avoiding isomerization: low isotherm 65 °C for 4 min; high isotherm 110 °C; temperature increment 5 °C/min; evaporator and detector 160 °C; nitrogen flow 30 mL/min. The relative retention times of 2 and 1 were 2.9:1. The dibromo derivatives were stable under the GLC conditions, and no changes in product composition were observed after repeated workup. Moreover, control experiments carried out with both dibromo derivatives 1 and 2 showed that at the highest concentration of dibromides obtained in the kinetic runs the presence of a 100-fold excess of pyridine caused only a negligible UV absorption in the 300–350-nm range within the time required to complete the kinetic runs, showing that no appreciable reaction of dibromides 1 and 2 with pyridine to give pyridinium bromides 3 or 6 occurred during these runs. No tetrabromo derivatives were formed under all bromination conditions employed. The product distributions obtained in the kinetic runs are reported in Tables I–III.

Preparative Brominations. With Molecular Bromine. Equal volumes (50 mL) of solutions of bromine and 1,3-butadiene of appropriate *concentrations* (Table IV) in 1,2-dichloroethane or dichloromethane were rapidly mixed at 20 °C. After 20 min, the resulting solutions were evaporated, and the residues, consisting of the dibromo derivatives 1 and 2, were weighed and subjected to GLC. The yields of dibromides and the 1/2 ratios are reported in Table IV.

With PyBr₂. (A) In 1,2-Dichloroethane. Equal volumes (50 mL) of solutions of diene and of PyBr₂ (prepared from the solid CTC and in some cases containing added pyridine) of appropriate concentrations (Table IV) were rapidly mixed and allowed to react at 20 °C. After about 10 min a white crystalline product started precipitating. Within 30 min the completely colorless solution was filtered off, and the precipitate, consisting of *N*-(4-bromo-1-buten-3-yl)pyridinium bromide (3), was collected and weighed. After crystallization from methanol–acetone, 3 had the following: mp 142–143 °C; ^{1}H NMR (D₂O) δ 4.12, 4.16 (2 d, J = 8.5 and 5.0 Hz, 2 diastereotopic H, CH₂Br), 5.51–5.82 (overlapping m, 3 H, =CH₂ and >CH–N$^+$<), 6.08–6.51 (m, 1 H, CH=), 8.17, 8.67, 9.00 (3 m, 5 H, C₅H₅N$^+$); ^{13}C NMR (D₂O) δ 34.95, 75.91, 126.47, 131.14, 133.24, 146.07, 149.64. In an off-resonance-irradiation experiment the signal at δ 34.95 became a triplet (CH₂Br) and that at 75.91 a doublet (>CH–N$^+$<).

Anal. Calcd for C₉H₁₁Br₂N: C, 36.89; H, 3.78; N, 4.78. Found: C, 37.00; H, 3.58; N, 4.95.

Small samples of the mother liquors were subjected to spectrophotometric measurements in the 330–360-nm range in order to calculate the amount of dissolved 3. At the same time the mother liquors were washed with 10% aqueous HCl and water, dried, and evaporated, and the residues, consisting of the dibromo

derivatives 1 and 2, were weighed and subjected to GLC. The yields of 1–3 and the 1/2 ratios are reported in Table IV.

(B) In CH₂Cl₂. The reaction was carried out at the concentrations reported in Table IV as described in section A, but no precipitation was observed within 30 min.[30] The concentration of the dissolved bromide 3 was then determined from the absorbances in the 320–360-nm range, the reaction mixture worked up as reported above, and the residue analyzed by GLC. The yields of 1–3 as well as the dibromide ratio are reported in Table IV.

With TBAT. Solutions of the diene and of preformed TBAT in 1,2-dichloroethane of concentrations reported in Table IV were mixed and allowed to react at 20 °C, until complete discoloration, then washed with water, dried, and evaporated. The residue was weighed and subjected to GLC. The yields of 1 and 2 and their ratio are shown in Table IV.

