Supporting Information

Diversity-driven and facile 1,3-dipolar cycloaddition to access dispirooxindole-imidazolidine scaffolds

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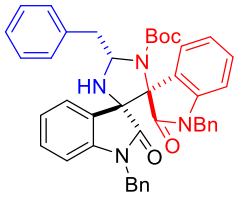
1. General Experimental Information

Unless otherwise noted, all the reagents were purchased from commercial suppliers and used without further purification. ^{1}H NMR spectra were recorded at 400 MHz. The chemical shifts were recorded in ppm relative to tetramethylsilane and with the solvent resonance as the internal standard. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, h = sextet), coupling constants (Hz), integration. ^{13}C NMR data were collected at 100 MHz with complete proton decoupling. Chemical shifts were reported in ppm from the tetramethylsilane with the solvent resonance as internal standard. Infrared spectra (IR) were measured by FT-IR apparatus. High resolution mass spectroscopy (HRMS) was recorded on TOF MS mass spectrometer and methanol was used to dissolve the sample. Column chromatography was carried out on silica gel (200-300 mesh).

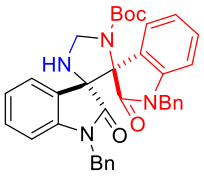
2. General Experimental Procedure

Isatins (0.20 mmol, 1 equiv.), amino acids (0.40 mmol, 2 equiv.), isatin-based imines (0.3 mmol, 1.5 equiv.) and DMSO (0.1 mL) were well mixed and stirred at room temperature. After the reaction was complete (monitored by TLC), the resulting residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 98:2) to yield the corresponding products.

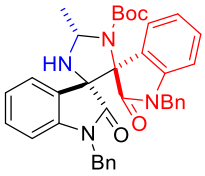
3. Characterization Data for All the New Compounds



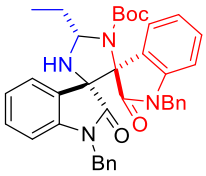
4aaa: white solid (140 mg, 0.207 mmol, 99% yield, *two diastereomers*, 73:27 *dr*) m.p. 238-243 °C; IR (KBr) *v* 3415, 3238, 2171, 1715, 1639, 1467, 1184, 762 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.51-7.35 (m, 5.0H), 7.30 (t, *J* = 7.4 Hz, 2.7H), 7.24-7.03 (m, 11.5H), 6.94 (d, *J* = 7.2 Hz, 2.5H), 6.90-6.74 (m, 3.0H), 6.70 (d, *J* = 7.5 Hz, 2.0H), 6.46 (d, *J* = 7.8 Hz, 1.2H), 6.31 (d, *J* = 7.8 Hz, 1.2H), 5.92 (td, *J* = 9.8, 2.9 Hz, 1.0H), 5.82 (t, *J* = 8.5 Hz, 0.2H), 5.04 (d, *J* = 15.9 Hz, 1.0H), 4.96 (d, *J* = 15.7 Hz, 0.5H), 4.82 (d, *J* = 15.8 Hz, 1.0H), 4.74 (d, *J* = 16.2 Hz, 0.2H), 4.67 (d, *J* = 15.8 Hz, 1.0H), 4.34 - 4.19 (m, 2.2H), 4.05 (d, *J* = 12.9 Hz, 0.2H), 3.29 (d, *J* = 9.8 Hz, 1.0H), 3.21-3.13 (m, 0.2H), 3.10 (dd, *J* = 14.0, 9.5 Hz, 1.0H), 0.93 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.1, 173.5, 151.6, 144.1, 143.4, 137.4, 135.1, 134.8, 130.4, 129.4, 128.9, 128.7, 128.6, 127.5, 127.3, 127.2, 126.8, 126.5, 125.8, 125.3, 124.8, 123.0, 122.9, 122.4, 109.5, 109.4, 80.4, 76.4, 73.2, 71.0, 43.9, 43.4, 39.7, 28.5, 27.7; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{43}H_{41}N_4O_4^+$ 677.3122, found 677.3111.



4aba: white solid (93 mg, 0.158 mmol, 79% yield, *two diastereomers*, 70:30 *dr*) m.p. 228-233 °C; IR (KBr) *v* 3418, 2977, 2921, 2171, 1720, 1384, 1176, 759 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.51-7.33 (m, 2.8H), 7.23-7.02 (m, 11.0H), 6.94-6.79 (m, 5.5H), 6.76 (d, *J* = 6.7 Hz, 0.7H), 6.71 (d, *J* = 7.2 Hz, 2.0H), 6.45 (d, *J* = 7.8 Hz, 1.0H), 6.42-6.38 (m, 1.7H), 5.41-5.31 (m, 1.4H), 5.10-4.96 (m, 3.8H), 4.89 (d, *J* = 16.2 Hz, 0.3H), 4.76 (d, *J* = 16.3 Hz, 0.3H), 4.50 (d, *J* = 15.9 Hz, 1.0H), 4.42 (d, *J* = 16.1 Hz, 0.3H), 4.40 (d, *J* = 16.4 Hz, 1.0H), 3.80 (dd, *J* = 11.2, 8.3 Hz, 0.3H), 3.73 (dd, *J* = 11.2, 8.3 Hz, 1.0H), 0.95 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.3, 173.5, 152.1, 143.9, 143.7, 134.9, 134.7, 130.5, 129.0, 128.6, 127.4, 127.3, 127.2, 126.8, 126.7, 125.6, 125.4, 125.0, 123.1, 123.0, 122.3, 109.5, 109.3, 80.4, 75.3, 69.9, 64.7, 43.9, 43.3, 28.4, 27.7; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{36}H_{35}N_4O_4^+$ 587.2653, found 587.2638.

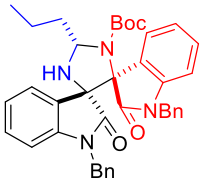


4aca: white solid (131 mg, 0.218 mmol, 99% yield, *two diastereomers*, 77:23 *dr*) m.p. 199-225 °C; IR (KBr) *v* 3414, 3030, 2967, 2170, 1709, 1491, 1364, 968 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.47-7.39 (m, 2.0H), 7.39-7.30 (m, 0.4H), 7.23-7.04 (m, 10.0H), 6.96-6.73 (m, 7.5H), 6.45 (d, *J* = 7.9 Hz, 1.2H), 6.38 (d, *J* = 7.8 Hz, 1.2H), 5.74 (dq, *J* = 11.1, 5.6 Hz, 1.0H), 5.65 (dq, *J* = 10.9, 5.5 Hz, 0.2H), 5.02 (d, *J* = 16.1 Hz, 1.0H), 4.99 (d, *J* = 15.8 Hz, 0.3H), 4.93 (d, *J* = 16.2 Hz, 0.2H), 4.84 (d, *J* = 15.8 Hz, 1.0H), 4.72 (d, *J* = 16.2 Hz, 0.3H), 4.64 (d, *J* = 15.8 Hz, 1.0H), 4.46 (d, *J* = 15.2 Hz, 1.0H), 4.42 (d, *J* = 16.0 Hz, 1.2H), 3.34 (d, *J* = 10.6 Hz, 0.2H), 3.25 (d, *J* = 10.7 Hz, 1.0H), 1.86 (d, *J* = 5.6 Hz, 3.0H), 1.81 (d, *J* = 5.5 Hz, 0.7H), 0.89 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.3, 173.6, 151.4, 144.0, 143.5, 135.0, 134.8, 130.4, 128.9, 128.6, 128.6, 127.5, 127.3, 127.2, 126.8, 126.7, 125.6, 125.5, 124.8, 123.0, 122.9, 122.4, 109.5, 109.4, 80.1, 73.2, 72.1, 71.1, 43.9, 43.3, 28.4, 27.7, 20.5, 19.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{37}H_{37}N_4O_4^+$ 601.2809, found 601.2818.

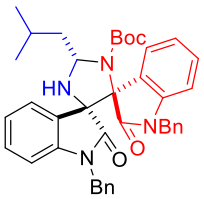


4ada: white solid (131 mg, 0.213 mmol, 99% yield, *two diastereomers*, 80:20 *dr*) m.p. 195-199 °C; IR (KBr) *v* 3552, 3414, 3030, 3000, 2171, 1691, 1496, 1185 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.42 (t, *J* = 8.2 Hz, 2.2H), 7.33 (d, *J* = 7.5 Hz, 0.2H), 7.2-7.02 (m, 9.7H), 6.94-6.75 (m, 4.9H), 6.72 (d, *J* = 7.3 Hz, 2.0H), 6.44 (d, *J* = 7.8 Hz, 1.2H), 6.37 (d, *J* = 7.8 Hz, 1.2H), 5.63 (t, *J* = 8.6 Hz, 1.0H), 5.54 (t, *J* = 9.3 Hz, 0.2H), 5.10 (d, *J* = 16.0 Hz, 1.2H), 4.96 (d, *J* = 16.2 Hz, 0.2H), 4.86 (d, *J* = 15.8 Hz, 1.0H), 4.68 (d, *J* = 16.2 Hz, 0.2H), 4.60 (d, *J* = 15.9 Hz, 1.0H), 4.35 (d, *J* = 16.1 Hz, 1.2H), 3.31 (d, *J* = 10.8 Hz, 0.2H), 3.22 (d, *J* = 10.2 Hz, 1.0H), 2.89-2.73 (m, 1.0H), 2.63-2.44 (m, 0.2H), 2.10-1.80 (m, 1.2H), 0.89 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.2, 173.5, 151.4, 144.0, 143.4, 135.0, 134.8, 130.4, 128.8, 128.6, 128.6, 127.4, 127.2, 127.1, 126.7, 125.8, 125.6, 124.9, 123.0, 122.9, 122.5, 109.5, 109.4, 80.1, 73.3, 71.0, 43.9, 43.4, 28.4, 27.7, 26.0,

9.6; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{38}H_{39}N_4O_4^+$ 615.2966, found 615.2989.

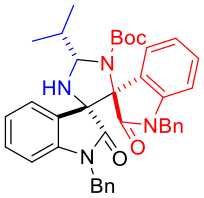


4aea: white solid (133 mg, 0.211 mmol, 99% yield, *two diastereomers*, 80:20 *dr*) m.p. 193-199 °C; IR (KBr) *v* 3415, 3320, 3058, 2929, 1706, 1491, 1153, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.41 (dd, *J* = 10.8, 7.3 Hz, 2.2H), 7.32 (d, *J* = 7.5 Hz, 0.2H), 7.2 -7.02 (m, 9.9H), 6.97-6.77 (m, 5.2H), 6.72 (d, *J* = 7.2 Hz, 2.0H), 6.45 (d, *J* = 7.8 Hz, 1.2H), 6.36 (d, *J* = 7.8 Hz, 1.2H), 5.66 (ddd, *J* = 11.3, 9.4, 2.5 Hz, 1.0H), 5.62-5.52 (m, 0.2H), 5.11 (d, *J* = 16.0 Hz, 1.0H), 5.07 (d, *J* = 15.9 Hz, 0.2H),4.95 (d, *J* = 16.2 Hz, 0.2H), 4.84 (d, *J* = 15.8 Hz, 1.0H), 4.69 (d, *J* = 16.4 Hz, 0.2H), 4.63 (d, *J* = 15.8 Hz, 1.0H), 4.38 (d, *J* = 16.1 Hz, 0.2H), 4.34 (d, *J* = 16.2 Hz, 1.0H), 3.32 (d, *J* = 10.7 Hz, 0.2H), 3.22 (d, *J* = 10.9 Hz, 1.0H), 2.83-2.75 (m, 1.0H), 2.56-2.41 (m, 0.2H), 2.12-1.95 (m, 0.2H), 1.91-1.82 (m, 1.0H), 1.61 (q, *J* = 7.7 Hz, 2.5H), 1.05 (t, *J* = 7.3 Hz, 3.7H), 0.89 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.3, 173.5, 151.4, 144.0, 143.4, 135.0, 134.8, 130.4, 128.8, 128.6, 128.6, 127.5, 127.3, 127.2, 126.8, 126.7, 125.8, 125.5, 124.9, 123.0, 122.9, 122.5, 109.5, 109.4, 80.1, 75.9, 73.3, 70.9, 43.9, 43.4, 35.3, 28.4, 27.7, 18.9, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{39}H_{41}N_4O_4^+$ 629.3122, found 629.3123.

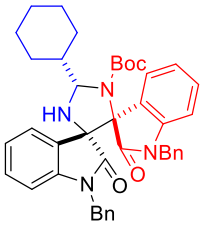


4afa: white solid (136 mg, 0.211 mmol, 99% yield, *two diastereomers*, 78:22 *dr*) m.p. 187-191 °C; IR (KBr) *v* 3415, 2961, 2171, 1718, 1490, 1456, 1173, 759 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.48-7.34 (m, 2.2H), 7.30 (d, *J* = 7.6 Hz, 0.2H), 7.24-7.01 (m, 10.0H), 6.94 (d, *J* = 7.4 Hz, 2.2H), 6.89-6.76 (m, 2.8H), 6.73 (d, *J* = 7.4 Hz, 2.0H), 6.45 (d, *J* = 7.8 Hz, 1.2H), 6.36 (d, *J* = 7.8 Hz, 1.2H), 5.73 (t, *J* = 8.7 Hz, 1.0H), 5.59 (d, *J* = 7.8 Hz, 0.2H), 5.11 (d, *J* = 16.2 Hz, 1.0H), 5.07 (d, *J* = 16.2 Hz, 0.2H), 4.93 (d, *J* = 16.2 Hz, 0.2H), 4.82 (d, *J* = 15.8 Hz, 1.0H), 4.71 (d, *J* = 15.8 Hz, 0.2H), 4.65 (d, *J* = 15.8 Hz, 1.0H), 4.40 (s, (d, *J* = 15.8 Hz, 0.2H), 4.34 (d, *J* = 16.1 Hz, 1.0H), 3.27 (d, *J* = 10.0 Hz, 0.2H), 3.19 (d, *J* = 10.0

Hz, 1.0H), 2.71 (ddd, *J* = 13.4, 10.4, 2.6 Hz, 1.0H), 2.41 (t, *J* = 12.5, 0.2H), 2.00-1.84 (m, 1.2H), 1.78 (ddd, *J* = 13.9, 9.9, 4.2 Hz, 1.2H), 1.10 (d, *J* = 6.5 Hz, 3.6H), 1.04 (d, *J* = 6.6 Hz, 3.6H), 0.89 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) *δ* 176.3, 173.4, 151.3, 144.1, 143.4, 135.1, 134.8, 130.4, 128.8, 128.6, 128.6, 127.5, 127.3, 127.2, 126.8, 125.7, 125.5, 124.8, 122.9, 122.5, 109.5, 109.4, 80.1, 74.8, 73.4, 70.8, 43.9, 43.4, 42.2, 28.4, 27.7, 25.5, 24.2, 21.6; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{40}H_{43}N_4O_4^+$ 643.3279, found 643.3306.

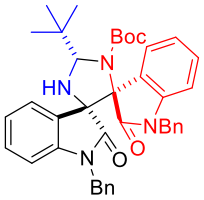


4aga: white solid (128 mg, 0.203 mmol, 99% yield, *two diastereomers*, 85:15 *dr*) m.p. 210-214 °C; IR (KBr) *ν* 3415, 3002, 2925, 2170, 1709, 1465, 1181, 752 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) *δ* 7.47 (t, *J* = 6.5 Hz, 2.2H), 7.37 (d, *J* = 7.4 Hz, 0.2H), 7.19-6.94 (m, 10.0H), 6.93-6.78 (m, 2.7H), 6.69 (d, *J* = 7.7 Hz, 3.0H), 6.57 (d, *J* = 7.5 Hz, 2.0H), 6.40 (d, *J* = 7.8 Hz, 1.0H), 6.34 (d, *J* = 7.8 Hz, 1.0H), 5.82 (dd, *J* = 11.6, 3.5 Hz, 1.0H), 5.73 (d, *J* = 11.4 Hz, 0.2H), 5.14 (d, *J* = 16.2 Hz, 1.2H), 5.04 (d, *J* = 15.9 Hz, 1.2H), 4.56 (d, *J* = 15.9 Hz, 0.2H), 4.37 (d, *J* = 15.9 Hz, 1.0H), 4.24 (d, *J* = 16.1 Hz, 1.2H), 3.45-2.84 (m, 2.5H), 1.25 (d, *J* = 7.0 Hz, 3.6H), 1.14 (d, *J* = 7.2 Hz, 3.7H), 0.93 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) *δ* 176.1, 173.8, 151.6, 144.0, 143.5, 135.0, 134.7, 130.3, 128.9, 128.6, 127.2, 127.1, 126.8, 126.5, 126.3, 125.9, 125.3, 123.1, 123.0, 122.9, 109.5, 109.2, 80.1, 79.6, 73.1, 71.6, 43.7, 43.3, 28.3, 27.7, 27.0, 19.8, 14.0; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{39}H_{41}N_4O_4^+$ 629.3122, found 629.3126.

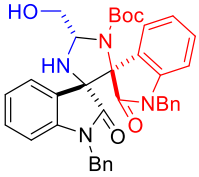


4aha: white solid (126 mg, 0.188 mmol, 94% yield, *two diastereomers*, 80:20 *dr*) m.p. 191-196 °C; IR (KBr) *ν* 3552, 3414, 2923, 1712, 1490, 1357, 1133, 754 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) *δ* 7.47 (t, *J* = 6.5 Hz, 2.2H), 7.38 (d, *J* = 7.5 Hz, 0.2H), 7.19-6.98 (m, 9.8H), 6.89-6.79 (m, 2.5H), 6.70 (d, *J* = 7.4 Hz, 2.5H), 6.62 (d, *J* = 7.6 Hz, 0.5H), 6.57 (d, *J* = 7.4 Hz, 2.0H), 6.39 (d, *J* = 7.8 Hz, 1.2H), 6.34 (d, *J* = 7.8 Hz, 1.2H), 5.78 (dd, *J* = 11.6, 3.5 Hz, 1.0H), 5.70 (dd, *J* = 11.5,

3.6 Hz, 0.2H), 5.15 (d, *J* = 16.2 Hz, 1.0H), 5.14 (d, *J* = 16.1 Hz, 0.2H), 5.03 (d, *J* = 16.0 Hz, 1.0H), 5.01 (d, *J* = 16.1 Hz, 0.2H), 4.58 (d, *J* = 16.3 Hz, 0.2H), 4.38 (d, *J* = 16.0 Hz, 1.0H), 4.27 (d, *J* = 16.0 Hz, 0.2H), 4.24 (d, *J* = 16.2 Hz, 1.0H), 3.40 (d, *J* = 11.8 Hz, 0.2H), 3.34 (d, *J* = 11.7 Hz, 1.0H), 2.94 (td, *J* = 10.9, 5.3 Hz, 1.0H), 2.66 (t, *J* = 11.0 Hz, 0.2H), 2.21-2.06 (m, 1.2H), 2.00-1.85 (m, 2.1H), 1.84-1.70 (m, 2.4H), 1.40-1.12 (m, 6.1H), 0.93 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.1, 173.7, 151.5, 144.0, 143.4, 135.0, 134.7, 130.3, 128.8, 128.6, 127.2, 127.1, 126.8, 126.5, 126.3, 125.9, 125.3, 123.1, 122.9, 122.9, 109.5, 109.3, 80.0, 79.3, 73.2, 71.4, 43.7, 43.3, 37.2, 30.6, 28.3, 27.7, 27.0, 26.8, 26.2, 24.9; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{42}H_{45}N_4O_4^+$ 669.3435, found 669.3423.

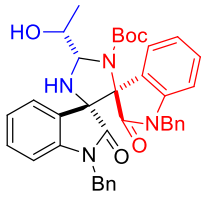


4aia: white solid (67 mg, 0.104 mmol, 52% yield, *single diastereomer*) m.p. 174-175 ℃; IR (KBr) *v* 3415, 2960, 2171, 1718, 1615, 1360, 1180, 758 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 1H), 7.20 - 7.10 (m, 2H), 7.12 - 7.03 (m, 6H), 6.84 (dt, *J* = 8.8, 4.4 Hz, 2H), 6.75 (d, *J* = 7.3 Hz, 2H), 6.65 (d, *J* = 7.5 Hz, 2H), 6.39 (d, *J* = 7.8 Hz, 1H), 6.35 (d, *J* = 7.8 Hz, 1H), 5.76 (d, *J* = 11.0 Hz, 1H), 5.12 (d, *J* = 16.1 Hz, 1H), 5.01 (d, *J* = 16.0 Hz, 1H), 4.46 (d, *J* = 16 Hz, 1H), 4.30 (d, *J* = 16.2 Hz, 1H), 3.28 (d, *J* = 11.1 Hz, 1H), 1.32 (s, 9H), 0.93 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 173.9, 153.6, 144.1, 143.2, 135.0, 134.8, 130.2, 128.9, 128.6, 127.2, 127.2, 126.8, 126.6, 126.1, 125.2, 123.0, 123.0, 122.8, 109.4, 109.2, 83.1, 72.7. 43.7, 43.3, 36.3, 28.3, 27.6; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{40}H_{43}N_4O_4^+$ 643.3279, found 643.3249.

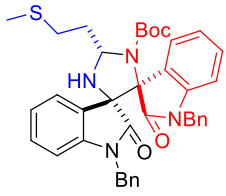


4aja: white solid (106 mg, 0.172 mmol, 86% yield, *two diastereomers*, 73:27 *dr*) m.p. 231-236 ℃; IR (KBr) *v* 3410, 3258, 2975, 2170, 1701, 1490, 1190, 749 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.44 (d, *J* = 7.6 Hz, 2.2H), 7.41-7.34 (m, 0.2H), 7.25-7.07 (m, 9.8H), 6.98-6.79 (m, 5.0H), 6.73 (d, *J* = 7.2 Hz, 2.2H), 6.50 (d, *J* = 7.8 Hz, 1.2H), 6.39 (d, *J* = 7.6 Hz, 1.2H), 5.77 (dd, *J* = 10.1, 1.6

Hz, 1.0H), 5.66 (d, *J* = 9.5 Hz, 0.2H), 5.03-4.93 (m, 1.5H), 4.82 (d, *J* = 15.8 Hz, 1.0H), 4.77-4.52 (m, 2.7H), 4.48-4.36 (m, 2.2H), 4.02 (d, *J* = 9.7 Hz, 0.2H), 3.93 (d, *J* = 10.0 Hz, 1.0H), 3.92-3.75 (m, 1.2H), 0.89 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 177.8, 173.9, 151.5, 144.0, 142.8, 134.7, 134.7, 130.6, 129.1, 128.7, 128.6, 127.7, 127.3, 127.2, 126.7, 126.0, 125.4, 124.6, 123.3, 123.1, 122.2, 109.7, 109.6, 80.9, 76.5, 73.7, 70.6, 60.1, 44.1, 43.4, 28.3, 27.6; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{37}H_{37}N_4O_5^+$ 617.2758, found 617.2743.

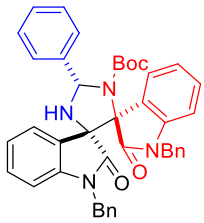


4aka: white solid (65 mg, 0.103 mmol, 50% yield, *two diastereomers*, 73:27 *dr*) m.p. 222-226 ℃; IR (KBr) *v* 3417, 2976, 2171, 1695, 1639, 1489, 1163, 741 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomer*s) δ 7.44 (t, *J* = 6.8 Hz, 2.2H), 7.36 (d, *J* = 7.7 Hz, 0.2H), 7.24-7.07 (m, 9.8H), 6.95-6.72 (m, 5.0H), 6.69 (d, *J* = 7.3 Hz, 2.0H), 6.49 (d, *J* = 7.9 Hz, 1.2H), 6.37 (d, *J* = 7.9 Hz, 1.2H), 5.63 (d, *J* = 9.9 Hz, 1.0H), 5.51 (d, *J* = 9.6 Hz, 0.2H), 5.08 (d, *J* = 16.0 Hz, 1.5H), 4.96 (q, *J* = 6.3 Hz, 1.2H), 4.83 (d, *J* = 15.8 Hz, 1.0H), 4.75 (s, 1.2H), 4.34 (d, *J* = 16.1 Hz, 1.2H), 3.98 (d, *J* = 10.0 Hz, 1.2H), 1.36 (d, *J* = 6.5 Hz, 3.6H), 0.89 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 178.1, 174.0, 151.3, 144.1, 142.8, 134.7, 134.6, 130.6, 129.0, 128.7, 128.6, 127.6, 127.3, 127.2, 126.7, 126.2, 125.3, 124.7, 123.3, 123.2, 122.4, 109.8, 109.6, 80.8, 79.8, 74.1, 70.7, 64.2, 44.1, 43.4, 28.3, 27.6, 18.9; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{38}H_{39}N_4O_5^+$ 631.2915, found 631.2897.

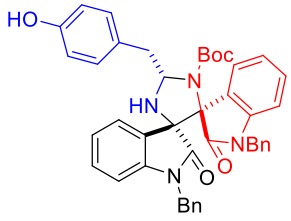


4ala: white solid (104 mg, 0.16 mmol, 77% yield, *two diastereomers*, 77:23 *dr*) m.p. 203-208 ℃; IR (KBr) *v* 3421, 2974, 2935, 2171, 1716, 1490, 1137, 755 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomer*s) δ 7.45 (d, *J* = 7.1 Hz, 1.0H), 7.41 (d, *J* = 7.1 Hz, 1.1H), 7.33 (d, *J* = 7.6 Hz, 0.3H), 7.23-7.03 (m, 9.2H), 6.94-6.76 (m, 5.0H), 6.71 (d, *J* = 7.3 Hz, 2.0H), 6.44 (d, *J* = 7.8 Hz, 1.2H), 6.37 (d, *J* = 7.7 Hz, 1.2H), 5.82-5.75 (m, 1.0H), 5.69 (d, *J* = 8.0 Hz, 0.2H), 5.08 (d, *J* = 16.1 Hz, 1.2H), 4.95 (d, *J* = 16.3 Hz, 0.2H), 4.88 (d, *J* = 15.8 Hz, 1.0H), 4.68 (d, *J* = 16.2 Hz, 0.3H),

4.59 (d, *J* = 15.9 Hz, 1.0H), 4.35 (d, *J* = 16.2 Hz, 1.3H), 3.64 (s, 1.2H), 3.04-2.85 (m, 2.3H), 2.82-2.78 (m, 1.5H), 2.42-2.28 (m, 1.2H), 2.20 (s, 3.4H), 0.90 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.2, 173.6, 151.3, 144.0, 143.4, 135.0, 134.7, 130.4, 128.9, 128.6, 128.6, 127.4, 127.3, 127.1, 126.7, 125.8, 125.5, 125.0, 123.1, 122.9, 122.5, 109.5, 109.4, 80.3, 75.4, 73.3, 70.9, 43.9, 43.4, 31.6, 29.5, 28.4, 27.7, 15.6; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{39}H_{41}N_4O_4S^+$ 661.2843, found 661.2847.

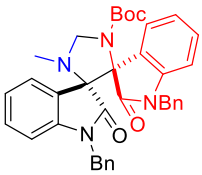


4ama: white solid (102 mg, 0.154 mmol, 77% yield, *two diastereomers*, 50:50 *dr*) m.p. 231-235 °C; IR (KBr) *v* 3415, 3237, 2171, 1616, 1490, 1358, 1153, 749 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 8.07 (d, *J* = 7.3 Hz, 2.0H), 8.03 (d, *J* = 7.3 Hz, 2.2H), 7.55 (d, *J* = 7.3 Hz, 1.0H), 7.53-7.42 (m, 7.2H), 7.41-7.32 (m, 2.1H), 7.21-7.05 (m, 16.2H), 6.96-6.75 (m, 8.0H), 6.73-6.63 (m, 5.1H), 6.56 (d, *J* = 10.9 Hz, 1.0H), 6.46 (d, *J* = 7.6 Hz, 1.0H), 6.44 (d, *J* = 7.6 Hz, 1.0H),6.37 (d, *J* = 7.8 Hz, 2.0H), 5.15-5.05 (m, 4.0H), 4.68 (d, *J* = 16.3 Hz, 1.0H), 4.52 (d, *J* = 15.9 Hz, 1.0H), 4.38 (d, *J* = 9.6 Hz, 1.0H), 4.34 (d, *J* = 9.2 Hz, 1.0H), 3.57 (d, *J* = 11.0 Hz, 1.0H), 3.43 (d, *J* = 11.0 Hz, 1.0H), 0.98 (s, 9.1H), 0.87 (s, 9.1H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.7, 173.7, 151.0, 143.9, 143.2, 140.9, 139.4, 134.9, 134.7, 130.5, 130.4, 129.2, 128.8, 128.7, 128.6, 128.0, 127.5, 127.3, 127.1, 126.9, 126.7, 126.6, 126.1, 125.6, 125.2, 124.3, 123.2, 123.1, 122.4, 109.7, 109.5, 80.4, 78.2, 74.3, 73.7, 71.1, 43.9, 43.4, 27.8; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{42}H_{39}N_4O_4^+$ 663.2966, found 663.2966.

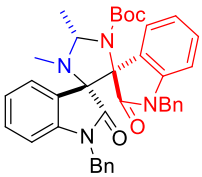


4ana: white solid (102 mg, 0.147 mmol, 74% yield, *two diastereomers*, 75:25 *dr*) m.p. 219-221 °C; IR (KBr) *v* 3413, 3063, 2977, 2171, 1721, 1614, 1188, 752 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.42 (d, *J* = 7.7 Hz, 2.3H), 7.33 (d, *J* = 7.5 Hz, 0.3H), 7.23-7.01 (m, 13.0H), 6.97-6.74 (m, 5.8H), 6.74-6.63 (m, 4.5H), 6.46 (d, *J* = 7.8 Hz, 1.3H), 6.32 (d, *J* = 7.8 Hz, 1.3H), 5.95-5.83

(m, 1.0H), 5.79 (t, *J* = 11.0 Hz, 0.3H), 5.00 (d, *J* = 16.1 Hz, 1.2H), 4.93 (d, *J* = 3.8 Hz, 0.3H), 4.82 (d, *J* = 15.8 Hz, 1.0H), 4.68 (d, *J* = 16.0 Hz, 1.3H), 4.35 (d, *J* = 16.2 Hz, 0.3H), 4.30 (d, *J* = 16.1 Hz, 1.0H), 4.17 (dd, *J* = 13.9, 2.6 Hz, 1.0H), 3.95 (dd, *J* = 13.9, 2.9 Hz, 0.3H), 3.39 (d, *J* = 10.0 Hz, 0.2H), 3.00 (dd, *J* = 13.9, 9.5 Hz, 1.0H), 0.93 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) *δ* 176.1, 173.6, 154.9, 151.6, 144.0, 143.3, 135.0, 134.6, 130.5, 130.3, 130.0, 129.0, 128.7, 128.6, 127.6, 127.3, 127.2, 126.8, 125.8, 125.1, 124.8, 123.1, 123.0, 122.2, 115.7, 109.6, 109.5, 80.5, 76.7, 73.1, 71.1, 43.9, 43.4, 38.8, 28.5, 27.7; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{43}H_{41}N_4O_5^+$ 693.3071, found 693.3054.

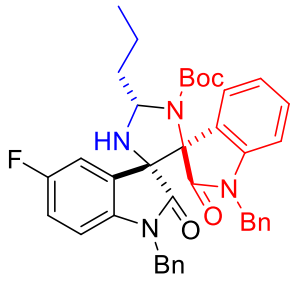


4aoa: white solid (61 mg, 0.101 mmol, 51% yield, *two diastereomers*, 57:43 *dr*) m.p. 231-235 °C; IR (KBr) *v* 3414, 2977, 2848, 2170, 1726, 1392, 1160, 754 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) *δ* 7.56-7.40 (m, 2.8H), 7.19-6.99 (m, 11.2H), 6.90-6.75 (m, 3.7H), 6.74-6.62 (m, 4.8H), 6.42-6.29 (m, 2.8H), 5.14 (d, *J* = 16.0 Hz, 1.0H), 5.10-4.88 (m, 4.3H), 4.61 (d, *J* = 16.3 Hz, 0.4H), 4.43 (d, *J* = 16.0 Hz, 1.4H), 4.29 (d, *J* = 16.0 Hz, 1.0H), 2.26 (s, 3.0H), 2.24 (s, 1.1H), 0.98 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) *δ* 175.1, 173.6, 151.8, 144.3, 143.9, 135.1, 134.8, 130.3, 129.3, 128.6, 128.5, 128.5, 127.2, 127.2, 127.0, 126.9, 126.6, 126.5, 126.1, 125.6, 123.4, 122.7, 121.8, 109.3, 109.0, 80.5, 77.8, 71.0, 68.3, 44.0, 43.0, 32.9, 28.4, 27.7; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{37}H_{37}N_4O_4^+$ 601.2809, found 601.2832.

