Efficient Synthesis of β-Acetamido Ketones Catalyzed by Cobalt Sulfate Heptahydrate Under Ultrasound Irradiation

Bao-Hua Chen[a,b,c], Ji-Tai Li*[,a], Guo-Feng Chen[a] and Ya-Li Song[b,c]

[a]*College of Chemistry and Environmental Science, Hebei University, Baoding 071002, P.R. China*

[b]*College of Pharmaceutical Sciences, Hebei University, Baoding 071002, P.R. China*

[c]*Key Laboratory of Pharmaceutical Quality Control of Hebei Province, Baoding 071002, P.R. China*

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Abstract: Ultrasound-promoted synthesis of β-acetamido ketones catalyzed by cobalt sulfate heptahydrate *via* one-pot multi-component reaction coupling of aromatic aldehyde, acetophenone and acetyl chloride in acetonitrile was carried out in excellent yields at 25-28 ^{o}C, providing an efficient synthesis of these compounds. The use of ultrasound increased the rate of reactions compared with reactions under reflux condition.

Keywords: β-Acetamido ketones, cobalt sulfate heptahydrate, condensation, synthesis, ultrasound irradiation.

INTRODUCTION

Multi-component reactions (MCRs) have emerged as a useful tool in modern synthetic organic chemistry and proved to be remarkably successful in generating molecular complexity in a single synthetic operation. Through MCRs, complicated molecules can be achieved in a very fast, efficient and time saving manner without the isolation of any intermediate. So the discovery of novel MCRs is of great interest for the chemists owing to their exceptional synthetic efficiency [1].

β-Acetamido ketones are valuable intermediates in organic synthesis and medicinal chemistry, and their skeletons exist in a large number of biologically or pharmacologically important compounds. For example, β-acetamido ketones can be used in the preparation of 1,3-aminoalcohols, β-amino acids, and various bioactive molecules such as antibiotic nikkomycin or neopolyoximes [2]. Therefore, the synthesis of β-acetamido ketones has gained considerable attention in recent years. Several strategies have been developed for the preparation of β-acetamido ketones, and one of them is the Dakin-West reaction using α-amino acids and acetic anhydride [3]. Later on, Iqbal *et al*. proposed another procedure for the formation of these compounds through the condensation of aromatic aldehyde, acetophenone and acetyl chloride in acetonitrile catalyzed by $CoCl_2$ or montmorillonite K-10 using one-pot multi-component reaction [4]. Subsequently, new and efficient methods for this multi-component reaction were investigated.

The one-pot synthesis of the title compounds from aromatic aldehyde, acetophenone, acetyl chloride and acetonitrile catalyzed by various catalysts, such as $CeCl_3$•$7H_2O$ [5], $FeCl_3$•$6H_2O$ [6], $ZrOCl_2$•$8H_2O$ [7], ZnO [8], $Mg(HSO_4)_2$ [9], $SiCl_4$-$ZnCl_2$ [10], $Cu(BF_4)_2$ [11], heteropoly acids [12], Amberlyst-15 [13], silica sulfuric acid [14], ionic liquid [15] and some other catalysts [16], has been reported. In spite of their potential utility, some of the reported methods suffer from draw-backs such as low yields, longer reaction time, expensive catalyst, requiring an inert atmosphere and harsh reaction conditions. Therefore, the development of simple, efficient and general methodology for the reaction is still desirable.

Ultrasound irradiation has been considered as a clean and useful protocol and widely used in organic synthesis in the last decades [17]. The most important effect of ultrasound by passing its waves through a liquid medium is the generation of many cavities. This leads to development of high temperatures and high pressures within the cavities during their collapse. The success and advantages of sonochemical reactions include shorter reaction times, higher yields and milder reaction conditions in comparison to classical methods [18].

Cobalt sulfate heptahydrate ($CoSO_4$•$7H_2O$), as an inexpensive commercial available solid, is a water-soluble cobalt salt with a variety of industrial uses and easy to handle, and also used as an efficient catalyst in organic synthesis [19]. In this article, we report an efficient and convenient procedure for the synthesis of β-acetamido ketones using cobalt sulfate heptahydrate as catalyst by one-pot multi-component reaction under ultrasound irradiation (Scheme **1**).

