Microwave-induced Monohydroxymethylation and Monoalkoxylation of 1,4-Naphthoquinones†

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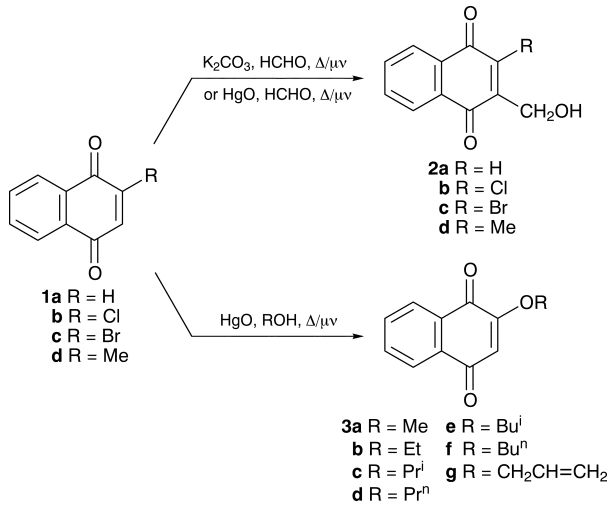
1,4-Naphthoquinones and its derivatives have been hydroxymethylated and alkoxylated in the quinone ring using, respectively, formalin or an alcohol, in the presence of K_2CO_3 or HgO by heating or microwave irradiation.

Several publications have described the use of commercially available microwave ovens for microwave induced organic reaction enhancement (MORE).[1,2] The technique is energy- and cost-efficient as well as convenient to use. The present communication reports the synthesis of hydroxymethylated and alkoxylated 1,4-naphthoquinones using microwave irradiation. It dramatically reduces the reaction time and increases the yield remarkably.



Scheme 1

Potassium carbonate or mercury(II) oxide in aqueous formalin were used for the introduction of hydroxymethyl group under thermal and microwave conditions at the active quinonoid position of 1,4-naphthoquinones **1** to give the 2-hydroxymethyl-1,4-naphthoquinones **2** (Scheme 1). Compounds **2a**–**d** were identified on the basis of their spectral data (Tables 1 and 2).

Mercury(II) oxide in various alcohols (methanol, ethanol, isopropyl alcohol, propanol, isobutyl alcohol, butanol and allyl alcohol) was used for the introduction of alkoxy groups under thermal and microwave conditions at the active quinonoid position of 1,4-naphthoquinones (**1a**–**c**), to give the corresponding alkoxy compounds (**3**) (Scheme 1, Table 3). Compounds (**3a**–**g**) were identified on the basis of spectral data (Table 4).

Table 2 Spectral data of quinones **2a–d**

Quinone	δ_H	ν/cm^{-1}
2a	2.50 (s, broad, 1 H, OH), 4.60 (s, 2 H, CH_2OH), 7.10 (s, 1 H, C_3-H), 7.80–8.10 (m, 4 H, Ar-H)	1620, 1650
2b	2.50 (s, broad, 1 H, OH), 4.60 (s, 2 H, CH_2OH), 7.60–8.20 (m, 4 H, Ar-H)	1625, 1650
2c	2.50 (s, broad, 1 H, OH), 4.60 (s, 2 H, CH_2OH), 7.60–8.10 (m, 4 H, Ar-H)	1625, 1650
2d	2.10 (s, 3 H, CH_3), 2.60 (s, broad, 1 H, OH), 4.70 (s, 2 H, CH_2OH), 7.20–8.00 (m, 4 H, Ar-H)	1625, 1655

Discussion

In the hydroxymethylation of various quinones, it was observed that the presence of the reagent (K_2CO_3 or HgO) was essential and the monohydroxymethylated products were obtained without any polymerization or replacement of halo group in **1b** and **1c** in Scheme 1. The reaction failed to proceed with other aldehydes, *e.g.* acetaldehyde and benzaldehyde. Yields were found to be higher with K_2CO_3 as compared to HgO. In the alkoxylation of various quinones, the presence of reagent (HgO) was also essential and the yield of alkoxy quinones decreased with the increase in the size of the alkyl group in the alcohol. The yield of alkoxy quinones is higher when halogenated quinones are alkoxylated because the halo group is a better leaving group. Microwave irradiation accelerates organic reactions by its high heating efficiency giving rise to a remarkable rate enhancement and a dramatic reduction in reaction times (Tables 1 and 3).