Reactions of Dibromides 1 and 2 with Pyridine. A. Equal volumes (15 mL) of a 0.04 M solution of the 1,4-dibromide 2 and of a 0.1 M solution of pyridine in 1,2-dichloroethane were mixed and stirred at room temperature. A white crystalline product began precipitating within 40 min. After the mixture was stirred for 24 h, the precipitate, consisting of the 1,4-dipyridinium adduct 6, was collected (0.74 g). After crystallization from methanol-acetone, the product, containing two molecules of crystallization water, had the following: mp 195–197 °C; ^{1}H NMR (D₂O) δ 5.38 (unresolved m, 4 H, 2 CH₂–N$^+$<), 6.32 (unresolved m, 2 H, 2 CH=), 8.13, 8.60, 8.90 (3 m, 10 H, 2 C₅H₅N$^+$).

Anal. Calcd for C₁₄H₁₆Br₂N₂·2H₂O: C, 41.19; H, 4.95; N, 6.86. Found: C, 41.40; H, 4.77; N, 6.92.

B. When the reaction of the 1,2-dibromo adduct 1 with pyridine was carried out as described in method A, only a very small amount of 6 (~0.01 g), identified by the IR spectrum, was obtained after 3 h. A further slight precipitate of 6 (~0.01 g) was collected after 24 h, and only comparably small amounts of this salt were formed after longer reaction times.

(30) No precipitation of 3 occurred even after a long time at low temperature.

Kinetics and Mechanism of the Oxidation of Primary Alcohols by *N*-Bromoacetamide in Acid Medium

Jogeshwar Mukherjee and Kalyan K. Banerji*

Department of Chemistry, University of Jodhpur, Jodhpur-342001, India

The kinetics of the oxidation of ten primary alcohols by *N*-bromoacetamide (NBA) has been studied in acid medium. The main product of the oxidation is the corresponding aldehyde. The reaction is first order in alcohol, NBA, and H$^+$. The oxidation of ethanol-*1,1-d₂* indicates no primary kinetic isotope effect. A solvent isotope effect, $k(D_2O)/k(H_2O) = 1.16$, was observed at 308 K. The rates were determined at four different temperatures and the activation parameters were evaluated. Addition of acetamide decreases the rate. (H₂OBr)$^+$ has been postulated as the oxidizing species. A mechanism involving formation of a hypobromite ester in the rate-determining step has been proposed. The reaction constant, ρ^*, has a value of −1.53 at 303 K.

NBA has been used in preparative organic chemistry as an oxidizing and halogenating reagent.[1] There seems to be no report in the literature about its mode of oxidation. However, its analogues, *N*-bromosuccinimide (NBS) and

N-chlorosuccinimide, have received substantial attention and several studies on the mechanism of their reaction have been reported in recent years.[2,3] The different

(1) R. Filler, *Chem. Rev.*, **63**, 21 (1963).

(2) N. Venkatasubramanian and V. Thiagarajan, *Tetrahedron Lett.* 3349 (1967); *Can. J. Chem.*, **47**, 694 (1969); *Indian J. Chem.*, **8**, 809 (1970).

Table I. Stoichiometry of the Oxidation of Ethanol
by N-Bromoacetamide

[H$^+$], M	moles of NBA consumed per mole of ethanol	% yield of DNP of acetaldehyde^a
0.2	1.07	
0.4	1.01	
0.6	0.91	
0.2		82
0.3		90
0.5		86

^{a} Based on NBA consumption.

mechanistic pathways[3] reported for these structurally related compounds prompted us to undertake this investigation. We report in this paper the kinetics of the oxidation of ten primary alcohols in 1:1 (v/v) acetic acid–water in the presence of perchloric acid. Mechanistic conclusions are discussed.

