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A straightforward synthesis of *N*-monosubstituted α-keto amides via aerobic benzylic oxidation of amides

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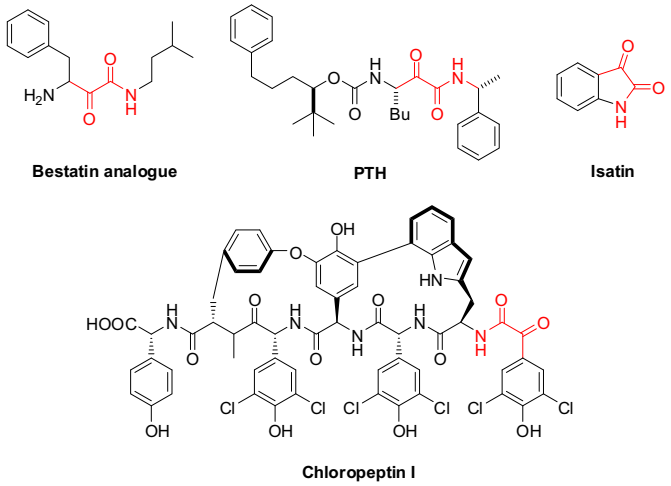
ABSTRACT

An efficient sodium bicarbonate promoted aerobic oxidation reaction to prepare *N*-monosubstituted α-keto amides in the presence of *n*-tetrabutylammonium hydrogensulfate (TBAHS) was described. This reaction provides a very simple and convenient synthetic route to *N*-monosubstituted α-keto amides from easily available aryl- or heteroarylacetamides in good to high yields without using toxic reagents and harsh conditions.

1. Introduction

Due to their specific structures and activities, *N*-monosubstituted α-keto amides have been paid great attentions. The α-keto amide scaffold is widely spread in natural products and some substances with potential bio-activities (Scheme 1). For example, Chloropeptin I and Complestatin are proved to inhibit HIV replication, and the studies on their total synthesis, modification, and activity attract the efforts of many chemists.[1] Bestatin and PTH analogues bearing the α-keto skeletons were found to be inhibitors of the serine proteinase elastase[2] and Cathepsin K,[3] respectively. Isatin and its derivatives are widely used in dye, food, and medicinal industry.[4] Besides, many other substances bearing the α-keto amide substructure were found to be fungicide and fungicide precursors,[5] antibiotics,[6] and various inhibitors.[7] Moreover, their usages as significant intermediates, versatile building blocks[8] and applications in NMR study[9] have also been added to their importance.

The synthesis of *N*-monosubstituted α-keto amides could date back to the early 1960s when Ugi and his co-workers developed the coupling reaction of acyl chloride with isonitrile.[10] After that, various synthetic methods were exploited including the direct amidation of α-keto acids and their derivatives,[11] photooxygenation of corresponding amides,[12] amido double carbonylation,[13] rearrangement reaction between Schiff base and isonitrile,[14] oxidation of α-hydroxyamides,[15] and direct α-oxidation of amides mainly using SeO_2 as metal oxidants.[8f,16] Recently, a copper-catalyzed oxidative amidation–diketonization of terminal alkynes[17] and a zinc



Scheme 1. Some bioactive products with α-keto amide moiety.

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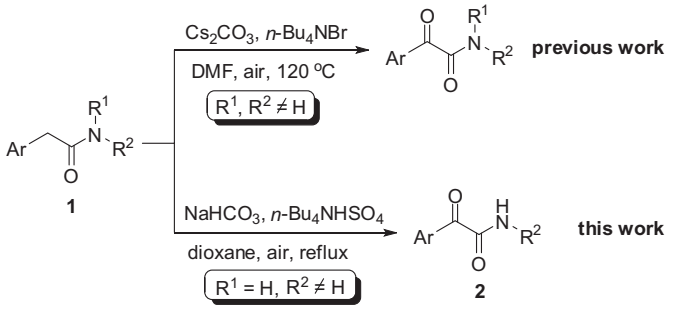
chloride promoted formal oxidative coupling of aromatic aldehydes and isocyanides to α-keto amides[18] were reported, which have provided new routes for this class of molecules. However, for some of the methods, the expensive and toxic reagents employed, the harsh conditions used and low yields achieved have turned them into limitations.

