Solid-State Synthesis of β-Enamino Ketones from Solid 1,3-Dicarbonyl Compounds and Ammonium Salts or Amines

Shi-Liang Xu,[a] Cheng-Ping Li,[b] Jing-Hua Li*[a]

[a] College of Pharmacuetical Sciences, Zhejiang University of Technology, 310032 Hangzhou, P. R. of China

[b] College of of Biology and Environmental Engineering, Zhejiang Shuren University, 310015 Hangzhou, P. R. of China
E-mail: lijh@zjut.edu.cn

Received 16 October 2008

Abstract: A facile amination of solid 1,3-dicarbonyl compounds with ammonium salts or amines in solid state has been achieved by mechanochemical grinding in the presence of $KHSO_4$ and SiO_2. Most of the reactions proceed smoothly at room temperature under solid-state conditions and give their corresponding β-imino derivatives in high yields. The method has the advantage of simple manipulation and mild conditions.

Key words: enamination, 1,3-dicarbonyl compounds, solid state, mechanochemistry

β-Enamino ketones have attracted considerable attention over the past decades and found wide application in synthetic chemistry and pharmaceutical chemistry.[1–3] Some drugs,[4] such as anticonvulsant,[5] anti-inflammatory agents,[6] and antitumor agents[7] can be prepared from β-enamino ketones. On the other hand, substituted β-enamino ketones are useful intermediates for the synthesis of heterocycles like pyridinones,[3a] quinolines,[3b] oxazoles,[3c] pyrroles,[3d] isoxazole derivatives,[3e] tetrahydrobenzoxazines,[3f] and polyazaheterocycles.[3g]

With growing interest in preparing biologically active compounds, it is important to find facile, 'green' and practical methods for preparation of β-enamino ketones. The most common route for the synthesis of β-enamino compounds involves the direct condensation of 1,3-dicarbonyl compounds with ammonium salts or amines in benzene or toluene at reflux temperature with azeotropic removal of water.[8] The condensation of β-keto esters with excess ammonium salts as the ammonia source in methanol[9] or acetic acid[10] was also reported. To improve the yield and speed up the reaction, some other catalysts or mediators have been developed, such as HCl,[11] H_2SO_4,[12] PTSA,[13] AcOH,[14] $HClO_4$,[15] TMSOTf,[16] montmorillonite K10,[17,18] I_2,[11b] $BF_3{\cdot}OEt_2$,[19] Al_2O_3,[20] silica gel,[21] $Zn(ClO_4)_2{\cdot}6H_2O$,[22] $CeCl_3{\cdot}7H_2O$,[23] $NaAuCl_4$,[24] erbium(III) triflate[25] and natural clays.[26] Recently, this condensation reaction has also been performed in water[27,28] or in ionic liquid medium.[29]

An improved procedure has been subsequently reported. The reaction of amines with β-keto esters catalyzed by $InBr_3$ under solvent-free conditions was carried out successfully.[30] However, for a solid 1,3-dicarbonyl compound it took a long reaction time to complete the reaction using excess ammonia source, and in many cases the reactions gave low yields.

Moreover, in the case of some Lewis acid catalyzed reactions, the failure of catalyst recycling renders these methods environmentally unsound. Although different methods are available for the synthesis of β-enaminones, development of convenient, high-yielding and 'green' approach is still highly desirable.

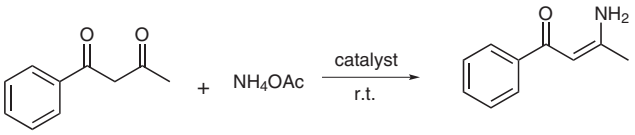
Organic solid-state reactions are highly promising new tools for solvent-free sustainable synthesis and production.[31] Costly workup is obsolete while few wastes are formed and resources and energy saved. Currently, growing efforts of the scientific community of chemistry rely upon the development of economical processes based on the principles of green chemistry.[24] Based on these, so our research interest is to realize an environmentally benign and efficiently synthetic methodology under solid-state conditions. We herein report a mechanochemical protocol for the condensation of solid 1,3-dicarbonyl compounds with ammonium salts or solid amines using a catalytic amount of $KHSO_4/SiO_2$ at solid phase and room temperature.

