Heteropoly acid catalyzed synthesis of 1-amidoalkyl-2-naphthols in the presence of molten tetraethylammonium chloride

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Abstract

An efficient and direct procedure has been developed for the preparation of amidoalkyl naphthols by a one-pot condensation of aryl aldehydes, β-naphthol and urea or acetamide in the presence of 12-tungstophosphoric acid as a heterogeneous catalyst. The reaction was carried out in molten tetraethylammonium chloride under solvent-free condition.

Keywords: Amidoalkyl naphthol, heteropoly acid, ionic liquid, tetraethylammonium chloride

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Introduction

The use of heteropoly acids (HPAs) in different areas of the organic chemistry has now reached significant levels, not only for the possibility to perform environmentally benign synthesis, but for the good yields.[1, 2] HPAs have several advantages as catalysts which make them economically and environmentally feasible. They are stronger acids than homogeneous acid catalysts such as sulfuric acid or ion exchange resins. The use of HPAs as a catalyst is important in the development of clean technologies, since it avoids the drawbacks of environmental pollution and prevents corrosion of the conventional technologies.

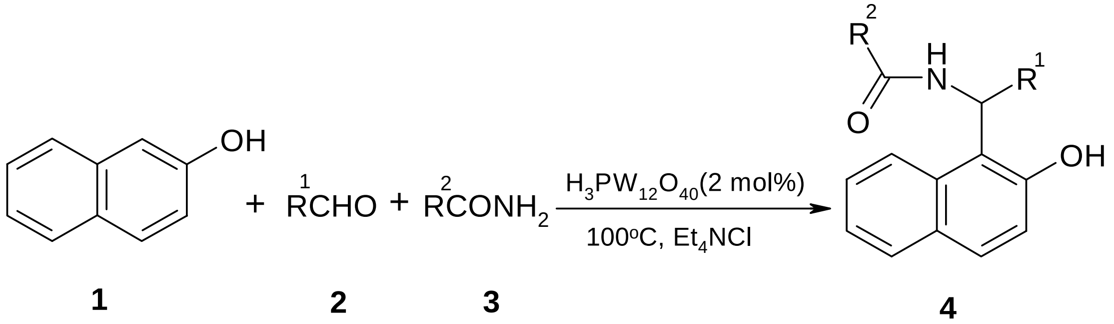
Multicomponent reactions (MCRs) have attracted considerable attention since they are performed without need to isolate any intermediate during their processes; this reduces time and saves both energy and raw materials.[3] They have merits over two-component reactions in several aspects including the simplicity of a one-pot procedure, possible structural variations and building up complex molecules.

One of these MCRs is the preparation of amidoalkyl naphthols. The preparation of 1-amidoalkyl-2-naphthols can be carried out by multi-component condensation of aryl aldehydes, 2-naphthol and acetonitrile or amide in the presence of Lewis or Brønsted acid catalysts such as montmorillonite K10 clay,[4] $HClO_4$-SiO_2,[5] Iodine,[6] $K_5CoW_{12}O_{40}.3H_2O$,[7] *p*-TSA,[8] Sulfamic acid[9] and cation-exchange resins.[10] One of the major drawbacks of these reactions is that in some cases when a solid aldehyde or high amounts of catalyst is used, an organic solvent such as dichloroethane is needed.[9] This problem can be solved by using of eco-friendly solvents such as ionic liquids.

Because of the volatile and toxic nature of many organic solvents, ionic liquids are emerging as effective solvents for 'green' processes.[11] These solvents are nonflammable, nonvolatile, easy to handle and possess high thermal stability.[12] Another promising class of new media are molten salts. They are good solvents for transition metal salts which are commonly used as catalyst. Molten salts are generally thermally stable and chemically resistant. Being composed entirely of ions, they possess negligible vapor pressures. This makes them environmentally benign media for industrial use. Wide range of possible cations and anions means that their properties may be directly controlled. Previously, molten tetraalkylammonium halides were used as cost-effective ionic liquids in a number of useful synthetic transformations. In this study we used tetraethylammonium chloride in molten state as the reaction media.

