Solvolytic Elimination and Hydrolysis promoted by an Aromatic Hydroxy-group. Part 2.[1] The Hydrolysis of 2-Bromo-4-dibromomethylphenol in 95% 1,4-Dioxane

Peter B. D. de la Mare* and Paul A. Newman
Chemistry Department, University of Auckland, Private Bag, Auckland, New Zealand

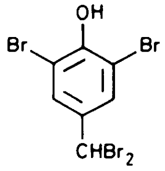
The reaction of 2-bromo-4-dibromomethylphenol with water in slightly aqueous (95%) 1,4-dioxane has been examined kinetically by using u.v. spectroscopy, which provides evidence for the transient formation of the quinone methide, 2-bromo-4-bromomethylenecyclohexa-2,5-dienone, during the hydrolysis. The final product is 3-bromo-4-hydroxybenzaldehyde. The rate of disappearance of starting material is independent of acidity, but is reduced by added or developing bromide ion. The rate of the loss of bromide ion from the phenol is very much greater than that of the corresponding reaction of 2-bromo-4-dibromomethylanisole under the same conditions. An estimate of the value of $\sigma_{p\text{-OH}}^+$ (−1.36), made by using these relative rates, is larger than the value (−0.92) based on relative rates of aromatic electrophilic substitution. Solvent kinetic isotope effects on these reactions are reported; the theoretical implications of variation in the substituent parameter for the hydroxy-group is discussed in terms of solvent effects on H–O hyperconjugation.

We showed in Part 1[1] that the solvolysis of 2,6-dibromo-4-dibromomethylphenol (**1**) in solvent mixtures containing water is very rapid. Kinetic evidence was adduced that at moderate acidities the rate-determining step is the conventional S_N1 solvolysis of the neutral phenol, proton-loss and capture of the carbocation by nucleophiles being processes subsequent to the initial ionization.

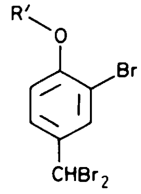
In any such system in which a conjugatively activating substituent R (OH in this case) is flanked by bulky groups, the electron-releasing power of R is modified by secondary steric effects whenever R is not spherically symmetrical.[2] This modification usually takes the form of steric inhibition of resonance. It would be small, but not necessarily negligible, for the hydroxy-group;[3,4] for this substituent, the effect might be tempered by the forces of internal hydrogen-bonding.[5] For substituents like the methoxy-, phenoxy-, and acetamido-groups, adjacent bromine substituents would strongly interfere with the normal electron-releasing properties of the group.

For these reasons, it is difficult to use 2,6-disubstituted compounds directly in an attempt to assess quantitatively the electron-releasing power of substituents in the 1-position. A provisional comparison of the hydroxy- and methoxy-group in the solvolysis of (**1**) and its methyl ether was attempted by using the additivity principle,[1] but this involved a long extrapolation, and rate differences were too large to enable direct comparisons to be made with suitable reference compounds in the same solvent.

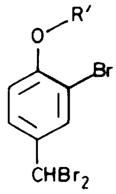
Consequently, attention has been turned to 2-bromo-4-dibromomethylphenol (**2a**) and its methyl ether (**2b**). Here the conformation shown, rather than the alternative (**3**), can be adopted for all substituents; and such steric inhibition of resonance as results from interaction between R′ and 6-H in conformation (**2**) affects all comparisons of the electron-releasing power of R′O groups. Phenol itself is most stable in the planar conformation, the barrier to free rotation of the hydroxy-group in phenol being small (14 kJ mol^{-1}).[6] So internal hydrogen-bonding in the hypothetical conformation (**3a**) cannot explain much enhancement of resonance in the phenol. A preliminary account of this work has been given.[7]



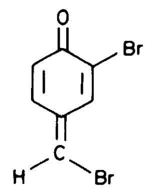
(**1**)



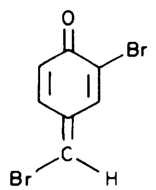
(**2**)
a; R′ = H
b; R′ = Me



(**3**)
a; R′ = H
b; R′ = Me



(**4**)



(**5**)

Experimental

Most of the materials and methods are described in Part 1;[1] the preparation and properties of 2-bromo-4-dibromomethylphenol (**2a**) have been described elsewhere.[8] This compound was converted by reaction with diazomethane into its *O*-methyl derivative, which was purified by chromatographing it on silica gel, hexane–diethyl ether (1:2 v/v) being used first as eluant. The resulting product was contaminated only by 3-bromo-4-methoxybenzaldehyde, which was removed by rapid chromatography on silica gel with CH_2Cl_2 as eluant, to give 2-bromo-4-dibromomethylanisole (**2b**). Its ^1H n.m.r. spectrum (CCl_4) had signals at δ 3.85 (3 H, s, OCH_3), 6.42 (1 H, s, $CHBr_2$), 6.67 (1 H, d, ArH, 6-H), 7.32 (1 H, d of d, ArH, 5-H), and 7.58 (1 H, d, ArH, 3-H). Its u.v. spectrum in dioxane had $\lambda_{max.}$ 253 nm (ε 8 600 l cm^{-1} mol^{-1}), being as expected practically identical with that of 2-bromo-4-dibromomethylphenol.

