Supporting Information

Diastereoselective construction of pyrrolo[2,1-*a*]isoquinoline-based bispirooxindoles through a three-component [3+2] cycloaddition

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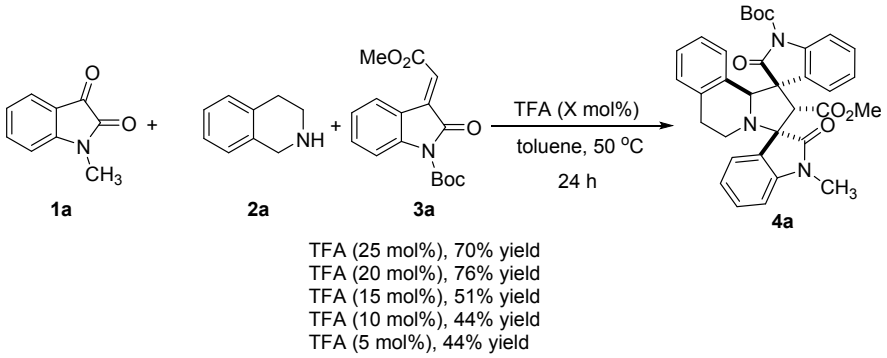
1. General methods

NMR spectra were recorded with tetramethylsilane as the internal standard. ^{1}H NMR spectra were recorded at 400 MHz, and ^{13}C NMR spectra were recorded at 100 MHz (Bruker Avance). ^{1}H NMR chemical shifts (δ) are reported in ppm relative to tetramethylsilane (TMS) with the solvent signal as the internal standard ($CDCl_3$ at 7.26 ppm, $(CD_3)_2SO$ at 2.50 ppm). ^{13}C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$ at 77.00 ppm, $(CD_3)_2SO$ at 39.52 ppm). Data are given as: s (singlet), d (doublet), t (triplet), q (quartet), dd (double of doublet), br (broad) or m (multiplets), coupling constants (Hz) and integration. Flash column chromatography was carried out using silica gel eluting with ethyl acetate and petroleum ether. High resolution mass spectra were obtained with the Q-TOF-Premier mass spectrometer. Reactions were monitored by TLC and visualized with ultraviolet light. IR spectra were recorded on a Thermo Fisher Nicolet Avatar 360 FTIR spectrometer on a KBr beam splitter. All the solvents were used directly without any purification.

2. Optimization of the TFA loadings



Scheme S1. Optimization of the loadings of TFA

Finally, we investigated the effect of the of TFA loadings to further improve the synthetic efficiency. When 25 mol% of TFA was employed, the yield was decreased to 70%. And much inferior results were obtained with less TFA. Thus, 20 mol% of TFA was proved to be optimal. Notably, we could detect a trace of product without Boc group in the reaction mixture by HRMS (Figure S1), and the Boc group could be removed completely by using 2.0 equivalent of TFA for 72 h.

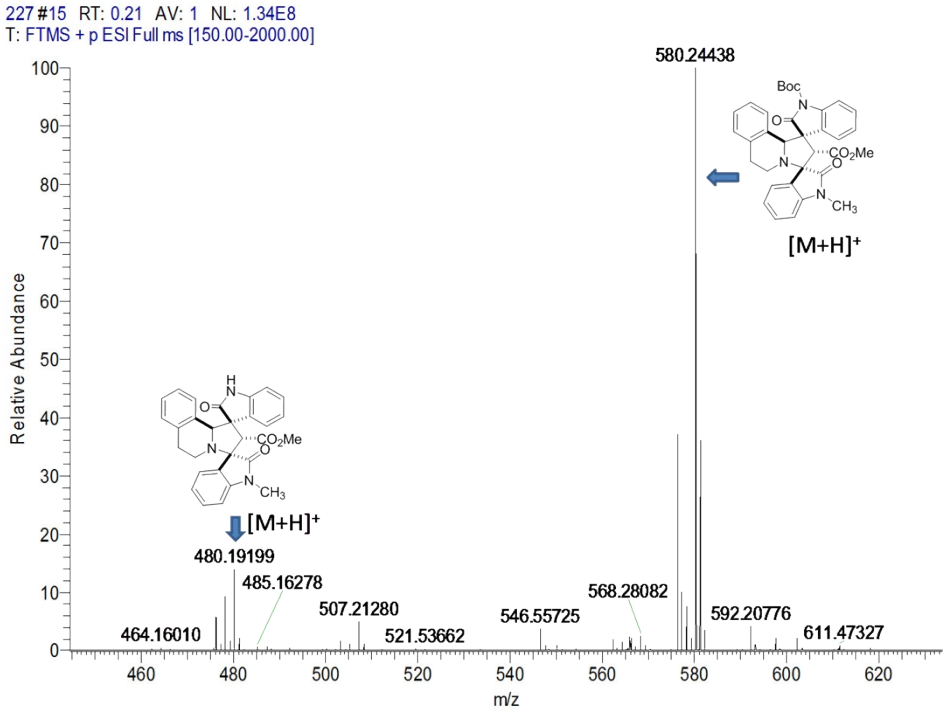
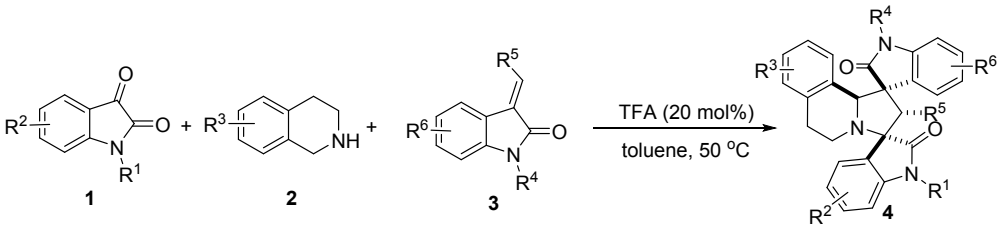
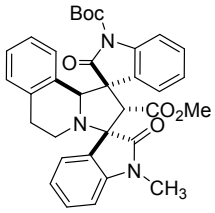


Figure S1. ESI-HRMS spectrum of the reaction of **1a**, **2a** and **3a** with 20 mol% of TFA in 1.0 mL of toluene after 72 h

3. Experimental data for pyrrolo[1,2-*a*]isoquinoline-based bispirooxindoles 4



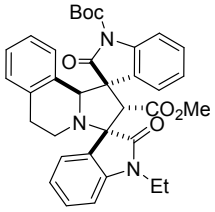
General procedure: To a 5.0 mL vial were successively added *N*-alkyl substituted isatin **1** (0.20 mmol), 1,2,3,4-tetrahydroisoquinoline **2** (0.24 mmol), methyleneindolinone **3** (0.24 mmol), TFA (0.04 mmol) and 1.0 mL toluene. The resulting mixture was stirred at 50 °C until almost full consumption of **1** as monitored by thin layer chromatography, and then the reaction mixture was directly subjected to flash column chromatography on silica gel (petroleum ether/ ethyl acetate) to afford the corresponding products **4**.



1-(*tert*-butyl) 2'-methyl 1''-methyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-

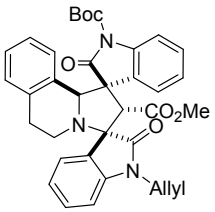
pyrrolo[2,1-*a*]isoquinoline-3',3"-indoline]-1,2'-dicarboxylate (**4a**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 25:1 to 20:1); 88.5 mg, 76% yield; reaction time = 72 h; mp 190.8-192.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.15 (d, *J* = 8.0 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.37 (q, *J* = 8.0 Hz, 2H), 7.27 (t, *J* = 8.0 Hz, 1H), 7.11 (t, *J* = 8.0 Hz, 1H), 7.02 (s, 2H), 6.87 (d, *J* = 8.0 Hz, 2H), 6.41 (d, *J* = 8.0 Hz, 1H), 5.75 (s, 1H), 4.33 (s, 1H), 3.32 (s, 3H), 3.10-2.99 (m, 4H), 2.71-2.55 (m, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 175.9, 168.2, 149.2, 144.9, 139.6, 134.9, 134.6, 129.9 (2C), 129.3, 128.7, 126.6, 126.5, 125.5, 125.3, 125.2, 124.5, 123.0, 122.8, 114.7, 108.0, 84.0, 70.3, 69.9, 63.8, 58.4, 51.3, 41.6, 29.7, 28.0, 26.0. IR (KBr) *v* 2980, 2941, 1771, 1736, 1721, 1296, 1154, 751 cm^{-1}. HRMS (ESI) calcd for $C_{34}H_{34}N_3O_6^+$ $[M+H]^+$ 580.2442, found 580.2445.



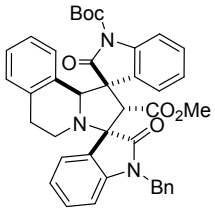
1-(*tert*-butyl) 2'-methyl 1"-ethyl-2,2"-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3"-indoline]-1,2'-dicarboxylate (**4b**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 18:1); 108.0 mg, 91% yield; reaction time = 24 h; mp 173.0-174.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.65 (d, *J* = 8.0 Hz, 1H), 7.41 (dd, $J_1 = J_2$ = 8.0 Hz, 2H), 7.24-6.96 (m, 8H), 6.55 (d, *J* = 8.0 Hz, 1H), 5.97 (d, *J* = 4.0 Hz, 1H), 3.99 (d, *J* = 8.0 Hz, 1H), 3.60 (q, *J* = 8.0 Hz, 1H), 3.39 (s, 3H), 3.14-3.04 (m, 2H), 2.89-2.84 (m, 1H), 2.72 (d, *J* = 16.0 Hz, 1H), 2.59 (t, *J* = 8.0 Hz, 1H), 1.52 (s, 9H), 0.72 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 173.7, 171.3, 148.7, 143.8, 139.7, 137.7, 134.4, 129.9, 129.0, 128.8, 126.6, 126.3, 125.7, 124.9, 123.8, 123.6, 123.4, 122.3, 114.0, 107.6, one carbon missing in the aromatic region, 83.7, 77.6, 62.2, 60.7, 55.0, 51.6, 42.7, 33.7, 29.6, 27.9, 12.1. IR (KBr) *v* 2979, 2935, 1738, 1701, 1474, 1360, 1163, 747 cm^{-1}. HRMS (ESI) calcd for $C_{35}H_{36}N_3O_6^+$ $[M+H]^+$594.2599, found 594.2597.



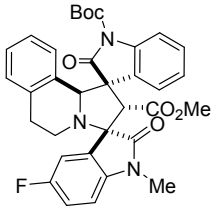
1-(*tert*-butyl) 2'-methyl 1''-allyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4c**)

White solid obtained by filtration of the precipitate; 90.5 mg, 75% yield; reaction time = 24 h; mp 172.8-174.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.67 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 8.0 Hz, 2H), 7.22-7.08 (m, 6H), 7.04-6.96 (m, 2H), 6.51 (d, J = 8.0 Hz, 1H), 5.97 (d, J = 12.0 Hz, 1H), 5.29-5.20 (m, 1H), 4.87 (d, J = 12.0 Hz, 1H), 4.51 (d, J = 16.0 Hz, 1H), 4.29-4.23 (m, 1H), 3.99 (d, J = 8.0 Hz, 1H), 3.66 (dd, J_1 = 4.0 Hz, J_2 = 8.0 Hz, 1H), 3.38 (s, 3H), 3.11-3.05 (m, 1H), 2.90-2.83 (m, 1H), 2.72 (dd, J_1 = J_2 = 4.0 Hz, 1H), 2.60 (dd, J_1 = J_2 = 4.0 Hz, 1H), 1.52 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 173.7, 171.3, 148.7, 144.0, 139.8, 137.6, 134.4, 130.6, 129.9, 129.1, 128.8, 126.5, 126.4 (2C), 125.8, 125.0, 123.8 (2C), 123.1, 122.5, 117.0, 114.1, 108.5, 83.8, 77.8, 62.1, 60.7, 55.1, 51.6, 42.8, 41.4, 29.6, 28.0. IR (KBr) v 3449, 2938, 1739, 1705, 1473, 1359, 1298, 1162, 747 cm^{-1}. HRMS (ESI) m/z calcd for $C_{36}H_{36}N_3O_6^+$ $[M+H]^+$ 606.2599, found606.2595.



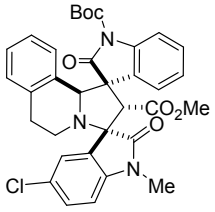
1-(*tert*-butyl) 2'-methyl 1''-benzyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4d**)

White solid obtained by filtration of the precipitate; 100.2 mg, 76% yield; reaction time = 28 h; mp 170.1-171.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.70 (d, J = 8.0 Hz, 1H), 7.43 (dd, J_1 = J_2 = 8.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 1H), 7.13-7.04 (m, 8H), 6.99-6.91 (m, 2H), 6.54 (d, J = 8.0 Hz, 2H), 6.30 (d, J = 8.0 Hz, 1H), 5.97 (d, J = 12.0 Hz, 1H), 4.89 (d, J = 16.0 Hz, 1H), 4.22 (d, J = 16.0 Hz, 1H), 3.99 (d, J = 8.0 Hz, 1H), 3.35 (s, 3H), 3.10-2.99 (m, 1H), 2.89-2.82 (m, 1H), 2.71 (dd, J_1 = J_2 = 4.0 Hz, 1H), 2.57 (dd, J_1 = J_2 = 8.0 Hz, 1H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 173.9, 171.2, 148.7, 144.0, 139.9, 137.5, 134.9, 134.3, 130.0, 129.2, 128.8, 128.6, 127.2, 126.7, 126.6, 126.4 (2C), 125.8, 125.0, 124.0, 123.9, 123.2, 122.6, 114.2, 108.8, 83.8, 77.5, 62.0, 60.6, 55.3, 51.6, 43.0, 42.7, 29.6, 27.9. IR (KBr) v 3437, 2924, 1767, 1736, 1467, 1355, 1294, 1161, 754 cm^{-1}. HRMS (ESI) calcd for $C_{40}H_{38}N_3O_6^+$ $[M+H]^+$ 656.2755, found 656.2754.



1-(*tert*-butyl) 2'-methyl 5''-fluoro-1''-methyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4e**)

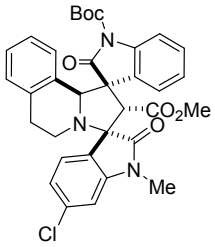
White solid obtained by filtration of the precipitate; 84.6 mg, 71% yield; reaction time = 72 h; mp 198.5-200.1 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.70 (d, J = 8.0 Hz, 1H), 7.39 (d, J = 8.0 Hz, 1H), 7.23-7.02 (m, 7H), 6.94 (t, J = 8.0 Hz, 1H), 6.45 (dd, J_1 = J_2 = 4.0 Hz, 1H), 5.97 (d, J = 8.0 Hz, 1H), 3.95 (d, J = 8.0 Hz, 1H), 3.39 (s, 3H), 3.15-3.06 (m, 1H), 2.91-2.86 (m, 1H), 2.74 (s, 4H), 2.60 (t, J = 8.0 Hz, 1H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.0, 173.9, 171.1, 158.9 (d, J = 240.0 Hz, 1C), 148.8, 140.6, 139.7, 137.4, 134.2, 129.3, 128.9, 126.4, 126.0, 125.8, 125.0, 124.9, 123.6, 123.4, 116.3 (d, J = 24.0 Hz, 1C), 114.5 (d, J = 26.0 Hz, 1C), 114.1, 108.1 (d, J = 8.0 Hz, 1C), 84.2, 77.9, 62.2, 60.9, 54.9, 51.7, 42.9, 29.6, 27.7, 25.3. IR (KBr) v 3406, 2973, 2924, 2850, 1760, 1615, 1490, 1351, 1300, 1165, 761 cm^{-1}. HRMS (ESI) calcd for $C_{34}H_{33}FN_3O_6^+$ $[M+H]^+$ 598.2348, found 598.2350.



1-(*tert*-butyl) 2'-methyl 5''-chloro-1''-methyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4f**)

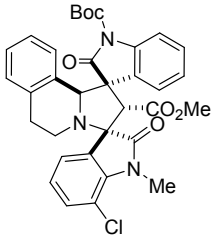
White solid obtained by filtration of the precipitate; 86.4 mg, 70% yield; reaction time = 24 h; mp 196.4-197.7 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.09 (d, J = 8.0 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 4.0 Hz, 1H), 7.41-7.24 (m, 3H), 7.05 (d, J = 8.0 Hz, 2H), 6.91-6.86 (m, 1H), 6.80 (d, J = 8.0 Hz, 1H), 6.39 (d, J = 12.0 Hz, 1H), 5.72 (s, 1H), 4.27 (s, 1H), 3.31 (s, 3H), 3.13-3.05 (m, 1H), 3.01 (s, 3H), 2.69-2.57 (m, 3H), 1.56 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 175.6, 168.2, 149.2, 143.5, 139.6, 134.8, 134.4, 130.0, 129.7, 129.4, 128.9, 128.5, 128.3, 126.6, 125.6, 125.3, 125.1, 125.0, 123.0, 114.8, 109.1, 84.2, 70.2, 69.9, 64.0, 58.2, 51.5, 41.7, 29.6, 28.0, 26.2. IR (KBr) v 3428, 2943, 1723, 1487, 1294, 1154, 755 cm^{-1}. HRMS (ESI) m/z calcd for

$C_{34}H_{33}ClN_3O_6^+$ $[M+H]^+$ 614.2052, found 614.20544.



1-(*tert*-butyl) 2'-methyl 6"-chloro-1"-methyl-2,2"-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3"-indoline]-1,2'-dicarboxylate (**4g**)

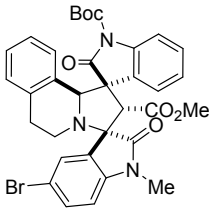
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 25:1 to 20:1); 89.3 mg, 73% yield; reaction time = 72 h; mp 153.5-155.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.09 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.38 (t, J = 8.0 Hz, 1H), 7.26 (t, J = 8.0 Hz, 1H), 7.09 (dd, J_1 = J_2 = 4.0 Hz, 1H), 7.04-7.02 (m, 2H), 6.90-6.86 (m, 2H), 6.39 (d, J = 4.0 Hz, 1H), 5.71 (s, 1H), 4.28 (s, 1H), 3.30 (s, 3H), 3.06-3.04 (m, 1H), 3.01 (s, 3H), 2.72-2.57 (m, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 175.9, 168.3, 149.2, 146.1, 139.6, 135.9, 134.9, 134.5, 129.7, 129.4, 128.9, 126.6, 125.6 (2C), 125.3, 125.2, 125.1, 123.0, 122.7, 114.8, 108.9, 84.2, 70.0, 69.9, 63.9, 58.3, 51.5, 41.6, 29.7, 28.0, 26.2. IR (KBr) ν 3435, 2940, 1720, 1607, 1488, 1363, 1294, 1152, 757 cm^{-1}. HRMS (ESI) calcd for $C_{34}H_{33}ClN_3O_6^+$ $[M+H]^+$ 614.2052, found 614.2056.



1-(*tert*-butyl) 2'-methyl 7"-chloro-1"-methyl-2,2"-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3"-indoline]-1,2'-dicarboxylate (**4h**)

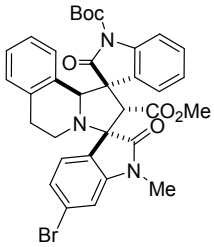
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 25:1 to 20:1); 97.5 mg, 79% yield; reaction time = 72 h; mp 210.5-211.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.09 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.39 (t, J = 8.0 Hz, 1H), 7.27 (t, J = 8.0 Hz, 2H), 7.06-7.00 (m, 3H), 6.91-6.86 (m, 1H), 6.40 (d, J = 8.0 Hz, 1H), 5.70 (s, 1H), 4.26 (s, 1H), 3.69 (s, 3H), 3.11-3.06 (m, 1H), 3.02 (s, 3H), 2.67-2.56 (m, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 176.2, 168.2, 149.2, 140.8, 139.6, 134.9, 134.6, 132.3, 129.8, 129.7, 129.4, 128.9, 126.6, 125.6, 125.3, 125.2, 123.6, 123.1, 123.0, 115.4, 114.8, 84.2,

69.9, 69.7, 64.3, 58.1, 51.5, 41.6, 29.7, 29.3, 28.0. IR (KBr) *v* 3430, 2983, 2916, 2831, 1746, 1701, 1601, 1483, 993, 836, 761 cm^{-1}. HRMS (ESI) calcd for $C_{34}H_{33}ClN_3O_6^+$ $[M+H]^+$ 614.2052, found 614.2053.



1-(*tert*-butyl) 2'-methyl 5''-bromo-1''-methyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4i**)

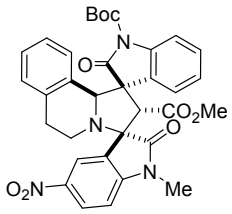
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 15:1); 91.3 mg, 69% yield; reaction time = 24 h; mp 201.8-203.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.09 (d, *J* = 8.0 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.67 (s, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.28 (s, 1H), 7.03 (s, 2H), 6.88 (s, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.39 (d, *J* = 4.0 Hz, 1H), 5.71 (s, 1H), 4.26 (s, 1H), 3.30 (s, 3H), 3.20-3.06 (m, 1H), 3.01 (s, 3H), 2.69-2.57 (m, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 175.5, 168.2, 149.2, 144.0, 139.7, 134.9, 134.5, 132.9, 129.7, 129.4, 128.9, 128.8, 127.7, 126.6, 125.6, 125.3, 125.2, 123.0, 115.5, 114.8, 109.5, 84.2, 70.2, 69.9, 64.0, 58.2, 51.5, 41.7, 29.7, 28.0, 26.2. IR (KBr) *v* 3407, 2939, 1735, 1713, 1606, 1481, 1357, 1290, 1246, 1153, 1100, 762 cm^{-1}. HRMS (ESI) calcd for $C_{34}H_{33}BrN_3O_6^+$ $[M+H]^+$ 658.1547, found 658.1549.



1-(*tert*-butyl) 2'-methyl 6''-bromo-1''-methyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4j**)

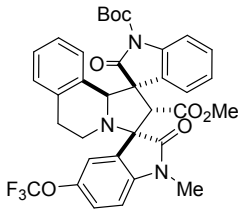
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 25:1 to 20:1); 96.0 mg, 73% yield; reaction time = 72 h; mp 165.3-166.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.08 (d, *J* = 8.0 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 2H), 7.26 (t, *J* = 8.0 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 3H), 6.90-6.86 (m, 1H), 6.39 (d, *J* = 4.0 Hz, 1H), 5.71 (s, 1H), 4.27 (s, 1H), 3.30 (s, 3H), 3.10-3.03 (m, 1H), 3.01 (s, 3H), 2.72-2.56 (m, 3H), 1.55 (s, 9H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 176.6, 175.9, 168.2, 149.2, 146.3, 139.7, 134.9, 134.5, 129.8, 129.3, 128.9, 126.6, 125.9, 125.7 (2C), 125.6, 125.3, 125.2, 123.8, 123.1, 114.8, 111.6, 84.2, 70.1, 70.0, 63.9, 58.3, 51.5, 41.7, 29.7, 28.0, 26.2. IR (KBr) *v* 3435, 2978, 2940, 1723, 1604, 1485, 1362, 1294, 1154, 757 cm^{-1}. HRMS (ESI) calcd for $C_{34}H_{33}BrN_3O_6^+$ $[M+H]^+$ 658.1547, found 658.1549.



1-(*tert*-butyl) 2'-methyl 1''-methyl-5''-nitro-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4k**)

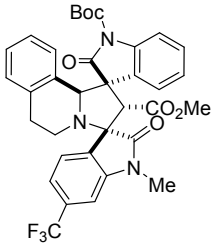
Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 15:1 to 5:1); 26.2 mg, 21% yield; reaction time = 24 h; mp 203.1-204.7 °C; ^1H NMR (400 MHz, $CDCl_3$), δ 8.41 (s, 1H), 8.34 (d, *J* = 8.0 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.27 (t, *J* = 8.0 Hz, 1H), 7.04 (s, 2H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.90 (t, *J* = 8.0 Hz, 1H), 6.40 (d, *J* = 8.0 Hz, 1H), 5.72 (s, 1H), 4.36 (s, 1H), 3.39 (s, 3H), 3.21-3.10 (m, 1H), 3.08 (s, 3H), 2.71-2.59 (m, 3H), 1.56 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 176.1, 168.2, 150.5, 149.1, 143.8, 139.8, 134.7, 134.1, 129.4 (2C), 129.0, 127.8, 127.2, 126.7, 125.7, 125.2, 125.0, 123.0, 120.5, 114.9, 107.8, 84.3, 70.1, 70.0, 64.2, 58.2, 51.6, 41.9, 29.6, 28.0, 26.5. IR (KBr) *v* 3441, 2945, 1772, 1728, 1614, 1339, 1152, 752 cm^{-1}. HRMS (ESI) calcd for $C_{34}H_{33}N_4O_8^+$ $[M+H]^+$ 625.2293, found 625.2293.



1-(*tert*-butyl) 2'-methyl 1''-methyl-2,2''-dioxo-5''-(trifluoromethoxy)-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4l**)

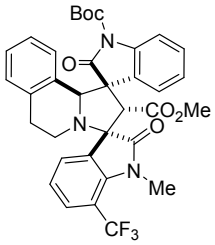
Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 12:1); 76.1 mg, 57% yield; reaction time = 36 h; mp 128.9-130.2 °C; ^1H NMR (400 MHz, $CDCl_3$), δ 8.11 (d, *J* = 8.0 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.40 (dd, $J_1 = J_2 = 8.0$ Hz, 2H), 7.29-7.22 (m, 2H), 7.03 (s, 2H), 6.91-6.84 (m, 2H), 6.40 (d, *J* = 8.0 Hz, 1H), 5.72 (s, 1H), 4.27 (s, 1H), 3.32 (s,

3H), 3.13-3.06 (m, 1H), 3.02 (s, 3H), 2.68-2.56 (m, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 175.8, 168.2, 149.2, 145.0 (2C), 143.6, 139.7, 134.8, 134.4, 129.7, 129.4, 128.9, 128.4, 126.6, 125.6, 125.2 (2C), 123.2, 123.0, 118.6, 114.8, 108.5, 84.2, 70.3, 69.9, 64.0, 58.3, 51.5, 41.7, 29.7, 28.0, 26.2. IR (KBr) *v* 3449, 1722, 1359, 1156, 756 cm^{-1}. HRMS (ESI) calcd for $C_{35}H_{33}F_3N_3O_7^+$ $[M+H]^+$ 664.2265, found 664.2268.



1-(*tert*-butyl) 2'-methyl 1''-methyl-2,2''-dioxo-6''-(trifluoromethyl)-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4m**)

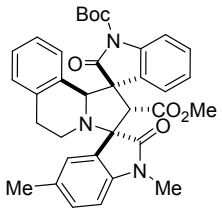
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 40:1 to 30:1); 67.1 mg, 52% yield; reaction time = 36 h; mp 198.3-199.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.09 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 2H), 7.27 (t, *J* = 8.0 Hz, 1H), 7.06 (d, *J* = 16.0 Hz, 3H), 6.89 (s, 1H), 6.40 (d, *J* = 8.0 Hz, 1H), 5.74 (s, 1H), 4.32 (s, 1H), 3.36 (s, 3H), 3.13-3.07 (m, 1H), 3.02 (s, 3H), 2.68-2.56 (m, 3H), 1.56 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 175.7, 168.2, 149.1, 145.6, 139.7, 134.8, 134.4, 132.6, 130.8, 129.6, 129.4, 128.9, 126.7, 125.7, 125.3, 125.2, 124.9, 123.0, 119.9 (2C), 114.9, 104.8, 84.3, 70.1, 70.0, 64.0, 58.3, 51.5, 41.8, 29.7, 28.0, 26.2. IR (KBr) *v* 3451, 2931, 1762, 1730, 1463, 1324, 1159, 777 cm^{-1}. HRMS (ESI) calcd for $C_{35}H_{33}F_3N_3O_6^+$ $[M+H]^+$ 648.2316, found 648.2318.



1-(*tert*-butyl) 2'-methyl 1''-methyl-2,2''-dioxo-7''-(trifluoromethyl)-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4n**)

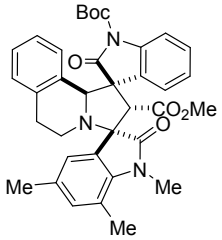
Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 50:1 to 40:1); 20.9 mg, 16% yield; reaction time = 18 h; mp 180.5-181.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.08 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 4.0 Hz, 1H), 7.19 (t, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 8.0 Hz,

2H), 6.89 (t, *J* = 8.0 Hz, 1H), 6.41 (d, *J* = 8.0 Hz, 1H), 5.72 (s, 1H), 4.28 (s, 1H), 3.52 (s, 3H), 3.10-3.06 (m, 1H), 3.02 (s, 3H), 2.64-2.56 (m, 3H), 1.56 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 176.6, 168.0, 149.1, 143.0, 139.6, 134.9, 134.5, 129.7, 129.6, 129.4, 128.9, 128.0, 127.9, 126.6, 125.7, 125.3, 125.2, 123.0, 122.2, 114.9, 112.6, 112.2, 84.2, 69.9, 68.4, 64.4, 58.1, 51.5, 41.5, 29.7, 28.7, 28.0. IR (KBr) *v* 3431, 2953, 1720, 1466, 1350, 1150, 746 cm^{-1}. HRMS (ESI) calcd for $C_{35}H_{33}F_3N_3O_6^+$ $[M+H]^+$ 648.2316, found 648.2316.



