Tetrahedron 69 (2013) 9063–9067

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

$SnCl_4$ mediated synthesis of γ-amino ketones derivatives via the ring-opening reaction of 4,5-dihydropyrroles

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ARTICLE INFO

Article history:
Received 16 May 2013
Received in revised form 23 July 2013
Accepted 15 August 2013
Available online 20 August 2013

Keywords:
4,5-Dihydropyrrole
$SnCl_4 \cdot 5H_2O$
Lewis acid
γ-Amino ketones
Pyrrole ring-opening

ABSTRACT

This paper presents an alternative route to γ-amino ketones via a $SnCl_4 \cdot 5H_2O$ mediated ring-opening reaction of the 4,5-dihydropyrroles with the advantages of readily available reactants, good to excellent yields and applicability to a wide range of substrates.

1. Introduction

The compounds with a side chain of γ-amino ketones are identified with diverse biological activities as anti-inflammatory phospholipase-A_2 inhibitors,[1] β-lactam inhibitors of human leukocyte elastase-1,[2] hypotensive agents,[3] central nervous system agents,[4] etc. Moreover, γ-amino ketones themselves are also useful intermediates in organic synthesis.[5] Among their applications, the preparation of highly functionalized tryptamines is a well-known example.[5a,6] In reviewing previous reports, γ-amino ketones can be prepared in several methods as follows (Scheme 1): (a) Hydrolysis of 4,5-dihydropyrrole derivatives in the presence of Brønsted acid, however, an obvious drawback of this method is that it can not provide structural diverse γ-amino ketones due to the substrate limitations.[5a,6,7] (b) Treating *N*-substituted 2-pyrrolidinones with RMgX.[5c,8] (c) Hydration reaction of the functional groups (such as alkene or alkyne) of which can be converted into a carbonyl group.[9] (d) Nucleophilic substitution of halide by amines.[10] (e) Ring-opening reaction of cyclopropyl aryl ketones with sulfonamides.[11] Besides, there are also some other synthetic methods, such as the ring-opening reaction of aziridines,[12] the conversion of carboxylic acids to γ-amino ketones.[5b,13] However, the existing synthetic methods for the preparation of γ-amino ketones more or less suffer from strong Brønsted acid, unsatisfactory yields, tedious reaction procedure, significant expensive reactants, and/or need of inert atmosphere, a remarkably limited substrate range and so on. So far as we know, only one case of Lewis acid mediated was that Shi et al. reported the synthesis of γ-amino ketones in the presence of $Zr(OTf)_4$ in 2004, but it encountered uncontrollable yield of the desired products.[11] Herein, we present a facile approach for the preparation of γ-amino ketones in good to excellent yields mediated by $SnCl_4 \cdot 5H_2O$ via ring-opening reaction of substituted 4,5-dihydropyrroles **1**, which were prepared in high yield by the reaction of amines and doubly activated cyclopropanes in EtOH at reflux (Scheme 1).[14]

2. Results and discussion

Combined with our recent research on the synthesis of nitrogen-containing heterocyclic compounds from readily available acetoacetamides precursors,[15] we made a lot of efforts to realize the intramolecular cyclization form **1** to **3** catalyzed by Lewis acids. We first focused on the reactivity of **1i** but the results were disappointing. The experiments showed that pyrrolo[3,2-*c*]quinolin-4-one **3i** could not be obtained in the presence of $FeCl_3$, $TiCl_4$, $AlCl_3$, and $BF_3 \cdot Et_2O$ (Scheme 2).[15c] However, after many attempts, it was

