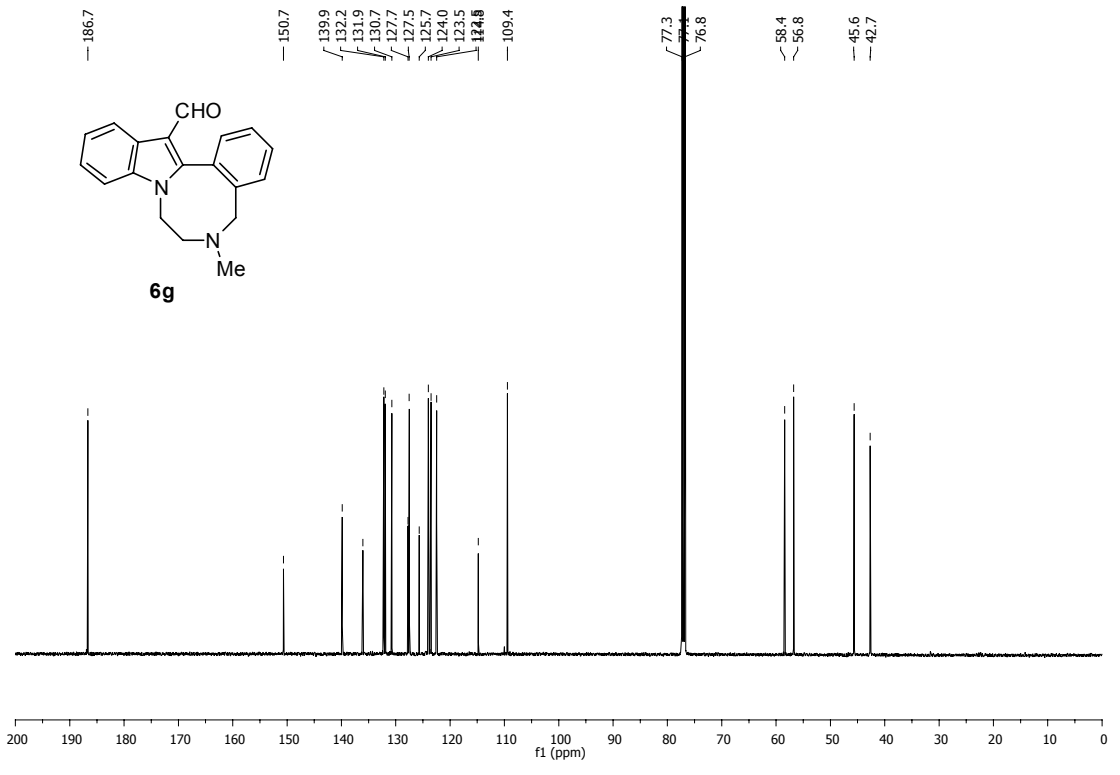
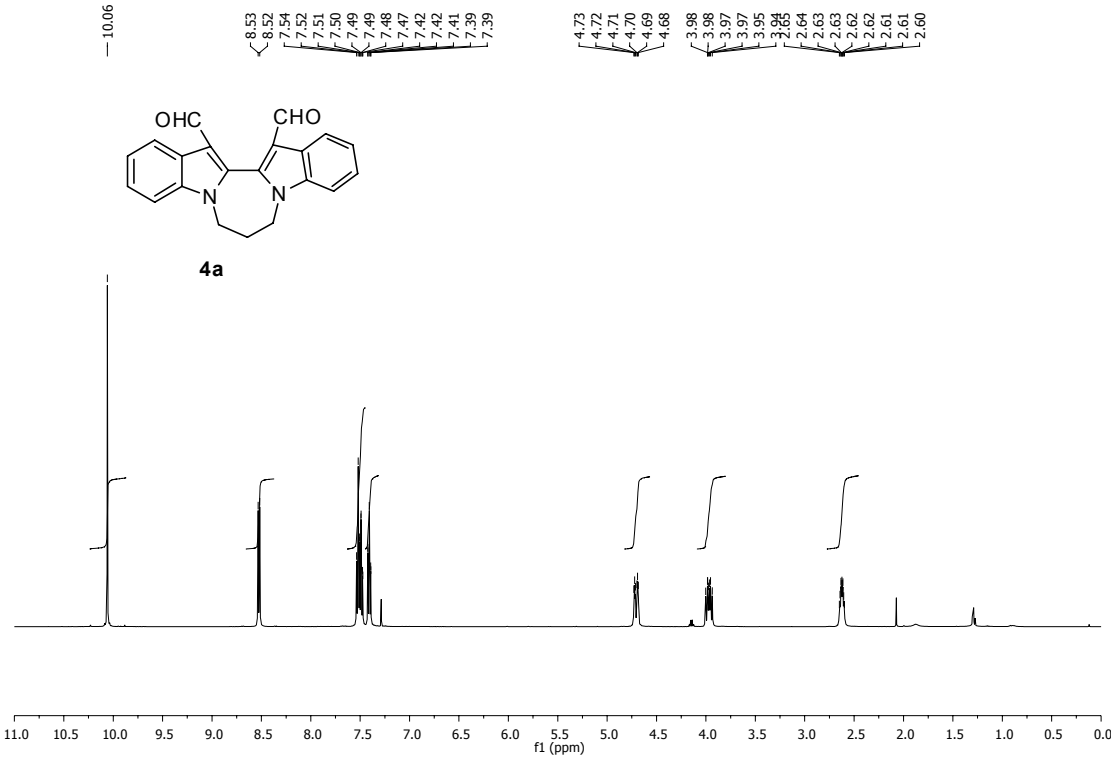
7.54
7.52
7.47
7.47
7.45
7.45
7.44
7.44
7.41
7.40
7.39
7.39
7.38
4.32
4.30
4.29
3.83
3.74
3.26
3.25
3.23
3.15
3.13
2.80
2.78
2.77
2.75
2.53
CHO
N
N
Me
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

6g


186.7
150.7
139.9
132.2
131.9
130.7
127.7
127.5
125.7
124.0
123.5
109.4
77.3
76.8
58.4
56.8
45.6
42.7
CHO
N
N
Me
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

