

93645-05-7; **12**, *t*-BuNH₃ClO₄, 93683-26-2; **13**, 71128-89-7; **16**, 71128-92-2; **17**, 73229-34-2; **18**, 93645-06-8; **19**, 83587-06-8; **20**, 83587-07-9; **21**, 93683-24-0; **22**, 83603-87-6; **23**, 93683-25-1; **24**, 93645-07-9; **25**, 93645-08-0; **26**, 93645-09-1; **27**, 83587-08-0; **28**, 93645-10-4; **29**, 93645-11-5; **30**, 93645-12-6; **31**, 93645-13-7; **32**, 71128-93-3; **33**, 93647-14-8; **34**, 17454-52-3; CH₂=CHCH₂Br, 106-95-6; Br(CH₂)₄Br, 110-52-1; Br(CH₂)₅Br, 111-24-0; Br(CH₂)₃Br, 109-64-8; *t*-BuNH₃ClO₄, 18720-49-5; Li⁺, 17341-24-1; Na⁺, 17341-25-2; K⁺, 24203-36-9; Rb⁺, 22537-38-8; Cs⁺, 18459-37-5; NH₄⁺, 14798-03-9; CH₃NH₃⁺, 17000-00-9; *t*-BuNH₃⁺, 22534-19-6; 3-(hydroxymethyl)-2'-[(2-propen-1-yl)-oxy]-5,5',5''-trimethyl[1,1':3',1'']terphenyl-2,2''-diol, 93645-15-9; di-

ethyleneglycol ditosylate, 7460-84-2; 2'-hydroxy-2,2''-dimethoxy-3,3''-bis(bromomethyl)-5,5',5''-trimethyl[1,1':3',1'']terphenyl, 93645-16-0; diethyleneglycol, 111-46-6; pyridine-2,6-dimethanol, 1195-59-1; 2,6-bis(bromomethyl)pyridine, 7703-74-4.

Supplementary Material Available: Experimental procedures for the syntheses of compounds **2**–**33**, their systematic names, characterization, and a modified method for determining K_a and $-\Delta G^\circ$ values at more dilute concentrations (24 pages). Ordering information is given on any current masthead page.

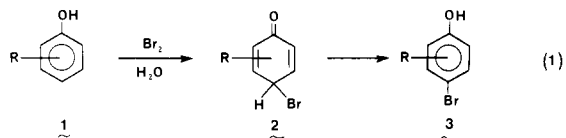
Observation of Transient Cyclohexadienones during the Aqueous Bromination of Phenols. Mechanisms of Enolization

Oswald S. Tee* and N. Rani Iyengar

Contribution from the Department of Chemistry, Concordia University, 1455 de Maisonneuve Quest, Montréal, Québec, Canada H3G 1M8. Received August 14, 1984

Abstract: Transient 4-bromo-2,5-cyclohexadienone intermediates have been observed during the aqueous bromination of phenol and several methylated derivatives. They enolize to the corresponding *p*-bromophenols by both acid-catalyzed and water-catalyzed pathways in the pH range 0–6. Studies carried out in buffers also indicate both general acid catalysis ($\alpha \approx 0.0$) and general base catalysis ($\beta = 0.54$). The latter is ascribed to simple rate-limiting proton abstraction, but the former is not so easily rationalized. The very low α is attributed to a termolecular transition state (water, substrate, and general acid) in which the dienone becomes more *anion-like* than cation-like. This seemingly anomalous behavior can be explained by the very large enol/keto ratio ($\sim 10^{11}$) for phenol.

Various evidence points to the intermediacy of cyclohexadienones in the electrophilic bromination of phenols (eq 1).¹ In particular, Ershov and Volod'kin isolated the dienone **2g** from the reaction of bromine with 2,6-di-*tert*-butylphenol in acetic acid.² Subsequently, its behavior in acetic acid was extensively studied by de la Mare and co-workers.^{1b} Using flow NMR methods, Fyfe and Van Veen observed several such dienones formed from 2,6-dialkylphenols and bromine, also in acetic acid.³



a, parent; b, R = 2-Me; c, R = 3-Me; d, R = 2,6-Me₂; e, R = 3,5-Me₂; f, R = 2,5-Me₂; g, R = 2,6-(*t*-Bu)₂

We recently reported that transient 4-bromo-2,5-cyclohexadienones (**2**) can be observed during the aqueous bromination of simple phenols.⁴ This ability allows, for the first time, a detailed study of the enolization of such dienones in aqueous solution, and such is the subject of the present paper. We have found general acid and general base catalysis, as one might expect by analogy with the enolization of simple ketones.⁵ However, the general acid catalysis observed cannot be explained by simple rate-limiting proton transfer from a general acid or by specific/general base catalysis.

