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AN EFFICIENT ULTRASOUND ASSISTED MULTICOMPONENT SYNTHESIS OF 1-AMIDOALKYL 2-NAPHTHOLS

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ABSTRACT

An ultrasound assisted one pot condensation of β-napahthol, acetamide/benzamide and aldehydes catalyzed by iodine, gives amidoalkyl naphthol in good to excellent yield, and short reaction time compare to other methods. It is an important fact that amido alkyl naphthols can be used as starting component for synthesizing some biologically important heterocycles and derivatives.

Key words: Ultrasound assisted synthesis, Multicomponent synthesis, Amido alkyl naphthol, Iodine.

INTRODUCTION

Multicomponent reactions (MCRs) are those in which several organic moieties are coupled in one step have emerged as a powerful strategy in organic, combinatorial, and medicinal chemistry[1]. Multicomponent condensation represents a possible technique to perform near ideal synthesis because they posses one of the aforementioned qualities namely the possibility of building up complex molecules with maximum simplicity and brevity. With increased environmental concern and regulatory constraints faced in the chemical and pharmaceuticals industries, development of environmentally benign organic reactions has become a crucial and demanding research area in modern organic chemical research[2]. For this purpose ultrasound irradiation technique has been increasingly used in organic synthesis in last three decades. Compared with traditional methods, the procedure is more convininient and can be carried out in higher yields, shorter reaction time under ultrasound irradiation[3,4]. Herein we have synthesized amido alkyl naphthol by ultrasound technique via multicomponent condensation reaction. Amido alkyl naphthols are the important synthetic building blocks[5,6] and are used as a precursor for synthesis of α-amino methyl β-naphthols, which exhibits cardiac activity[7].

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A number of lewis or Bronsted acid catalysts, have been used in the multi component condensation of β-naphthol, aryl aldehyde and acetamide such as montmorillonite k10 clay[8], p-TSA[9], sulfamic acid[10], cation exchange resin[11], $NaHSO_4.H_2O$[12] and $HClO_4/SiO_2$[13]. However, some of these methods are plagued by one or many drawbacks such as long reaction time, the use of expensive reagents, low yields of products, high catalyst loading etc. So here, a method of ultrasound technique using molecular iodine as a catalyst by using ethyl acetate as a solvent is reported. Iodine is a versatile catalyst, because of its mild Lewis acidity, it has recently received considerable attention as an inexpensive, nontoxic, readily available catalyst for various organic transformations. It is worth nothing that this method has none of the above mentioned disadvantages at all. Earlier reported method for preparation of 1-amido alky naphthol catalyzed by molecular iodine[14] contain longer reaction time 10-15 hr but in ultrasound method the reaction completed within 1-2 hour of period.

EXPERIMENTAL

All reagents used were AR grade and were used without further purification. Melting points are uncorrected for all produdcts. ^{1}H NMR spectras were recorded on a varian Gemini 200 MHz spectrometer.chemical shifts are reported in δ (ppm) unit relative to TMS as standard. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at the ionization potential of 70 eV. Sonication was performed in Toshcon ultrasonic cleaner (with a frequency of 25 KHz and a nominal power 250 W).

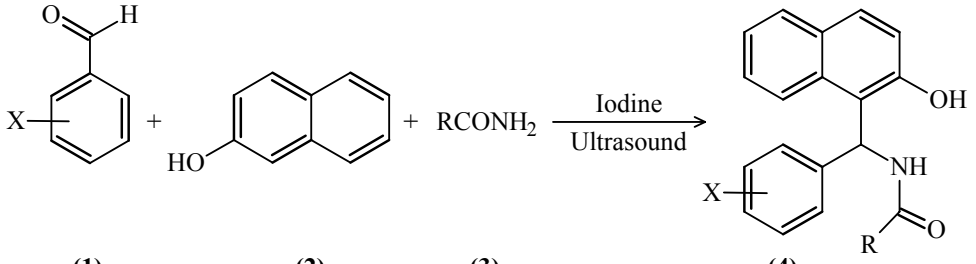
General procedure

β-naphthol (1 mmol), aromatic aldehydes (1 mmol), amide (1.1 mmol) and ethyl acetate (10 mL) and molecular iodine (10 mol %) irridiated in ultrasound bath for an appropriate time at 60^{o}C. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was treated with aqueous $Na_2S_2O_3$ solution and extracted with ethyl acetate. The extract was concentrated and the residue was purified by silica gel column chromatography (60–120 mesh silica gel) eluting with chloroform and methanol to afford the desired compound in a pure form.

Spectral data of N-((2-Hydroxynaphthalen-1-yl) (phenyl) methyl)acetamide (4a): White Solid; m.p. 242-244, IR (KBr): 3479, 3241, 2914, 1631, 1571, 1511, 1421, 1371, 1331, 1261, 1091, 1151, 1022, 974, 922, 862, 826, 803, 730 cm^{-1}. ^{1}H NMR (DMSO-d6) δ (ppm) 8.82 (brs, 1H), 8.1-8.23 (d, 1H), 7.82 (s, 1H), 7.71 (d, 1H), 7.61 (d, 1H), 7.44-7.23 (m, 9H, Ar-H), 1.97 (s, 3H) ppm. ^{13}C NMR (DMSO-d6): δ (ppm) = 23.5, 44.7, 119.3, 119.7, 123.2, 126.9, 127.2, 128.8, 129.4, 130.1, 133.2, 143.5, 155.0, 170.1.

