Marked Normal Salt Effects on the Stereoselectivity of the Ring Opening of an Aryloxirane in Acid Media

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The salt effect on the stereoselectivity of the ring opening of 1-phenyl- (**1a**) and 1-(*m*-chlorophenyl)cyclohexene oxide (**1b**) in acid media has been examined. The syn stereoselectivity of the reactions increases markedly with increasing amounts of added salt. The salt parameters b_c and b_t for the two parallel reactions leading to the cis and to the trans adduct have been calculated. The results show in all cases positive values both for b_c and for b_t, b_c being always much higher than the corresponding b_t. The b_c values are strongly dependent on the solvent, but they appear to be independent of the substituent on the phenyl group of 1. The relatively large b_c and the corresponding small b_t parameters observed are in accordance with the previously proposed mechanistic scheme.

A detailed knowledge of the mechanisms of the ring opening of aryloxiranes can be of some importance[1] in understanding the chemical behavior of K-region arene oxides,[2] which have been often proposed as the reactive metabolic intermediates responsible for the carcinogenic and mutagenic activity shown by some polycyclic arenes.[3]

Previous work carried out in these laboratories[4-6] has shown that the stereoselectivity observed in the ring opening of aryloxiranes depends to a large extent on several factors, such as the structure, configuration, and conformation of the epoxides, the nature of the aryl group, the solvent, the acid catalyst, the temperature, etc.,[4-6] with the reaction stereochemistry ranging from complete retention to complete inversion of configuration. The results obtained were rationalized through mechanisms[4-6] involving species with a high degree of positive charge on the benzylic carbon. A recent reformulation of these mechanisms[7] (schematized for 1-arylcyclohexene oxides (**1**), see Scheme I) has been proposed, which can be strictly related to the "ion–dipole pair" mechanisms,[8] a close analogue of the classical Winstein ion pair formulation of nucleophilic substitutions and eliminations.[9a,10,11] According to this interpretation the trans products (**5, 7**) arise by attack of a nucleophile (ROH) on the back side[9a,11] of an intramolecular intimate ion–dipole pair **3**, originating from the protonated oxirane (**2**), in which there is "an extended benzylic C–O bond with considerable ionic character".[12] The cis adducts (**6, 8**), on the other hand, can be formed by the collapse of a solvent-separated ion–dipole pair **4**. This collapse should take place with retention of configuration.[12,13]

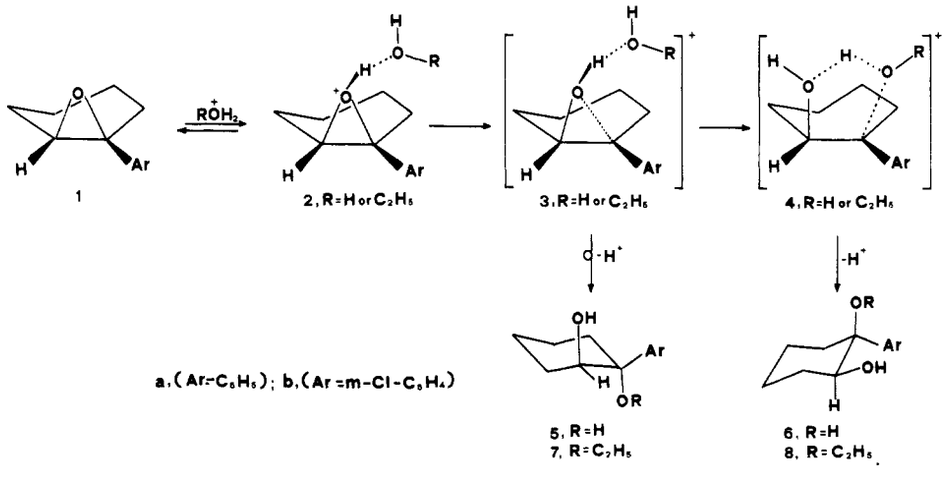
In such a mechanistic scheme, any factor which increases the stability of the benzylic carbocationic center should significantly favor intermediate **4**, and thus increase the syn/anti ratio.[4-7] The addition of inert salts produces a rate acceleration and this result has been quantitatively explained on the basis of an increase in polarity of the medium;[9,14] the addition of a salt should stabilize ionic transition states more than the reactants, and therefore result in an increase of the rate constant.[9,14] Several semiquantitative interpretations of such salt effects have been given,[9,15] but most of the theoretical treatments predict a linear relationship between log k and the concentration of the uni-univalent added salt.[9] This relation has been, however, inadequately tested[9,16] and the dependence of the rate constant on the salt concentration [S] can be better described by the empirical relationship:[9,16]

