Supporting Information

Palladium-catalyzed tandem reaction of 2-hydroxyarylacetonitriles with sodium sulfinates: one-pot synthesis of 2-arylbenzofurans

Jiuxi Chen,[a,b] Jianjun Li[a] and Weike Su*[a]

[a] *Key Laboratory for Green Pharmaceutical Technologies and Related Equipment of Ministry of Education, College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou 310014, China.*

E-mail: pharmlab@zjut.edu.cn

[b] *College of Chemistry & Materials Engineering, Wenzhou University, Wenzhou 325035, P. R. China.*

List of Contents

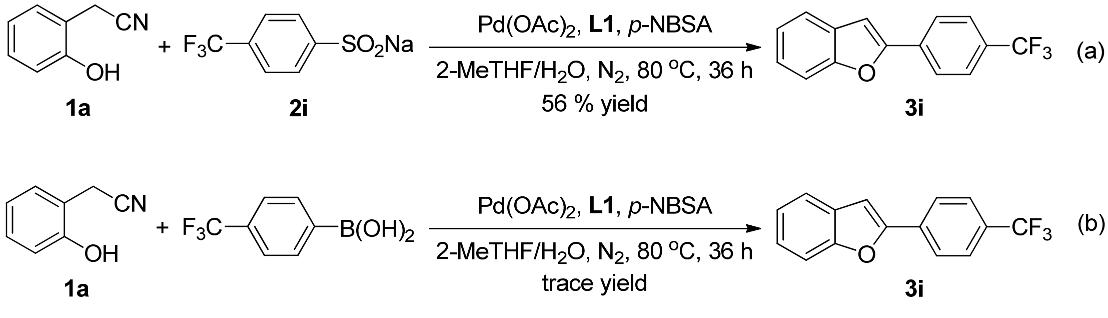
1. General experimental details

Chemicals were either purchased or purified by standard techniques without special instructions. ^{1}H NMR and ^{13}C NMR spectra were measured on a 500 MHz Bruker spectrometer, using $CDCl_3$ as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. Chemical shifts are given in δ relative to TMS, the coupling constants J are given in Hz. All reactions were conducted under air atmosphere. Column chromatography was performed using EM Silica gel 60 (300-400 mesh). All products are known compounds and identified by comparison with authentic samples. Analytical data and spectra (^{1}H and ^{13}C NMR) of all products are supplied in the Supporting Information.

2. General procedure

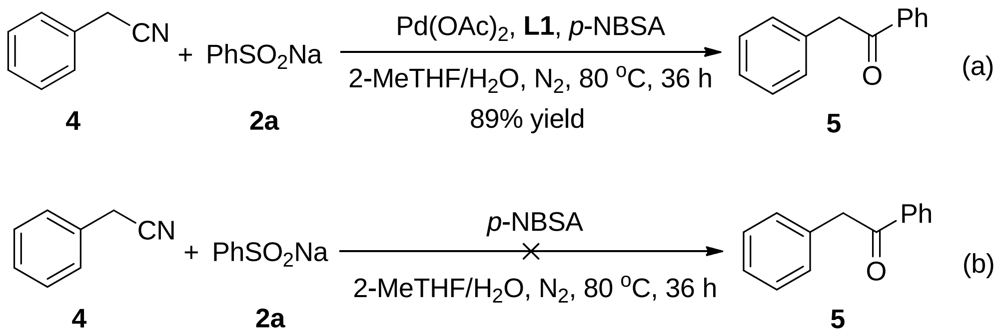
Under N_2 atmosphere, a Schlenk tube was charged with 2-hydroxyarylacetonitriles **1** (0.3 mmol), sodium sulfinates **2** (0.6 mmol), $Pd(OAc)_2$ (10 mol %), **L1** (20 mol %), *p*-NBSA (10 equiv), 2-MeTHF (2 mL), and H_2O (1 mL) at room temperature. The reaction mixture was stirred vigorously at 80 °C for 36 h. After the completion of the reaction, as monitored by TLC and GC-MS analysis, the reaction mixture was cooled to room temperature. The mixture was poured into ethyl acetate, which was washed with saturated $NaHCO_3$ (2 × 10 mL) and then brine (1 × 10 mL). After the aqueous layer was extracted with ethyl acetate, the combined organic layers were dried over anhydrous Na_2SO_4 and evaporated under a vacuum. The residue was purified by flash column chromatography (hexane/ethyl acetate as eluent) to afford the desired products **3**.

3. Control experiments



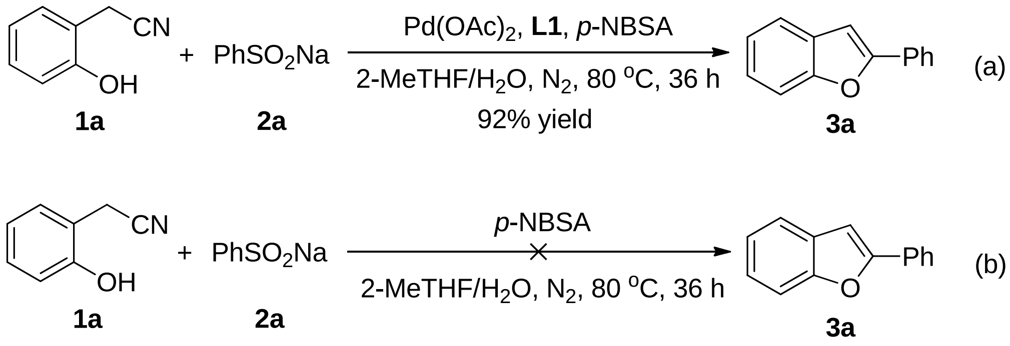
Scheme S1

Under N_2 atmosphere, a Schlenk tube was charged with **1a** (0.3 mmol), (4-(trifluoromethyl)phenyl)boronic acid (0.6 mmol), $Pd(OAc)_2$ (10 mol %), **L1** (20 mol %), *p*-NBSA (10 equiv), 2-MeTHF (2 mL), and H_2O (1 mL) at room temperature. The reaction mixture was stirred vigorously at 80 °C for 36 h. Trace target product **3i** was detected by GC/MS analysis.



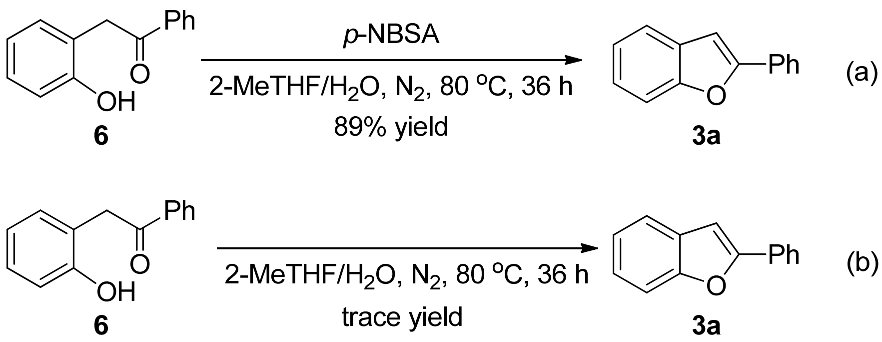
Scheme S2

Under N_2 atmosphere, a Schlenk tube was charged with **4** (0.3 mmol), **2a** (0.6 mmol), $Pd(OAc)_2$ (10 mol %), **L1** (20 mol %), *p*-NBSA (10 equiv), 2-MeTHF (2 mL), and H_2O (1 mL) at room temperature. The reaction mixture was stirred vigorously at 80 °C for 36 h. The mixture was poured into ethyl acetate, which was washed with saturated $NaHCO_3$ (2 × 10 mL) and then brine (1 × 10 mL). After the aqueous layer was extracted with ethyl acetate, the combined organic layers were dried over anhydrous Na_2SO_4 and evaporated under a vacuum. The residue was purified by flash column chromatography (hexane/ethyl acetate as eluent) to afford the desired products **5** (89% yield).



Scheme S3

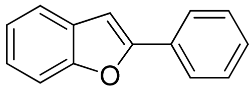
Under N_2 atmosphere, a Schlenk tube was charged with **1a** (0.3 mmol), **2a** (0.6 mmol), *p*-NBSA (10 equiv), 2-MeTHF (2 mL), and H_2O (1 mL) at room temperature. The reaction mixture was stirred vigorously at 80 °C for 36 h. No target product **3a** was detected by GC/MS analysis.



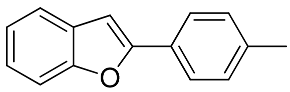
Scheme S4

Under N_2 atmosphere, a Schlenk tube was charged with **6** (0.3 mmol), *p*-NBSA (10 equiv), 2-MeTHF (2 mL), and H_2O (1 mL) at room temperature. The reaction mixture was stirred vigorously at 80 °C for 36 h. The mixture was poured into ethyl acetate, which was washed with saturated $NaHCO_3$ (2 × 10 mL) and then brine (1 × 10 mL). After the aqueous layer was extracted with ethyl acetate, the combined organic layers were dried over anhydrous Na_2SO_4 and evaporated under a vacuum. The residue was purified by flash column chromatography (hexane/ethyl acetate as eluent) to afford the desired products **3a** (89% yield). However, trace yield of desired product **3a** was observed by GC/MS analysis in the absence of *p*-NBSA.

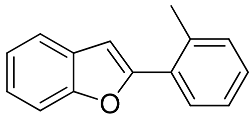
4. Analytical data for all products



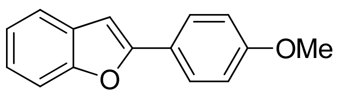
*2-Phenylbenzofuran (**3a**)*: White solid, mp 120−121 °C (Lit.[1] 121.6−122.2 °C); ^{1}H NMR($CDCl_3$, 500 MHz) δ 7.86 (d, *J* = 7.5Hz, 2H), 7.57 (d, *J*=7.6Hz, 1H), 7.52 (d, *J* = 8.1 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 1H), 7.29-7.27 (m, 1H), 7.24-7.21 (m, 1H), 7.01(s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.0, 155.0, 130.6, 129.3, 128.9, 128.6, 125.0, 124.4, 123.0, 121.0, 111.3, 101.4.



*2-p-Tolylbenzofuran (**3b**)*: White solid, mp 126−127 °C (Lit.[2] 126−128 °C); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.28-7.19 (m, 4H), 6.95 (s, 1H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.3, 154.8, 138.6, 129.5, 129.4, 127.8, 124.9, 124.0, 122.9, 120.8, 111.1, 100.6, 21.4.



*2-o-Tolylbenzofuran (**3c**)*: Oil,[3] ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.86 (d, *J* = 6.8 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 8.1 Hz, 1H), 7.31-7.22 (m, 5H), 6.89 (s, 1H), 2.58 (s, 3H); ^{13}C NMR ($CDCl_3$, 125MHz) δ 154.6, 153.3, 134.8, 130.2, 128.9, 128.1, 127.5, 127.1, 125.1, 123.2, 121.7, 119.9, 110.1, 104.1, 20.9.

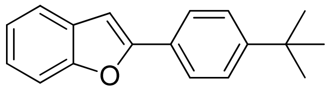


*2-(4-Methoxyphenyl)benzofuran (**3d**)*: White solid, mp 151−152 °C (Lit.[4] 148−150 °C); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.79 (d, *J* = 8.8 Hz, 2H), 7.54 (d, *J* = 7.1 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.24-7.19 (m, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 6.87 (s, 1H), 3.85 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 160.1, 156.1, 154.8, 129.6, 126.5, 123.8,

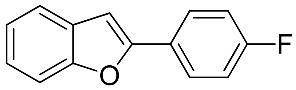
---

1 Ackermann, L.; Kaspar, L. T. *J. Org. Chem.* **2007**, *72*, 6149.
2 Kabalka, G. M.; Wang, L.; Pagni, R. M. *Tetrahedron* **2001**, *57*, 8017.
3 Astoin, J.; Demerseman, P.; Riveron, A.; Royer, R. *J. Heterocycl. Chem.* **1977**, *14*, 867.
4 Jaseer, E. A.; Prasad, D. J. C.; Sekar, G. *Tetrahedron* **2010**, 66, 2077.

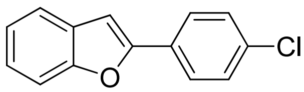
123.4, 122.9, 120.6, 114.3, 111.0, 99.7, 55.4.



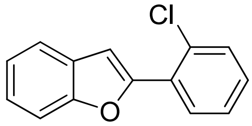
*2-(4-tert-Butylphenyl)benzofuran (**3e**)*: White solid, mp 131−132 °C (Lit.[5] 132 °C); ^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.82 (d, *J* = 8.5 Hz, 2H), 7.59 (d, *J* = 7.4 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.24 (t, *J* = 7.1 Hz, 1H), 6.99 (s, 1H), 1.38 (s, 9H); ^{13}C NMR (CDCl$_3$, 125 MHz) δ 156.0, 154.7, 151.6, 129.2, 127.6, 125.6, 124.6, 123.8, 122.7, 120.6, 110.9, 100.5, 34.6, 31.1.



*2-(4-Fluorophenyl)benzofuran (**3f**)*: White solid, mp 123−124 °C (Lit.[6] 122−124 °C); ^{1}H NMR (CDCl$_3$, 500 MHz): δ 7.86-7.83 (m, 2H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.52 (d, *J* = 8.1 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 1H), 7.24 (t, *J* = 7.4 Hz, 1H), 7.15 (t, *J* = 8.7 Hz, 2H), 6.96 (s, 1H); ^{13}C NMR (CDCl$_3$, 125 MHz) δ 163.7, 161.7, 154.9, 154.7, 129.0, 126.7, 126.6, 126.6, 124.1, 122.9, 120.7, 115.8, 115.6, 111.0, 100.84, 100.83.



