

NOTE

Synthesis of 1-Amidoalkyl-2-Naphthols by Two-Component Friedel-Crafts Reaction

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(Received: 22 May 2012;

Accepted: 30 January 2013)

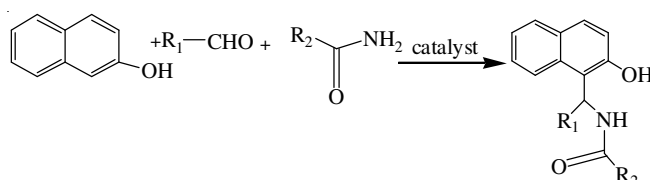
AJC-12775

A one-pot two-component Friedel-Crafts reaction of 1-amidoalkyl-2-naphthols by the condensation of 2-naphthol with various N-methyl hydrocarbon unsaturated amides in presence of the concentrated sulphuric acid as catalyst and anhydrous ethyl alcohol as solvent to form the corresponding amidoalkyl naphthols is described. This procedure offers advantages such as eco-friendly, shorter reaction times, simple work-up, excellent yields and recovery and reusability of the catalyst. The spectroscopic properties are assessed for their effectiveness and the fluorescent intensity sequence of three compounds in two different solvents follows the sequence: 1-N-methacrylamide-2-naphthol > 1-N-methyl phthalimide-2-naphthol > 1-N-methyl phthalimide-2-naphthol.

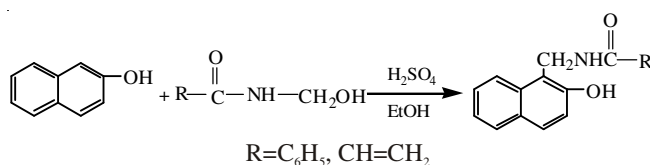
Key Words: 1-Amidoalkyl-2-naphthols, 2-Naphthole, N-methyl hydrocarbon unsaturated amides.

Amidoalkyl-2-naphthols can be converted to useful and important biological building blocks and to 1-aminomethyl-2-naphthols by an amide hydrolysis reaction, since compounds exhibit depressor and bradycardia effects in human^{1,2}. In recent years, 1-amidoalkyl-2-naphthols are mainly prepared by multi-component reactions of 2-naphthol with aryl aldehydes and amides in the presence of Lewis or Brønsted acid catalysts (**Scheme-I**) such as [Fem SILP] L-proline³, silica sulphuric acid⁴, silica chloride⁵, 1-hexane sulphonic acid sodium salt⁶, Montmorillonite K¹⁰ clay⁷, MoO₃-ZrO₂⁸, FeCl₃-SiO₂⁹, HClO₄-SiO₂¹⁰ and iodine¹¹. However, some of these reported procedures suffer from one or more drawbacks such as long reaction times, high temperatures, low yields of products, use of toxic organic solvents, use of the toxic, corrosive, expensive or non-reusable catalysts and tedious work up procedures. For developing a green protocol, we report the rapid synthesis of biologically significant amidoalkyl naphthols by a one-pot two-component Friedel-Crafts reaction using concentrated sulphuric acid as catalyst and anhydrous ethyl alcohol as solvent under extremely mild conditions (**Scheme-II**). This method offers significant advantages, such as high conversions, easy handling, cleaner reaction profile and shorter reaction times, which makes it a useful and attractive process for the rapid synthesis of substituted amidoalkyl naphthols.

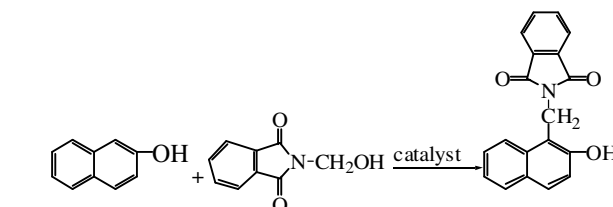
Chemicals and solvents used for synthesis are at least reagent grade quality and are used without further purification.