Firstly, the efficiency of various solid-acid catalysts was investigated in the model reaction conditions: benzoylacetone (5 mmol), ammonium acetate (5 mmol), and catalyst (10 mol%) in solid phase ground in a mortar at room temperature, and the results are summarized in Table 1. The results revealed that $KHSO_4/SiO_2$ (the weight ratio of $KHSO_4$ to SiO_2 was 1:1) was superior (Table 1, entry 10) with respect to the catalyst loadings, reaction times, and product yields. Using the recycled $KHSO_4/SiO_2$ as the catalyst, the catalytic efficiency shows almost no remarkable change (Table 1, entry 14). Entry 1 shows the reaction without addition of any catalyst, only 56% yield was obtained after 150 minutes. *p*-Toluenesulfonic acid gave a good result of the reaction, but it was laborious to separate it from the reaction mixture (Table 1, entry 2). Although the reaction also proceeded with SiO_2 or $KHSO_4$, respectively, it took long reaction time and gave low yield (Table 1, entries 8 and 9) compared to those obtained with the combination of $KHSO_4/SiO_2$. Lower catalyst loading can be used with a decline in reaction rate, and higher catalyst loading shows not to boost the reaction (Table 1, entries 11 and 12). If this reaction was carried out in a liquid solution, the reaction rate and yield were lower (Table 1,

SYNLETT 2009, No. 5, pp 0818–0822
Advanced online publication: 16.02.2009
DOI: 10.1055/s-0028-1087914; Art ID: W16308ST

entries 7 and 13). So we chose to perform the $KHSO_4$/SiO_2-catalyzed reaction in solid state as the standard conditions.

Table 1 Condensation of Benzoylacetone with Ammonium Acetate in the Presence of Various Solid Acids under Various Reaction Conditions[a]



Entry	Catalyst	Time (min)	Yield (%)[b]
1	neat	150	56
2	PTSA	20	97
3	phosphotungstic acid	60	89
4	phosphomolybdenum acid	80	78
5	cationic resin 732[c]	100	81
6	TiO_2, H_2SO_4	45	87
7	HCl[d]	150	69
8	SiO_2	150	54
9	$KHSO_4$	90	80
10	$KHSO_4$, SiO_2[e]	15	98
11	$KHSO_4$, SiO_2[f]	80	84
12	$KHSO_4$, SiO_2[g]	15	97
13	$KHSO_4$, SiO_2[h]	150	52
14	$KHSO_4$, SiO_2[i]	25	94

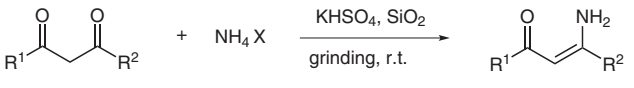
[a] General reaction conditions: grinding reactants with catalyst together at r.t.
[b] Isolated products.
[C] Cationic resin 732: polystyrene–sulfonic acid.
[d] Conditions: 5 mol% HCl at reflux temperature in benzene.
[e] Conditions: 10 mol% catalyst was used.
[f] Conditions: 5 mol% catalyst was used.
[g] Conditions: 30 mol% catalyst was used.
[h] Conditions: 5 mL of CH_2Cl_2 was added.
[i] The catalyst was reused.

To evaluate the scope and limitations of this solid-state reaction, various solid 1,3-dicarbonyl compounds were treated with a range of ammonium salts in the presence of catalytic amount (10 mol%) of $KHSO_4/SiO_2$ by grinding and the results are summarized in Table 2.[32]

First, benzoylacetone was treated with ammonium salts such as NH_4HCO_3, $(NH_4)_2CO_3$, NH_4OAc, NH_4SCN, $(NH_4)_2HPO_4$, $HCOONH_4$, NH_4Cl, $(NH_4)_2SO_4$. It was found that the ammonium salts of weak acids provided high yields of products in short reaction times. Other solid 1,3-dicarbonyl compounds also gave satisfying results (Table 2, entries 9–15). Compared to the corresponding reaction with benzoylacetone (Table 2, entry 3) under the same conditions, reactions of some solid 1,3-dicarbonyl compounds (Table 2, entries 13 and 14) took longer time due to steric factors.

In order to extend the present method to synthesize different kinds of β-enamino ketones, the condensation between solid 1,3-dicarbonyl compounds and solid substituted anilines was explored, and the results are summarized in Table 3.[32] For most of the solid substituted anilines tested, good yields were obtained when the reactions were carried out at room temperature. The presence of an electron-withdrawing group on the phenyl ring or some deactivating group in 1,3-diketones slightly decreased the reactivity of the substrate which led to a need for longer time to complete the reaction (Table 3, entries 8–11).

