

Supplementary Information

for

A Mild and Efficient Amide Formation Reaction Mediated by P(OEt)₃ and Iodine

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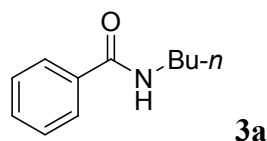
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General Remarks: The ^1H and ^{13}C NMR spectra were recorded on a Varian Mercury-Plus 300 or Varian INOVA 400 NMR instrument. All melting points are uncorrected. CH_2Cl_2 , CH_3CN , DMF, and Et_3N were distilled from CaH_2 , and THF was freshly distilled from Na prior to use. All other reagents were obtained from commercial sources and were used without further purification. Column chromatography was performed on 200–300 mesh silica gel. Thin-layer chromatography was conducted on Kieselgel60 F254.

General procedure for the synthesis of amides 3a-3r:

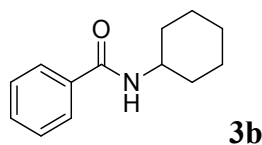
A solution of $\text{P}(\text{OEt})_3$ (1.0 mmol) in CH_2Cl_2 (5 mL) was added successively I_2 (1.0 mmol), **1** (1.0 mmol) and tertiary amine (Et_3N or N-methylmorpholine, 1.5 mmol) at 0 °C and then stirred at room temperature for 30 minutes. After addition of amine **2** (1.2 mmol) directly or the solution of amine's hydrochloride salt in DMF with one equivalent of tertiary amine to the mixture, the reaction mixture was stirred for 2–12 hours indicated in Table 2 and then diluted with CH_2Cl_2 (60 mL), washed with aqueous NH_4Cl , 5% NaOH and brine, dried (Na_2SO_4), and evaporated in vacuo. The residue was pure enough for the spectroscopic analysis, or purified by flash column chromatography on silica gel using hexane/EtOAc (12:1–4:1) as eluent, or recrystallize with ether to give the corresponding products **3a-3r**.

N-(n-butyl)benzamide (3a)^[1]



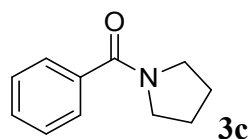
Oil. Yield: 75%. ^1H NMR (400 MHz, CDCl_3): δ 7.79 (d, $J = 7.7$ Hz, 2H), 7.52 (t, $J = 7.2$ Hz, 1H), 7.46 (t, $J = 7.5$ Hz, 2H), 6.21 (s, 1H), 3.54–3.44 (m, 2H), 1.69–1.58 (m, 2H), 1.51–1.39 (m, 2H), 0.99 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3): δ 167.7, 134.8, 131.3, 128.5, 126.9, 39.8, 31.7, 20.2, 13.8.

N-cyclohexylbenzamide (3b)^[2]



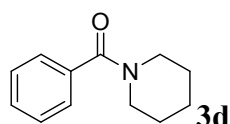
Oil. Yield: 95%. ^1H NMR (400 MHz, CDCl_3): δ 7.78 (d, $J = 7.8$ Hz, 2H), 7.47 (dt, $J = 26.8, 7.3$ Hz, 3H), 6.06 (s, 1H), 4.12 – 3.89 (m, 1H), 2.05 (d, $J = 10.0$ Hz, 2H), 1.78 (d, $J = 13.3$ Hz, 2H), 1.68 (d, $J = 12.9$ Hz, 1H), 1.45 (dd, $J = 24.8, 12.3$ Hz, 2H), 1.35 – 1.12 (m, 3H); ^{13}C NMR (101 MHz, CDCl_3): δ 166.6, 135.1, 131.2, 128.5, 126.8, 48.7, 33.3, 25.6, 24.9.

1-benzoyl-pyrrolidine (3c)^[3]



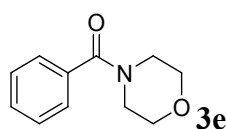
Oil. Yield: 82%. ¹H NMR (400 MHz, CDCl₃): δ 7.45–7.55 (m, 2H), 7.45–7.33 (m, 3H), 3.64 (s, 2H), 3.41 (s, 2H), 1.95 (s, 2H), 1.87 (s, 2H); ¹³C NMR (101 MHz, CDCl₃): δ 169.7, 137.2, 129.8, 128.2, 127.1, 49.6, 46.2, 26.4, 24.5.

1-benzoyl-piperidine (3d)^[4]



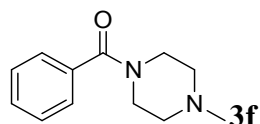
Oil. Yield: 97%. ¹H NMR (300 MHz, CDCl₃): δ 7.38 (s, 5H), 3.71 (s, 2H), 3.34 (s, 2H), 1.59–1.75 (m, 6H); ¹³C NMR (101 MHz, CDCl₃): δ 170.3, 136.5, 129.4, 128.4, 126.8, 48.8, 43.1, 26.5, 25.6, 24.6.

1-benzoyl-morpholine(3e)^[3]



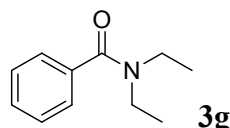
Oil. Yield: 91%. ¹H NMR (300 MHz, CDCl₃): δ 7.38 (s, 5H), 3.81–3.35 (m, 8H); ¹³C NMR (101 MHz, CDCl₃): δ 170.4, 135.3, 129.9, 128.6, 127.1, 66.9, 48.2, 42.6.

1-benzoyl-4-methylpiperazine(3f)^[5]



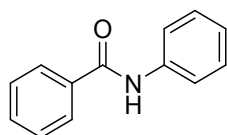
Oil. Yield: 90%. ¹H NMR (300 MHz, CDCl₃): δ 7.40 (s, 5H), 3.81 (s, 2H), 3.45 (s, 2H), 2.17–2.63 (m, 7H); ¹³C NMR (101 MHz, CDCl₃): δ 170.2, 135.7, 129.6, 128.4, 127.0, 55.2, 54.7, 47.6, 46.0, 42.0.

N,N-diethylbenzamide (3g)^[6]



Oil. Yield: 84%. ¹H NMR (300 MHz, CDCl₃): δ 7.35 (s, 5H), 3.53 (d, *J* = 4.9 Hz, 2H), 3.23 (d, *J* = 4.5 Hz, 2H), 1.24 (s, 3H), 1.09 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 171.3, 137.3, 129.1, 128.4, 126.2, 43.3, 39.2, 14.2, 12.9.

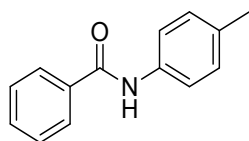
N-benzylbenzamide (3h)^[7]



3h

White solid. Mp161-163°C (lit.⁷ 162–163 °C). Yield: 91%. ¹H NMR (300 MHz, CDCl₃): δ 7.86 (d, *J* = 7.1 Hz, 3H), 7.64 (d, *J* = 7.9 Hz, 2H), 7.42–7.59 (m, 3H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃): δ 165.8, 137.9, 135.0, 131.9, 129.1, 128.8, 127.0, 124.6, 120.2.

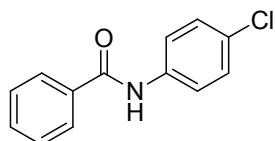
N-(*p*-tolyl)benzamide (3i)^[7]



3i

White solid. Mp154-157°C (lit.⁷ 154–157 °C). Yield: 82%. ¹H NMR (300 MHz, CDCl₃): δ 7.85 (d, *J* = 7.6 Hz, 2H), 7.80 (s, 1H), 7.44–7.56 (m, 4H), 7.17 (d, *J* = 7.3 Hz, 2H), 3.48 (s, 1H), 2.35 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 165.8, 135.4, 135.1, 134.2, 131.7, 129.6, 128.7, 127.1, 120.4, 21.0.

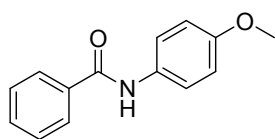
N-(4-chlorophenyl)benzamide (3j)^[7]



3j

White solid. Mp147-152°C (lit.⁷ 193–194 °C). Yield: 53%. ¹H NMR (400 MHz, CDCl₃): δ 7.90 (d, *J* = 7.9 Hz, 2H), 7.85 (s, 1H), 7.57–7.68 (m, 3H), 7.54 (t, *J* = 7.6 Hz, 2H), 7.38 (d, *J* = 8.5 Hz, 2H); ¹³C NMR (101 MHz, DMSO): δ 166.1, 138.7, 135.2, 132.2, 129.0, 128.9, 128.2, 127.7, 122.3.

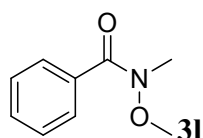
N-(4-methoxyphenyl)benzamide(3k)^[8]



3k

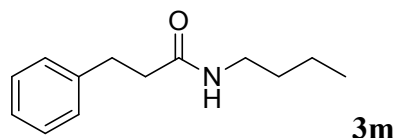
White solid. Mp154–156°C (lit.⁸ 154–155 °C). Yield: 67%. ¹H NMR (300 MHz, CDCl₃): δ 7.84 (d, *J* = 6.9 Hz, 3H), 7.61–7.39 (m, 5H), 6.89 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 3H); ¹³C NMR (101 MHz, CD₃OD): δ 167.3, 156.9, 134.9, 131.4, 131.3, 128.2, 127.1, 122.7, 113.5, 54.5.

N-methoxyl-N-methylbenzamide (3l)^[3]



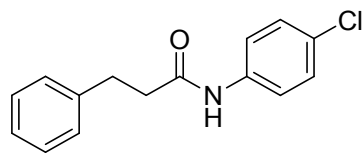
Oil. Yield: 75%. ^1H NMR (300 MHz, CDCl_3): δ 7.65 (d, $J = 7.1$ Hz, 2H), 7.48–7.31 (m, 3H), 3.55 (s, 3H), 3.36 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3): δ 167.0, 134.1, 130.6, 128.1, 128.0, 61.0, 33.8.

N-butyl-3-phenylpropanamide (3m)^[9]



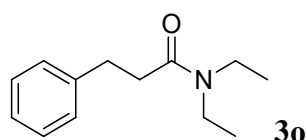
Oil. Yield: 65%. ^1H NMR (400 MHz, CDCl_3): δ 7.32–7.25 (m, 2H), 7.23–7.17 (m, 3H), 5.78 (s, 1H), 3.21 (td, $J = 7.1, 5.9$ Hz, 2H), 2.97 (t, $J = 8.0$ Hz, 2H), 2.47 (t, $J = 7.5$ Hz, 2H), 1.47–1.36 (m, 2H), 1.32–1.21 (m, 2H), 0.90 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3): δ 172.2, 140.9, 128.5, 128.3, 126.2, 39.2, 38.5, 31.9, 31.6, 20.0, 13.8.

N-(4-chlorophenyl)-3-phenylpropanamide (3n)^[10]



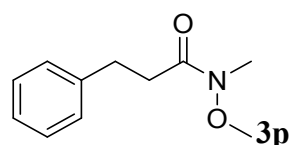
White solid. Mp 158–159°C (lit.¹⁰ 141.5–143 °C). Yield: 80%. ^1H NMR (400 MHz, CDCl_3): δ 7.57 (s, 1H), 7.40 (d, $J = 8.8$ Hz, 2H), 7.35–7.28 (m, 2H), 7.21–7.27 (m, 5H), 3.04 (t, $J = 7.6$ Hz, 2H), 2.67 (t, $J = 7.6$ Hz, 2H); ^{13}C NMR (101 MHz, CDCl_3): δ 170.8, 140.4, 136.3, 129.3, 129.0, 128.7, 128.4, 126.5, 121.4, 39.3, 31.5.

N,N-diethyl-3-phenylpropanamide (3o)^[11]



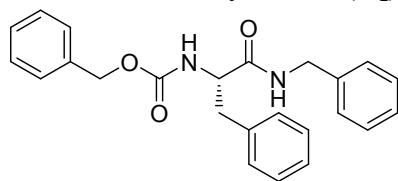
Oil. Yield: 67%. ^1H NMR (400 MHz, CDCl_3): δ 7.35–7.16 (m, 5H), 3.39 (q, $J = 7.1$ Hz, 2H), 3.23 (q, $J = 7.1$ Hz, 2H), 3.00 (t, $J = 8.2$ Hz, 2H), 2.61 (t, $J = 7.6$ Hz, 2H), 1.18–1.03 (m, 6H); ^{13}C NMR (101 MHz, CDCl_3): δ 171.3, 141.6, 128.5, 126.1, 41.9, 40.2, 35.1, 31.7, 14.3, 13.1.

N-methoxy-N-methyl-3-phenylpropanamide (3p)^[12]



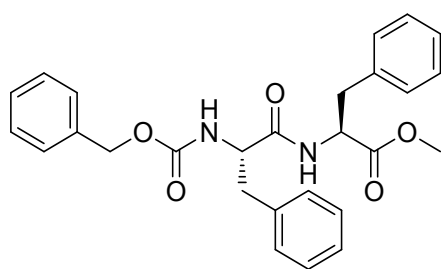
Oil. Yield: 86%. ^1H NMR (400 MHz, CDCl_3): δ 7.34–7.18 (m, 5H), 3.60 (s, 3H), 3.19 (s, 3H), 2.98 (t, $J = 8.3$ Hz, 2H), 2.76 (t, $J = 7.6$ Hz, 2H); ^{13}C NMR (101 MHz, CDCl_3): δ 173.7, 141.34, 128.5, 128.4, 126.1, 61.2, 33.8, 32.2, 30.7.

N-Cbz-Phe benzylamide (3q)^[13]



White Solid. Mp 160–162°C [lit.¹³ mp 162–164°C]. Yield: 85%. ¹H NMR (400 MHz, CDCl₃): δ 7.41–7.13 (m, 13H), 7.12–7.03 (m, 2H), 6.18 (s, 1H), 5.48 (d, *J* = 5.4 Hz, 1H), 5.12–4.98 (s, 2H), 4.47 (d, *J* = 6.7 Hz, 1H), 4.41–4.28 (m, 2H), 3.21–3.01 (m, 2H); ¹³C NMR (101 MHz, CDCl₃): δ 170.7, 155.9, 137.5, 136.4, 136.1, 129.4, 128.7, 128.6, 128.6, 128.2, 128.0, 127.7, 127.5, 127.0, 67.1, 56.5, 43.5, 38.8.

