IODINE-CATALYZED, RAPID AND EFFICIENT, ONE-POT SYNTHESIS OF 1,2-DIHYDRO-1-ARYLNAPHTHO[1,2-e][1,3]OXAZINE-3-ONES UNDER SOLVENT-FREE CONDITIONS

Aatika Nizam and M. A. Pasha
Department of Studies in Chemistry, Central College Campus, Bangalore University, Bangalore, India

A mixture of β-naphthol, aldehydes, and urea in the presence of a catalytic amount of iodine as catalyst under solvent-free condition was heated for 5 min on a preheated hot plate to get the corresponding 1,2-dihydro-1-aryl-naphto[1,2-e][1,3]oxazine-3-ones in very good yield.

Keywords: Aldehydes; iodine; β-naphthol; naphthoxazinones; solvent-free condition; urea

INTRODUCTION
Multicomponent condensations (MCCs) constitute attractive synthetic strategies for the rapid and efficient generation of molecules because the products are formed in a single step, and in MCCs, diversity can be achieved by varying the reacting components. Multicomponent reactions (MCRs) are also emerging as useful tools for carbon–carbon and carbon–heteroatom bond-forming reactions and for the synthesis of small molecules with several degrees of structural diversity.

If, in addition, these MCCs are done under solvent-free conditions, then the protocol becomes highly advantageous because solvent-free reactions are environmentally benign.

Naphthoxazinones, on the other hand, act as antibacterial agents and are used as precursors in the preparation of phosphonic ligands for asymmetric catalysis. However, to the best of our knowledge, not many reports are available for the synthesis of these compounds. One report by Szatmari et al. involves condensation of aminoalkynaphthols with phosgene in the presence of triethylamine, and another by Cimarelli and coworkers requires diimidazole instead of phosgene. In these procedures, reagents are either toxic and hazardous or require the preparation of starting aminoalkynaphthols (which again require harsh conditions for preparation). The reactions also require longer durations, and the yields of the products are moderate. Most recently, Dabiri et al. have reported the synthesis of

Received July 3, 2009.
Address correspondence to M. A. Pasha, Department of Studies in Chemistry, Central College Campus, Bangalore University, Bangalore 560 001, India. E-mail: m_a_pasha@ymail.com
naphthoxazinones by the condensation of β-naphthol, aromatic aldehydes, and urea in the presence of p-TsOH. However, the reaction takes a long time for completion (about 1.6 h) under conventional heating, and the same reaction under microwave irradiation is fast; however, the yields obtained under both the conditions are moderate.

It is well known that molecular iodine is an inexpensive, nontoxic, readily available catalyst employed for various organic transformations, affording the corresponding products in excellent yields with high selectivity. Because of numerous advantages associated with this ecofriendly element, iodine has been explored as a powerful catalyst for various organic transformations. As part our studies toward the development of new routes to the synthesis of biologically active heterocycles, we report the synthesis of naphthoxazinones by a one-pot, three-component reaction of β-naphthol, aldehydes, and urea in the presence of a catalytic amount of iodine as catalyst (Scheme 1).

RESULTS AND DISCUSSION

To successfully synthesize the naphthoxazinones, a number of preliminary experiments were carried out. We first performed the condensation of β-naphthol, aldehydes, and urea in the absence of any catalyst under solvent-free thermal

| Table 1. One-pot condensation of β-naphthol, aldehydes, and urea in the presence of catalytic amounts of iodine as catalyst under solvent-free conditions |
|-------------|-----|-----|-----|
| Product 4  | R   | Time (min) | Yield\(^a\) (%) | Mp\(^b\) (°C) |
| a           | H   | 5         | 96             | 218           |
| b           | 4-OMe | 5        | 96             | 167           |
| c           | 4-OH  | 5        | 94             | 181           |
| d           | 4-Cl   | 5        | 92             | 208           |
| e           | 4-F    | 5        | 92             | 204           |
| f           | 4-Br   | 5        | 90             | 221           |
| g           | 3-NO\(_2\) | 5        | 95             | 222-225\(^c\) |

