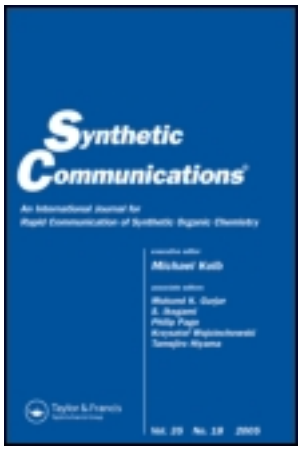

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One Pot Synthesis of Barbiturates on Reaction of Barbituric Acid with Aldehydes Under Microwave Irradiation Using a Variety of Catalysts

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ABSTRACT

The condensation of barbituric acid with aldehydes under microwave irradiation in dry media has been investigated in the presence of NH_4OAc/AcOH (4/3, w/w) (41–54%), Montmorillonite K-10 (49–60%), Silica gel (52–63%), basic Al_2O_3 (56–67%), NaCl (57–69%), Montmorillonite KSF (62–70%), and KSF + NaCl (1:1, w/w) (70–89%).

Key Words: Barbiturates; Aldehydes; K-10; KSF; NaCl; Silica gel; Alumina.

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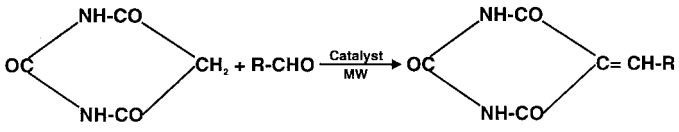

Scheme 1.

The barbiturates are associated with a number of biological activities such as antibacterial, hypotensive, and sedative.[1–3] They are synthesized by condensing barbituric acid with aldehydes under conventional refluxing conditions in aqueous medium (Sch. 1).[4] The method requires longer reaction times and tedious work-up. Villemin recently used microwave irradiation to prepare the barbiturates in the presence of Montmorillonite KSF clay as a catalyst.[5] Inspired by his research work, we describe herein our results of the synthesis of 5-arylidene barbiturates in the presence of a variety of catalysts – NH_4OAc/AcOH, (4/3 : w/w) Montmorillonite K-10, Silica gel, basic Alumina, NaCl, Montmorillonite KSF and KSF/NaCl (10/1:w/w) in dry media under microwave irradiation, a technique which has become very popular in organic chemistry.[6]

We started by reacting the readily available *p*-chloro benzaldehyde with barbituric acid in the presence of KSF Montmorillonite clay under a variety of irradiation levels (80 W, 160 W, 240 W, 320 W, 400W, 480 W, 560 W, 640 W, 720 W and 800 W). The best yield of 69% was obtained at 560 W after 7 min. Hence, we carried out all the catalytic reactions described herein at 560 W. The yields obtained in the presence of various catalysts are depicted in Table 1.

As can be seen, the NH_4OAc/AcOH, (4/3:w/w) Montmorillonite K-10, Silica gel and Alumina proved less effective yields (41–54%, 49–60%, 52–63% and 56–67% respectively). NaCl and KSF clay proved superior and gave almost comparable yields (57–69% and 62–70% respectively). In view of this we were interested in investigating the condensation reaction in presence of a mixture of KSF clay and NaCl. As expected the yields increased to 70–90%. Mechanistically, we believe that the Cl^- ions generate the desired barbiturate anion at 5-position and the Montmorillonite KSF clay provides the necessary Lewis and Bronsted acidities[6,7] in these Knoevenagel type condensations.

In conclusion, the mixture of the inexpensive and convenient catalysts, Montmorillonite KSF and NaCl (10/1:w/w) has proved the best among the catalysts used in these investigations. All the products were identified on the basis of their NMR and IR spectra and by comparison of their m.p. and Rf values with those of authentic samples.

Table 1. Condensation of aldehydes with barbituric acid in presence of various catalysts under microwave irradiation (560 W)[a].

Aldehydes (entry no.)	Yield (%) with catalyst							Melting points	
	NH_4-OAc/ AcOH	K-10 clay	Silica gel	Al_2O_3 basic	NaCl	KSF clay	KSF & NaCl	Observed (°C)	Lit. (°C)
Benzaldehyde (1)	52	58	60	65	68	70	90	256(d)	256(d)[4]
4-OH benzaldehyde (2)	41	50	52	57	61	62	81	275(d)	275(d)[4]
4-Cl benzaldehyde (3)	50	59	63	66	68	69	75	270(d)	271(d)[8]
2-NO_2 benzaldehyde (4)	43	51	54	58	60	62	70	260	260[4]
3,4-Dimethoxy benzaldehyde (5)	54	60	63	67	69	70	77	> 290	> 290[4]
Cinnamaldehyde (6)	46	54	55	60	63	65	86	270(d)	270(d)[4]
4-OCH_3 benzaldehyde (7)	48	55	58	62	64	64	85	279	279[4]

[a]The reactions were completed in ca 7 min.

TYPICAL EXPERIMENTAL PROCEDURE

Mixed barbituric acid (0.645 g, 5 mmol), 4-chlorobenzaldehyde (0.702 g, 5 mmol) and a catalyst NH_4OAc/AcOH, (40/30 mg) Montmorillonite K-10 (1 g), silica gel (1 g), alumina (chromatographic) (1 g), NaCl (100 mg), Montmorillonite KSF (1 g) and KSF/NaCl (1 g/100 mg) were taken in an Erlenmeyer flask (100 mL). The flask was subjected to irradiation at 560 W (70%) level in a Kenstar OM-9925E (800 W) unmodified domestic microwave oven operating at 2450 MHz. The flask was allowed to cool and DMF (50 mL) was added. The mixture was filtered and the solvent removed under reduced pressure (36°C/8 mmHg) to afford the desired barbiturate. [Orange-reddish solid; m.p. (dec) 271° lit.[8] m.p. dec 270°; H-NMR δ:7.5 (d, 2H, H arom, $J = 8$ Hz), 8.1 (d, 2H, H arom, $J = 8$ Hz), 8.3 (s, 1H, CH=), 11.27 (s, 1H, NH), 11.43 (s, 1H, NH); IR (KBr) ν in cm^{-1}: 3520–3480 (NH), 1750 (C=O), 1690 (NHCONH), 1650 (C=O), 1550, (C=C). Rf. 0.42 (benzene:ethyl acetate, 1:1).

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