Results

We have observed the transient dienones **2a**–**f** derived from phenol and various methyl derivatives (**1a**–**f**).⁶ We have failed

Table I. Rate Constants for the Enolization of 4-Bromo-2,5-cyclohexadienones (**2**) in Aqueous Acidic Solution;^a See Equation 2

dienone (2)	p <i>K</i> _a of 1 ^b	<i>k</i> ₀ , s ⁻¹	<i>k</i> _H , M ⁻¹ s ⁻¹
parent (2a)	9.95	16.1	111
2-methyl (2b)	10.28	3.22	48.2
3-methyl (2c)	10.08	9.98	36.1
2,6-dimethyl (2d)	10.63	0.572 ^c	3.17
3,5-dimethyl (2e)	10.19	4.81	1190
2,5-dimethyl (2f)	10.41	2.41	169

^aAt 25 °C, *I* = 0.1 M (KBr). ^bFrom: Jencks, W. P.; Regenstein, J. In "Handbook of Biochemistry and Molecular Biology", 3rd ed.; Fasman, G. D., Ed.; CRC Press: Cleveland, Ohio, 1976; Vol. I, p 314. ^cThe average value obtained from the intercepts of buffer plots (*I* = 1.0 M) is 0.425 s⁻¹.

to detect any cyclohexadienones derived from phenols bearing electron-withdrawing groups (see Discussion).

While measuring the rate of bromination of phenol at 265 nm (tribromide ion band), as is customary,⁷ we noted that the final absorbance value tailed downward slightly. However, when the reaction was followed at 275 nm no such tailing was apparent (Figure 1). Furthermore, at 235–240 nm we observed a trace (Figure 1) appropriate to the first-order formation and decay of a transient intermediate.^{8,9} The rate of the increase matches the decrease at 275 nm, and it is proportional to the phenol concentration.¹⁰ The extent of the increase at 237 nm varies in proportion

(6) Dienones arising from ipso bromine attack on *p*-cresol⁴ and other *p*-alkyl phenols have also been detected in this laboratory. Their decomposition, which does not involve enolization,⁴ is being studied separately.

(7) (a) Tee, O. S.; Berks, C. G. *J. Org. Chem.* **1980**, *45*, 830. (b) Tee, O. S.; Paventi, M. *J. Am. Chem. Soc.* **1982**, *104*, 4142. (c) Tee, O. S.; Thackray, D. C.; Berks, C. G. *Can. J. Chem.* **1978**, *56*, 2970.

(8) Moore, J. W.; Pearson, R. G. "Kinetics and Mechanism"; Wiley: New York, 1981; p 290.

(9) The 237-nm trace in Figure 1 can be computer simulated by using the appropriate equation from ref 8 with rate constants of 68 and 14 s⁻¹ and an apparent extinction coefficient for the intermediate of 8900.

(1) (a) de la Mare, P. B. D. "Electrophilic Halogenation"; Cambridge University Press: Cambridge, England, 1976. (b) de la Mare, P. B. D. *Acc. Chem. Res.* **1974**, *7*, 361 and references therein.

(2) Ershov, V. V.; Volod'kin, A. A. *Izv. Akad. Nauk. SSSR, Otd. Khim. Nauk.* **1962**, 730; *Chem. Abstr.* **1962**, *57*, 12337c.

(3) Fyfe, C. A.; Van Veen, L., Jr. *J. Am. Chem. Soc.* **1977**, *99*, 3366.

(4) Tee, O. S.; Iyengar, N. R.; Paventi, M. *J. Org. Chem.* **1983**, *48*, 759.

(5) Toulllec, J. *Adv. Phys. Org. Chem.* **1982**, *18*, 1 and references therein.

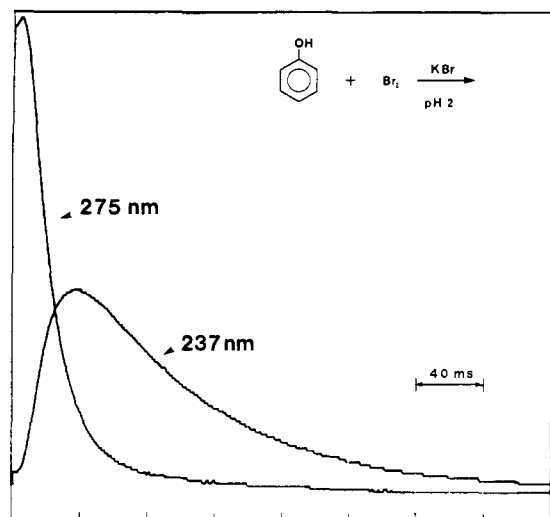


Figure 1. UV absorbance traces obtained during the aqueous bromination of phenol. The decrease at 275 nm is due to the consumption of bromine; the increase and decay at 237 nm are attributed to 4-bromo-2,5-cyclohexadienone (**2a**). Reaction conditions: $[\text{phenol}]_0 = 0.5 \text{ mM}$, $[\text{Br}_2]_0 = 0.05 \text{ mM}$, pH 2, 0.1 M KBr, 25 °C.