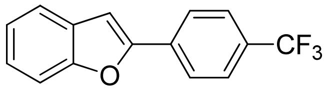
*2-(4-Chlorophenyl)benzofuran (**3g**)*: White solid; mp 147−148 °C (Lit.[7] 148−149 °C); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 7.79 (d, *J* = 8.6 Hz, 2H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.52 (d, *J* = 8.2 Hz, 1H), 7.42 (d, *J* = 8.6 Hz, 2H), 7.31 (t, *J* = 7.7 Hz, 1H), 7.25 (t, *J* = 7.4 Hz, 1H), 7.01 (s, 1H); ^{13}C NMR (CDCl$_3$, 125 MHz) δ 154.7, 154.6, 134.2, 128.9, 128.9, 128.8, 126.0, 124.4, 122.9, 120.8, 111.0, 101.6.



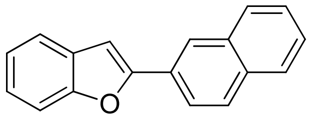
*2-(2-Chlorophenyl)benzofuran (**3h**)*: White solid; mp 46-47 °C (Lit.[8] 45−46 °C); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 8.06 (d, *J* = 7.9 Hz, 1H), 7.64 (d, *J* = 7.7 Hz, 1H), 7.54-7.49 (m, 3H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.34-7.30 (m, 2H), 7.29-7.27 (m, 1H); ^{13}C

[5] Astoin, J.; Demerseman, P.; Riveron, A.; Royer, R. *J. Heterocycl. Chem.* **1977**, *14*, 867.
[6] Chittimalla, S. K.; Chang, T.-C.; Liu, T.-C.; Hsieh, H.-P.; Liao, C.-C. *Tetrahedron* **2008**, *64*, 2586.
[7] Ghosh, S.; Das, J. *Tetrahedron Lett.* **2011**, *52*, 1112.
[8] Carril, M.; Martin, R. S.; Tellitu, I.; Domínguez, E. *Org. Lett.* **2006**, *8*, 1467

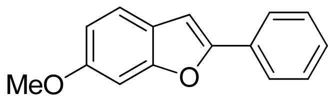
NMR ($CDCl_3$, 125 MHz) δ 154.2, 152.0, 149.2, 131.3, 130.9, 129.1, 129.0, 127.0, 124.9, 123.0, 121.5, 121.1, 111.1, 107.4.



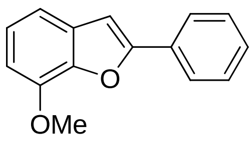
2-(4-(Trifluoromethyl)phenyl)benzofuran (**3i**): White solid; mp 159−161 °C (Lit.[9] 162−163 °C); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.94 (d, J = 8.2 Hz, 2H), 7.68 (d, J = 8.3 Hz, 2H), 7.60 (d, J = 7.7 Hz, 1H), 7.53 (d, J = 8.2 Hz, 1H), 7.32 (t, J = 7.2 Hz, 1H), 7.25-7.24 (m, 1H), 7.11 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 155.1, 154.1, 133.6, 129.9, 128.8, 125.8, 125.7, 125.7, 125.6, 125.1, 125.0, 124.9, 123.2, 121.2, 111.3, 103.2.



2-(Naphthalen-2-yl)benzofuran (**3j**): White solid, mp 162−163 °C (Lit.[10] 163 °C); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.37 (s, 1H), 7.94-7.87 (m, 3H), 7.83 (d, J = 8.8 Hz, 1H), 7.61 (d, J = 7.6 Hz, 1H), 7.56 (d, J = 8.1 Hz, 1H), 7.53-7.47 (m, 2H), 7.30 (t, J = 7.7 Hz, 1H), 7.24-7.23 (m, 1H), 7.13 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 155.8, 154.9, 133.3, 133.1, 128.3, 128.3, 127.6, 126.5, 126.3, 124.2, 123.7, 122.8, 122.6, 120.8, 111.0, 101.8.

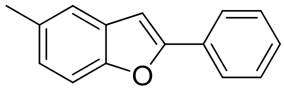


6-Methoxy-2-phenylbenzofuran (**3k**): White solid, mp 80−81 °C (Lit.[11] 79−81 °C); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.82 (d, J = 8.0 Hz, 2H), 7.44 (t, J = 8.5 Hz, 3H), 7.33 (t, J = 7.4 Hz, 1H), 7.08 (s, 1H), 6.96 (s, 1H), 6.87-6.90 (m, 1H), 3.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 158.1, 155.9, 155.2, 130.7, 128.8, 128.1, 124.5, 122.6, 120.9, 111.9, 101.2, 95.9, 55.8.

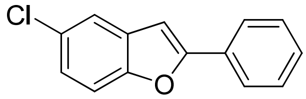


[9] Denmark, S. E.; Smith, R. C.; Chang, W.-T. T.; Muhuhi, J. M. *J. Am. Chem. Soc.* **2009**, *131*, 3104.
[10] Astoin, J.; Demerseman, P.; Riveron, A.; Royer, R. *J. Heterocycl. Chem.* **1977**, *14*, 867.
[11] Wang, X.; Liu, M.; Xu, L.; Wang, Q.; Chen, J.; Ding, J.; Wu, H. *J. Org. Chem.* **2013**, *78*, 5273.

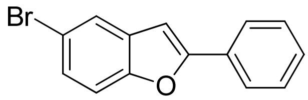
*7-Methoxy-2-phenylbenzofuran (**3l**)*: White solid, mp 80−81 °C (Lit.[12] 79−80 °C); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.91 (d, *J* = 8.2 Hz, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 1H), 7.21-7.15 (m, 2H), 7.03 (s, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 4.06 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 155.1, 144.4, 143.2, 130.0, 129.4, 127.7, 127.6, 124.1, 122.6, 112.4, 105.7, 100.7, 55.2.



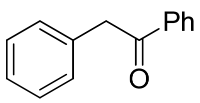
*5-Methyl-2-phenylbenzofuran (**3m**)*: White solid, mp 129−130 °C (Lit.[13] 128−129 °C); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.87 (d, *J* = 7.3 Hz, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 1H), 7.38-7.34 (m, 2H), 7.11 (d, *J* = 8.3 Hz, 1H), 6.96 (s, 1H), 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 156.3, 153.6, 132.6, 130.9, 129.6, 129.0, 128.7, 125.8, 125.1, 121.0, 110.9, 101.4, 21.6.



*5-Chloro-2-phenylbenzofuran (**3n**)*: White solid, mp 152−153 °C (Lit.[14] 154 °C); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.85 (d, *J* = 7.6 Hz, 2H), 7.55 (s, 1H), 7.48-7.43 (m, 3H), 7.38 (t, *J* = 7.4 Hz, 1H), 7.24 (d, *J* = 8.7 Hz, 1H), 6.96 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 157.2, 153.1, 130.4, 129.8, 128.8, 128.7, 128.3, 124.9, 124.2, 120.2, 111.9, 100.6.



*5-Bromo-2-phenylbenzofuran (**3o**)*: White solid, mp 159−160 °C (Lit.[15] 158−159 °C); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.85 (d, *J* = 7.3 Hz, 2H), 7.71 (s, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.41-7.36 (m, 3H), 6.96 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 157.0, 153.4, 131.0, 129.7, 128.8, 128.7, 126.9, 124.9, 123.3, 115.8, 112.4, 100.4.



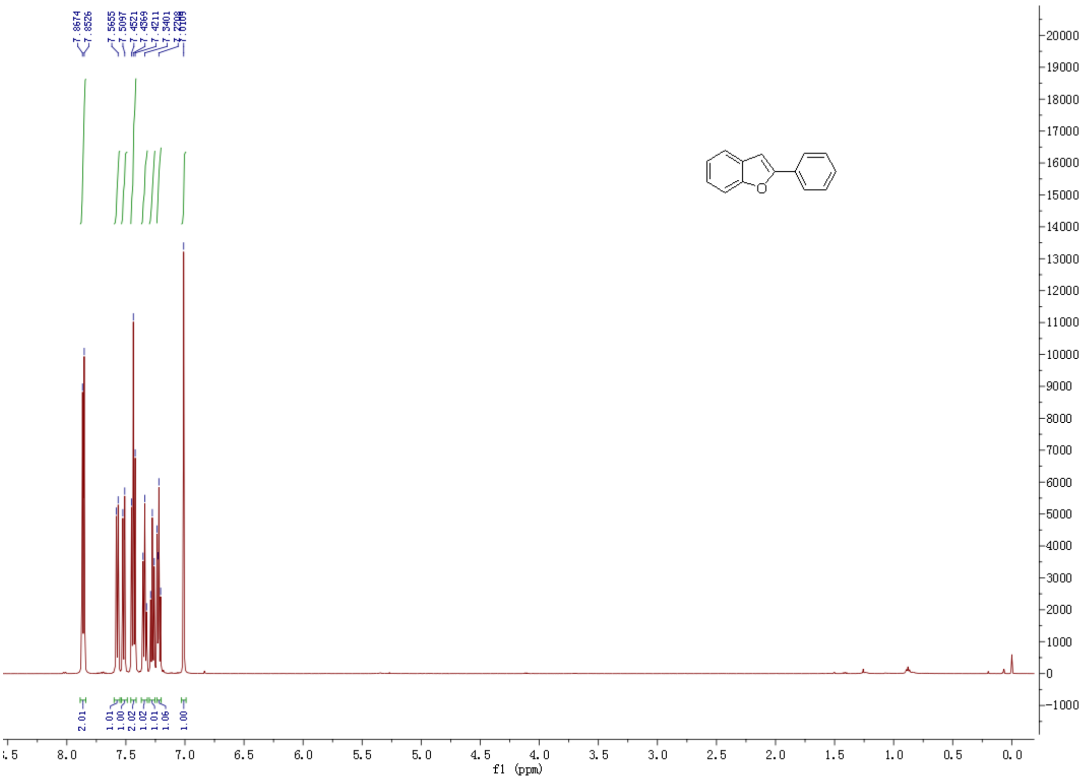
---

[12] Duan, X.-F.; Zeng, J.; Zhang, Z.-B.; Zi, G.-F. *J. Org. Chem.* **2007**, *72*, 10283.
[13] Duan, X.-F.; Zeng, J.; Zhang, Z.-B.; Zi, G.-F. *J. Org. Chem.* **2007**, *72*, 10283.
[14] Jaseer, E. A.; Prasad, D. J. C.; Sekar, G. *Tetrahedron* **2010**, 66, 2077.
[15] Takeda, N.; Miyata, O.; Naito, T. *Eur. J. Org. Chem.* **2007**, 1491.

1,2-Diphenylethanone (5). Yellow solid; mp 55-56 °C (Lit.[16] 59-60 °C); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.91 (d, *J* = 7.2 Hz, 2H), 7.44 (t, *J* = 7.7 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 2H), 7.22 (t, *J* = 7.4 Hz, 2H), 7.18-7.13 (m, 1H), 4.18 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 196.6, 135.6, 133.5, 132.1, 128.4, 127.62, 127.59, 127.56, 125.8, 44.4.

[16] Ye, C.; Twamley, B.; Shreeve, J. M. *Org. Lett.* **2005**, 7, 3961.

