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## Graphical Abstract

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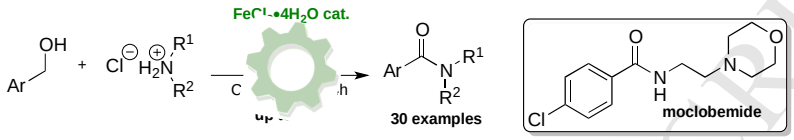

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# Iron-catalyzed benzamide formation. Application to the synthesis of moclobemide

Xavier Bantreil,[a]* Nasreddine Kanfar[a], Nicolas Gehin[a], Ethan Golliard[a], Pauline Ohlmann[a], Jean Martinez[a] and Frédéric Lamaty[a]*

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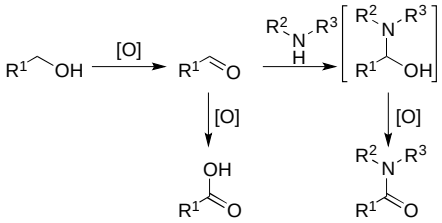
ABSTRACT

A convenient and user-friendly method to yield benzamides from primary and secondary amines and various benzylic alcohols in the presence of a cheap iron salt ($FeCl_2{\cdot}4H_2O$) and *tert*-butylhydroperoxide (70% in water) as a stoichiometric oxidant is described. Control experiments indicated that this reaction might involve radical species. This method proved to be general, generating a family of 30 benzamides and was applied to the preparative synthesis of anti-anxiety drug moclobemide.



## 1. Introduction

Amides are highly important functional groups due to their preponderance in many natural products such as peptides and proteins, pharmaceutical agents or man-made polymers, such as Nylon 6,6.[1] In most cases, common techniques to generate an amide bond involve the use of toxic coupling agents and toxic solvents. On industrial scale, these drawbacks directly impact environment and economics. To circumvent such issues, organometallic methodologies to form amides directly from alcohols and amines have recently emerged.[2] The general mechanism for this type of reaction involves the oxidation of an alcohol to the corresponding aldehyde, which will react with the amine to form an hemiaminal intermediate that is converted to the amide upon oxidation. It is important to note that in a competitive pathway, the aldehyde could be oxidised to the carboxylic acid, an undesired side-product (Scheme 1).




**Scheme 1.** General mechanism for amide formation

Efficient approaches have been reported using transition metals such as ruthenium[3] and rhodium,[4] and heterogeneous catalysts,[5] such $Au/TiO_2$ systems,[6] Au/DNA nanohybrids,[7] and alumina-supported silver clusters.[8] Such approaches are highly attractive as catalysis, step and atom economy are part of the 12 principles of green chemistry developed by Anastas and Warner.[9]

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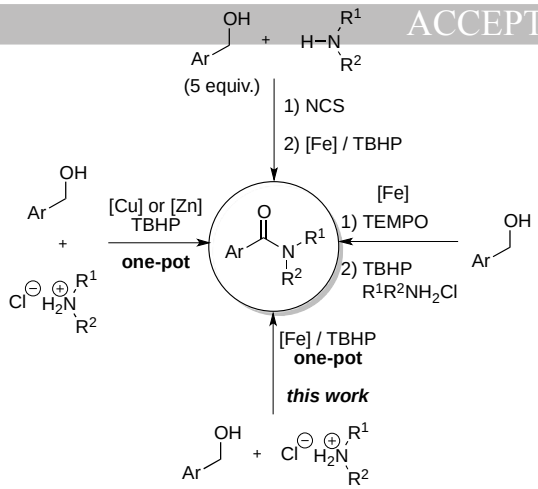



**Scheme 2.** Benzamide formation from alcohols in the litterature

To compete with those techniques involving expensive metals, studies on copper- or iron-catalyzed formation of amides from aldehydes have been reported.[10] As a part of our general interest in amide bonds,[11] we recently reported the copper-catalyzed amidation directly from benzylic alcohols and amines, which allowed to go one step further and realise a one-pot double oxidation.[12] Similar approach using zinc was developed (Scheme 2, left).[13] In 2013, Porcheddu et al. reported the iron-catalyzed amidation of *N*-chloramines, generated from toxic and non atom-economic *N*-chlorosuccinimide, which required the use of 5 equivalents of alcohols to obtain good yields (Scheme 2, top).[14] More recently, Ghosh et al. reported a stepwise iron-catalyzed synthesis of benzamides, requiring a first step of oxidation of alcohol into aldehyde prior to addition of the amine and TBHP (*tert*-butylhydroperoxide) as final oxidant (Scheme 2, right).[15] In here, we want to report a one-pot two steps convenient and practical method using a cheap iron salt as catalyst and readily available hydrochloric salt of amines (TON < 9, TOF < 0.9 $h^{-1}$).

## 2. Results/discussion

Optimisation of the reaction conditions was started using benzylic alcohol and cyclohexamine hydrochloric salt (1.5 equiv.) in the presence of TBHP (70% in $H_2O$) as oxidant and an iron salt in refluxing acetonitrile. It is worth noting that initial attempts to perform the amidation directly from free amines failed, proving that masking of the nitrogen as its ammonium salt was compulsory to the reaction. As already stated for copper catalysis,[12] calcium carbonate gave the best results. Its weak basicity and poor solubility induce a slow and controlled release of free amine within the reaction media. In the meantime, the alcohol would be oxidized to aldehyde that could react with free amine to yield corresponding amide after a second oxidation. This choice of base proved to be the key point for the feasibility of a one-pot two-steps reaction.

**Table 1**. Optimization of reaction conditions.[a]

| Entry | [Fe] (mol%) | [Ox] (equiv.) | Conversion (%)[b] |
|---|---|---|---|
| 1 | $FeSO_4 \cdot 7H_2O$ (5) | TBHP (4) | 84 |
| 2 | $FeCl_2 \cdot 4H_2O$ (5) | TBHP (4) | 87 |
| 3 | $K_4Fe(CN)_6 \cdot 3H_2O$ (5) | TBHP (4) | 53 |
| 4 | $Fe(acac)_3$ (5) | TBHP (4) | 78 |
| 5 | $Fe(NO_3)_3 \cdot 9$□□□ (5) | TBHP (4) | 84 |
| 6 | $FeCl_3$ (5) | TBHP (4) | 87 |
| 7 | $FeCl_2 \cdot 4H_2O$ (5) | TBHP (4)[c] | 45 |
| 8 | $FeCl_2 \cdot 4H_2O$ (5) | $H_2O_2$ (4) | <5 |

[a] Reaction conditions: benzyl alcohol (0.5 mmol), cyclohexylamine hydrochloride (0.75 mmol), $CaCO_3$ (0.75 mmol), TBHP (70% in $H_2O$, 270 µL, 4 equiv.), $CH_3CN$ (1 mL), 80°C, 4h.

[b] Conversion was determined by HPLC, based on **1a**.

[c] *tert*-butylhydroperoxide, 5.5M in nonane.

Screening of iron salts was realized. Apart from $K_4Fe(CN)_6 \cdot 3H_2O$ that gave only 53% conversion, all sources of iron tested gave around 80-85% conversion independently of the oxidation state of the metal (Table 1, entries 1-6). The best results were obtained using $FeCl_2 \cdot 4H_2O$ and $FeCl_3$, giving 87% conversion of amide **3aa**. As $FeCl_2 \cdot 4H_2O$ is less corrosive than $FeCl_3$, the optimisation was continued with this salt. Replacement of TBHP (70% in $H_2O$) by TBHP (5.5M in nonane) or hydrogen peroxide induced a decrease to respectively 45% and 5% conversion (entries 7-8).

**Table 2.** Optimization of the reaction conditions with a reverse stoichiometry.[a]

| Entry | [Fe] (mol%) | [Ox] (equiv.) | Ratio **2a**/**1a** | Yield (%)[b] |
|---|---|---|---|---|
| 1 | $FeCl_2 \cdot 4H_2O$ (5) | TBHP (5) | 1:1.3 | 72 |
| 2 | $FeCl_2 \cdot 4H_2O$ (10) | TBHP (5) | 1:1.3 | 89 |
| 3 | $FeCl_2 \cdot 4H_2O$ (10) | TBHP (4) | 1:1.3 | 89 |
| 4 | $FeCl_2 \cdot 4H_2O$ (10)[c] | TBHP (4) | 1:1.3 | 82 |
| 5 | - | TBHP (4) | 1:1.3 | 27 |

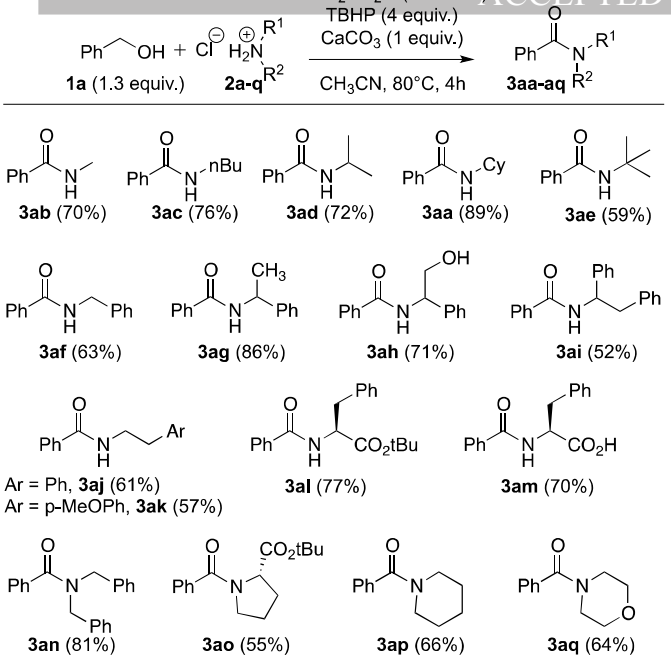
[a] Reaction conditions: benzyl alcohol (0.65 mmol), cyclohexylamine hydrochloride (0.5 mmol), $CaCO_3$ (0.5 mmol), TBHP (70% in $H_2O$, 270 µL, 4 equiv.), $CH_3CN$ (1 mL), 80°C, 4h.

[b] Isolated yield, based on **2a**.

[c] $FeCl_2 \cdot 4H_2O$ 99.99% and $CaCO_3$ 99.995% pure were used.

As explained above (Scheme 1), the main side-product formed during the amidation is carboxylic acid. During our previous study on copper-catalyzed amidation, we realized that alcohols featuring electron-donating groups were prone to convert quickly to corresponding benzoic acids. Thus, in view to develop the most general conditions and increase the isolated yield of this reaction, a reverse of the amine/alcohol stoichiometry was envisioned (Table 2). While the use of 1.3 equivalents of alcohols in the presence of 5 equivalents of TBHP and 5 mol% of $FeCl_2 \cdot 4H_2O$ gave a 72% yield (entry 1), increasing the quantity of iron salt to 10 mol% induced a satisfactory 89% yield (entry 2). Decreasing the excess of TBHP to 4 equivalents did not affect the isolated yield (89%, entry 3). As commercially available iron salts are often contaminated with other metals, the reaction was performed using extra pure iron source and base. Resulting amide was isolated in 82% (entry 4), indicating that traces of metals were not responsible for the amidation reaction. Finally, a control experiment in the absence of iron salt indicated that the transition metal was necessary to the reaction (27% without $FeCl_2 \cdot 4H_2O$, entry 5).

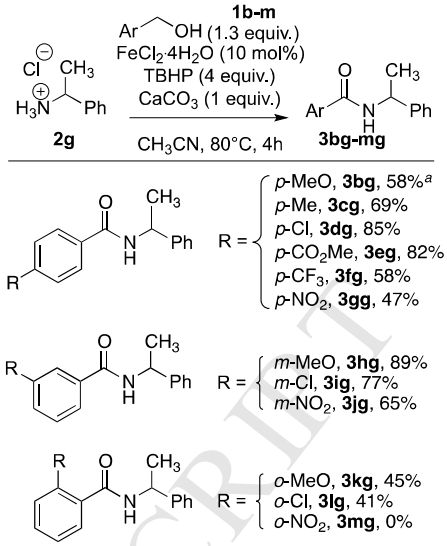
**Table 3.** Variation of primary and secondary amines in the amidation conditions.




Reaction conditions: benzyl alcohol (0.65 mmol), amine hydrochloride **2a-q** (0.5 mmol), $FeCl_2$·4H$_2$O (0.05 mmol), $CaCO_3$ (0.5 mmol), TBHP (70% in $H_2O$, 270 µL, 4 equiv.), $CH_3CN$ (1 mL), 80°C, 4h.

The scope of the reaction was then examined. First, variation of the amine was investigated (Table 3). For convenience, even if not specified, the amine hydrochloride salts were used throughout this study. Methyl andbutyl amine reacted efficiently yielding **3ab** and **3ac** in 70% and 76% respectively. Increasing the bulkiness with *iso*-propyl and cyclohexyl amine did not affect the amidation reaction (**3ad**, 72%; **3aa**, 89%). Even bulkier *tert*-butyl amine gave **3ae** in 59% yield. Benzyl amine, which was shown to yield easily benzamide in the presence of iron and TBHP,[16] was found to produce amide **3af** in 63% yield. Substituted benzylamines **2g-i** furnished corresponding amides in yields spanning from 52% to 86%. Phenethyl and *p*-methoxyphenethyl amines **2j** and **2k** gave corresponding amides in moderate yields (≈60%). Phenylalanine *tert*-butyl ester gave 77% of corresponding benzoylated aminoacid **3al**. To our delight, the use of unprotected phenylalanine hydrochloric salt allowed the coupling in 70% yield (**3am**), indicating the tolerance of the conditions toward the carboxylic acid functionality. To the best of our knowledge, such reaction with substrate featuring a free acid had never been accomplished in previous reports. The iron-catalyzed amidation was also performed in the presence of more nucleophilic but also more hindered secondary amines. Although bearing two benzylic oxidable positions, dibenzylamine gave a good 81% yield of **3an**. Cyclic amines reacted correctly, HCl-Pro-$^t$Bu (**2o**), piperidine (**2p**) and morpholine (**2q**) yielding the corresponding amides in respectively 55% (**3ao**), 65% (**3ap**) and 64% (**3aq**).

**Table 4.** Variation of benzylic alcohols in the amidation conditions.




Reaction conditions: benzyl alcohol **1b-m** (0.65 mmol), amine hydrochloride **2g** (0.5 mmol), $FeCl_2$·4H$_2$O (0.05 mmol), $CaCO_3$ (0.5 mmol), T-Hydro (270 µL, 4 equiv.), $CH_3CN$ (1 mL), 80°C, 4h. [a] 2 equiv. of *p*-methoxybenzylalcohol were used.

The diversification was continued using various benzylic alcohols in the presence of (□)-methylbenzyl amine **2g** (Table 4). Electron-donating substituents in *para* position gave a slight decrease in yield with 58% and 69% for respectively **3bg** and **3cg**. *p*-Chlorobenzyl alcohol was efficiently converted to amide **3dg** (85%). Introducing electron-withdrawing groups led to respectively 82% and 58% yield for *p*-$CO_2$Me and *p*-$CF_3$ groups. Surprisingly, *p*-$NO_2$ substitution, which accounted for the best yield in copper-catalyzed amidation, gave a poor 47% of corresponding amide **3gg**. When *meta*-substituted benzylic alcohols were used, yields from 65% to 89% were obtained, with methoxy (**3hg**), chloro (**3ig**) and nitro (**3jg**) substituents. Finally, *ortho* substitution, which combined steric and electronic influence, gave lower yields of amides **3kg** and **3lg**, bearing respectively methoxy (45%) and chloro groups (41%). *Ortho*-nitrobenzyl alcohol did not react as expected and amide **3mg** was not observed.

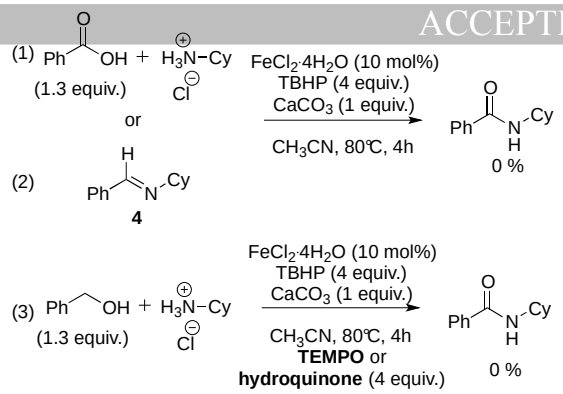
**Table 5.** Comparison of TON and TOF with literature.[a]

| | TON | TOF ($h^{-1}$) |
|---|---|---|
| $FeCl_2$·4H$_2$O/TBHP | < 8.9 | < 2.2 |
| CuO/TBHP (Lamaty)[12] | < 44 | < 11 |
| $ZnI_2$/TBHP (Beller)[13] | < 17 | < 1.1 |
| $Fe(NO_3)_3$·9H$_2$O/TEMPO/TBHP (Chen)[15] | < 16.2 | < 0.9 |
| $FeCl_3$·6H$_2$O/NCS/TBHP (De Luca)[14] | < 7 | n.d.[b] |

[a] TON=(mmol of product)/(mmol of catalyst). TOF=TON/(reaction time). TON and TOF were calculated using literature data.

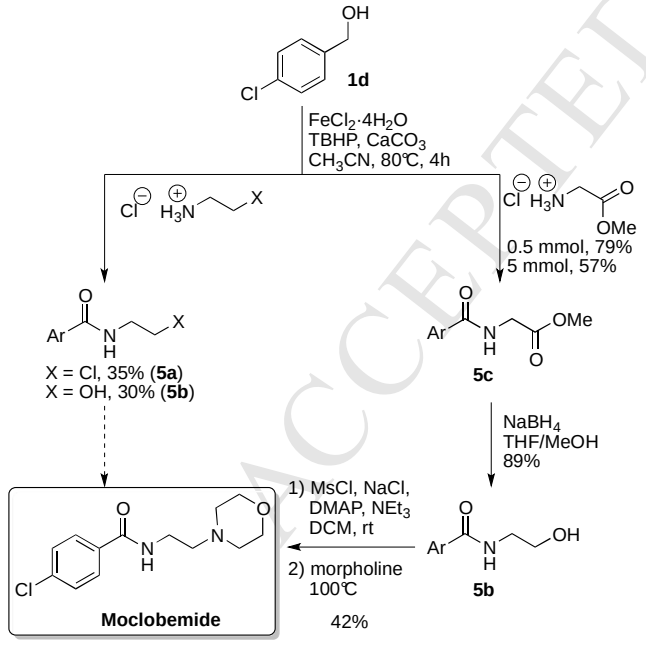
[b] Reaction time was not specified in the publication.

In order to compare this catalytic reaction with literature, TON (turnover number) and TOF (turnover frequency) were calculated using the best results reported in previous works and herein (Table 5). The copper catalyzed reaction[12] was by far the most efficient regarding TON (up to 44) and TOF (up to 11 $h^{-1}$), as only 2 mol% of CuO and 4h of reaction were necessary to obtain good yields. Apart from copper, considering TOF, the use of $FeCl_2$·4H$_2$O as catalyst (TOF up to 2.2 $h^{-1}$) gave better results than other catalytic systems involving zinc or iron (TOF up to 1.1 $h^{-1}$), therefore attesting that these reaction conditions represent a good alternative to reported procedures.




**Scheme 3.** Control experiments for amidation reaction

Control experiments were then run to assess if the iron-catalyzed amidation was indeed going through the general mechanism depicted in **Scheme 1**. First, when benzoic acid was used instead of benzylic alcohol in the presence of cyclohexylamine and under the exact optimized conditions used above, no reaction occurred, proving that no direct thermal condensation between acid and amine happened as described elsewhere (Scheme 3, eq. 1).[17] In addition, when aldimine **4** was reacted under the amidation conditions, no expected amide was observed, proving that formation of amide bond might result from oxidation of the hemiaminal rather than from corresponding aldimine (Scheme 3, eq. 2). Finally, reaction between benzylic alcohol and cyclohexylamine was performed in the presence of TEMPO or hydroquinone as radical scavengers (Scheme 3, eq. 3). Expected amide **3aa** could not be observed under those conditions, indicating that the iron-catalyzed amidation might certainly involve the formation of radical species during the oxidation process. However, no trapping intermediate could be isolated.




**Scheme 4.** Synthesis of moclobemide using iron-catalyzed amidation.

To prove that this methodology could be efficiently applied to the synthesis of compounds of interest, the synthesis of moclobemide was envisioned using an iron-catalyzed amidation as a first synthetic step (Scheme 4). Moclobemide, an Hoffmann-La Roche drug used against depression and social anxiety, could be readily obtained from 4-chloro-*N*-(2-chloroethyl)benzamide **5a**. Thus, *p*-chlorobenzyl alcohol **1d** was reacted with commercially available 2-chloroethylamine hydrochloride. The isolated yield of amide **5a** being only 35%, the synthesis of synthetic intermediates **5b** and **5c** was intended. While reacting **1d** with ethanolamine hydrochloride gave also a poor yield (**5b**, 30%), the use of glycine methylester yielded amide **5c** in 79% yield on a 0.5 mmol scale. On a 10-fold scale (5 mmol) under the exact same conditions, amide **5c** could be isolated with a slight depletion of the yield (57%). The final steps of the synthesis were achieved according to literature procedures. Reacting $NaBH_4$ in a mixture THF/MeOH[18] allowed the reduction of **5c** to alcohol **5b** in 89% yield. Quantitative substitution of the hydroxyl group by a chlorine atom and reaction with morpholine directly yielded moclobemide, with a 42% yield over 2 steps. This modest yield was consistent with the reported one (33%),[19] and moclobemide could be obtained from easily available substrates and in a more sustainable manner to generate the amide functionality.

## 3. Conclusions

In conclusion, we described a new protocol of iron-catalyzed direct formation of benzamides from alcohols and amines. This system required the use of a cheap iron salt and TBHP as a non-toxic stoichiometric oxidant, which decomposes only to form *tert*-butanol and water. Ammonium salts of amines, which are easily accessible, user-friendly and stable, were used in this study. Primary, secondary aliphatic and benzylic amines were well tolerated, as well as benzylic alcohols featuring electron-withdrawing and -donating groups. To validate the usefulness of this methodology, the synthesis of the anti-anxiety drug moclobemide was performed starting from easily available substrates.

## 4. Experimental section

### *4.1. General*

In a sealed tube were added $FeCl_2{\cdot}4H_2O$ (9.9 mg, 0.05 mmol, 10 mol%), cyclohexylamine·HCl (67.8 mg, 0.5 mmol, 1 equiv.) and $CaCO_3$ (50.1 mg, 0.5 mmol, 1 equiv.). 1 mL of $CH_3CN$, benzyl alcohol (67 µL, 0.65 mmol, 1.3 equiv) and *tert*-butylhydroperoxide (70% in $H_2O$, 140 µL, 2 equiv.) were then added. After 2h of stirring at 80°C, another 2 equiv. of *tert*-butylhydroperoxide (70% in $H_2O$) were added, and the mixture was further stirred for 2h. After cooling to rt, HCl 1N (5 mL) and AcOEt (5 mL) were added. The mixture was extracted with AcOEt (2 x 5 mL), and the combined organic phases were washed with saturated aqueous $NaHCO_3$ solution (10 mL), brine (10 mL), dried over magnesium sulfate and concentrated under reduced pressure. The crude mixture was purified by chromatography on silica gel using mixtures of cyclohexane and ethyl acetate as eluant.

**<u>*N*-cyclohexylbenzamide 3aa:</u>**[20] 89% yield (90.2 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.85-7.64 (m, 2H), 7.53-7.30 (m, 3H), 6.17 (d, 1H, *J* = 6.6 Hz), 3.95 (ttd, 1H, *J* = 11.9, 8.0, 3.8 Hz), 2.09-1.91 (m, 2H), 1.84-1.55 (m, 3H), 1.50-1.10 (m, 5H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 166.8, 135.2, 134.3, 128.6, 127.0, 48.8, 33.3, 25.7, 25.0.

**<u>*N*-methylbenzamide 3ab:</u>** 70% yield (48.7 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.84-7.67 (m, 2H), 7.52-7.30 (m, 3H), 6.71 (s, 1H), 2.96 (d, *J* = 4.8 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 168.5, 134.7, 131.4, 128.6, 127.0, 26.9.

**<u>*N*-*n*-butylbenzamide 3ac:</u>**[21] 76% yield (67.4 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.78-7.73 (m, 2H), 7.46-7.34 (m, 3H), 6.42 (br s, 1H), 3.42 (q, 2H, *J* = 6.5 Hz), 1.65-

1.47 (m, 2H), 1.43-1.24 (m, 2H), 0.93 (t, 3H, *J* = 7.2 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 167.7, 134.9, 131.3, 128.6, 127.0, 39.9, 31.8, 20.2, 13.9.

***N*-isopropylbenzamide 3ad:**[22] 72% yield (58.6 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.84-7.68 (m, 1H), 7.53-7.30 (m, 2H), 6.18 (s, 1H), 4.40-4.11 (m, 1H), 1.23 (d, J = 6.6 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 166.8, 135.1, 131.3, 128.5, 126.9, 41.9, 22.9.

***N*-*tert*-butylbenzamide 3ae:**[10d] 59% yield (52.0 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.93-7.60 (m, 2H), 7.42 (m, 3H), 5.99 (s, 1H), 1.46 (s, 9H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 167.0, 136.0, 131.2, 128.6, 126.8, 51.7, 20.0.

***N*-benzylbenzamide 3af:**[23] 63% yield (66.6 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.75-7.70 (m, 2H), 7.47-7.17 (m, 8H), 6.62 (br s, 1H), 4.55 (d, 2H, *J* = 5.7 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 167.6, 138.4, 134.4, 131.5, 128.8, 128.6, 127.9, 127.5, 127.1, 44.1.

***N*-(α-methylbenzyl)benzamide 3ag:**[24] 77% yield (86.2 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.89-7.65 (m, 2H), 7.59-7.20 (m, 8H), 6.56 (d, *J* = 7.1 Hz, 1H), 5.33 (p, *J* = 7.0 Hz, 1H), 1.59 (d, *J* = 6.9 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 166.7, 143.3, 134.7, 131.5, 128.8, 128.6, 127.5, 127.1, 126.3, 49.3, 21.8.

***N*-benzoyl-phenylglycinol 3ah:**[25] 71% yield (85.9 mg) as a white solid. $^1$H NMR (DMSO-$d_6$, 200 MHz): δ (ppm) = 8.70 (d, *J* = 8.1 Hz, 1H), 7.90 (d, *J* = 6.3 Hz, 2H), 7.64-7.11 (m, 8H), 5.07 (dd, *J* = 13.8, 8.1 Hz, 1H), 4.94 (t, *J* = 5.8 Hz, 1H), 3.80-3.55 (m, 2H). $^{13}$C NMR (DMSO-$d_6$, 75 MHz): δ (ppm) = 166.3, 141.4, 134.7, 131.2, 128.3, 128.2, 127.4, 127.0, 126.9, 64.6, 56.1.

***N*-(1,2-diphenylethyl)benzamide 3ai:**[26] 52% yield (78.4 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.75-7.55 (m, 2H), 7.51-7.13 (m, 11H), 7.08 (d, *J* = 5.9 Hz, 2H), 6.56 (d, *J* = 7.4 Hz, 1H), 5.45 (q, *J* = 7.2 Hz, 1H), 3.19 (d, *J* = 7.0 Hz, 2H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 166.9, 141.6, 137.35, 134.7, 131.55, 129.5, 128.7, 128.6, 128.5, 127.6, 127.0, 126.8, 54.9, 42.7.

***N*-phenethylbenzamide 3aj:**[10a, 27] 61% yield (69.0 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.77-7.60 (m, 2H), 7.54-7.16 (m, 8H), 6.23 (s, 1H), 3.72 (q, 2H, *J* = 6.9 Hz), 2.94 (t, 2H, *J* = 6.9 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 167.6, 139.0, 134.7, 131.5, 128.9, 128.8, 128.6, 126.9, 126.7, 41.3, 35.8.

***N*-*p*-methoxyphenethylbenzamide 3ak:**[28] 58% yield (73.8 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.72-7.68 (m, 2H), 7.51-7.34 (m, 3H), 7.16-7.12 (m, 2H), 6.87-6.83 (m, 2H), 6.36 (br s, 1H), 3.78 (s, 3H), 3.66 (q, 2H, *J* = 7.0 Hz), 2.86 (t, 2H, *J* = 7.0 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 167.6, 158.4, 134.8, 131.4, 131.0, 129.8, 128.6, 127.9, 126.9, 114.2, 55.3, 41.4, 34.9.

***N*-benzoylphenylalanine *tert*-butyl ester 3al:**[29] 77% yield (124.8 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.72-7.55 (m, 2H), 7.46-7.23 (m, 3H), 7.23-7.05 (m, 5H), 6.67 (d, 1H, *J* = 7.3 Hz), 4.88 (dt, 1H, *J* = 7.4, 5.8 Hz), 3.14 (d, 2H, *J* = 5.7 Hz), 1.34 (s, 9H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 170.8, 166.8, 136.3, 134.1, 131.7, 129.6, 128.6, 128.4, 127.0, 82.6, 54.0, 38.1, 28.0.

***N*-benzoylphenylalanine.½$H_2O$ 3am:** 70% yield (97.6 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.73 (d, *J* = 6.8 Hz, 2H), 7.64-7.28 (m, 8H), 6.87 (s, 1H, N*H*), 5.81 (s, 1H, $CO_2H$), 5.41 (s, 1H, ½ $H_2O$), 4.90 (s, 1H), 3.40-3.01 (m, 2H). $^{13}$C NMR ($CD_3OD$, 75 MHz): δ (ppm) = 176.3, 170.1, 138.7, 135.3, 132.8, 130.3, 129.5, 129.4, 128.4, 127.8, 56.3, 38.9.

***N*,*N*-dibenzylbenzamide 3an:**[29] 69% yield (104.0 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.65-7.29 (m, 7H), 7.18 (s, 1H), 4.73 (s, 1H), 4.42 (s, 1H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 172.3, 137.0, 136.5, 136.2, 129.7, 128.9, 128.6, 128.5, 127.6, 127.1, 126.8, 51.6, 46.9.

***N*-benzoyl proline *tert*-butyl ester 3ao:** 55% yield (76.4 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.56-7.51 (m, 2H), 7.42-7.29 (m, 3H), 4.52 (dd, *J* = 8.0, 5.5 Hz, 1H, 70%), 4.26-4.13 (m, 1H, 30%), 3.79-3.41 (m, 2H), 2.34-2.14 (m, 1H), 2.01-1.79 (m, 3H), 1.47 (s, 9H, 70%), 1.29 (s, 9H, 30%). $^{13}$C NMR ($CDCl_3$, 100 MHz): δ (ppm) = 171.5, 169.6, 136.6, 130.1, 128.3, 127.3, 126.8, 81.3, 60.0, 50.0, 29.5, 28.1, 27.8, 25.4 (major rotamer). δ (ppm) = 171.5, 170.5, 137.2, 129.7, 81.8, 62.1, 46.7, 31.6, 29.8, 22.7. (minor rotamer).

***N*-benzoyl piperidine 3ap:**[7] 66% yield (62.2 mg) as a translucid oil. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.36 (s, 5H), 3.68 (s, 2H), 3.31 (s, 2H), 1.64-1.51 (m, 6H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 170.3, 136.6, 129.4, 128.4, 126.8, 48.8, 43.1, 26.6, 25.7, 24.6.