Table 1 Hydroxymethylation of 1,4-naphthoquinones (**1a**–**d**)

		Yield (%)		*t*/min			Found (required) (%)		
Quinone	Reagent	Δ	μν	Δ	μν	Molecular formula	C	H	Lit. mp/°C
2a	K_2CO_3	92	90	30	5	$C_{11}H_8O_3$	70.2 (70.1)	4.25 (4.30)	115[3]
	HgO	90	80	90	6				
2b	K_2CO_3	95	95	30	5	$C_{11}H_7O_3Cl$	59.3 (59.1)	3.1 (3.2)	135[3]
	HgO	90	85	90	5				
2c	K_2CO_3	94	92	30	5	$C_{11}H_7O_3Br$	49.5 (49.6)	2.6 (2.4)	130[3]
	HgO	92	85	90	5				
2d	K_2CO_3	85	82	60	5	$C_{12}H_{10}O_3$	71.2 (71.0)	4.9 (4.7)	106
	HgO	80	78	90	6				

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Experimental

Melting points are uncorrected. IR spectra were recorded on a Shimadzu IR-435 spectrometer (Nujol, cm^{-1}). NMR spectra were recorded on a Perkin-Elmer R-32 (90 MHz) in $CDCl_3$, using TMS as internal standard. Chemical shifts were recorded on the δ scale.

Table 3 Alkoxylation of 1,4-naphthoquinones (**1a**–**c**)

Quinone	Alcohol	Product	Yield (%)		*t*/min		Mp/°C [lit. mp]
			Δ	*μν*	Δ	*μν*	
1a	CH_3OH	**3a**	70	80	120	5	182 [182–183][4]
1b			75	85	60	5	
1c			70	85	60	5	
1a	CH_3CH_2OH	**3b**	65	75	120	5	116 [115–117][4]
1b			80	85	60	5	
1c			82	85	60	5	
1a	$(CH_3)_2CHOH$	**3c**	65	72	180	6	115 [115][4]
1b			75	80	150	6	
1c			80	86	150	6	
1a	$CH_3(CH_2)_2OH$	**3d**	60	72	240	7	90
1b			65	75	180	6	
1c			62	78	210	6	
1a	$(CH_3)_2CHCH_2OH$	**3e**	55	65	240	7	78
1b			65	75	180	7	
1c			60	78	180	7	
1a	$CH_3(CH_2)_3OH$	**3f**	50	65	240	8	104 [104][5]
1b			60	75	180	7	
1c			62	75	180	7	
1a	$CH_2{=}CHCH_2OH$	**3g**	55	62	180	8	99 [98.5][6]
1b			58	70	150	8	
1c			60	72	150	8	

Table 4 Spectral data of quinones **3d**–**e**

Quinone	δ_H	ν/cm^{-1}
3d	1.00 (t, *J* 7.0, 3 H, CH_3), 1.50–2.10 (m, 2 H, CH_2CH_3), 3.80 (t, *J* 7.0, 2 H, OCH_2), 5.90 (s, 1 H, C_3-H), 7.30–7.90 (m, 4 H, Ar-H)	1620, 1680
3e	1.10 (d, *J* 7.0, 6 H, 2 CH_3), 1.90–2.40 (m, 1 H, OCH), 3.60 (d, *J* 7.0, 2 H, OCH_2), 5.90 (s, 1 H, C_3-H), 7.30–7.90 (m, 4 H, Ar-H)	1640, 1680

General Procedure—Method A.—To a solution of the substrate (0.1 mol, **1a**–**d**) in 30% aqueous formaldehyde (20 ml), potassium carbonate (0.1 mol) or yellow mercury(II) oxide (0.1 mol) was added. The solution was refluxed for specified time (Table 1). The reaction mixture was filtered and the filtrate concentrated under reduced pressure, diluted with water (100 ml) and the mixture extracted with ethyl acetate (2 × 20 ml). The organic extract was dried ($MgSO_4$) and evaporated under reduced pressure to give a solid which was purified by preparative TLC (silica gel) using benzene–ethyl acetate (9:1) as a solvent to afford the hydroxymethylated product (**2a**–**d**).

Method B.—To a solution of the substrate (0.1 mol, **1a**–**d**) in 30% aqueous formaldehyde (20 ml), potassium carbonate (0.1 mol) or yellow mercury(II) oxide (0.1 mol) was added. The mixture was subjected to microwave irradiation at 2450 MHz for a specified time (Table 1). The reaction mixture was worked up as described above to afford the hydroxymethylated product (**2a**–**d**).

Method C.—To a solution of the substrate (0.1 mol, **1a**–**c**) in the alcohol (20 ml), yellow mercury(II) (0.1 mol) was added. The solution was refluxed for specified time (Table 3), cooled and filtered. The filtrate was concentrated under reduced pressure, diluted with water (100 ml) and the mixture extracted with ethyl acetate (2 × 20 ml). The organic extract was dried ($MgSO_4$) and evaporated under reduced pressure to give a solid which was purified by preparative TLC using benzene–ethyl acetate (8:2) as a solvent to afford the alkoxylated product (**3a**–**g**).

Method D.—To a solution of the substrate (0.1 mol, **1a**–**c**) in alcohol (5 ml), mercury(II) oxide (0.1 mol) was added. The mixture was subjected to microwave irradiation at 2450 MHz for a specified time (Table 3). The reaction was worked up as described earlier to afford the alkoxylated product (**3a**–**g**).

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