An Improved Preparation of Enaminones from 1,3-Diketones and Ammonium Acetate or Amine Acetates

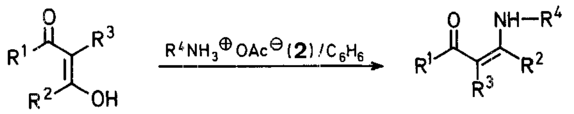
P. G. Baraldi, D. Simoni, S. Manfredini

Instituto Chimica Farmaceutica e Tossicologica, Università di Ferrara, Via Scandiana 21, I-44100 Ferrara, Italy

Enaminones are versatile intermediates in organic synthesis[1] both as synthons for the construction of heterocyclic compounds[2] and as precursors of important functionalities such as α,β-unsaturated ketones[3] and β-hydroxyketones[4].

The generally employed method for their preparation entails the reaction between ammonia or a primary or secondary amine with a 1,3-diketone in benzene solution with azeotropic removal of the water formed[5]. Very weak amines react only with activated forms of diketones, such as vinylogous acid halides or vinylogous esters[6]. Moreover, problems connected with the use of low boiling amines were recently discussed[7] and an improved procedure based on the utilization of a Lewis acid-amine complex was reported.

We report here a practical preparation of enaminones[2] starting from 1,3-diketones[1], characterized by the use of ammonium acetate as an active form of ammonia[8] and by the corresponding easily manipulable acetates in place of low boiling amines. The reaction is simply carried out by refluxing the components in the presence of acetic acid in benzene solution with azeotropic removal of water. In the absence of acetic acid, the reaction is slower and does not go to completion.



1 3

The yields obtained are very high as summarized in the Table. We consider the present method a useful and convenient alternative to the existing ones. The main advantages consist in: (a) the reaction is very simple to perform; (b) the reaction conditions are mild; (c) inexpensive and easy to handle reagents are involved; (d) the yields are always nearly quantitative.

Enaminones 3 from 1,3-Diketones 1; General Procedure:

To a stirred suspension of 1,3-diketone **1** (0.02 mol) in dry benzene (50 ml), containing acetic acid (1 ml), ammonium acetate (3.08 g, 0.04 mol) or ethylammonium acetate (4.2 g, 0.04 mol) (prepared *in situ* from equimolar amounts of ethylamine and acetic acid) is added. The mixture is heated under reflux and the water formed is removed azotropically using a Dean-Stark apparatus. After cooling the mixture is washed with saturated sodium hydrogen carbonate solution (2 × 50 ml), dried with sodium sulfate, evaporated in vacuo, and the residue crystallized (products **3c, f, g**) or purified by flash-chromatography using ethyl acetate/methanol (10 : 1) as eluent (products **3a, b, d, e**).

Table. Enaminones **3** prepared

Product No.	R^1	R^2	R^3	R^4	Reaction time [h]	Yield[a] [%]	m.p. [°C] or b.p. [°C]/torr found (solvent)	reported	I.R. (KBr)[b] ν [cm^{-1}]	^{1}H-N.M.R. (DMSO-d_6)[c] δ [ppm]
3a	CH_3	CH_3	H	H	0.3	90	40-41° (ether)	42-43°[9]	3350, 3160, 1620, 1540	1.85 (s, 3H); 1.9 (s, 3H); 4.95 (s, 1H); 7.3 (br. s, 1H); 9.5 (br. s, 1H)
3b	CH_3	CH_3	H	C_2H_5	0.5	92	78-79°/6	75-76°/5[7]	3340, 3150, 1680, 1645[d]	1.2 (t, 3H, $J=6$ Hz); 1.9 (s, 3H); 1.95 (s, 3H); 3.3 (m, 2H); 4.95 (s, 1H); 10.8 (br. s, 1H)
3c	C_6H_5	CH_3	H	H	8.0	70	144-145° (benzene)	143°[10]	3320, 3160, 1600, 1570, 1540	2.0 (s, 3H); 5.75 (s, 1H); 7.4 (m, 3H); 7.8 (m, 3H); 10.1 (br. s, 1H)
3d	$-(CH_2)_3-$		H	H	0.3	85	130-131° (ethyl acetate)	128-131°[11]	3340, 3140, 1680, 1560	1.7-2.3 (m, 6H); 4.95 (s, 1H); 6.7 (br. s, 2H)
3e	$-(CH_2)_3-$		H	C_2H_5	0.5	96	66-67° (ethyl acetate)	67-68°[13]	3420, 3220, 1570, 1520	1.2 (t, 3H, $J=6$ Hz); 1.85-2.15 (m, 2H); 2.2-2.5 (m, 4H); 3.0-3.3 (m, 2H); 5.0 (s, 1H); 6.5 (br. s, 1H)
3f	$-CH_2-C(CH_3)_2-CH_2-$		H	H	0.4	98	165° (ethyl acetate)	164-165°[5]	3320, 3140, 1680, 1550	1.0 (s, 6H); 1.95 (s, 2H); 2.15 (s, 2H); 4.95 (s, 1H); 6.7 (br. s, 2H)
3g	$-(CH_2)_3-$		$-CH_2-CH=CH_2$	H	1.0	95	112-113° (ethyl acetate)	113°[12]	3330, 3150, 1680, 1640, 1540	1.7-1.9 (m, 2H); 2.0-2.2 (m, 2H); 2.2-2.4 (m, 2H); 2.9 (m, 2H); 4.7-5.0 (m, 2H); 5.4-5.8 (m, 1H); 6.3 (br. s, 2H)

[a] Yield of pure, crystallized, isolated product.
[b] Measured on a Perkin-Elmer Model 257 infrared spectrometer.
[c] Recorded on a Perkin-Elmer Model R32 NMR spectrometer.
[d] In chloroform.

Received: April 19, 1983

---

[1] J. V. Greenhill, *Chem. Soc. Rev.* **6**, 277 (1977).

[2] A. G. Cook, *Enamines*, Marcel Dekker, New York, 1969.

[3] C. Kashima, Y. Yamamoto, Y. Tsuda, *J. Org. Chem.* **40**, 526 (1975).

[4] P. G. Baraldi, F. Moroder, G. P. Pollini, D. Simoni, A. Barco, S. Benetti, *J. Chem. Soc. Perkin Trans. 1* **1982**, 2983 and references cited therein.

[5] J. V. Greenhill, *J. Chem. Soc.* [C] **1971**, 2699.

[6] K. Dixon, J. V. Greenhill, *J. Chem. Soc. Perkin Trans. 1* **1976**, 2211.

[7] M. Azzaro, S. Geribaldi, B. Videan, *Synthesis* **1981**, 880.

[8] D. Y. Curtin, J. A. Kampmeier, M. L. Farmer, *J. Am. Chem. Soc.* **87**, 874 (1965). These authors described the conversion of 2-phenyl-1,3-indandione into 3-amino-2-phenylindenone by fusion with ammonium acetate at 120-140 °C.

[9] A. Combes, C. Combes, *Bull. Soc. Chim. Fr.* **7**, 778 (1892).

[10] E. Fischer, C. Bulow, *Ber. Dtsch. Chem. Ges.* **18**, 2131 (1885).

[11] F. Zymalkowski, H. Rimek, *Arch. Pharm. (Weinheim, Ger.)* **294**, 759 (1961).

[12] H. Iida, Y. Yuasa, C. Kibayashi, *Heterocycles* **9**, 1745 (1978).

[13] J. V. Greenhill, *J. Chem. Soc.* [B] **1969**, 299.