1-(*tert*-butyl) 2'-methyl 1",5"-dimethyl-2,2"-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3"-indoline]-1,2'-dicarboxylate (**4o**)

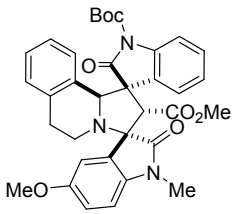
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 15:1); 57.5 mg, 48% yield; reaction time = 48 h; mp 199.4-200.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.15 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.38 (t, *J* = 8.0 Hz, 2H), 7.25 (t, *J* = 8.0 Hz, 1H), 7.15 (d, *J* = 8.0 Hz, 1H), 7.02 (d, *J* = 4.0 Hz, 2H), 6.90-6.85 (m, 1H), 6.76 (d, *J* = 8.0 Hz, 1H), 6.41 (d, *J* = 8.0 Hz, 1H), 5.74 (s, 1H), 4.31 (s, 1H), 3.30 (s, 3H), 3.13-3.04 (m, 1H), 3.00 (s, 3H), 2.70-2.56 (m, 3H), 2.34 (s, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 175.9, 168.3, 149.3, 142.6, 139.6, 135.0, 134.8, 132.5, 130.2, 130.0, 129.3, 128.7, 126.6, 126.5, 125.5, 125.3 (2C), 125.2, 123.1, 114.7, 107.7, 84.1, 70.4, 70.0, 63.8, 58.4, 51.3, 41.6, 29.7, 28.0, 26.0, 20.9. IR (KBr) *v* 3446, 2980, 2939, 2820, 1768, 1736, 1708, 1492, 1358, 1293, 1154, 760 cm^{-1}. HRMS (ESI) calcd for $C_{35}H_{36}N_3O_6^+$ $[M+H]^+$ 594.2599, found 594.2600.



1-(*tert*-butyl) 2'-methyl 1",5",7"-trimethyl-2,2"-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3"-indoline]-1,2'-dicarboxylate (**4p**)

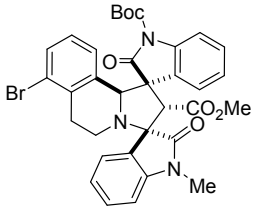
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 25:1 to 15:1); 80.9 mg, 67% yield; reaction time = 72 h; mp 200.2-201.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ

8.15 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 1H), 7.26 (t, *J* = 8.0 Hz, 1H), 7.21 (s, 1H), 7.03 (d, *J* = 4.0 Hz, 2H), 6.88-6.85 (m, 2H), 6.40 (d, *J* = 8.0 Hz, 1H), 5.72 (s, 1H), 4.26 (s, 1H), 3.57 (s, 3H), 3.12-3.04 (m, 1H), 3.00 (s, 3H), 2.72-2.59 (m, 3H), 2.56 (s, 3H), 2.28 (s, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 176.5, 168.3, 149.3, 140.2, 139.6, 135.0, 134.9, 134.2, 132.3, 130.1, 129.3, 128.7, 127.4, 126.4, 125.5, 125.3, 125.2, 123.1, 123.0, 119.2, 114.7, 84.1, 69.9, 69.6, 64.2, 58.2, 51.3, 41.5, 29.7, 29.3, 28.0, 20.6, 18.8. IR (KBr) *v* 3447, 2982, 2940, 1737, 1701, 1477, 1357, 1294, 1154, 1095, 759 cm^{-1}. HRMS (ESI) calcd for $C_{36}H_{38}N_3O_6^+$ $[M+H]^+$ 608.2755, found 608.2753.



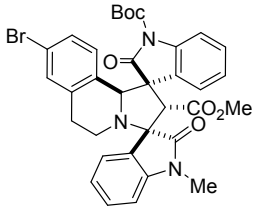
1-(*tert*-butyl) 2'-methyl 5''-methoxy-1''-methyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4q**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 12:1 to 8:1); 87.6 mg, 72% yield; reaction time = 72 h; mp 160.0-161.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.17 (d, *J* = 8.0 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 1H), 7.26 (t, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 4.0 Hz, 1H), 7.02 (d, *J* = 4.0 Hz, 2H), 6.91-6.85 (m, 2H), 6.77 (d, *J* = 12.0 Hz, 1H), 6.40 (d, *J* = 8.0 Hz, 1H), 5.75 (s, 1H), 4.29 (s, 1H), 3.81 (s, 3H), 3.30 (s, 3H), 3.13-3.05 (m, 1H), 3.00 (s, 3H), 2.73-2.64 (m, 2H), 2.58 (d, *J* = 16.0 Hz, 1H), 1.56 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 175.7, 168.2, 156.4, 149.2, 139.6, 138.4, 135.0, 134.8, 130.0, 129.4, 128.7, 128.0, 126.5, 125.6, 125.5, 125.3, 123.1, 115.2, 114.7, 111.0, 108.6, 84.2, 70.7, 70.0, 64.0, 58.4, 55.9, 51.3, 41.7, 29.7, 28.0, 26.1. IR (KBr) *v* 3394, 2942, 2829, 1707, 1607, 1494, 1360, 1158, 1035, 760 cm^{-1}. HRMS (ESI) calcd for $C_{35}H_{36}N_3O_7^+$ $[M+H]^+$ 610.2548, found 610.2544.



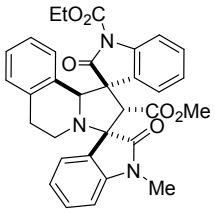
1-(*tert*-butyl) 2'-methyl 7'-bromo-1''-methyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4r**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 25:1 to 18:1); 117.2 mg, 89% yield; reaction time = 24 h; mp 143.2-144.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.16 (d, *J* = 8.0 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.38 (q, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.28 (t, *J* = 8.0 Hz, 1H), 7.12 (t, *J* = 8.0 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.78 (t, *J* = 8.0 Hz, 1H), 6.39 (d, *J* = 8.0 Hz, 1H), 5.74 (s, 1H), 4.32 (s, 1H), 3.33 (s, 3H), 3.00 (s, 3H), 2.91-2.85 (m, 1H), 2.77-2.61 (m, 3H), 1.57 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 175.8, 168.1, 149.1, 144.9, 139.5, 137.3, 134.9, 130.8, 130.1, 129.6, 128.9, 126.8, 126.4, 125.8, 125.4, 125.3, 124.5, 122.9, 122.2, 114.8, 108.1, 84.3, 70.0, 69.7, 63.9, 58.2, 51.4, 41.3, 31.0, 28.0, 26.0. IR (KBr) *v* 3448, 2978, 2942, 2826, 1716, 1610, 1472, 1361, 1295, 1248, 1153, 759 cm^{-1}. HRMS (ESI) calcd for $C_{34}H_{33}BrN_3O_6^+$ $[M+H]^+$ 658.1547, found 658.1549.



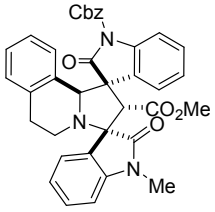
1-(*tert*-butyl) 2'-methyl 8'-bromo-1''-methyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4s**)

Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 16:1); 98.6 mg, 75% yield; reaction time = 72 h; mp 141.7-142.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.11 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.37 (q, *J* = 8.0 Hz, 2H), 7.27 (t, *J* = 8.0 Hz, 1H), 7.19 (s, 1H), 7.11 (t, *J* = 8.0 Hz, 1H), 7.00 (dd, $J_1 = J_2 = 4.0$ Hz, 1H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.25 (d, *J* = 8.0 Hz, 1H), 5.67 (s, 1H), 4.30 (s, 1H), 3.32 (s, 3H), 3.07-3.03 (m, 1H), 3.00 (s, 3H), 2.75-2.53 (m, 3H), 1.57 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 176.0, 168.2, 149.1, 144.9, 139.5, 137.5, 133.7, 132.1, 130.1, 129.6, 128.9, 128.6, 126.4, 125.3, 124.9, 124.6, 122.9, 120.3, 114.8, 108.1, one carbon missing in the aromatic region, 84.4, 70.3, 69.5, 63.6, 58.4, 51.4, 41.2, 29.6, 28.0, 26.1. IR (KBr) *v* 3442, 2977, 2941, 1717, 1609, 1476, 1361, 1294, 1248, 1153, 758 cm^{-1}. HRMS (ESI) calcd for $C_{34}H_{33}BrN_3O_6^+$ $[M+H]^+$ 658.1547, found 658.1544.



1-ethyl 2'-methyl 1''-methyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4t**)

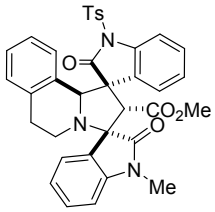
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 25:1 to 12:1); 44.8 mg, 41% yield; reaction time = 72 h; mp 209.2-210.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.15 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.42-7.34 (m, 2H), 7.29 (t, *J* = 8.0 Hz, 1H), 7.12 (t, *J* = 8.0 Hz, 1H), 7.03 (d, *J* = 4.0 Hz, 2H), 6.90-6.86 (m, 2H), 6.36 (d, *J* = 8.0 Hz, 1H), 5.78 (s, 1H), 4.45-4.35 (m, 2H), 4.31 (s, 1H), 3.32 (s, 3H), 3.07-3.02 (m, 1H), 3.00 (s, 3H), 2.75-2.56 (m, 3H), 1.36 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 176.0, 168.2, 150.8, 145.0, 139.3, 135.0, 134.5, 130.0 (2C), 129.4, 128.9, 126.7, 126.6, 125.8, 125.6, 125.4, 124.5, 123.0, 122.9, 114.8, 108.1, 70.2, 69.8, 64.2, 63.3, 58.4, 51.4, 41.6, 29.9, 26.0, 14.2. IR (KBr) *v* 3422, 2940, 1721, 1611, 1473, 1362, 1293, 1234, 756 cm^{-1}. HRMS (ESI) calcd for $C_{32}H_{30}N_3O_6^+$ $[M+H]^+$ 552.2129, found 552.2128.



1-benzyl 2'-methyl 1''-methyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4u**)

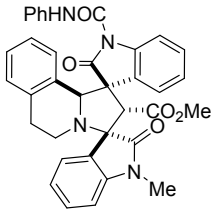
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 18:1); 57.2 mg, 47% yield; reaction time = 72 h; mp 176.7-178.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.17 (d, *J* = 8.0 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.39-7.28 (m, 8H), 7.13 (t, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 4.0 Hz, 2H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.82-6.78 (m, 1H), 6.36 (d, *J* = 8.0 Hz, 1H), 5.80 (s, 1H), 5.45 (d, *J* = 12.0 Hz, 1H), 5.35 (d, *J* = 12.0 Hz, 1H), 4.33 (s, 1H), 3.33 (s, 3H), 3.11-3.03 (m, 1H), 3.00 (s, 3H), 2.74-2.57 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 176.0, 168.1, 150.7, 145.0, 139.2, 135.1, 135.0, 134.5, 130.0, 129.9, 129.4, 128.9, 128.5, 128.2, 127.7, 126.6, 125.8, 125.6, 125.4, 124.5, 122.9 (2C), 114.8, 108.1, one carbon missing in

the aromatic region, 70.2, 69.9, 68.3, 64.1, 58.4, 51.4, 41.6, 29.8, 26.0. IR (KBr) *v* 3039, 2931, 1738, 1718, 1469, 1343, 1292, 1229, 1154, 756 cm^{-1}. HRMS (ESI) m/z calcd for $C_{37}H_{32}N_3O_6^+$ $[M+H]^+$ 614.2286, found 614.2284.



methyl 1''-methyl-2,2''-dioxo-1-tosyl-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-2'-carboxylate (**4v**)

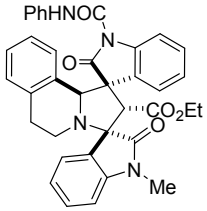
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 15:1); 73.9 mg, 58% yield; reaction time = 24 h; mp 227.4-228.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.15 (d, *J* = 8.0 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 2H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.41 (t, *J* = 8.0 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 1H), 7.29 (t, *J* = 4.0 Hz, 1H), 7.22 (d, *J* = 8.0 Hz, 2H), 7.11 (t, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.86 (dd, J_1 = 4.0 Hz, J_2 = 8.0 Hz, 2H), 6.32 (t, *J* = 8.0 Hz, 1H), 5.98 (d, *J* = 8.0 Hz, 1H), 5.71 (s, 1H), 4.17 (s, 1H), 3.29 (s, 3H), 3.01-2.95 (m, 1H), 2.92 (s, 3H), 2.68-2.51 (m, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.6, 175.8, 167.8, 145.3, 144.9, 139.1, 135.3, 134.7, 134.0, 130.1, 129.8, 129.6, 129.1, 129.2, 127.9, 126.4, 126.0 (2C), 125.7, 125.6, 124.5, 122.9, 122.6, 113.0, 108.1, 70.2, 69.3, 64.4, 58.0, 51.4, 41.6, 29.7, 26.0, 21.7. IR (KBr) *v* 3412, 2922, 1748, 1710, 1608, 1464, 1374, 1183, 1148, 1084, 753 cm^{-1}. HRMS (ESI) calcd for $C_{36}H_{32}N_3O_6S^+$ $[M+H]^+$ 634.2006, found 634.2000.



methyl 1''-methyl-2,2''-dioxo-1-(phenylcarbamoyl)-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-2'-carboxylate (**4w**)

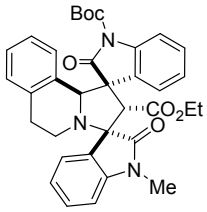
Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 15:1); 99.3 mg, 83% yield; reaction time = 40 h; mp 210.6-211.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 10.51 (s, 1H), 8.44 (d, *J* = 8.0 Hz, 1H), 8.19 (d, *J* = 4.0 Hz, 1H), 7.54 (dd, J_1 = J_2 = 8.0 Hz, 3H), 7.43 (dd, J_1 = 8.0 Hz, J_2 = 4.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.36-7.31 (m, 3H), 7.18-7.10 (m,

2H), 7.05 (t, J = 8.0 Hz, 2H), 6.91 (dd, $J_1 = J_2$ = 8.0 Hz, 2H), 6.39 (d, J = 8.0 Hz, 1H), 5.86 (s, 1H), 4.27 (s, 1H), 3.34 (s, 3H), 3.14-3.08 (m, 1H), 3.01 (s, 3H), 2.71 (d, J = 8.0 Hz, 2H), 2.63 (d, J = 16.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.6, 175.7, 167.8, 149.2, 145.0, 140.0, 137.1, 134.7, 134.5, 130.2, 129.6, 129.5, 129.2, 129.0, 126.9, 126.5, 126.3, 125.8, 125.2, 124.4, 124.2, 123.0, 122.8, 120.4, 116.3, 108.2, 70.2, 69.5, 64.2, 58.9, 51.6, 41.7, 29.7, 26.1. IR (KBr) v 3245, 2931, 1721, 1606, 1551, 1156, 749 cm^{-1}. HRMS (ESI) calcd for $C_{36}H_{31}N_4O_5^+$ $[M+H]^+$ 599.2289, found 599.2283.



ethyl 1'',5-dimethyl-2,2''-dioxo-1-(phenylcarbamoyl)-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-2'-carboxylate (**4x**)

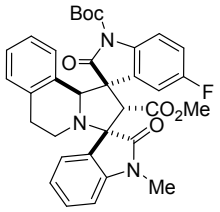
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 25:1 to 20:1); 87.8 mg, 72% yield; reaction time = 24 h; mp 166.4-168.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 10.53 (s, 1H), 8.46 (d, J = 8.0 Hz, 1H), 8.27 (d, J = 8.0 Hz, 1H), 7.56 (dd, $J_1 = J_2$ = 8.0 Hz, 3H), 7.46-7.33 (m, 5H), 7.18-7.04 (m, 4H), 6.91 (t, J = 8.0 Hz, 2H), 6.39 (d, J = 4.0 Hz, 1H), 5.87 (s, 1H), 4.29 (s, 1H), 3.58-3.49 (m, 2H), 3.35 (s, 3H), 3.15-3.07 (m, 1H), 2.68 (dd, J_1 = 8.0 Hz, J_2 = 16.0 Hz, 3H), 0.56 (t, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.7, 175.7, 167.2, 149.1, 145.0, 140.2, 137.1, 134.7, 134.6, 130.1, 129.8, 129.5, 129.2, 129.0, 126.8, 126.5, 126.2, 125.8, 125.5, 124.3, 124.2, 122.9, 122.8, 120.3, 116.3, 108.2, 70.2, 69.6, 64.1, 60.9, 58.9, 41.7, 29.7, 26.1, 13.1. IR (KBr) v 3257, 2927, 1721, 1607, 1549, 754 cm^{-1}. HRMS (ESI) calcd for $C_{37}H_{33}N_4O_5^+$ $[M+H]^+$ 613.2446, found 613.2447.



1-(*tert*-butyl) 2'-ethyl 1''-methyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4y**)

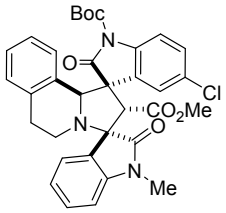
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 20:1 to 15:1);

74.4 mg, 63% yield; reaction time = 5 h; mp 148.9-150.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.19 (d, *J* = 8.0 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.35 (q, *J* = 8.0 Hz, 2H), 7.26 (t, *J* = 8.0 Hz, 1H), 7.15-7.09 (m, 1H), 7.03-7.02 (m, 2H), 6.87 (t, *J* = 8.0 Hz, 2H), 6.39 (d, *J* = 8.0 Hz, 1H), 5.74 (s, 1H), 4.32 (s, 1H), 3.51-3.48 (m, 2H), 3.32 (s, 3H), 3.09-3.04 (m, 1H), 2.71-2.56 (m, 3H), 1.56 (s, 9H), 0.54 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 176.0, 167.7, 149.2, 145.0, 139.8, 135.0, 134.7, 130.1, 129.9, 129.3, 128.7, 126.8, 126.5, 125.6 (2C), 125.3, 124.6, 123.1, 122.8, 114.7, 108.0, 84.1, 70.3, 70.1, 63.9, 60.6, 58.4, 41.7, 29.7, 28.0, 26.0, 13.1. IR (KBr) *v* 2980, 2934, 1724, 1473, 1296, 1155, 755 cm^{-1}. HRMS (ESI) calcd for $C_{35}H_{36}N_3O_6^+$ $[M+H]^+$ 594.2599, found 594.2593.



1-(*tert*-butyl) 2'-methyl 5-fluoro-1''-methyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4z**)

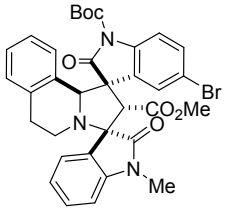
White solid obtained by column chromatography (petroleum ether/ethyl acetate = 25:1 to 20:1); 62.9 mg, 53% yield; reaction time = 24 h; mp 177.4-179.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.02 (d, *J* = 8.0 Hz, 1H), 7.96 (dd, $J_1 = J_2$ = 4.0 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.37 (t, *J* = 8.0 Hz, 1H), 7.13-7.03 (m, 4H), 6.88 (d, *J* = 8.0 Hz, 2H), 6.37 (d, *J* = 8.0 Hz, 1H), 5.70 (s, 1H), 4.31 (t, *J* = 8.0 Hz, 1H), 3.32 (s, 3H), 3.08-3.01 (m, 4H), 2.71-2.56 (m, 3H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 175.9, 168.0, 160.4 (d, *J* = 243.0 Hz, 1C), 149.2, 145.1, 135.6 (d, *J* = 3.0 Hz, 1C), 135.1, 134.4, 132.1 (d, *J* = 9.0 Hz, 1C), 130.1, 129.5, 126.7, 126.5, 125.7, 124.6, 123.0 (d, *J* = 12.0 Hz, 1C), 116.1 (d, *J* = 8.0 Hz, 1C), 115.5, 115.3, 113.1 (d, *J* = 25.0 Hz, 1C), 108.2, 84.4, 70.4, 70.2, 63.6, 58.7, 51.6, 41.7, 29.7, 28.1, 26.1. IR (KBr) *v* 3431, 2927, 1736, 1717, 1481, 1296, 1151, 753 cm^{-1}. HRMS (ESI) calcd for $C_{34}H_{33}FN_3O_6^+$ $[M+H]^+$ 598.2348, found 598.2349.



1-(*tert*-butyl) 2'-methyl 5-chloro-1''-methyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-

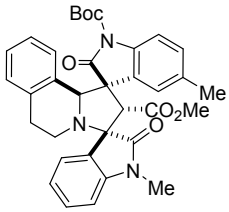
3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4aa**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 25:1 to 20:1); 41.1 mg, 34% yield; reaction time = 72 h; mp 138.2-140.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.22 (d, *J* = 4.0 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.38-7.35 (m, 2H), 7.11 (t, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.88 (d, *J* = 8.0 Hz, 2H), 6.36 (d, *J* = 8.0 Hz, 1H), 5.70 (s, 1H), 4.32 (s, 1H), 3.32 (s, 3H), 3.09-3.01 (m, 4H), 2.73-2.55 (m, 3H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.1, 175.7, 167.9, 149.0, 145.1, 138.2, 135.0, 134.3, 131.9, 130.7, 130.1, 129.4, 128.9, 126.7, 126.4, 125.6 (2C), 124.5, 122.9, 122.8, 116.0, 108.1, 84.5, 70.3, 70.1, 63.5, 58.4, 51.5, 41.6, 29.7, 28.0, 26.1. IR (KBr) *v* 3429, 2927, 1736, 1714, 1470, 1340, 1295, 1155, 752 cm^{-1}. HRMS (ESI) calcd for $C_{34}H_{33}ClN_3O_6^+$ $[M+H]^+$ 614.2052, found 614.2055.



1-(*tert*-butyl) 2'-methyl 5-bromo-1''-methyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-1,2'-dicarboxylate (**4ab**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 25:1 to 20:1); 55.2 mg, 42% yield; reaction time = 72 h; mp 162.2-163.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.35 (d, *J* = 4.0 Hz, 1H), 7.87 (d, *J* = 8.0 Hz, 1H), 7.54-7.51 (m, 2H), 7.36 (t, *J* = 8.0 Hz, 1H), 7.11 (t, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.88 (d, *J* = 8.0 Hz, 2H), 6.36 (d, *J* = 8.0 Hz, 1H), 5.69 (s, 1H), 4.31 (s, 1H), 3.32 (s, 3H), 3.09-3.00 (m, 4H), 2.72-2.55 (m, 3H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0, 175.7, 167.9, 149.0, 145.1, 138.8, 135.1, 134.3, 132.3, 131.9, 130.1, 129.4, 128.4, 126.7, 126.5, 125.6, 124.5, 123.0, 122.8, 118.2, 116.4, 108.1, 84.5, 70.3, 70.1, 63.5, 58.3, 51.6, 41.6, 29.7, 28.0, 26.1. IR (KBr) *v* 3440, 2941, 1738, 1713, 1469, 1339, 1295, 1155, 752 cm^{-1}. HRMS (ESI) calcd for $C_{34}H_{33}BrN_3O_6^+$ $[M+H]^+$ 658.1547, found 658.1541.

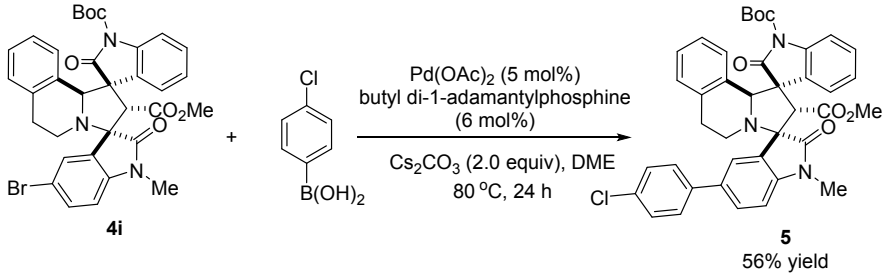


1-(*tert*-butyl) 2'-methyl 1'',5-dimethyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-

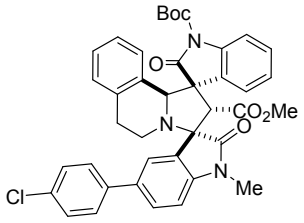
pyrrolo[2,1-*a*]isoquinoline-3',3"-indoline]-1,2'-dicarboxylate (**4ac**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 25:1 to 15:1); 70.8 mg, 60% yield; reaction time = 48 h; mp 139.5-141.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.94 (s, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 7.11 (t, *J* = 8.0 Hz, 1H), 7.01 (s, 2H), 6.86 (d, *J* = 4.0 Hz, 2H), 6.40 (d, *J* = 8.0 Hz, 1H), 5.71 (s, 1H), 4.33 (s, 1H), 3.32 (s, 3H), 3.09-3.02 (m, 4H), 2.71-2.55 (m, 3H), 2.40 (s, 3H), 1.55 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 175.8, 168.3, 149.2, 145.0, 137.2, 134.9, 134.8, 134.7, 129.9 (2C), 129.3, 129.2, 126.7, 126.4, 125.6, 125.5, 124.6, 123.1, 122.7, 114.5, 107.9, 83.9, 70.2, 69.9, 63.7, 58.4, 51.3, 41.6, 29.7, 28.0, 26.0, 21.3. IR (KBr) *v* 3419, 2940, 1720, 1486, 1341, 1295, 1156, 753 cm^{-1}. HRMS (ESI) calcd for $C_{35}H_{36}N_3O_6^+$ $[M+H]^+$ 594.2599, found 594.2598.

4. Experimental data for derivations of 4i and 4y

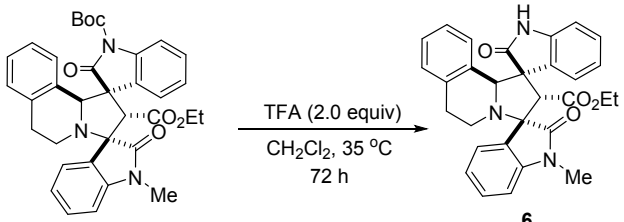


General procedure：Under nitrogen atmosphere, compound **4i** (131.7 mg, 0.20 mmol), 4-chlorophenyl boronic acid (1.5 equiv), Cs_2CO_3 (2.0 equiv), $Pd(OAc)_2$ (0.05 equiv) and butyl di-1-adamantylphosphine (0.06 equiv) were successively added to a 15 mL dried tube, followed by adding 2.0 mL DME. The resulting mixture was stirred at 80 °C for 24 h till almost full consumption of **4i** monitored by thin layer chromatography, and then the reaction mixture was directly subjected to flash column chromatography on silica gel (petroleum ether/ ethyl acetate) to afford the corresponding product **5**.

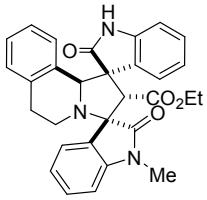


1-(*tert*-butyl) 2'-methyl 5"-(4-chlorophenyl)-1"-methyl-2,2"-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3"-indoline]-1,2'-dicarboxylate (**5**)

White solid obtained by column chromatography (petroleum ether/ethyl acetate = 18:1 to 15:1); 77.7 mg, 56% yield; reaction time = 24 h; mp 145.8-146.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.15 (d, *J* = 8.0 Hz, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.73 (d, *J* = 4.0 Hz, 1H), 7.58-7.51 (m, 3H), 7.39-7.33 (m, 3H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.05-7.03 (m, 2H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.91-6.87 (m, 1H), 6.42 (d, *J* = 8.0 Hz, 1H), 5.76 (s, 1H), 4.38 (s, 1H), 3.36 (s, 3H), 3.14-3.03 (m, 1H), 3.01 (s, 3H), 2.82-2.57 (m, 3H), 1.56 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 176.0, 168.3, 149.2, 144.6, 139.6, 138.7, 135.0, 134.9, 134.7, 133.1, 129.9, 129.4, 128.9, 128.8, 128.6, 128.1, 127.6, 126.6, 125.6, 125.3 (2C), 123.1, 123.0, 114.8, 108.4, 84.3, 70.5, 70.1, 64.1, 58.4, 51.4, 41.8, 29.7, 28.0, 26.2. IR (KBr) *v* 3425, 2929, 1719, 1482, 1153, 741 cm^{-1}. HRMS (ESI) calcd for $C_{40}H_{37}ClN_3O_6^+$ $[M+H]^+$ 690.2365, found 690.2367.



General procedure： To a 5.0 mL vial were successively added **4y** (75.6 mg, 0.13 mmol), TFA (29.6 mg, 0.26 mmol) and 1.0 mL CH_2Cl_2. The resulting mixture was stirred at 35 °C for 72 h, and then the reaction mixture was directly subjected to flash column chromatography on silica gel (petroleum ether/ ethyl acetate) to afford the corresponding products **6**.

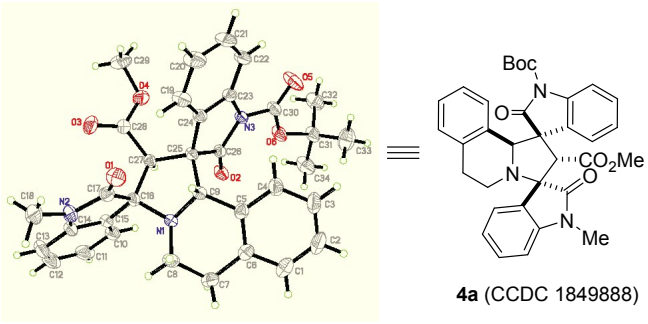


ethyl 1''-methyl-2,2''-dioxo-6',10b'-dihydro-2'*H*,5'*H*-dispiro[indoline-3,1'-pyrrolo[2,1-*a*]isoquinoline-3',3''-indoline]-2'-carboxylate (**6**)

Light yellow solid obtained by column chromatography (petroleum ether/ethyl acetate = 8:1 to 6:1); 44.9 mg, 70% yield; reaction time = 72 h; mp 131.9-133.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$), δ 8.12 (d, *J* = 4.0 Hz, 1H), 8.08 (s, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 1H), 7.26 (t, *J* = 8.0 Hz, 1H), 7.11 (t, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.90-6.84 (m, 3H), 6.45 (d, *J* = 8.0 Hz, 1H), 5.77 (s, 1H), 4.27 (s, 1H), 3.53-3.49 (m, 2H), 3.32 (s, 3H), 3.13-3.05 (m, 1H), 2.73-2.59 (m, 3H), 1.74-1.68 (m, 1H), 0.54 (t, *J* = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.2,

176.1, 168.0, 145.0, 140.9, 135.3, 134.8, 131.6, 129.9, 129.1, 128.5, 126.8, 126.5, 126.3, 125.7, 124.6, 123.4, 122.8, 109.4, 108.0, one carbon missing in the aromatic region, 70.5, 68.6, 63.2, 60.5, 58.0, 41.9, 29.8, 26.0, 13.1. IR (KBr) *v* 3277, 2927, 1723, 1471, 752 cm^{-1}. HRMS (ESI) calcd for $C_{30}H_{28}N_3O_4^+$ $[M+H]^+$ 494.2074, found 494.2073.

