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Kinetic Study of the Oxidation of Substituted Benzyl Alcohols by Ethyl Chlorocarbamate

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The kinetics of the oxidation of twenty-four monosubstituted benzyl alcohols by ethyl chlorocarbamate (ECC) have been studied in aqueous acetic acid solution, in the presence of perchloric acid. The main product of the oxidation is the corresponding benzaldehyde. The reaction is first order with respect to the alcohol, ECC, and hydrogen ion. The oxidation of [α,α-D_2]benzyl alcohol indicated a primary kinetic isotope effect, k_H/k_D=5.40 at 298 K. The value of solvent isotope effect, $k(H_2O)/k(D_2O)$, is 1.85 at 298 K. Addition of ethyl carbamate does not affect the reaction rate. $[EtOC(OH)NHCl]^+$ has been postulated as the reactive oxidizing species. The rates of oxidation of para- and meta-substituted benzyl alcohols show excellent correlation in Taft's dual substituent parameter equation, with negative reaction constants. The rates of the ortho-substituted compounds correlate well in Charton's equation of inductive, resonance and steric substituent parameters. A mechanism involving simultaneous transfer of a hydride ion from the C–H bond and of a proton from the O–H bond to the oxidant is proposed.

The use of halocarbamates in preparative organic chemistry is well documented.[1] We have been interested in the elucidation of the mechanism of the oxidations by *N*-halogeno reagents for quite some time[2] and have reported the oxidation of aliphatic alcohols by sodium ethyl chlorocarbamate recently.[3] In this article, we report the oxidation of several ortho-, meta-, and para-substituted benzyl alcohols by ethyl chlorocarbamate (ECC) in aqueous acetic acid solution, in the presence of perchloric acid. Attempts have been made to correlate rate and structure in this reaction. The mechanistic aspects are discussed.

Experimental

General. Acetylaminobenzyl alcohols were prepared by the reported methods.[4–6] All other alcohols were commercial products. They were purified by either recrystallization or distillation. [α,α-$^2D_2$]Benzyl alcohol was prepared by the reduction of ethyl benzoate by lithium aluminium deuteride.[7] ECC was prepared by treating ethyl carbamate (Merck) with sodium hypochlorite.[8] Perchloric acid (Merck) was used as a source of hydrogen ions. Deuterium oxide (99.4%) was supplied by BARC, Bombay.

Product Analysis. The product analysis was carried out under kinetic conditions i.e., with an excess of the alcohol over ECC.

In a typical experiment, benzyl alcohol (4.9 g, 0.05 mol) and ECC (1.46 g, 0.01 mol) were made up to 100 ml in 1:1 (v/v) acetic acid–water, in the presence of 0.5 M perchloric acid (1 M=1 mol dm^{-3}). The reaction mixture was allowed to stand in the dark for ca. 12 h to ensure completion of the reaction. It was then treated with an excess of (250 ml) of a saturated solution of 2,4-dinitrophenylhydrazine in 2 M HCl and kept in refrigerator for ca. 10 h. The precipitated 2,4-dinitrophenylhydrazone (DNP) was filtered off, dried, weighed, recrystallized from ethanol, and weighed again. The product was identical (mp and mixture mp) with an authentic sample of DNP of benzaldehyde. The yields of DNP, before and after recrystallization, were 2.75 g (96%) and 2.57 g (90%) respectively. In similar experiments, with other alcohols, the yields of DNP, after recrystallization, were 84 to 93%.

Kinetic Measurements. The pseudo-first-order conditions were attained by keeping a large excess (10-fold or greater) of the alcohol over ECC. The reactions were carried out at constant temperature (±0.1 K) and in flasks blackened from the outside to prevent any photochemical reaction. The reactions were followed iodometrically up to 70% of the reaction. The solvent was 1:1 (v/v) acetic acid–water. The pseudo-first-order rate constant, k_1, was computed from the linear (r>0.98) plots of log[ECC] versus time. The specific rate constant, k, was obtained by the relation $k=k_1/[H^+]\times[\text{Alcohol}]$. Preliminary experiments showed that the reaction is not sensitive to ionic strength (0.1—1.0 M) hence no attempt was made to keep it constant. Duplicate kinetic runs showed that the rates were reproducible to within ±3%. The average errors in the values of ΔH^*, ΔS^*, and ΔG^* (at 298 K) are ±3 kJ mol^{-1}, ±5 J mol^{-1} K^{-1}, and ±4 kJ mol^{-1} respectively.

