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Activator Free Diastereoselective 1,3-dipolar Cycloaddition: A Quick Access to Coumarin based Spiro Multi Heterocyclic Adducts.

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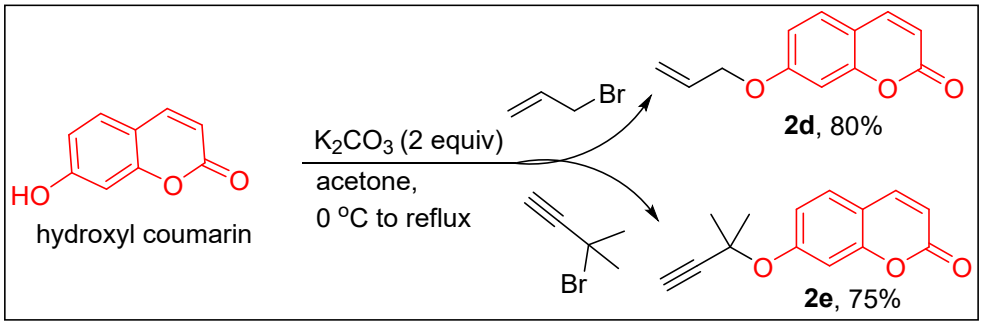
I. General Information

All reagents and solvents were purchased from commercial sources and used without purification. NMR spectra were recorded with a 300, 400 or 500 MHz spectrometer for ^{1}H NMR, 100 or 125 MHz for ^{13}C NMR spectroscopy. Chemical shifts are reported relative to the residual signals of tetramethylsilane in $CDCl_3$ or deuterated solvent $CDCl_3$ and DMSO-d_6 for ^{1}H and ^{13}C NMR spectroscopy. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of triplets (dt), triplet (t), quartet (q), multiplet (m). HRMS were recorded by using TOF, QTof, Orbitrap mass spectrometer. All reactions were monitored by using TLC. Characterizations of new compounds were further established by using HRMS.

II. Preparation of Starting materials

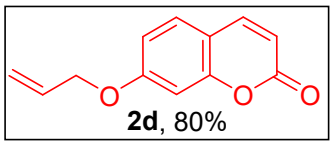
Starting materials indenoquinoxaline (**1**)[1] were prepared using reported condition

Synthesis of coumarin derivatives 2d and 2e:



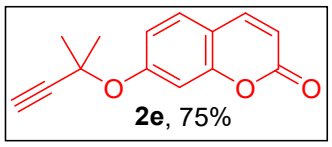
An oven dried 25 mL round bottom flask was added with a mixture of hydroxyl coumarin (500 mg, 3.06 mmol, 1 equiv) in acetone (10 mL), K_2CO_3 (847 mg, 6.13 mmol, 2 equiv), and allyl bromide (492 mg, 3.67 mmol, 1.2 equiv) or 3-bromo-3-methylbut-1-yne (536 mg, 3.67 mmol, 1.2 equiv) at 0 °C under a N_2 atmosphere, and the reaction mixture was stirred at RT then 60 °C until complete conversion of starting material. Then the solvent was removed under reduced pressure and the crude mixture was diluted with water and extracted with EtOAc (2×20 mL). Combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the resulted mixture was washed with pentane (3x 20 mL) to get **2d** (502 mg, 80%, pale yellow solid) **2e** (530 mg, 75%, off white solid).

7-(allyloxy)-2H-chromen-2-one (2d)[2a]: mp: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 9.5 Hz, 1H), 7.37 (d, *J* = 8.6 Hz, 1H), 6.87 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.83 (d, *J* = 2.4 Hz, 1H), 6.26 (d, *J* = 9.5 Hz, 1H), 6.05 (ddt, *J* = 17.3, 10.6, 5.3 Hz, 1H), 5.45 (dd, *J* = 17.3, 1.5 Hz, 1H), 5.35 (dd, *J* = 10.5, 1.3 Hz, 1H), 4.61 (dt, *J* = 5.3, 1.5 Hz, 2H).



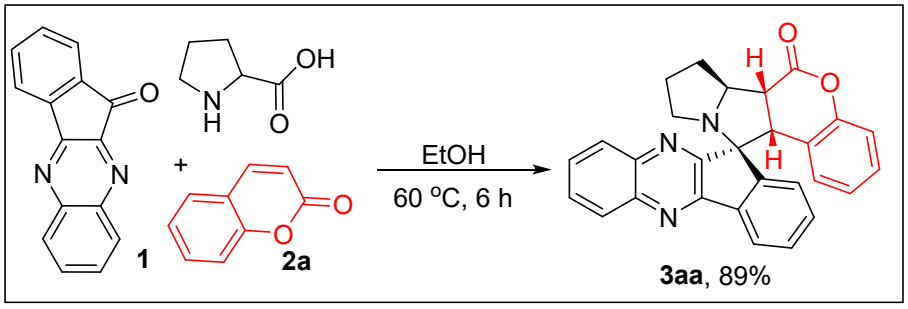
2d, 80%

7-((2-methylbut-3-yn-2-yl)oxy)-2H-chromen-2-one (2e)[2b]: mp: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 9.5 Hz, 1H), 7.37 (d, *J* = 8.6 Hz, 1H), 7.32 (d, *J* = 2.1 Hz, 1H), 7.05 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.28 (d, *J* = 9.5 Hz, 1H), 2.67 (s, 1H), 1.72 (s, 6H).



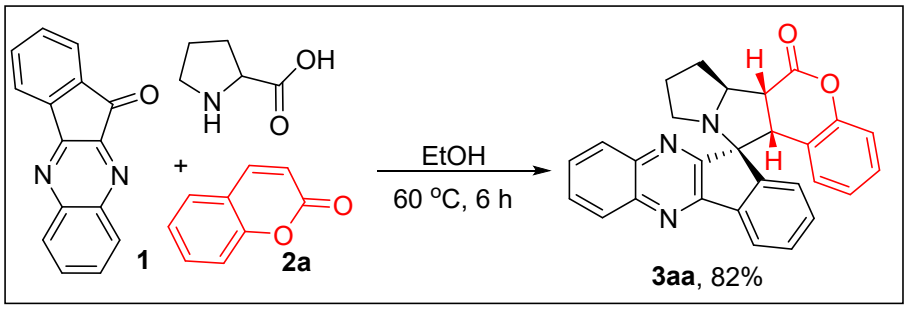
2e, 75%

III. General Procedure for the synthesis of 3, 5 and 7 taking synthesis of 3aa as an example:



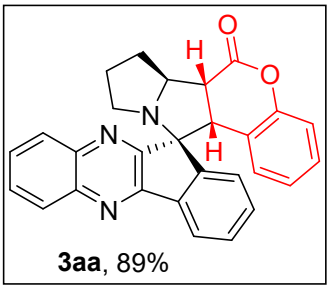
An oven dried 25 mL round bottom flask was charged with a mixture of indenoquinoxaline (**1a**) (116 mg, 0.5 mmol), coumarin (**2a**) (110 mg, 0.75 mmol) and proline (70 mg, 0.6 mmol) in ethanol (3 mL) was stirred at 60 °C (oil bath temperature) for 6 h. After completion of the reaction (monitored by TLC), the flask was cooled down to room temperature and the obtained solid material was filtered through buchner funnel and washed with pentane dried under vacuum to afford the desired product **3aa** as pale yellow solid 89% yield.

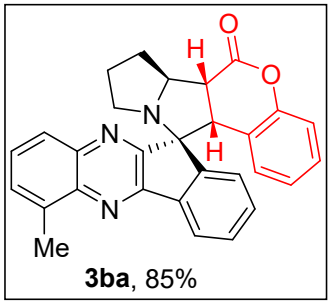
Procedure for the synthesis of 3aa in 1 gram scale:



An oven dried 100 mL round bottom flask was charged with a mixture of indenoquinoxaline (**1a**) (1 gm 4.31 mmol), coumarin (**2a**) (944 mg, 6.46 mmol) and proline (595 mg, 5.17 mmol) in ethanol (25 mL) was stirred at 60 °C (oil bath temperature) for 6 h. After completion of the reaction (monitored by TLC), the flask was cooled down to room temperature and the obtained solid material was filtered through buchner funnel and washed with cold ethanol (5 mL) and pentane dried under vacuum to afford the desired product **3aa** as pale yellow solid 82% (1.53) yield.

6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,11'-indeno[1,2-b]quinoxalin]-6-one (3aa): 3aa (192 mg) mp: 237-240 °C; R_f = 0.4 (hexanes:EtOAc = 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 7.0 Hz, 1H), 8.04 (s, 1H), 8.00 (d, *J* = 7.3 Hz, 1H), 7.93 (d, *J* = 3.9 Hz, 1H), 7.68 (dd, *J* = 13.1, 7.5 Hz, 2H), 7.63 (d, *J* = 4.0 Hz, 2H), 6.83 (t, *J* = 7.3 Hz, 1H), 6.65 (d, *J* = 7.8 Hz, 1H), 6.50 (t, *J* = 7.1 Hz, 1H), 6.22 (d, *J* = 7.2 Hz, 1H), 5.09 (s, 1H), 4.36 (d, *J* = 11.2 Hz, 1H), 3.41 – 3.27 (m, 2H), 2.98 (s, 1H), 2.75 (d, *J* = 8.5 Hz, 1H), 2.10 – 1.88 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 161.3, 152.3, 150.6, 143.9, 142.2, 140.7, 139.6, 131.3, 130.4, 129.6, 129.0, 128.6, 126.7, 126.5, 123.5, 122.9, 116.9, 116.8, 77.6, 68.6, 51.7, 49.5, 44.0, 34.1, 26.9; IR (KBr): δ 3070, 2928, 2864, 1726, 1674, 1456, 1252, 752 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{22}N_3O_2$ $[M+H]^+$ 432.1712 found 432.1718.

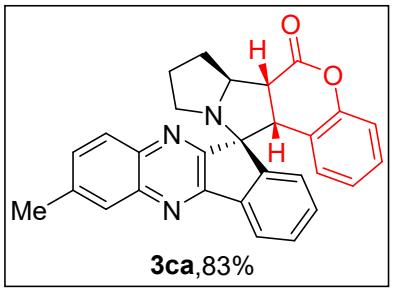




6'-methyl-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,11'-indeno[1,2-b]quinoxalin]-6-one (3ba): 3ba

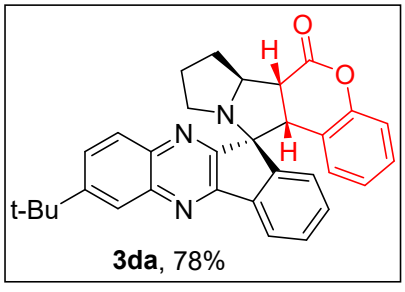
(190 mg) following general procedure **1b** (123 mg, 0.5 mmol); white solid; yield: 85%; mp: 257-260 °C; R_f = 0.42 (hexanes:EtOAc = 7:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, *J* = 7.2 Hz, 1H), 7.98 (d, *J* = 7.4 Hz, 1H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.71 – 7.62 (m, 2H), 7.48 (dt, *J* = 14.3, 7.1 Hz, 2H), 6.86 – 6.81 (m, 1H), 6.67 (d, *J* = 7.5 Hz, 1H), 6.51 (dd, *J* = 10.8, 4.2 Hz, 1H), 6.25 (d, *J* = 7.7 Hz, 1H), 5.10 – 5.05 (m, 1H), 4.36 (d, *J* = 11.3 Hz, 1H), 3.36 (dd, *J* = 11.3, 3.8 Hz, 1H), 3.31 (d, *J* = 2.6 Hz, 1H), 3.00 – 2.95 (m, 1H), 2.75 (d, *J* = 4.4 Hz, 1H), 2.72 (s, 3H), 2.10 – 2.03 (m, 1H), 2.03 – 1.86 (m, 2H);^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 160.7, 151.0, 150.7, 143.9, 141.4, 140.8, 140.1, 137.1, 130.9, 130.1, 129.7, 128.6, 128.5, 127.6, 126.8, 126.43, 123.4, 122.8, 117.2, 116.8, 76.9, 68.4, 51.7, 49.6, 43.8, 34.0, 26.9, 17.2; IR (KBr): δ 3064, 2925, 2859, 1753, 1457, 1256, 780 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{24}N_3O_2$ $[M+H]^+$ 446.1869 found 446.1878.

7'-methyl-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,11'-indeno[1,2-b]quinoxalin]-6-one (3ca): 3ca (184 mg) following general procedure **1c** (123 mg, 0.5 mmol); white solid; yield: 83%; mp: 207-210 °C; R_f = 0.42 (hexanes:EtOAc = 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 – 8.10 (m, 1H), 7.95 (dd, *J* = 25.3, 7.8 Hz, 1H), 7.81 (d, *J* = 8.3 Hz,1H), 7.73 – 7.61 (m, 3H), 7.45 (ddd, *J* = 8.5, 3.6, 2.0 Hz, 1H), 6.82 (ddd, *J* = 7.0, 4.9, 1.5 Hz, 1H), 6.70 – 6.61 (m, 1H), 6.50 (tdd, *J* = 7.5, 4.1, 1.2 Hz, 1H), 6.21 (t, *J* = 7.7 Hz, 1H), 5.09 (dd, *J* = 8.7, 5.2 Hz, 1H), 4.35 (dd, *J* = 11.3, 3.1 Hz, 1H), 3.49 (s, 1H), 3.41 – 3.26 (m, 2H), 2.99 (dd, *J* = 13.2, 5.4 Hz, 1H), 2.76 (dt, *J* = 11.4, 7.6 Hz, 1H), 2.52 (d, *J* = 9.1 Hz, 3H), 2.12 – 1.85 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.0, 161.3, 150.6, 143.9, 142.2, 140.7, 140.4, 139.6, 131.2, 130.3, 129.6, 129.1, 128.6, 126.8, 126.5, 123.5, 122.9, 116.8, 77.6, 68.6, 51.7, 49.5, 44.0, 34.1, 26.9; IR (KBr): δ 3064, 2925, 2859, 1753, 1457, 856 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{24}N_3O_2$ $[M+H]^+$ 446.1869 found 446.1872.



3ca,83%

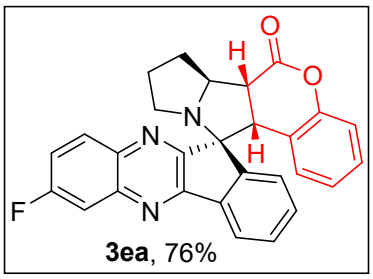
7'-(tert-butyl)-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,11'-indeno[1,2-b]quinoxalin]-6-one (3da): 3da (168 mg) following general procedure **1d** (144 mg, 0.5 mmol); white solid; yield: 78%; mp: 219-221 °C; R_f = 0.44 (hexanes:EtOAc = 7:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (dd, *J* = 9.6, 2.9 Hz,



3da, 78%

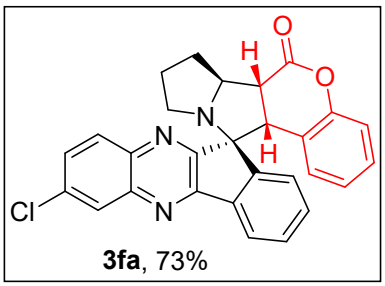
1H), 7.98 (dd, *J* = 10.9, 3.5 Hz, 1H), 7.93 (d, *J* = 2.1 Hz, 1H), 7.86 (d, *J* = 8.8 Hz, 1H), 7.73 – 7.61 (m, 3H), 6.86 – 6.81 (m, 1H), 6.68 (dd, *J* = 7.3, 4.9 Hz, 1H), 6.54 – 6.47 (m, 1H), 6.23 (d, *J* = 7.7 Hz, 1H), 5.13 – 5.03 (m, 1H), 4.36 (d, *J* = 11.4 Hz, 1H), 3.37 (ddd, *J* = 12.6, 8.9, 3.8 Hz, 1H), 3.30 (ddd, *J* = 10.9, 8.4, 5.1 Hz, 1H), 3.00 – 2.92 (m, 1H), 2.74 (dt, *J* = 12.4, 7.8 Hz, 1H), 2.06 (dt, *J* = 8.5, 5.1 Hz, 1H), 2.03 – 1.96 (m, 1H), 1.91 (ddd, *J* = 13.8, 10.5, 7.1 Hz, 1H), 1.42 (s, 7H), 1.39 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 152.6, 151.6, 150.8, 140.8, 140.5, 139.7, 130.9, 130.3, 128.8, 128.7, 128.5, 127.9, 126.8, 126.4, 124.9, 124.1, 123.7, 122.7, 116.8, 77.3, 68.5, 51.7, 44.0, 35.1, 33.0, 31.2, 31.0, 26.8; IR (KBr): δ 3689, 3019, 2402, 1527, 1214,740 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{32}H_{30}N_3O_2$ $[M+H]^+$ 488.2338 found 488.2332.

7'-fluoro-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,11'-indeno[1,2-b]quinoxalin]-6-one (3ea): 3ea (188 mg) following general procedure **1e** (125 mg, 0.5 mmol); white solid; yield: 76%; mp: 194-196 °C; R_f = 0.48 (hexanes:EtOAc = 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.1 Hz, 1H), 8.06 – 7.94 (m, 2H), 7.80 – 7.62 (m, 2H), 7.56 (dd, *J* = 9.4, 2.7 Hz, 1H), 7.39 (td, *J* = 9.0, 2.8 Hz, 1H), 6.85 (t, *J* = 7.2 Hz, 1H), 6.66 (d, *J* = 8.3 Hz, 1H), 6.51 (t, *J* = 7.1 Hz, 1H), 6.20 (d, *J* = 6.9 Hz, 1H), 5.07 (s, 1H), 4.36 (d, *J* = 11.2 Hz, 1H), 3.50 – 3.27 (m, 2H), 3.00 (s, 1H), 2.82 – 2.68 (m, 1H), 2.13 – 2.03 (m, 1H), 2.02 – 1.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 161.5, 151.7 (d, *J* = 242.2 Hz), 139.2, 137.6, 132.9, 131.6, 131.3, 131.2, 130.49, 128.7, 126.7, 126.5, 124.8, 123.5, 123.1, 122.7 (d, *J* = 25.2 Hz), 118.9 (d, *J* = 5.7 Hz), 116.8, 112.7, 112.5, 77.5, 68.6, 51.7, 49.4, 44.1, 34.0, 26.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -109.03. IR (KBr): δ 3685, 3017, 2399, 1418, 740 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{21}FN_3O_2$ $[M+H]^+$ 450.1618 found 450.1612.



3ea, 76%

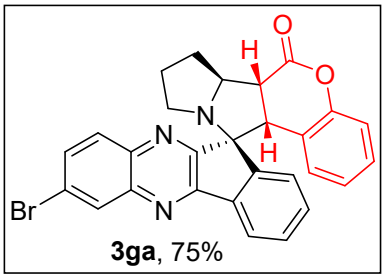
7'-chloro-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,11'-indeno[1,2-b]quinoxalin]-6-one (3fa): 3fa (171 mg) following general procedure **1f** (133 mg, 0.5 mmol); ash solid; yield: 73%; mp: 187-189 °C; R_f = 0.47 (hexanes:EtOAc = 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (d, *J* = 2.6 Hz, 1H), 8.47 – 8.40 (m,



3fa, 73%

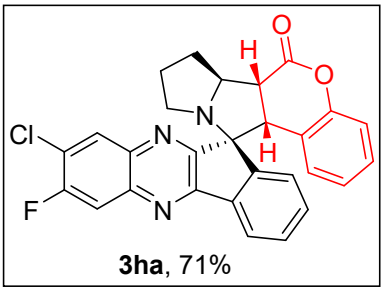
1H), 8.22 (d, J = 7.6 Hz, 1H), 8.07 – 7.95 (m, 2H), 7.87 (t, J = 7.4 Hz, 2H), 6.98 (t, J = 7.1 Hz, 1H), 6.79 (d, J = 7.7 Hz, 1H), 6.67 (t, J = 7.5 Hz, 1H), 6.24 (d, J = 6.9 Hz, 1H), 4.77 (s, 1H), 4.71 (d, J = 11.4 Hz, 1H), 3.79 (dd, J = 11.2, 3.6 Hz, 2H), 2.77 (t, J = 7.1 Hz, 1H), 2.55 – 2.48 (m, 1H), 2.11 (t, J = 19.1 Hz, 2H), 1.79 (s, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 163.8, 155.7, 154.7, 152.3, 150.4, 144.6, 138.6, 137.5, 136.4, 133.6, 132.4, 131.5, 130.7, 128.9, 126.7, 126.5, 125.1, 124.1, 123.7, 116.8, 77.5, 68.7, 51.6, 49.2, 44.3, 34.0, 26.9; IR (KBr): δ 3685, 3019, 2364, 1537, 1214, 740 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{21}ClN_3O_2$ $[M+H]^+$ 466.1308, found: 466.1316.

7'-bromo-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,11'-indeno[1,2-b]quinoxalin]-6-one (3ga): 3ga (192 mg) following general procedure **1g** (155 mg, 0.5 mmol); white solid; yield: 75%; mp: 220-223 °C; R_f = 0.47 (hexanes:EtOAc = 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (dd, J = 7.4, 6.6 Hz, 1H), 8.00 (d, J = 7.5 Hz, 1H), 7.90 (d, J = 8.8 Hz, 1H), 7.80 – 7.73 (m, 1H), 7.72 – 7.64 (m, 3H), 6.88 – 6.82 (m, 1H), 6.68 (ddd, J = 19.1, 8.2, 1.0 Hz, 3H), 6.51 (ddd, J = 7.5, 4.4, 1.2 Hz, 1H), 6.20 (dt, J = 7.8, 4.0 Hz, 1H), 5.08 – 5.00 (m, 1H), 4.35 (dd, J = 11.3, 5.6 Hz, 1H), 3.50 – 3.35 (m, 1H), 3.34 – 3.27 (m, 1H), 2.97 (dd, J = 13.9, 7.1 Hz, 1H), 2.80 – 2.70 (m, 1H), 2.11 – 1.88 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 153.0, 150.5, 144.1, 142.9, 139.1, 133.1, 132.4, 131.7, 131.5, 131.1, 130.7, 130.4, 129.9, 128.7, 126.7, 126.5, 123.5, 123.1, 116.9, 116.81, 77.6, 68.6, 51.7, 49.4, 44.1, 34.0, 26.9; IR (KBr): 2965, 1754, 151, 1494, 766 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{21}N_3O_2Br$ $[M+H]^+$ 510.0817 found 510.0826.



3ga, 75%

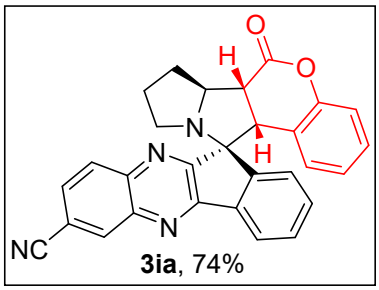
8'-chloro-7'-fluoro-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,11'-indeno[1,2-b]quinoxalin]-6-one (3ha): 3ha (172 mg) following general procedure **1h** (142 mg, 0.5 mmol); white solid; yield: 71%; mp: 226-229 °C; R_f = 0.45 (hexanes:EtOAc = 7:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 – 8.09 (m, 2H), 8.00 (d, J = 7.7 Hz, 1H), 7.80 – 7.69 (m, 1H), 7.66 (dd, J = 17.7, 8.6



3ha, 71%

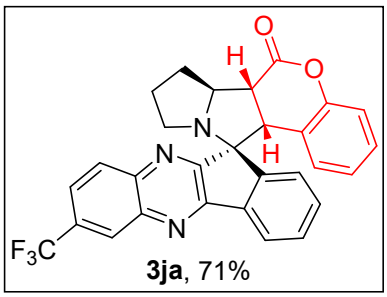
Hz, 2H), 6.87 (t, *J* = 7.5 Hz, 1H), 6.71 (t, *J* = 9.3 Hz, 1H), 6.52 (t, *J* = 7.5 Hz, 1H), 6.20 (d, *J* = 7.5 Hz, 1H), 5.02 (t, *J* = 8.9 Hz, 1H), 4.35 (d, *J* = 11.2 Hz, 1H), 3.38 (dd, *J* = 11.3, 3.6 Hz, 1H), 3.36 – 3.24 (m, 1H), 2.99 – 2.92 (m, 1H), 2.75 (dt, *J* = 15.3, 7.6 Hz, 1H), 2.12 – 2.04 (m, 1H), 2.03 – 1.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 161.7, 159.3, 151.7 (d, *J* = 265.9 Hz), 144.1, 141.6, 138.9, 137.4, 131.8, 130.4 (d, *J* = 8.8 Hz), 128.7, 126.7, 126.6, 126.0, 123.4 (d, *J* = 42.7 Hz), 121.8, 116.8, 116.7, 113.8, 113.5, 77.6, 68.6, 51.7, 49.3, 44.1, 34.0, 26.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.25.IR (KBr): δ 3686, 3018, 2404, 1629, 1214, 740 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{20}ClFN_3O_2$ $[M+H]^+$ 484.1228 found 484.1222

6-oxo-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,11'-indeno[1,2-b]quinoxaline]-7'-carbonitrile (3ia): 3ia (169 mg) following general procedure **1i** (118 mg, 0.5 mmol); white solid; yield: 74%; mp: 227-230 °C; R_f = 0.35 (hexanes:EtOAc = 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 1.7 Hz, 1H), 8.17 (d, *J* = 7.5 Hz, 1H), 8.01 (dd, *J* = 10.9, 8.2 Hz, 2H), 7.82 – 7.76 (m, 2H), 7.71 (t, *J* = 7.5 Hz, 1H), 6.96 – 6.78 (m, 1H), 6.70 (d, *J* = 7.5 Hz, 1H), 6.53 (td, *J* = 7.6, 1.1 Hz, 1H), 6.30 – 6.12 (m, 1H), 5.01 (ddd, *J* = 9.8, 6.3, 3.7 Hz, 1H), 4.36 (d, *J* = 11.3 Hz, 1H), 3.39 (dd, *J* = 11.3, 3.7 Hz, 1H), 3.31 (ddd, *J* = 10.6, 8.4, 5.0 Hz, 1H), 2.99 – 2.89 (m, 1H), 2.76 (dt, *J* = 15.4, 7.5 Hz, 1H), 2.08 (dd, *J* = 10.7, 6.2 Hz, 1H), 2.03 – 1.83 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 163.3, 154.8, 150.6, 144.5, 144.09, 139.8, 138.6, 135.0, 132.6, 130.9, 130.7, 130.2, 128.9, 126.8, 126.7, 123.7, 118.0, 117.0, 116.6, 112.3, 77.3, 68.6, 51.7, 49.3, 44.2, 34.1, 27.0; IR (KBr): δ 3210, 2977, 2942, 2232, 1588, 1218, 759 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{21}N_4O_2$ $[M+H]^+$ 457.1665, found: 457.1659.



3ia, 74%

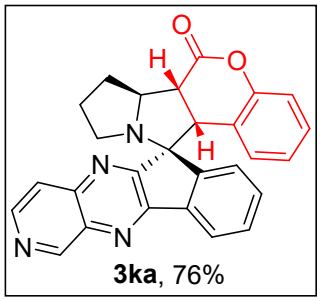
7'-(trifluoromethyl)-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,11'-indeno[1,2-b]quinoxalin]-6-one (3ja): 3ja (185 mg) following general procedure **1j** (158 mg, 0.5 mmol); white solid; yield: 71%; mp: 205-208 °C; R_f = 0.43 (hexanes:EtOAc = 5:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.18 (d, *J* = 7.6 Hz, 1H), 8.03 (t, *J* = 8.3 Hz, 2H), 7.85 – 7.74 (m, 2H), 7.70 (td, *J* = 7.5, 0.9 Hz, 1H), 6.91 – 6.81 (m, 1H), 6.74 – 6.65 (m, 1H), 6.52 (td, *J* = 7.5, 1.2 Hz, 1H), 6.22 (d, *J* = 7.7 Hz, 1H), 5.04 (ddd, *J* = 9.6, 6.0, 3.9 Hz, 1H), 4.38



3ja, 71%

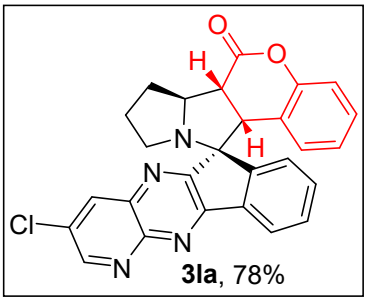
(d, J = 11.4 Hz, 1H), 3.41 (dd, J = 11.3, 3.8 Hz, 1H), 3.33 – 3.26 (m, 1H), 2.98 – 2.91 (m, 1H), 2.75 (dt, J = 12.1, 7.6 Hz, 1H), 2.17 (s, 1H), 2.10 – 1.98 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 162.8, 150.6, 144.4, 143.6, 139.7, 138.9, 132.1, 130.8, 130.6, 129.8, 128.8, 127.3, 126.7, 126.6, 125.5, 123.6, 123.4, 117.0, 116.7, 77.7, 68.7, 51.6, 49.6, 44.2, 34.0, 26.2; ^{19}F NMR (471 MHz, $CDCl_3$) δ -62.13. IR (KBr): δ 3686, 3019, 2399, 1534, 1214, 739 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{21}F_3N_3O_2$ $[M+H]^+$ 500.1586 found 500.1580.

6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,6'-indeno[1,2-b]pyrido[4,3-e]pyrazin]-6-one (3ka): 3ka (164 mg) following general procedure **1k** (116 mg, 0.5 mmol); white solid; yield: 76%; mp: 274-276 °C; R_f = 0.35 (hexanes:EtOAc = 5:5); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.61 (s, 1H), 8.89 (d, J = 5.7 Hz, 1H), 8.19 (d, J = 7.6 Hz, 2H), 7.99 (dd, J = 20.1, 6.6 Hz, 2H), 7.85 (s, 1H), 7.73 – 7.68 (m, 2H), 6.86 (t, J = 7.2 Hz, 1H), 6.70 (d, J = 8.1 Hz, 1H), 6.52 (t, J = 7.4 Hz, 1H), 6.20 (d, J = 7.4 Hz, 1H), 5.05 (t, J = 8.9 Hz, 1H), 4.38 (d, J = 11.3 Hz, 1H), 3.42 (dd, J = 11.3, 3.8 Hz, 1H), 3.31 (dd, J = 14.9, 9.3 Hz, 1H), 2.95 (t, J = 7.0 Hz, 1H), 2.76 (dd, J = 20.3, 7.8 Hz, 1H), 2.16 – 2.05 (m, 1H), 2.06 – 1.82 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.6, 160.1, 155.8, 153.9, 150.9, 150.0, 147.5, 146.2, 140.6, 137.2, 133.8, 132.7, 130.6, 128.8, 126.7, 125.1, 123.4, 122.1, 121.2, 117.0, 77.6, 68.8, 51.6, 49.3, 44.3, 34.0, 26.9; IR (KBr): δ 3687, 3019, 2401, 1523, 1410, 1214, 740 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{27}H_{21}N_4O_2$ $[M+H]^+$ 433.1665 found 433.1668.



