

Ceric Ammonium Nitrate (CAN) Enabled Concerted

Nitration/Ureation of Carbodiimides to Synthesize *o*-Nitroaryl Ureas

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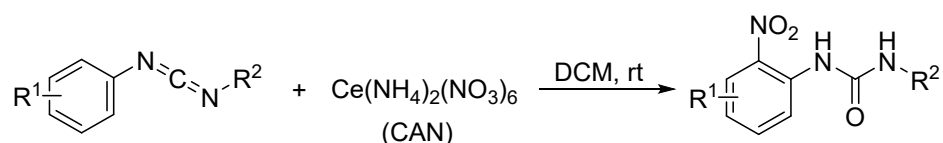
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1. General

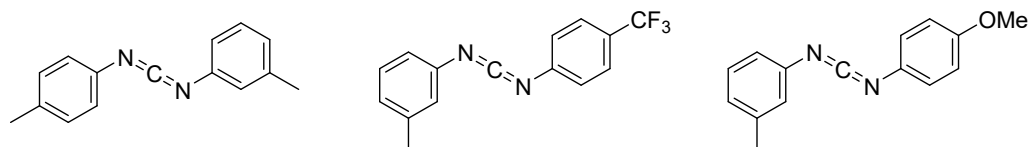
All reactions were performed in a glass vial under atmosphere. The boiling point of petroleum ether is between 60 °C and 90 °C. For chromatography, 200-300 mesh silica gel (Qingdao, China) was employed. ^1H , ^{13}C and ^{19}F NMR spectra were recorded on Ascend 400, Bruker Biospin GmbH 500 spectrometer. Chemical shifts are reported in ppm relative to CDCl_3 (^1H , TMS δ 0; ^{13}C , δ 77.16), $\text{DMSO-}d_6$ (^1H , δ 2.50; ^{13}C , δ 39.52). HMRS were obtained on a Bruker SolanX 70 FT-MS or Waters Xevo G2-XS QT spectrometer. All reagents and solvents were obtained from commercial sources and used as supplied unless otherwise noted. All carbodiimides^[1] were prepared according to literature methods.

2. General procedure for the synthesis of *o*-nitroaryl ureas

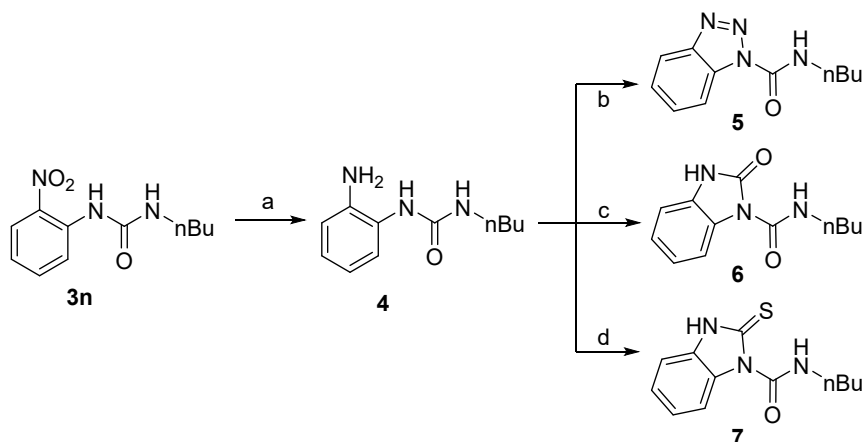


To a 10 mL dry thick walled tube equipped with a magnetic stir bar, was added CAN (0.3 mmol, 164.5 mg) and DCM (3 mL), the mixture was stirred for 5 min. Then, the carbodiimide **1a** (0.3 mmol, 56.4mg) was added. The tube was sealed and the reaction mixture was stirred at rt for 17 h. Upon the reaction completed, the mixture was concentrated under reduced pressure. The resulting crude residue was purified via flash column chromatography (petroleum ether/ethyl acetate = 10:1-5:1) on silica gel to afford the desired product **3a** (69.3 mg, 92%). *Note: the purity of the carbodiimide will affect its reactivity.*

For these *meta*-substituted diaryl carbodiimides, reaction systems were mixed.



3. Procedure for further transformation of **3n**



Procedure for the reduction of compound **3n.** To a solution of compound **3n** (105.8 mg, 0.446 mmol) in MeOH (10 mL) was added 5% Pd/C (20 mg). The reaction mixture was allowed to stir

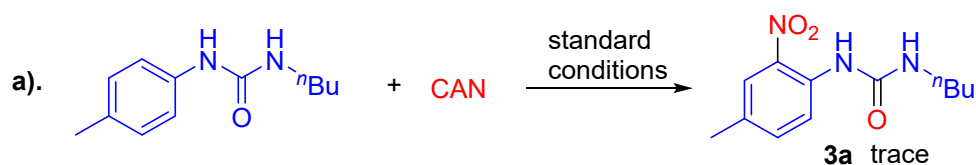
at room temperature under H₂. After 1 h, the mixture was filtered, concentrated in vacuo, and purified by column chromatography (petroleum ether/ethyl acetate 1:2) to give 64.7 mg (70%) of compound **4** as a solid.

Procedure for the synthesis of 5. The substance of **4** (0.3mmol, 62.1mg) was dissolved in 1 mL of glacial acetic acid at 25°C, and then 1M HCl were added. The mixture was cooled to 0-5 °C, stirring constantly. A separate solution of NaNO₂ (0.3mmol, 20.7mg) in 0.24 mL of water was then prepared and cooled to 0-5°C. The mixture is slowly added to the solution of **4**, maintaining the temperature at less than 10 °C, throughout. Upon the reaction completed, 15 mL H₂O was added to mixture and extracted with ethyl acetate (15 mL x 3). The combined organic layer was dried (anhydrous Na₂SO₄), filtered, and evaporated followed by a silica gel column chromatography (petroleum ether/ethyl acetate = 5:1) to afford desired product **5**.

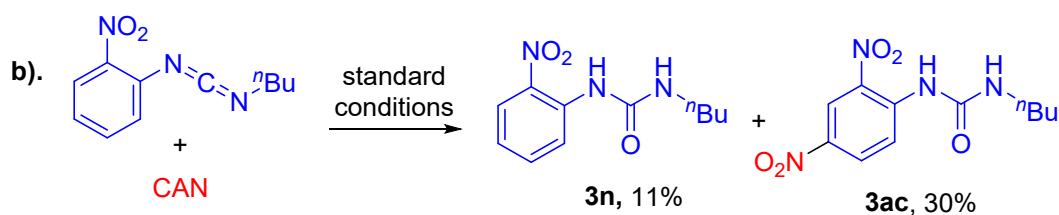
Procedure for the synthesis of 6. *N, N*-disuccinimidyl carbonate (84.54, 0.33mmol) was added to a solution of the substituted of **4** (0.3mmol) in acetonitrile (1.8ml). The mixture was stirred at room temperature for 13 h. The resulting suspension was filtered and washed with DCM, the separate solution evaporated followed by a silica gel column chromatography (DCM/MeOH = 20:1) to afford product **6**.

Procedure for the synthesis of 7. Thiophosgene (37.94mg, 0.33mmol) was added to a solution of the substituted of **4** (0.3mmol) in acetonitrile (1.8ml). The mixture was stirred at room temperature for 13 h. The separate solution evaporated followed by a silica gel column chromatography (petroleum ether/ethyl acetate = 5:1) to afford product **7**.

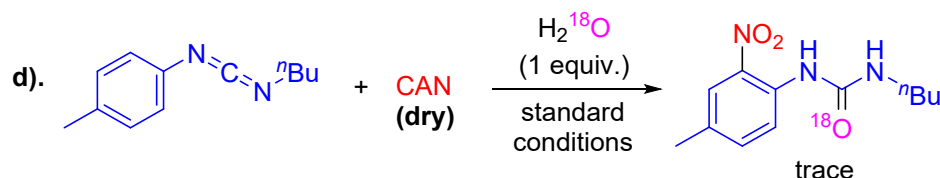
4. Control experiments



To a 10 mL dry thick walled tube equipped with a magnetic stir bar, was added 1-butyl-3-(*p*-tolyl) urea (41.3 mg 0.2 mmol) and CAN (109.6 mg 0.2 mmol) and dry DCM (2 mL) was added. The flask was sealed and the reaction mixture was stirred at 25 °C for 17 h, only trace amount of **3a** was detected.



To a 10 mL dry thick walled tube equipped with a magnetic stir bar, was added CAN (0.2 mmol, 109.6 mg) and dry DCM (2 mL), the mixture was stirred for 5 min. Then, the carbodiimide N-butyl-N-(2-nitrophenyl)methanediiimine (0.2 mmol, 43.8 mg) was added. The tube was sealed and the reaction mixture was stirred at rt for 9 h. Upon the reaction completed, the mixture was concentrated under reduced pressure. The resulting crude residue was purified via flash column chromatography (petroleum ether/ethyl acetate = 10:1) on silica gel to afford the desired product **3n** (5.2 mg, 11%) and **3ac** (16.9 mg, 30%).



To a 10 mL dry thick walled tube equipped with a magnetic stir bar, was added CAN (0.2 mmol, 109.6 mg, vacuum drying at 110 °C for 2 h) and dry DCM (2 mL), the mixture was stirred for 5 min. Then, the carbodiimide **1a** (0.2 mmol, 37.6 mg) and H_2^{18}O (4 μL) was added. The tube was sealed and the reaction mixture was stirred at rt for 17 h. Upon the reaction completed, the mixture was concentrated under reduced pressure. The resulting crude residue was purified via flash column chromatography (petroleum ether/ethyl acetate = 10:1) on silica gel to afford the desired product **3a** (19.1 mg, 77%), as shown in Figure SI 1, only trace amount of ^{18}O labeled product.

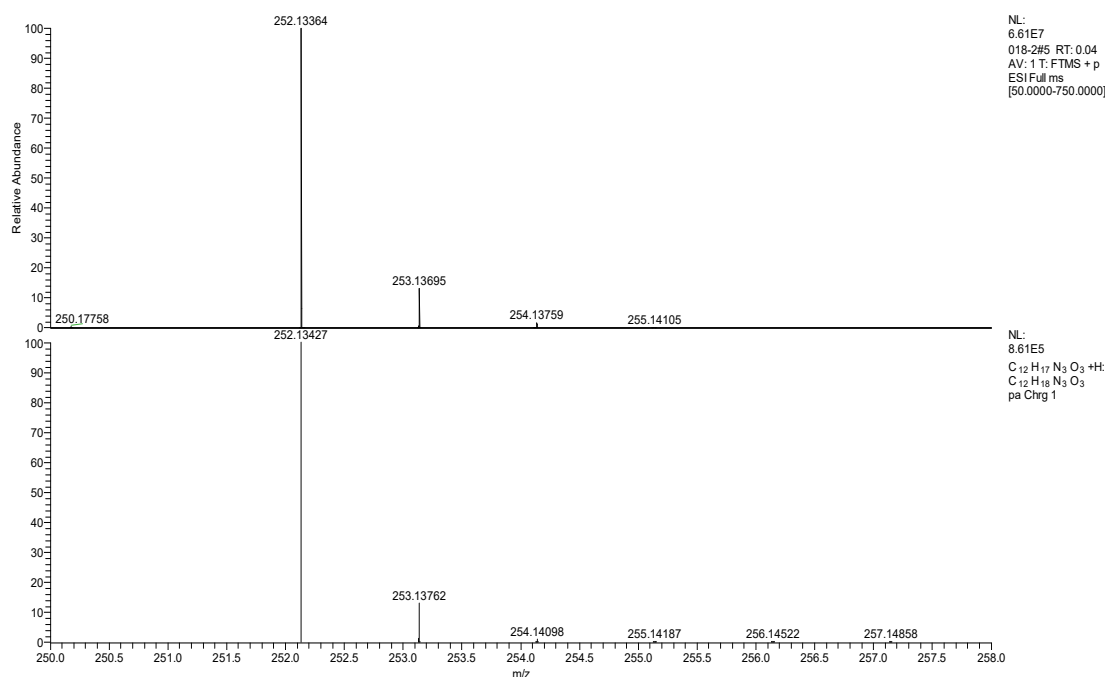
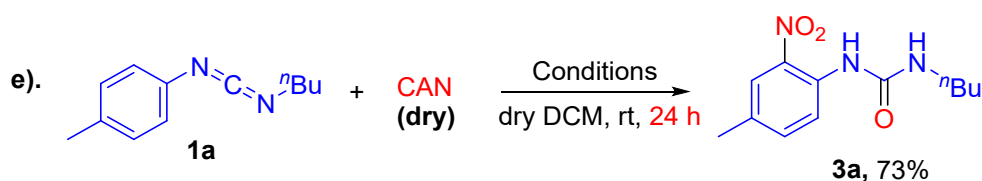


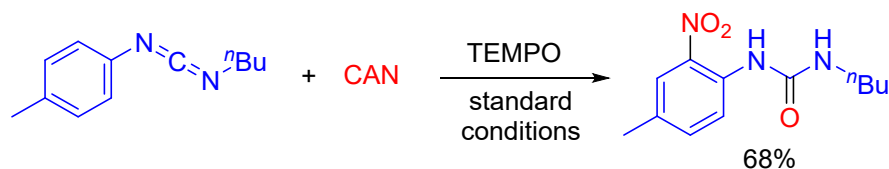
Figure SI 1 ^{18}O labeled result of Eq.d.



To a 10 mL dry thick walled tube equipped with a magnetic stir bar, was added CAN (0.1 mmol, 54.8 mg, vacuum drying at 110 °C for 2 h) and dry DCM (1 mL), the mixture was stirred for 5 min.

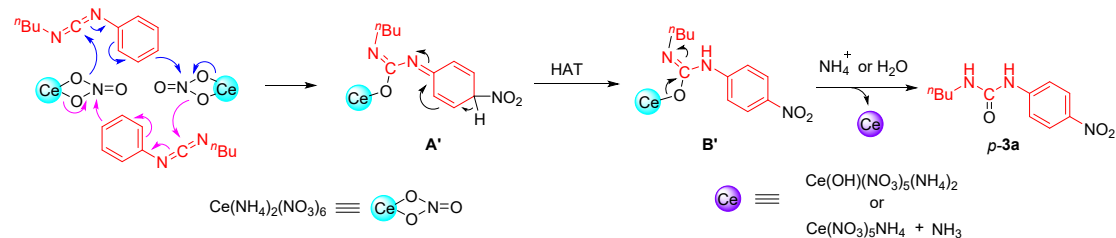
Then, the carbodiimide **1a** (0.1 mmol, 18.8 mg) was added. The tube was sealed and the reaction mixture was stirred at rt for 24 h. Upon the reaction completed, the mixture was concentrated under reduced pressure. The resulting crude residue was purified via flash column chromatography (petroleum ether/ethyl acetate = 10:1) on silica gel to afford the desired product **3a** (18.3 mg, 73%).

Rdical trapping experiment



To a 10 mL dry thick walled tube equipped with a magnetic stir bar, was added CAN (0.2 mmol, 109.6 mg) and dry DCM (2 mL), the mixture was stirred for 5 min. Then, the carbodiimide **1a** (0.2 mmol, 37.6 mg) and TEMPO (0.2 mmol, 18.2 mg) was added. The tube was sealed and the reaction mixture was stirred at rt for 17 h. Upon the reaction completed, the mixture was concentrated under reduced pressure. The resulting crude residue was purified via flash column chromatography (petroleum ether/ethyl acetate = 10:1) on silica gel to afford the desired product **3a** (16.9 mg, 68%).

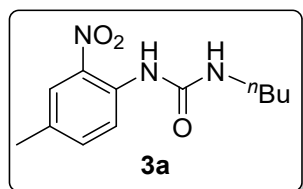
5. Proposed intermolecular mechanism



For the observed nitration in the para position, a probable intermolecular mechanism was proposed and described. The intermolecular nucleophilic addition of carbodiimides and electrophilic nitration of aromatic rings occur to give intermediate **A'**. Subsequently, hydrogen atom transfer (HAT) process result in the re-aromatized species **B'**, which undergoes isomerization and protonation with existing ammonium ion or external water to afford product *p*-**3a** and release cerium complex.

6. Characteristic Data of *o*-nitroaryl ureas

1-butyl-3-(4-methyl-2-nitrophenyl)urea (**3a**)



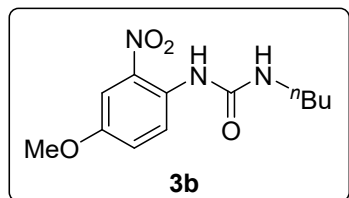
Yellow solid; yield 92% (69 mg); mp 144-145 °C;

¹H NMR (500 MHz, CDCl₃) δ 9.67 (s, 1H), 8.52 (d, *J* = 8.7 Hz, 1H), 7.97 (s, 1H), 7.40 (d, *J* = 8.7 Hz, 1H), 5.02 (s, 1H), 3.30 (q, *J* = 6.7 Hz, 2H), 2.35 (s, 3H), 1.57 (p, *J* = 7.3 Hz, 2H), 1.40 (h, *J* = 7.4 Hz, 2H), 0.95 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 154.40, 137.20, 135.37, 135.00, 131.44, 125.42, 121.52, 40.55, 32.10, 20.48, 20.16, 13.88.

HRMS (ESI): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{12}\text{H}_{18}\text{N}_3\text{O}_3^+$, 252.1343; found, 252.1348

1-butyl-3-(4-methoxy-2-nitrophenyl)urea (3b)



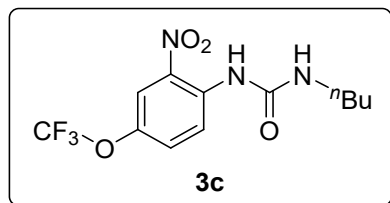
Yellow solid; yield 91% (73 mg); mp 164-166 °C;

^1H NMR (400 MHz, CDCl_3) δ 9.55 (s, 1H), 8.53 (d, $J = 9.4$ Hz, 1H), 7.61 (d, $J = 2.9$ Hz, 1H), 7.21 (dd, $J = 9.4, 2.9$ Hz, 1H), 4.94 (s, 1H), 3.83 (s, 3H), 3.30 (t, $J = 7.1$ Hz, 2H), 1.56 (p, $J = 7.3$ Hz, 2H), 1.40 (h, $J = 7.3$ Hz, 2H), 0.95 (t, $J = 7.3$ Hz, 3H).

^{13}C NMR (151 MHz, CDCl_3) δ 153.75, 135.90, 131.34, 124.57, 123.26, 107.79, 55.98, 40.56, 32.10, 20.16, 13.88.

HRMS (ESI): $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{12}\text{H}_{16}\text{N}_3\text{O}_4^-$, 266.1146; found, 266.1147

1-butyl-3-(2-nitro-4-(trifluoromethoxy)phenyl)urea (3c)



Yellow solid; yield 89% (86 mg); mp 136-138 °C;

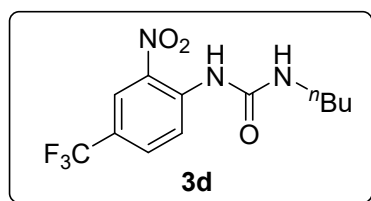
^1H NMR (500 MHz, CDCl_3) δ 9.75 (s, 1H), 8.76 (d, $J = 9.4$ Hz, 1H), 8.04 (s, 1H), 7.46 (d, $J = 8.7$ Hz, 1H), 5.48 (s, 1H), 3.31 (q, $J = 6.5$ Hz, 2H), 1.57 (p, $J = 6.9$ Hz, 2H), 1.40 (h, $J = 7.1$ Hz, 2H), 0.95 (t, $J = 7.3$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 154.13, 142.01, 136.25, 135.00, 129.19, 123.13, 120.48 (q, $J = 258.5$ Hz), 118.30, 40.56, 31.99, 20.13, 13.83.

^{19}F NMR (471 MHz, CDCl_3) δ -58.51.

HRMS (ESI): $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{12}\text{H}_{13}\text{F}_3\text{N}_3\text{O}_4^-$, 320.0864; found, 320.0863

1-butyl-3-(2-nitro-4-(trifluoromethyl)phenyl)urea (3d)



Yellow solid; yield 71% (65 mg); mp 144-145 °C;

^1H NMR (500 MHz, CDCl_3) δ 9.96 (s, 1H), 8.88 (d, $J = 9.1$ Hz, 1H), 8.46 (s, 1H), 7.78 (d, $J = 7.8$ Hz,

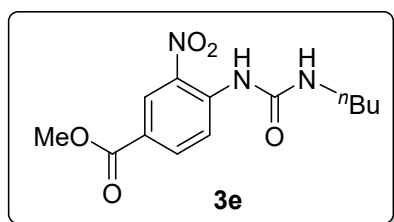
1H), 5.39 (s, 1H), 3.33 (q, $J = 6.9$ Hz, 2H), 1.59 (p, $J = 7.3$ Hz, 2H), 1.41 (h, $J = 7.3$ Hz, 2H), 0.96 (t, $J = 7.3$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 153.70, 140.10, 134.35, 132.26 (q, $J = 3.8$ Hz), 123.59 (q, $J = 3.7$ Hz), 123.42 (q, $J = 34.0$ Hz), 123.13 (q, $J = 272.2$ Hz), 122.02, 40.60, 31.97, 20.14, 13.84.

^{19}F NMR (471 MHz, CDCl_3) δ -62.56.

HRMS (ESI): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{12}\text{H}_{15}\text{F}_3\text{N}_3\text{O}_3^+$, 306.1060; found, 306.1066

methyl 4-(3-butylureido)-3-nitrobenzoate (3e)



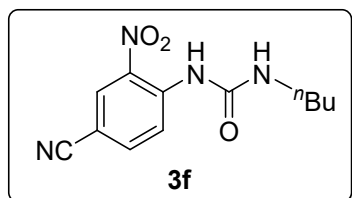
Yellow solid; yield 60% (47 mg); mp 134–135 °C;

^1H NMR (500 MHz, CDCl_3) δ 10.02 (s, 1H), 8.85 (d, $J = 2.1$ Hz, 1H), 8.79 (d, $J = 9.0$ Hz, 1H), 8.18 (dd, $J = 9.2, 2.1$ Hz, 1H), 5.46 (s, 1H), 3.94 (s, 3H), 3.33 (td, $J = 7.2, 5.6$ Hz, 2H), 1.59 (p, $J = 7.6$ Hz, 2H), 1.41 (h, $J = 7.3$ Hz, 2H), 0.96 (t, $J = 7.4$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 165.14, 153.71, 140.86, 136.38, 134.56, 127.91, 122.99, 120.99, 52.62, 40.57, 31.98, 20.14, 13.85.

HRMS (ESI): $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{13}\text{H}_{16}\text{N}_3\text{O}_5^-$, 294.1095; found, 294.1096

1-butyl-3-(4-cyano-2-nitrophenyl)urea (3f)



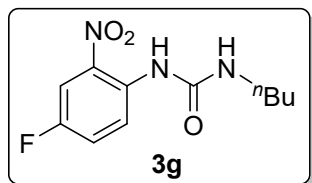
Yellow solid; yield 41% (32 mg); mp 137–139 °C;

^1H NMR (500 MHz, CDCl_3) δ 10.01 (s, 1H), 8.91 (d, $J = 9.0$ Hz, 1H), 8.52 (s, 1H), 7.79 (d, $J = 9.0$ Hz, 1H), 5.46 (s, 1H), 3.33 (q, $J = 6.4$ Hz, 2H), 1.58 (q, $J = 7.0$ Hz, 2H), 1.41 (h, $J = 7.0$ Hz, 2H), 0.96 (t, $J = 7.2$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 153.29, 140.96, 138.05, 134.37, 130.62, 122.12, 117.14, 104.48, 40.61, 31.87, 20.12, 13.83.

HRMS (ESI): $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{12}\text{H}_{13}\text{N}_4\text{O}_3^-$, 261.0993; found, 261.0993

1-butyl-3-(4-fluoro-2-nitrophenyl)urea (3g)



Yellow solid; yield 76% (58 mg); mp 128–129 °C;

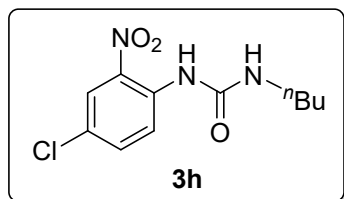
^1H NMR (400 MHz, CDCl_3) δ 9.64 (s, 1H), 8.69 (dd, $J = 9.4, 5.1$ Hz, 1H), 7.88 (dd, $J = 8.5, 2.8$ Hz, 1H), 7.39 – 7.32 (m, 1H), 5.03 (s, 1H), 3.31 (q, $J = 6.7$ Hz, 2H), 1.58 (dq, $J = 14.7, 7.4, 6.9$ Hz, 2H), 1.40 (h, $J = 7.2$ Hz, 2H), 0.96 (t, $J = 7.3$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 155.94 (d, $J = 245.4$ Hz), 154.37, 135.33 (d, $J = 8.1$ Hz), 133.94, 133.93, 123.87 (d, $J = 22.5$ Hz), 123.57 (d, $J = 7.0$ Hz), 111.81 (d, $J = 26.9$ Hz), 40.53, 32.02, 20.13, 13.85.

^{19}F NMR (471 MHz, CDCl_3) δ -119.31.

HRMS (ESI): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{11}\text{H}_{15}\text{FN}_3\text{O}_3^+$, 256.1092; found, 256.1095

1-butyl-3-(4-chloro-2-nitrophenyl)urea (3h)



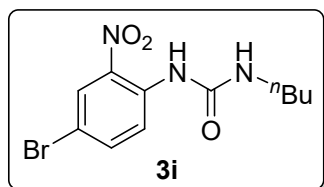
Yellow solid; yield 78% (64 mg); mp 148-150 °C;

^1H NMR (500 MHz, CDCl_3) δ 9.71 (s, 1H), 8.66 (d, $J = 9.2$ Hz, 1H), 8.16 (s, 1H), 7.53 (d, $J = 9.1$ Hz, 1H), 5.35 (s, 1H), 3.30 (q, $J = 6.6$ Hz, 2H), 1.57 (p, $J = 7.1$ Hz, 2H), 1.40 (h, $J = 7.2$ Hz, 2H), 0.95 (t, $J = 7.3$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 154.08, 136.07, 136.05, 135.44, 126.42, 125.18, 122.93, 40.54, 32.00, 20.14, 13.85.

HRMS (ESI): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{11}\text{H}_{15}\text{ClN}_3\text{O}_3^+$, 272.0796; found, 272.0805

1-(4-bromo-2-nitrophenyl)-3-butylurea (3i)



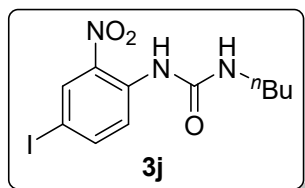
Yellow solid; yield 82% (78 mg); mp 163-164 °C;

^1H NMR (500 MHz, CDCl_3) δ 9.72 (s, 1H), 8.62 (d, $J = 9.2$ Hz, 1H), 8.31 (d, $J = 2.3$ Hz, 1H), 7.66 (dd, $J = 9.2, 2.3$ Hz, 1H), 5.14 (s, 1H), 3.31 (q, $J = 7.0$ Hz, 2H), 1.57 (p, $J = 7.4$ Hz, 2H), 1.40 (h, $J = 7.3$ Hz, 2H), 0.95 (t, $J = 7.4$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 153.92, 138.86, 136.51, 135.67, 128.16, 123.07, 113.21, 40.58, 32.02, 20.14, 13.86.

HRMS (ESI): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{11}\text{H}_{14}\text{BrN}_3\text{O}_3\text{Na}^+$, 338.0111; found, 338.0099

1-butyl-3-(4-iodo-2-nitrophenyl)urea (3j)



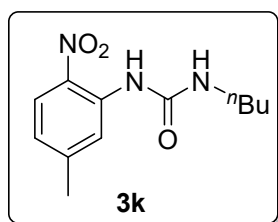
Yellow solid; yield 51% (56 mg); mp 176-178 °C;

^1H NMR (500 MHz, CDCl_3) δ 9.72 (s, 1H), 8.47 (s, 1H), 8.46 (s, 1H), 7.81 (d, $J = 8.7$ Hz, 1H), 5.15 (s, 1H), 3.30 (q, $J = 6.5$ Hz, 2H), 1.57 (p, $J = 7.0$ Hz, 2H), 1.40 (h, $J = 7.0$ Hz, 2H), 0.95 (t, $J = 7.3$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 153.88, 144.45, 137.10, 135.86, 134.00, 123.21, 82.30, 40.58, 32.01, 20.15, 13.87.

HRMS (ESI): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{11}\text{H}_{15}\text{IN}_3\text{O}_3^+$, 364.0153; found, 364.0143

1-butyl-3-(5-methyl-2-nitrophenyl)urea (3k)



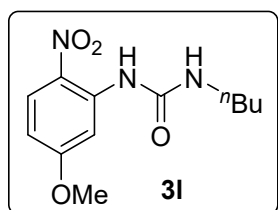
Yellow solid; yield 51% (o:p = 2.5:1) (24 mg:10 mg); mp 122-124 °C;

^1H NMR (500 MHz, CDCl_3) δ 9.88 (s, 1H), 8.50 (s, 1H), 8.08 (d, $J = 8.7$ Hz, 1H), 6.83 (d, $J = 8.5$ Hz, 1H), 4.98 (s, 1H), 3.31 (q, $J = 6.8$ Hz, 2H), 2.41 (s, 3H), 1.60 – 1.56 (m, 2H), 1.41 (h, $J = 7.3$ Hz, 2H), 0.96 (t, $J = 7.3$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 154.30, 148.16, 137.39, 133.38, 125.89, 122.59, 121.18, 40.56, 32.10, 22.31, 20.17, 13.89.

HRMS (ESI): $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{12}\text{H}_{16}\text{N}_3\text{O}_3^-$, 250.1197; found, 250.1197

1-butyl-3-(5-methoxy-2-nitrophenyl)urea (3l)



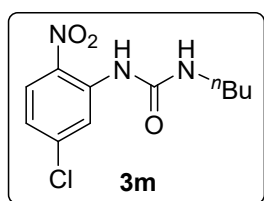
Yellow solid; yield 70% (o:p = 4:1) (45 mg:11 mg); mp 116-118 °C;

^1H NMR (400 MHz, CDCl_3) δ 10.29 (s, 1H), 8.36 (d, $J = 2.7$ Hz, 1H), 8.16 (d, $J = 9.7$ Hz, 1H), 6.54 (dd, $J = 9.5, 2.8$ Hz, 1H), 5.36 (s, 1H), 3.90 (s, 3H), 3.32 (q, $J = 6.7$ Hz, 2H), 1.58 (p, $J = 7.1$ Hz, 2H), 1.41 (h, $J = 7.2$ Hz, 2H), 0.95 (t, $J = 7.3$ Hz, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ 166.05, 154.41, 140.67, 128.59, 128.14, 110.21, 102.48, 56.17, 40.47, 32.08, 20.17, 13.89.

HRMS (ESI): $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{12}\text{H}_{17}\text{N}_3\text{O}_4\text{Na}^+$, 290.1111; found, 290.1102

1-butyl-3-(5-chloro-2-nitrophenyl)urea (3m)



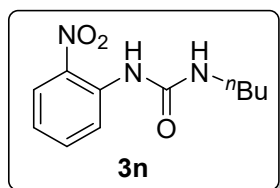
Yellow solid; yield 47% (o:p = 3:1) (29 mg:10 mg); mp 124-126 °C;

¹H NMR (500 MHz, CDCl₃) δ 9.89 (s, 1H), 8.81 (s, 1H), 8.13 (d, *J* = 9.1 Hz, 1H), 6.99 (d, *J* = 7.9 Hz, 1H), 5.23 (s, 1H), 3.32 (q, *J* = 6.6 Hz, 2H), 1.58 (p, *J* = 7.2 Hz, 2H), 1.41 (h, *J* = 7.2 Hz, 2H), 0.96 (t, *J* = 7.3 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 153.86, 143.01, 138.30, 133.49, 127.07, 121.69, 120.93, 40.58, 32.01, 20.14, 13.86.

HRMS (ESI): [M-H]⁻ calcd for C₁₁H₁₃ClN₃O₃⁻, 270.0651; found, 270.0653

1-butyl-3-(2-nitrophenyl)urea (3n)^[2]

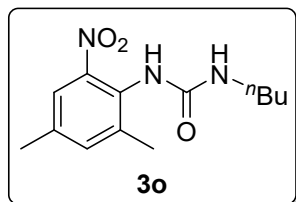


Yellow solid; yield 62% (o:p = 3:1) (33 mg:11 mg); mp 111-113 °C;

¹H NMR (400 MHz, CDCl₃) δ 9.79 (s, 1H), 8.65 (dd, *J* = 8.7, 1.2 Hz, 1H), 8.17 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.58 (ddd, *J* = 8.7, 7.2, 1.6 Hz, 1H), 7.03 (ddd, *J* = 8.5, 7.2, 1.3 Hz, 1H), 5.22 (s, 1H), 3.31 (td, *J* = 7.1, 5.8 Hz, 2H), 1.63 – 1.52 (m, 2H), 1.40 (dq, *J* = 14.4, 7.3 Hz, 2H), 0.95 (t, *J* = 7.3 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 154.34, 137.38, 136.08, 135.48, 125.82, 121.57, 121.34, 40.52, 32.06, 20.15, 13.87.

1-butyl-3-(2,4-dimethyl-6-nitrophenyl)urea (3o)



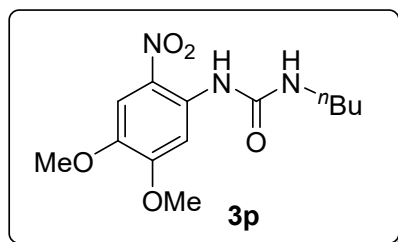
Yellow solid; yield 71% (57 mg); mp 172-174 °C;

¹H NMR (500 MHz, DMSO-*d*₆) δ 8.02 (s, 1H), 7.50 (s, 1H), 7.36 (s, 1H), 6.41 (s, 1H), 3.09 – 2.97 (m, 2H), 2.31 (s, 3H), 2.22 (s, 3H), 1.39 (s, 2H), 1.35 – 1.26 (m, 2H), 0.95 – 0.84 (m, 3H).

¹³C NMR (126 MHz, DMSO-*d*₆) δ 154.80, 145.28, 135.27, 135.14, 134.01, 128.12, 122.16, 31.91, 19.94, 19.42, 17.90, 13.68.

