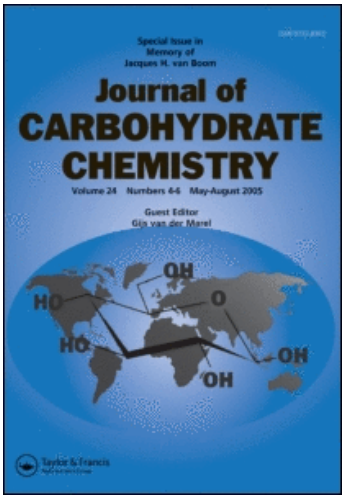

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KINETIC AND MECHANISTIC INVESTIGATION OF OXIDATION OF URONIC ACIDS BY SODIUM *N*-BROMOARYLSULFONAMIDES IN ALKALINE MEDIUM

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ABSTRACT

The kinetics of oxidation of uronic acids (UAs), D-glucuronic acid and D-galacturonic acid, by sodium *N*-bromo-*p*-toluenesulfonamide or bromamine-T (BAT) and sodium *N*-bromobenzenesulfonamide or bromamine-B (BAB) in alkaline medium at 30°C have been investigated and the rate law, rate = k [OX] [UA] [HO^-] where [OX][BAT] or [BAB] was observed. The product *p*-toluenesulfonamide (PTS) or benzenesulfonamide (BSA) and ionic strength have no influence on the rate. The rate decreased when the dielectric constant (ε) of the medium was decreased. The rate increased in D_2O medium. Proton inventory studies were made in D_2O–H_2O mixtures. Effect of temperature was studied and from the Arrhenius plots, activation parameters were computed. A mechanism involving the formation of enediol anion, which reacts with positive bromine of the bromamine in the rate-limiting step is suggested.

INTRODUCTION

In our broad program on the oxidation of monosaccharides by arylhaloamines, we have reported the studies of oxidation of a variety of monosaccharides by chloramines.[1–5] It is noted that RNX^- is the active oxidant species in the present experimental conditions (R═$CH_3C_6H_4SO_2$ for chloramine-T and bromamine-T, R═$C_6H_5SO_2$

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for chloramine-B and bromamine-B, and X═Cl for chloramines and Br for bromamines). Since there is a difference in the electrophilicities and the size of Cl and Br atoms, it was thought interesting to investigate the mechanism of oxidation of uronic acids by bromamines and to compare the results with those by their chlorine analogues.[4,5] From the present study, it is possible to draw some conclusion on the oxidation of uronic acids by *N*-arylhaloamines.

RESULTS AND DISCUSSION

The kinetics of oxidation of uronic aids by bromamines (OXs), BAT and BAB were investigated at several initial concentrations of the reactants. With substrate (UA) in excess and constant $[HO^-]$, plots of log [OX] vs. time were linear ($r > 0.9997$). Values of pseudo first order rate constants k_{obs} obtained from these plots were constant for different $[OX]_o$ employed (Table 1), indicating a first order dependence of rate on $[OX]_o$ (BAT or BAB). The k_{obs} values increased with increase in $[UA]_o$ (Table 1) and the plots of log k_{obs} vs. log $[UA]_o$ were found to be linear ($r > 0.9996$) with almost unit slope, indicating a first order dependence on [UA]. Furthermore, the plots of k_{obs} vs. $[UA]_o$ were linear (Figure 1, $r > 0.9998$) and passed through the origin, showing that the uronic acid–oxidant complex has a transient existence. The reaction rate increases with increase in $[HO^-]$ (Table 2). Plots of log k_{obs} vs. log $[HO^-]$ were found to be linear ($r > 0.9997$) with unit slope, showing a first order dependence on $[HO^-]$.

