SYNTHESIS OF TETRAPHENYL-FUROINDOLES VIA TANDEM REACTIONS

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Supporting Information

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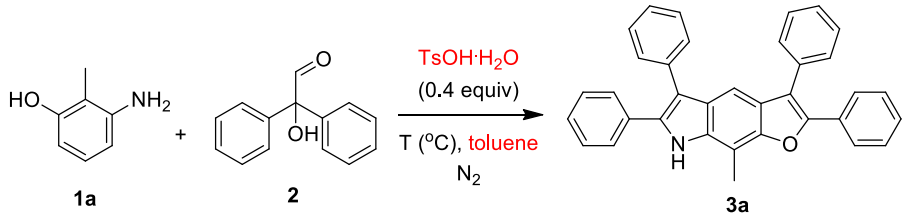
1. General information

Experimental: All non-aqueous manipulations were using standard Schlenk techniques. All reactions were carried out under nitrogen atmosphere. Reactions were monitored using thin-layer chromatography (TLC) on silica gel plates. Visualization of the developed plates was performed under UV light (254 nm) or $KMnO_4$ stain. Silica gel flash column chromatography was performed on SYNTHWARE 40-63 μm silica gel. Instrumentation: All NMR spectra were run at 400 MHz (^{1}H NMR) or 100 MHz (^{13}C NMR) in $CDCl_3$, or d_6-DMSO solution. ^{1}H NMR spectra were internally referenced to TMS. ^{13}C NMR spectra were internally referenced to the residual solvent signal. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constants (*J*) were reported in Hz. High resolution mass spectra (HRMS) were recorded on Bruker MicrOTOF-QII mass instrument (ESI). Materials: Unless otherwise indicated, starting catalysts and commercially available reagents were used without additional purification.

2. Optimization of reaction conditions

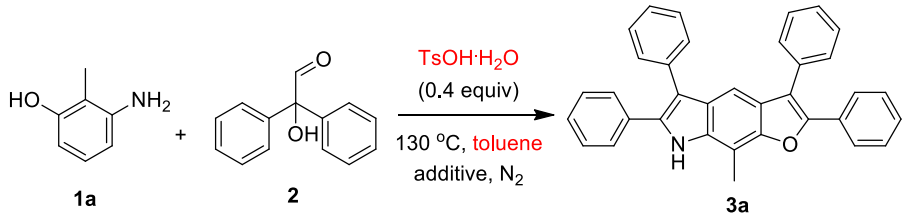
Table S1. Optimization of temperature[a]



entry	catalyst	T (°C)	yield (%)[b]
1	TsOH·H_2O	110	30
2	TsOH·H_2O	130	53
3	TsOH·H_2O	150	46

[a] Reaction conditions: **1a** (0.1 mmol), **2** (0.24 mmol, 1.2 eq), TsOH·H_2O (0.4 eq), reaction temperature: 25 °C (1.5 h), 60 °C (1.5 h), 80 °C (1 h), 100 °C (1 h), T (°C) (90 h), under an nitrogen atmosphere (the vial was evacuated and filled with nitrogen three times), toluene (2 mL), [b] Isolated yield.

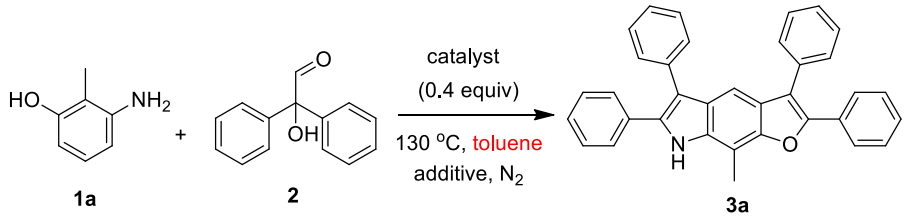
Table S2. Optimization of additive [a]



entry	catalyst	additives	yield (%)
1	TsOH·H_2O		53 [b]
2	TsOH·H_2O	$MgSO_4$	11
3	TsOH·H_2O	4 Å M.S.	n.d.[c]

[a] Reaction conditions: **1a** (0.1 mmol); **2** (0.24 mmol, 1.2 eq); TsOH·H_2O (0.4 eq); additive (100 mg); reaction temperature: 25 °C (1.5 h); 60 °C (1.5 h); 80 °C (1 h); 100 °C (1 h); 130 °C (90 h); under an nitrogen atmosphere (the vial was evacuated and filled with nitrogen three times); toluene (2 mL). [b] no additive. [c] n.d. = not detected.

