

Notes

Oxalic acid catalyzed solvent-free synthesis of α -amidoalkyl- β -naphthols

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Received 23 February 2009; revised 12 November 2009

An efficient one-pot synthesis of α -amidoalkyl- β -naphthols is described. This involves the three-component reaction of β -naphthol, aromatic aldehydes and amide or urea in the presence of a catalytic amount of oxalic acid under solvent-free conditions.

Keywords: Oxalic acid, One-pot reaction, β -Naphthol, Aryl aldehyde, Urea, Solvent free

Amidoalkyl naphthols are the important synthetic building blocks^{1,2} and are used as a precursor for synthesis of α -aminomethyl- β -naphthols, which exhibit cardiac activity³. The preparation of amidoalkyl naphthols can be carried out by one-pot reaction condensation of aldehydes, β -naphthol and amide or urea in the presence of Lewis or Brønsted acid⁴⁻¹⁰ heterogeneous catalysts like cation-exchange resins¹¹, silica supported perchloric acid^{12,13}, $\text{FeCl}_3\text{-SiO}_2$ ¹⁴, montmorillonite K10 clay¹⁵, silica sulphuric acid¹⁶ and sulphamic acid^{17,18}. However, some of the reported methods suffer from disadvantages such as long reaction time¹⁰, the use of expensive reagents⁸, low yields of products¹⁷, high catalyst loading¹⁶, corrosive reagents⁴, strongly acidic conditions^{12,13} and the use of an additional microwave oven⁷ or ultrasonic irradiation¹⁶. Therefore, to overcome these limitations, the search for a new, easily available catalyst with high catalytic activity and short reaction time for the preparation of amidoalkyl naphthols is strongly desirable. Oxalic acid, during the last few years, has emerged as a promising solid acid catalyst for acid catalyzed reaction, viz acetalisation¹⁹, esterification²⁰⁻²³, acetylation of alcohols/phenols²⁴ and nitrile formation²⁵. Recently the catalytic activity of oxalic acid for the synthesis of different heterocycles has

also been explored²⁶. In the present work, ureas and amides have been utilized to produce α -amidoalkyl- β -naphthols compounds using oxalic acid as a catalyst.

Experimental Procedure

All reagents used were of AR grade and were used without further purification. Melting points are uncorrected for all the products. ¹H NMR spectra were recorded on a Varian Gemini 200 MHz spectrometer. Chemical shifts are reported in δ units (ppm) relative to TMS as internal standard. Electron spray ionization mass spectra (ES-MS) were recorded on a Water-Micromass Quattro-II spectrometer. IR Spectra were recorded on Varian Spectrometer.

General procedure for preparation of naphthols (4a-q)

A mixture of aromatic aldehyde (1 mmol), β -naphthol (1 mmol), urea (**4a-4d**) /amide (**4e-4m**) or benzamide (**4n-4q**), (1.1 mmol) and oxalic acid (0.1 mmol) was magnetically stirred at 125°C under solvent-free condition for the appropriate time. The progress of the reaction was monitored by TLC [solvent system: (ethyl acetate): (hexane) = 1:4]. After completion of the reaction, the mixture was washed with H₂O. The pure products were obtained by recrystallization using EtOH-H₂O (1:3) in 80-98% yields and were subjected to characterization by melting point determination, and Infrared spectra and NMR studies.

Results and Discussion

The catalytic activity of oxalic acid was first investigated using 4-chlorobenzaldehyde, equimolar amount of β -naphthol and urea in the presence of 10 mol% oxalic acid. The mixture was magnetically stirred at 125°C under solvent-free condition for the appropriate time (Table 1). Having established the reaction conditions, various α -amidoalkyl- β -naphthols were synthesized in excellent yields by the reaction of different aromatic aldehydes with β -naphthol and urea. In all cases, α -amidoalkyl- β -naphthols were the sole products and no by-product was observed. The reaction of aromatic aldehydes with β -naphthol and different amides including acetamide and benzamide under similar reaction conditions also provided the corresponding α -amidoalkyl- β -naphthols in high

yields (Table 1). In all cases, aromatic aldehydes with substituents carrying either electron-donating or electron-withdrawing groups reacted successfully and gave the desired products in high yields. The reaction can be represented as given in scheme 1.