Results

The oxidation of benzyl alcohols by ECC in acid solutions results in the formation of the corresponding benzaldehydes. The overall reaction may be written as follows (Eq. 1).

$$PhCH_2OH + EtOOCNHCl \longrightarrow PhCHO + EtOOCNH_2 + H^+ + Cl^- \qquad (1)$$

Rate Laws. The reaction was found to be first order with respect to ECC. Individual kinetic runs were strictly first order with respect to ECC. Further the first-order rate coefficients do not vary with the initial concentration of the oxidant. The effect of variation of the concentration of alcohol on the reaction shows that the reaction is of first order with respect to the alcohol also. The reaction rate increases linearly with an increase in the concentration of hydrogen ion (Table 1).

Isotope Effects. To ascertain the importance of the cleavage of α-C–H bond in the rate-determining step, the oxidation of [α,α-D_2]benzyl alcohol was studied. The results show that the value of primary kinetic isotope effect, k_H/k_D, is 5.40 at 298 K (Table 2).

The oxidation of benzyl alcohol was studied in 95% deuterium oxide. The rate constants for the oxidation in H_2O and D_2O are $10^7k=15.3$ and $8.27\ M^{-2}s^{-1}$ respectively at 298 K. The value of solvent isotope effect, $k(H_2O)/k(D_2O)=1.85$. No acetic acid was added in this set of experiments.

Effect of Ethyl Carbamate. Addition of ethyl carbamate has no effect on the rate of oxidation (Table 3).

Induced Polymerization of Acrylonitrile. The oxidation of the alcohols by ECC in an atmosphere of nitrogen, failed to induce polymerization of acrylonitrile. Thus a one-electron oxidation, giving rise to free radicals, is unlikely.

Table 1. Rate Constants of the Oxidation of Benzyl Alcohol by ECC at 298 K

10^3[ECC]	[BA]	[H^+]	$k_1\times10^7$
M	M	M	s^{-1}
5.0	0.2	0.5	7.25
10.0	0.2	0.5	7.32
12.5	0.2	0.5	7.47
15.0	0.2	0.5	7.13
20.0	0.2	0.5	7.20
25.0	0.2	0.5	7.25
5.0	0.4	0.5	14.7
5.0	0.6	0.5	22.0
5.0	0.8	0.5	29.0
5.0	1.0	0.5	35.3
5.0	1.5	0.5	54.0
5.0	1.0	0.1	7.30
5.0	1.0	0.2	15.0
5.0	1.0	0.4	28.7
5.0	1.0	0.6	44.0
5.0	1.0	0.8	58.2
5.0	1.0	1.0	75.2

Effect of Substituents. The rates of the oxidation of a series of monosubstituted benzyl alcohols were obtained at different temperatures between 298 and 318 K and the activation parameters were evaluated (Table 4).

Table 2. Kinetic Isotope Effect in the Oxidation of Benzyl Alcohol by ECC[a)]

[BA]	Type	$k_1\times10^6$
M		s^{-1}
0.4	1,1-H_2	14.7
0.6	1,1-H_2	22.0
0.8	1,1-H_2	29.0
0.2	1,1-D_2	1.35
0.4	1,1-D_2	2.80
0.5	1,1-D_2	3.25

$10^6\,k_H=7.31\ M^{-2}s^{-1}$
$10^6\,k_D=1.35\ M^{-2}s^{-1}$
$k_H/k_D=5.40$

a) [ECC]=0.005 M, [H]=0.5 M, at 298 K.

Table 3. Effect of Ethyl Carbamate on the Oxidation of Benzyl Alcohol by ECC[a)]

10^3[Ethyl carbamate]/M	0.0	5.0	10.0	20.0
$10^7\,k_1/s^{-1}$	14.7	14.3	14.5	15.0

a) [ECC]=0.005 M, [Alcohol]=0.4 M, [H^+]=0.5 M, at 298 K.

Table 4. Rate Constants and the Activation Parameters of the Oxidation of Monosubstituted Benzyl Alcohols by ECC

