Res Chem Intermed (2011) 37:811–820
DOI 10.1007/s11164-011-0288-9

# One-pot synthesis of β-acetamido-β-arylpropiophenone employing trifluoroacetic acid as an efficient catalyst

**Xing-Hua Zhang · Li Fan · Jian Liu · Da-Cheng Yang**

Received: 8 December 2010 / Accepted: 17 January 2011 / Published online: 2 February 2011


**Abstract** Trifluoroacetic acid as an efficient catalyst promoting the Dakin–West reaction at ambient temperature is reported for the first time in this paper. A few efficacious auxiliary catalysts were also developed for the Dakin–West reaction. A variety of substituted aryl aldehydes and aryl ketones were found to be applicable to the preparation of some new β-acetamido-β-arylpropiophenones. This procedure has several advantages such as high yields, short reaction time, and smaller amount (0.30 mol%) of catalyst.

**Keywords** Trifluoroacetic acid · β-Acetamido ketones · One-pot · 3-Nitroacetophenone

## Introduction

β-Acetamido ketones are versatile intermediates in that their skeletons exist in a number of biologically or pharmacologically important compounds [1, 2]. Examples include the preparation of 1,3-amino alcohols [3, 4], β-amino acids [5], γ-lactams [6], and antibiotic nikkomycins or neopolyoxines [7, 8]. Moreover, it has recently been reported that β-acetamido ketones can act as α-glucosidase inhibitors [9]. This class of compounds is usually prepared by acylation of β-amino ketones [10], Michael addition of α,β-unsaturated ketones [11], or photoisomerization of phthalimides [12]. However, the most classical and facile method for the synthesis of β-acetamido ketones is the Dakin–West reaction. As a representative of multicomponent reactions, it plays a pivotal role in the building of complex organic molecules. A modified procedure involves a one-pot condensation of a ketone with an aldehyde and acetonitrile in the presence of acetyl chloride [13]. Several catalysts

X.-H. Zhang · L. Fan · J. Liu · D.-C. Yang (✉)
School of Chemistry and Chemical Engineering, Southwest University, Chongqing 400715, China
e-mail: hxydc@swu.edu.cn

have been exploited for the synthesis of $\beta$-acetamido ketones, for example silica sulfuric acid [14], $K_5CoW_{12}O_{40}\cdot 3H_2O$ [15], $H_6P_2W_{18}O_{62}$ [16], $ZrOCl_2\cdot 8H_2O$ [17], cyanuric chloride [18], selectfluor [19], $SnCl_2\cdot 2H_2O$ [20], $NaHSO_4\cdot H_2O$ [21], Montmorillonite K10 [22], etc. Although these catalysts are effective, they still suffer from disadvantages. Some are required in large amounts [14, 17, 20], some need a high temperature (80 °C) [14, 16, 21], some require column chromatography for separation of products [17, 20, 22], and others are expensive [15, 16], etc. Consequently, the development of new and efficient catalysts has become mandatory.

Trifluoroacetic acid (TFA) is a readily available organic acid. In recent years, TFA has been a useful intermediate in the synthesis of fluorine-containing organic compounds and an important starting material for fluoropolymers. TFA is also important in the synthesis of amino acids [23] and deprotection of peptides [24]. As a strongly acidic catalyst, TFA has been extensively used in alkylation [25], acylation of aromatic compounds, and olefin polymerization. As far as we are aware TFA has not been used for synthesis of $\beta$-acetamido ketones. Herein, it was our intent to utilize TFA in the Dakin–West reaction for the first time.

## Results and discussion

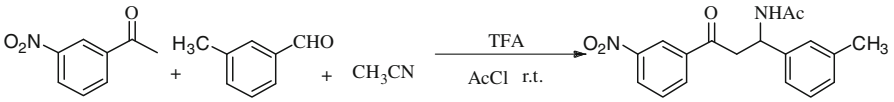
To optimize the reaction conditions, 3-nitroacteophenone (1 mmol), 4-methylbenzaldehyde (1 mmol), acetyl chloride (0.4 mL), and acetonitrile (3 mL) were selected as model substrates. Reactions were performed under different conditions to examine the effects of different amounts of TFA (Table 1). In the absence of catalyst, the $\beta$-acetamido ketone product was obtained only in 19.2% yield. When TFA was added as catalyst to the reaction mixture, the yield was over 80.0%. As can be seen from entry 3, the best yield was 98.6%, for reaction in the presence of 0.30 mol% TFA for 4.5 h. It is worth mentioning that the yield of product in the model reaction did not improve obviously with increasing of amount of TFA and the product could not be separated easily when the amount of TFA exceeded 0.30 mol%. So the optimized amount of catalyst was 0.30 mol% in Scheme 1.

