

Iodine catalyzed preparation of amidoalkyl naphthols in solution and under solvent-free conditions[☆]

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Abstract

A one-pot three-component reaction of 2-naphthol, aldehydes and urea or amides has efficiently been carried out in the presence of iodine in dichloroethane at room temperature or under solvent-free conditions at higher temperature to form the corresponding amidoalkyl naphthols in high yields.

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Recently we reported [1] the reaction of 2-naphthol and aldehydes in the presence of iodine to form xanthenes. The reaction proceeds through the in situ formation of *ortho*-quinone methides and 2-naphthol acted as a nucleophile (Scheme 1). We have now extended this iodine catalyzed procedure using urea or amides (to work as nucleophiles) along with 2-naphthol and aldehydes to produce the corresponding amidoalkyl naphthols (Scheme 2).

A series of amidoalkyl naphthols were prepared in high yields using various aldehydes and urea or amides (Table 1). The reaction was conducted in dichloroethane at room temperature or under neat conditions at 125 °C. The yields of the products were somewhat higher in the first case but the conversion times were much lower in the second case. Aromatic aldehydes underwent facile conversions but aliphatic aldehydes afforded the products in low yields. For example, the reaction of 2-naphthol, propanal and urea in the presence of iodine produced the corresponding amidoalkyl naphthol with yields of 34% (at room temperature in dichloroethane after 26 h) and 22% (under neat conditions after 9 h). The aromatic aldehydes containing both electron-donating and electron-withdrawing groups afforded the desired products. Polynuclear as well as *ortho*-substituted aromatic aldehydes also underwent the transformation conveniently. Urea and different

amides, such as acetamide and benzamide worked equally. α,β -Unsaturated amides also formed the products in high yields (Table 1). However, the reaction was unsuccessful with amines.

In recent years, multicomponent reactions have gained much importance in organic synthesis as they furnish the desired products in a single operation without isolating the intermediates [2]. Thus, the reaction times are reduced and both the energy and raw materials are also saved. The present one-pot three-component reaction catalyzed by iodine is a convenient and facile process for the synthesis of amidoalkyl naphthols. Iodine has currently been utilized by us as an efficiently catalyst in various chemical transformations [3]. It is inexpensive and readily available. Previously, amidoalkyl naphthols were prepared [4] by using *p*-TSA which may affect the acid sensitive groups. This problem would not come into play in the present iodine catalyzed conversions.

In conclusion, we have developed a very simple and efficient method for the high-yielding synthesis of amidoalkyl naphthols by one-pot three-component coupling of 2-naphthol, aromatic aldehydes and urea or amides in the presence of iodine as a catalyst. The reaction can be conducted in solution at room temperature or under solvent-free conditions at higher temperature.

1. Experimental

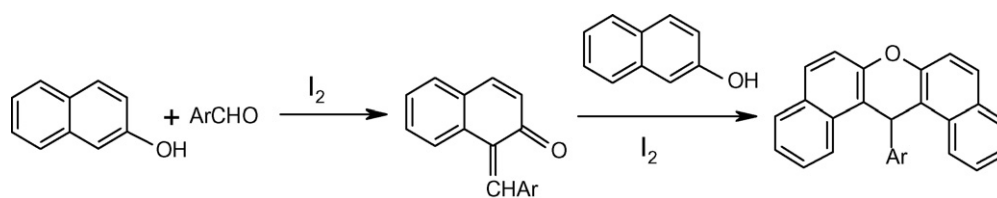
1.1. General procedure for the preparation of amidoalkyl naphthols

Method A: To a mixture of 2-naphthol (1 mmol), aldehyde (1 mmol) and urea or amide (1.3 mmol) in dichloroethane