***N*-benzoyl morpholine 3aq:**[10c] 64% yield (61.2 mg) as a white oil. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.39 (s, 5H), 3.69 (br s, 6H), 3.45 (br s, 2H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 170.5, 135.4, 129.9, 128.6, 127.1, 67.0.

***N*-(*p*-methoxybenzoyl)-α-methylbenzyl amine 3bg:**[30] 58% yield (74.4 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.71 (d, 2H, *J* = 8.9 Hz), 7.47-7.08 (m, 6H), 6.95-6.79 (m, 2H), 6.45 (d, 1H, *J* = 7.5 Hz), 5.28 (p, 1H, *J* = 7.0 Hz), 3.78 (s, 3H), 1.54 (d, 3H, *J* = 6.9 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 166.3, 162.2, 143.5, 128.9, 128.8, 127.4, 126.9, 126.3, 113.8, 55.5, 49.2, 21.9.

***N*-(*p*-methylbenzoyl)-α-methylbenzyl amine 3cg:**[31] 69% yield (83.8 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.65 (d, 2H, *J* = 8.2 Hz), 7.44-7.11 (m, 7H), 6.37 (d, 1H, *J* = 7.0 Hz), 5.31 (p, 1H, *J* = 7.0 Hz), 2.36 (s, 3H), 1.57 (d, 3H, *J* = 6.9 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 166.7, 143.4, 142.0, 131.8, 129.3, 128.8, 127.5, 127.1, 126.4, 49.2, 21.9, 21.5.

***N*-(*p*-chlorobenzoyl)-α-methylbenzyl amine 3dg:**[32] 85% yield (111.4 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.61 (dd, 2H, *J* = 8.2, 1.2 Hz), 7.34-7.13 (m, 7H), 6.59 (d, 1H, *J* = 7.2 Hz), 5.21 (p, 1H, *J* = 7.0 Hz), 1.50 (dd, 3H, *J* = 6.9, 1.0 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 165.7, 143.1, 137.7, 133.0, 128.8, 128.8, 128.6, 127.6, 126.3, 49.5, 21.8.

***N*-(*p*-(methoxycarbonyl)benzoyl)-α-methylbenzyl amine 3eg:**[31] 82% yield (115.5 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 8.09 (d, *J* = 8.6 Hz, 2H), 7.82 (d, *J* = 8.6 Hz, 2H), 7.45-7.28 (m, 5H), 6.34 (d, *J* = 6.7 Hz, 1H), 5.35 (p, *J* = 6.8 Hz, 1H), 1.63 (d, *J* = 6.9 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 166.4, 165.9, 143.0, 138.6, 132.6, 129.8, 128.8, 127.6, 127.2, 126.3, 52.4, 49.5, 21.7.

***N*-(*p*-trifluorobenzoyl)-α-methylbenzyl amine 3fg:** 58% yield (85.2 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.83 (d, *J* = 8.2 Hz, 2H), 7.60 (d, *J* = 8.3 Hz, 2H), 7.42-7.26 (m, 5H), 6.85 (d, *J* = 7.6 Hz, 1H), 5.30 (p, *J* = 7.0 Hz, 1H), 1.59 (d, *J* = 6.9 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 165.6, 142.9, 138.0, 133.2 (q, *J* = 32.5 Hz), 128.9, 127.7, 127.6, 126.3, 125.7, 125.6, 123.8 (q, *J* = 271 Hz), 49.6, 21.7. $^{19}$F NMR ($CDCl_3$, 282 MHz): δ (ppm) = -62.9. HRMS(ESI$^+$) m/z calculated for ($MH^+$): 294.1106. Found: 294.1107.

***N*-(*p*-trifluorobenzoyl)-α-methylbenzyl amine 3gg:**[33] 53% yield (71.8 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 8.31-8.12 (m, 2H), 7.98-7.83 (m, 2H), 7.44-7.27 (m, 5H), 6.70 (d, 1H, *J* = 7.3 Hz), 5.30 (p, 1H, *J* = 7.0 Hz), 1.61 (d, 3H, *J* = 6.9 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 164.8, 149.5, 142.7, 140.2, 128.9, 128.3, 127.8, 126.3, 123.7, 49.8, 21.7.

***N*-(*m*-methoxybenzoyl)-α-methylbenzyl amine 3hg:**[12] 89% yield (114.5 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.43-7.34 (m, 8H), 7.21-6.92 (m, 1H), 6.65 (d, *J* = 6.6 Hz, 1H), 5.56-5.23 (p, 1H, *J* = 7.0 Hz), 3.86 (s, 3H), 1.64 (d, 3H, *J* = 6.9 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 166.5, 159.9, 143.3, 136.1, 129.6, 128.8, 127.5, 126.3, 118.8, 117.7, 112.5, 55.5, 49.4, 21.8.

***N*-(*m*-chloro)-α-methylbenzyl amine 3ig:**[34] 77% yield (100.2 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.72 (t, *J* = 1.8 Hz, 1H), 7.64-7.54 (m, 1H), 7.45-7.17 (m, 7H), 6.74 (d, *J* = 7.5 Hz, 1H), 5.26 (p, *J* = 7.0 Hz, 1H), 1.54 (d, *J* = 6.9 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 165.5, 143.0, 136.5, 134.7, 131.5, 129.9, 128.8, 127.6, 127.4, 126.3, 125.2, 49.5, 21.7.

***N*-(*m*-nitro)-α-methylbenzyl amine 3jg:**[35] 65% yield (88.0 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 8.55 (s, 1H), 8.25 (d, *J* = 8.1 Hz, 1H), 8.10 (d, *J* = 7.7 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.35-7.21 (m, 4H), 7.12 (d, *J* = 7.1 Hz, 1H), 5.28 (p, *J* = 6.9 Hz, 1H), 1.58 (d, *J* = 6.9 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 164.4, 148.1, 142.8, 136.2, 133.5, 129.8, 128.8, 127.6, 126.3, 126.0, 122.0, 49.9, 21.7.

***N*-(*o*-methoxybenzoyl)-α-methylbenzyl amine 3kg:**[12] 45% yield (57.4 mg) as a slurry. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 8.27 (d, 1H, *J* = 6.7 Hz), 8.20 (dd, 1H, *J* = 7.8, 1.8 Hz), 7.55-7.18 (m, 6H), 7.08 (dt, 1H, *J* = 7.5, 0.8 Hz), 6.97 (d, 1H, *J* = 8.3 Hz), 5.35 (p, 1H, *J* = 6.9 Hz), 3.94 (s, 3H), 1.59 (d, *J* = 6.9 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 164.7, 157.6, 143.8, 133.0, 132.4, 128.8, 127.3, 126.2, 121.5, 111.5, 56.1, 49.3, 22.6.

***N*-(*o*-chlorobenzoyl)-α-methylbenzyl amine 3lg:**[36] 41% yield (53.4 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.65 (dd, *J* = 6.0, 3.1 Hz, 1H), 7.45-7.26 (m, 8H), 6.46 (s, 1H), 5.34 (p, *J* = 7.0 Hz, 1H), 1.62 (d, *J* = 6.9 Hz, 3H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 165.6, 142.9, 135.2, 131.4, 130.8, 130.4, 130.3, 128.9, 127.6, 127.2, 126.4, 49.8, 21.9.

***N*-(*p*-chlorobenzoyl)-glycine methyl ester 5c:**[10e] 79% yield (90.2 mg) as a white solid. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.82-7.68 (m, 2H), 7.48-7.36 (m, 2H), 6.64 (s, 1H), 4.24 (d, *J* = 5.0 Hz, 2H), 3.81 (s, 3H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 170.6, 166.5, 138.3, 132.2, 129.1, 128.7, 52.7, 41.9.

***N*-(*p*-chlorobenzoyl)-glycinol 5b:**[37] Following a literature procedure,[18] ester **5c** (488.2 mg, 2.15 mmol), $NaBH_4$ (408.8 mg, 10.75 mmol) and THF (1.8 mL) were stirred at 65°C for 15 min. Then MeOH (1.2 mL) was added and the resulting mixture was stirred for another 15 min at 65°C. The mixture was then cooled to room temperature, quenched with HCl 1M and extracted with $CH_2Cl_2$. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford the expected alcohol **5b** as a white solide in 89% yield (384.4 mg). The crude compound was found pure enough for further reactions.$^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.73-7.60 (m, 2H), 7.39-7.27 (m, 2H), 7.01 (s, 1H), 3.84-3.71 (m, 2H), 3.55 (dd, *J* = 10.2, 5.2 Hz, 2H), 3.46 (s, 1H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 167.7, 138.1, 132.6, 128.9, 128.6, 62.0, 42.9.

**Moclobemide:**[38] Alcohol **5b** (350 mg, 1.97 mmol), triethylamine (826 µL, 5.93 mmol) DMAP (24.1 mg, 0.20 mmol), and sodium chloride (346.6 mg, 5.93 mmol) were stirred in $CH_2Cl_2$ (9.9 mL) and methanesulfonyl chloride (460 µL, 5.93 mmol) was added dropwise. The mixture was stirred overnight and completion of the reaction was assessed by HPLC. Reaction was quenched using a saturated solution of $NH_4Cl$ and extracted with $CH_2Cl_2$. The combined organic layers were washed with a saturated solution of $NaHCO_3$, brine, dried over $MgSO_4$ filtered and concentrated under reduced pressure. The crude chloride was filtered through a pad of silica using $CH_2Cl_2$ as eluant. Filtered compound (white solid, 450 mg) was found pure enough for further reaction. $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.81-7.62 (m, 2H), 7.47-7.33 (m, 2H), 6.69 (s, 1H), 3.87-3.64 (m, 4H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 166.7, 138.2, 132.6, 129.1, 128.6, 44.2, 41.9. A mixture of compound **5a** (109.0 mg, 0.5 mmol) and morpholine (348 µL, 4 mmol) was then stirred at 100°C for 2h. After cooling to room temperature, 5 mL of $H_2O$ and then a 10% ammonia solution were added. The solution was extracted with $CH_2Cl_2$. The organic layers were combined, dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification on silica gel using a mixture $CH_2Cl_2$/MeOH 95:5 afforded 56.6 mg of moclobemide as a white solid (42 % yield). $^1$H NMR ($CDCl_3$, 200 MHz): δ (ppm) = 7.72 (dd, *J* = 8.9, 2.2 Hz, 2H), 7.41 (dd, *J* = 8.9, 2.2 Hz, 2H), 6.78 (s, 1H), 3.78-3.69 (m, 4H), 3.54 (dd, *J* = 11.4, 5.4 Hz, 2H), 2.67-2.56 (m, 2H), 2.56-2.46 (m, 4H). $^{13}$C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 166.4, 137.6, 133.0, 128.8, 128.4, 66.9, 56.9, 53.4, 36.2.

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# Iron-catalyzed benzamide formation. Application to the synthesis of moclobemide

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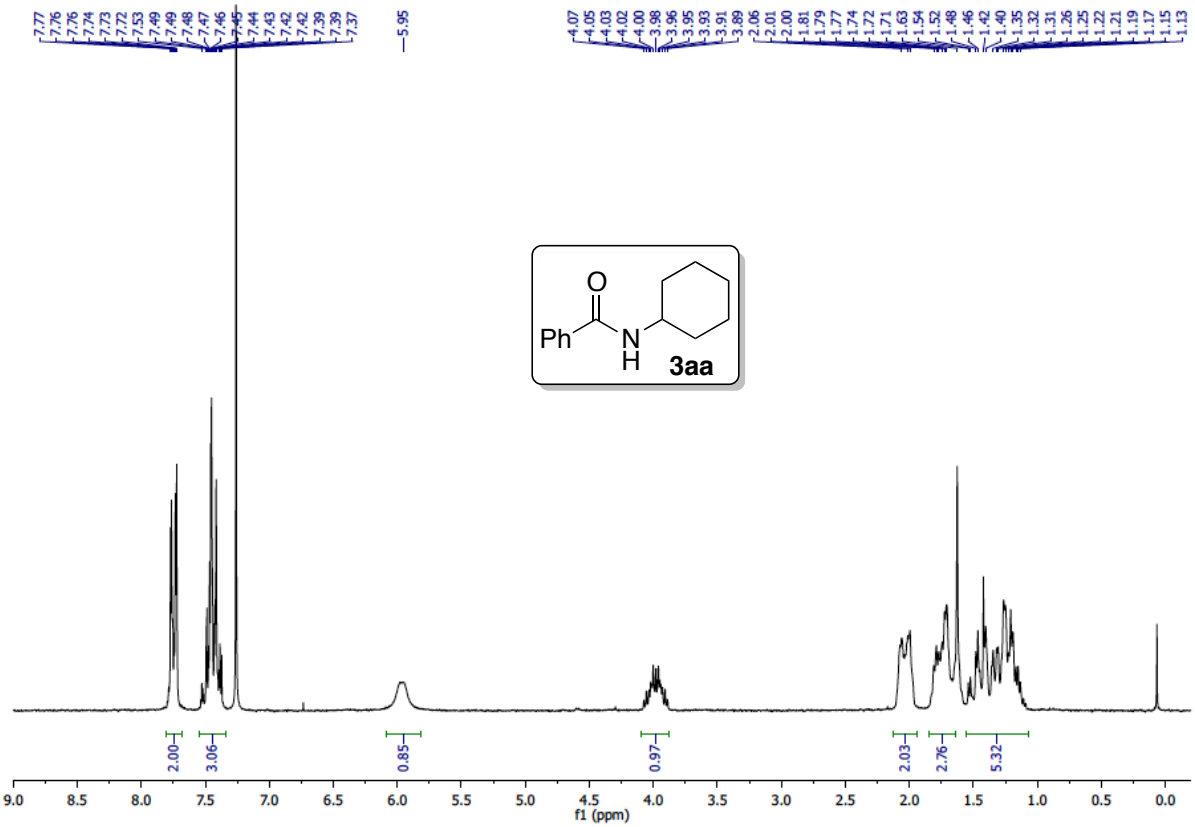
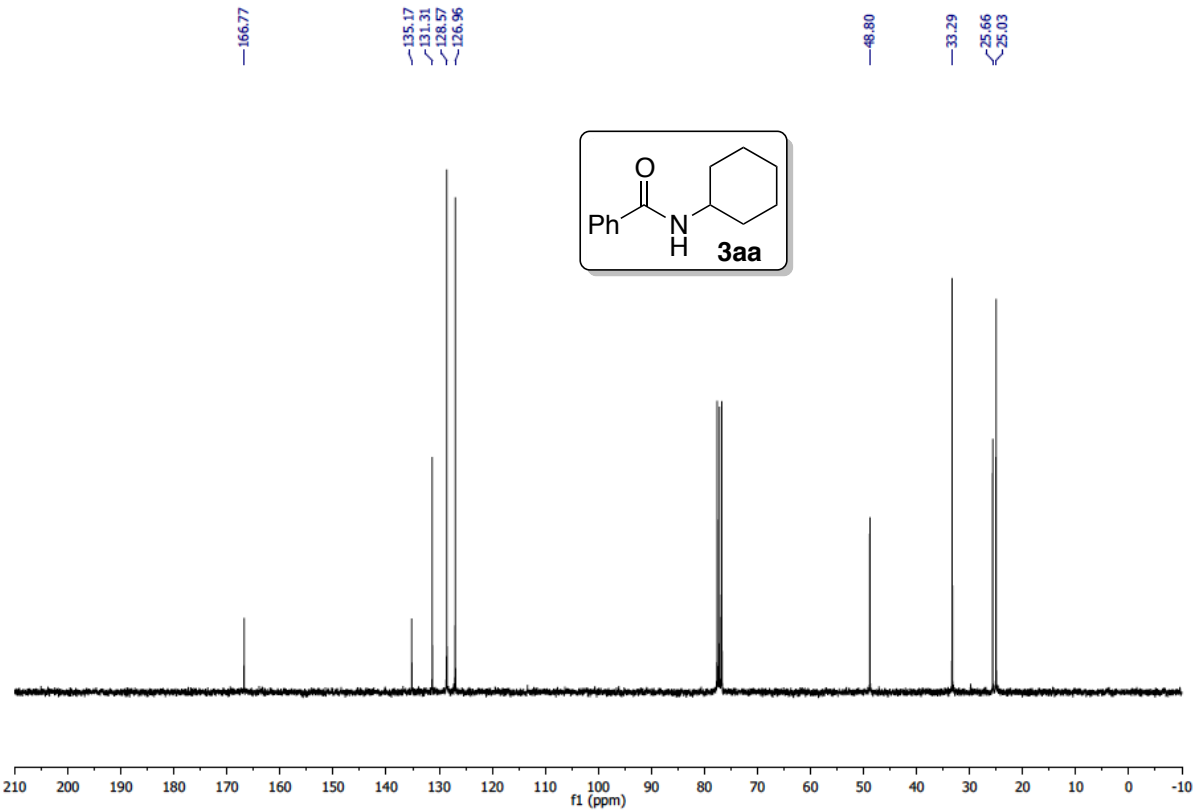
## Table of Content

# 1. NMR Spectra of Synthesized Compounds

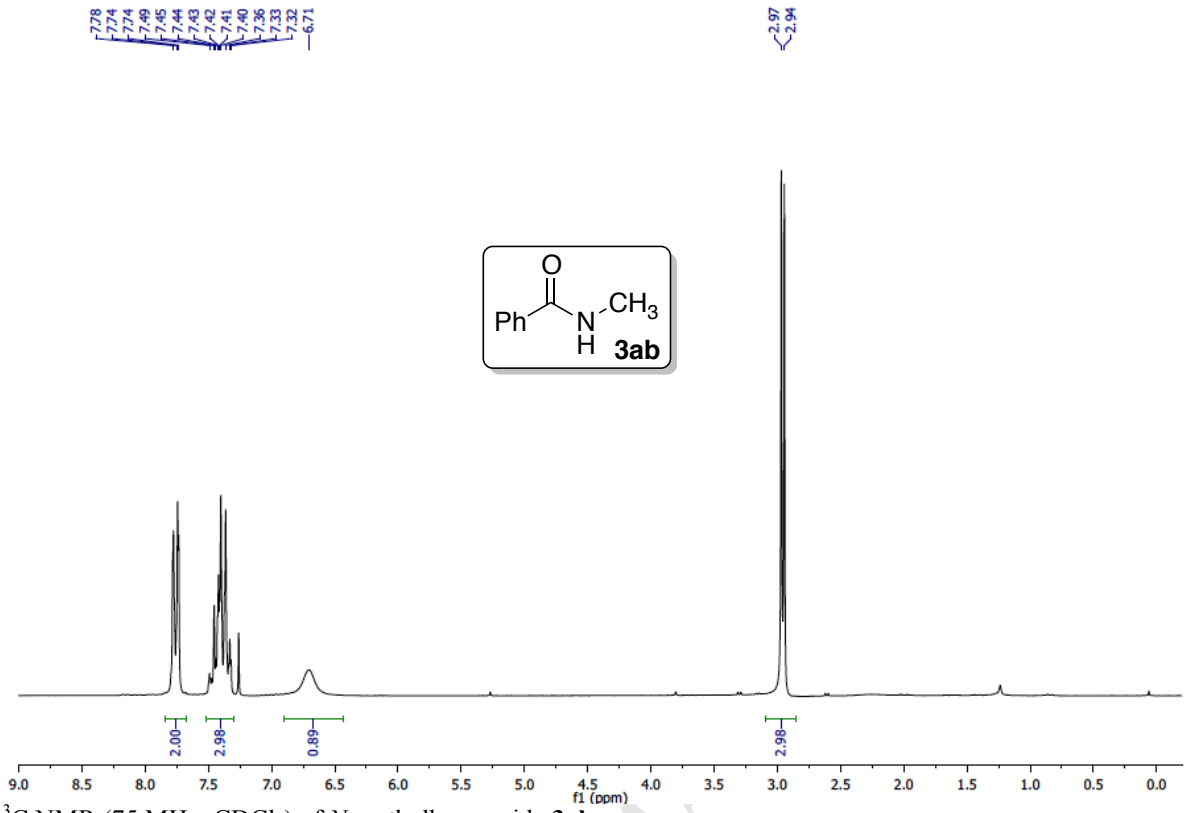
$^{1}$H NMR (200 MHz, $CDCl_3$) of *N*-cyclohexylbenzamide **3aa**



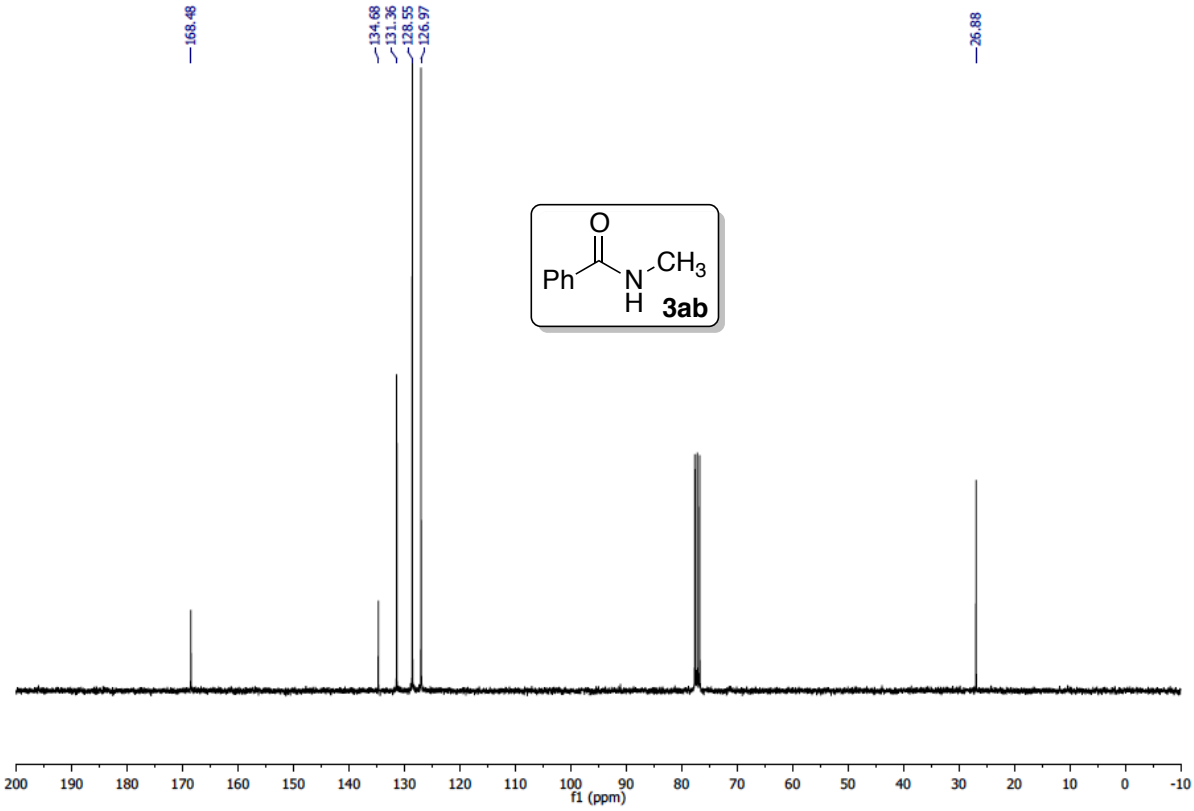

$^{13}$C NMR (75 MHz, $CDCl_3$) of *N*-cyclohexylbenzamide **3aa**



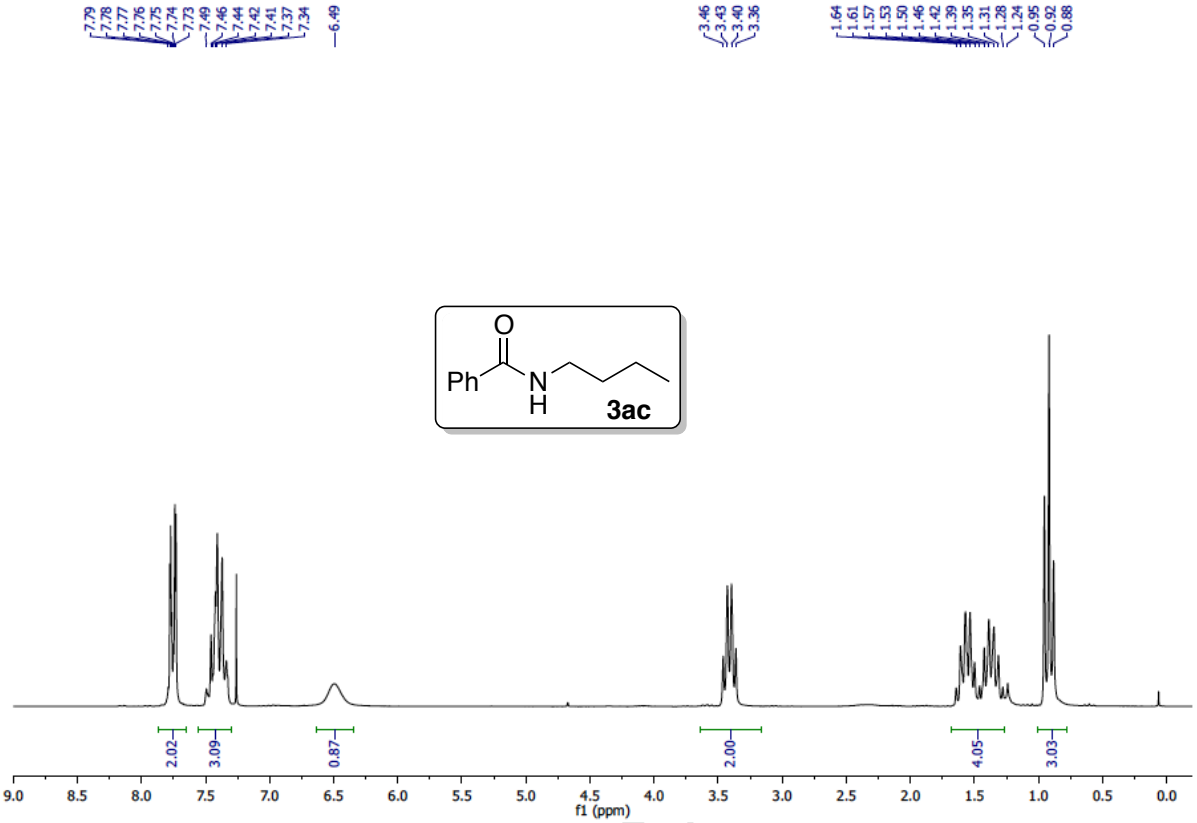
$^{1}$H NMR (200 MHz, $CDCl_3$) of *N*-methylbenzamide **3ab**