5. ^{1}H NMR and ^{13}C NMR spectra for all products



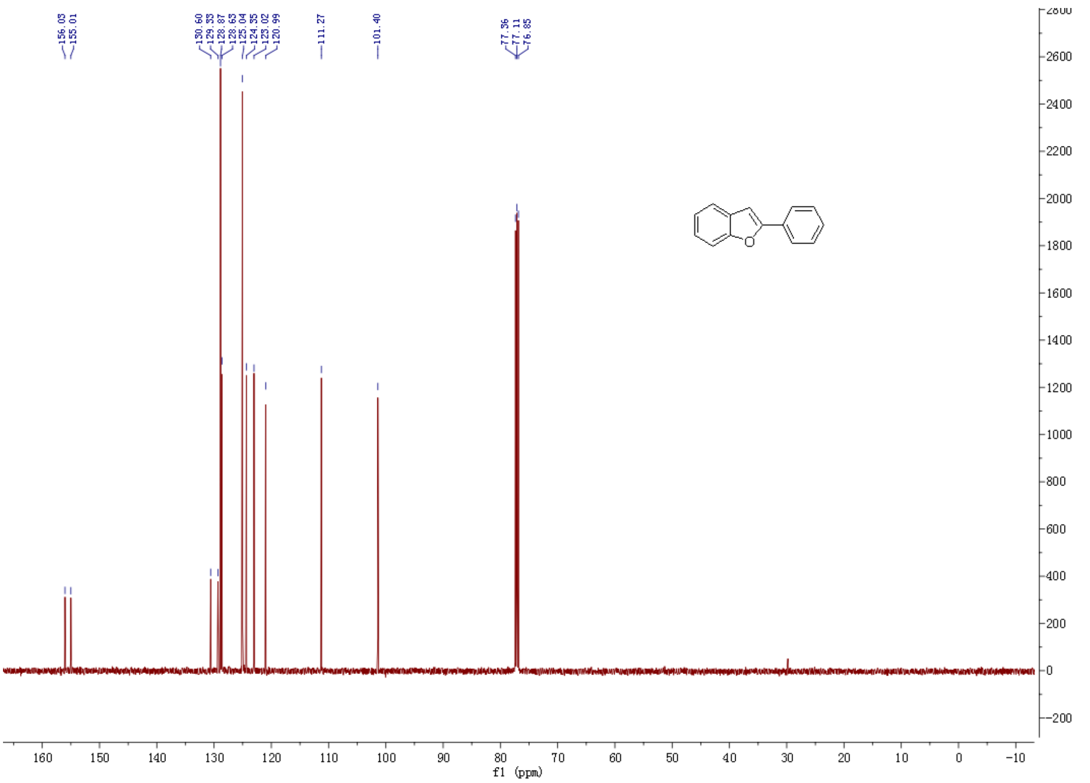
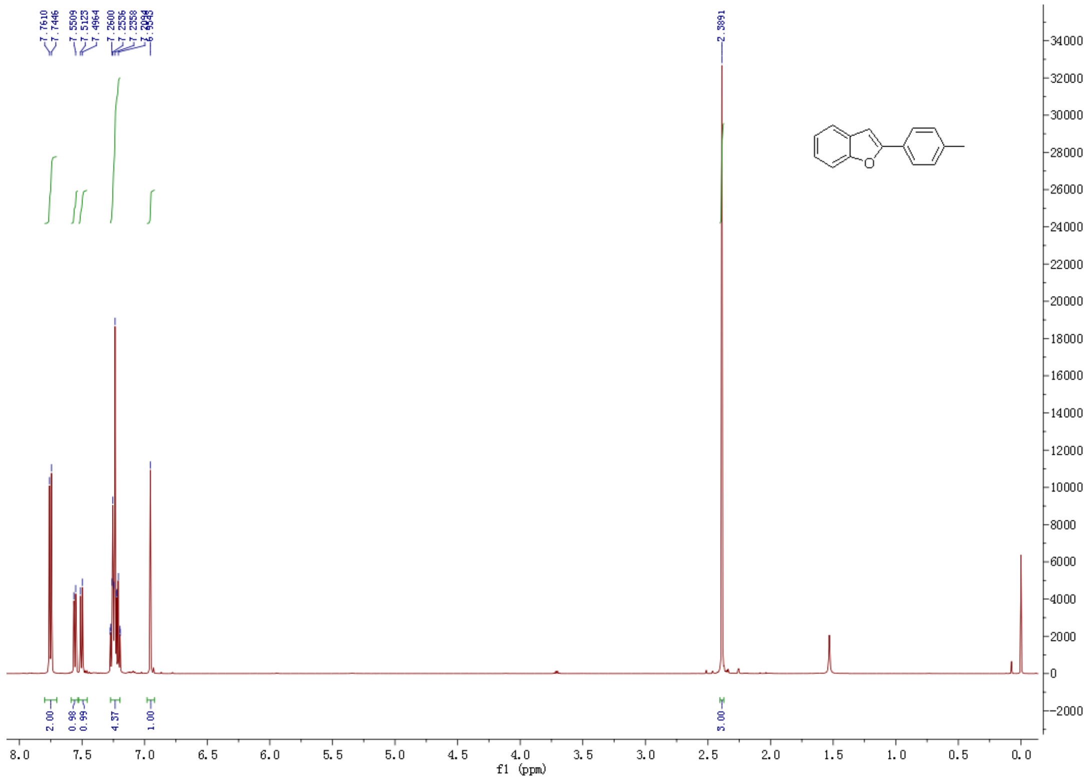


Figure S1. ^{1}H NMR of **3a** (500 MHz, $CDCl_3$) and ^{13}C NMR of **3a** (125 MHz, $CDCl_3$).



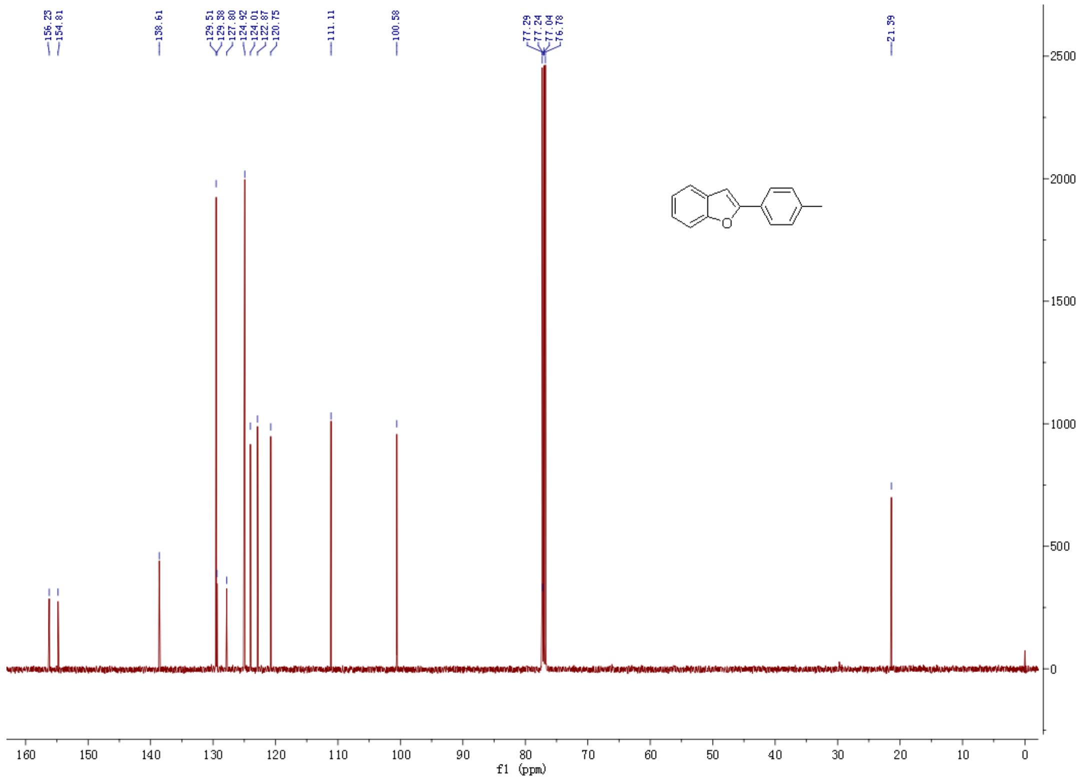
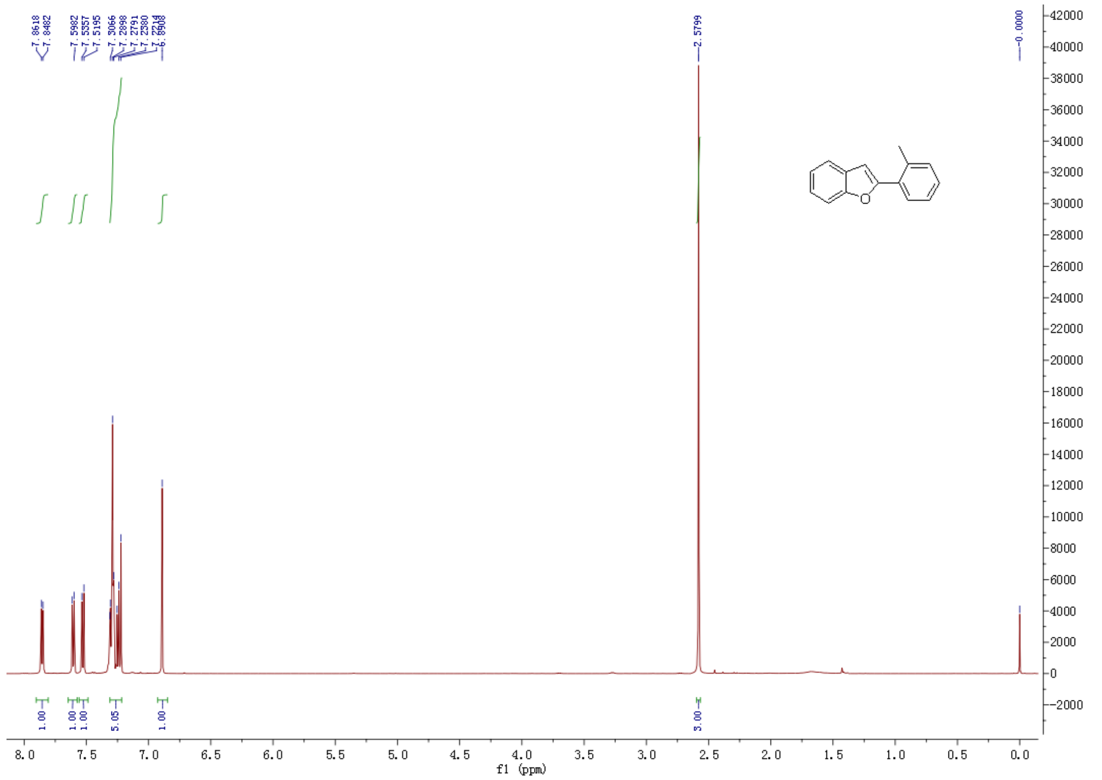


Figure S2. ^{1}H NMR of **3b** (500 MHz, $CDCl_3$) and ^{13}C NMR of **3b** (125 MHz, $CDCl_3$).



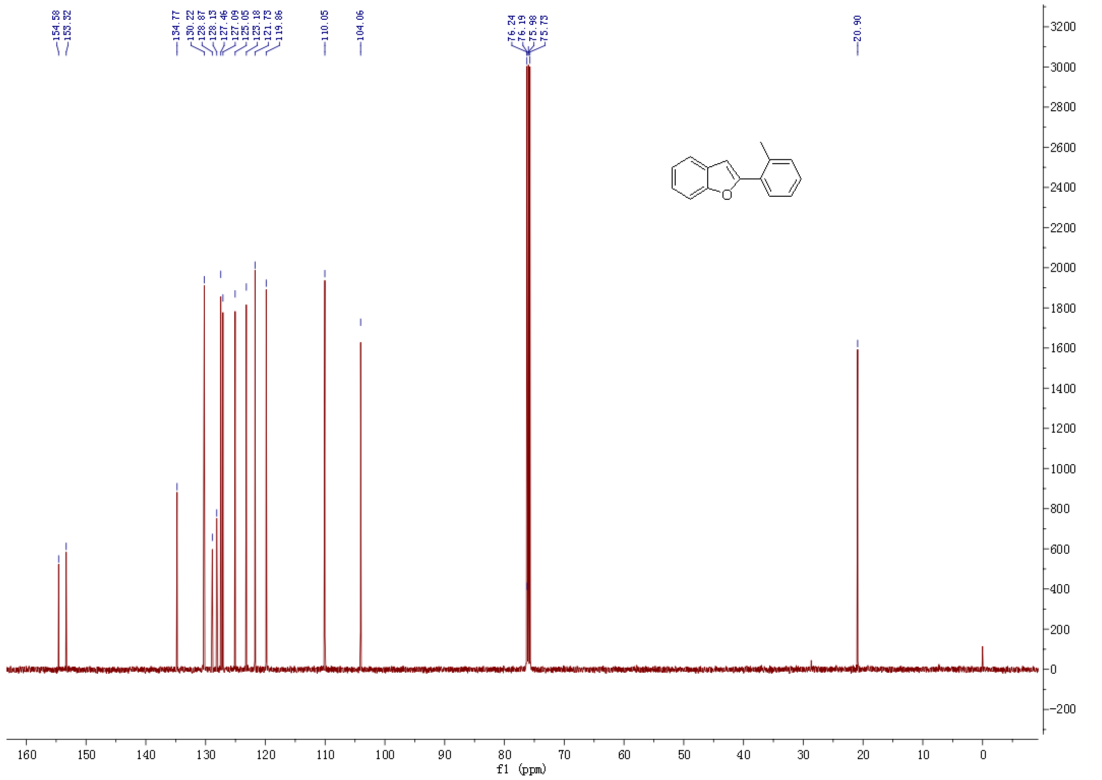
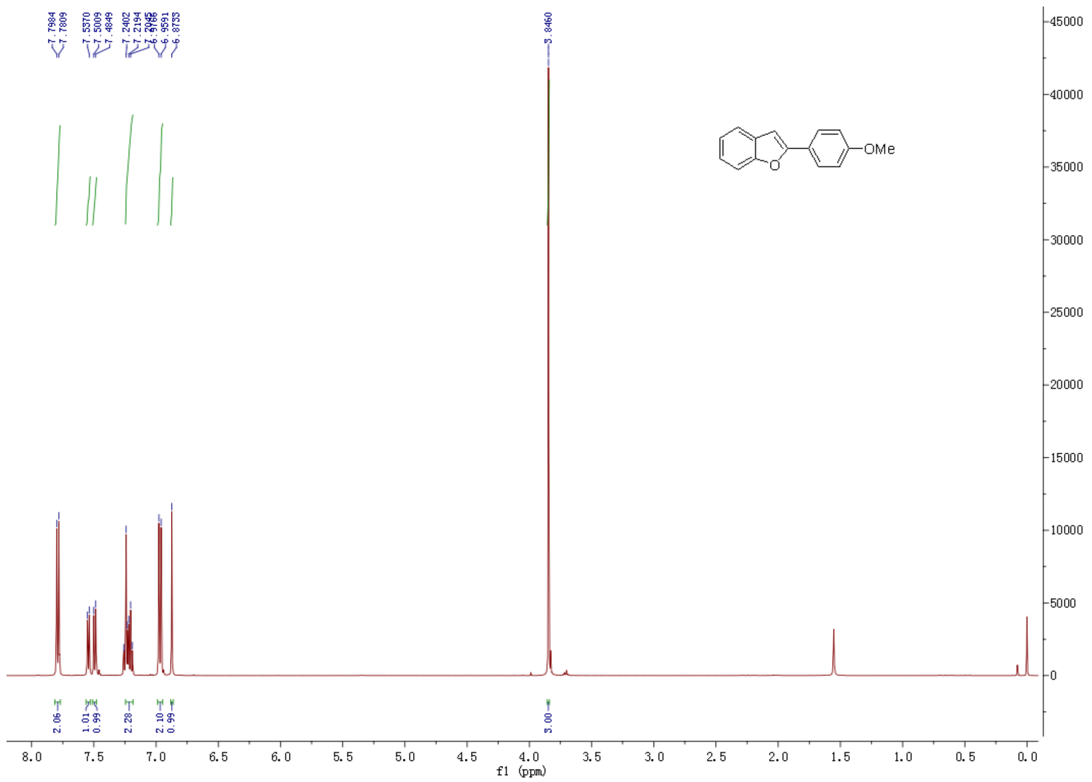


Figure S3. ¹H NMR of **3c** (500 MHz, $CDCl_3$) and ¹³C NMR of **3c** (125 MHz, $CDCl_3$).



