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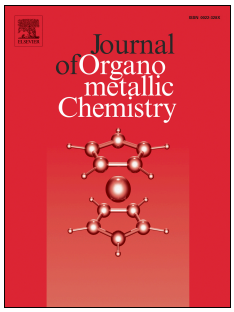

Mild Gold-Catalyzed Aerobic Dehydrogenative Coupling of Amines and Phenylglyoxal Derivatives

Ying Shao , Zhuhong Wu , Chunbao Miao , Li Liu

PII: S0022-328X(14)00245-9

DOI: 10.1016/j.jorganchem.2014.05.017

Reference: JOM 18589

To appear in: *Journal of Organometallic Chemistry*

Received Date: 29 March 2014

Revised Date: 16 May 2014

Accepted Date: 17 May 2014

Please cite this article as: Y. Shao, Z. Wu, C. Miao, L. Liu, Mild Gold-Catalyzed Aerobic Dehydrogenative Coupling of Amines and Phenylglyoxal Derivatives, *Journal of Organometallic Chemistry* (2014), doi: 10.1016/j.jorganchem.2014.05.017.

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Ying Shao, Zhuhong Wu, Chunbao Miao, Li Liu*

A simple and efficient gold-catalyzed coupling of secondary amine with phenylglyoxal derivatives has been developed, which provides a practical synthetic strategy for the synthesis of substituted *α*-ketoamides under mild reaction conditions.

Highlights

A novel method for the synthesis of a-ketoamides is developed.
Arylglyoxal can react with secondary amines effectively by $AuBr_3$ catalyst in air.
The scope of the present reaction is extended.
A radical involved mechanism is proposed.

Graphical Abstract

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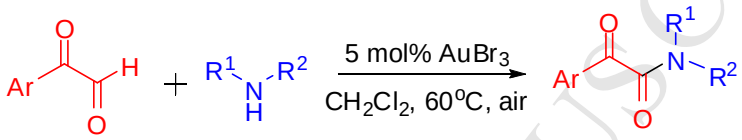
Ying Shao, Zhuhong Wu, Chunbao Miao, Li Liu [1]



53%-93% yield

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
α-ketoamide
gold-catalyzed
phenylglyoxal derivatives
secondary amine

ABSTRACT

A simple and efficient gold-catalyzed coupling of secondary amine with phenylglyoxal derivatives has been developed, which provides a practical synthetic strategy for the synthesis of substituted α-ketoamides under mild reaction conditions.

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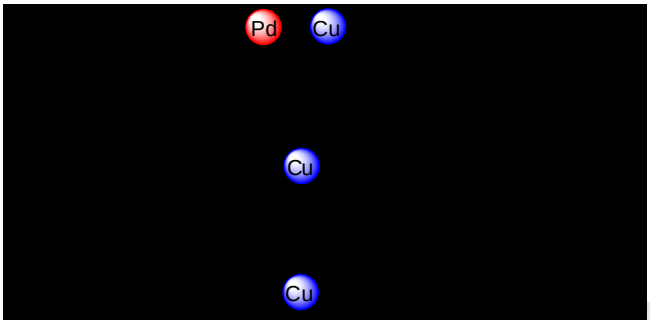
1. Introduction

The transition-metal-catalyzed amidation reaction is a widely used transformation that has been applied to the synthesis of complex organic molecules and commodity chemicals.[1] *α*-Ketoamides are omnipresent among the most abundant motifs in natural products and pharmaceuticals with important biologically active properties.[2] In addition, they also used as useful precursors for synthesis of *α*-hydroxy acids, *α*-amino acids and others.[3] The development of synthesis *α*-ketoamides has therefore attracted considerable attention. Among these methods, transition metal-catalyzed double carbonylative amination of aryl halides, aerobic oxidative coupling reactions have been explored, especially the formations involving secondary amine.[4] High reaction temperature and phosphine, *N*-heterocyclic carbene (NHC) or *N*-based ligands are usually required in these amidation reactions (Scheme 1).[5] Recently, Ji developed a novel copper-catalyzed direct oxidative synthesis of *α*-ketoamides from aryl methyl ketones.[4e] However, a general and simple catalytic system on the direct accessing *α*-ketoamides is still a great demand.



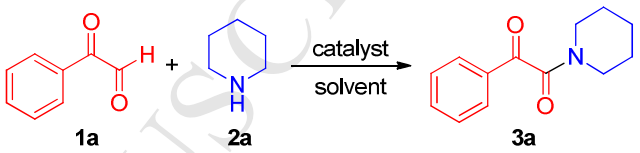
Scheme 1. Previous work on transition metal-catalyzed *α*-ketoamide construction.

Gold catalysts have recently gained growing attention and have become an important tool for the organic synthesis, owing to their soft lewis acidity and excellent reactivity.[6] Although many more reactions based on this theme are to be developed, further expansion of gold chemistry demands revelation of new reactivities. Recently, gold-catalyzed coupling reactions involving Au(I)/Au(III) catalytic cycles have been a hot research area in the presence of Selectfluor[7] or $PhI(OAc)_2$[8] as the external oxidants. However, the gold-catalyzed oxidative coupling under aerobic oxidative conditions is still a challenge. In 2012, the group of Zhu developed a highly efficient homogeneous gold-catalyzed oxidative C-C and C-P coupling methods by using air as the sole oxidant under mild conditions.[9] Wong and co-workers uncovered an efficient aerobic gold-catalyzed amide synthesis from aldehydes and amines with high functional group tolerance in aqueous medium under mild reaction conditions.[10] Herein, we report the example of gold(III)-catalyzed phenylglyoxal derivatives and secondary amines to give *α*-ketoamides under mild condition without ligand or additive.[11]

2. Results and discussion

Our initial studies focused on the phenylglyoxal monohydrate (**1a**) and piperidine (**2a**) in the presense of 5 mol% AuCl in DCM at room temperature for 12 h. The desired *α*-ketoamide **3a** was obtained in 10% yield (Table 1, entry 1). Among the gold catalysts tested (entries 2-5), $AuBr_3$ was the best which was found to afford the desired product in 34% yield, but the yield was still low. Interestingly, Ag_2CO_3 was found to be almost as effective as $AuBr_3$. No reaction product was observed in the absence of catalyst (Table 1, entry 6). The desired product **3a** was obtained along with phenyl(piperdine-1-yl)methanone in the presence of CuBr. When the reaction temperature was increased to 60 °C, the obtained yield was promoted to 72% (entry 6). The reactions showed lower yields when they were in other solvents such as DCE, MeOH, H_2O and toluene, even in higher reaction temperature.

Table 1. Optimization of reaction conditions for the preparation of **3a**.[a]



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

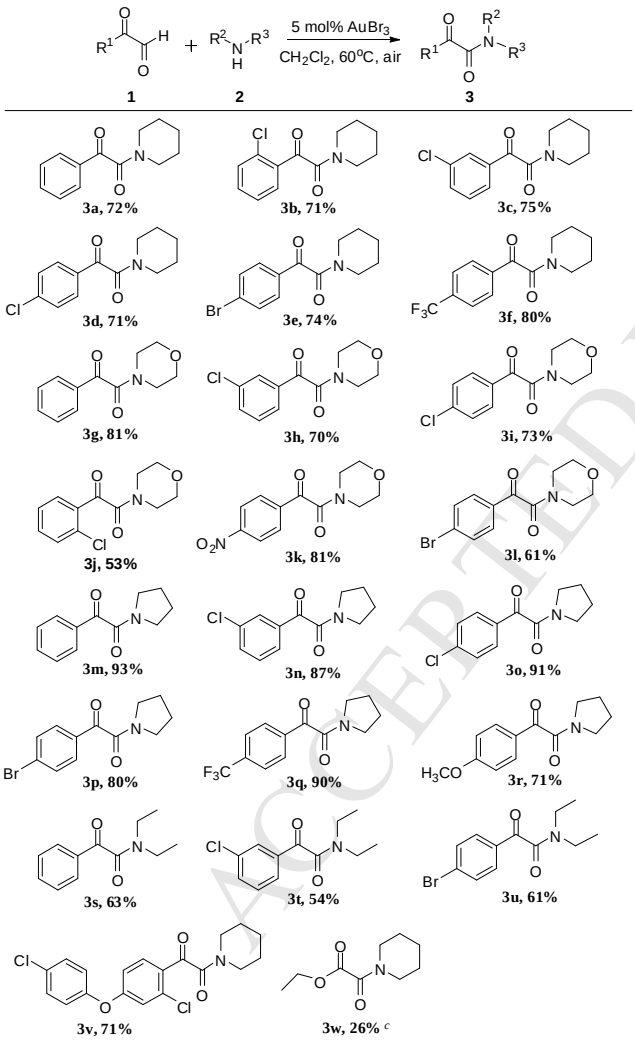
entry	catalyst	T(°C)	solvent	yield(%)[b]
1	AuCl	25	DCM	10
2	$AuCl_3$	25	DCM	17
3	$AuBr_3$	25	DCM	34
4	$NaAuCl_4 \cdot 2H_2O$	25	DCM	0
5	CuI	25	DCM	19
6	CuBr	25	DCM	16
7	Ag_2CO_3	25	DCM	31
8	--	25	DCM	0
9	$AuBr_3$	60	DCM	72
10	$AuBr_3$	60	DCE	61
11	$AuBr_3$	60	H_2O	14
12	$AuBr_3$	60	MeOH	15
13	$AuBr_3$	60	Toluene	54
14	$AuBr_3$	80	Toluene	23

[a] Standard reaction conditions: **1a** (1.0 mmol), **2a** (1.5 mmol), catalyst (5 mol%), solvent (2.0 mL) were heated in a sealed tube, 12 h. [b] Isolated yield.

With the optimized reaction conditions in hand, we then examined the scope of different phenylglyoxal derivatives and amines. As shown in table 2, both electron-rich and electron-deficient groups at different position (*para*-, *meta*-, and *ortho*-position) of phenylglyoxal derivatives could be smoothly transformed into the desired products with good yields. A wide range of different groups at the aromatic moiety of phenylglyoxal derivatives, such as halogen, trifluoromethyl, and methoxy, generated the corresponding coupling products

in 71-80% isolated yields (Table 2, **3a-3f**). The substrates bearing electron-withdrawing groups (**3n-3q**) was found suitable to afford higher yield than phenylglyoxal derivatives bearing electron-donating group (**3r**, Table 2). The results indicated that the electronic effect of phenylglyoxal derivatives would have influence on the *α*-ketoamides synthesis. However, aliphatic glyoxal such as ethyl glyoxalate with piperidine only gave 26% yield (GC yield) of the product (**3w**). Further investigation of the substrate scope involved a series of secondary amines was then explored. Piperdine, morpholine and pyrrolidine worked well in the reaction, provided the corresponding products in moderate to good yields (**3g-3r**). It's interesting to note that the pyrrolidine displays higher reactivity compared to the other amines. Acyclic amine such as diethylamine was also suitable for the reaction to give **3s-3u** in 54%-63% yields, respectively. It is noteworthy that 2-[2-chloro-4(4-chlorophenoxy)phenyl]-2-oxoacetaldehyde could also be

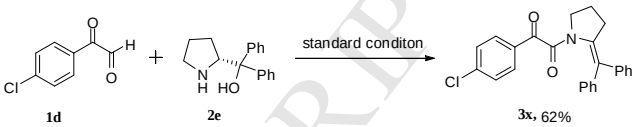
Table 2. Gold-Catalyzed Coupling of Secondary Amine and Glyoxals.[a]



[a] Reaction conditions: **1** (0.5 mmol), **2** (0.76 mmol), 5 mol% $AuBr_3$ in CH_2Cl_2 (2 mL) at 60 °C for 12 h in air; [b] Yield of isolated products; [c] Yield determined by GC.

smoothly transformed into the desired product **3v** in 71% yield. No desired products were observed when using primary amines including aniline.

It is interesting that when (*R*)-(+)-2-(diphenylhydroxymethyl)pyrrolidine **2e**, was used as secondary amine to condense with 2-oxoacetaldehyde **1d**, the corresponding dehydroxy product **3x** was obtained in 62% yield (Scheme 2). We speculate that alkene was formed after the amide bond formation due to dehydration the tertiary alcohol, because of using **2e** only in the same system, **2e** decomposed into benzophenone. In addition, the structure of **3x** was further confirmed by single-crystal X-ray analysis (Figure 1).



Scheme 2. Gold-catalyzed Coupling of **1d** and **2e**.

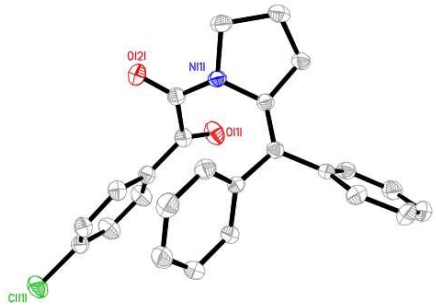
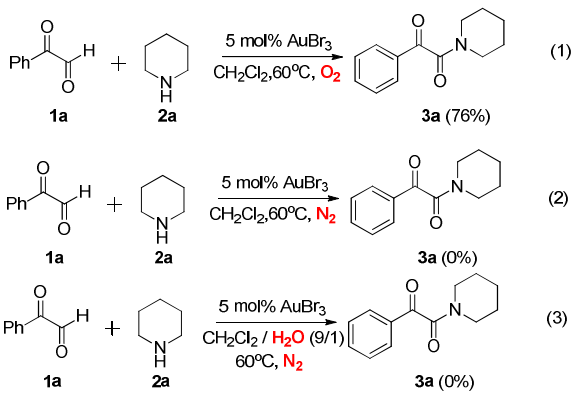


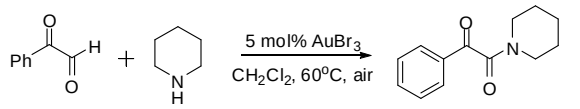
Figure 1. X-ray crystal structure of the product **3x**.

In order to obtain the reaction mechanism, some experiments were conducted. The transformation of **1a** and **2a** was conducted in the presence of O_2 and anhydrous solvent, **3a** was obtained in 76% yield (equation 1). When the reaction was performed in the presence of N_2 and anhydrous DCM, no product was detected (equation 2). Furthermore, it is noteworthy that the reaction didn't work when the transformation of **1a** and **2a** was performed in the presence of



H_2O under N_2 atmosphere. The results demonstrate that O_2 plays the key role of oxidation to facilitate this chemical process (equation 3). To gather further insight into our novel

gold-catalyzed direct amidation reactions, radical scavengers, such as TEMPO and 1,1-diphenylethylene, were employed in the reaction and the reactions significantly suppressed, which could indicate that this transformation involved radical intermediates (Scheme 3).

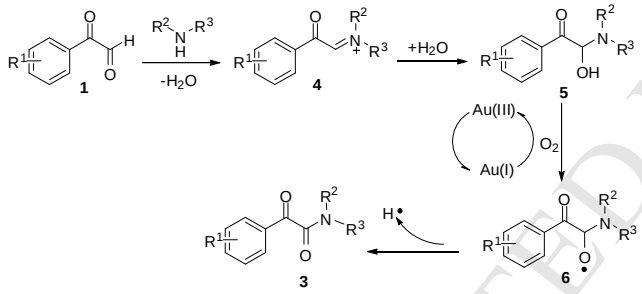


1a 2a 3a

No Scavenger	72%
TEMPO 1.0 equiv	5%
1,1-diphenylethylene 1.0 equiv	8%

Scheme 3. Radical Trapping Experiments.

On the basis of the above results and literatures,[10, 12] the proposed mechanism of this coupling reaction is depicted in Scheme 4. We speculate that iminium **4** could be formed by condensation, subsequently water addition to the iminium ion to form a hemiaminal **5**, and finally gold-catalyzed abstraction of the alpha-proton by dioxygen (likely alkoxy radical **6** involving) to form the amide C=O bond. In the presence of O_2, the resulting Au(I) species can be re-oxidized to the catalytically active Au(III) ion to complete the catalytic cycle.



Scheme 4. Proposed mechanism.

3. Conclusions

In summary, we have described a simple and efficient gold-catalyzed coupling of secondary amine with phenlglyoxal derivatives under ligand-free conditions. This method provides an avenue of the easy assembly of α-ketoamides. Further studies on the reaction mechanism, scope and synthetic applications are ongoing in our laboratory.

4. Experimental

4.1. Materials and methods

All experiments were conducted under an air atmosphere. All solvents were commercially avaliable. For column chromatography, 200-300 mesh silica gel was employed. ^{1}H NMR and ^{13}C NMR were recorded on 300 MHz, 400MHz or 500 MHz spectrometer in $CDCl_3$ or DMSO-d_6 solution and the chemical shifts were reported in parts per million (δ) relative to internal standard TMS (0 ppm). For HRMS measurements, the mass analyzer is GC-TOFMS. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification.

4.2. General procedure.

To a solution of $AuBr_3$ (10.9 mg, 5 mol%), glyoxal derivative **1** (0.5 mmol) and secondary amine **2** (0.75 mmol) in CH_2Cl_2 (2 mL) in a 10 mL Schlenk tube. The resulting solution was stirred at 60 ºC overnight. After cooling to room temperature, the resulting mixture was filtered through a pad of celite. The volatile compounds were removed in vacuum and the residue was purified by column chromatography (SiO_2, petroleum ether/ethyl acetate =10:1- 4:1) to give compounds **3**.

1-phenyl-2-(piperidin-1-yl)ethanone-1,2-dione ***(3a)***
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.3 Hz, 2H), 7.64 (t, J = 7.3 Hz, 1H), 7.52 (t, J = 7.6 Hz, 2H), 3.72-3.70 (m, 2H), 3.30 (t, J = 5.5 Hz, 2H), 1.71-1.70 (m, 4H), 1.56-1.54 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) 191.9, 165.5, 134.7, 133.3, 129.6, 129.0, 47.1, 42.2, 26.2, 25.5, 24.4.