Table 2 Solid-State Reactions of Solid 1,3-Dicarbonyl Compounds with Different Ammonium Salts



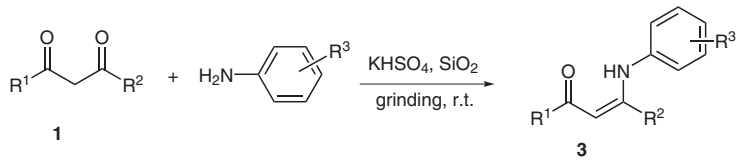
1 **2**

Entry	**1**, R^1 and R^2	Ammonium salt	Time (min)	**2**	Yield (%)[a]
1	**1a**, R^1 = Ph, R^2 = Me	NH_4HCO_3	15	**2a**	94
2	**1a**	$(NH_4)_2CO_3$	10	**2a**	98
3	**1a**	NH_4OAc	10	**2a**	96
4	**1a**	NH_4SCN	20	**2a**	91
5	**1a**	$(NH_4)_2HPO_4$	25	**2a**	94
6	**1a**	$HCOONH_4$	15	**2a**	98
7	**1a**	NH_4Cl	120	**2a**	49
8	**1a**	$(NH_4)_2SO_4$	120	**2a**	5
9	**1b**, R^1 = 4-$MeOC_6H_4$, R^2 = Me	NH_4OAc	20	**2b**	98
10	**1c**, R^1 = 4-FC_6H_4, R^2 = Me	NH_4OAc	15	**2c**	95
11	**1d**, R^1 = Ph, R^2 = COOEt	$(NH_4)_2HPO_4$	15	**2d**	98
12	**1e**, 1,3-cyclohexanedione	NH_4OAc	30	**2e**	92
13	**1f**, 5,5-dimethyl-1,3-cyclohexanedione	$HCOONH_4$	35	**2f**	94[b]
14	**1g**, R^1 = Ph, R^2 = Ph	NH_4OAc	70	**2g**	91[b]
15	**1h**, R^1 = 2-thienyl, R^2 = Me	NH_4OAc	20	**2h**	97

[a] Yields are given for isolated products.
[b] The reactions were performed at 50 °C.

In summary, this paper describes an efficient and practical process for the synthesis of β-enamino ketones. The reaction was carried out at room temperature in the solid state without solvent. The most important advantages of this

Table 3 Condensation of 1,3-Dicarbonyl Compounds with Substitutional Anilines



Entry	1	R^3	Time (min)	Product 3	Yield (%)[a]
1	**1a**	4-MeO	10	**3a**	99
2	**1a**	4-Cl	15	**3b**	98
3	**1a**	4-O_2N	30	**3c**	96
4	**1a**	4-Me	12	**3d**	96
5	**1b**	4-MeO	15	**3e**	97
6	**1c**	4-MeO	18	**3f**	96
7	**1d**	4-O_2N	15	**3g**	98
8	**1e**	4-O_2N	45	**3h**	93[b]
9	**1f**	4-MeO	35	**3i**	91[b]
10	**1f**	2,5-Cl_2	50	**3j**	90
11	**1g**	4-Me	120	**3k**	90[b]
12	**1h**	4-Cl	45	**3l**	95

[a] Yields are given for isolated products.
[b] The reactions were performed at 50 °C.

method are short reaction time, mild reaction conditions, clean product, high yield, and minimal waste.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

References and Notes

(1) (a) Tomioka, K.; Ando, K.; Takemasa, Y.; Koga, K. *J. Am. Chem. Soc.* **1984**, *106*, 2718. (b) Georg, I. G.; Kant, J. *Tetrahedron Lett.* **1988**, *29*, 403. (c) Lubell, W. D.; Kitamura, M.; Noyori, R. *Tetrahedron: Asymmetry* **1991**, *2*, 543. (d) Bartoli, G.; Cimarelli, C.; Marcantoni, E.; Palmieri, G.; Petrini, M. *J. Org. Chem.* **1994**, *59*, 5328.

(2) (a) Bartoli, G.; Bosco, M.; Cimarelli, C.; Dalpozzo, R.; Guercio, G.; Palmieri, G. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2081. (b) Bartoli, G.; Bosco, M.; Cimarelli, C.; Dalpozzo, R.; Palmieri, G. *J. Chem. Soc., Perkin Trans. 1* **1992**, 2095. (c) Bartoli, G.; Bosco, M.; Cimarelli, C.; Dalpozzo, R.; Munno, G. D.; Guercio, G.; Palmier, G. *J. Org. Chem.* **1992**, *57*, 6020.