Results and Discussion

Herein, we wish to describe a novel protocol for the rapid synthesis of a variety of amidoalkyl naphthols using a catalytic amount of 12-tungstophosphoric acid ($H_3PW_{12}O_{40}$) under extremely mild conditions (Scheme 1).



Scheme 1

To optimize the conditions, the reaction of benzaldehyde, β-naphthol and acetamide was selected as a model to investigate the effects of different amounts of catalyst on the yield. To test the general scope and versatility 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 acetamide. The best result was obtained by carrying out the reaction with equal molar amounts of aldehyde, β-naphthol and acetamide. The reaction mixture was heated to 100°C in the presence of 2 mol% of catalyst for 80 min in 1 eq. of Et_4NCl. The results are summarized in Table 1.

In the case of aromatic aldehydes the three-component reaction proceeded smoothly to give the corresponding amidoalkyl naphthols in good yields. Due to the availability of a vast number of aryl aldehydes this three component reaction can be very useful to synthesis the desired products. Moderate to high yields were obtained for the reaction of virtually all aryl aldehydes examined.

As table 1 shows in the case of all aryl aldehydes bearing electron-donating or electron-withdrawing substituents, gave desired amidoalkyl naphthols in good yields. Although as can be seen from the results of table 1, this reaction is affected by electronic and steric factors. Aldehydes with electron-withdrawing groups, give higher yields than aldehydes with electron-donating groups. Ortho substituents decrease the yield of the reaction probably due to the steric effect.

Attempts to bring aliphatic aldehydes such as isobutyryl aldehyde (entry **o**) into the reaction with naphthol and acetamide under these mild conditions were mostly unsuccessful. Therefore no other aliphatic aldehydes were examined.

Table 1. $H_3PW_{12}O_{40}$ catalyzed synthesis of amidoalkyl naphthols in molten tetraethyl ammonium chloride

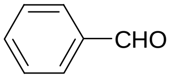
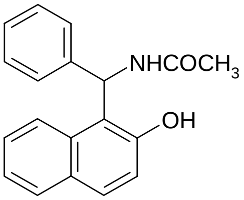
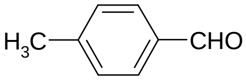
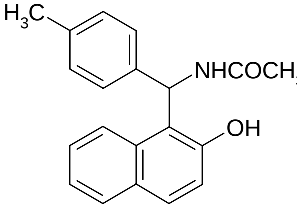
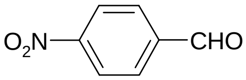
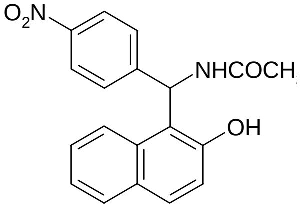
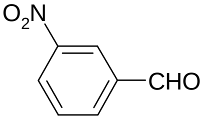
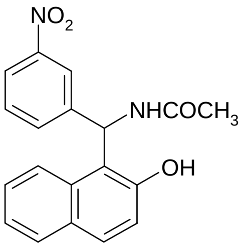
Entry	Aldehyde **2**	Urea/Acetamide **3**	Product **4**	Yield (%)	mp (°C)^{ref}
a		CH_3CONH_2		90	228-230[9a]
b		CH_3CONH_2		75	220-222[5a]
c		CH_3CONH_2		95	225-230[5a]
d		CH_3CONH_2		94	235-236[9a]