To evaluate the effect of the solvent, the reaction was carried out under similar reaction conditions but using different organic solvents. Various solvents, for example methanol, chloroform, and dichloromethane, were used, as shown in Table 2. No reaction was observed in methanol whereas reaction in chloroform and dichloromethane was completed with moderate yield. Unexpectedly, the best result was obtained when acetonitrile was used as solvent. Therefore, all the following

**Table 1** Effect of the amount of TFA on the model reaction

| Entry | TFA (mol%) | Time (h) | Yield (%)[a] |
|---|---|---|---|
| **1** | 0.00 | 4.5 | 19.2 |
| **2** | 0.15 | 4.5 | 80.1 |
| **3** | 0.30 | 4.5 | 98.6 |
| **4** | 0.45 | 4.5 | 93.5 |

[a] Isolated yield




**Scheme 1** Model reaction

**Table 2** Effect of solvents on the model reaction

| Entry | Solvent | Time (h) | Yield (%)[a] |
|---|---|---|---|
| **1** | $CH_3OH$[b] | 4.5 | None |
| **2** | $CH_2Cl_2$[b] | 4.5 | 70.0 |
| **3** | $CHCl_3$[b] | 4.5 | 58.6 |
| **4** | $CH_3CN$[c] | 4.5 | 95.6 |

[a] Isolated yield

[b] $CH_3CN$ used was 0.041 g (1 mmol), solvent used was 3 mL

[c] $CH_3CN$ used was 3 mL

**Table 3** Effect of the acyl chlorides and sulfochlorides

| Entry | Auxiliary catalyst | Time (h) | Yield (%) |
|---|---|---|---|
| 1 | $CH_3COCl$ | 4.5 | 95.6[a] |
| 2 | $ClCH_2COCl$ | 4.5 | 60.0[b] |
| 3 | $ClCH_2CH_2COCl$ | 4.5 | 30.0[b] |
| 4 | $ClCH_2CH_2CH_2COCl$ | 4.5 | 85.0[b] |
| 5 | *p*-$CH_3C_6H_4SO_2Cl$ | 4.5 | None |
| 6 | *p*-$NO_2C_6H_4SO_2Cl$ | 4.5 | None |
| 7 | *p*-$CH_3CONHC_6H_4SO_2Cl$ | 4.5 | None |

[a] Isolated yield

[b] Not isolated yield

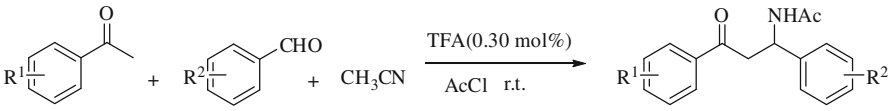
reactions were carried out in the presence of TFA in acetonitrile at ambient temperature.

To investigate the range of the acyl chloride, the model reaction was also carried out with different acyl chlorides and sulfochlorides. The results in Table 3 showed that the reaction proceeded effectively in the presence of both acetyl chloride and chlorobutyryl chloride, affording the corresponding β-acetamido ketones in good yields, whereas chloroacetyl chloride and chloropropionyl chloride did not work well enough. Surprisingly, sulfochlorides did not obviously promote the reaction.

To expand the scope of the TFA-catalyzed multi-component one-pot reaction, a variety of aromatic aldehydes and ketones containing both electron-donating and withdrawing substituents were used to produce the corresponding β-acetamido ketones. The experimental results in Table 4 revealed that these chose reactants afforded good to excellent yields under the optimized reaction conditions. It was

**Table 4** Experimental results under the optimum conditions

| Entry | $R^1$ | $R^2$ | Time (h) | Yield (%) | M.p. ( °C) |
|---|---|---|---|---|---|
| **1** | 3-$NO_2$ | 4-$CH_3$ | 5.0 | 92.6 | 125.1–126.8 |
| **2** | 3-$NO_2$ | 3-$CH_3$ | 4.5 | 98.6 | 150.1–152.5 |
| **3** | 3-$NO_2$ | 4-$OCH_3$ | 5.5 | 88.0 | 155.2–157.4 |
| **4** | 3-$NO_2$ | 3-$OCH_3$ | 5.0 | 86.2 | 95.4–96.2 |
| **5** | 3-$NO_2$ | 3,4,5-tri$OCH_3$ | 5.5 | 84.6 | 148.5–150.3 |
| **6** | 3-$NO_2$ | H | 5.0 | 96.0 | 132.1–133.2 |
| **7** | 3-$NO_2$ | 4-Cl | 7.0 | 87.5 | 128.0–129.0 |
| **8** | 3-$NO_2$ | 3-Cl | 6.5 | 86.9 | 147.4–149.1 |
| **9** | 3-$NO_2$ | 2-Cl | 5.5 | 84.5 | 178.1–179.9 |
| **10** | 3-$NO_2$ | 3-F | 4.0 | 88.0 | 149.5–151.2 |
| **11** | 3-$NO_2$ | 4-$NO_2$ | 5.5 | 83.1 | 207.7–208.9 |
| **12** | 3-$NO_2$ | 3-$NO_2$ | 4.0 | 79.4 | 204.9–206.4 |
| **13** | 3-$NO_2$ | 4-Br | 6.5 | 87.9 | 202.4–204.1 |
| **14** | 3-$NO_2$ | 3,4-diCl | 6.0 | 94.7 | 174.8–176.5 |
| **15** | 3-$NO_2$ | 2,4-diCl | 8.0 | 85.8 | 193.0–195.0 |
| **16** | 3-$NO_2$ | 3-$OCH_3$-4-OH | 6.0 | 80.0 | 198.0–200.4 |
| **17** | 4-Br | 3,4-diCl | 5.5 | 85.0 | 161.6–164.0 |
| **18** | 3,4-diCl | 3-F | 8.0 | 83.5 | 132.5–134.5 |
| **19** | 4-$OCH_3$ | 3,4-diCl | 5.5 | 85.0 | 137.9–139.7 |