6g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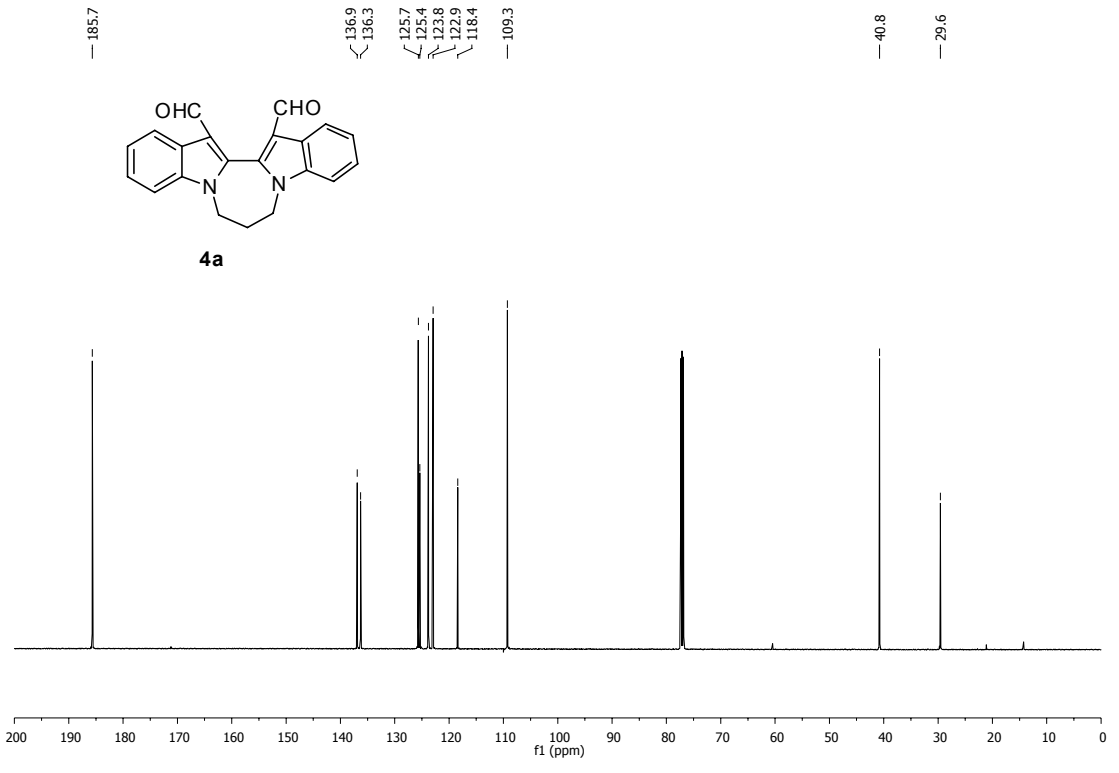
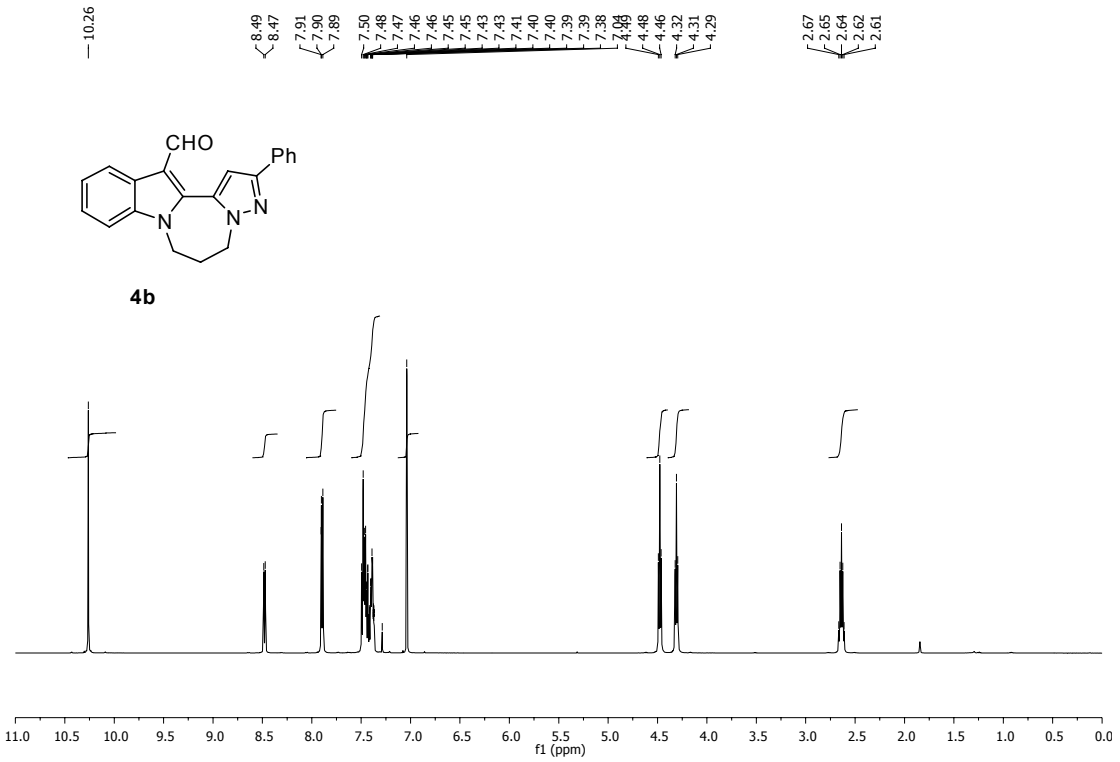
8.52
7.54
7.52
7.51
7.50
7.49
7.49
7.48
7.47
7.42
7.42
7.41
7.39
7.39
4.73
4.72
4.71
4.70
4.69
4.68
3.98
3.98
3.97
3.97
3.95
3.94
2.64
2.63
2.63
2.62
2.62
2.61
2.61
2.60
OHC
CHO
N
N
4a
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