Table S3. Optimization of catalyst [a]

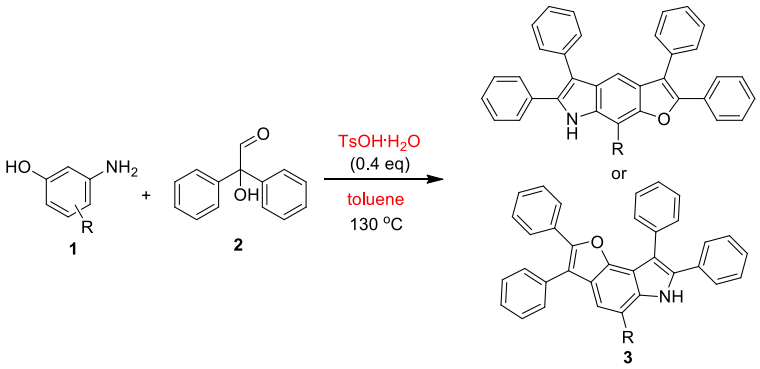


1a 2 3a

entry	catalyst	T (°C)	yield (%)
1	$TsOH·H_2O$	130	53
2	PPTS[b]	130	27

[a] Reaction conditions: **1a** (0.1 mmol); **2** (0.24 mmol, 1.2 eq); $TsOH·H_2O$ (0.4 eq); PPTS (0.4 eq); reaction temperature: 25 °C (1.5 h); 60 °C (1.5 h); 80 °C (1 h); 100 °C (1 h); 130 °C (90 h); under an nitrogen atmosphere (the vial was evacuated and filled with nitrogen three times); toluene (2 mL). [b] PPTS = pyridinium *p*-toluenesulfonate.

3. General procedure for the synthesis of furoindoles 3

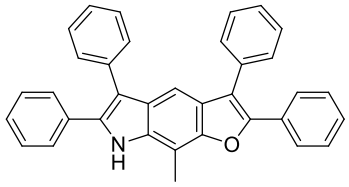


1 2 3

The reaction mixture of *m*-aminophenols **1** (0.1 mmol), α-hydroxyaldehydes **2** (0.24 mmol, 1.2 equiv., 51 mg), $TsOH·H_2O$ (0.04 mmol, 0.4 equiv., 7.6 mg) was stirred in toluene (2.0 mL) at 25 °C (1.5 h); 60 °C (1.5 h); 80 °C (1 h); 100 °C (1 h); 130 °C (90 h); under an nitrogen atmosphere (the vial was evacuated and filled with nitrogen three times). After the reaction was accomplished, the crude mixture purified by flash chromatography on silica gel use mixed eluents (petroleum ether/dichloromethane) to afford the desired pure compound **3**. The flow rate of eluent must be slowly.

4. Experimental characterization data for products

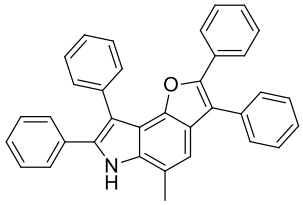
8-methyl-2,3,5,6-tetraphenyl-7*H*-furo[3,2-*f*]indole **(3a)**



3a

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.69 – 7.65 (m, 2H), 7.52 (dd, *J* = 10.3, 3.3 Hz, 3H), 7.44 (td, *J* = 7.2, 1.9 Hz, 6H), 7.37 – 7.25 (m, 10H), 2.78 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.61, 149.74, 135.34, 134.83, 134.53, 133.60, 133.02, 131.35, 130.28, 129.97, 128.96, 128.67, 128.59, 128.33, 128.16, 127.82, 127.56, 127.42, 126.81, 126.57, 126.22, 125.95, 118.05, 115.40, 106.50, 101.81, 9.88. HRMS (EI): m/z (M^+) calcd for $C_{35}H_{25}NO$: 475.1936; found: 475.1938.