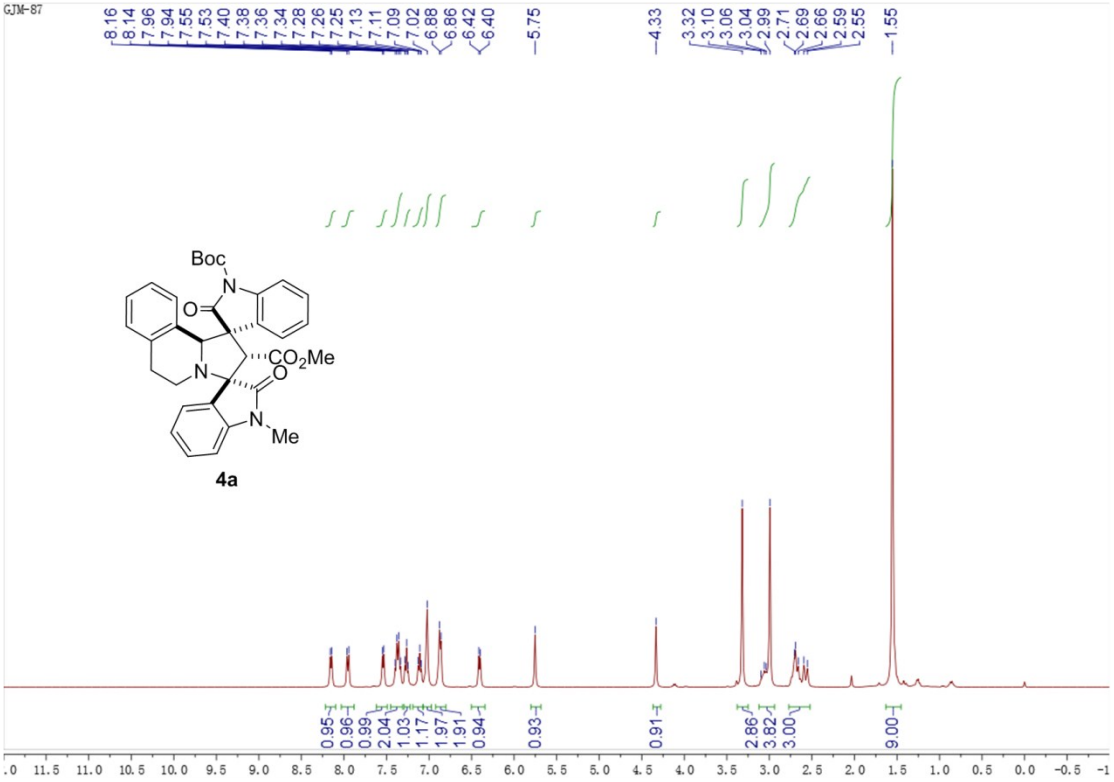
5. Crystal structure of 4a

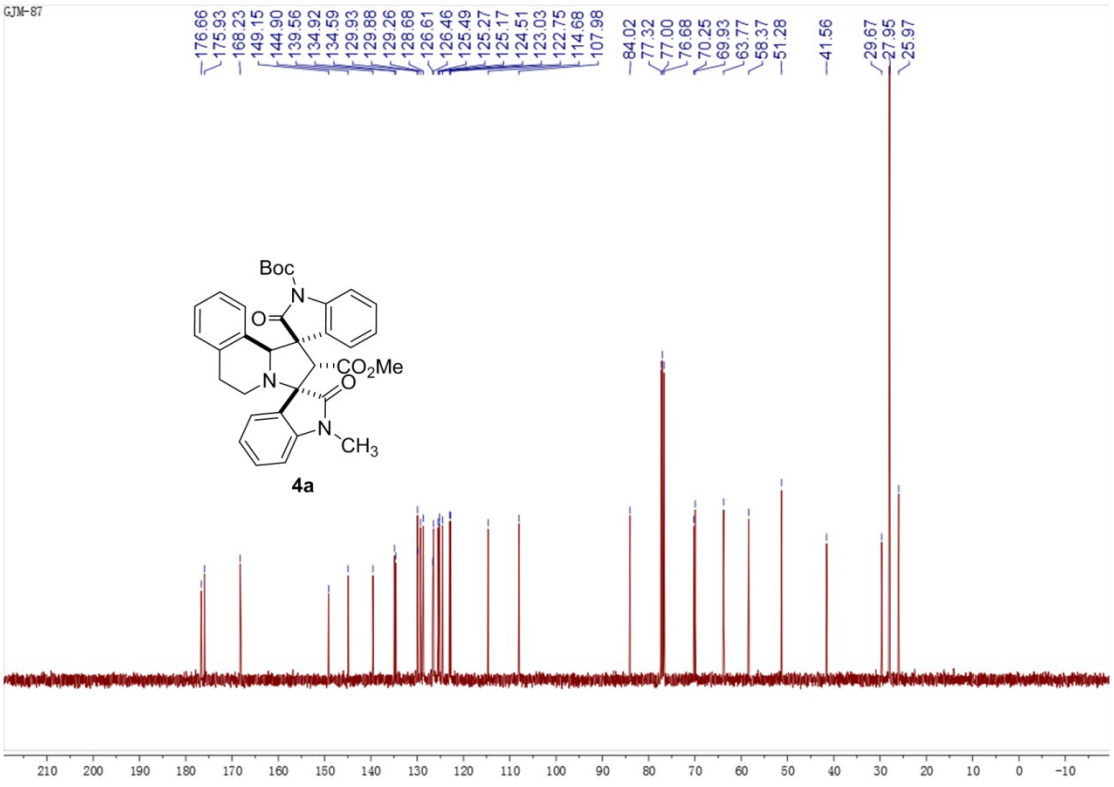


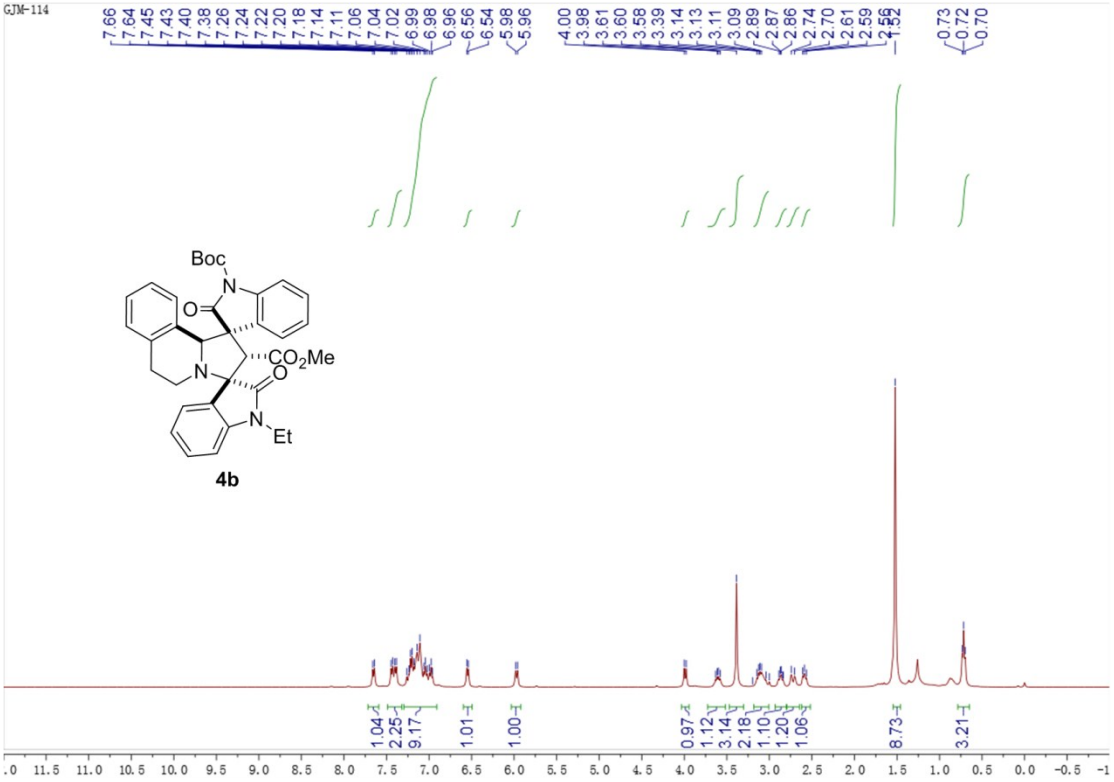
4a (CCDC 1849888)

Displacement ellipsoids are drawn at the 30% probability level.

6. ^{1}H NMR and ^{13}C NMR spectra



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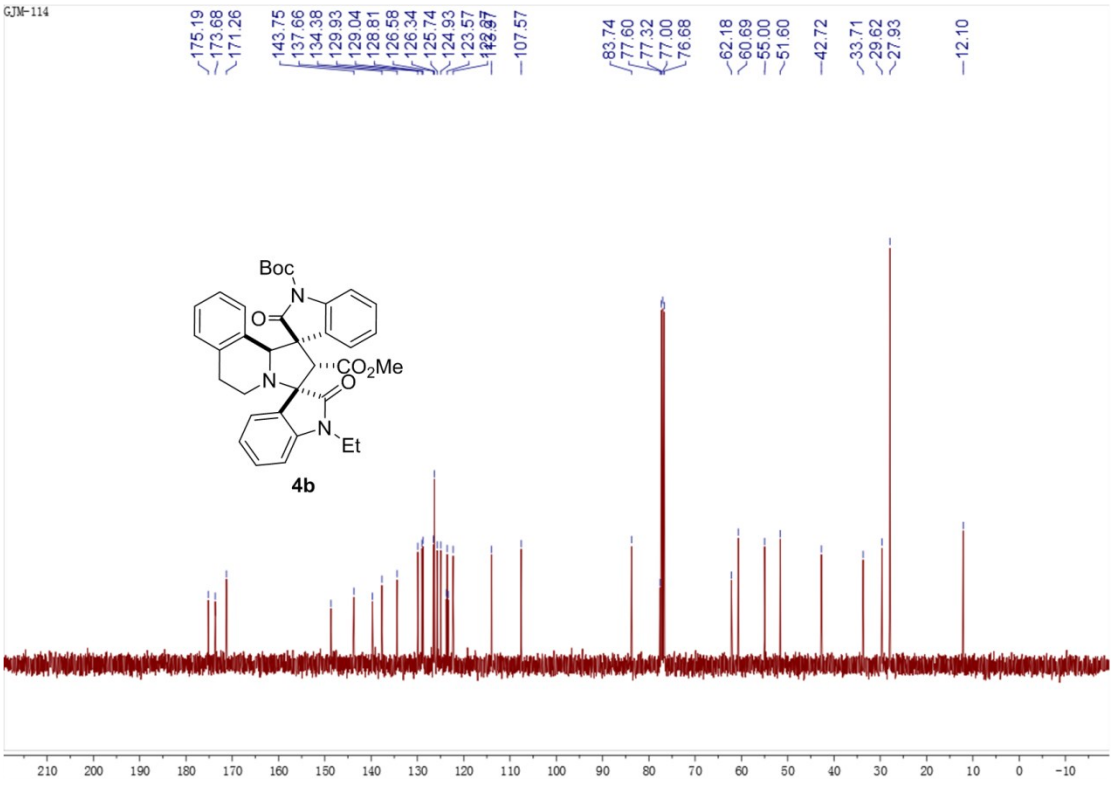
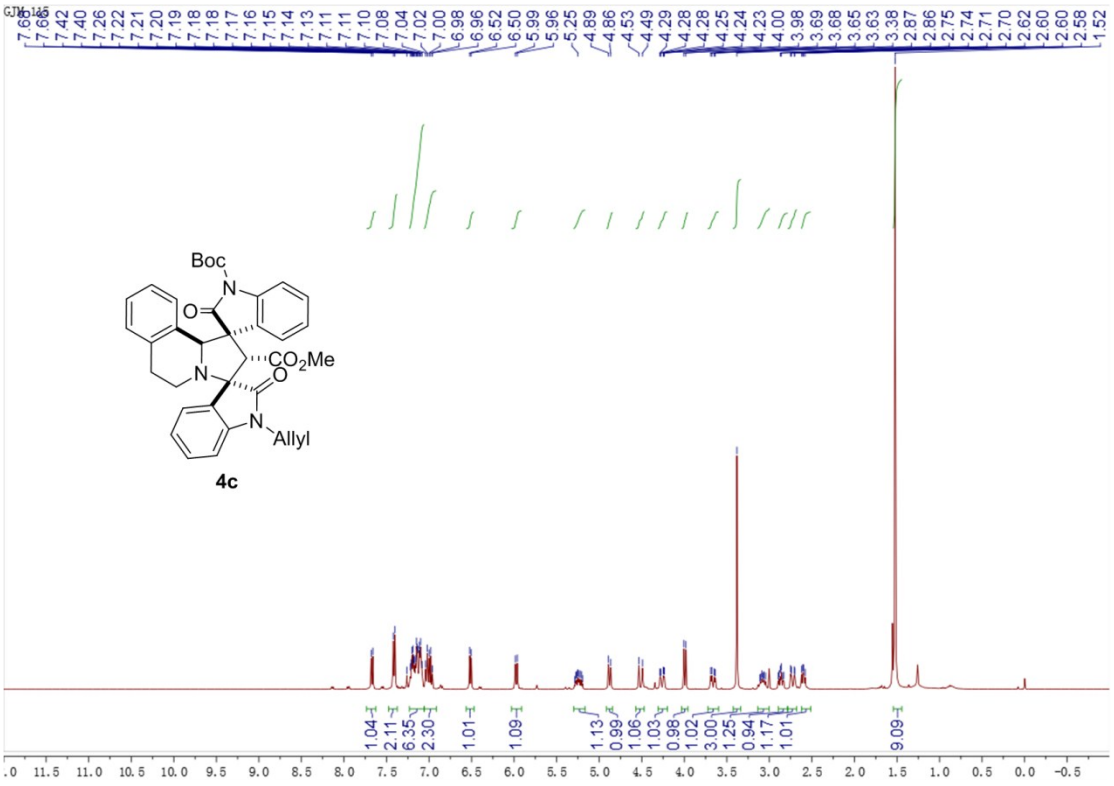
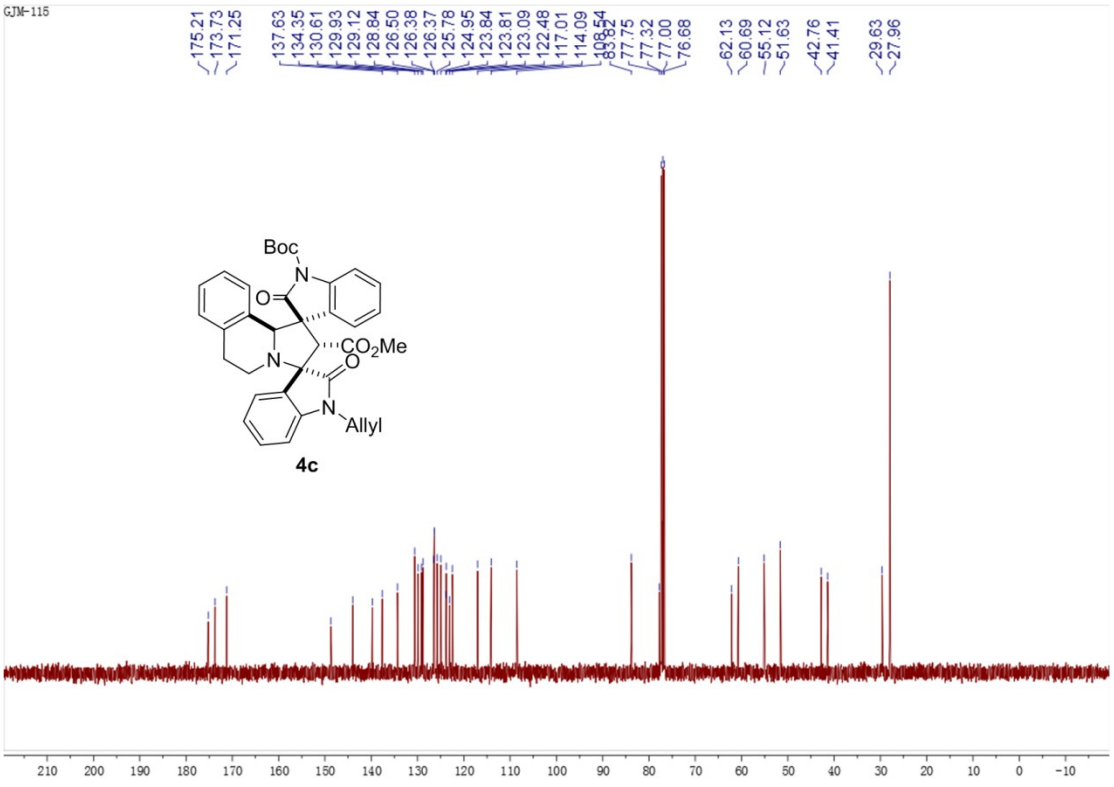
Boc
N
O
CO2Me
O
N
N
Et
4b

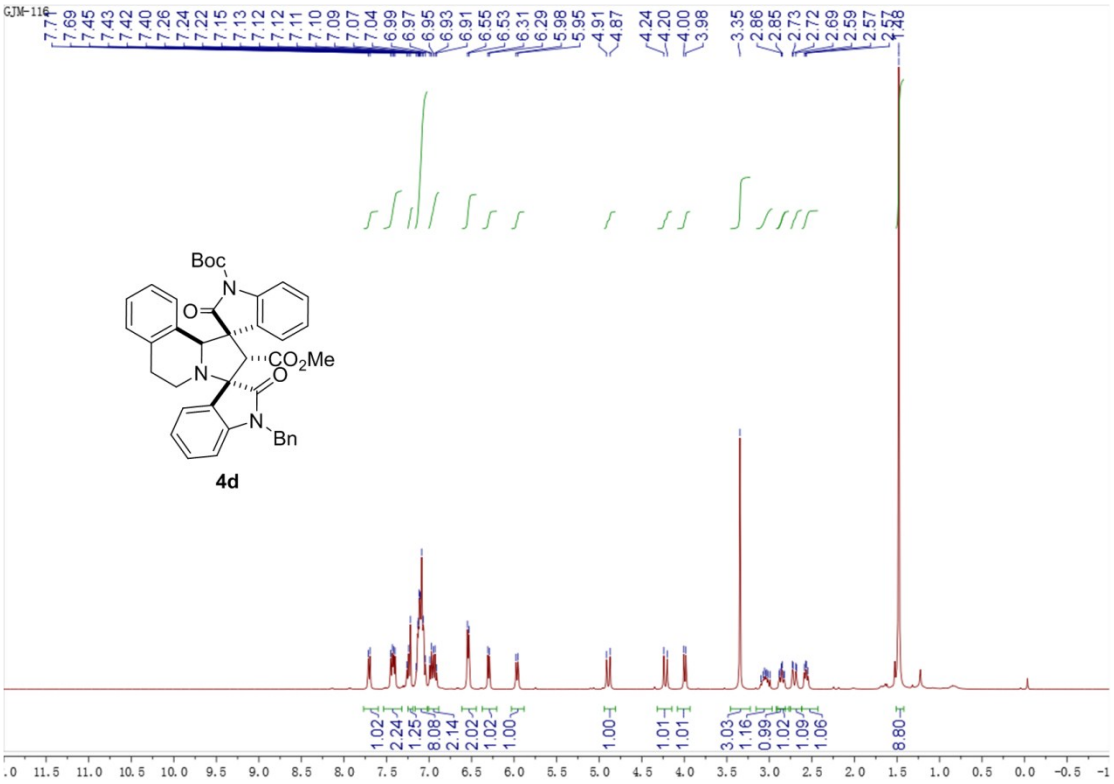

GJM-114
Boc
N
O
CO2Me
O
N
N
Et
4b



4c



4c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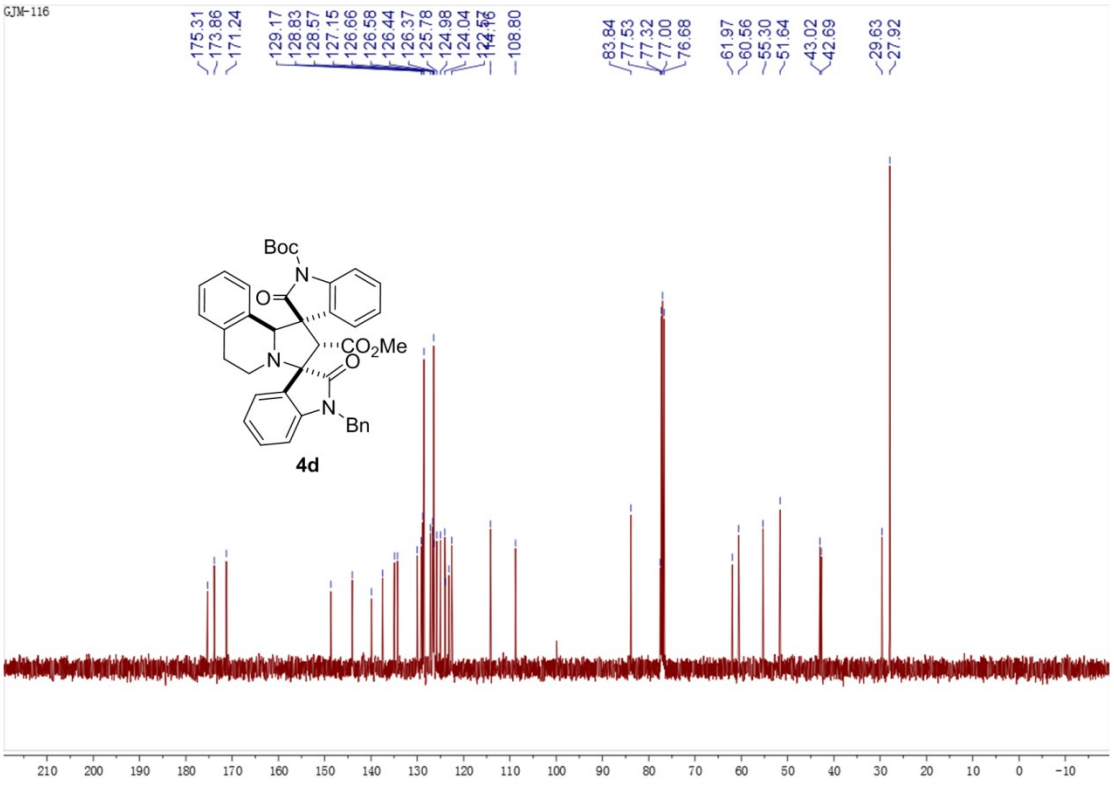
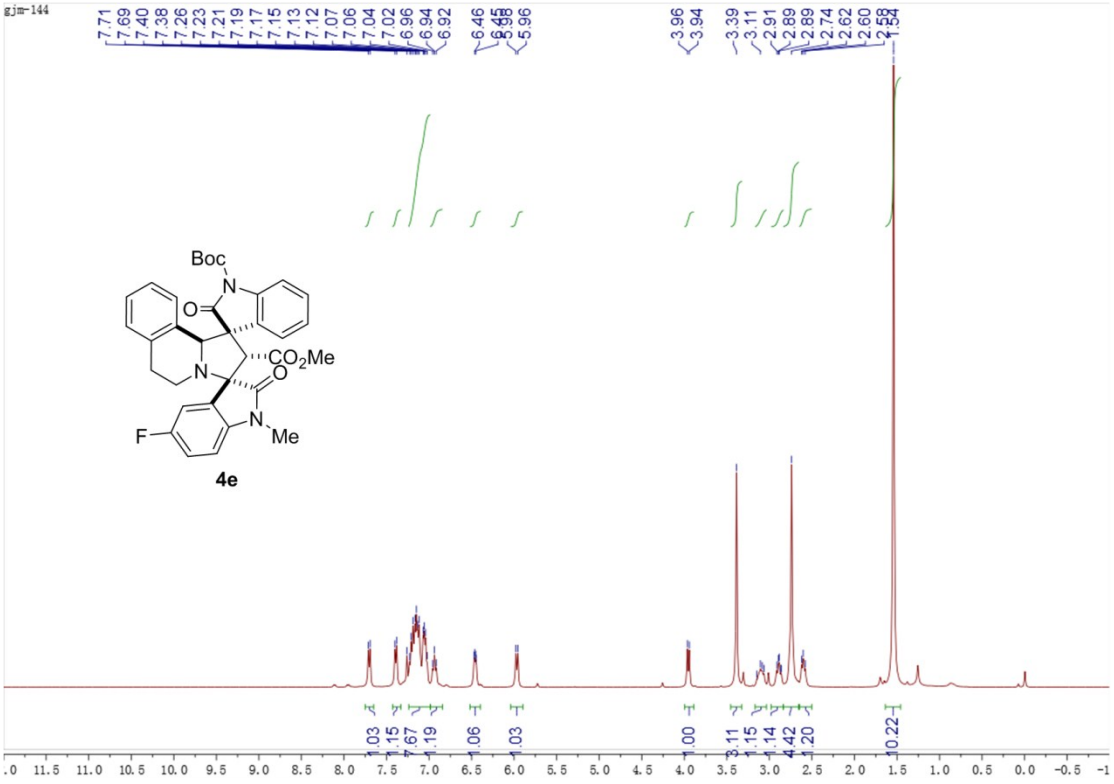
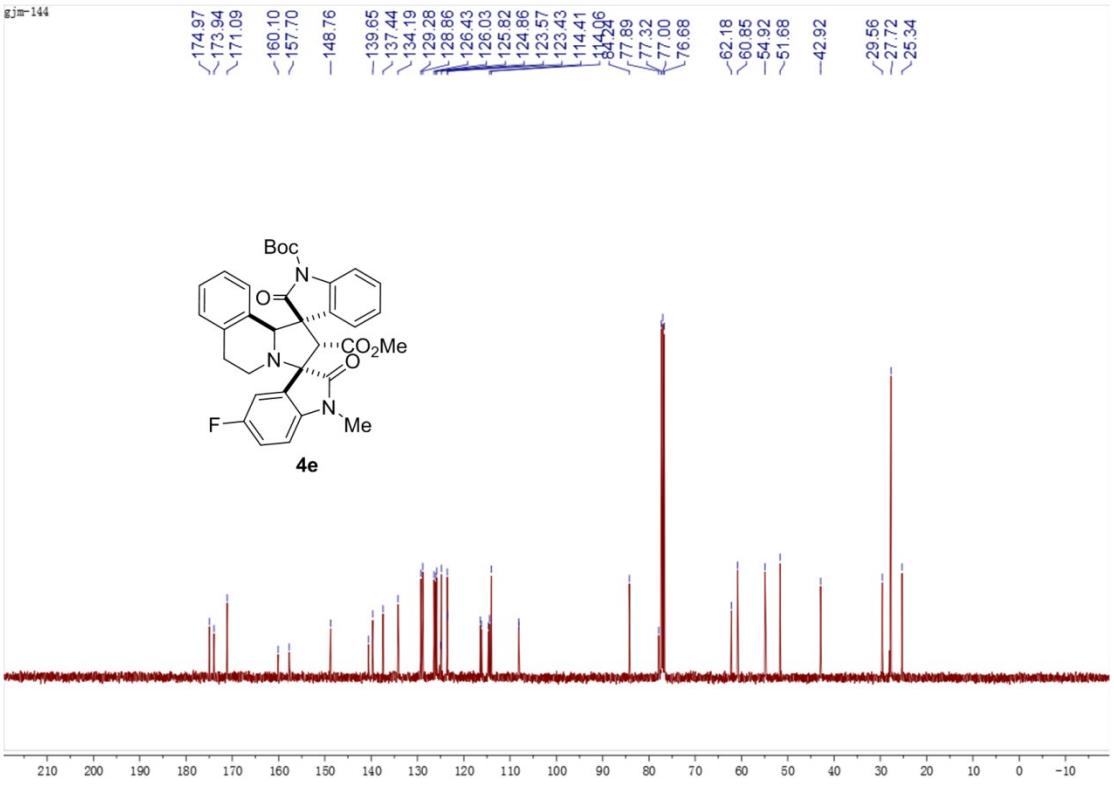
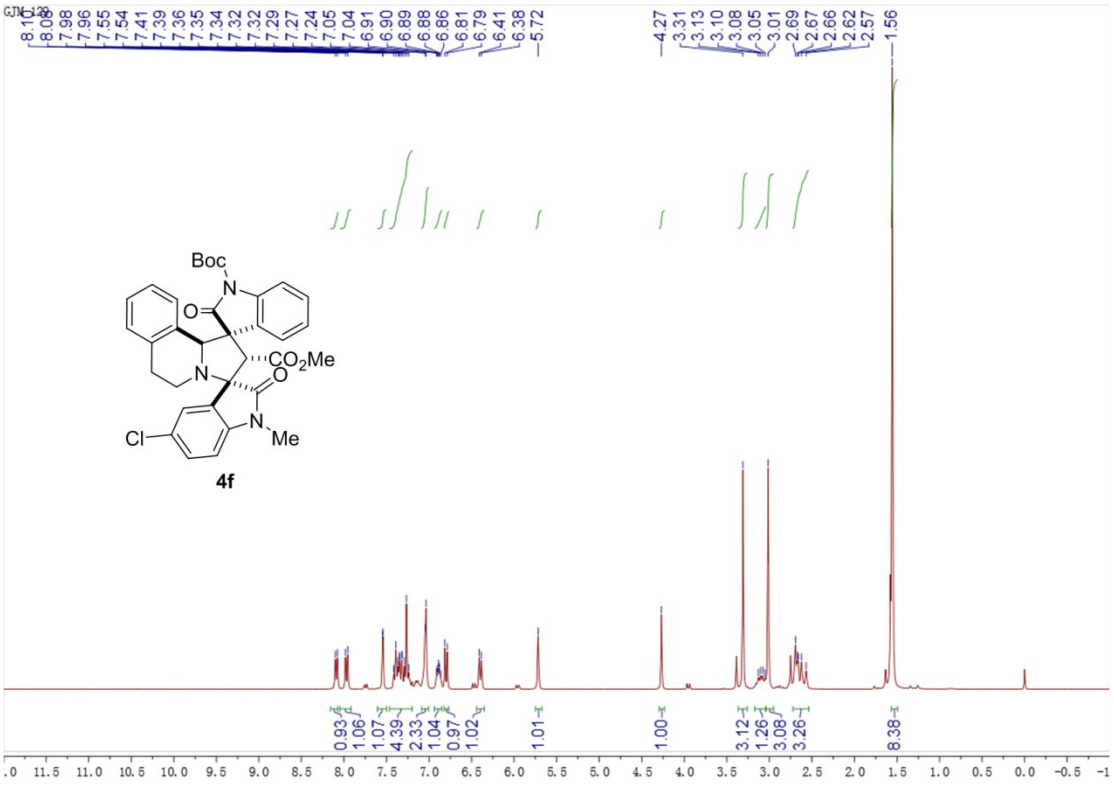
N
O
CO2Me
O
N
N
Bn
4d