185.7
136.9
136.3
125.7
125.4
123.8
122.9
118.4
109.3
40.8
29.6
OHC
CHO
N
N
4a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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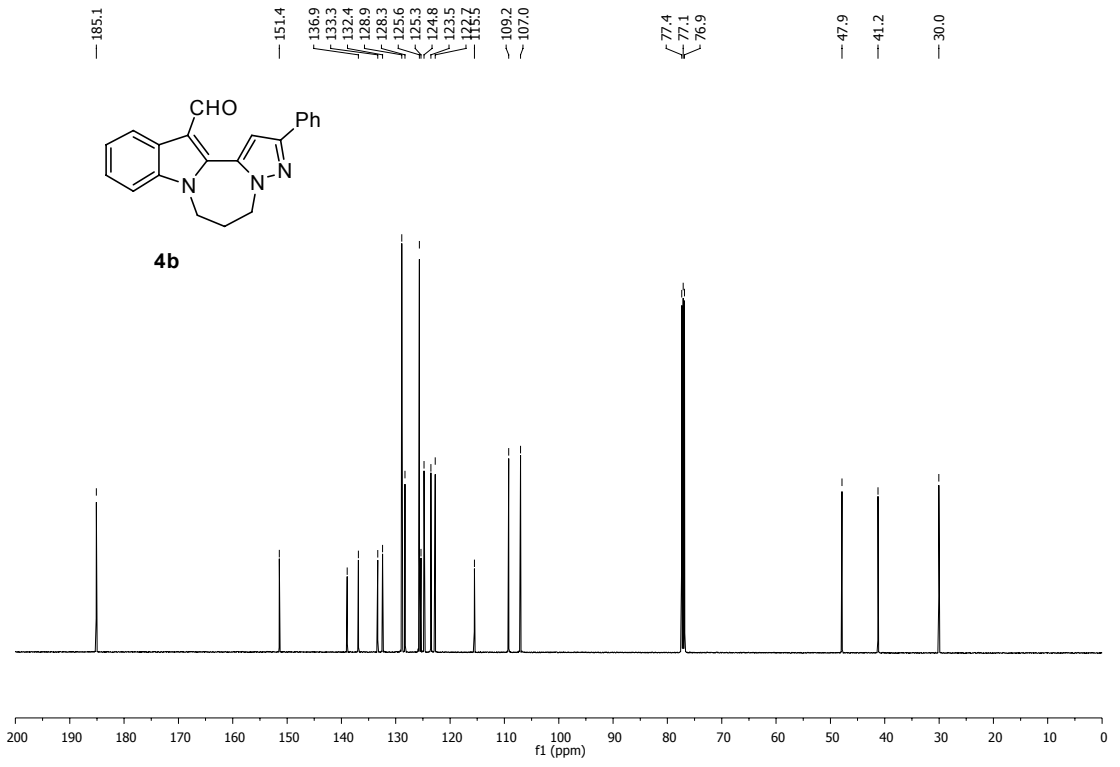
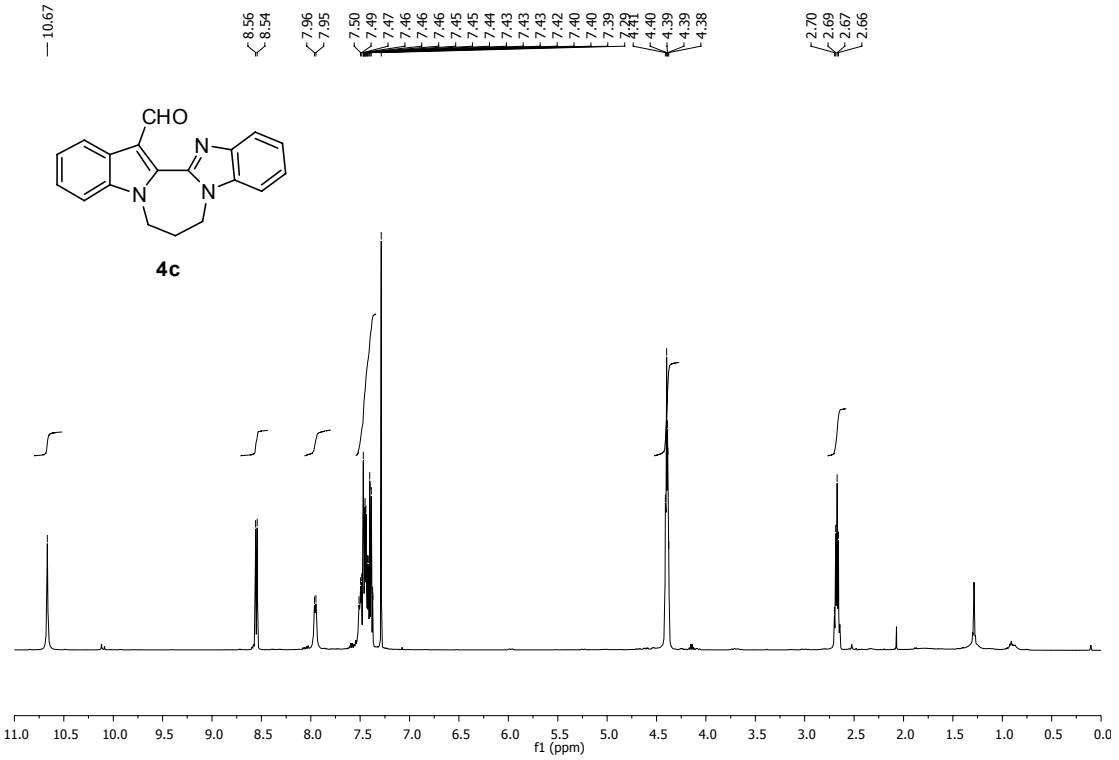
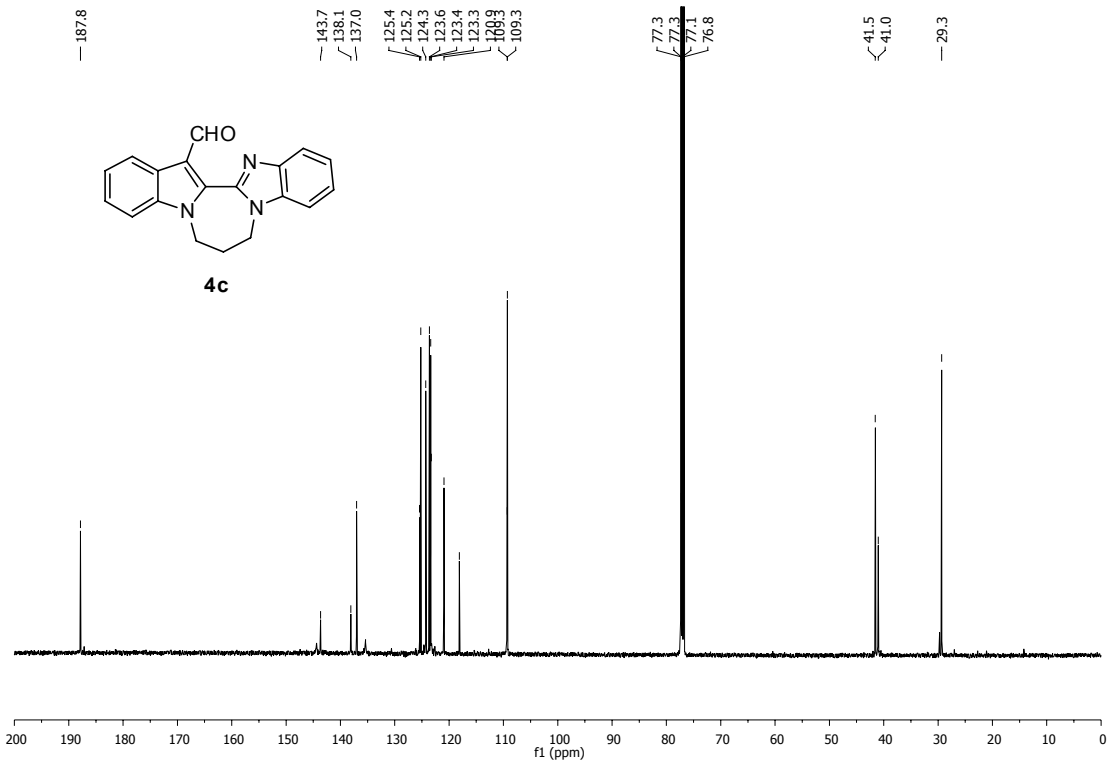
