Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Elemental Sulfur Accelerated the Reactivity of 3-Position of Indole for the Construction of Chromeno[2,3-b]indoles

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CONTENTS

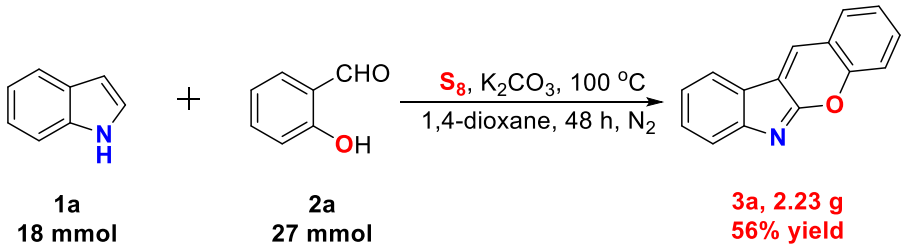
1. General experiment detail and materials

Experimental: All non-aqueous reactions and manipulations were using standard Schlenk techniques. All solvents before use were dried under N_2 atmosphere. NMR spectra were recorded on BRUKER Avance III (400 MHz and 600MHz) spectrometers. Chemical shifts were reported in parts per million (ppm) down field from TMS with the solvent resonance as the internal standard. Coupling constants (*J*) were reported in Hz and referred to apparent peak multiplications. High resolution mass spectra (HRMS) were recorded on Bruker MicroTOF-QII massinstrument (ESI). GS-MS analysis were performed with GC-MS-QP2010 system.

2. General procedure for the synthesis of chromeno[2,3-b]indoles

A mixture of indoles (0.30 mmol), salicylaldehydes (0.45 mmol), elemental sulfur (0.20 mmol), K_2CO_3 (0.45 mmol) and 1, 4-dioxane (2.0 mL) was added to a 25 mL flame-dried Young-type tube under nitrogen atmosphere. The mixture was stirred at 100 °C for 24 h. After the cool reaction to room temperature, the solvent was removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel and eluted with ethyl acetate/petroleum ether to afford the desired product.

3. Experimental procedure for on gram scale



Scheme 1

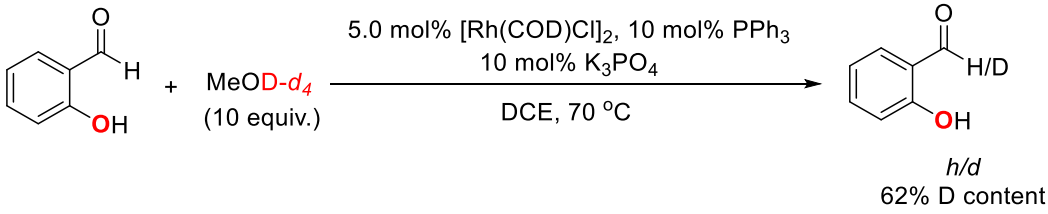
A mixture of indole (18 mmol), salicylaldehyde (27 mmol), elemental sulfur (12 mmol), K_2CO_3 (27 mmol) and 1, 4-dioxane (40 mL) was added to a 100 mL Schlenk

under nitrogen atmosphere. The mixture was stirred at 100 °C for 48 h. After cooling to room temperature, the residues were concentrated in *vacuum*. Then the residues were purified by chromatography on silica gel with petroleum ether/ethyl acetate as eluent to afford the desired product in 56% yield (Scheme 1).

4. Mechanistic studies

4.1 The cross-cyclization of indole and 62% D content of salicylaldehyde

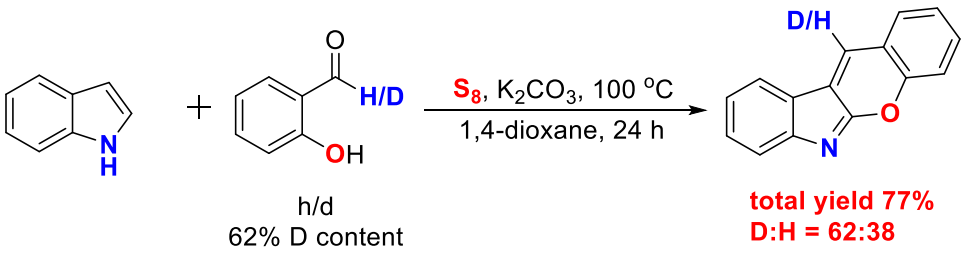
(a) Synthesis of deuterium-enriched salicylaldehyde *h/d*-1.[1] Under N_2, salicylaldehyde (244 mg, 2.0 mmol, 1.0 equiv.), $[Rh(COD)Cl]_2$ (49 mg, 0.10 mmol, 5.0 mol%), PPh_3 (52 mg, 0.20 mmol, 10 mol%) and K_3PO_4 (42 mg, 0.20 mmol, 10 mol%) were combined in DCE (0.50 mL) and methanol-d_4 (0.50 mL). The mixture was stirred at 70 °C for 40 h and passed through a plug of silica (elution with DCM). Purification by flash column chromatography furnished *h/d*-**1** as a light yellow oil (Scheme 2). The deuterium content in the aldehyde was determined to be 62% (^{1}H NMR).



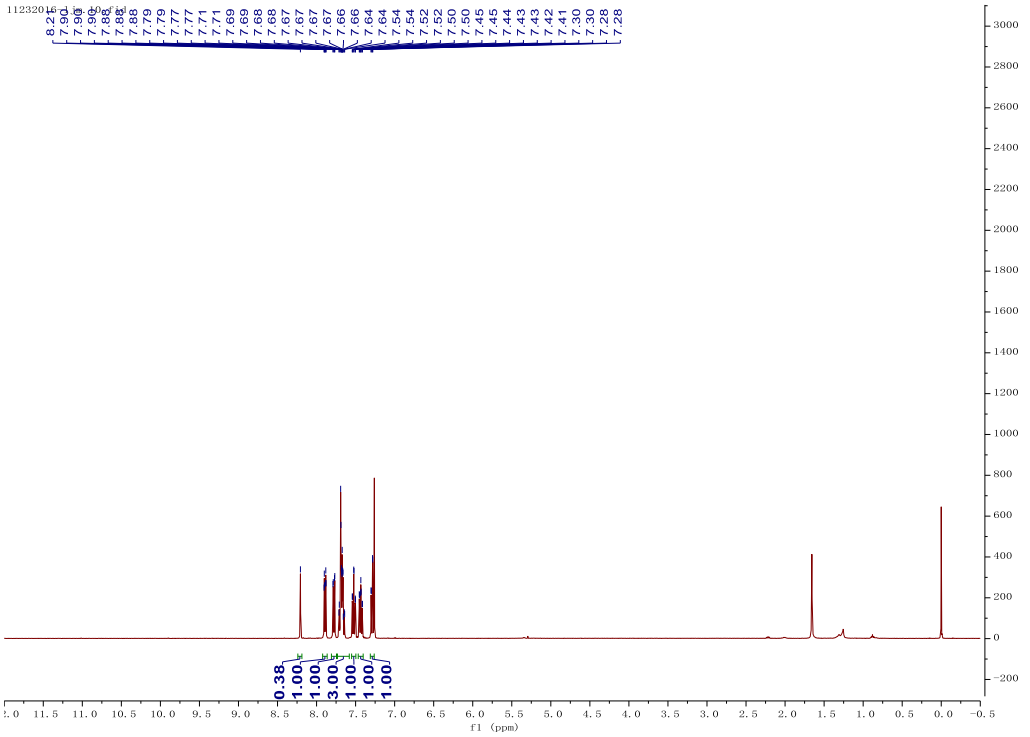
Scheme 2

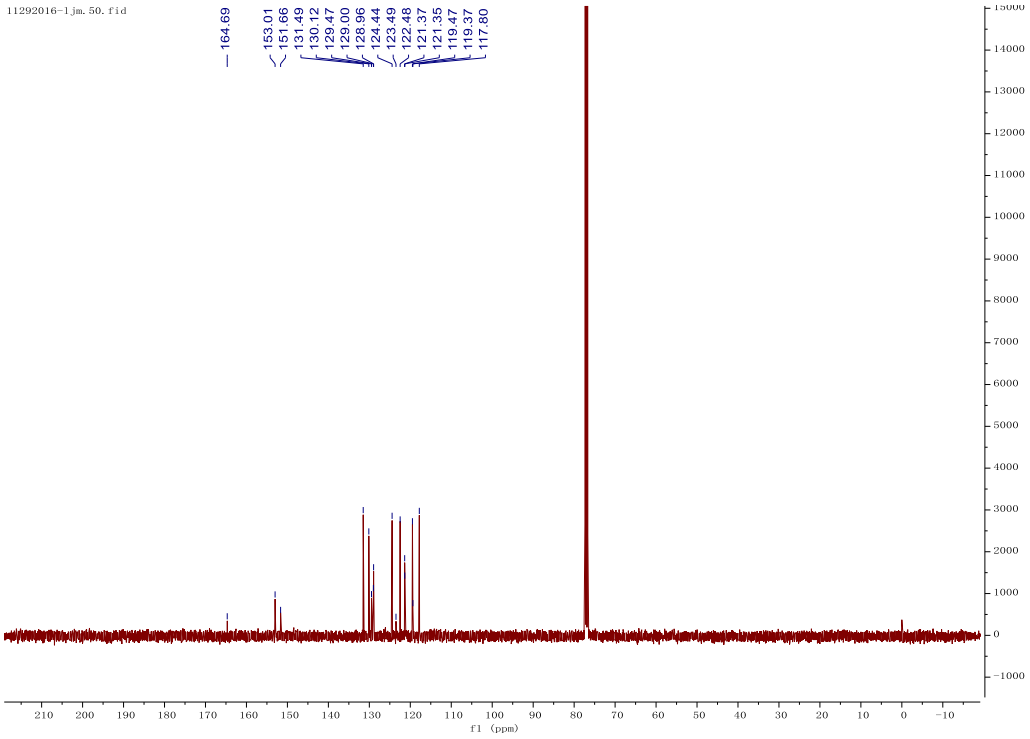
[1] D. E. Frantz, D. G. Weaver, J. P. Carey, M. H. Kress, U. H. Dolling, *Org. Lett.* **2002**, *4*, 4717-4718.

(b) A mixture of indoles (0.30 mmol), 62% D content of salicylaldehyde (0.45 mmol), elemental sulfur (0.20 mmol), K_2CO_3 (0.45 mmol) and 1, 4-dioxane (2.0 mL) was added to a 25 mL flame-dried Young-type tube under nitrogen atmosphere. The mixture was stirred at 100 °C for 24 h. After the cool reaction to room temperature, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel and eluted with ethyl acetate/petroleum ether to afford the desired product in 77% yield (Scheme 3).


O
H/D
OH
N
H
S8, K2CO3, 100 °C
1,4-dioxane, 24 h
D/H
O
N
h/d
62% D content
total yield 77%
D:H = 62:38

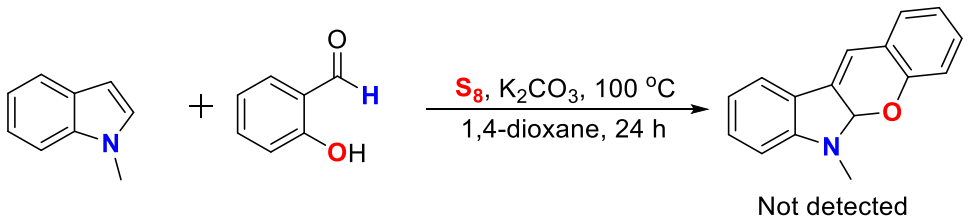
Scheme 3





4.2 The cross-cyclization of 1-methylindole and salicylaldehyde

A mixture of 1-methylindole (0.30 mmol), salicylaldehyde (0.45 mmol), elemental sulfur (0.20 mmol), K_2CO_3 (0.45 mmol) and 1, 4-dioxane (2.0 mL) was added to a 25 mL flame-dried Young-type tube under nitrogen atmosphere. The mixture was stirred at 100 °C for 24 h. After the cool reaction to room temperature, the mixture was detected by GC-MS. The result showed that no desired product was obtained and 1-methylindole did not undergo the reaction with elemental sulfur to form indole-sulfur species (Scheme 4).



Scheme 4

4.3 EPR experiment procedure for interaction of indole (1a) and salicylaldehyde (2a) with elemental sulfur.

a) Indole (0.30 mmol), K_2CO_3 (0.45 mmol), elemental sulfur (0.20 mmol), 1, 4-dioxane (2.0 mL), under N_2 atmosphere, 100 °C for 2.0 h, then preserved in liquid nitrogen for EPR examination. No organic radical was observed.

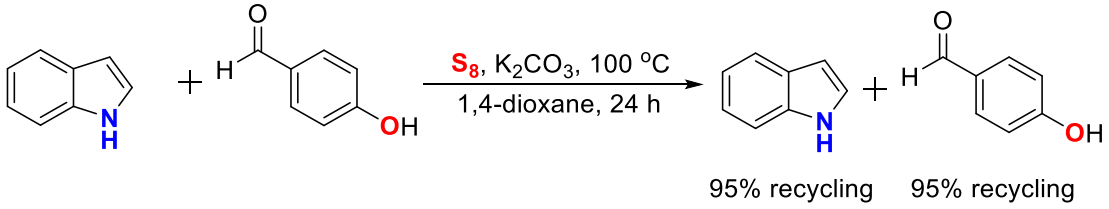
b) Salicylaldehyde (0.45 mmol), K_2CO_3 (0.45 mmol), elemental sulfur (0.20 mmol), 1,4-dioxane (2.0 mL), under N_2 atmosphere, 100 °C for 2.0 h, then preserved in liquid nitrogen for EPR examination. No organic radical was observed.

c) Indole (030 mmol), salicylaldehyde (0.45 mmol), K_2CO_3 (0.45 mmol), elemental sulfur (0.20 mmol), 1, 4-dioxane (2.0 mL), under N_2 atmosphere, 100 °C for 2.0 h, then preserved in liquid nitrogen for EPR examination. No organic radical was observed.

4.4 The cross-cyclization of indole and *p*-hydroxybenzaldehyde

A mixture of indoles (0.30 mmol), *p*-hydroxybenzaldehyde (0.45 mmol), elemental sulfur (0.20 mmol), K_2CO_3 (0.45 mmol) and 1, 4-dioxane (2.0 mL) was added to a 25 mL flame-dried Young-type tube under nitrogen atmosphere. The mixture was stirred

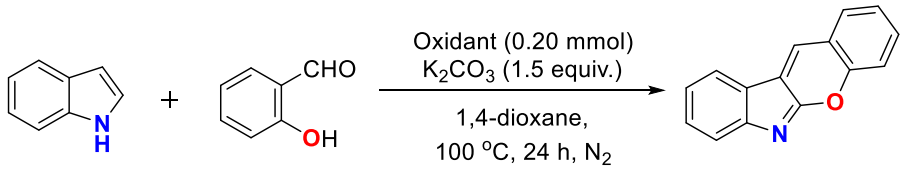
at 100 °C for 24 h. After the cool reaction to room temperature, the mixture was detected by GC-MS. Indole and *p*-hydroxybenzaldehyde was obtained in 95% yield by GC (Scheme 5).



Scheme 5

4.5 The cross-coupling reaction between indole (1a) and salicylaldehyde (2a) under the different oxidants

A mixture of indoles (0.30 mmol), salicylaldehydes (0.45 mmol), different oxidant (0.20 mmol), K_2CO_3 (0.45 mmol) and 1, 4-dioxane (2.0 mL) was added to a 25 mL flame-dried Young-type tube under nitrogen atmosphere. The mixture was stirred at 100 °C for 24 h. After the cool reaction to room temperature, the mixture was detected by GC-MS. No positive results were obtained in absence of elemental sulfur and starting materials were remained in reaction mixture (Scheme 6).



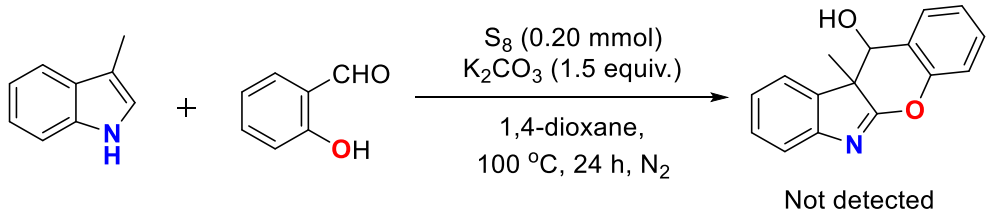
Oxidant	DTBP	TBHP	DDQ	$K_2S_2O_8$	O_2
Yield (%)	0%	0%	0%	0%	0%

Scheme 6

4.6 The cross-cyclization of 3-methylindole and salicyladehyde

A mixture of 3-methylindole (0.30 mmol), salicyladehyde (0.45 mmol), elemental sulfur (0.20 mmol), K_2CO_3 (0.45 mmol) and 1, 4-dioxane (2.0 mL) was added to a 25 mL flame-dried Young-type tube under nitrogen atmosphere. The mixture was stirred at 100 °C for 24 h. After the cool reaction to room temperature, the mixture was detected by GC-MS and no desired product was obtained (Scheme 7). 3-Methylindole

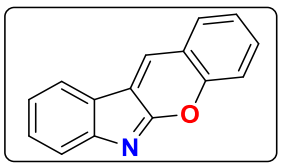
did not undergo the insertion of the aldehyde group.



Scheme 7

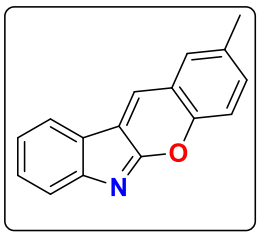
5 Experimental characterization data for products

Chromeno[2, 3-b]indole 3a



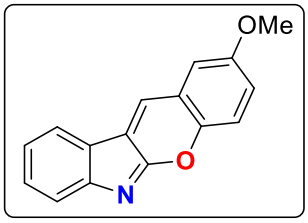
59.1 mg; Brown solid; m.p. 212-213°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.90 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.71-7.64 (m, 3H), 7.53 (td, *J* = 8.0, 4.0 Hz, 1H), 7.44 (td, *J* = 8.0, 4.0 Hz, 1H), 7.29 (td, *J* = 8.0, 4.0 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.7, 152.8, 151.6, 131.6, 130.2, 129.7, 129.1, 125.9, 124.5, 123.5, 122.6, 121.4, 119.4, 119.4, 117.8; HRMS, calculated for $C_{15}H_{10}NO$ ($M+H^+$): 220.0757, found: 220.0757.

2-Methylchromeno[2, 3-b]indole 3b



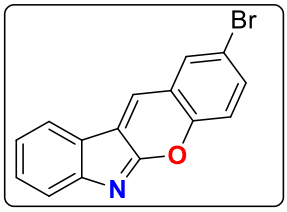
59.7 mg; Yellow solid; m.p. 225-226 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (s, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.55-7.51 (m, 2H), 7.48-7.45 (m, 1H), 7.27 (t, *J* = 8.0 Hz, 1H), 2.50 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.9, 153.0, 149.9, 134.2, 132.7, 130.0, 129.6, 128.8, 125.9, 123.6, 122.3, 121.3, 119.4, 119.2, 117.5, 20.9; HRMS, calculated for $C_{16}H_{12}NO$ ($M+H^+$): 234.0913, found: 234.0913.

2-Methoxychromeno[2, 3-b]indole 3c



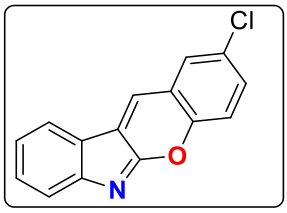
70.4 mg; Brown solid; m.p. 170-171 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 1H), 7.27-7.25 (m, 1H), 7.24-7.21 (m, 1H), 7.17 (d, *J* = 4.0 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.9, 156.1, 153.2, 146.2, 130.2, 129.3, 126.2, 123.3, 122.3, 121.4, 119.8, 119.4, 119.3, 118.6, 110.8, 55.9; HRMS, calculated for $C_{16}H_{12}NO_2$ ($M+H^+$): 250.0863, found: 250.0863.

2-Bromochromeno[2, 3-b]indole 3d



50.8 mg; Orange solid; m.p. 240-241 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.72 (s, 1H), 8.26 (s, 1H), 8.07 (d, *J* = 6.0 Hz, 1H), 7.93 (d, *J* = 12.0 Hz, 1H), 7.80 (d, *J* = 6.0 Hz, 1H), 7.59 (d, *J* = 12.0 Hz, 1H), 7.54 (t, *J* = 6.0 Hz, 1H), 7.33 (t, *J* = 9.0 Hz, 1H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 164.2, 153.0, 150.6, 134.7, 132.0, 130.7, 130.4, 126.3, 123.8, 123.1, 122.7, 121.7, 120.0, 119.4, 116.7; HRMS, calculated for $C_{15}H_9BrNO$ ($M+H^+$): 297.9862, found: 297.9865.

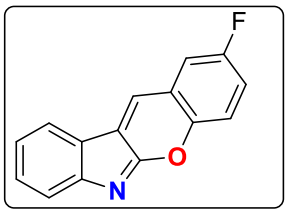
2-Chlorochromeno[2, 3-b]indole 3e



60.3 mg; Orange solid; m.p. 263-265 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.73 (s, 1H), 8.13 (s, 1H), 8.07 (d, *J* = 12.0 Hz, 1H), 7.86 (d, *J* = 12.0 Hz, 1H), 7.81 (d, *J* = 12.0 Hz, 1H), 7.59 (d, *J* = 6.0 Hz, 1H), 7.54 (t, *J* = 9.0 Hz, 1H), 7.32 (t, *J* = 6.0 Hz, 1H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 164.3, 153.0, 150.2, 131.9, 130.7, 130.5,

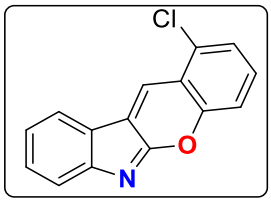
129.1, 128.9, 126.4, 123.8, 123.1, 122.8, 121.2, 119.7, 119.4; HRMS, calculated for $C_{15}H_9ClNO$ ($M+H^+$): 254.0367, found: 254.0367.

2-Fluorochromeno[2, 3-b]indole 3f



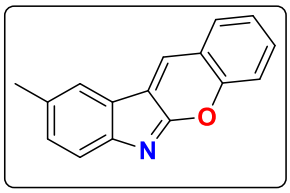
53.2 mg; Orange solid; m.p. 256-258 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.69-7.66 (m, 2H), 7.54 (t, J = 8.0 Hz, 1H), 7.46 (q, J = 4.0 Hz, 1H), 7.41-7.36 (m, 1H), 7.29 (t, J = 8.0 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.6, 158.7 (J_{CF} = 245 Hz), 153.2, 147.7, 130.7, 128.2 (J_{CF} = 3.0 Hz), 127.1, 123.1, 122.7, 121.7, 120.2 (J_{CF} = 7.6 Hz), 119.6, 119.2 (J_{CF} = 9.1 Hz), 118.9 (J_{CF} = 25.7 Hz), 114.0 (J_{CF} = 24.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.22 ppm; HRMS, calculated for $C_{15}H_8FNNaO$ ($M+Na^+$): 260.0482, found: 260.0487.

1-Chlorochromeno[2, 3-b]indole 3g



56.1 mg; Brown solid; m.p. 149-152 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.59-7.53 (m, 2H), 7.50 (d, J = 8.0 Hz, 1H), 7.31 (t, J = 8.0 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.1, 153.2, 152.3, 133.1, 131.1, 130.7, 126.9, 125.3, 125.2, 123.5, 122.9, 121.8, 119.7, 118.0, 116.7; HRMS, calculated for $C_{15}H_9ClNO$ ($M+H^+$): 254.0367, found: 254.0370.

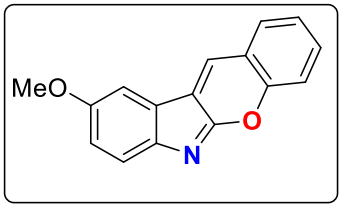
9-Methylchromeno[2, 3-b]indole 4a



65.0 mg; Orange solid; m.p. 190-196 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H),

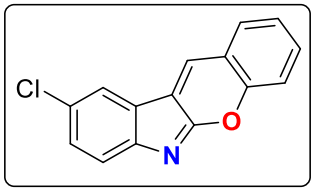
7.74 (d, J = 8.0 Hz, 1H), 7.67-7.61 (m, 3H), 7.55 (d, J = 8.0 Hz, 1H), 7.42-7.38 (m, 1H), 7.31 (d, J = 8.0 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.3, 151.6, 150.8, 132.0, 131.3, 131.0, 129.1, 129.0, 126.2, 124.3, 123.6, 121.8, 119.4, 119.0, 117.7, 21.5; HRMS, calculated for $C_{16}H_{12}NO$ ($M+H^+$): 234.0913, found: 234.0918.

9-Methoxychromeno[2, 3-b]indole 4b



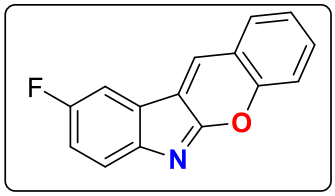
68.5 mg; Brown solid; m.p. 170-171 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.64-7.60 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H), 7.42-7.37 (m, 2H), 7.07 (dd, J = 8.0, 4.0 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.7, 155.9, 151.7, 146.7, 131.5, 129.5, 129.0, 126.3, 124.3, 124.2, 119.8, 119.2, 117.7, 116.5, 106.6, 55.9; HRMS, calculated for $C_{16}H_{12}NO_2$ ($M+H^+$): 250.0863, found: 250.0861.

9-Chlorochromeno[2, 3-b]indole 4c



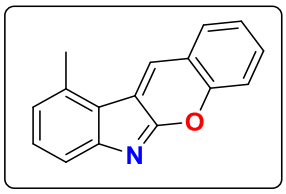
49.4 mg; Orange solid; m.p. 269-272 °C; ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.91 (s, 1H), 8.19 (s, 1H), 8.04 (d, J = 6.0 Hz, 1H), 7.86-7.81 (m, 2H), 7.60-7.56 (m, 2H), 7.54 (d, J = 6.0 Hz, 1H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 164.7, 151.8, 151.4, 134.0, 133.1, 130.6, 129.7, 127.0, 125.6, 125.5, 124.5, 122.4, 120.5, 119.6, 117.9; HRMS, calculated for $C_{15}H_9ClNO$ ($M+H^+$): 254.0367, found: 254.0367.

9-Fluorochromeno[2, 3-b]indole 4d



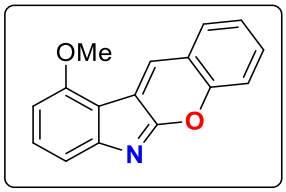
66.8 mg; Red solid; m.p. 250-252 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.71-7.69 (m, 2H), 7.62-7.55 (m, 2H), 7.47-7.43 (m, 1H), 7.25-7.20 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.4, 159.2 (J_{CF} = 240 Hz), 151.8, 148.9, 132.0, 130.8, 129.3, 125.8, 124.6, 124.2 (J_{CF} = 10.6 Hz), 120.1 (J_{CF} = 9.1 Hz), 119.1, 117.9, 117.0 (J_{CF} = 24.2 Hz), 108.2 (J_{CF} = 24.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.33 ppm; HRMS, calculated for $C_{15}H_9FNO$ ($M+H^+$): 238.0663, found: 238.0663.

10-Methylchromeno[2, 3-b]indole 4e



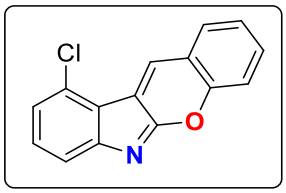
65.1 mg; Yellow solid; m.p. 188-192 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.77 (dd, J = 8.0, 4.0 Hz, 1H), 7.68-7.62 (m, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.44-7.39 (m, 2H), 7.07 (d, J = 8.0 Hz, 1H), 2.72 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.4, 152.8, 151.2, 134.4, 131.3, 130.9, 129.8, 129.0, 126.4, 124.4, 124.3, 122.0, 119.7, 117.7, 117.2, 19.9; HRMS, calculated for $C_{16}H_{12}NO$ ($M+H^+$): 234.0913, found: 234.0912.

10-Methoxychromeno[2, 3-b]indole 4f



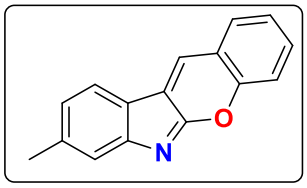
55.0 mg; Orange solid; m.p. 202-206 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.72 (d, J = 8.0 Hz, 1H), 7.65-7.57 (m, 2H), 7.46-7.36 (m, 2H), 7.30 (d, J = 8.0 Hz, 1H), 6.76 (d, J = 8.0 Hz, 1H), 4.04 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.6, 156.4, 154.0, 151.2, 131.0, 131.0, 130.9, 128.9, 124.7, 124.4, 120.1, 117.7, 112.6, 111.6, 104.6, 55.5; HRMS, calculated for $C_{16}H_{12}NO_2$ ($M+H^+$): 250.0863, found: 250.0862.