	$10^8\,k/M^{-2}s^{-1}$			ΔH^*	ΔS^*	ΔG^*
	298 K	308 K	318 K	kJ mol^{-1}	J mol^{-1} K^{-1}	kJ mol^{-1}
H	725	1770	4160	69.0	−105	100
p-NHCOMe	1400	3150	6320	65.1	−105	96.5
p-OMe	4610	7610	14000	44.4	−126	81.8
p-Me	1820	3990	7950	58.1	−113	91.8
p-F	679	1520	4000	69.9	−104	101
p-Cl	247	710	1900	80.8	−97	110
p-NO_2	11.0	63.4	267	126	−56	143
p-COOMe	73.2	157	800	93.4	−87	119
m-NHCOMe	285	675	2460	84.1	−91	111
m-OMe	535	1480	4010	78.9	−93	107
m-OPh	167	500	1320	81.7	−99	107
m-Me	1350	2300	5020	51.5	−125	88.9
m-F	91.4	387	1320	105	−69	126
m-Br	77.7	315	1000	101	−77	124
m-NO_2	8.90	52.6	252	132	−50	147
m-CN	14.6	68.0	310	121	−62	139
o-Me	12600	21300	31700	36.4	−129	74.7
o-F	458	1250	2610	70.0	−107	102
o-Cl	709	1800	5240	78.8	−91	106
o-Br	800	1420	3150	54.3	−126	91.7
o-I	1590	3500	6460	55.4	−118	90.7
o-NO_2	33.3	145	720	121	−54	137
o-NHCOMe	8940	15700	22400	36.4	−132	75.7
o-OMe	6350	12900	19200	43.7	−123	80.6

Discussion

The activation enthalpies and entropies of the oxidation of the alcohols are linearly related (r=0.9864). The correlation was tested and found genuine by applying Exner's criterion.[9] The value of isokinetic temperature determined by Exner's method is 371 K. Current views do not attach much significance to the value of isokinetic temperature.[10] The linear correlation however, is a necessary condition for the validity of linear free energy relationships. It also implies that all the alcohols are oxidized by the same mechanism and the changes in rates are governed by changes in both enthalpy and entropy of activation.

There seems to be no report about the various equilibria and species present in an acidified aqueous solution of ECC. However, based on the reactions of structurally related N-haloarenesulfonamides,[11] one can visualize the following equilibria:

$$\mathrm{EtOOCNHCl} + \mathrm{H_2O} \rightleftharpoons \mathrm{EtOOCNH_2} + \mathrm{HOCl} \qquad (2)$$

$$\mathrm{2EtOOCNHCl} \rightleftharpoons \mathrm{EtOOCNH_2} + \mathrm{EtOOCNCl_2} \qquad (3)$$

Hence the probable oxidizing species are ECC, $EtOOCNCl_2$, and HOCl. Ethyl dichlorocarbamate can be ruled out as the oxidizing species in view of the strict first order dependence of the reaction rate on ECC. Moreover, the absence of an effect of ethyl carbamate on the reaction precludes both HOCl and $EtOOCNCl_2$ as the reactive species. Thus, the most likely oxidizing species is EtOOCNHCl. The linear increase in the oxidation rate with acidity suggests that ethyl chlorocarbamate is protonated to give a stronger oxidant and electrophile (Eq. 4).

$$\mathrm{EtOOCNHCl} + \mathrm{H_3O^+} \rightleftharpoons \mathrm{EtO\overset{+}{C}(OH)NHCl} + \mathrm{H_2O} \qquad (4)$$

The presence of a primary kinetic isotope effect confirms that the C–H bond is cleaved in the rate-determining step.

The rate of an acid-catalyzed reaction involving the pre-equilibrium proton transfer step[12] is expected to be 2.5—3.0 times faster in D_2O than in H_2O. Labile hydrogens like those present in hydroxyl group undergo rapid exchange in D_2O, and the O–H/O–D isotope effect may neutralize the rate-enhancing effect of D_2O or even result in a slower rate in D_2O. The observed solvent isotope effect ($k(H_2O)/k(D_2O)=1.85$) shows that the k_{OH}/k_{OD} isotope effect is substantially large enough to cancel the effect of D_2O on pre-equilibrium(4). Thus a O–H bond rupture in the rate-determining step is indicated.

Correlation Analysis of Reactivity. (i) Para- and Meta-Substituted Benzyl Alcohols: Since the rates of the oxidation of para- and meta-monosubstituted benzyl alcohols failed to show satisfactory correlation with any single substituent parameter, the rates were subjected to analysis by Taft's[13] and Swain's[14] dual substituent parameter (DSP) equations. The oxidation rates of the p- and m- substituted compounds were separately correlated with σ_I and four different σ_R substituted constants in Taft's equation[13] and with the field and resonance substituents constants of Swain et al.[14] The results are summarized in Table 5. Both p- and m-series of substituted benzyl alcohols meet the basic requirements of minimum number of substituents required for the analysis by ESP equation,[15]

The results show that the rates of p-substituted benzyl alcohols show excellent correlation with σ_I and σ_R^{BA} values. The correlation with the other σ_R values and in Swain's equation[14] is relatively poor. We have used the standard deviation (SD) and f as the measure of goodness of fit. f has been defined by Dayal, et al.[13] as f=SD/RMS, where RMS is the root mean square of the data points (here $\log k/k_o$). The coefficient of multiple correlation, R, was also determined. The comparison on the f values shows that f is smaller for the σ_R^{BA} scale than those for other scales by the factors of ca. 3 to ca. 7. Therefore, it is apparent that the rates of the oxidation of p-substituted benzyl alcohols by ECC correlate best with σ_I and σ_R^{BA} values.