Table 1. Continued

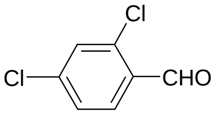
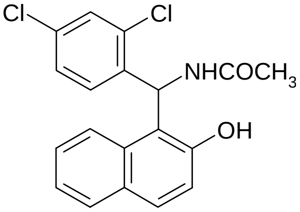
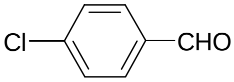
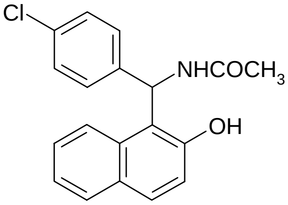
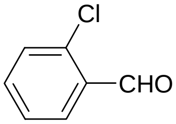
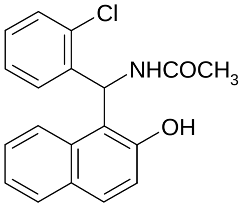
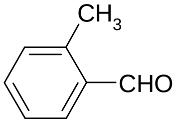
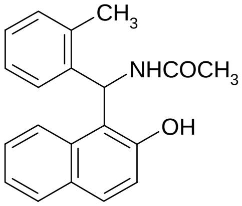
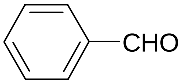
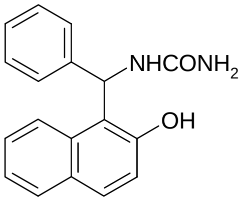
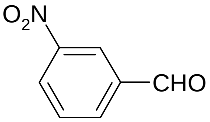
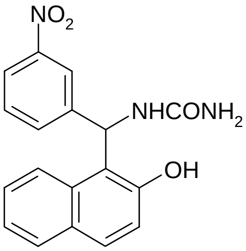
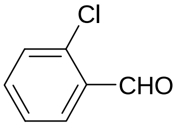
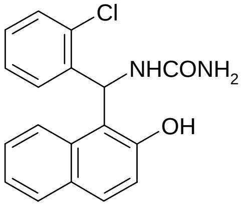
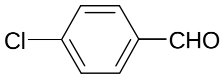
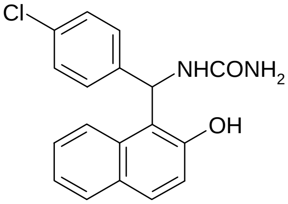
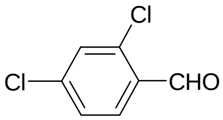
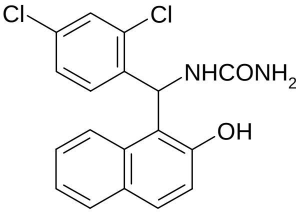
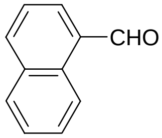
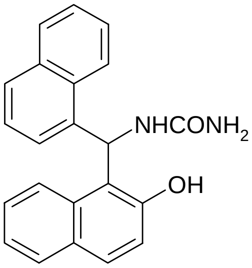
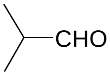
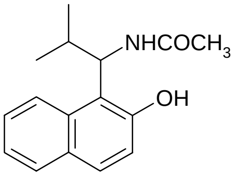
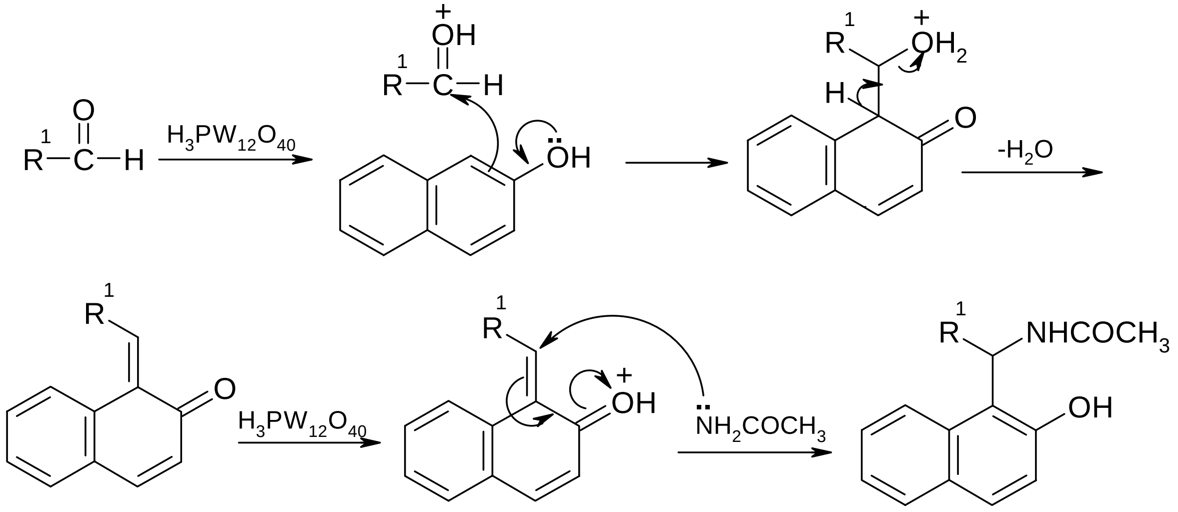
Entry	Aldehyde **2**	Urea/Acetamide **3**	Product **4**	Yield (%)	mp (^{o}C)^{ref}
e		CH_3CONH_2		85	200-202[4]
f		CH_3CONH_2		88	224-226[13]
g		CH_3CONH_2		85	193-195[9a]
h		CH_3CONH_2		65	200-202[9a]
i		NH_2CONH_2		95	171-173[9a]
j		NH2CONH2		95	184-1879a

