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Catalyst free synthesis of new 1,3-oxazines from β-naphtol, aldehyde and amonia

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Abstract: Some of new 1,3-oxazines have been synthesized *via* pseudo four component reaction, in which β-naphthol undergoes a ring closure reaction with substituted aryl aldehyde to give naphthoxazine derivatives. The structures were confirmed through elemental analysis, spectral studies.

Keywords: Naphthoxazine, MCRs, β-Naphthol, Aldehyde.

Introduction

Organic synthesis like any other human activity aims at achieving ideality. An ideal synthesis is one that can be performed in the most efficient and facile manner with maximum conversion. In this respect multicomponent reactions (MCRs) come very close to the concept of an ideal synthesis [1-2]. MCRs are ordered pot reactions, where three or more starting materials react in a sequence of steps, until a final one, to give a final product which contains most of the portions of all the initial components [3-4] a MCR is thus a domino process by definition [5-6]. The development of novel MCRs is an intellectually challenging task since one has to consider not only the reactivity match of the starting materials but also the reactivities of the intermediate molecules generated *in situ*, their compatibility and their compartmentalization [7-8]

Nitrogen-oxygen heterocycles are of synthetic interest because they constitute an important class of natural and non-natural products, many of which exhibit useful biological activities [9]. Among these the interest in six membered systems containing one oxygen and one nitrogen atoms (positions 1, 3 or 1, 4) stems from the occurrence of oxazines in biologically activated compounds and natural products [11].

As part of our continuing interest in the construction of novel heterocycles [12-14], we now report the results of our studies involving the reactions 2-naphthol (**1**) and Aromatic aldehydes (**2**) in the presence of aqueous ammonia (**3**), which constitutes a synthesis of new 1H-naphtho [1,3]oxazines derivatives (**4**) (Scheme **1**).

Results and discussion

The structures of compounds **4a–e** were deduced from their elemental analyses and their IR, ^{1}H NMR and ^{13}C NMR spectra. For example, the ^{1}H NMR spectrum of **4a** exhibited three singlets identified as methine (δ 5.54 and 5.68 ppm) and NH (δ 12.10 ppm) protons, along with multiplets for the aromatic region. The ^{1}H decoupled ^{13}C NMR spectrum of **4a** showed 20 distinct resonances, which confirmed the proposed structure. The IR spectrum of **4a-4e** displayed characteristic NH and aromatic bands. The ^{1}H NMR and ^{13}C NMR spectra of **4b-4e** were similar to those

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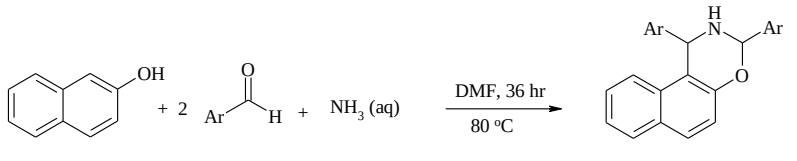
for **4a** except for the aromatic moieties, which exhibited characteristic resonances in appropriate regions of the spectrum.



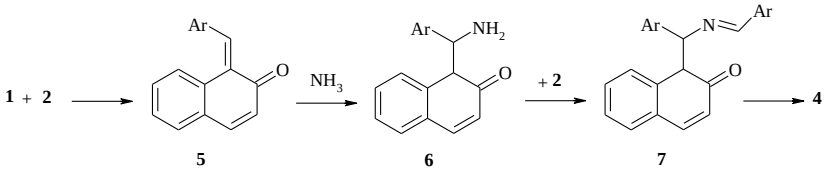
1

2	Ar	**3**
a	Ph	
b	4-Cl-Ph	
c	4-Br-Ph	
d	4-OMe-Ph	
e	4-NO_2-Ph	

4	Ar	Yield%
a	Ph	71
b	4-Cl-Ph	69
c	4-Br-Ph	70
d	4-OMe-Ph	72
e	4-NO_2-Ph	68

Scheme 1: Synthesis of new 1,3-oxazines.

