

# Supporting information

## Amine activation: Synthesis of *N*-(Hetero)arylamides from Isothioureas and Carboxylic Acids

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## **1. General information**

Unless stated otherwise, all solvents and commercially available reagents were used as received. Aniline was distilled prior to use and stored under nitrogen. In addition heptane and EtOAc, which were used for filtration and flash chromatography, were also distilled prior to use. Non-commercial starting materials were prepared as described below or according to literature procedures. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Advance 400 (100.62 MHz for  $^{13}\text{C}$ ) at ambient temperature using the non or partly deuterated solvent as internal standard ( $^1\text{H}$ :  $\delta$  2.50 ppm and  $^{13}\text{C}\{^1\text{H}\}$ :  $\delta$  39.5 ppm for DMSO- $d_6$  and  $^1\text{H}$ :  $\delta$  7.26 ppm and  $^{13}\text{C}\{^1\text{H}\}$ :  $\delta$  77.2 ppm for  $\text{CDCl}_3$ ). Chemical shifts ( $\delta$ ) are given in ppm and coupling constants (J) are quoted in hertz (Hz). Resonances are described as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad) or combinations thereof.  $^{13}\text{C}$  NMR spectra were recorded with complete proton decoupling. For high resolution mass-spectrometric analysis, samples were dissolved in  $\text{CH}_3\text{CN}$  and diluted to a concentration of approximately  $10^{-5}$  mol/L. 2  $\mu\text{L}$  was injected using a CapLC system and electrosprayed through the nanoelectrospray source. The nanoelectrospray source was operated in positive ion mode at an electrospray potential of 1.7 kV. The eluent used was 30 % A ( $\text{H}_2\text{O}$  0.1% formic acid) and 70 % B ( $\text{ACN}/\text{H}_2\text{O}$  95/5 0.1 % formic acid) at a flow rate of 6  $\mu\text{L}/\text{min}$ . Samples were injected with an interval of 3 minutes. Before analysis and after each seventh sample a 2  $\mu\text{L}$  volume of a 0.025 %  $\text{H}_3\text{PO}_4$  solution (50/50  $\text{MeOH}/\text{H}_2\text{O}$ ) was injected and used as lock mass. The MS was calibrated prior to use with a 0.015 %  $\text{H}_3\text{PO}_4$  solution. The spectra were lock mass corrected using the known mass of the nearest  $\text{H}_3\text{PO}_4$  cluster. Flash chromatography was performed manual on  $\text{SiO}_2$  (particle size 40-63  $\mu\text{m}$ , pore diameter 60  $\text{\AA}$ ) using the indicated eluent and visualized by UV detection (254 nm). The electronic laboratory notebook (ELN) codes of experiments are included for each compound.

## 2. Reagent and Substrate Synthesis

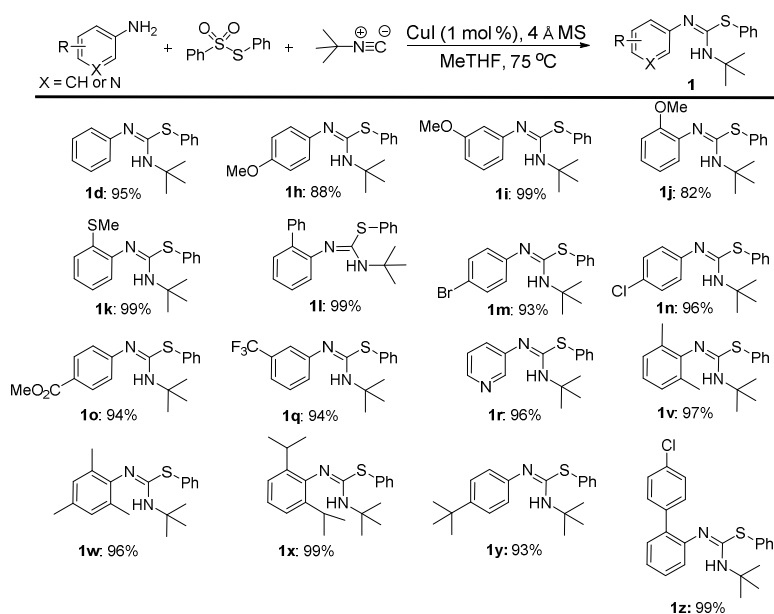
### S-Phenyl benzenethiosulfonate (yanping190)

S-Phenyl benzenethiosulfonate was synthesized according to literature procedure.<sup>1</sup>

### Synthesis of isothiureas

#### *N-t*-butyl-*N'*-(hetero)aryl-*S*-phenylisothiureas (**1**)

*N-t*-butyl-*N'*-(hetero)aryl-*S*-phenylisothiureas (**1**) were prepared from (hetero)arylamines, *S*-phenyl benzenethiosulfonate and *t*-butylisocyanide according to our previously established methodology.<sup>2</sup> The reaction showed a good tolerance to different substituted (hetero)arylamines. The results are listed in Scheme S1. The isothiureas **1a-1g** and *N-t*-butyl-*N'*-(4-trifluoromethylphenyl)-*S*-methylisothiurea (**1p**), *N*-(pyridin-4-yl)-*N'*-*t*-butyl-*S*-methylisothiurea (**1s**), *N-t*-butyl-*N'*-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)-*S*-methylisothiurea (**1t**), *N*-(benzo[*d*]thiazol-2-yl)-*N'*-*t*-butyl-*S*-methylisothiurea (**1u**), were reported in our previous paper.<sup>2</sup>



#### Scheme S1 Synthesis of *N-t*-butyl-*N'*-(hetero)aryl-*S*-phenylisothiureas (**1**)

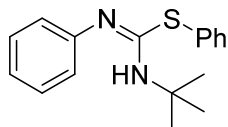
Reaction conditions: *S*-phenyl benzenethiosulfonate (250 mg, 1.0 mmol, 1.0 equiv), CuI (1.9 mg, 0.01 mmol, 1 mol %), (hetero)arylamine (1.7 mmol, 1.7 equiv), *t*-butylisocyanide (283  $\mu$ L, 2.5 mmol, 2.5 equiv) and 4 Å MS (300 mg) in 2-MeTHF (2.5 mL) under air were reacted at 75 °C for 20 h in a closed vessel.

<sup>1</sup> a) K. Fujuki, N. Tanifuji, Y. Sasaki, T. Yokoyama, *Synthesis*, **2002**, 343; b) S. Okumura, Y. Takeda, K. Kiyokawa, S. Minakata, *Chem. Commun.* **2013**, 49, 9266.

<sup>2</sup> P. Mampuy, Y. Zhu, T. Vlaar, E. Ruijter, R. V. A. Orru, B. U. W. Maes, *Angew. Chem. Int. Ed.* **2014**, 53, 12849.

### **3. Characterization Data of the Substrates**

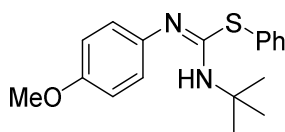
#### ***N-t-Butyl-N',S*-diphenylisothiourea (**1d**) (yanping95)**



A 10 mL microwave vial was charged with CuI (1.9 mg, 0.01 mmol, 1 mol %), *S*-phenyl benzenethiosulfonate (250 mg, 1.0 mmol, 1.0 equiv.), aniline (152  $\mu$ L, 1.7 mmol, 1.7 equiv.), *t*-butylisocyanide (283  $\mu$ L, 2.5 mmol, 2.5 equiv.), 4 Å MS (300 mg) and 2-MeTHF (2.5 mL). The vial was sealed and the reaction mixture was stirred at 75 °C for 20 h under air atmosphere. The mixture was filtered through Celite, the Celite cake was thoroughly washed (EtOAc), the filtrate was concentrated and dried under vacuum. The residue was purified by column chromatography on silica gel heptane/EtOAc as eluent. *N-t-Butyl-N',S*-diphenylisothiourea **1d** was obtained in 95% yield (270 mg). The use of a closed vial has no effect on the yield as we previously obtained 96% using a reflux set-up.<sup>2</sup>

White solid, m.p.: 69-71 °C, <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  (ppm) 7.34 (m, 5H), 7.15 (m, 2H), 6.89 (tt, *J* = 7.4, 1.1 Hz, 1H), 6.70 (dd, *J* = 8.4, 1.2 Hz, 2H), 5.41 (br, 1H), 1.30 (s, 9H). <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  (ppm) 149.7, 145.8, 132.7, 131.4, 129.4, 128.3, 128.2, 122.0, 121.8, 52.7, 28.1. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>17</sub>H<sub>21</sub>N<sub>2</sub>S: 285.1425; found: 285.1427.

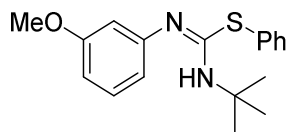
#### ***N-t-Butyl-N'*-(4-methoxyphenyl)-*S*-phenylisothiourea (**1h**) (yanping247)**



Prepared from 4-methoxyaniline (209 mg, 1.7 mmol, 1.7 equiv.), *S*-phenyl benzenethiosulfonate (250 mg, 1.0 mmol, 1.0 equiv.) and *t*-butylisocyanide (283  $\mu$ L, 2.5 mmol, 2.5 equiv.) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc as eluent. *N-t-Butyl-N'*-(4-methoxyphenyl)-*S*-phenylisothiourea was obtained in 88% yield (276 mg).

Yellow solid, m.p.: 85-87 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 7.44-7.47 (m, 2H), 7.31-7.34 (m, 3H), 6.79-6.86 (m, 4H), 3.88 (s, 1H), 3.76 (s, 3H), 1.29 (s, 9H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 155.28, 147.0, 143.3, 135.2, 130.9, 129.4, 129.1, 123.0, 113.8, 55.3, 52.9, 28.4. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>18</sub>H<sub>23</sub>N<sub>2</sub>OS: 315.1526; found: 315.1539.

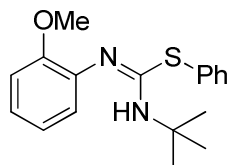
***N-t*-Butyl-*N'*-(3-methoxyphenyl)-*S*-phenylisothiourea (1i) (yanping248)**



Prepared from 3-methoxyaniline (209 mg, 1.7 mmol, 1.7 equiv.), *S*-phenyl benzenethiosulfonate (250 mg, 1.0 mmol, 1.0 equiv.) and *t*-butylisocyanide (283  $\mu$ L, 2.5 mmol, 2.5 equiv.) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc as eluent. *N-t*-Butyl-*N'*-(3-methoxyphenyl)-*S*-phenylisothiourea was obtained in 99% yield (311 mg).

White solid, m.p.: 67-69 °C,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 7.52-7.54 (m, 2H), 7.38-7.41 (m, 3H), 7.22 (t,  $J = 8.0$  Hz, 1H), 6.63 (dd,  $J_1 = 8.4$  Hz,  $J_2 = 2.4$  Hz, 1H), 6.59 (dd,  $J_1 = 7.6$  Hz,  $J_2 = 2.4$  Hz, 1H), 6.53 (t,  $J = 2.0$  Hz, 1H), 4.00 (s, 1H), 3.84 (s, 3H), 1.36 (s, 9H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 160.0, 151.2, 146.8, 135.2, 130.8, 129.4, 129.12, 129.10, 114.8, 108.3, 107.9, 55.1, 53.0, 28.4. HRMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{18}\text{H}_{23}\text{N}_2\text{OS}$ : 315.1526; found: 315.1533.

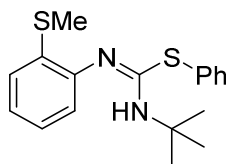
***N-t*-Butyl-*N'*-(2-methoxyphenyl)-*S*-phenylisothiourea (1j) (yanping249)**



Prepared from 2-methoxyaniline (209 mg, 1.7 mmol, 1.7 equiv.), *S*-phenyl benzenethiosulfonate (250 mg, 1.0 mmol, 1.0 equiv.) and *t*-butylisocyanide (283  $\mu$ L, 2.5 mmol, 2.5 equiv.) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc as eluent. *N-t*-Butyl-*N'*-(2-methoxyphenyl)-*S*-phenylisothiourea was obtained in 82% yield (257 mg).

White solid, m.p.: 85-87 °C,  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 7.48-7.52 (m, 2H), 7.35-7.38 (m, 3H), 7.01-7.05 (m, 1H), 6.92 (d,  $J = 5.2$  Hz, 2H), 6.90 (s, 1H), 4.03 (s, 1H), 3.86 (s, 3H), 1.38 (s, 9H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 151.6, 147.9, 139.7, 134.8, 131.5, 129.3, 128.8, 123.4, 123.3, 120.7, 112.2, 56.0, 53.1, 28.5. HRMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{18}\text{H}_{23}\text{N}_2\text{OS}$ : 315.1526; found: 315.1530.

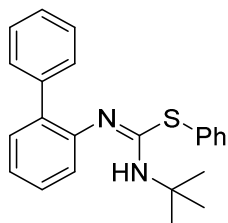
***N-t*-Butyl-*N'*-(2-methylthiophenyl)-*S*-phenylisothiourea (1k) (yanping250)**



Prepared from 2-(methylthio)aniline (236 mg, 1.7 mmol, 1.7 equiv.), *S*-phenyl benzenethiosulfonate (250 mg, 1.0 mmol, 1.0 equiv.) and *t*-butylisocyanide (283  $\mu$ L, 2.5 mmol, 2.5 equiv.) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc as eluent. *N-t*-Butyl-*N'*-(2-methylthiophenyl)-*S*-phenylisothiourea was obtained in 99% yield (327 mg).

White solid, m.p.: 81-83  $^{\circ}$ C,  $^1$ H-NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 7.53-7.55 (m, 2H), 7.37-7.40 (m, 3H), 7.15 (dd,  $J_1 = 7.6$  Hz,  $J_2 = 1.6$  Hz, 1H), 7.05-7.12 (m, 2H), 6.92 (dd,  $J_1 = 7.6$  Hz,  $J_2 = 1.6$  Hz, 1H), 4.06 (s, 1H), 2.46 (s, 3H), 1.39 (s, 9H).  $^{13}$ C-NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 148.4, 147.0, 135.2, 132.0, 130.7, 129.4, 129.1, 124.4, 124.2, 123.3, 121.7, 53.2, 28.6, 14.6. HRMS (ESI):  $m/z$   $[M+H]^+$  calcd for  $\text{C}_{18}\text{H}_{23}\text{N}_2\text{S}_2$ : 331.1297; found: 331.1283.

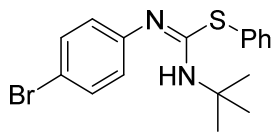
***N-t*-Butyl-*N'*-[(1,1'-biphenyl)-2-yl]-*S*-phenylisothiourea (1l) (yanping272)**



Prepared from [1,1'-biphenyl]-2-amine (287 mg, 1.7 mmol, 1.7 equiv.), *S*-phenyl benzenethiosulfonate (250 mg, 1.0 mmol, 1.0 equiv.) and *t*-butylisocyanide (283  $\mu$ L, 2.5 mmol, 2.5 equiv.) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc as eluent. *N-t*-Butyl-*N'*-[(1,1'-biphenyl)-2-yl]-*S*-phenylisothiourea was obtained in 99% yield (356 mg).

White solid, m.p.: 79-82  $^{\circ}$ C,  $^1$ H-NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 7.54 (d,  $J = 7.2$  Hz, 2H), 7.25-7.40 (m, 10H), 7.13 (t,  $J = 7.6$  Hz, 1H), 6.99 (dd,  $J_1 = 7.6$  Hz,  $J_2 = 1.2$  Hz, 1H), 3.78 (s, 1H), 1.17 (s, 9H).  $^{13}$ C-NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 147.7, 146.5, 141.0, 135.1, 134.7, 131.1, 130.1, 129.8, 129.4, 129.0, 127.7, 127.5, 126.2, 123.1, 123.0, 52.8, 28.5. HRMS (ESI):  $m/z$   $[M+H]^+$  calcd for  $\text{C}_{23}\text{H}_{25}\text{N}_2\text{S}$ : 361.1733; found: 361.1736.

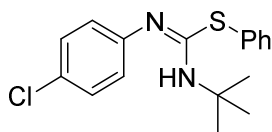
***N-t*-Butyl-*N'*-(4-bromophenyl)-*S*-phenylisothiourea (1m) (yanping253)**



Prepared from 4-bromoaniline (290.5 mg, 1.7 mmol, 1.7 equiv.), *S*-phenyl benzenethiosulfonate (250 mg, 1.0 mmol, 1.0 equiv.) and *t*-butylisocyanide (283  $\mu$ L, 2.5 mmol, 2.5 equiv.) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc as eluent. *N-t*-Butyl-*N'*-(4-bromophenyl)-*S*-phenylisothiourea was obtained in 93% yield (337 mg).

White solid, m.p.: 92-94  $^{\circ}$ C,  $^1$ H-NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 7.50-7.52 (m, 2H), 7.39-7.43 (m, 5H), 6.84 (d,  $J = 8.4$  Hz, 2H), 4.06 (s, 1H), 1.35 (s, 9H).  $^{13}$ C-NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 149.0, 147.3, 135.2, 131.5, 130.5, 129.5, 129.3, 124.2, 115.2, 53.2, 28.4. HRMS (ESI):  $m/z$   $[M+H]^+$  calcd for  $\text{C}_{17}\text{H}_{20}\text{BrN}_2\text{S}$ : 363.0525; found: 363.0526.

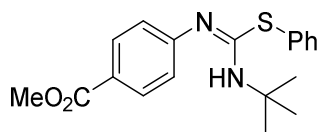
***N-t*-Butyl-*N'*-(4-chlorophenyl)-*S*-phenylisothiourea (1n) (yanping254)**



Prepared from 4-chloroaniline (216 mg, 1.7 mmol, 1.7 equiv.), *S*-phenyl benzenethiosulfonate (250 mg, 1.0 mmol, 1.0 equiv.) and *t*-butylisocyanide (283  $\mu$ L, 2.5 mmol, 2.5 equiv.) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc as eluent. *N-t*-Butyl-*N'*-(4-chlorophenyl)-*S*-phenylisothiourea was obtained in 96% yield (305 mg).

White solid, m.p.: 73-75  $^{\circ}$ C,  $^1$ H-NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 7.44-7.46 (m, 2H), 7.35-7.36 (m, 3H), 7.19 (d,  $J = 7.6$  Hz, 2H), 6.82 (d,  $J = 7.6$  Hz, 2H), 3.99 (s, 1H), 1.29 (s, 9H).  $^{13}$ C-NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 148.5, 147.4, 135.2, 130.5, 129.5, 129.3, 128.5, 127.6, 123.7, 53.2, 28.5. HRMS (ESI):  $m/z$   $[M+H]^+$  calcd for  $\text{C}_{17}\text{H}_{20}\text{ClN}_2\text{S}$ : 319.1030; found: 319.1031.

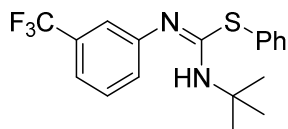
***N-t*-Butyl-*N'*-[4-(methoxycarbonyl)phenyl]-*S*-phenylisothiourea (1o) (yanping458)**



Prepared from methyl 4-aminobenzoate (345 mg, 1.7 mmol, 1.7 equiv.), *S*-phenyl benzenethiosulfonate (250 mg, 1.0 mmol, 1.0 equiv.) and *t*-butylisocyanide (283  $\mu$ L, 2.5 mmol, 2.5 equiv.) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc as eluent. Methyl *N-t*-Butyl-*N'*-[4-(methoxycarbonyl)phenyl]-*S*-phenylisothiourea was obtained in 94% yield (321 mg).

Yellow solid, m.p.: 104-106  $^{\circ}$ C,  $^1$ H-NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 7.97 (d,  $J = 8.4$  Hz, 2H), 7.55 (t,  $J = 3.6$  Hz, 1H), 7.46 (d,  $J = 7.6$  Hz, 2H), 7.39 (t,  $J = 3.6$  Hz, 1H), 7.34 (s, 1H), 7.34 (s, 1H), 6.96 (d,  $J = 8.4$  Hz, 2H), 3.89 (s, 3H), 1.33 (s, 9H).  $^{13}$ C-NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 167.0, 163.7, 154.3, 147.1, 135.0, 130.2, 129.4, 129.0, 123.7, 122.1, 53.1, 51.5, 28.3. HRMS (ESI):  $m/z$   $[M+H]^+$  calcd for  $\text{C}_{19}\text{H}_{23}\text{N}_2\text{O}_2\text{S}$ : 343.1475; found: 343.1490.

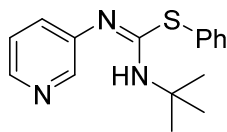
***N-t*-Butyl-*N'*-[3-(trifluoromethyl)phenyl]-*S*-phenylisothiourea (1q) (yanping460)**



Prepared from 3-(trifluoromethyl)aniline (274 mg, 1.7 mmol, 1.7 equiv.), *S*-phenyl benzenethiosulfonate (250 mg, 1.0 mmol, 1.0 equiv.) and *t*-butylisocyanide (283  $\mu$ L, 2.5 mmol, 2.5 equiv.) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc as eluent. *N-t*-Butyl-*N'*-[3-(trifluoromethyl)phenyl]-*S*-phenylisothiourea was obtained in 94% yield (331 mg).

Yellow solid, m.p.: 65-67  $^{\circ}$ C,  $^1$ H-NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 7.41 (dd,  $J = 2.4$  Hz, 7.6 Hz, 2H), 7.30 (t,  $J = 7.6$  Hz, 4H), 7.20 (d,  $J = 7.6$  Hz, 1H), 7.12 (s, 1H), 7.05 (d,  $J = 8.0$  Hz, 1H), 4.10 (s, 1H), 1.31 (s, 9H);  $^{13}$ C-NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 150.3, 148.0, 135.1, 130.8 (q,  $J = 31.8$  Hz), 130.2, 129.5, 129.4, 128.8, 125.8, 124.4 (q,  $J = 272.5$  Hz), 119.4 (q,  $J = 3.7$  Hz), 118.8 (q,  $J = 3.9$  Hz), 53.3, 28.4;  $^{19}$ F-NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) -62.39; HRMS (ESI):  $m/z$   $[M+H]^+$  calcd for  $\text{C}_{18}\text{H}_{20}\text{F}_3\text{N}_2\text{S}$ : 353.1294; found: 353.1284.

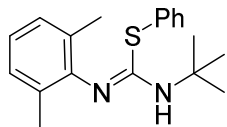
***N-t*-Butyl-*N'*-(3-pyridinyl)-*S*-phenylisothiourea (1r) (yanping270)**



Prepared from pyridin-3-amine (160 mg, 1.7 mmol, 1.7 equiv.), *S*-phenyl benzenethiosulfonate (250 mg, 1.0 mmol, 1.0 equiv.) and *t*-butylisocyanide (283  $\mu$ L, 2.5 mmol, 2.5 equiv.) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc as eluent. *N-t*-Butyl-*N'*-(3-pyridinyl)-*S*-phenylisothiourea was obtained in 96% yield (274 mg).

White solid, m.p.: 105-107  $^{\circ}$ C,  $^1$ H-NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 8.22-8.24 (m, 2H), 7.44-7.46 (m, 2H), 7.34-7.38 (m, 3H), 7.18-7.21 (dt,  $J = 1.6, 8.0$  Hz, 1H), 7.13 (q,  $J = 4.4$  Hz, 1H), 4.19 (s, 1H), 1.34 (s, 9H).  $^{13}$ C-NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 148.7, 146.0, 144.3, 143.4, 135.0, 130.2, 129.6, 129.35, 129.27, 123.0, 53.4, 28.4. HRMS (ESI):  $m/z$   $[M+H]^+$  calcd for  $\text{C}_{16}\text{H}_{20}\text{N}_3\text{S}$ : 286.1372; found: 286.1380.

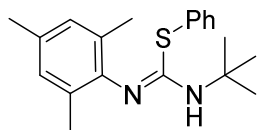
***N-t*-Butyl-*N'*-(2,6-dimethylphenyl)-*S*-phenylisothiourea (1v) (yanping288)**



Prepared from 2,6-dimethylaniline (206 mg, 1.7 mmol, 1.7 equiv.), *S*-phenyl benzenethiosulfonate (250 mg, 1.0 mmol, 1.0 equiv.) and *t*-butylisocyanide (283  $\mu$ L, 2.5 mmol, 2.5 equiv.) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc as eluent. *N-t*-Butyl-*N'*-(2,6-dimethylphenyl)-*S*-phenylisothiourea was obtained in 97% yield (303 mg).

White solid, m.p.: 59-61  $^{\circ}$ C,  $^1$ H-NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 7.56 (m, 2H), 7.42-7.44 (m, 3H), 7.11 (d,  $J = 7.6$  Hz, 2H), 6.97 (t,  $J = 7.6$  Hz, 1H), 3.93 (s, 1H), 2.32 (s, 6H), 1.43 (s, 9H).  $^{13}$ C-NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 147.6, 146.4, 135.6, 130.6, 129.5, 129.4, 127.6, 122.5, 52.7, 28.5, 18.4 (1C missing because of overlap). HRMS (ESI):  $m/z$   $[M+H]^+$  calcd for  $\text{C}_{19}\text{H}_{25}\text{N}_2\text{S}$ : 313.1733; found: 313.1741.

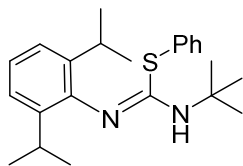
***N-t*-Butyl-*N'*-(2,4,6-trimethylphenyl)-*S*-phenylisothioureia (1w) (yanping291)**



Prepared from 2,4,6-trimethylaniline (229.5 mg, 1.7 mmol, 1.7 equiv.), *S*-phenyl benzenethiosulfonate (250 mg, 1.0 mmol, 1.0 equiv.) and *t*-butylisocyanide (283  $\mu$ L, 2.5 mmol, 2.5 equiv.) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc as eluent. *N-t*-Butyl-*N'*-(2,4,6-trimethylphenyl)-*S*-phenylisothioureia was obtained in 96% yield (313 mg).

White solid, m.p.: 88-90  $^{\circ}$ C,  $^1$ H-NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 7.47 (t,  $J = 7.6$  Hz, 2H), 7.34 (d,  $J = 5.2$  Hz, 2H), 7.33 (s, 1H), 6.84 (s, 2H), 3.80 (s, 1H), 2.25 (s, 3H), 2.19 (s, 6H), 1.33 (s, 9H).  $^{13}$ C-NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 146.5, 145.0, 135.6, 131.6, 130.8, 129.4, 129.3, 129.2, 128.3, 52.7, 28.5, 20.8, 18.3. HRMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{20}\text{H}_{27}\text{N}_2\text{S}$ : 327.1889; found: 327.1893.

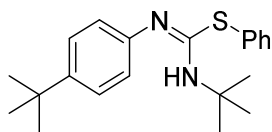
***N-t*-Butyl-*N'*-(2,6-diisopropylphenyl)-*S*-phenylisothioureia (1x) (yanping290)**



Prepared from 2,6-diisopropylaniline (301 mg, 1.7 mmol, 1.7 equiv.), *S*-phenyl benzenethiosulfonate (250 mg, 1.0 mmol, 1.0 equiv.) and *t*-butylisocyanide (283  $\mu$ L, 2.5 mmol, 2.5 equiv.) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc as eluent. *N-t*-Butyl-*N'*-(2,6-diisopropylphenyl)-*S*-phenylisothioureia was obtained in 99% yield (364 mg).

White solid, m.p.: 58-61  $^{\circ}$ C,  $^1$ H-NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 7.44-7.46 (m, 2H), 7.30-7.32 (m, 3H), 7.12 (d,  $J = 6.8$  Hz, 2H), 7.04 (t,  $J = 7.6$  Hz, 1H), 3.83 (s, 1H), 3.16 (sept,  $J = 6.8$  Hz, 2H), 1.36 (d,  $J = 7.2$  Hz, 6H), 1.32 (s, 9H), 1.18 (d,  $J = 7.2$  Hz, 6H);  $^{13}$ C-NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 146.5, 145.1, 139.6, 135.6, 130.9, 129.5, 129.4, 123.0, 122.7, 52.7, 28.5, 28.2, 23.9, 23.0. HRMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{23}\text{H}_{33}\text{N}_2\text{S}$ : 369.2359; found: 369.2362.

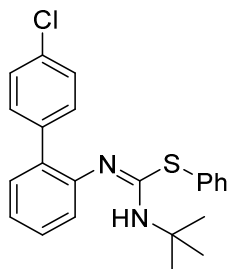
***N-t-Butyl-N'-(4-t-butylphenyl)-S-phenylisothiourea (1y) (yanping315)***



Prepared from 4-(*t*-butyl)aniline (253 mg, 1.7 mmol, 1.7 equiv.), *S*-phenyl benzenethiosulfonate (250 mg, 1.0 mmol, 1.0 equiv.) and *t*-butylisocyanide (283  $\mu$ L, 2.5 mmol, 2.5 equiv.) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc as eluent. *N-t-Butyl-N'-(4-t-butylphenyl)-S-phenylisothiourea* was obtained in 93% yield (316 mg).

Yellow solid, m.p.: 106-108  $^{\circ}$ C,  $^1$ H-NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 7.54-7.56 (m, 2H), 7.40-7.41 (m, 3H), 7.38 (s, 1H), 7.36 (s, 1H), 6.95 (d,  $J = 8.4$  Hz, 2H), 3.98 (s, 1H), 1.40 (s, 9H), 1.38 (s, 9H).  $^{13}$ C-NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 147.1, 146.3, 145.0, 135.2, 131.0, 129.3, 129.0, 125.3, 121.7, 53.0, 34.1, 31.5, 28.5. HRMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{21}\text{H}_{29}\text{N}_2\text{S}$ : 341.2046; found: 341.2036.

***N-Tert-butyl-N'-(4'-chloro[1,1'-biphenyl]-2-yl)-S-phenylisothiourea (1z) (yanping314)***

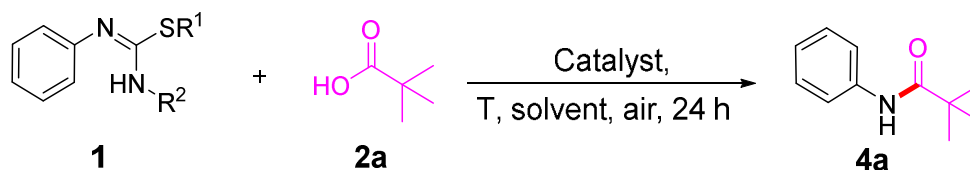


Prepared from 4'-chloro-[1,1'-biphenyl]-2-amine (346 mg, 1.7 mmol, 1.7 equiv.), *S*-phenyl benzenethiosulfonate (250 mg, 1.0 mmol, 1.0 equiv.) and *tert*-butyl isocyanide (283  $\mu$ L, 2.5 mmol, 2.5 equiv.) according to the general procedure. The residue was purified by column chromatography on silica gel with Heptane/EtOAc = 100:1 to 10:1 as eluent. *N-t-Butyl-N'-(4'-chloro[1,1'-biphenyl]-2-yl)-S-phenylisothiourea* was obtained in 99% yield.

White solid, m.p.: 91-93  $^{\circ}$ C,  $^1$ H-NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 7.34 (d,  $J = 6.8$  Hz, 2H), 7.21 (d,  $J = 7.6$  Hz, 3H), 7.11-7.18 (m, 6H), 6.97 (dt,  $J_1 = 0.8$  Hz,  $J_2 = 7.6$  Hz, 1H), 6.86 (d,  $J = 8.0$  Hz, 1H), 3.70 (s, 1H), 1.05 (s, 9H);  $^{13}$ C-NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  (ppm) 147.5, 146.6, 139.4, 135.0, 133.3, 132.1, 131.0, 130.6, 129.8, 129.4, 129.1, 128.0, 127.6, 123.2, 123.1, 52.8, 28.5. HRMS (ESI):  $m/z$   $[\text{M}+\text{H}]^+$  calcd for  $\text{C}_{23}\text{H}_{24}\text{N}_2\text{ClS}$ : 395.1343; found: 395.1345.

## 4. Optimization of the Reaction Conditions

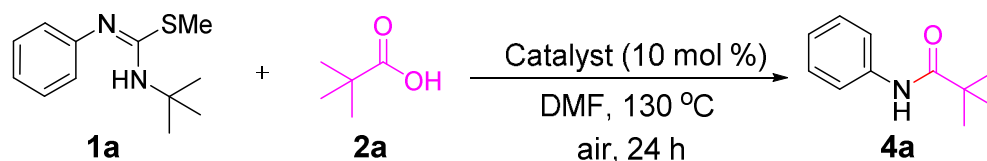
### 4.1. General procedure for the optimization



A 10 mL microwave vial was charged with isothiourea **1** (0.3 mmol), pivalic acid (**2a**), catalyst and solvent (2 mL) under air atmosphere. The vial was sealed and the reaction mixture was stirred for 24 hours at the indicated temperature. The mixture was concentrated under reduced pressure and dried under vacuum. The internal standard 1,3,5-trimethoxybenzene (50.4 mg, 0.3 mmol) was added to the dried mixture and everything was dissolved in CDCl<sub>3</sub>. The <sup>1</sup>H-NMR yield of reaction product and remaining substrate was subsequently determined.

### 4.2. Catalyst screening

The reaction conditions were optimized using *N*-*t*-butyl-*S*-methyl-*N'*-phenylisothiourea (**1a**) and pivalic acid (**2a**) as model substrate and reagent (Table S1). Several iron and copper catalysts were screened in DMF at 130 °C for 24 hours. Screening of a series of Fe(II) and Fe(III) catalysts revealed that Fe(SO<sub>4</sub>)<sub>2</sub>·7H<sub>2</sub>O, FeF<sub>2</sub> and Fe(acac)<sub>3</sub> were particularly effective catalysts, where the desired product could be obtained in 65%, 73% and 79% yield, respectively (entries 1, 7 and 8). Other iron catalysts, such as FeCl<sub>2</sub>·4H<sub>2</sub>O, FeCl<sub>3</sub>, Fe(OAc)<sub>2</sub>, FeBr<sub>2</sub>, FeCl<sub>3</sub>·6H<sub>2</sub>O and Fe<sub>2</sub>(SO<sub>4</sub>)<sub>3</sub>, gave a poor mass balance and only a low yield of reaction product **4a** (entries 2-6 and 9). In addition, we screened various Cu(I) and Cu(II) catalysts (entry 10-16). The results indicated that under copper catalysis the reaction generally afforded a low mass balance and the desired product was obtained in lower yield. While CuI and Cu(OAc)<sub>2</sub> gave still between 40 and 50% yield (entries 10 and 14) other Cu(I) (entry 11) and Cu(II) (entries 12-13, 15-16) catalysts gave the desired product in a low yield. Fe(acac)<sub>3</sub> was found to be the best catalyst for the reaction of **1a** and pivalic acid (**2a**) (entry 8) and was therefore selected for further optimization.

**Table S1.** Catalyst Screening<sup>[a]</sup>

Entry	Catalyst	Yield (%) <sup>[b]</sup>	
		Rec. <b>1a</b>	<b>4a</b>
1	Fe(SO <sub>4</sub> ) <sub>2</sub> ·7H <sub>2</sub> O	8	65
2	FeCl <sub>2</sub> ·4H <sub>2</sub> O	3	29
3	FeCl <sub>3</sub>	0	37
4	Fe(OAc) <sub>2</sub>	3	41
5	FeBr <sub>2</sub>	0	32
6	FeCl <sub>3</sub> ·6H <sub>2</sub> O	0	36
7	FeF <sub>2</sub>	5	73
<b>8</b>	<b>Fe(acac)<sub>3</sub></b>	<b>0</b>	<b>79</b>
9	Fe <sub>2</sub> (SO <sub>4</sub> ) <sub>3</sub>	7	17
10	CuI	5	48
11	CuBr	3	37
12	CuBr <sub>2</sub>	4	34
13	CuSO <sub>4</sub>	7	14
14	Cu(OAc) <sub>2</sub>	0	44
15	Cu(NO <sub>3</sub> ) <sub>2</sub>	3	37
16	Cu(OTf) <sub>2</sub>	0	36

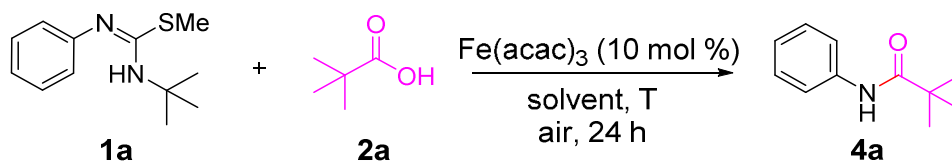
[a] Reaction conditions: **1a** (66.7 mg, 0.3 mmol), **2a** (61.2 mg, 0.6 mmol), catalyst (10 mol %) and DMF (2 mL) in a microwave vial under air at 130 °C for 24 h. [b] <sup>1</sup>H-NMR yield using 1,3,5-trimethoxybenzene as the internal standard.

### 4.3. Solvent screening and effect of temperature

With the best catalyst (Fe(acac)<sub>3</sub>) in hand, various solvents were subsequently tested for the reaction of **1a** with **2a** (Table S2). The reaction afforded the desired product in good to excellent yield using the solvents DMF, toluene, *o*-xylene, MeTHF, 1-propanol, isopropanol and *t*-butanol at their reflux temperature (entries 1-3 and 7-10). Other solvents such as dioxane, MeCN, THF, MeOH and EtOH did not perform well and gave the desired product in low yield (entries 4-6 and 11-12). Some solvents were further screened at 83 °C (entries 13-16), the temperature of the solvent which gave the best isolated yield (entry 10). The results

indicated that isopropanol (entry 10) and *o*-xylene (entry 15) were the best solvents. Based on the green solvent selection guide<sup>3</sup> (low toxicity and sustainability), isopropanol was finally selected as the standard solvent of choice for amide formation from isothiourea **1a** and **2a** (entry 10).

**Table S2.** Solvent screening and effect of temperature<sup>[a]</sup>



Entry	Solvent	Temp (°C)	Yield (%) <sup>[b]</sup>	
			Rec <b>1a</b>	<b>4a</b>
1	DMF	130	0	79
2	Toluene	111	11	79 (84) <sup>[c]</sup>
3	<i>o</i> -Xylene	130	9	94 (84) <sup>[c]</sup>
4	Dioxane	101	19	51
5	MeCN	101	24	58
6	THF	66	45	47
7	MeTHF	83	8	77 (78) <sup>[c]</sup>
8	1-Propanol	97	14	82 (76) <sup>[c]</sup>
9	<i>t</i> -Butanol	83	0	94 (74) <sup>[c]</sup>
<b>10</b>	<b>Isopropanol</b>	<b>83</b>	<b>10</b>	<b>85 (86)<sup>[c]</sup></b>
11	MeOH	65	32	56
12	EtOH	78	29	61
13	1-Propanol	83	6	86
14	DMF	83	0	85
15	<i>o</i> -Xylene	83	11	91
16	Toluene	83	37	66

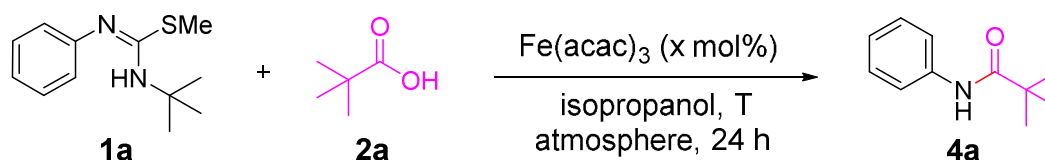
[a] Reaction conditions: **1a** (66.7 mg, 0.3 mmol), **2a** (61.2 mg, 0.6 mmol), Fe(acac)<sub>3</sub> (10.6 mg, 10 mol %), in solvent (2 mL) under air in a microwave vial at the indicated temperature for 24 h. [b] <sup>1</sup>H-NMR yield, using 1,3,5-trimethoxybenzene as the internal standard. [c] Isolated yield.

<sup>3</sup> a) R. K. Henderson, C. Jimenez-Gonzalez, D. J. C. Constable, S. R. Alston, G. G. A. Inglis, G. Fisher, J. Sherwood, S. P. Binks, A. D. Curzons, *Green Chem.* **2011**, *13*, 854; b) D. Prat, J. Hayler, A. Wells, *Green Chem.* **2014**, *16*, 4546.

#### 4.4. Fe(acac)<sub>3</sub> loading and amount of carboxylic acid

With the best catalyst and solvent in hand, the catalyst loading for reaction of **1a** with **2a** was screened. When the amount of Fe(acac)<sub>3</sub> was decreased to 5 mol %, the yield didn't change in within the same reaction time (Table S3, entry 2). However, the conversion and yield was significantly decreased when only 1 mol % of Fe(acac)<sub>3</sub> was used (entry 3). Higher loadings of Fe(acac)<sub>3</sub> (20 mol %) improved the conversion of **1a** and yield of **4a** (entry 4). The loading of pivalic acid (**2a**) could be decreased from 2 to 1 equivalent without decreasing the yield (entries 5-7). Reduction of the catalyst loading to 15 mol % gave a similar yield (entry 8). At 60 °C a significantly decreased conversion and yield were obtained (entry 9). Further reduction of the temperature to 40 °C or 25 °C shut down the reaction completely (entries 10-11). Considering that water or O<sub>2</sub> maybe important to the success of the reaction, Ar atmosphere, O<sub>2</sub> atmosphere and the addition of 4Å molecular sieves were also evaluated (entries 12-14). However, these had no negative influence on the yield and the reactions can therefore be executed under air. Thus, for reaction of isothioureia **1a** and **2a** the optimal catalyst loading is 15 mol % of Fe(acac)<sub>3</sub> and 1.2 equivalents of carboxylic acid (entry 8).

**Table S3.** Catalyst loading and amount of **2a** screening<sup>[a]</sup>



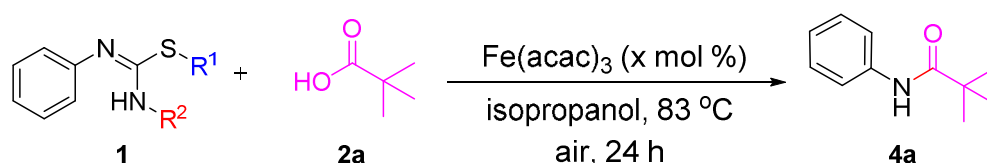
Entry	Fe(acac) <sub>3</sub> (x mol %)	Atmosphere	<b>2a</b> (y equiv.)	Temp. (°C)	Yield (%) <sup>[b]</sup>	
					<b>Rec 1a</b>	<b>4a</b>
1	10	Air	2.0	83	10	85 (86) <sup>[c]</sup>
2	5	Air	2.0	83	9	83 (83) <sup>[c]</sup>
3	1	Air	2.0	83	48	51
4	20	Air	2.0	83	0	quant (quant) <sup>[c]</sup>
5	20	Air	1.0	83	0	Quant
6	20	Air	1.2	83	0	Quant
7	20	Air	1.5	83	0	Quant
<b>8</b>	<b>15</b>	<b>Air</b>	<b>1.2</b>	<b>83</b>	<b>0</b>	<b>quant (93)<sup>[c]</sup></b>
9	15	Air	1.2	60	46	59
10	15	Air	1.2	40	90	0
11	15	Air	1.2	25	95	0
12	15	Ar	1.2	83	0	quant (quant) <sup>[c]</sup>
13	15	O <sub>2</sub>	1.2	83	0	quant (98) <sup>[c]</sup>
14	15	Ar + 4Å MS	1.2	83	0	quant (97) <sup>[c]</sup>

[a] Reaction conditions: **1a** (66.7 mg, 0.3 mmol), **2a** (y equiv.), and Fe(acac)<sub>3</sub> (x mol %), in isopropanol (2 mL) under the atmosphere indicated in a microwave vial at the indicated temperature for 24 h. [b] <sup>1</sup>H-NMR yield, using 1,3,5-trimethoxybenzene as the internal standard. [c] Isolated yield.

#### 4.5. Effect of the nitrogen and sulphur substituent in the isothiourea substrate

Considering that substituents on the sulphur and nitrogen atoms of the isothiourea can have a significant influence on the amide formation, a series of substituted isothioureas **1a-1g** was investigated (Table S4). After all, these can be freely selected by simply altering the thiosulfonate and isocyanide reagent in the activation step. These were subsequently tested in the amide forming reaction with **2a** under the conditions optimized for **1a** (entry 1). First the influence of the R<sup>2</sup> group was investigated with R<sup>1</sup> = Me (entries 1-3). When the R<sup>2</sup> was changed from a *t*-butyl to an isopropyl group the conversion and yield greatly decreased (entry 2). An aromatic rather than an aliphatic substituent, as exemplified by R<sup>2</sup> = Ph, had the same effect (entry 3). These results indicated that a sterically hindered *t*-butyl group is superior for the amide formation. Next, the influence of the R<sup>2</sup> group was investigated for R<sup>1</sup> = Ph. The reaction with R<sup>2</sup> = *t*-Bu gave a quantitative NMR yield and 95% isolated yield under the standard conditions (entry 4). Interestingly, the amount of catalyst could be dropped to 5 mol% (entries 5 and 6). However, a further decrease to 1 mol % gave no full conversion as 13% of substrate **1d** was recovered (entry 9). The minimal catalyst loading for full conversion in 24 h turned out to be 2.5 mol% (entry 7). A combination of R<sup>2</sup> = *t*-Bu with R<sup>1</sup> = Ph is required to achieve a good conversion at low catalyst loading as with a secondary (R<sup>2</sup> = isopropyl) or primary (R<sup>2</sup> = benzyl) alkyl the conversion and yield dropped significantly when applying the same catalyst loading (compare entries 7, 10 and 11). When a mild electron withdrawing group (4-Cl) was introduced in the *S*-phenyl group of *N-t*-butyl-*S,N'*-diphenylisothiourea full conversion was obtained with 1 mol % of catalyst (entry 12). R<sup>1</sup> = Ph and R<sup>2</sup> = *t*-Bu were selected as optimal substituents for the isothiourea. (Hetero)arylamine activation for amide formation therefore involves *S*-phenyl benzenethiosulfonate and *t*-butylisocyanide which are both commercially available reagents. Based on the commercial availability of *S*-phenyl benzenethiosulfonate it was preferred over its chlorinated analogue. Interestingly, byproduct PhSSPh was isolated in 72% yield during the purification of **4a** (entry 7). It can be transformed into *S*-phenyl benzenethiosulfonate reagent following a literature protocol allowing recycling.<sup>4</sup> The optimal reaction conditions for isothiourea **1d** with R<sup>1</sup> = Ph and R<sup>2</sup> = *t*-Bu are substrate (0.3 mmol), pivalic acid (**2a**) (0.36 mmol), Fe(acac)<sub>3</sub> (2.5 mol %) in isopropanol (2 mL) under air at 83 °C for 24 h (entry 7).

<sup>4</sup> S. Okumura, Y. Takeda, K. Kiyokawa, S. Minakata, *Chem. Commun.* **2013**, 49, 9266.

**Table S4.** R<sup>1</sup>, R<sup>2</sup> Screening<sup>[a]</sup>

Entry	Substrates	Fe(acac) <sub>3</sub> (x mol %)	Yield (%) <sup>[b]</sup>	
			Rec. <b>1</b>	<b>4a</b>
1	<b>1a</b> , R <sup>1</sup> = Me, R <sup>2</sup> = <i>t</i> -butyl	15	0	93
2	<b>1b</b> , R <sup>1</sup> = Me, R <sup>2</sup> = isopropyl	15	39	48
3	<b>1c</b> , R <sup>1</sup> = Me, R <sup>2</sup> = Ph	15	27	46
4	<b>1d</b> , R <sup>1</sup> = Ph, R <sup>2</sup> = <i>t</i> -butyl	15	0	quant (95) <sup>[c]</sup>
5	<b>1d</b> , R <sup>1</sup> = Ph, R <sup>2</sup> = <i>t</i> -butyl	10	0	Quant
6	<b>1d</b> , R <sup>1</sup> = Ph, R <sup>2</sup> = <i>t</i> -butyl	5	0	quant (94) <sup>[c]</sup>
<b>7</b>	<b>1d</b> , R <sup>1</sup> = Ph, R <sup>2</sup> = <i>t</i> -butyl	<b>2.5</b>	<b>0</b>	<b>quant (97)<sup>[c,d]</sup></b>
8	<b>1d</b> , R <sup>1</sup> = Ph, R <sup>2</sup> = <i>t</i> -butyl	2	5	quant (92) <sup>[c]</sup>
9	<b>1d</b> , R <sup>1</sup> = Ph, R <sup>2</sup> = <i>t</i> -butyl	1	13	87 (79) <sup>[c]</sup>
10	<b>1e</b> , R <sup>1</sup> = Ph, R <sup>2</sup> = isopropyl	1	21	79
11	<b>1f</b> , R <sup>1</sup> = Ph, R <sup>2</sup> = benzyl	1	31	46
12	<b>1g</b> , R <sup>1</sup> = 4-Cl-Ph, R <sup>2</sup> = <i>t</i> -butyl	1	0	91
13	<b>1d</b> , R <sup>1</sup> = Ph, R <sup>2</sup> = <i>t</i> -butyl	0	91	5

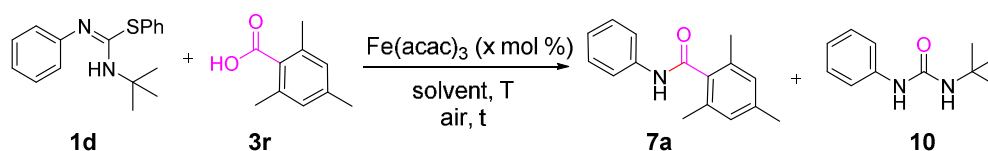
[a] Reaction conditions: **1** (66.7 mg, 0.3 mmol), **2a** (36.7 mg, 0.36 mmol), Fe(acac)<sub>3</sub> (x mol%) in isopropanol (2 mL) under air in a microwave vial at 83 °C for 24 h. [b] <sup>1</sup>H-NMR yield, using 1,3,5-trimethoxybenzene as internal standard. [c] Isolated yield. [d] 72% of PhSSPh was isolated.

#### 4.6. Sterically hindered carboxylic acids

The synthesis of sterically hindered (hetero)aromatic amides is still a challenge in synthetic chemistry. We therefore investigated the expansion of the scope towards sterically hindered carboxylic acids. The reaction of **1d** and **3r** were selected as model system (Table S5). When the reaction was performed in isopropanol at 83 °C for 48 h no full conversion was observed as 30% of substrate **1d** was recovered and 35% of the side compound *N-t*-butyl-*N'*-phenylurea (**10**) was observed. When the amount of catalyst and **3r** were increased, full conversion was achieved in 24 h, but the selectivity was still poor and **7a** was only obtained in 56% yield. Some higher boiling solvents were subsequently tested. 1-Propanol gave a full conversion but gave the desired product in a low yield only with poor selectivity versus urea **10** (entry 3). The reaction afforded the desired product **7a** in very good yield and with excellent selectivity using the solvents *o*-xylene and 2-butanol (entries 4 and 5). The optimal

reaction conditions selected were: **1d** (0.3 mmol), **3r** (0.36 mmol), Fe(acac)<sub>3</sub> (2.5 mol %) in 2-butanol (2 mL) under air at 98 °C for 24 hours.

**Table S5.** Optimization for sterically hindered carboxylic acids<sup>[a]</sup>

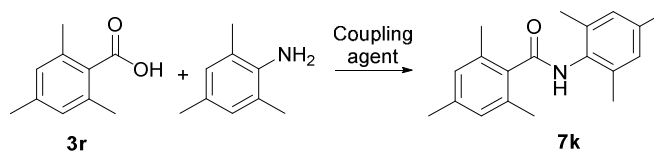


Entry	Solvent	Fe(acac) <sub>3</sub> (x mol %)	<b>3r</b> (y equiv.)	Temp (°C)	t (h)	Yield (%) <sup>[b]</sup>		
						<b>7a</b>	Rec. <b>1d</b>	<b>10</b>
1	Isopropanol	2.5	1.2	83	48	36	30	35
2	Isopropanol	5	1.5	83	48	56	0	35
3	1-Propanol	2.5	1.2	97	24	53	0	20
4	2-Butanol	2.5	1.2	98	24	89	5	0
5	<i>o</i> -Xylene	2.5	1.2	130	24	90	0	0

[a] Reaction conditions: **1d** (85 mg, 0.3 mmol), **3r** (y equiv.), Fe(acac)<sub>3</sub> (x mol %) in solvent (2 mL) under air in a microwave vial at the indicated temperature. [b] <sup>1</sup>H-NMR yield, using 1,3,5-trimethoxybenzene as the internal standard.

## 5. Comparison with classical approaches

For challenging amides, derived from sterically hindered carboxylic acids and electron deficient and/or sterically hindered (hetero)aromatic amines, for instance, the classical approaches give a low yield or often even fail, and no general efficient synthetic method is currently at hand. This is illustrated by the synthesis of N-mesityl-2,4,6-trimethylbenzamide from 2,4,6-trimethylbenzoic acid and 2,4,6-trimethylaniline (Scheme S2). A variety of classical coupling reagents under different conditions were tested but generally no reaction product was formed, only with PyBOP a moderate yield was obtained.



Coupling agent	Reaction conditions	Ref	Yield
DCC (1.08 equiv)	DMAP (0.25 equiv), DCM, 0-25 °C, 24 h	5	No reaction
DCC (1.1 equiv)	HOBt (1.1 equiv), THF, 0-25 °C, 24 h	6	No reaction

<sup>5</sup> Ju, X.; Liu, Z. China. Patent, CN101701016A, 2011. 20091103.

<sup>6</sup> Zhang, Y.; Feng, J.; Liu, C.; Fang, H.; Xu, W. *Bioorg. Med. Chem.* **2011**, *19*, 4437.

EDC (1.2 equiv)	HOBt (0.2 equiv), <i>i</i> -Pr <sub>2</sub> NEt (2.0 equiv), THF, 0-25 °C, 24 h	7	No reaction
HATU (1.5 equiv)	<i>i</i> -Pr <sub>2</sub> NEt (2.0 equiv), THF, 25 °C, 24 h	7, 8	Trace amount
T <sub>3</sub> P (1.5 equiv)	<i>i</i> -Pr <sub>2</sub> NEt (2.0 equiv), THF, 25 °C, 24 h	7, 8	No reaction
PyBOP (1.5 equiv)	<i>i</i> -Pr <sub>2</sub> NEt (2.0 equiv), THF, 25 °C, 24 h	7, 8	61%
CDI (1.1 equiv)	THF, 25 °C, 24 h	8	No reaction
CDI (1.1 equiv)	MeTHF, 25 °C, 3h, then DBU (0.5 equiv), 80 °C, 12 h	9	No reaction
This work	Scheme 4		86%

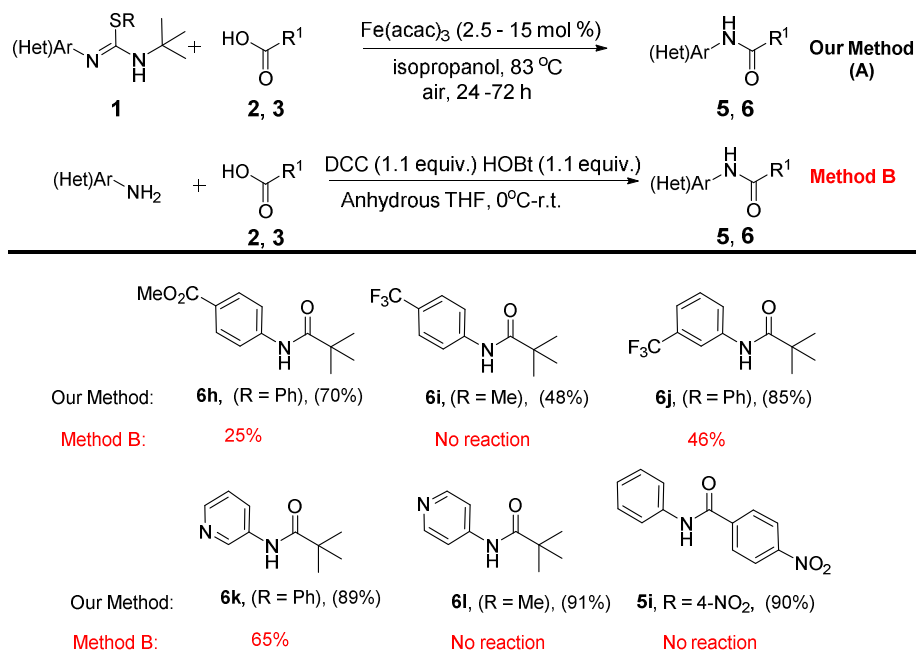
**Scheme S2. Screening of classical coupling agents for the synthesis of *N*-mesityl-2,4,6-trimethylbenzamide (7k).**

**General procedure for synthesis of challenging *N*-(hetero)arylamides 7 with DCC coupling (Scheme 4):**<sup>5</sup> A 25 mL round bottomed flask was charged with a carboxylic acid **2** or **3** (1.05 mmol) and 5 mL of DCM and cooled to 0 °C, then 1,3-dicyclohexylcarbodiimide (DCC) (1.08 mmol) and 4-dimethylaminopyridine (DMAP) (0.25 mmol) were dissolved in 5 mL DCM and added dropwise to the above mixture. The reaction mixture was subsequently stirred at 0 °C for 30 min, then an aniline (1.0 mmol) was added and the reaction mixture was stirred for 24 h at room temperature. The mixture was filtered through filter paper, the solid was thoroughly washed with EtOAc, and the combined filtrates concentrated and dried under vacuo. The residue was purified in the same way as used for our method.

<sup>7</sup> MacMillan, D. S.; Murray, J.; Sneddon, H. F.; Jamieson, C.; Watson, A. J. B. *Green Chem.* **2013**, *15*, 596.

<sup>8</sup> Junkers, M. *Aldrich ChemFiles*, 2007, 7.2, pp: 8-9.

<sup>9</sup> Larrivéé-Aboussafy, C.; Jones, B. P.; Price, K. E.; Hardink, M. A.; McLaughlin, R. W.; Lillie, B. M.; Hawkins, J. M.; Vaidyanathan, R. *Org. Lett.* **2010**, *12*, 324



**Scheme S3** Synthesis of examples of Scheme 2 and 3 using DCC (method B)

**Method B (Scheme 2 and Scheme 3):**<sup>10</sup> At 0 °C, to a solution of a carboxylic acid **2, 3** (1.0 mmol) and 1-hydroxybenzotriazole hydrate (1.1 mmol) in 5 mL of anhydrous THF a solution of 1,3-dicyclohexylcarbodiimide (1.1 mmol) (DCC) in 1 mL of anhydrous THF was added. After 20 mins an aniline (1.1 mmol) was added to the reaction mixture. After stirring the mixture at room temperature overnight, THF was evaporated and the residue was taken up in EtOAc (40 mL) and cooled in the refrigerator. Then *N,N*-dicyclohexylurea (DCU) was filtered off, the filtrate washed with saturated Na<sub>2</sub>CO<sub>3</sub> (3 x 10 mL), 1 N HCl (3 x 10 mL), brine (3 x 10 mL) and dried over MgSO<sub>4</sub>. The solvent was evaporated to give the crude product which was purified in the same way as used for our method.

## 7. Amide Synthesis from *N*-aryl-*N'*-*t*-butyl-*S*-phenylisothiourea

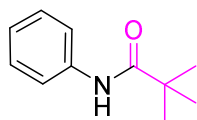
### 7.1. General procedure for amide synthesis

**Standard procedure for the synthesis of *N*-(hetero)arylamides (**4, 5, 7**):** A 10 mL microwave vial was charged with *N*-aryl-*N'*-*t*-butyl-*S*-phenylisothiourea (**1**) (0.3 mmol), carboxylic acid (0.36 mmol), Fe(acac)<sub>3</sub> (2.6 mg, 2.5 mol %) and isopropanol (2.0 mL) or 2-butanol (2.0 mL). The vial was sealed and the reaction mixture was respectively stirred at 83 °C or 98 °C for 24 h under an air atmosphere. The mixture was cooled down to room temperature, concentrated under reduced pressure and dried under vacuum. The residue was purified by flash column chromatography on silica gel or crystallization to yield the corresponding amide. Details of purification are given below for individual compounds.

<sup>10</sup> Y. Zhang, J. Feng, C. Liu, H. Fang, W. Xu, *Bio. Med. Chem.* **2011**, *19*, 4437-4444.

## 7.2. Characterization data for amides

### *N*-Phenylpivalamide (**4a**)<sup>11</sup> (yanping204)

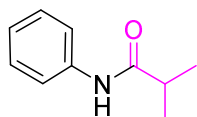


Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-phenylpivalamide was obtained in 97% yield (57 mg).

For the 5 mmol scale reaction a round-bottomed flask was used and a drying tube on top of the reflux condenser. In this case a reaction time of 48 h was used yielding 89% of *N*-phenylpivalamide (788 mg).

White solid, m.p.: 138-139 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.54 (d, *J* = 7.6 Hz, 2H), 7.47 (s, 1H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.10 (t, *J* = 7.6 Hz, 1H), 1.32 (s, 9H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 176.6, 138.0, 128.8, 124.1, 120.1, 39.5, 27.5; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>11</sub>H<sub>16</sub>NO: 178.1232; found: 178.1236.

### *N*-Phenylisobutyramide (**4b**)<sup>5</sup> (yanping215)

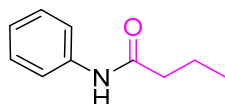


Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), isobutyric acid (**2b**) (32 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-Phenylisobutyramide was obtained in 94% yield (46 mg).

White solid, m.p.: 110-111 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.67 (br, 1H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 2H), 7.10 (t, *J* = 7.6 Hz, 1H), 2.55 (sept, *J* = 6.8 Hz, 1H), 1.25 (d, *J* = 6.8 Hz, 6H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 175.6, 138.1, 128.8, 124.0, 120.0, 36.5, 19.5. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>10</sub>H<sub>14</sub>NO: 164.1075; found: 164.1072.

<sup>11</sup> K. Kouki, A. Mitsuhiro, S. Satoshi, *J. Org. Chem.* **2008**, *73*, 9494.

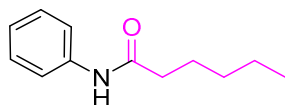
### *N*-Phenylbutyramide (**4c**)<sup>12</sup> (yanping198)



Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), butyric acid (**2c**) (32 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-Phenylbutyramide was obtained in 93% yield (45 mg).

White solid, m.p.: 94-96 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 8.28 (s, 1H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.29 (t, *J* = 8.0 Hz, 2H), 7.10 (t, *J* = 7.6 Hz, 1H), 2.34 (t, *J* = 7.6 Hz, 2H), 1.73 (sixtet, *J* = 7.6 Hz, 2H), 0.99 (t, *J* = 7.6 Hz, 3H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 172.0, 138.1, 128.7, 124.0, 120.1, 39.3, 19.1, 13.6. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>10</sub>H<sub>14</sub>NO: 164.1075; found: 164.1076.

### *N*-Phenylhexanamide (**4d**)<sup>13</sup> (yanping216)



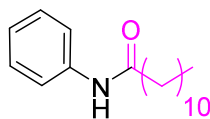
Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), caproic acid (**2d**) (42 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-Phenylhexanamide was obtained in 99% yield (57 mg).

White solid, m.p.: 97-98 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.91 (s, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.10 (t, *J* = 7.2 Hz, 1H), 2.36 (t, *J* = 7.6 Hz, 2H), 1.72 (t, *J* = 7.2 Hz, 2H), 1.34 (m, 4H), 0.92 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 172.0, 138.0, 128.8, 124.1, 120.0, 37.6, 31.3, 25.3, 22.3, 13.8. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>18</sub>NO: 192.1388; found: 192.1384.

<sup>12</sup> F. Tamaddon, F. Aboee, A. Nasiri, *Catalysis Commun.* **2011**, *16*, 194.

<sup>13</sup> S. Jammī, S. Sakthivel, L. Rout, T. Mukherjee, S. Mandal, R. Mitra, P. Saha, T. Punniyamurthy, *J. Org. Chem.* **2009**, *74*, 1971.

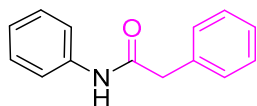
### *N*-Phenyldodecanamide (**4e**)<sup>14</sup> (yanping217)



Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), lauric acid (**2e**) (72 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-Phenyldodecanamide was obtained in 99% yield (82 mg).

