17829-41-3; $PhCH_2CH(H_3N^+)COOH$, 19665-03-3; 3,4-$(HO)_2PhCHC(CH_3)(H_3N^+)COOH$, 102108-06-5; $H_3N^+(CH_2)_4CH(H_3N^+)COOH$, 17829-44-6; $HOOCCH_2CH_2CH(H_3N^+)COOH$, 17806-34-7; $H_3N^+CH_2CH_2CH_2COOH$, 21029-90-3; $Me_2NH^+CH_2COOEt$ p-TsO^-, 102108-07-6; Me_2NCH_2COOEt, 33229-89-9; $Me_3N^+CH_2COOH$ Cl^-, 590-46-5; $Me_3N^+CH_2COO^-$, 107-43-7; $Me_2NH^+CH_2COOH$ Cl^-, 2491-06-7; $Me_2NH^+CH_2COO^-$, 1118-68-9; $H_3N^+CH_2COO^-$, 56-40-6; $H_3N^+CH_2COOEt$, 33888-04-9; $H_3N^+CH_2CN$, 73900-04-6; MeI, 74-88-4; MeCl, 74-87-3; Me_3PO_4, 512-56-1; MeOTs, 80-48-8; Me_2SO_4, 77-78-1; $PhCH_2Cl$, 100-44-7; $PhCH_2Br$, 100-39-0; LiBr, 7550-35-8; serine, 56-45-1; alanine, 56-41-7.

The Behavior of 4-Alkyl-4-bromo-2,5-cyclohexadienones Formed during the Aqueous Bromination of *p*-Alkylphenols

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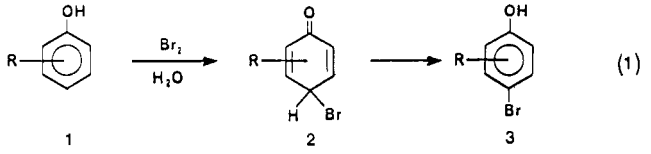
Received December 11, 1985

The title compounds ("ipso-dienones") **5** have been observed during the reaction of bromine with six *p*-alkylphenols **4** (R = Me, Et, *n*-Pr, *i*-Pr, *t*-Bu, 3,4-Me_2) in aqueous solutions of pH 0–3. Their formation by ipso bromine attack on **4** accounts for about 10% of the initial consumption of bromine. The decomposition of **5**, which is catalyzed by H^+ and by Br^-, is attributed to debromination. The rates of this reaction and of the attack of bromine on **4** are not very sensitive to the nature of the alkyl substituents. Studies of the behavior of **5** (R = Me) in buffers give curved buffer plots which provide additional support for the debromination mechanism and also demonstrate general acid catalysis. Decomposition of **5** (R = Me) in the presence of a trap for liberated bromine give straight buffer plots from which a Brønsted $\alpha \simeq 0.27$ is deduced. The ipso-dienone **8**, derived from 5-methylsalicyclic acid, shows intramolecular catalysis by the carboxyl group (EM = 58 M) and no catalysis by buffer acids.

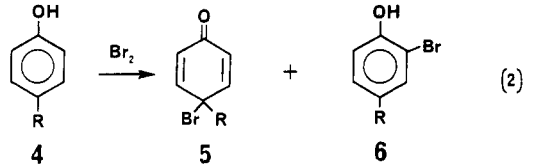
Recently, we showed that transient 4-bromo-2,5-cyclohexadienones **2** (eq 1) can be observed in the aqueous bromination of phenol and phenols bearing methyl groups at positions 2, 3, 5, and/or 6 (**1**).[1,2] This ability allowed



(1)

1 2 3

us to carry out a detailed study of the enolization of such dienones (**2** → **3**).[2] Our initial studies[1] also revealed that some ipso attack occurs in the bromination of *p*-cresol, resulting in the formation of a kinetically unstable 4-alkyl-4-bromo-2,5-cyclohexadienone (**5**, eq 2). The present paper describes more extensive studies on the breakdown of such "ipso-dienones" in dilute aqueous acidic solution.