\(^a\) Isolated yield.
\(^b\) 4c, 4d, 4e, and 4f were characterized by comparison on TLC and by their melting points with authentic samples prepared by the reported method.\(^9\)
\(^c\) Novel compounds 4g, 4a, and 4b were characterized by \(^1\)H NMR spectral analysis.
conditions. No desired product was obtained, and we decided to carry out the same reaction under solvent-free thermal conditions using catalytic amounts of iodine. When the condensation was done in the presence of iodine, we got the corresponding naphthoxazinones in very good yield. In a typical experiment, β-naphthol, benzaldehyde, and urea were taken in a conical flask, and a catalytic amount of iodine was added. The mixture was heated on a preheated hot plate for 5 min to get 1-phenyl-1,2-dihydro-naphtho[1,2-e][1,3]oxazin-3-one in 96% yield.

We then extended the same procedure to various other araldehydes with electron-withdrawing and electron-releasing groups, and regardless of the substituents, the yields of the products were excellent. Results of these experiments are presented in Table 1.

MECHANISM

We feel that the mechanism of formation of naphthoxazinones is similar to that proposed by Dabiri et al.\textsuperscript{[8]} It is assumed that in the first step of the reaction, there is complexation of I\textsubscript{2} with urea, and the activated urea then reacts with araldehyde to give an imine intermediate (not isolated), which may react with β-naphthol in the subsequent step, followed by cyclization to afford the corresponding naphthoxazinone as shown in Scheme 2.

CONCLUSION

In conclusion, we have successfully synthesized naphthoxazinones by the condensation of β-naphthol, araldehydes, and urea in the presence of catalytic amounts of an environmentally benign catalyst (iodine), avoiding use of any solvent. The methodology reported herein offers a useful alternative to the existing methodologies because of its efficiency and simplicity.
EXPERIMENTAL

All chemicals are commercial products and were used without further purification. The products were characterized by comparison of their physical data with those of authentic samples or by comparison of their $^1$H NMR spectra.

General Procedure for the Synthesis of 1,2-Dihydro-1-aryl-naphtho[1,2-e][1,3] Oxazine-3-ones

β-Naphthol (5 mmol), araldehyde (5 mmol), urea (5 mmol), and I$_2$ (0.25 g, 1 mmol) were taken in a 50-ml flat-bottomed flask, mixed well, and heated on a preheated hot plate at 80 °C for 5 min. The contents were then cooled to room temperature, water was added, and the solid was filtered and washed repeatedly with water to get the corresponding naphthoxazines. An analytical-grade sample was obtained by recrystallization from alcohol or by silica-gel column chromatography using 10% ethyl acetate in light petrol as an eluent.

$^1$H NMR Spectral Data of 4a, 4b, and 4g

1-Phenyl-1,2-dihydro-naphtho[1,2-e][1,3]oxazin-3-one (4a). Mp: 228 °C; $^1$H NMR (300 MHz, DMSO-d$_6$): δ = 6.18 (s, 1H, CH), 7.23–8.29 (m, 11H, Ar-H), 7.78 (d, J = 10.8 Hz, 1H, NH).

1-(4-Methoxy-phenyl)-1,2-dihydro-naphtho[1,2-e][1,3]oxazin-3-one (4b). Mp: 167 °C; $^1$H NMR (400 MHz, DMSO-d$_6$): δ = 6.14 (d, J = 2.8 Hz, 1H, CH), 6.87–7.99 (m, 10H, Ar-H), 8.79 (d, J = 2.8 Hz, 1H, NH).

1-(3-Nitro-phenyl)-1,2-dihydro-naphtho[1,2-e][1,3]oxazin-3-one (4g). Mp: 222–225 °C; $^1$H NMR (400 MHz, DMSO-d$_6$): δ = 6.48 (d, J = 2.8 Hz, 1H, CH), 7.42–8.29 (m, 10H, Ar-H), 9.02 (d, J = 2.8 Hz, 1H, NH).

REFERENCES