10-Chlorochromeno[2, 3-b]indole 4g



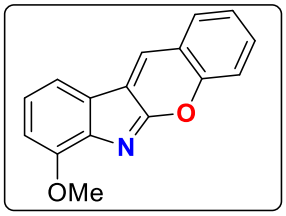
51.1 mg; Orange solid; m.p. 189-191 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.84 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.73-7.70 (m, 2H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.48-7.43 (m, 2H), 7.26 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.6, 154.0, 151.5, 133.4, 132.1, 130.4, 129.6, 129.4, 124.7, 124.6, 123.1, 121.2, 119.5, 118.0, 117.8; HRMS, calculated for $C_{15}H_9ClNO$ ($M+H^+$): 254.0367, found: 254.0367.

8-Methylchromeno[2, 3-b]indole 4h



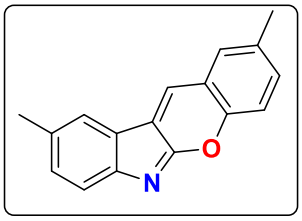
61.8 mg; Orange solid; m.p. 192-196 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.74-7.71 (m, 2H), 7.66-7.59 (m, 2H), 7.47 (d, *J* = 4.0 Hz, 1H), 7.41-7.37 (m, 1H), 7.07 (dd, *J* = 8.0, 4.0 Hz, 1H), 2.50 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.9, 153.3, 151.4, 140.8, 131.1, 128.8, 128.3, 126.0, 124.4, 123.5, 121.1, 120.9, 120.1, 119.5, 117.7, 22.4; HRMS, calculated for $C_{16}H_{12}NO_2$ ($M+H^+$): 234.0913, found: 234.0912.

7-Methoxychromeno[2, 3-b]indole 4i



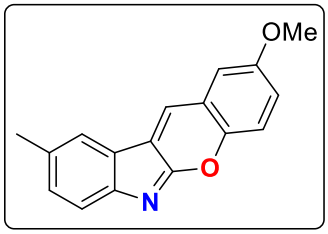
54.8 mg; Red solid; m.p. 167-169 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (s, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.70-7.63 (m, 2H), 7.53 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.44-7.40 (m, 1H), 7.23 (t, *J* = 8.0 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 1H), 4.06 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.2, 151.8, 150.6, 141.4, 131.6, 130.4, 129.0, 126.3, 124.8, 124.4, 123.3, 119.4, 117.9, 114.0, 113.0, 56.3; HRMS, calculated for $C_{16}H_{12}NO_2$ ($M+H^+$): 250.0863, found: 250.0863.

2, 9-Dimethylchromeno[2, 3-b]indole 4j



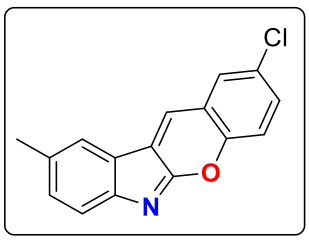
40.7 mg; Orange solid; m.p. 214-215 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.67 (s, 1H), 7.56-7.51 (m, 3H), 7.44 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 2.48 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.5, 150.8, 149.9, 134.0, 132.5, 131.8, 130.9, 129.1, 128.7, 126.0, 123.6, 121.7, 119.2, 118.9, 117.4, 21.4, 20.8; HRMS, calculated for $C_{17}H_{14}NO$ ($M+H^+$): 248.1070, found: 248.1068.

2-Methoxy-9-methylchromeno[2, 3-b]indole 4k



31.5 mg; Orange solid; m.p. 194-198 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.64 (s, 1H), 7.55 (dd, *J* = 12.0, 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 1H), 7.21-7.18 (m, 1H), 7.14 (d, *J* = 4.0 Hz, 1H), 3.89 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.5, 156.0, 150.9, 146.2, 131.8, 131.1, 128.9, 126.4, 123.4, 121.8, 119.8, 119.2, 118.9, 118.6, 110.8, 55.9, 21.4; HRMS, calculated for $C_{17}H_{14}NO_2$ ($M+H^+$): 264.1019, found: 264.1014.

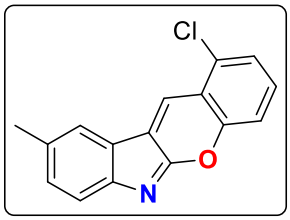
2-Chloro-9-methylchromeno[2, 3-b]indole 4l



34.3 mg; Orange solid; m.p. 277-281 ºC; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.65 (s, 1H), 8.11 (d, *J* = 4.0 Hz, 1H), 7.87 (s, 1H), 7.84 (d, *J* = 4.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 4.0 Hz, 1H), 2.45 (s, 3H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 163.8, 150.8, 150.1, 132.2, 131.8, 131.5, 123.0, 129.0, 128.8,

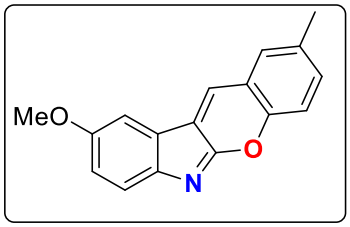
126.5, 123.9, 123.0, 121.2, 119.7, 119.0, 21.5; HRMS, calculated for $C_{16}H_{11}ClNO$ ($M+H^+$): 268.0524, found: 268.0525.

1-Chloro-9-methylchromeno[2, 3-b]indole 4m



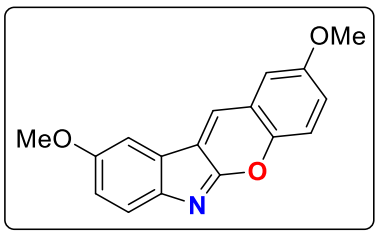
66.1 mg; Orange solid; m.p. 200-204 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 7.73 (s, 1H), 7.59-7.51 (m, 3H), 7.46 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.6, 152.2, 150.9, 133.1, 132.5, 131.5, 131.0, 127.0, 125.0, 124.8, 123.5, 122.2, 119.2, 118.0, 116.6, 21.4; HRMS, calculated for $C_{16}H_{11}ClNO$ ($M+H^+$): 268.0524, found: 268.0524.

9-Methoxy-2-methylchromeno[2, 3-b]indole 4n



58.4 mg; Brown solid; m.p. 194-199 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.55 (dd, *J* = 8.0, 4.0 Hz, 2H), 7.51 (s, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.41 (d, *J* = 4.0 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 3.89 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.9, 155.8, 150.0, 146.8, 134.0, 132.7, 129.6, 128.8, 126.2, 124.2, 119.7, 119.0, 117.4, 116.4, 106.6, 56.0, 20.9; HRMS, calculated for $C_{17}H_{14}NO_2$ ($M+H^+$): 264.1019, found: 264.1013.

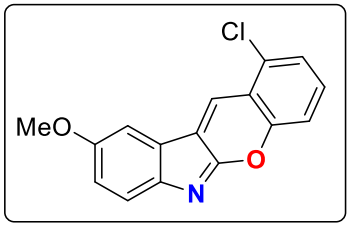
2, 9-Dimethoxychromeno[2, 3-b]indole 4o



59.6 mg; Brown solid; m.p. 169-171 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.56 (t, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 1.0 Hz, 1H), 7.22 (dd, *J* = 8.0, 4.0 Hz, 1H), 7.15

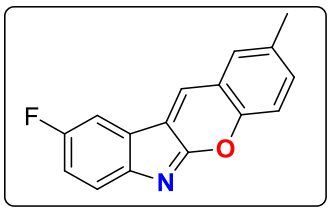
(d, J = 4.0 Hz 1H), 7.09 (dd, J = 8.0, 4.0 Hz, 1H), 3.90 (s, 3H), 3.89 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.9, 155.9, 155.8, 147.0, 146.3, 129.4, 126.6, 124.0, 119.7, 119.6, 119.3, 118.6, 116.5, 111.0, 106.7, 56.0, 55.9; HRMS, calculated for $C_{17}H_{14}NO_3$ ($M+H^+$): 280.0968, found: 280.0966.

1-Chloro-9-methoxychromeno[2, 3-b]indole 4p



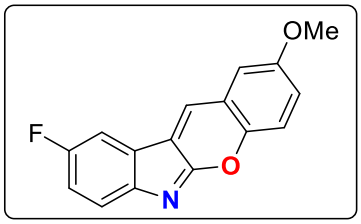
74.5 mg; Brown solid; m.p. 161-166 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.60-7.55 (m, 3H), 7.48-7.45 (m, 2H), 7.10 (dd, J = 8.0, 4.0 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.0, 156.2, 152.4, 146.9, 133.1, 131.1, 127.3, 125.3, 125.0, 124.1, 120.0, 117.8, 117.2, 116.6, 106.9, 56.0; HRMS, calculated for $C_{16}H_{11}ClNO_2$ ($M+H^+$): 284.0473, found: 284.0467.

9-Fluoro-2-methylchromeno[2, 3-b]indole 4q



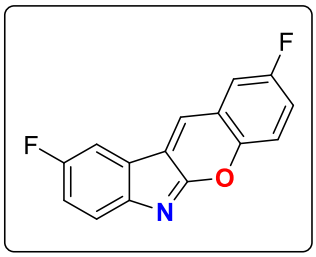
30.5 mg; Orange solid; m.p. 238-240 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 4.0 Hz 1H), 7.60-7.47 (m, 5H), 7.26-7.19 (m, 1H), 2.49 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.6, 159.1 (J_{CF} = 239 Hz), 150.1, 148.9, 134.3, 133.2, 130.8, 129.0, 125.6, 124.2 (J_{CF} = 10.6 Hz), 120.0 (J_{CF} = 9.1 Hz), 118.8, 117.5, 116.8 (J_{CF} = 24.2 Hz), 108.1 (J_{CF} = 25.7 Hz), 20.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.60 ppm; HRMS, calculated for $C_{16}H_{11}FNO$ ($M+H^+$): 252.0819, found: 252.0821.

9-Fluoro-2-methoxychromeno[2, 3-b]indole 4r



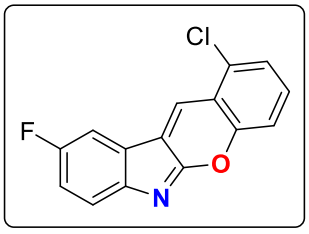
50.7 mg; Yellow solid; m.p. 203-207 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.63-7.54 (m, 3H), 7.26-7.19 (m, 3H), 3.92 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.6, 159.1 (J_{CF} = 240 Hz), 156.1, 149.1, 146.4, 130.6, 120.0 (J_{CF} = 9.1 Hz), 119.5, 118.7, 117.1 (J_{CF} = 24.2 Hz), 110.9, 108.2 (J_{CF} = 25.7 Hz), 55.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.64 ppm; HRMS, calculated for $C_{16}H_{11}FNO_2$(M+H$^+$): 268.0768, found: 268.0768.

2,9-Difluorochromeno[2, 3-b]indole 4s



45.0 mg; Red solid; m.p. 282-285 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.69 (q, J = 4.0 Hz, 1H), 7.62-7.56 (m, 2H), 7.49-7.39 (m, 2H), 7.26-7.22 (m, 1H); ^{13}C NMR (151 MHz, DMSO-d_6) δ 164.4, 158.9 (J_{CF} = 239 Hz), 158.5 (J_{CF} = 242 Hz), 149.3, 148.1, 132.5 (J_{CF} = 3.0 Hz), 126.1 (J_{CF} = 4.5 Hz), 124.6 (J_{CF} = 10.6 Hz), 120.5 (J_{CF} = 9.1 Hz), 120.3, 120.2 (J_{CF} = 9.1 Hz), 119.8 (J_{CF} = 9.1 Hz), 117.3, (J_{CF} = 24.2 Hz) 115.4 (J_{CF} = 24.2 Hz), 109.7 (J_{CF} = 25.7 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.92, -119.94 ppm; HRMS, calculated for $C_{15}H_8F_2NO$ (M+H$^+$): 256.0568, found: 256.0567.

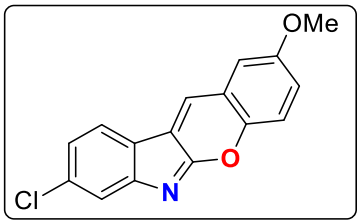
1-Chloro-9-fluorochromeno[2, 3-b]indole 4t



39.9 mg; Brown solid; m.p. 187-192 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 7.63-7.56 (m, 4H), 7.50 (q, J = 4.0 Hz, 1H), 7.25-7.21 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.7 (J_{CF} = 3.0 Hz), 159.3 (J_{CF} = 240 Hz), 152.4, 149.1 (J_{CF} = 1.5 Hz), 133.4, 131.6, 126.6 (J_{CF} = 6.0 Hz), 125.2, 124.1(J_{CF} =10.6 Hz), 120.3 (J_{CF} = 7.6 Hz), 117.6 (J_{CF} = 18.1 Hz), 117.4, 116.7, 108.6 (J_{CF} = 25.7 Hz); ^{19}F NMR (376 MHz,

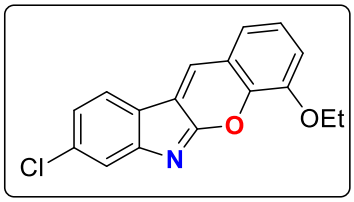
$CDCl_3$) δ -119.69 ppm; HRMS, calculated for $C_{15}H_7ClFNNaO$ ($M+Na^+$): 294.0092, found: 294.0098.

8-Chloro-2-methoxychromeno[2, 3-b]indole 4u



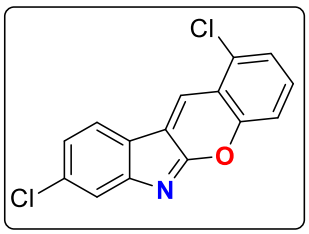
43 mg; Yellow solid; m.p. 226-228 ºC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.63 (d, *J* = 12.0 Hz, 2H), 7.28 (d, *J* = 4.0 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 1H), 7.19 (d, *J* = 4.0 Hz, 1H), 3.92 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.6, 156.3, 154.2, 146.2, 135.7, 130.0, 125.3, 122.5, 122.0, 121.7, 119.9, 119.8, 119.8, 118.8, 110.8, 56.0; HRMS, calculated for $C_{16}H_{11}ClNO$ ($M+H^+$): 284.0473, found: 284.0471.

8-Chloro-4-ethoxychromeno[2, 3-b]indole 4v



64.1 mg; Orange solid; m.p. 209-215 ºC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.60 (d, *J* = 1.0 Hz, 1H), 7.33-7.27 (m, 2H), 7.20-7.17 (m, 2H), 4.23 (q, *J* = 6.7 Hz, 2H), 1.55 (t, *J* = 6.0 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.2, 154.1, 147.8, 141.6, 135.6, 130.5, 125.0, 124.4, 122.5, 122.0, 121.7, 120.5, 120.0, 119.7, 115.2, 65.3, 14.9; HRMS, calculated for $C_{17}H_{13}ClNO_2$ ($M+H^+$): 298.0629, found: 298.0634.

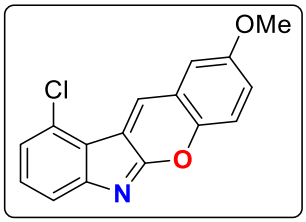
1,8-Dichlorochromeno[2, 3-b]indole 4w



48.8 mg; Red solid; m.p. 216-220 ºC; ^1H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H),

7.83 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 4.0 Hz, 1H), 7.61-7.57 (m, 2H), 7.51 (dd, J = 8.0, 4.0 Hz, 1H), 7.27 (t, J = 4.0 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.8, 154.2, 152.2, 136.3, 133.3, 131.5, 126.0, 125.9, 125.4, 123.1, 122.4, 121.8, 120.1, 118.0, 116.7; HRMS, calculated for $C_{15}H_7Cl_2NNaO$ ($M+Na^+$): 287.9977, found: 287.9980.

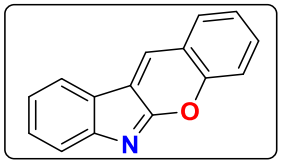
10-Chloro-2-methoxychromeno[2, 3-b]indole 4x

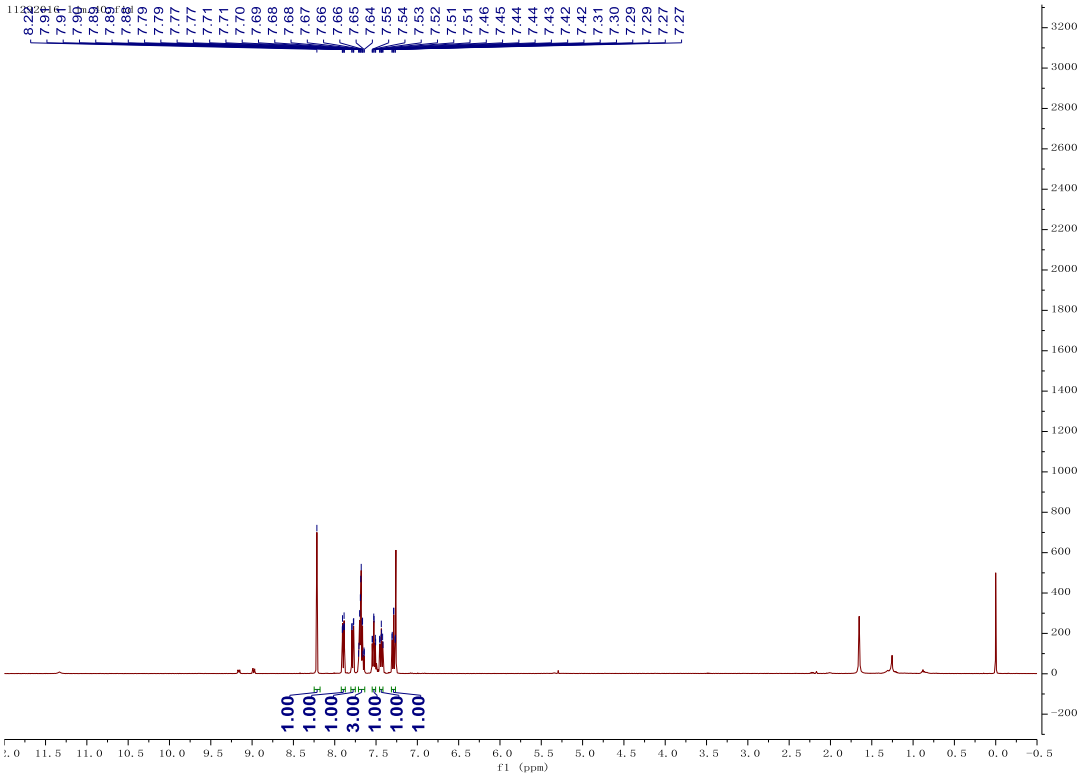


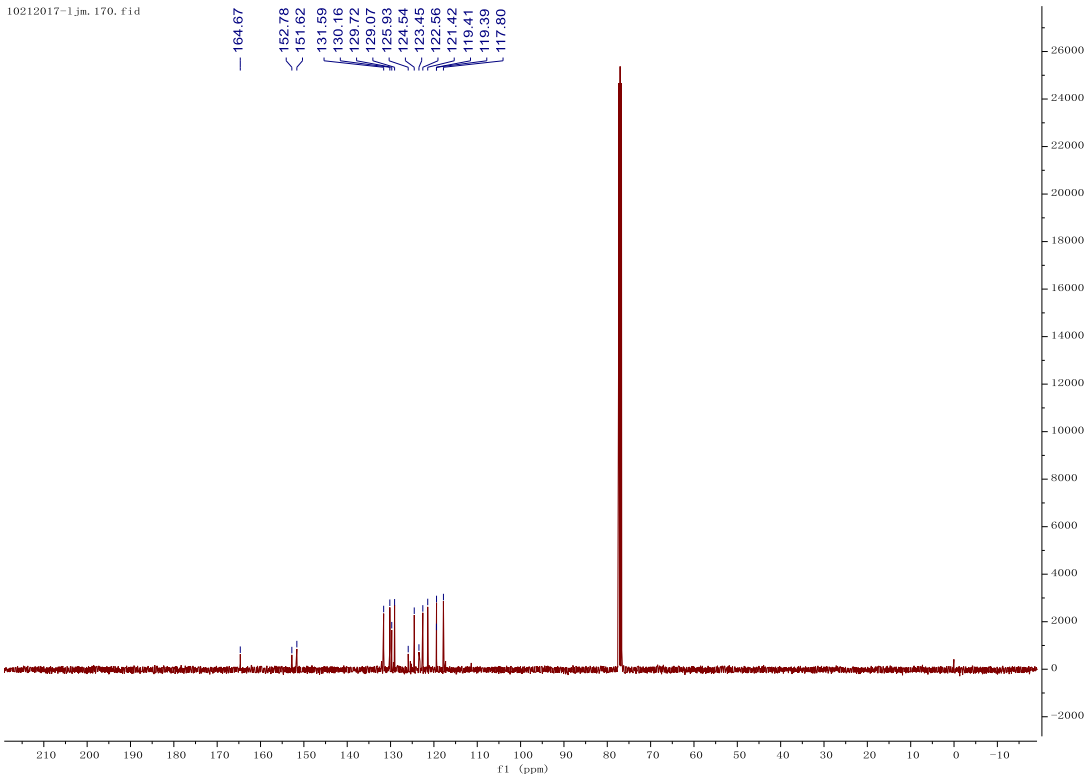
60.3 mg; Orange solid; m.p. 158-162 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 7.64 (d, J =12.0 Hz, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.44 (t, J = 8.0 Hz, 1H), 7.29 (d, J = 4.0 Hz, 1H), 7.25-7.23 (m, 2H), 3.92 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.7, 156.2, 154.2, 146.1, 133.2, 130.4, 129.4, 124.8, 122.9, 121.0, 120.4, 119.9, 118.7, 117.8, 110.9, 55.9; HRMS, calculated for $C_{16}H_{10}ClNNaO_2$ ($M+Na^+$): 284.0473, found: 284.0471.