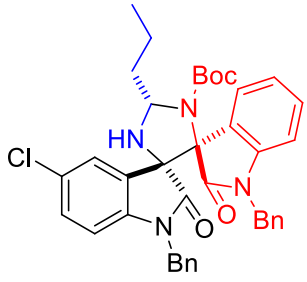


4apa: white solid (84 mg, 0.137 mmol, 69% yield, *two diastereomers*, 72:28 *dr*) m.p. 220-224 °C; IR (KBr) *v* 3415, 2978, 2851, 2171, 1701, 1488, 1147, 753 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) *δ* 7.48 (d, *J* = 7.5 Hz, 1.0H), 7.44 (d, *J* = 7.6 Hz, 0.2H), 7.41 (d, *J* = 7.5 Hz, 1.0H), 7.33 (d, *J* = 7.8 Hz, 0.3H), 7.21-7.01 (m, 10.0H), 6.88-6.77 (m, 5.0H), 6.74 (d, *J* = 7.3 Hz, 2.0H), 6.35 (t, *J* = 7.7 Hz, 2.5H), 5.26 (q, *J* = 5.2 Hz, 1.0H), 5.17 (q, *J* = 5.1 Hz, 0.2H), 4.99-4.82 (m, 2.5H),

4.62-4.42 (m, 2.5H), 2.19 (s, 3.0H), 2.18 (s, 0.6H), 1.80 (d, J = 5.2 Hz, 3.0H), 1.76 (d, J = 5.1 Hz, 0.6H), 0.90 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 175.0, 173.6, 151.1, 144.3, 143.8, 135.3, 135.0, 130.1, 129.0, 128.6, 128.5, 127.3, 127.2, 126.9, 126.8, 126.7, 126.0, 125.7, 123.2, 122.5, 122.3, 109.2, 109.1, 80.2, 74.8, 70.7, 44.0, 43.1, 32.1, 28.4, 27.7, 18.3; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{38}H_{39}N_4O_4^+$ 615.2966, found 615.2969.

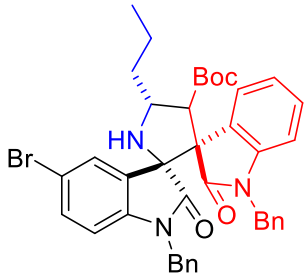


4bea: white solid (123 mg, 0.190 mmol, 95% yield, *two diastereomers*, 77:23 *dr*) m.p. 207-211 °C; IR (KBr) ν 3414, 3318, 2970, 2871, 2170, 1706, 1151, 755 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.40 (d, J = 7.8 Hz, 1.0H), 7.33 (d, J = 7.6 Hz, 0.2H), 7.26-7.06 (m, 9.8H), 7.04-6.75 (m, 5.3H), 6.72 (d, J = 7.2 Hz, 2.0H), 6.52 (d, J = 7.8 Hz, 1.0H), 6.45 (d, J = 7.8 Hz, 0.2H), 6.37 (d, J = 7.8 Hz, 0.2H), 6.28 (dd, J = 8.6, 4.2 Hz, 1.0H), 5.66 (t, J = 6.4 Hz, 1.0H), 5.57 (t, J = 6.3 Hz, 0.2H), 5.10 (d, J = 16.1 Hz, 1.2H), 4.96 (d, J = 16.1 Hz, 0.2H), 4.85 (d, J = 15.7 Hz, 1.0H), 4.78-4.59 (m, 1.2H), 4.33 (d, J = 16.1 Hz, 1.2H), 3.35-3.12 (m, 1.2H), 2.87-2.62 (m, 1.0H), 2.56-2.39 (m, 0.2H), 2.05-1.94 (m, 0.2H), 1.92-1.78 (m, 1.0H), 1.67-1.50 (m, 2.2H), 1.05 (t, J = 7.3 Hz, 3.6H), 0.89 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.0, 173.2, 159.0 (d, $^1J_{C\text{-}F}$= 240 Hz), 151.3, 143.4, 139.9(d, $^4J_{C\text{-}F}$ = 2 Hz), 135.0, 134.5, 129.0, 128.7, 128.7, 127.7, 127.4, 127.1, 126.7, 125.8, 125.3, 124.1, 124.0, 123.0, 116.8 (d, $^2J_{C\text{-}F}$ = 23 Hz), 113.4 (d, $^2J_{C\text{-}F}$ = 26 Hz), 110.1(d, $^3J_{C\text{-}F}$ = 8 Hz), 109.5, 80.2, 75.9, 73.2, 70.7, 44.0, 43.5, 35.3, 28.4, 27.7, 18.9, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{39}H_{40}F_1N_4O_4^+$ 647.3028, found 647.3014.



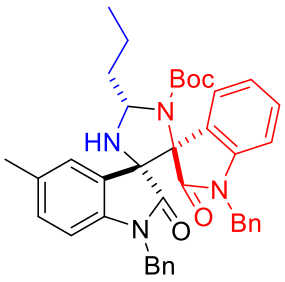
4cea: white solid (126 mg, 0.199 mmol, 95% yield, *two diastereomers*, 76:24 *dr*) m.p. 214-219 °C; IR (KBr) ν 3415, 3066, 2923, 2170, 1718, 1490, 1187, 744 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.50 (d,

J = 2.2 Hz, 1.2H), 7.38 (d, *J* = 7.5 Hz, 1.0H), 7.30 (d, *J* = 7.6 Hz, 0.2H), 7.25-7.07 (m, 9.8H), 7.02 (dd, *J* = 6.0, 2.4 Hz, 2.0H), 7.00-6.93 (m, 0.4H), 6.87 (t, *J* = 7.5 Hz, 1.0H), 6.86-6.73 (m, 0.6H), 6.72 (d, *J* = 7.3 Hz, 2.0H), 6.51 (d, *J* = 7.8 Hz, 1.0H), 6.46 (d, *J* = 7.8 Hz, 0.2H), 6.29 (d, *J* = 8.4 Hz, 1.2H), 5.65 (t, *J* = 8.5 Hz, 1.0H), 5.57 (t, *J* = 8.3 Hz, 0.2H), 5.07 (d, *J* = 16.1 Hz, 1.0H), 5.05-4.93 (m, 0.4H), 4.86 (d, *J* = 15.7 Hz, 1.0H), 4.69 (d, *J* = 15.7 Hz, 1.2H), 4.34 (d, *J* = 16.0 Hz, 1.2H), 3.30 (d, *J* = 8.9 Hz, 0.2H), 3.21 (d, *J* = 9.3 Hz, 1.0H), 2.87-2.68 (m, 1.0H), 2.57-2.41 (m, 0.2H), 2.08-1.92 (m, 0.2H), 1.90-1.82 (m, 1.0H), 1.65-1.55 (m, 2.4H), 1.05 (t, *J* = 7.3 Hz, 3.5H), 0.89 (s, 9.0H), ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) *δ* 176.0, 173.0, 151.3, 143.4, 142.6, 135.0, 134.3, 130.4, 129.0, 128.8, 128.7, 128.5, 127.6, 127.5, 127.1, 126.7, 125.7, 125.5, 125.1, 124.2, 123.0, 110.5, 109.6, 80.2, 75.9, 73.1, 70.7, 44.0, 43.5, 35.3, 28.4, 27.7, 18.9, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{39}H_{40}Cl_1N_4O_4^+$ 663.2733, found 663.2724.

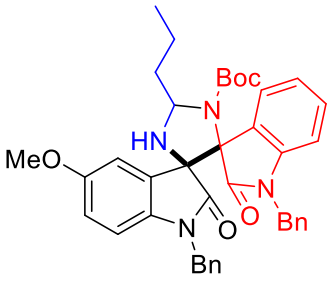


4dea: white solid (133 mg, 0.188 mmol, 94% yield, *two diastereomers*, 76:24 *dr*) m.p. 221-225 °C; IR (KBr) *v* 3414, 2974, 2869, 2170, 1717, 1489, 1187, 739 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) *δ* 7.63 (d, *J* = 2.1 Hz, 1.2H), 7.37 (d, *J* = 7.5 Hz, 1.0H), 7.34-7.27 (m, 0.4H), 7.28-7.07 (m, 9.6H), 7.06-7.01 (m, 2.0H), 6.99-6.95 (m, 0.4H), 6.87 (t, *J* = 7.5 Hz, 1.0H), 6.86-6.73 (m, 0.6H), 6.71 (d, *J* = 7.3 Hz, 2.0H), 6.50 (d, *J* = 7.8 Hz, 1.0H), 6.45 (d, *J* = 7.9 Hz, 0.2H), 6.24 (d, *J* = 8.4 Hz, 1.2H), 5.64 (t, *J* = 8.8 Hz, 1.0H), 5.56 (s, 0.2H), 5.06 (d, *J* = 16.1 Hz, 1.0H), 5.04-4.89 (m, 0.4H), 4.84 (d, *J* = 15.8 Hz, 1.0H), 4.71 (d, *J* = 15.6 Hz, 1.2H), 4.34 (d, *J* = 16.0 Hz, 1.2H), 3.30 (d, *J* = 10.2 Hz, 0.2H), 3.21 (d, *J* = 9.7 Hz, 1.0H), 2.91-2.64 (m, 1.0H), 2.56-2.32 (m, 0.2H), 2.08-1.95 (m, 0.2H), 1.94-1.78 (m, 1.0H), 1.63-1.57 (m, 2.4H), 1.05 (t, *J* = 7.3 Hz, 3.4H), 0.88 (s, 9.1H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) *δ* 176.3, 173.5, 151.4, 144.0, 143.4, 135.0, 134.8, 130.4, 128.8, 128.6, 128.6, 127.5, 127.3, 127.2, 126.7 ,125.8, 125.5, 124.9, 123.0, 122.9, 122.5, 109.5, 109.4, 80.1, 75.9, 73.3, 70.9, 43.9, 43.4, 35.3, 28.4, 27.7, 18.9, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for

$C_{39}H_{40}Br_1N_4O_4^+$ 707.2227, found 707.2217.

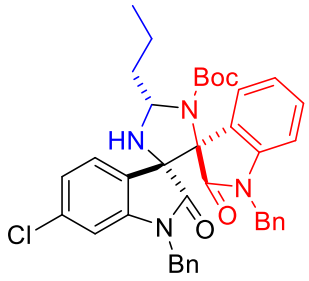


4eea: white solid (128 mg, 0.199 mmol, 99% yield, *two diastereomers*, 80:20 *dr*) m.p. 182-185 ℃; IR (KBr) *v* 3415, 2956, 2925, 2170, 1720, 1497, 1169, 744 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.41 (d, *J* = 7.3 Hz, 1.0H), 7.34-7.04 (m, 10.6H), 6.97-6.76 (m, 6.0H), 6.73 (d, *J* = 7.5 Hz, 2.0H), 6.45-6.36 (m, 1.6H), 6.26 (d, *J* = 7.8 Hz, 1.0H), 5.76-5.64 (m, 1.0H), 5.62-5.50 (m, 0.3H), 5.07 (d, *J* = 15.9 Hz, 1.6H), 4.96 (d, *J* = 16.0 Hz, 1.0H), 4.62 (d, *J* = 15.7 Hz, 0.3H), 4.56 (d, *J* = 16.0 Hz, 1.0H), 4.35 (d, *J* = 16.2 Hz, 1.3H), 3.42-3.13 (m, 1.3H), 2.88-2.67 (m, 1.0H), 2.56-2.41 (m, 0.2H), 2.07 (s, 3.0H), 2.02 (s, 1.0H), 1.96-1.77 (m, 1.1H), 1.66-1.57 (m, 2.6H), 1.05 (t, *J* = 7.3 Hz, 3.8H), 0.90 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.3, 173.5, 151.4, 143.5, 141.6, 135.1, 134.9, 132.7, 130.7, 128.8, 128.6, 128.5, 127.4, 127.2, 126.7, 126.7, 125.8, 125.6, 125.6, 122.9, 122.5, 109.4, 109.3, 80.0, 75.9, 73.4, 70.9, 43.7, 43.4, 35.3, 28.4, 27.7, 21.0, 18.9, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{40}H_{43}N_4O_4^+$ 643.3279, found 643.3268.

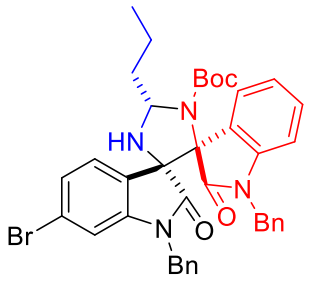


4fea: white solid (120 mg, 0.182 mmol, 91% yield, *two diastereomers*, 70:30 *dr*) m.p. 148-153 ℃; IR (KBr) *v* 3415, 2963, 2872, 2170, 1716, 1495, 1131, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.43 (d, *J* = 7.6 Hz, 1.0H), 7.35 (d, *J* = 7.5 Hz, 0.2H), 7.23-7.03 (m, 9.8H), 6.98-6.81 (m, 4.2H), 6.73 (d, *J* = 7.4 Hz, 2.0H), 6.67-6.55 (m, 1.2H), 6.46 (d, *J* = 7.9 Hz, 1.2H), 6.27 (d, *J* = 8.5 Hz, 1.2H), 5.67 (t, *J* = 7.8 Hz, 1.0H), 5.60 (t, *J* = 7.8 Hz, 0.2H), 5.06 (d, *J* = 16.1 Hz, 1.4H), 4.93 (d, *J* = 16.0 Hz, 1.0H), 4.62 (d, *J* = 15.9 Hz, 1.2H), 4.33 (d, *J* = 16.1 Hz, 1.2H), 3.52 (s, 3.0H), 3.46 (s, 0.6H), 3.30-3.11 (m, 1.2H), 2.90-2.59 (m, 1.0H), 2.58-2.37 (m, 0.2H), 2.07-1.93 (m, 0.2H), 1.94-1.79 (m, 1.1H), 1.66-1.56 (m, 2.4H), 1.05 (t, *J* = 7.3 Hz, 3.3H), 0.90 (s, 9.1H);

^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.3, 173.3, 156.0, 151.4, 143.5, 137.2, 135.0, 134.9, 128.8, 128.6, 128.6, 127.4, 127.2, 126.8, 126.8, 125.9, 125.5, 123.5, 122.9, 115.7, 111.6, 110.1, 109.4, 80.1, 76.0, 73.6, 70.9, 55.6, 43.8, 43.5, 35.3, 28.4, 27.7, 18.8, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{40}H_{43}N_4O_5^+$ 659.3228, found 659.3219.

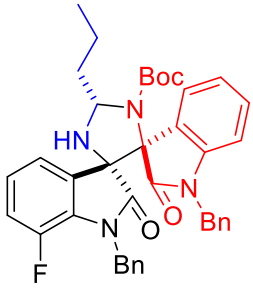


4gea: white solid (123 mg, 0.185 mmol, 93% yield, *two diastereomers*, 76:24 *dr*) m.p. 229-234 ℃; IR (KBr) *v* 3339, 3066, 2870, 2171, 1716, 1461, 1102, 729 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.37 (d, *J* = 7.2 Hz, 1.0H), 7.30 (d, *J* = 8.2 Hz, 1.2H), 7.26-7.06 (m, 8.8H), 6.98-6.81 (m, 3.7H), 6.80-6.68 (m, 3.5H), 6.64 (dd, *J* = 8.1, 1.9 Hz, 0.2H), 6.52 (d, *J* = 7.8 Hz, 1.2H), 6.35 (d, *J* = 1.9 Hz, 1.2H), 5.64 (t, *J* = 8.9 Hz, 1.0H), 5.56 (t, *J* = 9.4 Hz, 0.2H), 5.05 (d, *J* = 16.0 Hz, 1.0H), 5.03-4.92 (m, 0.4H), 4.87 (d, *J* = 15.8 Hz, 1.0H), 4.67 (d, *J* = 16.3 Hz, 0.2H), 4.61 (d, *J* = 15.8 Hz, 1.0H), 4.32 (d, *J* = 16.1 Hz, 1.2H), 3.26 (d, *J* = 10.6 Hz, 0.2H), 3.17 (d, *J* = 10.5 Hz, 1.0H), 2.81-2.73 (m, 1.0H), 2.60-2.35 (m, 0.2H), 2.03-1.93 (m, 0.2H), 1.93-1.77 (m, 1.0H), 1.64-1.54 (m, 2.5H), 1.04 (t, *J* = 7.3 Hz, 3.5H), 0.89 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.1, 173.4, 151.3, 145.3, 143.4, 136.4, 135.0, 134.2, 129.0, 128.8, 128.7, 127.6, 127.5, 127.2, 126.7, 126.0, 125.7, 125.3, 123.0, 122.9, 120.9, 110.0, 109.5, 80.2, 75.9, 72.9, 70.8, 43.8, 43.5, 35.2, 28.4, 27.7, 18.8, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{39}H_{40}Cl_1N_4O_4^+$ 663.2733, found 663.2722.

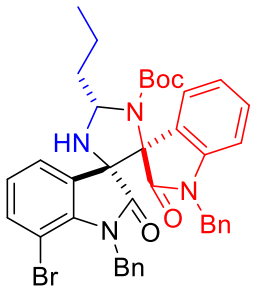


4hea: white solid (120 mg, 0.170 mmol, 85% yield, *two diastereomers*, 71:29 *dr*) m.p. 231-235 ℃; IR (KBr) *v* 3416, 2964, 2870, 2171, 1720, 1489, 1154, 751 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.36 (d, *J* = 7.5 Hz, 1.0H), 7.31-7.05 (m, 9.8H), 6.97-6.74 (m, 5.4H), 6.72 (d, *J* = 7.2 Hz, 2.0H), 6.57-6.49 (m, 2.4H), 5.64 (t, *J* = 8.8 Hz, 1.0H), 5.55 (t, *J* = 9.3 Hz, 0.2H), 5.04 (d, *J* = 16.1 Hz, 1.0H), 5.02-4.95 (m, 0.4H), 4.88 (d, *J* = 15.8 Hz,

1.0H), 4.66 (d, *J* = 16.3 Hz, 0.2H), 4.60 (d, *J* = 15.8 Hz, 1.0H), 4.32 (d, *J* = 16.1 Hz, 1.2H), 3.25 (d, *J* = 10.7 Hz, 0.2H), 3.16 (d, *J* = 10.4 Hz, 1.0H), 2.80-2.72 (m, *J* = 13.7, 8.1, 2.5 Hz, 1.0H), 2.47 (dt, *J* = 15.3, 8.8 Hz, 0.2H), 2.09-1.90 (m, 0.2H), 1.93-1.78 (m, 1.0H), 1.64-1.53 (m, 2.4H), 1.04 (t, *J* = 7.3 Hz, 3.6H), 0.89 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.1, 173.3, 151.3, 145.4, 143.4, 134.9, 134.2, 129.0, 128.8, 128.7, 127.6, 127.5, 127.1, 126.7, 126.2, 125.8, 125.7, 125.3, 124.4, 123.0, 121.5, 112.7, 109.5, 80.2, 75.9, 72.9, 70.7, 43.8, 43.5, 35.2, 28.3, 27.7, 18.8, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{39}H_{40}Br_1N_4O_4^+$ 707.2227, found 707.2221.

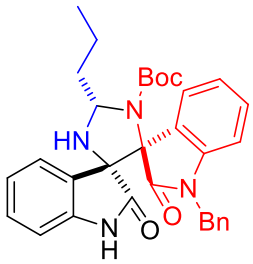


4iea : white solid (130 mg, 0.200 mmol, 99% yield, *two diastereomers*, 75:25 *dr*) m.p. 177-182 °C; IR (KBr) *v* 3418, 2962, 2873, 2171, 1719, 1455, 1162, 753 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.31 (d, *J* = 7.5 Hz, 1.0H), 7.19 (tt, *J* = 13.9, 7.3 Hz, 8.4H), 7.07 (t, *J* = 7.6 Hz, 1.2H), 7.02-6.84 (m, 6.0H), 6.82-6.73 (m, 2.2H), 6.73-6.63 (m, 0.2H), 6.49 (d, *J* = 7.8 Hz, 1.2H), 5.72-5.60 (m, 1.0H), 5.55 (s, 0.2H), 4.98 (d, *J* = 15.7 Hz, 1.0H), 4.99-4.91 (m, 0.4H), 4.81 (d, *J* = 15.7 Hz, 1.0H), 4.79-4.61 (m, 2.5H), 3.53-3.05 (m, 1.2H), 2.81-2.72 (m, 1.0H), 2.57-2.39 (m, 0.2H), 2.02-1.94 (m, 0.2H), 1.93-1.78 (m, 1.0H), 1.63-1.53 (m, 2.4H), 1.04 (t, *J* = 7.3 Hz, 3.6H), 0.89 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.1, 172.9, 151.3, 146.9 (d, $^1J_{C\text{-}F}$ = 243 Hz), 143.3, 136.2, 135.1, 130.9 (d, $^3J_{C\text{-}F}$ = 9 Hz), 129.0, 128.7, 128.4, 127.6, 127.3, 127.1, 126.9, 125.8, 125.3 (d, $^4J_{C\text{-}F}$ = 3 Hz), 125.0, 123.5 (d, $^3J_{C\text{-}F}$ = 6 Hz), 123.0, 120.9 (d, $^4J_{C\text{-}F}$ = 3 Hz) 118.6(d, $^2J_{C\text{-}F}$ = 19 Hz), 109.3, 80.1, 75.8, 73.1, 70.6, 45.0, 43.9, 35.3, 28.4, 27.7, 18.9, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{39}H_{40}F_1N_4O_4^+$ 647.3028, found 647.3009.

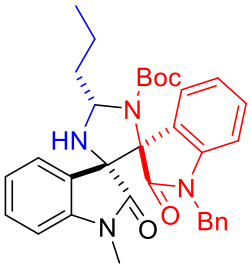


4jea : white solid (139 mg, 0.197 mmol, 98% yield, *two*

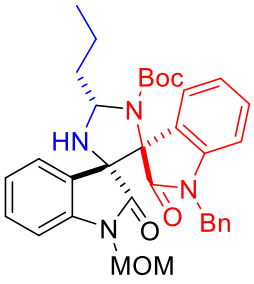
diastereomers, 71:29 *dr*) m.p. 229-233 °C;IR (KBr) *v* 3415, 2966, 2870, 2171, 1729, 1496, 1161, 768 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.43 (d, *J* = 7.5 Hz, 1.0H), 7.41-6.92 (m, 13.9H), 6.85-6.57 (m, 5.8H), 6.52 (d, *J* = 7.8 Hz, 1.0H), 5.60 (d, *J* = 9.0 Hz, 1.0H), 5.51 (d, *J* = 8.2 Hz, 0.3H), 5.30-5.10 (m, 2.5H), 4.95 (d, *J* = 16.1 Hz, 0.3H), 4.85 (d, *J* = 15.7 Hz, 1.0H), 4.65 (d, *J* = 15.7 Hz, 1.3H), 3.45-3.03 (m, 1.2H), 2.88-2.64 (m, 1.0H), 2.56-2.39 (m, 0.2H), 2.01-1.96 (m, 0.3H), 1.90-1.81 (m, 1.0H), 1.63-1.52 (m, 2.5H), 1.04 (t, *J* = 7.3 Hz, 3.7H), 0.87 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.1, 173.9, 151.3, 143.3, 141.7, 136.9, 136.5, 135.1, 129.0, 128.7, 128.4, 127.6, 127.3, 126.7, 126.0, 125.9, 125.7, 125.0, 124.1, 123.2, 109.4, 102.3, 80.2, 75.7, 72.4, 70.7, 44.4, 43.9, 35.3, 28.3, 27.7, 18.9, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{39}H_{40}Br_1N_4O_4^+$ 707.2227, found 707.2225.



4kea : white solid (99 mg, 0.184 mmol, 92% yield, *two diastereomers*, 80:20 *dr*) m.p. 238-241 °C; IR (KBr) *v* 3403, 2970, 2873, 2171, 1713, 1470, 1162, 748 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 8.16 (s, 1.0H), 7.88 (s, 0.2H), 7.47-7.30 (m, 2.4H), 7.25-7.11 (m, 4.8H), 7.04 (t, *J* = 7.7 Hz, 1.0H), 7.00-6.74 (m, 5.1H), 6.70 (d, *J* = 7.8 Hz, 1.2H), 6.42 (d, *J* = 7.8 Hz, 1.2H), 5.59 (t, *J* = 9.5 Hz, 1.0H), 5.50 (t, *J* = 8.5 Hz, 0.2H), 4.95 (d, *J* = 16.2 Hz, 0.2H), 4.85 (d, *J* = 15.8 Hz, 1.0H), 4.62 (d, *J* = 15.7 Hz, 1.2H), 3.28 (d, *J* = 10.4 Hz, 0.2H), 3.20 (d, *J* = 10.4 Hz, 1.0H), 2.88-2.59 (m, 1.0H), 2.50-2.41 (m, 0.1H), 2.07-1.95 (m, 0.2H), 1.91-1.79 (m, 1.0H), 1.63-1.52 (m, 2.0H), 1.02 (t, *J* = 7.3 Hz, 3.5H), 0.89 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.1, 175.4, 151.5, 143.3, 141.9, 135.1, 130.3, 129.0, 128.6, 127.5, 127.2, 125.3, 125.2, 125.1, 122.9, 122.8, 122.7, 110.1, 109.3, 80.1, 75.9, 73.5, 70.6, 43.8, 35.3, 28.4, 27.7, 18.9, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{32}H_{35}N_4O_4^+$ 539.2653, found 539.2637.

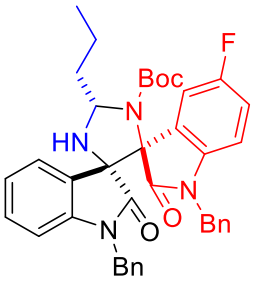


4lea： white solid (96 mg, 0.174 mmol, 87% yield, *two diastereomers*, 80:20 *dr*) m.p. 212-216 ℃; IR (KBr) *v* 3414, 2968, 2873, 2171, 1713, 1489, 1161, 753 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.37 (d, *J* = 7.5 Hz, 2.6H), 7.25-7.15 (m, 4.6H), 7.06-6.99 (m, 1.3H), 6.98-6.88 (m, 3.6H), 6.85 (t, *J* = 7.6 Hz, 1.1H), 6.79 (t, *J* = 7.7 Hz, 0.3H), 6.58 (d, *J* = 7.8 Hz, 1.3H), 6.39 (d, *J* = 7.7 Hz, 1.3H), 5.74-5.59 (m, 1.0H), 5.60-5.49 (m, 0.3H), 4.93 (d, *J* = 16.1 Hz, 0.3H), 4.81 (d, *J* = 15.8 Hz, 1.0H), 4.62 (d, *J* = 15.8 Hz, 1.3H), 3.31 (d, *J* = 11.2 Hz, 0.3H), 3.23 (d, *J* = 8.9 Hz, 1.0H), 2.95 (s, 3.7H), 2.83-2.63 (m, 1.0H), 2.46 (d, *J* = 8.2 Hz, 0.3H), 2.05-1.92 (m, 0.3H), 1.90-1.76 (m, 1.0H), 1.67-1.58 (m, 2.6H), 1.04 (t, *J* = 7.3 Hz, 3.8H), 0.89 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.1, 173.4, 151.4, 144.7, 143.3, 135.1, 130.3, 128.8, 128.6, 127.5, 127.2, 125.3, 125.1, 124.7, 122.8, 122.4, 122.3, 109.2, 108.1, 80.0, 76.1, 73.3, 70.6, 43.8, 35.3, 28.4, 27.7, 25.6, 18.9, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{33}H_{37}N_4O_4^+$ 553.2809, found 553.2796.

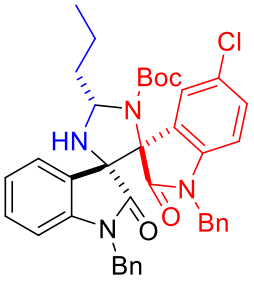


4mea： white solid (104 mg, 0.178 mmol, 89% yield, *two diastereomers*, 78:22 *dr*) m.p. 192-197 ℃; IR (KBr) *v* 3415, 2965, 2928, 2171, 1728, 1466, 1162, 795 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.42 (d, *J* = 7.5 Hz, 1.0H), 7.39 (d, *J* = 7.3 Hz, 1.3H),7.33-7.15 (m, 5.3H), 7.03 (t, *J* = 7.6 Hz, 1.3H), 6.98-6.80 (m, 6.0H), 6.42 (d, *J* = 7.7 Hz, 1.2H), 5.59 (t, *J* = 8.0 Hz, 1.0H), 5.51 (t, *J* = 8.0 Hz, 0.2H), 5.00 (d, *J* = 11.0 Hz, 1.4H), 4.90-4.77 (m, 2.2H), 4.66 (d, *J* = 15.9 Hz, 0.2H), 4.61 (d, *J* = 15.8 Hz, 1.0H), 3.29 (d, *J* = 10.5 Hz, 0.2H), 3.19 (d, *J* = 9.3 Hz, 1.0H), 3.06 (s, 0.5H), 3.02 (s, 3.0H), 2.82-2.69 (m, 1.0H), 2.55-2.38 (m, 0.2H), 2.09-1.91 (m, 0.2H), 1.92-1.77 (m, 1.0H), 1.63-1.53 (m, 2.5H), 1.03 (t, *J* = 7.3 Hz, 3.7H), 0.89 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.1, 173.7, 151.3, 143.4, 143.2, 135.0, 130.6, 129.0, 128.6, 127.5, 127.2, 125.6, 125.4, 124.9, 123.4, 122.5, 122.0, 109.7, 109.4, 80.1, 75.8, 73.6, 71.8, 70.6, 56.3, 43.9, 35.2, 28.4, 27.7, 18.9, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd

for $C_{34}H_{39}N_4O_5^+$ 583.2915, found 583.2905.

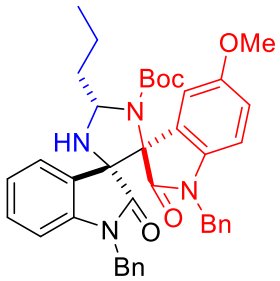


4aeb : white solid (62 mg, 0.096 mmol, 48% yield, *two diastereomers*, 68:32 *dr*) m.p. 207-212 ℃; IR (KBr) *v* 3416, 2957, 2871, 2171, 1725, 1455, 1173, 762 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.42 (d, J = 7.6 Hz, 1.0H), 7.39 (d, J = 7.9 Hz, 0.3H), 7.25-7.07 (m, 10.4H), 7.05-6.72 (m, 7.8H), 6.46 (d, J = 7.9 Hz, 1.3H), 6.35 (dd, J = 8.6, 4.1 Hz, 0.3H), 5.64 (t, J = 8.9 Hz, 1.0H), 5.54 (t, J = 8.4 Hz, 0.3H), 5.12 (d, J = 16.0 Hz, 1.3H), 4.92 (d, J = 16.2 Hz, 0.3H), 4.82 (d, J = 15.8 Hz, 1.0H), 4.62 (d, J = 15.9 Hz, 1.3H), 4.38 (d, J = 15.8 Hz, 1.3H), 3.33 (d, J = 10.7 Hz, 0.3H), 3.23 (d, J = 10.7 Hz, 1.0H), 2.90-2.64 (m, 1.0H), 2.57-2.39 (m, 0.3H), 2.04-1.94 (m, 0.3H), 1.92-1.77 (m, 1.0H), 1.66-1.53 (m, 2.7H), 1.05 (t, J = 7.3 Hz, 3.9H), 0.94 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.1, 173.2, 159.2 (d, $^1J_{C\text{-}F}$ = 241 Hz), 151.2, 144.1, 139.3, 134.7 (d, $^3J_{C\text{-}F}$ = 7 Hz), 130.6, 128.7, 128.7, 127.6, 127.5, 127.2, 126.7, 124.9, 123.1, 122.2, 115.1 (d, $^2J_{C\text{-}F}$ = 23 Hz), 114.0 (d, $^2J_{C\text{-}F}$ = 26 Hz), 109.9 (d, $^3J_{C\text{-}F}$ = 8 Hz), 109.6, 80.4, 76.0, 72.4, 70.7, 44.0, 43.5, 35.3, 28.4, 27.8, 18.9, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{39}H_{40}F_1N_4O_4^+$ 647.3028, found 647.3037.