HRMS (ESI): [M-H]⁻ calcd for C₁₃H₁₈N₃O₃⁻, 264.1354; found, 264.1355

1-butyl-3-(4,5-dimethoxy-2-nitrophenyl)urea (3p)



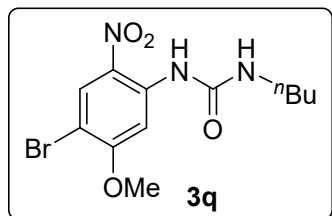
Yellow solid; yield 61% (54 mg); mp 202-204 °C;

^1H NMR (400 MHz, CDCl_3) δ 10.28 (s, 1H), 8.43 (s, 1H), 7.64 (s, 1H), 5.09 (s, 1H), 4.00 (s, 3H), 3.90 (s, 3H), 3.36 – 3.27 (m, 2H), 1.60 (s, 2H), 1.41 (dq, $J = 14.4, 7.2$ Hz, 2H), 0.96 (t, $J = 7.3$ Hz, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ 156.51, 154.52, 143.54, 135.31, 127.32, 106.84, 102.08, 56.77, 56.37, 40.53, 32.10, 20.19, 13.89.

HRMS (ESI): $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{13}\text{H}_{18}\text{N}_3\text{O}_5^-$, 296.1252; found, 296.1253

1-(4-bromo-5-methoxy-2-nitrophenyl)-3-butylurea (3q)



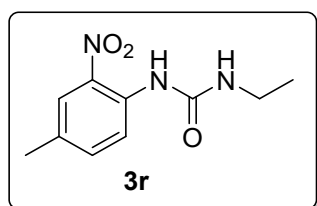
Yellow solid; yield 68% (71mg); mp 166-167 °C;

^1H NMR (500 MHz, CDCl_3) δ 10.21 (s, 1H), 8.51 (s, 1H), 8.42 (s, 1H), 5.47 (s, 1H), 4.00 (s, 3H), 3.32 (q, $J = 6.3$ Hz, 2H), 1.58 (q, $J = 7.1$ Hz, 2H), 1.41 (q, $J = 7.3$ Hz, 2H), 0.96 (t, $J = 7.2$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 162.03, 154.21, 139.81, 130.50, 128.47, 103.77, 101.97, 57.20, 40.47, 32.03, 20.17, 13.88.

HRMS (ESI): $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{12}\text{H}_{15}\text{BrN}_3\text{O}_4^-$, 344.0251; found, 344.0253

1-ethyl-3-(4-methyl-2-nitrophenyl)urea (3r)^[3]

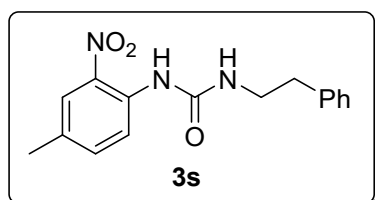


Yellow solid; yield 83% (56 mg); mp 182-183 °C;

^1H NMR (500 MHz, CDCl_3) δ 9.67 (s, 1H), 8.51 (d, $J = 8.7$ Hz, 1H), 7.96 (s, 1H), 7.40 (d, $J = 8.5$ Hz, 1H), 5.24 (s, 1H), 3.35 (p, $J = 6.8$ Hz, 2H), 2.34 (s, 3H), 1.22 (t, $J = 7.1$ Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 154.37, 137.18, 135.34, 135.01, 131.41, 125.38, 121.56, 35.59, 20.45, 15.26.

1-(4-methyl-2-nitrophenyl)-3-phenethylurea (3f)



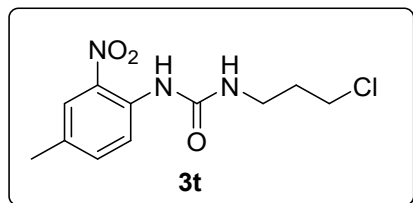
Yellow solid; yield 73% (66 mg); mp 156-158 °C;

^1H NMR (400 MHz, CDCl_3) δ 9.60 (s, 1H), 8.47 (s, 1H), 7.94 (s, 1H), 7.39 (dd, $J = 8.8, 2.0$ Hz, 1H), 7.30 (d, $J = 6.6$ Hz, 2H), 7.22 (d, $J = 7.1$ Hz, 3H), 5.22 (s, 1H), 3.57 (d, $J = 6.3$ Hz, 2H), 2.89 (d, $J = 5.4$ Hz, 2H), 2.34 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 154.32, 138.81, 137.17, 135.42, 134.85, 131.56, 128.95, 128.81, 126.76, 125.43, 121.56, 41.94, 36.23, 20.48.

HRMS (ESI): $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{16}\text{H}_{16}\text{N}_3\text{O}_3^-$, 298.1197; found, 298.1199

1-butyl-3-(4-cyano-2-nitrophenyl)urea (3f)



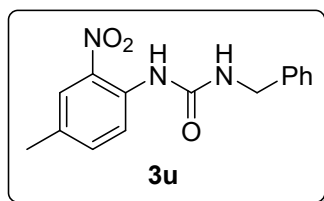
Yellow solid; yield 74% (60 mg); mp 150-151 °C;

^1H NMR (500 MHz, CDCl_3) δ 9.68 (s, 1H), 8.48 (d, $J = 8.7$ Hz, 1H), 7.94 (s, 1H), 7.40 (d, $J = 7.8$ Hz, 1H), 5.76 (s, 1H), 3.64 (t, $J = 6.3$ Hz, 2H), 3.48 (q, $J = 6.4$ Hz, 2H), 2.34 (s, 3H), 2.07 (p, $J = 6.4$ Hz, 2H).

^{13}C NMR (126 MHz, CDCl_3) δ 154.64, 137.23, 135.39, 134.81, 131.65, 125.41, 121.66, 42.49, 37.90, 32.60, 20.44.

HRMS (ESI): $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{11}\text{H}_{13}\text{N}_3\text{O}_3^-$, 270.0651; found, 270.0651

1-(3-chloropropyl)-3-(4-methyl-2-nitrophenyl)urea (3u)



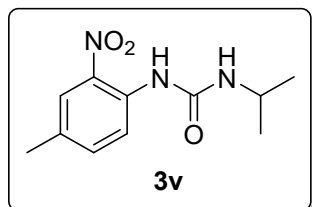
Yellow solid; yield 65% (56 mg); mp 170-171 °C;

^1H NMR (500 MHz, CDCl_3) δ 9.69 (s, 1H), 8.50 (d, $J = 8.6$ Hz, 1H), 7.93 (s, 1H), 7.34 (dd, $J = 19.1$, 6.1 Hz, 5H), 7.28 – 7.24 (m, 1H), 5.68 (s, 1H), 4.46 (d, $J = 5.3$ Hz, 2H), 2.33 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3) δ 154.38, 138.43, 137.15, 135.44, 134.77, 131.60, 128.84, 127.80, 127.68, 125.41, 121.63, 44.59, 20.46.

HRMS (ESI): $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{15}\text{H}_{14}\text{N}_3\text{O}_3^-$, 284.1041; found, 284.1040

1-isopropyl-3-(4-methyl-2-nitrophenyl)urea (3v)^[4]



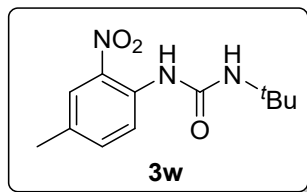
Yellow solid; yield 74% (53 mg); mp 177-178 °C;

^1H NMR (500 MHz, CDCl_3) δ 9.61 (s, 1H), 8.55 – 8.47 (m, 1H), 7.96 (s, 1H), 7.39 (d, $J = 8.7$ Hz, 1H), 4.94 (d, $J = 6.8$ Hz, 1H), 4.00 (dq, $J = 13.3$, 6.6 Hz, 1H), 2.34 (s, 3H), 1.24 (d, $J = 6.5$ Hz, 6H).

^{13}C NMR (126 MHz, CDCl_3) δ 153.63, 137.14, 135.37, 135.03, 131.36, 125.39, 121.54, 42.83, 23.21,

20.46.

1-(tert-butyl)-3-(4-methyl-2-nitrophenyl)urea (3w) [4]

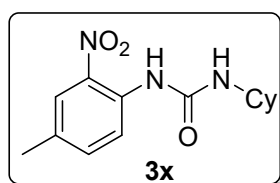


Yellow solid; yield 55% (41 mg); mp 156-158 °C;

¹H NMR (500 MHz, CDCl₃) δ 9.47 (s, 1H), 8.44 (d, *J* = 8.7 Hz, 1H), 7.94 (s, 1H), 7.37 (d, *J* = 8.7 Hz, 1H), 4.91 (s, 1H), 2.33 (s, 3H), 1.41 (s, 9H).

¹³C NMR (126 MHz, CDCl₃) δ 153.27, 136.98, 135.40, 135.09, 131.18, 125.37, 121.56, 51.47, 29.27, 20.44.

1-cyclohexyl-3-(4-methyl-2-nitrophenyl)urea (3x)



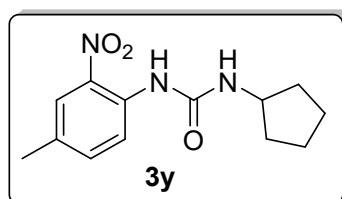
Yellow solid; yield 63% (52 mg); mp 213-215 °C;

¹H NMR (500 MHz, CDCl₃) δ 9.64 (s, 1H), 8.51 (d, *J* = 8.4 Hz, 1H), 7.96 (s, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 4.87 (s, 1H), 3.65 (s, 1H), 2.34 (s, 3H), 2.01 (d, *J* = 9.4 Hz, 2H), 1.75 (d, *J* = 11.5 Hz, 2H), 1.64 (d, *J* = 11.6 Hz, 2H), 1.43 – 1.35 (m, 2H), 1.23 – 1.18 (m, 2H).

¹³C NMR (126 MHz, CDCl₃) δ 153.56, 137.17, 135.36, 135.05, 131.35, 125.41, 121.48, 49.84, 33.68, 25.61, 25.04, 20.47

HRMS (ESI): [M-H]⁻ calcd for C₁₄H₁₈N₃O₃⁻, 276.1354; found, 276.1354

1-cyclopentyl-3-(4-methyl-2-nitrophenyl)urea (3y)



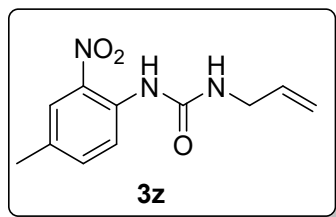
Yellow solid; yield 70% (55 mg); mp 178-179 °C;

¹H NMR (400 MHz, CDCl₃) δ 9.65 (s, 1H), 8.51 (d, *J* = 11.6 Hz, 1H), 7.95 (s, 1H), 7.39 (dd, *J* = 8.7, 1.9 Hz, 1H), 5.10 (s, 1H), 4.12 (h, *J* = 6.8 Hz, 1H), 2.34 (s, 3H), 2.05 (t, *J* = 9.3 Hz, 2H), 1.72 (s, 2H), 1.63 (s, 2H), 1.53 – 1.45 (m, 2H).

¹³C NMR (126 MHz, CDCl₃) δ 154.12, 137.12, 135.42, 134.94, 131.41, 125.39, 121.55, 52.61, 33.52, 23.80, 20.46.

HRMS (ESI): [M+H]⁺ calcd for C₁₃H₁₈N₃O₃⁺, 264.1343; found, 264.1338

1-allyl-3-(4-methyl-2-nitrophenyl)urea (3z)



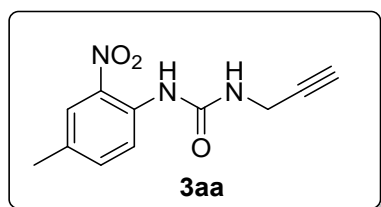
Yellow solid; yield 63% (48 mg); mp 166-168 °C;

¹H NMR (500 MHz, CDCl₃) δ 9.69 (s, 1H), 8.50 (d, *J* = 8.7 Hz, 1H), 7.95 (s, 1H), 7.39 (d, *J* = 8.7 Hz, 1H), 5.96 – 5.85 (m, 1H), 5.43 (s, 1H), 5.28 (d, *J* = 17.2 Hz, 1H), 5.17 (d, *J* = 10.2 Hz, 1H), 3.94 (s, 2H), 2.34 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 154.37, 137.15, 135.48, 134.78, 134.41, 131.61, 125.40, 121.67, 116.66, 43.09, 20.46

HRMS (ESI): [M-H]⁻ calcd for C₁₁H₁₂N₃O₃⁻, 234.0884; found, 234.0880

1-(4-methyl-2-nitrophenyl)-3-(prop-2-yn-1-yl)urea (3aa)



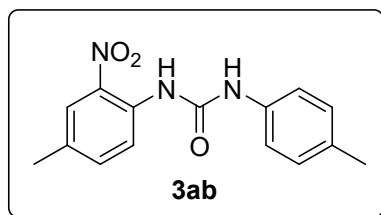
Yellow solid; yield 76% (53 mg); mp 149-151 °C;

¹H NMR (500 MHz, DMSO-*d*₆) δ 9.29 (s, 1H), 8.15 (d, *J* = 8.6 Hz, 1H), 7.84 (d, *J* = 15.4 Hz, 2H), 7.47 (d, *J* = 8.3 Hz, 1H), 3.98 – 3.82 (m, 2H), 3.14 (s, 1H), 2.31 (s, 3H).

¹³C NMR (126 MHz, DMSO-*d*₆) δ 154.03, 136.97, 135.83, 133.05, 131.43, 124.81, 122.23, 81.39, 73.23, 28.83, 19.73.

HRMS (ESI): [M+H]⁺ calcd for C₁₁H₁₂N₃O₃⁺, 234.0873; found, 234.0869

1-(4-methyl-2-nitrophenyl)-3-(p-tolyl)urea (3ab)

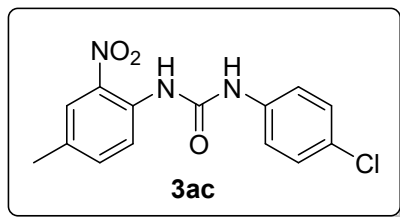


Yellow solid; yield 47% (40 mg); mp 209-210 °C;

¹H NMR (500 MHz, CDCl₃) δ 9.84 (s, 1H), 8.54 (d, *J* = 8.7 Hz, 1H), 7.96 (d, *J* = 2.4 Hz, 1H), 7.41 (d, *J* = 10.2 Hz, 1H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.19 (d, *J* = 8.2 Hz, 2H), 6.75 (s, 1H), 2.35 (s, 6H).

¹³C NMR (126 MHz, CDCl₃) δ 152.85, 137.06, 135.90, 135.65, 134.25, 134.13, 132.15, 130.25, 125.53, 123.06, 121.80, 21.10, 20.53.

HRMS (ESI): [M-H]⁻ calcd for C₁₅H₁₄N₃O₃⁻, 284.1041; found, 284.1042



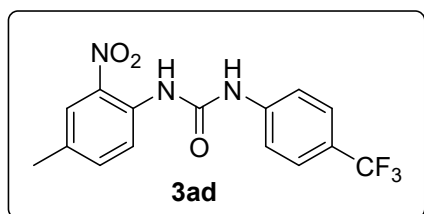
Yellow solid; yield 51% (47 mg); mp 207-208 °C;

^1H NMR (400 MHz, DMSO- d_6) δ 9.88 (s, 1H), 9.48 (s, 1H), 8.14 (d, J = 8.7 Hz, 1H), 7.90 (s, 1H), 7.57 – 7.47 (m, 3H), 7.34 (d, J = 8.8 Hz, 2H), 2.33 (s, 3H).

^{13}C NMR (101 MHz, DMSO- d_6) δ 151.86, 138.31, 137.70, 135.78, 132.24, 132.20, 128.72, 125.96, 124.94, 122.72, 120.01, 19.79.

HRMS (ESI): $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{14}\text{H}_{11}\text{ClN}_3\text{O}_3^-$, 304.0494; found, 304.0486

This structure was confirmed by reasonable fragment peak of HRMS



Yellow solid; yield 45% (46 mg); mp 216-217 °C;

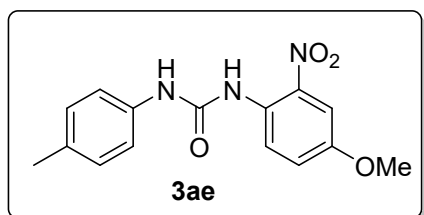
^1H NMR (400 MHz, DMSO- d_6) δ 10.14 (s, 1H), 9.54 (s, 1H), 8.14 (d, J = 8.5 Hz, 1H), 7.91 (s, 1H), 7.67 (q, J = 8.5 Hz, 4H), 7.53 (d, J = 8.5 Hz, 1H), 2.42 – 2.26 (m, 3H).

^{13}C NMR (101 MHz, DMSO- d_6) δ 151.82, 143.08, 137.92, 135.73, 132.48, 131.91, 126.12 (q, J = 3.8 Hz), 124.95, 124.48 (q, J = 271.1 Hz), 122.85, 122.29 (q, J = 32.1 Hz), 118.16, 40.14, 39.94, 39.73, 39.52, 39.31, 39.10, 38.89, 19.78.

HRMS (ESI): $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{15}\text{H}_{11}\text{F}_3\text{N}_3\text{O}_3^-$, 338.0758; found, 338.0758.

This structure was confirmed by reasonable fragment peak of HRMS

1-(4-methoxy-2-nitrophenyl)-3-(p-tolyl)urea (3ae)



Yellow solid; yield 49% (44 mg); mp 210–212 °C;

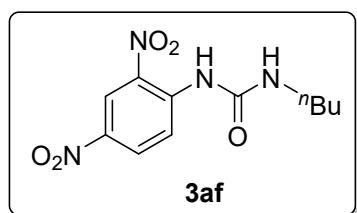
^1H NMR (400 MHz, DMSO- d_6) δ 9.55 (s, 1H), 9.27 (s, 1H), 8.12 (d, J = 9.2 Hz, 1H), 7.64 – 7.48 (m, 1H), 7.35 (d, J = 8.2 Hz, 3H), 7.09 (d, J = 8.2 Hz, 2H), 3.82 (s, 3H), 2.24 (s, 3H).

^{13}C NMR (101 MHz, DMSO- d_6) δ 153.86, 152.10, 138.64, 136.78, 131.17, 129.22, 128.22, 124.80, 122.28, 118.56, 108.22, 55.86, 20.35.

HRMS (ESI): $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{15}\text{H}_{14}\text{N}_3\text{O}_4^-$, 300.0990; found, 300.0983.

This structure was confirmed by reasonable fragment peak of HRMS

1-butyl-3-(2,4-dinitrophenyl)urea (3af)



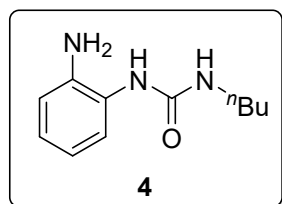
Yellow solid; yield 30% (21 mg); mp 134–135 °C;

¹H NMR (500 MHz, CDCl₃) δ 10.13 (s, 1H), 9.12 (d, *J* = 2.2 Hz, 1H), 8.98 (d, *J* = 9.5 Hz, 1H), 8.40 (dd, *J* = 9.5, 2.2 Hz, 1H), 5.30 (s, 1H), 3.35 (q, *J* = 6.8 Hz, 2H), 1.60 (p, *J* = 7.2 Hz, 2H), 1.42 (q, *J* = 7.4 Hz, 2H), 0.97 (t, *J* = 7.3 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 153.05, 142.30, 140.36, 133.76, 130.11, 122.47, 121.59, 40.69, 31.90, 20.13, 13.84.

HRMS (ESI): [M-H]⁻ calcd for C₁₁H₁₃N₄O₅⁻, 281.0891; found, 281.0892

1-(2-aminophenyl)-3-butylurea (4)



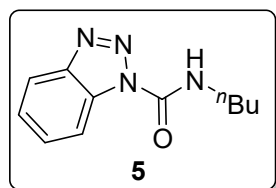
White solid; yield 70% (65 mg); mp 131-133 °C;

¹H NMR (400 MHz, CDCl₃) δ 7.09 (dd, *J* = 17.1, 7.5 Hz, 2H), 6.75 (q, *J* = 8.5, 7.8 Hz, 2H), 6.37 (br, 1H), 4.83 (br, 1H), 3.98 (s, 2H), 3.19 (p, *J* = 6.8 Hz, 2H), 1.44 (p, *J* = 7.6 Hz, 2H), 1.30 (h, *J* = 7.1 Hz, 2H), 0.89 (t, *J* = 7.1 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 157.44, 143.02, 128.07, 127.98, 123.22, 119.20, 116.67, 40.22, 32.34, 20.11, 13.91.

HRMS (ESI): [M-H]⁻ calcd for C₁₁H₁₆N₃O⁻, 206.1299; found, 206.1294

N-butyl-1*H*-benzo[*d*][1,2,3]triazole-1-carboxamide (5)^[5]

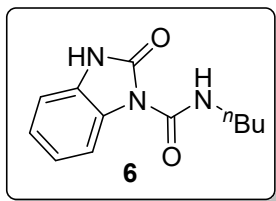


Yellow solid; yield 91% (60 mg); mp 198-200 °C;

¹H NMR (400 MHz, CDCl₃) δ 8.26 (d, *J* = 8.4 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 1H), 7.63 – 7.55 (m, 1H), 7.43 (dd, *J* = 8.2, 7.2 Hz, 1H), 7.34 (s, 1H), 3.58 – 3.50 (m, 2H), 1.74 – 1.64 (m, 2H), 1.45 (dq, *J* = 14.6, 7.4 Hz, 2H), 0.97 (t, *J* = 7.4 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃) δ 149.35, 146.37, 131.75, 129.94, 125.43, 120.03, 114.06, 40.36, 31.70, 20.07, 13.78.

N-butyl-2-oxo-2,3-dihydro-1*H*-benzo[*d*]imidazole-1-carboxamide (6)



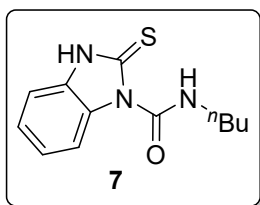
Yellow solid; yield 83% (58 mg); mp 157-159 °C;

^1H NMR (400 MHz, CDCl_3) δ 9.49 (s, 1H), 8.67 (s, 1H), 8.22 (d, $J = 8.1$ Hz, 1H), 7.13 (dd, $J = 37.1$, 8.2 Hz, 3H), 3.46 (q, $J = 6.9$ Hz, 2H), 1.65 (p, $J = 7.5$ Hz, 2H), 1.46 (p, $J = 7.6$ Hz, 2H), 0.98 (t, $J = 7.5$ Hz, 3H).

^{13}C NMR (101 MHz, CDCl_3) δ 154.58, 151.81, 127.90, 126.89, 123.96, 123.08, 115.74, 109.40, 39.86, 31.78, 20.25, 13.89.

HRMS (ESI): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{12}\text{H}_{16}\text{N}_3\text{O}_2^+$, 234.1237; found, 234.1234

N-butyl-2-thioxo-2,3-dihydro-1*H*-benzo[*d*]imidazole-1-carboxamide (7)



Yellow solid; yield 56% (42 mg); mp 180-181 °C;

^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ 13.49 (s, 1H), 10.15 (t, $J = 5.6$ Hz, 1H), 8.07 (d, $J = 7.9$ Hz, 1H), 7.42 – 7.14 (m, 3H), 3.38 (d, $J = 6.1$ Hz, 2H), 2.50 (s, 1H), 1.56 (q, $J = 7.0$ Hz, 2H), 1.41 (q, $J = 7.4$ Hz, 2H), 0.92 (t, $J = 7.4$ Hz, 3H).

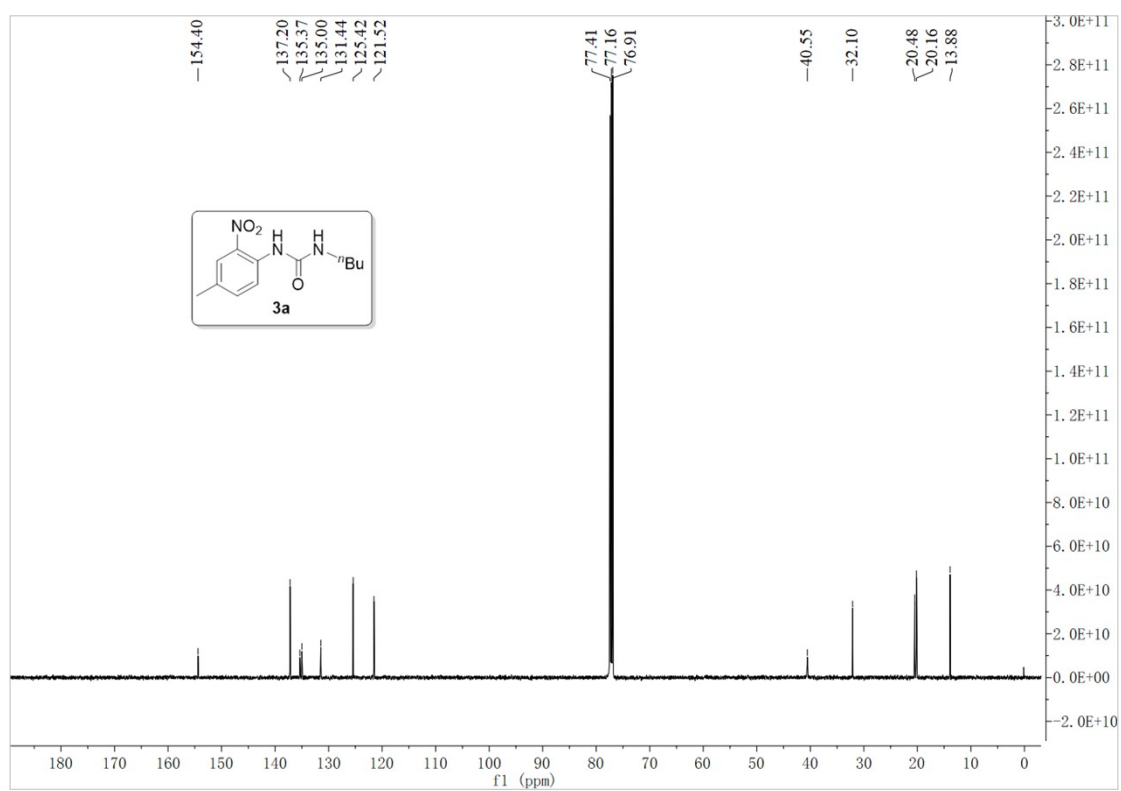
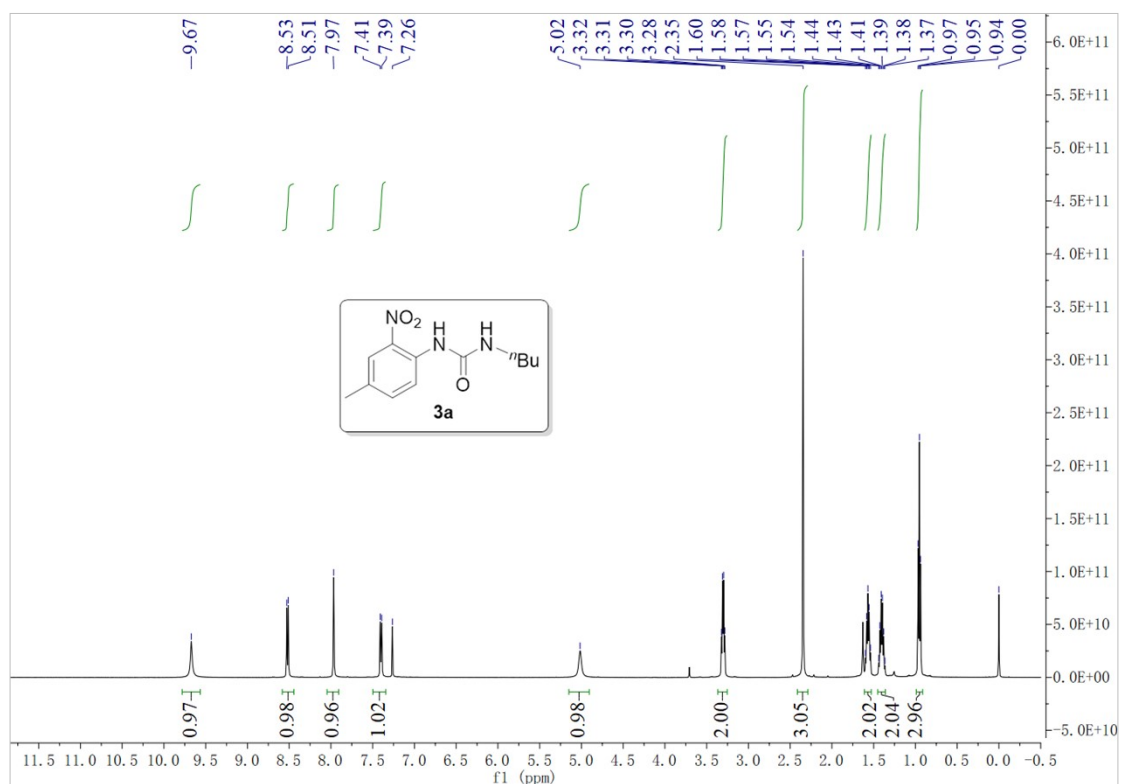
^{13}C NMR (126 MHz, $\text{DMSO-}d_6$) δ 167.03, 150.94, 131.20, 130.44, 124.68, 123.37, 115.28, 109.89, 30.72, 19.63, 13.54.