N-Cbz-L-Phe-L-Phe-OMe (3r)^[14]



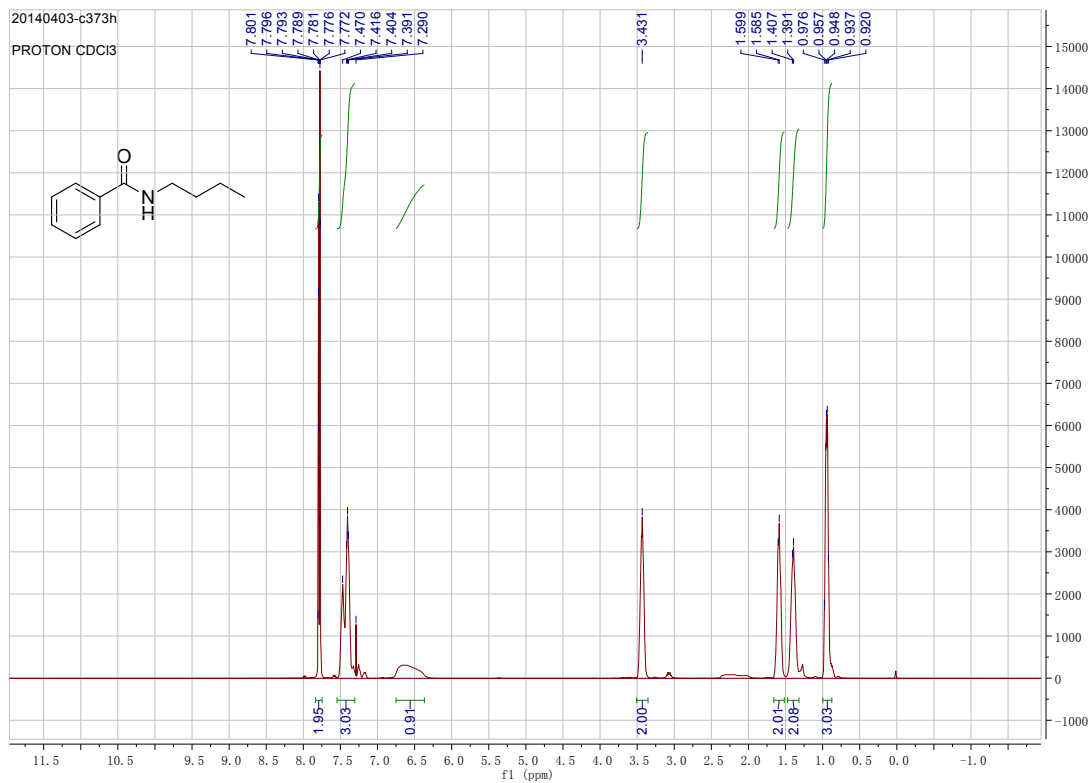
3r

White solid. Mp 146–147°C (lit.¹⁴ 134–136 °C). Yield: 90%. ¹H NMR (400 MHz, CDCl₃): δ 7.42–7.18 (m, 13H), 7.03–6.94 (m, 2H), 6.20 (d, *J* = 7.5 Hz, 1H), 5.24 (d, *J* = 7.2 Hz, 1H), 5.11 (s, 2H), 4.80 (dt, *J* = 7.5, 5.9 Hz, 1H), 4.42 (dd, *J* = 14.1, 6.9 Hz, 1H), 3.70 (s, 3H), 3.14–2.99 (m, 4H); ¹³C NMR (101 MHz, CDCl₃): δ 171.3, 170.4, 155.9, 136.2, 136.1, 135.5, 129.4, 129.2, 128.7, 128.6, 128.2, 128.0, 127.2, 127.1, 67.1, 56.0, 53.3, 52.4, 38.3, 37.9.

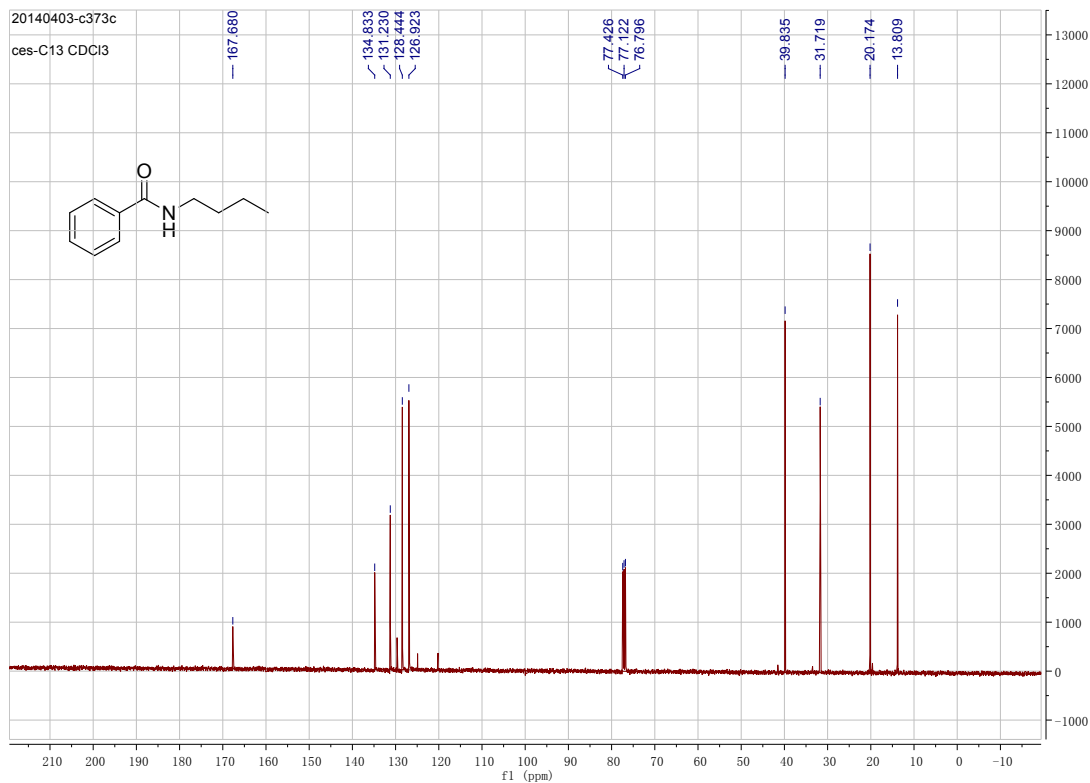
Referencee

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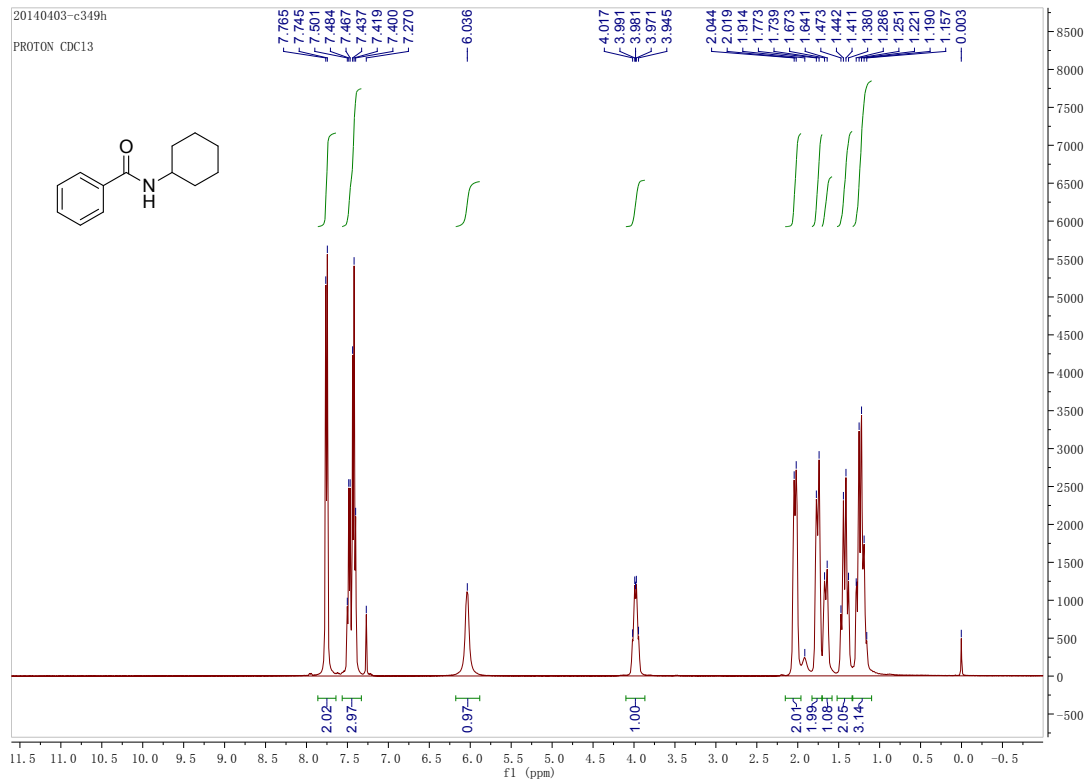
¹H NMR (400 MHz, CDCl₃) of 3a