$^{13}$C NMR (75 MHz, $CDCl_3$) of *N*-methylbenzamide **3ab**



$^{1}$H NMR (200 MHz, $CDCl_3$) of *N*-butylbenzamide **3ac**

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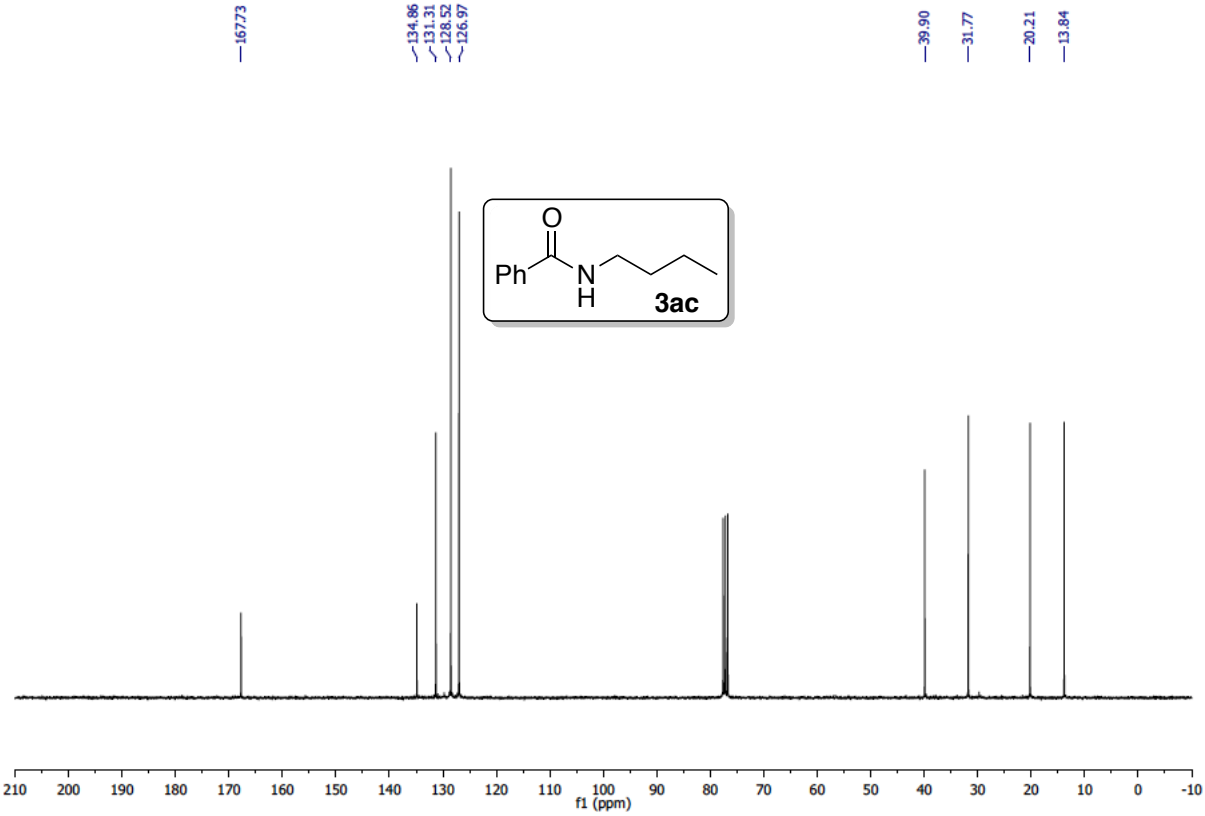
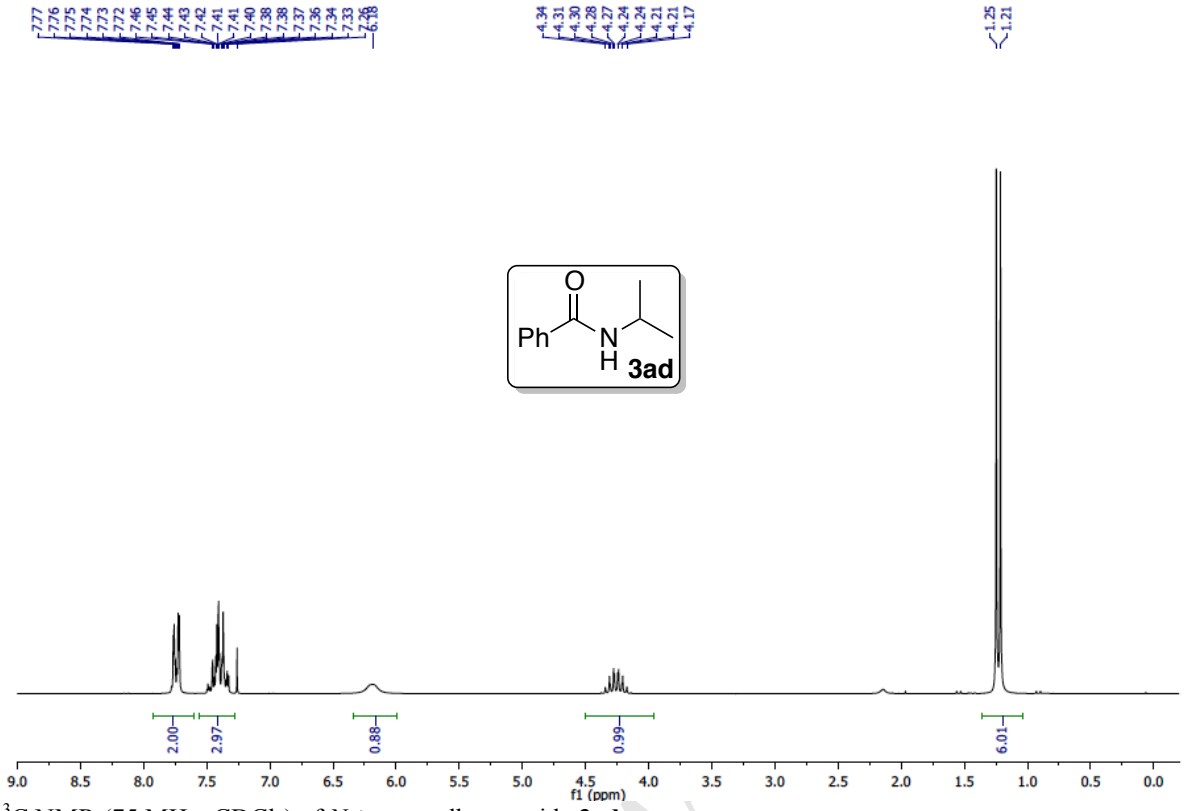
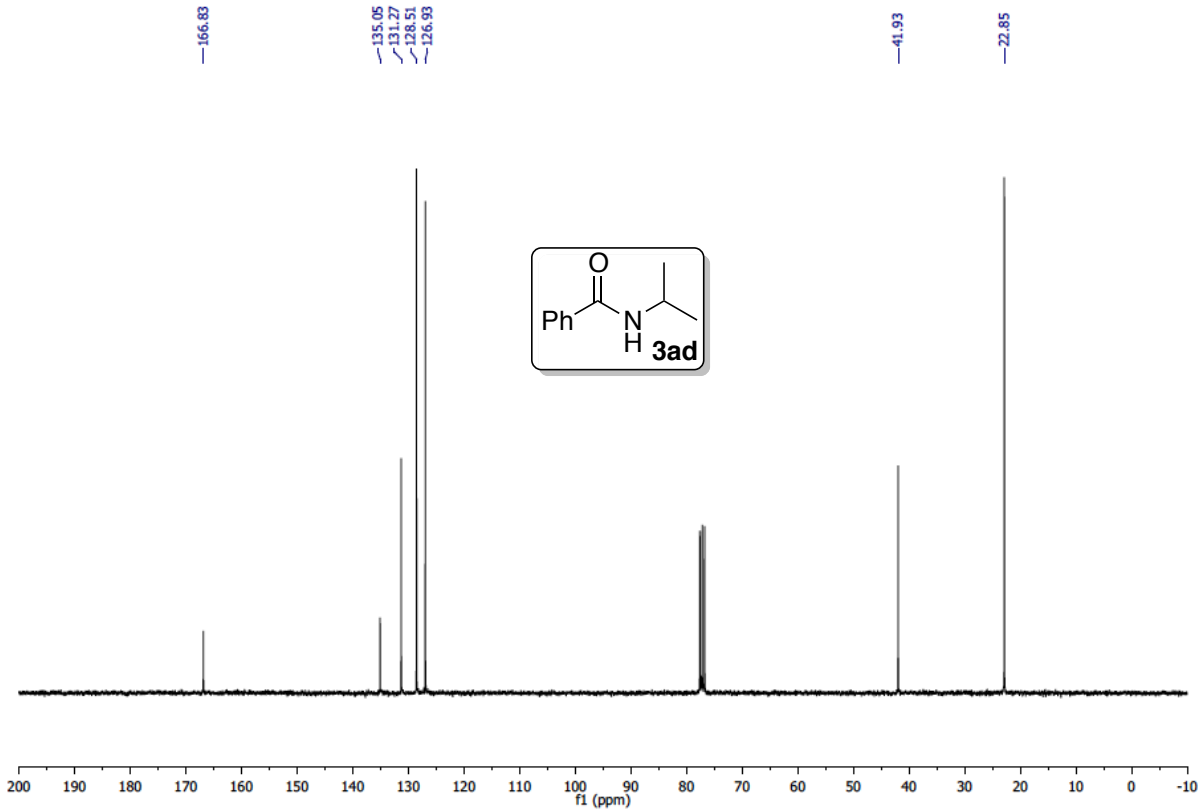


$^{1}$H NMR (200 MHz, $CDCl_3$) of *N-iso*propylbenzamide **3ad**




$^{13}$C NMR (75 MHz, $CDCl_3$) of *N-iso*propylbenzamide **3ad**



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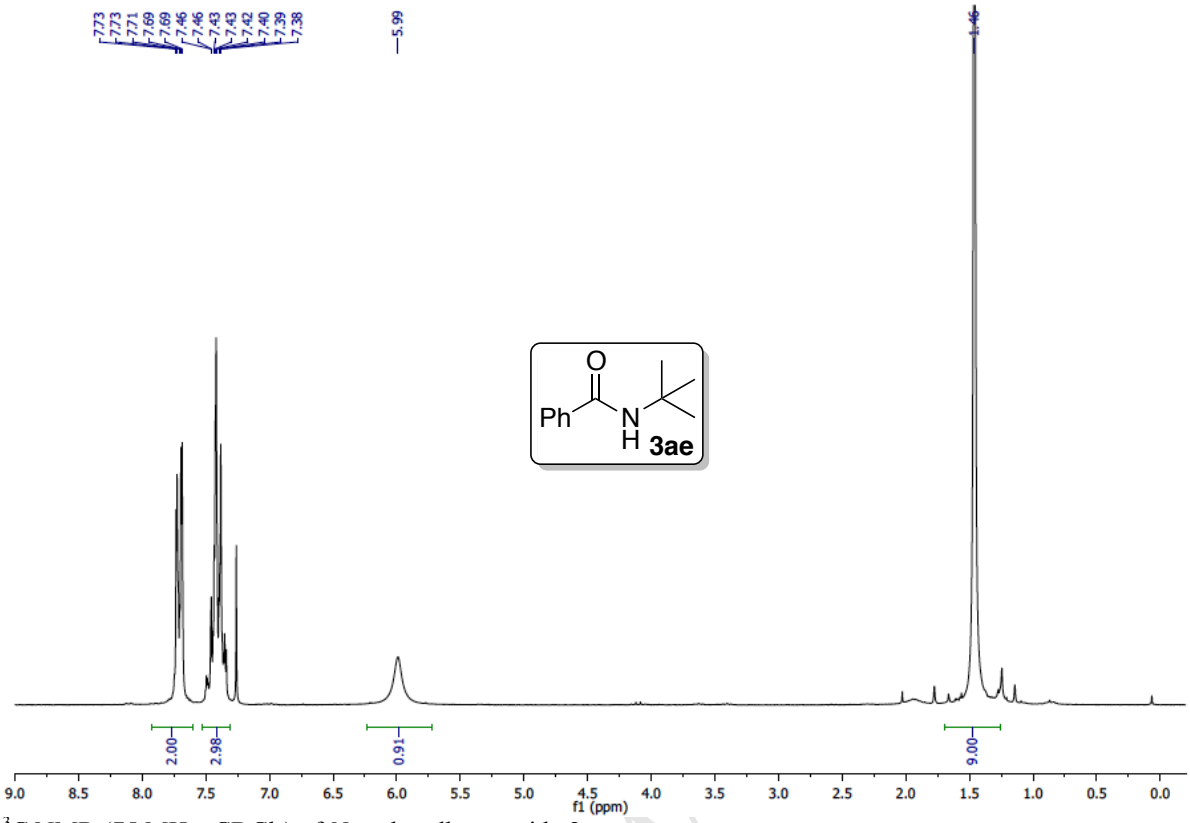


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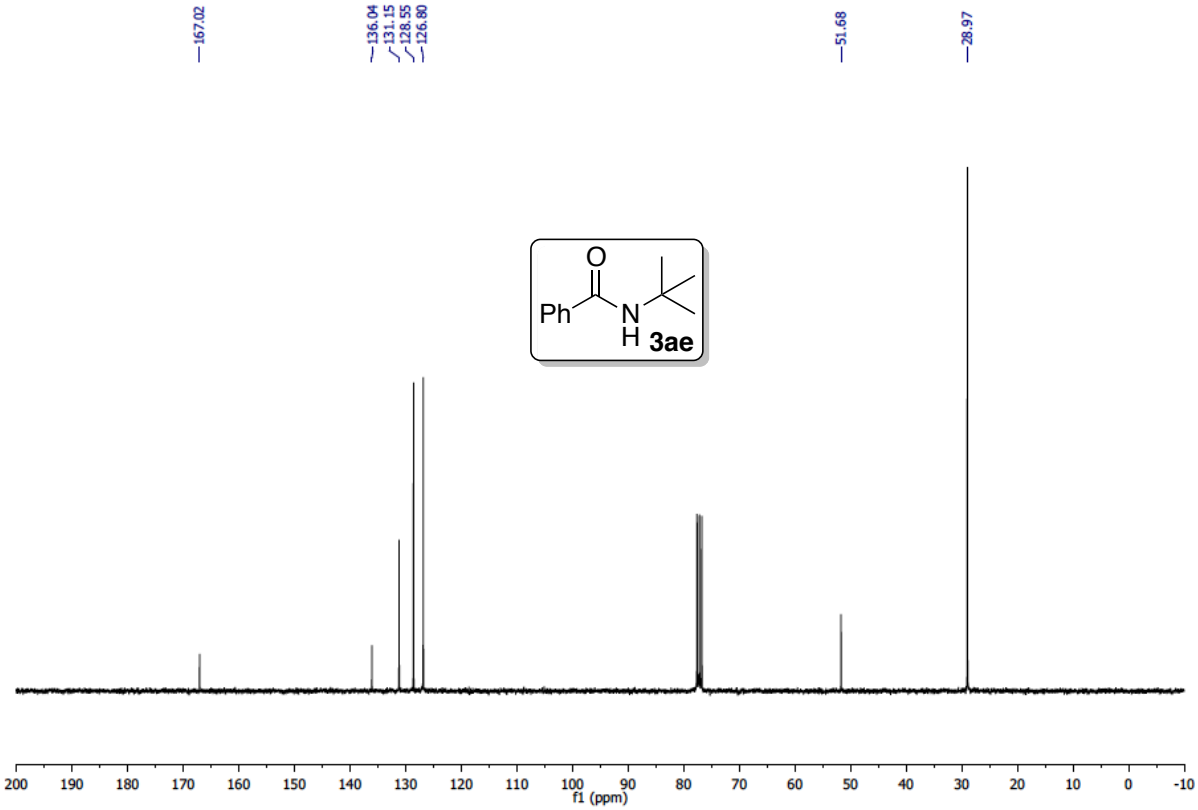
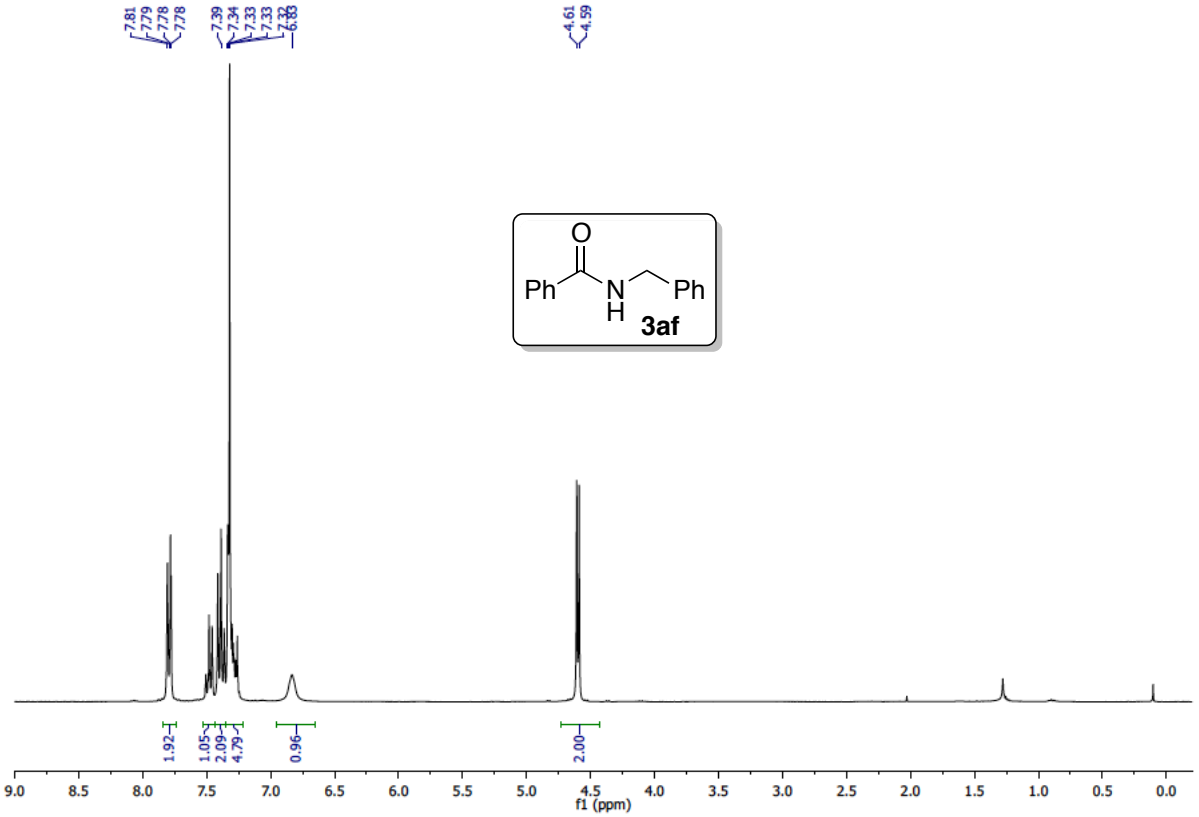
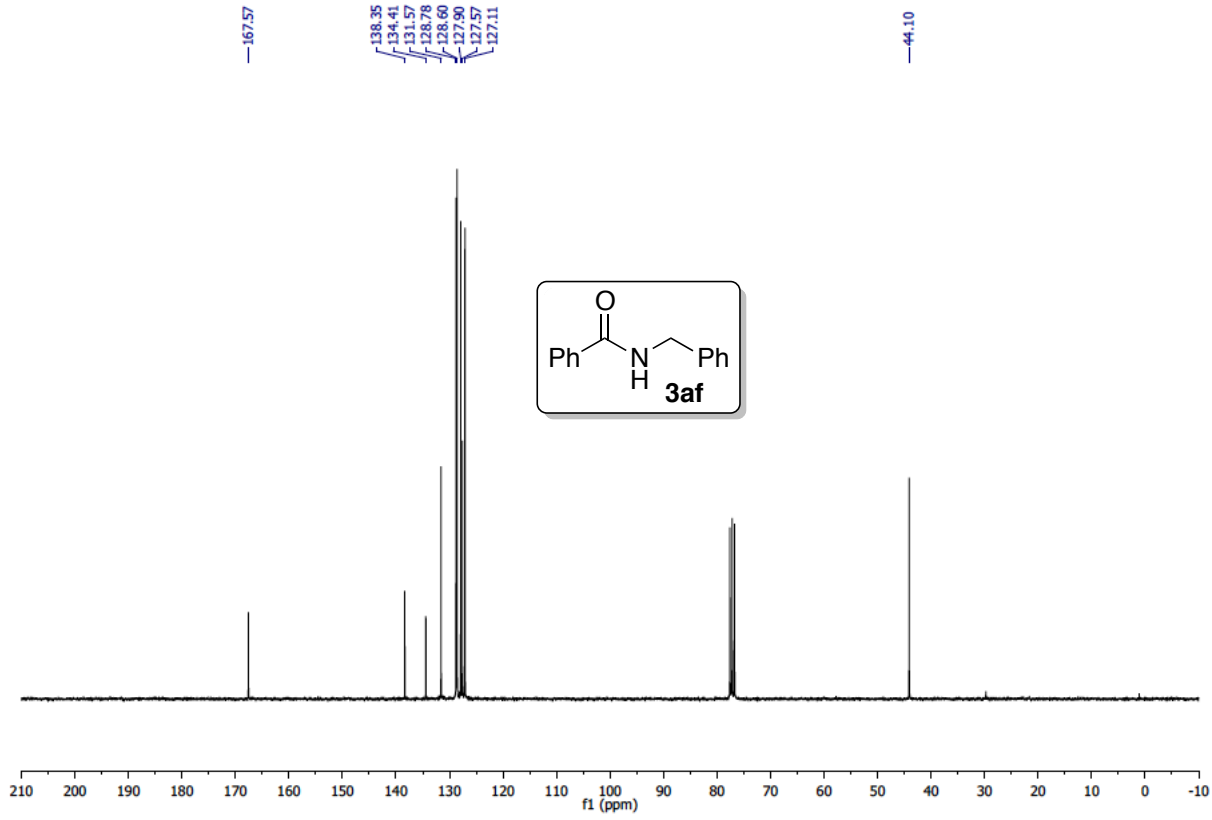


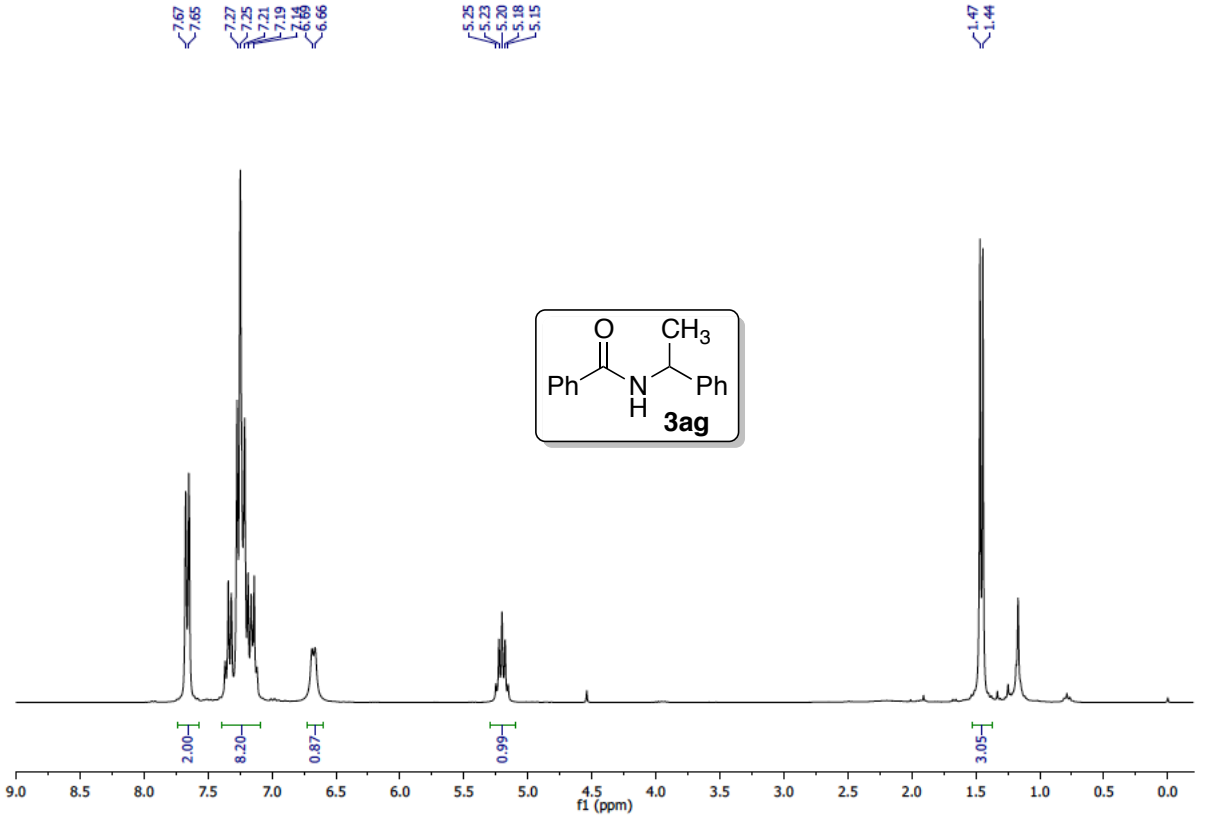
$^{1}$H NMR (200 MHz, $CDCl_3$) of *N*-benzylbenzamide **3af**



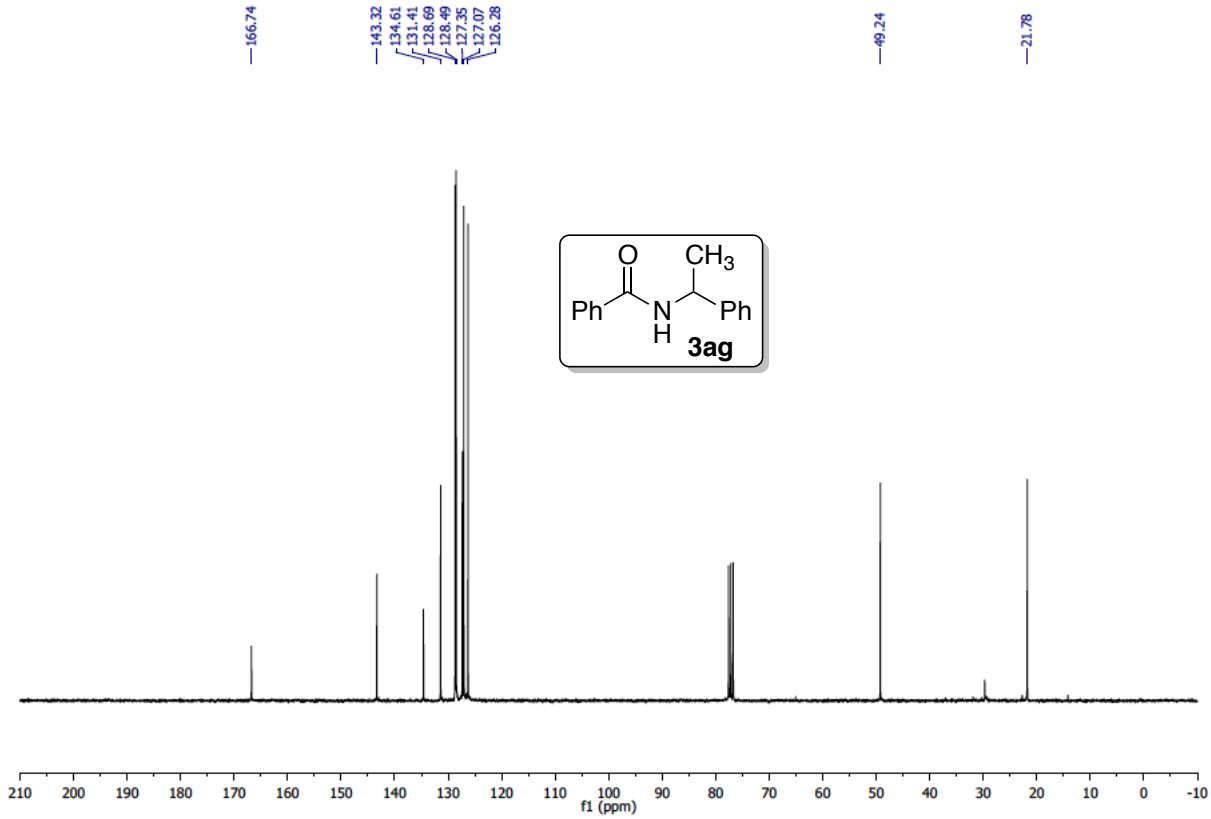

$^{13}$C NMR (75 MHz, $CDCl_3$) of *N*-benzylbenzamide **3af**



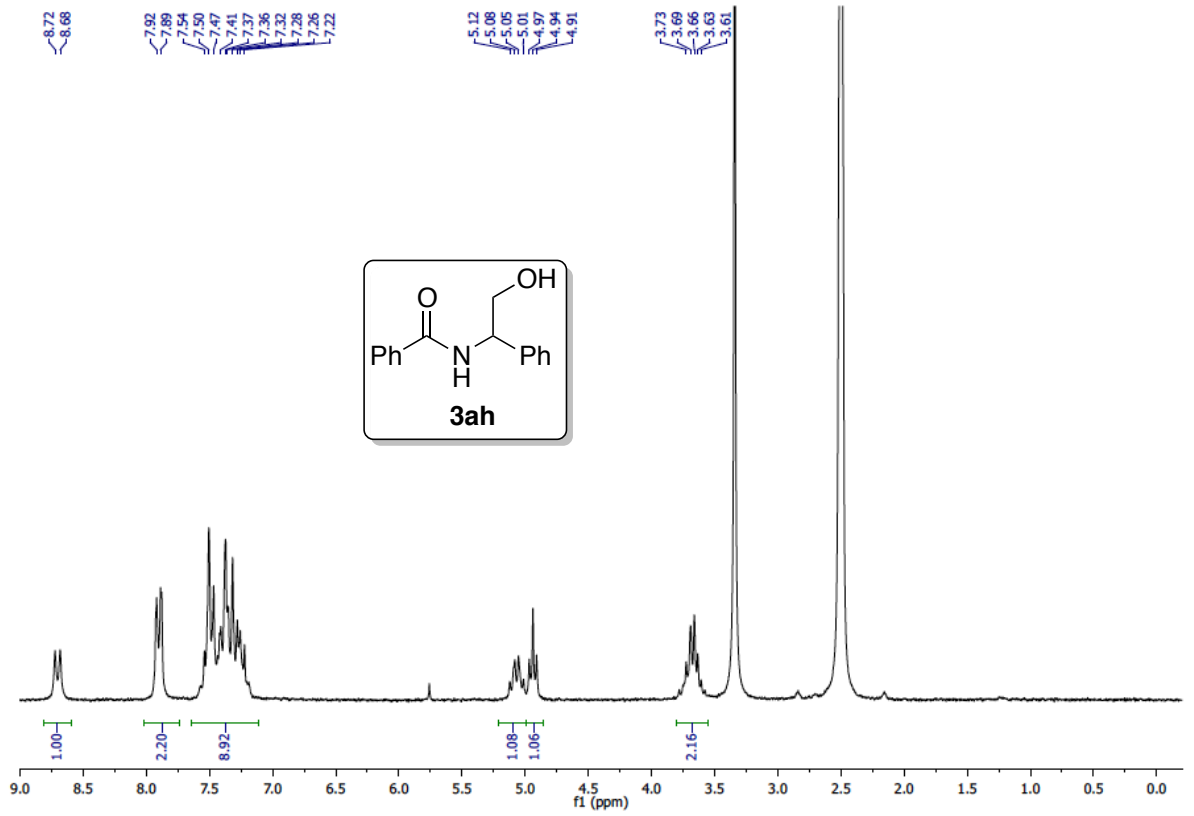
$^{1}$H NMR (200 MHz, $CDCl_3$) of *N*-[(±)-1-phenylethyl]benzamide **3ag**



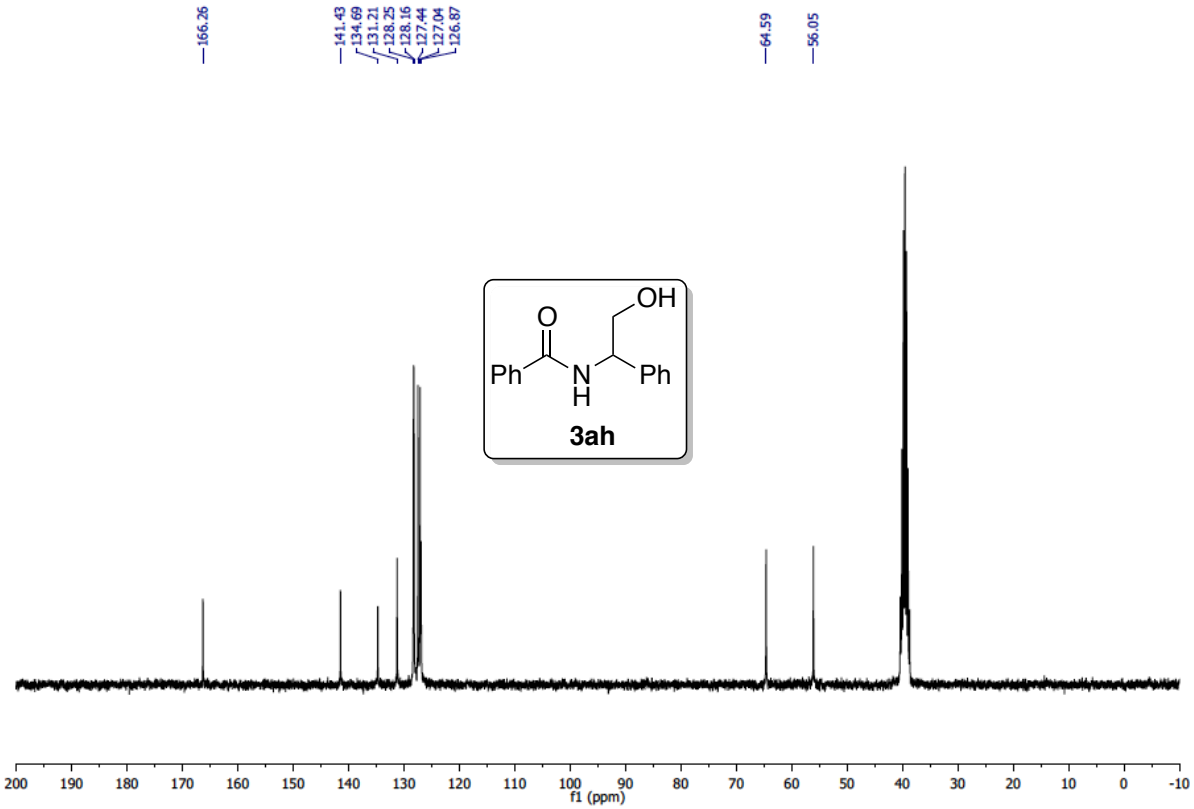

$^{13}$C NMR (75 MHz, $CDCl_3$) of *N*-[(±)-1-phenylethyl]benzamide **3ag**



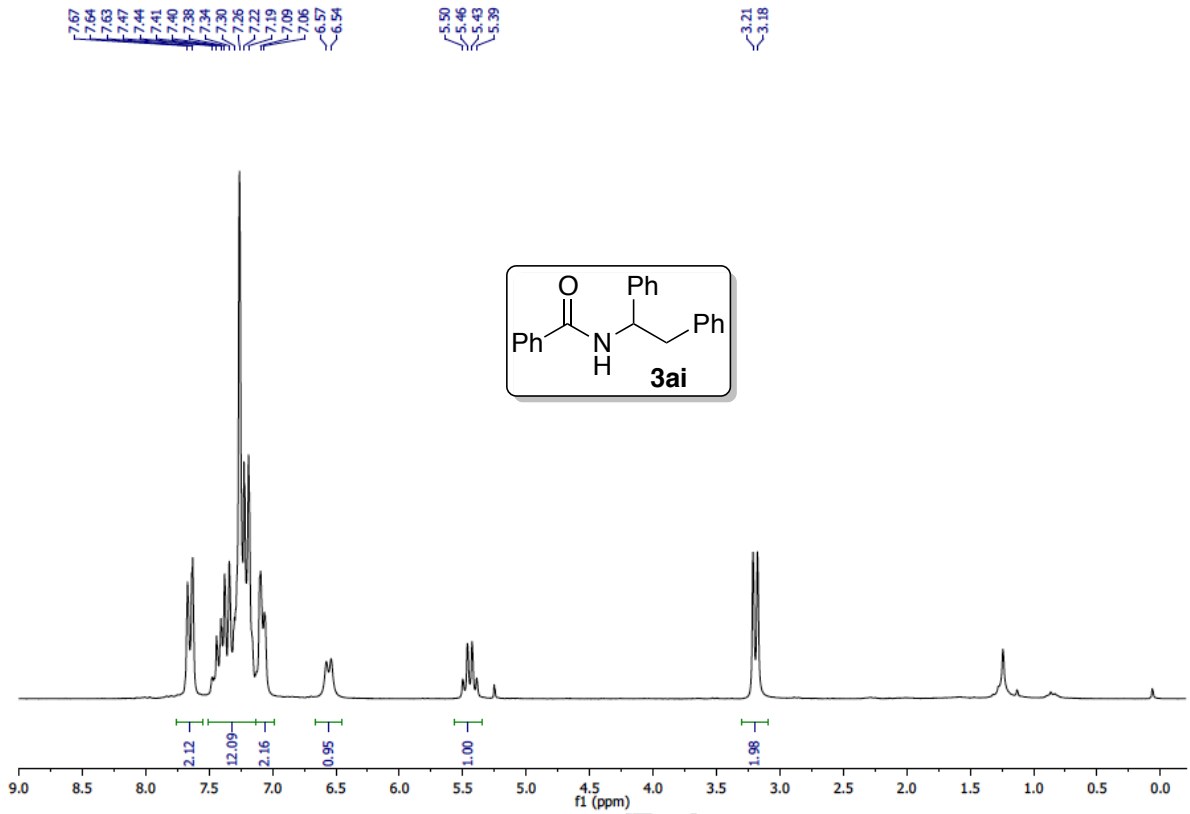
$^{1}$H NMR (200 MHz, DMSO-d6) of *N*-benzoylphenylglycinol **3ah**