We have recently reported an efficient access to *N*,*N*-disubstituted α-keto amides by treatment of easily available tertiary amides with Cs_2CO_3 and *n*-Bu_4NBr in the presence of atmospheric air.[19] However, the same reaction conditions failed to afford α-oxidized *N*-monosubstituted amides in good yields. It became a new synthetic challenge to find an efficient and convenient access to the *N*-monosubstituted α-keto amides via direct α-oxidation of the corresponding secondary amides without using any toxic or expensive reagents, or without employing harsh conditions. Herein, we developed a direct method for the efficient preparation of *N*-monosubstituted α-keto amides from readily available arylacetamides in good to high yields (Scheme 2). The reactions are effective in the presence of $NaHCO_3$ and *n*-Bu_4NHSO_4 with the reactions open to air in refluxed dioxane.



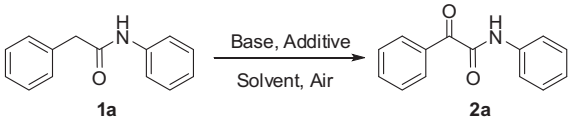
Scheme 2. Synthesis of α-keto arylacetamides.

2. Results and discussion

Initially, based on our previous results, we speculated whether the same conditions, which were successfully applied to give *N*,*N*-disubstituted α-keto amides, could be also effective for the preparation of *N*-monosubstituted amides. To our disappointment, **1a** in DMF in the presence of Cs_2CO_3 and *n*-Bu_4NBr gave **2a** in only 20% yield after reacted for 9 h (Table 1, entry 1). Improved yields could be achieved by increasing the amount of Cs_2CO_3 and *n*-Bu_4NBr (Table 1, entries 2 and 3). When *n*-Bu_4NHSO_4 was used instead as additive, the yield significantly dropped (Table 1, entry 4). However, the change of solvent turned out to be a good solution. Dioxane was proved to be the most favorable solvent (Table 1, entry 7). Other solvents, such as toluene and DCE gave no better results (Table 1, entries 5 and 6). Changing the additive from TBAHS to TEBAC gave trace amount of product (Table 1, entry 8) and the yields dropped with reduction of the amount of base or additive (Table 1, entries 9 and 10). No amelioration result could be afforded by using K_2CO_3, CsOAc, and NaOH as base (Table 1, entries 11–13). To our delight, the employment of $NaHCO_3$ as base gave **2a** in 89% yield after reacted for 12 h (Table 1, entry 14). However, when reducing the amount of *n*-Bu_4NHSO_4 to 1.0 equiv, the yield dropped to 70% (Table 1, entry 15) and less amount of $NaHCO_3$ gave only 22% yield of the oxidized product with a conversion of 25% after reacted for 43 h (Table 1, entry 16). When the reaction was conducted using oxygen atmosphere as oxidant (Table 1, entry 17) or using TBAB as additive instead of TBAHS (Table 1, entry 18), no better results were achieved.

To explore the scope of this method, a variety of aryl- or heteroarylacetamides **1a**–**r** were applied under the optimized conditions (Table 1, entry 14). The results are summarized in Table 2. As

Table 1
Reaction optimization of base, additive, and solvent[a]



Entry	Base (equiv)	Additive (equiv)	Solvent	Temp (°C)	Time (h)	Yield[b] (%)
1	Cs_2CO_3 (1.1)	TBAB (0.5)	DMF	120	9	20
2	Cs_2CO_3 (2.0)	TBAB (1.0)	DMF	120	6	31
3	Cs_2CO_3 (3.0)	TBAB (1.5)	DMF	120	5.5	41
4	Cs_2CO_3 (3.0)	TBAHS (1.5)	DMF	120	24	Trace
5	Cs_2CO_3 (3.0)	TBAHS (1.5)	Toluene	110	7	48
6	Cs_2CO_3 (3.0)	TBAHS (1.5)	DCE	85	24	<5
7	Cs_2CO_3 (3.0)	TBAHS (1.5)	Dioxane	Reflux	6	84
8	Cs_2CO_3 (3.0)	TEBAC (1.5)	Dioxane	Reflux	40	7
9	Cs_2CO_3 (2.5)	TBAHS (1.5)	Dioxane	Reflux	9	57
10	Cs_2CO_3 (3.0)	TBAHS (1.0)	Dioxane	Reflux	11	53
11	K_2CO_3 (3.0)	TBAHS (1.5)	Dioxane	Reflux	22	23
12	CsOAc (3.0)	TBAHS (1.5)	Dioxane	Reflux	24	0
13	NaOH (3.0)	TBAHS (1.5)	Dioxane	Reflux	24	10
14	**$NaHCO_3$ (3.0)**	**TBAHS (1.5)**	**Dioxane**	**Reflux**	**12**	**89**
15	$NaHCO_3$ (3.0)	TBAHS (1.0)	Dioxane	Reflux	14.5	70
16	$NaHCO_3$ (2.0)	TBAHS (1.5)	Dioxane	Reflux	43	22[c]
17	$NaHCO_3$ (3.0)	TBAHS (1.5)	Dioxane	Reflux	13	47[d]
18	$NaHCO_3$ (3.0)	TBAB (1.5)	Dioxane	Reflux	24	Trace

The bold values in the table are used for emphasizing the optimized reaction condition.

