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# Base-Strength Effects in Syn Eliminations from *trans*-2,3-Dichloro-2,3-dihydrobenzofuran in Dimethyl Sulfoxide

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Syn eliminations from *trans*-2,3-dichloro-2,3-dihydrobenzofuran (1), to give 3-chlorobenzofuran, promoted by substituted phenoxides (substituents: $p$-$CH_3$, H, $p$-Br, $p$-Cl, $m$-$NO_2$) and 4-chloro-2-nitroanilide anion have been investigated in 99% $Me_2SO$. The reaction rate is very sensitive to the base strength, and from the Brønsted plot a $\beta$ value of 0.67 can be calculated. Introduction of a chlorine substituent at the 5-position causes a 19-fold rate increase for the reaction with phenoxide ions, and with the same base a $k_H/k_D$ value (in comparison with the 3-deuterated counterpart of 1) of 2.4 is observed. These values clearly suggest that the reaction of 1 occurs by a highly carbanionic transition state. The substituent effect and $k_H/k_D$ value remain, however, substantially unchanged when the base strength is changed, thus indicating that the transition-state structure of the eliminations from 1 is not significantly influenced by the strength of the attacking base. These results are discussed in the light of the current theories concerning the effects of structural changes on the E2 transition state.

It has been long known that a close relationship exists between the transition-state structure of an E2 reaction (in the E1-like, central, E1cB-like spectrum) and the outcome of the reaction itself, with particular regard to geometrical and positional orientation as well as stereochemistry.[1] Therefore, both theoretical and experimental studies aimed at obtaining information regarding the influence of the nature of the reactants and of the reaction conditions on the transition state of concerted eliminations are of interest.

Concerning the effects of base structure, it has been observed that a rise in the strength of the attacking base generally increases the carbanion character of the transition state.[2-7] Such a shift appears to be mainly determined by a decrease in the extent of C leaving–group bond breaking in the transition state of the reaction with the stronger base, the degree of proton transfer undergoing changes of minor importance.[2-4]

However, according to theoretical treatments of the effects of structural changes on the E2 transition state[8,9] (particularly to that by Winey and Thornton[9]), the above behavior should not be general but should be limited to reactions occurring via central transition states. Accordingly, only for these reactions it is predicted that an increase in base strength modifies the geometry of the transition state by influencing both vibrational modes of the transition state itself, i.e., parallel and perpendicular to the reaction coordinate (parallel and perpendicular effects) as shown in Figure 1. The combination of these two effects, which theory suggests are of comparable magnitude, leads to a shift of the transition-state structure toward the carbanion side with little change in the degree of C–H bond rupture.

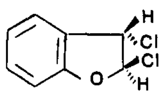
In contrast, for eliminations taking place via E1cB-like transition states, the reaction-coordinate motion is suggested to involve nearly exclusively the proton transfer (Figure 1); only parallel effects should therefore be of importance since the perpendicular ones do not involve the C–H motion. Thus, in this case, theory predicts that an increase in base strength will lead to a transition state with less carbanion character and a lesser degree of C–H bond cleavage. So far no example of elimination, with an E1cB-like transition state, conforming with this prediction has been observed.

Since it is felt that further experimental research in this area could be useful for an understanding of this phenomenon, we have kinetically investigated the eliminations from some *trans*-2,3-dichloro-2,3-dihydrobenzofurans promoted by phenoxides of different basicity in dimethyl sulfoxide ($Me_2SO$), determining the substituent effect and the deuterium kinetic isotope effect. For these reactions a highly carbanionic transition state can be expected.[10] Some eliminations from the same substrates induced by 4-chloro-2-nitroanilide ions have been also investigated to test for possible effects of the nature of the attacking atom in the base.

Since the elimination reactions from *trans*-2,3-dichloro-2,3-dihydrobenzofuran have a syn stereochemistry, the present study also gives information concerning base strength effects on syn eliminations.