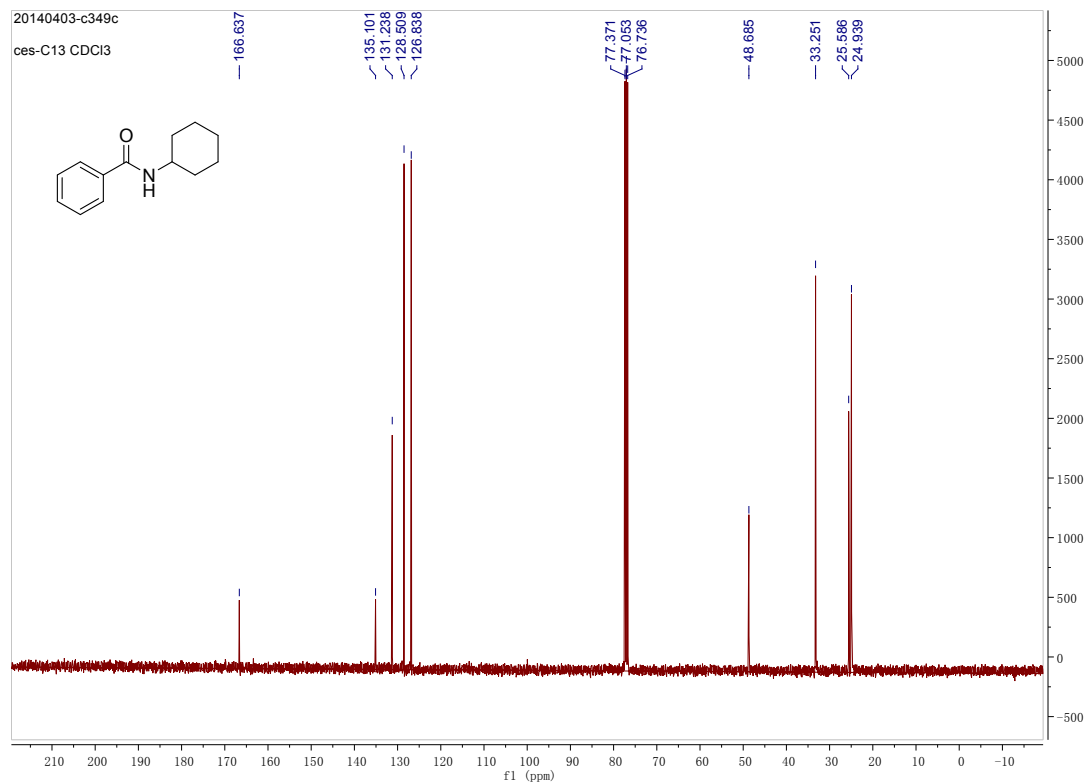
¹³C NMR (101 MHz, CDCl₃) of 3a



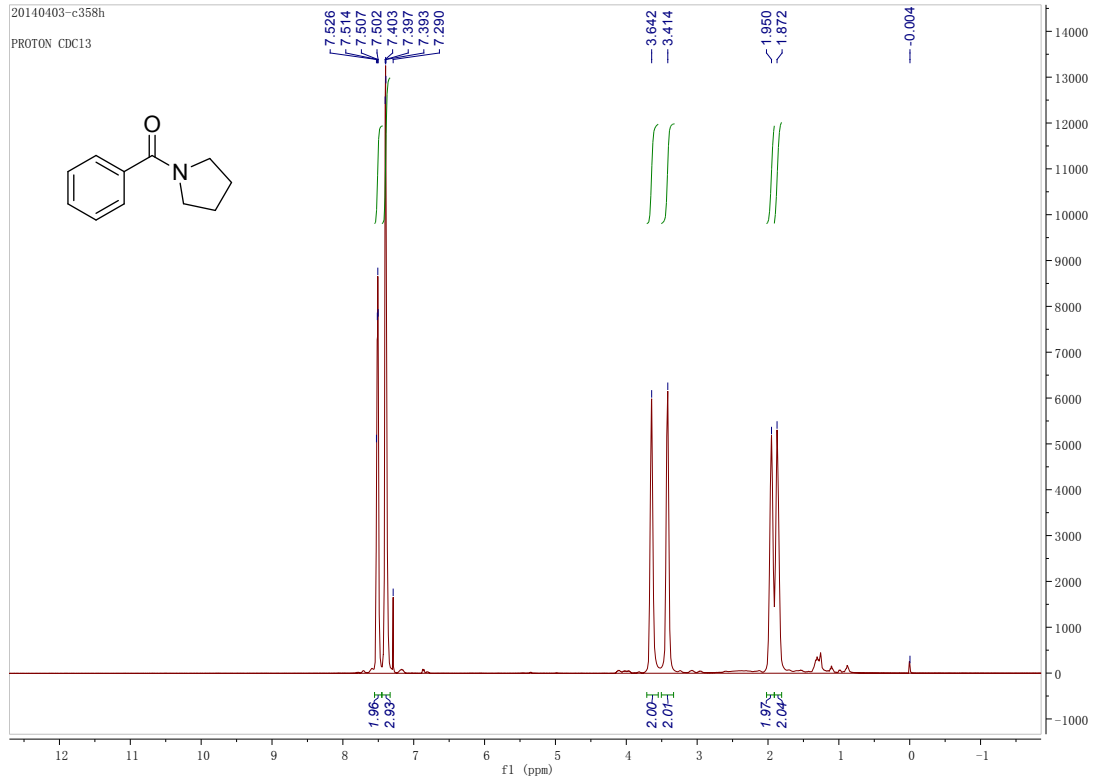
¹H NMR (400 MHz, CDCl₃) of **3b**



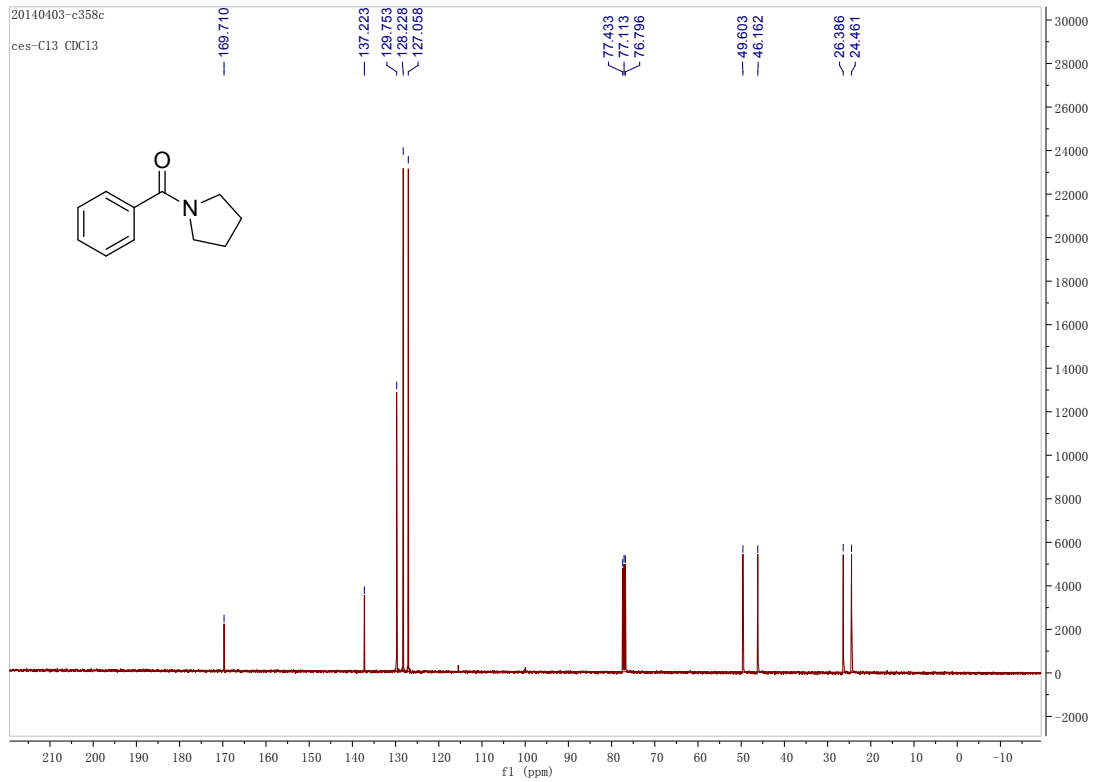
¹³C NMR (101 MHz, CDCl₃) of **3b**



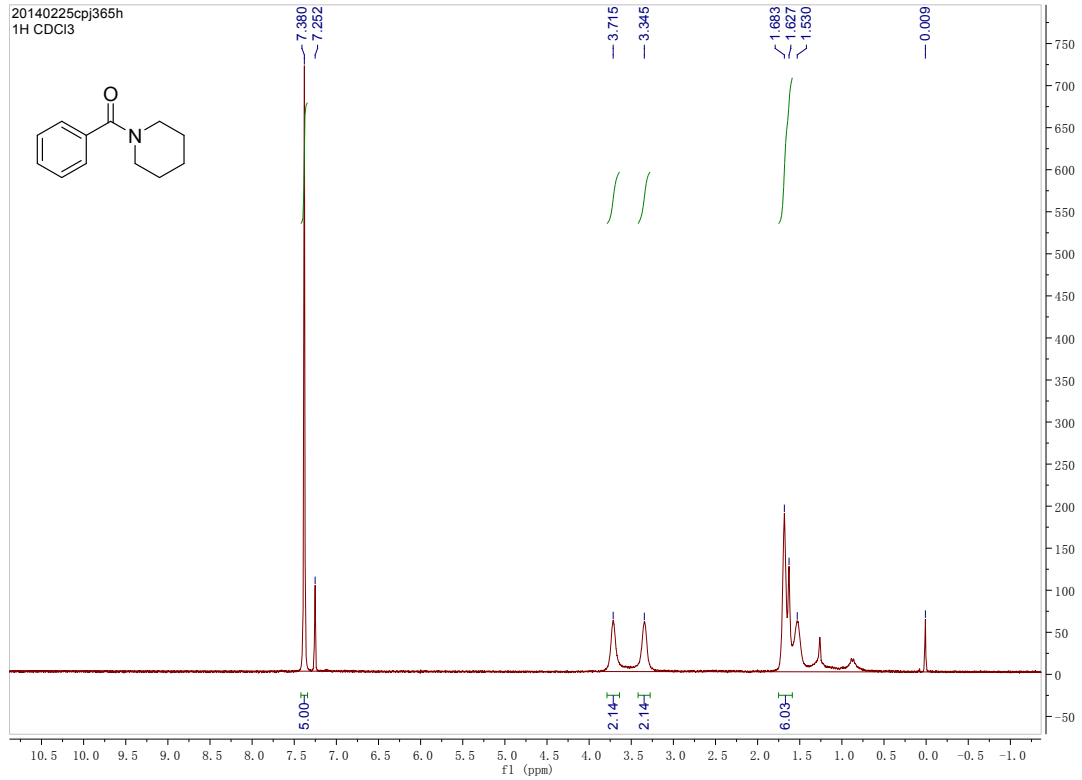
¹H NMR (400 MHz, CDCl₃) of **3c**



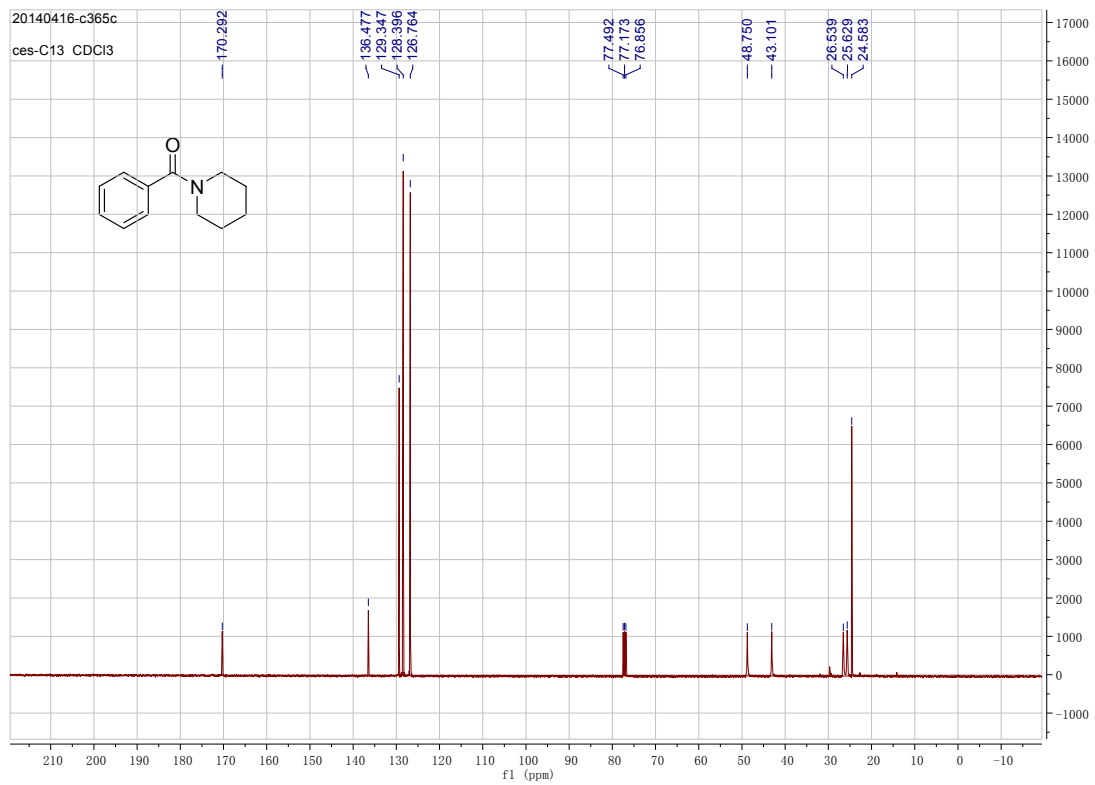
¹³C NMR (101 MHz, CDCl₃) of **3c**



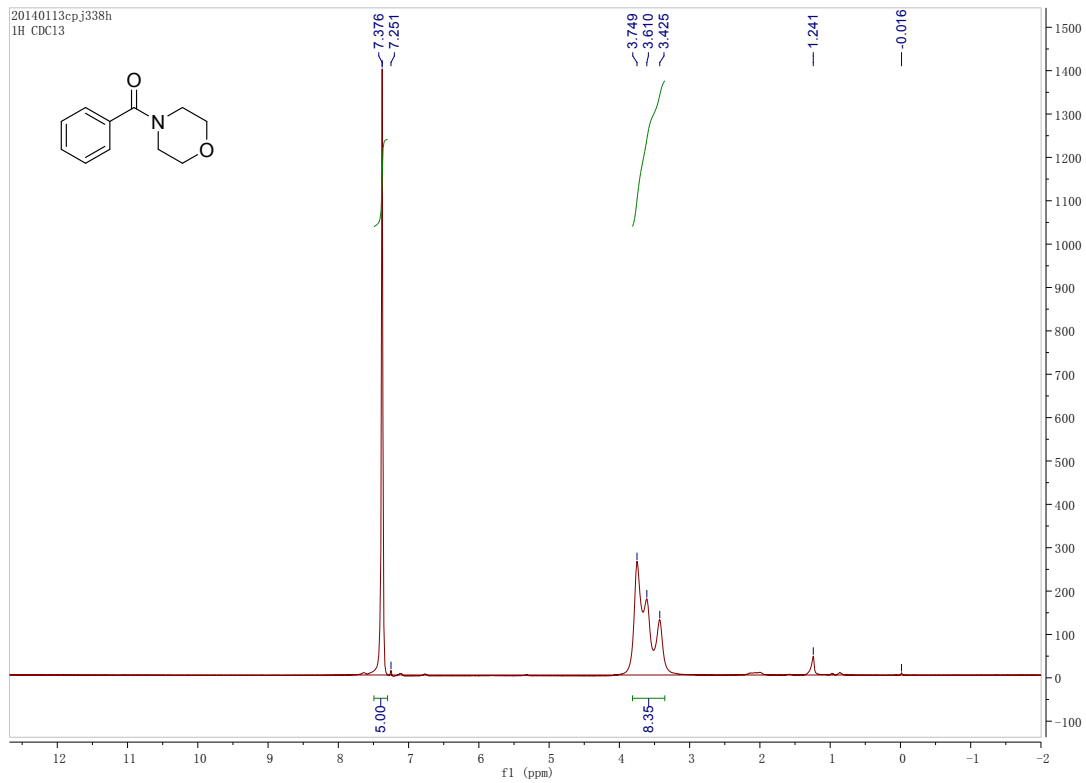
¹H NMR (300 MHz, CDCl₃) of **3d**



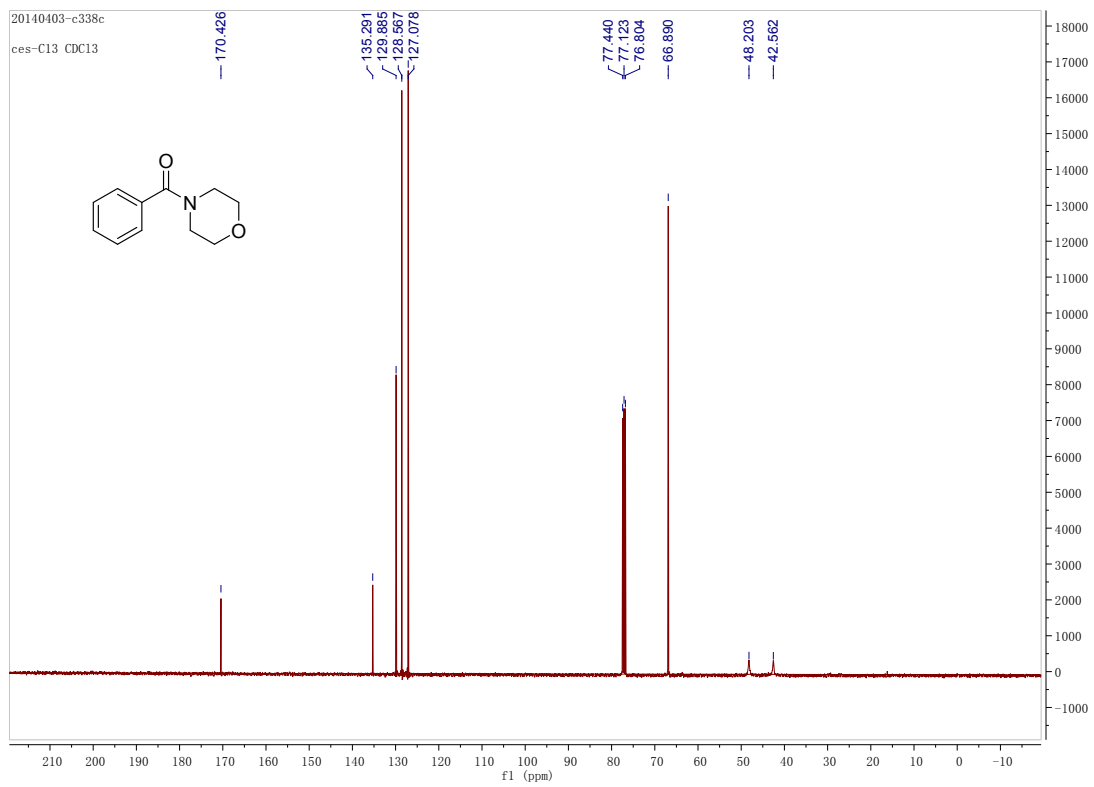
¹³C NMR (101 MHz, CDCl₃) of **3d**



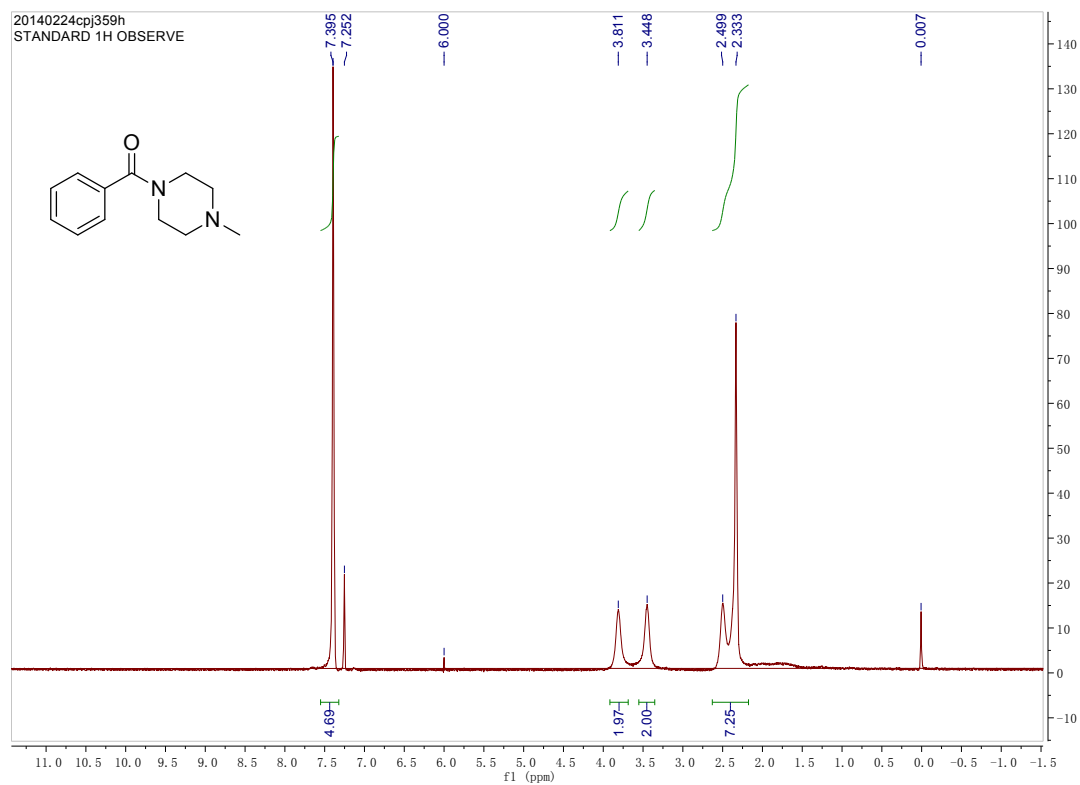