**Scheme 2**

also found that substituent groups in the *meta* position resulted in shorter reaction times than those in the *para* position (entries **1** and **2**, **3** and **4**, **7** and **8**, **11** and **12**), and that substituents groups on the acetophenone ring did not affect the reaction time obviously (entries **14**, **17**, **19**). Furthermore, for substituents in the *para* position, aromatic aldehydes with weak electron-withdrawing groups reacted faster than the others (for example entries **1**, **3**, **7**, **11** and **13**). With liquid aldehydes and aldehydes with substituents in the *meta* position, usually no solid was observed after completion of the reaction (entries **4**, **8**, **10**), with the exception of **entry 2**. When phenylacetaldehyde reacted with 3-nitroacteophenone and acetonitrile, the title product was obtained in trace amount (monitored by TLC). It is noteworthy that no acetylation of an aromatic hydroxyl group was observed and the corresponding *β*-acetamido ketones were isolated in an excellent yield (entry **16**) in Scheme 2.

In the course of our work, the effect of hydrogen chloride and concentrated hydrochloric acid on the model reaction were also examined carefully, but the results demonstrated that in the presence of hydrogen chloride or hydrochloric acid

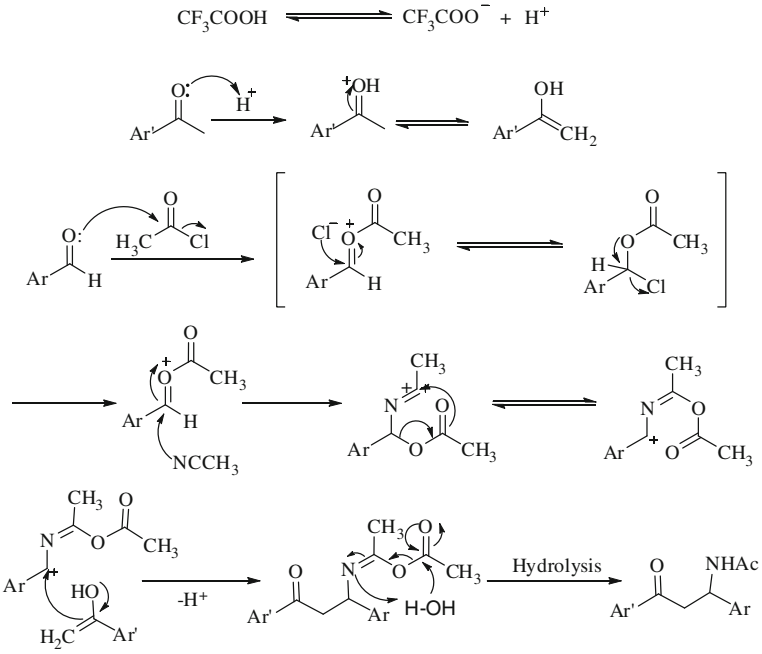



**Fig. 1**

acetyl chloride in the model reaction could not react thoroughly (only approximately 50%, monitored by TLC) within the same time, and there were some side products. Besides, the same reactants did not react when catalyzed by sulfochlorides without acetyl chloride. So, we consider TFA as the real catalyst of this reaction. On the basis of all the above results, we propose the mechanism as follows in Fig. 1.

## Conclusion

In summary, we discovered that TFA was a readily available and efficient catalyst for the one-pot synthesis of $\beta$-acetamido ketones. Especially, we found a few effective auxiliary catalysts for the first time. This methodology offers another choice to prepare $\beta$-acetamido ketones with several advantages, for example excellent yields, simple procedure, short reaction time, and mild conditions.

## Experimental

### General methods

Melting points were detected using an X-6 sophisticated micro-melting-point apparatus and were uncorrected. $^1$H NMR spectra were recorded in DMSO-$d_6$ on a Bruker AV-3000 spectrometer, and chemical shifts ($\delta$) were expressed in ppm,

downfield from the TMS used as the internal standard. Coupling constant ($J$) values were in Hz. The progress of the reactions was monitored by TLC using several solvent systems with different polarities. All solvents and reagents were of chemical grade or analytical grade.

General procedure for the synthesis of $\beta$-acetamido ketones

To a solution of an aldehyde (1.0 mmol), an enolizable ketone (1.0 mmol), and acetyl chloride (0.4 mL) in acetonitrile (2.0 mL), TFA (0.30 mol%) was added dropwise and the reaction mixture was stirred for 0.5 h at 0 °C, and then at ambient temperature (approx. 33 °C). The progress of the reaction was monitored by TLC. On completion, the reaction mixture was poured into ice water (20.0 mL), then the solution was adjusted to pH 7 with saturated $NaHCO_3$, which resulted in precipitation of the desired $\beta$-acetamido ketone. The precipitate was filtered and washed with diethyl ether (1.0 mL). The crude product obtained was recrystallized from a mixture of ethyl acetate and ethyl ether to afford analytically pure product. Eighteen title compounds are new and were characterized by $^1$H NMR and $^{13}$C NMR.