## Results and Discussion

The base-promoted eliminations of *trans*-2,3-dichloro-2,3-dihydrobenzofuran (1), *trans*-2,3-dichloro-3-deuterio-2,3-dihydrobenzofuran (2), and *trans*-2,3,5-trichloro-2,3-dihydrobenzofuran (3) have been carried out in 99% $Me_2SO$.[11] The bases were ring-substituted tetraethylammonium phenoxides (substituents: $p$-$CH_3$, H, $p$-Br, $p$-Cl, $m$-$NO_2$) and tetraethylammonium 4-chloro-2-nitroanilide. The reaction product was shown to be 3-chlorobenzofuran (from 1 and 2) and 3,5-dichlorobenzofuran (from 3) when the elimination was promoted by the weakest base, $m$-nitrophenoxide, as expected for base-in-



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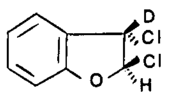

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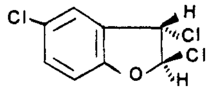

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[1] Bunnett, J. F. In "Survey of Progress in Chemistry"; Scott, A. F., Ed.; Academic Press: New York, 1969; Vol. 5, p 53.

[2] Alunni, S.; Baciocchi, E. *Tetrahedron Lett.* **1973**, 4665.

[3] Alunni, S.; Baciocchi, E.; Mancini, V. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1886.

[4] Alunni, S.; Baciocchi, E.; Perucci, P. *J. Org. Chem.* **1977**, *42*, 205.

[5] Yano, Y.; Oae, S. *Tetrahedron* **1970**, *26*, 27.

[6] McLennan, D. J.; Wong, R. J. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1818.

[7] Kevill, D. N.; Weiler, E. D.; Cromwell, N. M. *J. Am. Chem. Soc.* **1966**, *88*, 4489.

[8] More-O'Ferrall, R. A. *J. Chem. Soc. B* **1970**, 274.

[9] Winey, D. A.; Thornton, E. R. *J. Am. Chem. Soc.* **1975**, *97*, 3102.

[10] Baciocchi, E.; Ruzziconi, R.; Sebastiani, G. V. *J. Org. Chem.* **1979**, *44*, 28.

[11] The use of 99% $Me_2SO$ was considered opportune due to the fact that changes in the water content of the solvent, due to the use of slightly aqueous $Me_2SO$ solutions of tetraethylammonium hydroxide, could significantly influence the reaction rate.

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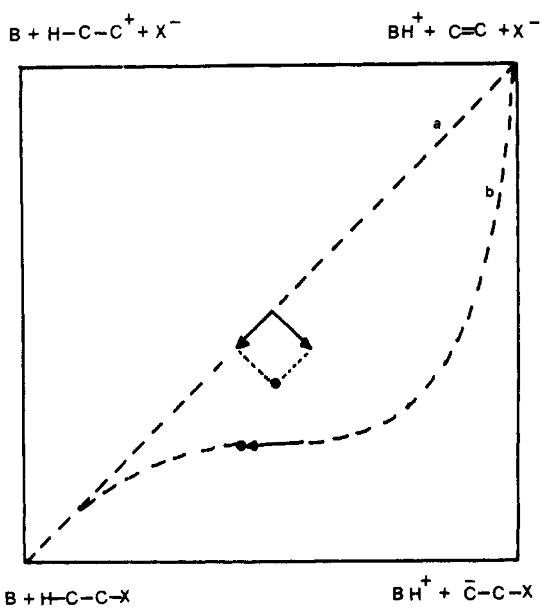

**Figure 1.** Changes in transition-state geometry of an E2 reaction caused by an increase in base strength evaluated by use of a schematic energy diagram (contour lines omitted) according to the Winey and Thornton theory (see text).[9] The dashed lines a and b indicate the reaction coordinates for eliminations taking place via central and E1cB-like transition states, respectively. The direction of parallel and perpendicular effects is given by the arrows. The position of the unperturbed transition state is at origin of the arrow(s). The new position results from the vector addition of parallel and perpendicular effects.

