W. Christensen, *Synthesis*, 534 (1973). (d) For example, J. L. Kice, C. A. Walters, and S B. Burton, *J. Org. Chem.*, **39**, 346 (1974) find that 4-nitrophenyl toluenesulfonate liberates the phenol at 70 °C in 20% acetonitrile with 0.1 M triethylamine–0.1 M triethylammonium ion with a rate constant $1.97 \times 10^{-5}\ s^{-1}$.

(20) (a) A. Williams and K. T. Douglas, *J. Chem. Soc., Perkin Trans. 2*, 1727 (1974); (b) A. Williams, *ibid.*, 808 (1972); 1244 (1973); (c) M. I. Page and W. P. Jencks, *J. Am. Chem. Soc.*, **94**, 8818 (1972).

(21) (a) J. R. Jones, "The Ionization of Carbon Acids", Academic Press, London, 1973, p 57; (b) A. I. Shatenshtein, *Adv. Phys. Org. Chem.*, **1**, 156 (1963); (c) A. Streitwieser and J. H. Hammons, *Prog. Phys. Org. Chem.*, **3**, 41 (1965); (d) R. E. Weston and J. Bigeleisen, *J. Am. Chem. Soc.*, **76**, 3074 (1954); (e) R. P. Bell, E. Gelles, and E. Möller, *Proc. R. Soc. London, Ser. A*, 176, 88 (1940); (f) R. F. Pratt and T. C. Bruice, *J. Am. Chem. Soc.*, **92**, 5956 (1970); (g) Professor F. G. Bordwell kindly supplied data for the pK_{SH} of carbon acids in Me_2SO; (h) M. H. Davies, J. R. Keefe, and B. H. Robinson, *Annu. Rep., Chem. Soc., Sect. A*, 123 (1973); (i) F. Hibbert, *J. Chem. Soc., Perkin Trans. 2*, 1289 (1973); (j) R. P. Bell and B. G. Cox, *J. Chem. Soc. B*, 652 (1971); (k) F. Hibbert and F. A. Long, *J. Am. Chem. Soc.*, **94**, 2647 (1972).

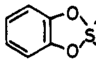
(22) (a) As far as we are aware the change from stepwise to a concerted process owing to the intermediate's lifetime becoming less than a vibration time has only recently been discussed with regard to carboxyl transfer.[22b–f] (b) W. P. Jencks, *Chem. Rev.*, **72**, 705 (1972); (c) J. P. Fox and W. P. Jencks, *J. Am. Chem. Soc.*, **96**, 1436 (1974); (d) M. I. Page and W. P. Jencks, *ibid.*, **94**, 8828 (1972); (e) W. P. Jencks and A. Satterthwait, *ibid.*, **96**, 7025 (1974); (f) N. Gravitz and W. P. Jencks, *ibid.*, **96**, 507 (1974).

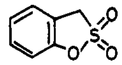
(23) (a) D. S. Kemp and M. L. Casey, *J. Am. Chem. Soc.*, **95**, 6672 (1973); (b) J. F. Bunnett, *Angew. Chem., Int. Ed. Engl.*, 1, 225 (1962); see also R. P. Bell "The Proton In Chemistry", Chapman and Hall, London, 1973, Chapter 11, and ref 21a, Chapter 9.

(24) (a) E. B. Wilson, *Chem. Soc. Rev.*, **1**, 293 (1972); (b) J. P. Lowe, *Prog. Phys. Org. Chem.*, **6**, 1 (1968).

(25) M. I. Page, *Chem. Soc. Rev.*, **2**, 295 (1973).

(26) From the pK_{SH} values for $C_6H_5CH_2SO_2CH_3$ (25.6), $C_6H_5CH_2SO_2C_6H_5$ (20.3), and $C_6H_5CH_2SO_2CF_3$ (14.6)[21g] in Me_2SO it might appear that applying Charton's σ_I values that the phenyl ester might have a low $pK_{SH} \sim 17$; however, the σ_I values ignore the considerable electron donating resonance interactions which could occur between the oxygen and the sulfone group. Evidence for this interaction in the sulfone series is the similarity in reactivity to hydroxide ion in the pair of esters: catechol sulfate and 2-hydroxyphenylmethanesulfonic acid sultone (E. T. Kaiser, I. R. Katz, and T. F.





Wulfers, *J. Am. Chem. Soc.*, **87**, 3781 (1965); O. R. Zaborsky and E. T. Kaiser, *ibid.*, **92**, 860 (1970)). Where measurements of pK_{SH} may be made on nitrophenyl and ethyl esters (CH_3COCH_2X, X = CH_3, OC_2H_5, OpNp, etc.) the esters do not have values agreeing with those calculated from a simple application of Taft σ_I values.

Nonenforced Catalysis of the Bisulfite Carbonyl Addition Reaction by Hydrogen Bonding[1]

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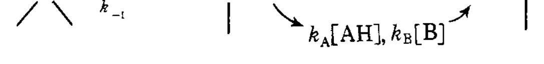
Abstract. The rates of dissociation of the bisulfite adducts of *p*-methoxyacetophenone and *p*-methoxy-, *p*-chloro-, and *p*-nitrobenzaldehyde have been measured spectrophotometrically in aqueous solution at 25 °C, ionic strength 1.0 with KCl or Me_4NCl. The reaction is catalyzed by oxygen and nitrogen bases with a Bronsted β of 0.94 ± 0.05 for both *p*-methoxyacetophenone and *p*-methoxybenzaldehyde. The reaction is also accelerated by mono- and divalent cations. The observed rate enhancements are correlated with the association constants for ion pair formation between these cations and sulfite dianion. A mechanism is suggested in which transition-state stabilization occurs through hydrogen bonding of the buffer acid with the dianionic transition state. Proton transfer from solvent to trap the initially formed dianionic addition compound is fast, so that catalysis is not enforced by a short lifetime of this intermediate. This reaction therefore provides an example of catalysis by hydrogen bonding in which the catalysis is not required or facilitated by the lifetime of unstable intermediates.

It would be helpful to our understanding of the mechanism of catalysis of carbonyl and acyl group reactions if we knew why some of these reactions are subject to general acid-base catalysis while others are not. There is a tendency for general acid catalysis of carbonyl addition reactions to become significant and to exhibit progressively increasing Bronsted α coefficients as the nucleophile becomes weaker and less basic, and this tendency has been rationalized in terms of "Hammond postulate" and related effects or generalizations such as "catalysis occurs when it is most needed".[3] However, Sayer et al. have pointed out that the appearance of general acid catalysis in this series of reactions corresponds to changes in the rate-determining step and mechanism rather than to a change in the structure of a common transition state as the nucleophile becomes weaker,[4] and it is now becoming apparent that the mechanism of catalysis for many, and perhaps most, reactions of this kind is *enforced* by the lifetime and acid-base properties of the initially formed intermediate.[5] In a simple carbonyl addition reaction (eq 1), for example, there *must* be catalysis of product formation through trapping of the addition intermediate by proton transfer after encounter with a molecule of buffer acid or base (k_A or k_B) whenever the intermediate breaks down to expel the nucleophile NH and regenerate reactants faster than it is trapped by proton transfer involving the solvent, i.e., when $k_{-1} > (k_h + k_s)$, in which k_h and k_s are the rate constants for proton transfer to or from solvent and through one or more solvent molecules, respectively. If the lifetime is so short that the intermediate breaks down faster than it separates from the catalyst, the intermediate *must* be formed within an encounter complex and exhibit catalysis by a "preassociation" mechanism, and if it is still shorter the intermediate cannot exist and the catalyzed reaction *must* be concerted. Since the catalyst is correctly located for subsequent proton transfer in a preassociation mechanism, there *must* be an opportunity for hydrogen bonding of the catalyst to the transition state[5] and for stabilization of the transition state by this hydrogen bonding.