RESULTS AND DISCUSSION

The synthesis of β-acetamido ketones using cobalt sulfate heptahydrate as catalyst was carried out by one-pot condensation of aromatic aldehyde, acetophenone and acetyl chloride in acetonitrile. To optimize the reaction conditions, the condensation of 4-chlorobenzaldehyde (**1b,** 2 mmol),

*Address correspondence to this author at the College of Chemistry and Environmental Science, Hebei University, Wusi East Road No.180, Baoding 071002, P.R. China. Tel: +86-312-5079361; Fax: +86-312-5079628; Email-address: lijitai@hbu.cn

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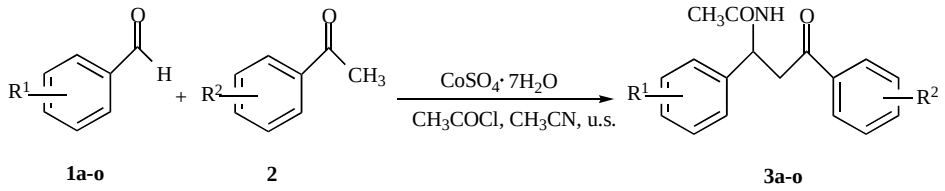

1a-o **2** **3a-o**

Scheme 1. One-pot synthesis of β-acetamido ketones catalyzed by cobalt sulfate heptahydrate.

acetophenone (**2b,** 2 mmol) and acetyl chloride (1 mL, 14 mmol) in acetonitrile (6 mL) was selected as model reaction.

As shown in Table **1**, without ultrasound under reflux condition by stirring alone for 8 h, the yields of the model reaction using various amount of $CoSO_4$•$7H_2O$ were obtained and compared. From the results, it can be concluded that the optimum amount of the catalyst was 30 mol% and the yield of **3b** was only 66% (Entry **3**).

Table 1. The Effect of Catalyst Amount on the Yield of 3b Under Reflux Condition without Ultrasound[a]

Entry	$CoSO_4$•$7H_2O$, mol%	Isolated yield, %
1	10	58
2	20	63
3	30	66
4	40	60
5	0	no product

[a]The reactions under reflux were performed for 8 h.

The effect of the amount of catalyst and reaction time on the yield of **3b** under ultrasound irradiation was also observed. As shown in Table **2**, the reaction was carried out using 20 mol% $CoSO_4$•$7H_2O$ at 25-28 ^oC for 2 h under ultrasound irradiation, **3b** can be obtained in 91% yield. It is clear that sonication can decrease the amount of catalyst, reduce the reaction time and improve the yield of **3b**. The effect of reaction temperature on the yield was not obvious, 25-28 ^oC was the appropriate temperature for the condensation.

From the results above, a typical experimental procedure was chosen as following: aromatic aldehyde (**1**, 2 mmol), acetophenone (**2,** 2 mmol), acetyl chloride (1 mL, 14 mmol), acetonitrile (6 mL) and $CoSO_4$•$7H_2O$ (0.4 mmol, 20 mol%). Using this system, we did a series of experiments to prepare β-acetamido ketones under ultrasound irradiation. The results are summarized in Table **3** (Method B).

In order to verify the effect of ultrasound irradiation, a series of experiments for the condensation of aromatic aldehydes, acetophenones, acetyl chloride and acetonitrile to form β-acetamido ketones **3**(**a-o**) were also completed under silent condition (Table **3**, method A). As shown in Table **3**, aromatic aldehydes or acetophenone in benzene ring with electron-rich and electron-poor substituents reacted to afford the corresponding β-acetamido ketones in high yields (86-91%) at 25-28 ^oC within 2 h under ultrasound irradiation. While in the absence of ultrasound the same reaction was refluxed for 8 h to provide the β-acetamido ketones in low yields (39-63%). It is apparently that ultrasound irradiation accelerated the condensation and improved the result.

Cavitation is the origin of sonochemistry. Cavitation is the production of microbubbles in a liquid when a large negative pressure is applied to it. These cavities can collapse violently with the release of large amounts of energy in and around these microbubbles. When the compression of bubbles occurs during cavitation, heating is more rapidly produced than thermal transport, creating a short lived localized hot spot, inducing molecular fragmentation, and highly reactive species are locally produced, which are responsible for the chemical effects of ultrasound on homogeneous solutions [21]. In some case, sonication can probably provide more efficient stirring. All of these can cause the reaction to take place rapidly.