Table I. Kinetic Data for the Elimination Reactions of *trans*-2,3-Dichloro-2,3-dihydrobenzofuran (1), *trans*-2,3-Dichloro-3-deuterio-2,3-dihydrobenzofuran (2), and *trans*-2,3,5-Trichloro-2,3-dihydrobenzofuran (3) with Substituted Phenoxides and 4-Chloro-2-nitroanilide in 99% $Me_2SO$ at 30 °C

| base[a] | p$K_a$[b] | $k_2$, $M^{-1}\ s^{-1}$ [c] | | |
|---|---|---|---|---|
| | | 1 | 2 | 3 |
| $p$-$CH_3C_6H_4O^-$ | 18.86 | 5.04 | 2.32 | |
| $C_6H_5O^-$ | 18.03 | 1.79<br>0.780[d]<br>0.599[e]<br>1.78[f] | 0.729<br><br>0.252[e] | 37.9 |
| $p$-$ClC_6H_4O^-$ | 16.74 | 0.260 | 0.116 | 5.11 |
| $p$-$BrC_6H_4O^-$ | | 0.195 | 0.0873 | 3.96 |
| $m$-$NO_2C_6H_4O^-$ | 14.39 | $5.55 \times 10^{-3}$ | $2.29 \times 10^{-3}$ | 0.108 |
| 4-Cl-2-$NO_2C_6H_3NH^-$ | 18.90 | 5.92 | 2.43 | |

[a] In all cases the counterion was $Et_4N^+$. [b] Data in anhydrous $Me_2SO$ from F. G. Bordwell (personal communication). [c] Average of at least two determinations. The average error is ±2%. [d] In the presence of added phenol, $3.77 \times 10^{-3}$ M. In the substitution reaction of $n$-butyl bromide with phenoxide ion $k_2$ is 0.26 $M^{-1}\ s^{-1}$ in the absence of added phenol and 0.117 $M^{-1}\ s^{-1}$ in the presence of added phenol, $3.77 \times 10^{-3}$ M, at 30 °C. [e] In the presence of added phenol, $5.39 \times 10^{-3}$ M. [f] In the presence of $Et_4N^+Br^-$, 0.0939 M.[15]

Table II. Deuterium Kinetic Isotope Effect and Substituent Effect in the Elimination Reactions of *trans*-2,3-Dichloro-2,3-dihydrobenzofuran with Substituted Phenoxides and 4-Chloro-2-nitroanilide in 99% $Me_2SO$ at 30 °C

| base | $k_H/k_D$[a] | $k_{5\text{-}Cl}/k_H$[b] |
|---|---|---|
| $p$-$CH_3C_6H_4O^-$ | 2.2 | |
| $C_6H_5O^-$ | 2.4<br>2.4[c] | 21.2 |
| $p$-$ClC_6H_4O^-$ | 2.2 | 19.7 |
| $p$-$BrC_6H_4O^-$ | 2.2 | 20.3 |
| $m$-$NO_2C_6H_4O^-$ | 2.4 | 19.5 |
| 4-Cl-2-$NO_2C_6H_3NH^-$ | 2.4 | |

[a] Reactivity ratio between 1 and 2. The average error is ±2.5%. [b] Reactivity ratio between 3 and 1. The average error is ±5%. [c] In the presence of added phenol, $5.39 \times 10^{-3}$ M.

duced eliminations from these substrates.[10,12] Attack at the 3-proton was therefore assumed for all of the other reactions investigated.

Kinetics were followed by determining the disappearance of the base spectrophotometrically. The reactions of **3** with $p$-methylphenoxide and 4-chloro-2-nitroanilide ions were, however, too fast to be studied kinetically. The concentration of the base was ca. $5 \times 10^{-4}$ M and that of the substrate (at least tenfold in excess) was in the range $5 \times 10^{-3}$–$4 \times 10^{-2}$ M. The first-order plots were satisfactorily linear; however, in several cases, a slight downward drift, after 50–60% of the reaction, was observed. Such a drift is attributed to base-conjugated acid association via hydrogen bonds.[13] The operation of an E1cB mechanism involving a reversibly formed carbanion, $(E1cB)_R$,[14] was excluded by the observation that the reaction of phenoxide ions with **1** and $n$-butyl bromide (a substitution reaction), when carried out in the presence of added phenol, underwent a very similar rate-retarding effect. An $(E1cB)_R$ mechanism is unlikely also on the basis of the substantial deuterium kinetic isotope effect[14] (vide infra) observed both in the presence and in the absence of added phenol. From the first-order plots the second-order rate constants ($k_2$) were obtained as usual.