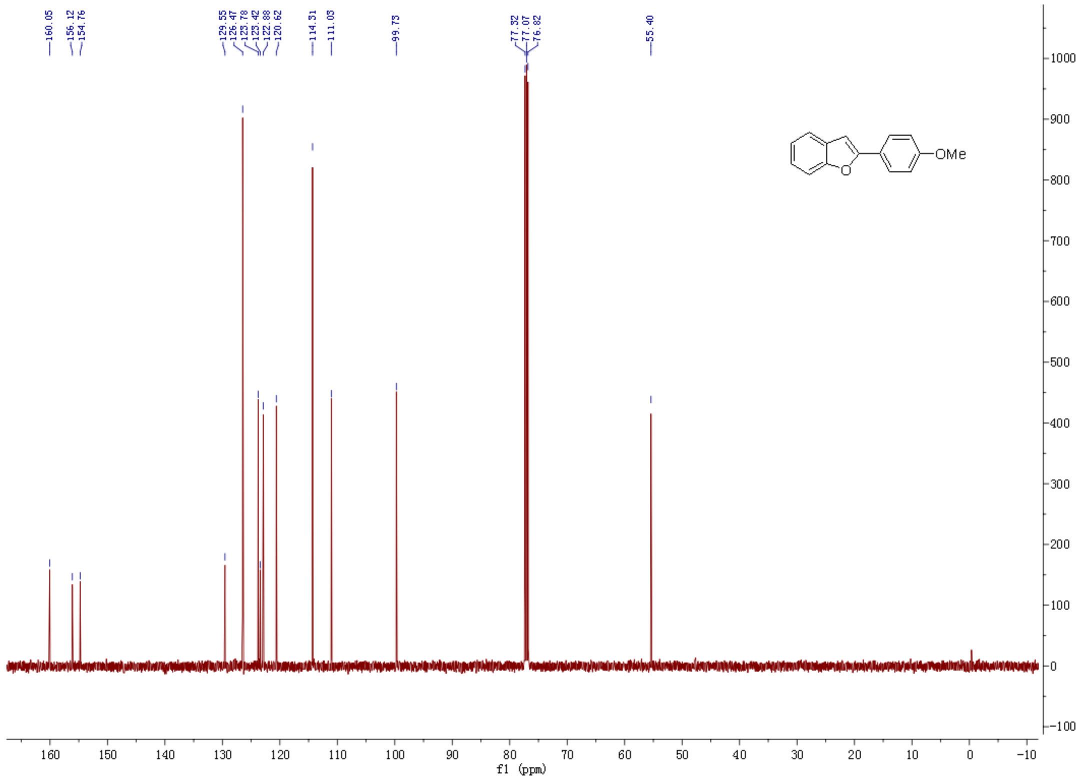
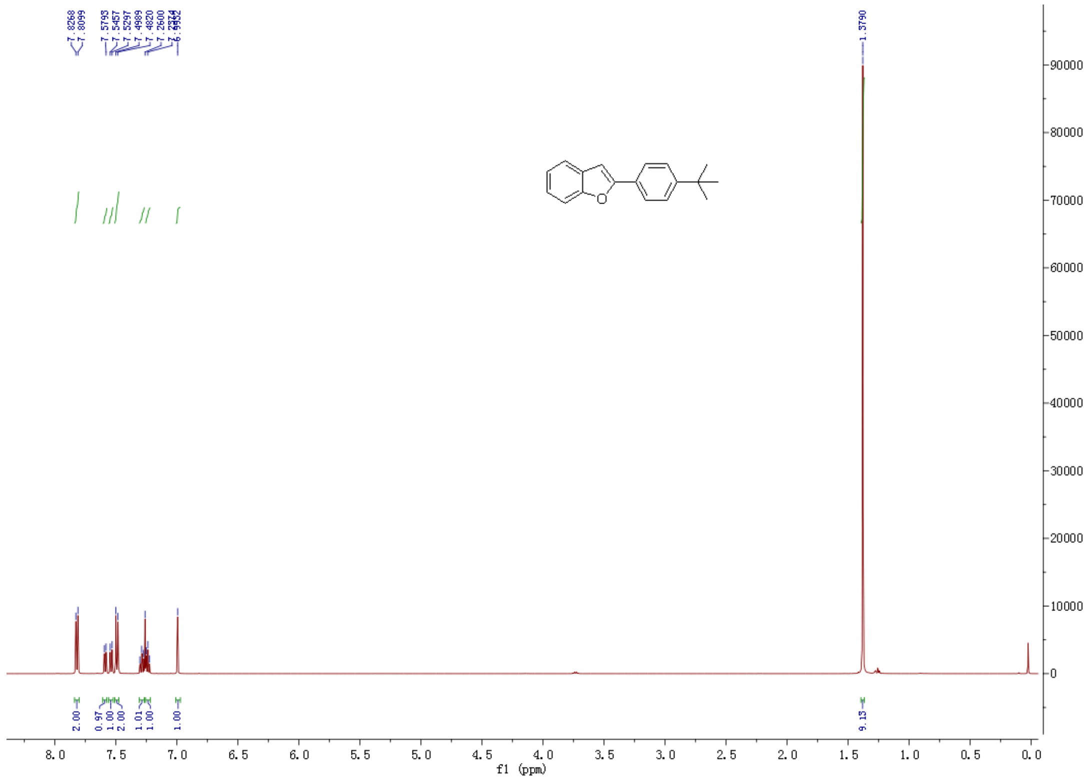


Figure S4. ^{1}H NMR of **3d** (500 MHz, $CDCl_3$) and ^{13}C NMR of **3d** (125 MHz, $CDCl_3$).



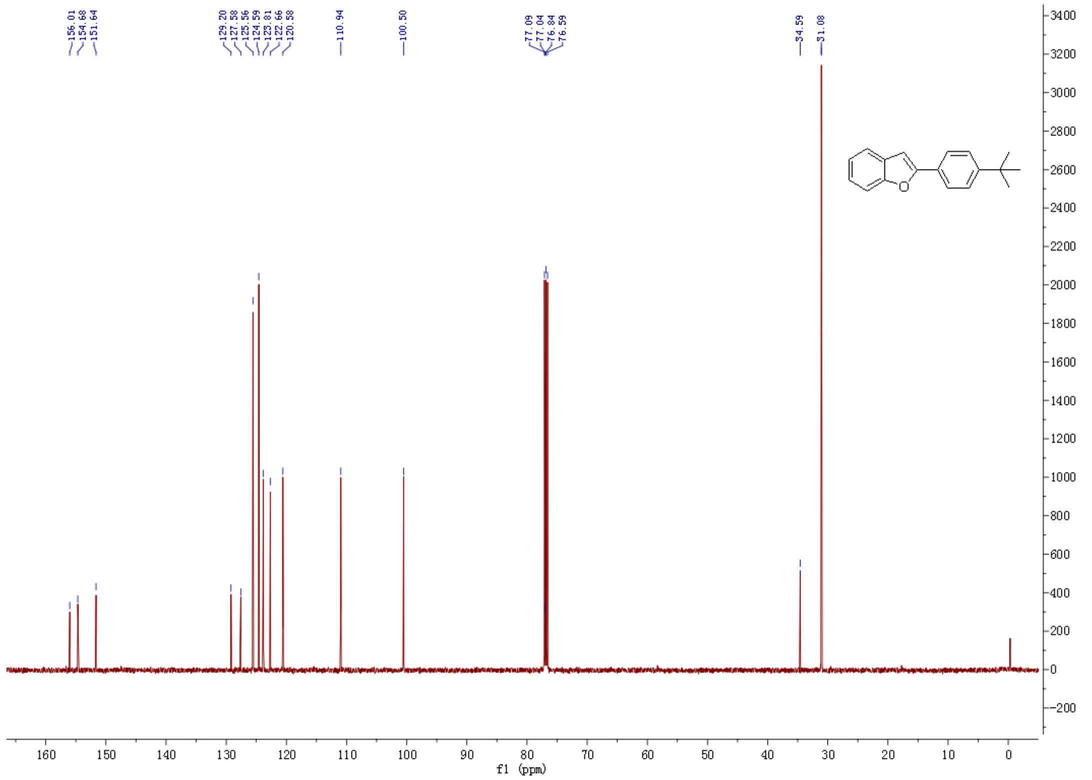
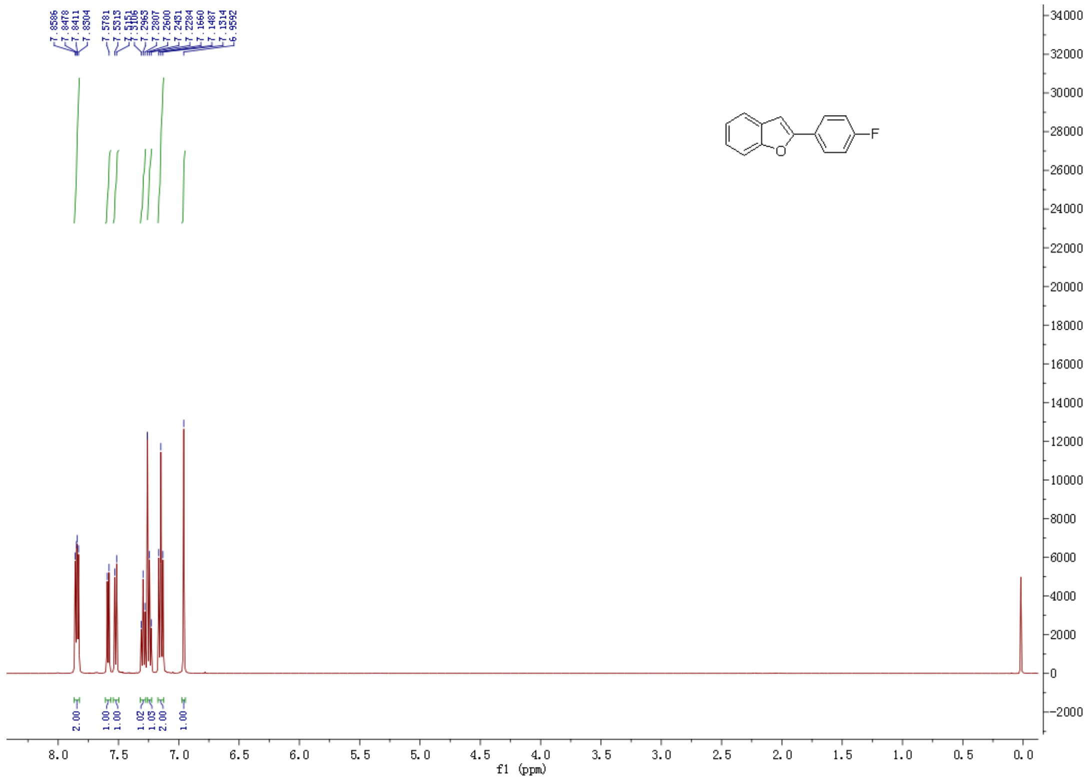


Figure S5. ^{1}H NMR of **3e** (500 MHz, $CDCl_3$) and ^{13}C NMR of **3e** (125 MHz, $CDCl_3$).



