Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

HFIP-mediated three-component imidization of electron-rich arenes with in situ formed spiroindolenines for facile construction of 2-arylspiroindolenines

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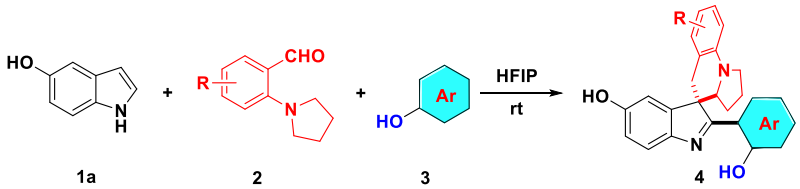
1. General Information

Unless otherwise noted, all reagents and solvents were purchased from the commercial sources and used as received. Thin layer chromatography (TLC) was used to monitor the reaction on Merck 60 F254 precoated silica gel plate (0.2 mm thickness). TLC spots were visualized by UV-light irradiation on Spectroline Model ENF-24061/F 254 nm. The products were purified by flash column chromatography (200-300 mesh silica gel) eluted with the gradient of petroleum ether and ethyl acetate. Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded on a Bruker 500 MHz NMR spectrometer ($CDCl_3$ or DMSO-d_6 solvent). The chemical shifts were reported in parts per million (ppm), downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-d (δ 7.26, singlet) or dimethyl sulfoxide-d_6 (δ 2.54, singlet). Multiplicities were afforded as: s (singlet); d (doublet); t (triplet); q (quartet); dd (doublets of doublet) or m (multiplets). The number of protons for a given resonance is indicated by nH. Coupling constants were reported as a *J* value in Hz. Carbon nuclear magnetic resonance spectra (^{13}C NMR) was referenced to the appropriate residual solvent peak. High resolution mass spectral analysis (HRMS) was performed on Waters XEVO G2 Q-TOF. All substituted 2-fluorobenzaldehydes, indole, 1-naphthol and sesamol were purchased from adamas-beta. All substituted *o*-aminobenzaldehydes[1] were prepared according to literature.

2. General Procedure

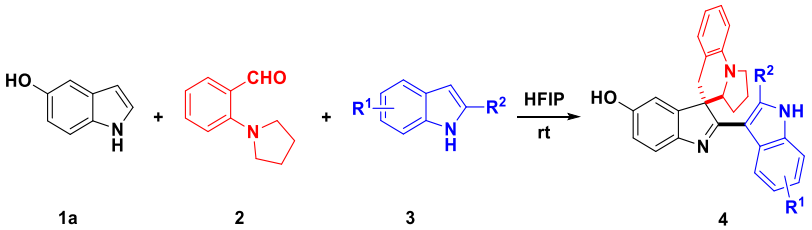
2.1 General Procedure for the Synthesis of 2-Arylspiroindolenine with the Employment of Phenols as Electron-rich Arenes



1a 2 3 4

A reaction tube was charged with 5-hydroxyindole **1a** (0.1 mmol), *o*-amino benzaldehyde **2** (0.13 mmol), phenol **3** (0.15 mmol) and HFIP (1.0 mL). The mixture was stirred at room temperature under an air atmosphere. Upon completion of the reaction as indicated by TLC analysis, the mixture was concentrated in vacuum and the residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:25) to afford the desired 2-arylspiroindolenine **4**.

2.2 General Procedure for the Synthesis of 2-Arylspiroindolenine with the Employment of Indoles as Electron-rich Arenes

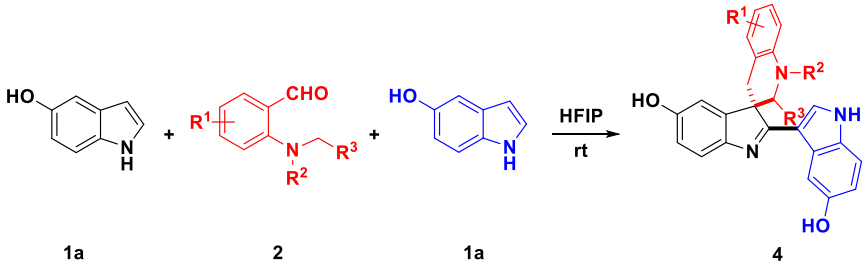


1a 2 3 4

A reaction tube was charged with 5-hydroxyindole **1a** (0.1 mmol), *o*-amino benzaldehyde **2** (0.13 mmol), indole **3** (0.15 mmol) and HFIP (1.0 mL). The mixture was stirred at room temperature under an air atmosphere. Upon completion of the reaction as indicated by TLC analysis, the mixture was concentrated in vacuum and the residue was directly purified by flash column chromatography on silica

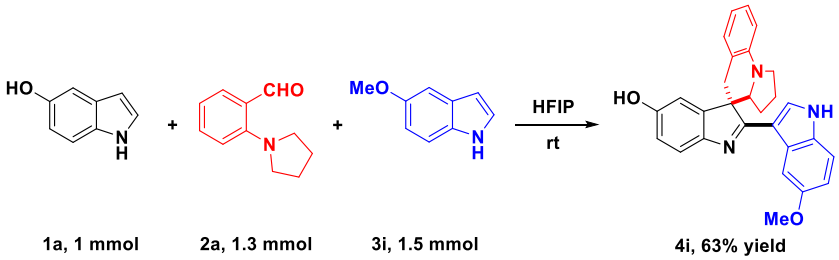
gel (eluent: ethyl acetate/petroleum ether, 1:15) to afford the desired 2-indolylspiroindolenine **4**.

2.3 General Procedure for the Synthesis of 2-Arylspiroindolenine with the Employment of 5-Hydroxyindole as Electron-rich Arene



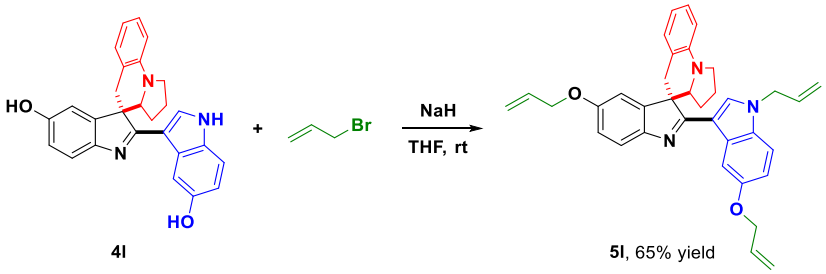
A reaction tube was charged with 5-hydroxyindole **1a** (0.24 mmol), *o*-amino benzaldehyde **2** (0.1 mmol), and HFIP (1.0 mL). The mixture was stirred at room temperature under an air atmosphere. Upon completion of the reaction as indicated by TLC analysis, the mixture was concentrated in vacuum and the residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:4) to afford the desired 2-indolylspiroindolenine **4**.

2.4 Large-scale synthesis



A round bottom flask was charged with 5-hydroxyindole **1a** (1.0 mmol), *o*-amino benzaldehyde **2a** (1.3 mmol), 5-methoxylindole **3i** (1.5 mmol) and HFIP (10.0 mL). The mixture was stirred at room temperature under an air atmosphere. Upon completion of the reaction as indicated by TLC analysis, the mixture was concentrated in vacuum and the residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:15) to afford the desired **4i** (286.9 mg, 63%) as a light yellow solid.

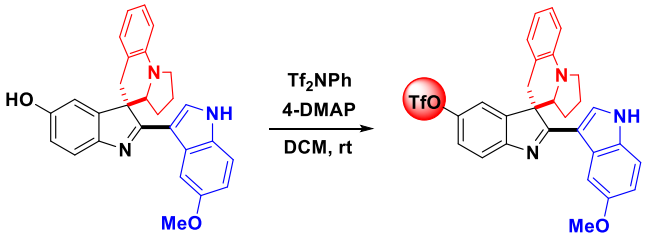
2.5 General Procedure for the Polyallylation of the Product 5l



To a 10 mL reaction tube was charged with **4l** (0.05 mmol), NaH (0.3 mmol), and dry THF (2.0 mL). The tube was stirred at room temperature. Upon completion of the reaction as indicated by TLC analysis, H_2O was added (5 mL) and the mixture was extracted with EtOAc (3 x 10 mL). Then the organic layers were dried with Na_2SO_4, and concentrated to dryness. The crude product was purified by silica gel

chromatography (eluent: ethyl acetate/petroleum ether, 1:25) to afford the polyallylated product **5l** in 65% yield as a light yellow solid.

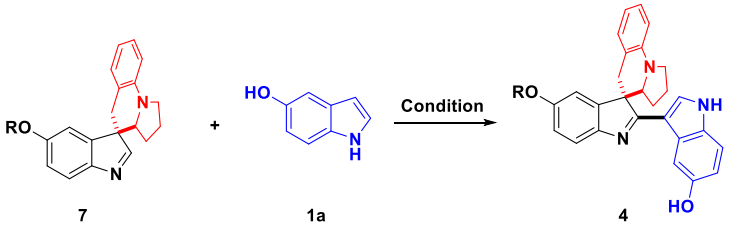
2.6 General Procedure for the Conversion of the Hydroxyl Group



4i **6i**, 68% yield

Compound **4i** (0.1 mmol) and 4-dimethylaminopyridine (0.3 mmol) were placed in a 10 mL Shrek tube. Then, the tube was purged with N_2 and CH_2Cl_2 (2 mL) was added. After 5 minutes, N-phenyl-bis(trifluoromethanesulfonimide) (0.2 mmol) was added and the mixture was stirred at room temperature. The reaction was monitored by thin layer chromatography eluting with CH_2Cl_2. When the starting material was consumed, H_2O was added (5 mL) and the mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine (30 mL) and dried under anhydrous Na_2SO_4. The organic solvents were removed under reduced pressure and the residue was purified by column chromatography eluting with (eluent: ethyl acetate/petroleum ether, 1:25) to afford the desired **6i** (53.9 mg, 68%) as a light yellow solid.

2.7 Control experiment



7 **1a** **4**

7a, R = H,	Condition: HFIP, rt	**4l**, 95%	(a)
7a, R = H,	Condition: HFIP, N_2, rt	**4l**, 30%	(b)
7a, R = H,	Condition: HFIP, O_2, rt	**4l**, 94%	(c)
7b, R = Me,	Condition: HFIP, rt	NR	(d)

Control experiment (a)

A reaction tube was charged with intermediate **7a** (0.1 mmol), 5-hydroxyindole **1a** (0.1 mmol), and HFIP (1.0 mL). The mixture was stirred at room temperature under an air atmosphere. Upon completion of the reaction as indicated by TLC analysis, the mixture was concentrated in vacuum and the residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:4) to afford the desired product **4l** in 95% yield as a light yellow solid.

Control experiment (b)

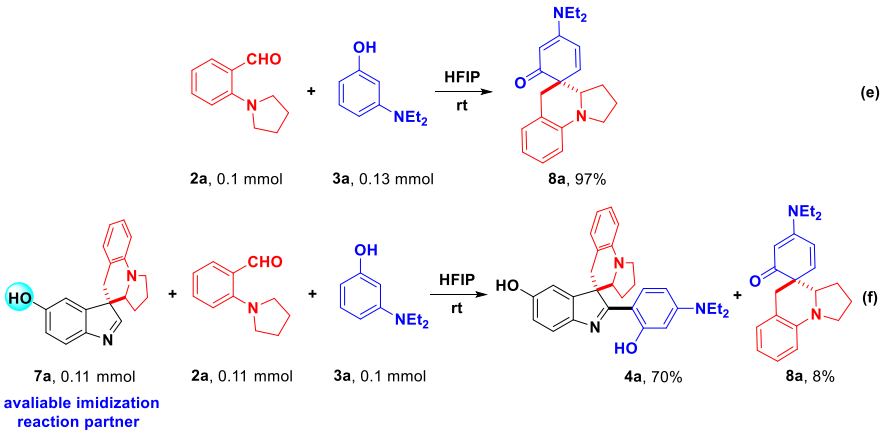
A reaction tube was charged with intermediate **7a** (0.1 mmol), 5-hydroxyindole **1a** (0.1 mmol), and HFIP (1.0 mL). The mixture was stirred at room temperature under N_2 atmosphere. Upon completion of the reaction as indicated by TLC analysis, the mixture was concentrated in vacuum and the residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:4) to afford the desired product **4l** in 30% yield as a light yellow solid.

Control experiment (c)

A reaction tube was charged with intermediate **7a** (0.1 mmol), 5-hydroxyindole **1a** (0.1 mmol), and HFIP (1.0 mL). The mixture was stirred at room temperature under O_2 atmosphere. Upon completion of the reaction as indicated by TLC analysis, the mixture was concentrated in vacuum and the residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:4) to afford the desired product **4l** in 94% yield as a light yellow solid.

Control experiment (d)

A reaction tube was charged with intermediate **7b**[2] (0.1 mmol), 5-hydroxyindole **1a** (0.1 mmol), and HFIP (1.0 mL). The mixture was stirred at room temperature under an air atmosphere. No reaction occurred by TLC analysis, albeit with prolonged reaction time.



Control experiment (e)

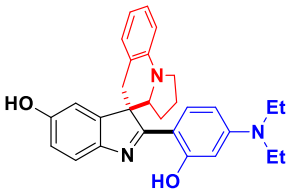
A reaction tube was charged with *o*-amino benzaldehyde **2a** (0.1 mmol), 3-aminophenol **3a** (0.13 mmol), and HFIP (1.0 mL). The mixture was stirred at room temperature under an air atmosphere. Upon completion of the reaction as indicated by TLC analysis, the mixture was concentrated in vacuum and the residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:8) to afford the product **8a** in 97% yield. And the structure of **8a** was determined by the literature[3].

Control experiment (f)

A reaction tube was charged with intermediate **7a** (0.11 mmol), *o*-amino benzaldehyde **2a** (0.11 mmol), 3-aminophenol **3a** (0.1 mmol), and HFIP (1.0 mL). The mixture was stirred at room temperature under an air atmosphere. Upon completion of the reaction as indicated by TLC analysis, the mixture was concentrated in vacuum and the residue was directly purified by flash column chromatography on silica gel (eluent: ethyl acetate/petroleum ether, 1:25) to afford the product **4a** in 70% yield and **8a** (eluent: ethyl acetate/petroleum ether, 1:8) in 8% yield.

3. Characterization of Products

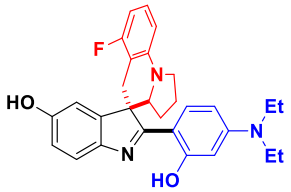
2-(4-(diethylamino)-2-hydroxyphenyl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4a)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:25) afforded the product (33.6 mg, 71% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, *J* = 9.1 Hz, 1H), 7.25 (d, *J* = 8.3 Hz, 1H), 7.19 – 7.14 (m, 2H), 6.96 (d, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 8.2 Hz, 1H), 6.60 (t, *J* = 7.3 Hz, 1H), 6.55 (d, *J* = 8.1 Hz, 1H), 6.24 (s, 1H), 6.12 (d, *J* = 8.9 Hz, 1H), 6.08 (s, 1H), 4.25 (dd, *J* = 9.3, 5.9 Hz, 1H), 3.81 (d, *J* = 16.6 Hz, 1H), 3.41 (dd, *J* = 8.6, 6.4 Hz, 1H), 3.31 (q, *J* = 6.9 Hz, 4H), 3.25 (dd, *J* = 16.6, 8.3 Hz, 1H), 2.66 (d, *J* = 16.6 Hz, 1H), 1.75 (dd, *J* = 19.5, 8.2 Hz, 2H), 1.59 – 1.51 (m, 2H), 1.13 (t, *J* = 7.0 Hz, 6H), 0.70 – 0.61 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 178.0, 164.5, 153.4, 150.9, 144.1, 140.1, 129.8, 129.3, 127.9, 118.5, 118.1, 116.0, 114.7, 111.9, 110.6, 105.2, 103.1, 98.9, 61.7, 57.6, 47.3, 44.4, 44.4, 36.5, 29.7, 26.9, 23.1, 12.8, 12.8. **HRMS (ESI):** calcd. for $C_{29}H_{32}N_3O_2$ [M+H]$^+$: 454.2489, found: 454.2490.

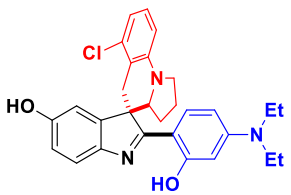
2-(4-(diethylamino)-2-hydroxyphenyl)-6'-fluoro-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4b)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:25) afforded the product (36.3 mg, 74% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (d, *J* = 9.0 Hz, 1H), 7.23 – 7.15 (m, 2H), 7.04 (dd, *J* = 14.3, 7.1 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 6.31 (dd, *J* = 16.9, 8.3 Hz, 2H), 6.21 (s, 1H), 6.13 (d, *J* = 9.9 Hz, 2H), 4.25 – 4.16 (m, 1H), 3.52 (d, *J* = 17.2 Hz, 1H), 3.39 (t, *J* = 8.1 Hz, 1H), 3.29 (d, *J* = 6.8 Hz, 4H), 3.22 (dd, *J* = 16.4, 8.1 Hz, 1H), 2.85 (d, *J* = 17.1 Hz, 1H), 1.71 (dd, *J* = 18.3, 8.8 Hz, 2H), 1.58 – 1.51 (m, 2H), 1.18 (s, 1H), 1.10 (t, *J* = 6.6 Hz, 6H), 0.71 – 0.63 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.7, 164.6, 162.0 (d, *J* = 237.5 Hz), 153.5, 151.0, 145.5, 145.4 (d, *J* = 3.75 Hz), 140.0, 129.2, 128.4 (d, *J* = 11.2 Hz), 118.5, 114.9, 111.7, 106.3, 105.4 (d, *J* = 20 Hz), 105.0, 103.3, 102.7 (d, *J* = 22.5 Hz), 98.9, 61.3, 56.7, 47.7, 44.4, 44.4, 29.6, 26.9, 23.0, 12.8, 12.8. **HRMS (ESI):** calcd. for $C_{29}H_{31}FN_3O_2$ [M+H]$^+$: 472.2395, found: 472.2407.

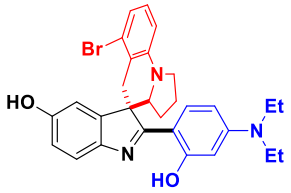
6'-chloro-2-(4-(diethylamino)-2-hydroxyphenyl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4c)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:25) afforded the product (28.9 mg, 57% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 9.0 Hz, 1H), 7.27 (d, *J* = 8.2 Hz, 1H), 7.19 (s, 1H), 7.07 (t, J = 8.0 Hz, 1H), 6.72 – 6.67 (m, 2H), 6.47 (d, *J* = 8.2 Hz, 1H), 6.25 (s, 1H), 6.15 (d, *J* = 9.3 Hz, 2H), 4.25 – 4.17 (m, 1H), 3.57 (d, *J* = 17.6 Hz, 1H), 3.40 (t, *J* = 8.6 Hz, 1H), 3.32 (dd, *J* = 13.9, 7.0 Hz, 4H), 3.29 – 3.24 (m, 1H), 2.93 (d, *J* = 17.6 Hz, 1H), 1.74 (dd, *J* = 17.4, 8.3 Hz, 2H), 1.66 (m, 2H), 1.13 (t, *J* = 6.8 Hz, 6H), 0.67 (dd, *J* = 20.4, 10.1 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.8, 164.4, 153.2, 150.9, 146.1, 145.3, 135.3, 129.2, 128.3, 118.7, 116.9, 116.3, 114.8, 114.2, 111.6, 109.1, 104.9, 103.1, 98.9, 61.2, 57.5, 47.6, 44.4, 44.4, 34.4, 26.9, 23.1, 12.8, 12.8. **HRMS (ESI):** calcd. for $C_{29}H_{31}ClN_3O_2$ $[M+H]^+$: 488.2099, found: 488.2085.

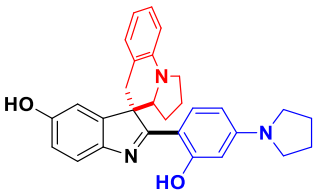
6'-bromo-2-(4-(diethylamino)-2-hydroxyphenyl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4d)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:25) afforded the product (36.4 mg, 66% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 9.1 Hz, 1H), 7.27 (d, *J* = 8.3 Hz, 1H), 7.19 (s, 2H), 7.01 (t, *J* = 8.0 Hz, 1H), 6.88 (d, *J* = 7.9 Hz, 1H), 6.70 (d, *J* = 8.1 Hz, 1H), 6.51 (d, *J* = 8.2 Hz, 1H), 6.25 (d, *J* = 1.9 Hz, 1H), 6.15 (d, *J* = 14.1 Hz, 2H), 4.20 (dd, *J* = 9.2, 6.0 Hz, 1H), 3.56 (d, *J* = 17.5 Hz, 1H), 3.40 (td, *J* = 8.8, 3.0 Hz, 1H), 3.33 (q, *J* = 7.1 Hz, 4H), 3.30 – 3.25 (m, 1H), 2.90 (d, *J* = 17.5 Hz, 1H), 1.81 – 1.68 (m, 2H), 1.53 (m, 2H), 1.14 (t, *J* = 7.0 Hz, 6H), 0.72 – 0.64 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 177.7, 164.4, 153.1, 150.9, 145.4, 140.4, 129.2, 129.0, 128.7, 126.2, 120.1, 118.7, 117.8, 114.8, 111.5, 109.8, 104.9, 103.2, 98.9, 61.2, 57.9, 47.6, 44.4, 44.4, 37.3, 26.8, 23.1, 12.8, 12.8. **HRMS (ESI):** calcd. for $C_{29}H_{31}BrN_3O_2$ $[M+H]^+$: 532.1594, found: 532.1585.