1-(2-chlorophenyl)-2-(piperidin-1-yl)ethane-1,2-dione ***(3b)***
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (dd, J = 7.7 Hz, 1.4Hz, 1H), 7.52-7.49 (m, 1H), 7.45-7.39 (m, 2H), 3.66 (t, J = 5.6 Hz, 2H), 3.44 (t, J = 5.6 Hz, 2H), 1.71-1.68 (m, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.1, 165.4, 134.3, 133.9, 133.3, 132.4, 130.9, 127.3, 46.9, 42.5, 25.6, 25.0, 24.4. HRMS (ESI) calcd for $C_{13}H_{14}ClNaNO_2$ ($[M+Na]^+$): 274.0611, found 274.0606.

1-(3-chlorophenyl)-2-(piperidin-1-yl)ethane-1,2-dione ***(3c)***
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.82 (d, J = 7.8 Hz, 1H), 7.6 (d, J = 8.0 Hz, 1H), 7.46 (t, J = 7.8 Hz, 1H), 3.71-3.70 (m, 2H), 3.29 (t, J = 5.6 Hz, 2H), 1.72-1.70 (m, 4H), 1.57-1.54 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.4, 164.7, 135.4, 134.9, 134.6, 130.3, 129.4, 127.8, 47.1, 42.3, 26.2, 25.5, 24.4. HRMS (ESI) calcd for $C_{13}H_{14}ClNaNO_2$ ($[M+Na]^+$): 274.0611, found 274.0607.

1-(4-chlorophenyl)-2-(piperidin-1-yl)ethane-1,2-dione ***(3d)***
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 8.6 Hz, 2H), 7.48 (d, J = 8.6 Hz, 2H), 3.69 (t, J = 5.5 Hz, 2H), 3.28 (t, J = 5.6 Hz, 2H), 1.71-1.69 (m, 4H), 1.57-1.54 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.5, 164.9, 141.2, 131.7, 130.9, 129.4, 47.0, 42.2, 26.2, 25.4, 24.3.

1-(4-bromophenyl)-2-(piperidin-1-yl)ethane-1,2-dione ***(3e)***
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 8.4 Hz, 2H), 3.72-3.69 (m, 2H), 3.28 (t, J = 5.5 Hz, 2H), 1.71-1.69 (m, 4H), 1.59-1.57 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) 190.7, 164.9, 132.4, 132.1, 130.9, 130.1, 47.1, 42.3, 26.3, 25.5, 24.4.

1-(piperidin-1-yl)-2[4-(trifluoromethyl)phenyl]ethane-1,2-dione ***(3f)***

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.2 Hz, 2H), 7.77 (d, J = 8.2 Hz, 2H), 3.73-3.71 (m, 2H), 3.30 (t, J = 5.5 Hz, 2H), 1.71-1.70 (m, 4H), 1.59-1.55 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.5, 164.6, 135.9, 135.8, 135.6, 129.9, 126.1, 126.0, 47.1, 42.4, 26.3, 25.5, 24.4. HRMS (ESI) calcd for $C_{14}H_{14}F_3NaNO_2$ ([M+Na]$^+$): 308.0874, found 308.0869.

*1-morpholino-2-phenylethane-1,2-dione (**3g**)*
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 7.2 Hz, 2H), 7.63 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.7 Hz, 2H), 3.77-3.74 (m, 4H), 3.62 (t, J = 4.8 Hz, 2H), 3.35 (t, J = 4.8 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) 191.1, 165.4, 134.9, 133.0, 129.6, 129.1, 66.7, 66.6, 46.2, 41.6.

*1-(3-chlorophenyl)-2-morpholinothane-1,2-dione (**3h**)*
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (t, J = 7.7 Hz, 1H), 7.85-7.82(m, 1H), 7.64-7.60 (m, 1H), 7.49-7.44 (m, 1H), 3.80-3.77 (m, 4H), 3.66 (t, J = 4.8 Hz, 2H), 3.38 (t, J = 4.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.6, 164.7, 135.5, 134.8, 134.7, 130.4, 129.4, 127.9, 66.7, 66.6, 46.3, 41.8. HRMS (ESI) calcd for $C_{12}H_{12}ClNaNO_3$ ([M+Na]$^+$):276.0403, found 276.0401.

*1-(4-chlorophenyl)-2-morpholinothane-1,2-dione (**3i**)*
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, J =8.6 Hz, 2H), 7.49 (d, J =8.6 Hz, 2H), 3.80-3.77 (m, 4H), 3.66 (t, J = 4.8 Hz, 2H), 3.38 (t, J = 4.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.7, 164.9, 141.6, 131.5, 131.0, 129.5, 66.7, 66.6, 46.3, 41.7.

*1-(2-chlorophenyl)-2-morpholinoethane-1,2-dione (**3j**)*
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (dd, J =7.8, 1.6 Hz, 1H), 7.55-7.50 (m, 1H), 7.46-7.40 (m, 2H), 3.82-3.79 (m, 2H), 3.78-3.73 (m, 4H), 3.56 (t, J = 4.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.7, 165.5, 134.5, 133.6, 133.5, 132.3, 130.8, 127.4, 66.3, 66.2, 46.2, 41.9. HRMS (ESI) calcd for $C_{12}H_{12}ClNaNO_3$ ([M+Na]$^+$): 276.0403, found 276.0403.

*1-morpholino-2-(4-nitrophenyl)ethane-1,2-dione (**3k**)*
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, J =8.9 Hz, 2H), 8.18 (d, J =8.9 Hz, 2H), 3.83-3.80 (m, 4H), 3.71 (t, J = 4.8 Hz, 2H), 3.44 (t, J = 4.8 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.7, 164.0, 151.2, 137.5, 130.9, 124.2, 66.8, 66.7, 46.4, 42.0.

*1-(4-bromophenyl)-2-morpholinothane-1,2-dione (**3l**)*
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, J =8.5 Hz, 2H), 7.67 (d, J = 8.5 Hz, 2H), 3.80-3.77 (m, 4H), 3.66 (t, J = 4.8 Hz, 2H), 3.38 (t, J = 4.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 189.5, 164.4, 132.1, 131.5, 130.6, 130.0, 66.3, 66.2, 45.9, 41.3.

*1-phenyl-2-(pyrrolidin-1-yl)ethane-1,2-dione (**3m**)*
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (d, J = 7.1 Hz, 2H), 7.66-7.61 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.5 Hz, 2H), 3.66 (t, J = 7.0 Hz, 2H), 3.42 (t, J = 6.8 Hz, 2H), 1.97-1.92 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.6, 164.9, 134.6, 132.9, 129.9, 128.9, 46.7, 45.2, 25.9, 24.0.

*1-(3-chlorophenyl)-2-(pyrrolidin-1-yl)ethane-1,2-dione (**3n**)*
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (t, J = 1.7 Hz, 1H), 7.87-7.85 (m, 1H), 7.58-7.56 (m, 1H), 7.44-7.40 (m, 1H), 3.62 (t, J = 6.9 Hz, 2H), 3.42 (t, J = 6.7 Hz, 2H), 1.95-1.91 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.9, 164.0, 135.2, 134.6, 134.5, 130.3, 129.7, 128.1, 46.8, 45.4, 25.9, 23.9. HRMS (ESI) calcd for $C_{12}H_{12}ClNaNO_2$ ([M+Na]$^+$): 260.0454, found 260.0449.

*1-(4-chlorophenyl)-2-(pyrrolidin-1-yl)ethane-1,2-dione (**3o**)*
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.6 Hz, 2H), 7.47 (d, J = 8.6 Hz, 2H), 3.64 (t, J = 6.9 Hz, 2H), 3.43 (t, J = 6.6 Hz, 2H), 1.97-1.92 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.1, 164.2, 141.1, 131.8, 131.3, 129.3, 46.8, 45.4, 25.9, 23.9. HRMS (ESI) calcd for $C_{12}H_{12}ClNaNO_2$ ([M+Na]$^+$): 260.0454, found 260.0451.

*1-(4-bromophenyl)-2-(pyrrolidin-1-yl)ethane-1,2-dione (**3p**)*
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.6 Hz, 2H), 7.64 (d, J = 8.6 Hz, 2H), 3.64 (t, J = 7.0 Hz, 2H), 3.43 (t, J = 6.7 Hz, 2H), 1.97-1.92 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.3, 164.2, 132.3, 131.9, 131.4, 130.1, 46.8, 45.4, 25.9, 23.9. HRMS (ESI) calcd for $C_{12}H_{12}BrNaNO_2$ ([M+Na]$^+$): 303.9949, found 303.9945.

*1-(pyrrolidin-1-yl)-2[4-(trifluoromethyl)phenyl]ethane-1,2-dione (**3q**)*
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, J = 8.1 Hz, 2H), 7.76 (d, J = 8.2 Hz, 2H), 3.67 (t, J = 7.0 Hz, 2H), 3.46 (t, J = 6.7 Hz, 2H), 1.98-1.93 (m, , 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.9, 163.8, 135.8, 130.3, 125.9, 125.8, 124.5, 46.8, 45.5, 25.9, 23.9.

*1-(4-methoxyphenyl)-2-(pyrrolidin-1-yl)ethane-1,2-dione (**3r**)*
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J = 9.0 Hz, 2H), 6.95 (d, J = 9.0 Hz, 2H), 3.88 (s, 3H), 3.63 (t, J = 6.7 Hz, 2H), 3.41 (t, J = 6.5 Hz, 2H), 1.96-1.92 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.3, 165.3, 164.8, 132.4, 126.0, 114.3, 55.6, 46.7, 45.2, 25.9, 24.1.

*N,N-diethyl-2-oxo-2-phenylacetamide (**3s**)*
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (d, J = 7.0 Hz, 2H),7.63 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.5 Hz, 2H), 3.57 (q, J = 7.2 Hz, 2H), 3.25 (q, J = 7.1 Hz, 2H), 1.29 (t, J = 7.2 Hz, 3H), 1.16 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 191.6, 166.7, 134.5, 133.3, 129.6, 128.9, 42.1, 38.8, 14.1, 12.8.

*2-(3-chlorophenyl)-N,N-diethyl-2-oxoacetamide (**3t**)*
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.81 (d, J = 7.7 Hz, 1H), 7.61-7.59 (m, 1H), 7.47-7.43 (m, 1H), 3.56 (q, J = 7.2 Hz, 2H), 3.24 (q, J = 7.1 Hz, 2H), 1.29 (t, J = 7.2 Hz, 3H), 1.17 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.0, 160.0, 135.4, 134.9, 134.5, 130.3, 129.4, 127.9, 42.2, 39.0, 14.2, 12.8.

*2-(4-bromophenyl)-N,N-diethyl-2-oxoacetamide (**3u**)*
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.5 Hz, 2H), 7.65 (d, J = 8.5 Hz, 2H), 3.55 (q, J = 7.2 Hz, 2H), 3.23 (q, J = 7.1

Hz, 2H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.4, 166.2, 132.4, 132.1, 131.0, 130.0, 42.2, 38.9, 14.2, 12.8.

*1-[2-chloro-4-(4-chlorophenoxy)phenyl]-2-(piperidin-1-yl)ethane-1,2-dione (**3v**)*

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.4 Hz, 1H), 7.37 (d, *J* = 8.8 Hz, 2H), 7.20 (dd, *J* = 8.4, 1.8 Hz, 1H), 7.03 (d, *J* = 8.8 Hz, 2H), 6.78 (d, *J* = 1.8 Hz, 1H), 3.45 (t, *J* = 5.6 Hz, 2H), 3.35 (t, *J* = 5.6 Hz, 2H), 1.60-1.58 (m, 4H), 1.41-1.39 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.9, 166.0, 158.5, 153.7, 141.5, 132.2, 130.6, 130.4, 124.4, 124.3, 121.4, 118.1, 46.8, 42.0, 25.7, 25.1, 24.3. HRMS (ESI) calcd for $C_{19}H_{17}Cl_2NaNO_3$ ($[M+Na]^+$): 400.0483, found 400.0478.

*1-(4-chlorophenyl)-2-[2-(diphenylmethylene)pyrrolidin-1-yl]ethane-1,2-dione (**3x**)*

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.40 (m, 2H), 7.28-7.26 (m, 4H), 7.17-7.14 (m, 2H), 7.11-7.08 (m, 2H), 6.86-6.82 (m, 4H), 3.91-3.81 (m, 2H), 2.69-2.62 (m, 2H), 2.13-2.03 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.4, 164.8, 141.5, 139.4, 139.3, 136.4, 131.4, 130.9, 129.9, 128.5, 128.0, 127.9, 127.3, 45.7, 29.8, 21.0. HRMS (ESI) calcd for $C_{25}H_{20}ClNaNO_2$ ($[M+Na]^+$): 424.1080, found 424.1079.

Acknowledgements

This work was supported by the National Natural Science Foundation of China (grant No. 21302015), the Natural Science Fundation for Colleges and Universities of Jiangsu Province(grant No. 12KJB150005), and the Priority Academic Program Development of Jiangsu Higher Education Institutions (PAPD).

Supplementary materials

Electronic Supplementary Information (ESI) available: [NMR spectra data for all the compounds and the cif file of the compound **3x** (CCDC 962698 has been deposited at the Cambridge Crystallographic Database Centre and is available on request from the Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www.ccdc.cam.ac.uk)].

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11 During our investigation, one gold-catalyzed oxidative coupling reaction of phenylglyoxal and piperidine was simply mentioned, without substrate scope broadening and mechanism investigation, see: Shi, S.; Wang, T.; Weingand, V.; Rudolph, M.; Stephen, A.; Hashmi, K. *Angew. Chem. Int. Ed.* **2013**, *52*, 1.

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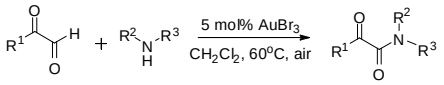
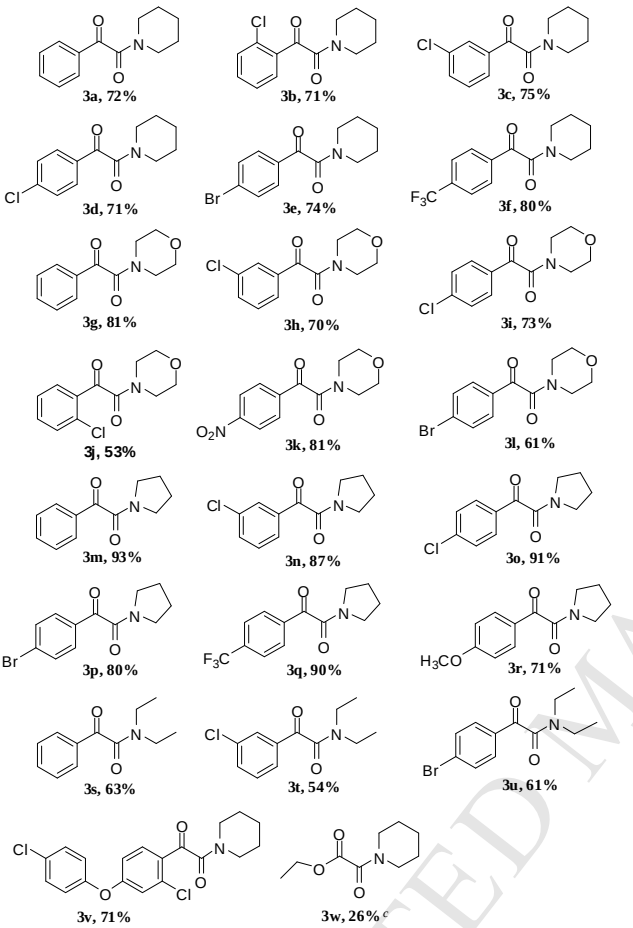
Table 2. Gold-Catalyzed Coupling of Secondary Amine and Glyoxals.[a]



1 2 3



[a] Reaction conditions: **1** (0.5 mmol), **2** (0.76 mmol), 5 mol% $AuBr_3$ in CH_2Cl_2 (2 mL) at 60 °C for 12 h in air; [b] Yield of isolated products; [c] Yield determined by GC.