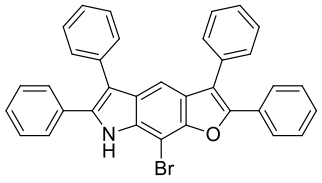
5-methyl-2,3,7,8-tetraphenyl-6*H*-furo[2,3-*e*]indole **(3b)**



3b

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.72 (d, *J* = 7.3 Hz, 2H), 7.57 – 7.52 (m, 4H), 7.49 (t, *J* = 7.2 Hz, 4H), 7.43 (t, *J* = 7.3 Hz, 3H), 7.35 – 7.30 (m, 4H), 7.25 - 7.17 (m, 3H), 7.05 (s, 1H), 2.55 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.68, 146.13, 135.01, 134.51, 133.93, 133.52, 132.87, 131.45, 130.80, 130.09, 128.97, 128.81, 128.47, 128.32, 127.98, 127.79, 127.50, 127.23, 126.44, 125.95, 123.59, 118.20, 116.44, 114.41, 114.09, 113.82, 16.85; HRMS (ESI): m/z $(M+H)^+$ calcd for $C_{35}H_{26}NO$: 476.2009; found: 476.2007.

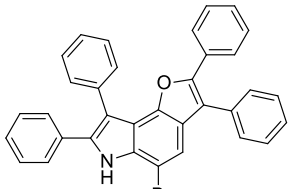
8-bromo-2,3,5,6-tetraphenyl-7*H*-furo[3,2-*f*]indole **(3c)**



3c

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.69 (t, *J* = 7.9 Hz, 4H), 7.61 – 7.52 (m, 4H), 7.46 – 7.37 (m, 5H), 7.32 (td, *J* = 7.7, 3.1 Hz, 4H), 7.25 (d, *J* = 7.1 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.76, 149.16, 135.20, 134.37, 132.77, 131.98, 130.84, 130.34, 129.73, 129.53, 128.73, 128.60, 128.49, 128.36, 128.28, 127.98, 127.64, 127.26, 126.42, 124.60, 116.78, 116.21, 115.88, 115.03, 105.45. HRMS (EI): m/z (M^+) calcd for $C_{34}H_{22}{}^{79}BrNO$: 539.0885; found: 539.0886; $C_{34}H_{22}{}^{81}BrNO$: 541.0864; found: 541.0871.

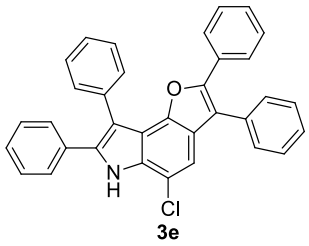
5-bromo-2,3,7,8-tetraphenyl-6*H*-furo[2,3-*e*]indole **(3d)**



3d

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.69 (d, *J* = 7.3 Hz, 2H), 7.55 – 7.49 (m, 8H), 7.46 – 7.41 (m, 4H), 7.39 – 7.35 (m, 3H), 7.27 – 7.19 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.52, 146.45, 134.43, 134.36, 133.10, 132.87, 132.13, 130.89, 130.71, 129.95, 129.11, 128.87, 128.49, 128.37, 128.18, 128.07, 127.80, 127.66, 126.75, 126.06, 124.91, 117.69, 116.36, 115.00, 114.55, 100.25. HRMS (EI): m/z (M^+) calcd for $C_{34}H_{22}{}^{79}BrNO$: 539.0885; found: 539.0884; $C_{34}H_{22}{}^{81}BrNO$: 541.0864; found: 541.0867.

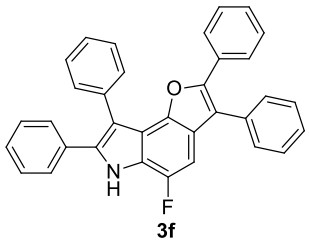
5-chloro-2,3,7,8-tetraphenyl-6*H*-furo[2,3-*e*]indole **(3e)**



3e

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H), 7.69 (d, *J* = 7.5 Hz, 2H), 7.54 -7.47 (m, 8H), 7.43 (t, *J* = 7.3 Hz, 3H), 7.39 – 7.32 (m, 4H), 7.27 – 7.20 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.60, 145.90, 134.42, 134.37, 133.13, 132.15, 131.66, 130.94, 130.73, 129.94, 129.10, 128.87, 128.47, 128.38, 128.17, 128.08, 127.79, 127.65, 126.76, 126.07, 124.28, 117.86, 115.14, 114.45, 113.40, 112.69. HRMS (EI): m/z (M^+) calcd for $C_{34}H_{22}{}^{35}ClNO$: 495.1390; found: 495.1386; $C_{34}H_{22}{}^{37}ClNO$: 497.1360; found: 497.1384