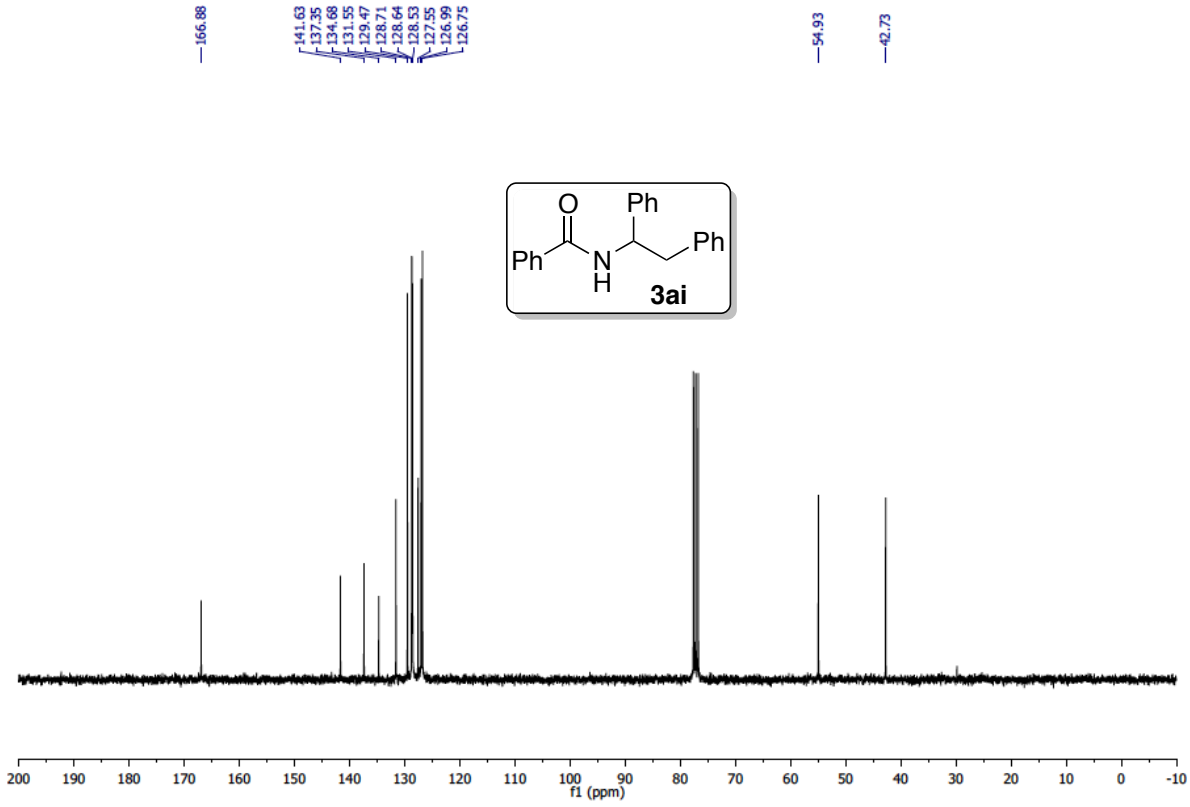

$^{13}$C NMR (75 MHz, DMSO-d6) of *N*-benzoylphenylglycinol **3ah**



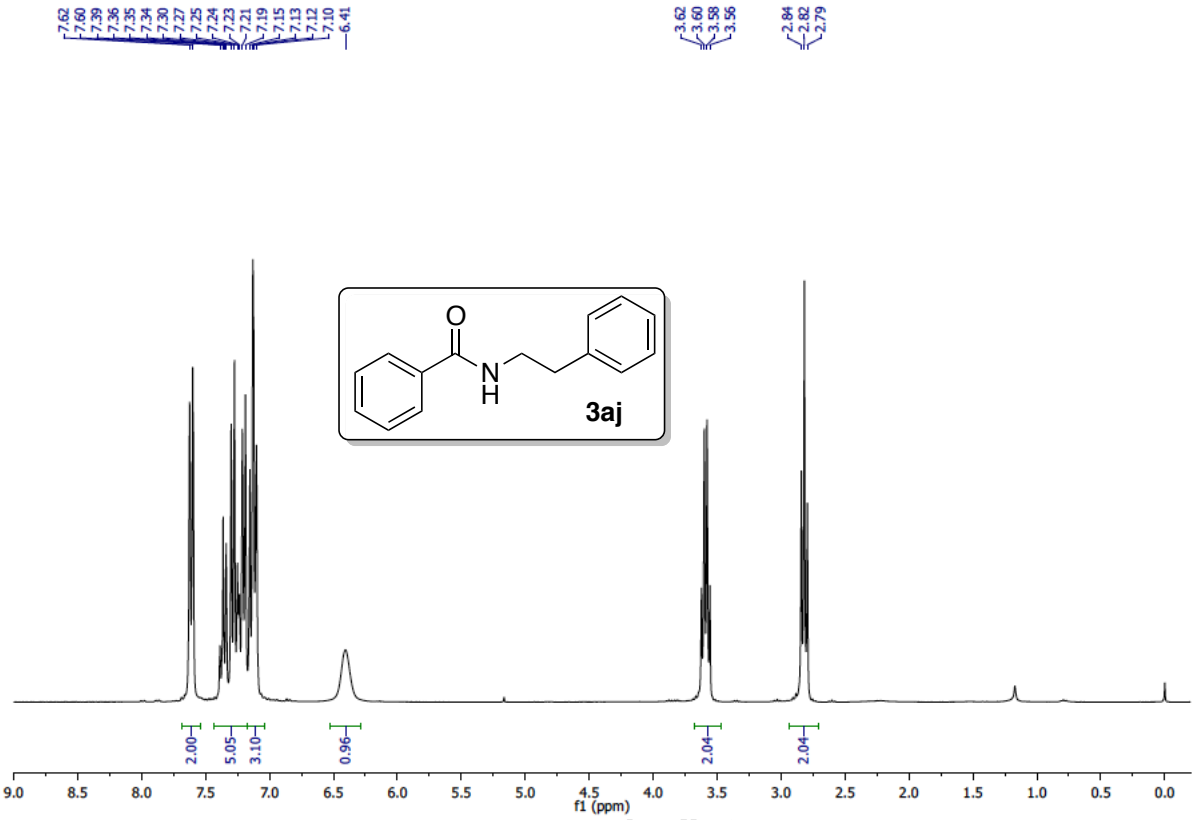
$^{1}$H NMR (200 MHz, $CDCl_3$) of *N*-[(±)-1-(phenyl)phenethyl]benzamide **3ai**



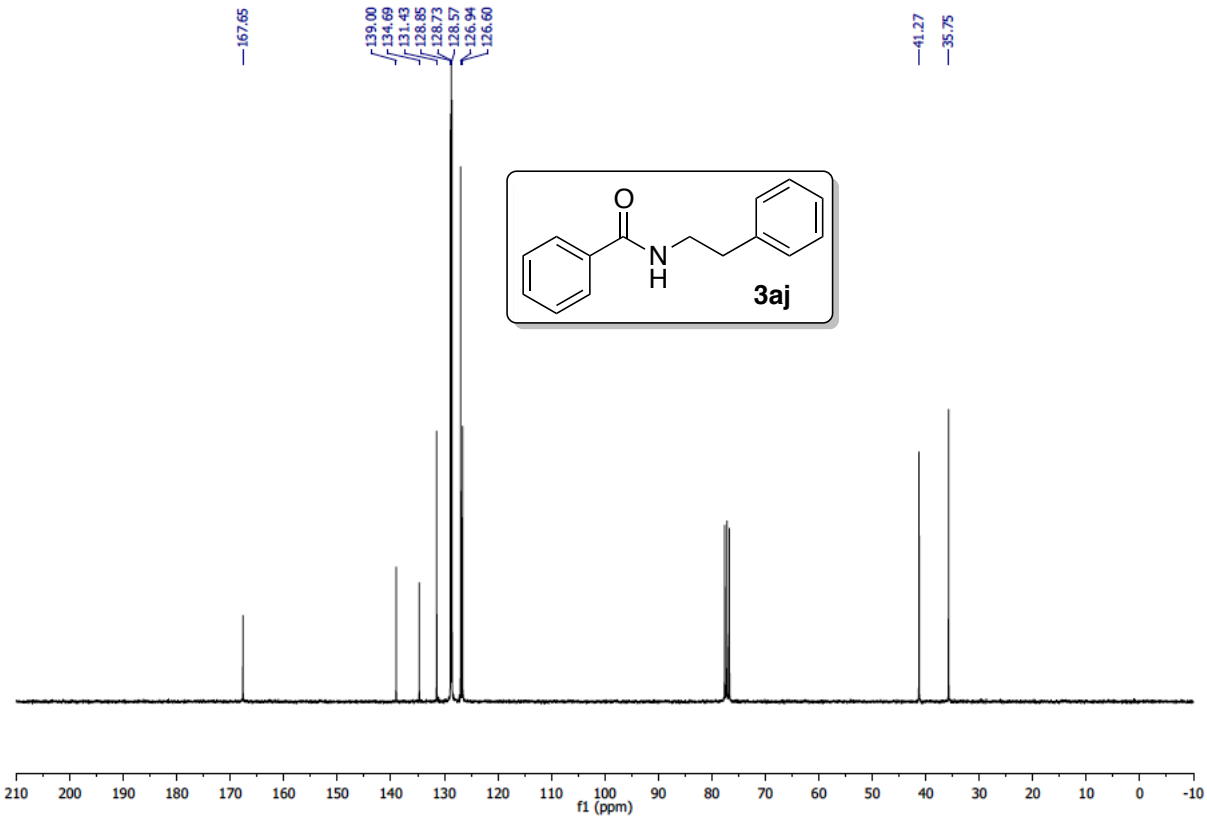

$^{13}$C NMR (75 MHz, $CDCl_3$) of *N*-[(±)-1-(phenyl)phenethyl]benzamide **3ai**



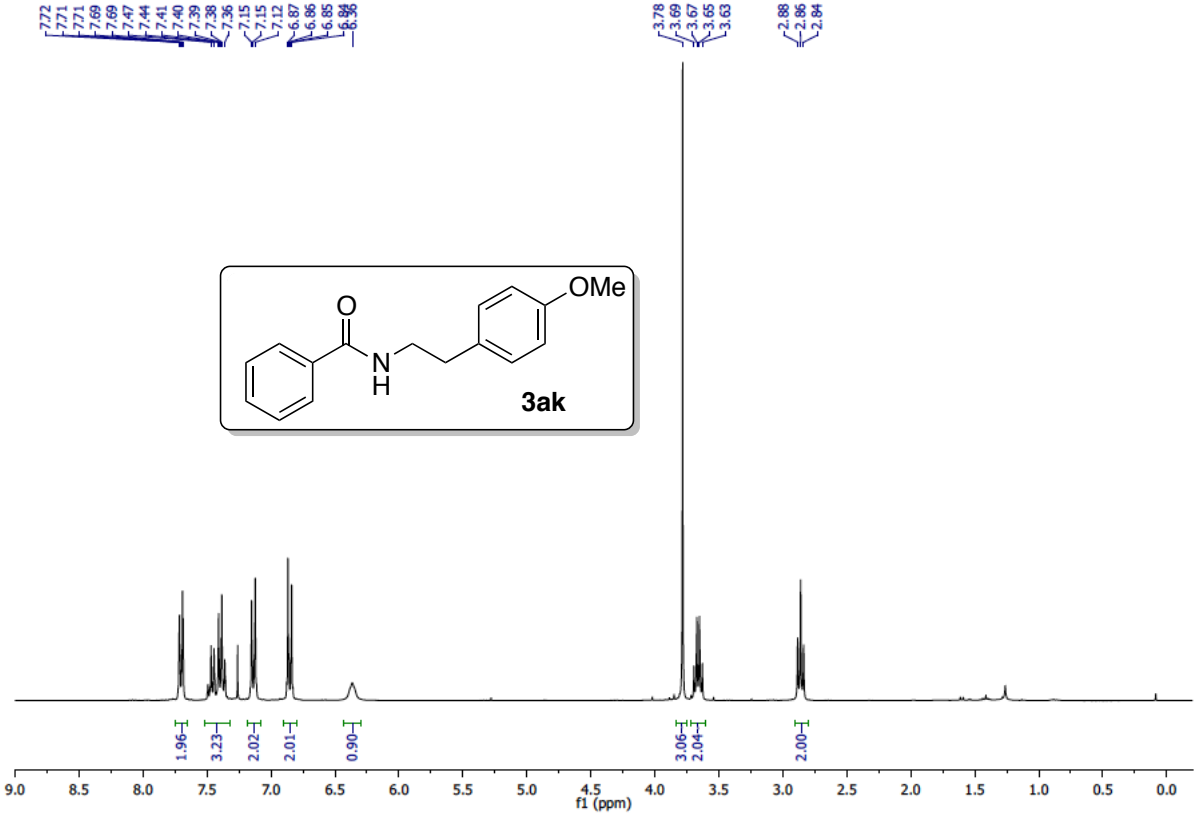
$^{1}$H NMR (200 MHz, $CDCl_3$) of *N*-[2-phenethyl]benzamide **3aj**



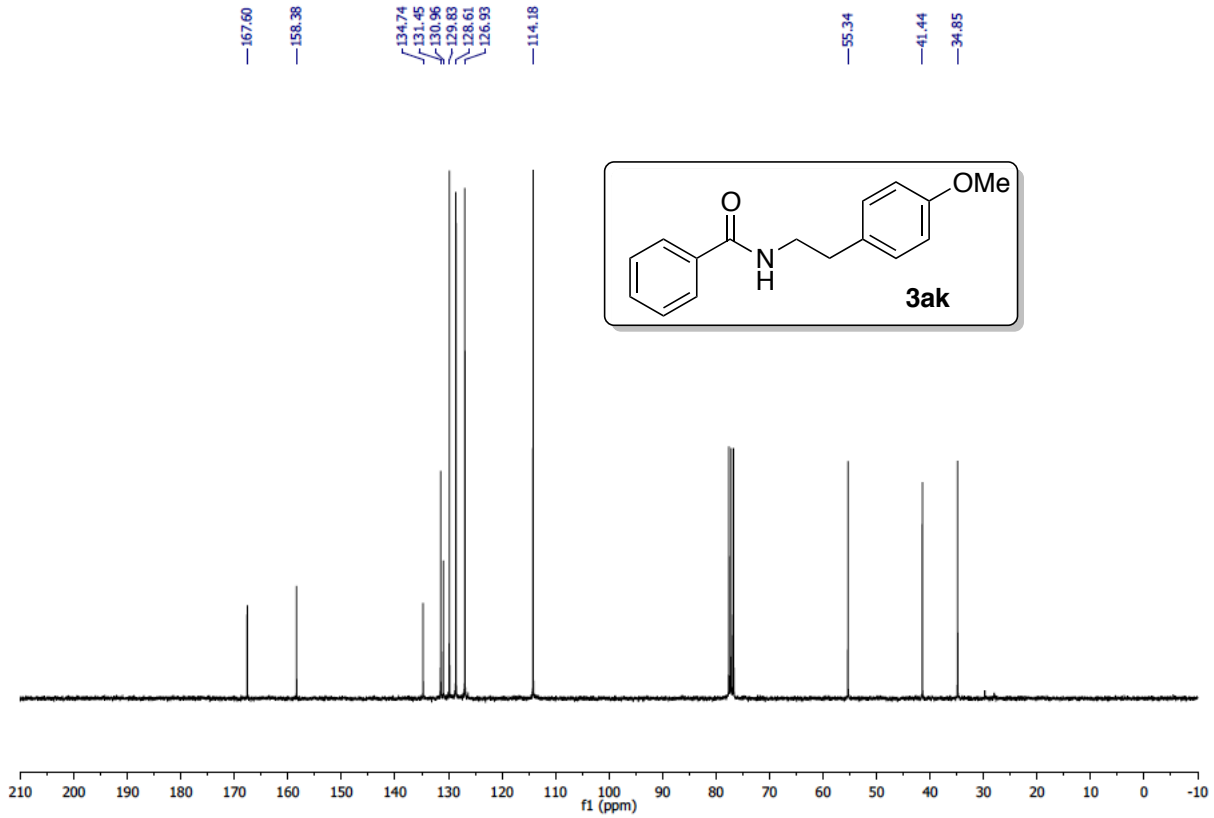

$^{13}$C NMR (75 MHz, $CDCl_3$) of *N*-[2-phenethyl]benzamide **3aj**



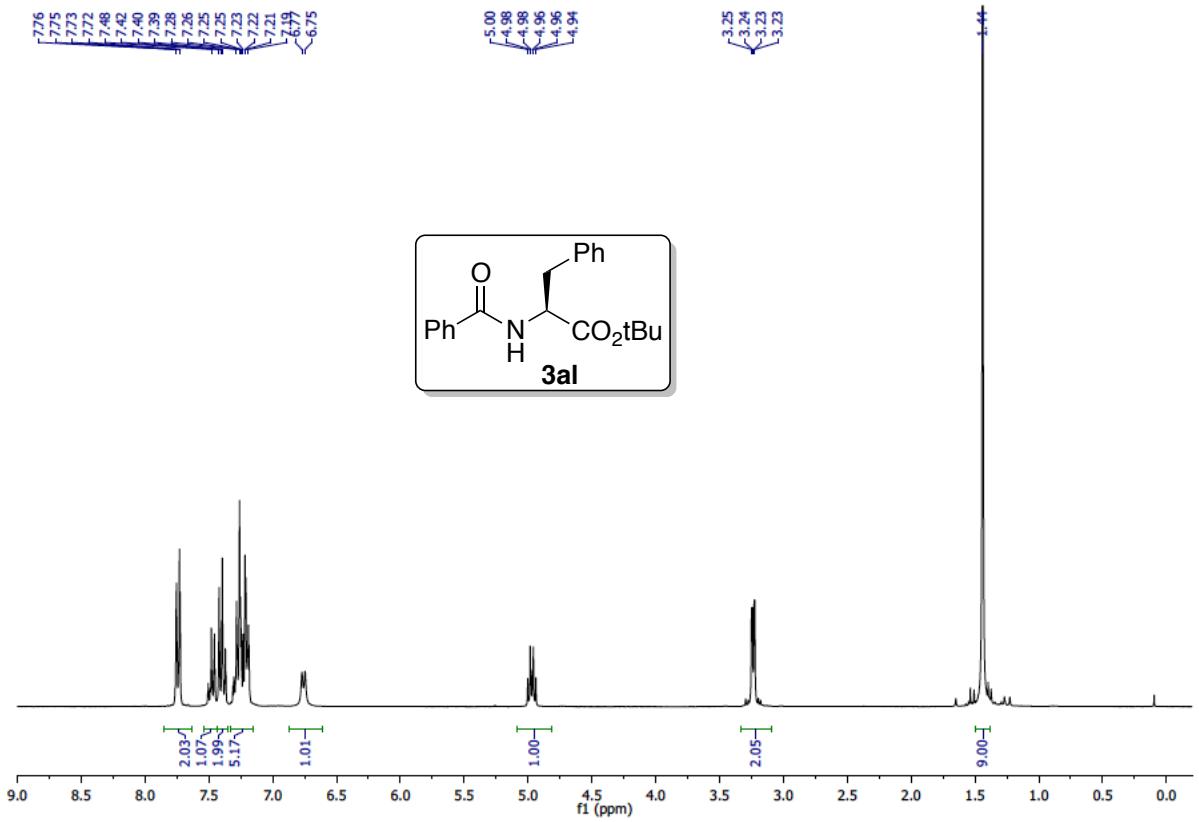
$^{1}$H NMR (200 MHz, $CDCl_3$) of *N*-[2-(4-methoxyphenyl)ethyl]benzamide **3ak**



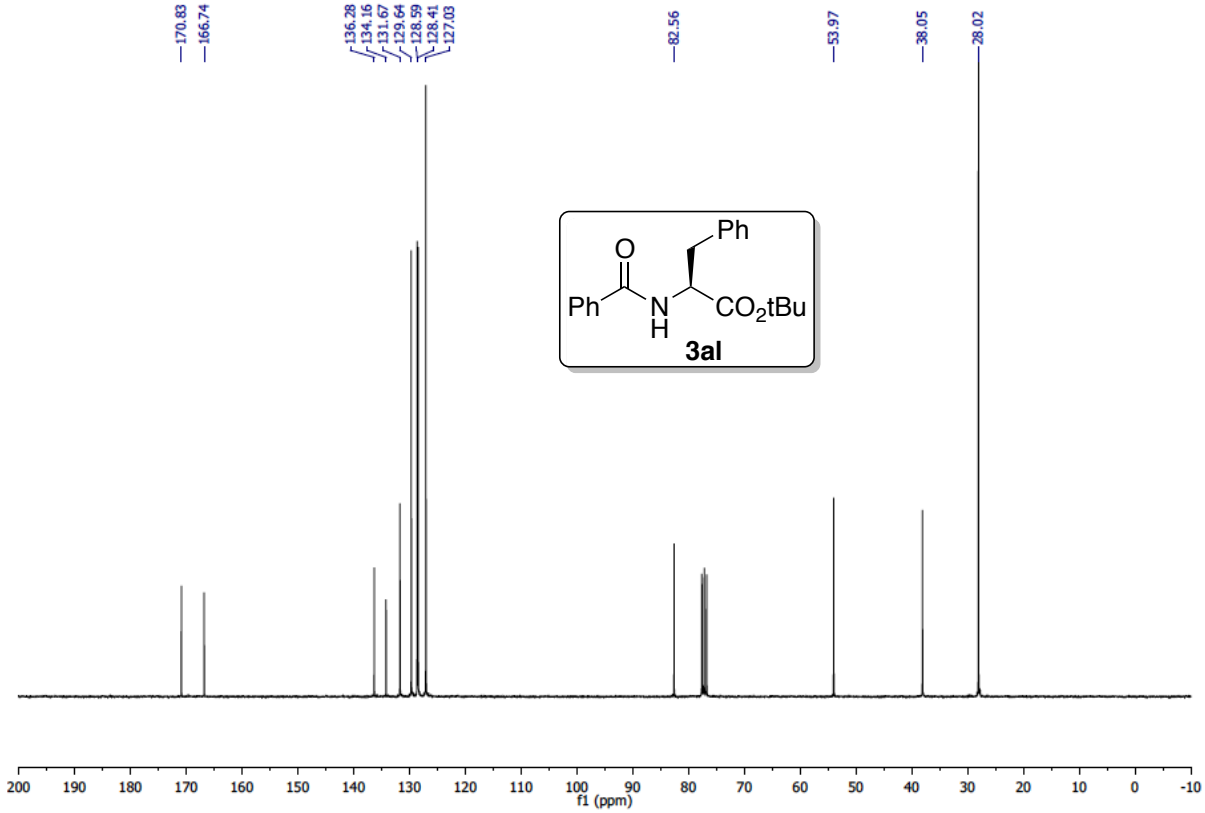

$^{13}$C NMR (75 MHz, $CDCl_3$) of *N*-[2-(4-methoxyphenyl)ethyl]benzamide **3ak**



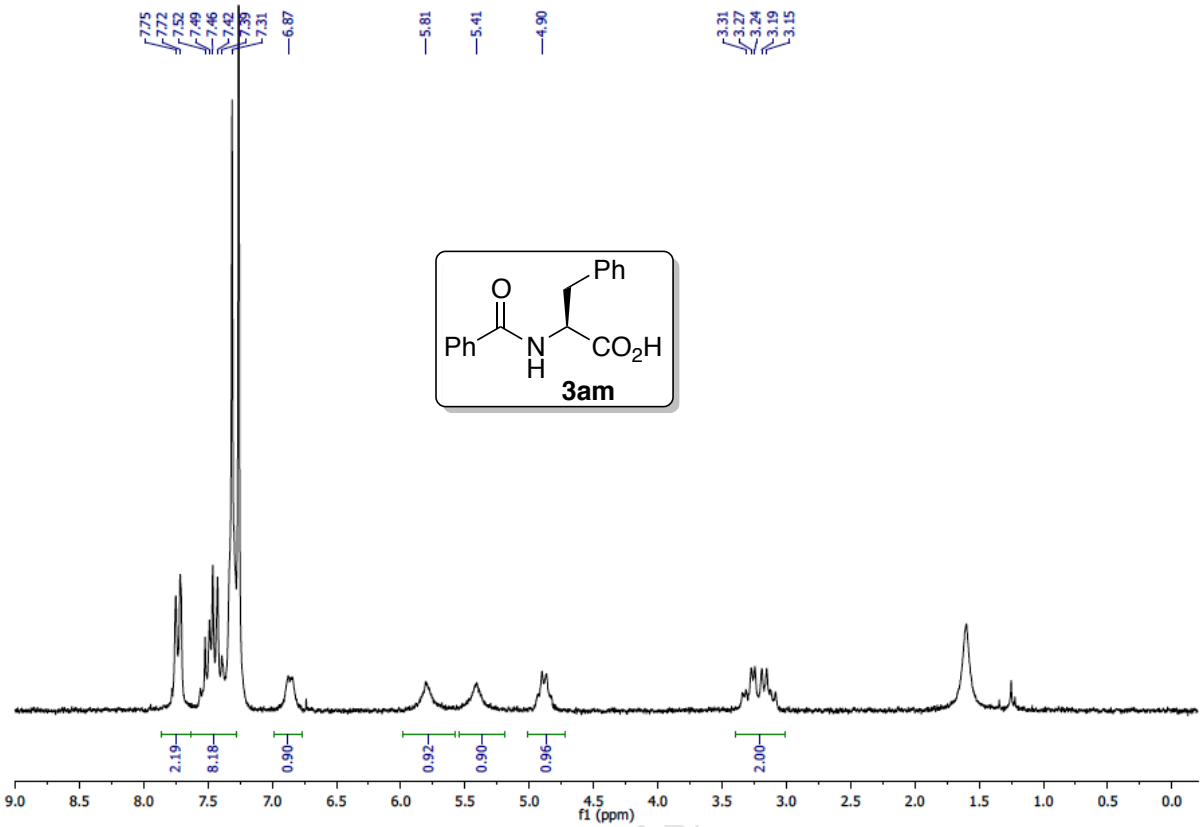
$^{1}$H NMR (200 MHz, $CDCl_3$) of *tert*-butyl-(2*S*)-(benzoylamino)-3-phenylpropanoate **3al**



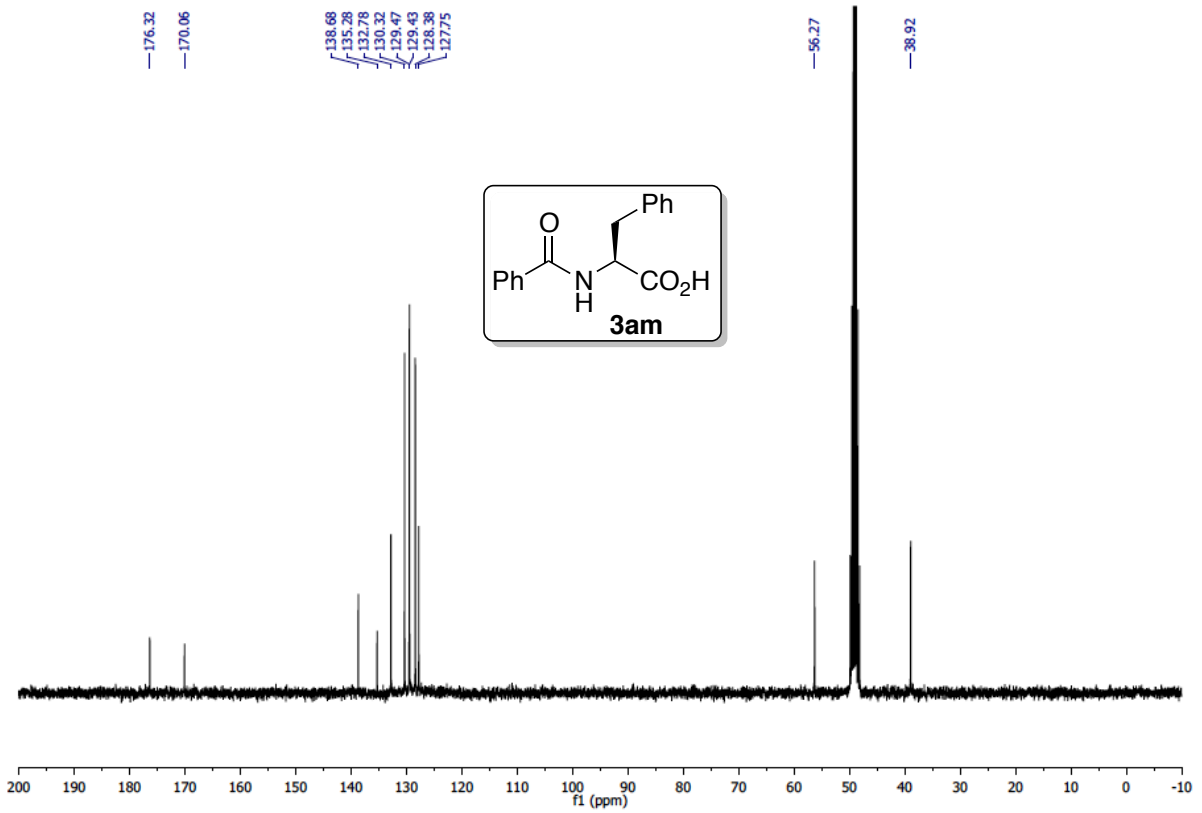

$^{13}$C NMR (75 MHz, $CDCl_3$) of *tert*-butyl-(2*S*)-(benzoylamino)-3-phenylpropanoate **3al**