6 Copies for ^{1}H NMR and ^{13}C NMR

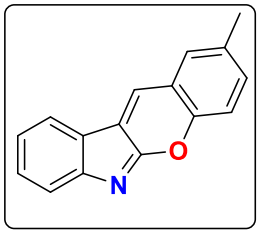
Chromeno[2, 3-b]indole 3a

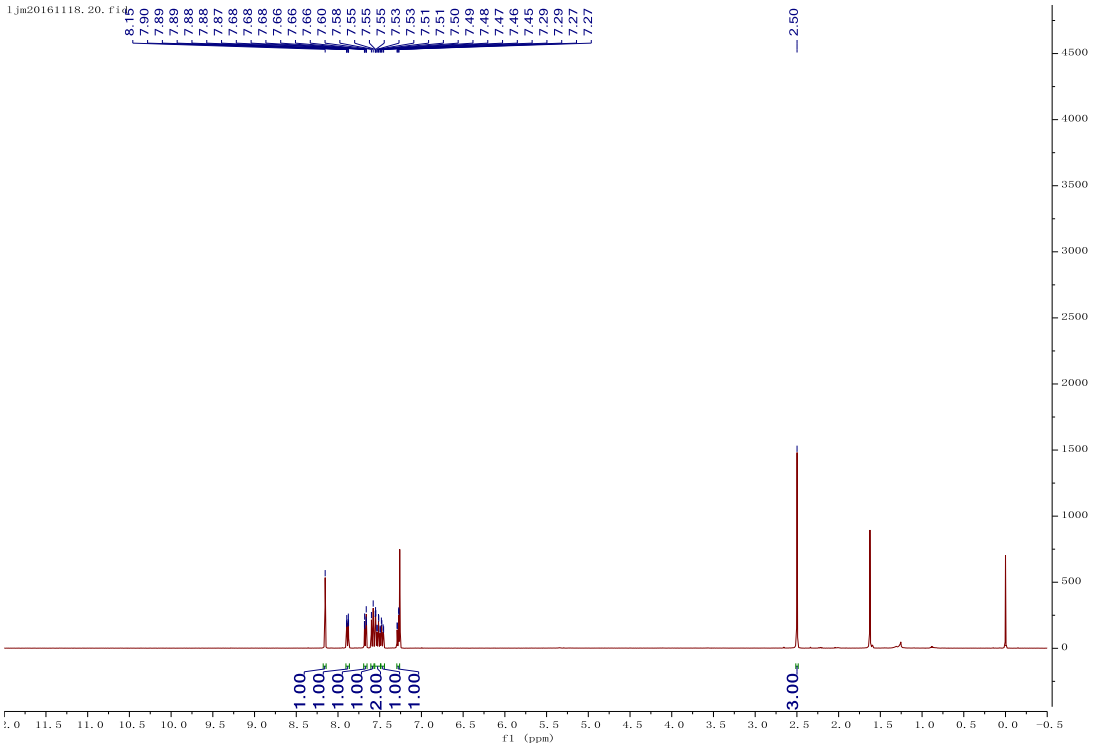


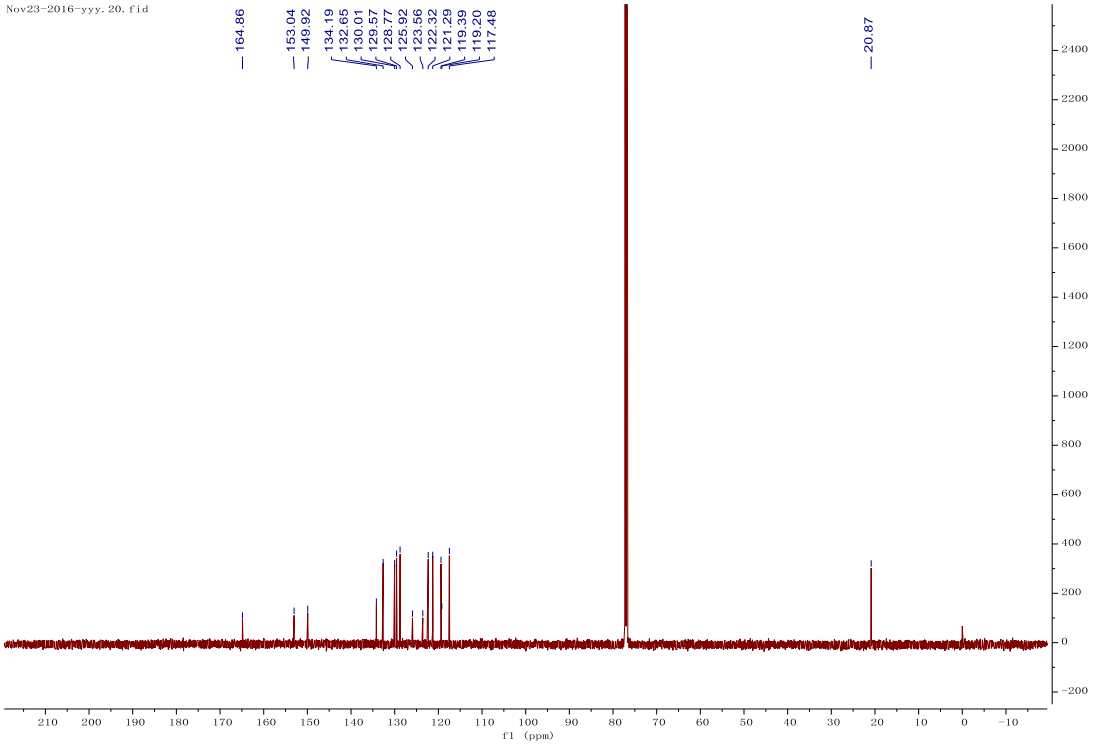




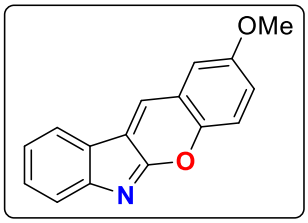
2-Methylchromeno[2, 3-b]indole 3b

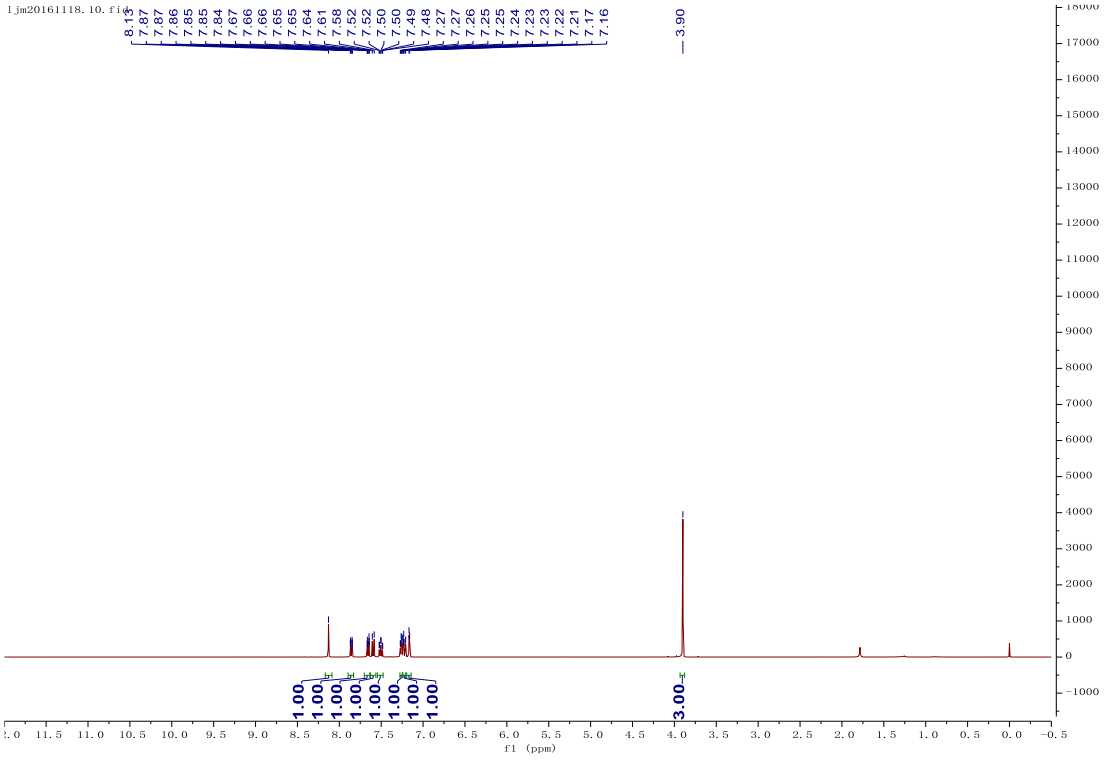


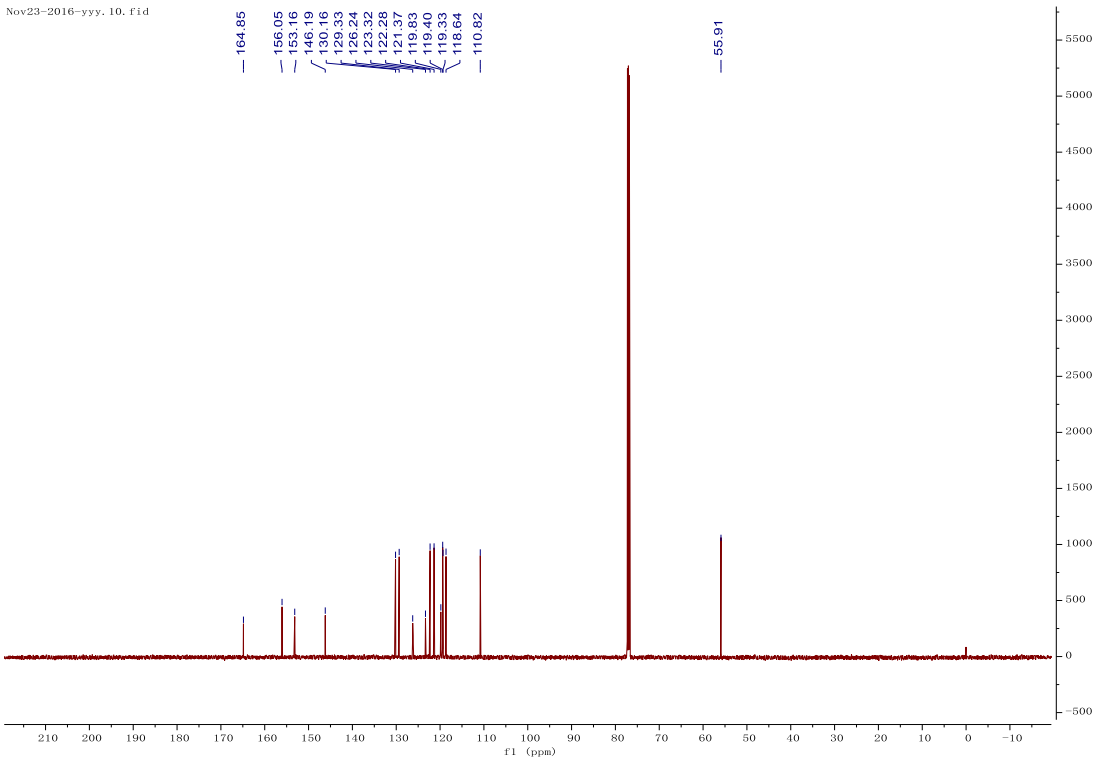




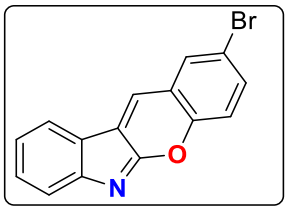
2-Methoxychromeno[2, 3-b]indole 3c

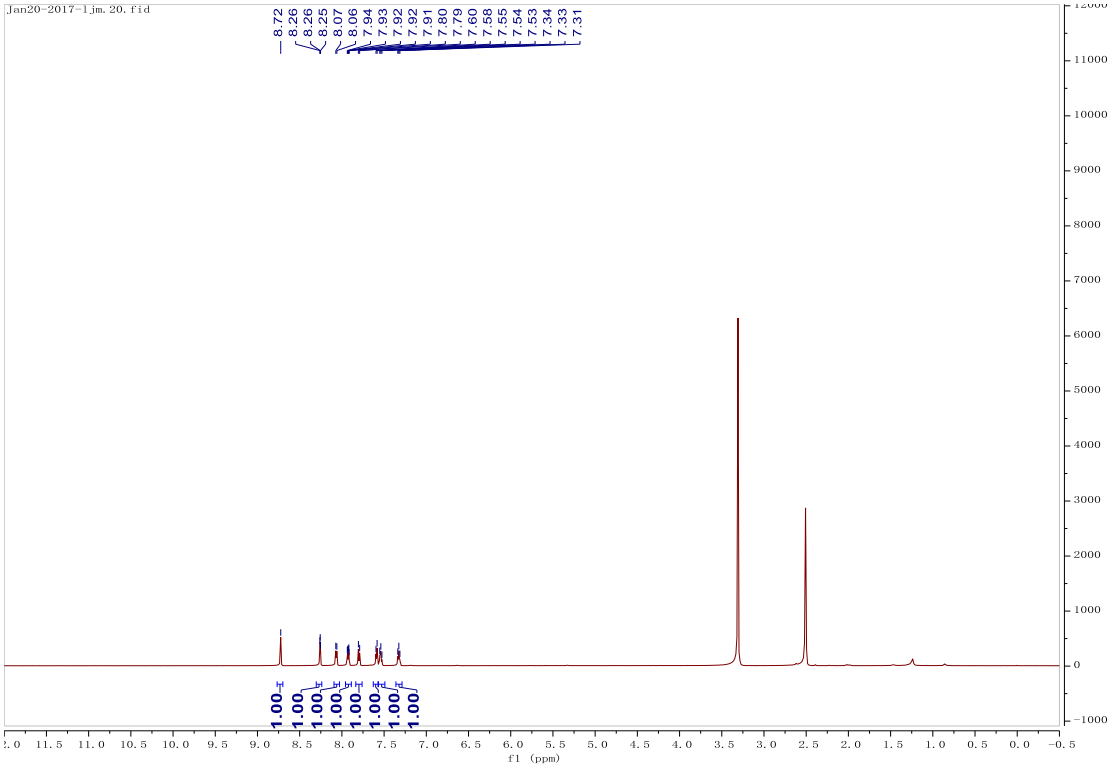


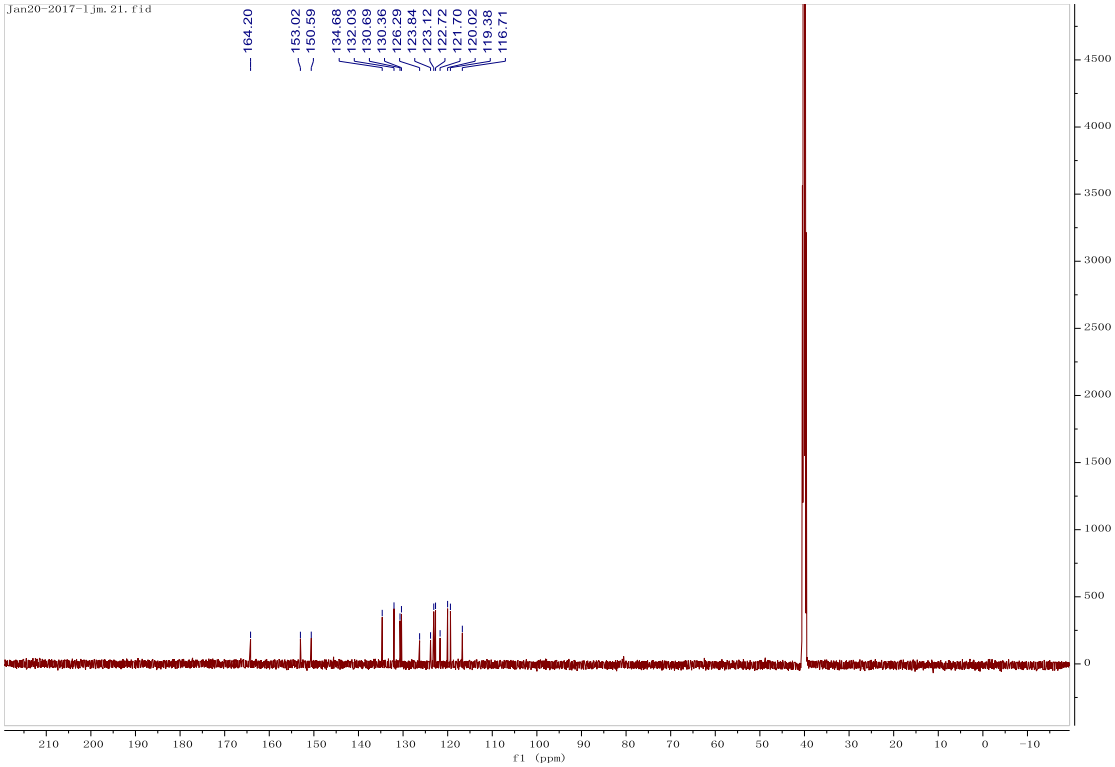




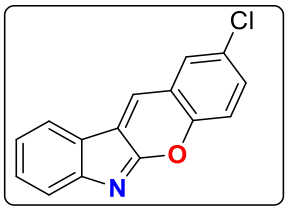
2-Bromochromeno[2, 3-b]indole 3d

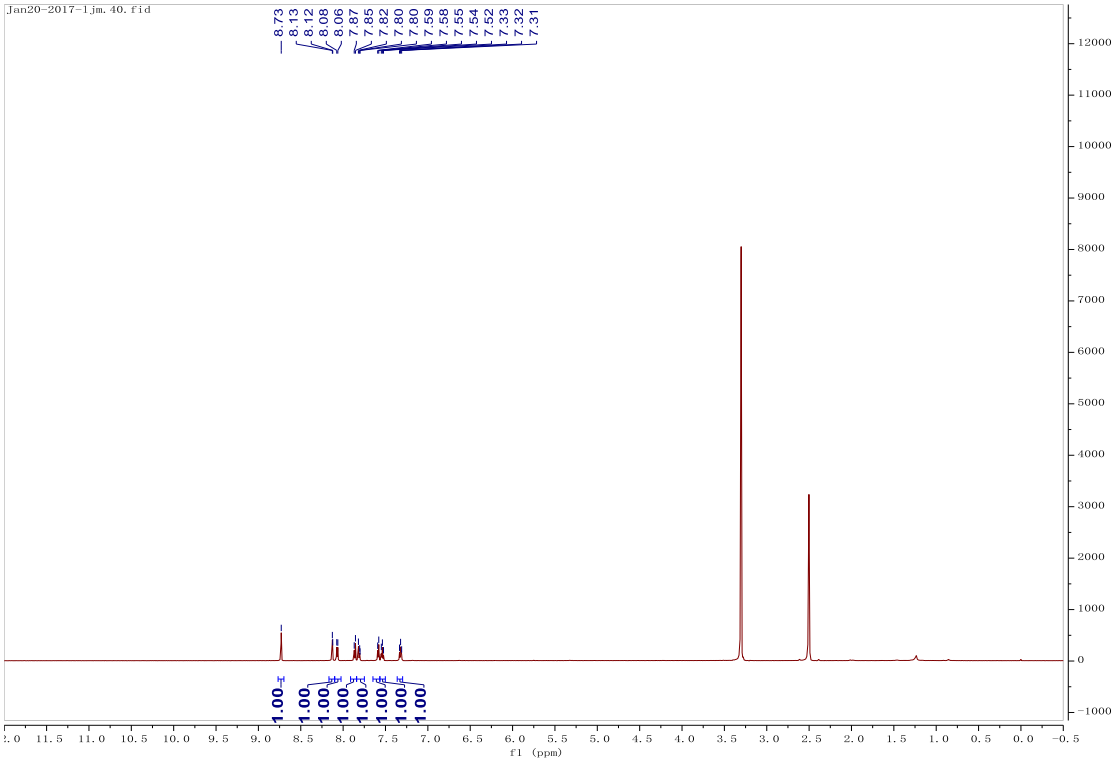


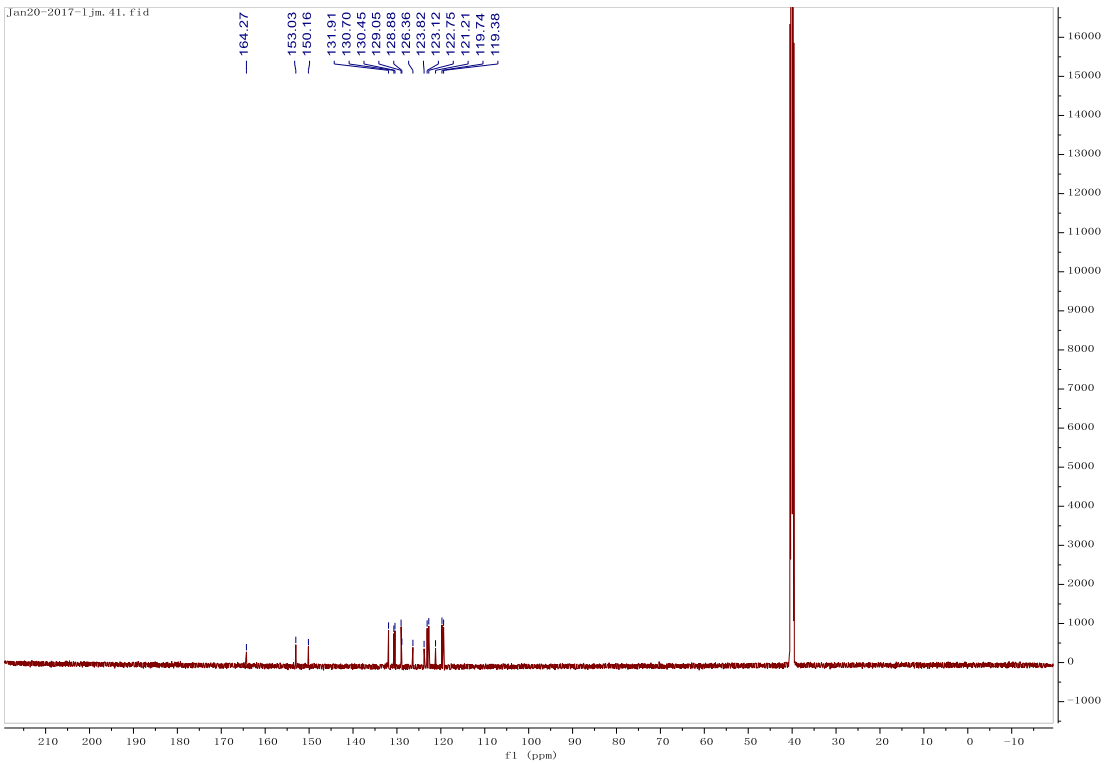




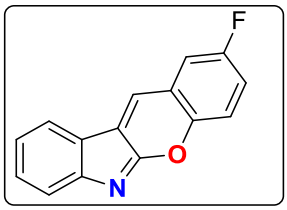
2-Chlorochromeno[2, 3-b]indole 3e

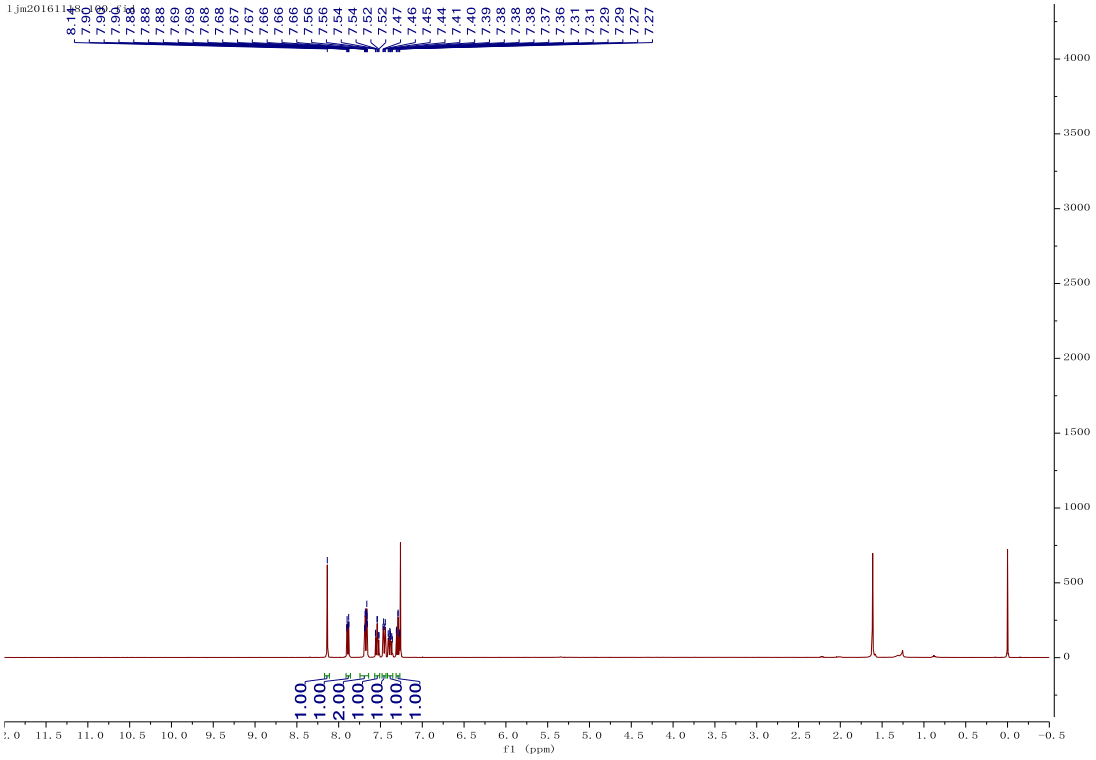


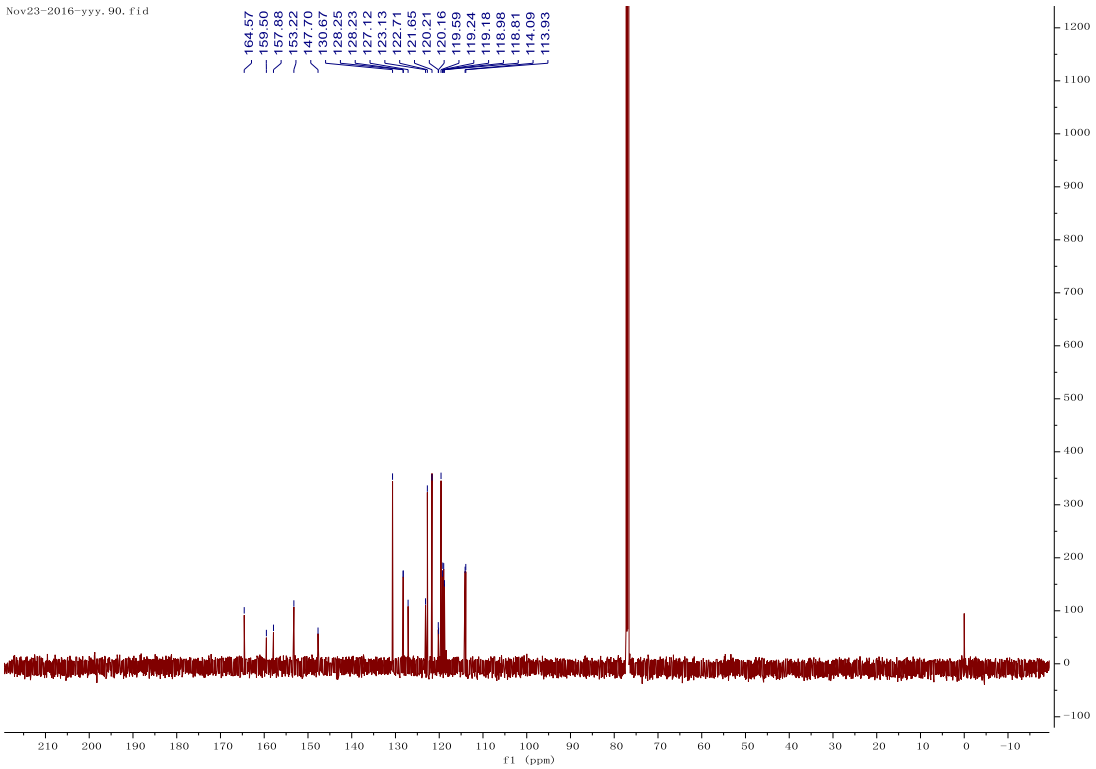


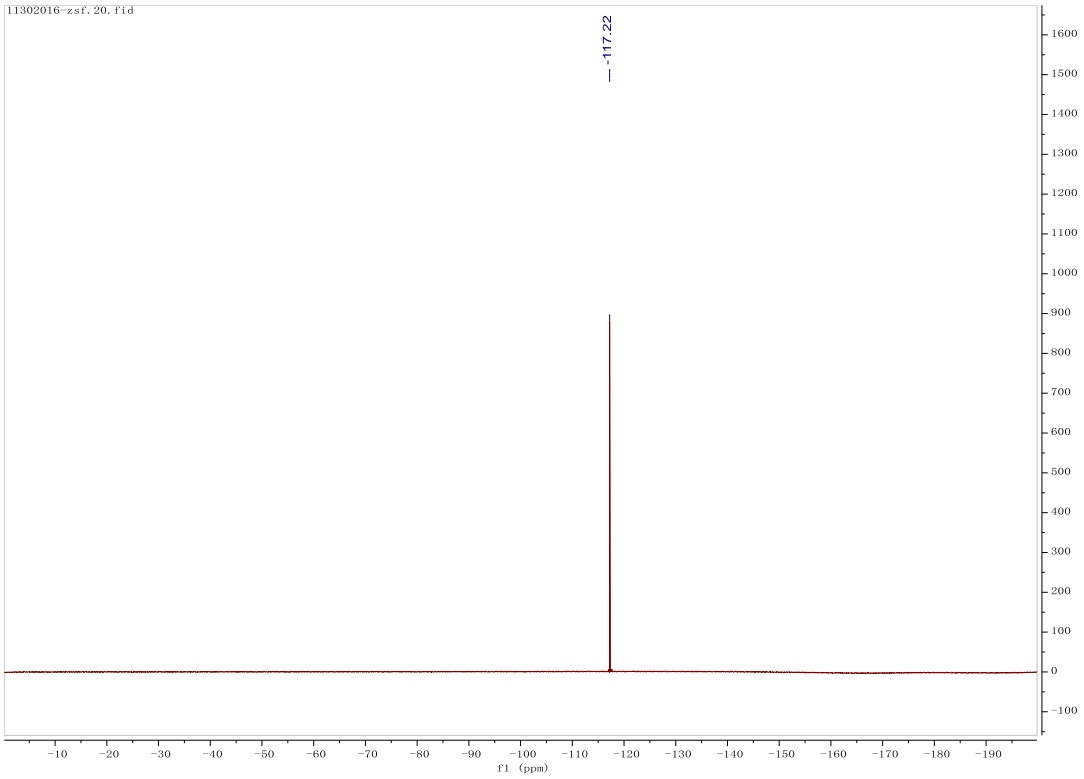


2-Fluorochromeno[2, 3-b]indole 3f





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-170
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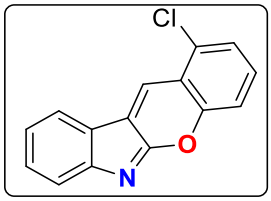
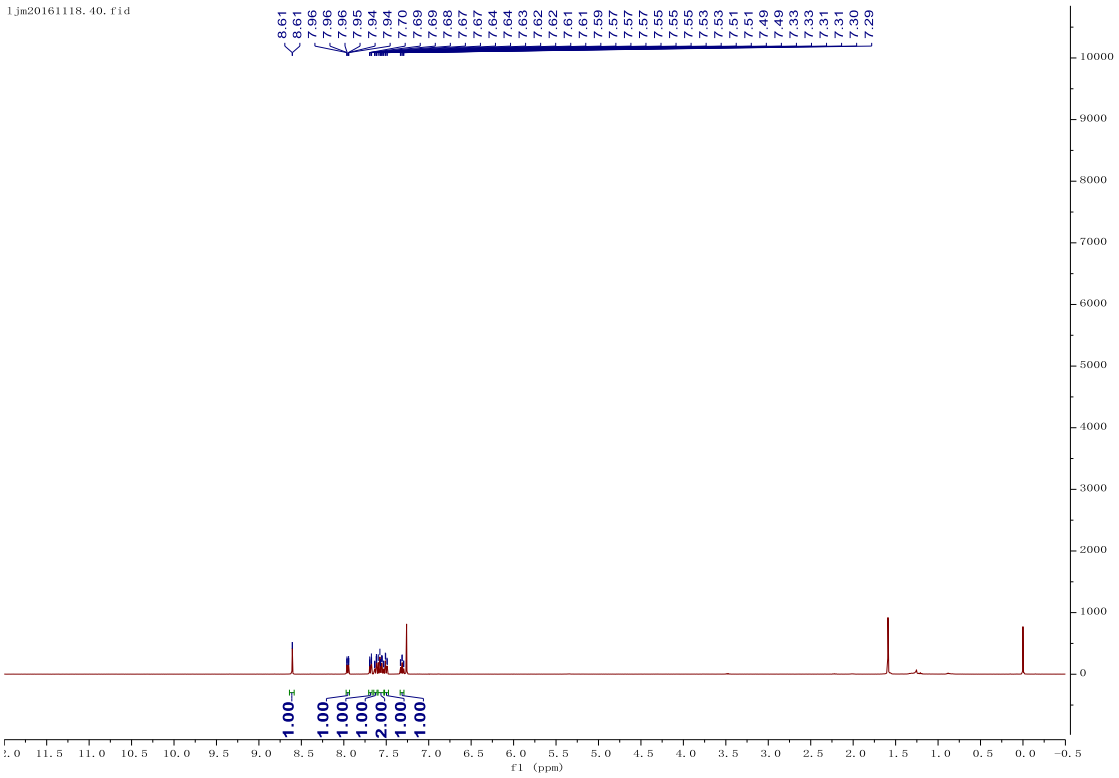
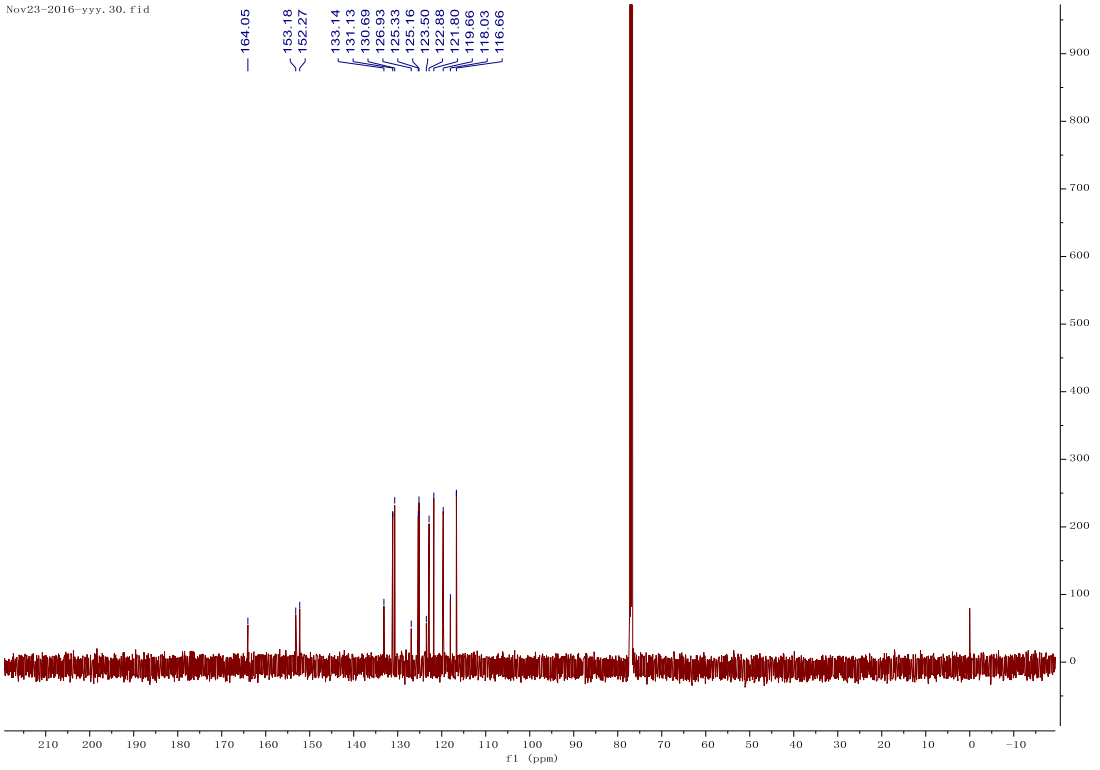
-190
f1 (ppm)