Hydrolysis of 2-bromo-4-dibromomethylphenol (aqueous $NaHCO_3$) gave 3-bromo-4-hydroxybenzaldehyde (**6**), m.p. 124 °C (lit.,[9] 124 °C). Its methyl ether was prepared by allowing 4-methoxybenzaldehyde (5.9 g) to react with bromine (6.9 g) in $CHCl_3$ (120 cm^3) in the dark, with iodine (0.2 g) as catalyst. After 7 days the solvent was removed under reduced pressure, and the residual brown oil was chromatographed on silica gel, CH_2Cl_2 being used as eluant. Middle fractions after removal of solvent were yellow solids; they were combined and recrystallized from hexane to give 3-bromo-4-methoxy-

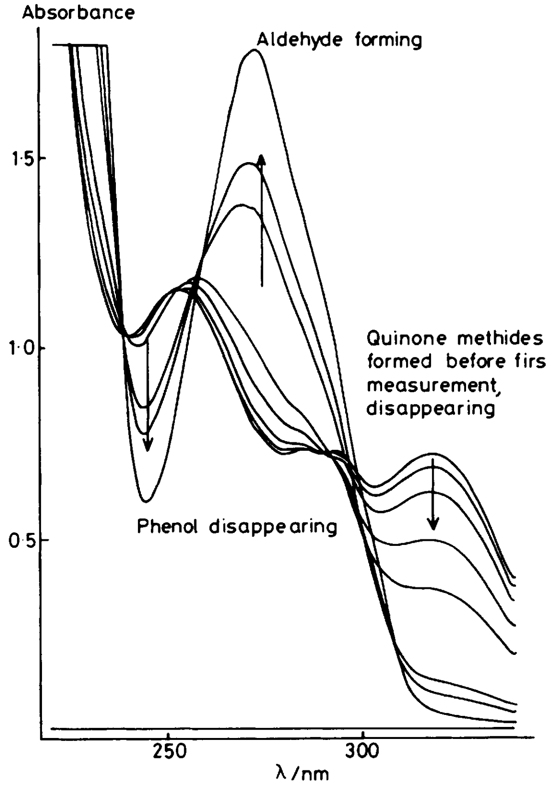


Figure 1. Spectral changes accompanying the hydrolysis of 2-bromo-4-dibromomethylphenol in 95% 1,4-dioxane at 34.0 °C; solution initially neutral

benzaldehyde (**9**), m.p. 52—53 °C (lit.,[10] 54 °C). Its ^1H n.m.r. spectrum had signals at δ 3.95 (3 H, s, OCH_3), 6.85 [1 H, d, ArH(6-H)], 7.63 [1 H, d of d, ArH(5-H)], 7.90 [1 H, d, ArH(3-H)], and 9.70 (1 H, s, CHO). Its u.v. spectrum in dioxane had $\lambda_{max.}$ 275 nm (ε 13 600 l cm^{-1} mol^{-1}).

The formation and subsequent decomposition of quinone methides [a mixture of the geometric isomers (**4**) and (**5**)] would be expected by analogy with the behaviour of 2,6-dibromo-4-dibromomethylphenol. These quinone methides are, however, too reactive to be prepared by the method used for their 2,6-dibromo-analogue;[1] their contribution to the solvolytic pathway can be inferred from the development and subsequent disappearance of weak absorption at *ca.* 330 nm. Figure 1 shows the complex spectral changes occurring during the reaction in initially neutral 95% dioxane. From the extinction coefficient at 300 nm, it would appear that *ca.* 25% of the starting material had been converted into the quinone methides by the time the first reading was made; this calculation is based on the assumption that the mixture of (**4**) and (**5**) would have the same molecular extinction coefficient as the dibromo-analogue.

Kinetic Measurements.—These were carried out as discussed in Part 1.[1] When the initial acidity of the solution was sufficiently great (10^{-4}M or greater), the solvolysis of 2-bromo-4-dibromomethylphenol was accompanied by very little build-up of the quinone methide. Figure 2 exemplifies the spectral changes typically accompanying the reaction under conditions used for the kinetic measurements. The slight absorption in the region of 330 nm indicates the presence of traces of (**4**) and/or (**5**), whilst good isosbestic points at 259 and 238 nm confirm that the concentration of any intermediates is low. The rate of reaction could be monitored, therefore, by measuring changes in absorption at 246 and 274 nm.

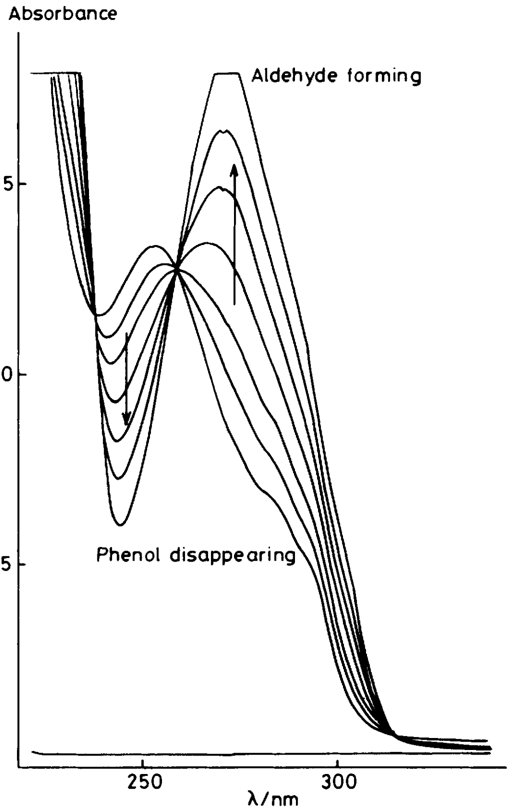


Figure 2. Spectral changes accompanying the hydrolysis of 2-bromo-4-dibromomethylphenol in 95% 1,4-dioxane at 34.0 °C; initial concentration of [H^+] 8.303 × 10^{-3}M

Table 1 gives an example of a typical kinetic run.