¹H NMR (300 MHz, CDCl₃) of **3e**



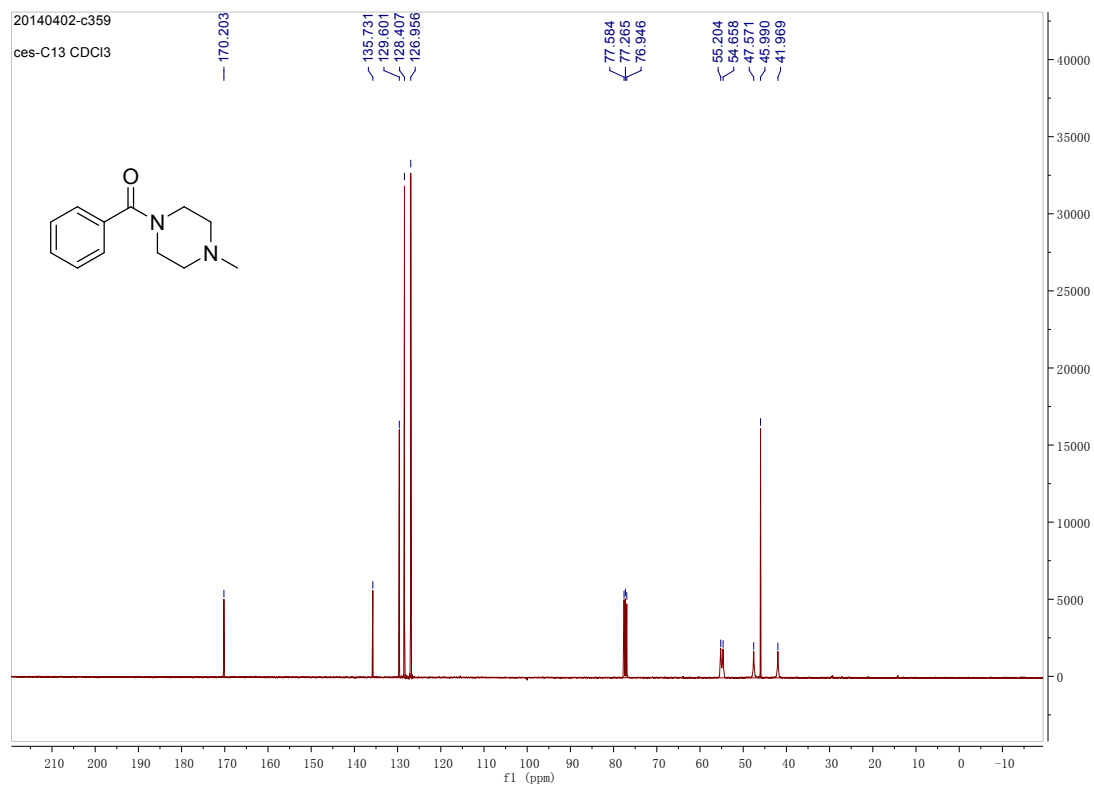
¹³C NMR (101 MHz, CDCl₃) of **3e**



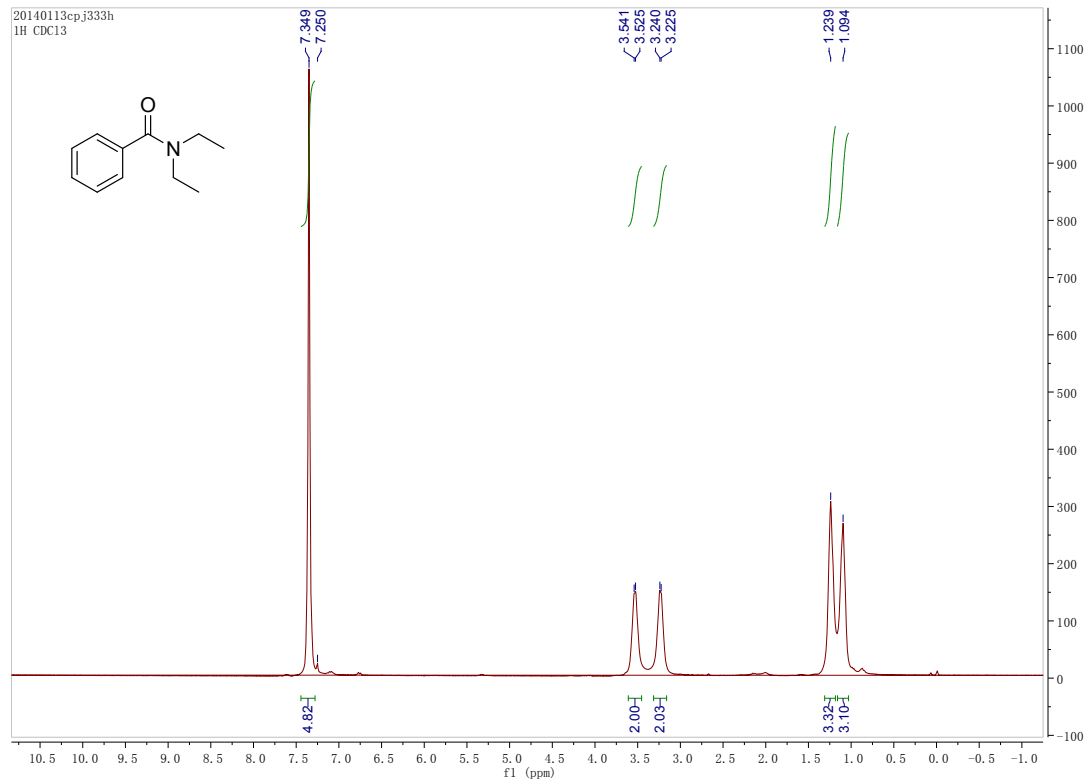
¹H NMR (300 MHz, CDCl₃) of **3f**



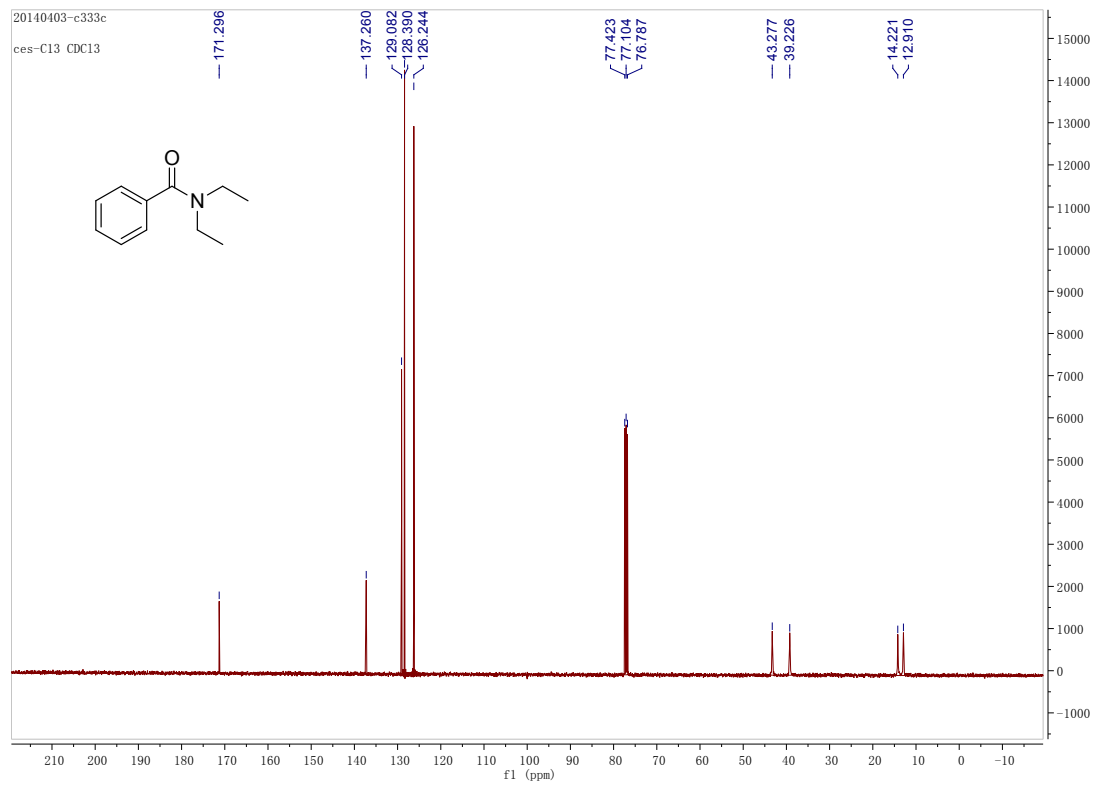
¹³C NMR (101 MHz, CDCl₃) of **3f**



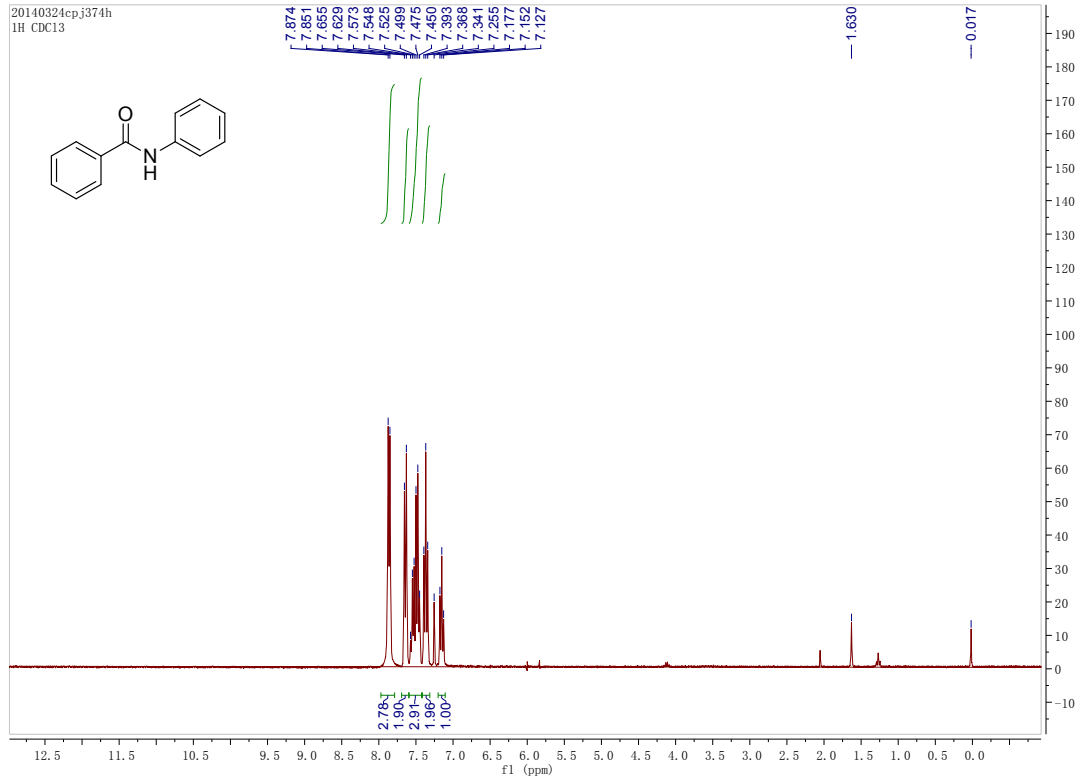
¹H NMR (300 MHz, CDCl₃) of **3g**



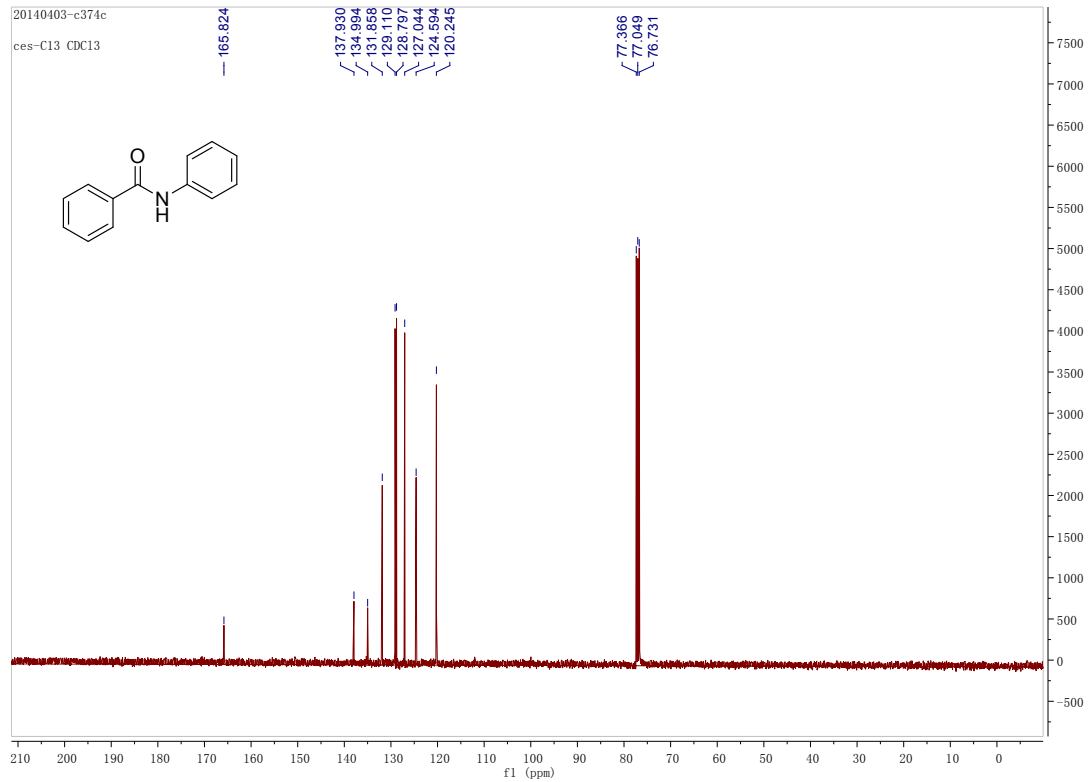
¹³C NMR (101 MHz, CDCl₃) of **3g**



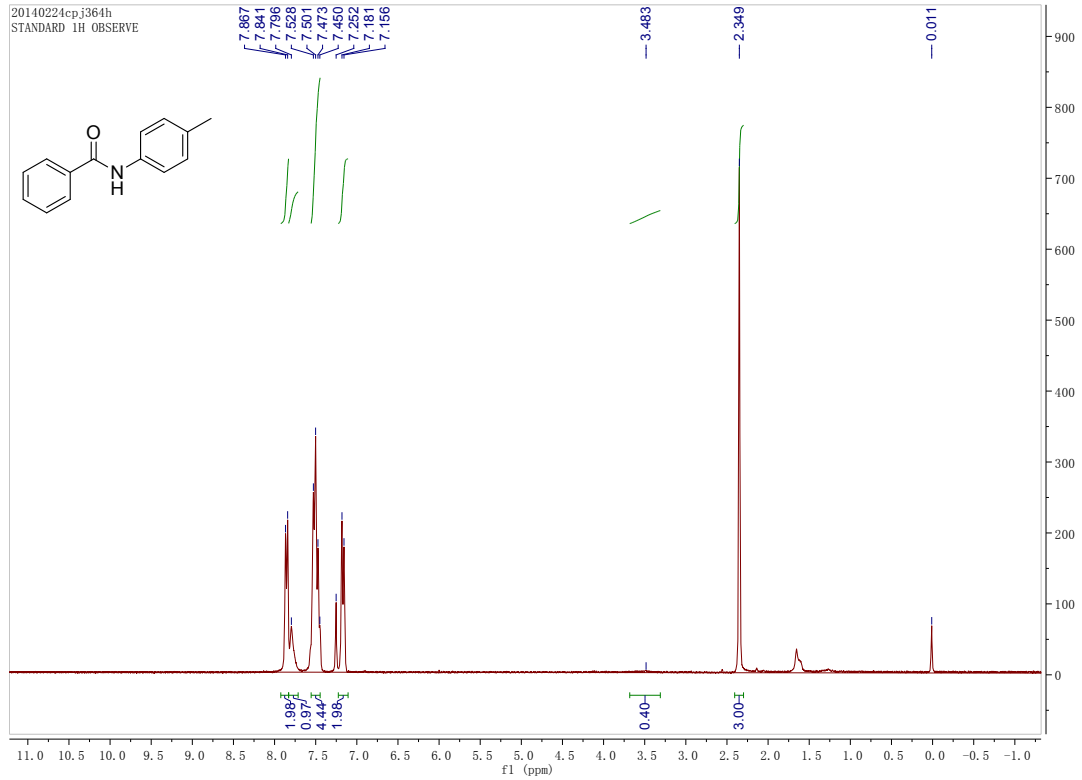
¹H NMR (300 MHz, CDCl₃) of **3h**



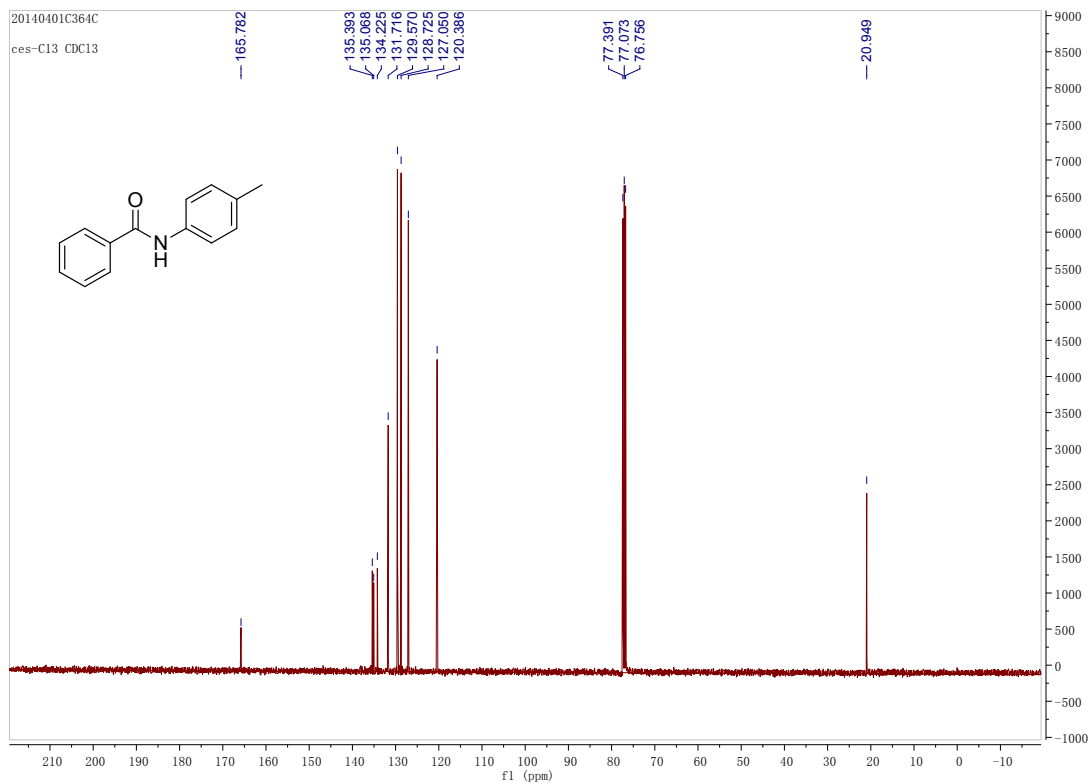
¹³C NMR (101 MHz, CDCl₃) of **3h**