Table 1. Continued

Entry	Aldehyde **2**	Urea/Acetamide **3**	Product **4**	Yield (%)	mp (°C)^{ref}
k		NH_2CONH_2		80	150-153[7]
l		NH_2CONH_2		85	210-212[9a]
m		NH_2CONH_2		80	140-142[6a]
n		NH_2CONH_2		90	163-165[6a]
o		CH_3CONH_2		0	-

All reactions were performed in 80 min at 100°C.

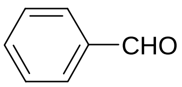
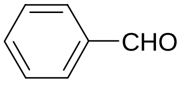
As reported in the literature,[6,8] the reaction of β-naphthol with aromatic aldehydes in the presence of acid catalyst is known to give ortho-quinone methides (O-QMs). The same O-QMs, generated in-situ, have been reacted with acetamide to form 1-amidoalkyl-2-naphthol derivatives. A reasonable explanation for this result can be given by considering the nucleophilic addition to O-QM intermediate favorable via conjugate addition on the α, β-unsaturated carbonyl group and finally this intermediate will aromatize to produce the final aromatic compound. A plausible mechanism for the formation of **4** is shown in scheme 2.



Scheme 2

To show the merit of this work in comparison with reported results in the literature, we compared our results with montmorillonite K10 clay,[4] I_2[6] and $K_5CoW_{12}O_{40}.3H_2O$[7] in the synthesis 1-amidomethyl-2-naphthol derivatives. As shown in Table 2, $H_3PW_{12}O_{40}$ can act as an effective catalyst with respect to reaction times and yields in the molten salt media.

Table 2. Comparison the results of synthesis of 1-amidoalkyl-2-naphthols in the presence of $H_3PW_{12}O_{40}$ in molten salt media with the literature

Entry	Amide	Aldehyde	Catalyst	Mol ratio of catalyst	Time	Yield (%)
			K 10	0.1g	90 min	89
			I_2	5 mol%	330 min	85
a	CH_3CONH_2		$K_5CoW_{12}O_{40}.3H_2O$	1 mol%	120 min	90
			$H_3PW_{12}O_{40}$	2 mol%	80 min	90
			K 10	0.1g	90 min	86
			I_2	5 mol%	270 min	87
b	NH_2CONH_2		$K_5CoW_{12}O_{40}.3H_2O$	1 mol%	180 min	80
			$H_3PW_{12}O_{40}$	2 mol%	80 min	95

The salient features of this method include a simple procedure, short reaction time, mild conditions, easy purification, generality and in addition not cumbersome apparatus are needed.

Experimental Section

General Procedures. All compounds are known and were identified by comparison of their spectral data and physical properties with those of the authentic samples. ^{1}H NMR spectra were recorded on a BRUKER DRX-500 AVANCE NMR spectrometer using DMSO-d_6 as a solvent. IR spectra were recorded on Mattson 1000 FT-IR spectrometer using KBr pellets. Melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected. Aldehydes, β-naphthol, urea, acetamide, 12-tungstophosphoric acid and Et_4NCl were purchased from Merck chemical company.