3ka, 76%

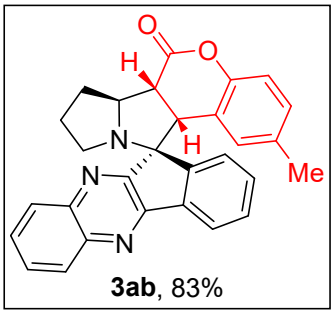
3'-chloro-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,6'-indeno[1,2-b]pyrido[3,2-e]pyrazin]-6-one (3la): 3la (182 mg) following general procedure **1l** (134 mg, 0.5 mmol); white solid; yield:78%; mp: 203-206 °C; R_f = 0.38 (hexanes:EtOAc = 5:5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 – 8.88 (m, 1H), 8.41 – 8.35 (m, 1H), 8.25 (dd, J = 5.6, 2.0 Hz, 1H), 8.00 (t, J = 8.3 Hz, 1H), 7.78 (ddd, J = 7.6, 4.5, 1.3 Hz, 1H), 7.70 (td, J = 7.5, 1.0 Hz, 1H), 6.91 – 6.84 (m, 1H), 6.77 – 6.66 (m, 1H), 6.57 – 6.50 (m, 1H), 6.20 (dd, J = 7.7, 1.3 Hz, 1H), 5.00



3la, 78%

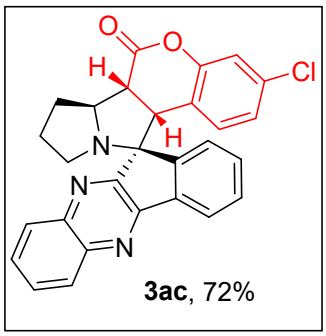
(ddd, J = 8.1, 6.3, 3.7 Hz, 1H), 4.40 – 4.28 (m, 1H), 3.43 – 3.36 (m, 1H), 3.34 – 3.26 (m, 1H), 2.96 (dd, J = 7.5, 6.3 Hz, 1H), 2.75 (dt, J = 15.4, 7.6 Hz, 1H), 2.08 (dt, J = 22.1, 8.2 Hz, 1H), 2.03 – 1.86 (m, 2H), 1.86 – 1.76 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.8, 163.8, 155.7, 152.3, 150.4, 149.6, 144.6, 138.6, 136.4, 135.5, 132.4, 131.5, 130.7, 128.9, 126.7, 126.5, 124.1, 123.8, 116.8, 116.4, 68.7, 51.6, 49.2, 44.3, 34.0, 26.9; IR (KBr): δ 3557, 2969, 2821, 1755, 1380, 1220, 765 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{27}H_{20}N_4O_2Cl$ $[M+H]^+$ 467.1275 found 467.1269.

2-methyl-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,11'-indeno[1,2-b]quinoxalin]-6-one (3ab): 3ab (184 mg) following general procedure **1a** (116 mg, 0.5 mmol); white solid; yield: 83%; mp: 260-263 °C; R_f = 0.40 (hexanes:EtOAc = 7:3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 7.2 Hz, 1H), 8.16 (d, J = 7.2 Hz, 1H), 8.04 (dd, J = 6.2, 3.4 Hz, 1H), 8.00 (d, J = 7.5 Hz, 1H), 7.93 (dd, J = 6.3, 3.3 Hz, 1H), 7.72 (t, J = 6.9 Hz, 1H), 7.67 (t, J = 5.3 Hz, 1H), 7.65 – 7.61 (m, 2H), 6.61 (d, J = 8.1 Hz, 1H), 6.52 (d, J = 6.5 Hz, 1H), 5.96 (s, 1H), 5.09 (dd, J = 10.6, 7.1 Hz, 1H), 4.30 (d, J = 11.3 Hz, 1H), 3.38 – 3.29 (m, 2H), 3.02 – 2.97 (m, 1H), 2.76 (dt, J = 14.9, 7.3 Hz, 1H), 2.11 – 2.05 (m, 1H), 1.95 (ddd, J = 16.9, 10.9, 4.8 Hz, 2H), 1.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 148.5, 144.1, 142.2, 140.7, 139.6, 132.9, 131.2, 130.3, 129.7, 129.2, 129.0, 128.6, 127.2, 126.6, 122.9, 116.4, 77.3, 68.7, 51.7, 50.0, 44.1, 34.1, 27.0, 20.4; IR (KBr): δ 3687, 3020, 2404, 1214, 740 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{24}N_3O_2$ $[M+H]^+$ 446.1864 found 446.1881.



3ab, 83%

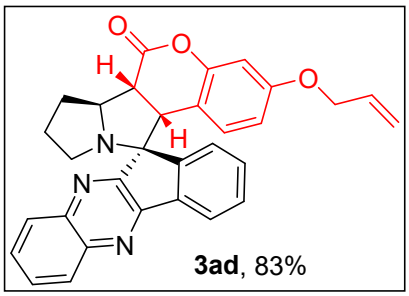
3-chloro-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,11'-indeno[1,2-b]quinoxalin]-6-one (3ac): 3ac (170 mg) following general procedure **1a** (116 mg, 0.5 mmol); white solid; yield: 72%; mp: 232-235 °C; R_f = 0.43 (hexanes:EtOAc = 7:3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (dd, J = 7.4, 0.8 Hz, 1H), 8.04 – 8.01 (m, 1H), 7.99 – 7.94 (m, 2H), 7.76 – 7.69 (m, 2H), 7.63 (dtd, J = 8.6, 6.9, 1.7 Hz, 2H), 6.79 (dd, J = 8.7, 2.5 Hz, 1H), 6.59 (d, J = 8.7 Hz, 1H), 6.16 (d, J = 2.4 Hz, 1H), 5.07 (ddd, J = 9.8, 6.1, 3.7 Hz, 1H), 4.29 (d, J = 11.3 Hz, 1H), 3.35 (dd, J = 11.3, 3.7 Hz, 1H), 3.29 (ddd, J = 10.8, 8.3, 5.1 Hz, 1H), 3.02 – 2.96 (m, 1H), 2.75 (dd, J = 14.0,



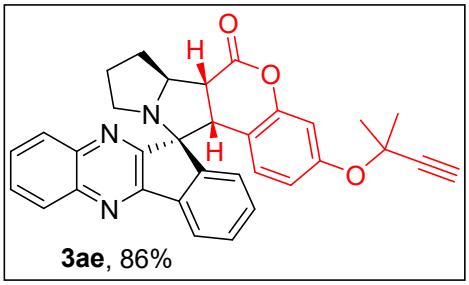
3ac, 72%

6.3 Hz, 1H), 2.11 – 2.04 (m, 1H), 2.04 – 1.95 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.4, 160.9, 152.2, 149.2, 143.3, 142.3, 140.6, 139.5, 131.4, 130.6, 129.8, 129.5, 129.1, 128.7, 128.6, 128.3, 126.5, 126.3, 123.1, 118.7, 118.1, 77.6, 68.6, 60.6, 51.7, 49.6, 43.9, 34.4, 26.8; IR (KBr): δ 3686, 3017, 2363, 1585, 1405, 714 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{21}ClN_3O_2$ $[M+H]^+$ 466.1311 found 466.1316.

3-(allyloxy)-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,11'-indeno[1,2-b]quinoxalin]-6-one (3ad): 3ad (203 mg) following general procedure **1a** (116 mg, 0.5 mmol); white solid; yield: 83%; mp: 207-209 °C; R_f = 0.38 (hexanes:EtOAc = 4:6); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 – 8.12 (m, 1H), 8.08 – 8.02 (m, 1H), 7.96 (ddd, *J* = 6.6, 6.2, 4.4 Hz, 2H), 7.73 – 7.65 (m, 2H), 7.64 – 7.57 (m, 2H), 6.20 (d, *J* = 1.8 Hz, 1H), 6.09 (d, *J* = 2.1 Hz, 2H), 5.85 – 5.74 (m, 1H), 5.19 (dq, *J* = 17.3, 1.5 Hz, 1H), 5.16 – 5.10 (m, 1H), 5.07 (ddd, *J* = 9.6, 6.1, 3.7 Hz, 1H), 4.30 (d, *J* = 11.3 Hz, 1H), 4.19 (dt, *J* = 5.4, 1.4 Hz, 2H), 3.37 – 3.26 (m, 2H), 3.01 – 2.93 (m, 1H), 2.75 (dt, *J* = 11.7, 7.2 Hz, 1H), 2.11 – 1.89 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 161.5, 155.5, 152.3, 150.7, 144.1, 142.2, 140.7, 139.6, 131.2, 130.3, 129.6, 129.5, 128.9, 128.7, 126.7, 126.5, 122.8, 116.5, 111.1, 109.2, 85.0, 76.7, 74.2, 72.6, 68.9, 51.8, 49.5, 44.0, 34.0, 29.4, 29.1, 26.9; IR (KBr): 3077, 2971, 1757, 1625, 1625, 1510, 780 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{31}H_{26}N_3O_3$ $[M+H]^+$ 488.1974 found 488.1977.

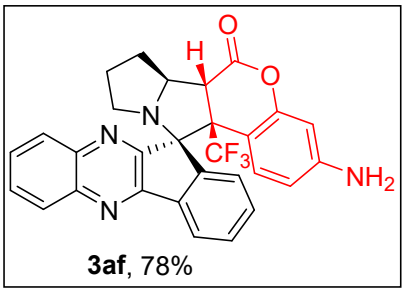


3-((2-methylbut-3-yn-2-yl)oxy)-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,11'-indeno[1,2-b]quinoxalin]-6-one (3ae): 3ae (221 mg) following general procedure **1a** (116 mg, 0.5 mmol); white solid; yield: 86%; mp: 237-240 °C; R_f = 0.40 (hexanes:EtOAc = 4:6); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 – 8.14 (m, 1H), 8.05 – 8.02 (m, 1H), 7.97 (d, *J* = 7.1 Hz, 1H), 7.94 – 7.91 (m, 1H), 7.73 – 7.64 (m, 2H), 7.62 (ddd, *J* = 5.6, 3.0, 1.3 Hz, 2H), 6.57 (d, *J* = 2.4 Hz, 1H), 6.30 (dd, *J* = 8.5, 2.4 Hz, 1H), 6.05 (d, *J* = 8.6 Hz, 1H), 5.08 (ddd, *J* = 9.6, 5.9, 3.8 Hz, 1H), 4.31 (d, *J* = 11.3 Hz, 1H), 3.37 (dd, *J* = 11.3, 3.8 Hz, 1H), 3.34 – 3.27



(m, 1H), 3.02 – 2.95 (m, 1H), 2.75 (dt, J = 11.6, 7.3 Hz, 1H), 2.22 (s, 1H), 2.11 – 1.87 (m, 3H), 1.38 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 161.2, 152.2, 148.5, 144.0, 142.6, 142.2, 140.7, 139.6, 132.8, 131.2, 130.3, 129.7, 129.2, 129.0, 128.6, 127.2, 126.6, 122.9, 116.4, 77.6, 77.3, 68.7, 51.7, 49.6, 44.1, 34.1, 26.0, 20.4; IR (KBr): δ 3302, 3020, 2358, 1747, 1215, 755 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{33}H_{28}N_3O_3$ $[M+H]^+$ 514.2131 found 514.2113.

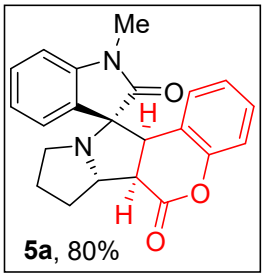
3-amino-11a-(trifluoromethyl)-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,11'-indeno[1,2-b]quinoxalin]-6-one (3af):



3af, 78%

3af (197 mg) following general procedure **1a** (116 mg, 0.5 mmol); white solid; yield: 78%; mp: 202-205°C; R_f = 0.35 (hexanes:EtOAc = 3:7); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 – 8.29 (m, 1H), 8.05 – 7.99 (m, 1H), 7.83 – 7.70 (m, 3H), 7.65 (d, J = 7.5 Hz, 2H), 7.09 (td, J = 7.5, 1.0 Hz, 1H), 6.65 (td, J = 7.7, 1.1 Hz, 1H), 6.15 (d, J = 7.8 Hz, 1H), 4.46 (d, J = 5.2 Hz, 1H), 2.53 (dd, J = 9.4, 6.7 Hz, 1H), 2.06 (d, J = 12.9 Hz, 1H), 1.96 (ddd, J = 21.3, 11.4, 4.4 Hz, 1H), 1.88 – 1.80 (m, 3H), 1.68 – 1.58 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4, 154.3, 146.1, 141.7, 140.5, 137.2, 131.1, 130.7, 129.7, 129.5, 129.3, 129.2, 129.1, 128.9, 128.8, 128.5, 128.4, 128.2, 126.9, 126.1, 121.7, 121.3, 77.2, 72.1, 61.1 (d, J = 126.4 Hz), 61.0, 47.2, 46.9 (q, J = 70.8, 40.8 Hz), 28.1, 21.4; ^{19}F NMR (471 MHz, $CDCl_3$) δ -113.17.IR (KBr): δ 3435, 3375, 2928, 1730, 1625, 1341, 768 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{22}F_3N_4O_2$ $[M+H]^+$ 515.1695 found 515.1687.

1'-methyl-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,3'-indoline]-2',6-dione (5a):

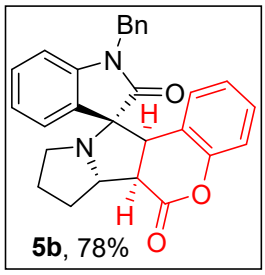


5a, 80%

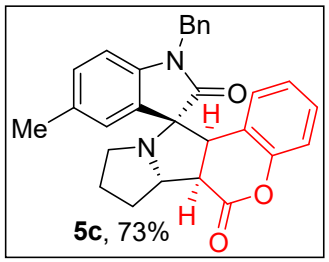
5a (145 mg) following general procedure **4a** (80 mg, 0.5 mmol); white solid; yield: 89%; mp: 237-240 °C; R_f = 0.48 (hexanes:EtOAc = 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 7.1 Hz, 1H), 7.40 (td, J = 7.8, 1.1 Hz, 1H), 7.18 (td, J = 7.6, 0.8 Hz, 1H), 7.15 – 7.09 (m, 1H), 7.01 (dd, J = 8.2, 0.9 Hz, 1H), 6.75 – 6.67 (m, 2H), 6.30 (d, J = 6.7 Hz, 1H), 4.84 – 4.75 (m, 1H), 3.96 (d, J = 11.2 Hz, 1H), 3.17 – 3.07 (m, 2H), 2.96 – 2.87 (m, 1H), 2.82 (s, 3H), 2.71 – 2.58 (m, 1H), 1.98 (d, J = 6.9 Hz, 1H), 1.95 – 1.76 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 167.7, 151.5, 145.4, 130.3, 128.8,

127.3, 125.9, 125.5, 123.5, 122.4, 117.4, 116.8, 108.7, 76.7, 67.8, 51.8, 48.6, 43.7, 33.9, 26.9, 25.7; IR (KBr): δ 3686, 3022, 2404, 1704, 1615, 1215, 742 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{22}H_{21}N_2O_3$ $[M+H]^+$ 361.1552 found 361.1527.

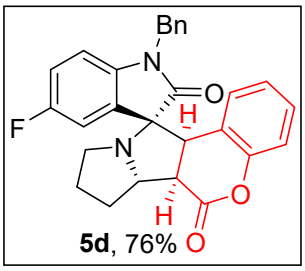
1'-benzyl-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,3'-indoline]-2',6-dione (5b): 5b (169 mg) following general procedure **4b** (118 mg, 0.5 mmol); white solid; yield: 78%; mp: 237-240 °C; R_f = 0.45 (hexanes:EtOAc = 6:4); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.4 Hz, 1H), 7.22 (d, *J* = 7.9 Hz, 2H), 7.12 (dd, *J* = 18.2, 7.7 Hz, 3H), 7.01 (t, *J* = 7.3 Hz, 2H), 6.75 (t, *J* = 7.4 Hz, 1H), 6.49 (d, *J* = 7.7 Hz, 1H), 6.37 (d, *J* = 7.0 Hz, 2H), 5.10 (d, *J* = 15.9 Hz, 1H), 4.87 (d, *J* = 7.0 Hz, 1H), 4.13 (d, *J* = 16.0 Hz, 1H), 4.02 (d, *J* = 11.1 Hz, 1H), 3.17 (dt, *J* = 14.8, 7.3 Hz, 2H), 2.94 (d, *J* = 7.1 Hz, 1H), 2.68 (d, *J* = 6.4 Hz, 1H), 2.00 (s, 1H), 1.96 – 1.75 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1, 167.6, 151.4, 144.8, 134.9, 130.8, 128.9, 128.5, 127.8, 127.1, 126.4, 125.8, 125.4, 123.7, 122.4, 117.6, 116.9, 109.9, 76.5, 67.9, 51.5, 48.1, 43.9, 43.4, 34.1, 29.7, 26.7; IR (KBr): δ 3682, 3018, 2402, 1628, 1410, 1214, 740 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{25}N_2O_3$ $[M+H]^+$ 437.1865 found 437.1863.



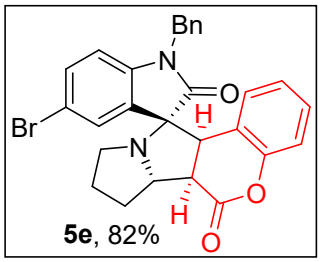
1'-benzyl-5'-methyl-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,3'-indoline]-2',6-dione (5c): 5c (167 mg) following general procedure **4c** (122 mg, 0.5 mmol); white solid; yield:76%; mp: 197-200 °C; R_f = 0.46 (hexanes:EtOAc = 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.2 Hz, 1H), 7.27 – 7.21 (m, 1H), 7.13 (dd, *J* = 17.4, 7.5 Hz, 2H), 7.02 (t, *J* = 7.3 Hz, 3H), 6.95 (d, *J* = 8.3 Hz, 1H), 6.49 (d, *J* = 7.7 Hz, 1H), 6.37 (d, *J* = 7.5 Hz, 2H), 6.07 (s, 1H), 5.11 (d, *J* = 15.9 Hz, 1H), 4.88 (s, 1H), 4.12 (d, *J* = 16.0 Hz, 1H), 3.99 (d, *J* = 11.0 Hz, 1H), 3.17 (d, *J* = 9.1 Hz, 2H), 3.00 (s, 1H), 2.72 – 2.62 (m, 1H), 2.06 – 1.99 (m, 1H), 1.91 (s, 3H), 1.84 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 167.7, 149.3, 144.9, 134.8, 133.3, 130.2, 129.6, 128.7, 128.0, 127.2, 126.4, 125.8, 122.5, 117.3, 109.9, 76.5, 68.1, 51.6, 48.0, 44.0, 43.4, 34.1, 26.7, 20.5; IR (KBr): δ 3159, 3017, 2935, 1713, 1464, 1215, 740 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{26}N_2O_3Na$ $[M+Na]^+$ 473.1841 found 473.1839.



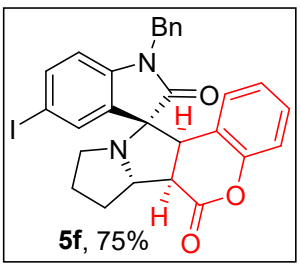
1'-benzyl-5'-fluoro-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,3'-indoline]-2',6-dione (5d): 5d (167 mg) following general procedure **4d** (122 mg, 0.5 mmol); white solid; yield: 76%; mp: 197-200 °C; R_f = 0.47 (hexanes:EtOAc = 6:4); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (s, 1H), 7.22 – 7.15 (m, 2H), 7.03 (t, *J* = 7.3 Hz, 1H), 6.99 – 6.92 (m, 2H), 6.87 (t, *J* = 8.6 Hz, 1H), 6.70 (t, *J* = 7.2 Hz, 1H), 6.38 – 6.24 (m, 3H), 4.98 (d, *J* = 15.9 Hz, 1H), 4.82 (s, 1H), 4.03 (d, *J* = 15.9 Hz, 2H), 3.14 (s, 1H), 2.96 (s, 1H), 2.61 (s, 1H), 1.97 (d, *J* = 13.8 Hz, 1H), 1.86 (s, 2H), 1.60 – 1.43 (m, 1H).^{13}C NMR (125 MHz, $CDCl_3$) δ ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 158.9 (d, *J* = 241.5 Hz), 151.3, 140.3, 134.4, 129.2, 128.6, 128.5, 127.8, 127.2, 127.1, 126.3, 123.9, 117.7, 116.8 (d, *J* = 23.3 Hz), 116.3, 114.0 (d, *J* = 24.0 Hz), 113.9, 110.6 (d, *J* = 6.1 Hz), 76.4, 68.1, 51.5, 47.8, 44.0, 43.5, 33.9, 26.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.80.IR (KBr): δ 3777, 3685, 3491, 2399, 1524, 1418, 1214, 740 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{24}FN_2O_3$ $[M+H]^+$ 455.1771 found 455.1765.



1'-benzyl-5'-bromo-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,3'-indoline]-2',6-dione (5e): 5e (210 mg) following general procedure **4e** (157 mg, 0.5 mmol); white solid; yield: 82%; mp: 210-212 °C; R_f = 0.46 (hexanes: EtOAc = 6:4); ^{1}H NMR (400 MHz, DMSO) δ 8.15 (s, 1H), 7.50 (d, *J* = 8.3 Hz, 1H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.14 – 7.10 (m, 1H), 7.03 (t, *J* = 8.2 Hz, 3H), 6.89 (t, *J* = 7.4 Hz, 1H), 6.59 (d, *J* = 8.4 Hz, 1H), 6.42 (d, *J* = 7.5 Hz, 1H), 6.35 (d, *J* = 7.4 Hz, 2H), 4.80 (s, 1H), 4.43 (d, *J* = 14.4 Hz, 2H), 4.40 – 4.33 (m, 2H), 3.24 (s, 1H), 2.62 (s, 1H), 2.39 (d, *J* = 12.1 Hz, 1H), 1.99 – 1.80 (m, 3H), 1.69 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 175.9, 167.9, 151.4, 143.4, 135.3, 133.2, 130.0, 129.5, 128.9, 128.2, 128.1, 127.5, 126.5, 124.5, 117.8, 117.2, 114.8, 111.8, 76.6, 67.8, 50.8, 47.3, 42.8, 42.5, 33.3, 26.6; IR (KBr): δ 3296, 3492, 3074, 2922, 1756, 1454,740 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{23}BrN_2O_3Na$ $[M+2+Na]^+$ 539.0790 found 539.0742.

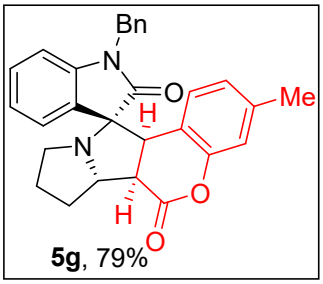


1'-benzyl-5'-iodo-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,3'-indoline]-2',6-dione (5f): 5f (210 mg) following general procedure **4f** (181 mg, 0.5 mmol); white solid; yield: 75%; mp: 217-219 °C; R_f = 0.46 (hexanes:EtOAc = 6:4); ^{1}H NMR (400 MHz, DMSO) δ 8.26 (d, *J*

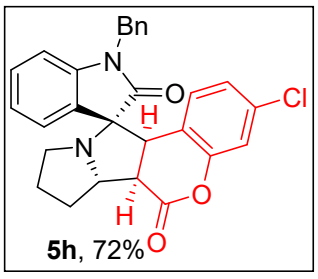


= 1.1 Hz, 1H), 7.64 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.34 (t, *J* = 7.3 Hz, 1H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.03 (t, *J* = 7.7 Hz, 3H), 6.89 (t, *J* = 7.4 Hz, 1H), 6.47 (d, *J* = 8.2 Hz, 1H), 6.41 (d, *J* = 7.4 Hz, 1H), 6.34 (d, *J* = 7.4 Hz, 2H), 4.81 (d, *J* = 16.2 Hz, 1H), 4.44 (td, *J* = 7.4, 2.8 Hz, 1H), 4.41 – 4.35 (m, 2H), 3.22 (dd, *J* = 15.9, 7.9 Hz, 1H), 2.61 (t, *J* = 6.9 Hz, 1H), 2.39 (dt, *J* = 15.0, 7.5 Hz, 1H), 2.00 – 1.77 (m, 3H), 1.72 – 1.63 (m, 1H). ^{13}C NMR (100 MHz, DMSO) δ 175.7, 167.9, 151.4, 143.8, 139.0, 135.4, 135.3, 129.5, 128.9, 128.3, 128.2, 127.4, 126.5, 124.3, 117.8, 117.2, 112.3, 86.0, 67.8, 50.8, 47.5, 42.8, 42.4, 33.3, 29.5, 26.6. IR (KBr): δ 3776, 3685, 3018, 2401, 1592, 1214, 740 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{23}IN_2O_3Na$ $[M+Na]^+$ 585.0651found 585.0619.

1'-benzyl-3-methyl-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,3'-indoline]-2',6-dione (5g): 5g (179 mg) following general procedure **4b** (181 mg, 0.5 mmol); off white solid; yield: 79%; mp: 221-223 °C; R_f = 0.45 (hexanes:EtOAc = 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.3 Hz, 1H), 7.15 (d, *J* = 7.6 Hz, 1H), 7.07 – 7.01 (m, 2H), 6.98 – 6.92 (m, 3H), 6.88 (d, *J* = 8.3 Hz, 1H), 6.42 (d, *J* = 7.3 Hz, 1H), 6.29 (d, *J* = 7.5 Hz, 2H), 6.00 (d, *J* = 1.2 Hz, 1H), 5.04 (d, *J* = 15.9 Hz, 1H), 4.81 (s, 1H), 4.05 (d, *J* = 16.0 Hz, 1H), 3.93 (d, *J* = 10.8 Hz, 1H), 3.17 – 3.07 (m, 2H), 2.94 (s, 1H), 2.66 – 2.56 (m, 1H), 1.99 (d, *J* = 10.1 Hz, 2H), 1.95 (d, *J* = 6.0 Hz, 1H), 1.84 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 171.0, 163.0, 144.0, 139.6, 130.1, 128.5, 125.5, 124.9, 123.7, 123.4, 122.4, 121.6, 121.1, 117.7, 112.5, 105.2, 72.5, 71.7, 63.3, 43.2, 39.2, 38.8, 29.3, 21.9, 15.8; IR (KBr): δ 3654, 3010, 2254, 1495, 1250, 765 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{26}N_2O_3Na$ $[M+Na]^+$ 473.1841 found 473.1814.

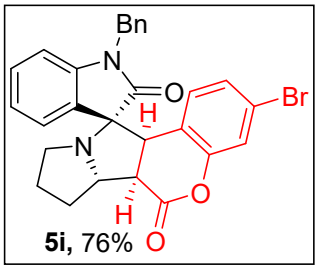


1'-benzyl-3-chloro-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,3'-indoline]-2',6-dione (5h): 5h (170 mg) following general procedure **4b** (118 mg, 0.5 mmol); white solid; yield: 72%; mp: 229-231 °C; R_f = 0.43 (hexanes:EtOAc = 6:4); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.4 Hz, 1H), 7.28 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.20 – 7.16 (m, 2H), 7.14 (d, *J* = 7.6 Hz, 1H), 7.09 (t, *J* = 7.3 Hz, 2H), 6.98 (d, *J* = 8.7 Hz, 1H), 6.55 (d, *J* = 7.8 Hz, 1H), 6.47 (d, *J* = 7.4 Hz, 2H), 6.28 (d, *J* =

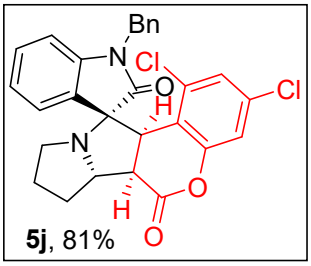


2.4 Hz, 1H), 5.07 (d, *J* = 16.0 Hz, 1H), 4.84 (td, *J* = 7.5, 3.2 Hz, 1H), 4.20 (d, *J* = 16.0 Hz, 1H), 3.95 (d, *J* = 11.2 Hz, 1H), 3.18 – 3.10 (m, 2H), 3.00 – 2.91 (m, 1H), 2.72 – 2.63 (m, 1H), 2.01 (d, *J* = 6.8 Hz, 1H), 1.97 – 1.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 167.0, 149.9, 144.3, 134.7, 130.8, 129.0, 128.6, 127.3, 126.3, 125.6, 124.9, 122.7, 118.9, 118.7, 110.2, 76.8, 68.1, 51.4, 47.8, 43.7, 43.4, 34.1, 26.6; IR (KBr): δ 3687, 3018, 2356, 1518, 1214, 740 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{24}ClN_2O_3$ $[M+H]^+$ 471.1475 found 471.1437.

1'-benzyl-3-bromo-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,3'-indoline]-2',6-dione (5i): 5i (195 mg) following general procedure **4b** (118 mg, 0.5 mmol); white solid; yield: 76%; mp: 225-228 °C; R_f = 0.44 (hexanes:EtOAc = 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.55 (m, 1H), 7.32 (dd, *J* = 8.7, 2.4 Hz, 1H), 7.28 (d, *J* = 1.2 Hz, 1H), 7.26 (d, *J* = 1.3 Hz, 1H), 7.20 – 7.16 (m, 1H), 7.15 – 7.08 (m, 3H), 6.92 (d, *J* = 8.7 Hz, 1H), 6.55 (d, *J* = 7.7 Hz, 1H), 6.44 (dd, *J* = 13.5, 4.6 Hz, 3H), 5.08 (d, *J* = 16.0 Hz, 1H), 4.84 (td, *J* = 7.4, 3.2 Hz, 1H), 4.20 (d, *J* = 16.0 Hz, 1H), 3.95 (d, *J* = 11.2 Hz, 1H), 3.20 – 3.08 (m, 2H), 2.97 (dd, *J* = 8.0, 5.7 Hz, 1H), 2.74 – 2.62 (m, 1H), 2.06 – 1.97 (m, 1H), 1.94 – 1.80 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 166.9, 150.4, 144.3, 134.7, 131.9, 130.5, 130.4, 128.7, 127.3, 126.2, 125.6, 124.9, 122.7, 119.3, 119.2, 116.1, 110.2, 77.4, 77.0, 76.7, 76.6, 68.1, 51.4, 47.7, 4.7, 4.41, 34.2, 26.6; IR (KBr): δ 3686, 3019, 2404, 1522, 1215, 740 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{23}BrN_2O_3Na$ $[M+Na]^+$ 537.0790 found 537.0760.

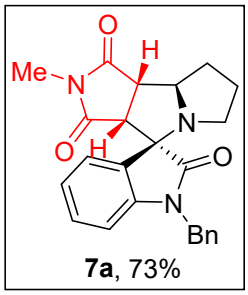


1'-benzyl-1,3-dichloro-6a,6b,7,8,9,11a-hexahydro-6H-spiro[chromeno[3,4-a]pyrrolizine-11,3'-indoline]-2',6-dione (5j): 5j (205 mg) following general procedure **4b** (118 mg, 0.5 mmol); white solid; yield: 81%; mp: 223-225 °C; R_f = 0.43 (hexanes:EtOAc = 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.4 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 2.3 Hz, 1H), 7.15 (dt, *J* = 14.3, 7.0 Hz, 4H), 6.62 (dd, *J* = 15.4, 7.4 Hz, 3H), 6.13 (d, *J* = 2.2 Hz, 1H), 5.03 (d, *J* = 15.7 Hz, 1H), 4.89 – 4.79 (m, 1H), 4.22 (d, *J* = 15.7 Hz, 1H), 3.93 (d, *J* = 11.2 Hz, 1H), 3.20 – 3.06 (m, 2H), 3.01 – 2.91 (m, 1H), 2.76 – 2.62 (m, 1H), 2.06 – 1.97 (m, 1H), 1.94 – 1.77 (m, 2H); ^{13}C NMR (100



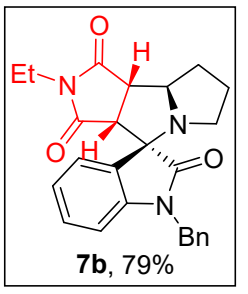
MHz, $CDCl_3$) δ 175.8, 166.9, 150.4, 144.3, 134.7, 131.9, 130.5, 130.3, 128.7, 127.3, 126.2, 125.6, 124.9, 122.7, 119.3, 119.2, 116.1, 110.2, 76.6, 68.1, 51.4, 47.7, 43.7, 43.4, 34.0, 26.6; IR (KBr): δ 3684, 3019, 2402, 1534, 1214, 740 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{28}H_{23}Cl_2N_2O_3$ $[M+H]^+$ 505.1086 found 505.1047.