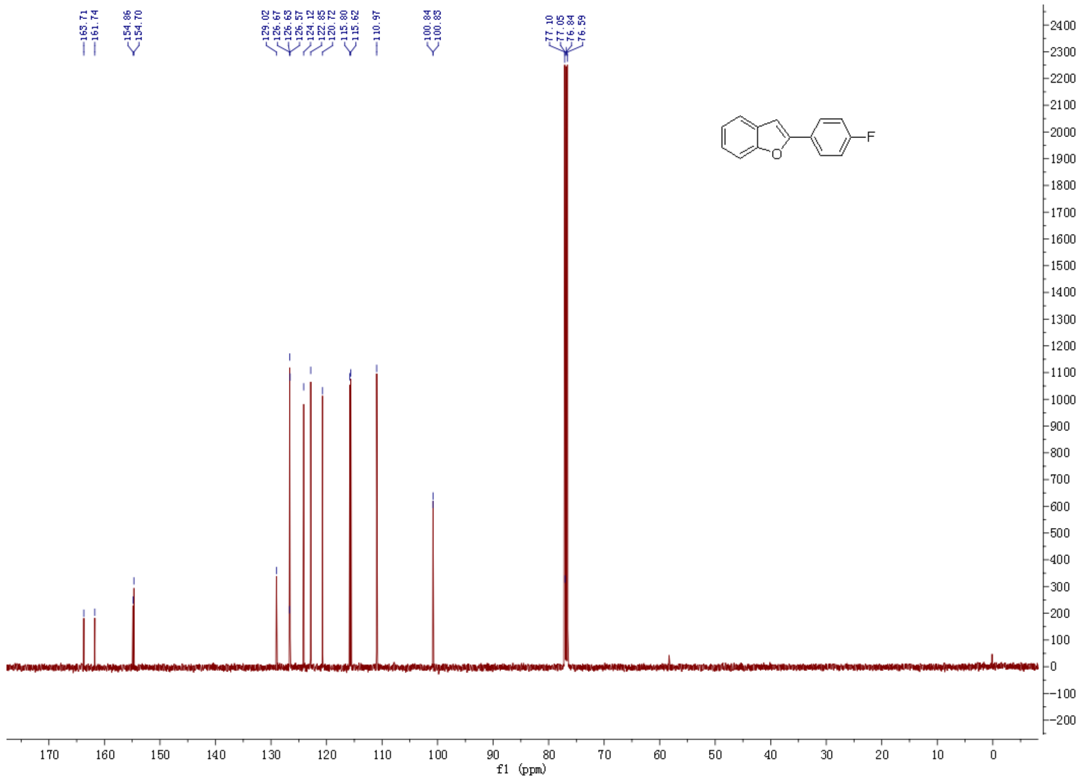
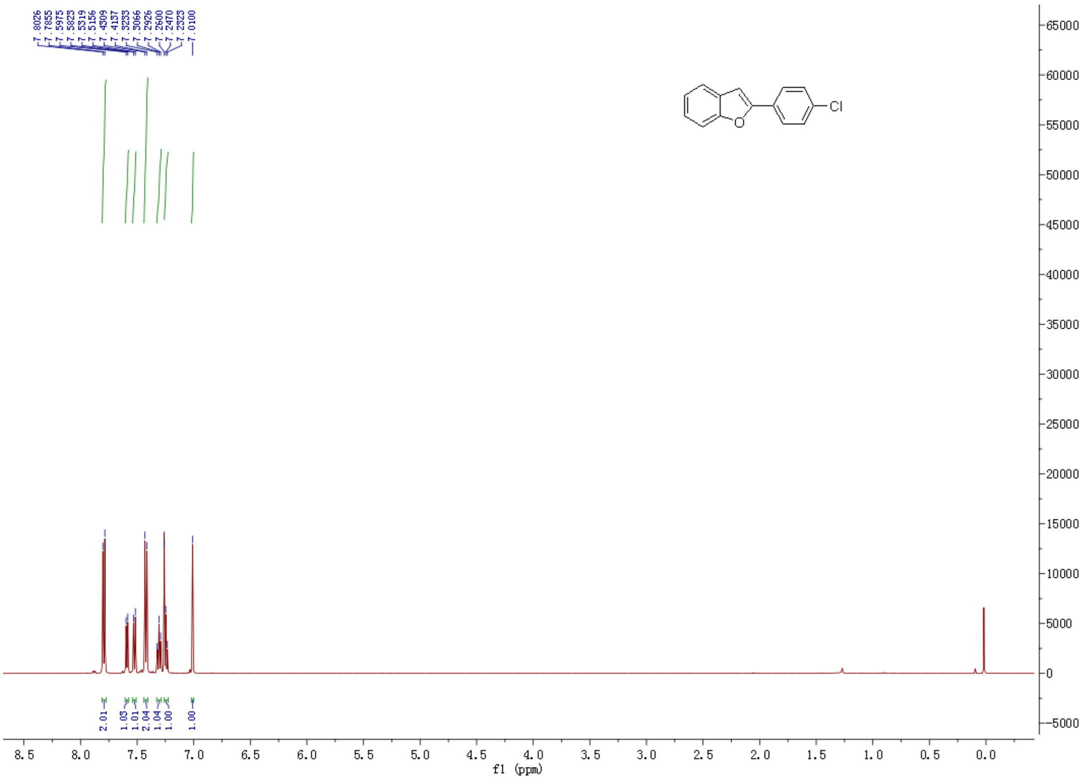


Figure S6. [1]H NMR of **3f** (500 MHz, $CDCl_3$) and [13]C NMR of **3f** (125 MHz, $CDCl_3$).



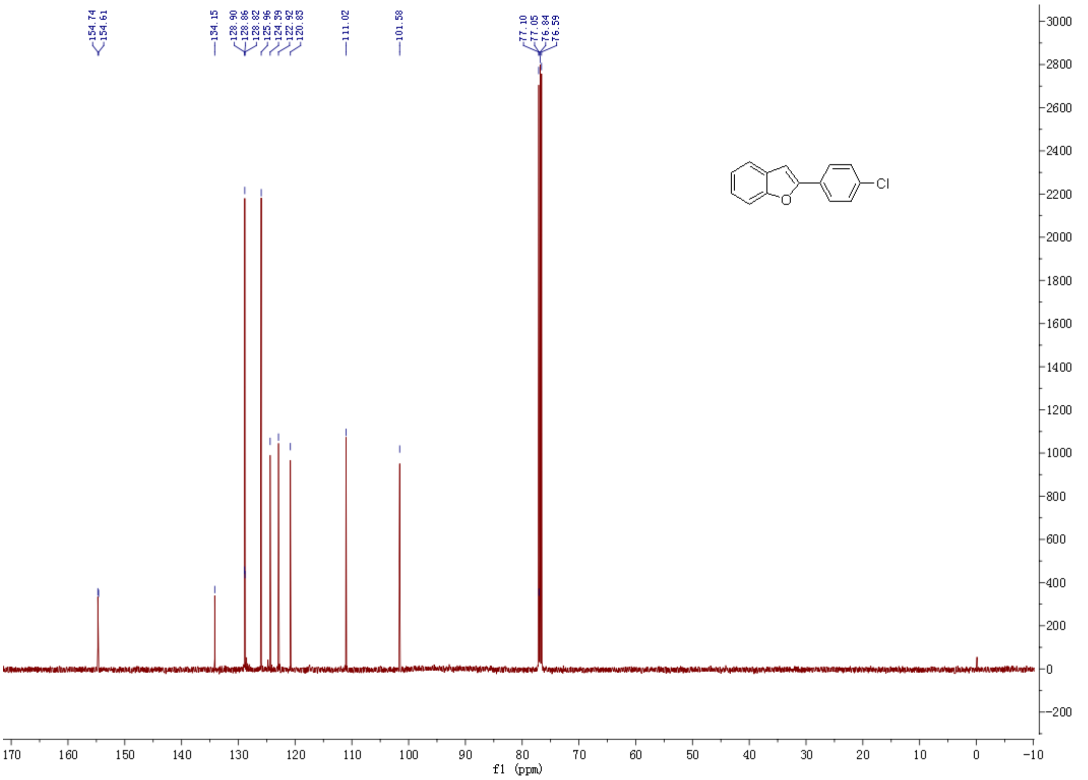
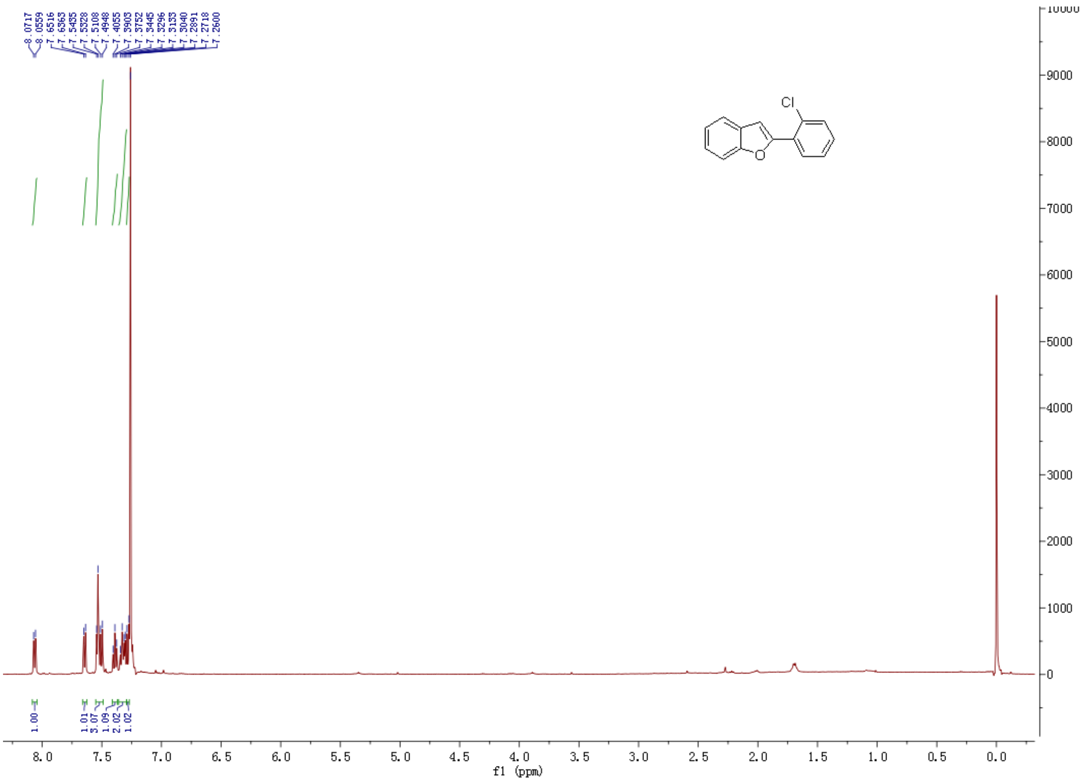


Figure S7. [1]H NMR of **3g** (500 MHz, $CDCl_3$) and [13]C NMR of **3g** (125 MHz, $CDCl_3$).



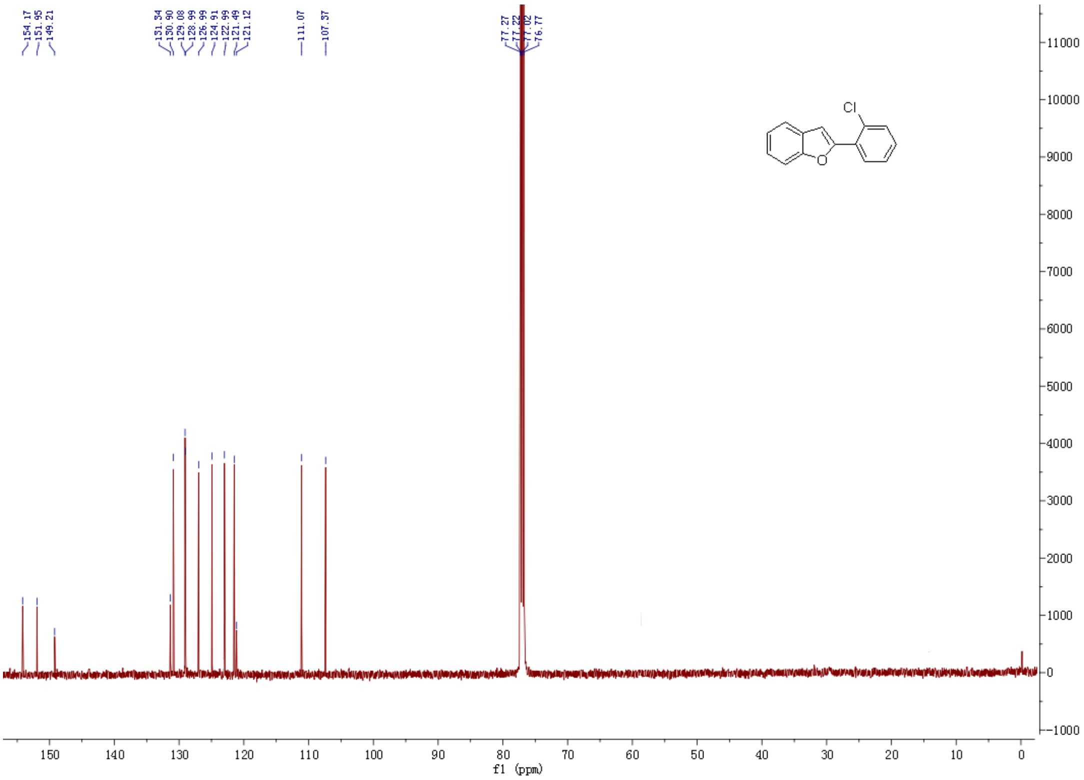
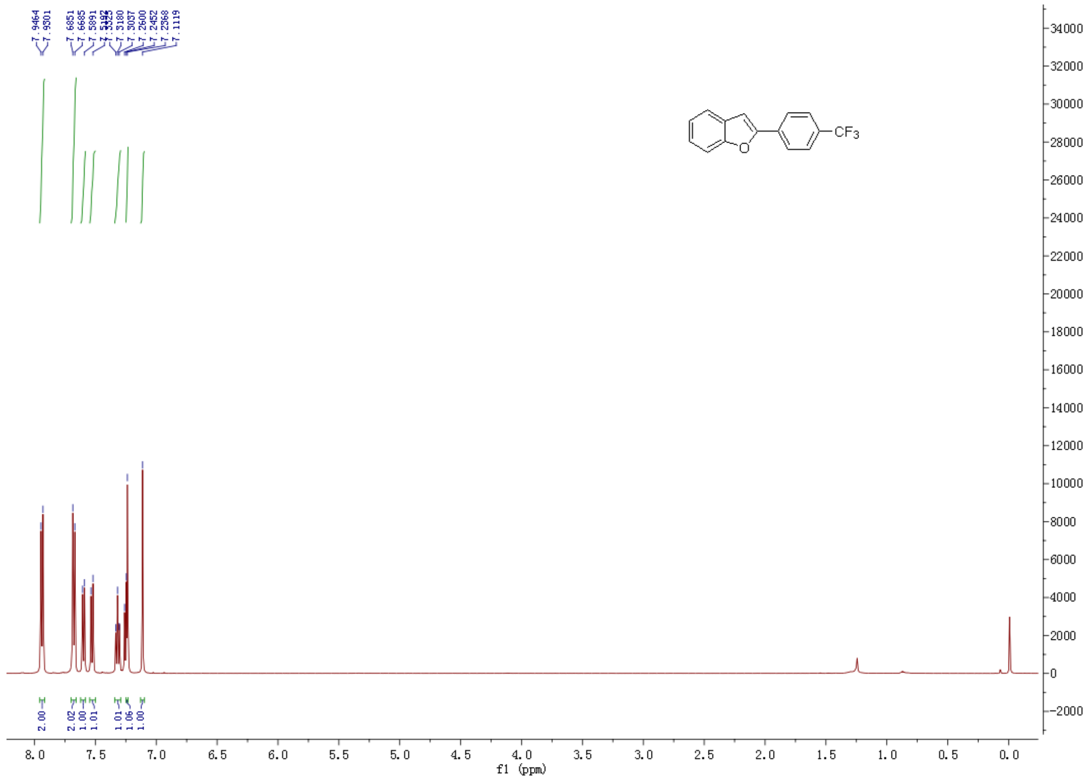


Figure S8. [1]H NMR of **3h** (500 MHz, $CDCl_3$) and [13]C NMR of **3h** (125 MHz, $CDCl_3$).