General procedure for the 12-tugstophosphoric acid catalyzed synthesis of 1-amidoalkyl-2-naphtols in molten salt media

A mixture of appropriate aldehyde (1 mmol), β-naphthol (1 mmol), acetamide/urea (1 mmol), Et_4NCl (1 mmol) and $H_3PW_{12}O_{40}$ (2 mol %) was heated in an oil bath at 100^{o}C for 80 minutes. Then the reaction mixture was washed thoroughly with water to remove the catalyst and Et_4NCl. The catalyst and Et_4NCl were recovered after evaporating of water. The resulting precipitate was recrystalyzed from ethanol:water (1:3) to afford pure amidoalkyl **4**.

Spectral data for the selected compounds

***N*-[(2-Hydroxynaphthlen-1-yl)phenylmethyl]acetamide (4a).** White solid; IR (KBr): 1520, 1660, 3063, 3251, 3390 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ (ppm) = 1.99 (s, 3H), 7.15-7.37 (m, 9H), 7.76-7.82 (m, 3H), 8.45 (d, J = 8.32 Hz, 1H), 9.99 (s, 1H). ^{13}C NMR (DMSO-d_6): δ (ppm) = 23.5, 48.7, 119.3, 119.7, 123.2, 126.9, 127.2, 128.8, 129.4, 130.1, 133.2, 143.5, 154.0, 170.1.

***N*-[(2-Hydroxy-naphthalen-1-yl)-p-tolyl-methyl]-acetamide (4b).** White solid; IR (KBr): 1519, 1659, 2970, 3063, 3391 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ (ppm) = 1.99 (s, 3H), 2.23 (s, 3H), 7.06-7.36 (m, 8H), 7.75-7.85 (m, 3H), 8.42 (d, J = 8.12 Hz, 1H), 9.97 (s, 1H). ^{13}C NMR (DMSO-d_6): δ (ppm) = 21.4, 23.5, 48.5, 119.4, 119.9, 123.2, 126.9, 127.1, 129.3, 129.4, 129.9, 133.2, 135.9, 140.4, 153.9, 170.0.

***N*-[(2-Hydroxy-naphthalen-1-yl)-(3-nitro-phenyl)-methyl]-acetamide (4d).** Pale yellow solid; IR (KBr): 1519, 1659, 2970, 3087, 3390 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ (ppm) = 2.03 (s, 3H), 7.20-8.07 (m, 11H), 8.64 (d, J = 6.96 Hz, 1H), 10.14 (s, 1H). ^{13}C NMR (DMSO-d_6): δ (ppm) = 23.4, 48.5, 118.7, 119.3, 121.3, 122.1, 123.5, 123.6, 127.6, 129.2, 129.6, 130.4, 130.8, 133.0, 133.7, 146.3, 148.6, 154.2, 170.5.

***N*-[(2, 4-Di-chloro-phenyl)-(2-hydroxy-naphthalen-1-yl)-methyl]-acetamide (4e).** White solid; IR (KBr): 1519, 1660, 3391 cm^{-1}. ^{1}H NMR (DMSO-d_6): δ (ppm) = 1.93 (s, 3H), 7.01 (d, J = 7.68 Hz, 1H), 7.12 (d, J = 8.79 Hz, 1H), 7.28 (t, J = 7.28 Hz, 1H), 7.41-7.47 (m, 3H), 7.60 (d, J

= 8.46 Hz, 1H), 7.75 (d, J = 8.81 Hz, 1H), 7.80 (d, J = 7.98 H, 1H), 7.97 (d, J = 8.57 Hz, 1H), 8.62 (d, J = 7.72 Hz, 1H), 9.98 (s, 1H). ^{13}C NMR (DMSO-d_6): δ (ppm) = 23.2, 48.1, 117.2, 119.4, 123.2, 123.4, 127.2, 127.3, 129.1, 129.3, 129.5, 130.5, 132.1, 132.5, 133.6, 133.7, 140.2, 154.5, 169.6.

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