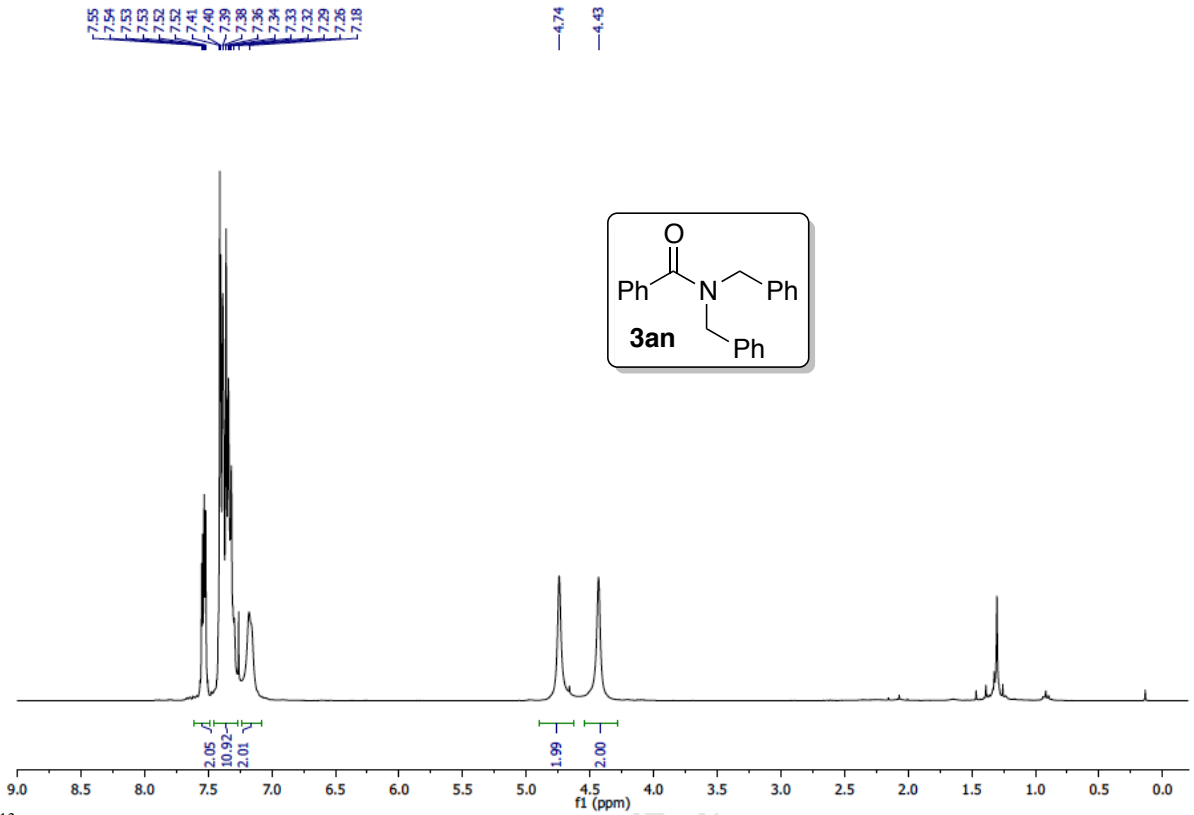
$^{1}$H NMR (200 MHz, $CDCl_3$) of *N*-benzoylphenylalanine **3am**



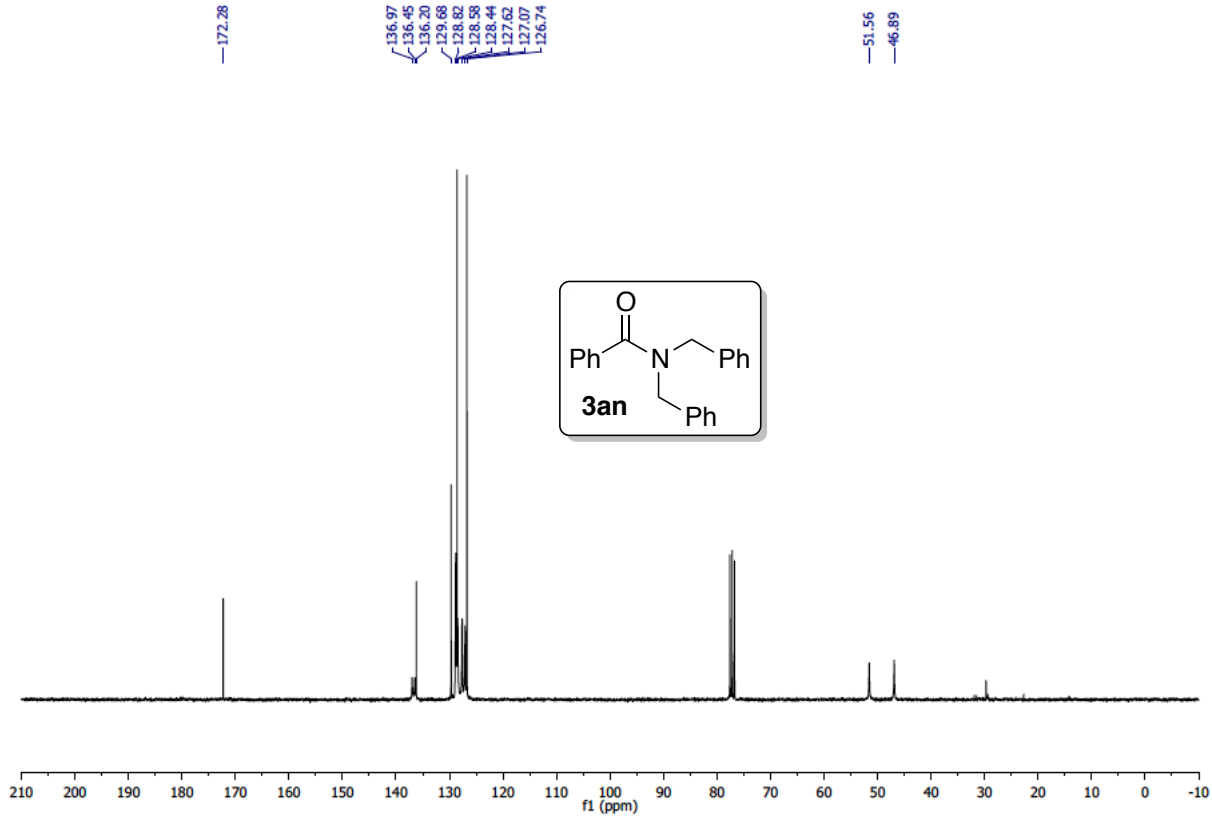

$^{13}$C NMR (75 MHz, $CD_3OD$) of *N*-benzoylphenylalanine **3am**



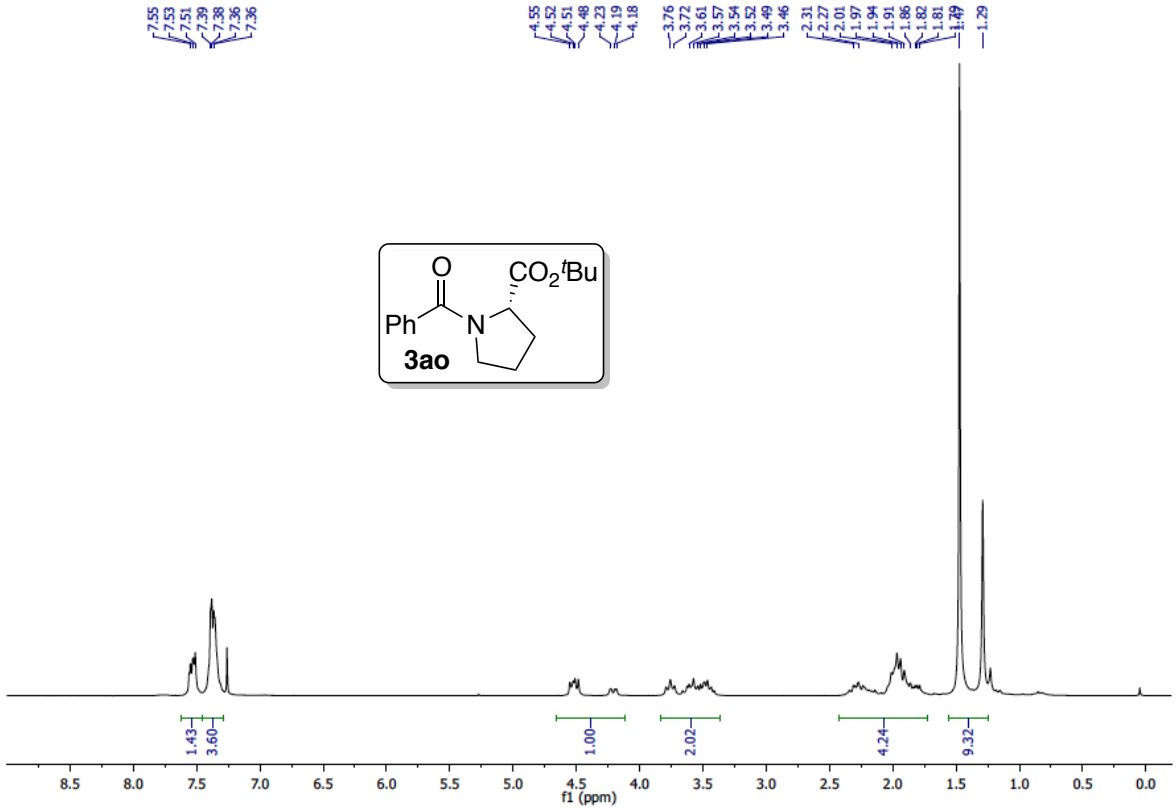
$^{1}$H NMR (200 MHz, $CDCl_3$) of *N*,*N*-dibenzylbenzamide **3an**



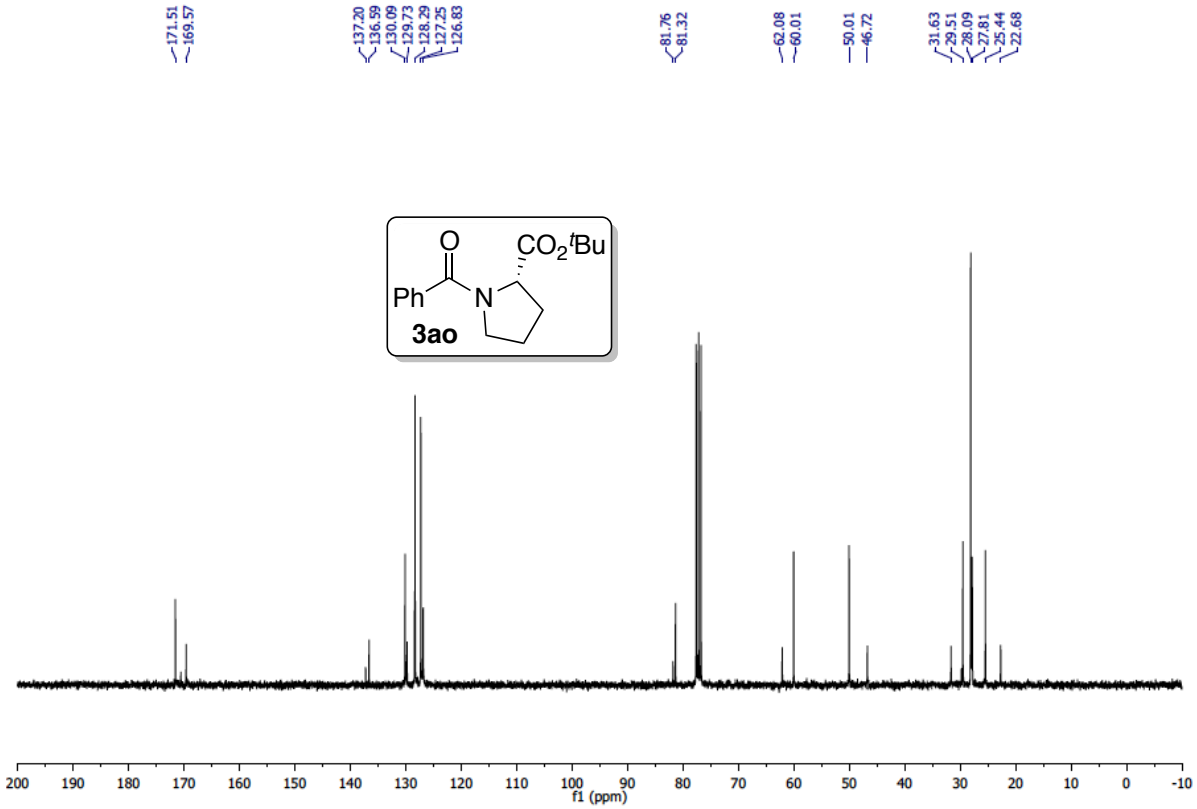

$^{13}$C NMR (75 MHz, $CDCl_3$) of *N*,*N*-dibenzylbenzamide **3an**



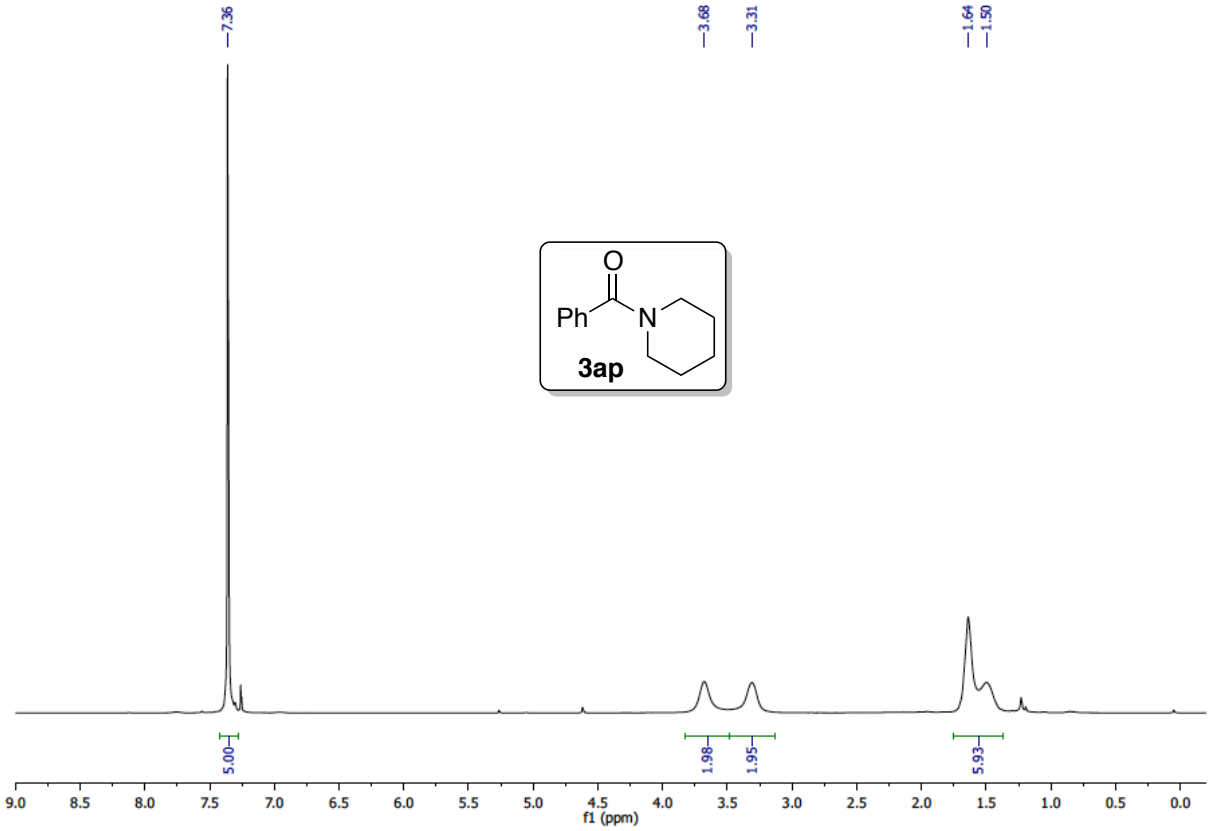
$^{1}$H NMR (200 MHz, $CDCl_3$) of *tert*-butyl-(2*S*)-1-benzoyl-2-pyrrolidinecarboxylate **3ao**



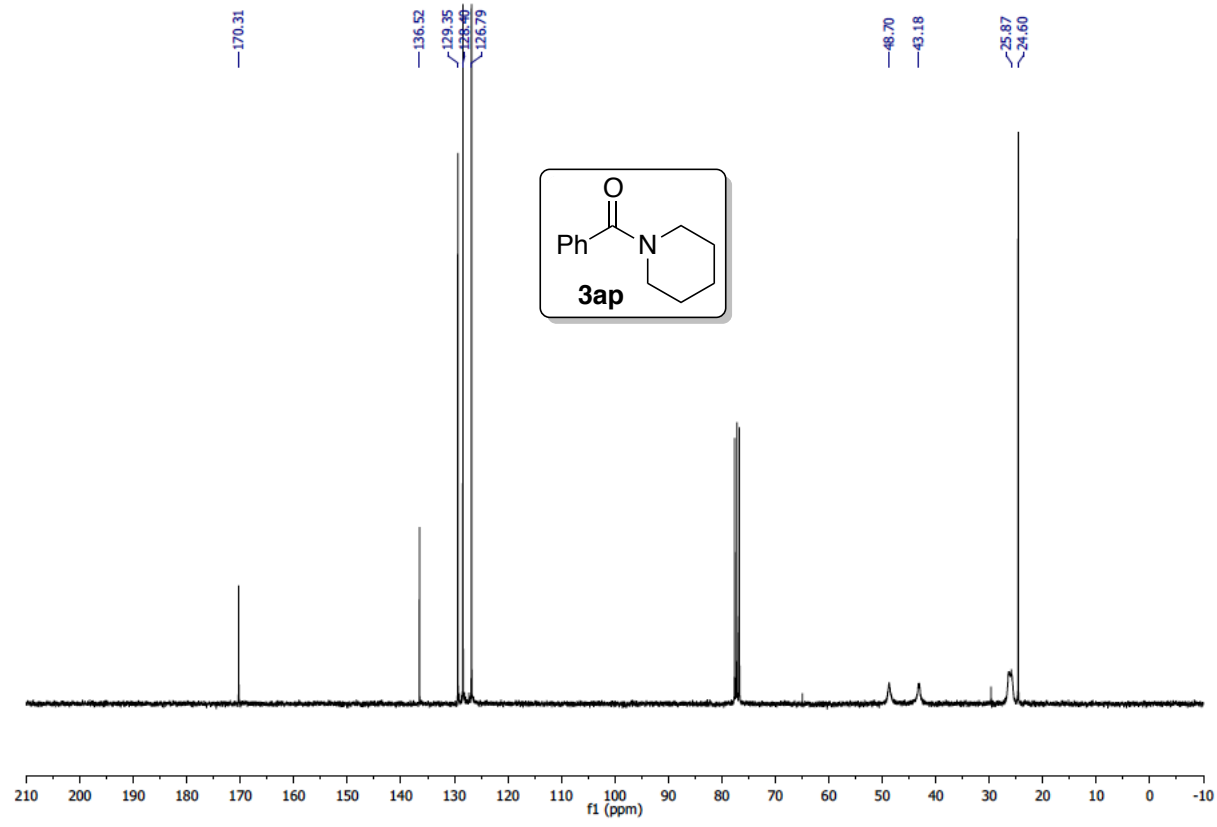

$^{13}$C NMR (75 MHz, $CDCl_3$) of *tert*-butyl-(2*S*)-1-benzoyl-2-pyrrolidinecarboxylate **3ao**



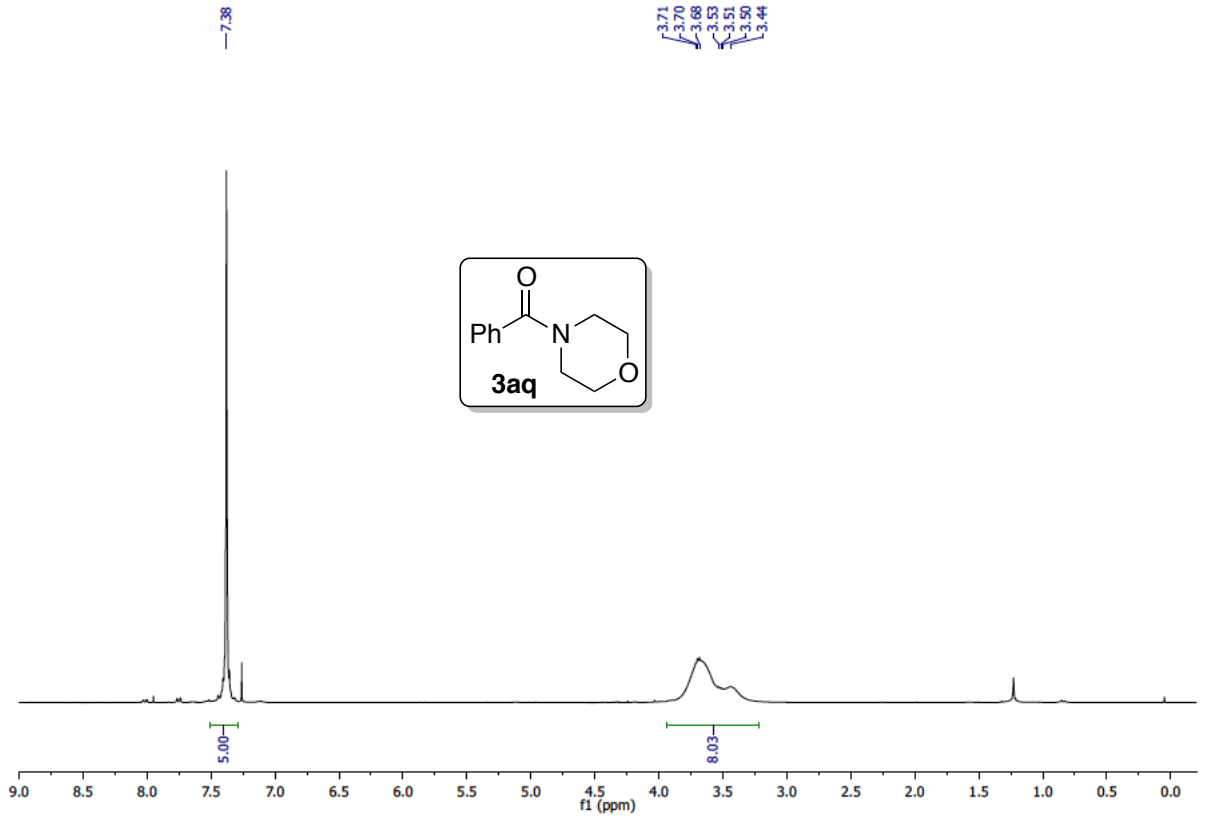
$^{1}$H NMR (200 MHz, $CDCl_3$) of *N*-benzoylpiperidine **3ap**



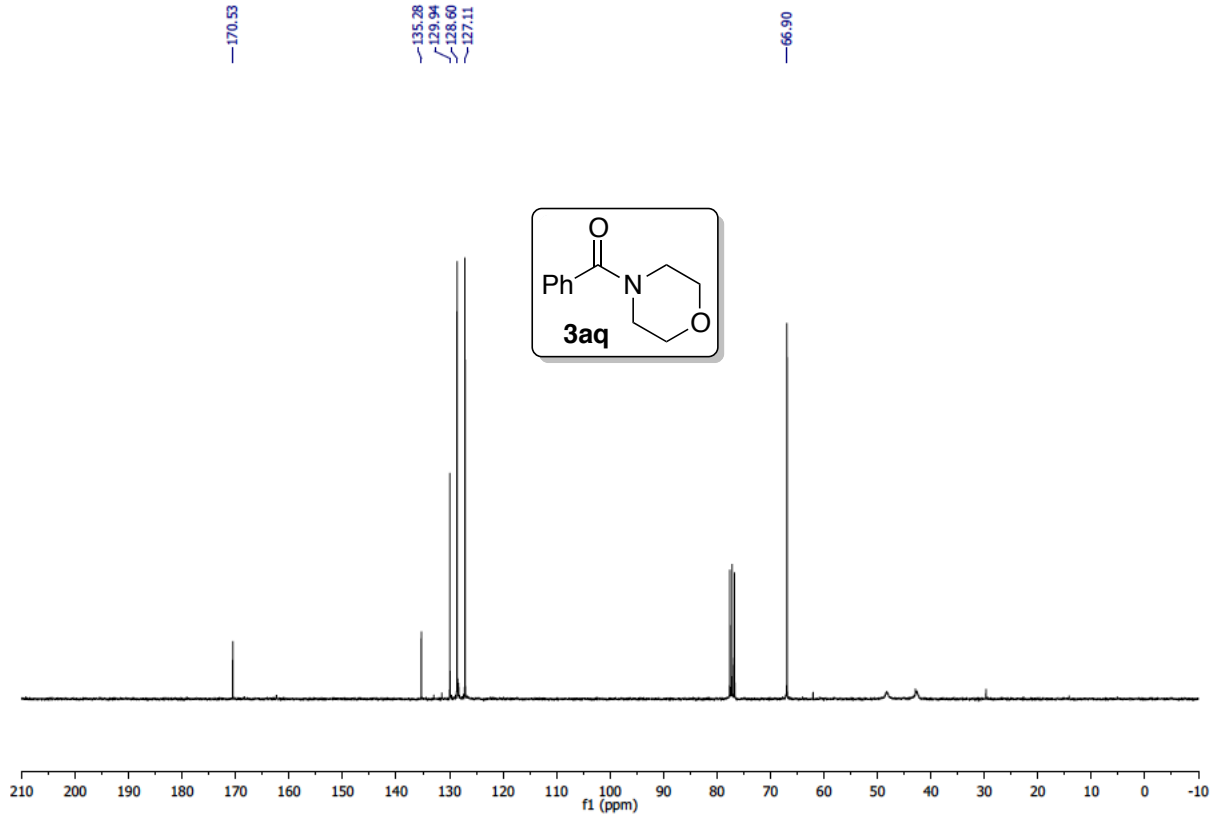

$^{13}$C NMR (75 MHz, $CDCl_3$) of *N*-benzoylpiperidine **3ap**



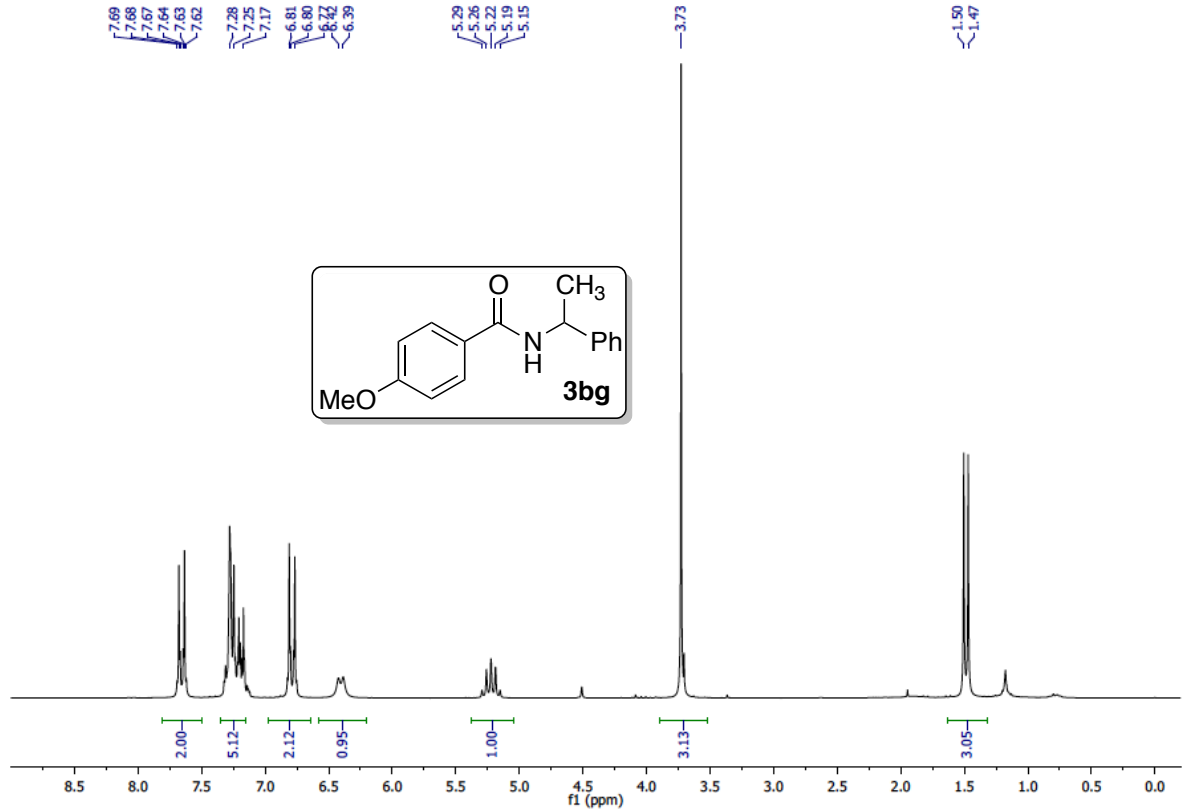
$^{1}$H NMR (200 MHz, $CDCl_3$) of *N*-benzoylmorpholine **3aq**