Addition of reaction products, *p*-toluenesulfonamide (PTS) in the case of BAT and benzenesulfonamide (BSA) in the case of BAB and Br^- or Cl^- ions did not alter

Table 1. Effect of Varying Reactant Concentration on the Reaction Rate at 30°C

10^4 $[BAT]_0$ or 10^4 $[BAB]_0$ M	10^3 $[UA]_0$ M	10^4 k_{obs} (s^{-1})			
		D-Glucuronic Acid		D-Galacturonic Acid	
		BAT	BAB	BAT	BAB
8.00	10.0	7.16	7.79	8.51	9.14
10.0	10.0	7.06	7.75	8.46	9.06
15.0	10.0	7.06	7.74	8.36	9.02
20.0	10.0	7.09	7.70	8.46	9.06
25.0	10.0	7.08	7.68	8.50	9.00
30.0	10.0	7.04	7.74	8.45	9.12
35.0	10.0	7.00	7.70	8.44	9.06
40.0	10.0	7.04	7.71	8.40	9.03
10.0	4.00	2.83	3.13	3.38	3.64
10.0	6.00	4.24	4.65	5.11	5.44
10.0	8.00	5.65	6.21	6.74	7.25
10.0	20.0	14.1	15.2	16.9	18.2
10.0	30.0	20.2	22.9	25.4	27.2
10.0	40.0	26.8	29.4	33.8	36.3

$[HO^-]_{eff} = 2.00 \times 10^{-2}$ M; I = 0.400 M.

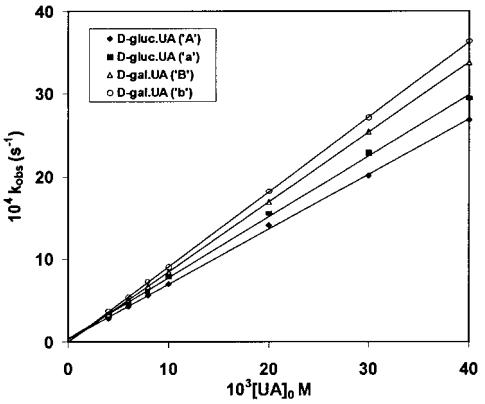


Figure 1. Plots of log k_{obs} vs. $[UA]_0$: 'A' and 'B' refer to BAT and 'a' and 'b' refer to BAB as oxidant at 30°C. $[BAT]_0 = [BAB]_0 = 1.00 \times 10^{-3}$ M; $[HO^-]_{eff} = 2.00 \times 10^{-2}$ M; I = 0.400 M.

the rate of reaction, indicating the absence of these compounds in pre-equilibrium to the rate-limiting step. The variation of ionic strength (I) of the medium maintained by the addition of $NaClO_4$ did not alter the rate of the reaction.

The rate decreased when the methanol content of the medium was increased. Plots of log k_{obs} vs. 1/ε (ε-dielectric constant) were linear with negative slope (Figure 2, $r > 0.9987$).

The reaction was studied over a range of temperature (298–318 K) and the Arrhenius plots of log k_{obs} vs. 1/T were linear ($r > 0.9989$). The activation energy E_a, was calculated from the slope. The other activation parameters $\Delta H^{\neq}$, $\Delta S^{\neq}$, $\Delta G^{\neq}$ and Arrhenius factor 'A' (in terms of log A) were calculated (Table 3).

The rate increased in D_2O medium and proton inventory studies were made in H_2O–D_2O mixtures of varying 'D' content (Table 4). Proton inventory plots relating the rate constant k_{obs} with the deuterium atom fraction 'n' in the solvent mixtures are shown in Figure 3.

Table 2. Effect of Varying $[HO^-]_{effective}$ on the Reaction Rate at 30°C

10^3 $[HO^-]_{eff}$ M	10^4 k_{obs} (s^{-1})			
	D-Glucuronic Acid		D-Galacturonic Acid	
	BAT	BAB	BAT	BAB
5.00	1.80	1.94	2.12	2.28
10.0	3.54	3.88	4.23	4.68
20.0	7.06	7.75	8.46	9.06
30.0	10.7	11.6	12.7	13.6
40.0	14.2	15.5	16.9	18.4
50.0	17.7	19.4	21.2	22.8

$[BAT]_0 = [BAB]_0 = 1.00 \times 10^{-3}$ M; $[UA]_0 = 1.00 \times 10^{-2}$ M; I = 0.400 M.