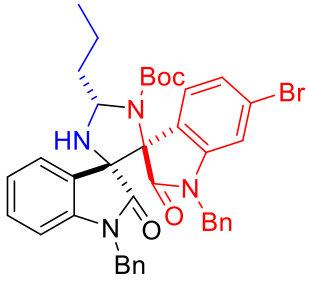


4aec : white solid (72 mg, 0.108 mmol, 54% yield, *two diastereomers*, 67:33 *dr*) m.p. 196-200 ℃; IR (KBr) *v* 3416, 2974, 2875, 2171, 1718, 1473, 1165, 763 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.46 (d, J = 2.2 Hz, 1.0H), 7.40 (d, J = 7.5 Hz, 1.6H), 7.25-7.01 (m, 10.5H), 6.96-6.73 (m, 6.6H), 6.44 (d, J = 7.9 Hz, 1.3H), 6.36 (d, J = 8.4 Hz, 1.3H), 5.64 (t, J = 8.6 Hz, 1.0H), 5.58 (t, J = 8.4 Hz, 0.3H), 5.17 (d, J = 15.9 Hz, 1.3H), 4.89 (d, J = 16.3 Hz, 0.3H), 4.79 (d, J = 15.8 Hz, 1.0H), 4.70 (d, J = 16.4 Hz, 0.3H), 4.64 (d, J = 15.9 Hz, 1.0H), 4.35 (d, J = 15.9 Hz, 1.3H), 3.31 (d, J = 9.0 Hz, 0.3H), 3.22 (d, J = 9.9 Hz, 1.0H), 2.90-2.67 (m, 1.0H), 2.57-2.40 (m, 0.3H), 2.09-1.91 (m, 0.3H), 1.92-1.72 (m, 1.0H), 1.67-1.54 (m, 2.6H), 1.05 (t, J = 7.3 Hz, 3.9H), 0.94 (s, 9.0H); ^{13}C NMR (100

MHz, $CDCl_3$, *major diastereomer*) δ 175.9, 173.1, 151.1, 144.1, 141.8, 134.8, 134.6, 130.6, 128.8, 128.7, 128.6, 127.7, 127.5, 127.2, 126.7, 126.2, 124.8, 123.1, 122.1, 110.4, 109.6, 80.4, 76.0, 73.4, 70.5, 44.0, 43.6, 35.3, 28.4, 27.8, 18.9, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{39}H_{40}Cl_1N_4O_4^+$ 663.2733, found 663.2742.

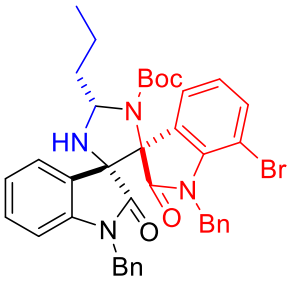


4aed: white solid (118 mg, 0.179 mmol, 90% yield, *two diastereomers*, 70:30 *dr*) m.p. 191-196 ℃; IR (KBr) ν 3415, 3027, 2873, 2171, 1717, 1473, 1186, 764 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.45 (d, J = 7.8 Hz, 1.0H), 7.42 (d, J = 7.7 Hz, 0.2H), 7.23-7.07 (m, 8.6H), 7.05 (d, J = 2.6 Hz, 1.0H), 7.00-6.89 (m, 2.4H), 6.85 (t, J = 7.7 Hz, 1.0H), 6.89-6.75 (m, 0.6H), 6.72 (d, J = 7.3 Hz, 2.0H), 6.63 (dd, J = 8.5, 2.6 Hz, 1.2H), 6.39 (d, J = 7.8 Hz, 1.2H), 6.35 (d, J = 8.5 Hz, 1.2H), 5.66 (t, J = 8.9 Hz, 1.0H), 5.57 (t, J = 9.2 Hz, 0.2H), 5.17 (d, J = 16.1 Hz, 1.2H), 4.89 (d, J = 16.1 Hz, 0.2H), 4.81 (d, J = 15.8 Hz, 1.0H), 4.70 (d, J = 16.2 Hz, 0.2H), 4.61 (d, J = 15.8 Hz, 1.0H), 4.33 (d, J = 16.1 Hz, 1.2H), 3.46 (s, 0.6H), 3.45 (s, 3.0H), 3.34 (d, J = 9.9 Hz, 0.2H), 3.25 (d, J = 10.1 Hz, 1.0H), 2.88-2.69 (m, 1.0H), 2.55-2.43 (m, 1.0H), 2.05-1.95 (m, 0.2H), 1.94-1.81 (m, 1.0H), 1.64-1.56 (m, 2.5H), 1.05 (t, J = 7.3 Hz, 3.7H), 0.93 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.0, 173.5, 156.1, 151.4, 144.2, 136.6, 135.2, 134.8, 130.4, 128.7, 128.6, 127.5, 127.3, 127.2, 126.8, 126.6, 126.5, 126.3, 125.0, 123.0, 122.5, 114.9, 111.5, 110.1, 109.4, 80.1, 75.9, 73.4, 71.1, 55.5, 44.0, 43.3, 35.3, 28.4, 27.8, 18.9, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{40}H_{43}N_4O_5^+$ 659.3228, found 659.3236.

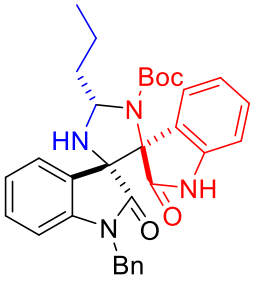


4aee: white solid (107 mg, 0.20 mmol, 75% yield, *two diastereomers*, 68:32 *dr*) m.p. 202-206 ℃; IR (KBr) ν 3416, 3060, 2870, 2171, 1726, 1455, 1162, 759 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.39 (d, J = 7.6 Hz, 1.0H), 7.35 (d, J = 7.6 Hz, 0.3H), 7.25-7.08 (m, 10.7H), 7.02-6.81 (m, 5.2H), 6.78 (d, J = 6.8 Hz, 0.7H), 6.74 (d, J = 6.4 Hz, 2.0H),

6.59 (d, *J* = 1.7 Hz, 1.0H), 6.57 (d, *J* = 1.7 Hz, 0.3H), 6.44 (d, *J* = 7.8 Hz, 1.3H), 5.63 (t, *J* = 8.3 Hz, 1.0H), 5.55 (t, *J* = 8.6 Hz, 0.3H), 5.11 (d, *J* = 16.1 Hz, 1.0H), 5.09 (d, *J* = 15.9 Hz, 0.3H), 4.89 (d, *J* = 16.2 Hz, 0.3H), 4.79 (d, *J* = 15.9 Hz, 1.0H), 4.65 (d, *J* = 16.4 Hz, 0.3H), 4.60 (d, *J* = 15.8 Hz, 1.0H), 4.35 (d, *J* = 16.0 Hz, 1.3H), 3.26 (d, *J* = 11.2 Hz, 0.3H), 3.17 (d, *J* = 7.9 Hz, 1.0H), 2.86-2.70 (m, 1.0H), 2.55-2.42 (m, 0.3H), 2.07-1.90 (m, 0.3H), 1.91-1.77 (m, 1.0H), 1.64-1.57 (m, 2.6H), 1.04 (t, *J* = 7.3 Hz, 3.9H), 0.92 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 176.1, 173.3, 151.1, 144.7, 144.0, 134.7, 134.4, 130.6, 128.8, 128.7, 127.7, 127.5, 127.1, 127.0, 126.7, 125.7, 124.8, 124.7, 123.1, 122.4, 122.2, 112.5, 109.6, 80.4, 76.0, 73.3, 70.5, 44.0, 43.4, 35.3, 28.4, 27.7, 18.8, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{39}H_{40}Br_1N_4O_4^+$ 707.2227, found 707.2236.



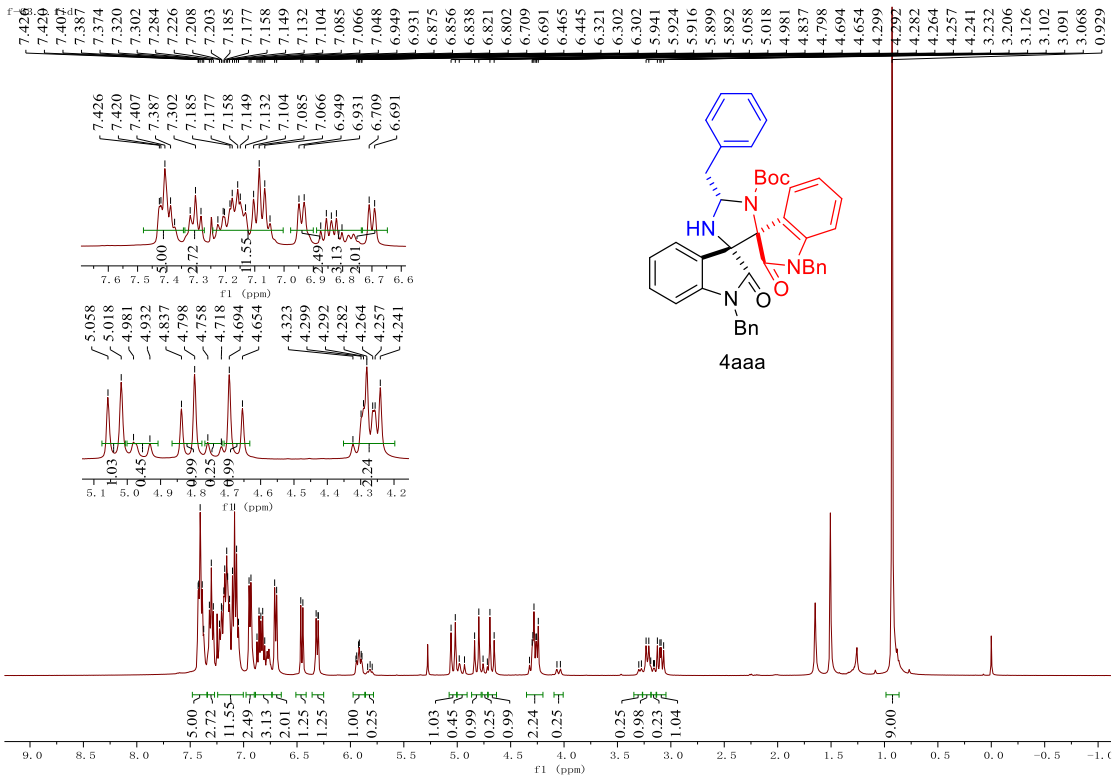
4aef: white solid (97 mg, 0.137 mmol, 68% yield, *two diastereomers*, 67:33 *dr*) m.p. 212-216 ℃; IR (KBr) *v* 3415, 3064, 2924, 2171, 1721, 1452, 1164, 733 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.43 (d, *J* = 7.5 Hz, 1.0H), 7.35-7.07 (m, 10.6H), 7.04-6.88 (m, 3.3H), 6.87-6.63 (m, 6.0H), 6.44 (d, *J* = 7.8 Hz, 1.3H), 5.65 (d, *J* = 8.9 Hz, 1.0H), 5.56 (d, *J* = 9.1 Hz, 0.3H), 5.40-4.93 (m, 4.0H), 4.40 (d, *J* = 15.8 Hz, 1.3H), 3.42-3.10 (m, 1.3H), 2.79-2.71 (m, 1.0H), 2.54-2.36 (m, 0.3H), 2.06-1.89 (m, 0.3H), 1.91-1.74 (m, 1.0H), 1.71-1.50 (m, 2.7H), 1.01 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 177.1, 173.3, 151.1, 143.9, 141.1, 136.9, 134.9, 134.8, 130.6, 129.0, 128.7, 128.4, 127.4, 127.0, 126.8, 126.5, 126.2, 125.0, 124.9, 124.0, 123.2, 121.9, 109.5, 102.2, 80.5, 76.1, 73.6, 70.0, 44.8, 43.4, 35.2, 28.4, 27.8, 18.8, 14.2; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{39}H_{40}Br_1N_4O_4^+$ 707.2227, found 707.2240.



4aeg: white solid (65 mg, 0.121 mmol, 60% yield, *two diastereomers*, 70:30 *dr*) m.p. 235-239 ℃; IR (KBr) *v* 3444,

2972, 2871, 2171, 1708, 1471, 1123, 754 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, *mixture of two diastereomers*) δ 7.58-7.44 (m, 2.6H), 7.38 (d, *J* = 7.6 Hz, 1.0H), 7.28 (d, *J* = 7.6 Hz, 0.3H), 7.23-7.06 (m, 6.6H), 6.95 (t, *J* = 7.7 Hz, 1.3H), 6.87 (t, *J* = 7.7 Hz, 1.3H), 6.79 (d, *J* = 7.3 Hz, 0.6H), 6.73 (d, *J* = 7.4 Hz, 2.0H), 6.63 (d, *J* = 7.8 Hz, 1.3H), 6.35 (d, *J* = 7.5 Hz, 1.3H), 5.63 (t, *J* = 9.9 Hz, 1.0H), 5.55 (t, *J* = 10.0 Hz, 0.3H), 5.11 (d, *J* = 15.8 Hz, 1.3H), 4.33 (d, *J* = 16.2 Hz, 1.3H), 3.26 (d, *J* = 10.8 Hz, 0.3H), 3.15 (d, *J* = 10.7 Hz, 0.9H), 2.91-2.71 (m, 1.0H), 2.49-2.44 (m, 0.3H), 2.05-1.91 (m, 0.3H), 1.85-1.75 (m, 1.1H), 1.63-1.53 (m, 2.6H), 1.03 (t, *J* = 7.3 Hz, 3.9H), 0.99 (s, 9.0H); ^{13}C NMR (100 MHz, $CDCl_3$, *major diastereomer*) δ 177.5, 173.3, 151.4, 144.0, 141.0, 134.8, 130.4, 128.8, 128.6, 127.3, 126.8, 126.2, 126.0, 124.7, 122.9, 122.8, 122.4, 110.0, 109.4, 80.1, 75.7, 73.2, 71.0, 43.4, 35.1, 28.4, 27.7, 18.8, 14.1; HRMS (TOF-ES+) m/z:$[M+H]^+$ calcd for $C_{32}H_{35}N_4O_4^+$ 539.2653, found 539.2659.

4. NMR Spectra of All New Compounds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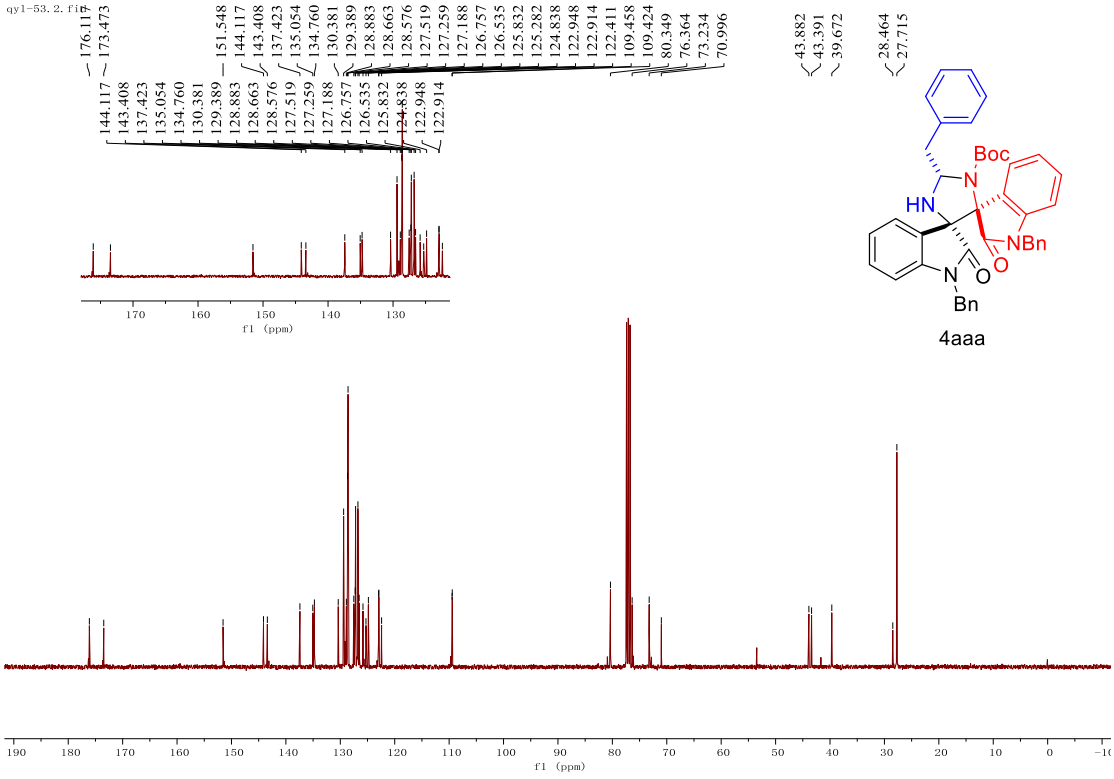
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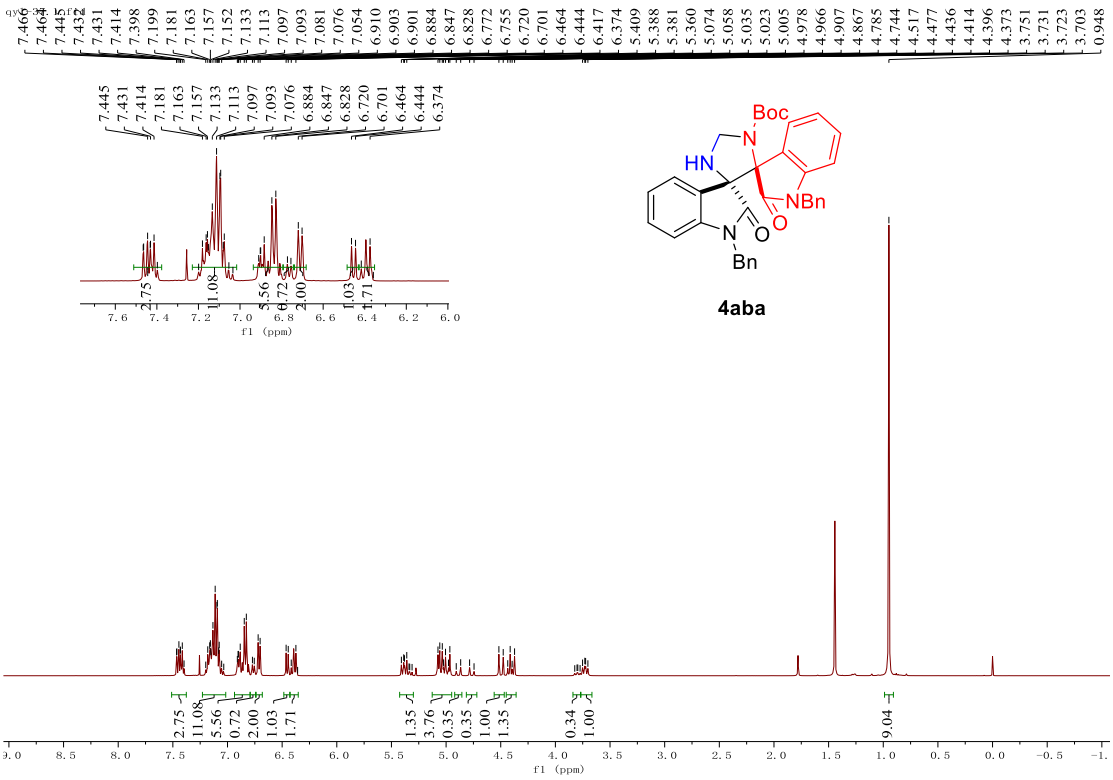
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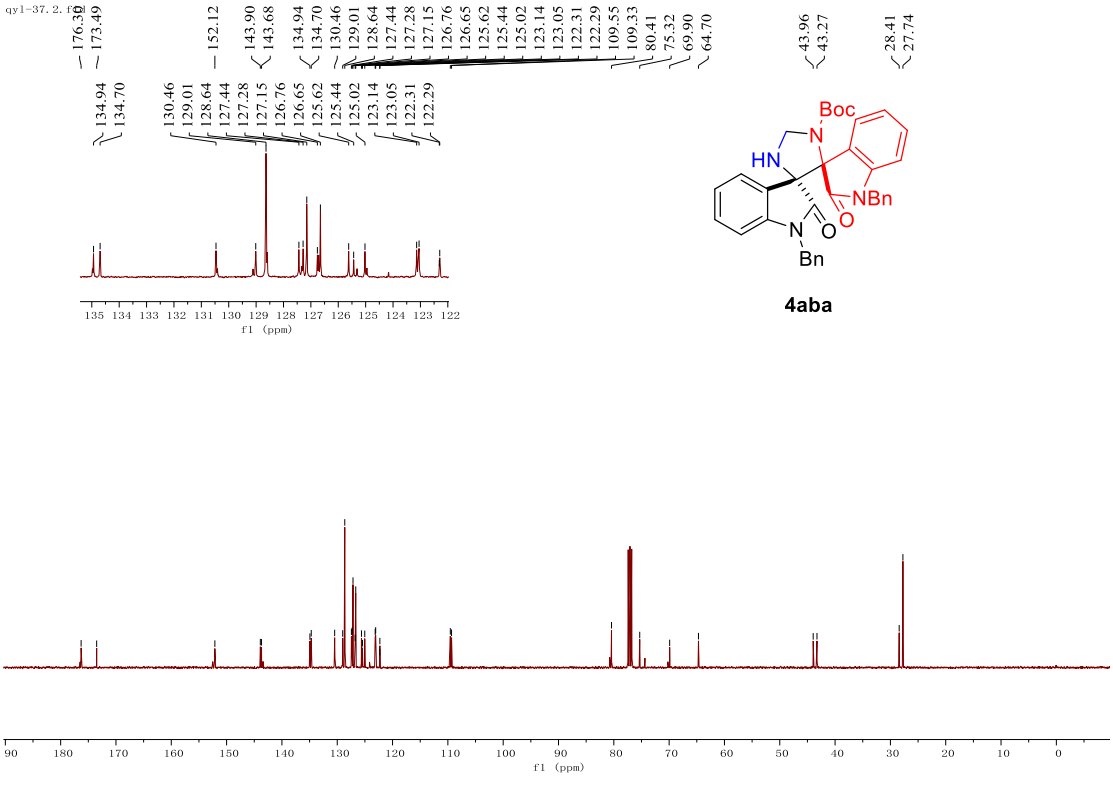
Boc
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HN
NBn
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N
O
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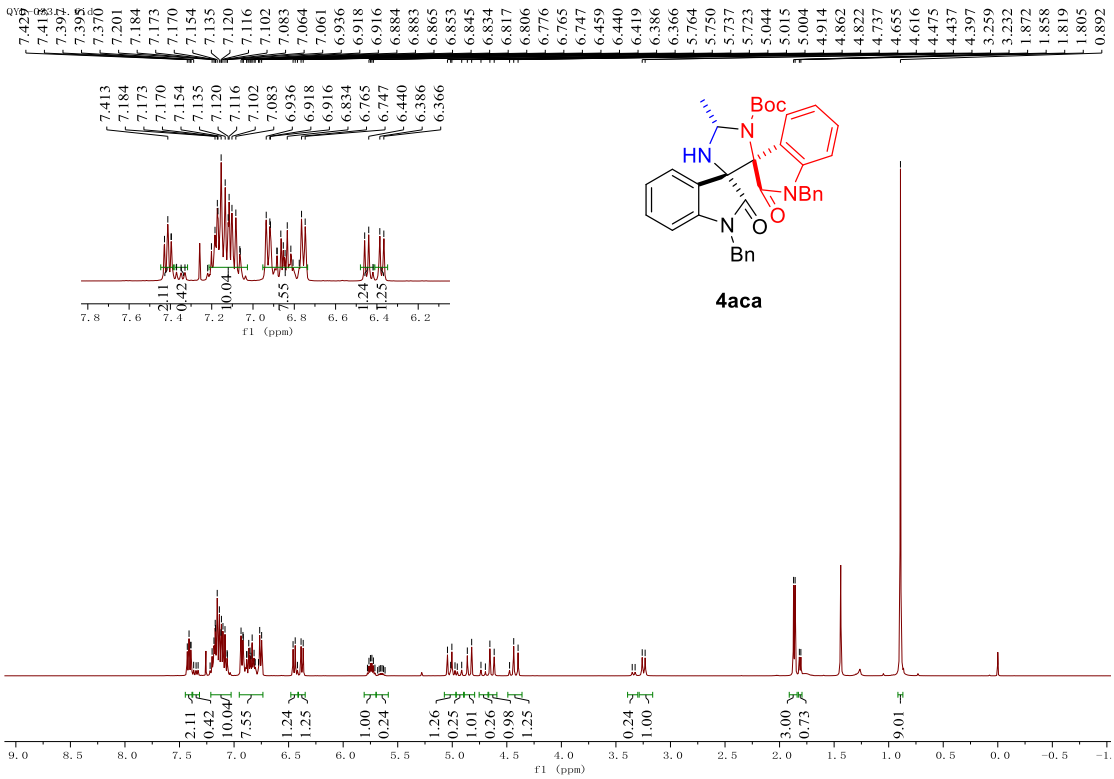
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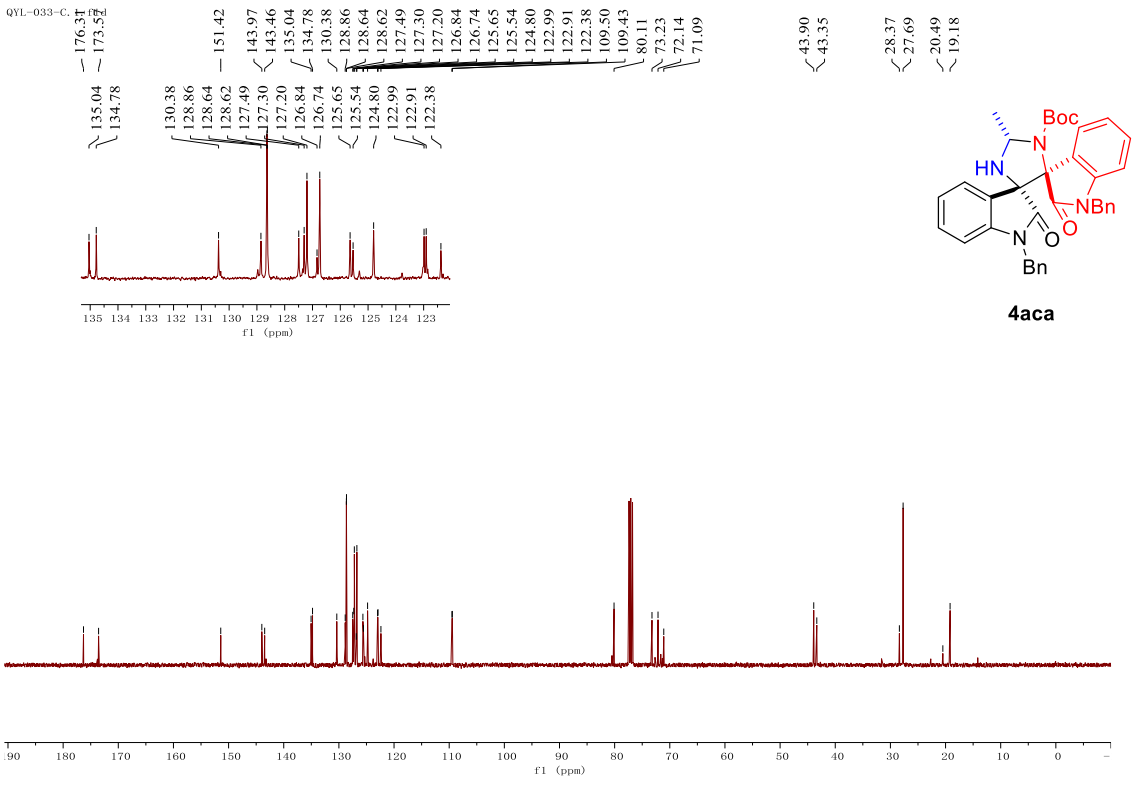
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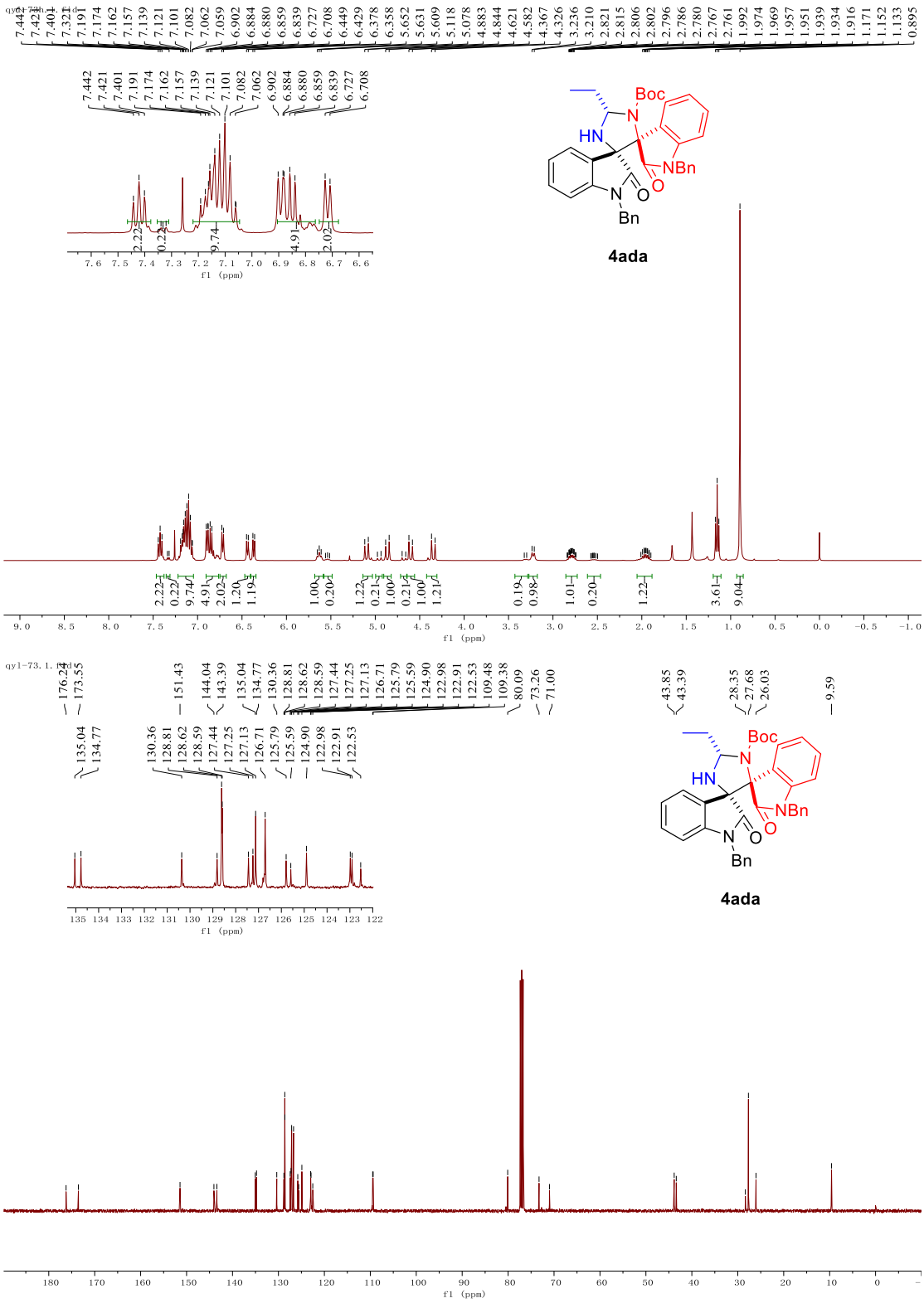
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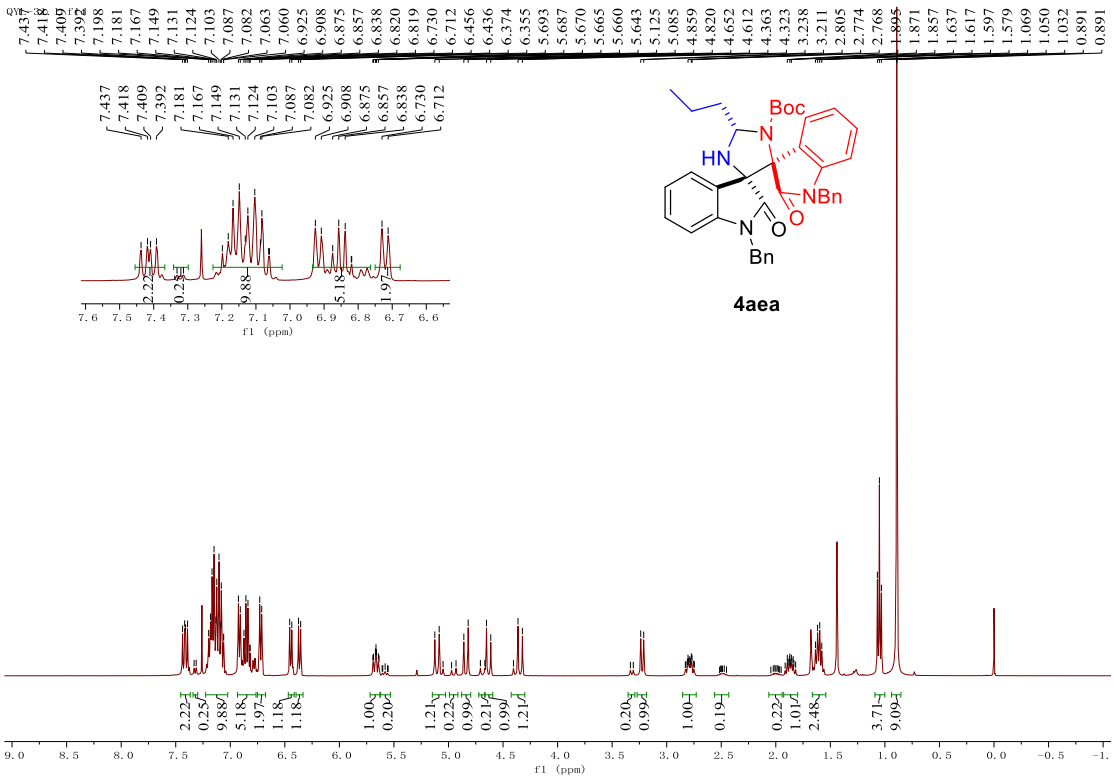