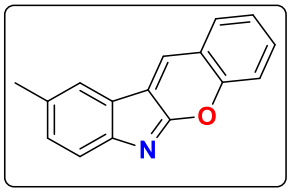
1-Chlorochromeno[2, 3-b]indole 3g

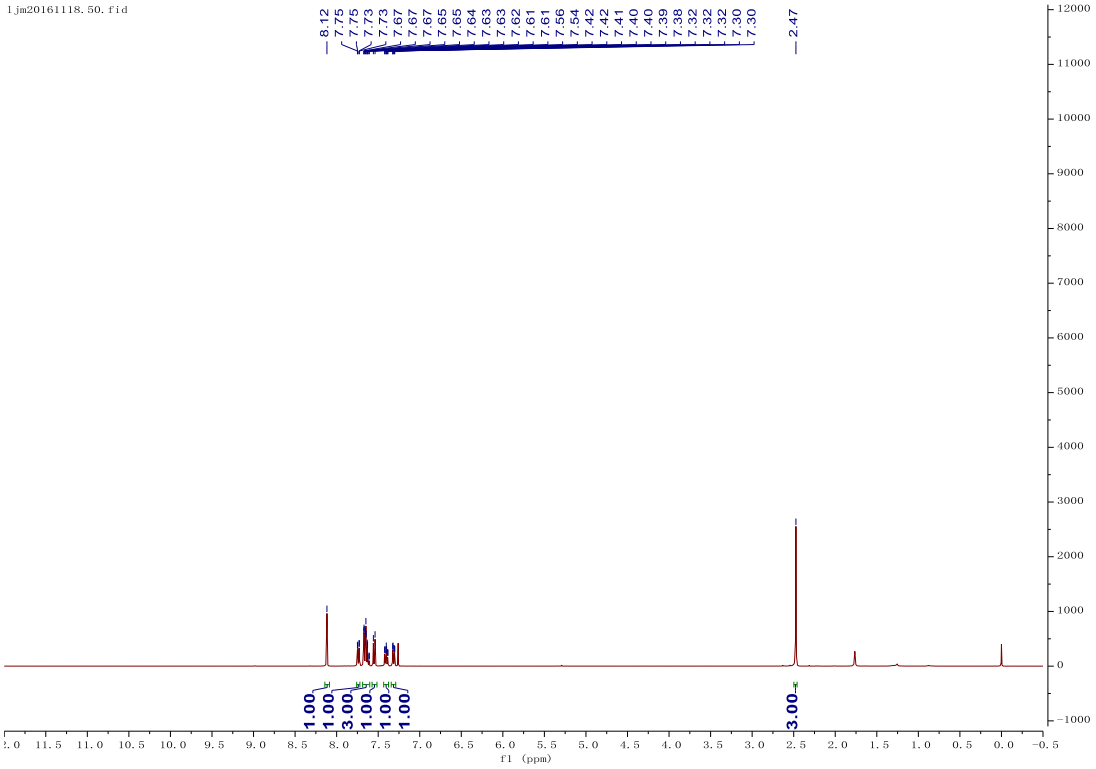


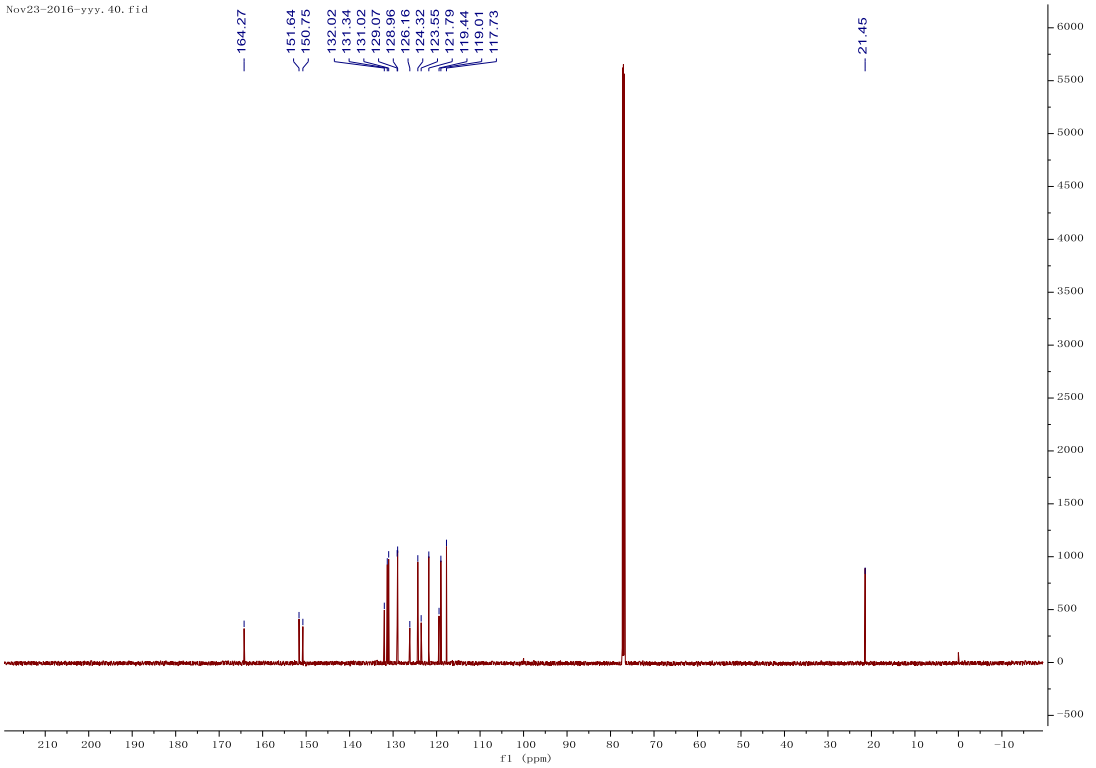




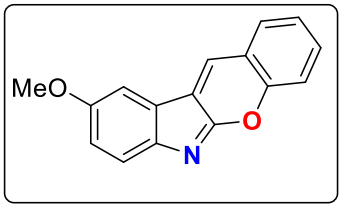
9-Methylchromeno[2, 3-b]indole 4a

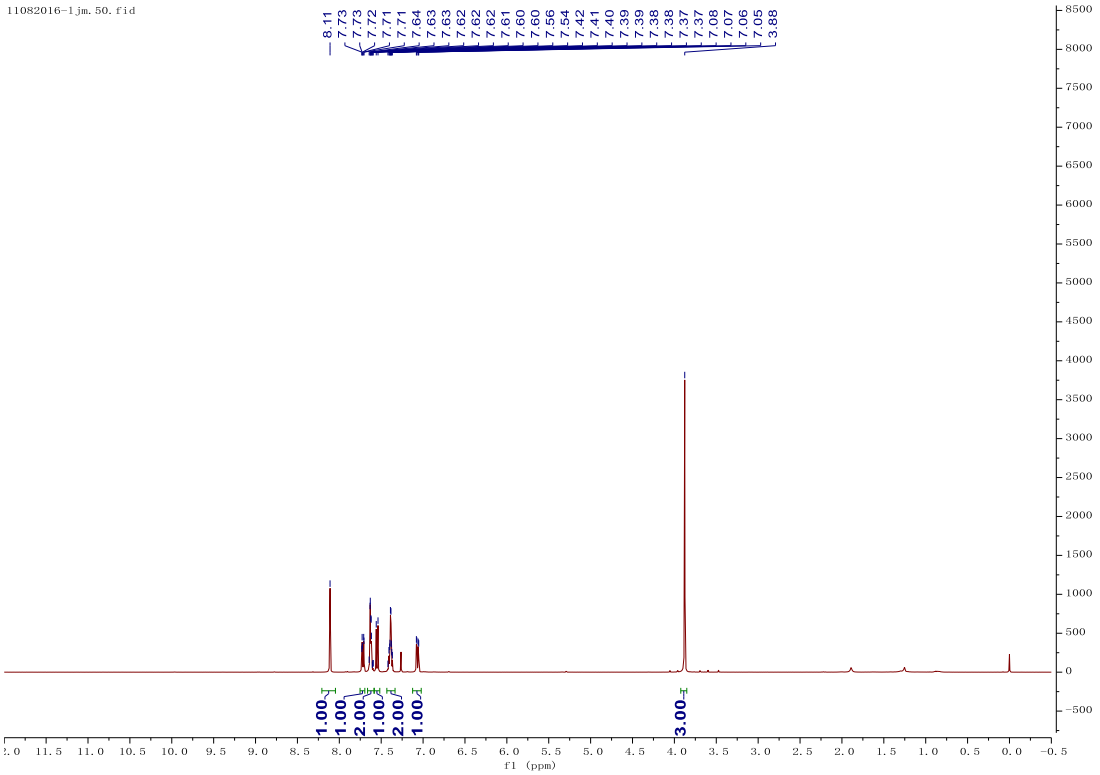


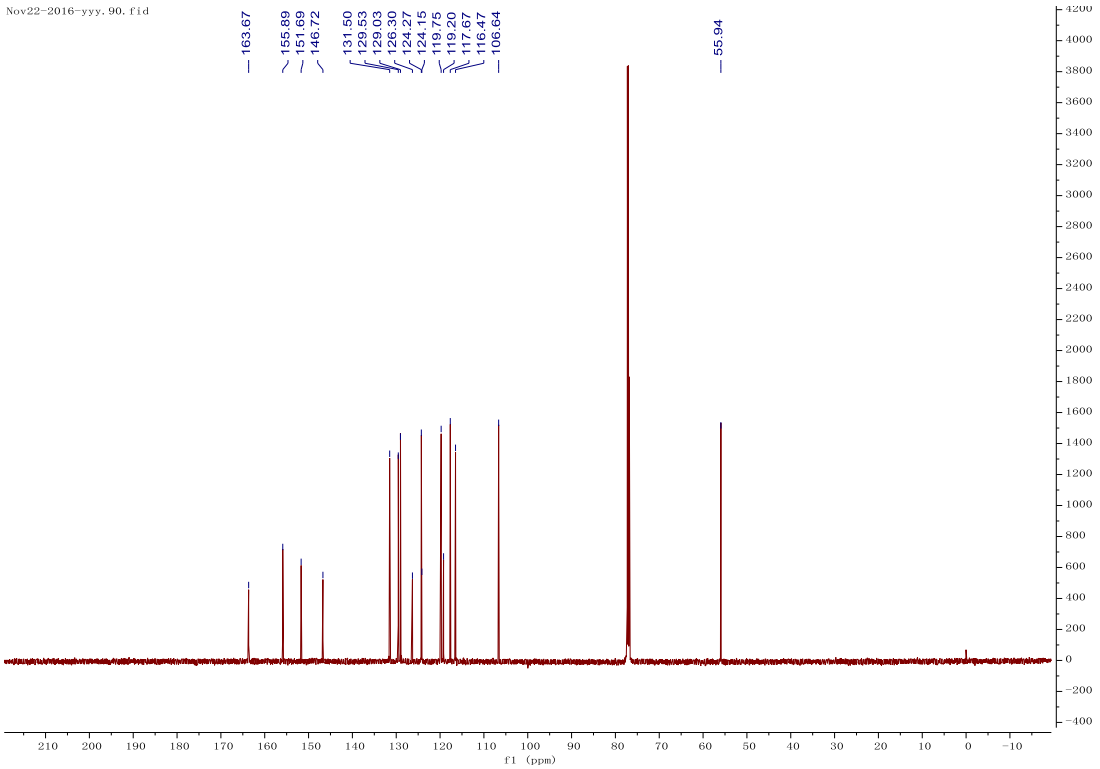




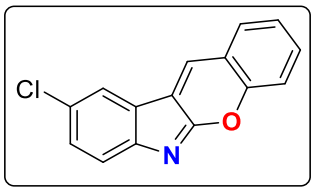
9-Methoxychromeno[2, 3-b]indole 4b

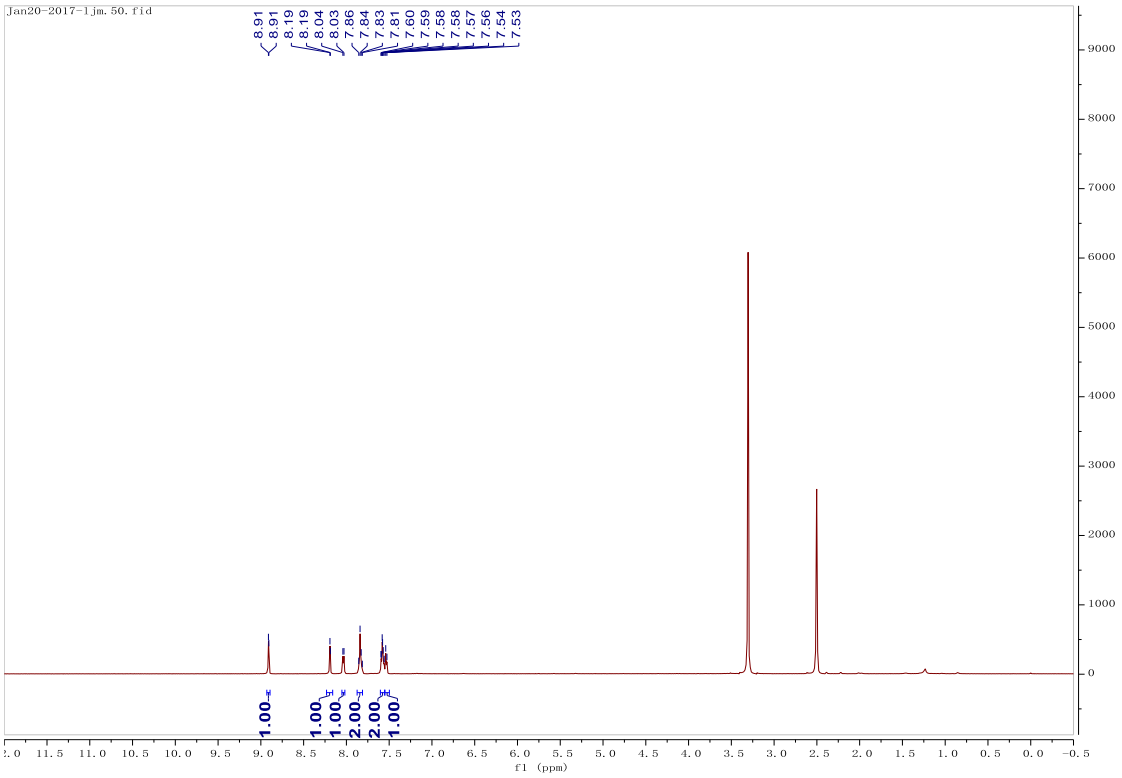


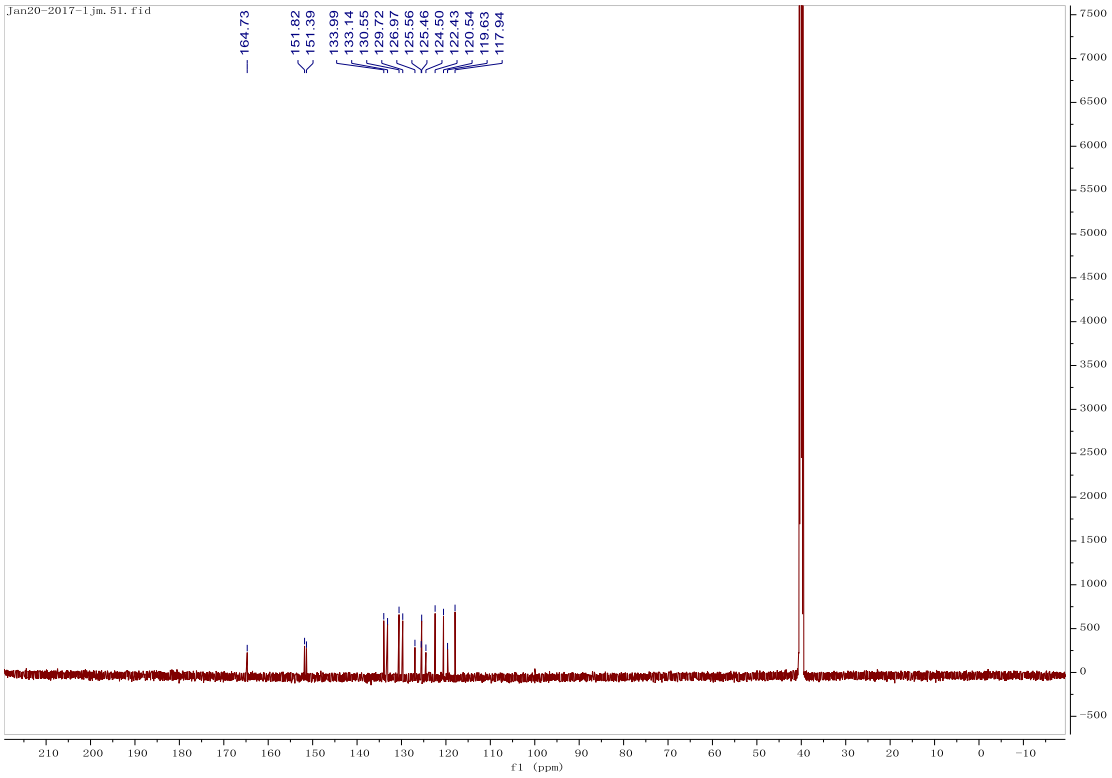




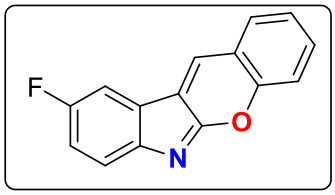
9-Chlorochromeno[2, 3-b]indole 4c

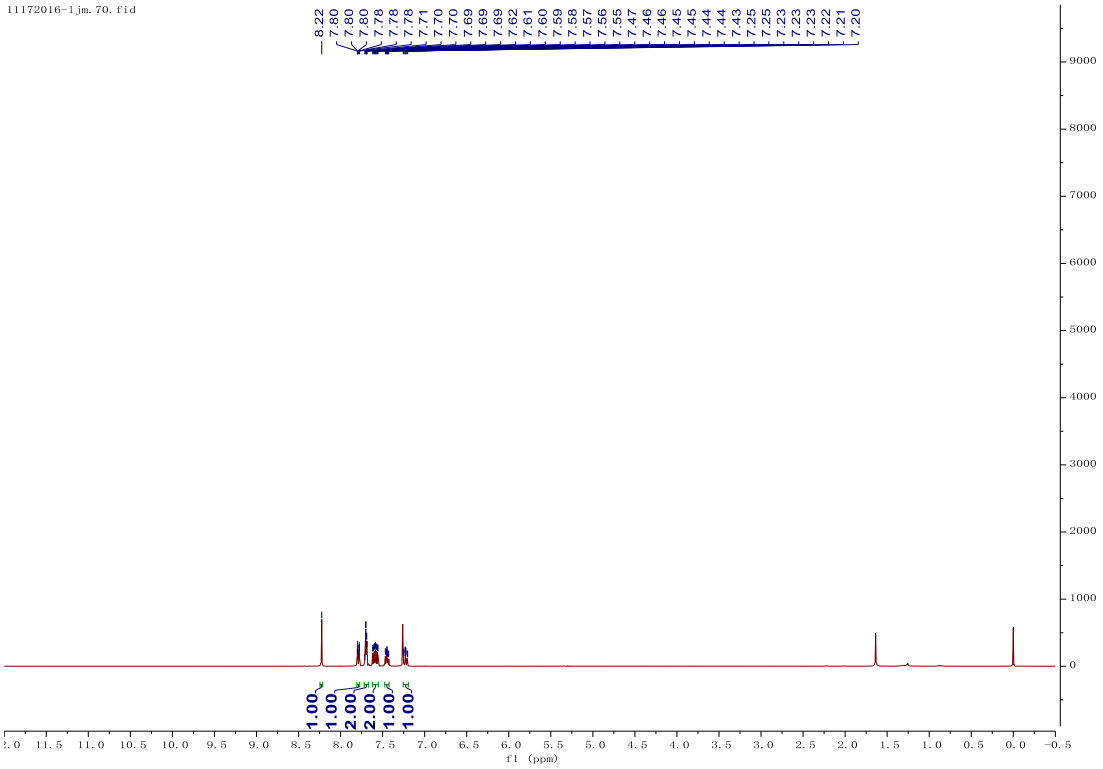


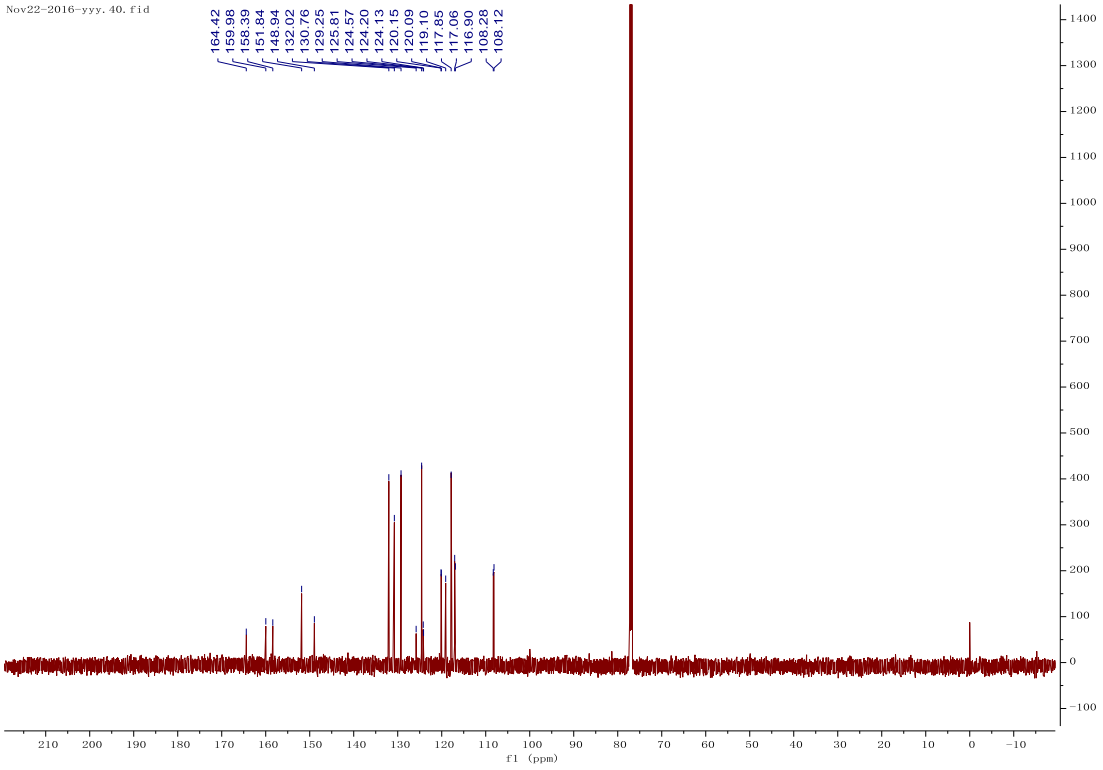


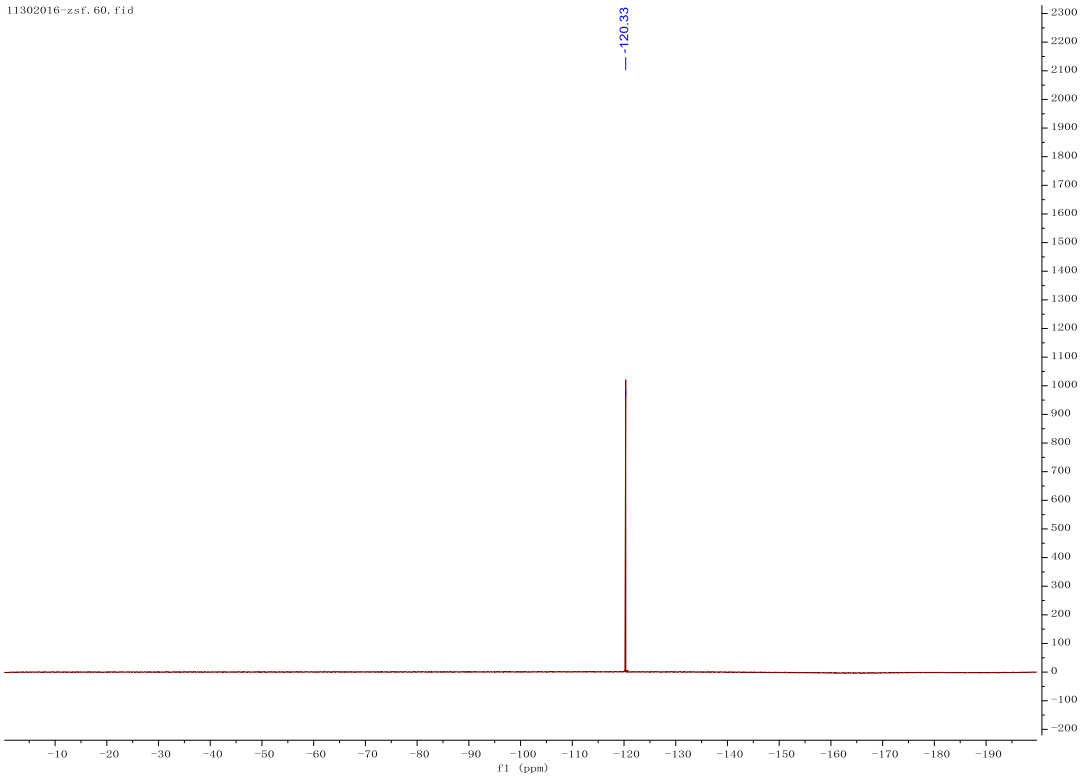


9-Fluorochromeno[2, 3-b]indole 4d





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-170
-180
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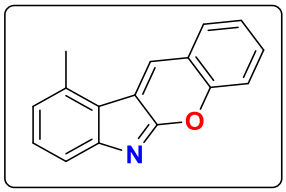
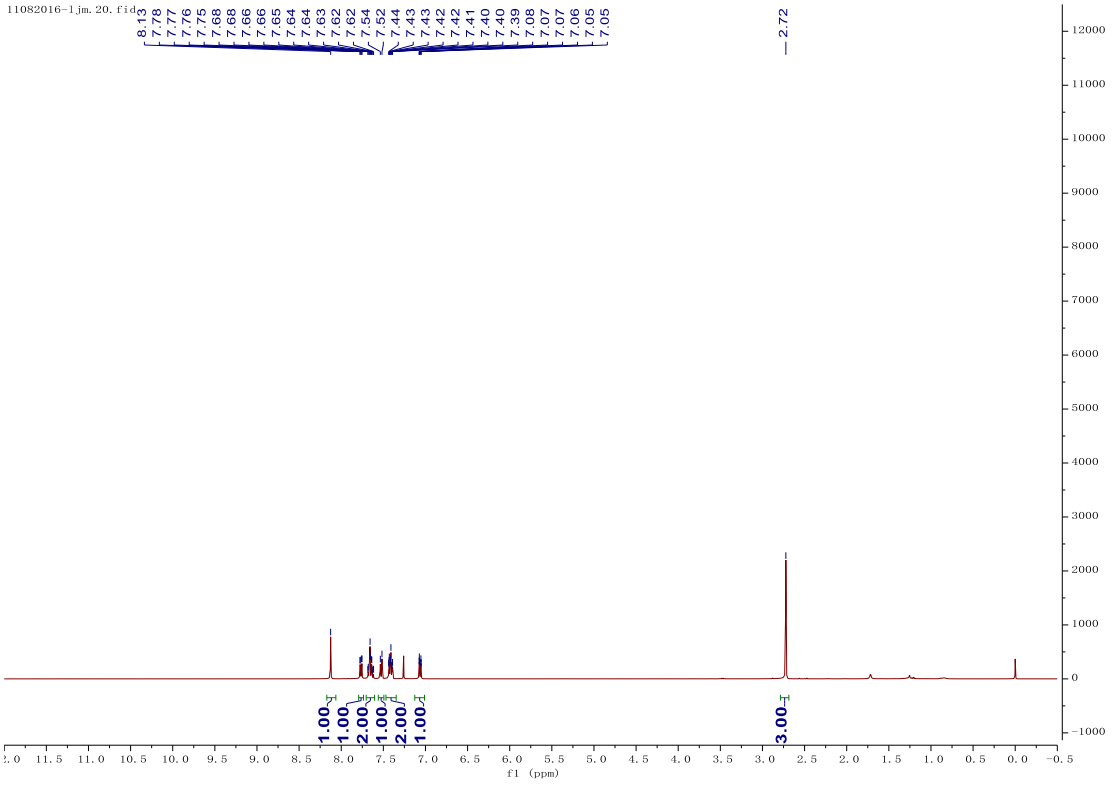
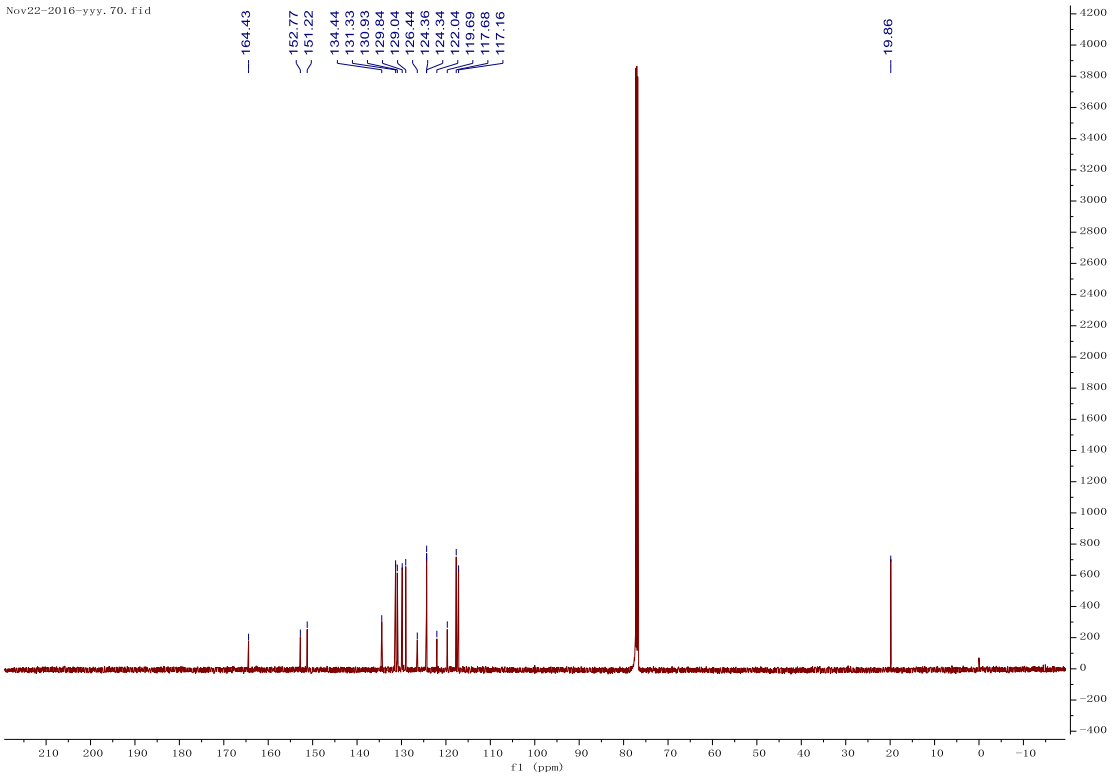
f1 (ppm)