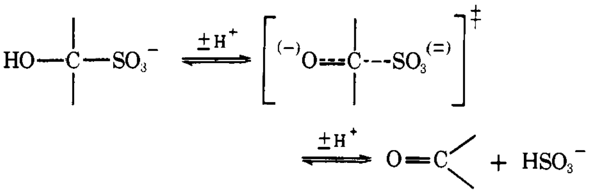


(1)

In general, catalysis by hydrogen bonding is more likely to be significant when the intermediate has a short lifetime (large k_{-1}). When nucleophile attack, k_1, is rate determining, a rate constant k_{HA}' for catalysis by hydrogen bonding to the transition state must be comparable with k_1 to be experimentally significant, whereas when trapping is rate determining k_{HA}'

need only be comparable with the smaller quantity $k_1(k_h + k_s)/k_{-1}$ to be significant; the advantage for the hydrogen-bonding mechanism in the latter case is given by the ratio $k_{-1}/(k_h + k_s)$. This provides one reason why general acid-base catalysis is frequently not observed for the attack of strong, basic nucleophiles but becomes significant for weakly basic nucleophiles that form a less stable addition intermediate (larger k_{-1}).[3]

It then becomes of interest to ask if catalysis of this type of reaction by hydrogen bonding is *ever* observed if it is not enforced or facilitated by the short lifetime of the addition intermediate.[6] We have reexamined the reversible addition of bisulfite to carbonyl compounds in an attempt to provide an answer to this question in a relatively simple system. This reaction requires the removal of a proton from the hydroxyl group of the addition compound and the addition of a proton to the leaving sulfite ion in the breakdown direction (eq 2) and



(2)

the corresponding proton transfers in the reverse direction for the addition reaction; the predominant mechanism involves a dianionic transition state. Catalysis of this reaction is not enforced and has not been detected previously.[7,8] We have studied this reaction with relatively stable carbonyl compounds, *p*-methoxyacetophenone and *p*-methoxybenzaldehyde, under experimental conditions that were designed to facilitate the detection of general acid-base catalysis.

Experimental Section

Materials. Reagent grade inorganic salts were used without further purification. Organic acids (with the exception of reagent grade formic and acetic acids) were purified by recrystallization or distillation. Ammonium salts (with the exception of spectrophotometric grade guanidine hydrochloride, Heico, Inc.) were recrystallized prior to use. Glass-distilled water was used throughout. *p*-Methoxybenzaldehyde was purified by distillation under reduced pressure; *p*-nitrobenzaldehyde was purified by recrystallization. The final purification of *p*-methoxyacetophenone and *p*-chlorobenzaldehyde was achieved by sublimation.

Stock solutions of the carbonyl bisulfites were prepared by dissolving a sufficient amount of the carbonyl compound in 4 M sodium bisulfite solution to give a final concentration of ~0.01 M. Stock solutions were stored at 4 °C under a nitrogen atmosphere. Aliquots (10–20 μl) were diluted into thermostated spectrophotometer cells containing 3.0 ml of the desired buffer solution and sufficient hydrogen peroxide (~10 μl of a 31% solution) to oxidize the excess sulfite to sulfate, thereby driving the reaction to completion. A small amount of strong base (~40 μl of 2 N KOH) was added to neutralize the acid produced by the oxidation. Under these conditions the initial and final pH values of the reaction solutions having moderate buffering capacity (>0.05 M total buffer) were unchanged within experimental error. Addition of excess hydrogen peroxide (or its total elimination in the case of *p*-methoxyacetophenone) gave no detectable change in the observed rate constant. The oxidation of sulfite under the conditions used was much faster than the breakdown of the carbonyl bisulfites, being complete in the mixing time. The same rate constants were obtained with stock solutions that had stood for several weeks (4 °C, under nitrogen) as with fresh solutions.

Kinetic Measurements. The rates of dissociation of the bisulfite addition compounds of *p*-methoxyacetophenone and *p*-methoxybenzaldehyde were followed by measuring the increase in carbonyl absorbance at 285 nm. The appearance of *p*-chlorobenzaldehyde and *p*-nitrobenzaldehyde were followed at 260 and 268 nm, respectively. Reaction rates were followed using a Zeiss PMQ II spectrophotometer or a Zeiss PM6KS spectrophotometer equipped with an automatic cell changer and a digital printout. Constant temperature was maintained at 25 °C by the use of a thermostated cell compartment; the ionic strength was adjusted to 1.0 with either KCl or Me_4NCl. First-order rate constants were determined from semilogarithmic plots of $(A_\infty - A_t)$ against time. Such plots were typically linear for over four half-times. The pH of each solution was determined at the completion of the experiment using a Radiometer PHM-25 pH meter equipped with a combined glass electrode. Minor variations in pH accompanying buffer dilution at constant buffer ratio were compensated for using the relationship:

$$k_{obsd(corr)} = k_{obsd} + \Delta(a_H/K_w)k_{OH^-} \qquad (3)$$

where k_{OH^-} is the apparent catalytic constant for hydroxide ion catalysis under the experimental conditions. All rate constants involving hydroxide ion are based on $10^{(pH - 14)}$. Catalytic constants for buffer catalysis (k_{app}) were determined from the least-squares slope of plots of $k_{obsd(corr)}$ against buffer concentration and typically were based on six to eight buffer concentrations.

Determinations of K_I. Association constants for ion pair formation:

$$K_I = \frac{[MSO_3]}{[M]_f[SO_3]_f} \qquad (4)$$

were determined from the pH change observed in a 0.1 M (50% ionized) bisulfite-sulfite buffer as various cations (previously adjusted to the pK_a' of bisulfite in Me_4NCl) were substituted for Me_4N^+ ion at a constant ionic strength of 1.0 and assuming that the observed decrease in pH may be accounted for by a decrease in the concentration of free sulfite dianion, $[SO_3]_f$, because of complex formation.[9] The value of $[SO_3]_f$ is then given by

$$[SO_3]_f = [SO_3]_t \text{ antilog}(-\Delta pH) \qquad (5)$$

and the concentration of MSO_3 is the difference between the concentration of added sulfite dianion, $[SO_3]_t$, and $[SO_3]_f$:

$$[MSO_3] = [SO_3]_t - [SO_3]_f \qquad (6)$$

Values of K_I were calculated from two-three determinations of ΔpH.

Product Analysis. The spectra of the reaction products from the dissociation of the various carbonyl bisulfite addition compounds were found to be identical with the sum of the spectra of the parent compound and the blank buffer solutions at the same concentrations.

Results

Catalysis by Hydrogen and Hydroxide Ions. The dependence on pH of the first-order rate constants for the dissociation of *p*-methoxyacetophenone bisulfite in the absence of general acids and bases (k_0) is shown in Figure 1. The data are consistent with the rate laws of the following equations:

$$k_0 = k_{H^+}[H^+] + k_{OH^-}[OH^-] + k_{H_2O}[H_2O] \qquad (7)$$

$$k_{obsd} = k_0 + k_{BH}[BH] + k_B[B] \qquad (8)$$

Values of k_0 were obtained from the ordinal intercept of plots of k_{obsd} against total buffer concentration (Figures 2 and 3). The pH-rate profile shows that the reaction is both acid and base catalyzed[8] and gives second-order rate constants, based on hydrogen ion activities, of $k_{H^+} = 1.1\ M^{-1}\ s^{-1}$ and $k_{OH^-} = 5.8 \times 10^8\ M^{-1}\ s^{-1}$ (ionic strength 1.0, KCl, 25 °C). The sum of the rate constants for the acid- and base-catalyzed reactions at the pH-rate minimum is ~23% less than the observed rate constants, suggesting the presence of a "water" reaction. The solid line in Figure 1 is calculated including the term k_{H_2O} (55.5 M) = $1.2 \times 10^{-3}\ s^{-1}$.

The rate of dissociation of the *p*-methoxybenzaldehyde bisulfite addition compound was found to increase linearly with increasing hydroxide ion activity in the pH range 3-5, giving $k_{OH^-} = 2.4 \times 10^7\ M^{-1}\ s^{-1}$ at ionic strength 1.0 with Me_4NCl.

General Base Catalysis. The effectiveness of amines as general base catalysts for the decomposition of *p*-methoxyacetophenone and *p*-methoxybenzaldehyde bisulfite addition

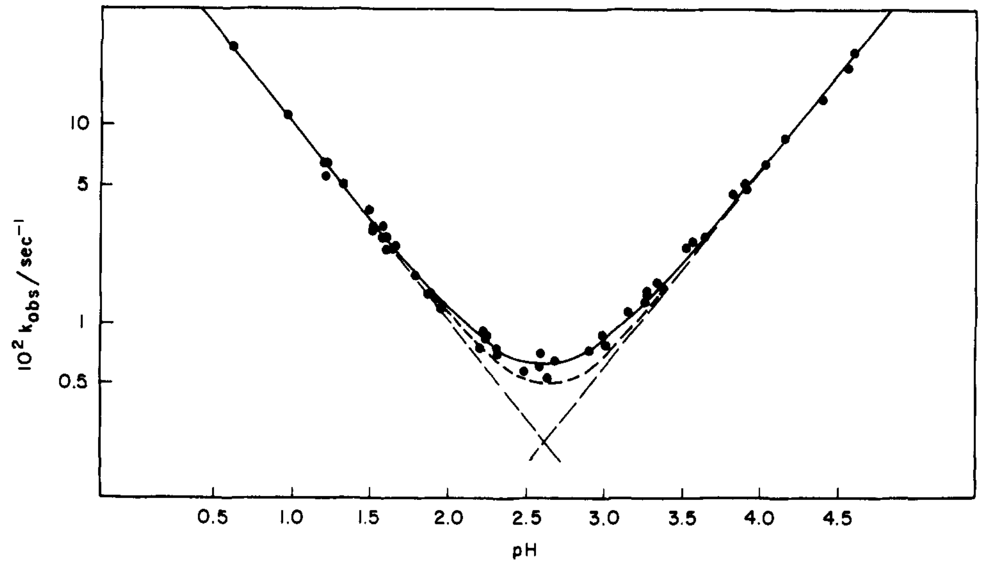


Figure 1. Dependence on pH of the observed first-order rate constants for the dissociation of *p*-methoxyacetophenone bisulfite extrapolated to zero buffer concentration at 25 °C, ionic strength 1.0 with KCl. The solid line is calculated from eq 7 and the rate constants in Table II. The dashed line is calculated similarly but omitting k_{H_2O}.