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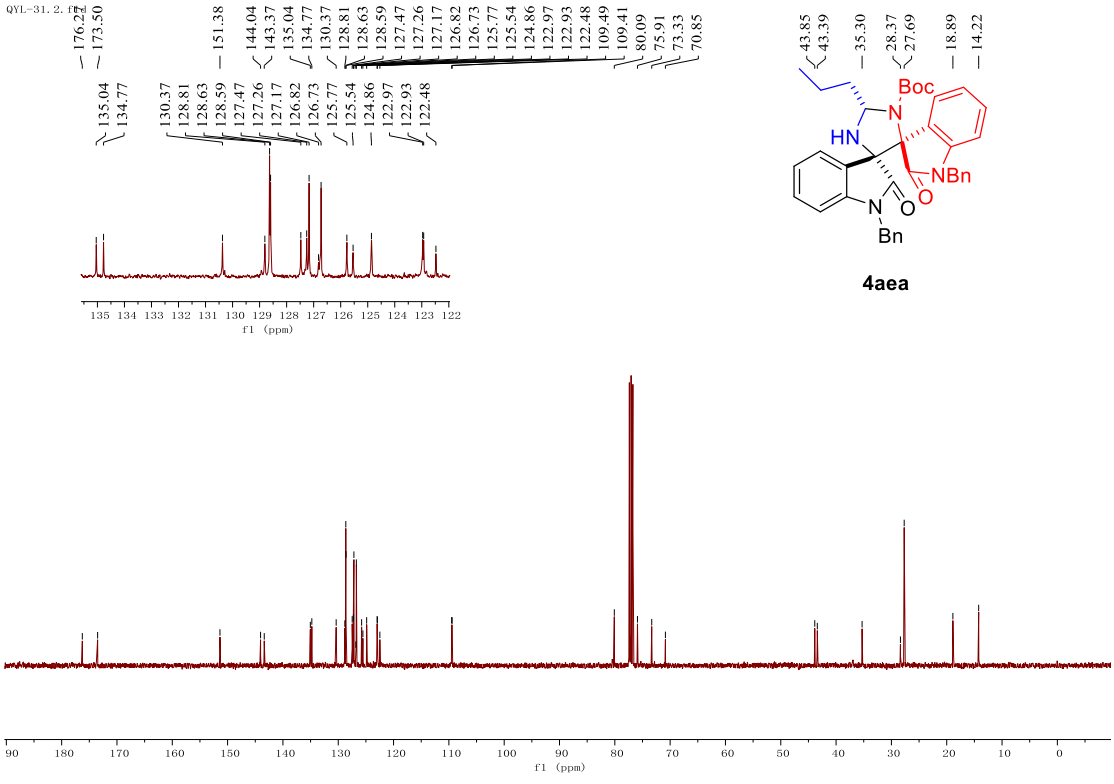

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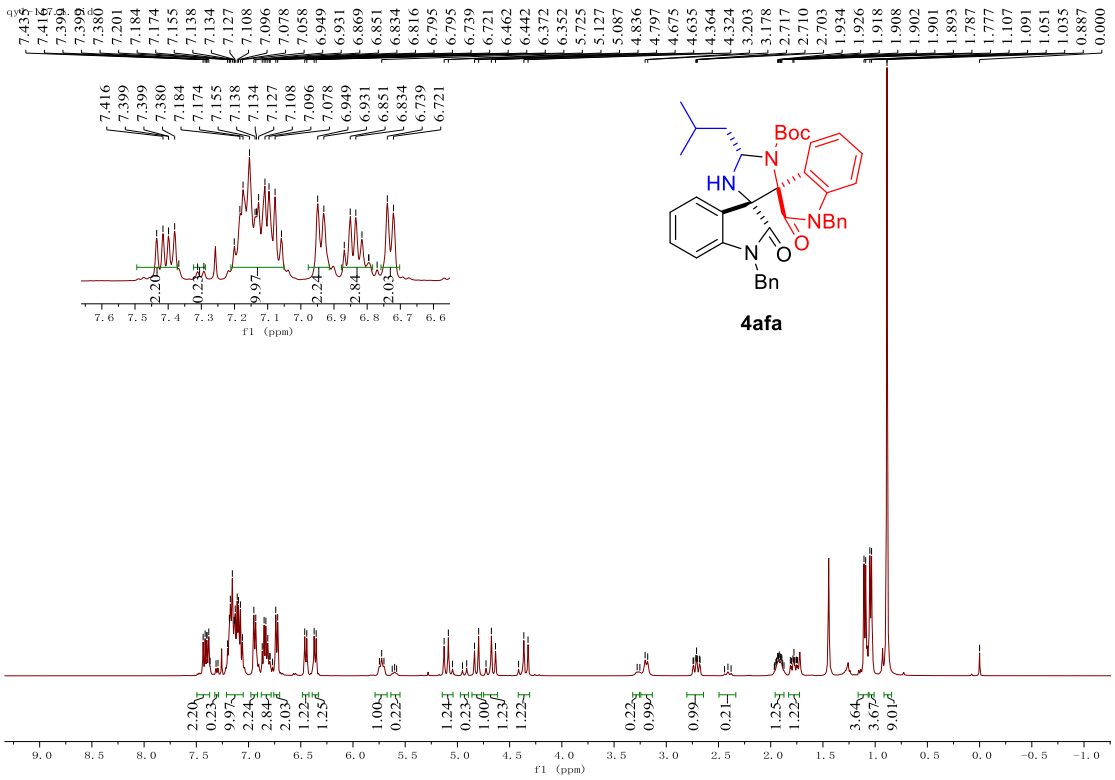
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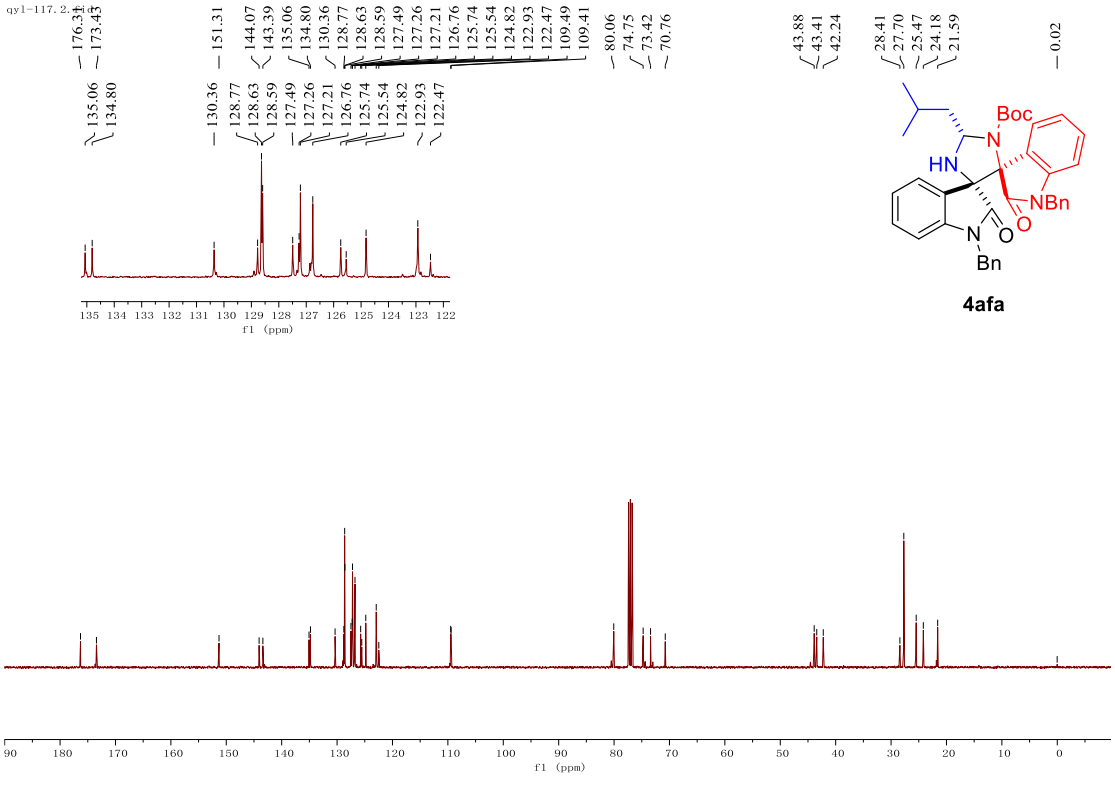
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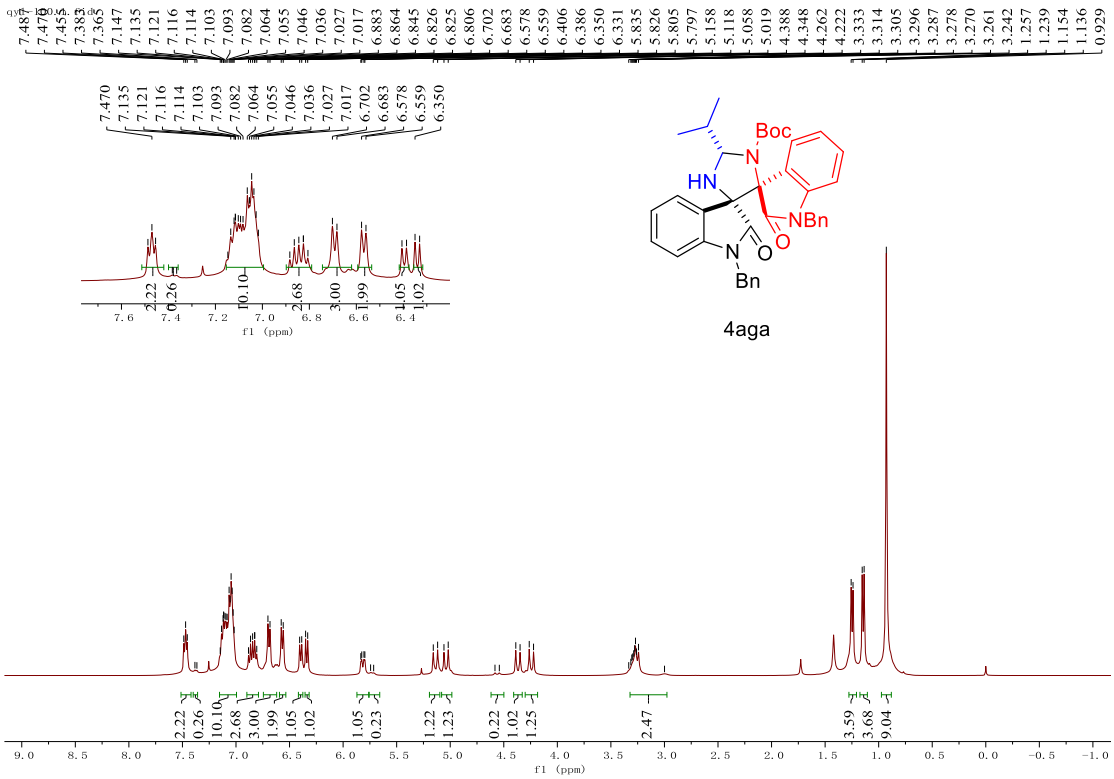

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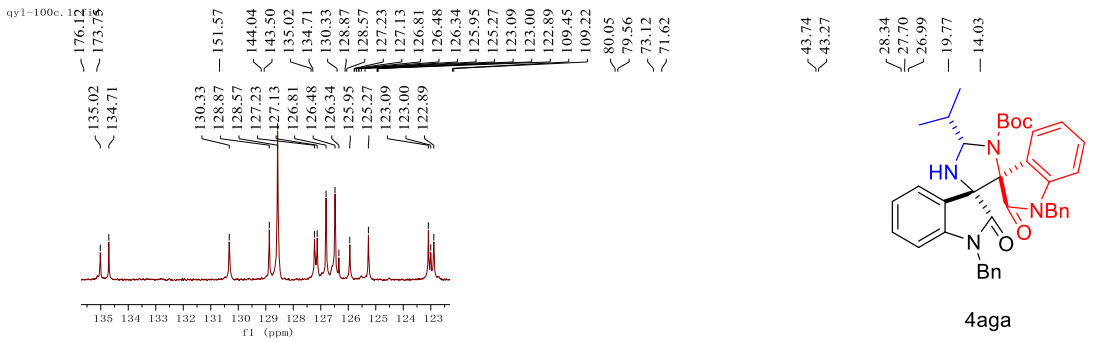

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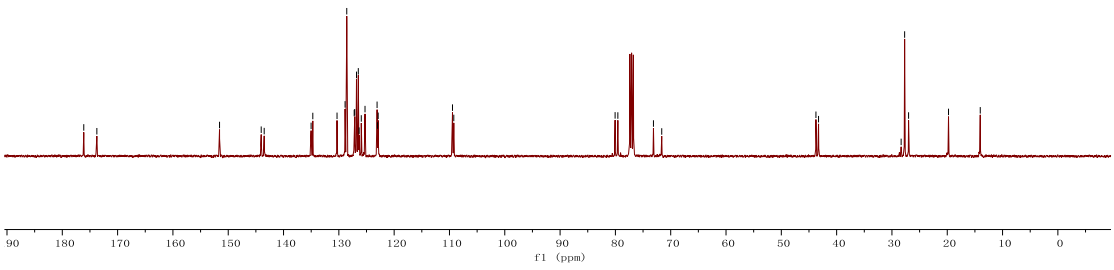

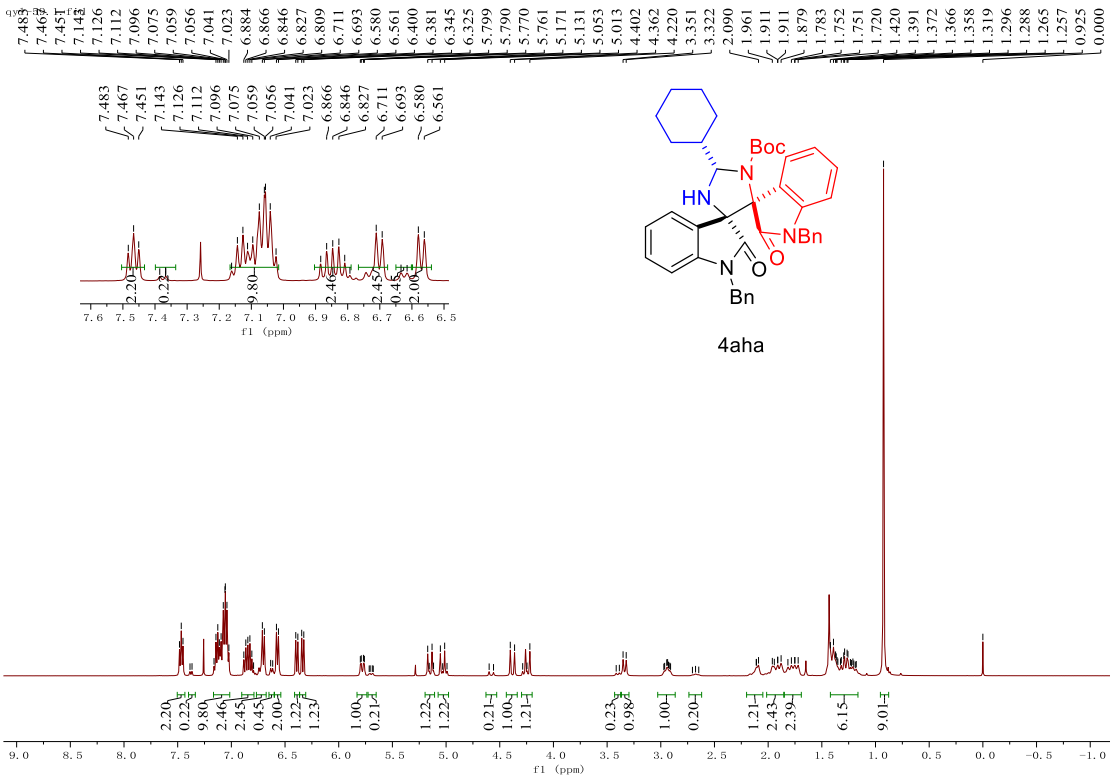

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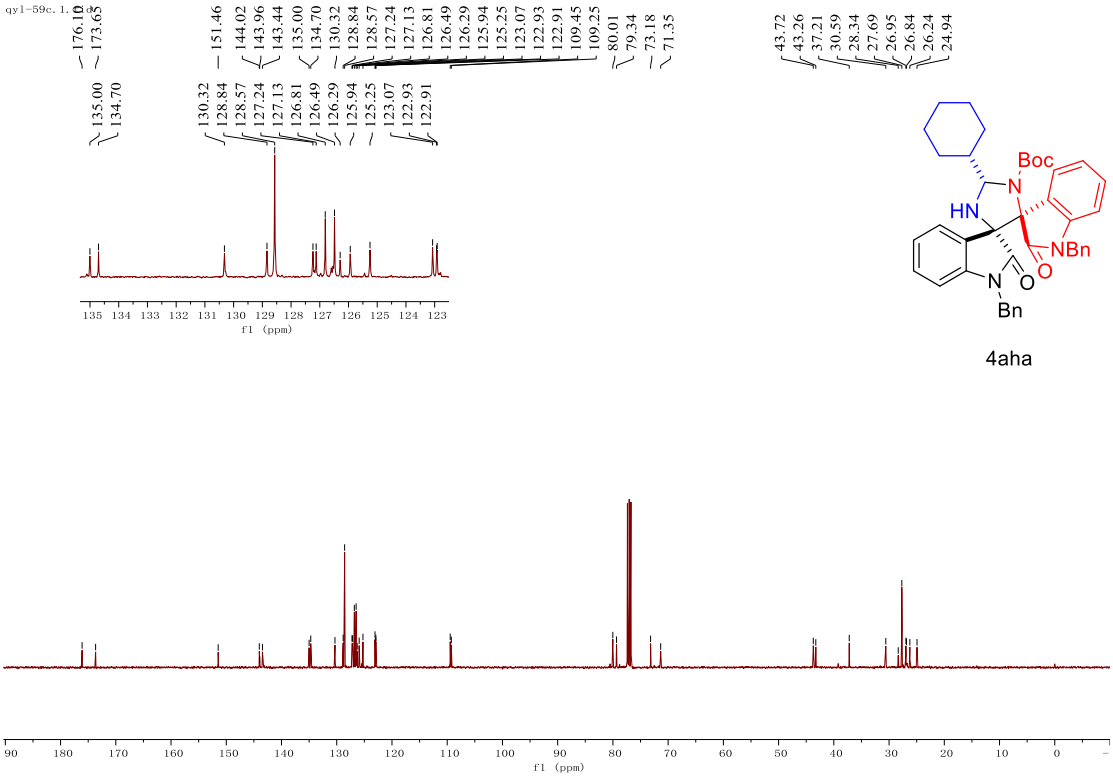

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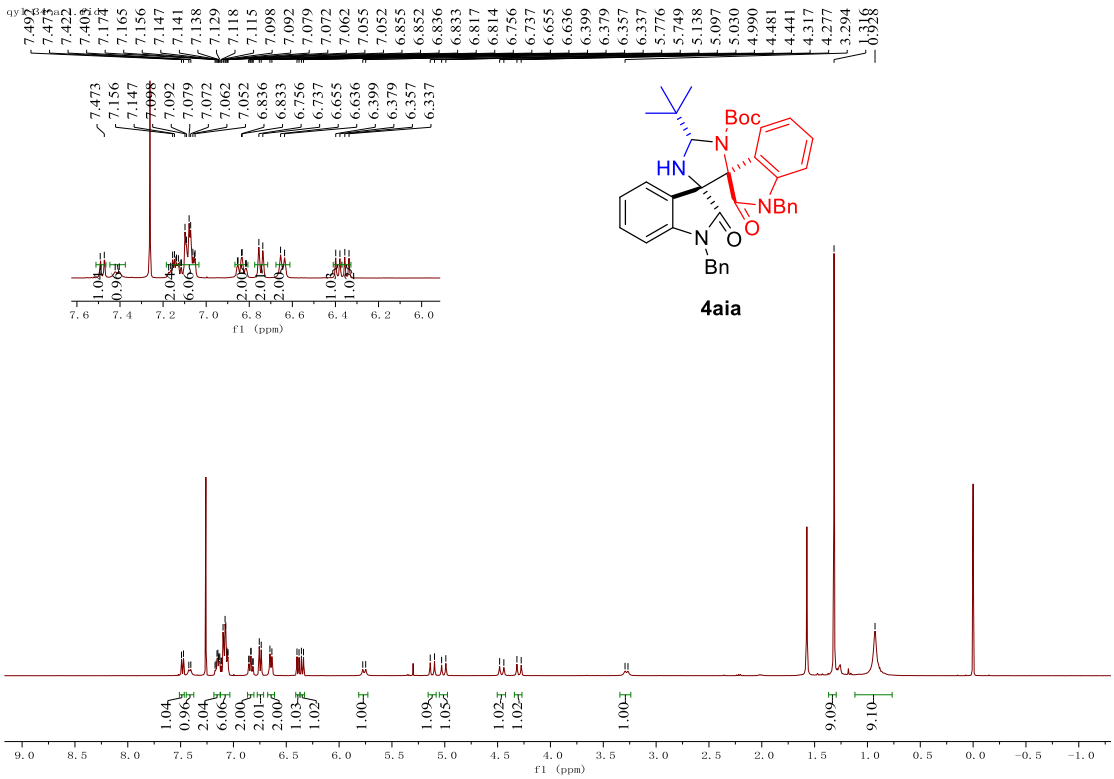

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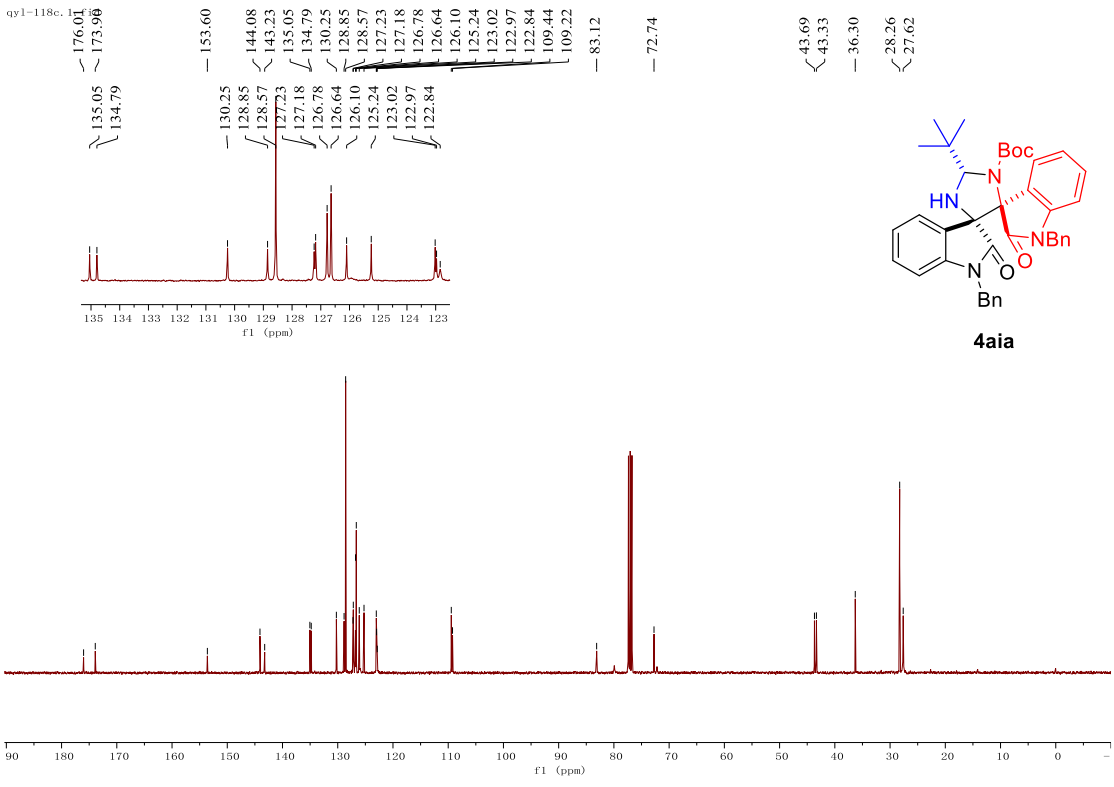

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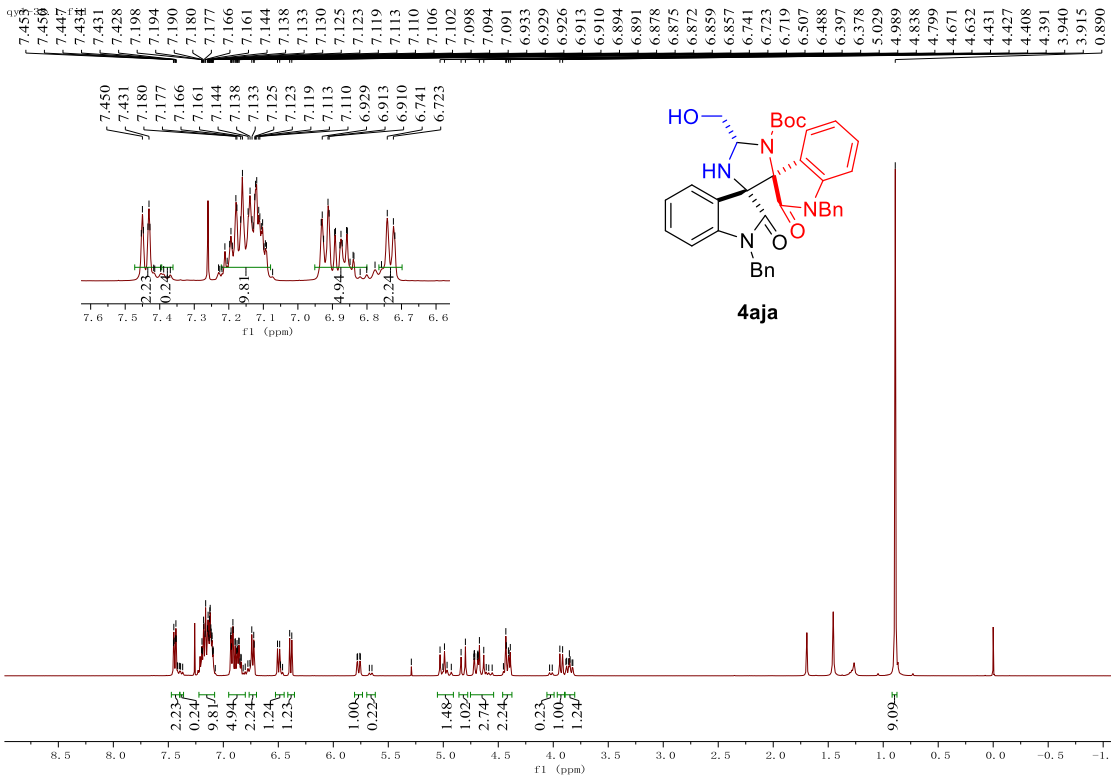

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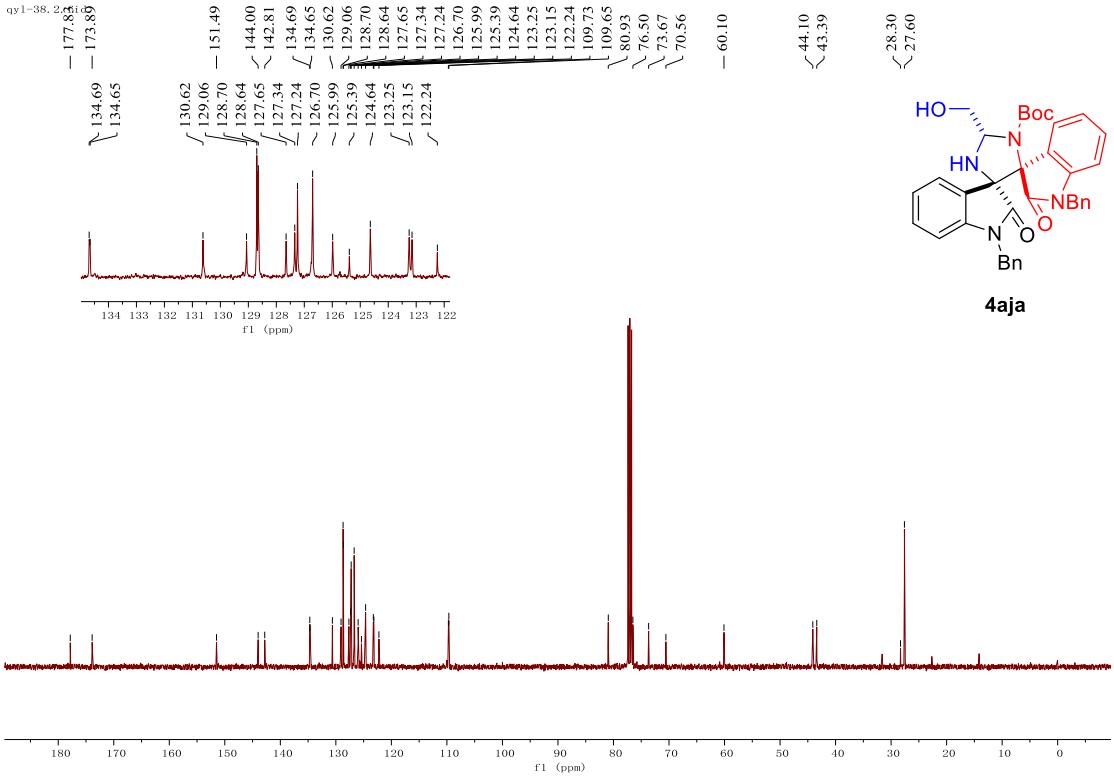