[a] Reaction conditions: **1a** (0.5 mmol), dioxane (2.5 mL), open to air, dried through a calcium chloride tube, reflux. DCE=1,2-dichloroethane, TBAB=Tetrabutylammonium bromide, TEBAC=Benzyltriethyl-ammonium chloride, TBAHS=Tetrabutylammonium hydrogensulfate.

[b] Isolated yields.

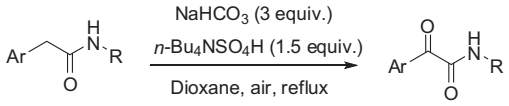
[c] With conversion of 25% based on **1a**.

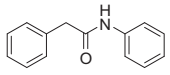
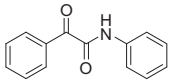
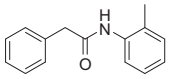
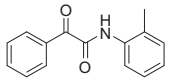
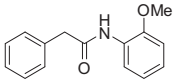
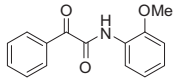
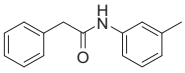
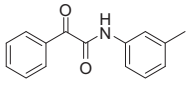
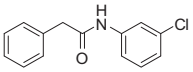
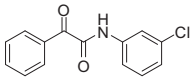
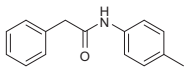
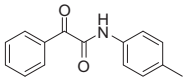
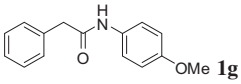
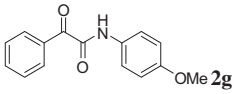
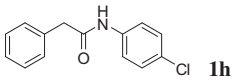
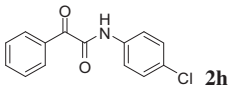
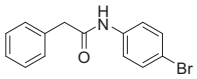
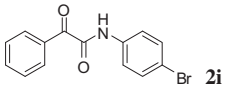
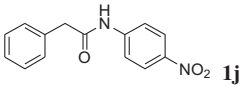
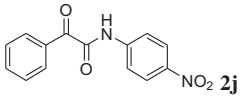
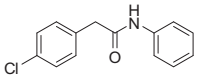
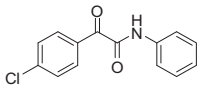
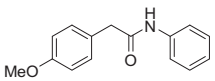
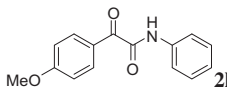
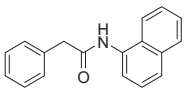
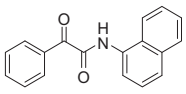
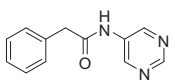
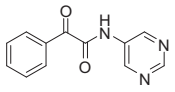
[d] Reaction was run under O_2 atmosphere.

shown in Table 2, the α-oxidation reaction proceeded readily to give the corresponding α-keto amides in moderate to good yields. Remarkably clean reactions were observed with functionalized molecules bearing *ortho*, *meta*, and *para* substitutions on the *N*-aryl ring (Table 2, entries 2–9). Electron-donating and electron-withdrawing groups substituted on the aryl ring were tolerated and readily to give the corresponding α-keto amides in good yields (Table 2, entries 11 and 12). However, substrate with strong electron-withdrawing group, e.g., nitro group, afforded lower yield (Table 2, entry 10). This oxidation reaction was not limited to simple benzene-containing aromatics, substrates containing the substructure of naphthalene (Table 2, entry 13), pyrimidine (Table 2, entry 14), pyridine (Table 2, entry 15), and aliphatic chain (Table 2, entry 16) also gave good yields. For sterically hindered or less reactive substrates, better results could be achieved using Cs_2CO_3 as base instead of $NaHCO_3$. For example, compound **2c** bearing an *ortho* methoxyl group was obtained in 84% yield (Table 2, entry 3), and **2h** and **2n** were obtained in both 93% yields under the same conditions (Table 2, entries 8 and 14). Nevertheless, for substrate with strong electron-withdrawing nitro group, amide **2j** was afforded in 29% yield even using Cs_2CO_3 as base (Table 2, entry 10). To further expand the scope of the reaction, substrates **1q** and **1r** with indol or thiophene moiety were investigated under standard conditions. Gratifyingly, the corresponding oxidation products **2q** and **2r** could be also well achieved in good yields, respectively (Table 2, entries 17 and 18). However, 2-phenylacetamide and cinnamamide derived substrate (*E*)-*N*,4-diphenylbut-3-enamide,[20] which was prepared from cinnamaldehyde and 4-methylbenzenesulfono-hydrazide, failed to react under the same conditions and gave no desired oxidation products.