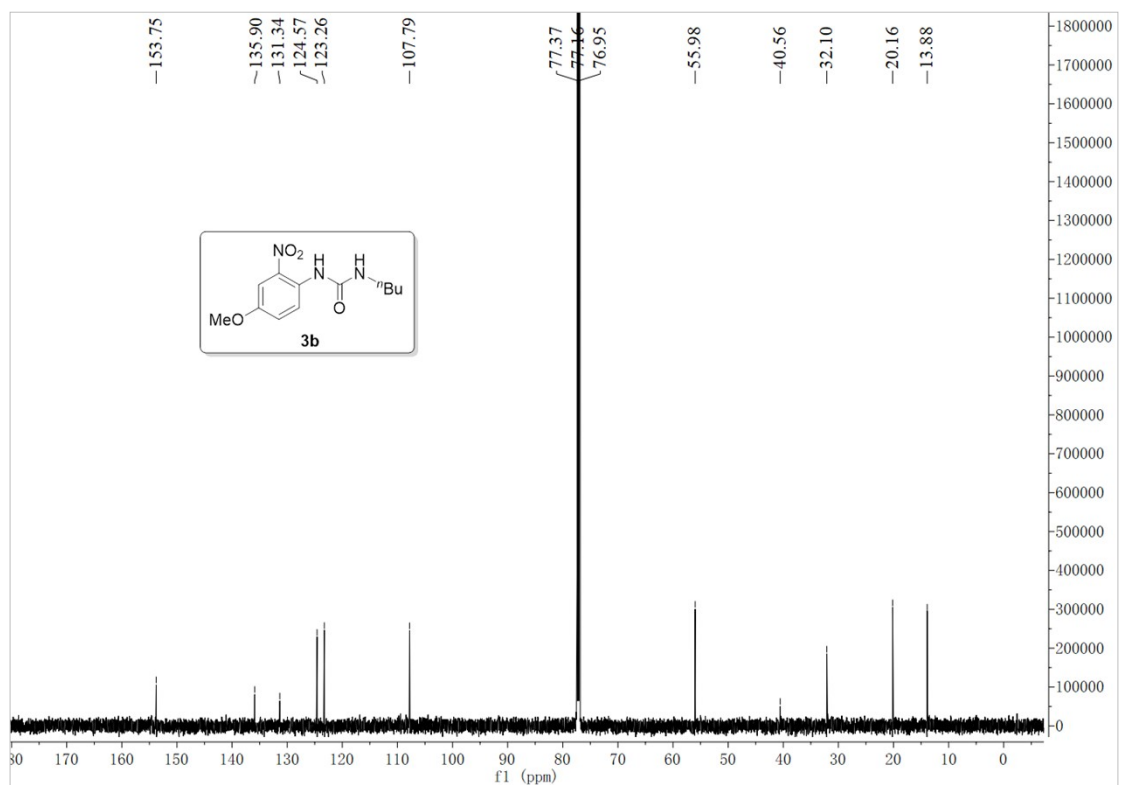
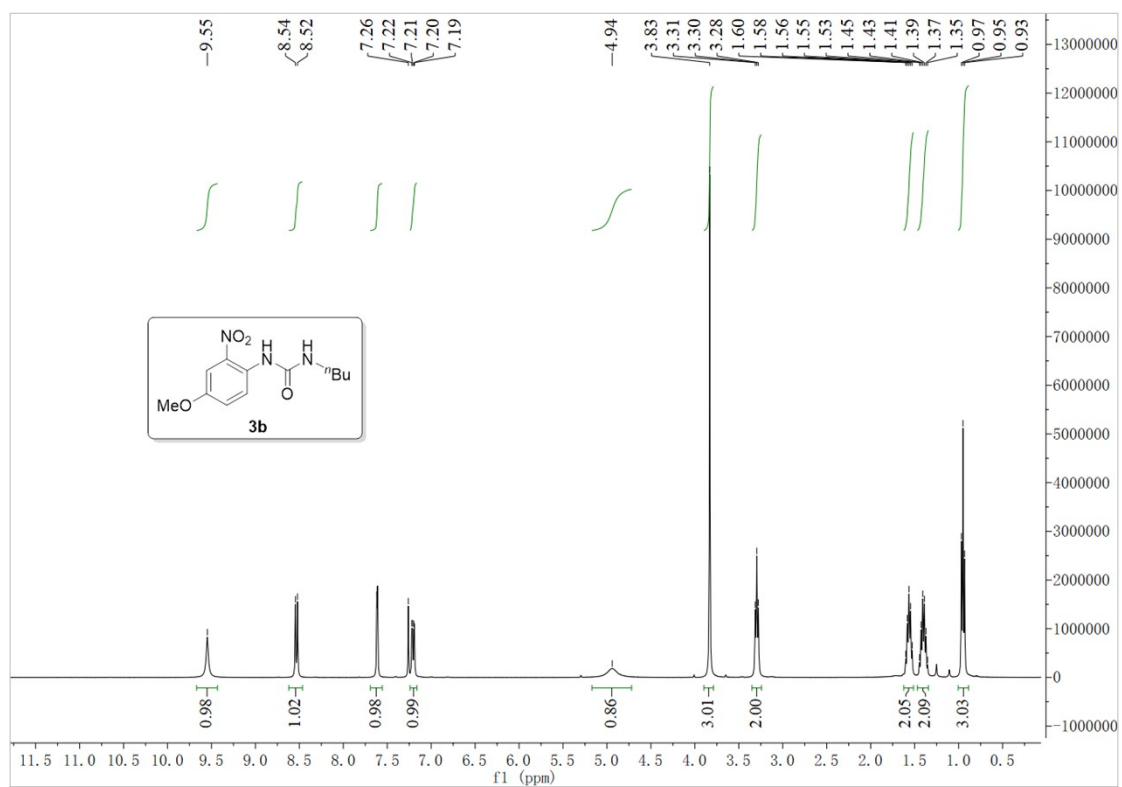
HRMS (ESI): $[\text{M}-\text{H}]^-$ calcd for $\text{C}_{12}\text{H}_{14}\text{N}_3\text{OS}^-$, 248.0863; found, 248.0860

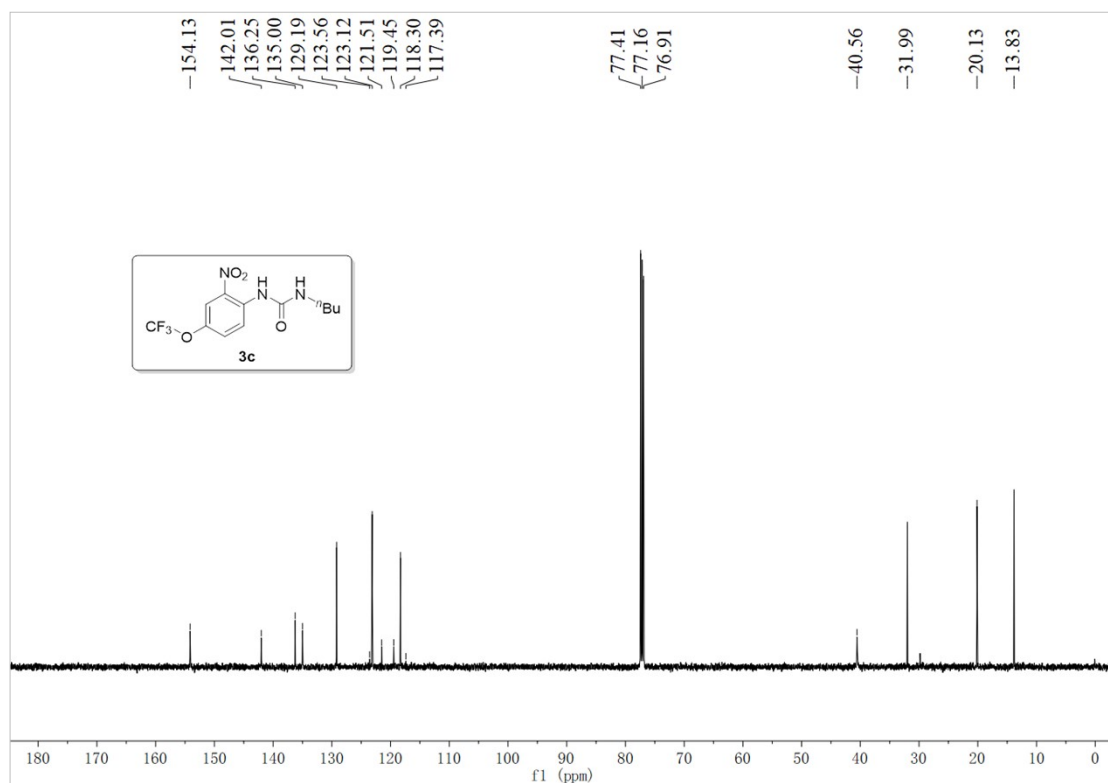
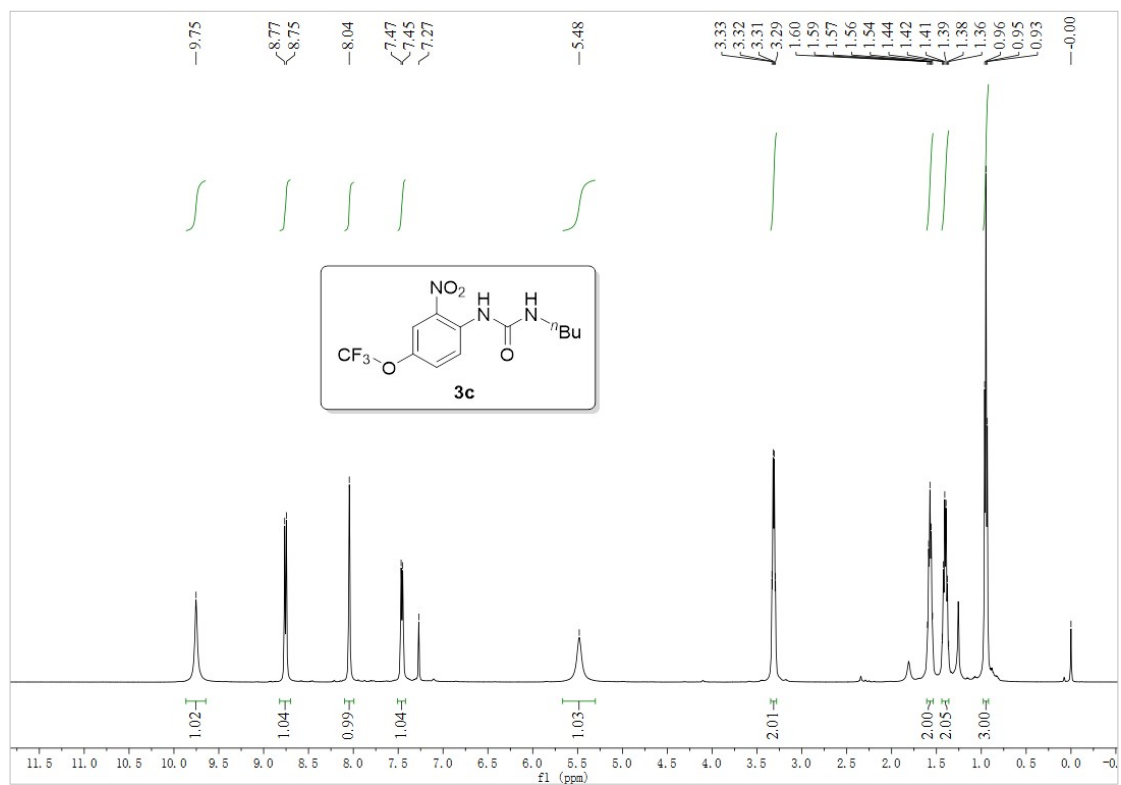
Reference

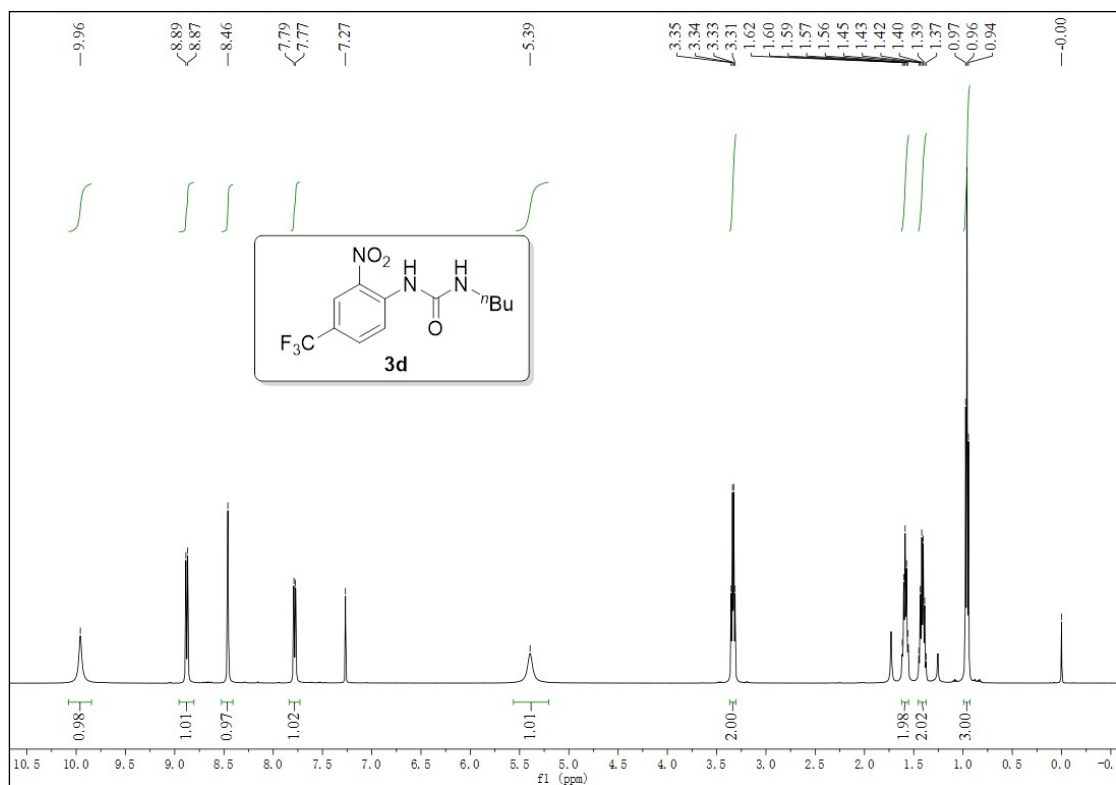
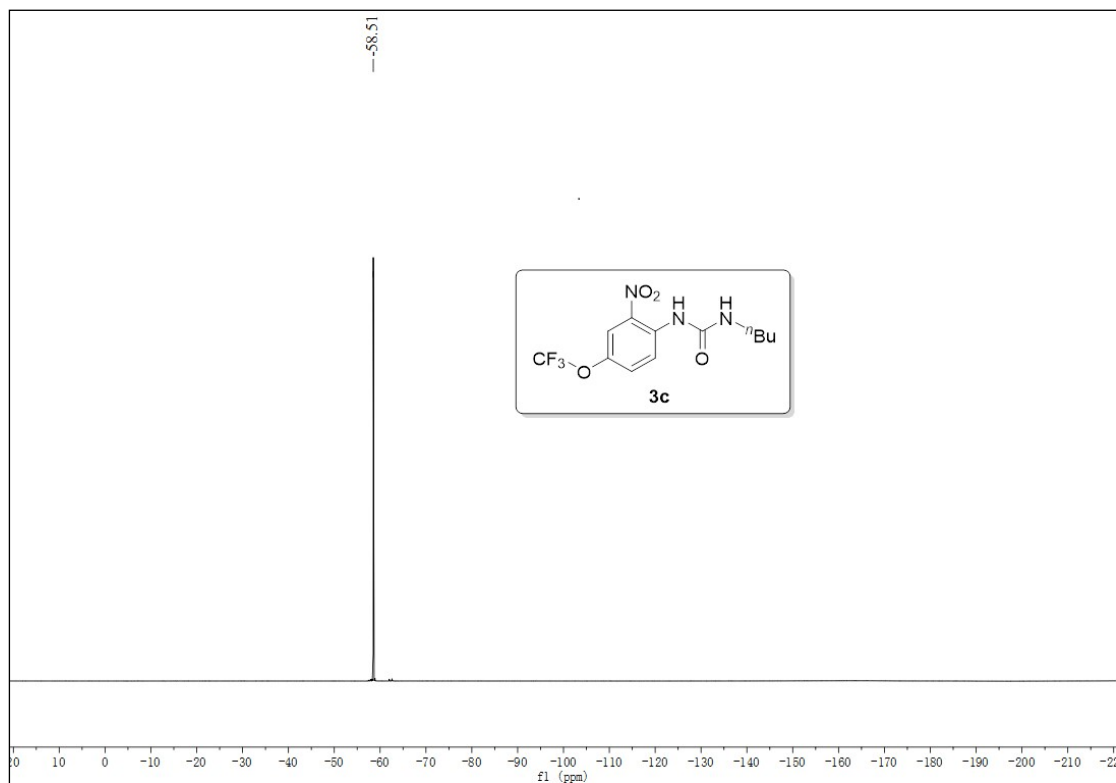
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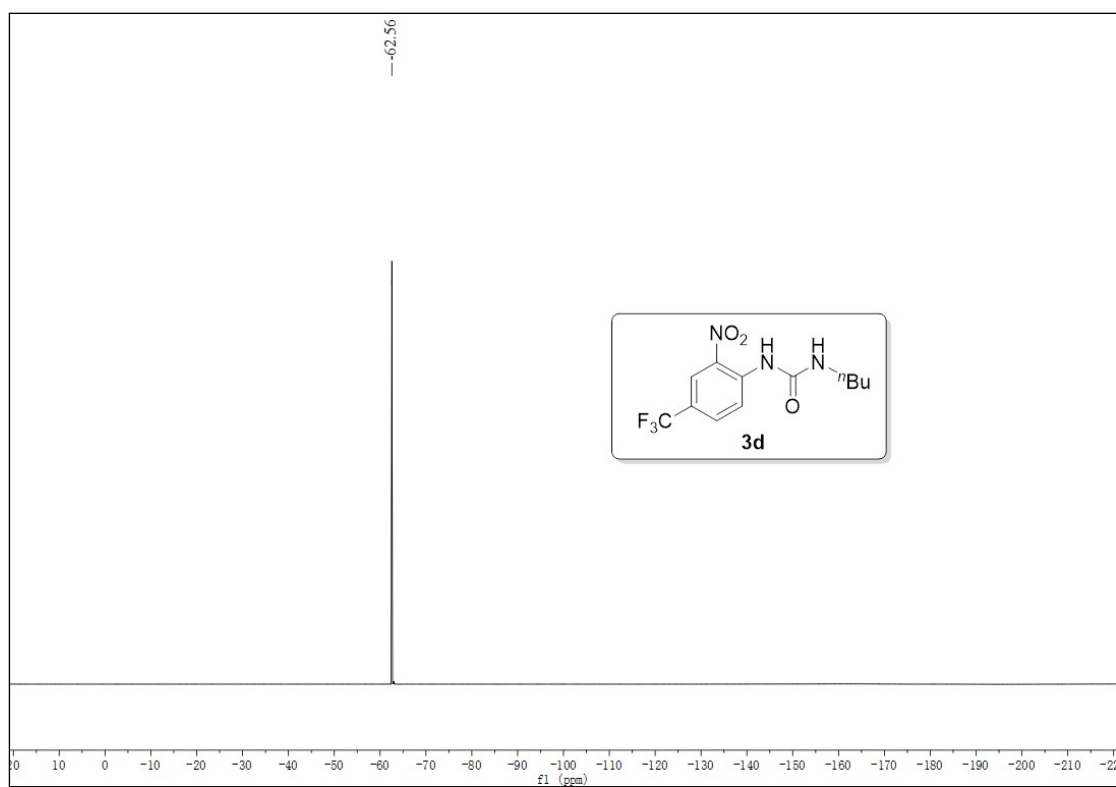
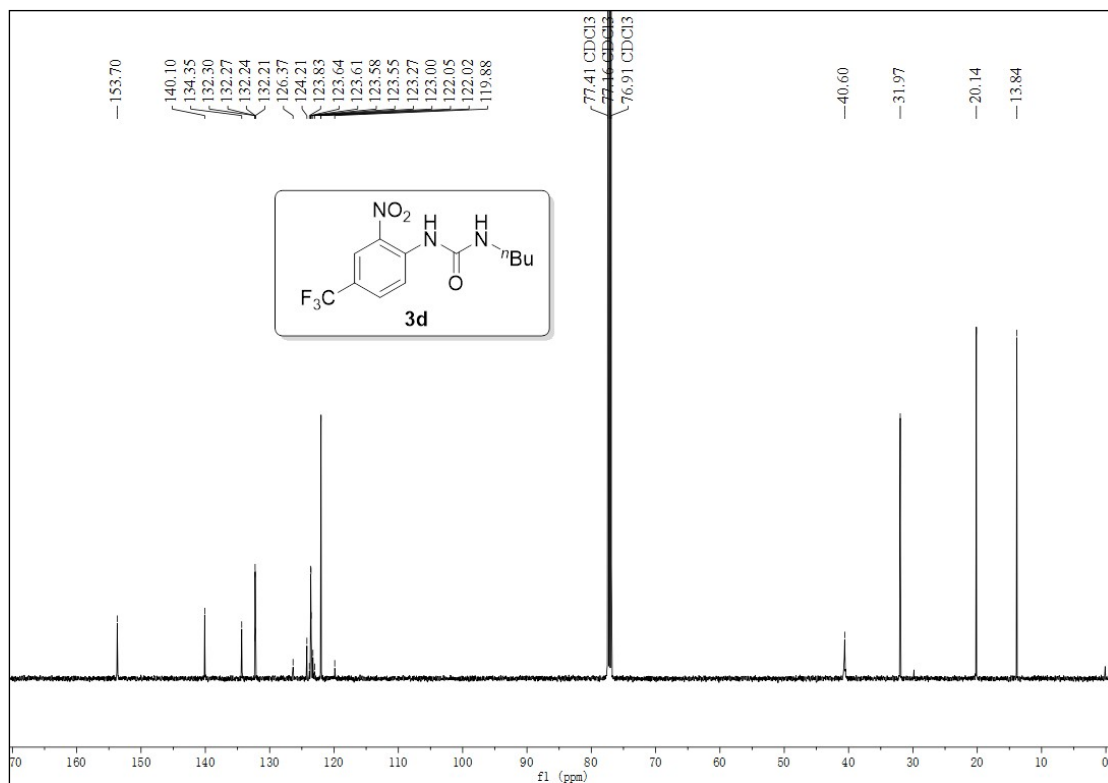
7. Copy of ^1H , ^{19}F and ^{13}C NMR for new Compounds

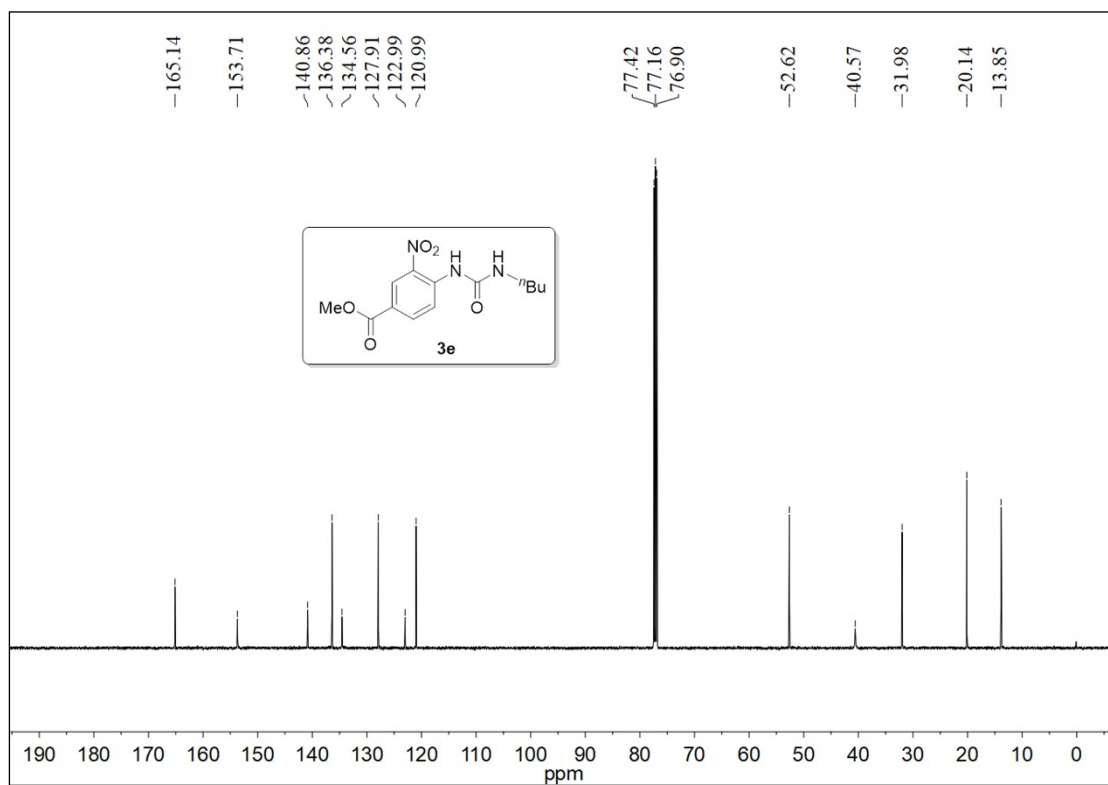
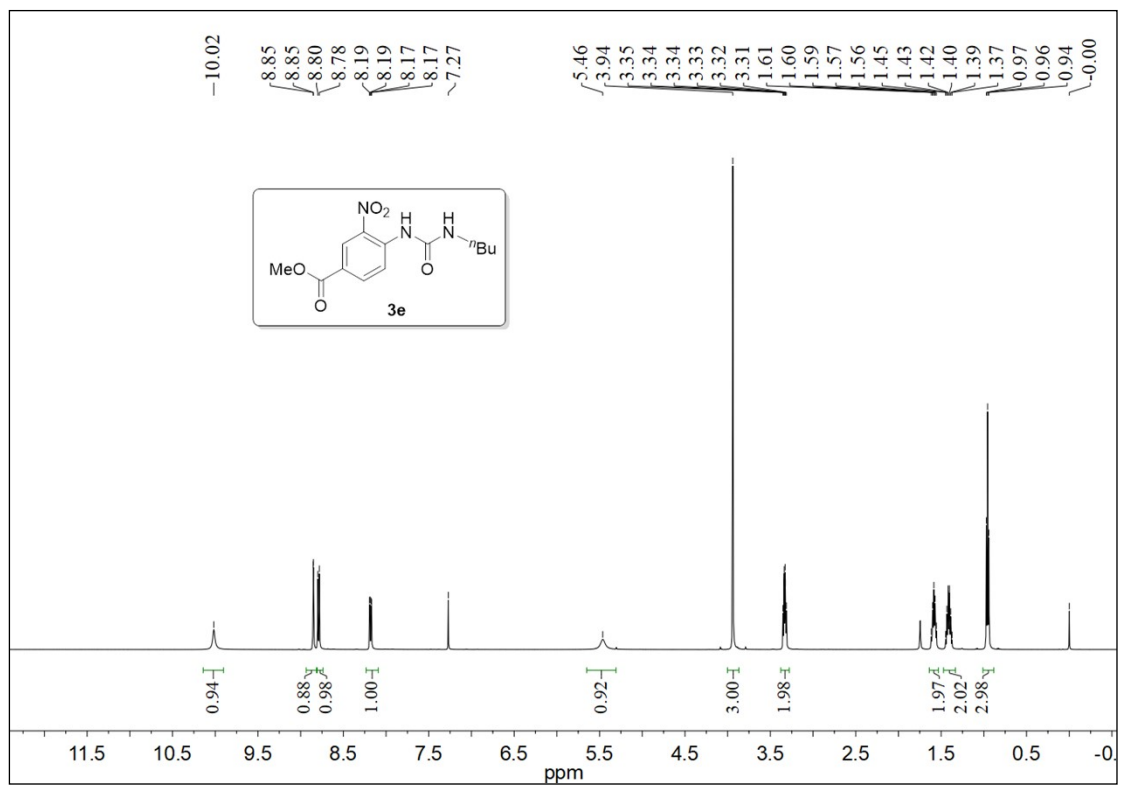


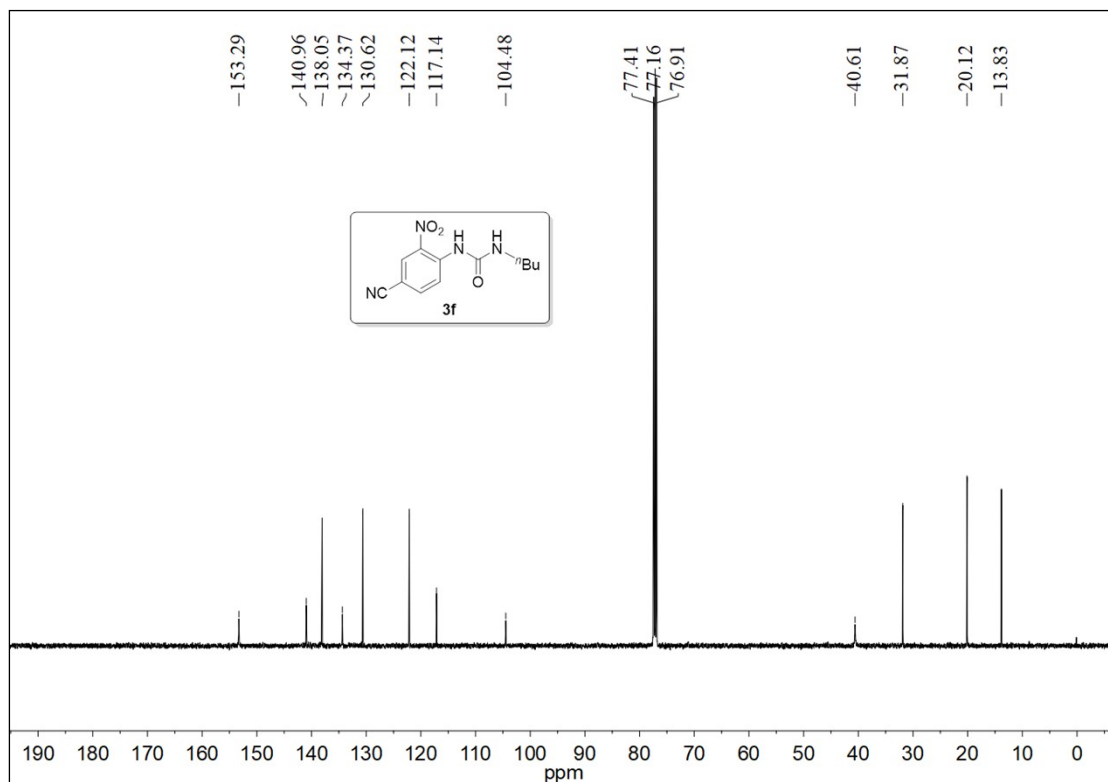
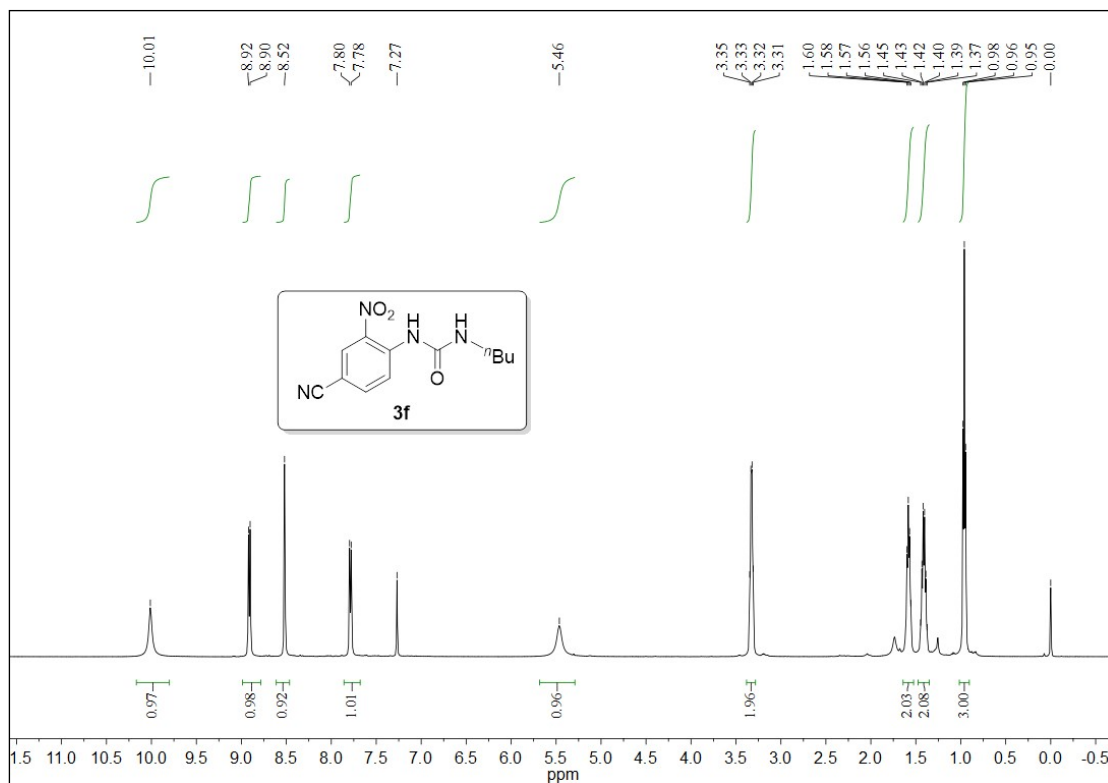


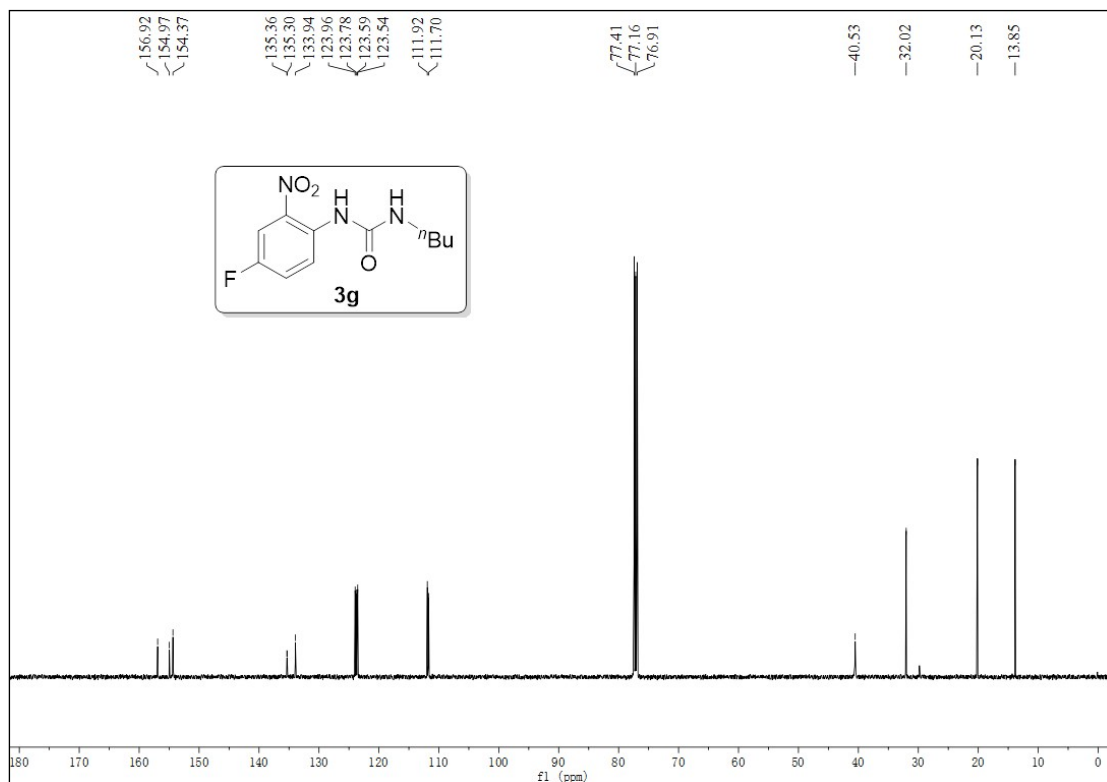
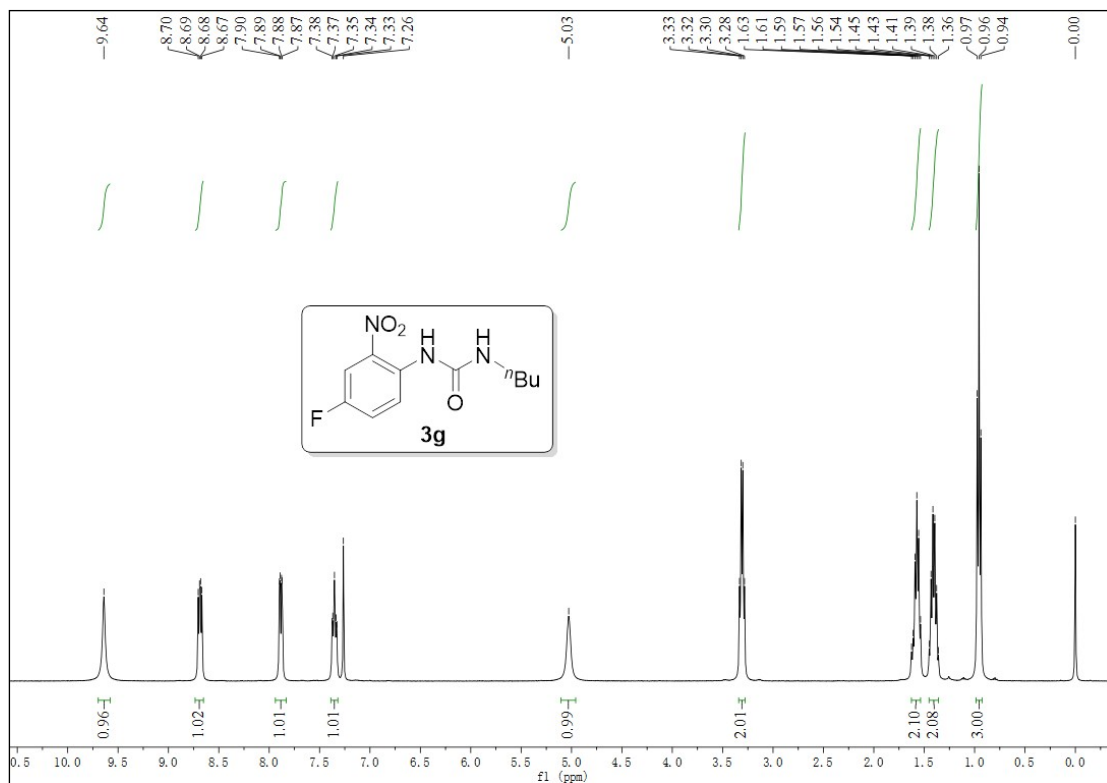