White solid, m.p.: 76-78 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.84 (s, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.10 (t, *J* = 7.6 Hz, 1H), 2.36 (t, *J* = 7.6 Hz, 2H), 1.72 (t, *J* = 7.2 Hz, 2H), 1.28-1.33 (m, 16H), 0.91 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 172.0, 138.1, 128.9, 124.1, 120.1, 37.7, 31.8, 29.56, 29.54, 29.44, 29.34, 29.26, 29.24, 26.7, 22.6, 14.0 (1 C missing because of overlap). HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>18</sub>H<sub>30</sub>NO: 276.2327; found: 276.2317.

### *N,2*-Diphenylacetamide (**4f**)<sup>15</sup> (yanping230)



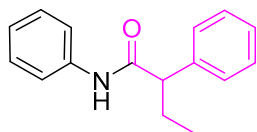
Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), phenylacetic acid (**2f**) (49 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N,2*-Diphenylacetamide was obtained in 98% yield (62 mg).

White solid, m.p.: 118-120 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.63 (s, 1H), 7.42 (d, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 6.4 Hz, 2H), 7.29 (s, 2H), 7.28 (s, 1H), 7.24 (t, *J* = 8.0 Hz, 2H), 7.05 (t, *J* = 7.6 Hz, 1H), 3.66 (s, 2H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 169.4, 137.7, 134.5, 129.3, 129.0, 128.8, 127.4, 124.3, 120.0, 44.5. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>14</sub>H<sub>14</sub>NO: 212.1075; found: 212.1074.

<sup>14</sup> M. Hosseini-Sarvari, E. Sodagar, M. M. Doroodmand, *J. Org. Chem.* **2011**, *76*, 2853.

<sup>15</sup> J. H. Dam, G. Osztrovsky, L. U. Nordstrøm, R. Madsen, *Chem. Eur. J.* **2010**, *16*, 6820.

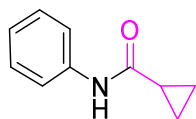
***rac*-N,2-Diphenylbutanamide (4g)<sup>16</sup> (yanping218)**



Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), (±)-2-phenylbutyric acid (**2g**) (59 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *rac*-N,2-Diphenylbutanamide was obtained in 93% yield (67 mg).

White solid, m.p.: 90-92 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.63 (s, 1H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.35-7.41 (m, 4H), 7.26-7.33 (m, 3H), 7.09 (t, *J* = 7.6 Hz, 1H), 3.47 (t, *J* = 7.6 Hz, 1H), 2.27-2.34 (m, *J* = 7.2 Hz, 1H), 1.86-1.97 (m, *J* = 7.6 Hz, 1H), 0.97 (t, *J* = 7.6 Hz, 3H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 172.0, 139.5, 137.9, 128.79, 128.75, 127.9, 127.3, 124.1, 119.9, 55.8, 26.4, 12.2. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>16</sub>H<sub>18</sub>NO: 240.1383; found: 240.1391.

***N*-Phenylcyclopropanecarboxamide (4h)<sup>17</sup> (yanping327)**



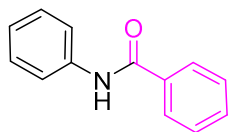
Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), cyclopropanecarboxylic acid (**2h**) (0.029 mL, 31 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 2/1 as eluent. *N*-Phenylcyclopropanecarboxamide was obtained in 96% yield (46 mg).

White solid, m.p.: 110-112 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.99 (s, 1H), 7.53 (d, *J* = 7.6 Hz, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.09 (t, *J* = 7.6 Hz, 1H), 1.53-1.59 (m, 1H), 1.06-1.10 (m, 2H), 0.79-0.84 (m, 2H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 172.3, 138.2, 128.8, 123.9, 119.9, 15.5, 7.8; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>10</sub>H<sub>12</sub>NO: 162.0919; found: 162.0917.

<sup>16</sup> G. S. Skinner, J. F. Perkins, *J. Am. Chem. Soc.* **1950**, *72*, 5569.

<sup>17</sup> Y.-H. Yang, M. Shi, *J. Org. Chem.* **2005**, *70*, 8645.

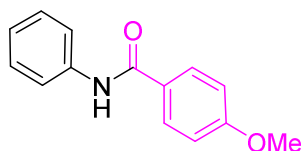
### ***N*-Phenylbenzamide (5a)<sup>18</sup> (yanping197)**



Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), benzoic acid (**3a**) (44 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-Phenylbenzamide was obtained in 90% yield (53 mg).

White solid, m.p.: 165-167 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 10.3 (s, 1H), 8.00 (d, *J* = 7.2 Hz, 2H), 7.84 (d, *J* = 7.6 Hz, 2H), 7.52-7.61 (m, 3H), 7.37 (t, *J* = 8.0 Hz, 2H), 7.12 (t, *J* = 7.6 Hz, 1H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 165.5, 139.2, 135.0, 131.4, 128.5, 128.3, 127.6, 123.6, 120.4; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>12</sub>NO: 198.0919; found: 198.0921.

### **4-Methoxy-*N*-phenylbenzamide (5b)<sup>13</sup> (yanping236)**

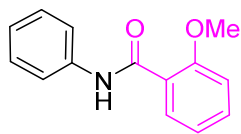


Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), *p*-methoxybenzoic acid (**3b**) (55 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 2:1 as eluent. 4-Methoxy-*N*-phenylbenzamide was obtained in 71% yield (48 mg).

White solid, m.p.: 170-172 °C, <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 10.1 (s, 1H), 7.97 (d, *J* = 8.4 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.05-7.10 (m, 3H), 3.84 (s, 3H); <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 164.8, 161.8, 139.3, 129.5, 128.5, 127.0, 123.3, 120.3, 113.5, 55.4; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>14</sub>H<sub>14</sub>NO<sub>2</sub>: 228.1025; found: 228.1034.

<sup>18</sup> X. F. Guo, L. Tang, Y. Yang, Z. G. Zha, Z. Y. Wang, *Green Chemistry* **2014**, *16*, 2443.

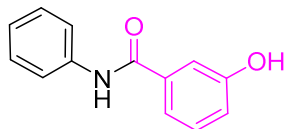
## 2-Methoxy-*N*-phenylbenzamide (**5c**)<sup>19</sup> (yanping237)



Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), 2-methoxybenzoic acid (**3c**) (55 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 2:1 as eluent. 2-Methoxy-*N*-phenylbenzamide was obtained in 78% yield (53 mg).

Light brown solid, m.p.: 78-80 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 9.77 (s, 1H), 8.26 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 7.6 Hz, 2H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.07-7.12 (m, 2H), 6.98 (d, *J* = 8.4 Hz, 1H), 3.99 (s, 3H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 163.1, 157.1, 138.3, 133.1, 132.3, 128.8, 124.0, 121.7, 121.5, 120.3, 111.5, 56.1; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>14</sub>H<sub>14</sub>NO<sub>2</sub>: 228.1025; found: 228.1034.

## 3-Hydroxy-*N*-phenylbenzamide (**5d**)<sup>20</sup> (yanping462)



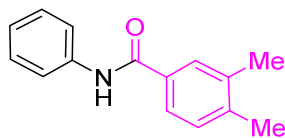
Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), 3-hydroxybenzoic acid (**3d**) (50 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 1:2 as eluent. 3-Hydroxy-*N*-phenylbenzamide was obtained in 85% yield (54 mg).

White solid, m.p.: 152-154 °C, <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 10.14 (s, 1H), 9.75 (s, 1H), 7.78 (d, *J* = 7.6 Hz, 2H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.30-7.36 (m, 4H), 7.09 (t, *J* = 7.6 Hz, 1H), 6.99 (dd, *J* = 1.6, 8.0 Hz, 1H); <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 155.6, 157.3, 139.2, 136.5, 129.4, 128.5, 123.5, 120.3, 118.5, 118.2, 114.5; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>12</sub>NO<sub>2</sub>: 214.0863; found: 214.0872.

<sup>19</sup> S. Shang, D. Zhang-Negrerie, Y. Du, K. Zhao, *Angew. Chem. Int. Ed.* **2014**, *53*, 6216

<sup>20</sup> N. Panda, R. Mothkuri, D. K. Nayak, *Eur. J. Org. Chem.* **2014**, *8*, 1602.

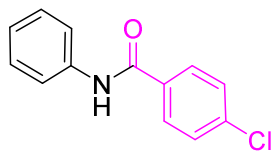
### 3,4-Dimethyl-*N*-phenylbenzamide (**5e**)<sup>21</sup> (yanping243)



Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), 3,4-dimethylbenzoic acid (**3e**) (54 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 2/1 as eluent. 3,4-Dimethyl-*N*-phenylbenzamide was obtained in 87% yield (59 mg).

White solid, m.p.: 102-104 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 8.26 (s, 1H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.65 (s, 1H), 7.58-7.60 (dd, *J*<sub>1</sub> = 8.0 Hz, *J*<sub>2</sub> = 2.4 Hz, 1H), 7.33 (t, *J* = 8.4 Hz, 2H), 7.15 (t, *J* = 7.2 Hz, 2H), 2.30 (s, 3H), 2.27 (s, 3H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 166.1, 140.7, 138.1, 136.9, 132.3, 129.6, 128.8, 128.3, 124.4, 124.1, 120.3, 19.7, 19.6; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>15</sub>H<sub>16</sub>NO: 226.1232; found 226.1241.

### 4-Chloro-*N*-phenylbenzamide (**5f**)<sup>13</sup> (yanping233)

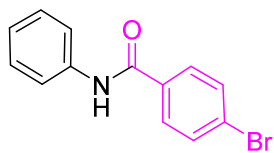


Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), 4-chlorobenzoic acid (**3f**) (56 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 2/1 as eluent. 4-Chloro-*N*-phenylbenzamide was obtained in 88% yield (61 mg).

White solid, m.p.: 152-154 °C, <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 10.29 (s, 1H), 7.99 (d, *J* = 8.0 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.11 (t, *J* = 7.2 Hz, 1H); <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 164.4, 138.9, 136.3, 133.6, 129.5, 128.5, 128.4, 123.8, 120.4; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>11</sub>NOCl: 232.0529; found: 232.0535.

<sup>21</sup> M. Kissane, D. Lynch, J. Chopra, S. E. Lawrence, A. R. Maguire, *Org. Biomol. Chem.* **2010**, *8*, 5602.

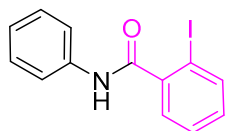
#### 4-Bromo-*N*-phenylbenzamide (**5g**)<sup>13</sup> (yanping232)



Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), 4-bromobenzoic acid (**3g**) (72 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 2/1 as eluent. 4-Bromo-*N*-phenylbenzamide was obtained in 83% yield (69 mg).

Brown solid, m.p.: 194-197 °C, <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 10.29 (s, 1H), 7.92 (d, *J* = 8.4 Hz, 2H), 7.73-7.78 (m, 4H), 7.35 (t, *J* = 8.0 Hz, 2H), 7.11 (t, *J* = 7.2 Hz, 1H); <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 164.5, 138.9, 134.0, 131.3, 129.7, 128.6, 125.3, 123.8, 120.4; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>11</sub>NOBr: 276.0024; found: 276.0013.

#### 2-Iodo-*N*-phenylbenzamide (**5h**)<sup>22</sup> (yanping244)

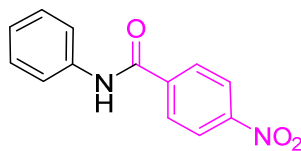


Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), 4-iodobenzoic acid (**3h**) (89 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 2/1 as eluent. 2-Iodo-*N*-phenylbenzamide was obtained in 88% yield (85 mg).

White solid, m.p.: 136-139 °C, <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 10.41 (s, 1H), 7.95 (d, *J* = 7.6 Hz, 1H), 7.75 (d, *J* = 7.6 Hz, 2H), 7.50 (t, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.22-7.26 (m, 1H), 7.14 (t, *J* = 7.6 Hz, 1H); <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 167.5, 143.1, 139.02, 139.00, 131.0, 128.7, 128.1, 128.0, 123.8, 119.7, 93.6; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>11</sub>NOI: 323.9885; found 323.9878.

<sup>22</sup> Y. Nishiyama, M. Nakamura, T. Misawa, M. Nakagomi, M. Makishima, M. Ishikawa, Y. Hashimoto, *Bioorg. Med. Chem.* **2014**, *22*, 2799.

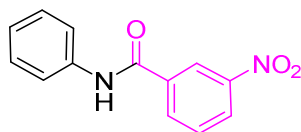
#### 4-Nitro-*N*-phenylbenzamide (**5i**)<sup>13</sup> (yanping342)



Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), 4-nitrobenzoic acid (**3i**) (60 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) in *o*-xylene at 130 °C according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 2/1 as eluent. 4-Nitro-*N*-phenylbenzamide was obtained in 90% yield (65 mg).

Off white solid, m.p.: 214-216 °C, <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 10.53 (s, 1H), 8.36 (d, *J* = 8.8 Hz, 2H), 8.19 (d, *J* = 8.8 Hz, 2H), 7.78 (d, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.14 (t, *J* = 7.6 Hz, 1H); <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 163.8, 149.1, 140.6, 138.6, 129.1, 128.6, 124.1, 123.5, 120.5; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>11</sub>N<sub>2</sub>O<sub>3</sub>: 243.0770; found: 243.0772.

#### 3-Nitro-*N*-phenylbenzamide (**5j**)<sup>23</sup> (yanping235)

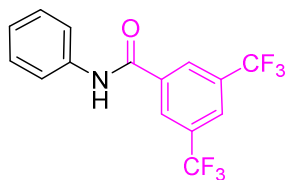


Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), 3-nitrobenzoic acid (**3j**) (60 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 2/1 as eluent. 3-Nitro-*N*-phenylbenzamide was obtained in 74% yield (54 mg).

White solid, m.p.: 152-154 °C, <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 10.65 (s, 1H), 8.15 (d, *J* = 7.6 Hz, 1H), 7.87 (t, *J* = 7.6 Hz, 1H), 7.70-7.79 (m, 2H), 7.69 (d, *J* = 7.6 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.13 (t, *J* = 7.6 Hz, 1H); <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 164.1, 146.4, 138.8, 134.0, 132.7, 130.9, 129.2, 128.8, 124.2, 123.9, 119.7; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>11</sub>N<sub>2</sub>O<sub>3</sub>: 243.0770; found: 243.0778.

<sup>23</sup> V. K. Das, R. R. Devi, A. J. Thakur, *Applied Catalysis A: General* **2013**, 456, 118.

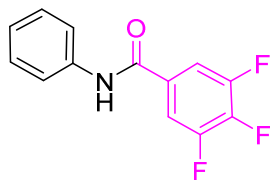
### ***N*-Phenyl-3,5-bis(trifluoromethyl)benzamide (5k) (yanping368)**



Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), 3,5-bis(trifluoromethyl)benzoic acid (**3k**) (93 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure in *o*-xylene at 130 °C. The residue was purified by column chromatography on silica gel with heptane/EtOAc 2/1 as eluent. *N*-Phenyl-3,5-bis(trifluoromethyl)benzamide was obtained in 82% yield (82 mg).

White solid, m.p.: 175-177 °C, <sup>1</sup>H-NMR (400 MHz, DMSO-d<sub>6</sub>): δ (ppm) 10.63 (s, 2H), 8.61 (s, 1H), 8.35 (s, 1H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.40 (t, *J* = 7.6 Hz, 2H), 7.16 (t, *J* = 7.6 Hz, 1H); <sup>13</sup>C-NMR (100 MHz, DMSO-d<sub>6</sub>): δ (ppm) 162.4, 138.4, 137.1, 130.5 (q, *J* = 33.3 Hz), 128.7, 128.5 (m), 125.0 (m), 124.3, 123.0 (q, *J* = 272.9 Hz), 120.7; <sup>19</sup>F-NMR (100 MHz, DMSO-d<sub>6</sub>): δ (ppm) -61.33; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>15</sub>H<sub>10</sub>F<sub>6</sub>NO: 334.0661; found 334.0655.

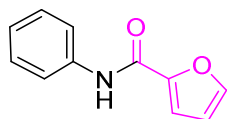
### **3,4,5-Trifluoro-*N*-phenylbenzamide (5l) (yanping367)**



Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), 3,4,5-trifluorobenzoic acid (**3l**) (63 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure in *o*-xylene at 130 °C. The residue was purified by column chromatography on silica gel with heptane/EtOAc 2/1 as eluent. 3,4,5-Trifluoro-*N*-phenylbenzamide was obtained in 95% yield (72 mg).

White solid, m.p.: 145-147 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.75 (s, 1H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.52 (t, *J* = 7.2 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.19 (t, *J* = 7.6 Hz, 1H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 162.0, 150.0 (ddd, *J* = 248.5, 10.0, 3.4 Hz), 140.8 (dt, *J* = 254.0, 15.7 Hz), 138.5, 131.1 (td, *J* = 6.6, 4.1 Hz), 128.6, 124.1, 120.5, 112.8 (dd, *J* = 16.4, 6.0 Hz); <sup>19</sup>F-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) -134 (dd, *J* = 9.2, 22.8 Hz, 1F), -156.7 (tt, *J* = 6.8, 22.4 Hz, 1F); HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>9</sub>F<sub>3</sub>NO: 252.0631; found 252.0632.

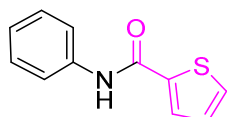
### ***N*-Phenylfuran-2-carboxamide (5m)<sup>24</sup> (yanping258)**



Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), furan-2-carboxylic acid (**3m**) (40 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-Phenylfuran-2-carboxamide was obtained in 83% yield (47 mg).

Light yellow solid, m.p.: 125-126 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 8.18 (s, 1H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.50 (s, 1H), 7.37 (t, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 7.2 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 6.55 (dd, *J* = 1.6 Hz, 3.6 Hz, 1H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 156.1, 147.8, 144.1, 137.4, 129.0, 124.4, 120.0, 115.1, 112.5; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>11</sub>H<sub>10</sub>NO<sub>2</sub>: 188.0712; found: 188.0718.

### ***N*-Phenylthiophene-2-carboxamide (5n)<sup>25</sup> (yanping240)**



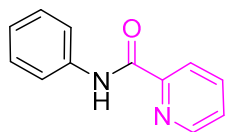
Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), thiophene-2-carboxylic acid (**3n**) (46 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-Phenylthiophene-2-carboxamide was obtained in 87% yield (53 mg).

White solid, m.p.: 136-138 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.88 (s, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 2H), 7.52 (dd, *J*<sub>1</sub> = 5.2 Hz, *J*<sub>2</sub> = 0.8 Hz, 1H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.14 (d, *J* = 7.6 Hz, 1H), 7.08-7.11 (m, 1H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 160.1, 139.3, 137.6, 130.7, 129.0, 128.5, 127.8, 124.6, 120.3; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>11</sub>H<sub>10</sub>NOS: 204.0483; found 204.0480.

<sup>24</sup> Y. Wang, D. Zhu, L. Tang, S. Wang, Z. Wang, *Angew. Chem. Int. Ed.* **2011**, *50*, 8917.

<sup>25</sup> A. Schoenberg, R. F. Heck, *J. Org. Chem.* **1974**, *39*, 3327.

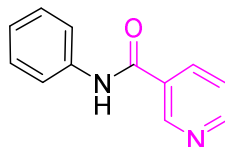
### *N*-Phenylpicolinamide (**5o**)<sup>19</sup> (yanping238)



Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), picolinic acid (**3o**) (44 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) in 2-butanol at 98 °C according to the general procedure with 48 hours reaction time. The residue was purified by column chromatography on silica gel with heptane/EtOAc = 1/3 as eluent. *N*-Phenylpicolinamide was obtained in 80% yield (47 mg).

Yellow solid, m.p.: 74-76 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 10.01 (s, 1H), 8.59 (d, *J* = 4.8 Hz, 1H), 8.29 (d, *J* = 7.6 Hz, 1H), 7.88 (t, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 2H), 7.43-7.47 (m, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.14 (t, *J* = 7.6 Hz, 1H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 161.9, 149.8, 147.9, 137.7, 137.6, 129.0, 126.3, 124.2, 122.3, 119.6; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>11</sub>N<sub>2</sub>O: 198.0866; found: 198.0874.

### *N*-Phenylnicotinamide (**5p**)<sup>26</sup> (yanping259)

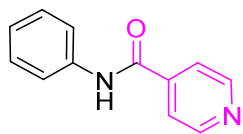


Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), nicotinic acid (**3p**) (44 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) in 2-butanol at 98 °C according to the general procedure with 48 hours reaction time. The residue was purified by recrystallizing from EtOAc/MeOH 9/1. *N*-Phenylnicotinamide was obtained in 86% yield (51 mg).

White solid, m.p.: 122-123 °C, <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 10.45 (s, 1H), 9.10 (d, *J* = 1.6 Hz, 1H), 8.76 (dd, *J* = 1.6, 4.8 Hz, 1H), 8.29 (dt, *J* = 2.0, 8.0 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 2H), 7.57 (dq, *J* = 0.8, 4.8 Hz, 1H), 7.37 (t, *J* = 7.2 Hz, 2H), 7.13 (t, *J* = 7.6 Hz, 1H); <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 164.0, 153.2, 152.0, 148.6, 138.8, 136.9, 135.4, 128.6, 123.9, 120.4; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>11</sub>N<sub>2</sub>O: 198.0866; found: 198.0870.

<sup>26</sup> J. R. Martinelli, T. P. Clark, D. A. Watson, R. H. Munday, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2007**, *46*, 8460.

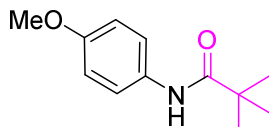
### ***N*-Phenylisonicotinamide (5q)<sup>27</sup> (yanping260)**



Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), isonicotinic acid (**3q**) (44 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) in 2-butanol at 98 °C according to the general procedure with 48 hours reaction time. The residue was purified by recrystallizing from EtOAc/MeOH 9/1. *N*-Phenylisonicotinamide was obtained in 99% yield (59 mg).

White solid, m.p.: 170-172 °C, <sup>1</sup>H-NMR (400 MHz, DMSO-d<sub>6</sub>): δ (ppm) 10.51 (s, 1H), 8.79 (d, *J* = 6.0 Hz, 2H), 7.86 (d, *J* = 6.0 Hz, 2H), 7.78 (d, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.14 (t, *J* = 7.2 Hz, 1H); <sup>13</sup>C-NMR (100 MHz, DMSO-d<sub>6</sub>): δ (ppm) 164.0, 150.2, 141.9, 138.6, 128.7, 124.2, 121.6, 120.5; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>11</sub>N<sub>2</sub>O: 198.0866; found: 198.0872.

### ***N*-(4-Methoxyphenyl)pivalamide (6a)<sup>28</sup> (yanping280)**



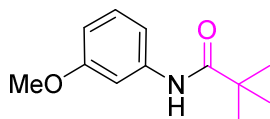
Prepared from *N*-*t*-butyl-*N'*-(4-methoxyphenyl)-*S*-phenylisothiourea (**1h**) (94 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-(4-Methoxyphenyl)pivalamide was obtained in 97% yield (60 mg).

White solid, m.p.: 124-126 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.40 (d, *J* = 8.0 Hz, 2H), 7.35 (s, 1H), 6.82 (d, *J* = 9.2 Hz, 2H), 3.76 (s, 3H), 1.28 (s, 9H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 176.4, 156.3, 131.1, 122.0, 114.0, 55.4, 39.3, 27.5; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>18</sub>NO<sub>2</sub>: 208.1338; found 208.1346.

<sup>27</sup> C.-H. Ge, X.-D. Zhang, W. Guan, F. Guo, Q.-T. Liu, *Chinese Journal of Chemistry* **2005**, *23*, 1001.

<sup>28</sup> W. Fuhrer, H. W. Gschwend, *J. Org. Chem.* **1979**, *44*, 1133.

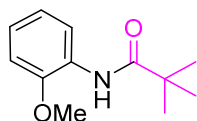
### *N*-(3-Methoxyphenyl)pivalamide (**6b**)<sup>22</sup> (yanping281)



Prepared from *N*-*t*-butyl-*N'*-(3-methoxyphenyl)-*S*-phenylisothiourea (**1i**) (94 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-(3-Methoxyphenyl)pivalamide was obtained in 97% yield (60 mg).

White solid, m.p.: 130-131 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.43 (s, 1H), 7.37 (t, *J* = 2.4 Hz, 1H), 7.17 (t, *J* = 8.0 Hz, 1H), 6.94 (dd, *J* = 8.0, 1.2 Hz, 1H), 6.64 (dd, *J* = 8.0, 2.0 Hz, 1H), 3.77 (s, 3H), 1.21 (s, 9H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 176.6, 160.1, 139.3, 129.4, 111.9, 110.2, 105.5, 55.2, 39.6, 27.5; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>18</sub>NO<sub>2</sub>: 208.1338; found 208.1340.

### *N*-(2-Methoxyphenyl)pivalamide (**6c**)<sup>29</sup> (yanping282)

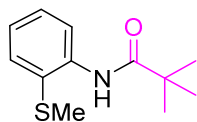


Prepared from *N*-*t*-butyl-*N'*-(2-methoxyphenyl)-*S*-phenylisothiourea (**1j**) (94 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 2/1 as eluent. *N*-(2-Methoxyphenyl)pivalamide was obtained in 71% yield (44 mg).

White solid, m.p.: 39-41 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 8.39 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.13 (s, 1H), 7.01 (td, *J* = 7.6, 1.6 Hz, 1H), 6.94 (td, *J* = 7.6, 1.6 Hz, 1H), 6.87 (dd, *J* = 8.0, 1.2 Hz, 1H), 3.88 (s, 3H), 1.32 (s, 9H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 176.4, 148.0, 127.8, 123.3, 121.0, 119.5, 109.7, 55.7, 27.5, 25.2; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>18</sub>NO<sub>2</sub>: 208.1338; found 208.1344.

<sup>29</sup> G. W. Gribble, F. P. Bousquet, *Tetrahedron*. **1971**, *27*, 3785.

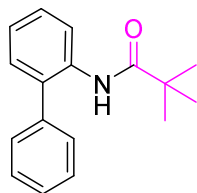
### *N*-[2-(Methylthio)phenyl]pivalamide (**6d**)<sup>30</sup> (yanping283)



Prepared from *N*-*t*-butyl-*N'*-[2-(methylthio)phenyl]-*S*-phenylisothiourea (**1k**) (99 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-[2-(Methylthio)phenyl]pivalamide was obtained in 73% yield (49 mg).

White solid, m.p.: 40-44 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 8.73 (s, 1H), 8.37 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.48 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.29 (dt, *J* = 8.4, 1.6 Hz, 1H), 7.04 (dt, *J* = 7.6, 1.6 Hz, 1H), 2.37 (s, 3H), 1.35 (s, 9H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 176.6, 138.7, 133.1, 129.0, 125.1, 124.0, 120.3, 40.1, 27.6, 18.8; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>18</sub>NOS: 224.1109; found 224.1107.

### *N*-[(1,1'-Biphenyl)-2-yl]pivalamide (**6e**)<sup>31</sup> (yanping296)



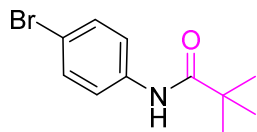
Prepared from *N*-*t*-butyl-*N'*-[(1,1'-biphenyl-2-yl)-*S*-phenylisothiourea (**1l**) (108 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-[(1,1'-Biphenyl)-2-yl]pivalamide was obtained in 82% yield (62 mg).

White solid, m.p.: 70-72 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 8.39 (d, *J* = 8.0 Hz, 1H), 7.50-7.53 (m, 3H), 7.44-7.46 (m, 1H), 7.37-7.41 (m, 3H), 7.26 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.17 (dd, *J* = 7.6, 1.2 Hz, 1H), 1.12 (s, 9H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 176.2, 138.1, 135.1, 132.2, 129.6, 129.3, 129.0, 128.4, 128.0, 123.8, 120.9, 39.7, 27.3; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>17</sub>H<sub>20</sub>NO: 254.1545; found 254.1534.

<sup>30</sup> M. G. Cabiddu, S. Cabiddu, E. Cadoni, S. De Montis, C. Fattuoni, S. Melis, *Tetrahedron* **2003**, *59*, 2893.

<sup>31</sup> W. M. Seganish, P. DeShong, *J. Org. Chem.* **2004**, *69*, 6790.

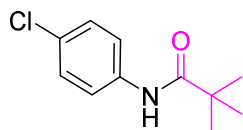
### ***N*-(4-Bromophenyl)pivalamide (6f)<sup>32</sup> (yanping292)**



Prepared from *N*'-(4-bromophenyl)-*N*-*t*-butyl-*S*-phenylisothiourea (**1m**) (109 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-(4-Bromophenyl)pivalamide was obtained in 90% yield (69 mg).

White solid, m.p.: 150-152 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.43 (d, *J* = 2.4 Hz, 2H), 7.40 (d, *J* = 3.2 Hz, 2H), 7.38 (s, 1H), 1.29 (s, 9H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 176.6, 137.1, 131.8, 121.6, 116.7, 39.6, 27.5; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>11</sub>H<sub>15</sub>NOBr: 256.0337; found 256.0347.

### ***N*-(4-Chlorophenyl)pivalamide (6g)<sup>24</sup> (yanping293)**

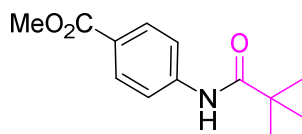


Prepared from *N*-*t*-butyl-*N*'-(4-chlorophenyl)-*S*-phenylisothiourea (**1n**) (95 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-(4-Chlorophenyl)pivalamide was obtained in 91% yield (58 mg).

White solid, m.p.: 144-146 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.47 (d, *J* = 8.8 Hz, 2H), 7.42 (s, 1H), 7.25 (d, *J* = 8.8 Hz, 2H), 1.30 (s, 9H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 176.7, 136.6, 129.1, 128.8, 121.4, 39.6, 27.5; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>11</sub>H<sub>15</sub>NOCl: 212.0842; found 212.0842.

<sup>32</sup> K. Sasaki, D. Crich, *Org. Lett.* **2011**, *13*, 2256.

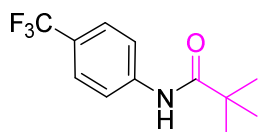
### Methyl 4-pivalamidobenzoate (**6h**) (yanping463)



Prepared from *N*-*t*-butyl-*N'*-(4-methoxycarbonylphenyl)-*S*-phenylisothiourea (**1o**) (103 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. Methyl 4-pivalamidobenzoate was obtained in 70% yield (49 mg).

White solid, m.p.: 126-128 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.98 (d, *J* = 8.8 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 2H), 7.51 (s, 1H), 3.89 (s, 3H), 1.32 (s, 9H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 176.8, 166.6, 142.3, 130.7, 125.5, 119.0, 51.9, 39.8, 27.5; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>18</sub>NO<sub>3</sub>: 236.1281; found 236.1294.

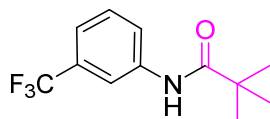
### *N*-[4-(Trifluoromethyl)phenyl]pivalamide (**6i**)<sup>27</sup> (yanping294)



Prepared from *N*-*t*-butyl-*N'*-[4-(trifluoromethyl)phenyl]-*S*-methylisothiourea (**1p**) (87 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (16 mg, 15 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 2/1 as eluent. *N*-[4-(Trifluoromethyl)phenyl]pivalamide was obtained in 48% yield (35 mg).

Yellow solid, m.p.: 154-156 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.66 (d, *J* = 8.8 Hz, 2H), 7.57 (d, *J* = 8.8 Hz, 2H), 7.42 (s, 1H), 1.33 (s, 9H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 177.0, 143.1, 124.2 (q, *J* = 271.2 Hz), 125.5 (q, *J* = 3.8 Hz), 123.3 (q, *J* = 32.0 Hz), 119.9, 39.3, 27.0; <sup>19</sup>F-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) -62.16; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>15</sub>F<sub>3</sub>NO: 246.1100; found 246.1109.

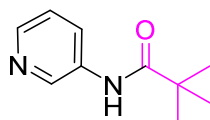
### *N*-[3-(Trifluoromethyl)phenyl]pivalamide (**6j**)<sup>33</sup> (yanping465)



Prepared from *N*-*t*-butyl-*N'*-[3-(trifluoromethyl)phenyl]-*S*-phenylisothiourea (**1q**) (106 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 2/1 as eluent. *N*-[3-(Trifluoromethyl)phenyl]pivalamide was obtained in 85% yield (62 mg).

Yellow solid, m.p.: 107-109 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.85 (s, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.52 (s, 1H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 1.32 (s, 9H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 176.9, 138.6, 131.3 (q, *J* = 32.4 Hz), 129.4, 124.1 (q, *J* = 272.5 Hz), 123.1, 120.7 (q, *J* = 3.8 Hz), 116.8 (q, *J* = 4.0 Hz), 39.7, 27.5; <sup>19</sup>F-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) -62.81; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>15</sub>F<sub>3</sub>NO: 246.1100; found 246.1111.

### *N*-(Pyridin-3-yl)pivalamide (**6k**)<sup>34</sup> (yanping295)



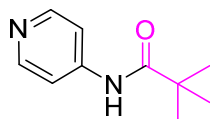
Prepared from *N*-*t*-butyl-*N'*-(3-pyridinyl)-*S*-phenylisothiourea (**1r**) (86 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 1/1 as eluent. *N*-(Pyridin-3-yl)pivalamide was obtained in 89% yield (48 mg).

Brown solid, m.p.: 129-131 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 8.54 (d, *J* = 2.4 Hz, 1H), 8.27 (dd, *J*<sub>1</sub> = 4.4 Hz, *J*<sub>2</sub> = 1.6 Hz, 1H), 8.10 (ddd, *J* = 1.2, 2.4, 8.4 Hz, 1H), 7.82 (s, 1H), 7.20 (dd, *J* = 4.8, 8.4 Hz, 1H), 1.28 (s, 9H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 177.3, 145.0, 141.6, 135.0, 127.6, 123.5, 39.6, 27.4; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>10</sub>H<sub>15</sub>N<sub>2</sub>O: 179.1184; found 179.1176.

<sup>33</sup> R. Jaouhari, P. Quinn, *Heterocycles*, **1994**, *38*, 2243.

<sup>34</sup> S. Thies, H. Sell, C. Schütt, C. Bornholdt, C. Näther, F. Tuzcek, R. Herges, *J. Am. Chem. Soc.* **2011**, *133*, 16243.

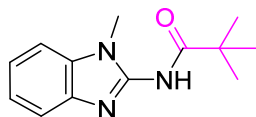
### *N*-(Pyridin-4-yl)pivalamide (**6l**)<sup>35</sup> (yanping287)



Prepared from *N*-*t*-butyl-*N'*-(4-pyridinyl)-*S*-methylisothiourea (**1s**) (67 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (16 mg, 15 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-(Pyridin-4-yl)pivalamide was obtained in 91% yield (49 mg).

White solid, m.p.: 133-135 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 8.47 (d, *J* = 6.4 Hz, 2H), 7.78 (s, 1H), 7.51 (d, *J* = 6.0 Hz, 2H), 1.32 (s, 9H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 177.4, 150.5, 145.3, 113.7, 39.9, 27.4; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>10</sub>H<sub>15</sub>N<sub>2</sub>O: 179.1184; found 179.1179.

### *N*-(1-Methyl-1*H*-benzo[*d*]imidazol-2-yl)pivalamide (**6m**)<sup>36</sup> (yanping286)



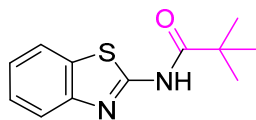
Prepared from *N*-*t*-butyl-*N'*-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)-*S*-methylisothiourea (**1t**) (83 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (16 mg, 15 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-(1-Methyl-1*H*-benzo[*d*]imidazol-2-yl)pivalamide was obtained in 76% yield (53 mg).

Brown solid, m.p.: 114-116 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 10.45 (s, 1H), 7.28 (s, 1H), 7.19 (s, 3H), 3.61 (br, 3H), 1.30 (s, 9H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 189.4, 153.0, 130.8, 130.0, 122.6, 122.57, 112.0, 108.7, 40.8, 28.3, 28.0; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>18</sub>N<sub>3</sub>O: 232.1444; found 232.1442.

<sup>35</sup> K. Walczyński, O. P. Zuiderveld, H. Timmerman, *Eur. J. Med. Chem.* **2005**, *40*, 15.

<sup>36</sup> Q. Wang, S. L. Schreiber, *Org. Lett.* **2009**, *11*, 5178.

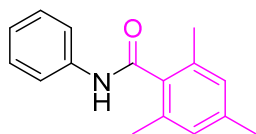
### *N*-(Benzo[*d*]thiazol-2-yl)pivalamide (**6n**)<sup>37</sup> (yanping335)



Prepared from *N*-*t*-butyl-*N'*-(benzo[*d*]thiazol-2-yl)-*S*-methylisothiourea (**1u**) (84 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (16 mg, 15 mol %) according to the general procedure in *o*-xylene at 130 °C. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-(Benzo[*d*]thiazol-2-yl)pivalamide was obtained in 73% yield (51 mg).

White solid, m.p.: 86-89 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 9.45 (s, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.45 (t, *J* = 8.0 Hz, 1H), 7.33 (t, *J* = 8.0 Hz, 1H), 1.38 (s, 9H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 176.7, 158.5, 148.1, 132.1, 126.2, 123.9, 121.4, 120.7, 39.4, 27.1; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>15</sub>N<sub>2</sub>OS: 235.0900; found 235.0907.

### 2,4,6-Trimethyl-*N*-phenylbenzamide (**7a**)<sup>38</sup> (yanping196)



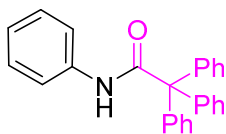
Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), 2,4,6-trimethylbenzoic acid (**3r**) (59 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) in 2-butanol (2.0 mL) at 98 °C according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. 2,4,6-Trimethyl-*N*-phenylbenzamide was obtained in 91% yield (65 mg).

White solid, m.p.: 156-157 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.63 (d, *J* = 7.6 Hz, 2H), 7.52 (s, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.17 (t, *J* = 7.2 Hz, 1H), 6.90 (s, 2H), 2.36 (s, 6H), 2.33 (s, 3H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 168.8, 138.8, 137.9, 135.0, 134.3, 129.1, 128.3, 124.5, 119.8, 21.1, 19.1; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>16</sub>H<sub>18</sub>NO: 240.1388; found: 240.1393.

<sup>37</sup> D. Fajkusova, M. Pesko, S. Keltosova, J. Guo, Z. Oktabec, M. Vejsova, P. Kollar, A. Coffey, J. Csollei, K. Kralova, J. Jampilek, *Bioorg. Med. Chem.* **2012**, *20*, 7059.

<sup>38</sup> L. Zhang, S. Su, H. Wu, S. Wang, *Tetrahedron* **2009**, *65*, 10022.

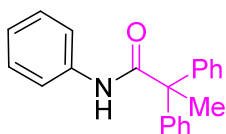
### *N*,2,2,2-Tetraphenylacetamide (**7b**)<sup>35</sup> (yanping266)



Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), 2,2,2-triphenylacetic acid (**2j**) (104 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) in 2-butanol (2.0 mL) at 98 °C according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*,2,2,2-Tetraphenylacetamide was obtained in 90% yield (98 mg).

White solid, m.p.: 167-168 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.40 (d, *J* = 7.6 Hz, 3H), 7.27-7.34 (m, 17H), 7.07 (t, *J* = 7.6 Hz, 1H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 171.4, 143.0, 137.6, 130.5, 128.9, 128.1, 127.2, 124.5, 119.8, 68.6; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>26</sub>H<sub>22</sub>NO: 364.1701; found 364.1709.

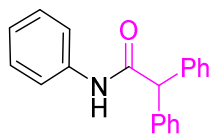
### *N*,2,2-Triphenylpropanamide (**7c**) (yanping264)



Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), 2,2-diphenylpropanoic acid (**2k**) (81 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) in 2-butanol (2.0 mL) at 98 °C according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*,2,2-Triphenylpropanamide was obtained in 95% yield (86 mg).

White solid, m.p.: 115-117 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.30-7.46 (m, 14H), 7.24 (s, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 2.14 (s, 3H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 173.1, 144.6, 137.6, 128.9, 128.7, 128.1, 127.2, 124.4, 119.6, 57.9, 27.1; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>21</sub>H<sub>20</sub>NO: 302.1545; found 302.1558.

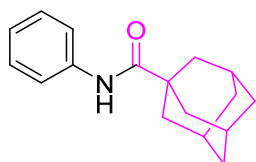
### ***N*,2,2-Triphenylacetamide (7d)<sup>39</sup> (yanping265)**



Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), 2,2-diphenylacetic acid (**2i**) (76 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) in 2-butanol (2.0 mL) at 98 °C according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*,2,2-Triphenylacetamide was obtained in 92% yield (79 mg).

White solid, m.p.: 180-182 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.55 (s, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.28-7.40 (m, 12 H), 7.12 (t, *J* = 7.6 Hz, 1H), 5.11 (s, 1H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 170.1, 139.1, 137.6, 128.93, 128.90, 128.8, 127.4, 124.5, 119.8, 59.9; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>20</sub>H<sub>18</sub>NO: 288.1388; found 288.1389.

### ***N*-Phenyladamantane-1-carboxamide (7e)<sup>40</sup> (yanping263)**



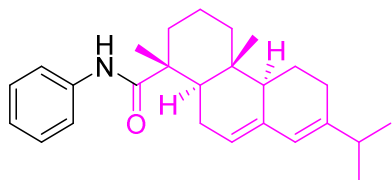
Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiourea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), 1-adamantanecarboxylic acid (**2m**) (65 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) in 2-butanol (2.0 mL) at 98 °C according to the general procedure. The residue was purified by recrystallization from EtOAc/MeOH 9/1. *N*-Phenyladamantane-1-carboxamide was obtained in 94% yield (72 mg).

White solid, m.p.: 189-191 °C, <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 9.06 (s, 1H), 7.64 (s, 2H), 7.26 (s, 2H), 7.02 (s, 1H), 1.90 (s, 9H), 1.70 (s, 6H); <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>): δ (ppm) 175.8, 139.3, 128.3, 123.0, 120.2, 40.8, 38.3, 36.0, 27.7; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>17</sub>H<sub>22</sub>NO: 256.1701; found 256.1702.

<sup>39</sup> W. Ye, J. Mo, T. Zhao, B. Xu, *Chem. Commun.* **2009**, 3246.

<sup>40</sup> W. Wu, Z. Zhang, L. S. Liebeskind, *J. Am. Chem. Soc.* **2011**, *133*, 14256.

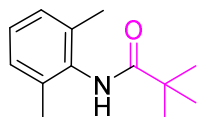
**(1*R*,4*aR*,4*bR*,10*aR*)-7-Isopropyl-1,4*a*-dimethyl-*N*-phenyl-1,2,3,4,4*a*,4*b*,5,6,10,10*a*-decahydrophenanthrene-1-carboxamide (7f)<sup>41</sup> (yanping300)**



Prepared from *N*-*t*-butyl-*S,N'*-diphenylisothiurea (**1d**) (85 mg, 0.3 mmol, 1.0 equiv.), abietic acid (**2i**) (109 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 2/1 as eluent. (1*R*,4*aR*,4*bR*,10*aR*)-7-Isopropyl-1,4*a*-dimethyl-*N*-phenyl-1,2,3,4,4*a*,4*b*,5,6,10,10*a*-decahydrophenanthrene-1-carboxamide was obtained in 62% yield (70 mg).

White solid, m.p.: 86-89 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.52-7.54 (m, 2H), 7.49 (s, 1H), 7.28-7.34 (m, 2H), 7.11 (t, *J* = 7.6 Hz, 1H), 5.78 (s, 1H), 5.35 (t, *J* = 2.8 Hz, 1H), 7.24 (t, *J* = 7.2 Hz, 1H), 2.10 (t, *J* = 4.8 Hz, 3H), 1.91-1.95 (m, 3H), 1.82-1.86 (m, 1H), 1.77 (s, 1H), 1.65-1.68 (m, 3H), 1.41 (s, 3H), 1.33 (s, 3H), 1.20-1.28 (m, 5H), 1.02-1.04 (q, *J* = 3.2 Hz, 4H), 0.88-0.92 (m, 4H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 176.5, 145.2, 138.0, 135.5, 128.8, 124.1, 122.4, 120.3, 120.2, 51.0, 47.2, 46.0, 38.2, 37.5, 35.4, 34.8, 34.7, 27.4, 26.4, 25.4, 22.4, 22.1, 21.4, 20.8, 18.3, 17.1, 14.1. HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>26</sub>H<sub>36</sub>NO: 378.2797; found 378.2780.

***N*-(2,6-Dimethylphenyl)pivalamide (7g)<sup>42</sup> (yanping303)**



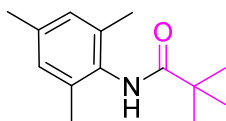
Prepared from *N*-*t*-butyl-*N'*-(2,6-dimethylphenyl)-*S*-phenylisothiurea (**1v**) (94 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) in 2-butanol (2.0 mL) at 98 °C according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-(2,6-Dimethylphenyl)pivalamide was obtained in 81% yield (50 mg).

White solid, m.p.: 193-195 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.13 (s, 1H), 7.08 (dd, *J*<sub>1</sub> = 9.2 Hz, *J*<sub>2</sub> = 5.6 Hz, 1H), 7.03-7.05 (m, 2H), 2.15 (s, 6H), 1.31 (s, 9H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 176.5, 135.4, 134.1, 127.8, 126.8, 39.0, 27.5, 18.0; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>20</sub>NO: 206.1545; found 206.1537.

<sup>41</sup> F. Paul, *Synth. Commun.* **1995**, 25, 959.

<sup>42</sup> J. E. Steves, M. D. Kennedy, K. P. Chiang, W. S. Kassel, W. G. Dougherty, T. J. Dudley, D. L. Zubris, *Dalton Transactions* **2009**, 1214.

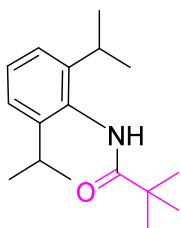
### *N*-Mesitylpivalamide (**7h**)<sup>43</sup> (yanping304)



Prepared from *N*-*t*-butyl-*N'*-(2,4,6-trimethylphenyl)-*S*-phenylisothiurea (**1w**) (118 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) in 2-butanol (2.0 mL) at 98 °C according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-Mesitylpivalamide was obtained in 85% yield (56 mg).

White solid, m.p.: 184-186 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 6.94 (s, 1H), 6.85 (s, 2H), 2.26 (s, 3H), 2.12 (s, 6H), 1.31 (s, 9H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 176.6, 136.4, 135.1, 131.4, 128.7, 39.1, 27.7, 20.8, 18.0; HRMS (ESI): m/z [M+H]<sup>+</sup> calcd for C<sub>14</sub>H<sub>22</sub>NO: 220.1701; found 220.1699.

### *N*-(2,6-Diisopropylphenyl)pivalamide (**7i**)<sup>44</sup> (yanping305)



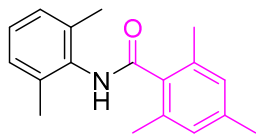
Prepared from *N*-*t*-butyl-*N'*-(2,6-diisopropylphenyl)-*S*-phenylisothiurea (**1x**) (132 mg, 0.3 mmol, 1.0 equiv.), pivalic acid (**2a**) (37 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) in 2-butanol (2.0 mL) at 98 °C according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-(2,6-Diisopropylphenyl)pivalamide was obtained in 88% yield (69 mg).

White solid, m.p.: 269-270 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.24 (t, *J* = 7.2 Hz, 1H), 7.13 (d, *J* = 7.6 Hz, 2H), 6.82 (s, 1H), 2.98 (sept, *J* = 7.2 Hz, 2H), 1.32 (s, 9H), 1.16 (d, *J* = 7.2 Hz, 12H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 177.1, 146.2, 131.5, 128.0, 123.3, 39.2, 28.7, 27.8, 23.5; HRMS (ESI): m/z [M+H]<sup>+</sup> calcd for C<sub>17</sub>H<sub>28</sub>NO: 262.2171; found 262.2174.

<sup>43</sup> B. T. Gowda1, K. M. Usha1, K. Jyoth, *Zeitschrift fuer Naturforschung, A: Physical Sciences*. **2004**, 59, 69.

<sup>44</sup> C. Loh, S. Seupel, H. Görls, S. Kriek, M. Westerhausen, *Eur. J. Inorg. Chem.* **2014**, 2014, 1312.

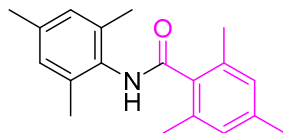
***N*-(2,6-Dimethylphenyl)-2,4,6-trimethylbenzamide (7j)<sup>45</sup> (yanping307)**



Prepared from *N*-*t*-butyl-*N'*-(2,6-dimethylphenyl)-*S*-phenylisothiourea (**1v**) (94 mg, 0.3 mmol, 1.0 equiv.), 2,4,6-trimethylbenzoic acid (**3r**) (59 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) in 2-butanol (2.0 mL) at 98 °C according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-(2,6-Dimethylphenyl)-2,4,6-trimethylbenzamide was obtained in 84% yield (67 mg).

White solid, m.p.: 197-199 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.15 (t, *J* = 4.8 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 2H), 7.11 (s, 1H), 6.89 (s, 2H), 2.42 (s, 6H), 2.35 (s, 6H), 2.32 (s, 3H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 168.6, 138.4, 135.1, 134.8, 134.4, 133.6, 128.40, 128.38, 127.2, 20.9, 19.8, 19.3; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>18</sub>H<sub>22</sub>NO: 268.1701; found 268.1707.

***N*-Mesityl-2,4,6-trimethylbenzamide (7k)<sup>46</sup> (yanping308)**



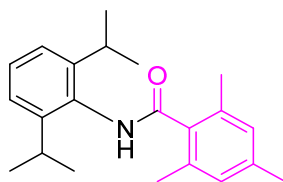
Prepared from *N*-*t*-butyl-*N'*-(2,4,6-trimethylphenyl)-*S*-phenylisothiourea (**1w**) (118 mg, 0.3 mmol, 1.0 equiv.), 2,4,6-trimethylbenzoic acid (**3r**) (59 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) in 2-butanol (2.0 mL) at 98 °C according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-Mesityl-2,4,6-trimethylbenzamide was obtained in 86% yield (72 mg).

White solid, m.p.: 205-207 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 6.99 (s, 1H), 6.92 (s, 2H), 6.87 (s, 2H), 2.41 (s, 6H), 2.30 (s, 9H), 2.28 (s, 3H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 168.7, 138.3, 136.8, 134.9, 134.4, 130.9, 129.1, 128.4, 20.9, 20.7, 19.8, 19.2 (1C missing because of overlap); HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>19</sub>H<sub>24</sub>NO: 282.1858; found 282.1855.

<sup>45</sup> Y.-y. Wang, S.-a. Lin, F.-m. Zhu, H.-y. Gao, Q. Wu, *Eur. Poly. J.* **2008**, *44*, 2308.

<sup>46</sup> C. R. Hauser, D. S. Hoffenberg, *J. Am. Chem. Soc.* **1955**, *77*, 4885.

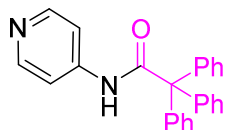
### *N*-(2,6-Diisopropylphenyl)-2,4,6-trimethylbenzamide (7l)<sup>47</sup> (yanping309)



Prepared from *N*-*t*-butyl-*N'*-(2,6-diisopropylphenyl)-*S*-phenylisothiourea (**1x**) (132 mg, 0.3 mmol, 1.0 equiv.), 2,4,6-trimethylbenzoic acid (**3r**) (59 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) in 2-butanol (2.0 mL) at 98 °C according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 3/1 as eluent. *N*-(2,6-Diisopropylphenyl)-2,4,6-trimethylbenzamide was obtained in 89% yield (86 mg).

White solid, m.p.: 202-205 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 7.37 (t, *J* = 7.6 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.09 (s, 1H), 6.95 (s, 2H), 3.40 (sept, *J* = 7.2 Hz, 2H), 2.51 (s, 6H), 2.36 (s, 3H), 1.29 (d, *J* = 7.2 Hz, 12H) <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 169.8, 146.0, 138.5, 134.65, 134.61, 130.4, 128.7, 128.3, 123.5, 28.5, 23.8, 20.9, 19.7; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>22</sub>H<sub>30</sub>NO: 324.2327; found 324.2336.

### *N*,2,2,2-Triphenyl-*N*-(pyridin-4-yl)acetamide (7m)<sup>48</sup> (yanping623)



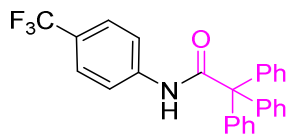
Prepared from *N*-*t*-butyl-*N'*-(4-pyridinyl)-*S*-methylisothiourea (**1s**) (67 mg, 0.3 mmol, 1.0 equiv.), 2,2,2-triphenylacetic acid (**2j**) (104 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (16 mg, 15 mol %) in 2-butanol (2.0 mL) at 98 °C according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 1/3 as eluent. *N*,2,2,2-triphenyl-*N*-(pyridin-4-yl)acetamide was obtained in 89% yield (97 mg).

White solid, m.p.: 186-187 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 8.47 (d, *J* = 5.9 Hz, 2H), 7.55 (s, 1H), 7.24-7.38 (m, 17H), <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 172.2, 150.0, 142.3, 130.5, 130.3, 128.3, 127.49, 127.48, 68.8; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>25</sub>H<sub>21</sub>N<sub>2</sub>O: 365.1576; found 365.1642.

<sup>47</sup> G. Schäfer, C. Matthey, J. W. Bode, *Angew. Chem. Int. Ed.* **2012**, *51*, 9173.

<sup>48</sup> C. A. Faler and M. M. Joullié, *Tetrahedron Letters*, **2006**, *47*, 7229-7231

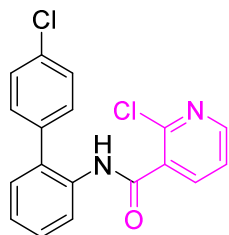
### *N*,2,2,2-Triphenyl-*N*-[4-(trifluoromethyl)phenyl]acetamide (**7n**) (yanping624)



Prepared from *N*-*t*-butyl-*N*'-[4-(trifluoromethyl)phenyl]-*S*-methylisothiurea (**1p**) (87 mg, 0.3 mmol, 1.0 equiv.), 2,2,2-triphenylacetic acid (**2j**) (104 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (16 mg, 15 mol %) in 2-butanol (2.0 mL) at 98 °C according to the general procedure. The residue was purified by column chromatography on silica gel with heptane/EtOAc 1/1 as eluent. *N*,2,2,2-triphenyl-*N*-(4-(trifluoromethyl)phenyl)acetamide was obtained in 48% yield (62 mg).

White solid, m.p.: 168-171 °C, <sup>1</sup>H-NMR (400 MHz, DMSO): δ (ppm) 9.43 (s, 1H), 7.79 (d, *J* = 8.8 Hz, 2H), 7.63 (d, *J* = 8.8 Hz, 2H), 7.30-7.36 (m, 12H), 7.24-7.27 (m, 3H); <sup>13</sup>C-NMR (100 MHz, DMSO): δ (ppm) 171.6, 143.0, 142.3, 130.1, 127.8, 126.6, 125.6 (q, *J* = 15.6 Hz), 123.5 (q, *J* = 127.2 Hz), 120.8, 68.4; <sup>19</sup>F-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) -100.0; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>27</sub>H<sub>21</sub>F<sub>3</sub>NO: 432.1497; found 432.1573.

### 2-Chloro-*N*-(4'-chloro-[1,1'-biphenyl]-2-yl)nicotinamide (**8**),<sup>49</sup> yanping319-2

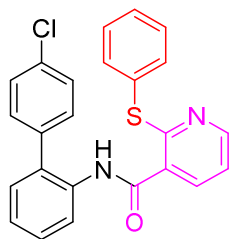


Prepared from *N*-*tert*-butyl-*N*'-(4'-chloro[1,1'-biphenyl]-2-yl)-*S*-phenylisothiurea (**1z**) (85 mg, 0.3 mmol, 1.0 equiv.), 2-chloronicotinic acid (**3s**) (57 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) in 2-butanol at 90 °C under oxygen atmosphere according to the general procedure. The residue was purified by column chromatography on silica gel with Heptane/EtOAc 3:1 to 1:1 as eluent. 2-Chloro-*N*-(4'-chloro-[1,1'-biphenyl]-2-yl)nicotinamide was obtained in 74% yield.

White solid, m.p.: 143-145 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 8.39 (dd, *J* = 2.4, 4.8 Hz, 1H), 8.36 (d, *J* = 8.0 Hz, 1H), 8.23 (s, 1H), 8.08 (d, *J* = 7.6 Hz, 1H), 7.44-7.47 (m, 1H), 7.43 (s, 1H), 7.41 (s, 1H), 7.31-7.35 (m, 3H), 7.28 (d, *J* = 8.4 Hz, 2H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 162.5, 151.1, 146.6, 139.8, 136.3, 134.25, 134.18, 132.4, 131.1, 130.7, 130.1, 129.1, 128.7, 125.3, 122.7, 122.4; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>18</sub>H<sub>12</sub>N<sub>2</sub>OCl<sub>2</sub>: 343.0405; found 343.0409.

<sup>49</sup> P. Debnath, M. Baeten, N. Lefèvre, S. V. Daele, B. U. W. Maes, *Adv. Synth. Catal.* **2015**, 357, 197.

