Kinetics and Mechanism of the Reaction of 2,3-Dimethoxy-1,4-naphthoquinone with Alkoxide Ions in Alcoholic Solvents

Vivian M. Flaten, José G. Santos,* and Jaime A. Valderrama
Facultad de Química (502), Pontifica Universidad Católica de Chile, Casilla 6177, Santiago, Chile

The reaction of 2,3-dimethoxy-1,4-naphthoquinone with ethoxide, n-propoxide, n-butoxide, and isopropoxide ion in the respective alcohols as solvents has been subjected to kinetic study. The reaction leads to 2,3-dialkoxy-1,4-naphthoquinones (**2a**—**d**) through 2-alkoxy-3-methoxy-1,4-naphthoquinones (**3a**—**d**) as intermediates. Catalytic behaviour by the alkoxide ions is observed. Rate constants and activation parameters have been measured for the two steps. The nucleophilic rate constants are related to the acidity of the respective alcohols, leading to linear behaviour in log k-$E_T(30)$ plots. Activation parameters of the two steps are discussed in terms of stabilization of reactants and transition states and the differences between the first and second substitution in terms of the effect of the sustituent in the vicinal position.

Nucleophilic substitution reactions are important in the synthesis of quinones since many quinones can be obtained using a suitable nucleophile and a quinone bearing a labile group.[1] Several studies to establish the mechanism of these transformations have been described using halogenoquinones and nitrogenated nucleophiles, showing that the product is obtained through an inner π complex[2,3] or by a radical anion[4] depending on the nature of the amine.

Furthermore, Hewgill,[5] studying substitutions of halogeno- and alkoxy-quinones with alcohols in alkaline solution, detected semiquinone radicals generated during the reaction.

It is interesting that substitution in monohalogenated quinones with methoxy anion as nucleophile occurs on the carbon atom that supports the halogen and/or on the vicinal carbon atom.[5,6]

Because of our interest in quinones[7] we decided to undertake kinetic studies on the addition and nucleophilic substitution reactions of quinones since the mechanism has received little attention. The results could also be used for some regioselective transformations with synthetic applications. We report here the results of a kinetic study of the alcoholysis of 2,3-dimethoxy-1,4-naphthoquinone in alkaline medium. This substrate was selected in order to study only the kinetic characteristics of substitution because the possibilities of geminal or vicinal attack are indistinguishable.

Experimental

H.p.l.c. chromatograms were obtained with a Series 2 Perkin-Elmer apparatus with an analytical silica column and a UV, LC-15 Perkin-Elmer detector using cyclohexane–chloroform (3:1 v/v) as eluant in the isocratic mode; flow rate 1.5 ml min^{-1}; temperature ambient. The m.p. of compound (**3a**) was determined on a Kofler hot-stage microscope apparatus and is uncorrected. I.r. (KBr) spectra were obtained with a Perkin-Elmer model 567 spectrophotometer. ^{1}H N.m.r. ($CDCl_3$) spectra were taken with a Varian XL-100 spectrometer with tetramethylsilane as internal standard. Elemental analyses were performed with a Heraeus CH Mikro-Standard apparatus.

Materials.—2,3-Dimethoxy-1,4-naphthoquinone (**1**) was prepared as described.[8] The solvents (ethanol, n- and iso-propyl alcohol, n-butyl alcohol, and benzene) were Merck analytical reagents.

Ethanol was dried with molecular sieves 3 Å—4 Å (B.D.H.). Benzene and n- and iso-propyl alcohols were dried by reaction with metallic sodium and distilled under N_2, and n-butyl alcohol was dried with K_2CO_3 and distilled under N_2.

Sodium alkoxide solutions were prepared adding the appropriate alcohol (6 ml) through a serum cap, over accurately weighed sodium into dry benzene (4 ml).