Values of the instantaneous rate coefficient, calculated from the increase in absorbance at 274 nm and thus representing the rate of appearance of the product, fell rapidly with the progress of the reaction and consequent development of bromide ion. Results obtained by using the absorbance at 246 nm gave good agreement in the early stages of the reaction, but diverged a little towards its end, perhaps because the spectrum of the starting material could not be determined independently in the aqueous solvent.

A plot of $1/k_1$ (where k_1 is the instantaneous first-order rate coefficient calculated between successive experimental points) against the average concentration of bromide ion between each corresponding pair of points is given in Figure 3 (circles). Extrapolation to give the rate coefficient at zero concentration of bromide is possible, but the accuracy of this procedure depends critically on the early points, which are the most subject to experimental error. Consequently we have determined also 'average' rate coefficients corresponding to average concentrations of bromide ion within each kinetic run, and used the results of experiments in which bromide ion was added initially. Under these circumstances the concentration of bromide ion and hence the successive values of k_1 were much more nearly constant through the course of a run. The results of such measurements at constant initial acidity and ionic strength are given in Table 2, and plotted in Figure 3 (crosses).

From the results given in Table 2, the value of the initial first-order rate coefficient for solvolysis of 2-bromo-4-dibromomethylphenol (**2a**) in 95% 1,4-dioxane at 34.0 °C with initial [H^+] 8.303 × 10^{-3} and ionic strength 2.00 × 10^{-2} mol l^{-1} at zero concentration of bromide ion extrapolates to 0.442 min^{-1}. This value represents the intrinsic solvolytic reactivity of

Table 1. Hydrolysis of 2-bromo-4-dibromomethylphenol in 95% 1,4-dioxane at 34.0 °C (initial concentrations $[CHBr_2]_0$, 1.76×10^{4}; $[Br^-]_0$, 0; $[H^+]_0$, 8.308×10^{3}; ionic strength, 2.00×10^{2} mol l^{1})

t/min	Absorbance 274 nm	246 nm	$10^4[CHBr_2]$/ l mol ^{1}	$10^4[Br^-]_{av}$/ l mol $^{1\,b}$	k_1/min $^{1\,c}$	k_1 ^{1}/min
0	0.832	1.496	1.762[a]	0		
1	1.168	1.285	1.350	0.412	0.265	3.77
2	1.313	1.169	1.166	1.008	0.140	7.14
3	1.442	1.109	1.057	1.301	0.144	6.94
4	1.523	1.053	0.965	1.502	0.102	9.80
5	1.597	1.005	0.885	1.674	0.104	9.61
6	1.658	0.969	0.824	1.814	0.095	10.5
8	1.756	0.904	0.716	1.984	0.087	11.5
10	1.821	0.856	0.638	2.170	0.067	14.9
12	1.884	0.815	0.570	2.334	0.075	13.3
15	1.952	0.767	0.492	2.462	0.064	15.6
20	2.046	0.707	0.391	2.641	0.069	14.5
25	2.097	0.665	0.325	2.808	0.051	19.6
30	2.141	0.634	0.274	2.925	0.057	17.5
56	2.236	0.562	0.158	3.091	0.049	20.4
∞	2.273[a]	0.493[a]	0			

[a] Calculated from the spectrum of the starting material in dioxane (A_{274} 4 720; A_{246} 8 490) and of the product (A_{274} 12 900; A_{246} 2800) in 95% dioxane. [b] Average concentration of bromide ion over the interval between each pair of points. [c] Instantaneous values of k_1 calculated from point to point from the increase in absorbance at 274 nm.

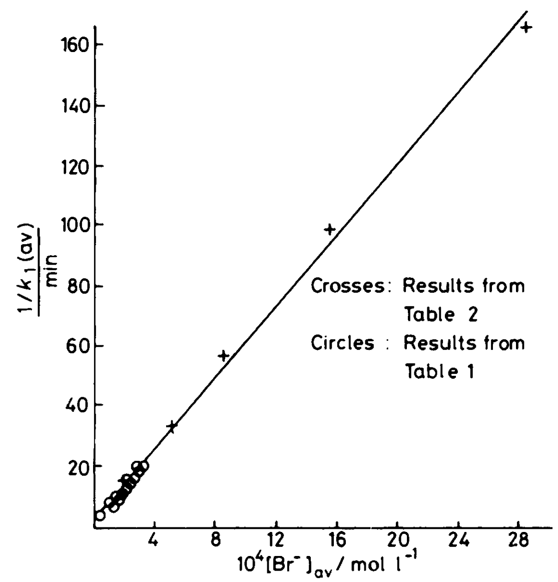


Figure 3. Variation with $[Br^-]$ in the rate of hydrolysis of 2-bromo-4-dibromomethylphenol in 95% 1,4-dioxane at 34.0 °C, with initial $[Br^-]$ 8.303×10^{-3} and ionic strength 2.00×10^{-2} mol l^{-1}

Table 2. Variation with $[Br^-]$ in the rate of hydrolysis of 2-bromo-4-dibromomethylphenol (**2a**) in 95% 1,4-dioxane at 34.0 °C, with initial $[H^+]$ 8.303×10^{3} and ionic strength 2.00×10^{2} mol l^{1}

$10^4[Br^-]_0$/ mol l^{1}	$10^4[Br^-]_{av}$/ mol l^{1}	$10^2k_{1(av)}$/min ^{1}	$k_{1(av)}$ ^{1}/min
0	1.98	7.76[a]	14.8
3.51	5.19	2.99	33.4
7.02	8.45	1.78	56.2
14.04	15.4	1.01	98.9
24.57	26.3	0.602	166.3

[a] From the results of Table 1, k_1 now calculated from the rate of disappearance of starting material.

