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Correlation analysis of reactivity in the oxidation of substituted benzyl alcohols by hexamethylenetetramine-bromine

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Correlation analyses of the effect of substituents on the oxidation of benzyl alcohols by hexamethylenetetramine-bromine indicate the presence of a carbocationic centre in the transition state and steric acceleration of the reaction.

Keywords: correlation analysis, benzyl alchols, hexamethylenetetramine-bromine

In 1994, hexamethylenetetramine-bromine (HABR) was reported as a mild and selective synthetic reagent for the oxidation of alcohols to carbonyl compounds.[1] It has also been used for the regeneration of carbonyl compounds from oximes and hydrazones.[2] We have initiated a study of kinetics and mechanism of oxidation reactions of HABR and a few reports have emanated from our laboratory.[3–6] In this paper, we report the kinetics and mechanism of the oxidation of benzyl alcohol and 33 monosubstituted benzyl alcohols by HABR in glacial acetic acid. The major emphasis of this investigation is to correlate the structure and reactivity in this oxidation.

HABR was prepared by the reported method[1] and its purity was checked by an iodometric method and melting point determination. Contrary to the earlier report[1] we found that, in glacial acetic acid, the active bromine content of this complex is 2 mole per mole of the reagent.[6] α,α-Dideuteriobenzyl alcohol ($PhCD_2OH$) was prepared by the reported method.[7] The reactions were studied under pseudo-first-order conditions by keeping an excess (× 20 or greater) of the alcohol over HABR. The solvent was glacial acetic acid. The reactions were studied at constant temperature (± 0.1 K) and were followed by monitoring the decrease in the [HABR] spectrophotometrically at 380 nm for up to 80% reaction. Pseudo-first-order rate constants, k_{obs}, were evaluated from linear plots ($r^2 > 0.995$) of log [HABR] against time.

The oxidation of benzyl alcohols results in the formation of the corresponding benzaldehydes. The overall reaction may be represented as Equation (1).

$$2ArCH_2OH + (CH_2)_6N_4Br_4 \rightarrow 2ArCHO + (CH_2)_6N_4 + 4HBr \quad (1)$$

The reactions are of first order with respect to both the alcohol and HABR. An addition of hexamethylenetetramine (HXA) or sodium bromide had no effect on the rate of oxidation. The oxidation of benzyl alcohol, in an atmosphere of nitrogen, failed to induce the polymerisation of acrylonitrile. Further, an addition of acrylonitrile had no effect on the rate of oxidation. Thus a one-electron oxidation, giving rise to free radicals, is unlikely. The rates of oxidation were determined at different temperatures and the activation parameters were calculated.

To ascertain the importance of the cleavage of the α-C–H bond in the rate-determining step, the oxidation of deuteriated benzyl alcohol was studied. The results showed the presence of a substantial primary kinetic isotope effect ($k_H/k_D = 5.44$ at 298 K). This confirmed the cleavage of an α-C–H bond in the rate-determining step.

In solutions, HABR may dissociate to form molecular bromine and HXA.

$$(CH_2)_6N_4Br_4 \rightleftharpoons 2\,Br_2 + (CH_2)_6N_4 \quad (2)$$

The nil effects of added hexamethylenetetramine (HXA) or bromide ion on the rate of oxidation are reminiscent of the results obtained earlier[3,4] and indicate that the reactive oxidising species is HABR itself. The spectral data and isolation of unchanged HABR support this.

The rates of the *ortho*-, *meta*- and *para*-compounds failed to exhibit a significant correlation in terms of any single- or dual-substituent parameter equations. The rate constants, k_2, were, therefore, analysed in terms of Charton's[16] LDR/LDRS equations.

$$\log k_2 = L\,\sigma_l + D\,\sigma_d + R\,\sigma_e + h \quad (7)$$

$$\log k_2 = L\,\sigma_l + D\,\sigma_d + R\,\sigma_e + S\,\upsilon + h \quad (9)$$

The latter two substituent parameters are related by Equation (8),

$$\sigma_D = \eta\,\sigma_e + \sigma_d \quad (8)$$

where η , represents the electronic demand of the reaction site which is given by $\eta = R/D$, and σ_D represents the delocalised electrical parameter of the diparametric LD equation.

The rates of oxidation of the *ortho*-, *meta*- and *para*-substituted benzyl alcohols showed excellent correlations with LDR/LDRS equations. All the three regression coefficients, L, D and R, are negative indicating an electron-deficient carbon centre in the transition state of the reaction. The positive value of η adds a negative increment to σ_d, increasing the donor effect of the substituent where σ_d is negative and decreasing the acceptor effect where σ_d is positive. The substituent is, therefore, better able to stabilise a cationic reaction site. The large magnitude of η, which represents the electronic demand of the reaction, indicates a large charge separation in the transition state.

The positive value of S indicates that the reaction is subjected to a steric acceleration by the *ortho*-substituent. This may be due to high ground state energy of the sterically crowded alcohols. Since the crowding is relieved in the transition state as well as in the product formed, the transition state energy of the crowded and uncrowded alcohols do not differ much and steric acceleration, therefore, results.