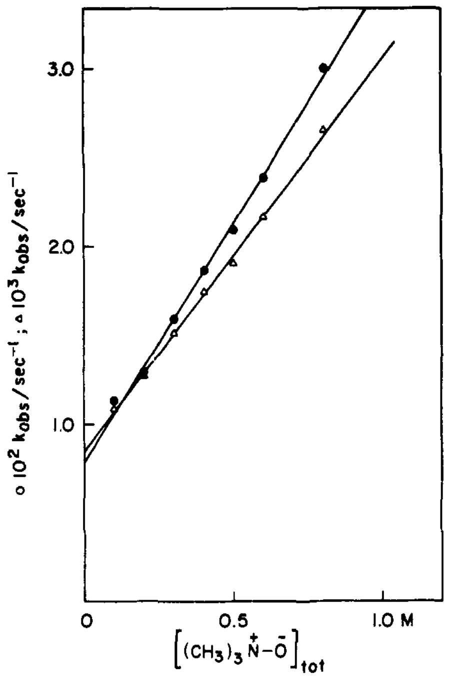


Figure 2. Dependence of the observed first-order rate constants for the dissociation of *p*-methoxyacetophenone bisulfite (circles) and of *p*-methoxybenzaldehyde bisulfite (triangles) on the concentration of trimethylamine *N*-oxide buffer at pH 3.72, ionic strength 1.0 with Me_4NCl, 25 °C.

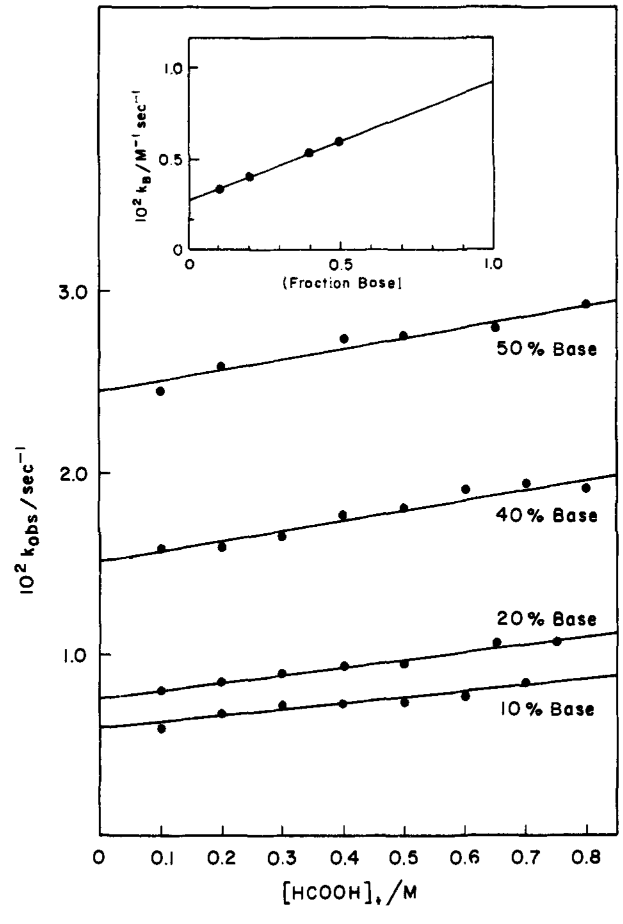


Figure 3. Dependence of the observed firs [illegible] constants for the dissociation of *p*-methoxyacetophenone bisulfite on the concentration of formic acid buffers at four buffer ratios, ionic strength 1.0 with KCl, 25 °C.

compounds was measured by obtaining values of k_{obsd} in the presence of increasing concentrations of amine hydrochlorides maintained at pH 3.5–4.5 with 0.1 M formate or acetate buffers, ionic strength 1.0 with Me_4NCl (Figure 2). The catalytic constant, k_B, was obtained by dividing the slope of such plots by the fraction of free amine, calculated from the pK_a and the experimental pH. Values of k_B for a series of amines are listed in Table I. Catalytic constants determined in this manner at different pH values agree satisfactorily, showing that the catalytically active species of the buffer is the free base. General base catalysis can be detected in this system far below the pK_a of the buffer because of the absence of a significant uncatalyzed or proton-catalyzed reaction until moderately low pH values are reached and because hydroxide ion falls significantly low on the Bronsted plot (Figure 4). The fact that the point for hydroxide ion is low shows that there is no additional specific base catalyzed reaction that is distinct from the reaction described by the Bronsted plot.

For *p*-methoxyacetophenone, increasing the concentration of carboxylic acid buffers from 0 to 1 M increases k_{obsd} 30-

Table I. General Base Catalysis of Carbonyl Bisulfite Breakdown[a]

Base	pK_a	Concn range, M[b]	pH[c]	10^2k_{app}, $M^{-1}\ s^{-1}$ [d]	k_B, $M^{-1}\ s^{-1}$ [e]
p-Methoxybenzaldehyde					
Trimethylamine *N*-oxide (TMAO)	5.01[f]	0.1-1.0	3.72[g]	0.21	0.043
Trifluoroethylamine (TFEA)	5.81[h]	0.1-1.0	4.75[i]	2.30	0.29
Ethyl glycinate (EG)	7.90[j,k]	0.1-0.9	4.56	2.15	47
Ammonia	9.48[h]	0.1-0.7	4.56	1.78	1.5×10^3
		0.1-0.9	3.57	0.16	1.3×10^3
Triethylamine (TEA)	10.93[k,l]	0.1-0.9	4.62	0.40	8.2×10^3
Ethylamine (EA)	10.97[j,k]	0.1-0.9	4.58	2.15	5.3×10^4
		0.1-0.9	3.55	0.20	5.3×10^4
Quinuclidine (Q)	11.5[m]	0.1-0.9	4.63	1.57	1.2×10^5
Guanidine (Gu)	13.6[n,k]	0.1-0.9	4.58	5.3	5.5×10^7
p-Methoxyacetophenone					
Trimethylamine *N*-oxide (TMAO)	5.01[f]	0.1-1.0	3.72[g]	2.60	0.53 ± 0.02
		0.1-0.5	4.20[o]	3.19[o]	0.27 ± 0.02[o]
Ammonia	9.48[h]	0.2-0.9	3.50	3.05	2.9×10^4
Ethylamine (EA)	10.97[j,k]	0.1-0.9	3.57	1.78	4.5×10^5
Guanidine (Gu)	13.6[n,k]	0.1-0.9	3.53	3.67	3.1×10^8

[a] Ionic strength maintained at 1.0 with Me_4NCl; $T = 25$ °C. [b] Total buffer concentration. [c] Maintained with 0.1 M formate or acetate except as noted. [d] Observed second-order rate constant for buffer catalysis. [e] Observed second-order rate constant divided by the fraction of buffer free base as calculated from the pK_a and the experimental pH. [f] Determined from observed pH and buffer ratio. [g] 95% acid. [h] J. P. Fox and W. P. Jencks, *J. Am. Chem. Soc.*, **96,** 1436 (1974). [i] 92% acid. [j] Ionic strength 1.0 with KCl; M. Gilchrist and W. P. Jencks, *J. Am. Chem. Soc.*, **90,** 2622 (1968). [k] pK_a's for a number of amines are essentially identical in KCl and in Me_4NCl.[h] [l] Ionic strength 0.18 with KCl; W. S. Fyfe, *J. Chem. Soc.*, 1347 (1955). [m] M. J. Gresser and W. P. Jencks, in preparation. [n] Ionic strength 2.0 with KCl; N. F. Hall and M. R. Sprinkle, *J. Am. Chem. Soc.*, 54, 3469 (1932). [o] 89% acid, pH meter reading, in 96% D_2O; see text.