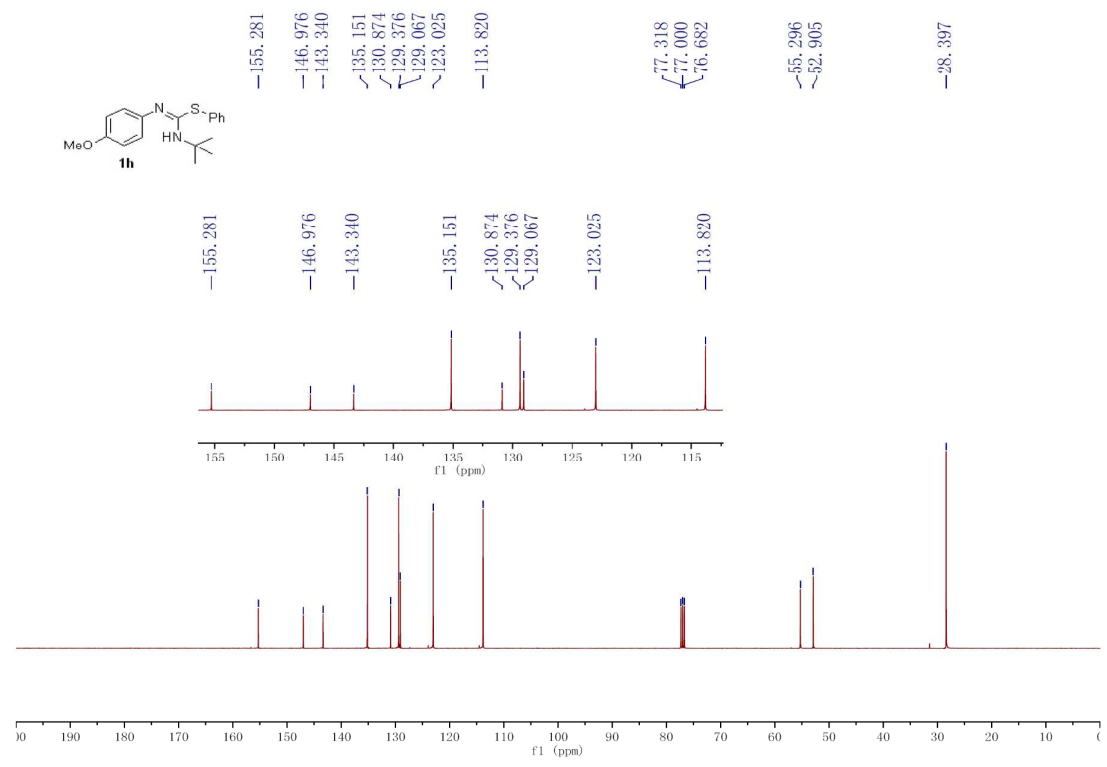
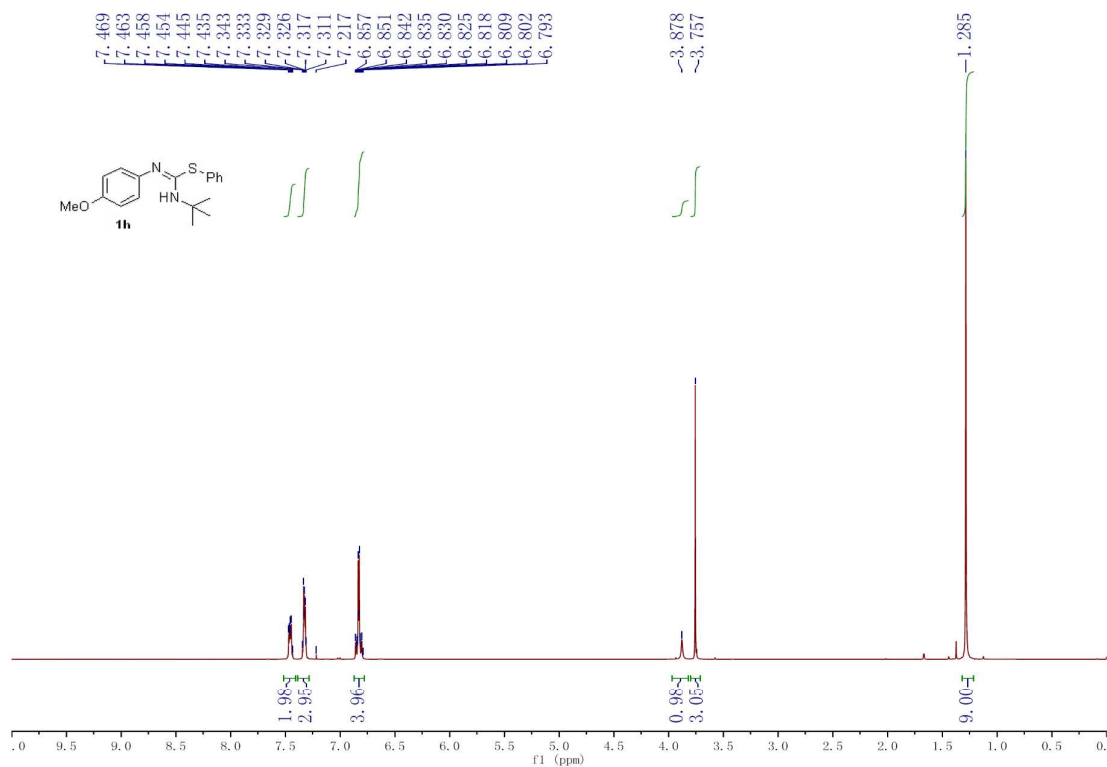
***N*-(4'-Chloro-[1,1'-biphenyl]-2-yl)-2-(phenylthio)nicotinamide (9), yanping319-1**

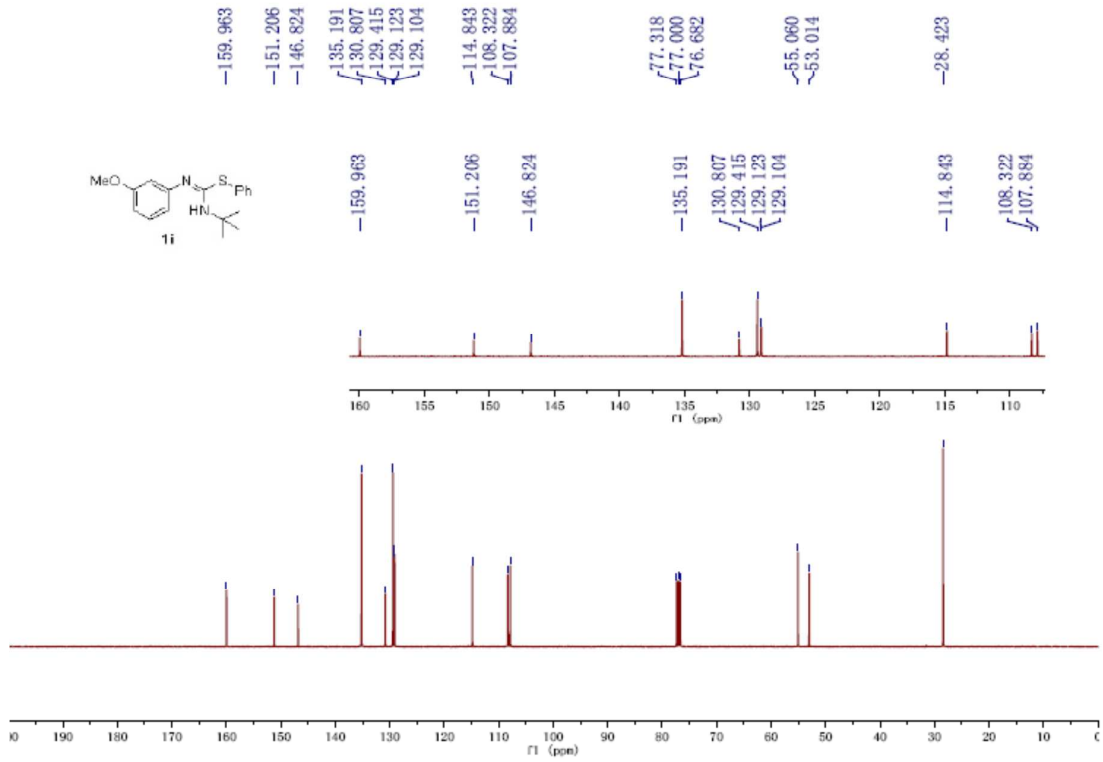
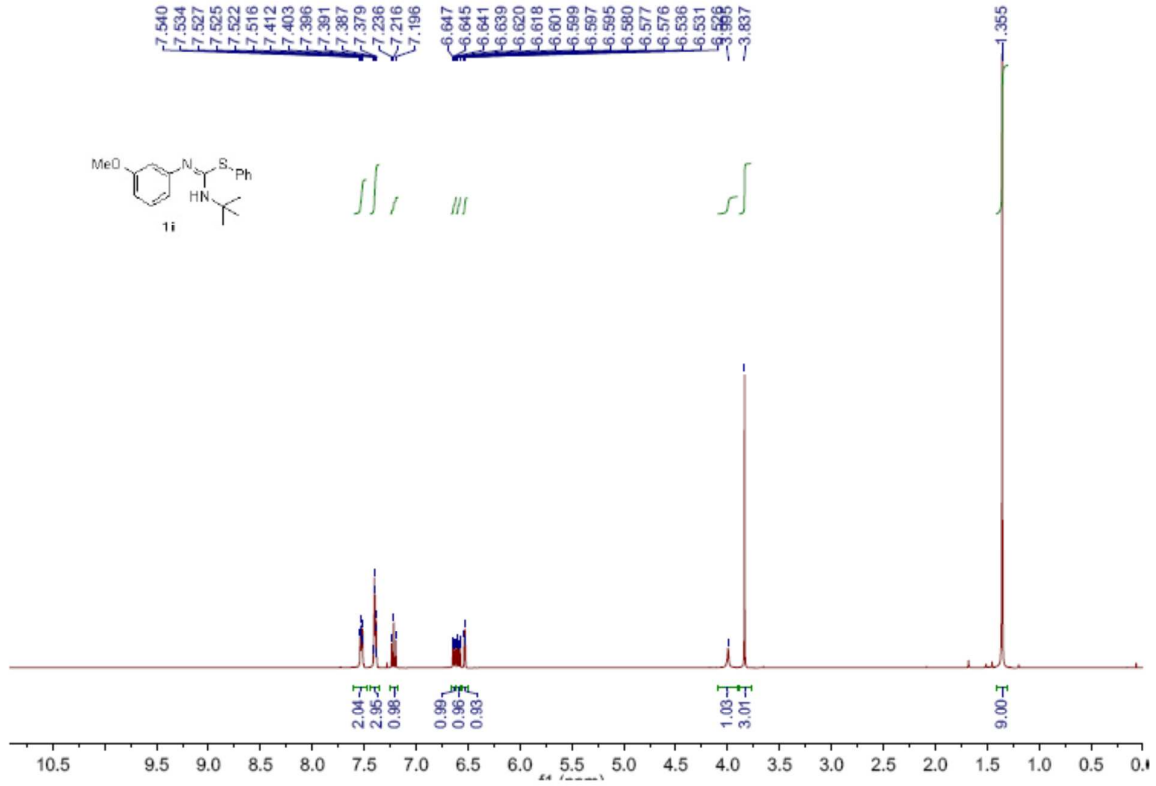


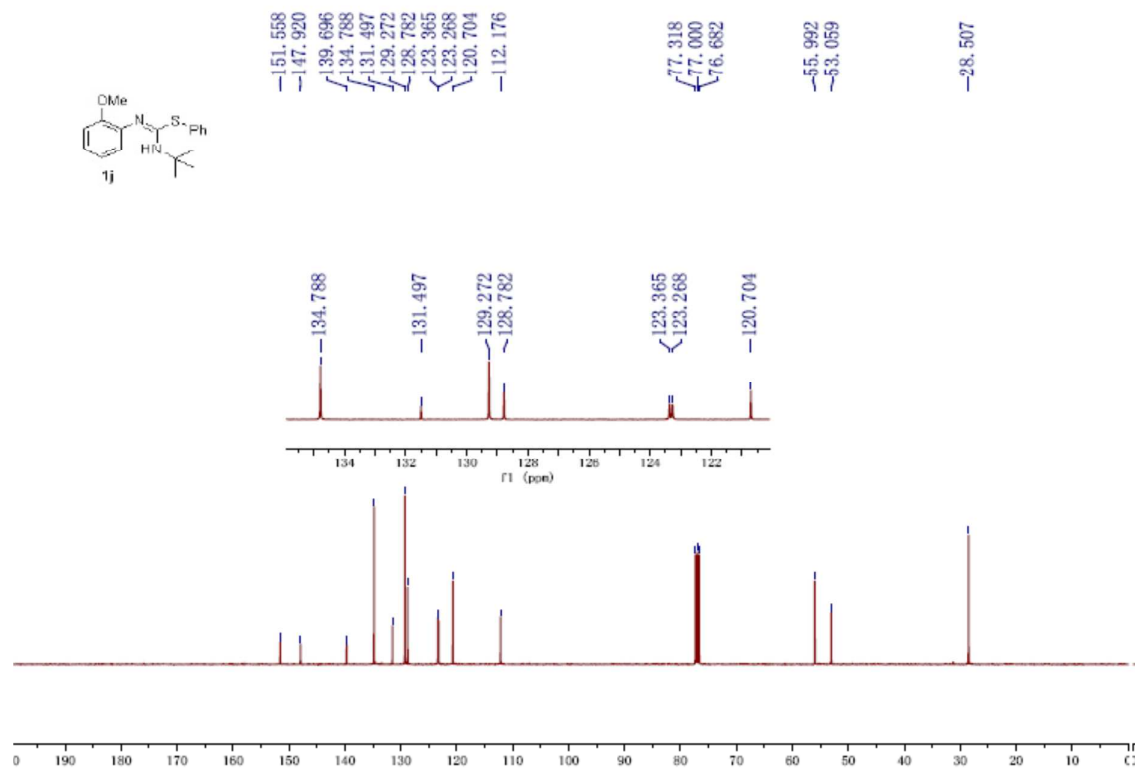
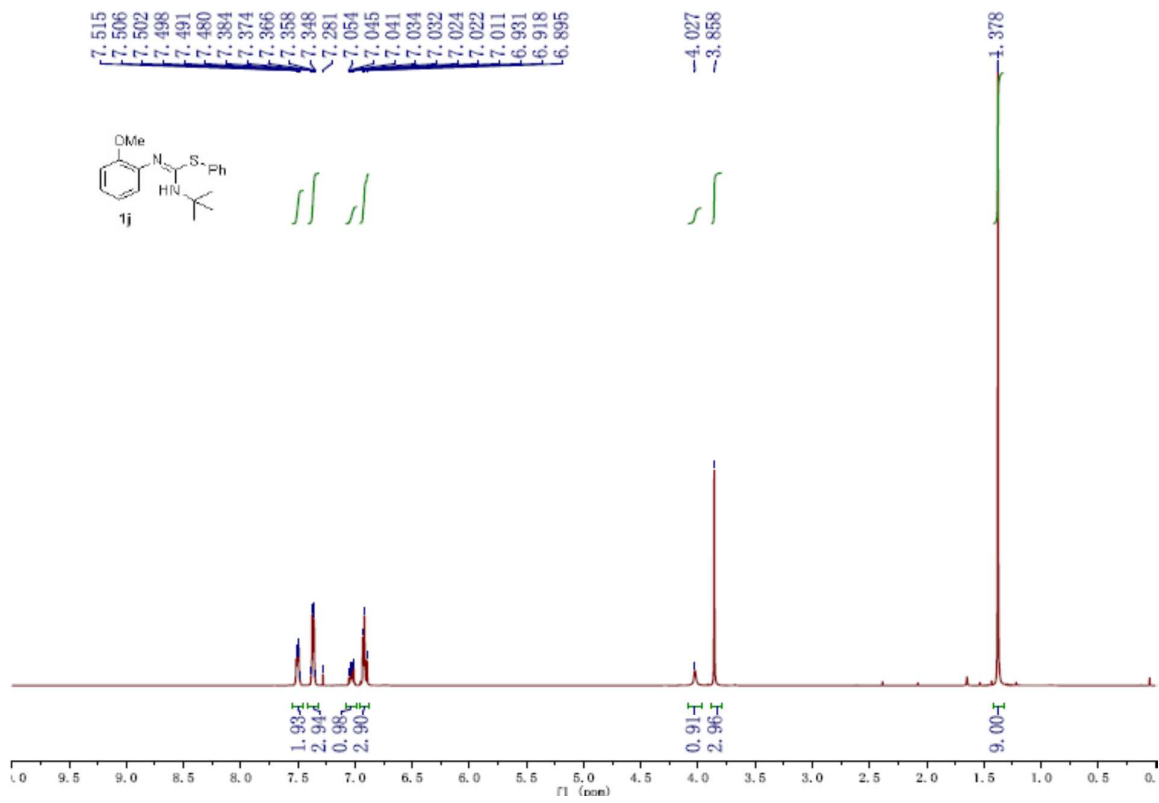
Prepared from *N-tert*-butyl-*N'*-(4'-chloro[1,1'-biphenyl]-2-yl)-*S*-phenylisothiourea (**1z**) (85 mg, 0.3 mmol, 1.0 equiv.), 2-chloronicotinic acid (**3s**) (57 mg, 0.36 mmol, 1.2 equiv.) and Fe(acac)<sub>3</sub> (2.65 mg, 2.5 mol %) in 2-butanol at 90 °C under Ar according to the general procedure. The residue was purified by column chromatography on silica gel with Heptane/EtOAc 3:1 to 1:1 as eluent. *N*-(4'-Chloro-[1,1'-biphenyl]-2-yl)-2-(phenylthio)nicotinamide was obtained in 72% yield.

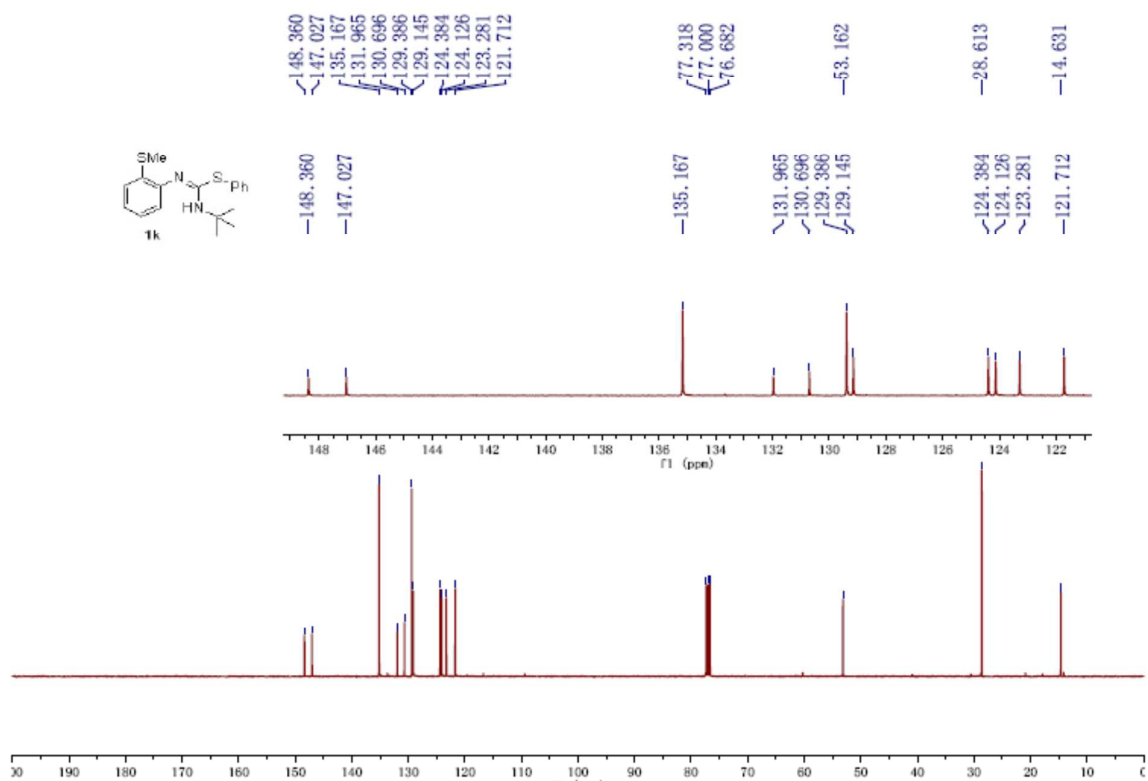
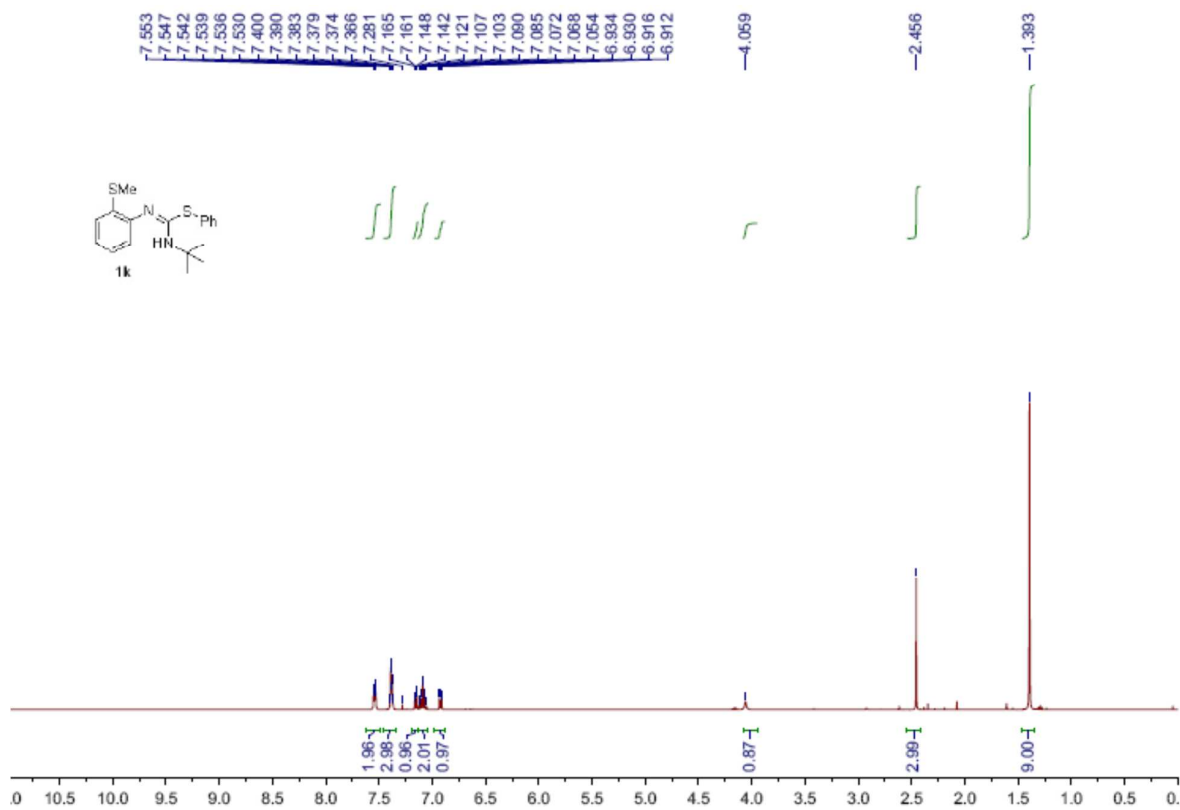
White solid, m.p.: 180-183 °C, <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): δ (ppm) 8.74 (s, 1H), 8.56 (dd, *J* = 1.2, 4.8 Hz, 1H), 8.52 (d, *J* = 8.4 Hz, 1H), 8.38 (dd, *J* = 3.2, 4.8 Hz, 1H), 8.26 (dd, *J* = 1.6 Hz, 7.6 Hz, 1H), 7.85 (dd, *J* = 1.6 Hz, 7.6 Hz, 1H), 7.62 (dd, *J* = 1.2, 8.0 Hz, 1H), 7.43-7.49 (m, 2H), 7.38 (m, overlap, 5H), 7.27 (t, *J* = 7.2 Hz, 1H), 7.07-7.12 (m, 2H); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): δ (ppm) 162.6, 156.5, 151.5, 151.3, 147.1, 140.2, 136.9, 135.4, 134.5, 132.6, 130.9, 130.2, 129.2, 128.8, 128.5, 126.1, 125.0, 122.9, 122.4, 120.3; HRMS (ESI): *m/z* [M+H]<sup>+</sup> calcd for C<sub>24</sub>H<sub>18</sub>N<sub>2</sub>OCIS: 417.0823; found 417.0820.

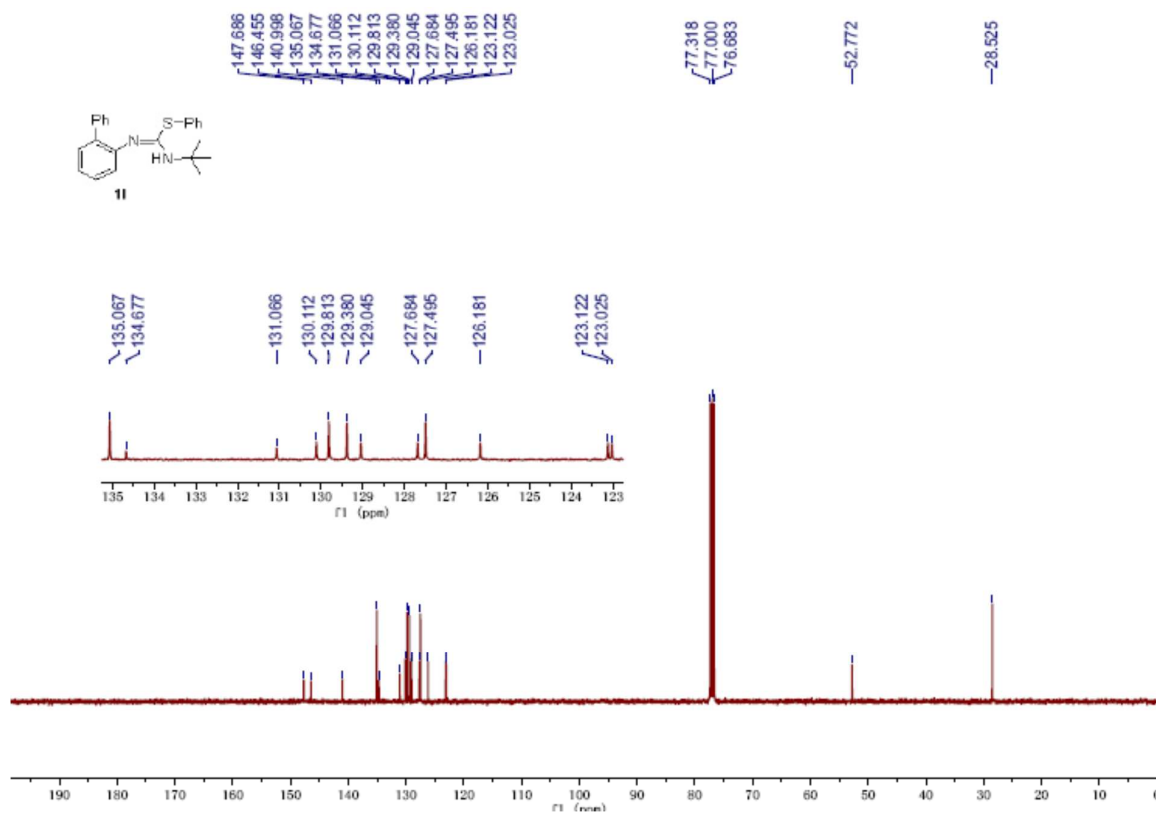
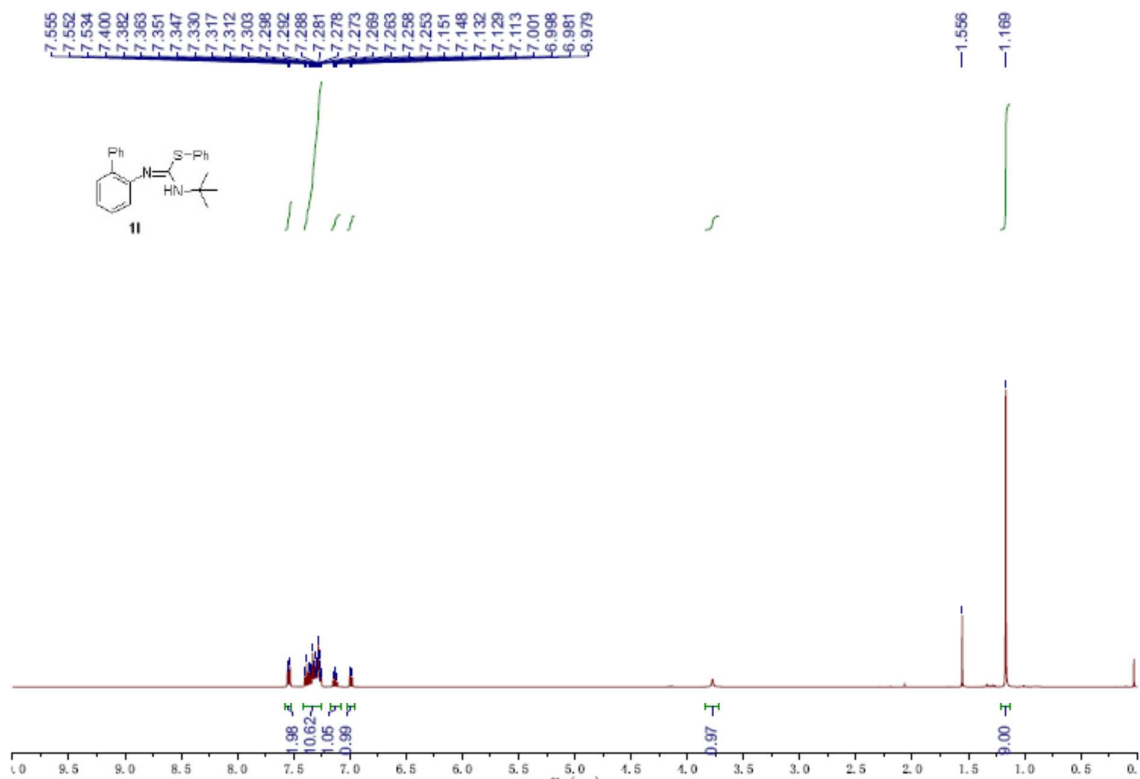
## 9. Copies of NMR spectra

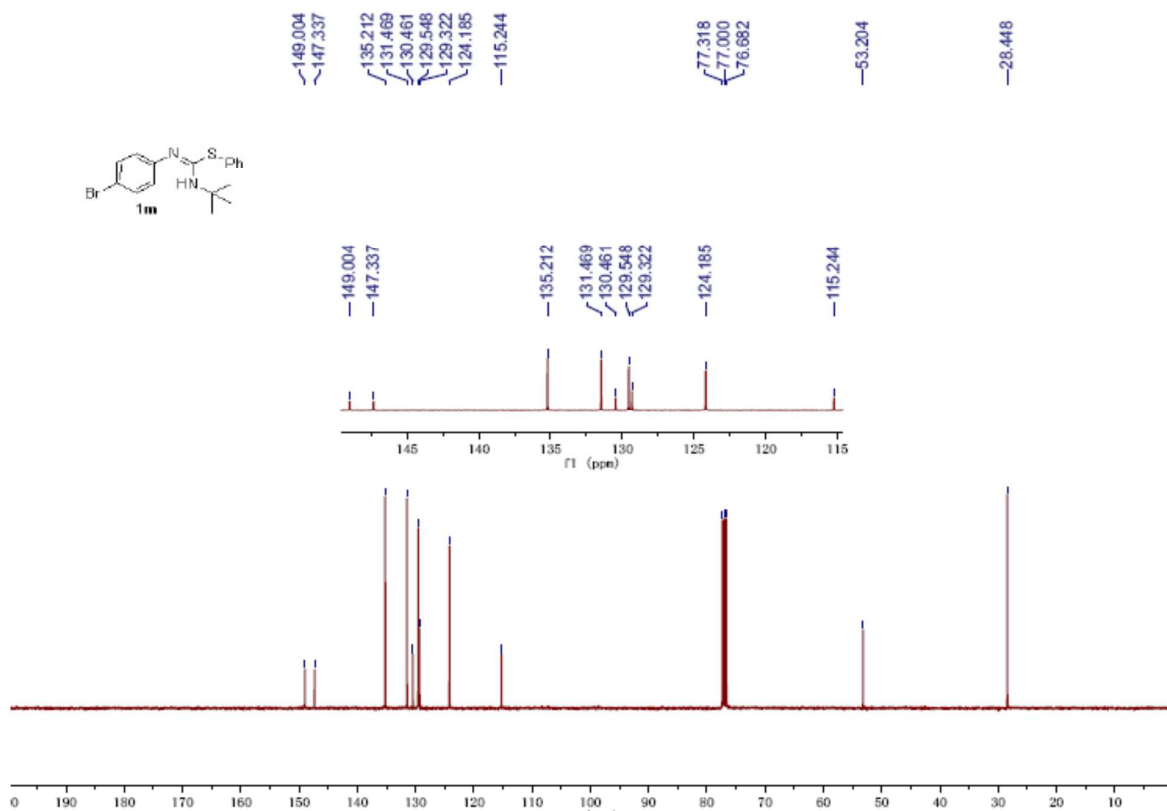
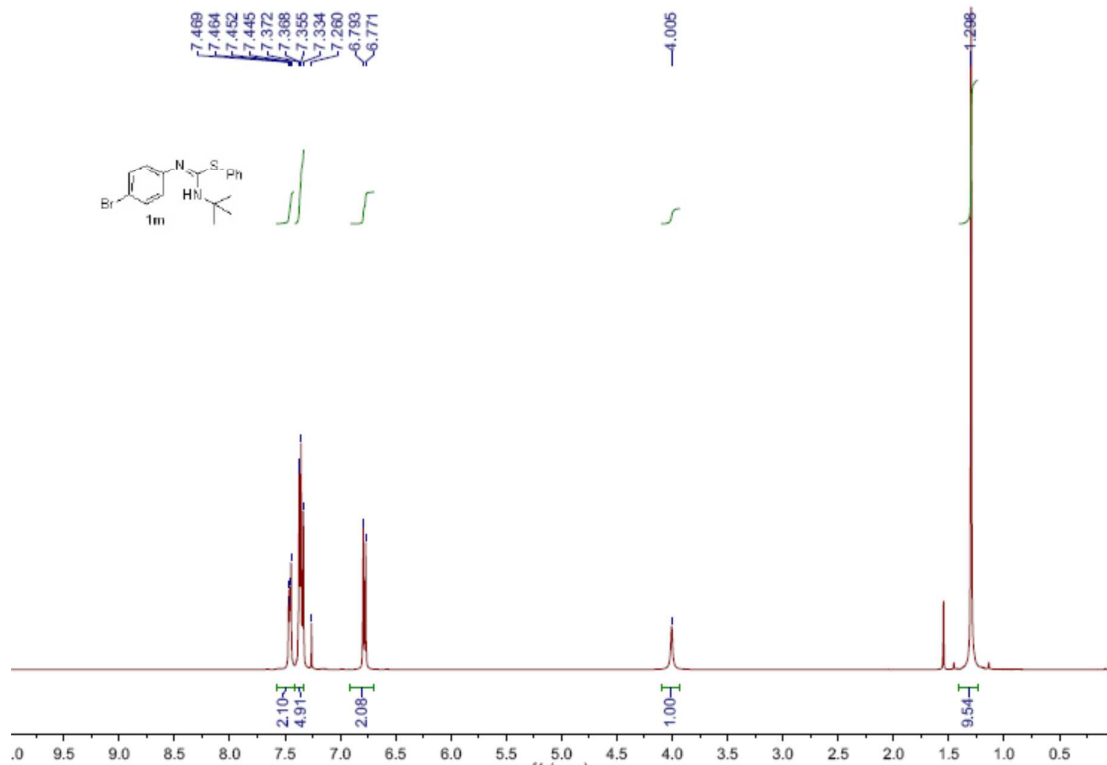


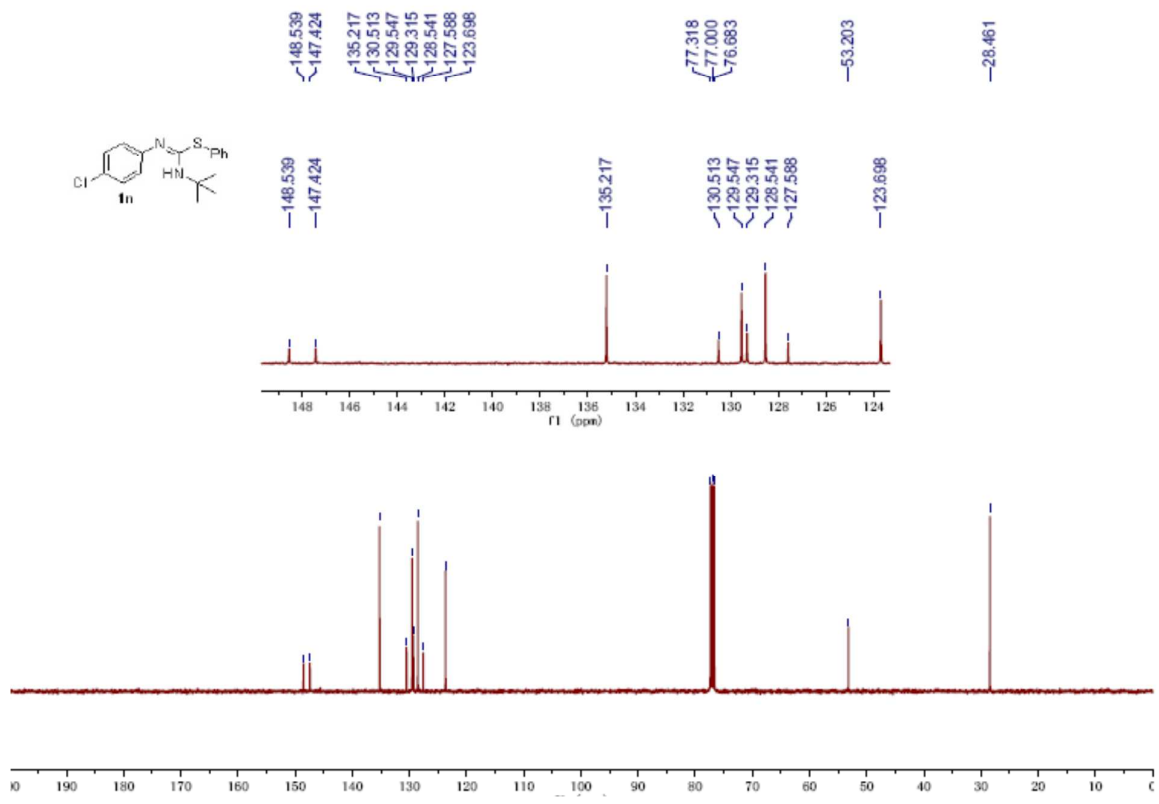
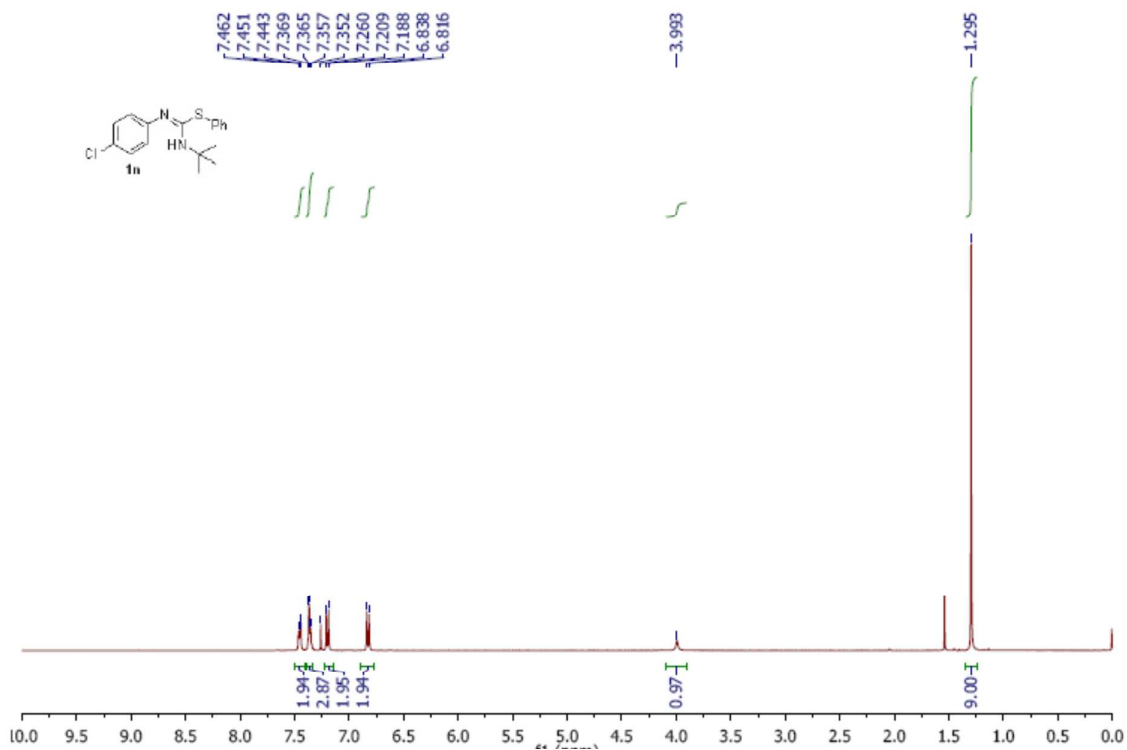


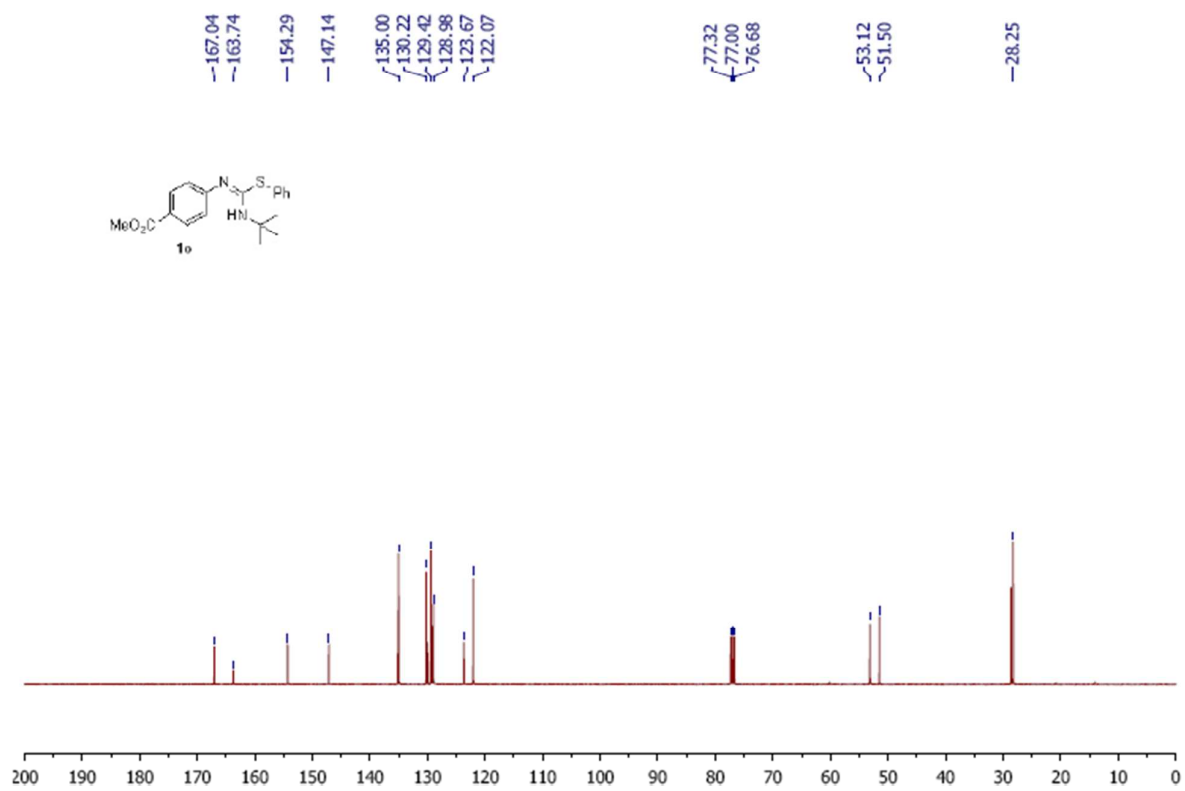
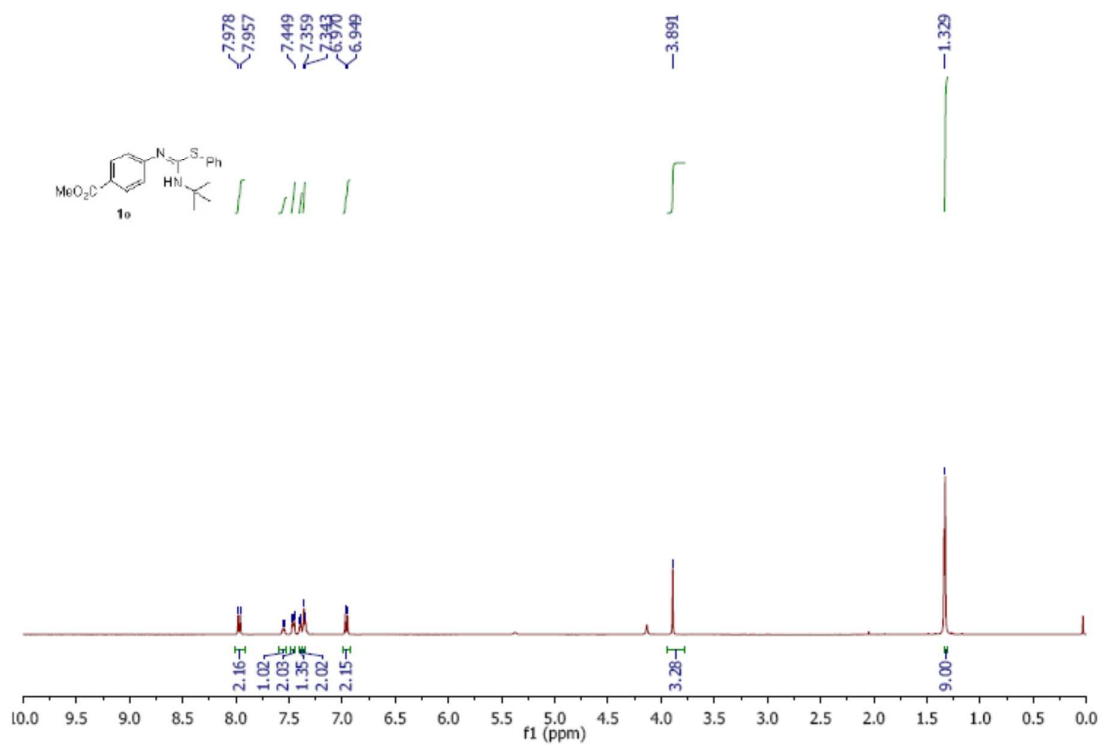


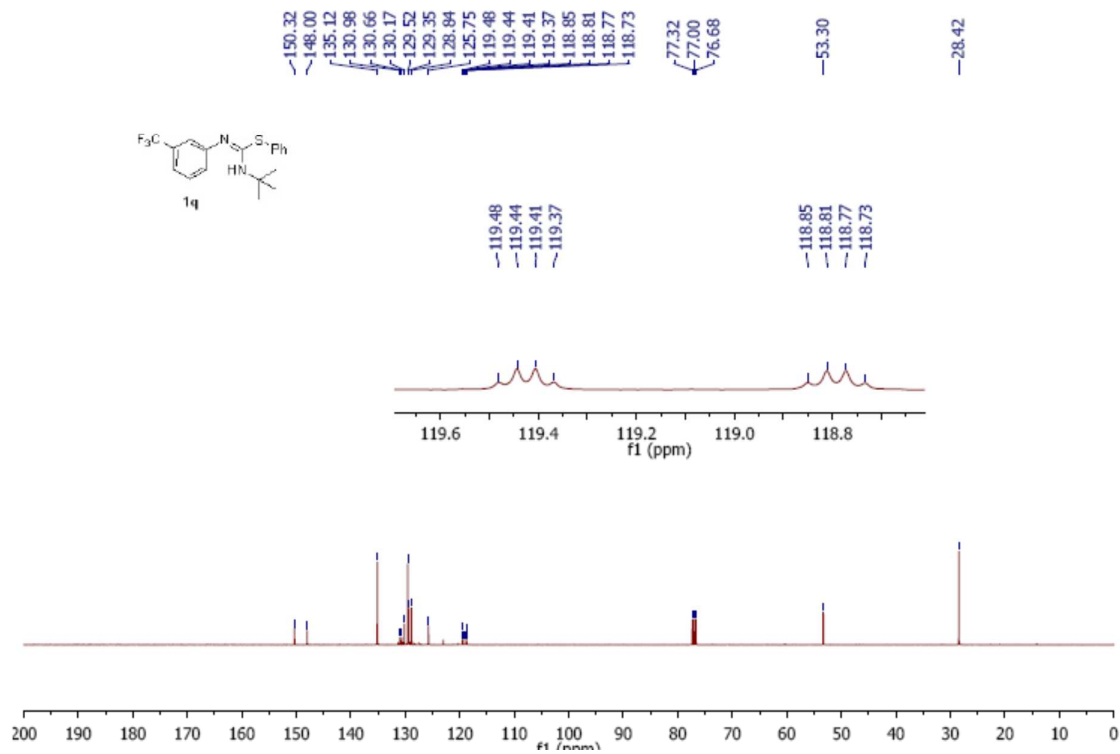
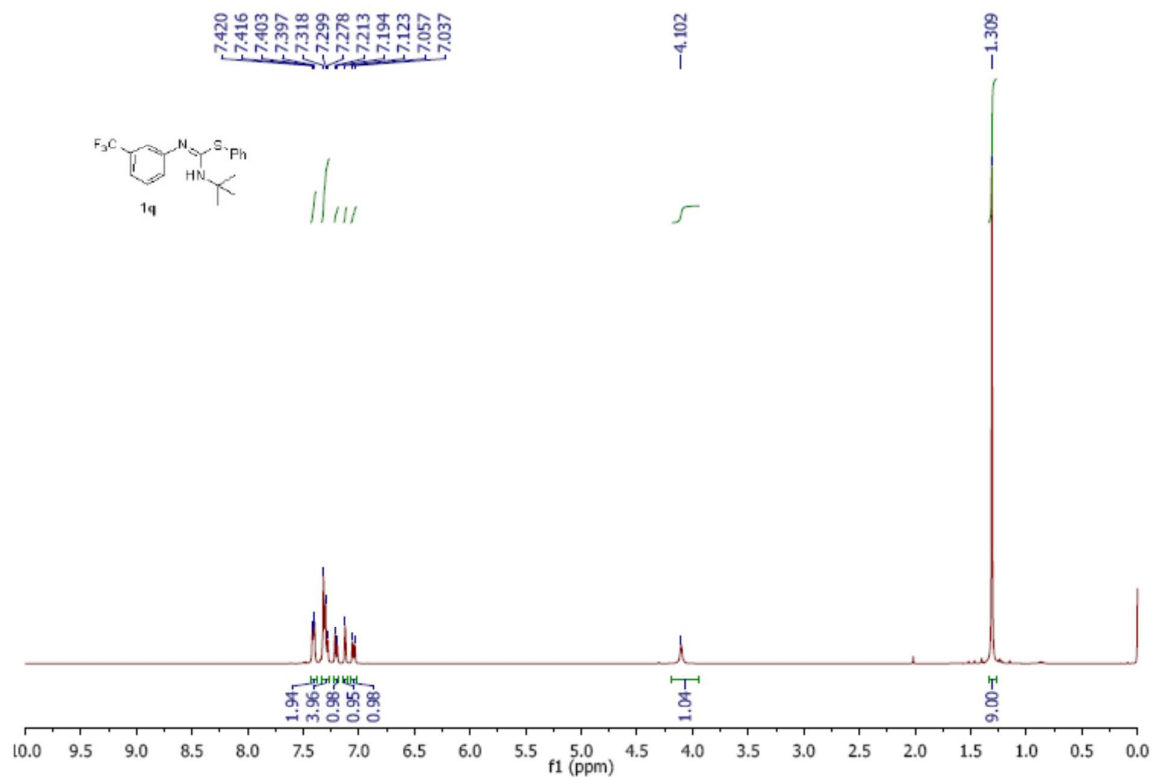


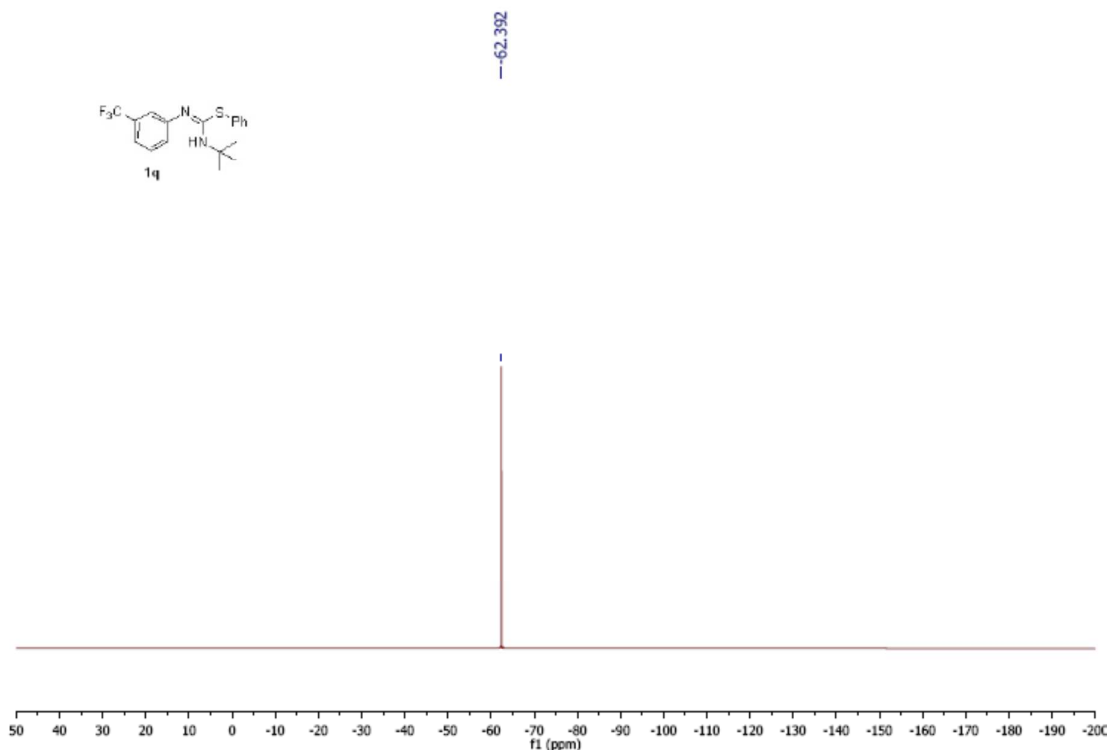


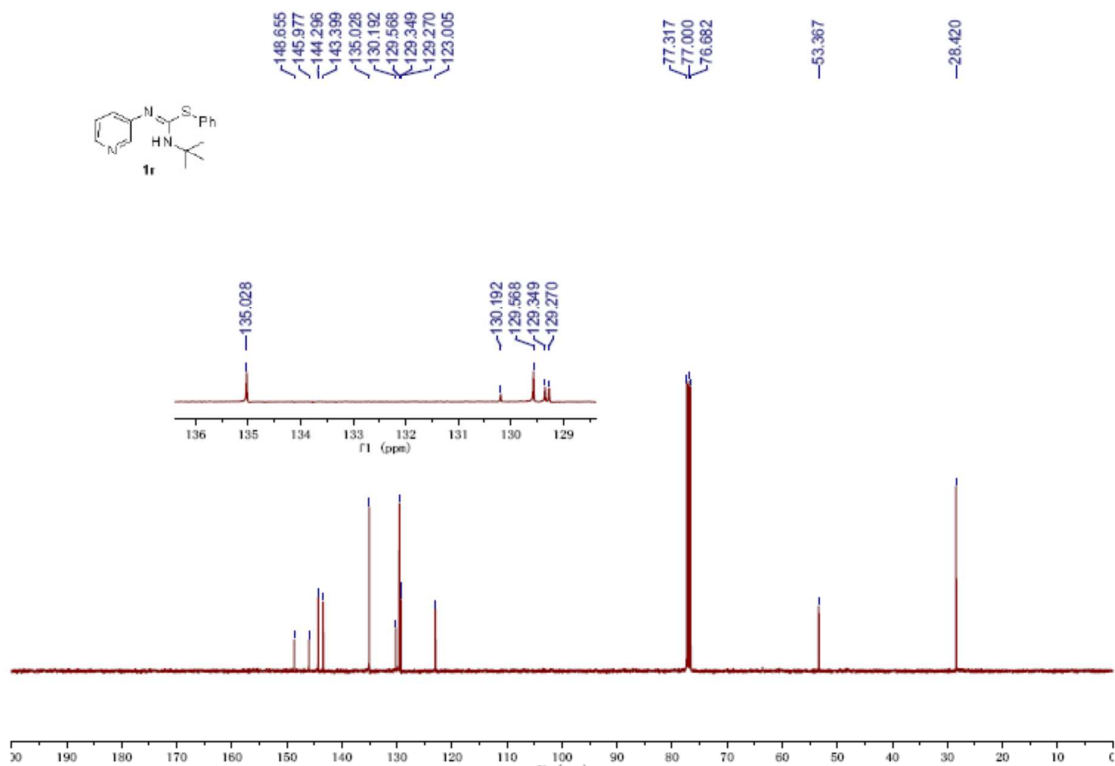
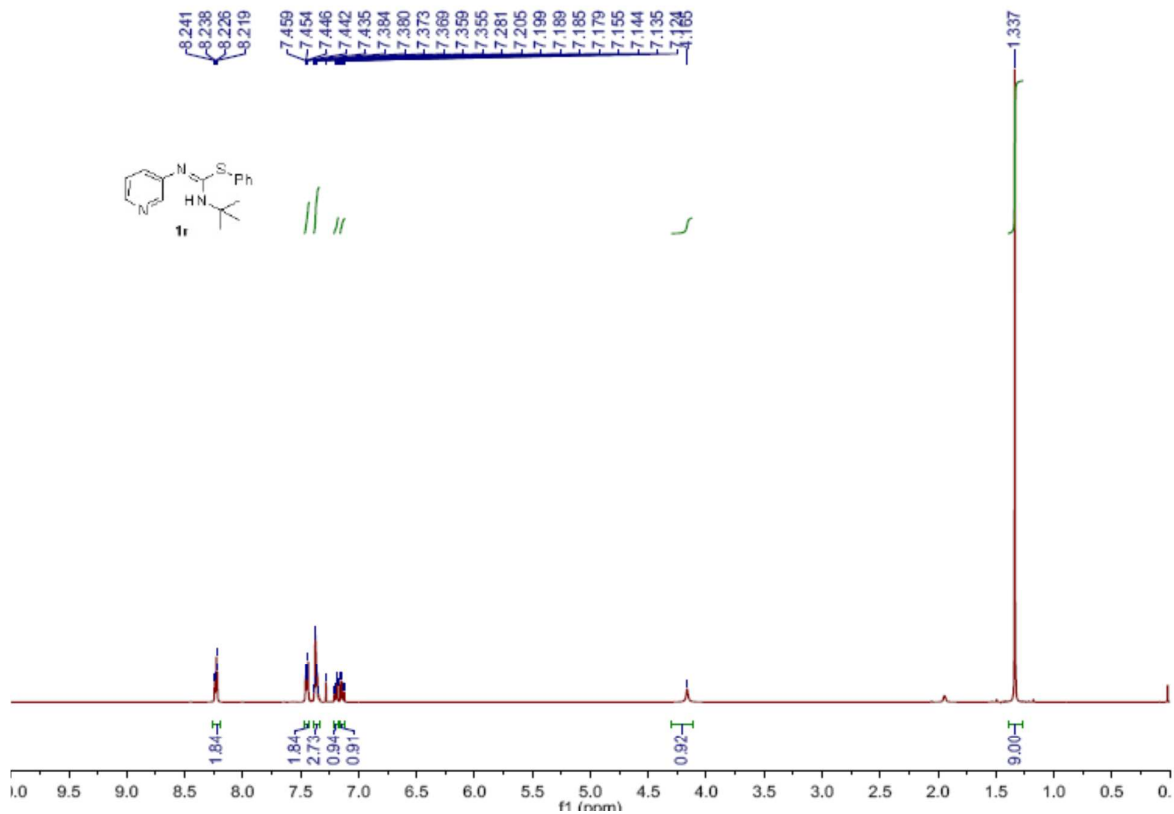


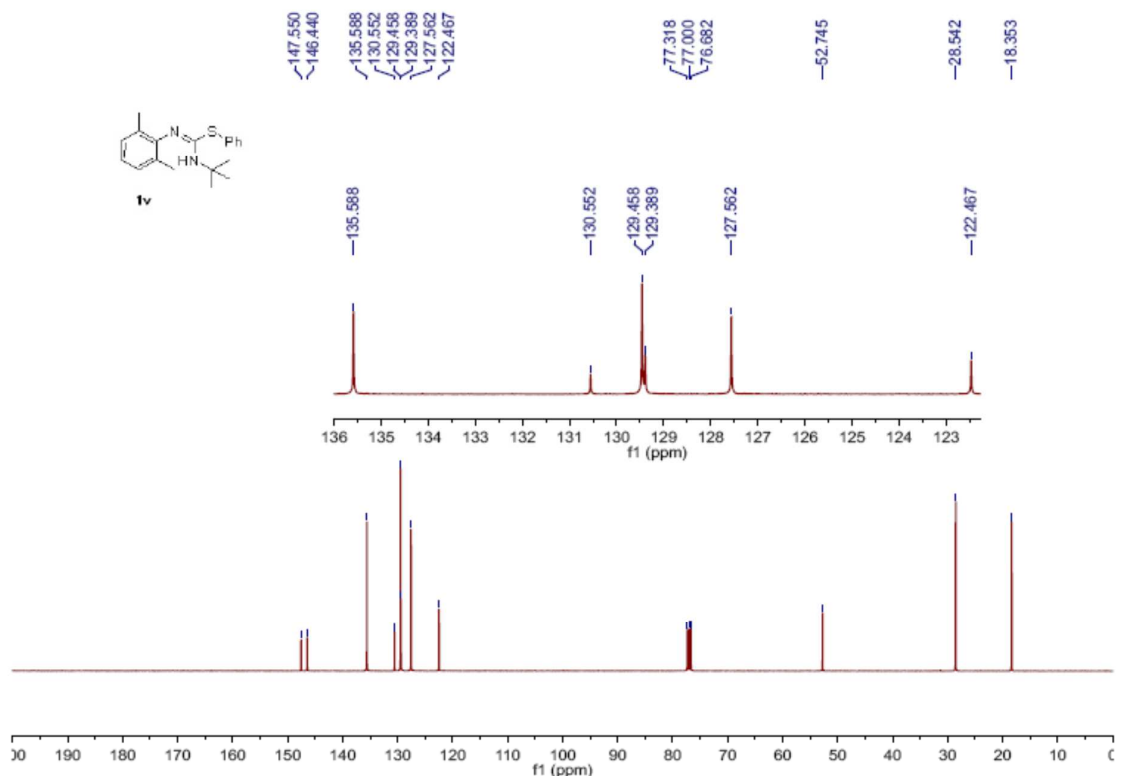
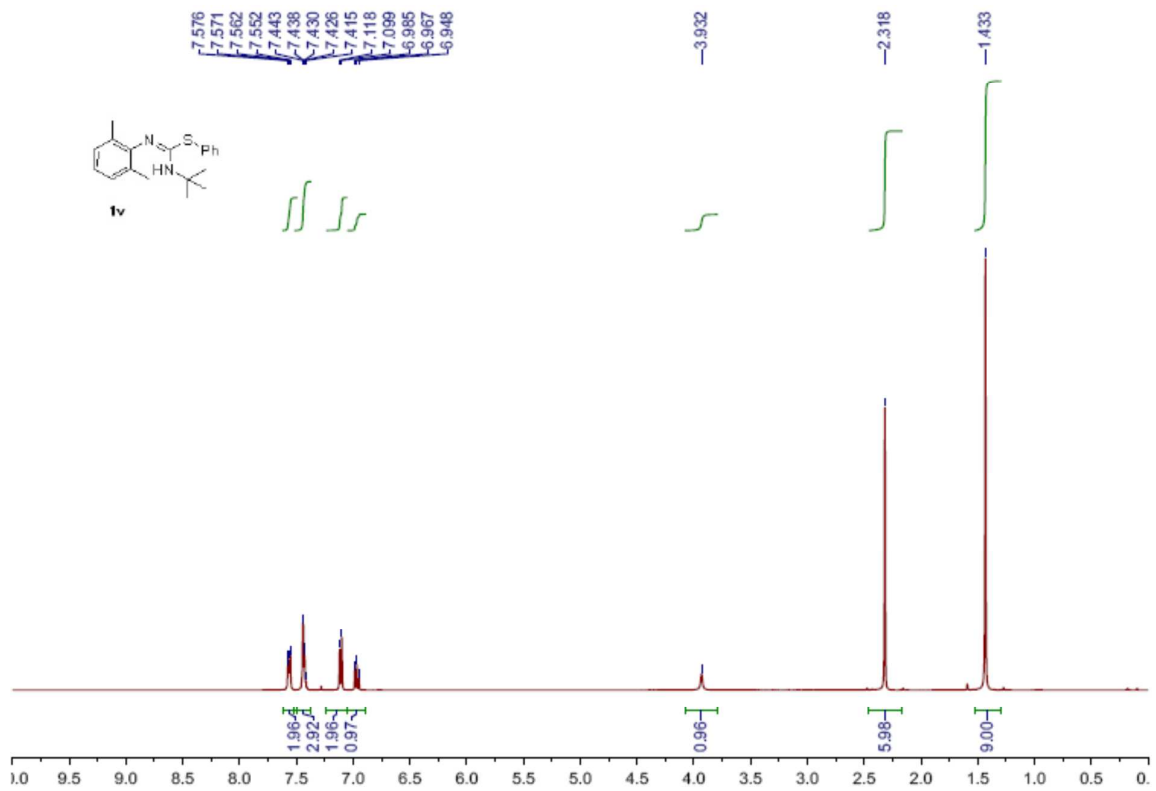


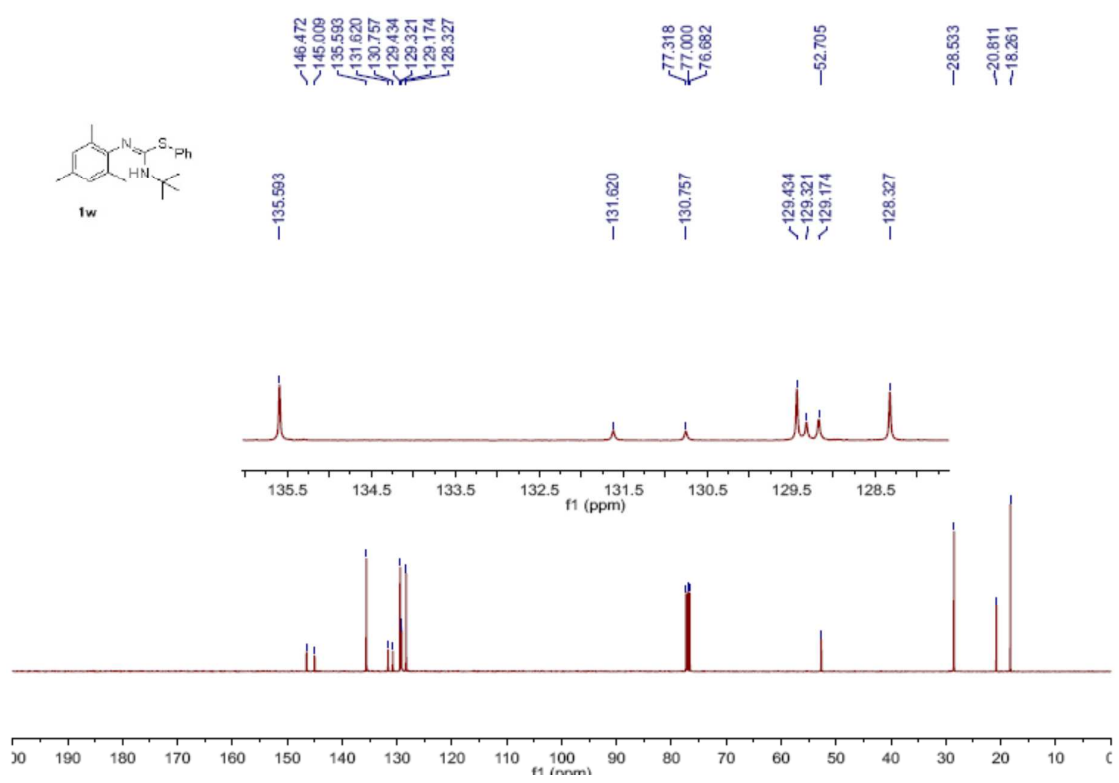
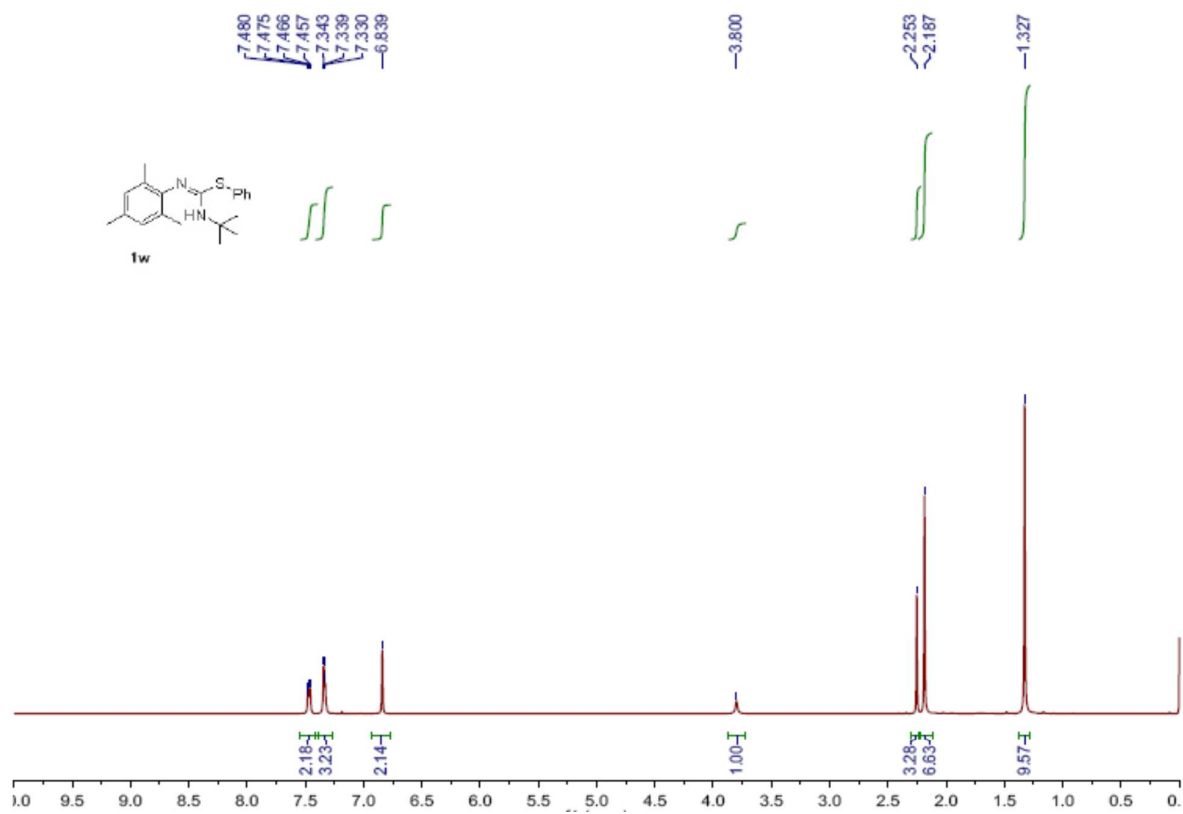