Spectral data for the new products

*β-Acetamido-β-(4-methylphenyl)-3-nitropropiophenone (1)*

$^1$H NMR (300 MHz, DMSO-$d_6$,): 1.76 (s, 3H, $COCH_3$), 2.25 (s, 3H, $CH_3$), 3.46 (dd, $J = 5.40$ and 17.1 Hz, 1H, $CH_2$), 3.62 (dd, $J = 8.40$ and 17.1 Hz, 1H, $CH_2$), 5.28–5.35 (m, 1H, CHN), 7.10 (d, $J = 7.80$ Hz, 2H, Ar–H), 7.24 (d, $J = 7.80$ Hz, 2H, Ar–H), 7.81 (t, $J = 8.10$ Hz, 1H, Ar–H), 8.40 (d, $J = 6.60$ Hz, 2H, Ar–H), 8.45 (d, $J = 8.10$ Hz, 1H, Ar–H), 8.61 (s, 1H, Ar–H). $^{13}$C NMR(75 MHz, DMSO-$d_6$):196.3, 168.8, 148.5, 140.1, 138.2, 136.4, 134.7, 131.0, 129.2, 127.8, 127.0, 122.8, 48.1, 45.3, 23.0, 21.0.

*β-Acetamido-β-(3-methylphenyl)-3-nitropropiophenone (2)*

$^1$H NMR (300 MHz, DMSO-$d_6$): 1.78 (s, 3H, $COCH_3$), 2.27 (s, 3H, $CH_3$), 3.47 (dd, $J = 8.40$ and 17.1 Hz, 1H, $CH_2$), 3.64 (dd, $J = 5.70$ and 17.1 Hz, 1H, $CH_2$), 5.28–5.35 (m, 1H, CHN), 7.02 (d, $J = 6.90$ Hz, 1H, Ar–H,), 7.16–7.18 (m, 3H, Ar–H), 7.81 (t, $J = 8.10$ Hz, 1H, Ar–H,), 8.36–8.46 (m, 3H, NH, Ar–H), 8.60 (s, 1H, Ar–H). $^{13}$C NMR (75 MHz, DMSO-$d_6$): 196.3, 168.9, 148.4, 143.1, 138.2, 137.7, 134.7, 131.0, 128.6, 128.0, 127.8, 124.4, 122.8, 49.3, 45.3, 23.0, 21.5.

*β-Acetamido-β-(4-methoxylphenyl)-3-nitropropiophenone (3)*

$^1$H NMR (300 MHz, DMSO-$d_6$): 1.78 (s, 3H, $COCH_3$), 2.27 (s, 3H, $CH_3$), 3.43-3.41 (m, 1H, $CH_2$), 3.60-3.70 (m, 1H, $CH_2$), 5.28–5.35 (m, 1H, CHN), 6.86 (d, $J = 7.80$ Hz, 2H, Ar–H), 7.27–7.32 (m, 3H, Ar–H), 7.64–7.72 (m, 1H, Ar–H), 8.27 (d, $J = 7.50$ Hz, 1H, Ar–H), 8.41 (d, $J = 8.10$ Hz,1H, NH), 8.72 (s, 1H, Ar–H).$^{13}$C

NMR (75 MHz, DMSO-$d_6$): 196.3, 168.9, 158.6, 148.4, 138.2, 135.0, 134.7, 131.0, 128.3, 127.8, 122.7, 114.0, 55.5, 48.9, 45.3, 22.9.

*β-Acetamido-β-(3-methoxylphenyl)-3-nitropropiophenone (4)*

$^1$H NMR (300 MHz, $CDCl_3$): 2.04 (s, 3H, $COCH_3$), 3.49 (dd, $J = 6.60$ and 17.1 Hz, 1H, $CH_2$), 3.85 (dd, $J = 9.30$ and 17.1 Hz, 1H, $CH_2$), 3.79 (s, 1H, $OCH_3$), 3.83–3.88 (m, 1H, $CH_2$), 5.50–5.56 (m, 1H, CHN), 6.41 (d, $J = 7.80$ Hz, 1H, Ar–H,), 6.80 (d, $J = 8.40$ Hz, 1H, Ar–H,), 6.89–6.93 (m, 2H, Ar–H), 7.23–7.27 (m, 1H, Ar–H), 7.67 (t, $J = 7.80$ Hz, 1H, Ar–H), 8.24 (d, $J = 7.80$ Hz, 1H, Ar–H), 8.41 (d, $J = 7.80$ Hz, 1H, NH), 8.72 (s, 1H, Ar–H).$^{13}$C NMR (75 MHz, $CDCl_3$): 196.0, 184.8, 169.6, 141.9, 137.3, 133.7, 130.0, 129.9, 127.7, 123.0, 118.7, 112.8, 112.7, 55.2, 50.1, 43.8, 23.4

