Supplementary information

Visible-light-mediated amidation from carboxylic acids and tertiary amines via C-N cleavage

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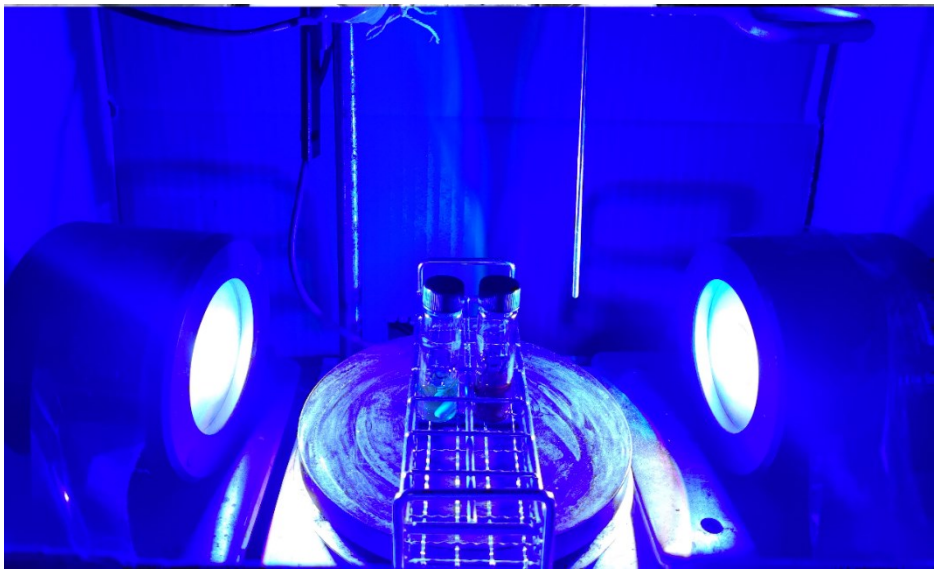
1. General

NMR spectra were recorded on Bruker 400 MHz (^{1}H NMR at 400 MHz, ^{13}C NMR at 101 MHz) or Bruker 500 MHz (^{1}H NMR at 500 MHz, ^{13}C NMR at 126 MHz) using $CDCl_3$ as the solvent (δH = 7.26 ppm, δC = 77.0 ppm as standard). NMR data are presented in the following format: chemical shift (multiplicity [s = single, d = doublet, t = triplet, q = quartet, br = broad, dd = doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, ddd = doublet of doublet of doublets, m = multiplet], coupling constant (Hz), number of equivalent nuclei by integration).

Gas chromatographic (GC) analysis were performed on a GC equipped with a flame-ionization detector and an rtx@-65 (30 m × 0.32 mm ID × 0.25 μm df) column. GC-MS analyses were performed on a GC-MS with an EI mode. High-resolution mass spectra were obtained by ESI on a TOF mass analyzer. The blue LEDs light was purchased from Kessil.

All the reactions were conducted in transparent glass vials under air. All solvents were obtained from commercial suppliers and used without further purification. Reagents were purchased from Energy Chemical, Adamas-beta, and etc. The photocatalyst was prepared following the literature procedure[1]. Flash column chromatographic purification of products was accomplished using forced-flow chromatography on Silica Gel (300-400 mesh).

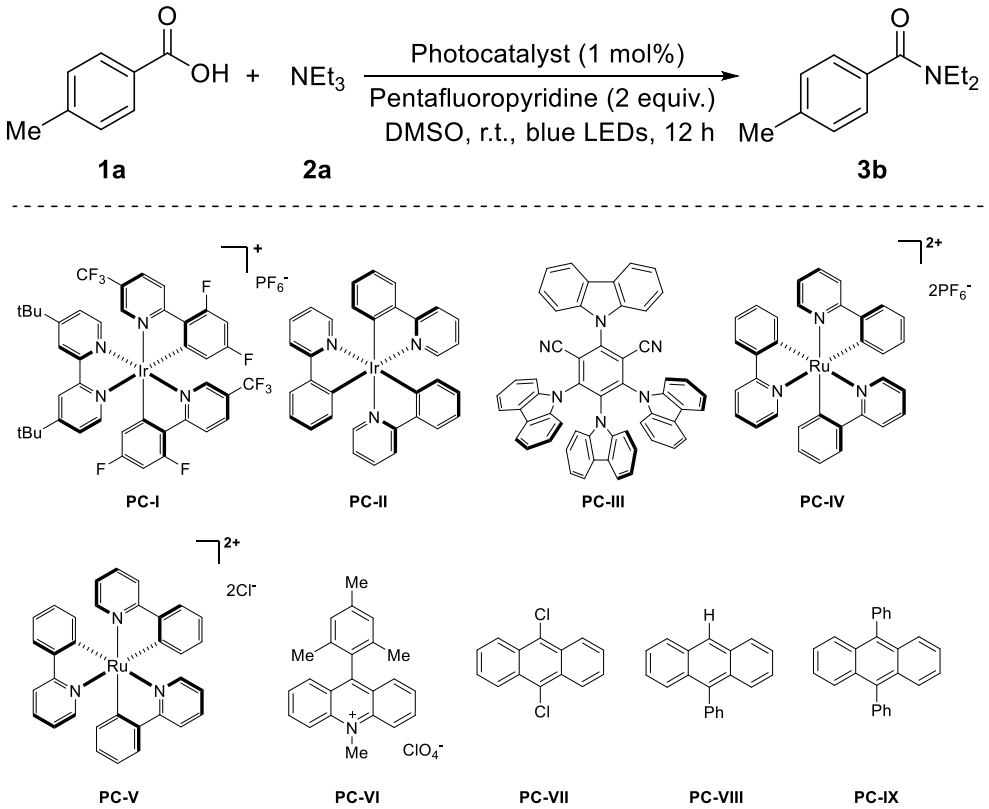
2. Photoreactor Set-up



The blue LEDs was purchased from Kessil. The fan was used at the top to make the reaction temperature around room temperature or so.

3. Optimization Details

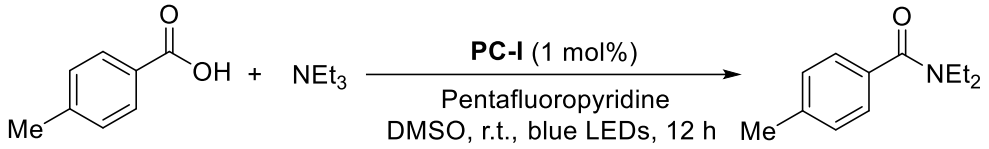
Table S1. Screening of the photocatalyst



Entry [a]	Photocatalyst (1 mol%)	Yield [%] [b]
1	**PC-I**	82
2	**PC-II**	64
3	**PC-III**	66
4	**PC-IV**	32
5	**PC-V**	33
6	**PC-VI**	9
7	**PC-VII**	10
8	**PC-VIII**	7
9	**PC-IX**	7

[a] Standard condition: **1a** (0.2 mmol), **2a** (0.72 mmol, 100 μL), photocatalyst (1 mol%), pentafluoropyridine (2.0 equiv.), DMSO (2 ml), blue LEDs, rt, 12 h, air. [b] Yields determined by gas chromatography using biphenyl as the internal standard.

Table S2. Screening of the reactant ratio

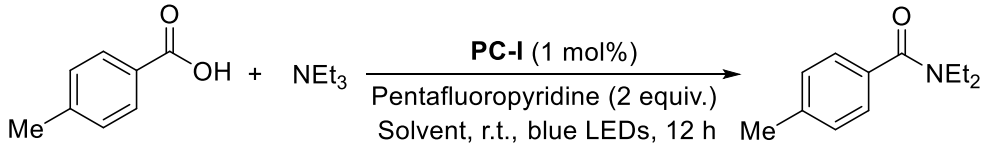


1a **2a** **3b**

Entry [a]	**1a**: **2a**: Pentafluopyridine	Yield [%] [b]
1	1: 1.2: 1.5	20
2	1: 2: 1.5	36
3	1: 3: 1.5	75
4	1: 3.6: 1.5	80
5	1: 3.6: 0	n.d.
6	1: 3.6: 0.1	3
7	1: 3.6: 0.5	18
8	1: 3.6: 1	30
9	1: 3.6: 2	82
10	1: 3.6: 3	10

[a] Standard condition: **1a** (0.2 mmol), **2a**, photocatalyst (1 mol%), pentafluoropyridine, DMSO (2 ml), blue LEDs, rt, 12 h, air. [b] Yields determined by gas chromatography using biphenyl as the internal standard.

Table S3. Screening of the solvent



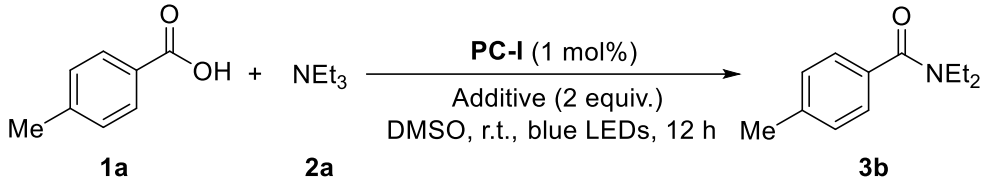
1a **2a** **3b**

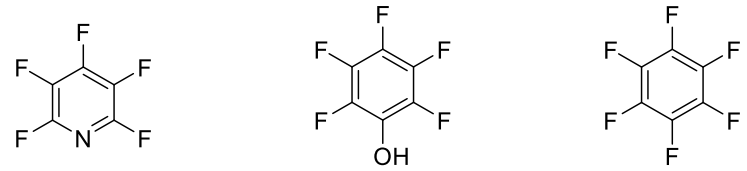
Entry [a]	Solvent (2 ml)	Yield [%] [b]
1	MeCN	70
2	Acetone	36
3	DMF	68
4	DCM	28
5	DMSO	82
6	CyH	10
7	Dioxane	n.d.
8	EtOH	n.d.
9	MTBE	n.d.

10	THF	n.d.
11	DMSO + H_2O (0.4 ml)	68
12	DMSO + H_2O (20 μL)	65

[a] Standard condition: **1a** (0.2 mmol), **2a** (0.72 mmol, 100 μL), **PC-I** (1 mol%), pentafluoropyridine (2.0 equiv.), solvent (2 ml), blue LEDs, rt, 12 h, air. [b] Yields determined by gas chromatography using biphenyl as the internal standard.

Table S4. Screening of the additive



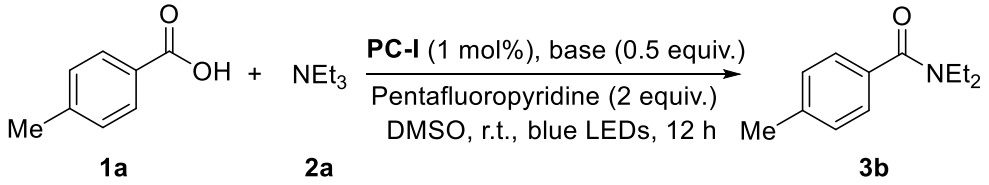


Pentafluoropyrodine Pentafluorophenol Hexafluorobenzene

Entry [a]	Additives (2 equiv.)	Yield [%] [b]
1	Pentafluoropyridine	82
2	Pentafluorophenol	n.d.
3	Hexafluorobenzene	n.d.

[a] Standard condition: **1a** (0.2 mmol), **2a** (0.72 mmol, 100 μL), **PC-I** (1 mol%), additives (2.0 equiv.), DMSO (2 ml), blue LEDs, rt, 12 h, air. [b] Yields determined by gas chromatography using biphenyl as the internal standard.

Table S5. Screening of the base

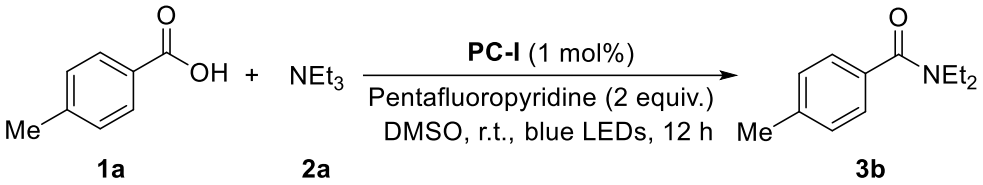


Entry [a]	Bases (0.5 equiv.)	Yield [%] [b]
1	None	82
2	$NaHCO_3$	34
3	CH_3COONa	n.d.
4	K_2HPO_4	28
5	$CaCO_3$	50

6	$Ca(OH)_2$	22

[a] Standard condition: **1a** (0.2 mmol), **2a** (0.72 mmol, 100 μL), **PC-I** (1 mol%), pentafluoropyridine (2.0 equiv.), DMSO (2 ml), blue LEDs, rt, 12 h, air. [b] Yields determined by gas chromatography using biphenyl as the internal standard.

Table S6. Control experiments



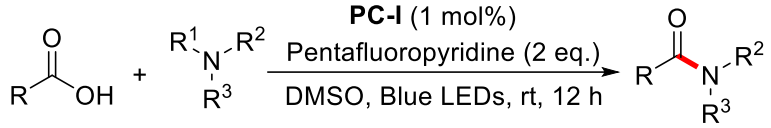
1a **2a** **3b**

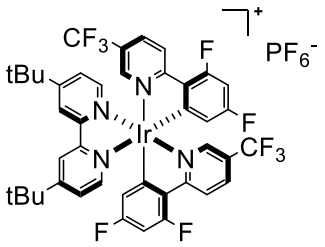
Entry [a]	Variety	Yield [%] [b]
1	No light	n.d.
2	No pentafluoropyridine	n.d.
3	No Photocatalyst	trace
4	Heated 80℃ and no light	n.d.

[a] Standard condition: **1a** (0.2 mmol), **2a** (0.72 mmol, 100 μL), **PC-I** (1 mol%), pentafluoropyridine (2.0 equiv.), DMSO (2 ml), blue LEDs, rt, 12 h, air. [b] Yields determined by gas chromatography using biphenyl as the internal standard.

4. Synthesis of Tertiary Amide Products

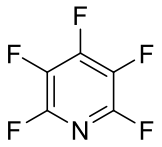
General procedure:





$[Ir(dF(CF_3)ppy)_2(dtbbpy)]PF_6$

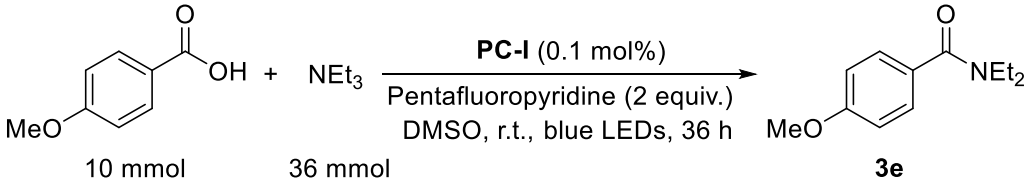
PC-I



Pentafluoropyridine

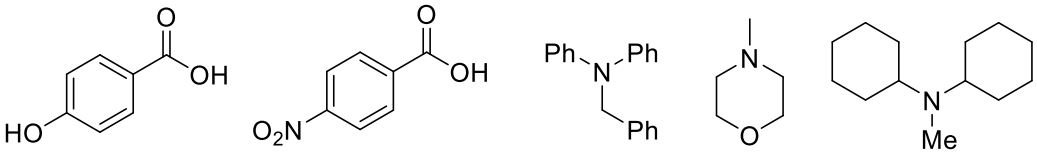
To a clean 10 mL glass vial was charged carboxylic acid (0.2 mmol), tertiary amine (3.6 equiv., 0.72 mmol), pentafluoropyridine (2 equiv., 0.4 mmol, 68 mg, 45 μL), **PC-I** (1 mol%, 0.002 mmol, 2.3 mg) and DMSO (2 mL), and then sealed with a screw cap. The reactants were irradiated with blue light under stirring for 12 hours. Afterwards, add 2 mL sodium bicarbonate solution into the reaction mixture, and extract the organic phase with 2 mL EA for several times. Combined organics were concentrated in vacuo and purified via silica gel column chromatography (EA:PE=1:5-1:3 if not stated otherwise) to give the tertiary amide product. If the product looks yellow or brown, add some activated carbon during purification.

Gram-scale experiment procedure:



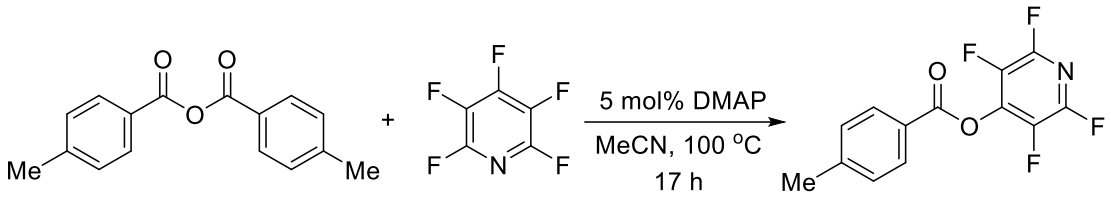
To a clean 250 mL flask was charged *p*-anisic acid (10 mmol, 1522 mg), triethylamine (3.6 equiv., 36 mmol, 5 mL), pentafluoropyridine (2 equiv., 20 mmol, 3381 mg, 2.05 mL), **PC-I** (0.1 mol%, 11.5 mg) and DMSO (100 mL). The reactants were irradiated with blue light under stirring for 36 hours. Afterwards, add 100 mL sodium bicarbonate solution into the reaction mixture, and extract the organic phase with 100 mL EA for several times. Combined organics were concentrated in vacuo and purified via silica gel column chromatography (EA:PE=1:3) to give the product.

Unsuccessful substrates



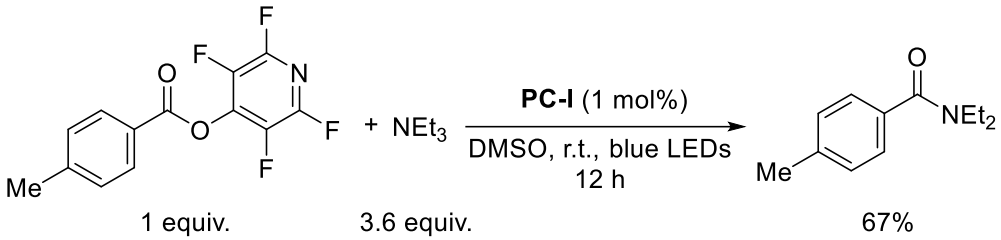
5. Mechanistic Studies

5.1 Verification of ester 5 as the intermediate[2]



To a clean 10 mL glass vial was charged 4-methylbenzoic anhydride (1.4 mmol, 356 mg), pentafluoropyridine (0.7 mmol, 118 mg), DMAP (5 mol%, 4.3 mg) and MeCN (2 mL), and then sealed with a screw cap. The reactants were heated at 100℃ for 17 hours and then concentrated in vacuo and purified via silica gel column chromatography (EA:PE=1:30-1:10) to give the product.

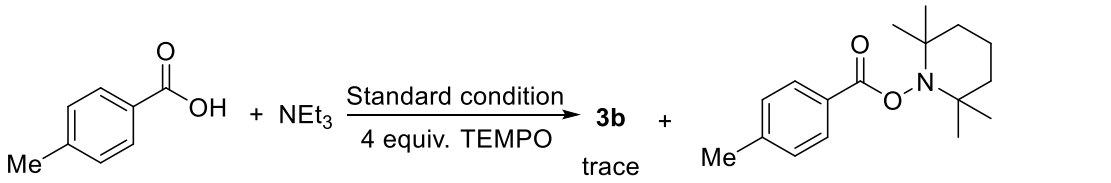
Ester **5** (perfluoropyridin-4-yl 4-methylbenzoate): White solid (m.p. = 56-58℃), 101.1 mg, 51% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.09 (d, *J* = 8.2 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 1H), 2.49 (s, 2H).



To a clean 10 mL glass vial was charged ester **35** (0.175 mmol, 50.0 mg), triethylamine (0.631 mmol, 88 μL r.t.), **PC-I** (1 mol%, 2,0 mg) and DMSO (1.75 mL), and then sealed with a screw cap. The reactants were irradiated with blue light under stirring for 12 hours. Afterwards, add 2 mL water and 2 mL sodium bicarbonate solution into the reaction mixture, and extract the organic phase with 2 mL EA for several times. Combined organics were concentrated in vacuo and purified via silica gel column chromatography (EA:PE=1:3) to give tertiary amide product.

Product (*N,N*-diethyl-4-methylbenzamide): Colorless oil, 22.4 mg, 67% yield. Structure and purity verified by ^{1}H NMR and GC-MS.

5.2 TEMPO Inhibition Experiment



Chemical Formula (+H$^+$): $C_{17}H_{25}NO_2H^+$
calculated: 276.1958
found: 276.1952

We added 4.0 equivalent 2,2,6,6-tetramethyl-1-piperinedinyloxy (TEMPO) into the model reaction. It was found that the reaction was almost inhibited completely. And a part of the acyl radical derivated from ester can be trapped by TEMPO, which could be detected by high-resolution mass spectrometry (calculated: 276.1958, found: 276.1952).

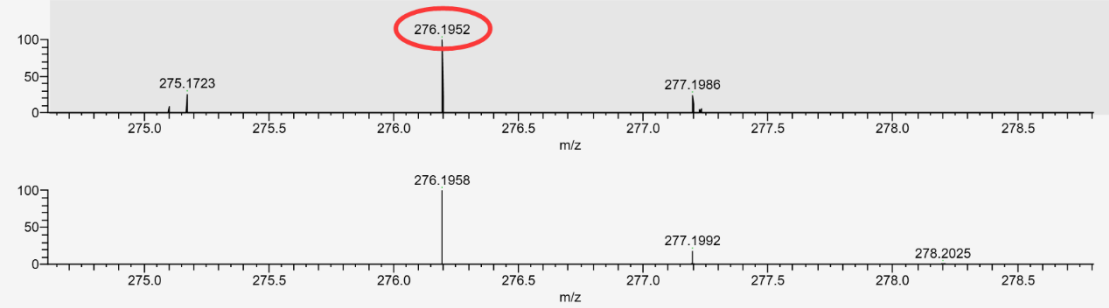


Figure S1. Detection of acyl radicals by HRMS

5.3 Light-on/Dark Experiment

To conduct the light/dark experiment, the model reaction underwent under the light for 1 hour and without the light for another hour, and on and on it went. The reaction system was added 30 mg biphenyl as the internal standard previously. Each time we turn on/off the light, we determined the reaction progress by gas chromatography.

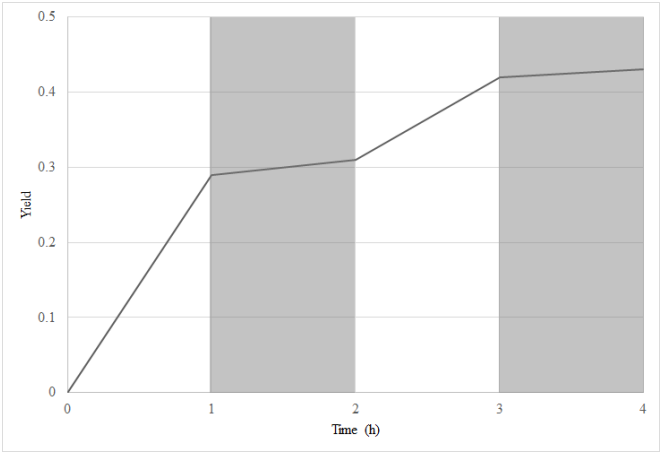


Figure S2. Result of the light/dark experiment

Obviously, the reaction occurs when the light is on. When the light is off, the reaction is almost stagnant. When we turn on the light again, the reaction continues in progress. This phenomenon could basically rule out the possibility of the radical chain propagation.

5.4 Luminescence Quenching Experiment

The experiments were carried out in 5×10^{-6} mol/L of Ir[dFCF$_3$(ppy)]$_2$(dtbbpy)PF$_6$ (**PC-I**) in DMSO at 25 °C. The emission intensity was collected at 478 nm. The concentrations of quencher (p-Toluic acid, triethylamine, pentafluoropyridine, ester **5**) in DMSO were 0.5 mmol/L, 1.5 mmol/L, 3 mmol/L, 5 mmol/L, 10 mmol/L. Based on the data shown (Fig. S3 and Fig. S4), photoexcited Ir[dFCF$_3$(ppy)]$_2$(dtbbpy)PF$_6$ (**PC-I**) can be quenched by triethylamine.

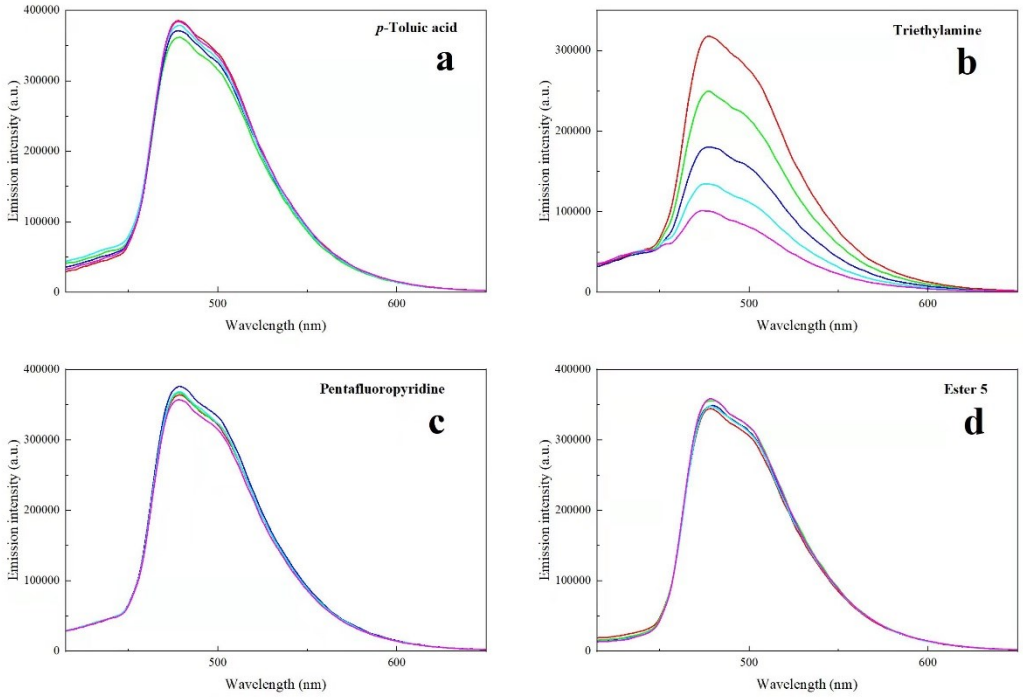


Figure S3. The data of fluorescence quenching of Ir[dFCF$_3$(ppy)]$_2$(dtbbpy)PF$_6$ quenched by **(a)** p-Toluic acid, **(b)** triethylamine, **(c)** pentafluoropyridine, **(d)** ester **5**

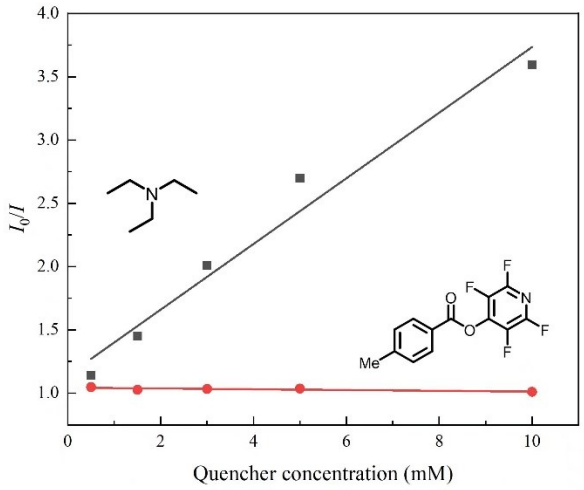


Figure S4. The standard curve of fluorescence quenching of Ir[dFCF$_3$(ppy)]$_2$(dtbbpy)PF$_6$ quenched by triethylamine and ester **5**.

5.5 ^{19}F NMR Study of the Reaction[3]

To a clean 10 mL glass vial was charged carboxylic acid (0.2 mmol), tertiary amine (3.6 equiv., 0.72 mmol), pentafluoropyridine (2 equiv., 0.4 mmol, 68 mg, 45 μL), **PC-I** (1 mol%, 0.002 mmol, 2.3 mg) and DMSO-d_6 (2 mL), and then sealed with a screw cap. The reactants were irradiated

with blue light under stirring for 6 hours. And then reaction products and by-products were identified by ^{19}F NMR (Figure S5).

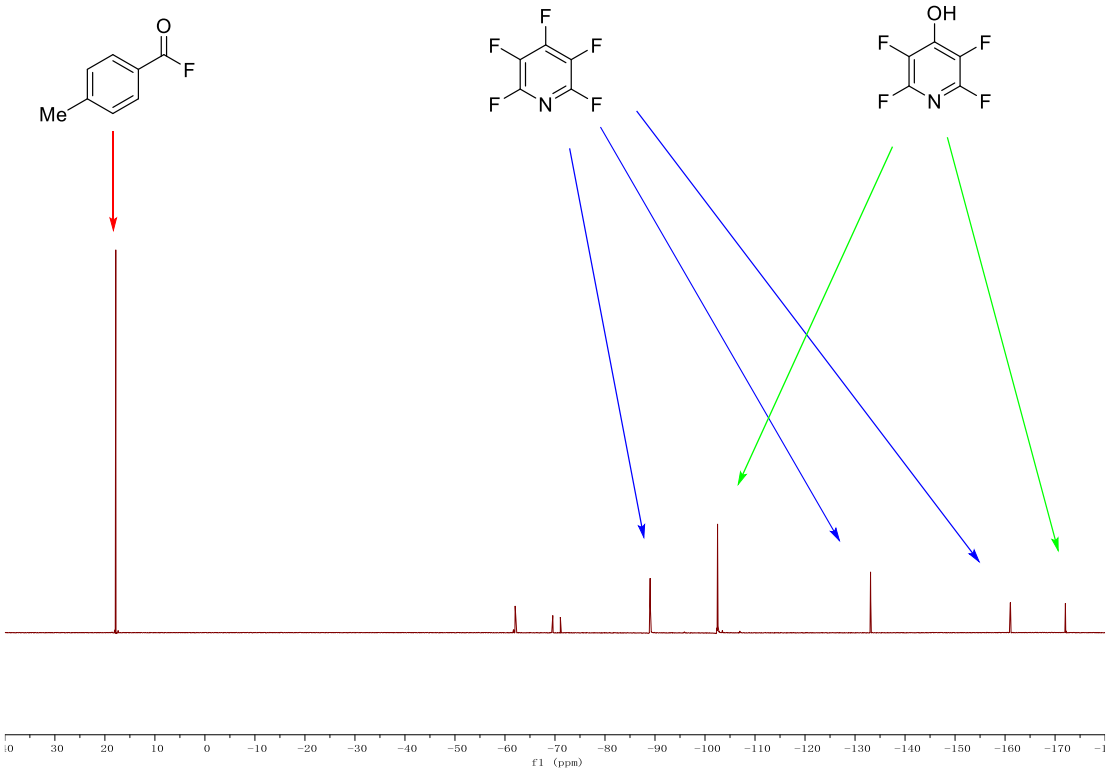


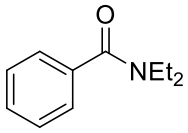
Figure S5. ^{19}F NMR study of the reaction

This spectrum is consistent with that reported in the literature[3].

The 4-methylbenzoyl fluoride, was also detected by GC-MS. However, when we used the prepared active ester instead of carboxylic acids under the standard conditions without the addition of pentafluoropyridine, the desired products can still be formed. This might imply that the formation of benzoyl fluorides might not be the intermediate for C-N bond formation under the photoredox conditions.

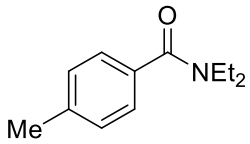
6. Characterization Data of Products

_N,N_-diethylbenzamide (3a)



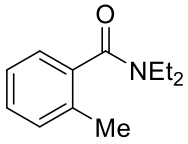
The compound was synthesized according to the general procedure in 0.2 mmol (from benzoic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 27.4 mg, 77% yield. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.49 – 7.30 (m, 5H), 3.54 (s, 2H), 3.24 (s, 2H), 1.32 – 1.00 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.2, 137.3, 129.0, 128.3, 126.2, 43.2, 39.2, 14.2, 12.9. **IR** (ATR): ν = 2972, 2934, 1624, 1425, 1285, 1071, 704 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{11}H_{16}NO$ $(M + H)^+$: 178.1226; found: 178.1227.