$$k = k^0(1 + b[S]) \quad (1)$$

where k and k^0 are the rate constants in the presence and absence of salt, and b is the salt parameter representing the magnitude of the normal salt effect. The b value varies with the nature and the polarity of solvent, substrate, added salt, and temperature.[9,16] Deviations from linearity occur at relatively high concentration of salt when the observed rates increase more rapidly than predicted.[9,16] In some cases, however, the addition of small amounts of salt can induce an initial sharp acceleration followed by a normal linear acceleration (special salt effect).[9]

The present paper deals with the study of the salt effect on the course and stereoselectivity of the acid-catalyzed ring opening of aryloxiranes **1a** and **1b**. As a text of our mechanistic hypothesis it would be of significance to determine the salt parameters b_c and b_t for the two parallel reactions leading to the cis (**6, 8**) and the trans compounds (**5, 7**) from the epoxides **1**. This information can be obtained from a determination of

Scheme I



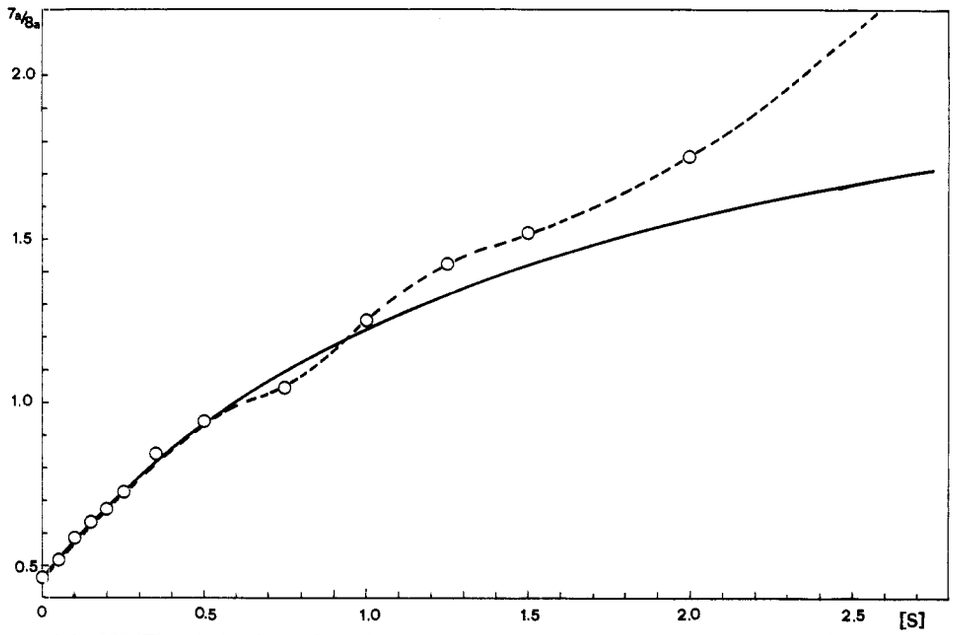


Figure 1. Dependence of the [C]/[T] ratio for the acid-catalyzed ethanolysis of **1a** on the salt concentration [S]. Experimental points and curve (O, broken line); curve calculated on the basis of eq 3 (solid line).