to the concentration of the limiting reagent, bromine, and it corresponds to an apparent extinction coefficient of about 9000.⁹

All these observations are consistent with the transient species being 4-bromo-2,5-cyclohexadienone (**2a**) since analogous stable dienones have absorption maxima at 230–260 nm and extinction coefficients around 10 000.^{1b,3,11}

Similar dienones **2b–f** have been detected at 240–260 nm, starting from the methyl-substituted phenols **1b–f**.⁶ Of these the easiest to observe is **2d** since its formation is faster but its decay is much slower. Consequently, curves for its decay are cleanly first order. From the (extrapolated) initial absorbance values at various wavelengths one can construct a spectrum of **2d** which shows a clear maximum at 250 nm and an extinction coefficient of about 8000 (Figure 2).

Since bromination of phenol under aqueous acidic conditions gives 82% para substitution,¹² eq 1 represents the principal pathway. The 2-bromo-3,5-cyclohexadienone, which is presumably involved in the minor amount of ortho bromination, has not been detected. It should absorb around 310 nm with an extinction coefficient of a few thousand.¹³ Analogous "ortho dienones" derived from other phenols have also eluded detection. They probably enolize too fast to permit detection since, in general, 2,4-cyclohexadienones are kinetically less stable than their 2,5-isomers.¹⁴

Analysis of the absorbance–time curves for the dienones **2** gives first-order rate constants (k_{obsd}) which are independent of the initial concentrations of the phenol, bromine, and bromide ion, indicating that formation of the dienones is irreversible on the time scale of the experiments. However, values of k_{obsd} vary with pH (Table S1 and Figure 3), and their acidity dependence may be expressed by eq 2. Appropriate values of k_{H} and k_0 for the dienones **2a–f** are collected in Table I.

$$k_{\text{obsd}} = k_{\text{H}}[\text{H}^+] + k_0 \quad (2)$$

The involvement of water acting as a base in the k_0 process is supported by deuterium solvent isotope effects¹⁵ of 1.6 for **2** at

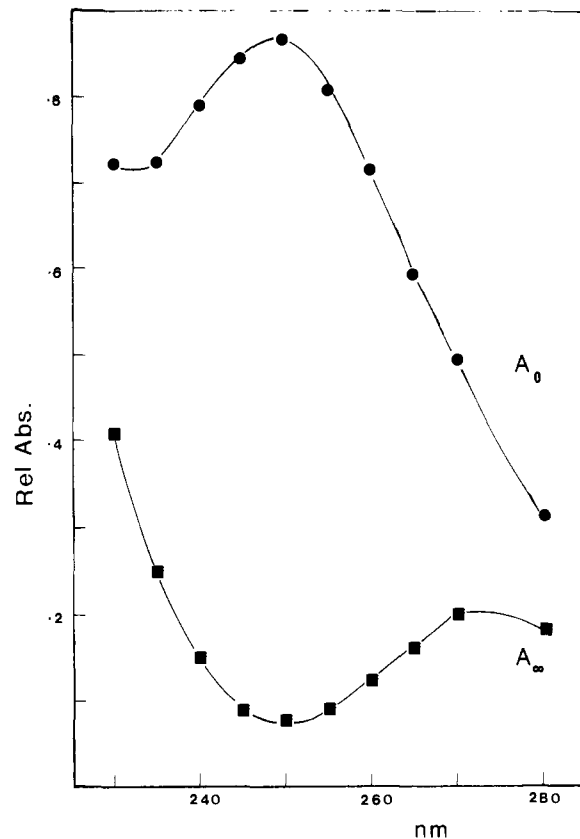


Figure 2. Wavelength dependence of initial and final absorbance values obtained from decay traces for the dienone **2d** derived from 2,6-dimethylphenol (**1d**). Reaction conditions: $[\text{1d}]_0 = [\text{Br}_2]_0 = 0.1 \text{ mM}$, pH 3.42, 0.1 M KBr, 25 °C.

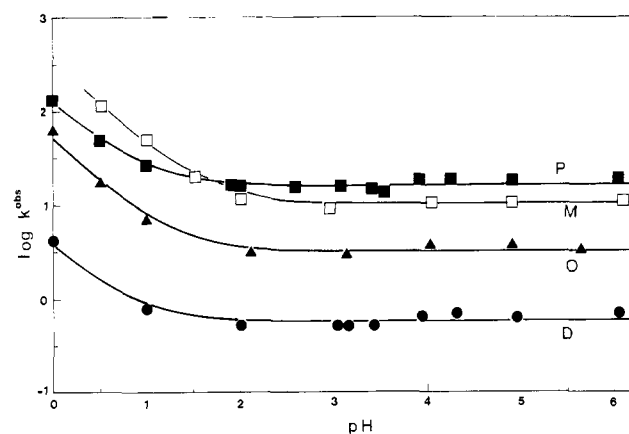


Figure 3. pH–rate profiles for the enolization of 4-bromo-2,5-cyclohexadienones (**2a–d**). The profiles for **2e** and **2f**, which cross those shown, have been omitted for the sake of clarity.