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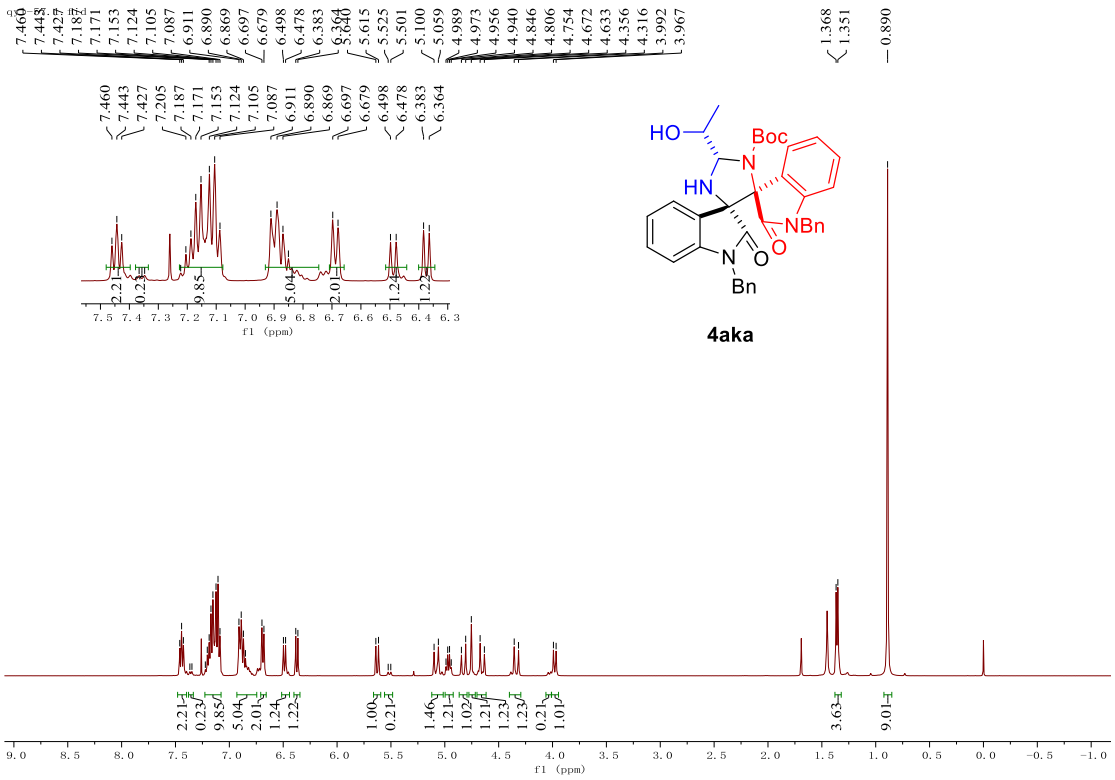

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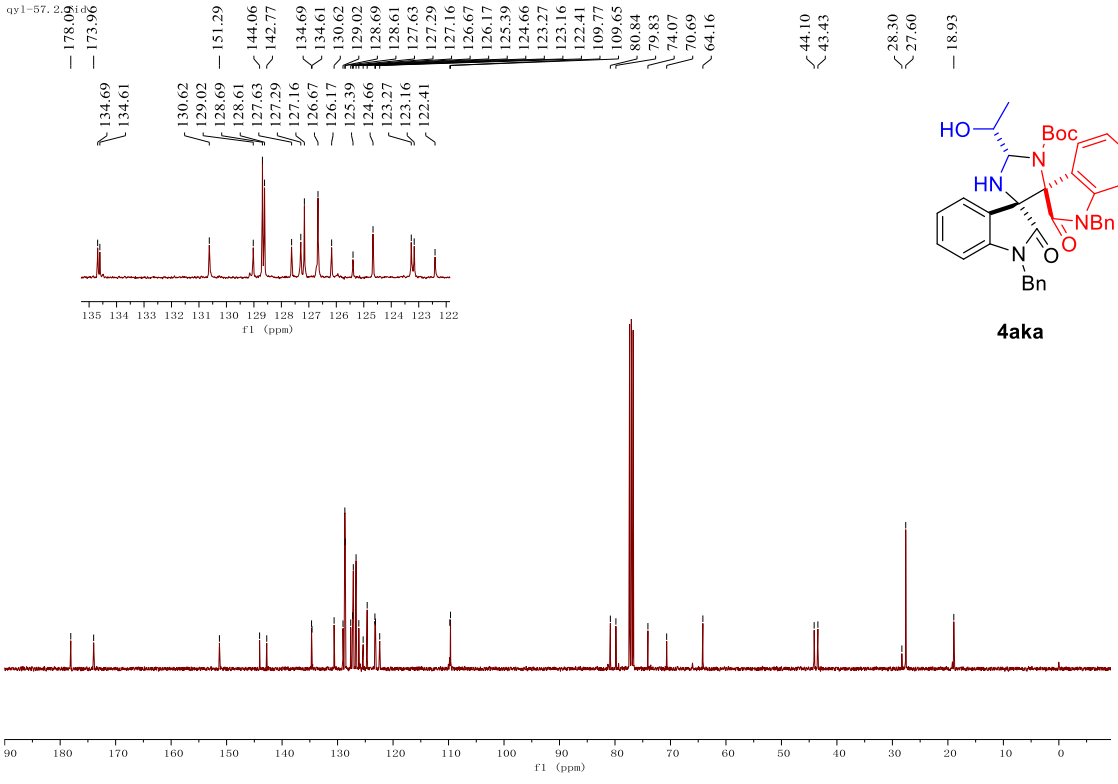

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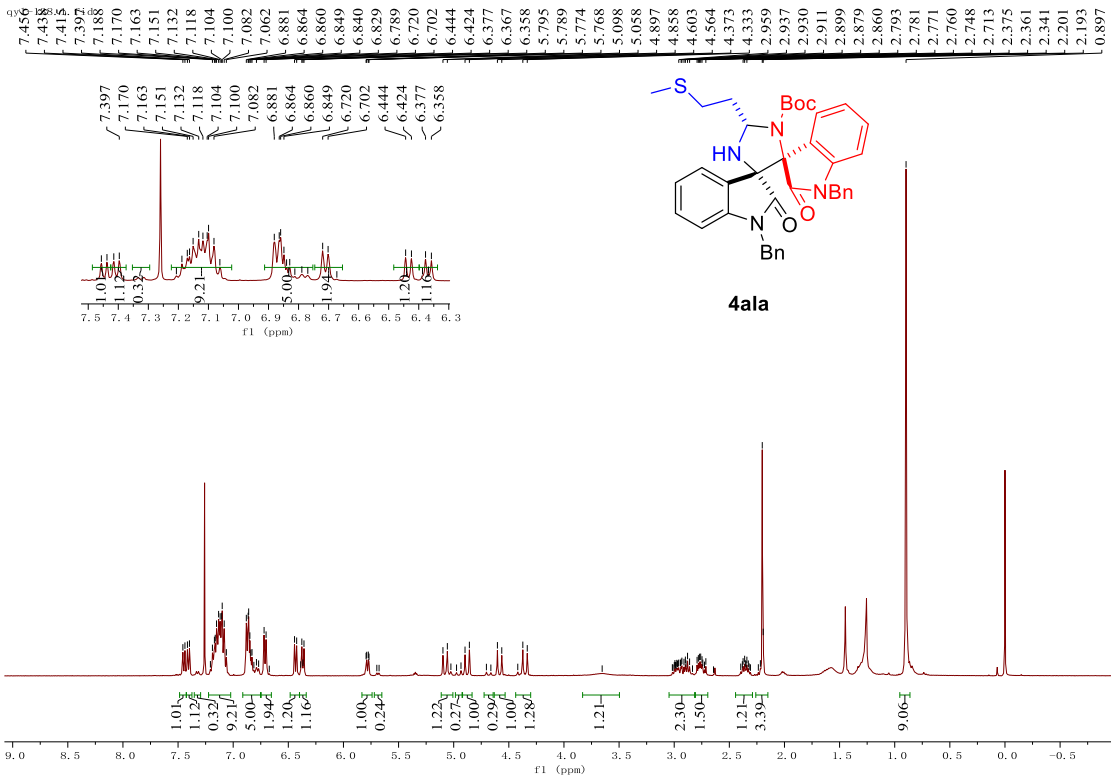
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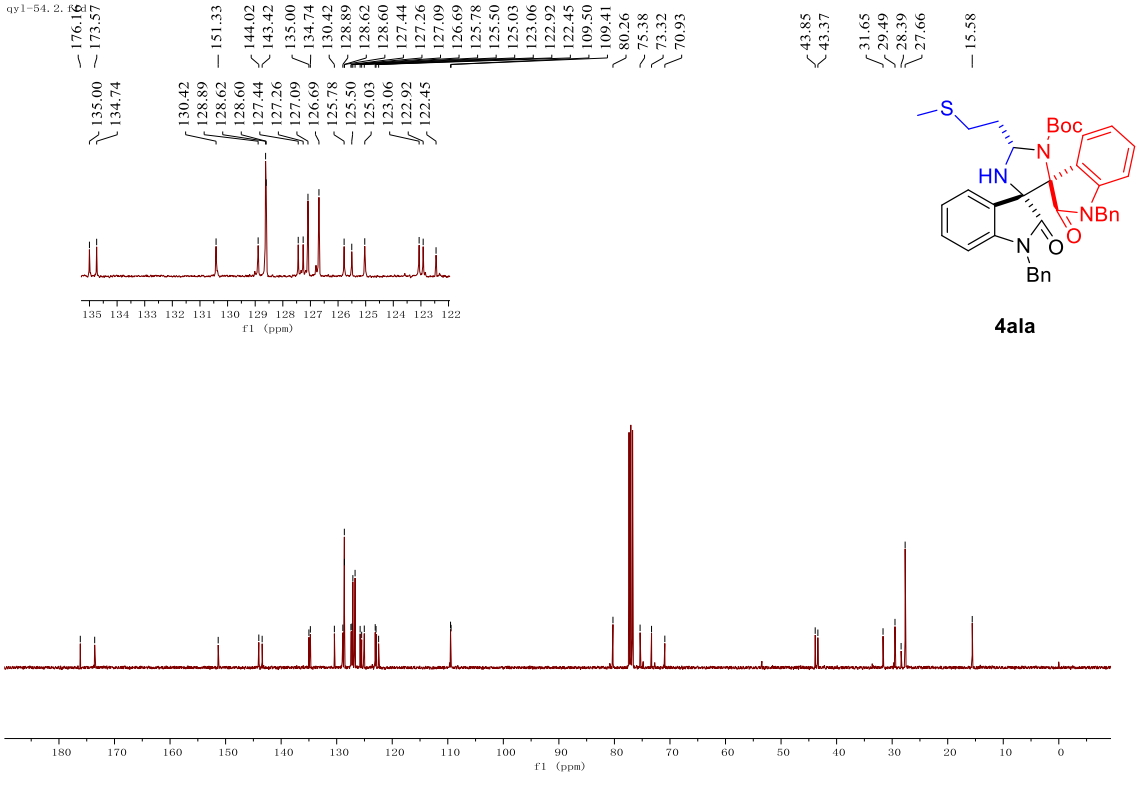
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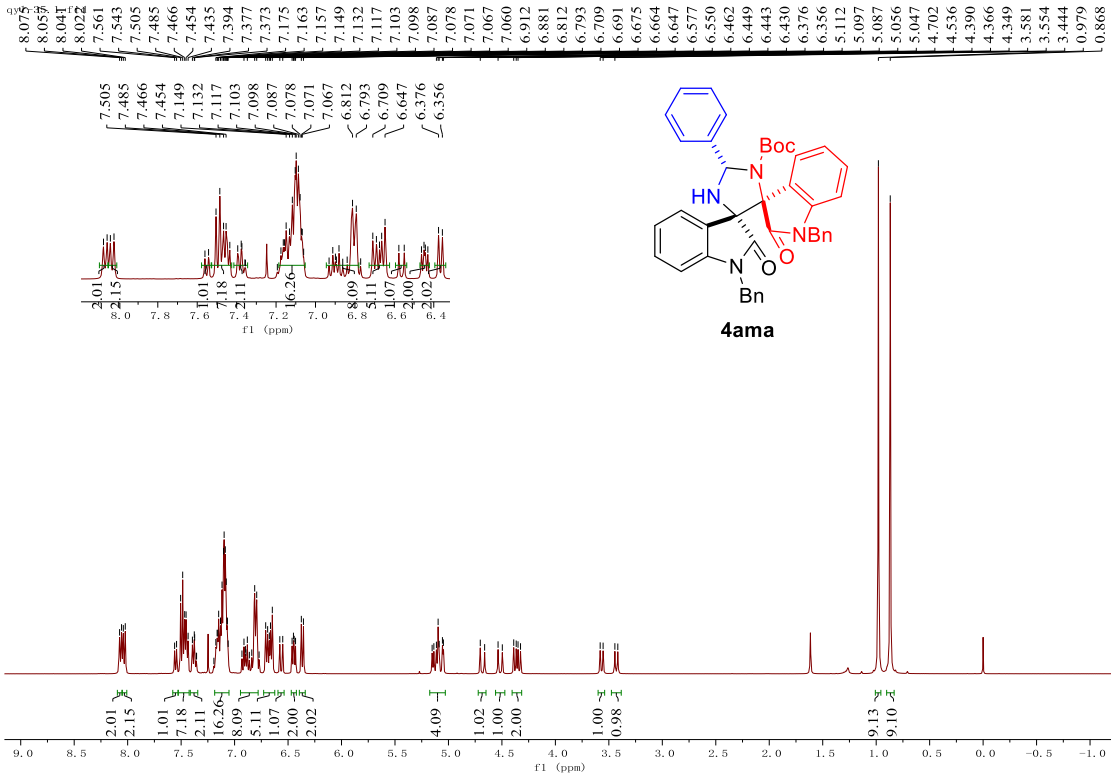
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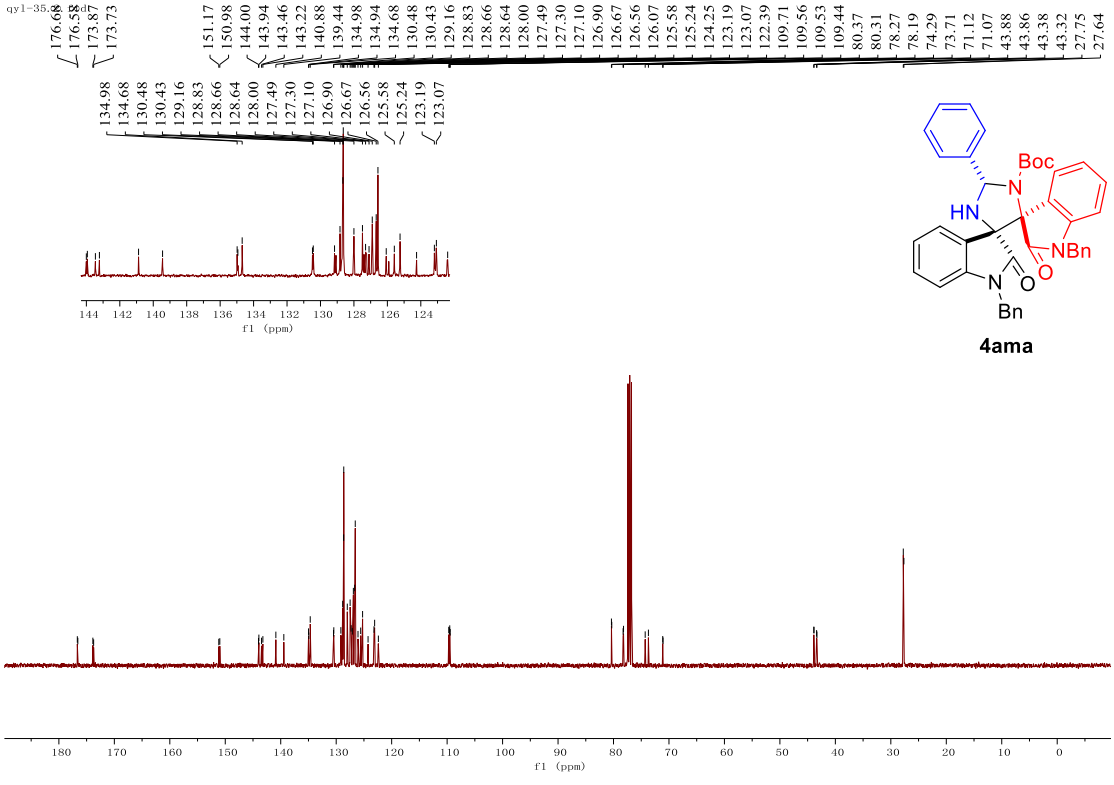
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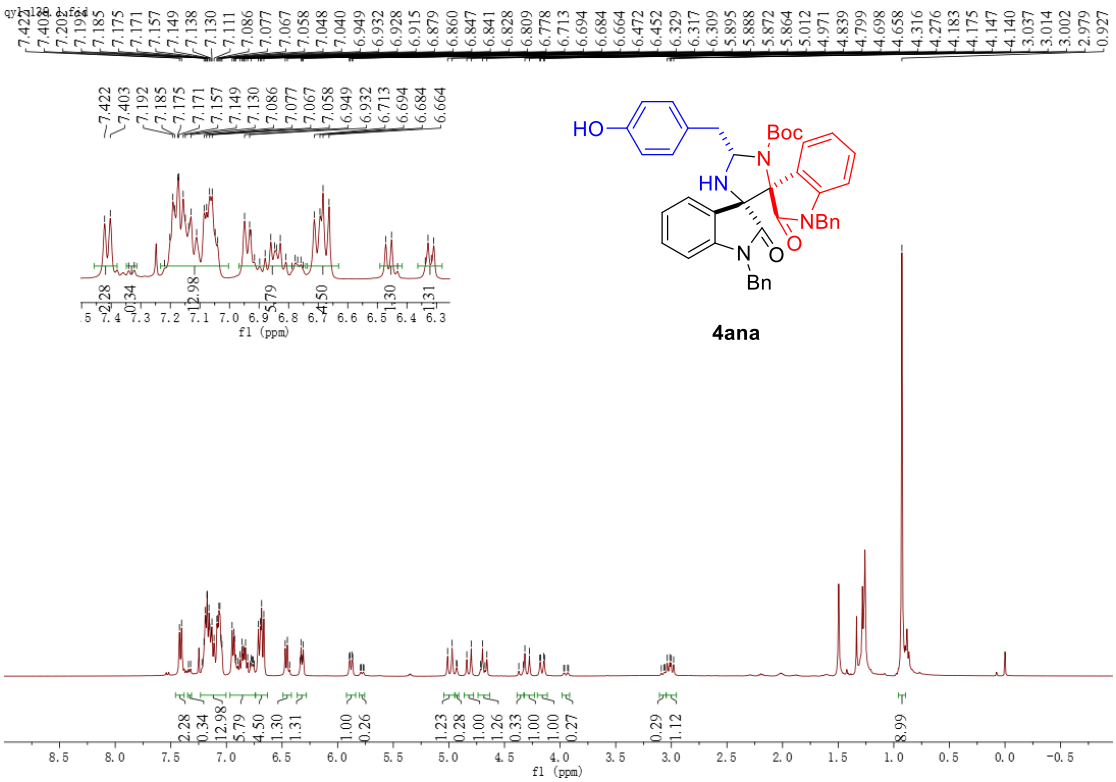
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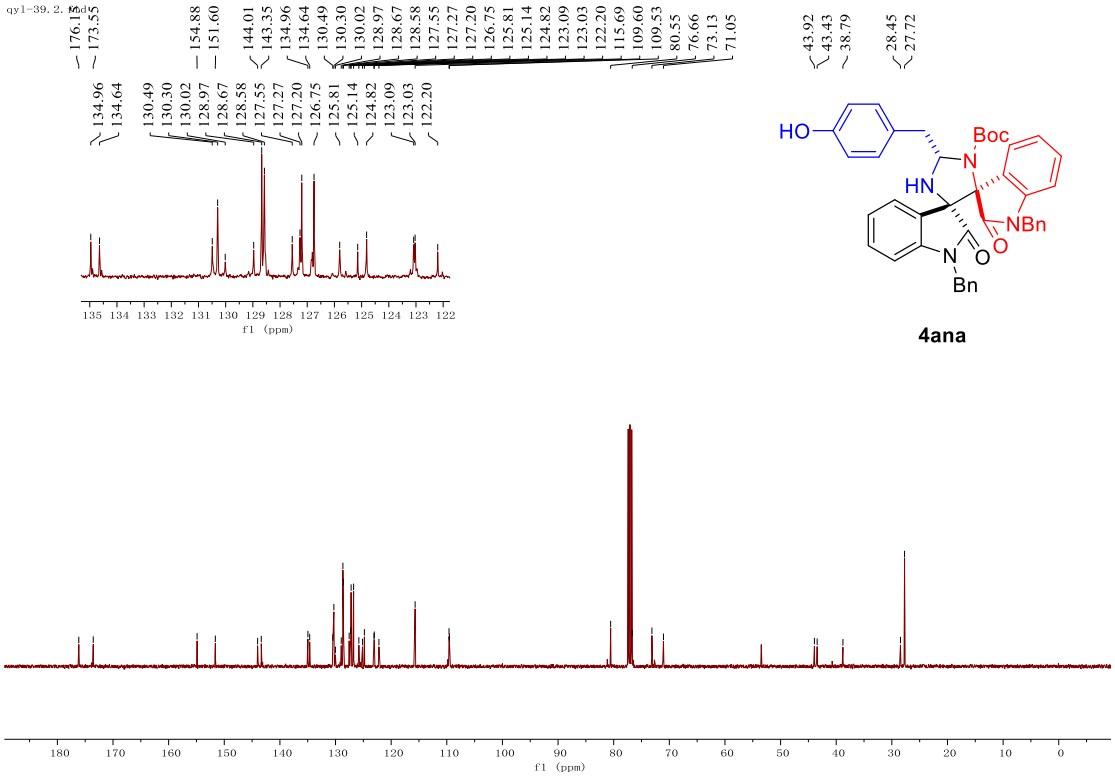
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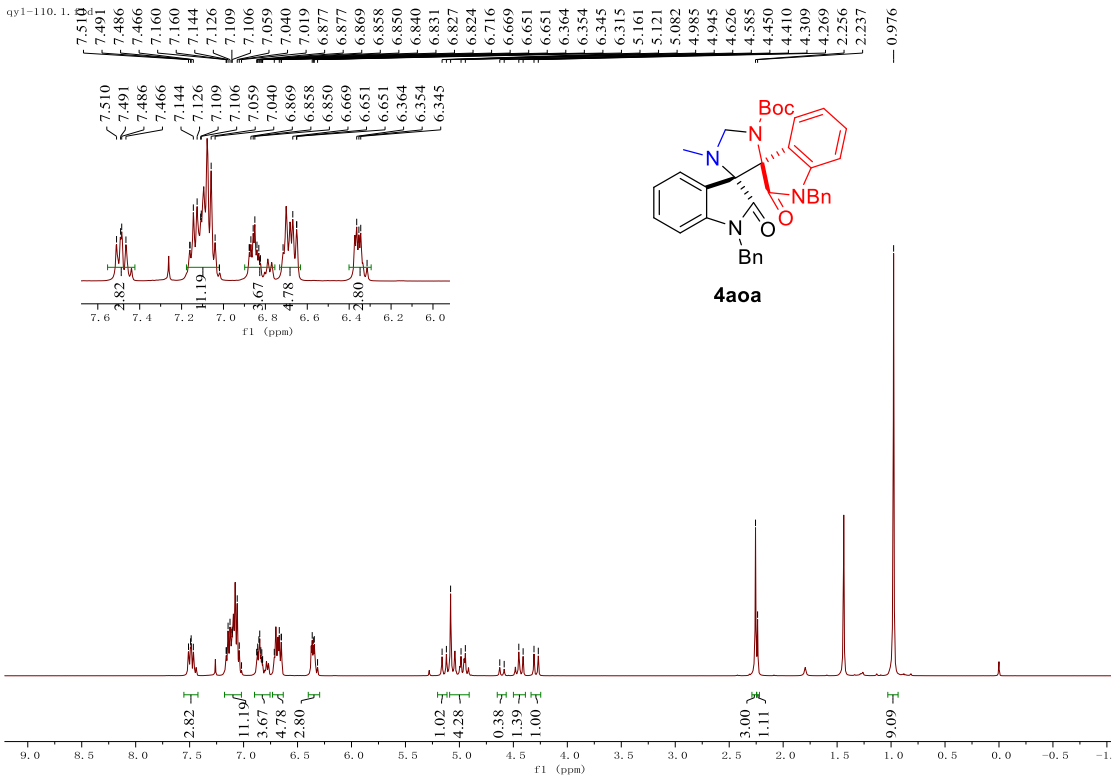
f1 (ppm)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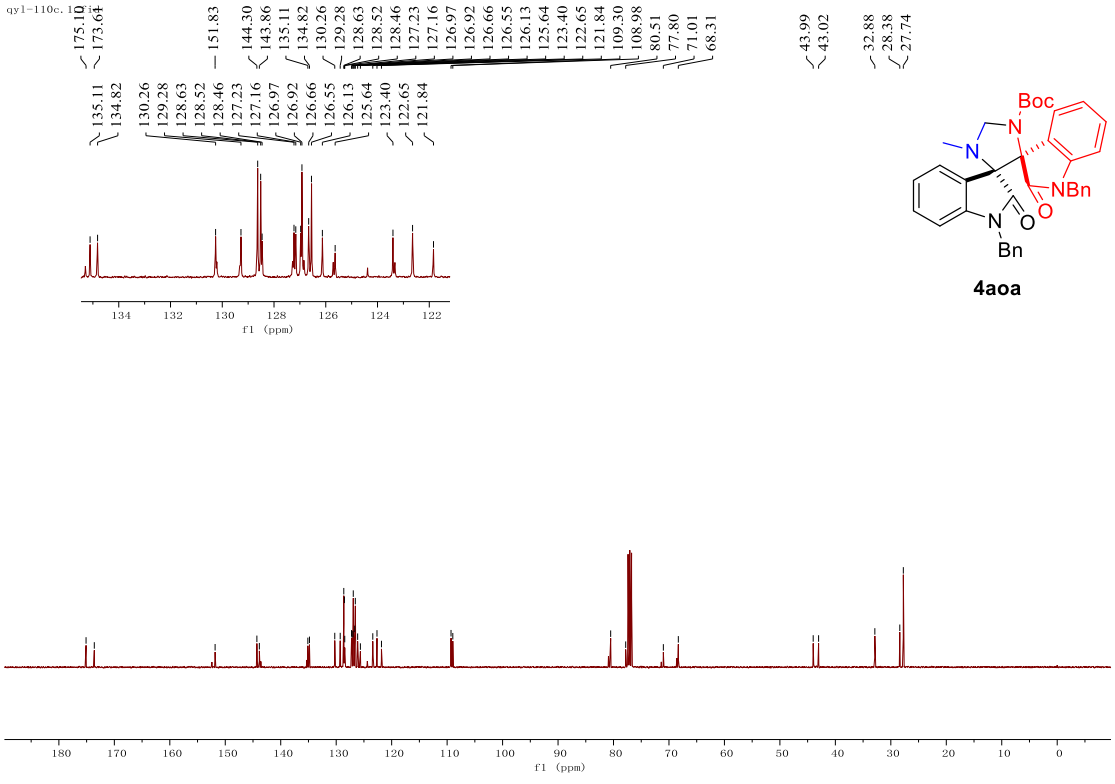
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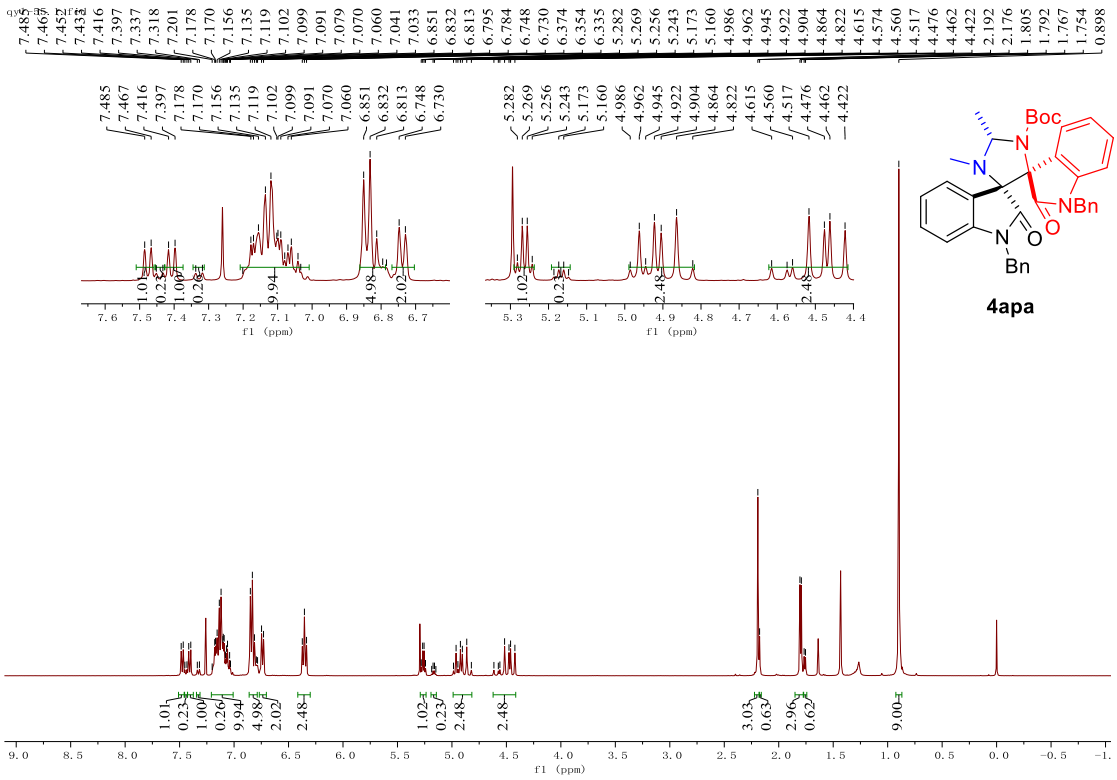
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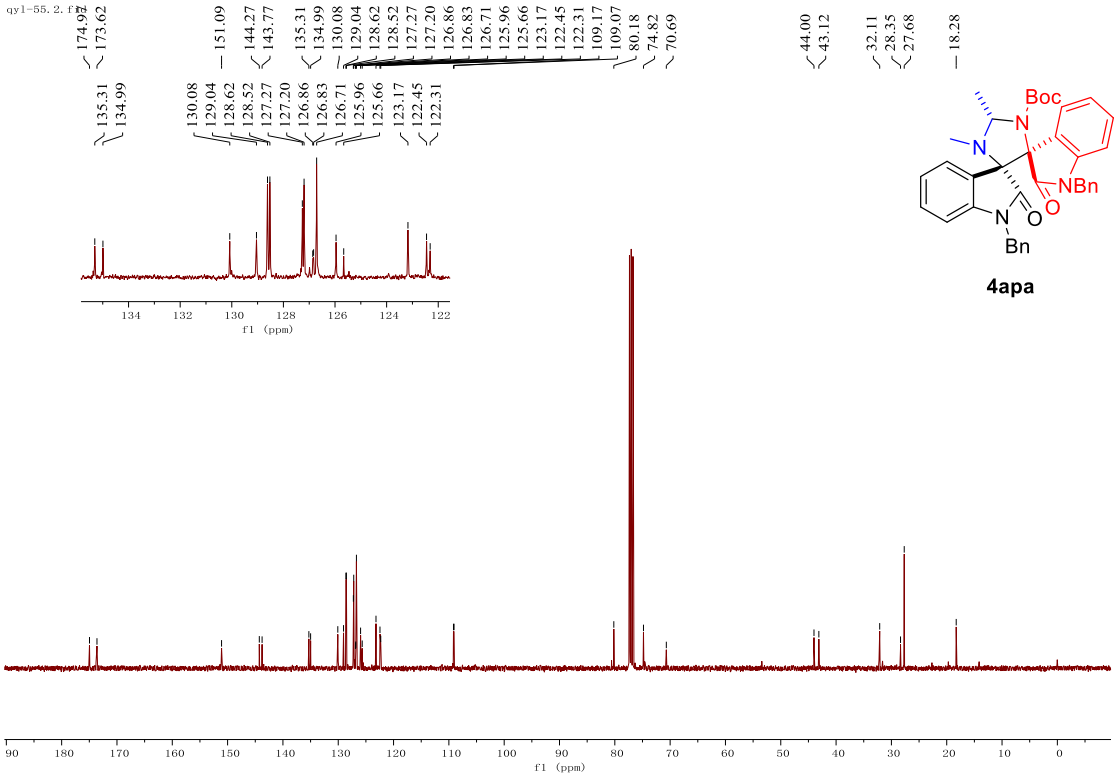
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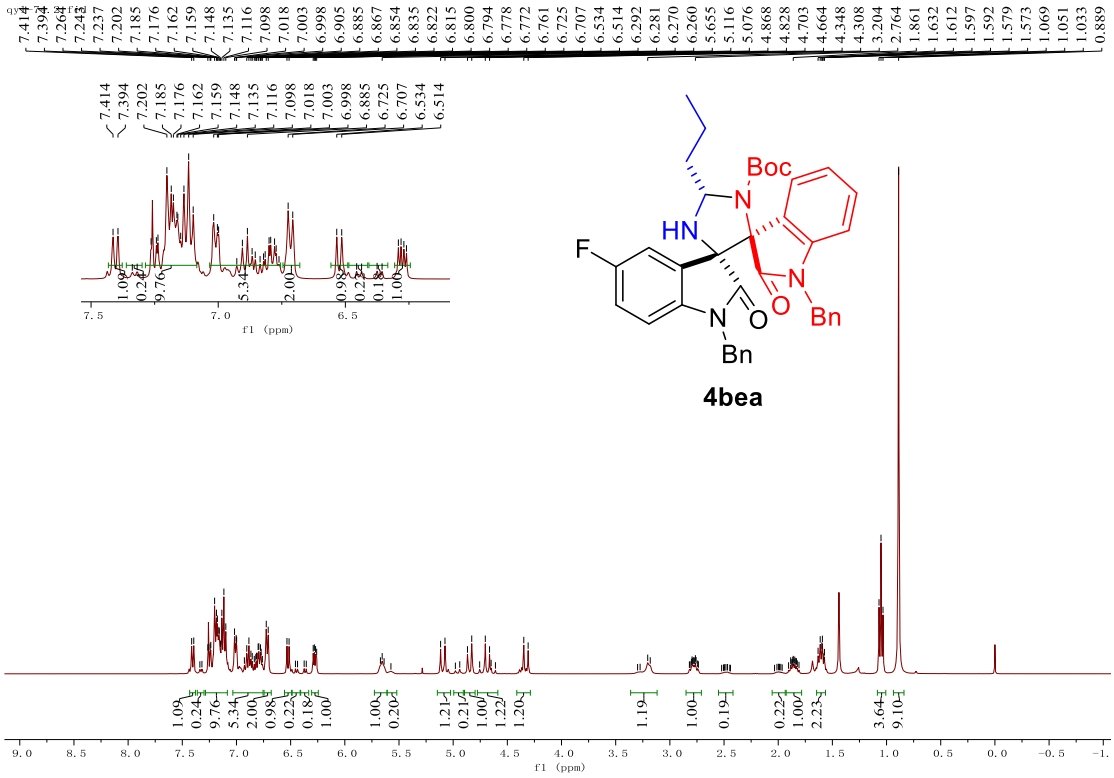
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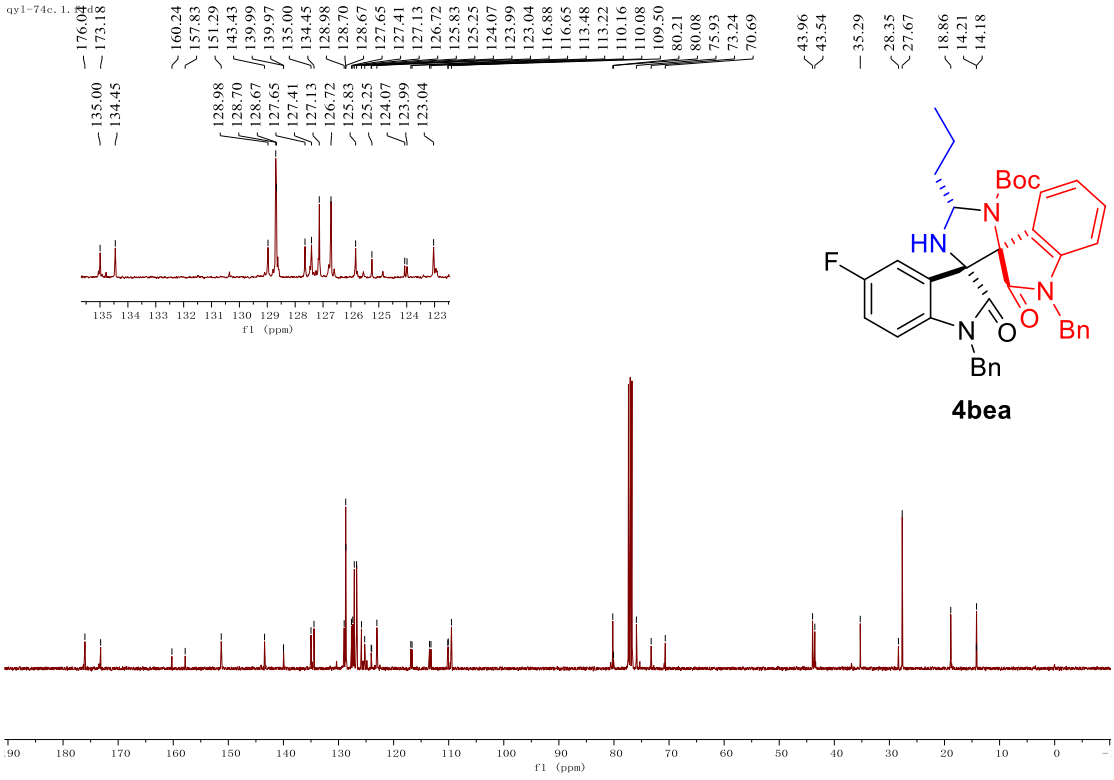
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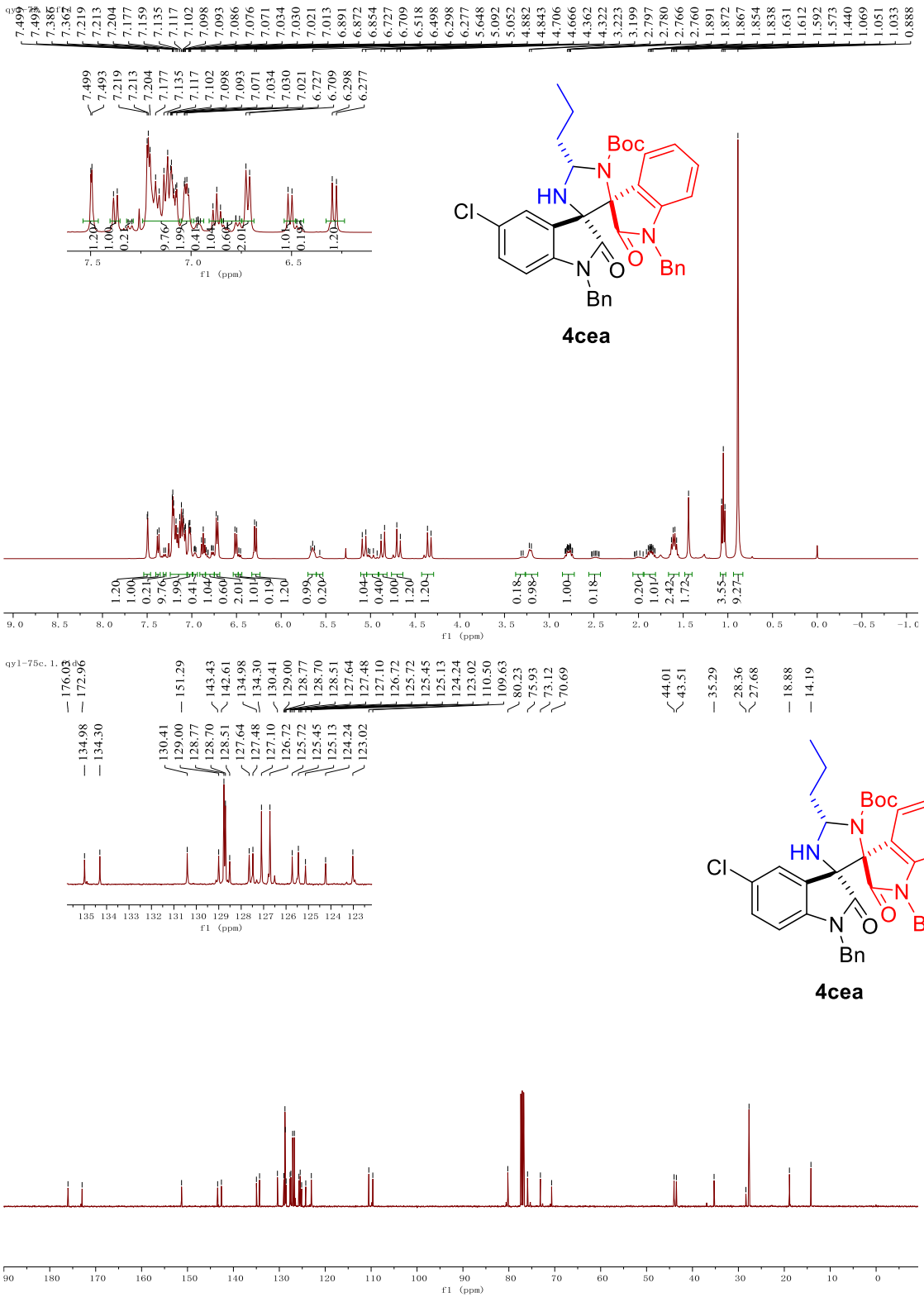
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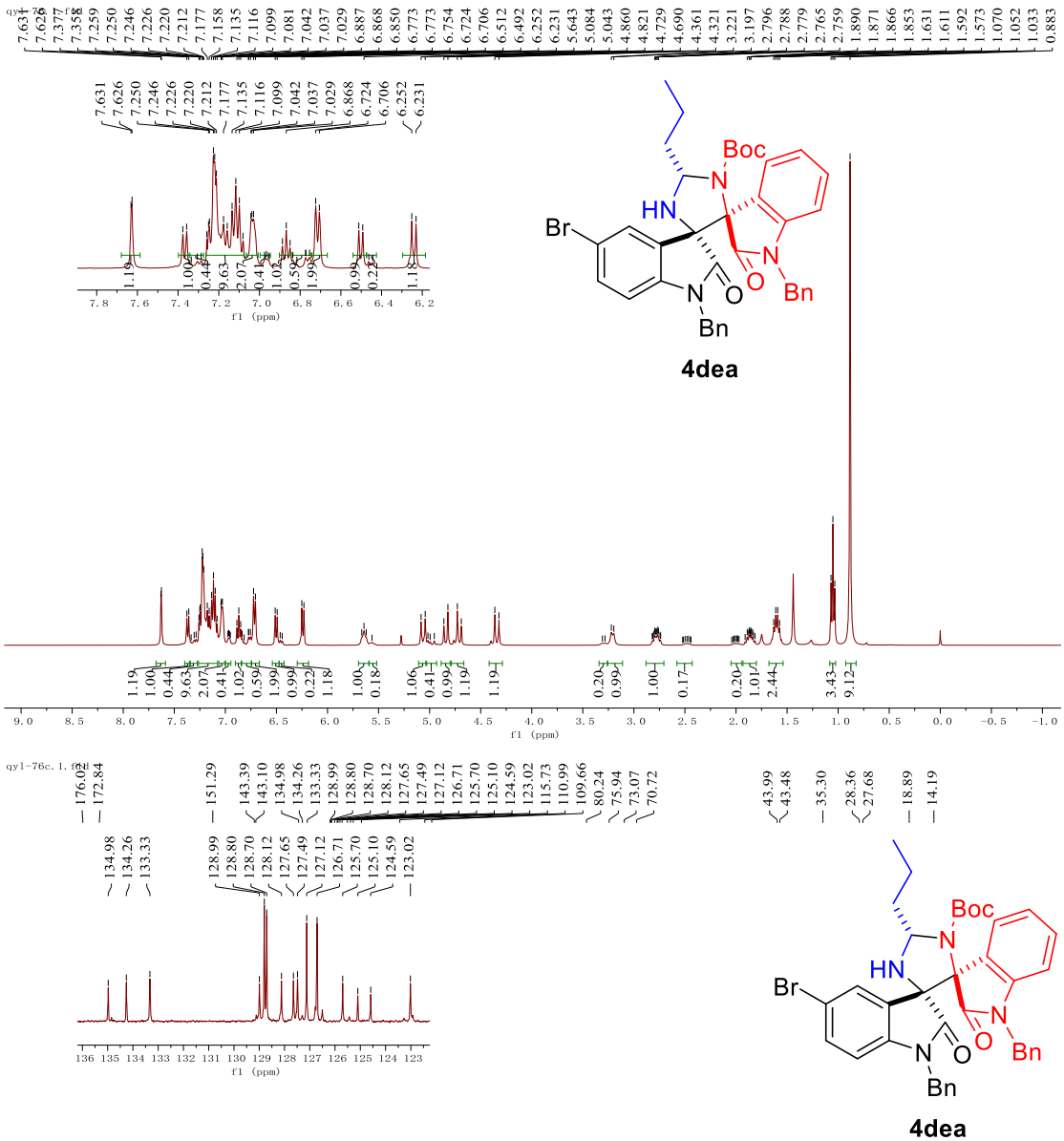
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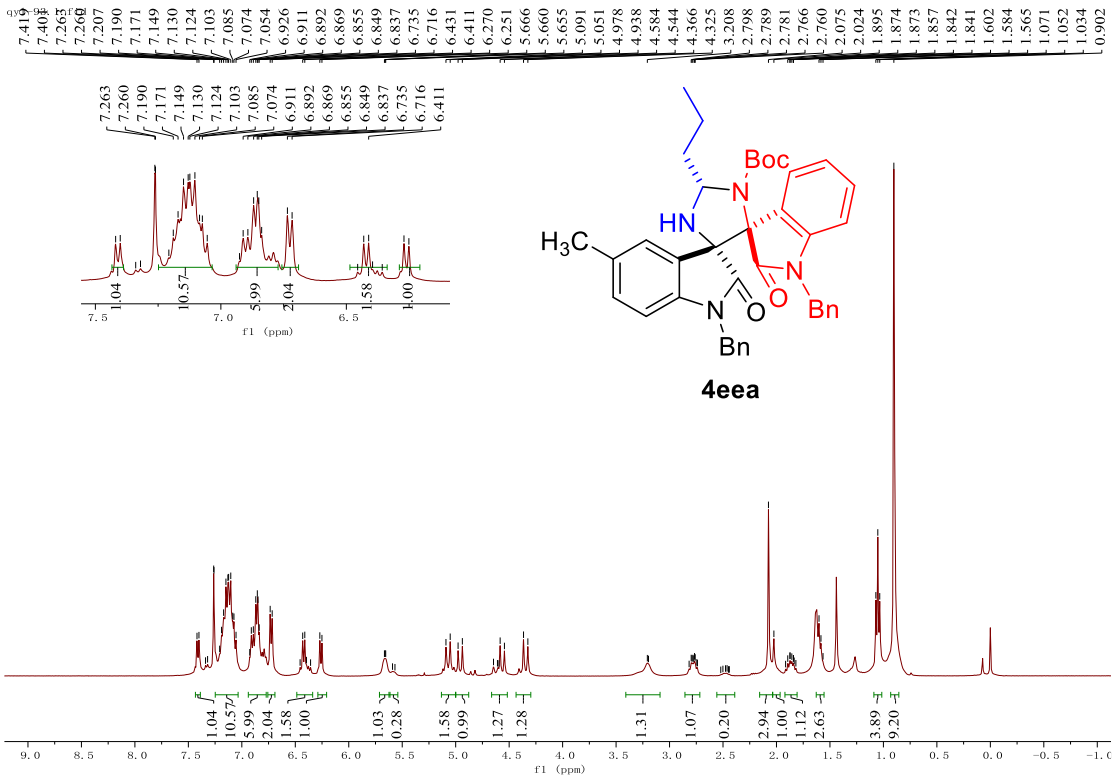
f1 (ppm)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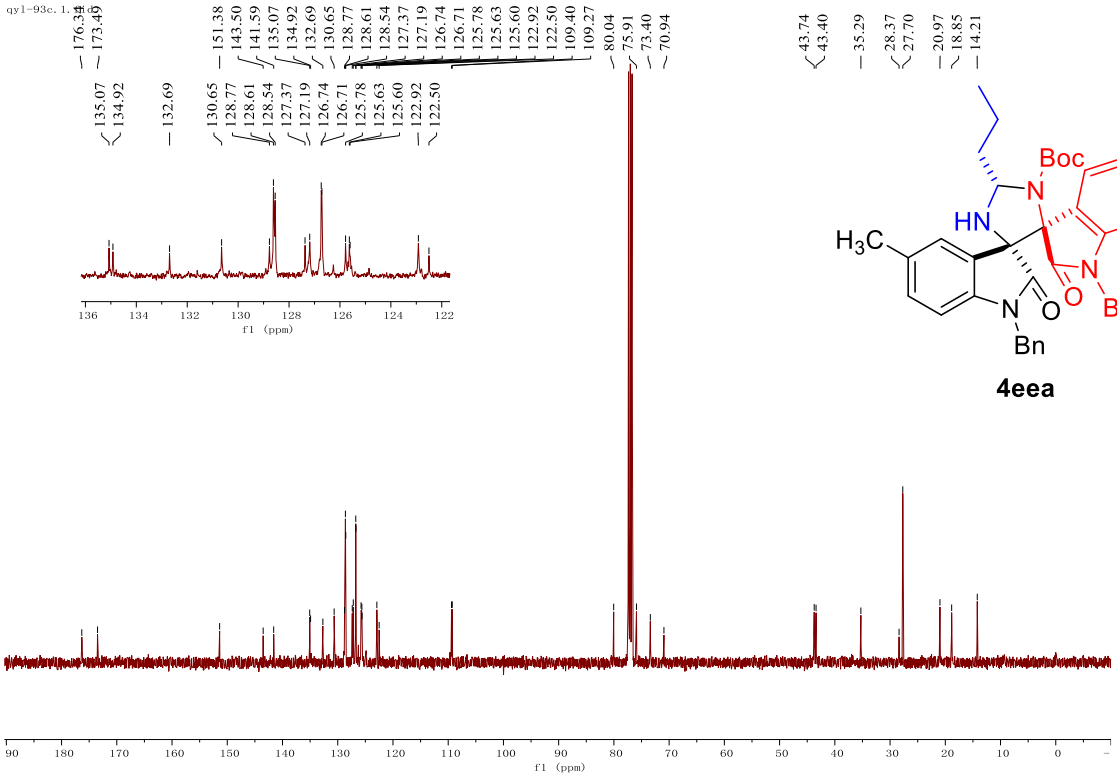
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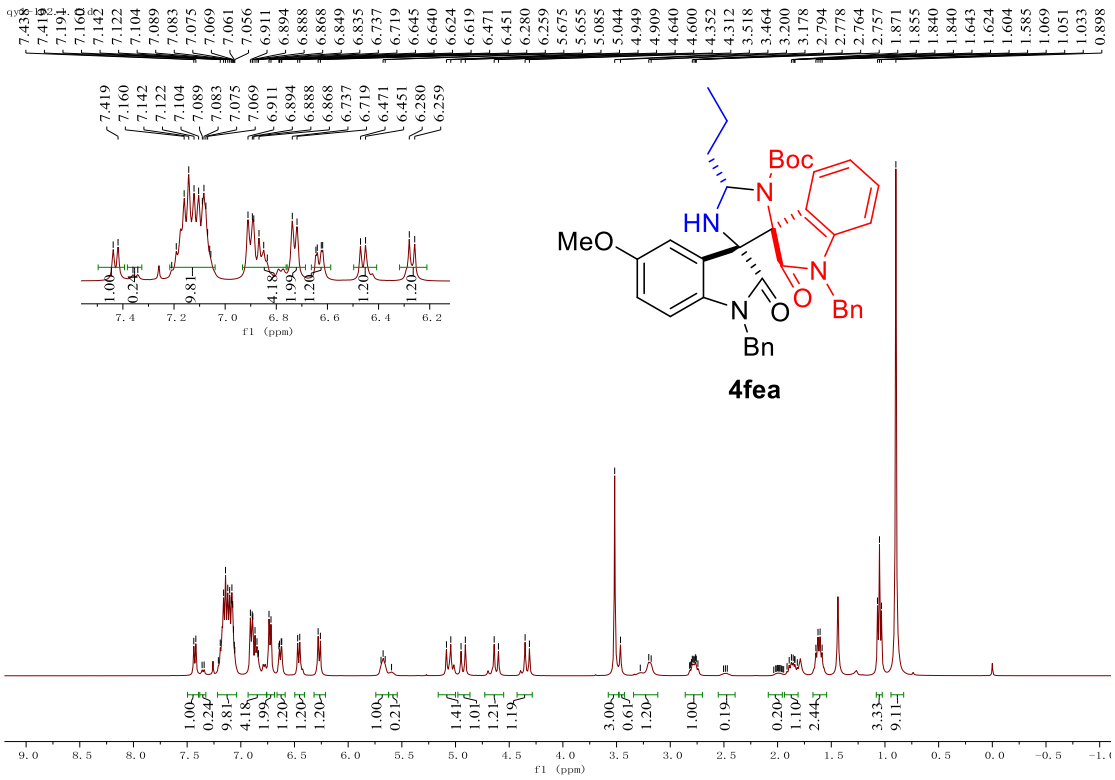