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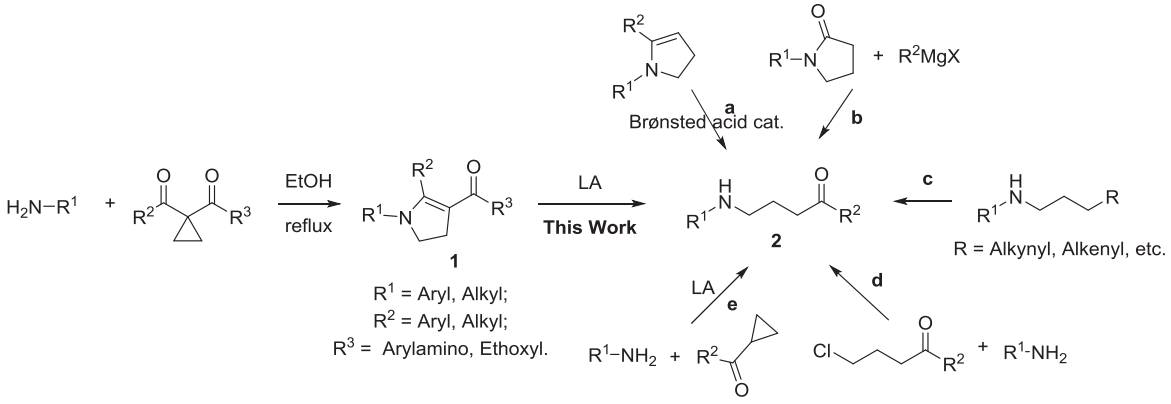
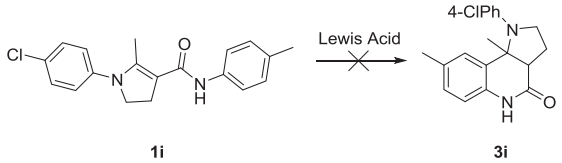
http://dx.doi.org/10.1016/j.tet.2013.08.027



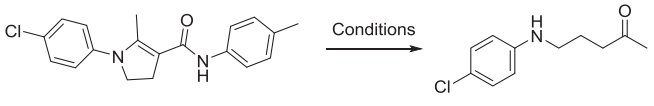
Scheme 1. Synthetic approaches of γ-amino ketones **2**.



Scheme 2. The reaction of 4,5-dihydropyrroles **1i** in the presence of Lewis acid.

found that the ring-opening product 5-((4-chlorophenyl)amino) pentan-2-one **2i** could be isolated in the yield of 85% by treating **1i** (0.5 mmol) with $SnCl_4·5H_2O$ (0.6 mmol) in xylene (2.0 mL) at reflux after 18 h (Table 1, entry 1). Further exploration disclosed that lowering the reaction temperature had significant influence on the conversion (entry 1 vs 2 and 3). Similarly, treatment of **1i** with 1.0 equiv of $SnCl_4·5H_2O$ for 20 h could only afford **2i** in 63% yield along with the recovered **1i** (30%) (entry 4). The screening also

Table 1
Survey of the reaction conditions[a]



Entry	Catalyst (equiv)	Solvent	*T*/°C	Time/h	Yield/%[b]
1	$SnCl_4·5H_2O$ (1.2)	Xylene	Reflux	18	85
2	$SnCl_4·5H_2O$ (1.2)	Xylene	120	24	63[c]
3	$SnCl_4·5H_2O$ (1.2)	Xylene	90	48	0[d]
4	$SnCl_4·5H_2O$ (1.0)	Xylene	Reflux	20	63[e]
5	$SnCl_4·5H_2O$ (1.2)	Xylene	Reflux	13	77[f]
6	$SnCl_4·5H_2O$ (1.2)	DMSO	145	5.5	0[g]
7	$SnCl_4·5H_2O$ (1.2)	$MeNO_2$	Reflux	5.5	52[g]
8	$SnCl_4·5H_2O$ (1.2)	Dioxane	Reflux	18	69[h]
9	$SnCl_4$ (1.2)	Xylene	Reflux	8	Trace[i]
10	$SnCl_4$ (1.2)+H_2O (6.0)	Xylene	Reflux	8	80%
11	$FeCl_3$ (1.2)	Xylene	Reflux	18	0%
12	$TiCl_4$ (1.2)	Xylene	Reflux	18	0%[j]
13	$BF_3·Et_2O$ (1.2)	Xylene	Reflux	18	70%[k]
14	$AlCl_3$ (1.2)	Xylene	Reflux	18	57%[l]