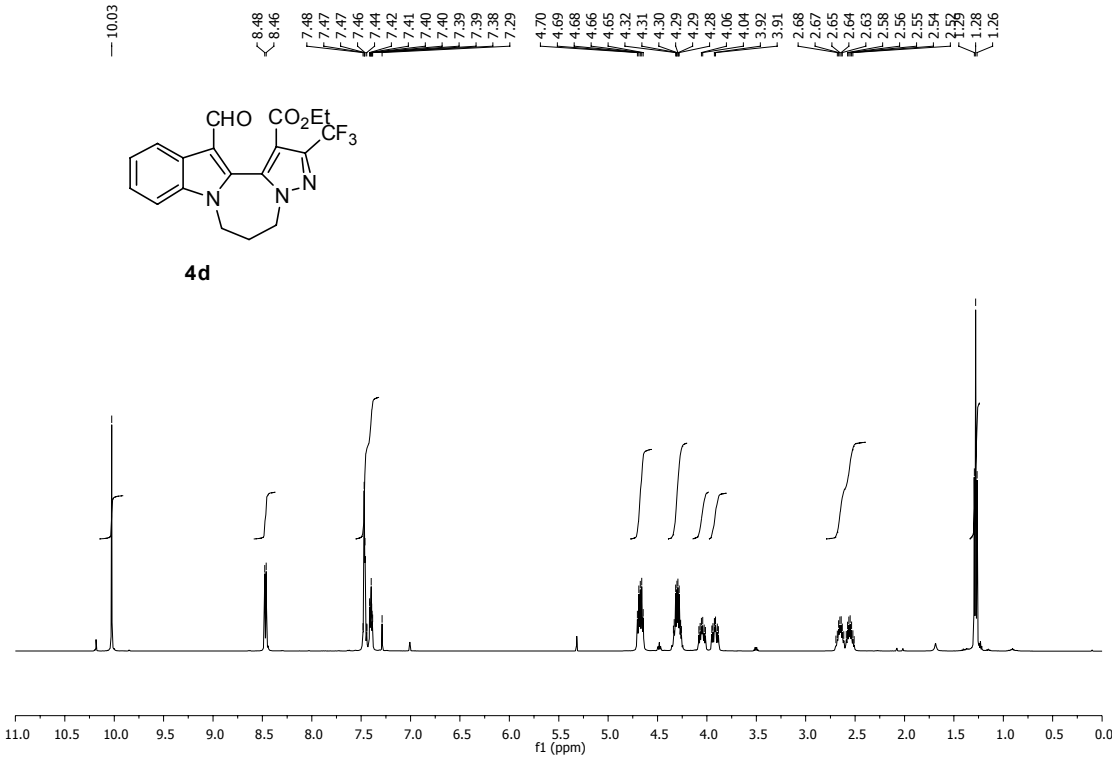
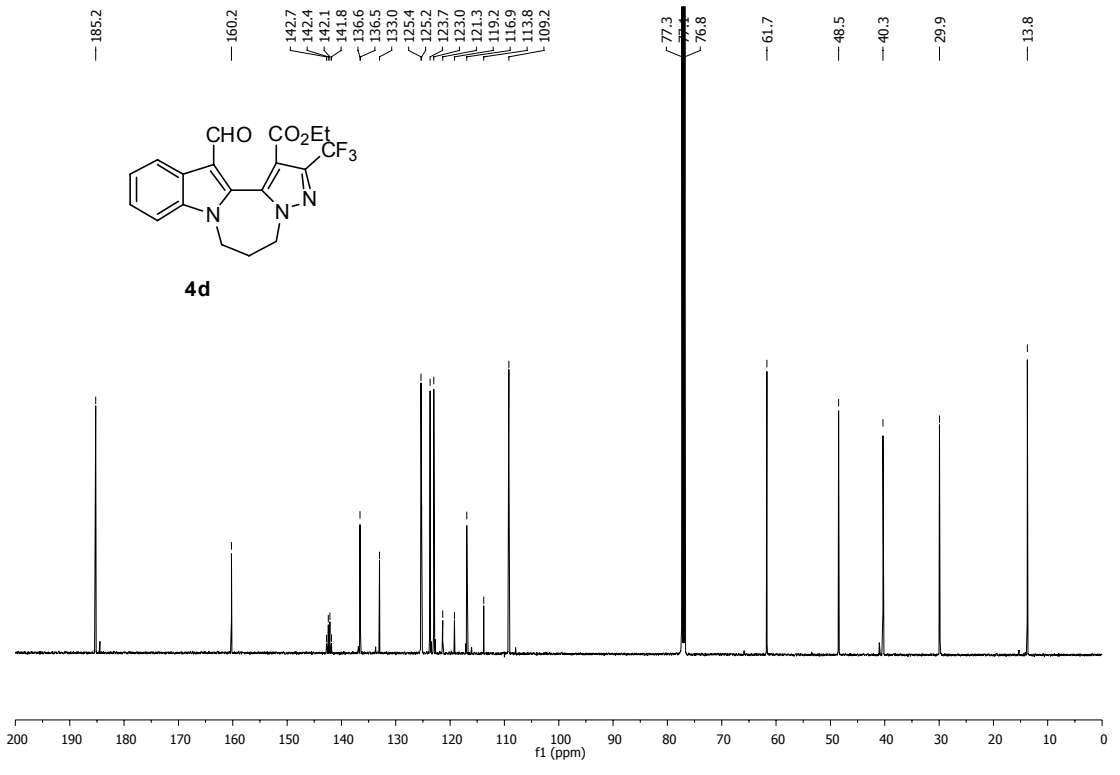
7.89
7.50
7.48
7.47
7.46
7.46
7.45
7.45
7.43
7.41
7.40
7.40
7.39
7.39
7.38
7.04
4.49
4.48
4.46
4.32
4.31
4.29
2.67
2.65
2.64
2.62
2.61
CHO
Ph
N
N
N
4b
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