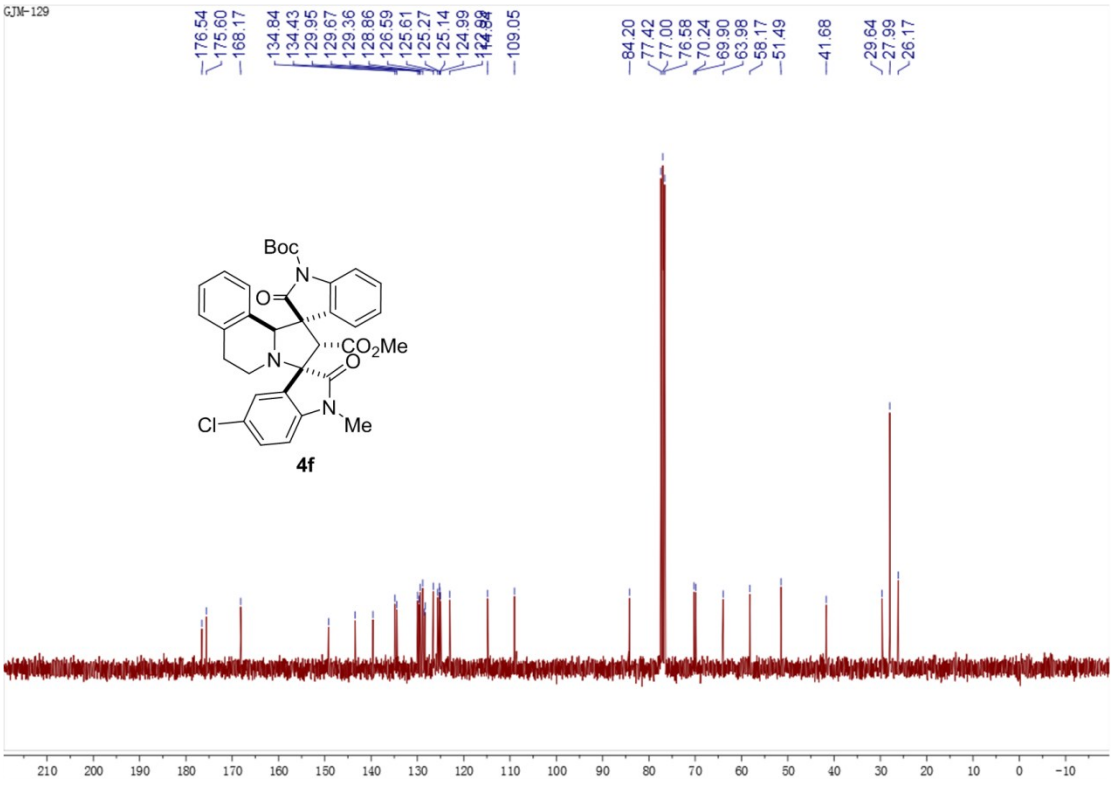

GJM-116
Boc
N
O
CO2Me
O
N
N
Bn
4d


gjm-144
Boc
CO2Me
F
Me
4e


gjm-144
Boc
CO2Me
F
Me
4e



4f



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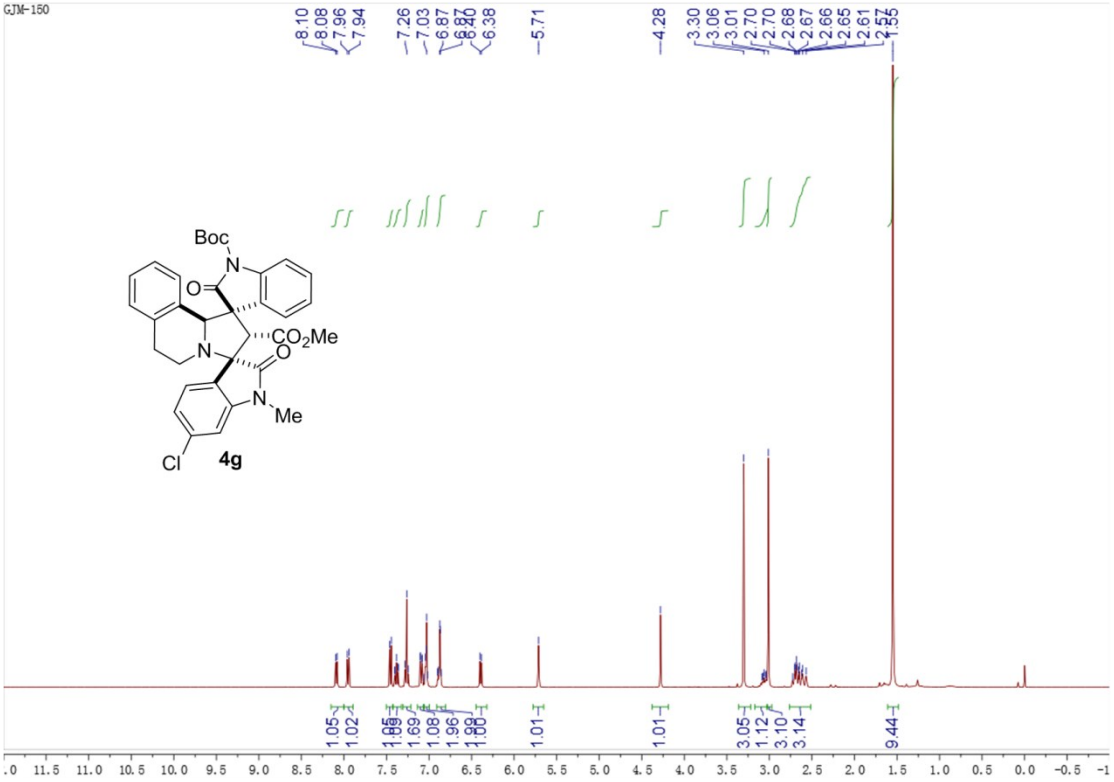
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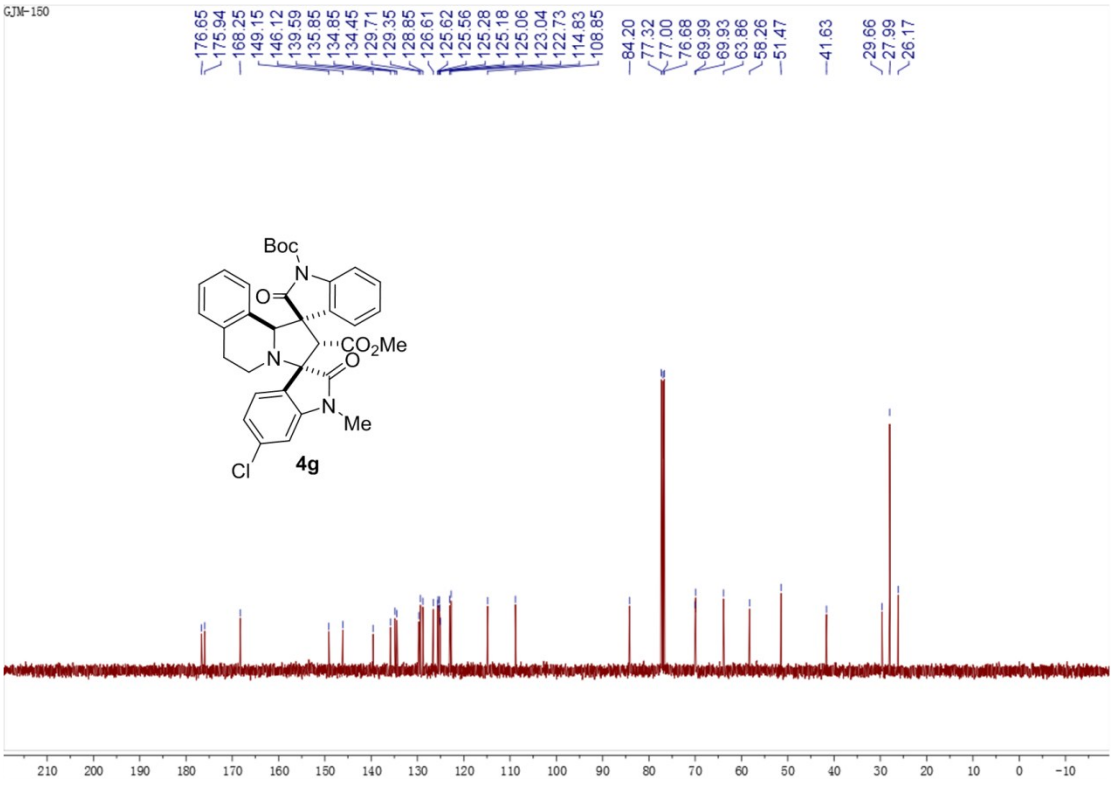
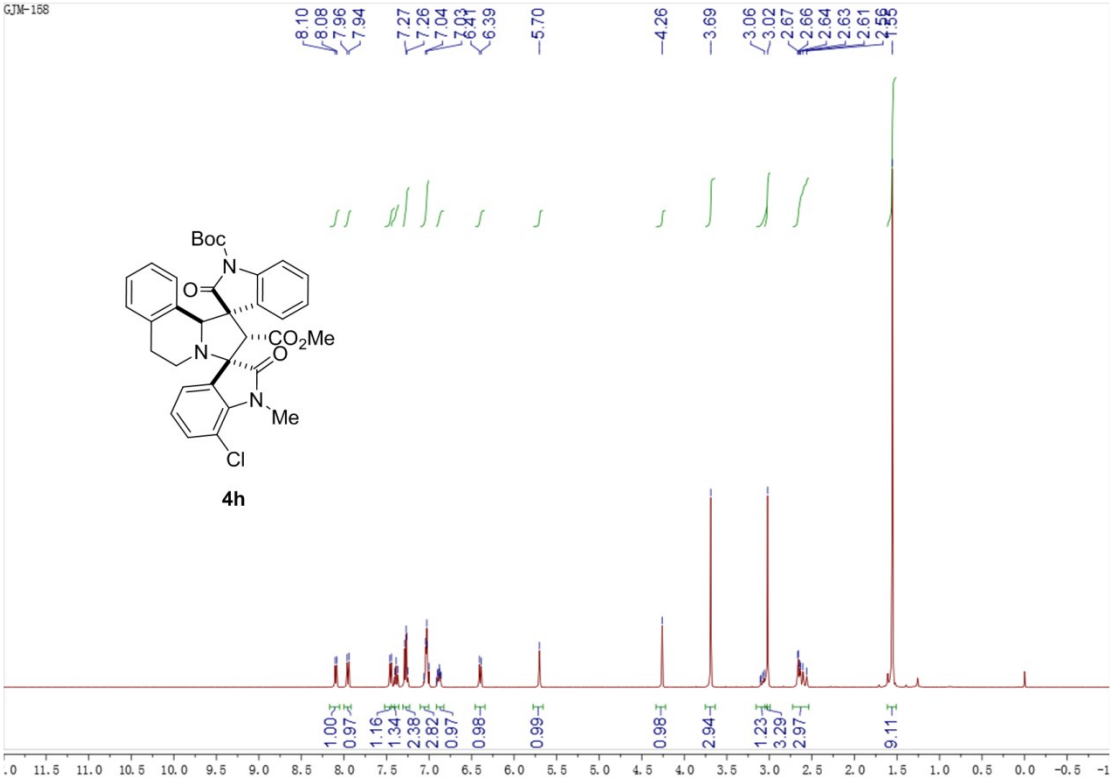
N
O
CO2Me
O
N
N
Me
Cl
4g


GJM-150
Boc
N
O
CO2Me
O
N
N
Me
Cl
4g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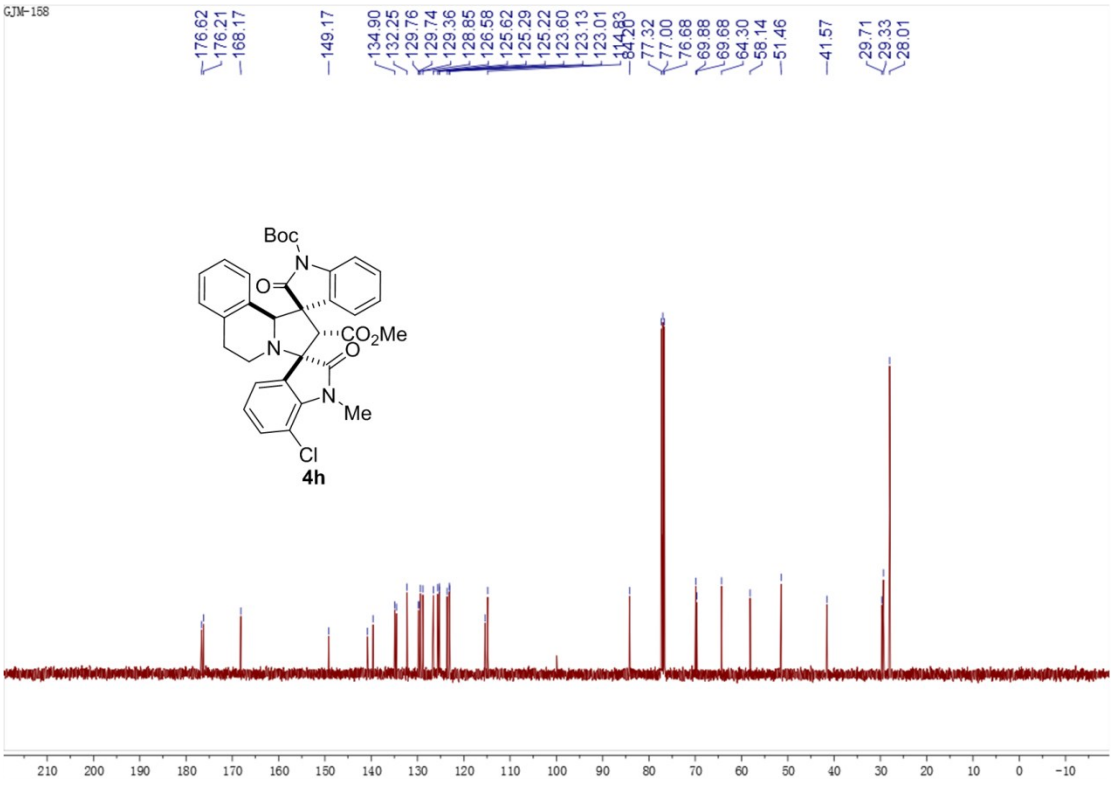
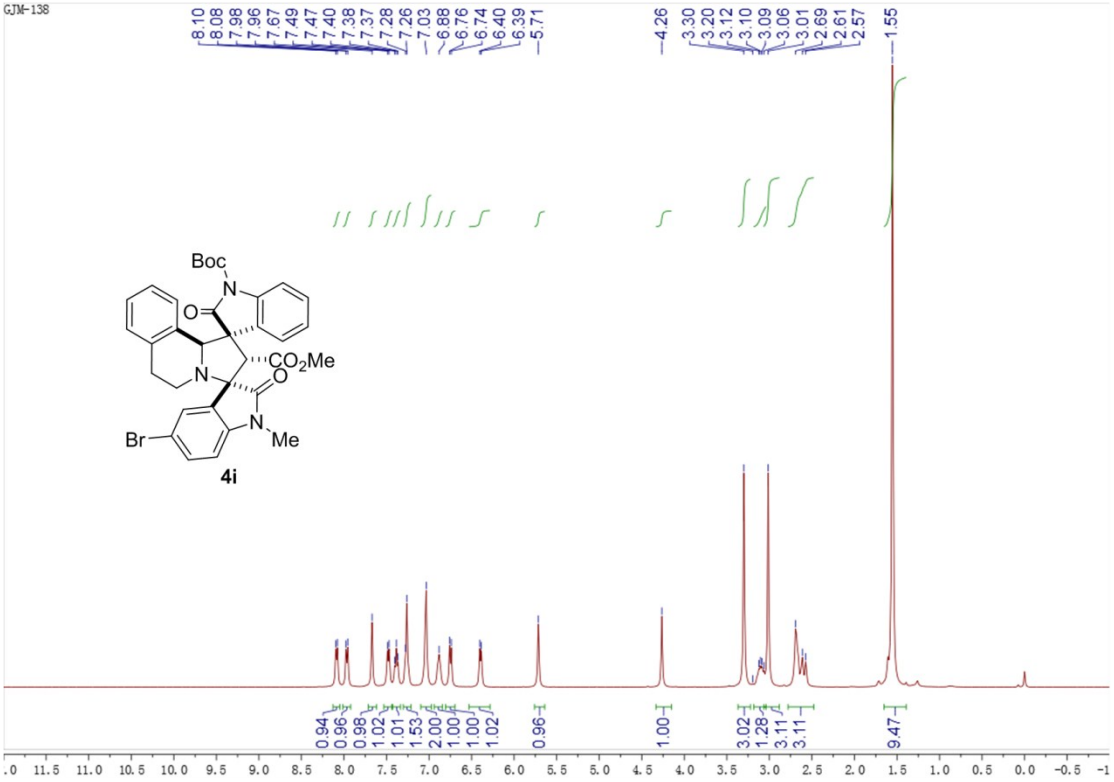
O
CO2Me
O
N
N
Me
Cl
4h


GJM-158
Boc
N
O
CO2Me
O
N
N
Me
Cl
4h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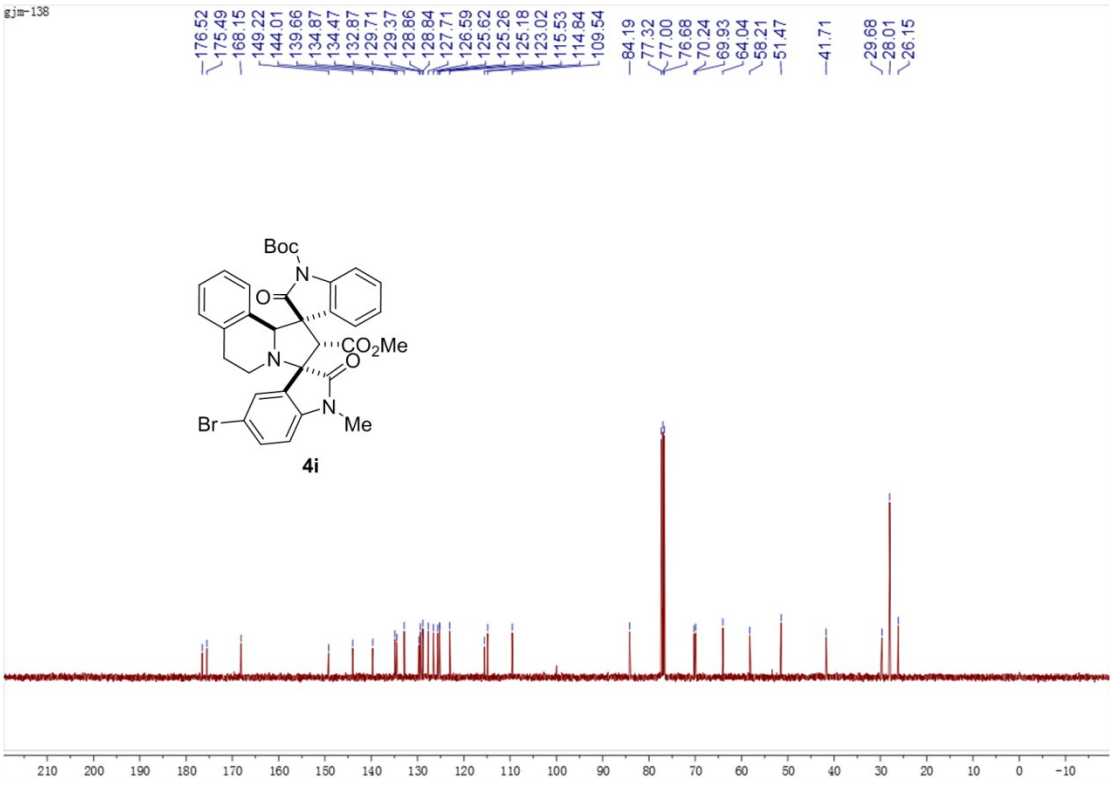
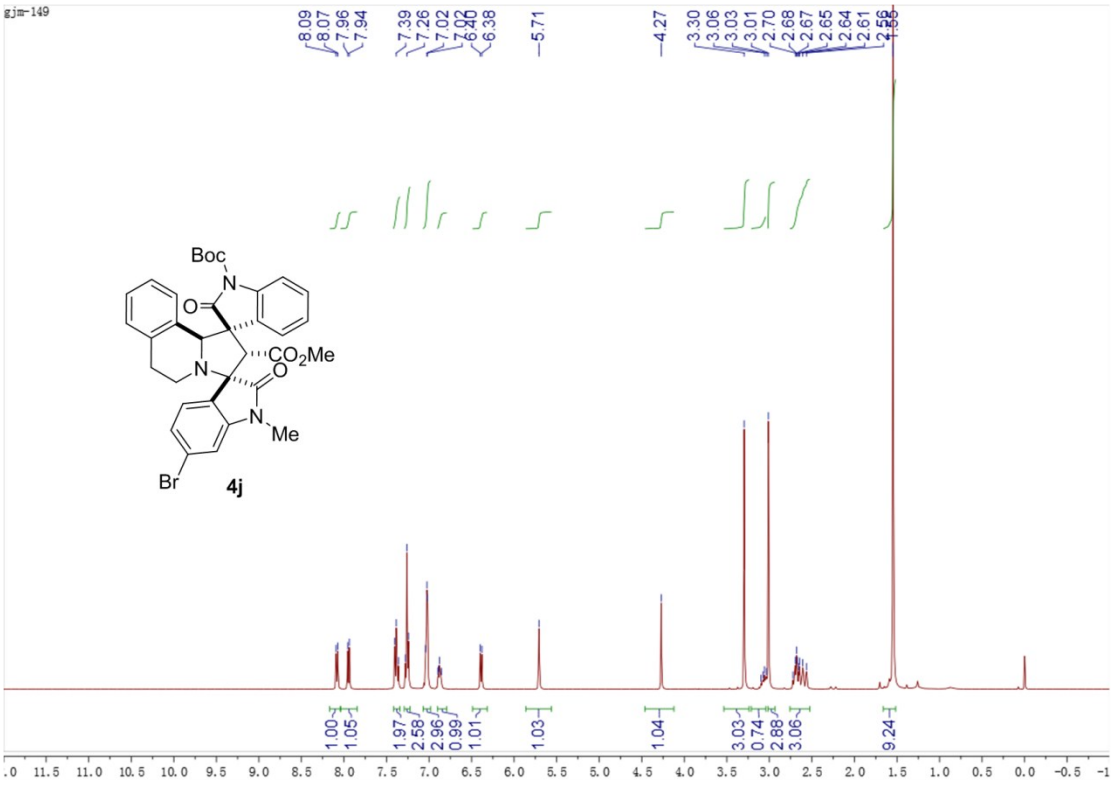
8.08
7.98
7.96
7.67
7.49
7.47
7.40
7.38
7.37
7.28
7.26
7.03
6.88
6.76
6.74
6.40
6.39
5.71
4.26
3.30
3.20
3.12
3.10
3.09
3.06
3.01
2.69
2.61
2.57
1.55
Boc
N
O
CO2Me
N
O
N
Me
Br
4i
0.94
0.96
0.98
1.02
1.01
1.53
2.00
1.00
1.00
1.02
0.96
1.00
3.02
1.28
3.11
3.11
9.47


gjm-138
176.52
175.49
168.15
149.22
144.01
139.66
134.87
134.47
132.87
129.71
129.37
128.86
128.84
127.71
126.59
125.62
125.26
125.18
123.02
115.53
114.84
109.54
84.19
77.32
77.00
76.68
70.24
69.93
64.04
58.21
51.47
41.71
29.68
28.01
26.15
Boc
N
O
CO2Me
N
O
N
Me
Br
4i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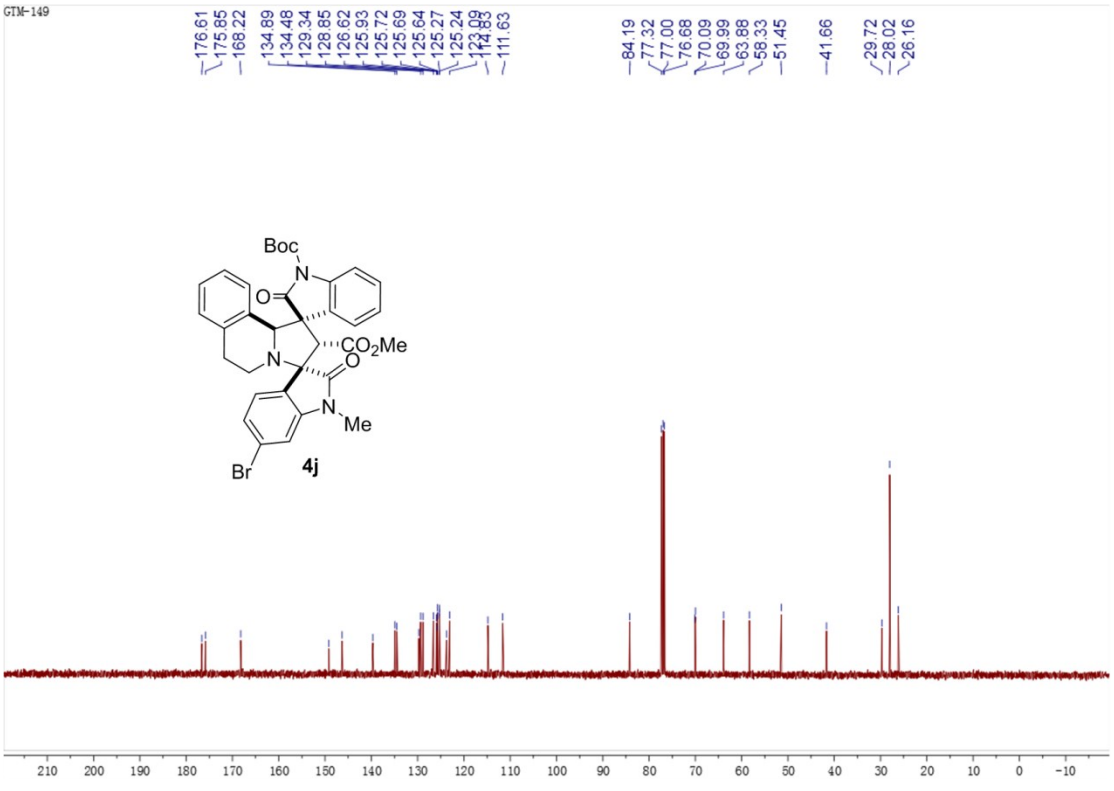
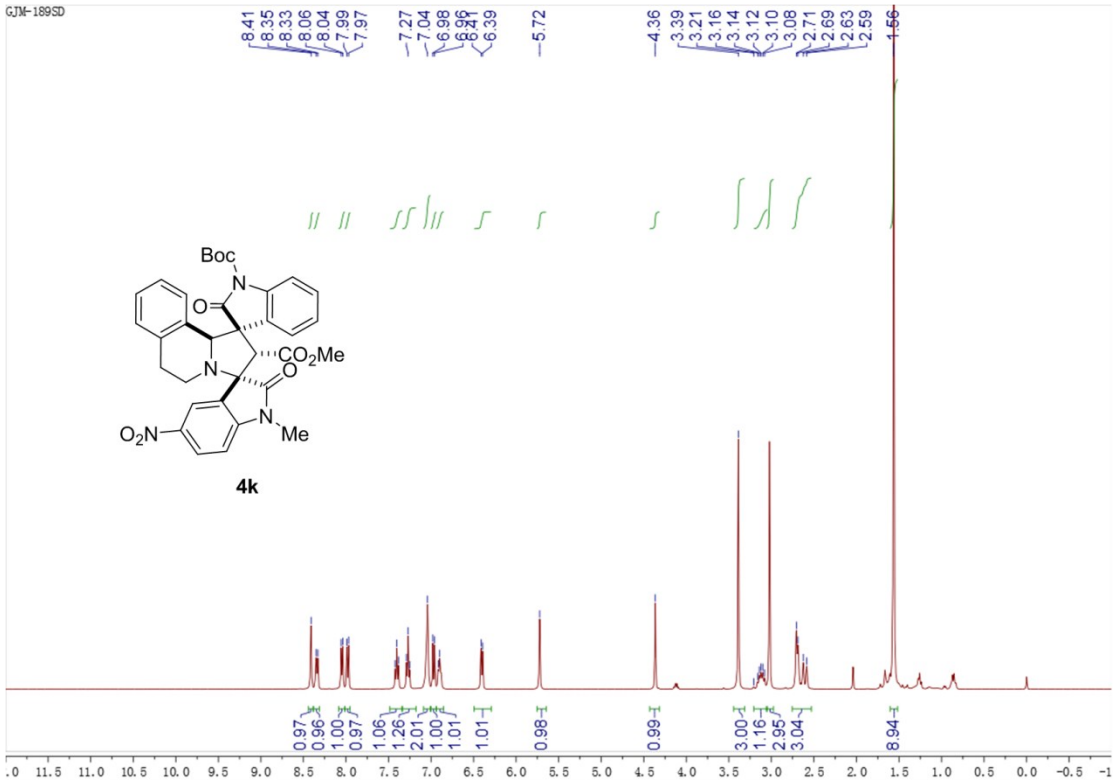
Boc
CO2Me
Me
Br
4j