_N,N_-diethyl-4-methylbenzamide (3b)



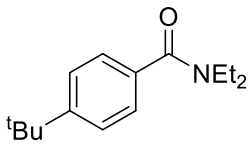
The compound was synthesized according to the general procedure in 0.2 mmol (from *p*-toluic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 31.4 mg, 83% yield. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.24 (d, *J* = 8.1 Hz, 2H), 7.16 (d, *J* = 7.8 Hz, 2H), 3.50 (s, 2H), 3.25 (s, 2H), 2.34 (s, 3H), 1.31 – 0.97 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.5, 139.0, 134.3, 128.9, 126.3, 43.3, 39.3, 21.3, 14.3, 12.9. **IR** (ATR): ν = 2970, 2933, 1625, 1423, 1287, 1093, 827 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{12}H_{18}NO$ $(M + H)^+$: 192.1383; found: 192.1382.

_N,N_-diethyl-2-methylbenzamide (3c)



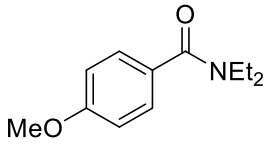
The compound was synthesized according to the general procedure in 0.2 mmol (from *o*-toluic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 35.5 mg, 93% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.32 – 7.08 (m, 4H), 3.88 – 3.30 (br, 2H), 3.11 (q, *J* = 7.0 Hz, 2H), 2.28 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.02 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.8, 137.1, 133.8, 130.2, 128.4, 125.7, 125.4, 42.5, 38.6, 18.7, 13.9, 12.8. **IR** (ATR): ν = 2973, 2933, 1627, 1425, 1292, 1082, 768 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{12}H_{18}NO$ $(M + H)^+$: 192.1383; found: 192.1383.

4-(tert-butyl)-_N,N_-diethylbenzamide (3d)



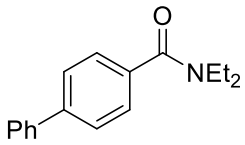
The compound was synthesized according to the general procedure in 0.2 mmol (from 4-tert-butylbenzoic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 39.2 mg, 84% yield. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.42 – 7.27 (m, 4H), 3.60 – 3.40 (m, 2H), 3.28 (s, 2H), 1.31 (s, 9H), 1.26 – 1.06 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.4, 152.1, 134.3, 126.1, 125.2, 43.2, 39.1, 34.7, 31.2, 31.1, 14.2, 12.9. **IR** (ATR): ν = 2966, 2906, 1625, 1424, 1288, 1113, 835, 733, 586 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{15}H_{24}NO$ $(M + H)^+$: 234.1852; found: 234.1850.

_N,N_-diethyl-4-methoxybenzamide (3e)



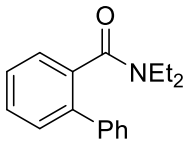
The compound was synthesized according to the general procedure in 0.2 mmol (from *p*-anisic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 37.5 mg, 90% yield. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.38 – 7.24 (m, 2H), 6.98 – 6.74 (m, 2H), 3.80 (s, 3H), 3.40 (s, 4H), 1.16 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.1, 160.2, 129.5, 128.1, 113.6, 55.2, 43.0, 39.3, 13.9, 13.3. **IR** (ATR): ν = 2972, 2936, 1608, 1423, 1245, 1172, 1028, 839, 764, 590 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{12}H_{18}NO_2$ $(M + H)^+$: 208.1332; found: 208.1330.

_N,N_-diethyl-[1,1'-biphenyl]-4-carboxamide (3f)



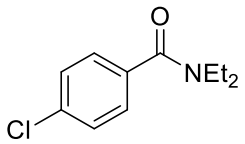
The compound was synthesized according to the general procedure in 0.2 mmol (from 4-biphenylcarboxylic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 32.1 mg, 64% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*): δ 7.63 – 7.58 (m, 4H), 7.48 – 7.42 (m, 4H), 7.39 – 7.34 (m, 1H), 3.57 (s, 2H), 3.32 (s, 2H), 1.38 – 1.03 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.0, 141.9, 140.3, 136.0, 128.8, 127.6, 127.1, 126.8, 43.3, 39.2, 14.2, 12.9. **IR** (ATR): ν = 2972, 2933, 1628, 1427, 12892, 1097, 846, 749, 698 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{17}H_{20}NO$ $(M + H)^+$: 254.1539; found: 254.1538.

_N,N_-diethyl-[1,1'-biphenyl]-2-carboxamide (3g)



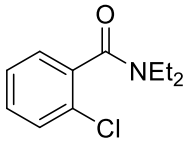
The compound was synthesized according to the general procedure in 0.2 mmol (from 2-biphenylcarboxylic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 26.9 mg, 53% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.59 – 7.29 (m, 9H), 3.82 – 3.69 (m, 1H), 3.05 – 2.88 (m, 2H), 2.69 – 2.59 (m, 1H), 0.88 (t, *J* = 7.1 Hz, 3H), 0.73 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.5, 139.8, 138.3, 136.3, 129.4, 128.9, 128.8, 128.2, 127.5, 127.0, 42.2, 38.3, 13.3, 11.9. **IR** (ATR): ν = 2972, 2933, 1623, 1425, 1286, 1096, 747, 696 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{17}H_{20}NO$ $(M + H)^+$: 254.1539; found: 254.1535.

4-chloro-_N,N_-diethylbenzamide (3h)



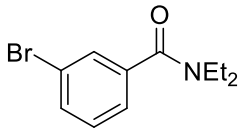
The compound was synthesized according to the general procedure in 0.2 mmol (from 4-chlorobenzoic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 31.5 mg, 74% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.38 – 7.34 (m, 2H), 7.32 – 7.28 (m, 2H), 3.52 (s, 2H), 3.23 (s, 2H), 1.42 – 0.93 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.1, 135.6, 135.1, 128.6, 127.8, 43.3, 39.3, 14.1, 12.8. **IR** (ATR): ν = 2974, 2935, 1630, 1426, 1288, 1096, 837 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{11}H_{15}NOCl$ $(M + H)^+$: 212.0837; found: 212.0838.

2-chloro-*N,N*-diethylbenzamide (3i)



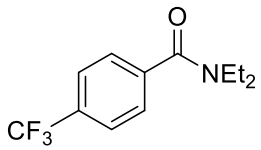
The compound was synthesized according to the general procedure in 0.2 mmol (from 2-chlorobenzoic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 37.4 mg, 87% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.41 – 7.36 (m, 1H), 7.34 – 7.24 (m, 3H), 3.83 – 3.73 (m, 1H), 3.43 – 3.33 (m, 1H), 3.20 – 3.09 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.05 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.6, 136.6, 130.2, 129.7, 129.5, 127.3, 126.9, 42.6, 38.8, 13.8, 12.5. **IR** (ATR): ν = 2974, 2935, 1629, 1427, 1290, 1106, 767 cm^{-1}. **HRMS** *m/z* (ESI) calcd for $C_{11}H_{15}NOCl$ $(M + H)^+$: 212.0837; found: 212.0837.

3-bromo-*N,N*-diethylbenzamide (3j)



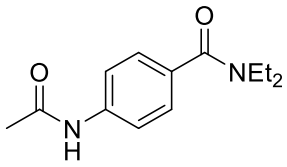
The compound was synthesized according to the general procedure in 0.2 mmol (from 3-bromobenzoic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 38.3 mg, 75% yield. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.64 – 7.17 (m, 4H), 3.53 (s, 2H), 3.24 (s, 2H), 1.32-1.00 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.4, 139.1, 132.1, 130.0, 129.3, 124.7, 122.4, 43.2, 39.3, 14.1, 12.8. **IR** (ATR): ν = 2973, 2934, 1627, 1429, 1285, 1102, 791, 733 cm^{-1}. **HRMS** *m/z* (ESI) calcd for $C_{11}H_{15}NOBr$ $(M + H)^+$: 256.0332 (^{79}Br); found: 256.0330 (^{79}Br).

***N,N*-diethyl-4-(trifluoromethyl)benzamide (3k)**



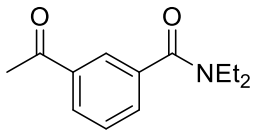
The compound was synthesized according to the general procedure in 0.2 mmol (from 4-trifluoromethylbenzoic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 30.8 mg, 63% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 8.0 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 3.63 – 3.48 (m, 2H), 3.28 – 3.15 (m, 2H), 1.35 – 1.18 (m, 3H), 1.18 – 1.01 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.8, 140.8, 131.1 (q, *J* = 35.3 Hz), 126.6, 125.5 (q, *J* = 3.8 Hz), 123.8 (q, *J* = 270.0 Hz), 43.2, 39.3, 14.2, 12.8. **IR** (ATR): ν = 2977, 2938, 1630, 1431, 1323, 1164, 1124, 1097, 847 cm^{-1}. **HRMS** *m/z* (ESI) calcd for $C_{12}H_{15}NOF_3$ $(M + H)^+$: 246.1100; found: 246.1096.

***N,N*-diethyl-4-ethynylbenzamide (3l)**



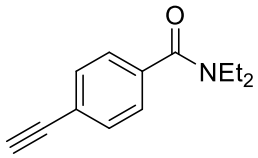
The compound was synthesized according to the general procedure in 0.2 mmol (from 4-acetylamino benzoic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 28.3 mg, 62% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.25 (s, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 3.65 – 3.40 (m, 2H), 3.39 – 3.16 (m, 2H), 2.15 (s, 3H), 1.36 – 0.99 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.2, 168.9, 139.1, 132.4, 127.0, 119.8, 43.4, 39.4, 24.4, 14.1, 12.8. **IR** (ATR): ν = 3379, 2988, 2920, 1659, 1607, 1469, 1436, 1315, 1015, 951, 703 cm^{-1}. **HRMS** *m/z* (ESI) calcd for $C_{13}H_{19}N_2O_2$ $(M + H)^+$: 235.1441; found: 235.1439.

3-acetyl-*N*,*N*-diethylbenzamide (3m)



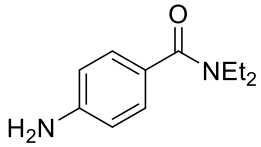
The compound was synthesized according to the general procedure in 0.2 mmol (from 3-acetylbenzoic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 27.1 mg, 61% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.01 – 7.94 (m, 2H), 7.59 – 7.55 (m, 1H), 7.53 – 7.48 (m, 1H), 3.56 (s, 2H), 3.24 (s, 2H), 2.61 (s, 3H), 1.26 (s, 3H), 1.12 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 197.4, 170.2, 137.7, 137.2, 130.8, 128.9, 128.8, 126.3, 43.4, 39.4, 26.7, 14.2, 12.9. **IR** (ATR): ν = 2973, 2934, 1685, 1625, 1420, 1252, 796 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{13}H_{18}NO_2$ $(M + H)^+$: 220.1332; found: 220.1330.

***N*,*N*-diethyl-4-ethynylbenzamide (3n)**



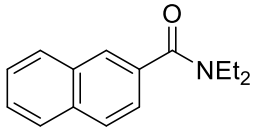
The compound was synthesized according to the general procedure in 0.2 mmol (from 4-ethynylbenzoic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 20.4 mg, 50% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.51 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 3.54 (s, 2H), 3.23 (s, 2H), 3.12 (s, 1H), 1.24 (s, 3H), 1.10 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.4, 137.5, 132.2, 126.3, 123.0, 82.9, 78.3, 43.3, 39.3, 14.2, 12.8. **IR** (ATR): ν = 3291, 2973, 2934, 1621, 1426, 1287, 1094, 843, 763 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{13}H_{16}NO$ $(M + H)^+$: 202.1226; found: 202.1226.

4-amino-*N*,*N*-diethylbenzamide (3o)



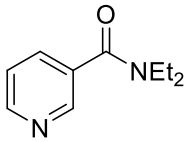
The compound was synthesized according to the general procedure in 0.2 mmol (from 4-amino benzoic acid and triethylamine) and purified by flash chromatography (PE/EA = 1:1). White solid (m.p. = 91-93 ℃), 20.2 mg, 52% yield. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.24 – 7.17 (m, 2H), 6.66 – 6.60 (m, 2H), 3.83 (s, 2H), 3.41 (s, 4H), 1.16 (t, *J* = 6.9 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.6, 146.4, 128.2, 127.6, 115.0, 29.3, 13.4. **IR** (ATR): ν = 3339, 3224, 2972, 2933, 1596, 1422, 1282, 1096, 838 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{11}H_{17}N_2O$ (Mj+ $H)^+$: 193.1335; found: 193.1335.

***N*,*N*-diethyl-2-naphthamide (3p)**



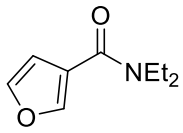
The compound was synthesized according to the general procedure in 0.2 mmol (from 2-naphthoic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 38.1 mg, 84% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.15 – 7.80 (m, 4H), 7.68 – 7.28 (m, 3H), 3.60 (s, 2H), 3.30 (s, 2H), 1.53 – 0.90 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.2, 134.5, 133.3, 132.7, 128.2, 127.7, 126.7, 125.6, 123.8, 43.3, 39.2, 14.2, 12.9. **IR** (ATR): ν = 2972, 2934, 1622, 1424, 1288, 1088, 864, 757 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{15}H_{18}NO$ $(M + H)^+$: 228.1383; found: 228.1379.

***N,N*-diethylnicotinamide (3q)**



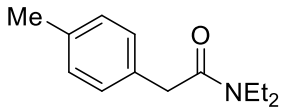
The compound was synthesized according to the general procedure in 0.2 mmol (from nicotinic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 29.6 mg, 85% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 8.58 – 8.55 (m, 1H), 7.79 – 7.73 (m, 1H), 7.58 – 7.53 (m, 1H), 7.33 – 7.28 (m, 1H), 3.56 (q, *J* = 7.1 Hz, 2H), 3.37 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H), 1.14 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 168.5, 155.2, 148.3, 136.8, 124.0, 122.9, 43.1, 40.1, 14.3, 12.8. **IR** (ATR): ν = 2973, 2934, 1625, 1420, 1107, 749 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{10}H_{15}N_2O$ $(M + H)^+$: 179.1179; found: 179.1178.

***N,N*-diethylfuran-3-carboxamide (3r)**



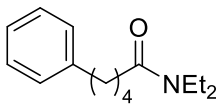
The compound was synthesized according to the general procedure in 0.2 mmol (from 3-furoic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 29.9 mg, 84% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.69 – 7.68 (m, 1H), 7.41 – 7.38 (m, 1H), 6.58 – 6.57 (m, 1H), 3.52 – 3.40 (m, 4H), 1.20 (t, *J* = 7.1 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 164.1, 142.7, 121.8, 110.1, 42.8, 39.9, 14.5, 12.7. **IR** (ATR): ν = 2974, 2935, 1614, 1429, 1024, 751 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_9H_{14}NO_2$ $(M + H)^+$: 168.1019; found: 168.1018.

***N,N*-diethyl-2-(p-tolyl)acetamide (3s)**



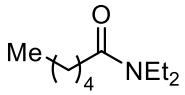
The compound was synthesized according to the general procedure in 0.2 mmol (from 4-methylphenylacetic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 27.6 mg, 66% yield. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.17 – 7.08 (m, 4H), 3.65 (s, 2H), 3.38 (q, *J* = 7.1 Hz, 2H), 3.29 (q, *J* = 7.1 Hz, 2H), 2.32 (s, 3H), 1.16 – 1.04 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.3, 136.1, 132.4, 129.3, 128.5, 42.3, 40.5, 40.1, 29.7, 21.0, 14.2, 12.9. **IR** (ATR): ν = 2971, 2925, 1638, 1461, 1258, 1075, 790 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{13}H_{20}NO$ $(M + H)^+$: 206.1539; found: 206.1538.

***N,N*-diethyl-5-phenylpentanamide (3t)**



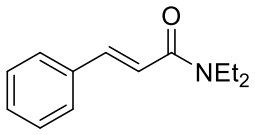
The compound was synthesized according to the general procedure in 0.2 mmol (from 5-phenylvaleric acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 41.0 mg, 88% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.32 – 7.25 (m, 2H), 7.23 – 7.16 (m, 3H), 3.38 (q, *J* = 7.1 Hz, 2H), 3.29 (q, *J* = 7.2 Hz, 2H), 2.66 (t, *J* = 7.2 Hz, 2H), 2.32 (t, *J* = 7.2 Hz, 2H), 1.77 – 1.65 (m, 4H), 1.16 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.9, 142.3, 128.3, 125.6, 41.9, 40.0, 35.7, 32.9, 31.2, 25.1, 14.3, 13.0. **IR** (ATR): ν = 2971, 2931, 1636, 1427, 1263, 1081, 745, 699 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{15}H_{24}NO$ $(M + H)^+$: 234.1852; found: 234.1850.

***N,N*-diethylhexanamide (3u)**



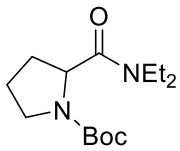
The compound was synthesized according to the general procedure in 0.2 mmol (from hexanoic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless liquid, 28.4 mg, 86% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 3.37 – 3.22 (m, 4H), 2.33 – 2.14 (m, 2H), 1.66 – 1.55 (m, 2H), 1.35 – 1.23 (m, 4H), 1.13 (t, *J* = 7.1 Hz, 3H), 1.06 (t, *J* = 7.1 Hz, 3H), 0.86 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.3, 41.9, 39.9, 33.0, 31.6, 25.1, 22.4, 14.3, 13.9, 13.0. **IR** (ATR): ν = 2959, 2930, 1637, 1426, 1260, 1096 cm^{-1}. **HRMS** *m/z* (ESI) calcd for $C_{10}H_{22}NO$ $(M + H)^+$: 172.1696; found: 172.1696.

***N,N*-diethylcinnamamide (3v)**



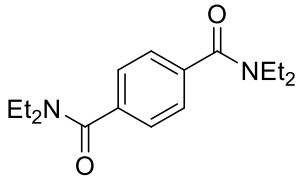
The compound was synthesized according to the general procedure in 0.2 mmol (from cinnamic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 29.4 mg, 72% yield. **^{1}H NMR** (400 MHz, Chloroform-*d*) δ 7.45 – 7.40 (m, 2H), 7.37 – 7.21 (m, 3H), 6.62 (d, *J* = 12.7 Hz, 1H), 6.08 (d, *J* = 12.7 Hz, 1H), 3.49 (q, *J* = 7.1 Hz, 2H), 3.28 (q, *J* = 7.1 Hz, 2H), 1.19 (t, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.3, 136.2, 132.4, 129.3, 128.5, 42.3, 40.5, 40.1, 21.0, 14.2, 12.9. **IR** (ATR): ν = 2972, 2933, 1611, 1430, 1270, 1142, 1077, 781, 698 cm^{-1}. **HRMS** *m/z* (ESI) calcd for $C_{13}H_{18}NO$ $(M + H)^+$: 204.1383; found: 204.1382.

tert-butyl 2-(diethylcarbamoyl)pyrrolidine-1-carboxylate (3w)



The compound was synthesized according to the general procedure in 0.2 mmol (from N-BOC-L-proline and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless crystal (m.p. = 49-51 °C), 38.0 mg, 70% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 4.61 – 4.54 (m, 0.4H), 4.45 – 4.38 (m, 0.6H), 3.77 – 3.05 (m, 6H), 2.22 – 1.94 (m, 2H), 1.89 – 1.74 (m, 2H), 1.42 (s, 3H), 1.38 (s, 6H), 1.26 – 1.16 (m, 3H), 1.15 – 1.04 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.9, 154.4, 153.9, 79.4, 79.2, 56.4, 56.1, 46.9, 46.8, 41.7, 40.9, 40.7, 31.2, 30.2, 28.5, 28.4, 24.1, 23.4, 14.7, 13.1, 12.9. **IR** (ATR): ν = 2973, 2932, 1694, 1949, 1393, 1257, 1163, 1119 cm^{-1}. **HRMS** *m/z* (ESI) calcd for $C_{14}H_{27}N_2O_3$ $(M + H)^+$: 271.2016; found: 271.2009.

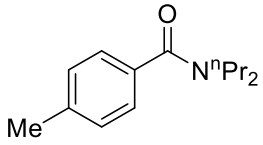
***N*^{1},*N*^{1},*N*^{4},*N*^{4}-tetraethylterephthalamide (3x)**



The compound was synthesized according to the modified procedure in 0.2 mmol (with 1 equiv. terephthalic acid, 7.2 equiv. triethylamine, 4 equiv. pentafluoropyridine, 2 mol% **PC-I** and 4 mL DMSO), and purified by flash chromatography (PE/EA = 1:1). White solid (m.p. = 110-112 °C), 23.3 mg, 42% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.39 (s, 4H), 3.62 – 3.47 (m, 4H), 3.31 – 3.16 (m, 4H), 1.33 – 1.18 (m, 6H), 1.15 – 1.02 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.6, 138.0, 126.4, 43.2, 39.2, 14.2, 12.9. **IR** (ATR): ν = 2974, 2935, 1616,

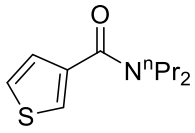
1433, 1291, 1102, 840, 733 cm^{-1}. **HRMS** *m/z* (ESI) calcd for $C_{16}H_{25}N_2O_2$ $(M + H)^+$: 277.1911; found: 277.1904.

4-methyl-*N,N*-dipropylbenzamide (3y)



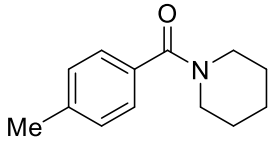
The compound was synthesized according to the general procedure in 0.2 mmol (from *p*-toluic acid and tripropylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 24.1 mg, 55% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.23 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 3.43 (s, 2H), 3.16 (s, 2H), 2.35 (s, 3H), 1.66 (s, 2H), 1.51 (s, 2H), 0.95 (s, 3H), 0.73 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 171.9, 138.9, 134.4, 128.9, 126.4, 50.7, 46.2, 21.8, 21.3, 20.6, 11.4, 11.0. **IR** (ATR): ν = 2963, 2932, 1627, 1420, 1256, 1097, 828, 752 cm^{-1}. **HRMS** *m/z* (ESI) calcd for $C_{14}H_{22}NO$ $(M + H)^+$: 220.1696; found: 220.1693.

***N,N*-dipropylthiophene-3-carboxamide (3z)**



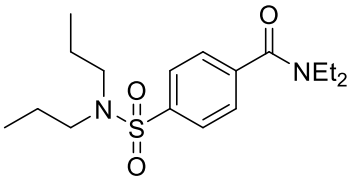
The compound was synthesized according to the general procedure in 0.2 mmol (from 3-thiophenezoic acid and tripropylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 33.9 mg, 80% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.43 (dd, *J* = 2.9, 1.2 Hz, 1H), 7.32 – 7.28 (m, 1H), 7.15 (dd, *J* = 5.0, 1.2 Hz, 1H), 3.56 – 3.07 (m, 4H), 1.77 – 1.42 (m, 4H), 1.05 – 0.66 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 167.1, 137.5, 126.8, 125.6, 124.9, 50.6, 46.8, 22.1, 20.6, 11.4, 11.0. **IR** (ATR): ν = 2964, 2933, 1624, 1427, 1252, 1098, 740 cm^{-1}. **HRMS** *m/z* (ESI) calcd for $C_{11}H_{18}NOS$ $(M + H)^+$: 212.1104; found: 212.1104.

piperidin-1-yl(p-tolyl)methanone (3aa)



The compound was synthesized according to the general procedure in 0.2 mmol (from *p*-toluic acid and N-methylpiperidine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 12.8 mg, 32% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.28 (d, *J* = 8.1 Hz, 2H), 7.19 (d, *J* = 7.8 Hz, 2H), 3.69 (s, 2H), 3.35 (s, 2H), 2.36 (s, 3H), 1.72 – 1.45 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.5, 139.4, 133.5, 128.9, 126.9, 48.8, 43.1, 26.5, 25.6, 24.6, 21.3. **IR** (ATR): ν = 2934, 2856, 1628, 1431, 1274, 1109, 1002, 829, 752 cm^{-1}. **HRMS** *m/z* (ESI) calcd for $C_{13}H_{18}NO$ $(M + H)^+$: 204.1383; found: 204.1382.

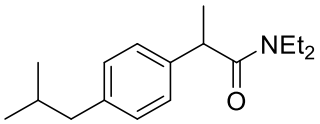
4-(N,N-dipropylsulfamoyl)-N,N-diethylbenzamide (4a)



The compound was synthesized according to the general procedure in 0.2 mmol and purified by flash chromatography (PE/EA = 3:1). White solid (m.p. = 58-60 °C), 30.5 mg, 48% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 7.8 Hz,

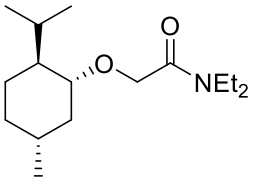
2H), 7.48 (d, *J* = 7.8 Hz, 2H), 3.61 – 3.48 (m, 2H), 3.27 – 3.14 (m, 2H), 3.13 – 3.01 (m, 4H), 1.60 – 1.51 (m, 4H), 1.30 – 1.20 (m, 3H), 1.14 – 1.04 (m, 3H), 0.87 (t, *J* = 7.3 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.6, 141.0, 140.8, 127.3, 126.9, 50.1, 43.3, 39.4, 22.0, 14.2, 12.8, 11.1. **IR** (ATR): ν = 2969, 2935, 2876, 1630, 1459, 1428, 1338, 1286, 1155, 1084, 991, 843, 751, 595 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{17}H_{29}N_2O_3S$ $(M + H)^+$: 341.1893; found: 341.1891.

N,N-diethyl-2-(4-isobutylphenyl)propenamide (4b)



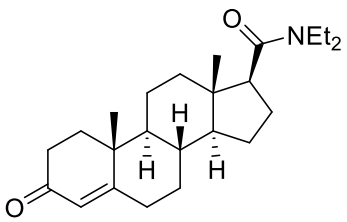
The compound was synthesized according to the general procedure in 0.2 mmol (from probenecid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 44.2 mg, 84% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.15 (d, *J* = 7.8 Hz, 2H), 7.06 (d, *J* = 7.8 Hz, 2H), 3.79 (q, *J* = 6.8 Hz, 1H), 3.50 – 3.41 (m, 1H), 3.34 – 3.21 (m, 2H), 3.16 – 3.08 (m, 1H), 2.42 (d, *J* = 7.2 Hz, 2H), 1.87 – 1.78 (m, 1H), 1.41 (d, *J* = 6.9 Hz, 3H), 1.08 (t, *J* = 7.1 Hz, 3H), 0.94 (t, *J* = 7.1 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.9, 139.9, 139.6, 129.4, 126.9, 45.0, 42.7, 41.6, 40.2, 30.1, 22.3, 20.9, 14.1, 12.8. **IR** (ATR): ν = 2968, 2929, 1640, 1461, 1429, 1267, 1066 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{17}H_{28}NO$ $(M + H)^+$: 262.2165; found: 262.2162.

N,N-diethyl-2-(((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)oxy)acetamide (4c)



The compound was synthesized according to the general procedure in 0.2 mmol (from (-)-menthoxyacetic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 43.1 mg, 67% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 4.18 – 4.10 (m, 2H), 4.08 – 4.00 (m, 2H), 3.46 – 3.26 (m, 4H), 3.20 – 3.11 (m, 1H), 2.27 – 2.16 (m, 1H), 2.15 – 2.07 (m, 1H), 1.66 – 1.54 (m, 2H), 1.39 – 1.17 (m, 3H), 1.14 (t, *J* = 7.1 Hz, 3H), 1.09 (t, *J* = 7.1 Hz, 3H), 1.00 – 0.76 (m, 8H), 0.75 – 0.72 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 168.8, 79.7, 68.3, 48.2, 41.2, 39.9, 39.7, 34.4, 31.4, 25.4, 23.1, 22.2, 20.9, 16.1, 14.2, 12.7. **IR** (ATR): ν = 2954, 2924, 2869, 1645, 1457, 1381, 1368, 1099 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{16}H_{32}NO_2$ $(M + H)^+$: 270.2428; found: 270.2422.

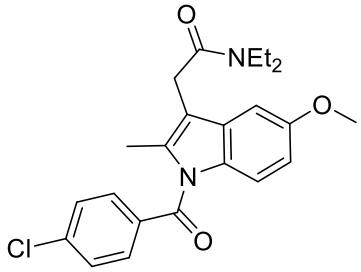
(8S,9S,10R,13S,14S,17S)-N,N-diethyl-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthrene-17-carboxamide (4d)



The compound was synthesized according to the general procedure in 0.2 mmol (from AD-17-carboxylic acid and triethylamine) and purified by flash chromatography (PE/EA = 3:1). White solid (m.p. = 96-98°C), 33.2 mg, 44% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 5.71 (s, 1H), 3.79 – 3.69 (m, 1H), 3.68 – 3.58 (m, 1H), 3.15 – 3.05 (m, 1H), 3.03 – 2.94 (m, 1H), 2.64 (t, *J* = 9.0 Hz, 1H), 2.45 – 2.32 (m, 3H),

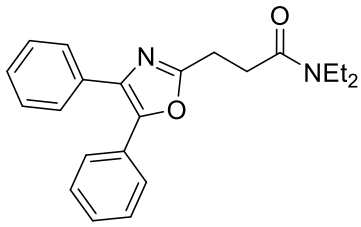
2.29 – 2.23 (m, 2H), 2.04 – 1.96 (m, 1H), 1.89 – 1.83 (m, 1H), 1.82 – 1.77 (m, 1H), 1.75 – 1.65 (m, 3H), 1.62 – 1.53 (m, 2H), 1.46 (qd, *J* = 13.2, 3.9 Hz, 1H), 1.39 – 1.20 (m, 3H), 1.17 (s, 3H), 1.13 – 1.06 (m, 6H), 1.05 – 0.97 (m, 1H), 0.97 – 1.90 (m, 1H), 0.78 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 199.4, 172.1, 171.1, 123.8, 55.8, 53.8, 50.9, 44.9, 41.8, 40.2, 38.7, 38.6, 35.7, 35.6, 33.9, 32.8, 32.0, 25.8, 24.6, 20.9, 17.3, 14.7, 13.9, 13.5. **IR** (ATR): ν = 2970, 2937, 1669, 1629, 1449, 1429,1381, 1263, 1132, 1067, 867, 732, 701 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{24}H_{38}NO_2$ $(M + H)^+$: 372.2897; found: 372.2891.

2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)-N,N-diethylacetamid (4e)



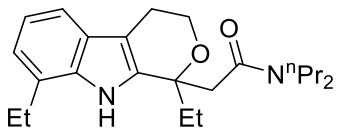
The compound was synthesized according to the general procedure in 0.2 mmol (from indometacin and triethylamine) and purified by flash chromatography (PE/EA = 3:1). Colorless oil, 48.5 mg, 59% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.68 – 7.64 (m, 2H), 7.48 – 7.44 (m, 2H), 7.02 (d, *J* = 2.5 Hz, 1H), 6.82 (d, *J* = 9.0 Hz, 1H), 6.66 – 6.62 (m, 1H), 3.82 (s, 3H), 3.70 (s, 2H), 3.44 – 3.35 (m, 4H), 2.38 (s, 3H), 1.18 – 1.09 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 169.1, 168.3, 155.9, 139.1, 135.1, 134.0, 131.1, 130.9, 130.8, 129.0, 114.8, 113.8, 111.5, 101.5, 55.6, 42.3, 40.6, 30.5, 14.2, 13.4, 13.1. **IR** (ATR): ν = 2972, 2931, 1678, 1637, 1476, 1454, 1356, 1314, 1221, 1087, 1066, 833, 755 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{23}H_{26}N_2O_3Cl$ $(M + H)^+$: 413.3626; found: 413.3617.

3-(4,5-diphenyloxazol-2-yl)-N,N-diethylpropanamide (4f)



The compound was synthesized according to the general procedure in 0.2 mmol (from oxaprozin and triethylamine) and purified by flash chromatography (PE/EA = 1:1). Colorless oil, 63.3 mg, 90% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 7.68 – 7.59 (m, 2H), 7.59 – 7.52 (m, 2H), 7.38 – 7.26 (m, 6H), 3.45 – 3.33 (m, 4H), 3.26 – 3.20 (m, 2H), 2.92 – 2.86 (m, 2H), 1.20 (t, *J* = 7.2, 7.2 Hz, 3H), 1.12 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.0, 162.7, 145.1, 134.9, 132.5, 128.9, 128.5, 128.4, 128.2, 127.9, 127.8, 126.3, 41.8, 40.2, 29.8, 23.8, 14.2, 13.0. **IR** (ATR): ν = 2974, 2932, 1638, 1446, 1265, 1221, 1058, 764, 733, 693 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{22}H_{25}N_2O_2$ $(M + H)^+$: 349.1911; found: 349.1904.