Based on literature reports and our previous work,[19,21] a possible reaction mechanism for this direct formation of α-keto amides was illustrated involving deprotonation at the benzyl position of

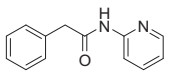
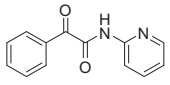
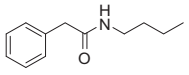
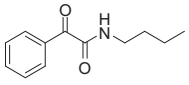
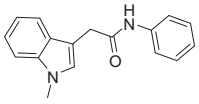
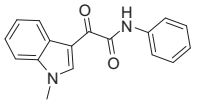
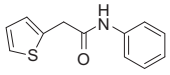
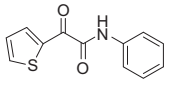
Table 2
Synthesis of *N*-monosubstituted α-keto amides by oxidation of amides[a]



Entry	Reactant	Product	Time (h)	Yield[b] (%)
1	 **1a**	 **2a**	12	89
2	 **1b**	 **2b**	14.5	85
3	 **1c**	 **2c**	16	84[c]
4	 **1d**	 **2d**	13	81
5	 **1e**	 **2e**	12	83
6	 **1f**	 **2f**	14	80
7	 **1g**	 **2g**	11.5	85
8	 **1h**	 **2h**	18	93[c]
9	 **1i**	 **2i**	18	80
10	 **1j**	 **2j**	11	29[c]
11	 **1k**	 **2k**	10	83
12	 **1l**	 **2l**	11	84
13	 **1m**	 **2m**	12	64
14	 **1n**	 **2n**	11.5	93[c]

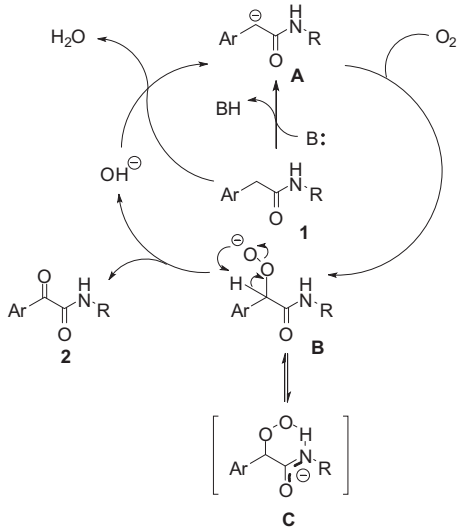
(*continued on next page*)

Table 2 (*continued*)

Entry	Reactant	Product	Time (h)	Yield[b] (%)
15	 **1o**	 **2o**	10	52
16	 **1p**	 **2p**	14.5	55
17	 **1q**	 **2q**	10	59
18	 **1r**	 **2r**	7	44

[a] Reaction conditions: amides (**1a**–**r**, 0.5 mmol), $NaHCO_3$ (1.5 mmol), *n*-Bu_4NHSO_4 (0.75 mmol), dioxane (2.5 mL), open to air, dried through a calcium chloride tube, reflux.
[b] Isolated yields.
[c] Cs_2CO_3 (3.0 equiv) was used instead of $NaHCO_3$.

the amides **1** and the formation of carbanion **A**, which then reacted with molecule oxygen to provide peroxy anion **B** (Scheme 3). Intermediate **B** could be assumed to exist in form **C** with a six-membered ring by intermolecular hydrogen bond interaction. Intra or intermolecular abstraction of a proton from the benzylic site of the intermediate **B** leading to loss of hydroxide ion and formation of a carbonyl group of **2**.[21c] The effect of ammonium salt in this reaction may account for the deprotonation step. The detailed mechanism is still unconfirmed at this time and need further investigation in our laboratory.



Scheme 3. Plausible mechanism of α-oxidation reaction.

3. Conclusion

In summary, we describe here an efficient sodium bicarbonate promoted aerobic oxidation reaction in the presence of tetra-*n*-butylammonium bisulfate to afford *N*-monosubstituted α-keto amides. Compared with other reported methods, the current approach provides a very simple and convenient route to α-keto amides from easily available aryl- or heteroarylacetamides in good to high yields. This reaction avoids using toxic reagents and harsh conditions. The usage of the reaction and its applications for the synthesis of bioactive compounds are currently under further investigation in our laboratory and will be reported in due course.