Supporting Information for

Mild Gold-Catalyzed Aerobic Dehydrogenative Coupling of Amines and Phenylglyoxal Derivatives

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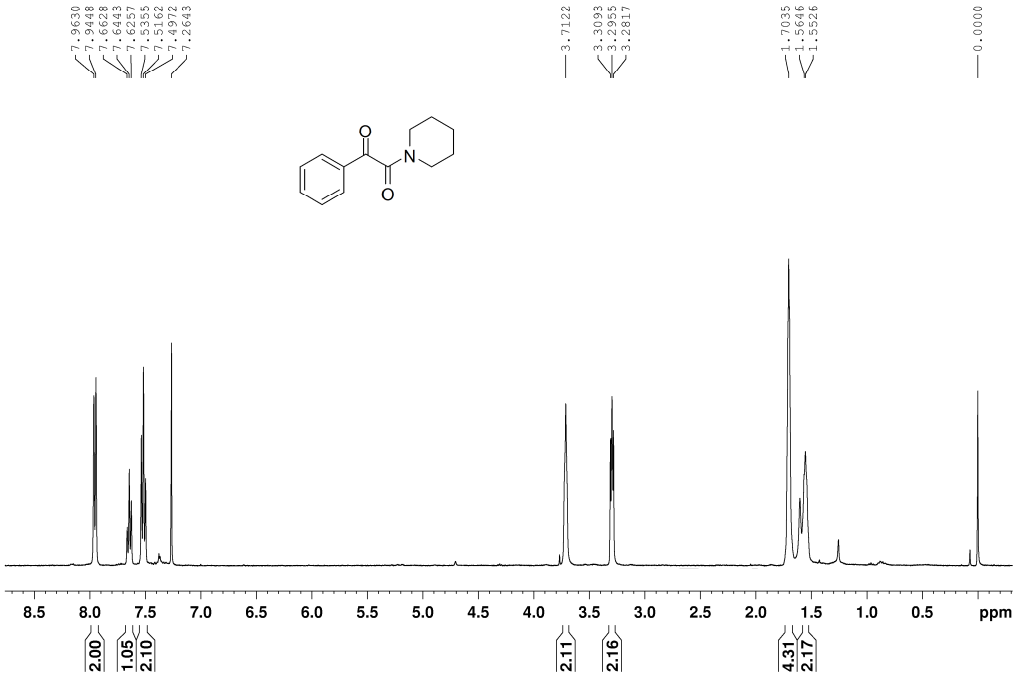
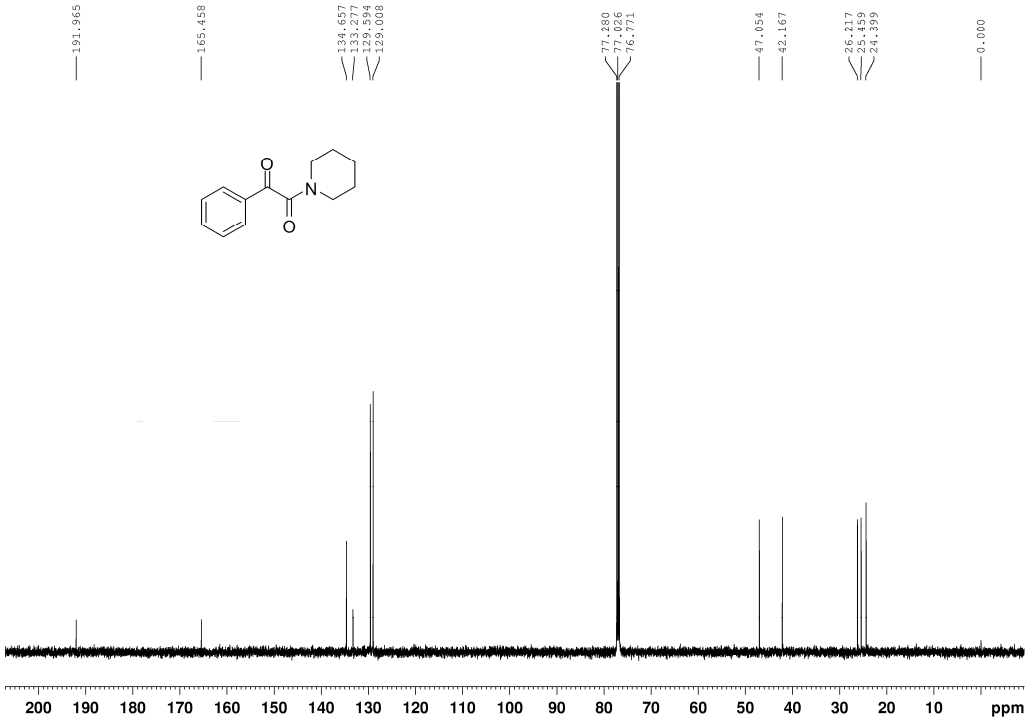
3a:



^{1}H NMR (400 MHz, $CDCl_3$) of **3a**.



^{13}C NMR (125 MHz, $CDCl_3$) of **3a**.

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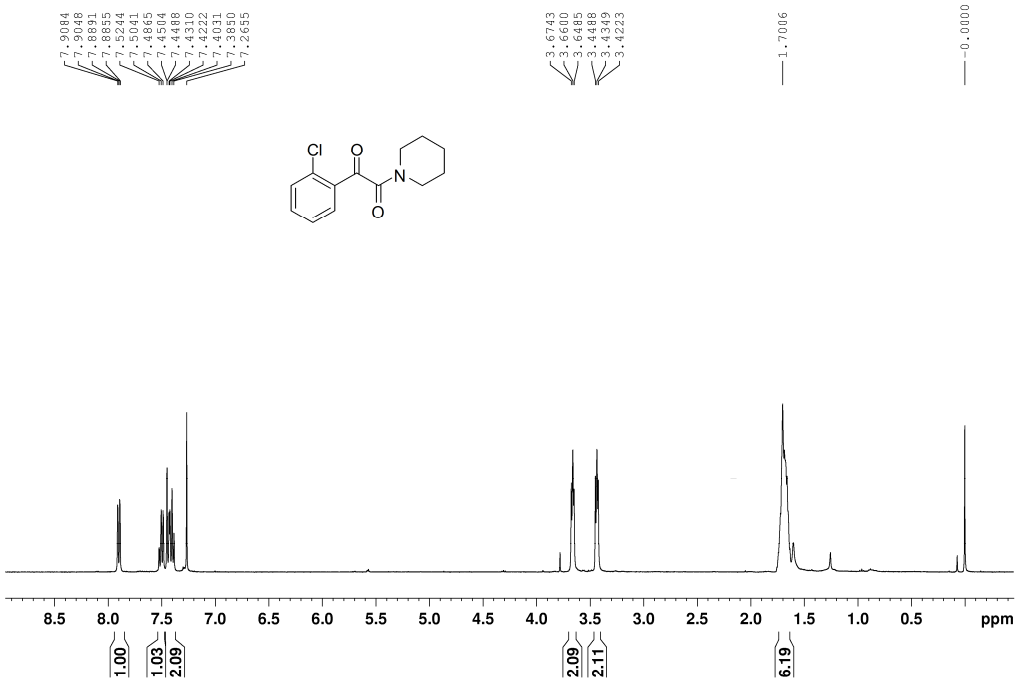

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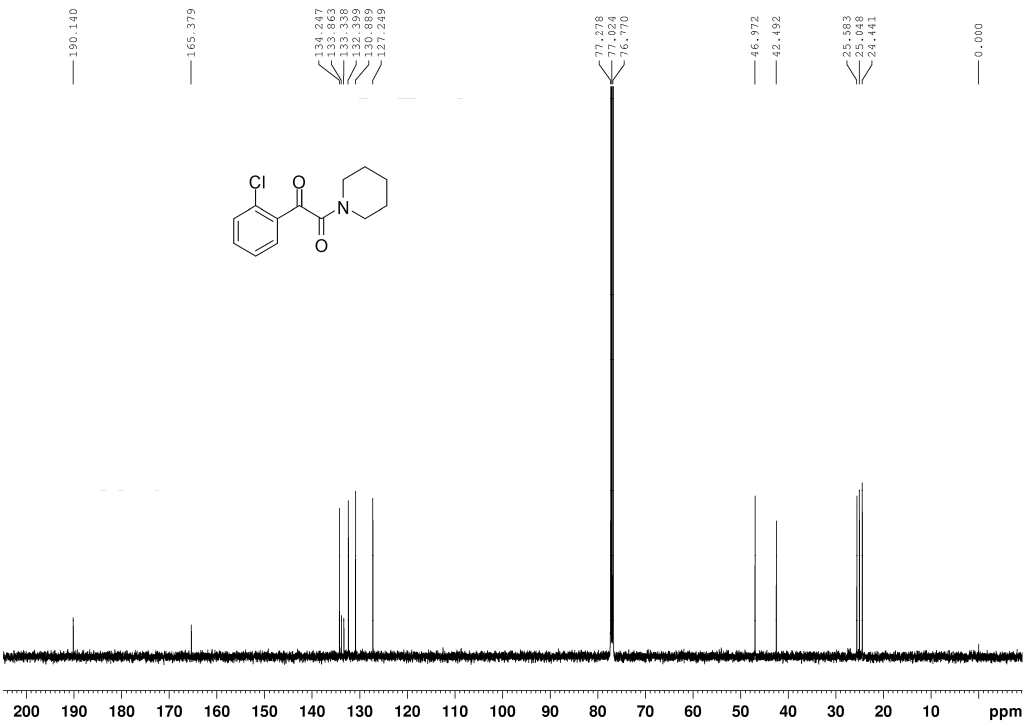

^{13}C NMR (125 MHz, $CDCl_3$) of **3b**.

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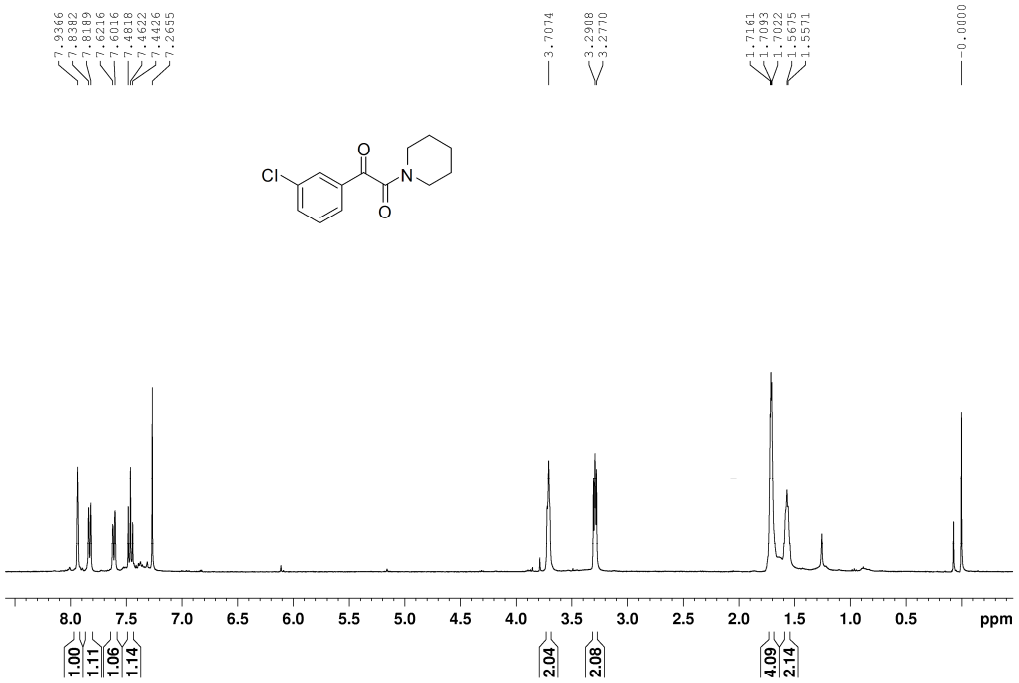
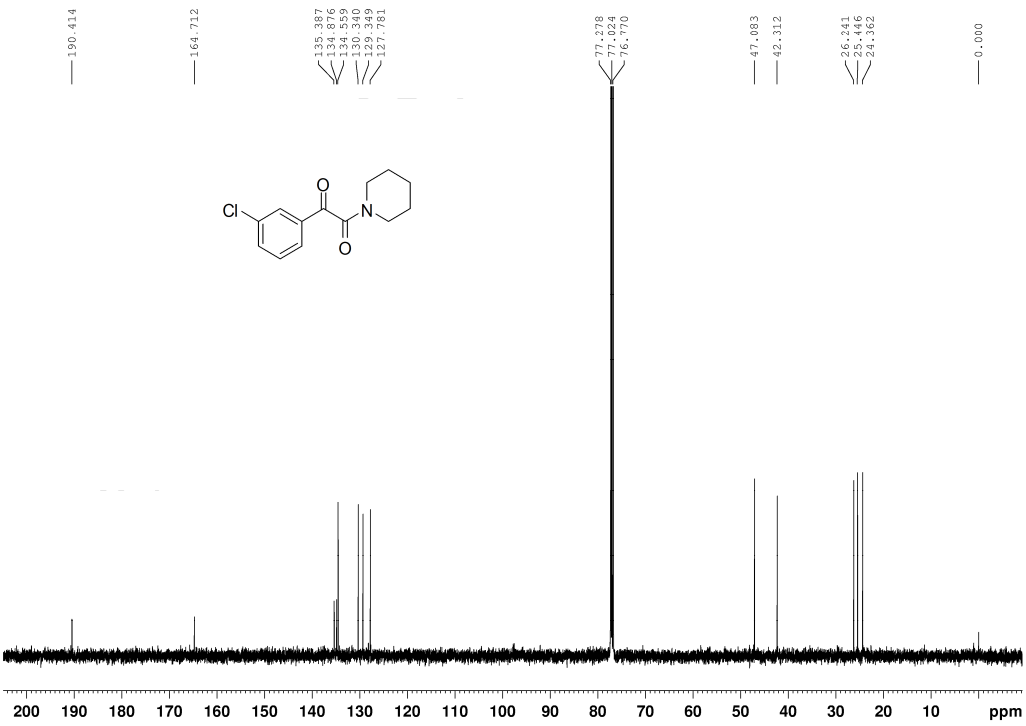


^{1}H NMR (400 MHz, $CDCl_3$) of **3c**.



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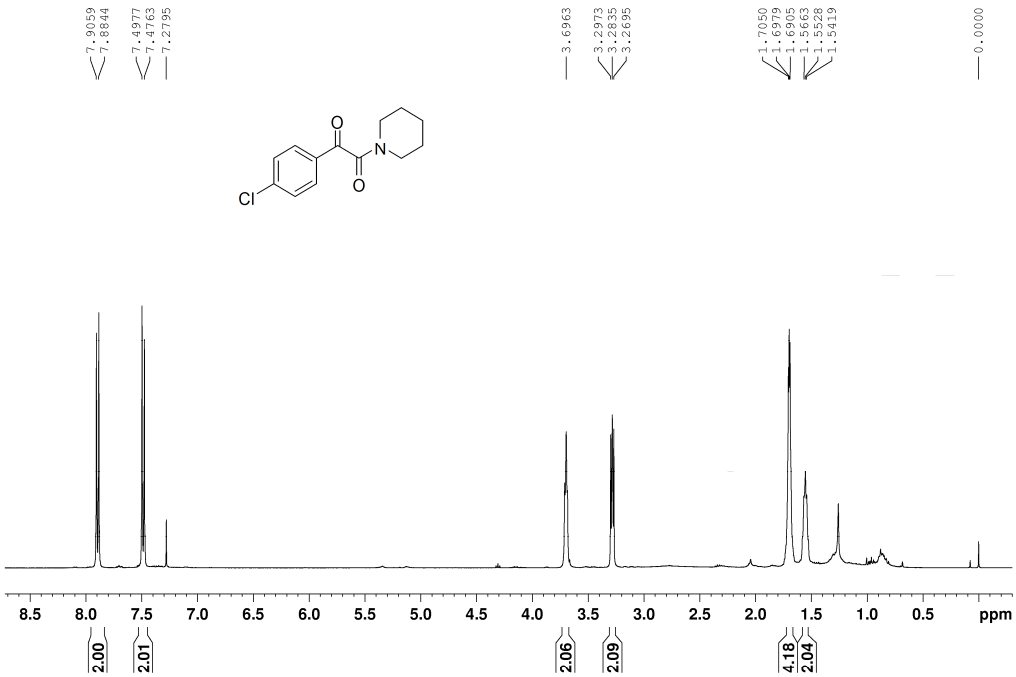
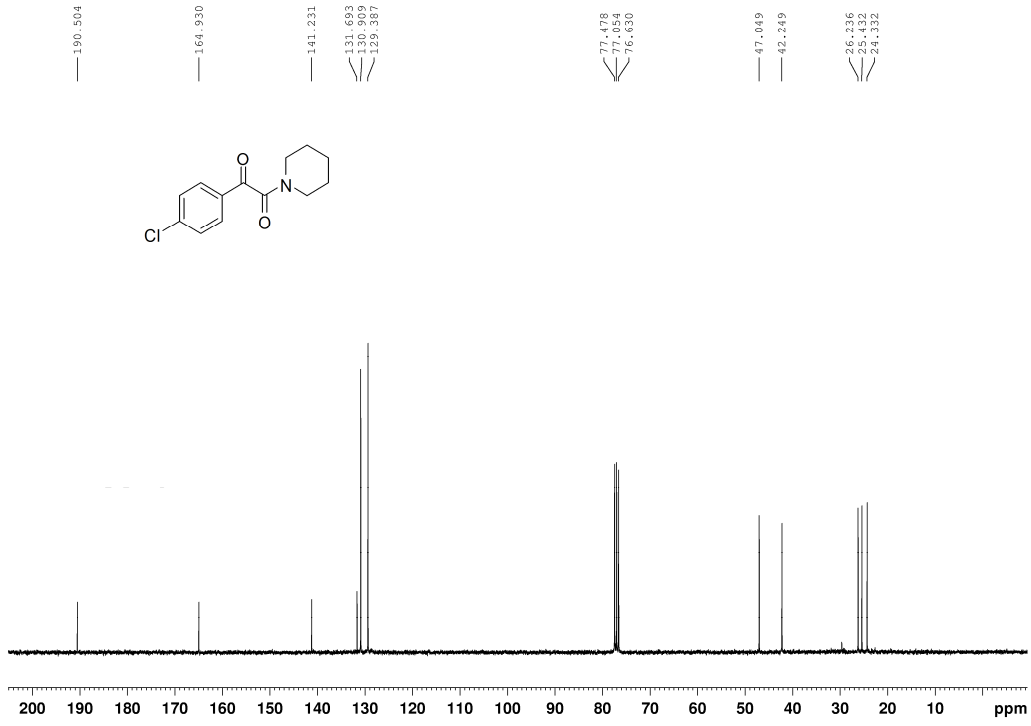


^{1}H NMR (400 MHz, $CDCl_3$) of **3d**.