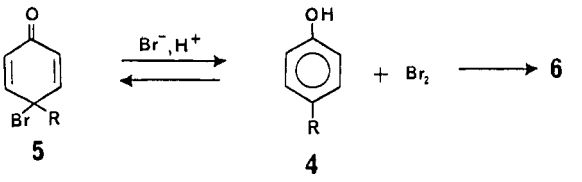


(2)

4 5 6

The occurrence of ipso halogen attack on 2,4,6-trisubstituted phenols has long been known.[3] Moreover, such attack must occur in electrophilic substitution reactions

Scheme I



5 4

in which halogen replaces a substituent other than hydrogen.[6] That it can also be of significance in the halogenation of simple *p*-alkylphenols has recently been demonstrated by Fischer and Henderson.[4,5] They were able to isolate chloro analogues of **5** from various organic media[4] but not the bromo derivatives which proved to be too labile.[5] These studies suggested to us that the dienones **5** are probably formed during the aqueous bromination of *p*-alkylphenols but that they had escaped attention up to now because of their lability. Our findings support this view and provide information about their mode of breakdown.

Results

The transient dienones **2** have absorption maxima at 230–260 nm with extinction coefficients of about 10 000, in accord with the values found for analogous stable structures.[1,2] Therefore, using stopped-flow UV spectrophotometry, we monitored the region around 250 nm during the course of the reaction of bromine with an excess of *p*-cresol (**4**, R = Me) in aqueous solutions of pH 0–3. After the initial fast consumption of bromine ($k_2 = 6.2 \times 10^5$ M^{-1} s^{-1}),[7] there is a slower decrease in absorbance which

(1) Tee, O. S.; Iyengar, N. R.; Paventi, M. *J. Org. Chem.* **1983**, *48*, 759.
(2) Tee, O. S.; Iyengar, N. R. *J. Am. Chem. Soc.* **1985**, *107*, 455.
(3) (a) de la Mare, P. B. D. *Electrophilic Halogenation*; Cambridge University: Cambridge, England, 1976. (b) de la Mare, P. B. D. *Acc. Chem. Res.* **1974**, *7*, 361. (c) Waring, A. J. *Adv. Alicyclic Chem.* **1966**, *1*, 129. (d) Ershov, V. V.; Volod'kin, A. A.; Bogdanov, G. N. *Russ. Chem. Rev. (Engl. Transl.)* **1963**, *32*, 75. (e) Brittain, J. M.; de la Mare, P. B. D. In *The Chemistry of Functional Groups*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1983; Supplement D, Chapter 12. (f) Additional background references are given by Fischer and Henderson.[4,5]
(4) Fischer, A.; Henderson, G. N. *Can. J. Chem.* **1979**, *57*, 552.
(5) Fischer, A.; Henderson, G. N. *Can. J. Chem.* **1983**, *61*, 1045.
(6) Norman, R. O. C.; Taylor, R. *Electrophilic Substitution in Benzenoid Compounds*; Elsevier: London, England, 1965.

0022-3263/86/1951-2585$01.50/0

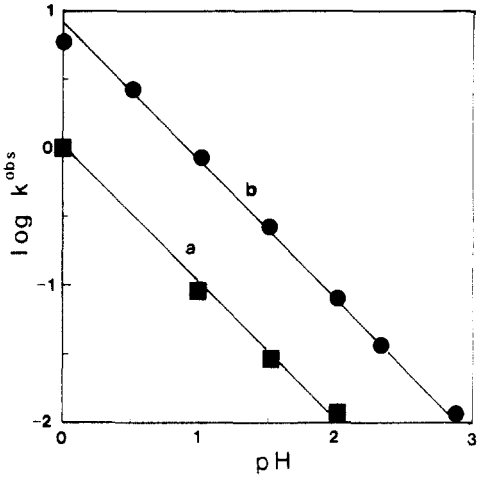


Figure 1. Rate constants for the decomposition of **5** (R = Me) in aqueous acidic solutions containing (a) 0.1 M KBr or (b) 1.0 M KBr. Similar data were obtained for other **5** (see Table S1, supplementary material).

is ascribed to the decay of the ipso-dienone **5** (R = Me).

The extent of this slow absorbance change is about 10% of that expected if all of the bromine were to be converted to **5** (R = Me), assuming that $\epsilon = 10000$. Therefore, as an initial estimate, the attack of bromine on *p*-cresol is partitioned between ~90% ortho attack (which leads rapidly[8] to the *o*-bromo product **6**) and ~10% para (ipso) attack which results in the formation of the dienone **5** (R = Me). Also, the size of the absorbance change associated with the decay of **5** (R = Me) varies in direct proportion to the concentration of the limiting reagent, bromine but is independent of the concentration of the *p*-cresol which is present in excess. These observations are consistent with the initial formation of the dienone **5** (R = Me) being essentially irreversible on the time scale of the bromine attack.