4. Experimental section

4.1. General

All solvents were purified before used.[22] All melting points were taken on a melting point tube. Infrared spectra were recorded on a Nicolet AVATAR 370 FT-IR spectrometer. ^1H and ^{13}C NMR spectra were obtained on a Bruker AV-500 spectrometer. Chemical shifts are reported relative to chloroform (δ=7.26 ppm) or dimethyl sulfoxide (δ=2.50 ppm) for ^1H NMR and chloroform (δ=77.16 ppm) or dimethyl sulfoxide (δ=39.52 ppm) for ^{13}C NMR. GC-MS was carried out on an Agilent 5975 N mass spectrometer (EI, 70 eV). Elemental analyses were carried out on a VARIO EL111 elemental analyzer. Silica gel plate GF_{254} were used for thin layer chromatography (TLC) and silica gel H or 300–400 mesh were used for flash column chromatography. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise indicated.

4.2. General procedure for synthesis of *N*-monosubstituted α-keto amides (2a–r)

To a 25 mL round-bottom flask dried through a calcium chloride tube, **1a**–**r** (0.5 mmol), $NaHCO_3$ (1.5 mmol), and *n*-Bu_4NHSO_4 (0.75 mmol) in dioxane (2.5 mL) were added in the presence of atmospheric oxygen. The reaction mixture was stirred under reflux until **1a**–**r** was disappeared monitored by TLC. After that, the mixture was filtered and washed with ethyl acetate. The filtrate was concentrated under reduced pressure and the crude product was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate) to give **2a**–**r**.

*4.2.1. 2-Oxo-N,2-diphenylacetamide (**2a**)*[23]. Light yellow solid, 89% yield, mp 43–45 °C. IR (KBr): 3436, 3338, 3059, 2925, 1667, 1596, 1281 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 9.04 (s, 1H), 8.40 (dd, *J*=7.5, 1.0 Hz, 2H), 7.71 (d, *J*=7.5 Hz, 2H), 7.66–7.63 (m, 1H), 7.50 (t, *J*=8.0 Hz, 2H), 7.39 (t, *J*=8.0 Hz, 2H), 7.19 (t, *J*=7.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.57, 159.09, 136.76, 134.71, 133.16, 131.53,

129.30, 128.65, 125.38, 120.06. MS (EI): *m*/*z* (%) 225 (27) [M^+], 211 (10), 120 (10), 119 (10), 106 (21), 105 (100), 91 (18), 77 (47).

*4.2.2. 2-Oxo-2-phenyl-N-o-tolylacetamide (**2b**)*[17,24]. Light yellow solid, 85% yield, mp 89.5–91.5 °C. IR (KBr): 3231, 2910, 1677, 1253 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 8.96 (s, 1H), 8.46–8.44 (m, 2H), 8.12 (d, *J*=8.0 Hz, 1H), 7.66 (tt, *J*=7.5, 1.0 Hz, 1H), 7.51 (t, *J*=7.5 Hz, 2H), 7.31–7.24 (m, 2H), 7.15 (td, *J*=7.5, 1.0 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.60, 158.97, 134.70, 133.19, 131.56, 130.75, 128.82, 128.64, 127.02, 127.00, 125.75, 121.80, 17.66. MS (EI): *m*/*z* (%) 239 (28) [M^+], 106 (15), 105 (100), 77 (38).

*4.2.3. N-(2-Methoxyphenyl)-2-oxo-2-phenylacetamide (**2c**).* Light yellow solid, 84% yield, mp 81–84 °C. IR (KBr): 3437, 3384, 2967, 1693, 1663, 1524, 1280 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 9.53 (s, 1H), 8.50 (dd, *J*=8.0, 1.5 Hz, 1H), 8.49–8.40 (m, 2H), 7.65 (tt, *J*=7.5, 1.5 Hz, 1H), 7.53–7.50 (m, 2H), 7.14 (td, *J*=7.5, 1.5 Hz, 1H), 7.02 (td, *J*=7.5, 1.0 Hz, 1H), 6.94 (dd, *J*=8.5, 1.5 Hz, 1H), 3.94 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.63, 159.12, 148.93, 134.60, 133.40, 131.52, 128.68, 126.55, 125.19, 121.17, 119.97, 110.32, 55.93. MS (EI): *m*/*z* (%) 225 (3) [M^+], 215 (12), 214 (100), 212 (99), 133 (25), 105 (86), 77 (35). Anal. Calcd for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.45; H, 4.85; N, 5.59.