*β-Acetamido-β-(3,4,5-trimethoxylphenyl)-3-nitropropiophenone (5)*

$^1$H NMR(300 MHz, $CDCl_3$): 2.04 (s, 3H, $COCH_3$), 3.43–3.41 (m, 1H, $CH_2$), 3.65–3.84 (m, 1H, $CH_2$,$OCH_3$), 5.43–5.49 (m, 1H, CHN), 6.41 (d, $J = 7.50$ Hz, 1H, Ar–H), 6.56 (s, 1H, Ar–H), 7.68 (t, $J = 7.80$ Hz, 1H, Ar–H), 8.27 (d, $J = 7.80$ Hz, 1H, Ar–H), 8.42 (d, $J = 9.60$ Hz, 1H, NH), 8.73 (s, 1H, Ar–H). $^{13}$C NMR (75 MHz, $CDCl_3$): 196.0, 168.6, 153.4, 148.4, 137.7, 136.2, 133.7, 130.0, 127.6, 123.0, 104.0, 60.7, 56.1, 50.6, 44.0, 23.3.

*β-Acetamido-β-phenyl-3-nitropropiophenone (6)*

$^1$H NMR (300 MHz, DMSO-$d_6$): 1.78(s, 3H, $COCH_3$), 3.47–3.55 (m, 1H, $CH_2$), 3.60–3.69 (m, 1H, $CH_2$), 5.33–5.40 (m, 1H, CHN), 7.22–7.38 (m, 5H, Ar–H), 7.82 (t, $J = 8.10$ Hz, 1H, Ar–H), 8.32–8.62 (m, 3H, Ar–H, NH), 8.63 (s, 1H, Ar–H).

*β-Acetamido-β-(4-chlorophenyl)-3-nitropropiophenone (7)*

$^1$H NMR (300 MHz, $CDCl_3$): 2.04(s, 3H, $COCH_3$), 3.51 (dd, $J = 5.40$ and 17.4 Hz, 1H, $CH_2$), 3.83 (dd, $J = 6.60$ and 17.4 Hz, 1H, $CH_2$), 5.51–5.58 (m, 1H, CHN), 6.49 (d, $J = 7.50$ Hz, 1H, Ar–H), 7.27–7.30 (m, 4H, Ar–H), 7.69 (t, $J = 7.80$ Hz, 1H, Ar–H), 8.24 (d, $J = 7.20$ Hz, 1H, Ar–H), 8.43 (d, $J = 9.60$ Hz, 1H, NH), 8.72(s, 1H, Ar–H).$^{13}$C NMR(75 MHz, DMSO-$d_6$): 196.3, 168.9, 148.4, 142.2, 138.1, 134.7, 131.9, 131.0, 129.0, 128.6, 127.9, 122.8, 48.7, 45.0, 23.0.

*β-Acetamido-β-(3-chlorophenyl)-3-nitropropiophenone (8)*

$^1$H NMR (300 MHz, $CDCl_3$): 2.05(s, 3H, $COCH_3$), 3.51 (dd, $J = 5.70$ and 16.5 Hz, 1H, $CH_2$), 3.83 (dd, $J = 5.10$ and 16.5 Hz, 1H, $CH_2$), 5.55–5.57 (m, 1H, CHN), 6.56 (d, $J = 6.60$ Hz, 1H, Ar–H), 7.25–7.27 (m, 2H, Ar–H), 7.34 (s, 1H, Ar–H), 7.69 (t, $J = 7.80$ Hz, 1H, Ar–H), 8.25 (d, $J = 7.80$ Hz, 1H, Ar–H), 8.43 (d, $J = 8.10$ Hz, 1H, NH), 8.72 (s, 1H, Ar–H). $^{13}$C NMR(75 MHz, $CDCl_3$): 195.6,

169.8, 148.4, 142.8, 137.6, 134.6, 133.6, 130.0, 129.9, 127.8, 126.8, 126.7, 124.9, 122.9, 49.3, 43.7, 23.3.

*β-Acetamido-β-(2-chlorophenyl)-3-nitropropiophenone (9)*

$^1$H NMR (300 MHz, $CDCl_3$): 2.06(s, 3H, $COCH_3$), 3.58 (dd, $J = 5.70$ and 16.5 Hz, 1H, $CH_2$), 3.83 (dd, $J = 6.00$ and 16.5 Hz, 1H, $CH_2$), 5.83–5.90 (m, 1H, CHN), 6.68 (d, 1H, $J = 7.80$ Hz, Ar–H), 7.17–7.26 (m, 2H, Ar–H), 7.35–7.38 (m, 1H, Ar–H), 7.42–7.47 (m, 1H, Ar–H), 7.68 (t, $J = 7.80$ Hz, 1H, Ar–H), 8.26 (d, $J = 7.50$ Hz, 1H, Ar–H), 8.42 (d, $J = 7.80$ Hz, 1H, NH), 8.75 (s, 1H, Ar–H).$^{13}$C NMR(75 MHz, $CDCl_3$): 195.6, 168.9, 148.4, 140.4, 137.9, 134.5, 132.1, 130.8, 129.6, 128.9, 128.0, 127.7, 127.6, 122.8, 46.6, 43.9, 22.9.