2-(1,8-diethyl-1,3,4,9-tetrahydropyrano[3,4-b]indol-1-yl)-N,N-dipropylacetamide (4g)

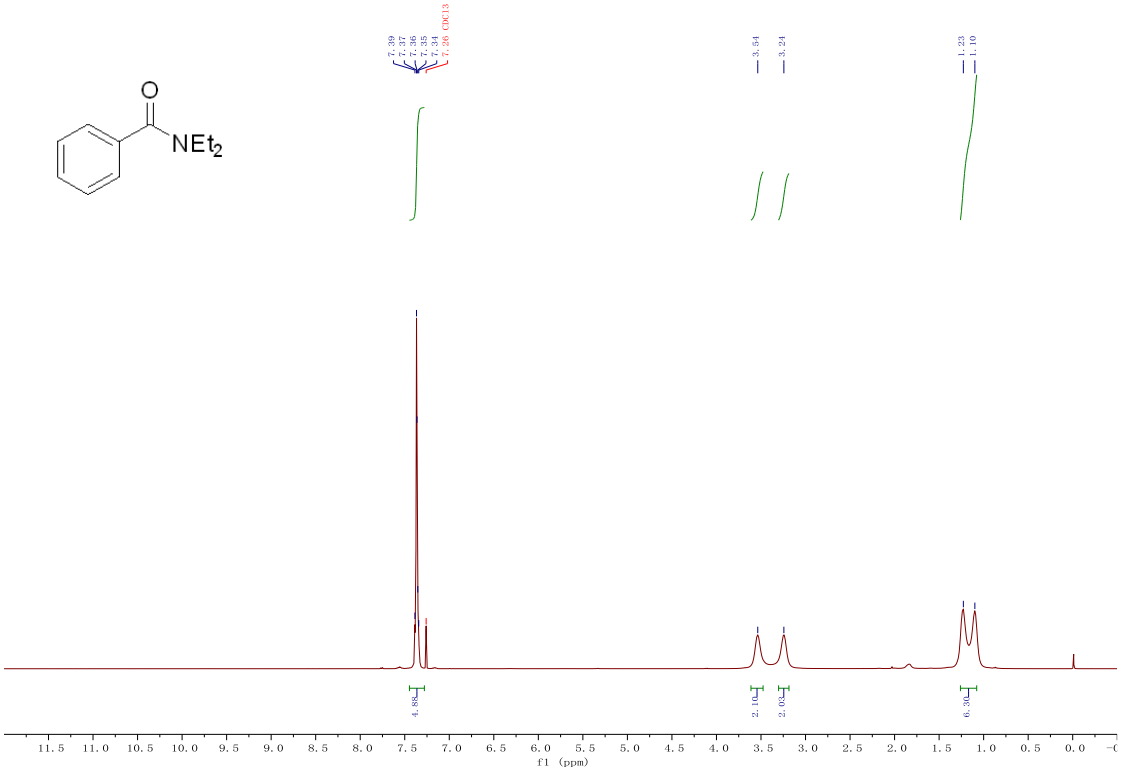


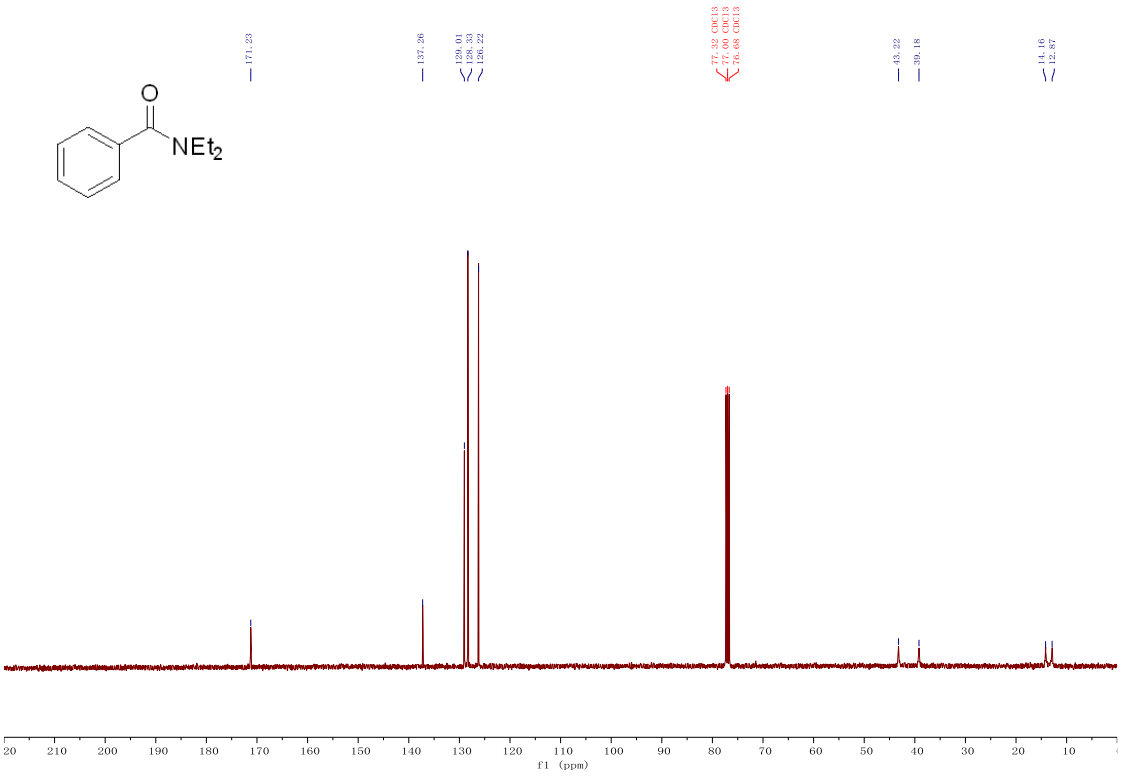
The compound was synthesized according to the general procedure in 0.2 mmol (from etodolac and tripropylamine) and purified by flash chromatography (PE/EA = 5:1). Colorless oil, 47.8 mg, 65% yield. **^{1}H NMR** (500 MHz, Chloroform-*d*) δ 10.09 (s, 1H), 7.36 (d, *J* = 7.7 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 6.8 Hz, 1H), 4.08 – 4.02 (m, 1H), 4.01 – 3.95 (m, 1H), 3.41 – 3.32 (m, 1H), 3.31 – 3.24 (m, 1H), 3.24 – 3.15 (m, 2H), 2.97 – 2.77 (m, 6H), 2.27 – 2.19 (m, 2H), 1.63 – 1.50 (m, 4H), 1.37 (t, *J* = 7.6 Hz, 3H), 0.92 (td, *J* = 7.4, 2.4 Hz, 6H), 0.86 (t, *J* =

7.4 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.8, 137.2, 134.1, 126.8, 126.1, 119.9, 119.1, 115.7, 107.0, 77.3, 60.4, 50.2, 48.0, 41.5, 29.8, 24.3, 22.5, 22.0, 20.9, 13.8, 11.4, 11.2, 7.8. **IR** (ATR): ν = 3327, 2964, 2933, 2875, 1630, 1607, 1455, 1228, 1100, 1076, 1051, 924, 743, 630, 613 cm^{-1}. **HRMS** *m*/*z* (ESI) calcd for $C_{23}H_{35}N_2O_2$ $(M + H)^+$: 371.2693; found: 371.2685.

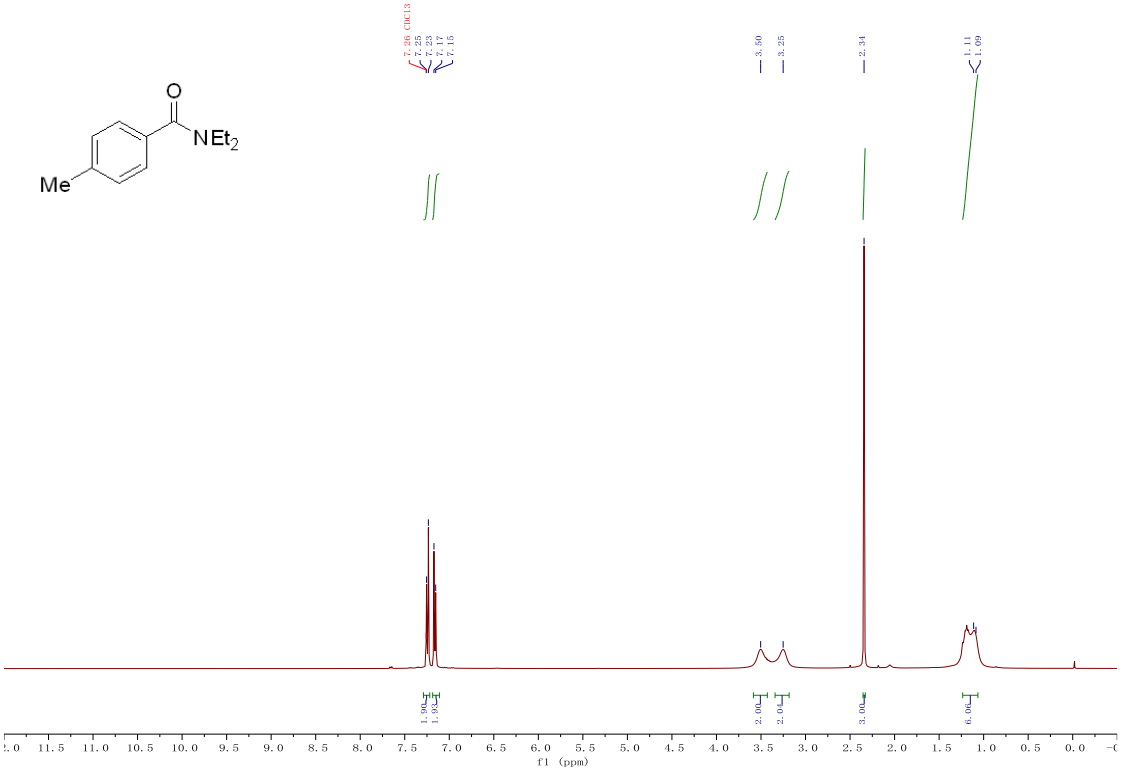
7. NMR Spectra

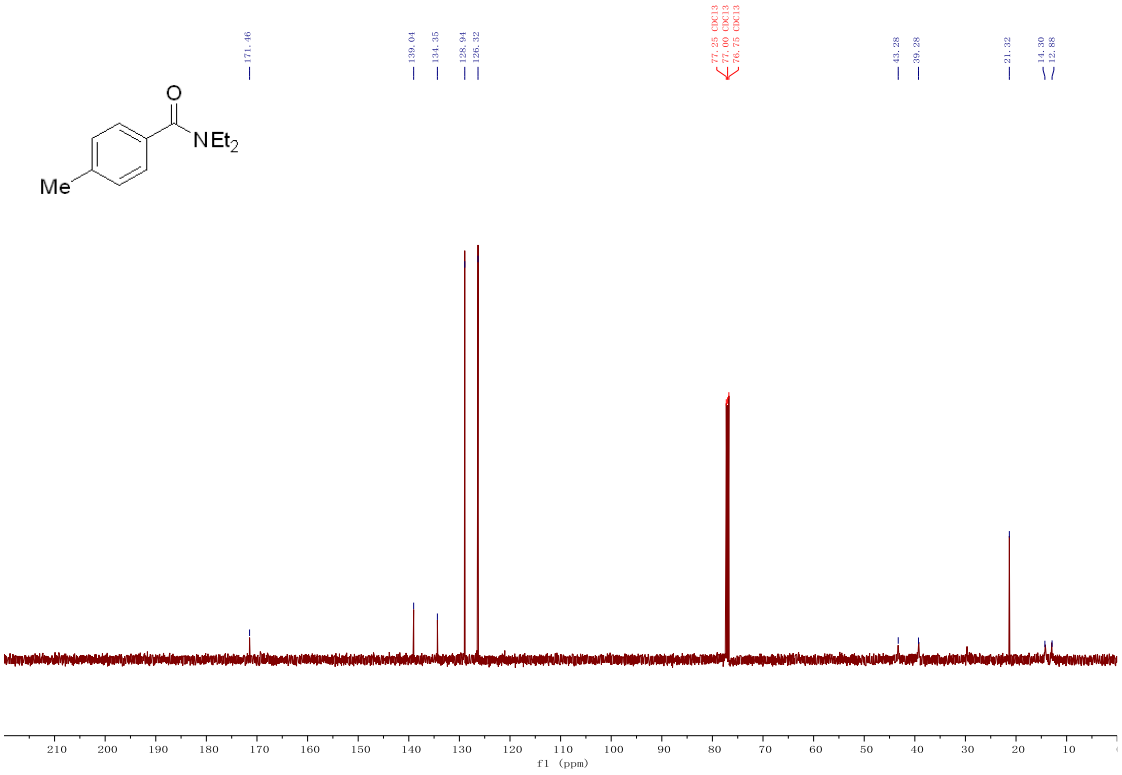
N,N-diethylbenzamide (3a)



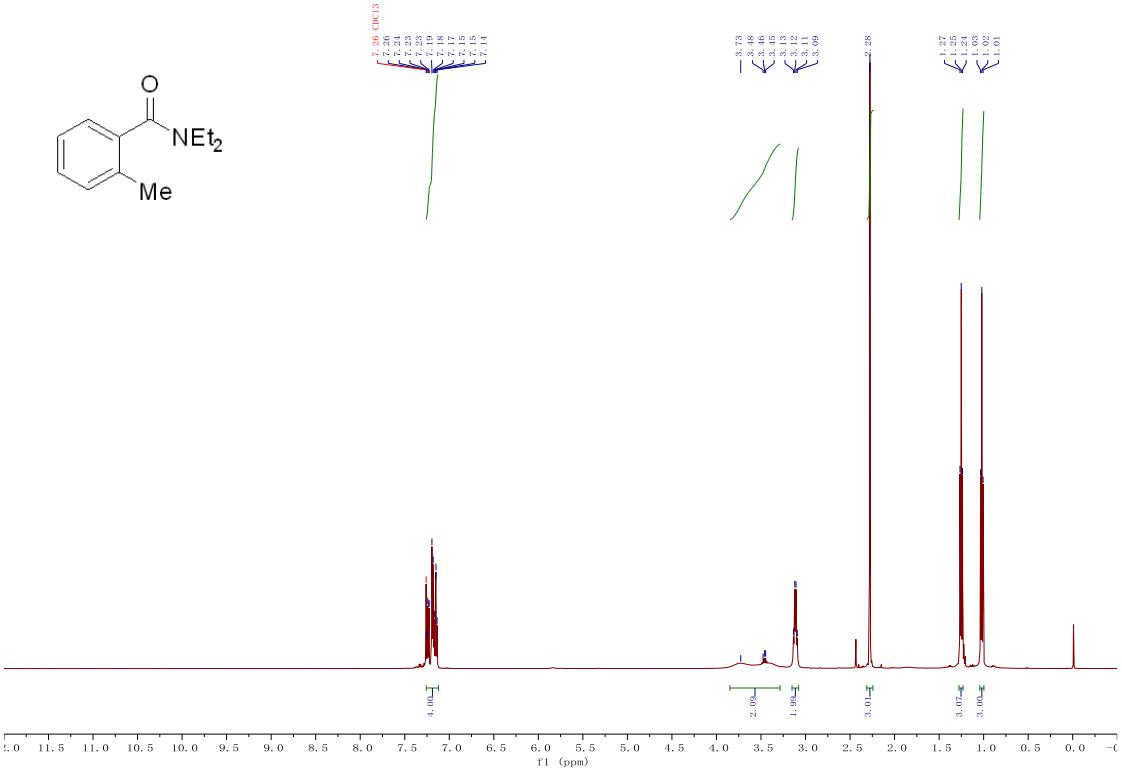


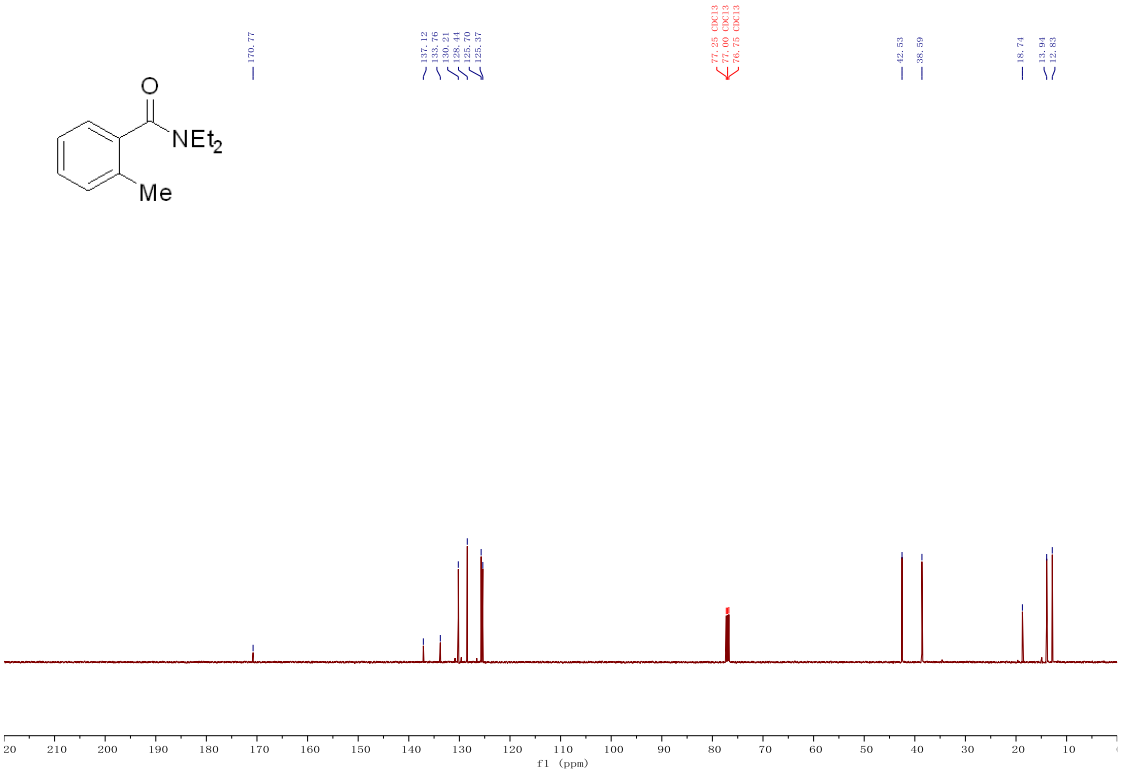
N,N-diethyl-4-methylbenzamide (3b)



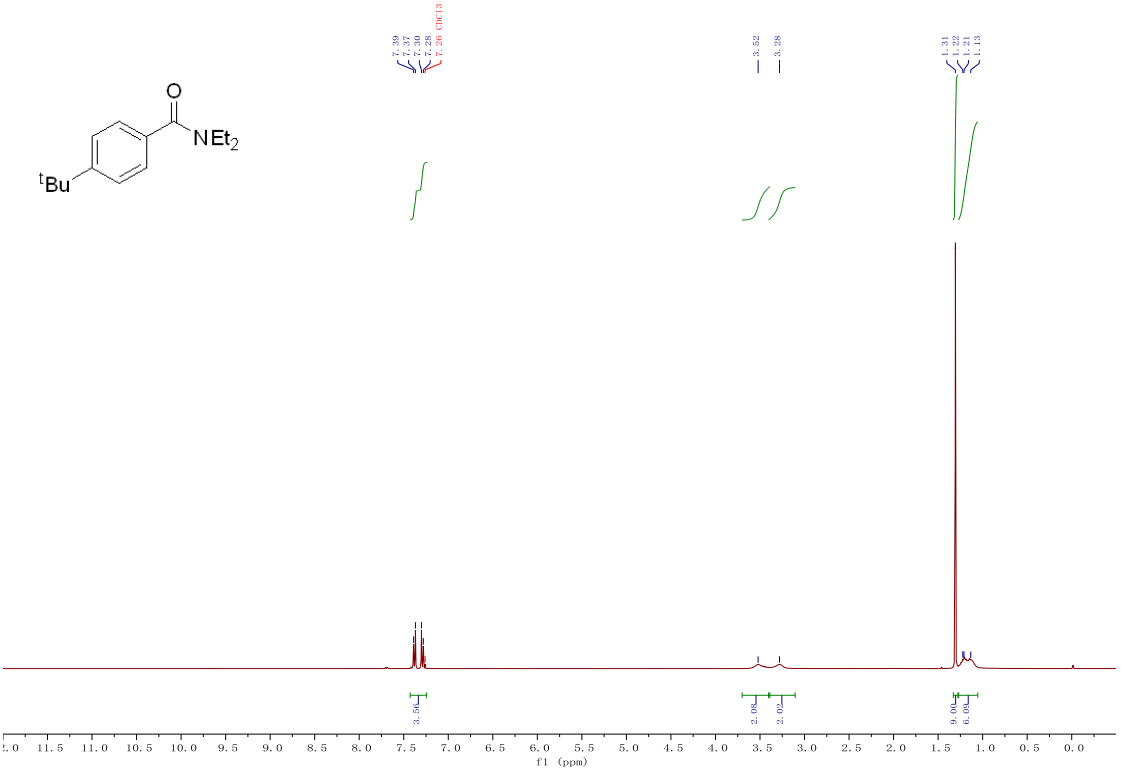


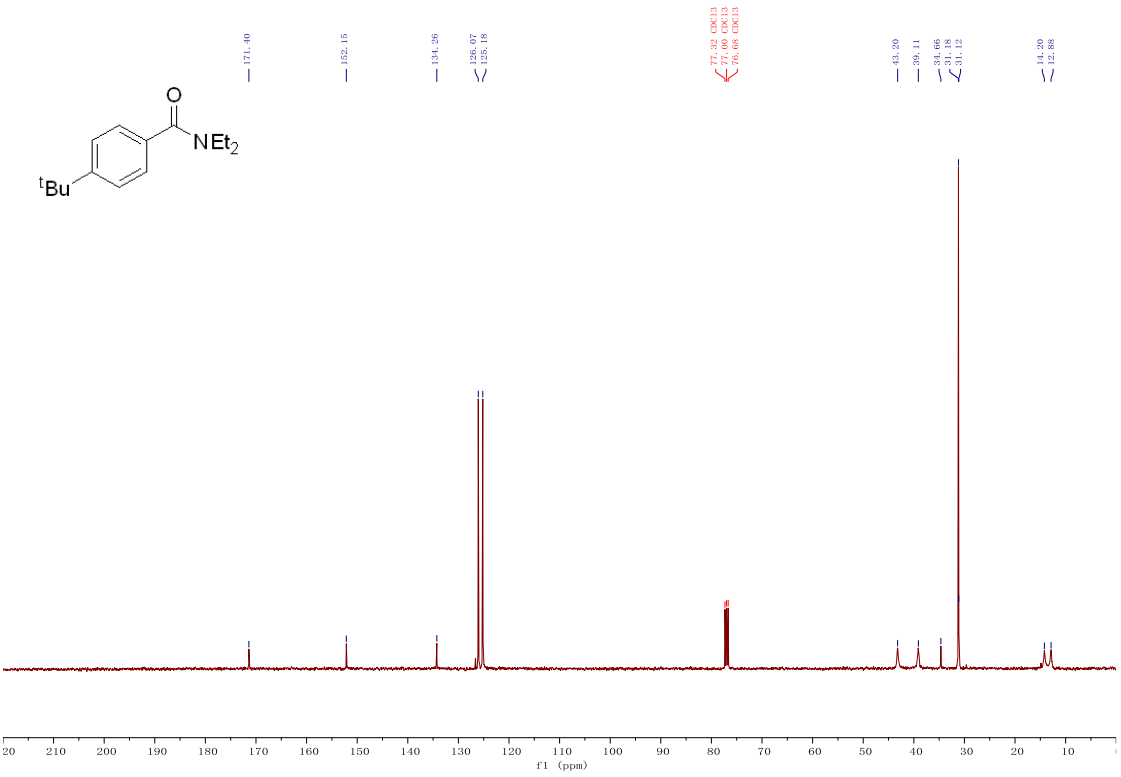
N,N-diethyl-2-methylbenzamide (3c)



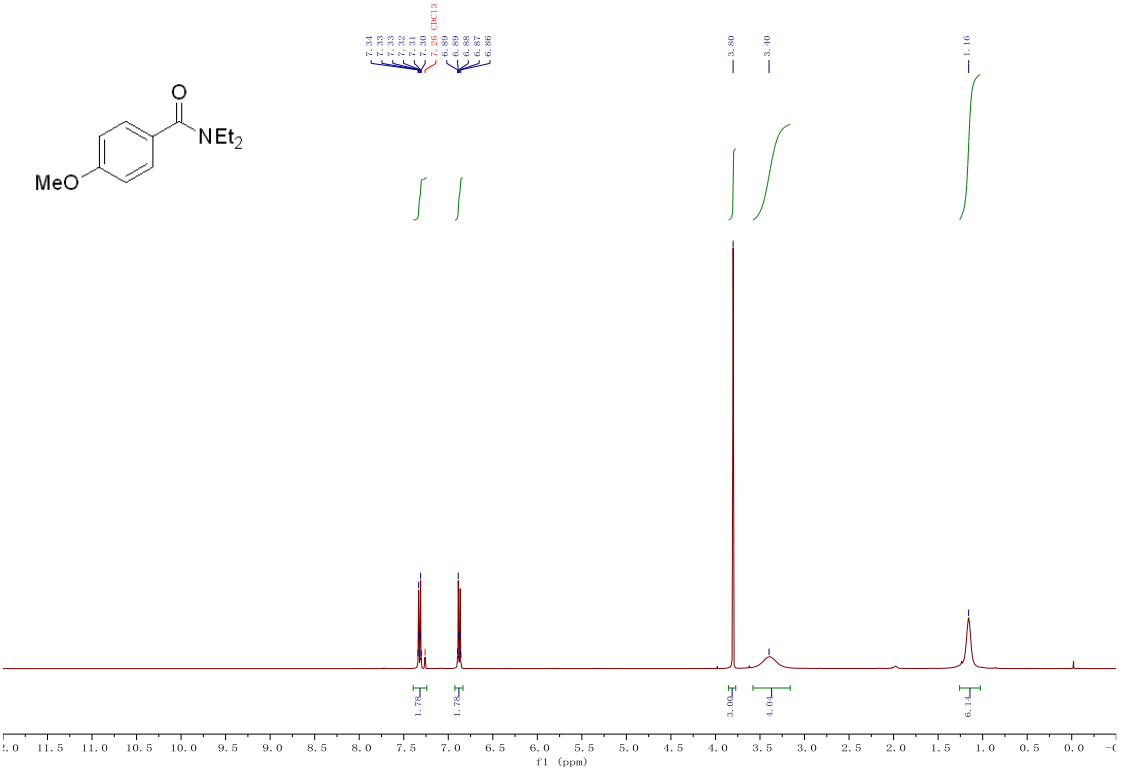


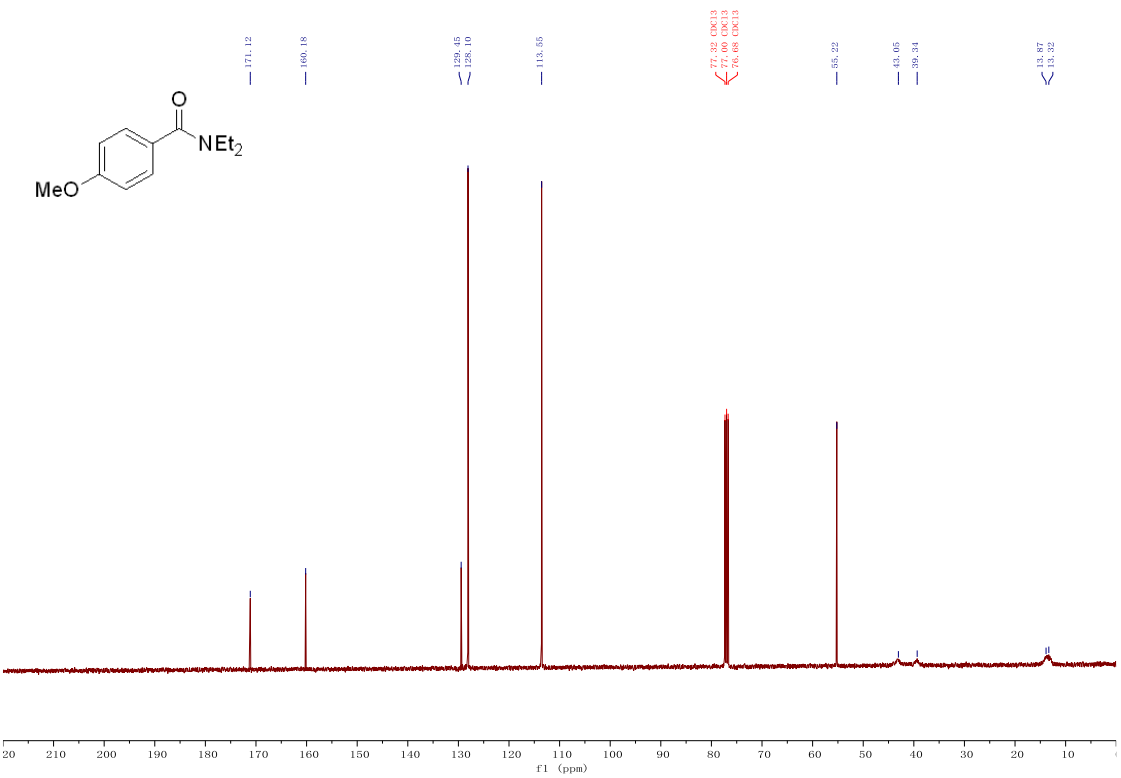
4-(tert-butyl)-N,N-diethylbenzamide (3d)



