Microwave-induced Selective Alkoxylation of 1,4-Naphthoquinones†

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Mazaahir Kidwai,* Parven Kumar and Seema Kohli

Department of Chemistry, University of Delhi, Delhi-110007, India

A new efficient alkoxylation of 1,4-naphthoquinones at the active quinonoid position is reported using alkanols and an alkenol in the presence of cerium chloride and iodine under microwave irradiation.

Alkoxy-1,4-naphthoquinones occur in nature and some are biologically important.[1,2] Recently 2,3-disubstituted analogues of 1,4-naphthoquinones have shown potent antiplatelet, antiallergic and antiinflammatory activities.[3] Alkoxylation of 1,4-quinones has been reported using alkanols in the presence of metal/metal salts,[4,5] Cu-bronze/I_2,[6] silica gel[6] and Raney Ni.[6] Khanna *et al.*[7] have reported the use of transition metal salts in the presence of iodine for the alkoxylation of 1,4-napthoquinones.

Keeping in mind the current interest in lanthanide salts and the importance of microwaves in organic synthesis, we report $CeCl_3/I_2$ as a new reagent for the selective alkoxylation of 1,4-naphthoquinones at the active quinonoid position. In order to show the general use of the reagent we used substituted 1,4-naphthoquinones as starting materials and different alkanols and an alkenol as alkoxylating agents. All the reactions were carried out with conventional heating as well as microwave irradiation. A comparative study (method A and method B, Table 1) showed that the use of microwaves substantially reduces the reaction time and appreciably increases the yields. All the products (**6–13**) were characterised and compared with authentic samples (TLC, mp and IR).

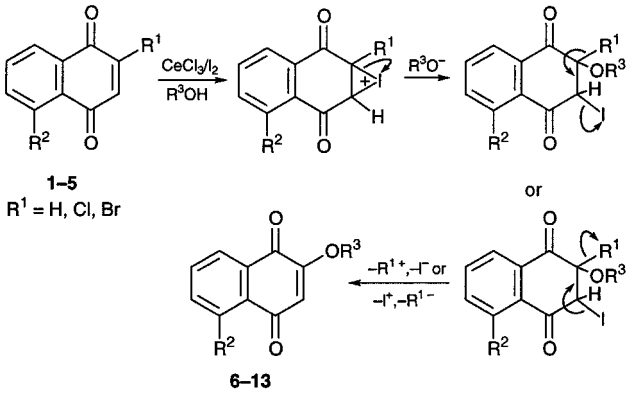

Table 1 Comparison of reaction times and yields obtained using method A and method B

		Reaction time[a] [Yield (%)]				
		Reactant				
Compound	Method	**1**	**2**	**3**	**4**	**5**
6[7]	A	4 [70]	3 [75]	2 [78]	—	—
	B	[82]	[85]	[90]	—	—
7[7]	A	4.5 [68]	4 [70]	3.5 [75]	—	—
	B	[70]	[78]	[83]	—	—
8[6]	A	5.5 [65]	5.5 [62]	5.5 [65]	—	—
	B	[70]	[70]	[78]	—	—
9[7]	A	6 [60]	6 [60]	5.5 [60]	—	—
	B	[65]	[63]	[67]	—	—
10[11]	A	7 [54]	6.5 [57]	6 [58]	—	—
	B	[60]	[60]	[65]	—	—
11[6]	A	7.5 [50]	7 [55]	6.5 [55]	—	—
	B	[57]	[60[]	[60]	—	–
12[12]	A	8 [55]	7 [60]	7 [68]	—	—
	B	[60]	[65]	[75]	—	—
13[7]	A	—	—	—	7.0 [60]	8.0 [57]
	B	—	—	—	[62]	[60]

[a]Reaction time for method A is in hours and all method B reactions were carried out for 5 min.

Alkoxylation of 1,4-naphthoquinones in the presence of $CeCl_3/I_2$ follows an ionic pathway as the reaction is not quenched by the addition of a radical quencher like hydroquinone. Georgoulis *et al.*[8] have showed that the metal salt aids the abstraction of the iodide ion due to the reversible attack of the alkoxy ion on the double bond and no organometallic intermediates are involved during this process. It has also been reported[9–10] that molecular iodine is activated by complexation, with the metal salt facilitating an electrophilic attack on the olefinic double bond. In our case, alkoxylation does not proceed in the absence of either iodine or cerium chloride, implying that the initial step is the electrophilic attack of iodine on the quinonoid double bond to form an iodonium intermediate which is then attacked by the alkoxy anion from the corresponding alkanol to give the alkoxylated 1,4-napthoquinone.