Scheme-I: Synthesis of 1-amidoalkyl-2-naphthols from one-pot multicomponent reaction



Scheme-II: Synthesis of 1-amidoalkyl-2-naphthols from one-pot two-component reaction



Scheme-II: Synthesis of 1-amidoalkyl-2-naphthols from one-pot two-component reaction

Fourier transform infrared (FT-IR) spectra is recorded using a Thermo Nicolet AVATAR-360 FT-IR spectra spectrometer. ¹H NMR spectra is recorded on a Bruker AVCEIII600 Hz

spectrometer with tetramethylsilane as internal reference. Elemental analyses are done on a Vario EL Elementar. Fluorescence spectra is determined with a Hitachi High Technologies F-4600 fluorescent spectrometer at EX/EM slit width of 2.5 nm.

β -Naphthol and *N*-methyl unsaturated hydrocarbon amides dissolved in 100 mL of dehydrated alcohol are put into a 250 mL three-necked round-bottom flask equipped with a heating oil bath and stirrer. Then concentrated sulfuric acid (10 mL) is dropped stepwise as the catalyst under oil bath. The reactant mixture is heated to specific temperature for a time. After cooling down, the resulting mixture is washed with NaOH (aq) to terminate the reaction. The organic phase is separated and recrystallized to remove the excess β -naphthol, finally placed in the *vacuum* oven to remove the traces of alcohol and water. Table-1 shows the optimal reactive conditions of compounds.

Product	Reactant mole ratio	$V_{\text{catalyst}} \cdot V$		Time
		Solvent	Solvent	
NMAMN	1:1	1:10	50	5h
NMBAN	1:1	1:10	40	7h
NMPN	1:1	1:10	60	24h

The spectral data of three compounds are given below:

1-*N*-Methacrylamide-2-naphthol (NMAMN): IR (KBr, pellet, cm^{-1}): Yield, 86 %. m.p. 147 °C, 3326 ($\nu_{\text{O-H}}$), 3205 ($\nu_{\text{N-H}}$), 1644 ($\nu_{\text{C=O}}$), 1543 ($\delta_{\text{N-H}}$), 3063 ($\nu_{\text{C-H}}$), 1591, 1464 1435 ($\nu_{\text{C=C}}$, naphthalene), 3063 ($\nu_{\text{C-H}}$, naphthalene), 2784 (ν_{CH_2}), 1252 ($\nu_{\text{C-O}}$, phenol), 948,973 ($\gamma_{\text{C-H}}$). ^1H NMR (acetone, TMS): 10.42 (s, OH, 1H), 8.69 (s, NH, 1H), 8.05 (d, naphthalene, 1H), 7.81 (d, naphthalene, 1H), 7.78 (d, naphthalene, 1H), 7.49 (t, naphthalene, 1H), 7.33 (t, naphthalene, 1H), 7.17 (d, naphthalene, 1H), 6.33 (q, =CH₂, 2H), 5.68 (q, CH=, 1H), 5.00 (d, -CH₂-, 2H). Anal. calcd for C₁₄H₁₃NO₂: C, 73.99; H, 5.7; N, 6.1. Found: C, 73.3; H, 5.6; N, 6.1.

1-*N*-Methy benzoyl amide-2-naphthol (NMBAN): IR (KBr, pellet, cm^{-1}): Yield, 89 %. m.p. 186 °C, 3627 ($\nu_{\text{O-H}}$), 3186 ($\nu_{\text{N-H}}$), 1621 ($\nu_{\text{C=O}}$), 1544 ($\delta_{\text{N-H}}$), 1600, 1544, 1451 ($\nu_{\text{C=C}}$, naphthalene), 3132 ($\nu_{\text{C-H}}$, naphthalene), 2768 (ν_{CH_2}), 1226 ($\nu_{\text{C-O}}$, phenol). ^1H NMR (acetone, TMS): 10.61 (s, OH, 1H), 9.12 (s, NH, 1H), 8.20 (d, naphthalene, 1H), 7.95 (t, naphthalene, 2H), 7.82 (q, naphthalene, 2H), 7.55 (t, naphthalene, 1H), 7.51 (m, benzene, 3H), 7.33 (t, benzene, 1H), 7.19 (d, benzene, 1H), 4.99 (d, -CH₂-, 2H); Anal. calcd for C₁₈H₁₅NO₂: C, 77.96; H, 5.45; N, 5.05. Found: C, 78.4; H, 5.45; N, 11.09.