70% over the k_0 value ($\mu = 1.0$ with KCl, Figure 3); this increase is smaller than the rate increases observed with amine buffers ($\mu = 1.0$ with Me_4NCl). The slopes of such plots represent apparent second-order rate constants for buffer catalysis, k_{app}. The second-order rate constants for the acidic and basic components of the buffer (k_{BH} and k_B, respectively) were obtained from the ordinal intercepts of plots of k_{app} against the fraction of basic component in the buffer (inset, Figure 3). Values of k_B for a series of carboxylate ions are summarized in Table II. General acid catalysis of this reaction and the values of k_{BH} will be described in a separate communication.

Since relatively high buffer concentrations were required to determine the catalytic constants, it is important to determine the effects of salts and organic solvents on k_{OH^-} as this represents a large fraction of k_{obsd}. The results are summarized in Table III. There is no significant effect of 0-1.0 M Me_4NCl on the rate, but the value of k_{OH^-} is sensitive to the concentration of most other added salts and solvents. Since the addition of organic solvents or the substitution of other salts for potassium chloride cause a *decrease* in k_{obsd}, the rate increases observed with carboxylate buffer represent lower limits of k_{app}. Approximate corrections for these negative salt and solvent effects on k_{app} were made using:

$$k_{app}' = [0.3(\text{fraction acid}) + 0.2(\text{fraction base})]k_0 + k_{app} \quad (9)$$

and an average value of $-30\%\ M^{-1}$ for solvent effects and $-20\%\ M^{-1}$ for salt effects, these being the average molar percent perturbation on k_{OH^-} caused by ethanol, acetamide, and 2-propanol (solvent effects) and trifluoroacetate and nitrate (salt effects, Table III). Thus, the first term in eq 9 provides an estimate of the amount by which 1 M buffer decreases k_0 simply due to solvent and specific salt effects. This value plus the observed rate increase (k_{app}) gives the second-order rate constant for buffer catalysis that would be expected if there were no such solvent or salt effects. The values of k_B' listed in Table II were determined from plots of k_{app}' against the fraction of the basic form of the buffer. Catalytic constants for trifluoroethanol, hexafluoro-2-propanol, and hexafluoroacetone hydrate were determined at pH ~3.6 by a procedure analogous to that described for amine catalysis. An approximate compensation for solvent effects with these compounds was carried out experimentally by maintaining a constant total concentration of ethanol plus trifluoroethanol and of 2-propanol plus hexafluoro-2-propanol or hexafluoroacetone hydrate in the reaction mixtures. Values or upper limits for k_B' were determined directly from the slopes of plots of k_{obsd} against the concentration of added catalyst. Approximate uncorrected values of k_B were determined from values of k_0 calculated from the experimental pH and k_{OH^-} in the absence of added solvents and the extrapolated value for k_{obsd} in the presence of 1 M buffer.

In the Bronsted plot of Figure 4, the corrected values of the catalytic constants ($\mu = 1.0$, KCl) are plotted as closed circles and the uncorrected values are indicated as lower limits. The least-squares Bronsted slope of the line through these lower limits ($\beta = 0.92$) does not differ significantly from the value of $\beta = 0.94$ calculated from all points except those for hydroxide ion and water. Although the points for amine catalysts (determined in Me_4NCl) fall on the same line as those for oxygen catalysts (determined in KCl), it is probable that there is a small electrostatic effect favoring the former catalysts because the catalytic constant for acetate is smaller in Me_4NCl (open circle) than in KCl (closed circle). There is a larger favorable salt effect of KCl on the hydroxide ion reaction (Table III and Figure 4), which accounts for the smaller percentage rate increases observed with buffers in the presence of KCl.

Catalysis of the breakdown of *p*-methoxybenzaldehyde, *p*-chlorobenzaldehyde, and *p*-nitrobenzaldehyde bisulfites by formic acid buffers was also observed, giving the approximate k_{app}/k_0 ratios listed in Table IV.

Table II. General Base Catalysis of *p*-Methoxyacetophenone Bisulfite Breakdown[a]

Base	pK_a	Concn range,[b] M	Fraction base	$10^2 k_{app}$,[c] $M^{-1}\,s^{-1}$	k_B, $M^{-1}\,s^{-1}$ [d]	k_B', $M^{-1}\,s^{-1}$ [e]
Formate (F)	3.56[f]	0.1–0.8	0.5	0.60	9.2×10^{-3}	2.1×10^{-2}
		0.1–1.0[g]	0.5	0.40		
		0.1–0.8	0.4	0.53		
		0.1–0.75	0.2	0.42		
		0.1–0.7	0.1	0.33		
Glycolate	3.62[h]	0.1–1.0	0.5	0.60	9.3×10^{-3}	2.2×10^{-2}
		0.1–0.8	0.3	0.45		
		0.1–1.0	0.15	0.37		
β-Chloropropionate	3.93[f]	0.1–0.8	0.5	<1.07	$1.5\ (\pm 0.45) \times 10^{-2}$	3×10^{-2}
		0.1–0.8	0.1	0.35		
Acetate	4.65[f]	0.1–1.0	0.05	0.43	8.7×10^{-2}	1.8×10^{-1}
		0.1–1.0[g]	0.05	0.23	4.7×10^{-2}	7.3×10^{-2}

Base	pK_a	Concn range,[b] M	pH[i]	$10^2 k_{app}$,[c] $M^{-1}\,s^{-1}$	k_B, $M^{-1}\,s^{-1}$ [d]	k_B', $M^{-1}\,s^{-1}$ [e]
Hexafluoroacetone hydrate anion (HFAH)	6.45[j]	0.3–0.9	3.62	0.82	5.5[k]	8.23[l]
Hexafluoro-2-propanol anion (HFIP)	9.22[f]	0.1–0.45	3.61	0.22	900[k]	2.6×10^{3} [l]
Trifluoroethanol anion (TFE)	12.43[m]	0.3–0.9	3.62	0.20	1.3×10^{6} [k]	2.5×10^{6} [l]
H_2O	−1.74				2.1×10^{-5} [n]	
HO^-	15.74				5.8×10^{8} 1.6×10^{8} [g] 2.2×10^{8} [g,o]	

[a] Ionic strength maintained at 1.0 with KCl; $T = 25$ °C. [b] Total buffer concentration. [c] Observed second-order rate constant for buffer catalysis. [d] Determined from ordinal intercept of a plot of k_{app} vs. fraction base. [e] Determined from the ordinal intercept of a plot of solvent and salt corrected values of k'_{app} (eq 9) vs. fraction base. [f] J. M. Sayer and W. P. Jencks, *J. Am. Chem. Soc.*, **91,** 6353 (1969). [g] Ionic strength and W. P. Jencks, *J. Am. Chem. Soc.*, **96,** 7031 (1974). [k] Second-order rate constant divided by the fraction of buffer free base as calculated from the pK_a and the experimental pH (see text). [l] Second-order rate constant corrected for salt and solvent effects (eq 4) divided by the fraction of buffer free base as calculated from the pK_a and the experimental pH. [m] C. K. Sauers, W. P. Jencks, and S. Groh, *J. Am. Chem. Soc.*, **97,** 5546 (1975). [n] k_{H_2O}, $M^{-1}\,s^{-1}$; see text. [o] In 96% D_2O. pD was calculated by adding 0.40 to the observed pH meter reading; $[OD^-]$ was calculated as a_D/K_w taking $K_w = 10^{-14.81}$ in D_2O.[10]

Table III. Salt and Solvent Effects on the Breakdown of Bisulfite Addition Compounds[a]

Additions	Concn, M	pH[b]	k_{OH^-}, $M^{-1}\,s^{-1}$ [c]
		p-Methoxybenzaldehyde	
None[d]		3.85	2.5×10^{7}
KCl	0.6	3.87	6.0×10^{7}
KCl	1.0	3.83	6.83×10^{7}
Me_4NCl	0.6	3.86	2.7×10^{7}
Me_4NCl	1.0	3.85	2.35×10^{7}
Pr_4NCl	1.0	3.85	2.5×10^{7}
		p-Methoxyacetophenone	
KCl	1.0	3.50	5.8×10^{8}
Me_4NCl	1.0	3.50	1.6×10^{8}
EtOH[e]	1.0	3.56	4.3×10^{8}
CH_3CONH_2[e]	1.0	3.55	3.3×10^{8}
KNO_3	1.0	3.55	5.7×10^{8}
$K^+CF_3COO^-$	1.0	3.55	3.7×10^{8}
2-Propanol[e]	1.0	3.64	4.2×10^{8}

[a] Temperature 25 °C. [b] pH maintained with 0.1 M formate buffers. [c] Observed second-order rate constant for hydroxide ion catalysis calculated as $k_{obsd}/(a_H/K_w)$, taking $K_w = 10^{-14}$ and assuming $a_H = 10^{-pH}$. [d] Determined from the intercept of a plot of k_{OH^-} against [KCl]. [e] Ionic strength 1.0 with KCl.