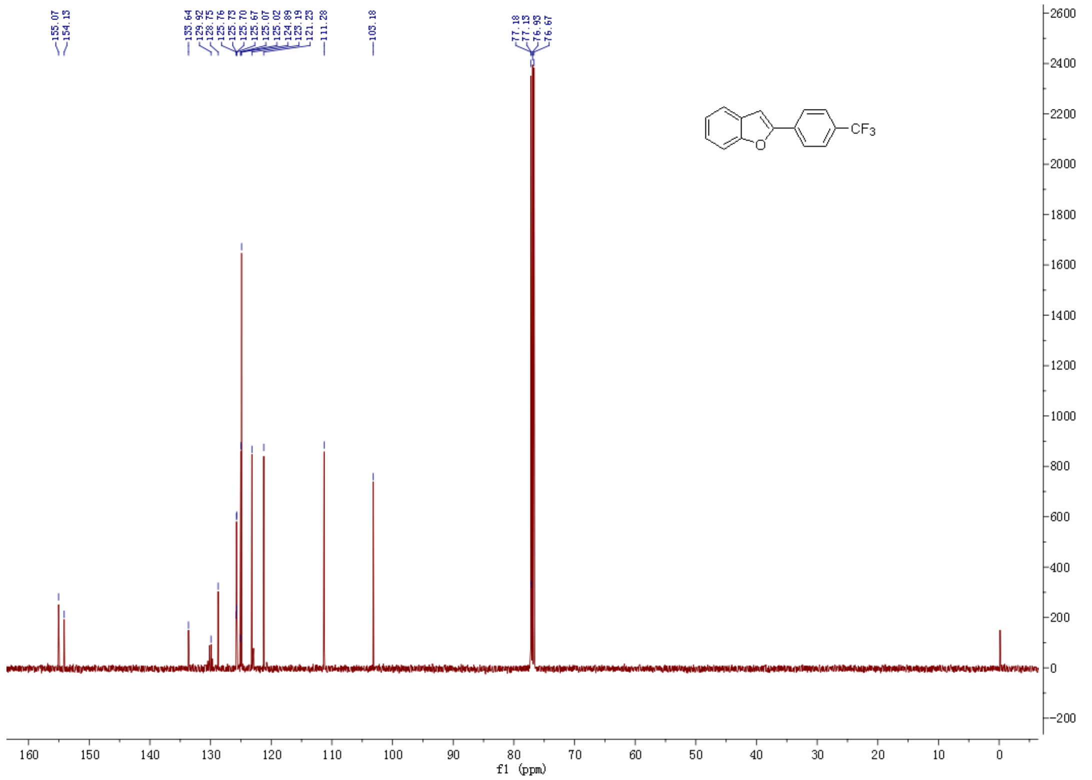
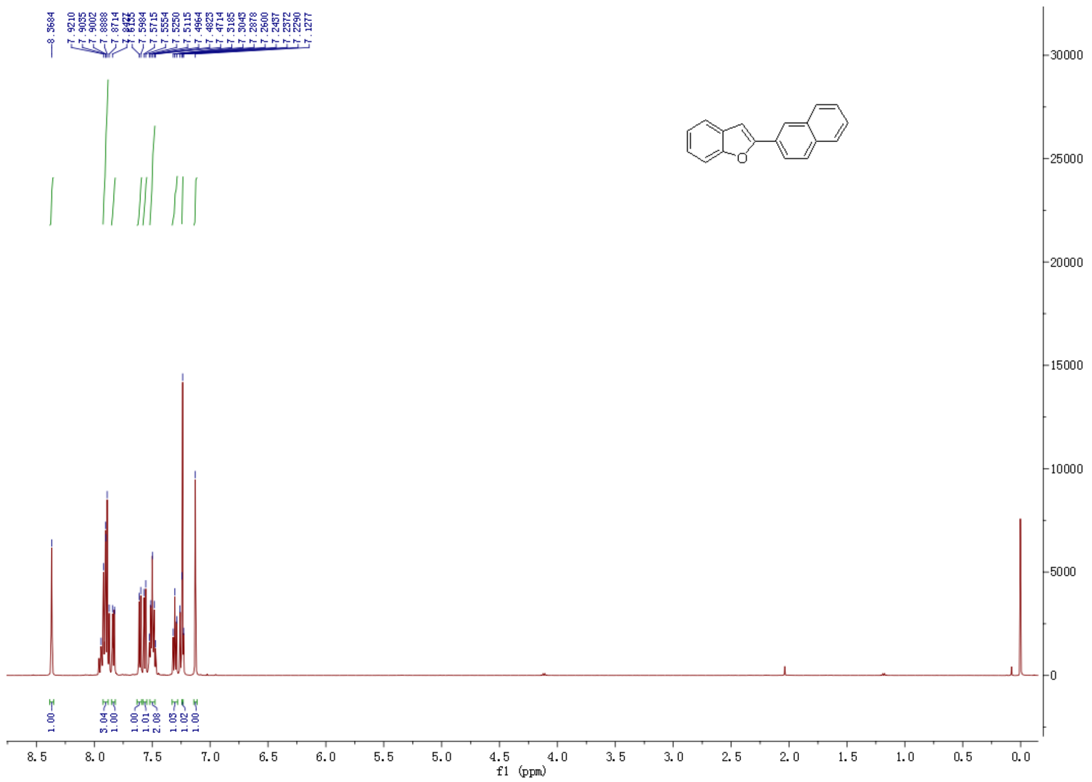


Figure S9. ^{1}H NMR of **3i** (500 MHz, $CDCl_3$) and ^{13}C NMR of **3i** (125 MHz, $CDCl_3$).



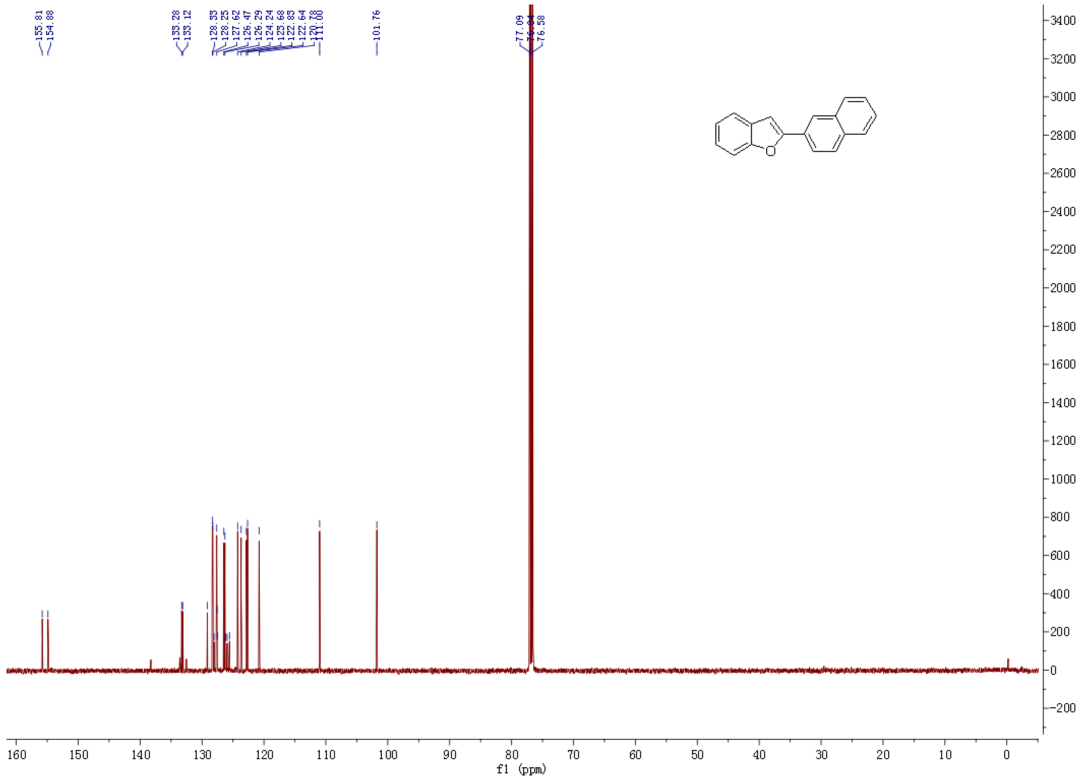
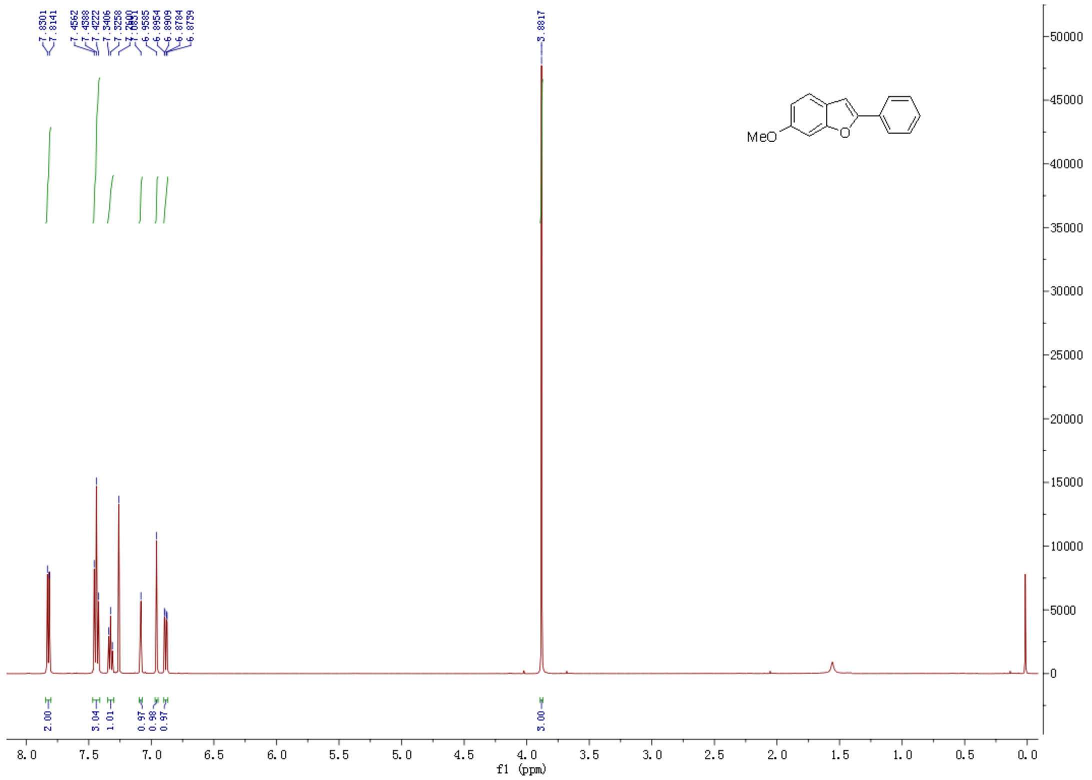


Figure S10. [1]H NMR of **3j** (500 MHz, $CDCl_3$) and [13]C NMR of **3j** (125 MHz, $CDCl_3$).