GTM-149
Boc
CO2Me
Me
Br
4j


GJM-189SD
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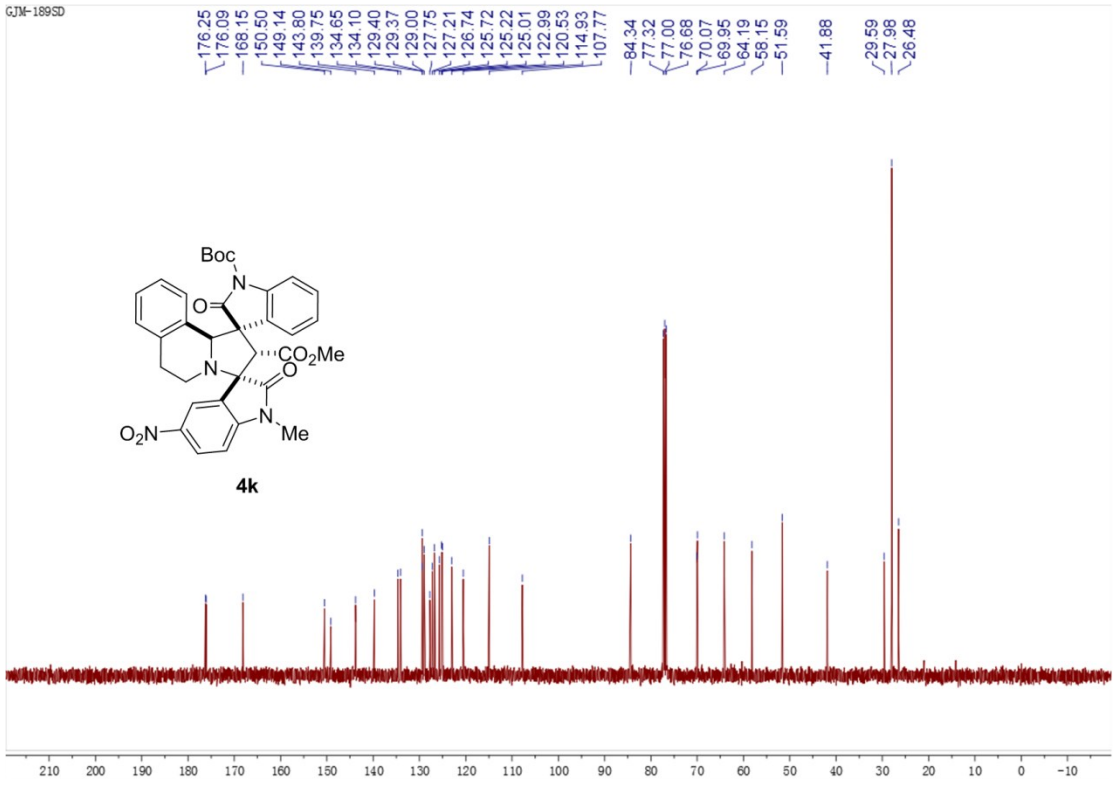
8.33
8.06
8.04
7.99
7.97
7.27
7.04
6.98
6.96
6.91
6.39
5.72
4.36
3.39
3.21
3.16
3.14
3.12
3.10
3.08
2.71
2.69
2.63
2.59
1.56
Boc
N
O
CO2Me
N
O
N
Me
O2N
4k
0.97
0.96
1.00
0.97
1.06
1.26
2.01
1.00
1.01
1.01
0.98
0.99
3.00
1.16
2.95
3.04
8.94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139.75
134.65
134.10
129.40
129.37
129.00
127.75
127.21
126.74
125.72
125.22
125.01
122.99
120.53
114.93
107.77
84.34
77.32
77.00
76.68
70.07
69.95
64.19
58.15
51.59
41.88
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27.98
26.48
Boc
N
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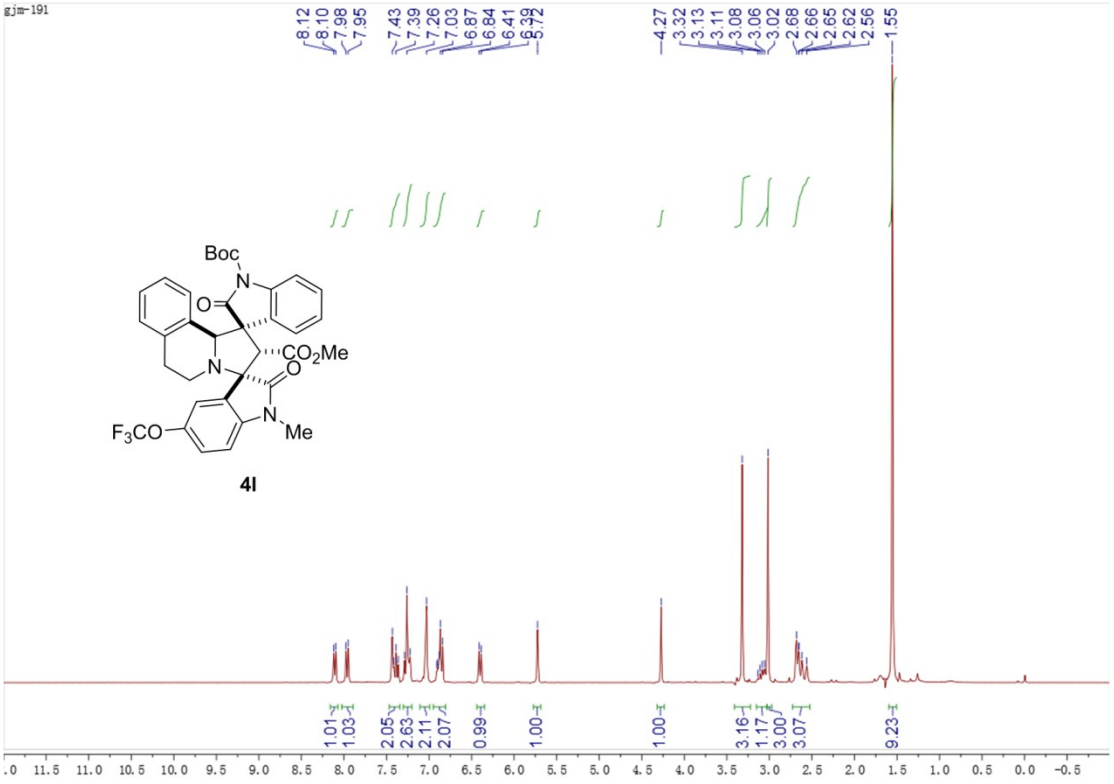
CO2Me
N
O
N
Me
O2N
4k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6.39
5.72
4.27
3.32
3.13
3.11
3.08
3.06
3.02
2.68
2.66
2.65
2.62
2.56
1.55
Boc
N
O
CO2Me
N
O
F3CO
N
Me
1.01
1.03
2.05
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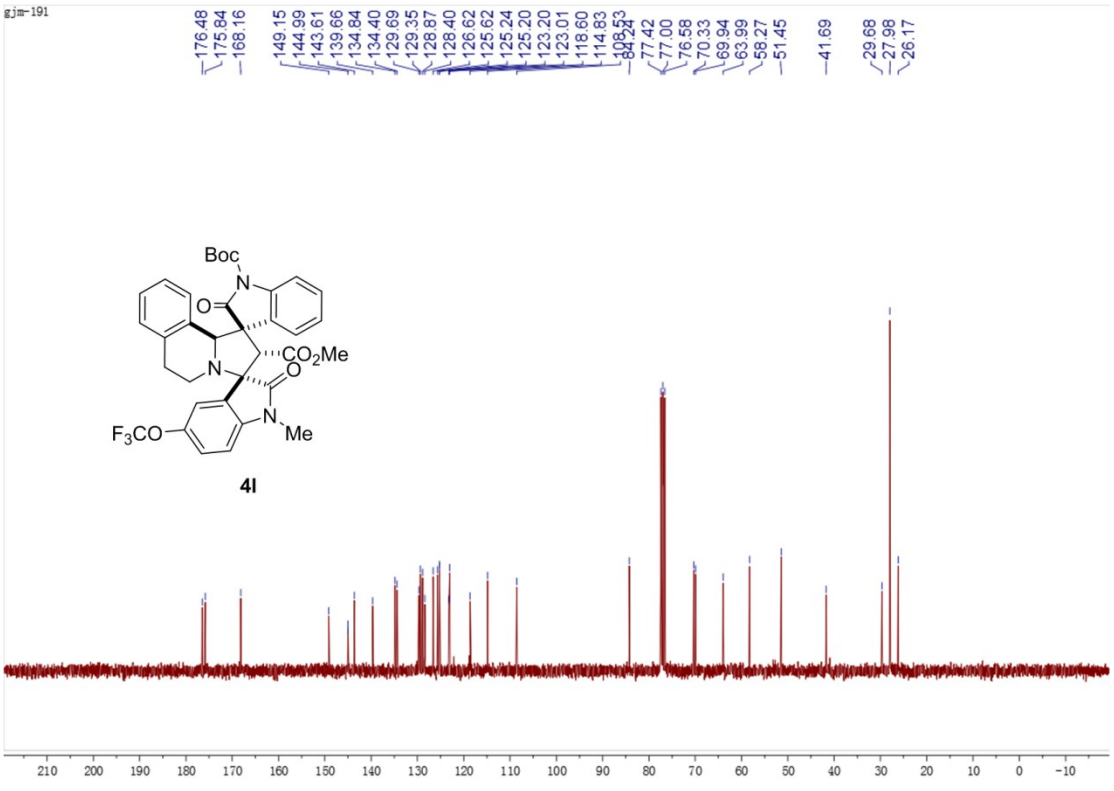
2.11
2.07
0.99
1.00
1.00
3.16
1.17
3.00
3.07
9.23

4l


gjm-191
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175.84
168.16
149.15
144.99
143.61
139.66
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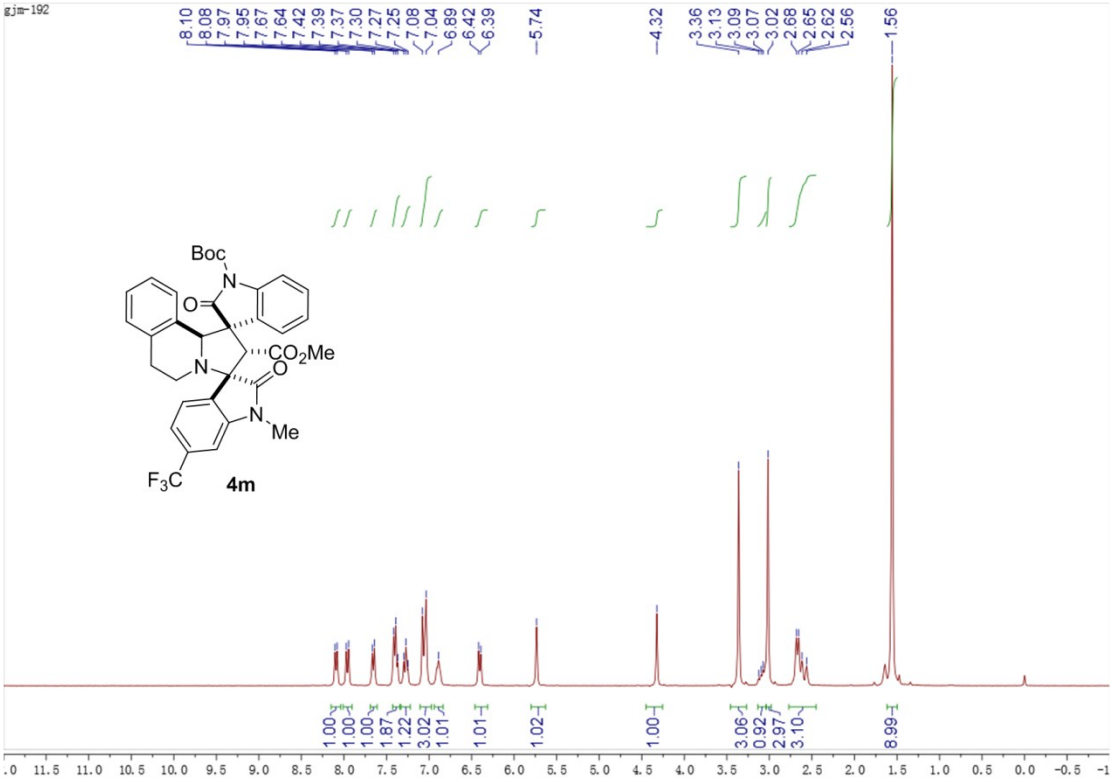
134.40
129.69
129.35
128.87
128.40
126.62
125.62
125.24
125.20
123.20
123.01
118.60
114.83
77.42
77.00
76.58
70.33
69.94
63.99
58.27
51.45
41.69
29.68
27.98
26.17
Boc
N
O
CO2Me
N
O
F3CO
N
Me

4l


gjm-192
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8.08
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7.37
7.30
7.27
7.25
7.08
7.04
6.89
6.42
6.39
5.74
4.32
3.36
3.13
3.09
3.07
3.02
2.68
2.65
2.62
2.56
1.56
Boc
N
O
CO2Me
O
N
N
Me
F3C
4m
1.00
1.00
1.00
1.87
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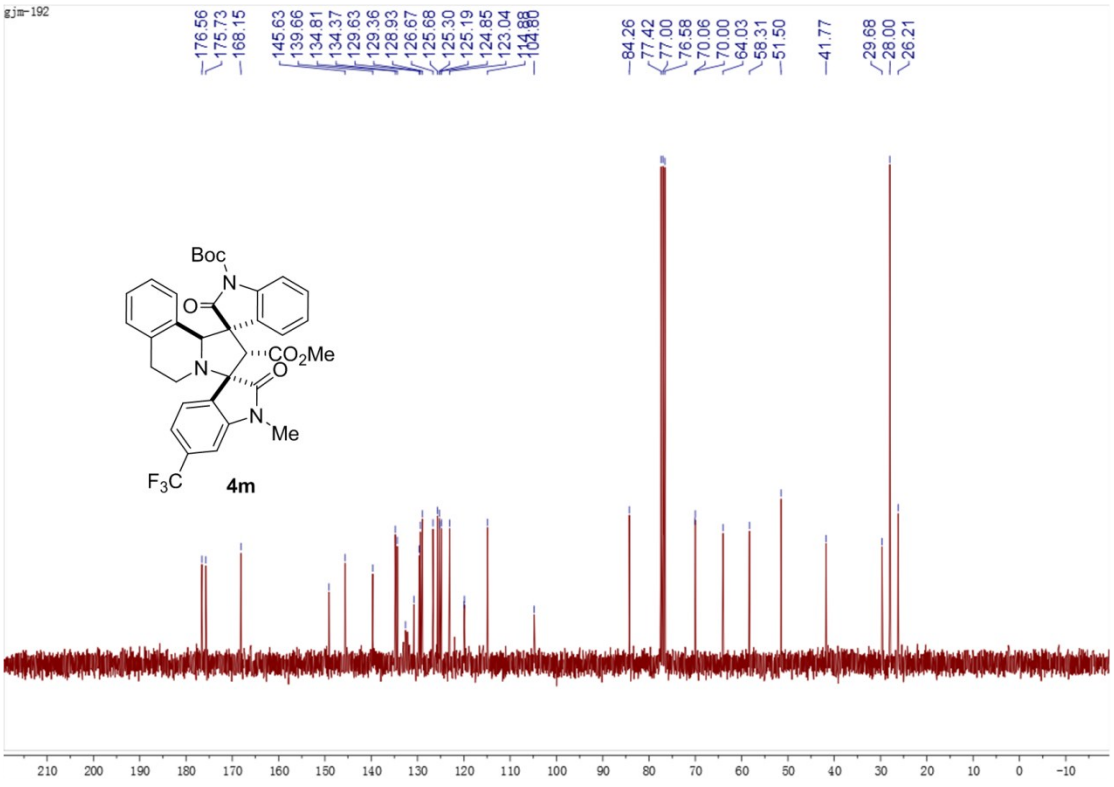
1.01
1.01
1.02
1.00
3.06
0.92
2.97
3.10
8.99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134.37
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129.36
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126.67
125.68
125.30
125.19
124.85
123.04
84.26
77.42
77.00
76.58
70.06
70.00
64.03
58.31
51.50
41.77
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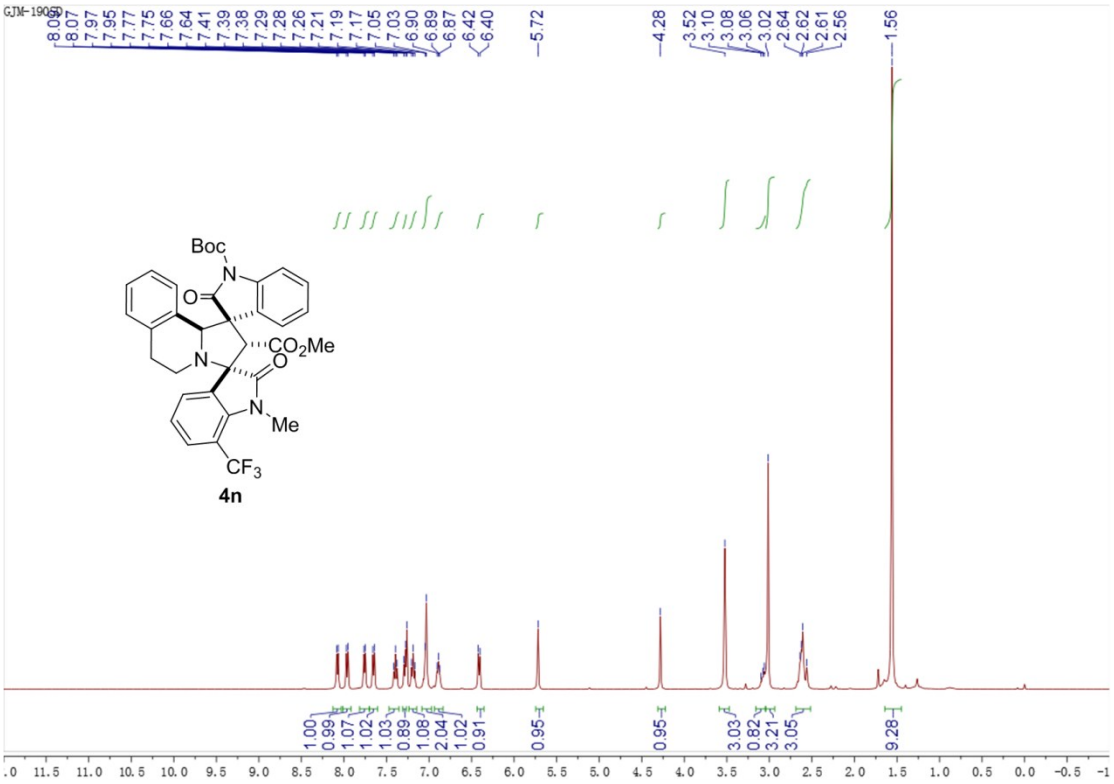
O
CO2Me
O
N
N
Me
F3C
4m


GJM-190SD
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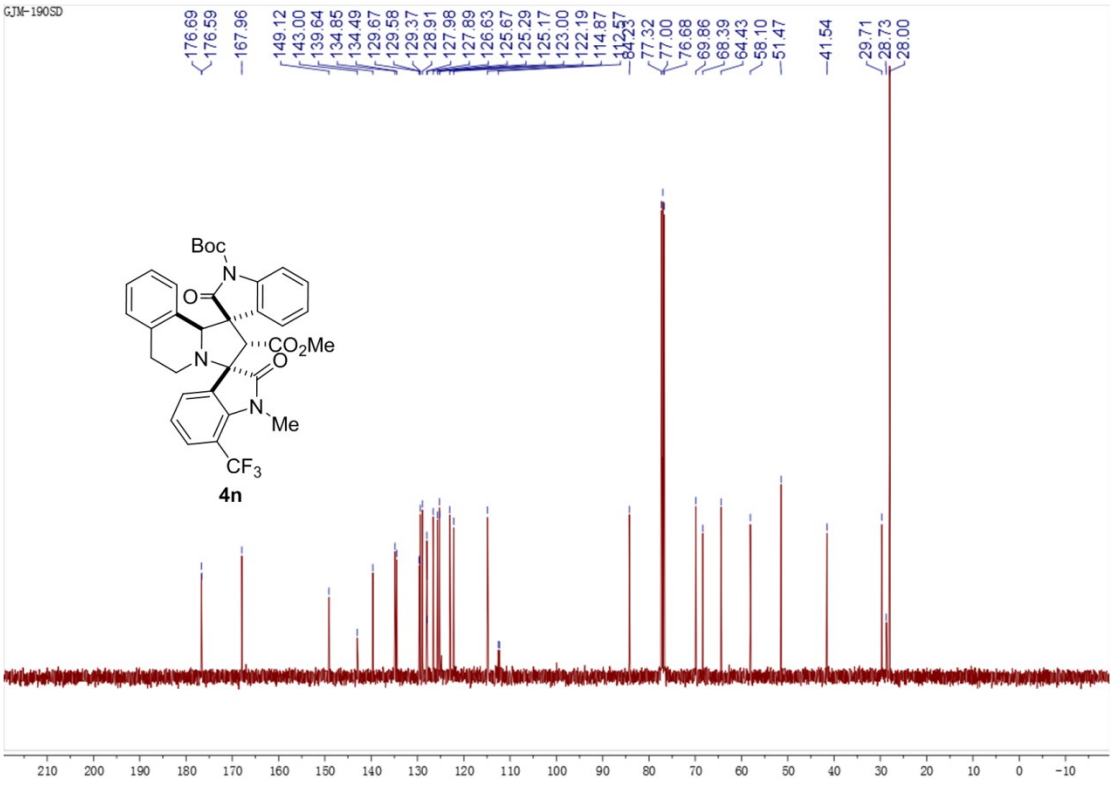
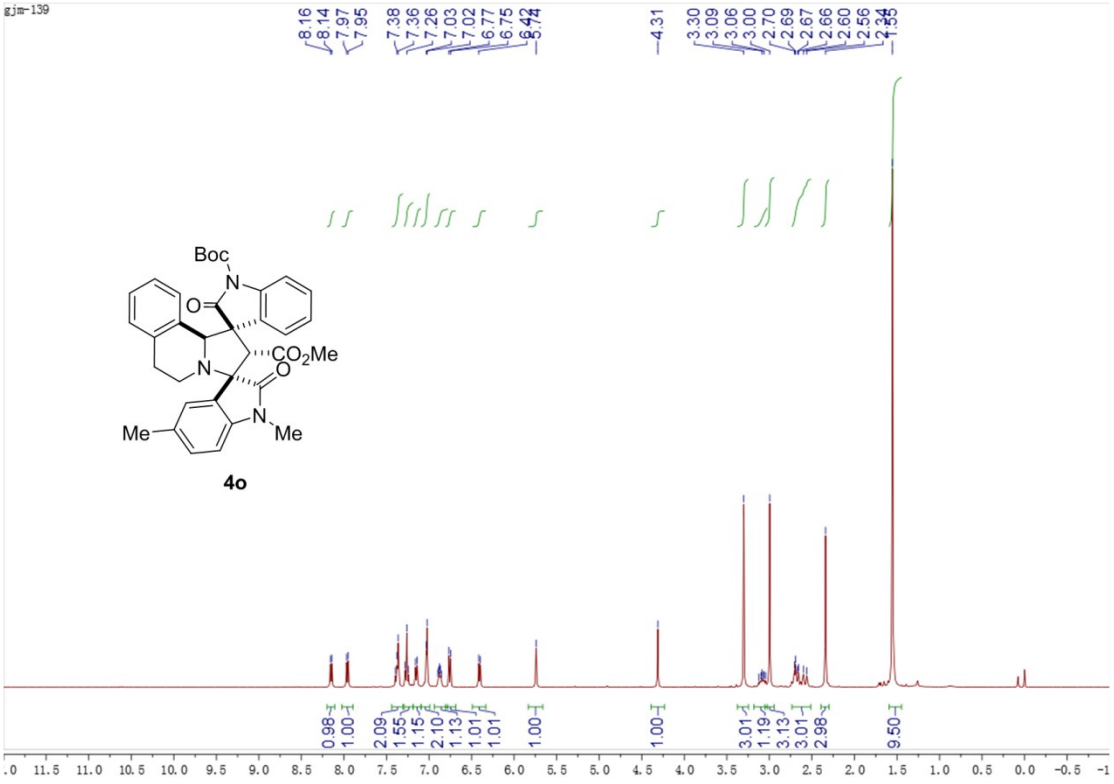
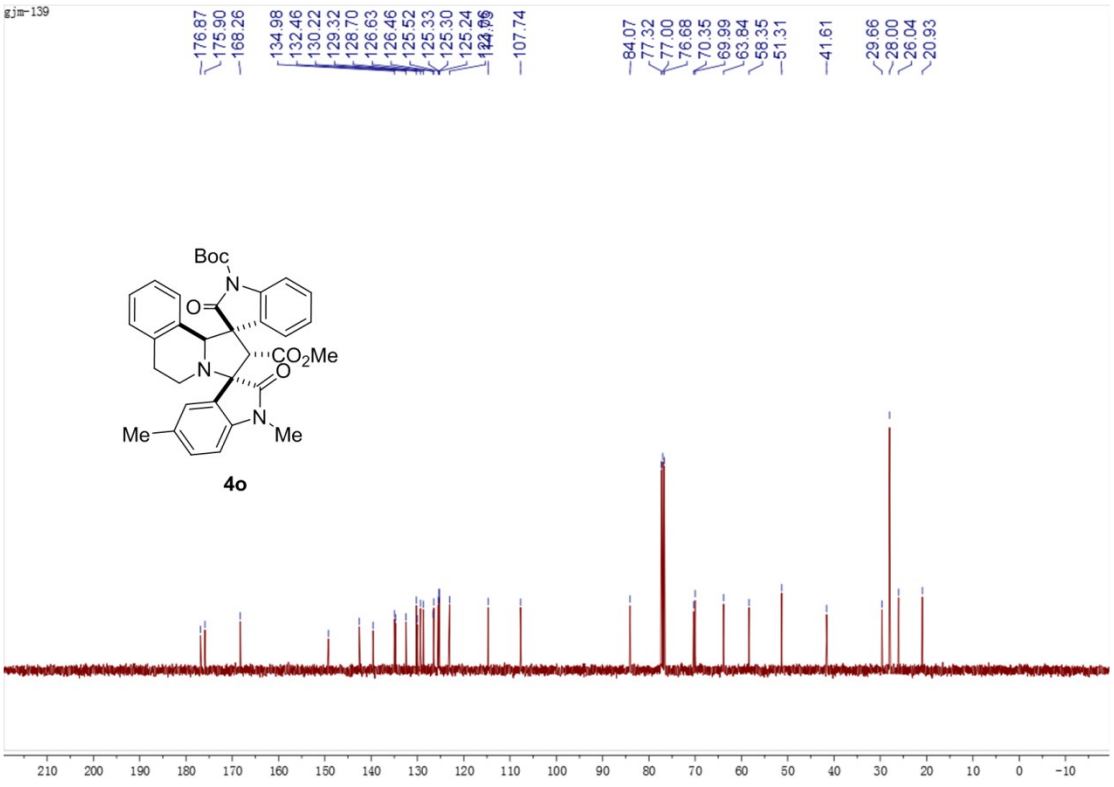
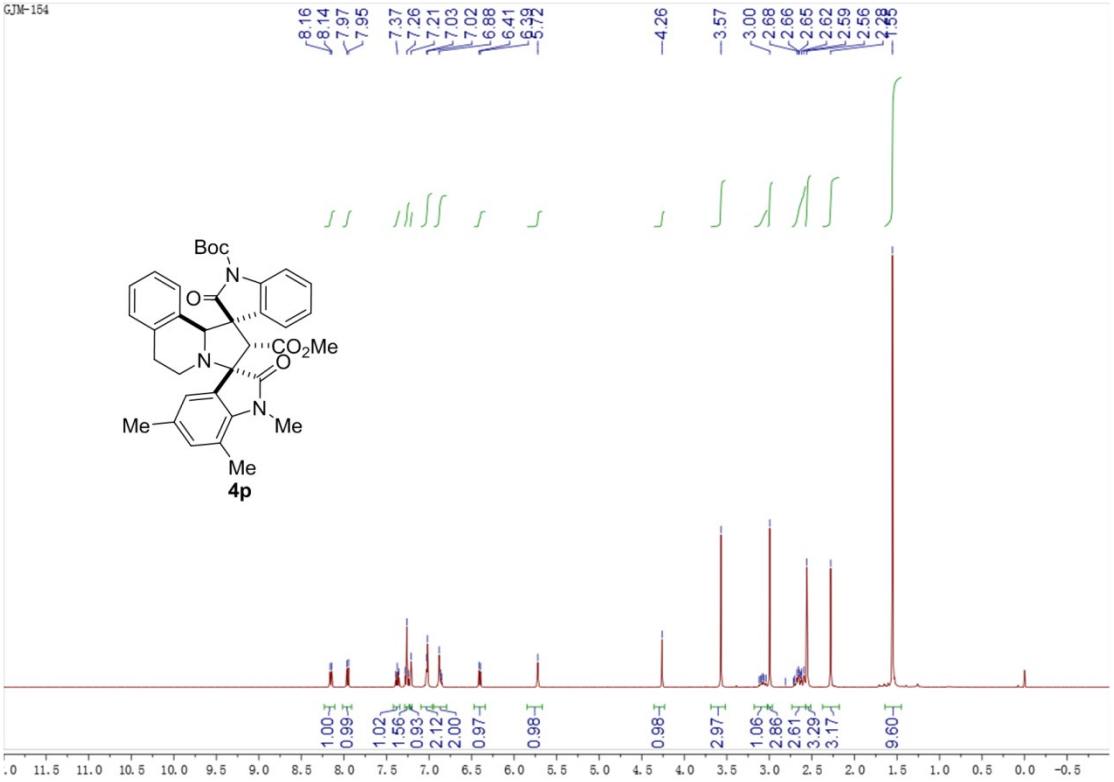
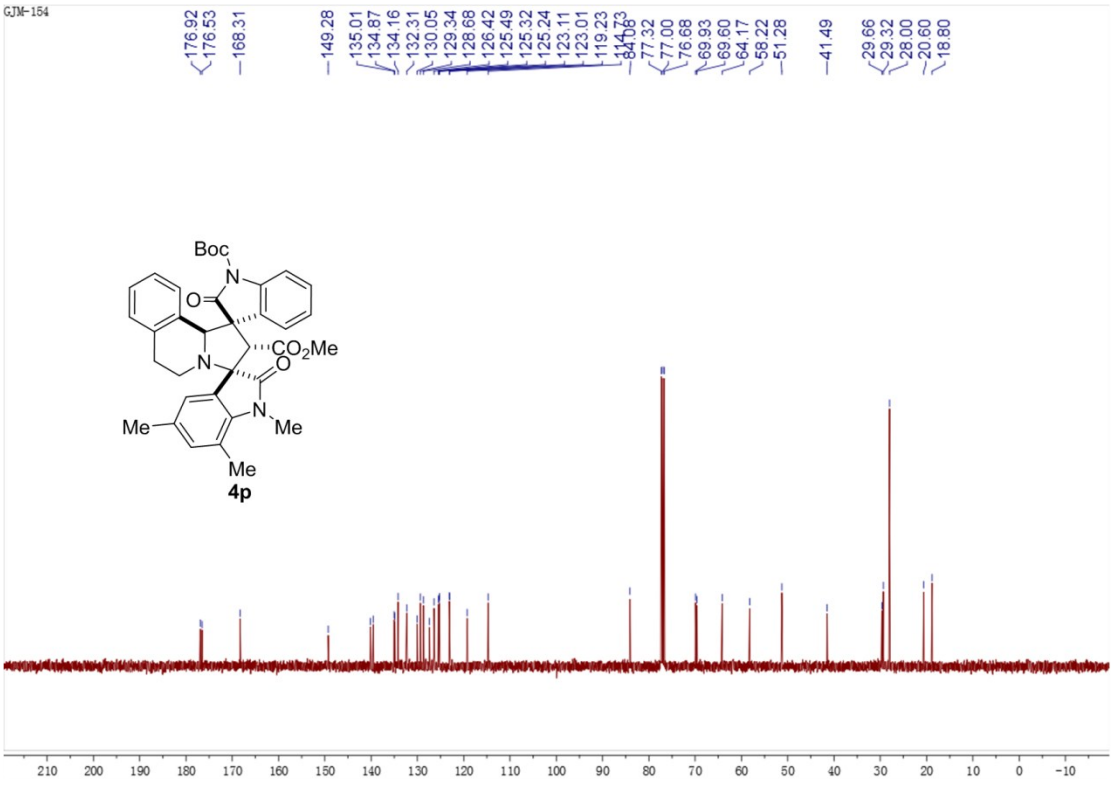
7.26
7.21
7.19
7.17
7.05
7.03
6.90
6.89
6.87
6.42
6.40
5.72
4.28
3.52
3.10
3.08
3.06
3.02
2.64
2.62
2.61
2.56
1.56
Boc
N
O
CO2Me
O
N
N
Me
CF3
4n
1.00
0.99
1.07
1.02
1.03
0.89
1.08
2.04
1.02
0.91
0.95
0.95
3.03
0.82
3.21
3.05
9.28