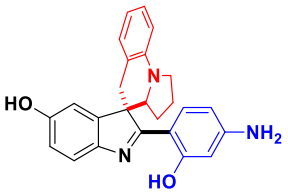
(2-hydroxy-4-(pyrrolidin-1-yl)phenyl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4e)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:25) afforded the product (28.3 mg, 60% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.9 Hz, 1H), 7.25 (d, *J* = 8.3 Hz, 1H), 7.16 (m, 2H), 6.96 (d, *J* = 7.4 Hz, 1H), 6.70 – 6.66 (m, 1H), 6.60 (t, *J* = 7.3 Hz, 1H), 6.55 (d, *J* = 8.1 Hz, 1H), 6.14 (s, 1H), 6.08 (s, 1H), 6.04 (d, *J* = 8.9 Hz, 1H), 4.25 (m, 1H), 3.82 (d, *J* = 16.6 Hz, 1H), 3.45 – 3.37 (m, 1H), 3.27 (d, *J* = 11.5 Hz, 5H), 2.67 (d, *J* = 16.6 Hz, 1H), 1.95 (d, *J* = 15.9 Hz, 4H), 1.72 (m, 2H), 1.52 (m, 2H), 0.65 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 178.3, 164.3, 153.2, 150.6, 145.8, 144.1, 140.2, 129.8, 129.2, 128.0, 118.6, 118.1, 116.0, 114.7, 111.8, 110.6, 105.4, 103.6, 99.4, 61.7, 57.6, 47.5, 47.5, 47.3, 36.4, 26.9 , 25.5, 25.5, 23.1. **HRMS (ESI):** calcd. for $C_{29}H_{30}N_3O_2$ $[M+H]^+$: 452.2333, found: 452.2325.

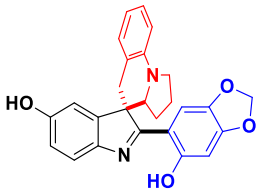
2-(4-amino-2-hydroxyphenyl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4f)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:25) afforded the product (27.5 mg, 66% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.7 Hz, 1H), 7.27 (d, *J* = 8.3 Hz, 1H), 7.19 (m, 2H), 6.96 (d, *J* = 7.3 Hz, 1H), 6.69 (d, *J* = 8.3 Hz, 1H), 6.60 (t, *J* = 7.3 Hz, 1H), 6.55 (d, *J* = 8.1 Hz, 1H), 6.27 (s, 1H), 6.10 (d, *J* = 7.7 Hz, 2H), 4.23 (m, 1H), 4.08 – 3.96 (m, 2H), 3.84 – 3.78 (m,1H), 3.41 (m, 1H), 3.25 (m, 1H), 2.65 (d, *J* = 16.6 Hz, 1H), 1.76 (m, 2H), 1.52 (m, 2H), 1.20 (d, *J* = 22.0 Hz, 2H), 0.72 – 0.59 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 178.3, 164.5, 153.6, 150.5, 145.3, 144.0, 140.3, 129.8, 129.5, 128.0, 119.0, 117.9, 116.1, 114.8, 111.8, 110.6, 107.7, 106.2, 102.6, 61.6, 57.8, 47.3, 36.3, 26.9, 23.0. **HRMS (ESI):** calcd. for $C_{25}H_{24}N_3O_2$ $[M+H]^+$: 398.1863, found: 398.1857.

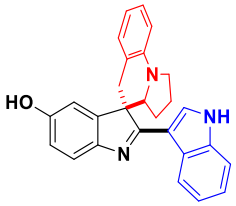
2-(6-hydroxybenzo[d][1,3]dioxol-5-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4g)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:25) afforded the product (27.7mg, 62% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 15.27 (s, 1H), 9.40 (s, 1H), 7.38 (d, *J* = 8.3 Hz, 1H), 7.31 (s, 1H), 7.21 (t, *J* = 7.7 Hz, 1H), 7.02 (d, *J* = 7.3 Hz, 1H), 6.72 (dd, *J* = 8.3, 1.9 Hz, 1H), 6.68 (d, *J* = 6.7 Hz, 2H), 6.63 (t, *J* = 7.3 Hz, 1H), 6.07 (d, *J* = 1.9 Hz, 1H), 6.04 (d, *J* = 5.1 Hz, 2H), 4.42 (dd, *J* = 9.5, 5.9 Hz, 1H), 3.84 (d, *J* = 16.3 Hz, 1H), 3.50 (dd, *J* = 9.0, 7.1 Hz, 1H), 3.23 (q, *J* = 8.4 Hz, 1H), 2.60 (d, *J* = 16.4 Hz, 1H), 1.89 – 1.80 (m, 1H), 1.75 (dd, *J* = 12.3, 5.3 Hz, 1H), 1.47 (dt, *J* = 12.0, 5.9 Hz, 1H), 0.56 (dd, *J* = 19.5, 10.2 Hz, 1H); **^{13}C NMR** (125 MHz, DMSO) δ 178.0, 160.2, 156.1, 151.1, 144.3, 143.4, 140.6, 129.7, 128.2, 119.4, 118.1, 116.0, 115.1, 112.3, 111.1, 107.6, 106.3, 102.1, 99.4, 60.6, 58.1, 47.4, 35.9, 26.9, 26.8, 22.9. **HRMS (ESI):** calcd. for $C_{26}H_{23}N_2O_4$ $[M+H]^+$: 427.1652, found: 427.1645.

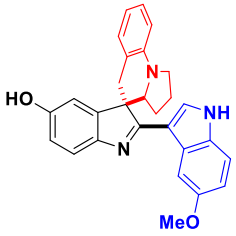
2-(1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4h)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) afforded the product (26.8 mg, 68% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.78 (s, 1H), 9.07 (s, 1H), 8.74 (d, *J* = 7.6 Hz, 1H), 8.19 (s, 1H), 7.46 (d, *J* = 7.7 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 1H), 7.26 – 7.17 (m, 3H), 7.01 (d, *J* = 7.3 Hz, 1H), 6.67 (dd, *J* = 15.5, 8.2 Hz, 2H), 6.60 (t, *J* = 7.3 Hz, 1H), 6.02 (s, 1H), 4.35 (dd, *J* = 9.3, 6.0 Hz, 1H), 3.77 (d, *J* = 15.9 Hz, 1H), 3.52 (t, *J* = 8.5 Hz, 1H), 3.22 (dd, *J* = 16.9, 8.5 Hz, 1H), 2.55 (s, 1H), 1.79 (dd, *J* = 21.0, 9.2 Hz, 2H), 1.42 (m, 1H), 0.66 – 0.46 (m, 1H); **^{13}C NMR** (125 MHz, DMSO) δ 174.9, 154.6, 149.1, 144.6, 141.4, 136.8, 129.6, 129.2, 128.1, 126.9, 123.9, 123.0, 121.1, 119.8, 119.2, 115.6, 114.5, 111.9, 111.8, 110.7, 109.5, 62.7, 57.1, 47.7, 38.2, 27.0, 23.2. **HRMS (ESI):** calcd. for $C_{27}H_{24}N_3O$ $[M+H]^+$: 406.1914, found: 406.1906.

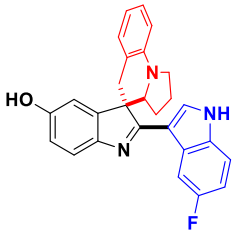
2-(5-methoxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4i)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) afforded the product (28.2 mg, 62% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.63 (d, *J* = 2.0 Hz, 1H), 9.09 (s, 1H), 8.31 (d, *J* = 2.5 Hz, 1H), 8.11 (d, *J* = 2.9 Hz, 1H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.19 (s, 1H), 7.01 (d, *J* = 7.3 Hz, 1H), 6.89 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.68 (dd, *J* = 8.2, 2.4 Hz, 1H), 6.64 (d, *J* = 8.1 Hz, 1H), 6.60 (t, *J* = 7.3 Hz, 1H), 6.01 (d, *J* = 2.4 Hz, 1H), 4.32 (dd, *J* = 9.6, 5.9 Hz, 1H), 3.85 (s, 3H), 3.74 (d, *J* = 15.9 Hz, 1H), 3.21 (d, *J* = 8.1 Hz, 1H), 2.51 (dd, *J* = 3.6, 1.9 Hz, 2H), 1.84 – 1.70 (m, 2H), 1.41 (m, 1H), 0.63 – 0.53 (m, 1H); **^{13}C NMR** (125 MHz, DMSO) δ 175.0, 155.2, 154.5, 149.0, 144.5, 141.3, 131.9, 129.6, 129.5, 128.1, 127.5, 119.8, 119.1, 115.6, 114.5, 112.7, 112.6, 111.9, 110.7, 109.3, 106.1, 62.7, 57.1, 55.9, 47.7, 38.2, 27.0, 23.2. **HRMS (ESI):** calcd. for $C_{28}H_{26}N_3O_2$ $[M+H]^+$: 436.2020, found: 436.2014.

2-(5-fluoro-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4j)

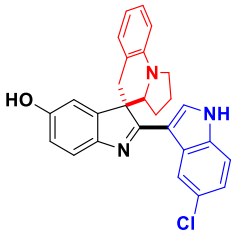


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) afforded the product (26.6 mg, 60% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.87 (s, 1H), 9.16 (s, 1H), 8.47 – 8.42 (m, 1H), 8.23 (d, *J* = 2.8 Hz, 1H), 7.48 (dd, *J* = 8.8, 4.7 Hz, 1H), 7.39 (d, *J* = 8.2 Hz, 1H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.12 – 7.07 (m, 1H), 7.00 (d, *J* = 7.3 Hz, 1H), 6.69 (dd, *J* = 8.2, 2.4 Hz, 1H), 6.64 (d, *J* = 8.1 Hz, 1H), 6.59 (t, *J* = 7.3 Hz, 1H), 6.00 (d, *J* = 2.3 Hz, 1H), 4.32 (dd, *J* = 9.6, 5.9 Hz, 1H), 3.72 (s, 1H), 3.50 (d, *J* = 7.0 Hz, 1H), 3.20 (q, *J* = 8.7 Hz, 1H), 2.54 (s, 1H), 1.82 – 1.70 (m, 2H), 1.40 (m, 1H), 0.55 (dd, *J* = 19.2, 10.2 Hz, 1H); **^{13}C NMR** (125 MHz, DMSO) δ 174.7, 158.5 (d, *J* =230.0 Hz), 154.7, 148.9, 144.5, 141.3, 133.5, 130.8,

129.6, 128.2, 127.2 (d, *J* =11.3 Hz), 119.9, 119.0, 115.7, 114.5, 113.1 (d, *J* =10.0 Hz), 111.9, 111.2 (d, *J* =26.3 Hz), 110.7, 109.6 (d, *J* =3.8 Hz), 108.4 (d, *J* =23.8 Hz), 62.6, 57.1, 47.7, 38.0, 26.9, 23.2. **HRMS (ESI) :** calcd. for $C_{27}H_{23}FN_3O$ $[M+H]^+$: 424.1820, found: 424.1807.

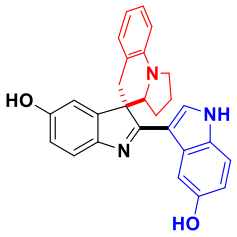
2-(5-chloro-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4k)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) afforded the product (25.3 mg, 55% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.98 (s, 1H), 9.10 (s, 1H), 8.75 (s, 1H), 8.28 (s, 1H), 7.48 (d, *J* = 8.6 Hz, 1H), 7.41 (d, *J* = 8.2 Hz, 1H), 7.25 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.01 (d, *J* = 7.2 Hz, 1H), 6.69 (dd, *J* = 8.3, 2.3 Hz, 1H), 6.65 (d, *J* = 8.1 Hz, 1H), 6.60 (t, *J* = 7.3 Hz, 1H), 6.02 (s, 1H), 4.33 (dd, *J* = 9.6, 5.9 Hz, 1H), 3.76 (d, *J* = 15.9 Hz, 1H), 3.52 (t, *J* = 7.8 Hz, 1H), 3.25 – 3.19 (m, 1H), 2.55 (s, 1H), 1.83 – 1.74 (m, 2H), 1.44 – 1.37 (m, 1H), 0.62 – 0.53 (m, 1H); **^{13}C NMR** (125 MHz, DMSO) δ 174.5, 154.8, 148.8, 144.5, 141.3, 135.4, 130.6, 129.6, 128.2, 127.9, 125.8, 122.9, 122.8, 120.0, 119.1, 115.6, 114.5, 113.6, 111.9, 110.7, 109.2, 62.6, 57.2, 47.7, 37.9, 26.9, 23.2. **HRMS (ESI):** calcd. for $C_{27}H_{23}ClN_3O$ $[M+H]^+$: 440.1524, found: 440.1503.

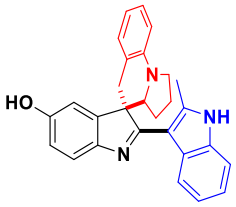
2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4l)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) afforded the product (37.5 mg, 85% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.54 (s, 1H), 9.06 (s, 1H), 8.93 (s, 1H), 8.17 (s, 1H), 8.08 (s, 1H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.27 (d, *J* = 8.6 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.02 (d, *J* = 7.1 Hz, 1H), 6.79 – 6.73 (m, 1H), 6.72 – 6.68 (m, 1H), 6.64 (d, *J* = 8.1 Hz, 1H), 6.60 (t, *J* = 7.3 Hz, 1H), 6.04 (s, 1H), 4.32 (dd, *J* = 9.1, 6.1 Hz, 1H), 3.76 (d, *J* = 16.0 Hz, 1H), 3.51 (t, *J* = 8.0 Hz, 1H), 3.22 (d, *J* = 8.3 Hz, 1H), 2.52 (d, *J* = 5.7 Hz, 1H), 1.78 (dd, *J* = 21.1, 9.2 Hz, 2H), 1.48 – 1.37 (m, 1H), 0.65 – 0.53 (m, 1H); **^{13}C NMR** (125 MHz, DMSO) δ 174.9, 154.6, 149.1, 144.6, 141.4, 136.8, 129.6, 129.2, 128.1,126.9, 123.9, 122.9, 121.1, 119.8, 119.2, 115.6, 114.5, 112.0, 111.9, 110.7, 109.5, 62.7, 57.1, 47.7, 38.2, 26.9, 23.2. **HRMS (ESI):** calcd. for $C_{27}H_{24}N_3O_2$ $[M+H]^+$: 422.1863, found: 422.1853.

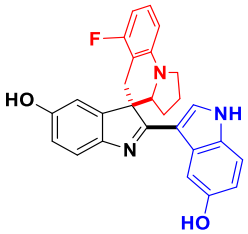
2-(2-methy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4m)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:15) afforded the product (22.4 mg, 51% yield, dr 4:1) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 10.77 (d, *J* = 21.5 Hz, 1H), 8.62 (s, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.24 (dd, *J* = 7.5, 0.8 Hz, 1H), 7.22 (d, *J* = 2.7 Hz, 1H), 7.20 (d, *J* = 8.9 Hz, 1H), 7.17 (t, *J* = 7.9 Hz, 1H), 6.95 (d, *J* = 7.2 Hz, 1H), 6.91 (d, *J* = 7.2 Hz, 1H), 6.88 (d, *J* = 2.2 Hz, 1H), 6.63 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.60 – 6.56 (m, 2H), 6.41 (d, *J* = 7.4 Hz, 1H), 6.27 – 6.21 (m, 1H), 4.04 – 3.96 (m, 1H), 3.10 (dd, *J* = 16.5, 9.1 Hz, 1H), 2.53 – 2.49 (m, 1H), 2.28 (s, 3H), 1.82 (m, 1H), 1.73 – 1.67 (m, 1H), 1.61 (m, 1H), 0.45 – 0.36 (m, 1H); **^{13}C NMR** (125 MHz, DMSO) δ 184.9, 155.5, 151.0, 144.3, 139.6, 130.9, 129.6, 128.9, 128.9, 128.1, 125.9, 125.1, 123.7, 119.8, 118.3, 115.8, 112.1, 111.7, 110.5, 104.3, 100.7, 61.0, 56.2, 47.6, 35.7, 26.7, 23.3, 16.4. **HRMS (ESI):** calcd. for $C_{28}H_{26}N_3O$ $[M+H]^+$**:** 420.2070, found: 420.2099.

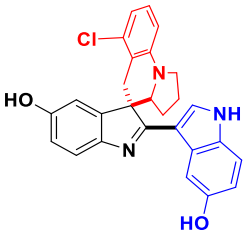
6'-fluoro-2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4n)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:4) afforded the product (35.7 mg, 78% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.54 (d, *J* = 2.4 Hz, 1H), 9.14 (s, 1H), 8.96 (s, 1H), 8.11 (dd, *J* = 13.4, 2.7 Hz, 2H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.26 (d, *J* = 8.6 Hz, 1H), 7.21 (dd, *J* = 15.2, 8.0 Hz, 1H), 6.72 (m, 2H), 6.50 (d, *J* = 8.2 Hz, 1H), 6.44 (t, *J* = 8.7 Hz, 1H), 6.03 (d, *J* = 2.4 Hz, 1H), 4.29 (dd, *J* = 9.6, 6.0 Hz, 1H), 3.58 – 3.53 (m, 2H), 3.21 (dd, *J* = 16.8, 8.9 Hz, 1H), 2.61 (d, *J* = 15.7 Hz, 1H), 1.83 – 1.69 (m, 2H), 1.43 (dt, *J* = 12.0, 5.8 Hz, 1H), 0.62 – 0.52 (m, 1H); **^{13}C NMR** (125 MHz, DMSO) δ 174.7, 161.5 (d, *J* = 237.5 Hz), 154.6, 152.7, 149.1, 146.1 (d, *J* = 7.5 Hz), 141.1, 131.2, 129.4, 128.9 (d, *J* = 11.3 Hz), 127.7, 119.6, 114.7, 113.1, 112.3, 111.5, 108.7, 108.1, 106.9, 106.0 (d, *J* = 20.0 Hz), 102.1 (d, *J* = 22.5 Hz), 62.2, 56.1, 48.1, 31.1, 26.9, 23.1. **HRMS (ESI):** calcd. for $C_{27}H_{23}FN_3O_2$ $[M+H]^+$: 440.1769, found: 440.1753.

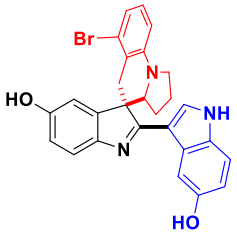
6'-chloro-2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4o)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:4) afforded the product (32.4 mg, 68% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.52 (d, *J* = 2.1 Hz, 1H), 9.20 (s, 1H), 9.02 (s, 1H), 8.11 (d, *J* = 2.4 Hz, 1H), 8.07 (d, *J* = 2.9 Hz, 1H), 7.36 (d, *J* = 8.3 Hz, 1H), 7.28 (d, *J* = 8.6 Hz, 1H), 7.20 (t, *J* = 8.1 Hz, 1H), 6.74 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.72 (d, *J* = 2.8 Hz, 1H), 6.70 (d, *J* = 2.7 Hz, 1H), 6.63 (d, *J* = 8.2 Hz, 1H), 6.04 (d, *J* = 2.4 Hz, 1H), 4.29 (dd, *J* = 9.5, 6.0 Hz, 1H), 3.50 (dd, *J* = 16.1, 12.3 Hz, 2H), 3.22 (dd, *J* = 17.0, 8.7 Hz, 1H), 2.68 (d, *J* = 16.7 Hz, 1H), 1.83 – 1.70 (m, 2H), 1.44 (dt, *J* = 11.5, 5.8 Hz, 1H), 0.59 (dd, *J* = 19.2, 10.3 Hz, 1H); **^{13}C NMR** (125 MHz, DMSO) δ 174.6, 154.5, 152.7, 149.1, 146.0, 141.2, 134.1, 131.2, 129.4, 129.0, 127.6, 119.7, 116.6, 115.9, 114.8, 113.2, 112.4, 111.5, 109.8, 108.7, 108.1, 62.1, 56.8, 48.0, 36.3, 27.0, 23.2. **HRMS (ESI):** calcd. for $C_{27}H_{23}ClN_3O_2$ $[M+H]^+$: 456.1473, found: 456.1455.

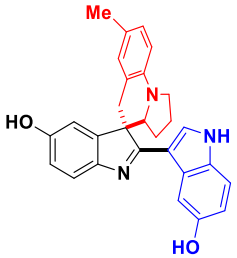
6'-bromo-2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4p)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:4) afforded the product (36.5 mg, 70% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.56 (d, *J* = 2.3 Hz, 1H), 9.13 (s, 1H), 8.93 (s, 1H), 8.13 (s, 2H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.26 (d, *J* = 8.6 Hz, 1H), 7.14 (t, *J* = 8.1 Hz, 1H), 6.88 (d, *J* = 7.7 Hz, 1H), 6.75 – 6.67 (m, 3H), 6.06 (d, *J* = 2.3 Hz, 1H), 4.33 (dd, *J* = 9.5, 6.0 Hz, 1H), 3.56 – 3.49 (m, 2H), 3.24 (dd, *J* = 17.1, 8.7 Hz, 1H), 2.66 (d, *J* = 16.6 Hz, 1H), 1.87 – 1.73 (m, 2H), 1.45 (m, 1H), 0.65 – 0.53 (m, 1H); **^{13}C NMR** (125 MHz, DMSO) δ 174.5, 154.6, 152.8, 149.1, 146.1, 141.2, 131.2, 129.5, 129.4, 127.7, 125.4, 119.7, 119.1, 118.3, 114.8, 113.1, 112.3, 111.5, 110.3, 108.7, 108.1, 62.1, 57.0, 48.0, 39.3, 26.9, 23.3. **HRMS (ESI):** calcd. for $C_{27}H_{23}BrN_3O_2$ $[M+H]^+$: 500.0968, found: 500.0954.