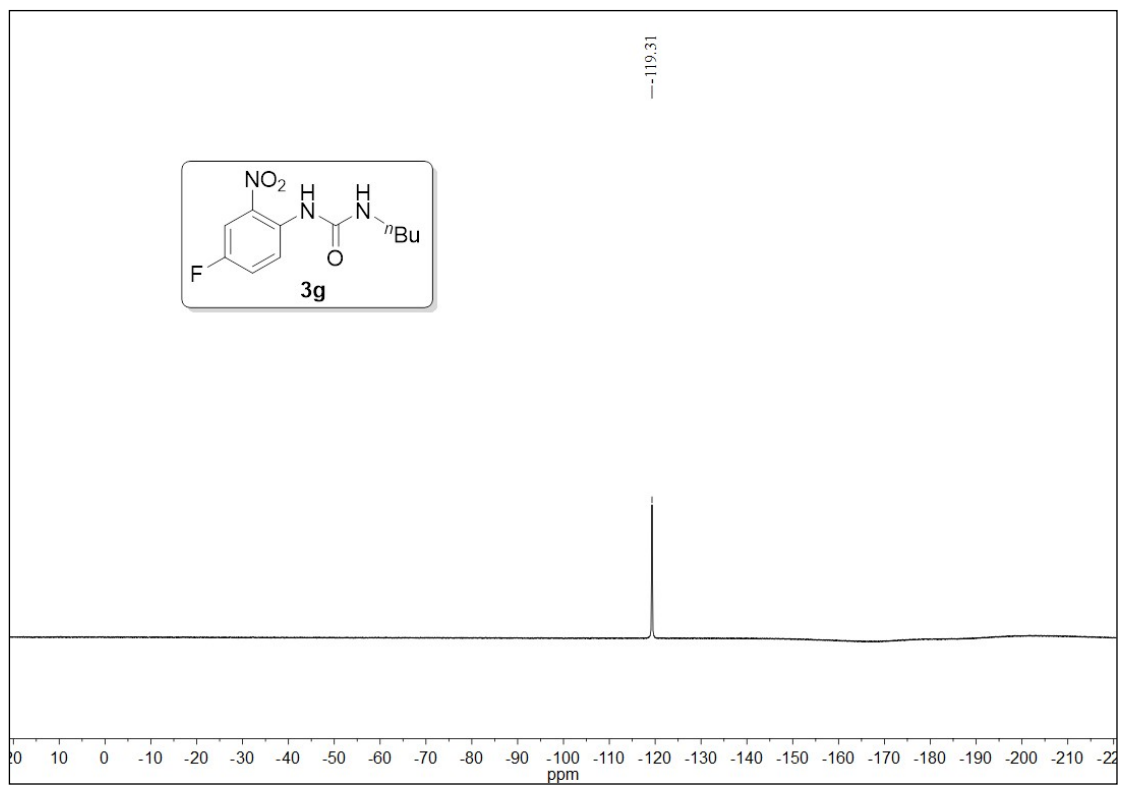


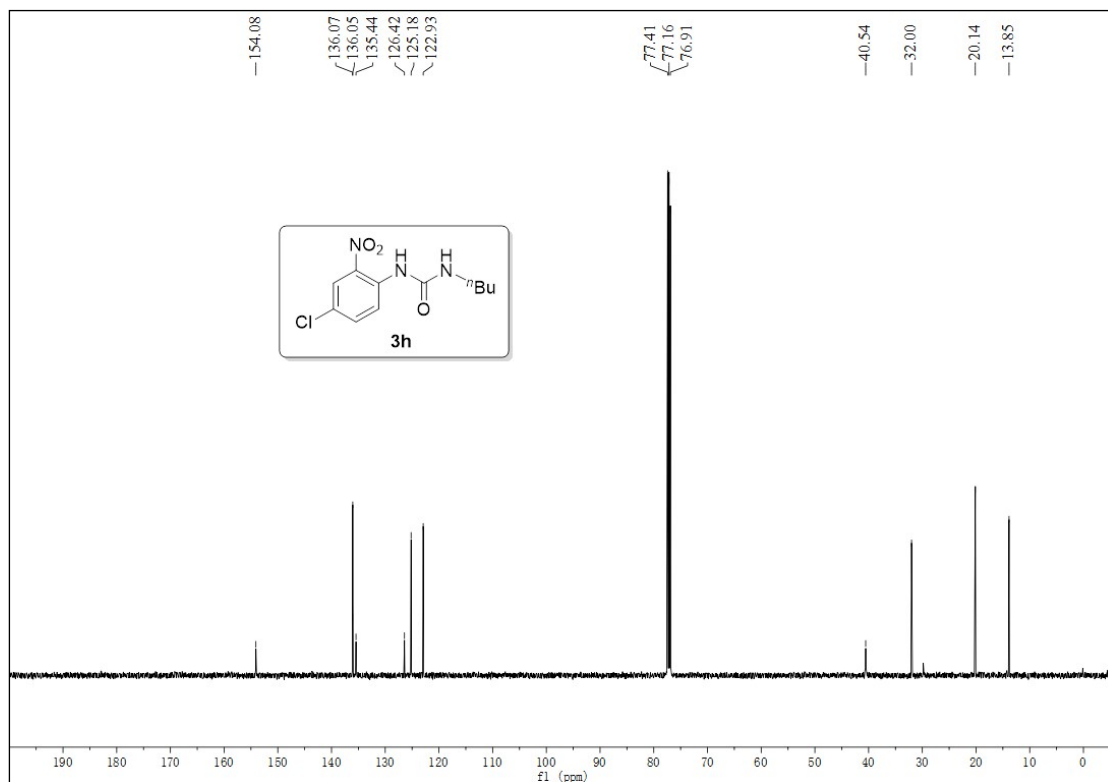
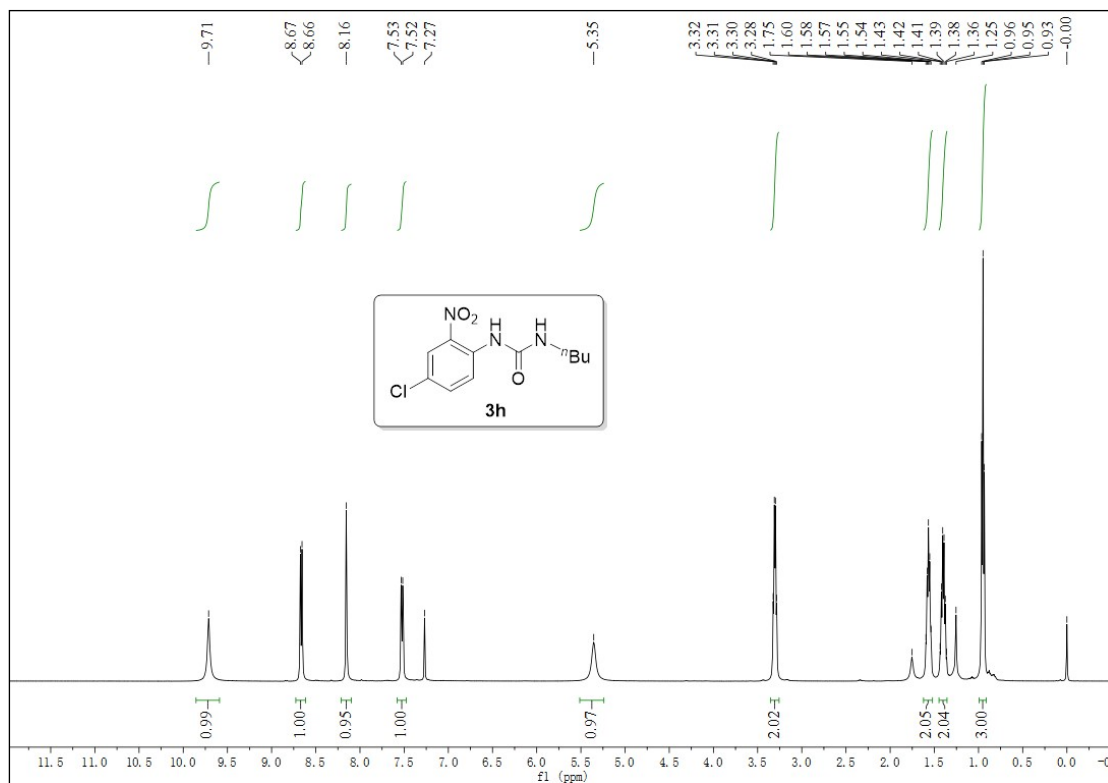


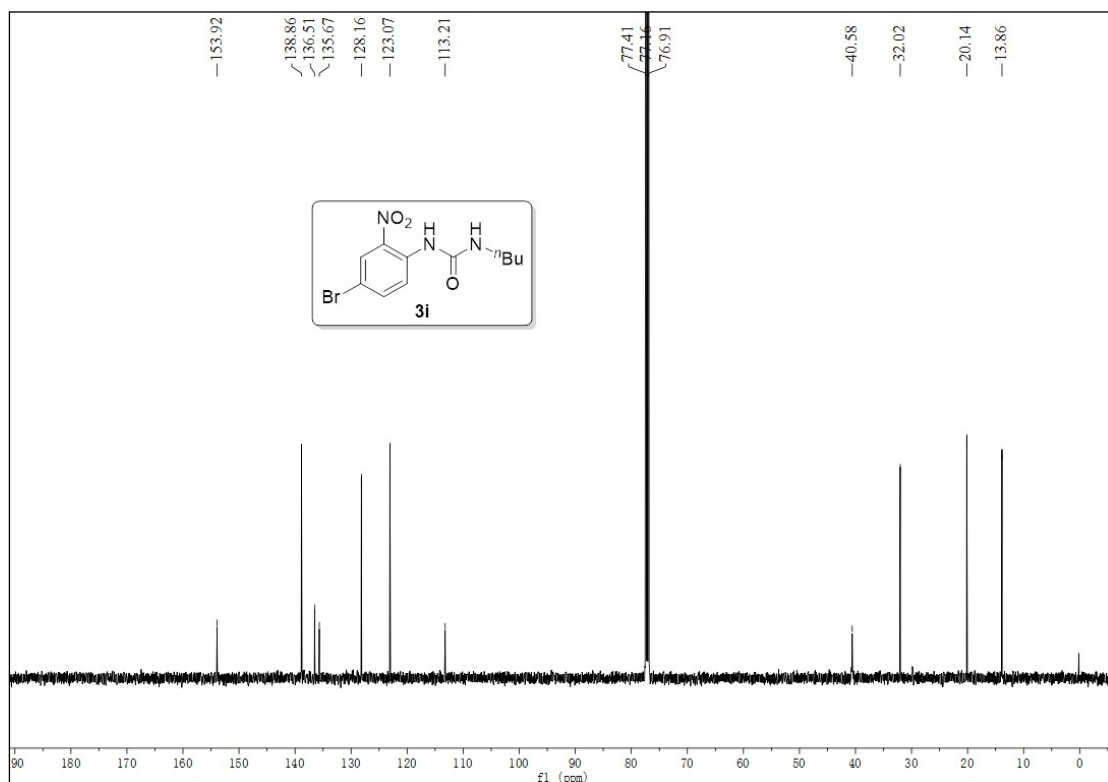
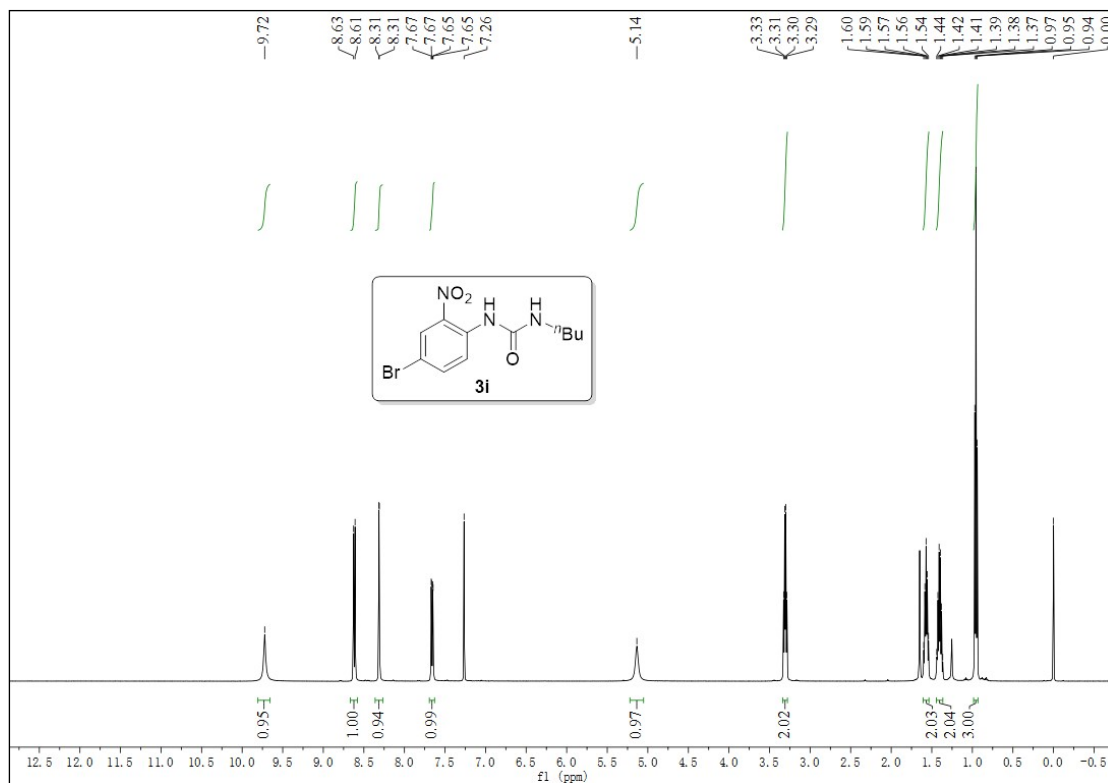


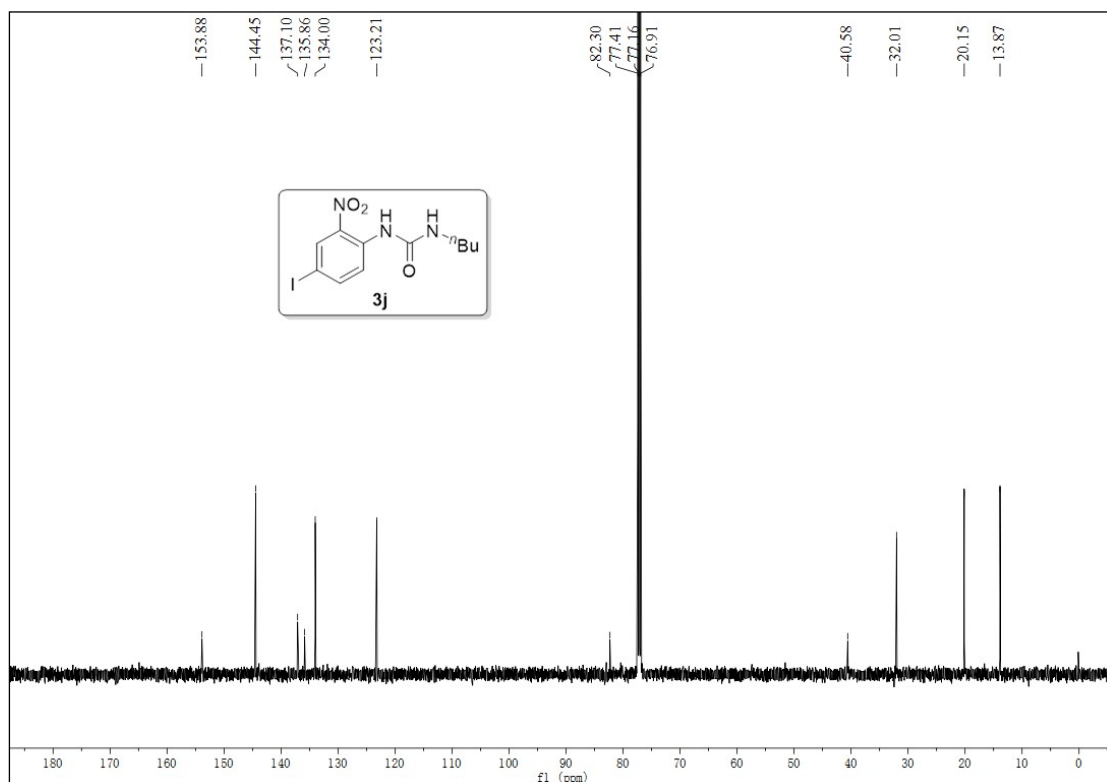
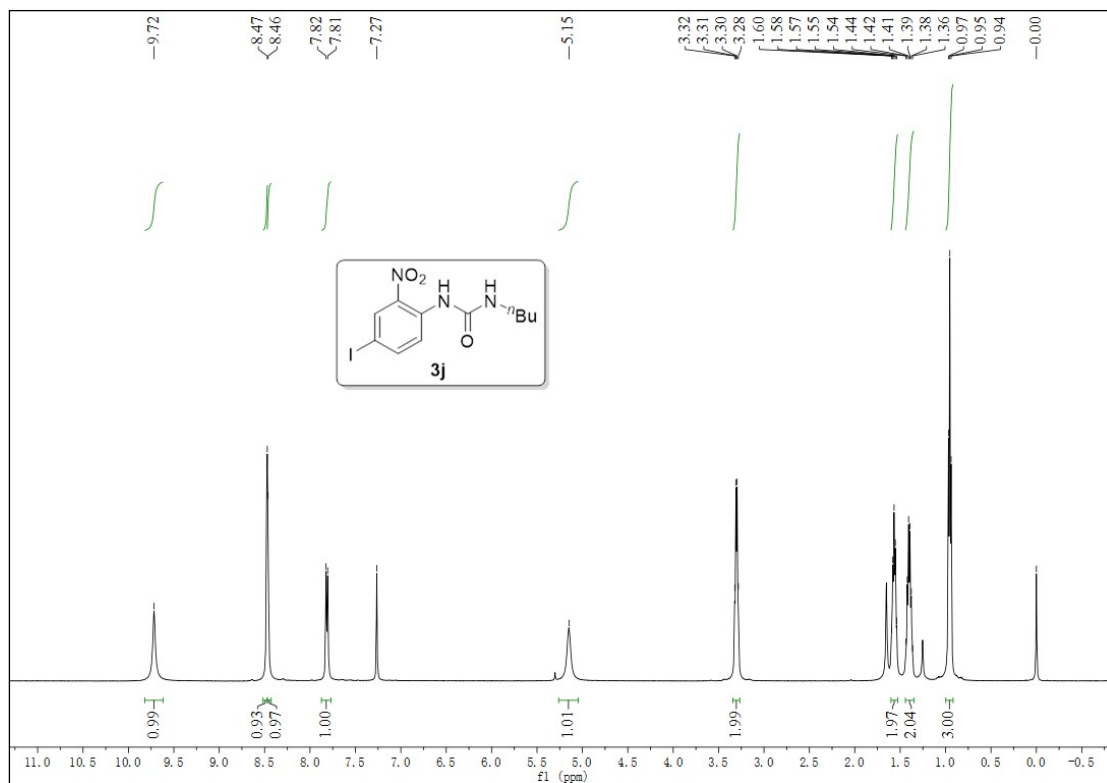


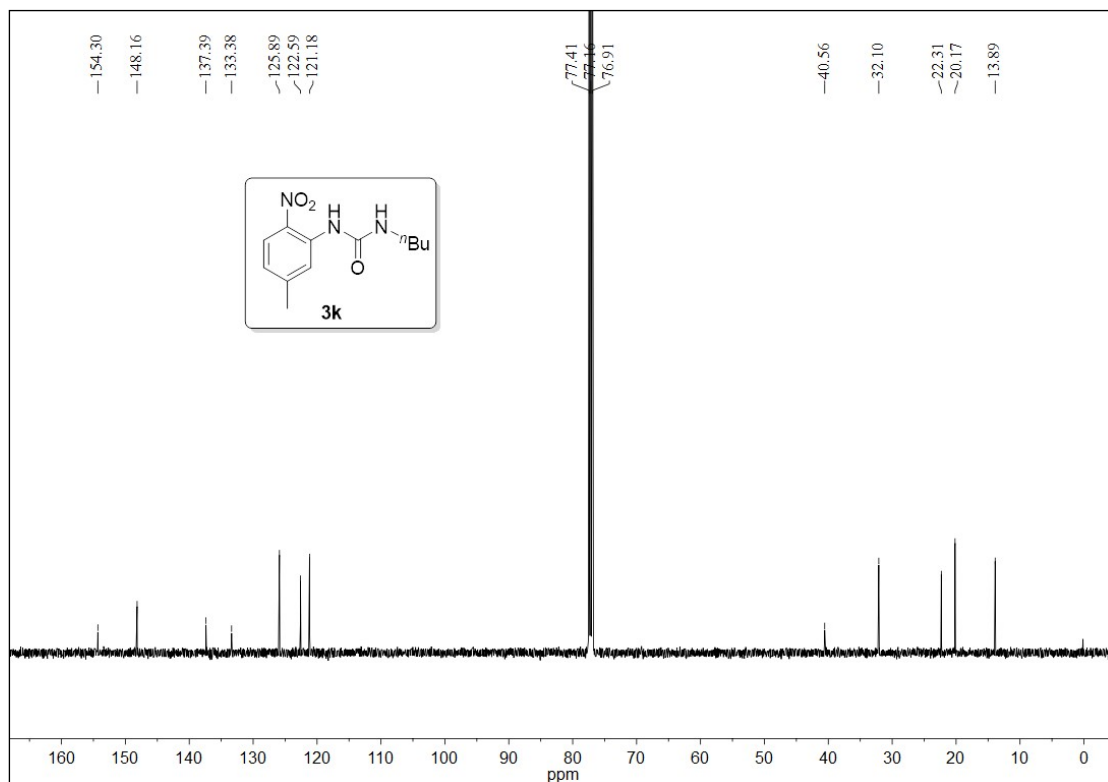
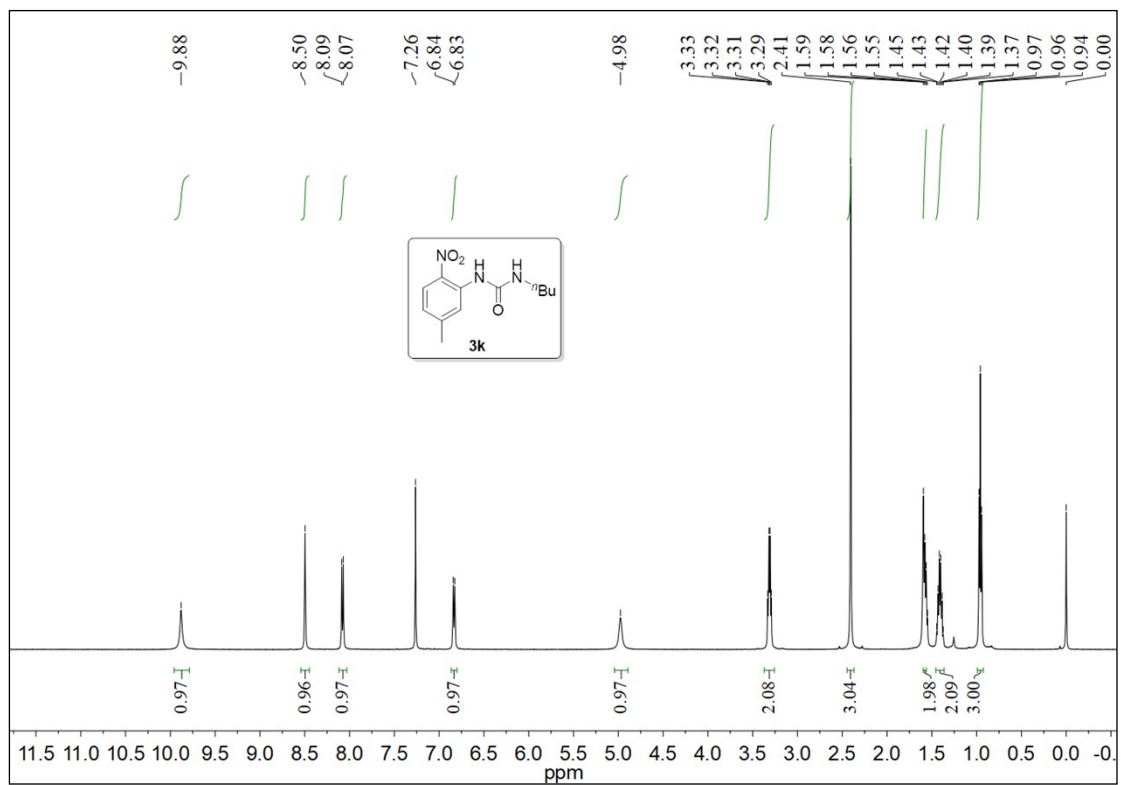


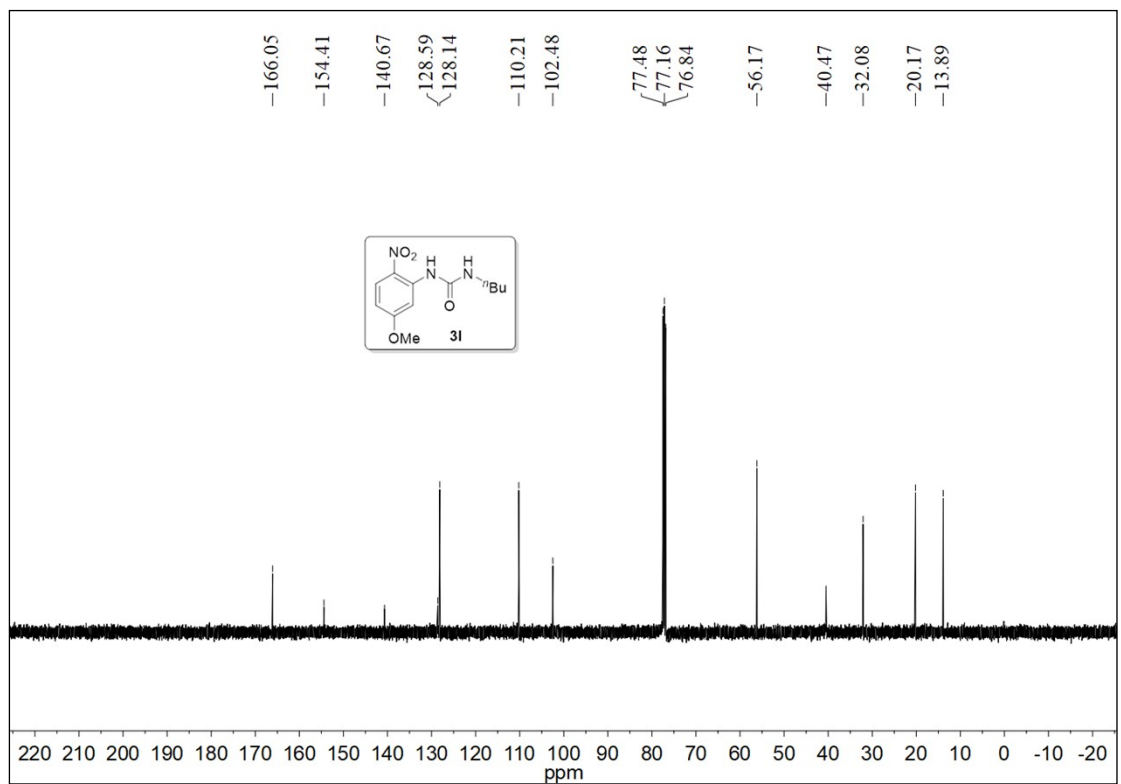
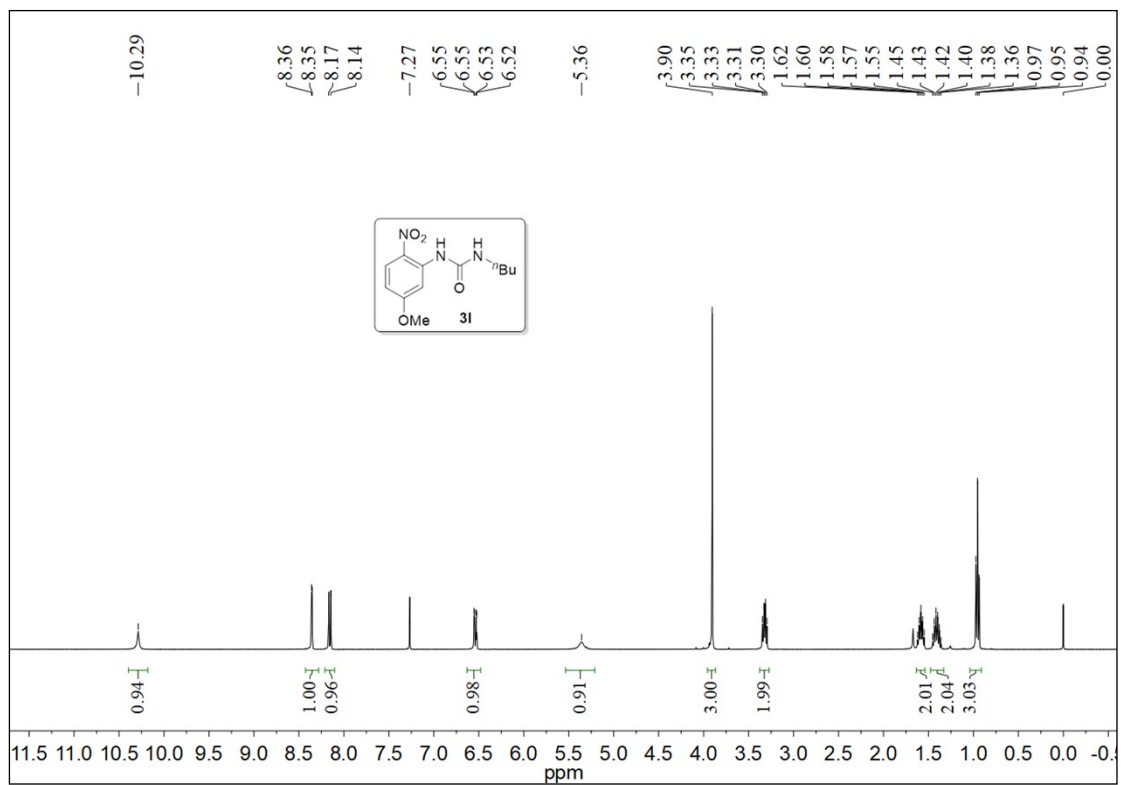


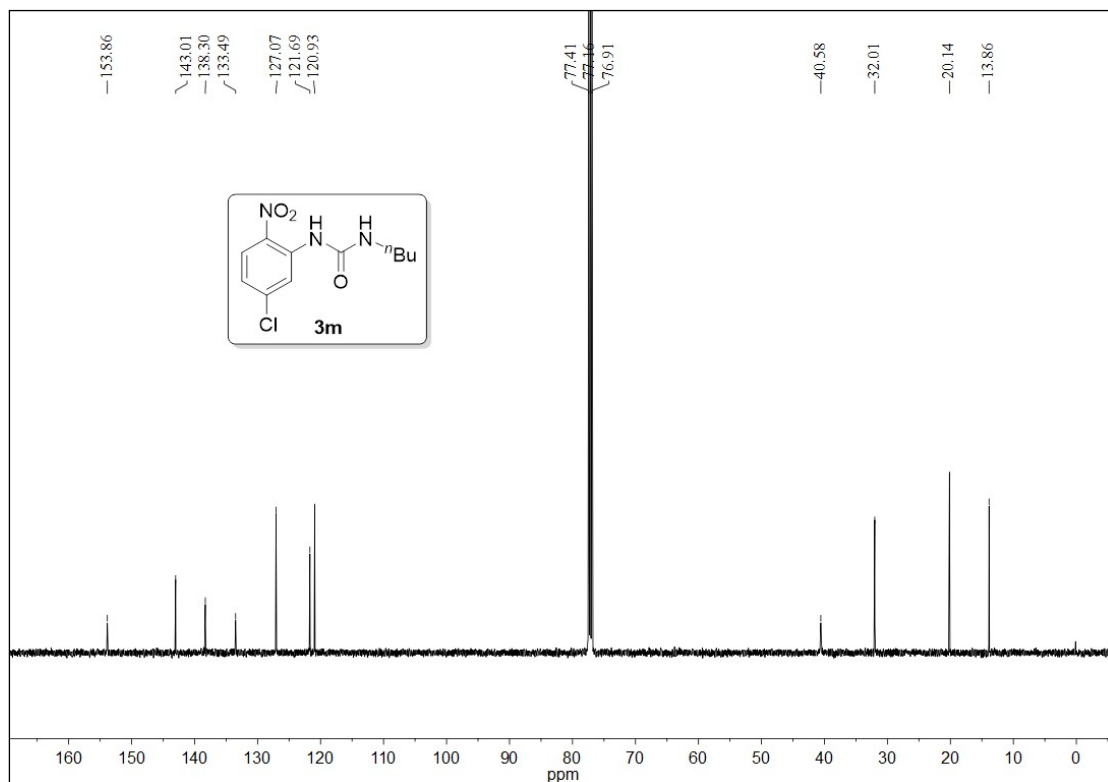
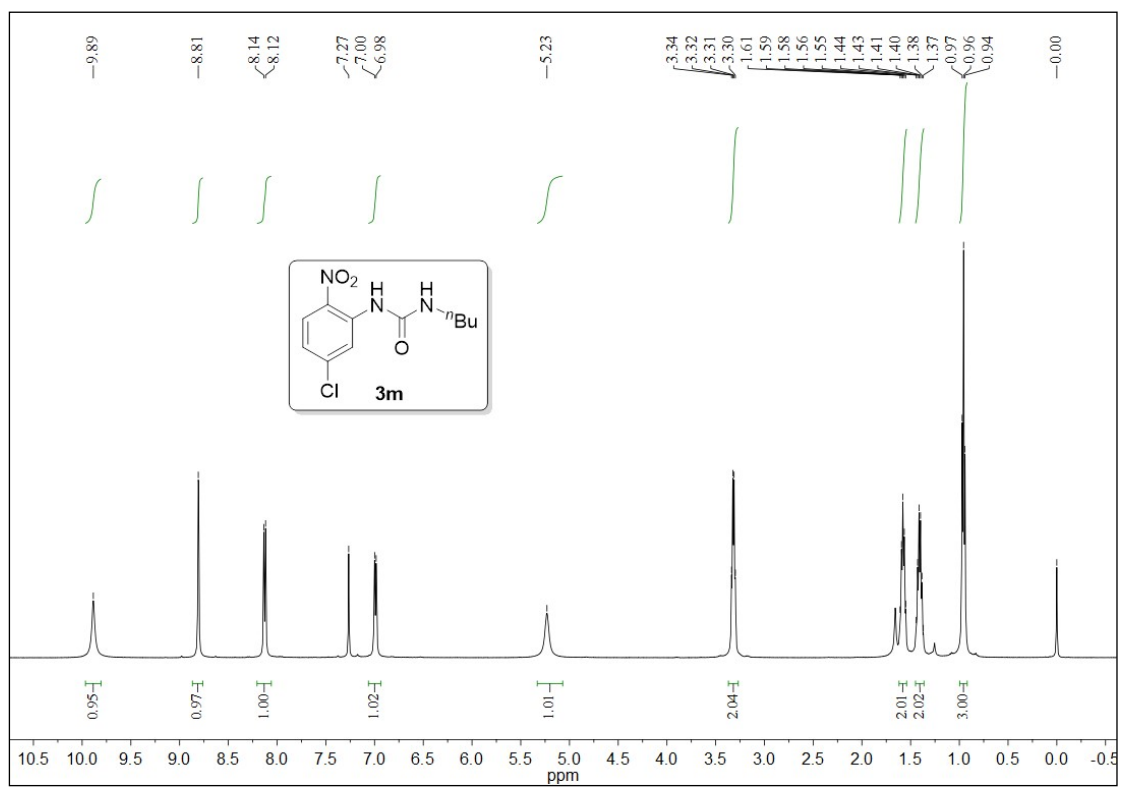