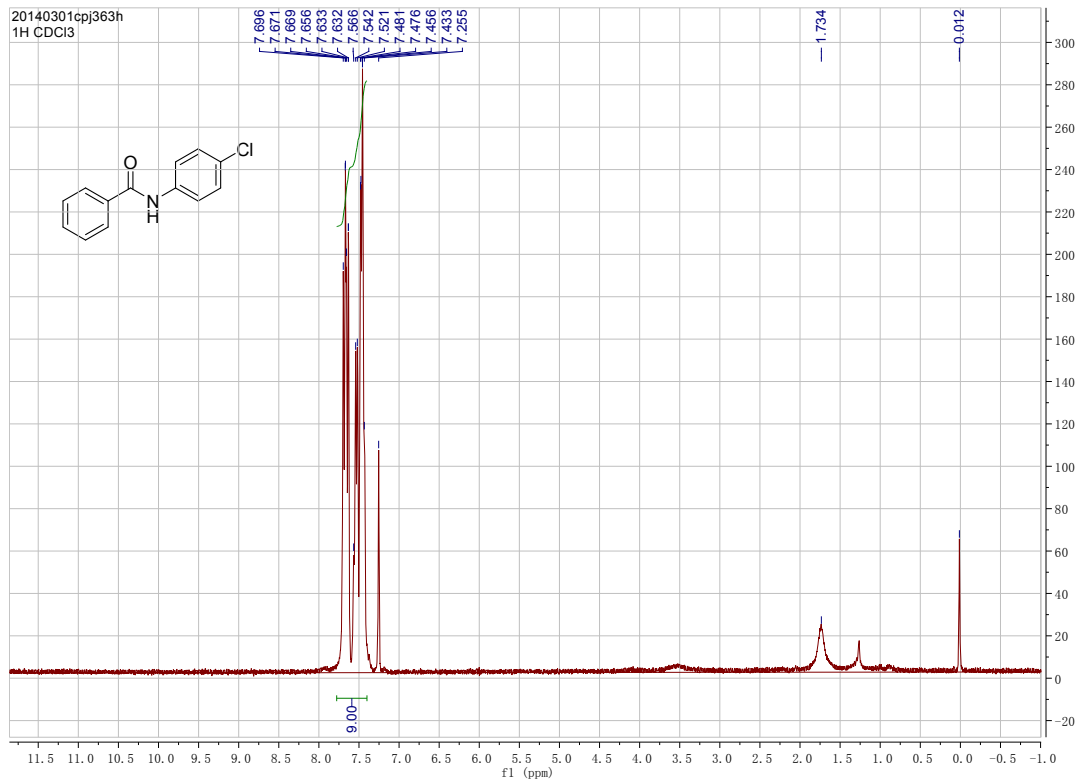
¹H NMR (300 MHz, CDCl₃) of **3i**



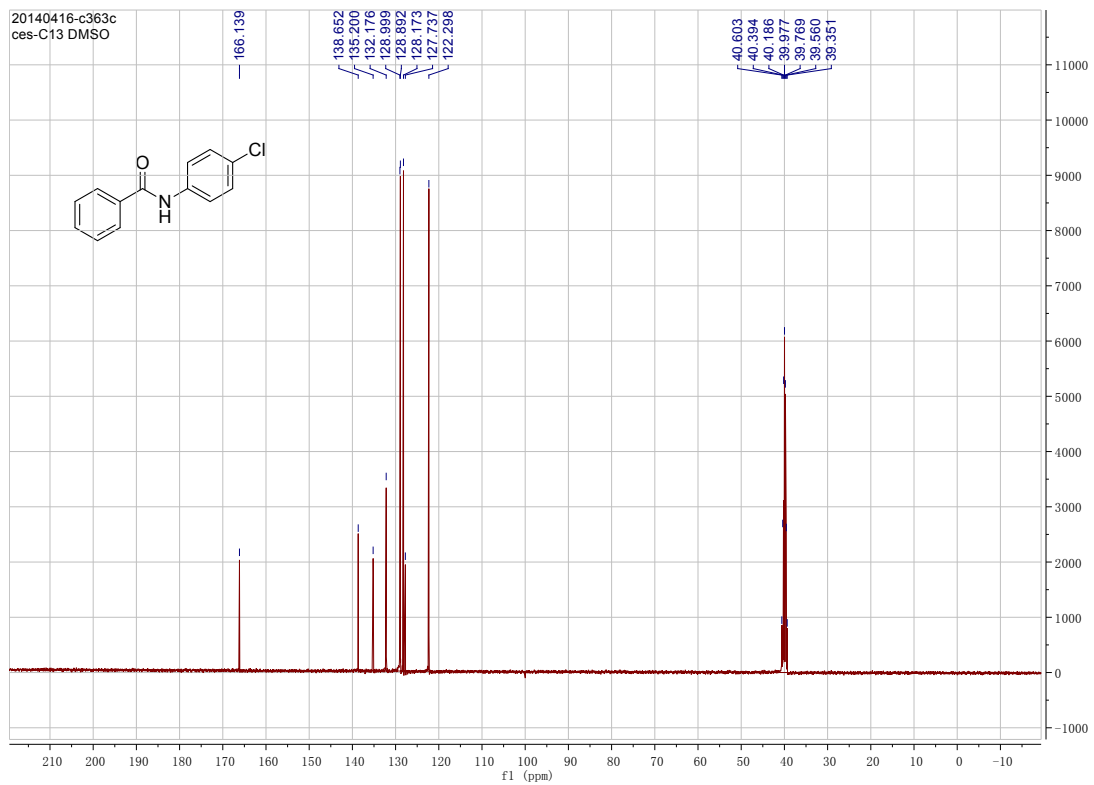
¹³C NMR (101 MHz, CDCl₃) of **3i**



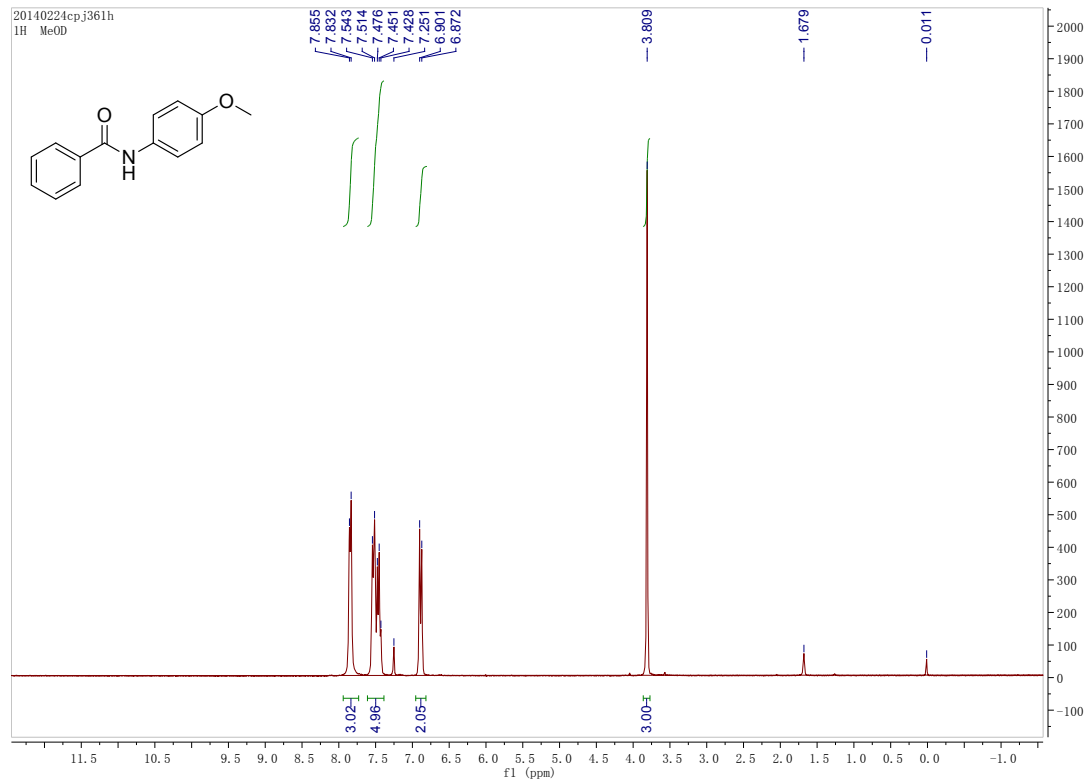
¹H NMR (400 MHz, CDCl₃) of **3j**



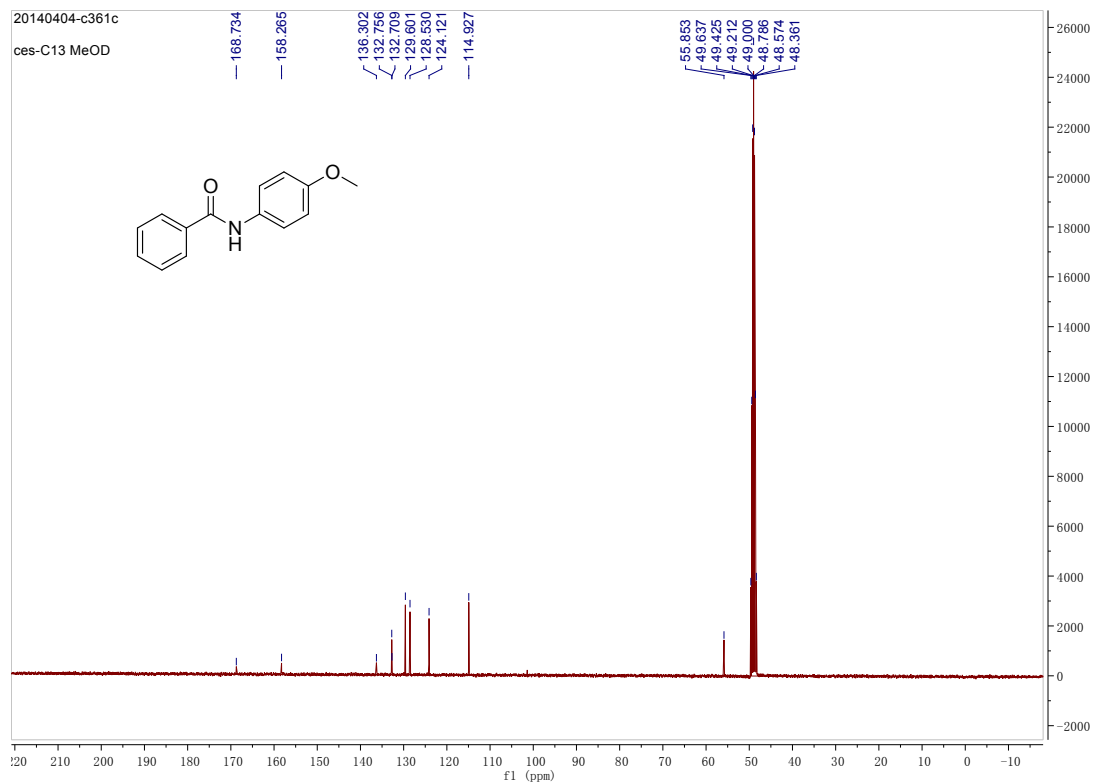
¹³C NMR (101 MHz, DMSO) of **3j**



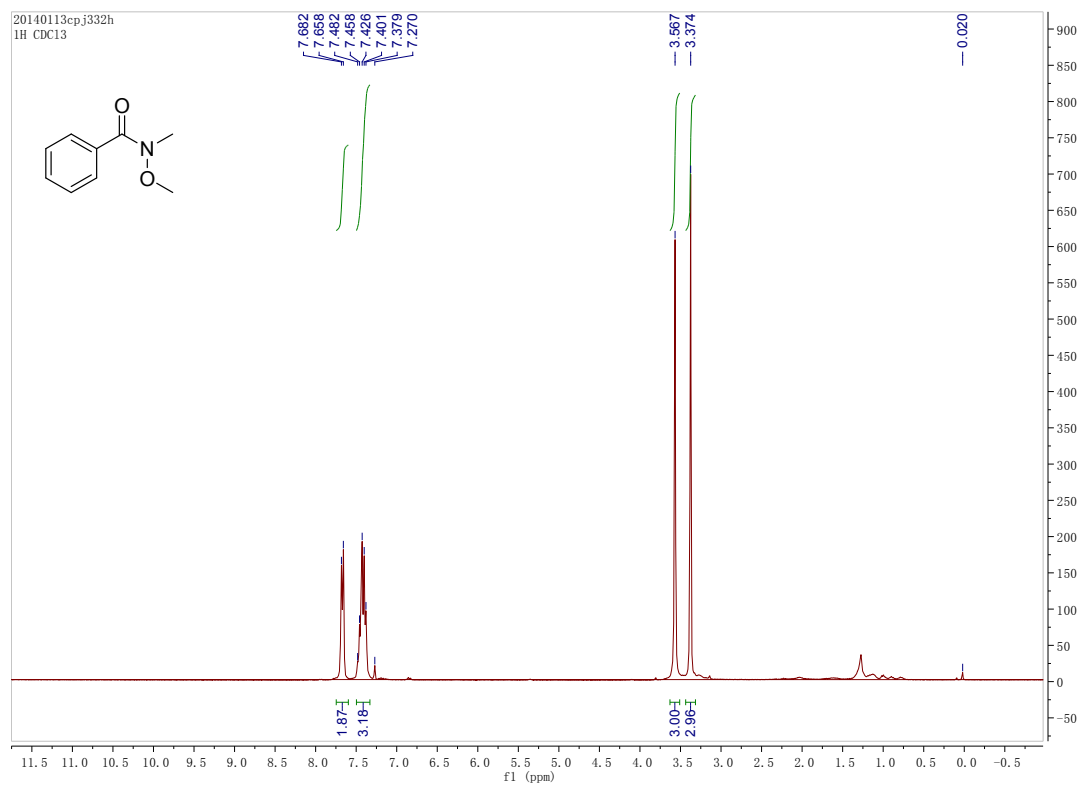
¹H NMR (300 MHz, CDCl₃) of 3k



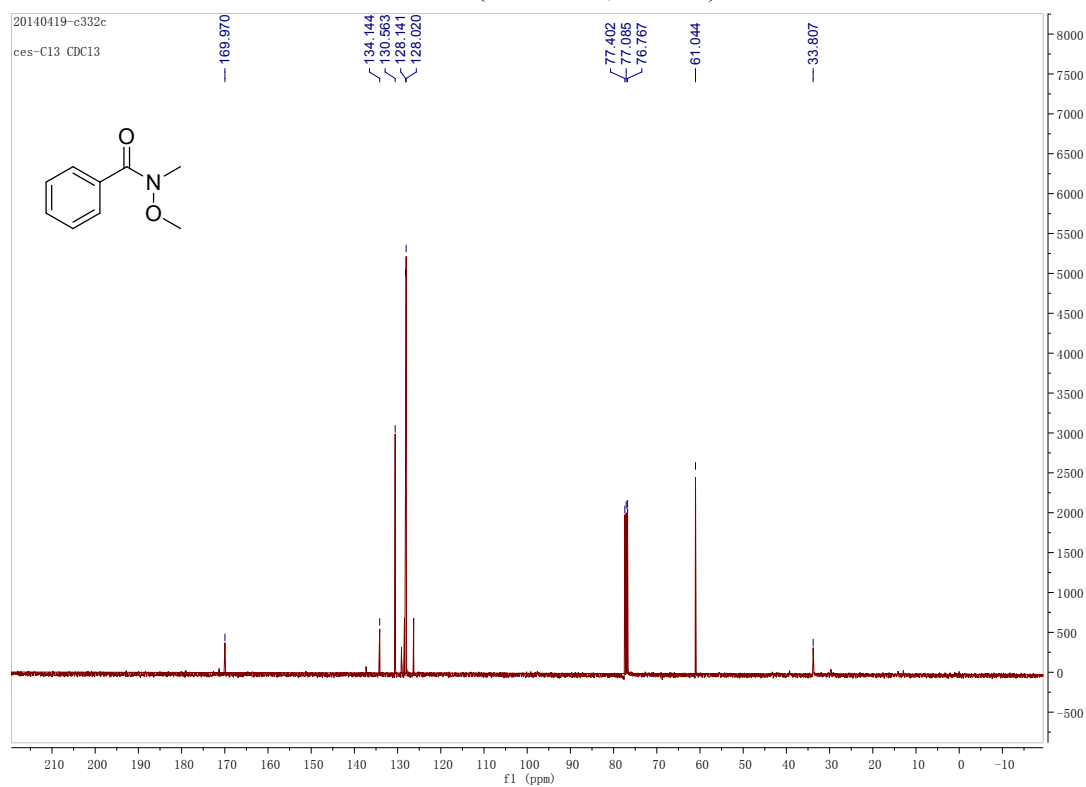
¹³C NMR (101 MHz, CDCl₃) of 3k



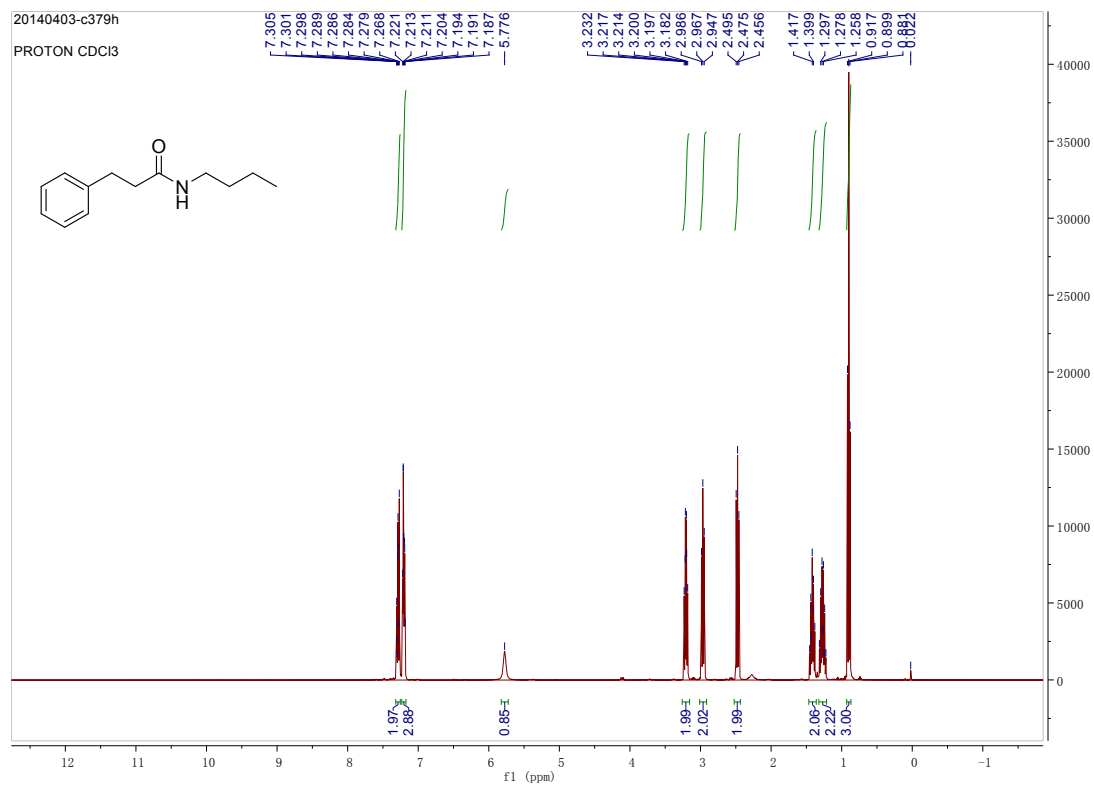
¹H NMR (300 MHz, CDCl₃) of **3I**



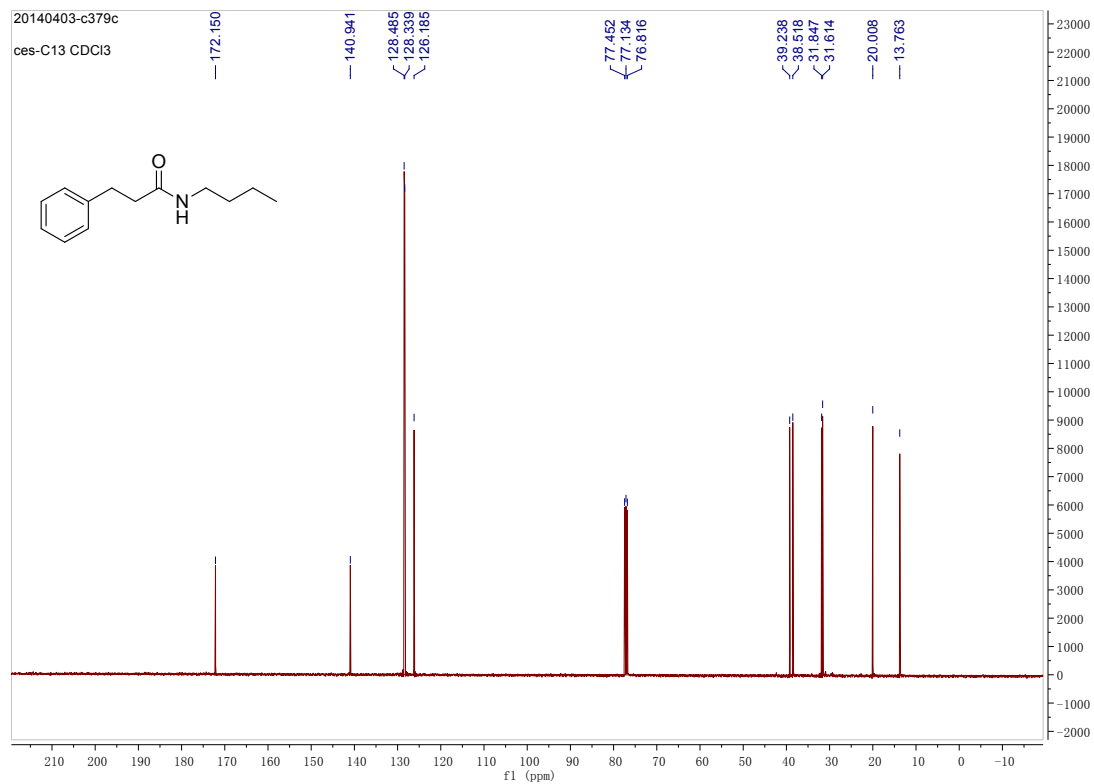