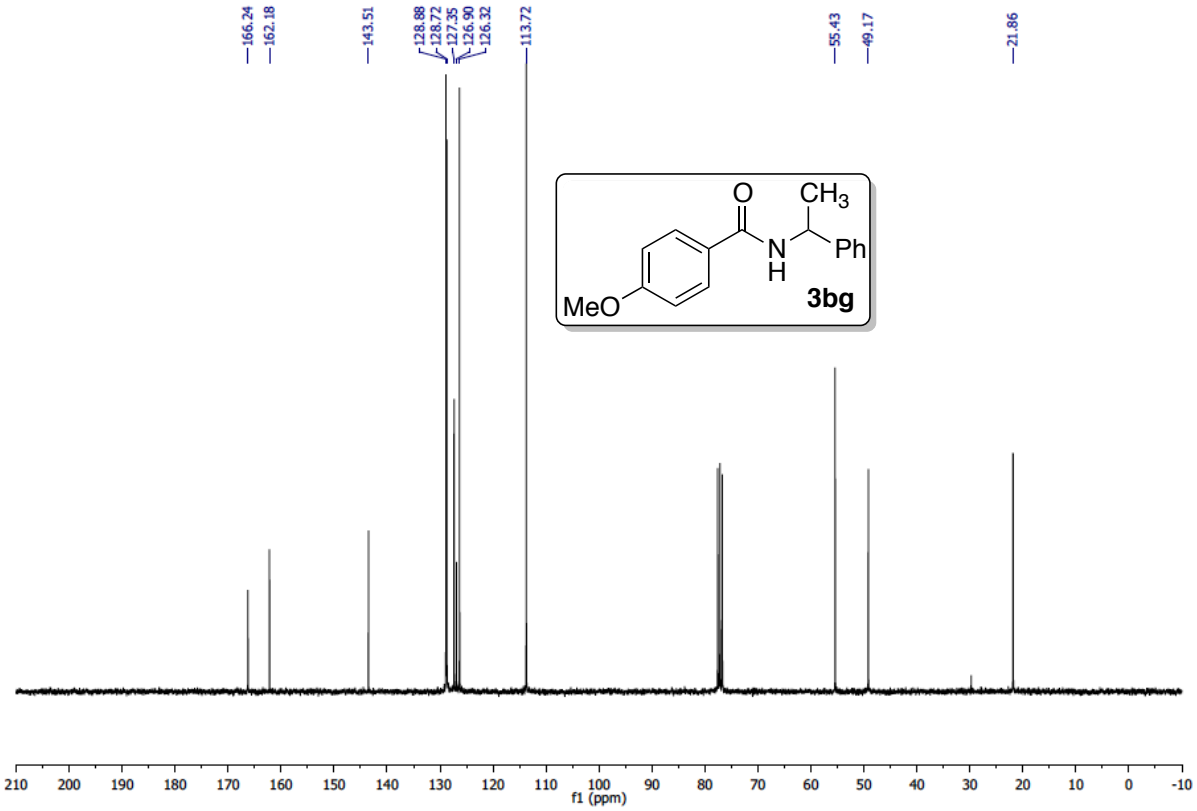

$^{13}$C NMR (75 MHz, $CDCl_3$) of *N*-benzoylmorpholine **3aq**



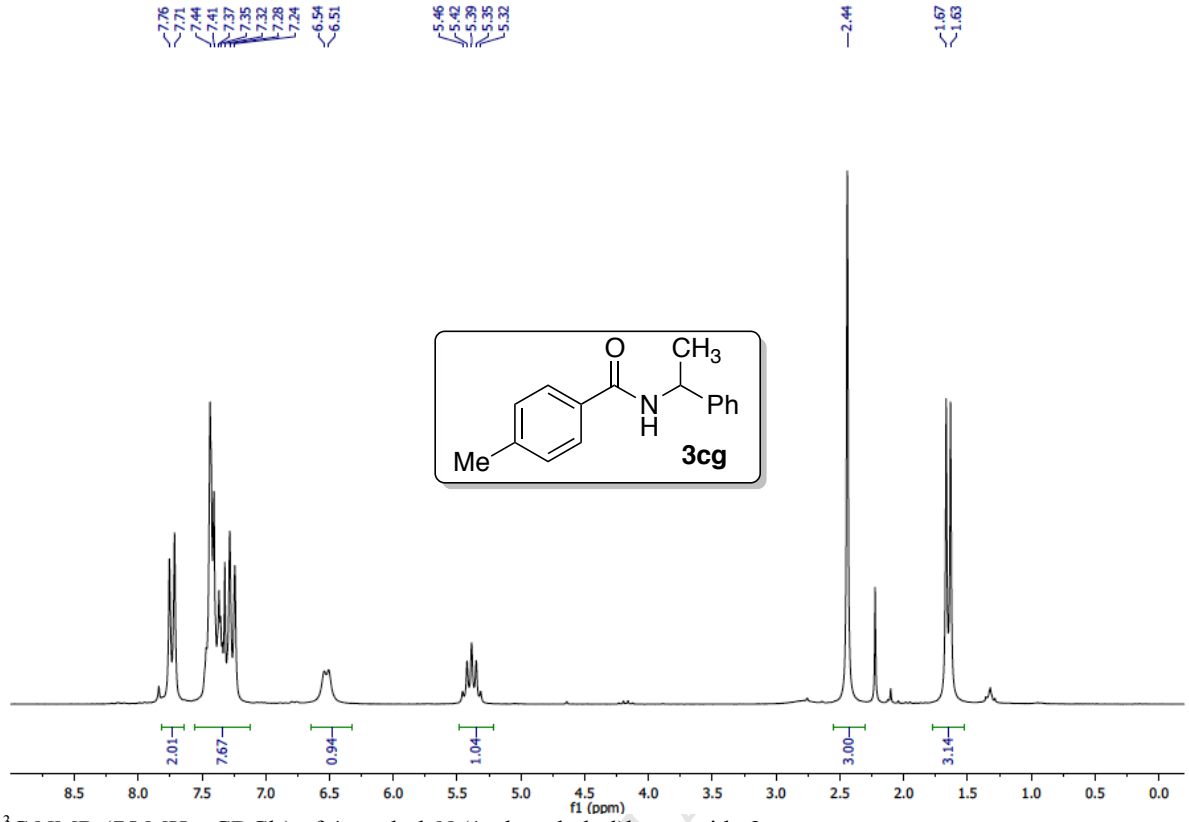
$^{1}$H NMR (200 MHz, $CDCl_3$) of 4-methoxy-*N*-(1-phenylethyl)benzamide **3bg**



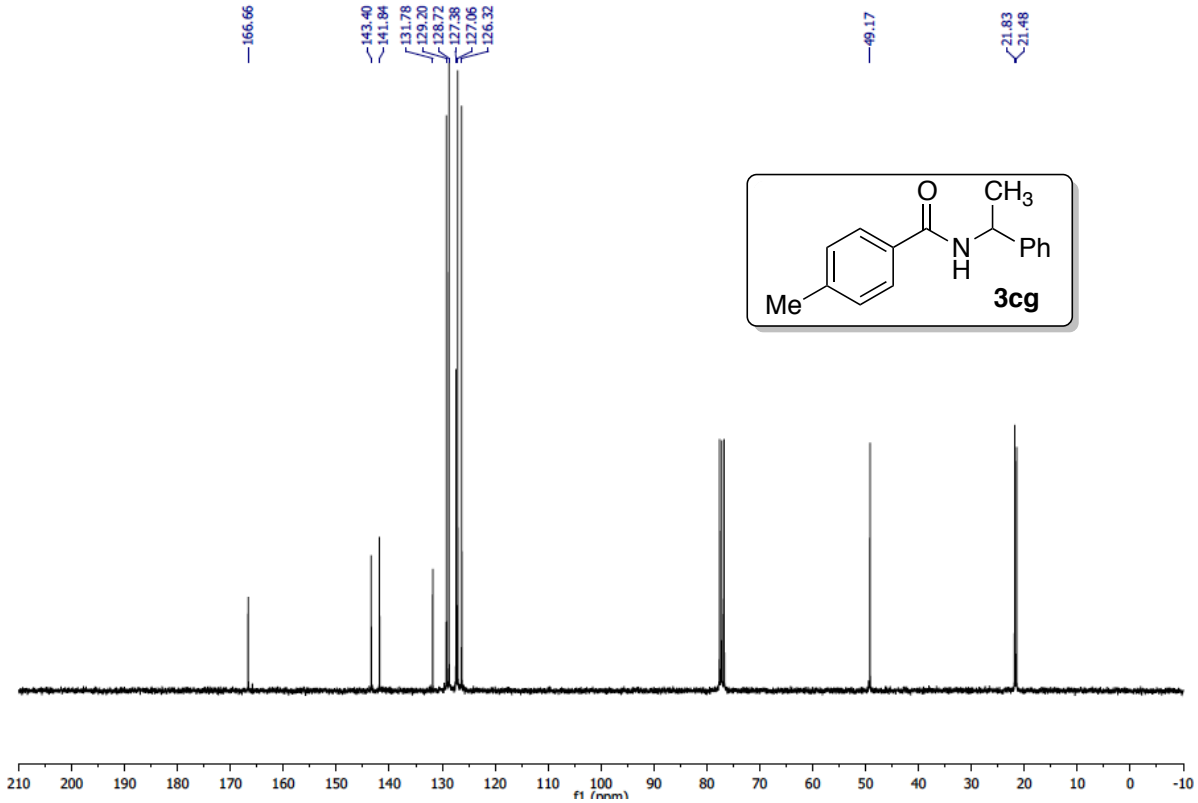

$^{13}$C NMR (75 MHz, $CDCl_3$) of 4-methoxy-*N*-(1-phenylethyl)benzamide **3bg**



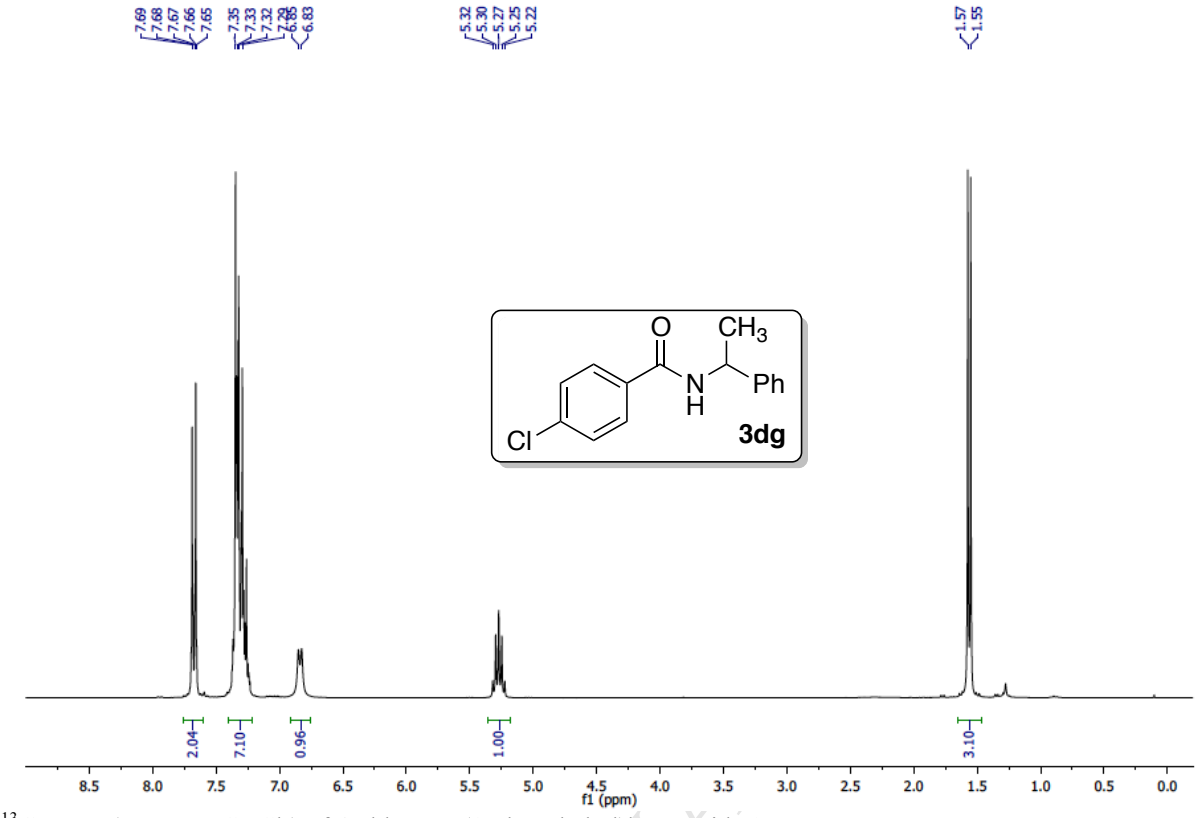
$^{1}$H NMR (200 MHz, $CDCl_3$) of 4-methyl-*N*-(1-phenylethyl)benzamide **3cg**



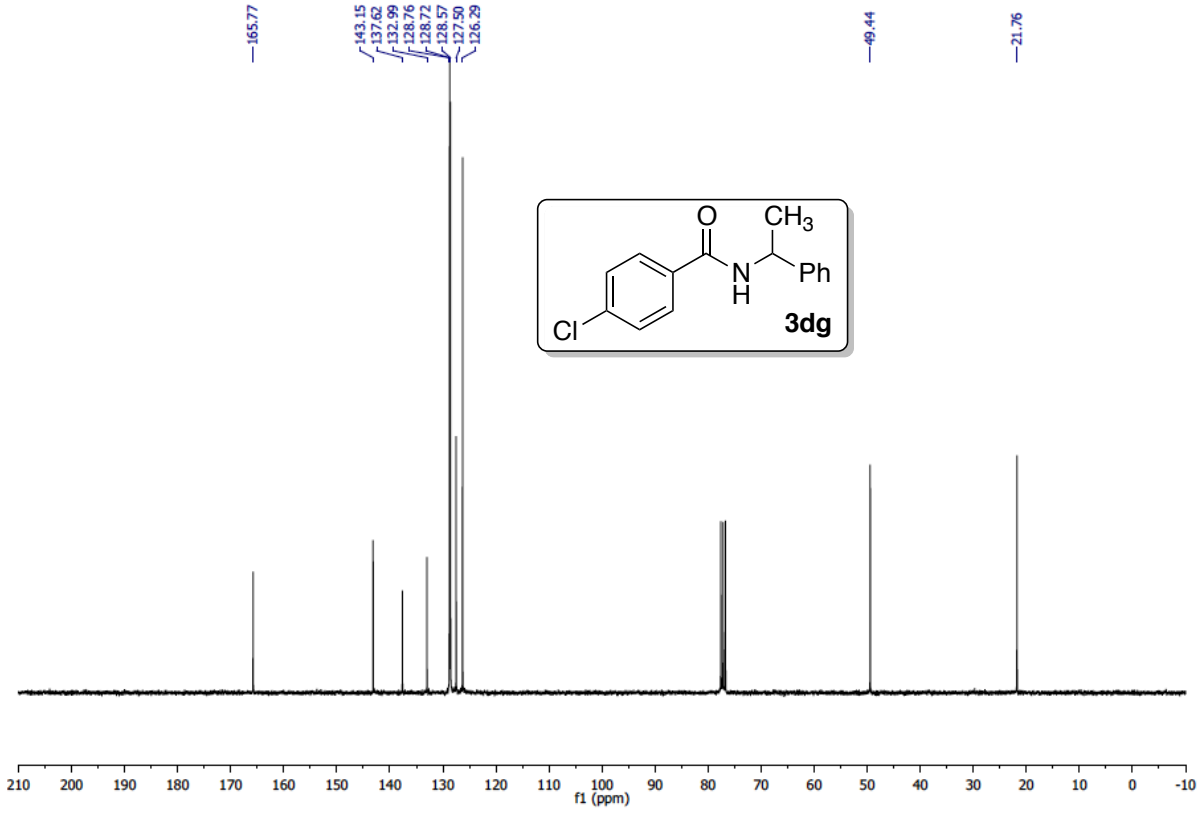

$^{13}$C NMR (75 MHz, $CDCl_3$) of 4-methyl-*N*-(1-phenylethyl)benzamide **3cg**



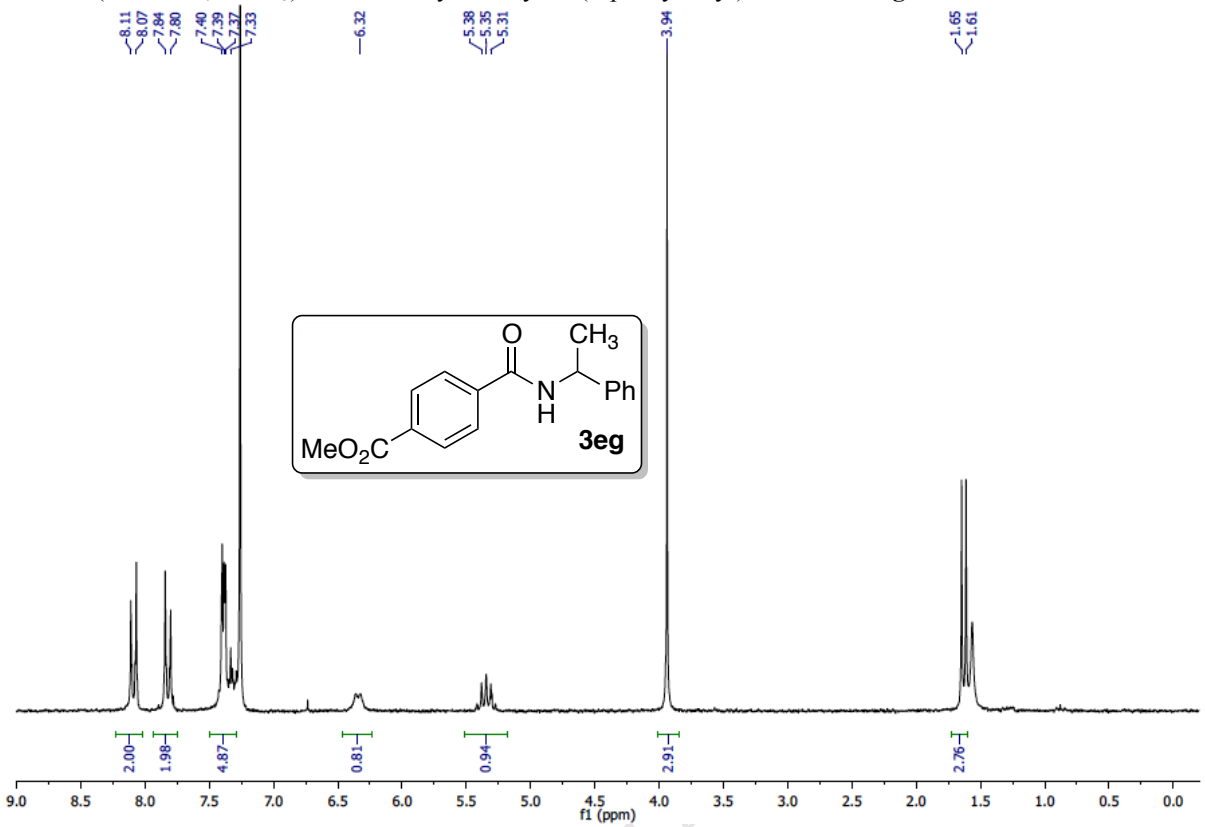
$^{1}$H NMR (200 MHz, $CDCl_3$) of 4-chloro-*N*-(1-phenylethyl)benzamide **3dg**




$^{13}$C NMR (75 MHz, $CDCl_3$) of 4-chloro-*N*-(1-phenylethyl)benzamide **3dg**



$^{1}$H NMR (200 MHz, $CDCl_3$) of 4-methoxycarbonyl-*N*-(1-phenylethyl)benzamide **3eg**

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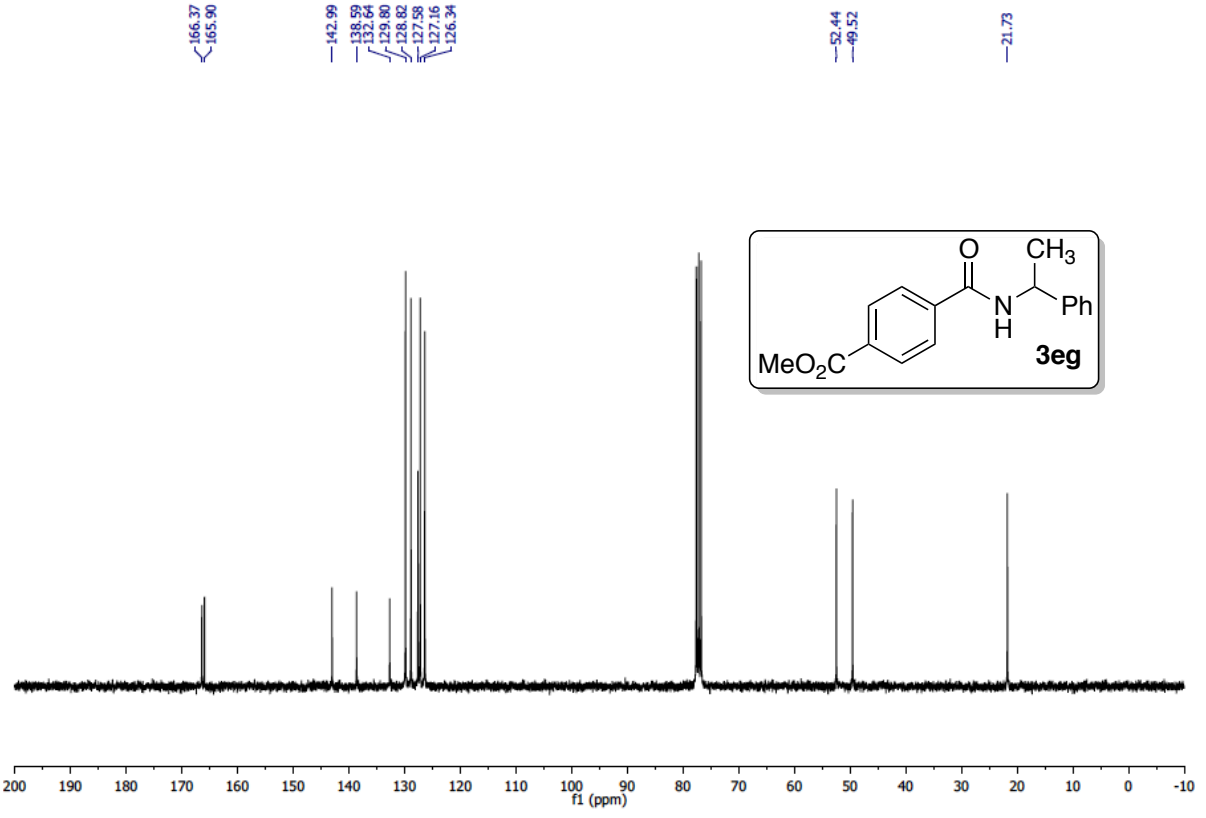
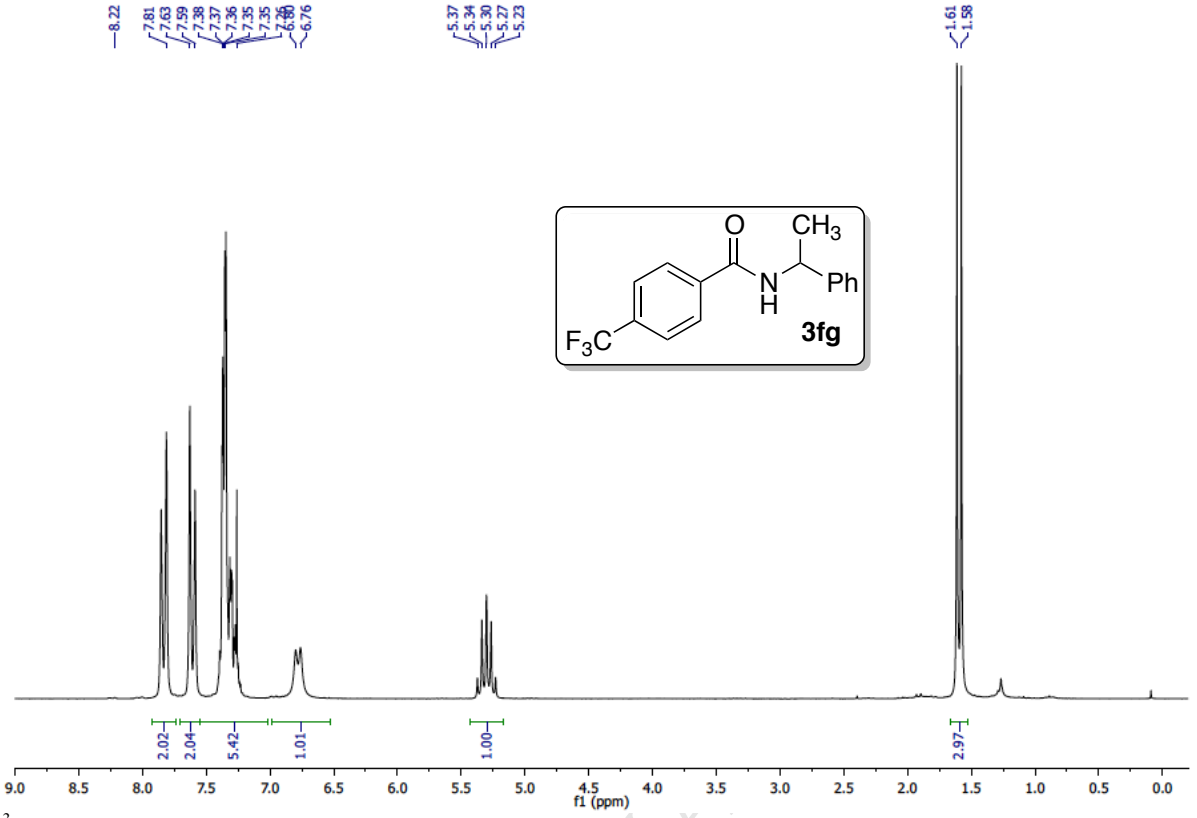
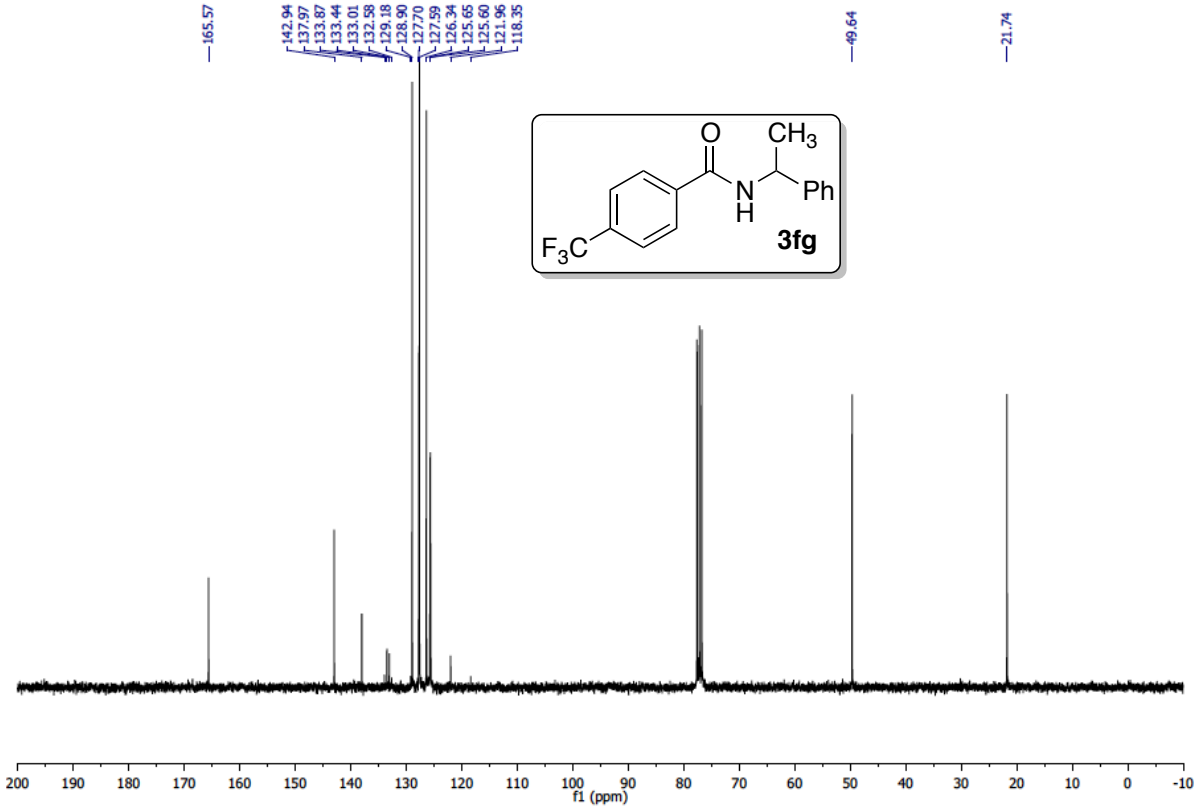


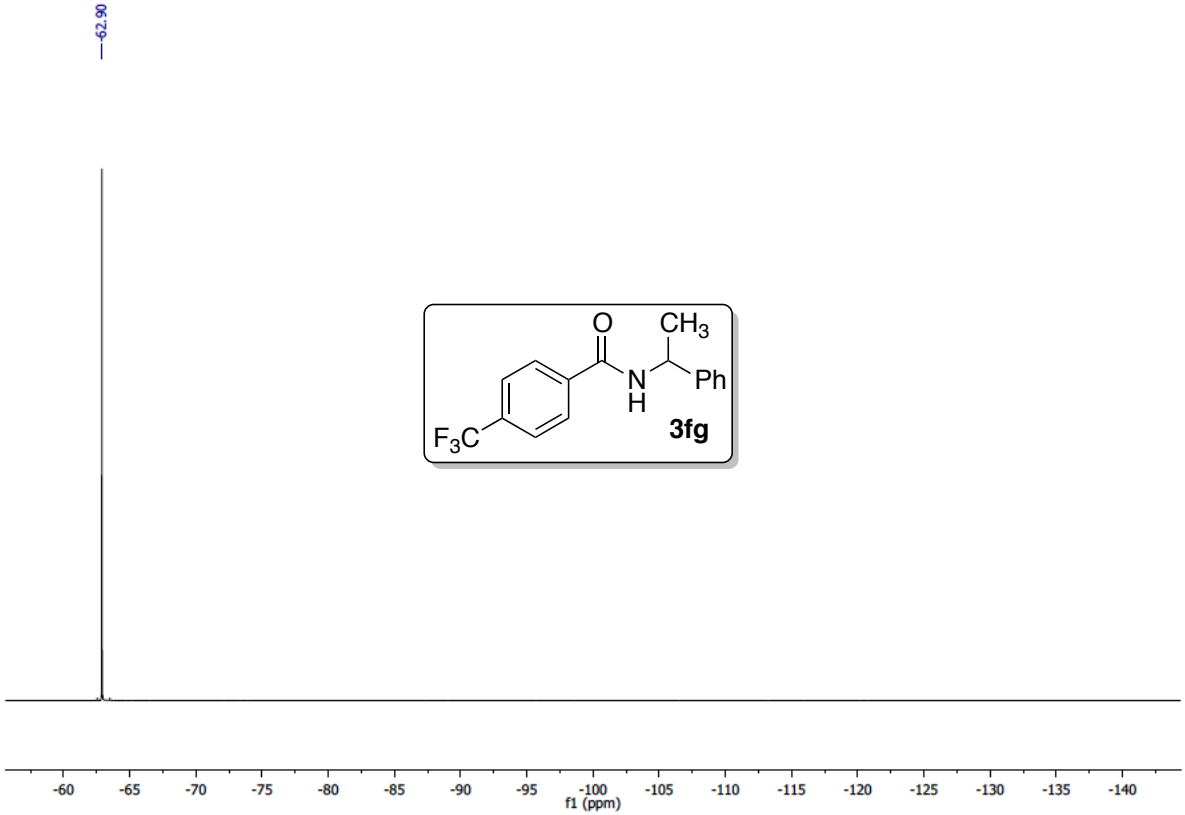
$^{1}$H NMR (200 MHz, $CDCl_3$) of 4-trifluoro-*N*-(1-phenylethyl)benzamide **3fg**