1-benzyl-2'-methyl-3a',6',7',8',8a',8b'-hexahydro-1'H-spiro[indoline-3,4'-pyrrolo[3,4-a]pyrrolizine]-1',2,3'(2'H)-trione (7a): 7a (139 mg) following general procedure **4b** (118 mg, 0.5 mmol); white solid; yield: 73%; MP: 197-199 °C; R_f = 0.42 (hexanes:EtOAc = 5:5); ^1H NMR (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 6.1 Hz, 3H), 7.20 (s, 3H), 6.95 (d, *J* = 7.0 Hz, 2H), 6.67 (d, *J* = 7.3 Hz, 1H), 4.83 (dd, *J* = 53.2, 15.3 Hz, 2H), 4.54 (s, 1H), 3.68 – 3.53 (m, 2H), 2.98 (s, 3H), 2.50 (s, 2H), 1.97 (d, *J* = 23.1 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 175.2, 143.3, 135.4, 130.0, 128.9, 127.7, 127.2, 126.6, 122.5, 109.6, 68.4, 64.8, 56.2, 45.4, 43.8, 26.2, 25.1, 23.7; IR (KBr): δ 3684, 3019, 2404, 1701, 1618, 1214, 741 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{24}H_{24}N_3O_3$ $[M+H]^+$ 402.1818 found 402.1787.



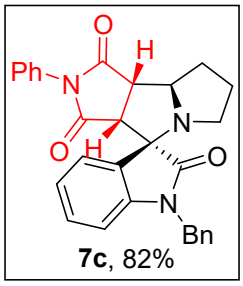
7a, 73%

1-benzyl-2'-ethyl-3a',6',7',8',8a',8b'-hexahydro-1'H-spiro[indoline-3,4'-pyrrolo[3,4-a]pyrrolizine]-1',2,3'(2'H)-trione (7b): 7b (155 mg) following general procedure **4b** (118 mg, 0.5 mmol); white solid; yield: 79%; mp: 167-169 °C; R_f = 0.43 (hexanes:EtOAc = 5:5); ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.25 (m, 1H), 7.25 – 7.22 (m, 2H), 7.22 – 7.19 (m, 2H), 7.18 – 7.14 (m, 1H), 6.95 (dd, *J* = 7.6, 5.3 Hz, 2H), 6.66 (d, *J* = 7.9 Hz, 1H), 4.89 (d, *J* = 15.7 Hz, 1H), 4.74 (d, *J* = 15.8 Hz, 1H), 4.42 (s, 1H), 3.60 (d, *J* = 7.9 Hz, 1H), 3.54 (qd, *J* = 7.1, 3.0 Hz, 2H), 3.46 (t, *J* = 7.4 Hz, 1H), 2.44 (s, 1H), 1.93 (s, 3H), 1.51 (s, 1H), 1.17 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 175.1, 143.3, 135.5, 129.9, 128.9, 127.7, 127.2, 127.1, 126.9, 122.4, 109.5, 77.3, 68.7, 64.8, 45.6, 43.8, 34.0, 26.0, 23.8, 13.0; IR (KBr): δ 3687, 3618, 3020, 2397, 1526, 1214, 740 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{25}H_{26}N_3O_3$ $[M+H]^+$ 416.1974 found 416.1943.



7b, 79%

1-benzyl-2'-phenyl-3a',6',7',8',8a',8b'-hexahydro-1'H-spiro[indoline-3,4'-pyrrolo[3,4-a]pyrrolizine]-1',2,3'(2'H)-trione (7c): 7c (190 mg)



7c, 82%

following general procedure **4b** (118 mg, 0.5 mmol); white solid; yield: 82%; mp: 194-196 °C, R_f = 0.43 (hexanes:EtOAc = 6:4); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.47 (m, 2H), 7.44 – 7.39 (m, 1H), 7.35 – 7.33 (m, 2H), 7.32 – 7.30 (m, 3H), 7.28 (dd, *J* = 6.3, 2.2 Hz, 2H), 7.22 (td, *J* = 7.7, 1.3 Hz, 1H), 7.10 (dd, *J* = 7.5, 0.9 Hz, 1H), 6.99 (td, *J* = 7.6, 0.9 Hz, 1H), 6.73 (d, *J* = 7.8 Hz, 1H), 5.00 (d, *J* = 15.7 Hz, 1H), 4.81 (d, *J* = 15.7 Hz, 1H), 4.58 (dd, *J* = 14.7, 7.3 Hz, 1H), 3.87 (d, *J* = 8.0 Hz, 1H), 3.71 (t, *J* = 8.0 Hz, 1H), 2.88 – 2.86 (m, 1H), 2.66 – 2.46 (m, 2H), 2.16 – 1.94 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.8, 175.8, 174.3, 143.3, 135.6, 131.9, 129.9, 129.3, 128.9, 128.7, 127.7, 127.2, 126.9, 126.3, 124.2, 122.5, 109.5, 69.3, 65.5, 56.1, 50.8, 44.9, 26.2, 24.0; IR (KBr): δ 3684, 3019, 2404, 1525, 1214, 740 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{29}H_{26}N_3O_3$ $[M+H]^+$ 464.1974 found 464.1983.

IV. References

1. (a) A. S. Filatov, N. A. Knyazev, M. N. Ryazantsev, V. V. Suslonov, A. G. Larina, A. P. Molchanov, R. R. Kostikov, V. M. Boitsov and A. V. Stepakov, *Org. Chem. Front.* 2018, **5**, 595-605.

2. (a) J. Wang, W. Xu, S. Xue, T. Yu and H. Xie, *Org. Biomol. Chem*. 2020, **18**, 4029-4033. (b) C. Guillon, Y.-H. Jan, D. E. Heck, T. M. Mariano, R. D. Rapp, M. Jetter, K. Kardos, M. Whittemore, E. Akyea, I. Jabin, J. D. Laskin and N. D. Heindel, *Bioorganic Chemistry* 2019, **89**, 103014-103024.

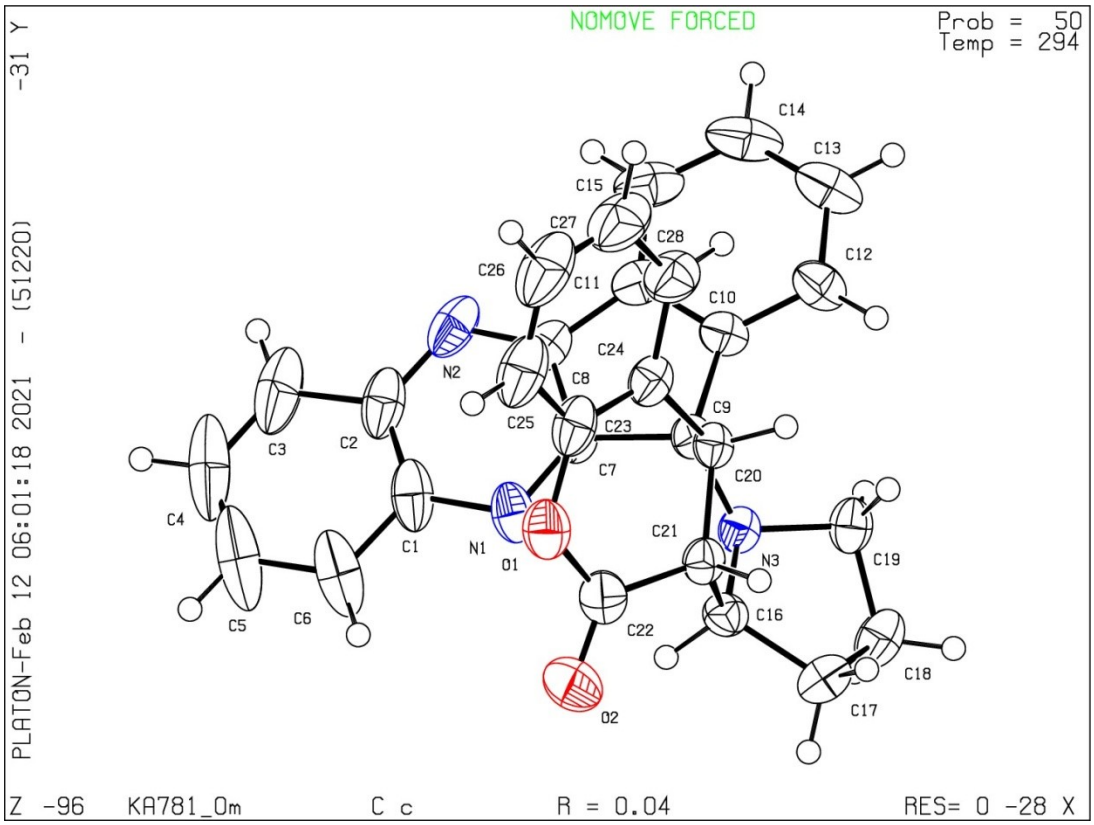
V. X-ray Crystallography.

X-ray data for compounds **3aa**, **5a** and **7b** were collected at room temperature using a Bruker Smart Apex CCD diffractometer with graphite monochromated MoKα radiation (λ=0.71073Å) with ω-scan method [1]. Preliminary lattice parameters and orientation matrices were obtained from four sets of frames.

Integration and scaling of intensity data was accomplished using SAINT program [1]. The structure was solved by direct methods using SHELXS97 [2] and refinement was carried out by full-matrix least-squares technique using SHELXL97 [2]. Anisotropic displacement parameters were included for all non-hydrogen atoms. All H atoms were positioned geometrically and

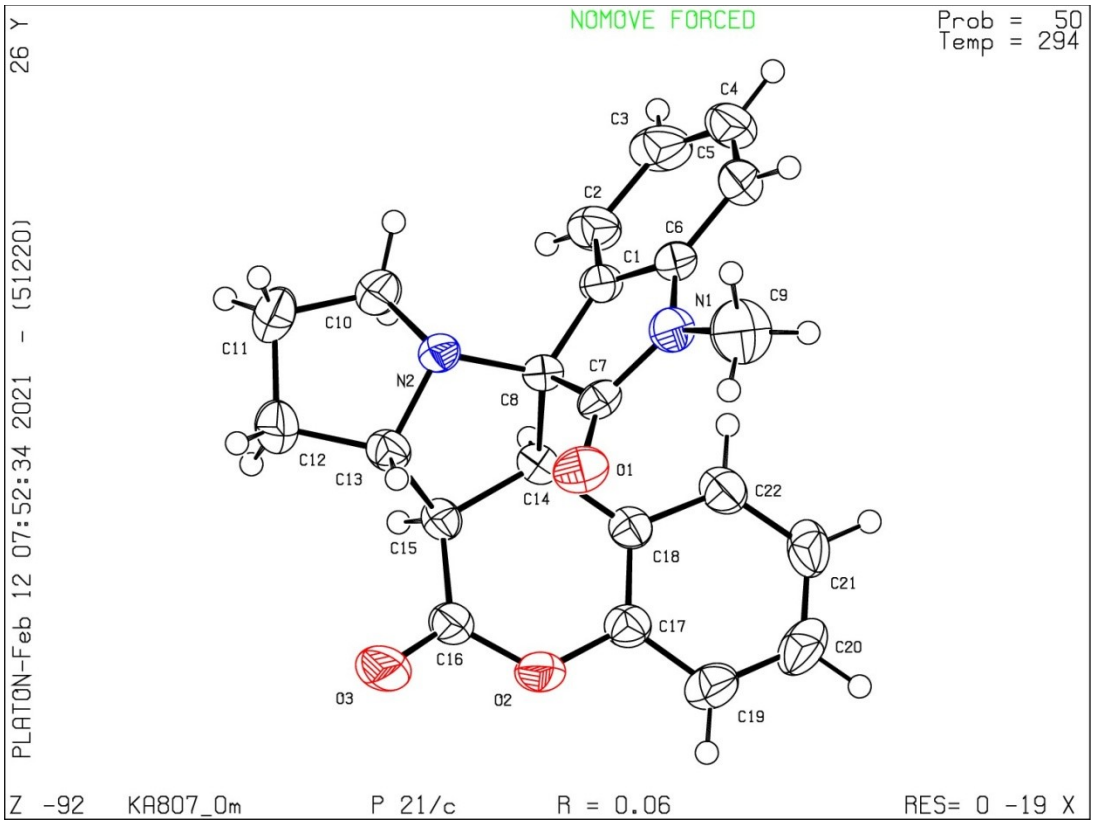
treated as riding on their parent C atoms [C-H = 0.93-0.97 Å and $U_{iso}(H) = 1.5U_{eq}(C)$ for methyl H or $1.2U_{eq}(c)$ for other H atoms]. The methyl groups were allowed to rotate but not to tip.

Crystal structure determination of [3aa]



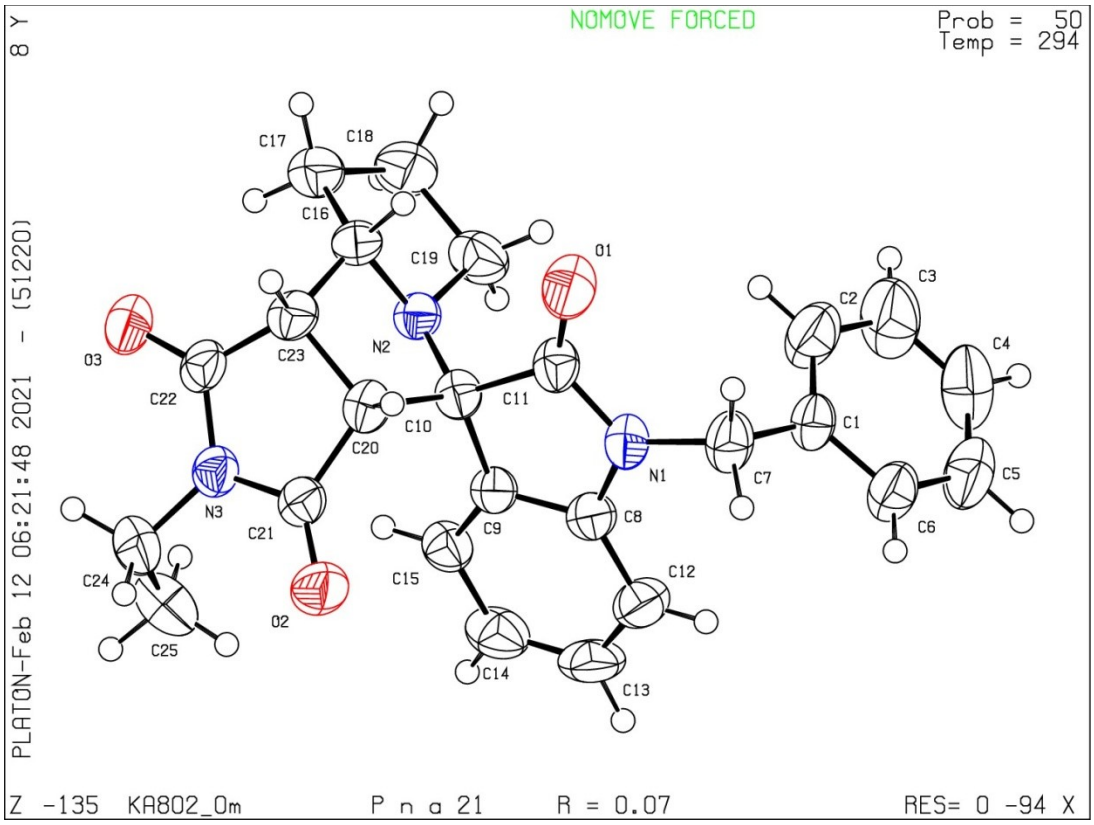
Crystal Data for $C_{28}H_{21}N_3O_2$ (M =431.48 g/mol): monoclinic, space group Cc (no. 9), a = 10.5012(10) Å, b = 21.4163(19) Å, c = 10.7561(9) Å, β = 116.366(3)°, V = 2167.4(3) Å^3, Z = 4, T = 294.15 K, μ(MoKα) = 0.085 mm^{-1}, *Dcalc* = 1.322 g/cm^3, 31296 reflections measured (4.896° ≤ 2Θ ≤ 61.13°), 6275 unique (R_{int} = 0.0252, R_{sigma} = 0.0227) which were used in all calculations. The final R_1 was 0.0411 (I > 2σ(I)) and wR_2 was 0.1105 (all data). CCDC **2065302** contains supplementary Crystallographic data for the structure.

Crystal structure determination of [5a]



Crystal Data for $C_{22}H_{20}N_2O_3$ (M =360.40 g/mol): monoclinic, space group $P2_1/c$ (no. 14), a = 14.0372(2) Å, b = 9.4978(2) Å, c = 14.4733(3) Å, β = 113.2323(10)°, V = 1773.15(6) Å^3, Z = 4, T = 294.15 K, μ(MoKα) = 0.091 mm^{-1}, *Dcalc* = 1.350 g/cm^3, 25150 reflections measured (5.27° ≤ 2Θ ≤ 52.492°), 3571 unique (R_{int} = 0.0733, R_{sigma} = 0.0465) which were used in all calculations. The final R_1 was 0.0638 (I > 2σ(I)) and wR_2 was 0.1470 (all data). CCDC **2065304** contains supplementary Crystallographic data for the structure.

Crystal structure determination of [7b]



Crystal Data for $C_{25}H_{25}N_3O_3$ (M =415.48 g/mol): orthorhombic, space group $Pna2_1$ (no. 33), a = 10.5361(2) Å, b = 20.5984(4) Å, c = 9.9179(2) Å, V = 2152.45(7) Å^3, Z = 4, T = 294.15 K, μ(MoKα) = 0.085 mm^{-1}, *Dcalc* = 1.282 g/cm^3, 15870 reflections measured (4.342° ≤ 2Θ ≤ 61.028°), 5861 unique (R_{int} = 0.0547, R_{sigma} = 0.0844) which were used in all calculations. The final R_1 was 0.0677 (I > 2σ(I)) and wR_2 was 0.1328 (all data). CCDC **2065303** contains supplementary Crystallographic data for the structure.

These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk].

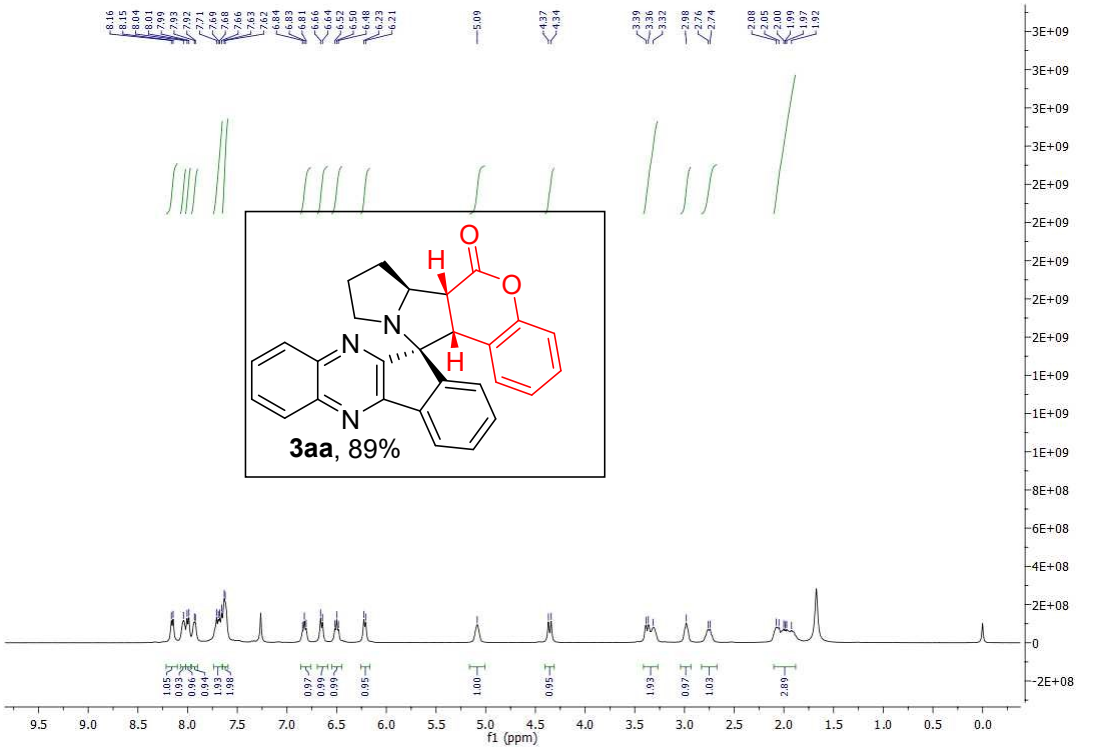
1. Bruker (2001). SAINT (Version 6.28a) & SMART (Version 5.625). Bruker AXS Inc., Madison, Wisconsin, USA.
2. Sheldrick, G. M. (2015). Acta Cryst. C71, 3--8..

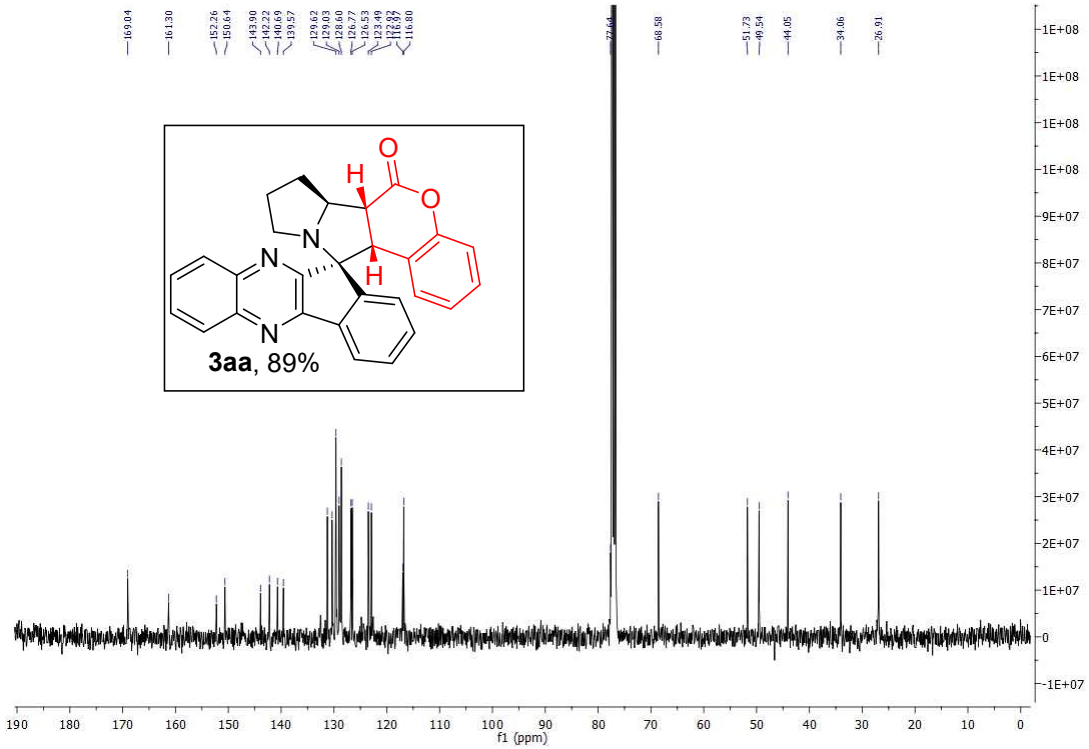
Figure Captions

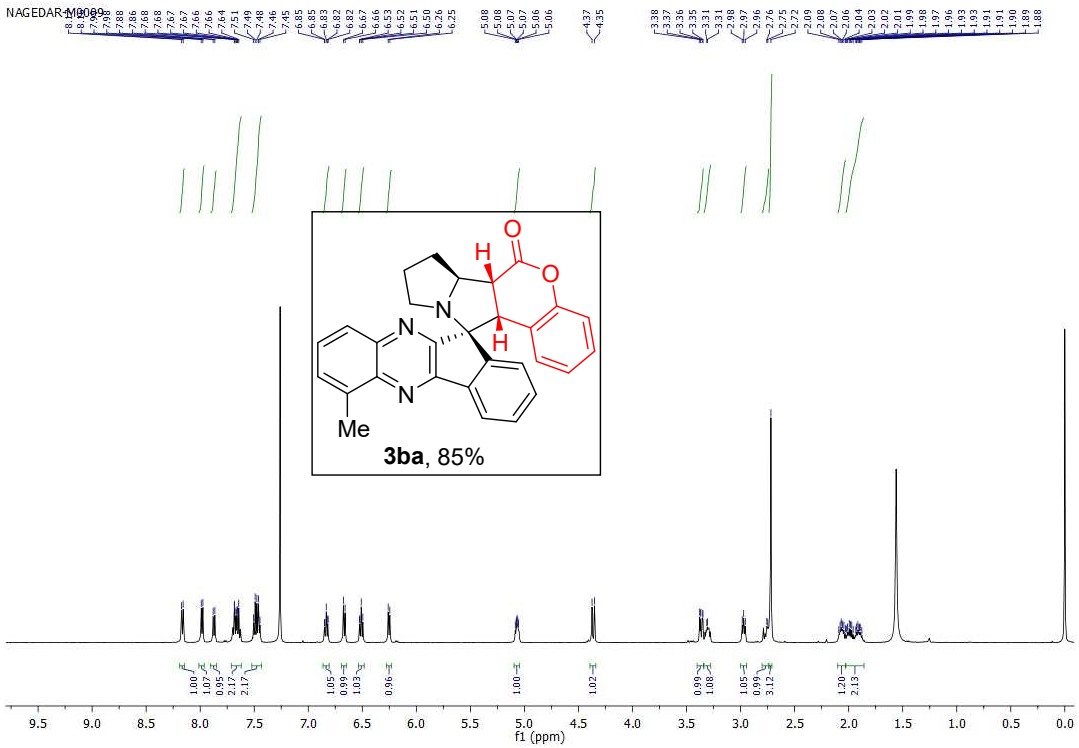
1. A view of **3aa**_0m, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are represented by circles of arbitrary radii.

2. A view of **5a**_0m, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are represented by circles of arbitrary radii.
3. A view of **7b**_0m, showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are represented by circles of arbitrary radii.

Copies of ^{1}H and ^{13}C NMR data of **3aa-3la**, **3ab-3af**, **5a-5j** and **7a-c**:



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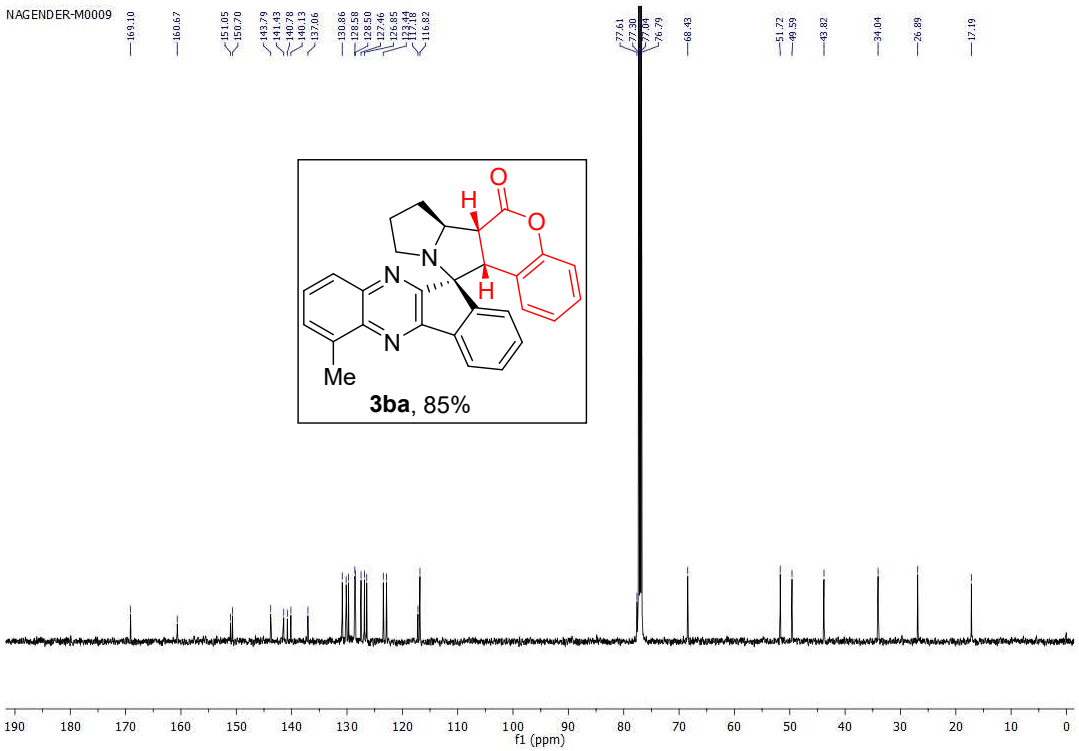
f1 (ppm)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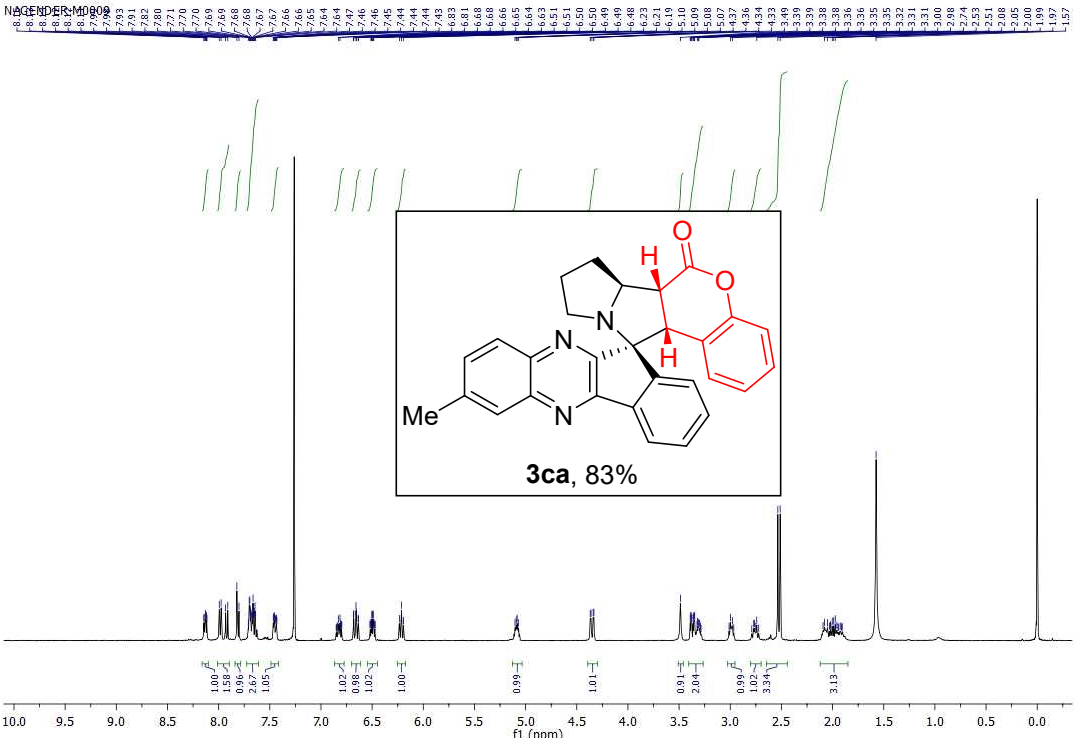
3ba, 85%
f1 (ppm)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N
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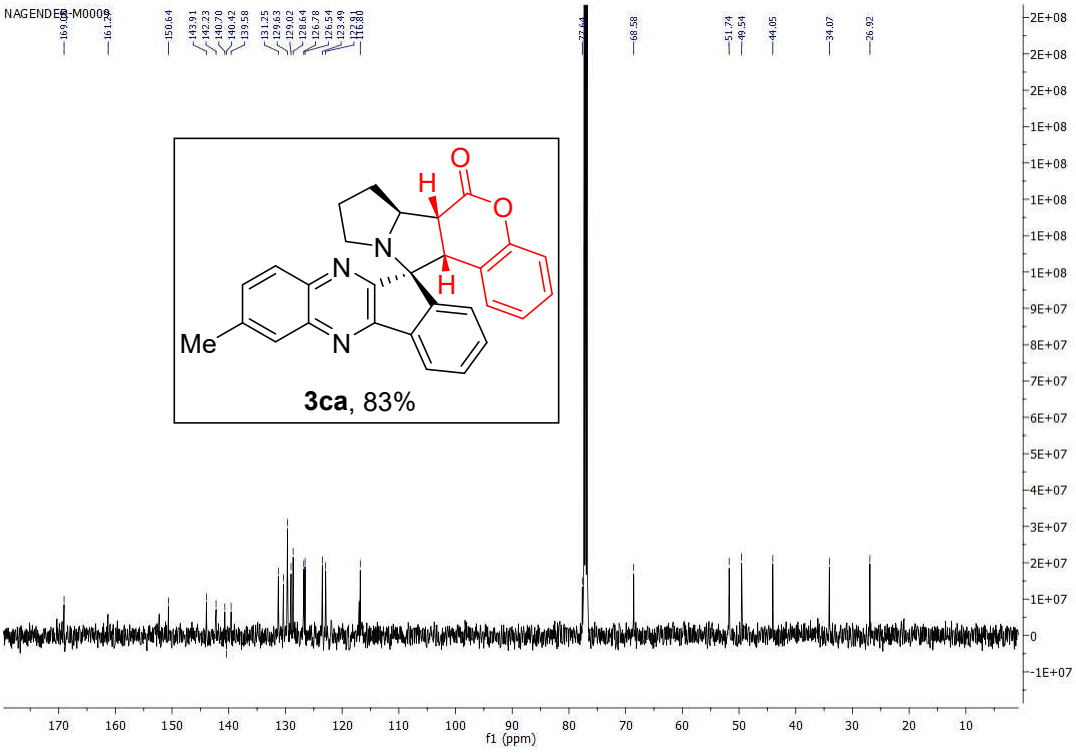
Me
N
3ca, 83%
f1 (ppm)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O
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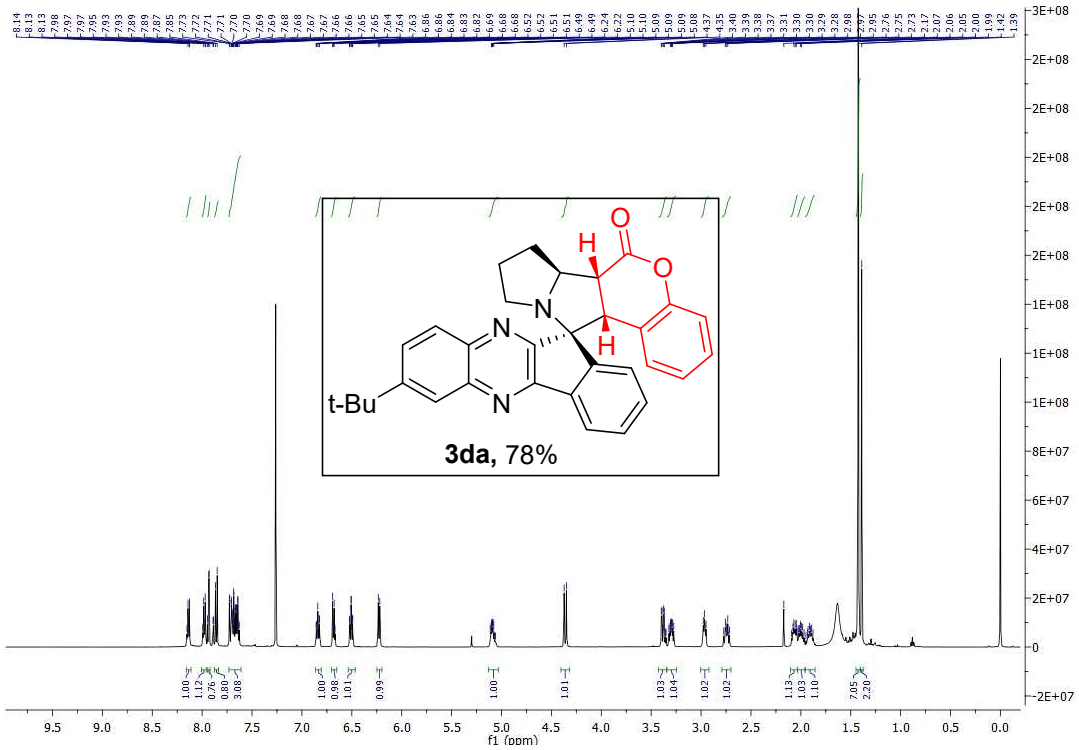
N
H
Me
N
3ca, 83%
f1 (ppm)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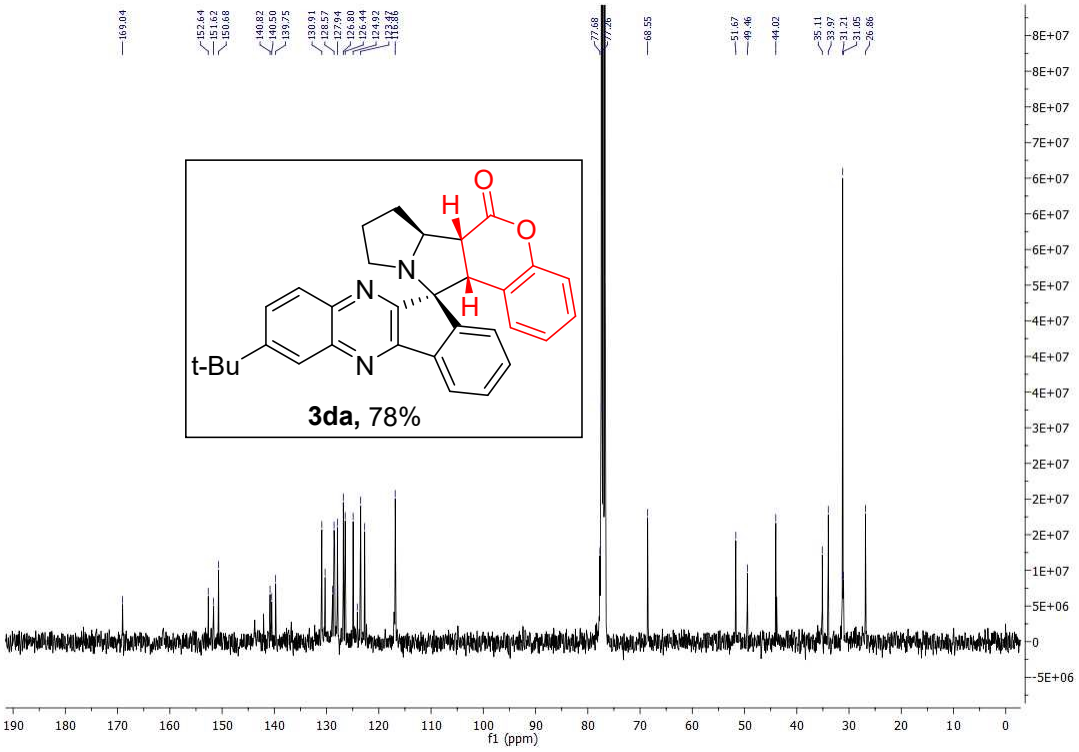
f1 (ppm)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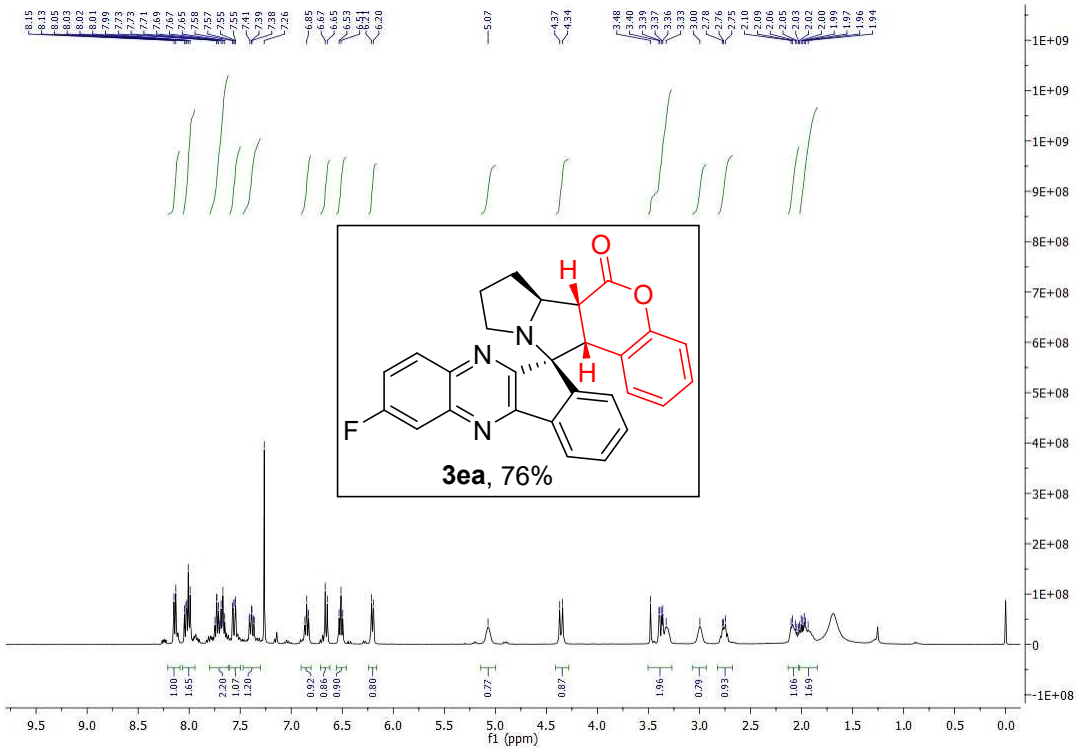
3da, 78%
f1 (ppm)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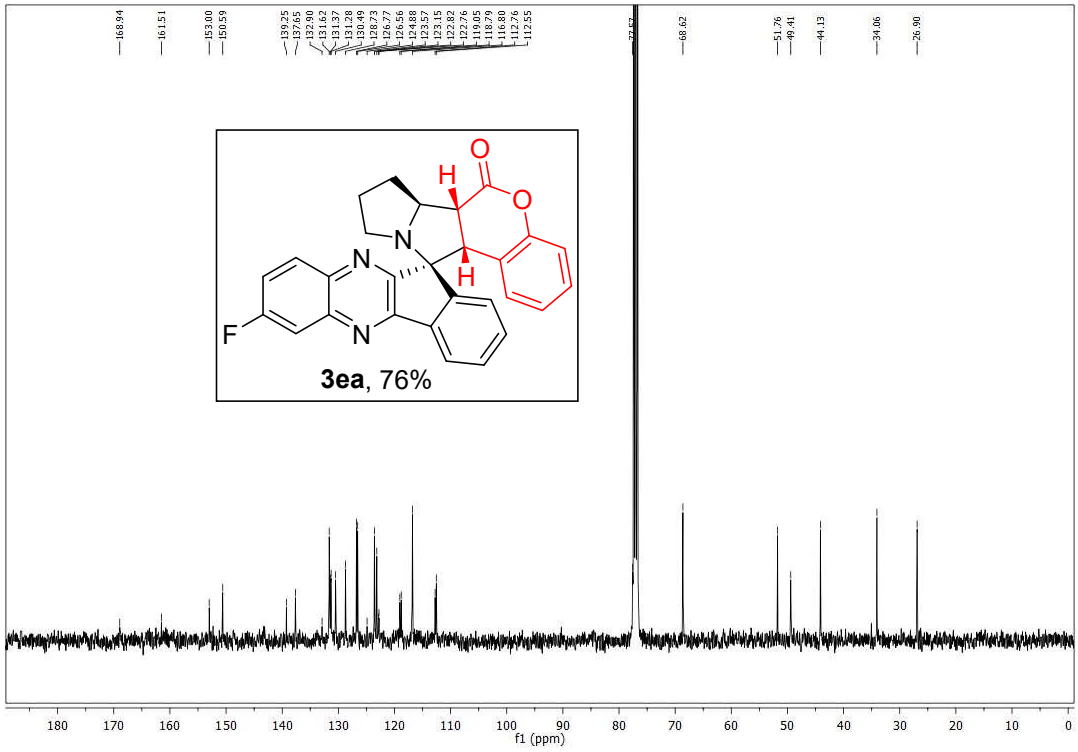
f1 (ppm)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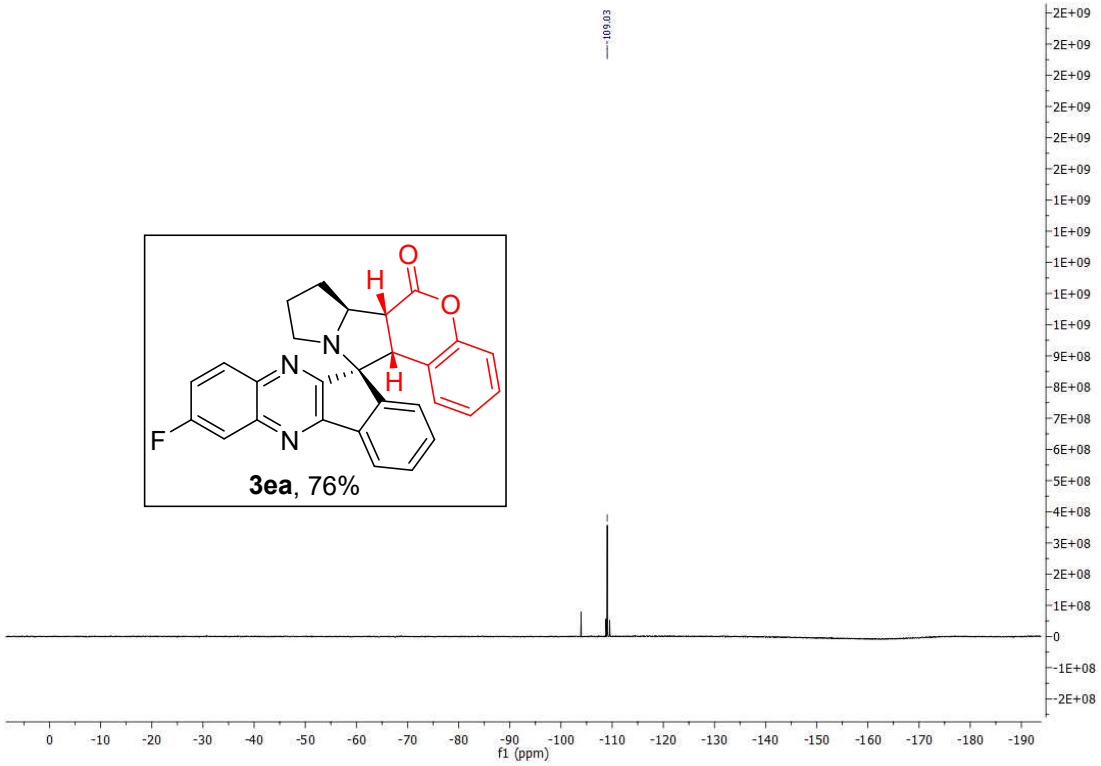
-109.03
O
H
O
N
N
H
F
N
3ea, 76%
2E+09
2E+09
2E+09
2E+09
2E+09
2E+09
1E+09
1E+09
1E+09
1E+09
1E+09
1E+09
9E+08
8E+08
7E+08
6E+08
5E+08
4E+08
3E+08
2E+08
1E+08
0
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-2E+08
0
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-50
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-170
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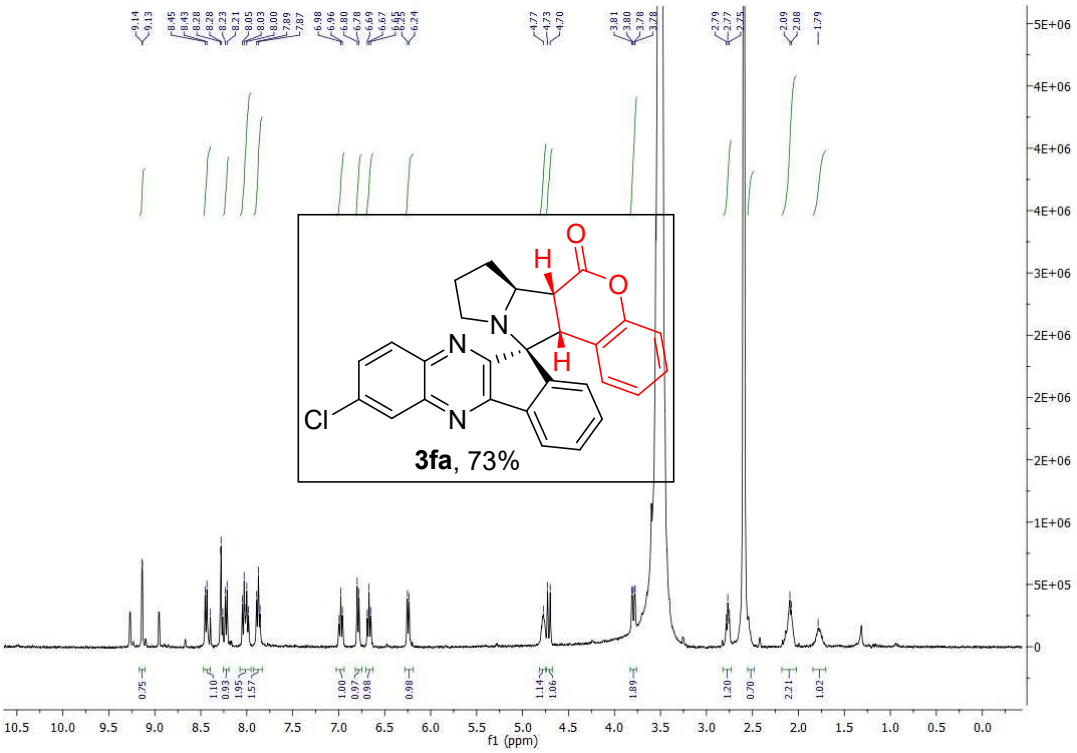
-190
f1 (ppm)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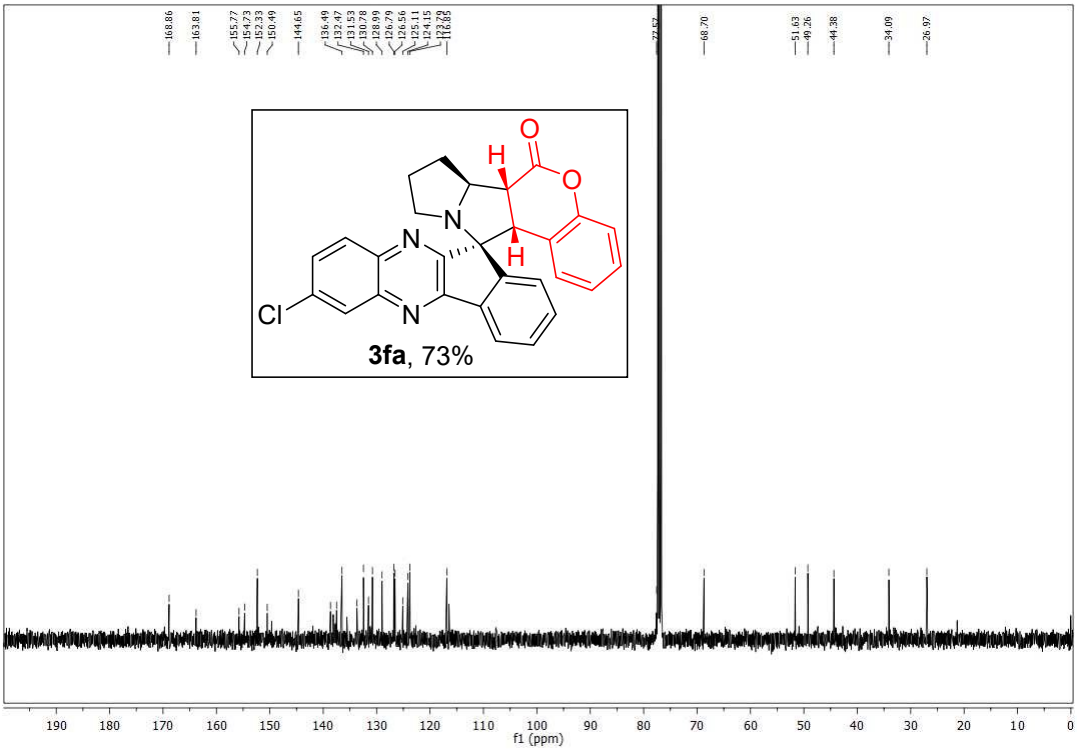
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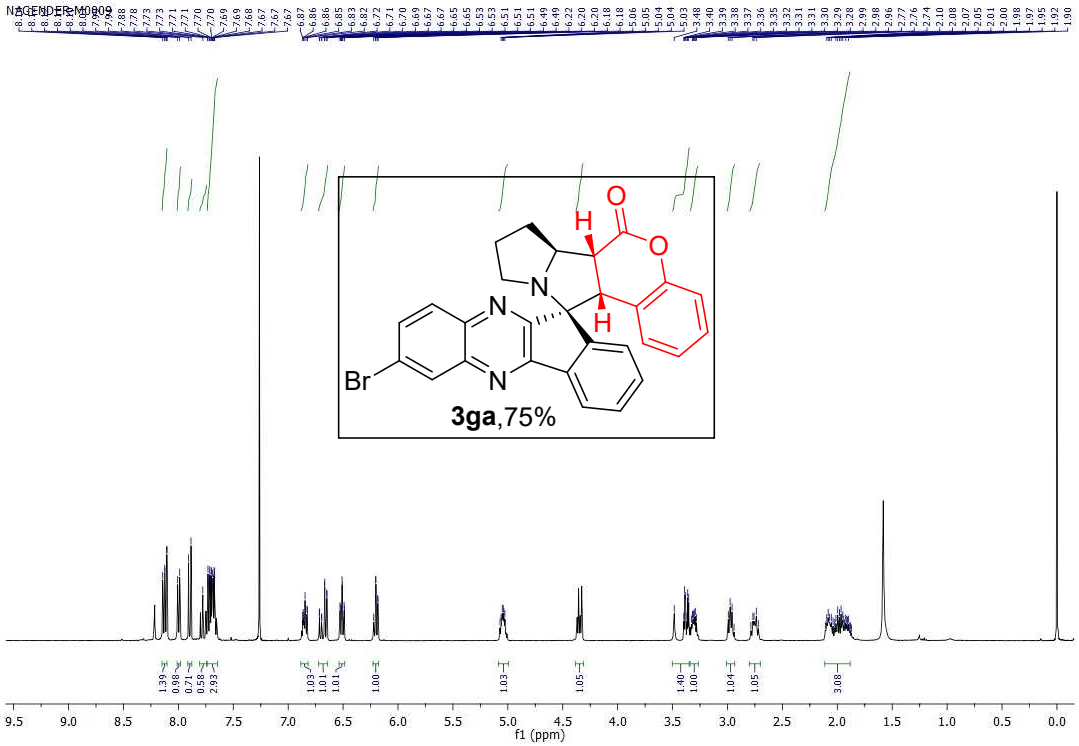
f1 (ppm)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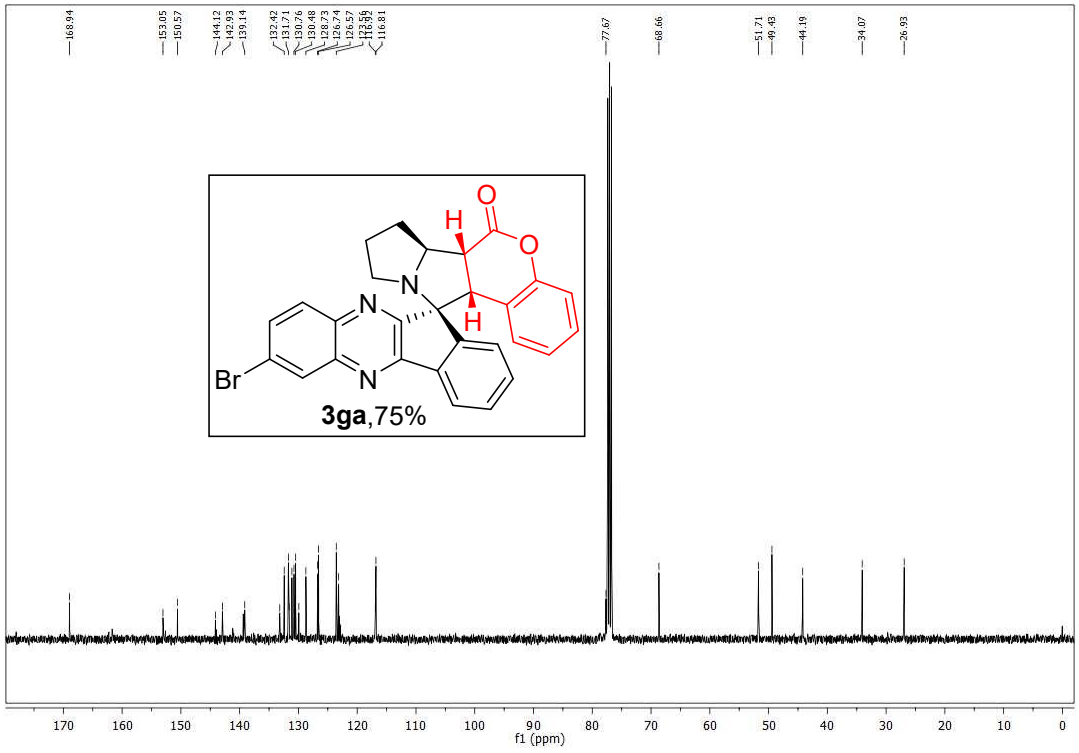
H
N
Br
N
3ga,75%
f1 (ppm)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H
N
Br
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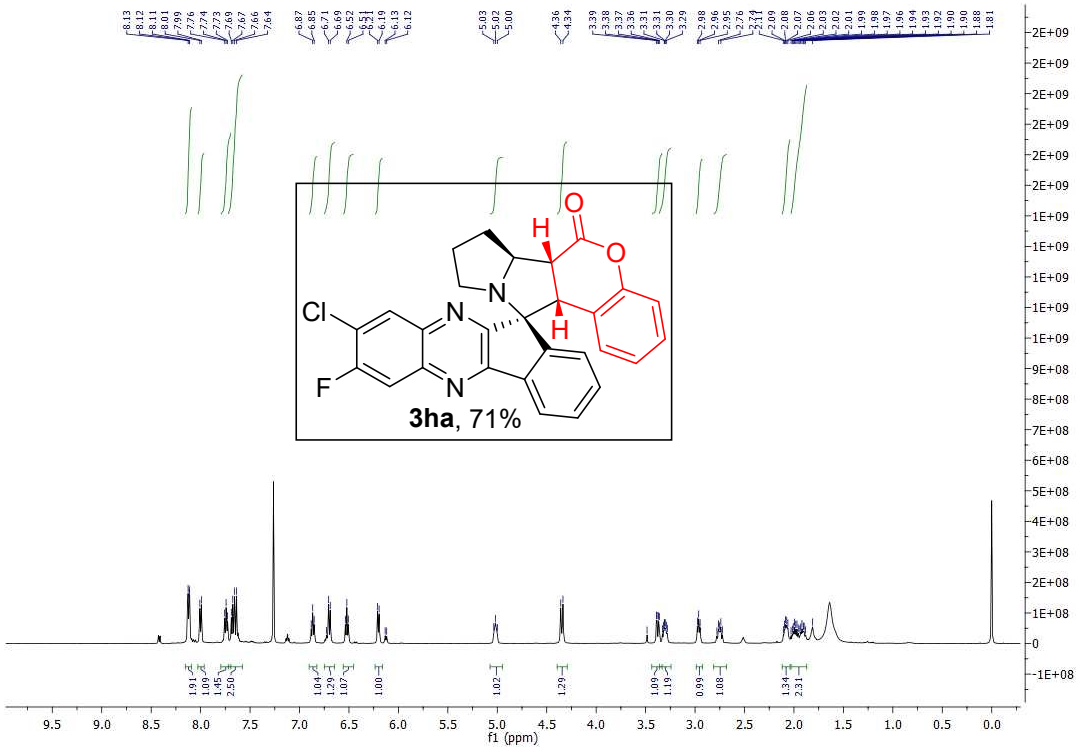
f1 (ppm)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N
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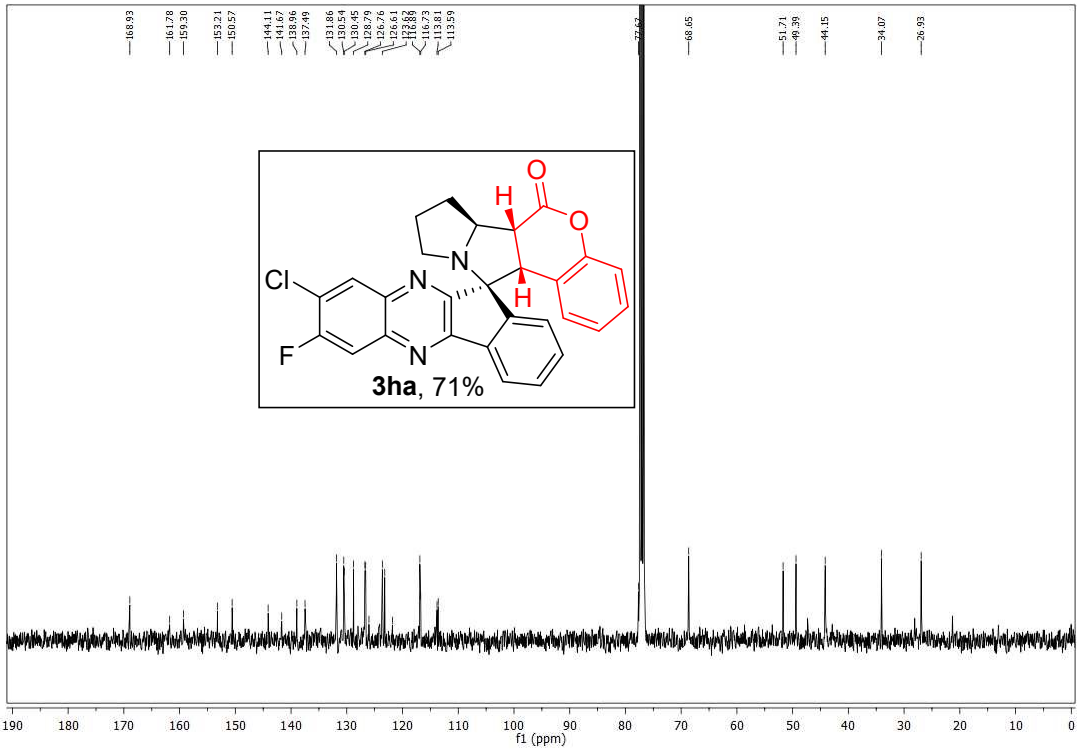
H
H
O
O
3ha, 71%
f1 (ppm)