Table 3. Variation with acidity in the rate of hydrolysis of 2-bromo-4-dibromomethylphenol in 95% 1,4-dioxane at 34.0 °C, with $[Br^-]_0$ 15.1×10^{-4} and ionic strength 2.00×10^{-2} mol l^{-1}

$10^3[H^+]_0$/mol l^{-1}	$10^3[H^+)_{av}$/mol l^{1}	$10^2k_{1(av)}$/min ^{1}
1.196	1.37	0.80
8.303	8.35	1.01[a]
9.969	10.12	1.00

[a] Interpolated from Figure 3.

this compound under the specified conditions. The general accord with the results obtained from a run with zero initial concentration of bromide is evident from Figure 3. The mass law constant[1] α, derivable from the results, is 27 600 l mol^{-1}.

For this compound there was no need to extrapolate also to high acidity, since there was no indication of reaction through the phenoxide ion. The rate in fact increased slightly with acidity, even at constant ionic strength, probably because of specific salt effects in this solvent. Results are given in Table 3. The trend with acidity was confirmed from results obtained with no initial bromide ion and lower ionic strength, now using average rate coefficients for each run. Results are in Table 4.

Hydrolysis of 2-bromo-4-dibromomethylanisole (**2b**) was also followed spectrophotometrically by monitoring the changes in absorption at 274 and 246 nm. This reaction was much slower, and the operation of a mass law effect was not apparent from the results obtained within a single run, so rate coefficients could be determined without the necessity of extrapolation to zero concentration of bromide ion. The operation of a small specific salt effect was evident here, as for the phenol, as is shown by the results given in Table 5.

In these solvolyses the absorption spectrum of the starting material was converted cleanly into that of the expected product, with no indication of the presence of any other absorbing species throughout the measured course of the reaction, which was normally followed to *ca.* 50% completion. When bromide ion (2.808×10^{-3} mol l^{-1}) was included in the reaction medium, with $[H^+_0]$ 8.308×10^{-3} mol l^{1} and ionic strength 2.00×10^{-2} mol l^{1}, the disappearance of absorption at 246 nm paralleled the increase at 270 nm only for the first

Table 4. Variation with acidity in the rate of hydrolysis of 2-bromo-4-dibromomethylphenol in 95% 1,4-dioxane at 34.0 °C, with $[Br^-]_0$ 0 and ionic strength 0.700 × 10^{-2} mol l^{-1}

$10^3[H^+]_0$/mol l^{-1}	$10^3[H^+]_{av}$/mol l^{-1}	$10^2k_{1(av)}$/min$^{-1\,a}$
1.196	1.38	2.99
2.990	3.18	3.06
4.485	4.68	3.29
5.980	6.17	3.44

[a] 'Average' rate coefficient through each run, corresponding with an average concentration of bromide ion, 1.85 × 10^{-4} mol l^{-1}.

Table 5. Variation with acidity in the rate of hydrolysis of 2-bromo-4-dibromomethylanisole (**2b**) in 95% 1,4-dioxane at 34.0 °C, with $[Br^-]_0$ 0, ionic strength 2.00 × 10^{-3} mol l^{-1}

$10^3[H^+]_0$/mol l^{-1}	$10^3[H^+]_{av}$/mol l^{-1}	10^4k_1/min^{-1}
1.495	1.54	1.28
8.31	8.35	1.39

Table 6. Solvent deuterium isotope effects for the solvolyses of 2-bromo-4-dibromomethyl-phenol (**2a**) and -anisole (**2b**) in 95% 1,4-dioxane at 34.0 °C, with $[Br^-]_0$ 0, ionic strength 2.387 × 10^{-2} mol l^{-1}

Compound	$\frac{k_1(H_2O)}{\text{min}^{-1}}$	$\frac{k_1(D_2O)}{\text{min}^{-1}}$	$\frac{k_{1(av)}(H_2O)}{\text{min}^{-1\,a}}$	$\frac{k_{1(av)}(D_2O)}{\text{min}^{-1\,a}}$	$k(H_2O)/k(D_2O)$
(**2a**)			7.6 × 10^{-2}	4.5 × 10^{-2}	1.71
(**2b**)	1.39 × 10^{-4}	1.07 × 10^{-4}			1.30

[a] Average first-order rate coefficients for the run, over the range with $[Br^-]_{av}$ 1.8 × 10^{-4} mol l^{-1}.