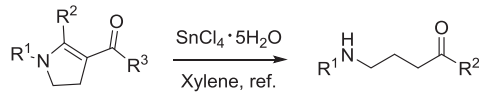
[a] All reactions were carried out with **1i** (0.5 mmol) in solvent (2.0 mL).
[b] Isolated yield.
[c] 20% **1i** was recovered.
[d] 80% **1i** was recovered.
[e] 30% **1i** was recovered.
[f] 13% **1i** was recovered.
[g] Along with a complex mixture without any recognizable product.
[h] 17% **1i** was recovered.
[i] Reaction was carried out in N_2 atmosphere, 23% **1i** was recovered along with unidentified complex mixture.
[j] 75% **1i** was recovered.
[k] 10% **1i** was recovered.
[l] 20% **1i** was recovered.

demonstrated that other solvents, such as DMSO, $MeNO_2$, and dioxane were proved to be fundamentally ineffective (entry 6) or low efficiency (entries 7, 8). It was observed that $FeCl_3$, $TiCl_4$, $AlCl_3$, and $BF_3·Et_2O$ were proved to be ineffective or less effective for the transformation (entries 11–14).

Under the optimal conditions (Table 1, entry 1), a range of substrates **1** was carried out to extend the scope of the ring-opening reaction, and some of the results were summarized in Table 2. It has been found that the reactions of **1a**–**r** proceeded smoothly to afford the corresponding substituted γ-amino ketones **2** in the presence of $SnCl_4·5H_2O$ at reflux (Table 2). Obviously, the substituents on the 4,5-dihydro-1*H*-pyrrole ring had significant effects on the yields and reaction times of the ring-opening reaction. For compounds **1a**–**c** with an electron donating group (EDG) (OMe) on the benzene ring of the *N*-phenyl moiety, the isolated yield of **2b** (92%) with a methoxy group at *meta*-position was slightly higher than that of the products with a methoxy group at *ortho*- (**2a**: 85%) and *para*- (**2c**: 65%) positions (entries 1–3). Quite similar with the phenyl non-substituted product **2d** (entry 4), it required a dramatically longer reaction times to provide the product **2g** in approximately equal yield to **2e**, **2f**, and **2h** when the substrates **1e**–**h** with an electron withdrawing group (EWG) (Cl, CO_2Et) on the *N*-phenyl moiety were used for the conversion (entries 5–8). For α-methyl substituted reactants **1i**–**l**, the small change of the electronic effects of the aryl group on *N*-phenyl moiety could affect the yields of the reaction. The γ-amino ketone **2i** with an EWG on the benzene ring was obtained in the yields of 85% and 86%, respectively (entries 9 and 10), which were little higher than the yields of **2j** and **2k** in entries 11, 12, and 13 (60%, 63%, and 67%, respectively) with an EDG on the benzene ring. To our delight, all of the 3-ester substituted pyrroles **1n**–**q** could also smoothly slide into the corresponding products **2** in high yields (82–96%) regardless of the electronic nature of the diversity substituent (entries 14–17). However, *N*-benzyl substituted 4,5-dihydro-1*H*-pyrrole derivatives **1r** provided an unidentified complex mixture instead of the desired **2m** (entry 18). It is worth noting that all the synthesized compounds **2** are unstable, and should be stored under an inert atmosphere in the dark.