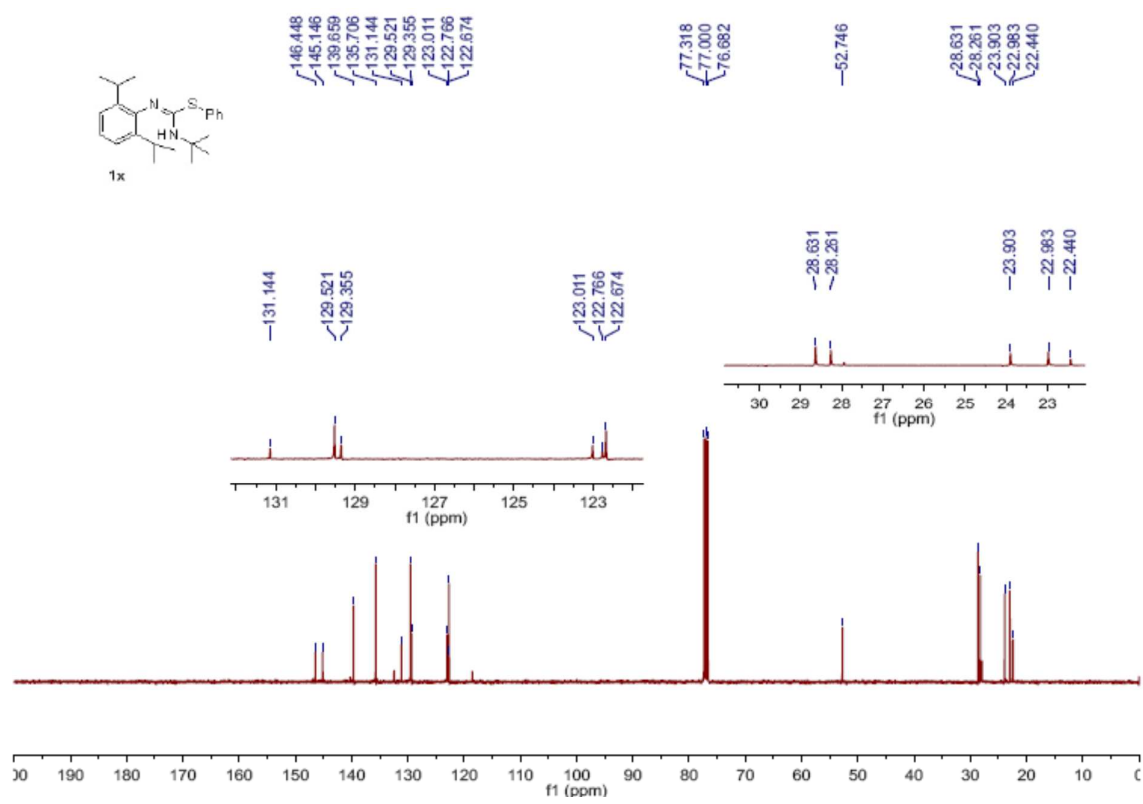
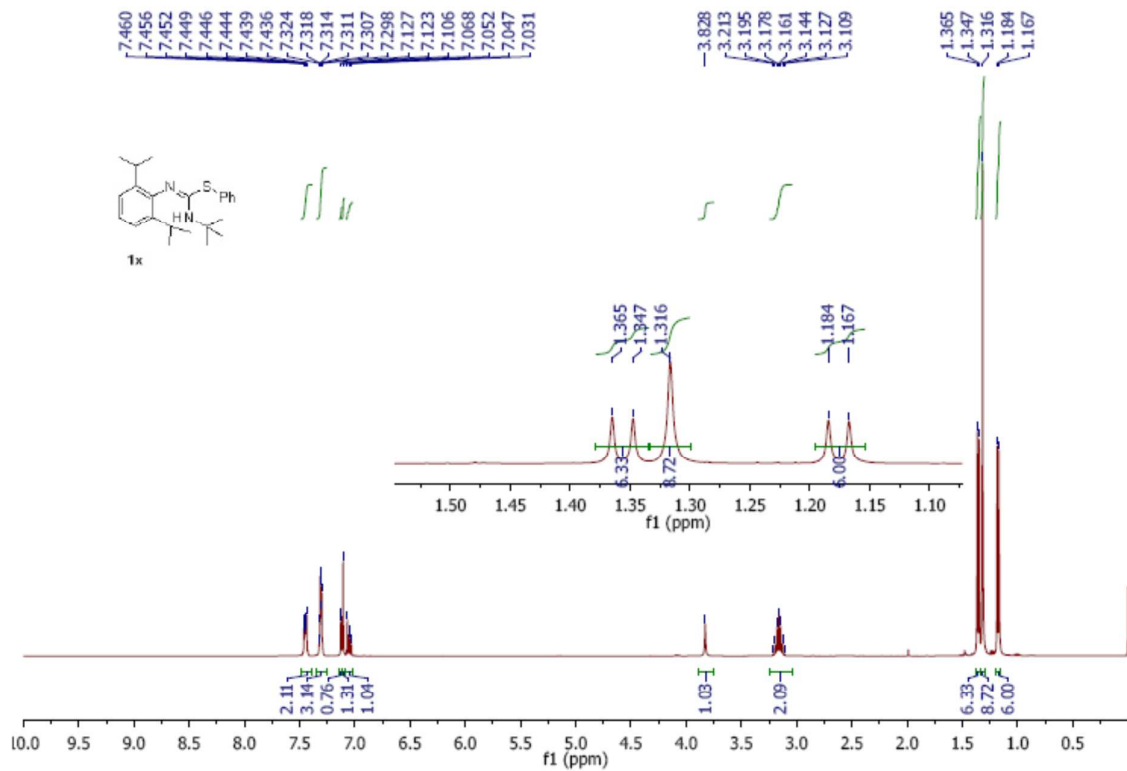


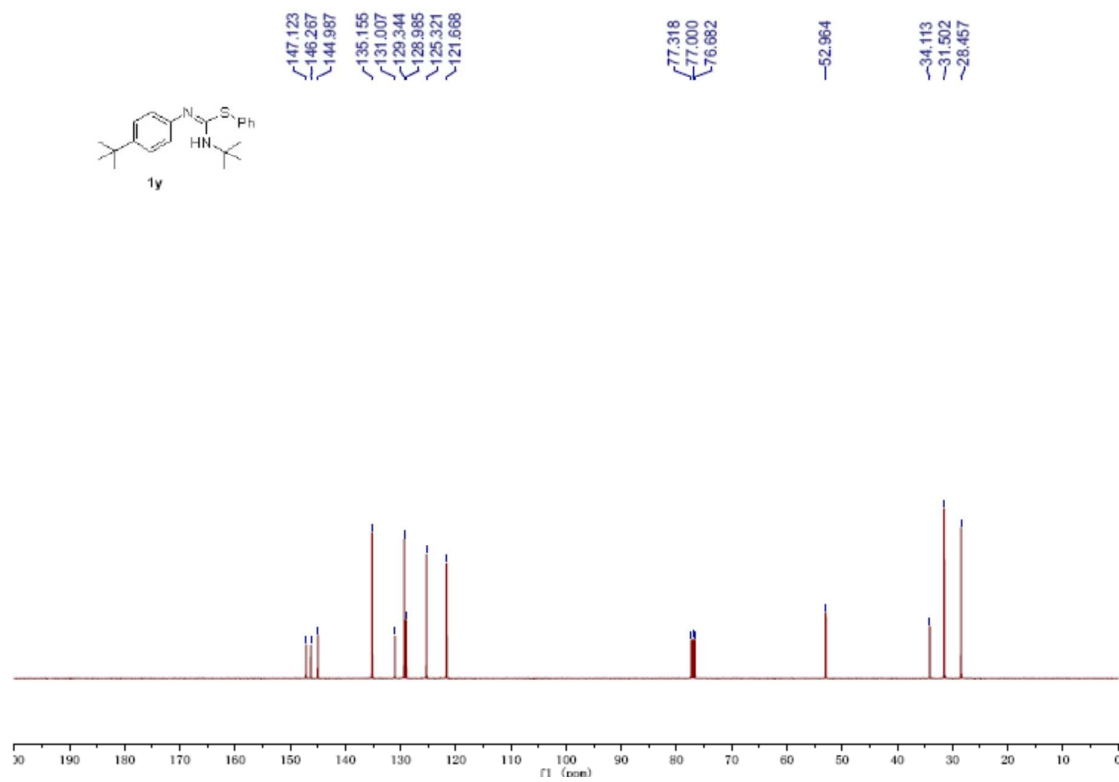
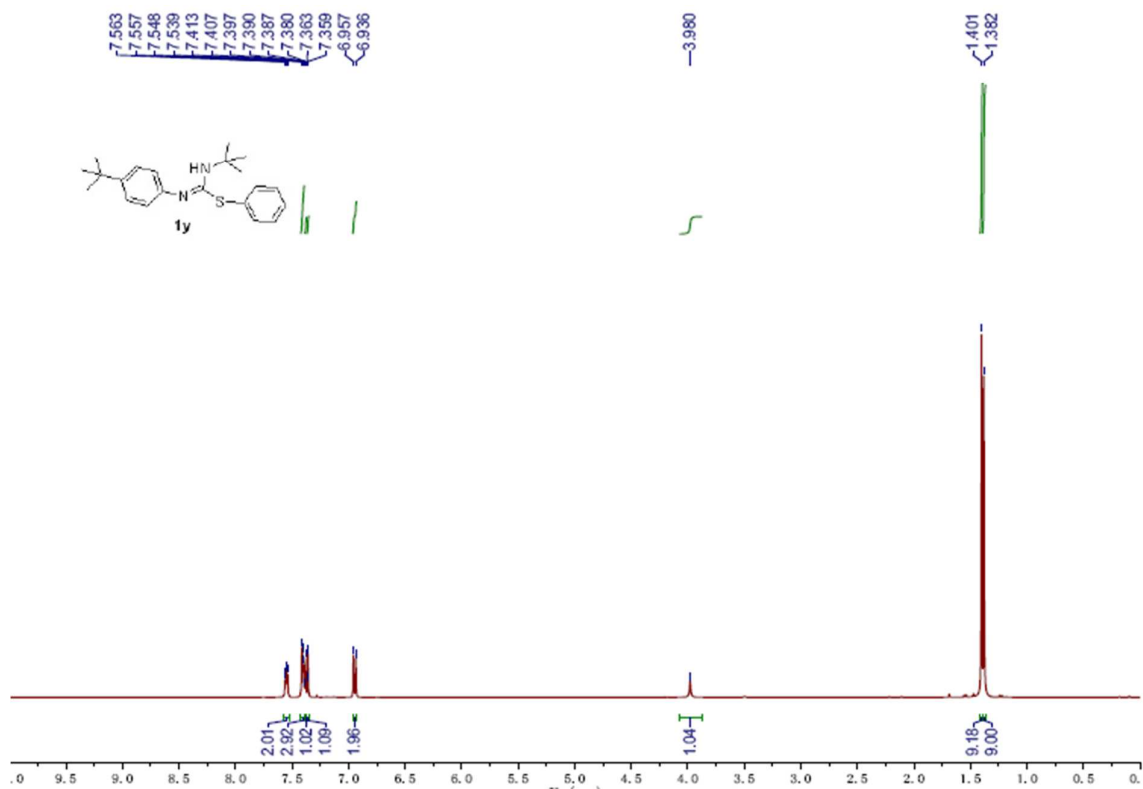


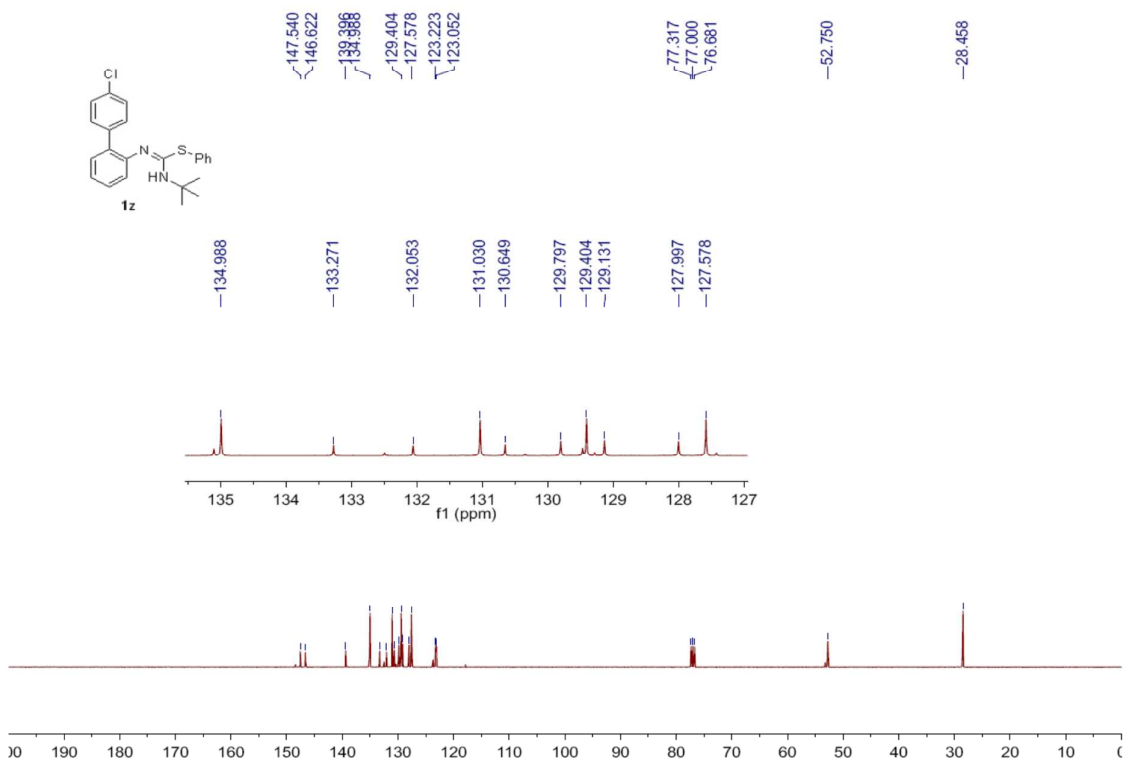
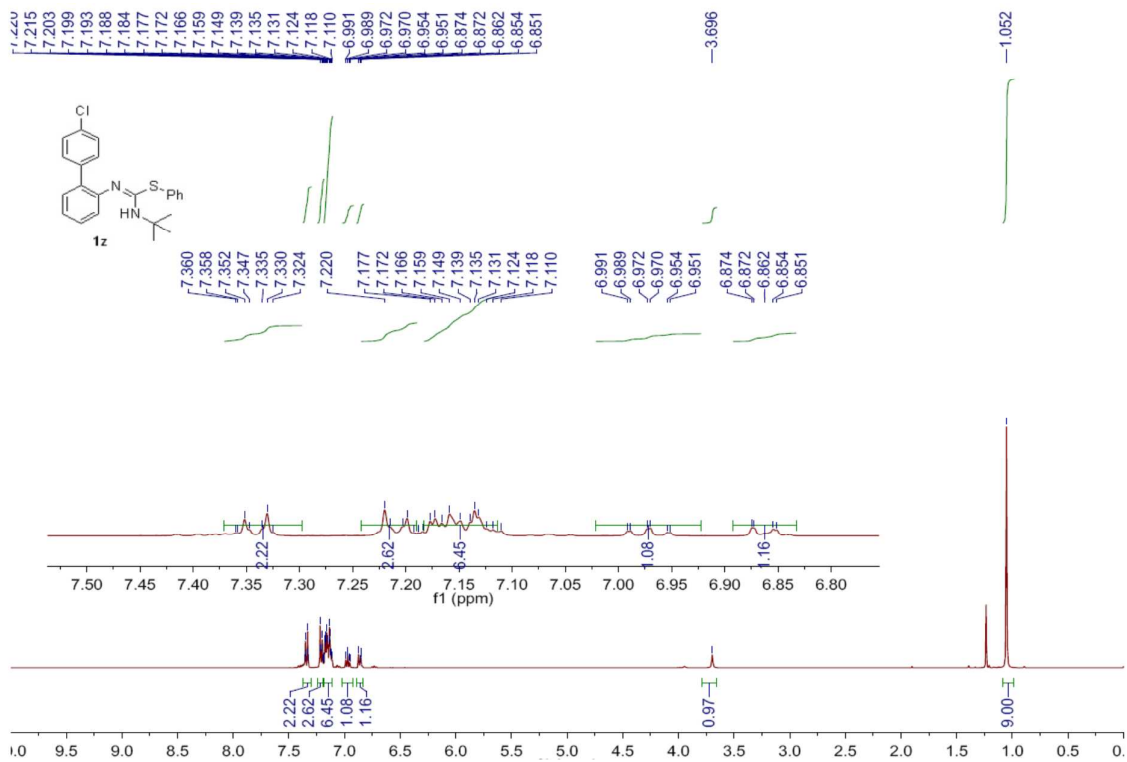


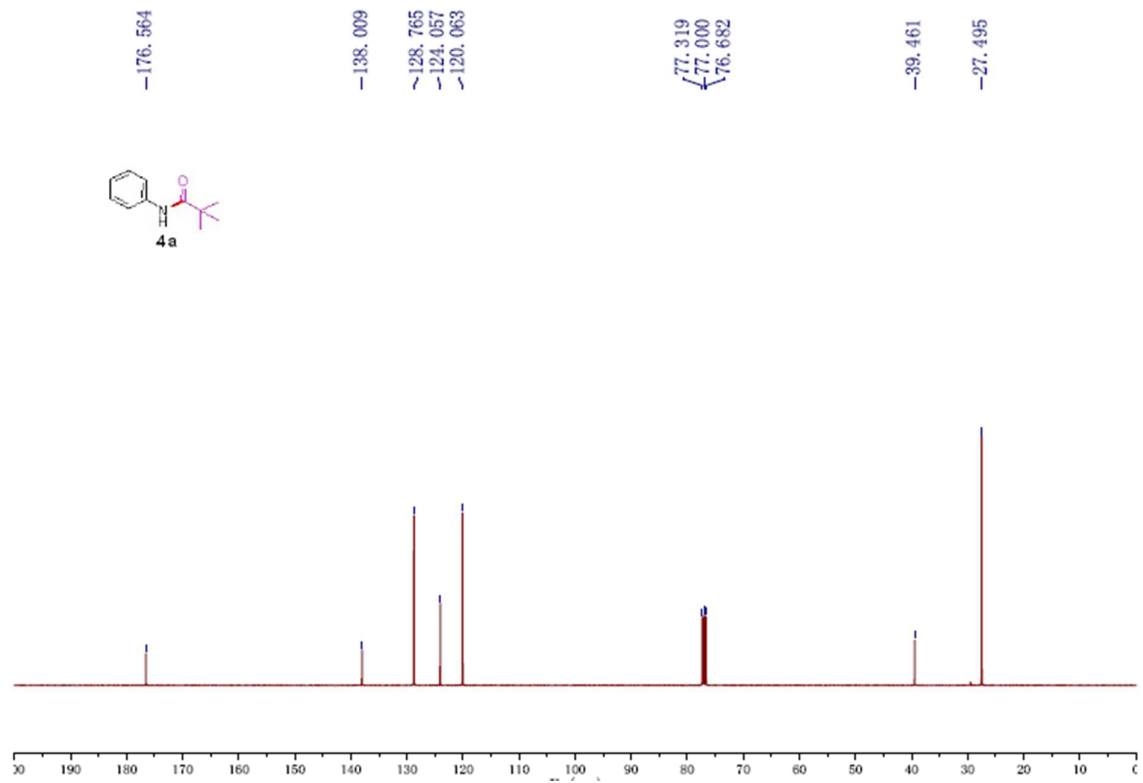
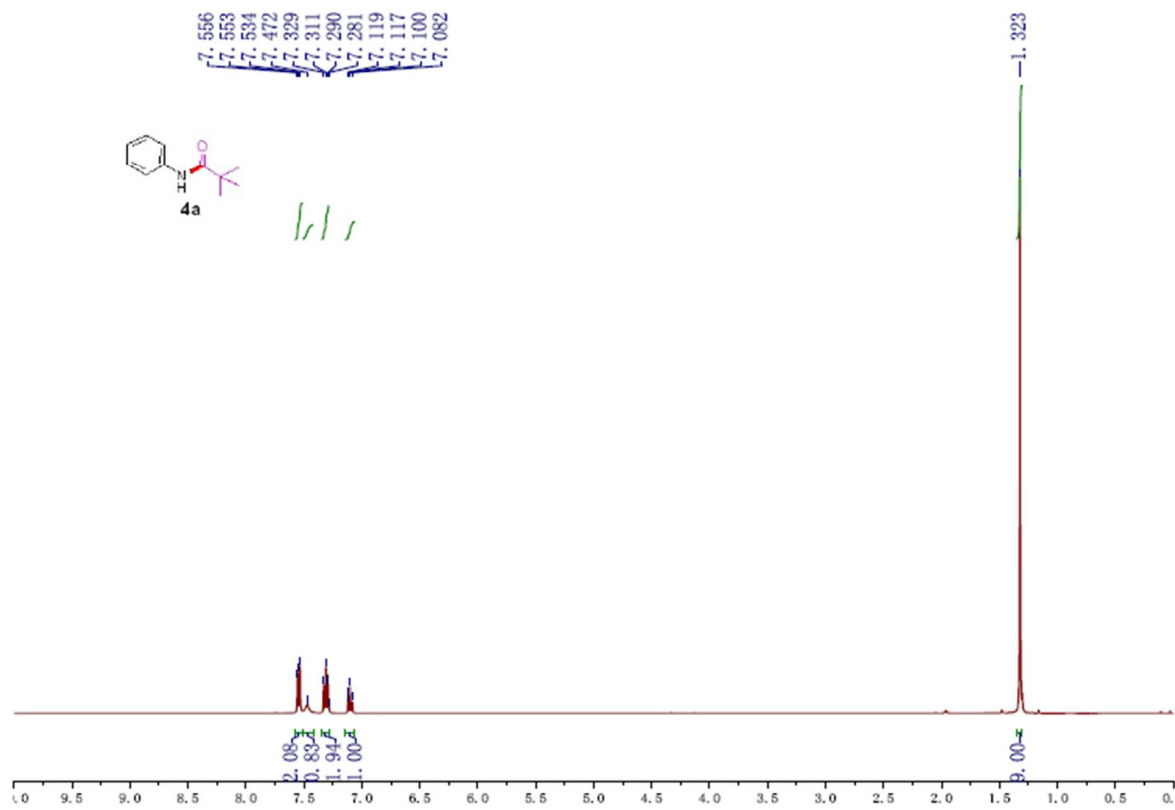


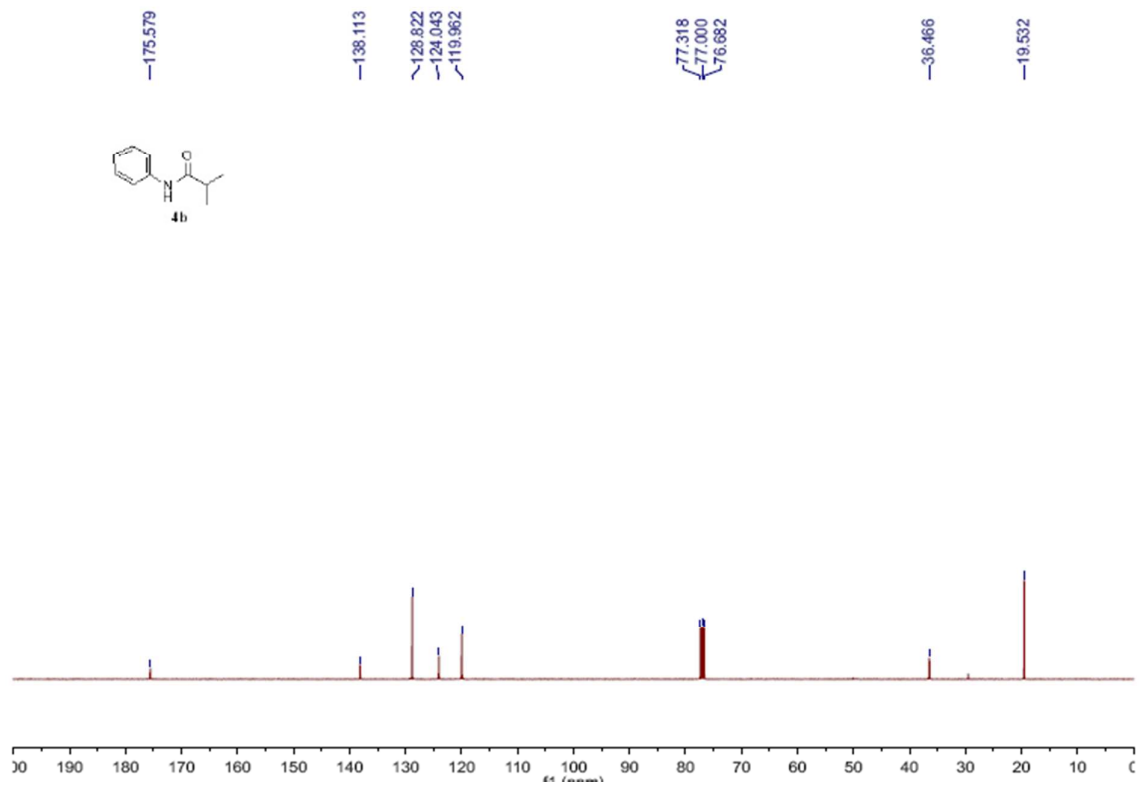
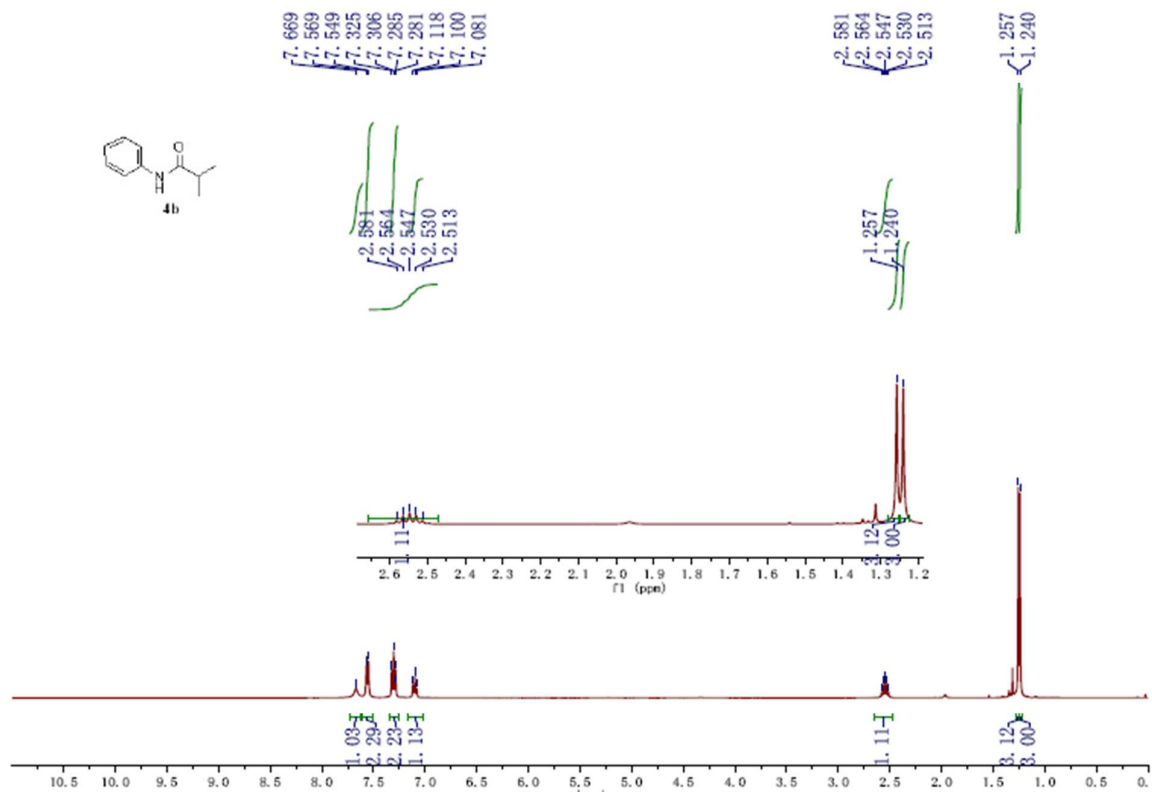


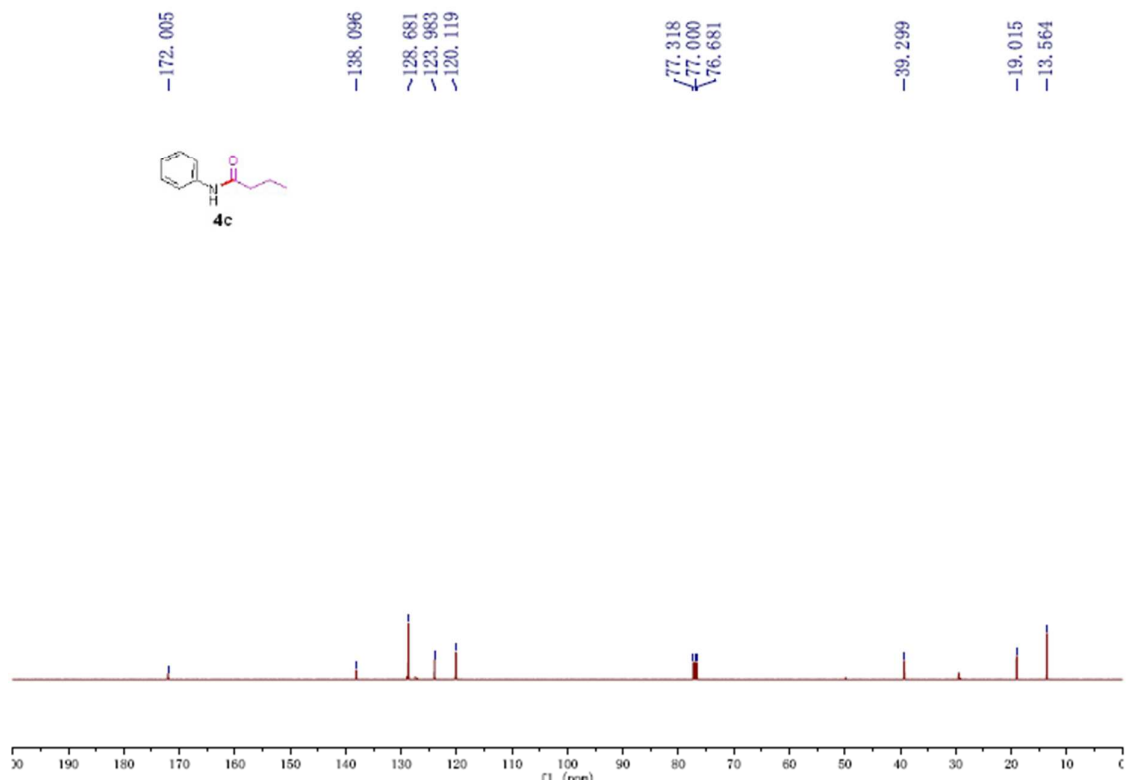
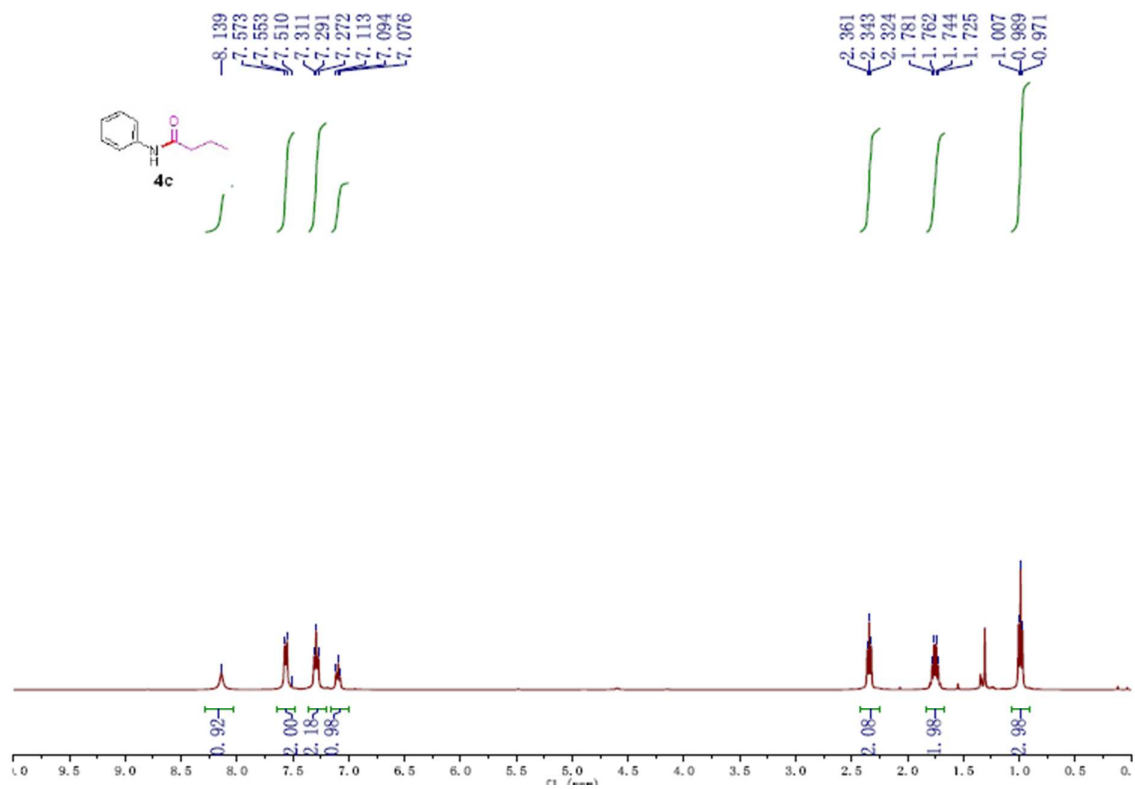


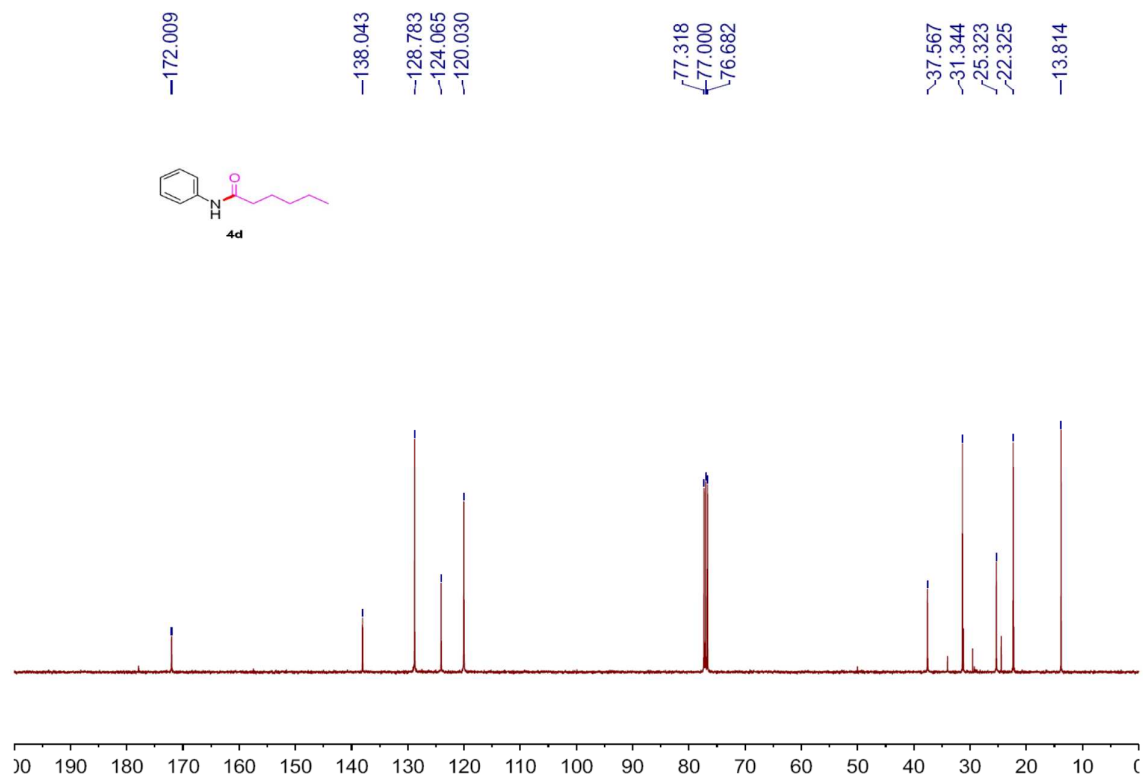
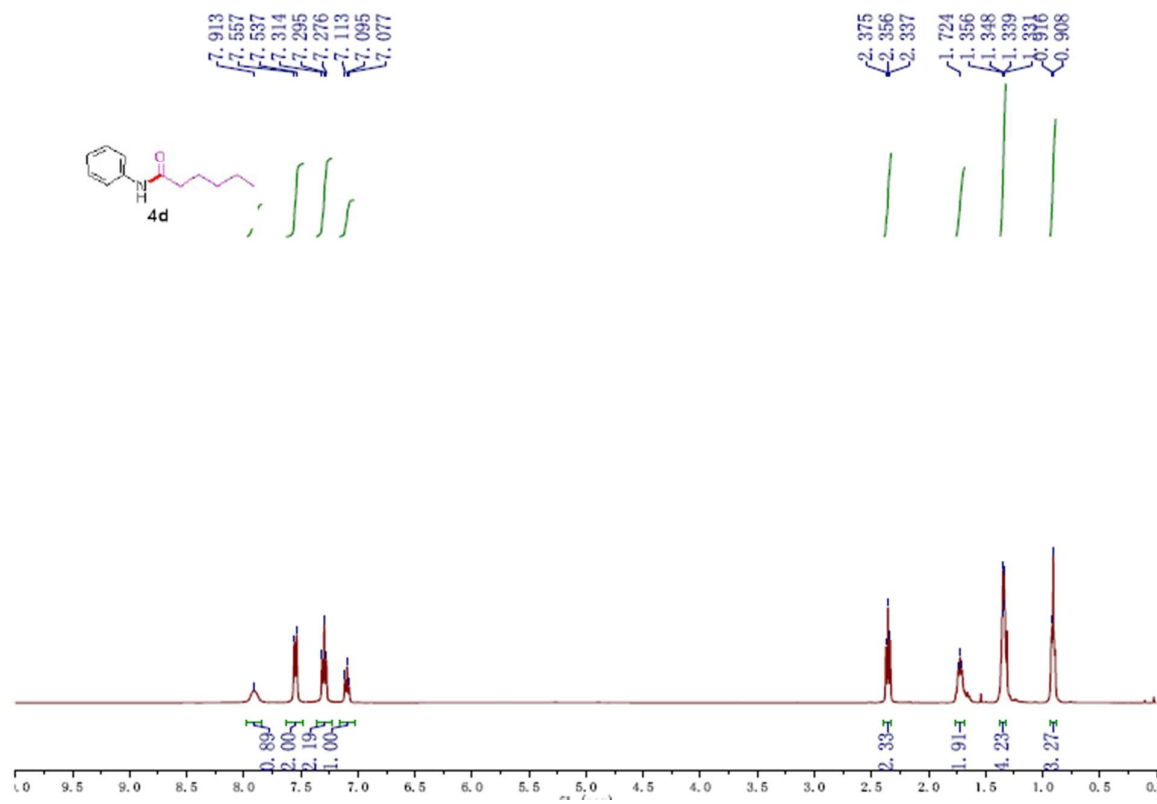


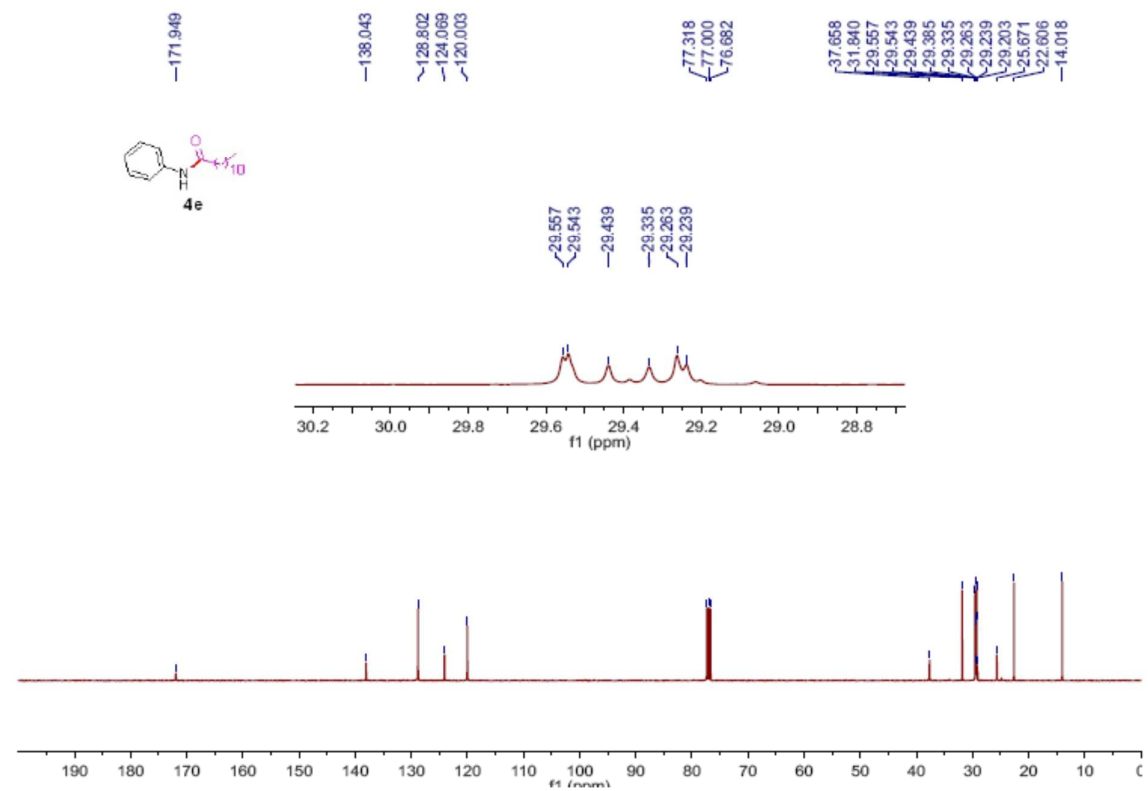
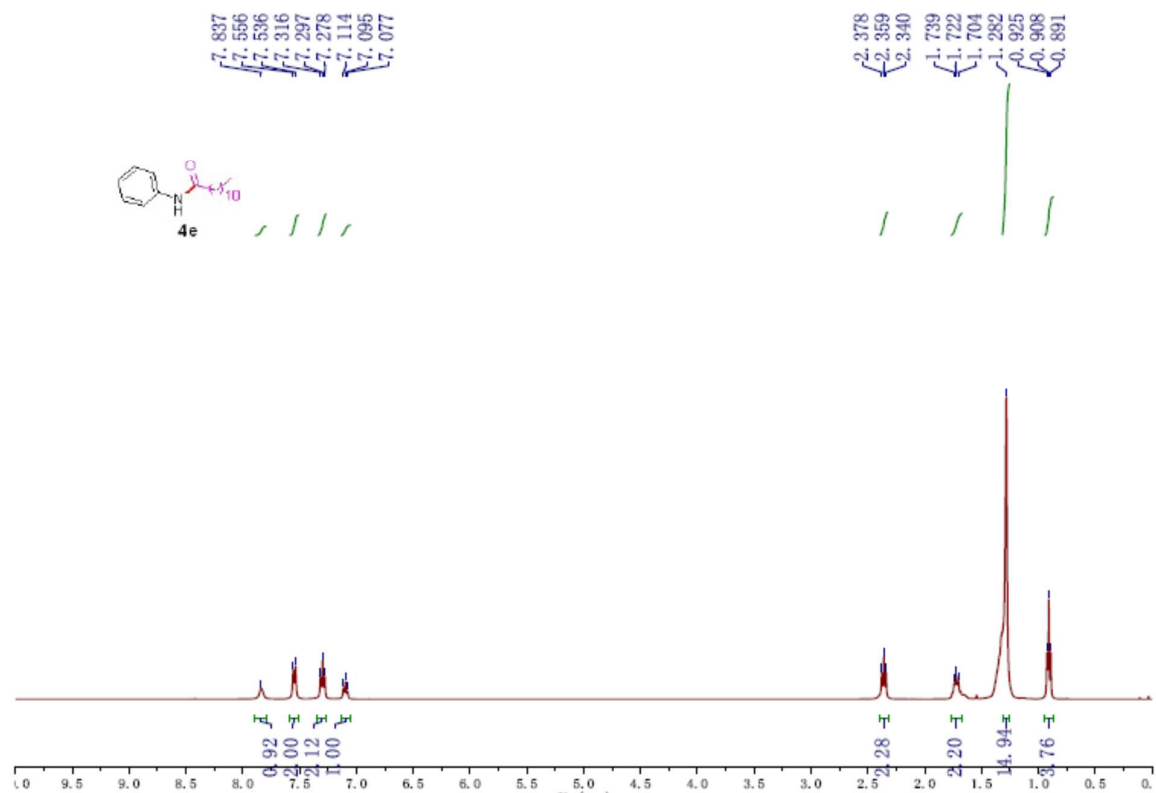


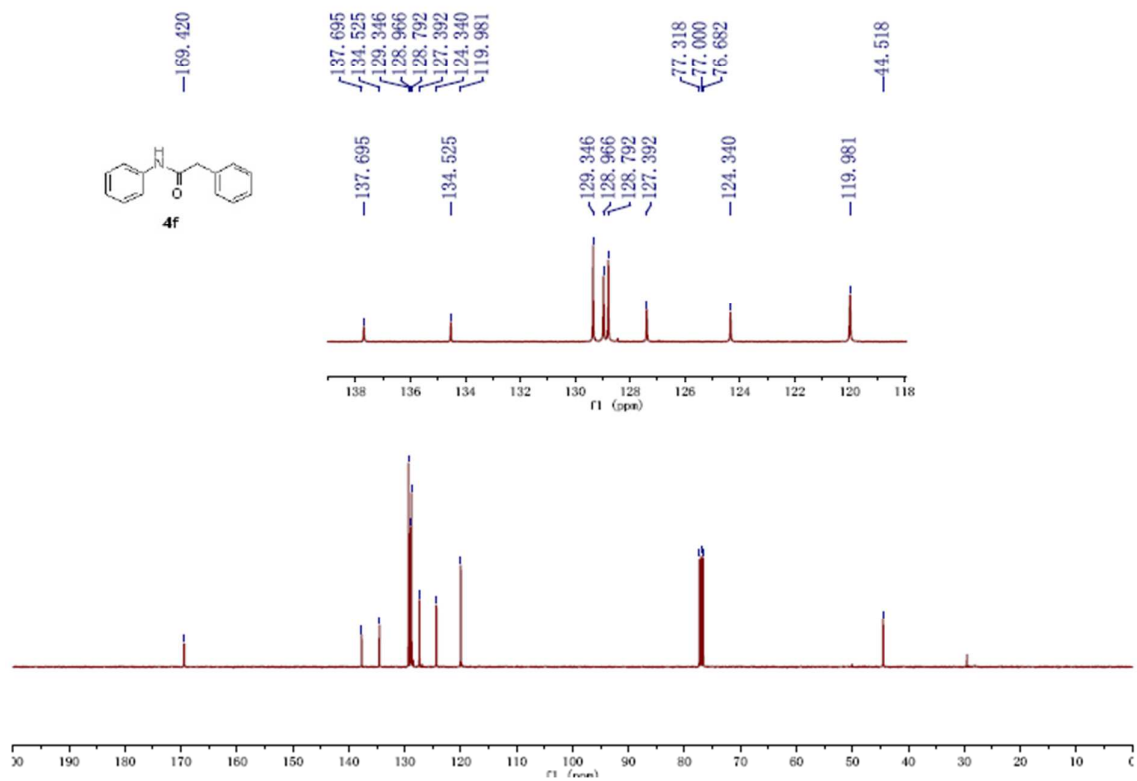
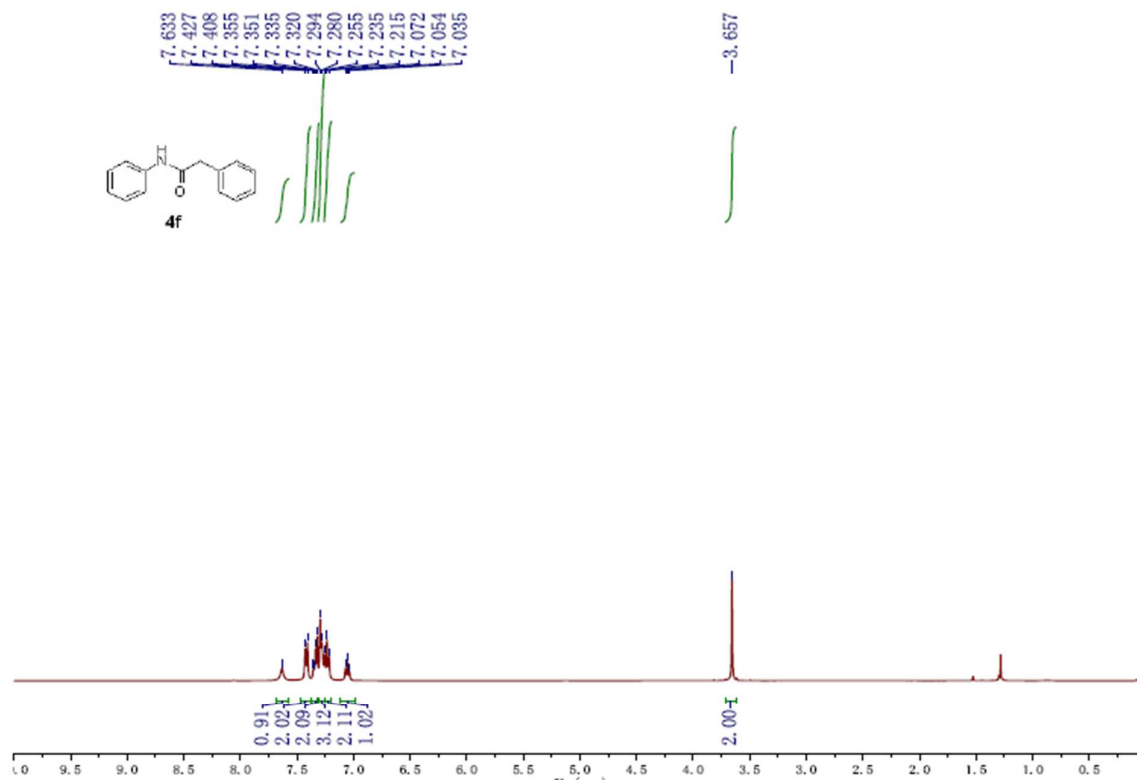


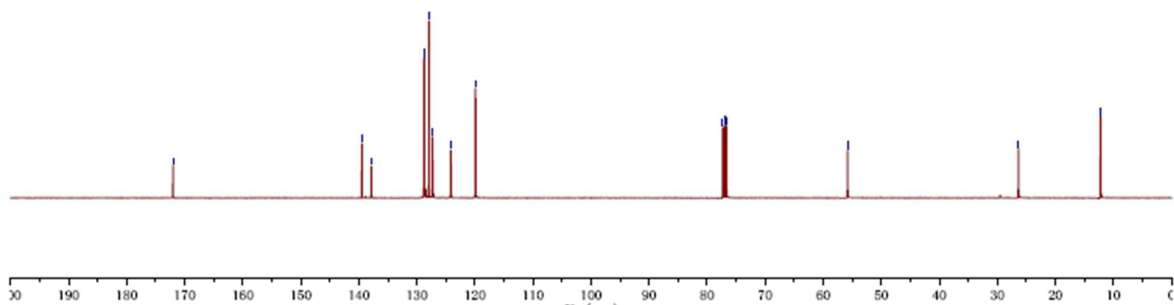
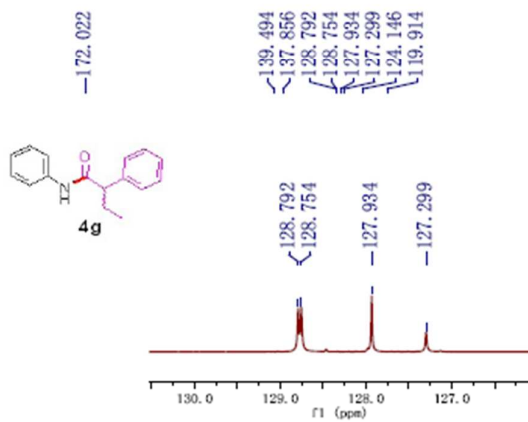
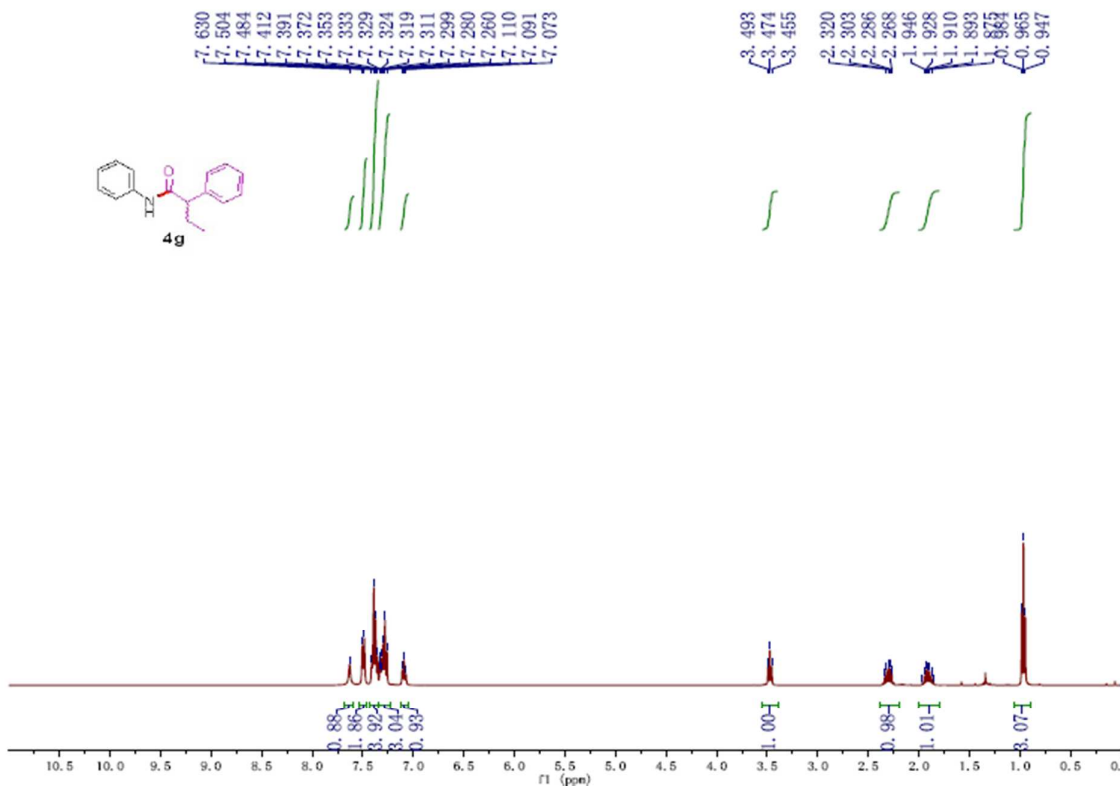
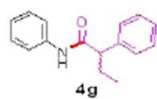


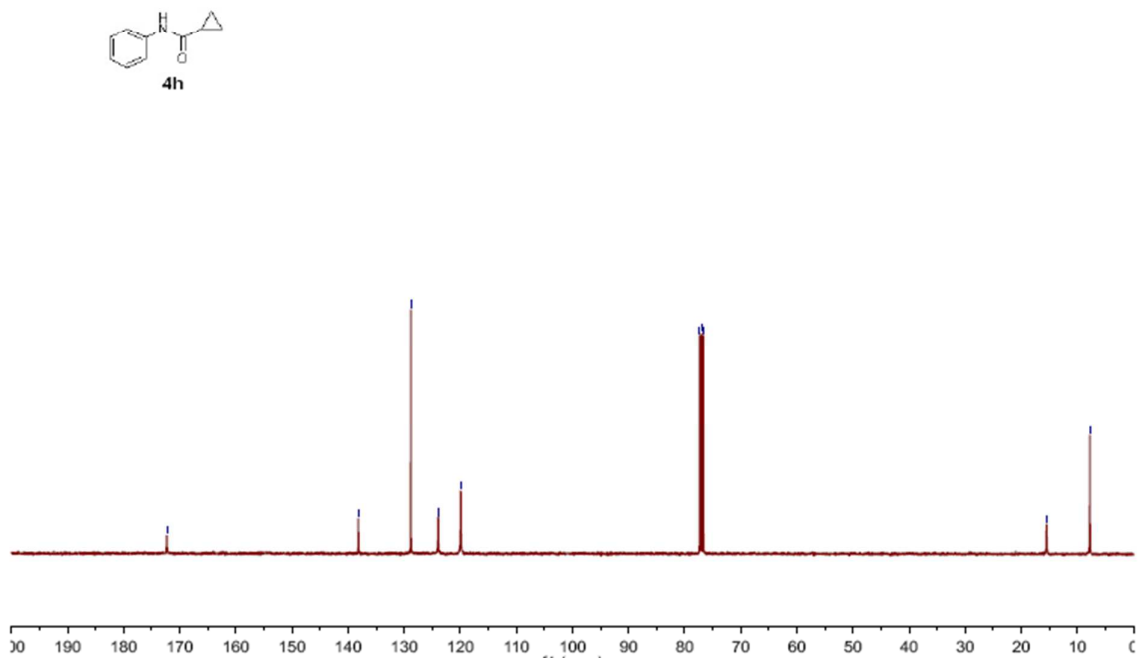
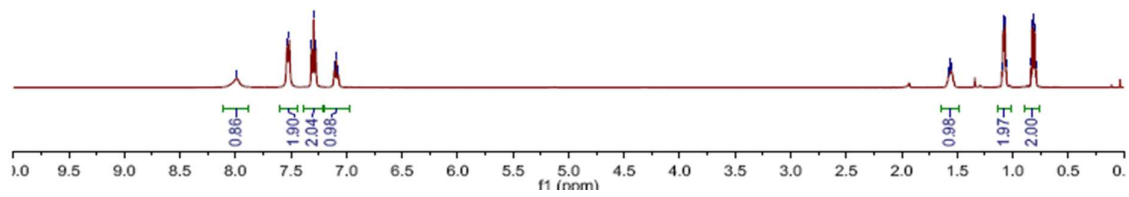


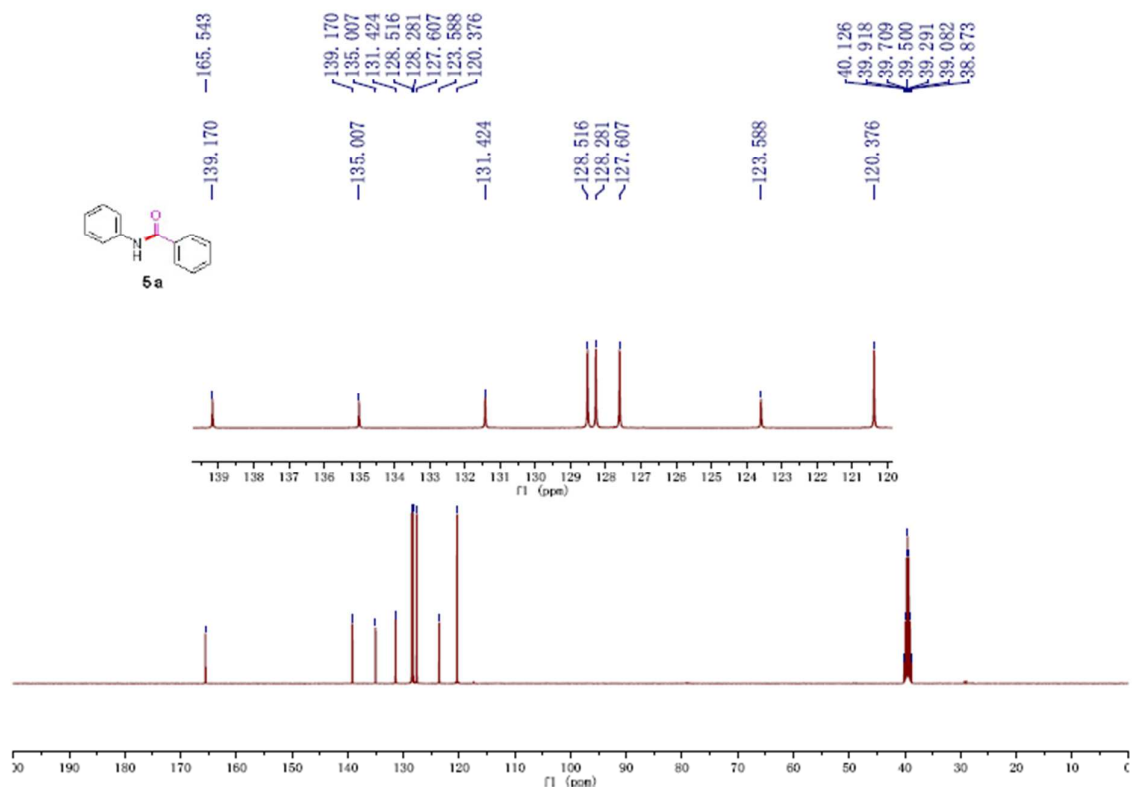
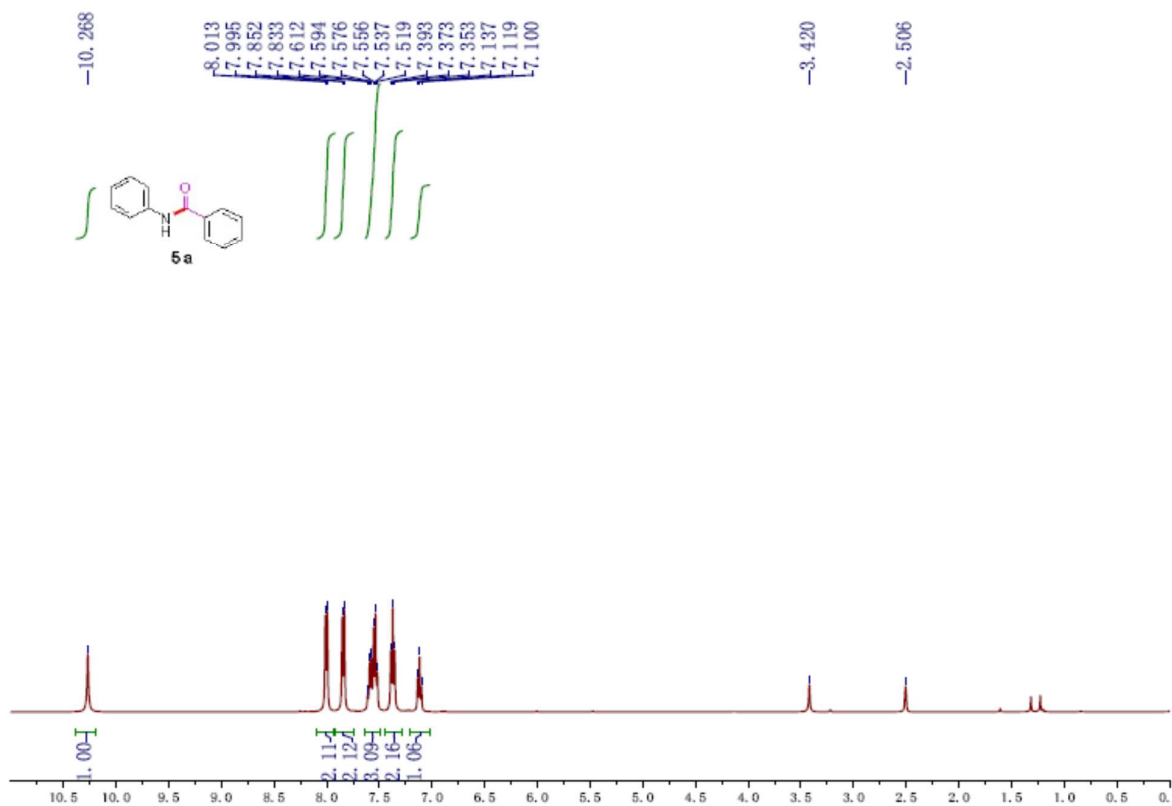