Although the mechanistic details of the reaction are not known, a plausible rationalization may be advanced to explain the product formation (Scheme **2**). Presumably, the unsaturated keton **5** [15-16], formed from 2-naphtole and the aryl aldehyde is attackted by **3** to furnish intermediate **6**, which is condensed by another aryl aldehyde to produce **7**. This intermediate is converted to final product (**4**) by intermolecular ring closing.



Scheme 2: Proposed mechanism for the formation of the compounds **4.**

Conclusion

In summary, we have reported a catalyst free transformation involving β-naphthol (**1**) and Aromatic aldehydes (**2**) in the presence of aqueous ammonia (**3**), which affords a new route to the synthesis of new 1,3-oxazines. The present procedure has the advantage that not only is the reaction performed under neutral conditions, but also the reactants can be mixed without any prior activation or modification.

Experimental

General procedure:

All compounds were obtained from Fluka, Merck. M.p.: Electrothermal-9100 apparatus. IR Spectra: Shimadzu IR-460 spectrometer. ^{1}H-, ^{13}C- NMR spectra: Bruker DRX-500 AVANCE instrument; in $CDCl_3$ 500, 125 MHz, respectively; δ in ppm. Elemental analyses (C, H, N) were performed with a Heraeus CHNS-O-Rapid analyzer.

*General procedure for the synthesis of 1,3- oxazines (**4a-f**):*

To the stirred solution of β-naphthol (0.223 g, 1 mmol) in DMF (10 ml) was added aryl aldehyde (4 mmol) and 1 ml of 25% aqueous ammonia. Then heated at 80 ºC for 36 hours. 10 cc water was added and the mixture was extracted by ethyl acetate (3*10 cc). Collected ethyl acetate dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude precipitate was purified by flash column chromatography (CC) (SiO_2; Hexane/AcOEt 3 : 1) to afford the pure title compounds **4a-f**.

1,3-diphenyl-2,3-dihydro-1H-naphto[1,2-e][1,3] oxazine (**4a**):

Yellow powder; 146–148 °C, yield: 0.24 g (71%). IR (KBr) (ν_{max}/cm^{-1}): 3200, 2944, 1651, 1416, 1145. Anal. Calcd for $C_{24}H_{19}NO$ (337.4): C, 85.43; H, 5.68; N, 4.15. Found: C, 85.31; H, 5.72; N, 4.18. ^{1}H-NMR ($CDCl_3$, δ: ppm): 5.54 (1H, s, CH), 5.68 (1H, s, CH), 7.18-8.10 (16H, m, ArH), 12.10 (br s, NH). ^{13}C-NMR ($CDCl_3$, δ: ppm): 54.5 (CH), 79.1 (CH), 114.6 (CH), 114.8 (CH), 115.2 (CH), 115.9 (CH), 117.0 (CH), 117.4 (CH), 120.3 (CH), 125.2 (CH), 125.7 (C), 127.6 (2CH), 128.3 (2CH), 128.5 (2CH), 129.2 (2CH), 130.3 (C), 130.6 (C), 134.4 (C), 135.4 (C), 148.2 (C).

1,3-bis(4-chlorophenyl)-2,3-dihydro-1H-naphto[1,2-e][1,3]oxazine (**4b**):

Yellow powder; 165–167 °C, yield: 0.28 g (69%). IR (KBr) (ν_{max}/cm^{-1}): 3210, 2923, 1664, 1412. Anal. Calcd for $C_{24}H_{17}Cl_2NO$ (406.3): C, 70.95; H, 4.22; N, 3.45. Found: C, 71.11; H, 4.32; N, 3.48. ^{1}H NMR ($CDCl_3$, δ: ppm): 5.63 (1H, s, CH), 5.71 (1H, s, CH), 7.19-8.09 (14H, m, ArH), 12.18 (br s, NH). ^{13}C-NMR ($CDCl_3$, δ: ppm): 53.6 (CH), 79.3 (CH), 113.9 (CH), 114.0 (CH), 115.1 (CH), 115.8 (CH), 116.1 (CH), 117.5 (CH), 125.9 (C), 127.6 (2CH), 127.9 (2CH), 128.5 (2CH), 128.8 (2CH), 129.7 (C), 130.1 (C), 130.3 (C), 130.6 (C), 134.4 (C), 135.4 (C), 149.2 (C).