*4.2.4. 2-Oxo-2-phenyl-N-m-tolylacetamide (**2d**)*[17]. Light yellow solid, 81% yield, mp 91–93 °C. IR (KBr): 3470, 3341, 1688, 1661, 1279 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 8.99 (s, 1H), 8.41 (d, *J*=7.5 Hz, 2H), 7.65 (t, *J*=7.5 Hz, 1H), 7.57 (s, 1H), 7.51 (t, *J*=7.5 Hz, 3H), 7.28 (t, *J*=7.5 Hz, 1H), 7.02 (d, *J*=7.5 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.58, 159.04, 139.27, 136.66, 134.67, 133.19, 131.53, 129.11, 128.62, 126.19, 120.63, 117.15, 21.59. MS (EI): *m*/*z* (%) 239 (30) [M^+], 134 (14), 133 (10), 106 (15), 105 (100), 77 (38).

*4.2.5. N-(3-Chlorophenyl)-2-oxo-2-phenylacetamide (**2e**)*[25]. Light yellow solid, 83% yield, mp 120–121 °C. IR (KBr): 3474, 3348, 1688, 1660, 1594, 1538, 1484, 1443 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 9.01 (s, 1H), 8.41 (dd, *J*=9.5, 1.0 Hz, 2H), 7.87 (t, *J*=2.0 Hz, 1H), 7.67 (tt, *J*=7.5, 1.0 Hz, 1H), 7.53–7.50 (m, 3H), 7.32 (t, *J*=8.0 Hz, 1H), 7.18–7.17 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.09, 159.00, 137.88, 135.05, 134.94, 132.97, 131.61, 130.32, 128.74, 125.47, 120.16, 118.06. MS (EI): *m*/*z* (%) 261 (4) [M^+ (^{37}Cl)], 259 (12) [M^+ (^{35}Cl)], 105 (100), 77 (28).

*4.2.6. 2-Oxo-2-phenyl-N-p-tolylacetamide (**2f**)*[17]. Light yellow solid, 80% yield, mp 114.5–116.4 °C. IR (KBr): 3444, 3340, 2923, 1671, 1535, 1281 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 8.92 (s, 1H), 8.41 (d, *J*=7.0 Hz, 2H), 7.66 (t, *J*=7.5 Hz, 1H), 7.59 (AA′ of AA′BB′, *J*=8.5 Hz, 2H), 7.51 (t, *J*=8.0 Hz, 2H), 7.20 (BB′ of AA′BB′, *J*=8.5 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.66, 158.89, 135.20, 134.71, 134.22, 133.28, 131.60, 129.87, 128.67, 120.03, 21.12. MS (EI): *m*/*z* (%) 239 (37) [M^+], 106 (17), 105 (100), 77 (38).

*4.2.7. N-(4-Methoxyphenyl)-2-oxo-2-phenylacetamide (**2g**)*[17]. Light yellow solid, 85% yield, mp 94–95 °C. IR (KBr): 3367, 3341, 2957, 2928, 1664, 1511, 1245 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 8.90 (s, 1H), 8.41 (AA′ of AA′BB′, *J*=7.0 Hz, 2H), 7.67–7.61 (m, 3H), 7.50 (t, *J*=8.0 Hz, 2H), 6.94 (BB′ of AA′BB′, *J*=7.0 Hz, 2H), 3.82 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.74, 158.80, 157.16, 134.68, 133.32, 131.57, 129.93, 128.66, 121.63, 114.47, 55.61. MS (EI): *m*/*z* (%) 255 (46) [M^+], 149 (10), 122 (11), 105 (100), 77 (35).

*4.2.8. N-(4-Chlorophenyl)-2-oxo-2-phenylacetamide (**2h**)*[17]. Light yellow solid, 93% yield, mp 158–160 °C. IR (KBr): 3339, 1696, 1663, 1532, 1278, 1166 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 9.02 (s, 1H), 8.49 (dd, *J*=8.0, 1.0 Hz, 2H), 7.66 (AA′ of AA′BB′, *J*=9.0 Hz, 2H), 7.68–7.64 (m, 1H), 7.51 (t, *J*=8.0 Hz, 2H), 7.35 (BB′ of AA′BB′, *J*=9.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.19, 158.92, 135.33, 134.91, 133.02, 131.60, 130.49, 129.41, 128.73, 121.26. MS (EI): *m*/*z* (%) 261 (5) [M^+ (^{37}Cl)], 259 (15) [M^+ (^{35}Cl)], 105 (100), 77 (31).