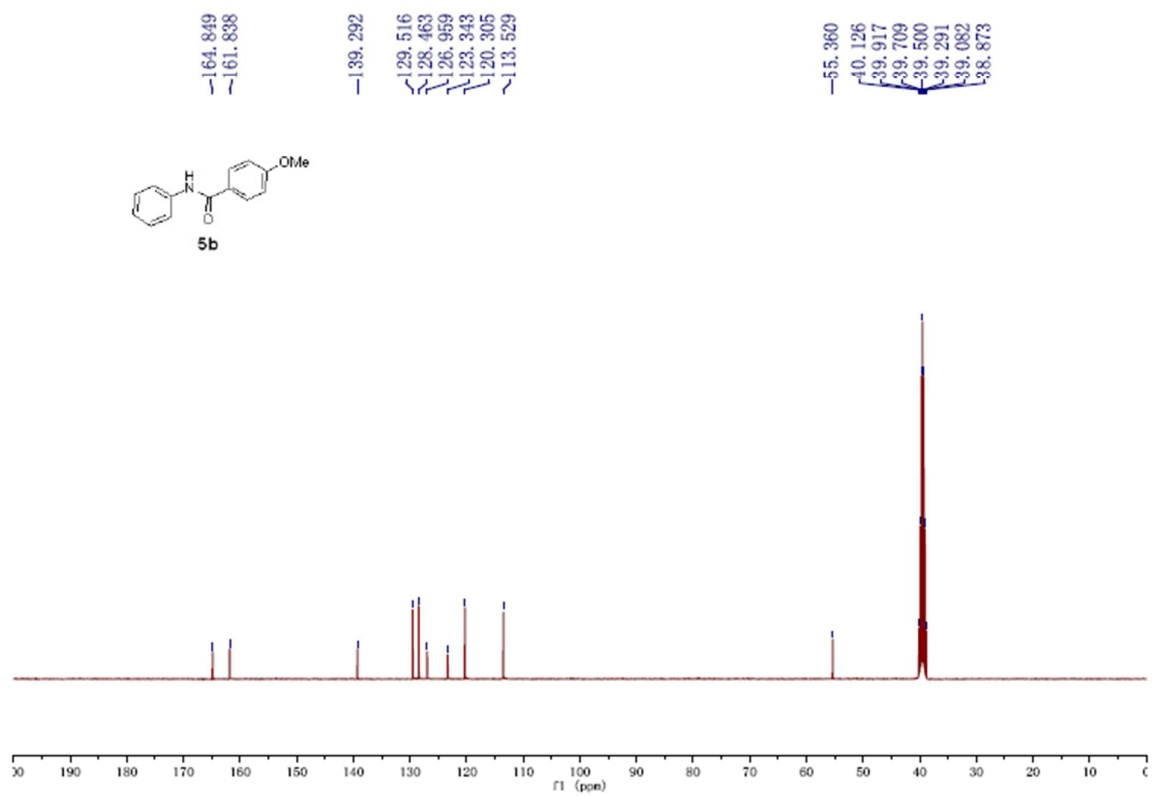
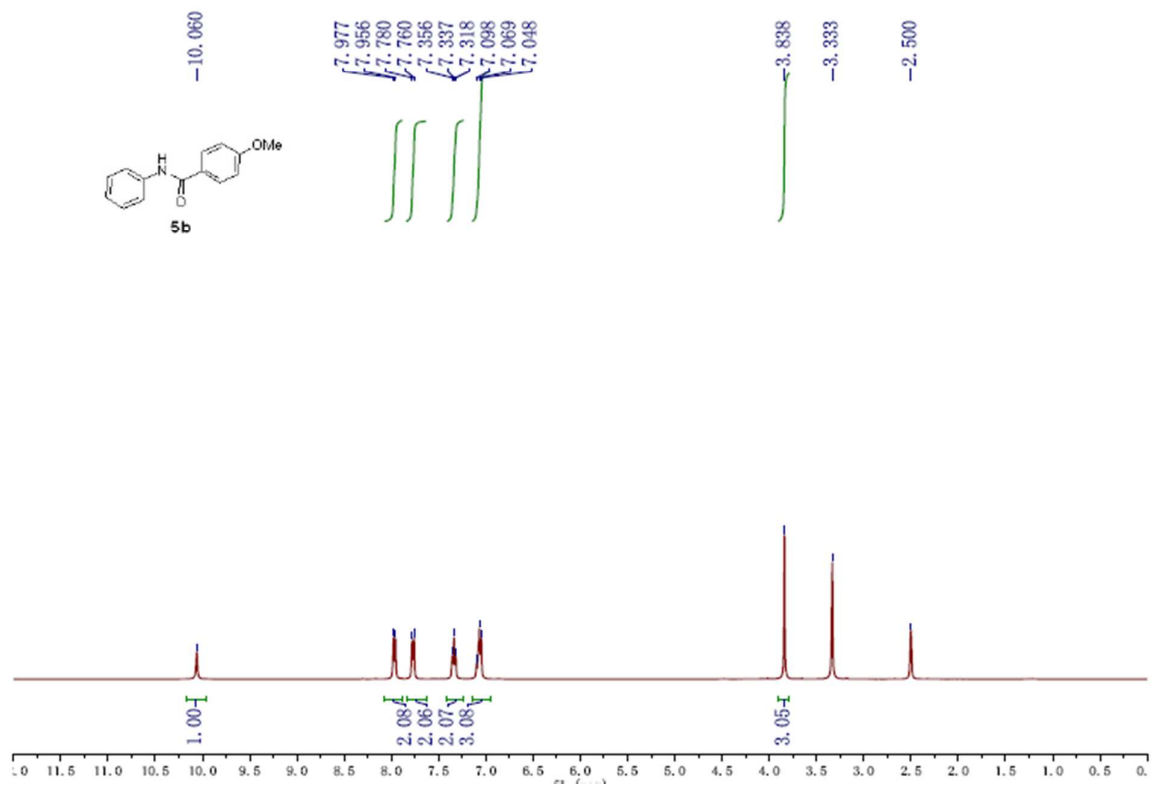


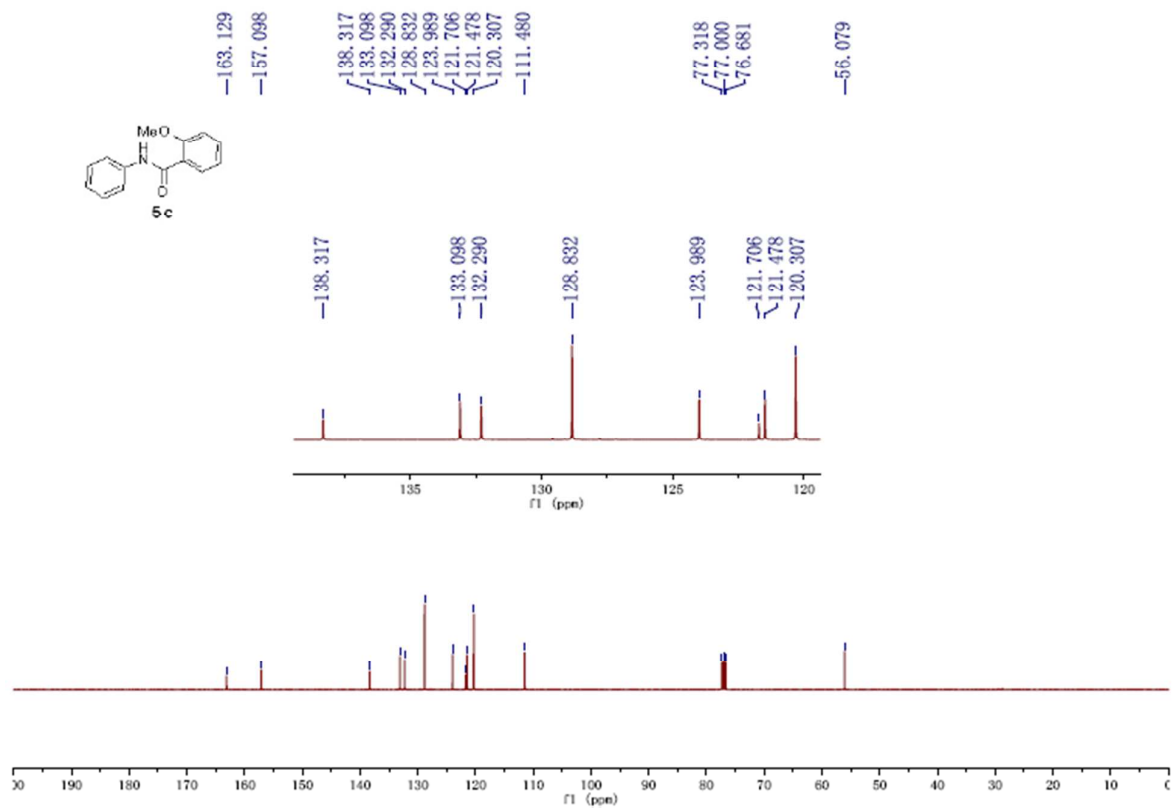
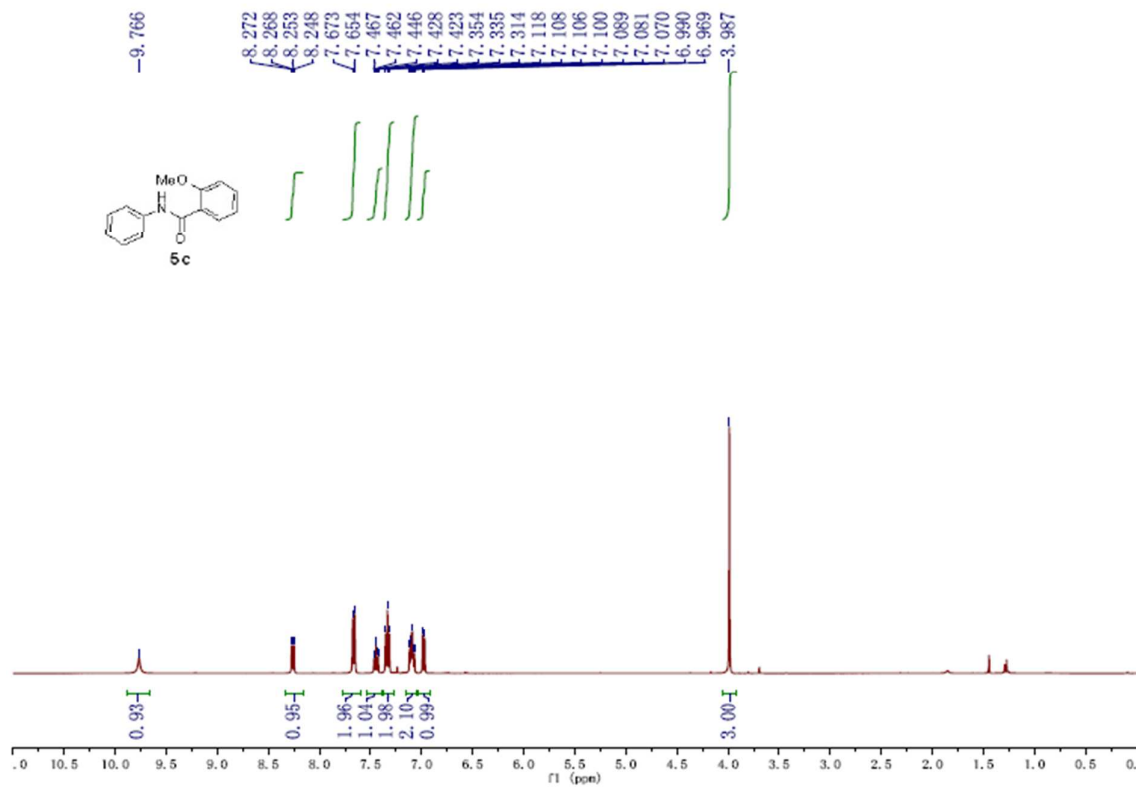


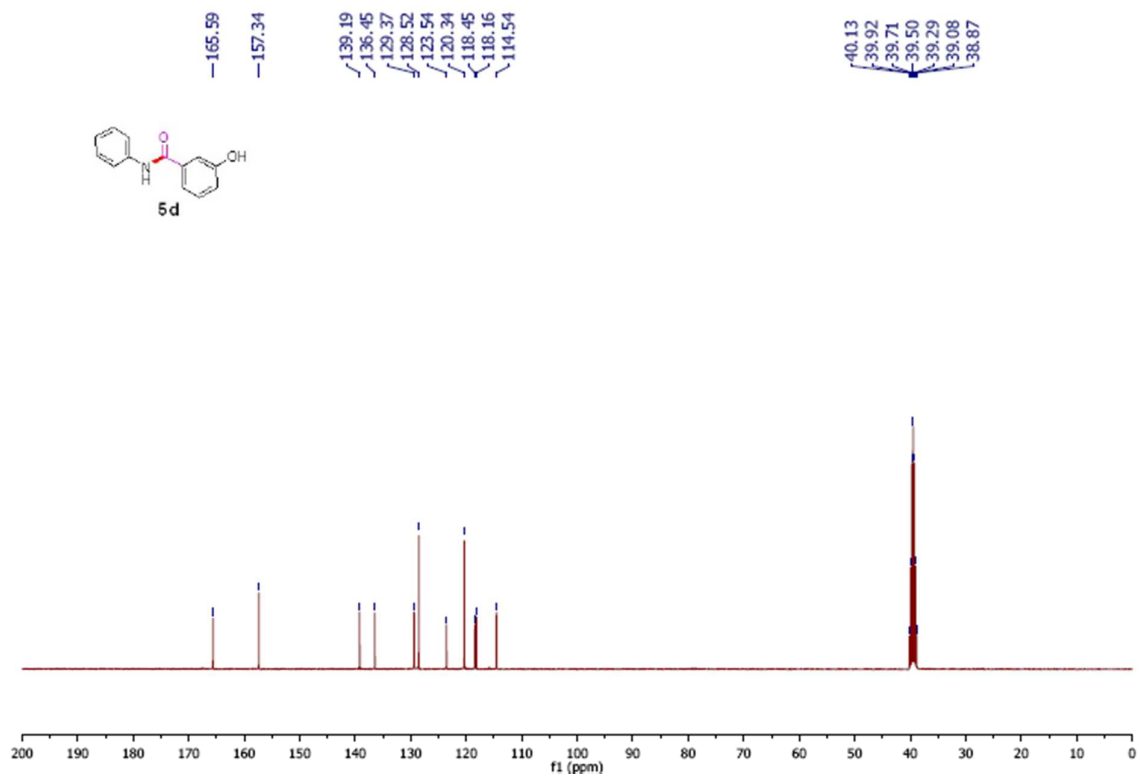
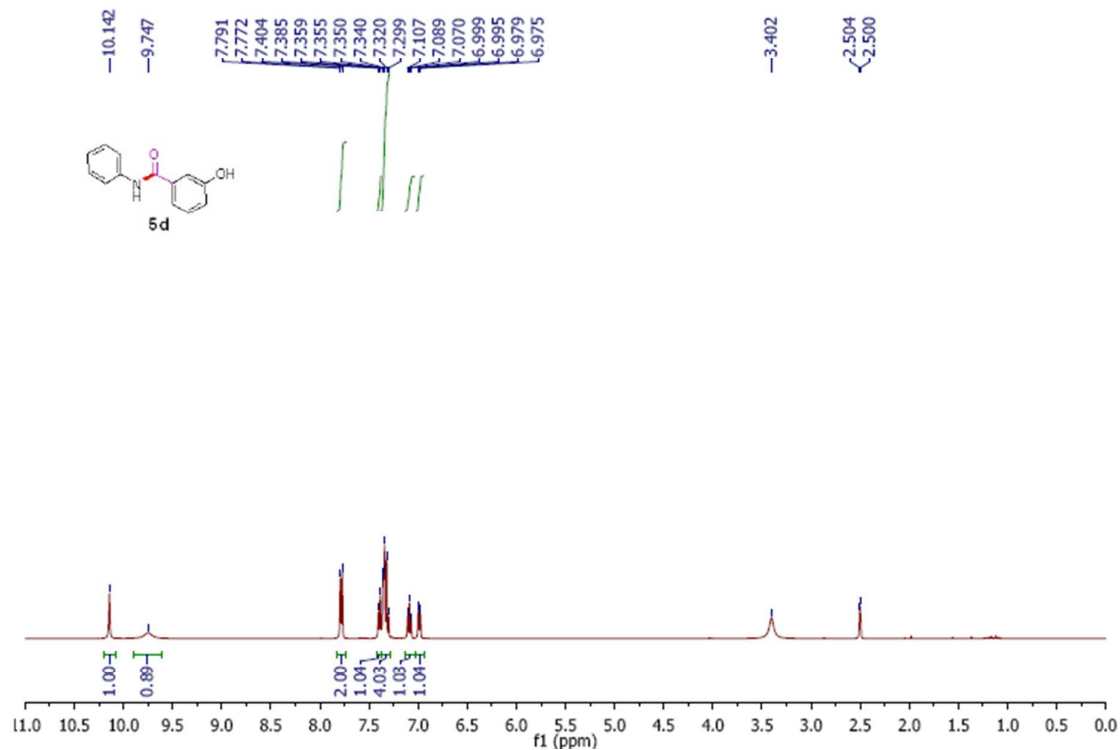


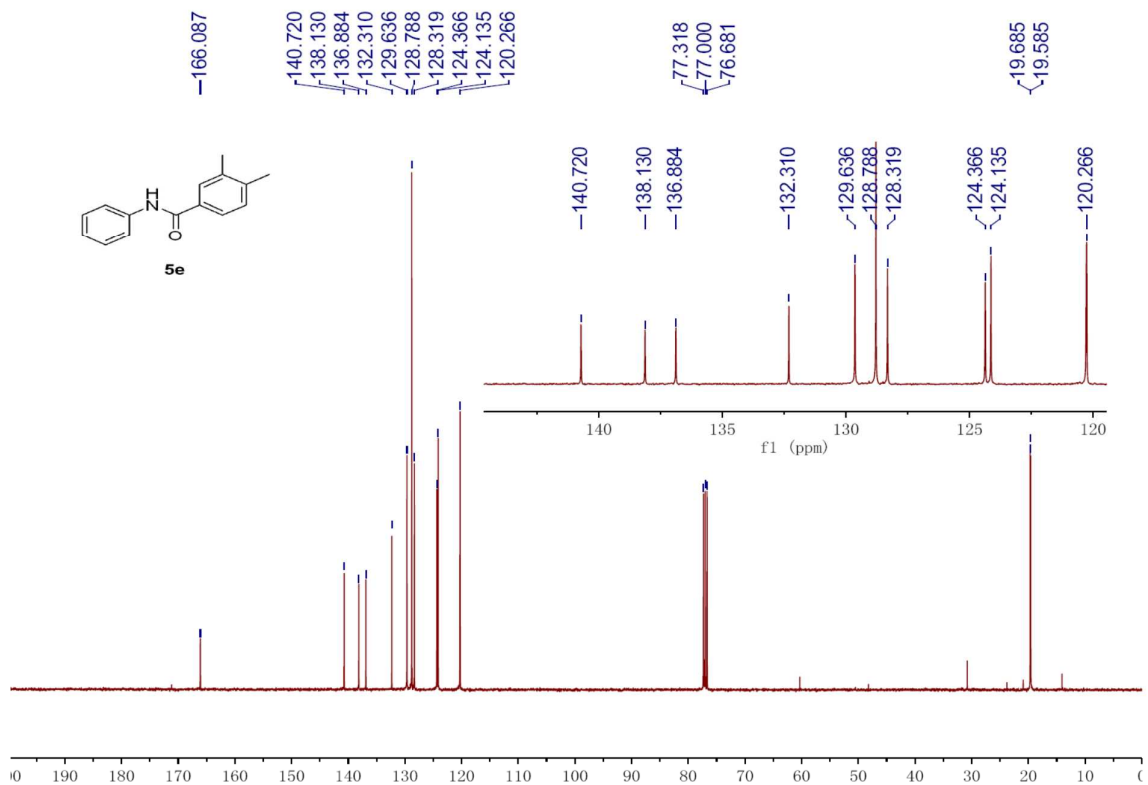
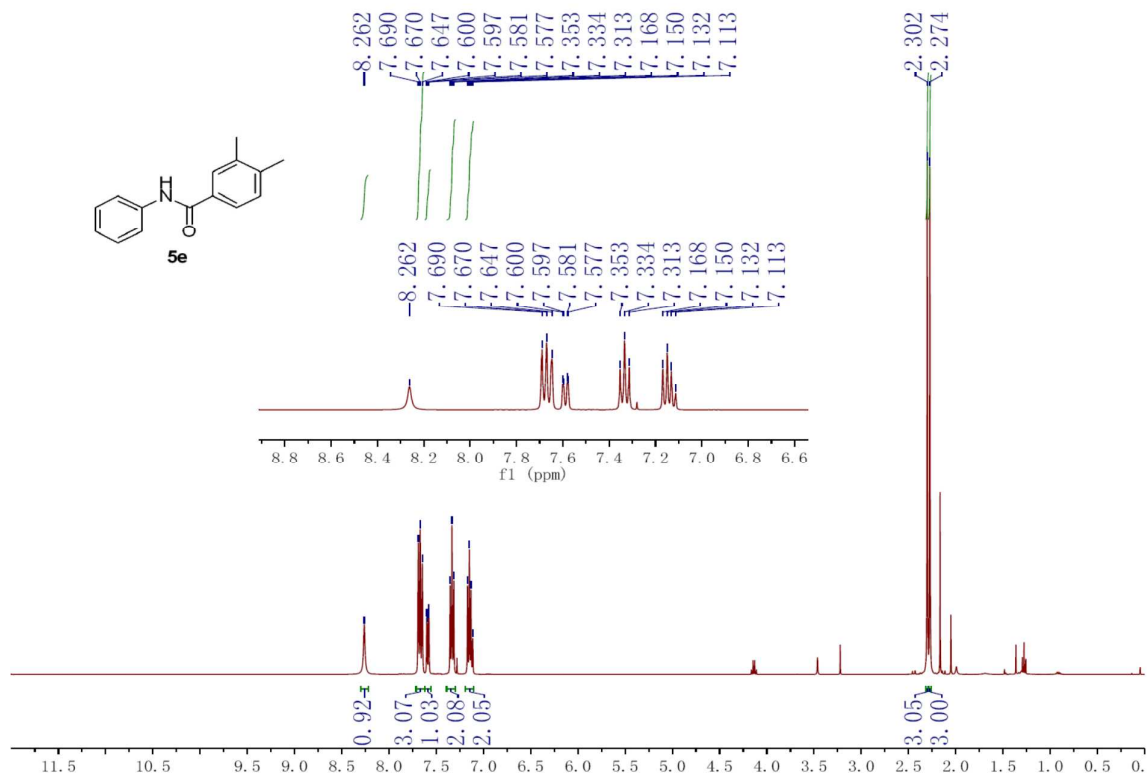


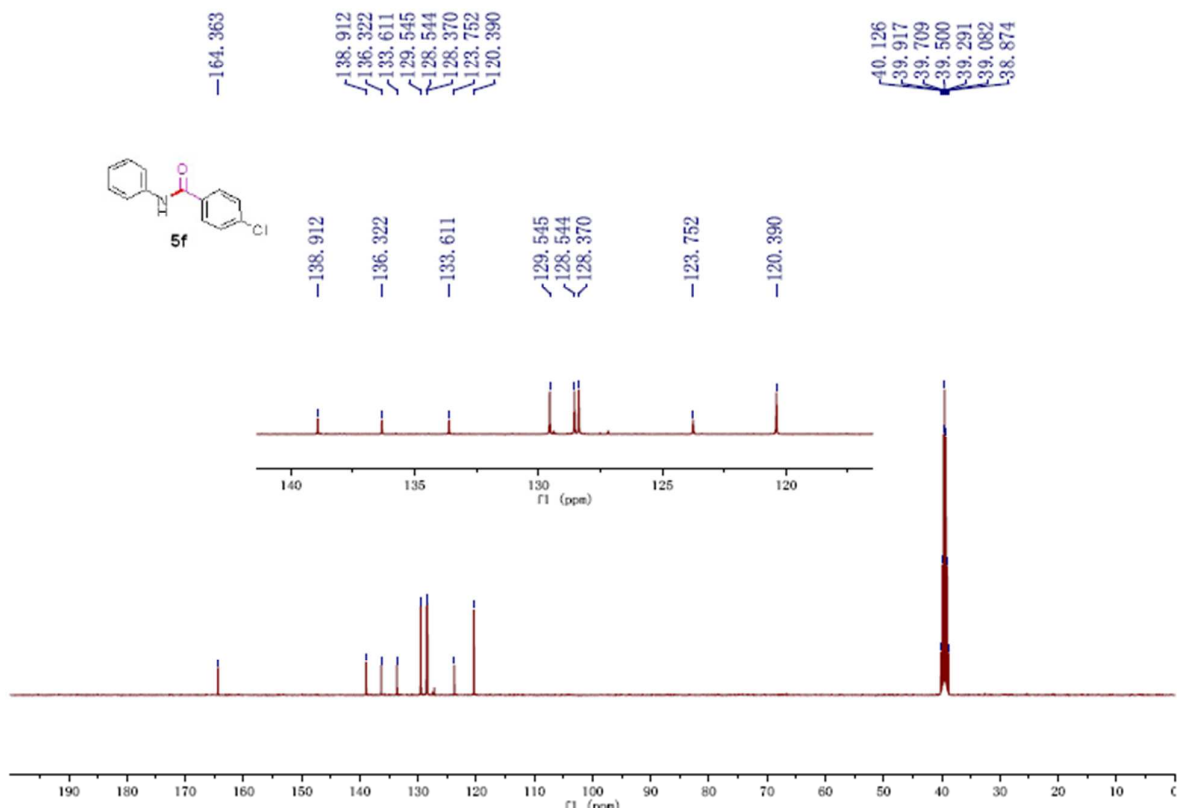
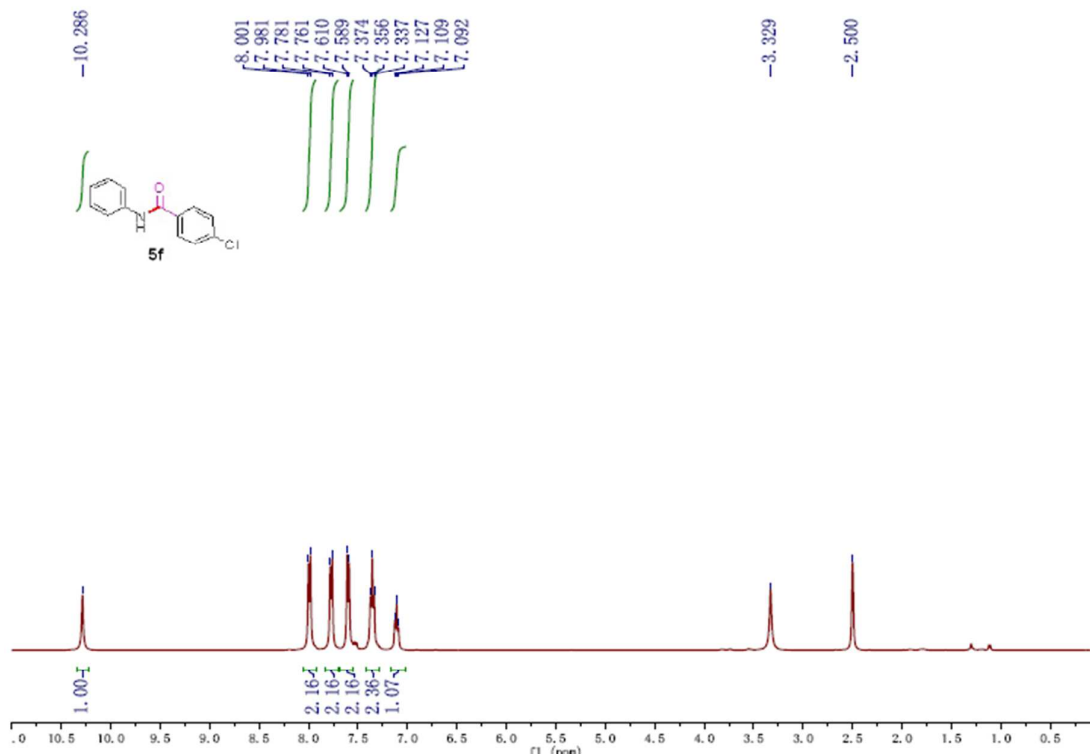


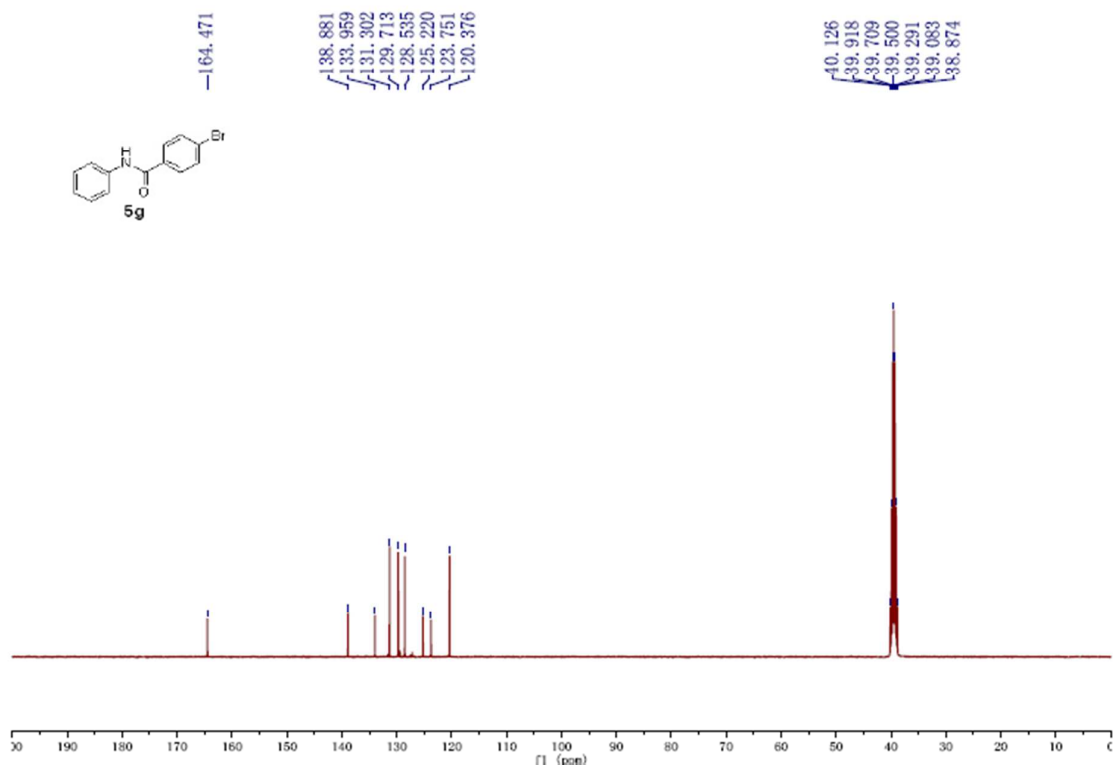
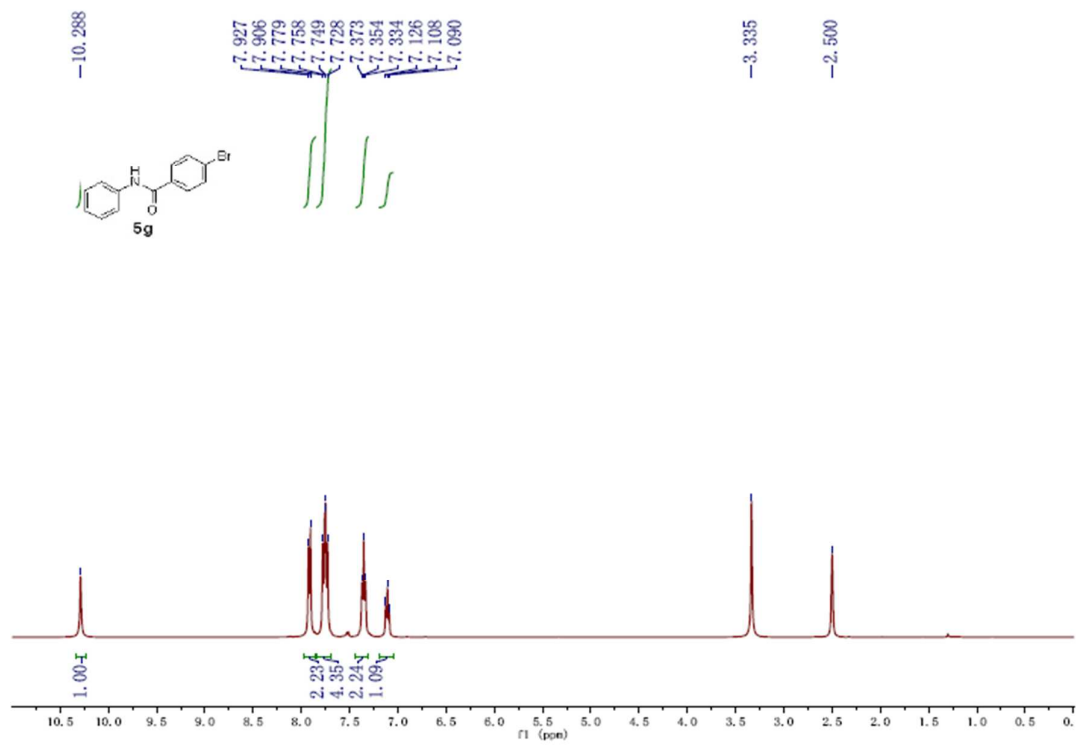


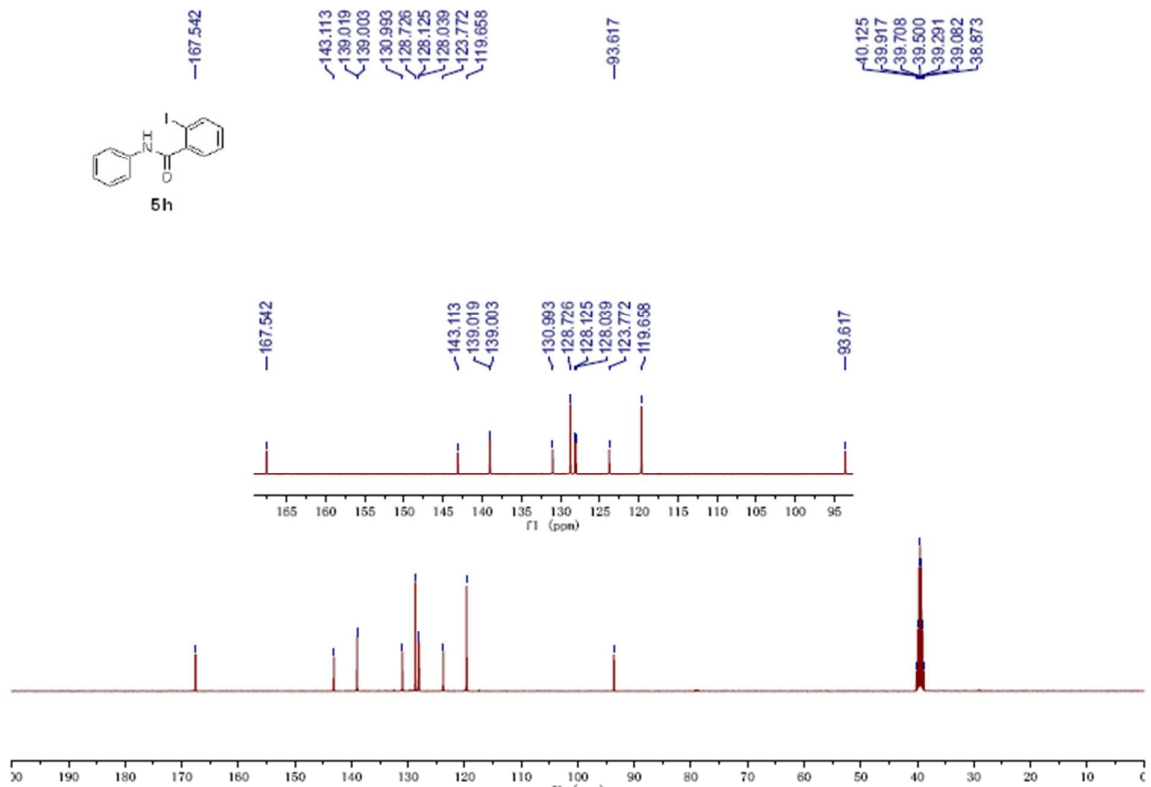
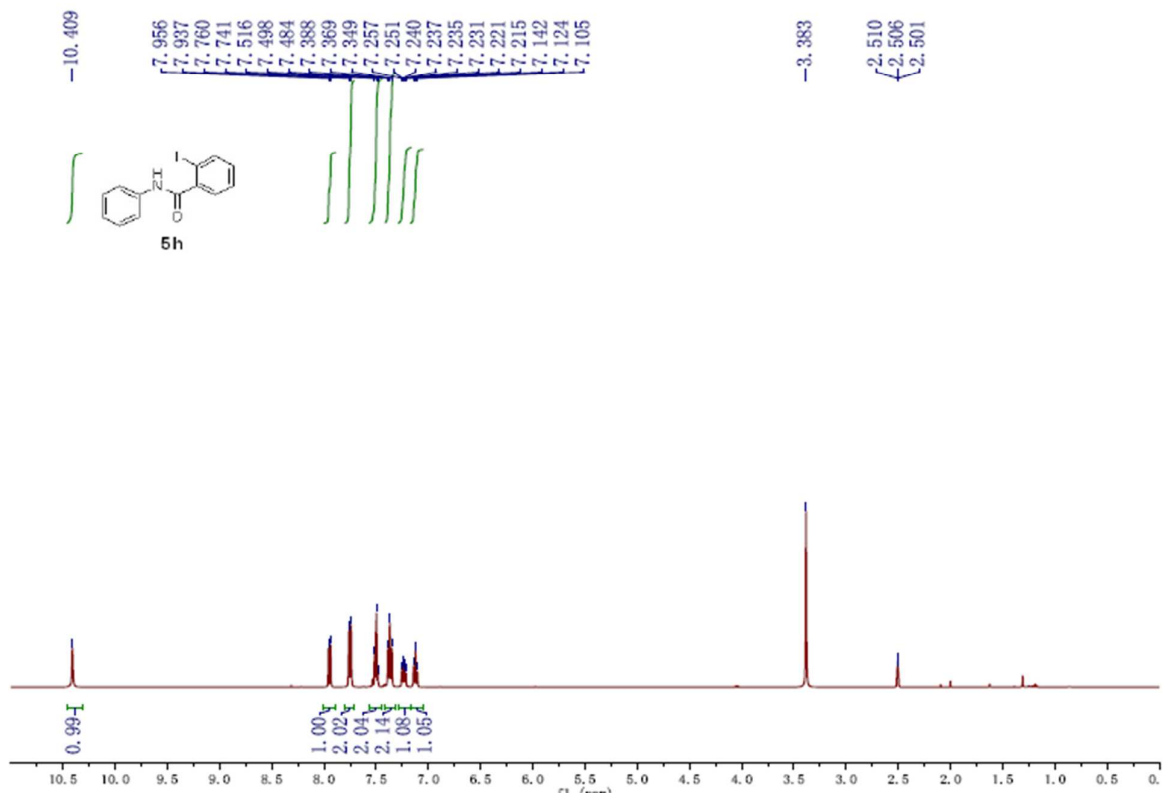


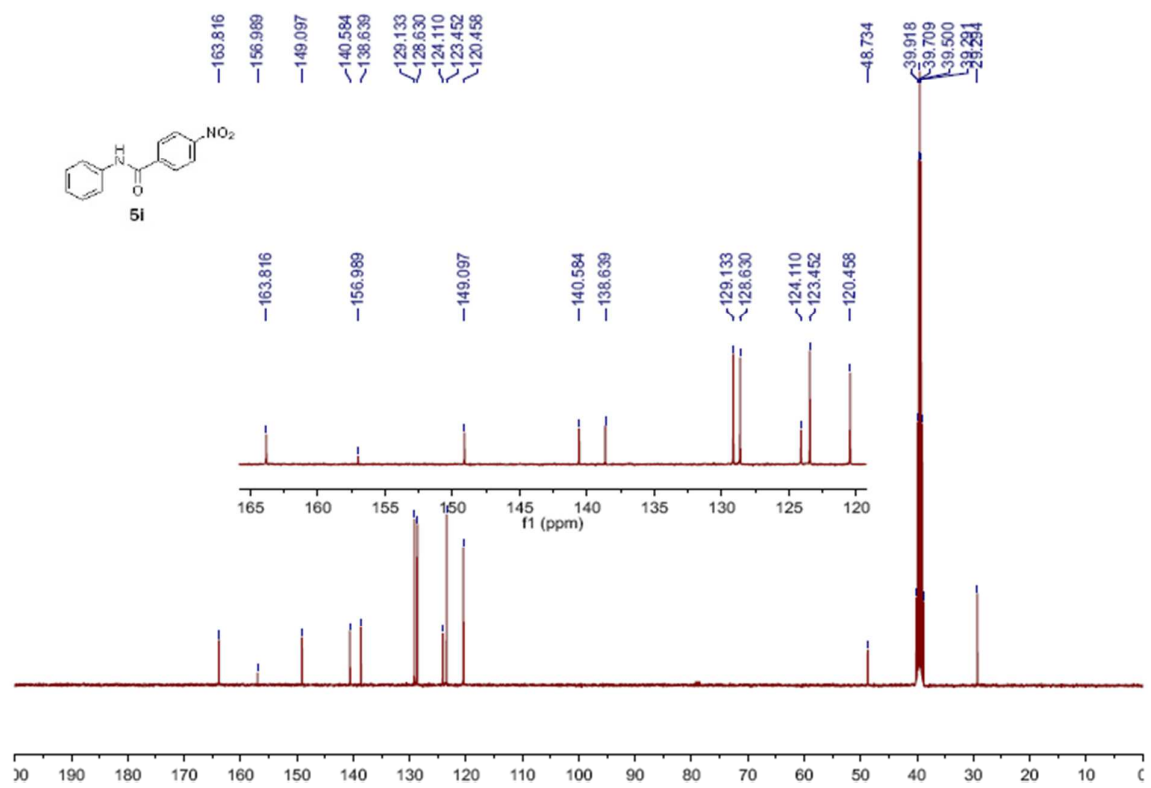
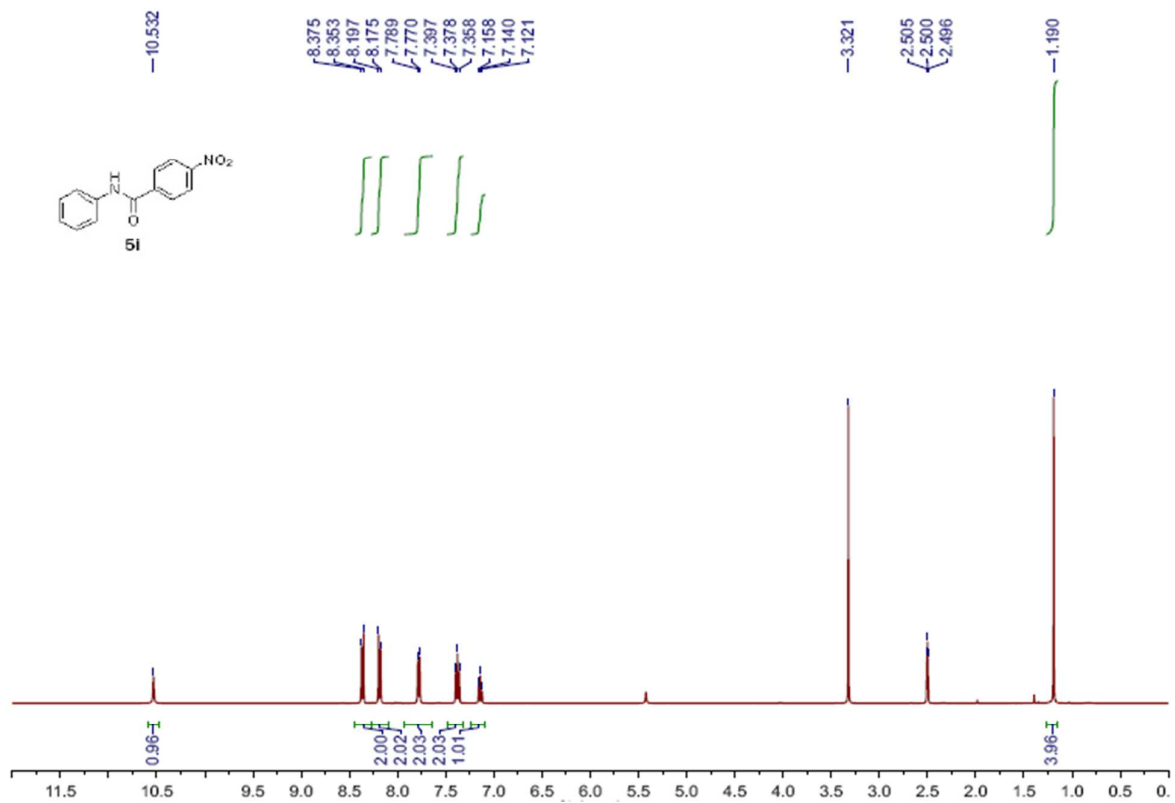


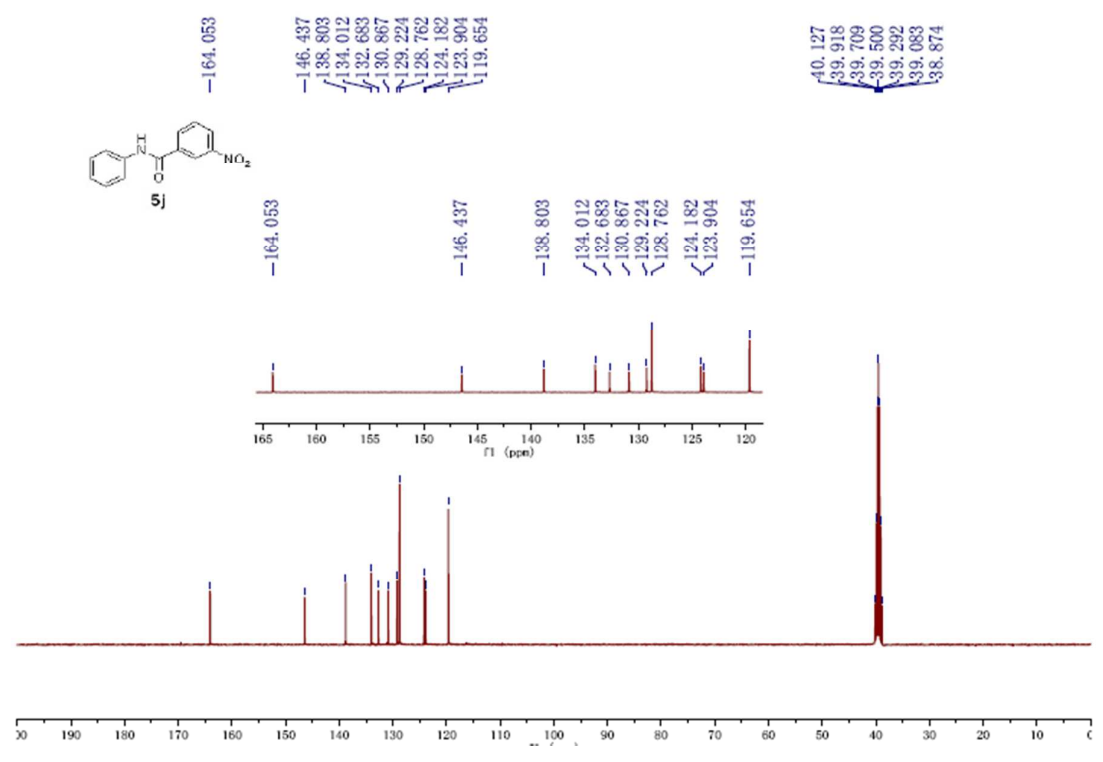
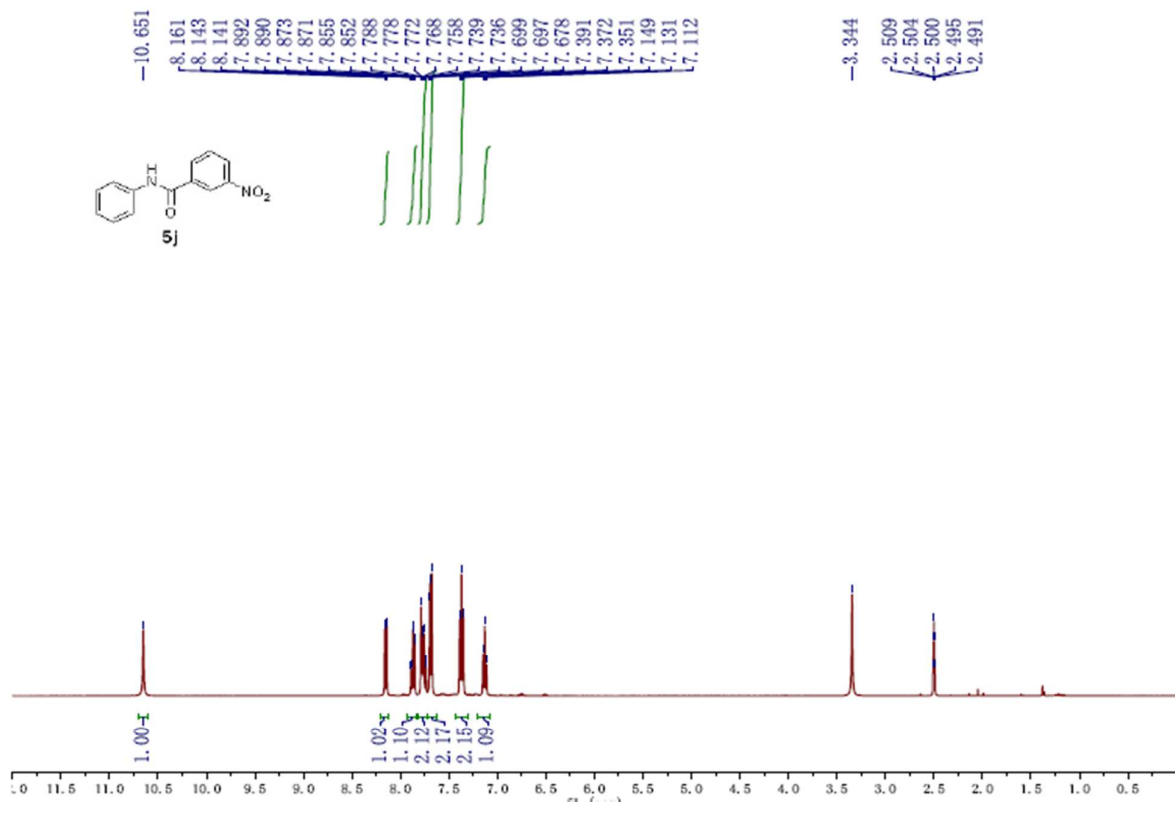


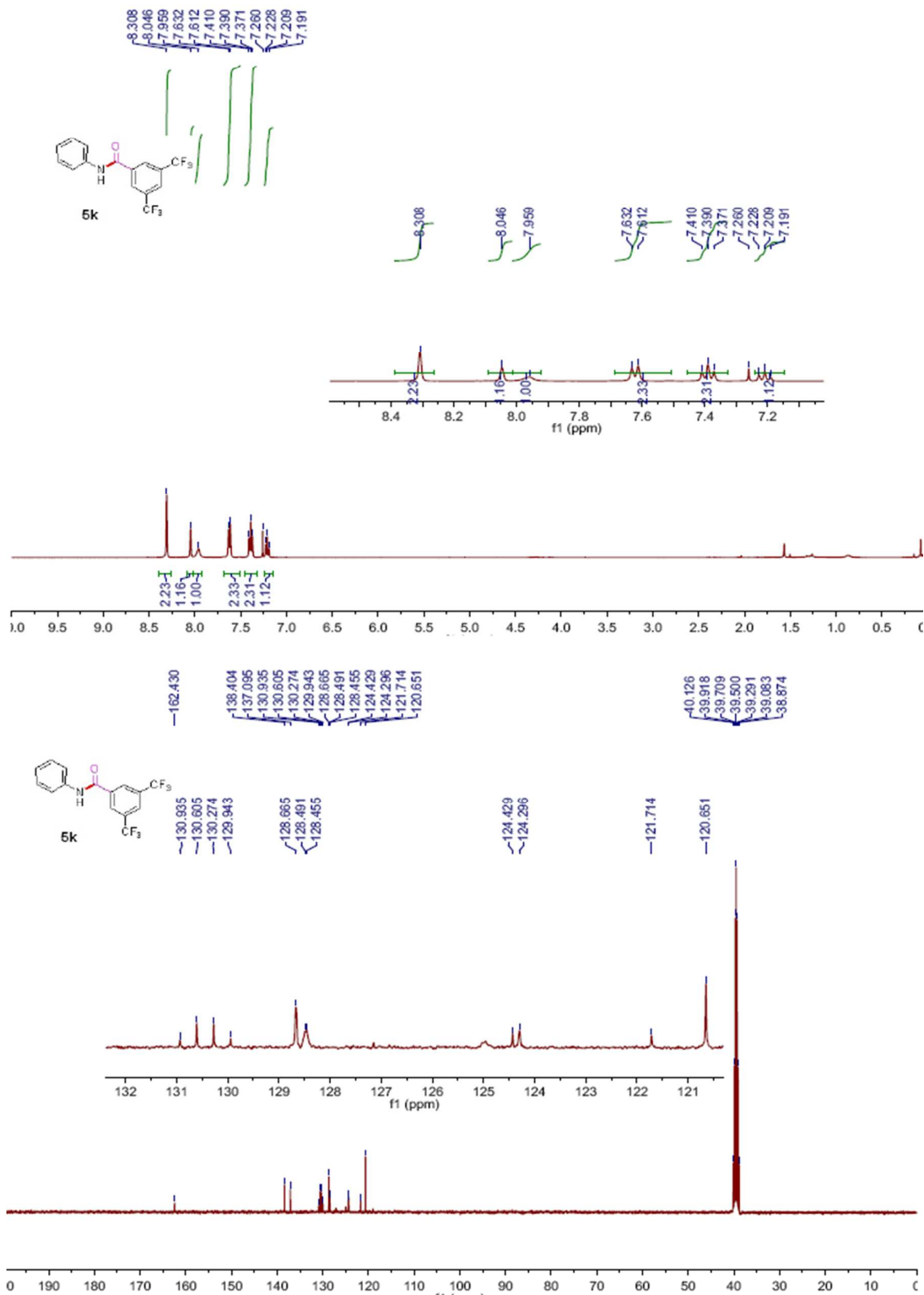


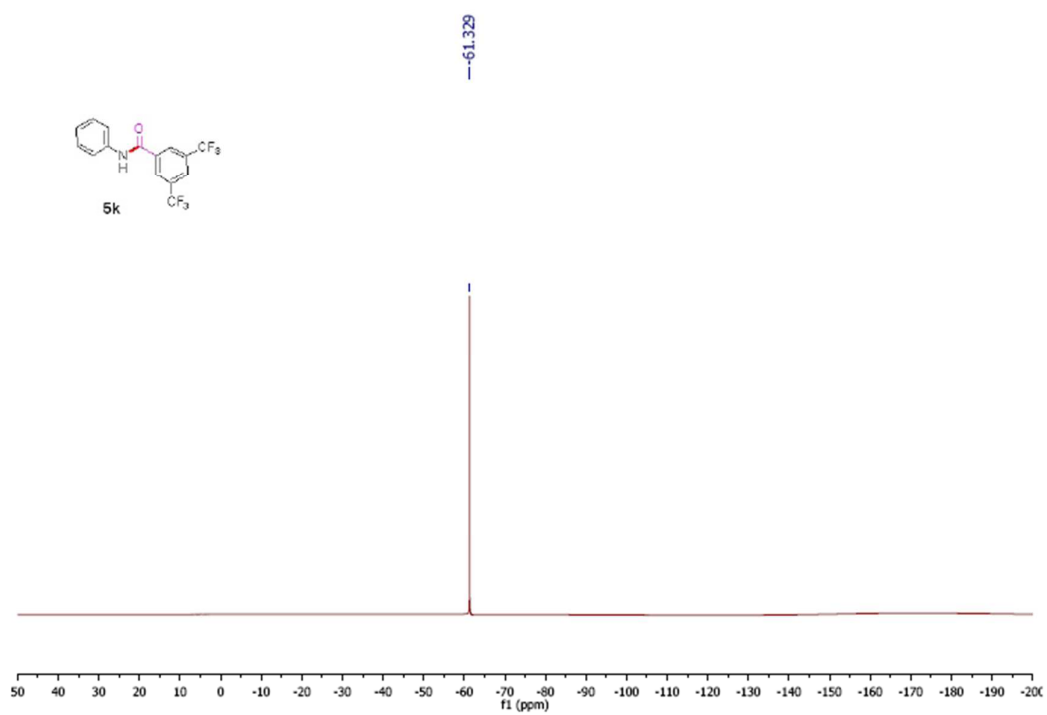


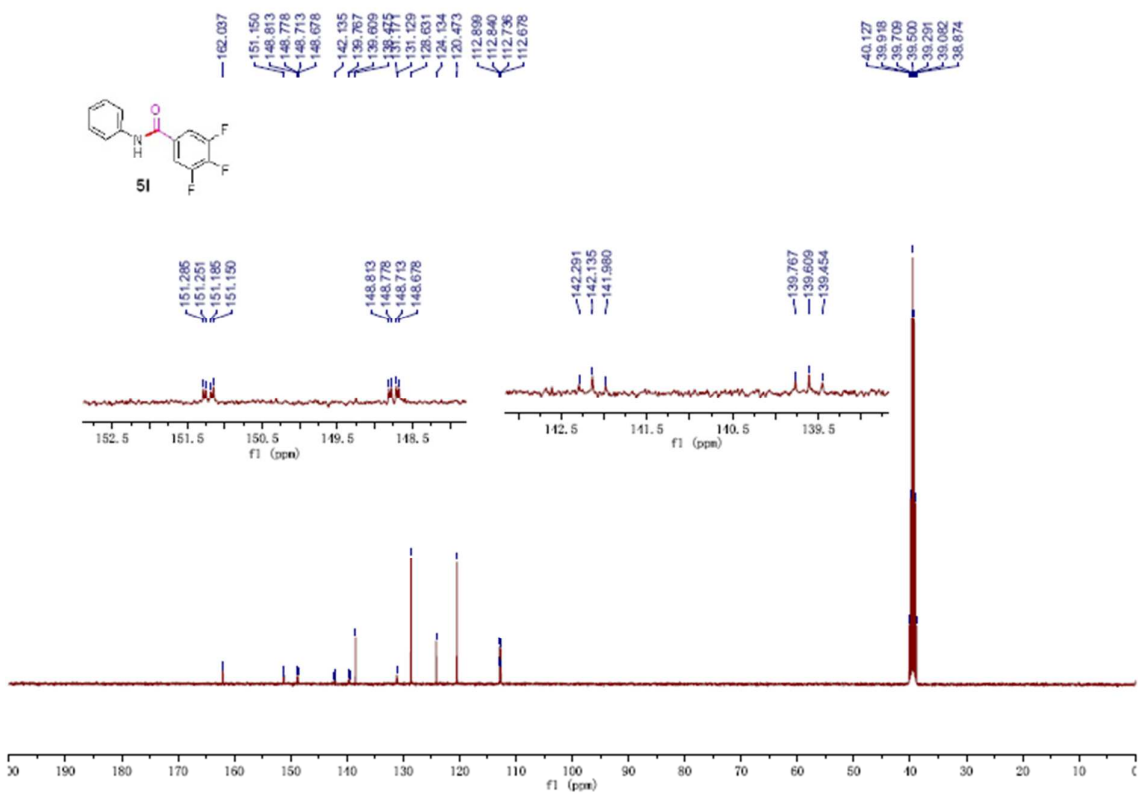
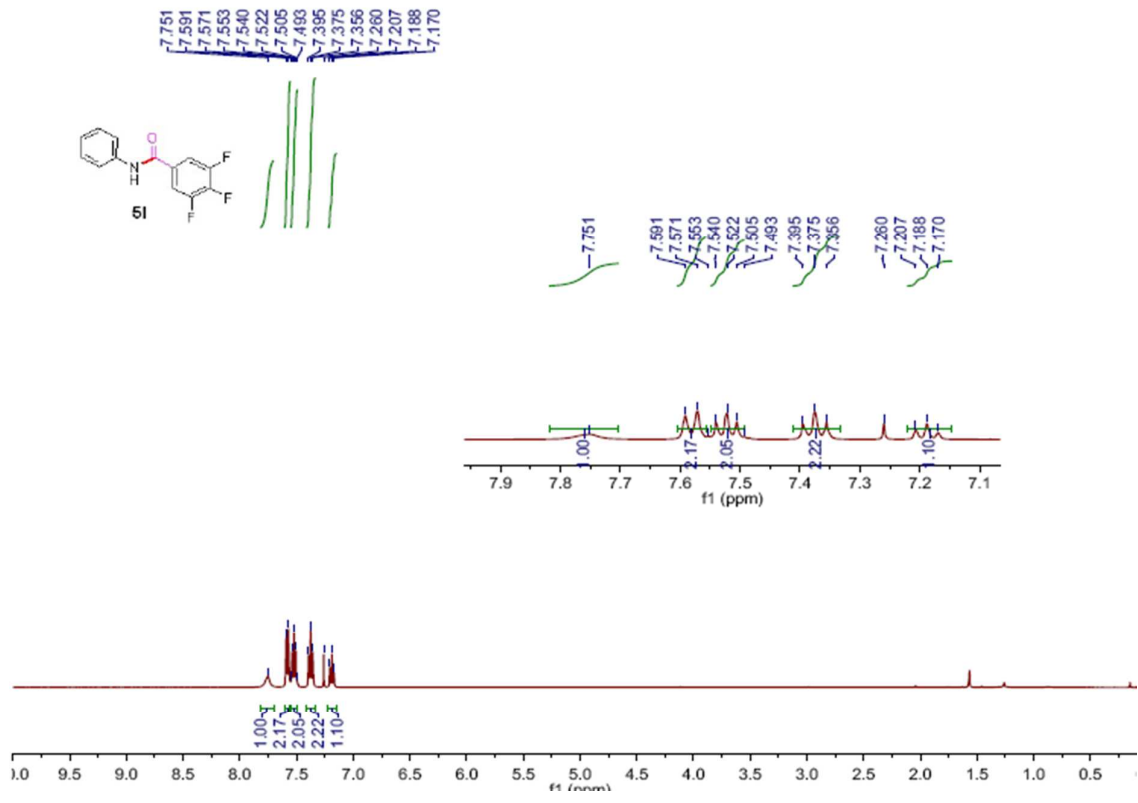