*β-Acetamido-β-(3-fluorophenyl)-3-nitropropiophenone (10)*

$^1$H NMR (300 MHz, $CDCl_3$): 2.05(s, 3H, $COCH_3$), 3.50 (dd, $J = 6.30$ and 17.1 Hz, 1H, $CH_2$), 3.83 (dd, $J = 5.10$ and 17.1 Hz, 1H, $CH_2$), 5.55–5.61 (m, 1H, CHN), 6.56 (d, $J = 7.80$ Hz, 1H, Ar–H), 6.92–6.99 (m, 1H, Ar–H), 7.05–7.14 (m, 2H, Ar–H), 7.27–7.34 (m, 1H, Ar–H), 7.69 (m, 1H, Ar–H), 8.25 (d, $J = 8.10$ Hz, 1H, Ar–H), 8.42 (d, $J = 8.10$ Hz, 1H, NH), 8.72(s, 1H, Ar–H).$^{13}$C NMR (75 MHz, $CDCl_3$): 195.8, 169.7, 161.3, 148.4, 143.1, 137.6, 133.6, 130.4, 130.1, 127.8, 122.9, 122.1, 114.8, 113.8, 46.6, 43.9, 22.9.

*β-Acetamido-β-(4-nitrophenyl)-3-nitropropiophenone (11)*

$^1$H NMR (300 MHz, DMSO-$d_6$): 1.83(s, 3H, $COCH_3$), 3.60 (dd, $J = 5.10$ and 18.0 Hz, 1H, $CH_2$), 3.77 (dd, $J = 8.40$ and 18.0 Hz, 1H, $CH_2$), 5.42–5.49 (m, 1H, CHN), 7.66 (d, $J = 8.40$ Hz, 2H, Ar–H), 7.84 (t, $J = 8.40$ Hz, 1H, Ar–H), 8.20 (d, $J = 8.40$ Hz, 2H, Ar–H), 8.40 (d, $J = 7.80$ Hz, 1H, NH), 8.49 (m, 2H, Ar–H), 8.66(s, 1H, Ar–H). $^{13}$C NMR (75 MHz, DMSO-$d_6$): 195.6, 169.2, 151.2, 148.4, 146.9, 138.0, 134.6, 131.0, 128.4, 128.0, 123.9, 122.8, 48.9, 44.6, 23.0.

*β-Acetamido-β-(3-nitrophenyl)-3-nitropropiophenone (12)*

$^1$H NMR (300 MHz, DMSO-$d_6$): 1.84 (s, 3H, $COCH_3$), 3.58–3.66 (dd, $J = 5.10$ and 17.7 Hz,1H, $CH_2$), 3.79–3.87 (dd, $J = 8.70$and 17.7 Hz, 1H, $CH_2$), 5.45–5.52 (m, 1H, CHN), 7.22–7.39 (m, 1H, Ar–H), 7.62 (t, $J = 7.80$ Hz, 2H, Ar–H), 8.12 (d, $J = 8.70$ Hz, 1H, Ar–H), 8.27 (s, 1H, Ar–H), 8.42 (d, $J = 7.80$ Hz, Ar–H), 8.48 (d, $J = 8.40$ Hz, Ar–H), 8.66(s, 1H, Ar–H), 8.74(d, $J = 6.90$ Hz, NH) $^{13}$C NMR(75 MHz, DMSO-$d_6$): 195.8, 169.3, 148.4, 148.2, 145.7, 138.0, 134.7, 134.2, 131.0, 130.2, 127.9, 123.9, 122.8, 122.3, 121.8, 48.8, 44.7, 22.9.

*β-Acetamido-β-(4-bromophenyl)-3-nitropropiophenone (13)*

$^1$H NMR (300 MHz, DMSO-$d_6$): 1.78(s, 3H, $COCH_3$), 3.51 (dd, $J = 5.40$ and 17.1 Hz,1H, $CH_2$), 3.66 (dd, $J = 8.40$ and 17.7 Hz, 1H, $CH_2$), 5.28–5.35 (m, 1H,

CH), 7.33 (d, $J = 8.40$ Hz, 2H, Ar–H), 7.51 (d, $J = 8.40$ Hz, 2H, Ar–H), 7.82 (t, $J = 8.10$ Hz, 1H, Ar–H), 8.36 (m, 2H, NH, Ar–H), 8.45–8.49 (m, 1H, Ar–H), 8.63(s, 1H, Ar–H). $^{13}$C NMR(75 MHz, DMSO-$d_6$): 196.0, 168.9, 148.4, 142.7, 138.0, 134.6, 131.5, 131.0, 129.4, 127.9, 122.8, 120.4, 48.7, 44.7, 23.0.