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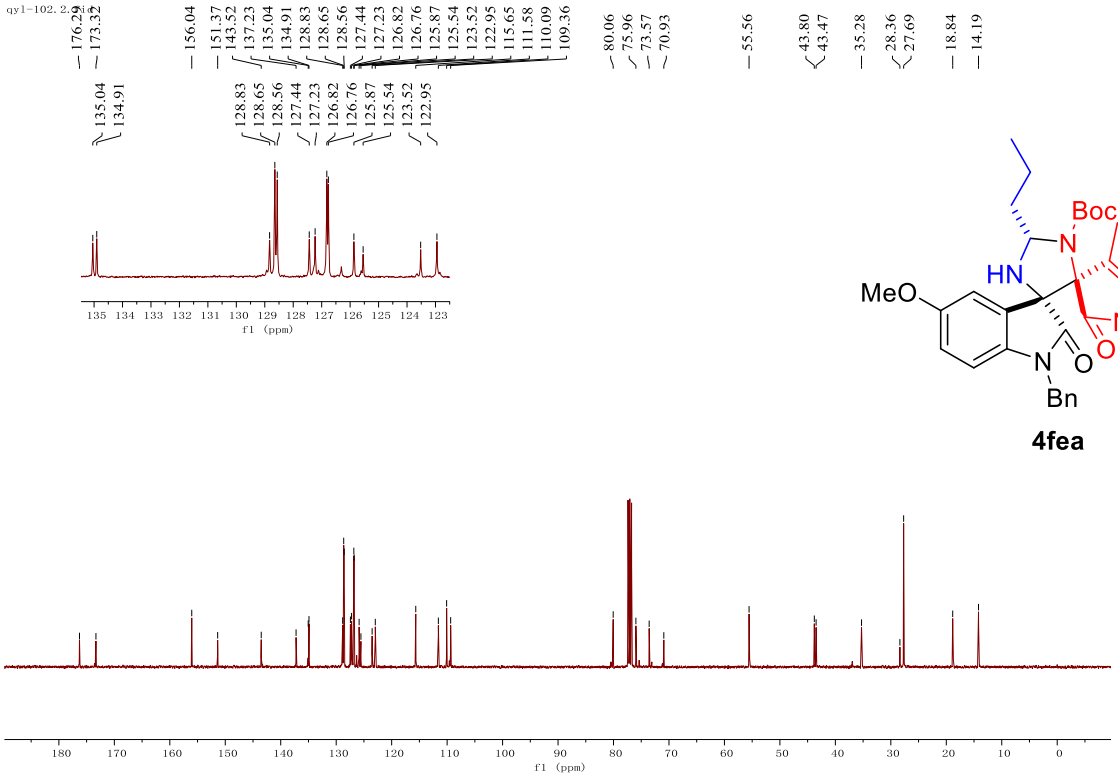