pH (pD) 3.6 and 2.0 for **2d** at pH (pD) 4.3. If the k_{H} process involved specific acid/general base catalysis, with water acting as the base (cf. simple ketones⁵), a solvent isotope effect of <1.0 should be observed.¹⁵ However, for the dienone **2d** at pH (pD) 0.0 we find a value of 1.2, suggesting that some other type of acid catalysis is operative.

Studies carried out on the transient dienone derived from perdeuteriophenol show sizable primary isotope effects. At pH 0, where the term $k_{\text{H}}[\text{H}^+]$ in eq 2 is dominant, the effect is 3.8 whereas at pH 4.4, where the reaction is largely water catalyzed, the effect is 7.8. Clearly then, both k_{H} and k_0 (eq 2) are associated with processes which involve rate-limiting C–H bond rupture, as expected for the enolization **2** → **3**.

(15) Laughton, P. M.; Robertson, R. E. In "Solute–Solvent Interactions"; Coetzee, J. F., Ritchie, C. D., Eds.; Dekker: New York, 1969; Chapter 7.

(10) (a) The disappearance of bromine is second order with a rate constant of $4.2 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$ at 25 °C, $I = 0.1 \text{ M}$ (KBr) pH 0–4.⁴ The literature value of $1.8 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$ (extrapolated to $I = 0$) was admitted to be of low accuracy.^{10b} (b) Bell, R. P.; Rawlinson, D. *J. Chem. Soc.* **1961**, 63.

(11) Cook, K. L.; Waring, A. J. *J. Chem. Soc., Perkin Trans. 2* **1973**, 84.

(12) Paventi, M. Ph.D. Thesis, Concordia University, 1984. Tee, O. S.; Paventi, M., manuscript in preparation.

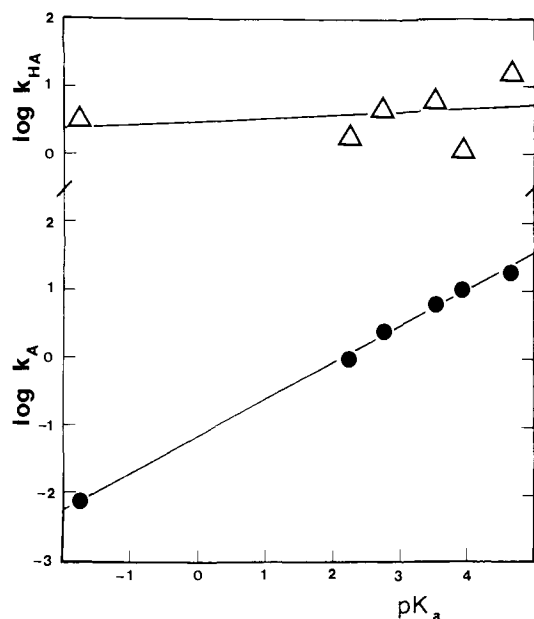
(13) Miller, B. *J. Am. Chem. Soc.* **1970**, *92*, 6246, 6252. Quinkert, G.; Durner, G.; Kleiner, E.; Haupt, E.; Leibfritz, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 556. Lasne, M. C.; Ripoll, J. L.; Denis, J. *Chem. Tetrahedron Lett.* **1980**, *21*, 463.

(14) Fischer, A.; Henderson, G. N. *Can. J. Chem.* **1979**, *57*, 552; **1983**, *61*, 1045. Miller, B. *Acc. Chem. Res.* **1975**, *8*, 245.

Table II. Catalytic Constants for the Enolization of the Cyclohexadienone **2d** Derived from 2,6-Dimethylphenol (**1d**)^a

acid (HA)	pK _a	k _A ^b	k _{HA}
hydronium ion	-1.74	0.00766	3.17
cynoacetic	2.23	0.956	1.97
chloroacetic	2.74	2.64	4.78
methoxyacetic	3.52	6.37	6.50
3-chloropropionic	3.93	10.5	1.21
acetic	4.65	18.2	15.6
(succinate monoanion	5.49	11.9	17.2) ^c

^aAt 25 °C, *I* = 1.0 M (NaCl). pK values are averages from various papers by Jencks (see ref 27c and 36 and references therein). Units of k_A and k_{HA} are M⁻¹ s⁻¹. ^bEquals k₀/55.5, where k₀ = 0.425 s⁻¹, the average value of the intercepts of the buffer plots. ^cOmitted from the Brønsted plots because of the ambiguity of the k_{HA} value; the succinate monoanion may function as both an acid and a base.