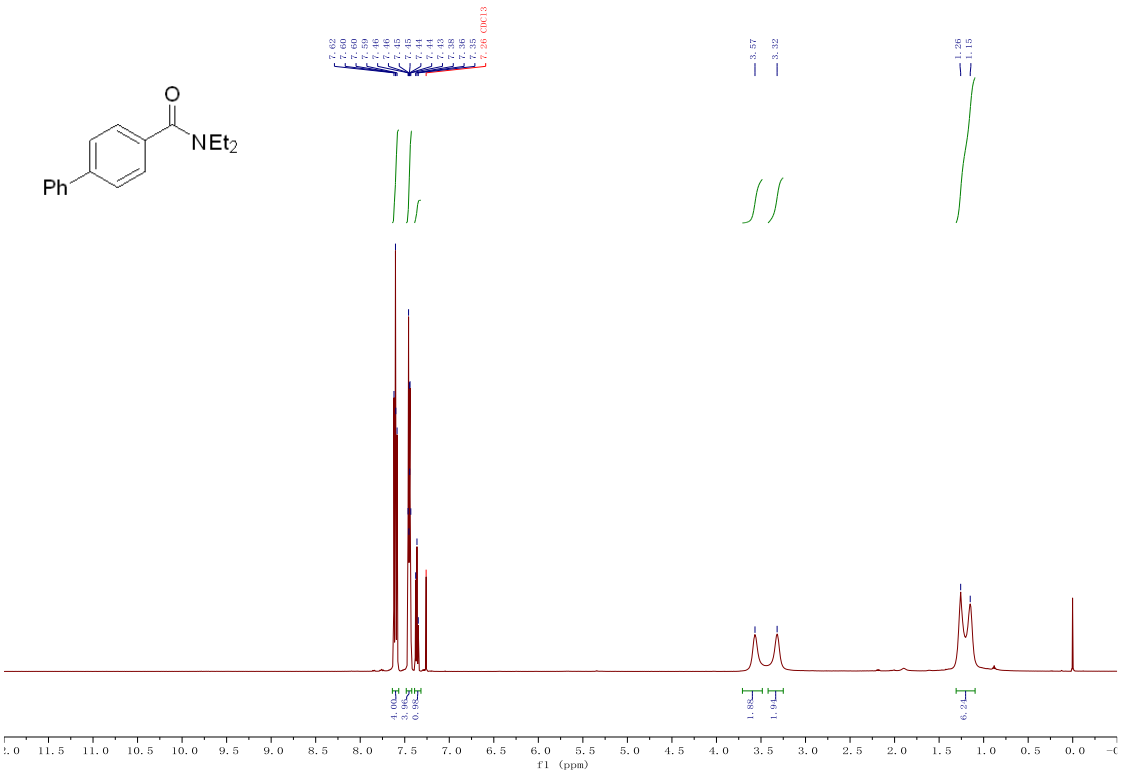


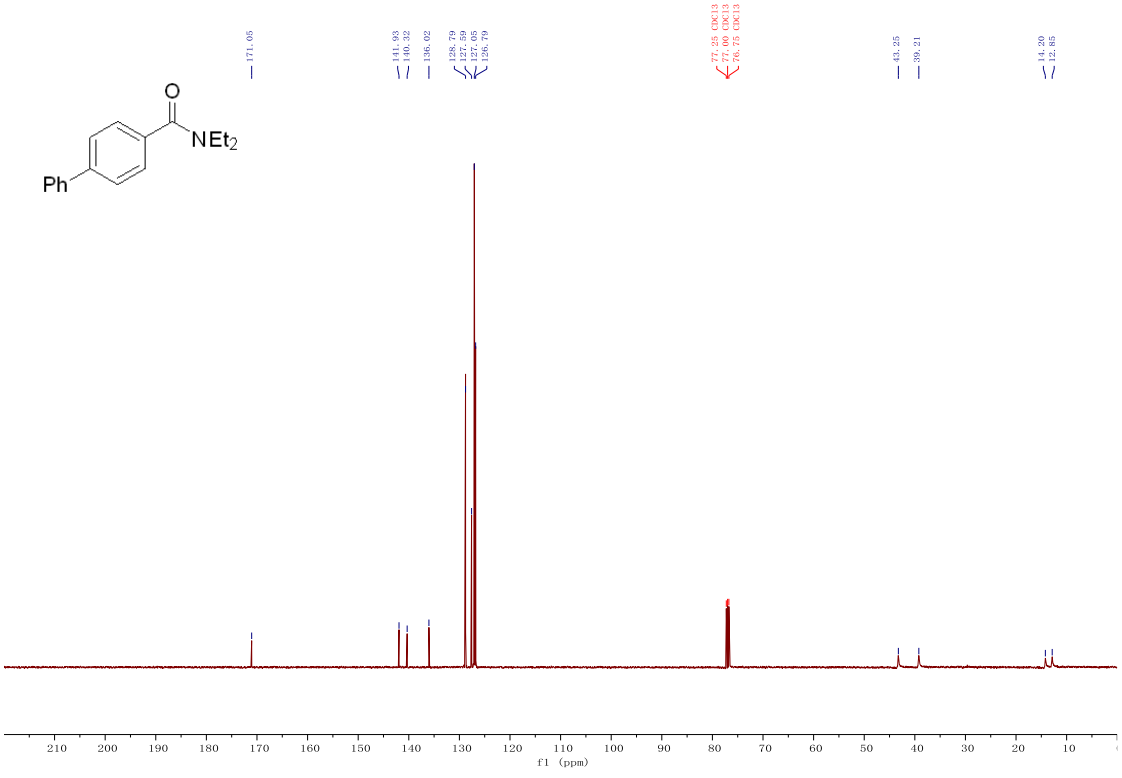
N,N-diethyl-4-methoxybenzamide (3e)



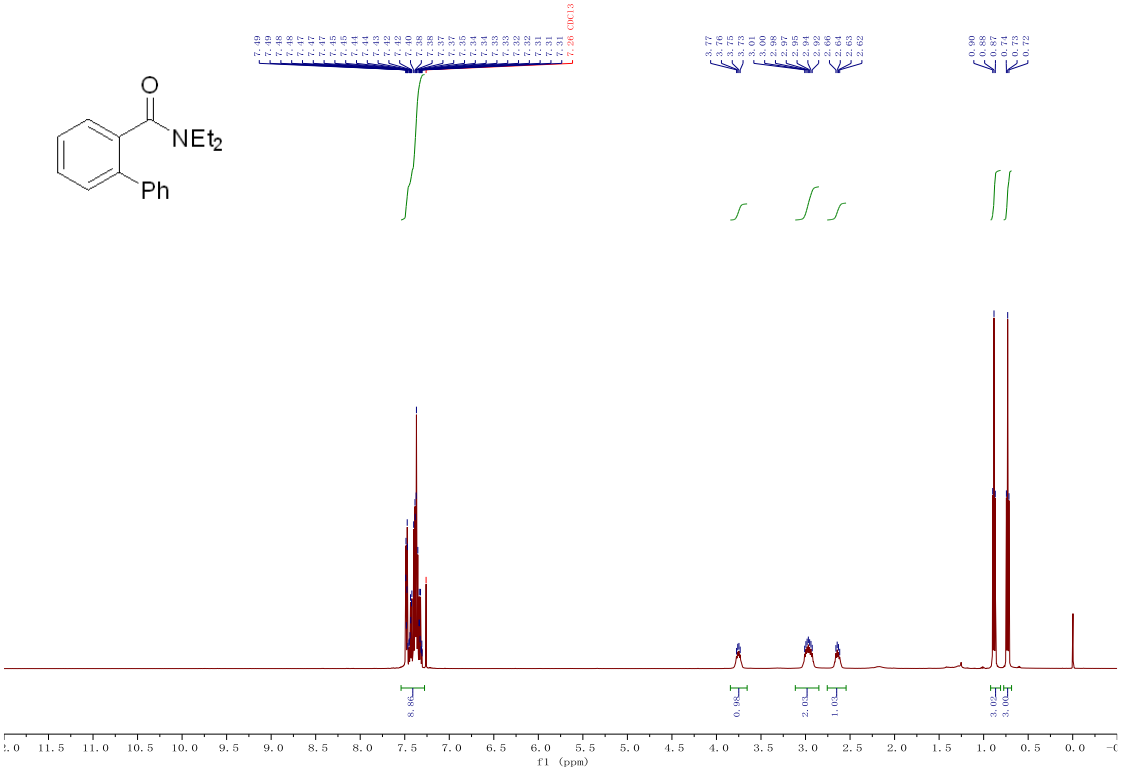


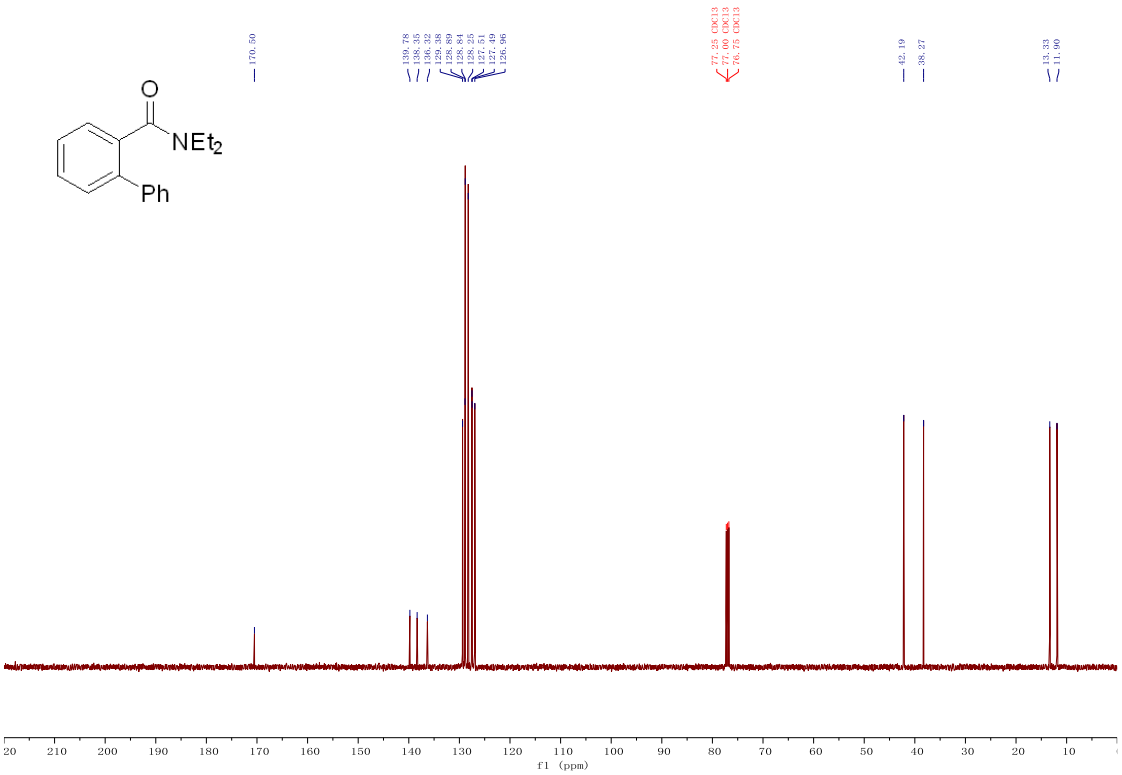
N,N-diethyl-[1,1'-biphenyl]-4-carboxamide (3f)



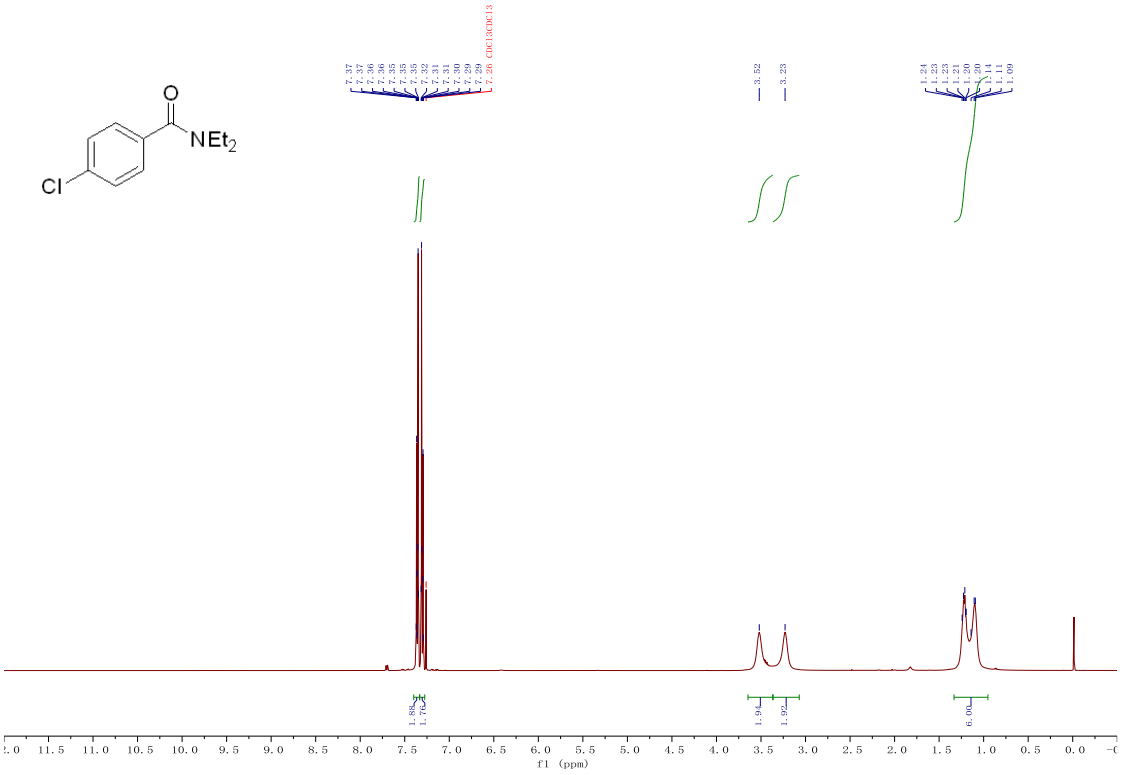


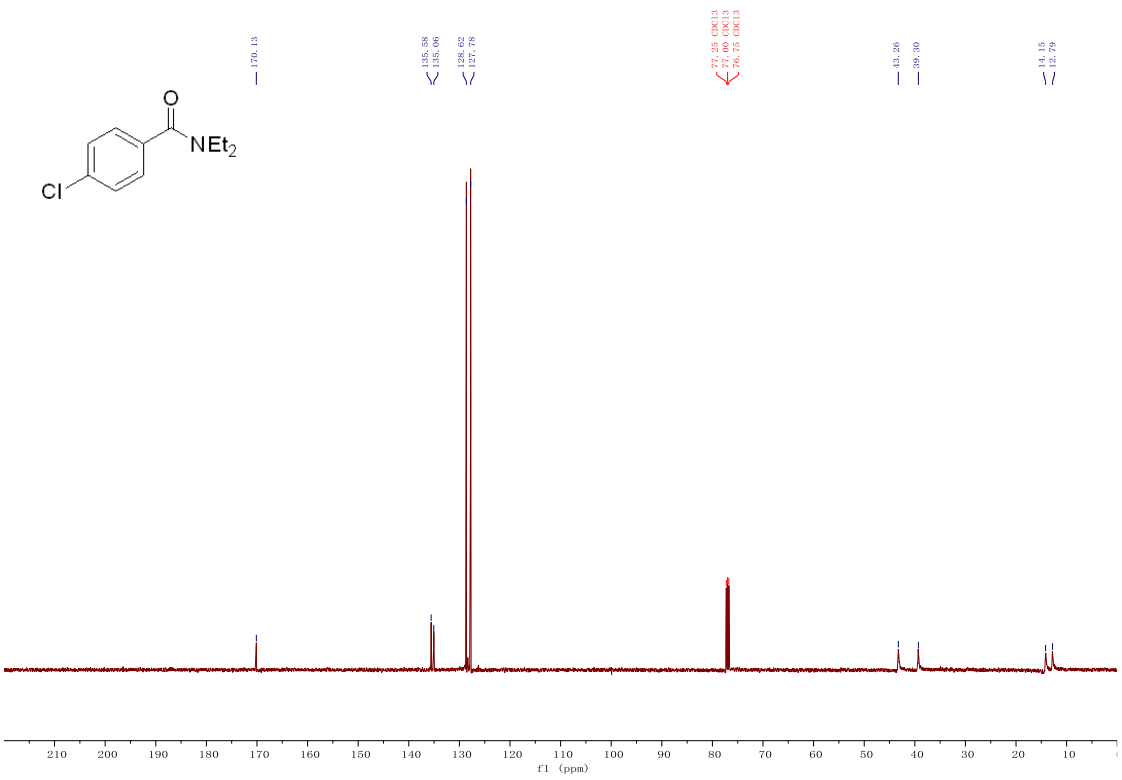
N,N-diethyl-[1,1'-biphenyl]-2-carboxamide (3g)



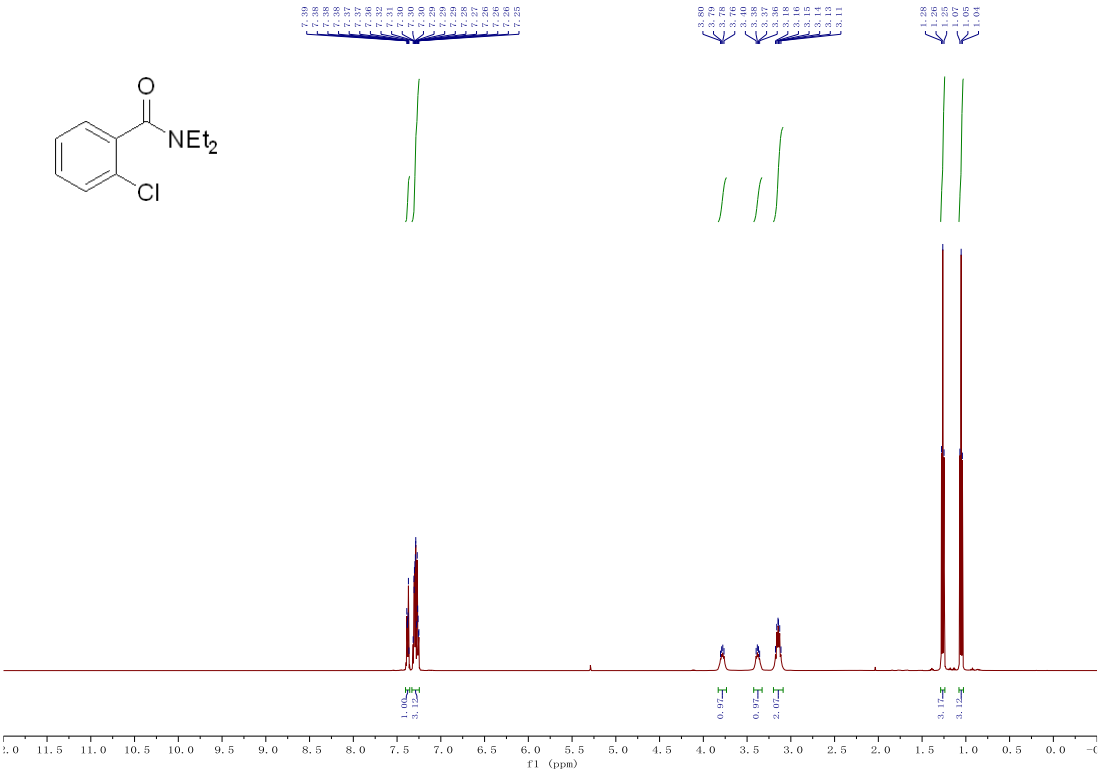


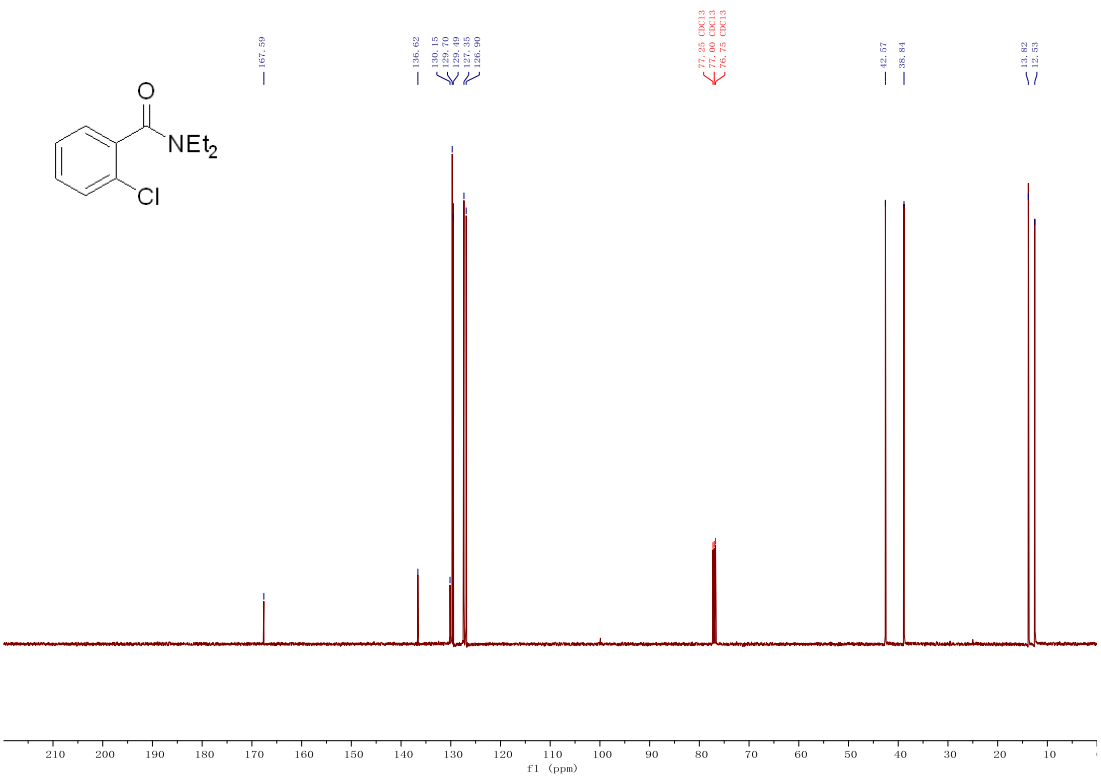
4-chloro-N,N-diethylbenzamide (3h)



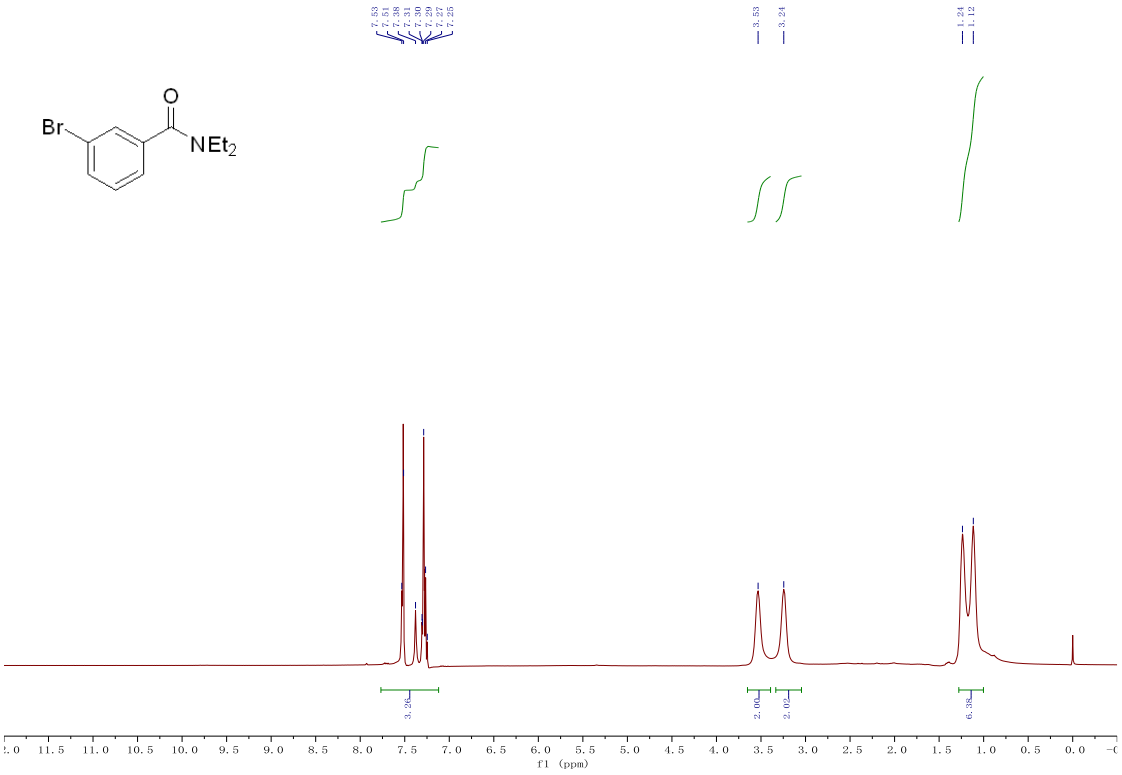


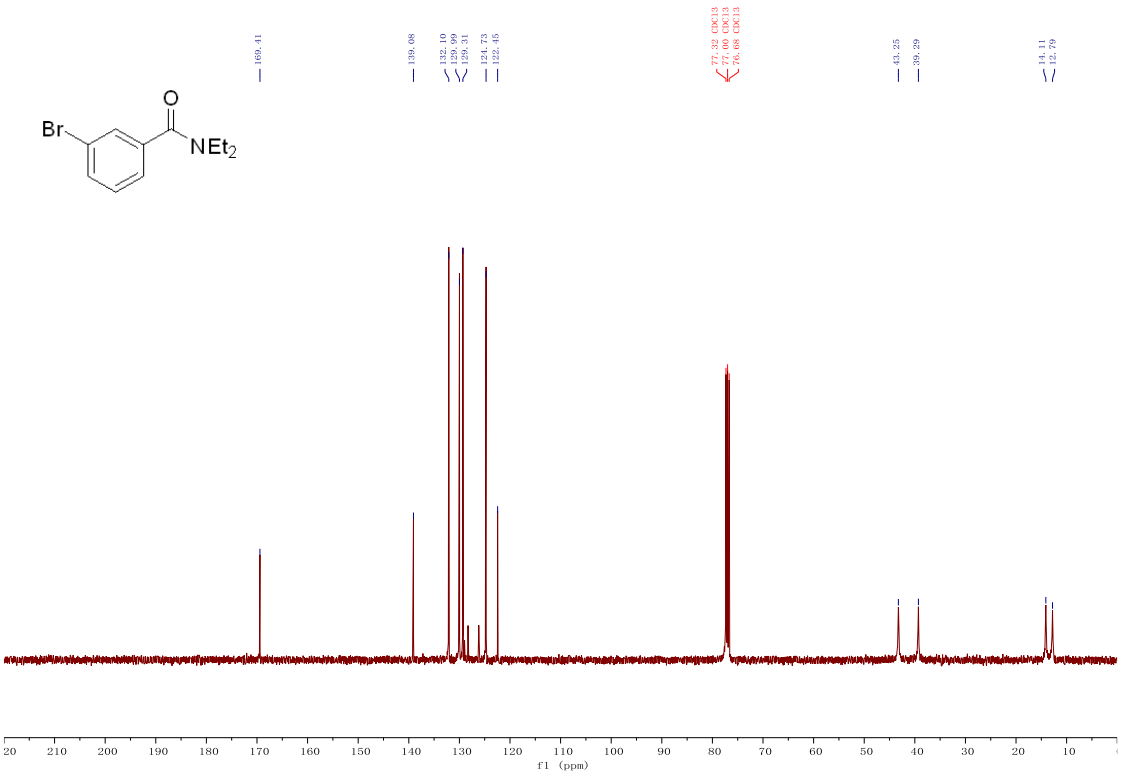
2-chloro-N,N-diethylbenzamide (3i)



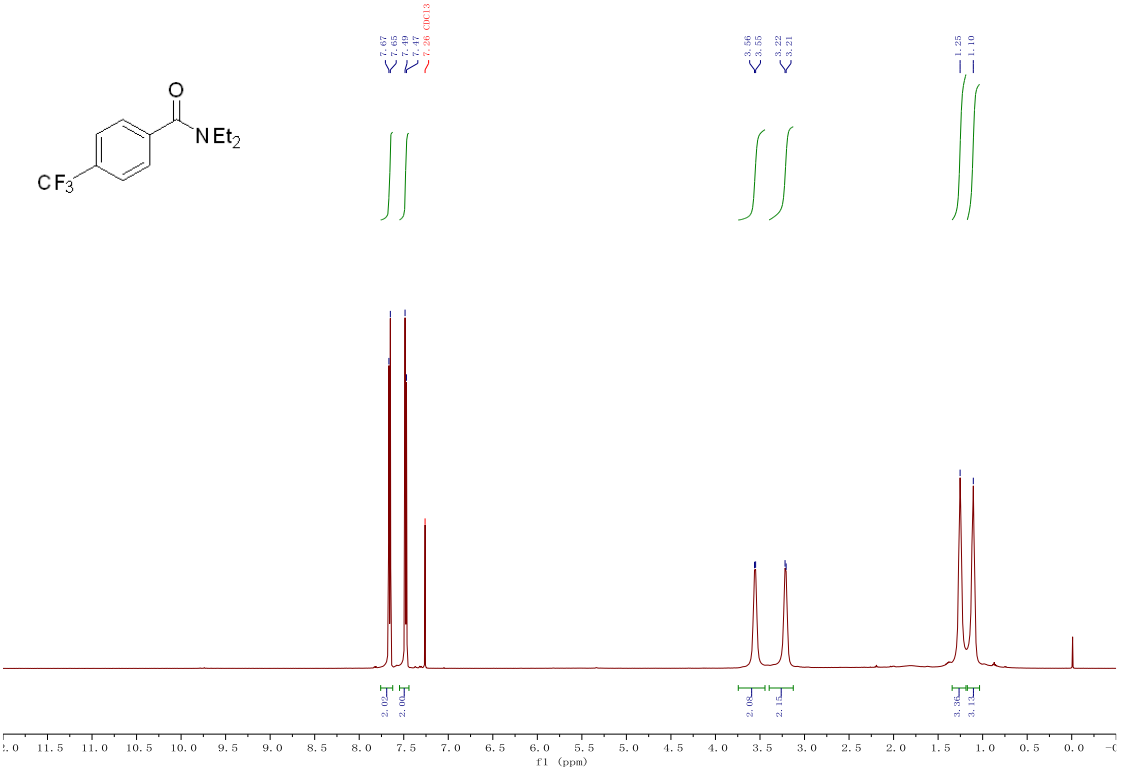


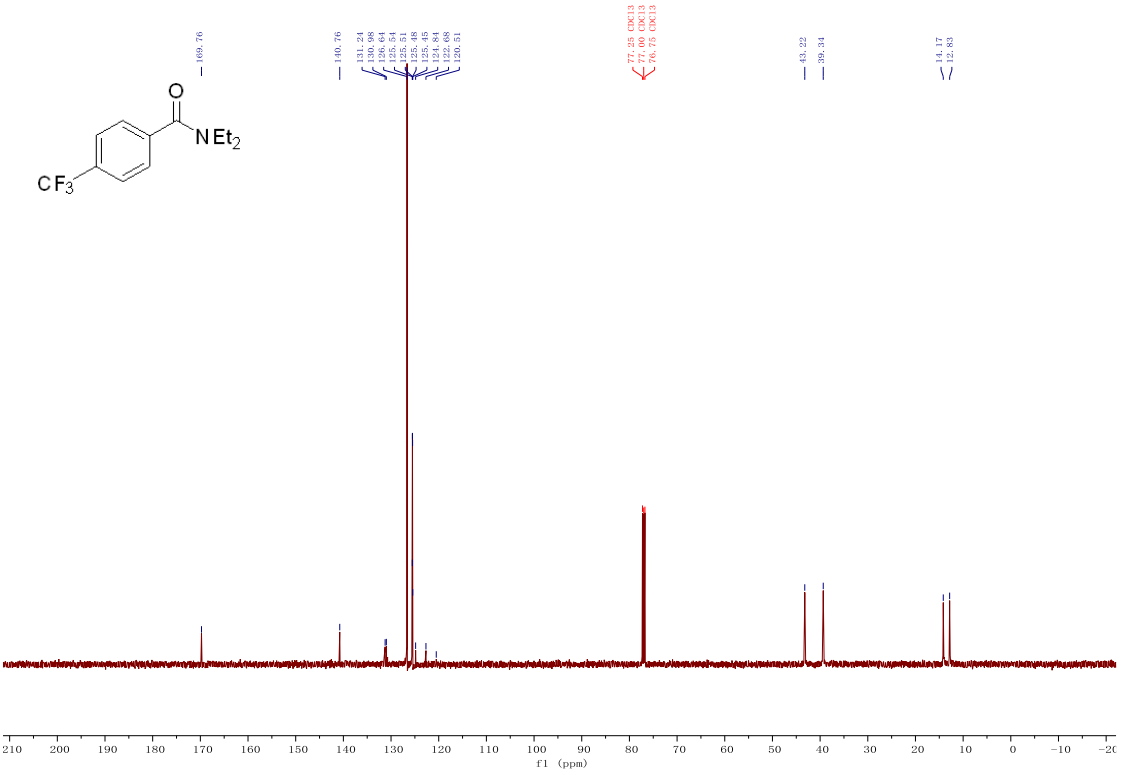
3-bromo-N,N-diethylbenzamide (3j)