Table I. $LiClO_4$ Salt Effects upon the Acid-Catalyzed Solvolysis of Epoxides 1

	1a in EtOH			**1b** in EtOH		**1a** in H_2O		**1b** in CH_3COOH	
$[LiClO_4]$	**8a**	**7a**	Carbonyl products, %[a]	**8b**	**7b**	**6a**	**5a**	**6b**	**5b**[b]
0	31.6	68.4	4.1	10.3	89.7	62.6	37.4	64.0	36.0
0.05	34.2	65.8	5.6	11.7	88.3	63.7	36.3	72.2	27.8
0.10	37.1	62.9	5.7	12.5	87.5	64.0	36.0	77.9	22.1
0.15	38.7	61.3	7.0	13.5	86.5	65.2	34.8	82.1	17.9
0.20	40.3	59.7	7.7	14.0	86.0	66.0	34.0	84.9	15.1
0.25	42.1	57.9	5.9	14.9	85.1	66.0	34.0	87.4	12.6
0.35	45.8	54.2	7.7	16.9	83.1	67.5	32.5	88.0	12.0
0.50	48.5	51.5	6.7	18.4	81.6	69.7	30.3	90.8	9.2
0.75	51.2	48.8	6.9	20.3	79.7	71.3	28.7	92.4	7.6
1.00	55.6	44.4	9.1						
1.25	58.7	41.3	7.4						
1.50	60.3	39.7	13.9						
2.00	63.7	36.3	15.3						
3.00	73.5	26.5	27.0						

[a] 2-Phenylcyclohexanone and 1-phenylcyclopentane-1-carboxaldehyde in a ratio of about 9:1; yields are expressed in moles. [b] After saponification of the monoacetates.

Table II. Correlation Coefficients r for Equation 4 and Salt Parameters b_c and b_t for Acid-Catalyzed Solvolysis of Epoxides 1

	1a in EtOH	**1b** in EtOH	**1a** in H_2O	**1b** in CH_3COOH
b_c	3.29	3.27	1.32	12.57
b_t	0.62	0.72	0.49	0.63
r	0.9968	0.9924	0.9819	0.9886

the ratios of these products in the reaction mixtures. Thus, division of eq 1 for the cis products (subscript c) by the corresponding equation for the trans products (subscript t) affords eq 2. Furthermore, k_c/k_t can be equated to the concentration ratios [C]/[T] on the very likely assumption that the two parallel reactions follow the same kinetic equation,[5,6,17] yielding eq 3. Equation 3 can be further transformed into a linear relationship (eq 4) with respect to 1/[S], which allows one to obtain the $1/(b_c - b_t)$ and the $b_t/(b_c - b_t)$ values, and from these the parameters b_c and b_t.

$$\frac{k_c}{k_t} = \frac{k_c^0}{k_t^0}\left\{1 + \frac{(b_c - b_t)[S]}{1 + b_t[S]}\right\} \quad (2)$$

$$\frac{[C]}{[T]} = \frac{[C^0]}{[T^0]}\left\{1 + \frac{(b_c - b_t)[S]}{1 + b_t[S]}\right\} \quad (3)$$

$$\frac{1}{([C][T^0]/[T][C^0]) - 1} = \frac{1}{(b_c - b_t)}\frac{1}{[S]} + \frac{b_t}{b_c - b_t} \quad (4)$$

The effect of lithium perchlorate on the acid-catalyzed ethanolysis of epoxide **1a** was investigated over a wide range of salt concentrations (up to 3 M) (see Figure 1). In all cases the reaction yielded exclusively mixtures of the two hydroxy ethers *cis*-**8a** and *trans*-**7a**[17] together with minor amounts of carbonylic products (2-phenylcyclohexanone and 1-phenylcyclopentane-1-carboxaldehyde).[17] The syn stereoselectivity of the reaction rises on increasing the amount of salt added, whereas the increase in rearrangement products becomes marked only at very high salt concentration (see Table I). The [C]/[T] variation could be described nicely by equations of type 3, but at salt concentration higher than 0.75 M the ratios observed increase much more rapidly than predicted. Strong

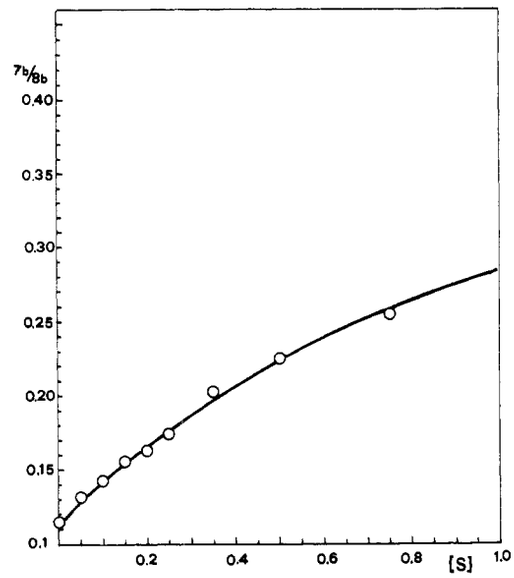


Figure 2. Dependence of the [C]/[T] ratio for the acid-catalyzed ethanolysis of **1b** on the salt concentration [S]. Experimental points (O); curve calculated on the basis of eq 3 (solid line).