The reaction was carried using thiourea, β -naphthol and aromatic aldehyde but it was observed that corresponding products were not formed. Also, amines such as aniline were utilized and but no α -amidoalkyl- β -naphthols were obtained. Although

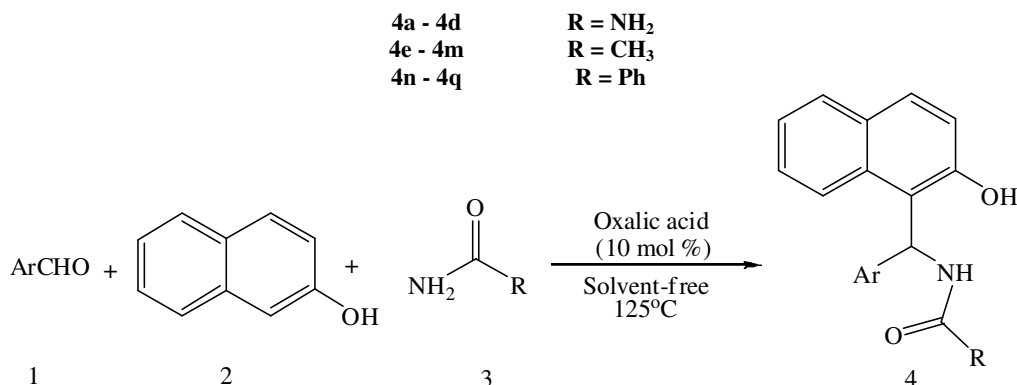
all the products were characterized by IR and MNR studies, only the representative data for **4b** is given below:

IR (KBr, cm^{-1}): 3450 (-OH s), 3348 (-NH, amide), 3215 (-CH, aromatic), 2245 (C=C, s), 1625 (-C=O, s), 1580 (C=C), 1520, 1380 (-OH, def), 820 (-C-Cl).

^1H NMR (CDCl_3 -200 MHz): δ : 9.98 (bs, 1H, -CONH), 7.45-7.10 (m, 3H aromatic), 7.85-7.55 (m, 7H aromatic), 6.95 (bs, 2H), 6.69 (s, 2H) ES/MS m/z (%): 325 (M+H).

Table 1—Details of synthesis of α -amidoalkyl- β -naphthols in solvent-free conditions

Entry	Aldehyde	Time (min)	Yield (%)	Melting point ($^{\circ}\text{C}$)	
				Found	Reported
4a	PhCHO	8	98	175-176	174-175 ⁸
4b	4-ClC ₆ H ₄ CHO	8	98	169-170	168-169 ¹¹
4c	4-MeC ₆ H ₄ CHO	24	88	118-120	117-118 ⁸
4d	3-NO ₂ C ₆ H ₄ CHO	10	92	178-180	179-180 ⁸
4e	PhCHO	8	96	244-245	241-243 ²⁷
4f	4-NO ₂ C ₆ H ₄ CHO	8	94	247-248	248-250 ²⁸
4g	4-ClC ₆ H ₄ CHO	8	98	223-225	224-227 ²⁷
4h	4-MeOC ₆ H ₄ CHO	20	87	182-185	184-186 ²⁷
4i	4-MeC ₆ H ₄ CHO	24	88	221-222	222-223 ²⁸
4j	4-Me ₂ NC ₆ H ₄ CHO	8	91	82-83	78-79 ²⁷
4k	2,5-(MeO) ₂ C ₆ H ₃ CHO	7	94	252-253	251-253 ²⁸
4l	4-NO ₂ C ₆ H ₄ CHO	10	97	241-242	241-242 ⁶
4m	3,4-(MeO) ₂ C ₆ H ₃ CHO	8	91	234-236	235-236 ²⁷
4n	PhCHO	8	96	240-241	242-243 ¹²
4o	4-MeC ₆ H ₄ CHO	8	94	215-216	216-217 ⁸
4p	4-ClC ₆ H ₄ CHO	10	96	187-189	187-188 ⁸
4q	4-NO ₂ C ₆ H ₄ CHO	18	96	239-241	241-242 ⁸



Scheme 1—Preparation of α -amidoalkyl- β -naphthols using oxalic acid catalyst under solvent free condition.

From the results of the above study it can be concluded that a novel and highly efficient methodology for the synthesis of α -amidoalkyl- β -naphthols by one-pot condensation reaction of aromatic aldehyde, β -naphthol and urea or amides, catalyzed by oxalic acid has been established. This method offers several significant advantages such as, high conversions, easy handling, clean reaction profile and shorter reaction times, which makes it a useful and attractive process for the rapid synthesis of substituted α -amidoalkyl- β -naphthols.

Acknowledgement

The authors are thankful to the Head of the Department of Chemical Technology, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad 431 004, India for providing the laboratory facility.

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