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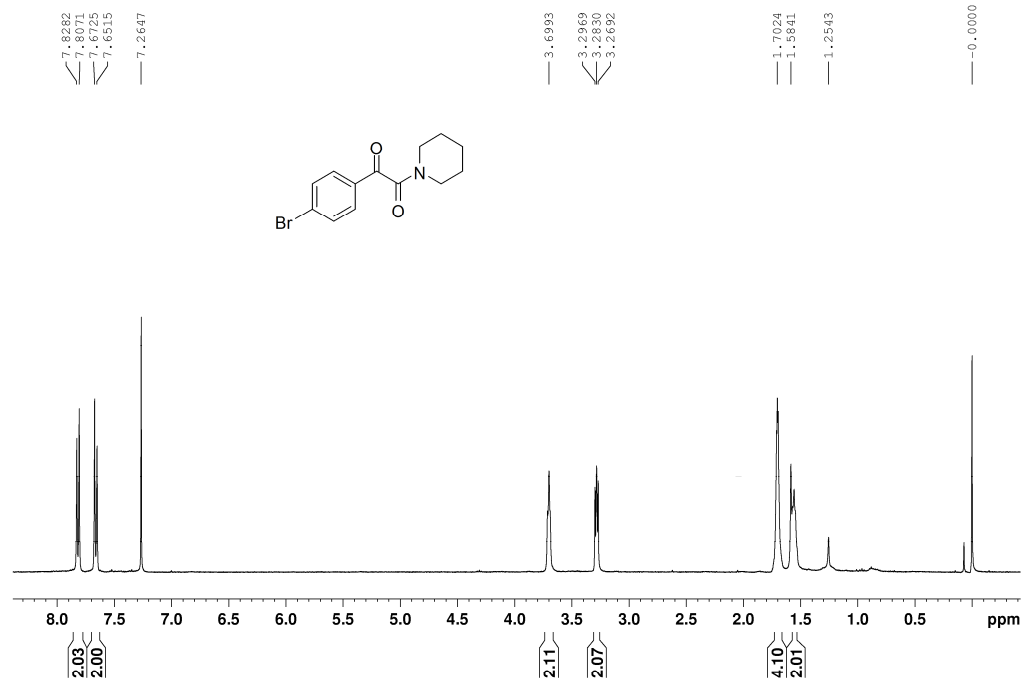

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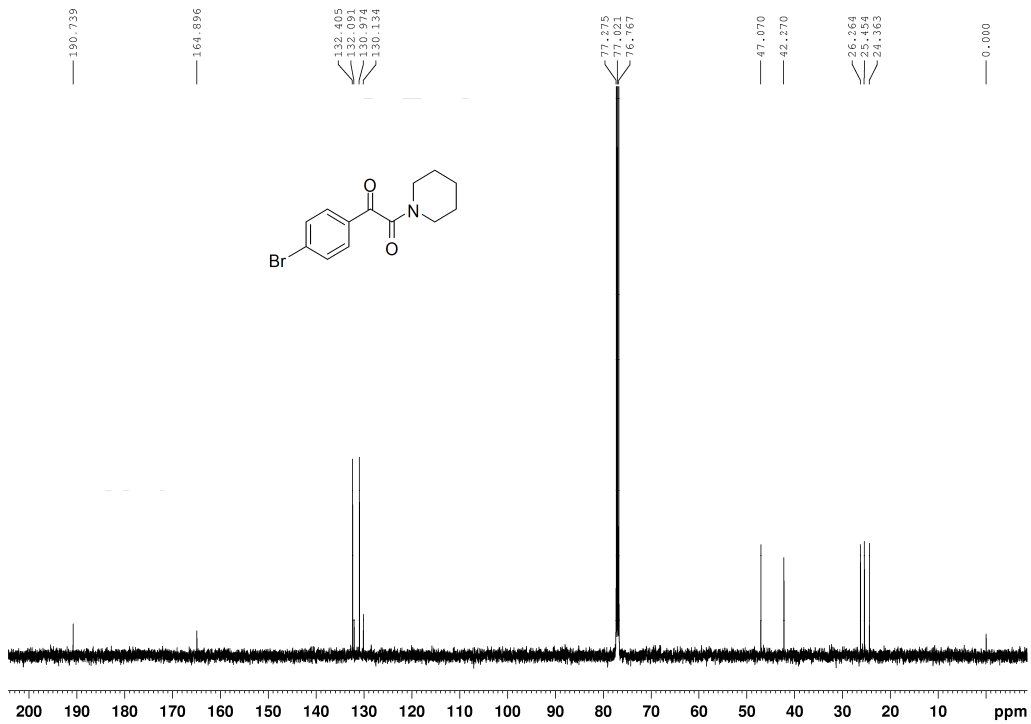

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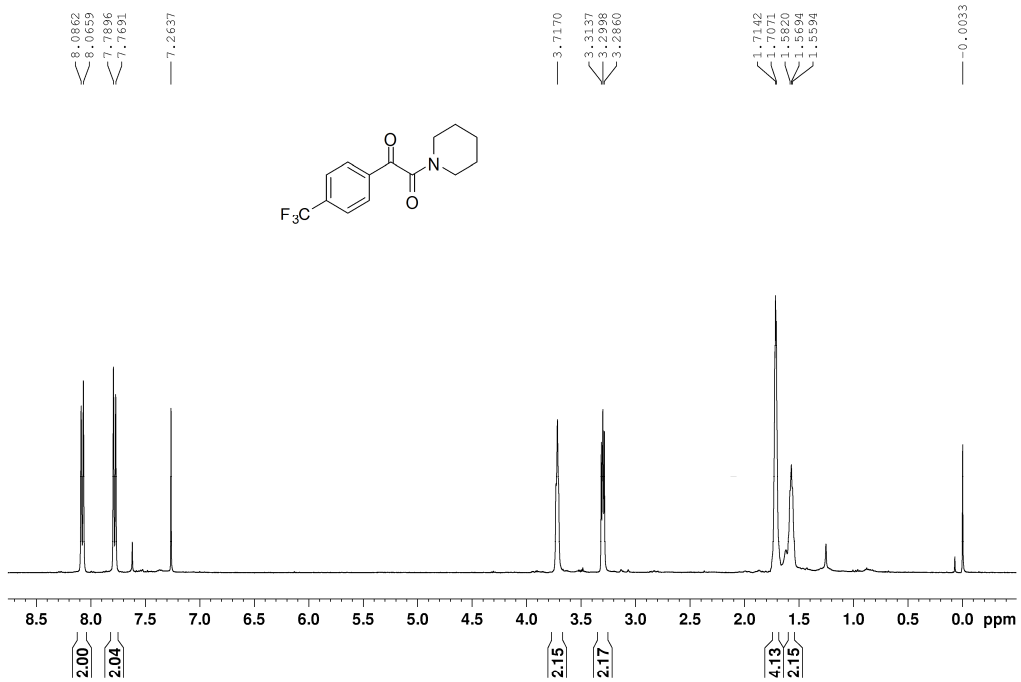

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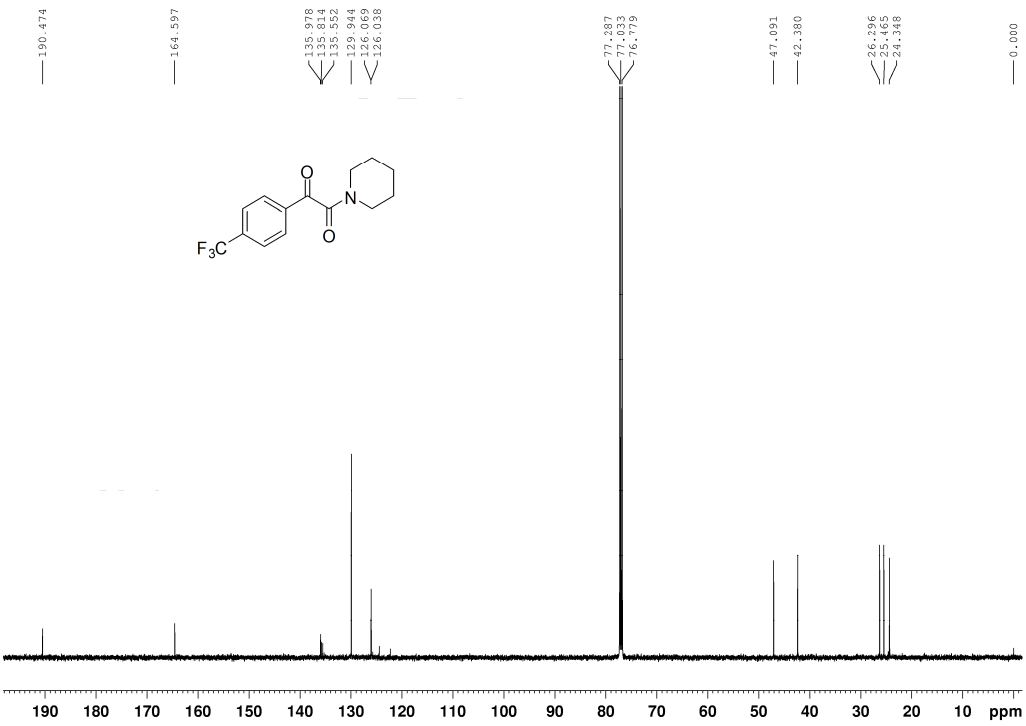

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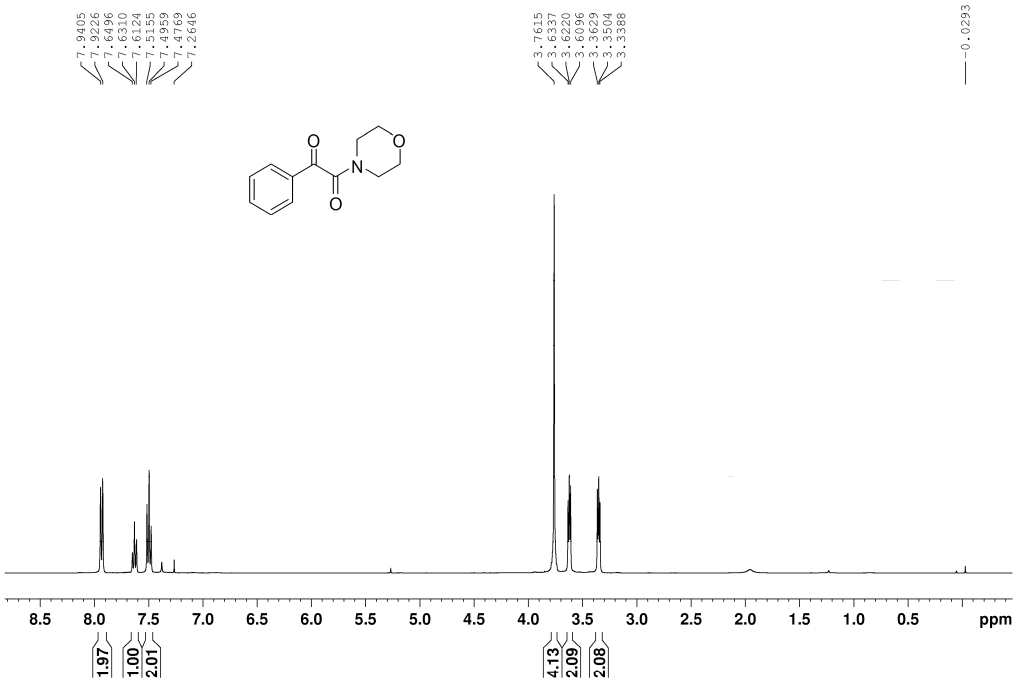

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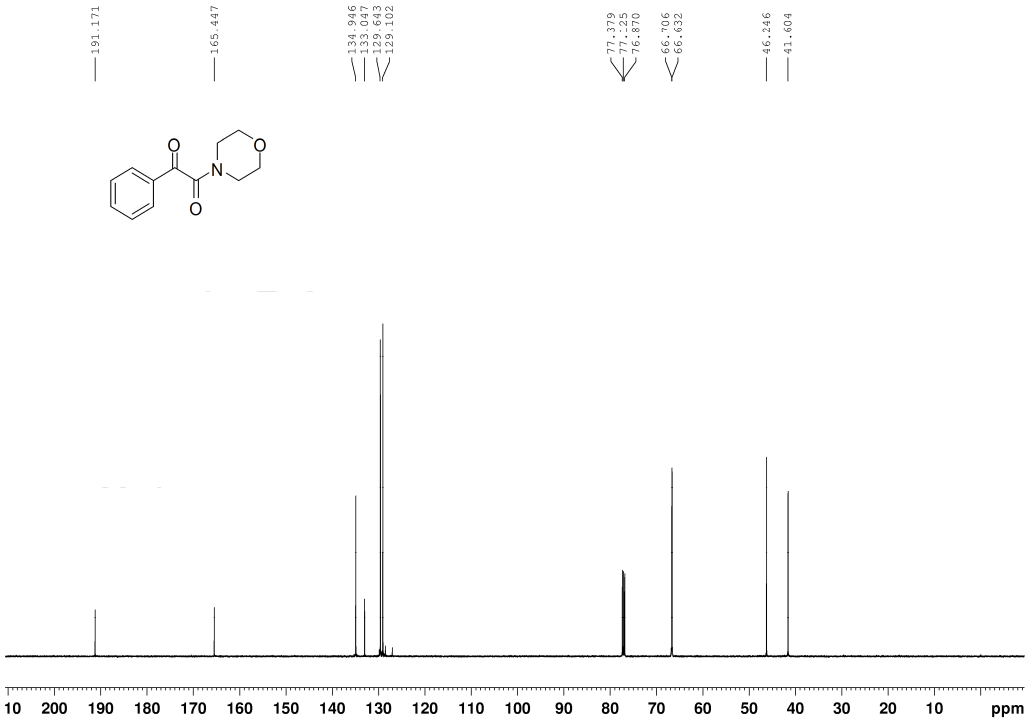

^{13}C NMR (125 MHz, $CDCl_3$) of **3g**.

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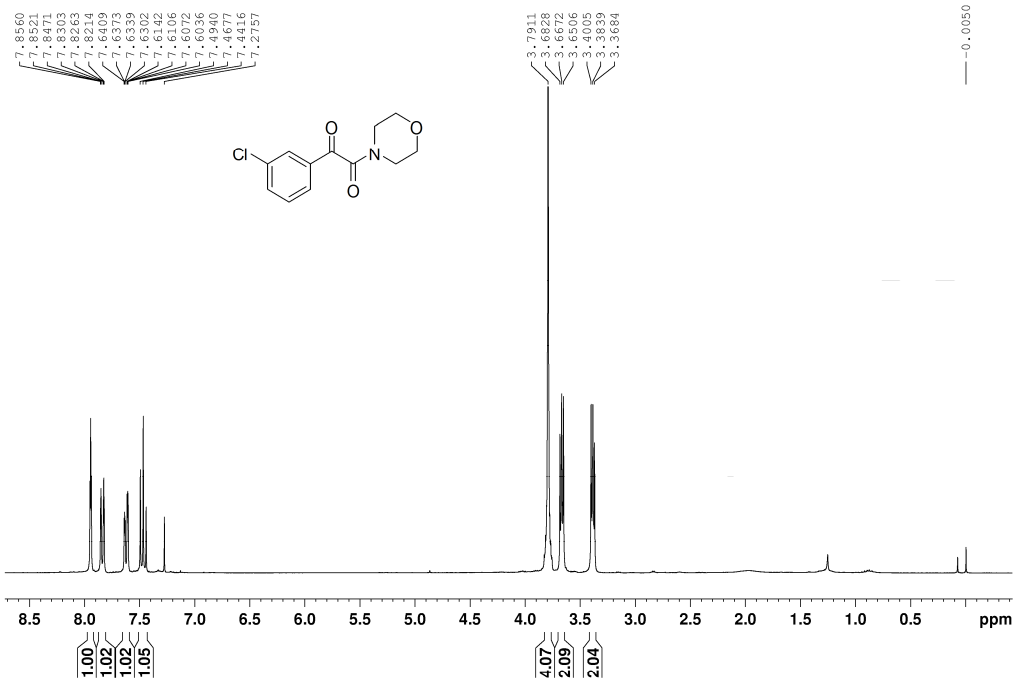

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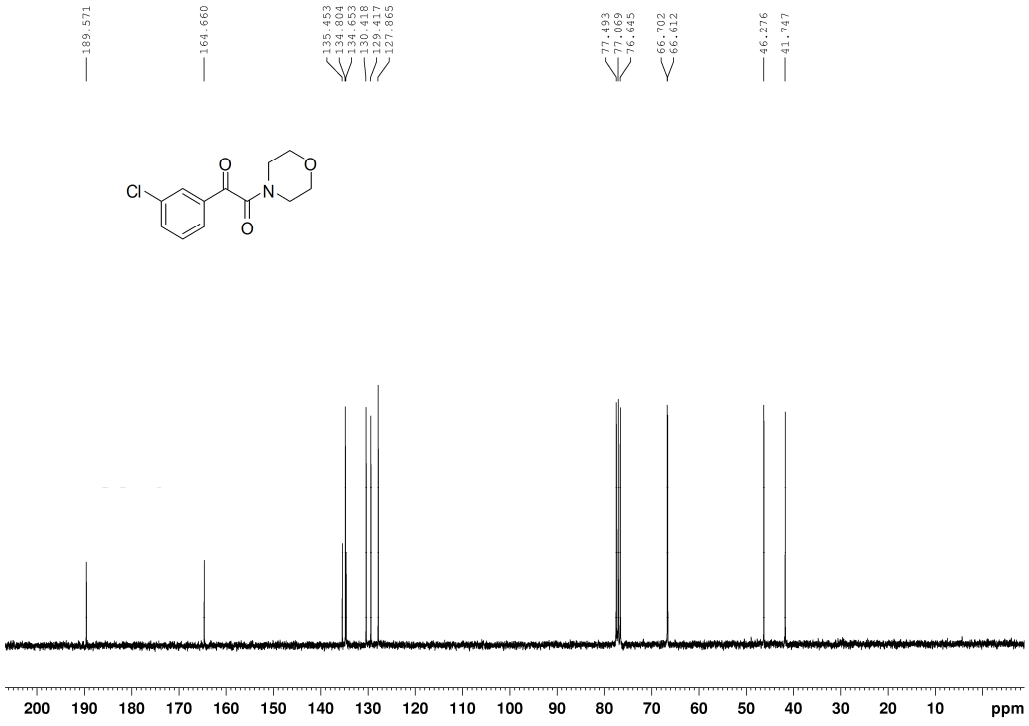