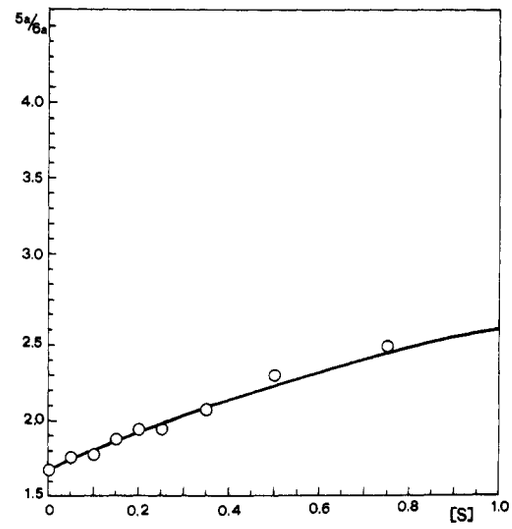


Figure 3. Dependence of the [C]/[T] ratio for the acid-catalyzed hydrolysis of **1a** on the salt concentration [S]. Experimental points (O); curve calculated on the basis of eq 3 (solid line).

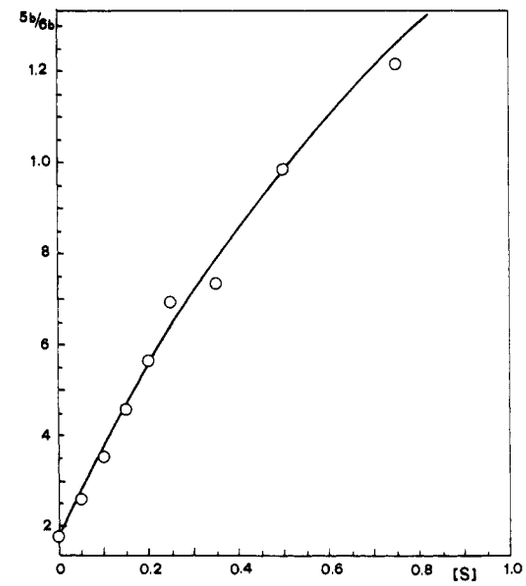


Figure 4. Dependence of the [C]/[T] ratio for the acetolysis of **1b** on the salt concentration [S]. Experimental points (O); curve calculated on the basis of eq 3 (solid line).

deviations from the linear relationship (eq 1) have been previously observed for high salt concentrations.[16a] By making use of eq 4 a fairly good linear correlation is obtained between $1/([C][T^0]/[T][C^0] - 1)$ and $1/[S]$ for lithium perchlorate concentrations up to 0.75 M (the correlation coeficient was $r = 0.9968$). The points for 0.05 and 0.10 M lithium perchlorate concentrations have been excluded in the calculations due to the large relative error in the ratios $1/([C][T^0]/[T][C^0] - 1)$ at such low salt ratios. The b values obtained are reported in Table II. As anticipated the [C]/[T] ratio can be described by eq 3 using the b parameters obtained, and the calculated curve superimposes satisfactorily on the experimental one up to 0.75 M lithium perchlorate concentrations (see Figure 1).