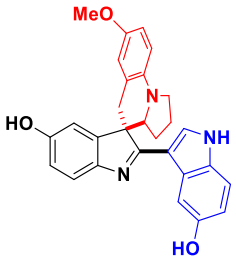
5'-methyl-2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4q)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:4) afforded the product (31.9 mg, 70% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.51 (s, 1H), 9.05 (s, 1H), 8.92 (s, 1H), 8.15 (d, *J* = 2.4 Hz, 1H), 8.03 (d, *J* = 2.0 Hz, 1H), 7.36 – 7.30 (m, 1H), 7.26 (d, *J* = 8.6 Hz, 1H), 7.00 (d, *J* = 8.2 Hz, 1H), 6.84 (s, 1H), 6.73 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.69 (dd, *J* = 8.2, 2.4 Hz, 1H), 6.55 (d, *J* = 8.2 Hz, 1H), 6.04 (d, *J* = 2.4 Hz, 1H), 4.27 (dd, *J* = 9.5, 6.0 Hz, 1H), 3.71 (d, *J* = 16.1 Hz, 1H), 3.50 – 3.44 (m, 1H), 3.20 (q, *J* = 8.5 Hz, 1H), 2.53 – 2.50 (m, 1H), 2.20 (s, 3H), 1.84 – 1.67 (m, 2H), 1.40 (m, 1H), 0.59 (dd, *J* = 19.2, 10.3 Hz, 1H); **^{13}C NMR** (125 MHz, DMSO) δ 175.1, 154.4, 152.7, 149.2, 142.5, 141.4, 131.1, 130.2, 129.2, 128.5, 127.8, 123.8, 119.4, 119.2, 114.4, 113.0, 112.3, 112.0, 110.8, 109.0, 108.2, 62.8, 57.3, 47.7, 38.2, 27.0, 23.2, 20.6. **HRMS (ESI):** calcd. for $C_{28}H_{26}N_3O_2$ $[M+H]^+$: 436.2020, found: 436.2015.

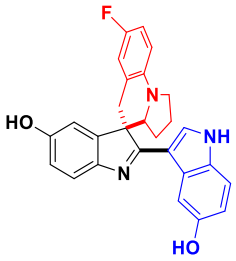
5'-methoxyl-2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4r)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:4) afforded the product (34.5 mg, 73% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.51 (s, 1H), 9.03 (s, 1H), 8.90 (s, 1H), 8.13 (s, 1H), 8.04 (d, *J* = 2.8 Hz, 1H), 7.32 (d, *J* = 8.2 Hz, 1H), 7.25 (d, *J* = 8.6 Hz, 1H), 6.82 (dd, *J* = 8.7, 2.9 Hz, 1H), 6.72 (dd, *J* = 8.8, 2.4 Hz, 2H), 6.68 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.59 (d, *J* = 8.8 Hz, 1H), 6.06 (d, *J* = 2.1 Hz, 1H), 4.24 (dd, *J* = 9.3, 6.0 Hz, 1H), 3.72 (d, *J* = 16.2 Hz, 1H), 3.67 (s, 3H), 3.47 – 3.42 (m, 1H), 3.27 – 3.19 (m, 1H), 2.54 (s, 1H), 1.82 – 1.66 (m, 2H), 1.40 (m, 1H), 0.61 – 0.50 (m, 1H); **^{13}C NMR** (125 MHz, DMSO) δ 175.1, 154.4, 152.7, 150.5, 149.2, 141.5, 139.2, 131.1, 129.3, 127.8, 120.4, 119.4, 115.6, 114.4, 113.7, 113.0, 112.3, 112.0, 111.5, 109.0, 108.2, 62.9, 57.4, 55.7, 48.0, 38.4, 26.9, 23.2. **HRMS (ESI):** calcd. for $C_{28}H_{26}N_3O_3$ $[M+H]^+$: 452.1969, found: 452.1985.

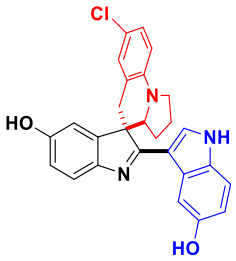
5'-fluoro-2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4s)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:4) afforded the product (33.9 mg, 74% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.51 (s, 1H), 9.12 (t, *J* = 4.1 Hz, 1H), 8.98 (t, *J* = 4.1 Hz, 1H), 8.11 (s, 1H), 8.04 (s, 1H), 7.34 (dt, *J* = 8.3, 4.3 Hz, 1H), 7.27 (dt, *J* = 8.6, 4.2 Hz, 1H), 7.03 (dd, *J* = 11.8, 5.5 Hz, 1H), 6.93 (d, *J* = 9.1 Hz, 1H), 6.76 – 6.71 (m, 1H), 6.69 (dt, *J* = 8.3, 2.6 Hz, 1H), 6.61 (dd, *J* = 6.9, 4.1 Hz, 1H), 6.00 (d, *J* = 2.4 Hz, 1H), 4.29 – 4.25 (m, 1H), 3.73 (s, 2H), 3.22 – 3.16 (m, 1H), 2.56 (s, 1H), 1.77 (dd, *J* = 21.3, 12.4 Hz, 2H), 1.40 (s, 1H), 0.61 – 0.51 (m, 1H); **^{13}C NMR** (125 MHz, DMSO) δ 174.9, 154.4, 154.2 (d, *J* = 220.3 Hz), 152.6, 149.2, 141.4, 141.1, 131.1, 129.3, 127.7, 120.7 (d, *J* = 7.5 Hz), 119.5, 116.1 (d, *J* = 22.5 Hz), 114.5, 114.2 (d, *J* = 21.3 Hz), 113.1, 112.3, 111.8, 111.1 (d, *J* = 8.8 Hz), 108.8, 108.1, 62.8, 56.8, 48.1, 38.1, 26.9, 23.2. **HRMS (ESI):** calcd. for $C_{27}H_{23}FN_3O_2$ $[M+H]^+$: 440.1769, found: 440.1753.

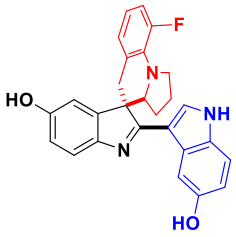
5'-chloro-2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4t)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:4) afforded the product (28.6 mg, 60% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.52 (d, *J* = 2.4 Hz, 1H), 9.13 (s, 1H), 8.97 (s, 1H), 8.11 (d, *J* = 2.4 Hz, 1H), 8.05 (d, *J* = 3.0 Hz, 1H), 7.34 (d, *J* = 8.2 Hz, 1H), 7.26 (d, *J* = 8.6 Hz, 1H), 7.20 (dd, *J* = 8.6, 2.4 Hz, 1H), 7.08 (d, *J* = 2.3 Hz, 1H), 6.73 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.69 (dd, *J* = 8.3, 2.4 Hz, 1H), 6.62 (d, *J* = 8.8 Hz, 1H), 5.97 (d, *J* = 2.4 Hz, 1H), 4.30 (dd, *J* = 9.7, 5.9 Hz, 1H), 3.70 (d, *J* = 16.2 Hz, 1H), 3.17 (dd, *J* = 16.8, 8.9 Hz, 1H), 2.55 (d, *J* = 16.4 Hz, 1H), 1.83 – 1.70 (m, 2H), 1.44 – 1.37 (m, 1H), 0.61 – 0.52 (m, 1H); **^{13}C NMR** (125 MHz, DMSO) δ 174.7, 154.5, 152.7, 149.2, 143.4, 141.0, 131.1, 129.3, 129.0, 127.7, 127.6, 121.3, 119.6, 118.9, 114.6, 113.1, 112.3, 111.9, 111.7, 108.8, 108.1, 62.8, 56.6, 47.9,37.9, 26.9, 23.2. **HRMS (ESI):** calcd. for $C_{27}H_{23}ClN_3O_2$ $[M+H]^+$: 456.1473, found:456.1457.

3'-fluoro-2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4u)

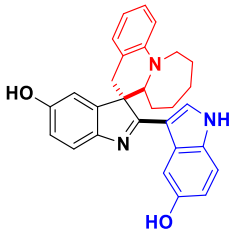


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:4) afforded the product (34.4 mg, 75% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.52 (s, 1H), 9.14 (s, 1H), 8.96 (s, 1H), 8.13 (d, *J* = 2.1 Hz, 1H), 8.08 (d, *J* = 2.8 Hz, 1H), 7.35 (d, *J* = 8.2 Hz, 1H), 7.26 (d, *J* = 8.6 Hz, 1H), 7.06 (dd, *J* = 14.0, 8.1 Hz, 1H), 6.89 (d, *J* = 7.4 Hz, 1H), 6.74 – 6.68 (m, 2H), 6.63 (td, *J* = 7.8, 4.8 Hz, 1H), 6.23 (d, *J* = 2.2 Hz, 1H), 4.31 (t, *J* = 7.0 Hz, 1H), 3.93 – 3.89 (m, 1H), 3.73 (d, *J* = 16.3 Hz, 2H), 2.60 (d, *J* = 16.4 Hz, 1H), 1.71

– 1.63 (m, 1H), 1.51 – 1.42 (m, 2H), 0.65 – 0.57 (m, 1H); **^{13}C NMR** (125 MHz, DMSO) δ 174.9, 154.4, 152.7, 150.8 (d, *J* = 236.3 Hz), 149.3, 141.4, 133.4 (d, *J* = 8.8 Hz), 131.1, 129.3, 127.7, 125.9, 123.6 (d, *J* = 5.0 Hz), 119.6, 116.6 (d, *J* = 7.5 Hz), 114.9 (d, *J* = 21.3 Hz), 114.7, 113.1, 112.3, 111.7, 108.9, 108.2, 63.5, 56.8, 51.4, 38.2, 26.0, 23.8. **HRMS (ESI):** calcd. for $C_{27}H_{23}FN_3O_2$ $[M+H]^+$: 440.1769, found: 440.1760.

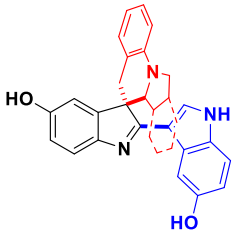
2'-(5-hydroxy-1H-indol-3-yl)-6a,7,8,9,10,11-hexahydro-5H-spiro[azepino[1,2-a]quinoline-6,3'-indol]-5'-ol (4v)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:4) afforded the product (30.1 mg, 64% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.48 (s, 1H), 9.05 (s, 1H), 8.92 (s, 1H), 8.13 (s, 1H), 8.02 (s, 1H), 7.33 (d, *J* = 8.1 Hz, 1H), 7.26 (d, *J* = 8.6 Hz, 1H), 7.18 (t, *J* = 7.7 Hz, 1H), 6.99 (d, *J* = 7.3 Hz, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 6.73 (d, *J* = 8.6 Hz, 1H), 6.69 (d, *J* = 8.2 Hz, 1H), 6.65 (t, *J* = 7.3 Hz, 1H), 6.31 (s, 1H), 4.13 (dd, *J* = 9.1, 3.8 Hz, 1H), 3.73 – 3.69 (m, 1H), 3.63 – 3.61 (m,1H), 3.34 (s, 1H), 2.44 (d, *J* = 16.5 Hz, 1H), 1.78 (d, *J* = 6.5 Hz, 2H), 1.55 – 1.52 (m, 2H), 1.50 – 1.48 (m, 1H), 1.16 (dd, *J* = 20.8, 10.3 Hz, 2H), 0.91 – 0.87 (m, 1H); **^{13}C NMR** (125 MHz, DMSO) δ 175.6, 154.3, 152.7, 149.1, 148.4, 142.1, 131.2, 129.9, 129.0, 127.7, 127.6, 120.8, 119.5, 116.8, 114.4, 113.6, 113.0, 112.3, 112.3, 109.1, 108.1, 63.1, 59.7, 50.4, 38.9, 30.3, 29.2, 28.1, 26.8. **HRMS (ESI):** calcd. for $C_{29}H_{28}N_3O_2$ $[M+H]^+$: 450.2176, found: 450.2164.

2-(5-hydroxy-1H-indol-3-yl)-6a',6b',7',8',9',10',10a',11'-octahydro-5'H-spiro[indole-3,6'-isoindolo[2,1-a]quinolin]-5-ol (4w)

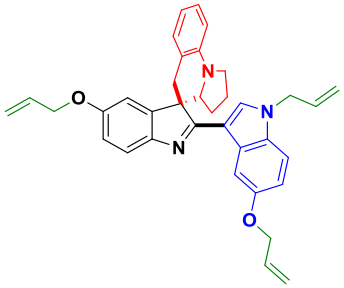


Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:4) afforded the product (27.3 mg, 55% yield) as a yellow solid.

^{1}H NMR (500 MHz, DMSO) δ 11.47 (d, *J* = 1.9 Hz, 1H), 9.07 (s, 1H), 8.94 (s, 1H), 8.17 (d, *J* = 2.8 Hz, 1H), 8.13 (d, *J* = 2.2 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 1H), 7.25 (d, *J* = 8.6 Hz, 1H), 7.17 (t, *J* = 7.7 Hz, 1H), 6.96 (d, *J* = 7.3 Hz, 1H), 6.72 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.66 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.62 (d, *J* = 8.2 Hz, 1H), 6.55 (t, *J* = 7.3 Hz, 1H), 5.93 (d, *J* = 2.3 Hz, 1H), 4.55 (d, *J* = 9.8 Hz, 1H), 3.76 (d, *J* = 15.8 Hz, 1H), 3.22 (q, *J* = 9.5 Hz, 2H), 2.43 (d, *J* = 16.0 Hz, 1H), 1.93 (dd, *J* = 11.3, 5.5 Hz, 1H), 1.63 – 1.54 (m, 1H), 1.46 (d, *J* = 12.6 Hz, 1H), 1.37 (dd, *J* = 25.1, 12.5 Hz, 1H), 1.23 (s, 1H), 1.16 (d, *J* = 12.9 Hz, 1H), 1.08 – 0.95 (m, 2H), 0.83 (t, *J* = 11.5 Hz, 2H); **^{13}C NMR** (125 MHz, DMSO) δ 175.7, 154.3, 152.6, 149.2, 145.0, 141.4, 131.1, 129.8, 129.4, 128.2, 127.7, 119.7, 118.9, 115.2, 114.3, 112.9, 112.2, 111.9,

110.2, 109.5, 108.2, 61.6, 56.6, 56.6, 55.3, 53.9, 36.9, 28.8, 25.2, 25.0, 21.5. **HRMS (ESI):** calcd. for $C_{31}H_{30}N_3O_2$ $[M+H]^+$: 476.2333, found: 476.2303.

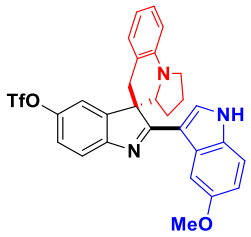
2-(1-allyl-5-allyloxy-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-allyloxy (5l)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:25) afforded the product (17.6 mg, 65% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42 (d, *J* = 2.4 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.43 (s, 1H), 7.19 – 7.14 (m, 3H), 6.97 – 6.91 (m, 2H), 6.78 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.61 – 6.53 (m, 2H), 6.17 (d, *J* = 2.4 Hz, 1H), 6.10 (m, 1H), 5.93 (m, 1H), 5.82 (m, 1H), 5.45 (dd, *J* = 17.2, 1.3 Hz, 1H), 5.25 (d, *J* = 10.5 Hz, 1H), 5.18 (m, 2H), 5.10 (s, 1H), 5.08 (d, *J* = 6.5 Hz, 1H), 4.65 (d, *J* = 5.4 Hz, 4H), 4.19 (d, *J* = 5.4 Hz, 2H), 4.11 (dd, *J* = 9.6, 5.8 Hz, 1H), 3.63 (dd, *J* = 15.0, 5.9 Hz, 1H), 3.44 (td, *J* = 8.6, 2.8 Hz, 1H), 3.22 (dd, *J* = 16.7, 8.5 Hz, 1H), 2.65 (d, *J* = 16.3 Hz, 1H), 1.75 – 1.67 (m, 2H), 1.16 (m, 1H), 0.73 – 0.63 (m, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 175.1, 155.9, 154.9, 144.2, 140.8, 134.1, 133.5, 132.6, 131.8, 129.7, 128.9, 128.2, 120.0, 118.5, 118.4, 117.6, 117.5, 115.9, 114.2, 110.8, 110.4, 110.2, 107.3, 69.7, 69.1, 63.3, 57.6, 49.5, 47.6, 38.0, 30.6, 29.7, 26.9, 23.3, 19.2, 13.7. **HRMS (ESI):** calcd. for $C_{36}H_{36}N_3O_2$ $[M+H]^+$: 542.2802, found: 542.2789.

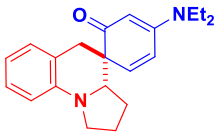
2-(5-methoxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-trifluoromethanesulfonate (6i)



Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:25) afforded the product (53.9 mg, 68% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.31 (d, *J* = 2.4 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.38 (s, 1H), 7.22 (d, *J* = 7.7 Hz, 1H), 7.17 (dd, *J* = 12.3, 7.9 Hz, 1H), 7.14 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.10 (d, *J* = 8.8 Hz, 1H), 6.91 (d, *J* = 7.4 Hz, 1H), 6.84 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.62 (t, *J* = 7.4 Hz, 1H), 6.59 (s, 1H), 6.42 (d, *J* = 2.4 Hz, 1H), 3.96 (dd, *J* = 9.2, 6.1 Hz, 1H), 3.84 (s, 3H), 3.53 – 3.47 (m, 1H), 3.43 (td, *J* = 8.7, 3.2 Hz, 1H), 3.21 (q, *J* = 8.3 Hz, 1H), 2.59 (d, *J* = 16.2 Hz, 1H), 1.72 – 1.61 (m, 2H), 1.43 (m, 1H), 1.35 (s, 1H), 1.25 – 1.16 (m, 1H), 0.81 – 0.74 (m, 1H), 0.54 (dd, *J* = 20.8, 10.8 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 179.4, 156.2, 155.7, 146.4, 143.8, 141.0, 131.1, 129.6, 128.5, 128.2, 127.2, 123.8, 121.2, 120.2, 117.8, 117.3, 116.3, 114.2, 111.9, 110.6, 110.3, 105.7, 63.5, 58.3, 55.9, 47.4, 38.1, 26.9, 23.1. **HRMS (ESI):** calcd. for $C_{29}H_{25}F_3N_3O_4S$ $[M+H]^+$: 568.1512, found: 568.1503.

4-(diethylamino)-1',2',3',3a'-tetrahydro-5'H-spiro[cyclohexane-1,4'-pyrrolo[1,2-a]quinoline]-2,4-dien-6-one (8a)



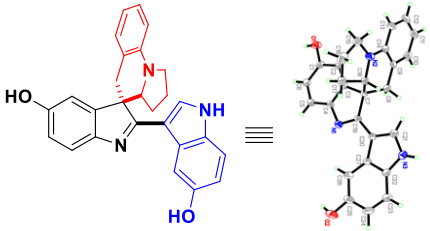
Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1:8) gave the product (31.2 mg, 97% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$) 7.12 (t, *J* = 7.7 Hz, 1H), 7.02 (d, *J* = 7.3 Hz, 1H), 6.57 (t, *J* = 7.3 Hz, 1H), 6.49 (d, *J* = 8.1 Hz, 1H), 6.39 (dd, *J* = 10.5, 1.9 Hz, 1H), 6.15 (dd, *J* = 10.4, 2.1 Hz, 1H), 5.33 (s, 1H), 3.85 (dd, *J* = 9.9, 5.0 Hz, 1H), 3.52 – 3.43 (m, 2H), 3.37 (q, *J* = 7.0 Hz, 4H), 3.18 (d, *J* = 7.5 Hz, 1H), 2.61 (d, *J* = 15.8 Hz, 1H), 2.00 – 1.86 (m, 3H), 1.30 (dd, *J* = 10.3, 7.9 Hz, 1H), 1.21 (t, *J* = 7.0 Hz, 6H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 197.4, 156.5, 143.9, 143.2, 129.1, 127.3, 119.9, 118.6, 114.9, 110.1, 96.6, 64.4, 47.2, 45.7, 44.9, 39.8, 27.8, 23.5. **HRMS (ESI):** calcd. for $C_{21}H_{26}N_2O$ $[M+H]^+$: 323.2045, found: 323.2047.

Reference

1. I. D. Jurberg, B. Peng, E. W çstefeld, M. Wasserloos and N. Maulide, *Angew. Chem. Int. Ed.*, 2012, **51**, 1950.
2. G. Bai, F. Dong, L. Xu, Y. Liu, L. Wang and S.-S. Li, *Org. Lett.* 2019, **21**, 6225.
3. S.-S. Li, X. Lv, D. Ren, C.-L. Shao, Q. Liu and J. Xiao, *Chem. Sci.* 2018, **9**, 8253.

