Microwave Enhanced Knoevenagel Condensation of Barbituric Acid with Aromatic Aldehydes on Basic Alumina

Khalafi-Nezhad, Ali and Hashemi, Aboulghasem*
Department of Chemistry, Faculty of Sciences, Shiraz University,
Zip code 71454, Shiraz, I. R. Iran

ABSTRACT: *Efficient Knoevenagel condensation of barbituric acid with different aromatic aldehydes on basic alumina was performed in a conventional microwave oven in the absence of solvent.*

KEY WORDS: *Barbituric acid, Aldehydes, Alumina, Condensation, Microwave*

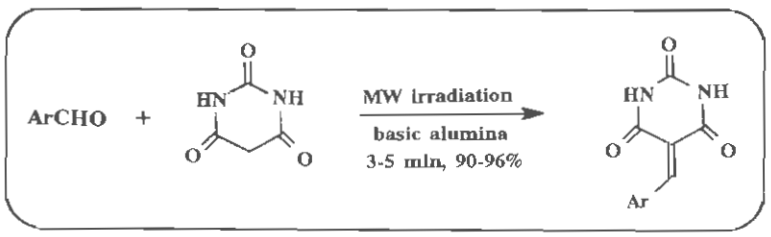
INTRODUCTION

In the recent years, the application of microwave irradiation in a variety of organic reactions has been rapidly increasing due to the short reactions time and the operational simplicities [1-13]. The ability of inorganic supports [14] to enhance the reaction rates is well demonstrated in several types of organic reactions using this technique.

Recently the microwave methodology was applied for Knoevenagel condensation of diethyl malonate [15], ethyl cyanoacetate [16,17] and different types of aldehydes in monochlorobenzene as solvent. The Knoevenagel condensation reaction of malonic acid and its derivatives with aldehydes on basic alumina [18] and the new solid phase Knoevenagel catalyst have also been reported [19].

Knoevenagel condensation reaction of barbituric acid with aldehydes has been reported to occur in refluxing aqueous solutions in good yields [20].

We wish to report a novel and efficient method for the Knoevenagel condensation of barbituric acid and various aromatic aldehydes on basic alumina in the absence of organic solvents under microwave irradiation (Scheme). This method was found to be very efficient and clean with an easy work up procedure. The reactions were completed within 3-5 min. with excellent product yields (Scheme, Table).



Scheme

* *To whom correspondence should be addressed.*

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Table

Aldehyde	Time(min)	Isolated yield(%)	m.p.[°C]
Benzaldehyde(a)	5	90	263-264(Lit. [20], 263-265)
3-Nitrobenzaldehyde(b)	3	94	254-255(Lit. [20], 254-255)
4-Chlorobenzaldehyde(c)	3	92	228-230
2-Methoxybenzaldehyde(d)	4	96	268-269
1-Naphthaldehyde(e)	4	90	284-286
4-*iso*-Propylbenzaldehyde(f)	4	91	209-210
3-Methylbenzaldehyde(g)	4	90	—
4-Methylbenzaldehyde(h)	4	91	270-272
4-Bromobenzaldehyde(i)	3	92	246-247
2,6-Dichlorobenzaldehyde(j)	4	96	208-210

The products are designed as (a-j) and the NMR data of products (c-j) are given in the experimental section

It is interesting to note that the nature of substitutent on the aromatic ring does not affect on the yield of Knoevenagel condensation. The condensation reactions of aromatic aldehydes carrying electron-donating or electron-withdrawing groups were also successfully carried out with this method.

In conclusion, using microwave irradiation and basic alumina as solid support, the Knoevenagel condensation of barbituric acid and aromatic aldehydes with electron-donating or -withdrawing groups can occur efficiently. Short reaction times, easy procedure and work up and excellent yields of the reactions, make this technique a suitable method for this type of condensation.

EXPERIMENTAL

Chemicals were purchased from Fluka (Switzerland), Aldrich (U.S.A) and Merck (Germany) companies. This layer chromatography (TLC) on commerical silica gel plates 60 F_{254} was used to monitor the progress of the reactions. Yields refer to isolated pure products after purification. Products were characterized by comparison of their physical data (m.p, IR and NMR spectra) with samples prepared from known method [20].

General procedure for the condensation of barbituric acid with aromatic aldehydes

Aldehyde, basic alumina and barituric acid in molar ratio of 1.2:1:1 were well mixed in a flask at room temperature and then irradiated at 700 watt for 3-5 min. in the microwave oven (Scheme). The reaction mixture was then washed with *n*-hexane followed by cold water to remove excess of aldehyde and any of unreacted barbituric acid. The mixture was then placed in ethanol and heated to dissolve the product. After filtration of alumina, the solvent was evaporated. A solid was obtained which was recrystallized from ethanol to give the desired product in 90-96% yield. The ^{1}H NMR(250 MHz) of products (Table, compounds **c-j**)in DMSO-d_6 are given bellow; (**c**) δ: 7.89-7.44(m, 4H, Ar), 8.35(s, 1H, =CH-), 11.31(s, 1H, NH), 11.52(s, 1H, NH), (**d**) δ: 3.92(s, 3H, OCH_3), 8.06-7.09(m, 4H, Ar), 8.55(s, 1H, =CH-), 11.21(s, 1H, NH), 11.39(s, 1H, NH), (**e**) δ: 8.08-7.64 (m, 4H, Ar), 8.86(s, 1H, =CH-), 11.23(s, 1H, NH), 11.52(s, 1H, NH), (**f**) δ: 1.27(d, 6H, CH_3), 3.06-2.95 (m, 1H, CH), 8.14-7.39(m, 4H, Ar), 8.30(s, 1H, =CH-), 11.25(s, 1H, NH), 11.40(s, 1H, NH), (**g**) δ: 2.4(s, 3H, OCH_3), 8.1-7.0(m, 4H, Ar), 8.26(s, 1H, =CH-), 11.22 (s, 1H, NH), 11.37(s, 1H, NH), (**h**) δ: 2.39(s, 3H, OCH_3), 8.12-7.29(m, 4H, Ar), 8.26(s, 1H, =CH-), 11.23 (s, 1H, NH), 11.39(s, 1H, NH), (**i**) δ: 7.97-7.69(m, 4H, Ar), 8.23(s, 1H, =CH-), 11.49(s, 1H, NH), 11.65(s, 1H, NH), (**j**) δ: 7.57-7.17(m, 4H, Ar), 8.16(s, 1H, =CH-), 11.48(s, 1H, NH), 11.63(s, 1H, NH).

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