Similarly good results (see Tables I and II and Figures 2–4) have been obtained for the acid-catalyzed hydrolysis of **1a**, for the acid-catalyzed ethanolysis of **1b**, and for the acetolysis of **1b** in the presence of *p*-toluenesulfonic acid. These reactions have been carried out for salt concentrations up to 0.75 M. The reaction mixtures consisted mainly of the known diols **5a** and **6a** for the hydrolysis reactions of **1a**, and of the hydroxy ethers **7b** and **8b** for the ethanolysis of **1b** (see Table I). Within the salt concentration range used only small amounts (~5%) of side products (2-arylcyclohexanone and 1-arylcyclopentane-1-carboxaldehyde) were present in the crude reaction mixtures, and their variation with the salt added was practically negligible. The structure and the configurations of **7b** and **8b** were shown by their oxidation to 2-(*m*-chlorophenyl)-2-ethoxycyclohexanone (**9b**), and by their ^1H NMR and IR spectra in the 3-μm range in dilute solution of CCl_4, which are in agreement with those of the corresponding hydroxy ethers unsubstituted on the phenyl **7a** and **8a**.[17] In the case of the acetolysis of **1b** the reaction mixtures were analyzed after hydrolysis of the monoacetates to the corresponding diols (**5b** and **6b**). Also in these cases the points for 0.05 and 0.10 M lithium perchlorate concentrations have been excluded in the calculations of the parameters of eq 4 (see Table II and Figures 2–4). The consistency of the results obtained argues for the validity of the approach.

The results show in all cases positive b values for the formation of both the cis and the trans products, the b_c values being always much higher than the corresponding b_t ones. Furthermore the b_c values are strongly dependent on the solvent, but they appear to be independent of the substituent on the phenyl group of the epoxide. The relatively large salt effects observed for the paths leading to the cis products (**6** and **8**) and the corresponding small effects on the reaction leading to the trans compounds (**5** and **7**) are in good agreement with the mechanistic scheme suggested above; the addition of the salt, leading to an increase in the polarity of the medium, should greatly stabilize the separated ion–dipole pair **4**, which is much more polar than the starting compound, as expected for an A-1 type reaction.[9,18] On the contrary, the salt added should have little effect on the intimate ion–dipole pair **3**, which resembles more an A-2 or borderline A-1 type of structure in which the positive charge on the benzylic carbon is more distributed between carbon and oxygen.[9,18] However, it may be pointed out that a certain degree of breaking must have occurred between the benzylic carbon and the epoxidic oxygen in structure **3**; this can be shown on the basis of the same regiospecificity of the ring opening of **1** for both the cis (**6**, **8**) and the trans products (**5**, **7**),[17,19] and of a previous study on the dependence of the stereoselectivity of these reactions on the substituents on the phenyl.[5] Furthermore, as required

by the theory,[9,18] the magnitude of the salt effect (expressed by the salt parameter b) for the reaction proceeding through the highly polar structure **4**, markedly increases in the series of solvents (water, ethanol, acetic acid), i.e., when the polarity of the solvent is decreased.[9,18] The salt effect for the formation of the trans adducts remains almost constant in the three solvents.

The marked increase in the yield of carbonyl products as the salt concentration becomes very high (this has been checked only in the ethanolysis of **1a**) could be due either to the increase in the polarity of the medium, thus favoring paths leading to the rearranged products, and/or to a "drying" of the solvent by the salt. Large amounts of electrolyte will compete with the carbocationic structures of type **3** and **4** by attracting solvent molecules, thus making them less available as nucleophiles and making the rearrangement paths more competitive.[1b,20]

Experimental Section

Melting points were determined on a Kofler apparatus. IR spectra were taken on a Perkin–Elmer Model 257 double beam grating spectrometer in dried (P_2O_5) CCl_4, using the indene band at 3110 cm^{-1} as a calibration standard; a quartz cell of 2 cm optical length was employed. The NMR spectrum of **7b** has been determined with a Jeol C-60 HL spectrometer and that of **8b** has been measured on a Bruker HXS 360 NMR spectrometer on ~10% $CDCl_3$ solutions using Me_4Si as an internal standard. Preparative TLC was performed on 2-mm silica gel plates (Merck 254) containing a fluorescent indicator; spots were detected under UV light (245 nm). The relative percentages of compounds **5a** and **6a**, and **7** and **8a,b** were determined on a Fractovap GV apparatus with a flame ionization detector, using a dual column system with glass columns. **5a** and **6a** (columns packed with 10% Carbowax 20M on 80–100 mesh silanized Chromosorb W, 2.5 mm × 1 m): temperature of columns 185 °C, evaporator and detector 200 °C; nitrogen flow 35 mL/min; order of increasing retention times, **6a** < **5a**. **7a** and **8a** (columns packed with 10% ethylene glycol succinate on 80–100 mesh silanized Chromosorb W, 2.5 mm × 1 m): temperature of columns 135 °C, evaporator and detector 200 °C; nitrogen flow 35 mL/min; order of increasing retention times, 1-phenylcyclopentane-1-carbaldehyde < 2-phenylcyclohexanone < **7a** < **8a**. **7b** and **8b** (columns packed with 10% Carbowax 20M on 80–100 mesh silanized Chromosorb W, 2.5 mm × 1 m); temperature of columns 175 °C, evaporator and detector 220 °C; nitrogen flow 35 mL/min; order of increasing retention times, **7b** < **8b**. The relative percentages of **5b** and **6b** were determined on a Perkin-Elmer Model F-11 apparatus using a glass column (2.5 mm × 1 m) packed with 10% ethylene glycol succinate on 80–100 mesh silanized Chromosorb W, temperature of column 215 °C evaporator and detector 250 °C, nitrogen flow 45 mL/min; order of increasing retention times, **6b** < **5b**.