The rates of the oxidation of m-substituted compounds show excellent correlation with σ_I and σ_R^0

Table 5. Correlation of the Rates of the Oxidation of Para- and Meta-Substituted Benzyl Alcohols by ECC with Dual Substituent Parameters[a]

σ_R^0		σ_R^{BA}		σ_R^-[b]		σ_R^+		Swain et al.[c]	
SD	f	SD	f	SD	f	SD	f	SD	f
				Para-substituted					
0.09	0.11	0.03	0.04	0.21	0.24	0.21	0.26	0.11	0.13
				Meta-substituted					
0.03	0.03	0.06	0.06	0.09	0.09	0.11	0.11	0.07	0.07

a) Temperature 298 K, SD=standard deviation, f=SD/RMS of $\log k/k_o$, σ_I and σ_R values are from Ref. 13. b) Data for NHCOMe and OPh were not considered, σ_R^- values are not available. c) Field and resonance substituents constants are from Ref. 14.

Table 6. Temperature Dependance of the Reaction Constant[a)]

Temp/K	ρ_I	ρ_R[b)]	λ	R	SD	f
			Para-substituted			
298	−2.27	−2.35	1.04	0.9996	0.03	0.04
308	−1.87	−2.00	1.07	0.9923	0.10	0.11
318	−1.51	1.58	1.05	0.9986	0.04	0.06
			Meta-substituted			
298	−2.70	−1.28	0.47	0.9995	0.03	0.03
308	−2.06	−1.10	0.53	0.9944	0.07	0.09
318	−1.73	−1.05	0.61	0.9825	0.11	0.16

a) R=Coefficient of multiple correlation, $\lambda=\rho_R/\rho_I$, SD=standard deviation, f=SD/RMS of $\log k/k_o$. b) ρ_R is ρ_R^{BA} and ρ_R^{o} for para- and meta-substituted compounds respectively.

substituent constants, though the discriminating factor for the precision of fit with the other σ_R scales or in Swain's equation[14)] is not as sharp as in the case of *p*-substituted compounds. In fact the correlation with σ_R^{BA}, $\sigma_{\bar{R}}$, and in Swain's equation meet the requirement[16)] for a satisfactory fit (f<0.1). Even the correlation with σ_R^+ is not very poor. This agrees with the observation of Ehrenson, Brownlee and Taft[16)] that the correlation of *m*-substituted compounds is generally best with σ_R^o constants and *m*-substituted compounds are less discriminating.

The reaction constants and statistical data at different temperatures are given in Table 6.

The value of λ^p (1.05) shows that the oxidation of *p*-substituted compounds is almost equally susceptible to localized and delocalized effects. The selectivity of the reaction decreases at higher temperatures and the decrease is of similar order for both the localized and delocalized effects, reflected in the almost constant value of λ^p at different temperatures.

In the oxidation of *m*-substituted compounds, the values of λ are between 0.47 and 0.61, suggesting the greater importance of the localized effect. In this case, at higher temperatures, the decrease is more pronounced in the localized reaction constant, resulting in a gradual increase in the value of λ^m with an increase in the temperature.

(ii) **Ortho-Substituted Benzyl Alcohols:** The rates of the oxidation of *o*-substituted benzyl alcohols were analyzed in the terms of Taft's polar and steric substituent constants separately.[17)] The results are given in Eqs. 5 and 6.

$$\log k/k_o = -2.10\,\sigma_o^* \qquad (5)$$

R = 0.9324; SD=0.41; n=8

$$\log k/k = -0.33E_s \qquad (6)$$

R=0.2783; SD=0.54; n=8

The substituent NHCOMe was not included since the substituent constants are not available. The results show that the observed reactivity is not compatible with either the size of the substituents or with their Taft's polar substituent constant.