The decay of the absorbance attributed to the ipso-dienone **5** (R = Me) is first order (at fixed pH and $[Br^-]$), and the observed rate constants (k_{obsd}) are invariant to changes in the *p*-cresol or bromine concentrations. However, the values of k_{obsd} do vary with pH and with $[Br^-]$. Figure 1 shows pH–rate profiles obtained at two different bromide ion concentrations which clearly indicate that the disappearance of **5** (R = Me) is catalyzed by H^+ and by bromide ion.

Since the product of the decay of **5** (R = Me) is 2-bromo-4-methylphenol[10] (**6**, R = Me), the simplest mechanism to explain the above results is that set out in Scheme I. In this mechanism the ipso-dienone **5** breaks down by debromination[11] back to substrate **4** and bromine. The bromine is then repartitioned between ortho attack (~90%), leading to **6**, and ipso attack (~10%), and so eventually all of it is converted to **6**. In terms of the overall reaction (**4** + Br_2 → **6**) then, the formation of the ipso-dienone **5**, under the present conditions, is a minor diversion: a dead-end from which the only way out[12] is by reversal.

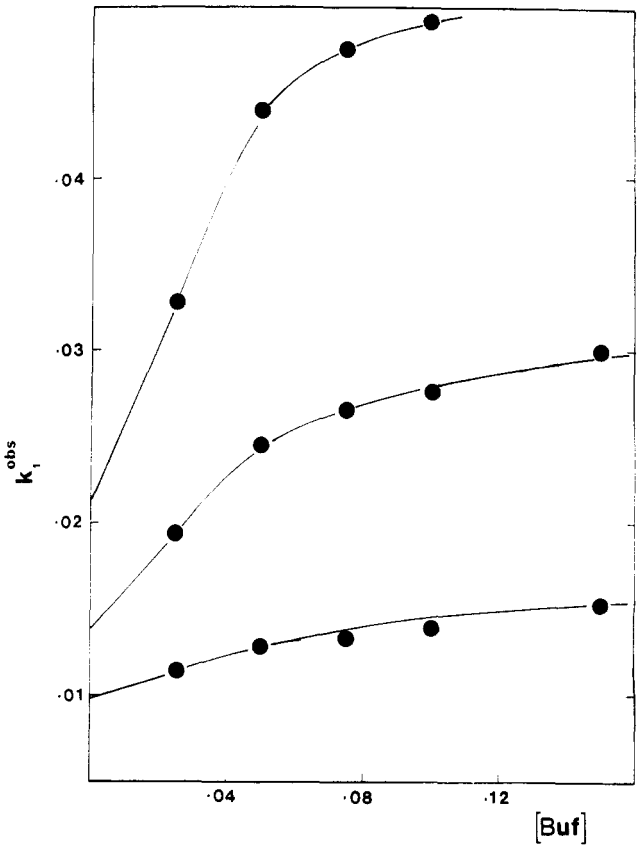


Figure 2. Rate constants for the decomposition of **5** (R = Me) generated in cyanoacetate buffers of pH 1.73 (upper curve), 2.24 (middle), and 2.52 (lower). Similar curved plots were obtained for chloroacetate buffers (see Table S2, supplementary material).

In the isomerization of **5** to **6** (Scheme I) the liberated bromine can be treated as a steady-state intermediate[15] since it is formed slowly but consumed rapidly. For this situation, with the rate constants[16] as set out in eq 3, the

$$5 + H^+ + Br^- \underset{k_p}{\overset{k_d}{\rightleftharpoons}} 4 + Br_2 \xrightarrow{k_0} 6 \qquad (3)$$

$$k_{obsd} = \frac{k_d k_0 [H^+][Br^-]}{(k_0 + k_p)} \qquad (4)$$

expected form of the observed rate constant is as given by eq 4.[17] This expression is consistent with the observed dependence of k_{obsd} on pH and bromide ion (Figure 1 and Table S1, supplementary material).

The behavior described above for *p*-cresol and rationalized by Scheme I has been found for five other *p*-al-

(7) Tee, O. S.; Iyengar, N. R.; Kraus, B. *J. Org. Chem.* **1985**, *50*, 973. Values of k_2 are corrected for tribromide ion formation.

(8) We have been unable to detect the 2-bromo-4-methyl-3,5-cyclohexadienone which is presumably involved in the ortho bromination of *p*-cresol and likewise analogous "*o*-dienones" derived from other phenols. They probably enolize faster than **2**[2] since, in general, *o*-dienones are more labile than *p*-dienones.[4,5,9]

(9) Miller, B. *Acc. Chem. Res.* **1975**, *8*, 245.

