J. Indian Chem. Soc.,
Vol. 84, October 2007, pp. 1035-1036

NOTE

Microwave assisted Knoevenagel condensation : A facile method for the synthesis of 5-arylidine barbituric acid derivatives under solvent free conditions†

S. S. Pandit*, B. N. Jejurkar and R. L. Harde

P. G. and Research Center, Department of Chemistry, Padmashri Vikhe Patil College, Pravaranagar (Loni kd.), Tal. Rahata, Dist. Ahmednagar-413 713, Maharashtra, India

E-mail : akankshapandit2002@yahoo.com

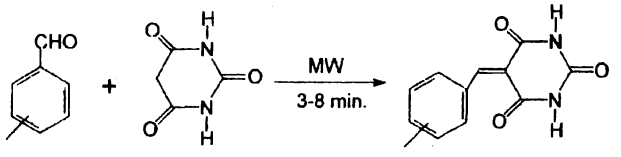
Manuscript received 22 June 2006, revised 14 June 2007, accepted 20 July 2007

Abstract : Several benzaldehydes were condensed with barbituric acid under microwave irradiation in absence of solvent affording the corresponding 5-arylidine barbituric acid derivatives in short reaction period with high yields.

Keywords : Knoevenagel condensation, barbituric acid, microwave irradiation.

The list of biologically active substituted barbituric acid is very long and with time the synthesis and applications of these compounds have only increased[1].

This work deals with the potential of microwave irradiation for the formation of 5-arylidine barbituric acid. These molecules were obtained by means of a Knoevenagel condensation between barbituric acid and aldehydes. Barbituric acid itself (pyrimidine-2,4,6-trione) is commercially available and is highly inexpensive (Scheme 1).



1 2 3

Scheme 1

There are a large number of medicinal uses of barbiturates in present day use[2].

Results and discussion

Table 1 summarizes the Knoevenagel condensation reaction between barbituric acid and various aldehydes for the synthesis 5-arylidine barbituric acid derivatives under microwave irradiation (Entry a-j). The arylidine barbituric acid derivatives were obtained in good to excellent yields with in short reaction period. The aldehydes consisting of electron donating substituents (Entry b, c, g, h, i) as well as electron withdrawing substituents (Entry d, e, f, j) react with barbituric acid very smoothly to produce good to excellent yields. The electron donating groups (Entry b, c, g, h, i) present on aromatic aldehydes substantially decreases the reaction time.

To improve the efficiency and reduce the waste production we optimized the reaction conditions used in the literature[6], first times the microwave energy source has been used for the synthesis of 5-benzylidene barbituric acid derivatives in solvent free condition.

Experimental

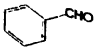
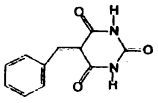
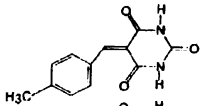
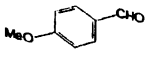
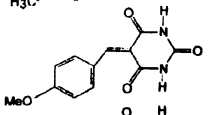
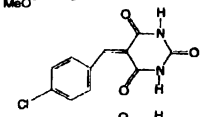
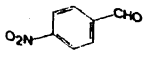
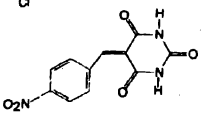
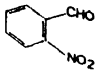
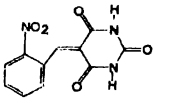
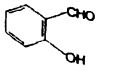
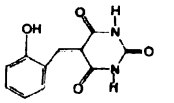
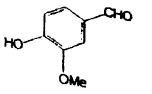
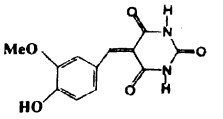
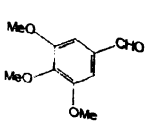
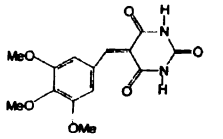
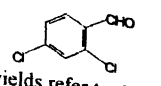
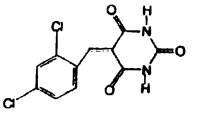
All chemicals were analytical grade. The melting points were determined on the open capillary tube and are uncorrected. All the reactions were carried out in a domestic Bajaj 2800 ET-B microwave oven having power sources 230 V, 50 Hz, input power 1300 W (microwave), operating frequency 2450 MHz. The IR spectra were recorded on Bomen FT-IR MB-104 spectrophotometer with zinc selenide optics. ^{1}H NMR were recorded on Brucker AC-300 MHz in $CDCl_3$ using TMS as an internal standard.