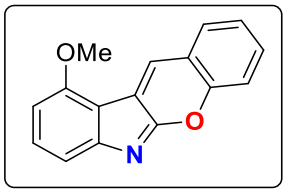
10-Methylchromeno[2, 3-b]indole 4e

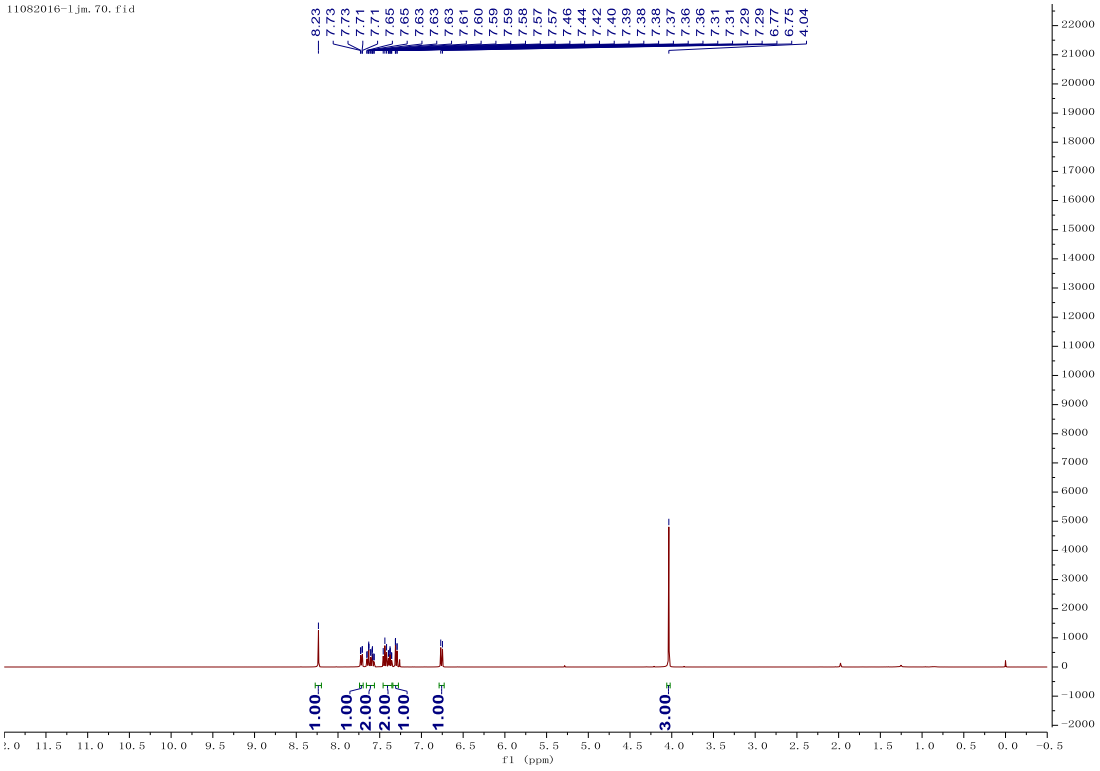


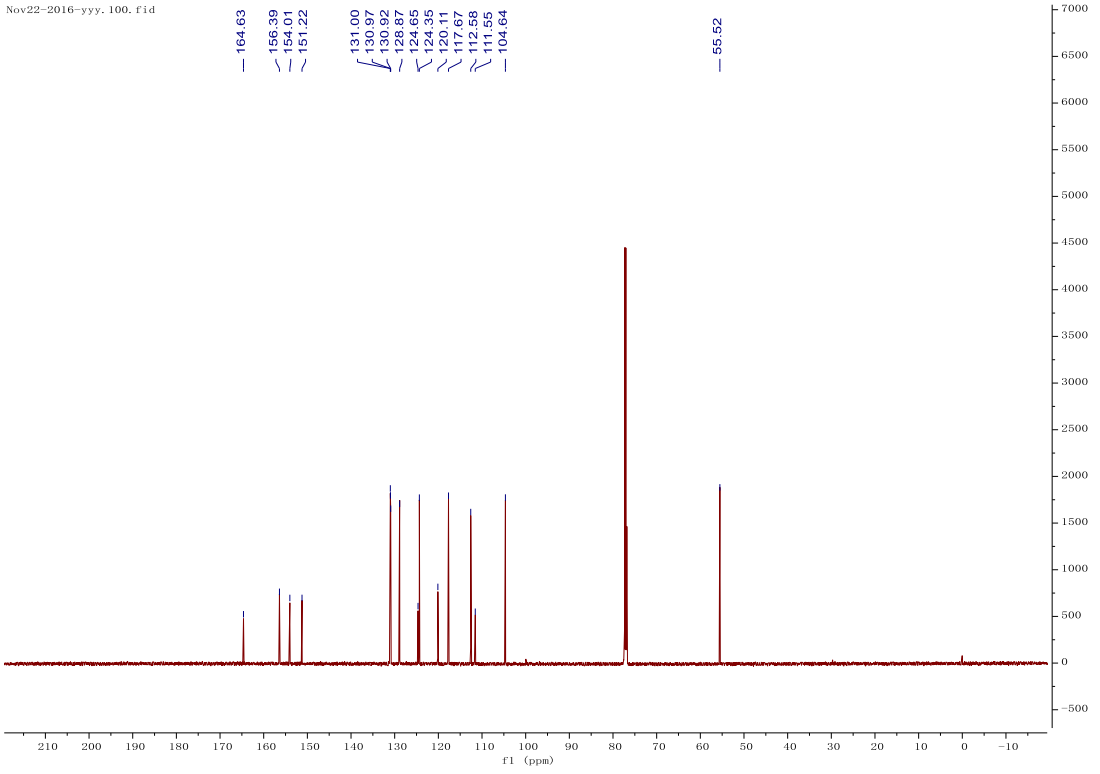




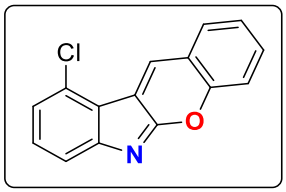
10-Methoxychromeno[2, 3-b]indole 4f

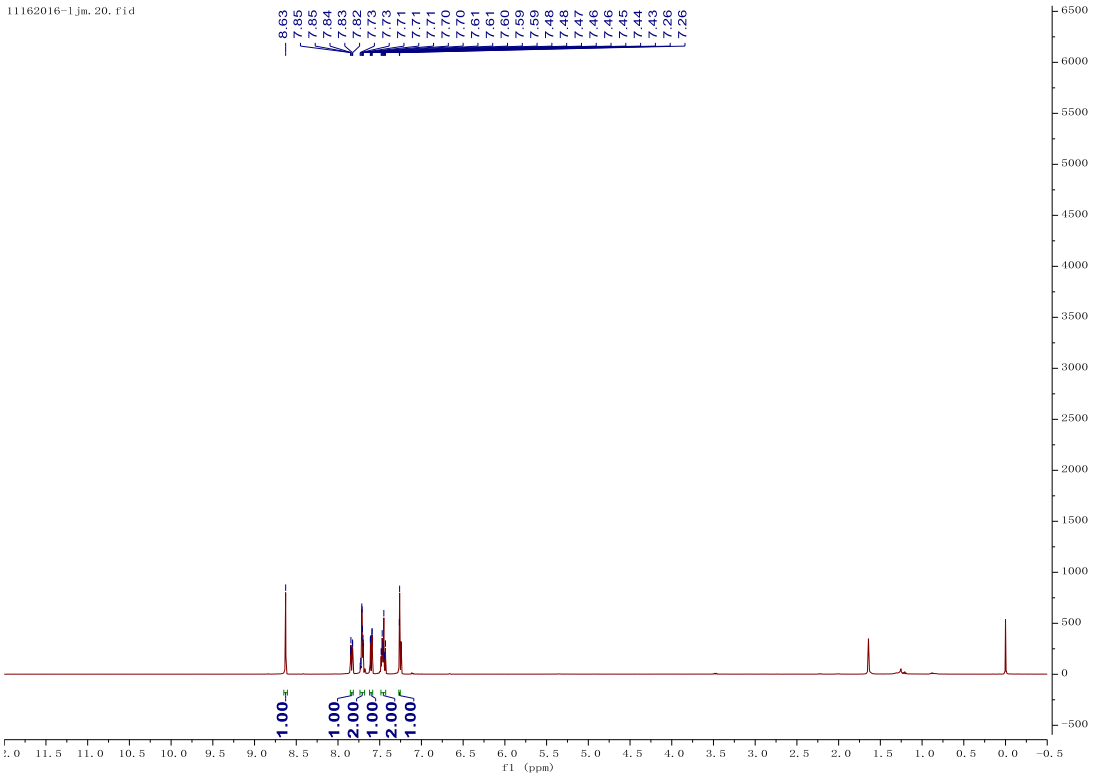


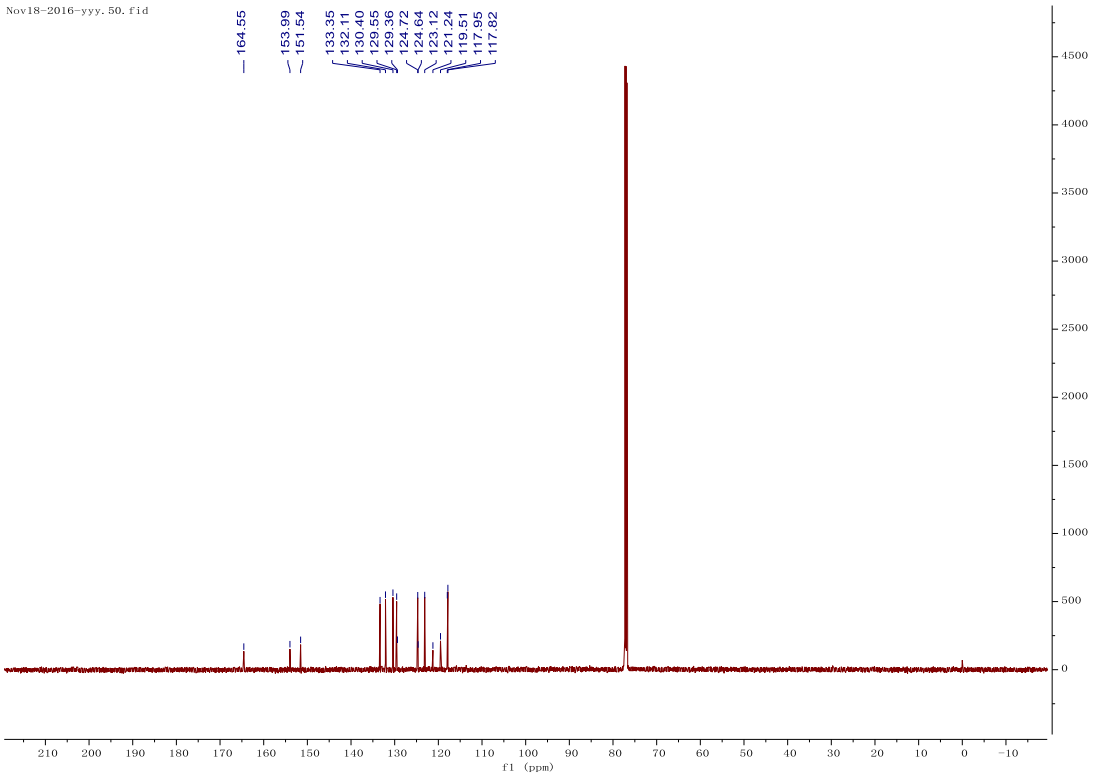




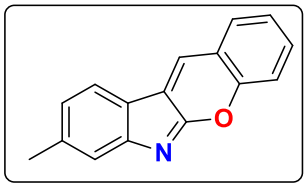
10-Chlorochromeno[2, 3-b]indole 4g

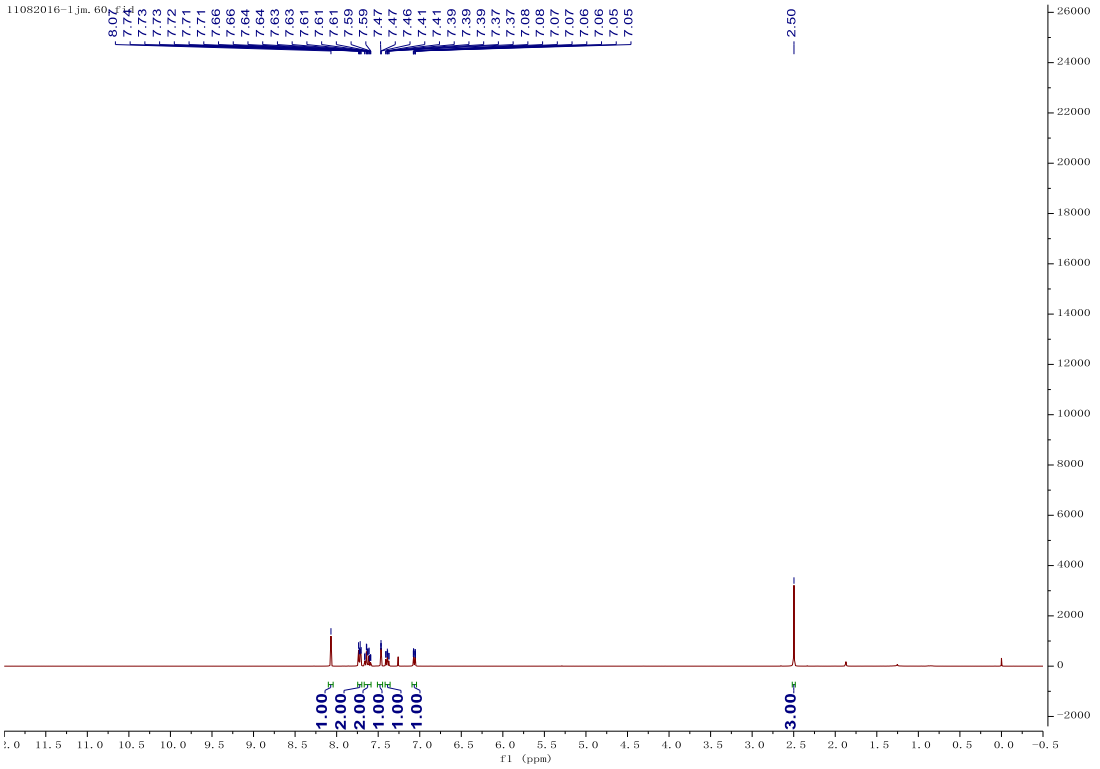


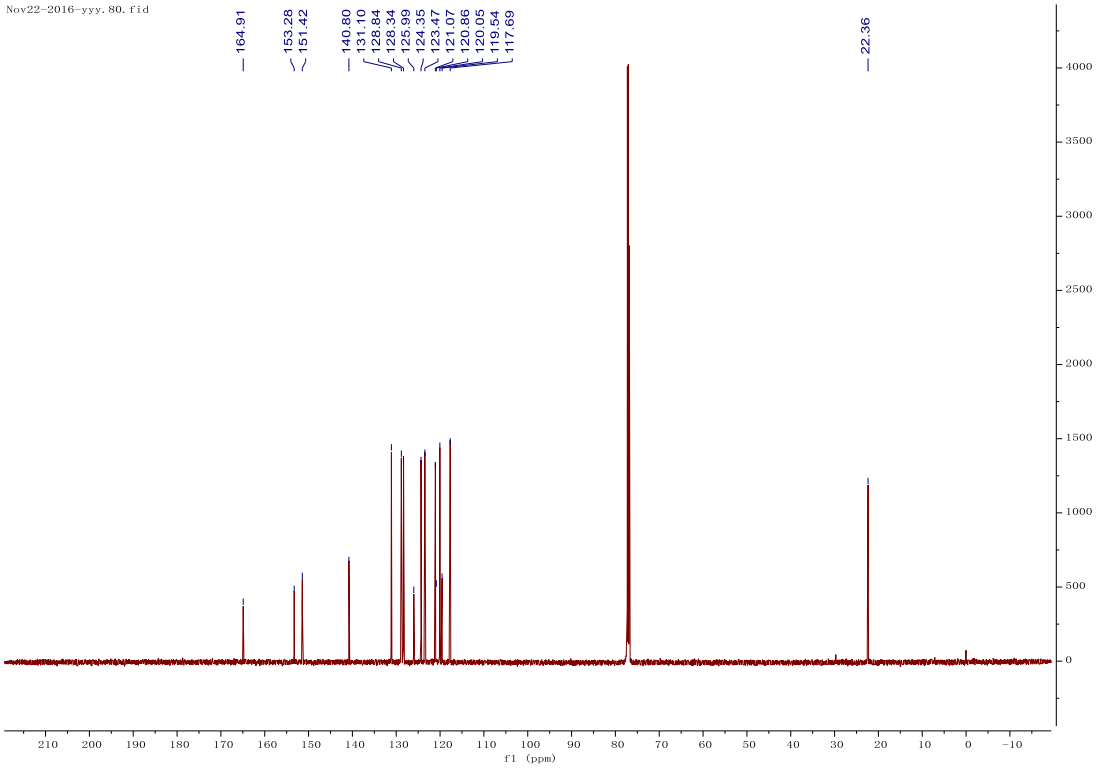




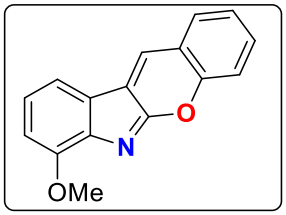
8-Methylchromeno[2, 3-b]indole 4h

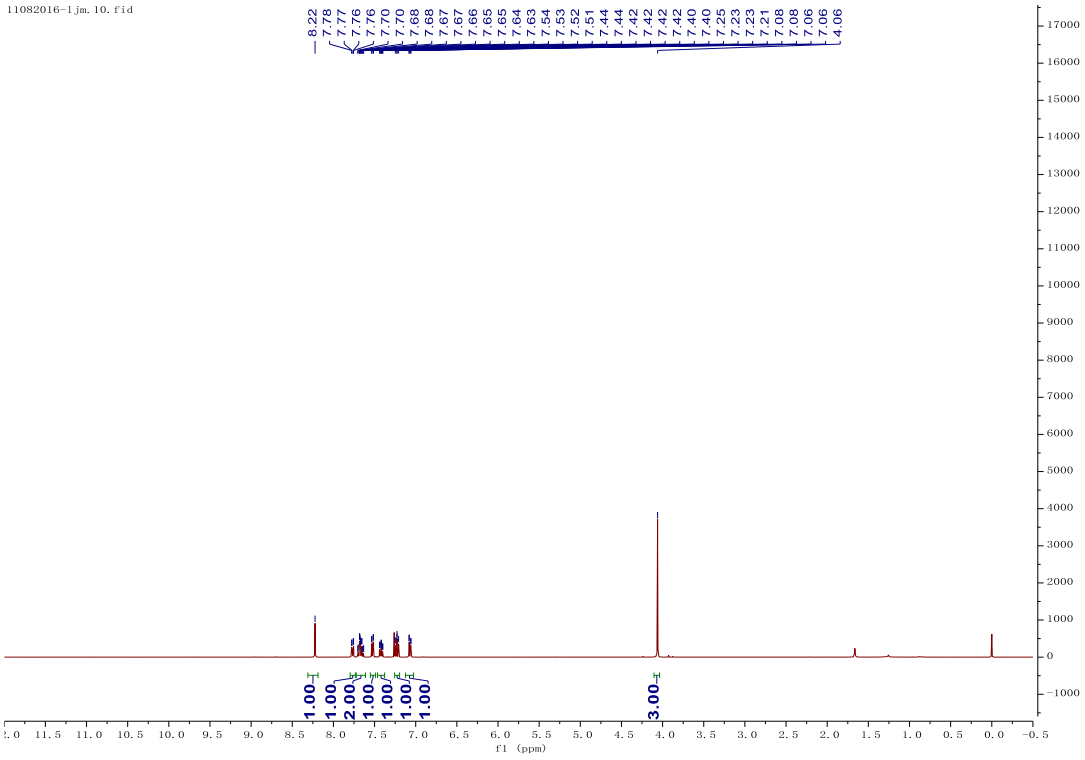


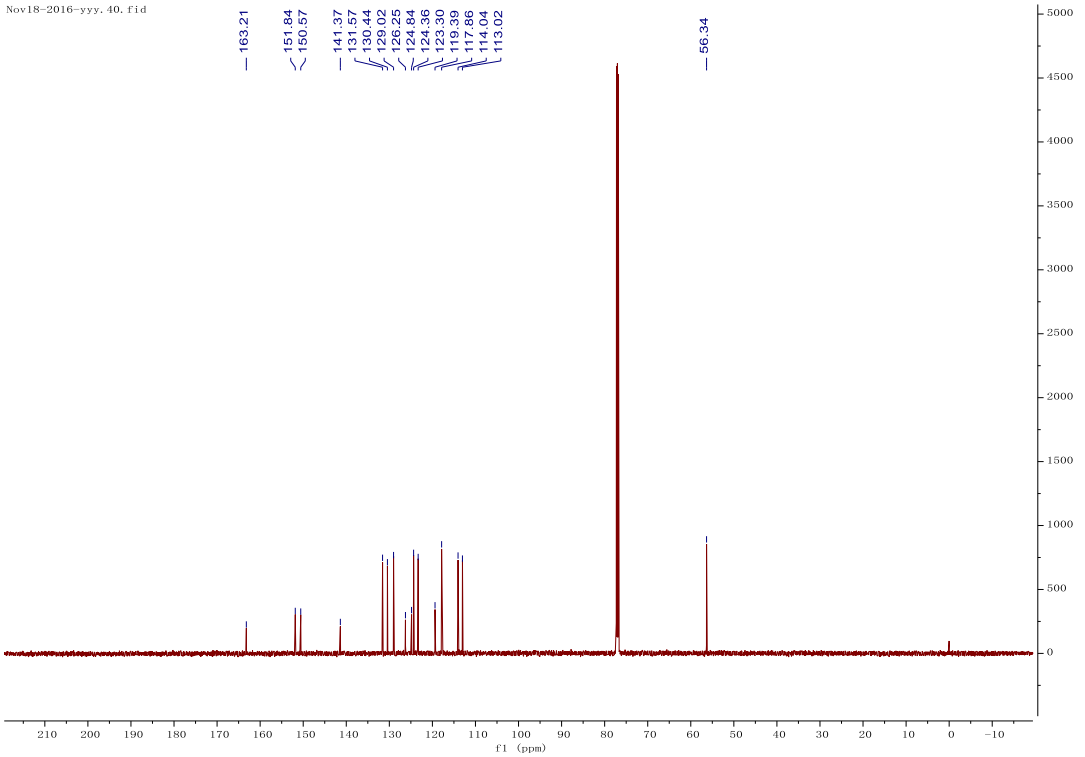




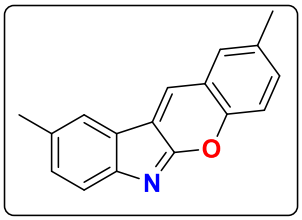
7-Methoxychromeno[2, 3-b]indole 4i

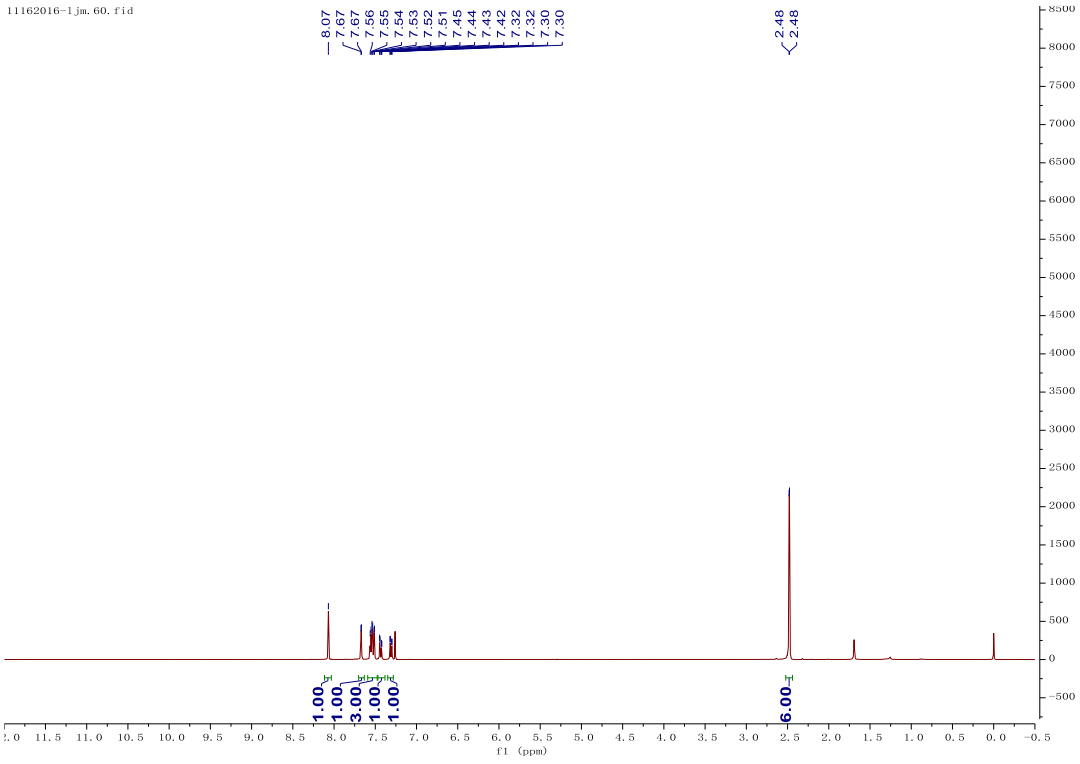