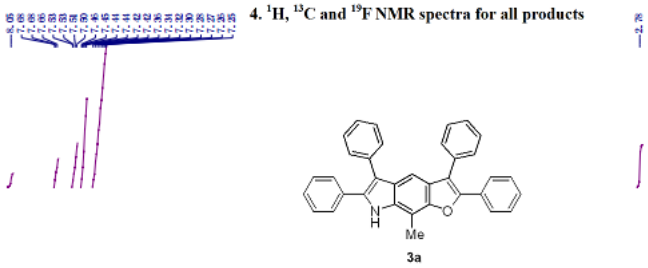
5-fluoro-2,3,7,8-tetraphenyl-6*H*-furo[2,3-*e*]indole **(3f)**



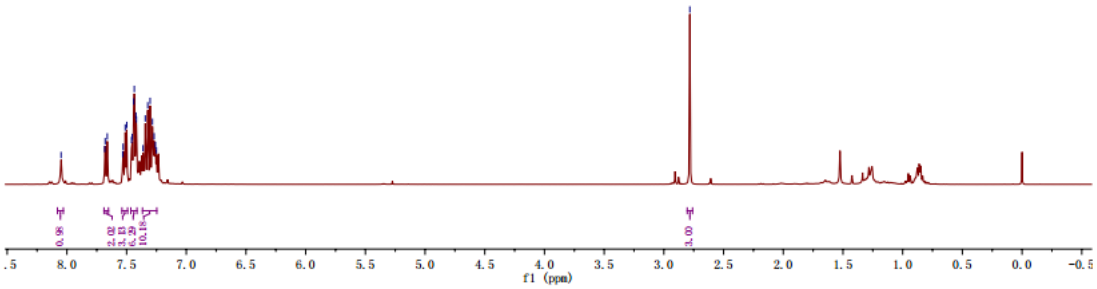
3f

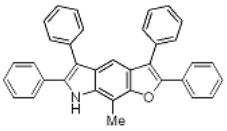
^{1}H NMR (400 MHz, DMSO-d_6) δ 12.31 (s, 1H), 7.58 (d, *J* = 7.6 Hz, 2H), 7.53 - 7.46 (m, 8H), 7.43 – 7.36 (m, 6H), 7.33 – 7.24 (m, 4H), 6.90 (d, *J* = 10.6 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 148.20, 147.68 (d, J_{1F} = 239.8 Hz), 143.06, 136.07, 134.85, 132.76, 132.03, 130.90, 130.78, 129.93, 129.75, 129.41, 129.14, 128.94, 128.54, 128.50, 128.44, 127.10, 125.91, 123.79 (d, J_{2F} = 17.4 Hz), 121.78 (d, J_{3F} = 8.8 Hz), 118.71 (d, J_{4F} = 3.5 Hz), 116.41 (d, J_{3F} = 5.6 Hz), 113.23, 113.22, 97.70 (d, J_{2F} = 20.4 Hz). ^{19}F NMR (377 MHz, DMSO-d_6) δ -136.69. HRMS (EI): m/z (M^+) calcd for $C_{34}H_{22}FNO$: 479.1685; found: 479.1683.