The $k_2$ values, collected in Table I, can be confidently considered to represent the reactivity of the nonassociated base, owing to the very low concentrations used and the nature of the cation (tetraethylammonium ion). This is further confirmed by previous observations[15] indicating that the rate of the reaction of **1** with tetraethylammonium phenoxide remains unchanged in the presence of 0.1 M tetraethylammonium bromide. Thus, from the data in Table I, quantitative information concerning the base-strength effect on the elimination rate can be obtained.

It can be at once observed, in this respect, that the elimination rate is strongly influenced by the base strength; accordingly, changes in rate by a factor of $10^3$ for p$K_a$ variations of 4 units are observed. A quantitative assessment of the base dependence of the rate can be provided by the Brønsted plot which exhibits an excellent linearity ($r$ = 0.999, $S$ = 0.064), in agreement with the previous assumption that the reactivity of the various bases is not significantly influenced by association phenomena. Interestingly, the $k_2$ value for 4-chloro-2-nitroanilide ions also nicely fits the Brønsted plot. Thus, the nitrogen base appears to behave exactly as an oxygen base with respect to the rate sensitivity to the base strength. In contrast, the sensitivity of positional orientation of E2 reactions to base strength is larger for oxygen than for nitrogen bases.[16]

From the Brønsted plot a $\beta$ value of 0.67 can be calculated. Even though the actual significance of $\beta$ values is at present the subject of controversy,[17] the calculated value

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[12] Palmer, M. H. "The Structure and Reactions of Heterocyclic Compounds", 1st ed.; Edward Arnold Ltd.: London, 1967; Chapter 12, p 321.

[13] Kolthoff, I. M.; Chantooni, M. K., Jr.; Bhownik, S. *J. Am. Chem. Soc.* **1968**, *90*, 23.

[14] Bordwell, F. G. *Acc. Chem. Res.* **1972**, *5*, 374.

[15] Baciocchi, E.; Ruzziconi, R.; Sebastiani, G. V. *J. Org. Chem.* **1979**, *44*, 3718.

[16] Bartsch, R. A.; Wiegers, K. E.; Guritz, D. M. *J. Am. Chem. Soc.* **1974**, *96*, 430.

suggests a transition-state structure with a significant degree of proton transfer to the base. This suggestion finds support in the values of the substituent effect ($k_{5\text{-Cl}}/k_{\text{H}}$) and the deuterium kinetic isotope effect ($k_{\text{H}}/k_{\text{D}}$), reactivity ratios between 3 and 1 and between 1 and 2, respectively, collected in Table II. The chlorine substituent at the 5-position, acting from a *meta*-type position (with respect to the $\beta$-hydrogen), exerts a very significant accelerating effect in all cases, thus indicating a transition state where considerable buildup of negative charge at the $\beta$-carbon has taken place. The $k_{\text{H}}/k_{\text{D}}$ values, much smaller than the maximum value expected for a 50% proton transfer, are also in agreement with this conclusion since they can be reasonably interpreted in terms of highly asymmetric transition states where the proton is more than 50% transferred to the base. On the other hand, an E1cB-like transition-state structure for the investigated eliminations was certainly expected on the basis of the substrate structure (a $\beta$-chloro and a $\beta$-phenyl group are present) and previous results.[10]

Even though the reactions of 1 are discussed as belonging to the class of E2 reactions, it is recognized that a stepwise mechanism involving an irreversibly formed carbanion, (E1cB)$_{\text{I}}$, could also be compatible with the above results.[18] A distinction of this mechanism from the E2 one is, however, most difficult[14] and rests mainly on indirect evidence. Our preference for the concerted mechanism derives from the observation that the reactivity of 1 with phenoxide is significantly smaller (20–30-fold) than that of its dibromo derivative analogue, thus indicating the presence of a leaving-group effect.[20] However, as opposed to the case with *t*-BuOK-*t*-BuOH,[10] a precise measure of such an effect is not possible, owing to the quite fast $\text{Me}_2\text{SO}$-promoted decomposition of *trans*-2,3-dibromo-2,3-dihydrobenzofuran.

Anyway, it can be noted that for the (E1cB)$_{\text{I}}$ mechanism and the E2 mechanism with a E1cB-like transition state, the same base dependence of the transition-state structure is theoretically predicted. Thus, most of the following discussion should remain valid even though 1 reacts by an (E1cB)$_{\text{I}}$ mechanism.