(3) (a) Alberola, A.; Calvo, L. A.; Ortega, A. G.; Ruiz, M. C. S.; Yustos, P. *J. Org. Chem.* **1999**, *64*, 9493. (b) Chaaban, I.; Greenhill, J. V.; Akhtar, P. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1593. (c) Augusti, R.; Kascheres, C. *J. Org. Chem.* **1993**, *58*, 7079. (d) Eberlin, M. N.; Kascheres, C. *J. Org. Chem.* **1988**, *53*, 2084. (e) Al-Omran, F.; El-Khair, A. A. *J. Heterocycl. Chem.* **2005**, *45*, 307. (f) Müller, A.; Maier, A.; Neumann, R.; Maas, G. *Eur. J. Org. Chem.* **1998**, 1177. (g) Bejan, E.; Aït-Haddou, H.; Daran, J. C.; Balavoine, G. G. A. *Eur. J. Org. Chem.* **1998**, 2907.

(4) Eddington, N. D.; Cox, D. S.; Khurana, M.; Salama, N. N.; Stables, J. P.; Harrison, S. J.; Negussie, A.; Taylor, R. S.; Tran, U. Q.; Moore, J. A.; Barrow, J. C.; Scott, K. R. *Eur. J. Med. Chem.* **2003**, 49.

(5) Azzaro, M.; Geribaldi, S.; Videau, B. *Synthesis* **1981**, 880.

(6) Dannhardt, G.; Bauer, A.; Nowe, U. *J. Prakt. Chem.* **1998**, *340*, 256.

(7) Boger, D. L.; Ishizaki, T.; Wysocki, J. R.; Munk, S. A.; Kitos, P. A.; Suntornwat, O. *J. Am. Chem. Soc.* **1989**, *111*, 6461.

(8) (a) Baraladi, P. G.; Simoni, D.; Manfredini, S. *Synthesis* **1983**, 902. (b) Martin, D. F.; Janusonis, G. A.; Martin, B. B. *J. Am. Chem. Soc.* **1961**, *83*, 73. (c) Ferraz, H. M. C.; Oliceira, E. O.; Payret-Arrua, M. E.; Brandt, C. A. *J. Org. Chem.* **1995**, *60*, 7357. (d) Kloek, J. A.; Leschinsky, K. L. *J. Org. Chem.* **1978**, *43*, 1460. (e) Soloshonok, V. A.; Kukhar, V. *Tetrahedron* **1996**, *52*, 6953. (f) Leflemme, N.; Dallemange, P.; Rault, S. *Synthesis* **2002**, 1740.

(9) (a) Zhu, G.; Chen, Z.; Zhang, X. *J. Org. Chem.* **1999**, *64*, 6907. (b) Garaldi, P. G.; Simoni, D.; Manfredini, S. *Synthesis* **1983**, 902. (c) Marchalin, S.; Kuthan, J. *Collect. Czech. Chem. Commun.* **1983**, *48*, 3112. (d) Marchalin, S.; Kuthan, J. *Collect. Czech. Chem. Commun.* **1984**, *49*, 1395.

(10) Rodríguez, H.; Reyes, O.; Suarez, M.; Garay, H. E.; Pérez, R.; Cruz, L. J.; Verdecia, Y.; Martín, N.; Seoane, C. *Tetrahedron Lett.* **2002**, *43*, 439.

(11) (a) Saeed, A. A. H. *J. Chem. Eng. Data* **1984**, *29*, 358. (b) Hauser, C. R.; Reynolds, G. A. *J. Am. Chem. Soc.* **1948**, *70*, 2402. (c) Coffey, S.; Thomson, J. K.; Wilson, F. J. *J. Chem. Soc.* **1936**, 856.

(12) Martin, D. F.; Janusonis, G. A.; Martin, B. B. *J. Am. Chem. Soc.* **1961**, *83*, 73.