(10) From isolation experiments the only organic product was **6** (R = Me). From spectral studies the majority of this (ca. 90%) is formed during the initial fast attack of bromine and the remainder as the result of the decay of the ipso-dienone **5** (R = Me).

(11) Cf.: Banerjee, S.; Tee, O. S. *J. Org. Chem.* **1974**, *39*, 3120. This reference describes studies on the debromination of some bromopyrimidinones.

(12) In strong acids (e.g., triflic acid) some ipso-dienones undergo an acid-catalyzed [1,2] shift to give a meta-substituted product (see ref 3e, 5, 9, 13, and 14 and references therein). This reaction, however, does not require halide ion.

(13) Fischer, A.; Henderson, G. N. *J. Chem. Soc., Chem. Commun.* **1979**, 279.

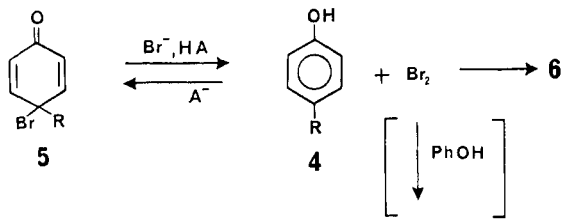
(14) Brittain, J. M.; de la Mare, P. B. D.; Newman, P. A.; Chin, W. S. *J. Chem. Soc., Perkin Trans. 2* **1982**, 1193.

(15) Even though the substrate **4** is present in excess it also may be treated as a steady-state species since its concentration remains constant during the course of **5** → **6**.

(16) The subscripts indicate: d, debromination; o, ortho attack; p, para (ipso) attack.

(17) Bromine and Br^- are also involved in the equilibrium formation of tribromide ion. However, this affects the k_0 and k_p steps to exactly the same extent and so cancels from the expression.

Scheme II



kylphenols (4, R = Me, Et, *n*-Pr, *i*-Pr, *t*-Bu, 3,4-Me_2) (see data in Table S1), but it is not found for 2,4-dimethylphenol.[18] The five substrates listed above all react rapidly with bromine ($k_2 > 5 \times 10^5$ M^{-1} s^{-1}), but again only about 10% of the bromine appears to be converted to the respective dienone **5**. Moreover, as shown in Table I, the rates of decomposition of the various ipso-dienones are all quite similar.

The enolization of the dienones **2** to **3** is catalyzed by general acids and shows a low Brønsted $\alpha \simeq 0$.[2] In view of the chemical similarity of this reaction to the debromination of the ipso-dienones **5**, we have also investigated the behavior of **5** (R = Me) in buffers. When this dienone is formed and allowed to decompose in solutions of varying buffer strength curved buffer plots are obtained as shown by the examples in Figure 2. As discussed below, these curved plots provide additional support for the debromination mechanism and also show that the reaction is catalyzed by buffer acids.

If the breakdown of **5** is catalyzed by the buffer acid (HA) then, according to the principle of microscopic reversibility, the formation of **5** from **4** and bromine must be catalyzed by the buffer base (A^-),[19] as shown in eq 5 and Scheme II. Correspondingly, the equation for k_{obsd} (eq

$$5 + HA + Br^- \underset{k_p^A}{\overset{k_d^{HA}}{\rightleftharpoons}} 4 + A^- + Br_2 \xrightarrow{k_0} 6 \qquad (5)$$

4) must be replaced by the more complex expression shown in eq 6[17] which represents the sum of the reactions depicted in eq 3 and 5. This expression gives rise to curved buffer

$$k_{obsd} = \frac{(k_d[H^+] + k_d^{HA}[HA])k_0[Br^-]}{(k_0 + k_p + k_p^A[A^-])} \qquad (6)$$

plots at fixed pH since k_{obsd} approaches a plateau value for high concentrations of the buffer. Analysis of the data in terms of eq 6 is difficult unless one has reliable values for the intercept and/or plateau values of k_{obsd}. To overcome this difficulty we designed and executed a series of experiments in which the curvature of the buffer plots is removed.