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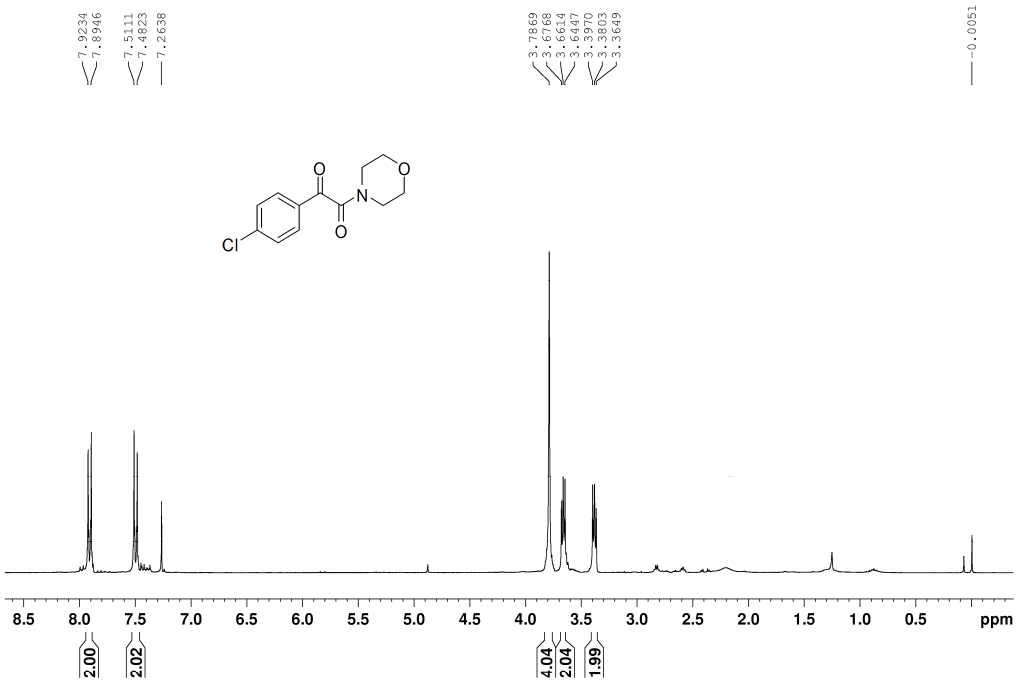

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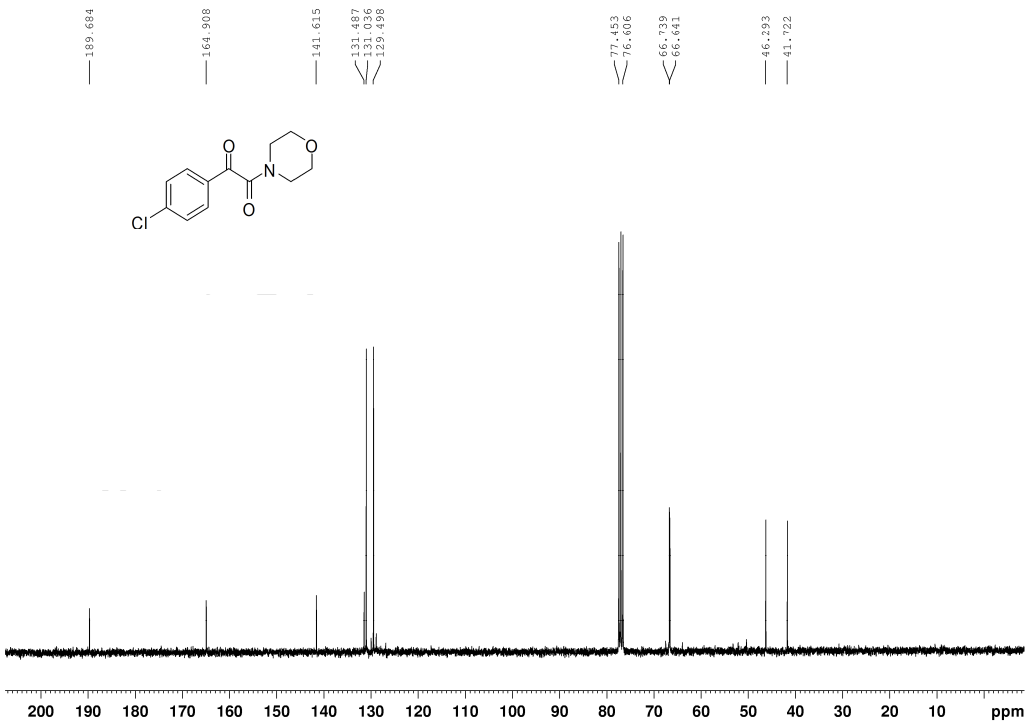

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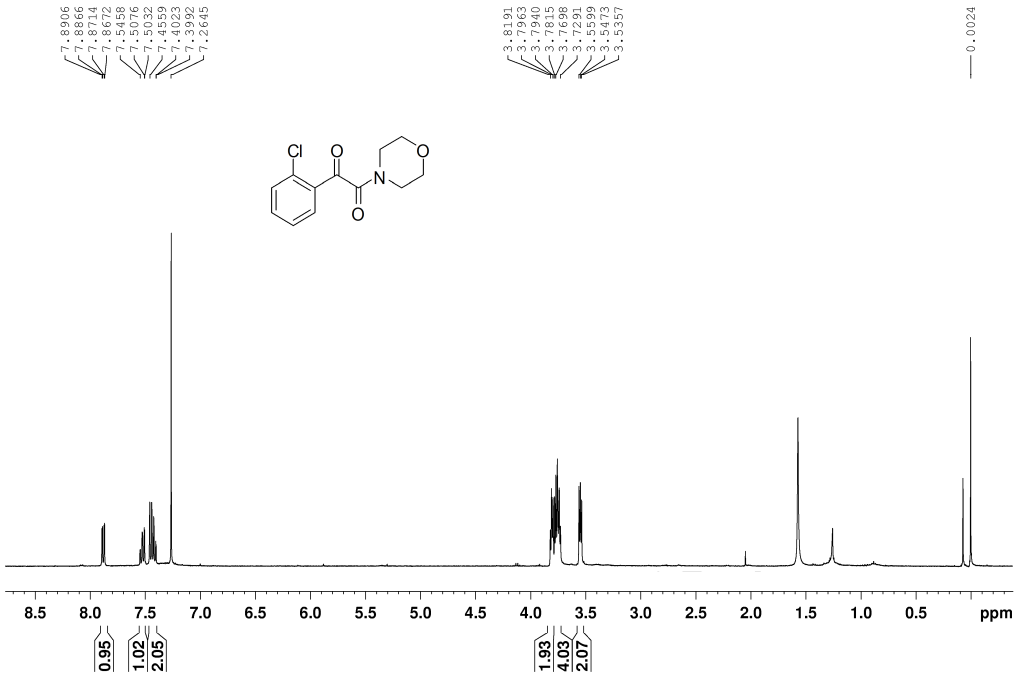

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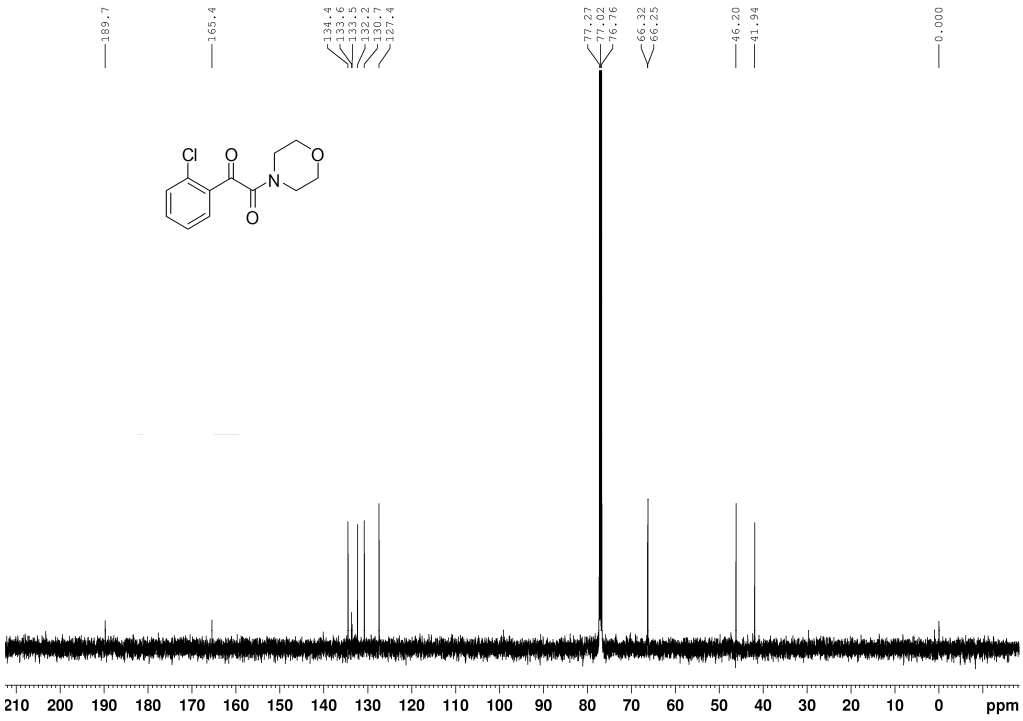

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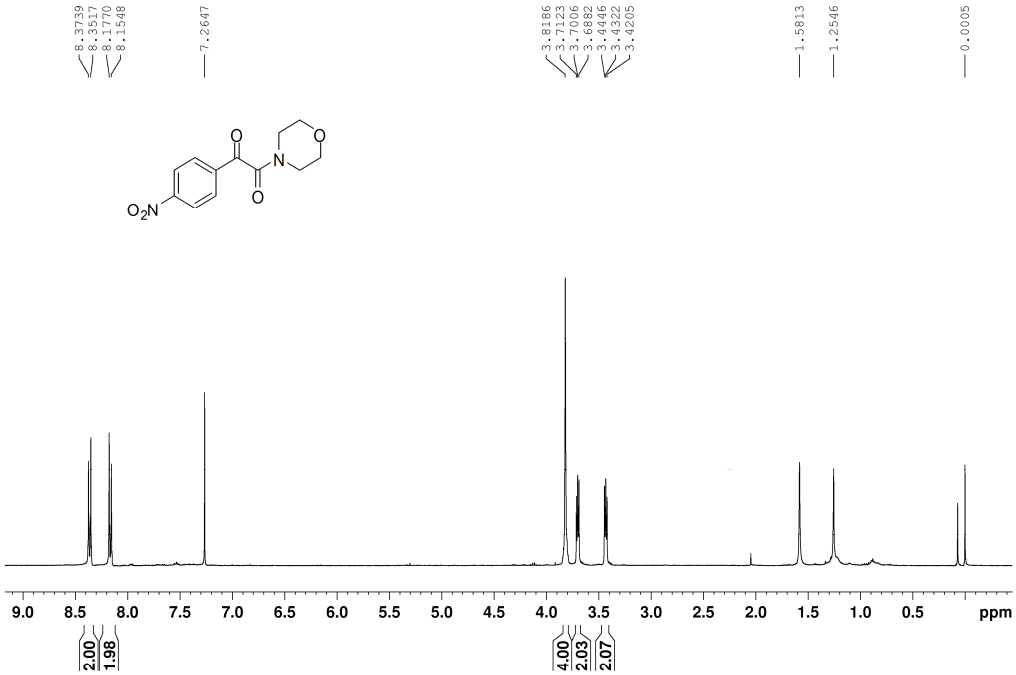

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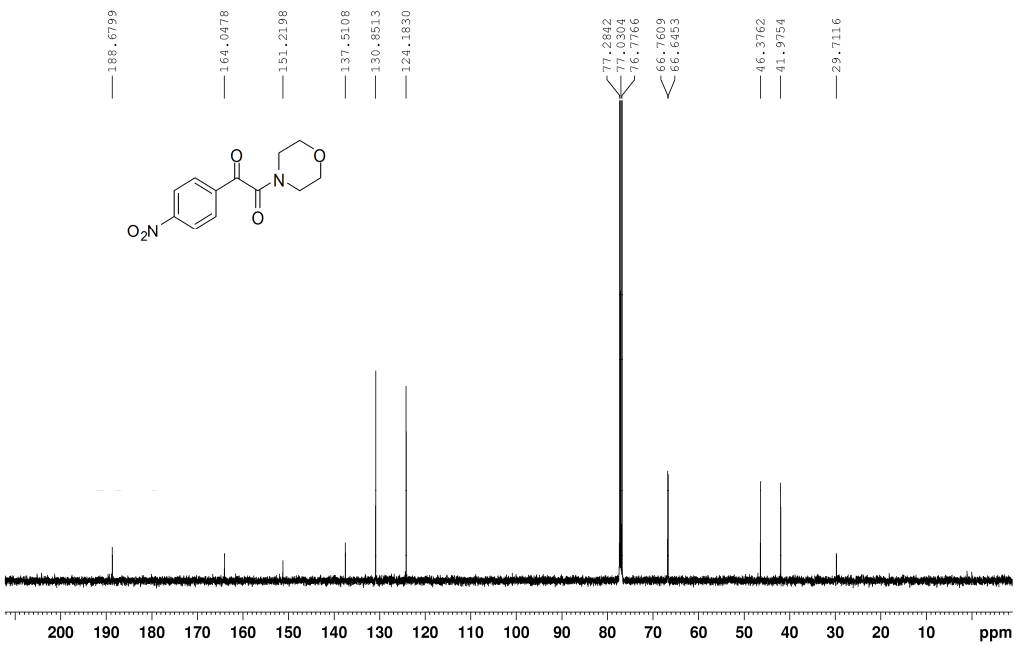

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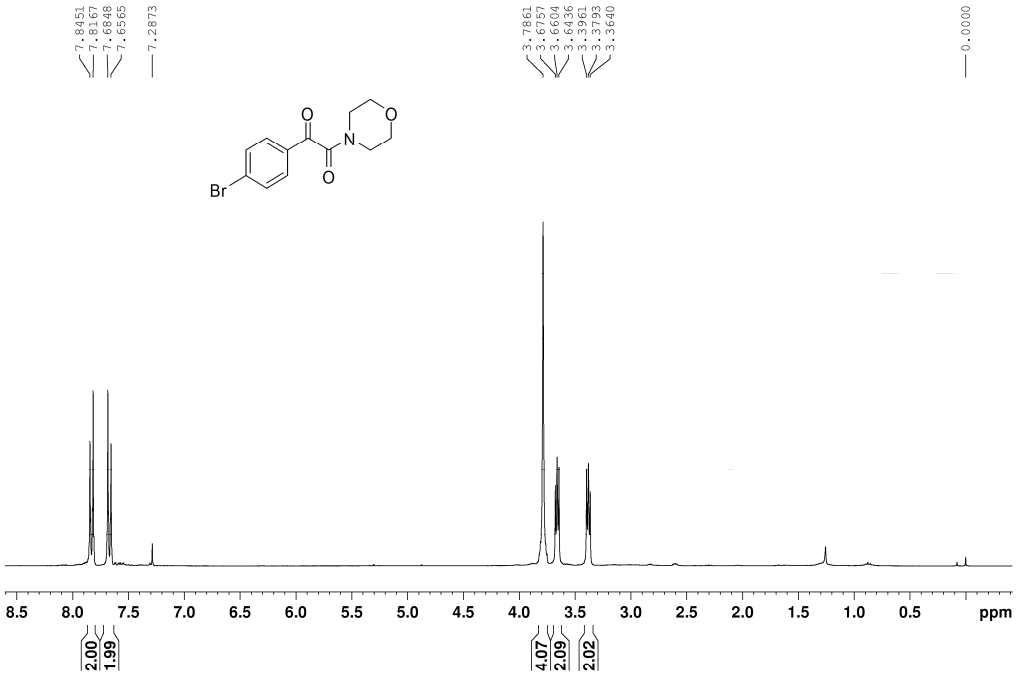

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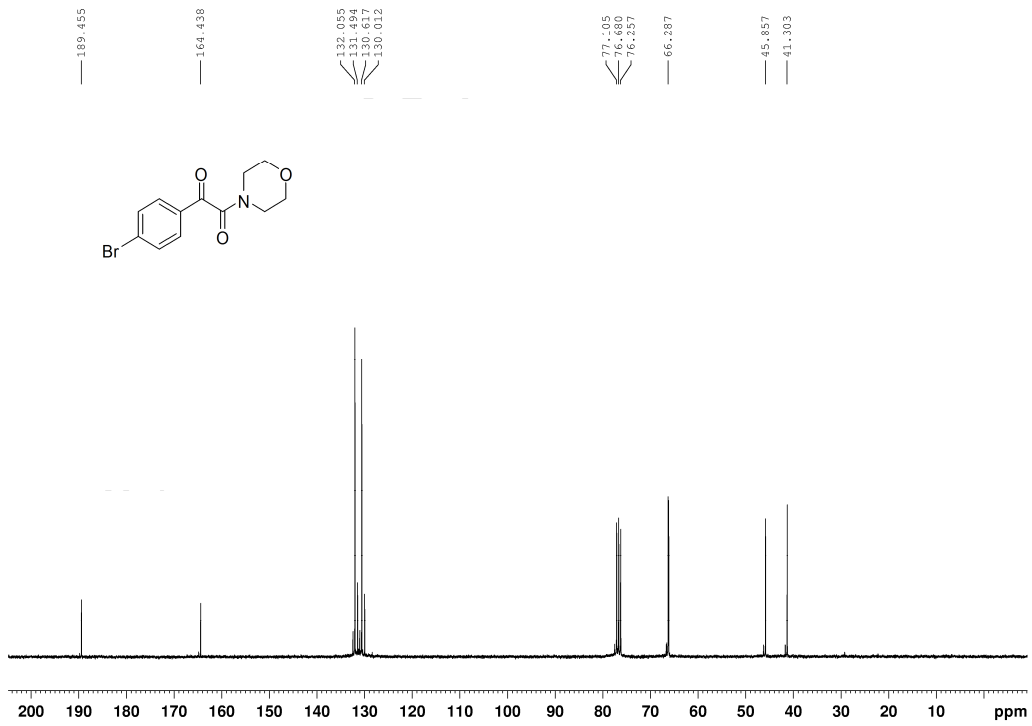