1,3-bis(4-bromophenyl)-2,3-dihydro-1H-naphto[1,2-e][1,3]oxazine (**4c**):

Yellow powder; 169–171 °C, yield: 0.20 g (70%). IR (KBr) (ν_{max}/cm^{-1}): 3220, 2940, 1668, 1440. Anal. Calcd for $C_{24}H_{17}Br_2NO$ (495.2): C, 58.21; H, 3.46; N, 2.83. Found: C, 58.31; H, 3.42; N, 2.87. ^{1}H NMR ($CDCl_3$, δ: ppm): 5.75 1H, (s, CH), 5.81 (1H, s, CH), 7.02-8.16 (14H, m, ArH), 11.88 (br s, NH). ^{13}C-NMR ($CDCl_3$, δ: ppm): 54.1 (CH), 78.8 (CH), 114.7 (CH), 114.8 (CH), 115.3 (CH), 115.6 (CH), 116.8 (CH), 120.2 (CH), 125.7 (C), 127.9 (2CH), 128.2 (2CH), 128.6 (2CH), 128.9 (2CH), 129.4 (C), 130.1 (C), 130.4 (C), 130.8 (C), 134.2 (C), 134.5 (C), 147.2 (C).

1,3-bis(4-methoxyphenyl)-2,3-dihydro-1H-naphto [1,2-e][1,3]oxazine (**4d**):

Brown powder; 165–167 °C, yield: 0.36 g (72%). IR (KBr) (ν_{max}/cm^{-1}): 3240, 2980, 1655, 1420. Anal. Calcd for $C_{26}H_{22}NO_3$ (497.4): C, 78.57; H, 5.83; N, 3.52. Found: C, 78.51; H, 5.41; N, 3.55. ^{1}H NMR ($CDCl_3$, δ: ppm): 3.44 (3H, s, OCH_3), 3.65 (3H, s, OCH_3), 6.01 (1H, s, CH), 6.10 (1H, s, CH), 6.89-8.05 (13H, m, ArH), 12.61 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, δ: ppm): 53.6 (CH), 55.5 (CH_3), 55.7 (CH_3), 80.4 (CH), 111.9 (CH), 114.7 (CH), 116.9 (CH), 120.1 (CH), 121.1(CH), 121.2 (CH), 121.5 (CH), 123.4 (CH), 123. 6 (CH), 127.9 (2CH), 128.01 (2 CH), 128.8 (2CH), 129.5 (2CH), 130.48 (C), 133.02(C), 145. 4 (C), 156.77 (C), 159.28(C).

1,3-bis(4-nitrophenyl)-2,3-dihydro-1H-naphto[1,2-e][1,3]oxazine (**4e**):

Brown powder; 165–167 °C, yield: 0.29 g (68%). IR (KBr) (ν_{max}/cm^{-1}): 3235, 2990, 1665, 1443. Anal. Calcd for $C_{24}H_{17}N_3O_5$ (427.4): C, 67.44; H, 4.01; N, 9.83. Found: C, 67.51; H, 4.10; N, 9.95. ^{1}H NMR ($CDCl_3$, δ: ppm): 5.68 (1H, s, CH), 5.85 (1H, s, CH), 7.12-8.08 (10H, m, ArH), 8.57 (2 H, d, *J*=8.0 Hz, 2CH), 8.75 (2 H, d, *J*=8.2 Hz, 2CH), 11.56 (br s, NH). ^{13}C-NMR ($CDCl_3$, δ: ppm): 52.9 (CH), 84.2 (CH), 113.7 (CH), 114.8 (CH), 116.1 (CH), 116.6 (CH), 118.3 (CH), 121.4 (CH), 126.1 (C), 128.0 (2CH), 128.2 (2CH), 128.4 (2CH), 128.9 (2CH), 129.9 (C), 130.3 (C), 131.1 (C), 131.4 (C), 134.6 (C), 134.5 (C), 147.6 (C).

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