Alcoholysis Reaction.—For the preparations of 2,3-dialkoxy-1,4-naphthoquinones (**2a**—**d**), sodium alkoxide (0.3 mmol) in dry benzene–alcohol (3:2 v/v; 0.5 ml) was added (at room temperature through a silicone rubber cap) to a stirred solution of 2,3-dimethoxy-1,4-naphthoquinone (0.15 g, 0.69 mmol) in benzene–alcohol (1:4 v/v; 10 ml). After 2 h the mixture was filtered through silica gel (70—230 mesh), evaporated under reduced pressure, and the residue dissolved in chloroform (2 ml) and purified by column chromatography on 70—230 mesh silica gel with chloroform as eluant. For the preparation of the 2-methoxy-3-alkoxy-1,4-naphthoquinones (**3a**—**d**) sodium alkoxide (0.3 mmol) in dry benzene–alcohol (3:2 v/v; 0.5 ml) was added (through a silicone serum cap) to a stirred solution of 2,3-dimethoxy-1,4-naphthoquinone (**1**) (0.15 g, 0.69 mmol) in dry benzene (10 ml). The reaction was followed by t.l.c. until an appreciable quantity of product was obtained; the reaction was then quenched by rapid filtration through a short column silica gel (70—230 mesh) and the resulting solution was chromatographed on a silica gel column (70—230 mesh) with benzene–chloroform (3:7 v/v) as eluant. As these compounds were obtained as intermediates, yields cannot be reported because they were functions of the reaction time.

2,3-*Diethoxy*-1,4-*naphthoquinone* (**2a**). This was a yellow liquid (88%), $\nu_{max.}$ 1 665 (C=O) and 1 265 (C–O) cm^{-1}; δ_H 1.41 (t, 6 H, *J ca.* 7 Hz), 4.38 (q, 4 H, *J ca.* 6 Hz), 7.84 (m, 2 H, 6- and 7-H), and 7.98 (m, 2 H, 5- and 8-H) (Found: C, 68.6; H, 5.9. Calc. for $C_{14}H_{14}O_4$: C, 68.3; H, 5.7%).

2,3-*Di-n-propoxy*-1,4-*naphthoquinone* (**2b**). This was a yellow liquid (89%), $\nu_{max.}$ 1 660 (C=O) and 1 265 (C–O) cm^{-1}; δ_H 1.12 (t, 6 H, *J ca.* 7 Hz), 1.88 (m, 4 H), 4.33 (t, 4 H, *J ca.* 6 Hz), 7.63 (m, 2 H, 6- and 7-H), and 7.98 (m, 2 H, 5- and 8-H) (Found: C, 69.8; H, 6.8. Calc. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.6%).

2,3-*Di-n-butoxy*-1,4-*naphthoquinone* (**2c**). This was a yellow liquid (90%), $\nu_{max.}$ 1 660 (C=O) and 1 265 (C–O) cm^{-1}; δ_H 1.02 (t, 6 H, *J ca.* 7 Hz), 1.24—2.05 (m, 8 H), 4.36 (t, 4 H, *J ca.* 6 Hz), 7.84 (m, 2 H, 6- and 7-H), and 8.09 (m, 2 H, 5- and 8-H) (Found: C, 71.75; H, 7.0. Calc. for $C_{18}H_{22}O_4$: C, 71.5; H, 7.3%).

2,3-*Di-isopropoxy*-1,4-*naphthoquinone* (**2d**). This was a yellow liquid (87%), $\nu_{max.}$ 1 660 (C=O) and 1 265 (C–O) cm^{-1}; δ_H 1.36 (d, 12 H, *J ca.* 6 Hz), 4.96 (m, 2 H), 7.7 (m, 2 H, 6- and 7-H), and

Table 1. Experimental conditions and second-order rate constants k_{app_1} and k_{app_2} for the reactions studied