RESULTS AND DESCUSSION

Herein, we wish to describe a novel protocol for the rapid synthesis of a variety of amidoalkyl naphthols using a catalytic amount molecular iodine under ultrasound waves.



(1) **(2)** **(3)** **(4)**

Some of the reported methods in which amido alkyl naphthols have been synthesized by using molecular iodine[14] contain longer reaction time and low yields of products compare to ultrasound methods. To test the general significance and efficiency of this procedure in the synthesis of a variety of substituted amidoalkyl naphthols, we examined a number of differently substituted aryl aldehydes, β-naphthols and amides (Table 1). The best result was obtained by carrying out the reaction with equal molar amounts of aldehyde, β-naphthol and acetamide/benzamide.

Table 1: Synthesis of amido alkyl naphthols by ultrasound method catalysed by iodine[a]

Entry	Compds.	Aldehydes	R	Yield (%)[b]	Time (hr.)	M.P. (^oC)
1	**4a**	C_6H_5CHO	CH_3	84	1.5	242-244
2	**4b**	4-OMe C_6H_4CHO	CH_3	82	2	184-186
3	**4c**	4-Br C_6H_4CHO	CH_3	86	2	228-230
4	**4d**	3-Nitro C_6H_5CHO	CH_3	89	1.5	182-184
5	**4e**	2-Chloro C_6H_4CHO	CH_3	90	1.5	193-195
6	**4f**	4-Chloro C_6H_5CHO	CH_3	85	1.5	220-222
7	**4g**	C_6H_5CHO	Ph	82	1.6	242-243
8	**4h**	4-Chloro C_6H_5CHO	Ph	88	2	187-188
9	**4i**	4-OMe C_6H_5CHO	Ph	89	1.4	196-198
10	**4j**	2,5-$(OMe)_2C_6H_4CHO$	CH_3	80	1.7	249-251
11	**4k**	3,4-$(OMe)_2C_6H_4CHO$	CH_3	81	1.65	234-236

[a]Reaction conditions: Aldehydes (1 mmol), β-naphthol (1 mmol), amide (1.1 mmol), I_2 (10 mol %), ethyl acetate, 60^{o}C. [b]isolated yields

Using this method, all aldehydes including benzaldehyde as well as aromatic aldehydes possessing electron-withdrawing and electron-donating substituent's such as –Me, –OMe, –F, –Cl, –Br, $–NO_2$ were treated (Table 1). Aldehydes with electron-withdrawing substituent's reacts faster than donating groups and gives maximum yields. The reaction can be proceed with amides and urea also. On the other hand thiourea and amines instead of amide/urea were utilized but no corresponding products were obtained.

Effect of catalyst composition

Various amounts of molecular iodine have been studied and the results are summarized in Table 2. It is observed that in the absence of catalyst no desired product was formed. As the catalyst concentration increases there is an increase in the product yield and decrease in the time required. It is observed that 10 mol % of catalyst is just sufficient to achieve maximum yield at reduced time periods Table 2 (entry 8).

Table 2: Effect of catalyst concentration on the reaction[a]

S. No.	Catalyst mol (%)	Time (min)	Yield (%)[b]
1	-	200	-
2	0.5	190	38
3	1	180	44
4	2	165	55
5	3	140	66
6	4	120	72
7	5	100	78
8	**10**	**90**	**84**
9	15	90	86

[a]benzaldehyde (1 mmol), β-naphthol (1 mmol), acetamide (1.1 mmol), I_2, [b]isolated yields.

Effect of solvent

Among the solvents studied, ethyl acetate was proved to be efficient (Table 3, entry 1) in terms of its relative higher yield and short reaction time period in ultrasonic conditions. Application of ultrasound shortened the reaction time for generation of amidoalkyl naphthols from 12-20 hr under classical conditions to 1-2 hr referred with

reported methods[14]. In addition, the yields of the products were improved by 20-30% in comparison with those obtained by the other method.

Table 3: Solvent effect on the reaction of benzaldehyde, β-naphthol, acetamide under ultrasonic conditions[a]

Entry	Solvent	Time (hr)	Yield (%)[b]
1	EtOAc	**1.5**	**84**
2	MeCN	6	55
3	EtOH	8	40
4	DMF	10	32
5	Water	18	Trace

[a]benzaldehyde (1 mmol), β-naphthol (1 mmol), acetamide (1.1 mmol), I_2,
[b]isolated yields

CONCLUSION

In summary, this work describes a convenient and efficient new procedure for the synthesis of biologically interesting 1-amidoalkyl 2-naphthols via the one-pot multi-components condensation of 2-naphthol, aromatic aldehydes and amides using ultrasound radiation catalyzed by molecular iodine. Present methodology offers very attractive features such as relatively short reaction time, high yield, cleaner reaction profile, simplicity and easy workup protocol.

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