The values given in Table I were the average of at least three measurements done on at least two different runs for each point. The accuracy is ±1%.

1-Phenylcyclohexene oxide (**1a**),[21] 1-(*m*-chlorophenyl)cyclohexene oxide (**1b**),[22] 1-phenyl-*r*-1-*cis*-2-cyclohexanediol (**6a**),[21] 1-phenyl-*r*-1-*trans*-2-cyclohexanediol (**5a**),[23] 1-(*m*-chlorophenyl)-*r*-1-*cis*-2-cyclohexanediol (**6b**),[22] 1-(*m*-chlorophenyl)-*r*-1-*trans*-2-cyclohexanediol (**5b**),[22] 2-phenyl-*cis*-2-ethoxy-*r*-1-cyclohexanol (**8a**),[17] 2-phenyl-*trans*-2-ethoxy-*r*-1-cyclohexanol (**7a**),[17] 2-phenylcyclohexanone,[24] and 1-phenylcyclopentane-1-carboxaldehyde[24] were prepared as previously described.

2-(*m*-Chlorophenyl)-*trans*-2-ethoxy-*r*-1-cyclohexanol (7b). A solution of **1b** (2.0 g) in 0.2 N H_2SO_4 in anhydrous ethanol was left at −25 °C for 4 days, then quenched with solid $NaHCO_3$ and saturated $NaHCO_3$, diluted with water, and extracted with ether. Evaporation of the washed (H_2O) and dried ($MgSO_4$) ether extracts yielded an oily residue (2.05 g) consisting mostly of **7b**, which was subjected to preparative TLC (eluent: 75/25 petroleum ether and ether mixture). Extraction of the main band yielded pure **7b** (1.70 g), which crystallyzed from petroleum ether at −25 °C: mp 33–34 °C; IR ν_{OH} (CCl_4) 3608 cm^{-1} (OH···π); NMR δ 3.76 (m, 1, $W_{1/2}$ = 7.0 Hz, CHO). Anal. Calcd for $C_{14}H_{19}ClO_2$: C, 66.01; H, 7.52. Found: C, 66.21; H, 7.59.

2-(*m*-Chlorphenyl)-*cis*-2-ethoxy-*r*-1-cyclohexanol (8b). A solution of **1b** (2.0 g, 9.6 mmol) in anhydrous CH_2Cl_2 (200 mL) and anhydrous ethanol (3.35 mL, 57.4 mmol) was treated with *p*-toluenesulfonic acid (0.182 g, 0.9 mmol). The resulting solution was stirred for 24 h at room temperature, then treated with solid $NaHCO_3$ and saturated aqueous $NaHCO_3$. Evaporation of the washed (H_2O) organic solvent yielded an oily residue (1.96 g) consisting of a mixture of **7a** and **8a** together with carbonylic compounds [mainly 2-(*m*-chlorophenyl)cyclohexanone and 1-(*m*-chlorophenyl)cyclopentane-1-carboxaldehyde], which was subjected to preparative TLC (a 75/25 mixture of petroleum ether and ether was used as the eluent). Extraction of the band corresponding to the *cis*-hydroxy ether **8b** (the trans isomer **7b** has higher R_f) yielded **8b**, impure with carbonylic compounds (0.95 g), as an oil from which pure **8b** has been obtained by crystallization from petroleum ether at −25 °C: mp 47.5–48 °C; IR ν_{OH}(CCl_4) 3591 cm^{-1} (OH···O); NMR δ 3.46 (dd, 1, J = 9.4, 4.4 Hz, CHO). Anal. Calcd for $C_{14}H_{19}ClO_2$: C, 66.01; H, 7.52. Found: C, 66.24; H, 7.72.