Temperature (°C)	10^4[AlkONa]/M	$10^3k_{obs_1}$/s^{-1}	$10^4k_{obs_2}$/s^{-1}	k_{app_1}/l mol^{-1} s^{-1}	k_{app_2}/l mol^{-1} s^{-1}
(a) Sodium ethoxide in ethanol					
9.4	6.9—34.6	0.49—4.32	0.8—9.63	1.39 ± 0.02	0.32 ± 0.02
14.4	27.7—48.4	5.25—9.79	12.8—24.3	2.19 ± 0.02	0.55 ± 0.05
19.4	20.7—41.5	5.78—12.6	14.4—31.6	3.3 ± 0.1	0.84 ± 0.03
24.3	13.8—27.6	5.50—12.7	14.7—32.0	5.22 ± 0.09	1.27 ± 0.07
(b) Sodium n-propoxide in n-propyl alcohol					
5.0	23.2—46.4	6.38—14.3	9.67—21.0	3.4 ± 0.5	0.5 ± 0.1
10.1	15.5—38.6	6.18—17.3	9.10—25.7	4.8 ± 0.1	0.7 ± 0.1
15.3	15.5—38.6	7.90—23.1	13.1—37.3	6.6 ± 0.1	1.05 ± 0.01
20.3	15.5—38.6	8.90—28.9	14.5—48.1	8.6 ± 0.2	1.42 ± 0.07
(c) Sodium n-butoxide in n-butyl alcohol					
4.3	17.3—43.2	6.96—19.0	10.0—27.5	4.46 ± 0.03	0.67 ± 0.01
9.3	17.3—34.6	10.05—21.3	14.2—30.7	6.52 ± 0.07	0.97 ± 0.05
14.3	17.3—31.1	12.5—24.1	20.3—39.2	8.4 ± 0.3	1.34 ± 0.05
20.1	8.6—34.6	8.12—36.0	11.8—59.2	10.9 ± 0.2	1.84 ± 0.07
(d) Sodium isopropoxide in isopropyl alcohol					
1.1	7.8—12.0	10.4—20.6	7.1—14.4	24.3 ± 0.1	1.74 ± 0.01
5.1	7.2—12.0	13.3—26.7	10.2—21.0	28.2 ± 0.9	2.28 ± 0.07
9.2	6.0—12.0	15.0—35.0	11.2—27.2	33 ± 1	2.69 ± 0.05
13.1	7.2—9.6	20.0—29.7	15.0—23.1	40.3 ± 0.5	3.4 ± 0.9

8.01 (m, 2 H, 5- and 8-H) (Found: C, 69.9; H, 6.6. Calc. for $C_{16}H_{18}O_4$: C, 70.05; H, 6.6%).

2-Methoxy-3-ethoxy-1,4-naphthoquinone (**3a**). This formed yellow needles, m.p. 60—61 °C; $\nu_{max.}$ 1 660 (C=O) and 1 260 (C–O) cm^{-1}; δ_H 1.45 (t, 3 H, *J ca.* 7 Hz), 4.2 (s, 3 H), 4.41 (q, 2 H, *J ca.* 7 Hz), 7.74 (m, 2 H, 6- and 7-H), and 8.12 (m, 2 H, 5- and 8-H) (Found: C, 67.4; H, 5.0. Calc. for $C_{13}H_{12}O_4$: C, 67.2; H, 5.2%).

2-Methoxy-3-n-propoxy-1,4-naphthoquinone (**3b**). This was a yellow liquid, $\nu_{max.}$ 1 655 (C=O) and 1 260 (C–O) cm^{-1}; δ_H 1.07 (t, 3 H, *J ca.* 7 Hz), 1.88 (m, 2 H), 4.17 (s, 3 H), 4.32 (t, 2 H, *J ca.* 6 Hz), 7.79 (m, 2 H, 6- and 7-H), and 8.16 (m, 2 H, 5- and 8-H) (Found: C, 68.1; H, 5.7. Calc. for $C_{14}H_{14}O_4$: C, 68.3; H, 5.7%).

2-Methoxy-3-n-butoxy-1,4-naphthoquinone (**3c**). This was a yellow liquid, $\nu_{max.}$ 1 655 (C=O) and 1 260 (C–O), δ_H 0.99 (t, 3 H, *J ca.* 7 Hz), 1.37—1.92 (m, 4 H), 4.17 (s, 3 H), 4.35 (t, 2 H, *J ca.* 6 Hz), 7.73 (m, 2 H, 6- and 7-H), and 8.10 (m, 2 H, 5- and 8-H) (Found: C, 69.15; H, 6.1. Calc. for $C_{15}H_{16}O_4$: C, 69.2; H, 6.2%).