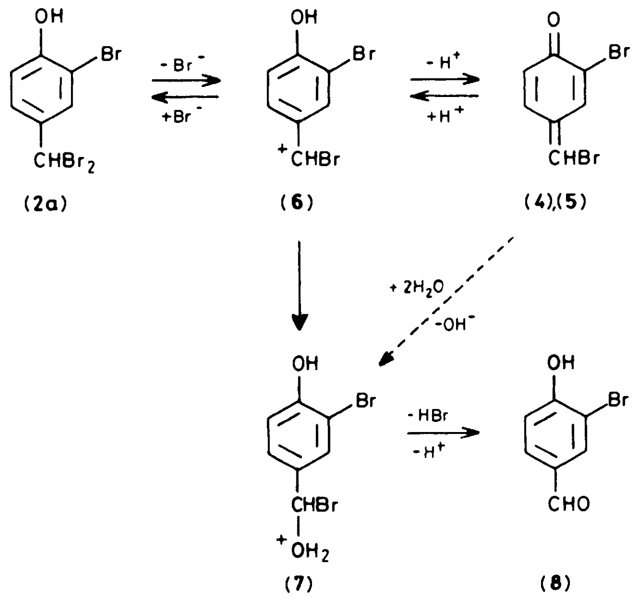
13% of reaction; thereafter an unexpected side reaction occurred. From reaction followed only over the initial period, k_1 was 1.11 × 10^{-4} min^{-1}, as compared with 1.39 × 10^{-4} min^{-1} with zero initial bromide. This gives an estimate of α = 90 for the mass law constant for this compound.

Solvent deuterium isotope effects on the rates of solvolysis of (**2a**) and (**2b**) were determined also. As for the 2,6-dibromo-compound,[1] a procedure was adopted which gave solvents containing exactly the same molar percentages of protium or deuterium oxide, and for this reason the solvent containing protium oxide did not have exactly the same composition as was used for the normal experiments. Results are given in Table 6.

Discussion

(a) *Course taken in the Hydrolysis of* 2-*Bromo*-4-*dibromomethylphenol*.—The hydrolysis of 2-bromo-4-dibromomethylphenol (**2a**) evidently follows a course which corresponds with that attributed[1] to its 2,6-dibromo-analogue (Scheme).

Proton-loss resulting in the formation of the quinone methides (**4**), (**5**) neither precedes nor is synchronous with loss of bromide ion, since mass-law retardation of the rate by developing or added bromide ion is not accompanied by a corresponding effect of hydrogen ion. The conventional carbocationic intermediate (**6**) is thus the first intermediate on the reaction path. The initial rate of reaction when compared with rates of reaction of suitable reference compounds can therefore be used to determine the influence of the hydroxy-group on the rate of this S_N1 heterolysis.



Scheme. Course taken in the hydrolysis of 2-bromo-4-dibromomethylphenol in 95% dioxane

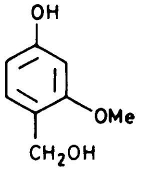
(b) *Estimate of the Value of* $\sigma_{p\text{-OH}}^+$.—Because the mass-law effect of added bromide ion is very large, it is necessary to make a fairly inaccurate extrapolation to obtain the required initial rate (see Figure 3). We regard our value (k_1 0.44 min^{-1} for reaction in 95% dioxane at 34.0 °C with initial $[H^+]$ 8.303 × 10^{-3} and ionic strength 2.00 × 10^{-2} mol l^{-1}) as being the best that can be obtained from the experimental data; a generous assessment of the possible error would be ±0.1 min^{-1}. The comparisons which follow are hardly affected by an uncertainty of this magnitude.

The corresponding rate of reaction of 2-bromo-4-dibromomethylanisole (**2b**) is 1.39 × 10^{-4} min^{-1}, and is therefore *ca.* 3 200 times less than that of the phenol. It is immediately evident that for this reaction the hydroxy-group is very much more strongly activating than the methoxy-group. To give this comparison a quantitative basis, a ρ value for these hydrolyses is needed. Quemeneur *et al.*[11] have measured the rates of hydrolysis of dibromomethylbenzene and its 4-methyl analogue in acetone–water mixtures at 25 °C. The value of $\sigma_{p\text{-Me}}^+$ being taken as -0.31,[12] the results are well represented by a ρ value of -6.0, and this value is almost independent of the proportion of water in the solvent over the range 60—33% acetone.

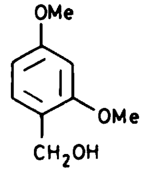
We think that this value of ρ can quite reasonably be assumed to apply to our conditions of reaction. On the further assumption that $\sigma_{p\text{-OMe}}^+$ can be accorded its standard value[12] of -0.78, the value of $\sigma_{p\text{-OH}}^+$ is -1.36.

The standard reactions used originally[13] to determine the values of $\sigma_{p\text{-OMe}}^+$ were the S_N1 solvolyses of aryldimethylcarbinyl chlorides, $RC_6H_4CMe_2Cl$. Good linear free-energy correlations are known to exist with other S_N1 solvolyses.[12] In principle, hydrolyses of the kind discussed in the present paper would for most substituents be expected to provide generally applicable measures of their electronic properties.

No other estimate of $\sigma_{p\text{-OH}}^+$ has been obtained from solvolysis of a halide as far as we know. Instead, the value usually tabulated[12] ($\sigma_{p\text{-OH}}^+$ -0.92) comes from a set of satisfactorily concordant estimates in which aromatic replacements having widely different ρ values have been used.[14] Included in the correlation were the results for ionization of substituted triarylmethanols, for which reaction also the conjugative electron-releasing power of the hydroxy-group has been shown to be superior to that of the methoxy-group.[15] The formation of quinone methides from the solvolyses of benzyl



(9)



(10)

halides[16] has been presumed to proceed by preliminary loss of a proton, as probably it does when the reagent is an effective base. Similarly, Ivnas and Lindberg[17] attributed different mechanisms to the much faster reaction of vanillyl alcohol (**9**) than of veratryl alcohol (**10**) with sulphite ions.