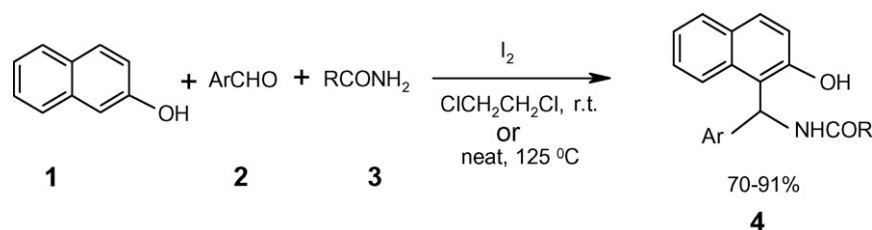
[☆] ICT Communication No. 060828 Part 105 in the series “Studies on novel synthetic methodologies”.

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Scheme 1.



Scheme 2.

Table 1
Preparation of amidoalkyl naphthols^a

Entry	Aldehyde	Urea or amide	Product	Method A		Method B	
				Time (h)	Yield (%)	Time (h)	Yield (%)
a		NH ₂ CONH ₂		12	91	4.5	87
b		NH ₂ CONH ₂		16	90	4.5	85
c		NH ₂ CONH ₂		11	90	4	89
d		NH ₂ CONH ₂		15	89	5	76
e		NH ₂ CONH ₂		20	75	6	70

Table 1 (Continued)

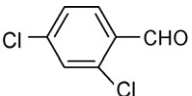
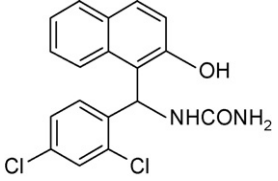
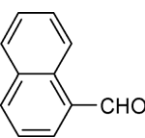
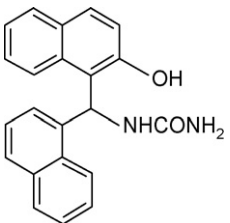
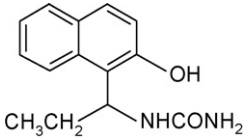
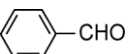
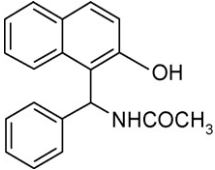
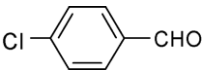
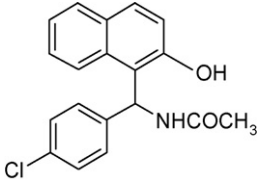
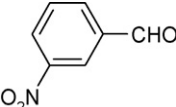
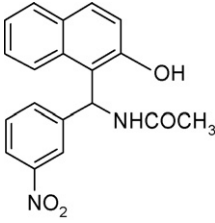
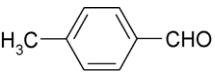
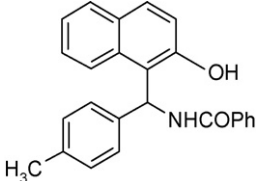
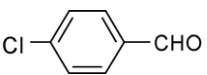
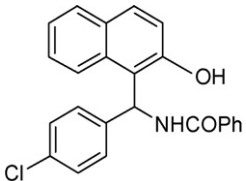
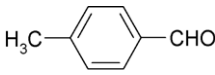
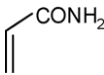
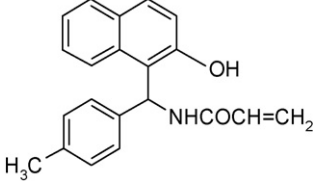
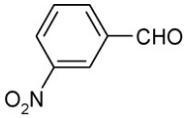
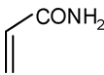
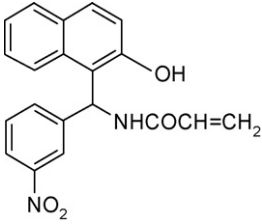
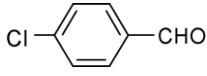
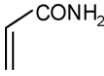
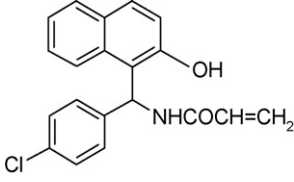
Entry	Aldehyde	Urea or amide	Product	Method A		Method B	
				Time (h)	Yield (%)	Time (h)	Yield (%)
f		NH ₂ CONH ₂		17	89	6.5	82
g		NH ₂ CONH ₂		20	71	7	70
h	CH ₃ CH ₂ CHO	NH ₂ CONH ₂		26	35	9	20
i		CH ₃ CONH ₂		11	89	5.5	85
j		CH ₃ CONH ₂		11.5	90	4.5	86
k		CH ₃ CONH ₂		10	85	5	81
l		PhCONH ₂		14	90	7.5	78
m		PhCONH ₂		16	89	8	88