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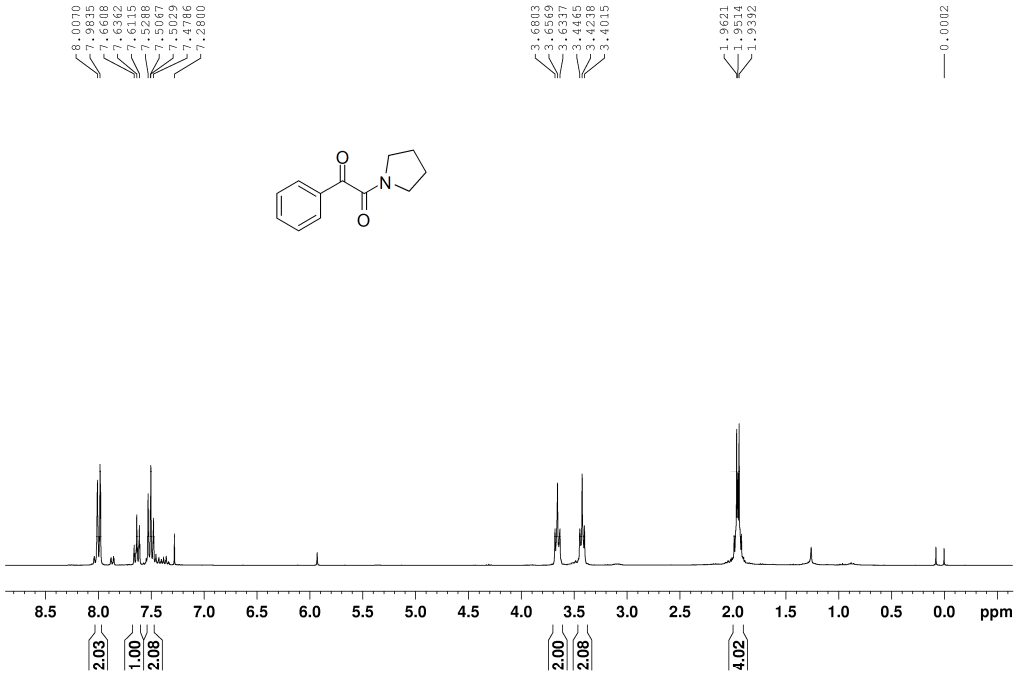

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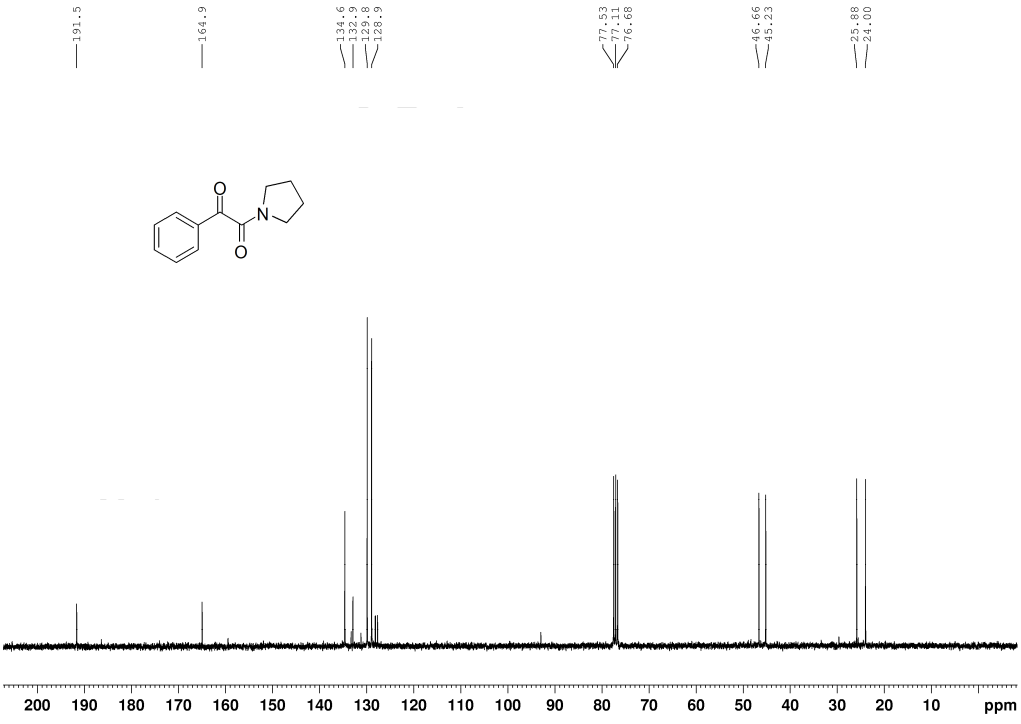

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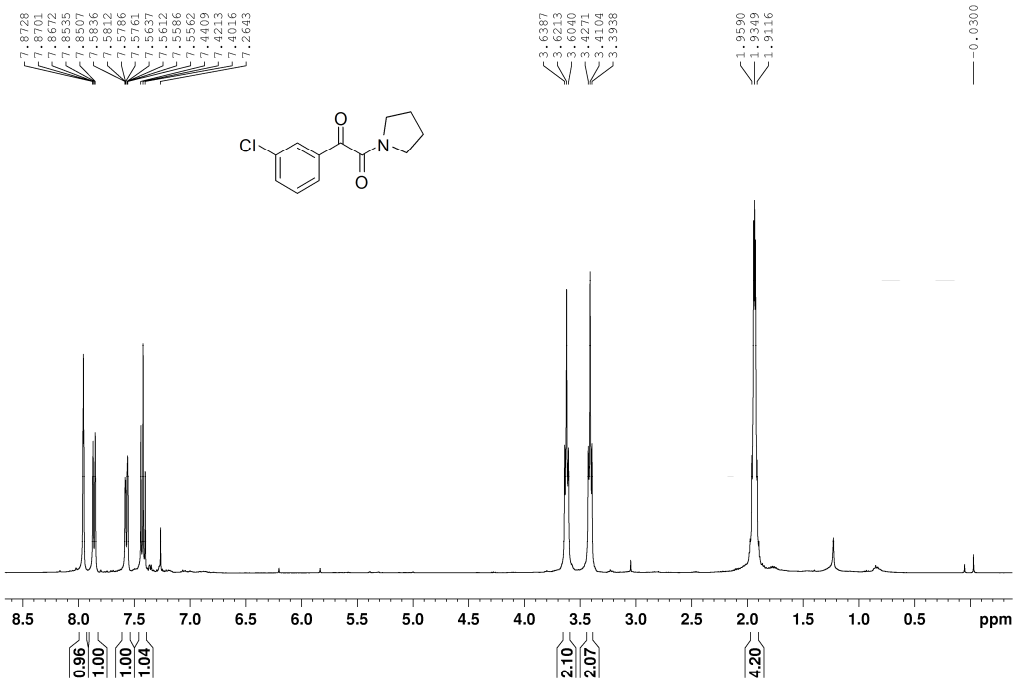
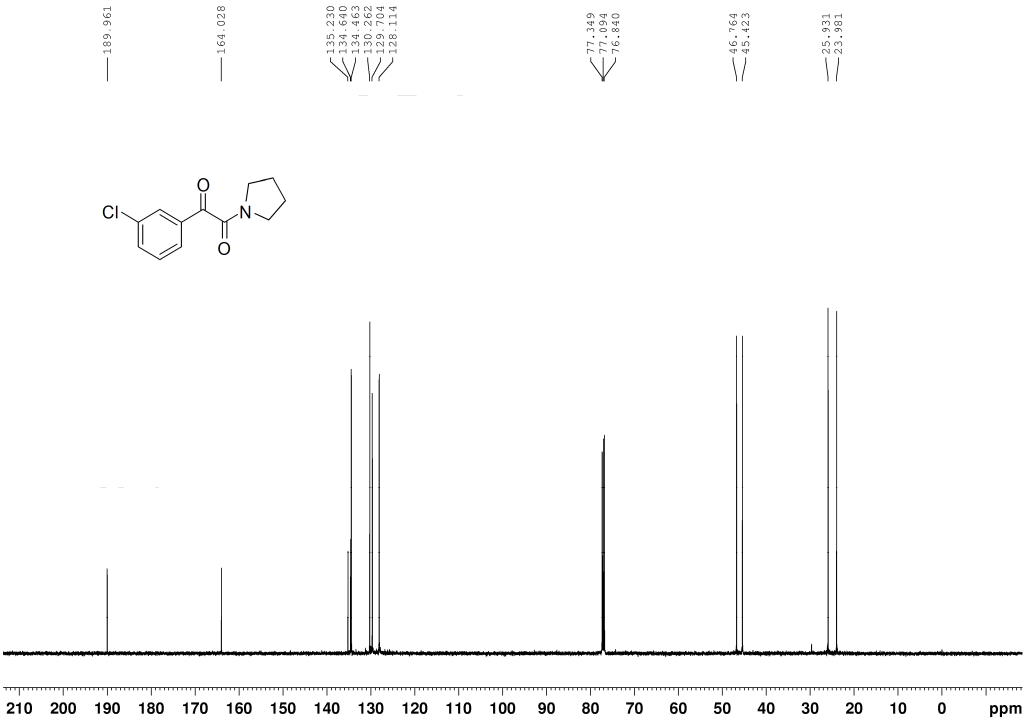
3n:

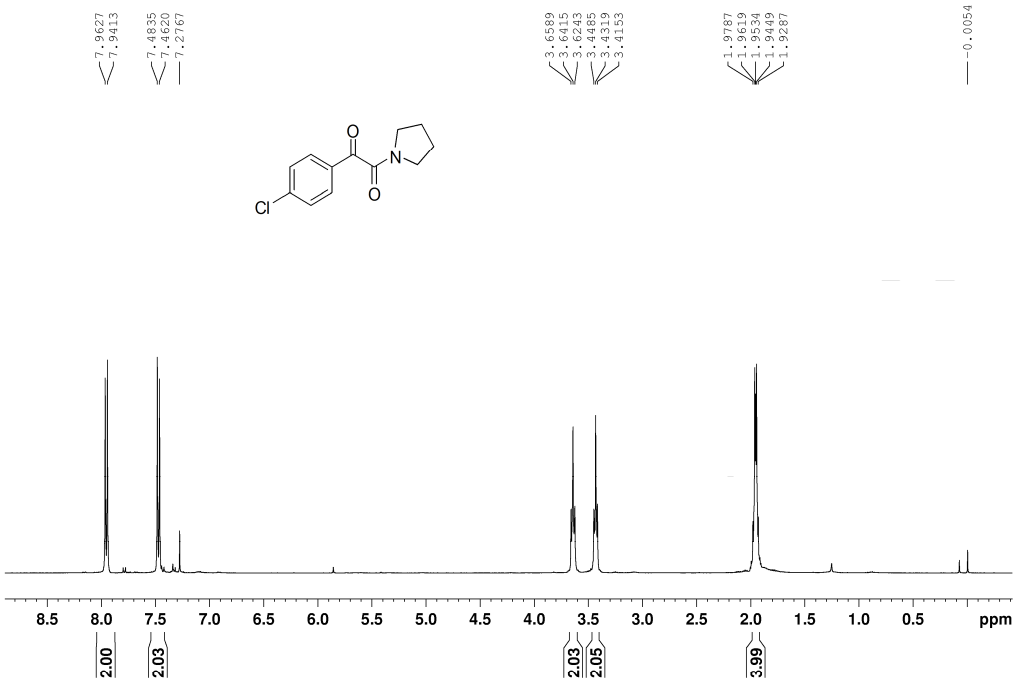


^{1}H NMR (400 MHz, $CDCl_3$) of **3n**.

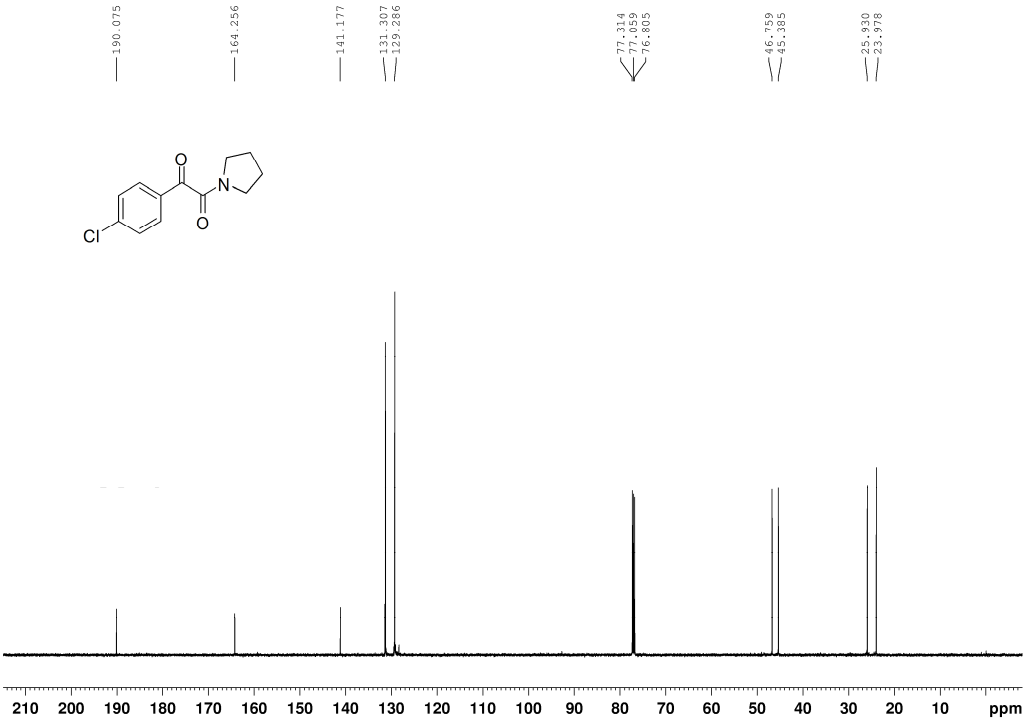


^{13}C NMR (125 MHz, $CDCl_3$) of **3n**.

3o:

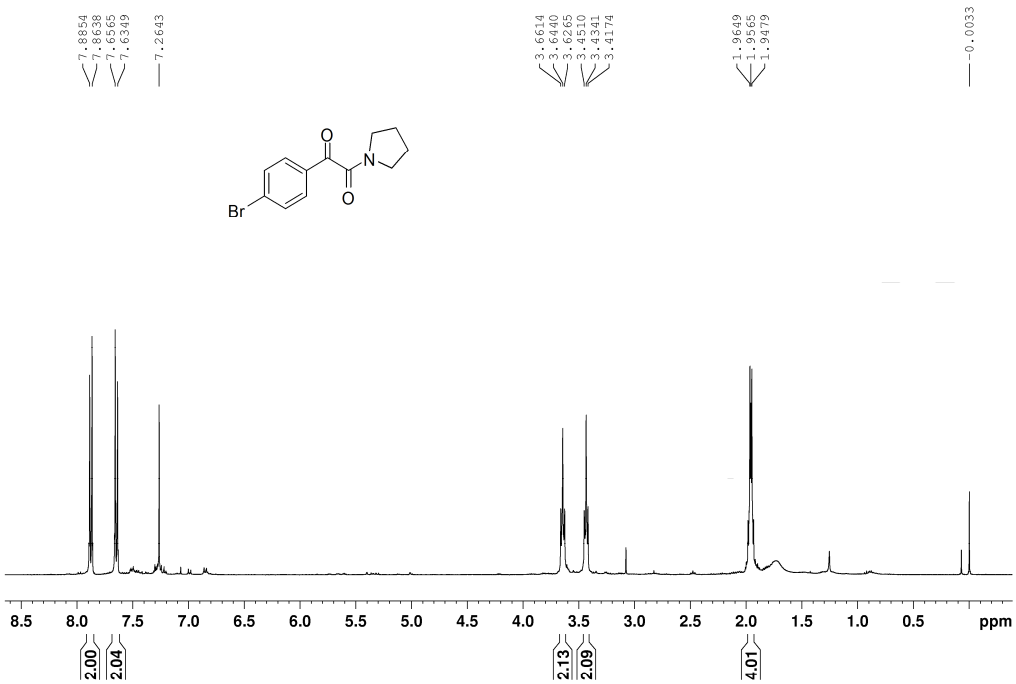


^{1}H NMR (400 MHz, $CDCl_3$) of **3o**.