General procedure :

In a borosil 50 ml beaker a mixture of aldehyde (5 mmol) and barbituric acid (5 mmol) were taken, the mixture was stirred well and put into the microwave oven for irradiation for the appropriate time. After completion of reaction (monitored by TLC) the reaction mixture was washed with

†Dedicated to Loknete Balasaheb Vikhe Patil on the occasion of his 75th birthday.

Table 1. Knoevenagel condensation reaction between various aldehydes and barbituric acid

Entry	Aldehyde 1	Product 3	Time (min)	Yields[a,b] (%)	Ref.
a			5	92	3
b			3	91	4
c			3	87	5
d			8	75	3
e			5	76	5
f			5	82	5
g			5	83	3
h			4	93	*c*
i			3	91	*c*
			7	80	3

[a]The yields refer to the pure isolated products.
[b]All products are characterized by IR and ^{1}H NMR and compared with authentic samples.
[c]Spectroscopic data is given.

sodium bicarbonate (20 ml × 2) and with water then recrystallised from n-hexane and ethyl acetate.

Spectroscopic data :

(3h) : Yellow solid (93%), m.p. 270–272 °C; IR (KBr) : 3095, 3070, 1710, 1670, 1650, 1550, 1250 cm^{-1}; ^{1}H NMR δ : 11.24 (1H, s, NH), 11.11 (1H, s, NH), 8.30 (1H, d, *J* 2 Hz) and 8.20 (1H, s, C=CH), 8.1 (2H, s), 3.7 (3H, s), 4.2 (1H, s).

(3i) : Orange solid (91%), m.p. 263–265 °C; IR (KBr) : 3095, 3080, 1706, 1680, 1660, 1550, 1250 cm^{-1}; ^{1}H NMR δ : 11.24 (1H, s, NH), 11.10 (1H, s, NH), 8.7 (1H, s, C=CH), 8.3 (2H, s), 3.8 (9H, s).

Acknowledgement

The authors BNJ and RLH thank the Chairman, Pravara Rural Education Society, Pravaranagar and Principal, Padmashri Vikhe Patil College, Pravaranagar for providing all the facilities for the completion of project work under restructuring programme affiliated to University of Pune, Poona, Maharashtra, India for the partial fulfillment of degree Bachelor of Science.

References

1. G. M. Smith and A. M. Reynard,"Essentials of Pharmacology", W. B. Sanders. Philadelpia, 1995; M. K. Carter, *J. Chem. Ed.*, 1951.
2. "The Merck Index", ed. S. Budavari, 11th ed., Rahway, New Jersy, USA, 1989; F. Yoneda, R. Hirayama and M. Yamashita, *Heterocyclic Chem.*, 1992, 301; J. T. Pinhey and B. A. Rowe, *Tetrahedron Lett.*, 1980, **21**, 695; M. E. Wolff, "Burgers Medical Chemistry and Drug Discovery : Thearapeutical Agents", 5th ed., Wiley, New York, 1997, Vol. II-V; K. Tanaka, X. Cheng and F. Yoneda, *Chem. Pharm. Bull.*, 1980, **34**, 3945; J. D. Figueroa-Villar and C. E. Rangel, *Synth. Commun.*, 1992, **22**, 1159; K. Tanaka, X. Cheng and F. Yoneda, *Tetrahedron*, 1988, **44**, 3241.
3. V. D. Vvedenski, *Khim. Geteroski. Soedin*, 1969, **5**, 1092.
4. M. Sekiya and C. Yanaihara, *Chem. Pharm. Bull.*, 1969, **17**, 747.
5. C. N. Robinson and C. C. Irving, *Heterocyclic Chem.*, 1969, **16**, 921.
6. D. Villemin and B. Labiad, *Synth. Commun.*, 1990, **20**, 3333; B. S. Jursic and D. M. Neuman, *Tetrahedron Lett.*, 2001, **42**, 4103; P. Singh and K. Paul, *Indian J. Chem., Sect. B*, 2001, **48**, 247.