Coming now to compare the $k_{\text{H}}/k_{\text{D}}$ and $k_{5\text{-Cl}}/k_{\text{H}}$ values obtained with the various bases, one observes the substantial independence of these values from base strength. Of course, this implies $\beta$ values which are practically identical for the reactions of 1, 2, and 3. In this case too, the nitrogen base behaves like the oxygen base, 4-chloro-2-nitroanilide giving a $k_{\text{H}}/k_{\text{D}}$ value similar to those observed with phenoxides. Clearly, the transition state of these reactions undergoes little change as the base strength is changed, especially with respect to the extent of C–H bond breaking and the density of negative charge at the $\beta$-carbon.

Thus, the present result also does not agree with theoretical predictions concerning the base-strength effects on the E1cB-like transition state, according to which an increase in $k_{\text{H}}/k_{\text{D}}$ (less C–H bond breaking) and a decrease in $k_{5\text{-Cl}}/k_{\text{H}}$ (less carbanion character) would have been expected. However, this further confirmation of the failure of the theory to make correct predictions in this respect does not necessarily mean that there is something wrong with its basic premises.[21] It is, instead, more probable that the situation where only the parallel effects are of importance represents a limit which is, in practice, very difficult to reach. In other words, perpendicular effects can be significant even in transition states characterized by a high carbanion character.

It is useful to point out that, for the reasons mentioned above, the same kind of disagreement between theoretical and experimental results would exist even if the elimination from 1 is (E1cB)$_{\text{I}}$. Interestingly, in this case too, the operation of perpendicular effects would offer a reasonable explanation,[22] and it is worthwhile to note that such effects have been called into play to rationalize the finding that in the (E1cB)$_{\text{I}}$ elimination from 1,1-diaryl-2,2,2-trichloroethanes the $\rho$ value is slightly increased by increasing the base strength.[25]

An additional observation is that the results obtained with *trans*-2,3-dichloro-2,3-dihydrobenzofurans are at variance not only with theoretical expectations but also with the results obtained in other elimination reactions occurring via E1cB-like transition states where an increase in base strength caused an increase in the carbanion character of the transition state. Thus, in the reactions of (2-arylethyl)trimethylammonium ions in DMF the $\rho$ value was found to increase from 3.81 to 4.25 when the base was changed from *m*-nitrophenoxide to phenoxide,[4] and in the reactions of 2-(arylsulfonyl)ethyl chlorides with amines the $\rho$ value increases from 1.64 to 1.81 for a 3.7-unit increase in the p$K_{\text{a}}$ of the base.[5] It could be tentatively suggested that as the transition-state structure moves from the center of the spectrum (where a stronger base makes the transition state *more* carbanionic) to the E1cB-like extreme (where a stronger base *should* make the transition state *less* carbanionic), a situation may obtain where it exhibits very little sensitivity to changes in base strength. It should also be noted that the stereochemistry of the eliminations from 1 (syn) is different from that (presumably anti) of the reactions of (2-arylethyl)trimethylammonium ions and 2-(arylsulfonyl)ethyl chlorides. However, a different response to changes in base strength for transition states of syn and anti eliminations (possible in principle for reactions promoted by associated bases)[26] appears unlikely in this case since the syn eliminations from 1 should be promoted by solvated anions. Therefore, the geometry of the transition state of these reactions

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[17] Kresge, A. J. "Proton Transfer Reactions"; Caudin, E. F., Gold, V., Eds.; Chapman and Hall: London, 1975; p 179.

[18] An E1cB mechanism involving a tightly solvated carbanion, (E1cB)$_{\text{ip}}$,[14] should be also considered. This mechanism is, however, practically undistinguishable from the E2 one since according to recent suggestions,[19] it can also exhibit a substantial deuterium kinetic isotope effect. Perhaps, since the (E1cB)$_{\text{ip}}$ mechanism involves a preequilibrium acid–base reaction, it should probably be characterized by a $\beta$ value which is very close to unity and therefore larger than that observed in our system.