¹³C NMR (101 MHz, CDCl₃) of **3I**



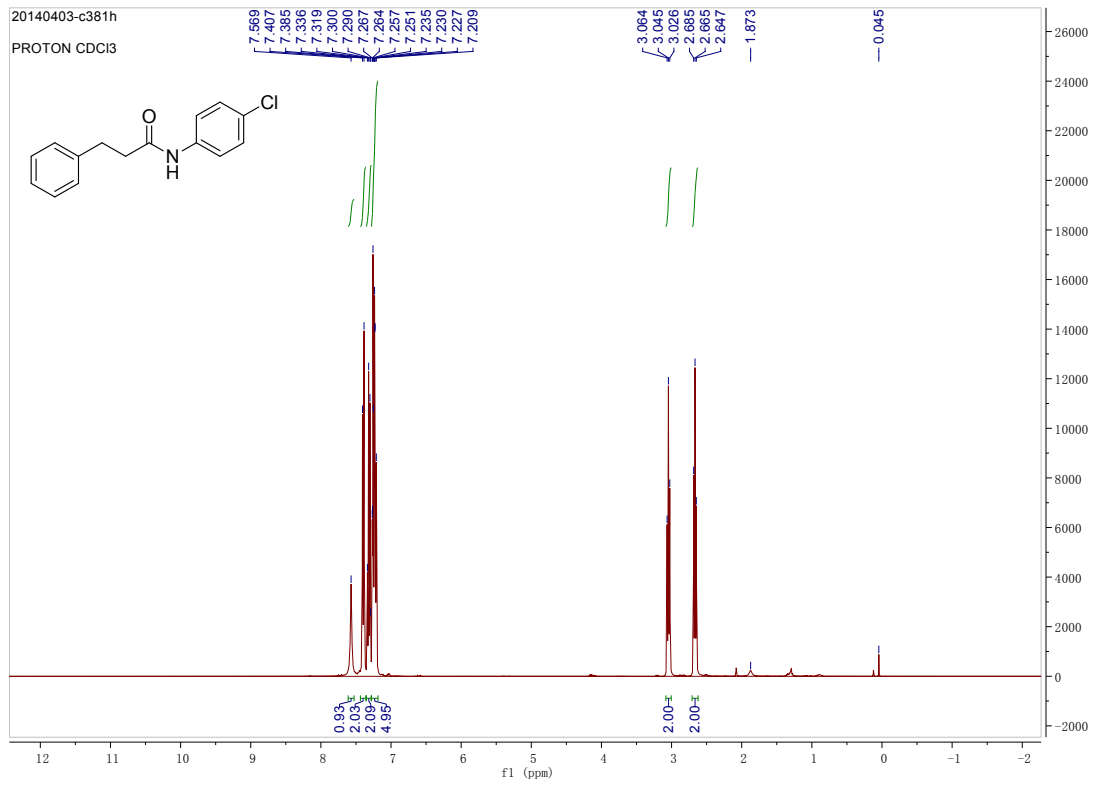
¹H NMR (400 MHz, CDCl₃) of **3m**



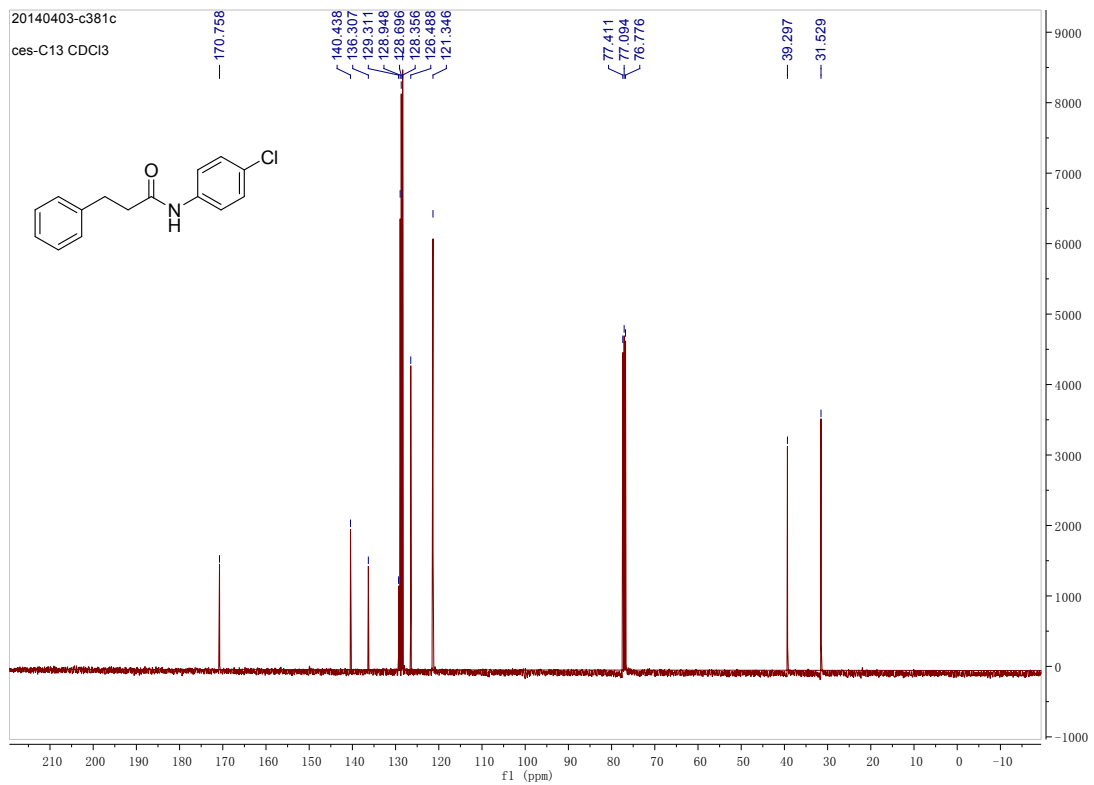
¹³C NMR (101 MHz, CDCl₃) of **3m**



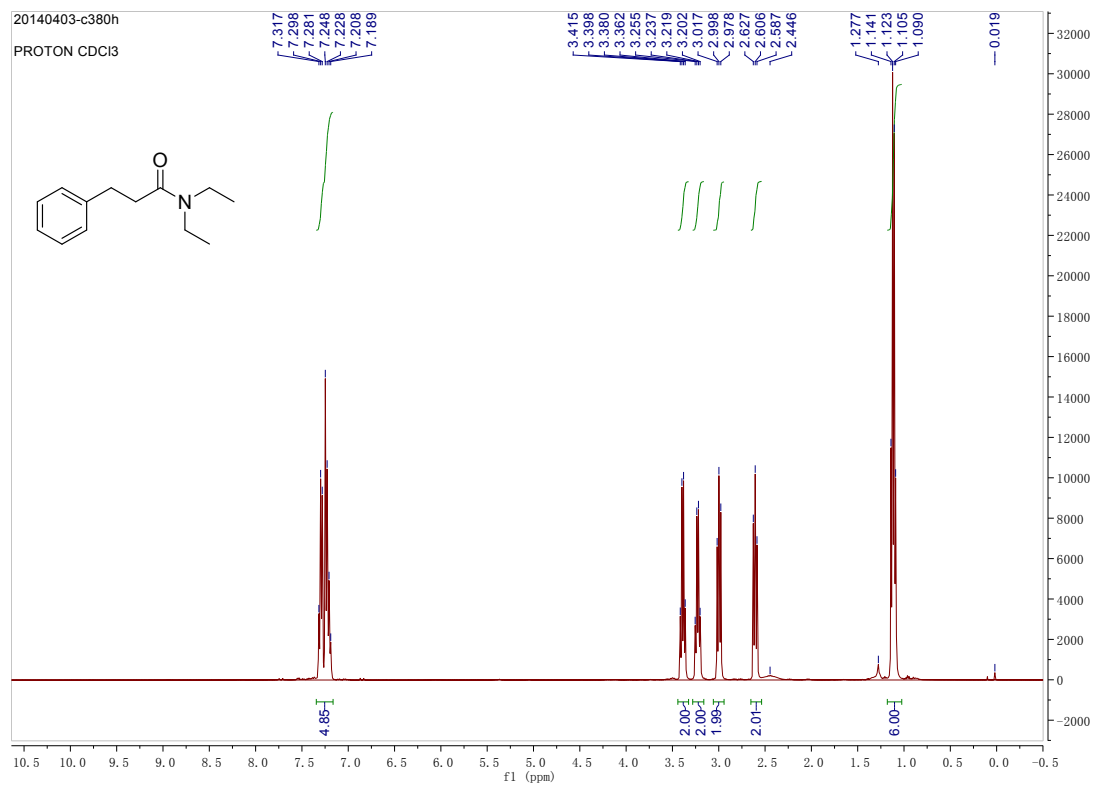
¹H NMR (400 MHz, CDCl₃) of **3n**



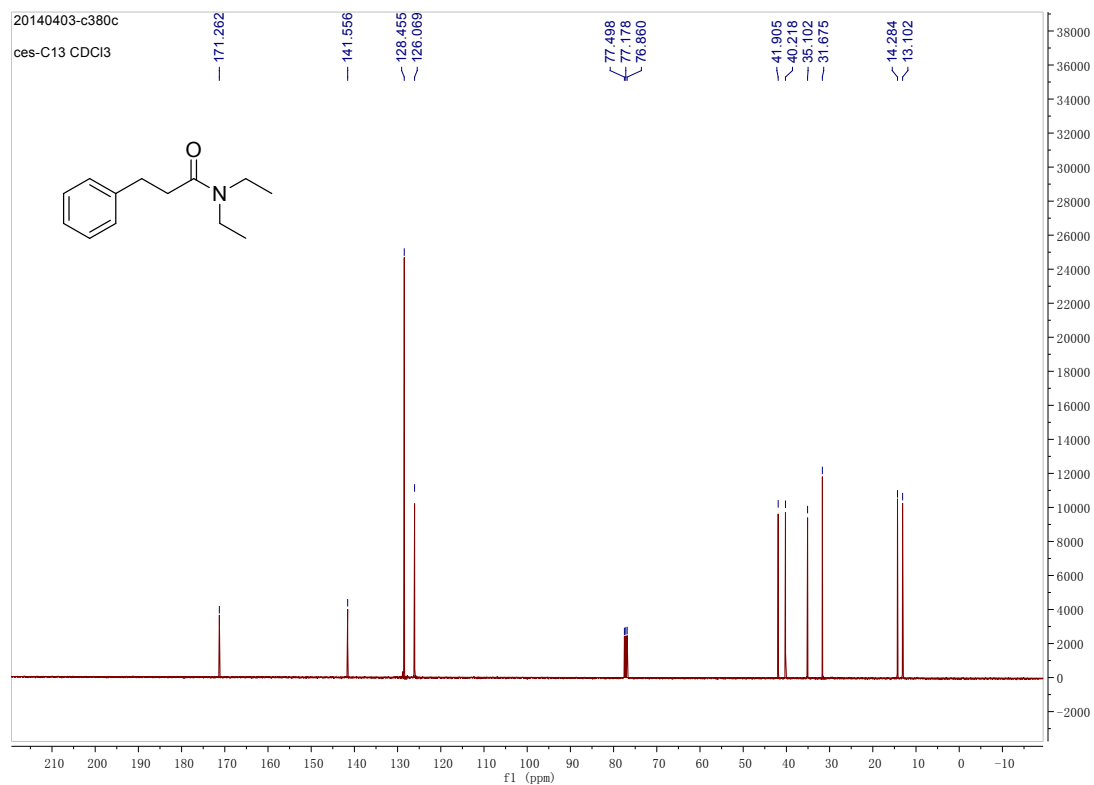
¹³C NMR (101 MHz, CDCl₃) of **3n**



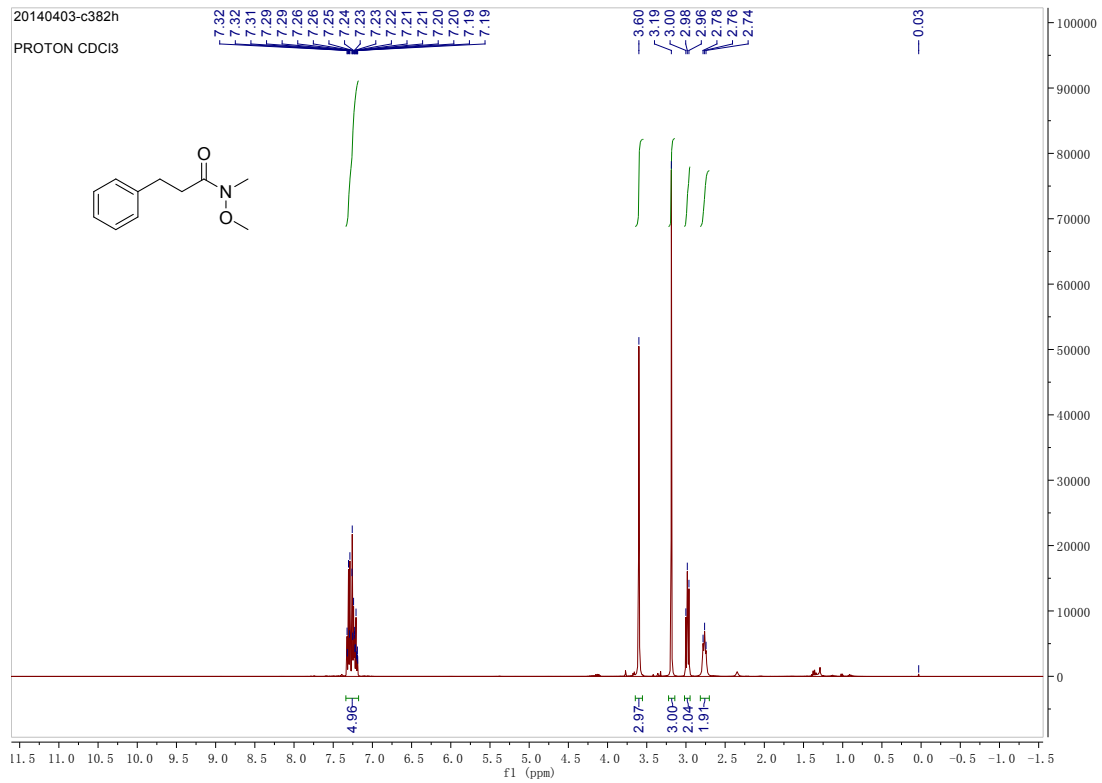
¹H NMR (400 MHz, CDCl₃) of **3o**



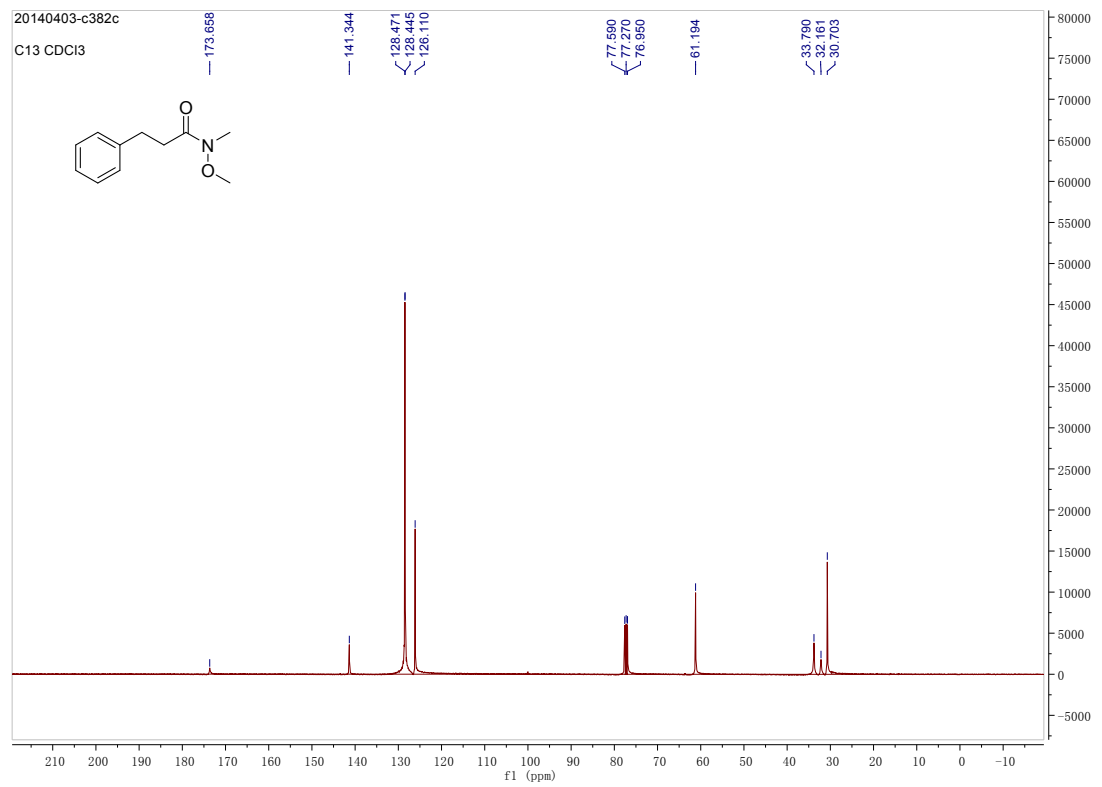
¹³C NMR (101 MHz, CDCl₃) of **3o**



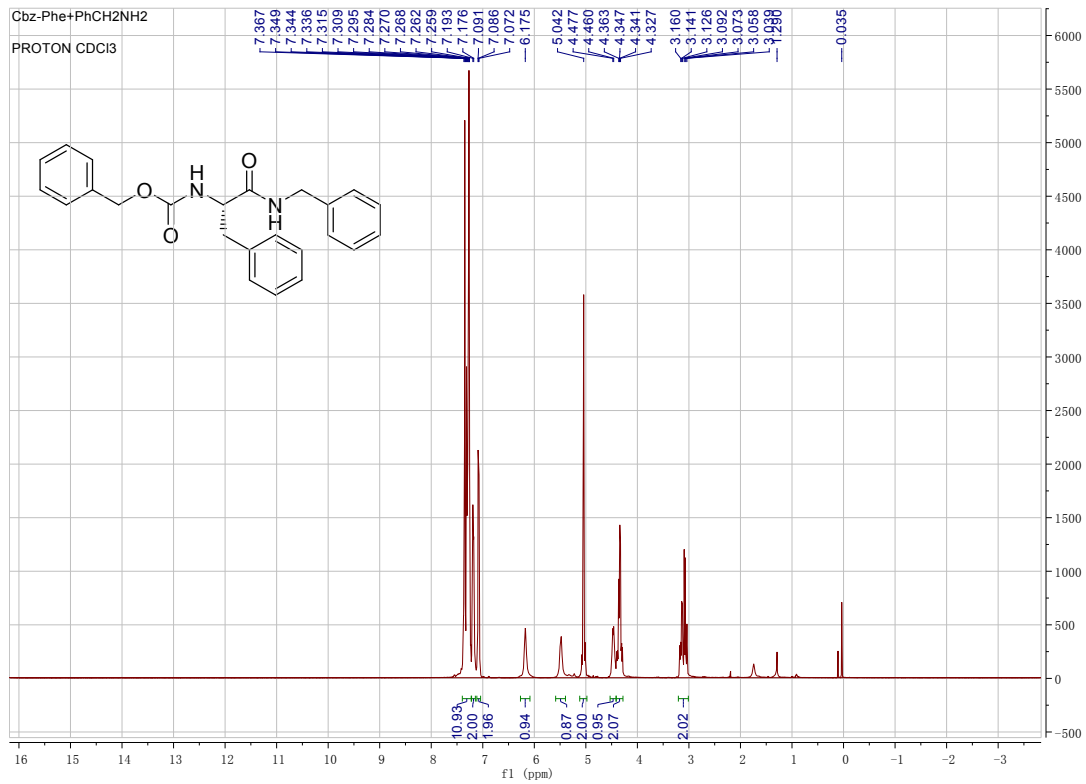