On alkoxylation, 2-chloro-5-hydroxy-1,4-naphthoquinones (**4**) and 5-hydroxy-1,4-naphthoquinones (**5**) both afforded 2-alkoxy-5-hydroxy-1,4-naphthoquinones (**13**) in comparable yields, which indicates that the ease of elimination of H and Cl are almost identical under the above reaction conditions.

Experimental

General Procedure.—Method A (thermal). In a 100 ml conical flask, a mixture of cerium chloride (1.0 mmol), iodine (0.1 mmol) and a solution of 1,4-naphthoquinone (1.0 mmol) in alkanol/alke-

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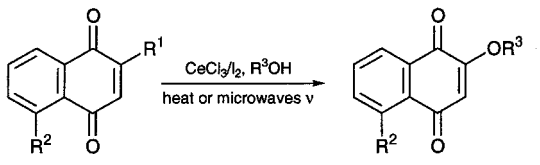

1 R^1 = H, R^2 = H
2 R^1 = Cl, R^2 = H
3 R^1 = Br, R^2 = H
4 R^1 = Cl, R^2 = OH
5 R^1 = H, R^2 = OH

6 R^2 = H, R^3 = Me
7 R^2 = H, R^3 = Et
8 R^2 = H, R^3 = Pr
9 R^2 = H, R^3 = $CH(Me)_2$
10 R^2 = H, R^3 = $CH_2(CH_2)_2Me$
11 R^2 = H, R^3 = $CH_2CH(Me)_2$
12 R^2 = H, R^3 = $CH_2CH{=}CH_2$
13 R^2 = OH, R^3 = Et

nol (50 ml) was stirred for a specified time (Table 1) at 60–70 °C (oil bath). The reaction progress was monitored by TLC. After completion the mixture was filtered and the filtrate was concentrated under reduced pressure. The concentrate was diluted with water (100 ml) and extracted with ethyl acetate (3 × 50 ml). The organic extract was dried (anhydrous Na_2SO_4) and evaporated under reduced pressure to give a solid which was purified by column chromatography to afford the pure alkoxylated product.

Method B (microwave irradiation). In a 100 ml conical flask, a mixture of cerium chloride (1.0 mmol), iodine (0.1 mmol) and a solution of 1,4-napthoquinone (1.0 mmol) in alkanol/alkenol (50 ml) was irradiated in a microwave oven for 5 min at 2450 MHz. The reaction mixture was worked up as described earlier to give alkoxylated products.

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References

1 R. H. Thomson, *Naturally Occurring Quinones*, Academic Press, London, 1971, p. 293.
2 T. R. Sheshadri, *Rev. Pure Appl. Chem*., 1951, **1**, 186.
3 Jin-Cherng Lien, Li-Jiau Huang, Jih-Pyang Wang, Che-Ming Teng, Kuo-Hsiung Lee and Sheng-Chu Kuo, *Chem. Pharm. Bull*., 1996, **44**, 1181.
4 J. N. Ashley, W. K. Anslow and H. Raistrick, *J. Chem. Soc*., 1938, 438.
5 F. Farina and V. Valderrama, *Synthesis*, 1971, 315.
6 P. C. Thapliyal, N. Seth, J. Sharma, S. Kanodia, K. P. Singh and R. N. Khanna, *Indian J. Chem*., 1996, **35B**, 381.
7 R. N. Khanna, K. P. Singh, S. K. Yadav and S. Srinivas, *Synth. Commun*., 1989, **19**, 3151.
8 C. Georgoulis, E. Paillasseur and J. M. Valery, *Synthesis*, 1979, 69.
9 C. Georgoulis and J. M. Valery, *Synthesis*, 1978, 402.
10 O. Akira, U. Sakae and M. Okauo, *Bull. Chem. Soc. Jpn*., 1974, **47**, 2818.
11 L. F. Fieser, *J. Am. Chem. Soc*., 1926, **48**, 2922.
12 L. F. Fieser, *J. Am. Chem. Soc*., 1926, **48**, 3201.