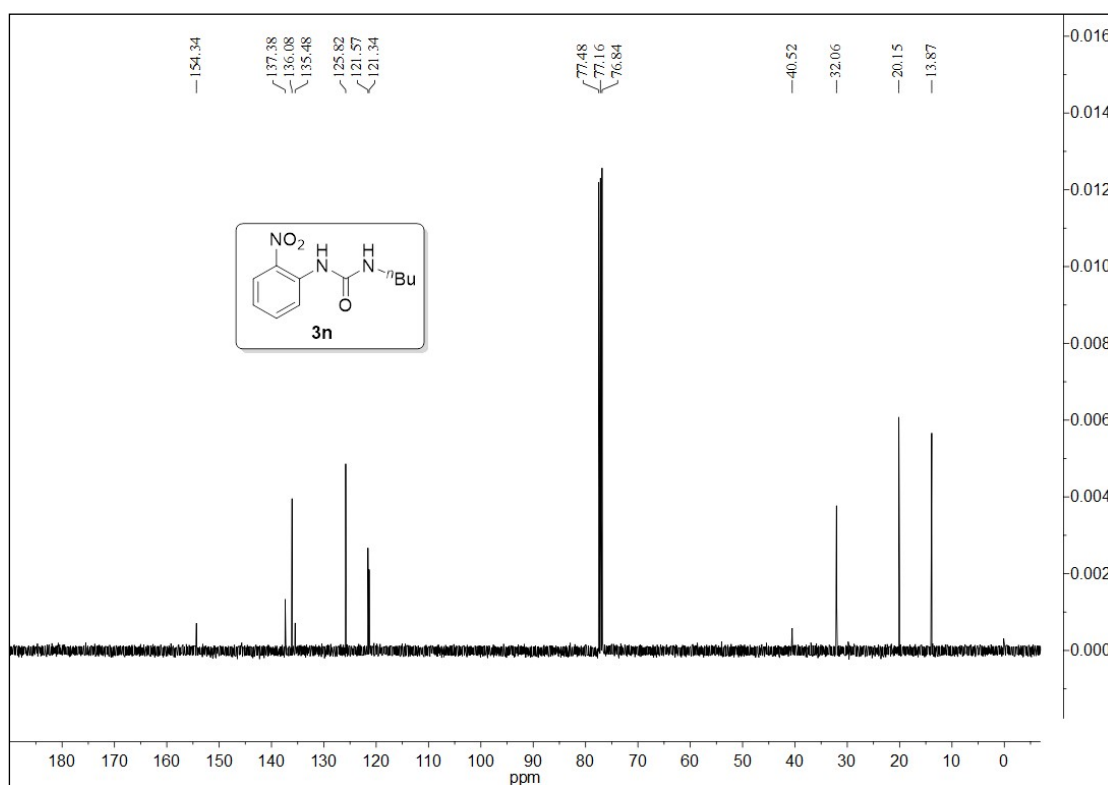
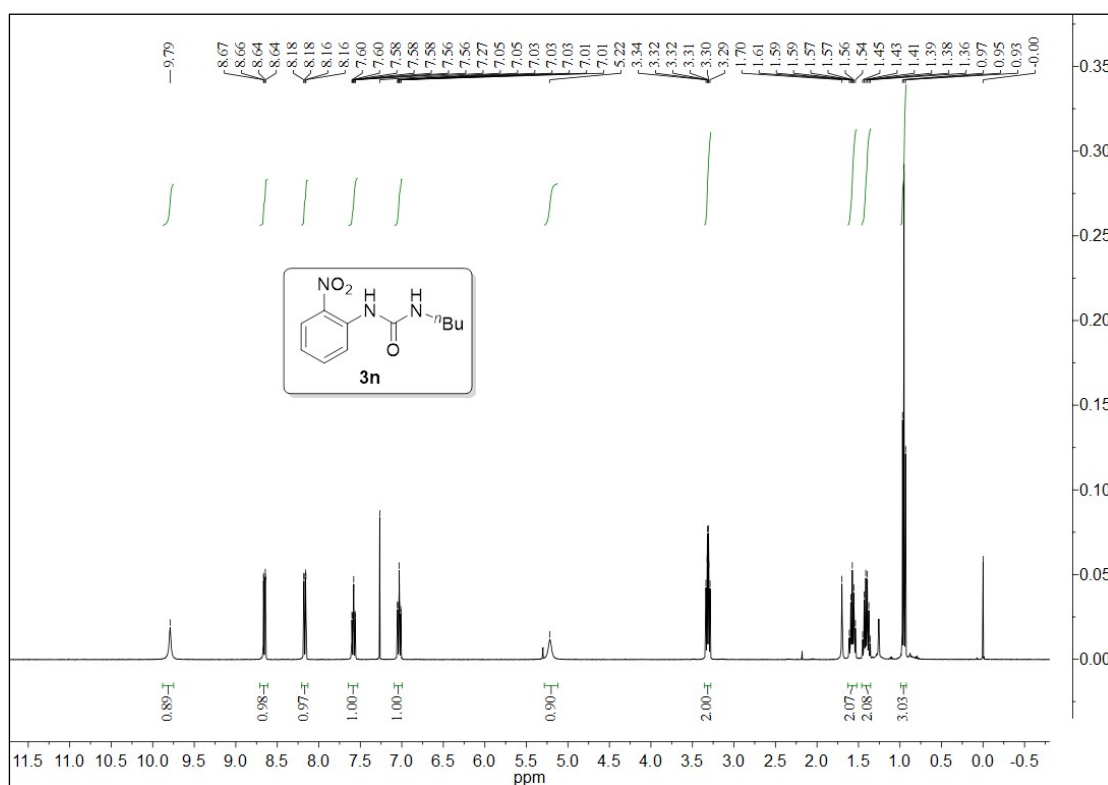


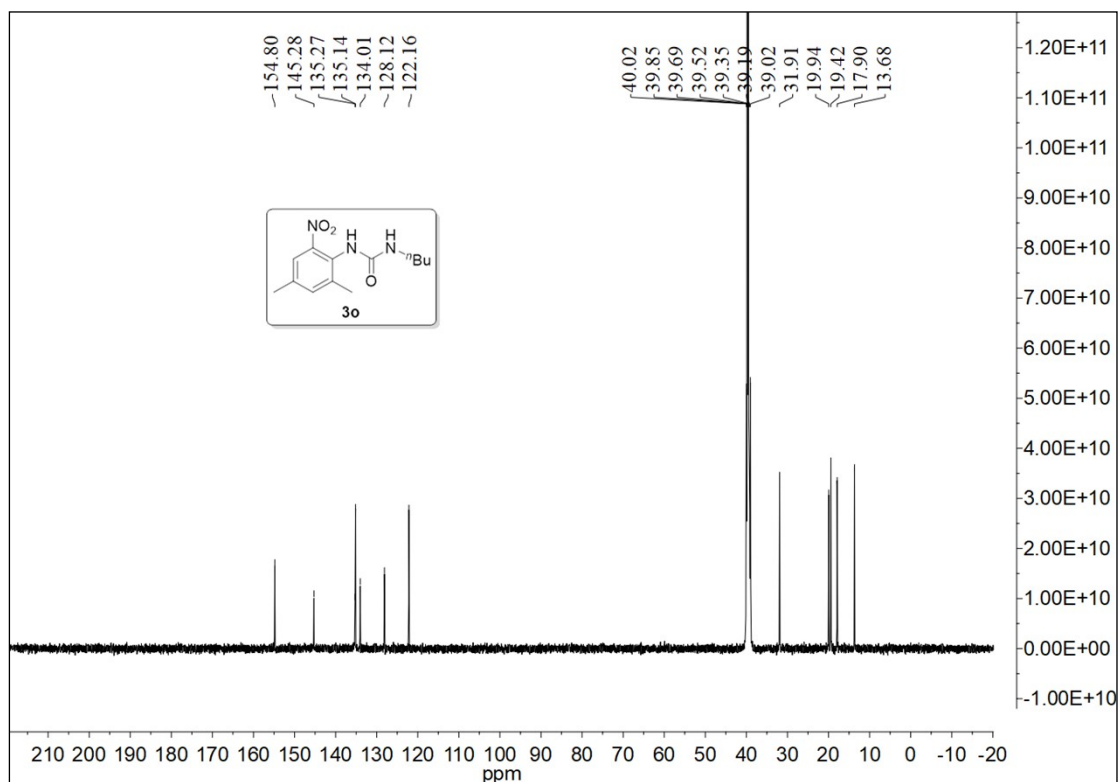
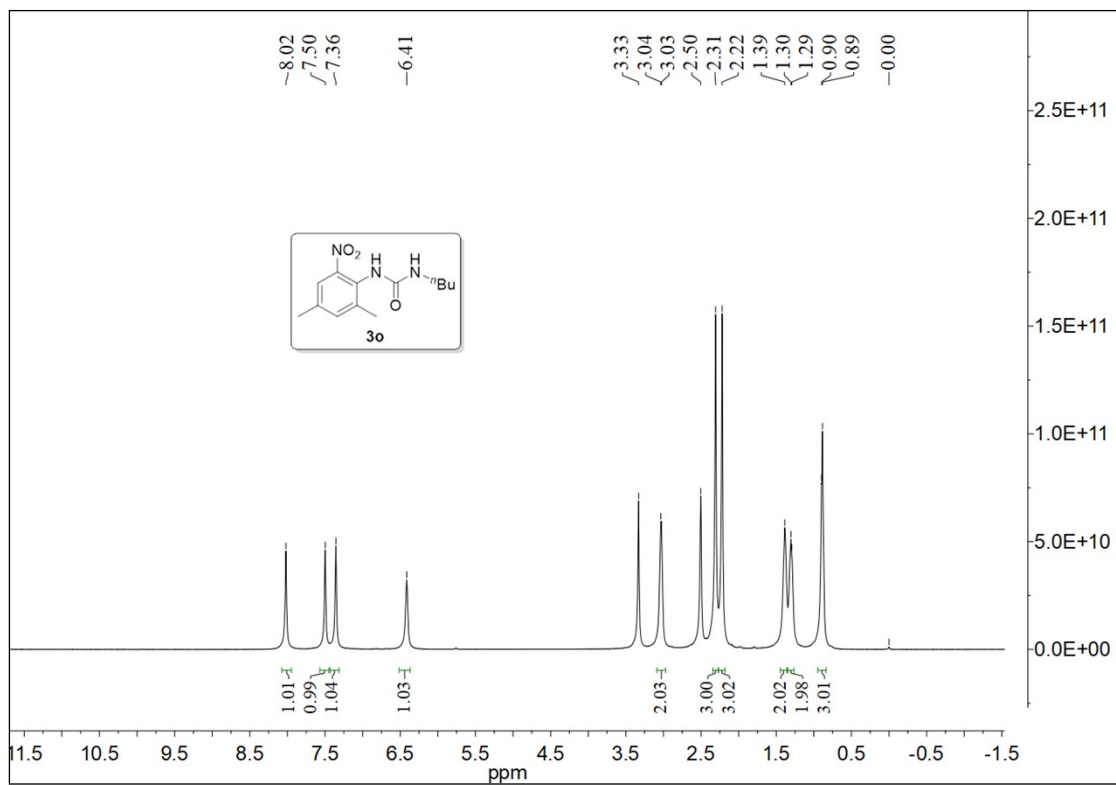


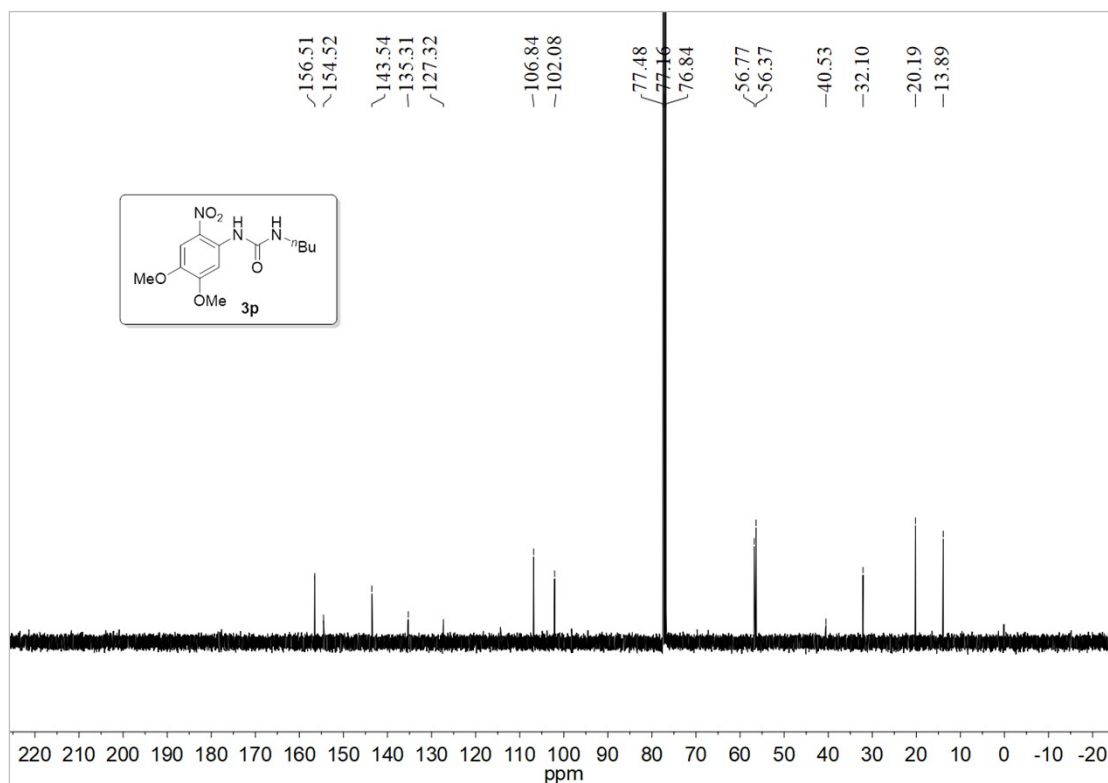
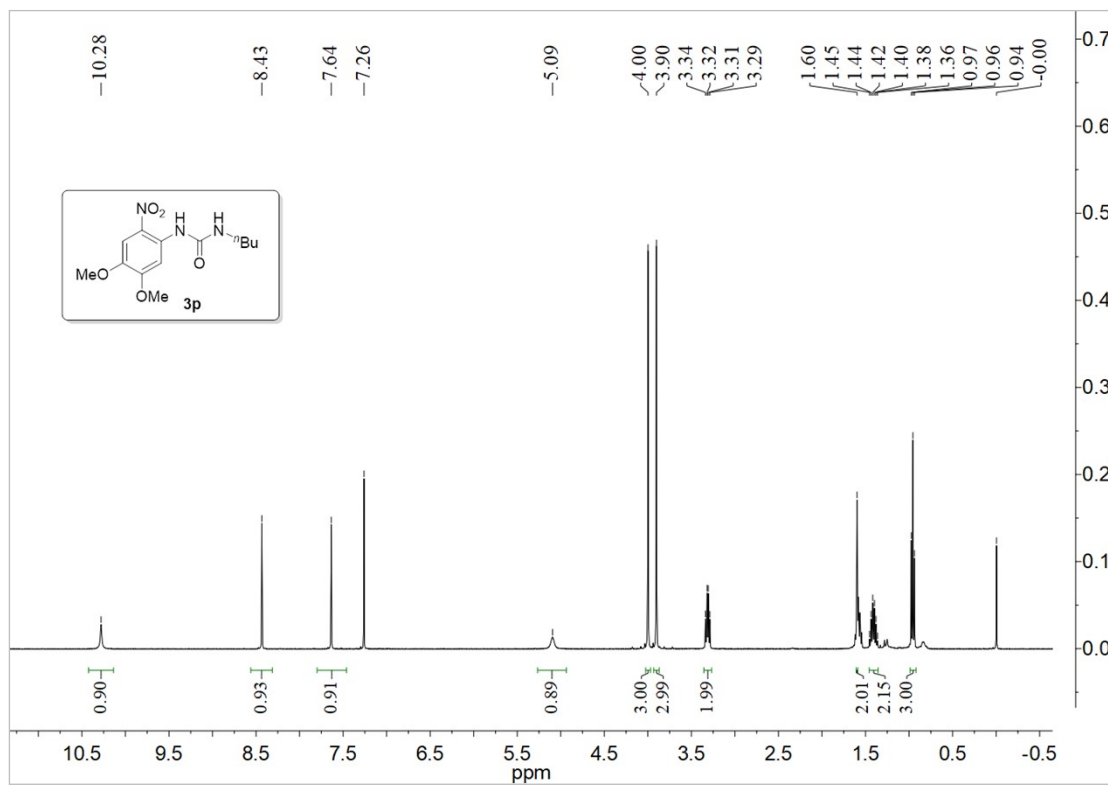


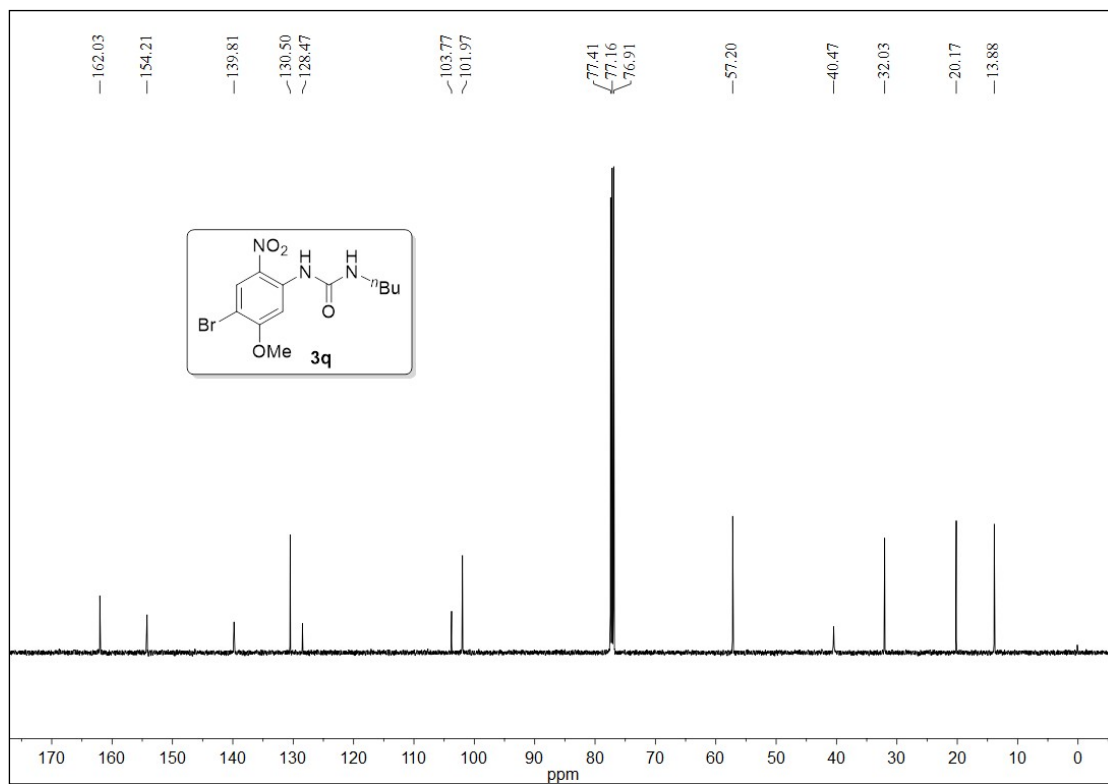
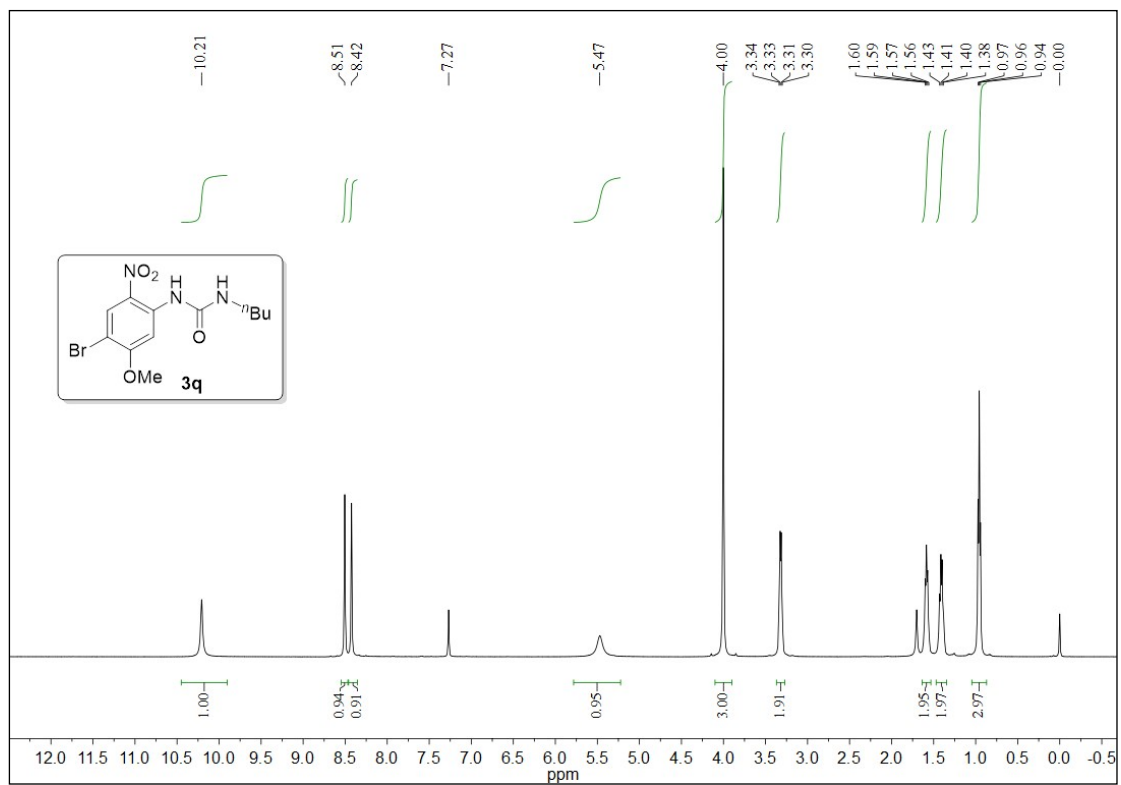


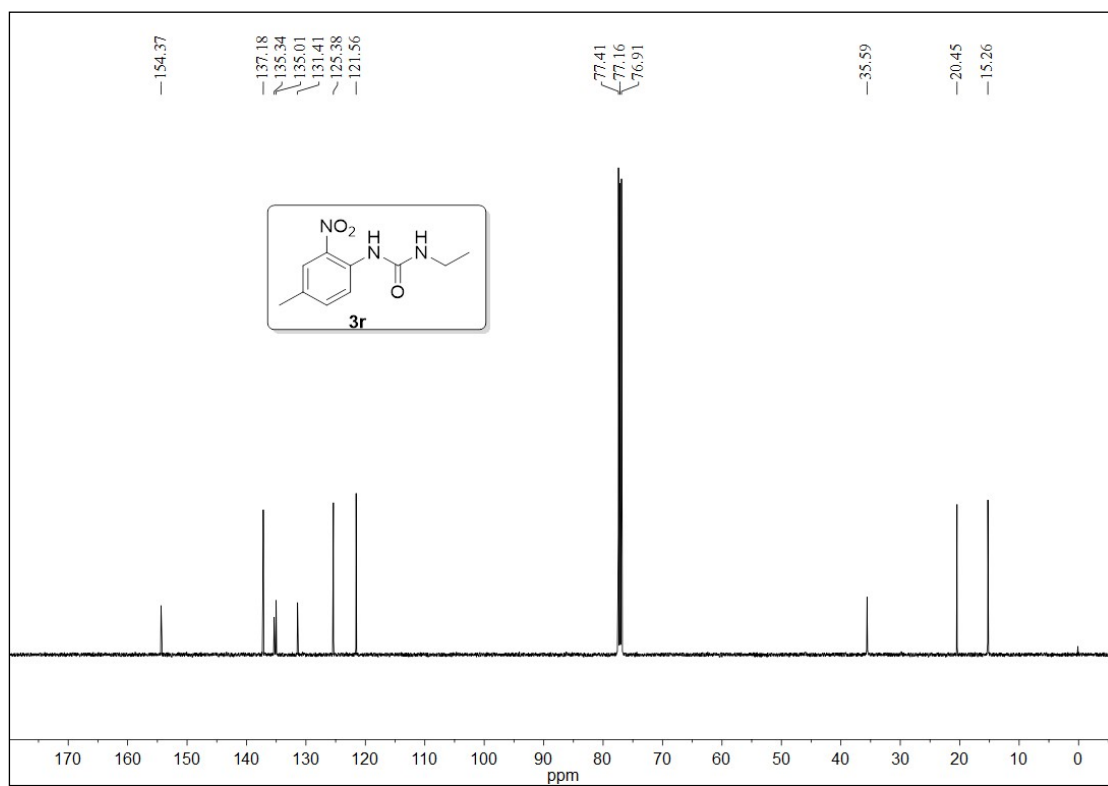
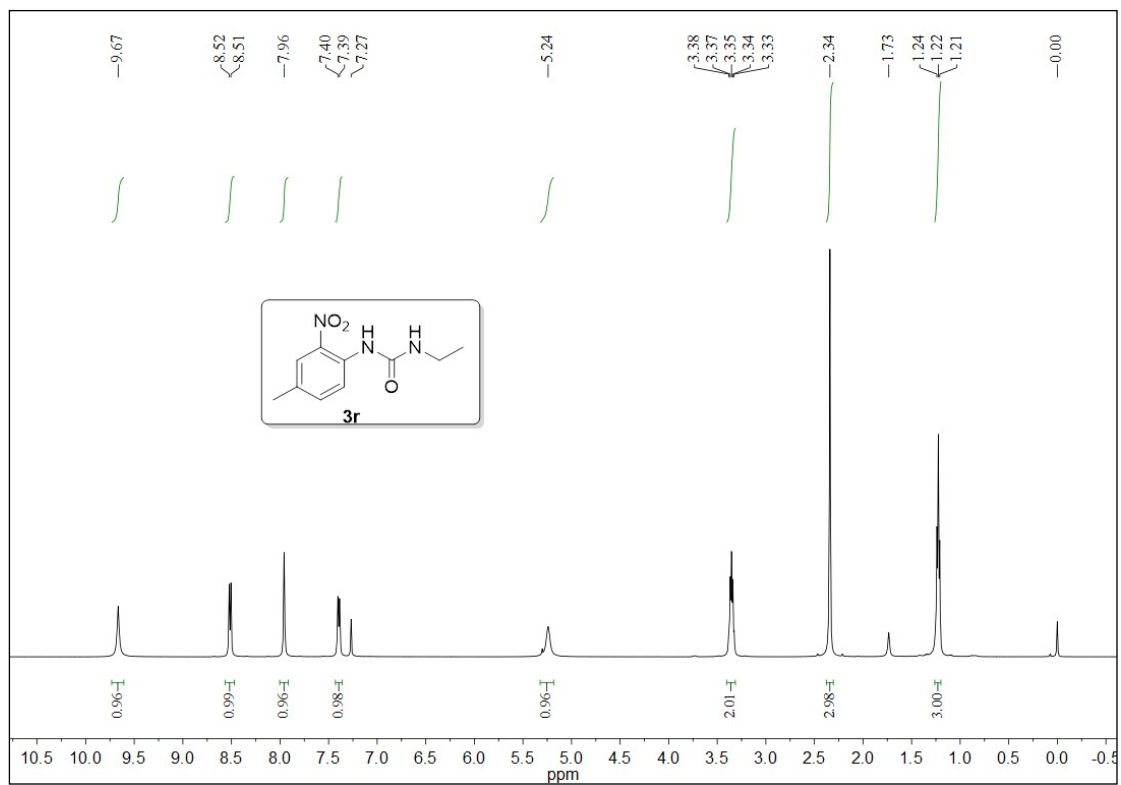


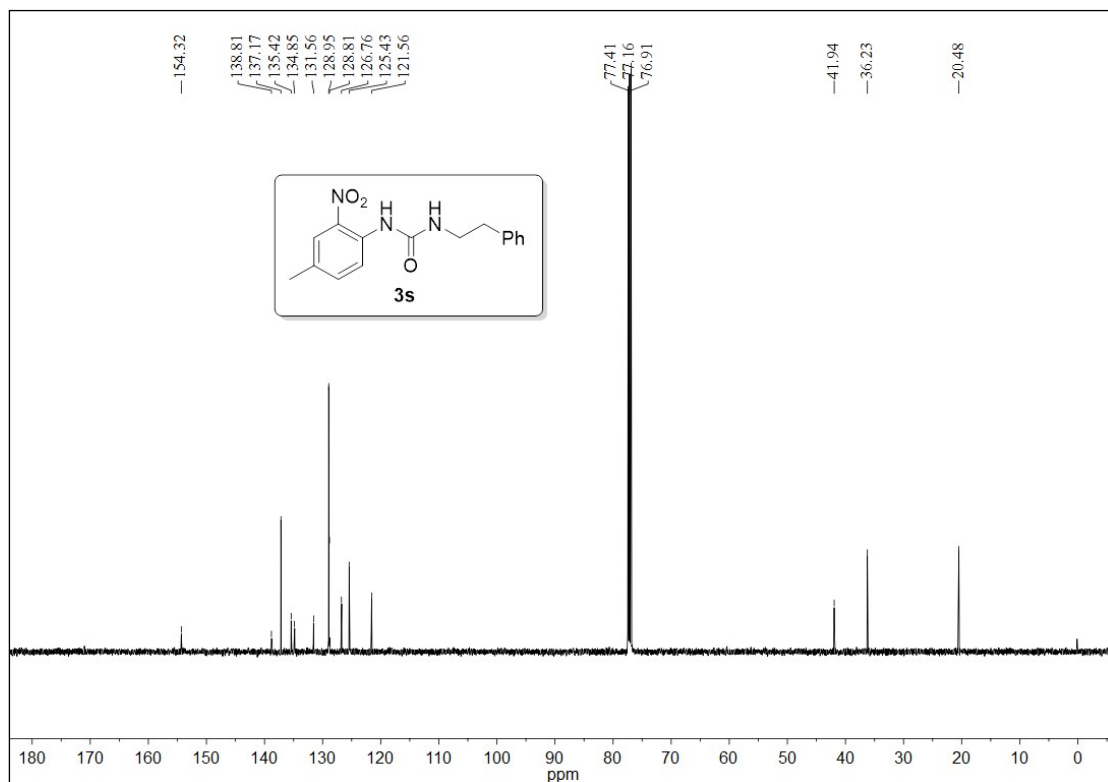
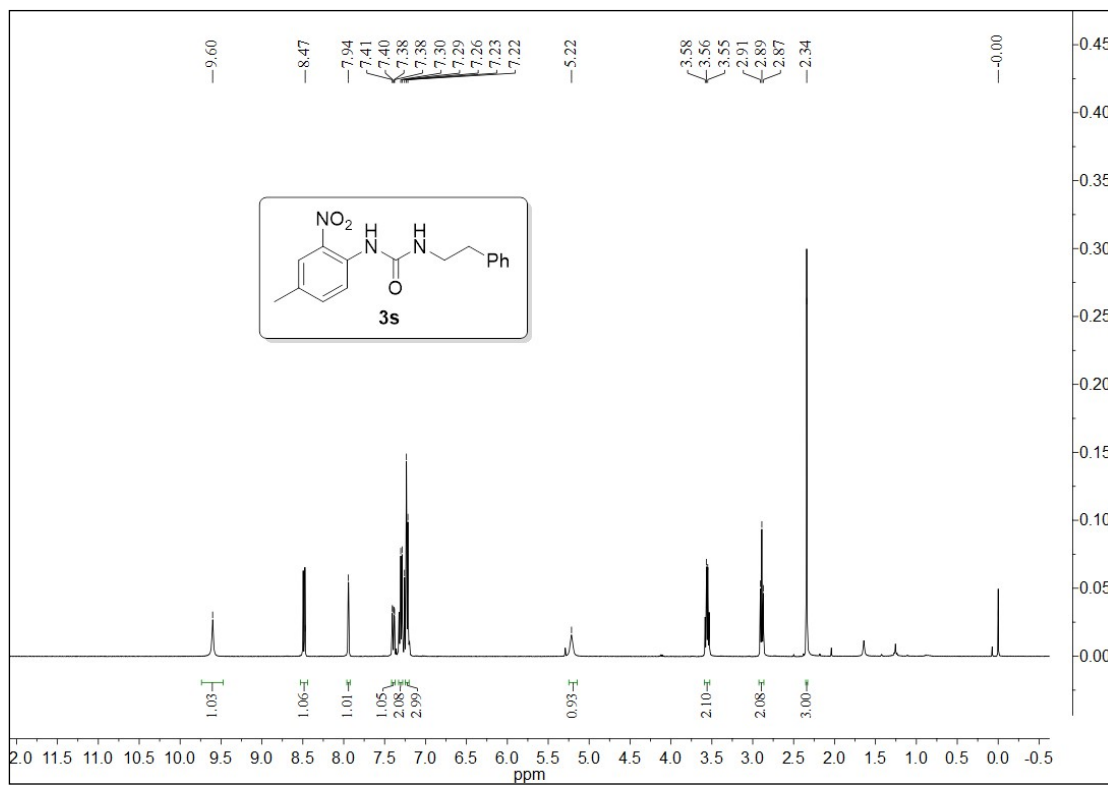