Table IV. Buffer Catalysis of Carbonyl Bisulfite Breakdown[a]

Compound	pH	$10^{-7} k_{OH^-}$,[b] $M^{-1}\,s^{-1}$	$(k_{app}/k_0)_{obsd}$,[c] M^{-1}	$(k_{app}/k_0)_{corr}$,[d] M^{-1}
p-Methoxybenzaldehyde	3.60	6.83[e]	0.42[f]	0.60
p-Chlorobenzaldehyde	3.60	5.57[e]	0.19[f]	0.39
p-Nitrobenzaldehyde	3.60	4.94	0.55[f]	0.39
p-Methoxyacetophenone	3.53	58.0	0.24[g]	0.50

[a] In formate buffers, 50% ionized, ionic strength 1.0 with KCl. [b] Observed second-order rate constant for hydroxide ion catalysis calculated as $k_{obsd}(a_H/K_w)$, taking $K_w = 10^{-14}$ and assuming $a_H = 10^{-pH}$. [c] Observed second-order rate constants for buffer catalysis divided by the rate constant in the absence of added buffers. [d] Observed second-order rate constant for buffer catalysis corrected for salt and solvent effects by eq 9 based on (salt:solvent) correction factors of $-0.26{:}-0.10\ M^{-1}$, $-0.31{:}-0.08\ M^{-1}$, $0.03{:}0.31\ M^{-1}$ from the effect of $(EtOH{:}CF_3COO^-)$ on k_{OH^-} for *p*-methoxy-, *p*-chloro-, and *p*-nitrobenzaldehyde, respectively. [e] Values of $k_{OH} = 3.7 \times 10^{7}$ $M^{-1}\,s^{-1}$ and 2.8×10^{7} $M^{-1}\,s^{-1}$ for *p*-methoxy- and *p*-chlorobenzaldehyde, respectively, based on experiments in 1.5 M acetate buffer, 25 °C, have been reported in ref 20. [f] General acid catalysis is estimated to account for less than 1% of k_{app}. [g] General acid catalysis comprises ~50% of k_{app}.

The solvent isotope effects in 96% deuterium oxide are $k_B^{H_2O}/k_B^{D_2O} = 2.0 \pm 0.2$ and $k_{OH^-}/k_{OD^-} = 0.73$ for the re-

Table V. Effect of Cations on the Breakdown of Carbonyl Bisulfites[a]

Cation	(k_{app}/k_0), M^{-1} [b]			ΔpH	K_1, M^{-1} [c]
	p-Methoxybenzaldehyde	*p*-Methoxyacetophenone	*p*-Chlorobenzaldehyde		
Zn^{2+}	80[d]		72	1.50[e]	200
Mg^{2+}	24[d]	18[d]	20[d]	1.00[e]	35.3
Guanidinium$^+$ (Gu)	9.8			0.59[f]	3.35
NH_4^+	4.4	4.0	3.8	0.56[f]	3.05
$CH_3CH_2NH_3^+$ (EA)	2.6	2.7		0.50[f]	2.50
Ethyl glycinate$^+$ (EG)	3.7			0.41[f]	1.81
Quinuclidinium$^+$ (Q)	2.2			0.38[f]	1.61
K^+	2.2	2.7	2.2	0.35[f]	1.42
Cs^+	1.2			0.26[f]	0.93
Triethylammonium$^+$ (TEA)	0.57		0.55	0.11[f]	0.32

[a] Ionic strength maintained at 1.0 with Me_4NCl, $T = 25$ °C, pH maintained with 0.1 M acetate buffer (50% ionized). [b] Apparent second-order rate constant for cation catalysis divided by the rate constant in Me_4NCl at the experimental pH. [c] Association constants for ion pair formation between cations and sulfite dianion (eq 4). [d] Calculated from the ordinal intercept of a plot of k_{app}/k_0 vs. $[M^{2+}]$. [e] pH change observed in 0.1 M bisulfite buffer (50% ionized) when 0.3 M cation was substituted for Me_4N^+ ion at a constant ionic strength of 1.0. [f] pH change observed in 0.1 M bisulfite buffer (50% ionized) when 0.9 M cation was substituted for Me_4N^+ ion at a constant ionic strength of 1.0.

actions catalyzed by trimethylamine *N*-oxide and lyoxide ion, respectively (Tables I and II). These isotope effects can be expressed in terms of the kinetically equivalent reaction of the conjugate acid of the catalyst with the dianion of the addition compound by multiplying by the ratio of the isotope effects on the ionization constants of BH^+ and the α-hydroxysulfonic acid anion. If this difference is given by antilog 0.017 ΔpK_a,[10] the solvent isotope effect on the general acid catalyzed reaction is $k_{BH^+}/k_{BD^+} = 1.5$. Similarly, based on an isotope effect of $\Delta pK_a = 0.81$ for water[10] and $\Delta pK_a = 0.65$ for the α-hydroxysulfonic acid anion, estimated from the equation of Bell and Kuhn,[10] the isotope effect for breakdown of the dianion is $k_{H_2O}/k_{D_2O} = 1.05$.

"Cation Catalysis". In addition to the salt and solvent effects already described, the value of k_{obsd} is sensitive to the nature of the cationic species used to maintain constant ionic strength, being minimum with Me_4N^+ and maximum with the divalent ions Mg^{2+} and Zn^{2+}. Linear increases in k_{obsd} were observed as potassium or cesium ions were substituted for Me_4N^+ at constant pH and ionic strength. The ratios of the slopes of these plots to the background reaction at the experimental pH (k_{app}/k_0, $k_0 = k_{OH^-}[OH^-]$ in 1 M $Me_4N^+Cl^-$) for these cations and for various ammonium ions are given in Table V. Nonlinear plots of k_{obsd} vs. metal ion concentration having slight upward curvature were observed for Zn^{2+} and to a lesser extent for Mg^{2+}. For these cations the initial k_{app}/k_0 ratios in Table V were determined from extrapolated ordinal intercepts of plots of k_{app}/k_0 vs. $[M^{2+}]$.

Association constants (K_1, Table V) for cation-sulfite ion pair formation were determined from the change in observed pH and bisulfite-sulfite ratio as various cations were substituted for Me_4N^+ ion at a constant ionic strength of 1.0 (eq 4-6). The magnitudes and trends of these association constants are similar to those for these cations and sulfate dianion that were determined by other methods.[11]

Estimation of pK_a Values. The acid dissociation constants of Scheme I were estimated by the method of Fox and Jencks, based on $\rho_I = -8.4$ for the ionization of the hydroxyl group of $X\text{-}CR_2\text{-}OH$;[12] the values of σ_I are from Charton.[13]

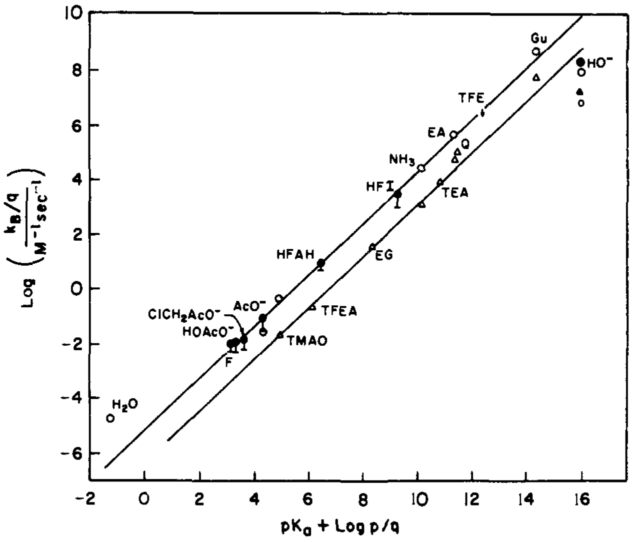
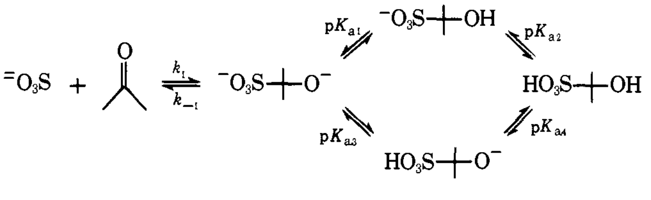


Figure 4. Bronsted plot for the general base catalyzed dissociation of *p*-methoxyacetophenone bisulfite (circles) and *p*-methoxybenzaldehyde bisulfite (triangles). The catalysts used are listed in Tables I and II. The least-squares slope of the line for the *p*-methoxyacetophenone reaction (excluding the points for hydroxide ion and water) is $\beta = 0.94$ and both lines are drawn with this slope. The ionic strength was maintained at 1.0 with KCl (closed symbols) or Me_4NCl (open symbols).