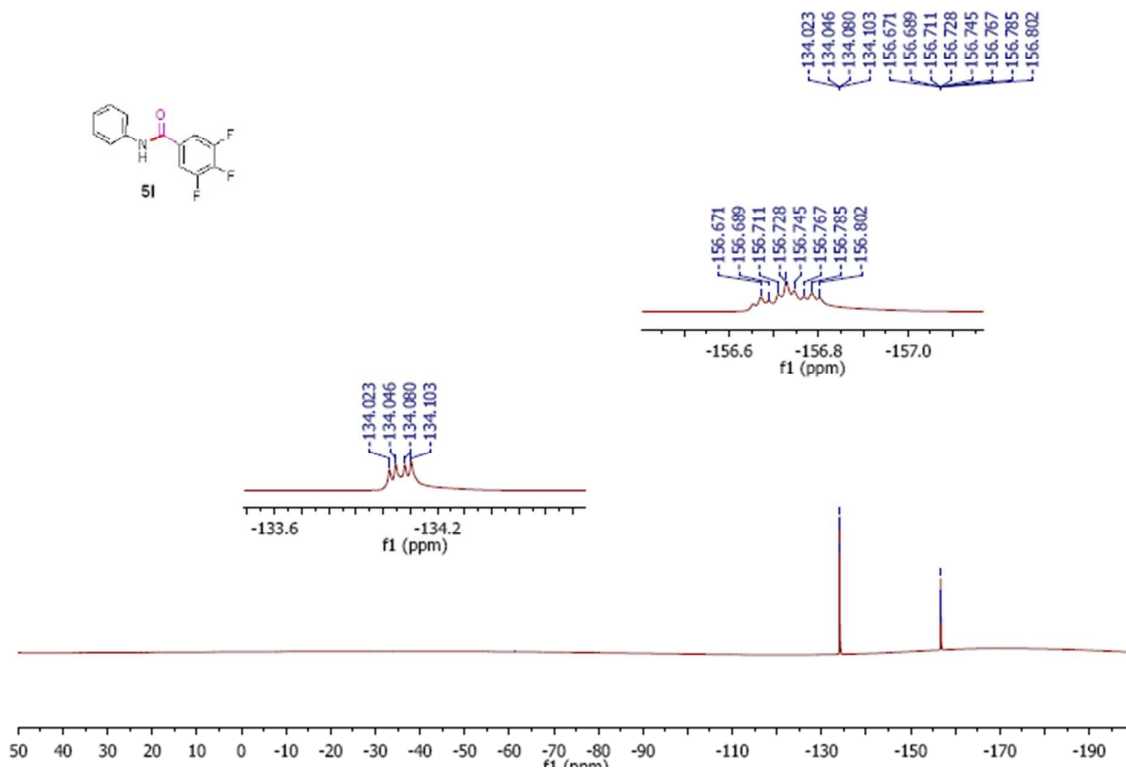
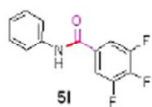


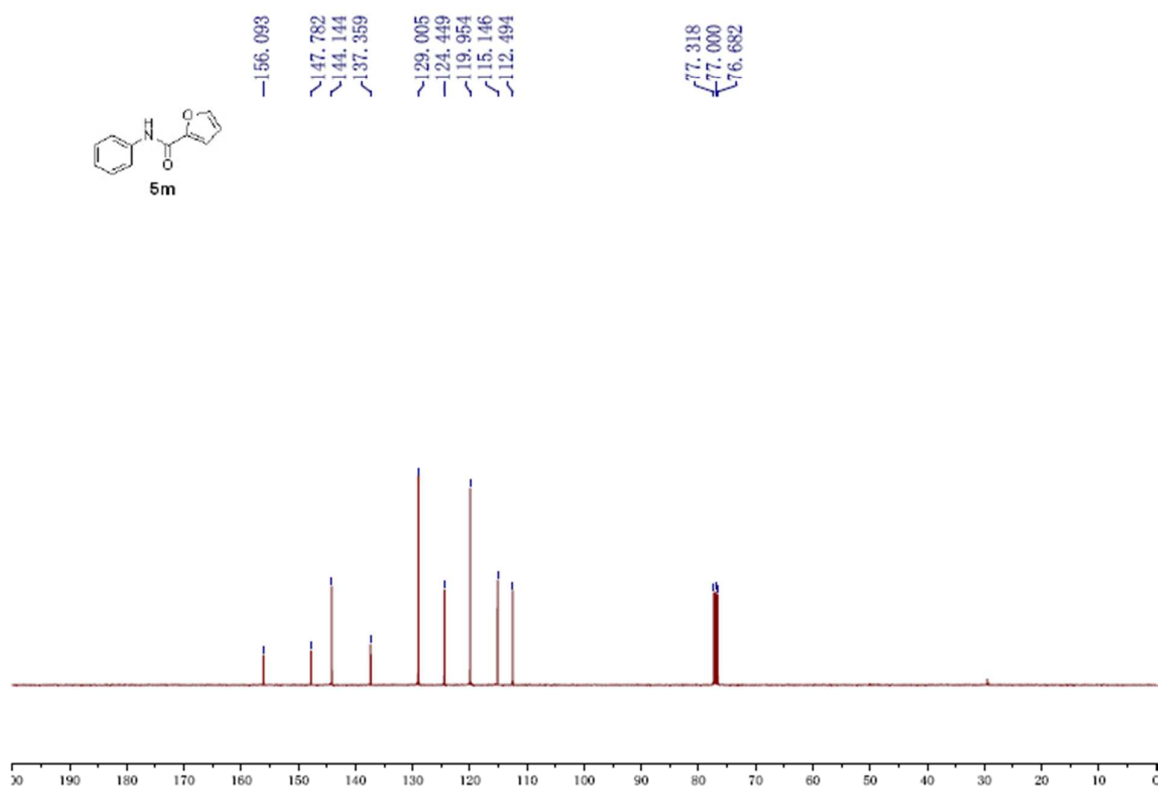
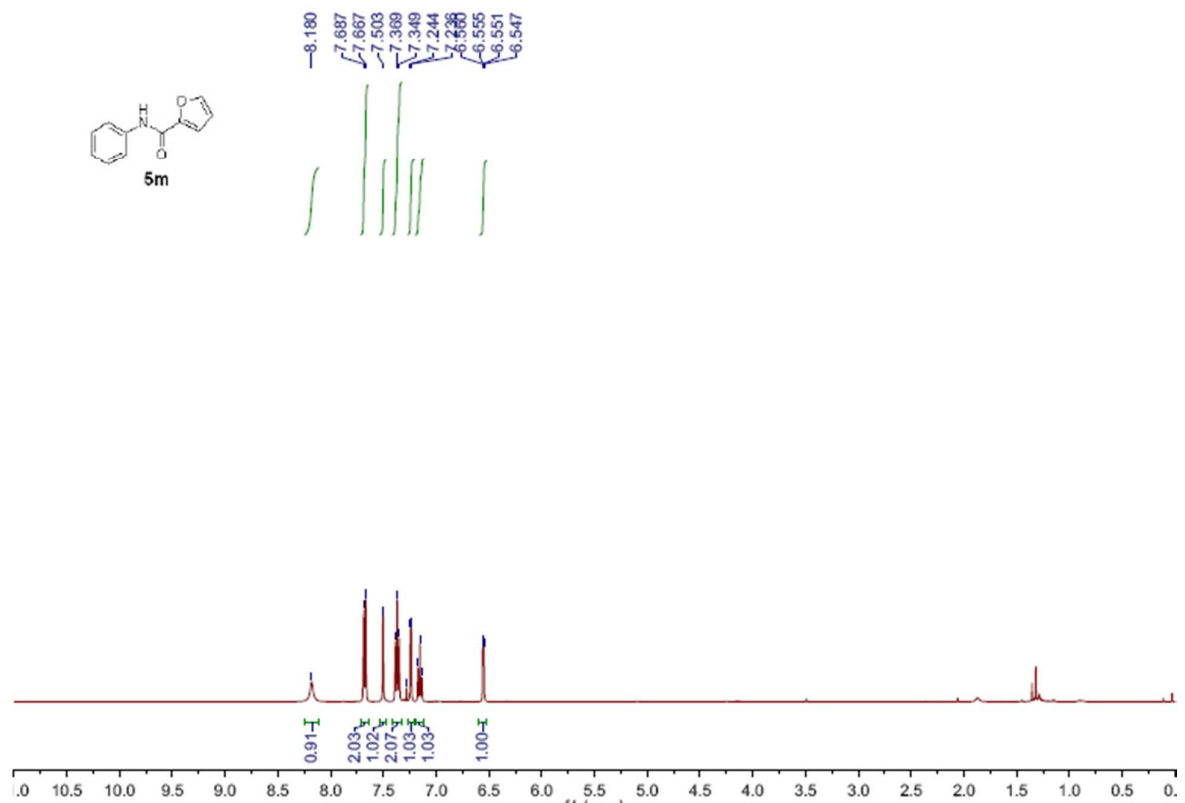


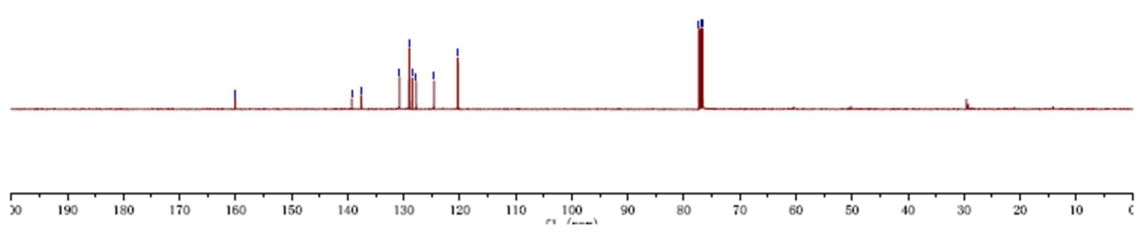
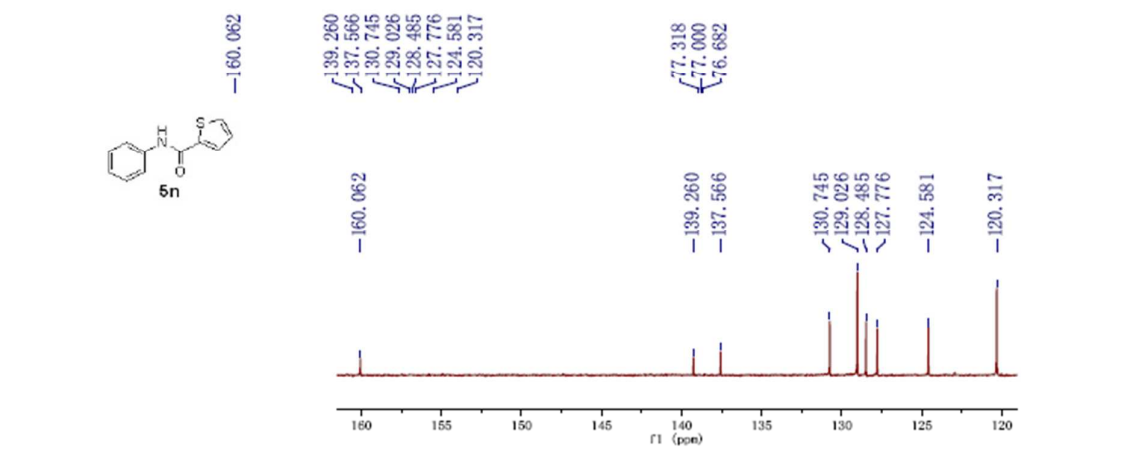
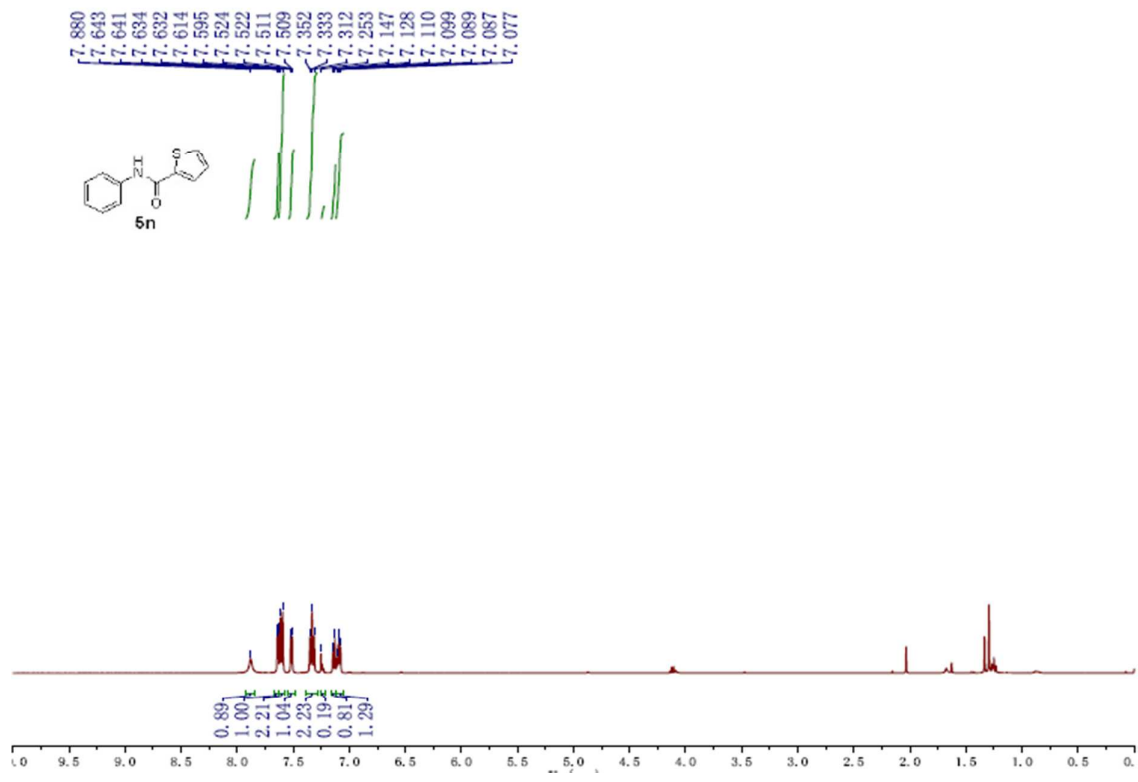


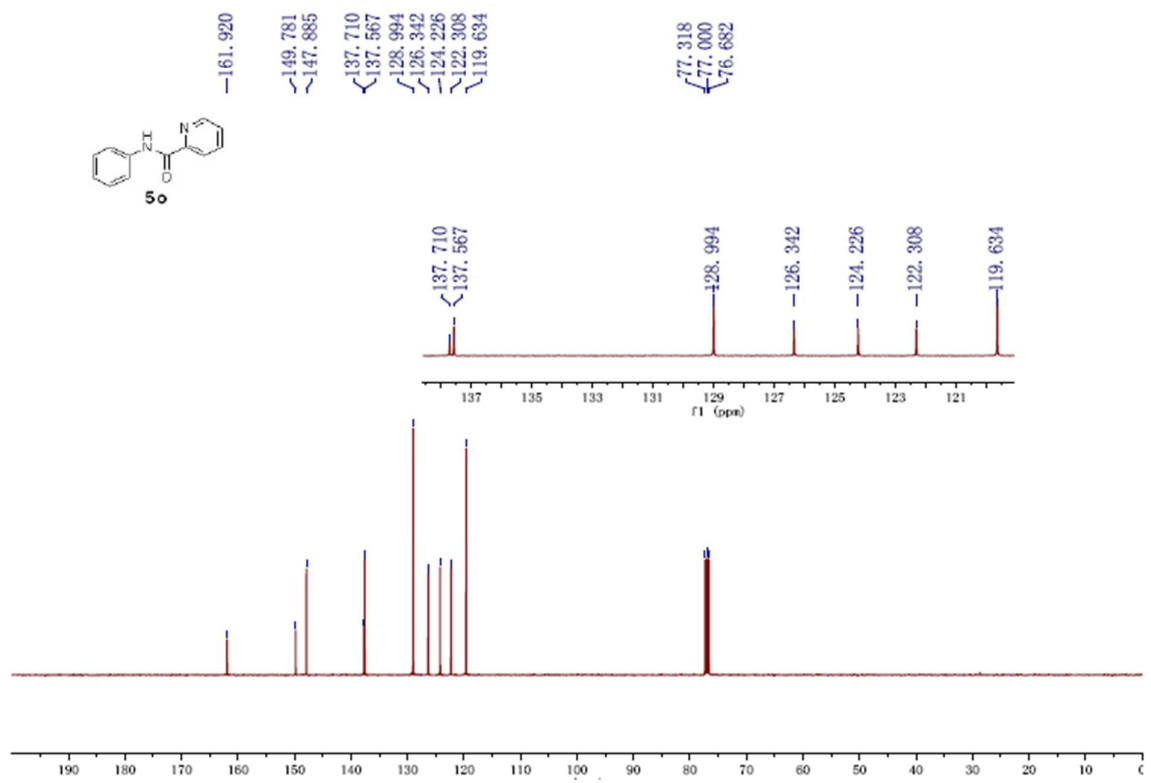
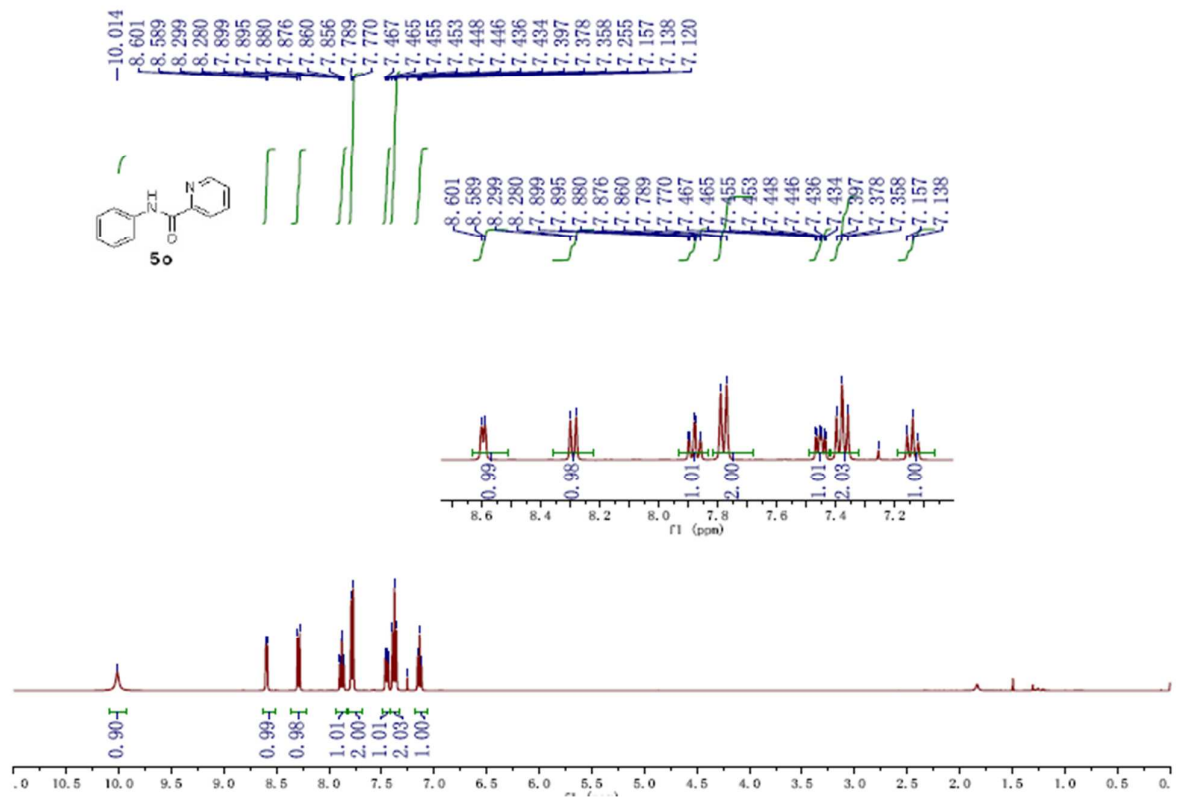


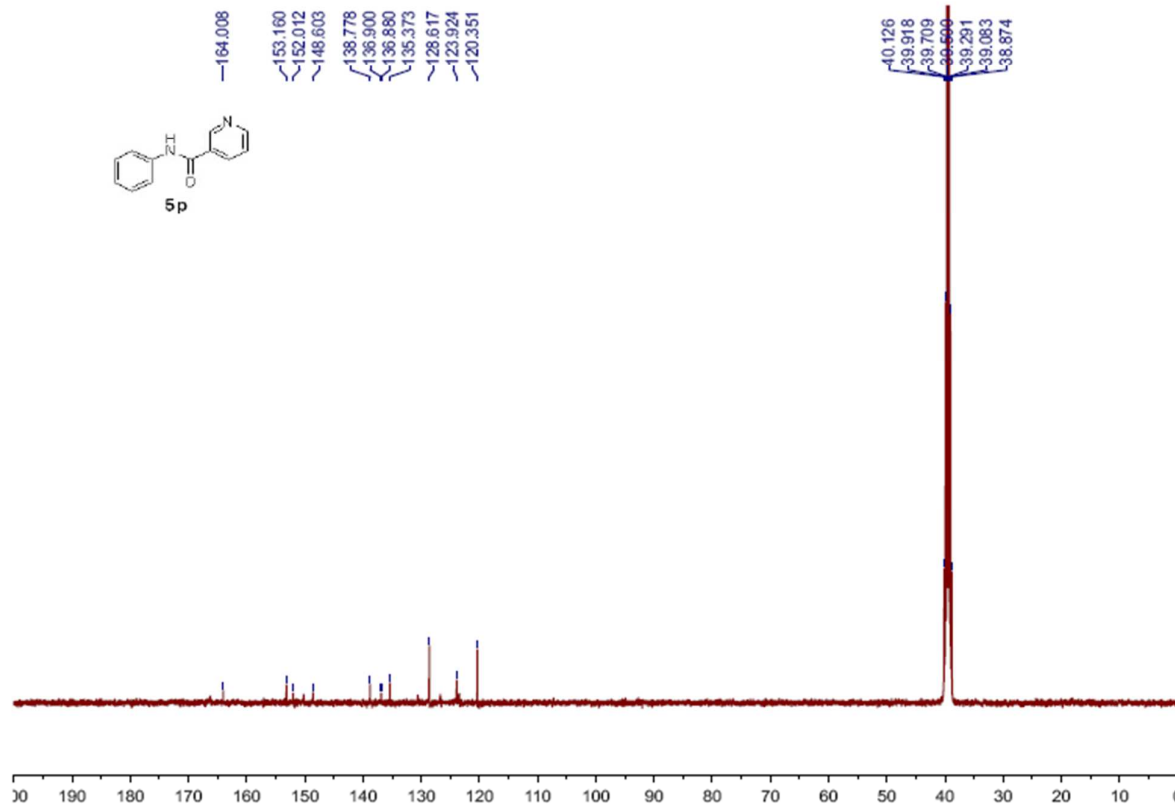
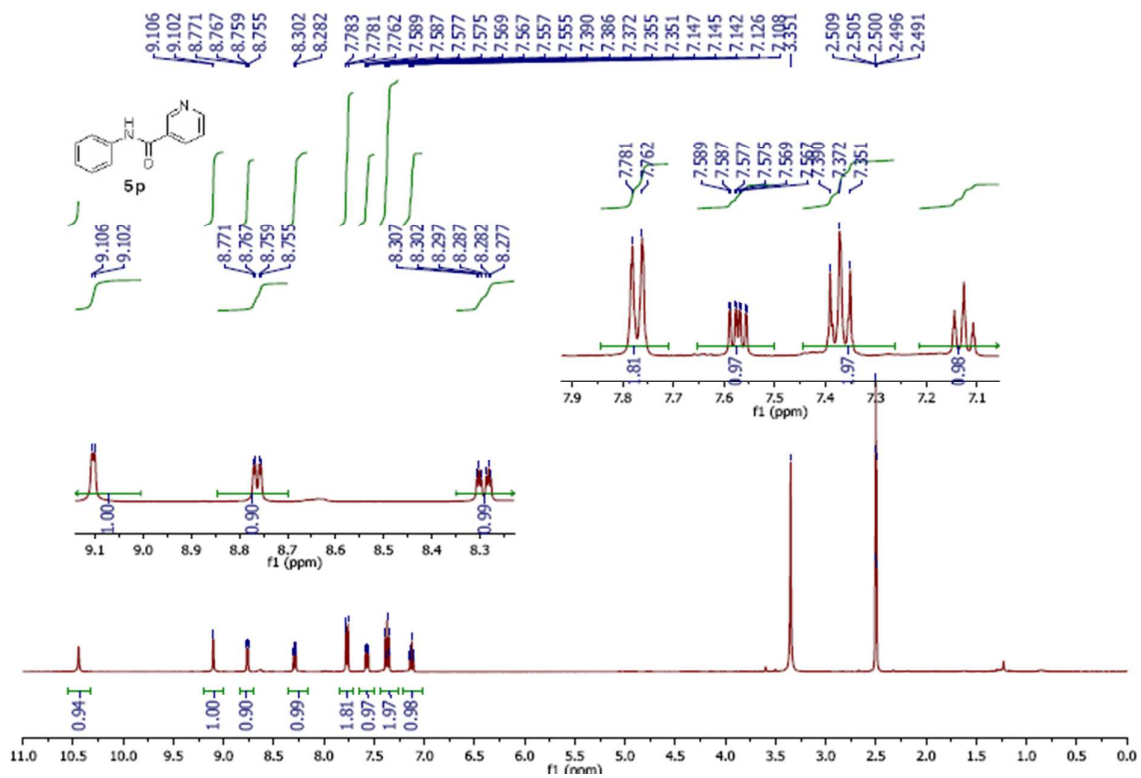


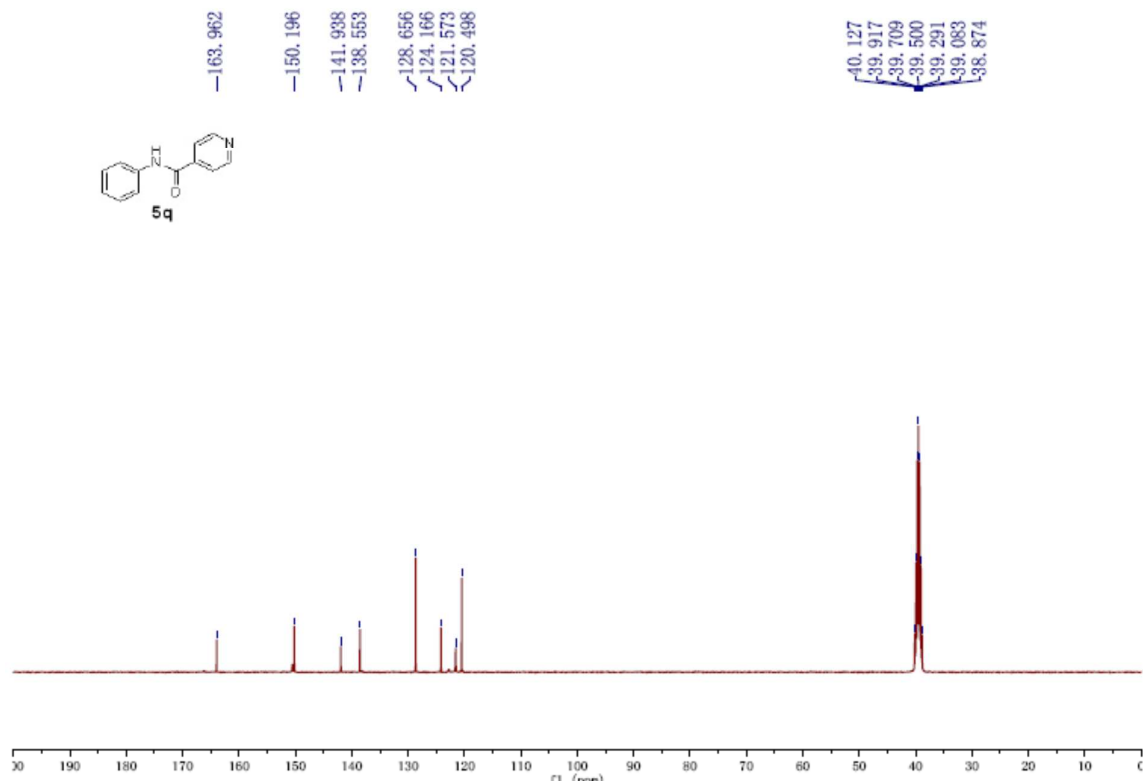
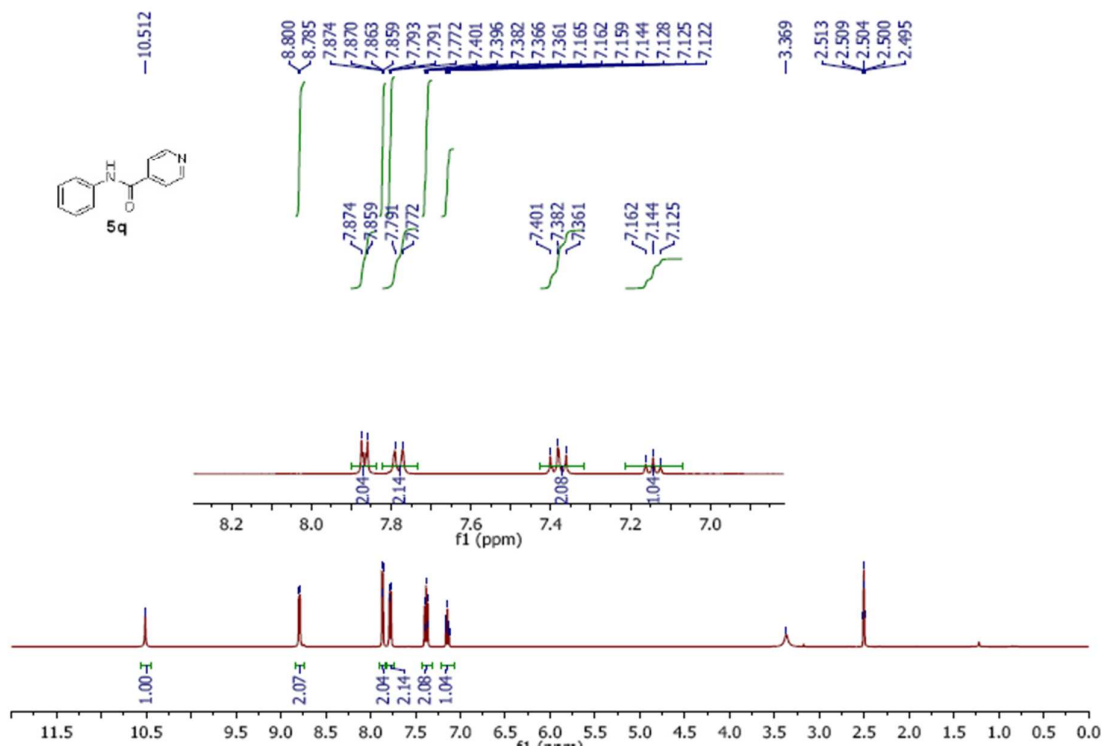


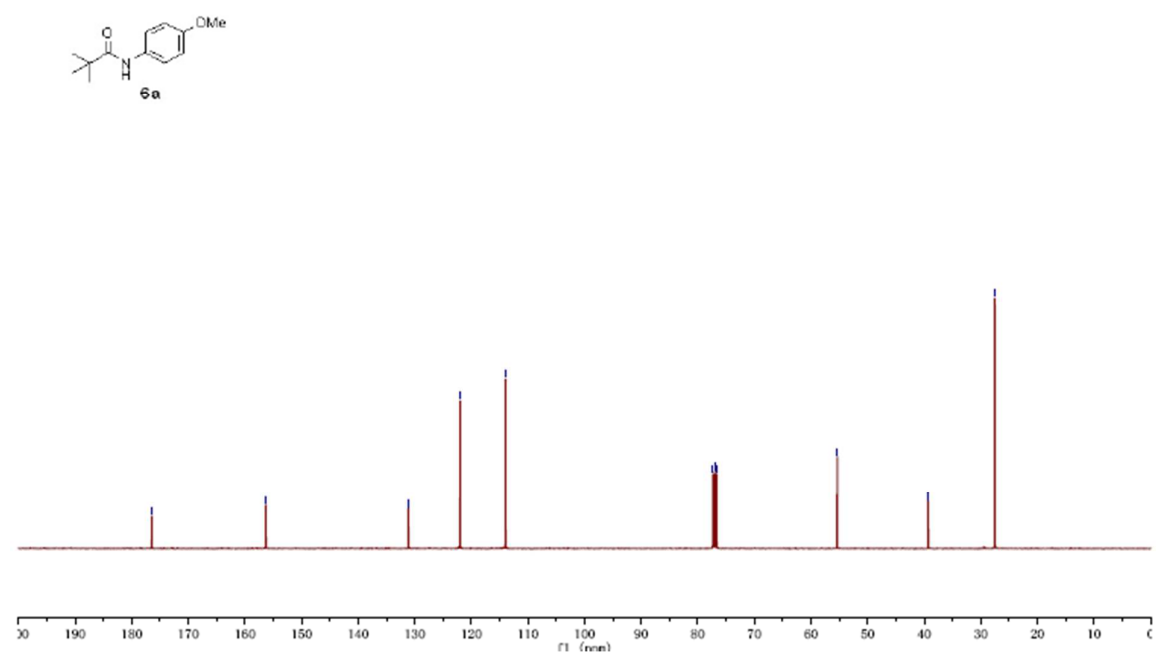
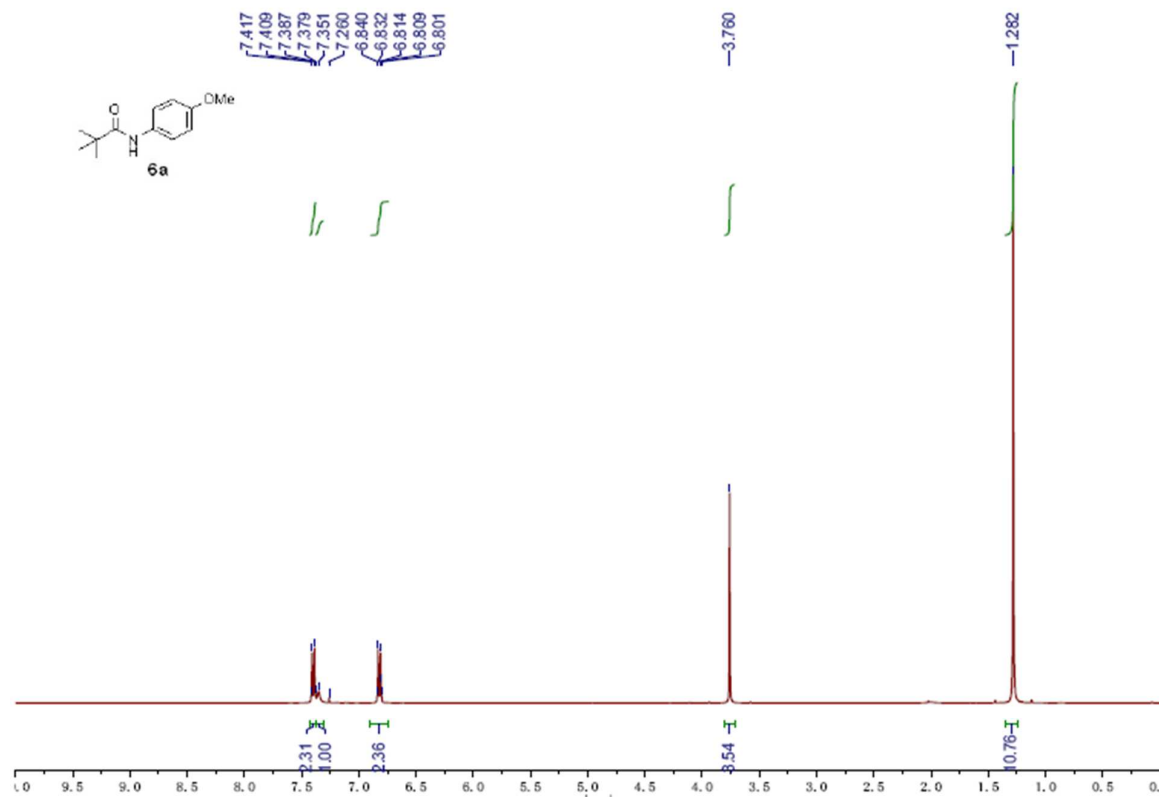


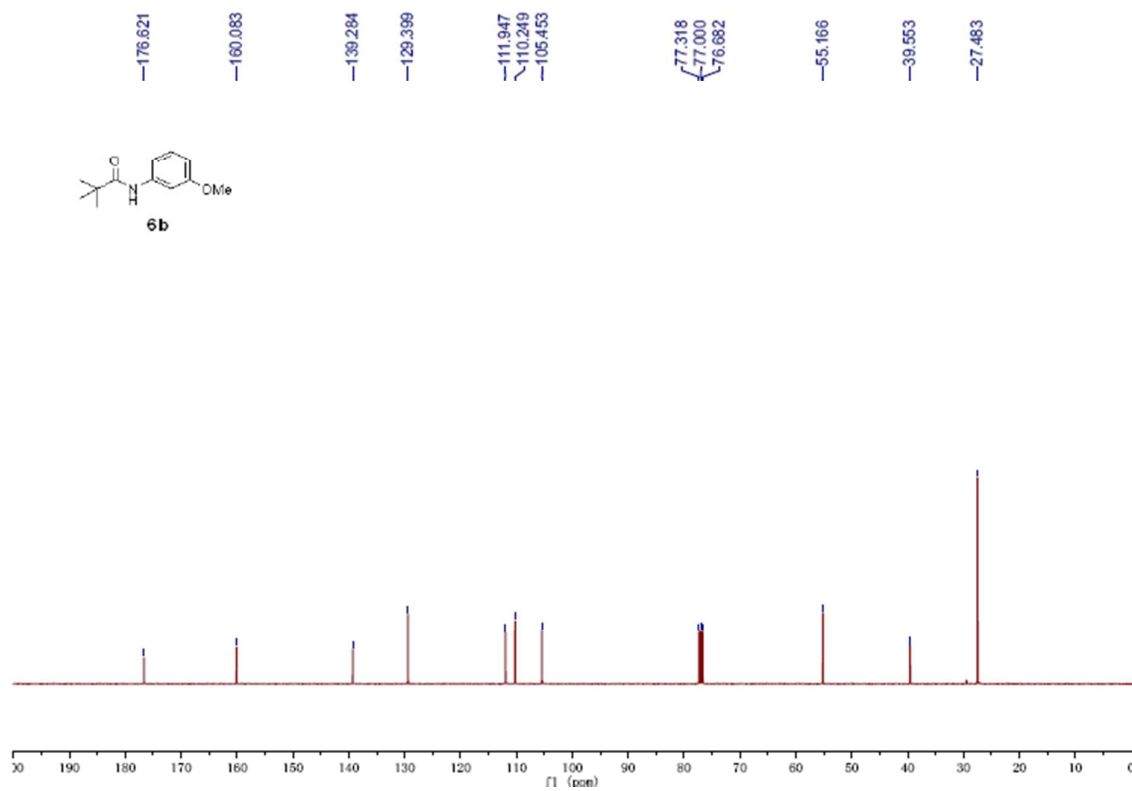
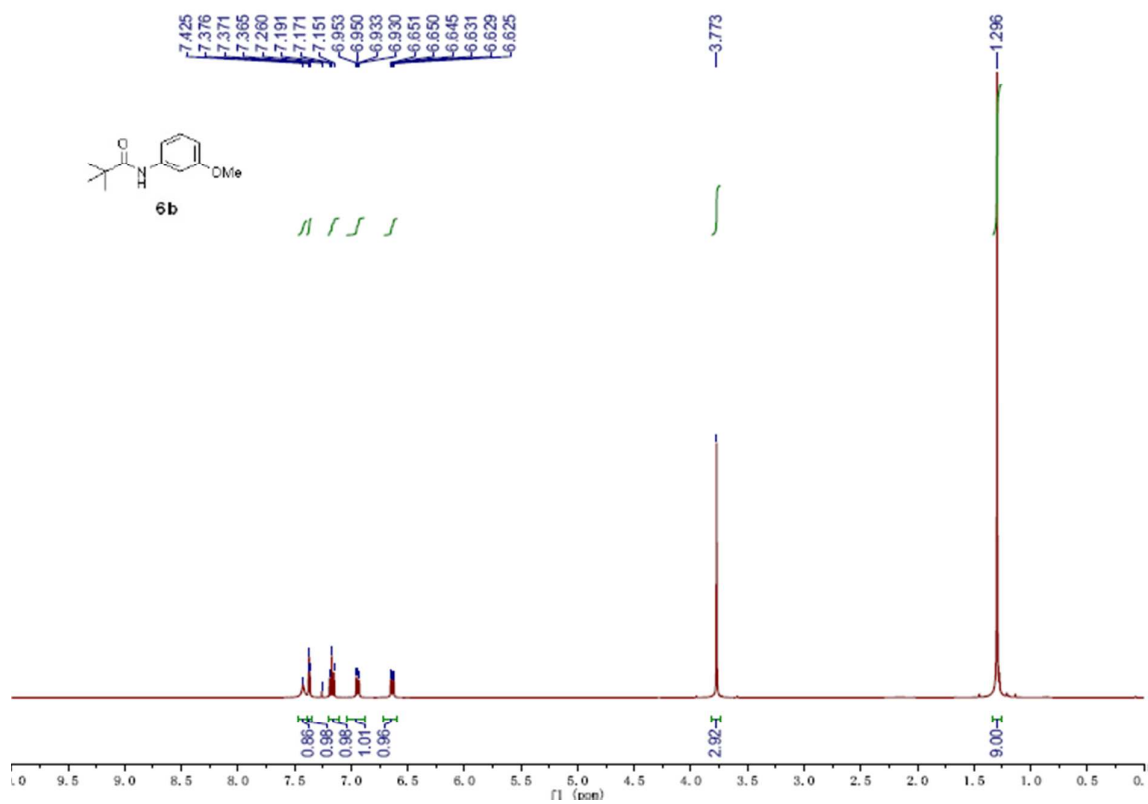


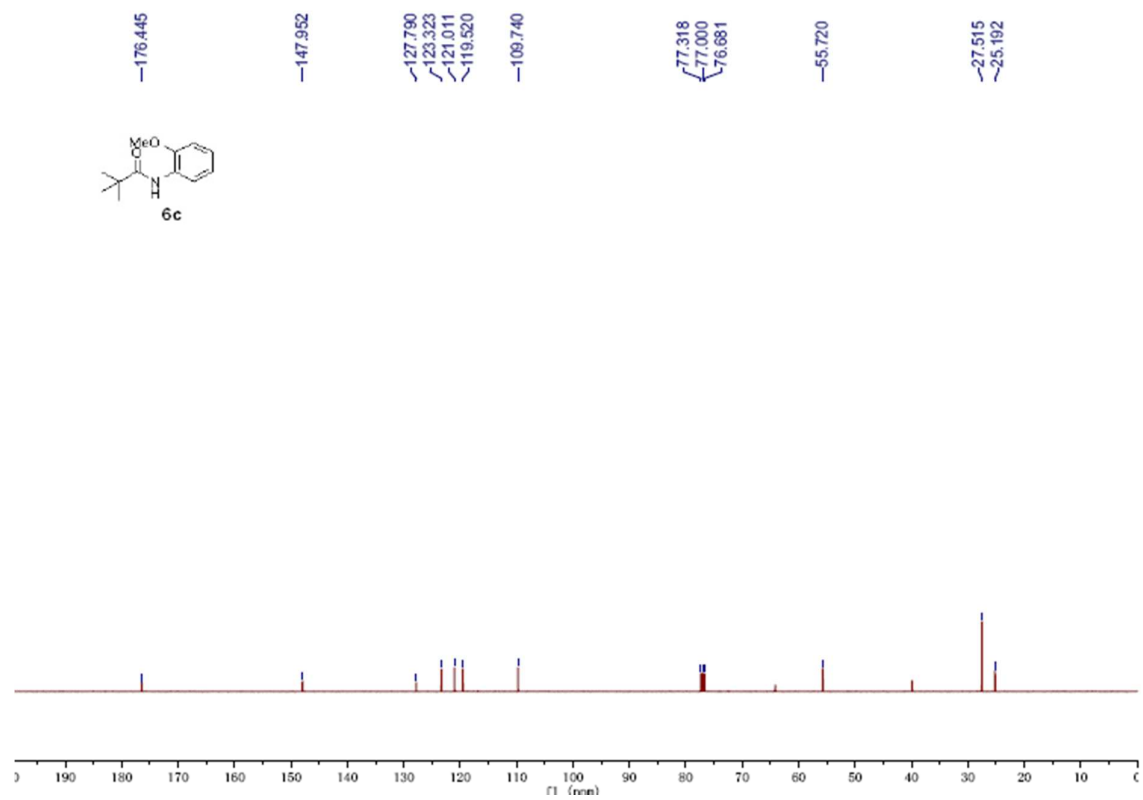
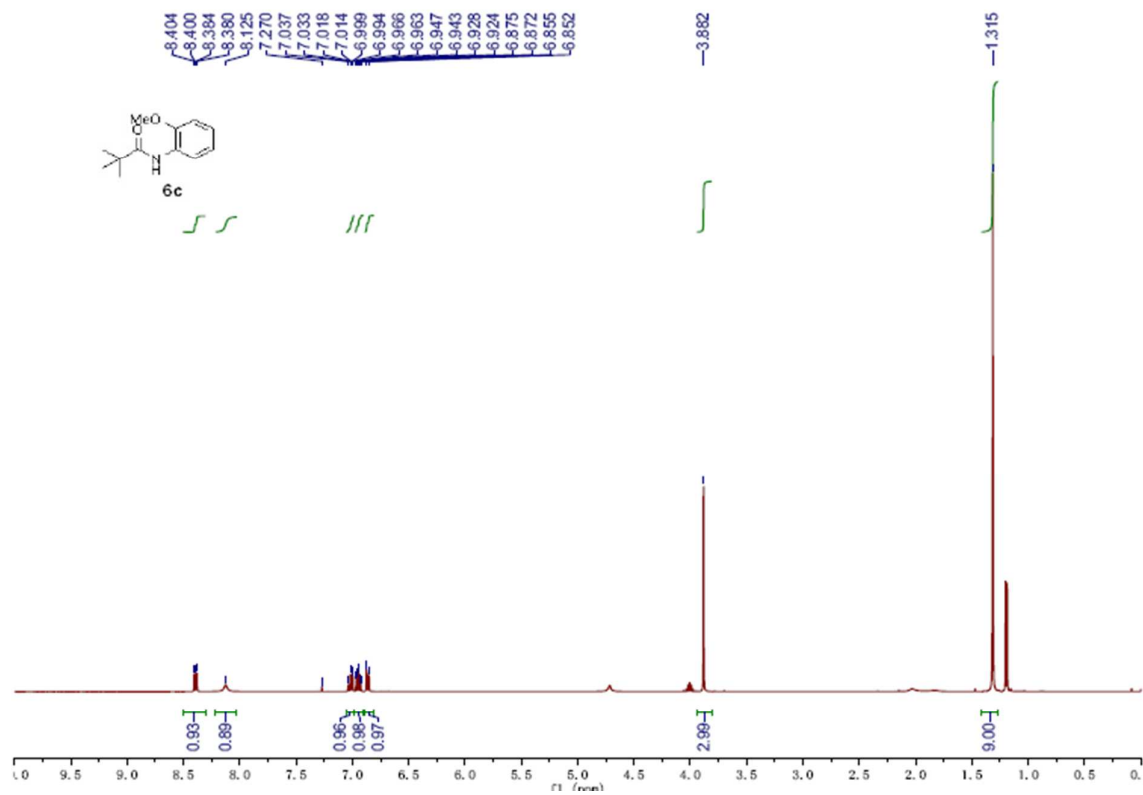


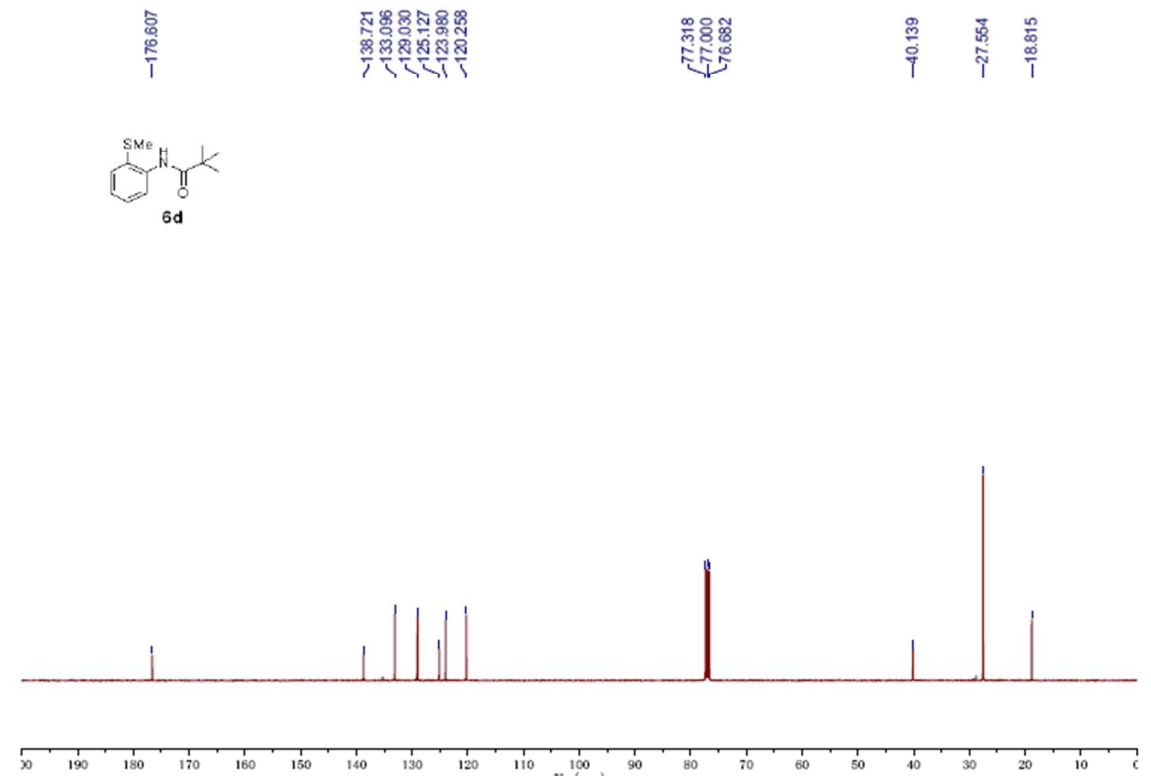
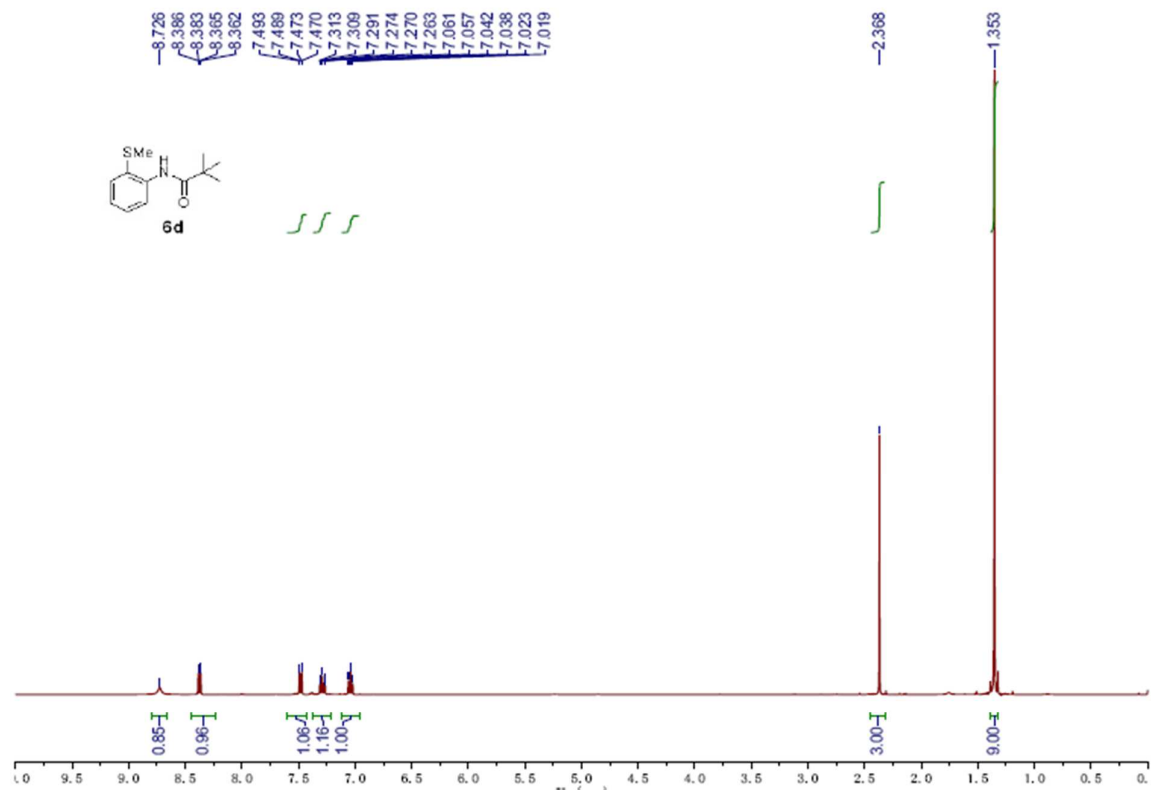


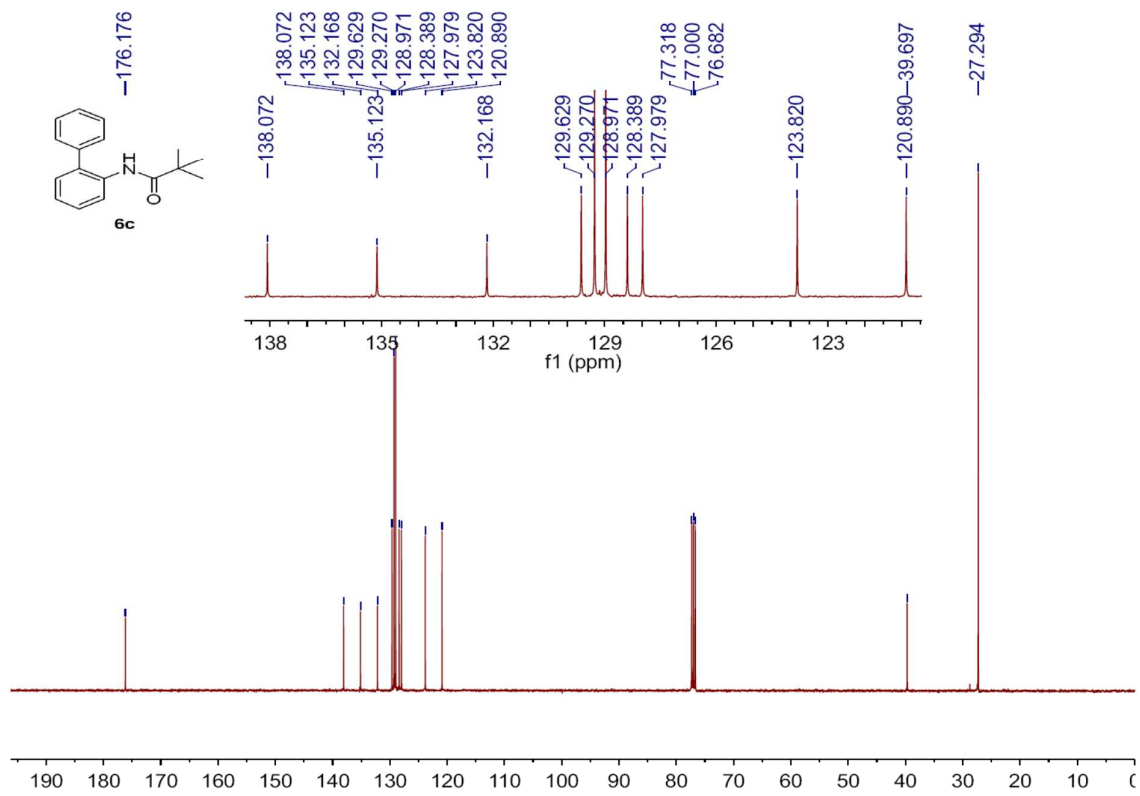
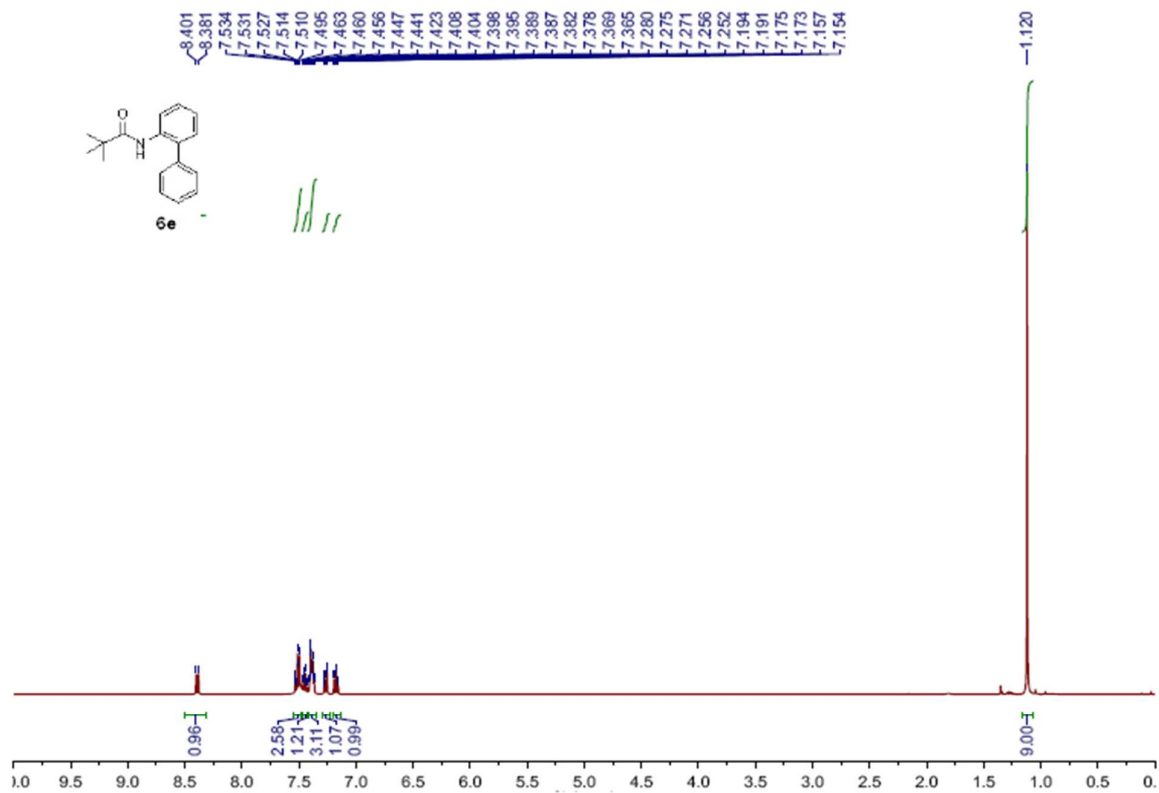


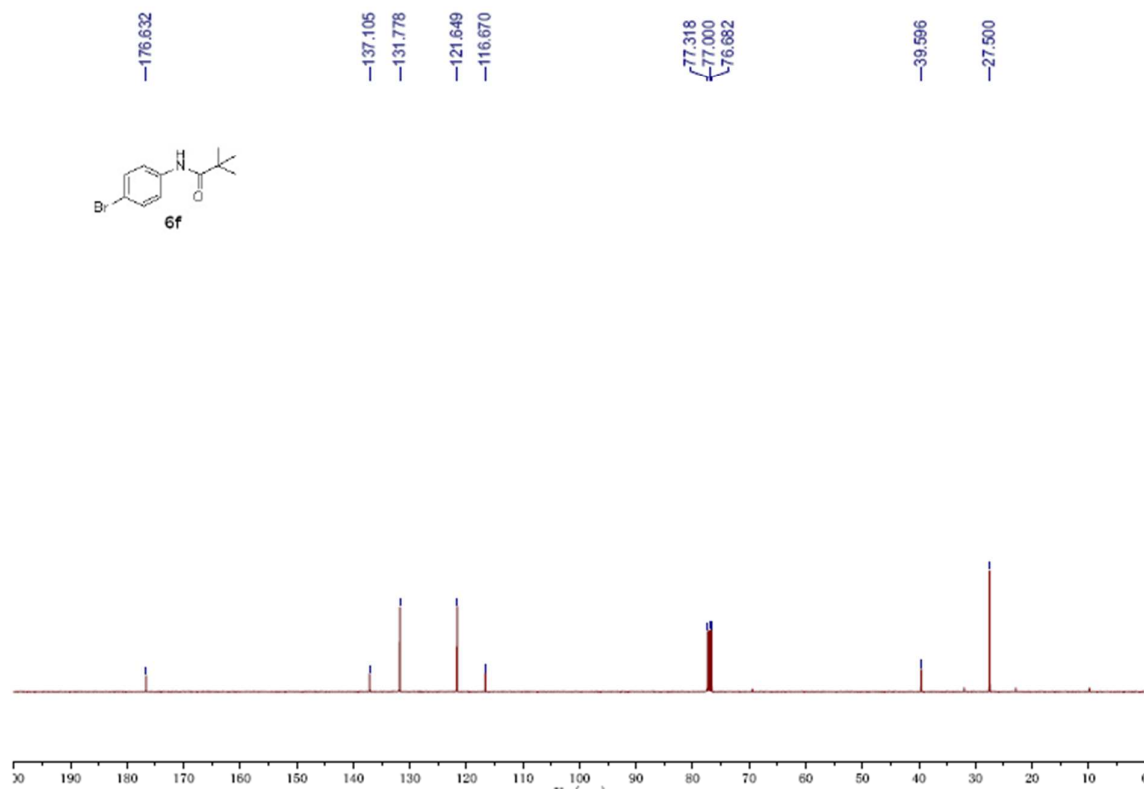
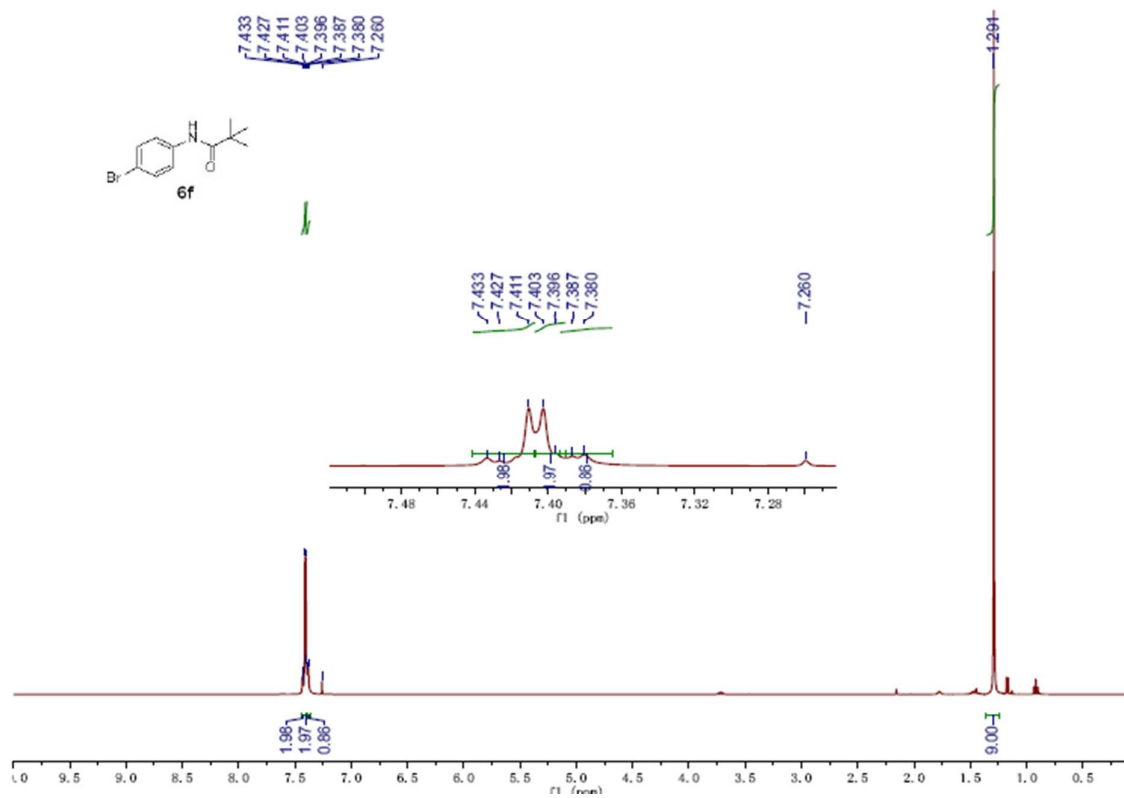