In preliminary experiment, we tried to prepare **3a** according to the reported one-pot method in the literature [12b], but the result was poor, **3a** was afforded in 30% yield only at r.t. for 1 h. Then we decided to investigate the reaction catalyzed by cobalt sulfate heptahydrate under ultrasound. The yield and reaction time of **3a** catalyzed by

Table 2. The Effect of Reaction Conditions on the Yield of 3b Under Ultrasound Irradiation

Entry	$CoSO_4$•$7H_2O$, mol%	Temperature, ^oC	Time, h	Isolated yield, %
1	20	25-28	1	80
2	10	25-28	2	80
3	20	25-28	2	91
4	30	25-28	2	90
5	20	25-28	3	88
6	0	25-28	2	no product
7	20	38-40	2	91
8	20	18-20	2	89

Table 3. The Preparation of β-Acetamido Ketones Catalyzed by Cobalt Sulfate Heptahydrate Under Different Conditions[a]

Entry	R^1	R^2	Product	Isolated yield, %		m.p., °C [Lit.]
				A	B	
a	H	H	**3a**	51	90	101-103(102-104) [11]
b	4-Cl	H	**3b**	63	91	145-147(146-148) [11]
c	3-Cl	H	**3c**	45	88	103-105(105-108)[15]
d	2-NO_2	H	**3d**	40	88	185-187(186-188) [11]
e	3-NO_2	H	**3e**	39	86	138-140(139-140) [11]
f	4-NO_2	H	**3f**	44	89	147-149(148-150) [11]
g	4-CH_3O	H	**3g**	42	91	112-114(112-114) [11]
h	H	4-NO_2	**3h**	45	91	73-75(74-76) [12b]
i	4-Cl	4-NO_2	**3i**	48	91	118-120(116-118) [12b]
j	2-NO_2	4-NO_2	**3j**	43	88	215-217
k	4-NO_2	4-NO_2	**3k**	48	90	185-187(187-188) [12c]
l	4-OH	4-NO_2	**3l**	50	89	130-132
m	4-CH_3O	4-NO_2	**3m**	44	87	89-91(87-89) [12b]
n	H	4-CH_3O	**3n**	46	88	128-130(130) [7]
o	4-Cl	4-CH_3O	**3o**	43	89	59-61(59-61) [20]

[a]Method(A) refluxing for 8 h and (B) ultrasound irradiation at 25-28 °C for 2 h.

$CoSO_4$•$7H_2O$ under ultrasound were compared with various catalysts and conditions reported in some previous works. As shown in Table **4**, the yield of **3a** catalyzed by cobalt sulfate heptahydrate under ultrasound irradiation is, in general, similar or higher than those described in literatures (except for Entry **2**), and the reaction time is also reduced from 4-8 to 2 h (except for Entry **7**). We can deduce that the present method represented a better procedure for the synthesis of β-acetamido ketones.

In conclusion, we have developed an efficient procedure for the preparation of β-acetamido ketones *via* multi-component reaction in the presence of cobalt sulfate heptahydrate under ultrasound irradiation. This method has many advantages such as short reaction time, mild conditions and high yields, which make it a useful strategy for the synthesis of β-acetamido ketones.

EXPERIMENTAL SECTION

Melting points were uncorrected. The ^1H NMR and ^{13}C NMR spectra were measured on a Bruker AVANCE 600 (600 MHz) spectrometer using TMS as the internal standard and $CDCl_3$ as a solvent. MS were determined on Shimadzu GCMS-QP2010 spectrometer (ESI). Sonication was performed in Shanghai Branson-BUG40-06 ultrasonic cleaner (with a frequency of 40 kHz and a nominal power 250 W).