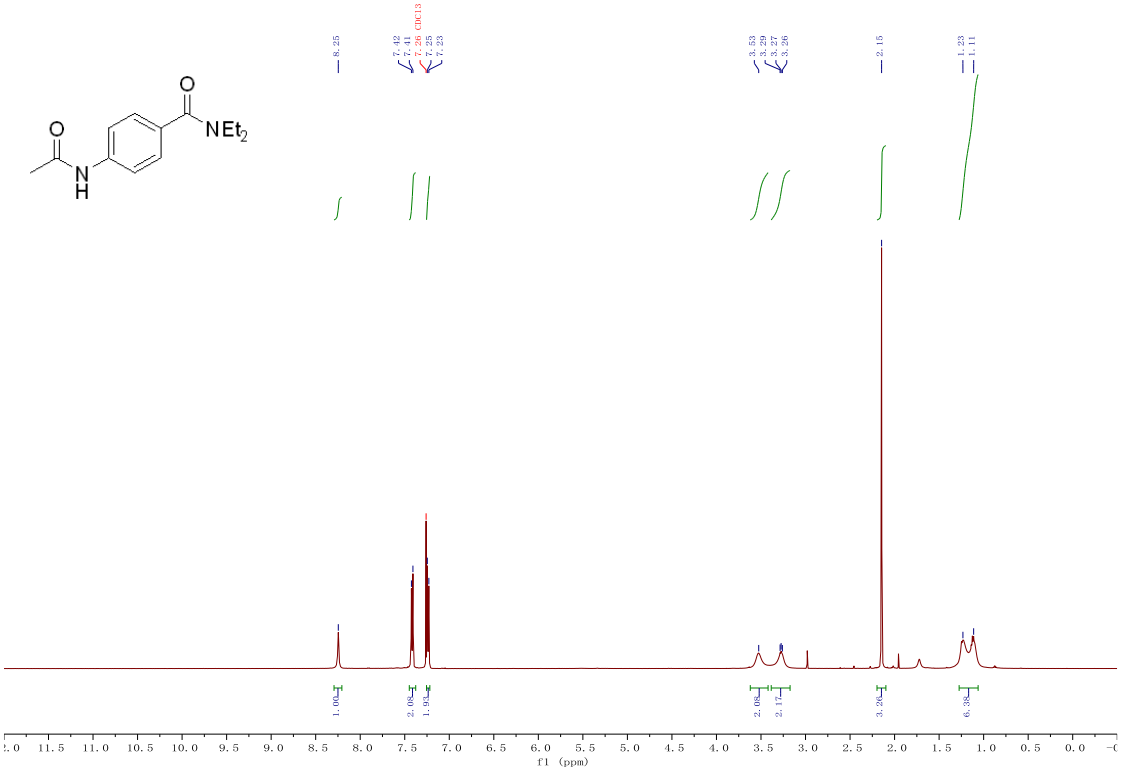


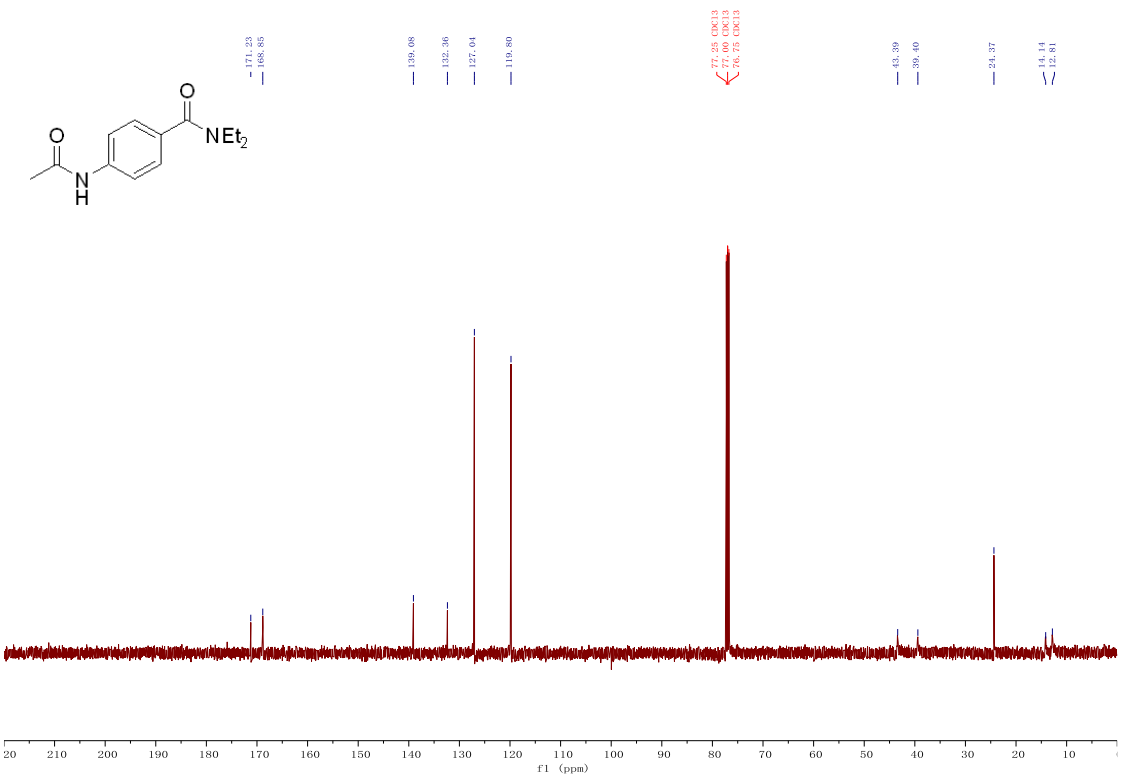
N,N-diethyl-4-(trifluoromethyl)benzamide (3k)



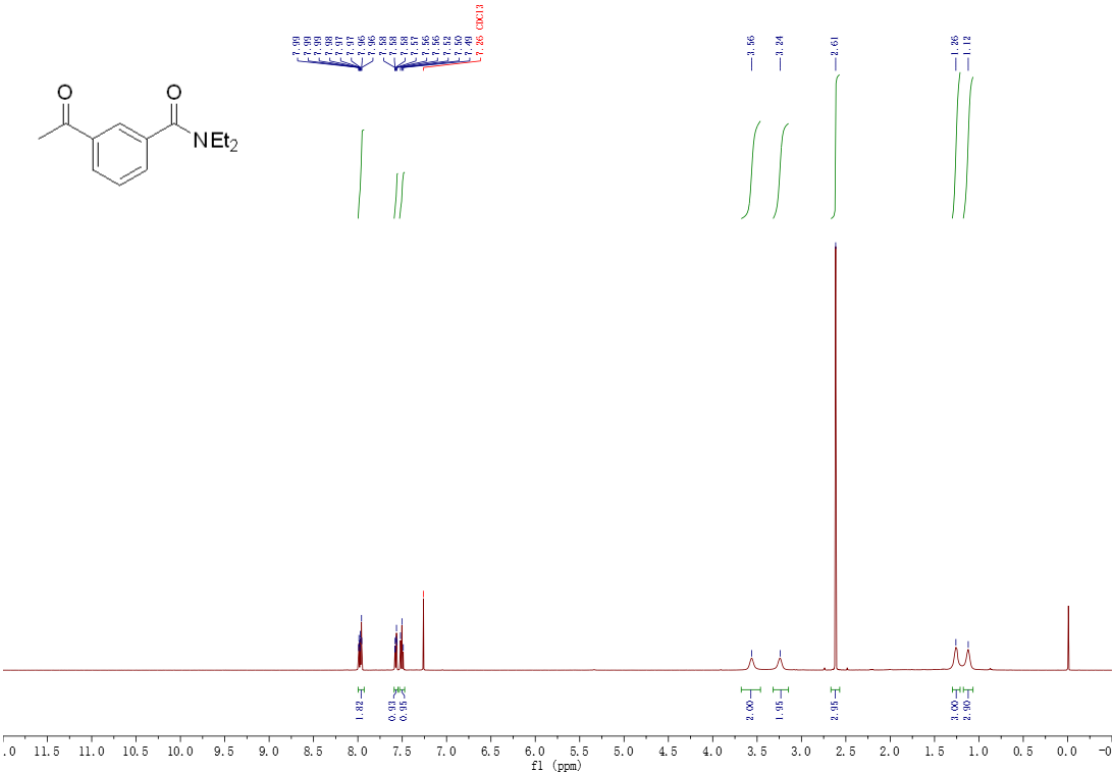


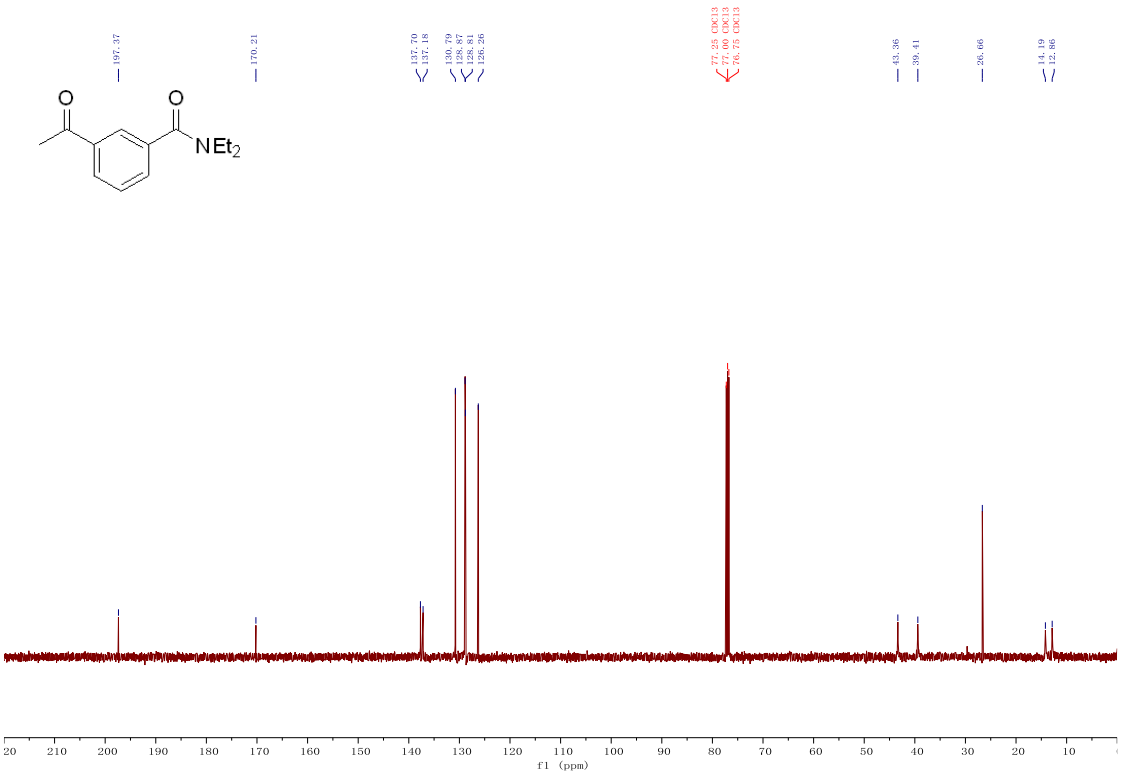
N,N-diethyl-4-ethynylbenzamide (3l)



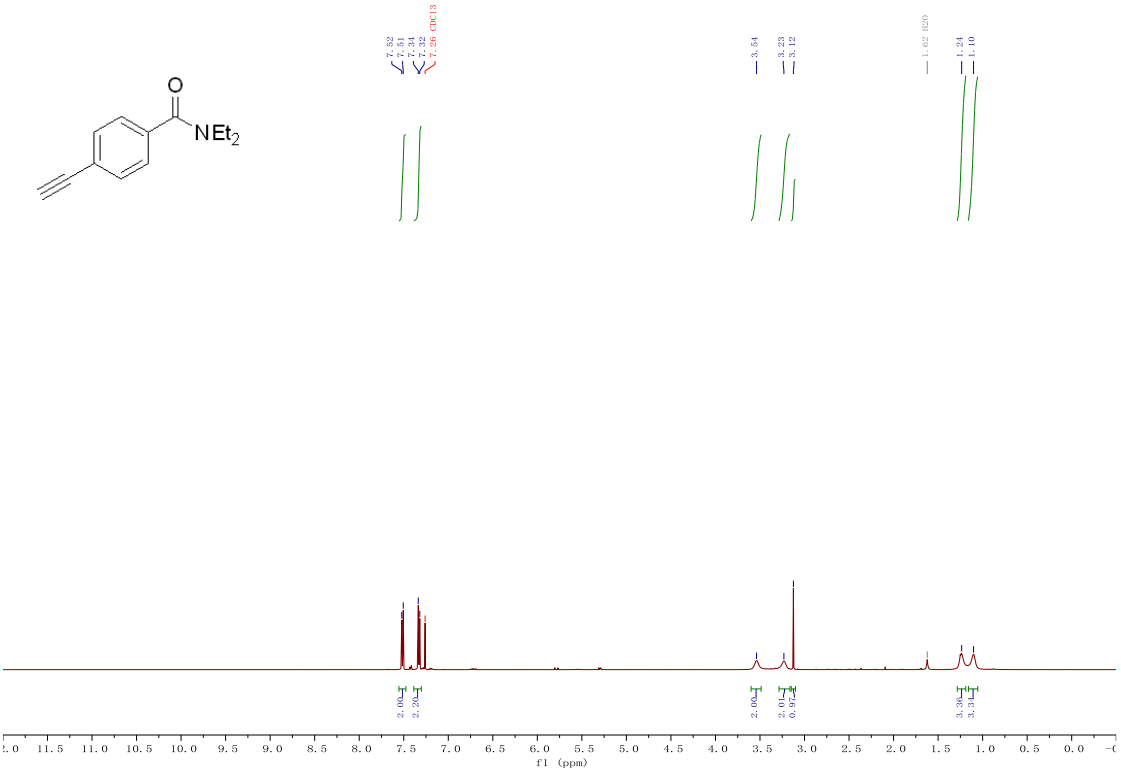


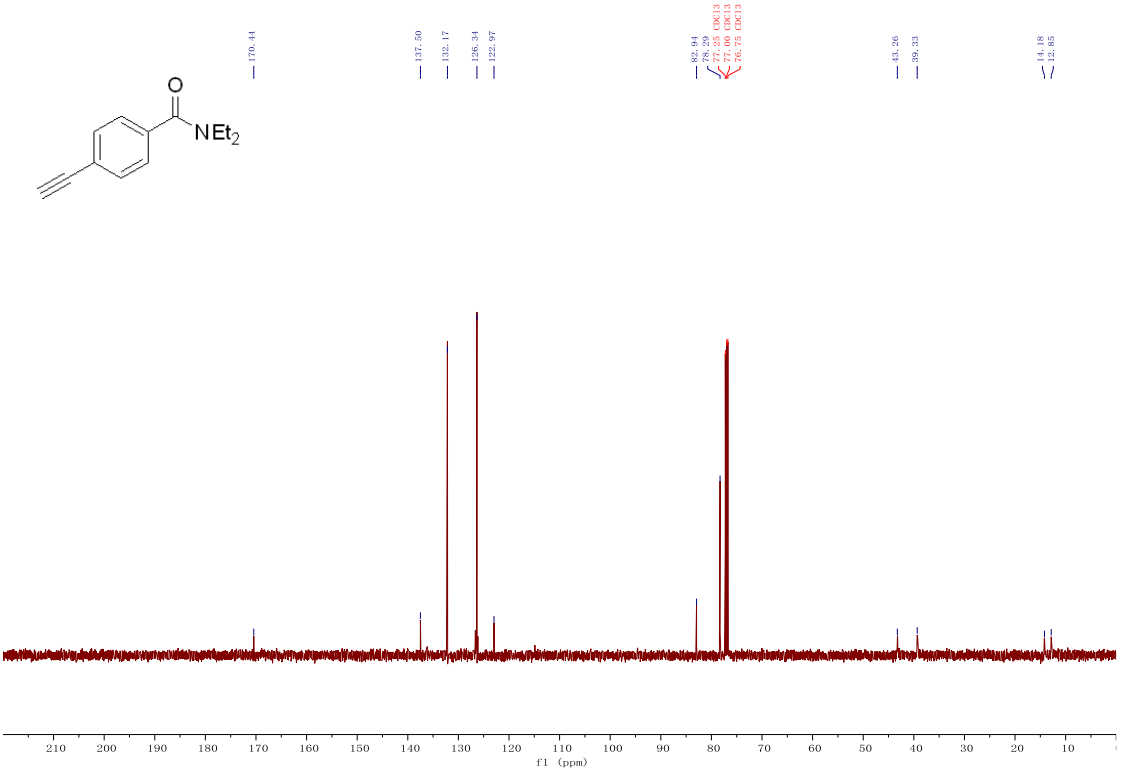
3-acetyl-N,N-diethylbenzamide (3m)



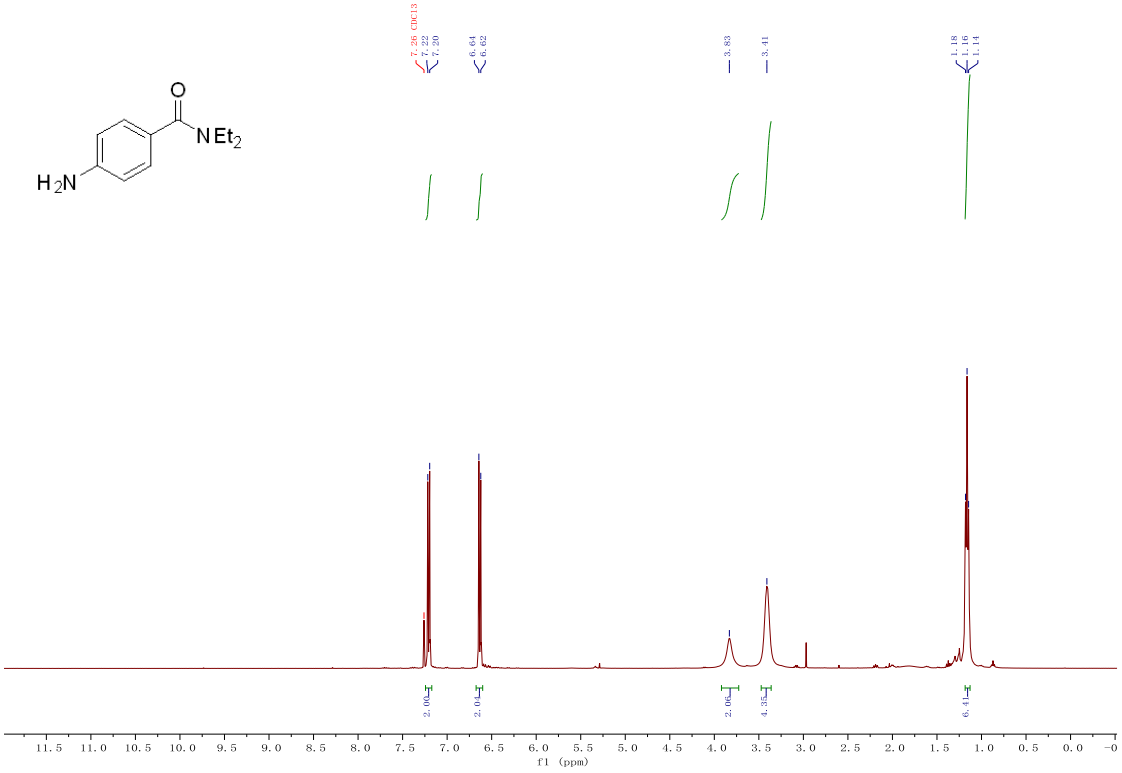


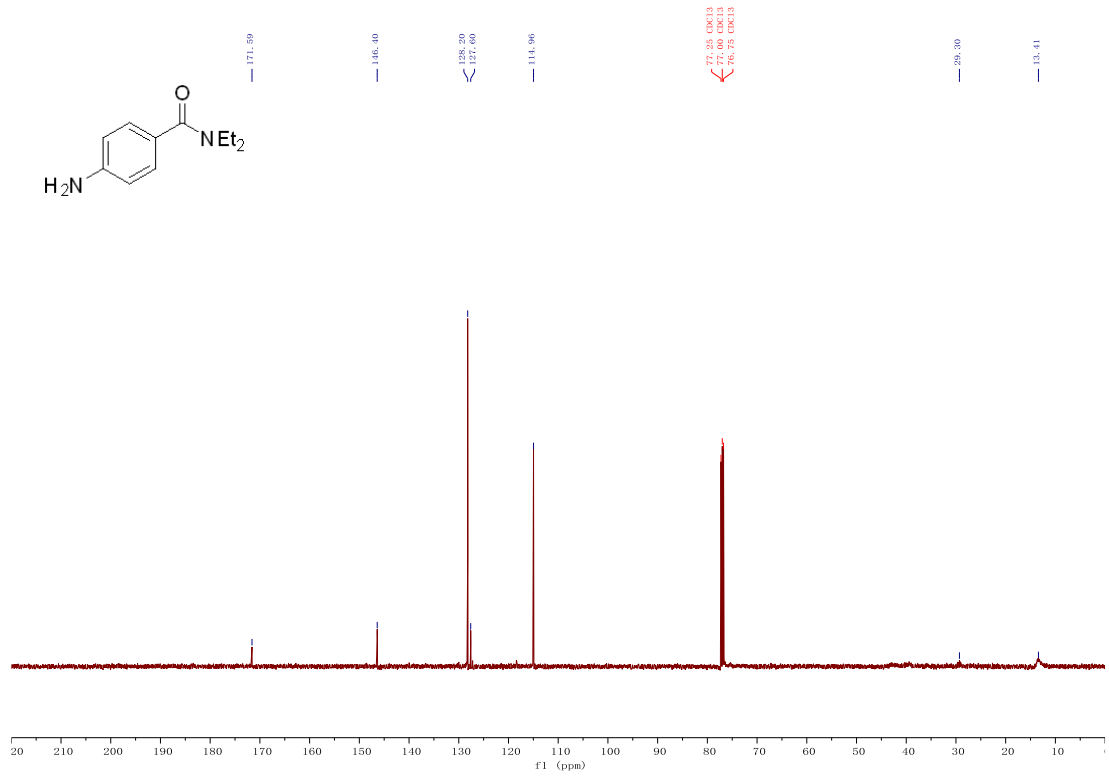
N,N-diethyl-4-ethynylbenzamide (3n)



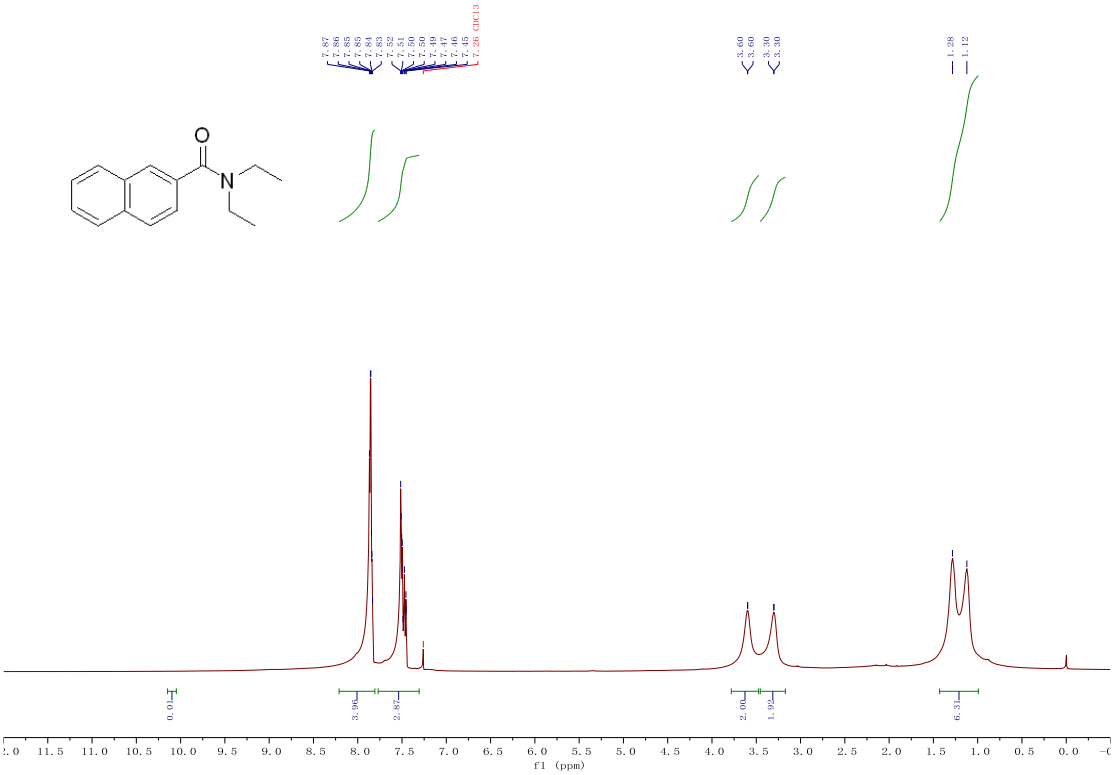


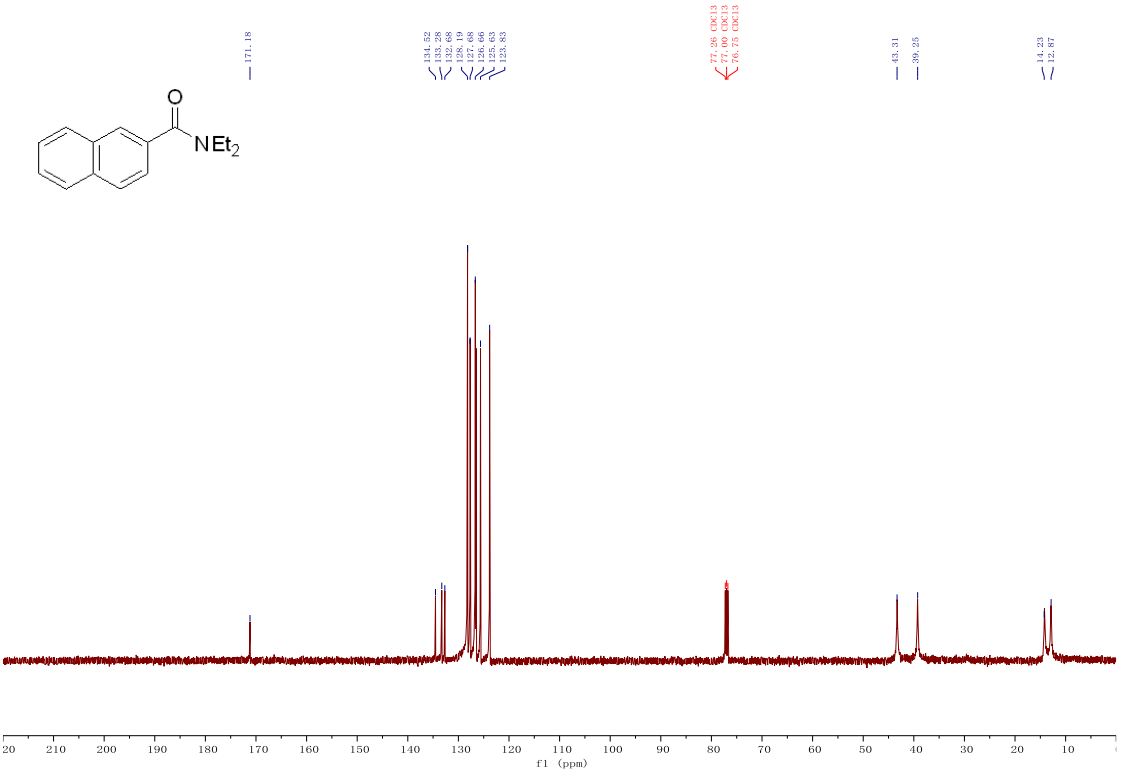
4-amino-N,N-diethylbenzamide (3o)



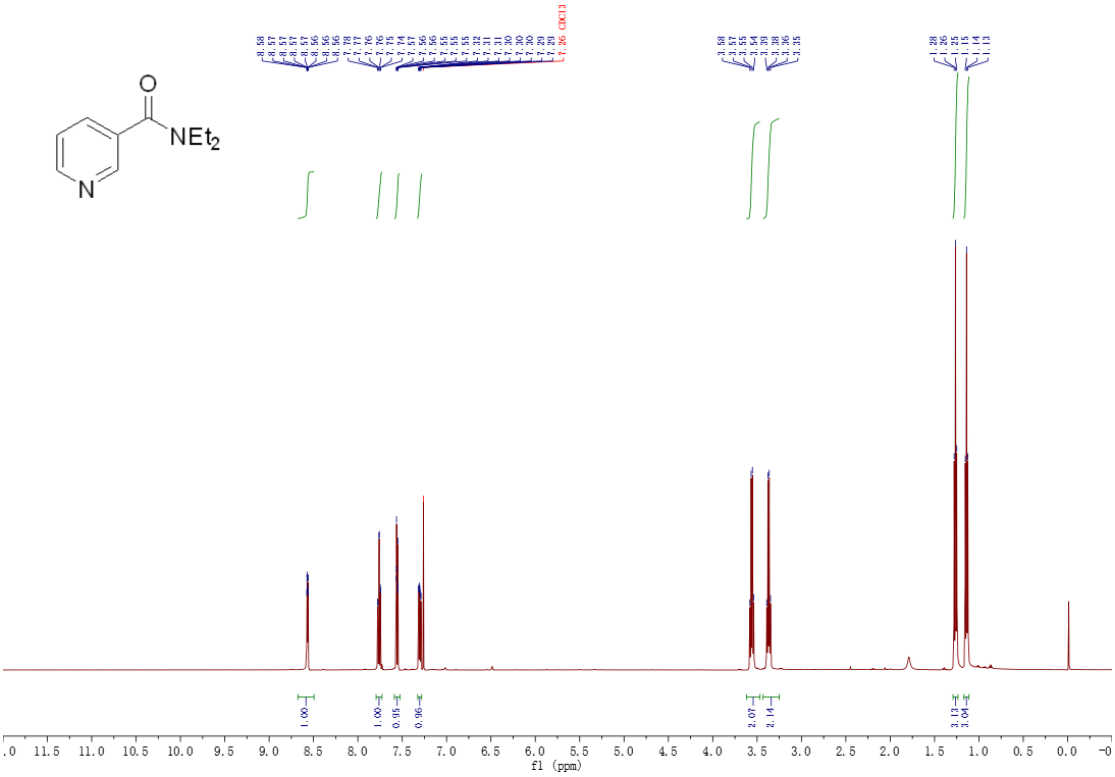


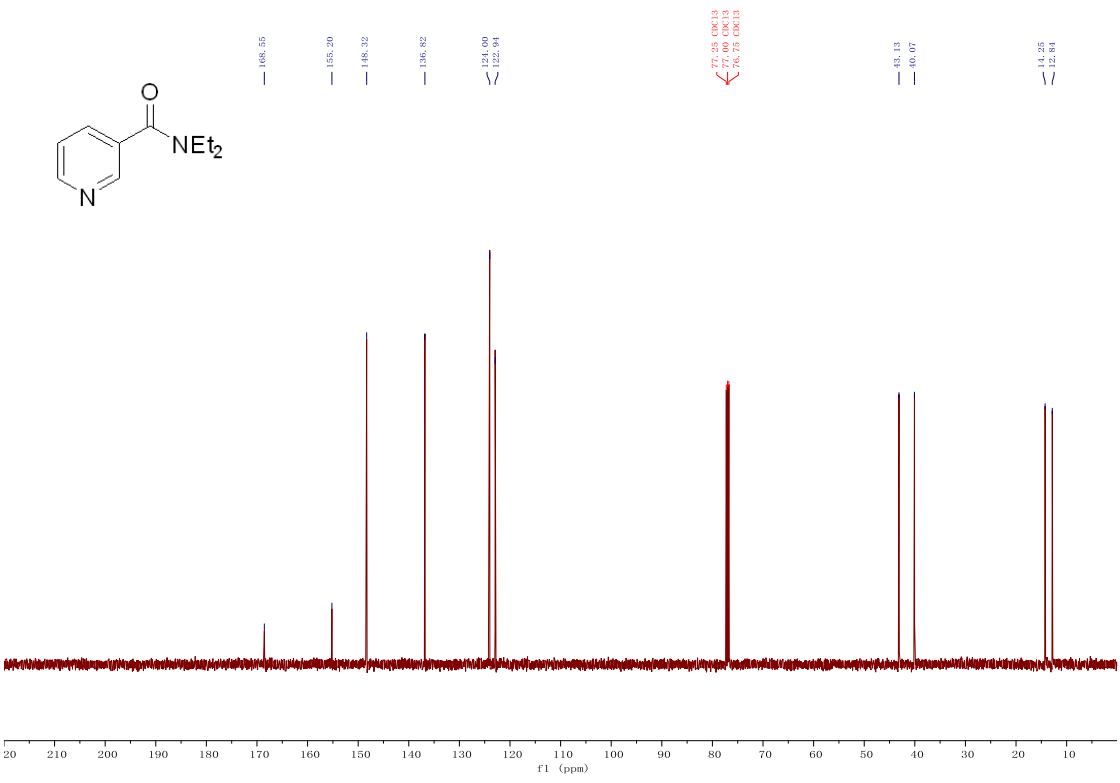
N,N-diethyl-2-naphthamide (3p)