The negative values of localised and delocalised coefficients, L, D, and R indicate that the electron-demand of the reaction on the substituents is high, suggesting an electron-deficient reactive centre in the transition state of the rate-determining step. It is further supported by the positive value of η, which indicates that the substituent is better able to stabilise a cationic or electron-deficient reactive site. The large negative reaction constants coupled with a large value of η and the large deuterium isotope effect point to a considerable carbocationic character in the transition state. Hence the rate-determining step can be visualised as a hydride-ion transfer involving a late product-like transition state. Therefore, a mechanism involving a hydride-ion transfer from the alcohol

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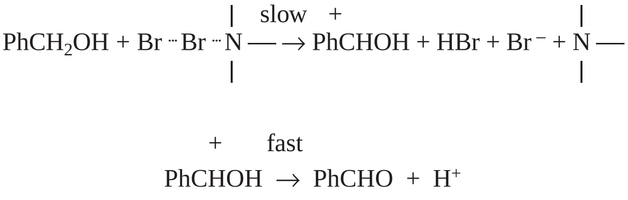
Table 7 Reaction constants of the oxidation reactions in terms of LDR/LDRS equations at 298 K

Oxidant/reductant	L	D	R	η	S	Ref.
			para-substituted			
BTMACB/ArCHO	–1.59	–1.75	–1.31	0.75	–	21
PhPB/ArSMe	–1.43	–2.11	–2.89	1.37	–	22
BTMAB/ArSMe	–1.40	–2.09	–2.85	1.36	–	20
BTMACl/ArCH$_2$OH	–1.59	–2.15	–3.10	1.44	–	19
HABR/ArSMe	–1.41	–2.09	–3.01	1.44	–	4
HABR/ArCH$_2$OH	–1.58	–2.25	–3.18	1.41	–	This work
			meta-substituted			
BTMACB/ArCHO	–1.64	–1.08	–0.72	0.67	–	21
PhPB/ArSMe	–1.72	–0.99	–0.95	0.96	–	22
BTMAB/ArSMe	–1.68	–1.01	–1.03	1.02	–	20
BTMACl/ArCH$_2$OH	–1.89	–1.04	–1.46	1.40	–	19
HABR/ArSMe	–1.72	–1.05	–1.29	1.23	–	4
HABR/ArCH$_2$OH	–1.77	–1.05	–1.48	1.41	–	This work
			ortho-substituted			
BTMACB/ArCHO	–1.61	–1.53	–1.10	0.79	–1.03	21
PhPB/ArSMe	–1.46	–1.66	–2.25	1.36	–1.13	22
BTMAB/ArSMe	–1.42	–1.72	–2.10	1.22	–1.15	20
BTMACl/ArCH$_2$OH	–1.87	–1.69	–2.53	1.50	1.23	19
HABR/ArSMe	–1.47	–1.71	–2.67	1.56	–1.14	4
HABR/ArCH$_2$OH	–1.92	–2.08	–3.05	1.47	1.26	This work

BTMACB = benzyltrimethylammonium chlorobromate; BTMAB = benzyltrimethylammonium tribromide; BTMACl = benzyltrimethylammonium dichloroiodate; PHPB = pyridinium hydrobromide perbromide.

to the oxidant is postulated (Scheme 1). It is of interest to compare here the results obtained in earlier studies using Charton's LDR/LDRS equations.[4,19–22] The values of the reaction constants are recorded in Table 7. These reactions[4,19,20,22] involve the formation of a cationic species in the rate-determining step either by a hydride-ion transfer from the reductant to the oxidant or by an addition of halogen to the sulfide. The magnitudes of R and η in the oxidation of aromatic aldehydes by benzyltrimethylammonium chlorobromate (BTMACB)[21] are lower than that observed in the present reaction. This shows that in the oxidation by BTMACB,[21] the transition state is more reactant-like rather than product-like. In the rest of the reactions, the polar reaction constants have comparable values. The negative steric constant in the reactions[4,20–22] implies a steric hindrance by the *ortho*-substituents, whereas in the oxidation of alcohols,[19] a positive steric constant indicates a steric acceleration. The above comparison supports the proposed mechanism. The observed negative value of the entropy of activation also supports the proposed mechanism. As HABR and the alcohol come together in the transition state to form a single activated complex, their freedom to move separately is curtailed. This results in a loss of entropy.



$$\mathrm{PhCH_2OH + Br\cdots Br\cdots \overset{|}{\underset{|}{N}} \xrightarrow{slow} Ph\overset{+}{C}HOH + HBr + Br^- + \overset{|}{\underset{|}{N}}—}$$

$$\mathrm{Ph\overset{+}{C}HOH \xrightarrow{fast} PhCHO + H^+}$$

Scheme 1

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Equations: 11
Figure: 1
References: 22

Table 1. Rate constants for the oxidation of benzyl alcohol by HABR at 308 K

Table 2. Rate constants for the oxidation of substituted benzyl alcohols by HABR and the activation parameters

Table 3. Effect of hexamethylenetetramine on the oxidation of benzyl alcohol by HABR

Table 4. Effect of bromide ion on the oxidation of benzyl alcohol by HABR

Table 5. Correlation analysis of the rates of oxidation of *meta*- and *para*-substituted benzyl alcohols by HABR with Taft's dual substituent-parameters at 298 K

Table 6. Temperature dependence for the reaction constants for the oxidation of substituted benzyl alcohols by HABR

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