1-*N*-Methy phthalimide-2-naphthol (NMPN): Yield, 85 %. m.p. 207 °C, IR (KBr, pellet, cm^{-1}): 3221 ($\nu_{\text{O-H}}$), 1692 ($\nu_{\text{C=O}}$), 1610, 1518, 1463 ($\nu_{\text{C=C}}$, naphthalene), 3066 ($\nu_{\text{C-H}}$, naphthalene), 723 (δ_{CH_2}), 1309 ($\nu_{\text{C-O}}$, phenol). ^1H NMR (acetone, TMS): 9.05 (s, OH, 1H), 8.41 (d, naphthalene, 1H), 7.89 (m, 4H), 7.82 (d, 2H), 7.53 (d, 1H), 7.34 (m, 1H), 7.32 (t, 1H), 5.30 (s, 2H); Anal. calcd. for C₁₉H₁₃NO₃: C, 75.24 %; H, 4.32 %; N, 4.62 %. Found: C, 74.27 %; H, 4.3 %; N, 4.65 %.

Fig. 1 shows the fluorescence spectra of three compounds in THF and DMSO at the same concentration ($M = 1 \times 10^{-5}$ mol/L). The fluorescence intensity of NMAMN is the largest,

NMBAN is lower and NMPN is the lowest in two solvents. It is immediately obvious that the fluorescence spectra show a remarkably strong dependence on the nature of the medium. Compared to THF, the fluorescence intensity is enhanced significantly in the DMSO solvent. Apart from the intensity enhancement, the fluorescence peaks in the DMSO solvent also exhibit a prominent red-shift. This may be caused by the polarity factor of solvents.

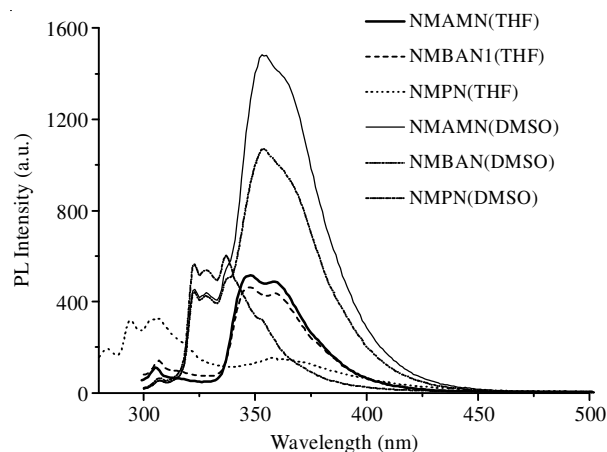


Fig. 1. Fluorescence spectra of compounds in different solvent ($M = 1 \times 10^{-5}$ mol/L)

Conclusion

In conclusion, three kinds of *N*-methyl hydrocarbon unsaturated amides are synthesized by a one-pot two-component Friedel-Crafts reaction. This procedure offers advantages such as eco-friendly, shorter reaction times, simple work-up, excellent yields and recovery and reusability of the catalyst. The fluorescence intensity sequence of three compounds in two different solvents follows the same sequence: 1-*N*-methacrylamide-2-naphthol > 1-*N*-methyl phthalimide-2-naphthol > 1-*N*-methyl phthalimide-2-naphthol.

ACKNOWLEDGEMENTS

This work is financially supported by the NSFC (No. 50673085), National "863" Project (2010AA09Z203, 2010AA065104) and Cheung Kong Scholars Programme of China.

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