*β-Acetamido-β-(3,4-chlorophenyl)-3-nitropropiophenone (14)*

$^1$H NMR (300 MHz, DMSO-$d_6$): 1.82(s, 3H, $COCH_3$), 3.54–3.62 (m, 1H, $CH_2$), 3.68–3.77 (m, 1H, $CH_2$), 5.31–5.38 (m, 1H, CH), 7.37–7.41 (m, 1H, Ar–H), 7.61 (d, $J = 8.10$ Hz, 1H, Ar–H), 7.66 (s, 1H, Ar–H), 7.85 (t, $J = 7.80$ Hz, 1H, Ar–H), 8.41 (m, 2H, NH, Ar–H), 8.49 (d, $J = 7.80$ Hz, 1H, Ar–H), 8.67 (s, 1H, Ar–H). $^{13}$C NMR (75 MHz, DMSO-$d_6$): 195.8, 169.1, 148.4, 144.5, 138.0, 134.7, 131.3, 131.0, 130.8, 129.8, 129.2, 127.9, 127.7, 122.8, 48.4, 44.7, 23.0.

*β-Acetamido-β-(2,4-chlorophenyl)-3-nitropropiophenone (15)*

$^1$H NMR (300 MHz, DMSO-$d_6$): 1.81 (s, 3H, $COCH_3$), 3.44 (dd, $J = 4.20$ and 17.7 Hz, 1H, $CH_2$), 3.62 (dd, $J = 9.00$ and 17.7 Hz, 1H, $CH_2$), 5.62–5.69 (m, 1H, CH), 7.44–7.53 (m, 2H, Ar–H), 7.60 (s, 1H, Ar–H), 7.84 (t, $J = 7.80$ Hz, 1H, Ar–H), 8.39–8.50 (m, 3H, NH, Ar–H), 8.68 (s, 1H, Ar–H).$^{13}$C NMR(75 MHz, DMSO-$d_6$): 195.6, 169.1, 148.4, 139.8, 137.9, 134.7, 133.0, 132.7, 131.0, 129.6, 129.1, 128.0, 127.9, 122.9, 46.3, 43.7, 22.9.

*β-Acetamido-β-(4-hydroxy-3–methoxyphenyl)-3-nitropropiophenone (16)*

$^1$H NMR (300 MHz, DMSO -$d_6$): 1.77 (s, 3H, $COCH_3$), 3.45-3.61 (m, 2H, $CH_2$), 3.75 (s, 1H, $OCH_3$), 5.23–5.30 (m, 1H, CH), 6.66–6.75 (m, 2H, Ar–H), 6.93 (s, 1H, Ar–H), 7.81 (t, 1H, Ar–H, $J = 8.40$ Hz), 8.22 (d, 1H, $J = 8.10$ Hz, Ar–H), 8.37 (d, $J = 7.80$ Hz, 1H, Ar–H), 8.43–8.46 (m, 2H, NH, Ar–H), 8.60 (s, 1H, Ar–H), 8.84 (s, 1H, Ar–H). $^{13}$C NMR(75 MHz, DMSO-$d_6$): 196.5, 168.7, 148.4, 147.8, 146.0, 138.2, 134.7, 133.7, 131.0, 127.8, 122.8, 119.4, 115.5, 111.5, 56.0, 49.3, 45.6, 23.0.

*β-Acetamido-β-(3,4-chlorophenyl)-4-bromopropiophenone (17)*

$^1$H NMR (300 MHz, DMSO-$d_6$): 1.81 (s, 3H, $COCH_3$), 3.39-3.47 (m, 1H, $CH_2$), 3.54–3.63 (m, 1H, $CH_2$), 5.28–5.37 (m, 1H, CHN), 7.34–7.41 (m, 4H, Ar–H), 7.35 (d, $J = 8.10$ Hz, 2H, Ar–H),7.58 (s, 1H, Ar–H) 7.60 (d, $J = 7.80$ Hz, 1H, Ar–H), 7.74 (d, $J = 8.70$ Hz, 2H, Ar–H), 7.90 (d, $J = 7.80$ Hz, 2H, Ar–H), 8.38 (d, $J = 7.50$ Hz, 1H, NH). $^{13}$C NMR(75 MHz, DMSO-$d_6$):196.6, 168.8, 150.9, 145.2, 135.9, 132.2, 130.5, 129.7, 127.8, 124.5, 120.8, 120.2, 48.8, 44.8, 23.1.

*β-Acetamido-β-(3-fluorophenyl)-3,4-chloropropiophenone (18)*

$^1$H NMR (300 MHz, DMSO-$d_6$): 1.80 (s, 3H, $COCH_3$), 3.42 (dd, $J = 5.10$ and 17.4 Hz, 1H, $CH_2$), 3.57 (dd, $J = 8.40$ and 17.4 Hz, 1H, $CH_2$), 5.23-5.33 (m, 1H, CHN), 7.07–7.21 (m, 3H, Ar–H), 7.35–7.38 (m, 1H, Ar–H), 7.80 (d, $J = 8.38$ Hz,

1H, Ar–H), 7.93 (d, $J = 8.38$ Hz, 1H, Ar–H), 8.19 (s, 1H, Ar–H), 8.34 (d, $J = 7.35$ Hz, 1H, NH).$^{13}$C NMR(100 MHz, DMSO-$d_6$): 195.1, 168.4, 163.3, 145.7, 136.6, 135.9, 131.7, 130.1, 130.0, 129.9, 127.9, 122.7, 113.6, 113.2, 48.3, 44.2, 22.5.