(c) *Variations in the Electronic Properties of the Hydroxy-group with Solvent and Reaction.*—A most conspicuous general feature of the electronic properties of the hydroxy-group is, however, a variability with solvent and reaction. The parameters most generally quoted,[12] $\sigma_{m\text{-OH}}$ 0.12 and $\sigma_{p\text{-OH}}$ −0.37, are derived from the ionization of benzoic acids in water. But they give rise frequently to substantial deviations in correlations of reactions in solvents other than water,[18,19] so that Charton[20] has concluded that the HO group resembles ionic groups in showing a very great dependence of its substituent parameters on the nature of the medium.

(d) HO *Hyperconjugation.*—Elsewhere,[1,4] it has been emphasized that H–O hyperconjugation can contribute to the conjugative electron-releasing power of the hydroxy-group. In discussing this in relation to aromatic substitution, we have earlier thought that an extreme form of hyperconjugation was under observation, in which the hyperconjugating H–O bond was breaking in the transition state for the reaction. In the present case, this has been established not to be so; the hyperconjugative influence resembles instead those of the H–C and Me–C bonds, which are not accompanied by their cleavage in the course of the reaction.[21]

It is well recognized now that the contribution of H–C hyperconjugation to the electronic effect of the methyl and related groups varies extensively with solvent and with reaction.[22,23] It is not at all surprising, therefore, that conjugative electron-release by the hydroxy-group, with its contribution from H–O hyperconjugation, can vary in the same way. The difference between the values of $\sigma_{p\text{-OH}}^+$ obtained from solvolysis (−1.36) and from aromatic substitution (−0.92) can be attributed to a combination of an effect of solvent and of reaction.

(e) *Solvent Deuterium Isotope Effects.*—Solvent deuterium isotope effects on the rates of solvolysis of 2-bromo-4-dibromomethylphenol and its methyl ether (Table 6) support the view that hyperconjugation contributes to the electron-releasing power of the hydroxy-group. For reactions of alkyl chlorides in water,[24] S_N1 processes are subject to a normal solvent deuterium isotope effect of *ca.* 1.3. Accordingly, the isotope effect in the solvolysis of 2-bromo-4-dibromomethylanisole has been found to be 1.30. The total effect found for 2-bromo-4-dibromomethylphenol is 1.71; so the effect attributable to the specific effect of the hydroxy-group,* and thence to H–O hyperconjugation, is 1.32. For comparison, the deuterium isotope effect on H–C hyperconjugation is typically *ca.* 1.1 per hydrogen atom,[25,26] and is smaller when the effect is transmitted through a vinyl or phenyl group.[27] A greater effect on HO than on HC hyperconjugation is consistent with its larger contribution to facilitation of the reaction.

It should be emphasized that, as we have argued before,[4] the fact that the OH group in the gas phase may be nearly in the plane of the benzene ring does not preclude an influence of HO hyperconjugation on electron release from the group, for two reasons. First, the potential for hyperconjugation arises from the fact that the H–O bond is polarisable in the sense $H^{\delta+}$—$O^{\delta-}$; it is particularly effective in doing this because of its power to participate in hydrogen-bonding with an electronegative group in the solvent. The random orientation of hydrogen-bonding solvent molecules is likely to reduce the barrier which favours the coplanarity of the HO group and the ring. Secondly, the barrier for free rotation in phenols, as we have noted elsewhere, is relatively small, and at the temperature of kinetic measurements the rotational states with the H–O group out of the plane of the ring will be significantly populated and easily attainable in the transition state. For these reasons, we do not think that H–O hyperconjugation in these phenols would be as limited by stereoelectronic factors as H–C hyperconjugation can be when atomic movements are restricted rigidly.[26]

(f) *An Estimate of the Value of* $\sigma_{p\text{-O}^-}^+$ *from Unimolecular Solvolysis.*—It has been stated[28] that the determination of σ^+ constants of anionic substituents by the standard chemical method is obviously impossible. This view is unduly pessimistic, provided that the principles of linear free-energy analysis are accepted, as indeed they are by the authors cited.[28]

The rate coefficient for the solvolysis of 2,6-dibromo-4-dibromomethylphenol as a function of acidity contains the term $2.37 \times 10^{-6}/[H^+]$ min^{-1} which represents the rate of reaction of this compound through its phenoxide ion under the prevailing conditions, when its absolute concentration is very small. The true rate-coefficient for its phenoxide ion, $k_{1(O^-)}$, is $2.37 \times 10^{-6}[ArOH]/[H^+][ArO^-] = 2.37 \times 10^{-6}/K_a^{ArOH}$ min^{-1} where K_a^{ArOH} is the dissociation constant of the phenol. This dissociation constant cannot be determined directly, but it can be estimated by using linear free-energy correlations. It has been shown[29] that the pK_a of 2,6-dichlorophenol is 6.8 in water and 10.0 in 95% dioxane,† and that in the latter solvent the effects of 4-substituents can be expressed to a good approximation by the expression $K_a^R/K_a^H = 3.66\ \sigma$. The corresponding value of pK_a for 2,6-dibromophenol[30] is 6.7, and the value of $\sigma_{p\text{-CHBr}_2}$ has been estimated[12] from Sheppard's data[31] to be +0.32. From these values, linear free-energy correlation analysis gives pK_a 8.7 (K_a 2×10^{-9} mol l^{-1}) for 2,6-dibromo-4-dibromomethylphenol in 95% dioxane. The rate-coefficient for the solvolysis of 2,6-dibromo-4-dibromomethylphenolate must then be 2.37×10^{-6} mol l^{-1} min^{-1}/2×10^{-9} mol l^{-1} = 1.2×10^3 min^{-1}. Comparison of this value with the rate of solvolysis of 2-bromo-4-dibromomethylanisole, allowance being made for the additional nuclear bromine ($\sigma_m = \sigma_m^+ = +0.39$),[12] gives $\sigma_{p\text{-O}^-}^+ = \{\log_{10}(1.2 \times 10^3/0.0001\ 39)\} - 6.0 - 0.78 - 0.39 = -2.33$.