Scheme I



pK_{a1}: Kokesh and Hall[14] reported pK_{a1} for the benzaldehyde bisulfite addition compound to be 10.40. The effect of the *p*-methoxy group is to raise the pK_a 0.18 unit, as estimated from substituent effects on the pK_a of substituted trifluoroacetophenone hydrates,[15] and the substitution of $-CH_3$ for $-H$ raises the pK_a by 0.3 unit.[12] pK_{a1} is therefore $10.40 + 0.18 + 0.3 = 10.88$.

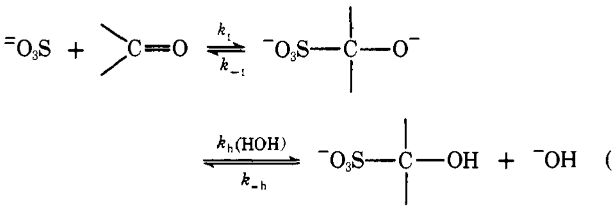
pK_{a2}: The pK_a of benzylsulfonic acid is reported to be approximately -6.5.[16] The α-hydroxyl group will lower this by $(0.25)(-8.4) = -2.1$. Correction for the *p*-OCH_3 and α-methyl groups gives p$K_{a2} = -6.5 + (-2.1) + 0.18 + 0.3 = -8.1$.

pK_{a3}: The electrostatic effect of ionizing the $-OH$ group is estimated to be 4.7 units.[12] pK_{a3} is therefore approximately $-8.1 + 4.7 = -3.4$.

pK_{a4}: The value of pK_{a4} is therefore pK_{a1} + pK_{a2} − pK_{a3} = 6.2.

Discussion

The rate constants for the individual steps of the bisulfite-*p*-methoxyacetophenone reaction in the absence of added catalysts (eq 10) may be calculated from the observed rate constants, the pK_a of the addition compound of 10.88, and the rate constants for simple proton transfer reactions in water.[17] The observed rate constant of 5.8×10^8 M^{-1} s^{-1} for the hydroxide ion catalyzed breakdown reaction is at least an order of magnitude slower than that expected for proton removal by hydroxide ion,[17] so that proton transfer is not rate determining. The still slower rate constants for the benzaldehyde addition compounds (Table IV) confirm this conclusion. From the pK_a of 10.88, $K_w = 10^{-14}$, and assuming[17] $k_{-h} = 6 \times 10^9$ M^{-1} s^{-1}, the value of k_h is 4.6×10^6 s^{-1}. The rate-determining step for the breakdown reaction is expulsion of the sulfite dianion, and the rate constant for this step of $k_{-1} = 4.4 \times 10^5$ s^{-1} is an order of magnitude slower than k_h. Similar calculations for the benzaldehyde bisulfite compounds give even larger k_h/k_{-1} ratios of 88, 108, and 121 for the *p*-methoxy-, *p*-chloro-, and *p*-nitro-substituted compounds, respectively.[18] Thus, in the forward direction the dianionic addition intermediate abstracts a proton from water (k_h) faster than it reverts to starting materials (k_{-1}), and there is no requirement for catalysis by a trapping, preassociation, or concerted mechanism. The small value of the ratio $k_{-1}/(k_h + k_s)$ also means that there is no facilitation of catalysis by hydrogen bonding because of a short lifetime of the addition intermediate.



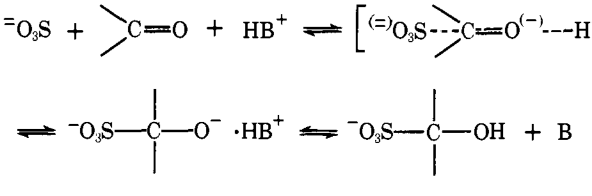
$$ {}^{=}O_3S + {>}C{=}O \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} {}^{-}O_3S{-}C{-}O^{-} \underset{k_{-h}}{\overset{k_h(HOH)}{\rightleftharpoons}} {}^{-}O_3S{-}C{-}OH + {}^{-}OH \qquad (10)$$

The large slope of the Bronsted plot for general base catalysis of the breakdown reaction with $\beta = 0.94 \pm 0.05$ (Figure 4) means that proton transfer is almost complete and the catalyst closely resembles its conjugate acid in the transition state. Catalysis with this large β value is detectable only because the points for hydroxide ion exhibit negative deviations from the Bronsted line. This large slope is consistent with a mechanism for catalysis in which there is modest stabilization of the transition state by hydrogen bonding to BH^+. The observed general base catalysis of breakdown of the monoanion of the addition compound with the rate constant k_B can be described by the kinetically equivalent rate law for general acid catalysis of the breakdown of the dianion with the rate constant k_{BH}':

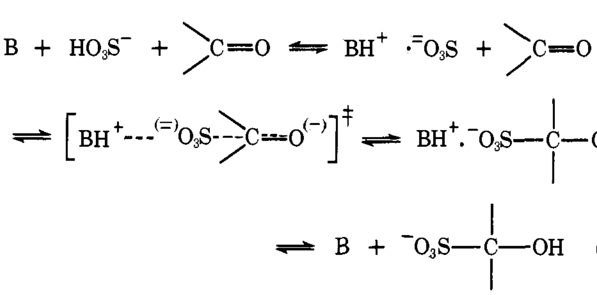
$$v = k_B[B][{}^{-}O_3SCHArOH] = k_{BH}'[BH^+] \times [{}^{-}O_3SCHArO^{-}] \qquad (11)$$

The small value of $\alpha = 1 - \beta = 0.06$ suggests that there is only a small perturbation of the B-H bond of the catalyzing acid by a weakly basic transition state.

The two simplest mechanisms for this catalysis, shown in eq 12 and 13, differ depending upon whether the catalysis involves the carbonyl oxygen atom (eq 12) or the attacking-leaving sulfite ion (eq 13). Catalysis at the carbonyl oxygen atom stabilizes the developing negative charge by hydrogen bonding to the acid in the forward direction and increases the concentration of the reacting dianion in the reverse direction (eq 12). Catalysis at the sulfite group stabilizes the developing negative charge on the leaving sulfite dianion by hydrogen bonding to the acid in the breakdown direction and increases the concentration of the attacking sulfite dianion in the forward direction (eq 13).



$$ {}^{=}O_3S + {>}C{=}O + HB^+ \rightleftharpoons \left[{}^{(=)}O_3S{--}C{=\!=}O^{(-)}{---}HB^+\right]^{\ddagger} \rightleftharpoons {}^{-}O_3S{-}C{-}O^{-}\cdot HB^+ \rightleftharpoons {}^{-}O_3S{-}C{-}OH + B \qquad (12)$$



$$ B + HO_3S^{-} + {>}C{=}O \rightleftharpoons BH^+\cdot{}^{=}O_3S + {>}C{=}O \rightleftharpoons \left[BH^+{---}{}^{(=)}O_3S{--}C{=\!=}O^{(-)}\right]^{\ddagger} \rightleftharpoons BH^+\cdot{}^{-}O_3S{-}C{-}O^{-} \rightleftharpoons B + {}^{-}O_3S{-}C{-}OH \qquad (13)$$

Hine[19] has suggested that approximate equilibrium constants K_{AB} for hydrogen bond formation in aqueous solution can be estimated from

$$\log K_{AB} = \tau(pK_{HA} - pK_{H_2O})(pK_{H_3O^+} - pK_B) - 1.74 \qquad (14)$$

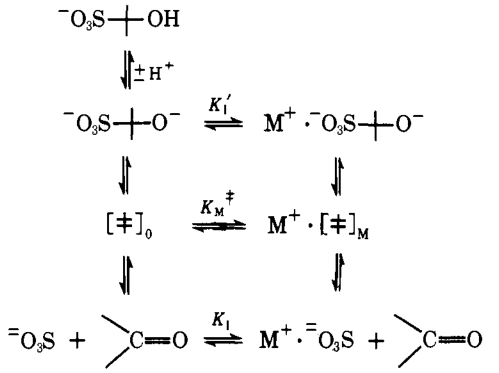
in which HA refers to the proton donor (BH^+ in the above discussion), and pK_B is the pK of the conjugate acid of the proton acceptor, corresponding to the basic site in the transition states of eq 12 and 13. The association constant K_{AB} corresponds to the ratio of the rate constants for the general acid catalyzed and uncatalyzed reactions and $\Delta\log K_{AB}/\Delta pK_{HA}$ gives the Bronsted slope α. The pK of the transition state is given by

$$(\alpha/\tau) - 1.74 = pK^{\ddagger} \qquad (\tau = 0.024) \qquad (15)$$

and is equal to ~1 for $\alpha = 0.06$.