(13) (a) Hickmot, P. W.; Sheppard, G. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1038. (b) Bieräugel, H.; Akkerman, J. M.; Lapierre Armande, J. C.; Pandit, U. K. *Recl. Trav. Chim. Pays-Bas* **1976**, *95*, 266. (c) Gravel, D.; Labelle, M. *Can. J. Chem.* **1985**, *63*, 1874. (d) Yapi, A. D.; Mustofa, M.; Valentin, A.; Chavignon, O.; Teulade, J. C.; Mallie, M.; Chapat, J.-P.; Blache, Y. *Chem. Pharm. Bull.* **2000**, *48*, 1886.
(14) (a) Naringrekar, V. H.; Stella, V. J. *J. Pharm. Sci.* **1990**, *79*, 138. (b) Brown, R. J.; Carver, F. W. S.; Hollingsworth, B. L. *J. Org. Chem.* **1967**, *32*, 2624. (c) Brandt, C. A.; Da Silva, A. C. M. P.; Pancote, C. G.; Brito, C. L.; Da Silveira, M. A. B. *Synthesis* **2004**, 1557.
(15) Das, B.; Venkateswarlu, K.; Majhi, A.; Reddy, R. M.; Reddy, N. K.; Rao, K. Y.; Ravikumar, K.; Sridhar, B. *J. Mol. Catal. A: Chem.* **2006**, *246*, 276.
(16) Cartaya-Marin, C. P.; Henderson, D. G.; Soeder, R. W. *Synth. Commun.* **1997**, *27*, 4275.
(17) (a) Rechsteimer, B.; Texier-Boullet, F.; Hamelin, J. *Tetrahedron Lett.* **1993**, *34*, 5071. (b) Braibante, H. T. S.; Braibante, M. E. F.; Rosso, G. B.; Oriques, D. A. *J. Braz. Chem. Soc.* **2003**, *14*, 994.
(18) Valduga, C. J.; Squizani, A.; Braibante, H. S.; Braibante, M. E. F. *Synthesis* **1998**, 1019.
(19) Stefane, B.; Polanc, S. *Synlett* **2004**, 698.
(20) Texier-Bouliet, F. *Synthesis* **1985**, 679.
(21) Gao, Y.-H.; Zhang, Q.-H.; Xu, J.-X. *Synth. Commun.* **2004**, *34*, 909.
(22) Bartoli, G.; Bosco, M.; Locatelli, M.; Marcantoni, E.; Melchiorre, P.; Sambri, L. *Synlett* **2004**, 239.
(23) Khodaei, M. M.; Khosropour, A. R.; Kookhazadeh, M. *Synlett* **2004**, 1980.
(24) Arcadi, A.; Bianchi, G.; Di Giuseppe, S.; Marinelli, F. *Green Chem.* **2003**, *5*, 64.
(25) Dalpozzo, R.; Nino, A. D.; Nardi, M.; Russo, B.; Procopio, A. *Synthesis* **2006**, 1127.
(26) Silva, F. C.; De Souza, M. C. B. V.; Ferreira, V. F.; Sabino, S. J.; Antunes, O. A. C. *Catal. Commun.* **2004**, *5*, 151.
(27) Stefani, H. A.; Costa, I. M.; de O. Silva, D. *Synthesis* **2000**, 1526.
(28) Khosropour, A. R.; Khodaei, M. M.; Kookhazadeh, M. *Tetrahedron Lett.* **2004**, *45*, 1725.
(29) Khodaei, M. M.; Khosropour, A. R.; Kookhazadeh, M. *Can. J. Chem.* **2005**, *83*, 209.
(30) Zhang, Z.-H.; Yin, L.; Wang, Y.-M. *Adv. Synth. Catal.* **2006**, *348*, 184.
(31) Kaupp, G.; Schmeyers, J.; Boy, J. *Chemosphere* **2001**, *43*, 55.

(32) **General Procedure for the Preparation of β-Enamino Ketones**

A mixture of the solid 1,3-dicarbonyl compound (5 mmol), amine (or ammonium, 5 mmol), and $KHSO_4/SiO_2$ (0.136 g, weight ratio 1:1) was ground in a mortar at r.t. for the appropriate time. After completion of the reaction as indicated by TLC, the reaction mixture was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure to give a product with high purity. The solid product could be further purified by recrystallization in PE (Table 2, entries 1–15) or in EtOH (Table 3, entries 1–12).

3-Amino-1-phenylbut-2-en-1-one (2a)

Mp 138–140 °C; lit.[33a] 144–145 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.06 (s, 3 H), 5.21 (br, 1 H, NH), 5.74 (s, 1 H), 7.39–7.45 (m, 3 H), 7.87–7.89 (m, 2 H), 10.22 (br, 1 H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.92, 92.34, 127.10, 128.22, 130.83, 140.20, 162.91, 189.54.

3-Amino-1-(4-methoxyphenyl)but-2-en-1-one (2b)[33b]

Mp 106–108 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.04 (s, 3 H), 3.85 (s, 3 H), 5.11 (br, 1 H,NH), 5.70 (s, 1 H), 6.89–6.92 (m, 2 H), 7.85–7.88 (m, 2 H), 10.13 (br, 1 H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.95, 55.36, 91.88, 113.43, 129.03, 132.90, 161.89, 162.14, 188.65.