¹H NMR (400 MHz, CDCl₃) of **3p**



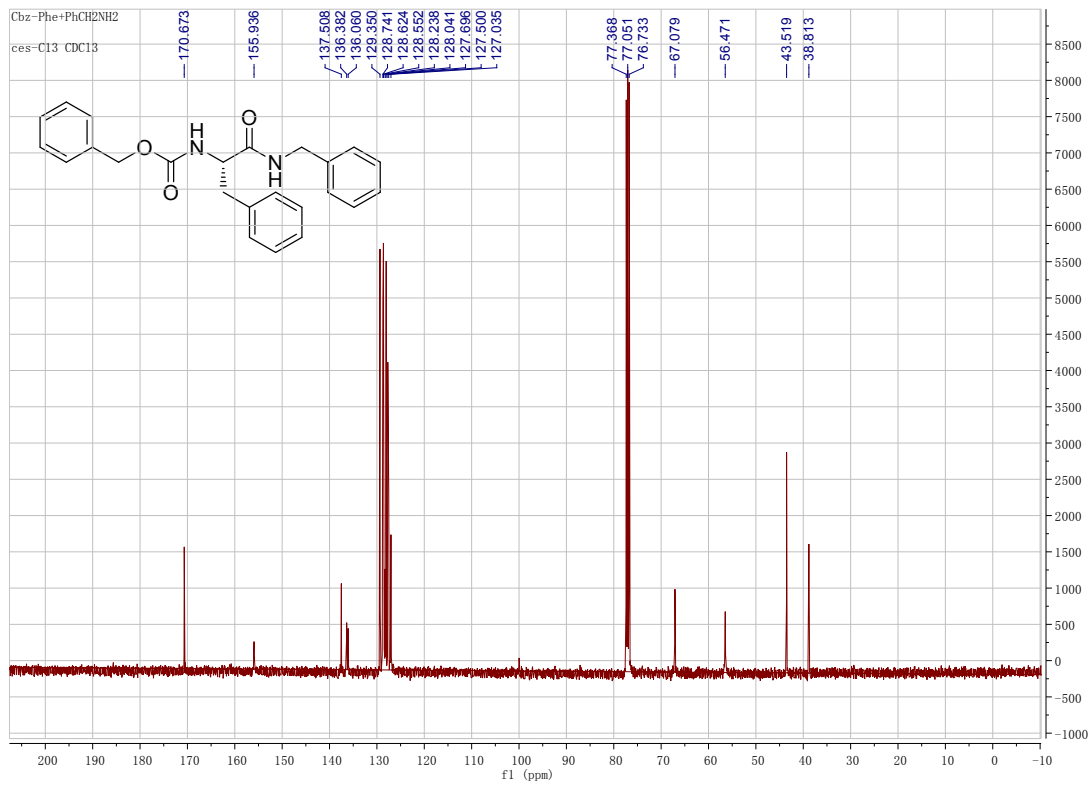
¹³C NMR (101 MHz, CDCl₃) of **3p**



¹H NMR (400 MHz, CDCl₃) of **3q**

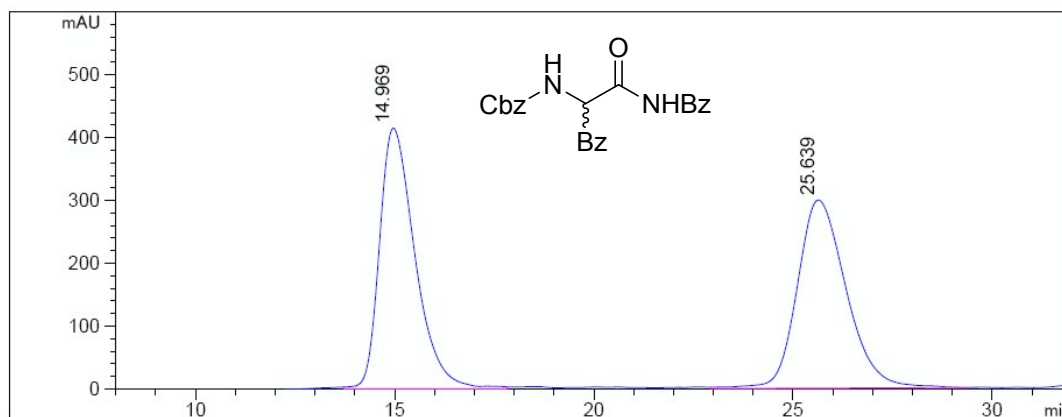


¹³C NMR (101 MHz, CDCl₃) of **3q**



The HPLC result of the racemer of **3q**

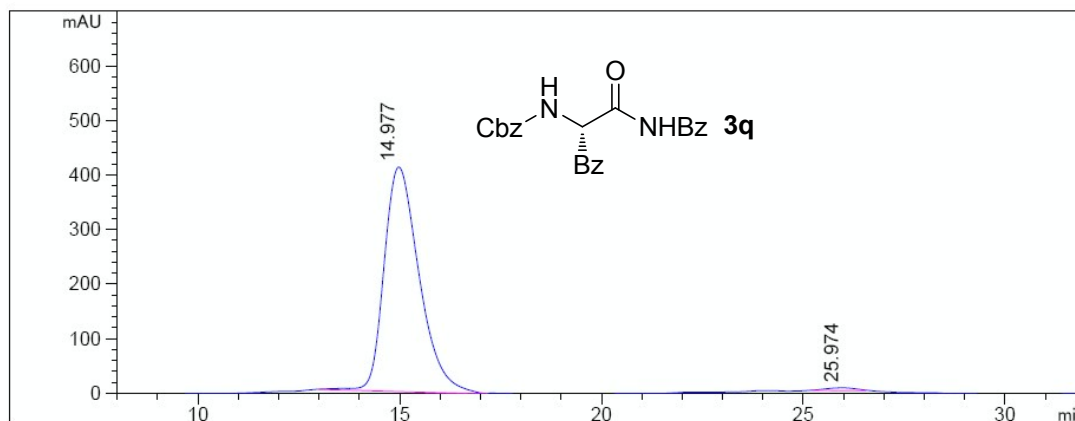
Conditions: Chiralcel AS column, hexane:IPA=90:10, $v = 1.0$ mL/min



Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	14.97	25698.631	414.859	1.032	50.14
2	25.64	25552.738	299.293	1.304	49.85

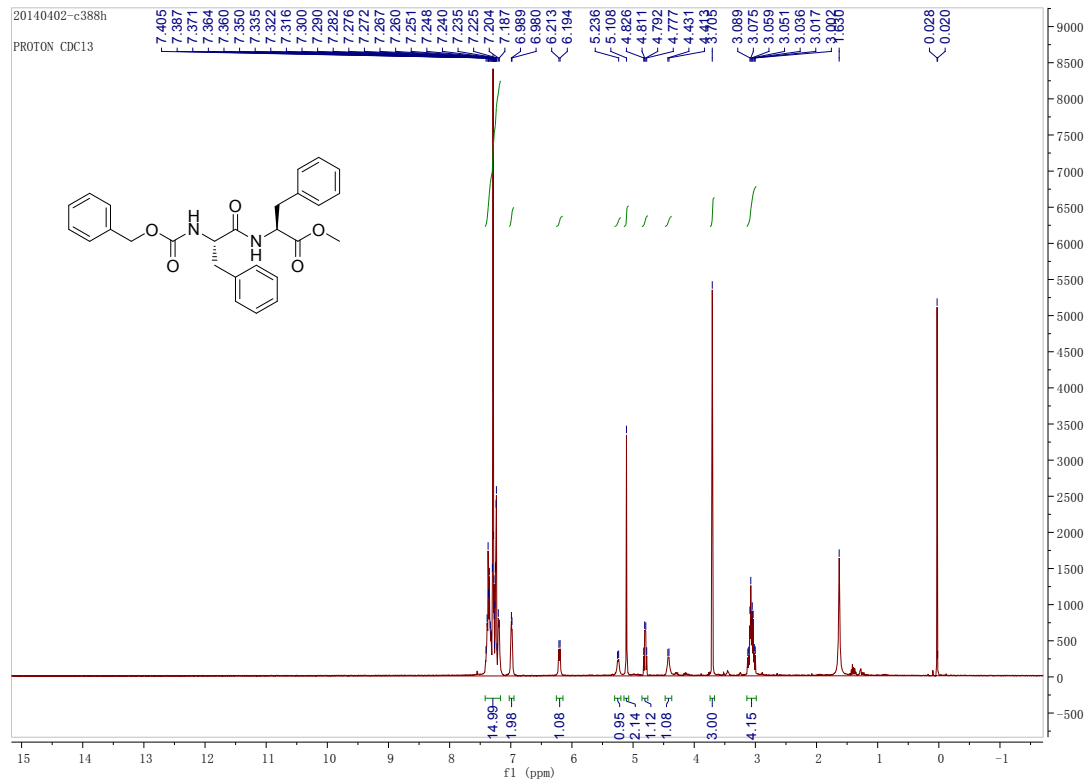
The HPLC result of the racemer of **3q**