Experimental Section

General Procedures. All alcohols were commercial products. Methanol, ethanol, and 1-propanol were purified by the magnesium alkoxide method.[4] 2-Methoxyethanol and 2-chloroethanol were dried over anhydrous calcium sulfate and fractionated. Other alcohols were dried over anhydrous potassium carbonate and then fractionated. NBA was prepared by the reported method,[5] and its purity checked by iodometric titration of active bromine. Ethanol-*1,1-d$_2$* was prepared by Kaplan's method.[6] Its isotopic purity as ascertained by its NMR spectra was 92 ± 5%. Deuterium oxide (purity 99.4%) was supplied by BARC, Bombay (India). Perchloric acid (E. Merck) was used as a source of hydrogen ions. Acetic acid was first refluxed with chromic oxide and acetic anhydride for 3 h and then fractionated.[7] The fraction coming over between 116–118 °C was collected. While the effect of the varying concentration of perchloric acid on the reaction rate was studied, ionic strength was kept constant at 0.8 M by using sodium perchlorate.

Product Analysis and Stoichiometry. The product analysis was made under kinetic conditions. Ethanol (2.30 g, 0.05 mol) and NBA (1.39 g, 0.01 mol) made up to 50 mL in perchloric acid (0.2–0.5 M) were kept in the dark for 8 h until completion of oxidation. The solution was then treated overnight with an excess (200 mL) of a freshly filtered saturated solution of 2,4-dinitrophenylhydrazine in 2 M hydrochloric acid. The precipitated 2,4-dinitrophenylhydrazone (DNP) was collected by filtration. It was weighed both before and after being recrystallized from ethanol. The difference in the crude yield and yield determined after recrystallization was about 2%. Mixture melting point and mixture TLC of the DNP of the product and that of an authentic sample confirmed that the product was acetaldehyde. Similar experiments were carried out with other alcohols.

Stoichiometry was ascertained by treating ethanol (0.46 g, 0.01 mol) with NBA (6.95 g, 0.05 mol) in the presence of perchloric acid (0.2–0.6 M). The residual NBA was determined iodometrically.

Kinetic Measurements. The reactions were carried out under pseudo-first-order conditions by keeping an excess (×15 or greater) of the alcohol over NBA. The solvent was 1:1 (v/v) acetic acid–water unless mentioned otherwise. All reactions were carried out in blackened flasks to avoid any photochemical reactions. Aliquots were withdrawn at suitable time intervals by means of a pipet and the amount of unreacted NBA was determined by iodometric
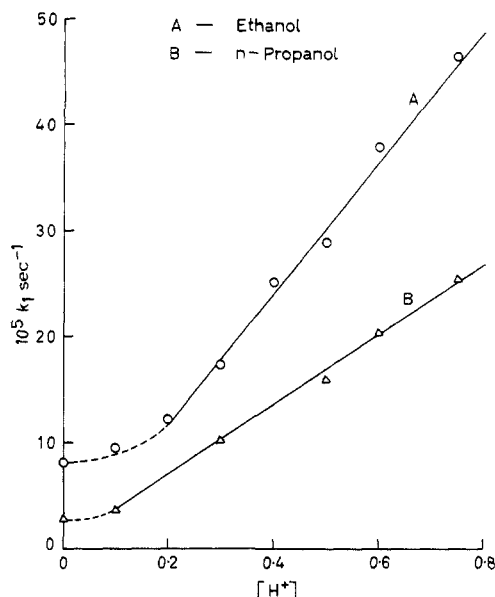
(3) N. S. Srinivasan and N. Venkatasubramanian, *Tetrahedron*, **30**, 419 (1974).

(4) A. I. Vogel, "A Text Book of Practical Organic Chemistry", Longmans, London, 1967, p 167.

(5) E. P. Oliveto and C. Gerold in "Organic Syntheses", Collect. Vol. IV, H. Gilman, Ed., John Wiley, New York, 1963, p 104.

(6) L. Kaplan, *J. Am. Chem. Soc.* **80**, 2639 (1958).

(7) K. J. Orton and A. Bradfield, *J. Chem. Soc.*, 960 (1924); *ibid*; 983 (1927).