Cl
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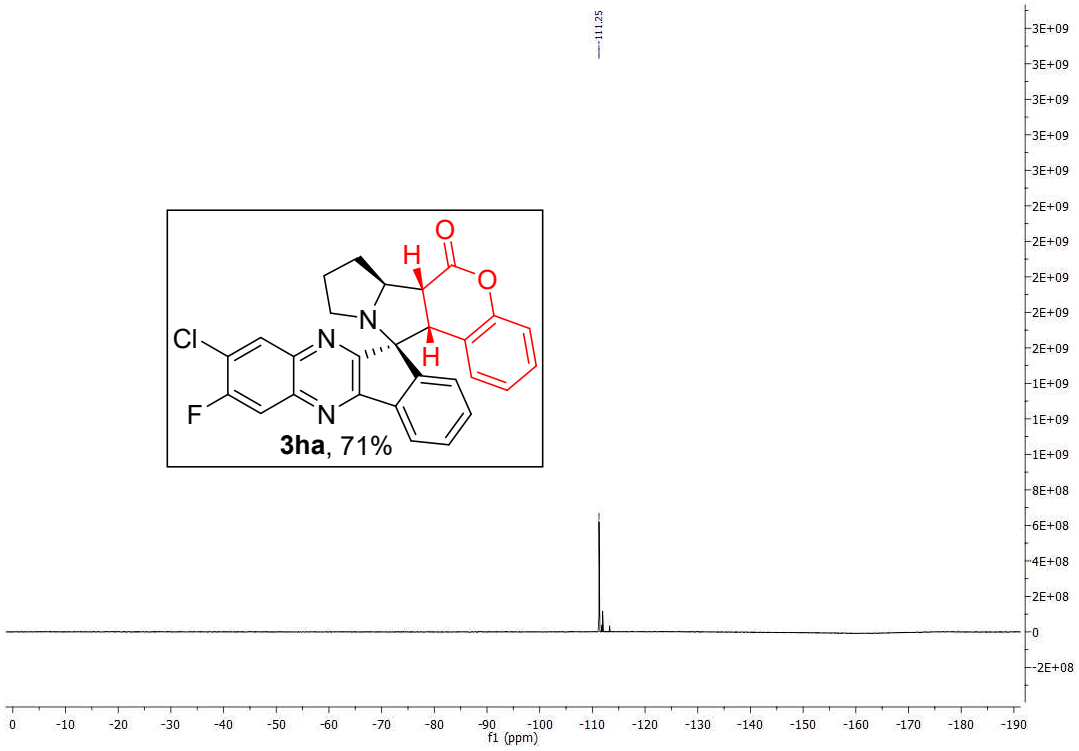
N
N
H
H
O
O
3ha, 71%
f1 (ppm)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1E+09
1E+09
1E+09
8E+08
6E+08
4E+08
2E+08
0
-2E+08
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-30
-40
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-60
-70
-80
-90
-100
-110
-120
-130
-140
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-190
f1 (ppm)
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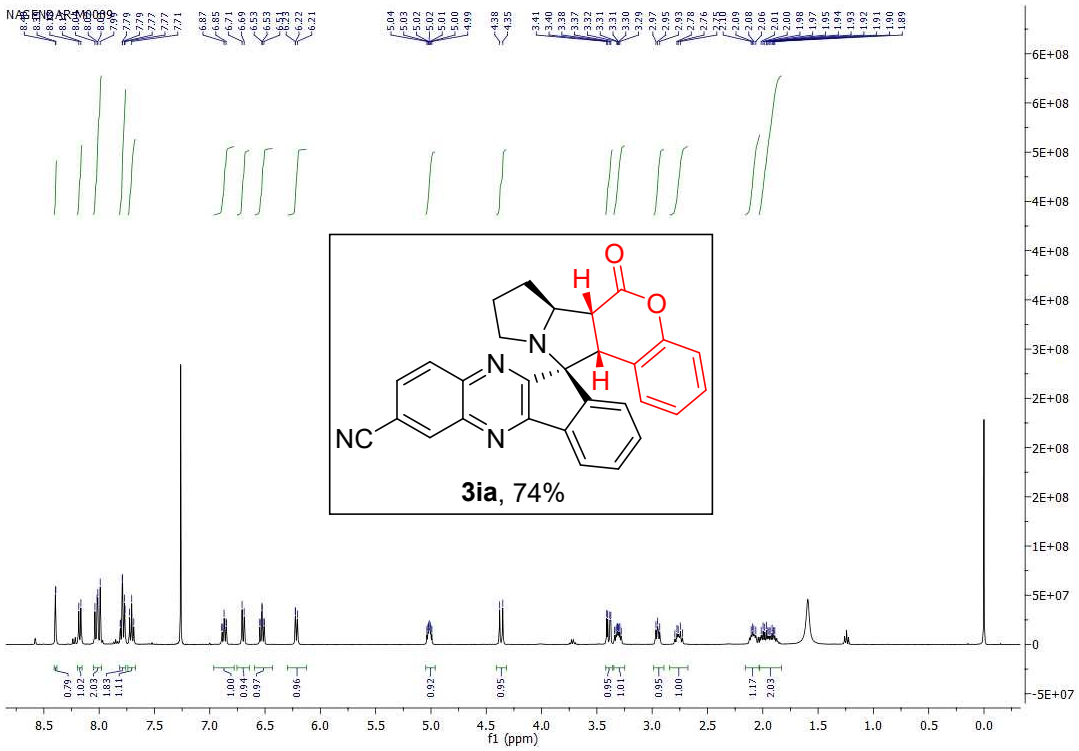
H
O
N
Cl
N
H
F
N
3ha, 71%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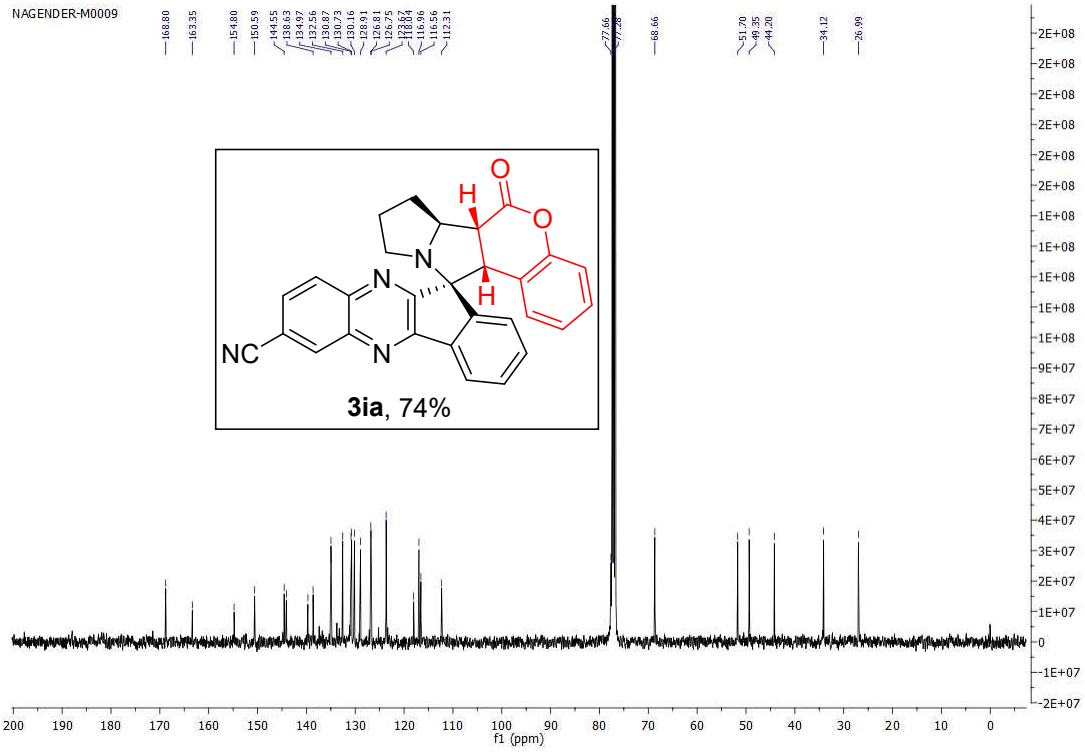
3ia, 74%
f1 (ppm)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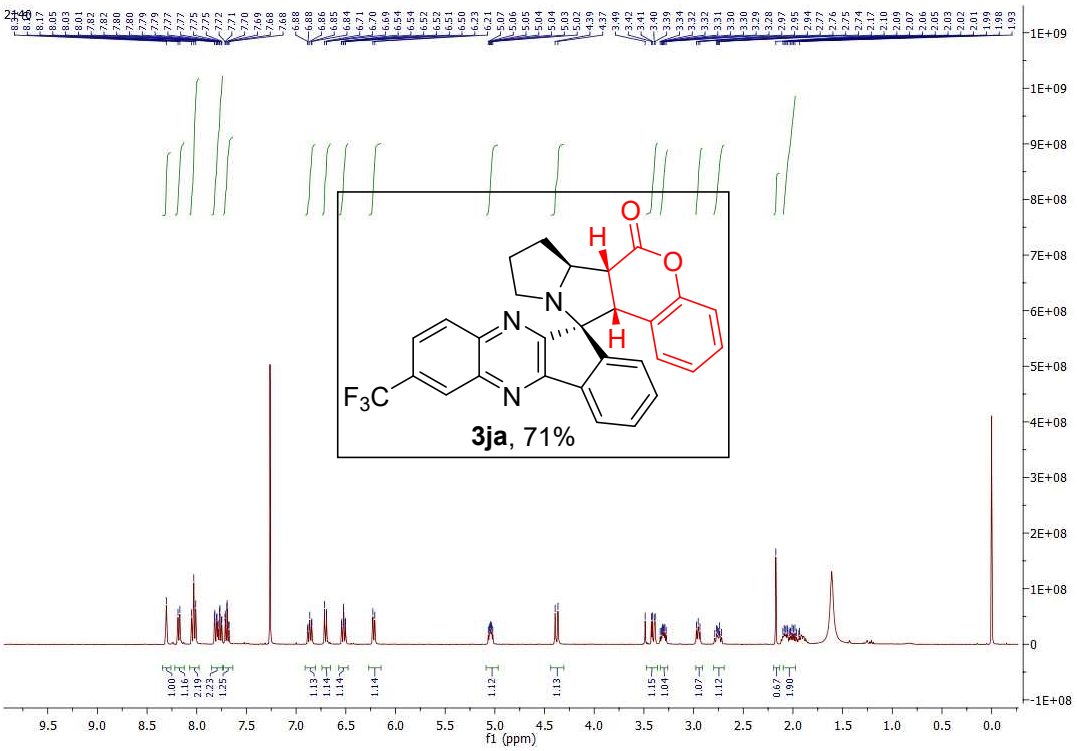
3ia, 74%
f1 (ppm)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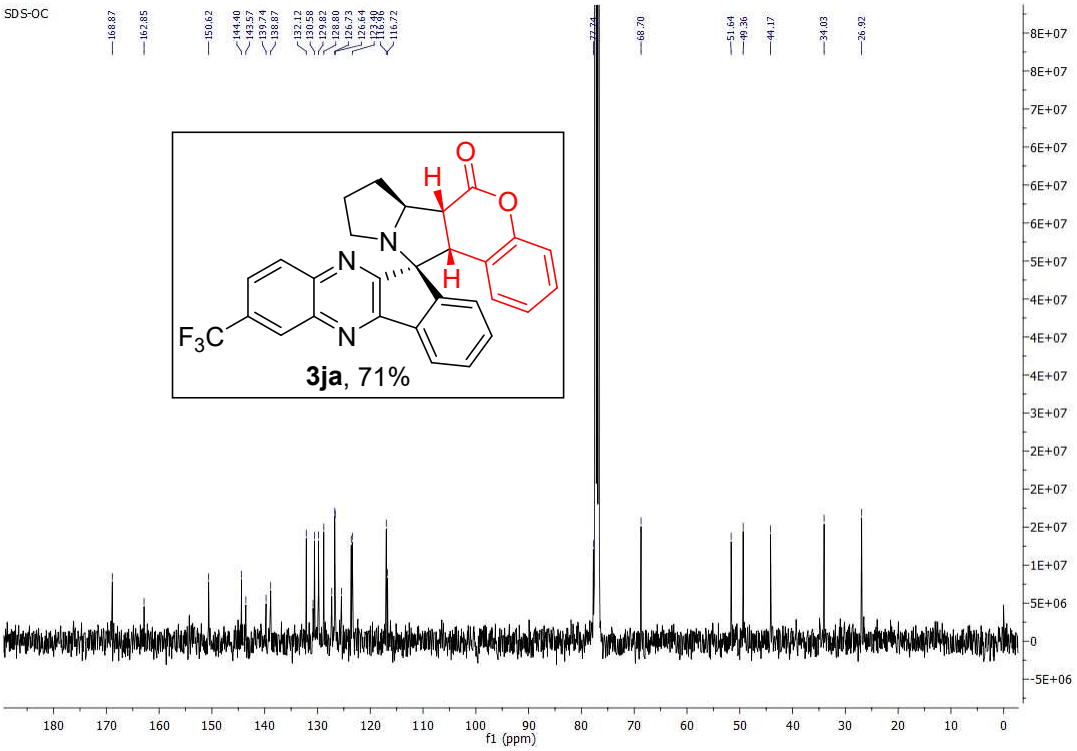
N
H
F3C
N
3ja, 71%
f1 (ppm)


SDS-OC
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N
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H
F3C
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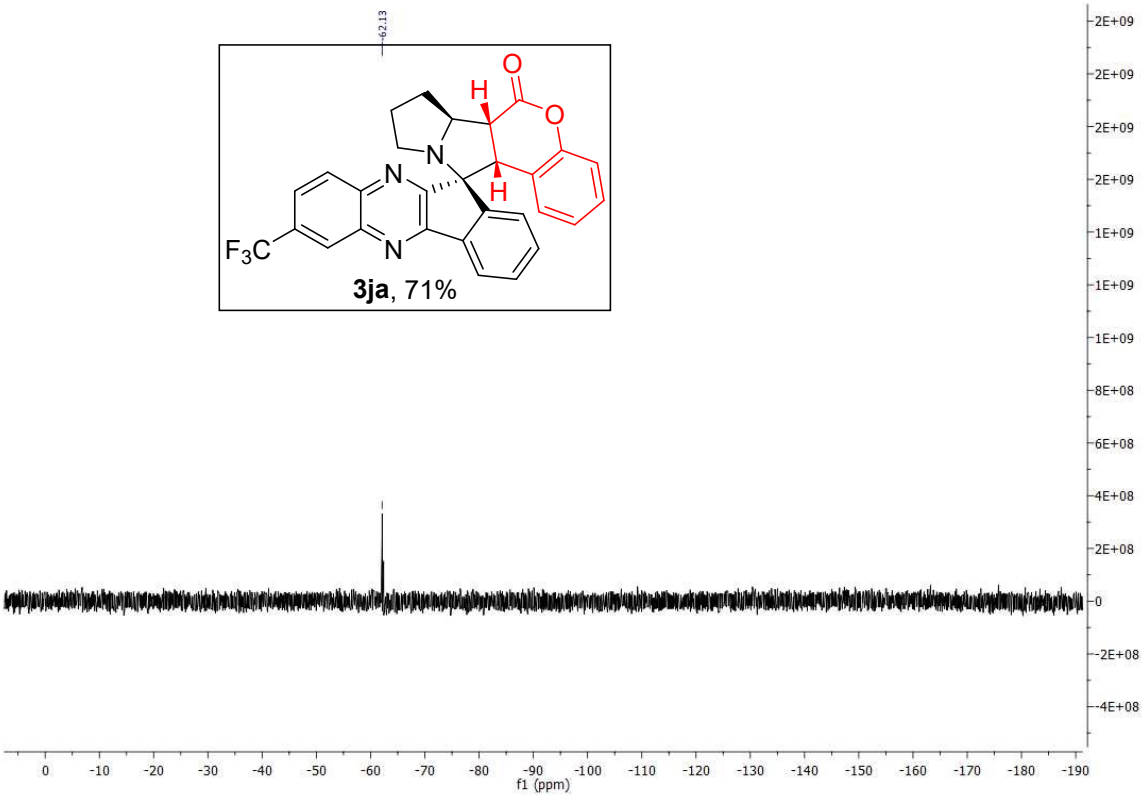
f1 (ppm)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N
H
F3C
N
3ja, 71%
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2E+09
2E+09
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1E+09
1E+09
1E+09
8E+08
6E+08
4E+08
2E+08
0
-2E+08
-4E+08
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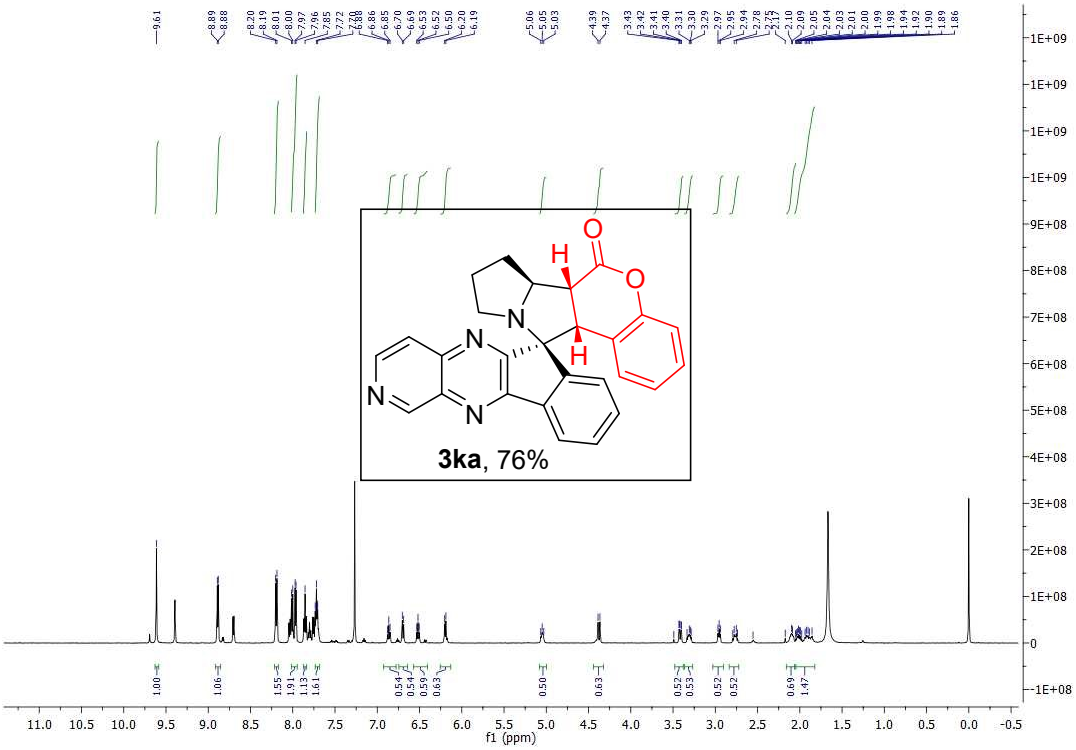
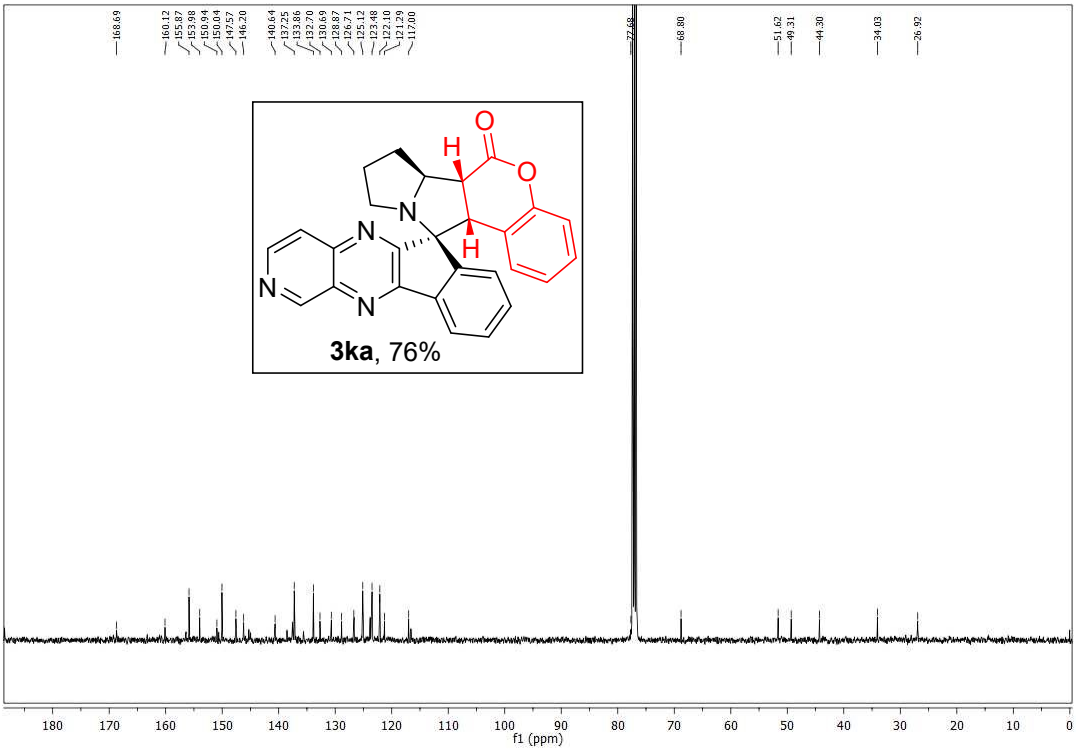
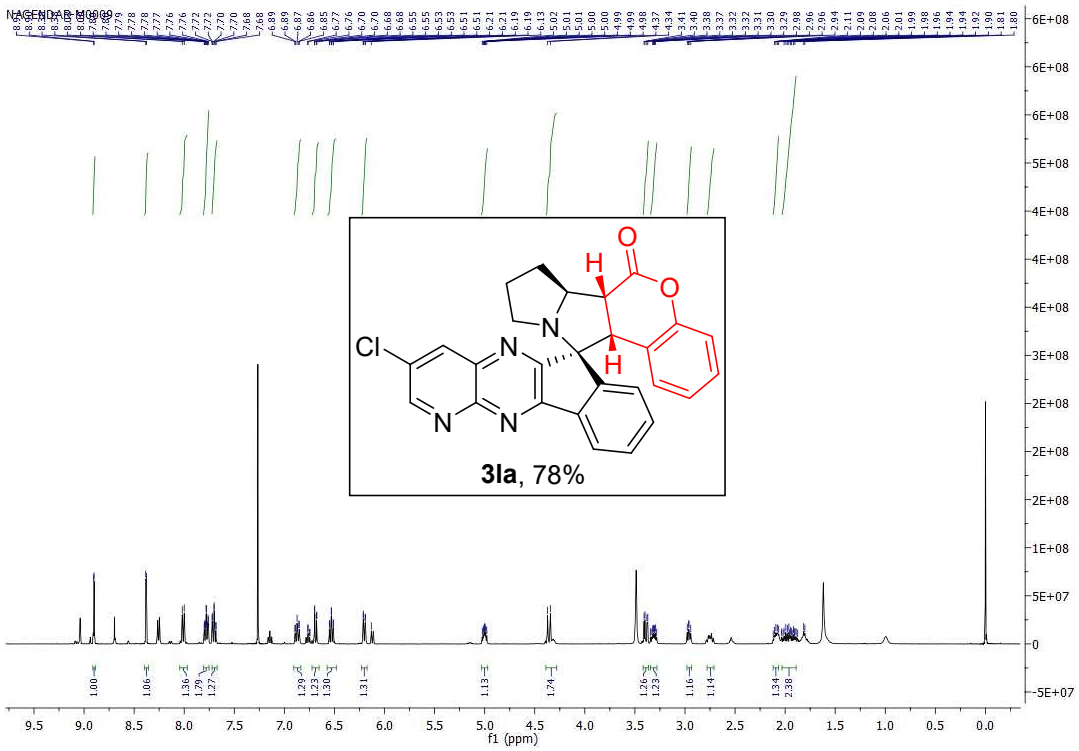
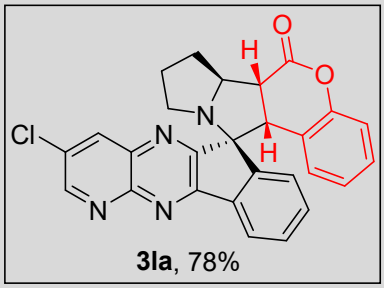
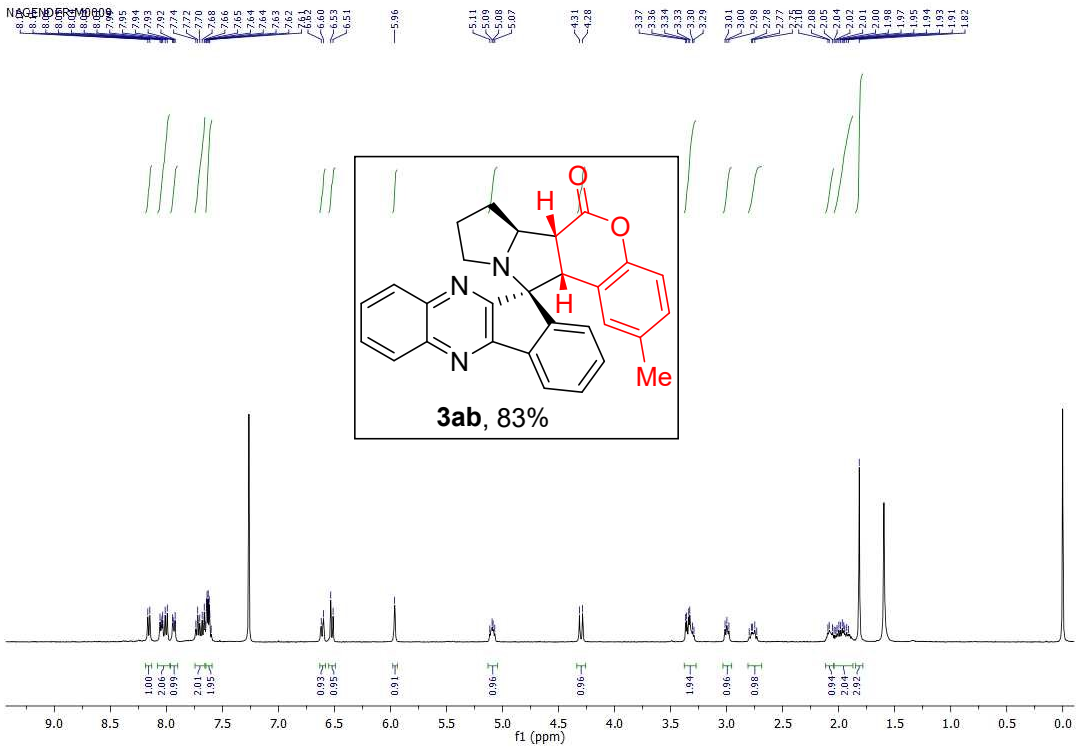
f1 (ppm)

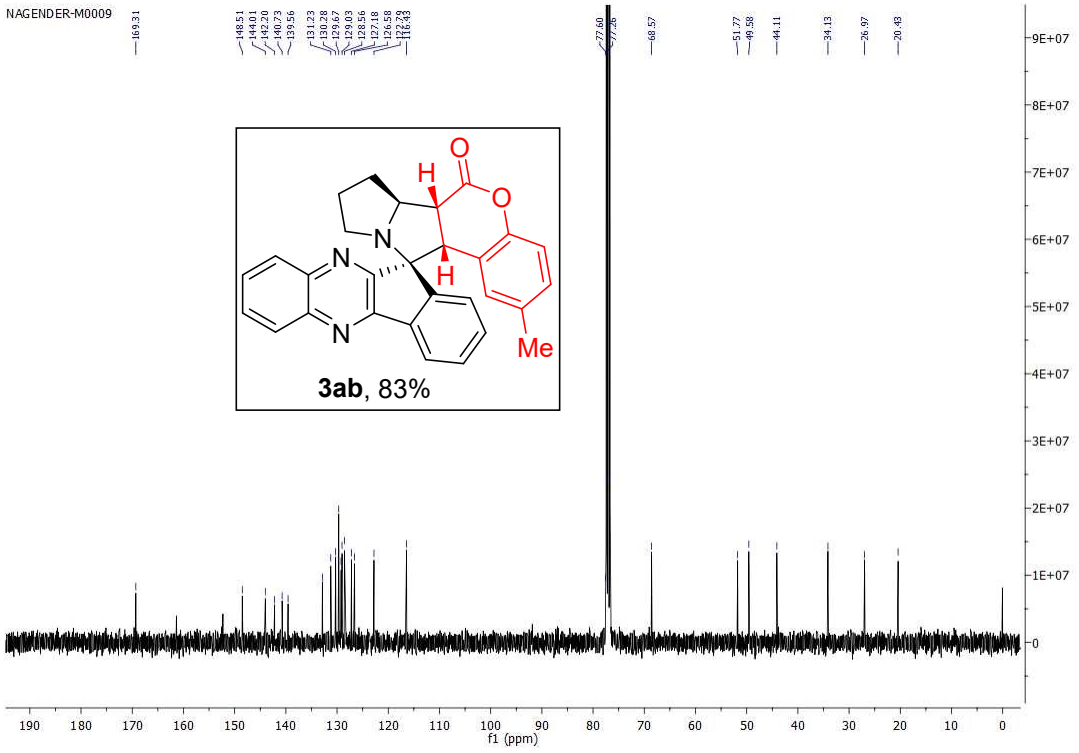

3ka, 76%
f1 (ppm)

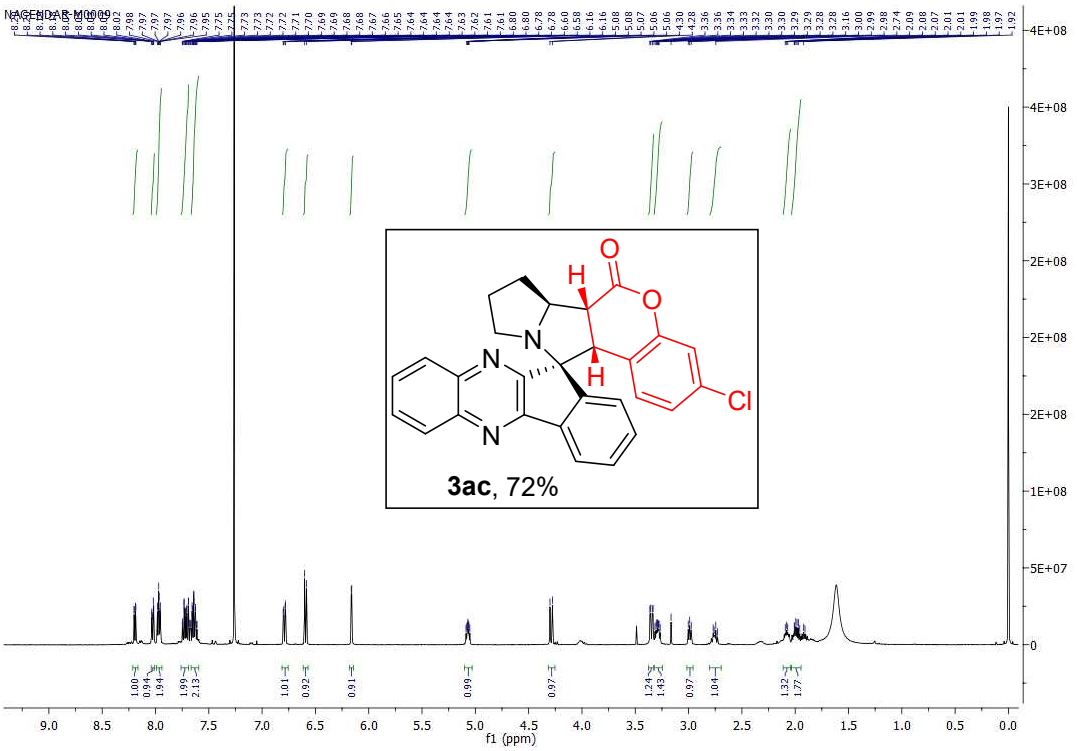

3ka, 76%
f1 (ppm)