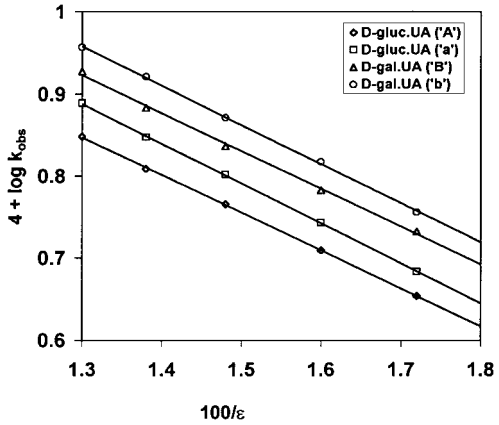


Figure 2. Plots of log k_{obs} vs. 1/ε: 'A' and 'B' refer to BAT and 'a' and 'b' refer to BAB as oxidant at 30°C. $[BAT]_0 = [BAB]_0 = 1.00 \times 10^{-3}$ M; $[UA]_0 = 1.00 \times 10^{-2}$ M; $[HO^-]_{eff} = 2.00 \times 10^{-2}$ M; I = 0.400 M.

Addition of acrylamide to the reaction mixture did not initiate polymerization, showing the absence of free-radical species.

The identical order with respect to both oxidant (BAT or BAB) and uronic acids suggests a common mechanism for the oxidation of uronic acids by bromamines. The arylhaloamines behave as strong electrolytes in aqueous solutions and several equilibria present are predominantly pH dependent.[6–8] Since kinetic investigations of D-glucuronic acid and D-galacturonic acid have been made in alkaline medium, $RNBr^-$, OBr^- and RNBrH are the likely oxidizing species. But the formation of RNBrH envisages the retardation of the rate by HO^- ion and also by the added reaction product RNH_2 (PTS or BSA). Since no such kinetic effect was noticed, it is probable that the anion $RNBr^-$ itself is the active oxidant.[7–9]

In alkaline medium sugars undergo the familiar Lobry de Bruyn–Alberda Van Ekenstein transformation[4] and the enediol anions (UA^-) formed react with the oxidant in a rate-limiting step to form the products. The proposed mechanism is given by Scheme 1.

Table 3. Activation Parameters for the Oxidation of Sugars by BAT and BAB in Alkaline Medium

Activation Parameter	D-Glucuronic Acid		D-Galacturonic Acid	
	BAT	BAB	BAT	BAB
E_a kJ mol^{-1}	98.9	96.6	95.6	94.7
$\Delta H^{\neq}$ kJ mol^{-1}	96.3	94.0	93.0	92.1
$\Delta G^{\neq}$ kJ mol^{-1}	83.3	92.1	92.0	91.9
$\Delta S^{\neq}$ J K^{-1} mol^{-1}	12.0	6.00	3.25	0.940
Log A	17.6	17.3	17.1	17.0

$[BAT]_0 = [BAB]_0 = 1.00 \times 10^{-3}$ M; $[UA]_0 = 1.00 \times 10^{-2}$ M; $[HO^-]_{eff} = 2.00 \times 10^{-2}$ M; I = 0.400 M.

Table 4. Proton Inventory Studies for the Oxidation of Uronic Acids by BAT and BAB in H_2O-D_2O Mixtures at 30°C

	10^4 k_{obs} (s^{-1})			
	D-Glucuronic Acid		D-Galacturonic Acid	
Atom Fraction of Deuterium (n)	BAT	BAB	BAT	BAB
000	7.06	7.75	8.46	9.06
0.250	7.80	8.49	8.86	9.90
0.500	9.02	9.92	10.4	11.8
0.750	11.0	11.9	12.7	13.8
0.940	12.9	13.6	16.1	17.4

$[BAT]_0 = [BAB]_0 = 1.00 \times 10^{-3}$ M; $[UA]_0 = 1.00 \times 10^{-2}$ M; $[HO^-]_{eff} = 2.00 \times 10^{-2}$ M; I = 0.400 M.