Unfortunately, any intermediate, as direct evidence for the mechanism of the ring-opening reactions, was not isolated in the control experiments of quenching the reaction in 13 h (Table 1, entry 5) or performing the reaction at slightly lower temperature (Table 1, entries 2 and 3). But by analysis of the structure of the product **2**, we can see that it should experience the hydrolysis and decarboxylation steps during the conversion from **1** to **2**. So we deduced that it should not afford the desired product **2** under anhydrous conditions. The controlled experiments were carried out under anhydrous conditions. **1i** was subjected into anhydrous $SnCl_4$

Table 2
Reaction extension[a,b]



1 **2**

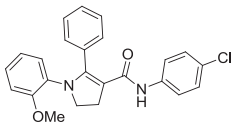
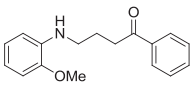
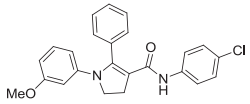
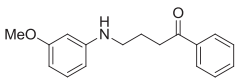
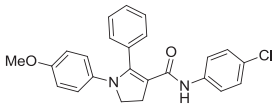
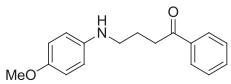
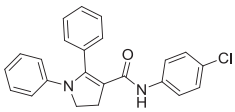
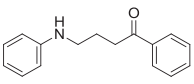
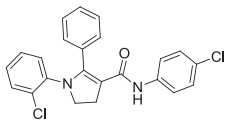
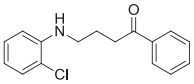
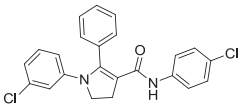
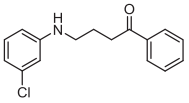
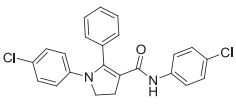
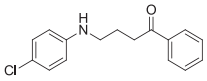
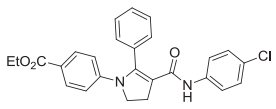
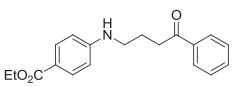
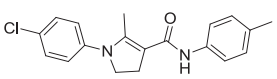
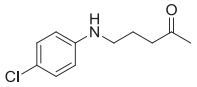
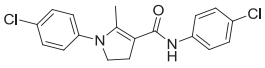
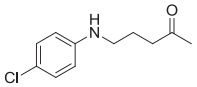
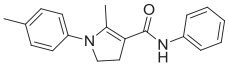
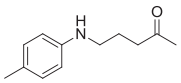
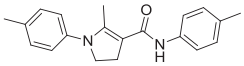
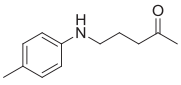
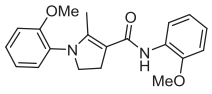
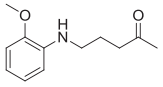
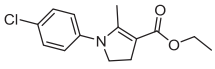
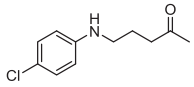
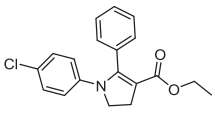
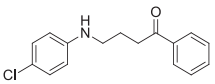
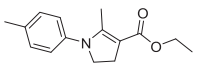
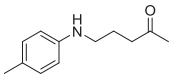
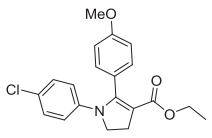
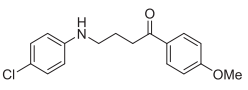
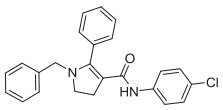
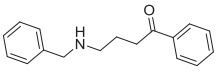
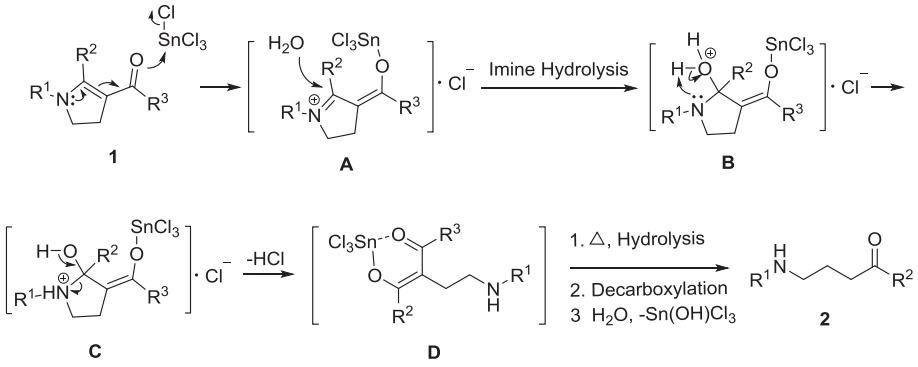
Entry	Substrates **1**	Products **2**
1	 **1a**	 **2a**: 13 h, 85%
2	 **1b**	 **2b**: 12 h, 92%
3	 **1c**	 **2c**: 12 h, 65%
4	 **1d**	 **2d**: 13 h, 94%
5	 **1e**	 **2e**: 4.0 h, 85%
6	 **1f**	 **2f**: 5.0 h, 90%
7	 **1g**	 **2g**: 19 h, 92%
8	 **1h**	 **2h**: 4.0 h, 87%