Table 1 (Continued)

Entry	Aldehyde	Urea or amide	Product	Method A		Method B	
				Time (h)	Yield (%)	Time (h)	Yield (%)
n				15	83	7	80
o				14	93	6	90
p				11	92	6	83

^a All the products were characterized from spectral (¹H NMR and MS) data.

(10 ml) molecular iodine (5 mol%) was added. The mixture was stirred at room temperature and the reaction was followed by TLC. After completion, the mixture was treated with aqueous Na₂S₂O₃ solution and extracted with EtOAc (3 × 10 ml). The extract was concentrated and the residue was purified by column chromatography (silica gel, 20% EtOAc in hexane) to obtain pure amidoalkyl naphthol.

Method B: A mixture of 2-naphthol (1 mmol), aldehyde (1 mmol) and urea or amide (1.3 mmol) was heated at 125 °C. The reaction was monitored by TLC. After completion, the reaction was worked up following the above procedure to obtain pure amidoalkyl naphthol.

The spectral (¹H NMR and MS) data of some representative compounds are given below:

Compound **4b**: ¹H NMR (200 MHz, DMSO-*d*₆): δ 9.70 (1H, brs), 7.92 (1H, m), 7.68 (1H, d, *J* = 8.0 Hz), 7.60 (1H, d, *J* = 8.0 Hz), 7.36–6.86 (9H, m), 5.42 (2H, brs), 2.22 (3H, s); FABMS: *m/z* 307 [*M* + H]⁺.

Compound **4g**: ¹H NMR (200 MHz, DMSO-*d*₆): δ 9.72 (1H, brs), 8.02 (1H, m), 7.80–7.58 (6H, m), 7.20–7.08 (8H, m), 5.46 (2H, brs); FABMS: *m/z* 343 [*M* + H]⁺.

Compound **4j**: ¹H NMR (200 MHz, DMSO-*d*₆): δ 9.68 (1H, brs), 8.12–7.98 (2H, m), 7.78–7.59 (2H, m), 7.30 (1H, m), 7.28–7.06 (7H, m), 2.02 (3H, s); FABMS: *m/z* 329, 327 [*M* + H]⁺.

Compound **4i**: ¹H NMR (200 MHz, DMSO-*d*₆): δ 9.88 (1H, brs), 8.86 (1H, d, *J* = 8.0 Hz), 8.14 (1H, d, *J* = 8.0 Hz), 7.90–7.68

(2H, m), 7.46–7.20 (11H, m), 7.01 (2H, d, *J* = 8.0 Hz), 2.24 (3H, s); FABMS: *m/z* 368 [*M* + H]⁺.

Compound **4n**: ¹H NMR (200 MHz, DMSO-*d*₆): δ 9.61 (1H, brs), 8.22 (1H, d, *J* = 8.0 Hz), 8.01 (1H, d, *J* = 8.0 Hz), 7.78–7.62 (2H, m), 7.33–7.22 (2H, m), 7.24–6.90 (6H, m), 6.26 (1H, d, *J* = 12.0 Hz), 6.24 (1H, d, *J* = 10.0 Hz), 5.61 (1H, dd, *J* = 12.0, 10.0 Hz), 2.22 (3H, s); FABMS: *m/z* 318 [*M* + H]⁺.

Acknowledgements

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