If, as proposed in eq 3 and 5, the dienones **5** decompose by liberating bromine then efficient trapping of this bromine should eliminate the back reaction **5** ← **4** + Br_2, and

$$5 + Br^- \xrightarrow[k_d^{HA}[HA]]{k_d[H^+]} 4 + Br_2 \xrightarrow{\text{trap}} \qquad (7)$$

the forward reaction should become solely rate-limiting (eq 7 and Scheme II). Under these circumstances the form

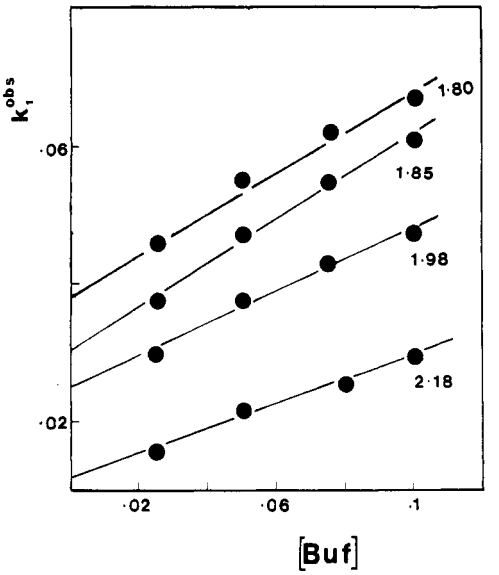


Figure 3. Rate constants for the decomposition of preformed **5** (R = Me) in cyanoacetate buffers containing phenol as a trap for liberated bromine. pHs were as indicated.

of k_{obsd} should simply be as in eq 8 and linear buffer plots should be obtained.

$$k_{obsd} = (k_d[H^+] + k_d^{HA}[HA])[Br^-] \qquad (8)$$

To carry out the appropriate type of experiments **5** (R = Me) was preformed from *p*-cresol and bromine in the absence of added bromide ion and in a weak acetate buffer of pH 4–5. Because the rate of decay of **5** depends on $[H^+]$ and $[Br^-]$, this approach provides solutions of **5** (R = Me) which are stable enough for further experimentation.[20] Such solutions were mixed in the stopped-flow apparatus with a series of cyanoacetate buffers containing a fixed concentration of Br^- and an excess of phenol as the trap for liberated bromine.[21] As shown by Figure 3 the use of this procedure gives buffer plots which are essentially straight[22] and from which one can calculate a value of k_d^{HA}. Moreover, the very fact that the approach works provides additional support for the debromination mechanisms involving liberated bromine (Schemes I and II).

Trapping experiments carried out in dilute HCl (described below) yield a value of $k_d = 8.9$ M^{-2} s^{-1} ($I = 1.0$ M) for the catalytic coefficient of the proton. From the variation of the slopes of the buffer plots (Figure 3) with pH (Table S3, supplementary material) we obtain a value of $k_d^{HA} = 0.76$ M^{-2} s^{-1} ($I = 1.0$ M) for catalysis by cyanoacetic acid. Using these two rate constants, we estimate a Brønsted α of 0.27 for the debromination of **5** (R = Me).

Bromine trapping experiments also furnish a better way of estimating the fractions of ortho and para (ipso) bromine

(18) The reaction of 2,4-dimethylphenol with aqueous bromine is more complex: two kinetic phases are observable, after the initial consumption of bromine, and the variations of each with pH, $[Br^-]$, and the initial concentrations of the reagents are not simple (Takasaki, B. K.; Tee, O. S., unpublished results).

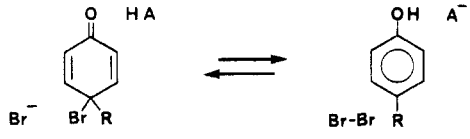
(19) If the formation of **5** from **4** + Br_2 is catalyzed by general bases it is likely that the formation of **6** is also. For the sake of simplicity and since the present data do not clearly require it, this likelihood is ignored in eq 5 and 6. However, the possibility is considered again in the Discussion.

(20) This approach was originally employed to study the effect of cyclodextrins on the decompositions of **5** (Bennett, J. M.; Tee, O. S., unpublished results).

(21) Other traps were tried, but they led to problems due to their spectral properties or side reactions. Furthermore, one must avoid bromine traps which are "too" reactive since they may abstract Br^+ from **5** directly (e.g., I^-) and so subvert the desired experiments. Phenol seemed a reasonable choice since it is almost as reactive toward bromine as *p*-cresol (rate ratio 4.2:6.2),[1,7] and so, when it is present in reasonable excess, it can compete effectively with the latter for bromine. Values of k_{obsd} for the decomposition of **5** increase and level off as the concentration of phenol is raised to 1 mM. This behavior is consistent with bromine trapping and not with direct attack of phenol on **5**.

(22) Some of the plots curve slightly at the highest buffer concentration, suggesting that the trapping of Br_2 is not 100% efficient. Nonetheless, we feel that the experiments are convincing confirmation of the debromination mechanism and that the plots yield a reasonable estimate of the catalytic coefficient for cyanoacetic acid.