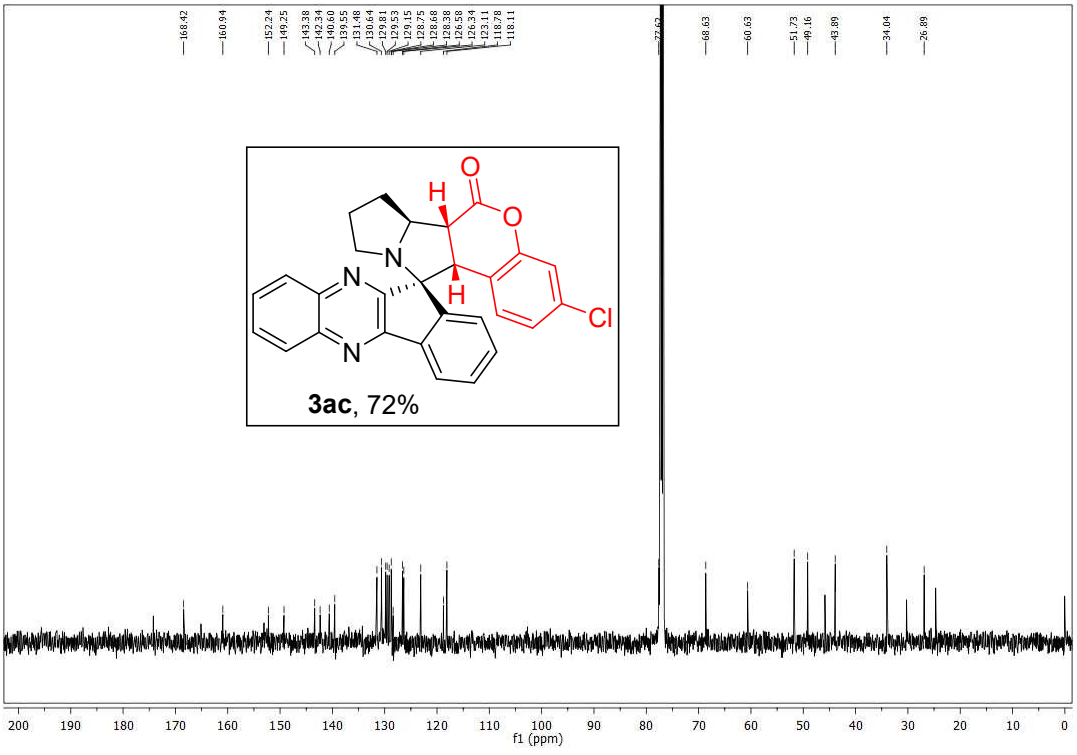

3la, 78%
f1 (ppm)

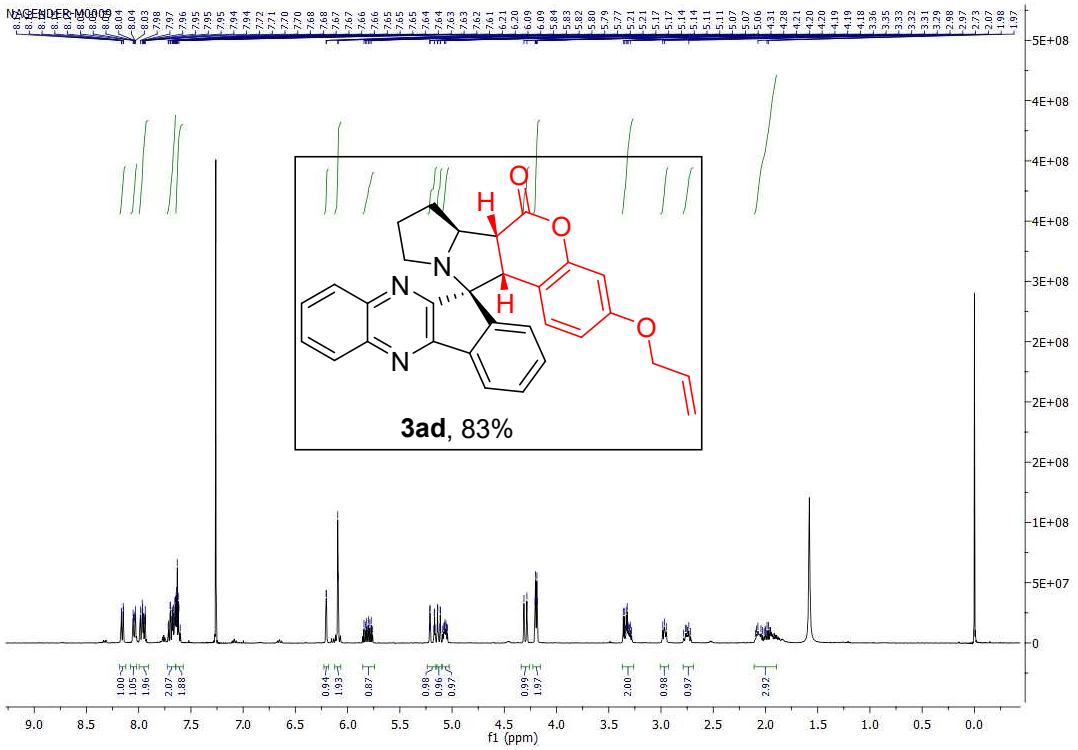

3la, 78%

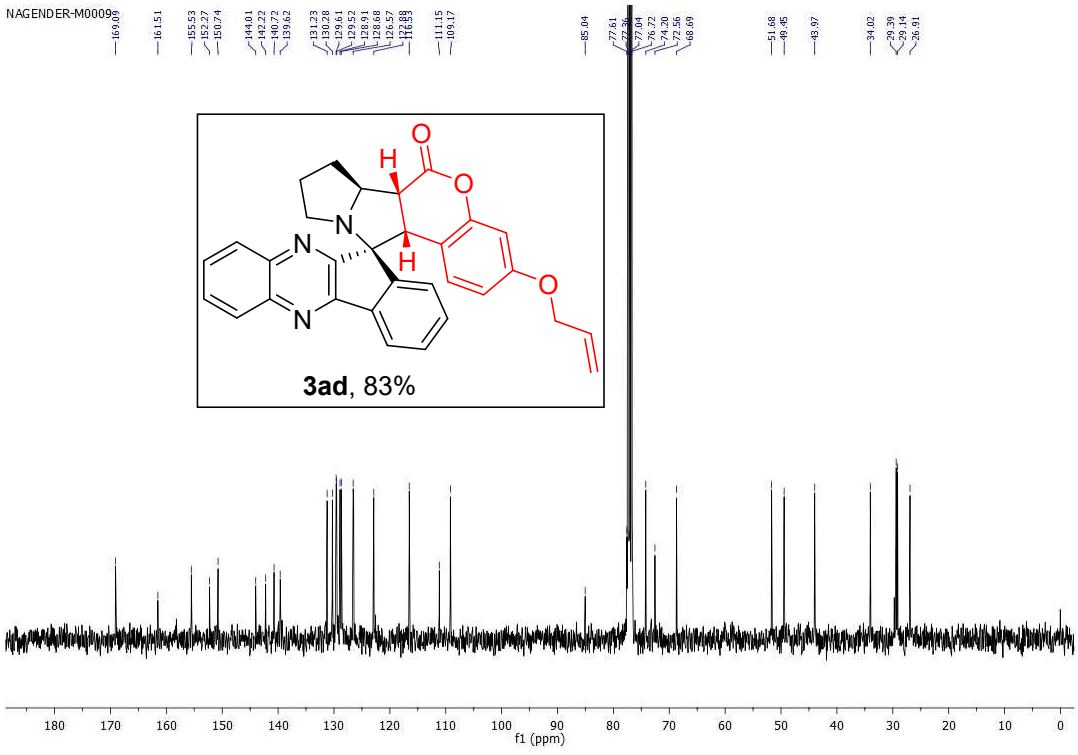

NAGENDER-M0009
3ab, 83%
f1 (ppm)

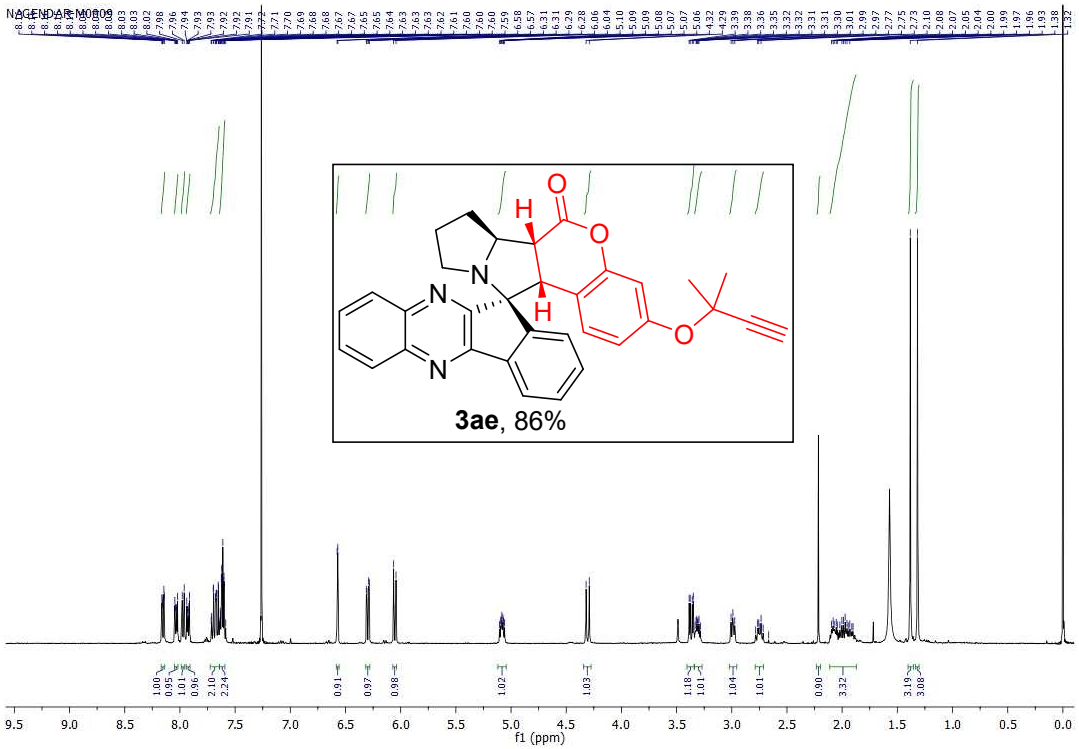

NAGENDER-M0009
3ab, 83%
f1 (ppm)

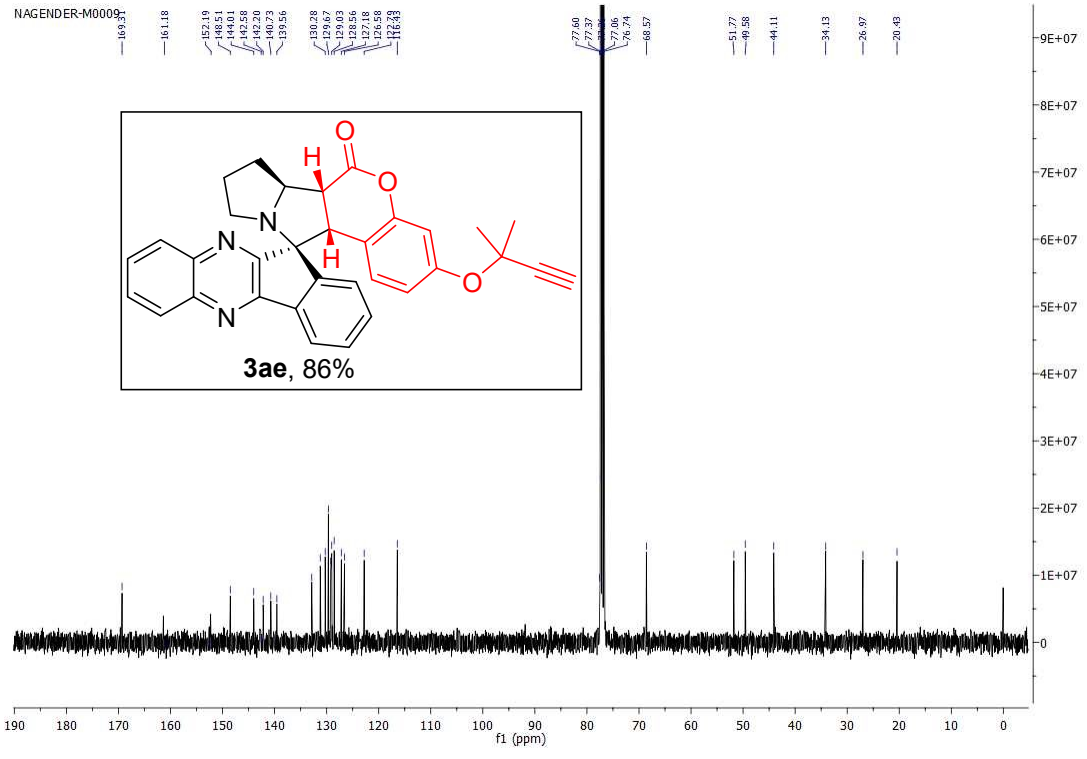

3ac, 72%
f1 (ppm)

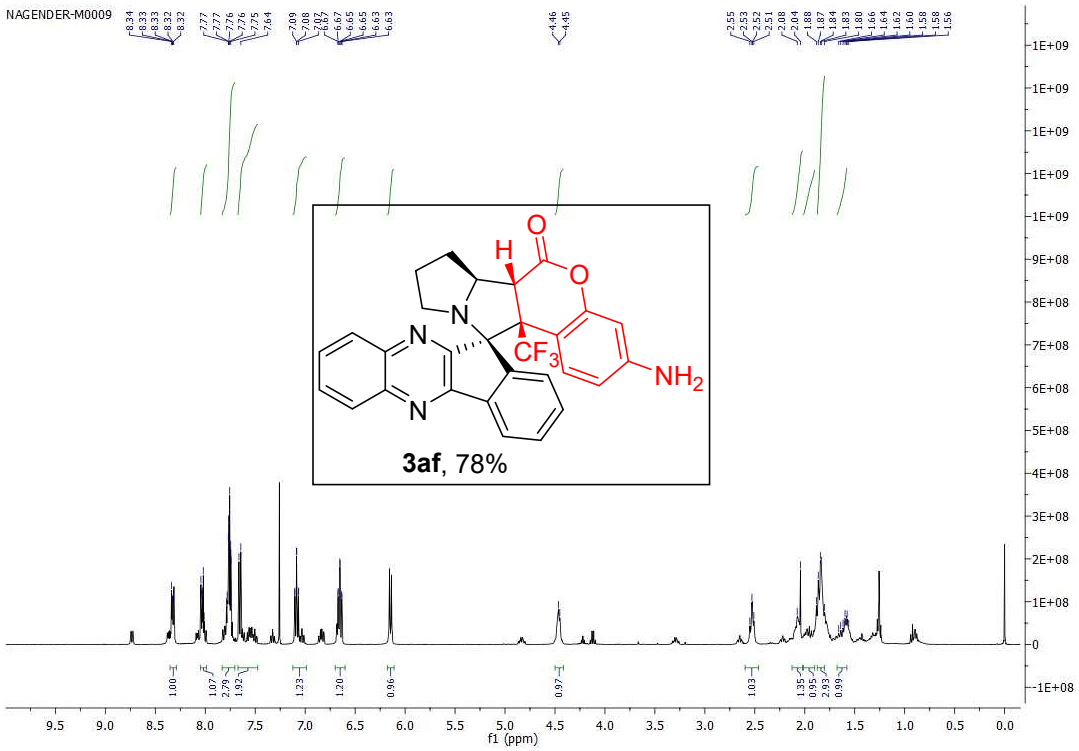

3ac, 72%
f1 (ppm)

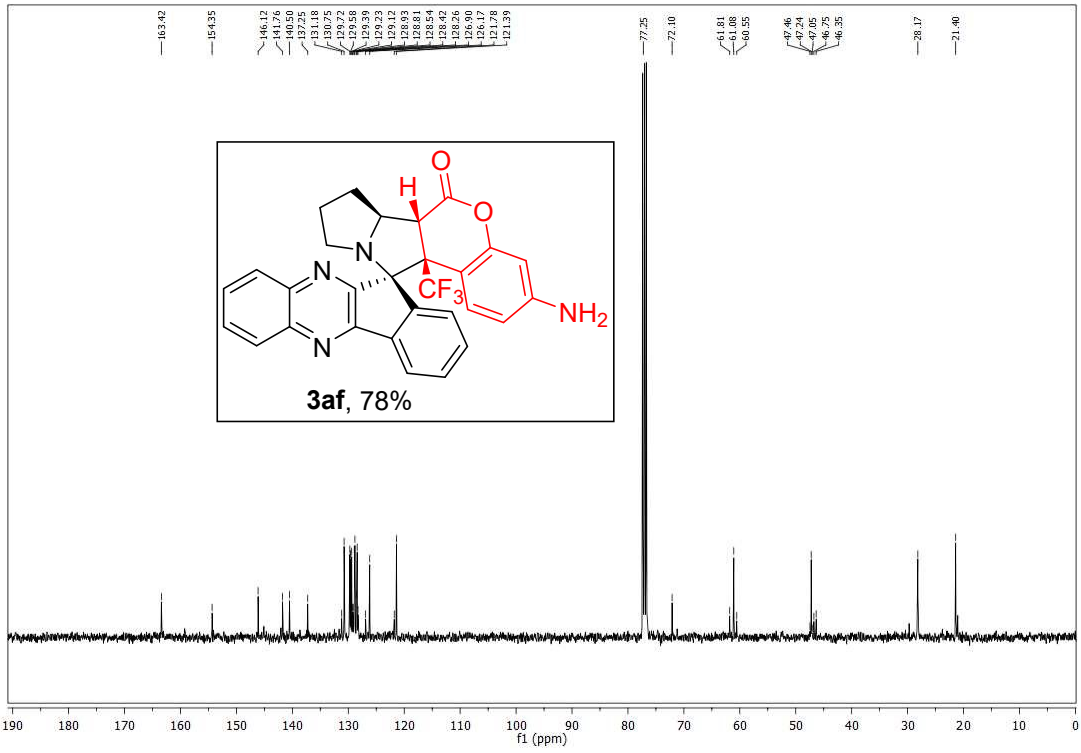

3ad, 83%
f1 (ppm)

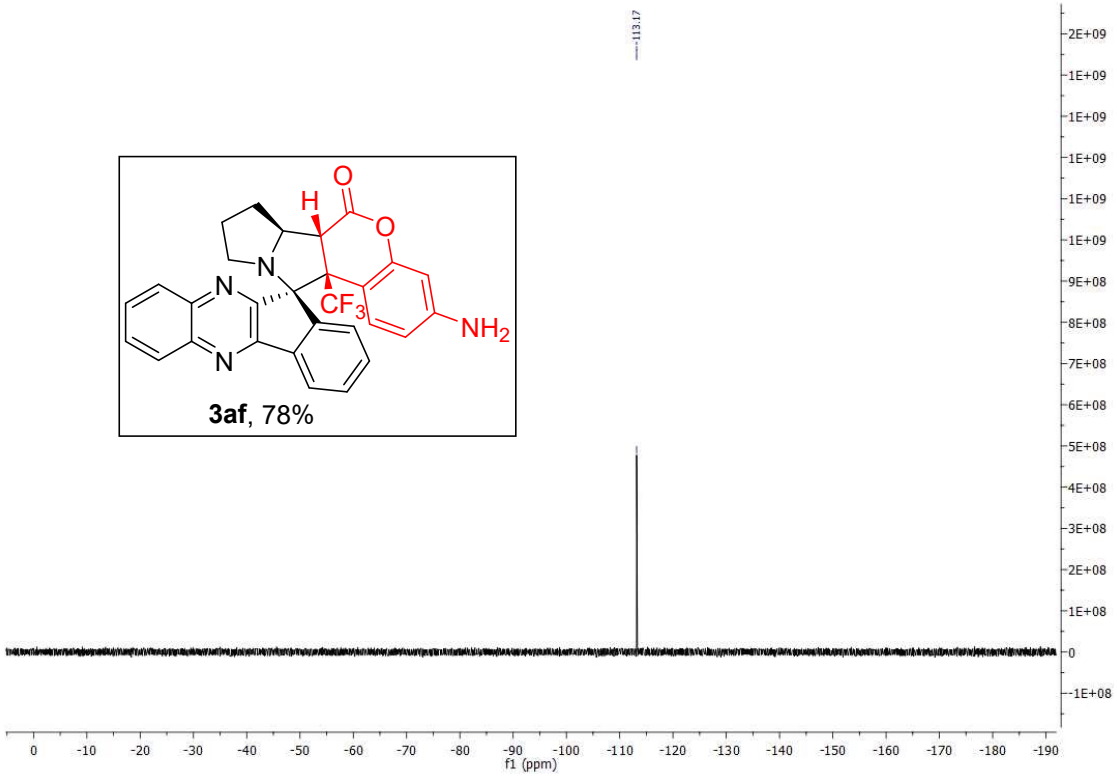

NAGENDER-M0009
3ad, 83%
f1 (ppm)

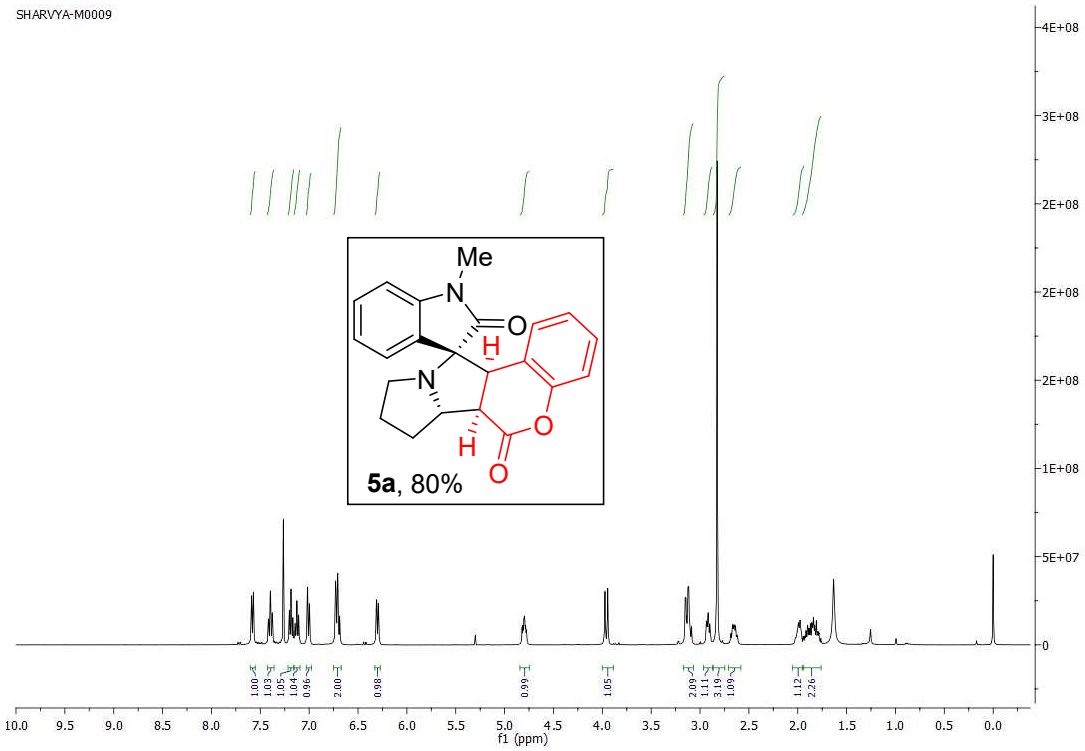

NAGENDAR-M0009
3ae, 86%
f1 (ppm)

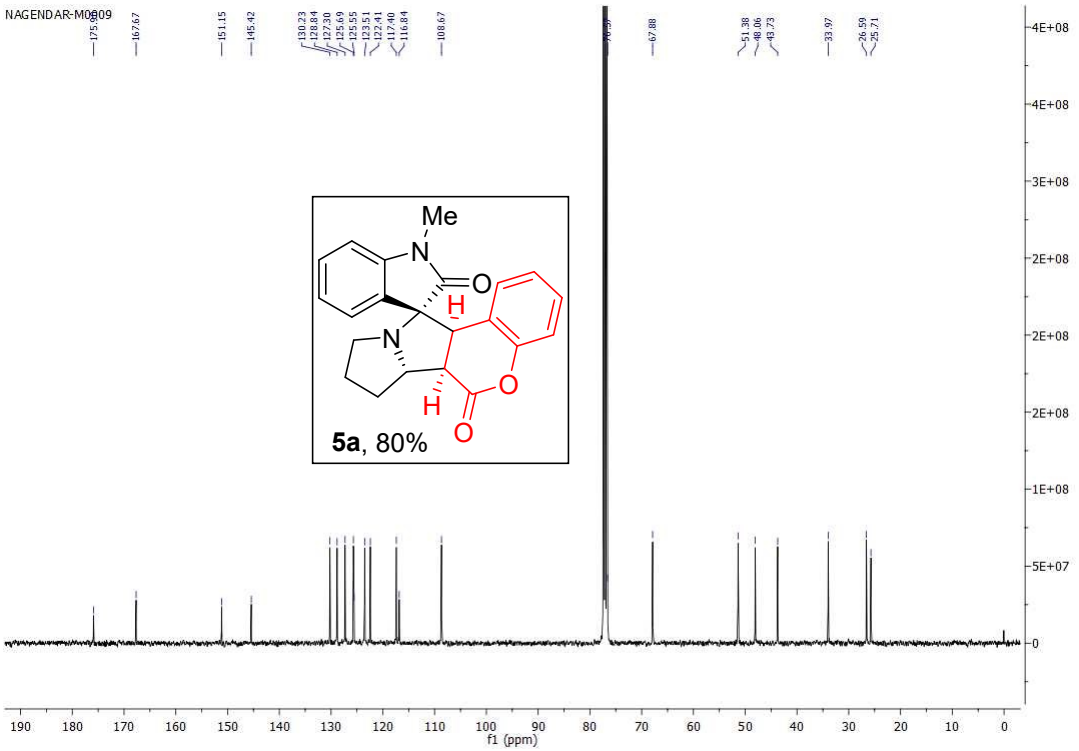

NAGENDER-M0009
3ae, 86%
f1 (ppm)

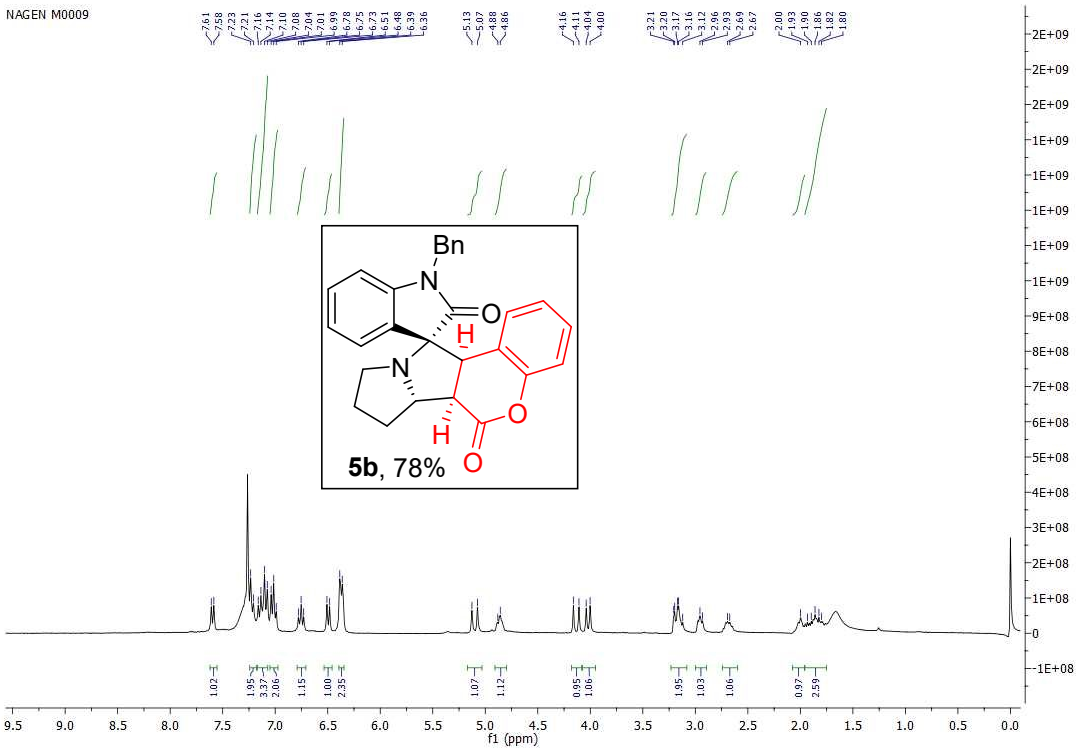

NAGENDER-M0009
3af, 78%
f1 (ppm)

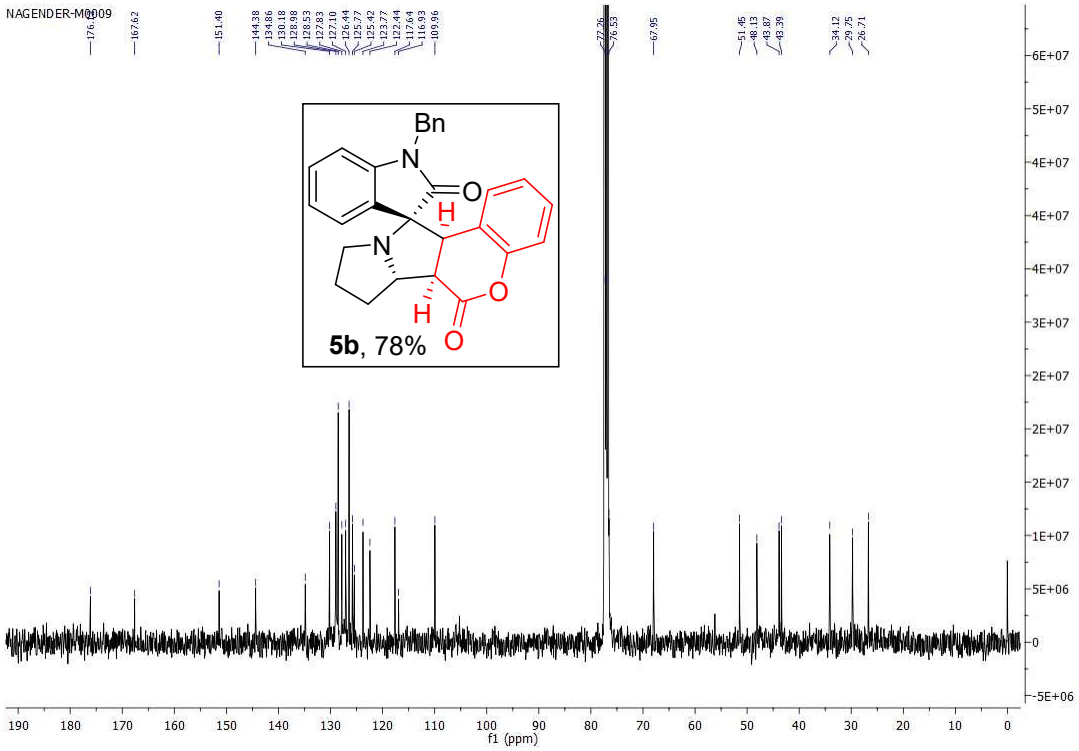

3af, 78%
f1 (ppm)