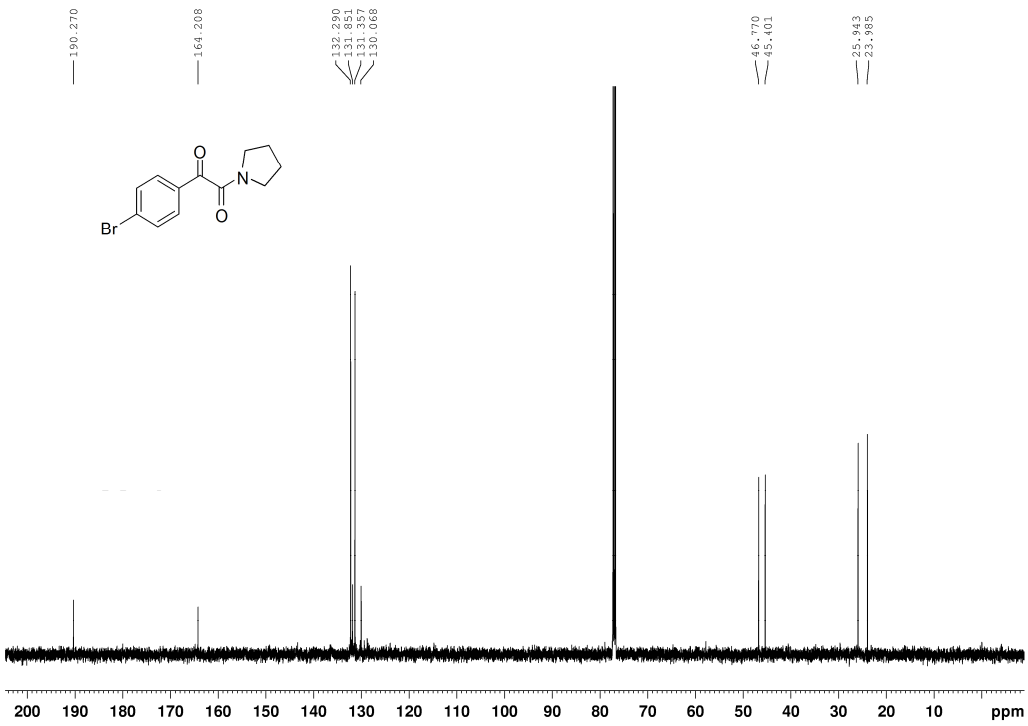


^{13}C NMR (125 MHz, $CDCl_3$) of **3o**.

3p:

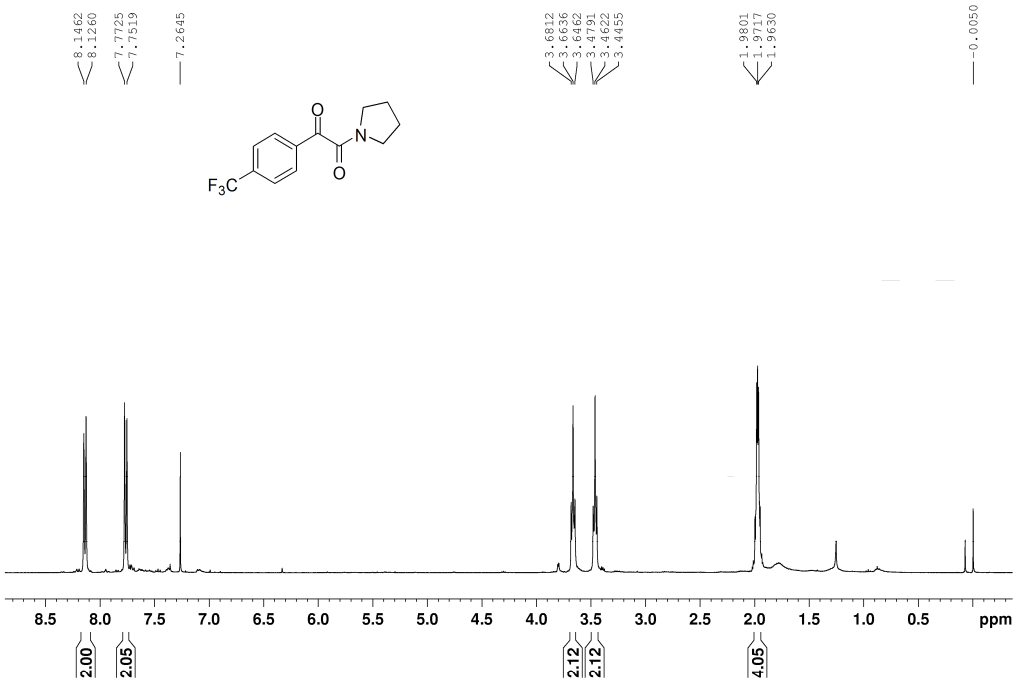


^{1}H NMR (400 MHz, $CDCl_3$) of **3p**.

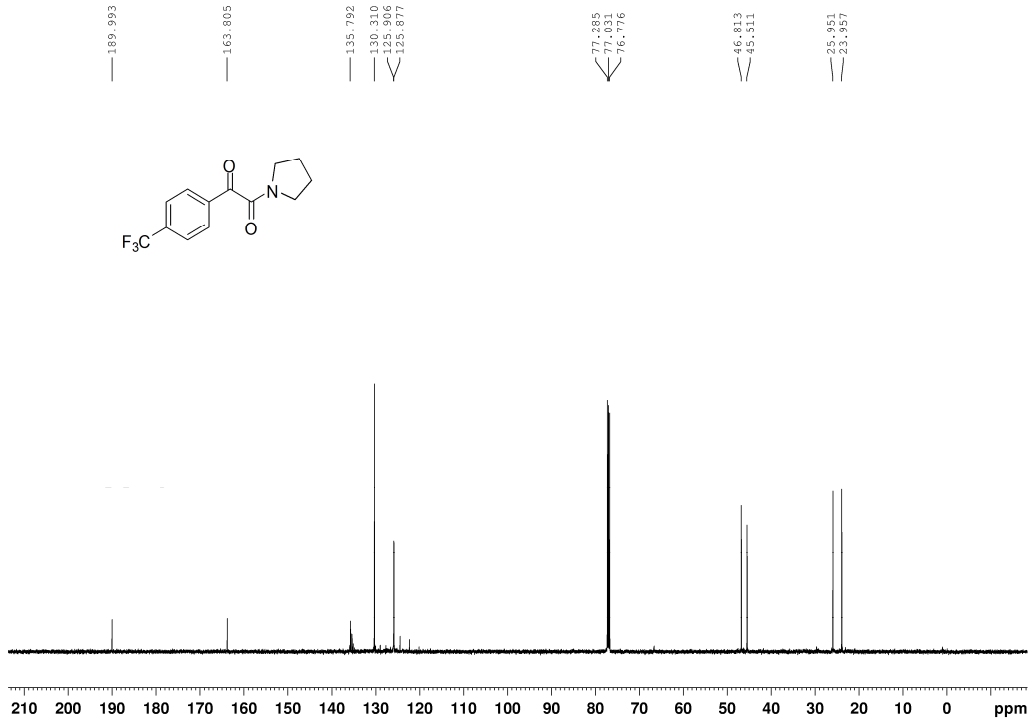


^{13}C NMR (125 MHz, $CDCl_3$) of **3p**.

3q:

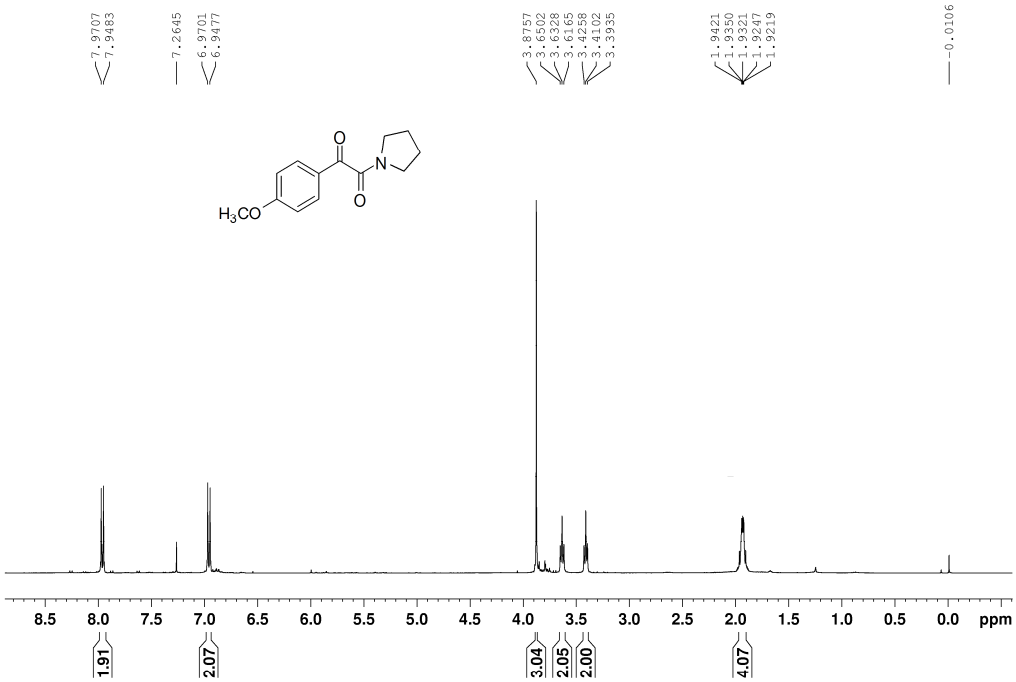


^{1}H NMR (400 MHz, $CDCl_3$) of **3q**.

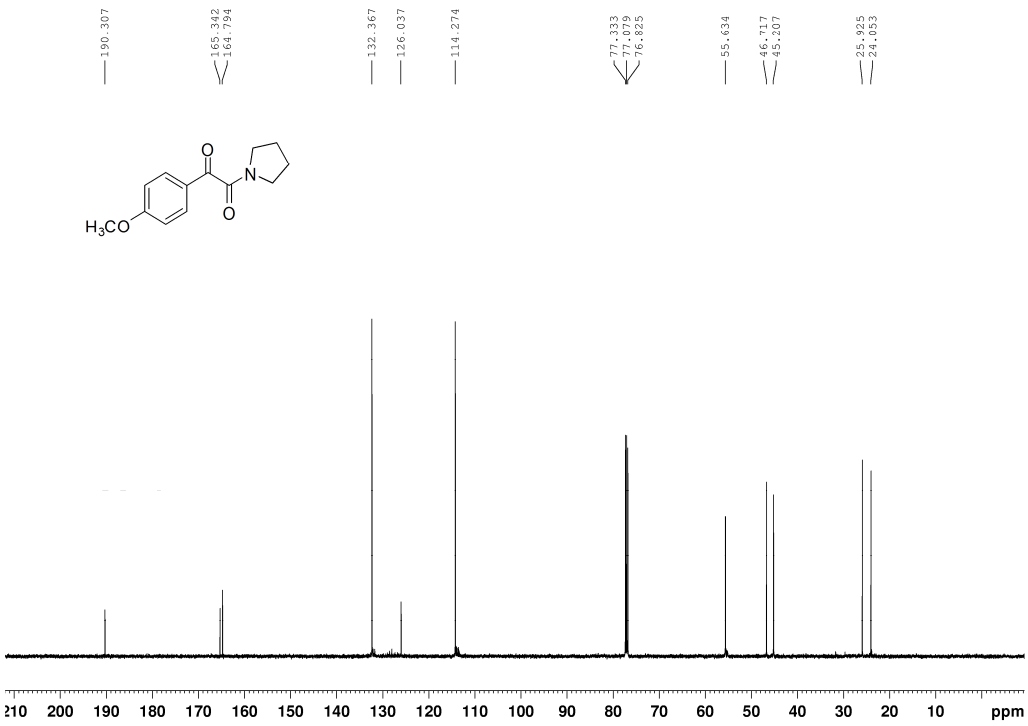


^{13}C NMR (125 MHz, $CDCl_3$) of **3q**.

3r

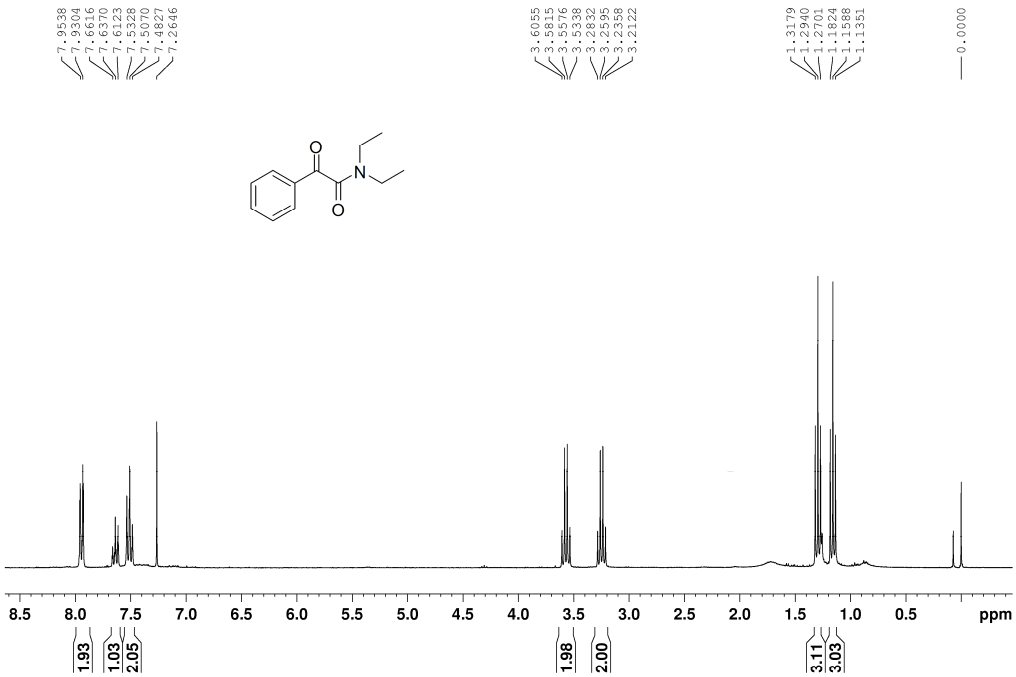


^{1}H NMR (400 MHz, $CDCl_3$) of **3r**.

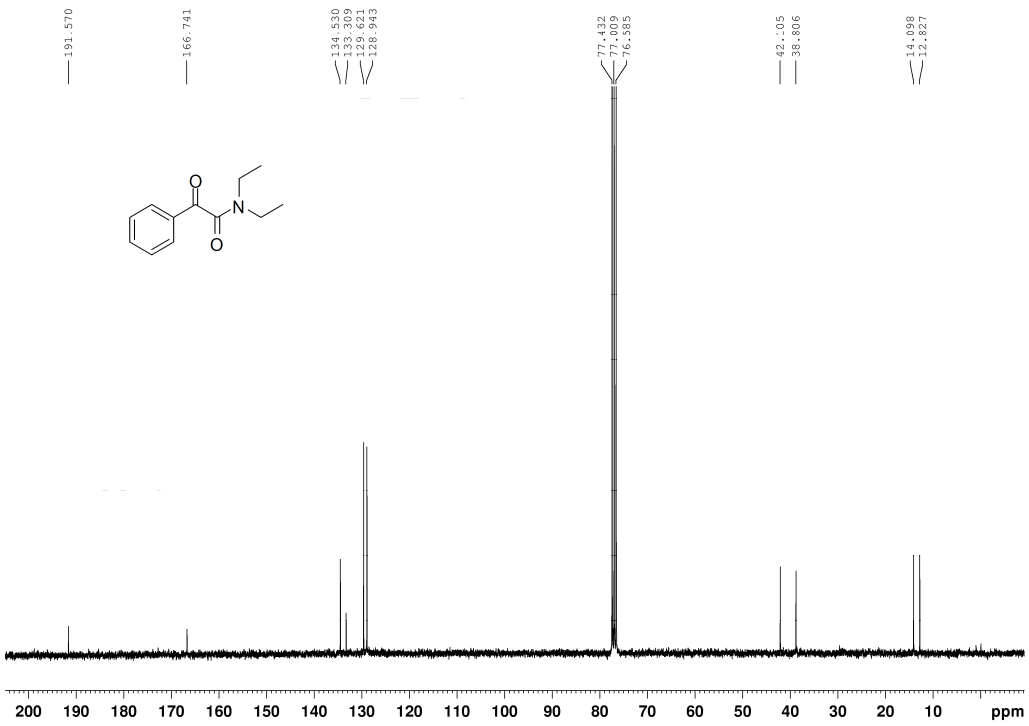


^{13}C NMR (125 MHz, $CDCl_3$) of **3r**.

3s:

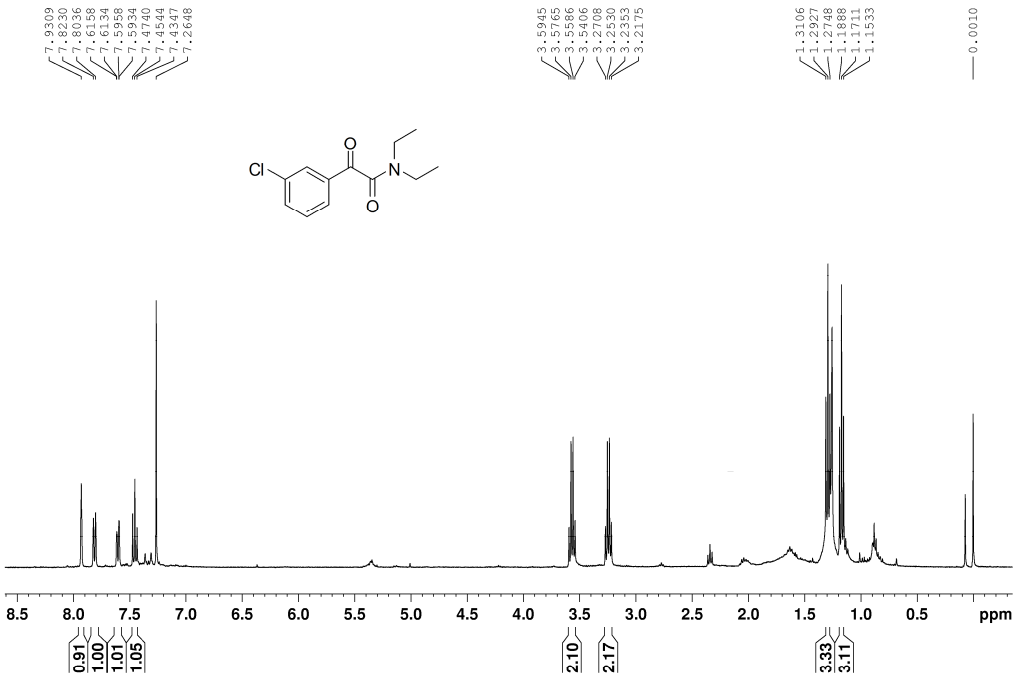


^{1}H NMR (300 MHz, $CDCl_3$) of **3s**.