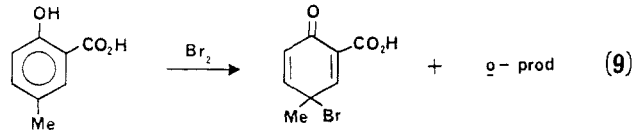
Scheme III



5 4

attack. Decomposition of preformed **5** (R = Me) in aqueous 0.1 M HCl + 0.4 M NaCl + 0.5 M KBr (total I = 1.0 M) containing 1 mM phenol (as the bromine trap) gave k_{obsd} = 0.447 s^{-1}. This value represents the intercept term of eq 8, namely, $k_d[H^+][Br^-]$. From a similar experiment carried out *without* a bromine trap, where eq 4 is valid, a value of k_{obsd} = 0.410 s^{-1} was obtained. Division of the latter rate constant by the former yields the fraction of ortho attack as $k_o/(k_o + k_p)$ = 0.410/0.447 = 0.92 and hence that there is 8% of ipso (para) attack by bromine on *p*-cresol. We feel that this value is better than the initial estimate of 10%, which was based on a guess of the extinction coefficient for the dienone **5** (R = Me).

Having found catalysis of the decomposition of **5** (R = Me) by carboxylic acids, we also considered that it might be possible to find intramolecular catalysis in an ipso-dienone bearing a suitably placed carboxyl group. Therefore, as reported recently in a paper on the bromination of salicylate ions,[23] we have studied the behavior of the ipso-dienone **8** derived from the reaction of bromine with 5-methylsalicylic acid (**7**, eq 9). From the pH–rate



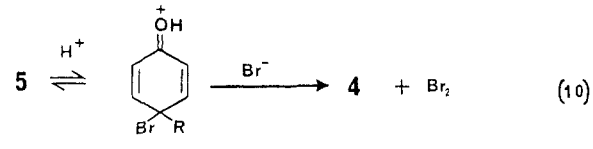
7 8 (9)

profile for the decomposition of **8**[23] it was concluded that the internal carboxyl group does catalyze the reaction since, if the reaction involved H^+ catalysis on the anion of **8**, this anion would have to be 2300 times more reactive than **5** (R = Me). Moreover, *no* catalysis by external general acids was found for **8**.[23]

Discussion

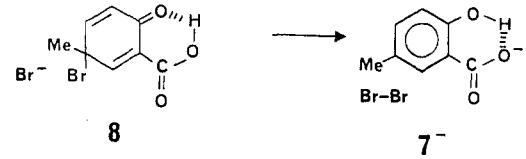
On the evidence given above, the ipso-dienones **5** are formed during the bromination of *p*-alkylphenols **4** in aqueous solutions of low pH, but they only account for about 10% of the initial consumption of bromine. Under the reactions conditions they are labile and they decompose by debromination which is induced by Br^- and catalyzed by the proton and general acids (Schemes I and II). As a consequence they are converted to the *o*-bromo products **6** (eq 3 and 5).

Previously,[1] it was suggested that the proton catalysis arises from bromide ion attack on the protonated form of **5** (**9**, eq 10). However, since we have now found catalysis by carboxylic acids as well, it seems more reasonable to propose a mechanism of debromination in which bromide



9 (10)

Scheme IV



8 7^-

ion attack and proton transfer occur within the same encounter complex[24] (Scheme III). This mechanism provides a route from **5** to **4** which avoids the protonated form **9**. The low Brønsted α of 0.27 implies a small but significant amount of HA bond rupture at the transition state of the reaction although it is not mandatory that proton transfer and bromide ion attack be completely synchronous.

Support for the type of mechanism depicted in Scheme III comes from the behavior of the ipso-dienone **8**, generated from bromine and 5-methylsalicylic acid.[23] With this species, which does *not* exhibit catalysis by external carboxylic acids, the internal carboxyl group facilitates reaction and the rate data are consistent with intramolecular catalysis (Scheme IV). Furthermore, from the rate data for **8**, its pK_a of 3.06, and the Brønsted α of 0.27 obtained in the present work, one can calculate an effective molarity[25] of 58 M for the internal COOH.[23] This value is modest but quite reasonable for a process involving intramolecular general acid catalysis.[25]

The conclusions reached with respect to the debromination of **5** and **8** obviously have implications with respect to the reverse reactions: the ipso attack of bromine on **4** and **7**, respectively. In the latter case, Scheme IV requires that the attack of bromine on the anion 7^- be catalyzed by the ortho carboxylate group. This conclusion is supported by our recent studies of various salicylic acid derivatives which indicate an enhanced reactivity of salicylate ions toward bromine.[23]

As pointed out earlier, the principle of microscopic reversibility also requires that the ipso attack of bromine on **4** be general base catalyzed if the debromination of **5** is general acid catalyzed. We have looked for buffer catalysis of bromine attack (ortho + ipso) on *p*-cresol and do find evidence for it. However, the reactivity of the substrate requires working near the limits of the stopped-flow apparatus, and so the results are not of sufficient quality for proper analysis. Studies are in progress using less reactive substrates to try to circumvent this problem.