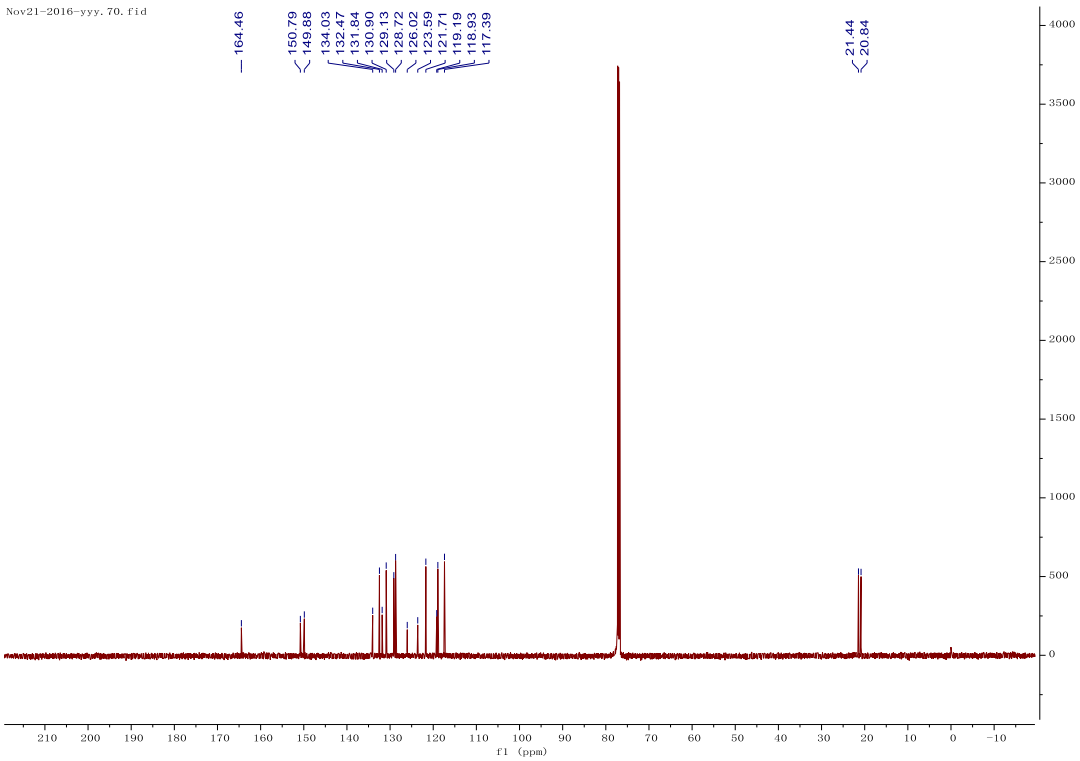




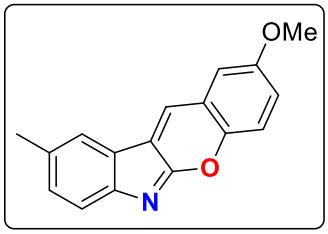
2, 9-Dimethylchromeno[2, 3-b]indole 4j

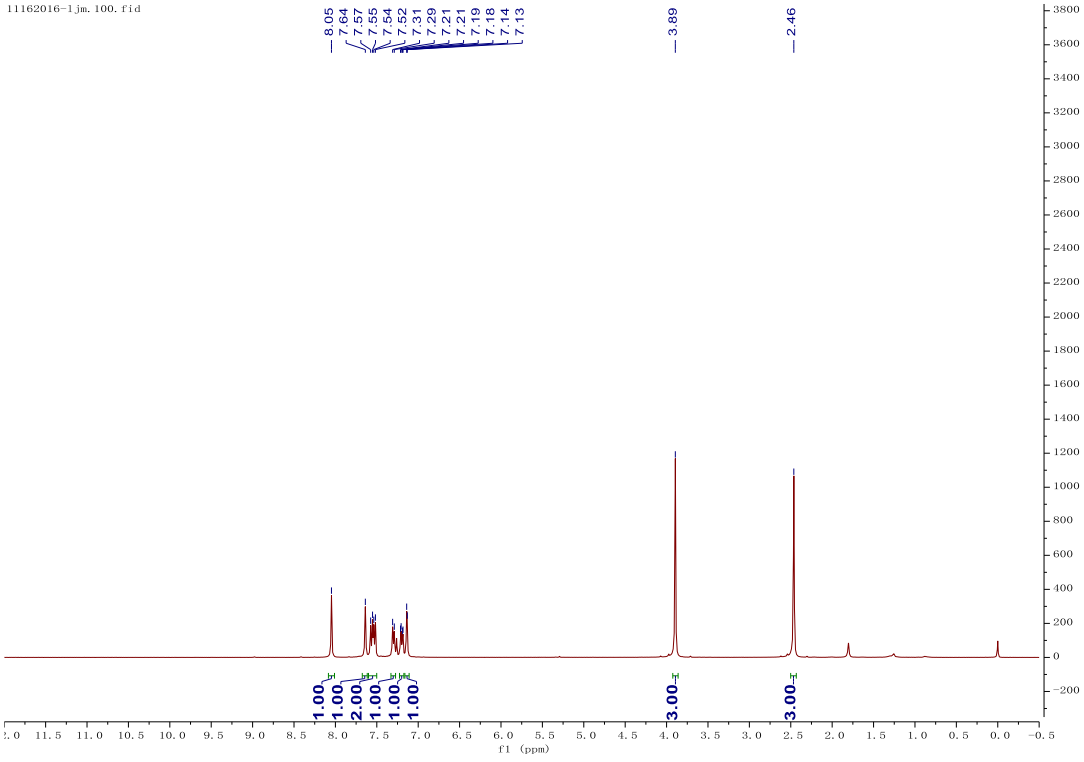


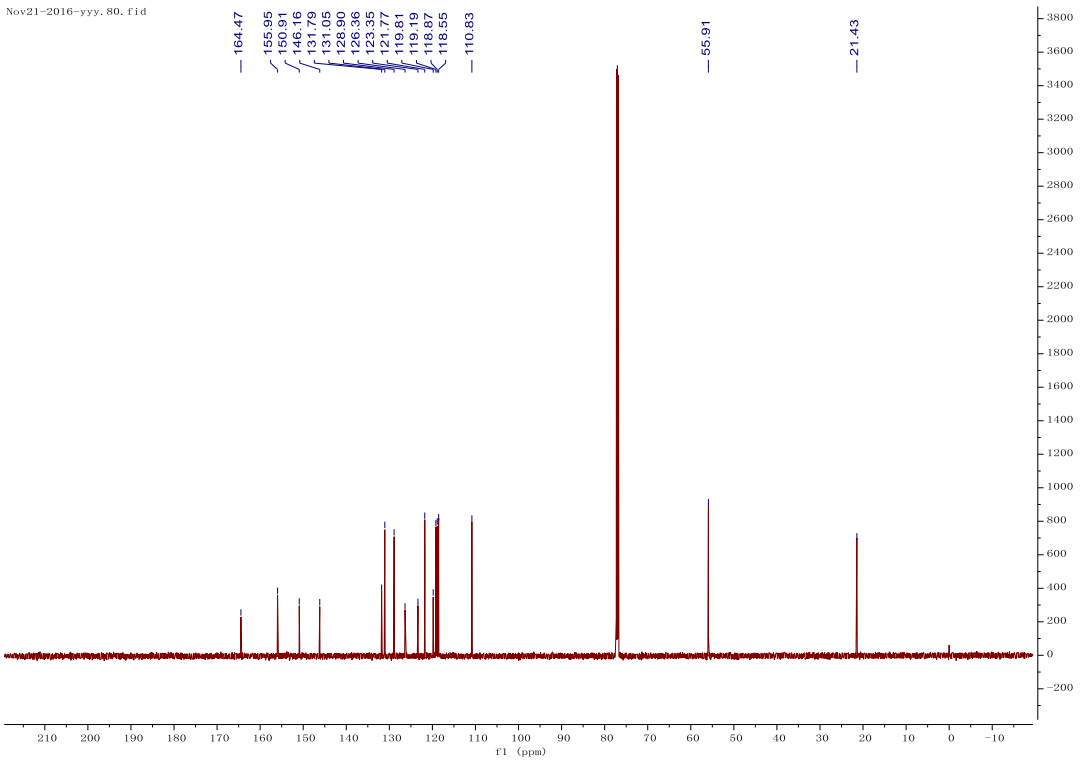




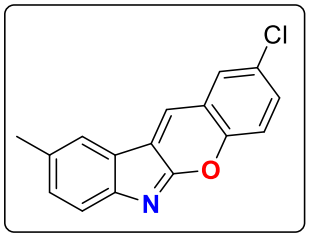
2-Methoxy-9-methylchromeno[2, 3-b]indole 4k

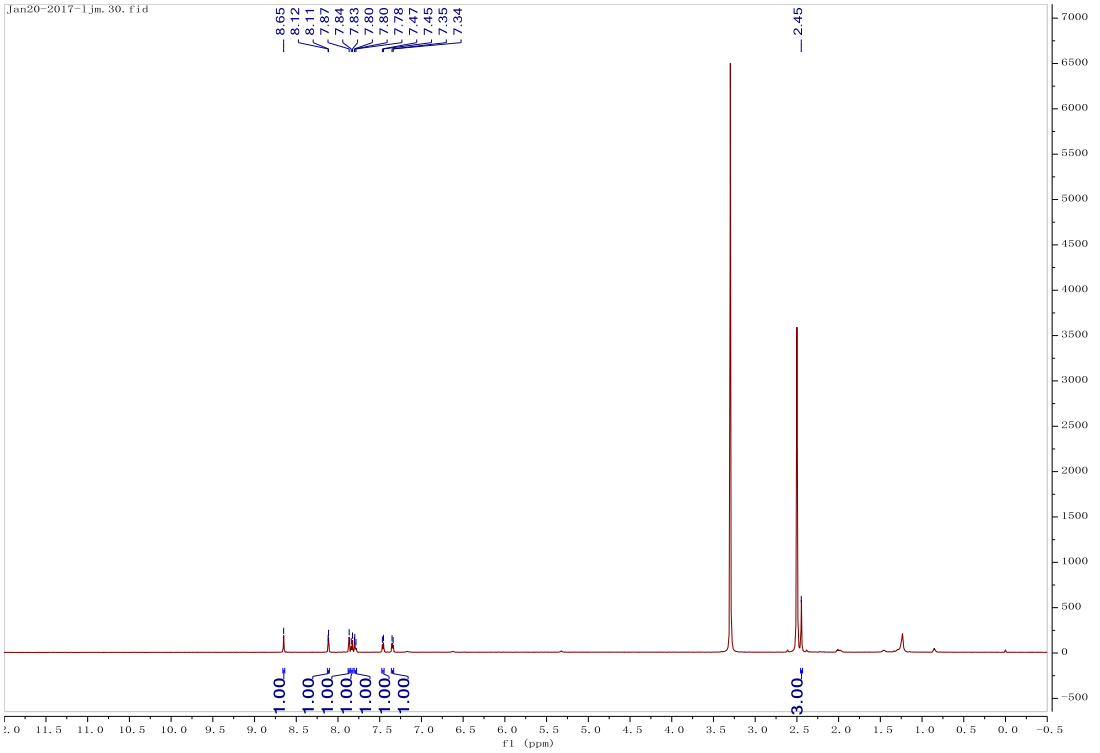


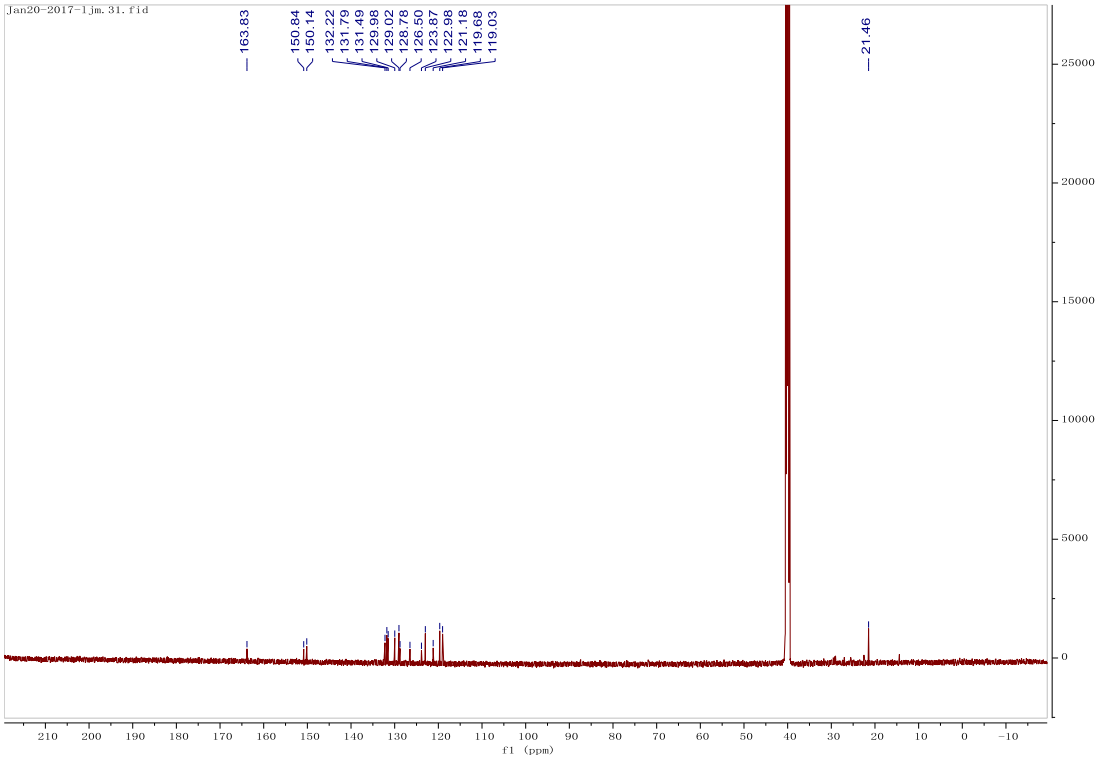




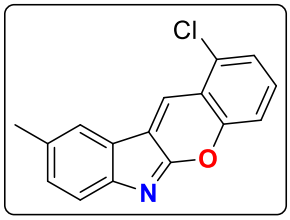
2-Chloro-9-methylchromeno[2, 3-b]indole 4l

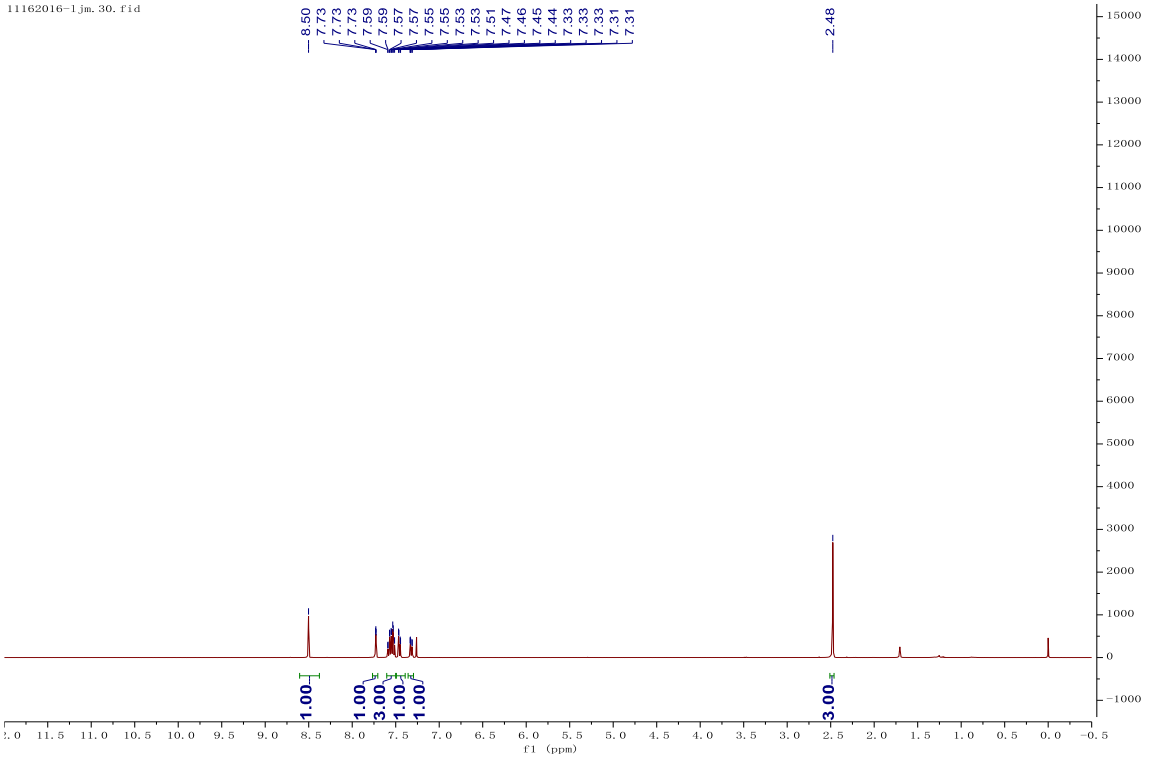


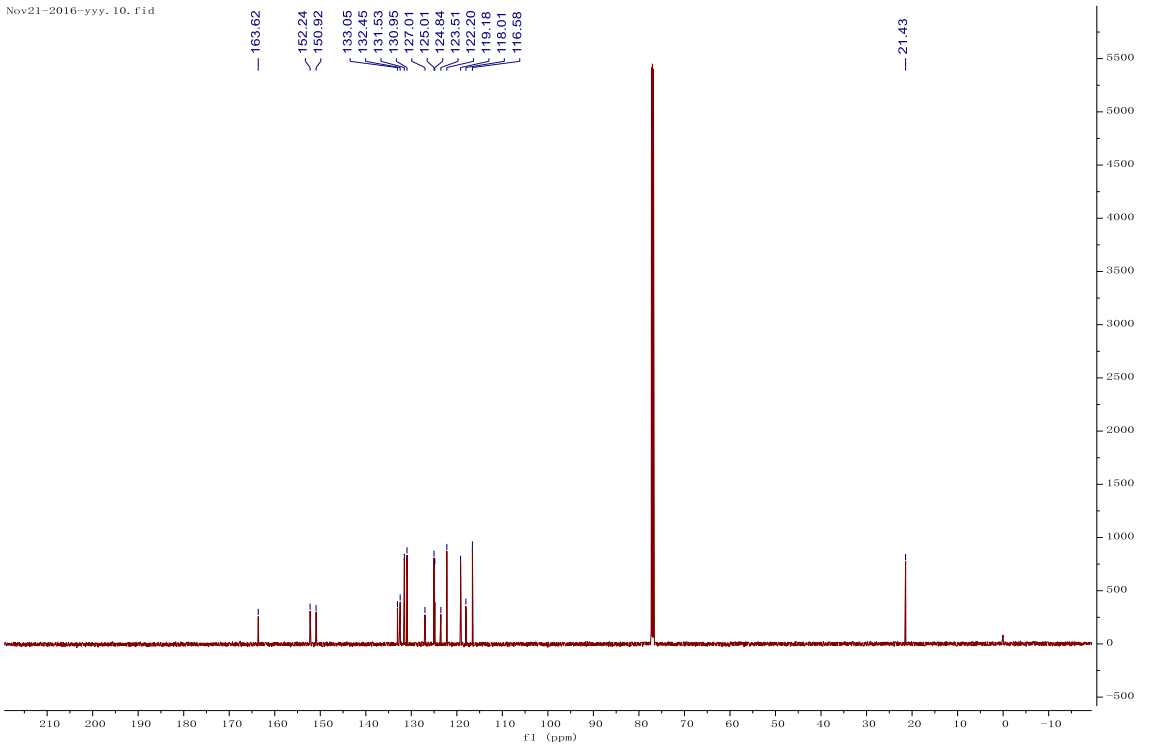




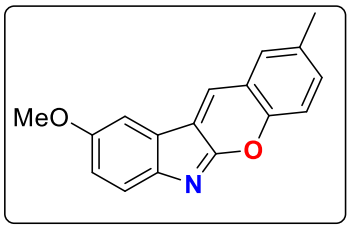
1-Chloro-9-methylchromeno[2, 3-b]indole 4m

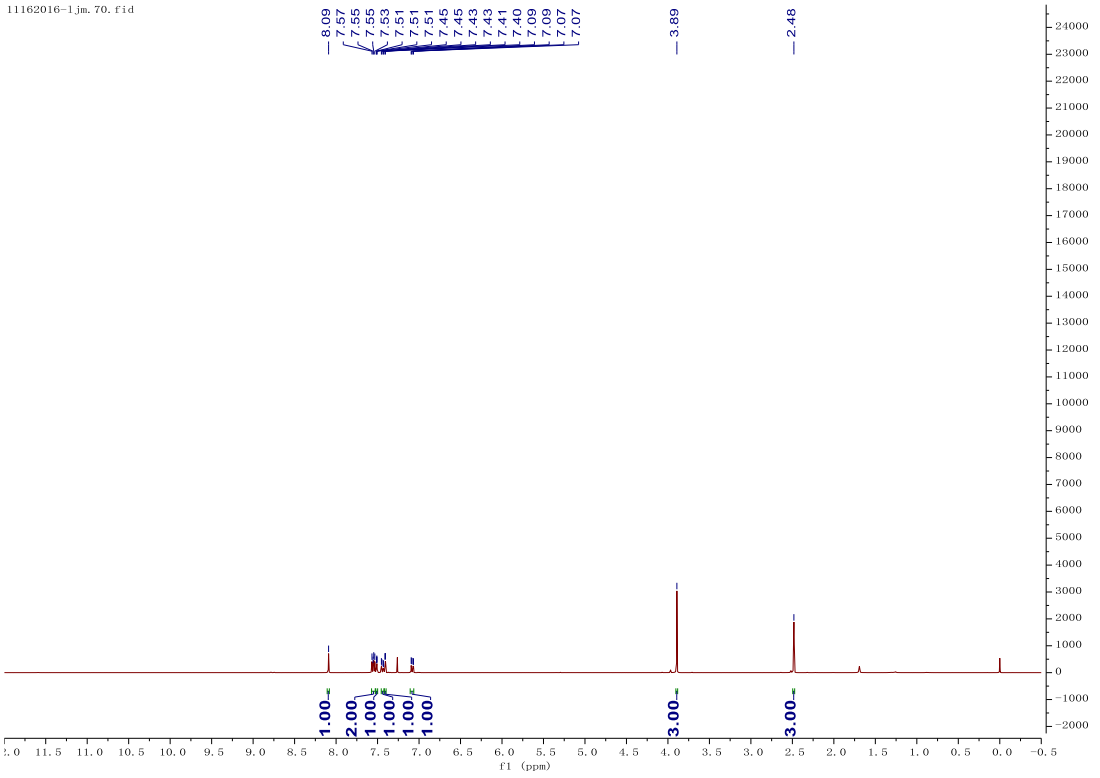


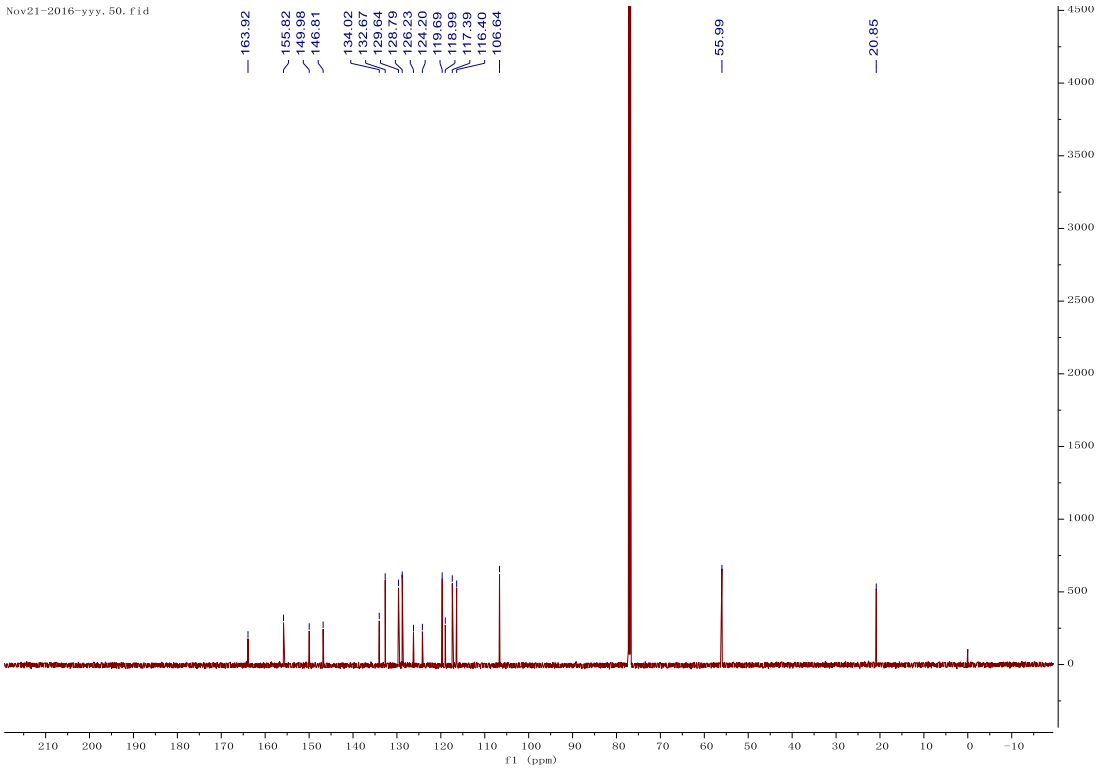




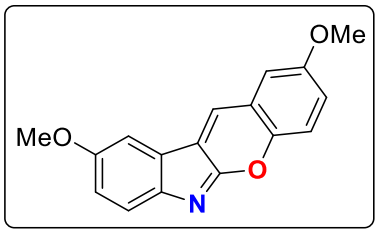
9-Methoxy-2-methylchromeno[2, 3-b]indole 4n