*β-Acetamido-β-(3,4-chlorophenyl)-4-methoxylpropiophenone (19)*

$^1$H NMR (300 MHz, DMSO -$d_6$): 1.79 (s, 3H, $COCH_3$), 3.34–3.40 (m, 1H, $CH_2$), 3.52–3.60 (m 1H, $CH_2$), 5.29–5.36 (m 1H, CHN), 7.15 (d, $J = 8.70$ Hz, 2H, Ar–H), 7.21(s, 1H, Ar–H), 7.25 (d, $J = 7.50$ Hz, 1H, Ar–H), 7.58 (d, $J = 7.50$ Hz, 1H, Ar–H), 7.92 (d, $J = 8.70$ Hz, 2H, Ar–H,), 8.53 (d, $J = 7.50$ Hz, 1H, NH). $^{13}$C NMR (75 MHz, DMSO-$d_6$):195.5, 169.1, 163.6, 144.9, 131.2, 130.8, 130.7, 129.8, 129.7, 129.2, 127.7, 114.3, 55.9, 48.7, 44.1, 22.9

## References


1. J.R. Casimir, C. Turetta, L. Ettouati, J. Paris, Tetrahedron Lett. **36**(27), 4797–4800 (1995)
2. A. Godfrey, D.A. Brooks, L.A. Hay, M. Peters, J.R. McCarthy, D. Mitchell, J. Org. Chem. **68**, 2623–2632 (2003)
3. J. Barluenga, A.L. Viado, E. Aguilar, S. Fustero, B. Olano, J. Org. Chem. **58**, 5972–5975 (1993)
4. D. Enders, M. Moser, G. Geibel, M.C. Laufer, Synthesis **12**, 2040–2046 (2004)
5. M. Mukhopodhyay, B. Bhatia, J. Iqbal, Tetrahedron Lett. **38**(6), 1083–1086 (1997)
6. I. Rao, E.N. Prabhakaran, S.K. Das, J. Iqbal, J. Org. Chem. **68**(10), 4079–4082 (2003)
7. K. Kobinata, M. Uramoto, M. Nishii, H. Kusakabe, G. Nakamura, K. Isono, Agri. Biol. Chem. **44**, 1709–1711 (1980)
8. U. Daehn, H. Hagenmaier, H. Hoehne, W.A. Koenig, G. Wolf, H. Zaehner, Arch. Microbiol. **107**, 249–256 (1976)
9. A.K. Tiwari, R.M. Kumbhare, S.B. Agawane, A.Z. Ali, K.V. Kumar, Bioorg. Med. Chem. Lett. **18**(14), 4130–4132 (2008)
10. P. Dallemagne, S. Rault, M. Severicourt, K.M. Hassan, M. Robba, Tetrahedron Lett. **27**(23), 2607–2610 (1986)
11. P.W. Jeffs, R. Redfearn, J. Wolfram, J. Org. Chem. **48**, 3861–3863 (1983)
12. M.R. Paleo, D. Dominguez, L. Castedo, Tetrahedron Lett. **34**(14), 2369–2370 (1993)
13. B. Bhatia, M.M. Reddy, J. Iqbal, J. Chem. Soc. Chem. Commun. 713–714 (1994)
14. M.M. Khodaei, A.R. Khosropour, P. Fattahpour, Tetrahedron Lett. **46**, 2105–2108 (2005)
15. L. Nagarapu, S. Kantevari, V.N. Cheemalapati, S. Apuri, N.V. Kumari, J. Mol. Catal. A Chem. **264**, 22–25 (2007)
16. M.M. Heravi, L. Ranjbar, F. Derikvand, F.F. Bamoharram, Catal. Commun. **8**, 289–291 (2007)
17. R. Ghosh, S. Maiti, A. Chakraborty, S. Chakraborty, A.K. MukherJee, Tetrahedron **62**, 4059–4064 (2006)
18. B. Das, M. Srilatha, B. VeeranJaneyulu, B.R. Rao, Synthesis **5**, 0803–0807 (2010)
19. V.S. Shinu, B. SheeJa, E. Purushothaman, D. Bahulayan, Tetrahedron Lett. **50**, 4838–4843 (2009)
20. L. Nagarapu, R. Bantu, R. Puttireddy, Appl. Catal. A Gen. **332**, 304–309 (2007)
21. A. Hassankhani, M.T. Maghsoodlou, S.M. Habibi-Khorassani, H. Hosseini-Mahdiabad, G. Marandi, Arkivoc **ii**, 134–140 (2008)
22. D. Bahulayan, S.K. Das, J. Iqbal, J. Org. Chem. **68**(14), 5735–5738 (2003)
23. A.A. Beushev, V.V. Kon'shin, N.A. Chemeris, M.M. Chemeris, Russ. J. Appl. Chem. **81**(10), 1856–1859 (2008)
24. C.A. Guy, G.B. Fields, Methods Enzymol. **289**, 67–83 (1997)
25. V. Cadierno, J. Francos, J. Gimeno, Chem. Commun. **46**(23), 4175–4177 (2010)