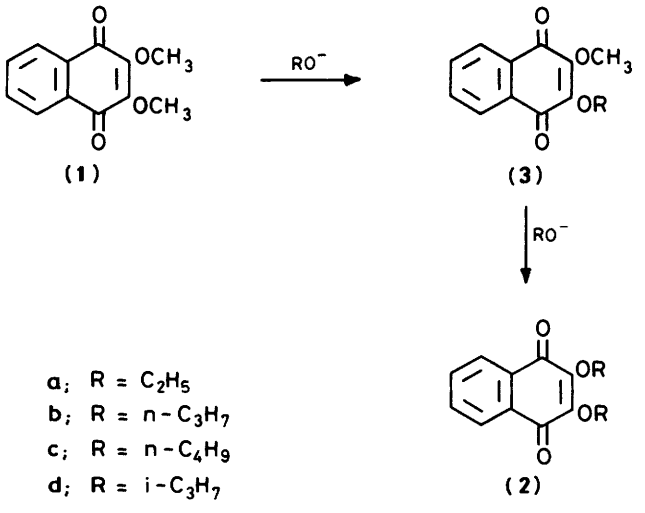
2-Methoxy-3-isopropoxy-1,4-naphthoquinone (**3d**). This was a yellow liquid, $\nu_{max.}$ 1 660 (C=O) and 1 270 (C–O) cm^{-1}; δ_H 1.42 (d, 6 H, *J ca.* 7 Hz), 4.16 (s, 3 H), 4.91 (m, 1 H), 7.72 (m, 2 H, 6- and 7-H), and 8.05 (m, 2 H, 5- and 8-H) (Found: C, 68.1; H, 5.65. Calc. for $C_{14}H_{14}O_4$: C, 68.3; H, 5.7%).

Kinetic Measurements.—In a water-jacketed flask (3 ml) was placed a solution of 2,3-dimethoxy-1,4-naphthoquinone (**1**) (1.16 × 10^{-2}M) in benzene–alcohol (1:9 v/v; 2 ml). After allowing *ca.* 10 min for the temperature to equilibrate, reaction was initiated by adding a portion (5—35 μl) of the appropriate sodium alkoxide solution prepared as above (the concentration ranges of sodium alkoxide are in Table 1). After appropriate times, samples (*ca.* 50 μl) were withdrawn through a silicone serum cap and quenched by addition to an alcoholic acetic acid solution.

The reactions were followed by h.p.l.c., from the height of the signal for (**1**) (h_1) and for (**3a, d**) (h_3) relative to that of benzene used as internal standard (h_b). Plots of $\ln(h_1/h_b)$ against time were linear for at least four half-lives. The slopes of these plots are the pseudo-first-order rate constants (k_{obs_1}). When (**1**) was practically consumed plots of $\ln(h_3/h_b)$ against time were linear with slopes k_{obs_2}. To check the accuracy of k_{obs_1} and k_{obs_2} a simulation of the concentration of (**3a, d**) was made using solutions in the corresponding benzene–alcohol solution as standard. The second-order rate constants k_{app_1} and k_{app_2} were determined from plots of k_{obs} against [alkoxide ion]. The activation parameters were obtained from Eyring plots.

Results and Discussion

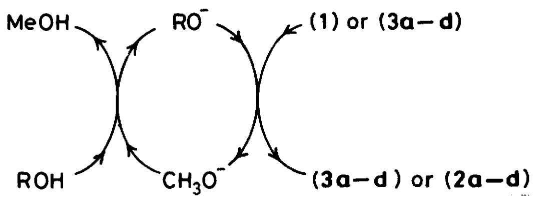
Preliminary examination, by h.p.l.c. and t.l.c. of mixtures of 2,3-dimethoxy-1,4-naphthoquinone (**1**) with alkoxide (ethoxide, n-propoxide, n-butoxide, and isopropoxide) ions in the corresponding alcohol, showed the rapid formation of 2,3-dialkoxy-1,4-naphthoquinones (**2a**—**d**). When the reactions were carried out in benzene–alcohol the presence of 2-alkoxy-3-methoxy-1,4-naphthoquinones (**3a**—**d**) as intermediates was observed (Scheme 1). In alcohol solution (without benzene) the reactions



Scheme 1.

are fast and the intermediates cannot be observed. Alcoholyses like these were described by Hewgill and Mullings for methoxyquinone systems.[5]

Although these reactions do not occur in the absence of alkoxide ions, they go completely to (**2a**—**d**) in alcohol solutions even for a stoicheiometric deficit of alkoxide ion. This suggests that methoxide ion formed as product in the alcoholyses reacts with the alcohol in the media producing methanol and regenerating the alkoxide ion which continues the reaction. When the reactions were carried out in benzene with alkoxide ion, in stoicheiometric deficit of alcohol, mixtures of quinones (**1**)—(**3**) were obtained. On the other hand, when methoxide ion was added to a solution of (**1**) in isopropyl alcohol, only (**2d**) was obtained suggesting the catalytic behaviour shown in Scheme 2.