4. Crystal Structures and Data



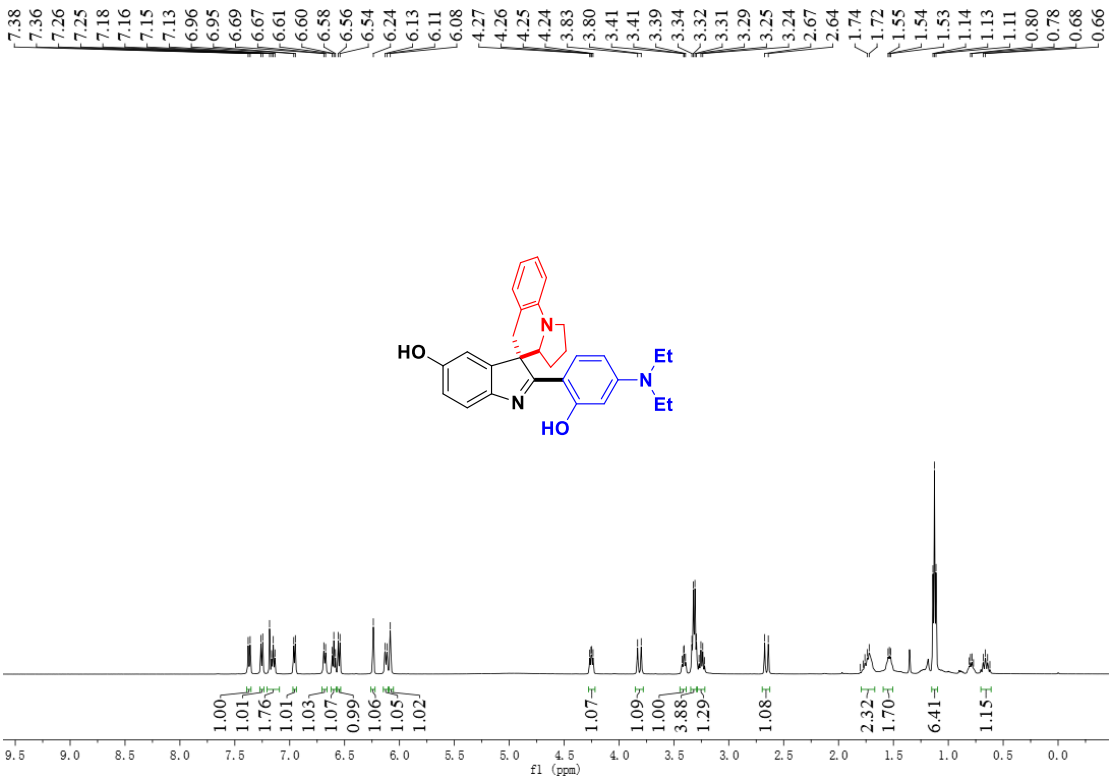
4l (**CCDC 2098243**)

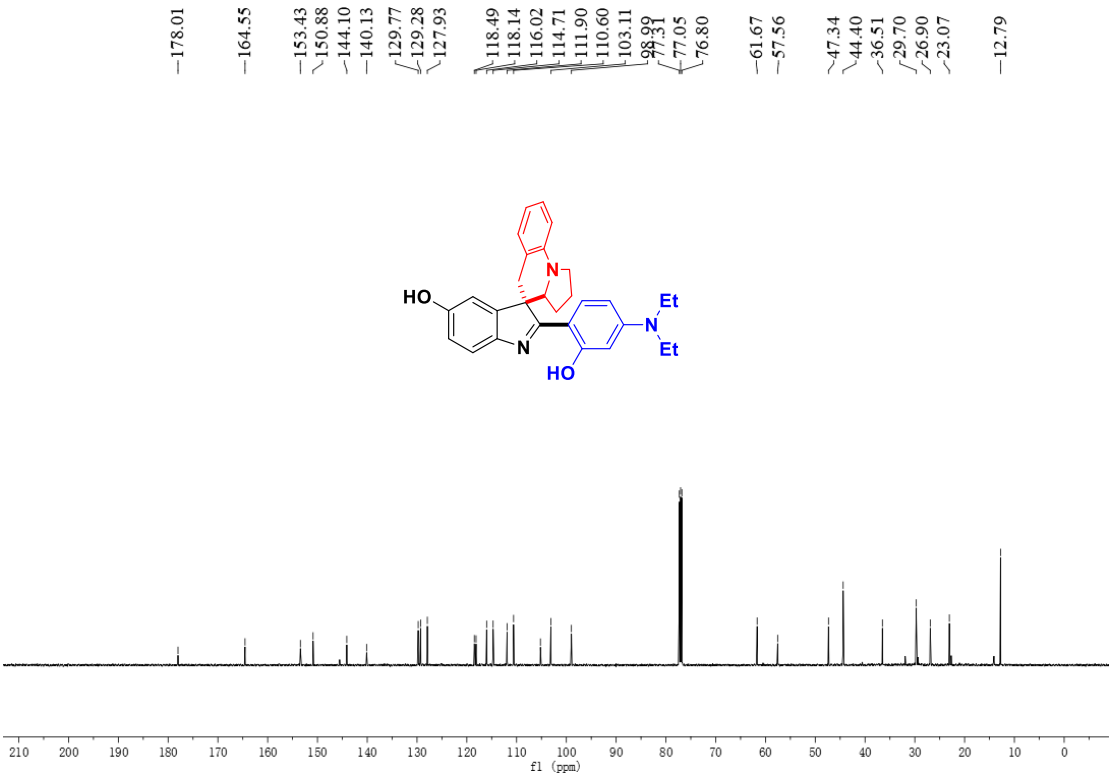
Table 1. Crystal data and structure refinement for **4l**.

Identification code	**4l**
Empirical formula	$C_{27}H_{23}N_3O_2$
Formula weight	842.97
Temperature	293(2) K
Wavelength	1.54184 A
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 10.0368(4) A alpha = 92.957(4) deg.
	b = 13.6087(6) A beta = 95.422(3) deg.
	c = 20.5575(9) A gamma = 90.160(4) deg.
Volume	2791.5(2) A^3
Z, Calculated density	2, 1.003 Mg/m^3
Absorption coefficient	0.511 mm^-1
F(000)	888
Crystal size	0.120 x 0.110 x 0.110 mm
Theta range for data collection	3.811 to 67.230 deg.
Limiting indices	-8<=h<=12, -16<=k<=16, -24<=l<=24
Reflections collected / unique	20183 / 9964 [R(int) = 0.0496]
Completeness to theta = 67.230	99.7 %
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	9964 / 0 / 581
Goodness-of-fit on F^2	1.044
Final R indices [I>2sigma(I)]	R1 = 0.0754, wR2 = 0.2702
R indices (all data)	R1 = 0.1157, wR2 = 0.3100
Extinction coefficient	n/a
Largest diff. peak and hole	0.753 and -0.262 e.A^-3

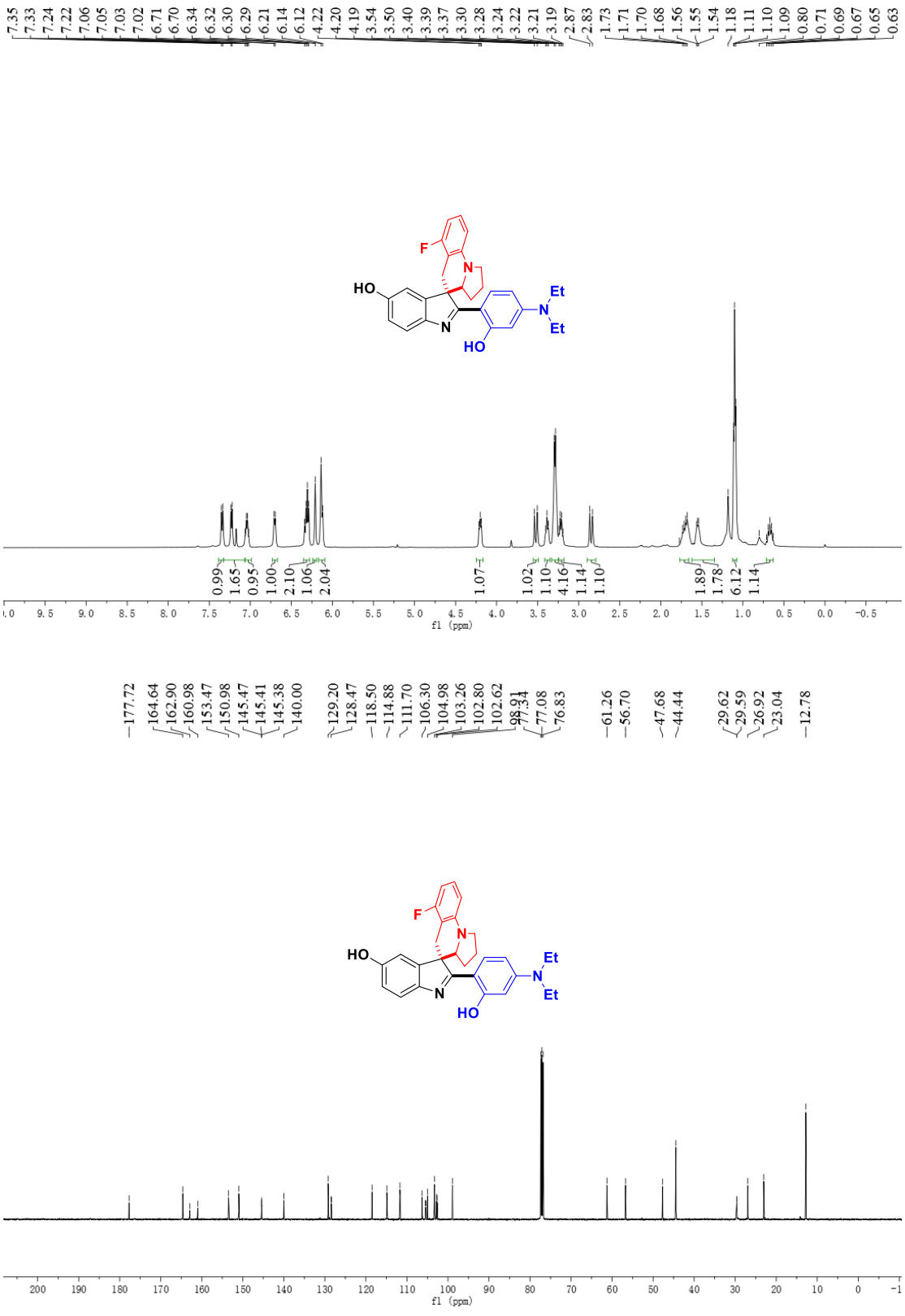
5. ^{1}H and ^{13}C NMR Spectra

2-(4-(diethylamino)-2-hydroxyphenyl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4a)

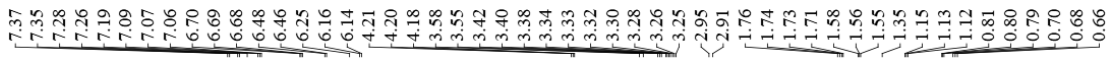


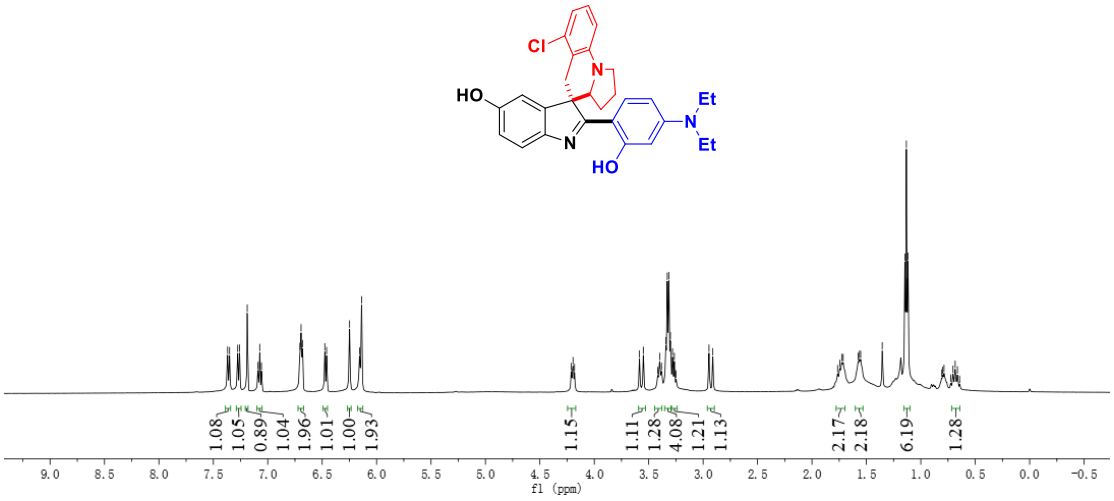


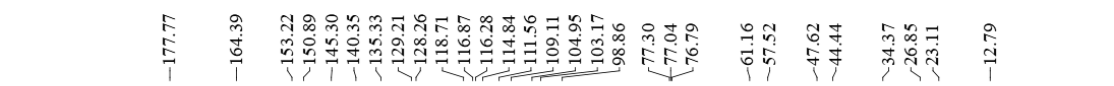
2-(4-(diethylamino)-2-hydroxyphenyl)-6'-fluoro-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4b)

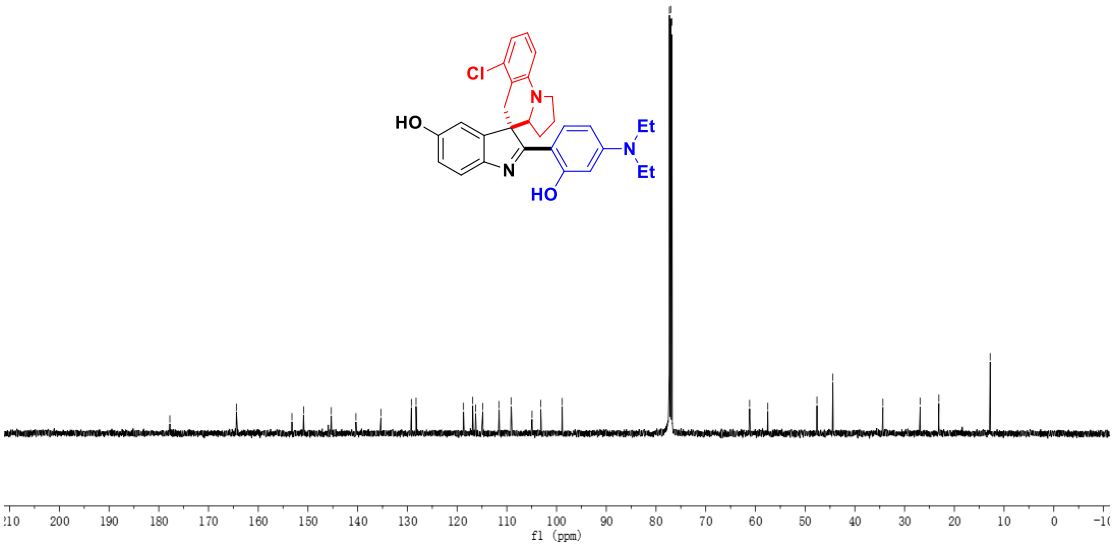


6'-chloro-2-(4-(diethylamino)-2-hydroxyphenyl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4c)

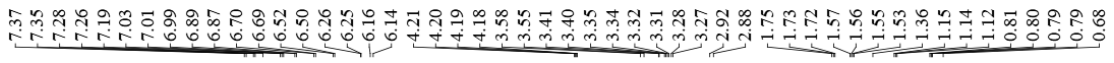


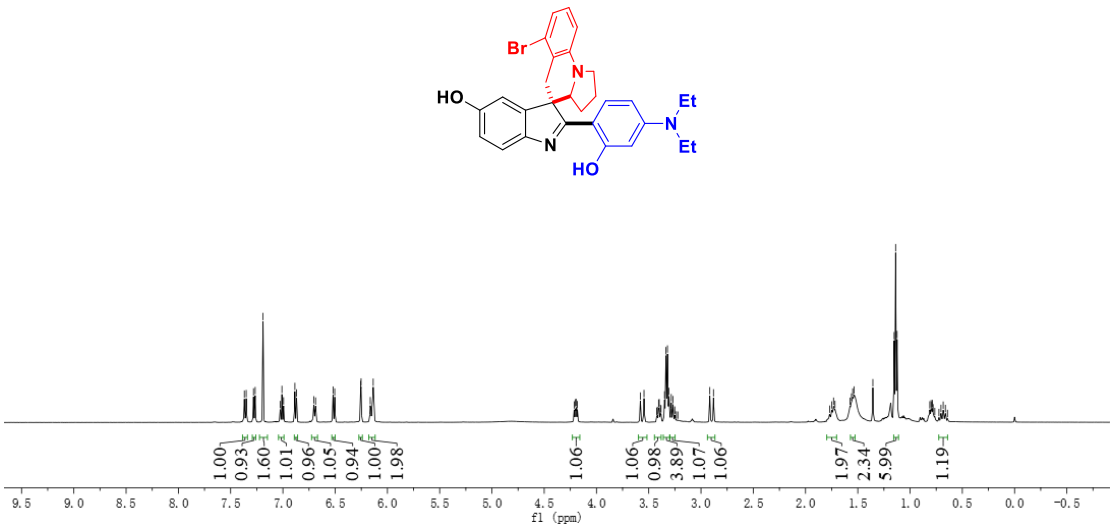


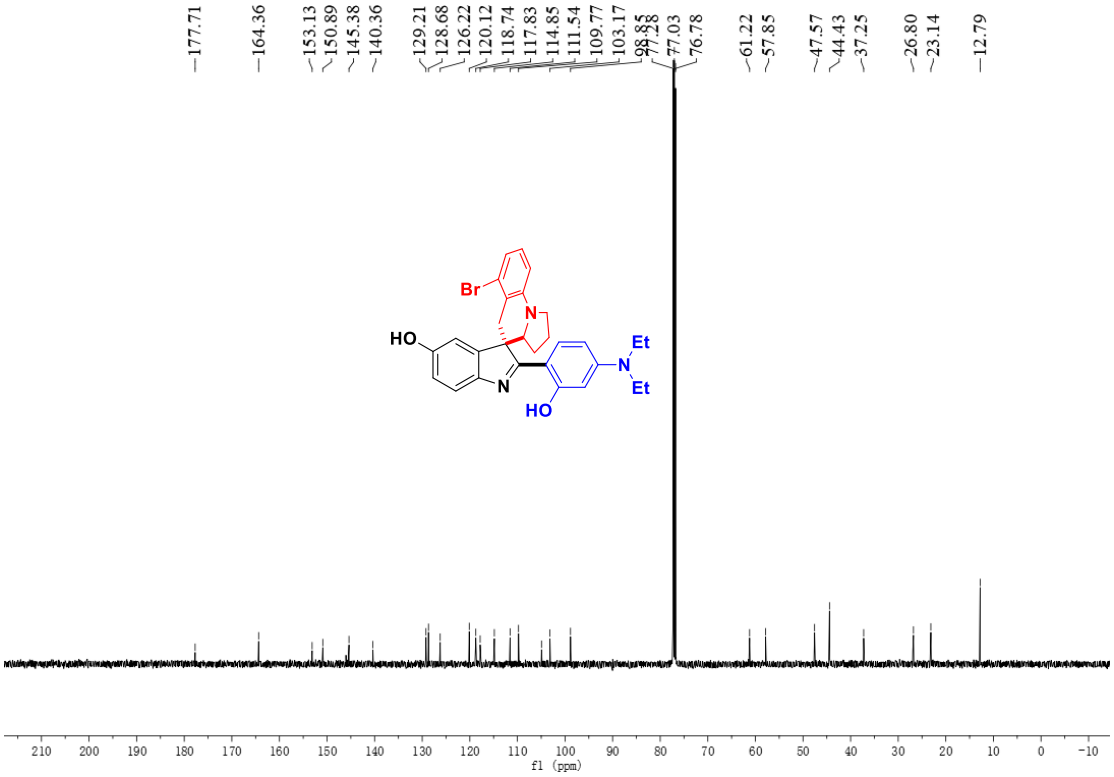




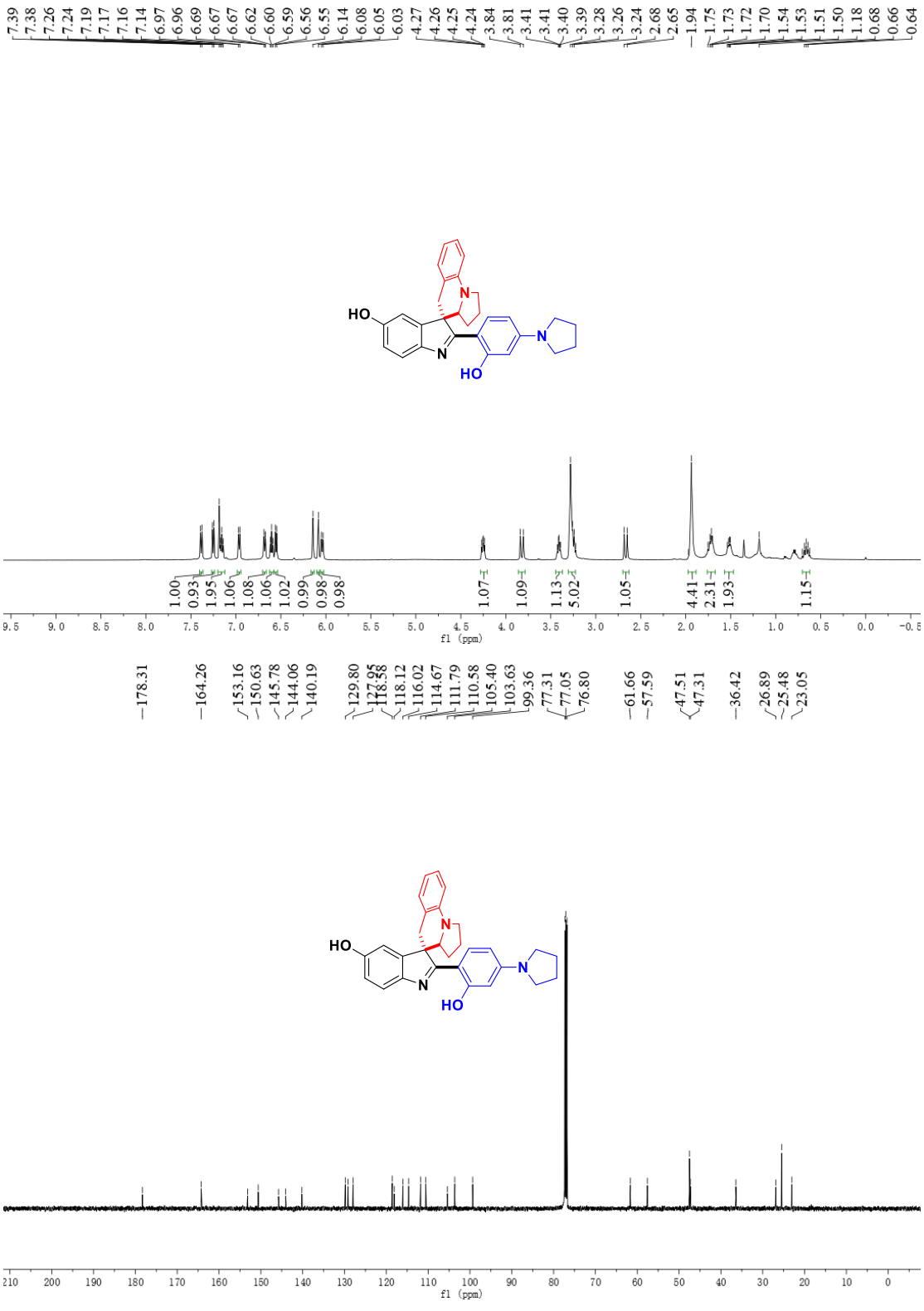
6'-bromo-2-(4-(diethylamino)-2-hydroxyphenyl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4d)