Figure 1. Plot of observed rate constant k_1 vs. [H$^+$]: [NBA] = 0.005 M; [Hg(II)] = 0.005 M; I = 0.80 M; [EtOH] = 1.72 M; [n-PrOH] = 0.65 M; T = 308 K.

titrations. The reactions were followed up to 70% reaction. The pseudo-first-order rate constant, k_1, was computed from plots of log [NBA] against time. Duplicate kinetic runs showed that the rate constants are reproducible within ±3%. Experiments carried out at different initial [alcohol] and [H$^+$] indicated a rate law of the form, rate = k[NBA][Alcohol][H$^+$], where k = k_1/[alcohol][H$^+$].

Results and Discussion

The oxidation of alcohols results in the formation of corresponding aldehydes. The amount of NBA consumed and the aldehyde formed (Table I) indicate the overall reaction of eq 1.

$$RCH_2OH + MeCONHBr \rightarrow$$
$$RCHO + MeCONH_2 + Br^- + H^+ \quad (1)$$
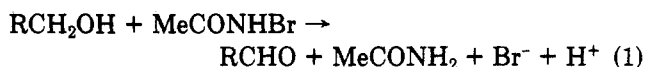
When the concentration of the alcohol is in excess, the plot of log [NBA] against time shows that the reaction is composed of two successive reactions. The initial slow reaction is followed by a faster reaction. Such an observation has been recorded in NBS oxidations also[2] and the faster reaction has been attributed to bromine oxidation. We also observed a yellow color (perhaps of liberated bromine) in the reaction mixture after the reaction has proceeded to about 15%. The liberation of the yellow color and the second faster reaction were suppressed by the addition of 0.005 M of mercury(II) acetate.[2] All reactions were, therefore, carried out in the presence of 0.005 M mercury(II) acetate. Under these conditions, the first-order plots were linear (r > 0.98) for over 70% of the reaction. The rate of the reaction in the presence of mercury(II) was nearly the same as the rate of the slow initial reaction without Hg(II).

The first-order dependence both in NBA and the alcohol was established by effecting a manifold variation in the respective concentration at the constant concentration of other components. (These data are available as supplementary material; see paragraph at the end of the paper.) The reaction is catalyzed by perchloric acid. The reaction rate increases slowly at lower acidity but above [H$^+$] = 0.2 M the order is one. (These data are also available as supplementary material; see paragraph at the end of the paper.) The linear plot between observed k_1 and [H$^+$] (Figure 1) indicates that the oxidation proceeds even in

Table II. Temperature Dependence of Reaction Rate and Activation Parameters for Oxidation of Primary Alcohols, RCH_2OH, by *N*-Bromoacetamide

substituent	10^5k, M^{-2} s^{-1}, at T, K				ΔH^*, kJ mol^{-1}	$-\Delta S^*$, J mol^{-1} K^{-1}	ΔF^*, kJ mol^{-1}
	303	308	313	318			
H	6.55	9.12	11.8	16.1	47.4	153	94.4
Me	29.2	45.9	81.3	131	83.6	62	103
Et	42.0	58.8	83.5	138	55.6	128	95
n-Pr	54.9	78.8	107	175	60.9	109	94
n-Bu	57.9	75.1	98.0	130	43.6	166	95
i-Pr	82.4	94	105	125	22.1	234	94
i-Bu	88.3	104	109	120	18.2	246	94
$ClCH_2$	1.20	1.90	2.44	3.60	57.8	151	104
$MeOCH_2$	4.0	4.3	5.4	6.0	27.4	242	102
$MeCH(OMe)CH_2$	77.4	102	137	186	42.9	166	94

Table III. Effect of Acetamide on the Rate of Oxidation of Ethanol by *N*-Bromoacetamide[a]

10^3[acetamide], M	0.00	2.0	2.5	5.0	7.5	10.0
10^5k_1, s^{-1}		19.7	16.7	16.0	13.5	11.5	10.2

[a] [NBA] = 0.005 M; [EtOH] = 0.858 M; [H⁺] = 0.5 M; [Hg(II)] = 0.005 M; T = 308 K.

the absence of added mineral acid. To avoid complications all rate data were obtained in the [H⁺] range where the rate is first order with respect to H⁺. Table II records the rate constants for the oxidation of alcohols at different temperatures and the activation parameters.