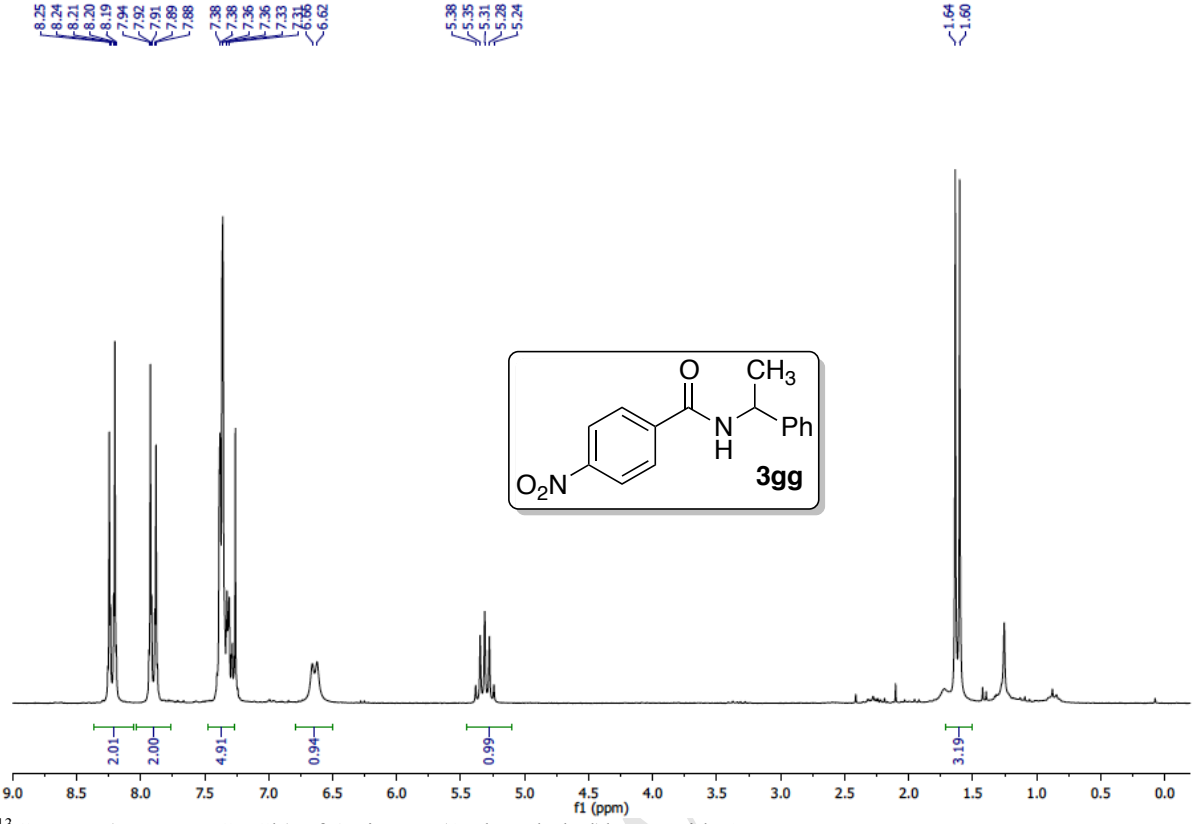

$^{13}$C NMR (75 MHz, $CDCl_3$) of 4-trifluoro-*N*-(1-phenylethyl)benzamide **3fg**



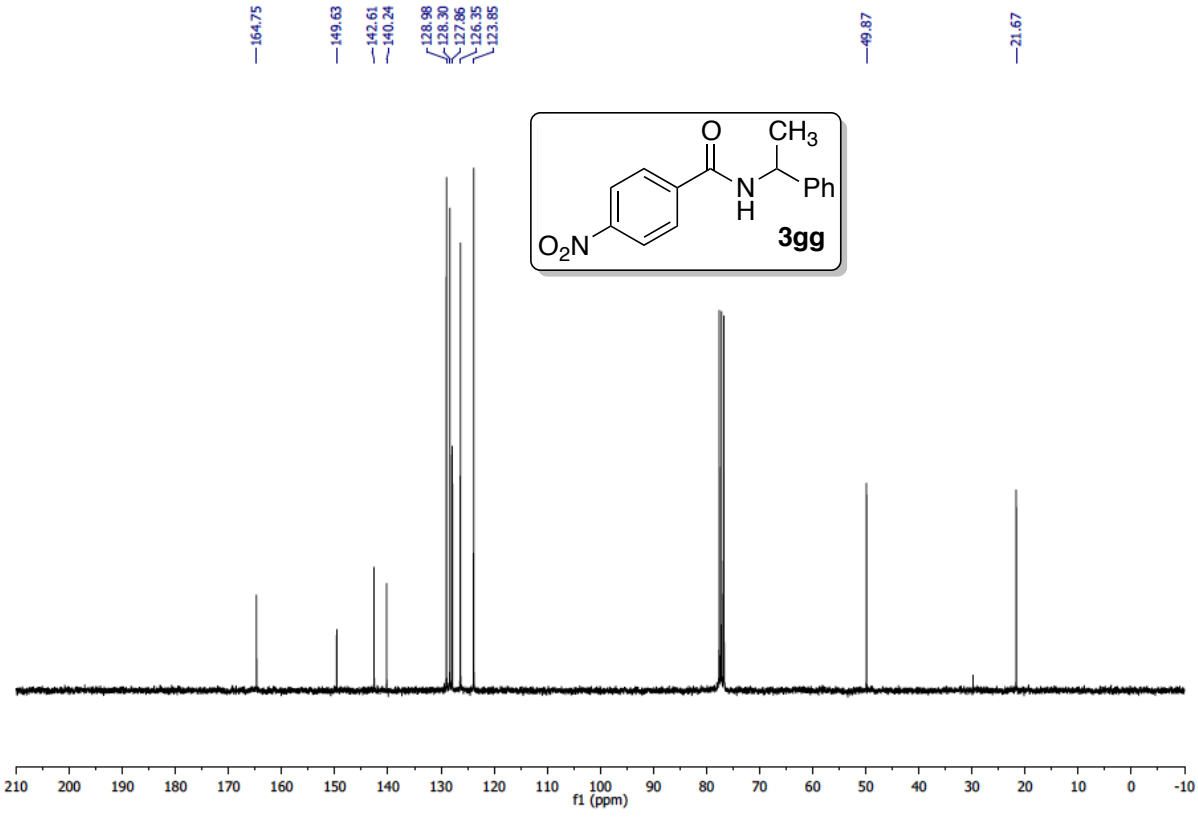
$^{19}$F NMR (282 MHz, $CDCl_3$) of 4-trifluoro-*N*-(1-phenylethyl)benzamide **3fg**



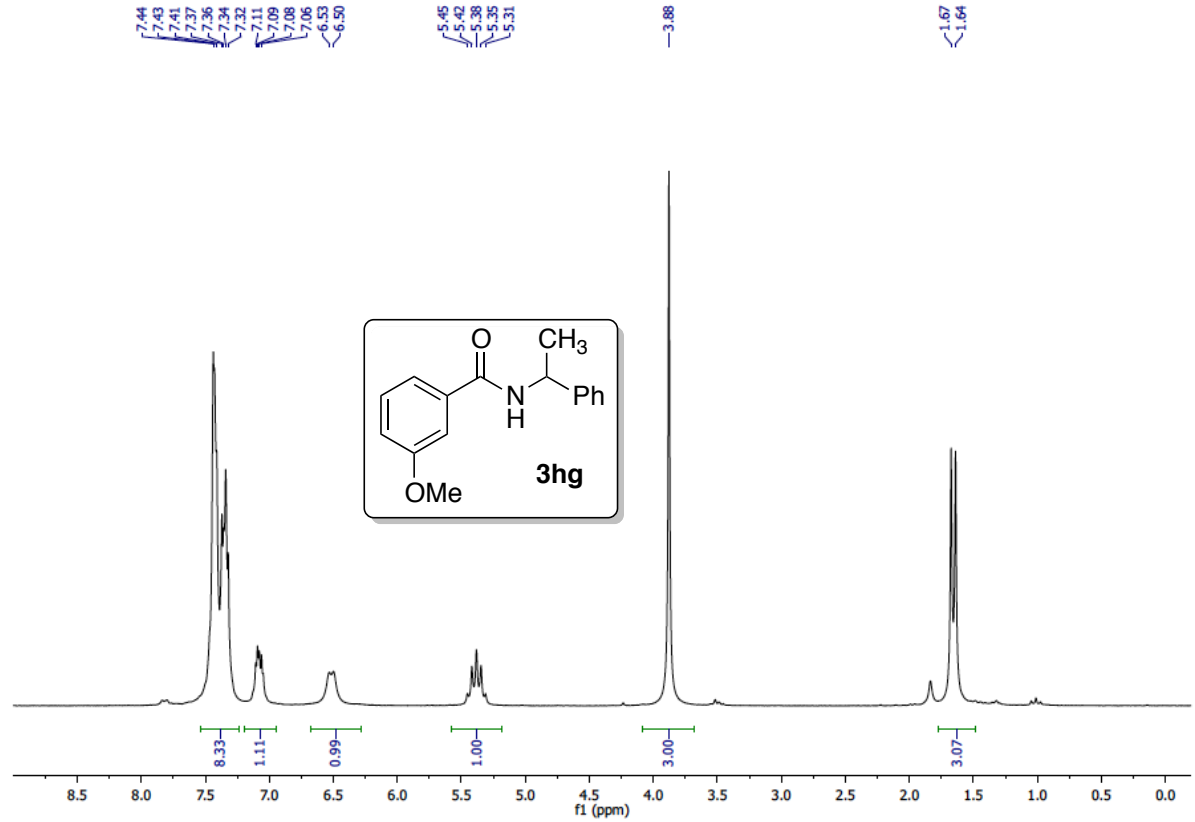
$^{1}$H NMR (200 MHz, $CDCl_3$) of 4-nitro-*N*-(1-phenylethyl)benzamide **3gg**



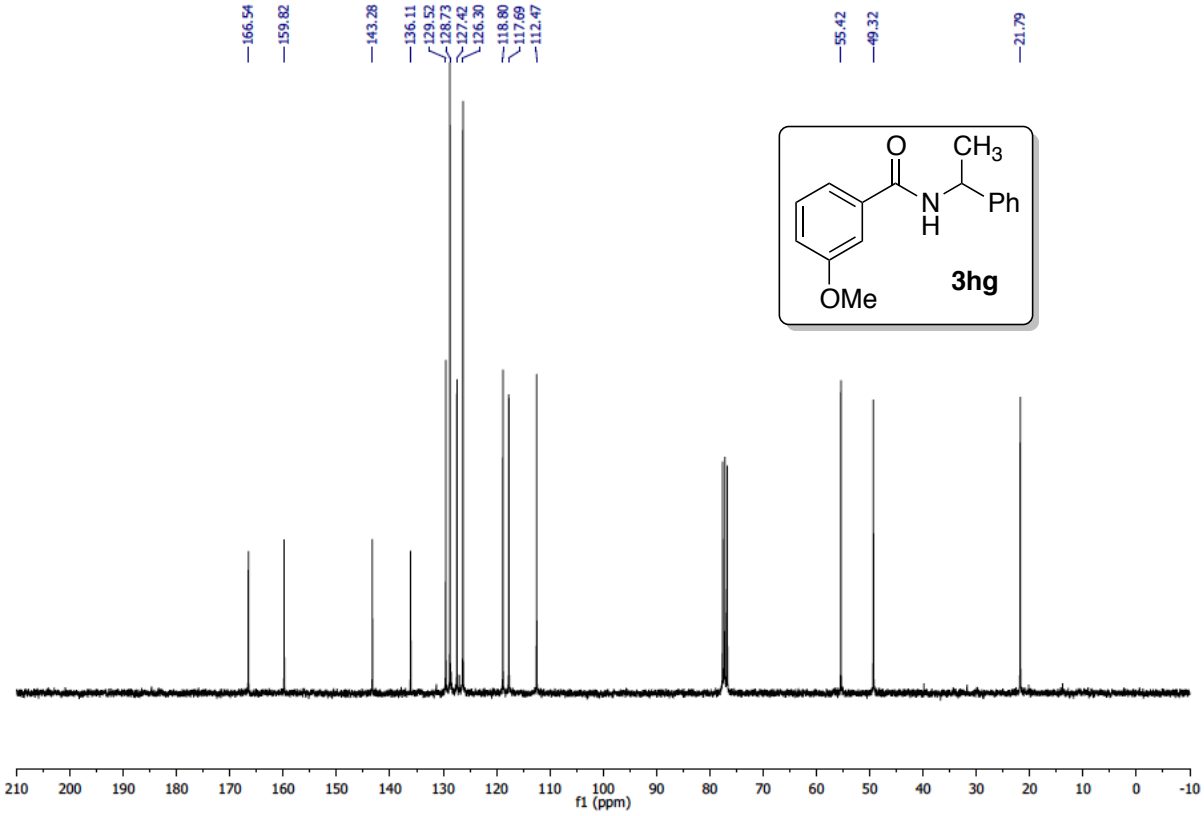

$^{13}$C NMR (75 MHz, $CDCl_3$) of 4-nitro-*N*-(1-phenylethyl)benzamide **3gg**



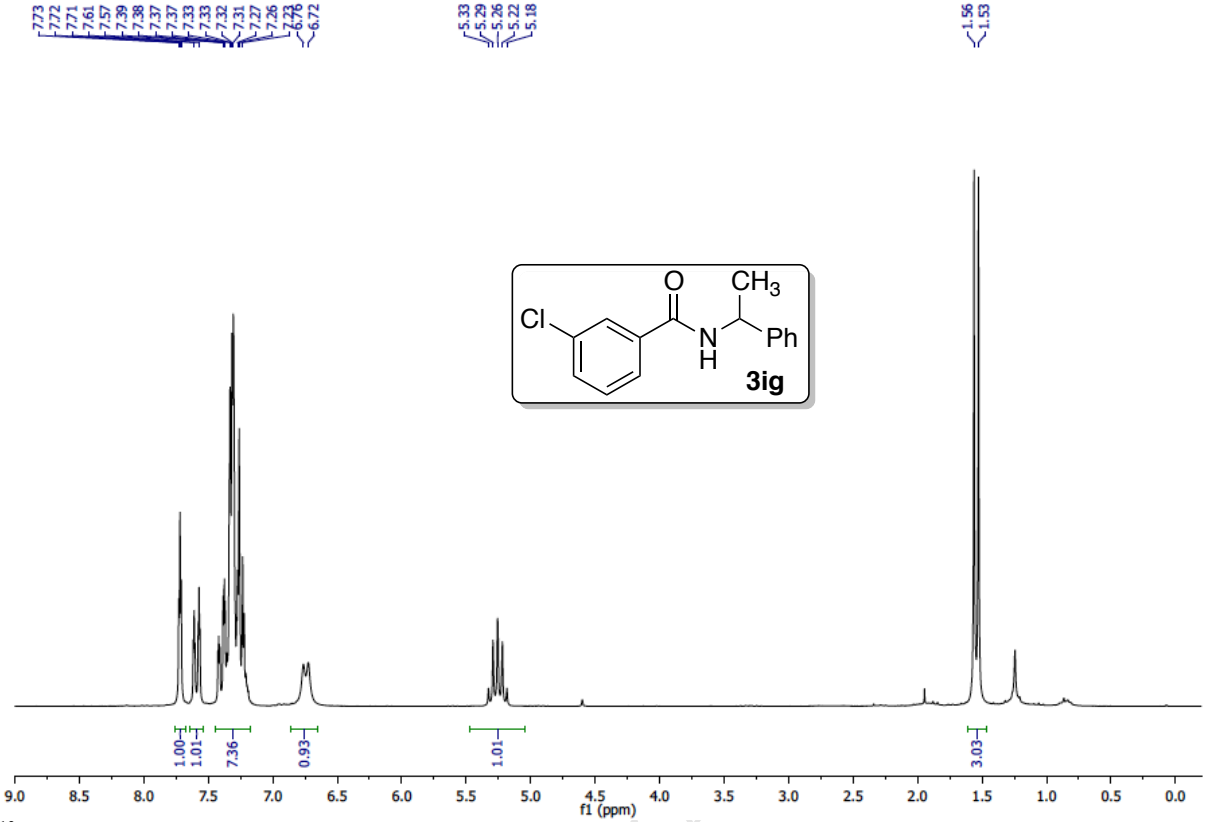
$^{1}$H NMR (200 MHz, $CDCl_3$) of 3-methoxy-*N*-(1-phenylethyl)benzamide **3hg**



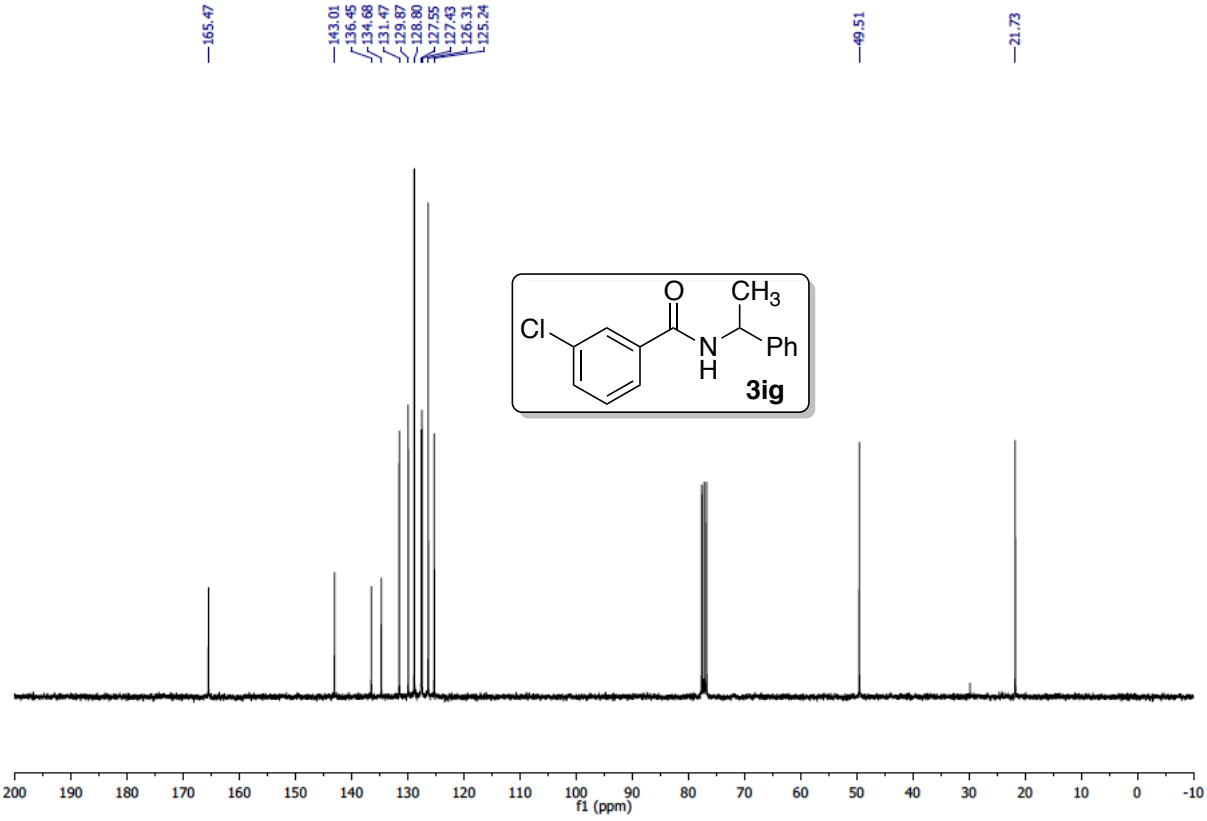

$^{13}$C NMR (75 MHz, $CDCl_3$) of 3-methoxy-*N*-(1-phenylethyl)benzamide **3hg**



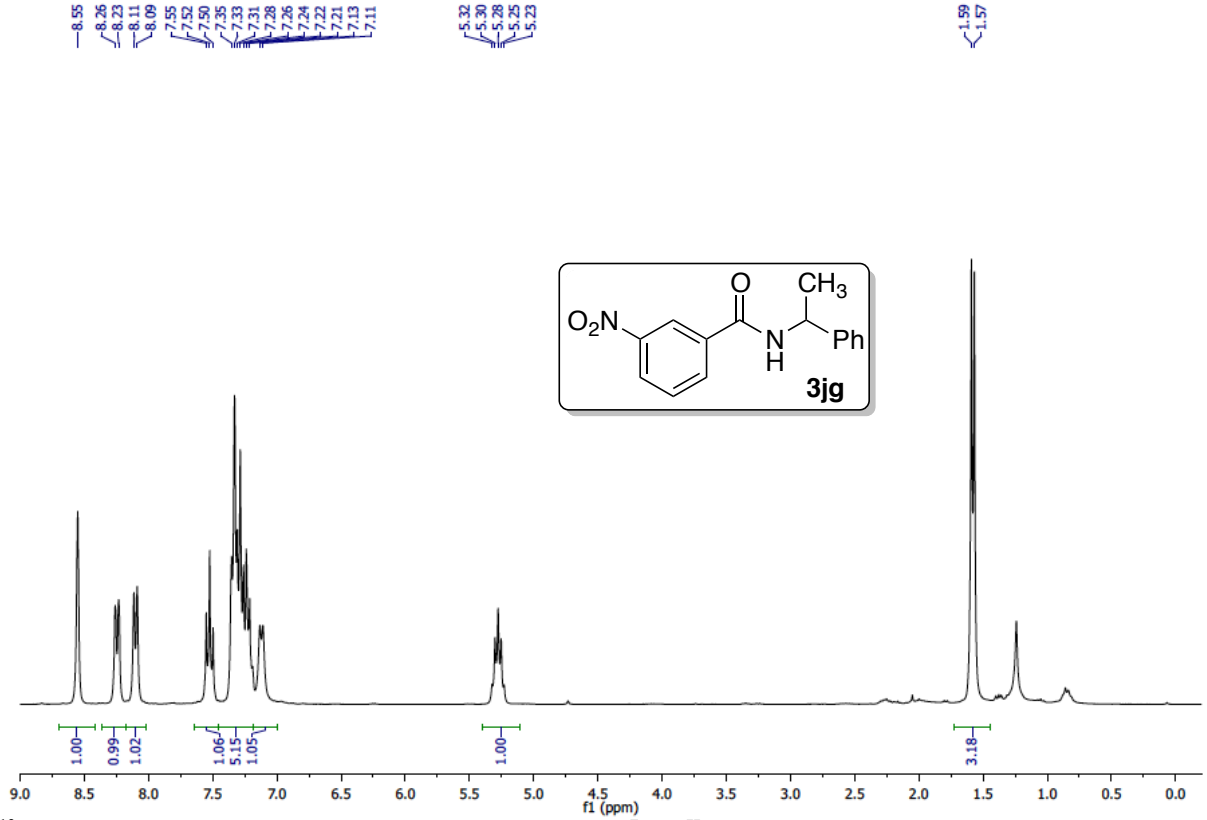
$^{1}$H NMR (200 MHz, $CDCl_3$) of 3-chloro-*N*-(1-phenylethyl)benzamide **3ig**



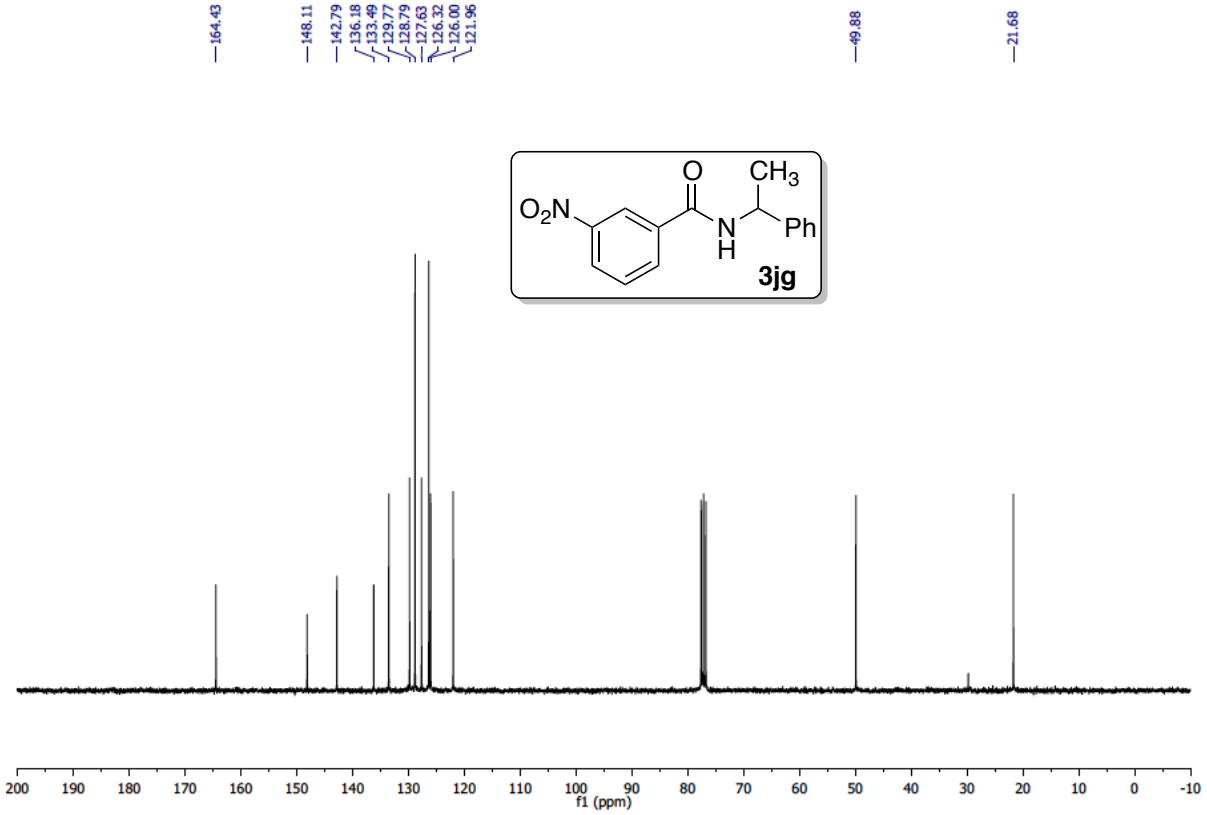

$^{13}$C NMR (75 MHz, $CDCl_3$) of 3-chloro-*N*-(1-phenylethyl)benzamide **3ig**



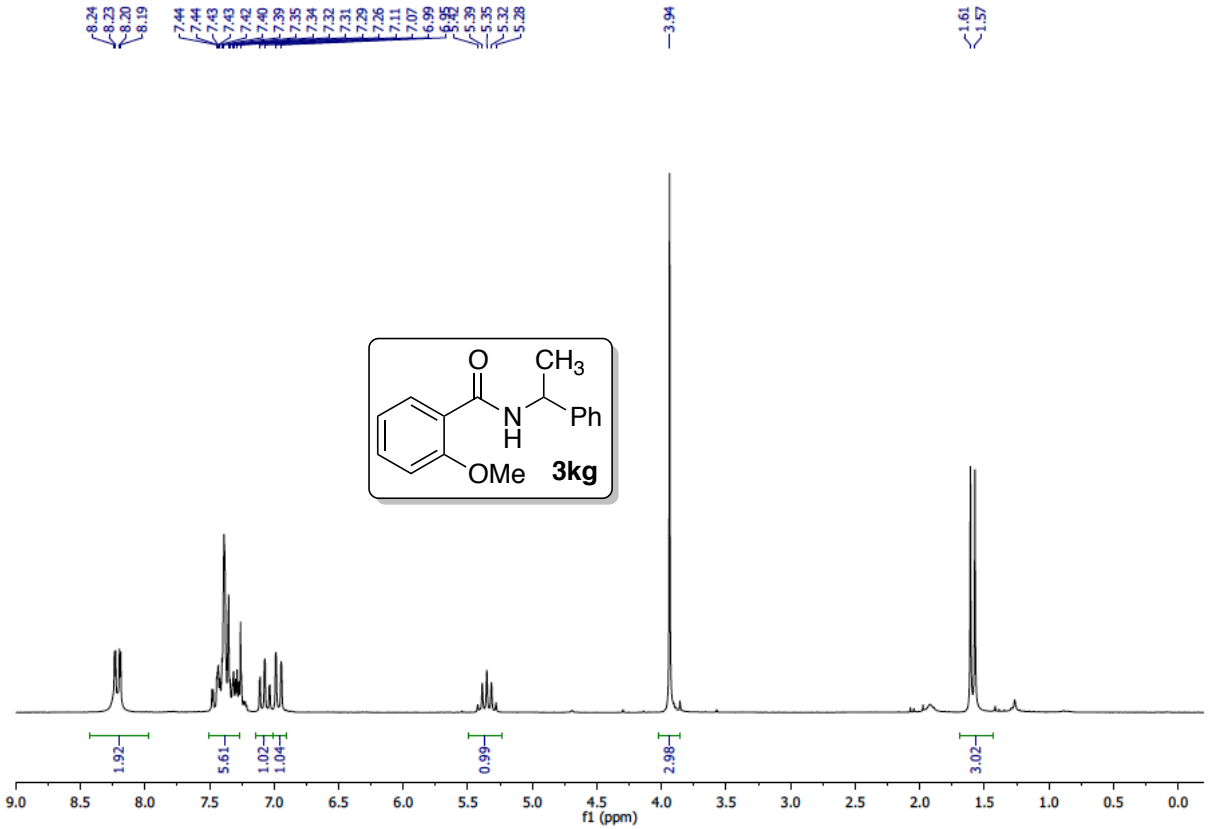
$^{1}$H NMR (200 MHz, $CDCl_3$) of 3-nitro-*N*-(1-phenylethyl)benzamide **3jg**