General Procedure for the Synthesis of β-Acetamido Ketones

A 25 mL round-bottomed flask was charged with aromatic aldehyde (**1**, 2 mmol), acetophenone (**2**, 2 mmol), acetyl chloride (1 mL, 14 mmol), acetonitrile (6 mL) and the

Table 4. Comparison Among Synthesis of 3a *via* One-Pot Reaction Using Various Catalysts

Entry	Catalyst	Temperature, °C	Time, h	Yield, %
1	$FeCl_3$•$6H_2O$	r. t.	8	88 [6]
2	$CeCl_3$•$7H_2O$	r. t.	7	96 [5]
3	$ZrOCl_2$•$8H_2O$	r. t.	5	90[7]
4	Selectfluor™	r. t.	4	74 [16d]
5	Mont. K10	70	7	80 [4c]
6	ZnO	80	6	90 [8]
7	Silica sulfuric acid	80	65 min	91 [14]
8	$CoSO_4$•$7H_2O$	25-28	2	90

given amount of $CoSO_4$•$7H_2O$ was added. The reaction flask was located in the cleaner bath, where the surface of reactants is slightly lower than the level of the water. Observation of the surface of the reaction solution during vertical adjustment of vessel depth will show the optimum position by the point at which maximum surface disturbance occurs. The reaction temperature was controlled by addition or removal of water from ultrasonic bath. The mixture was irradiated by ultrasound at 25-28 ^oC (bath temperature, the temperature inside the reactor was also the same) in the water bath of the ultrasonic cleaner for the period as indicated in Table **3**. The reaction was monitored by TLC (petroleum ether: ethyl acetate = 3:1, V/V). After the completion of the reaction, the mixture was poured into 50 mL water and neutralized by diluted sodium hydroxide solution. The solid was filtered and washed with water. The crude product was further purified by column chromatography on silica gel (200–300 mesh), eluted with petroleum ether (b.p. 60-90 ^oC) or a mixture of petroleum ether and ethyl acetate (1/2, V/V). The authenticity of the unknown compounds **3j** and **3l** were established by their spectral data of ^1H NMR, ^{13}C NMR and MS; the rest known compounds were established by their spectral data of ^1H NMR, ^{13}C NMR and their melting points compared with that reported in literatures.

Compound 3a

β-Acetamido-β-(phenyl)propiophenone, white solid. ^1H NMR: δ_H 1.80 (s, 3H, CH_3), 3.40 (dd, *J*=5.7 and 16.9 Hz, 1H, CH_2), 3.54 (dd, *J*=8.4 and 16.9 Hz, 1H, CH_2), 5.37-5.40 (m, 1H, CH), 6.71 (s, 1H, NH), 7.22-7.36 (m, 5H, Ar-H), 7.52 (t, *J*=15.4 Hz, 2H, Ar-H), 7.63 (t, *J*=14.8 Hz, 1H, Ar-H), 7.95 (d, *J*=7.4 Hz, 2H, Ar-H). ^{13}C NMR: δ 23.1, 45.1, 49.4, 127.1, 127.3, 128.5, 128.7, 129.2, 133.7, 137.0, 143.5, 168.8, 197.6.

Compound 3b

β-Acetamido-β-(4-chlorophenyl)propiophenone, white solid. ^1H NMR: δ_H 2.00 (s, 3H, CH_3), 3.42 (dd, *J*=5.8 and 17.1 Hz, 1H, CH_2), 3.73 (dd, *J*=4.9 and 17.1 Hz, 1H, CH_2), 5.53 (d, *J*=7.8 Hz, 1H, CH), 6.75 (d, *J*=7.4 Hz, 1H, NH), 7.27 (s, 4H, Ar-H), 7.46 (t, *J*=15.2 Hz, 2H, Ar-H), 7.58 (t, *J*=14.6 Hz, 1H, Ar-H), 7.89 (d, *J*=7.7 Hz, 2H, Ar-H). ^{13}C NMR: δ 23.4, 43.0, 49.3, 127.9, 128.1, 128.7, 128.8, 133.1, 133.7, 136.5, 139.6, 198.4.