[19] Koch, H. F.; Dahlberg, D. B.; McEntee, M. F.; Klecha, C. J. *J. Am. Chem. Soc.* **1976**, *98*, 1060. Koch, H. F.; Dahlberg, D. B.; Toezko, A. G.; Solsky, R. L. *Ibid.* **1973**, *95*, 2029.

[20] Similar rate effects can be predicted for bromine and chlorine when bonded at the $\beta$-position.[10]

[21] Actually, the theory works quite satisfactorily when structural changes on the substrate are considered.[9] See also: Smith, P. J.; Bourns, A. N. *Can. J. Chem.* **1974**, *52*, 749.

[22] An alternative explanation[23] calls into play the effects on the transition-state structure of the changes in the steric requirements of the solvated base (the stronger base should be the more solvated). Such an explanation might also be valid for E2 eliminations involving an E1cB-like transition state; however, it does not appear that changes in the steric requirement of the base modify the transition-state geometry of concerted eliminations.[24]

[23] McLennan, D. J. *J. Chem. Soc., Faraday Trans. 1* **1974**, *71*, 1515.

[24] Alunni, S.; Baciocchi, E.; Perucci, P.; Ruzziconi, R. *J. Org. Chem.* **1978**, *43*, 2414.

[25] McLennan, D. J.; Wong, R. J. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1373.

[26] In syn eliminations with associated bases the transition state can have a cyclic structure where the cation of the base is coordinated with the leaving group.[27] This transition state could respond to changes in base strength in a different way than the transition state of an anti elimination.

[27] Závada, J.; Svoboda, M.; Sicher, J. *Collect. Czech. Chem. Commun.* **1968**, *33*, 4027. Svoboda, M.; Závada, J.; Sicher, J. *Ibid.* **1968**, *33*, 1415.

should not be significantly different from that of the transition state of anti eliminations.

## Experimental Section

**Materials.** *trans*-2,3-Dichloro-2,3-dihydrobenzofuran (1),[10] *trans*-2,3-dichloro-2,3-dihydro-3-deuteriobenzofuran (2),[15] and *trans*-2,3,5-trichloro-2,3-dihydrobenzofuran (3) were prepared by chlorine addition in $Et_2O$ at −5 to 0 °C to the corresponding benzofuran.[10] The NMR spectrum ($CCl_4$) of 3 exhibited the following peaks: $\delta$ 5.32 (1 H, s, 3-H), 6.40 (1 H, s, 2-H), 6.82–7.50 (3 H, m, ArH). The UV spectra (99% $Me_2SO$) of these compounds exhibited very broad maxima at 284 (1 and 2) and 296 nm (3). 3-Chlorobenzofuran[10] and 3,5-dichlorobenzofuran were obtained by dehydrohalogenation of 1 and 3, respectively, with alcoholic potassium hydroxide.[10] The NMR spectrum ($CCl_4$) of the latter compound exhibited the following peaks: $\delta$ 7.51 (1 H, s, 2-H), 7.05–7.55 (3 H, m, ArH). The UV spectra (99% $Me_2SO$) exhibited very sharp absorption maxima at 277 and 284 nm (3-chlorobenzofuran) and at 284 and 292 nm (3,5-dichlorobenzofuran). 4-Chloro-2-nitroaniline (Fluka AG) and phenol and its derivatives (Erba RPE) were used without further purification.

**The solvent and bases** were prepared as previously described.[15]

**Kinetic Study.** Kinetic experiments were carried out by following spectrophotometrically the disappearance of the base at 330 nm for phenoxide and *p*-methyl-, *p*-chloro-, and *p*-bromophenoxide, 480 nm for *m*-nitrophenoxide, and 560 nm for 4-chloro-2-nitroanilide. At these wavelengths no appreciable absorbance is exhibited by the reaction products. The reactions were brought about in a stoppered two-limbed silica cell. In one limb was placed the substrate solution (1 mL), and in the other was placed at first the phenol solution (1 mL) and then successively, under nitrogen, an amount of 0.0116 M tetraethylammonium hydroxide solution calculated on the basis of previous spectrophotometric titration of the phenol solution as described in the literature[28] (100–200 $\mu$L). The cell was placed in the thermostated compartment of a Beckman DB-GT spectrophotometer. After 20 min the solutions were mixed throughly, and the cell was rapidly placed again in the cell compartment of the spectrophotometer. The final product from the reactions of 1–3 with *m*-nitrophenoxide was the corresponding 3-chlorobenzofuran as shown by comparison (GPC analysis[10] at 120 °C) with an authentic specimen.