Table 2 (*continued*)

Entry	Substrates **1**	Products **2**
9	 **1i**	 **2i**: 18 h, 85%
10	 **1j**	 **2i**: 24 h, 86%
11	 **1k**	 **2j**: 22 h, 60%
12	 **1l**	 **2j**: 22 h, 63%
13	 **1m**	 **2k**: 6.5 h, 67%
14	 **1n**	 **2i**: 4.0 h, 96%
15	 **1o**	 **2g**: 4.0 h, 95%
16	 **1p**	 **2j**: 4.0 h, 89%
17	 **1q**	 **2l**: 4.0 h, 82%
18	 **1r**	 **2m**: 4.0 d, trace

[a] All reactions were carried out with **1** (0.5 mmol), $SnCl_4 \cdot 5H_2O$ (0.6 mmol) in xylene (2.0 mL) at reflux.
[b] Isolated yield.

at 130 °C for 8.0 h in N_2, then the reaction was quenched. After work-up, the residue was investigated by means of LC-MS. We found 23% **1i** and only a trace amount of **2i** in the reaction mixture along with some unrecognizable products (Table 1, entry 9). Additionally, it could provide **2i** in the yield of 80% when 6.0 equiv water was added to the reaction mixture in the presence of anhydrous $SnCl_4$ after 8.0 h (Table 1, entry 10). All of these controlled experiments indicated the importance of water on the transformation. We deduced the plausible mechanism according to the conditions screening and above controlled experiments together with some previous literature results. In a simplified, generally accepted mechanistic model as shown in Scheme 3, highly



Scheme 3. Proposed mechanism.

substituted 4,5-dihydro-1*H*-pyrroles **1** initially coordinated with the $SnCl_4 \cdot 5H_2O$ to generate *N*-arylpyrrolinium analogue **A**. Subsequently, species **A** further converted into the chain α-monosubstituted β-dicarbonyl intermediate **D** via the hydrolysis of the imine[5a,6,7,8b] and dehydrochlorination process.[15b,c] Finally, the intermediates **D** produced the γ-amino ketones **2** via the hydrolysis and decarboxylation reaction.[12a,15b,c]

3. Conclusion

In summary, a facile and efficient method for the synthesis of γ-amino ketones **2** has been developed from readily available multi-substituted-4,5-dihydropyrroles. The procedure involves a continuous multiple bond cleavage process in the presence of $SnCl_4 \cdot 5H_2O$. This protocol is associated with readily available starting materials, a wide range of substrates scope, excellent yields, dense, and flexible substituted patterns, and important synthetic potential of the products.

4. Experimental

4.1. General

All reagents were purchased from commercial sources and used without further treatment, unless otherwise indicated. Xylene were distilled from sodium/benzophenone ketyl and purged with nitrogen atmosphere prior to use. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance/400 (^{1}H: 400 MHz, ^{13}C: 100 MHz at 25 °C) and TMS as internal standard. Data are represented as follows: chemical shift, integration, multiplicity (br=broad, s=singlet, d=doublet, dd=double doublet, t=triplet, q=quartet, m=multiplet), coupling constants in Hertz (Hz). All high-resolution mass spectras (HRMS) were measured on a Bruker MicroTOF mass spectrometer Bruker microTOF (ESI-oa-TOF). Melting points were measured on a YuHua X-5 apparatus.