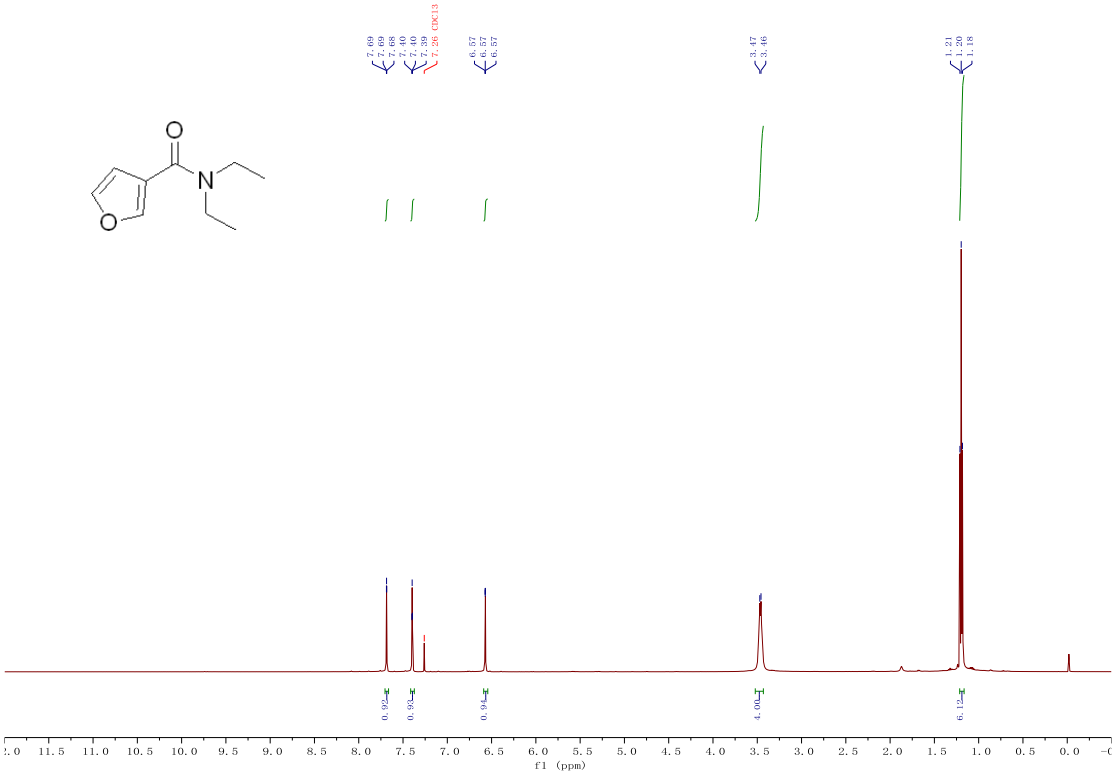


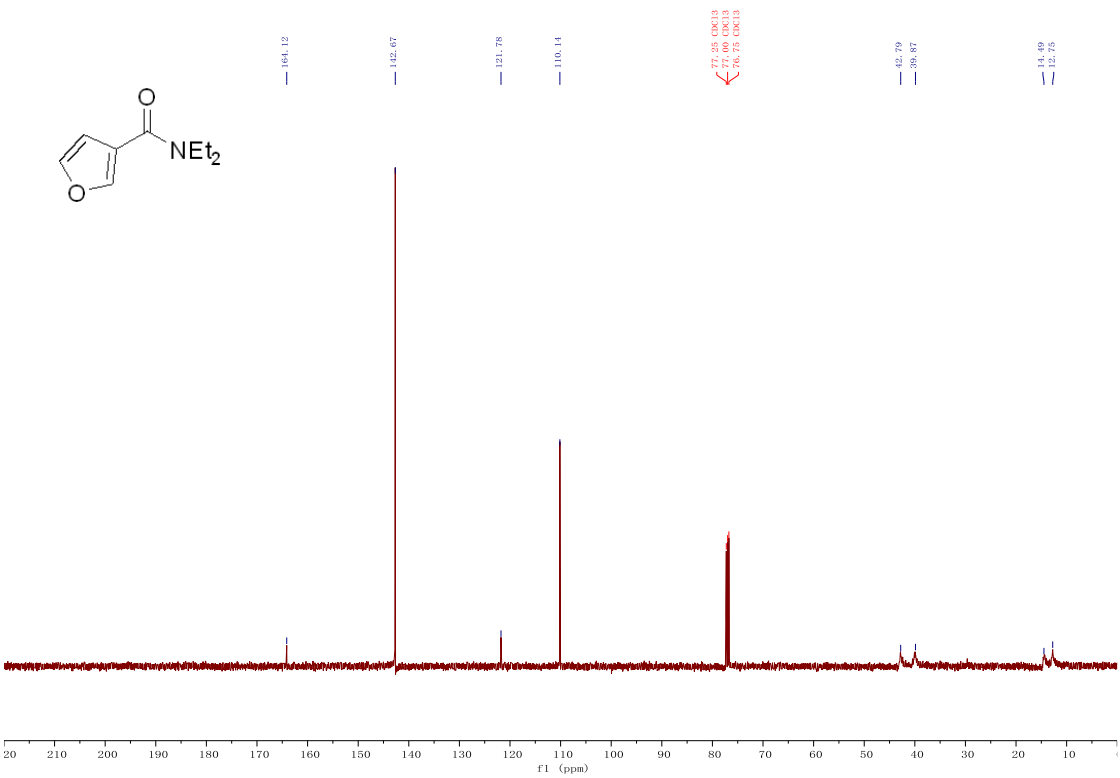
N,N-diethylnicotinamide (3q)



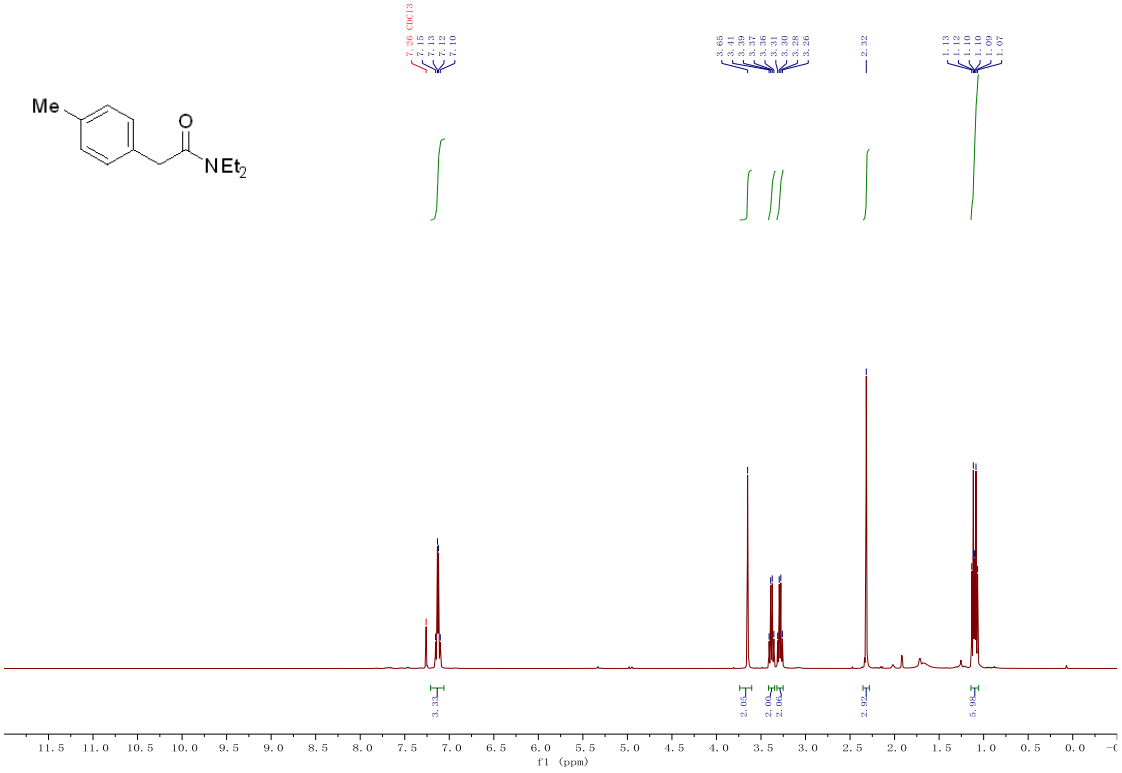


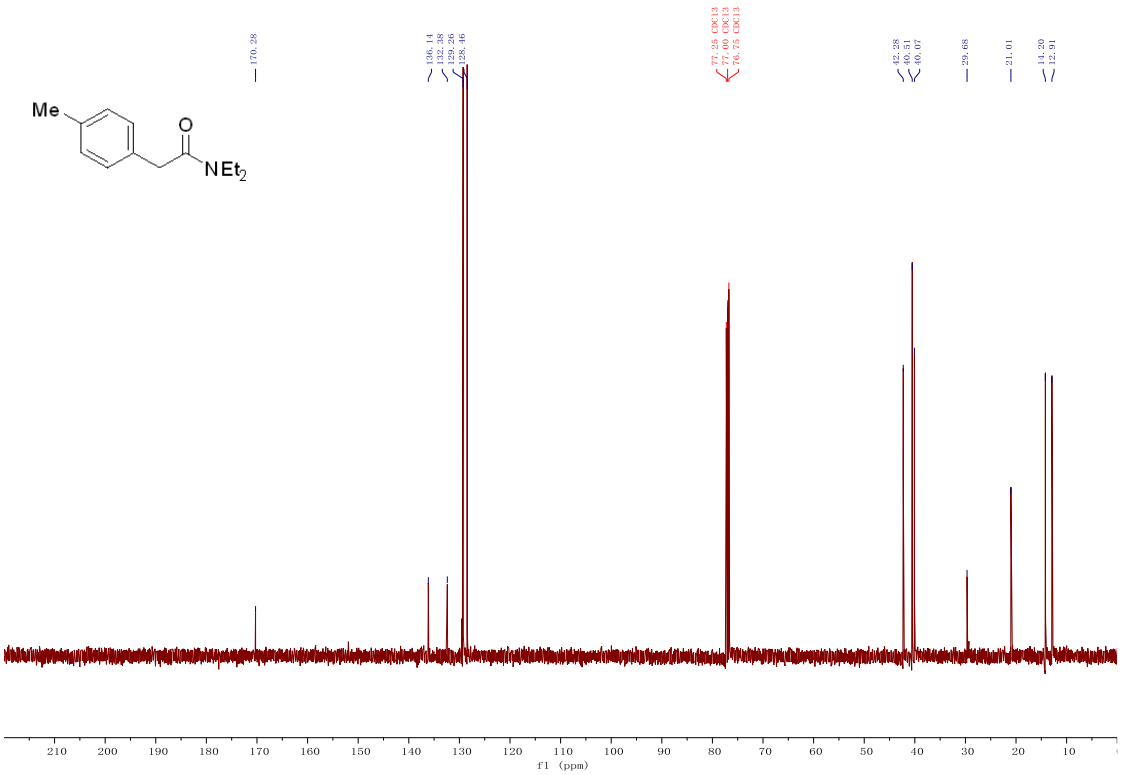
N,N-diethylfuran-3-carboxamide (3r)



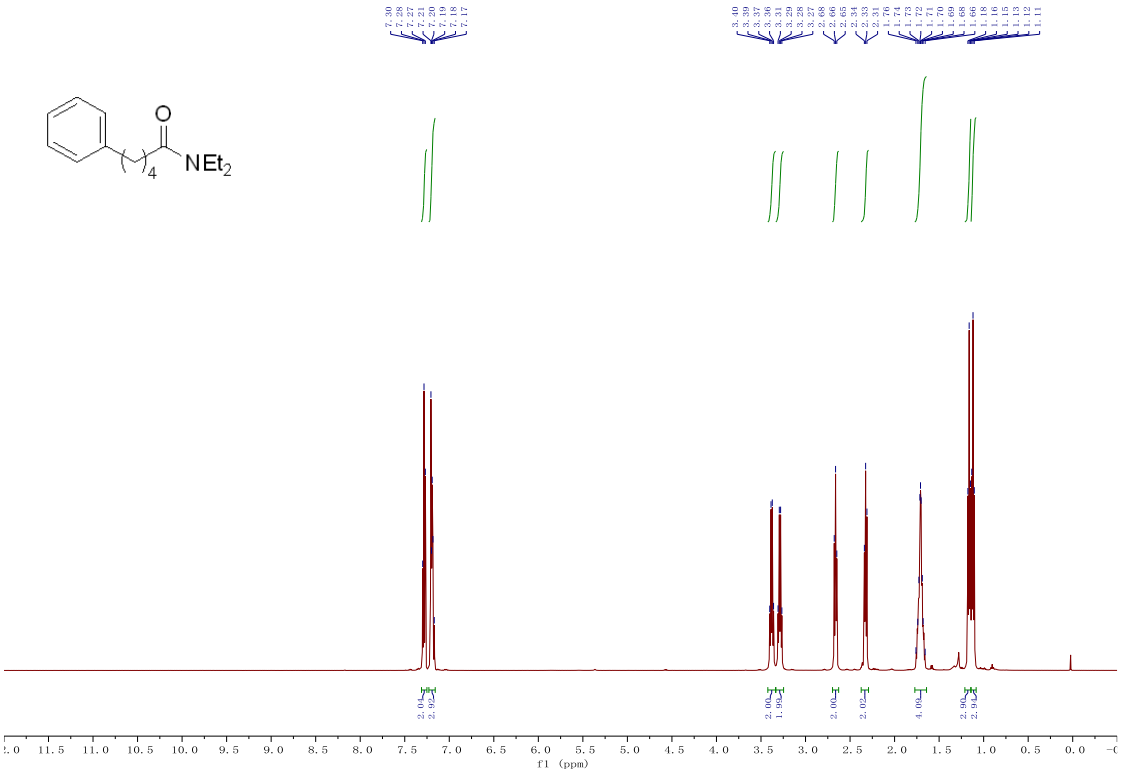


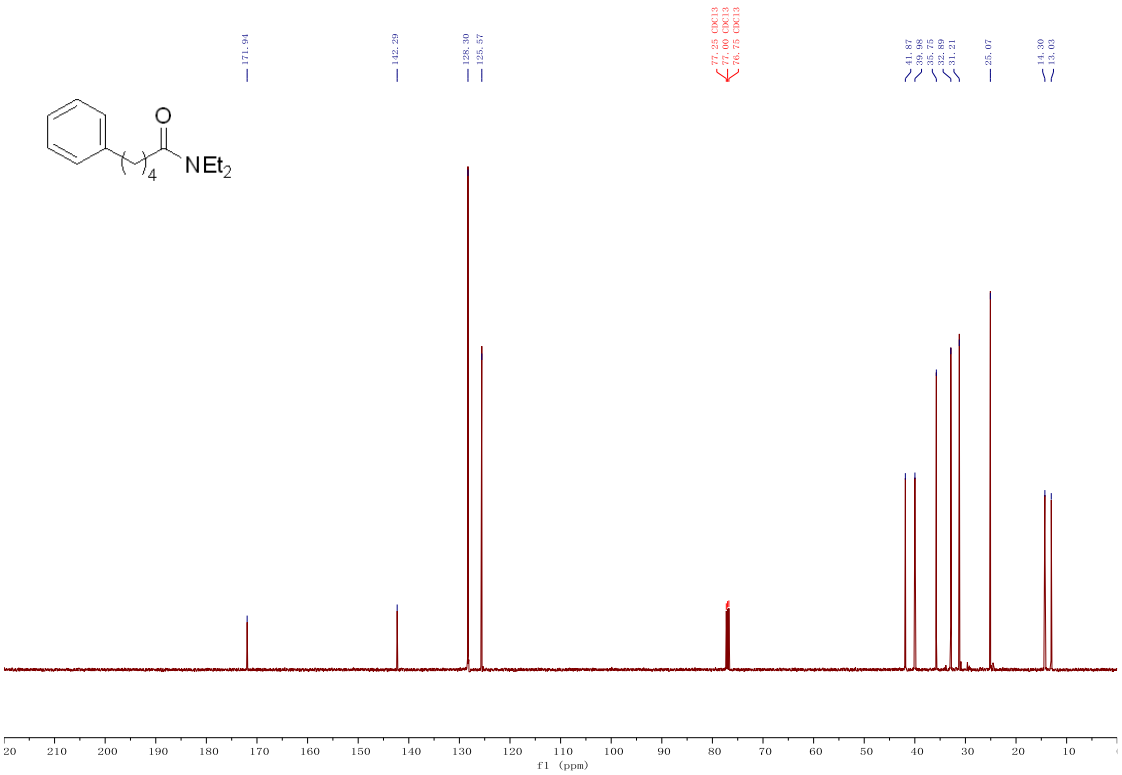
N,N-diethyl-2-(p-tolyl)acetamide (3s)



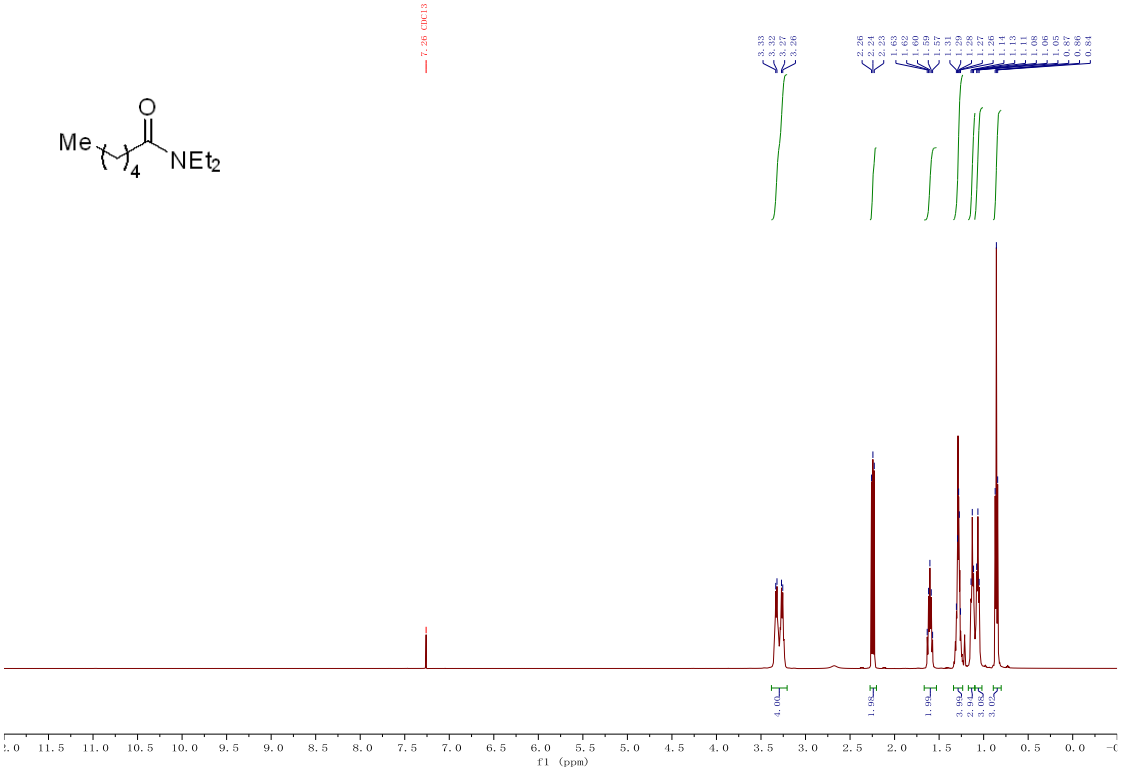


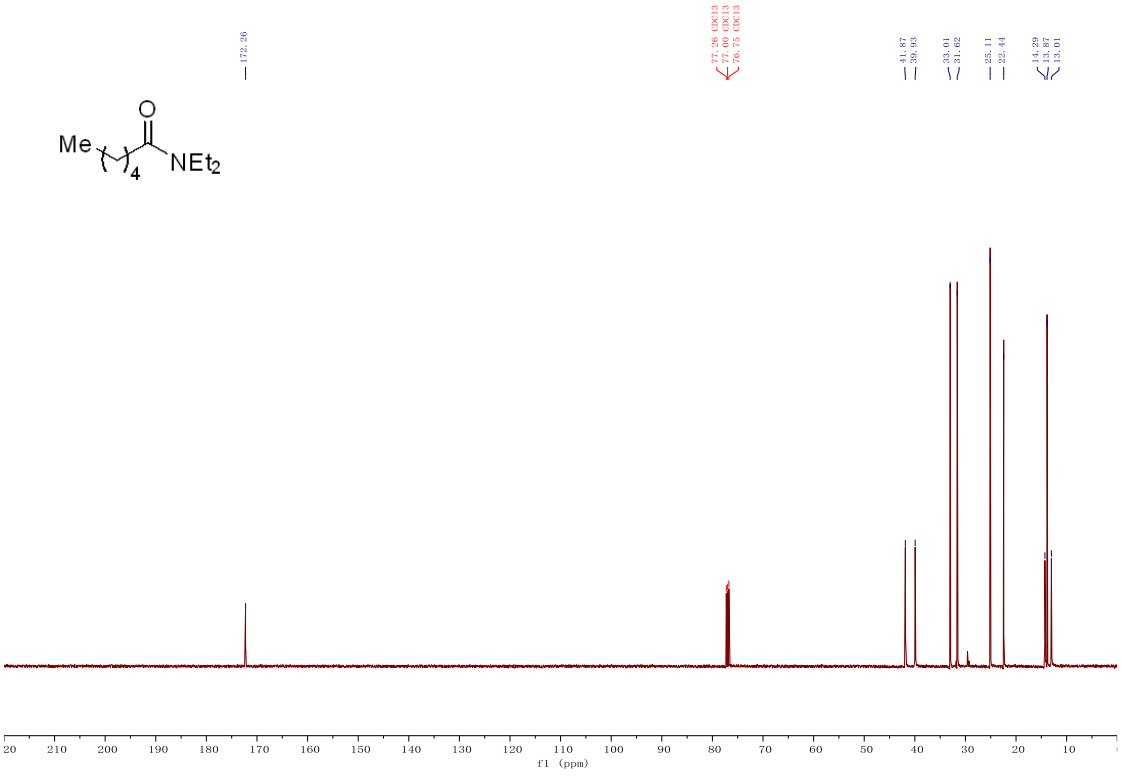
N,N-diethyl-5-phenylpentanamide (3t)



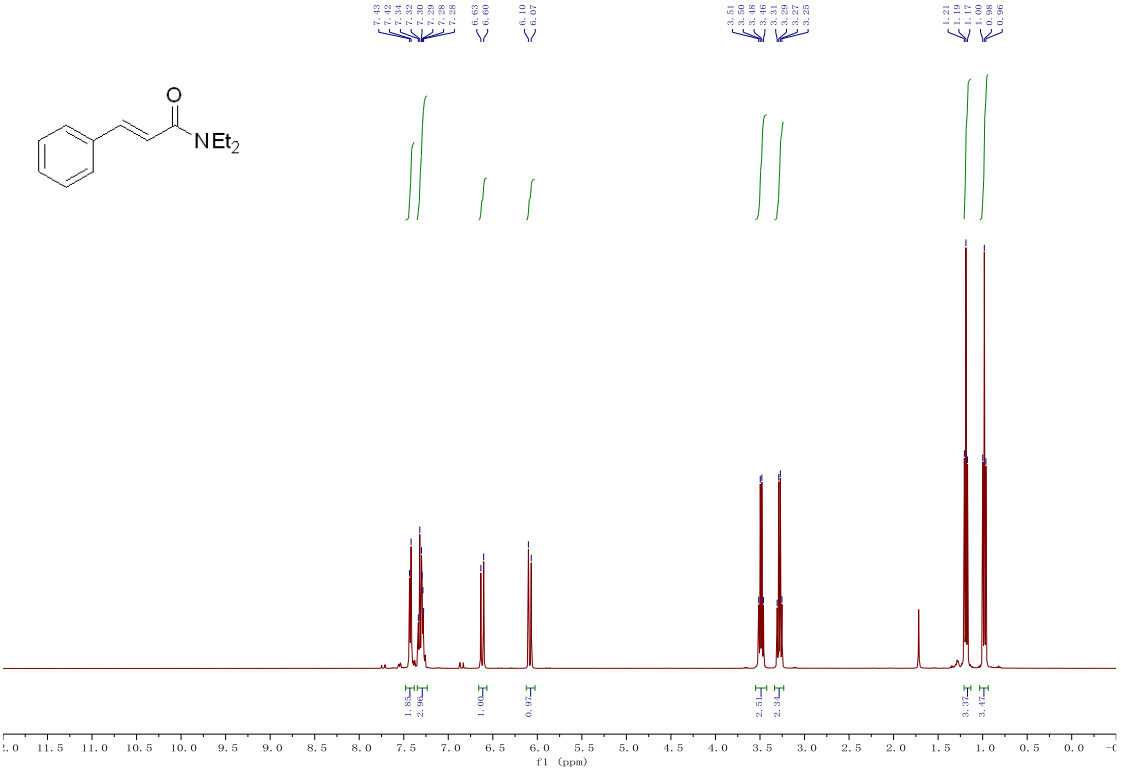


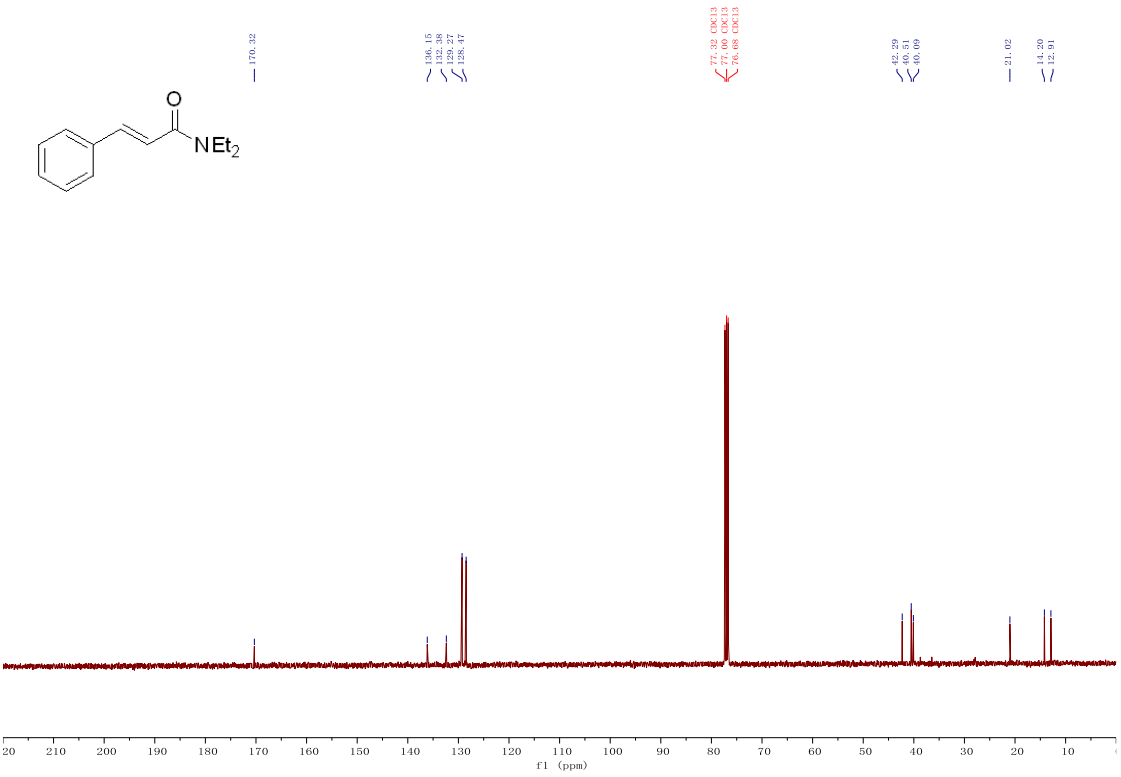
N,N-diethylhexanamide (3u)



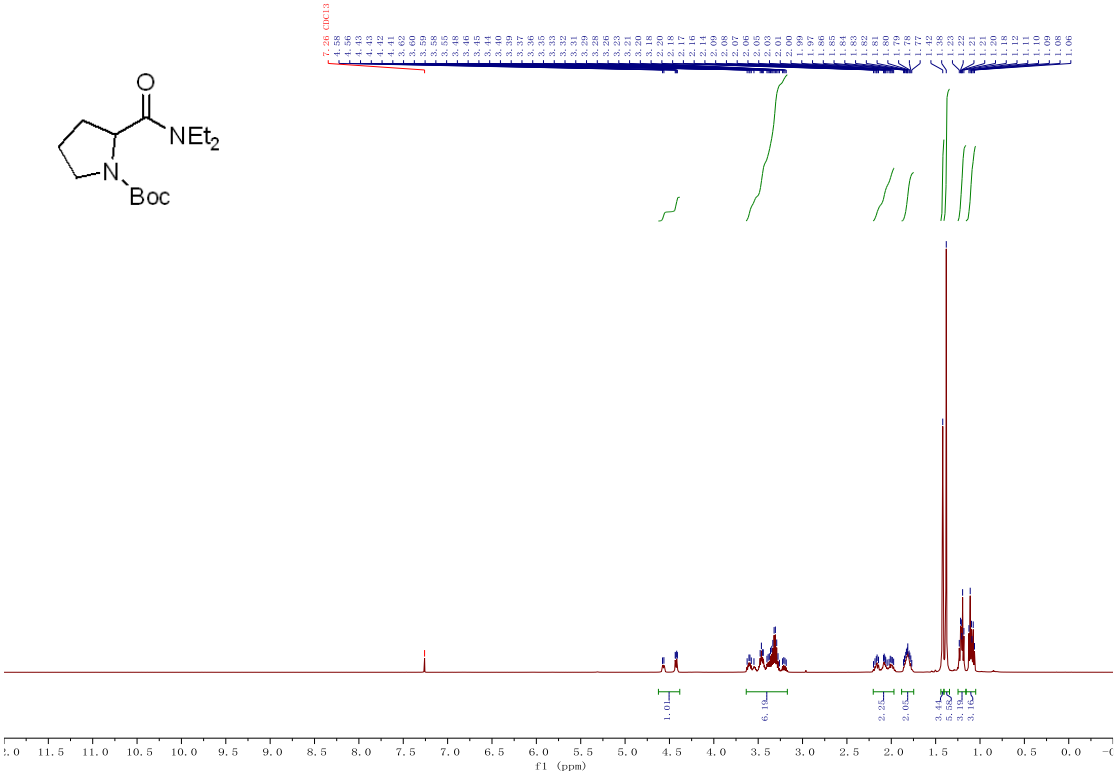


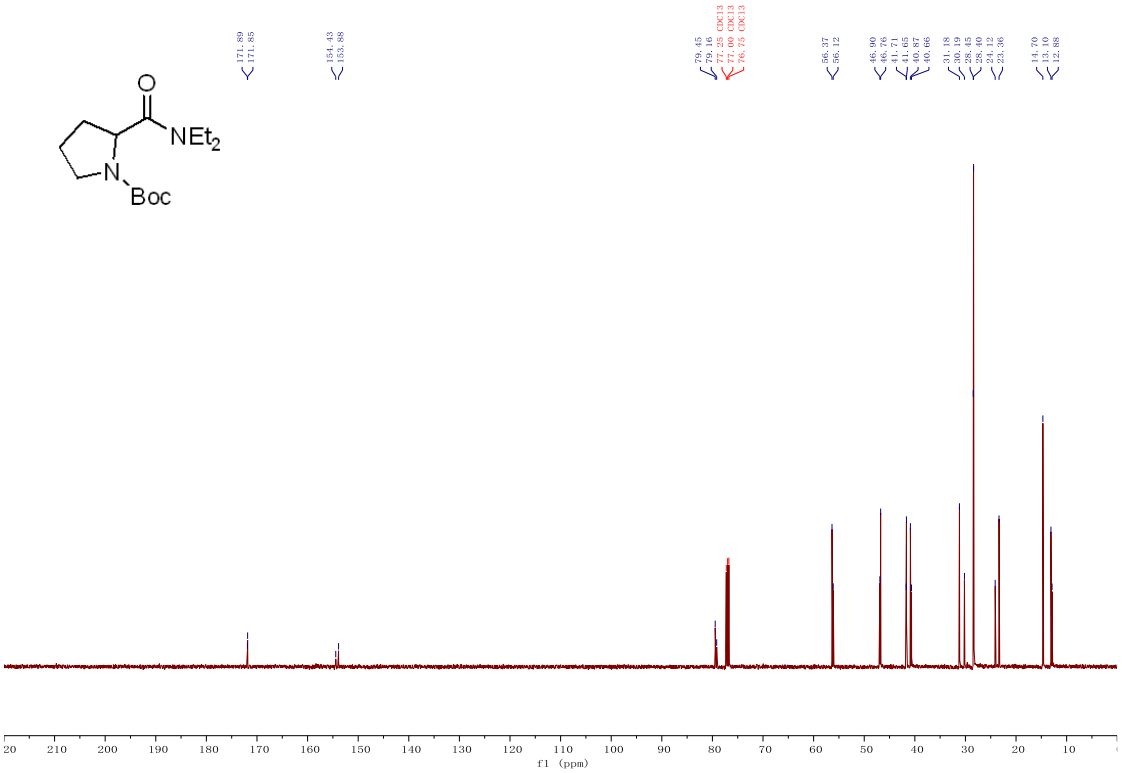
N,N-diethylcinnamamide (3v)