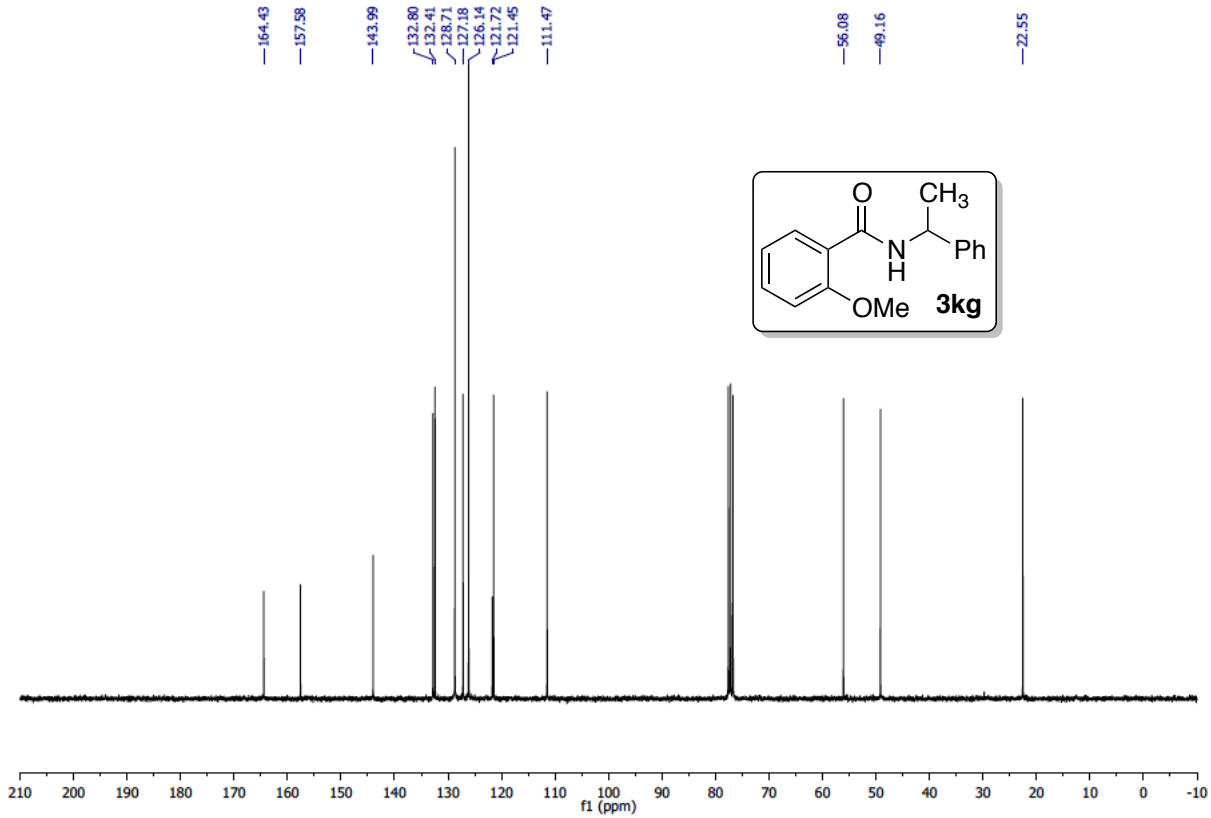

$^{13}$C NMR (75 MHz, $CDCl_3$) of 3-nitro-*N*-(1-phenylethyl)benzamide **3jg**



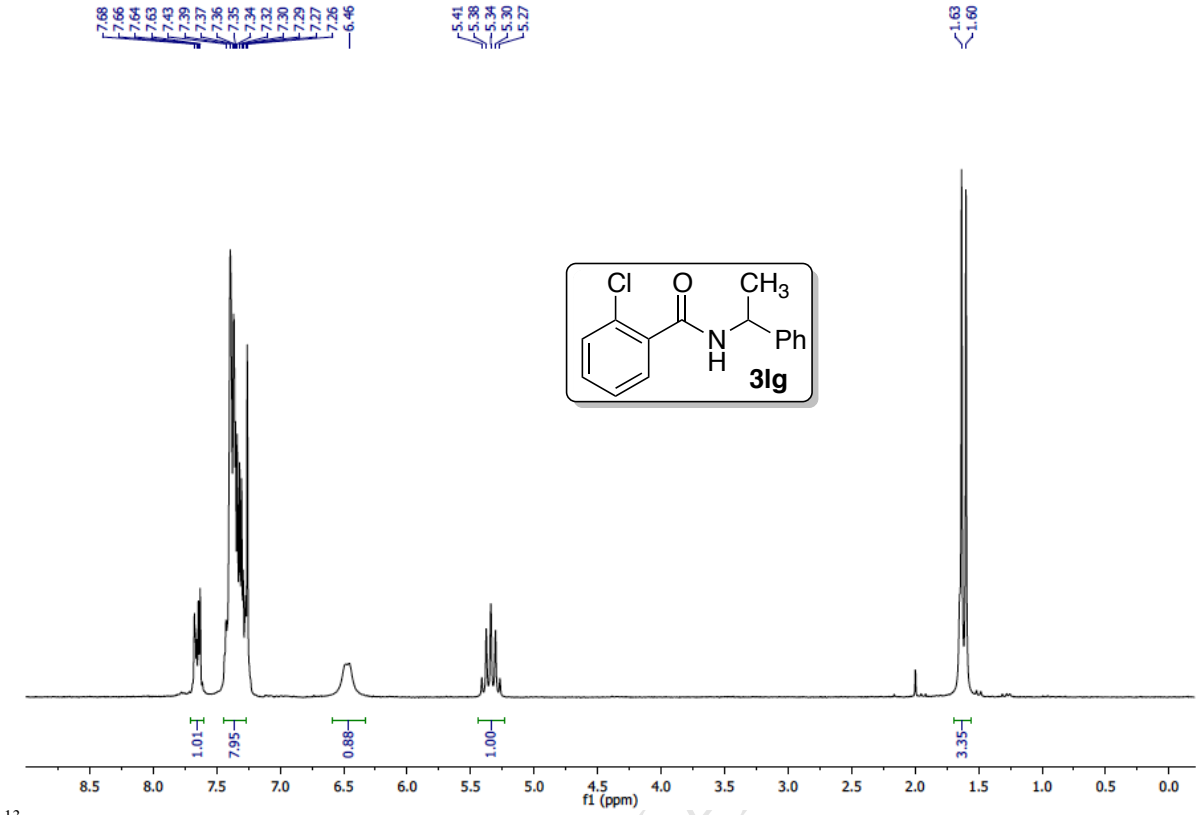
$^{1}$H NMR (200 MHz, $CDCl_3$) of 2-methoxy-*N*-(1-phenylethyl)benzamide **3kg**



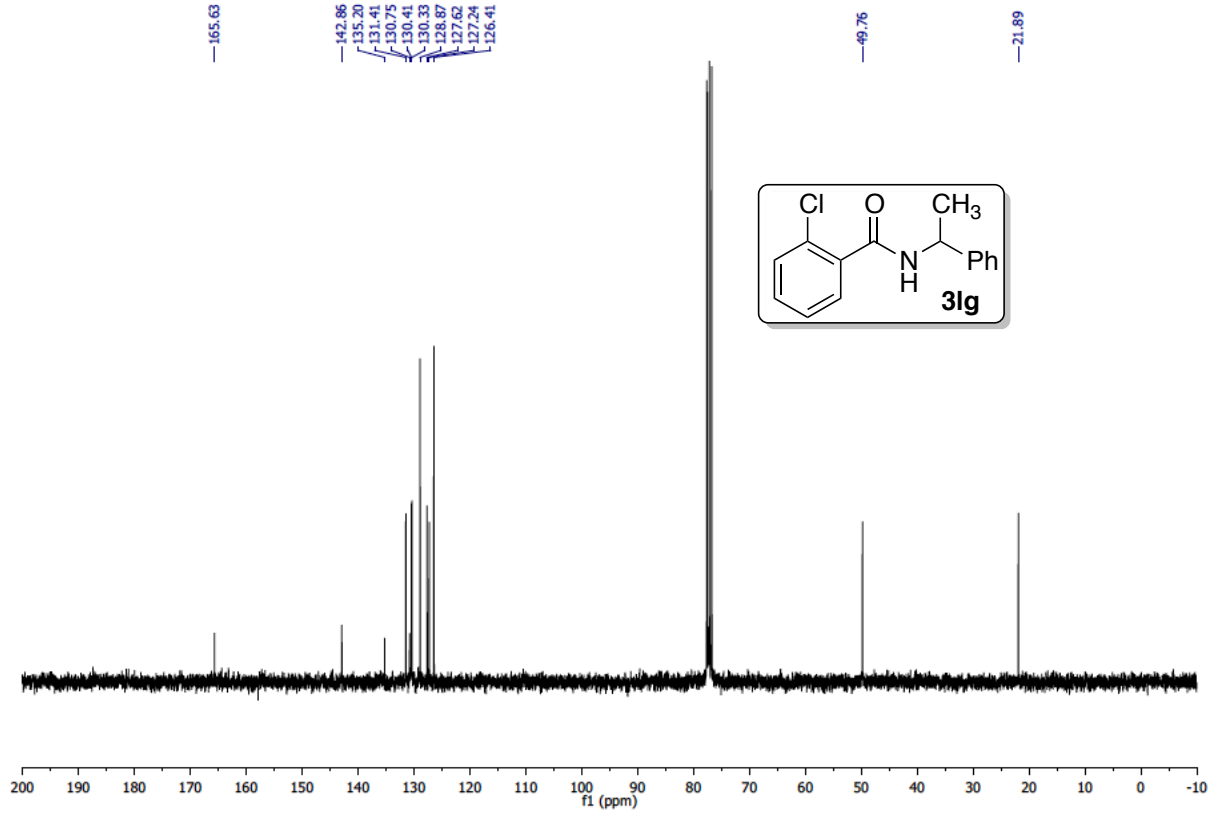

$^{13}$C NMR (75 MHz, $CDCl_3$) of 2-methoxy-*N*-(1-phenylethyl)benzamide **3kg**



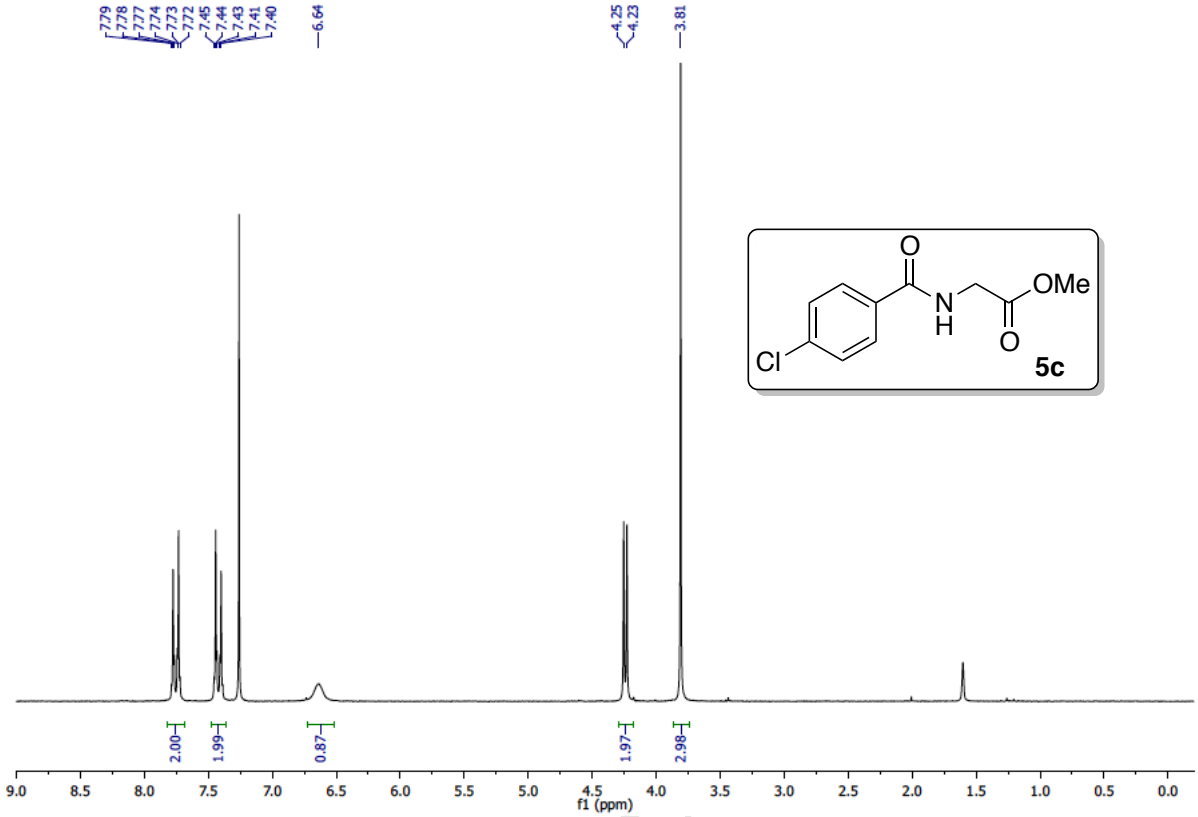
$^{1}$H NMR (200 MHz, $CDCl_3$) of 2-chloro-*N*-(1-phenylethyl)benzamide **3lg**



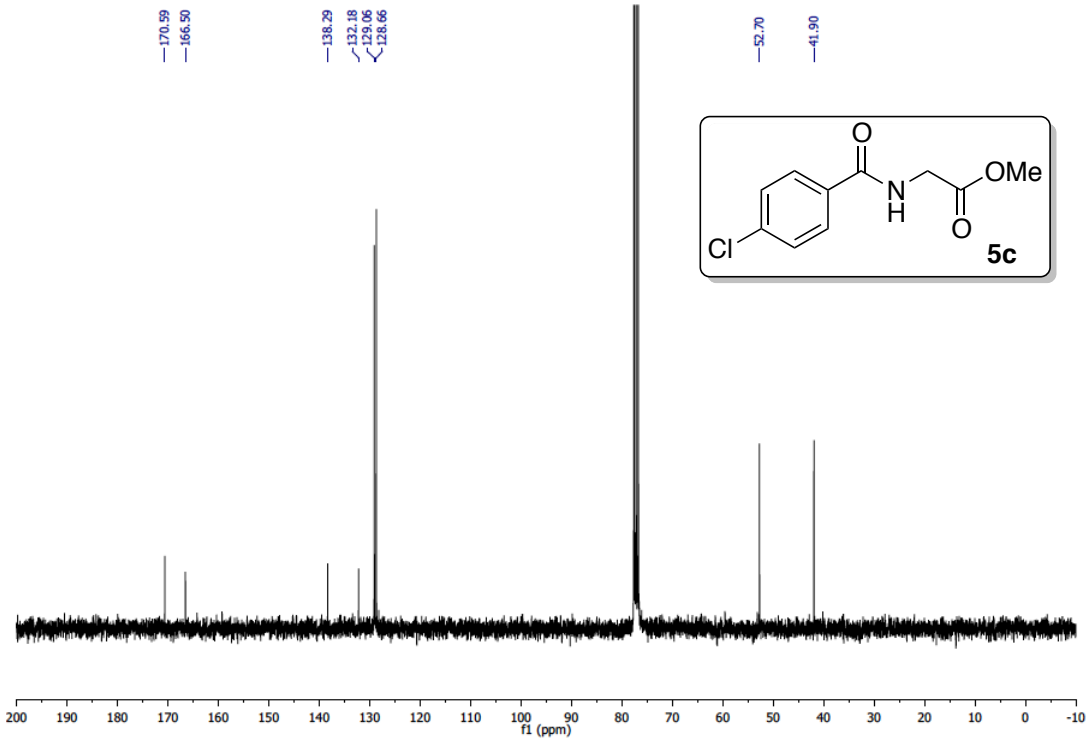

$^{13}$C NMR (75 MHz, $CDCl_3$) of 2-chloro-*N*-(1-phenylethyl)benzamide **3lg**



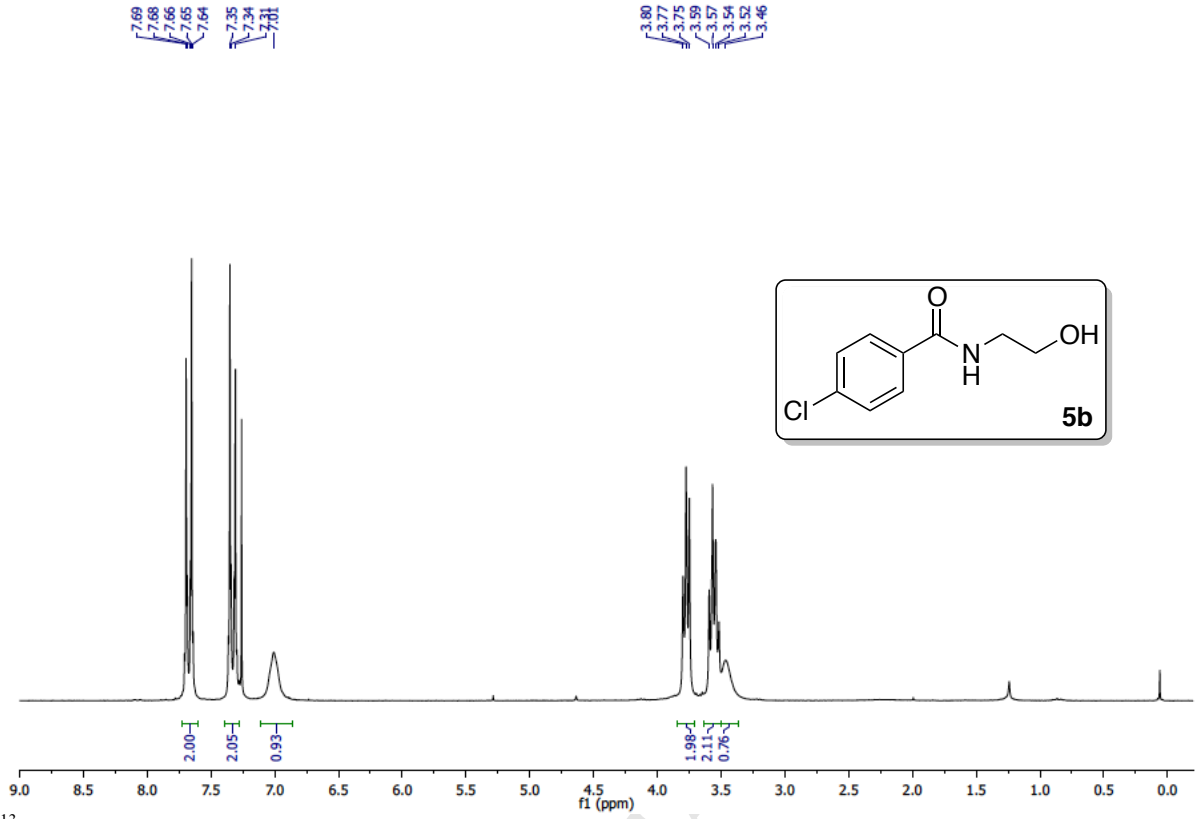
$^{1}$H NMR (200 MHz, $CDCl_3$) of *N*-(*p*-chlorobenzoyl)glycine methyl ester **5c**



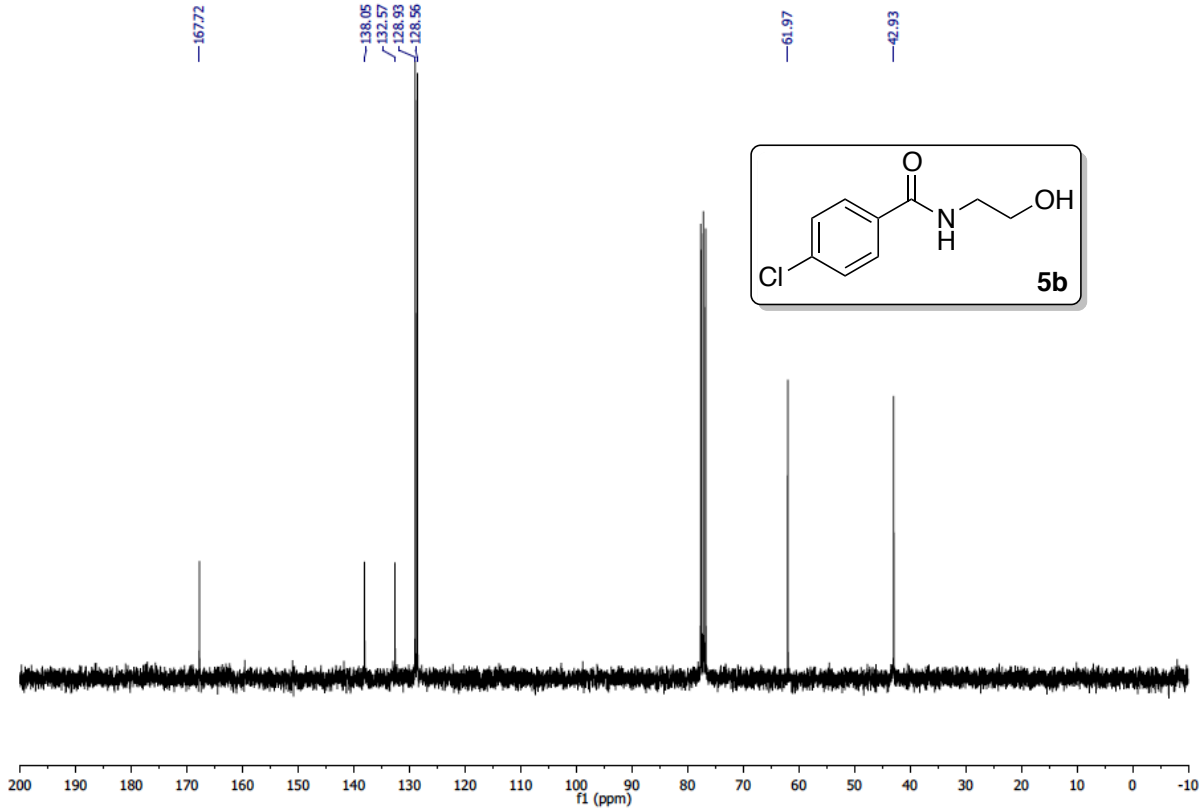

$^{13}$C NMR (75 MHz, $CDCl_3$) of *N*-(*p*-chlorobenzoyl)glycine methyl ester **5c**



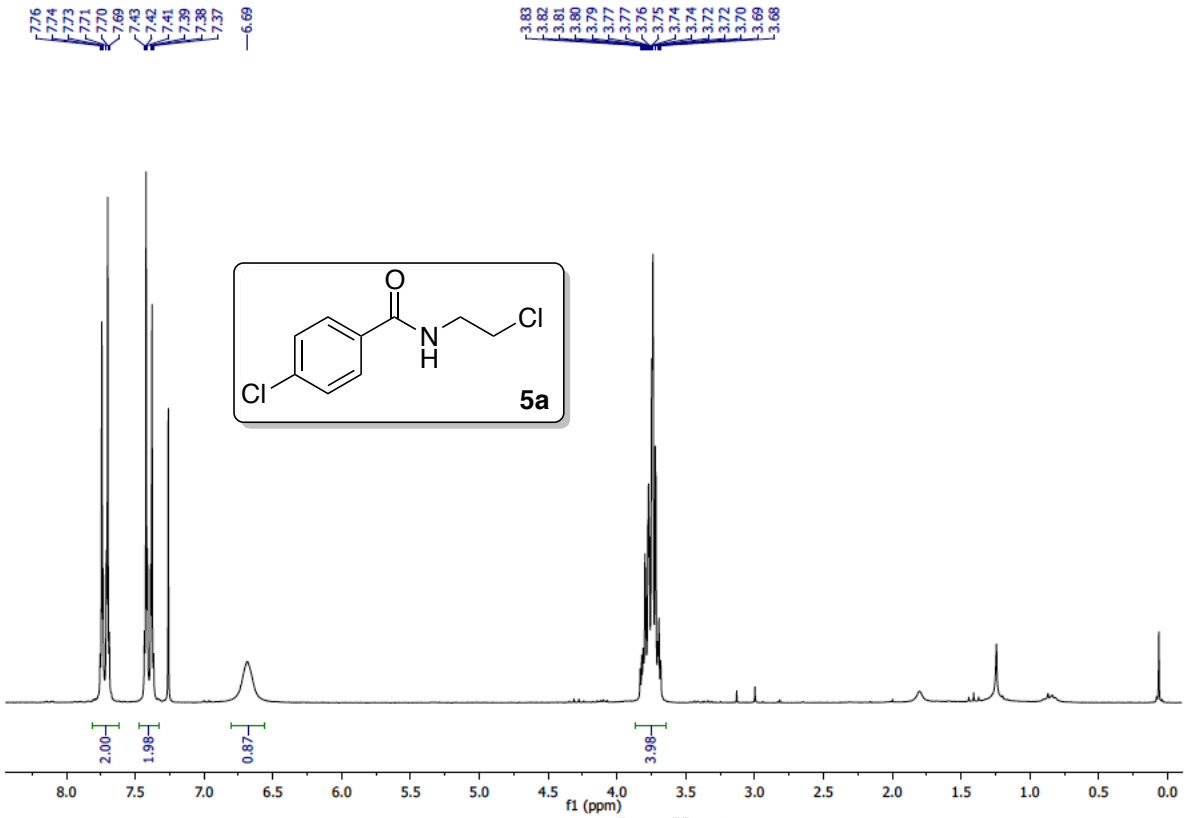
$^{1}$H NMR (200 MHz, $CDCl_3$) of *N*-(*p*-chlorobenzoyl)glycinol **5b**



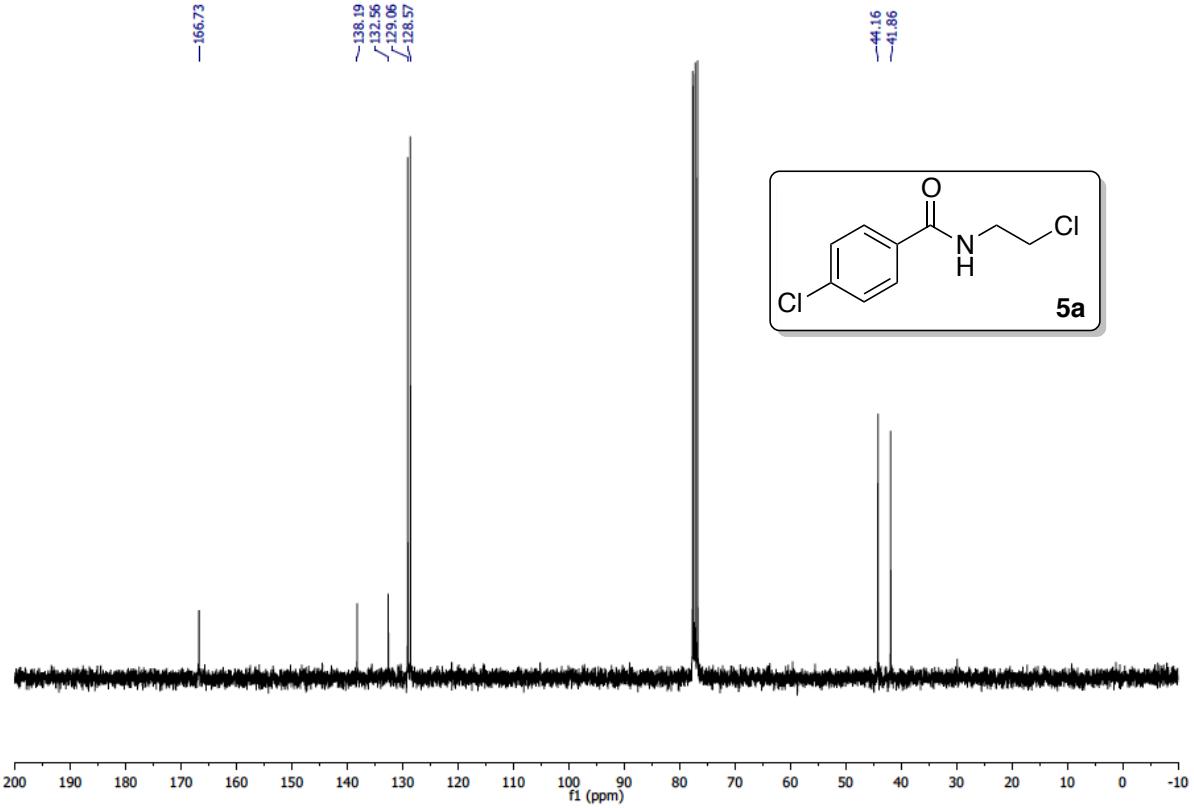

$^{13}$C NMR (75 MHz, $CDCl_3$) of *N*-(*p*-chlorobenzoyl)glycinol **5b**



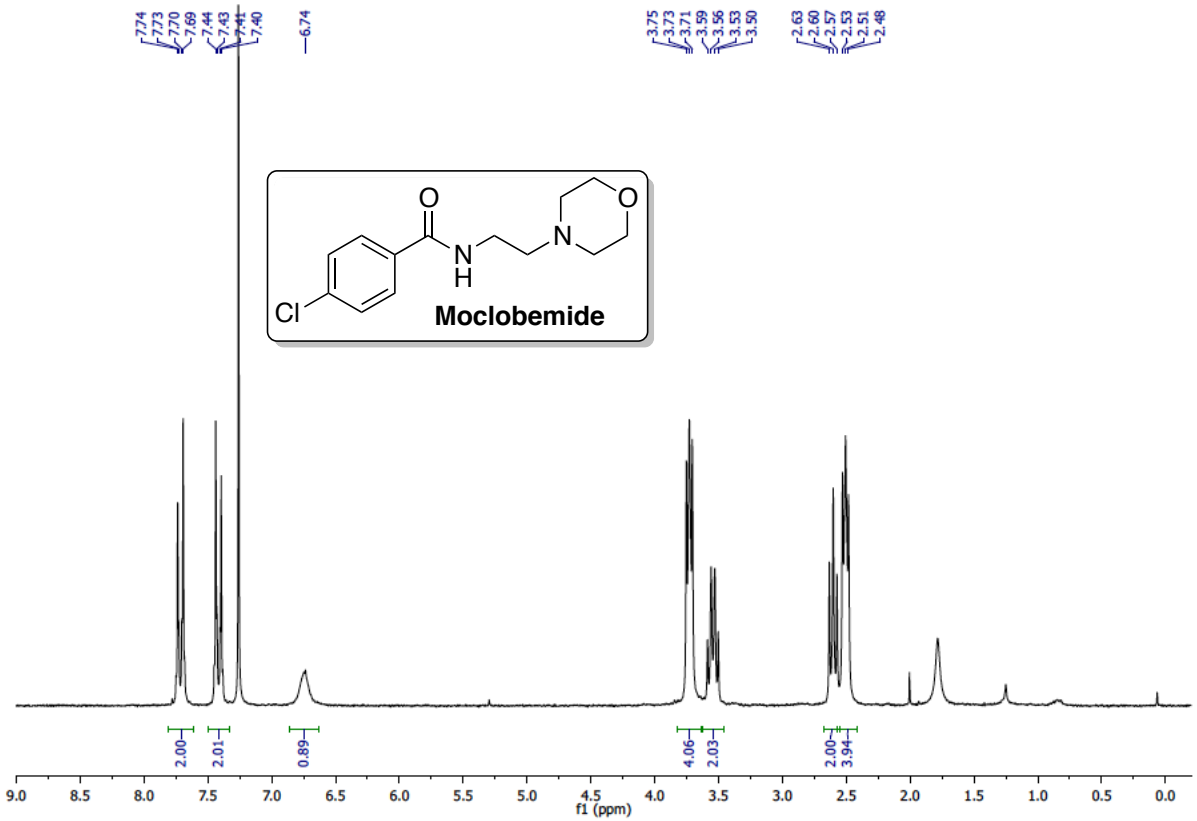
$^{1}$H NMR (200 MHz, $CDCl_3$) of *p*-chloro-*N*-(2-chloroethyl)-benzamide **5a**




$^{13}$C NMR (75 MHz, $CDCl_3$) of *p*-chloro-*N*-(2-chloroethyl)-benzamide **5a**



$^{1}$H NMR (200 MHz, $CDCl_3$) of *p*-chloro-*N*-(2-morpholinoethyl)-benzamide




$^{13}$C NMR (75 MHz, $CDCl_3$) of *p*-chloro-*N*-(2-morpholinoethyl)-benzamide