The ρ^+ value for the equilibrium formation of the dianionic addition compound from a series of substituted benzaldehydes is approximately 2.36, based on a value of $\rho^+ = 1.25$ for the equilibrium formation of the monoanion of the addition compound[20] and $\rho = 1.11$ for ionization of the α-hydroxy proton.[15] The ρ^+ value of 1.12 for the rate constant of the forward reaction indicates that the transition state is about halfway between starting materials and products as measured by substituent effects on the benzaldehyde. The secondary deuterium isotope effects on the rate and equilibrium constants for the addition of sulfite to acetone are $k_H/k_D = 0.91$ and $K_H/K_D = 0.77$, respectively, which also suggests a transition state that has proceeded roughly halfway or slightly less toward completion.[21] If the dubious assumption is made that the pK values of the reacting groups have also changed halfway toward those of the products in the transition state, the pK values of the sulfite and carbonyl oxygen atoms are roughly -0.9 and 3.7, respectively, in the transition state.[22] In view of the uncertainties in these assumptions and eq 14 and 15, either of these values is consistent with catalysis by hydrogen bonding, the observed value of $\alpha = 0.06$, and the estimated pK of the transition state, but it is not possible to distinguish between the mechanisms of eq 12 and 13 on this basis. A distinction between mechanisms can also be made, in principle, from the effect of polar substituents in the aldehyde on the Bronsted slope,[23] but the absence of a significant change in the ratio k_{app}/k_0 with a series of substituted benzaldehydes (Table IV) provides no basis for such a distinction in this reaction.

The reaction is also accelerated by the dications Mg^{2+} and Zn^{2+} and, to a lesser extent, by the substitution of alkali monocations for tetramethylammonium ions at constant ionic strength. This acceleration may be described either in terms of a specific salt effect on the activity coefficient ratio of the reactants and transition state or in terms of cation binding to the transition state. As shown in Figure 5, the increases in the rates of the *p*-methoxyacetophenone, *p*-methoxybenzaldehyde, and *p*-chlorobenzaldehyde reactions that are brought about by cations are correlated with the association constants of the same cations with sulfite dianion, except for a positive deviation by guanidinium ion. Catalysis by amine buffers can be described in terms of catalysis by the amine base of the reaction of the monoanionic substrate or catalysis by the protonated amine of the reaction of the dianionic substrate (eq 11). When the catalysis is expressed in terms of the amine cation, the rate accelerations that are brought about by a number of weak acid catalysts (for which association constants with sulfite dianion could be determined) fall on the same correlation line (Figure 5). This suggests that stabilization by both metal cations and acid catalysts of the dianionic transition state resembles the stabilization of the dianionic sulfite product and that the equilibrium constant for the binding of metal or catalyst to the transition state ($K_M{}^{\ddagger}$, eq 16) is approximately 0.7 times as

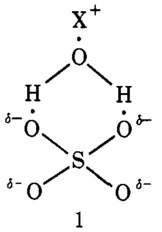

(16)

sensitive to changes in structure as the equilibrium constant K_I for binding to the sulfite product. Thus, the observed rate accelerations may reasonably be ascribed to binding to the leaving sulfite dianion or to a structurally similar species in the transition state. This mechanism of catalysis is not available for the addition of other basic nucleophiles such as cyanide ion, basic thiol anions, and trimethylamine, which may help to account for the failure to detect catalysis of these reactions.[3,24]

Ultrasonic absorption studies suggest that ion pair formation in water between magnesium and sulfate ions can be described by:

$$\mathrm{Mg_{(aq)}}^{2+} + \mathrm{SO_{4(aq)}}^{=} \overset{K_1}{\rightleftharpoons} [\mathrm{Mg}\cdot(\mathrm{W}\cdot\mathrm{W})\cdot\mathrm{SO_4}] \overset{K_2}{\rightleftharpoons} [\mathrm{Mg}\cdot(\mathrm{W})\cdot\mathrm{SO_4}] \overset{K_3}{\rightleftharpoons} [\mathrm{Mg}\cdot\mathrm{SO_4}] \qquad (17)$$

with values of $K_1 = 50\ \mathrm{M}^{-1}$, $K_2 = 1.96$, and $K_3 = 0.17$.[25,26] The predominant species is that in which the ions are separated by a single water molecule, presumably with the structure **1** ($X^+ = Mg^{++}$). Furthermore, Ralph and Grunwald[27] have demonstrated the existence in water of hydrogen-bonded acid-base pairs in which the proton donor and acceptor are separated by a water molecule. Therefore, it appears reasonable to suggest that similar structures are involved in stabilization of the transition state of the bisulfite reaction by both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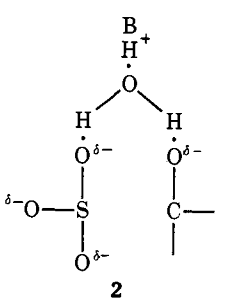
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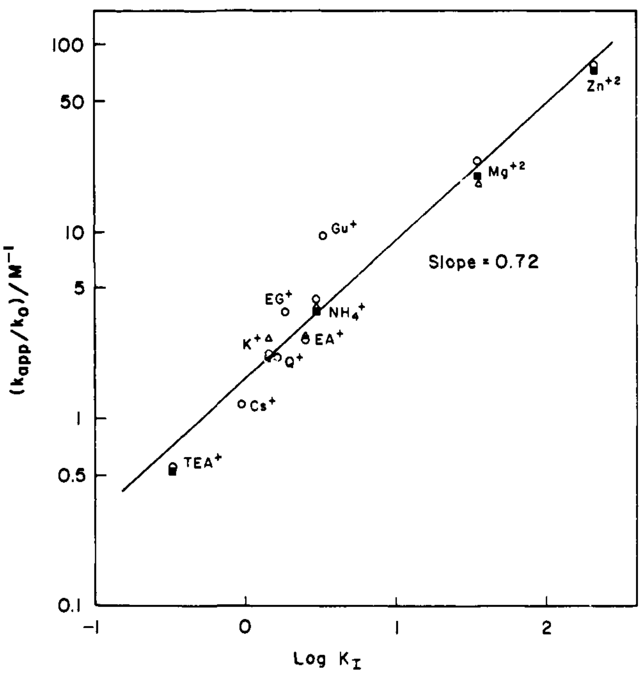
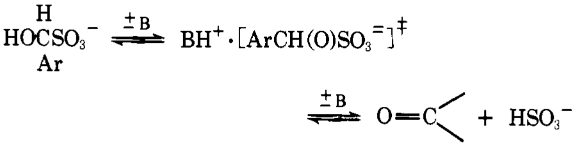


Figure 5. The relationship between the observed (k_{app}/k_0) ratios for the dissociation of *p*-methoxyacetophenone bisulfite (triangles) and of *p*-methoxy- and *p*-chlorobenzaldehyde bisulfites (circles and squares, respectively) and the association constants for ion pair formation between the various cations and sulfite dianion. The cations used are listed in Table IV. The line has a slope of 0.72.

cations and hydrated acid catalysts ($X^+ = BH^+$). This would explain the catalytic activity of both monofunctional catalysts, such as quinuclidinium ion, and bifunctional catalysts, such as guanidinium ion, which may bind directly to the transition state. The similar catalytic activity of neutral and cationic acids suggests that the electrostatic contribution to catalysis by buffer acids is small and that hydrogen bonding to the acidic proton is the principal source of catalysis. The same conclusion may be drawn from the experimental fact that catalysis by amines is observed at constant total cation concentration when the only change in the medium is the substitution of R_3NH^+, with an acidic proton, for Me_4N^+.

The catalysis could involve transition-state stabilization by hydrogen bonding to two oxygen atoms of the leaving sulfite dianion (eq 13). However, an equally or more attractive mechanism involves hydrogen bonding to the partial negative charge on the carbonyl oxygen atom as well as to sulfite (**2**) because this mechanism provides stabilization to the two most basic sites in the transition state. This mechanism provides the advantages of the mechanisms of both eq 12 and 13 through a bifunctional interaction of the catalyst with the transition state and is consistent with the observed correlation of catalytic effectiveness with the association constants for complex formation between cations and the structurally similar sulfite dianion (Figure 5). Regardless of the detailed mechanism, the observed catalysis can be described simply in terms of a stabilization of the dianionic transition state, and also the dianionic intermediates from which it is formed, by hydrogen bonding to a catalyzing acid:



$$\mathrm{HO}\underset{\mathrm{Ar}}{\overset{\mathrm{H}}{\mathrm{C}}}\mathrm{SO_3}^- \overset{\pm B}{\rightleftharpoons} \mathrm{BH^+}\cdot[\mathrm{ArCH(O)SO_3}^=]^{\ddagger} \overset{\pm B}{\rightleftharpoons} \mathrm{O{=}C}\!< + \mathrm{HSO_3}^- \qquad (18)$$

References and Notes

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(2) P.R.Y. was partially supported by a fellowship (CA 05356) from the National Cancer Institute of the National Institutes of Health.