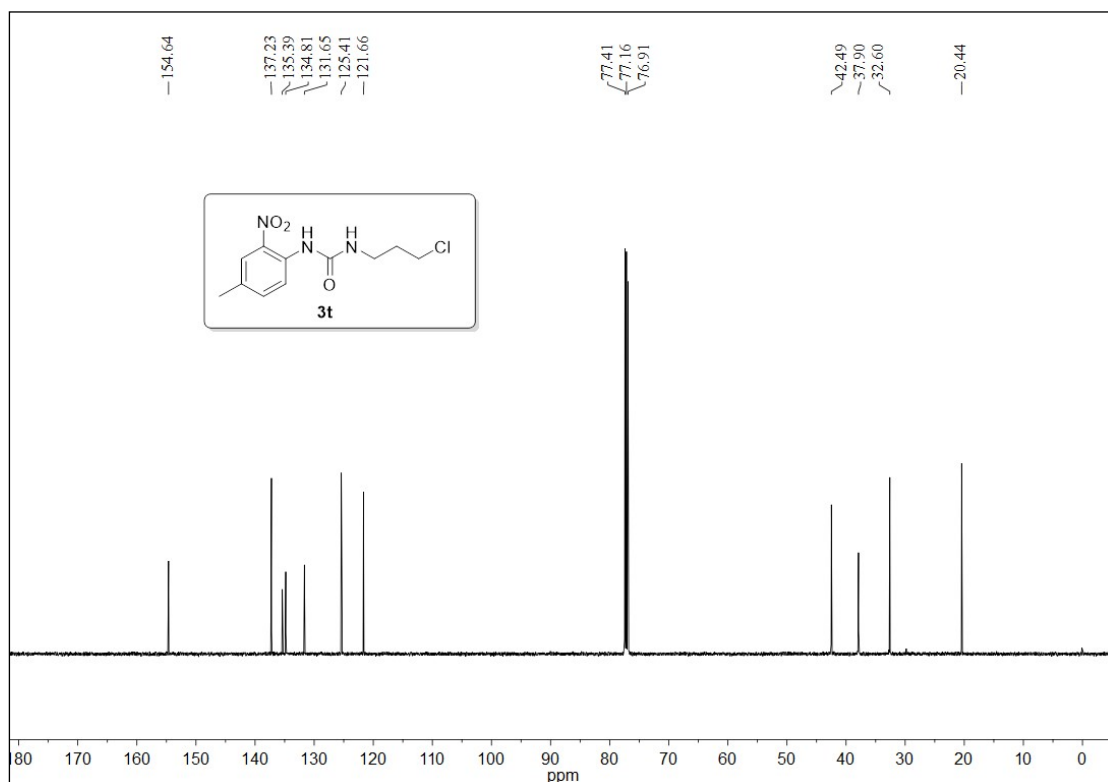
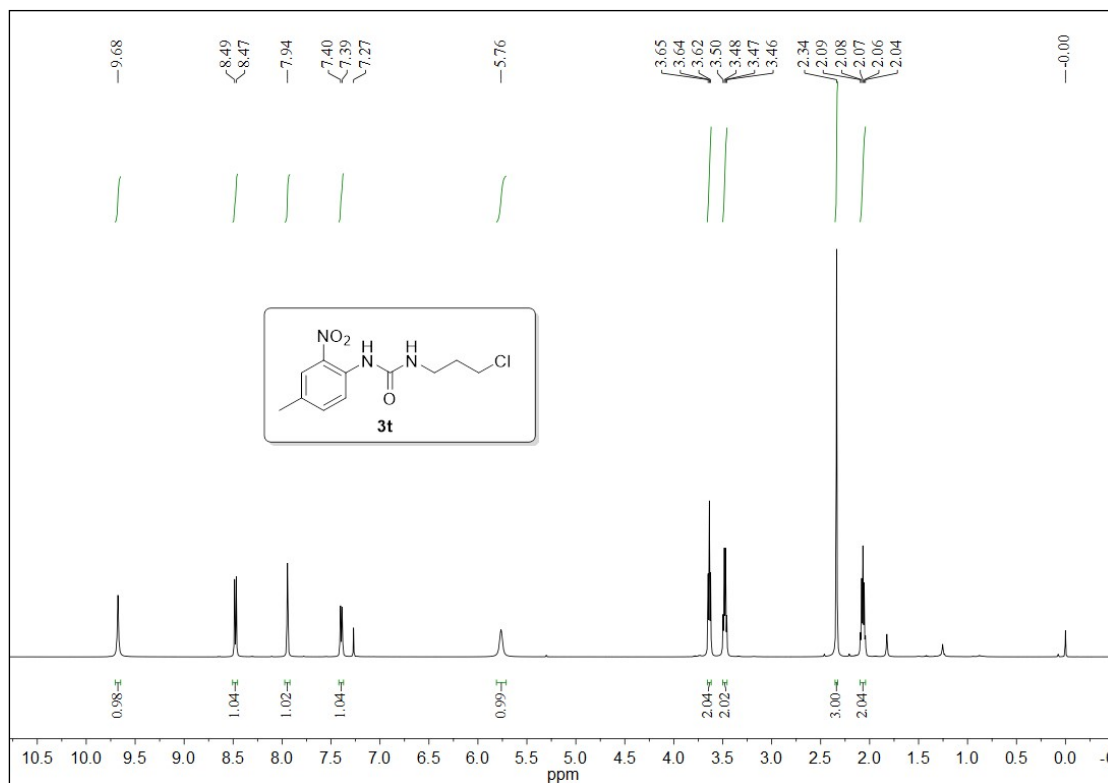


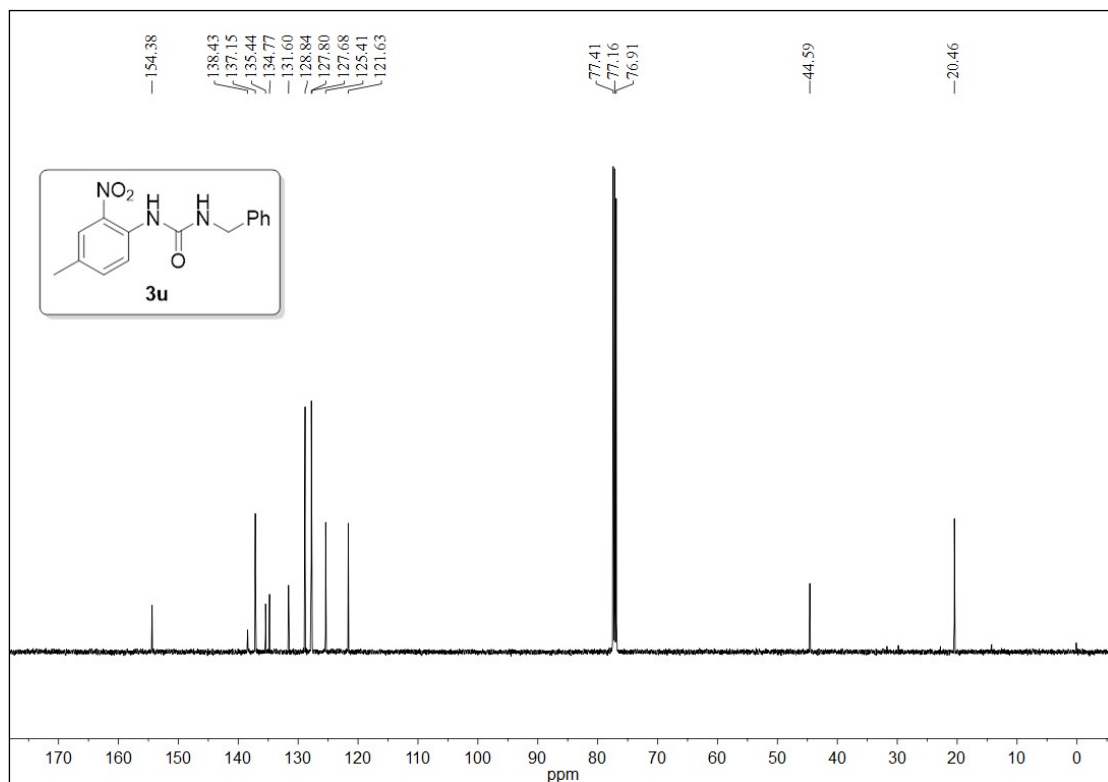
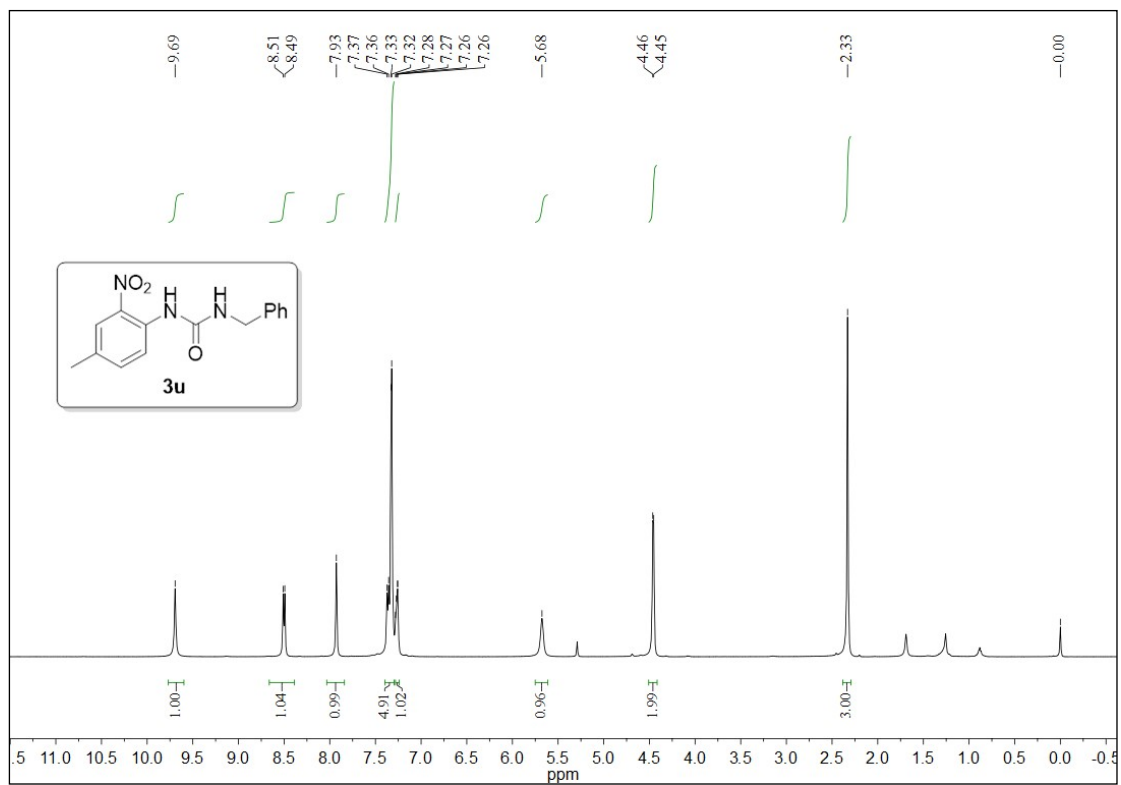


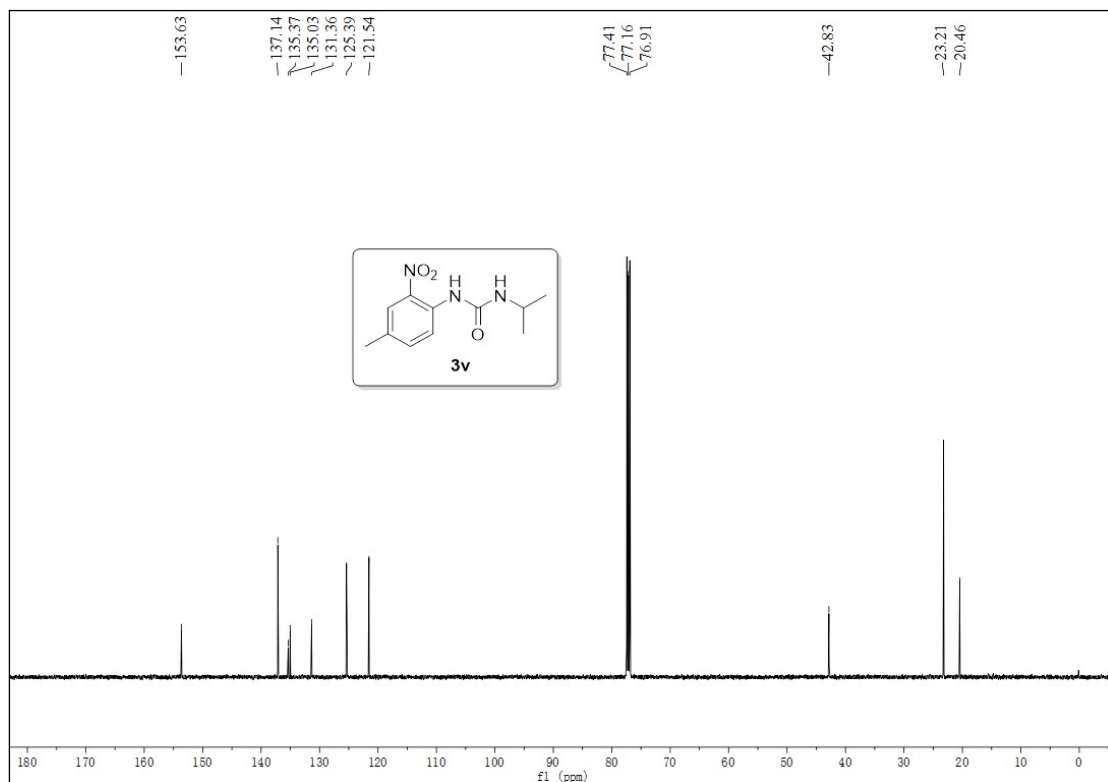
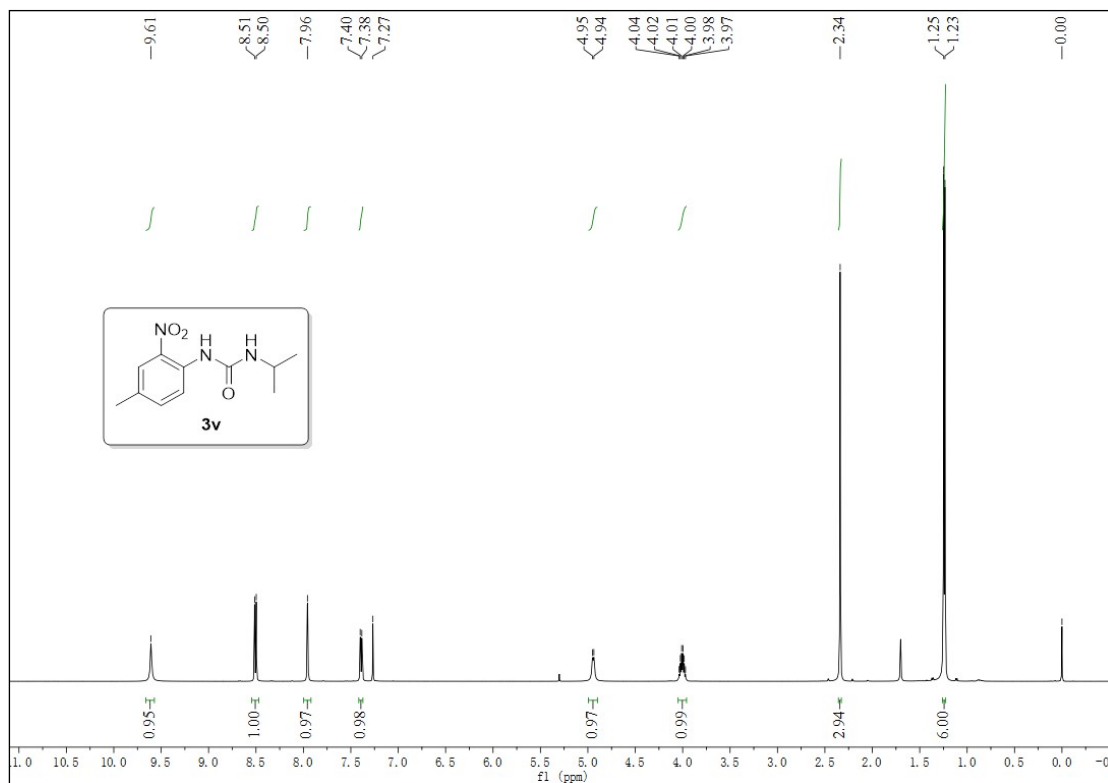


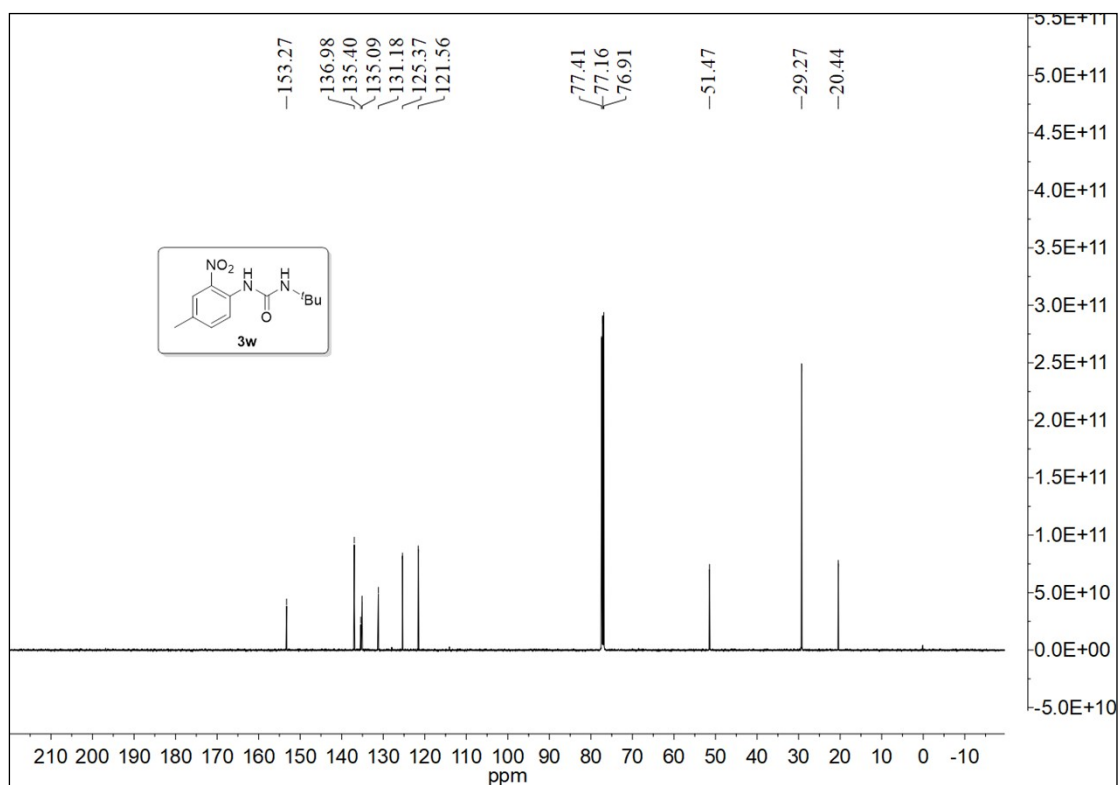
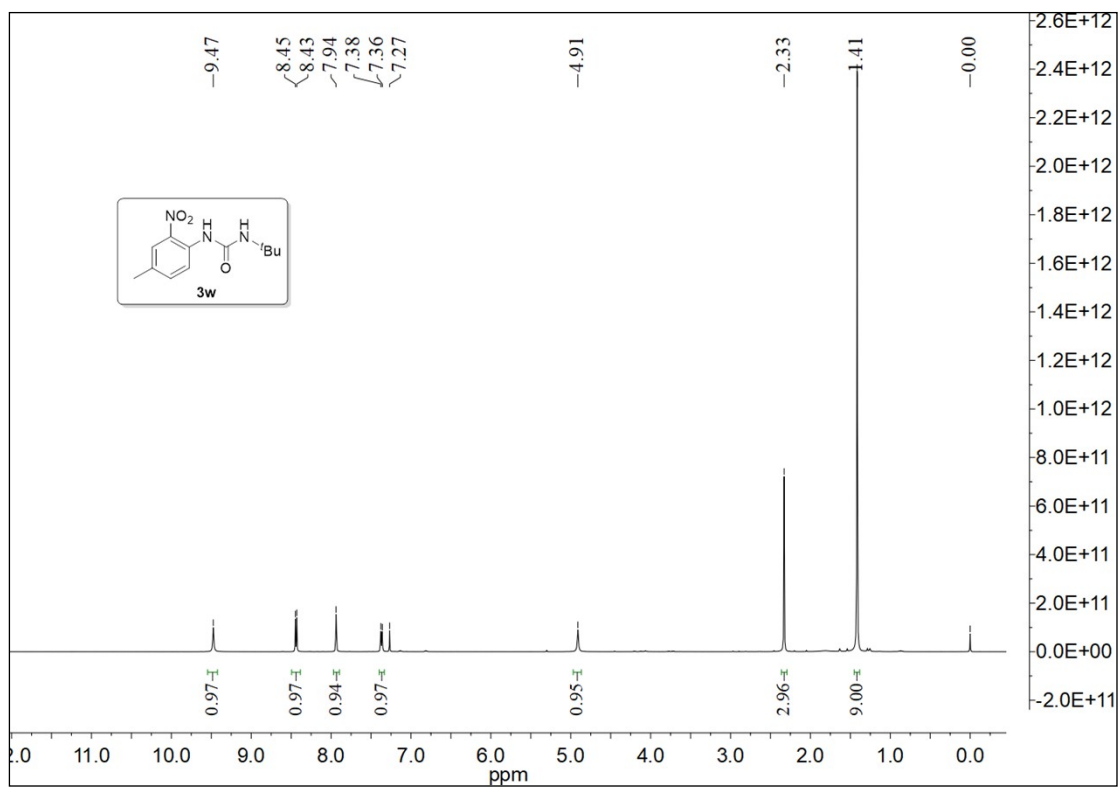


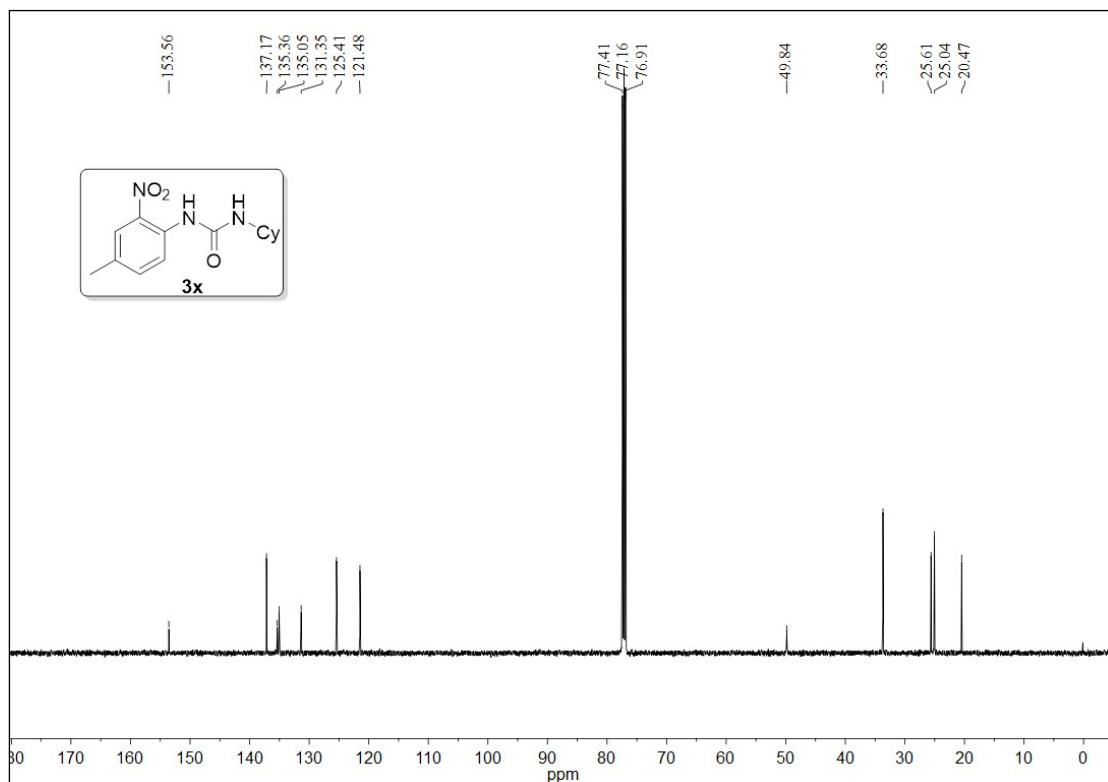
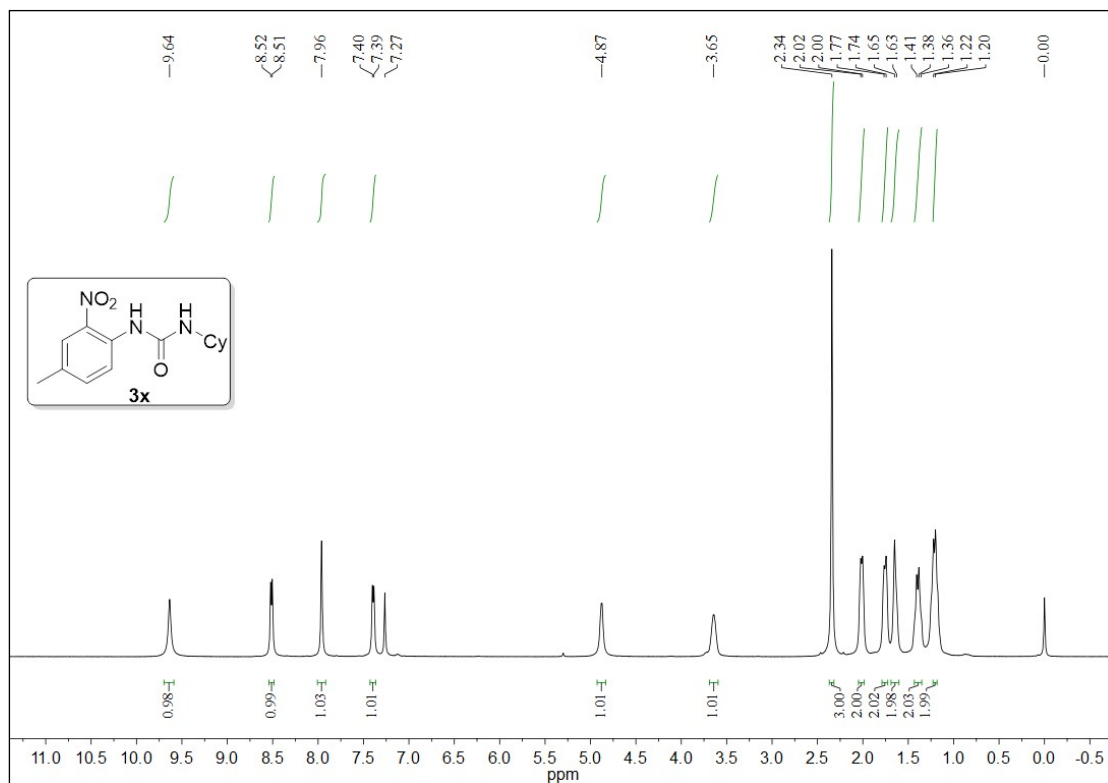


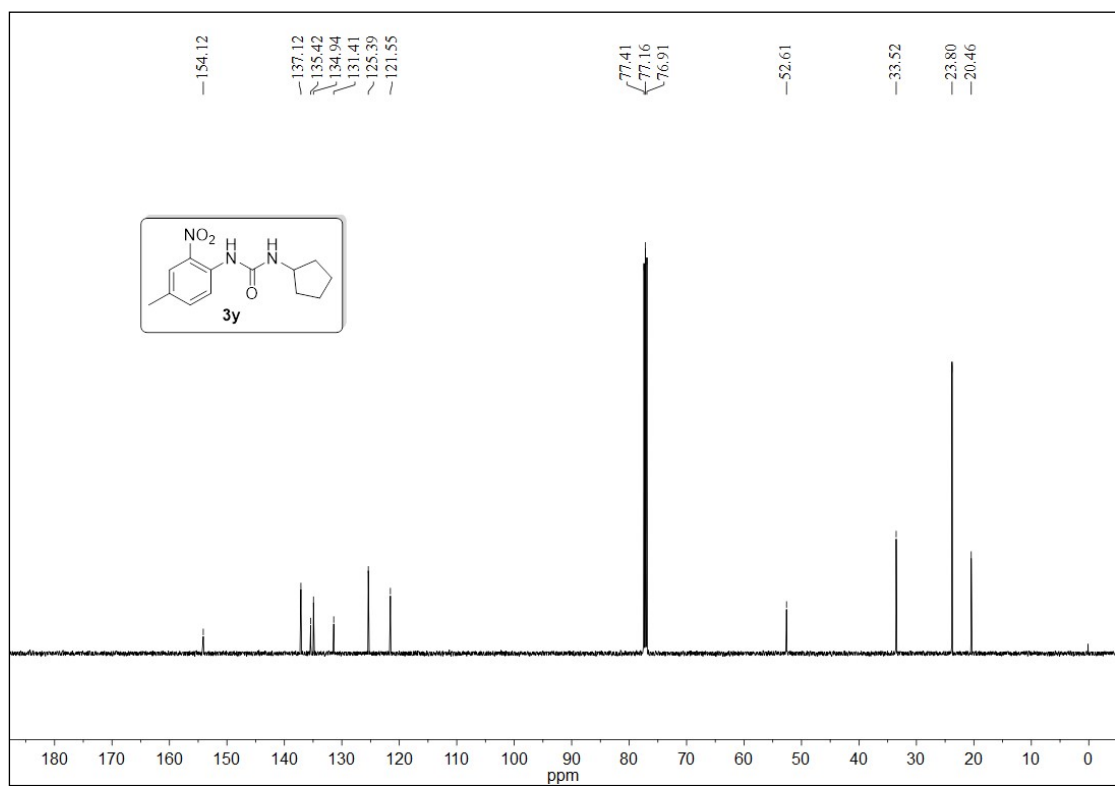
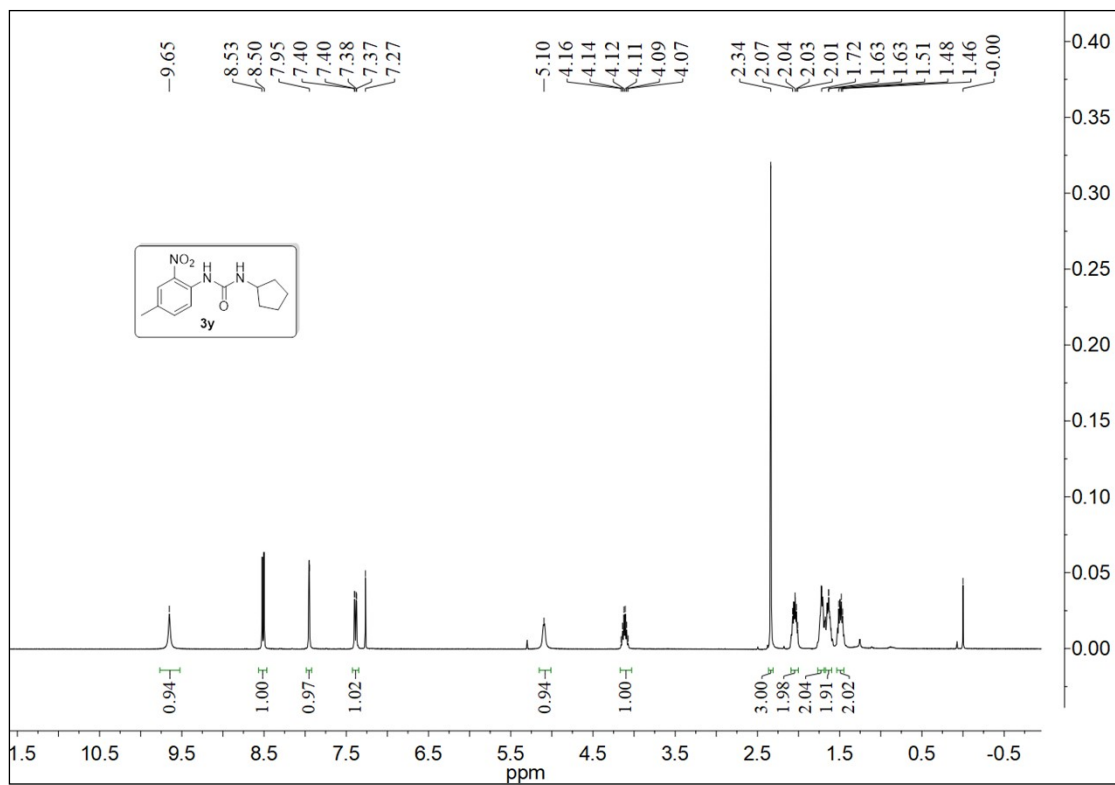