To examine the possibility of one-electron oxidation, the reaction was carried out in the presence of acrylonitrile in an atmosphere of nitrogen. One-electron oxidation produces free radicals which are known to induce polymerization of acrylonitrile.[8] The oxidation of alcohols by NBA in an atmosphere of nitrogen, however, failed to induce polymerization of acrylonitrile. Thus one-electron oxidation is highly unlikely.

Addition of acetamide decreases the rate of oxidation (Table III). This retarding effect suggests that the preequilibrium step involves a process in which acetamide is one of the products (2).

The linear increase in the rate of reaction with acidity may well be due to protonation of HOBr to give a cationic bromine species (3). From this observation it is likely that in the absence of added mineral acid the oxidizing species is HOBr.

Venkatasubramanian and Thiagarajan[2] also observed a retarding effect of the parent amide on the oxidation rate in the alcohol–NBS reaction, but no explanation has been given. They did suggest that the effect of amide could be traced to the equilibrium producing "positive" bromine but assumed NBS or NBSH⁺ to be the reactive species. They have not reported any effect of acidity. We propose that the reactive species in the oxidation by *N*-bromoamides in acid solution is $(H_2OBr)^+$.

An increase in the amount of acetic acid in the solvent results in an increase in the rate of oxidation. (The data for the effect of solvent composition are included in the supplementary material; see paragraph at the end of the paper.) Values of the dielectric constant of acetic acid–water mixtures have been estimated earlier.[9] A plot of log k_1 against the inverse of the dielectric constant gives a straight line (Figure 2) for water-rich mixtures; the increase is less than expected when more organic component is present. Thus according to Amis[10] an interaction be-
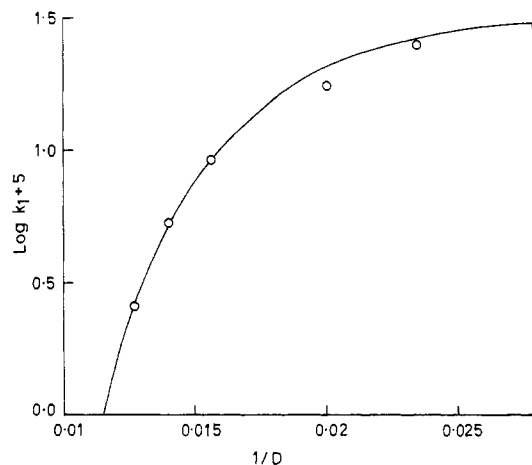
Figure 2. Plot of log (observed rate constant k_1) vs. inverse of the dielectric constant of the solution: [NBA] = 0.005 M; [Hg(II)] = 0.005 M; [EtOH] = 1.72 M; [H⁺] = 0.5 M; T 303 K.

Table IV. Kinetic Isotope Effect in Oxidation of Ethanol by *N*-Bromoacetamide[a]

[EtOH], M	type	10^5k_1, s^{-1}
0.858	$\alpha,\alpha\text{-}^1H_2$	19.7
1.716	$\alpha,\alpha\text{-}^1H_2$	39.4
2.574	$\alpha,\alpha\text{-}^1H_2$	58.2
0.83	$\alpha,\alpha\text{-}^2H_2$	18.0
1.66	$\alpha,\alpha\text{-}^2H_2$	37.2
2.49	$\alpha,\alpha\text{-}^2H_2$	55.0

[a] 10^4k_H = 4.60 M^{-2} s^{-1}; 10^4k_D = 4.41 M^{-2} s^{-1}; k_H/k_D = 1.05; [NBA] = 0.005 M; [H⁺] = 0.5 M; [Hg(II)] = 0.005 M; T = K.

tween a dipole and a positive ion is indicated, though the behavior is not ideal. The increases in the reaction rate may, however, be simply explained by assuming that if a cationic bromine reacts with a neutral alcohol in the rate-determining step, then charge will be dispersed over a somewhat larger area in the transition state. Since the charge density has been thus diminished, the transition state requires less solvation.[11] Therefore, the reaction should be more rapid in solutions of lower dielectric constants.