Applying steady state conditions to $[UA^-]$, the following rate law can be derived:

$$\text{Rate} = \frac{-d[OX]}{dt} = \frac{k_1 k_2 [UA][HO^-][RNBr^-]}{k_{-1}[H_2O] + k_2[RNBr^-]} = k_1'[UA][HO^-][RNBr^-]$$

where

$$k_1' = \frac{k_1 k_2}{k_{-1}[H_2O]}$$

and assuming $k_2[RNBr^-] <<< k_{-1}[H_2O]$ or $k_{obs} = k_1'[UA][HO^-]$ as rate $= k_{obs}[RNBr^-]$ under pseudo first order conditions of $[UA]_o \gg [RNBr^-]_o$.

A possible mechanism of oxidation of glucuronic acid is shown in Scheme 2. The uronic acid reacts in the pyranose form with HO^- to give the anion UA^-, which is

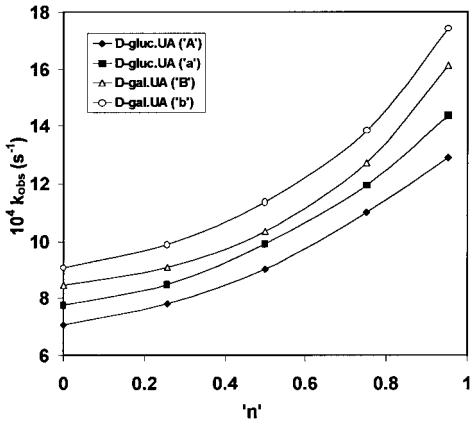


Figure 3. Proton inventory plots of the oxidation of uronic acids. 'A' and 'B' refer to BAT and 'a' and 'b' refer to BAB as oxidant at 30°C. $[BAT]_0 = [BAB]_0 = 1.00 \times 10^{-3}$ M; $[UA]_0 = 1.00 \times 10^{-2}$ M; $[HO^-]_{eff} = 2.00 \times 10^{-2}$ M; I = 0.400 M.

$$UA + HO^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} UA^- + H_2O \qquad \text{fast.....(i)}$$

$$UA^- + RNBr^- \xrightarrow{k_2} \text{products.} \qquad \text{slow and rate determining.....(ii)}$$

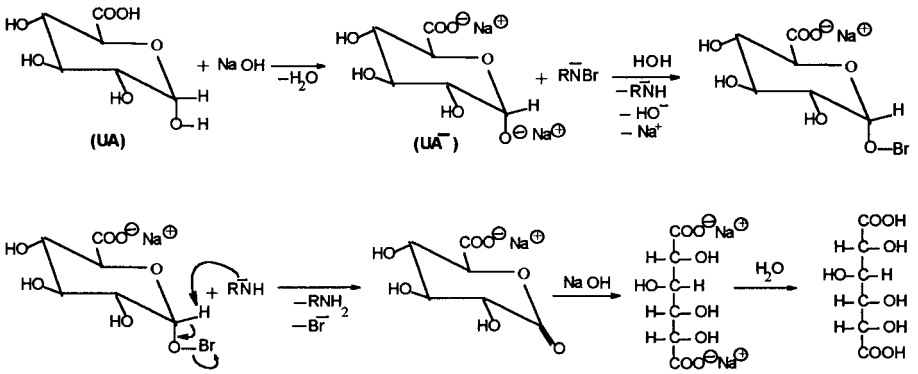
Scheme 1.

subsequently attacked by the positive bromine species of the oxidant, $RNBr^-$. Elimination of sulfonamide (RNH_2) followed by bromide ion results in a lactone which on hydrolysis forms the aldaric acid.