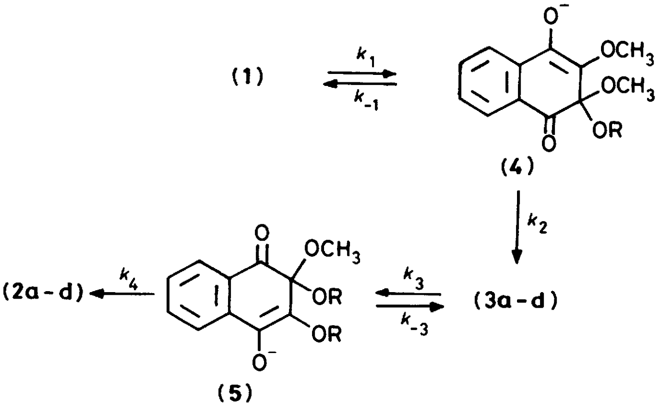
Scheme 2.

For the conditions in Scheme 2 it is clear that it is difficult to obtain quinones (**3a**—**d**) because (i) the yield of these products depends on the number of cycles (or the time of reaction), (ii) these products are probably accompanied by (**1**) and/or (**2a**—**d**), and (iii) the rate constants for the two substitutions are not very different (Table 1). Table 1 shows the rate constant for the substitution of one methoxy group in (**1**) (k_{obs_1}) and in the corresponding quinone (**3a**—**d**) (k_{obs_2}) at several temperatures. With these values we can determine the maximum concentration of (**3a**—**d**) from the time for this maximum ($t_{\text{max.}}$) at each temperature for each alkoxide ion using equation (1) and applying the equations for consecutive reactions.[9] The result depends on each alkoxide ion and is *ca.* 63% for ethoxide and 81% for isopropoxide ion.

$$t_{\text{max.}} = (k_{\text{obs}_1} - k_{\text{obs}_2})^{-1} \ln(k_{\text{obs}_1}/k_{\text{obs}_2}) \qquad (1)$$

Plots of k_{obs_1} and k_{obs_2} against alkoxide ion concentration were straight lines showing first-order dependence on [RO⁻]. The apparent second-order rate constants k_{app_1} and k_{app_2} obtained from the slopes are also summarized in Table 1.

A possible mechanism for the reactions under study is shown in Scheme 3. Assuming the steady-state condition for the intermediates (**4a**—**d**) and (**5a**—**d**) the observed and the apparent rate constants are expressed by equation (2).



Scheme 3.

$$\begin{aligned} k_{\text{obs}_1} &= k_1k_2(k_{-1} + k_2)^{-1}[\text{RO}^-]; \\ k_{\text{obs}_2} &= k_3k_4(k_{-3} + k_4)^{-1}[\text{RO}^-] \\ k_{\text{app}_1} &= k_1k_2(k_{-1} + k_2)^{-1}; k_{\text{app}_2} = k_3k_4(k_{-3} + k_4)^{-1} \end{aligned} \qquad (2)$$

It is known, at least for nucleophilic displacement of the alkoxy group in substituted alkyl phenyl ethers, that alkoxy groups are poor nucleofuges and the reactions do not occur in a single step, usually the breakdown of the intermediate being the rate-determinging step.[10,11] In our case intermediates (**4**) and (**5**) go to product or return to reactants when an alkoxy group leaves and there is no rate-determining step.