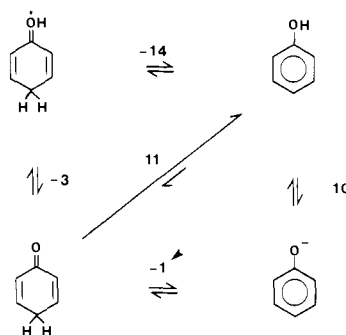
**Figure 4.** Brønsted plots for the catalysis of the enolization of **2d** to **3d**. The upper plot is for general acid catalysis; the lower plot is for general base catalysis.

For the dienone **2d** we have found catalysis by carboxylic acid buffers. Individual buffer plots are strictly linear (Table S2), and analysis of their slopes provided the catalytic constants (k_A and k_{HA}) given in Table II. Thus enolization of the dienone **2d** displays both general acid catalysis and general base catalysis, as does the enolization of simple ketones.⁵

Figure 4 shows the Brønsted plots generated from the data in Table II. The values of k_A give a Brønsted β of 0.54 for general base catalysis which is readily explicable (vide infra). In contrast, the values of k_{HA} show little variation for acids whose pK_as span ~7 pK units (Table II). The Brønsted plot shown (Figure 4, upper) has a slope of 0.05 (SD = 0.08) so that α is essentially 0. This low value is quite unusual for the enolization of a ketone.¹⁶

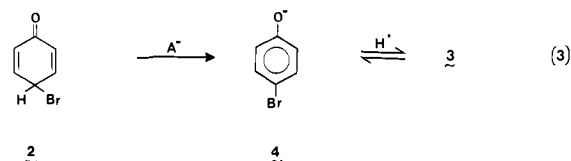
Discussion

From the evidence presented above and its relationship to earlier studies,^{1,3} there seems little doubt that the transients observed in the present work are 4-bromo-2,5-cyclohexadienones (**2**). The finding of pH dependence and buffer catalysis is reasonable for the enolization of **2** to **3**, and the primary isotope effects (PKIEs) determined for the dienone **2a** are very similar to those found by de la Mare and co-workers¹⁷ for the acid- and base-catalyzed decomposition of **2g** in acetic acid and to those found by Gro-

**Figure 5.** The tautomerization of phenol. The numbers refer to pK values estimated in the text. Note the very acidic pK_a of the cyclohexadienone tautomer.

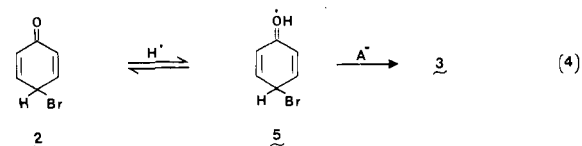
venstein et al.¹⁸ in the aqueous iodination of phenol at high iodide concentration.

Our earlier proposal⁴ that the k₀ term of eq 2 is due to water acting as a general base is supported by the solvent isotope effects and by the Brønsted plot for general bases (Figure 4, lower). The Brønsted β of 0.54 and the PKIE of 7.8 are consistent^{19,20} with general bases abstracting the C₄ proton of **2** in the rate-limiting step (eq 3), with the proton being about half-transferred at the transition state.²¹ The results for general acid catalysis of the



enolization of **2d** to **3d** are more intriguing since they are not so readily explained. They correspond to α ≈ 0.0 for genuine general acid catalysis or β ≈ 1.0 for specific acid/general base catalysis. Neither of these values is compatible with a simple mechanism.

For the protonated form of **2** (viz. **5**, eq 4), we estimate a pK_a < -3, based on the pKs of cyclohexadienones which cannot enolize.^{11,24} Thus, simple rate-limiting proton transfer from the general acids in Table II would be energetically unfavorable and should show a value of α > 0.5.¹⁹ On the other hand, if the reaction involved specific acid/general base catalysis, as shown in eq 4 and as suggested earlier,⁴ the value of β for the depro-



tonation step should be <0.5 for two reasons. First, the proton transfer from **5** to A⁺ would be energetically favorable (vide infra), and second the β for **5** → **3** should be much less than the value of 0.54 observed for **2** → **4**.²⁵ In contrast, the results in Table II correspond to a β of 1.0. The solvent isotope effect of 1.2 found

(18) Grovenstein, E., Jr.; Aprahamian, N. S.; Bryan, C. J.; Gnanaprasam, N. S.; Kilby, D. C.; McKelvey, J. M., Jr.; Sullivan, R. J. *J. Am. Chem. Soc.* **1973**, *95*, 4261.

(19) (a) Kresge, A. J.; *Chem. Soc. Rev.* **1973**, *2*, 475. (b) Kresge, A. J. In "Proton Transfer Reactions"; Caldin, E. F., Gold, W., Eds.; Chapman and Hall: London, 1975; Chapter 7. (c) Bell, R. P. In "Correlation Analysis in Chemistry"; Chapman, N. B., Shorter, J., Eds.; Plenum Press: New York, 1978; Chapter 2.