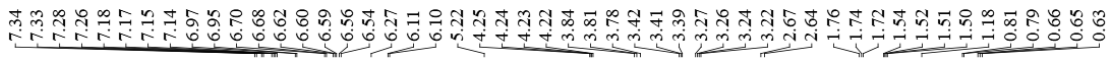


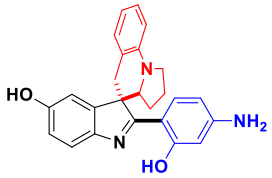


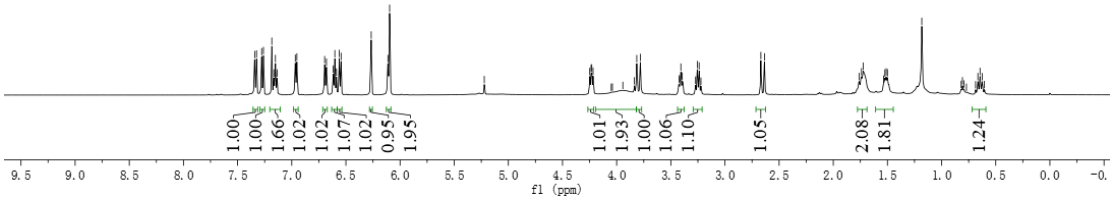
(2-hydroxy-4-(pyrrolidin-1-yl)phenyl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4e)

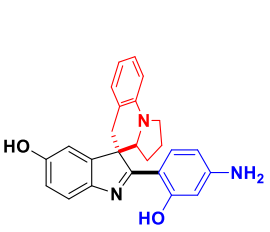


2-(4-amino-2-hydroxyphenyl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4f)

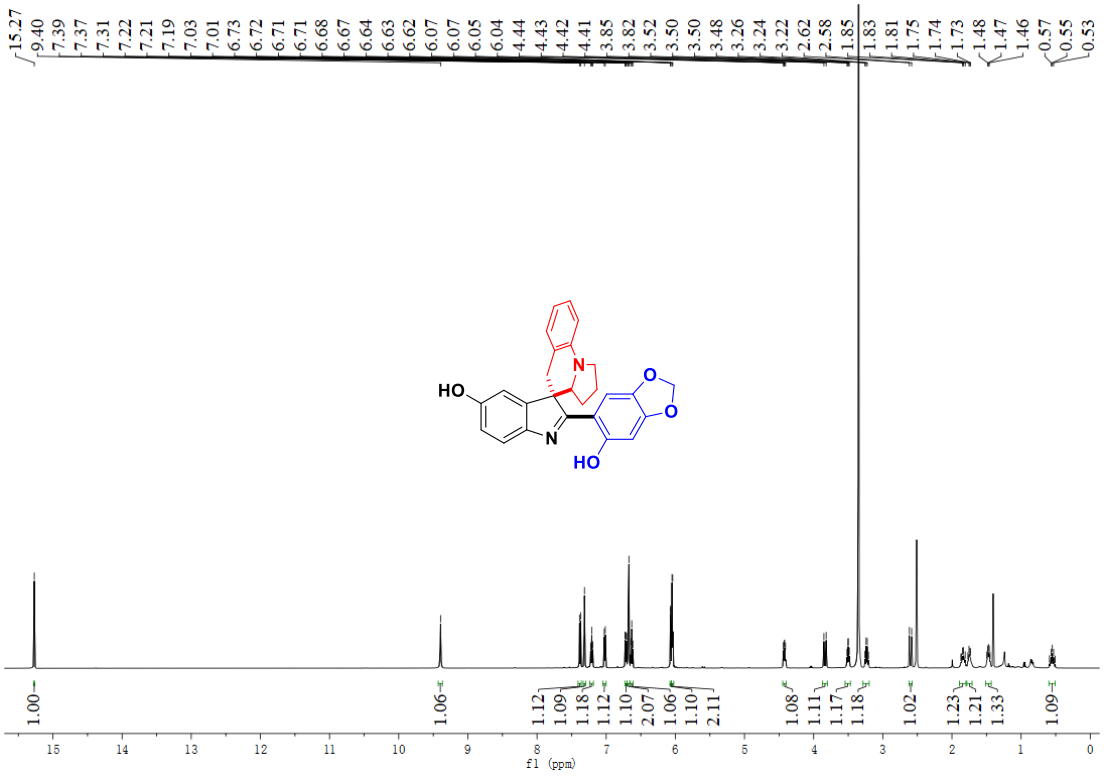


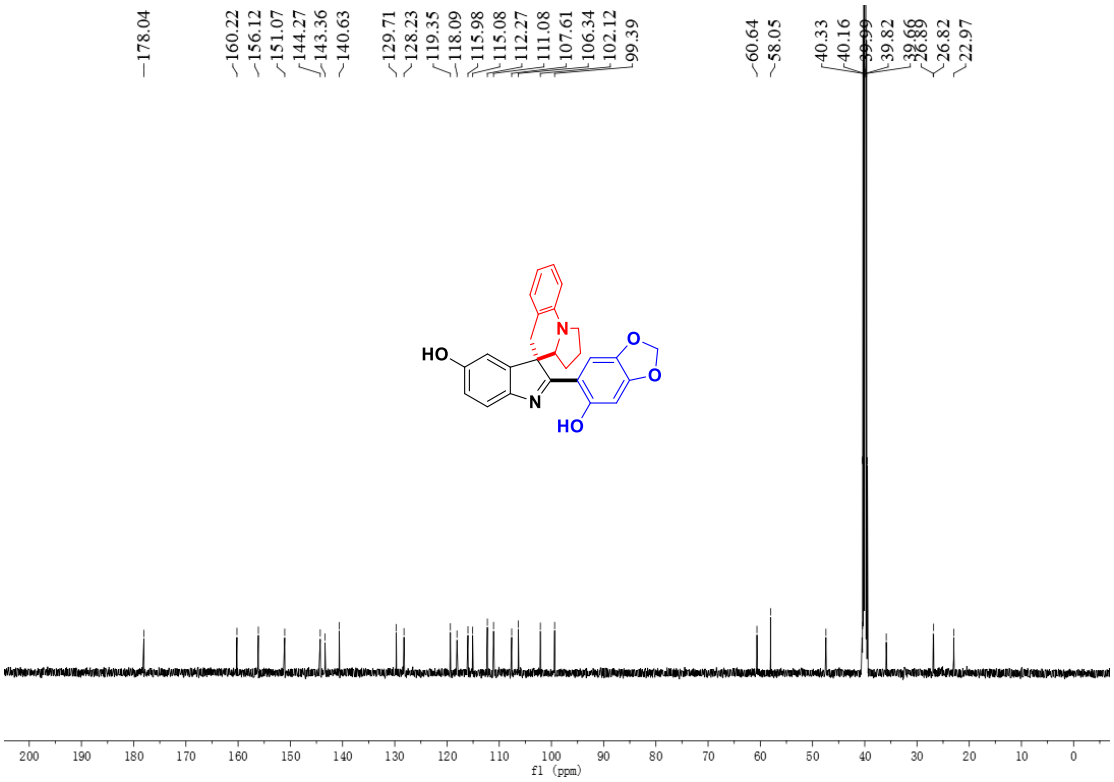




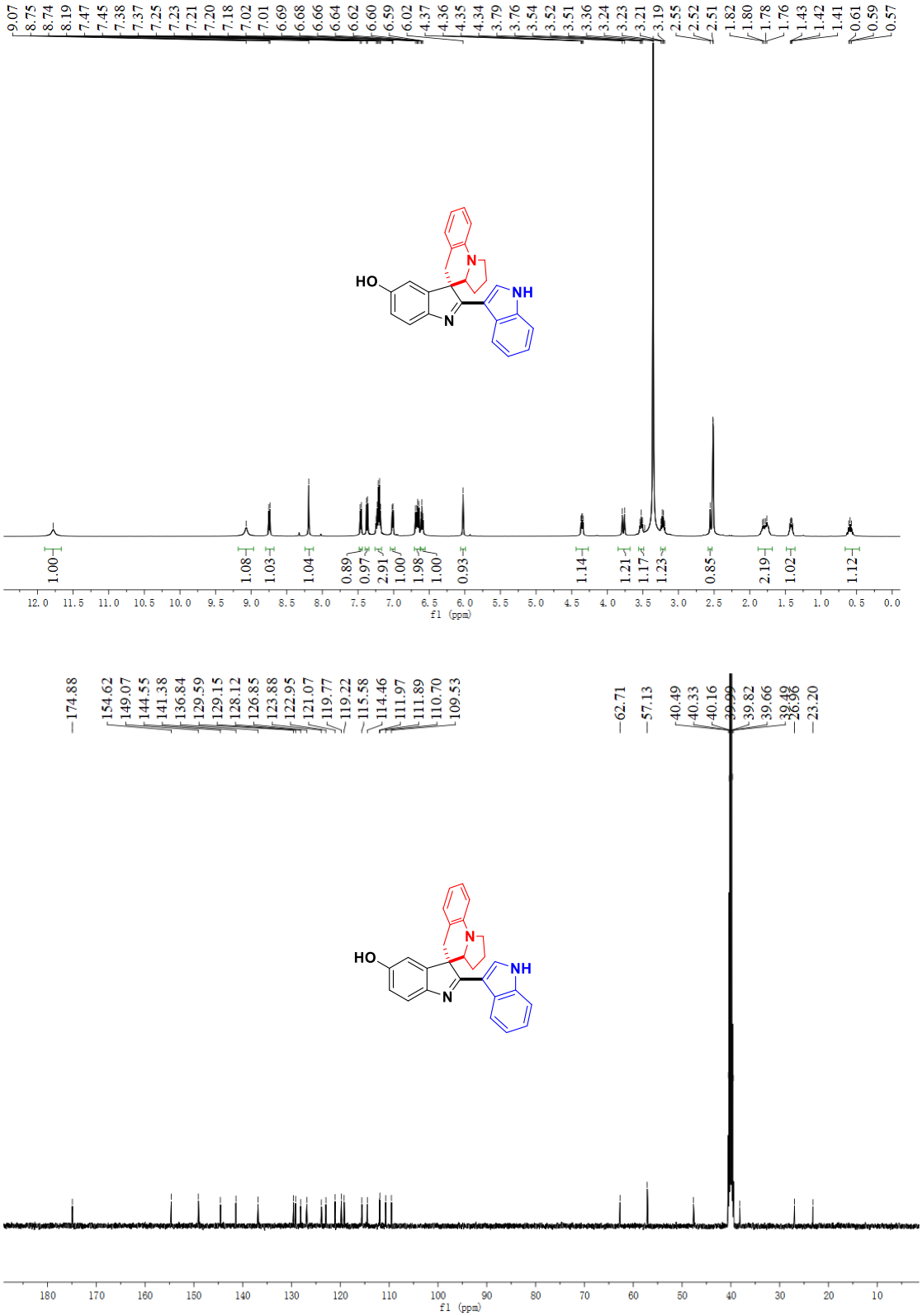


2-(6-hydroxybenzo[d][1,3]dioxol-5-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4g)

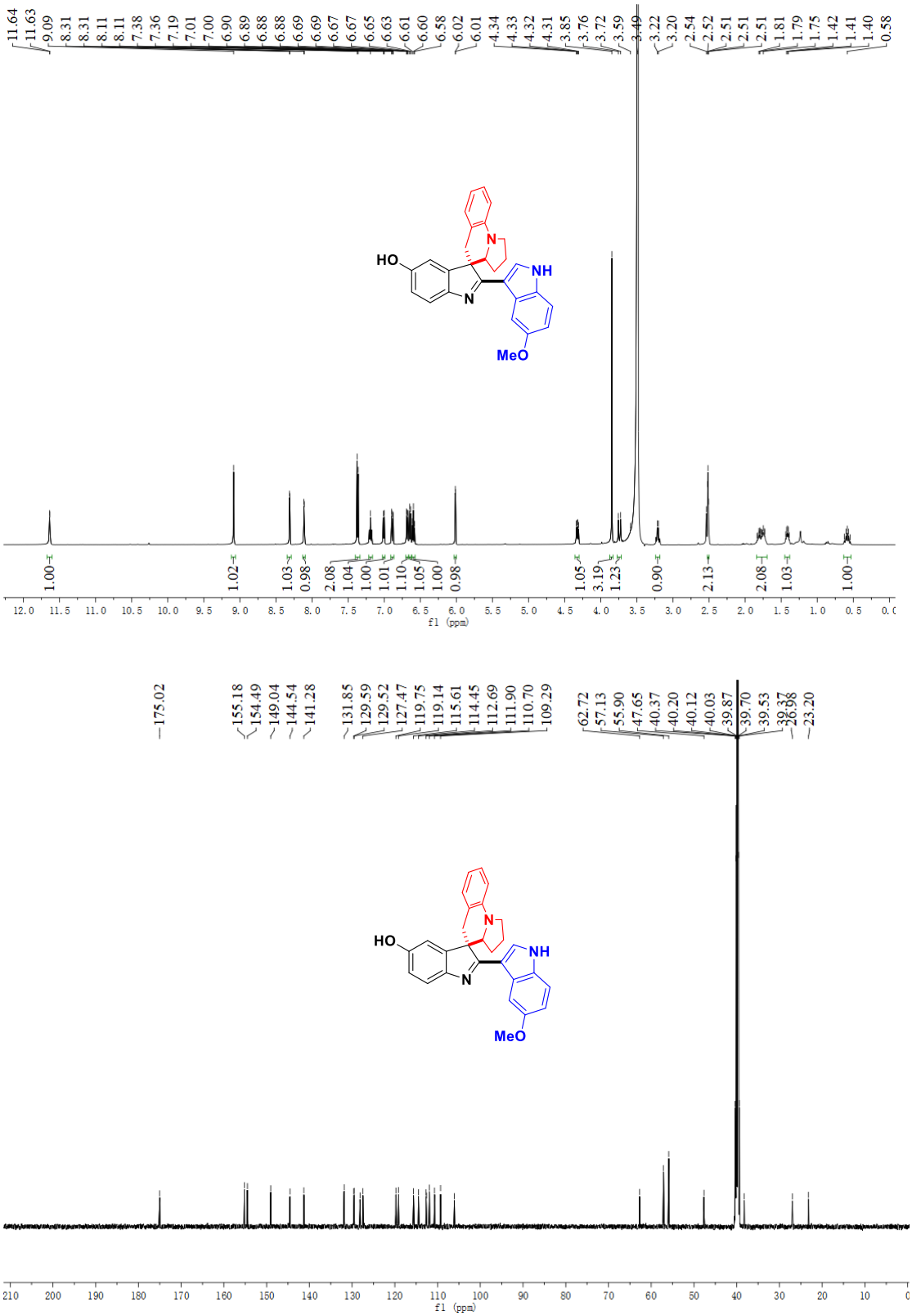




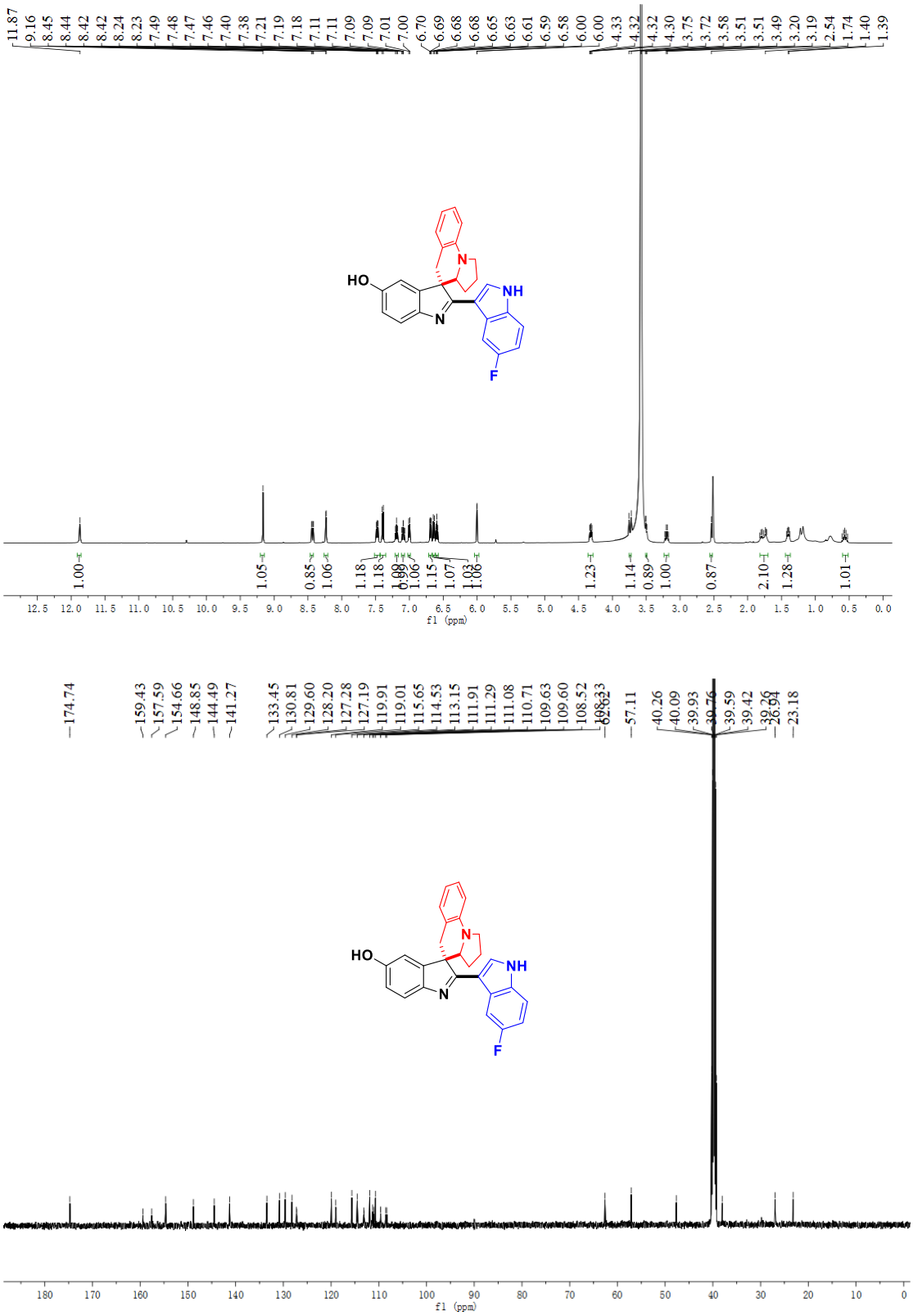
2-(1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4h)