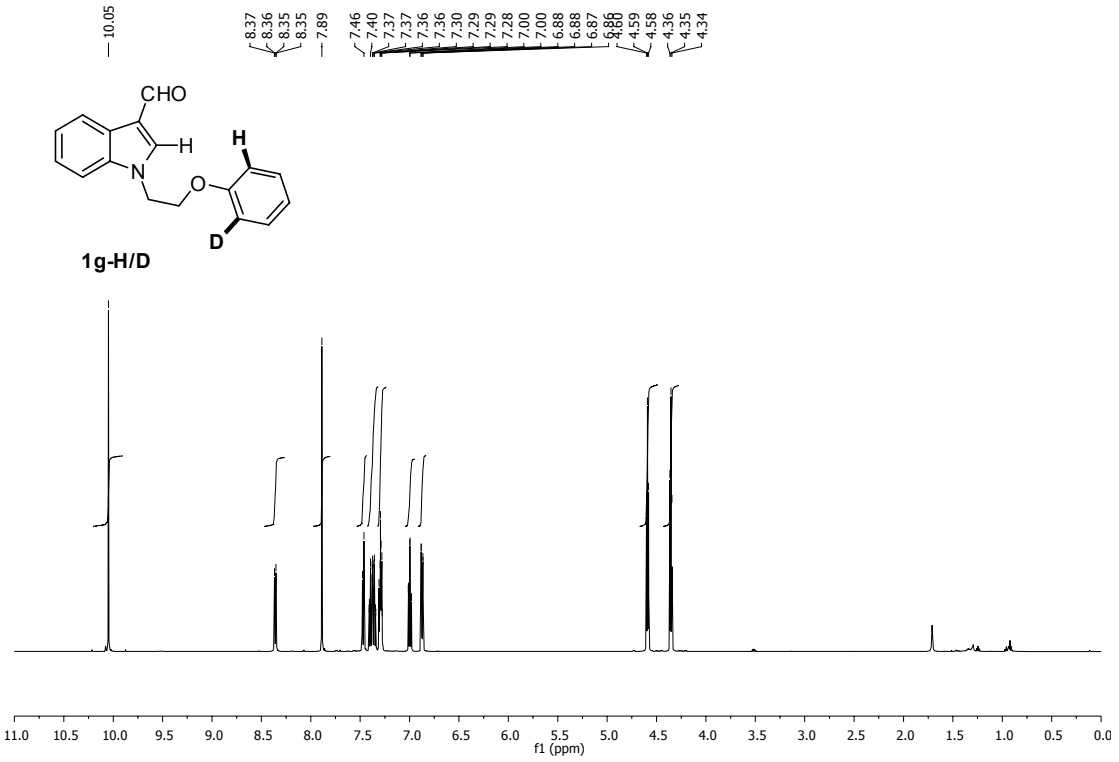

185.1
151.4
136.9
133.3
132.4
128.9
128.3
125.6
125.3
124.8
123.5
122.7
115.5
109.2
107.0
77.4
77.1
76.9
47.9
41.2
30.0
CHO
Ph
N
N
N
4b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