2-(*m*-Chlorophenyl)-2-ethoxycyclohexanone (9b). (**A**) A solution of **7b** (0.050 g, 0.196 mmol) in acetone (4 mL) was treated with Jones reagent[25] (0.15 mL). After 15 min at room temperature the mixture was diluted with water and extracted with ether. Evaporation of the washed (H_2O, saturated aqueous $NaHCO_3$, and H_2O) and dried ether extracts gave an oily residue of **9b** (0.045 g): IR λ 5.80 μm (C=O); 2,4-dinitrophenylhydrazone,[26] mp 51.5–52 °C (from ethanol). Anal. Calcd for $C_{20}H_{21}ClN_4O_5$: C, 55.50; H, 4.89; N, 12.94. Found: C, 55.80; H, 4.89; N, 12.66.

(**B**) **8b** (0.050 g) was oxidized under the conditions used above to give **9b** (0.044 g): 2,4-dinitrophenylhydrazone,[26] mp 51.5–52 °C.

Acid-Catalyzed Solvolyses of 1-Arylcyclohexene Oxides (1) in the Presence of $LiClO_4$. The reactions were carried out in the following way. A suspension (water) or a solution (other solvents) of 1 (100 mg) in a 0.2 N solution of the acid (H_2SO_4 for the reactions in water and monohydrate *p*-toluenesulfonic acid for the reactions in the other solvents) in the solvent (see Table I) containing anhydrous $LiClO_4$ in the concentrations shown in Table I (10 mL) was stirred at 25 °C for 0.5 h (2 h in the case of the reactions in water), then quenched with solid $NaHCO_3$ and saturated acqueous $NaHCO_3$ (in the case of the reactions in acetic acid the mixtures were diluted with water) and thoroughly extracted with ether. Evaporation of the washed (H_2O, saturated aqueous $NaHCO_3$, and H_2O) and dried ($MgSO_4$) ether extracts yielded crudes consisting of the diols **5** and **6** (reactions in water), or the hydroxy ethers **7** and **8** (reactions in ethanol), or monoacetates (reactions in acetic acid) accompained by minor amounts of 2-arylcyclohexanone and 1-phenylcyclopentane-1-carboxaldehyde, which were directly analyzed by GLC, except for the reactions carried out in acetic acid. The crudes obtained from the reactions in acetic acid were analyzed by GLC after hydrolysis of the monoacetates formed to the corresponding diols **5** and **6**: the crude residues were dissolved in THF (5 mL), treated with 1 M KOH in ethanol (2 mL), and left for 5 h at room temperature. Dilution with water, extraction with ether and evaporation of the washed (H_2O) and dried ($MgSO_4$) ether extracts yielded residues consisting practically of **5** and **6**.

The solvolysis addition products of epoxides **1** were completely stable under the reaction conditions used, and rearrangement products (2-arylcyclohexanones and 1-arylcyclopentane-1-carboxaldehyde) were shown to be not derived from a further transformation of the addition products of epoxides **1**.

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Registry No.—**1a**, 4829-01-0; **1b**, 54637-84-2; **7b**, 63641-45-2; **8b**, 63641-46-3; **9b**, 63641-47-4; **9b** DNP, 63641-48-5; $LiClO_4$, 7791-03-9.

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Synthesis and Interconversion by Hydrogen Exchange of Isomeric Quinhydrones[1,2]

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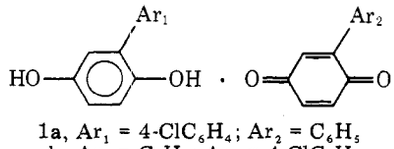
Isomeric quinhydrones, 2-phenylquinone/2-(4′-chlorophenyl)hydroquinone (1:1) (**1a**) and 2-(4′-chlorophenyl)-quinone/2-phenylhydroquinone (1:1) (**1b**), have been prepared as crystalline solids and shown to resist interconversion by a redox (hydrogen exchange) process even at temperatures as high as 140 °C when kept in the solid state. It is suggested that these unsymmetrically substituted complexes are inert to oxidation–reduction interconversions because of a stabilizing combination of hydrogen bonding and charge-transfer forces. A semiquantitative survey of the rates in solution of the redox equilibration of a number of quinone–hydroquinone pairs has been studied by NMR spectroscopy as the basis for the rational selection of the pair of quinhydrones described above.