Conditions: Chiralcel AS column, hexane:IPA=90:10, $v = 1.0$ mL/min

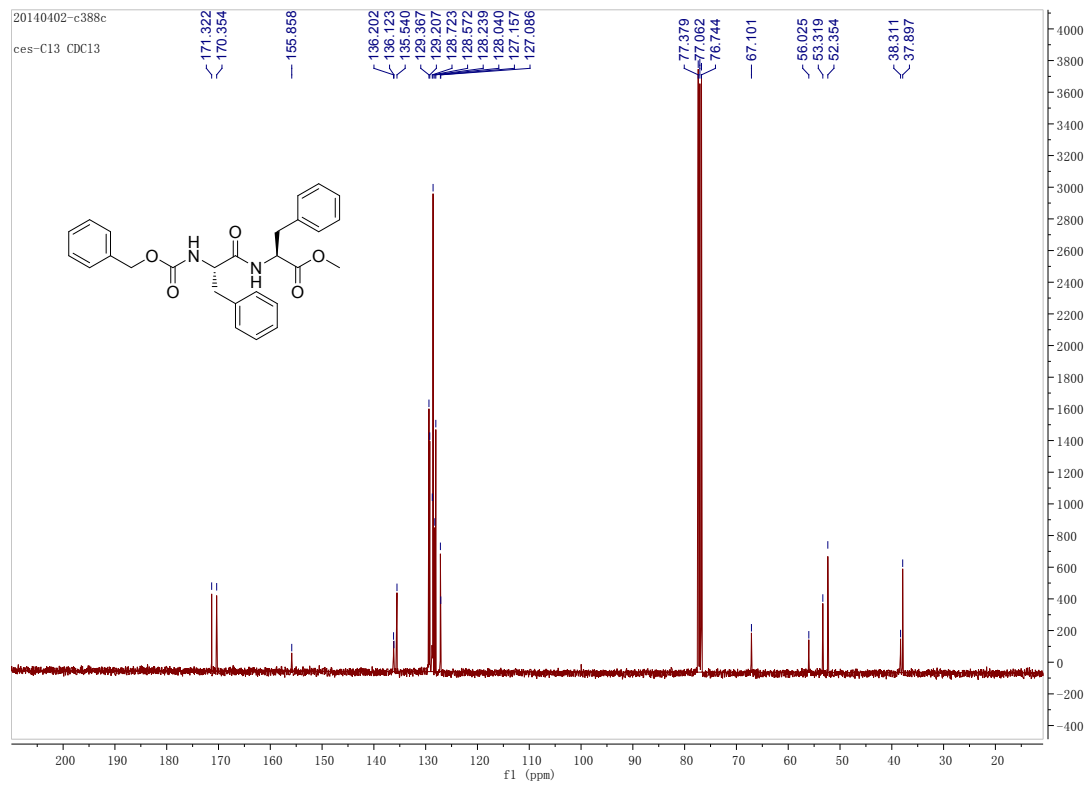


Entry #	RetTime [min]	Area [mAU*s]	Height [mAU]	Width [min]	Area %
1	14.98	24920.051	411.338	1.010	98.87
2	25.97	283.455	5.377	0.879	1.12

¹H NMR (400 MHz, CDCl₃) of 3r

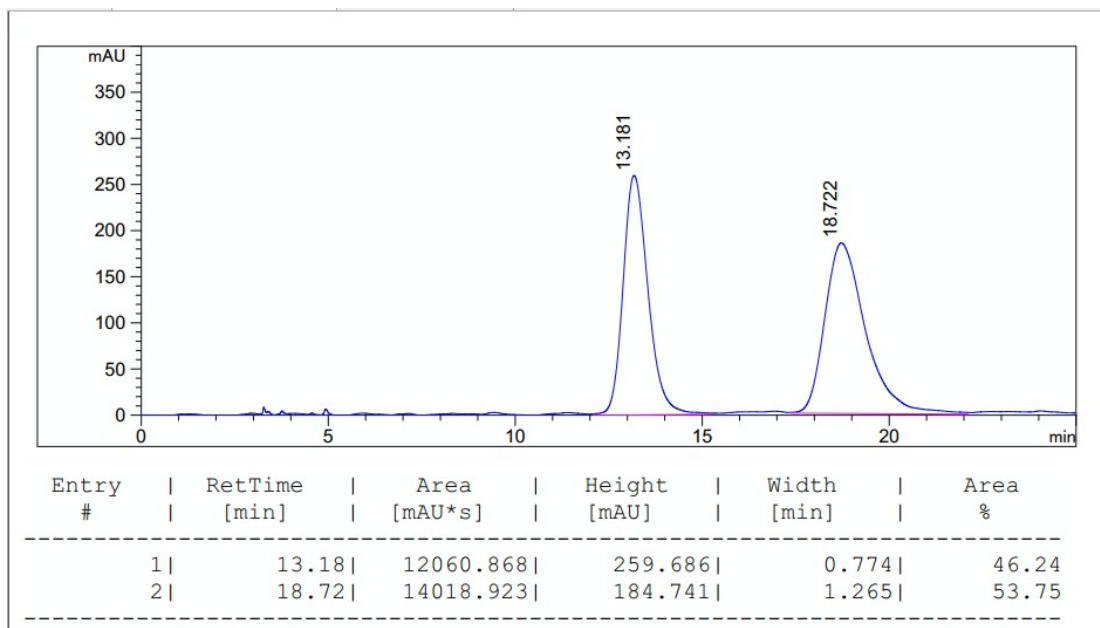


¹³C NMR (101 MHz, CDCl₃) of 3r



The HPLC result of the diastereomer of **3r**

Conditions: Chiralcel OD column, hexanes:IPA=90:10, $v = 1.0$ mL/min



The HPLC result of **3r**

Conditions: Chiralcel OD column, hexanes:IPA=90:10, $v = 1.0$ mL/min