Absence of a primary kinetic isotope effect (Table IV) suggests that the C–H bond is not cleaved in the rate-determining step. Venkatasubramanian and Thiagarajan[2] suggested that a C–H bond ruptures in the rate-determining step in the alcohol–NBS reaction. However, there seems to be no evidence for C–H bond rupture in their reports. They mostly relied on the similarity of rate laws between bromine and NBS oxidations. In fact their data

(8) A. Y. Drummond and W. A. Waters, *J. Chem. Soc.*, 2836 (1953); J. S. Littler and W. A. Waters, *ibid.*, 1299 (1959).

(9) K. K. Banerji, *Indian J. Chem.*, **16A**, 595 (1978).

(10) E. S. Amis, "Solvent Effects on Reaction Rates and Mechanism", Academic Press, New York, 1967, p 43.
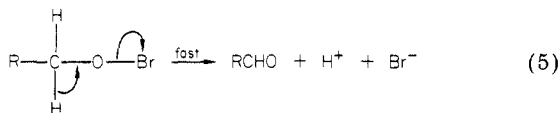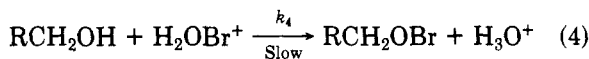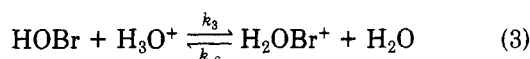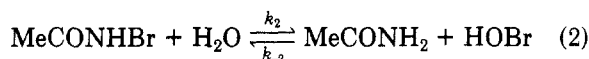
(11) E. S. Gould, "Mechanism and Structure in Organic Chemistry", Holt, Rinehart and Winston, New York, 1964, p 184.

Table V. Temperature Dependence of the Reaction Constant in Oxidation of Alcohols by NBA

T, K	303	308	313	318
$-\rho^*$	1.53	1.49	1.48	1.47
regression coeff	0.9859	0.9817	0.9804	0.9641

can be very well explained on the basis of the mechanism proposed by us. Balyeat[12] has shown that during cleavage of deuterated ketone by NBS there is no loss of deuterium.

The oxidation of ethanol was studied in deuterium oxide (overall deuterium content of the solvent was 90%). The rate constants for the oxidation in H_2O and D_2O at 308 K are $10^4 k$ = 5.0 and 5.8 M^{-2} s^{-1}, respectively. The solvent isotope effect, $k(D_2O)/k(H_2O)$ = 1.16 at 308 K. This set of experiments was carried out in aqueous solution. The rate of an acid-catalyzed reaction in D_2O is expected to be nearly 2.5–3.0 times the rate in water.[13] In the present case the solvent isotope effect is much less. If we assume that O–H bond rupture is involved in the rate-determining step, we can explain this observation. The hydroxyl group will undergo rapid interchange in D_2O and O–H/O–D isotope effect will neutralize the rate-enhancing effect of D_2O. Therefore, it is proposed that the rate-determining step involves formation of a hypobromite ester which then decomposes to the aldehyde in a fast step. The hypohalite esters are known to decompose to carbonyl compounds,[14] eq 2–5.

$$MeCONHBr + H_2O \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} MeCONH_2 + HOBr \quad (2)$$

$$HOBr + H_3O^+ \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} H_2OBr^+ + H_2O \quad (3)$$

$$RCH_2OH + H_2OBr^+ \underset{Slow}{\overset{k_4}{\longrightarrow}} RCH_2OBr + H_3O^+ \quad (4)$$

$$R{-}\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}{-}O{-}Br \xrightarrow{fast} RCHO + H^+ + Br^- \quad (5)$$

The above mechanism leads to the rate expression of eq 6.