*4.2.9. N-(4-Bromophenyl)-2-oxo-2-phenylacetamide (**2i**)*[17]. Light yellow solid, 80% yield, mp 160–162 °C. IR (KBr): 3340, 2925, 1488, 1279, 1166, 1069 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 8.98 (s, 1H), 8.40 (d, *J*=7.5 Hz, 2H), 7.67 (t, *J*=7.5 Hz, 1H), 7.61 (AA′ of AA′BB′, *J*=8.5 Hz, 2H), 7.51 (BB′ of AA′BB′, *J*=9.0 Hz, 2H), 7.53–7.50 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.14, 158.89, 135.84, 134.95, 133.04, 132.40, 131.64, 128.77, 121.57, 118.22. MS (EI): *m*/*z* (%) 304 (10) [M^+ (^{81}Br)], 303 (10) [M^+ (^{79}Br)], 105 (100), 77 (33).

*4.2.10. N-(4-Nitro-phenyl)-2-oxo-2-phenyl-acetamide (**2j**)*[26]. Light yellow solid, 29% yield, mp 170–172 °C. IR (KBr): 3329, 2958, 2925, 1509, 1339, 1264 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 9.29 (br, 1H), 8.43 (d, *J*=8.0 Hz, 2H), 8.30 (AA′ of AA′BB′, *J*=9.0 Hz, 2H), 7.90 (BB′ of AA′BB′, *J*=9.0 Hz, 2H), 7.70 (t, *J*=7.0 Hz, 1H), 7.55 (t, *J*=8.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 186.39, 158.90, 142.37, 135.31, 132.69, 131.73, 128.91, 125.39, 119.73. MS (EI): *m*/*z* (%) 270 (4) [M^+], 105 (100), 77 (31).

*4.2.11. 2-(4-Chlorophenyl)-2-oxo-N-phenylacetamide (**2k**).* Light yellow solid, 83% yield, mp 127–128 °C. IR (KBr): 3458, 3338, 1655, 1535, 1277, 1165 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 8.96 (br, 1H), 8.41 (d, *J*=8.5 Hz, 2H), 7.69 (AA′ of AA′BB′, *J*=7.5 Hz, 2H), 7.48 (BB′ of AA′BB′, *J*=8.5 Hz, 2H), 7.41 (t, *J*=8.0 Hz, 2H), 7.21 (t, *J*=7.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 186.19, 158.66, 141.64, 136.59, 133.11, 131.53, 129.41, 129.12, 125.60, 120.08. MS (EI): *m*/*z* (%) 261 (6) [M^+ (^{37}Cl)], 259 (16) [M^+ (^{35}Cl)], 149 (9), 105 (100), 77 (32). Anal. Calcd for $C_{14}H_{10}ClNO_2$: C, 64.75; H, 3.88; N, 5.39. Found: C, 64.55; H, 3.82; N, 5.42.

*4.2.12. 2-(4-Methoxyphenyl)-2-oxo-N-phenyl-acetamide (**2l**)*[27]. Light yellow solid, 84% yield, mp 110.0–111.0 °C. IR (KBr): 3441, 3353, 2849, 1688, 1642, 1595, 1565, 1531, 1445, 1164 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 9.07 (s, 1H), 8.48 (d, *J*=9.0 Hz, 2H), 7.70 (AA′ of AA′BB′, *J*=8.0 Hz, 2H), 7.38 (t, *J*=8.0 Hz, 2H), 7.18 (d, *J*=7.5 Hz, 1H), 6.96 (BB′ of AA′BB′, *J*=8.5 Hz, 2H), 3.89 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 185.35, 165.00, 159.66, 136.89, 134.35, 129.28, 126.18, 125.25, 120.02, 114.02, 55.69. MS (EI): *m*/*z* (%) 255 (12) [M^+], 135 (100), 77 (12).

*4.2.13. N-(Naphthalen-1-yl)-2-oxo-2-phenylacetamide (**2m**)*[28]. Light yellow solid, 64% yield, mp 102–103 °C. IR (KBr): 3441, 3178, 1667, 1656, 1594, 1535, 1502, 1442 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 9.56 (s, 1H), 8.51–8.49 (m, 2H), 8.25 (d, *J*=7.5 Hz, 1H), 7.97 (d, *J*=8.5 Hz, 1H), 7.91 (dd, *J*=8.0, 0.5 Hz, 1H), 7.77 (d, *J*=8.0 Hz, 1H), 7.70–7.67 (m, 1H), 7.62–7.58 (m, 1H), 7.57–7.53 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 187.60, 159.45, 134.86, 134.21, 133.27, 131.72, 131.25, 129.04, 128.76, 126.81, 126.61, 126.41, 125.86, 120.35, 119.65. MS (EI): *m*/*z* (%) 275 (38) [M^+], 270 (28), 150 (37), 120 (71), 105 (100), 77(64).