Compound 3c

β-Acetamido-β-(3-chlorophenyl)propiophenone, white solid. ^1H NMR: δ_H 2.01 (s, 3H, CH_3), 3.41 (dd, *J*=5.6 and 17.2 Hz, 1H, CH_2), 3.71 (dd, *J*=5.2 and 17.2 Hz, 1H, CH_2), 5.53 (d, *J*=8.0 Hz, 1H, CH), 6.94 (s, 1H, NH), 7.18-7.23 (m, 3H, Ar-H), 7.33 (s, 1H, Ar-H), 7.45 (t, *J*=15.4 Hz, 2H, Ar-H), 7.57 (t, *J*=14.8 Hz, 1H, Ar-H), 7.89 (d, *J*=7.4 Hz, 2H, Ar-H). ^{13}C NMR: δ 23.3, 43.3, 49.4, 124.9, 126.7, 127.5, 128.1, 128.8, 129.9, 133.7, 134.4, 136.4, 143.5, 169.8, 198.0. *m/z* (ESI): 302 $[M]^+$, 324 $[M+Na]^+$.

Compound 3d

β-Acetamido-β-(2-nitrophenyl)propiophenone, white solid. ^1H NMR: δ_H 1.99 (s, 3H, CH_3), 3.62 (dd, *J*=5.4 and 16.7 Hz, 1H, CH_2), 3.71 (dd, *J*=6.4 and 16.8 Hz, 1H, CH_2), 5.94-5.97 (m, 1H, CH), 7.09 (s, 1H, NH), 7.39 (t, *J*=15.4 Hz, 1H, Ar-H), 7.45 (t, *J*=15.2 Hz, 2H, Ar-H), 7.57 (t, *J*=13.4 Hz, 2H, Ar-H), 7.70 (d, *J*=7.8 Hz, 1H, Ar-H), 7.92 (d, *J*=7.3 Hz, 2H, Ar-H), 7.94 (s, 1H, Ar-H). ^{13}C NMR: δ 23.3, 42.3, 47.4, 125.1, 128.3, 128.4, 128.8, 129.8, 133.5, 133.9, 136.3, 136.7, 148.4, 198.6.

Compound 3e

β-Acetamido-β-(3-nitrophenyl)propiophenone, white solid. ^1H NMR: δ_H1.99 (s, 3H, CH_3), 3.62 (dd, *J*=5.4 and 16.8 Hz, 1H, CH_2), 3.71 (dd, *J*=6.4 and 16.9 Hz, 1H, CH_2), 5.95 (d, *J*=6.5 Hz, 1H, CH), 7.06 (d, *J*=6.2 Hz, 1H, NH), 7.39 (t, *J*=15.2 Hz, 1H, Ar-H), 7.45 (t, *J*=15.2 Hz, 2H, Ar-H), 7.57 (t, *J*=11.3 Hz, 2H, Ar-H), 7.70 (d, *J*=7.8 Hz, 1H, Ar-H), 7.93 (t, *J*=14.5 Hz, 3H, Ar-H). ^{13}C NMR: δ 22.8, 44.0, 45.7, 124.3, 128.0, 128.1, 128.8, 128.9, 133.4, 133.5, 136.6, 138.6, 148.4, 169.6, 196.1.

Compound 3f

β-Acetamido-β-(4-nitrophenyl)propiophenone, white solid. ^1H NMR: δ_H 2.05 (s, 3H, CH_3), 3.49 (dd, *J*=5.6 and 17.5 Hz, 1H, CH_2), 3.79 (dd, *J*=5.2 and 17.5 Hz, 1H, CH_2), 5.63-5.67 (m, 1H, CH), 7.07 (d, *J*=8.1 Hz, 1H, NH), 7.45 (t, *J*=15.6 Hz, 2H, Ar-H), 7.52 (d, *J*=8.7 Hz, 2H, Ar-H), 7.59 (t, *J*=9.4 Hz, 1H, Ar-H), 7.88 (d, *J*=7.4 Hz, 2H, Ar-H), 8.13 (d, *J*=8.8 Hz, 2H, Ar-H). ^{13}C NMR: δ 23.3, 42.7, 49.2, 123.8, 127.4, 128.1, 128.9, 134.0, 136.2, 147.1, 148.7, 169.8, 198.0.