Molecular complexes (1:1) (quinhydrones) of benzoquinones and hydroquinones have long been known as stable solids which, however, in solution separate into their components.[3] The possibility of preparing isomeric quinhydrones by virtue of the presence of different substituents on the quinone and hydroquinone ring has been recognized, and investigations of deuterium- and carbon-14-labeled compounds have been carried out as a method of studying the redox interconversions in solution of such compounds.[4] In other cases where preparation of isomeric pairs of substituted quinhydrones has been attempted, the rapid redox interconversion in solution coupled with a lack of adequate methods of characterization has led to confusing results.[5] Nevertheless crystals of unsymmetrically substituted complexes of this type as, for example, **1a** and **1b**, could be of great interest, because of their possible optical and electrical properties coupled with the fact that their interconversion requires only the transfer between oxygen atoms of hydrogen atoms (or hydride ions plus protons). Furthermore, determinations of the crystal structures of the monoclinic[6a] and triclinic[6b] forms of the parent symmetrical quinhydrone (1 with $Ar_1 = Ar_2 = H$) have shown that in each case the structures are composed of chains of alternating, well-defined, quinone and hydroquinone molecules hydrogen bonded in such a way that it might be hoped that hydrogen switching could be induced without seriously disrupting the structure.[7] With the proper choice of substituents, spectral or other properties should differ sufficiently for the isomers analogous to **1a** and **1b** to permit ready recognition of whether a crystal is in state **1a** or state **1b**.



1a, Ar_1 = 4-ClC_6H_4; Ar_2 = C_6H_5
b, Ar_1 = C_6H_5; Ar_2 = 4-ClC_6H_4
c, $Ar_1 = Ar_2 = C_6H_5$
d, $Ar_1 = Ar_2$ = 4-ClC_6H_4

This paper describes a study of the factors affecting the redox interconversion of hydroquinone–quinone pairs in solution and the synthesis of the crystalline redox isomers **1a** and **1b**.

Experimental Section

Spectra and other supplementary experimental data are available in ref 1.

Synthesis of Quinones and Hydroquinones. Hydroquinone-*2,3,5,6-d*$_4$. To 40 mL of acetyl chloride was added, over 30–45 min, 20 mL of D_2O (90% D, Columbia Organic Chemicals) with regular stirring and such that the evolution of gas was not too vigorous. The hydrolyzed mixture was added to 2.1 g of hydroquinone (Mallinckrodt, twice sublimed, mp 171 °C) and 4.0 g of amalgamated zinc and the resulting mixture was heated under reflux for 24 h.[8] The reaction was arrested with about 150 mL of water and the reaction mixture was repeatedly extracted with ether. The combined ethereal extracts were washed with $NaHCO_3$ solution until the washings remained alkaline. The organic layer was dried and the ether was removed to leave the crude deuterated hydroquinone which was sublimed at 70 °C and at 0.04 Torr to give 1.75 g (82%) of product that showed approximately 88% deuterium incorporation (by NMR and mass spectrometry). A final recrystallization from ethanol–benzene yielded 1.42 g (68%) of solid: mp 171–173 °C (lit. mp 175 °C);[9] IR (KBr) 3270, 2234, and 1210 cm^{-1}; mass spectrum (CH-5, 10 eV) M^+ (base peak) (*m/e*) 114, 113 (39%), 112 (22%).

Anal. Calcd for $C_6D_4(OH)_2$ with 88% D: C, 63.44; H, 5.29. Found: C, 63.08; H, 5.53.

2,5-Dichlorohydroquinone-*3,6-d*$_2$. 2,5-Dichloro-1,4-benzoquinone was reduced to the hydroquinone with $SnCl_2$ in virtually quantitative yield.[10,11] This hydroquinone (250 mg) was deuterated