4.2. General procedure for the ring-opening reaction (Table 2)

A mixture of **1** (0.5 mmol) and $SnCl_4 \cdot 5H_2O$ (210 mg, 0.6 mmol) in xylene (2.0 mL) in a round-bottom flask (25 mL) equipped with a spherical condenser (40 cm length) was well stirred for 18 h at reflux. After cooling off, the mixture was added water (5.0 mL) and NaOH (144 mg) at stirring. After 10 min, the mixture was extract with CH_2Cl_2 (5.0 mL×3) and the combined organic phases were dried over anhydrous $MgSO_4$, then removed under reduced pressure, and the residue was purified through a short flash silica gel column chromatography to give compound **2**.

*4.2.1. 4-((2-Methoxyphenyl)amino)-1-phenylbutan-1-one (**2a**).* White solid. Mp: 78–80 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98–7.96 (m, 2H), 7.57–7.55 (m, 1H), 7.48–7.44 (m, 2H), 6.90–6.86 (m, 1H), 6.78–6.76 (m, 1H), 6.69–6.63 (m, 2H), 4.27 (br, 1H), 3.84 (s, 3H), 3.26–3.25 (m, 2H), 3.14 (t, *J*=7.2 Hz, 2H), 2.15–2.08 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.94, 146.95, 138.40, 137.13, 133.13, 128.71, 128.17, 121.49, 116.51, 109.99, 109.64, 55.55, 43.29, 36.22, 24.17. HRMS (ESI), *m*/*z* calcd for $C_{17}H_{19}NO_2$ ($[M+H]^+$) 270.1489, found: 270.1489.

*4.2.2. 4-((3-Methoxyphenyl)amino)-1-phenylbutan-1-one (**2b**).* White solid. Mp: 67–69 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.96 (s, 1H), 7.57 (t, *J*=7.6 Hz, 1H), 7.46 (t, *J*=8.0 Hz, 2H), 7.10–7.06 (m, 1H), 6.28–6.23 (m, 2H), 6.18 (t, *J*=2.4 Hz, 1H), 3.80 (br, 1H), 3.77 (s, 3H), 3.22 (t, *J*=6.8 Hz, 2H), 3.12 (t, *J*=6.8 Hz, 2H), 2.12–2.05 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.95, 160.96, 149.78, 136.95, 133.23, 130.10, 128.74, 128.14, 106.02, 102.56, 98.73, 55.20, 43.57, 36.16, 23.86. HRMS (ESI), *m*/*z* calcd for $C_{17}H_{19}NO_2$ ($[M+H]^+$) 270.1489, found: 270.1489.

*4.2.3. 4-((4-Methoxyphenyl)amino)-1-phenylbutan-1-one (**2c**).* Yellow solid. Mp: 77–79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J*=7.6 Hz, 2H), 7.57 (t, *J*=7.2 Hz, 1H), 7.46 (t, *J*=7.6 Hz, 2H), 6.78 (d, *J*=8.8 Hz, 2H), 6.59 (d, *J*=8.8 Hz, 2H), 3.74 (s, 3H), 3.47 (br, 1H), 3.18 (t, *J*=6.8 Hz, 2H), 3.12 (t, *J*=7.2 Hz, 2H), 2.12–2.03 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.05, 152.19, 142.65, 137.00, 133.23, 128.75, 128.17, 115.04, 114.20, 55.96, 44.56, 36.24, 24.10. HRMS (ESI), *m*/*z* calcd for $C_{17}H_{19}NO_2$ ($[M+H]^+$) 270.1489, found: 270.1489.