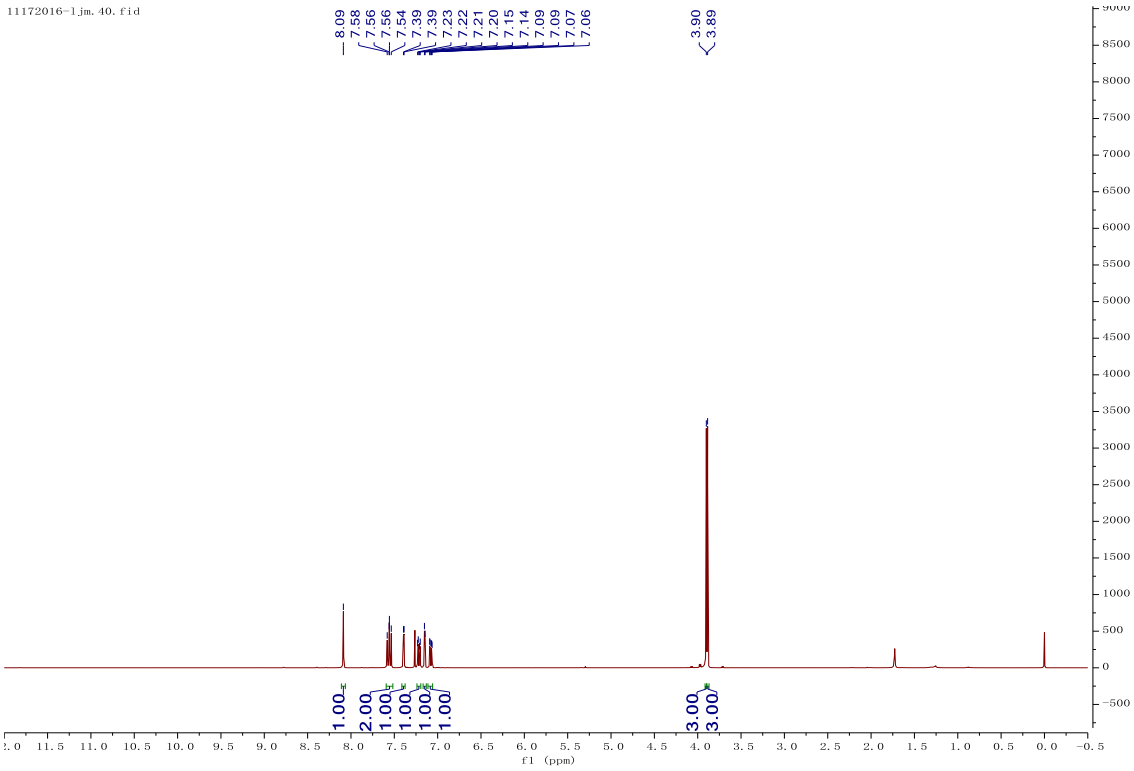


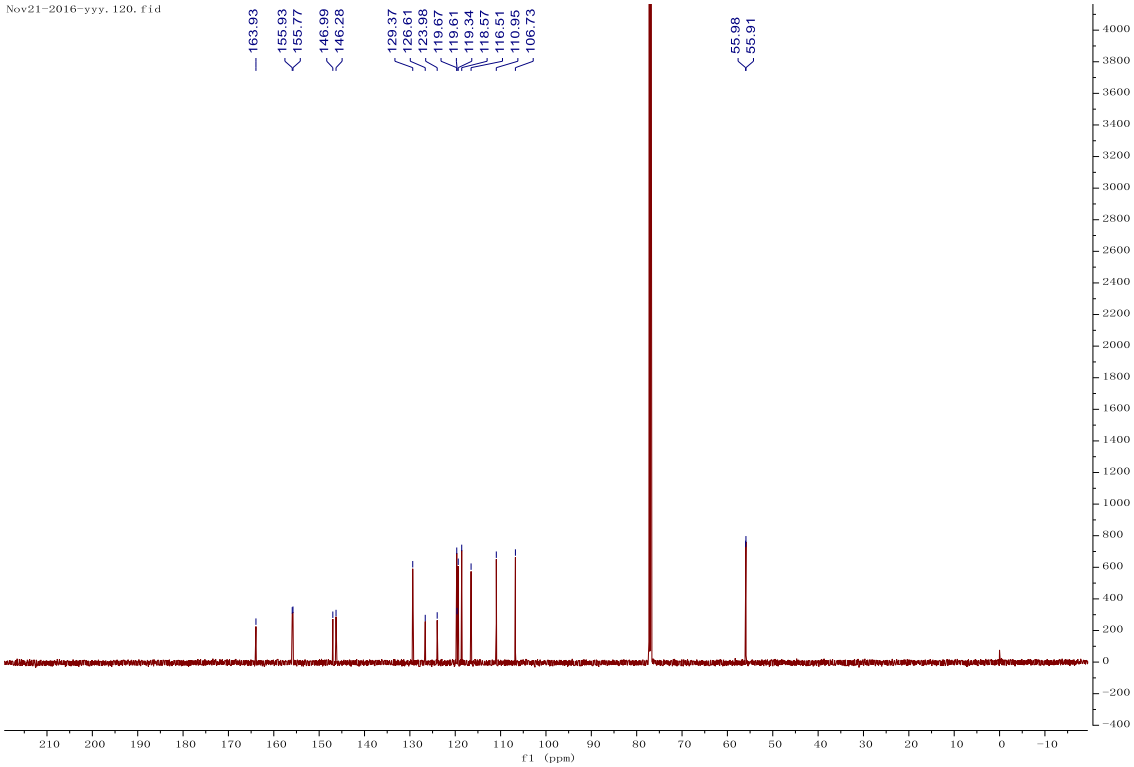




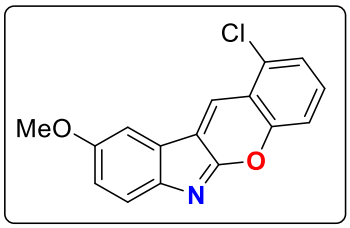
2, 9-Dimethoxychromeno[2, 3-b]indole 4o

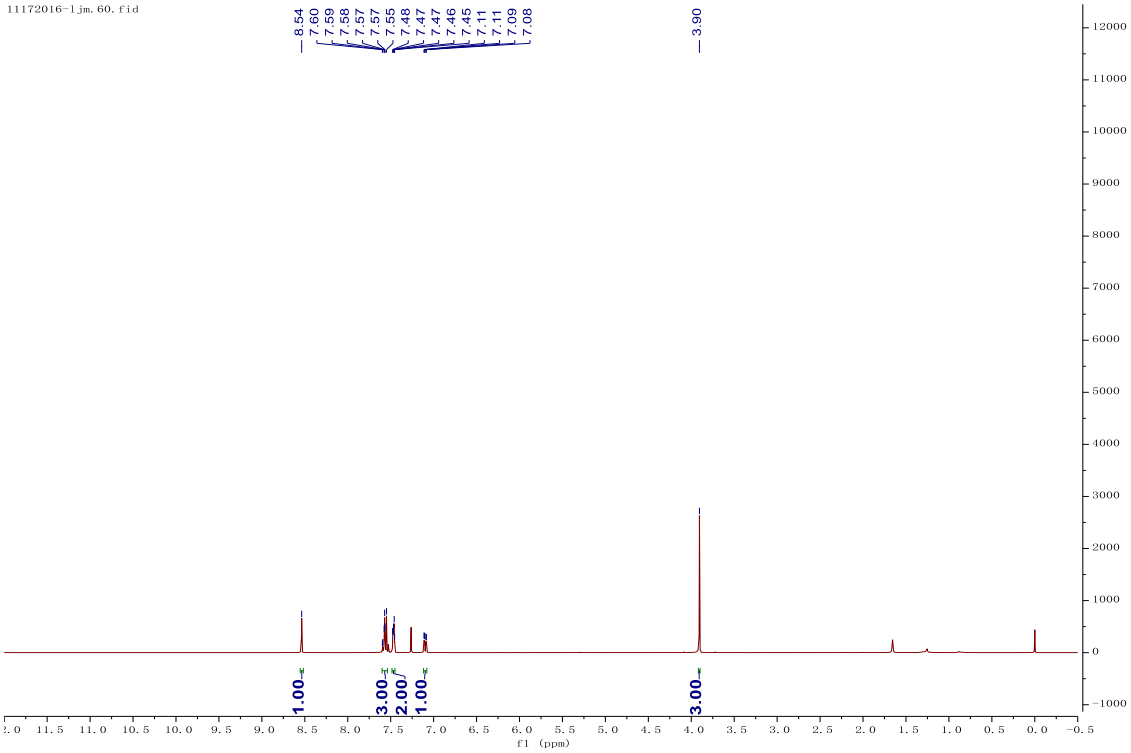


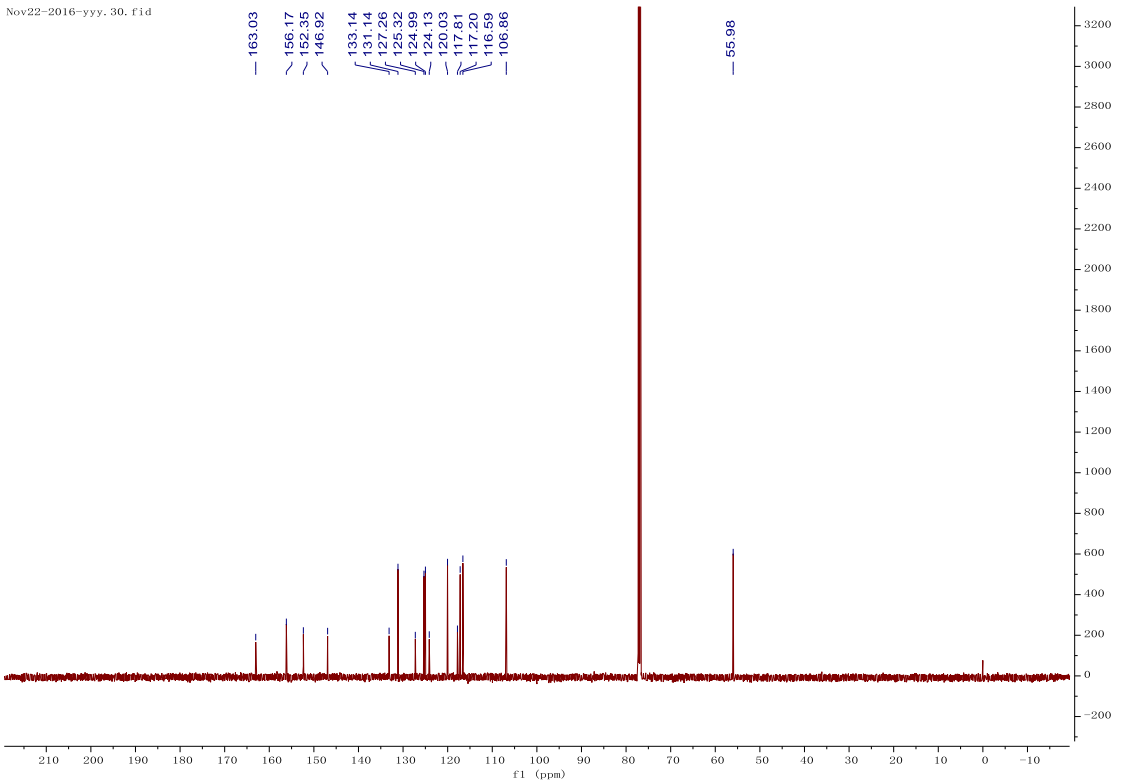




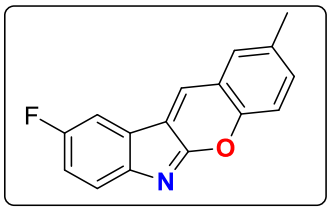
1-Chloro-9-methoxychromeno[2, 3-b]indole 4p

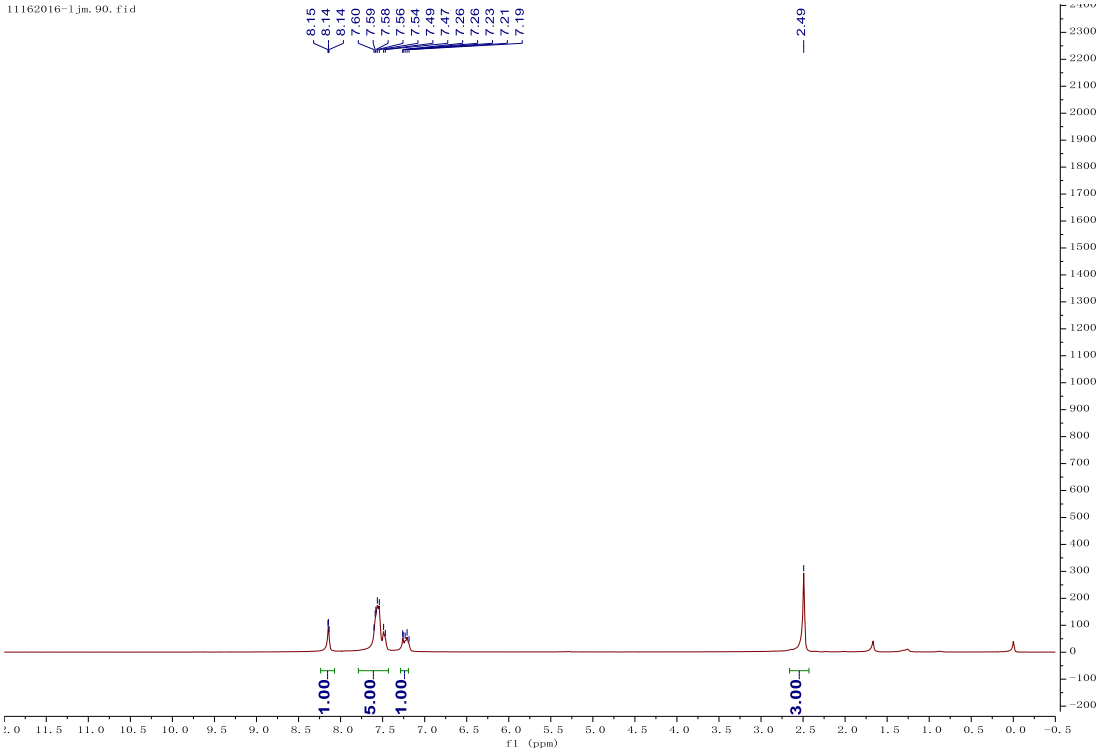


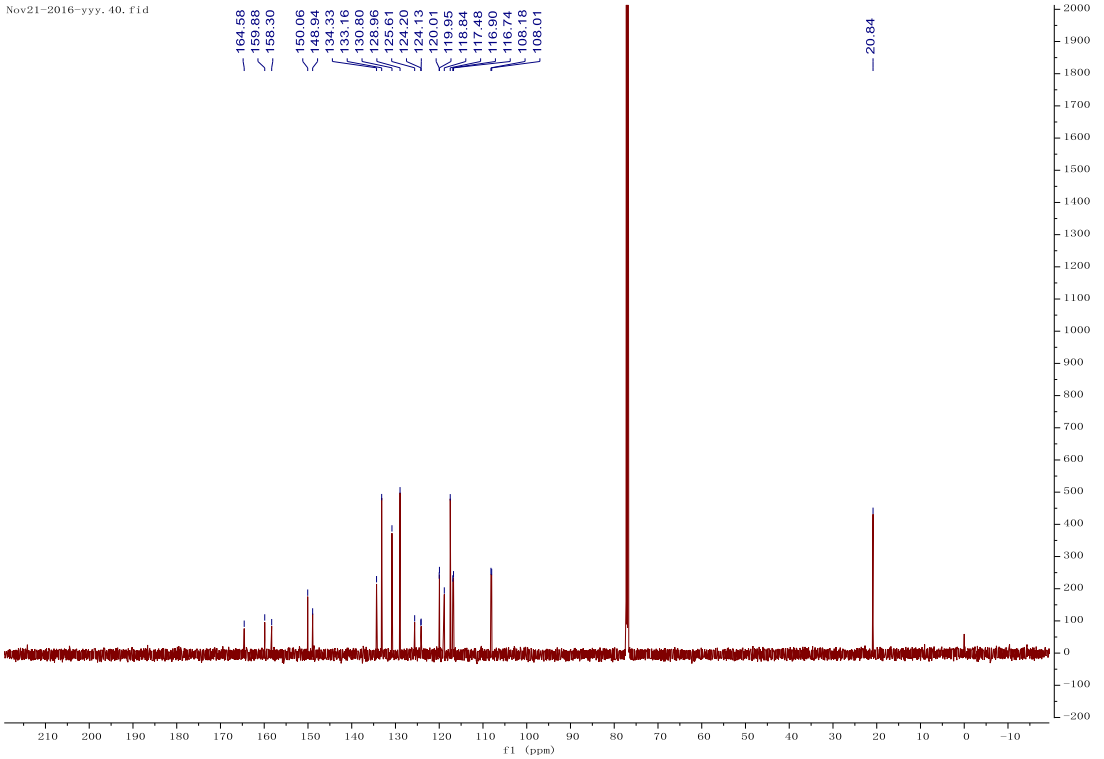


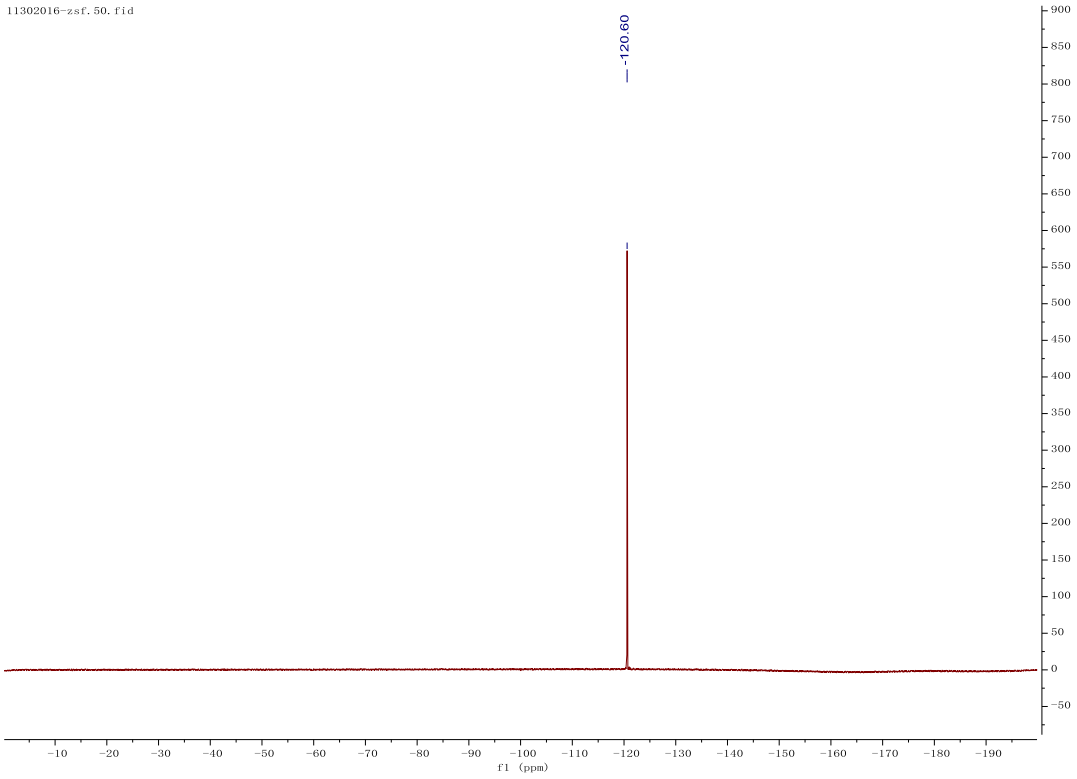


9-Fluoro-2-methylchromeno[2, 3-b]indole 4q





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-60
-70
-80
-90
-100
-110
-120
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-140
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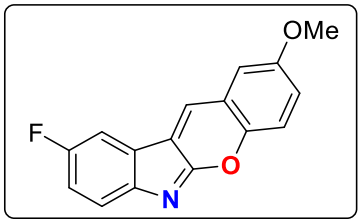
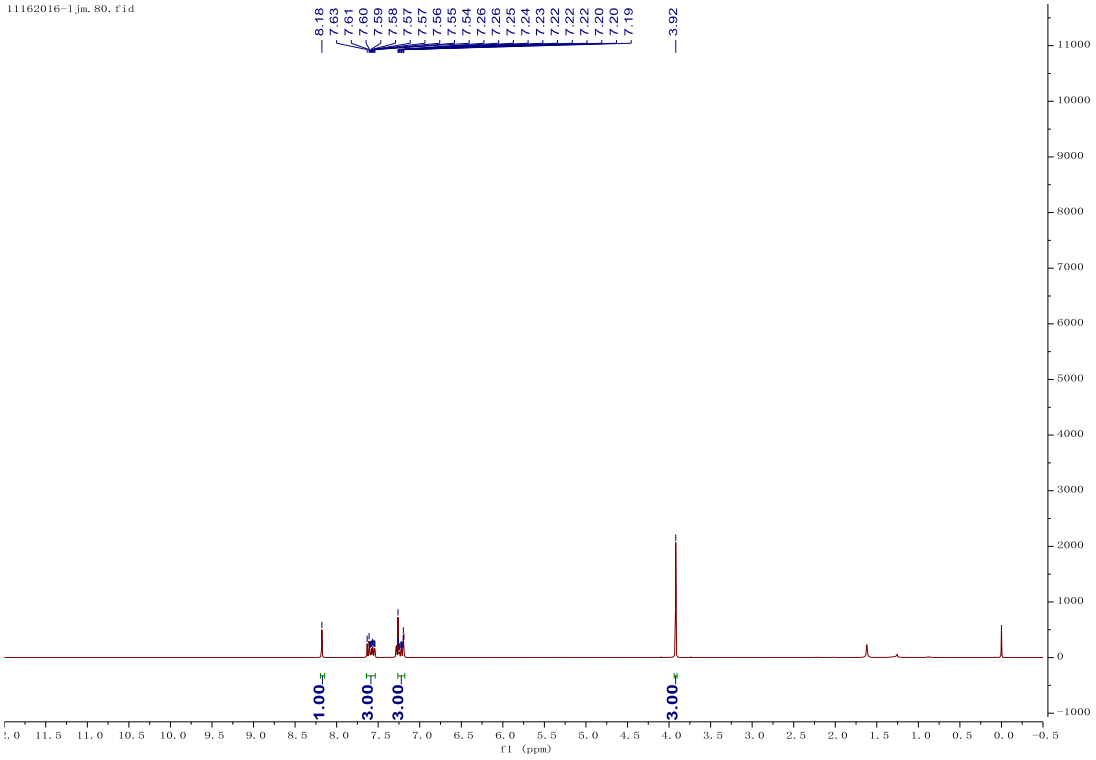
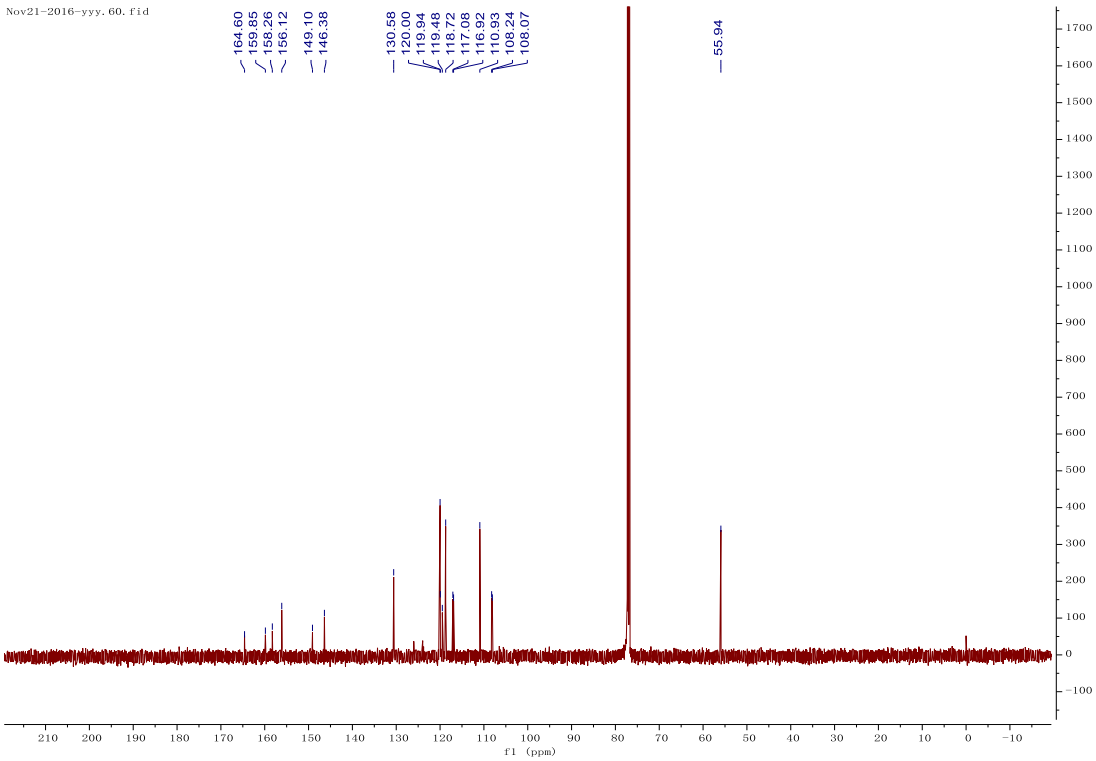
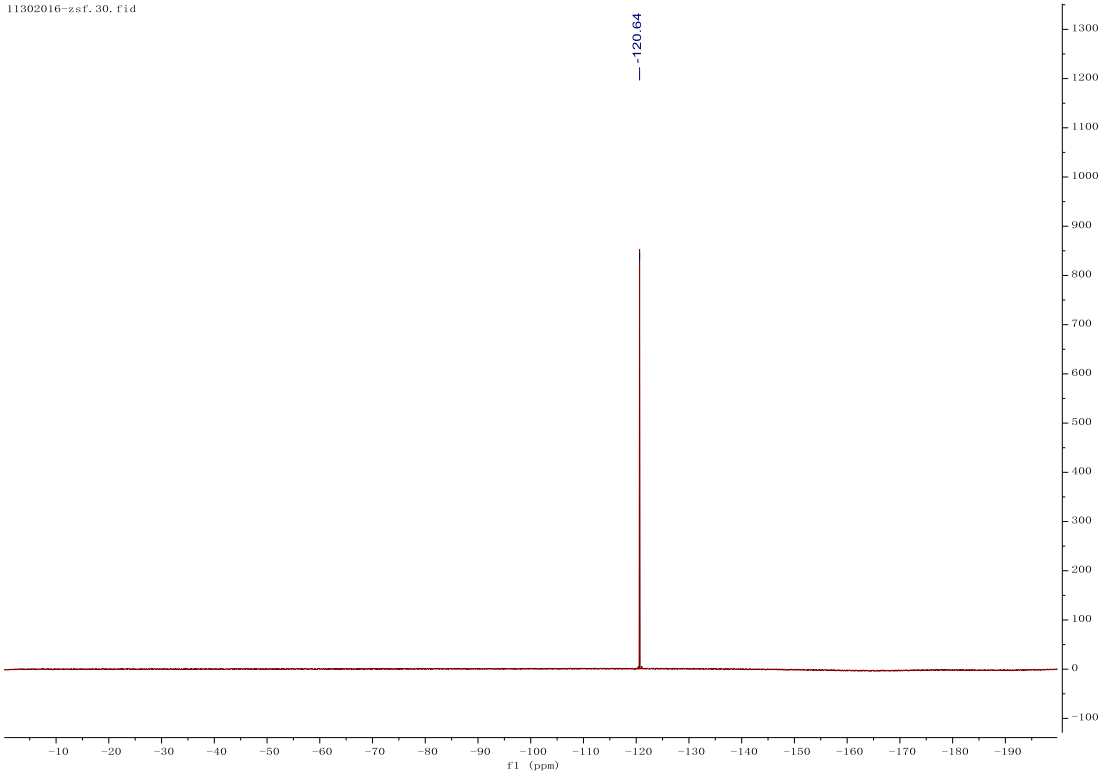
-160
-170
-180
-190
f1 (ppm)

9-Fluoro-2-methoxychromeno[2, 3-b]indole 4r





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-80
-90
-100
-110
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-160
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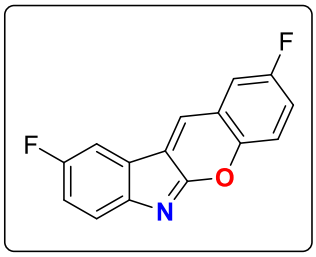
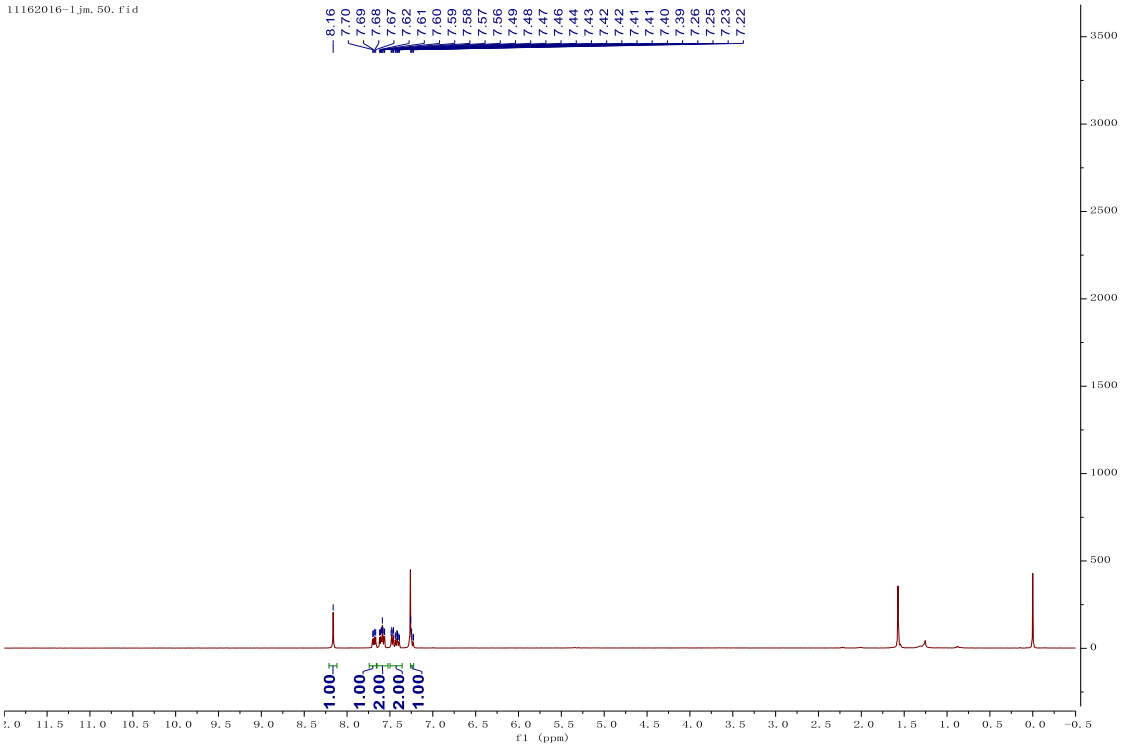
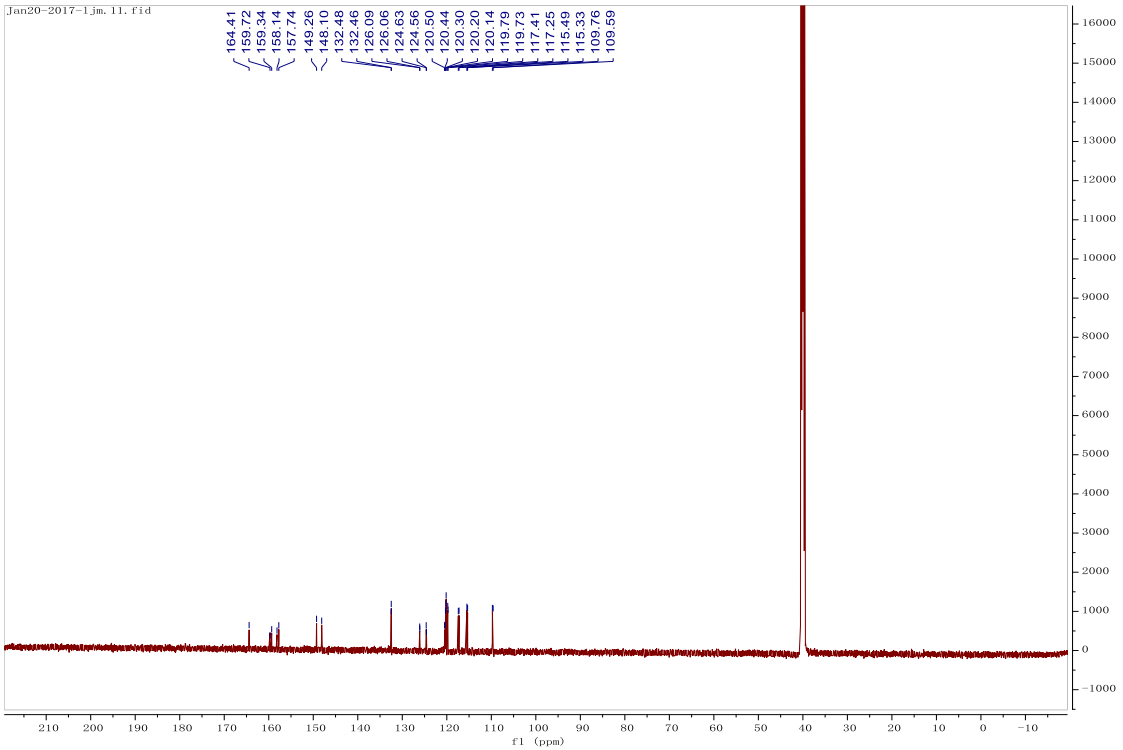
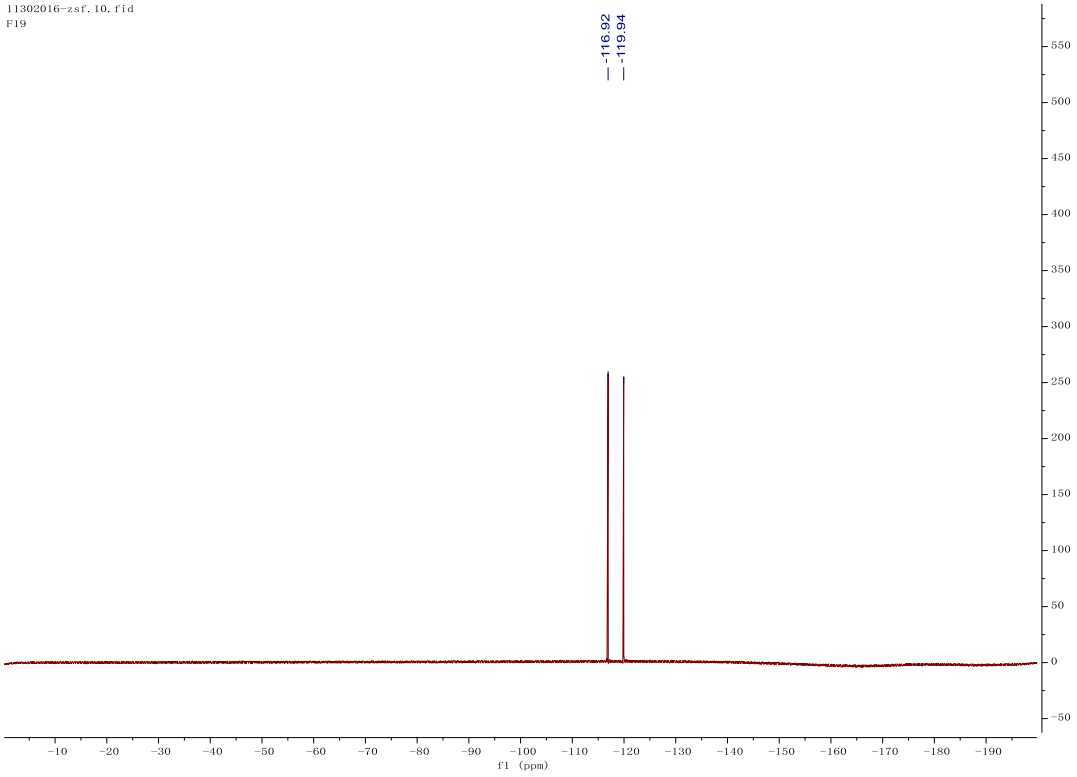
-180
-190
f1 (ppm)