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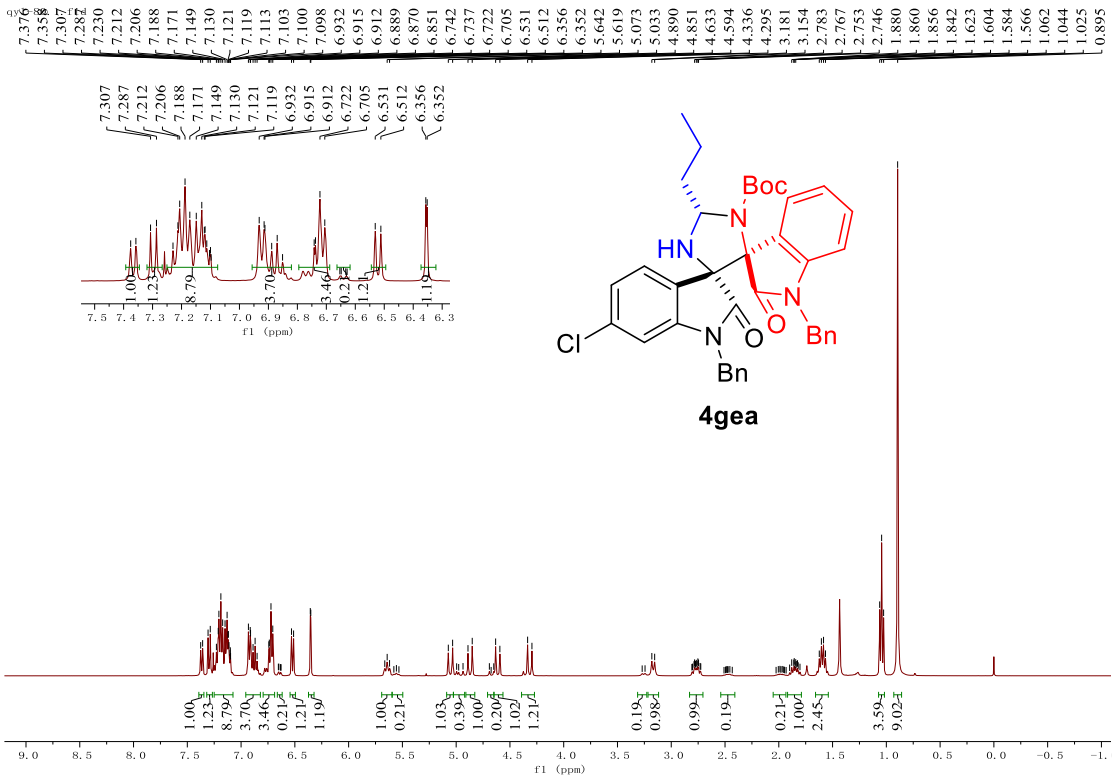
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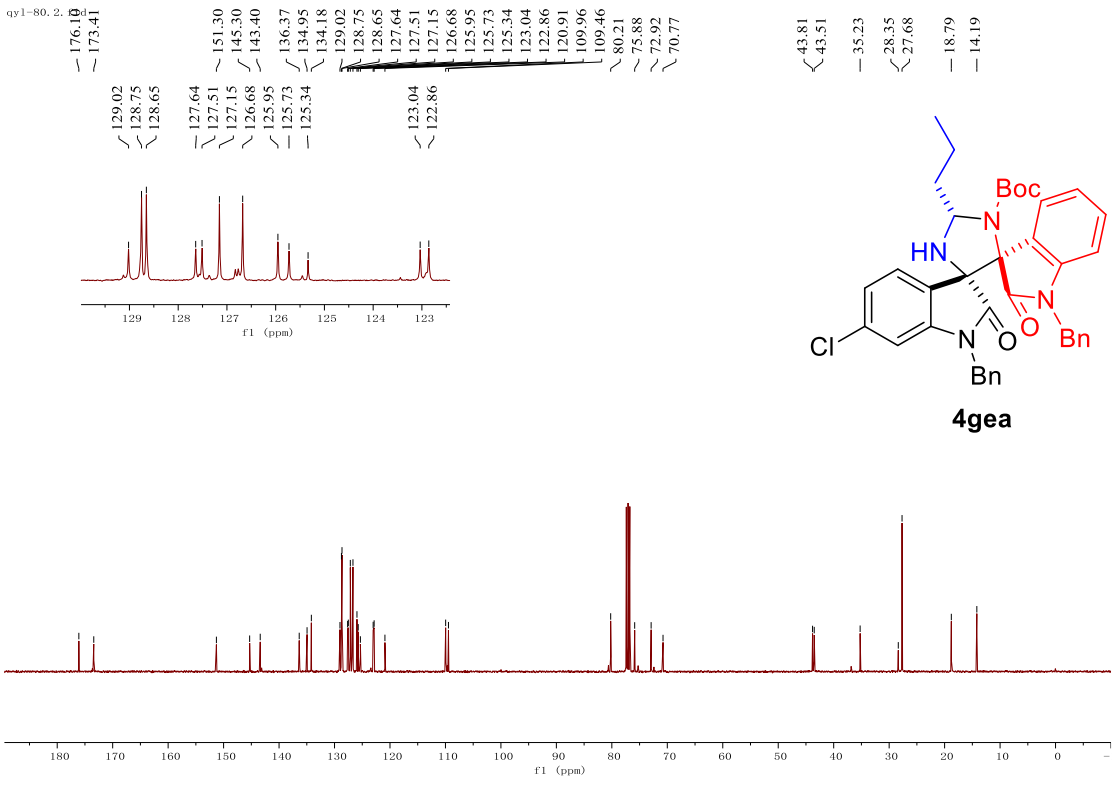
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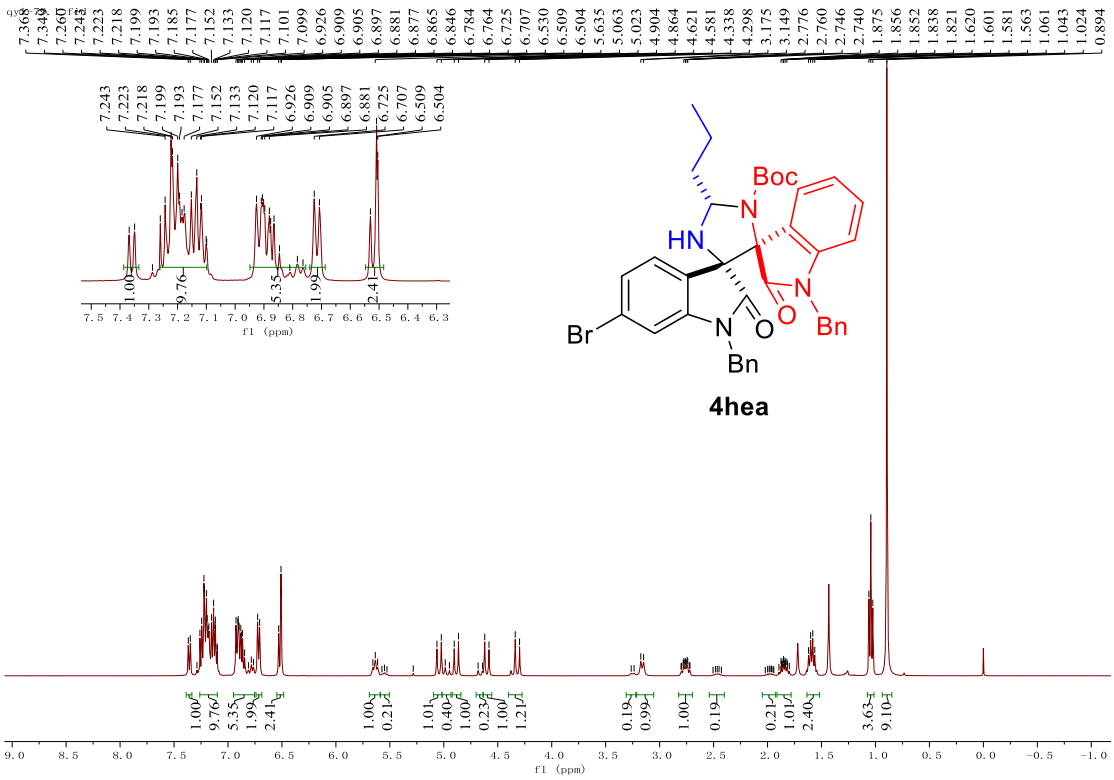
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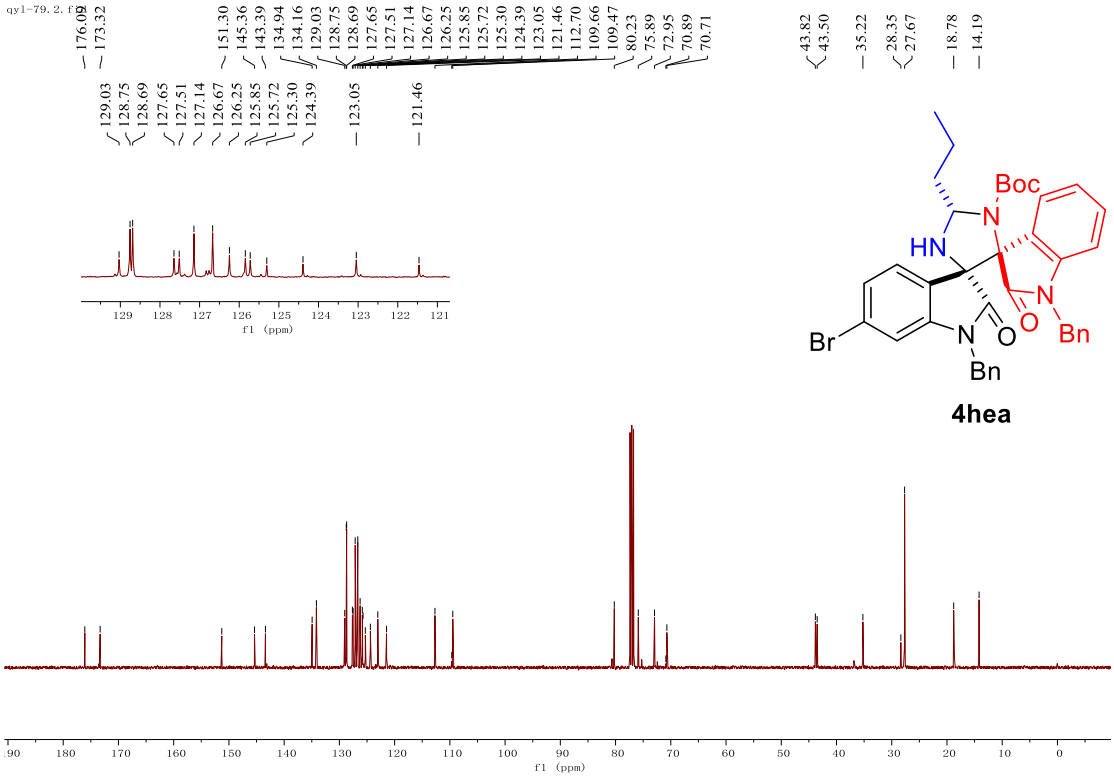
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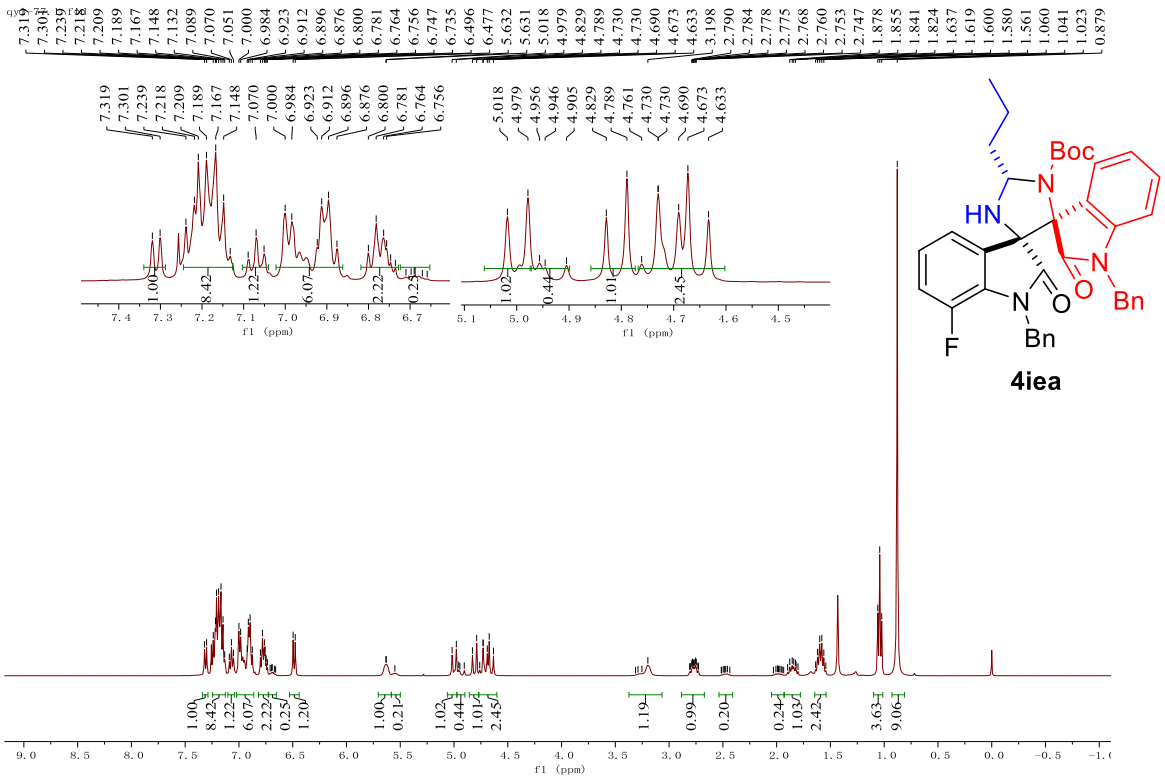
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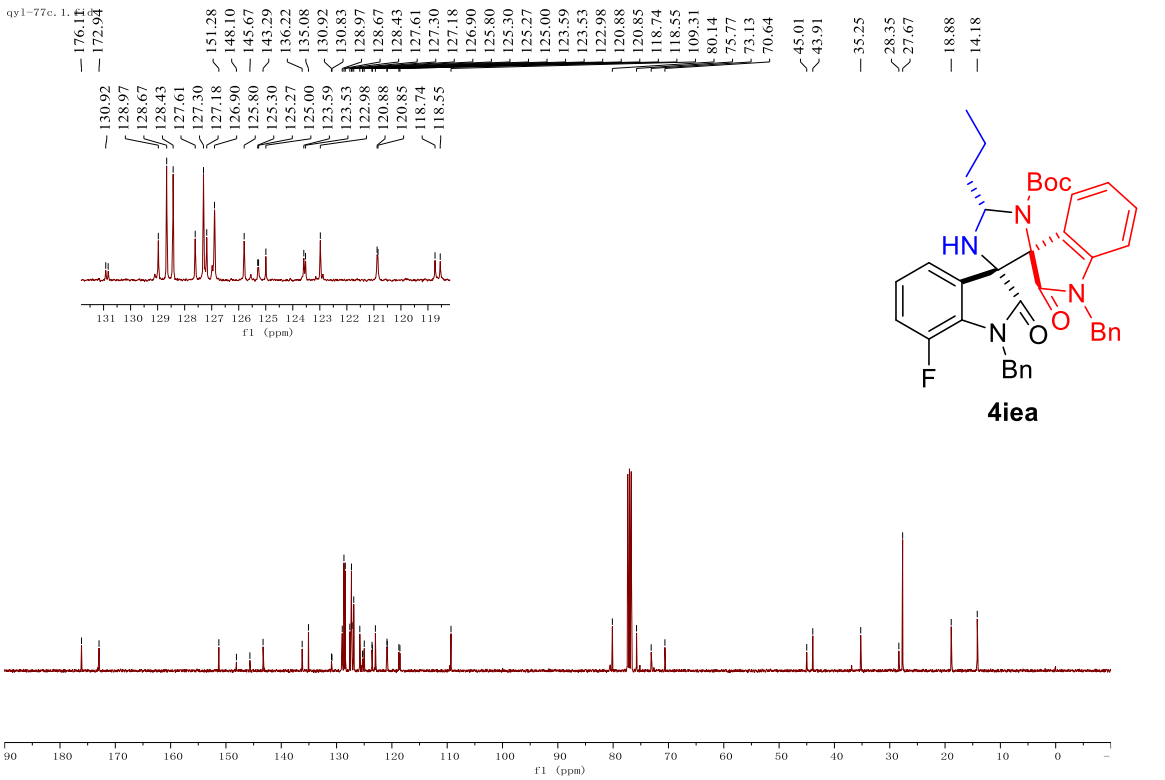
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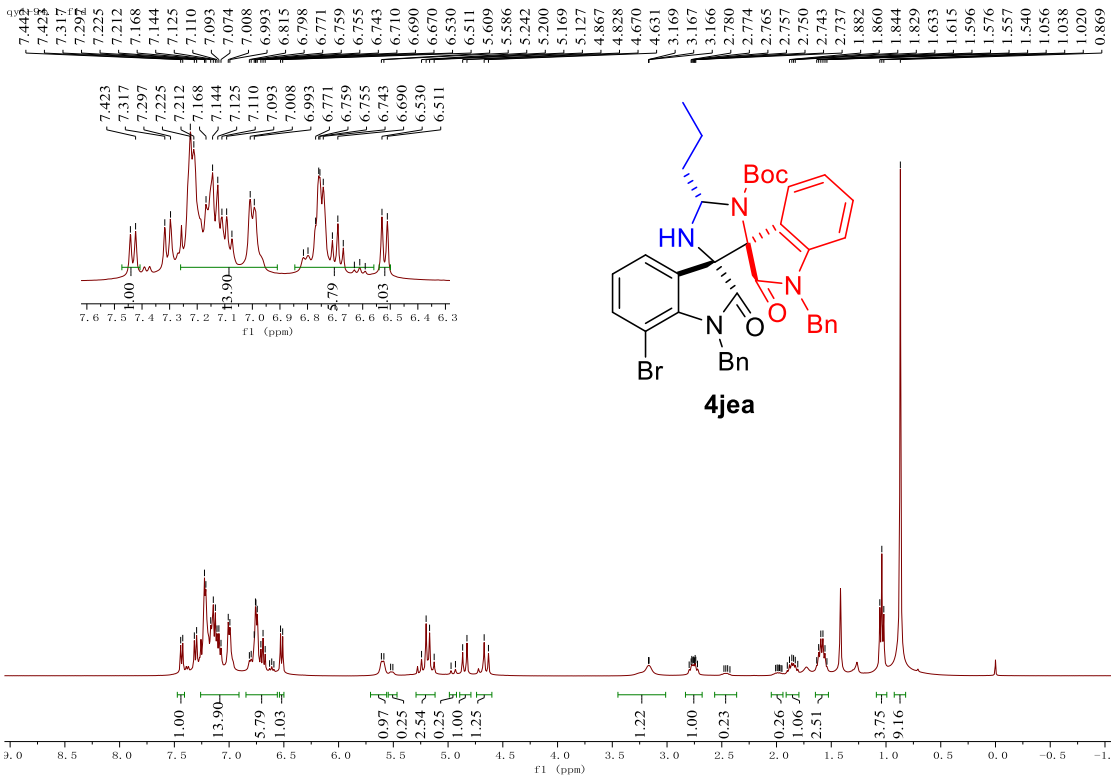
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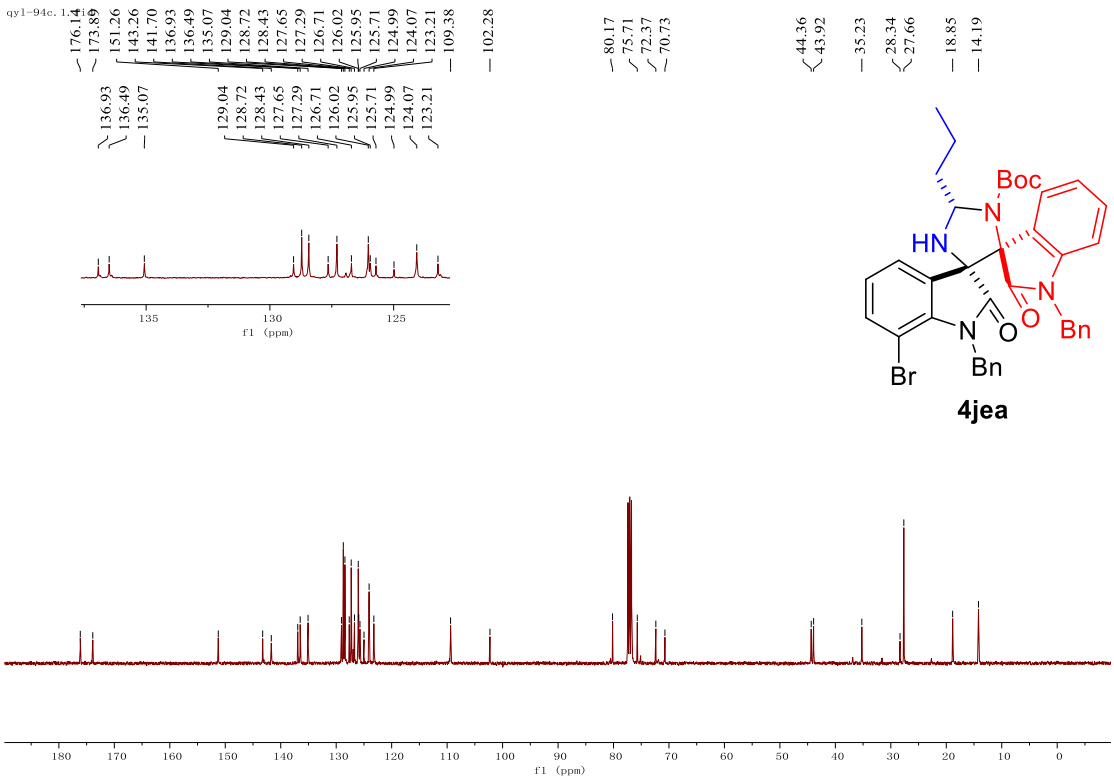
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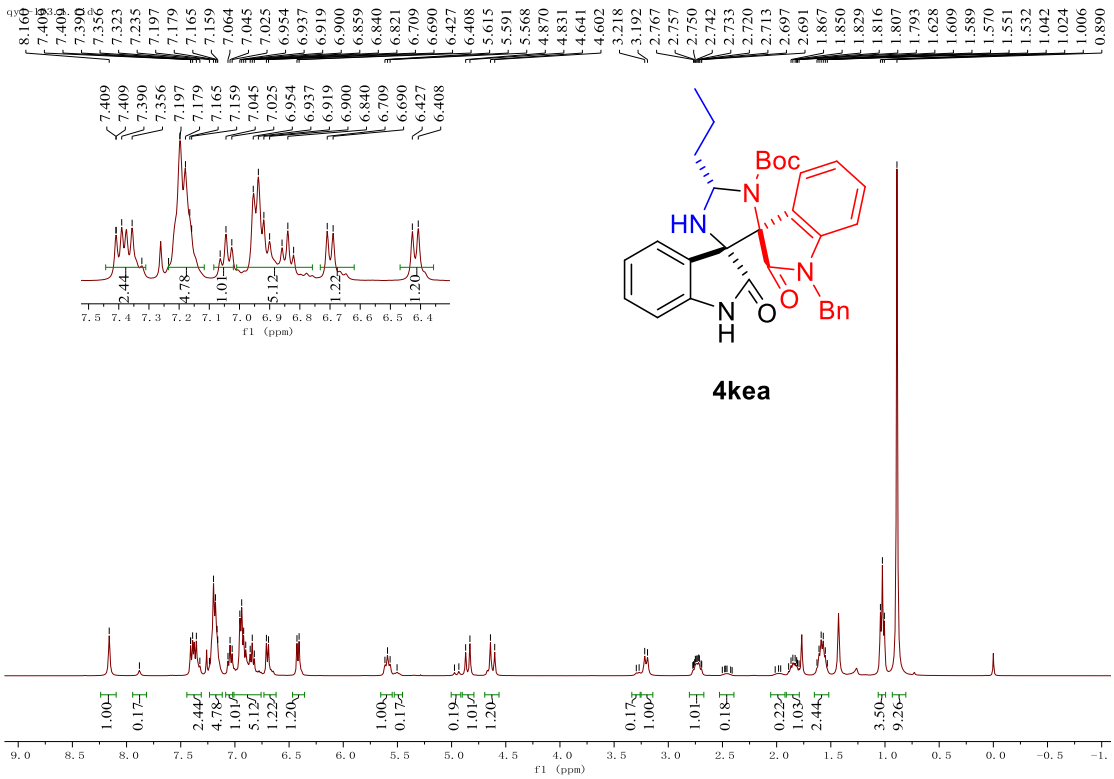

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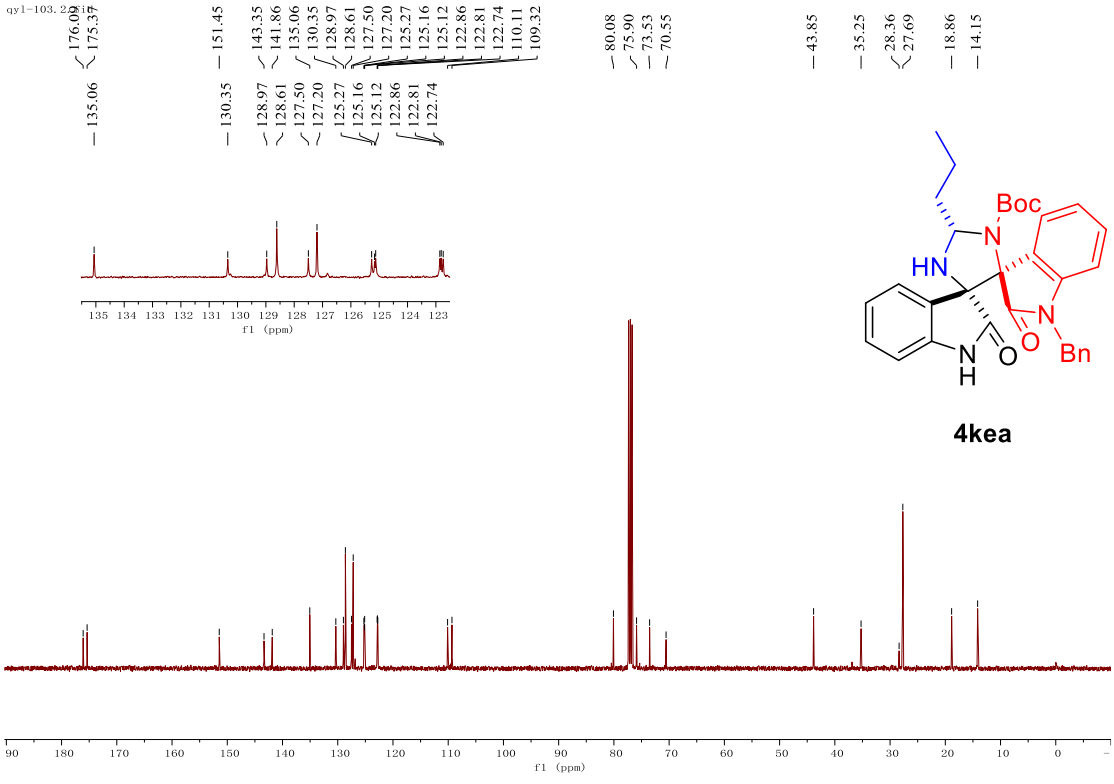

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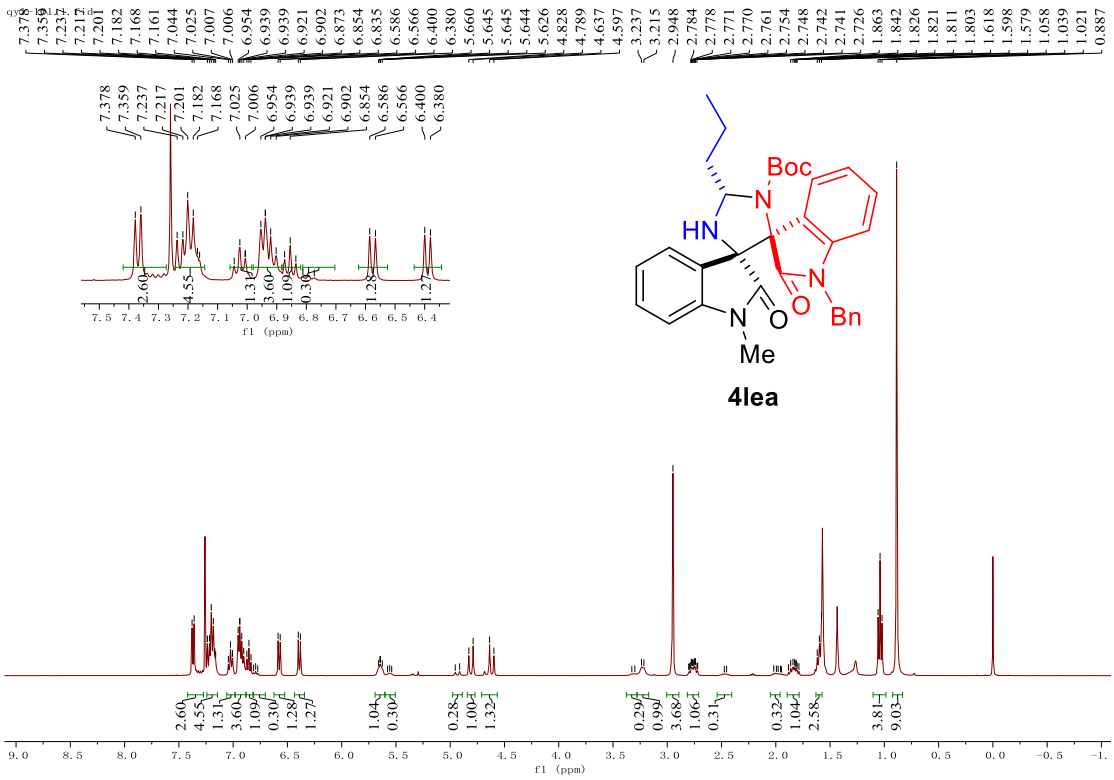
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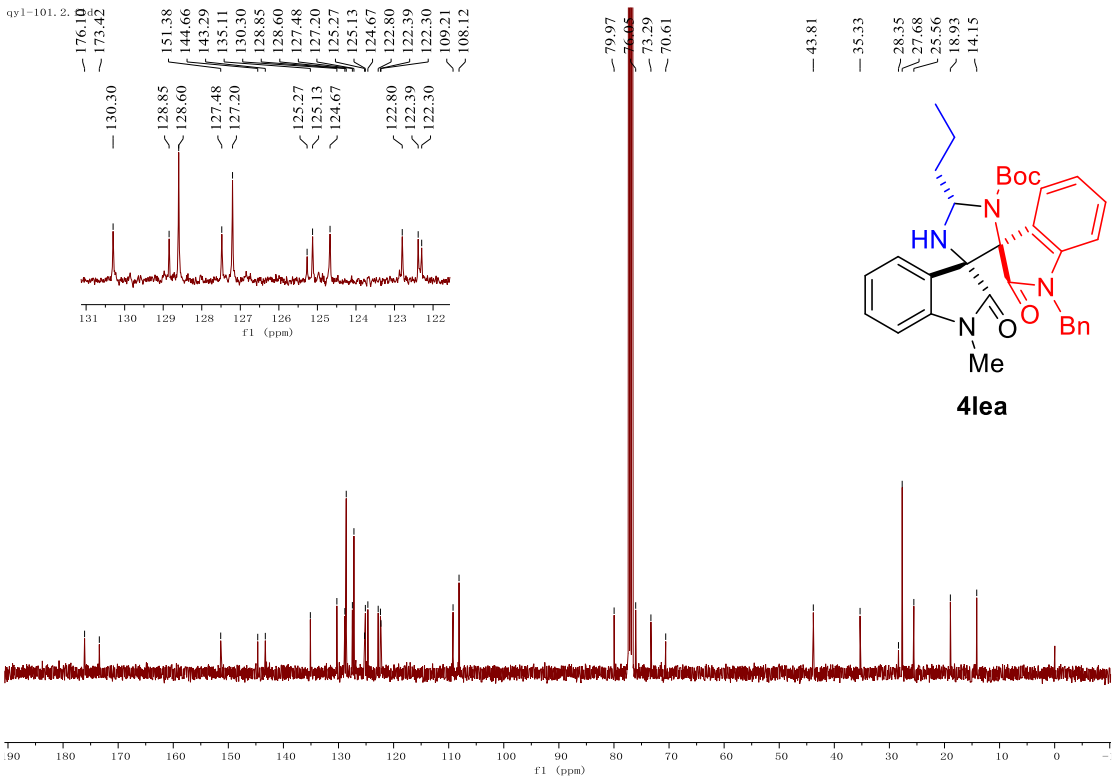
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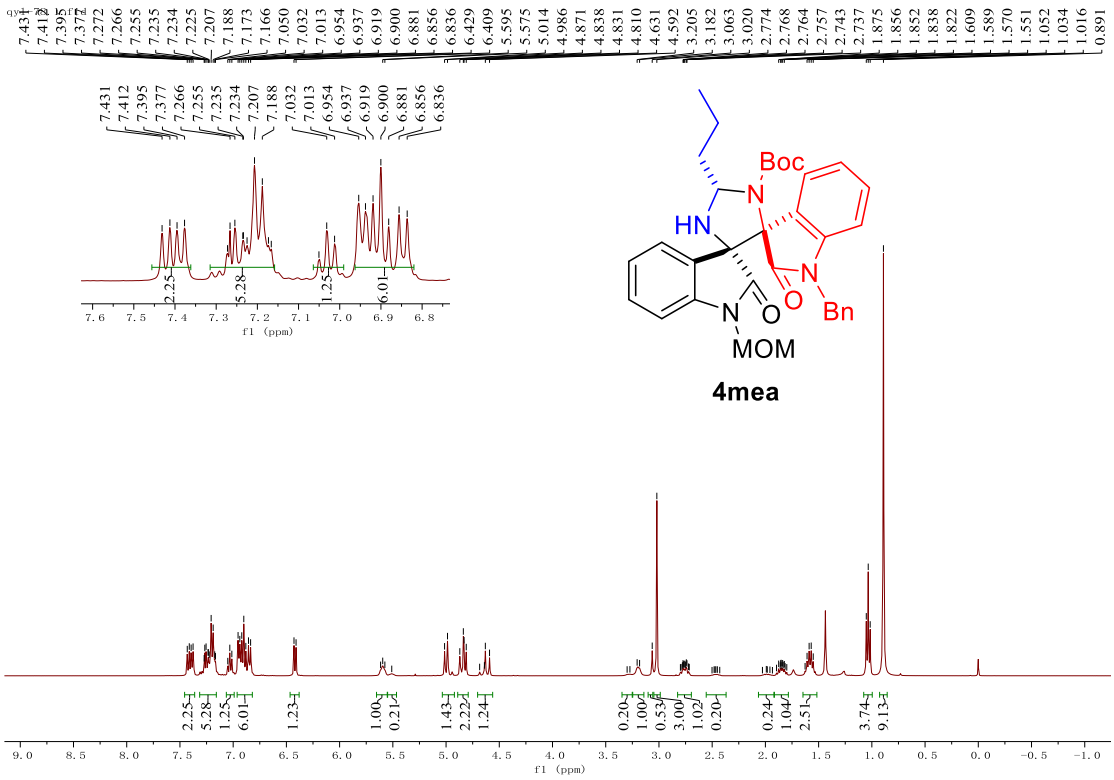

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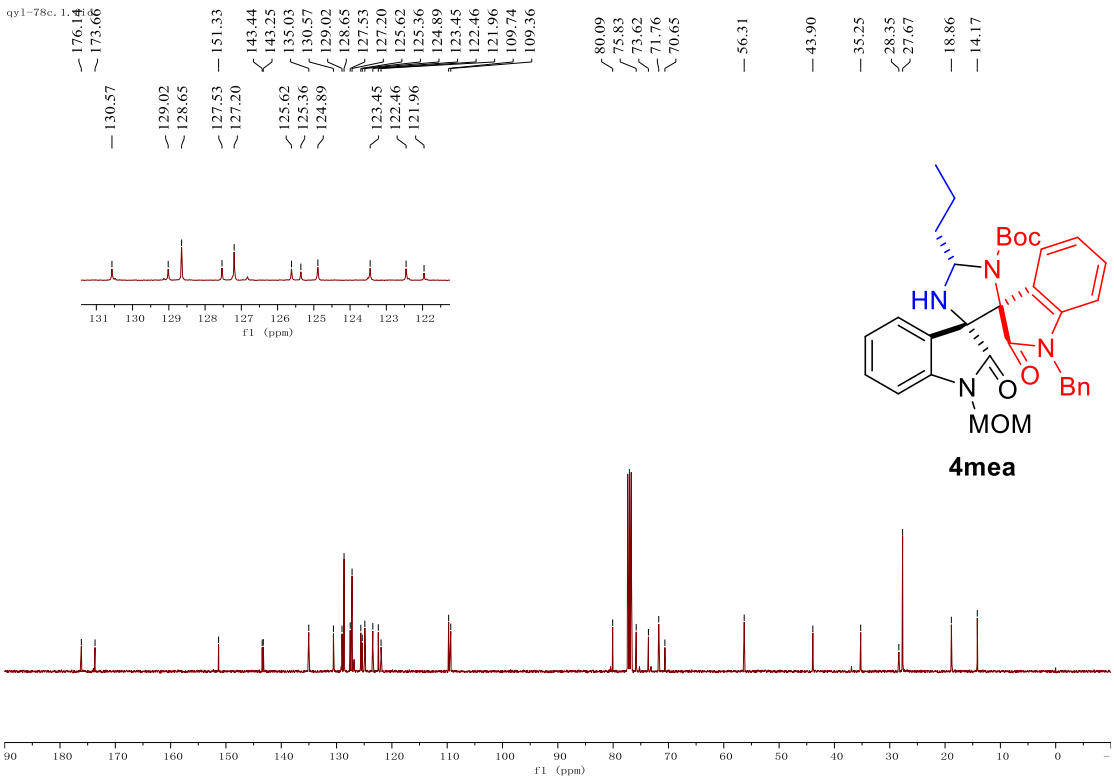

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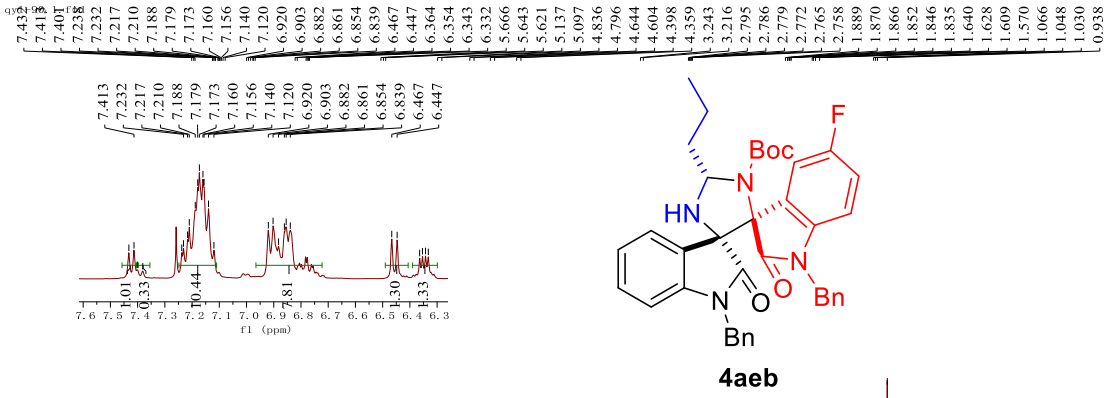