*4.2.4. 1-Phenyl-4-(phenylamino)butan-1-one (**2d**).*[16] White solid. Mp: 76–78 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J*=7.2 Hz, 2H),

7.57 (t, J=6.8 Hz, 1H), 7.47 (t, J=7.2 Hz, 2H), 7.18 (t, J=6.8 Hz, 2H), 6.70 (t, J=6.8 Hz, 1H), 6.63 (d, J=7.6 Hz, 2H), 3.75 (br, 1H), 3.24 (t, J=6.4 Hz, 2H), 3.12 (t, J=6.8 Hz, 2H), 2.13–2.05 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.94, 148.43, 137.08, 133.19, 129.39, 128.74, 128.16, 117.45, 112.91, 43.65, 36.22, 24.04. HRMS (ESI), m/z calcd for $C_{16}H_{17}NO$ ($[M+H]^+$) 240.1386, found: 240.1383.

*4.2.5. 4-((2-Chlorophenyl)amino)-1-phenylbutan-1-one (**2e**).* White solid. Mp: 63–65 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J=7.6 Hz, 2H), 7.57 (t, J=7.2 Hz, 1H), 7.47 (t, J=8.0 Hz, 2H), 7.25 (d, J=8.0 Hz, 1H), 7.14 (t, J=8.0 Hz, 1H), 6.70 (d, J=8.0 Hz, 1H), 6.62 (t, J=8.0 Hz, 1H), 4.40 (br, 1H), 3.29 (dd, J=12.4, 6.4 Hz, 2H), 3.14 (t, J=6.8 Hz, 2H), 2.17–2.10 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.73, 144.09, 136.95, 133.27, 129.23, 128.76, 128.16, 127.95, 119.20, 117.22, 111.27, 43.23, 35.98, 23.66. HRMS (ESI), m/z calcd for $C_{16}H_{16}ClNO$ ($[M+H]^+$) 274.0993, found: 274.0993.

*4.2.6. 4-((3-Chlorophenyl)amino)-1-phenylbutan-1-one (**2f**).* White solid. Mp: 102–104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J=7.2 Hz, 2H), 7.58 (t, J=7.2 Hz, 1H), 7.47 (t, J=8.0 Hz, 2H), 7.06 (t, J=8.0 Hz, 1H), 6.64 (dd, J_1=8.0 Hz, J_2=1.6 Hz, 1H), 6.58 (t, J=2.0 Hz, 1H), 6.47 (dd, J_1=8.0 Hz, J_2=1.6 Hz, 1H), 3.90 (br, 1H), 3.20–3.19 (m, 2H), 3.12 (t, J=6.8 Hz, 2H), 2.12–2.05 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.88, 149.47, 136.84, 135.11, 133.33, 130.29, 128.77, 128.13, 117.13, 112.31, 111.18, 43.43, 36.11, 23.59. HRMS (ESI), m/z calcd for $C_{16}H_{16}ClNO$ ($[M+H]^+$) 274.0989, found: 274.0993.

*4.2.7. 4-((4-Chlorophenyl)amino)-1-phenylbutan-1-one (**2g**).* White solid. Mp: 126–129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J=7.6 Hz, 2H), 7.57 (t, J=7.2 Hz, 1H), 7.46 (t, J=7.6 Hz, 2H), 7.12–7.08 (m, 2H), 6.56–6.51 (m, 2H), 3.83 (br, 1H), 3.18 (t, J=6.8 Hz, 2H), 3.10 (t, J=7.2 Hz, 2H), 2.10–2.03 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.81, 146.81, 136.79, 133.21, 129.05, 128.67, 128.03, 121.76, 113.82, 43.64, 36.01, 23.61. HRMS (ESI), m/z calcd for $C_{16}H_{16}ClNO$ ($[M+H]^+$) 274.0991, found: 274.0993.