4. ^{1}H, ^{13}C and ^{19}F NMR spectra for all products

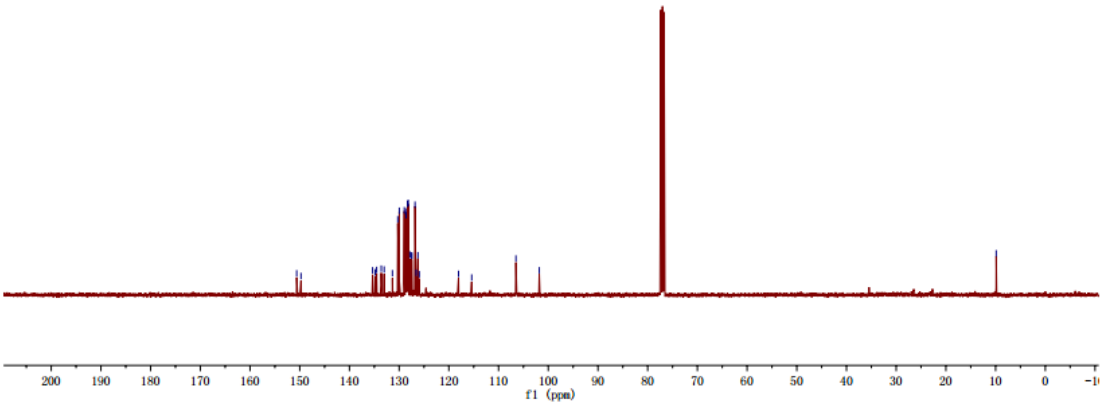


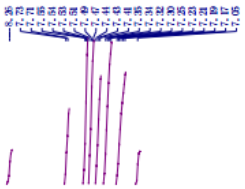
3a

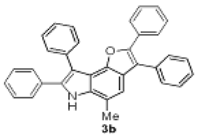


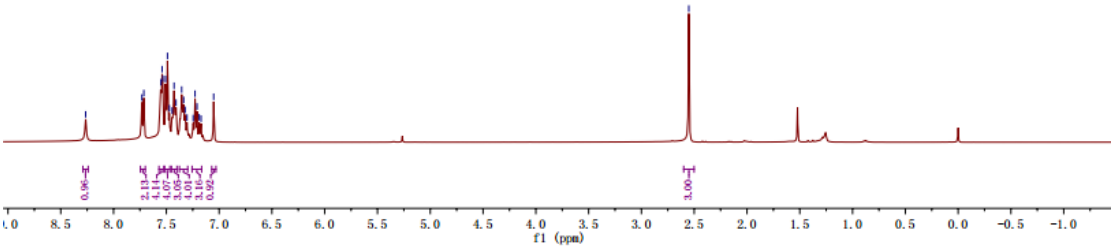


3a






Me
3b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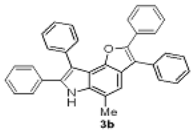
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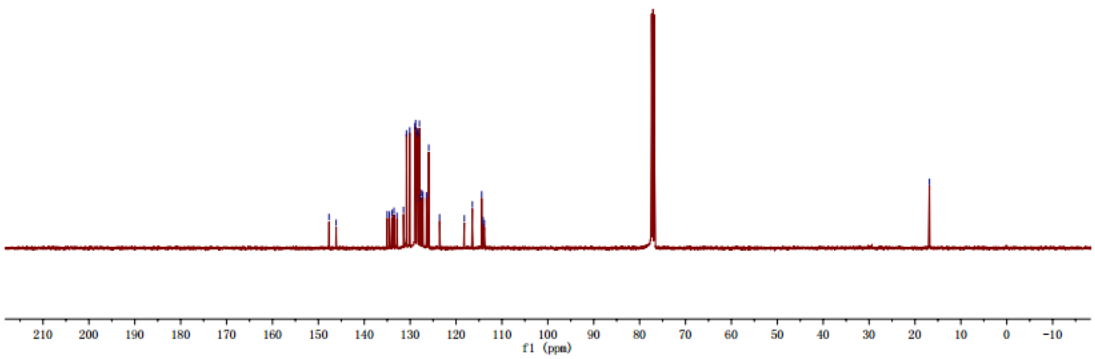
3b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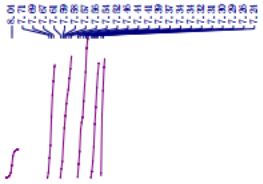
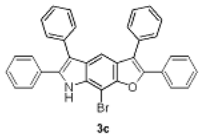
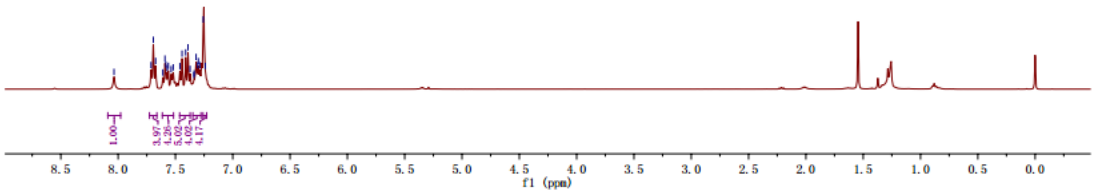
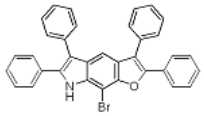