(20) More O'Ferrall, R. A. In "Proton Transfer Reactions"; Caldin, E. F., Golod, V., Eds.; Chapman and Hall: London, 1975; Chapter 8.

(21) The validity of using a Brønsted exponent as a direct measure of the degree of proton transfer at the transition state may break down when considerable heavy-atom motion is involved or when some of the bond-making and bond-breaking processes are not completely synchronous.^{19b,22,23}

(22) Jencks, W. P. "Catalysis in Chemistry and Enzymology"; McGraw-Hill: New York, 1969; p 240.

(23) Guthrie, J. P. *J. Am. Chem. Soc.* **1980**, *102*, 5286.

(24) Vitullo, V. P.; Grossman, N. *J. Am. Chem. Soc.* **1972**, *94*, 3844.

(25) In support of this contention we note that the α for C-protonation of anisole is 0.71,²⁶ implying that β for the reverse reaction (analogous to **5** → **3**) is 0.29.

(16) Reference 5, p 8.

(17) (a) de la Mare, P. B. D.; Singh, A.; Tillet, J. G.; Zeltner, M. *J. Chem. Soc. B* **1971**, 1122. (b) de la Mare, P. B. D.; Singh, A. *J. Chem. Soc., Perkin Trans. 2* **1972**, 1801. (c) de la Mare, P. B. D.; Singh, A. *J. Chem. Soc., Perkin Trans. 2* **1973**, 59.

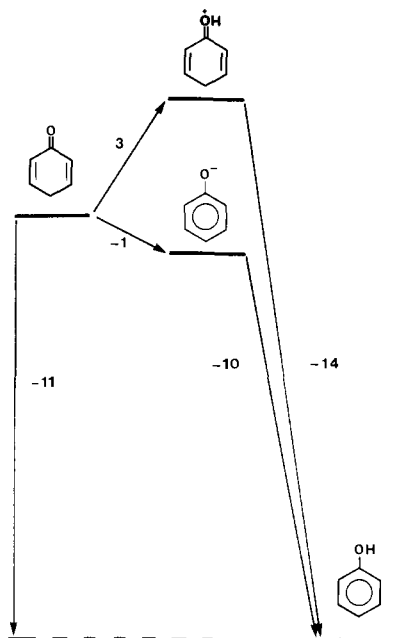
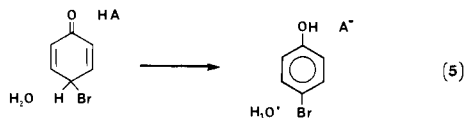


Figure 6. Relative free energies of species involved in the tautomerization of phenol at pH 0. Energies in pK units (1 unit = 1.364 kcal/mol, at 25 °C).

for **2d** at pH 0 also militates against the mechanism¹⁵ shown in eq 4. However, the results for general acid catalysis can be explained by a termolecular mechanism in which water abstracts the C₄ proton of **2** and the general acid HA protonates the incipient phenoxide ion (eq 5). The situation appears to be similar to that



found for the attack of strong nucleophiles on carbonyl groups where general acid catalysis shows α values down to 0.²⁷ Probable origins of such low values have been discussed by Jencks.²⁷

We believe the origin of the enolization mechanism shown in eq 5 lies in the thermodynamics of the tautomerization of phenol (Figure 5). The pK for protonation of phenol on carbon has been estimated by Kresge to be -14,²⁸ whereas for protonation of the oxygen of the 2,5-cyclohexadienone tautomer the pK should be about -3.²⁹ Accordingly, we estimate the enol/keto ratio for phenol in water to be about 10¹¹. Furthermore, since the deprotonation pK_a of phenol is 10, this ratio implies that the C₄ proton of the cyclohexadienone tautomer is very acidic with a pK_a of -1! Thus, even in 1 M HCl (pH \approx 0), where each pK is directly proportional to ΔG_0 for the individual step, the pathway from the dienone to phenol *via the anion* is potentially of lower energy than that *via the cation* (see Figure 6).³⁰ For the observed dienone **2a** the presence of the 4--bromo substituent should stabilize the anion (**4a**) but destabilize the cation (**5a**) and so favor the anionic pathway even more. In particular, the pK_a for the ionization **2a** \rightleftharpoons **4a** should be about -2³¹ so that deprotonation by water should

(26) Kresge, A. J.; Mylonakis, S. G.; Sata, Y.; Vitullo, V. P. *J. Am. Chem. Soc.* **1971**, *93*, 6181.

(27) (a) Reference 22, p 198. (b) Jencks, W. P. *Acc. Chem. Res.* **1976**, *9*, 425. (c) Funderburk, L. H.; Aldwin, L.; Jencks, W. P. *J. Am. Chem. Soc.* **1978**, *100*, 5444.