*4.2.8. Ethyl 4-((4-oxo-4-phenylbutyl)amino)benzoate (**2h**).* White solid. Mp: 83–85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J=6.8 Hz, 2H), 7.86 (d, J=8.8 Hz, 2H), 7.58–7.55 (m, 1H), 7.46 (t, J=7.6 Hz, 2H), 6.56 (d, J=8.8 Hz, 2H), 4.39 (br, 1H), 4.30 (dd, J=7.2 Hz, 2H), 3.26 (dd, J=6.4 Hz, 2H), 3.12 (t, J=6.8 Hz, 2H), 2.13–2.06 (m, 2H), 1.35 (t, J=7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.82, 167.00, 151.99, 136.76, 133.35, 131.60, 128.76, 128.09, 118.59, 111.44, 60.27, 43.06, 36.04, 23.45, 14.56. HRMS (ESI), m/z calcd for $C_{19}H_{21}NO_3$ ($[M+H]^+$) 312.1597, found: 312.1594.

*4.2.9. 5-((4-Chlorophenyl)amino)pentan-2-one (**2i**).* White solid. Mp: 100–102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (d, J=8.2 Hz, 2H), 6.43 (d, J=8.2 Hz, 2H), 3.66 (br, 1H), 3.01 (t, J=6.8 Hz, 2H), 2.48 (t, J=6.8 Hz, 2H), 2.08 (s, 3H), 1.84–1.77 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.62, 146.91, 129.15, 121.87, 113.83, 43.64, 41.21, 30.13, 23.27. HRMS (ESI), m/z calcd for $C_{11}H_{14}ClNO$ ($[M+H]^+$) 212.0834, found: 212.0837.

*4.2.10. 5-(p-Tolylamino)pentan-2-one (**2j**).* White solid. Mp: 72–74 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (d, J=8.0 Hz, 2H), 6.53 (d, J=8.0 Hz, 2H), 3.53 (br, 1H), 3.11 (t, J=6.8 Hz, 2H), 2.56 (t, J=6.8 Hz, 2H), 2.24 (s, 3H), 2.15 (s, 3H), 1.92–1.86 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.74, 146.07, 129.84, 126.62, 112.98, 77.48, 76.84, 43.82, 41.30, 30.13, 23.56, 20.47. HRMS (ESI), m/z calcd for $C_{12}H_{17}NO$ ($[M+H]^+$) 192.1383, found: 192.1377.

*4.2.11. 5-((2-Methoxyphenyl)amino)pentan-2-one (**2k**).* Brown liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 (t, J=7.6 Hz, 1H), 6.76 (d, J=7.6 Hz, 1H), 6.66 (t, J=7.6 Hz, 1H), 6.60 (d, J=8.0 Hz, 1H), 4.19 (br, 1H), 3.84 (s, 3H), 3.15 (t, J=6.8 Hz, 2H), 2.58 (t, J=7.2 Hz, 2H), 2.16 (s, 3H), 1.96–1.89 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.62, 146.87, 138.30, 121.43, 116.50, 109.83, 109.53, 55.53, 43.09, 41.27, 30.14, 23.63. HRMS (ESI), m/z calcd for $C_{12}H_{17}NO_2$ ($[M+H]^+$) 208.1332, found: 208.1335.

*4.2.12. 4-((4-Chlorophenyl)amino)-1-(4-methoxyphenyl)butan-1-one (**2l**).* White solid. Mp: 125–127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95–7.92 (m, 2H), 7.12–7.08 (m, 2H), 6.94–6.91 (m, 2H), 6.54–6.50 (m, 2H), 3.86 (s, 3H), 3.83 (br, 1H), 3.17 (t, J=6.8 Hz, 2H), 3.05 (t, J=6.8 Hz, 2H), 2.08–2.02 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.45, 163.63, 146.97, 130.40, 129.98, 129.13, 121.75, 113.86, 113.85, 55.59, 43.77, 35.74, 23.85. HRMS (ESI), m/z calcd for $C_{17}H_{18}ClNO_2$ ($[M+H]^+$) 304.1099, found: 304.1092.

Acknowledgements

We thank the NSFC (21002051, 21172056, and 21272057), PCSIRT (IRT1061), China Postdoctoral Science Foundation funded project (2012M521397 and 2013M530339), Key Project of Henan Educational Committee (13A150546), and the Foundation and Frontier Technology Research Program of Henan Province (112300410312) for financial supports of this research.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.08.027.

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