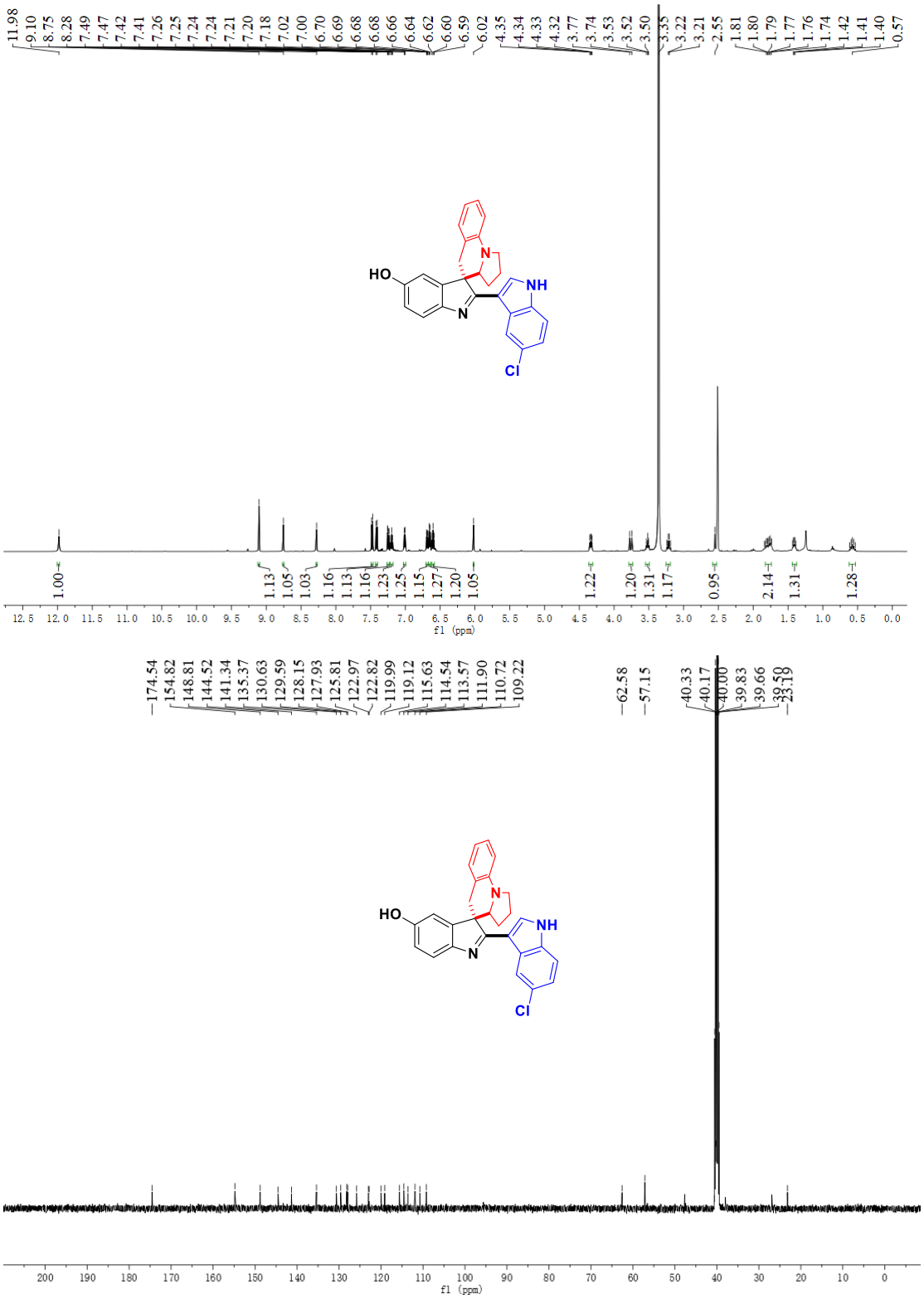
2-(5-methoxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4i)



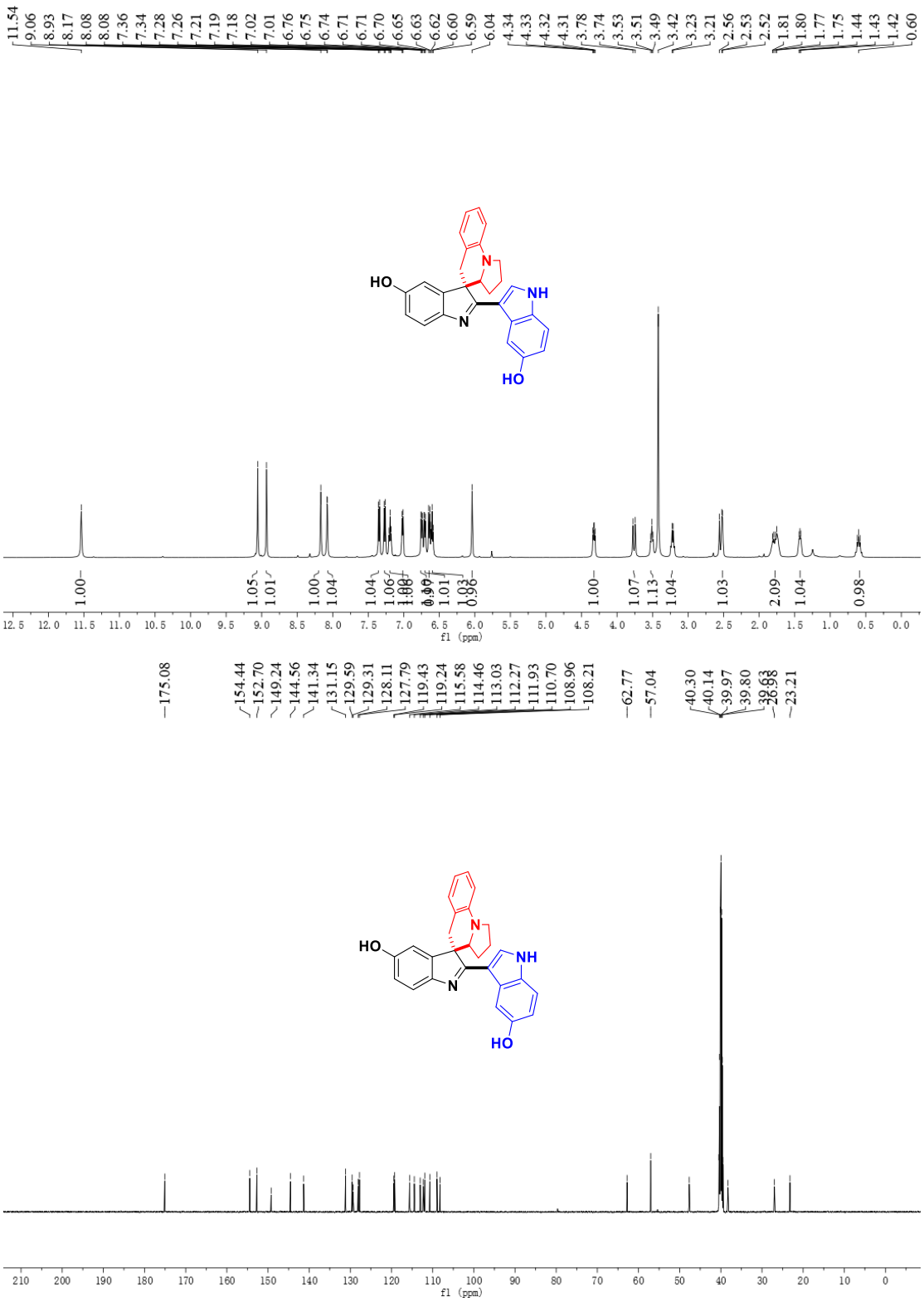
2-(5-fluoro-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4j)



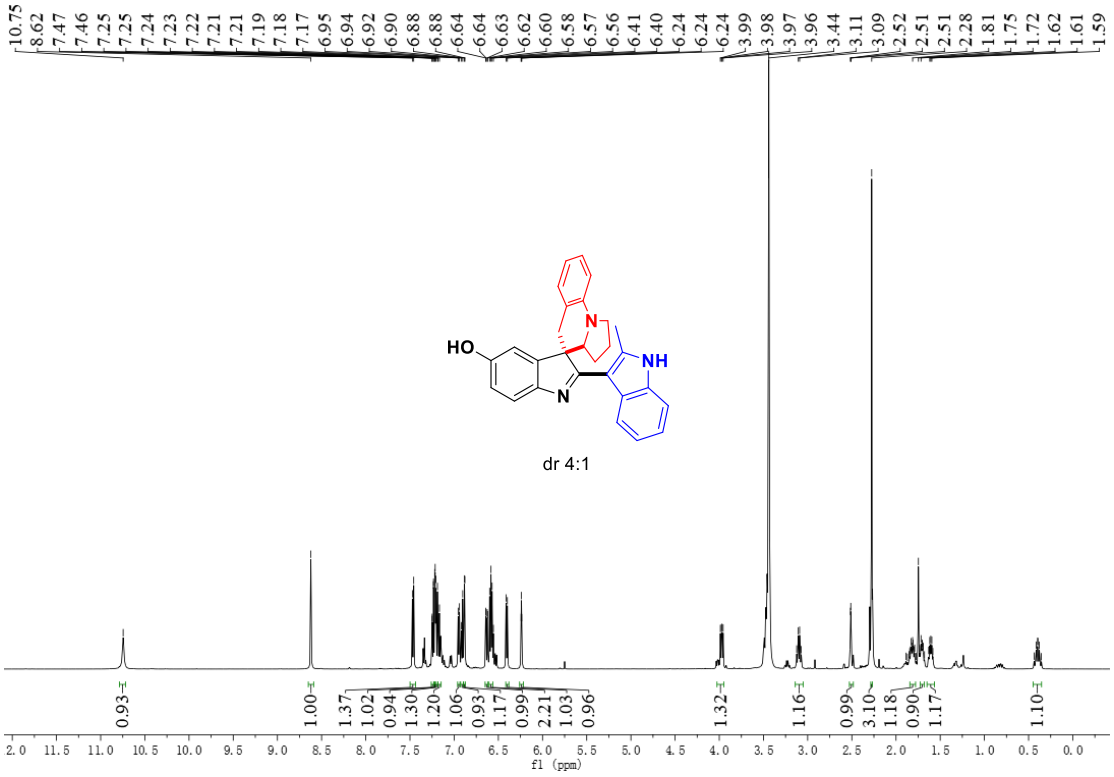
2-(5-chloro-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4k)

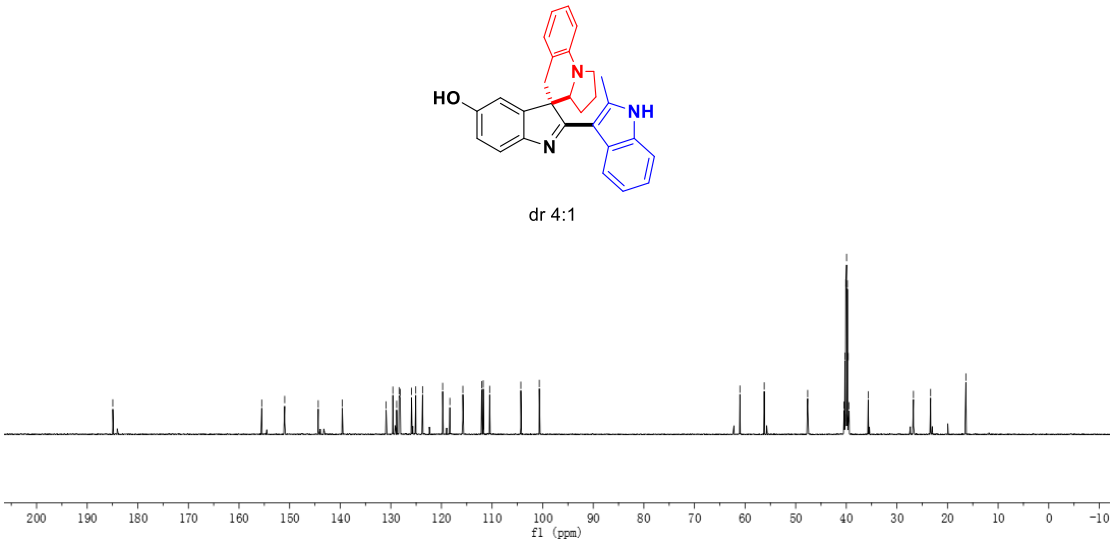


2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4l)

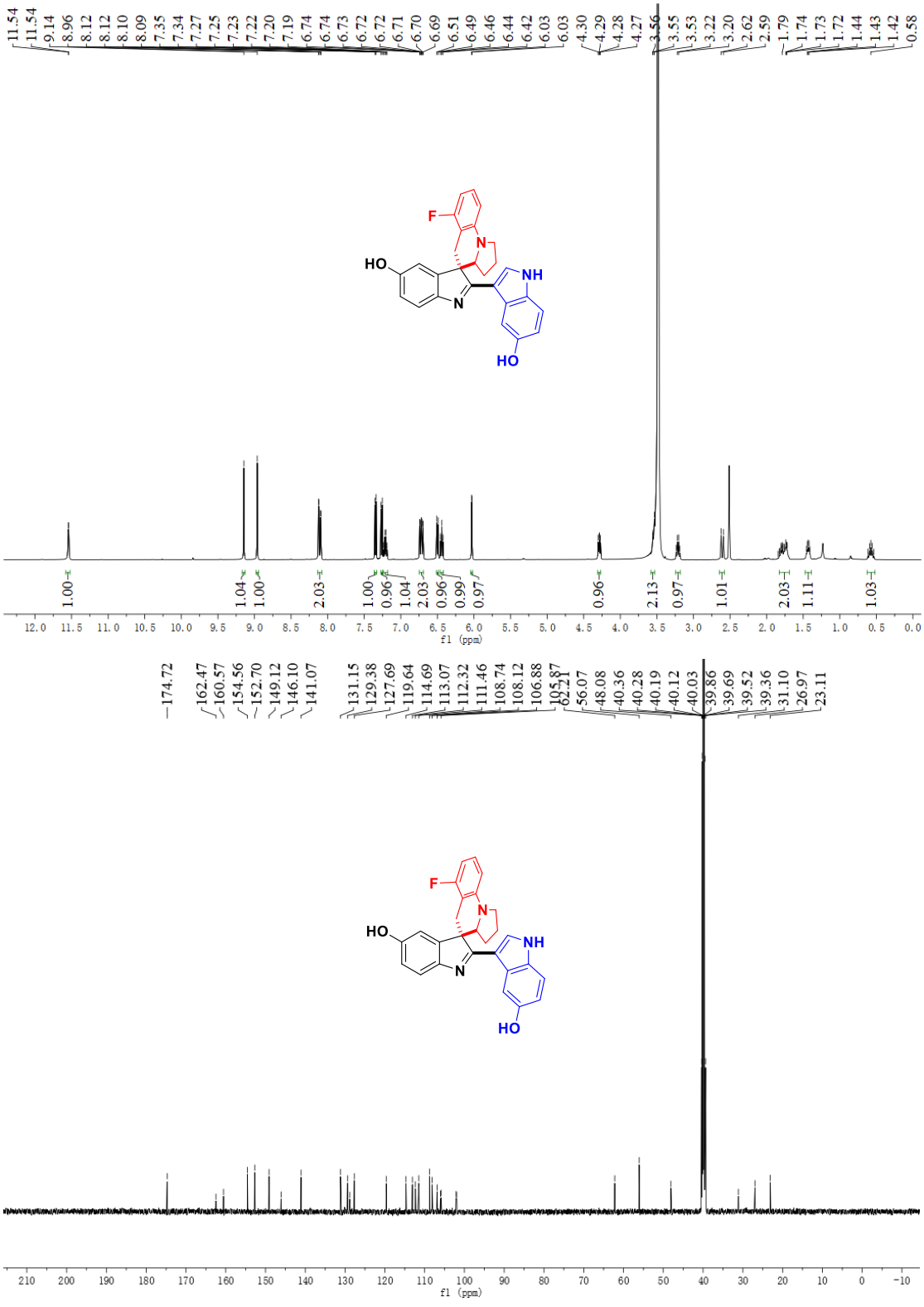


2-(2-methy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4m)

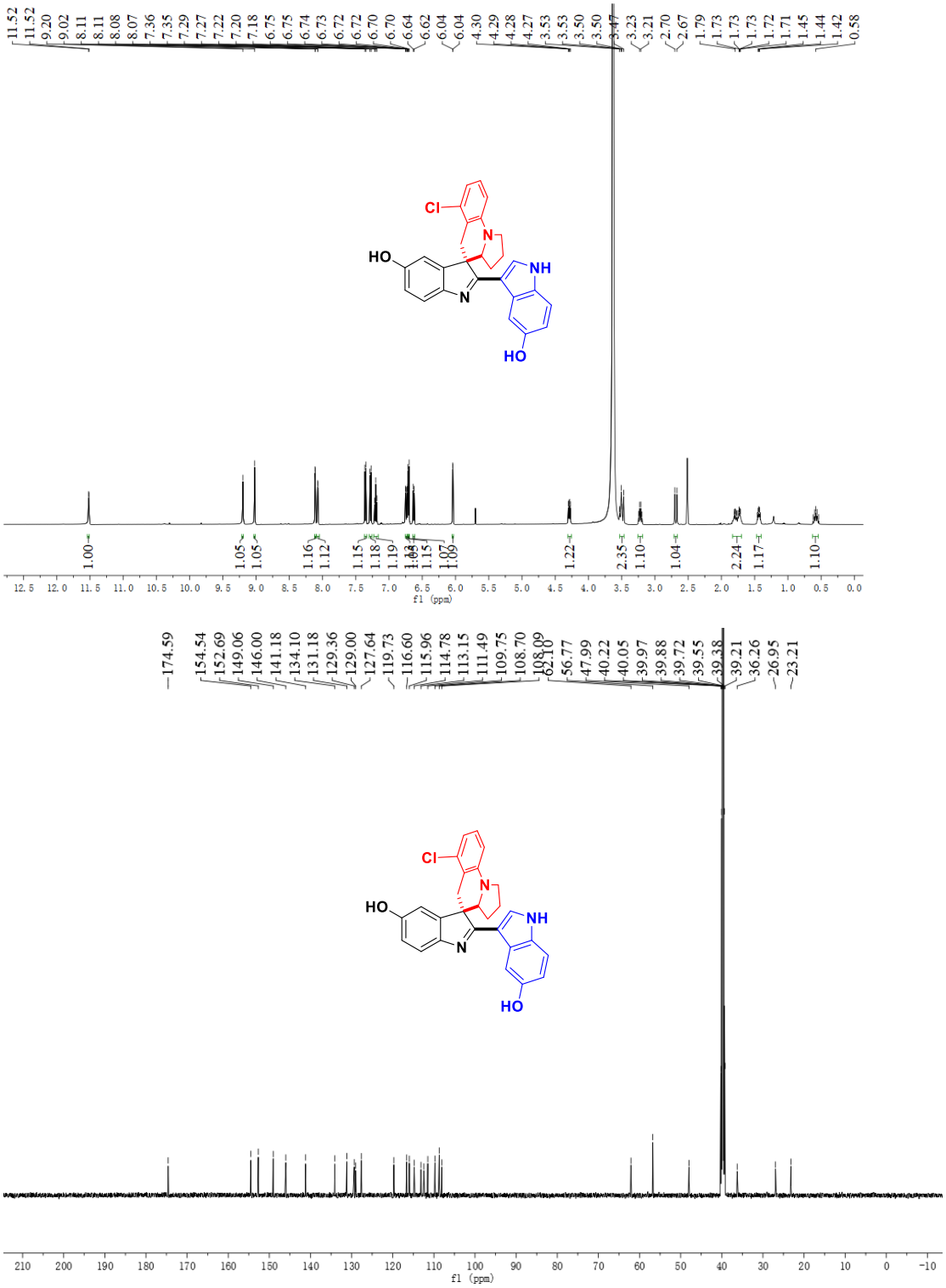




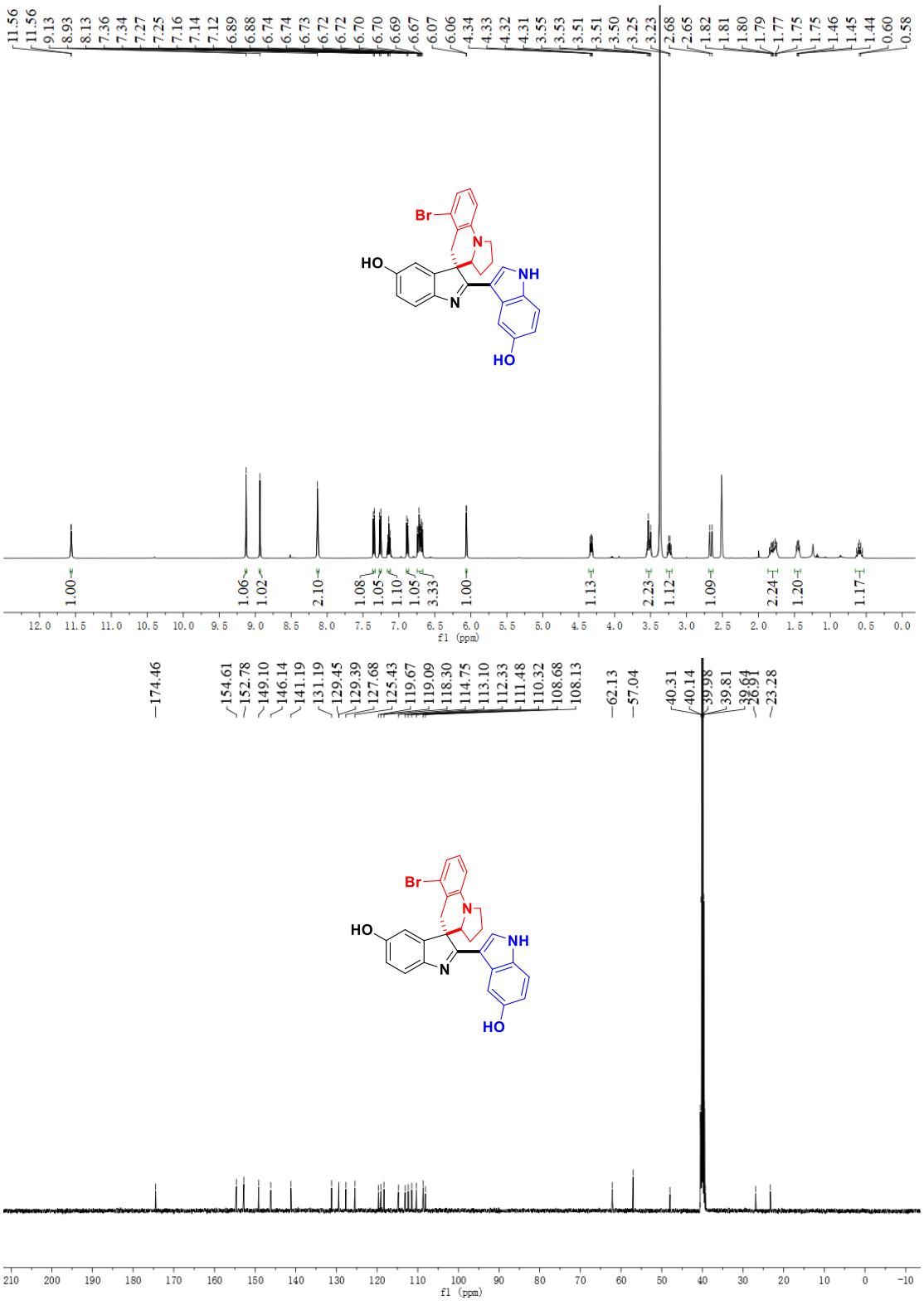
6'-fluoro-2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4n)