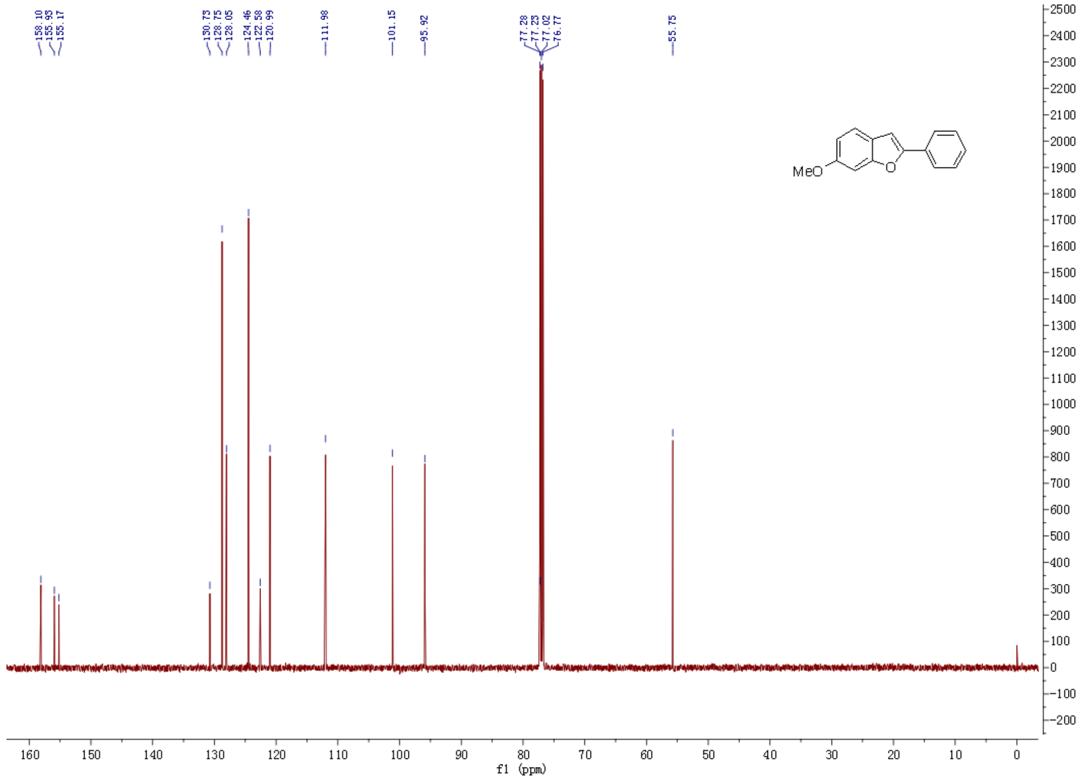
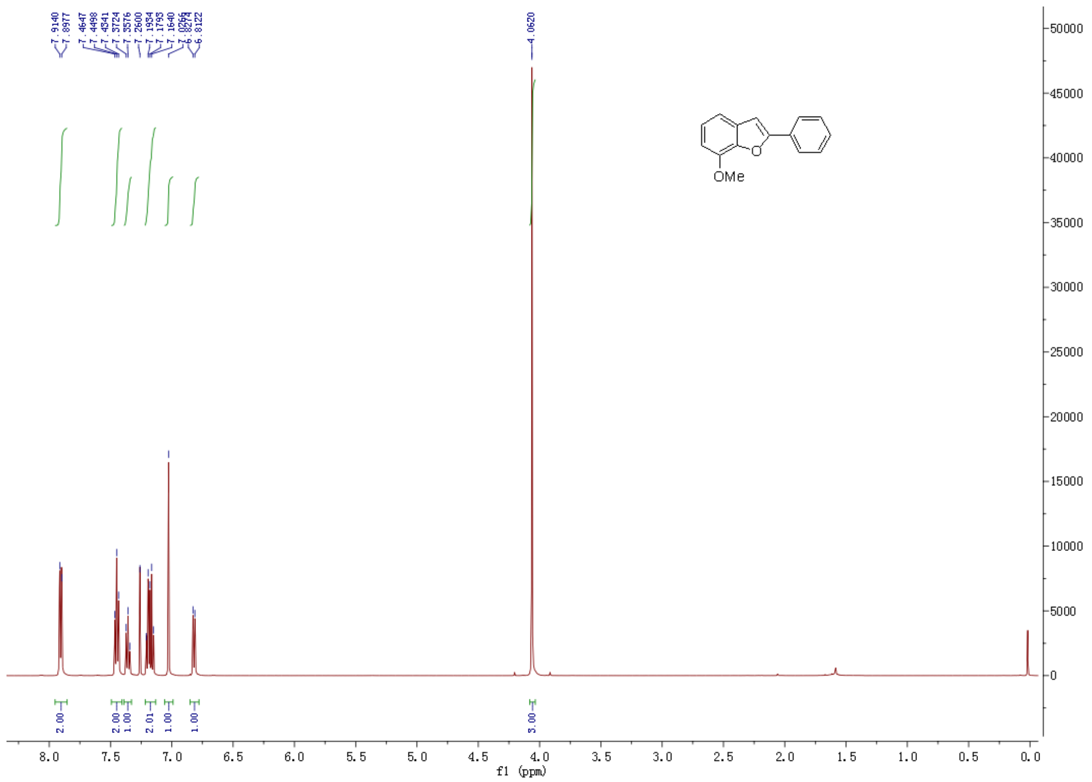


Figure S11. ^{1}H NMR of **3k** (500 MHz, $CDCl_3$) and ^{13}C NMR of **3k** (125 MHz, $CDCl_3$).



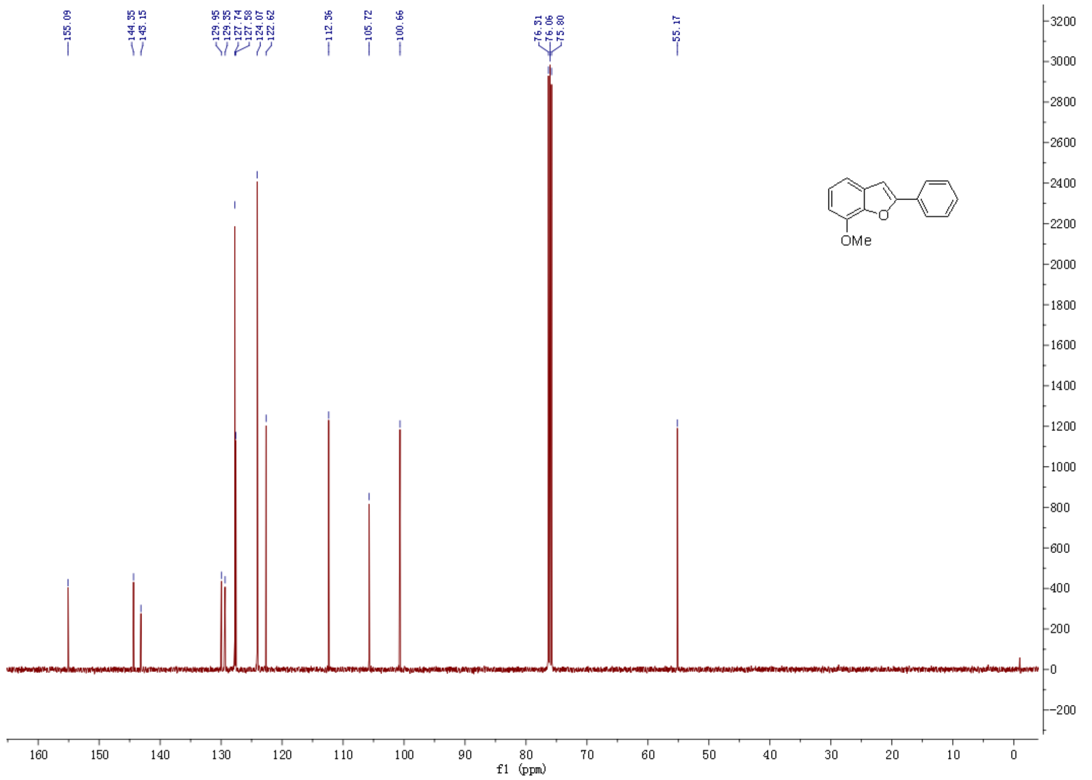
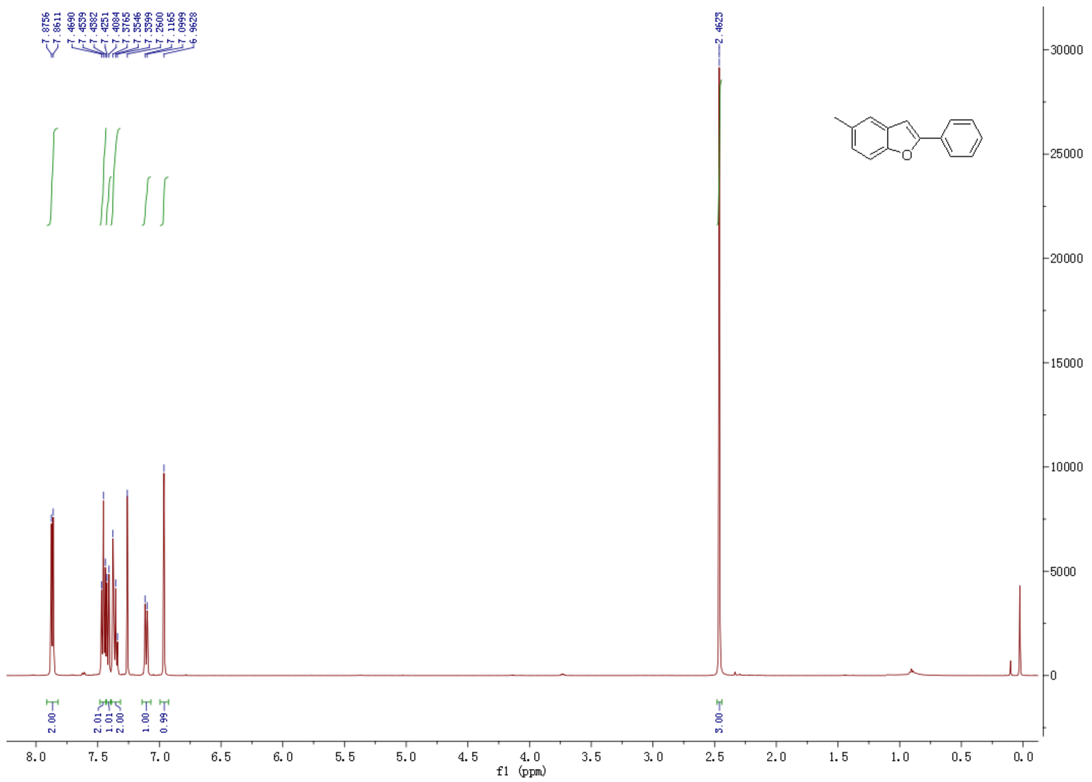


Figure S12. ^{1}H NMR of **3l** (500 MHz, $CDCl_3$) and ^{13}C NMR of **3l** (125 MHz, $CDCl_3$).



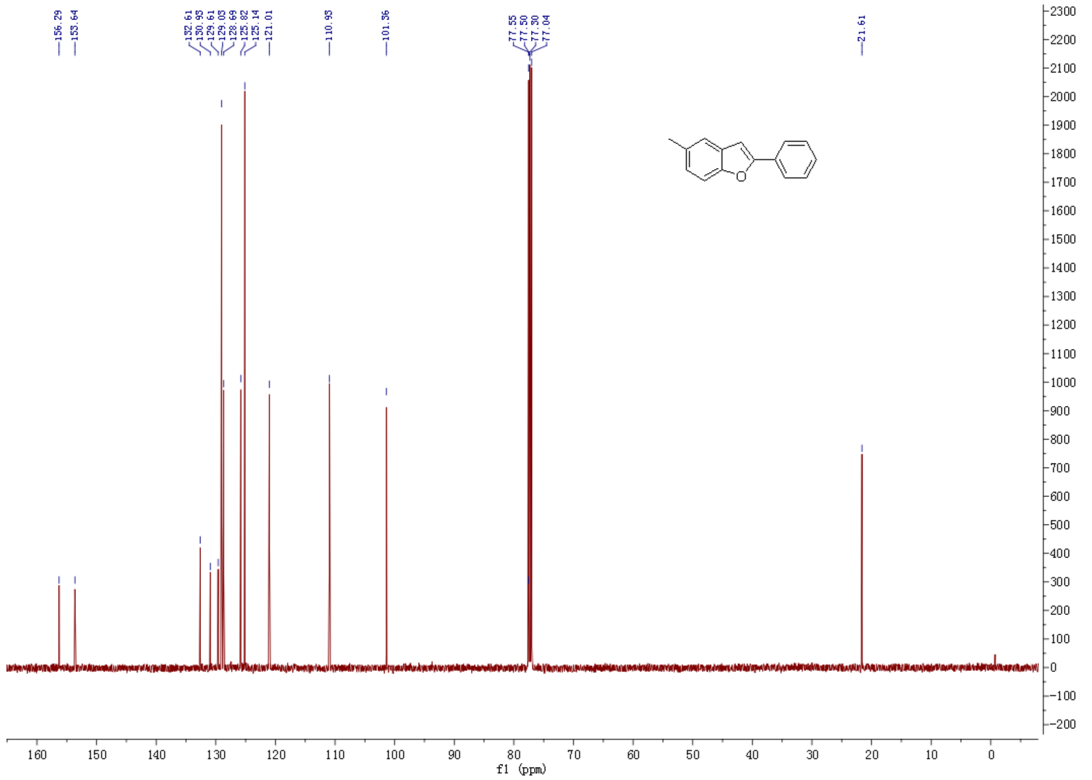
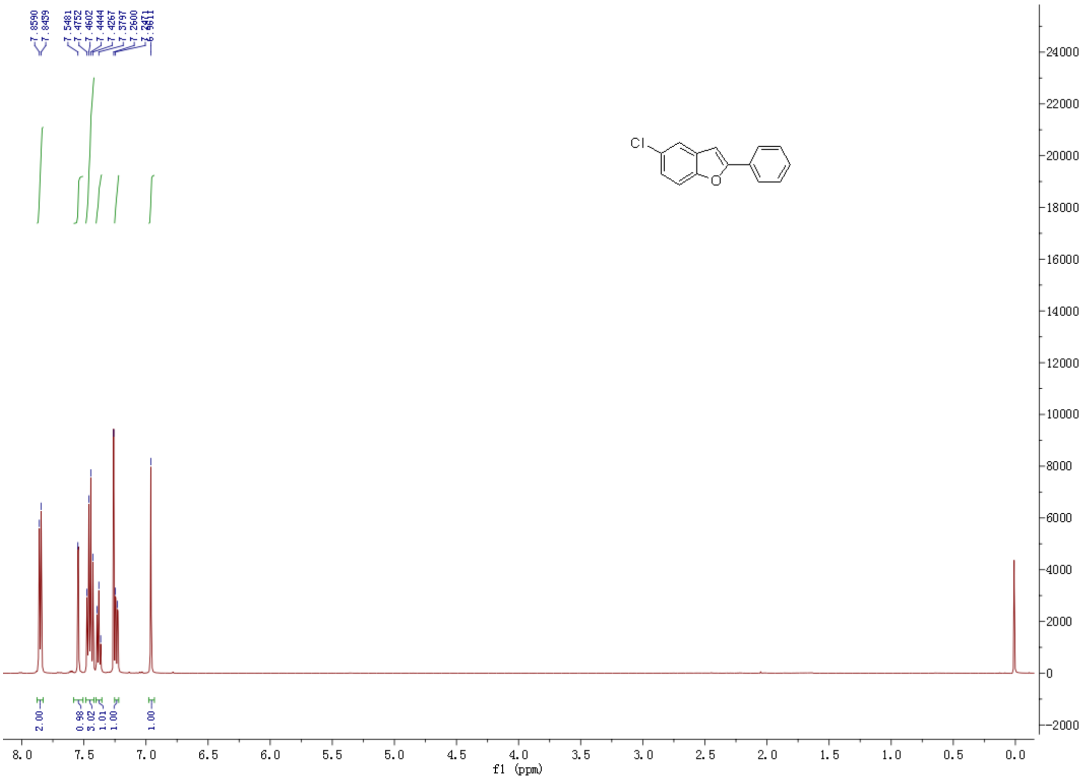


Figure S13. ^{1}H NMR of **3m** (500 MHz, $CDCl_3$) and ^{13}C NMR of **3m** (125 MHz, $CDCl_3$).