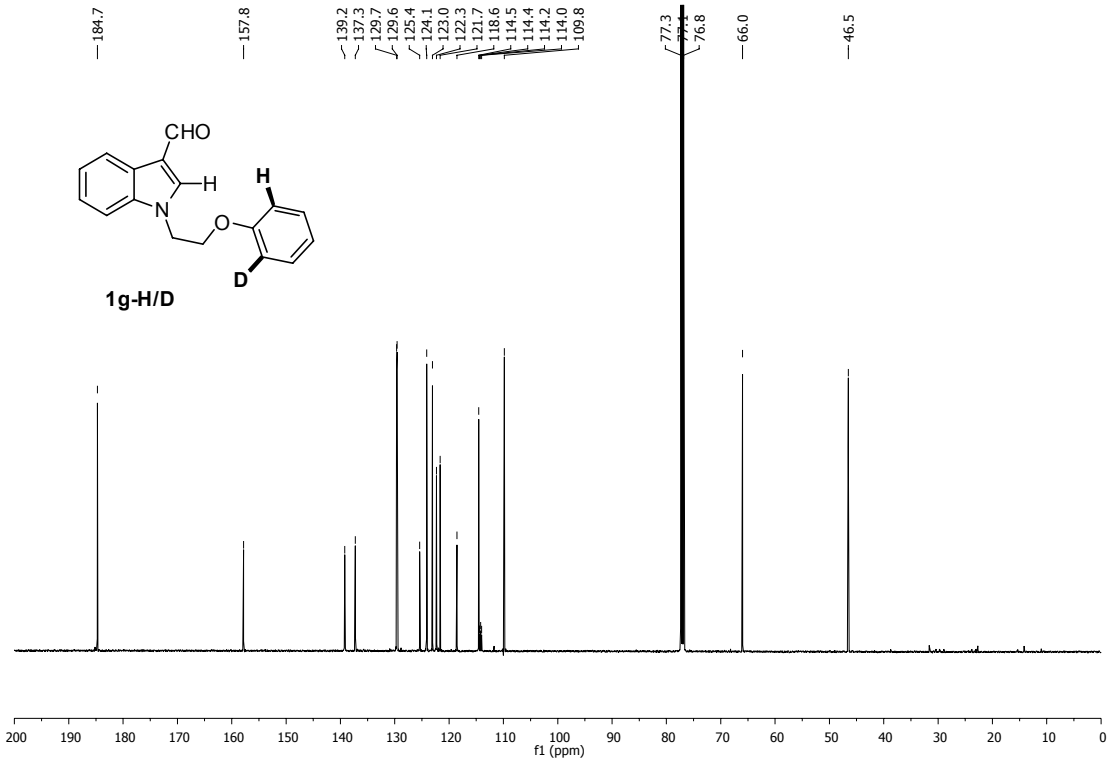

10.67
8.56
8.54
7.96
7.95
7.50
7.49
7.47
7.46
7.46
7.46
7.45
7.45
7.44
7.43
7.43
7.43
7.42
7.40
7.40
7.39
4.41
4.40
4.39
4.39
4.38
2.70
2.69
2.67
2.66
CHO
N
N
N
4c
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


187.8
143.7
138.1
137.0
125.4
125.2
124.3
123.6
123.4
123.3
109.3
109.3
77.3
77.3
77.1
76.8
41.5
41.0
29.3
CHO
N
N
N
4c
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

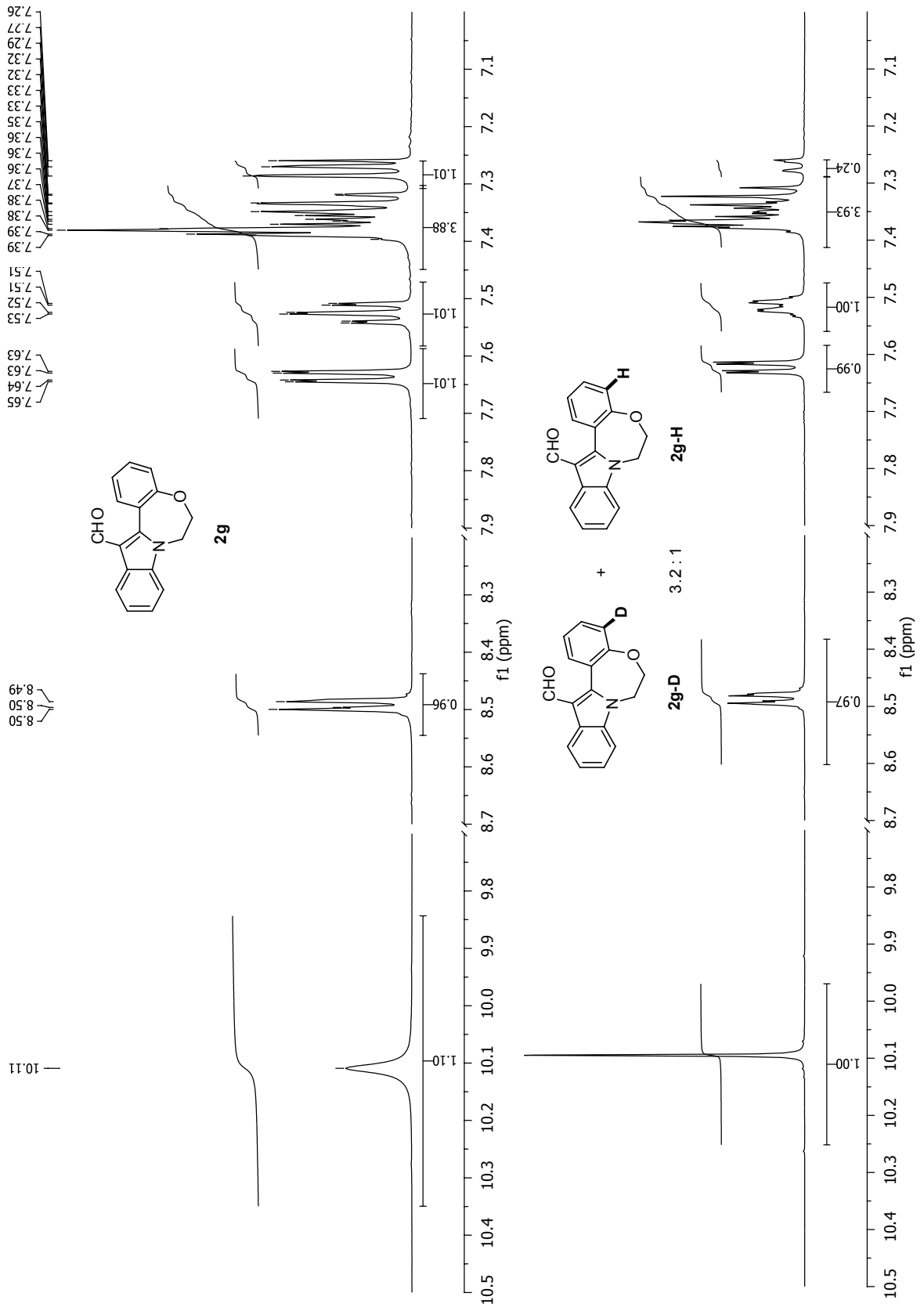

10.03
8.48
8.46
7.48
7.47
7.47
7.46
7.44
7.42
7.41
7.40
7.40
7.39
7.39
7.38
7.29
4.70
4.69
4.68
4.66
4.65
4.32
4.31
4.30
4.29
4.29
4.28
4.06
4.04
3.92
3.91
2.68
2.67
2.65
2.64
2.63
2.58
2.56
2.55
2.54
1.29
1.28
1.26
CHO
CO2Et
CF3
N
N-N
4d
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