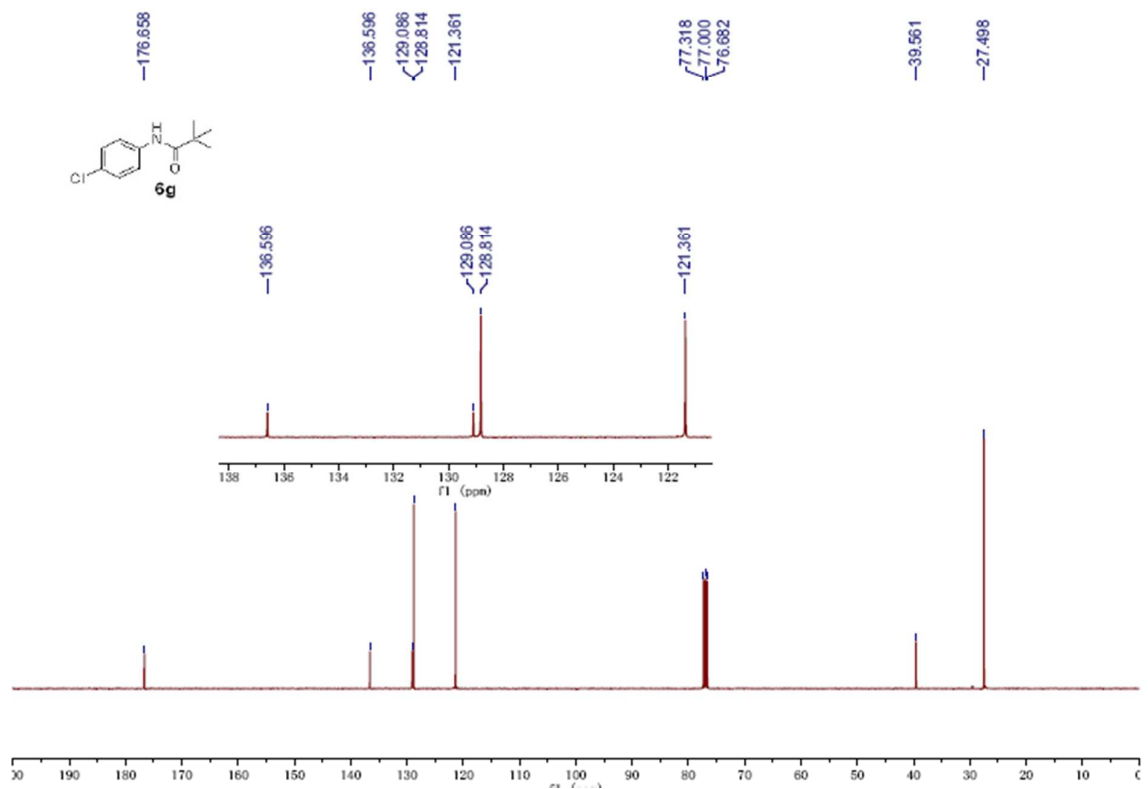
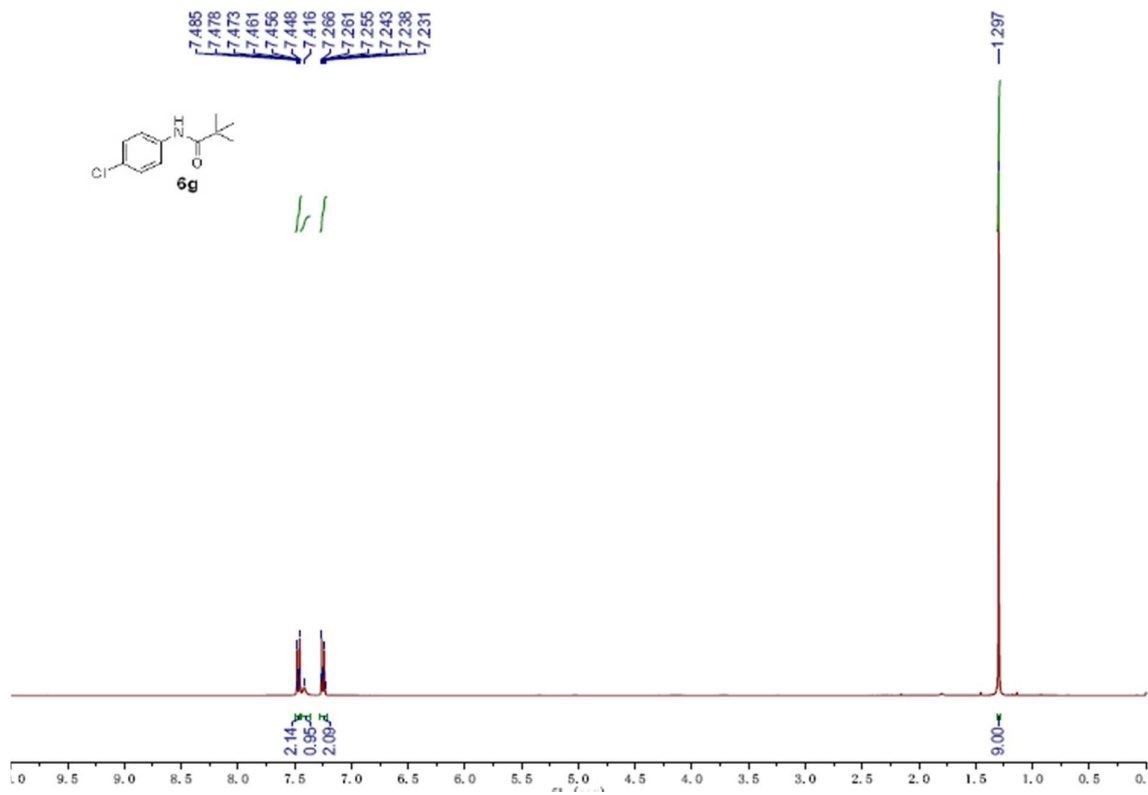


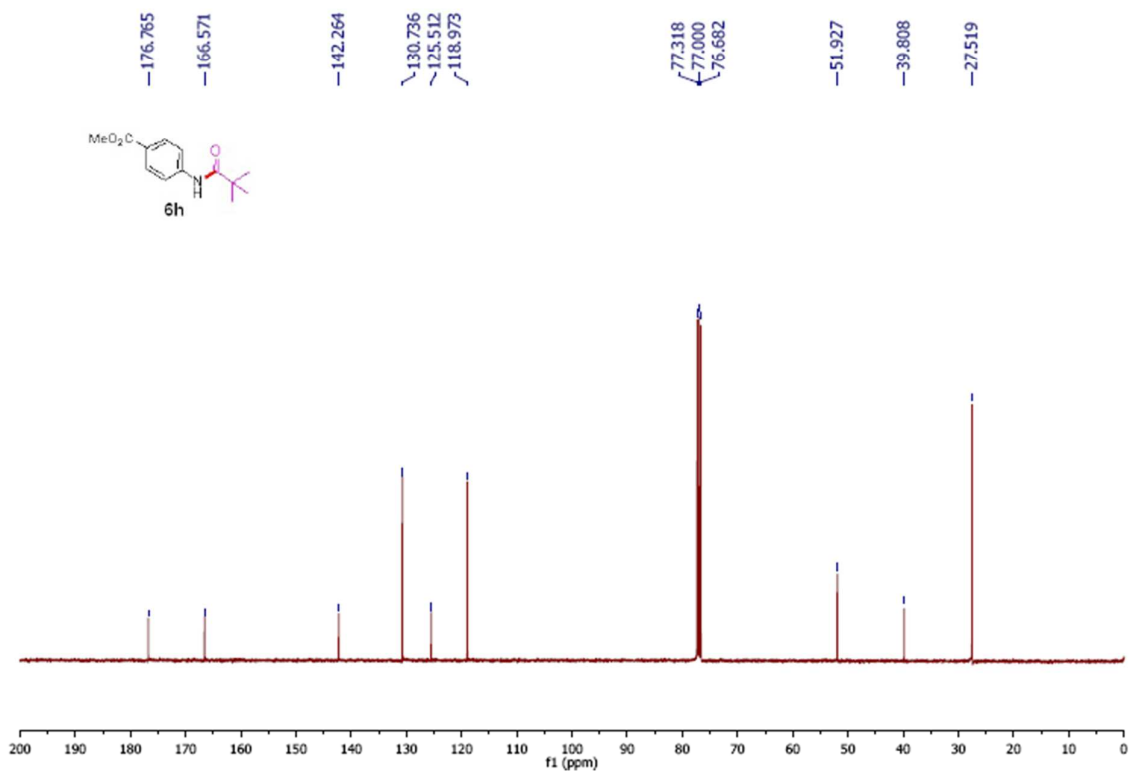
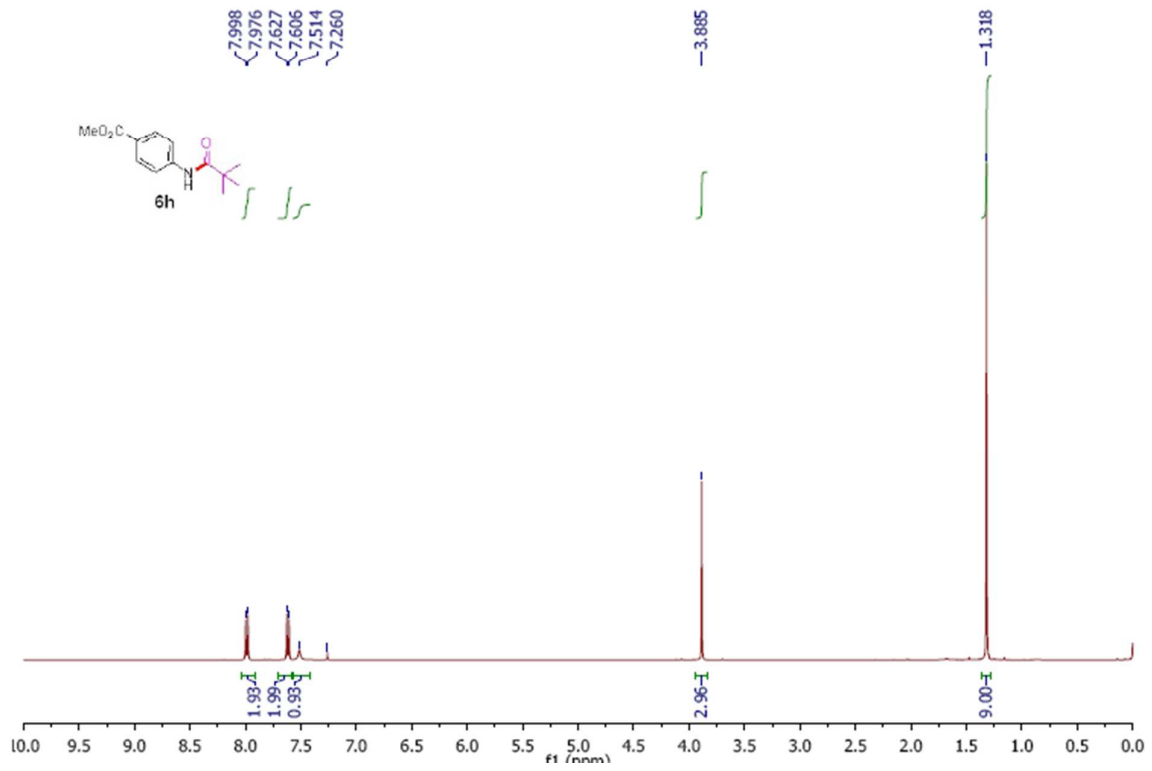


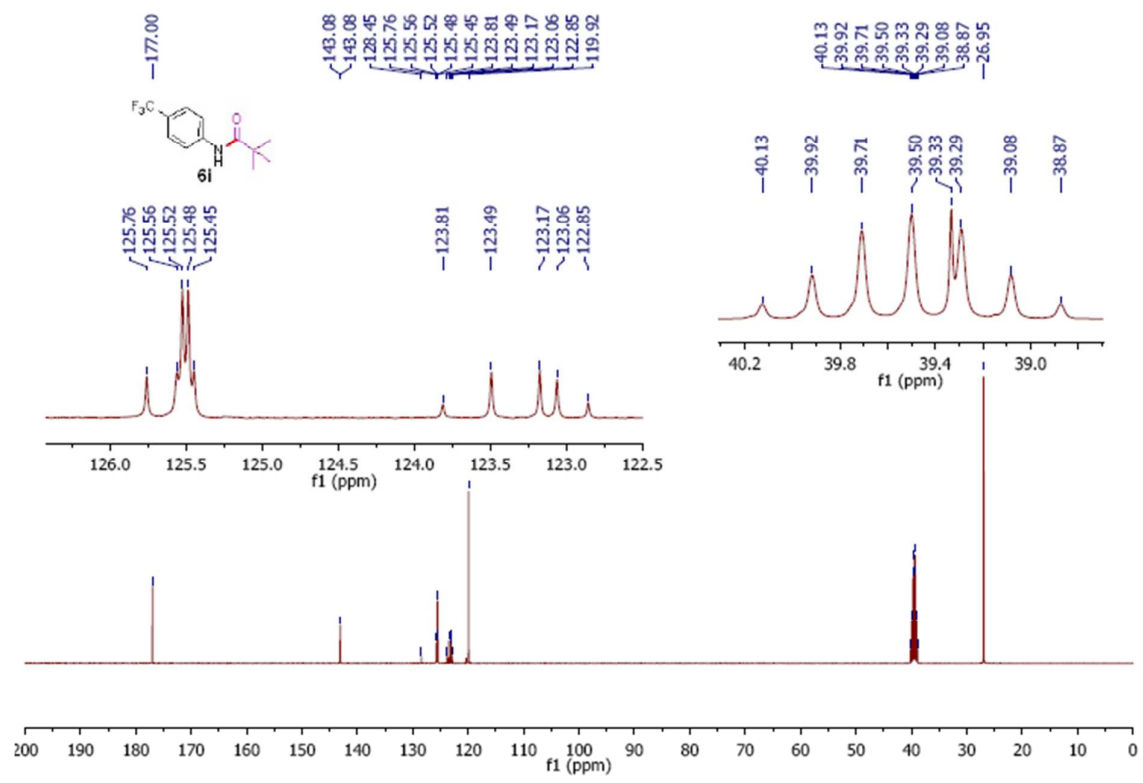
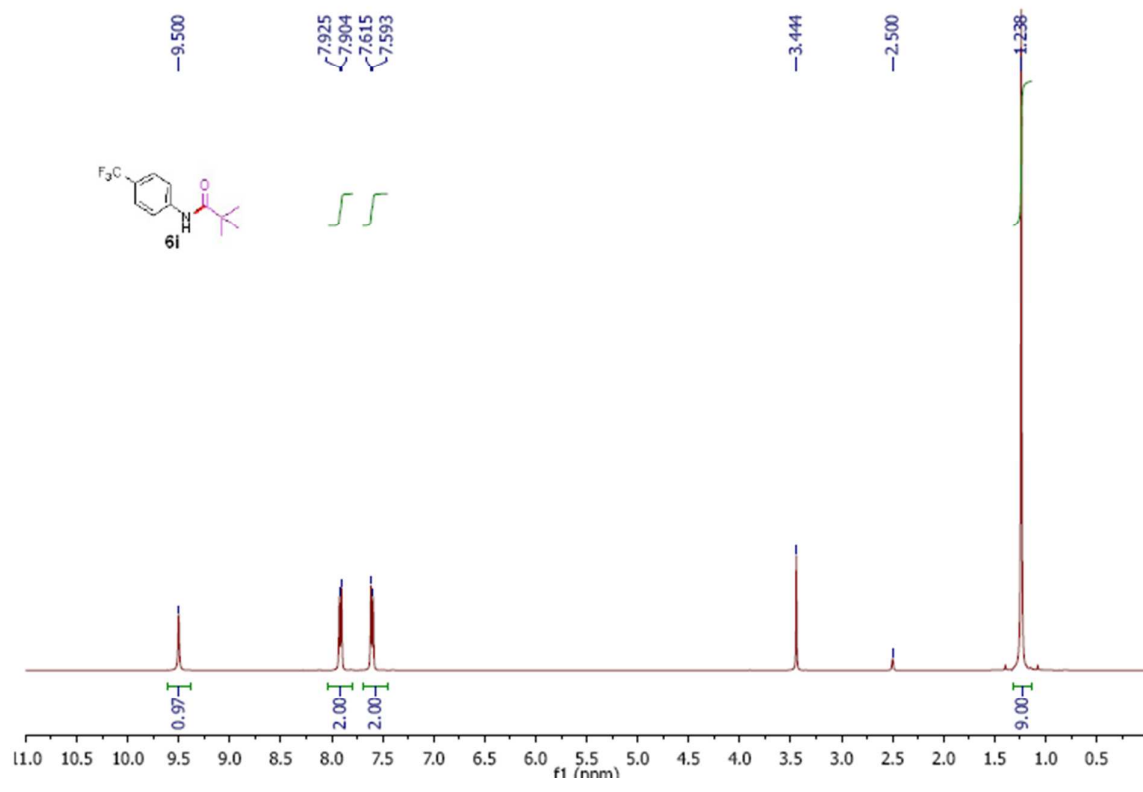


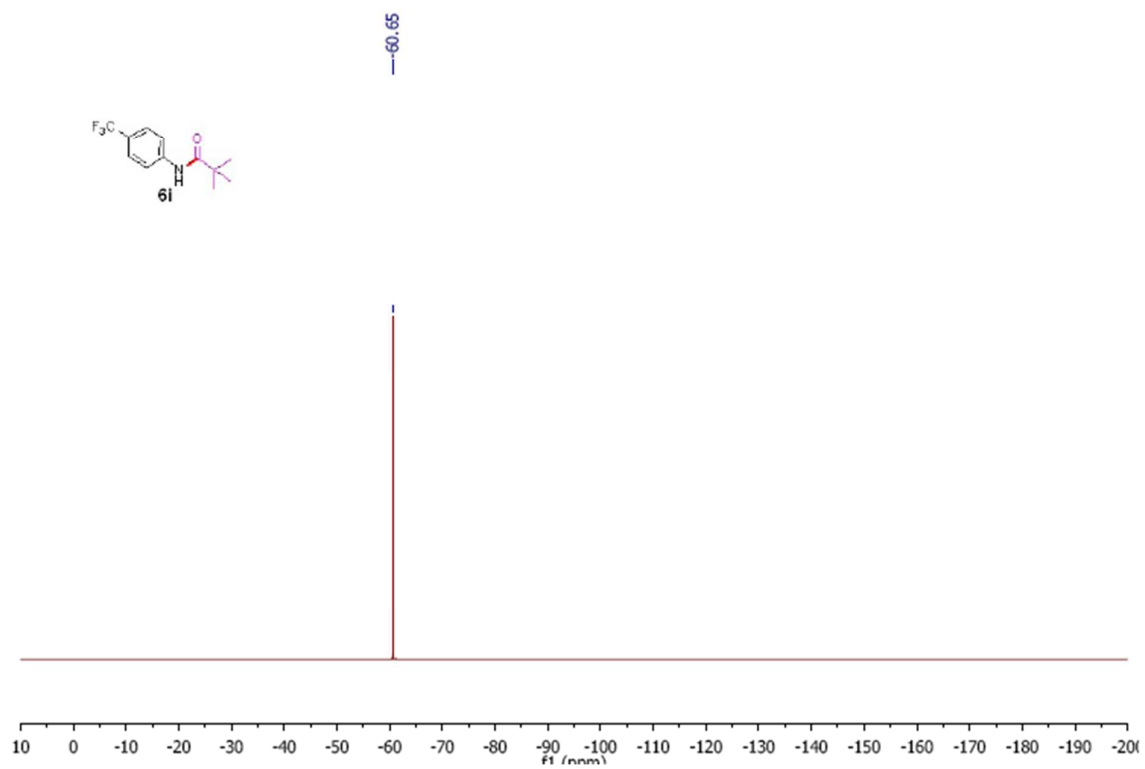


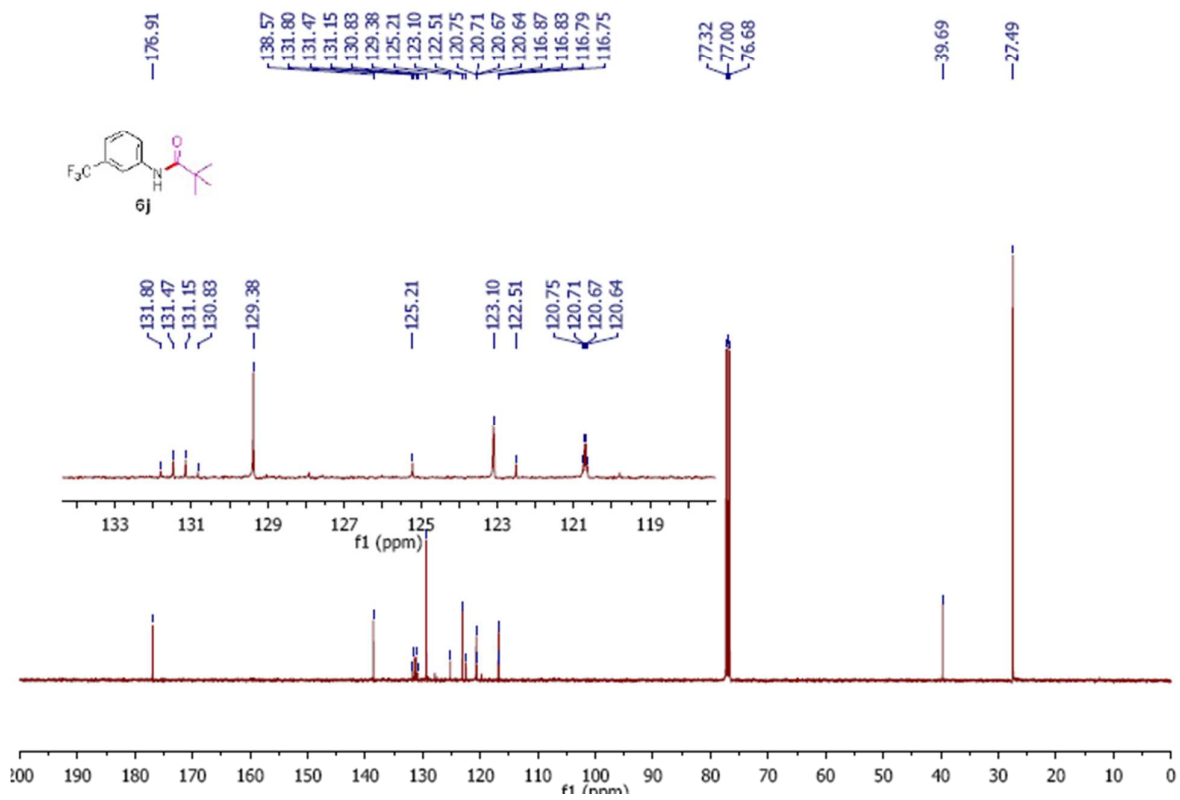
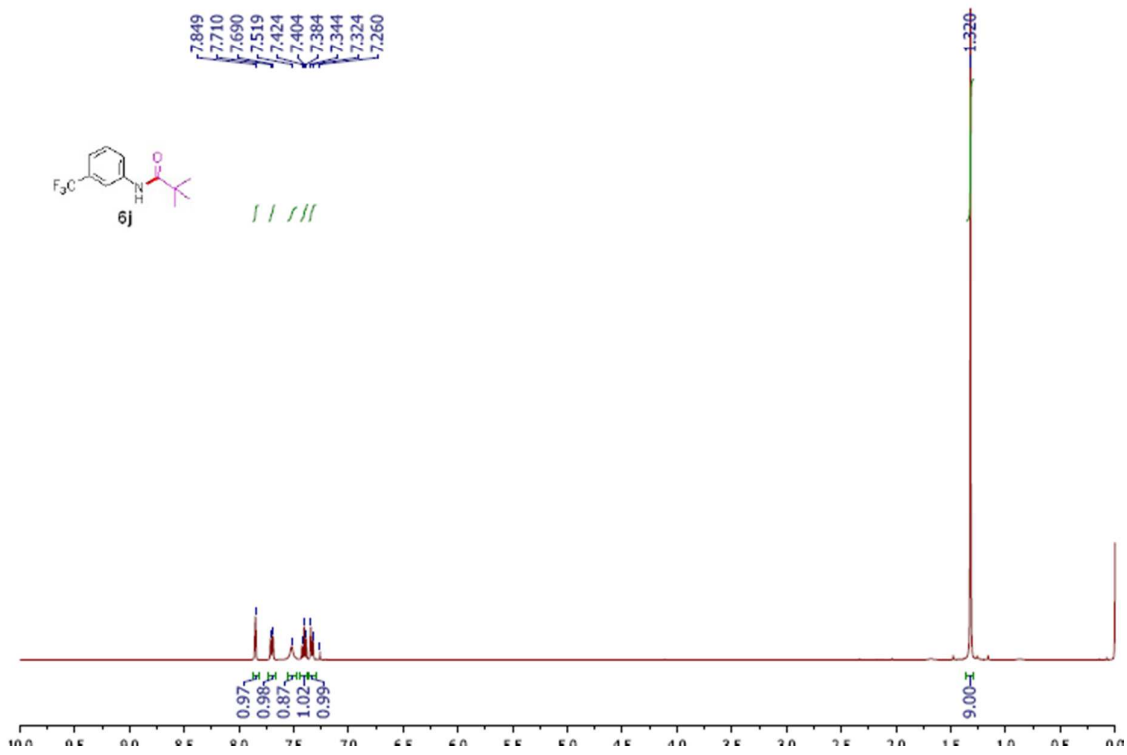


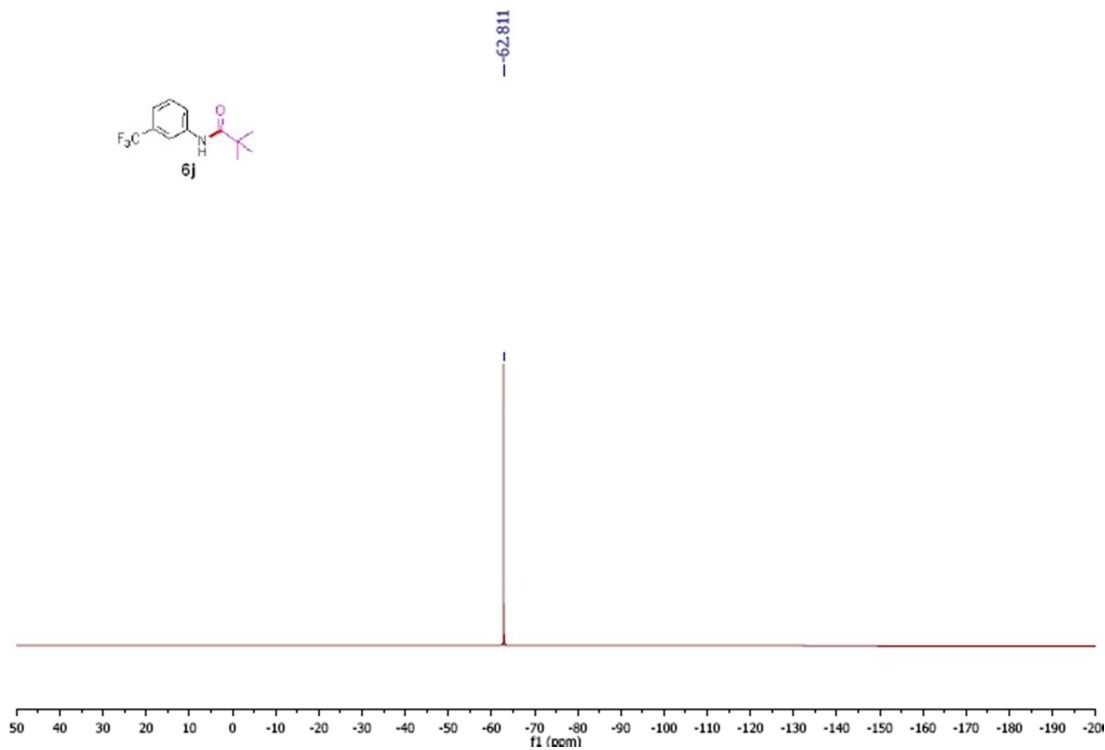
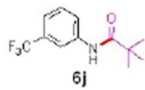


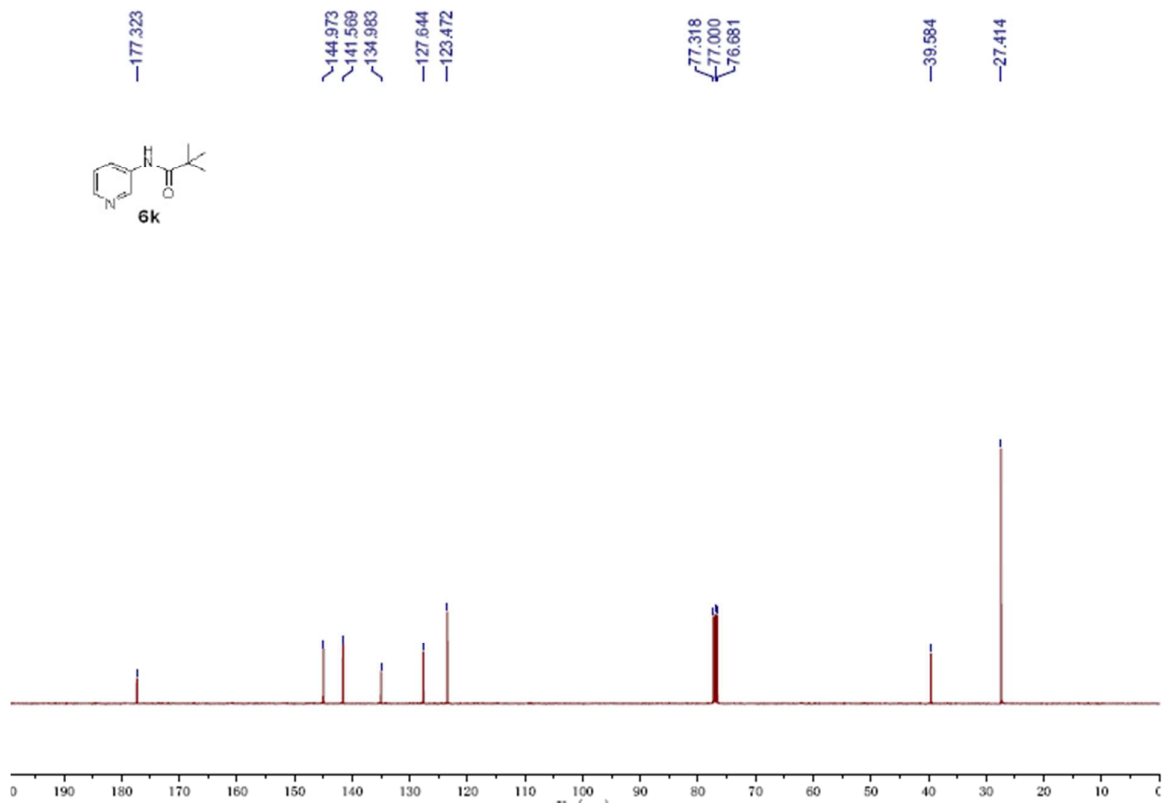
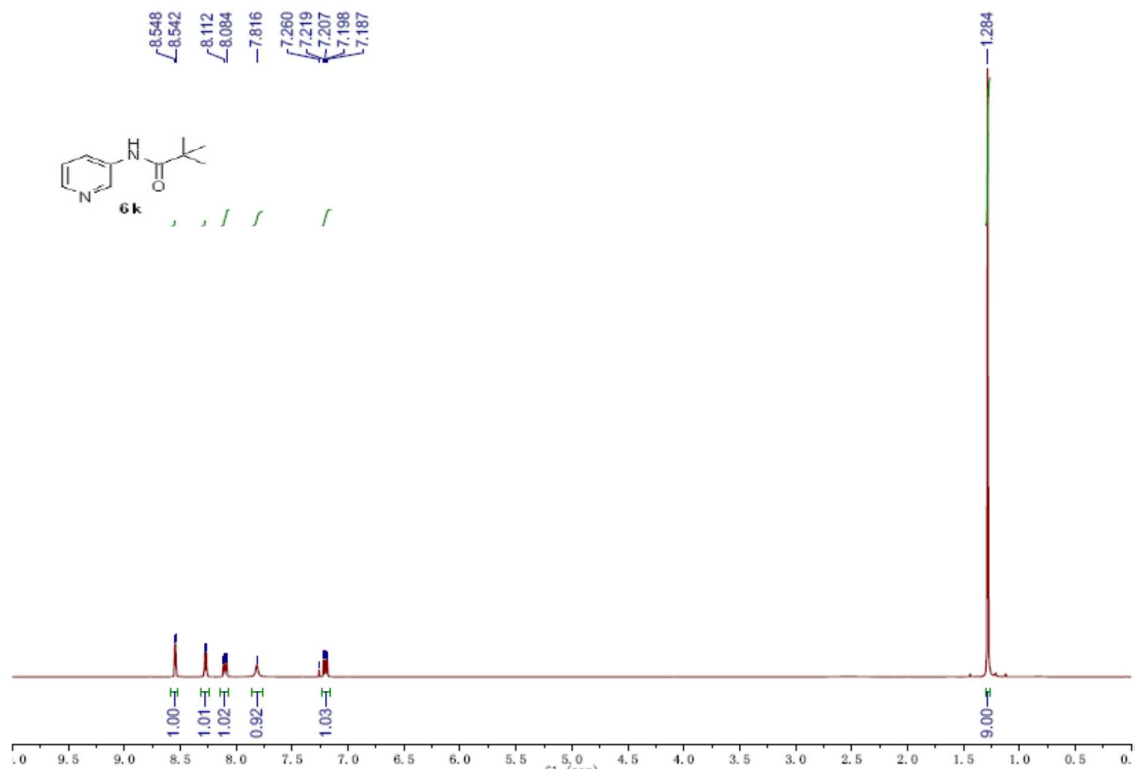


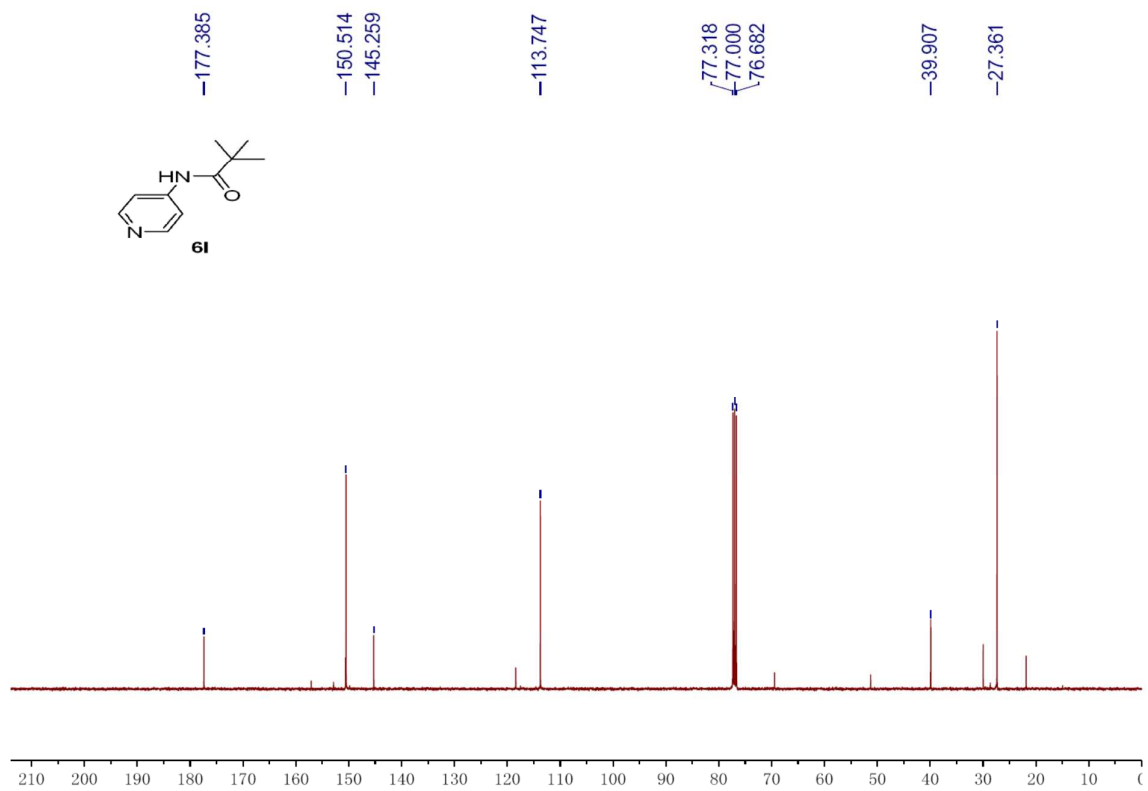
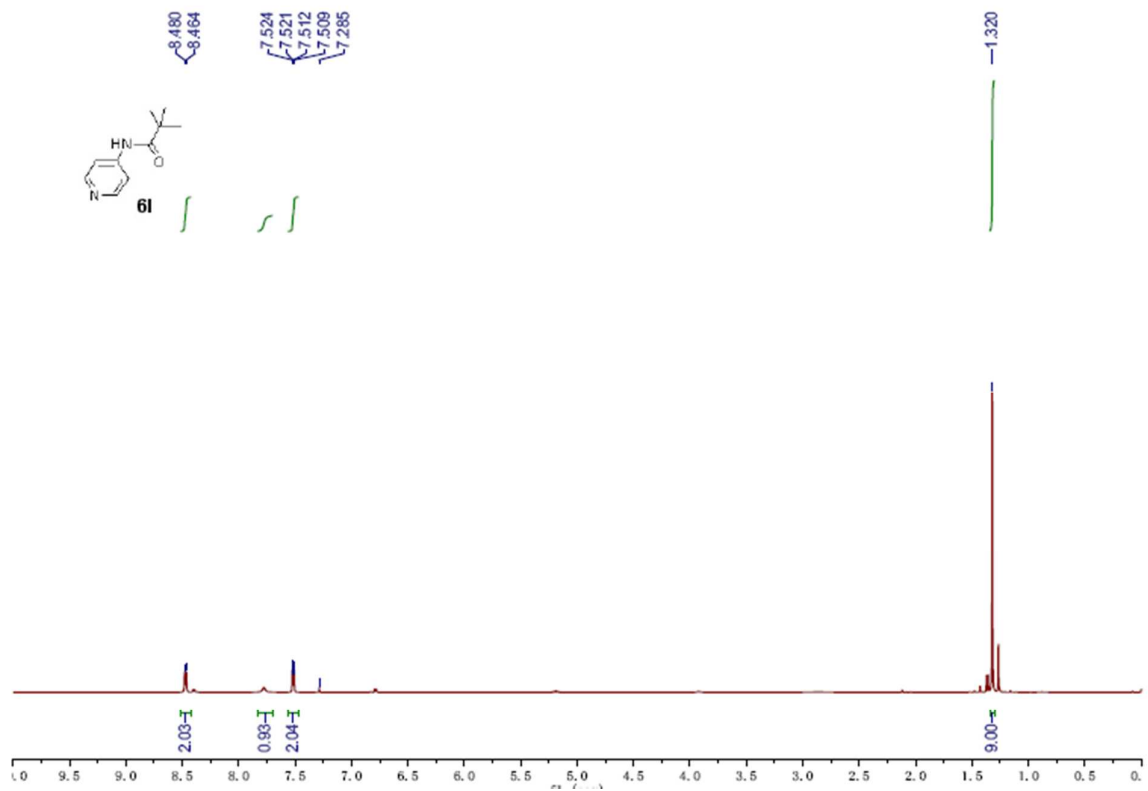


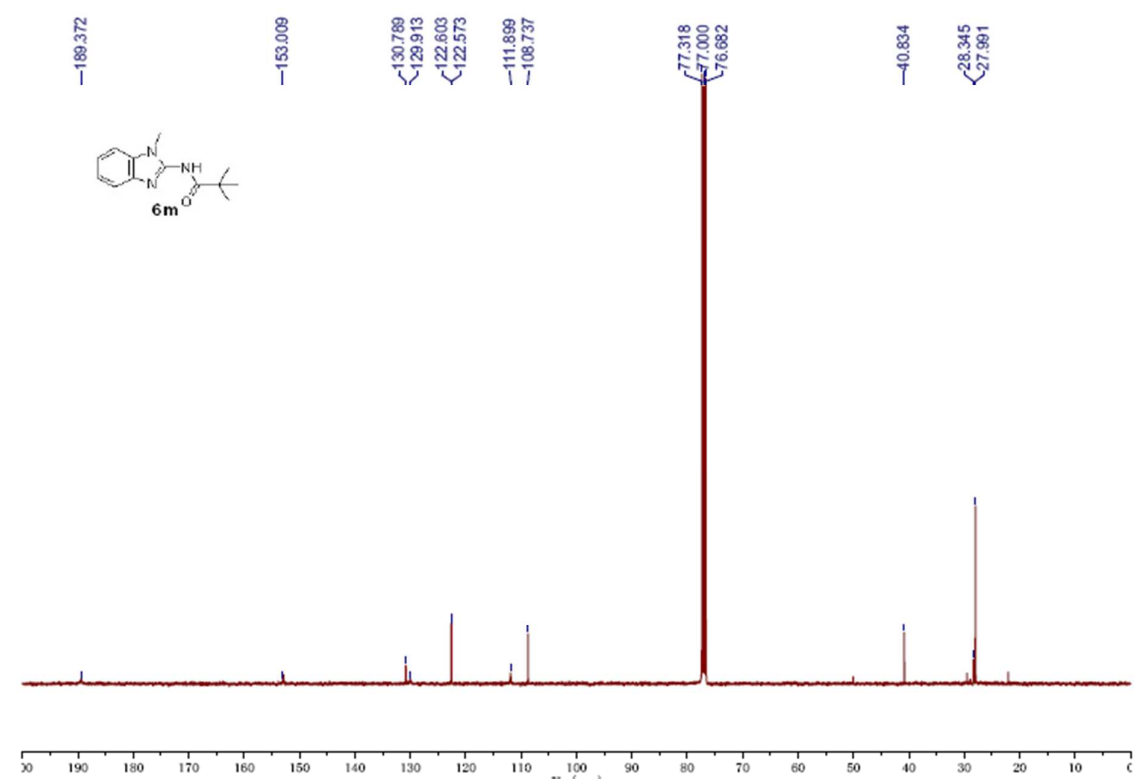
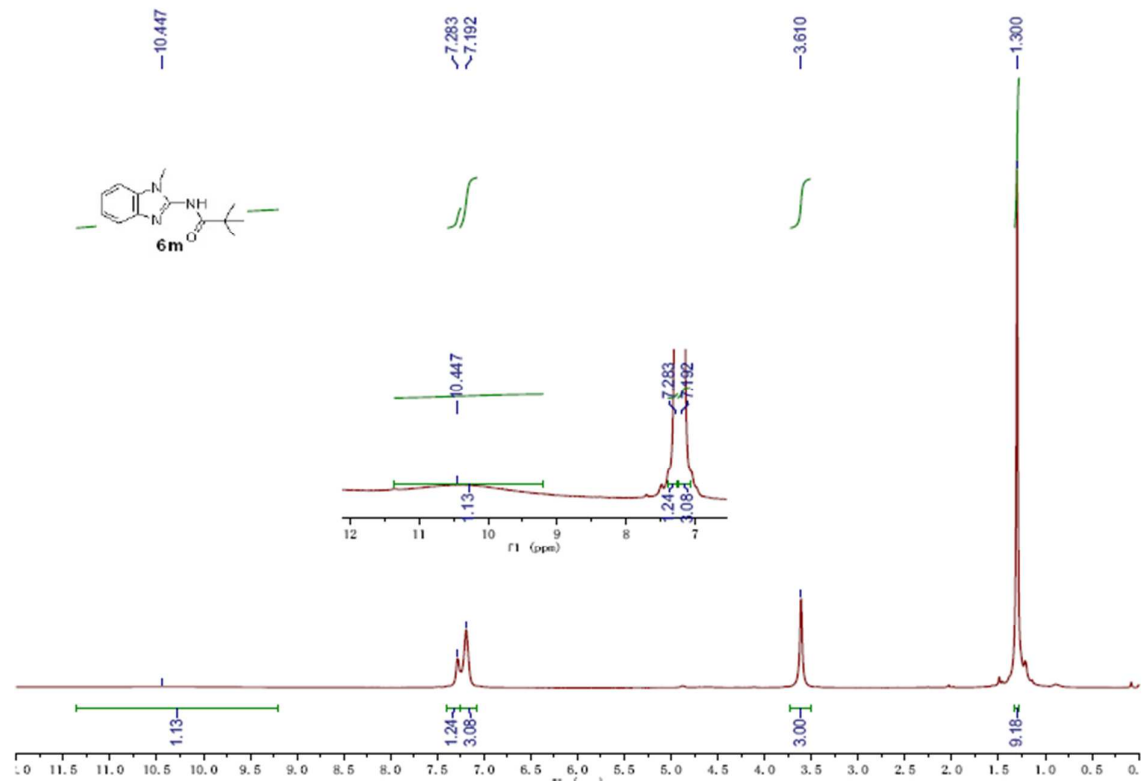


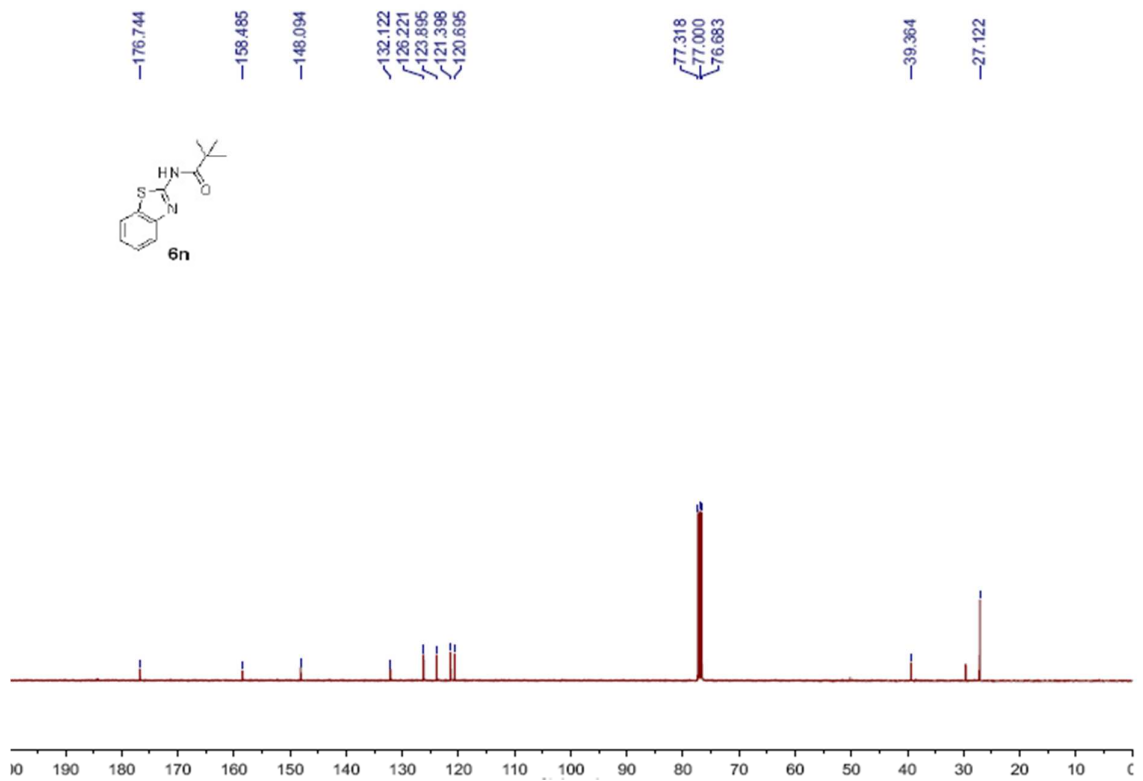
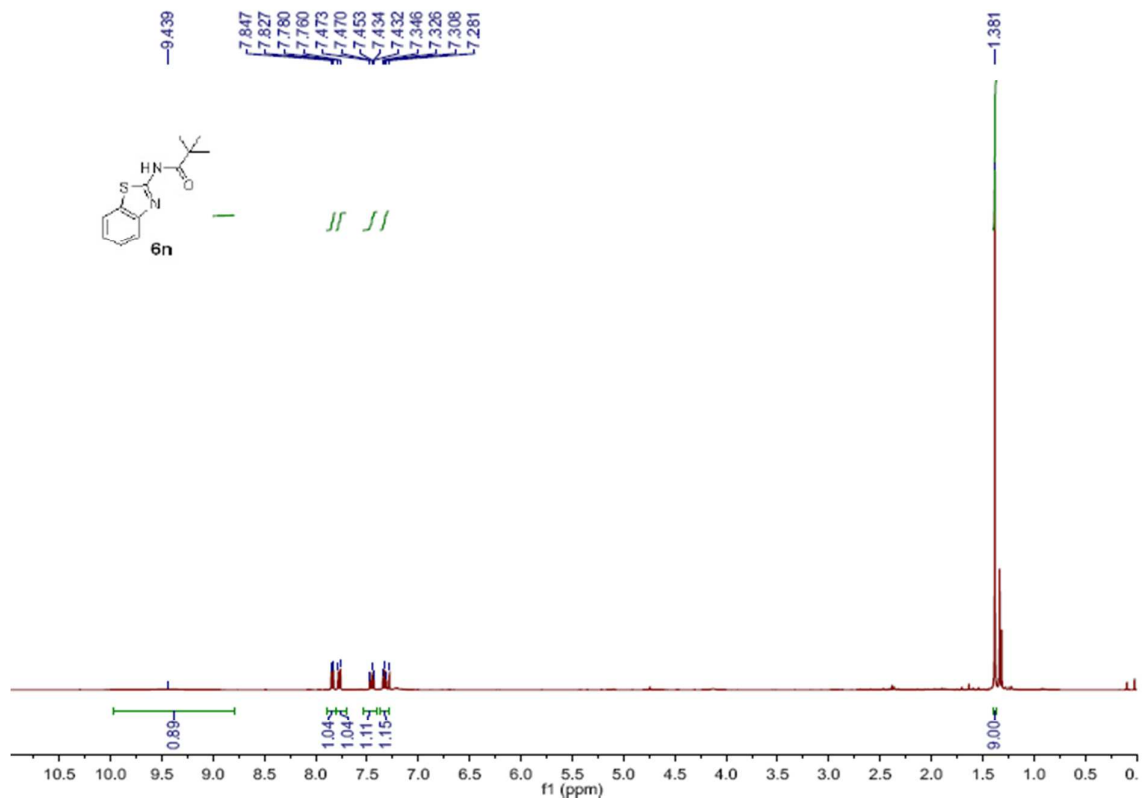


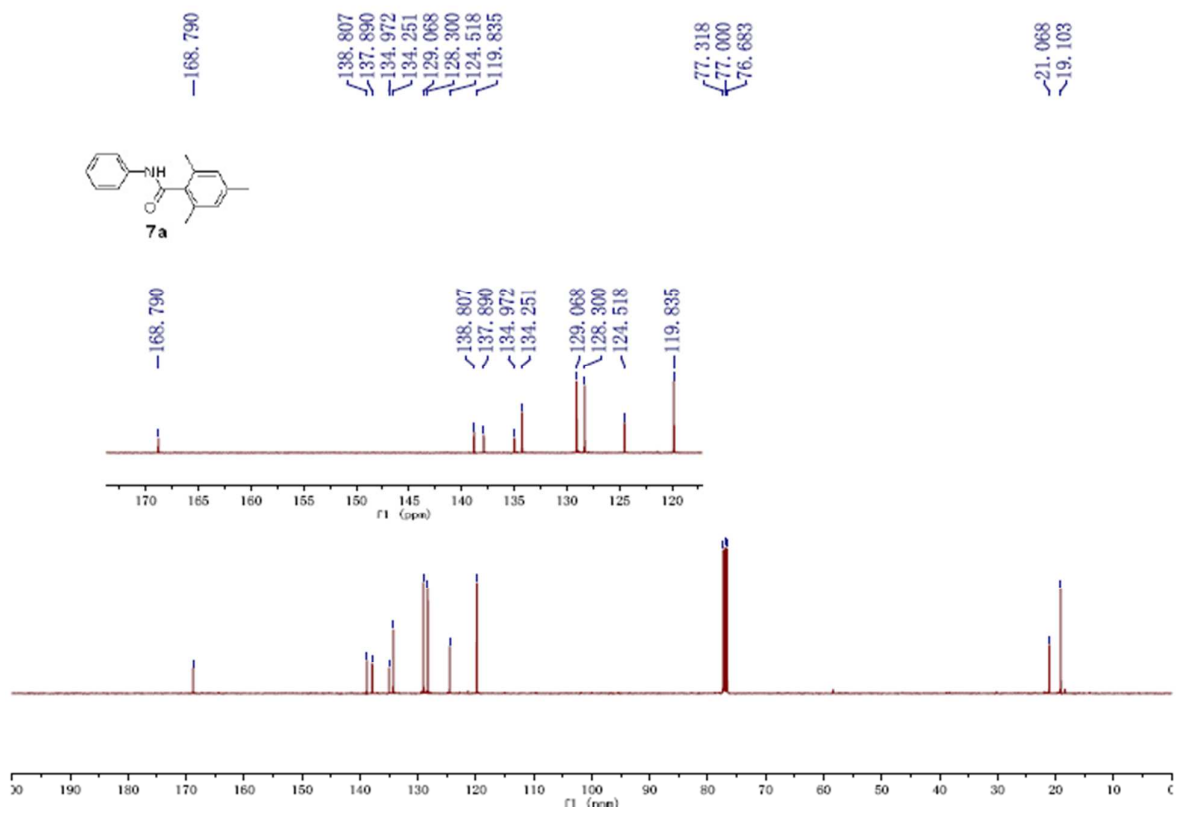
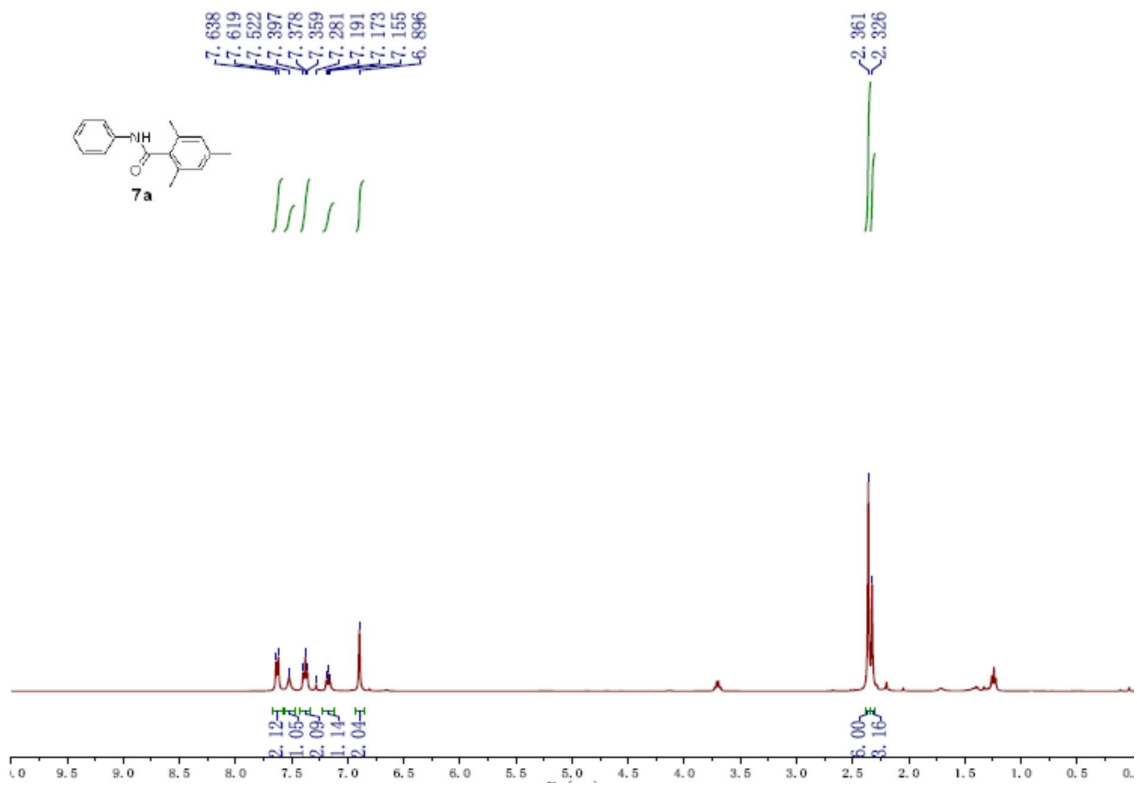


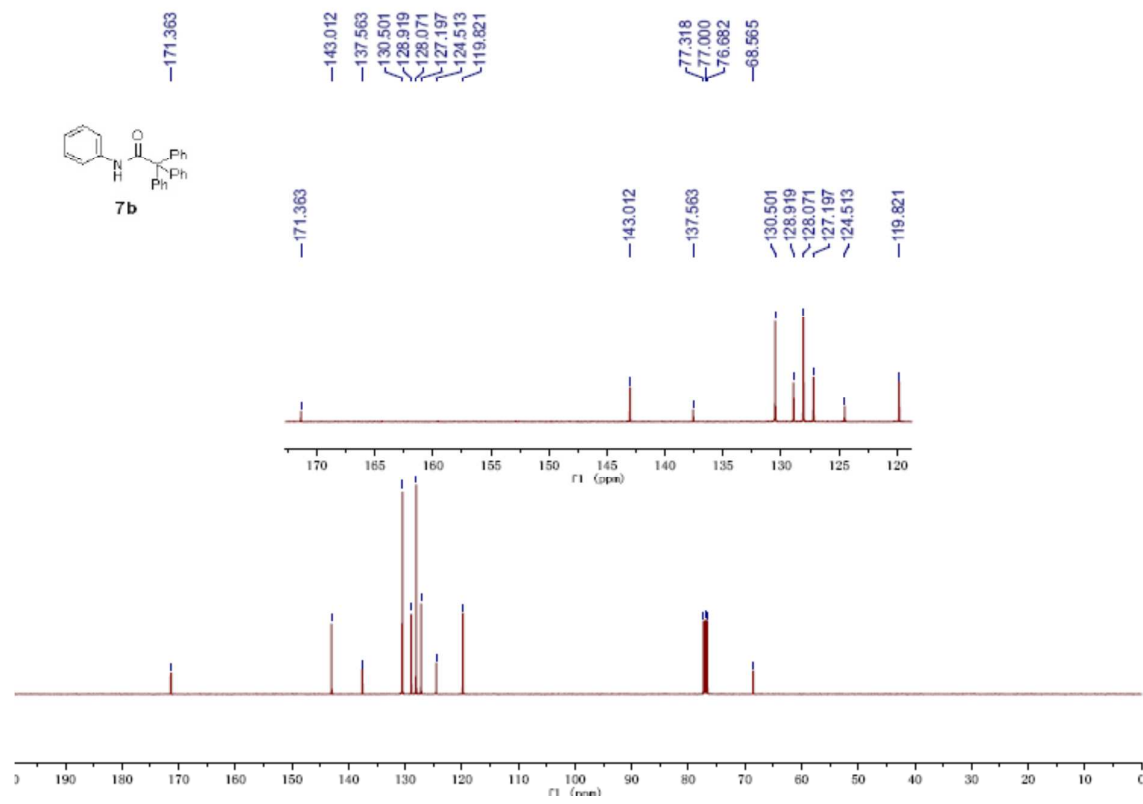
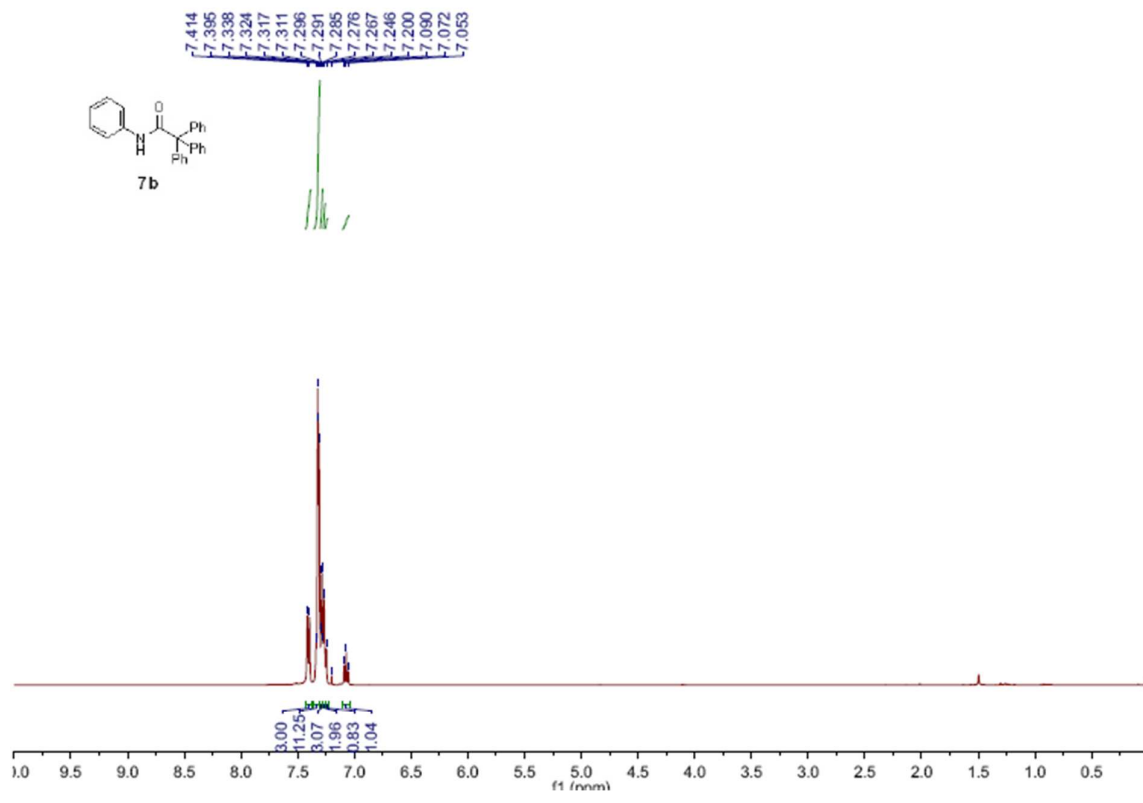