(3) E. H. Cordes and W. P. Jencks, *J. Am. Chem. Soc.*, **84**, 4319 (1962); W. P. Jencks, *Prog. Phys. Org. Chem.*, **2**, 63 (1964); L. do Amaral, W. A. Sandstrom, and E. H. Cordes, *J. Am. Chem. Soc.*, **88**, 2225 (1966).

(4) J. M. Sayer, B. Pinsky, A. Schonbrunn, and W. Washtien, *J. Am. Chem. Soc.*, **96**, 7998 (1974).

(5) W. P. Jencks and J. M. Sayer, *Faraday Symp. Chem. Soc.*, **10**, 41–49 (1974); W. P. Jencks, *Acc. Chem. Res.*, **9**, 425 (1976).

(6) Catalysis by hydrogen bonding has also been suggested for the general acid catalyzed addition of hydrogen peroxide to benzaldehydes[5] [E. G. Sander and W. P. Jencks, *J. Am. Chem. Soc.*, **90**, 4377 (1968)]. However, in this reaction, proton transfer from the catalyzing acid is almost complete in the transition state, and the lifetime of the protonated intermediate is not known.

(7) L. R. Green and J. Hine, *J. Org. Chem.*, **39**, 3896 (1974).

(8) T. D. Stewart and L. H. Donnally, *J. Am. Chem. Soc.*, **54**, 2333 (1932).

(9) U. K. Klaning and O. Osterby, *J. Chem. Soc., Faraday Trans. 1*, 513 (1976).

(10) P. M. Laughton and R. E. Robertson in "Solute-Solvent Interactions", J. G. Coetzee and C. D. Ritchie, Ed., Marcel Dekker, New York, N.Y., 1969, pp 415–420, and references cited therein; R. P. Bell and A. T. Kuhn, *Trans. Faraday Soc.*, **59**, 1789 (1963).

(11) C. Davies, "Ion Association", Butterworths, Washington, 1962, pp 168–170; E. J. Reardon, *J. Phys. Chem.*, **79**, 422 (1975).

(12) J. P. Fox and W. P. Jencks, *J. Am. Chem. Soc.*, **96**, 1436 (1974).

(13) M. Charton, *J. Org. Chem.*, **29**, 1222 (1964).

(14) F. C. Kokesh and R. E. Hall, *J. Org. Chem.*, **40**, 1632 (1975).

(15) R. Stewart and R. Van der Linden, *Can. J. Chem.*, **38**, 399 (1960).

(16) A. Koeberg-Telder and H. Cerfontain, *J. Chem. Soc., Perkin Trans. 2*, 226 (1975).

(17) M. Eigen, *Angew. Chem., Int. Ed. Engl.*, **3**, 1 (1964), reports $k_{OH^-} \sim 6 \times 10^9$ M^{-1} s^{-1} for deprotonation of bicarbonate monoanion, to give the dianion.

(18) (k_h/k_{-1}) for *p*-methoxy-, *p*-chloro-, and *p*-nitrobenzaldehyde bisulfites are: $(2.3 \times 10^6$ $s^{-1}/2.6 \times 10^4$ $s^{-1})$, $(8.5 \times 10^5$ $s^{-1}/7.9 \times 10^3$ $s^{-1})$, $(2.3 \times 10^5$ $s^{-1}/1.9 \times 10^3$ $s^{-1})$, respectively.

(19) J. Hine, *J. Am. Chem. Soc.*, **94**, 5766 (1972).

(20) P. Geneste, G. Lamaty, and J. P. Roque, *Recl. Trav. Chim. Pays-Bas*, **91**, 188 (1972).

(21) P. Geneste, G. Lamaty, and J. P. Roque, *Tetrahedron*, **27**, 5539 (1971).

(22) The value of pK_{a3} (Scheme I) is −8.1, and the pK_a of bisulfite is 6.42 (μ = 1.0, KCl), giving a total ΔpK of 14.5. The pK of the conjugate acid of *p*-methoxyacetophenone is −3.39 [A. Levi, G. Medena, and G. Scorrano, *J. Am. Chem. Soc.*, **96**, 6585 (1974)] and pK_{a1} of the product (Scheme I) is 10.88, giving a total ΔpK of 14.27.

(23) W. P. Jencks, *Chem. Rev.*, **72**, 705 (1972). Since $k_{app} \cong k_B$ and k_0 is a measure of k_{OH^-}, the absence of a trend in the ratio k_{app}/k_0 means that there is no detectable change in the Bronsted slope β.

(24) W. J. Svirbely and J. F. Roth, *J. Am. Chem. Soc.*, **75**, 3106 (1953); G. E. Lienhard and W. P. Jencks, *ibid.*, **88**, 3982 (1966); T. D. Stewart and H. P. Kung, *ibid.*, **55**, 4813 (1933); J. Hine and F. C. Kokesh, *ibid.*, **92**, 4383 (1970).

(25) G. Atkinson and S. Petrucci, *J. Phys. Chem.*, **70**, 3122 (1966).

(26) M. Eigen and K. Tamm, *Z. Elektrochem.*, **66**, 93, 107 (1962).

(27) E. K. Ralph and E. Grunwald, *J. Am. Chem. Soc.*, **91**, 2422 (1969).

Sulfonation of Acyclic Fluorovinyl Ethers

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Abstract: Contrary to implications in the literature, polyfluorovinyl ethers have been shown to form unstable sultones with sulfur trioxide. Near 25 °C these sultones isomerize easily to β-carbonylsulfonate esters. A fluorovinyl diether was found to lead preferentially to cyclic sulfate, a convenient precursor to a perfluoro α-diketone. Mechanisms for these transformations are proposed. These reactions offer superior routes to the two classes of difunctional fluoroorganics, β-carbonylsulfonates and α-diketones.

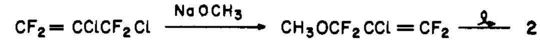
Electrophilic attack on fluoroolefins by sulfur trioxide to form fluorinated sultones is a well-documented reaction.[1,2] Terminal olefins are particularly susceptible to the reaction, which appears to proceed through a dipolar intermediate.[2] Stabilization of positive charge by α-fluorine atoms in the intermediate and destabilization by β-fluorine atoms[3] account for the observed orientation and for the fact that internal fluoroolefins are rarely reported to undergo the cycloaddition. In view of the special effectiveness of α-alkoxy groups in stabilization of cations, the known[4] facile addition of sulfur trioxide with fluorovinyl ethers is also compatible with formation of a dipolar intermediate. For the limited number of such reactions already in the literature, sultone and cyclic sulfonate–sulfate anhydride are the reported products.[2,4] As described below, we find the reaction of sulfur trioxide with a series of acyclic fluorovinyl ethers is at variance with these reports.[5]

Syntheses of Representative Fluorovinyl Ethers. A selection of vinyl ethers with varied substituents on the vinyl group was required for this study. Those with a trifluoromethyl group in the 1 position are best obtained by the action of a trialkyl phosphite on hexafluoroacetone;[6] yields of **1** by this route were generally 60% for preparations on a molar scale.

$$CH_3CH_2OC(CF_3)=CF_2 \qquad CH_3OCF=CClCF_3$$

1 **2**

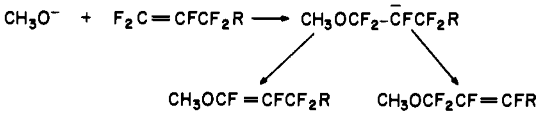
Vinyl ether **2** was obtained by an unusually facile rearrangement of the allyl ether **3**, which was itself prepared by an S_N2' displacement on **4**.[7]



$$CF_2=CClCF_2Cl \xrightarrow{NaOCH_3} CH_3OCF_2CCl=CF_2 \longrightarrow 2$$

4 **3**

Methyl perfluoro-1-alkenyl ethers (**5**) were prepared by treatment of terminal perfluoroalkenes with 1 mol of sodium methoxide. Hexafluoropropene in this reaction gives the vinyl ether in good yield; none of the allylic ether potentially available from S_N2' displacement of fluoride is observed.[8] The intermediate carbanion apparently undergoes loss of the fluoride ion which leads to the more thermodynamically stable product, difluorovinyl ether **5** (R = F) rather than the trifluorovinyl product **6** (R = F).



5 **6**

Although such displacements of vinylic halogen are well known,[9] there seems to be no report of a case in which a longer