In the hydrolysis of alkyl di-isopropyl- and alkyl di-t-butylmaleates[12] it was found that the rate is indeed highly sensitive to the basicity of the leaving group and the rate-determining step is the breakdown of the tetrahedral intermediate with alkoxide ion as the leaving group. A plot of log k_{hy} against pK_a for alkoxy leaving groups was a straight line with slope −1.43 in good agreement with the −1.4 value suggested by Jencks and Gilchrist[13] for elimination of alkoxy groups, showing that intramolecular catalysis in the maleate case is not important for the relative elimination rate of alkoxy groups.[12] Therefore, we expect that equation (3) can be used to estimate the relative values of k_{-1}/k_2 and k_{-3}/k_4 for the reactions studied. In equation (3) the subindices M and A correspond to methanol and another alcohol, respectively, and the k values are the reaction rate constants for alkoxy group elimination from the tetrahedral intermediates.

$$\log(k_M/k_A) = -1.43(\text{p}K_M - \text{p}K_A) \qquad (3)$$

Equation (3) was derived from a reaction in water solution and our study is in alcoholic medium. Obviously the acidities are different in these media. In this respect, it is noteworthy that if the alcohols are considered as substituted methanol, the log K_a values in water can be correlated with the σ* values of the

Table 2. Nucleophilic rate constants determined from the k_{app} values (Table 1) and equation (3)[a]

Alkoxide–alcohol	pK_a	$E_T(30)$[e]	T/°C	k_1/l mol⁻¹ s⁻¹	k_3/l mol⁻¹ s⁻¹
Ethoxide–ethanol	15.9[b]	51.9	9.4	2.17	0.50
			10.0	2.29[f]	0.55[f]
			14.4	3.43	0.86
			19.4	5.16	1.31
			24.3	8.17	1.99
n-Propoxide–n-propyl alcohol	16.1[c]	50.7	5.0	4.84	0.70
			10.0	6.74[f]	1.01[f]
			10.1	6.84	1.01
			15.3	9.40	1.50
			20.3	12.3	2.02
n-Butoxide–n-butyl alcohol	16.1[c]	50.2	4.3	6.35	0.95
			9.3	9.28	1.38
			10.0	9.20[f]	1.42[f]
			14.3	11.8	1.91
			20.1	15.5	2.62
Isopropoxide–isopropyl alcohol	16.57[d]	48.6	1.1	29.6	2.12
			5.1	34.3	2.77
			9.2	40.1	3.27
			10.0	42.5[f]	3.51[f]
			13.1	49.0	4.14

[a] For methanol pK_a 15.5 from ref. 15. [b] From ref. 15. [c] From ref. 18. [d] From ref. 14. [e] From ref. 19. [f] Interpolated from Eyring plots.

Table 3. Activation parameters[a] for the reaction of (**1**) and (**3a**—**d**) with alkoxide bases in the corresponding alcohols

Substrate	Alkoxide	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J K^{-1} mol^{-1}
(**1**)	Ethoxide	59 ± 1	$-28 \pm 4\ (-34 \pm 4)^b$
(**1**)	n-Propoxide	39 ± 1	$-91 \pm 4\ (-97 \pm 4)^b$
(**1**)	n-Butoxide	35 ± 3	$-100 \pm 10\ (-107 \pm 10)^b$
(**1**)	Isopropoxide	25 ± 2	$-126 \pm 6\ (-132 \pm 6)^b$
(**3a**)	Ethoxide	62 ± 2	-31 ± 8
(**3b**)	n-Propoxide	45 ± 1	-85 ± 4
(**3c**)	n-Butoxide	41 ± 2	-96 ± 6
(**3d**)	Isopropoxide	33 ± 2	-117 ± 8

[a] Errors are standard errors. [b] This value results from the Eyring plot by dividing k_1 by a factor of 2.

substituents, showing ρ^* values of 1.316[14] and 1.42[15] in very good agreement with ρ^* 1.36 obtained by Taft[16] in the treatment of the dissociation constants of alcohols in isopropyl alcohol obtained by Hine and Hine.[17] These results suggest that the ΔpK_a values remains constant when the medium is changed. Although the pK_a (in water) against $\log K_a$ (in isopropyl alcohol) plot of Murto[18] does not produce a straight line it must be emphasized that if the plot is drawn with methanol, ethanol, and isopropyl alcohol a straight line is obtained showing that in our series equation (3) can be used for our purpose. Assuming that the ΔpK_a values do not change significantly we can calculate the nucleophilic constants k_1 and k_3 with the aid of equations (3) and (2). These are shown in Table 2.