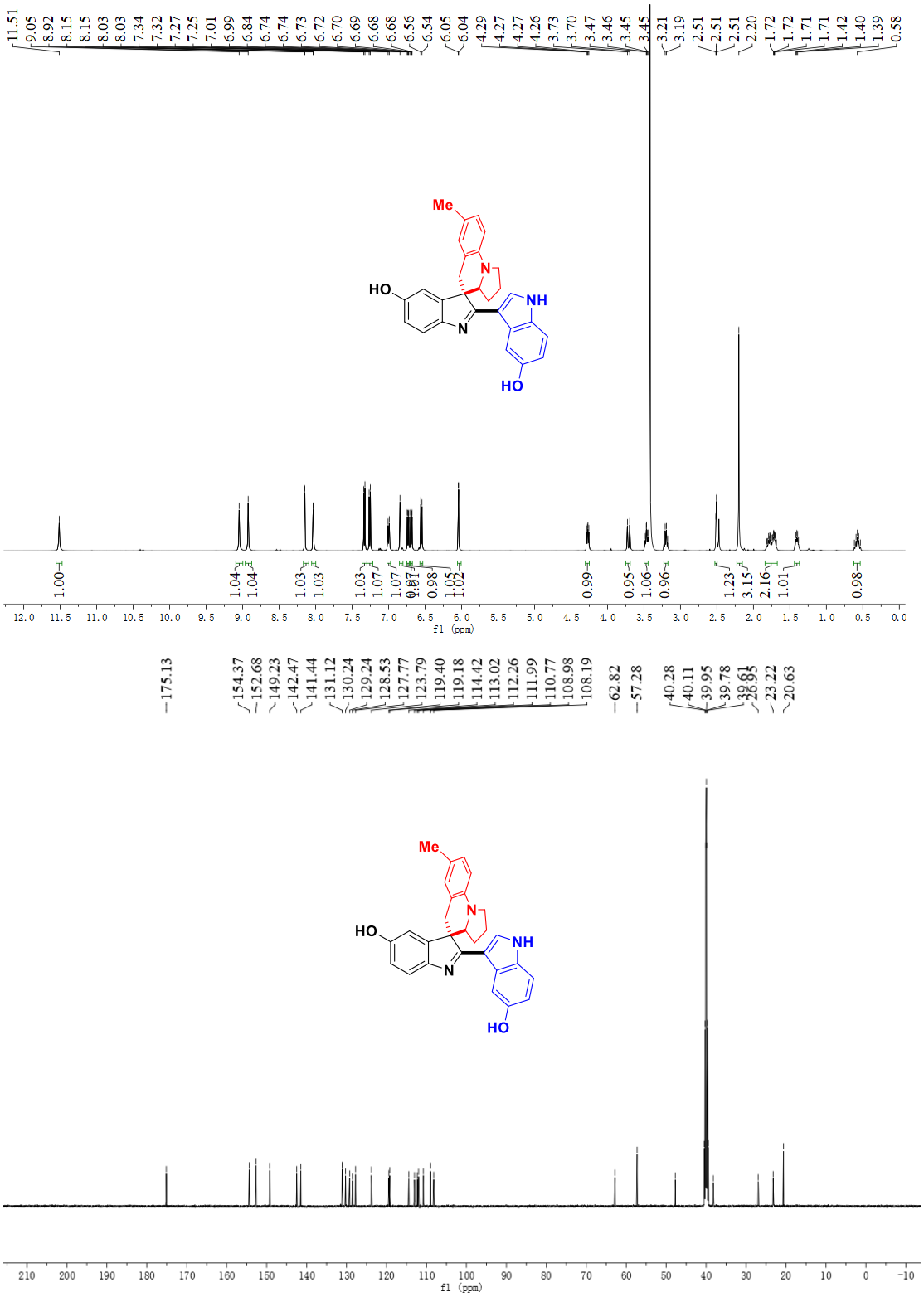
6'-chloro-2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4o)



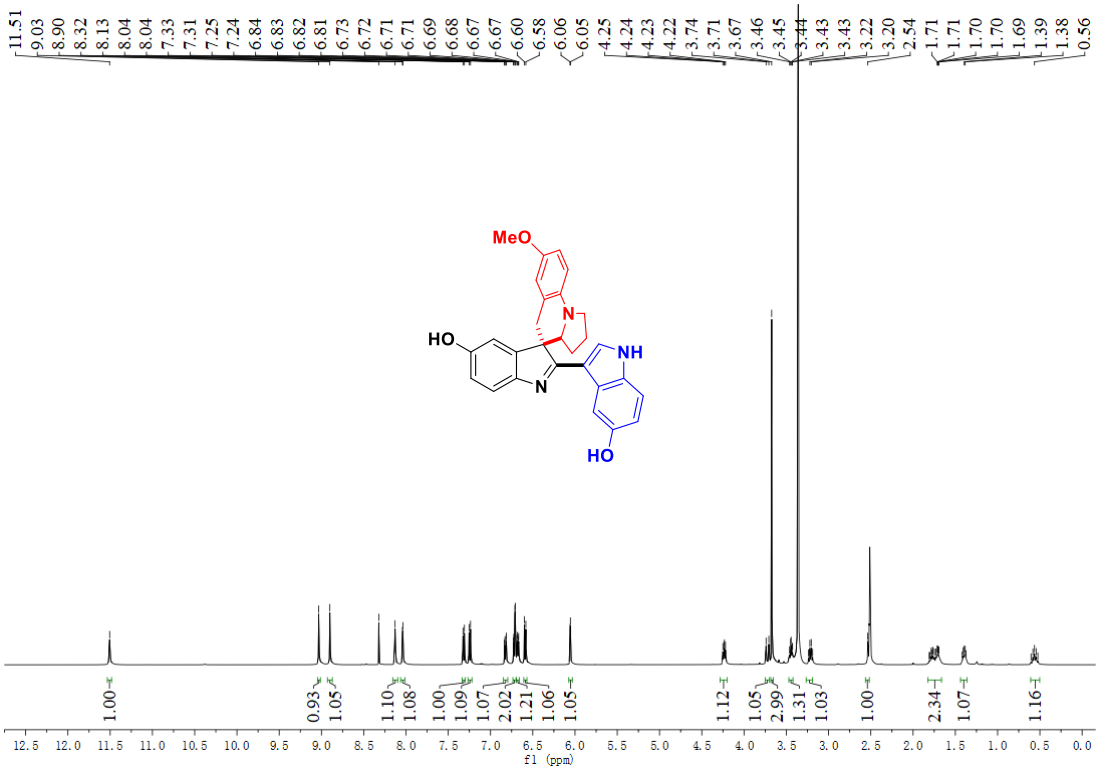
6'-bromo-2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4p)

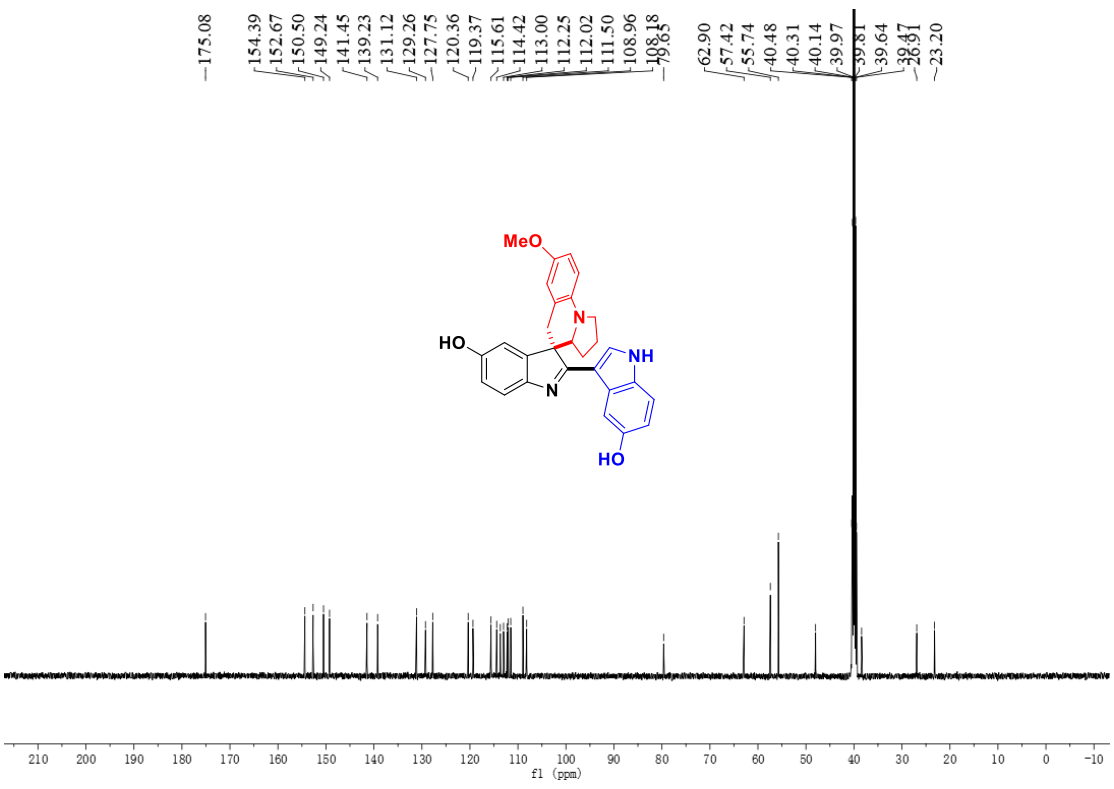


5'-methyl-2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4q)

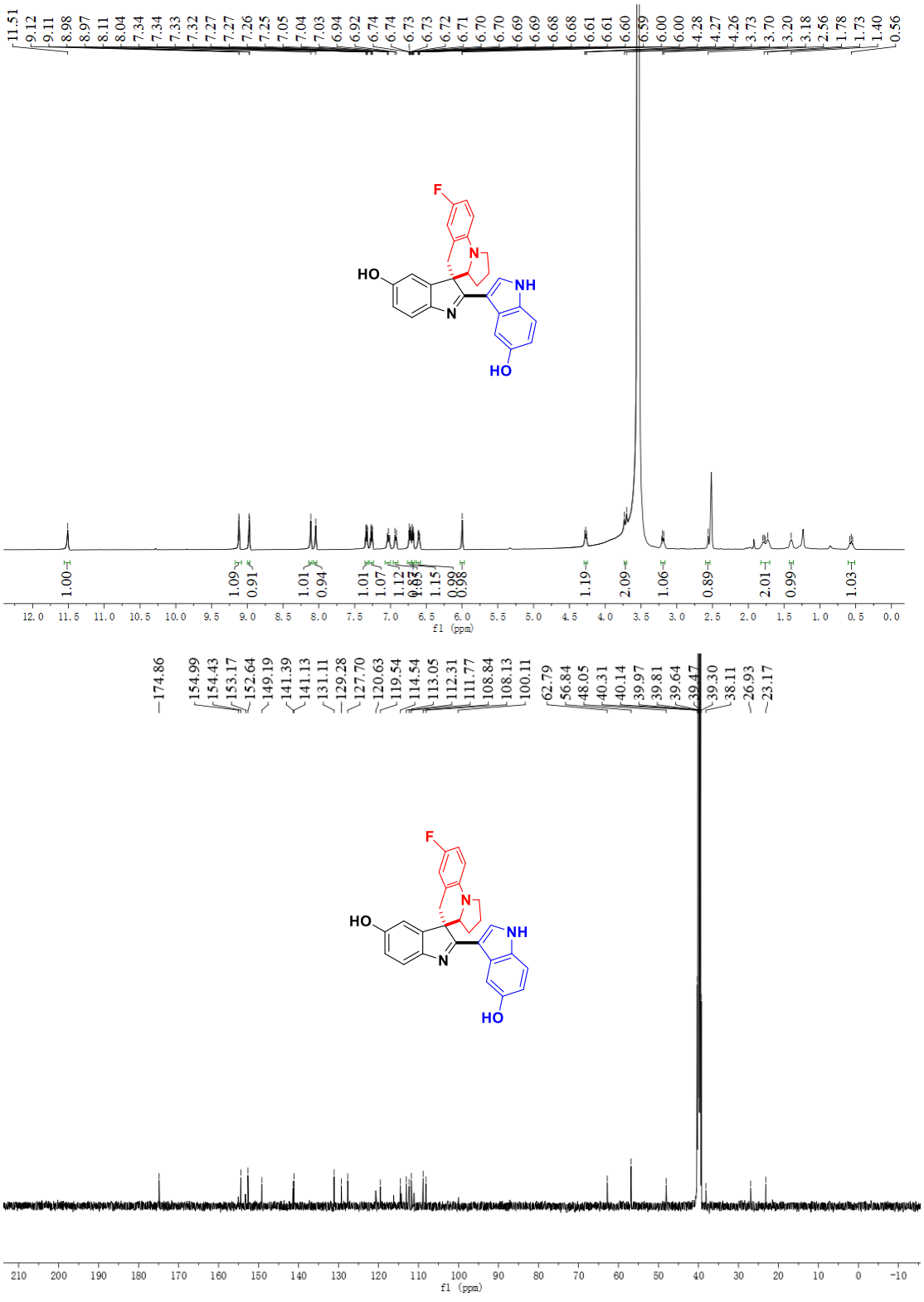


5'-methoxyl-2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4r)

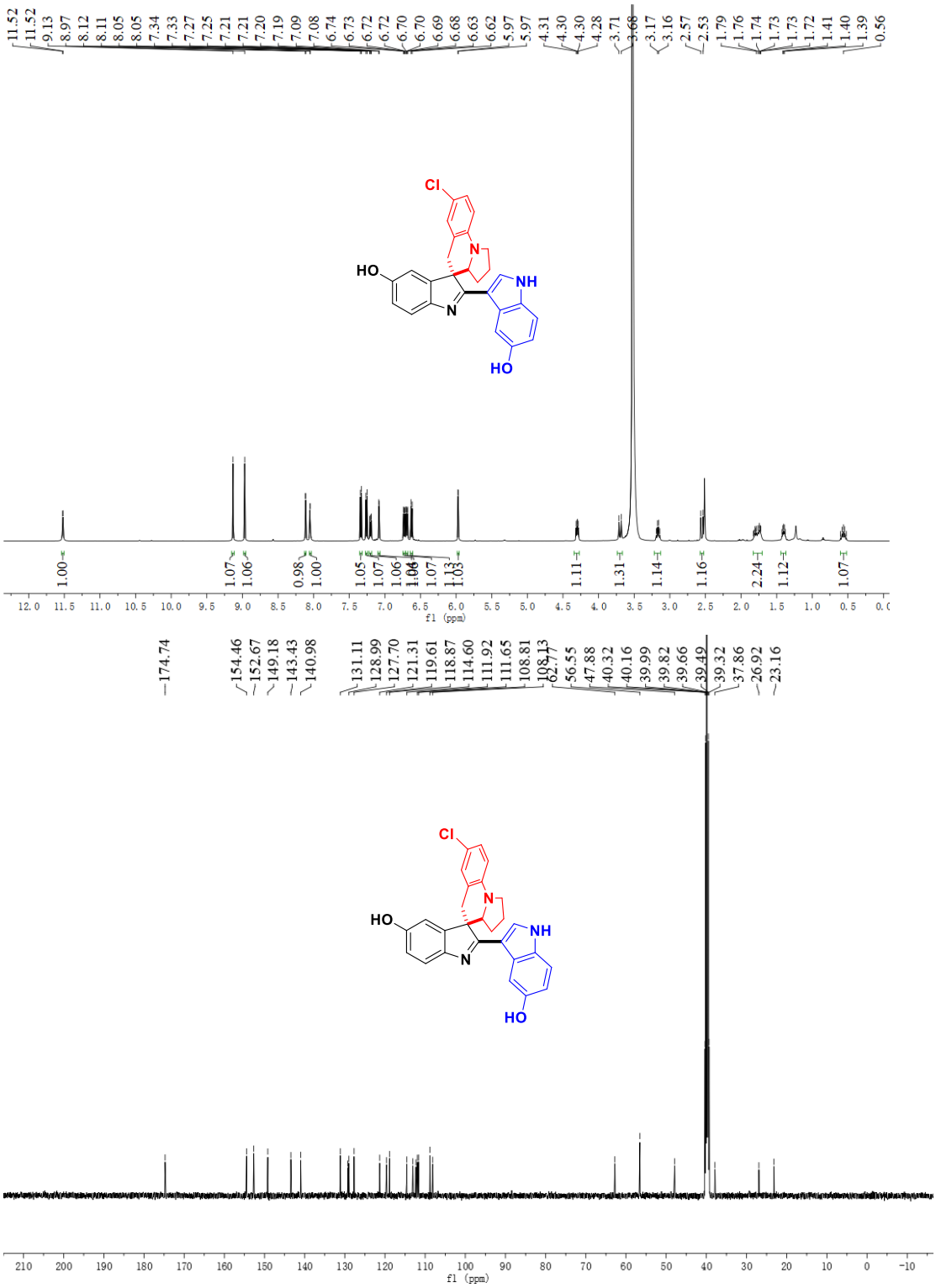




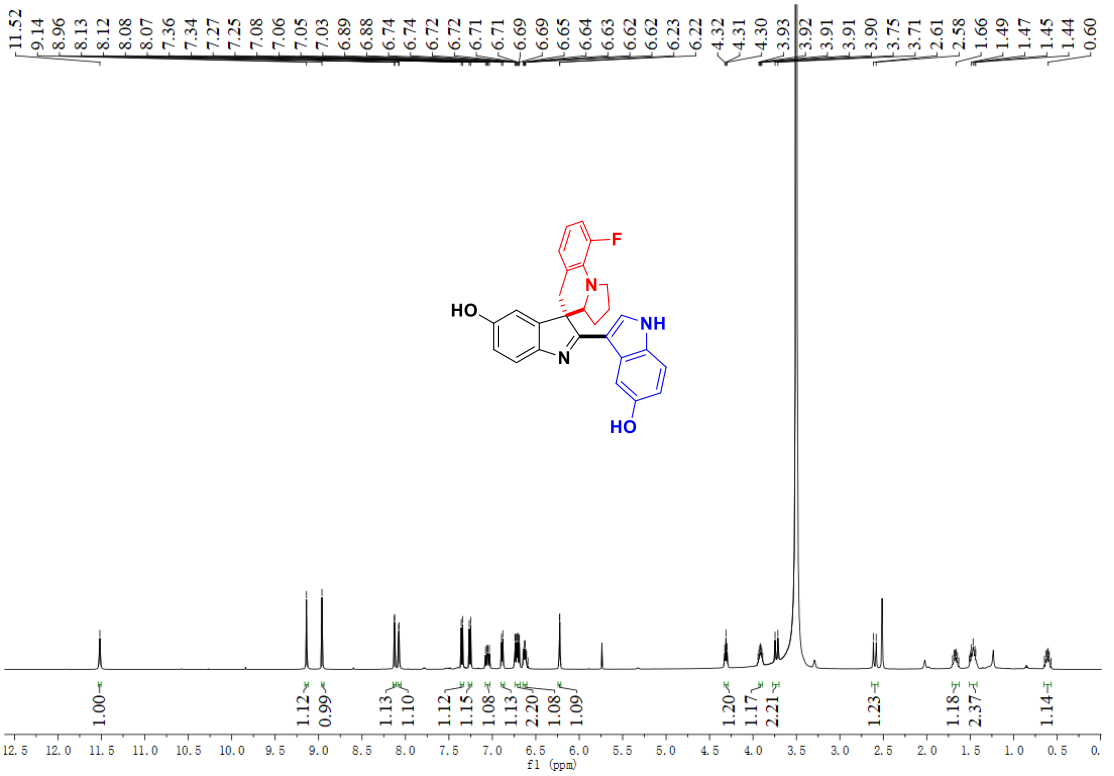
5'-fluoro-2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4s)