(g) *Other Estimates of the Value of* $\sigma_{p\text{-O}^-}^+$.—Hoefnagel and Wepster[32] have used a complicated argument based on the strengths of arylacetic acids and the rates of alkaline hydrolysis of substituted ethyl benzoates to estimate a value for this quantity of −2.3. This excellence of the agreement with our value from rates of S_N1 solvolysis is probably fortuitous in view

---

* We have assumed that H-D exchange between water in the solvent and the phenolic hydroxy-group is very rapid, so that the observed solvent isotope effect is composite of a true solvent effect and a structural isotope effect.

† This value, obtained by electrochemical methods, should probably be corrected by an unknown junction potential involving the two solvents; we think that this can be neglected in view of the other approximations necessary for our present estimate.

of the assumptions in both treatments. It would be useful to have a comparable estimate based on rates of aromatic substitution. Both for electrophilic halogenation and for diazo-coupling, it is well known that the O^--group is much more activating than the OH-group. Thus it has been shown by Berliner[33] that the rate coefficients for the iodination of phenol, aniline, and the phenoxide ion under similar conditions have the relative values 1:3.7 × 10^5:0.2 × 10^9. If it is assumed that a linear free-energy relationship applies to these results, then the conventional values $\sigma_{p\text{-OH}}{}^+$ -0.92, $\sigma_{p\text{-NH}_2}{}^+$ -1.31 lead to ρ − 14.3, $\sigma_{p\text{-O}^-}{}^+$ -1.62. Adoption instead of Hoefnagel and Wepster's preferred values ($\sigma_{p\text{-OH}}{}^+$ -0.91, $\sigma_{p\text{-NH}_2}{}^+$ -1.47) leads instead to ρ -9.94, $\sigma_{p\text{-O}^-}{}^+$ -1.91. On either basis, $\sigma_{p\text{-O}^-}{}^+$ is given a large value, but one which is smaller than our estimated value from solvolysis. It is possible that the difference is real, *i.e.* that the O^--substituent varies by this amount in its activating power for the two reactions. The results for iodination are, however, subject to the difficulty that the true concentration of the iodinating reagent is not known, and must be very small. Since the concentration of the phenoxide ion was also small, it is possible that this rate is in the region where it would be controlled by diffusion, and that the true activating power of the O^--group for iodination is greater than these experiments reveal.

A similar estimate could be made for diazo-coupling if a ρ value for this reaction were known. Thus the rate-sequence below shows the slightly greater activating power of the hydroxy- than of the methoxy-group, and the enormously greater influence of the oxido-group:

Compound	3-Methoxyphenol	1,3-Dihydroxybenzene	3-Methoxyphenolate
Relative rate of diazo-coupling[34]	1.58	3.47	2.1 × 10^8

The additional activation attributable to the O^--group gives a rate acceleration of similar magnitude to that found in iodination; but, as far as we are aware, the ρ value for this reaction is not known and cannot be estimated reliably. If it is *ca.* -10, then $\sigma_{p\text{-O}^-}{}^+$ from this reaction is *ca.* -1.7.

None of these estimates based on chemical methods lead plausibly to a value of $\sigma_{p\text{-O}^-}{}^+$ higher than -2.5. Binev *et al.*[28] have used a dual-parameter approach based on correlations of i.r. frequencies and intensities of nitriles in polar aprotic solvents, and have compared them with carbonyl i.r. frequencies in ketones and esters. Their preferrred treatment gives $\sigma_{p\text{-O}^-}{}^+$ -4.27, with limits -3.99 to -4.53. Such a very high value does not seem to represent well the effect of the O^--substituent on the rates of chemical reactions, and emphasizes the fact that the attempts up to this time to develop a theory of substituent effects applicable both to chemical reactions and to physical properties are still only partially successful.

(h) *The Mechanism of the Formation of Dienones in Aromatic Substitution.*—There exist many electrophilic replacements in phenols which necessarily involve the formation of dienones,[35] and it can be presumed that ring substitutions are often preceded by the formation of these intermediates.[35—37] We showed[4,38] that the bromination of phenol in acetic acid is associated with a solvent deuterium isotope effect, small but sufficient in magnitude to indicate the weakening of the H–O bond in the transition state. Up till now, there has been no evidence on which to base an opinion whether this weakening resulted in proton loss (when the first intermediate would be the dienone) or not (when the first intermediate would be the carbocation). The results presented in the present paper indicate that in the solvolysis of 4-dibromomethylphenols in acidic 95% dioxane the proton is retained in the first intermediate on the reaction path. It seems likely, therefore, that in brominations in acetic acid the proton is also retained in the first intermediate, and that proton-loss to form the dienone is a subsequent reaction. This view is supported by the relatively small magnitude of the observed isotope effect ($k_{\text{HOAc}}/k_{\text{DOAc}}$ 1.8—1.9), which might be expected to be larger if the transition state were such as to allow the breaking of the H–O bond, and is in any case composite of a true solvent isotope effect and a structural isotope effect. The conclusion which we now prefer does not preclude the possibility that under other conditions evidence could be adduced for a synchronous electrophilic attack and proton loss.