Since the single parameter equations did not yield satisfactory correlations, the rates were analyzed using Charton's method.[18)] The rate constants were correlated with Eqs. 7 and 8, where σ_I, σ_R, and V are inductive, resonance, and steric substituent constants respectively and the values used were those compiled by Aslam et al.[19)]

$$\log k_{ortho} = \alpha\sigma_I + \beta\sigma_R + h \qquad (7)$$

$$\log k_{ortho} = \alpha\sigma_I + \beta\sigma_R + \phi V + h \qquad (8)$$

In multiple regression analysis using Eq. 7, the correlation coefficient is poor and the standard deviation is high (Eq. 9).

$$\log k_{ortho} = -2.66\sigma_I - 2.21\alpha_R - 4.66 \qquad (9)$$

R=0.8714; SD=0.45; n=9

The absence of a significant correlation with Eq. 7 leads to the conclusion that the electrical effects alone are not sufficient to account for the ortho-substituent effect in this reaction.

The correlation with Eq. 8 were performed at temperatures 298, 308, and 318 K. The results are given in Eqs. 10—12 respectively.

$$\log k = -3.01\sigma_I - 2.04\sigma_R + 1.58V - 5.10 \qquad (10)$$

R=0.9962; SD=0.09; n=9

$$\log k = -2.57\sigma_I - 1.79\sigma_R + 1.27V = 4.96 \qquad (11)$$

R=0.9877; SD=0.14; n=9

$$\log k = -1.97\sigma_I - 1.25\sigma_R + 0.98V - 4.30 \qquad (12)$$

R =0.9827; SD=0.15; n=9

The effect of *o*-NO_2 group is consistent with the orthogonal conformation.

The significance of the correlation was tested by means of an F-test. The confidence levels for the F-test are greater than 99%. The confidence levels for the significance of α, β, and ϕ terms were obtained by means of a Student's T-test. The confidence level of the T-test is >99%, indicating the operation of significant inductive, resonance and steric effects. These results show that this reaction belongs to Case 1 of the classification given by Charton.[18)]

The contribution of the resonance effect to the polar effect[18)] is given by Eq. 13.

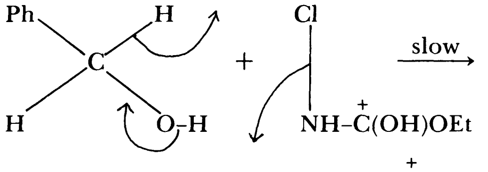
$$p_R = \frac{100|\beta|}{|\alpha| + |\beta|} \tag{13}$$

The value of P_R is found to vary between 38.8 and 41.1. This shows that the inductive effect is more pronounced than the resonance effect. The contribution of the steric effect, p_S, was calculated using the Eq. 14.

$$p_S = \frac{|\phi|\,100}{|\alpha| + |\beta| + |\phi|} \tag{14}$$

The percentage contribution of the steric effect is ca. 23%, pointing to a considerable steric effect in the reaction.

Mechanism. The presence of a primary kinetic isotope effect confirms that in the rate-determining step, α-C–H bond is cleaved. In this respect this reaction resembles the oxidation by chloramine-B and bromamine-B.[2)] However, it differs from the other oxidations in the observation of a solvent isotope effect. In the oxidations by chloramine-B and bromamine-B[2)] the rate in D_2O is more than that in H_2O. This indicates that the rupture of the O–H bond is also taking place in the rate-determining step. Thus a simultaneous transfer of a hydride ion from the C–H bond and a proton from hydroxyl groups is indicated (15). The negative polar reaction constants points to an electron-deficient carbon center in the transition state. The correlation of the rates of *p*-substituted benzyl alcohols with σ_R^{BA} constants also suggests a weak resonance interaction between a developing positive center and the substituent. Thus it seems that in the transition state the cleavage of the C–H is somewhat ahead of the rupture of the O–H bond. However, it may be mentioned here that the formation of a carbonyl group is also expected to be favored by an electron-releasing substituent.



$$PhCHO + HCl + H_2N\text{-}\overset{+}{C}(OH)OEt \tag{15}$$

$$H_2N\text{-}\overset{+}{C}(OH)OEt \xrightarrow{\text{fast}} H_2NCOOEt + H^+ \tag{16}$$

The positive regression coefficient for the steric term corresponds to a steric acceleration of the reaction by the ortho-substituent. This can be explained on the basis of high ground state energy level of the starting material. Since the crowding is relieved in the product aldehyde as well as in the transition state leading to it, the transition state energy of the crowded (ortho-stbstituted) and uncrowded alcohols do not differ much and steric acceleration, therefore, results.

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