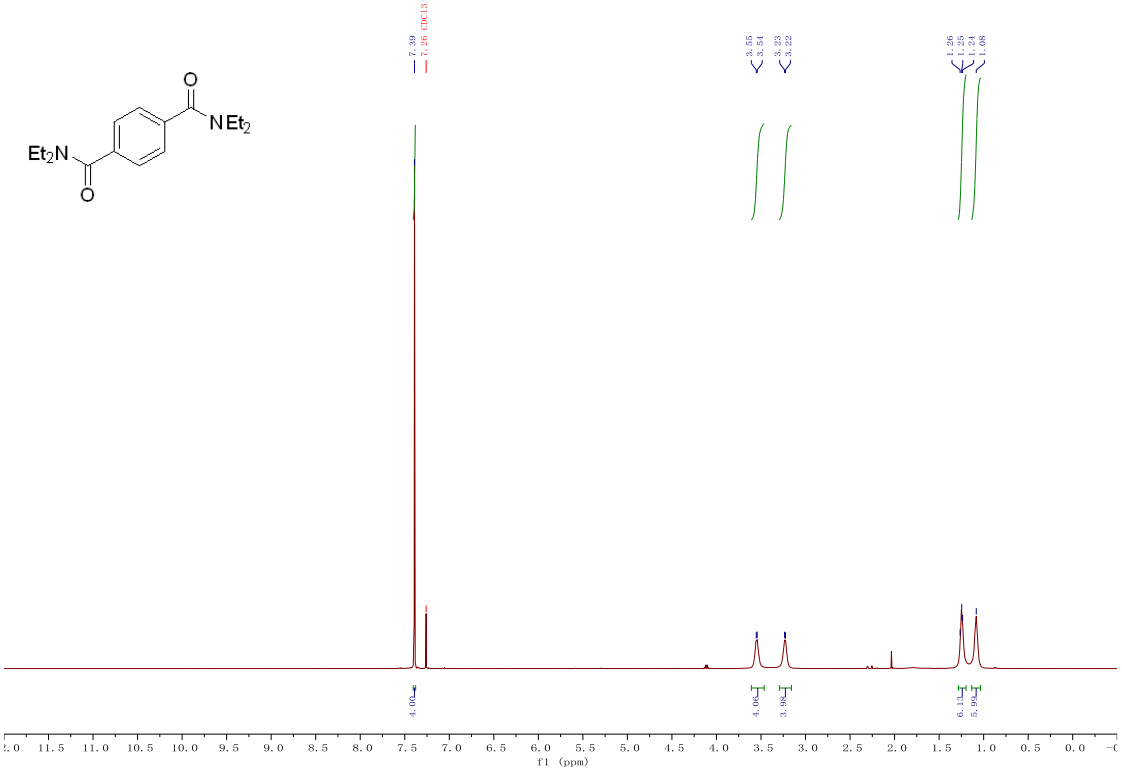


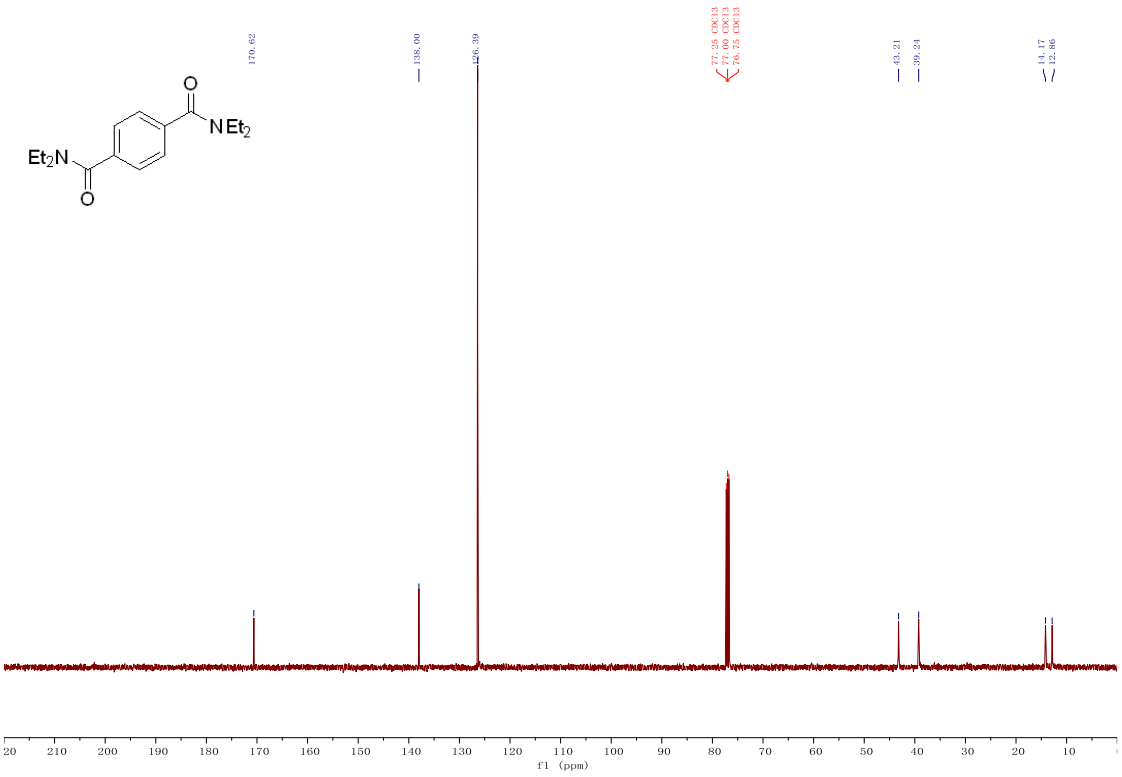
tert-butyl 2-(diethylcarbamoyl)pyrrolidine-1-carboxylate (3w)



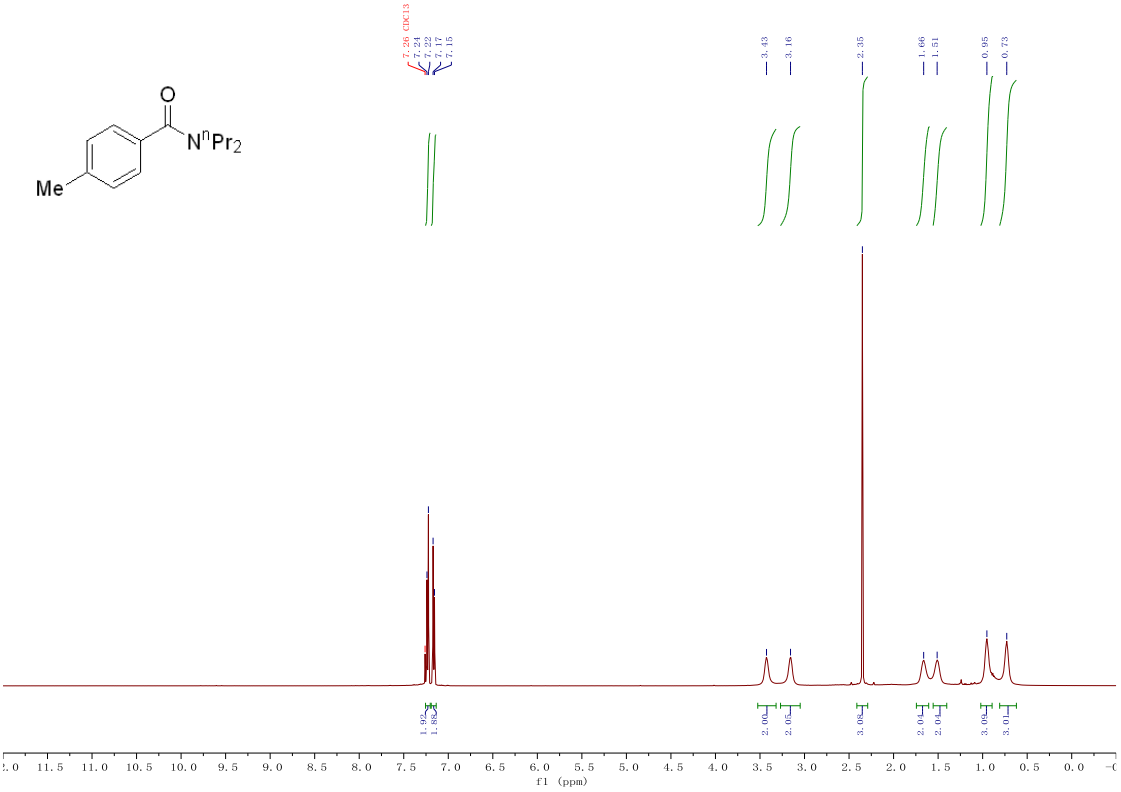


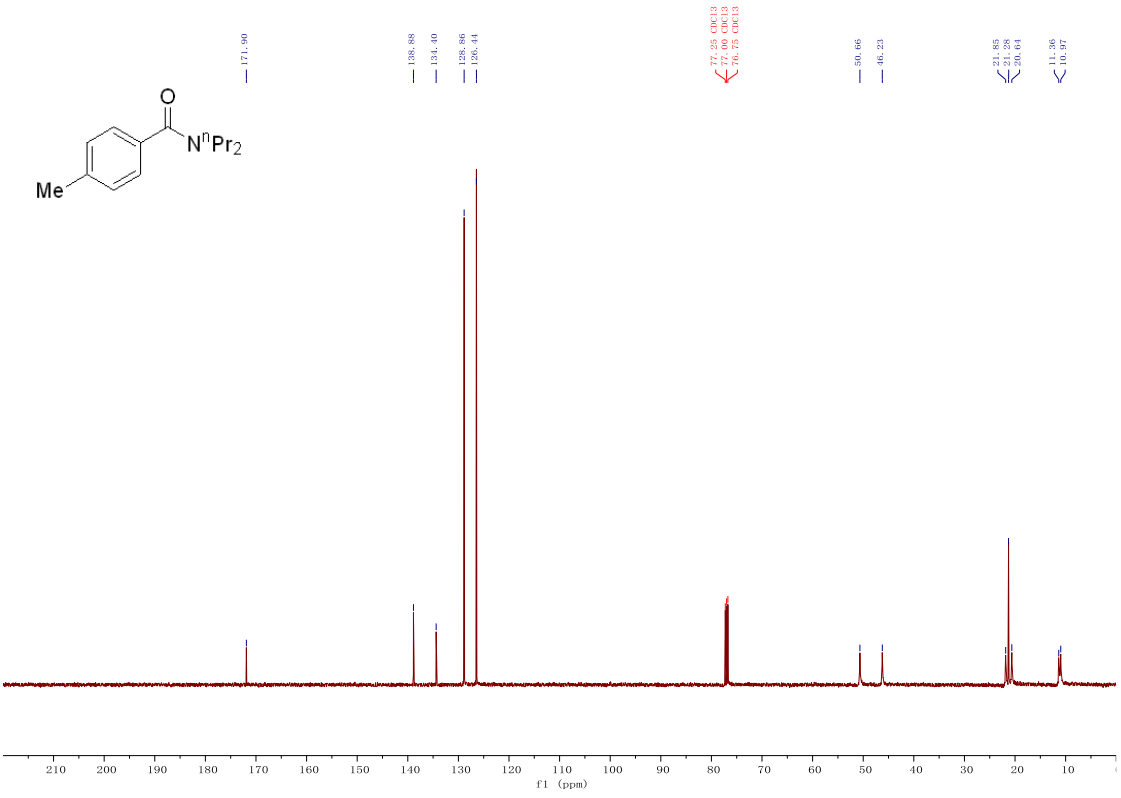
N^1,N^1,N^4,N^4-tetraethylterephthalamide (3x)



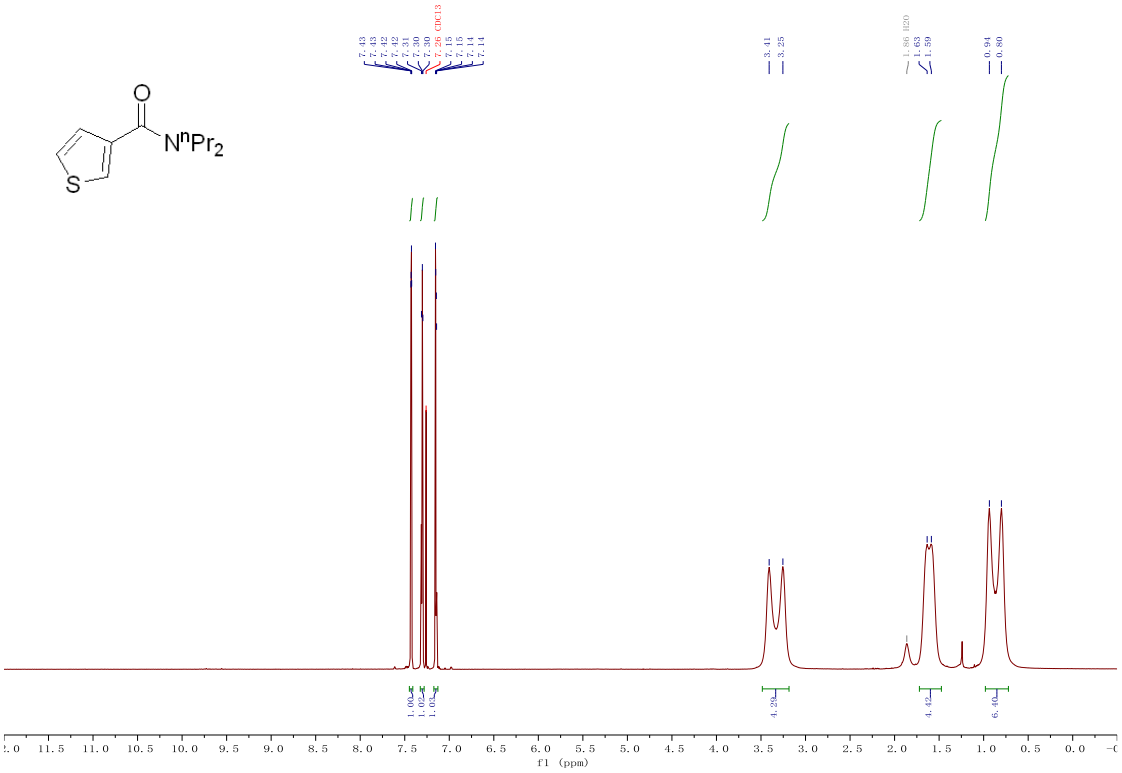


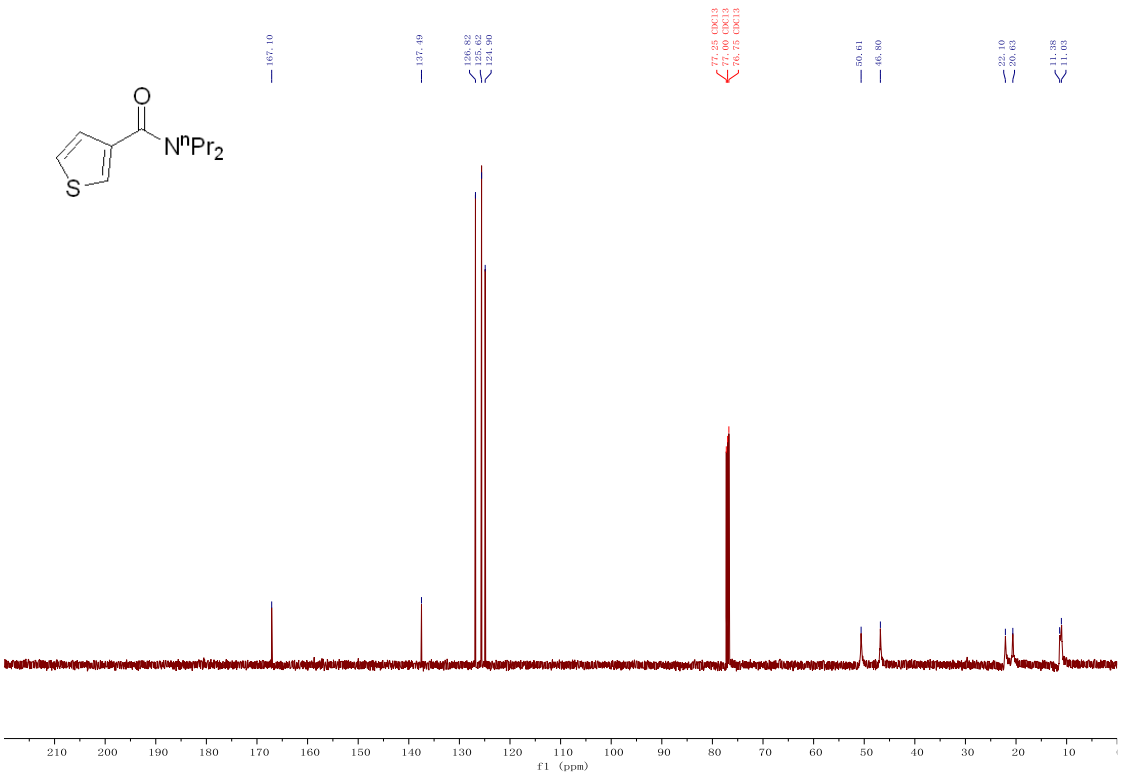
4-methyl-N,N-dipropylbenzamide (3y)



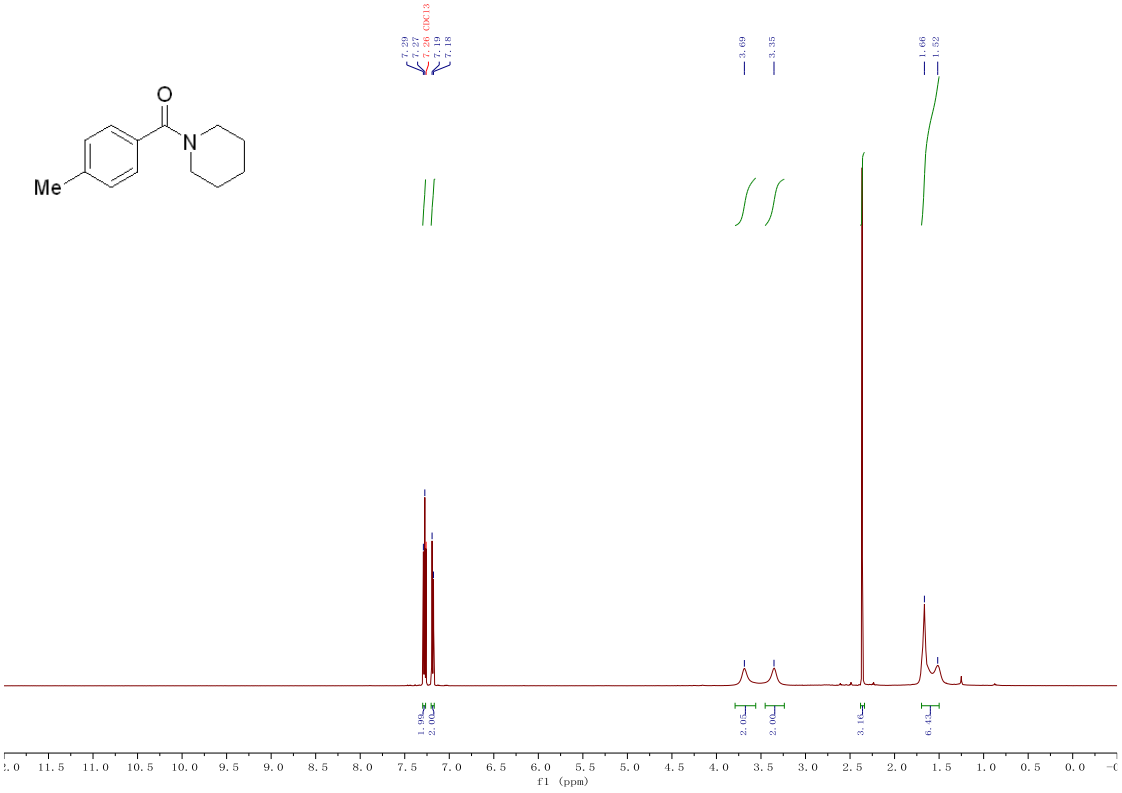


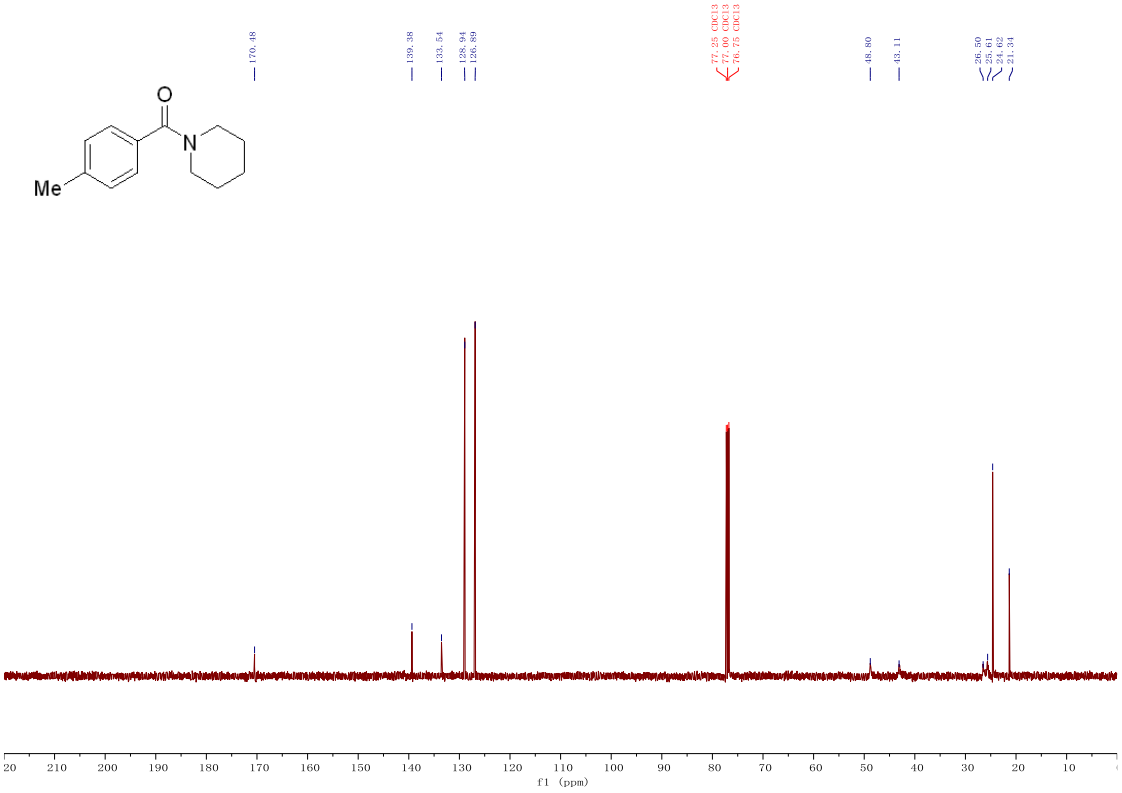
N,N-dipropylthiophene-3-carboxamide (3z)



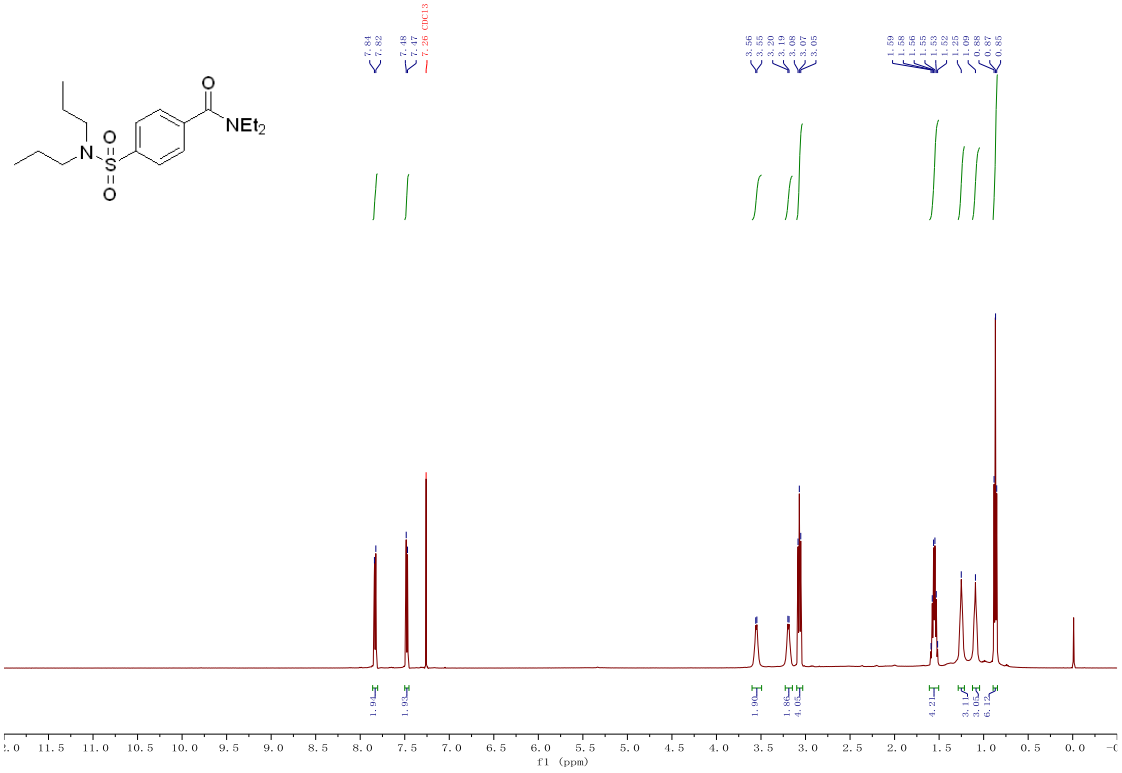


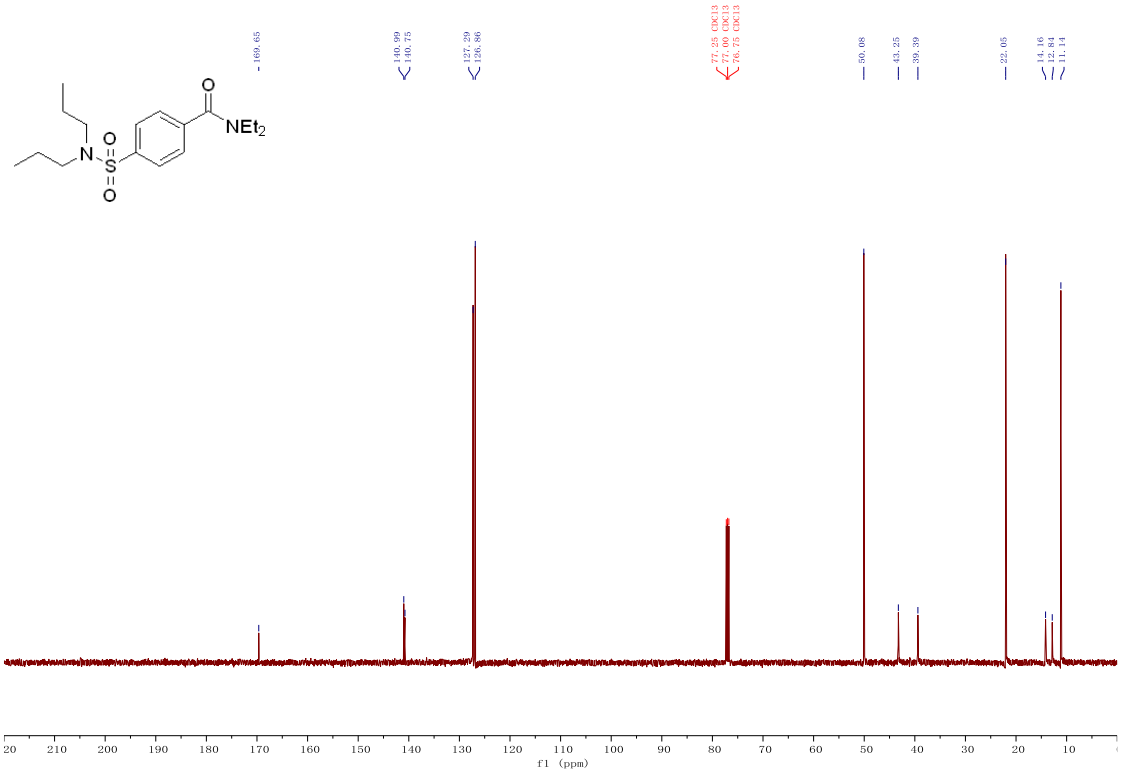
piperidin-1-yl(p-tolyl)methanone (3aa)



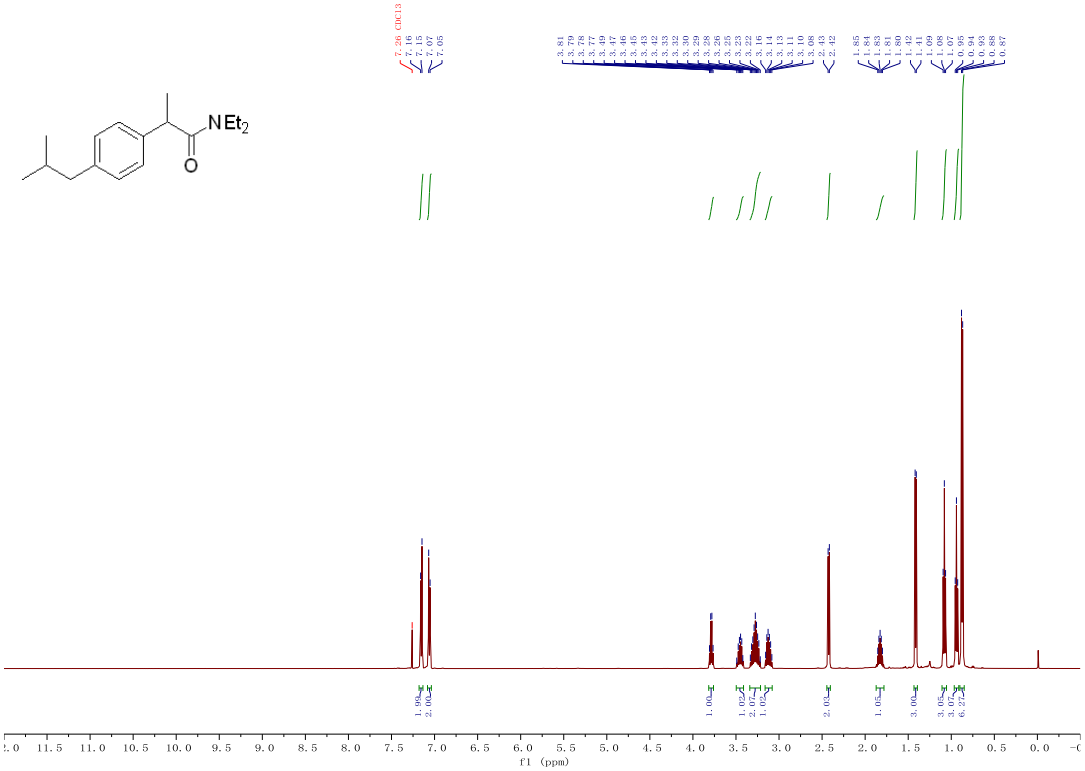


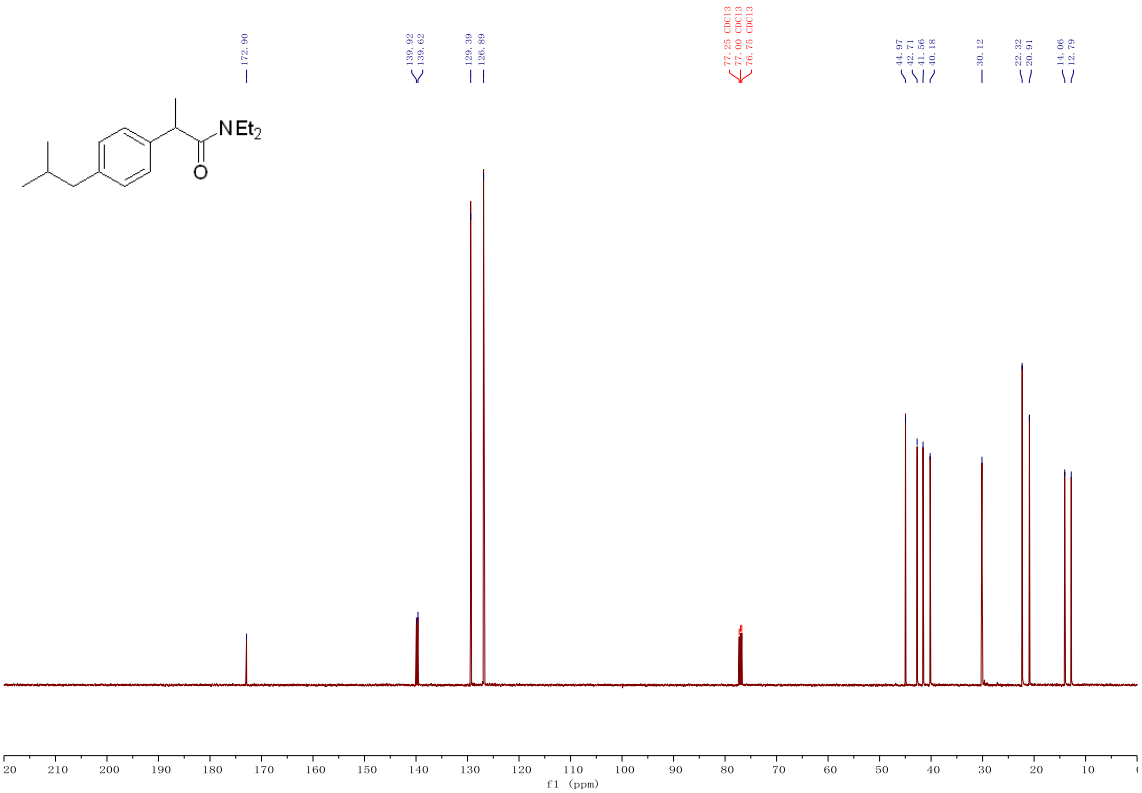
4-(N,N-dipropylsulfamoyl)-N,N-diethylbenzamide (4a)