3c





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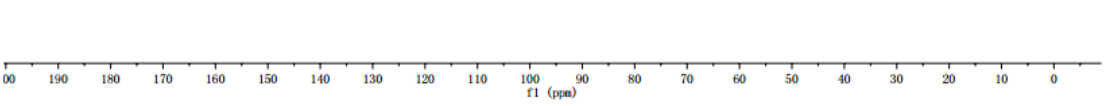
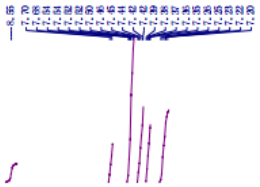
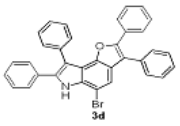
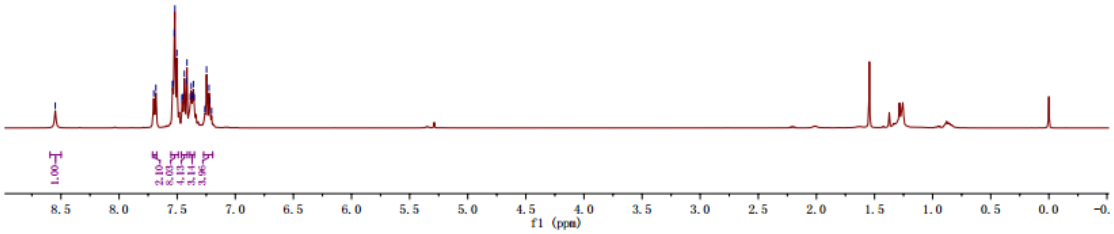





Br
3d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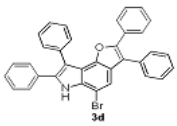
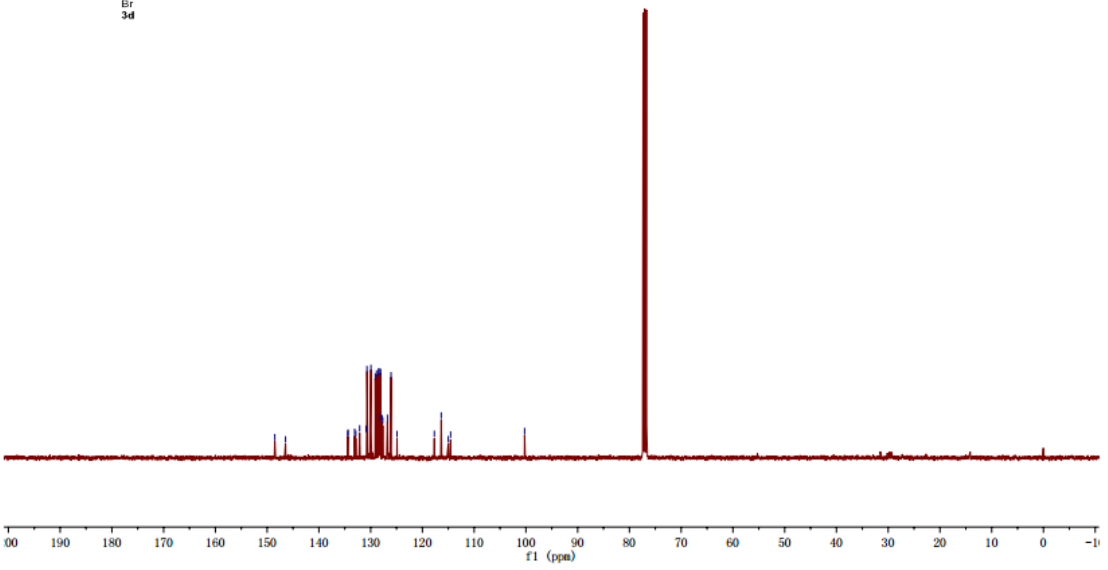
4.13
3.96
f1 (ppm)


Br
3d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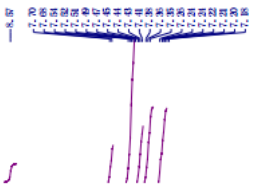
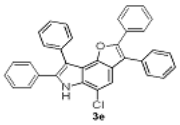
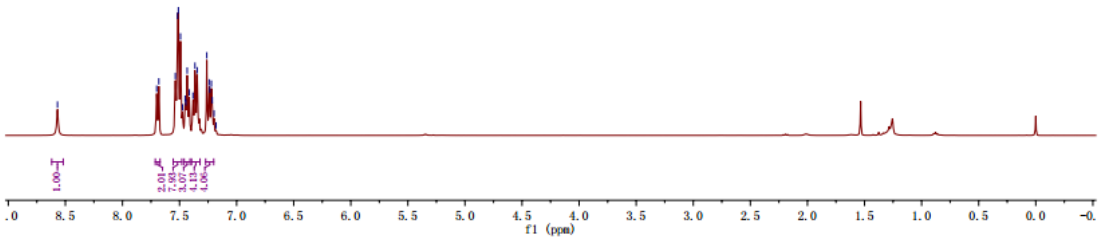