Compound 3g

β-Acetamido-β-(4-methoxyphenyl)propiophenone, white solid. ^1H NMR: δ_H 1.95 (s, 3H, CH_3), 3.36-3.40 (m, 1H, CH_2), 3.67-3.71 (m, 1H, CH_2), 3.73 (s, 3H, CH_3O), 5.50 (d, *J*=6.2 and 13.9 Hz, 1H, CH), 6.8 (d, *J*=7.8 Hz, 2H, Ar-H), 6.87-6.90 (m, 1H, NH), 7.24 (d, *J*=8.8 Hz, 2H, Ar-H), 7.42 (t, *J*=14.5 Hz, 2H, Ar-H), 7.54 (t, *J*=14.4 Hz, 1H, Ar-H), 7.89 (d, *J*=8.1 Hz, 2H, Ar-H). ^{13}C NMR: δ 23.4, 43.5, 49.6, 55.2, 114.0, 127.8, 128.2, 128.7, 133.2, 133.4, 136.7, 158.8, 169.5, 198.5.

Compound 3h

β-Acetamido-β-(phenyl)-4-nitropropiophenone, white solid. ^1H NMR: δ_H 2.01 (s, 3H, CH_3), 3.47 (dd, *J*=6.7 and 16.7 Hz, 1H, CH_2), 3.83 (dd, *J*=5.3 and 16.6 Hz, 1H, CH_2), 5.53 (dd, *J*=6.8 and 12.8 Hz, 1H, CH), 6.47 (d, *J*=7.0 Hz, 1H, NH), 7.26-7.33 (m, 5H, Ar-H), 8.06 (d, *J*=8.8 Hz, 2H, Ar-H), 8.28 (d, *J*=8.8 Hz, 2H, Ar-H). ^{13}C NMR: δ 23.4, 44.1, 50.3, 123.9, 126.6, 127.9, 128.9, 129.2, 140.2, 141.0, 150.5, 169.6, 196.8.

Compound 3i

β-Acetamido-β-(4-chlorophenyl)-4-nitropropiophenone, white solid. ^1H NMR: δ_H 2.01 (s, 3H, CH_3), 3.46 (dd, *J*=6.5 and 17.1 Hz, 1H, CH_2), 3.80 (dd, *J*=5.3 and 17.1 Hz, 1H, CH_2), 5.51 (dd, *J*=6.3 and 13.4 Hz, 1H, CH), 6.66 (d, *J*=7.8 Hz, 1H, NH), 7.28 (s, 4H, Ar-H), 8.06 (d, *J*=8.8 Hz, 2H, Ar-H), 8.28 (d, *J*=8.8 Hz, 2H, Ar-H). ^{13}C NMR: δ 23.3, 43.9, 49.4, 124.0, 128.0, 129.0, 129.2, 133.6, 138.9, 140.7, 150.5, 169.7, 196.5.

Compound 3j

β-Acetamido-β-(2-nitrophenyl)-4-nitropropiophenone, white solid. ^1H NMR: δ_H 1.78 (s, 3H, CH_3), 3.36 (d, *J*=14.1 Hz, 1H, CH_2), 3.51 (dd, *J*=3.3 and 18.0 Hz, 1H, CH_2), 3.75 (dd, *J*=9.8 and 18.0 Hz, 1H, CH), 5.74-5.77 (m, 1H, NH), 7.52-7.55 (m, 1H, Ar-H), 7.72-7.78 (m, 2H, Ar-H), 7.95 (d,

J=8.2 Hz, 1H, Ar-H), 8.24 (d, *J*=8.8 Hz, 2H, Ar-H), 8.35 (d, *J*=8.8 Hz, 2H, Ar-H). ^{13}C NMR: δ 22.9, 44.7, 45.1, 124.3, 124.6, 128.8, 129.0, 130.0, 134.1, 138.5, 141.3, 148.5, 150.5, 169.3, 195.9. *m/z* (ESI): 358 $[M]^+$.

Compound 3k

β-Acetamido-β-(4-nitrophenyl)-4-nitropropiophenone, white solid. ^{1}H NMR: δ_H 2.08 (s, 3H, CH_3), 3.57 (dd, *J*=5.9 and 17.7 Hz, 1H, CH_2), 3.88 (dd, *J*=5.0 and 17.7 Hz, 1H, CH_2), 5.65-5.69 (m, 1H, CH), 6.66 (d, *J*=8.0 Hz, 1H, NH), 7.54 (d, *J*=8.7 Hz, 2H, Ar-H), 8.07 (d, *J*=8.8 Hz, 2H, Ar-H), 8.18 (d, *J*=7.2 Hz, 2H, Ar-H), 8.31 (d, *J*=8.8 Hz, 2H, Ar-H). ^{13}C NMR: δ 23.4, 43.4, 49.2, 124.0, 124.1, 127.5, 129.2, 140.4, 147.3, 147.8, 150.8, 169.7, 196.3.