The present results also supply the information required to work out an equilibrium constant for ipso attack of bromine on *p*-cresol (eq 11).

$$4 + Br_2 \overset{K}{\rightleftharpoons} 5 + H^+ + Br^- \qquad (11)$$

For the equilibrium shown in eq 11 we define

$$K = \frac{k_p}{k_d} = \frac{[5][H^+][Br^-]}{[4][Br_2]} \qquad (12)$$

A value of $k_p = 5.0 \times 10^4$ M^{-1} s^{-1} is obtained from the rate constant for bromine attack on *p*-cresol[7] and the fraction of ipso attack (0.08), evaluated above. From the trapping experiments carried out in dilute acid we get k_d = 8.9 M^{-2} s^{-1} and so K = 5600 M (at 25 °C and I = 1.0 M).

The high value of K means that, except for highly acidic media containing high bromide ion and low substrate concentrations, the right-hand side of the equilibrium (eq 11) is favored. Moreover, rate measurements show that toward neutral pH and at low Br^- concentrations the

(23) Tee, O. S.; Iyengar, N. R. *J. Org. Chem.* **1985**, *50*, 4468.

(24) Ridd, J. H. *Adv. Phys. Org. Chem.* **1978**, *16*, 1.
(25) Kirby, A. J. *Adv. Phys. Org. Chem.* **1980**, *17*, 183.

Table I. Rate Constants for the Decomposition of the Ipso-dienones 5 in Aqueous Acid[a]

R	k_{obsd}, s^{-1}	R	k_{obsd}, s^{-1}
Me	1.01	*i*-Pr	0.755
Et	0.624	*t*-Bu	1.08
n-Pr	1.29	3,4-Me_2	2.00

[a] At 25 °C, in 1.0 M HCl containing 0.1 M KBr. Values of k_{obsd} vary with pH and [Br^-], as described for **5** (R = Me). More extensive data are given in Table S1 (supplementary material).

ipso-dienones **5** can be sufficiently long-lived as to permit other reactions to be carried out (as evidenced by the trapping experiments). Note, however, that at some point the decrease in the rate of decay of **5** with increasing pH will level out when unassisted attack of Br^- on **5** takes over. This reaction is the microscopic reverse of ipso bromine attack on the anion of **4** (eq 13) which is anticipated since reaction between bromine and phenoxide ions is well documented.[26,27] Furthermore, at low Br^- there may well be pathways for debromination of **5** involving attack by H_2O or OH^-.[28]

$$\mathbf{5} + Br^- \rightleftarrows \mathbf{4}^- + Br_2 \rightarrow \mathbf{6} \qquad (13)$$

As noted earlier, the rates of debromination of **5** are not particularly sensitive to the size of the alkyl group R (Table I). This also seems to be true for the step which forms **5** since the rates of bromine attack ($k_0 + k_p$) for **4** (R = Me) and **4** (R = *t*-Bu) are very close (6.2×10^5 and 5.9×10^5 M^{-1} s^{-1})[7] and the fraction of ipso attack appears to be about 10% in all the cases considered. Taken as a whole, these observations mean that the value of K (eq 12) is very similar for the various substrates studied.

Under the reaction conditions used (pH 0–3, [Br^-] = 0.1–1.0 M, [**4**] $\simeq$ 1 mM) the right-hand side of the equilibrium in eq 11 is favored by 1.0–6.5 kcal/mol (for R = Me). Thus, the conversion of **5** to **4** is slightly endoergonic, whereas the enolization of **2** to **3** (eq 1) is highly exoergonic.[2] Therefore, despite the formal similarity of the two reactions, mechanistic differences between them are to be expected because of their different thermochemistries. Indeed, for the conversion of **5** to **4** we have found a Brønsted α of 0.27, whereas for **2** to **3** it is 0.[2]