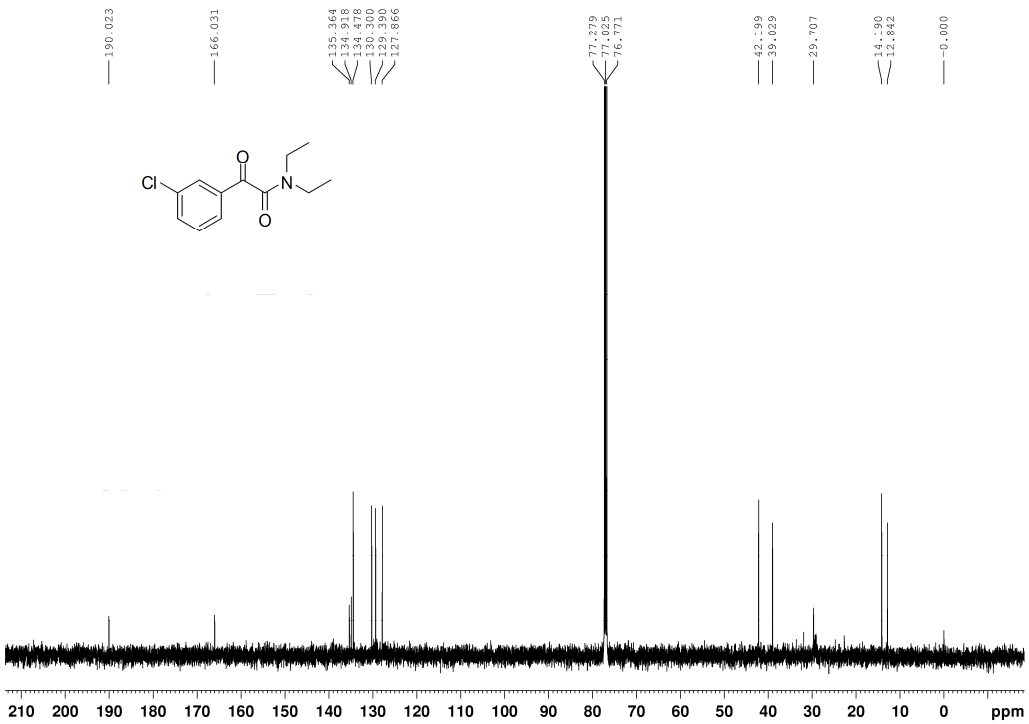


^{13}C NMR (75 MHz, $CDCl_3$) of **3s**.

3t:

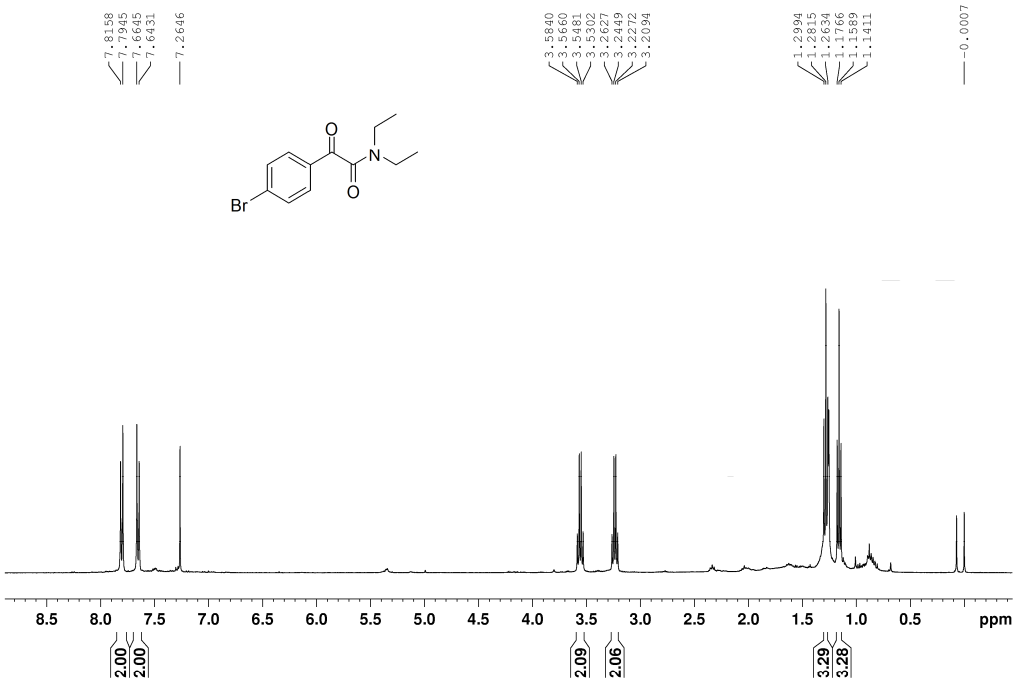


^{1}H NMR (400 MHz, $CDCl_3$) of **3t**.

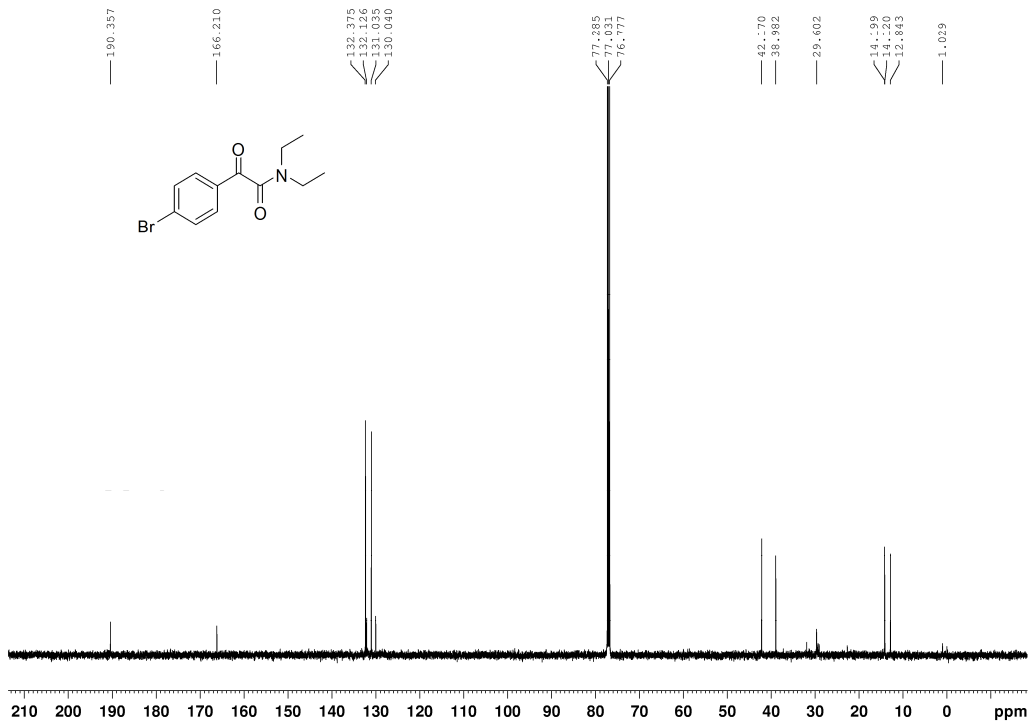


^{13}C NMR (75 MHz, $CDCl_3$) of **3t**.

3u:

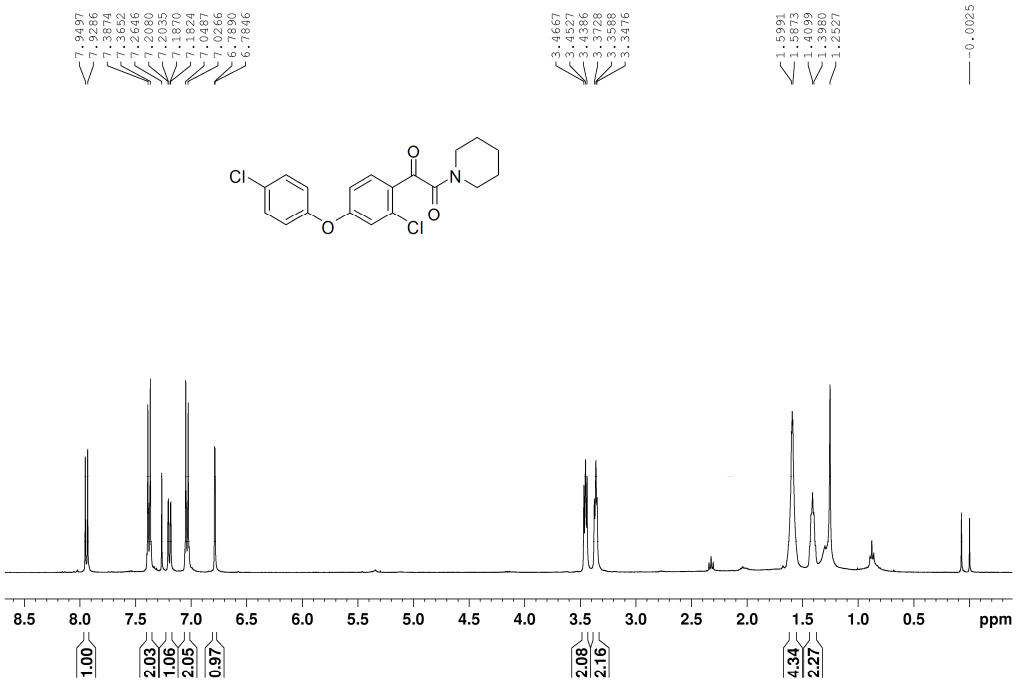


^{1}H NMR (400 MHz, $CDCl_3$) of **3u**.

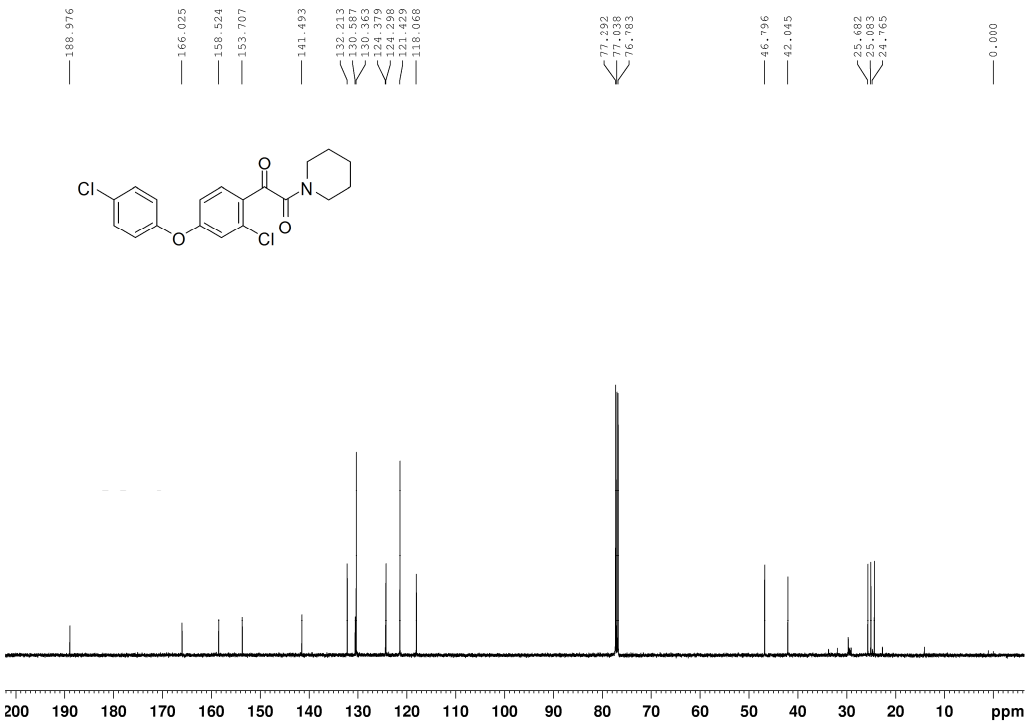


^{13}C NMR (125 MHz, $CDCl_3$) of **3u**.

3v:

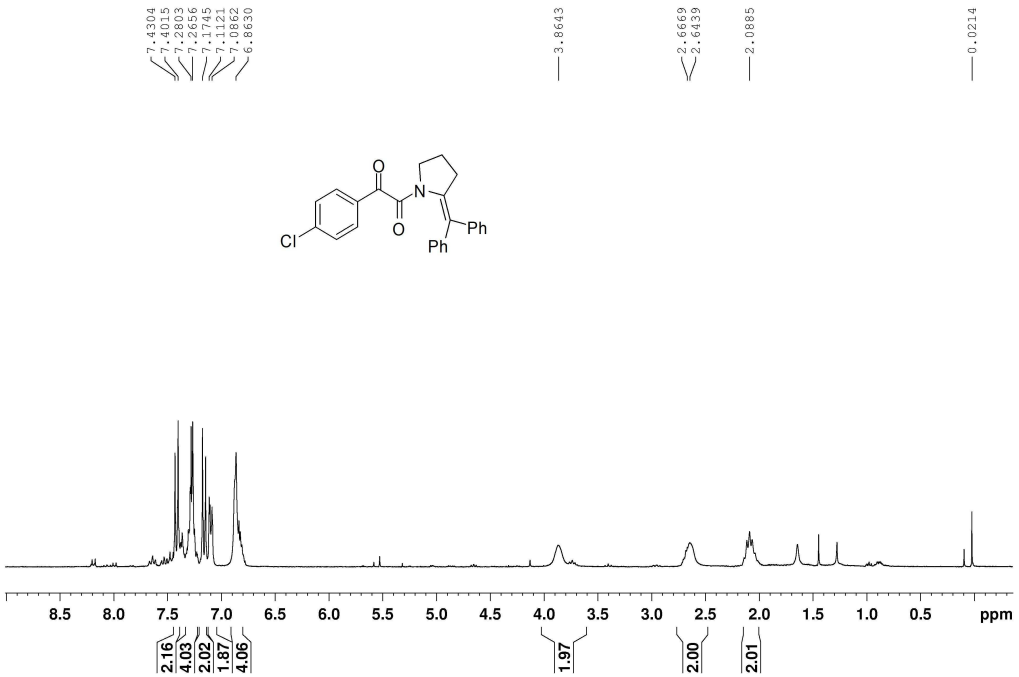


^{1}H NMR (400 MHz, $CDCl_3$) of **3v**.

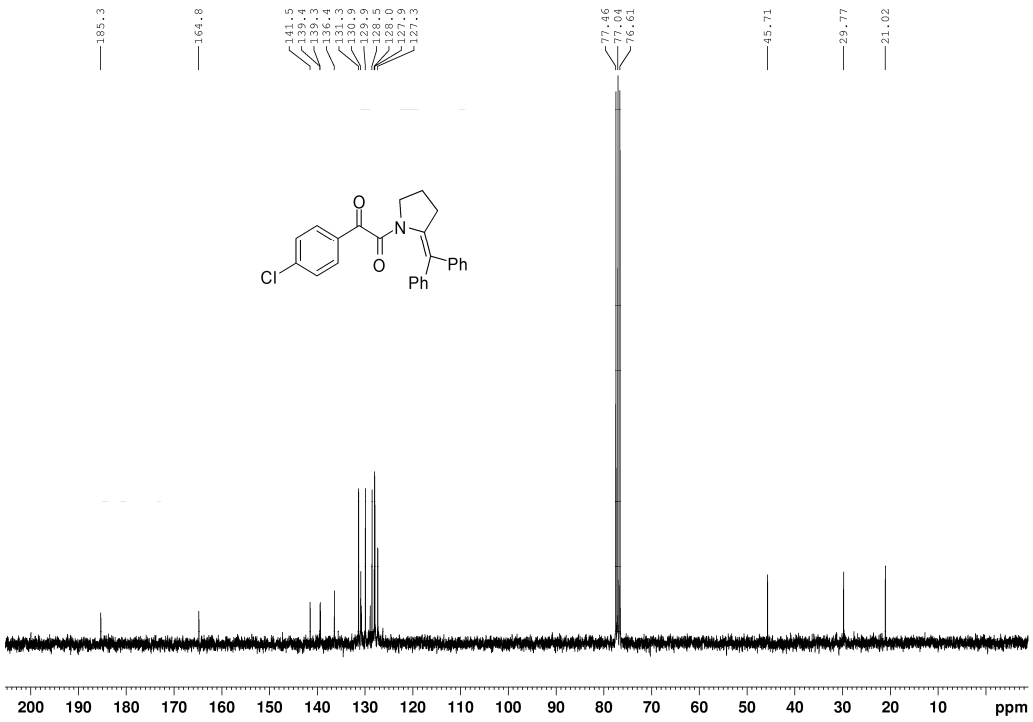


^{13}C NMR (125 MHz, $CDCl_3$) of **3v**.

3x:



^{1}H NMR (400 MHz, $CDCl_3$) of **3x**.



^{13}C NMR (125 MHz, $CDCl_3$) of **3x**.