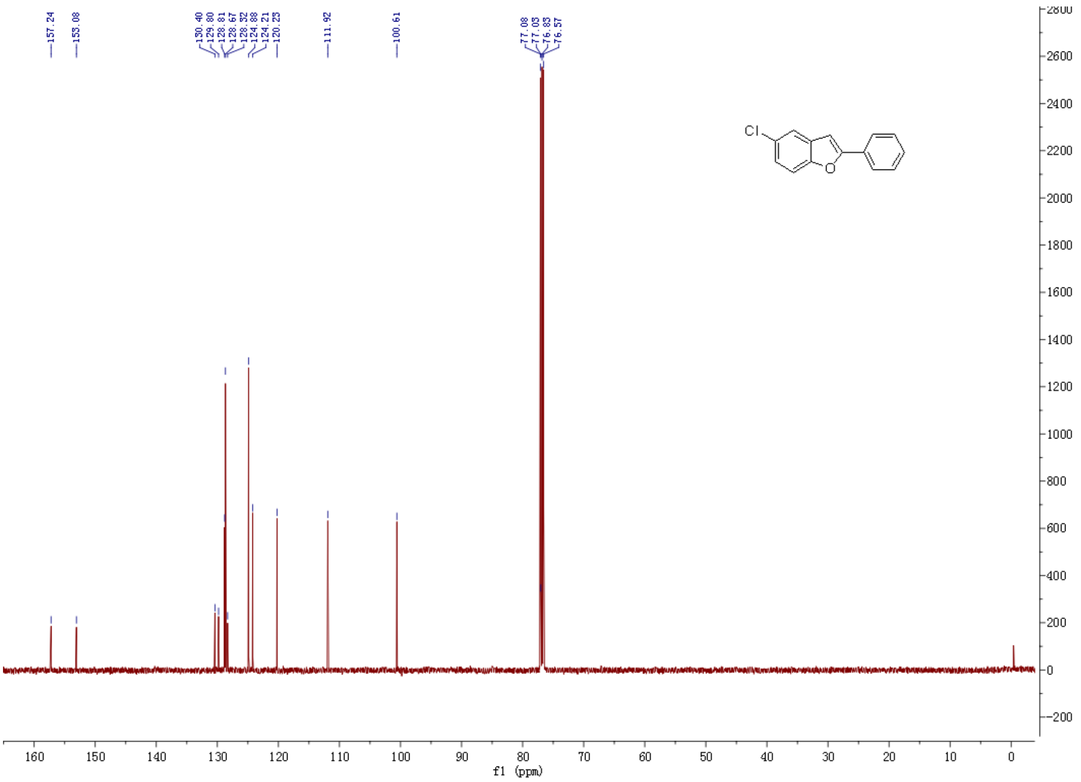
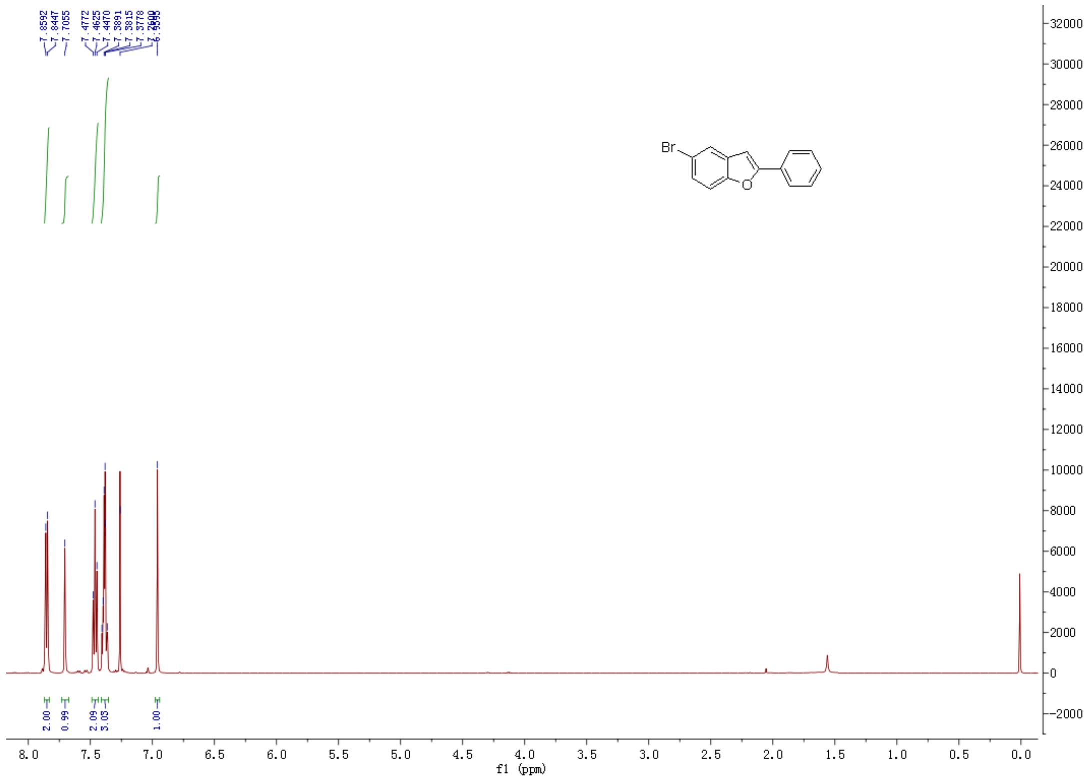


Figure S14. [1]H NMR of **3n** (500 MHz, $CDCl_3$) and [13]C NMR of **3n** (125 MHz, $CDCl_3$).



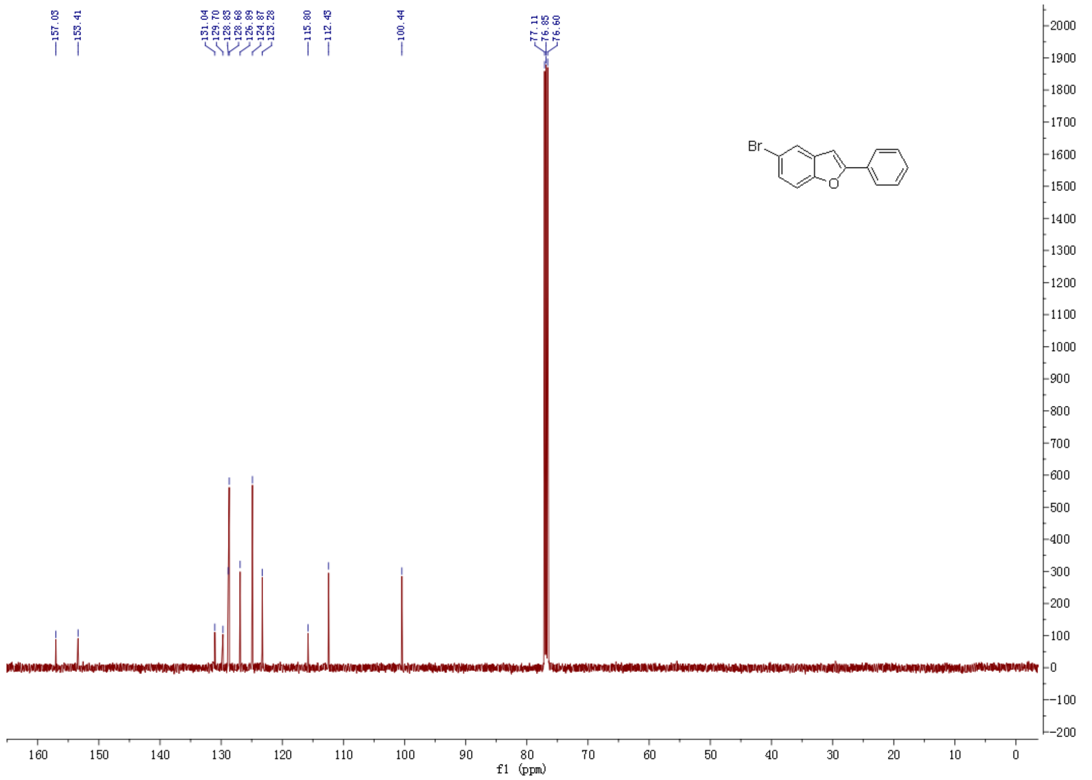
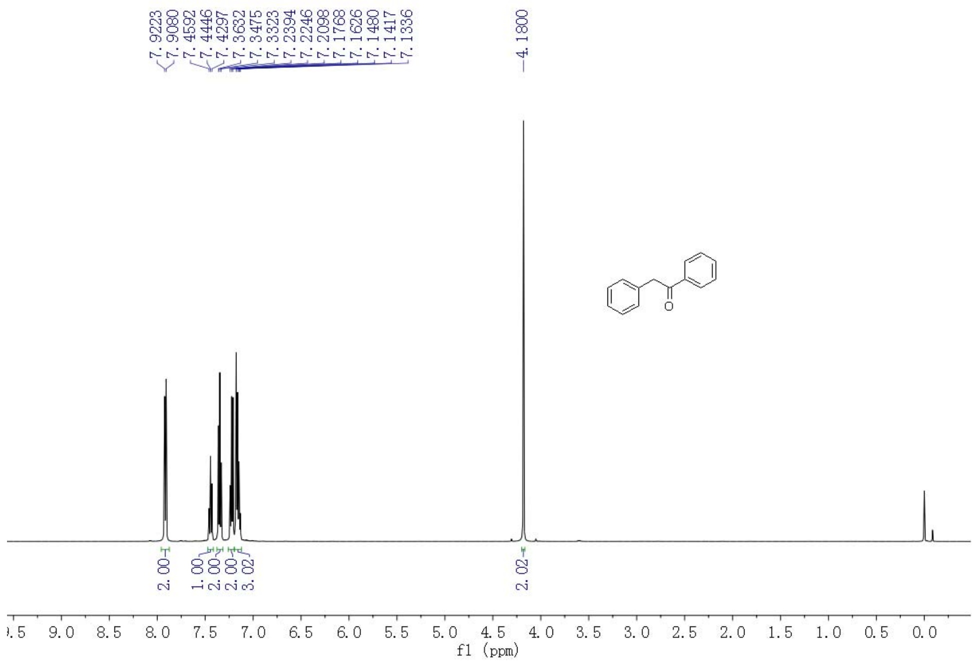


Figure S15. [1]H NMR of **3o** (500 MHz, $CDCl_3$) and [13]C NMR of **3o** (125 MHz, $CDCl_3$).



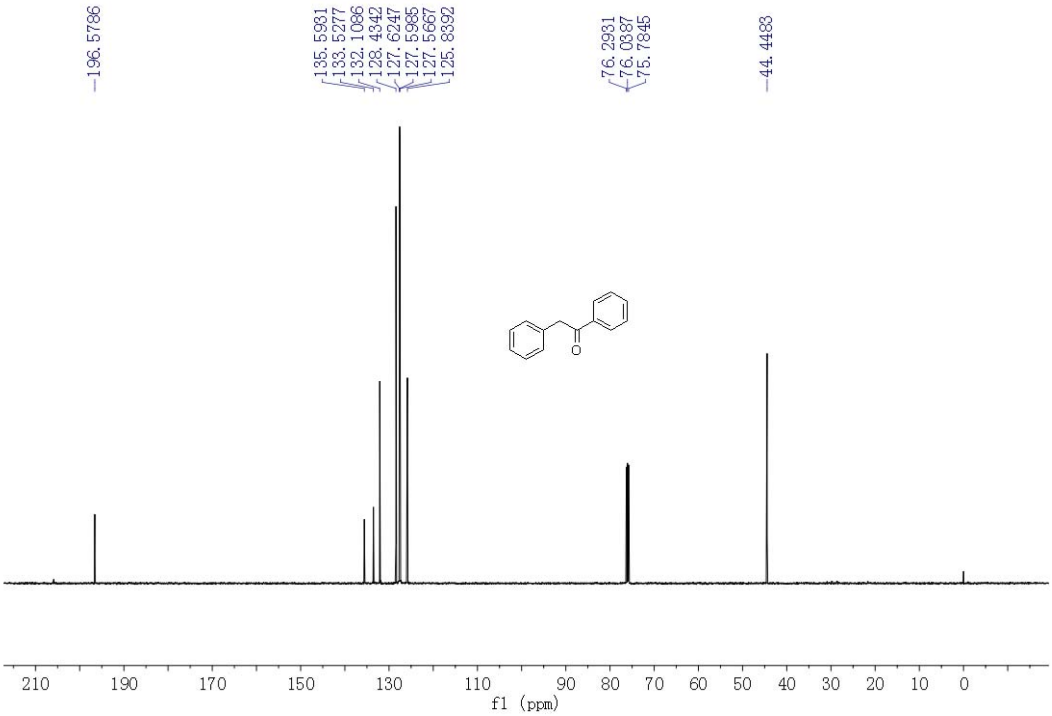


Figure S16. [1]H NMR of **5** (500 MHz, $CDCl_3$) and [13]C NMR of **5** (125 MHz, $CDCl_3$).