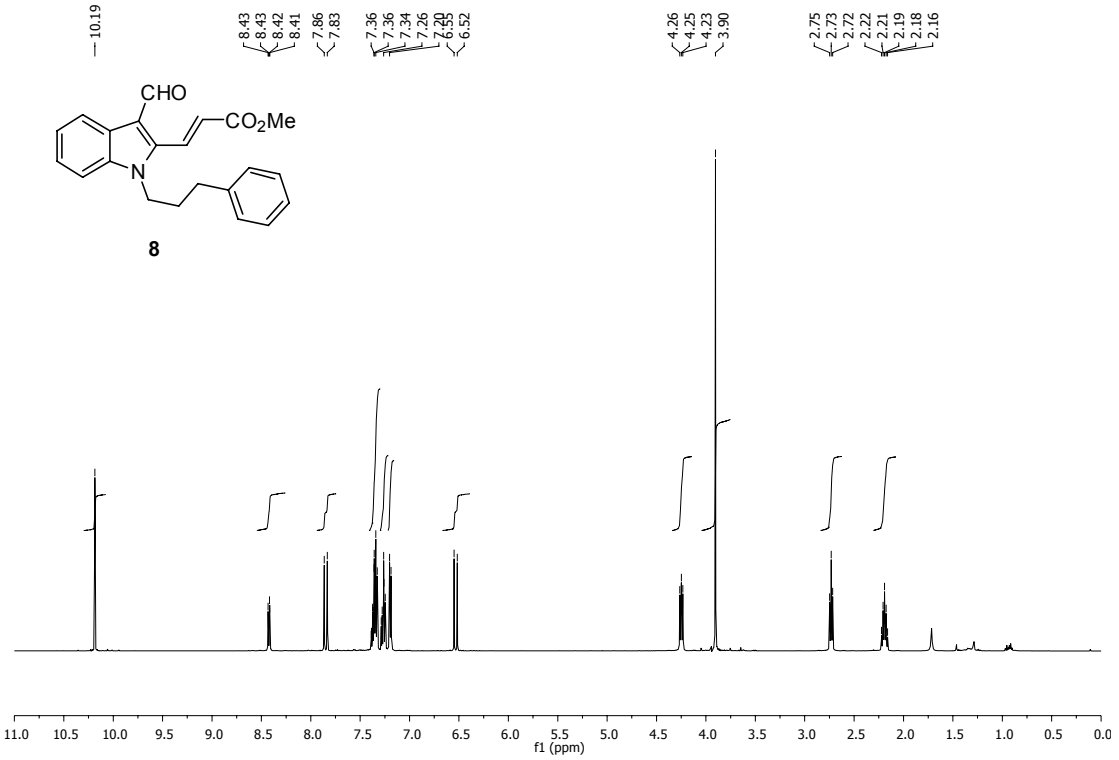

185.2
160.2
142.7
142.4
142.1
141.8
136.6
136.5
133.0
125.4
125.2
123.7
123.0
121.3
119.2
116.9
113.8
109.2
77.3
76.8
61.7
48.5
40.3
29.9
13.8
CHO
CO2Et
CF3
N
N-N
4d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

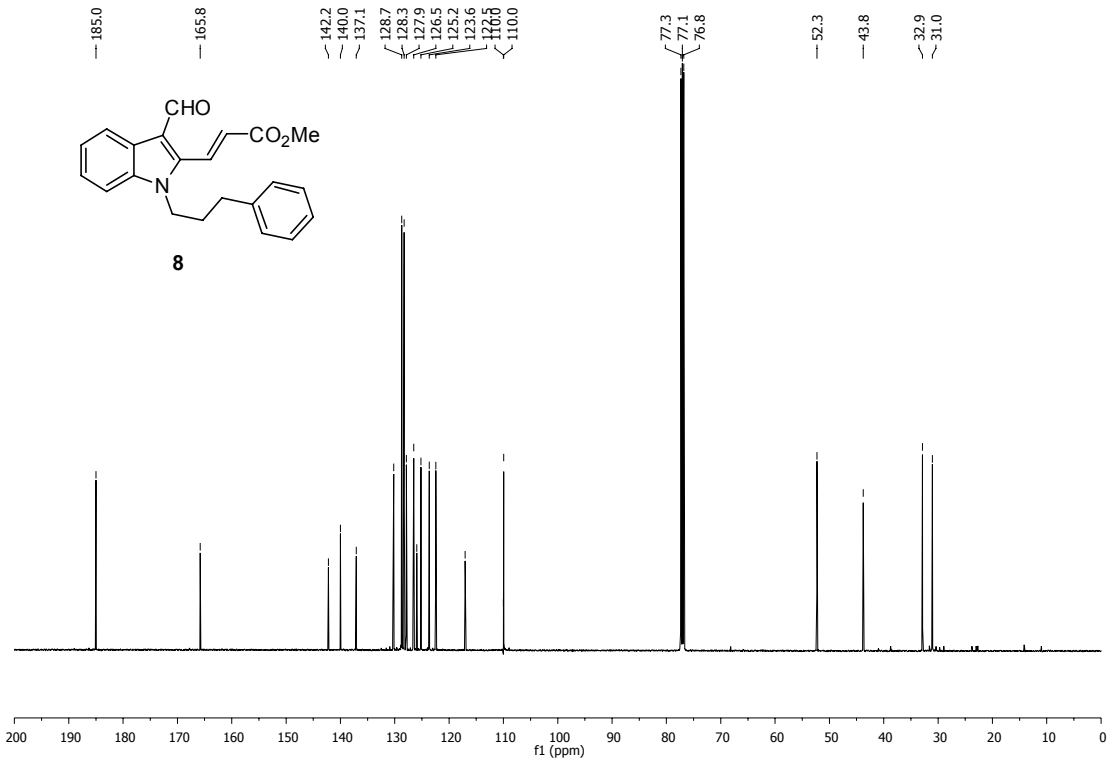

10.05
8.37
8.36
8.35
8.35
7.89
7.46
7.40
7.37
7.37
7.36
7.36
7.30
7.29
7.29
7.28
7.00
7.00
6.88
6.88
6.87
6.86
4.60
4.59
4.58
4.36
4.35
4.34
CHO
H
H
N
O
D
1g-H/D
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


184.7
157.8
139.2
137.3
129.7
129.6
125.4
124.1
123.0
122.3
121.7
118.6
114.5
114.4
114.2
114.0
109.8
77.3
76.8
66.0
46.5
CHO
H
H
N
O
D
1g-H/D
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