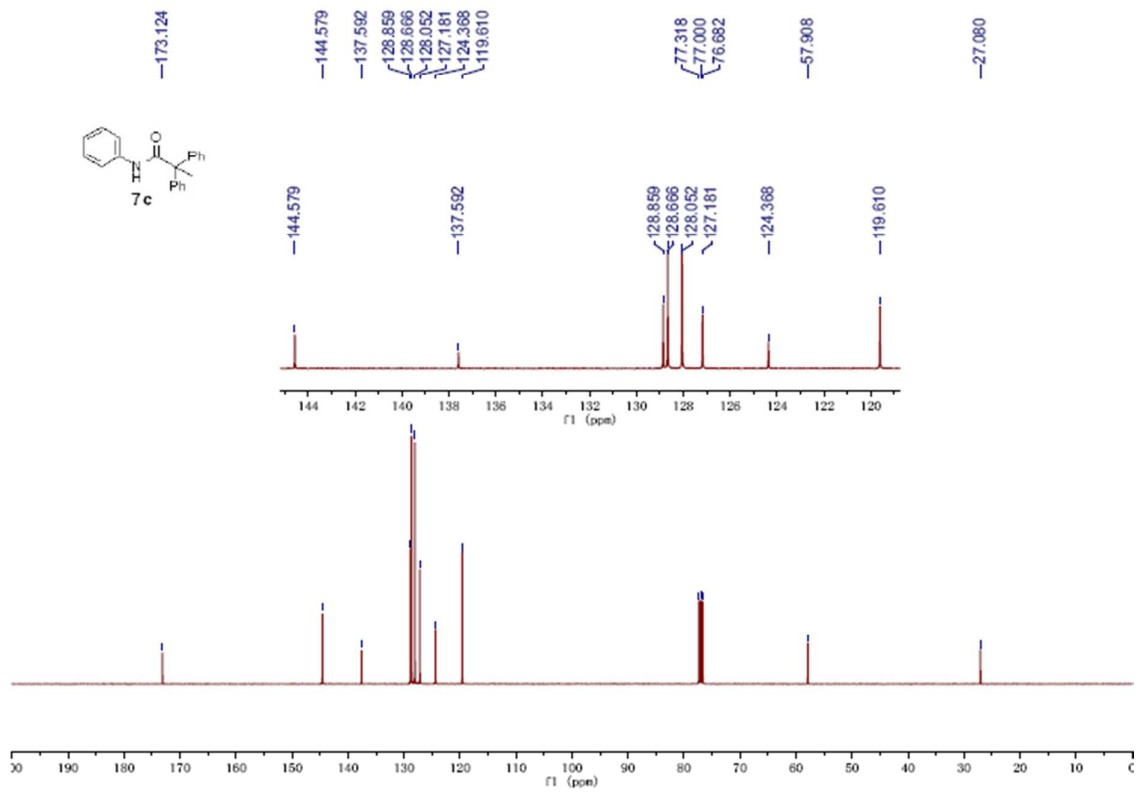
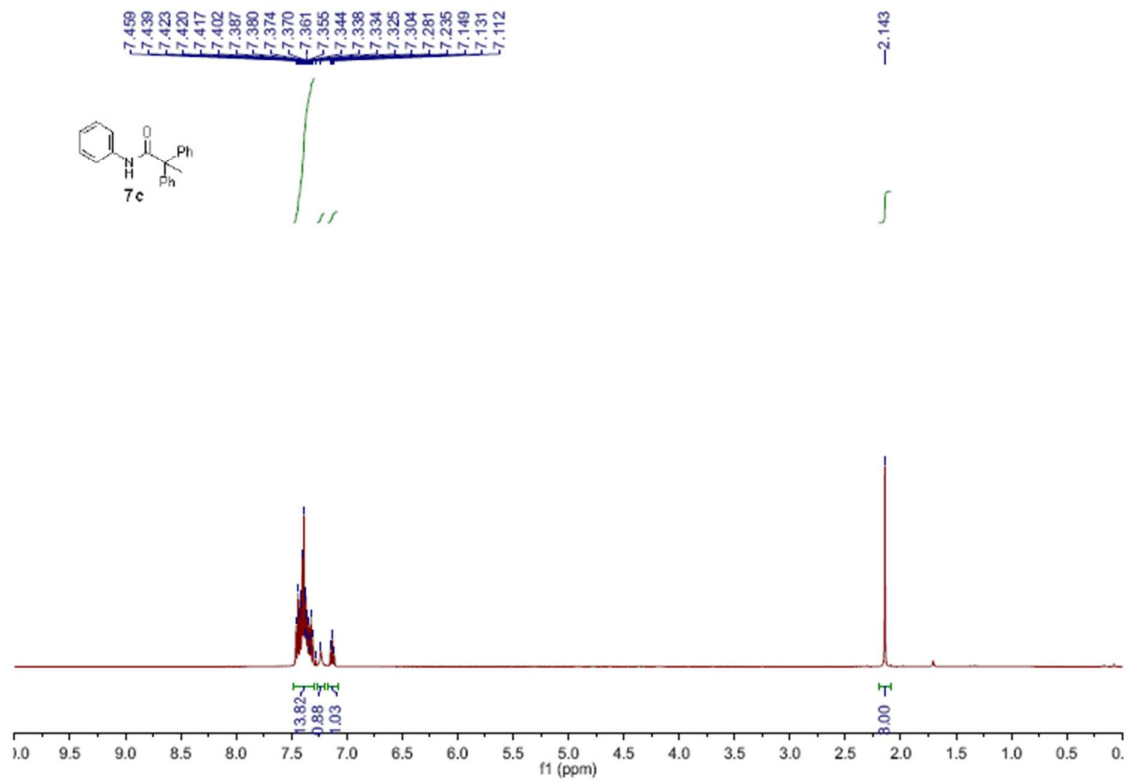


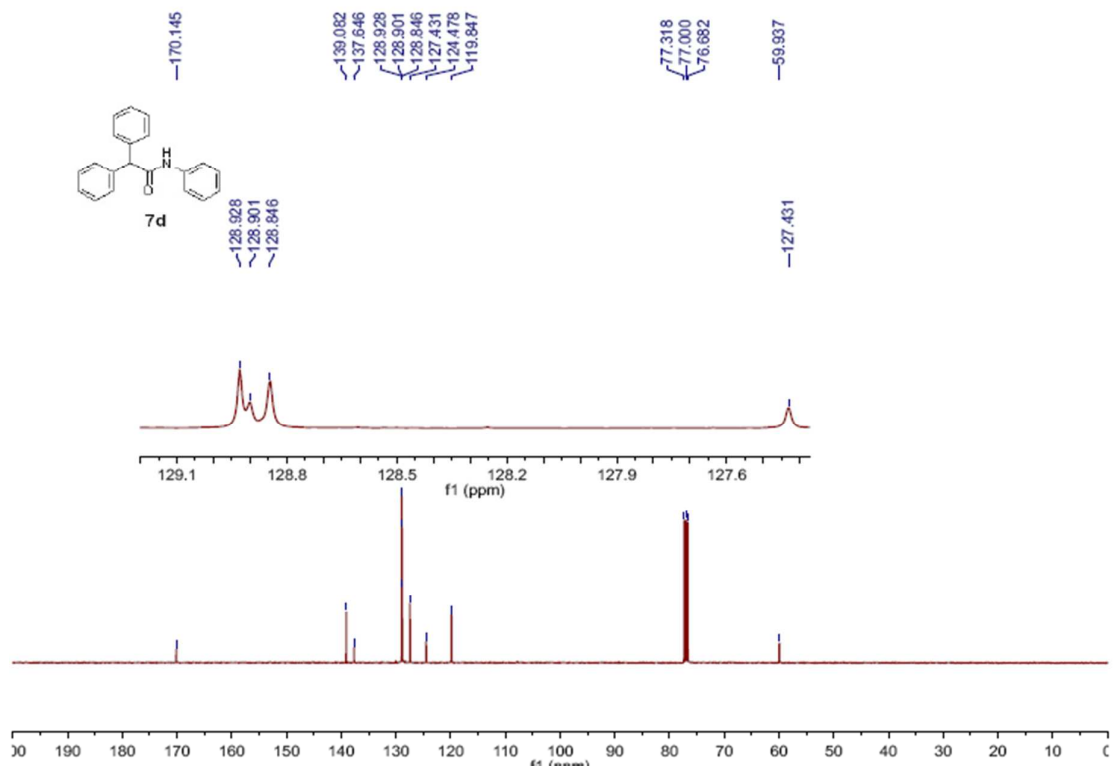
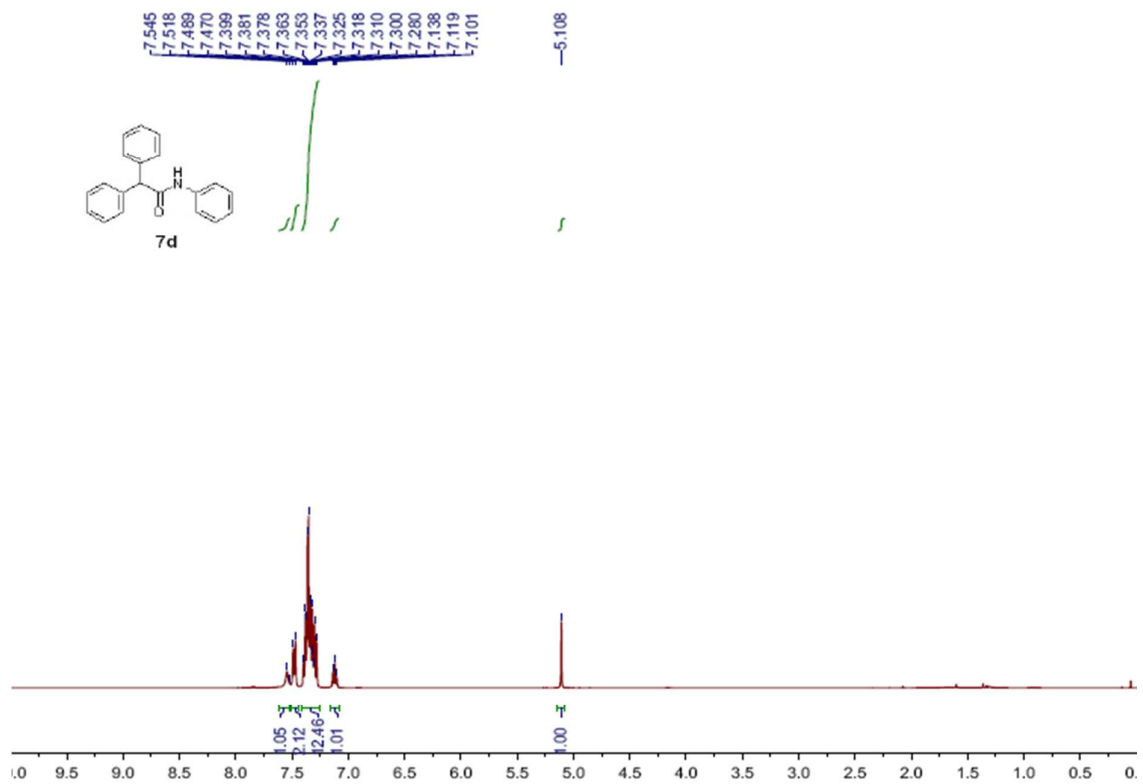


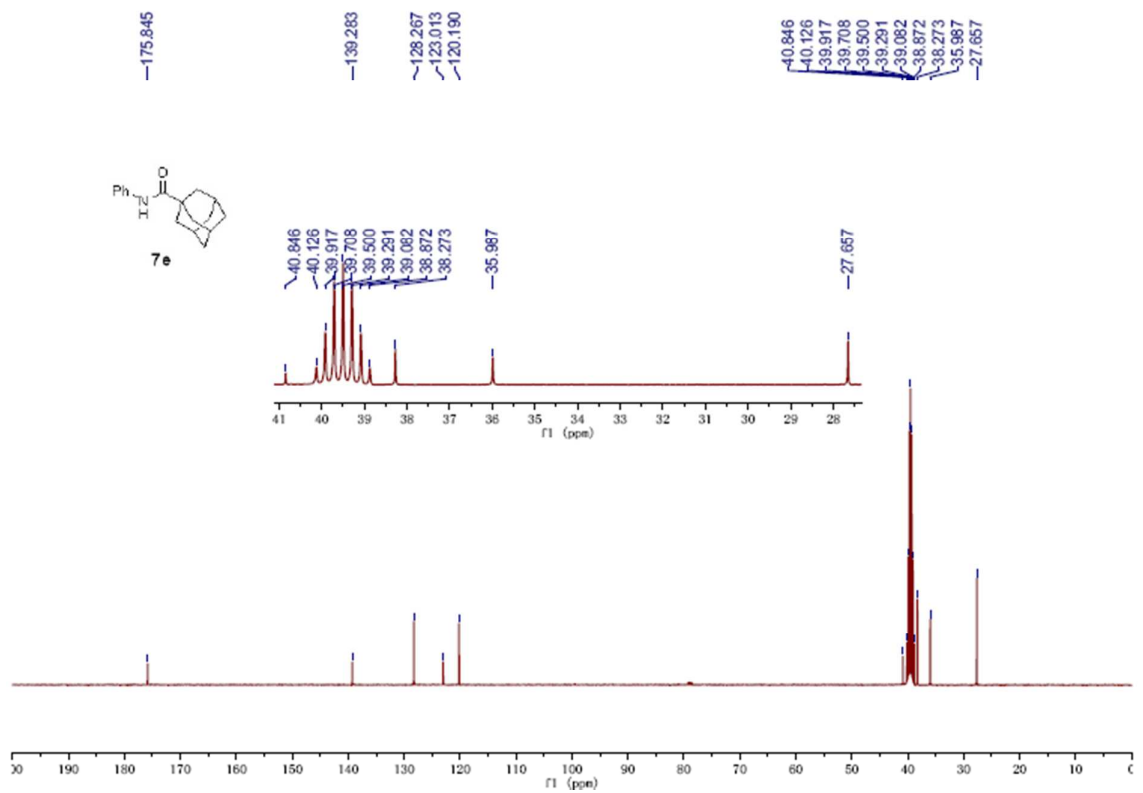
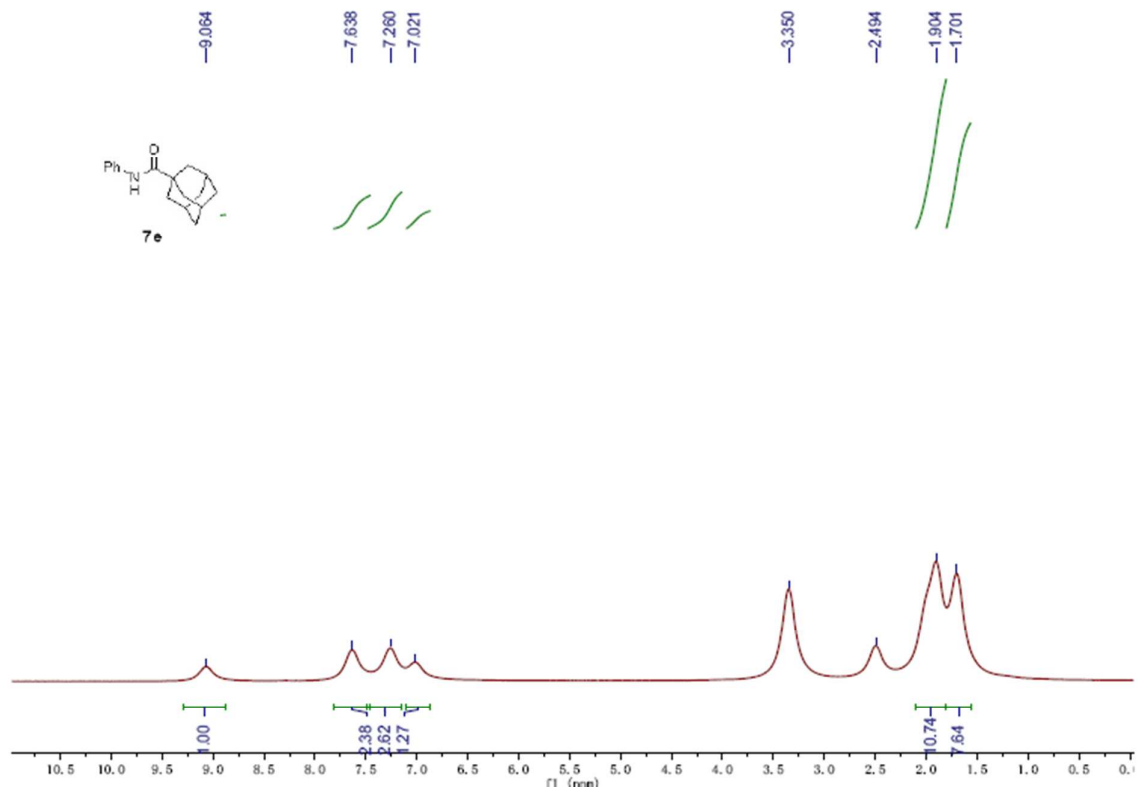


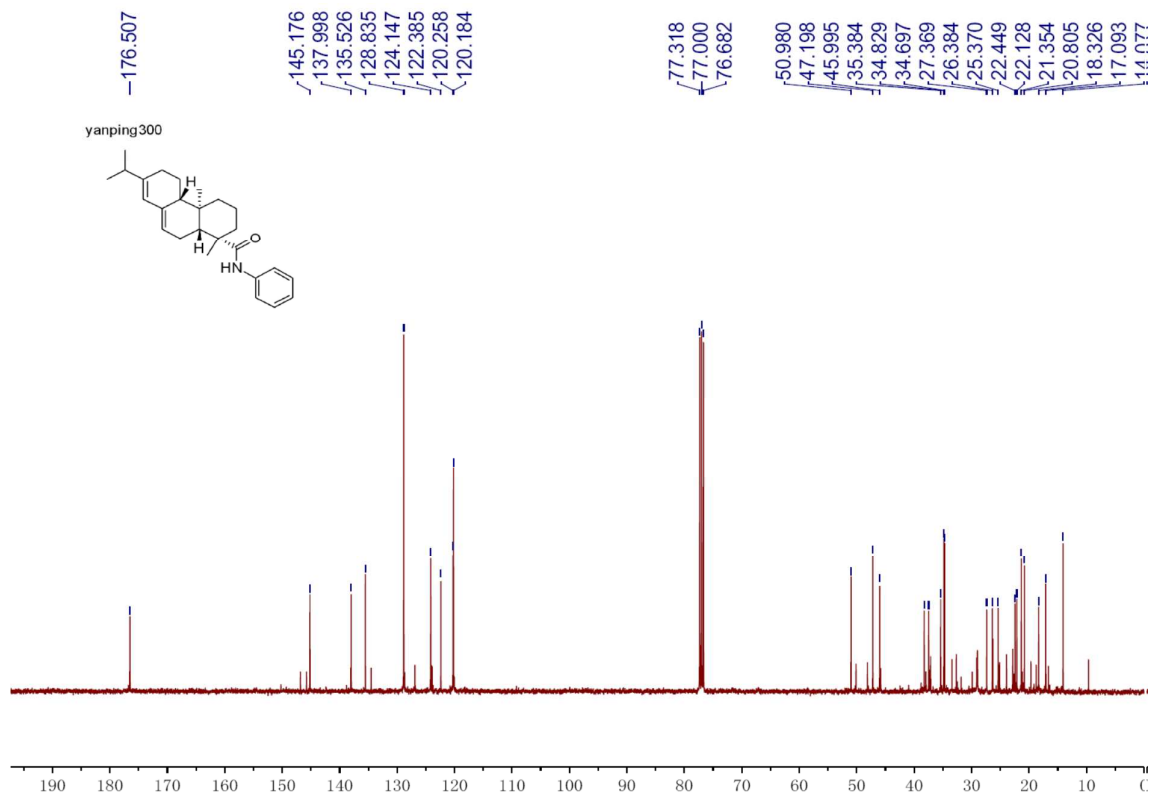
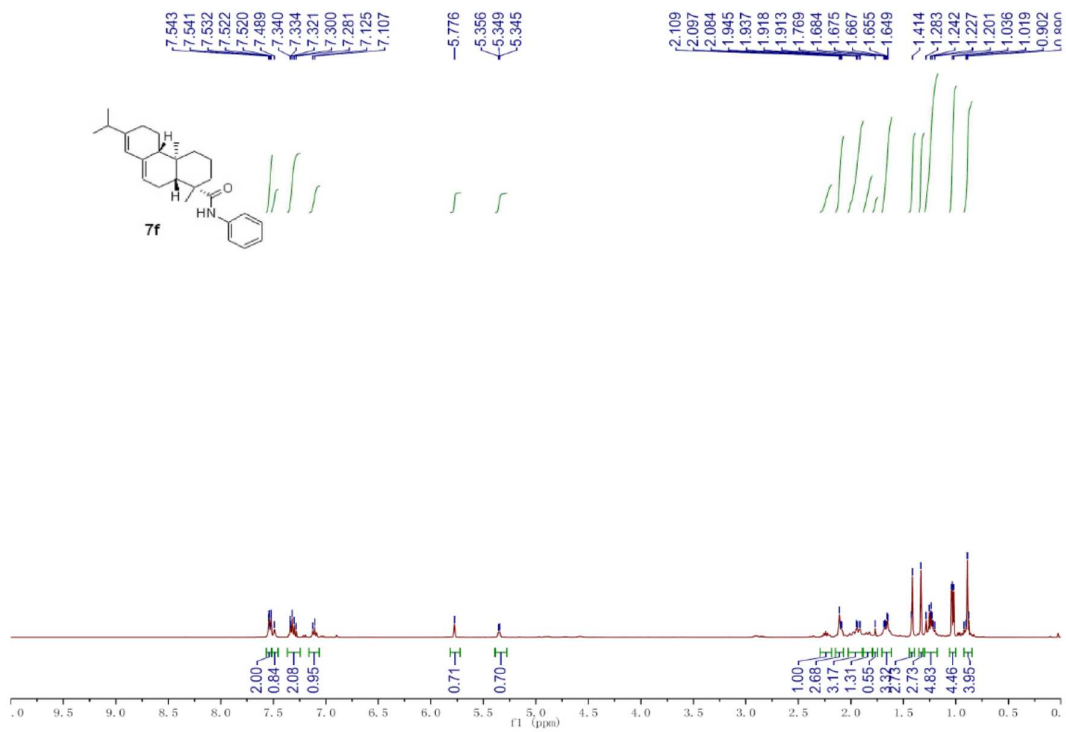


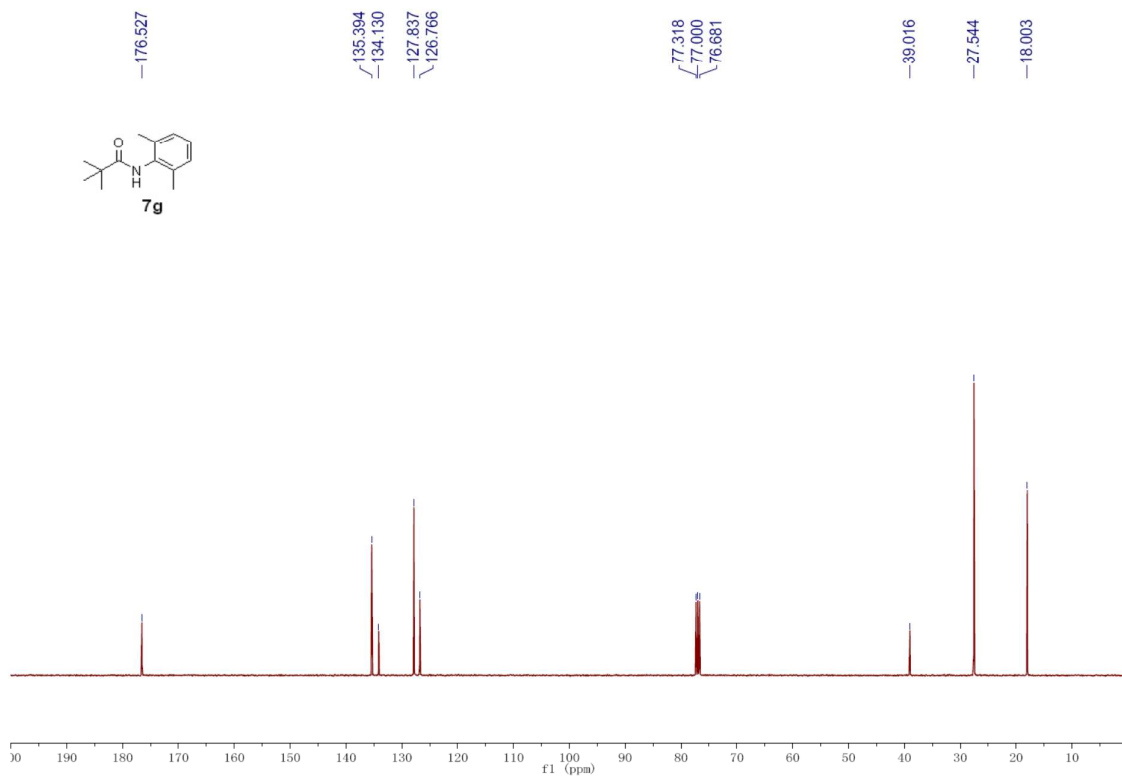
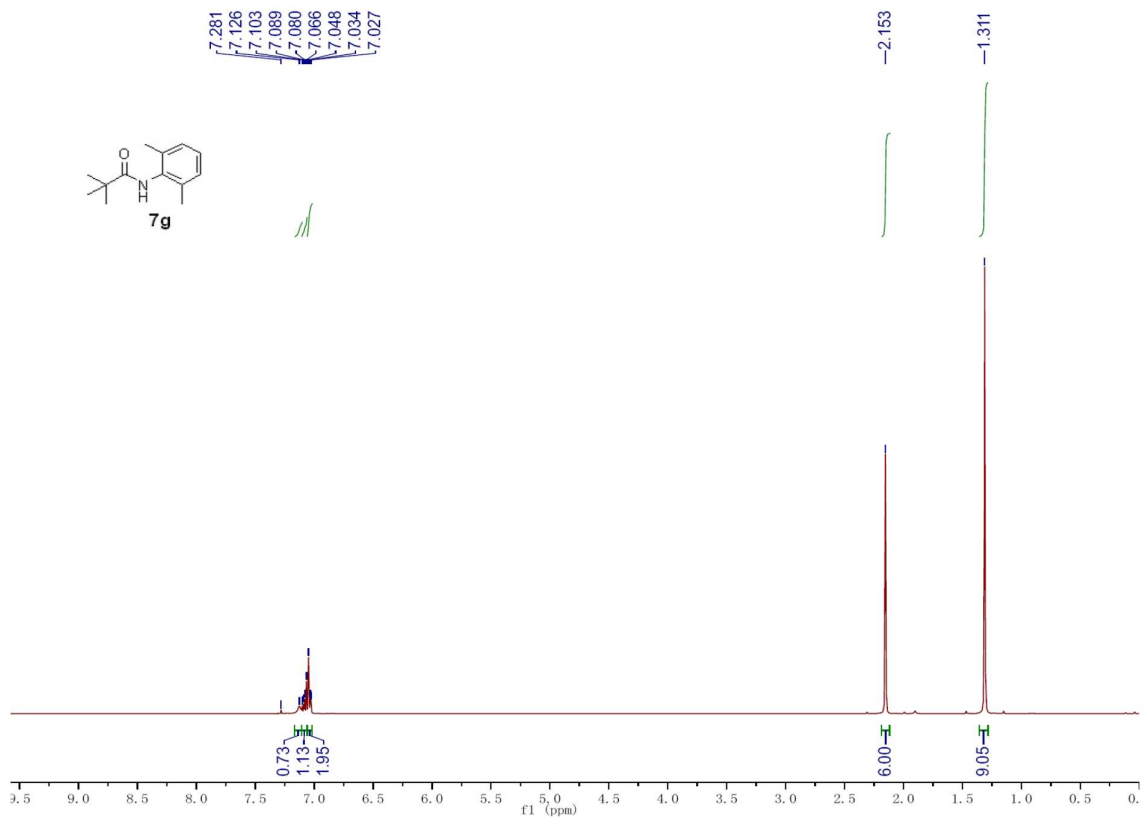


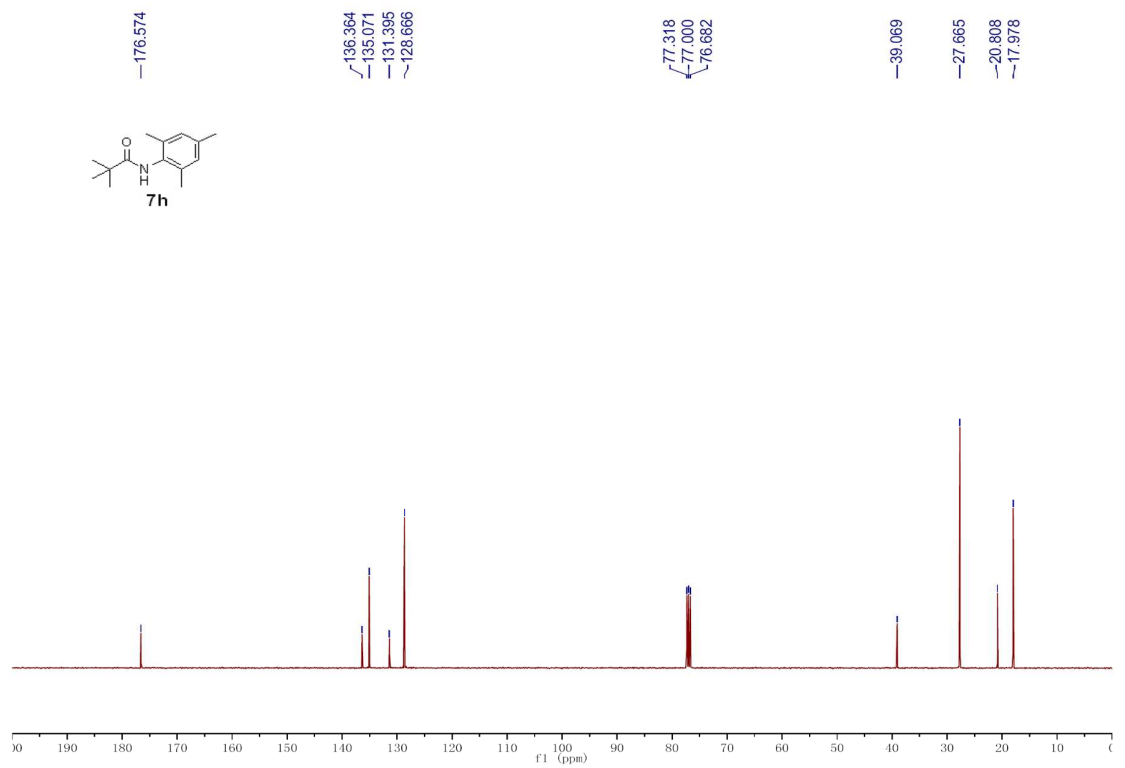
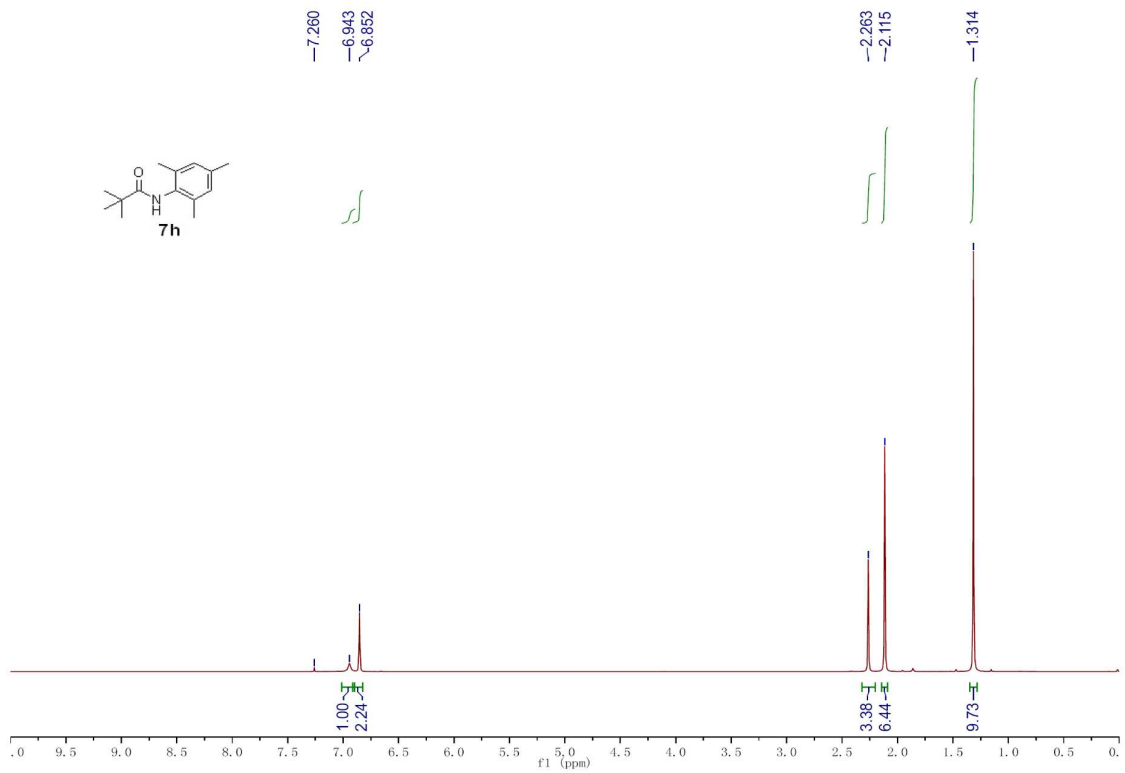


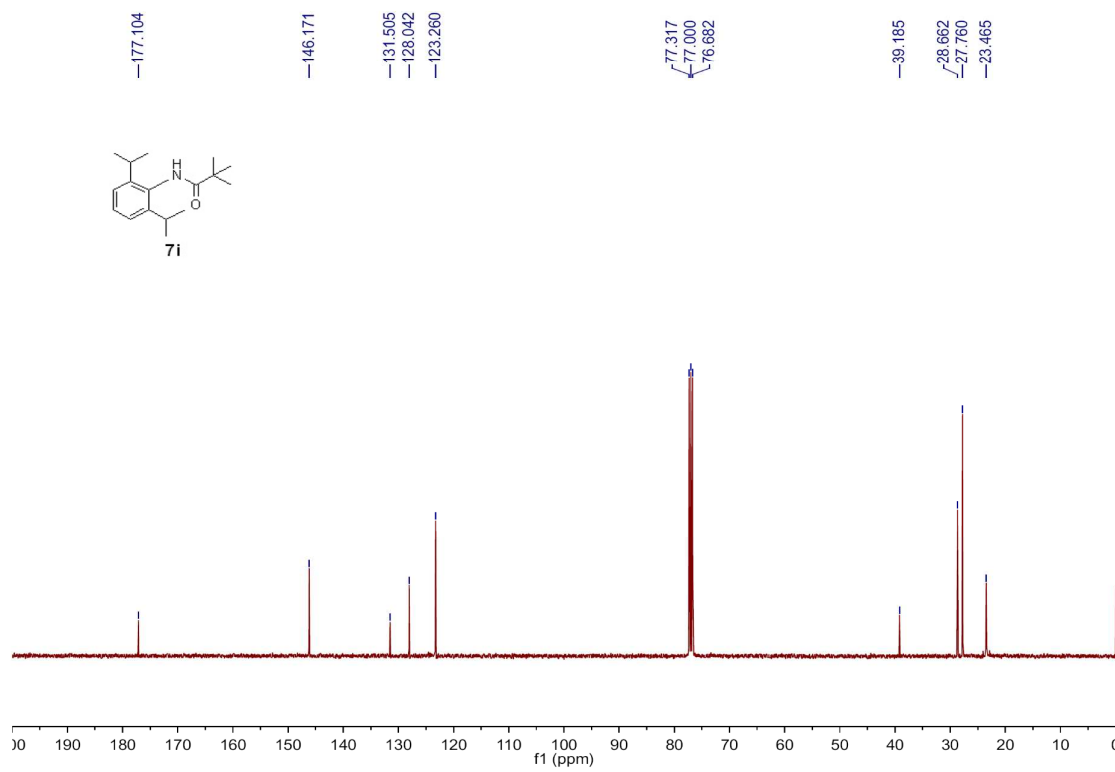
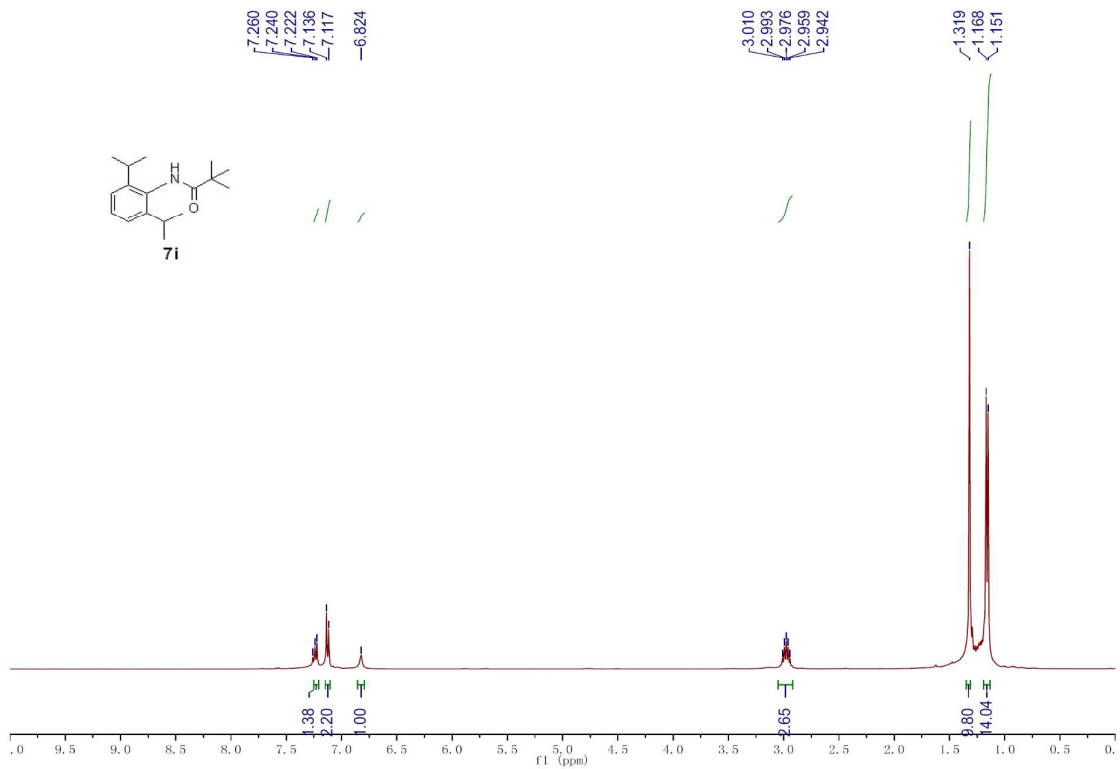


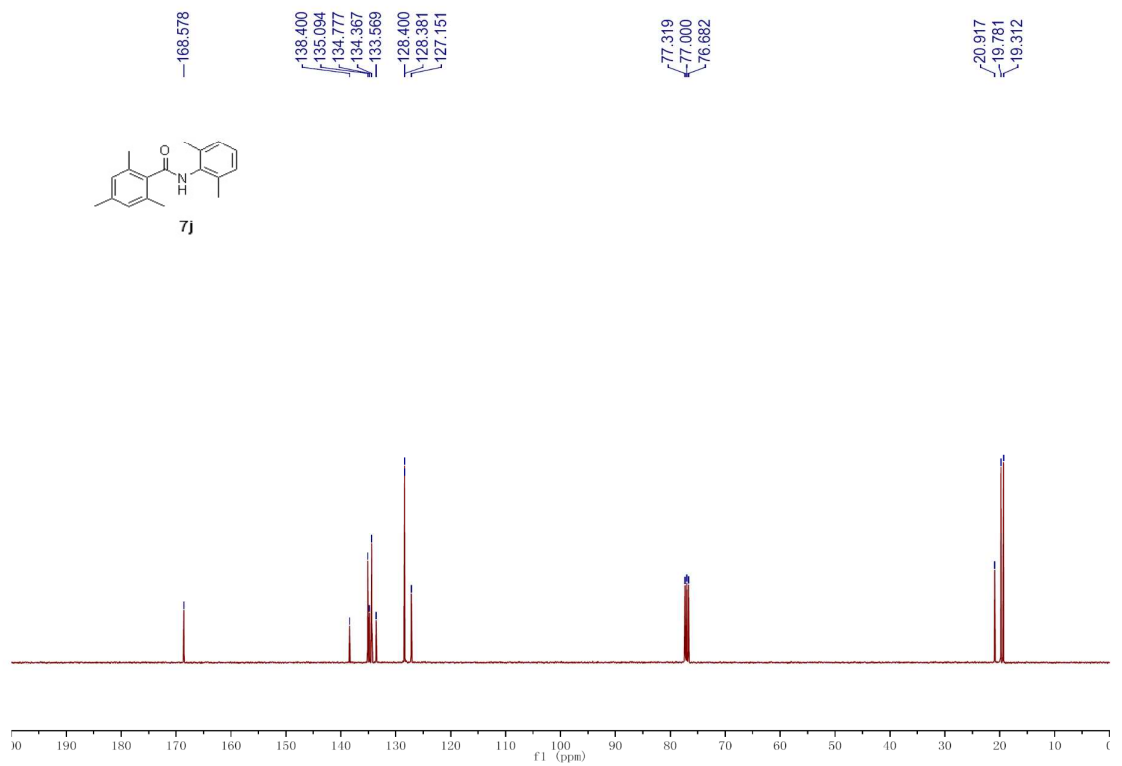
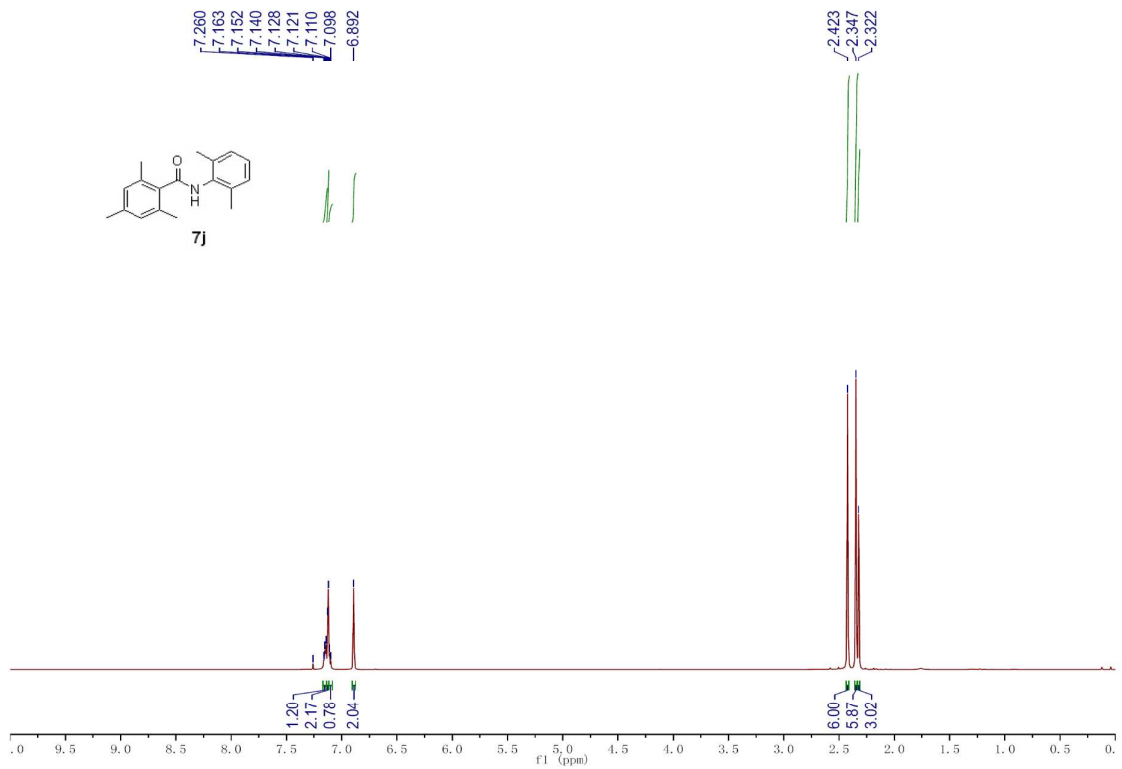


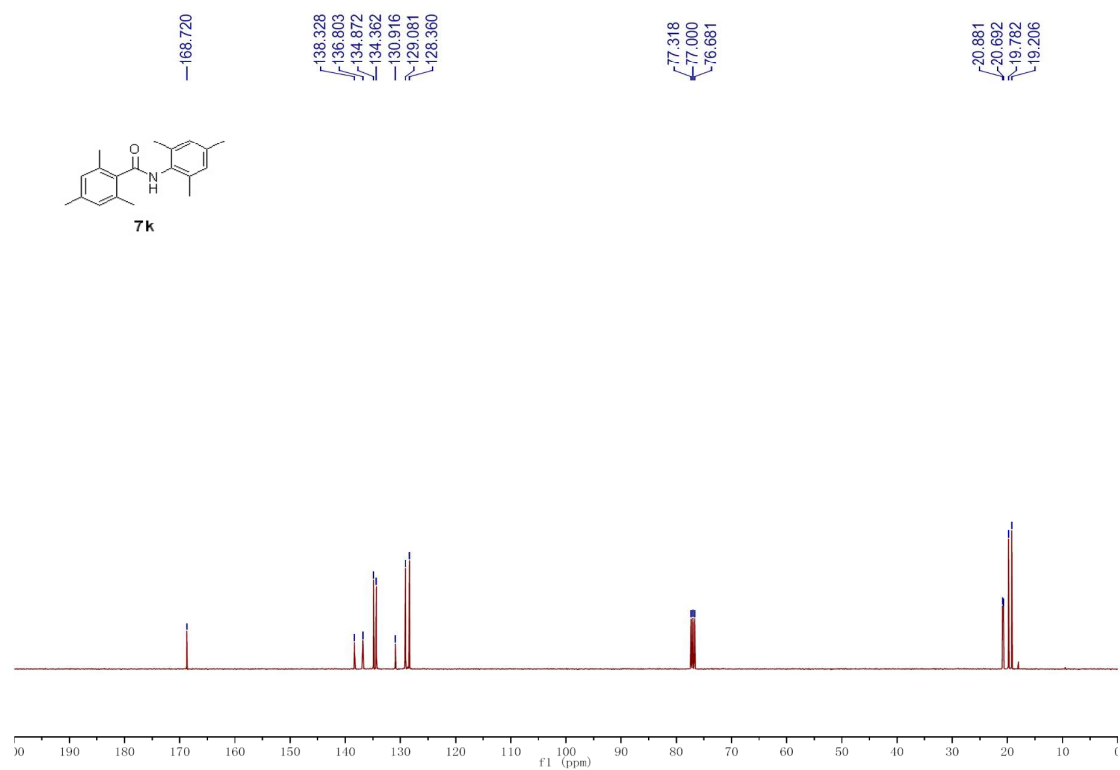
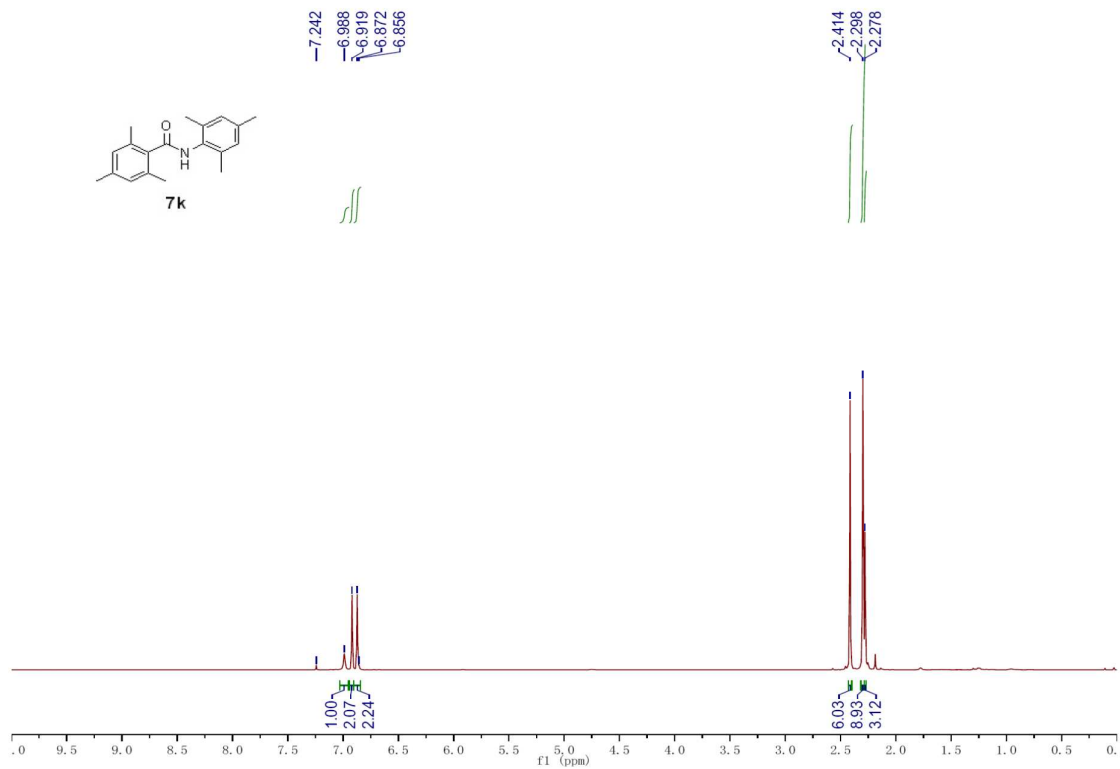


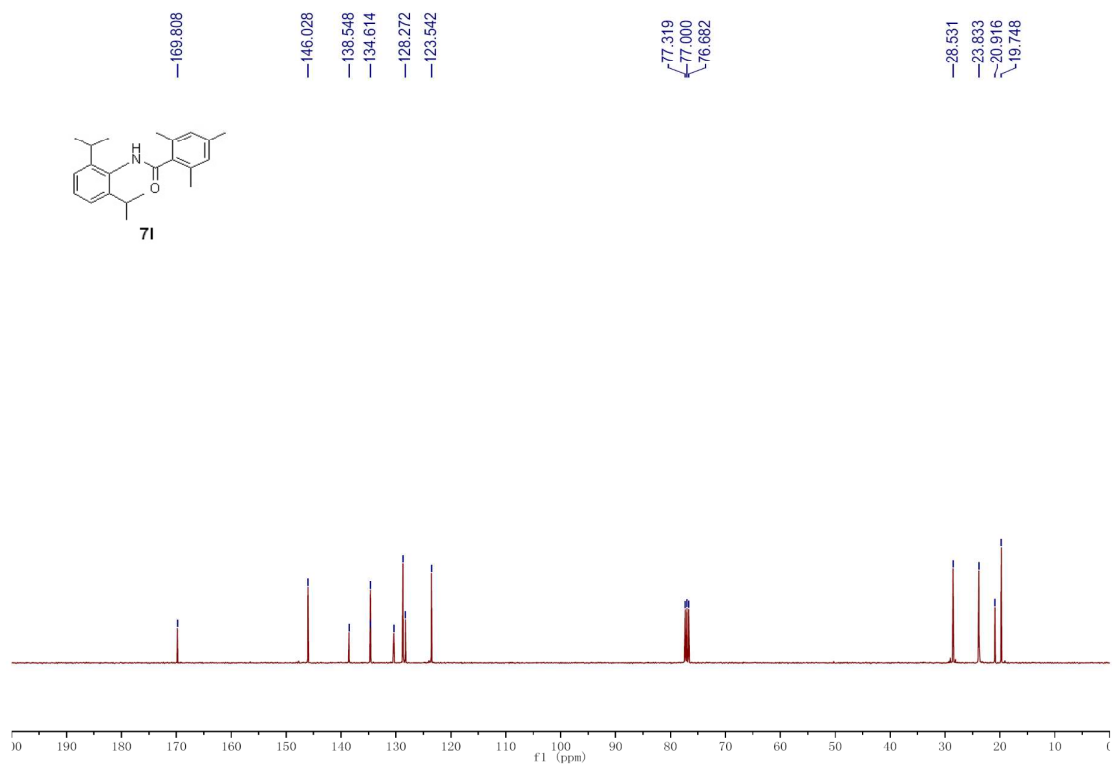
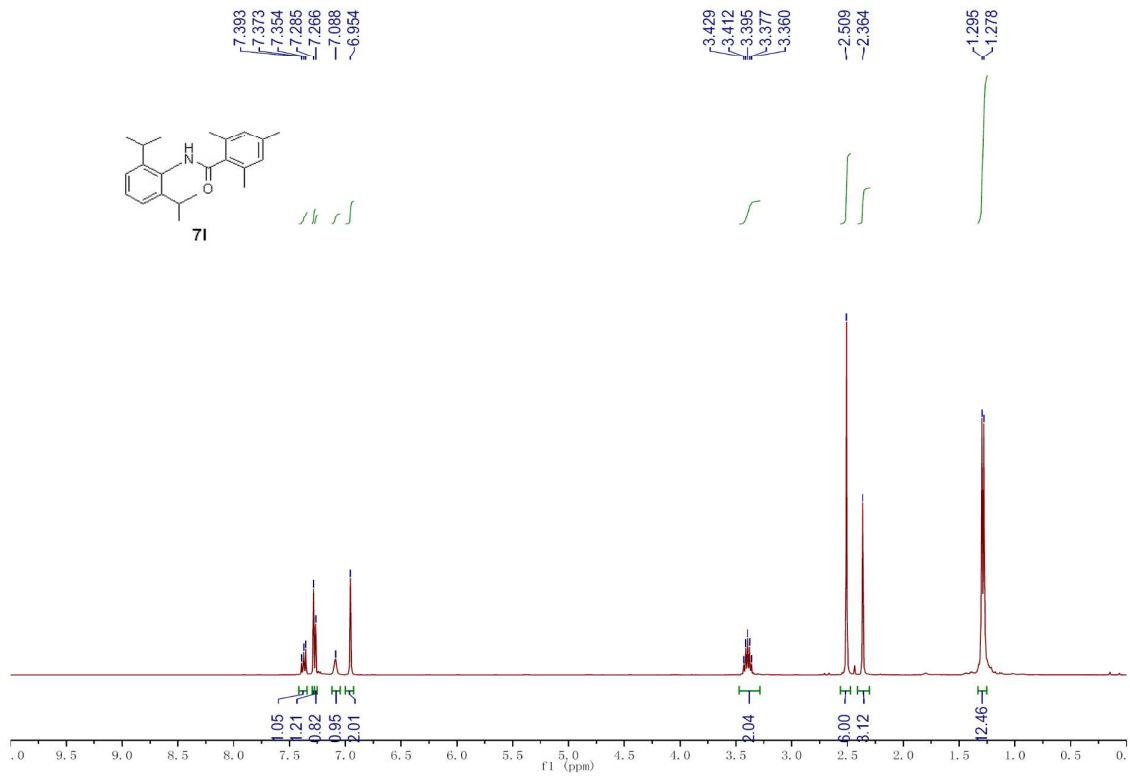


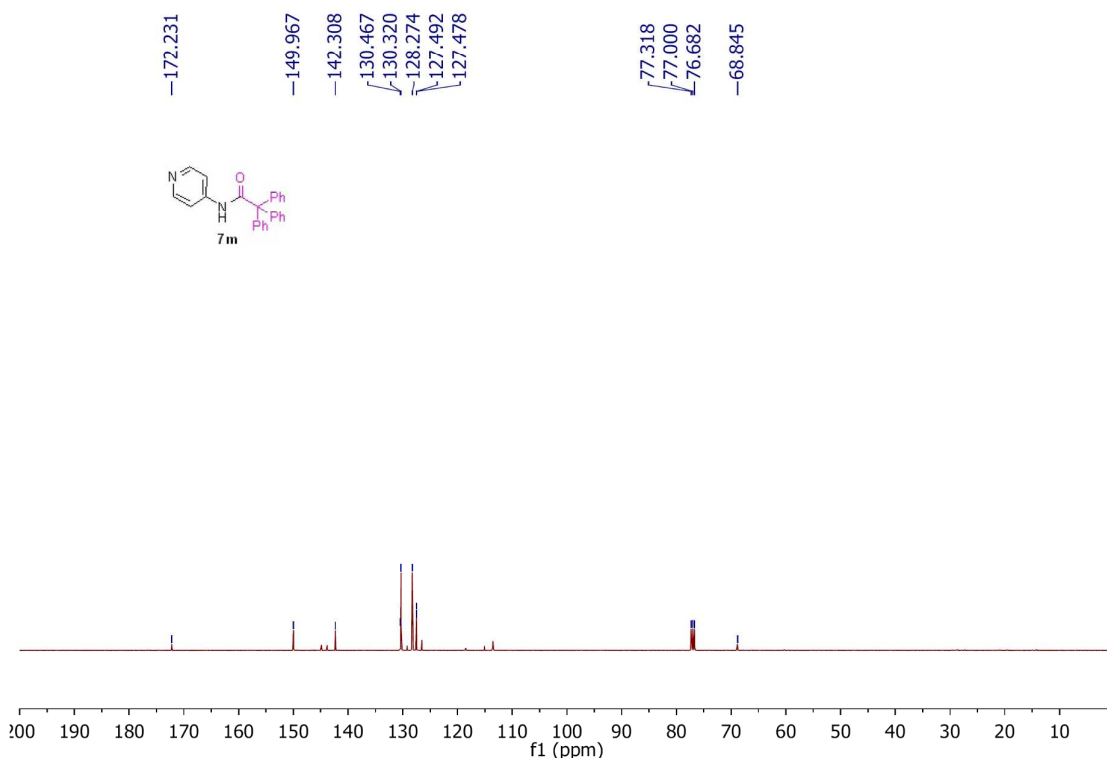
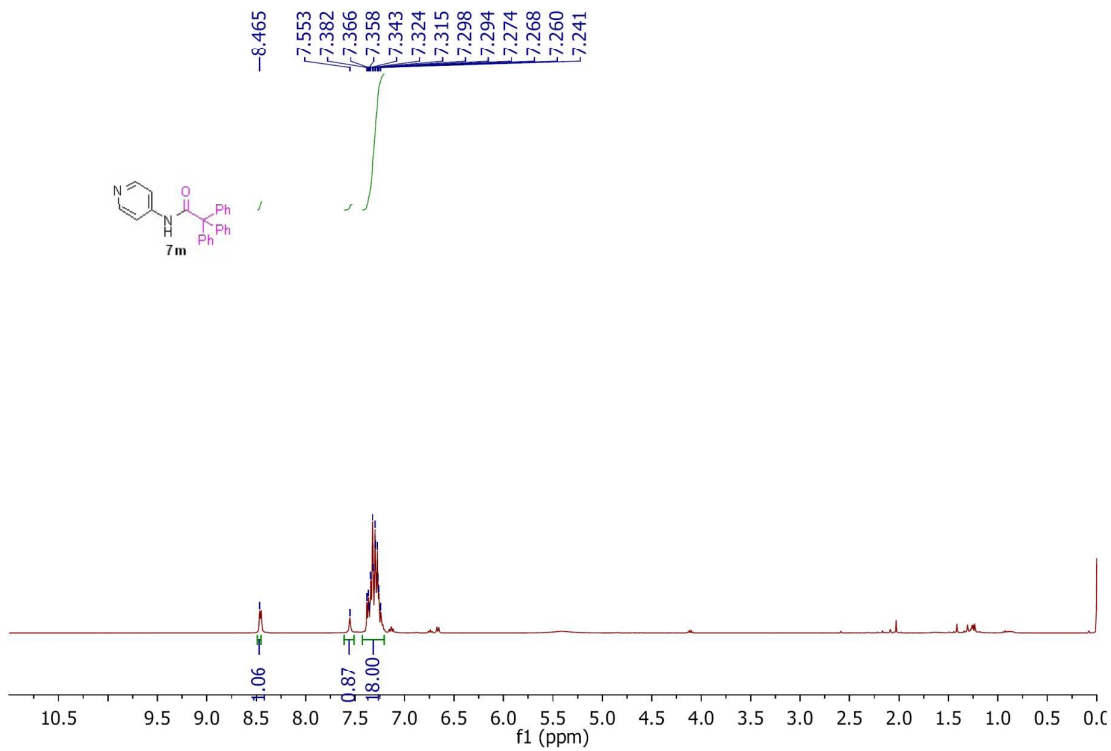


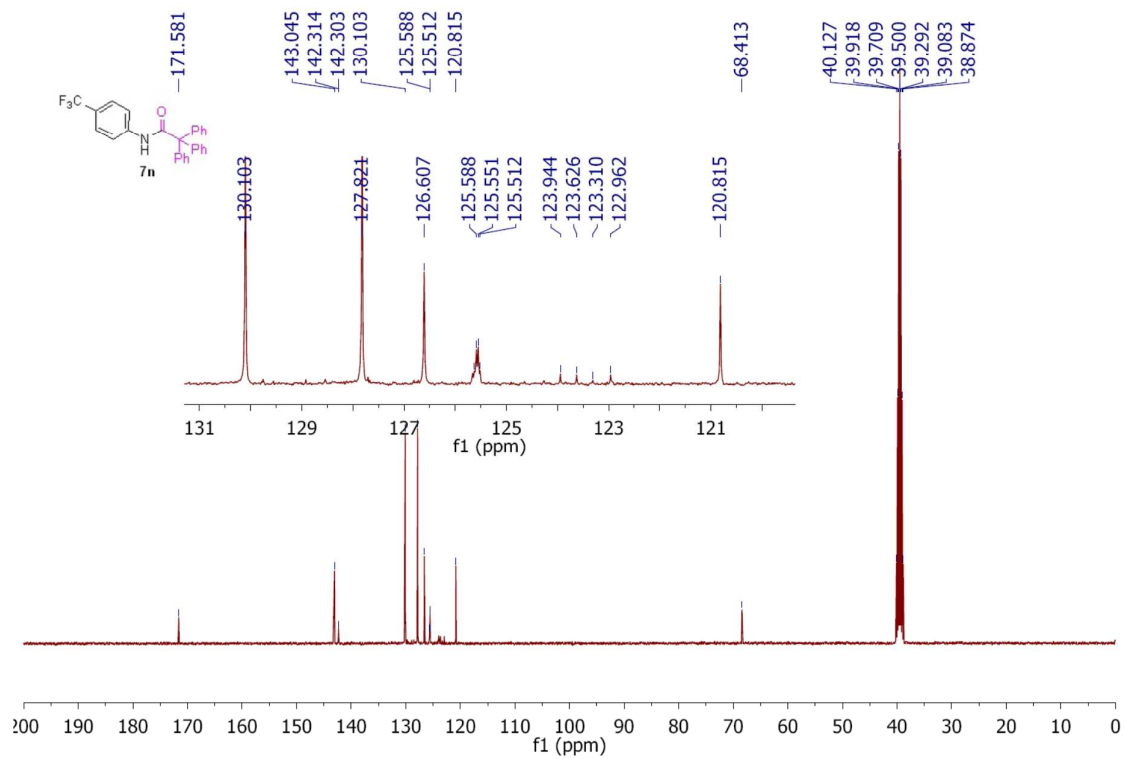
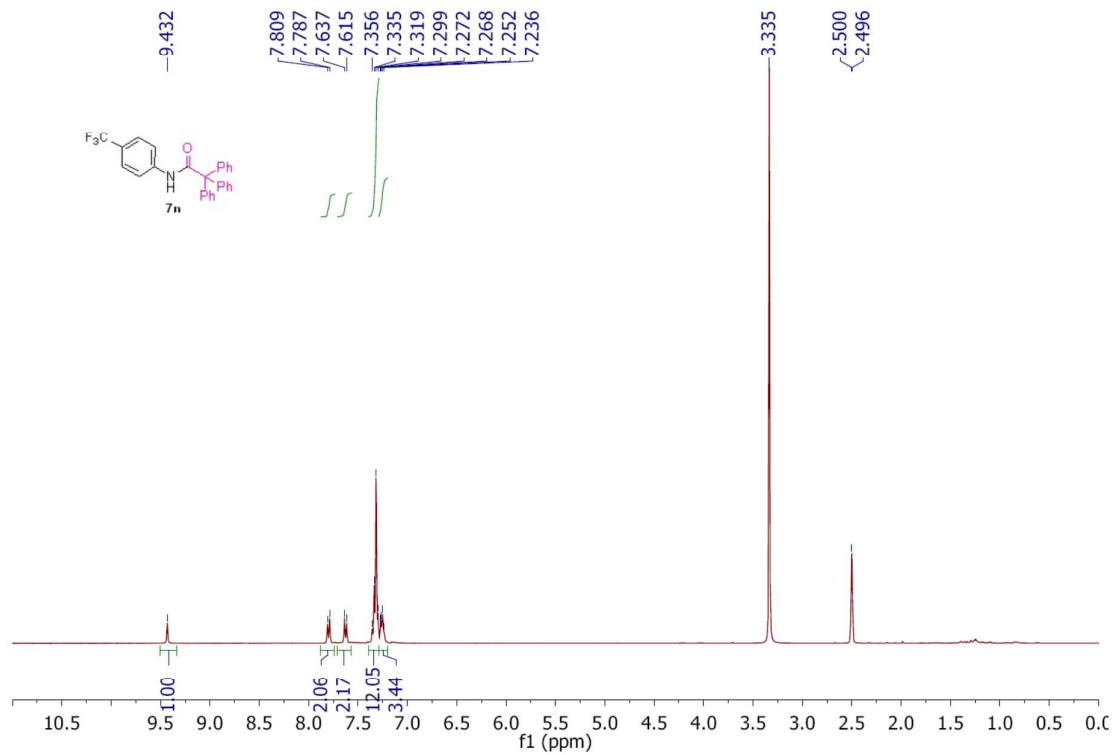


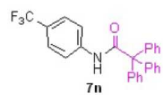












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