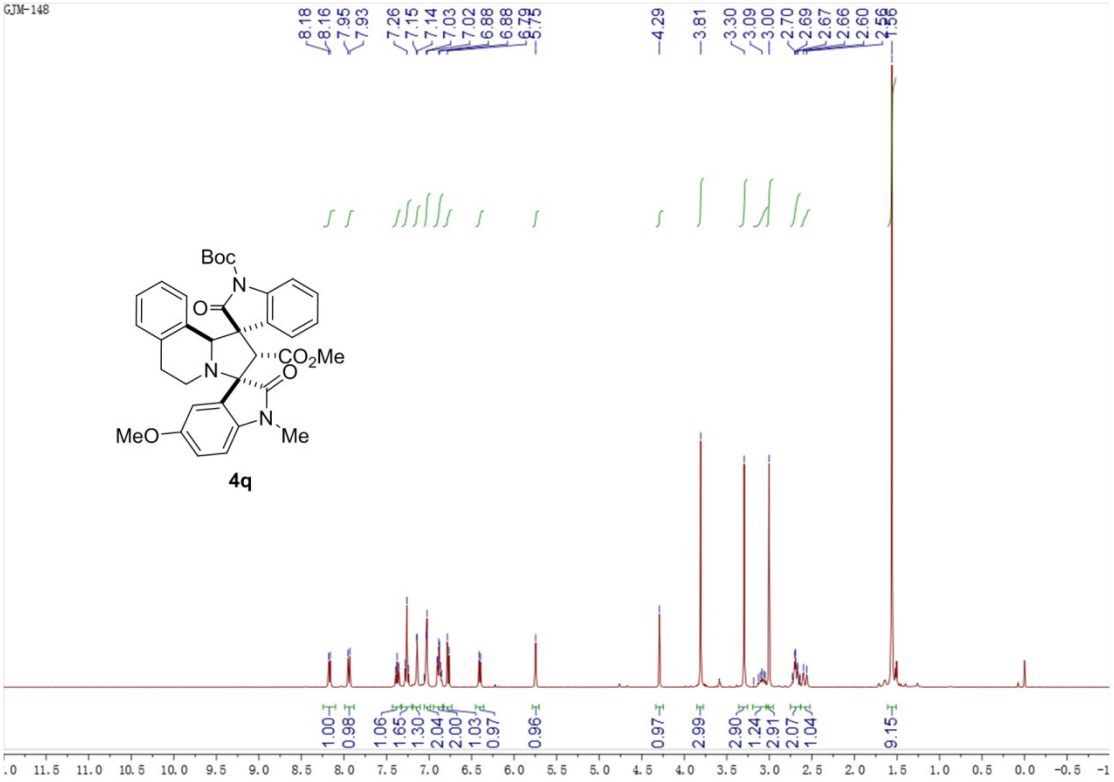

GJM-190SD
176.69
176.59
167.96
149.12
143.00
139.64
134.85
134.49
129.67
129.58
129.37
128.91
127.98
127.89
126.63
125.67
125.29
125.17
123.00
122.19
114.87
77.32
77.00
76.68
69.86
68.39
64.43
58.10
51.47
41.54
29.71
28.73
28.00
Boc
N
O
CO2Me
O
N
N
Me
CF3
4n