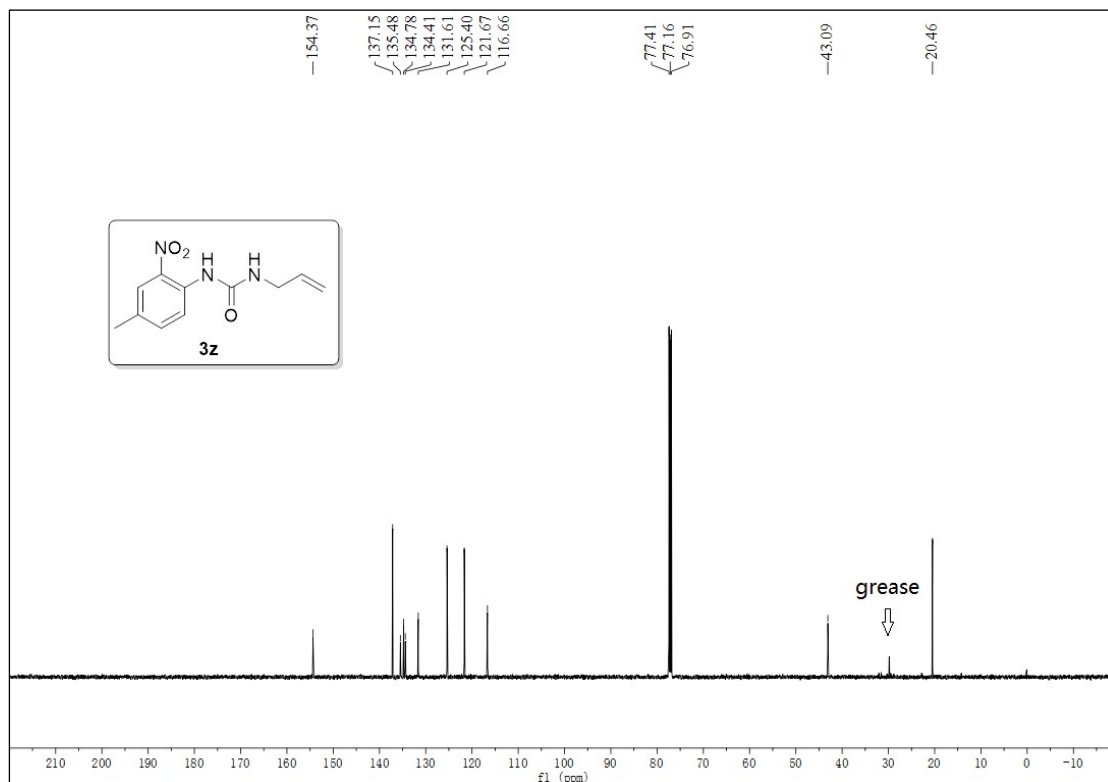
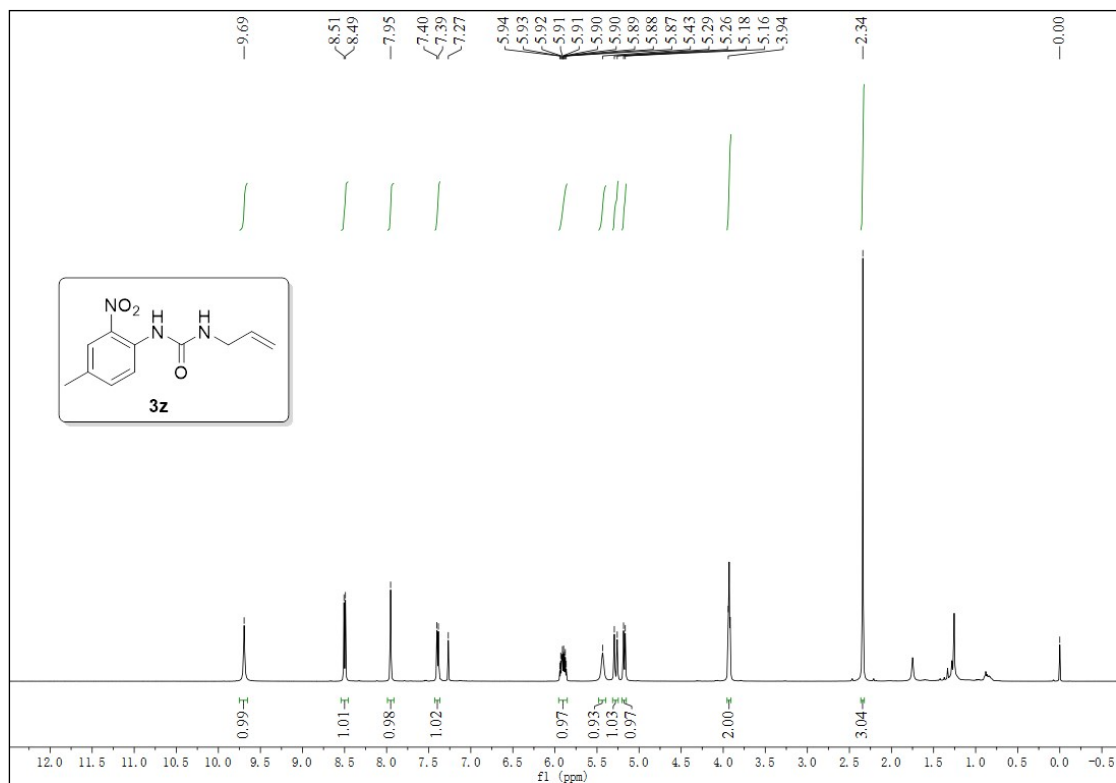


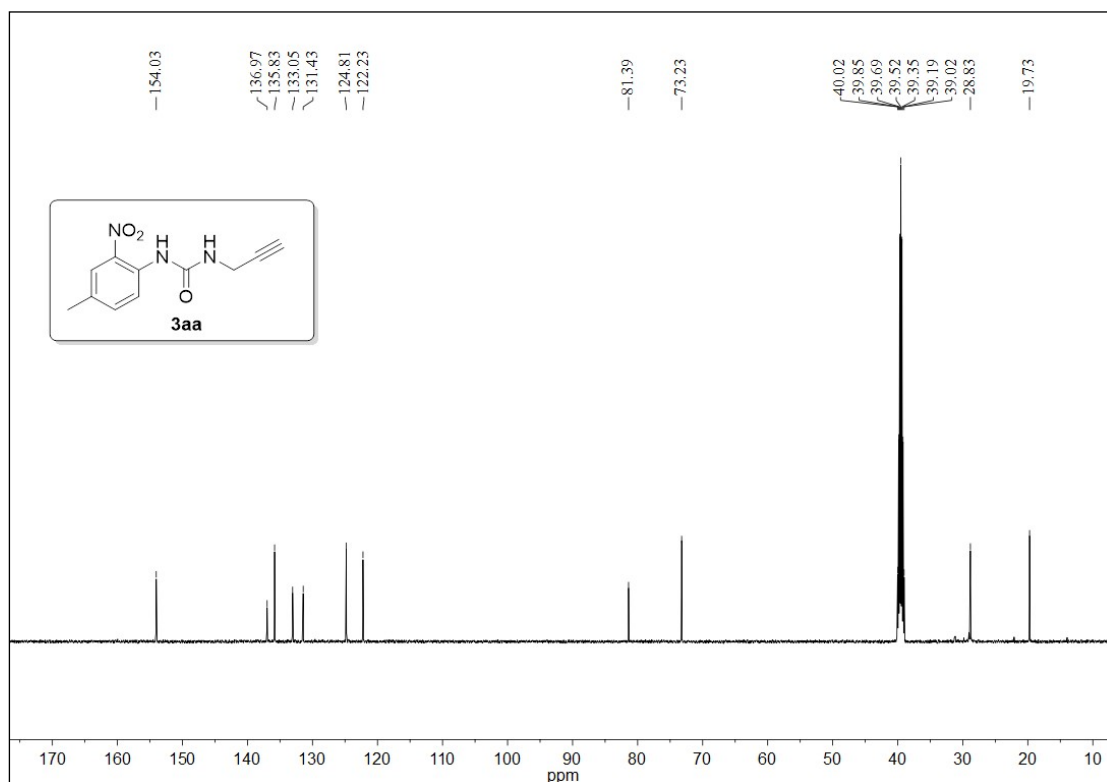
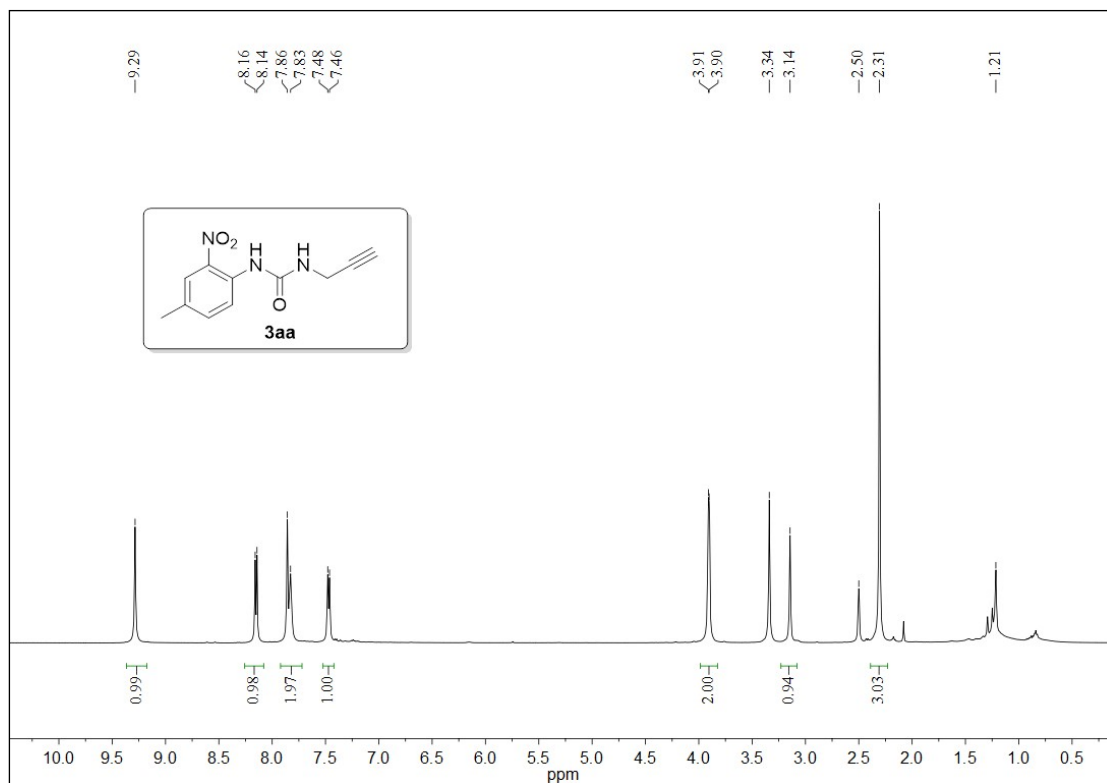


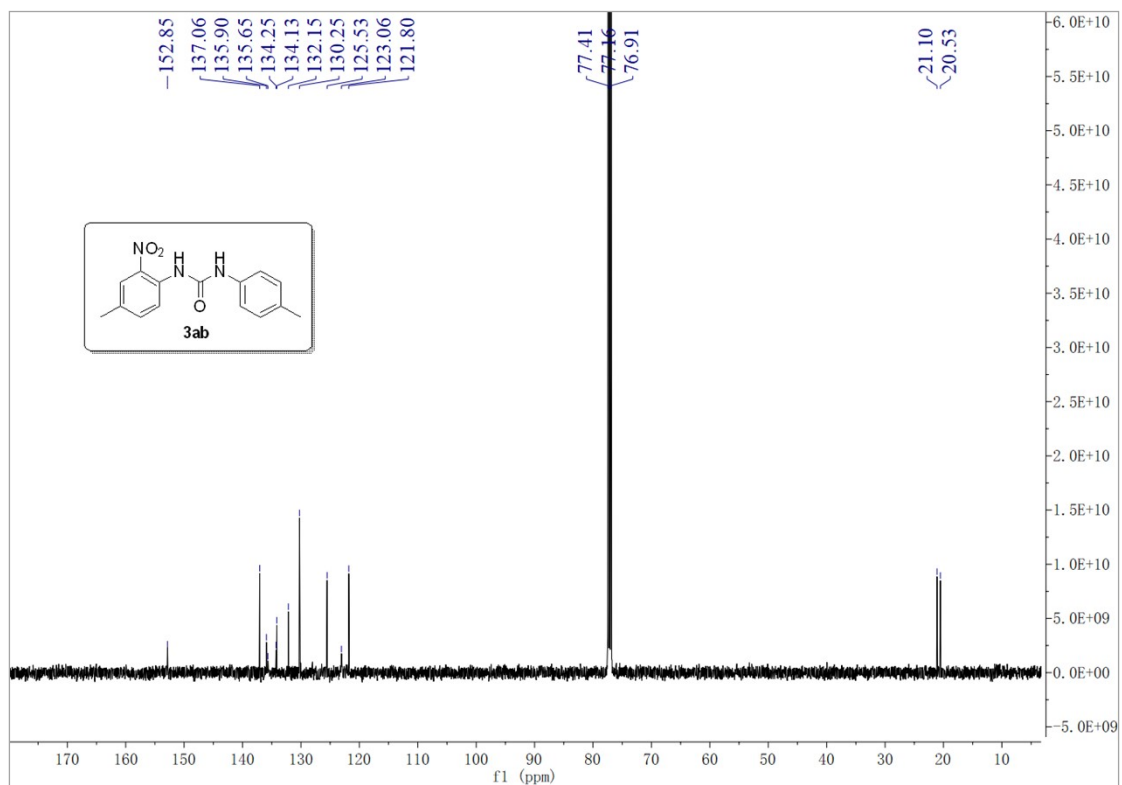
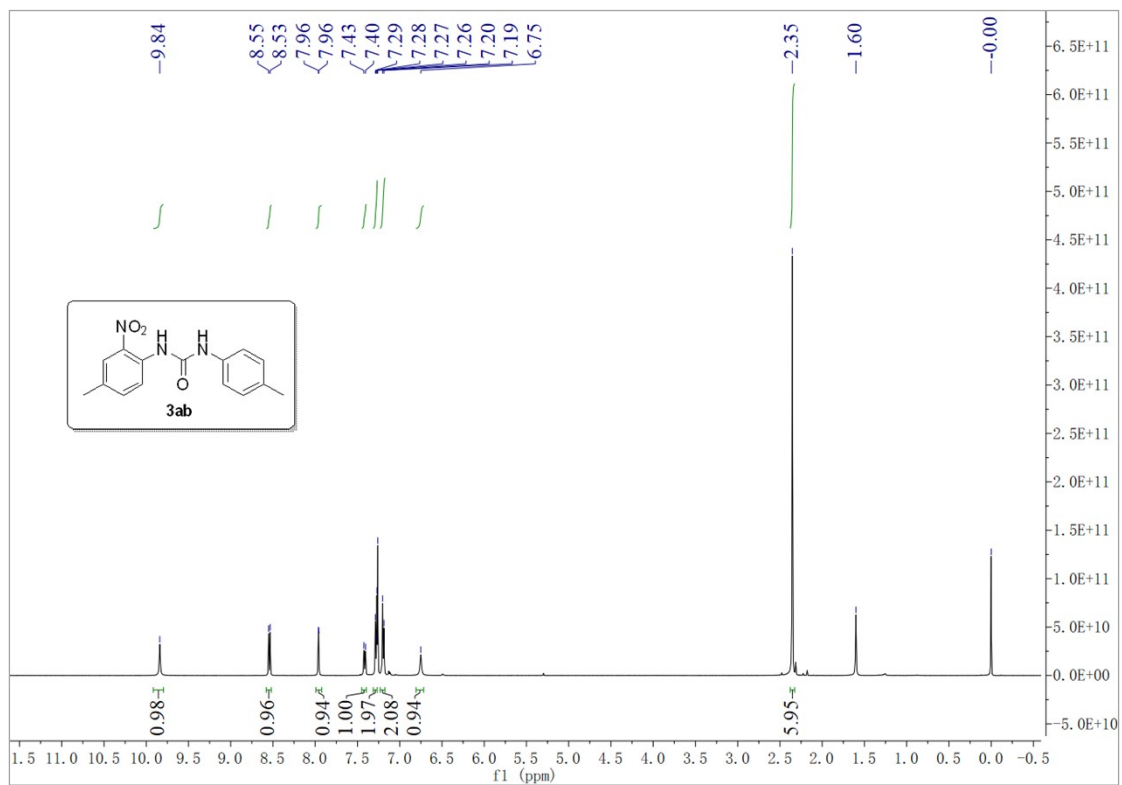


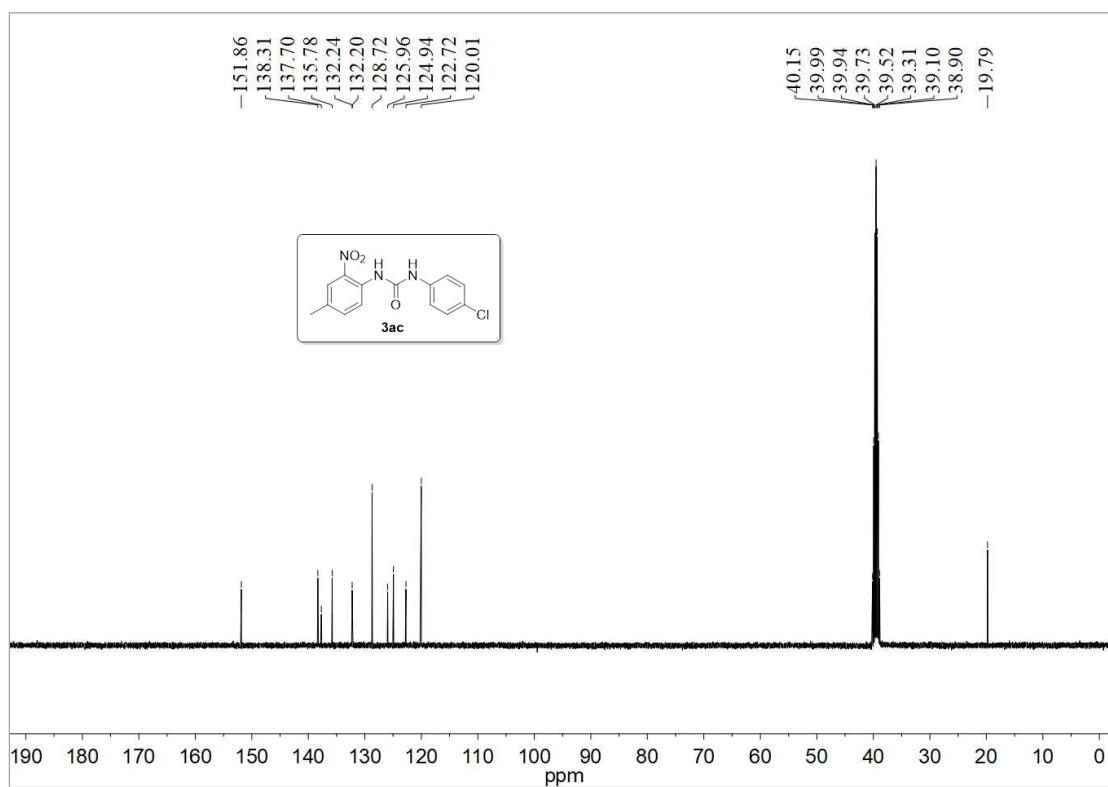
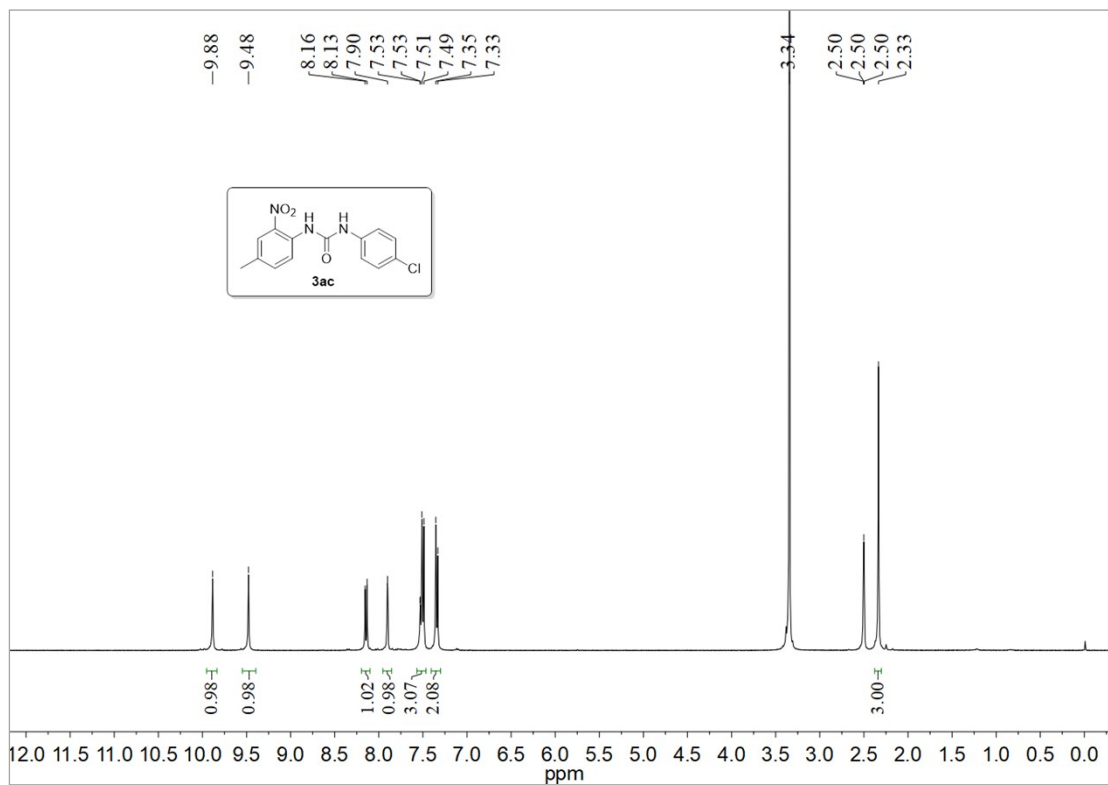


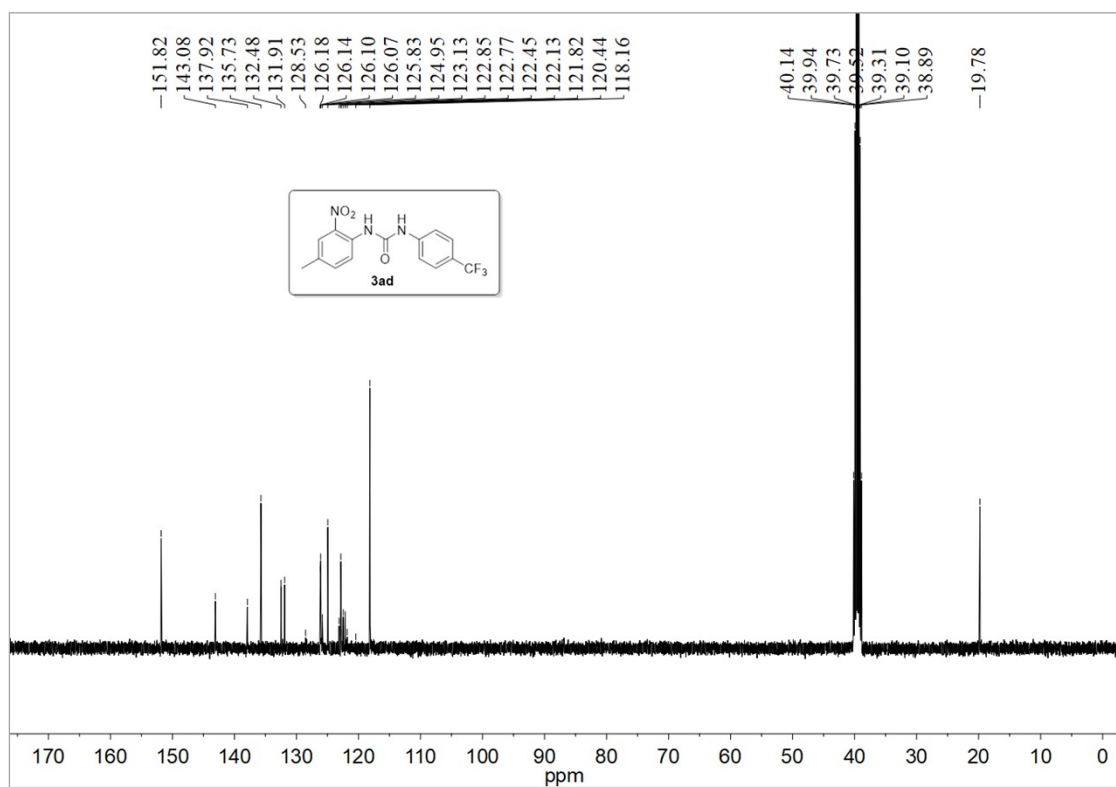
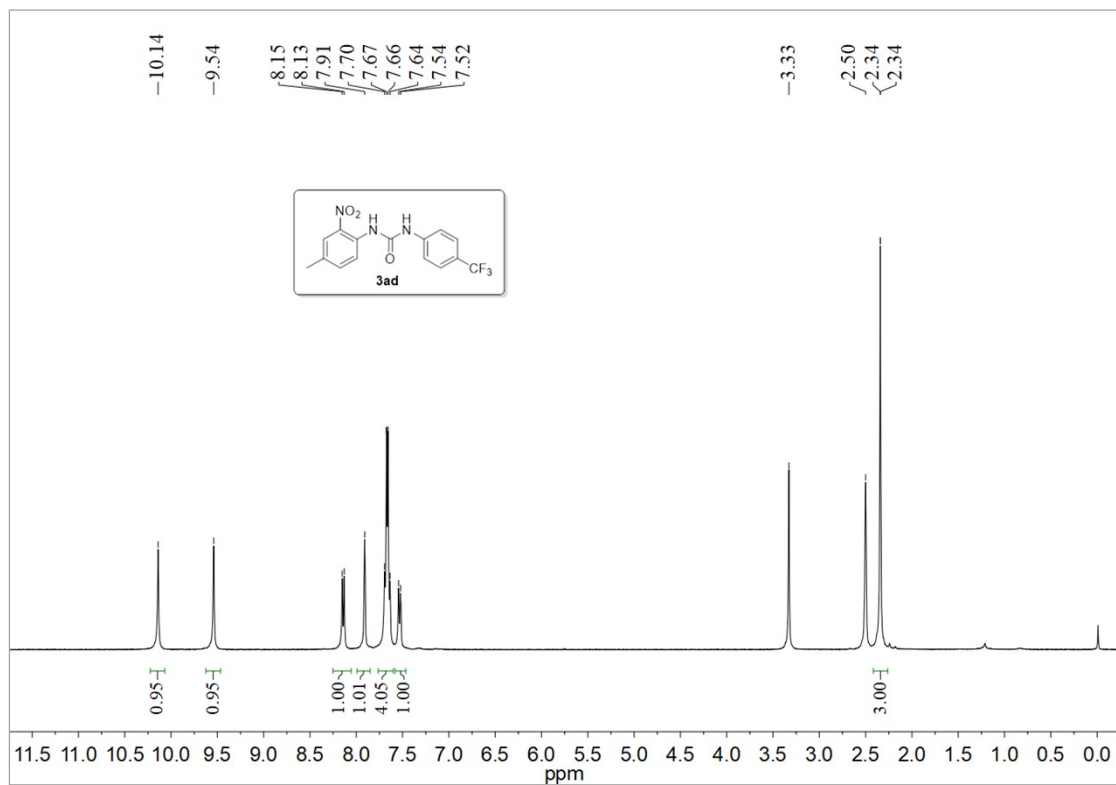


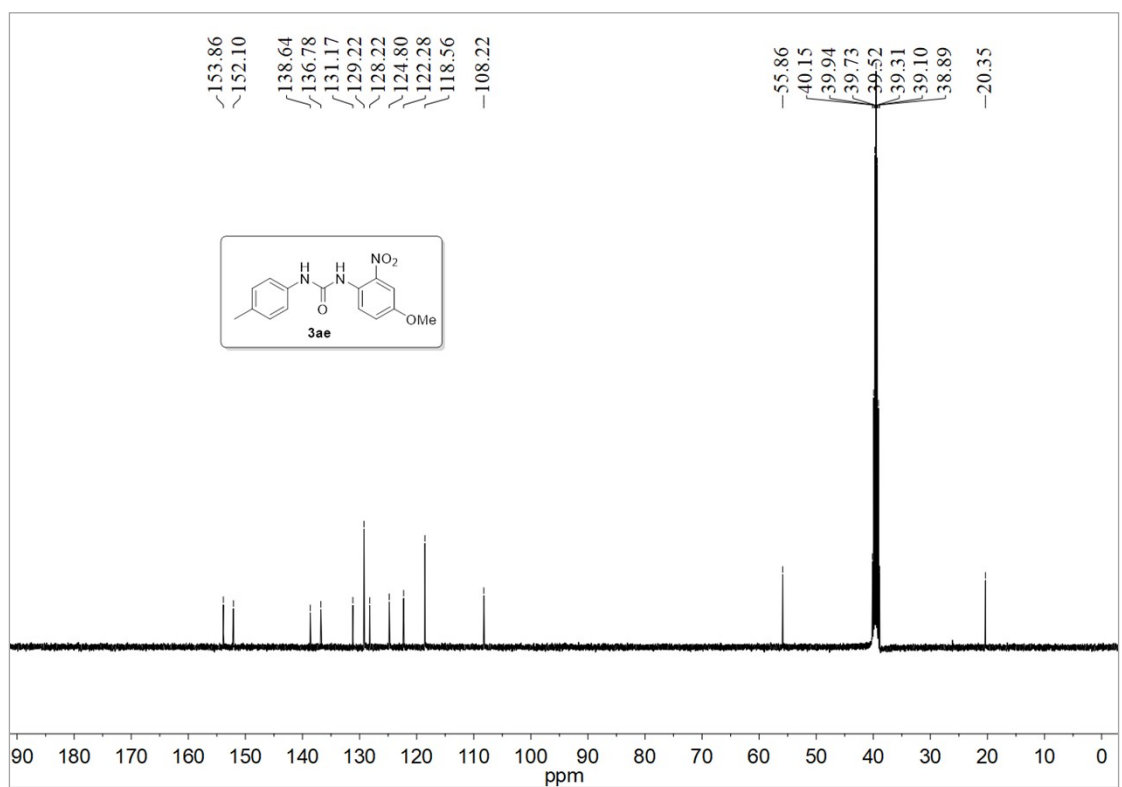
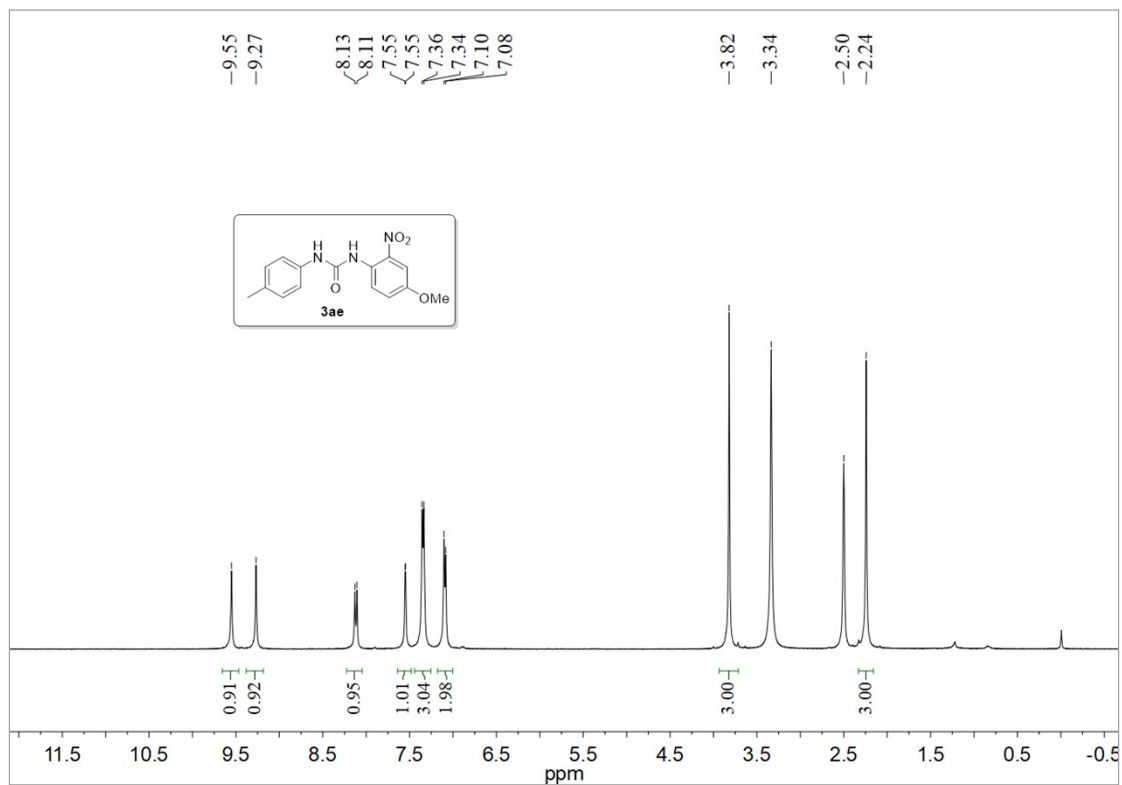