(28) Kresge, A. J.; Chen, H. J.; Hakka, L. E.; Kouba, J. E. *J. Am. Chem. Soc.* **1971**, *93*, 6174.

(29) The protonation pK of 4,4-dimethyl-2,5-cyclohexadienone is -2.4.¹¹ Without the two methyl groups it should be slightly more negative.

(30) This picture would not change substantially unless the phenol protonation pK of -14 is too negative by 4 or more units. Since this estimate is based on a measured value of -10 for 3,5-dimethylphenol, this seems unlikely.²⁸

(31) A *p*-bromo substituent lowers the pK_a of phenol by 0.6 (see Table I, footnote b).

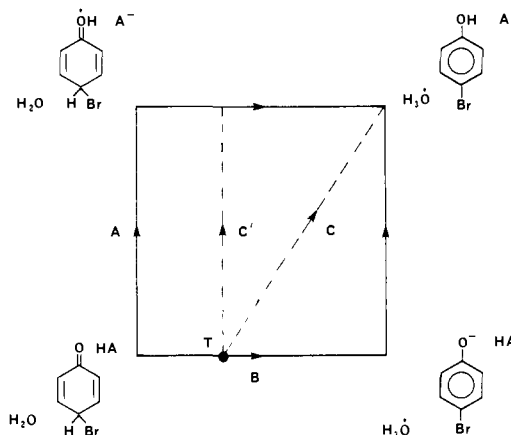


Figure 7. Free energy reaction-coordinate surface³⁶ for the general acid catalyzed enolization of **2** to **3**. The location of the transition state T is based on $\alpha \approx 0$ (vertical direction) and PKIE ≈ 3.8 (horizontal direction).

have $\Delta G_0 \approx 0$, consistent with the observed PKIE of 7.8 for the k_0 process.

Given the free energy relationships shown in Figure 6 it is not surprising that in dilute acid the mechanism of enolization of the dienones **2** differs markedly from that for simple ketones.⁵ In the case of acetone the corresponding relationship are quite different as the enol/keto ratio³² is 10⁻⁸ and the enolization³³⁻³⁵ is energetically uphill.

The proposed mechanism for general acid catalyzed enolization of the dienones **2** (eq 5) is best appreciated by reference to the free energy/reaction coordinate surface³⁶ depicted in Figure 7. Pathway A, reaction via the cation, should be more than 4×1.364 kcal/mol higher in energy than pathway B through the anion. Since we observe general acid catalysis with $\alpha \approx 0$, the actual pathway followed is possibly like that labeled C, with a transition state T that has some anionic character. The catalyzing acid HA, through hydrogen bonding to the incipient phenoxide oxygen, may afford modest stabilization of the transition state^{27b,37} and only transfer its proton after sufficient charge has developed on the oxygen to make the transfer favorable.^{23,38}

A possible variant of this mechanism, kindly suggested to us by Guthrie, is that labeled C' in Figure 7. After sufficient charge has formed on the oxygen the proton "jumps" across the preformed hydrogen bond with only a small barrier,²³ effectively causing a switch from the pathway B to pathway A, thereby avoiding the energy maxima on both these pathways. Such "orthogonal" pathways have been proposed by Guthrie for various reactions showing buffer catalysis.²³

The proposed pathway (C or C', Figure 7) is in essence a preassociation mechanism.^{27b} The product anion **4** can have no real lifetime at low pH³⁹ since proton transfer within encounter complexes (**4**·HA) can occur faster than diffusional separation of the partners.^{27b,39} Accordingly, the general acid HA involved in this transfer must be present before the proton abstraction from C₄ of the dienone **2** which produces the anion **4**.

A kinetic equivalent to the mechanism proposed in eq 5 would be a general base A⁻ abstracting the C₄ proton of **2** with hydronium ion donating a proton to carbonyl oxygen (eq 6). This mechanism can be ruled out in the same way as specific acid/general base

(32) Chiang, Y.; Kresge, A. J.; Tang, Y. S.; Wirz, J. *J. Am. Chem. Soc.* **1984**, *106*, 460.

(33) Tapuhi, E.; Jencks, W. P. *J. Am. Chem. Soc.* **1982**, *104*, 5758.

(34) Guthrie, J. P.; Cossar, J.; Klym, A. *J. Am. Chem. Soc.* **1984**, *106*, 1351.

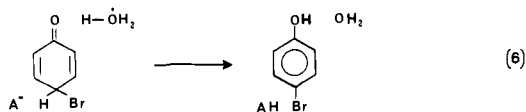
(35) For a detailed analysis of the modes of enolization of acetone see: Albery, W. J. *J. Chem. Soc., Faraday Trans. 1* **1982**, *78*, 1579.