References

1 Part 1, P. B. D. de la Mare and P. A. Newman, *J. Chem. Soc., Perkin Trans. 2*, 1984, 231.
2 B. M. Wepster, *Prog. Stereochem.*, 1958, **2**, 99.
3 P. B. D. de la Mare, *Tetrahedron*, 1959, **5**, 107.
4 P. B. D. de la Mare, O. M. H. el Dusouqui, J. G. Tillett, and M. Zeltner, *J. Chem. Soc.*, 1964, 5306.
5 L. Hunter, *Prog. Stereochem.*, 1954, **1**, 223.
6 T. Kojima, *J. Phys. Chem. Jpn.*, 1960, **15**, 284.
7 P. B. D. de la Mare and P. A. Newman, *Tetrahedron Lett.*, 1982, **23**, 1305.
8 J. M. Brittain, P. B. D. de la Mare, and P. A. Newman, *J. Chem. Soc., Perkin Trans. 2*, 1979, 933.
9 C. Paal, *Ber.*, 1895, **28**, 2407.
10 E. P. Kohler and J. B. Conant, *J. Am. Chem. Soc.*, 1917, **39**, 1699.
11 F. Quemeneur, B. Bariou, and M. Kerfanto, *Compt. Rend. Acad. Sci., Ser. C*, 1974, **278**, 299.
12 O. Exner, in 'Correlation Analysis in Chemistry–Recent Advances,' eds. N. B. Chapman and J. Shorter, Plenum Press, New York and London, 1978.
13 H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, 1957, **79**, 1913.
14 S. Clementi and P. Linda, *J. Chem. Soc., Perkin Trans. 2*, 1973, 1887.
15 N. C. Deno and A. Schriesheim, *J. Am. Chem. Soc.*, 1955, **77**, 3051; N. C. Deno and W. L. Evans, *ibid.* 1957, **79**, 5804.
16 S. Winstein, *Tetrahedron Lett.*, 1960, 12.
17 L. Ivnas and B. Lindberg, *Acta Chem. Scand.*, 1961, **15**, 1081.
18 H. H. Jaffe, *Chem. Rev.*, 1953, **53**, 191.
19 R. W. Taft, *J. Phys. Chem.*, 1960, **64**, 1805.
20 M. Charton, *Prog. Phys. Org. Chem.*, 1981, **13**, 119.
21 E. D. Hughes, C. K. Ingold, and N. A. Taher, *J. Chem. Soc.*, 1940, 949.
22 E. S. Lewis and C. E. Boozer, *J. Am. Chem. Soc.*, 1954, **76**, 791.
23 H. Kloosterziel and H. J. Backer, *J. Am. Chem. Soc.*, 1952, **74**, 5306.
24 R. L. Schowen, *Prog. Phys. Org. Chem.*, 1972, **9**, 275.
25 K. T. Leffek, J. A. Llewellyn, and R. E. Robertson, *Can. J. Chem.*, 1960, **38**, 2171.
26 V. J. Shiner, Jr., B. L. Murr, and B. Heinemann, *J. Am. Chem. Soc.*, 1963, **85**, 2413; V. J. Shiner, Jr. and J. S. Humphrey, Jr., *ibid.*, p. 2416.
27 J. G. Jewett and R. P. Dunlop, *J. Am. Chem. Soc.*, 1968, **90**, 809; E. S. Lewis, R. R. Johnson, and G. M. Coppinger, *ibid.*, 1959, **81**, 3140.
28 I. G. Binev, R. B. Kuzmanova, J. Kaneti, and I. N. Jucknovski, *J. Chem. Soc., Perkin Trans. 2*, 1982, 1533.
29 A. Fischer, G. J. Leary, R. D. Topsom, and J. Vaughan, *J. Chem. Soc. B*, 1967, 846.
30 R. A. Robinson, *J. Res. Nat. Bur. Stand.*, 1967, **71**, 213.
31 W. A. Sheppard, *Tetrahedron*, 1971, **27**, 945.
32 A. J. Hoefnagel and B. M. Wepster, *J. Am. Chem. Soc.*, 1973, **95**, 5357.
33 E. Berliner, *J. Am. Chem. Soc.*, 1951, **73**, 4307.
34 O. Macháčková, V. Sterba, and K. Valter, *Collect. Czech. Chem. Commun.*, 1972, **37**, 1851.
35 A. J. Waring, *Adv. Alicyclic Chem.*, 1966, **1**, 129.
36 J. M. Brittain and P. B. D. de la Mare, in 'The Chemistry of Functional Groups, Supplement D,' eds. S. Patai and Z. Rappoport, Wiley, Chichester, 1983, p. 483.
37 O. S. Tee, N. R. Iyengar, and M. Paventi, *J. Org. Chem.*, 1983, **48**, 759.
38 P. B. D. de la Mare and O. M. H. el Dusouqui, *J. Chem. Soc. B*, 1967, 25.

Received 14*th February* 1984; *Paper* 4/257