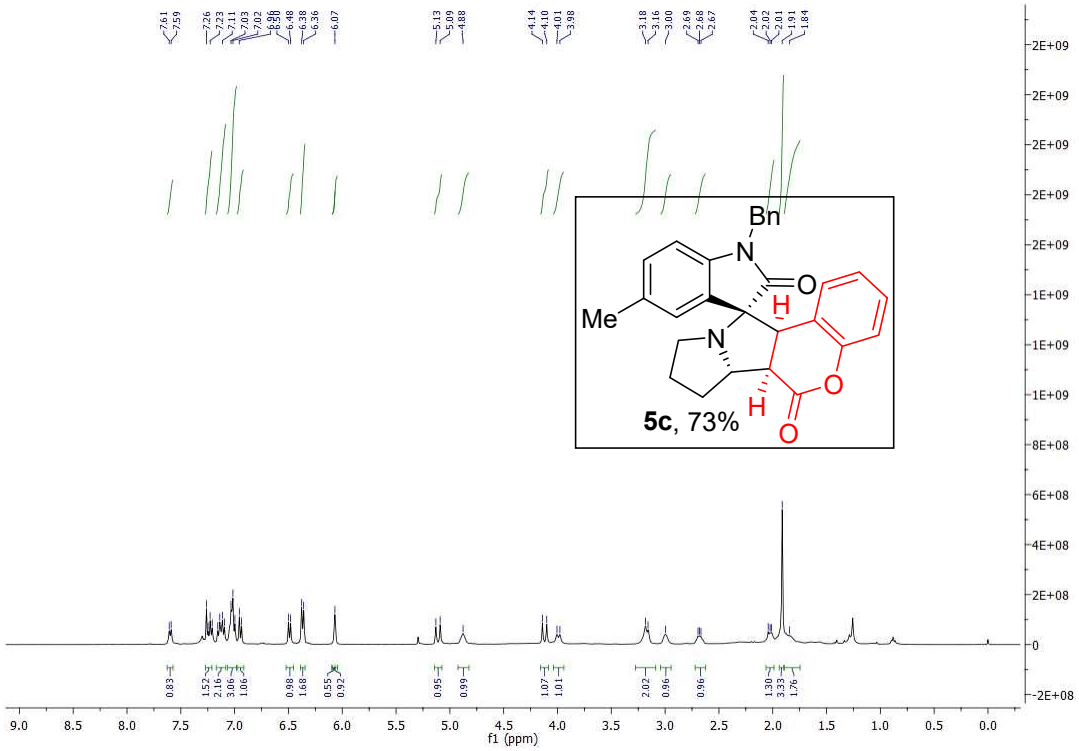

O
H
O
N
N
N
CF3
NH2
3af, 78%
-113.17
2E+09
1E+09
1E+09
1E+09
1E+09
1E+09
1E+09
9E+08
8E+08
7E+08
6E+08
5E+08
4E+08
3E+08
2E+08
1E+08
0
-1E+08
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

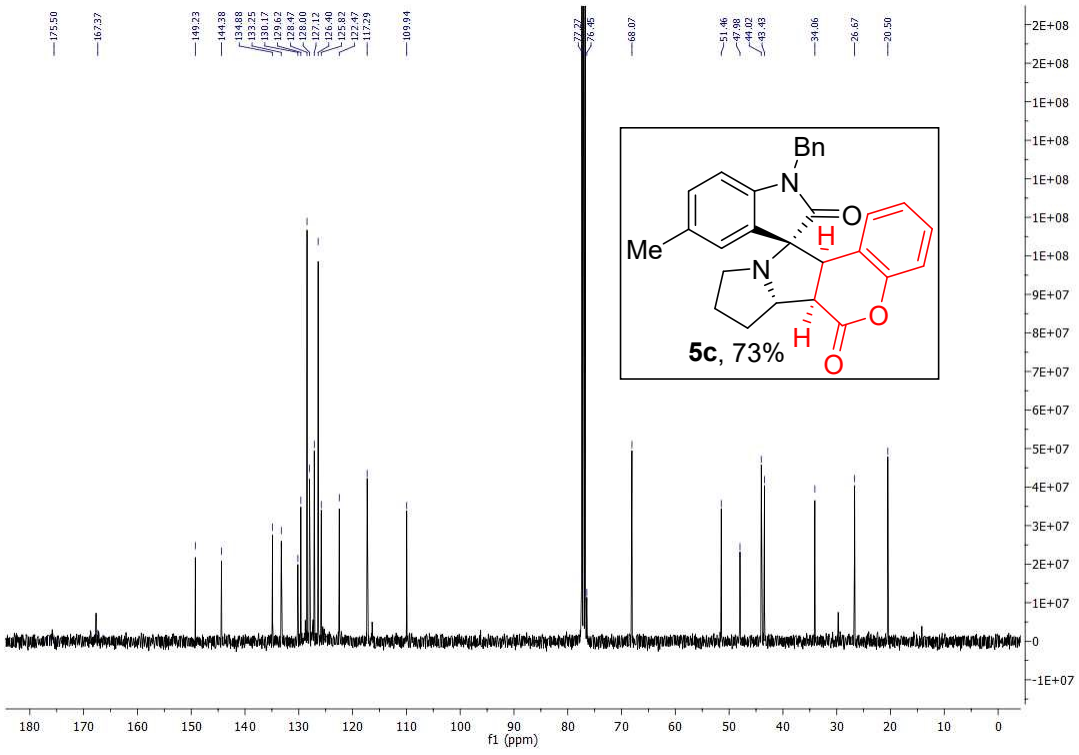

SHARVYA-M0009
Me
N
O
H
N
O
H
O
5a, 80%
f1 (ppm)

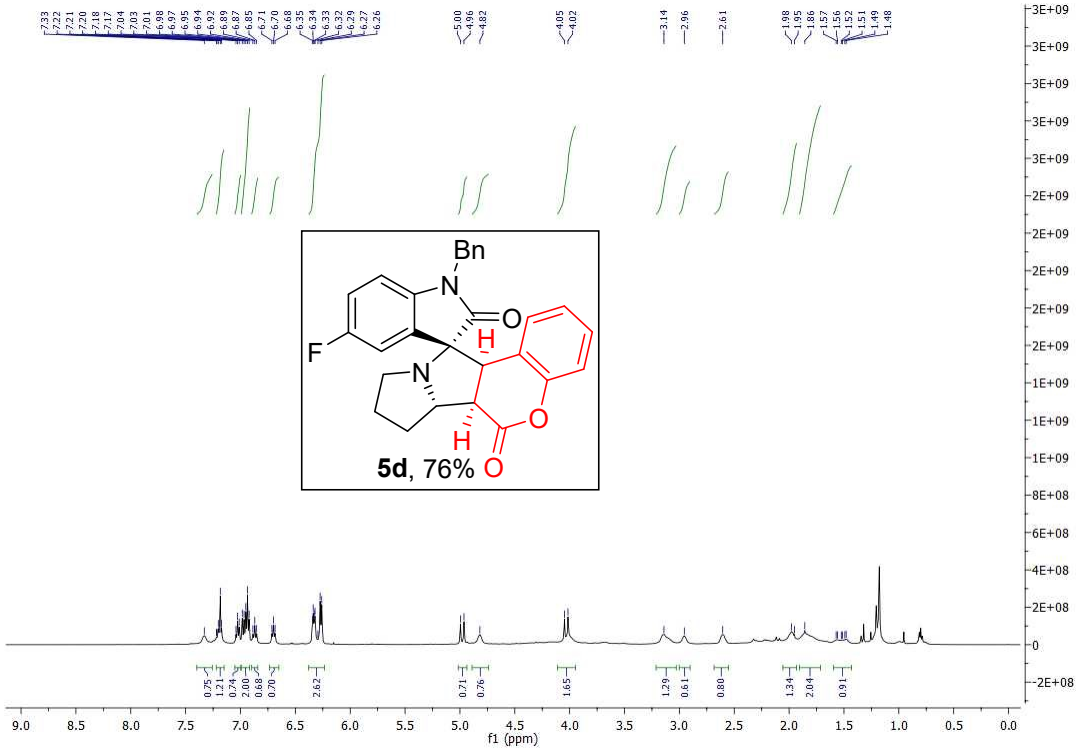

NAGENDAR-M0809
Me
N
O
H
N
O
H
O
5a, 80%
f1 (ppm)

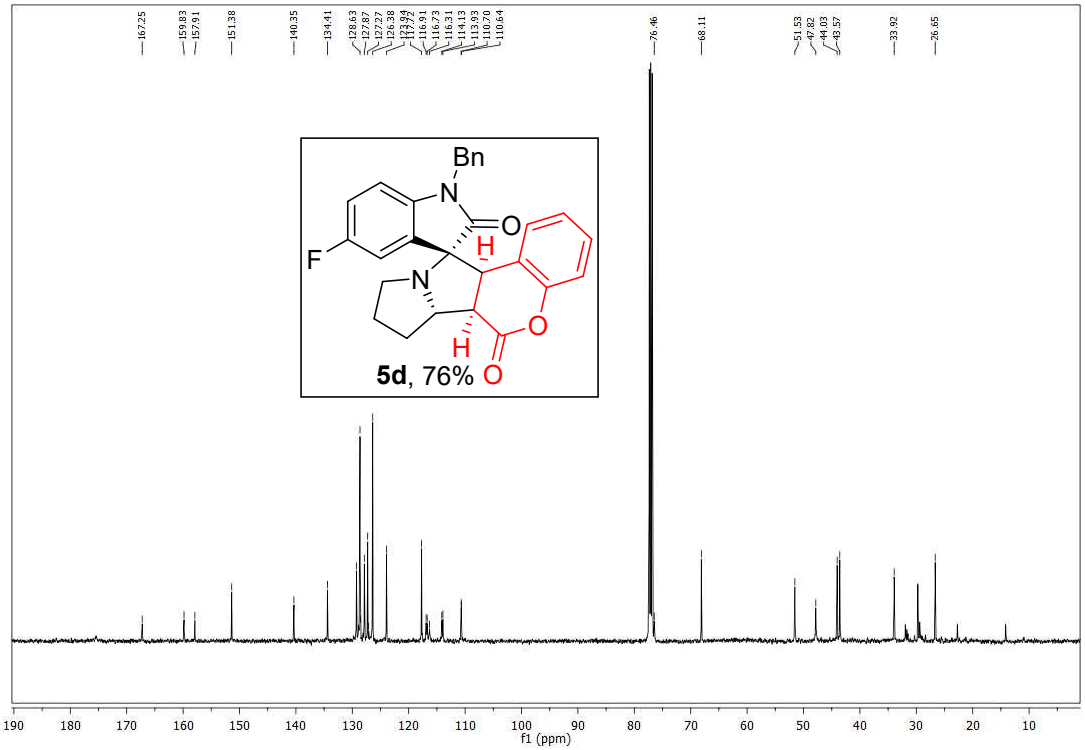

NAGEN M0009
Bn
N
O
H
N
O
H
O
5b, 78%
f1 (ppm)

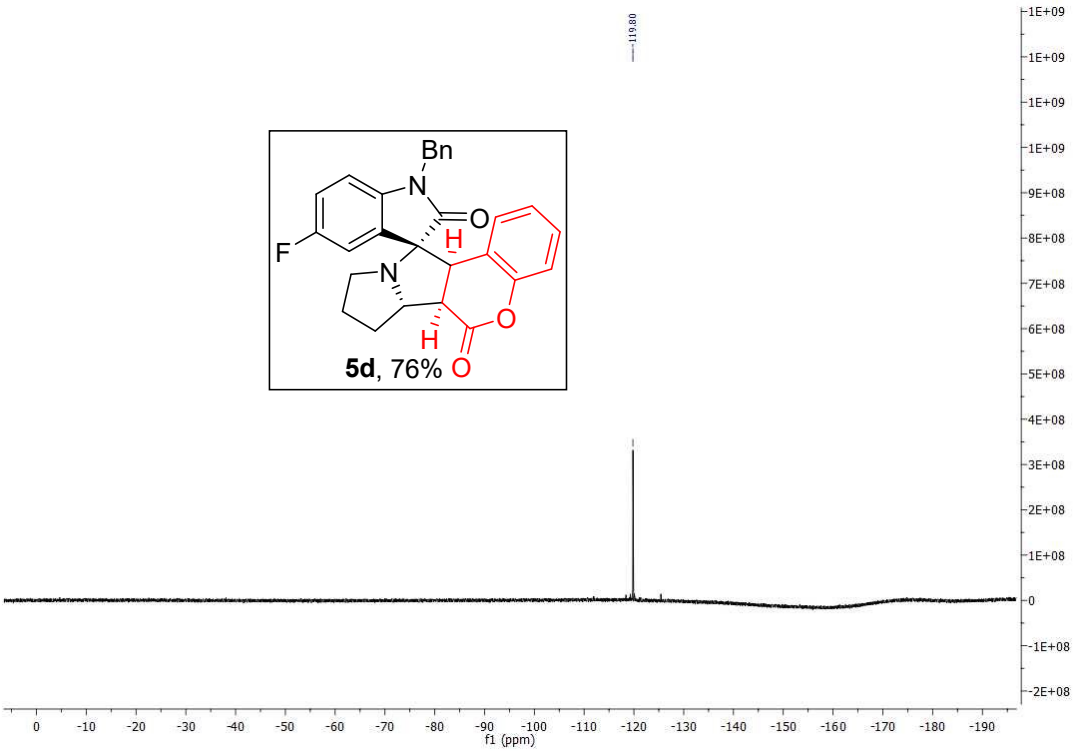

NAGENDER-M0009
Bn
N
O
H
N
O
H
O
5b, 78%
f1 (ppm)

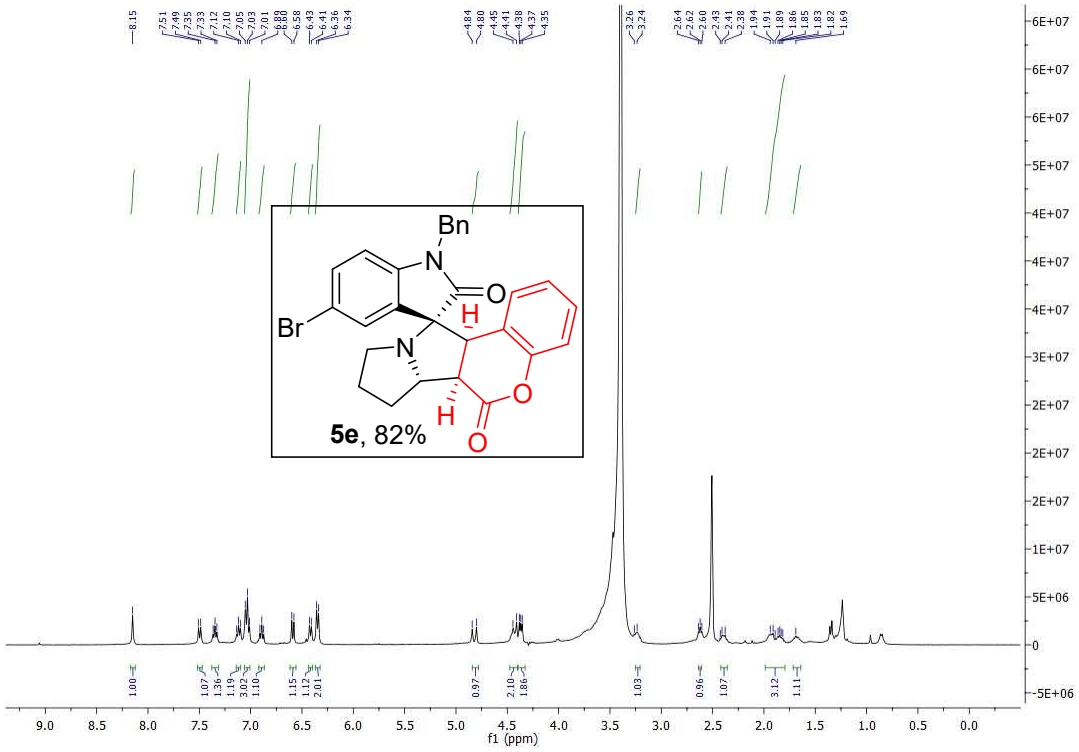

Bn
N
O
H
Me
N
O
H
O
5c, 73%
f1 (ppm)

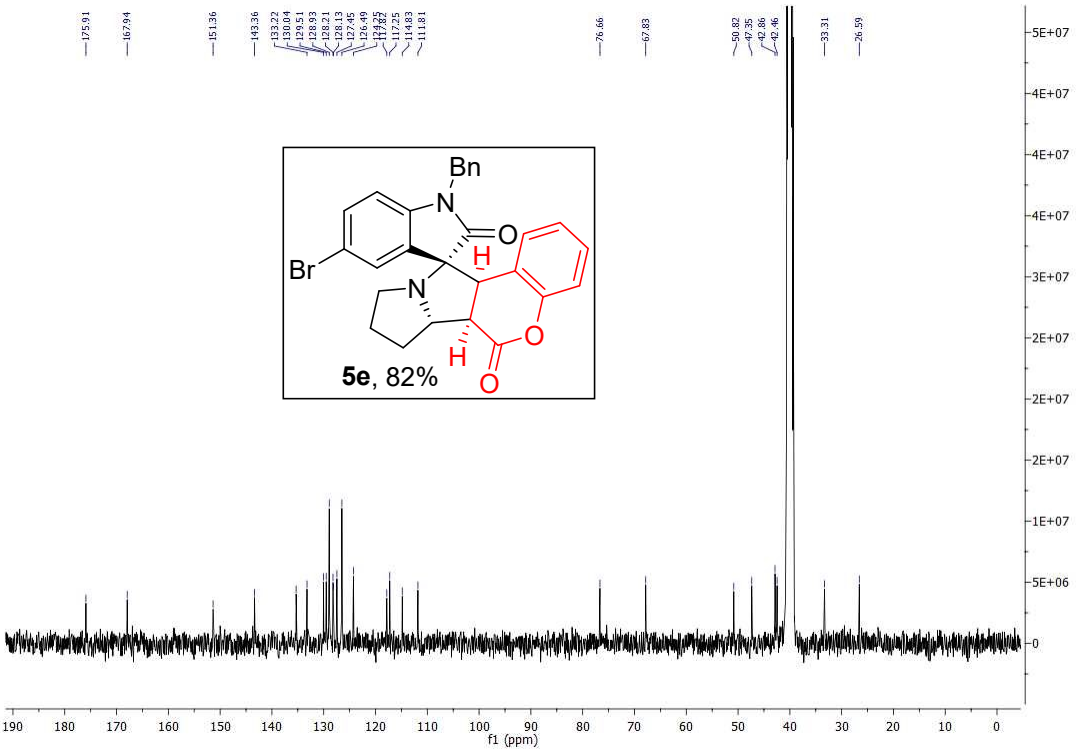

Bn
N
O
H
Me
N
O
H
O
5c, 73%
f1 (ppm)

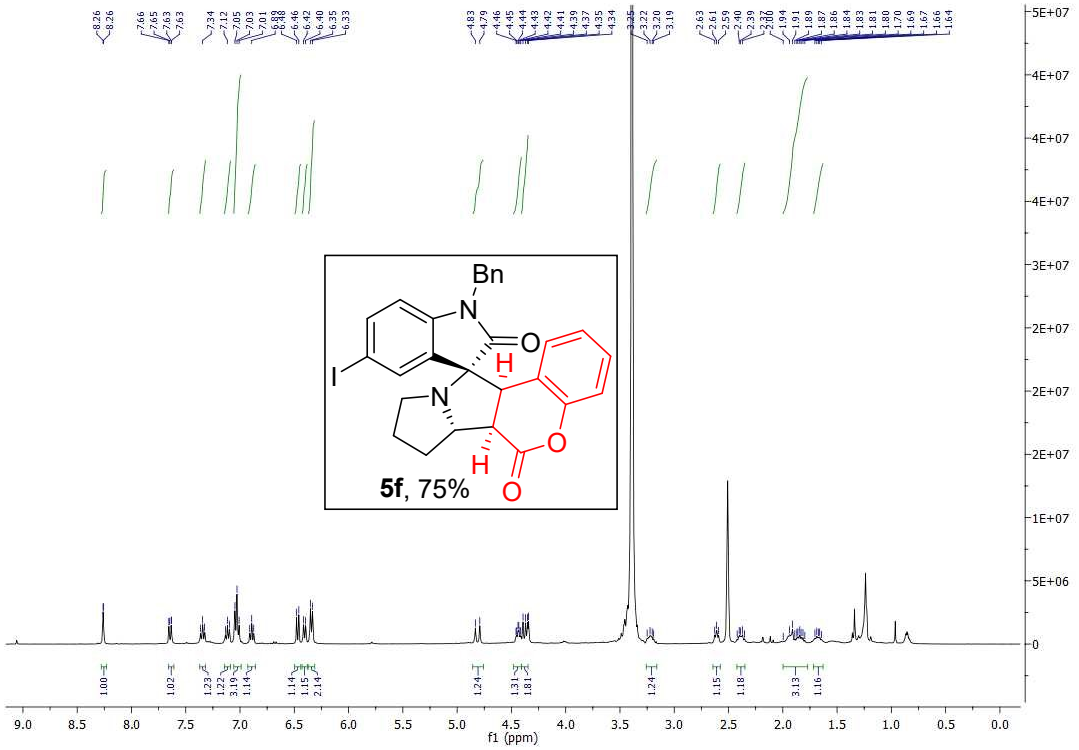

Bn
N
O
F
H
N
O
H
O
5d, 76% O
f1 (ppm)

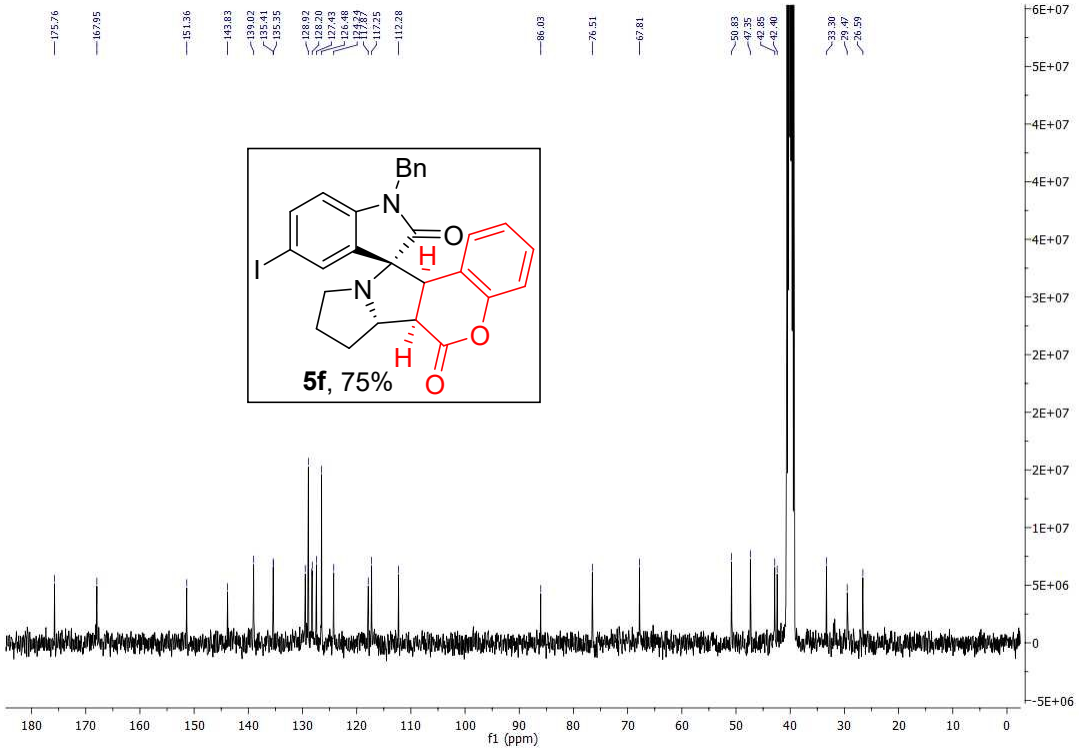

Bn
N
O
F
H
N
O
H
O
5d, 76% O
f1 (ppm)

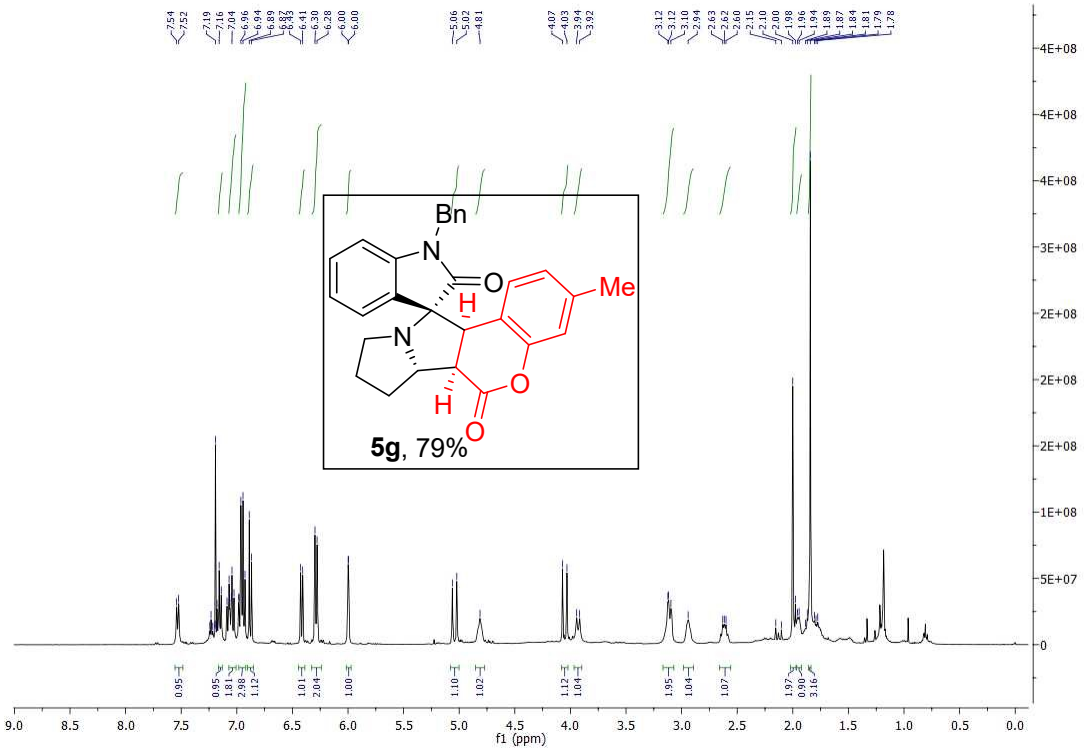

Bn
N
O
H
F
N
O
H
O
5d, 76%
-119.080
1E+09
1E+09
1E+09
1E+09
9E+08
8E+08
7E+08
6E+08
5E+08
4E+08
3E+08
2E+08
1E+08
0
-1E+08
-2E+08
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190
f1 (ppm)

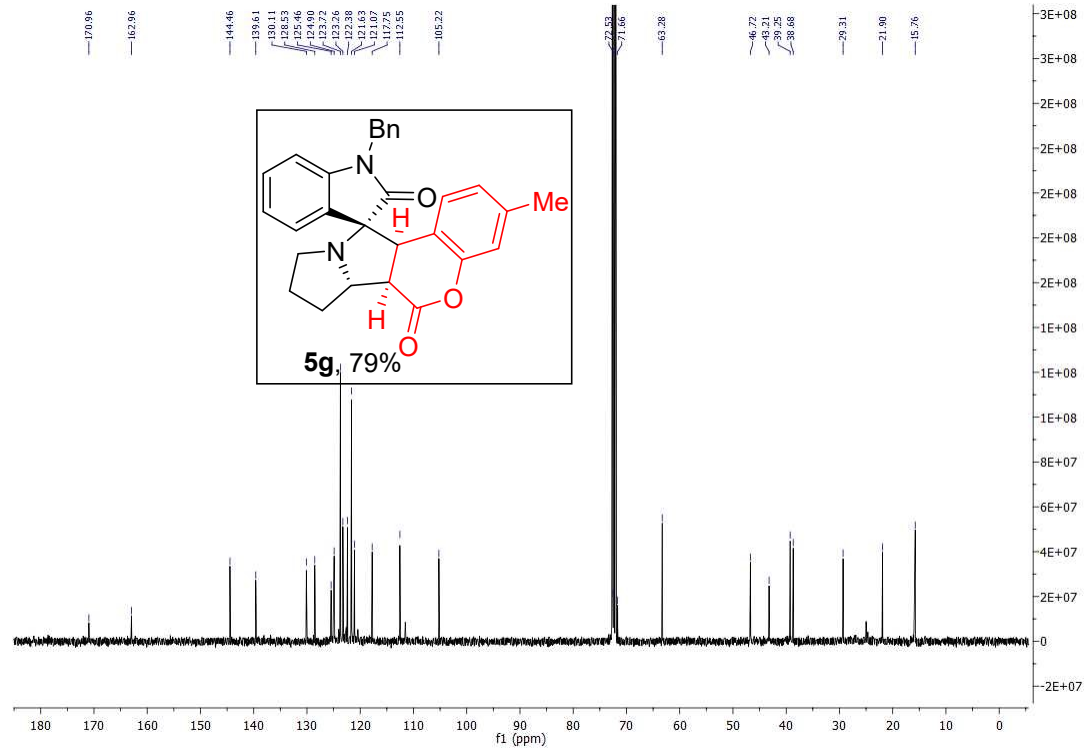

Bn
N
O
H
Br
N
O
H
O
5e, 82%
f1 (ppm)