As final points we consider the related questions of halogen attack at ipso and nonipso positions and the effect of *p*-alkyl substituents on reactivity. In the case of *p*-cresol (**4**, R = Me) 8% of the bromine attack occurs ipso to the methyl group, and so $k_{ipso} = (0.08)(6.2 \times 10^5) = 5.0 \times 10^4$ M^{-1} s^{-1}. For comparison, phenol ($k_2 = 4.2 \times 10^5$ M^{-1} s^{-1})[1,27] undergoes 82% para attack[27] and hence $k_{para} = 3.4 \times 10^5$ M^{-1} s^{-1}. Thus, ipso attack in *p*-cresol is 6.8 times slower than para attack in phenol. In view of its similar k_2 and fraction of ipso attack, a comparable figure must also apply to *p-tert*-butylphenol. These findings parallel those of Baciocchi and Illuminati who measured the rates of bromine attack on 2,6-di-*tert*-butyl-4-R-phenols in acetic acid.[29] They found that for R = Me or *t*-Bu the reaction is about 4 times slower than for R = H.

The introduction of a *p*-alkyl substituent into phenol clearly has two opposing effects on bromine attack: it raises the intrinsic reactivity of the substrate, but it also removes the most reactive position (para) and replaces it with a less reactive one (ipso). Thus, in the case of *p*-cresol the ortho positions are 7.5 times more reactive than those of phenol, while the ipso (para) position is 6.8 times less reactive. The net result is that *p*-cresol is only 1.5 times more reactive toward bromine than is phenol. Again, a similar situation pertains to *p-tert*-butylphenol which has a similar reactivity to *p*-cresol.[7]

Experimental Section

All of the starting phenols were of the highest purity available from Aldrich. Any old or discolored samples were distilled or recrystallized before use. Other reagents were likewise of the highest purity available. Water was deionized and distilled from glass.

Buffer solutions and bromine solutions were made up according to standard practice in this laboratory.[2,7,23,30] Unless specified otherwise, all of the aqueous solutions contained a fixed concentration of KBr for reasons given earlier.[31]

The initial experiments were carried out by mixing in a stopped-flow apparatus a substrate solution (0.4, 1.0, or 2.0 mM) with bromine (0.1 or 0.2 mM), both in the desired aqueous medium. For buffers that slowly react with bromine[2] only the substrate solution contained the buffer before mixing.

For the trapping experiments carried out in buffers a solution of preformed **5** (R = Me) was generated from *p*-cresol (0.8 mM) and bromine (0.8 mM) in 1 mM aqueous sodium acetate. This solution, which deteriorates slowly, was then mixed in the stopped-flow apparatus with a buffer solution containing KBr, NaCl, and 0.8 mM phenol (as the trap for liberated bromine). The final ionic strength was 1.0 M (due to 0.5 M KBr + NaCl + buffer). Similar experiments were also carried out by using dilute HCl in place of buffers (see Results). For reactions conducted in buffered media the quoted pHs are all final measured values. For dilute HCl solutions we have simply used pH = −log [HCl].

The decomposition of the dienones **5** was monitored at an optimum wavelength near 250 nm relative to little or no change at 320–340 nm by using an Aminco-Morrow stopped-flow accessory on an Aminco DW-2 spectrophotometer. The observation cell was thermostated at 25.0 ± 0.1 °C. For fast runs the absorbance signal traces were captured with a Biomation 805 waveform recorder and transferred to an Apple II microcomputer as described previously.[32] For slower runs the output voltage of the spectrophotometer was recorded by using a Cyborg Isaac 91a connected to the Apple II. Analysis of the absorbance data covering ~90% reaction followed standard practice.[30–32] Each of the observed rate constants (k_{obsd}) is the average of three to five runs differing by <10% and usually by <5%.

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Registry No. **4** (R = Me), 106-44-5; **4** (R = Et), 123-07-9; **4** (R = Pr), 645-56-7; **4** (R = *i*-Pr), 99-89-8; **4** (R = *t*-Bu), 98-54-4; **4** (R = 3,4-Me_2), 95-65-8; **5** (R = Me), 84559-80-8; **5** (R = Et), 102260-53-7; **5** (R = Pr), 102260-54-8; **5** (R = *i*-Pr), 102260-55-9; **5** (R = *t*-Bu), 102260-56-0; **5** (R = 3,4-Me_2), 102260-57-1; **7**, 89-56-5; **8**, 102260-58-2.

Supplementary Material Available: Tables of rate constants for the decomposition of the dienones **5** (R = Me, Et, *n*-Pr, *i*-Pr, *t*-Bu, 3,4-Me_2) as a function of pH (Table S1) and for the decomposition of **5** (R = Me) as a function of buffer concentration at various pHs in the presence and absence of a bromine trap (Table S2 and S3) (4 pages). Ordering information is given on any current masthead page.

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