Compound 3l

β-Acetamido-β-(4-hydroxyphenyl)-4-nitropropiophenone, white solid. ^{1}H NMR: δ_H 1.92 (s, 3H, CH_3), 3.45 (dd, *J*=6.2 and 16.9 Hz, 1H, CH_2), 3.72 (dd, *J*=7.5 and 16.8 Hz, 1H, CH_2), 5.37-5.54 (m, 1H, CH), 6.75 (d, *J*=8.4 Hz, 1H, NH), 7.02-7.96 (m, 4H, Ar-H), 8.13-8.32 (m, 5H, Ar-H+OH). ^{13}C NMR: δ 22.0, 40.1, 47.1, 115.5, 121.7, 123.8, 128.0, 129.4, 139.3, 141.2, 150.1, 169.4, 196.1. *m/z* (ESI): 329 $[M]^+$.

Compound 3m

β-Acetamido-β-(4-methoxyphenyl)-4-nitropropiophenone, white solid. ^{1}H NMR: δ_H1.99 (s, 3H, CH_3), 3.44 (dd, *J*=7.1 and 16.5 Hz, 1H, CH_2), 3.76 (s, 3H, CH_3O), 3.80 (dd, *J*=5.4 and 16.4 Hz, 1H, CH_2), 5.46 (dd, *J*=7.2 and 12.8 Hz, 1H, CH), 6.50 (d, *J*=7.6 Hz, 1H, NH), 6.84 (d, *J*=8.7 Hz, 2H, Ar-H), 7.24 (d, *J*=8.7 Hz, 2H, Ar-H), 8.07 (d, *J*=7.0 Hz, 2H, Ar-H), 8.27 (d, *J*=7.0 Hz, 2H, Ar-H). ^{13}C NMR: δ 23.4, 44.4, 49.9, 55.3, 114.2, 123.9, 127.9, 129.2, 132.3, 141.1, 150.4, 159.2, 169.6, 196.8. *m/z* (ESI): 343 $[M]^+$.

Compound 3n

β-Acetamido-β-(phenyl)-4-methoxypropiophenone, white solid. ^{1}H NMR: δ_H1.99 (s, 3H, CH_3), 3.34 (dd, *J*=5.8 and 16.6 Hz, 1H, CH_2), 3.66 (dd, *J*=5.2 and 16.6 Hz, 1H, CH_2), 3.85 (d, *J*=10.5 Hz, 3H, CH_3O), 5.54 (d, *J*=6.8 Hz, 1H, CH), 6.89-6.95 (m, 4H, Ar-H), 7.21 (d, *J*=7.0 Hz, 1H, NH), 7.32 (d, *J*=7.4 Hz, 2H, Ar-H), 7.90 (dd, *J*=8.5 and 31.9 Hz, 3H, Ar-H). ^{13}C NMR: δ 23.4, 26.4, 42.9, 50.1, 55.5, 113.7, 113.9, 126.5, 127.3, 128.6, 129.8, 130.5, 130.6, 141.2, 163.8, 169.5, 197.1.

Compound 3o

β-Acetamido-β-(4-chlorophenyl)-4-methoxypropiophenone, white solid. ^{1}H NMR: δ_H1.97 (s, 3H, CH_3), 3.31 (dd, *J*=6.0 and 16.8 Hz, 1H, CH_2), 3.63 (dd, *J*=5.4 and 16.8 Hz, 1H, CH_2), 3.84 (s, 3H, CH_3O), 5.49 (dd, *J*=5.7 and 13.8 Hz, 1H, CH), 6.89 (d, *J*=8.9 Hz, 2H, Ar-H), 7.16 (t, *J*=14.5 Hz, 1H, NH), 7.24 (dd, *J*=8.6 and 15.8 Hz, 4H, Ar-H), 7.86 (d, *J*=8.9 Hz, 2H, Ar-H). ^{13}C NMR: δ 23.3, 42.7, 49.4, 55.5, 113.9, 128.0, 128.7, 129.6, 130.5, 133.0, 140.0, 163.9, 169.7, 196.7.

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