3-Amino-1-(4-fluorophenyl)but-2-en-1-one (2c)[33b]

Mp 106–108 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.06 (s, 3 H), 5.21 (br, 1 H, NH), 5.67 (s, 1 H), 7.06–7.09 (m, 2 H), 7.87–7.90 (m, 2 H), 10.19 (br, 1 H, NH). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 22.95 91.99, 115.14 (d, *J* = 20 Hz), 129.39 (d, *J* = 9 Hz), 136.40, 136.42 163.30 (d, *J* = 56 Hz), 165.52, 188.08.

Ethyl 2-Amino-4-oxo-4-phenylbut-2-enoate (2d)

Mp 49–51 °C; lit.[33c] 50–51 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.41 (t, 3 H, *J* = 7 Hz), 4.38 (q, 2 H, *J* = 7 Hz), 6.04 (br, 1 H, NH), 6.67 (s, 1 H), 7.46–7.54 (m, 3 H), 7.96–9.98 (m, 2 H), 9.49 (br, 1 H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.13, 62.70, 93.26, 127.45, 128.44, 131.29, 139.28, 147.49, 163.88, 191.80.

3-Aminocyclohex-2-enone (2e)

Mp 128–130 °C; lit.[33d] 133 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.97 (m, 2H), 2.29 (t, 2H, *J* = 6 Hz), 2.35 (t, 2H, *J* = 6 Hz), 4.67 (br, 2H, NH), 5.26 (s, 1H). ^{13}C NMR (125 MHz, D_2O) δ = 23.89, 30.60, 36.94, 99.56, 177.00, 203.01.

3-Amino-5,5-dimethylcyclohex-2-enone (2f)

Mp 164–166 °C; lit.[33d] 165–167 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.08 (s, 6 H), 2.16 (s, 2 H), 2.20 (s, 2 H), 4.71 (br, 2 H, NH), 5.25 (s, 1 H). ^{13}C NMR (125 MHz, D_2O) δ = 28.35, 32.88, 42.65, 49.86, 99.27, 163.46, 197.31.

3-Amino-1,3-diphenylprop-2-en-1-one (2g)[33e]

Mp 78–79 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ = 5.46 (br, 1 H, NH), 6.16 (s, 1 H), 7.42–7.53 (m, 6 H), 7.64–7.65 (m, 2 H), 7.94–7.96 (m, 2 H), 10.43 (br, 1 H, NH). ^{13}C NMR (125 MHz, $CDCl_3$) δ = 91.93, 126.36, 127.24, 128.32, 129.06, 130.74, 131.06, 137.63, 140.36, 162.88, 190.26.

3-Amino-1-(thiophen-2-yl)but-2-en-1-one (2h)

Mp 168–170 °C; lit.[33b] 168–170 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.03 (s, 3 H), 5.31 (br, 1 H,NH), 5.60 (s, 1 H), 7.05–7.56 (m, 3 H), 9.91 (br, 1 H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 22.73, 92.00, 127.73, 127.87, 130.21, 146.99, 162.82, 182.21.

3-(4-Methoxyphenylamino)-1-phenylbut-2-en-1-one (3a)[33f]

Mp 100–102 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.07 (s, 3 H), 3.82 (s, 3 H), 5.86 (s, 1 H), 6.89–6.91 (m, 2 H), 7.10–7.12 (m, 2 H), 7.41–7.46 (m, 3 H), 7.90–7.92 (m, 2 H), 12.92 (br, 1 H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.27, 55.52, 93.59, 114.37, 126.64, 127.05, 128.28, 130.80, 131.46, 140.16, 157.89, 163.21, 188.47.

3-(4-Chlorophenylamino)-1-phenylbut-2-en-1-one (3b)

Mp 126–128 °C; lit.[33g] 128–129 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.12 (s, 3 H), 5.91 (s, 1 H), 7.09–7.15 (m, 2 H), 7.31–7.34 (m, 2 H), 7.41–7.48 (m, 3 H), 7.90–7.92 (m, 2 H), 13.07 (br, 1 H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.30, 94.63, 125.80, 127.01, 128.26, 129.23, 131.02, 131.15, 137.20, 139.71, 161.63, 188.88.

3-(4-Nitrophenylamino)-1-phenylbut-2-en-1-one (3c)[33h]

Mp 140–142 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.33 (s, 3 H), 6.04 (s, 1 H), 7.25–7.28 (m, 2 H), 7.44–7.47 (m, 2 H), 7.50–7.52 (m, 1 H), 7.88–7.93 (m, 2 H), 8.21–8.25 (m, 2 H), 13.41 (br, 1 H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.18, 97.54, 122.26, 125.22, 127.30, 128.50, 131.73, 139.20, 144.13, 145.18, 159.16, 189.99.