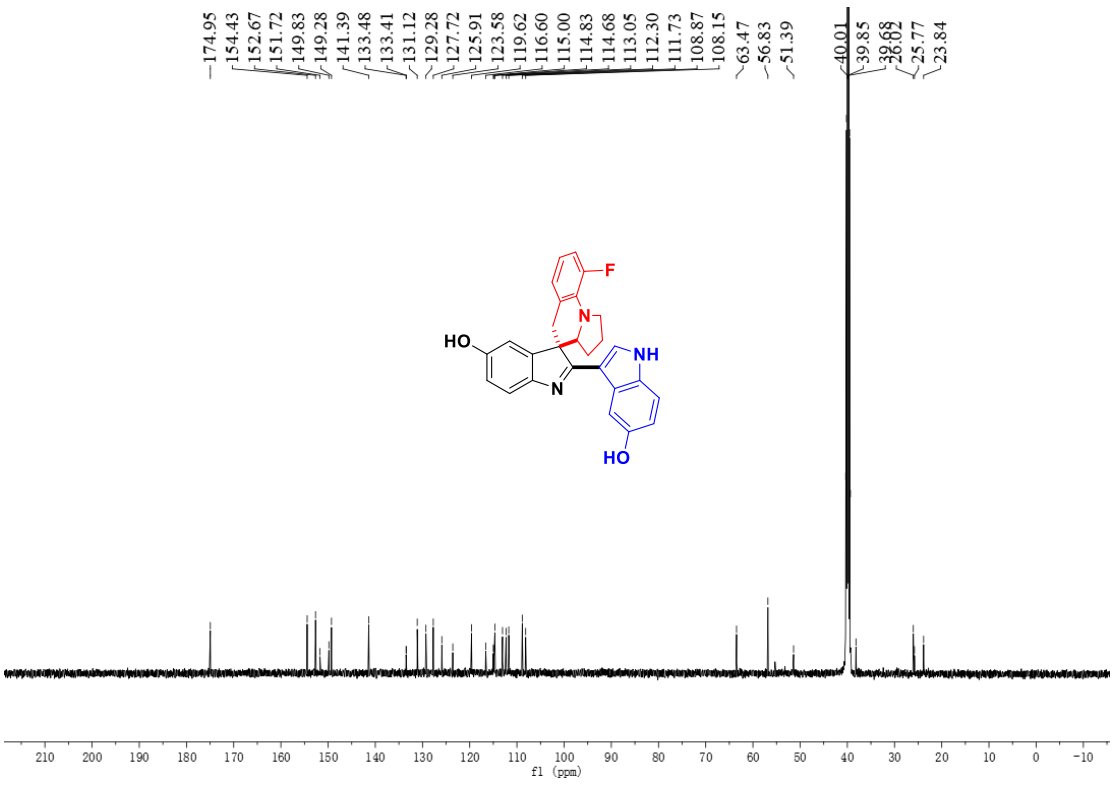


5'-chloro-2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4t)

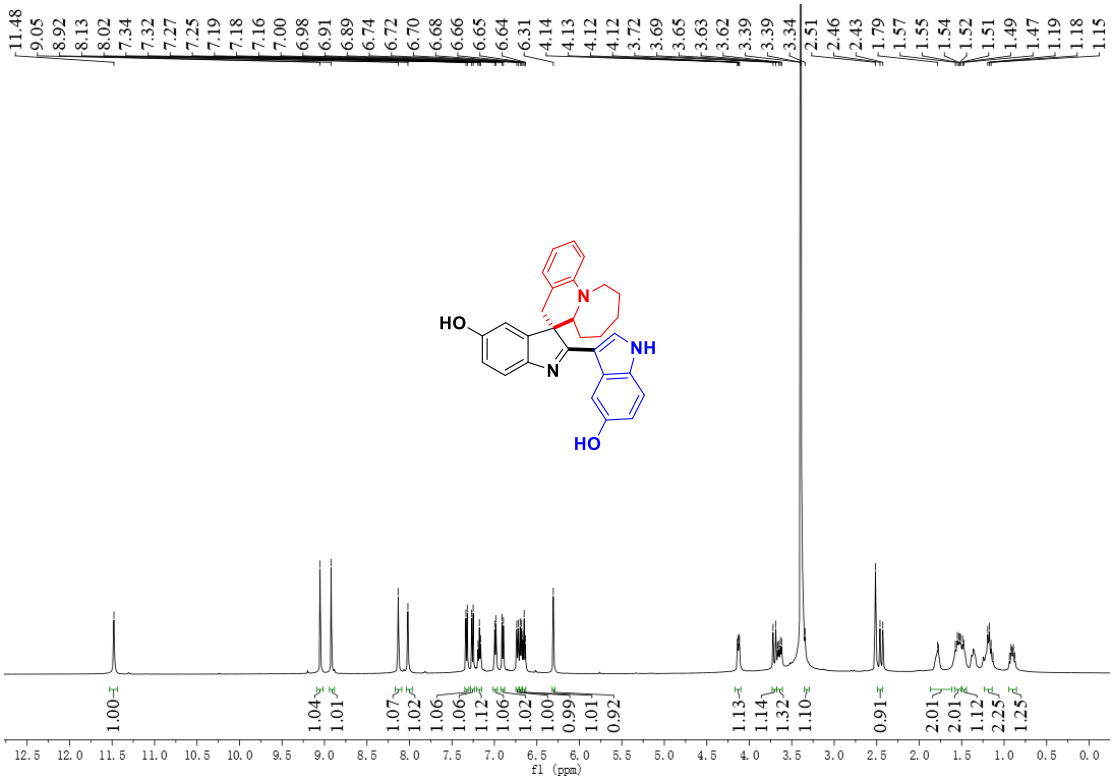


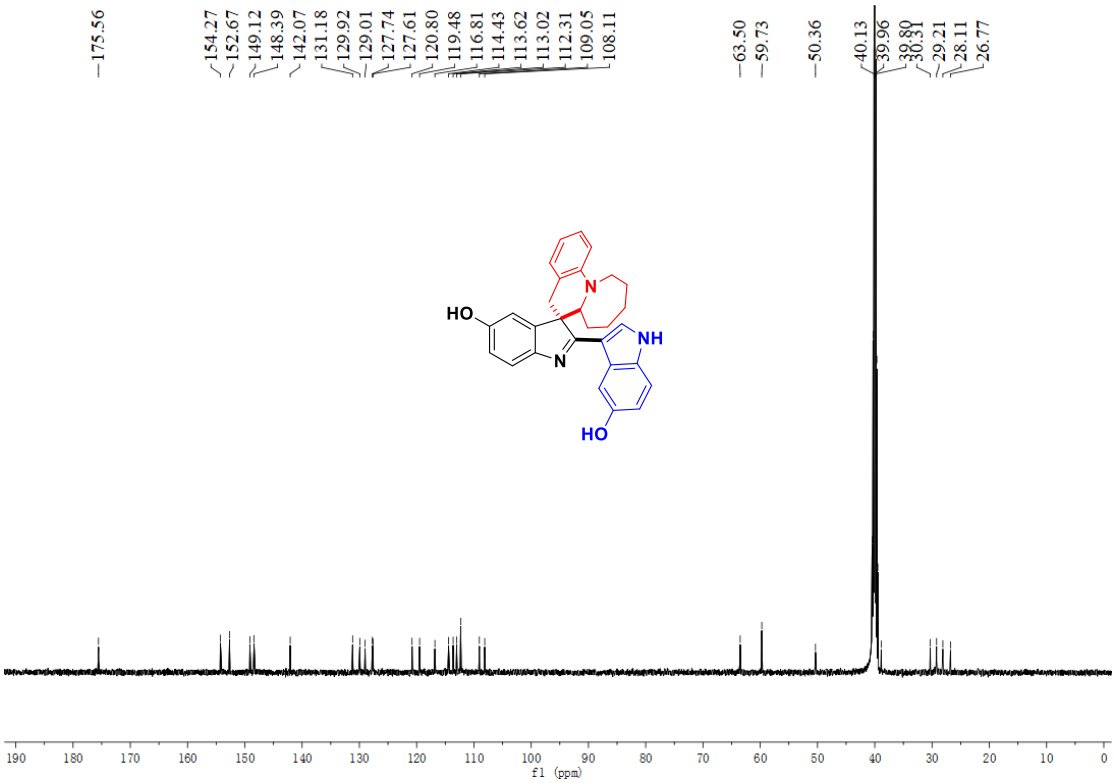
3'-fluoro-2-(5-hydroxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-ol (4u)



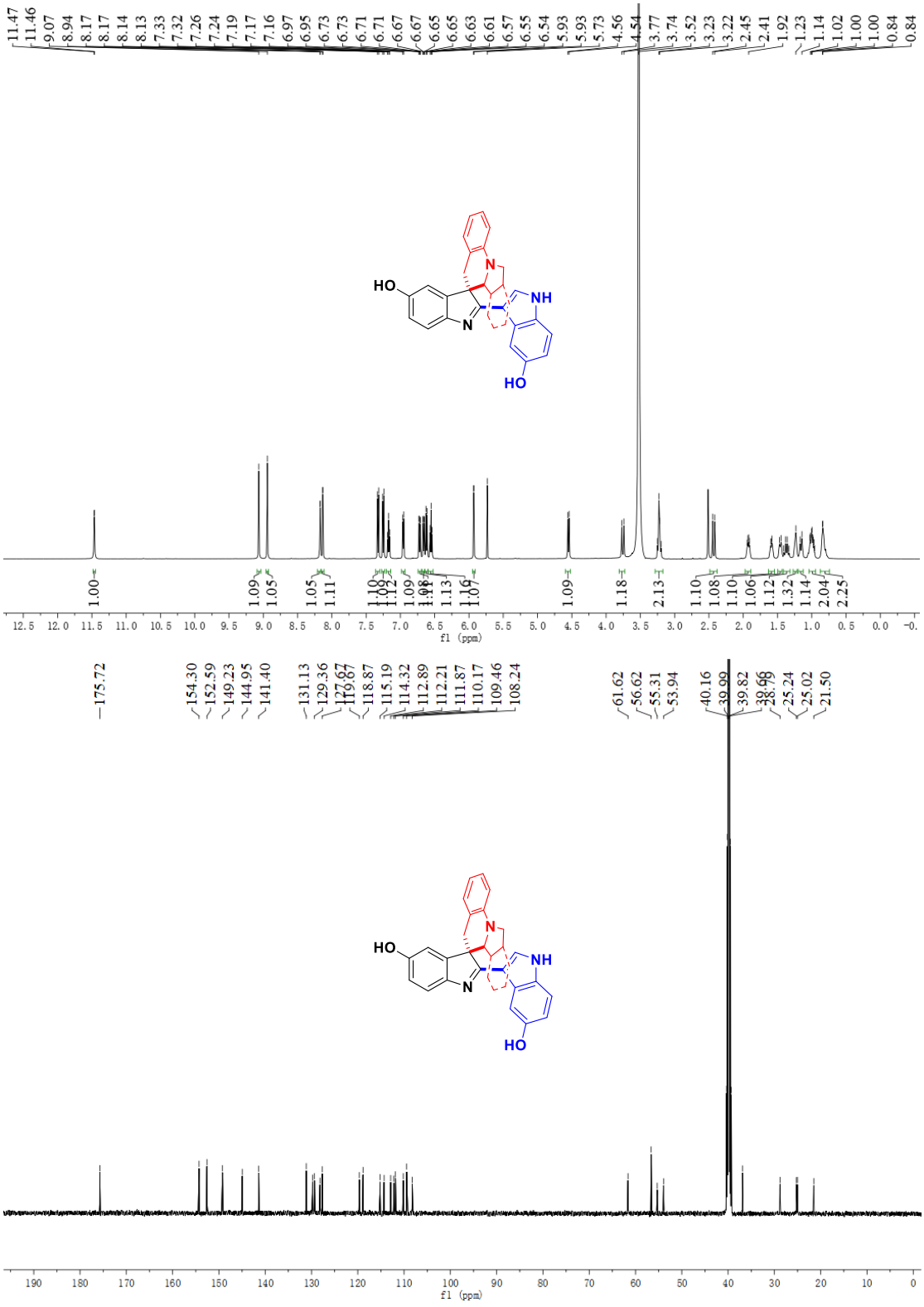


2'-(5-hydroxy-1H-indol-3-yl)-6a,7,8,9,10,11-hexahydro-5H-spiro[azepino[1,2-a]quinoline-6,3'-indol]-5'-ol (4v)

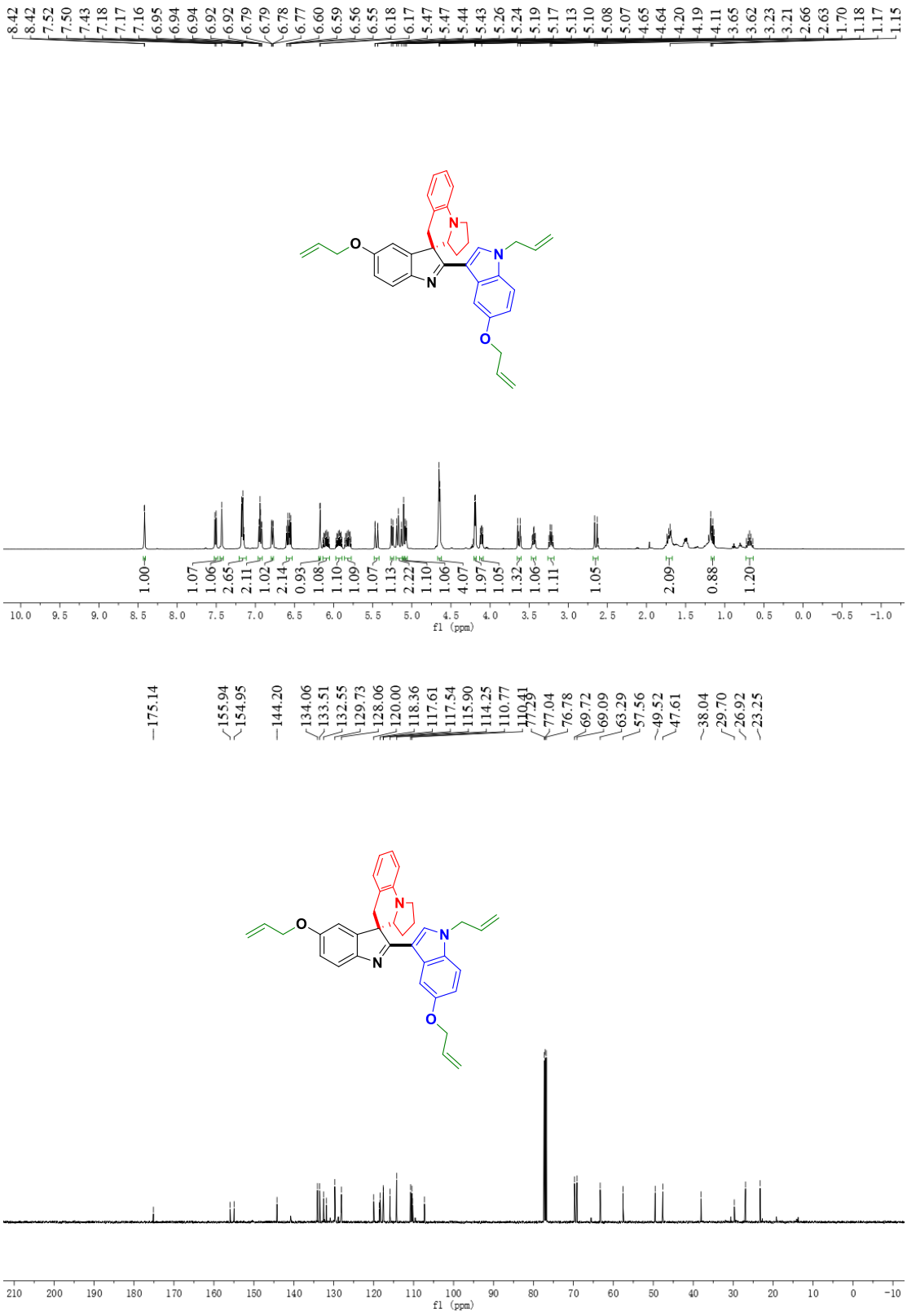




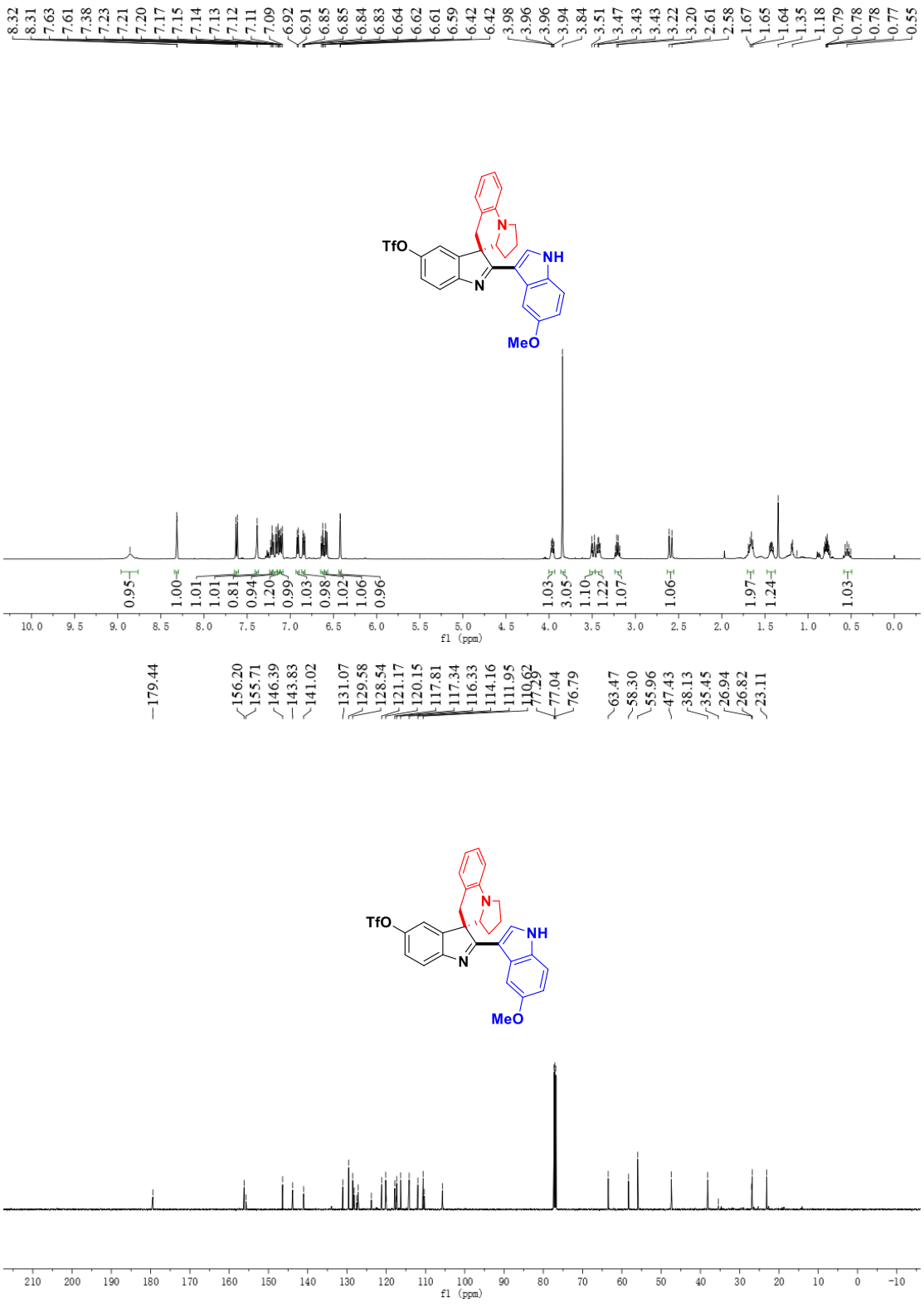
2-(5-hydroxy-1H-indol-3-yl)-6a',6b',7',8',9',10',10a',11'-octahydro-5'H-spiro[indole-3,6'-isoindolo[2,1-a]quinolin]-5-ol (4w)



2-(1-allyl-5-allyloxy-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-allyloxy (5l)



2-(5-methoxy-1H-indol-3-yl)-1',2',3',3a'-tetrahydro-5'H-spiro[indole-3,4'-pyrrolo[1,2-a]quinolin]-5-trifluoromethanesulfonate (6i)



4-(diethylamino)-1',2',3',3a'-tetrahydro-5'H-spiro[cyclohexane-1,4'-pyrrolo[1,2-a]quinoline]-2,4-dien-6-one (8a)