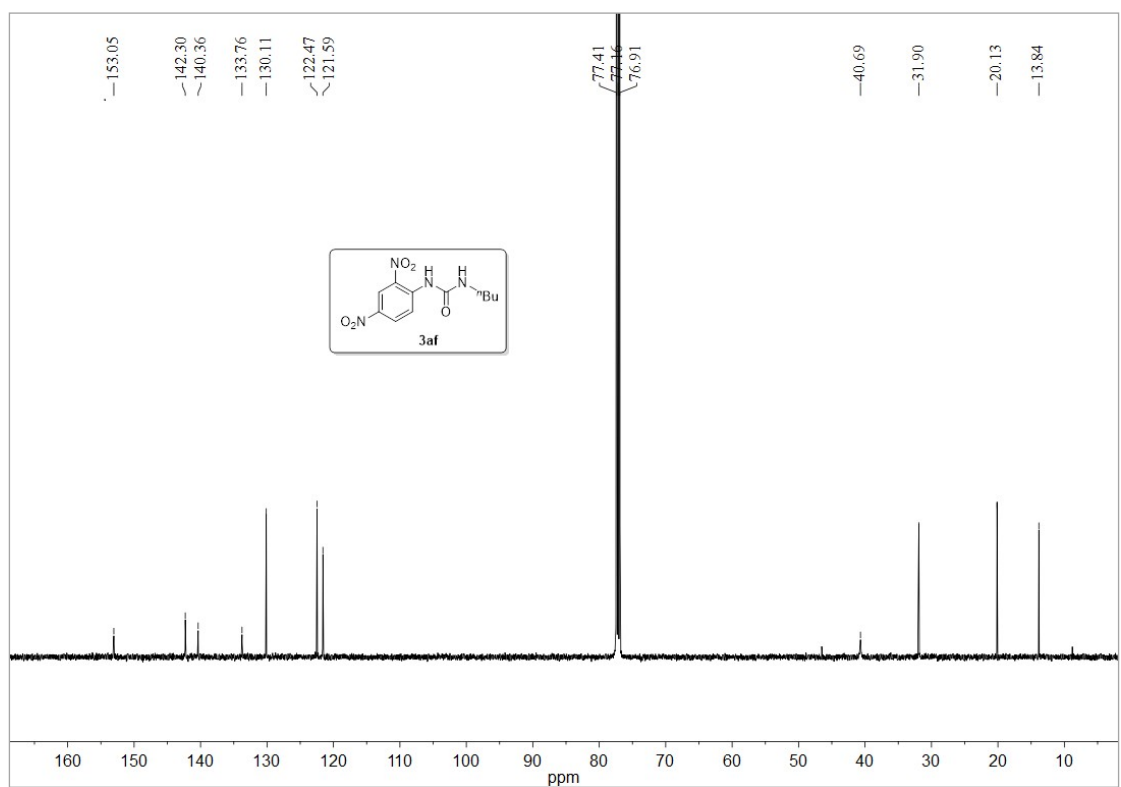
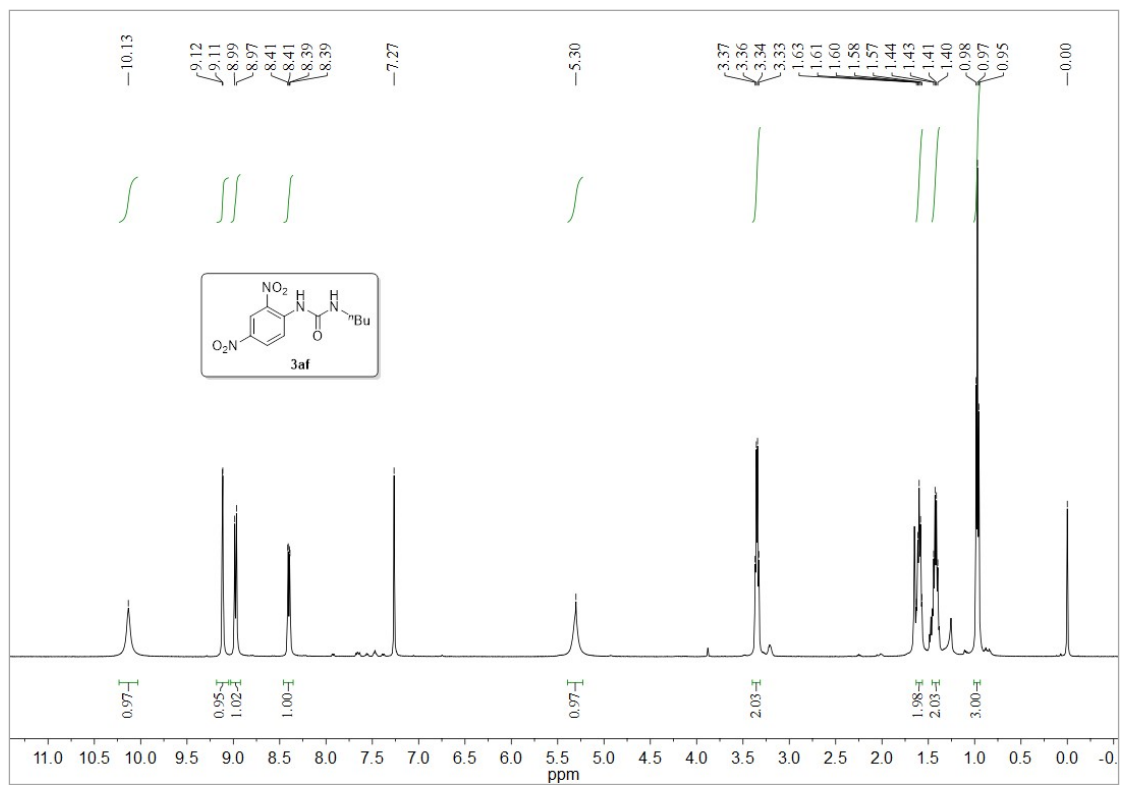


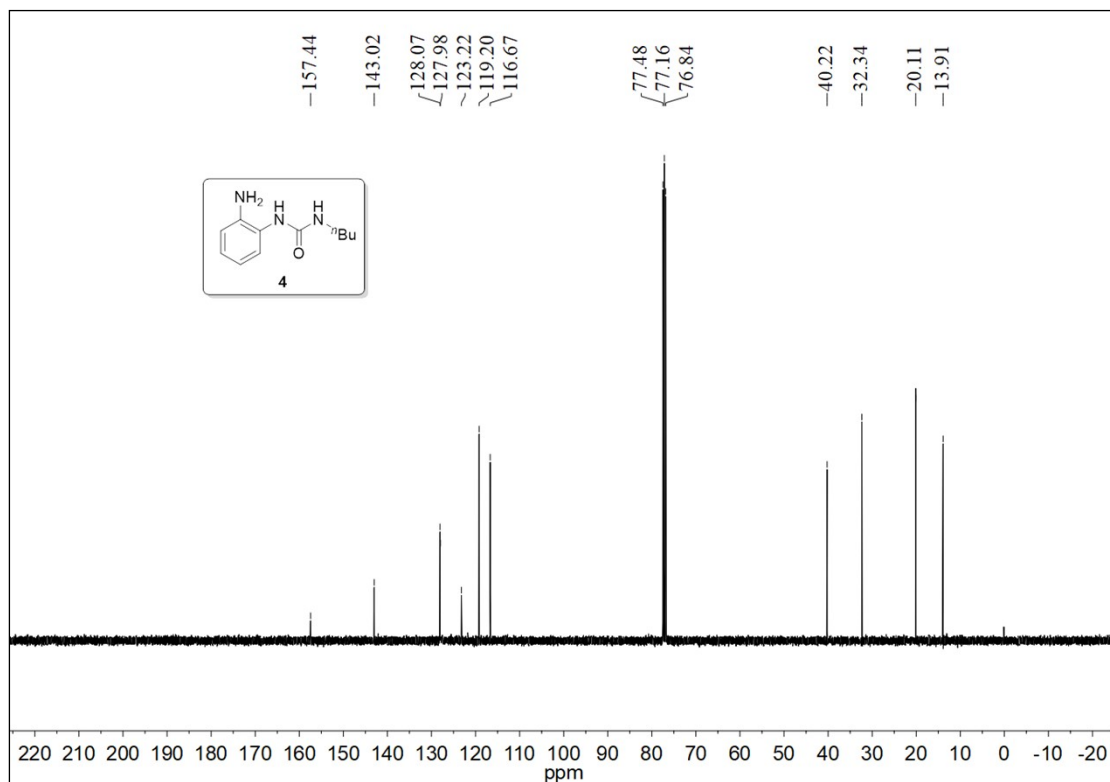
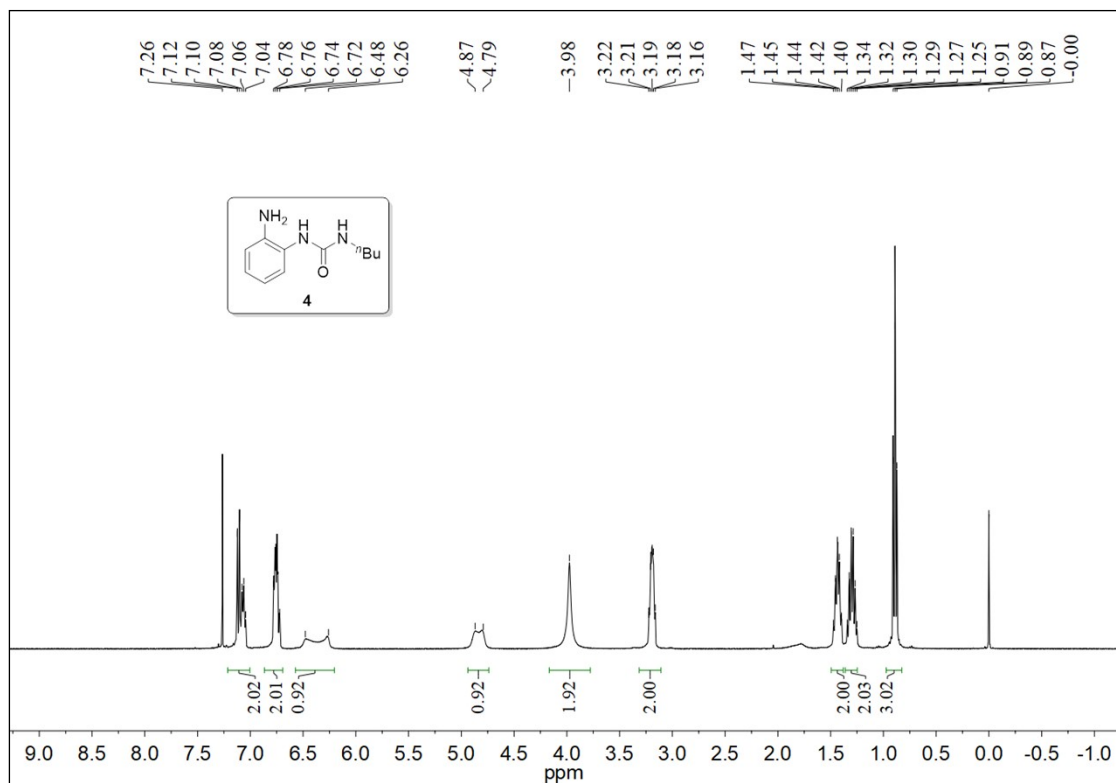


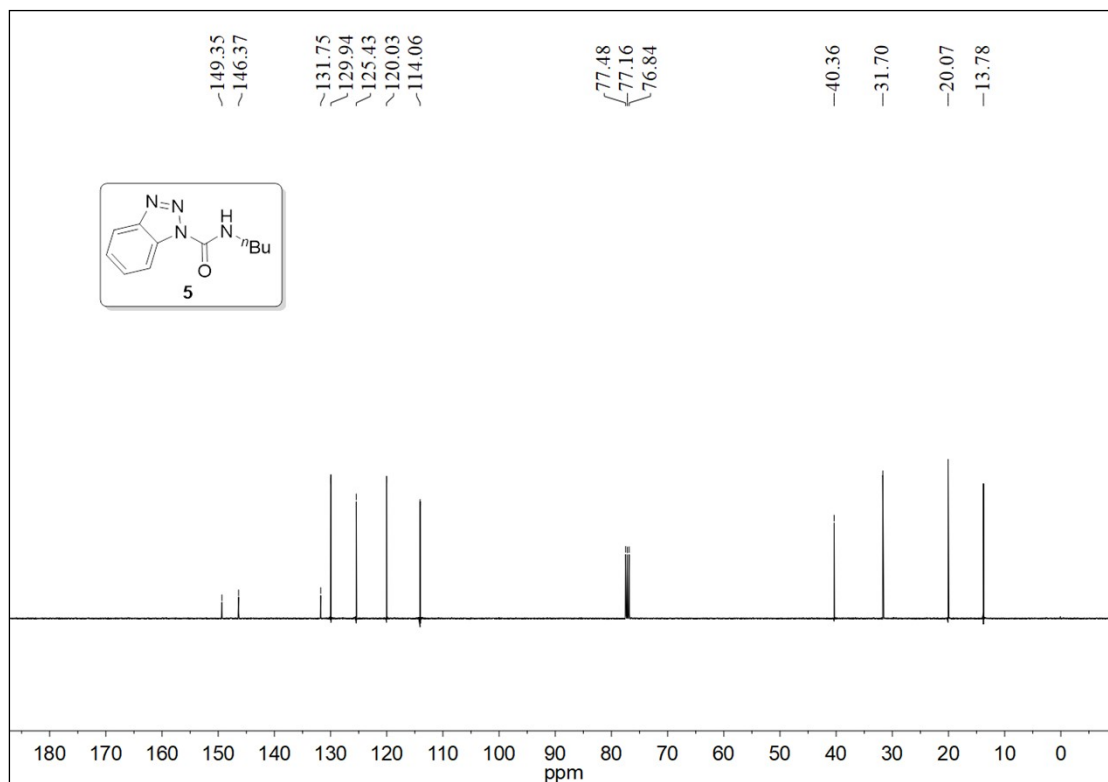
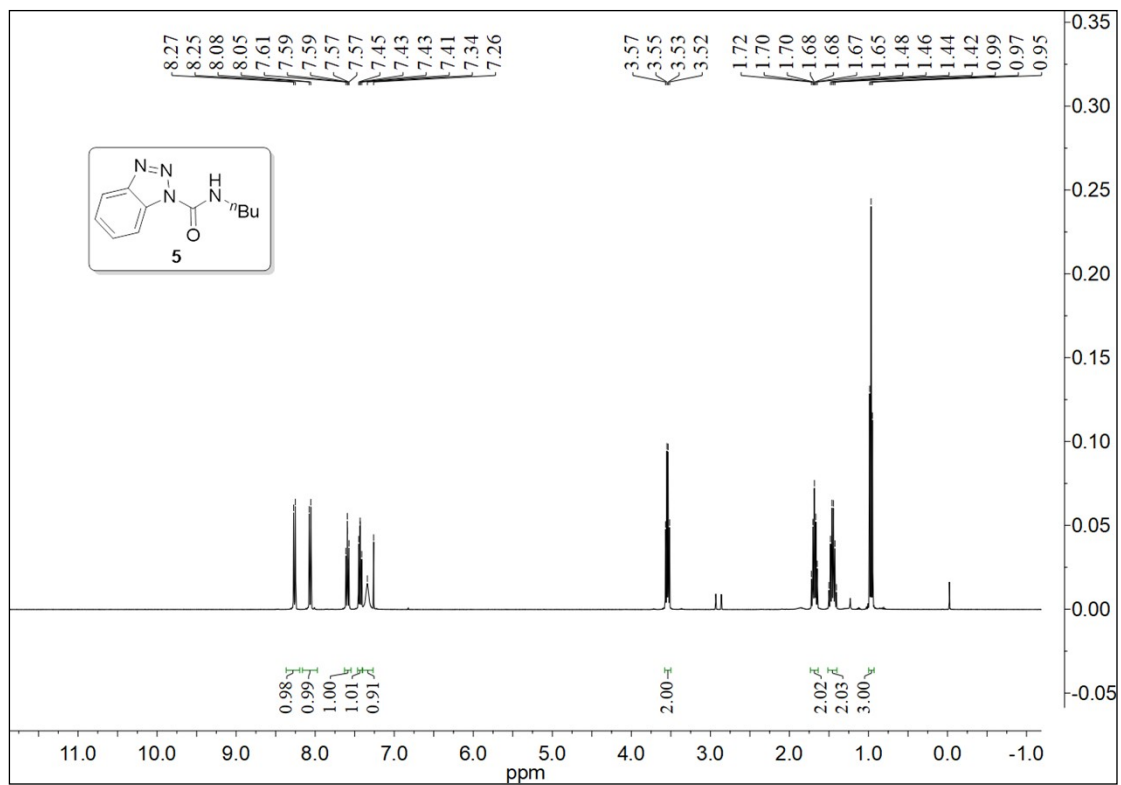


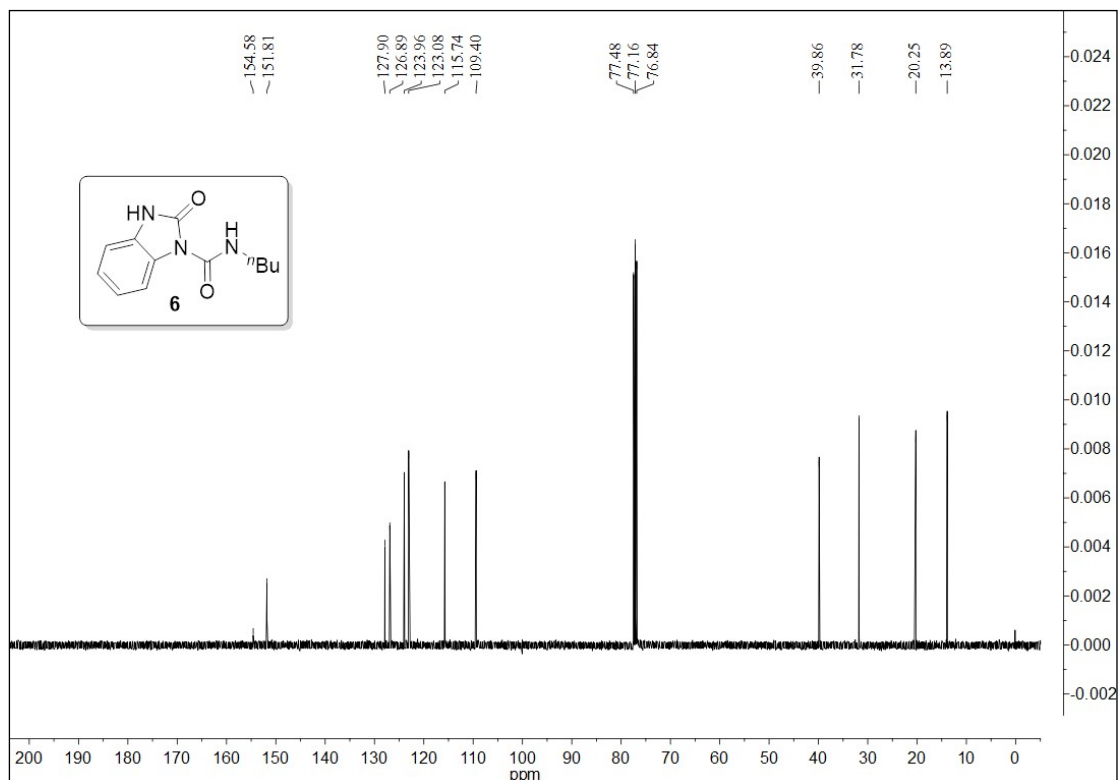
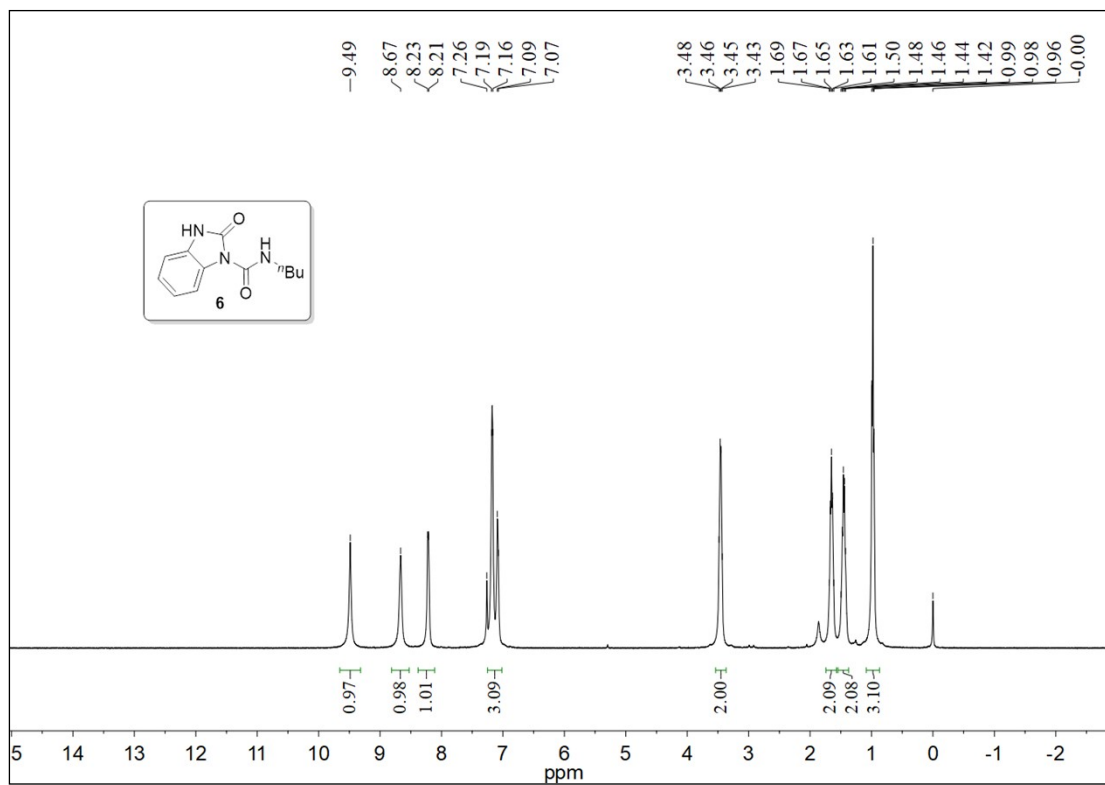


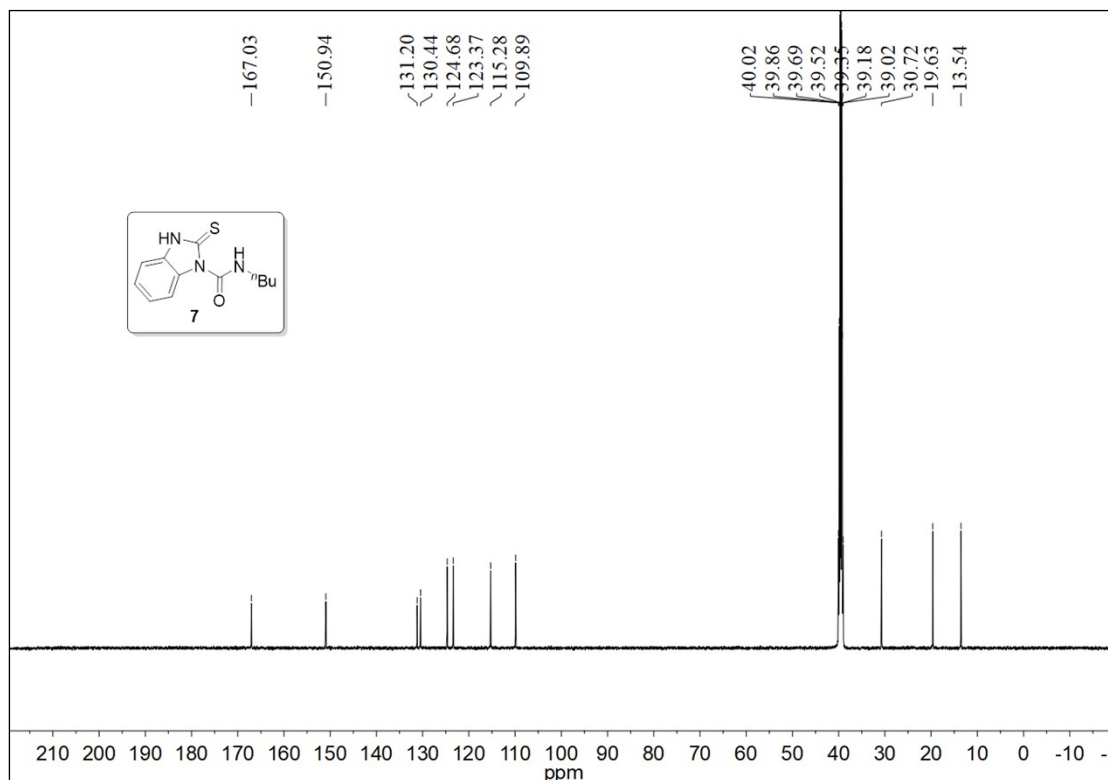
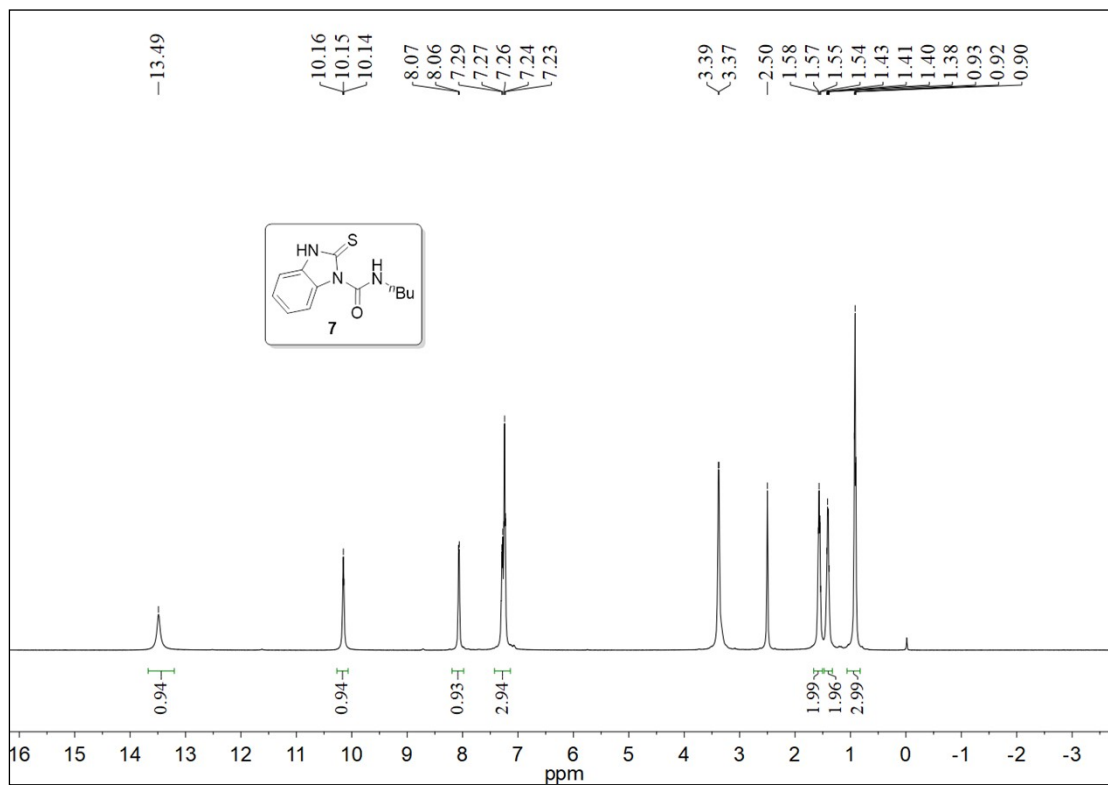




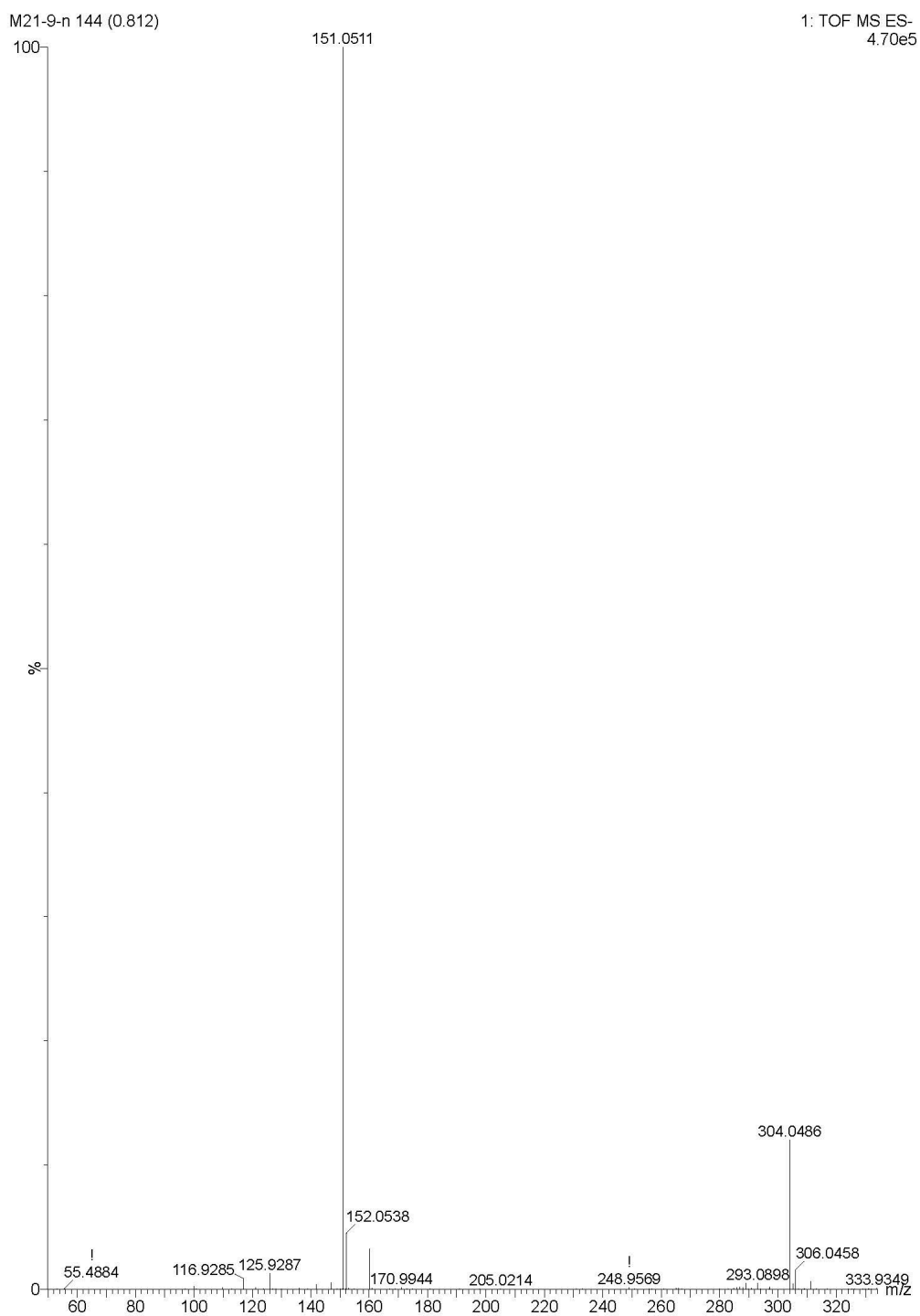




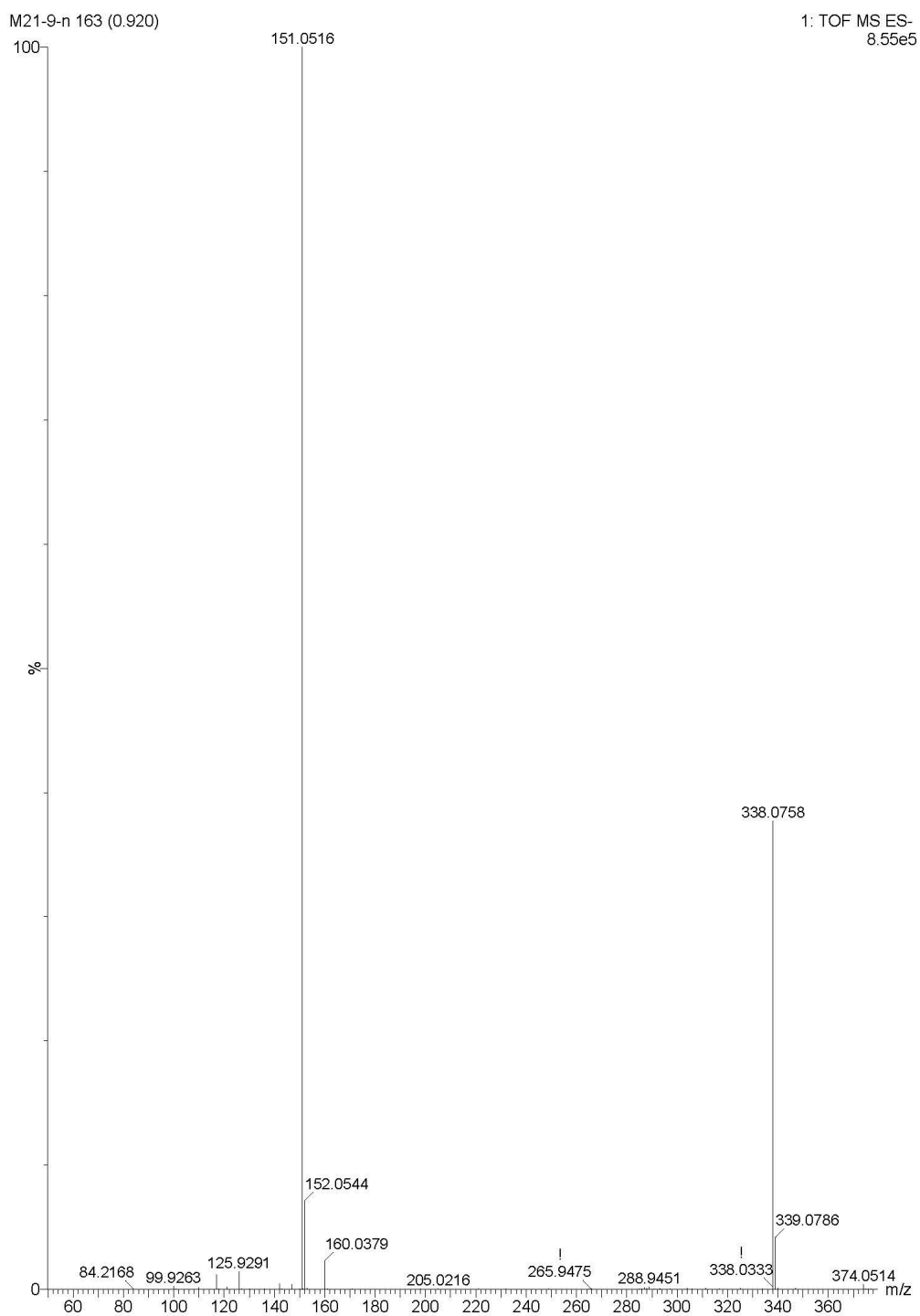




Copy of HRMS for **3ac**



Copy of HRMS for **3ad**



Copy of HRMS for **3ae**