1-Phenyl-3-(*p*-tolylamino)but-2-en-1-one (3d)[33i]

Mp 114–116 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.10 (s,

3 H), 2.35 (s, 3 H), 5.87 (s, 1 H), 7.05–7.07 (m, 2 H), 7.15–7.25 (m, 2 H), 7.40–7.46 (m, 3 H), 7.90–7.93 (m, 2 H), 13.03 (br, 1 H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.38, 20.97, 93.92, 124.85, 127.06, 128.27, 129.76, 130.82, 135.72, 136.02, 140.14, 162.60, 188.48.

1-(4-Methoxyphenyl)-3-(4-methoxyphenylamino)but-2-en-1-one (3e)[33j]

Mp 142–143 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.05 (s, 3 H), 3.82 (s, 3 H), 3.86 (s, 3 H), 5.82 (s, 1 H), 6.88–6.94 (m, 4 H), 7.09–7.11 (m, 2 H), 7.89–7.91 (m, 2 H), 12.85 (br, 1 H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.26, 55.36, 55.49, 93.05, 113.47, 114.31, 126.57, 128.90, 131.67, 132.81, 157.74, 161.87, 162.41, 187.62.

1-(4-Fluorophenyl)-3-(4-methoxyphenylamino)but-2-en-1-one (3f)

Mp 116–118 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.06 (s, 3 H), 3.82 (s, 3 H), 5.80 (s, 1 H), 6.89–6.91 (m, 2 H), 7.07–7.11 (m, 4 H), 7.90–7.93 (m, 2 H), 12.87 (br, 1 H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.25, 55.49, 93.15, 114.37, 115.16 (d, *J* = 21 Hz), 126.63, 129.24 (d, *J* = 9 Hz), 131.35, 136.36 (d, *J* = 4 Hz), 157.94, 163.38 (d, *J* = 22 Hz), 165.47, 186.94. IR (KBr): 3440, 1599, 1543, 1515, 1496, 1462, 1436, 1328, 1251, 1198, 1105, 1031, 855, 779, 520 cm^{-1}. MS (EI): *m/z* (%) = 286 (18), 285 (100) [M$^+$], 284 (70), 270 (18), 190 (11), 162 (36), 147 (22), 123 (71), 108 (9), 95 (27). Anal. Calcd for $C_{17}H_{16}FNO_2$: C, 71.56; H, 5.65; N, 4.91. Found: C, 71.51; H, 5.60; N, 4.87.

Ethyl 2-(4-Nitrophenylamino)-4-oxo-4-phenylbut-2-enoate (3g)

Mp 98–99 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.22 (t, 3 H, *J* = 7 Hz), 4.28 (q, 2 H, *J* = 7 Hz), 6.67 (s, 1 H), 7.04–7.05 (m, 2 H), 7.47–7.51 (m, 2 H), 7.57–7.60 (m, 1 H), 7.97–7.99 (m, 2 H), 8.19–8.21 (m, 2 H), 11.95 (br, 1 H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 13.83, 62.79, 101.02, 120.30, 125.09, 127.77, 128.76, 132.95, 138.10, 143.72, 145.72, 146.95, 163.64, 191.94. IR (KBr): 3441, 2981, 1373, 1619, 1585, 1510, 1337, 1281, 1226, 1163, 1108, 1051, 1016, 831, 853, 750, 591, 552, 493 cm^{-1}. MS (EI): *m/z* (%) = 341 (5), 340 (33) [M$^+$], 339 (31), 294 (14), 268 (18), 267 (84), 236 (26), 221 (15), 105 (100), 77 (42). Anal. Calcd for $C_{18}H_{16}N_2O_5$: C, 63.52; H, 4.74; N, 8.23. Found: C, 63.50; H, 4.67; N, 8.14.

3-(4-Nitrophenylamino)cyclohex-2-enone (3h)[33k]

Mp 176–178 °C.^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.07–2.11 (m, 2 H), 2.42 (t, 2 H, *J* = 7 Hz), 2.56 (t, 2 H, *J* = 6 Hz), 5.85 (s, 1 H), 6.83 (br, 1 H, NH), 7.26–7.29 (m, 2 H), 8.19–8.21 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.65, 29.82, 36.55, 103.13, 121.31, 125.32, 143.35, 144.94, 159.90, 198.94.