2, 9-Difluorochromeno[2, 3-b]indole 4s





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-120
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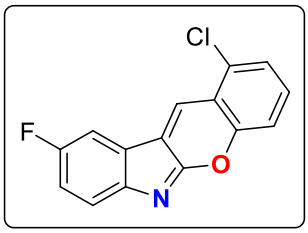
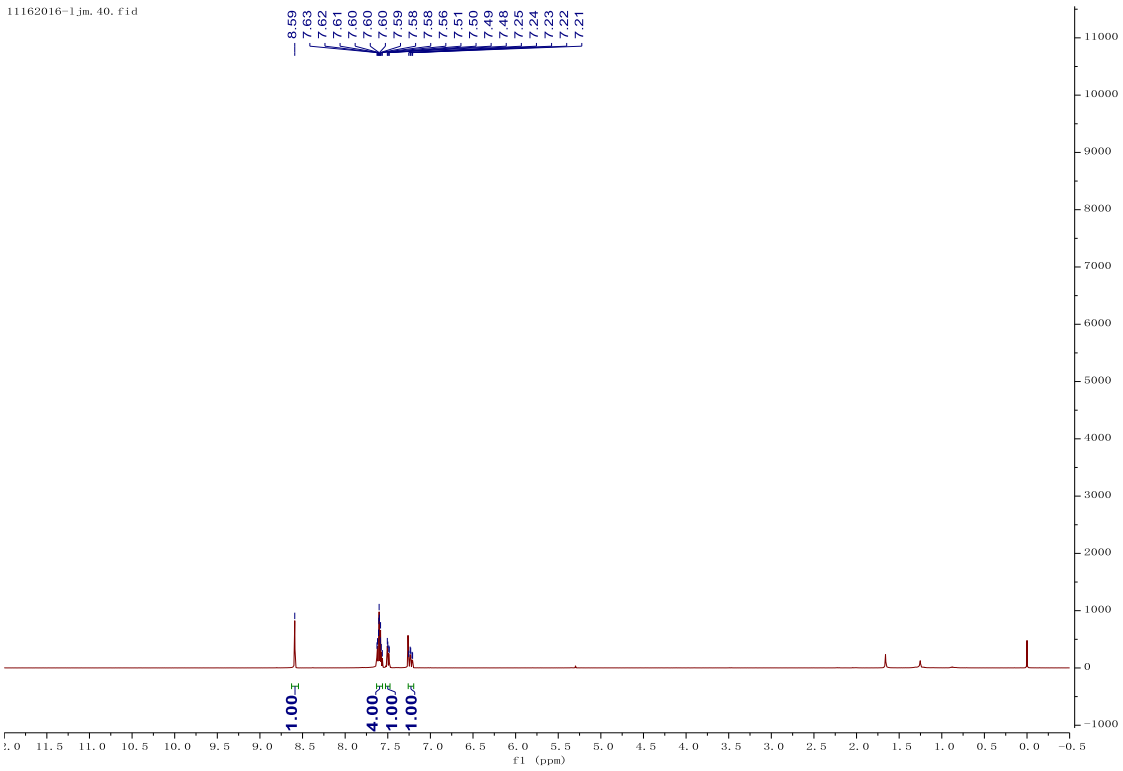
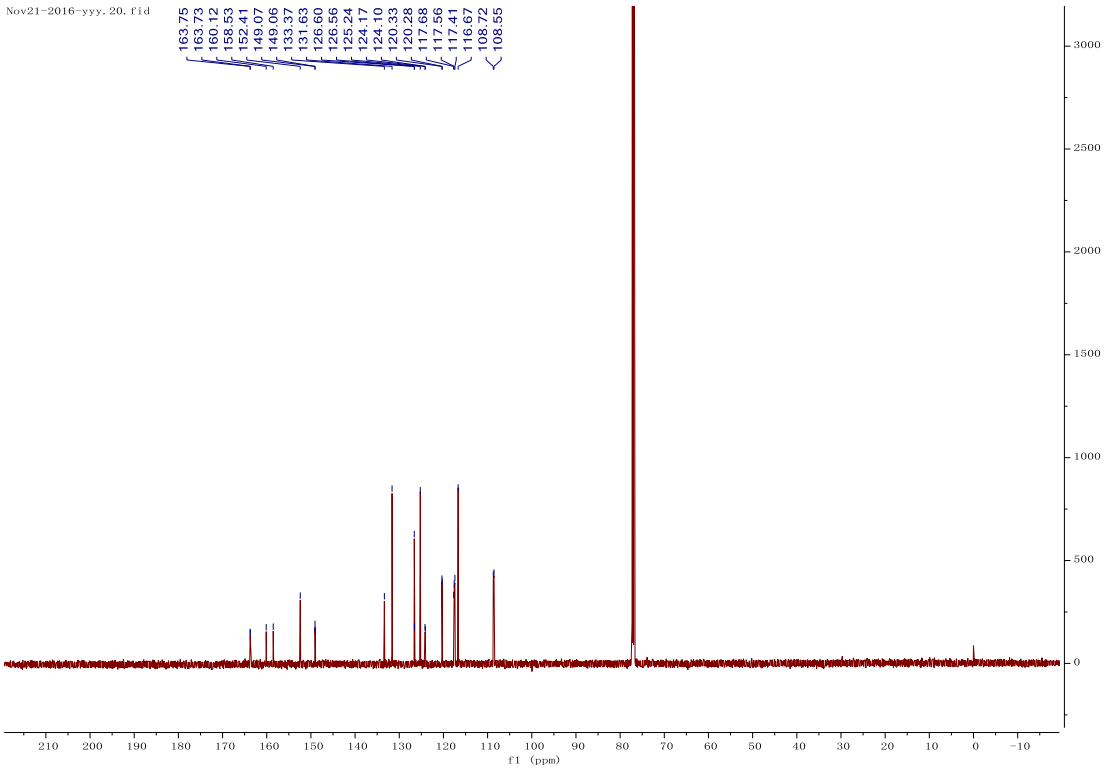
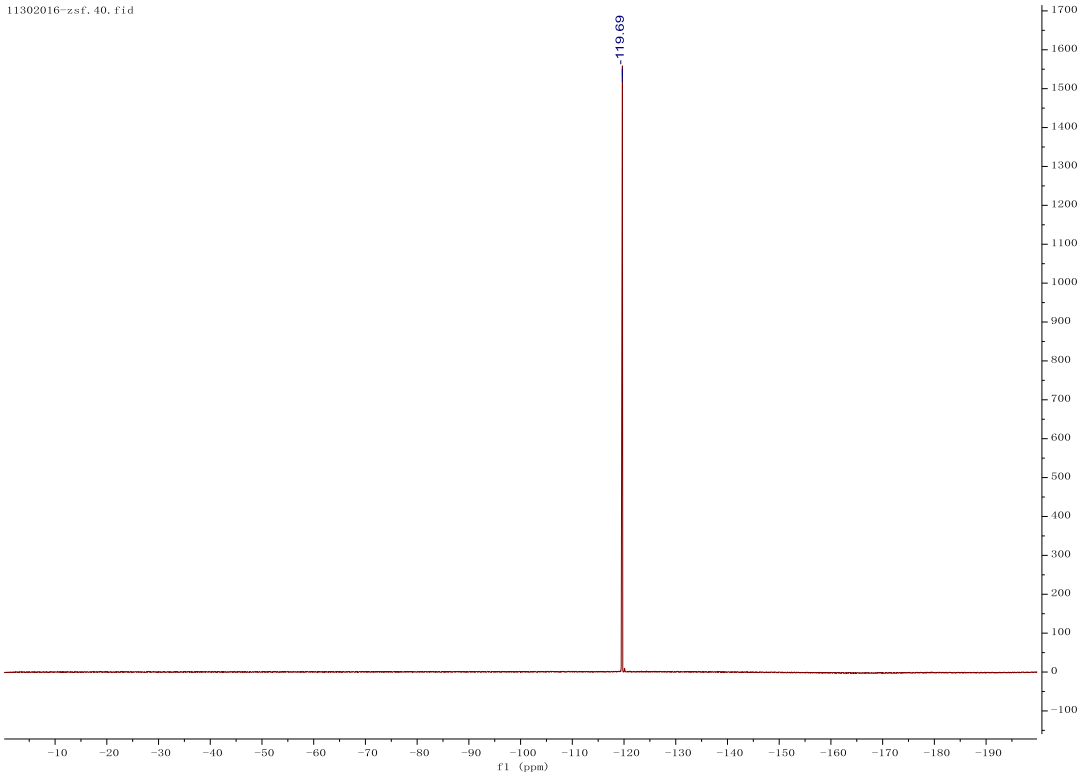
-170
-180
-190
f1 (ppm)

1-Chloro-9-fluorochromeno[2, 3-b]indole 4t





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-60
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-80
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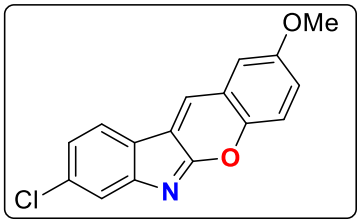
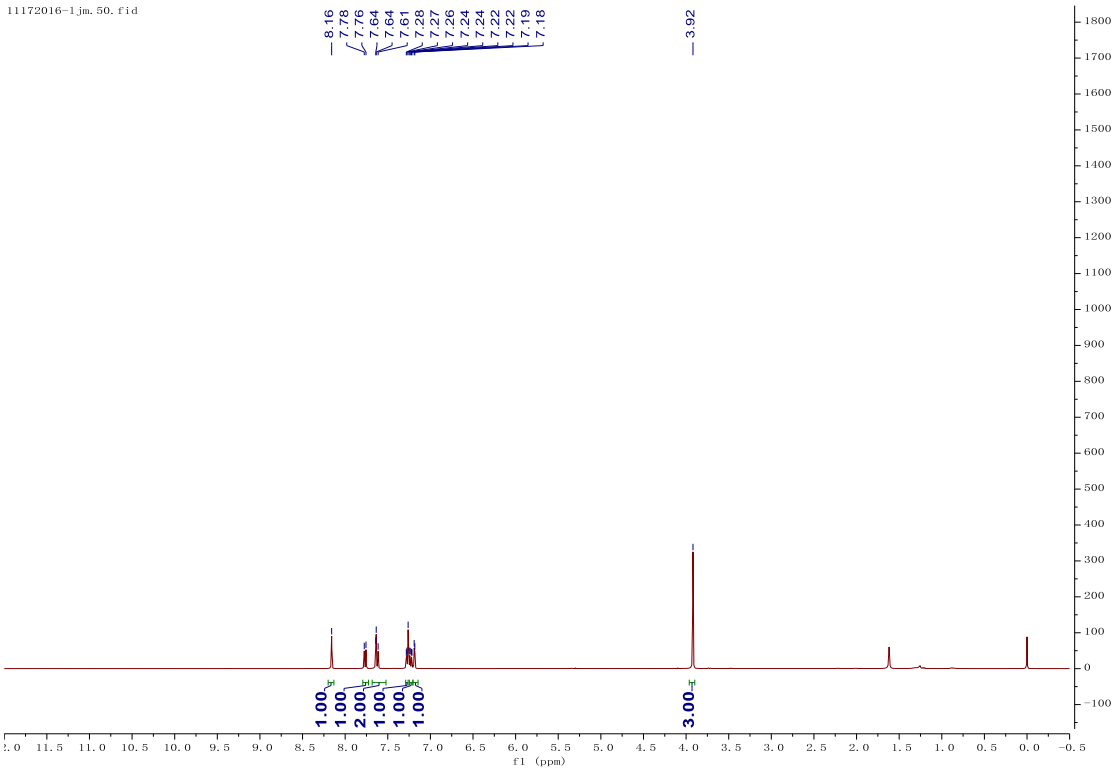
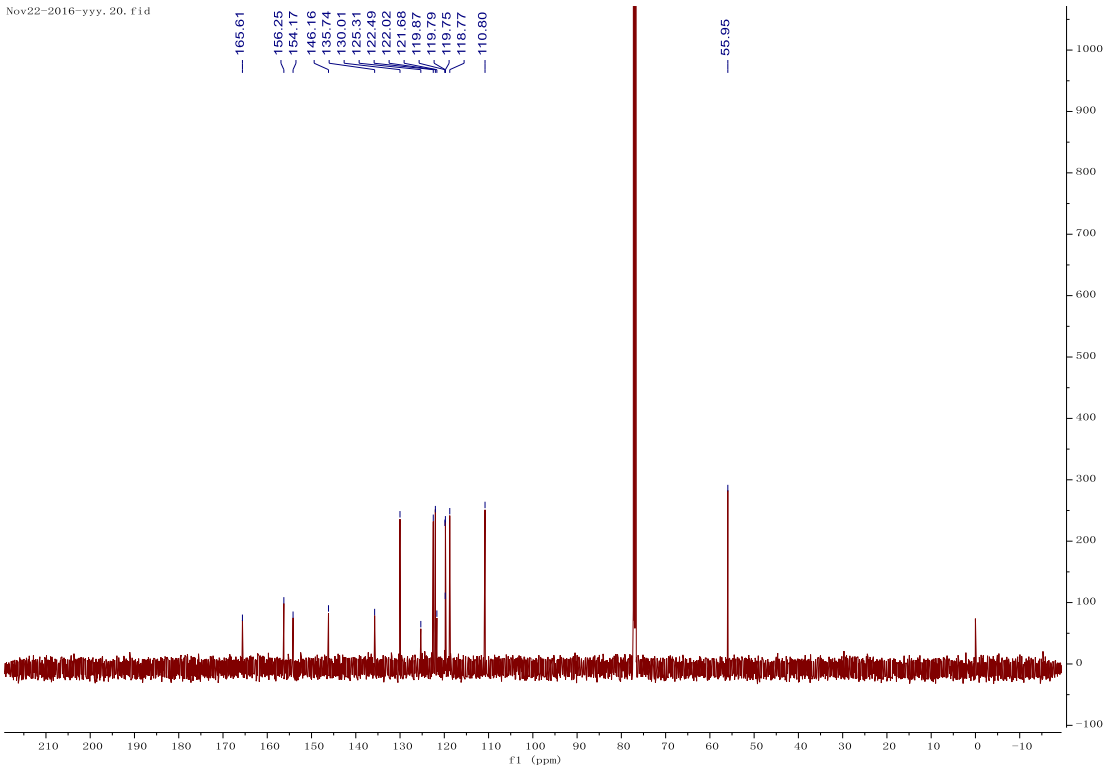
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

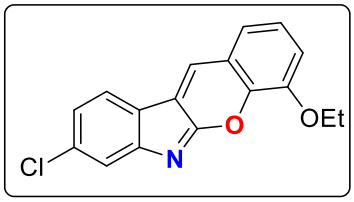
8-Chloro-2-methoxychromeno[2, 3-b]indole 4u

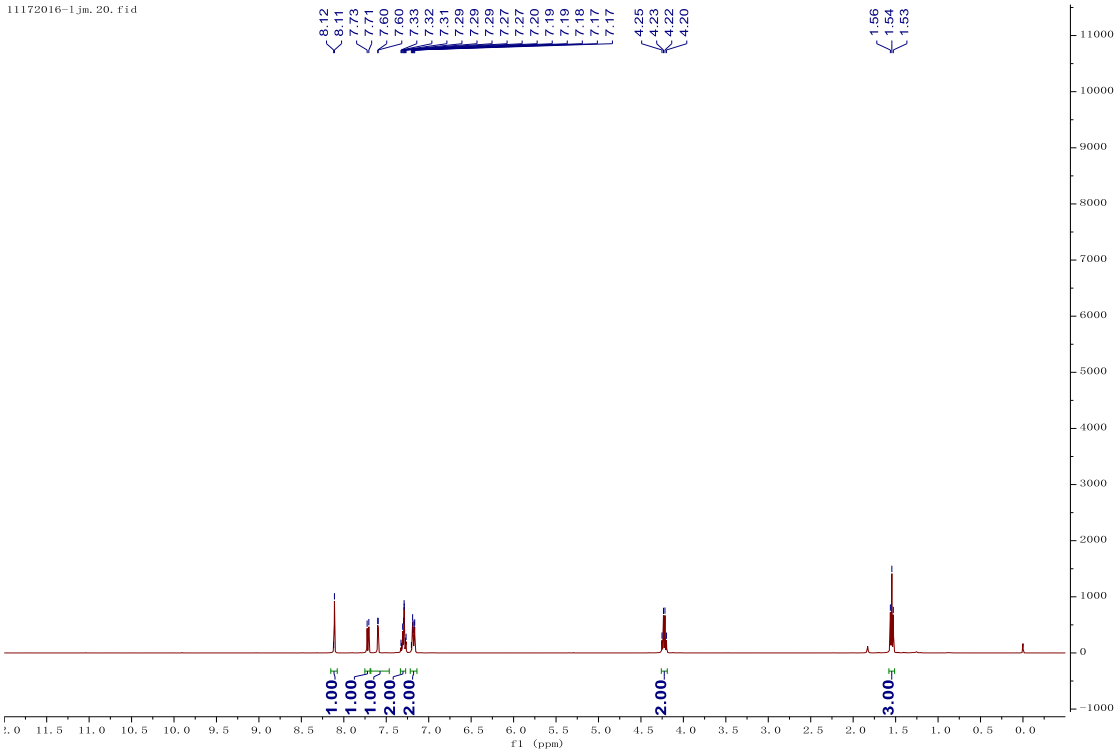


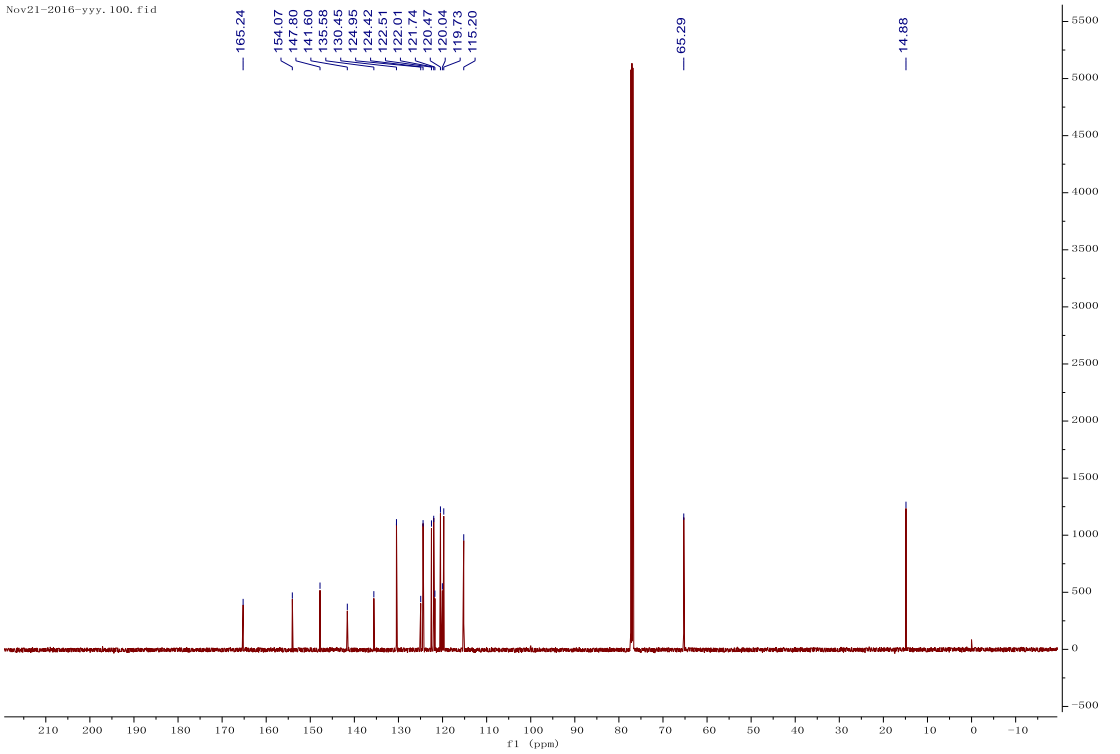




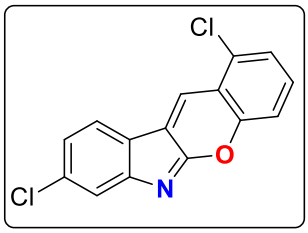
8-Chloro-4-ethoxychromeno[2, 3-b]indole 4v

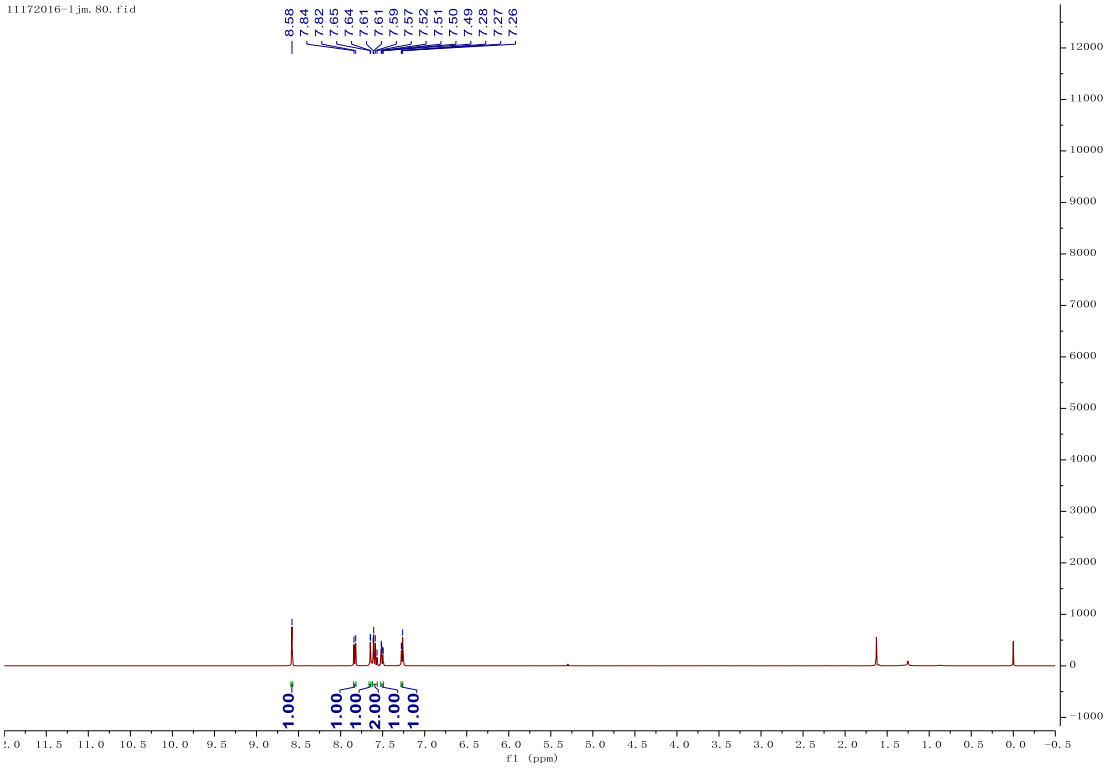


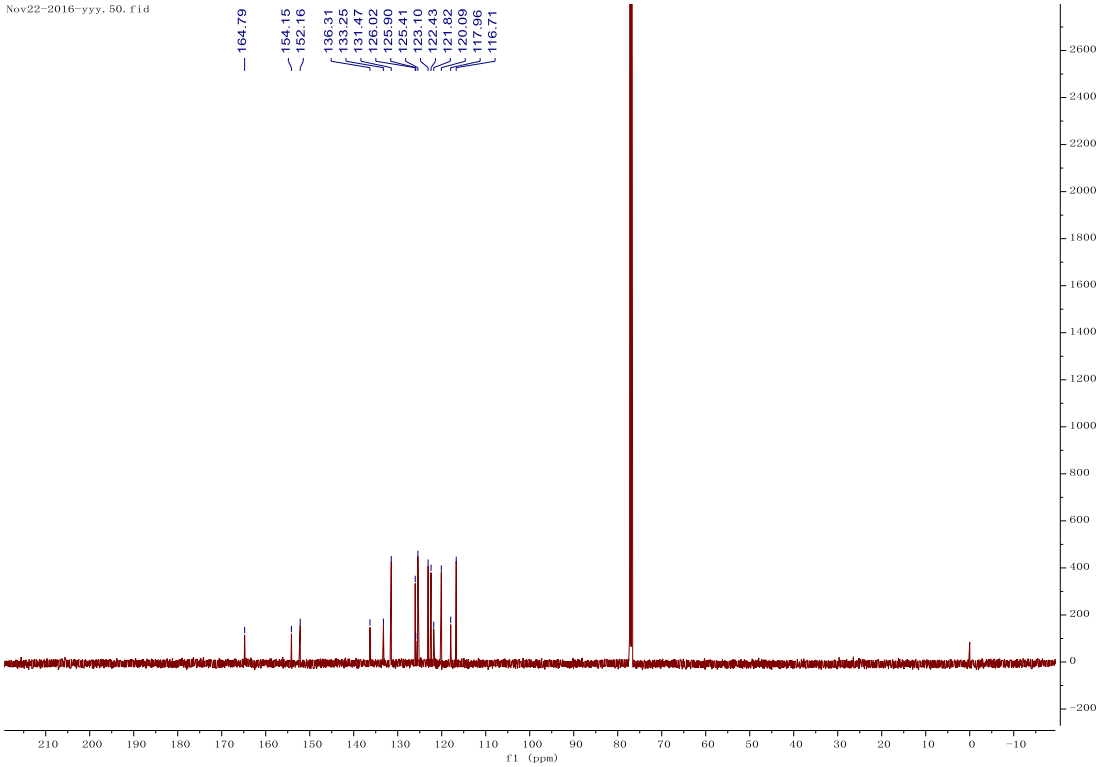




1, 8-Dichlorochromeno[2, 3-b]indole 4w







10-Chloro-2-methoxychromeno[2, 3-b]indole 4x