For any of the reactions studied the $2k_3/k_1$ value * is the effect on the substitution of a methoxy by an alkoxy group when there is a methoxy or alkoxy group in the vicinal position. In each case the solvent and nucleophile are the same and the effect can be attributed fundamentally to the substituent effect in the vicinal position. The relative values obtained at 10 °C show the following sequence: $\mathrm{Pr^iO^-} > \mathrm{Bu^nO^-} > \mathrm{Pr^nO^-} > \mathrm{EtO^-}$. This effect is probably due to the fact in the quinone that the substituents are localized one above and the other below the quinone ring in order to diminish electrical and steric hindrance. Therefore, the alkoxide ion must attack at the side opposite to the group being substituted and in the case of the second alcoholysis reaction, this is the side occupied by the more bulky group. In this respect, we must not disregard the possible inductive effect of the groups because the greater the inductive effect of the substituent the less electrophilic is the C-3 position and the lower is the reaction rate.

Table 3 summarizes the activation parameters for the reactions studied (for comparative purposes the values of k_1 of Table 2 have been corrected statistically by dividing them by two). The negative values found for $\Delta S^{\ddagger}$ can be explained by the bimolecular character of the reaction but also by the different solvation of reactants and transition states; in fact, the sequence (Table 3) shows greater changes for reaction with the larger alkoxide ions. The shorter-chain alcohols are more solvated, resulting in less entropy for the initial state. On the other hand, if the transition state is polar (as expected) it would diminish its entropy by solvation, but due to its relatively greater size its solvation would be similar in the different solvents reducing its entropy proportionally less than in the initial state. For these reasons it is possible to expect greater changes in entropy for the reaction with the larger alkoxide ions (*i.e.* more basic), as observed experimentally. The comparison between n-propoxide and isopropoxide ions leads us to the same conclusion.

Table 3 shows that for both substitutions $\Delta H^{\ddagger}$ decreases with the increase of basicity of the alkoxide ion. This fact can be related to the greater stabilization (relative to the transition state) by solvation of the less basic alkoxide ion (also of smaller size) by its corresponding alcohol. On the other hand, the differences in stabilization of quinones and transition states may be similar in the four solvents, and all the differences may be attributed to solvation of the alkoxide ion by the corresponding alcohol.

From a comparison of the $\Delta H^{\ddagger}$ values for the substitution of the first and second methoxy group by the same alkoxide ion, differences of 2—8 kJ mol^{-1} can be observed, small but greater than experimental error. Given that we have the alkoxide ion in the corresponding alcohol and that we cannot suppose significant differences in the stabilization of (**1**) and (**3a**—**d**), it is probable that these differences are due to the higher energy of the transition state for the k_3 step (due to steric hindrance) relative to that for the k_1 step. The establishment of a similar comparison between the $\Delta S^{\ddagger}$ values is complicated because of the relatively greater experimental error, but the similarity in $\Delta S^{\ddagger}$ values for the two substitutions in each case probably indicates that the $\Delta S^{\ddagger}$ values are mainly due to the solvation of alkoxide ions.

We observe that the $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ terms operate in different directions in $\Delta G^{\ddagger}$. Indeed, for an increase in basicity $\Delta G^{\ddagger}$ is decreased by $\Delta H^{\ddagger}$ contribution but increased by $\Delta S^{\ddagger}$. The values for $\Delta G^{\ddagger}$ show that the more basic alkoxide ions are the more reactive and in consequence the enthalpy effect is more important. Because of the relative errors in $\Delta G^{\ddagger}$ it is preferable to analyse the variation in k_1 values calculated at 10 °C; in this case we observe a clear increase as the basicity increases: $\mathrm{EtO^-} < \mathrm{Pr^nO^-} < \mathrm{Bu^nO^-} < \mathrm{Pr^iO^-}$. Although, as discussed for the substitution of the second methoxy group, there is an effect by the vicinal substituent (different in each case) the k_3 values calculated at 10 °C show the same sequence as the k_1 values. The sequence is $\mathrm{EtO^-}:\mathrm{Pr^nO^-}:\mathrm{Bu^nO^-}:\mathrm{Pr^iO^-}$ 1:3:4:20 for the first substitution and 1:2:3:7 for the second. In the first sequence (k_1) the effect is principally due to the polarity of the alkoxy group and its stabilization but in the second sequence we also must take into account steric hindrance in the substrate and, therefore, the increase in reactivity of $\mathrm{Pr^iO^-}$ due to its lowest stabilization by solvation is diminished by steric hindrance in (**3d**).