(36) Gilbert, H. F.; Jencks, W. P. *J. Am. Chem. Soc.* **1982**, *104*, 6769.

(37) See ref 22, Chapter 6.

(38) A manifestation of the "libido" rule. See: Jencks, W. P. *J. Am. Chem. Soc.* **1972**, *94*, 4731.

(39) Ridd, J. H. *Adv. Phys. Org. Chem.* **1978**, *16*, 1.



catalysis (eq 4). Any degree of proton transfer to the oxygen of the dienone should lower β below 0.5 (the value for general base catalysis) whereas the observed data require a value of 1.0.

Finally, we discuss the effects of substituents on the enolization and on the ability to observe dienones other than **2a-g**. For the general base catalyzed route (eq 3) it seems reasonable to look for a correlation of rates with the stability of the incipient 4-bromophenoxide ions, **4**. Since the pK_a s of the product phenols **3a-f** are not all available, we have chosen those of the substrate phenols **1a-f** (Table I) in the hope that the effect of a 4-bromo substituent is relatively constant. Indeed, there is quite a good correlation between $\log k_0$ and these pK_a values: the least-squares line has slope (SD) = -2.09 (0.13), intercept (SD) = 22.01 (1.37), and $r = 0.9919$. The magnitude of the slope indicates a significant sensitivity to the pK_a of the starting phenol and, presumably, to that of the product 4-bromophenol also, as anticipated for rate-limiting formation of the anions **4** (eq 3). Clearly, for phenols possessing electron-withdrawing groups, which are more acidic than those studied here, the lifetimes of the cyclohexadienones must be so short as to preclude observation by stopped-flow methods.⁴⁰

For the rate constants for acid catalysis (k_H , Table I) no simple correlation is apparent. This probably reflects the differing and conflicting effects of the methyls at the 2(6)- and 3(5)-positions on the two proton transfers involved in the mechanism shown in eq 5.

Experimental Section

The substrate phenols were all of commercial origin and of the highest purity available. Unless recently purchased, they were recrystallized or distilled before use. Likewise, buffer acids were of the highest quality available.

All buffer solutions were freshly prepared before use since they deteriorate with time and some become reactive toward bromine. Cyanoacetic acid and methoxyacetic acid buffers react noticeably with bromine and so reactions involving these were initiated by mixing the substrate in buffer with bromine in aqueous NaCl in the stopped-flow apparatus.

For the pH dependence studies (Table S1), dilute aqueous HCl solutions were used for pH 0-2 and Perrin's buffers (0.01 M strength)⁴¹ for pH >2. All solutions contained 0.1 M KBr so that the total ionic strength was 0.11 M, except at the highest acidities (pH <2).

For buffer catalysis studies 0.3-0.1 M stock solutions were prepared by using the Henderson-Hasselbach equation and employing pK_a s for 1 M ionic strength (Table II). Buffers of the desired concentration were made by dilution of the stock with 1 M aqueous NaCl so that the total ionic strength was 1 M.

After being mixed in the stopped-flow apparatus the reacting solutions were normally 0.5 mM in substrate and 0.1 mM in bromine (for details see Tables S1 and S2).

Disappearance of each of the intermediates **2** was monitored at an optimum wavelength in the range 235-260 nm relative to little or no change at 320-340 nm. The stopped-flow apparatus, data acquisition system, and data analysis were as in other recent work.^{7,42} The observation cell was maintained at 25.0 ± 0.1 °C by water circulation. Each of the observed first-order rate constants (Tables S1 and S2) is the average of 3-5 kinetic runs differing by <10% and usually <5%.

Acknowledgment. This research was made possible by an operating grant to O.S.T. from the Natural Sciences and Engineering Research Council of Canada. The authors also thank Professors W. J. Albery, J. P. Guthrie, and W. P. Jencks for stimulating comments.

Registry No. **1a**, 108-95-2; **1b**, 95-48-7; **1c**, 108-39-4; **1d**, 576-26-1; **1e**, 108-68-9; **1f**, 95-87-4; **1g**, 128-39-2; **2a**, 84559-79-5; **2b**, 93684-14-1; **2c**, 93684-15-2; **2d**, 84559-81-9; **2e**, 93684-16-3; **2f**, 93684-17-4; **D**₂, 7782-39-0.

Supplementary Material Available: Tables of rate constants for the enolization of **2a-f** as a function of pH (S1) and for the buffer catalysis of the enolization of **2d** (S2) (7 pages). Ordering information is given on any current masthead page.

(41) Perrin, D. D. *Aust. J. Chem.* **1963**, *16*, 572.

(42) Tee, O. S.; Trani, M.; McClelland, R. A.; Seaman, N. E. *J. Am. Chem. Soc.* **1982**, *104*, 7219.

(40) Kulic, J.; Vecera, M. *Collect. Czech. Chem. Commun.* **1974**, *39*, 71.