$$1/\text{rate} = \frac{1}{k_2[\text{NBA}]}\left(1 + \frac{k_{-3}}{k_4[\text{RCH}_2\text{OH}]}\right)\left(1 + \frac{k_{-2}[\text{acetamide}]}{k_3[\text{H}^+]}\right) \quad (6)$$

According to eq 6 the plot of 1/rate and [acetamide] should be linear. Figure 3 shows that this is actually so in practice (r = 0.9886). However, the protonation step may preceed the hydrolysis (eq 7, 8) to form the cationic

$$MeCONHBr + H_3O^+ \rightleftharpoons (MeCONH_2Br)^+ + H_2O \quad (7)$$

$$(MeCONH_2Br)^+ + H_2O \rightleftharpoons MeCONH_2 + H_2OBr^+ \quad (8)$$
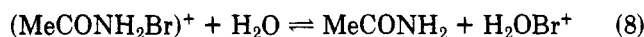
bromine species. It is not possible to distinguish kinetically between the two alternatives.

Effect of Substituent. The introduction of electron-withdrawing groups decreases the rate of oxidation. The rate of the oxidation of nine alcohols correlates well with

Figure 3. Plot of inverse of the observed rate constant k_1 vs. [acetamide]: [NBA] = 0.005 M; [Hg(II)] = 0.005 M; [EtOH] = 0.858 M; [H$^+$] = 0.5 M; T = 308 K.
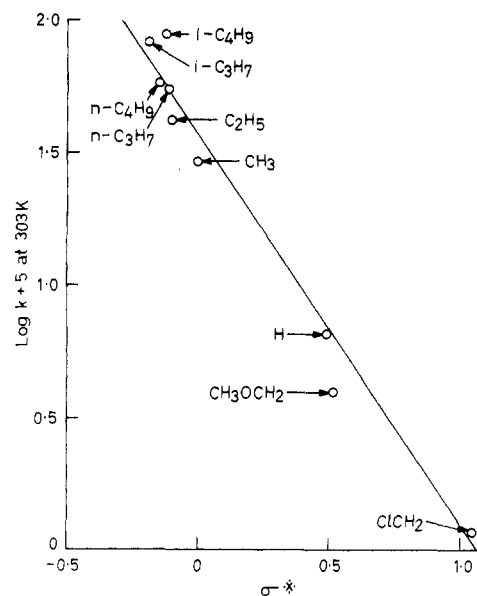
Figure 4. Plot of log k vs. Taft's σ^* substituent constant for oxidation of primary alcohols, RCH_2OH, by NBA at 303 K.

Taft's σ^* substituent constants with negative reaction constants (Table V). The substituent constant for the $MeCH(OMe)CH_2^-$ group is not available in literature; its value computed from Taft's plot (Figure 4) is -0.221 ± 0.008.

(12) J. R. Balyeat, Gov. Rep. Announce. Index (U.S.), 79, 106 (1979); Chem. Abstr., 90 107608 (1979).

(13) J. March, "Advanced Organic Chemistry", Academic Press, New York, 1977, p 399.

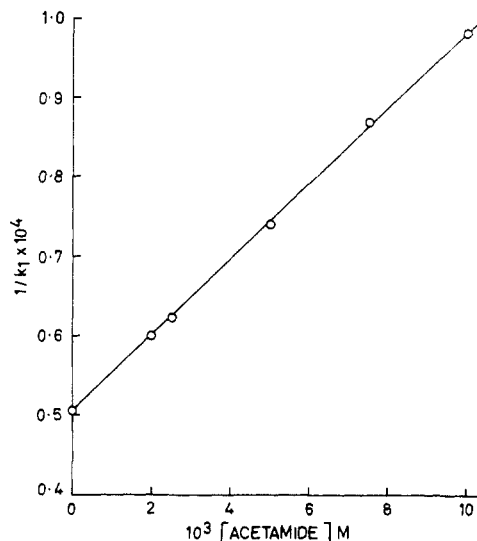(14) L. S. Levitt and E. R. Malinowskii, J. Am. Chem. Soc., 77, 4517 (1955).