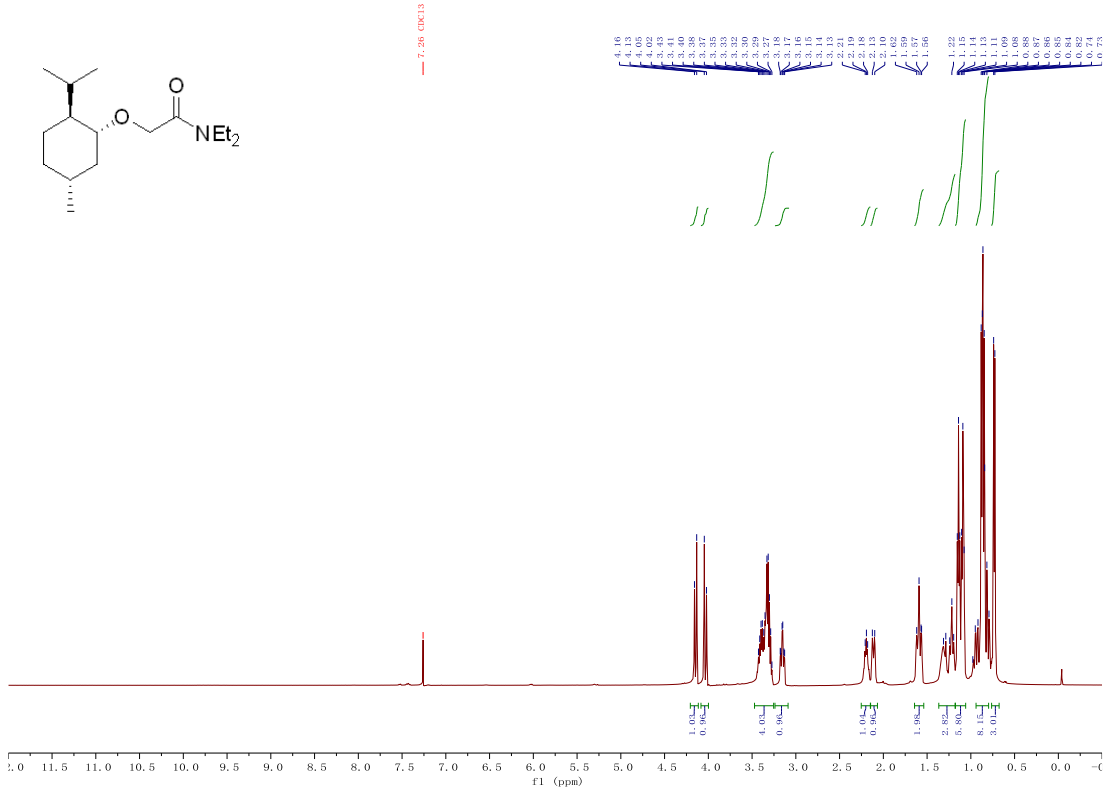


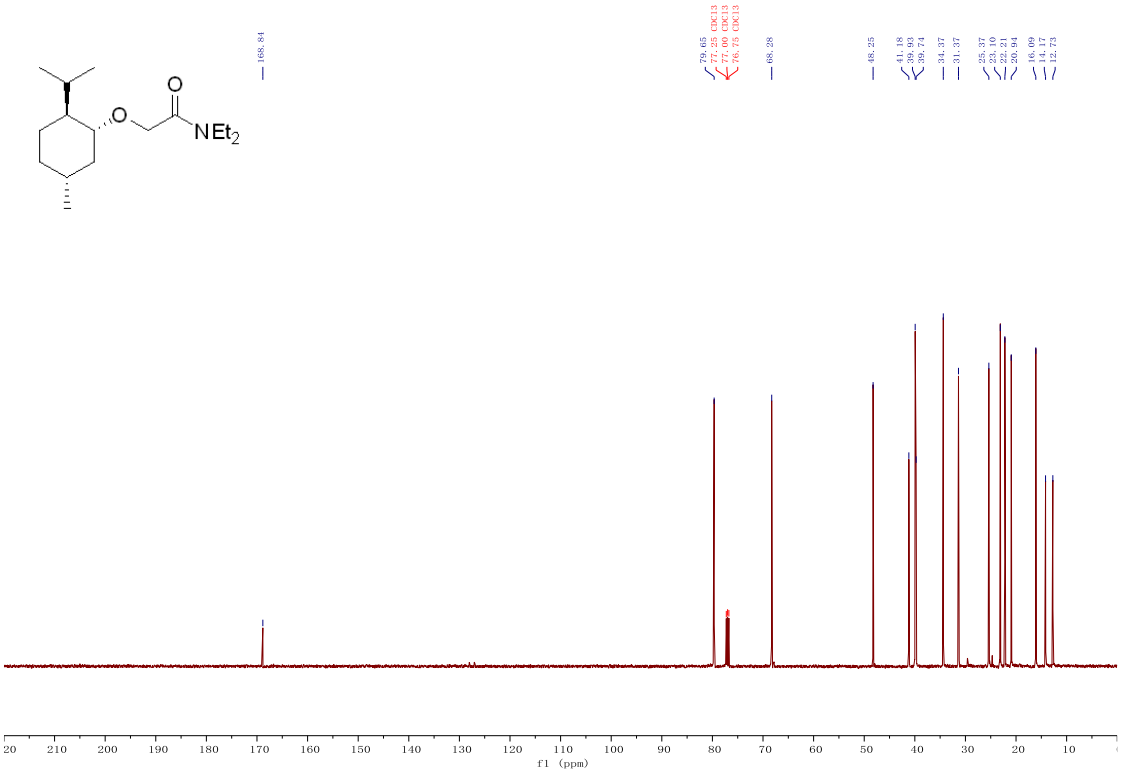
N,N-diethyl-2-(4-isobutylphenyl)propenamide (4b)



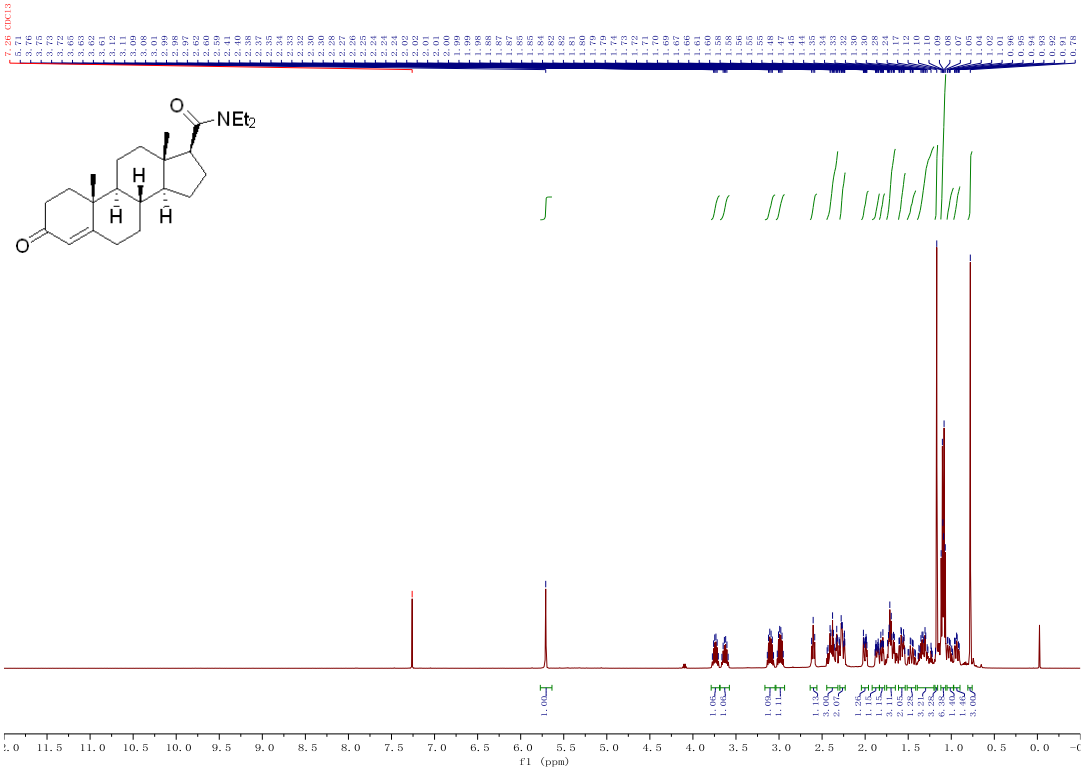


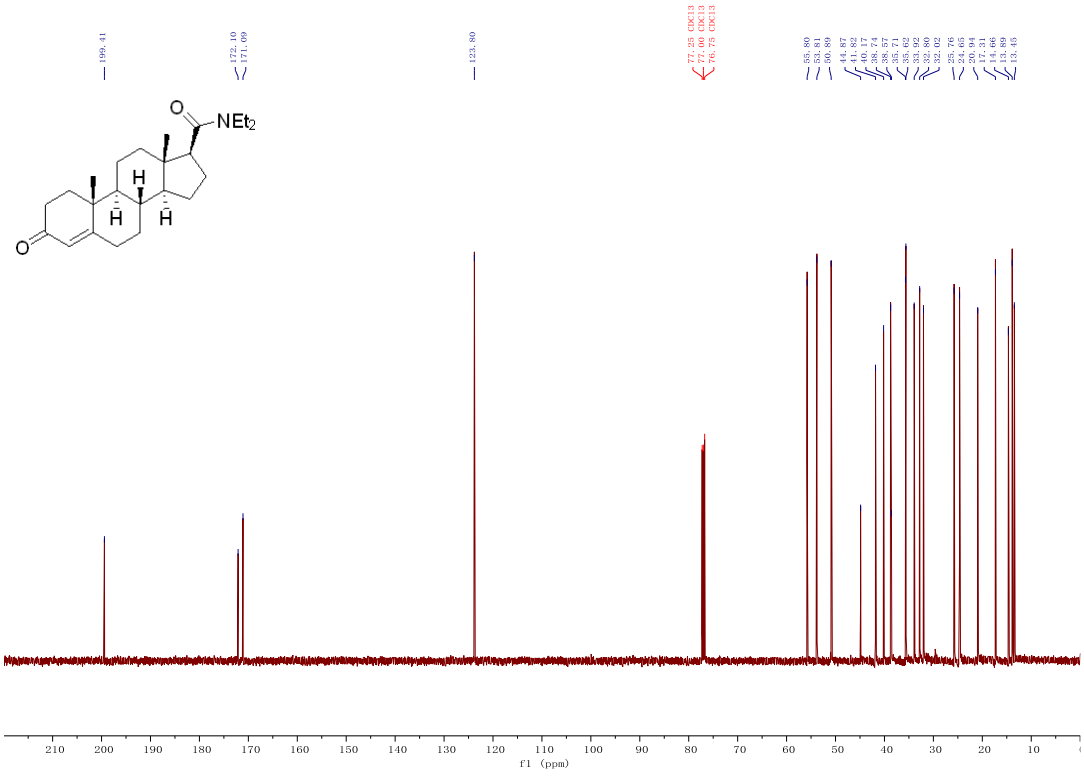
N,N-diethyl-2-(((1R,2S,5R)-2-isopropyl-5-methylcyclohexyl)oxy)acetamide (4c)



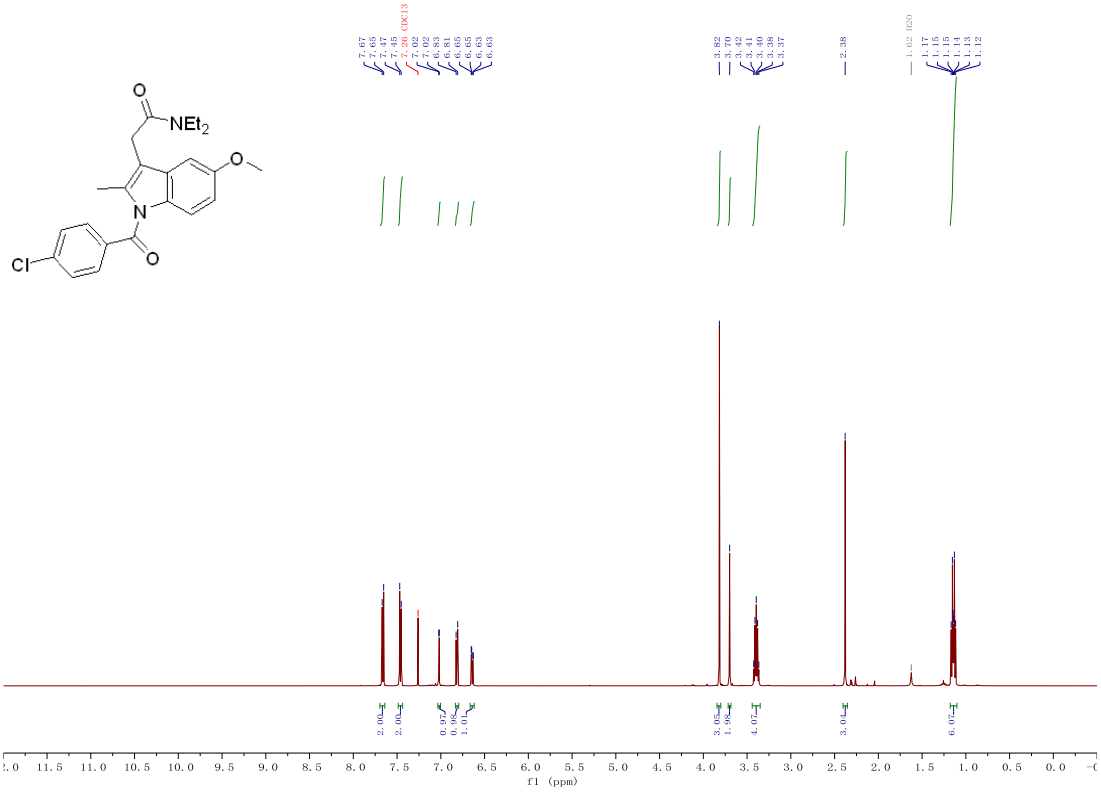


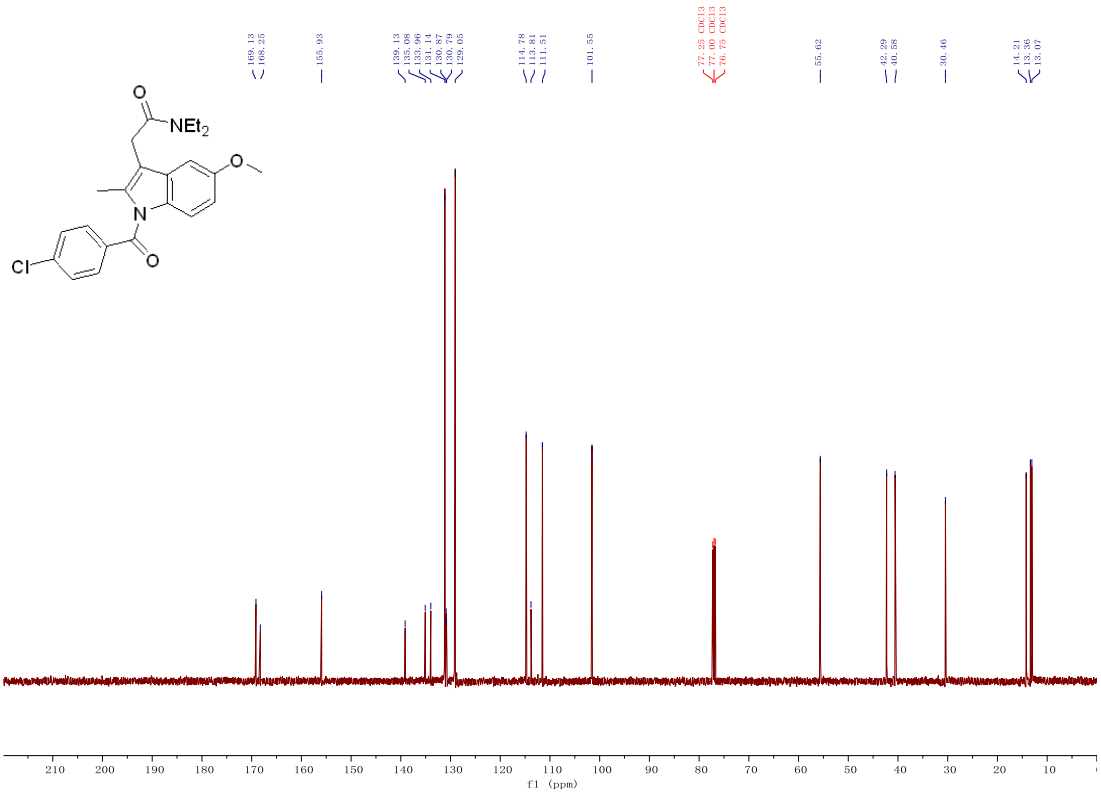
(8S,9S,10R,13S,14S,17S)-N,N-diethyl-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthrene-17-carboxamide (4d)



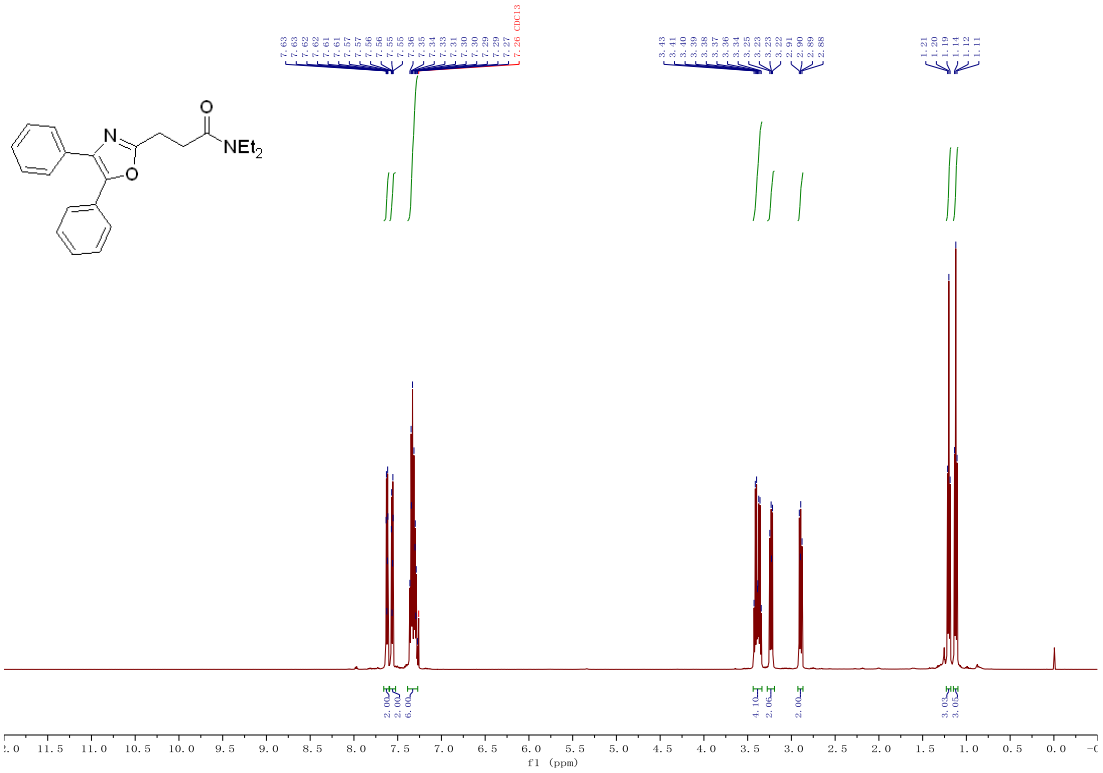


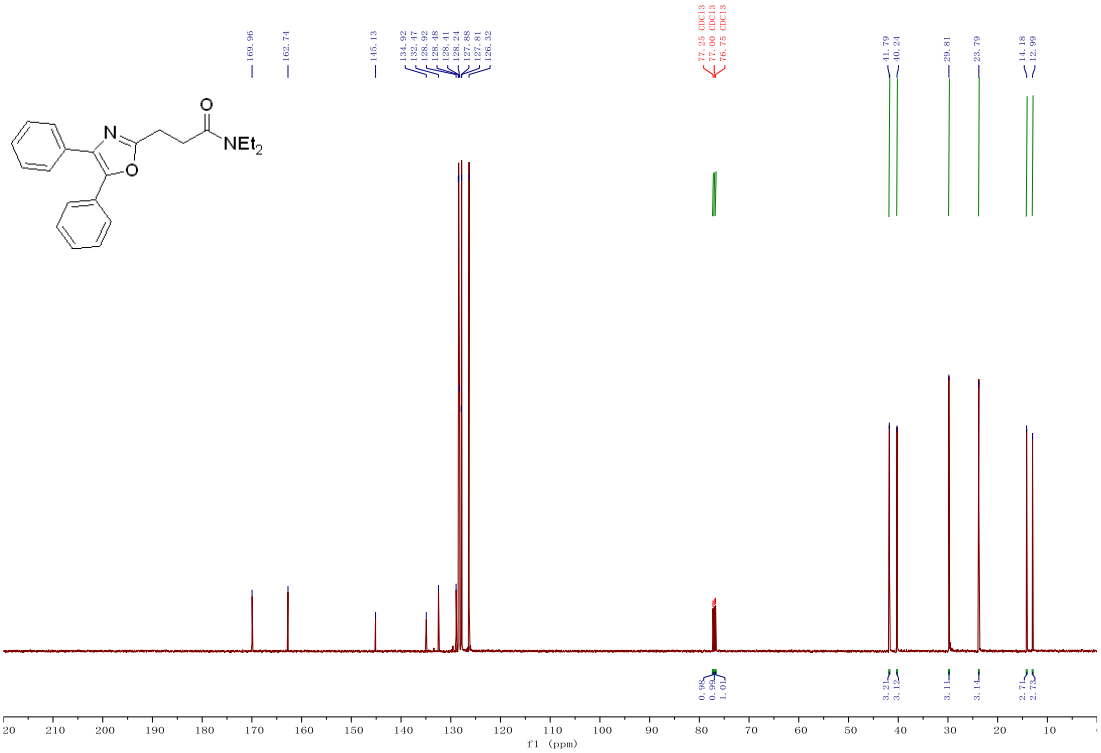
2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)-N,N-diethylacetamid (4e)



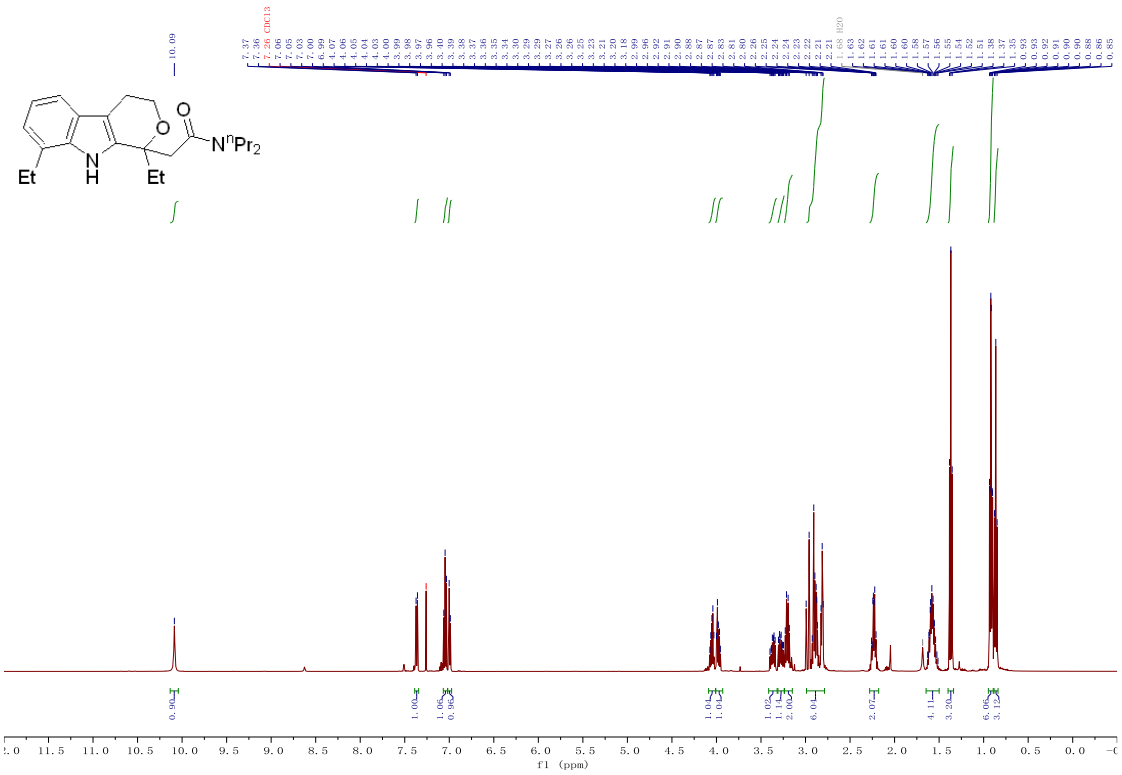


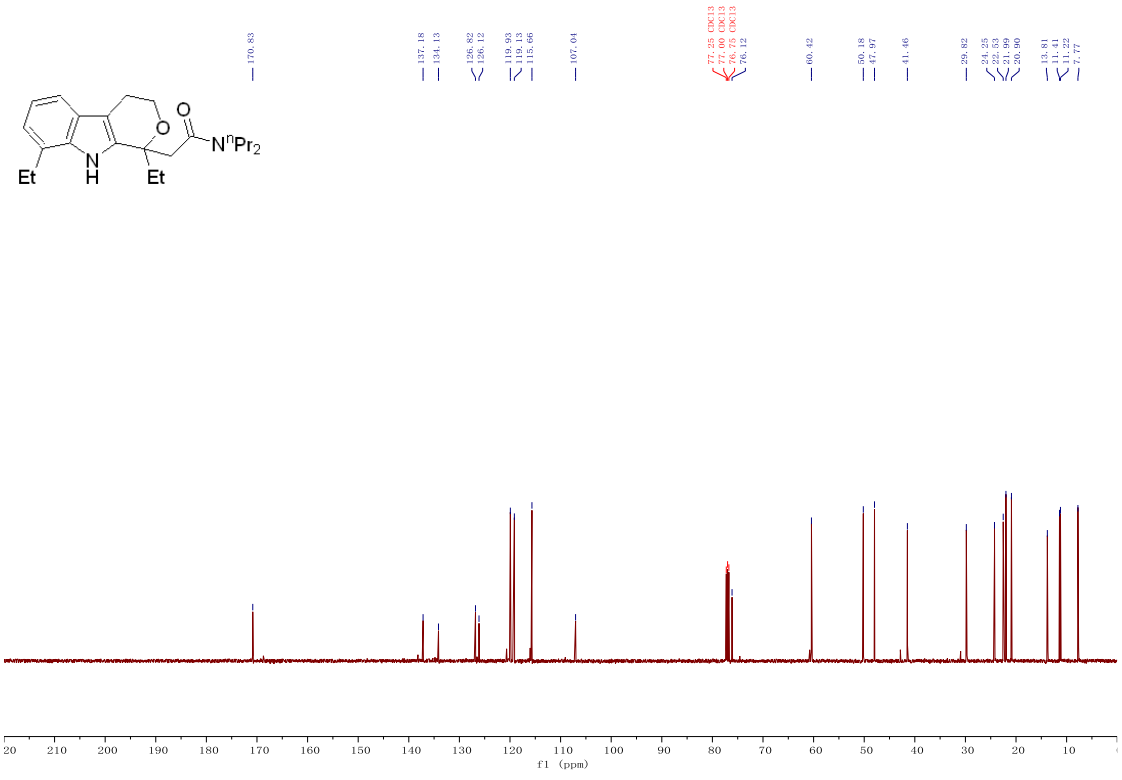
3-(4,5-diphenyloxazol-2-yl)-N,N-diethylpropanamide (4f)



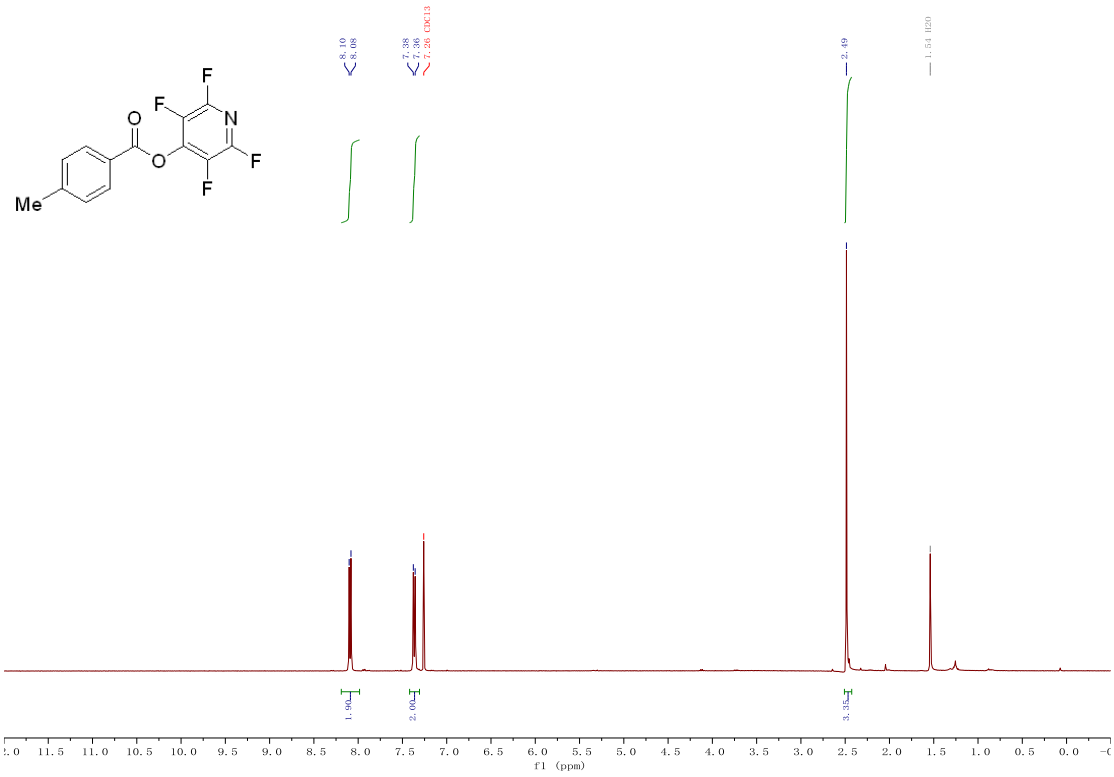


2-(1,8-diethyl-1,3,4,9-tetrahydropyrano[3,4-b]indol-1-yl)-N,N-dipropylacetamide (4g)





perfluoropyridin-4-yl 4-methylbenzoate (5)



8. References

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3 W. D. G. Brittain and S. L. Cobb, *Org. Lett.* 2021, **23**, 5793–5798.