*4.2.14. 2-Oxo-2-phenyl-N-(pyrimidin-5-yl)acetamide (**2n**).* Light yellow solid, 93% yield, mp 169–170 °C. IR (KBr): 3441, 2831, 1669, 1438, 1277, 1200 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 9.18 (s, 2H), 9.12 (s, 1H), 9.08 (s, 1H), 8.44–8.42 (m, 2H), 7.72–7.69 (m, 1H), 7.54 (t, *J*=8.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 185.97, 159.31, 155.22, 148.08, 135.40, 132.62, 131.73, 128.94. MS (EI): *m*/*z* (%) 227 (7) [M^+], 199 (23), 105 (100), 83 (40), 77 (45). Anal. Calcd for $C_{12}H_9N_3O_2$: C, 63.43; H, 3.99; N, 18.49. Found: C, 63.46; H, 4.03; N, 18.43.

*4.2.15. 2-Oxo-2-phenyl-N-(pyridin-2-yl)acetamide (**2o**).* Light yellow solid, 52% yield, mp 69–70 °C. IR (KBr): 3436, 1675, 1620, 1594,

1579, 1531, 1465 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 9.55 (s, 1H), 8.39–8.37 (m, 3H), 8.32 (d, J=8.0 Hz, 1H), 7.78 (td, J=7.5, 2.0 Hz, 1H), 7.66 (tt, J=7.5, 1.5 Hz, 1H), 7.53–7.50 (m, 2H), 7.13 (dd, J=7.5, 1.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 186.91, 159.84, 150.43, 148.53, 138.54, 134.75, 132.98, 131.36, 128.70, 120.77, 114.43. MS (EI): m/z (%) 226 (9) [M^+], 105 (100), 77 (45). Anal. Calcd for $C_{13}H_{10}N_2O$: C, 69.02; H, 4.46; N, 12.38. Found: C, 69.02; H, 4.26; N, 12.42.

*4.2.16. N-Butyl-2-oxo-2-phenylacetamide (**2p**)*[29]. Light yellow liquid, 55% yield. IR (film): 3314, 2959, 2932, 2872, 1666, 1596, 1527, 1448, 747 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 8.30 (dd, J=8.0, 1.0 Hz, 2H), 7.61–7.58 (m, 1H), 7.45 (t, J=8.0 Hz, 2H), 7.17 (br, 1H), 3.37 (q, J=7.0 Hz, 2H), 1.67 (quint, J=7.5 Hz, 2H), 1.38 (sextet, J=7.5 Hz, 2H), 0.93 (t, J=7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 188.08, 161.93, 134.41, 133.46, 131.25, 128.54, 39.24, 31.40, 20.14, 13.78. MS (EI): m/z (%) 205 (17) [M^+], 105 (100), 77 (30), 57 (27).

*4.2.17. 2-(1-Methyl-1H-indol-3-yl)-2-oxo-N-phenylacetamide (**2q**)*[30]. Yellow solid, 59% yield, mp 151–152 °C. IR (KBr): 3356, 3149, 1682, 1630, 1589, 1508, 1440, 1368, 1078 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 9.42 (s, 1H), 9.04 (s, 1H), 8.47–8.45 (m, 1H), 7.72 (d, J=8.0 Hz, 2H), 7.42–7.38 (m, 5H), 7.19 (t, J=7.5 Hz, 1H), 3.88 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 179.60, 160.23, 142.35, 137.06, 137.00, 129.18, 127.74, 124.93, 124.07, 123.67, 122.67, 119.86, 111.66, 110.04, 33.85. MS (EI): m/z (%) 278 (15) [M^+], 158 (100), 77 (14).

*4.2.18. 2-Oxo-N-phenyl-2-(thiophen-2-yl)acetamide (**2r**).* Yellow solid, 44% yield, mp 129–130 °C. IR (KBr): 3307, 1689, 1643, 1407, 1361, 1283, 1050, 744 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 9.15 (s, 1H), 8.47 (d, J=4.0 Hz, 1H), 7.86 (dd, J=5.0, 1.0 Hz, 1H), 7.71 (d, J=8.0 Hz, 2H), 7.39 (t, J=8.0 Hz, 2H), 7.22–7.18 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.38, 158.32, 139.23, 138.58, 136.44, 136.27, 129.26, 128.39, 125.43, 120.00. m/z (%) 231 (29) [M^+], 111 (100), 77 (11). Anal. Calcd for $C_{12}H_9NO_2S$: C, 62.32; H, 3.92; N, 6.06. Found: C, 62.23; H, 3.96; N, 6.10.

Acknowledgements

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Supplementary data

^1H NMR and ^{13}C NMR spectra of all compounds. Supplementary data of ^1H NMR and ^{13}C NMR spectra of all compounds are available. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.11.005.

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