In relation to the acidity of the alcohols, in Table 2 it can be observed that k_1 and k_3 increase as the $E_T(30)$ values of the alcohols decrease (at 10 °C). Plots of $\ln k_1$ and $\ln k_3$ against $E_T(30)$ are linear, $\ln k_1 = (46.5 \pm 1.6) - (0.88 \pm 0.03)E_T(30)$ (R^2 0.998) and $\ln k_3 = (28.7 \pm 0.8) - (0.57 \pm 0.01)E_T(30)$ (R^2 0.998), showing that the acidity of the solvents stabilizes the reactants (*i.e.* alkoxide ions) more than respective transition states, in accord with the proposed mechanism.

In consequence, from our results we can conclude that an ionic mechanism is the most likely for the reactions studied, and that the most important effects found can be attributed to the solvation and basicity of alkoxide ion and also to the acidity of the alcohols used as solvent.

Acknowledgements

Financial support by the Dirección de Investigación de la Pontificia Universidad Católica de Chile (DIUC) is gratefully acknowledged.

References

1 K. T. Finley, 'The Chemistry of Quinonoid Compounds,' ed. S. Patai, Wiley, 1974, Part 2, ch. 17.
2 B. K. Das and B. Majee, *J. Indian Chem. Soc.*, 1968, **45**, 1054.

---

* A factor of 2 is included because of the statistical correction for k_1 for the two equivalent positions in (**1**).

3 T. Nagami, K. Yoshihara, H. Hosoya, and S. Nagakura, *J. Phys. Chem.*, 1969, **73**, 2670.
4 T. Yamaoka and S. Nagakura, *Bull. Chem. Soc. Jpn.*, 1971, **44**, 2971.
5 F. R. Hewgill and L. R. Mullings, *J. Chem. Soc. B*, 1969, 1155.
6 D. W. Cameron, P. J. Chalmers, and G. I. Feutrill, *Tetrahedron Lett.*, 1984, **25**, 6031.
7 R. Cassis, M. Scholz, R. Tapia, and J. A. Valderrama, *Tetrahedron Lett.*, 1985, **26**, 6281 and references cited therein.
8 L. F. Fieser and R. H. Brown, *J. Am. Chem. Soc.*, 1949, **71**, 3609.
9 A. A. Frost and R. G. Pearson, 'Kinetics and Mechanism,' Wiley New York, 1961, 2nd edn.
10 J. F. Bunnett and C. F. Bernasconi, *J. Am. Chem. Soc.*, 1965, **87**, 5209.
11 C. F. Bernasconi, *J. Org. Chem.*, 1967, **32**, 2947.
12 M. F. Aldersley, A. J. Kirby, and P. W. Lancaster, *J. Chem. Soc., Perkin Trans. 2*, 1974, 1504.
13 W. P. Jencks and M. Gilchrist, *J. Am. Chem. Soc.*, 1968, **90**, 2622.
14 S. Takahashi, L. A. Cohen, H. K. Miller, and E. G. Peake, *J. Org. Chem.*, 1971, **36**, 1205.
15 P. Ballinger and F. A. Long, *J. Am. Chem. Soc.*, 1960, **82**, 795.
16 R. W. Taft, Jr., *J. Am. Chem. Soc.*, 1953, **75**, 4231.
17 J. Hine and M. Hine, *J. Am. Chem. Soc.*, 1952, **74**, 5266.
18 J. Murto, *Acta Chem. Scand.*, 1964, **18**, 1043.
19 C. Reichardt, *Angew. Chem., Int. Ed. Engl.*, 1979, **18**, 98.

Received 3rd *February* 1987; *Paper* 7/184