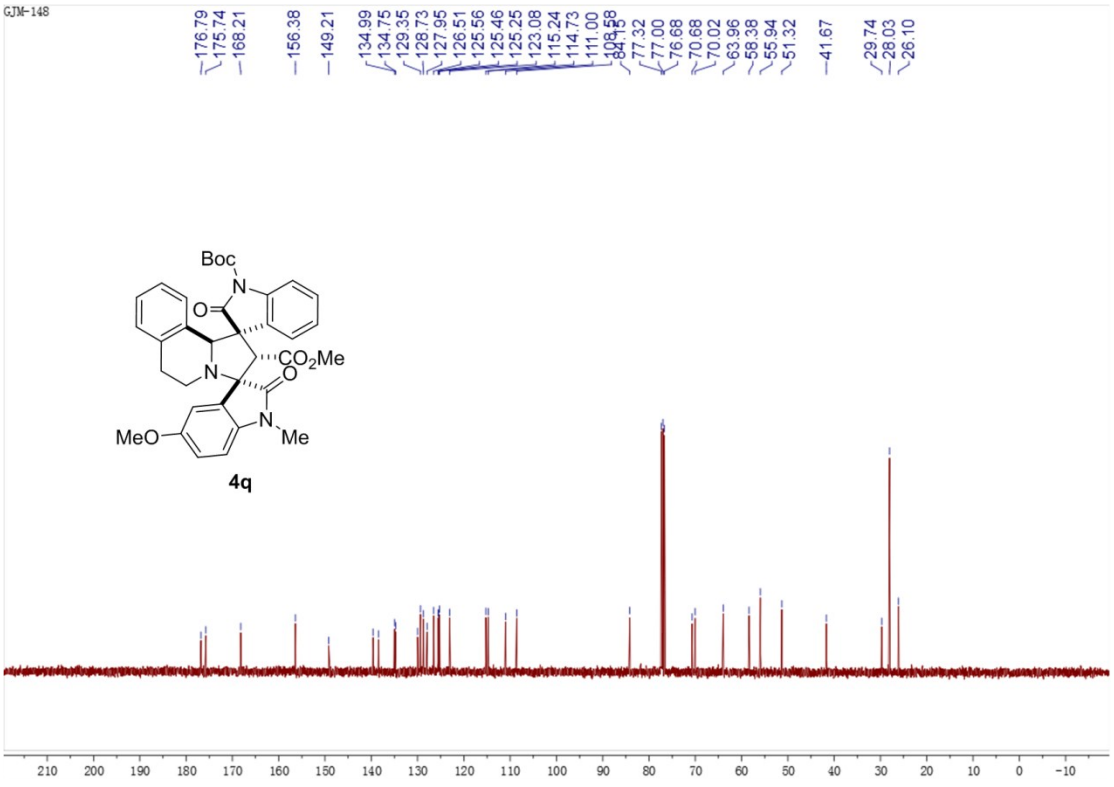

gjm-139
Boc
N
O
CO2Me
O
N
Me
N
Me
4o

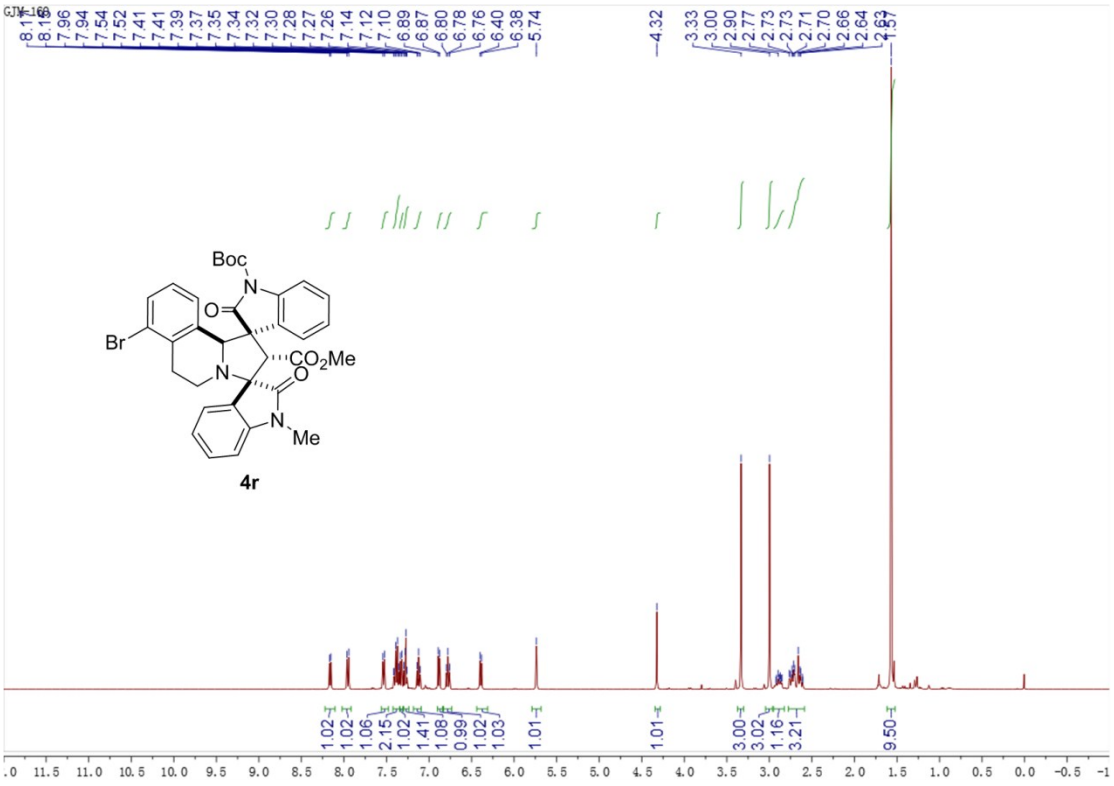

gjm-139
Boc
N
O
CO2Me
O
N
Me
N
Me
4o


GJM-154
Boc
N
O
CO2Me
O
N
N
Me
Me
Me
4p

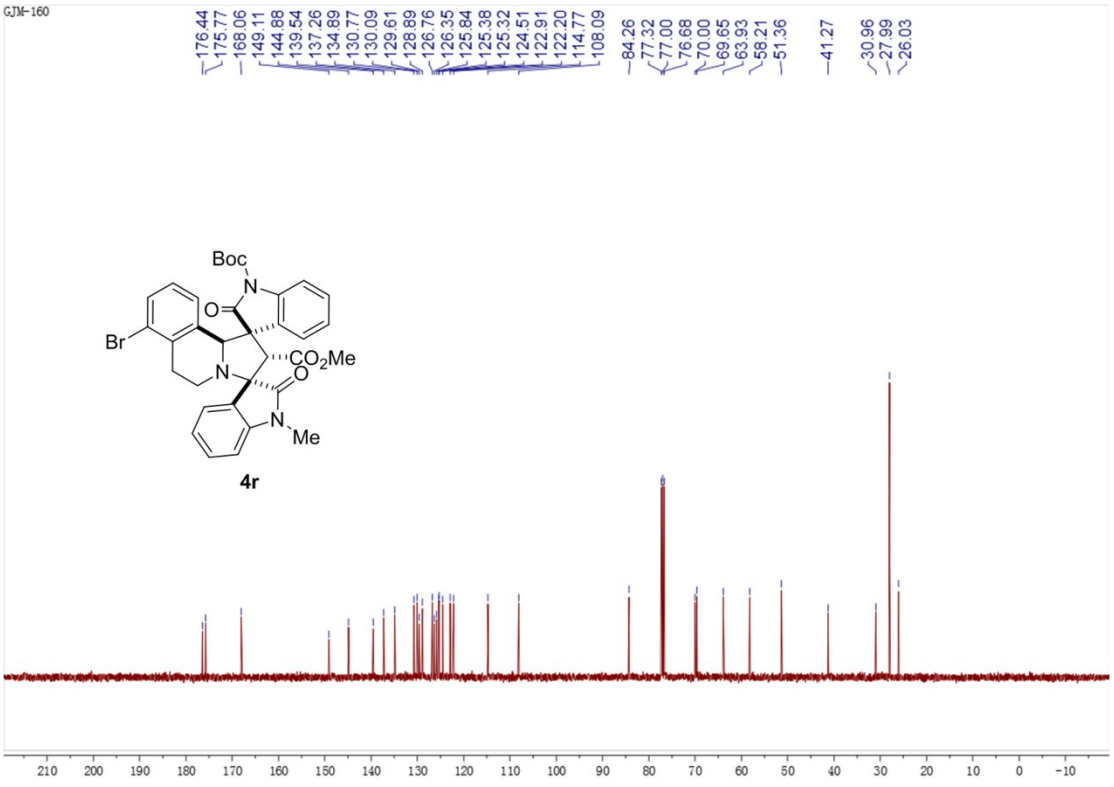

GJM-154
Boc
N
O
CO2Me
O
N
N
Me
Me
Me
4p


GJM-148
Boc
N
O
CO2Me
N
O
N
Me
MeO
4q

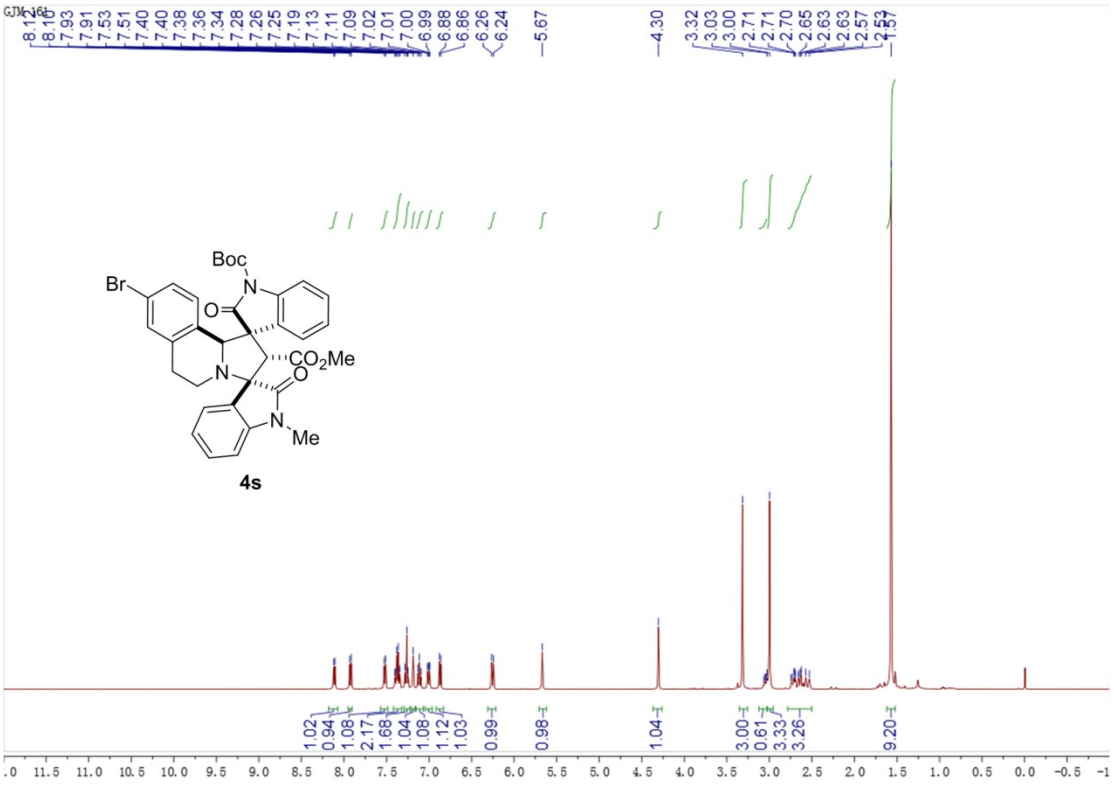

GJM-148
Boc
N
O
CO2Me
N
O
N
Me
MeO
4q

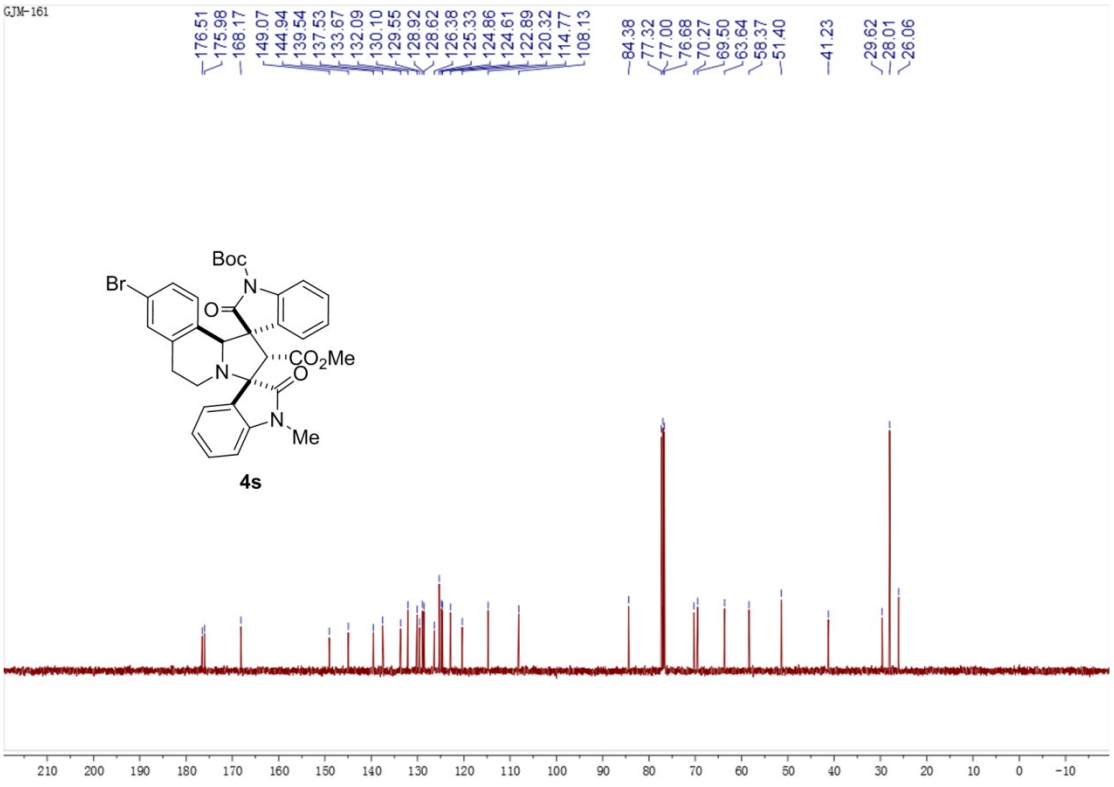


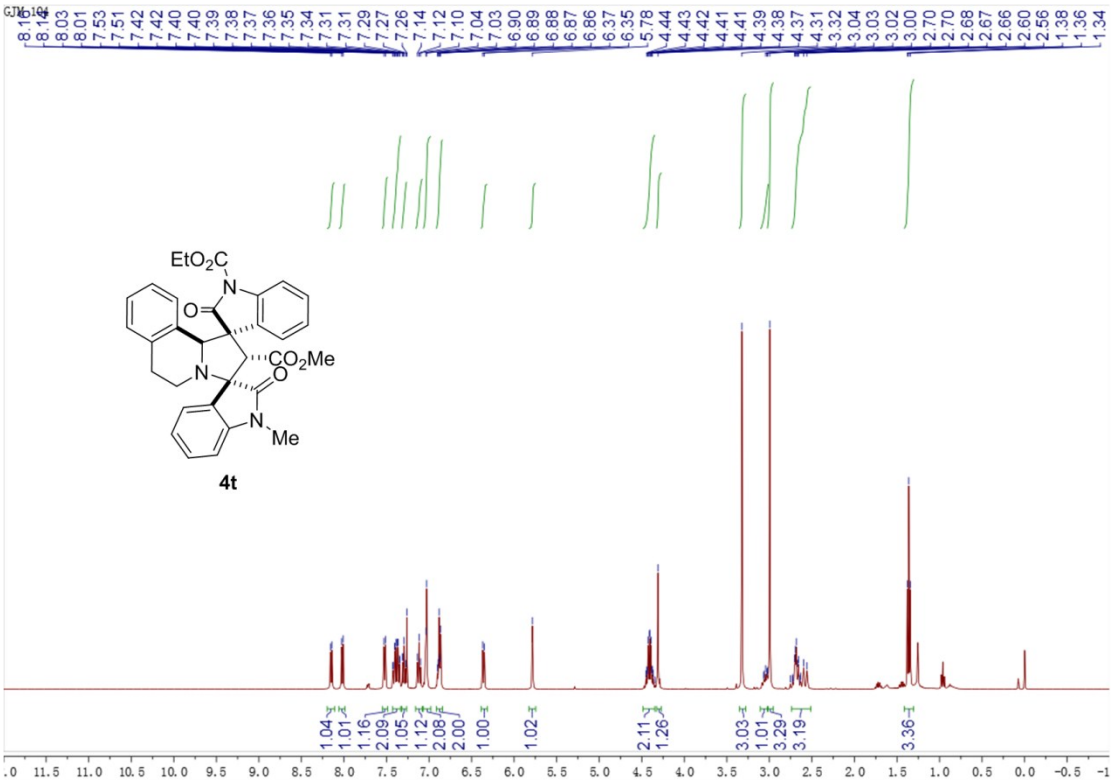
4r

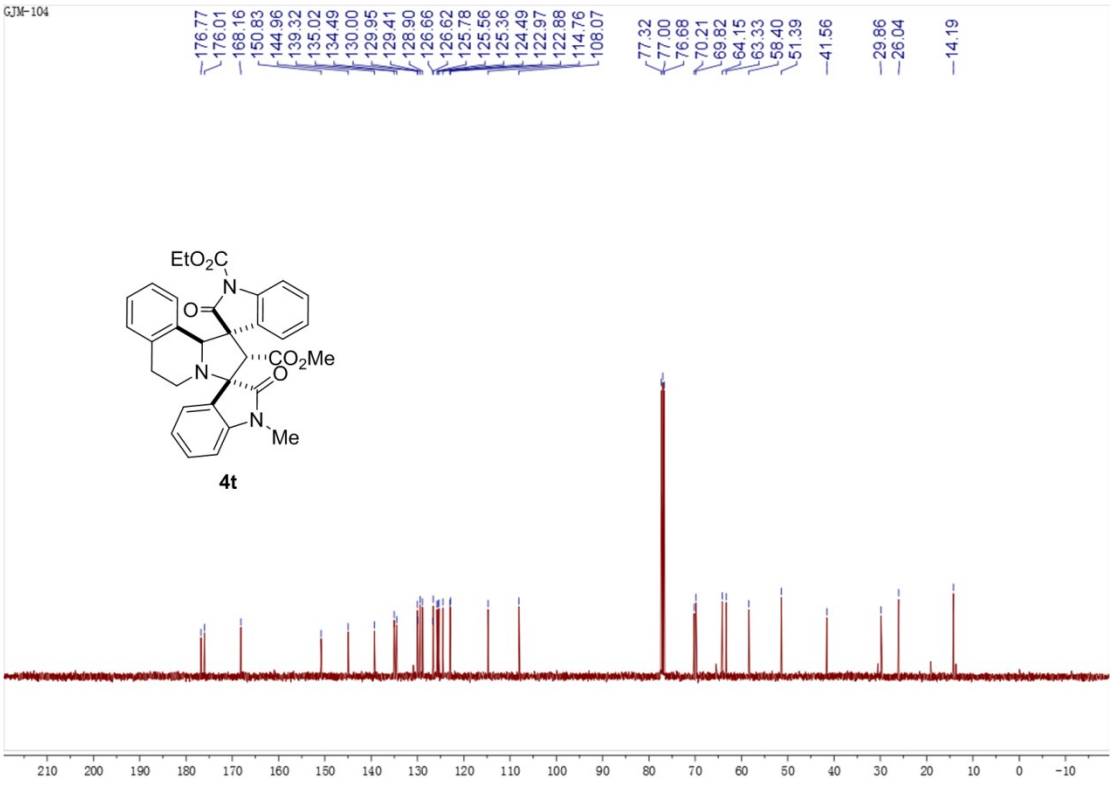


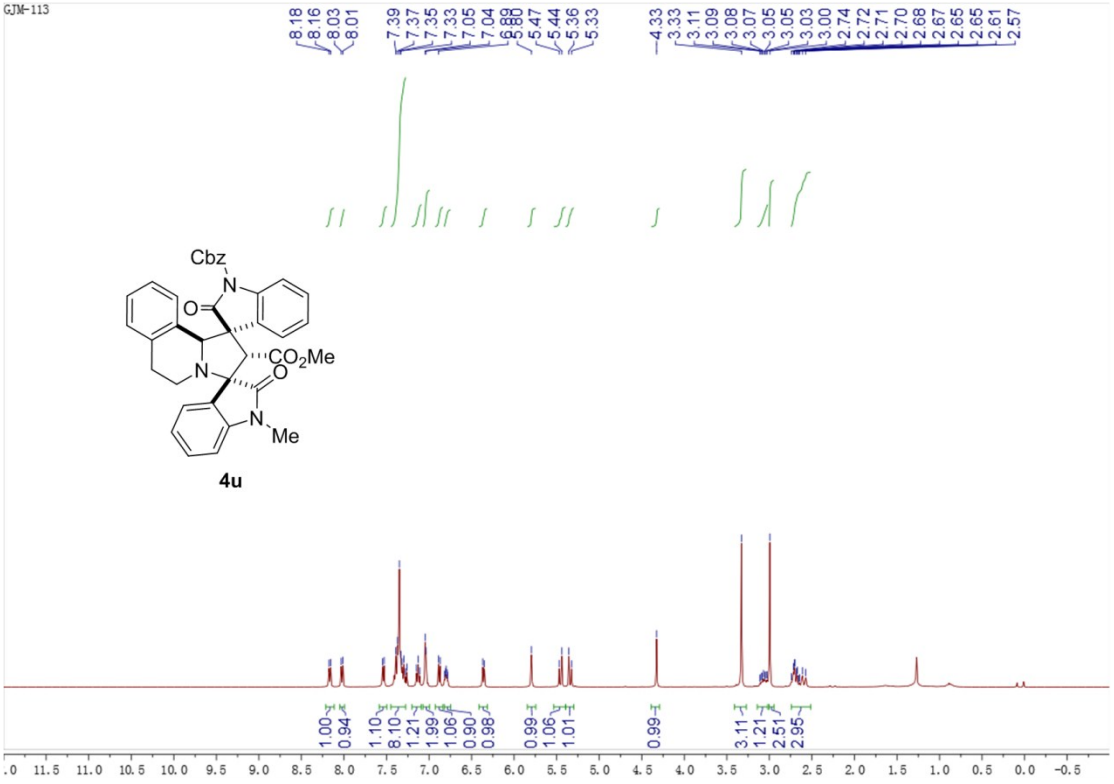
4r

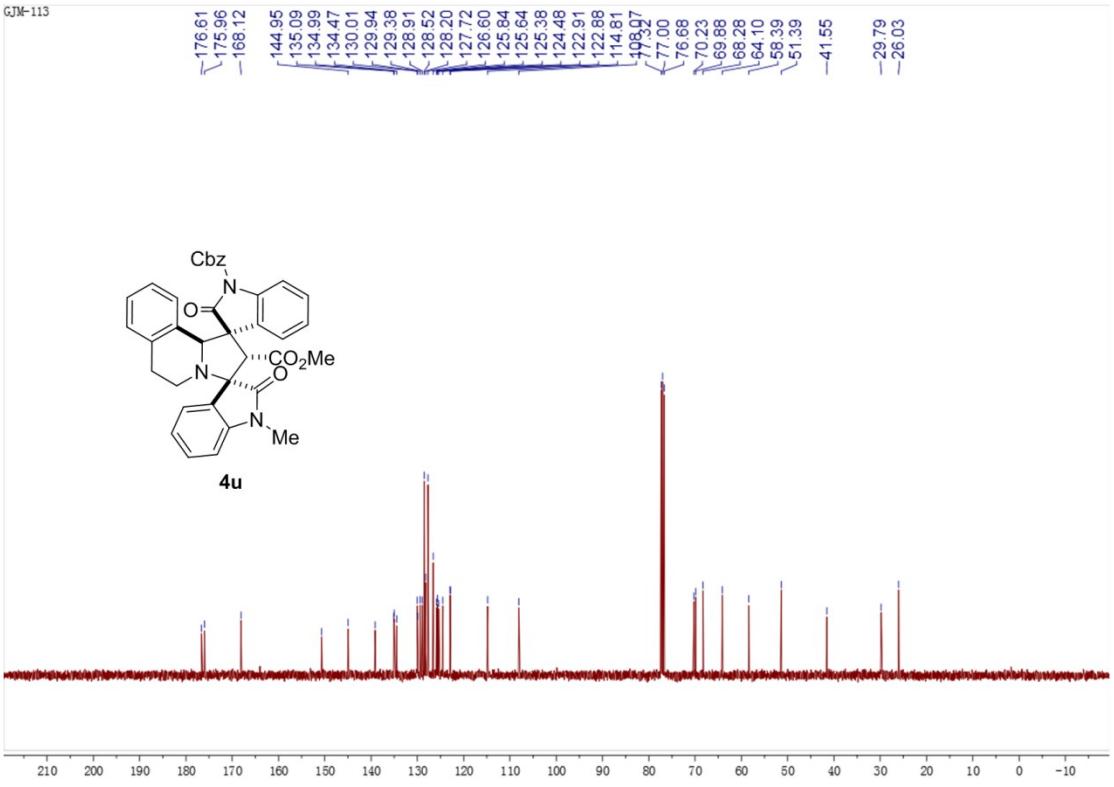

Boc
Br
O
N
CO2Me
O
N
Me
4s

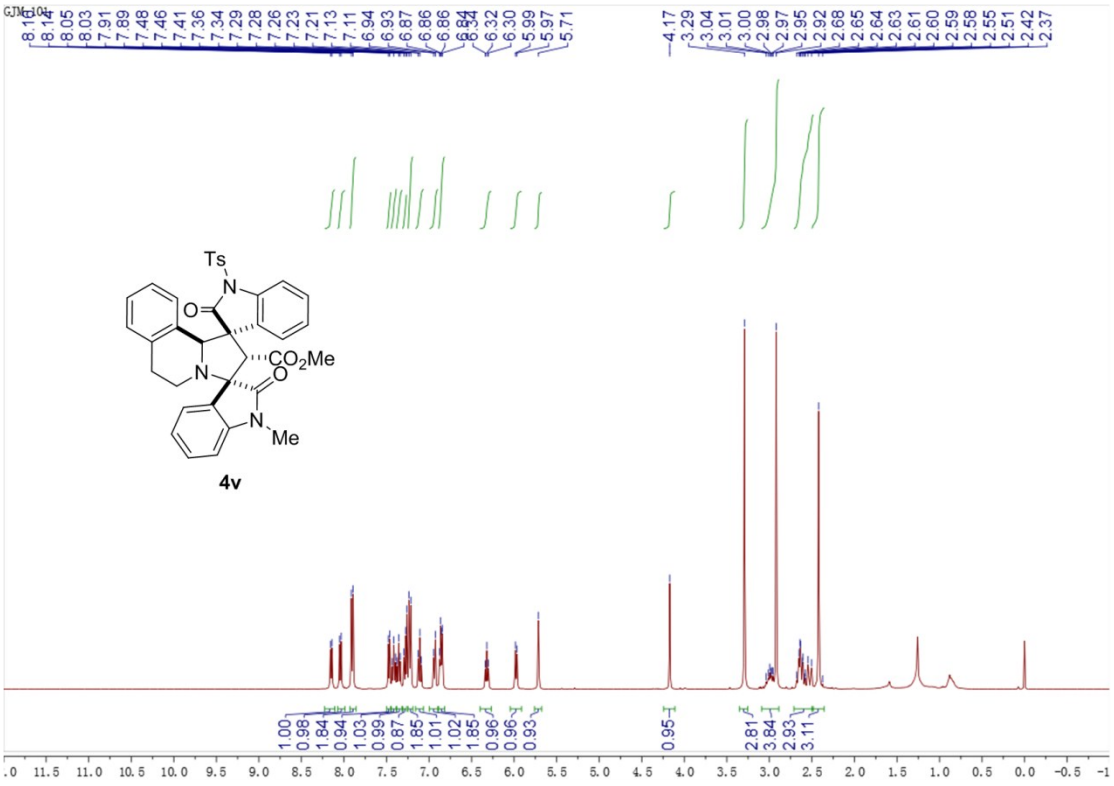

Boc
Br
O
N
CO2Me
O
N
Me
4s


EtO2C
CO2Me
Me
4t

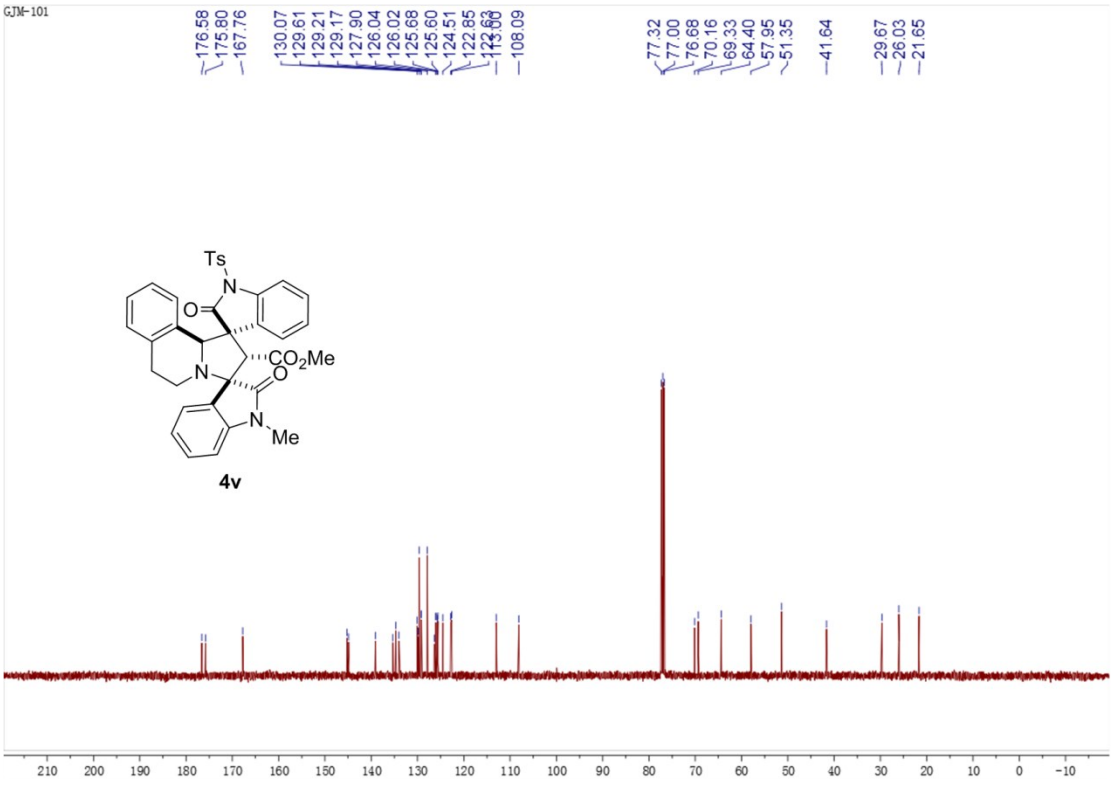

GJM-104
EtO2C
CO2Me
Me
4t


GJM-113
Cbz
CO2Me
Me
4u

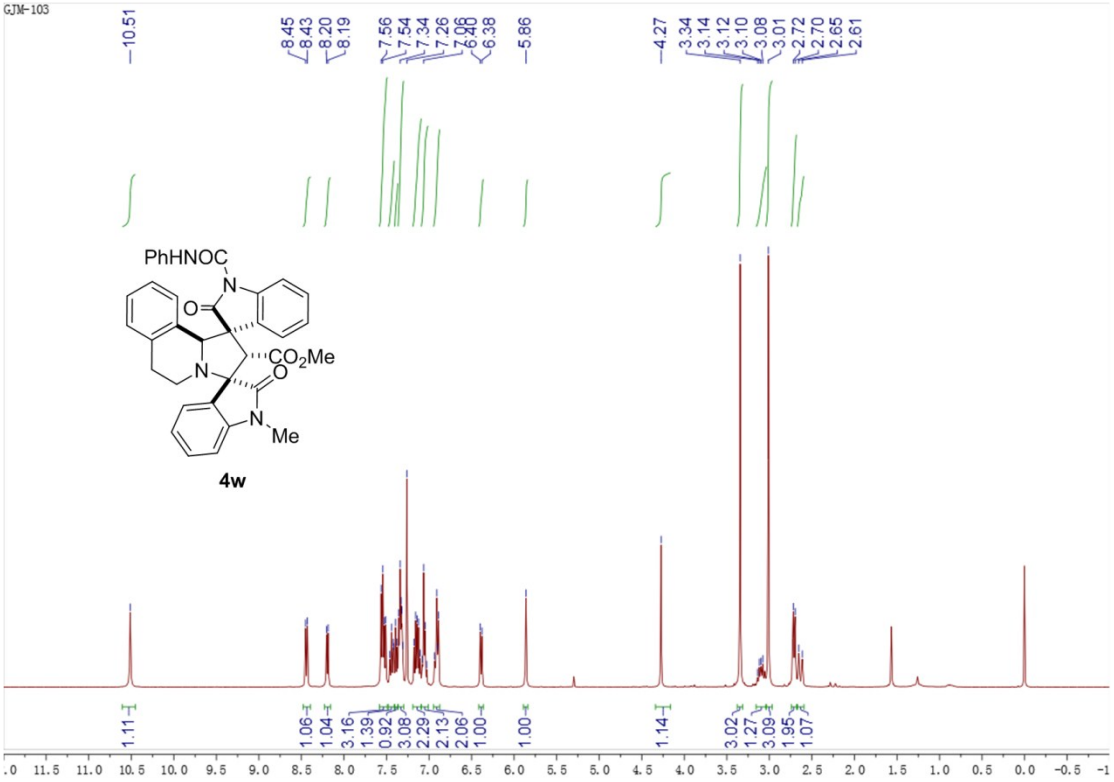

GJM-113
Cbz
CO2Me
Me
4u

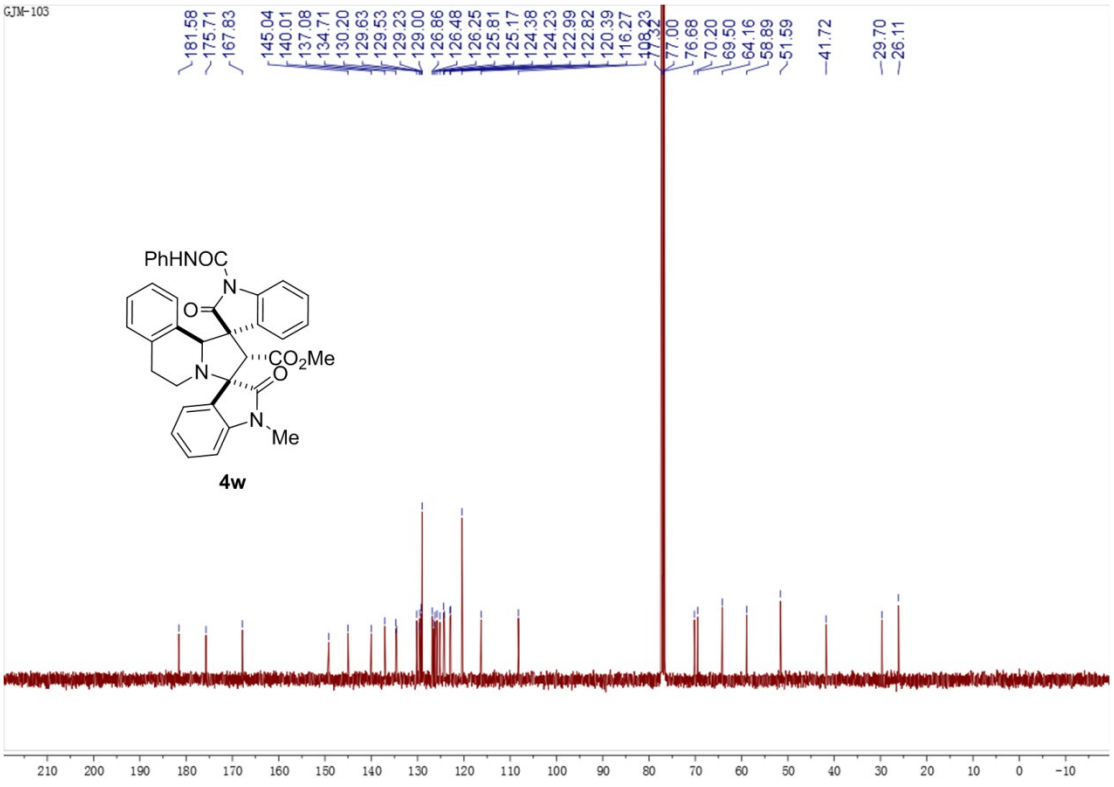


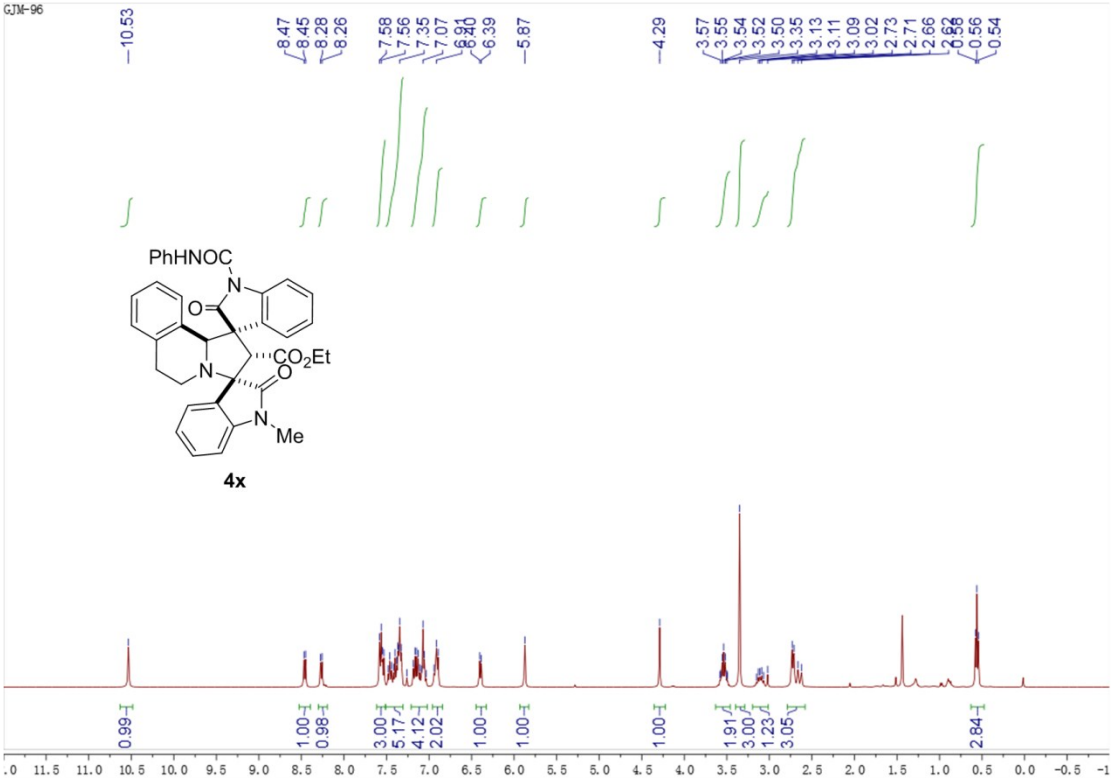
4v

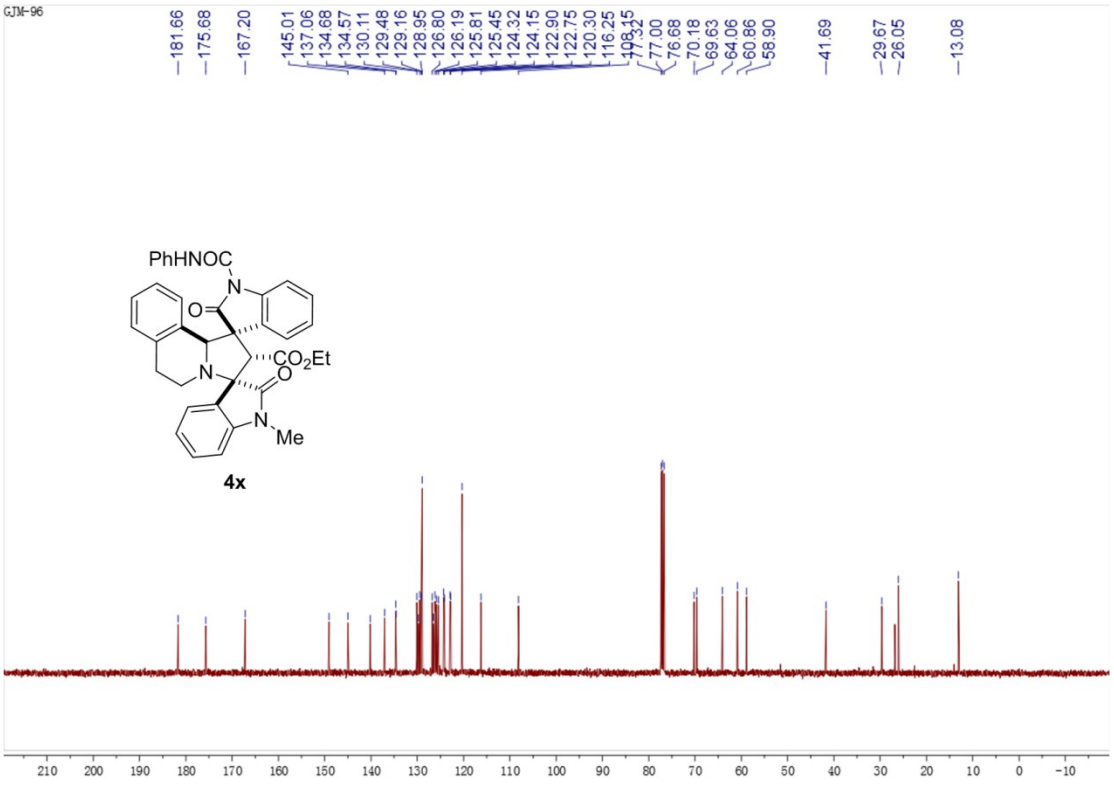


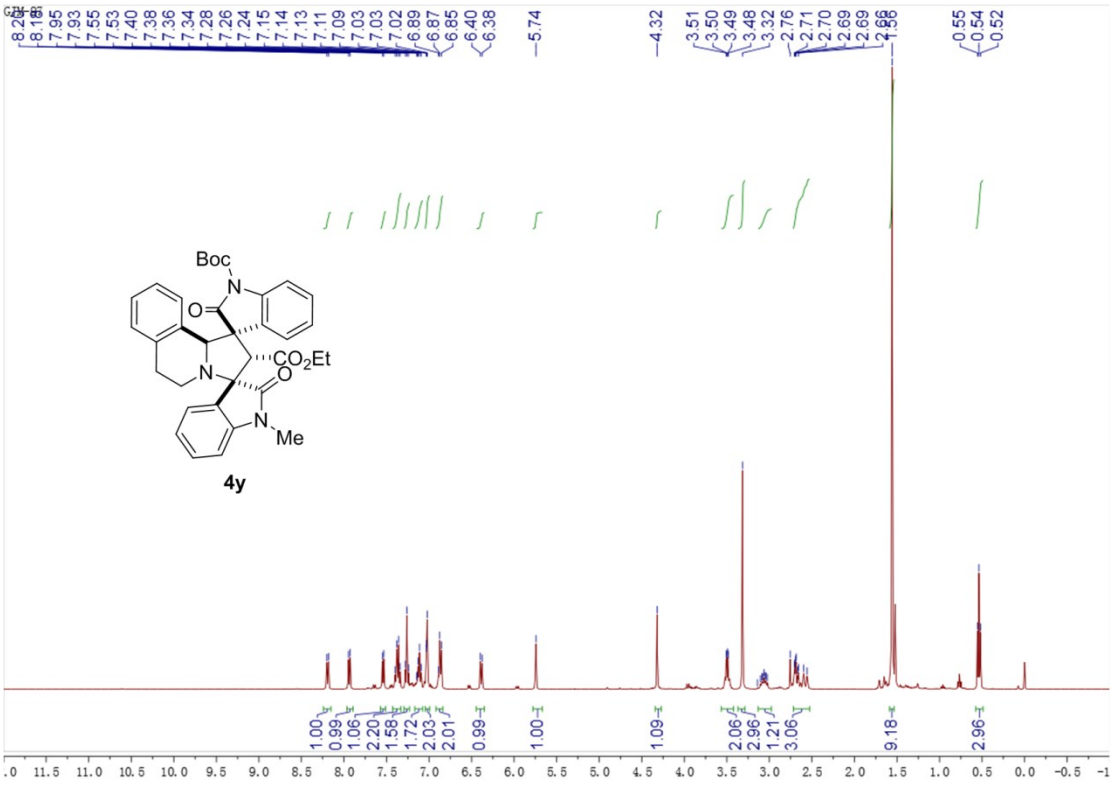
4v


GJM-103
PhHNOC
CO2Me
Me
4w

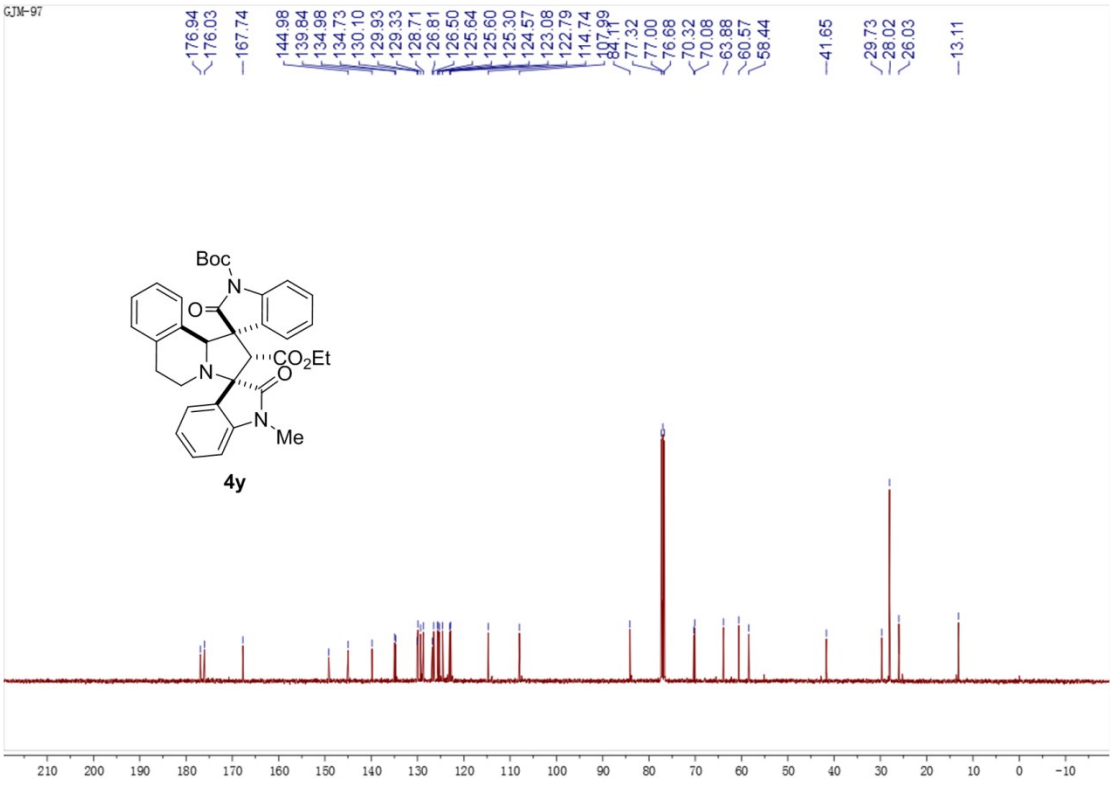

GJM-103
PhHNOC
CO2Me
Me
4w


GJM-96
PhHNOC
CO2Et
Me
4x

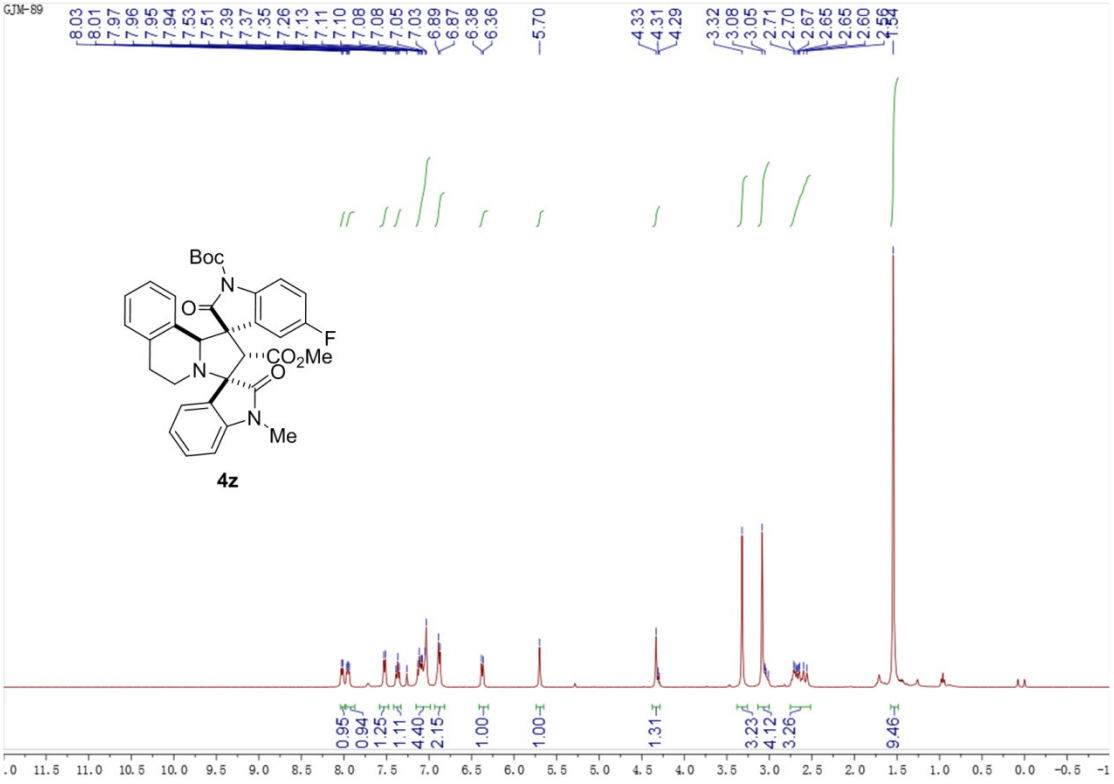

GJM-96
PhHNOC
CO2Et
Me
4x

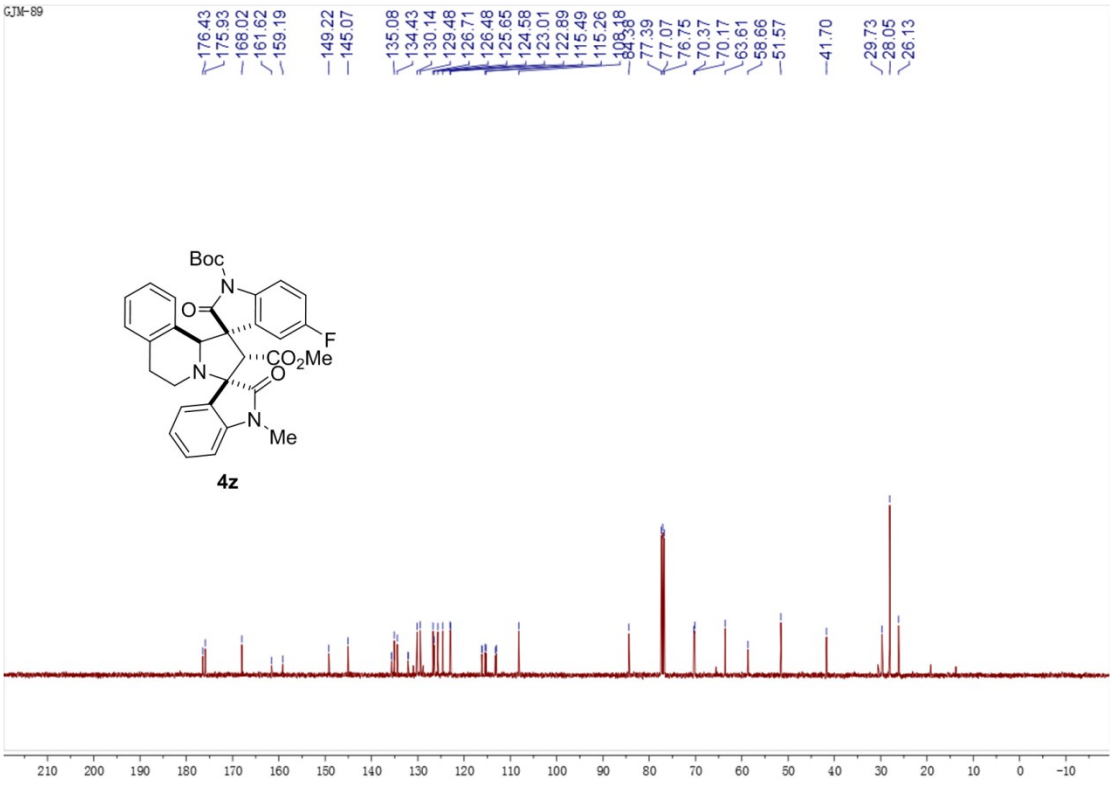


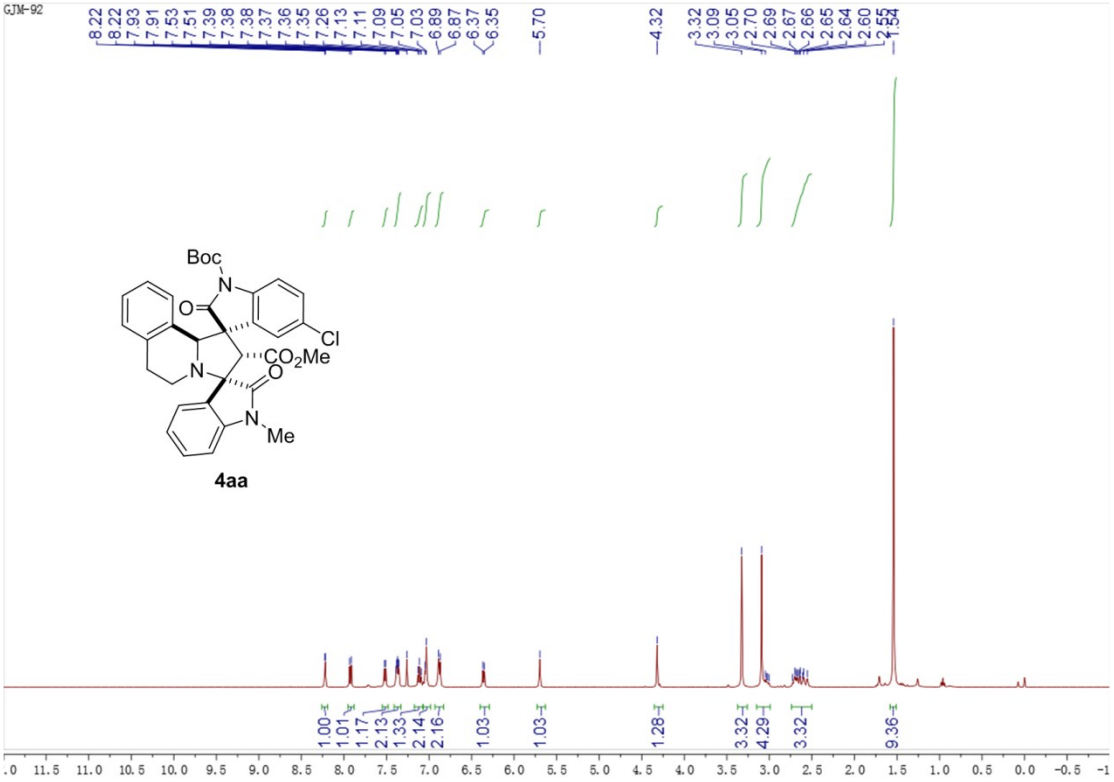
4y

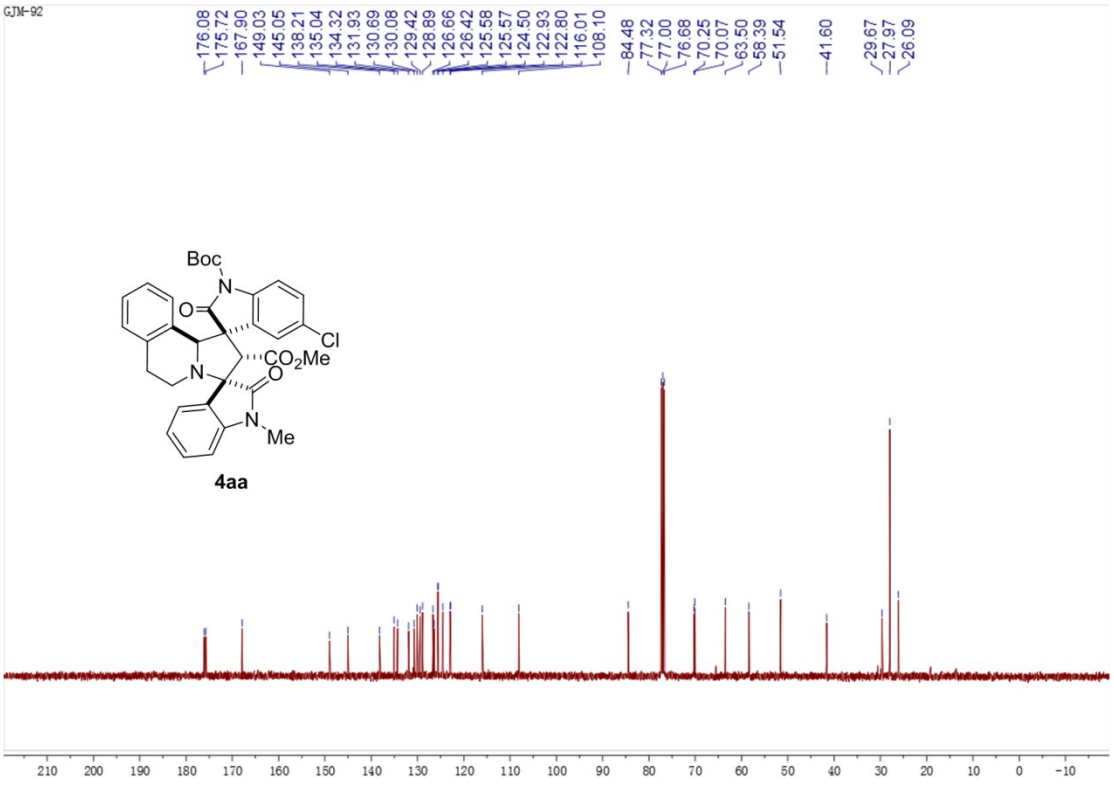