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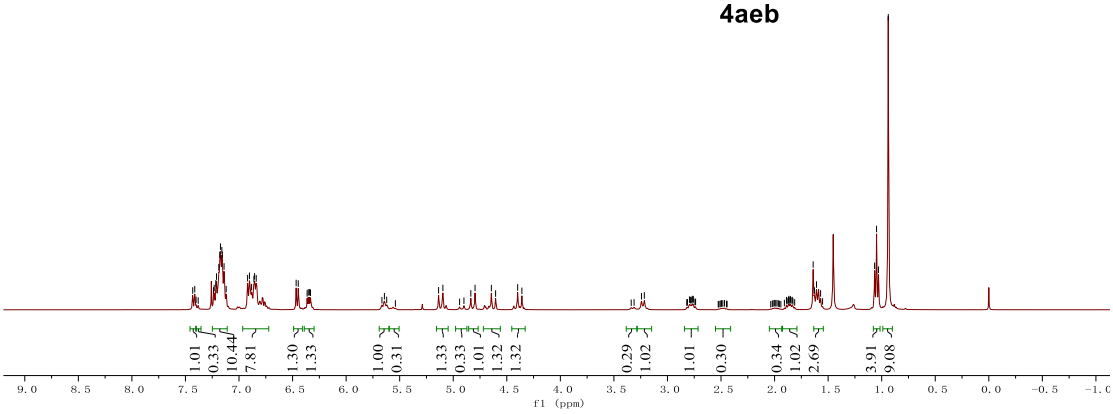

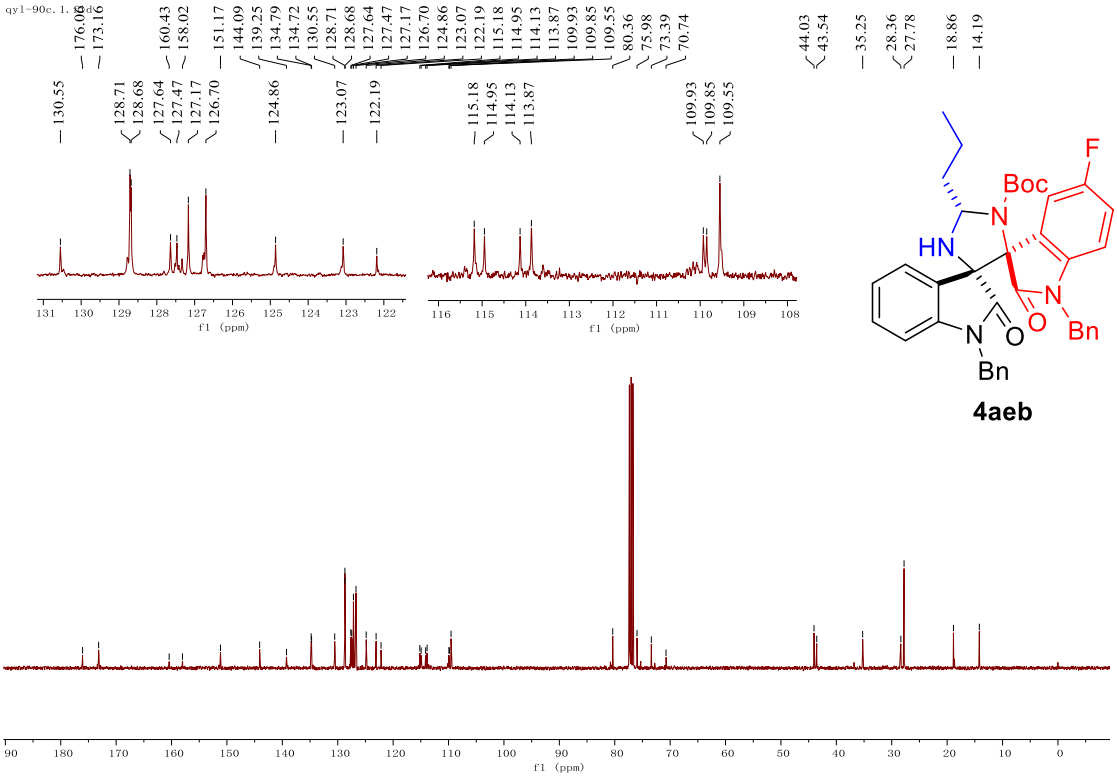

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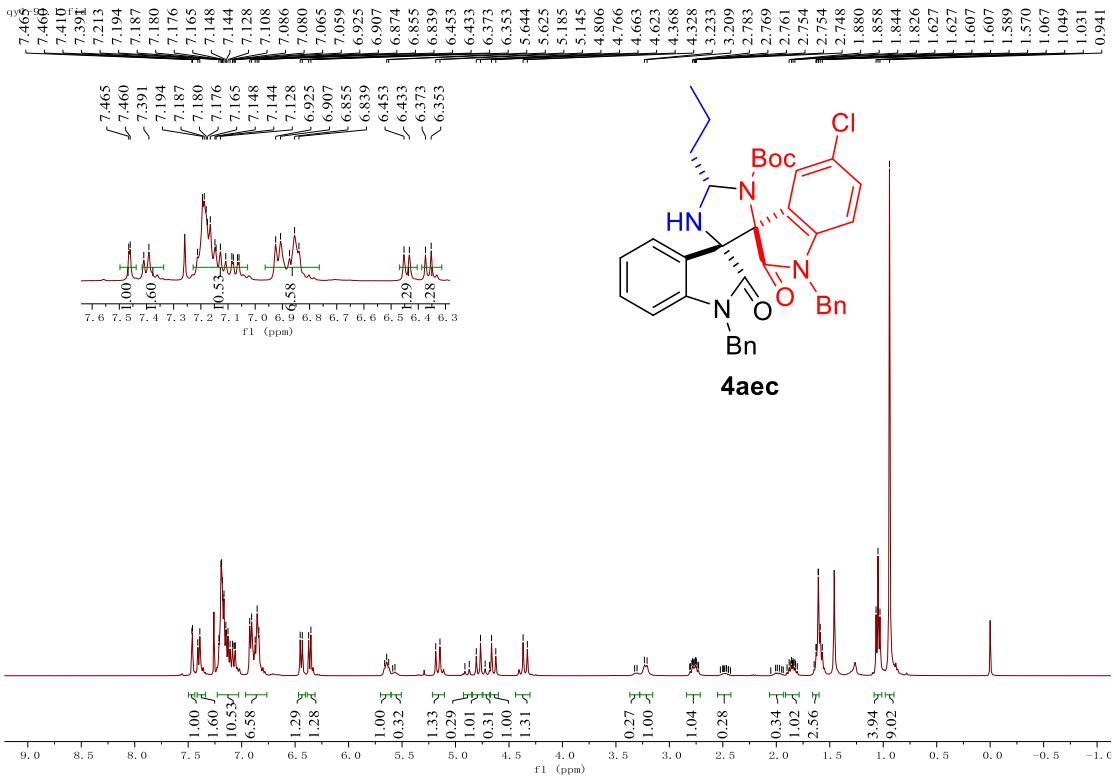
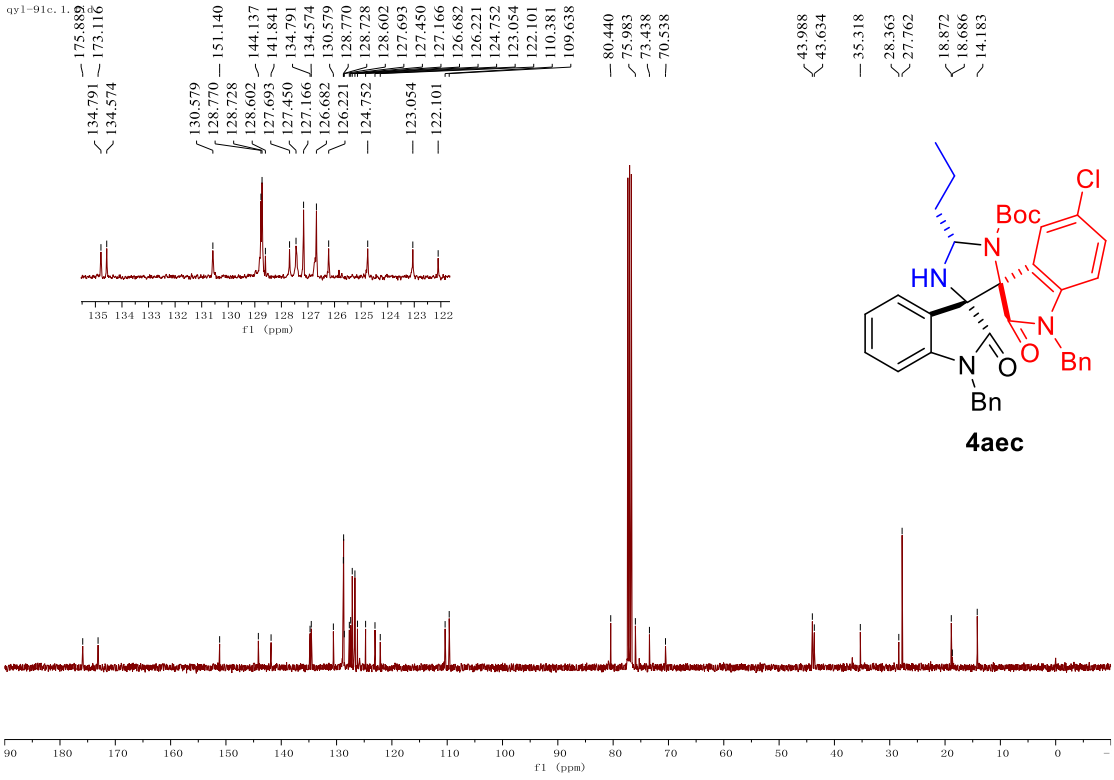
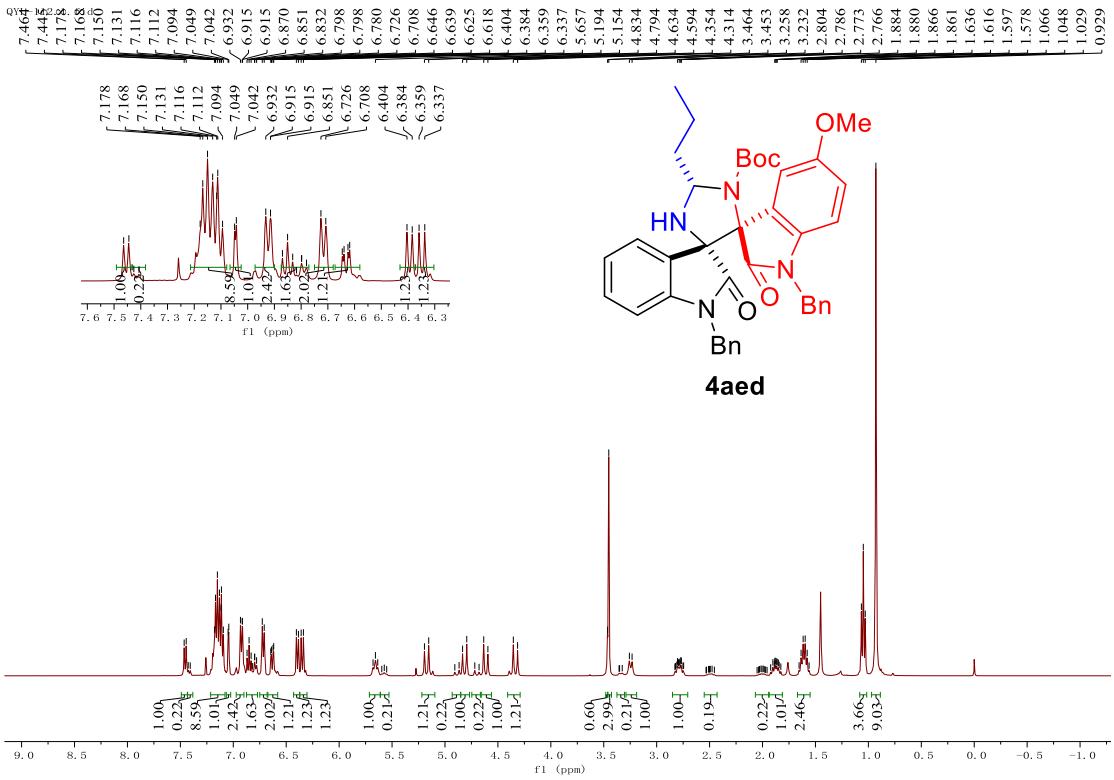


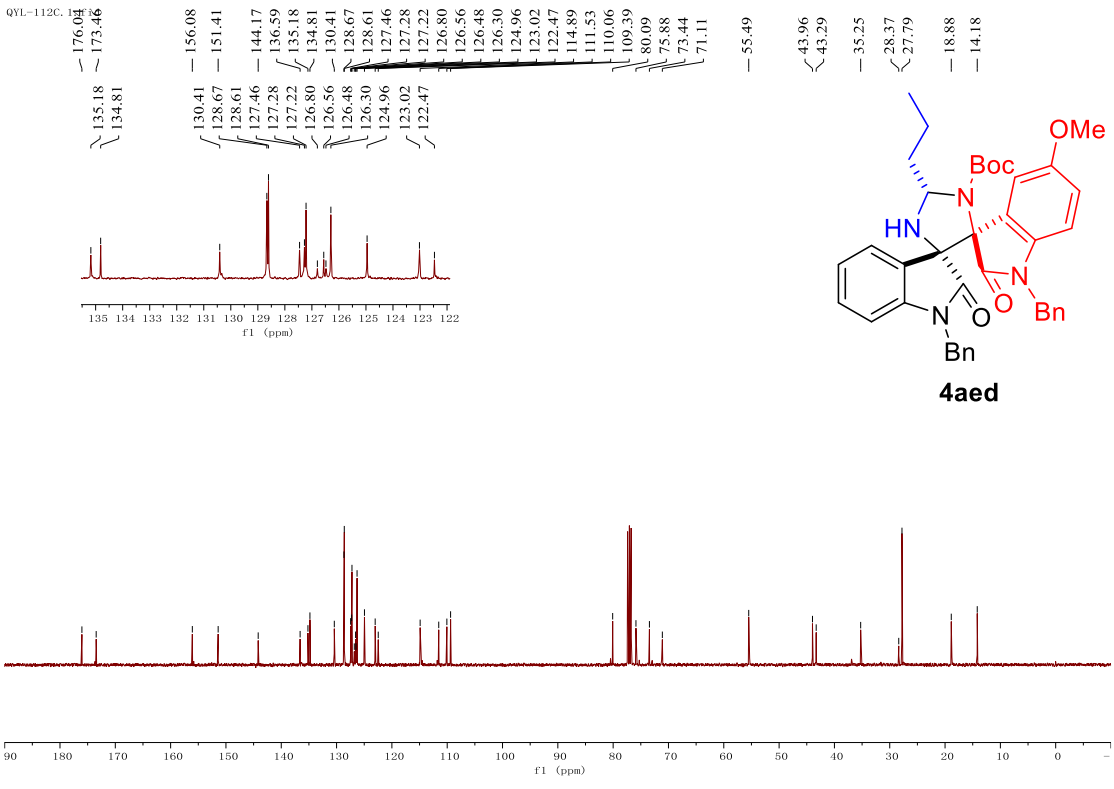
4aec



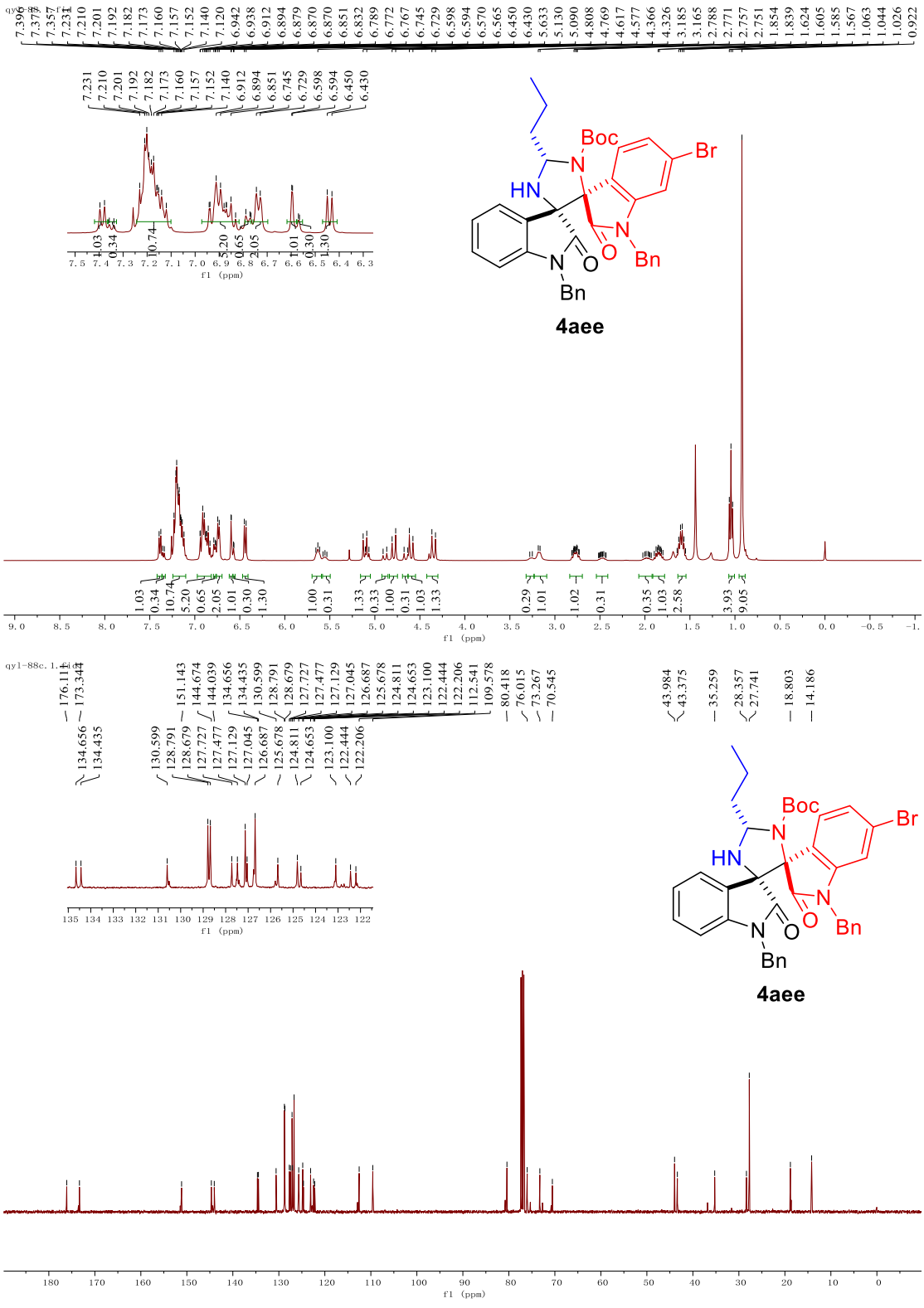
4aec

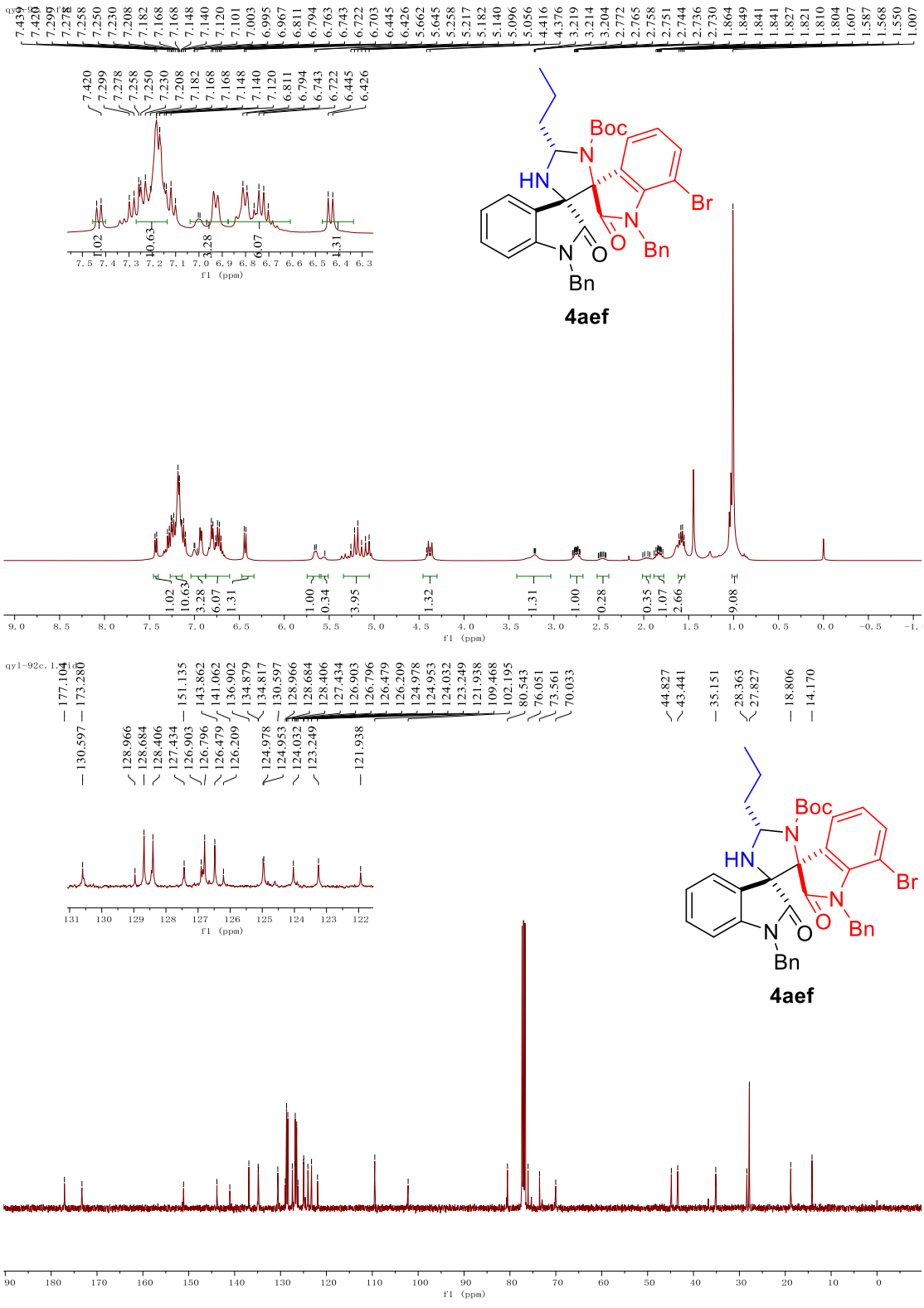


4aed



4aed


Boc
Br
HN
N
O
N
Bn
O
N
Bn
4aee


Boc
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HN
Br
N
O
Bn
N
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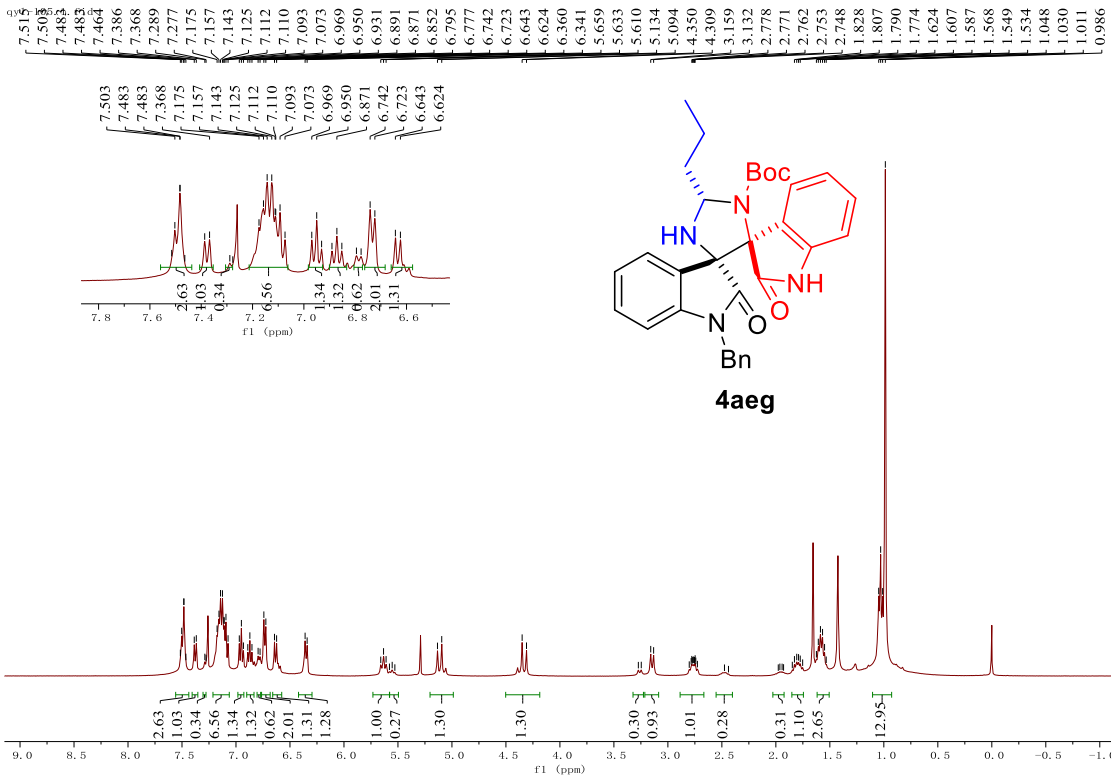
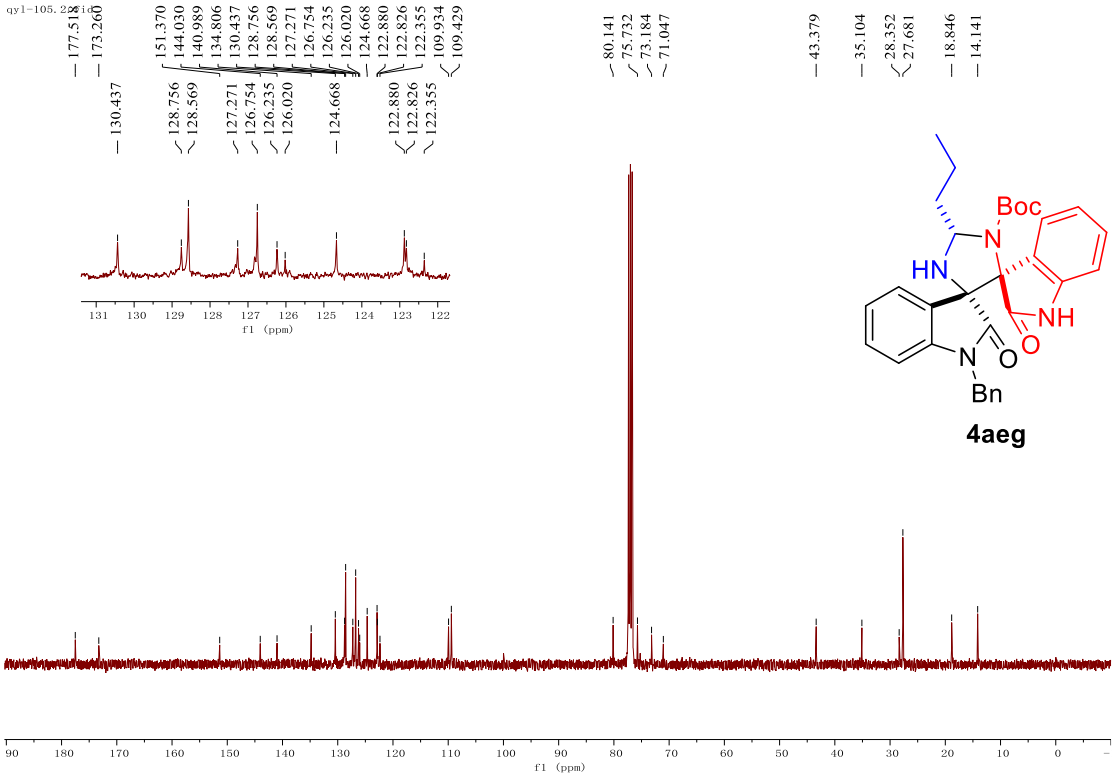
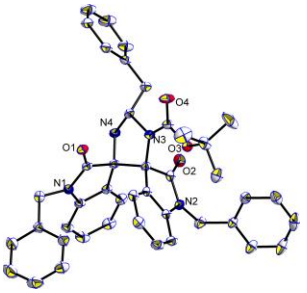
Bn
4aef

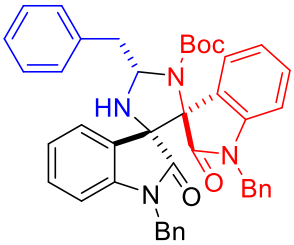

Boc
N
HN
NH
O
N
O
Bn
4aeg


Boc
N
HN
NH
O
N
O
Bn
4aeg

5. X-ray crystallographic data of compound 4aaa and 4lea

i. X-ray crystallographic data of compound **4aaa** **(CCDC 1571120)**





Bond precision: C-C = 0.0039 A Wavelength=0.71073

Cell: a=19.078(2) b=17.996(2) c=20.823(3)
alpha=90 beta=90 gamma=90
Temperature: 296 K

	Calculated	Reported
Volume	7149.1(15)	7149.0(15)
Space group	P b c a	Pbca
Hall group	-P 2ac 2ab	?
Moiety formula	C43 H40 N4 O4	?
Sum formula	C43 H40 N4 O4	C2.41 H2.24 N0.22 O0.22
Mr	676.79	37.86
Dx,g cm-3	1.258	1.258
Z	8	143
Mu (mm-1)	0.081	0.081
F000	2864.0	2864.0
F000'	2865.19	
h,k,lmax	23,21,25	23,21,25
Nref	6779	6780
Tmin,Tmax	0.981,0.984	
Tmin'	0.976	

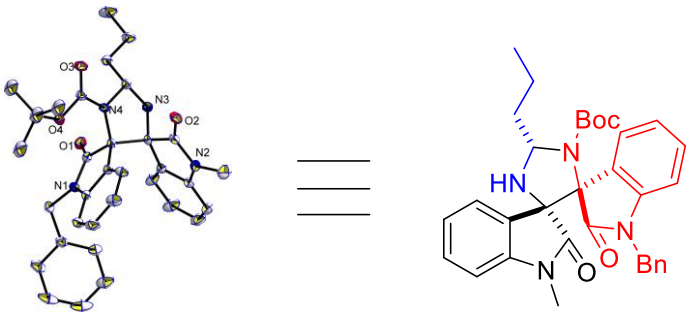
Correction method= Not given

Data completeness= 1.000 Theta(max)= 25.680

R(reflections)= 0.0531(3492) wR2(reflections)= 0.1495(6780)

S = 1.007 Npar= 460

ii. X-ray crystallographic data of compound **4lea (CCDC 1571121)**



Bond precision: C-C = 0.0047 A Wavelength=0.71073

Cell: a=10.1477(4) b=21.6478(8) c=13.5815(4)
alpha=90 beta=94.959(2) gamma=90
Temperature: 296 K

	Calculated	Reported
Volume	2972.35(18)	2972.35(18)
Space group	P 21/n	P2(1)/n
Hall group	-P 2yn	?
Moiety formula	C33 H36 N4 O4	?
Sum formula	C33 H36 N4 O4	C33 H36 N4 O4
Mr	552.66	552.66
Dx,g cm-3	1.235	1.235
Z	4	4
Mu (mm-1)	0.082	0.082
F000	1176.0	1176.0
F000'	1176.49	
h,k,lmax	12,26,16	12,26,16
Nref	5654	5654
Tmin,Tmax	0.981,0.984	
Tmin'	0.976	

Correction method= Not given

Data completeness= 1.000 Theta(max)= 25.680

R(reflections)= 0.0694(3959) wR2(reflections)= 0.1996(5654)

S = 1.040 Npar= 357