3-(4-Methoxyphenylamino)-5,5-dimethylcyclohex-2-enone (3i)

Mp 186–188 °C; lit.[33l] 186–188 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.05 (s, 6 H), 2.15 (s, 2 H), 2.32 (s, 2 H), 3.78 (s, 3 H), 5.34 (s, 1 H), 6.82 (dd, 2 H, *J* = 2, 7 Hz), 7.04 (dd, 2 H, *J* = 2, 7 Hz), 7.28 (s, 1 H).^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.27, 32.76, 43.02, 50.36, 55.46, 96.96, 114.37, 126.07, 131.14, 157.46, 162.87, 197.61.

3-(2,5-Dichlorophenylamino)-5,5-dimethylcyclohex-2-enone (3j)

Mp 182–184 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.14 (s, 6 H), 2.26 (s, 2 H), 2.39 (s, 2 H), 5.61 (s, 1 H), 6.12 (br, 1 H), 7.07–7.42 (m, 3 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 28.28, 32.89, 43.74, 50.34, 100.78, 124.56, 125.27, 125.96, 130.79, 133.30, 136.28, 158.05, 198.18. IR (KBr) 3442, 3225, 2953, 2873, 1597, 1537, 1464, 1402, 1364, 1269, 1092, 1048, 925, 893, 827, 743, 519 cm^{-1}. MS (EI): *m/z* (%) = 285 (42), 283 (50), 268 (20), 266 (20), 227 (36), 192 (100), 164 (28). Anal. Calcd for $C_{14}H_{15}Cl_2NO$: C, 59.17; H, 5.32; N, 4.93. Found: C, 59.09; H, 5.28; N, 4.90.

1,3-Diphenyl-3-(*p*-tolylamino)prop-2-en-1-one (3k)[33m]

Mp 120–122 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.23 (s, 3 H), 6.05 (s, 1 H), 6.68–7.95 (m, 14 H), 12.90 (br, 1 H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.79, 96.57, 123.21, 127.22, 128.33, 128.38, 128.49, 129.31, 129.55, 131.17, 133.86, 135.94, 136.80, 139.98, 161.74, 189.43.

3-(4-Chlorophenylamino)-1-(thiophen-2-yl)but-2-en-1-one (3l)

Mp 80–82 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.11 (s, 3 H), 5.78 (s, 1 H), 7.06–7.61 (m, 7 H), 12.71 (br, 1 H, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.31, 94.51, 125.74, 127.89, 128.14, 129.34, 130.66, 131.21, 137.24, 146.56, 161.33, 181.88. IR (KBr): 3441, 3095, 1623, 1562, 1481, 1418, 1373, 1381, 1229, 1093, 1031, 824, 834, 766, 722, 502 cm^{-1}. MS (EI): *m/z* (%) = 279 (25), 278 (39), 277 (67), 276 (84), 244 (87), 111 (100), 83 (8). Anal. Calcd for $C_{14}H_{12}ClNOS$: C, 60.54; H, 4.35; N, 5.04. Found: C, 60.50; H, 4.31; N, 5.01.

(33) (a) Baraldi, P. G. *Synthesis* **1983**, 902. (b) Singh, B.; Lesher, G. Y. *J. Heterocycl. Chem.* **1990**, *27*, 2085. (c) Baraldi, P. G. *Tetrahedron* **1987**, *43*, 235. (d) Wang, G.-W. *Green Chem.* **2006**, *8*, 1080. (e) Sviridov, S. I. *Tetrahedron* **2007**, *63*, 12195. (f) Simunek, P. *Tetrahedron* **2005**, *61*, 8130. (g) Boatman, S. *J. Org. Chem.* **1966**, *31*, 1785. (h) Tan, S. F.; Ang, K. P.; Jayachandran, H. *J. Chem. Soc., Perkin Trans. 2* **1983**, 1011. (i) Khodaei, M. M.; Khosropour, A. R.; Kookhazadeh, M. *Can. J. Chem.* **2005**, *83*, 209. (j) Lyubchanskaya, V. M.; Mukhanova, T. I.; Panisheva, E. K.; Alekseeva, L. M.; Granik, V. G. *Khim. Farm. Zh.* **1995**, *29*, 40; *Chem. Abstr.* **1995**, *124*, 145843. (k) Zhuo, J.-C. *Magn. Reson. Chem.* **1997**, *355*, 311. (l) Vovk, M. B. *Russ. J. Org. Chem.* **2007**, *43*, 256. (m) Bannikova, Y. N.; Khalturina, V. V.; Sedegova, E. A.; Maslivets, A. N. *Russ. J. Org. Chem.* **2007**, *43*, 154.