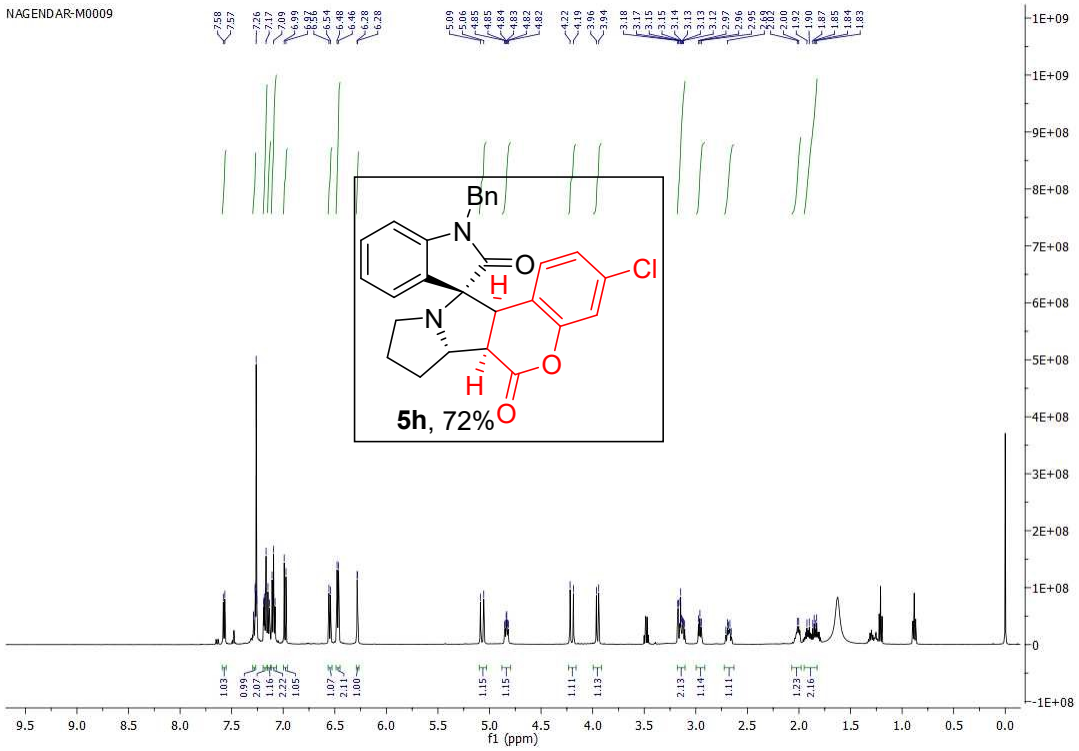

Bn
N
O
H
Br
N
O
H
O
5e, 82%
f1 (ppm)

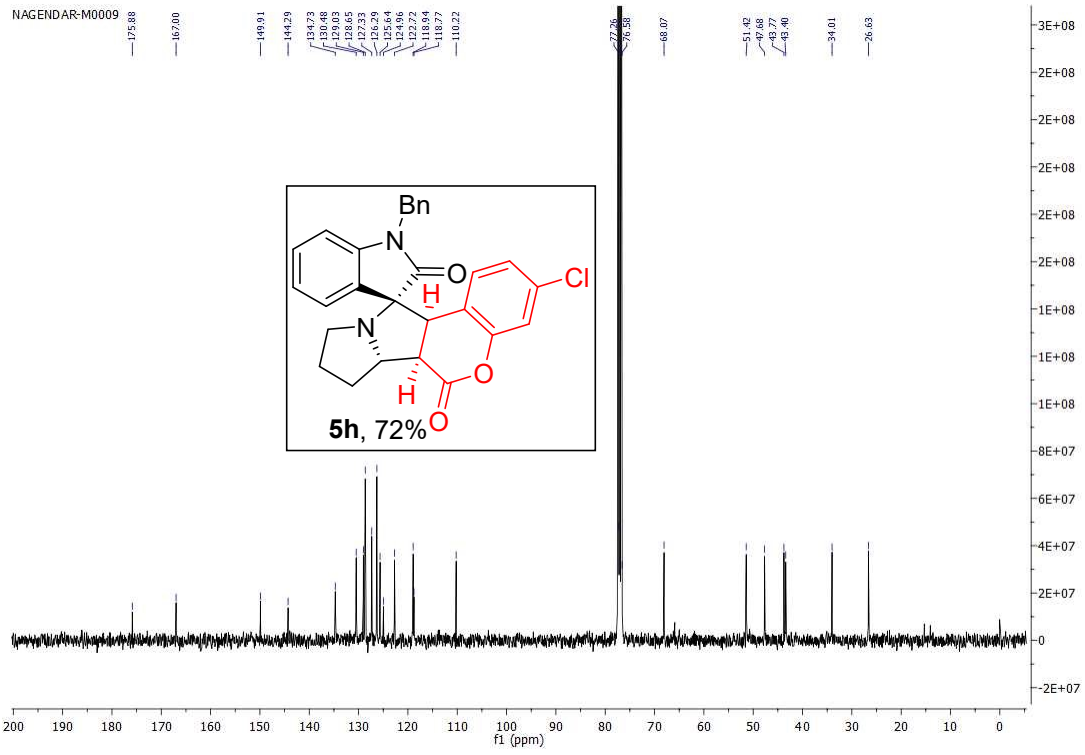

Bn
N
O
H
I
N
O
H
O
5f, 75%
f1 (ppm)

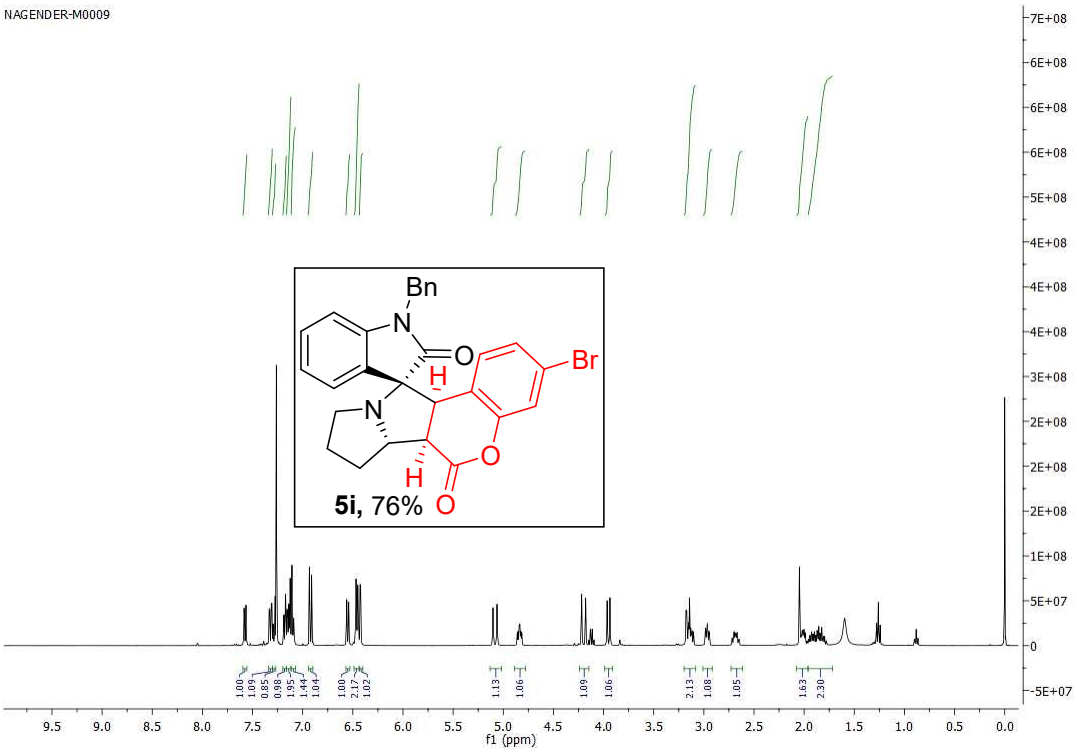

Bn
N
O
H
I
N
O
H
O
5f, 75%
f1 (ppm)

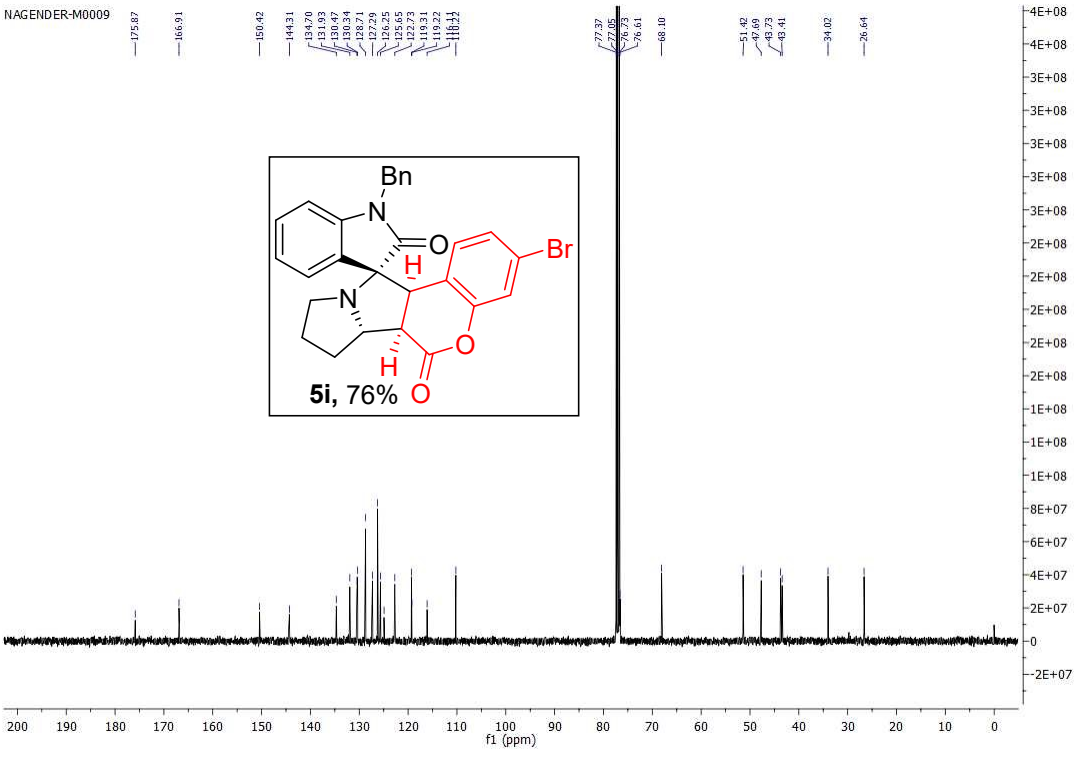

Bn
N
O
H
Me
N
O
H
O
5g, 79%
f1 (ppm)

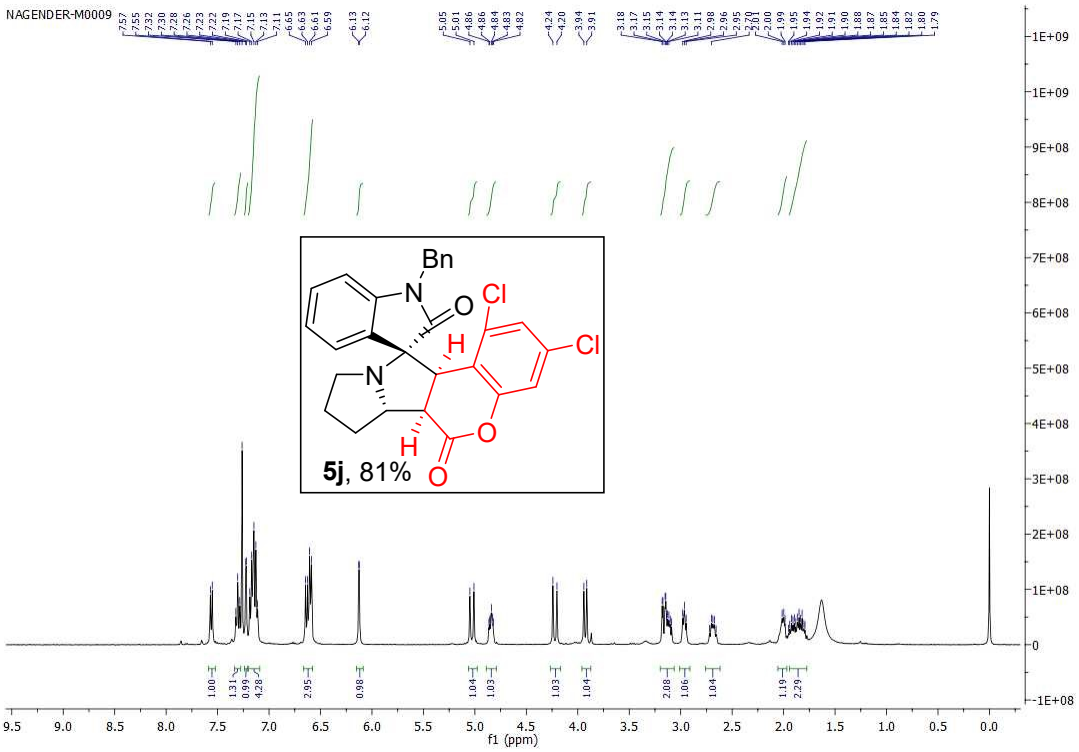

Bn
N
O
H
Me
N
O
H
O
5g, 79%
f1 (ppm)

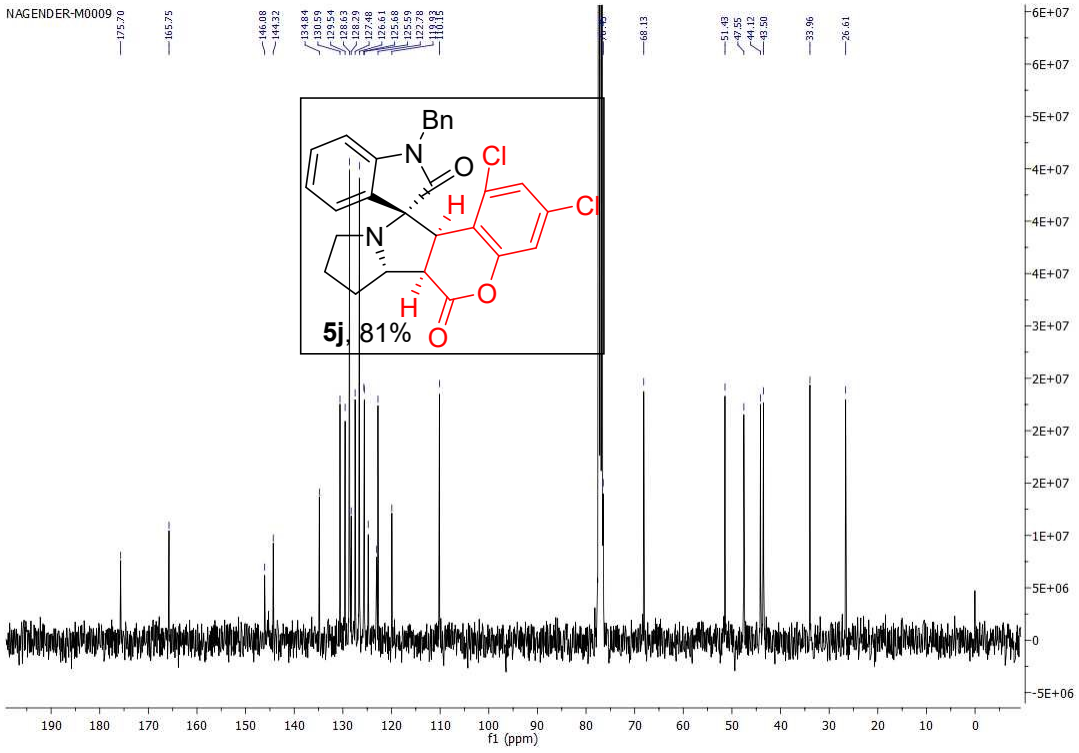

NAGENDAR-M0009
Bn
N
O
H
Cl
N
O
H
O
5h, 72%
f1 (ppm)

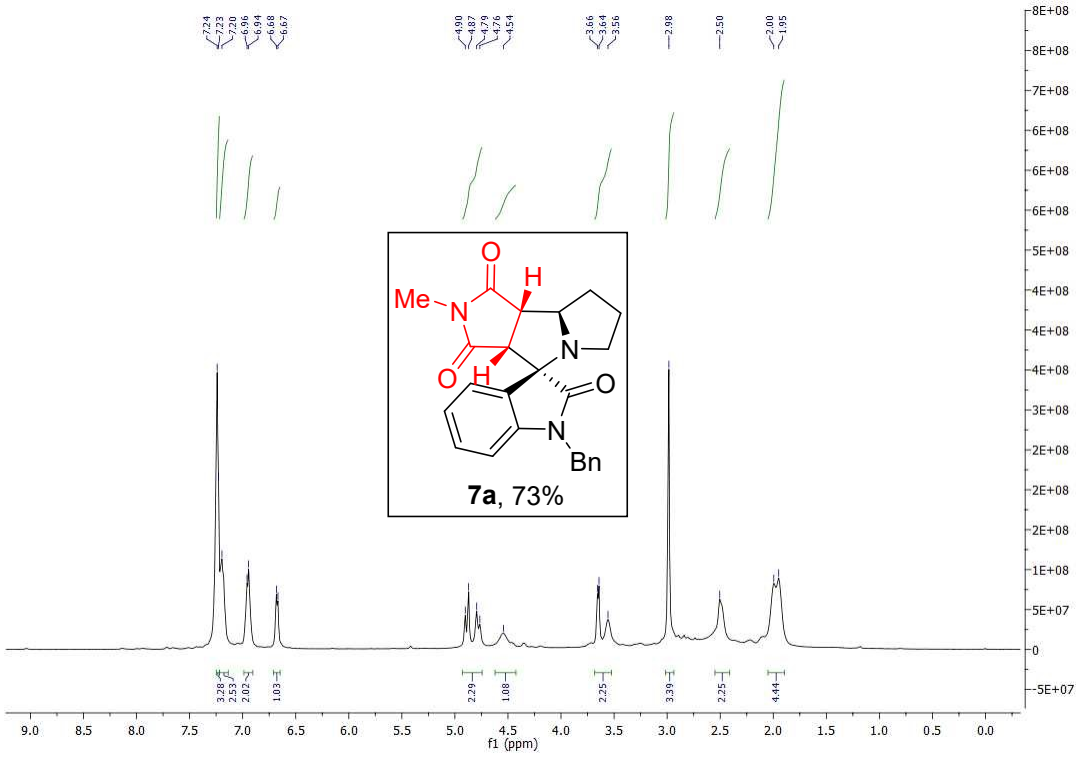

NAGENDAR-M0009
Bn
N
O
H
Cl
N
O
H
O
5h, 72%
f1 (ppm)

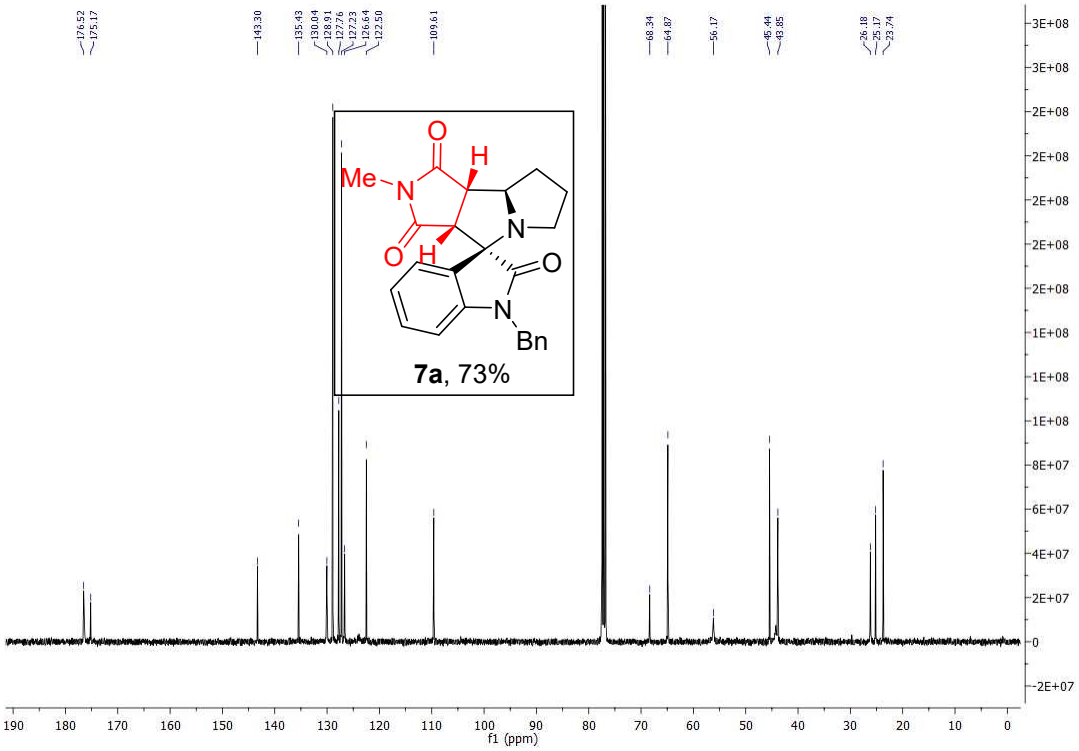

NAGENDER-M0009
Bn
N
O
H
Br
N
O
H
O
5i, 76%
f1 (ppm)

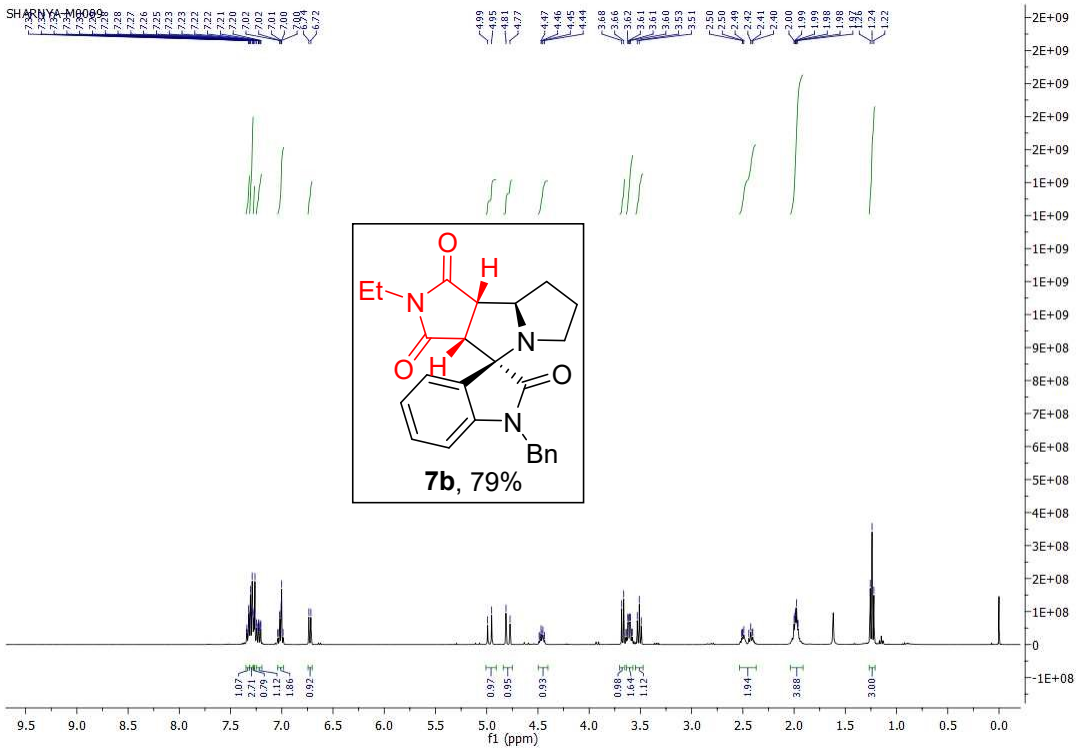

NAGENDER-M0009
175.87
166.91
150.42
144.31
134.70
131.93
130.47
130.34
128.71
127.29
126.25
125.65
122.73
119.31
119.22
118.41
118.22
77.37
77.05
76.73
76.61
68.10
51.42
47.69
43.73
43.41
34.02
26.64
Bn
N
O
H
Br
N
O
H
O
5i, 76%
f1 (ppm)

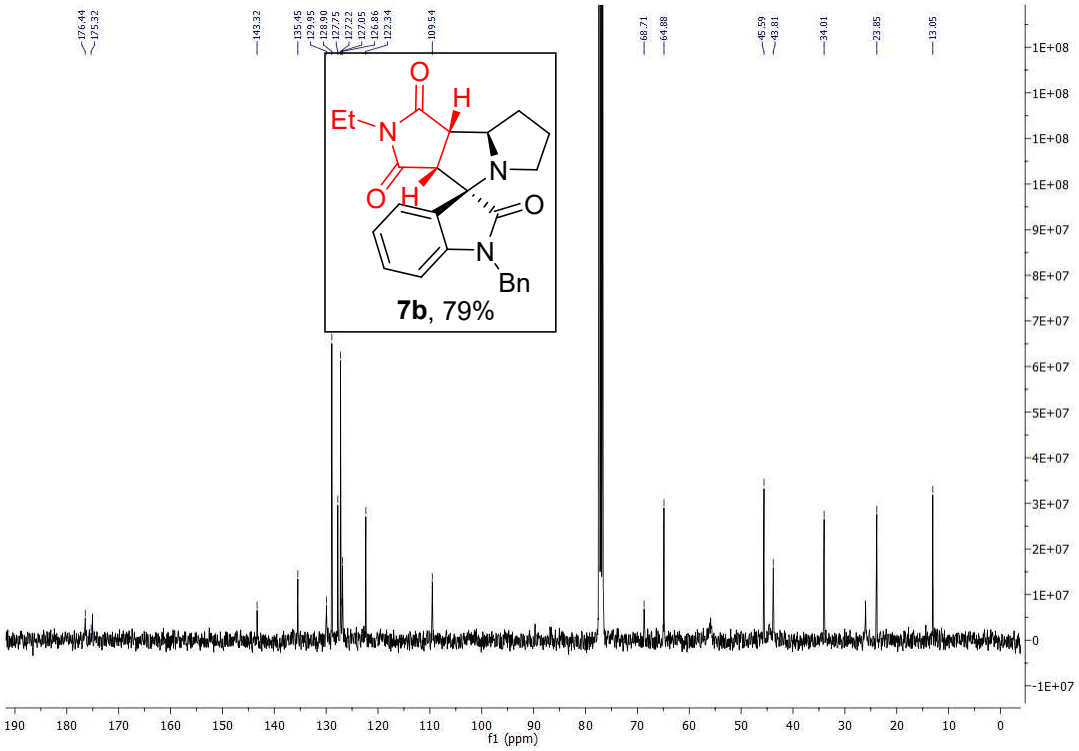

NAGENDER-M0009
Bn
N
O
Cl
H
Cl
N
H
O
O
5j, 81%
f1 (ppm)

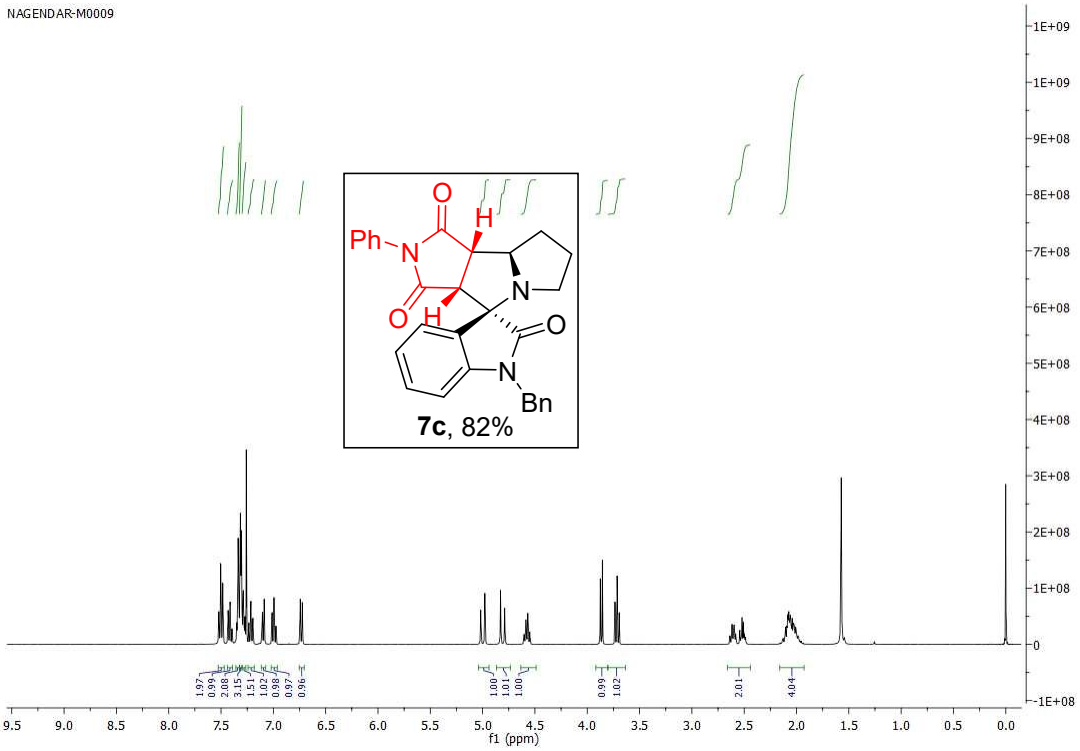

NAGENDER-M0009
Bn
N
O
Cl
H
Cl
N
H
O
O
5j, 81%
f1 (ppm)

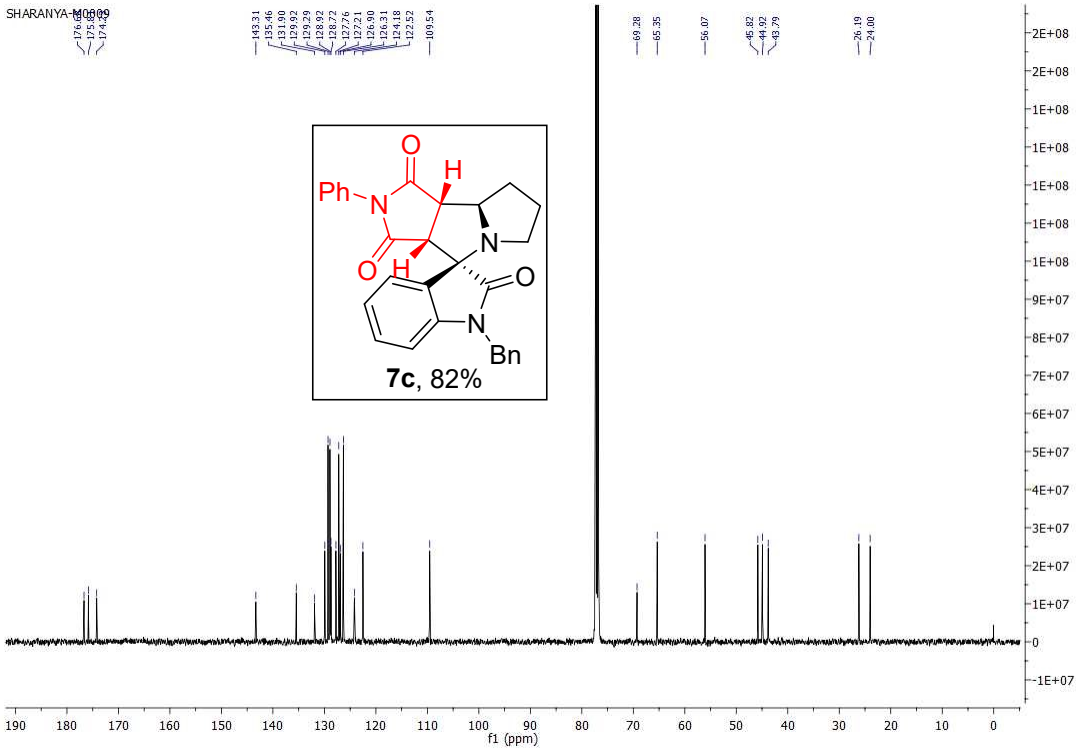

7a, 73%
f1 (ppm)


7a, 73%
f1 (ppm)


SHARNYA-M8089
Et
N
O
H
O
H
N
O
N
Bn
7b, 79%
f1 (ppm)


Et
N
O
H
O
H
N
O
N
Bn
7b, 79%
f1 (ppm)


NAGENDAR-M0009
Ph
N
O
H
O
H
N
O
N
Bn
7c, 82%
f1 (ppm)


SHARANYA-M0009
Ph
N
O
H
O
H
N
O
N
Bn
7c, 82%
f1 (ppm)