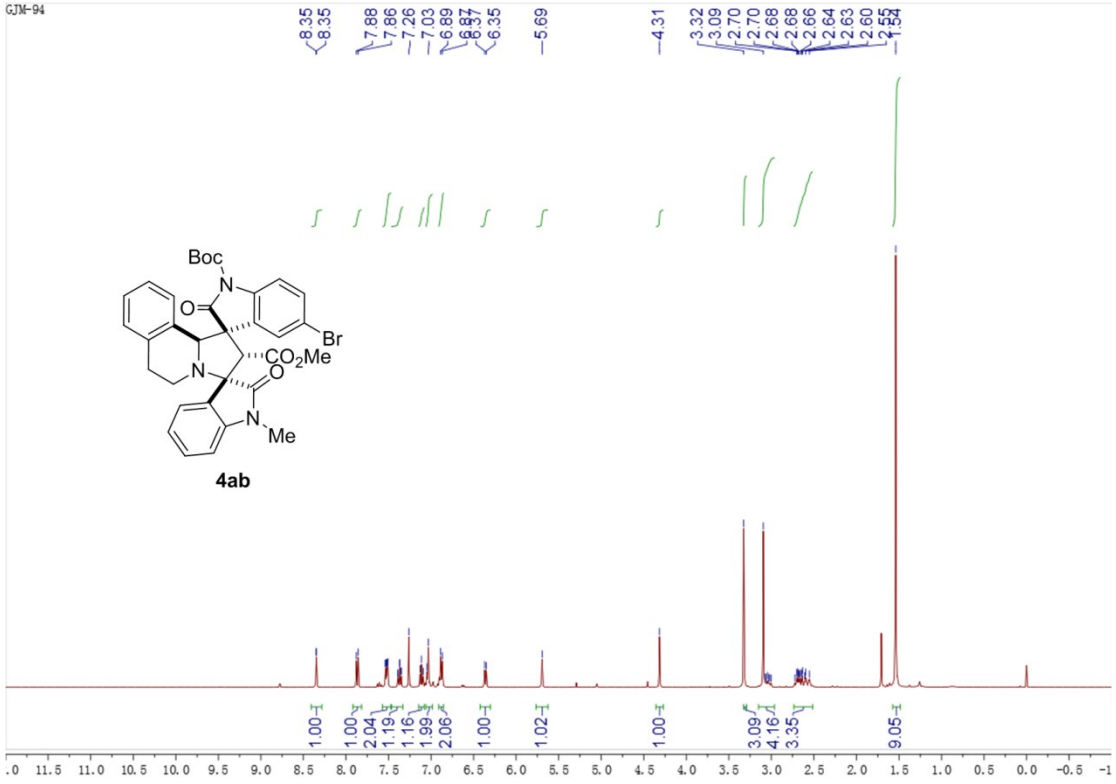
4y

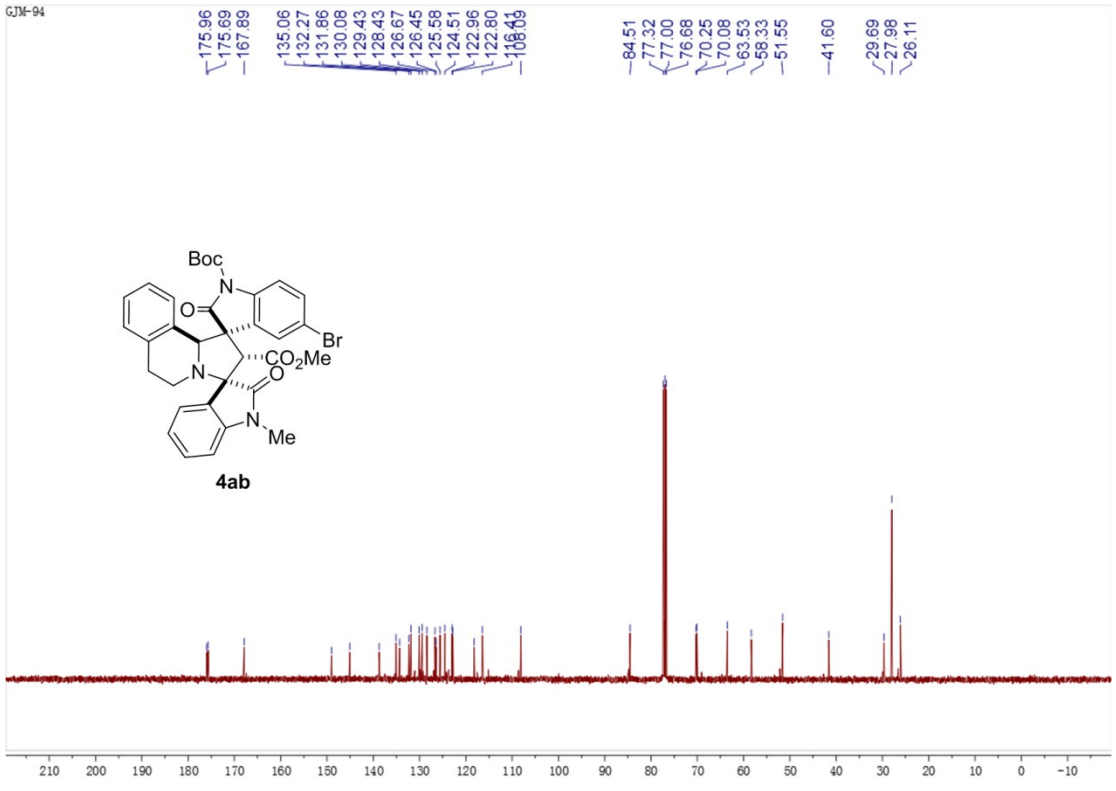

GJM-89
Boc
N
O
F
CO2Me
O
N
N
Me
4z

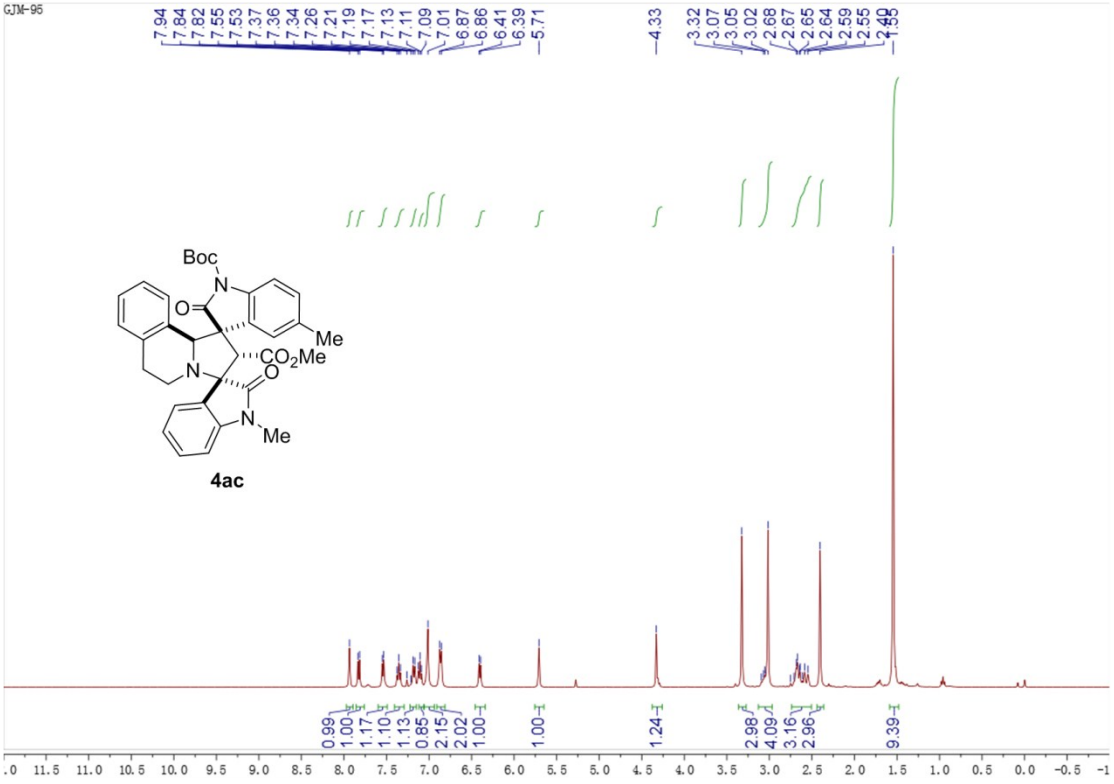

GJM-89
Boc
N
O
F
CO2Me
O
N
N
Me
4z

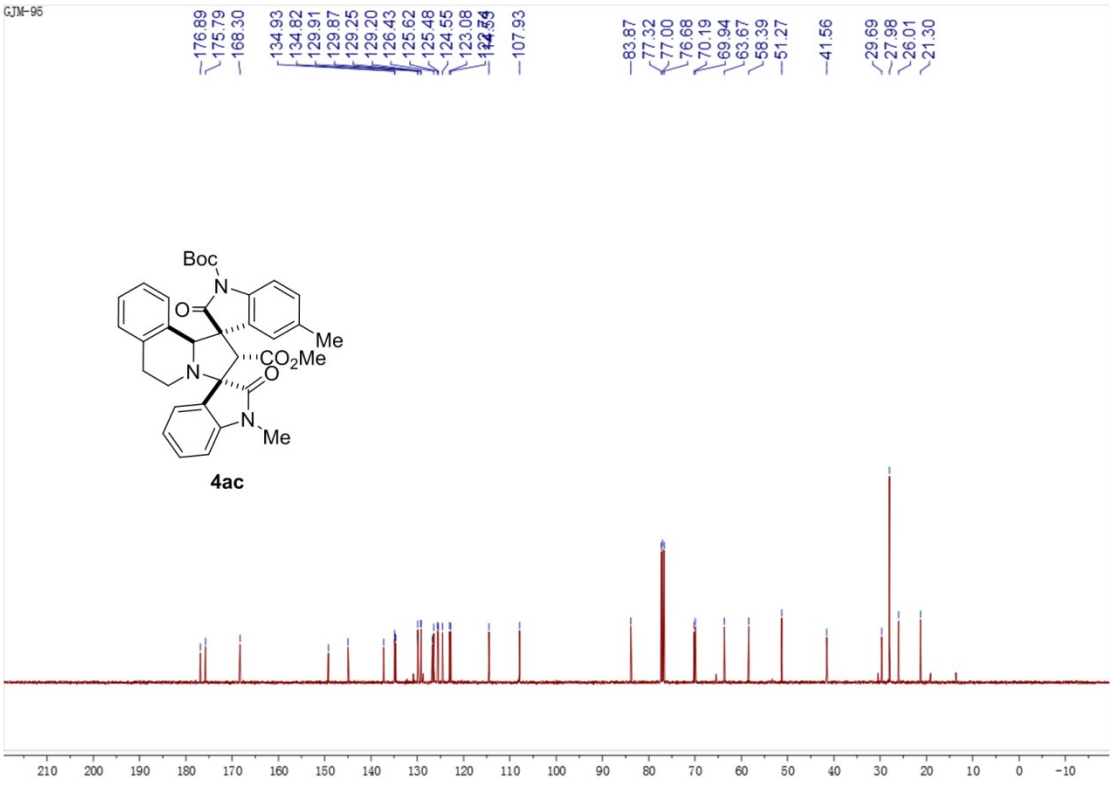

GJM-92
Boc
N
O
Cl
CO2Me
O
N
N
Me
4aa

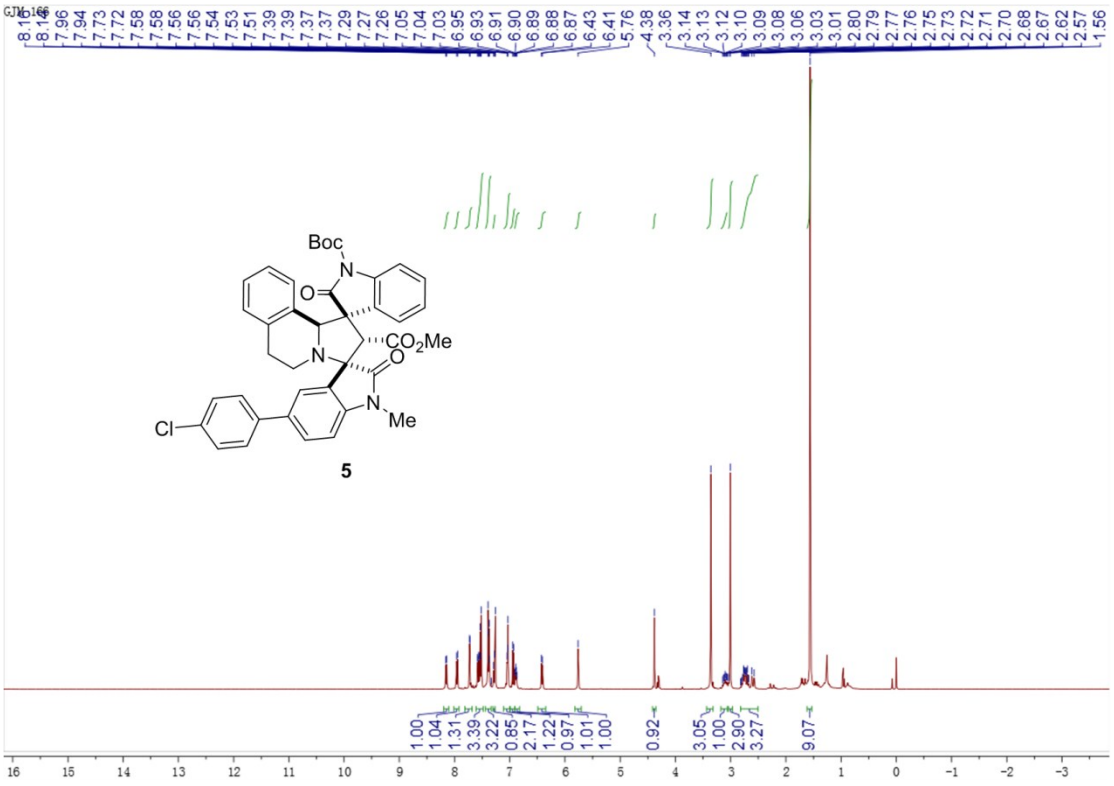

GJM-92
Boc
N
O
Cl
CO2Me
O
N
N
Me
4aa

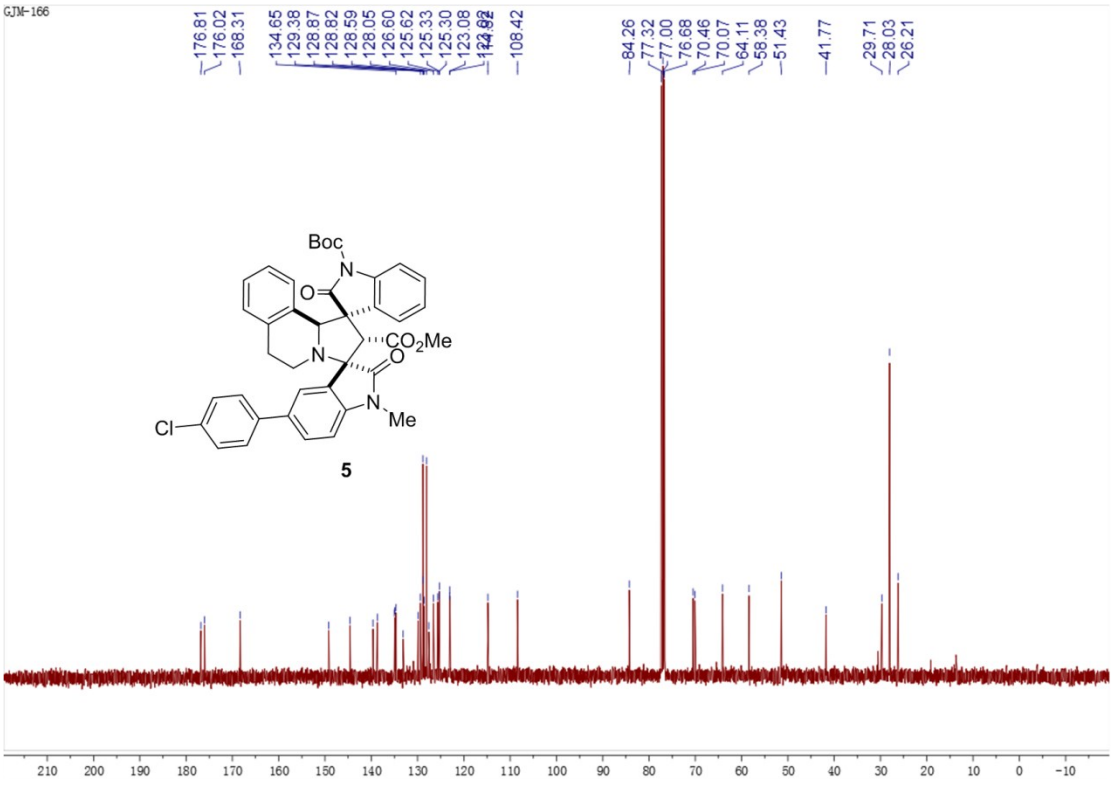

GJM-94
Boc
N
O
Br
CO2Me
O
N
N
Me
4ab

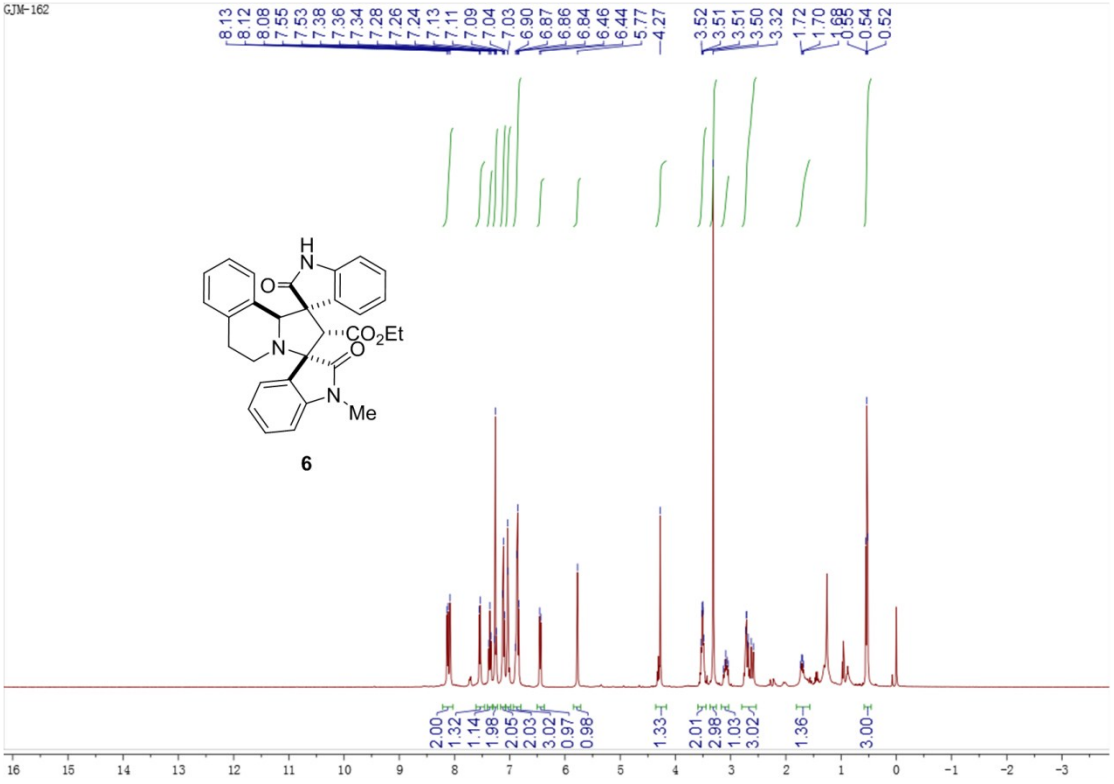

GJM-94
Boc
N
O
Br
CO2Me
O
N
N
Me
4ab


GJM-95
Boc
N
O
Me
CO2Me
N
O
N
Me
4ac


GJM-95
Boc
N
O
Me
CO2Me
N
O
N
Me
4ac


GJM-166
Boc
N
O
CO2Me
O
N
N
Me
Cl
5


GJM-166
Boc
N
O
CO2Me
O
N
N
Me
Cl
5


GJM-162
8.13
8.12
8.08
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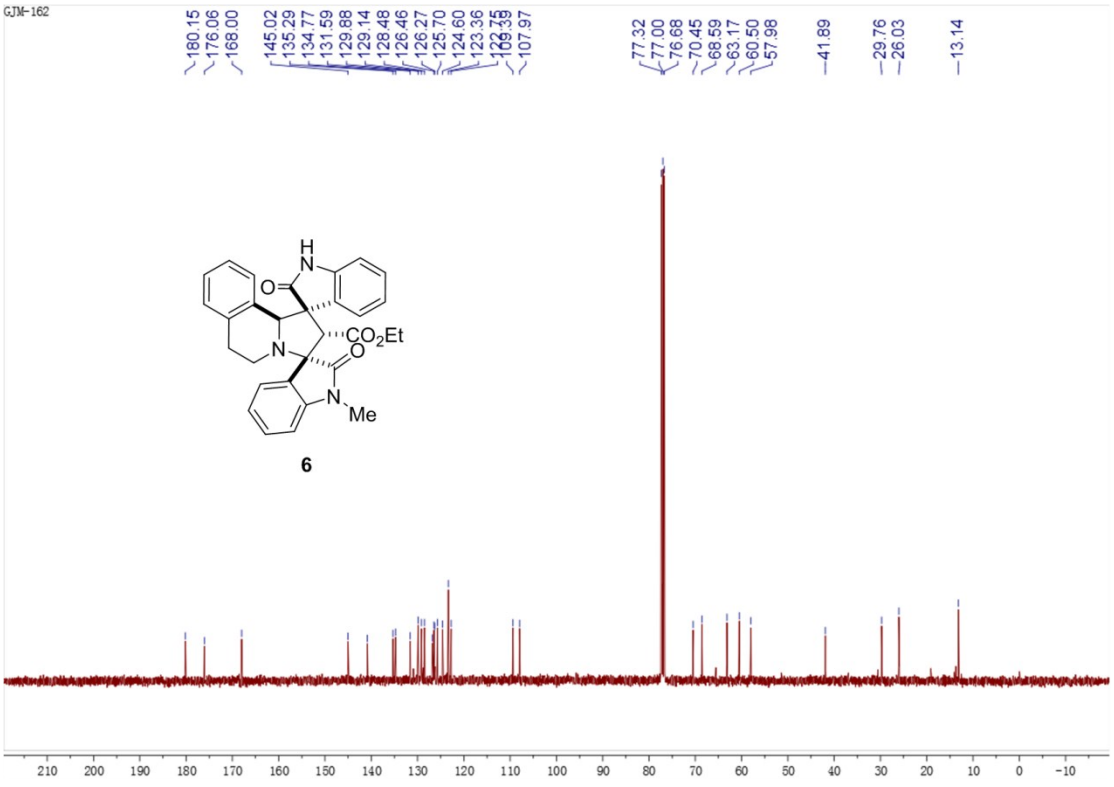
7.53
7.38
7.36
7.34
7.28
7.26
7.24
7.13
7.11
7.09
7.04
7.03
6.90
6.87
6.86
6.84
6.46
6.44
5.77
4.27
3.52
3.51
3.51
3.50
3.32
1.72
1.70
1.68
1.55
0.54
0.52
2.00
1.32
1.14
1.98
2.05
2.03
3.02
0.97
0.98
1.33
2.01
2.98
1.03
3.02
1.36
3.00
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3

H
N
O
CO2Et
N
O
N
Me

6


GJM-162
180.15
176.06
168.00
145.02
135.29
134.77
131.59
129.88
129.14
128.48
126.46
126.27
125.70
124.60
123.36
107.97
77.32
77.00
76.68
70.45
68.59
63.17
60.50
57.98
41.89
29.76
26.03
13.14
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10

H
N
O
CO2Et
N
O
N
Me

6