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**Registry No. 1**, 63361-57-9; **2**, 70749-80-3; **3**, 72360-51-1; *p*-$CH_3C_6H_4O^-$, 3174-48-9; $C_6H_5O^-$, 3229-70-7; *p*-$ClC_6H_4O^-$, 24573-38-4; *p*-$BrC_6H_4O^-$, 2042-41-3; *m*-$NO_2C_6H_4O^-$, 14609-74-6; 4-Cl-2-$NO_2C_6H_3NH^-$, 72360-52-2.

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[28] Mandolini, L.; Masci, B.; Roelens, S. *J. Org. Chem.* **1977**, *42*, 3733.

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# Mechanisms of Bromination of Uracil Derivatives. 5.[1] Reaction of Uracil and 5-Bromouracil via Their Anions in Weakly Acidic Aqueous Solution

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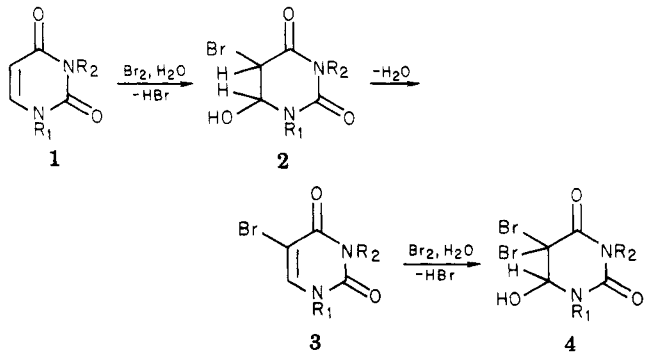
The rates of reaction of bromine with uracil, 1-methyluracil, 3-methyluracil, 1,3-dimethyluracil, 5-bromouracil, and 5-bromo-1,3-dimethyluracil have been measured in acidic, aqueous solutions (pH 0–5). For those derivatives having a methyl group at $N_1$ the observed second-order rate constants are invariant with acidity, whereas for those derivatives having hydrogen at $N_1$ they increase with decreasing acidity. These results suggest that reaction upon the anions of uracil, 3-methyluracil, and 5-bromouracil predominates at higher pH. The mechanistic implications of these findings are discussed.

In a recent paper[1] we presented evidence which supports the overall mechanism of bromination of uracils in aqueous solution first proposed by Wang.[2] In this mechanism (Scheme I) bromine reacts rapidly with the uracil 1 ($R_1$ and $R_2$ = H or Me), leading to an observable[1] intermediate, 2, which undergoes relatively slow dehydration to give the substitution product 3, a 5-bromouracil. Details of the mechanism of the conversion 2 → 3 were afforded by a kinetic study of the appearance of 3 in acidic media.[1] 5-Bromouracils 3 also react with aqueous bromine and yield 5,5-dibromo derivatives 4.[2] The reverse reaction, 4 → 3, which occurs in strong acid,[2] has been studied kinetically for the 6-methyl homologue.[3]

Heretofore no study of the fast reactions of bromine with uracils 1 or 5-bromouracils 3 has appeared. In this paper we report such a study carried out by using the stopped-flow method, the object being to provide mechanistic details of the steps 1 → 2 and 3 → 4.

Scheme I



## Results

We have measured the rates of reaction of bromine with uracil (1, $R_1 = R_2 =$ H), 1-methyluracil (1, $R_1$ = Me, $R_2$ = H), 3-methyluracil (1, $R_1$ = H, $R_2$ = Me), 1,3-di-

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[1] Part 4: O. S. Tee and S. Banerjee, *Can. J. Chem.*, **57**, 626 (1979).

[2] S. Y. Wang, *J. Org. Chem.*, **24**, 11 (1959).

[3] S. Banerjee and O. S. Tee, *J. Org. Chem.*, **39**, 3120 (1974).

0022-3263/80/1945-0830$01.00/0