Cl
3e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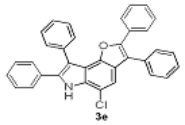
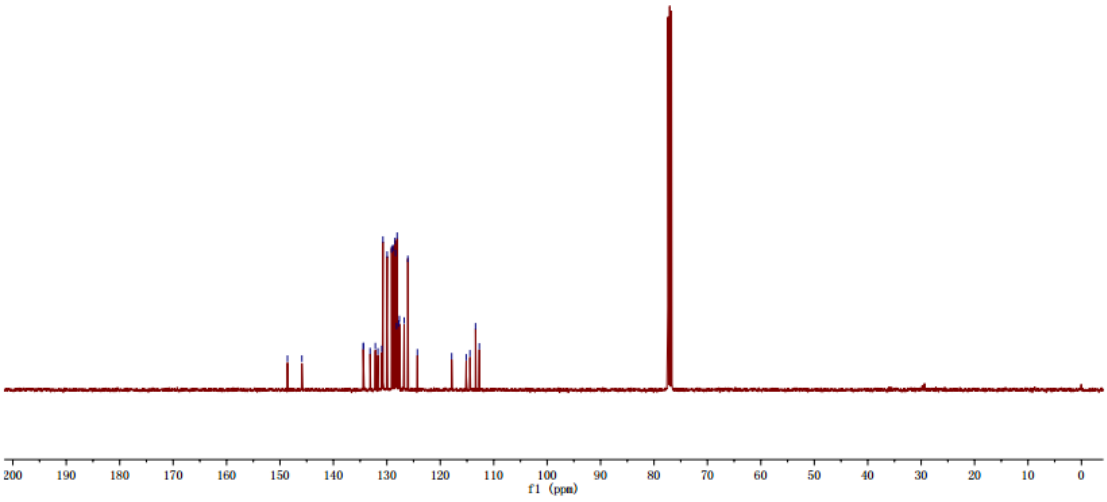
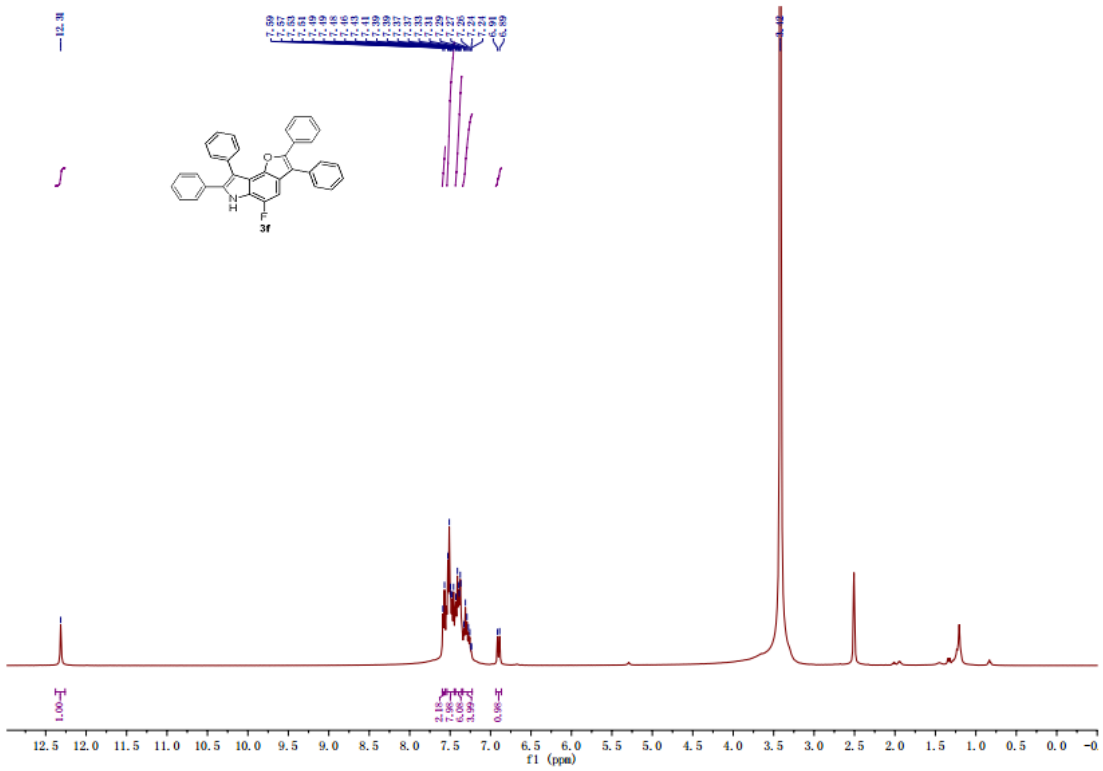
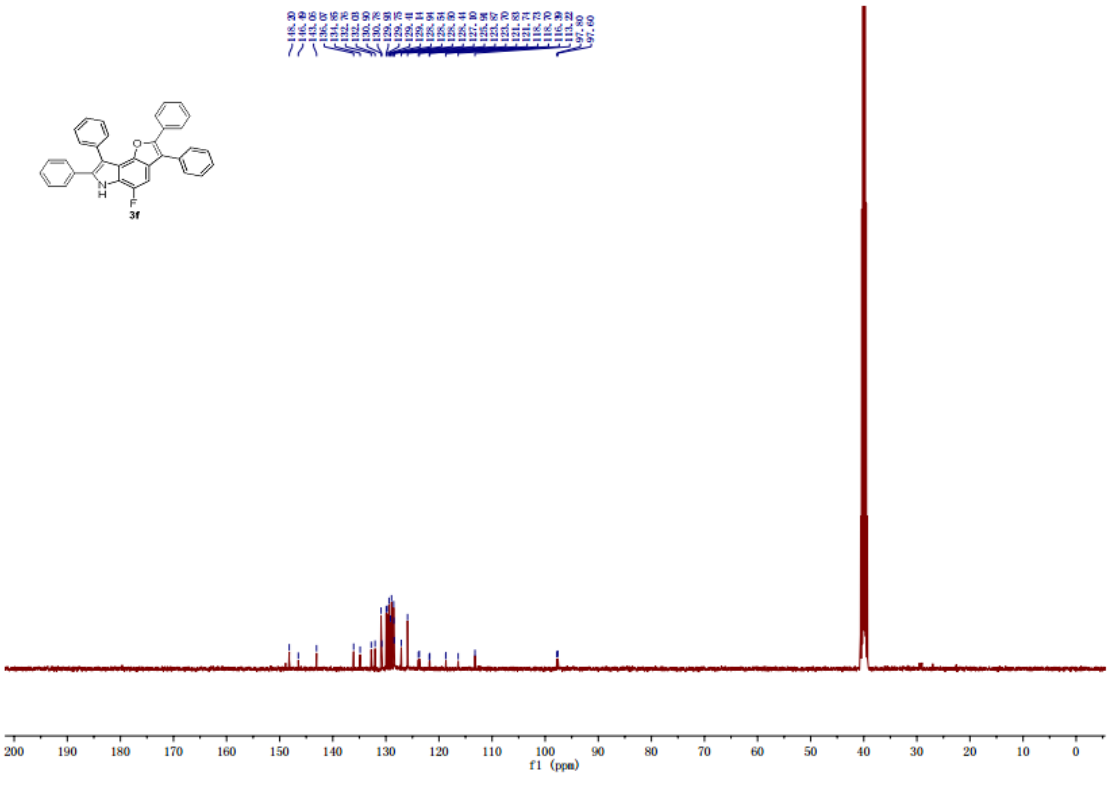
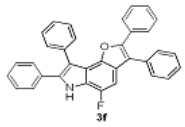
1.07
4.13
4.06
f1 (ppm)


Cl
3e


f1 (ppm)


12.38
7.59
7.57
7.53
7.51
7.49
7.48
7.46
7.43
7.41
7.39
7.39
7.37
7.33
7.31
7.29
7.27
7.26
7.24
7.21
6.94
6.89
4.49
1.00
2.15
7.98
6.08
3.99
0.98
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0
f1 (ppm)
3f


148.20
146.49
143.05
136.07
134.85
134.76
132.01
130.90
130.78
130.59
129.75
129.48
129.34
128.84
128.80
128.44
127.80
127.58
123.87
123.70
121.83
121.71
118.73
118.70
116.39
116.22
97.80
97.60
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
3f


O
N
H
F

3f

-136.69
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)