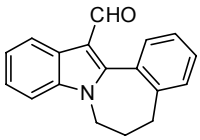
Intramolecular KIE



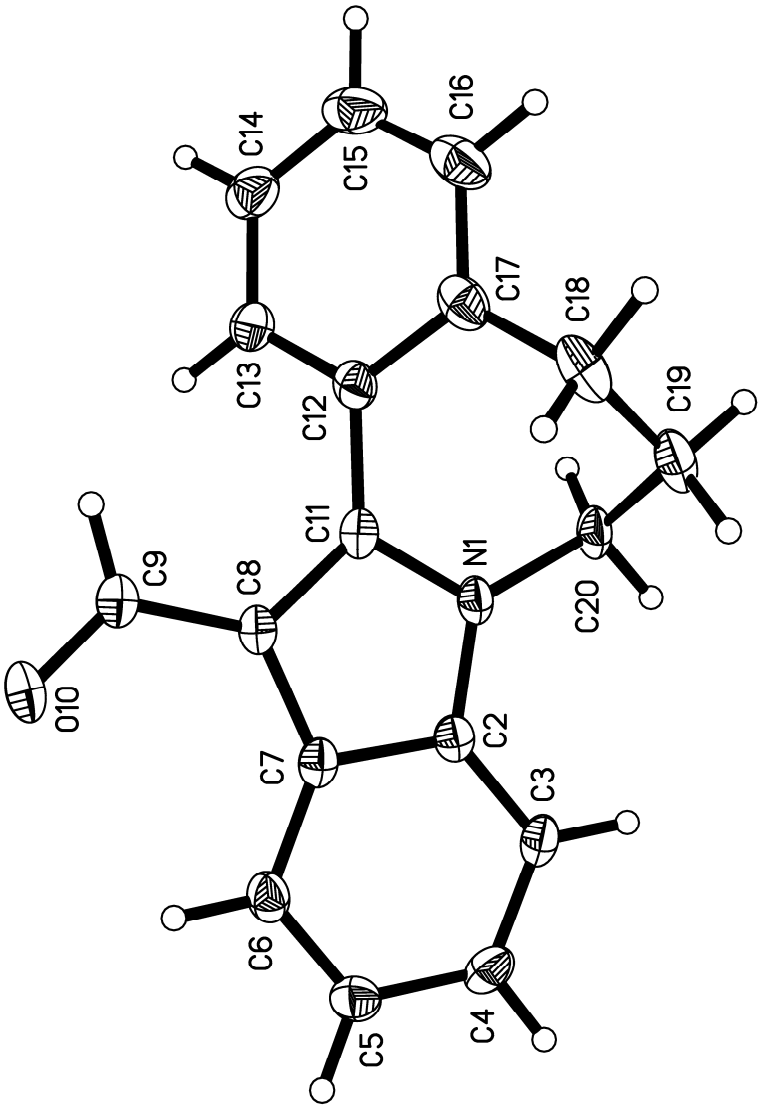

10.19
8.43
8.43
8.42
8.41
7.86
7.83
7.36
7.36
7.34
7.26
6.55
6.52
4.26
4.25
4.23
3.90
2.75
2.73
2.72
2.22
2.21
2.19
2.18
2.16
CHO
CO2Me
N
8
f1 (ppm)

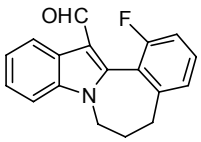

185.0
165.8
142.2
140.0
137.1
128.7
128.3
127.9
126.5
125.2
123.6
110.0
77.3
77.1
76.8
52.3
43.8
32.9
31.0
CHO
CO2Me
N
8
f1 (ppm)

IV: X-Ray Structures

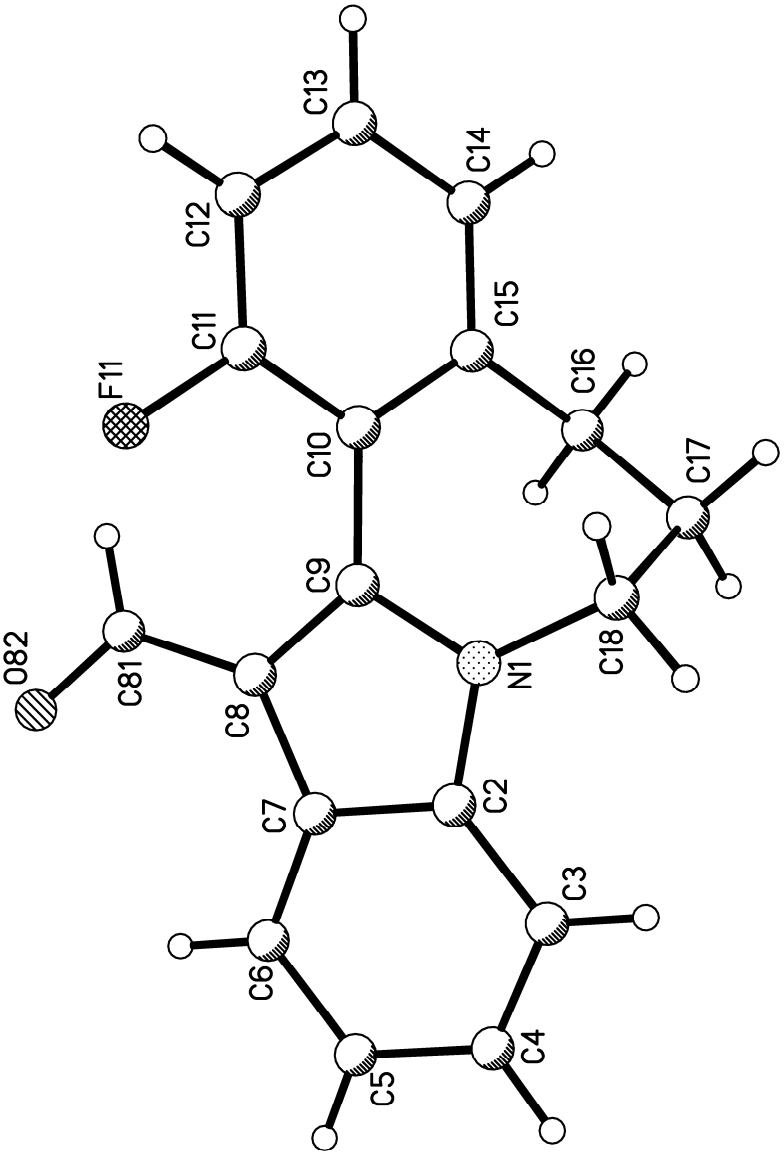


2a




OHC
F
N

2d


C13
C14
C12
C15
C11
F11
C16
C10
C17
C9
O82
C81
C8
N1
C18
C7
C2
C3
C6
C4
C5