The proposed mechanism is supported by the following factors:

(i) We expect a doubling of the reaction rate in D_2O medium, since DO^- is a stronger base than HO^- by a factor of 2. The value of $k_{obs}(D_2O)/k_{obs}(H_2O)$ is found to be = 1.9 (Table 4), thus justifying our expectation and also supporting a pre-equilibrium transfer of HO^- ion.[10] Proton inventory plots could throw light on the nature of the transition state.[11,12] Comparison of proton inventory plots (Figure 3) with the standard curves available in the literature[13] shows that there is single transition state and one HO^- ion is involved in its formation.

(ii) The decrease in the rate with decrease in the dielectric constant (ε) of the medium suggests an ion–ion interaction and supports the derived rate law. The plots of log k_{obs} vs. $1/\varepsilon$ were linear (Figure 2) with negative slopes (slope = $-Z_AZ_Be^2/KTd_{AB}$),[14] which enable us to compute the size d_{AB}, of the activated complex of the reaction. It is found to be 4.98 Å and 5.16 Å when BAT is the oxidant, and 4.68 Å and 5.03 Å when BAB is the oxidant for D-glucuronic acid and D-galacturonic acid, respectively. The values are found to be quite reasonable when compared with those of other reactions of similar nature.[15]



Scheme 2.

(iii) The rate determining step (ii) of Scheme 1 involves an interaction between two negatively charged ions, which require high activation energy. The values of E_a obtained are very high supporting the proposed mechanism. The positive value of $\Delta S^{\neq}$ shows that there is more disorder in the transition state while constancy of $\Delta G^{\neq}$ values (Table 3) indicates that a similar mechanism is operative in the oxidation of both the uronic acids carried out with BAT and BAB as oxidants.

(iv) When we compare the rates of oxidation of uronic acids by bromamines with the rates of oxidation of uronic acids by chloramines,[4,5] it is clear that the rate of oxidation by bromamines is grater than that by chloramines.

CONCLUSION

Kinetic investigations of two uronic acids, D-glucuronic acid and D-galacturonic acid, reveal that there is no difference in their oxidative behaviour with BAT and BAB in alkaline medium. The structural differences at C-4 of D-glucuronic acid and D-galacturonic acid have no influence on macroscopic rate constants and other kinetic parameters. The oxidation rates are faster in BAB than in BAT. This may be due to a strong inductive effect of the methyl group present in BAT, which pushes the electron density at the polar N–Br bond and reduces the elecrophilicity of the Br atom. The oxidation of uronic acids is faster with bromamines than with chloramines, this may be due to the difference in the size and electrophilicities of Cl and Br atoms. The sequence of reactivity is found to be BAB > BAT > CAB > CAT.

EXPERIMENTAL

Materials. D-glucuronic acid and D-galacturonic acids were purchased from Sigma. Bromamine-T (BAT) and bromamine-B (BAB) were prepared in the laboratory by standard procedures available in the literature.[16,17] The aqueous solutions of BAT and BAB were prepared, standardized iodometrically and preserved in brown bottles to prevent their photochemical deterioration. The concentrated aqueous solution of $NaClO_4$ was used to maintain the ionic strength of the reaction mixture. All other chemicals used were of analytical grades of purity. Triply distilled water was used to prepare aqueous solutions. The D_2O (99.4%) used for solvent isotope studies was supplied by BARC, Bombay (India).

Kinetic measurements. Appropriate amounts of uronic acid, $NaClO_4$, NaOH, and H_2O (to keep the total volumeconstant for all runs) were placed in a stoppered Pyrex glass tube (the alkali concentration was adjusted to allow for neutralization of carboxylic group at C-6 carbon) and thermostated at 30°C. A measured amount of oxidant (BAT or BAB) solution, also thermostated at the same temperature, was rapidly added to the mixture. The progress of the reaction was monitored by withdrawing aliquots from the reaction mixture at regular intervals of time and determining the unreacted oxidant by iodometric titrations. The course of the reaction was studied up to

two half-lives. The calculated pseudo first order rate constants, k_{obs}, were reproducible within ±3% error.

Stoichiometry and product analysis. Reaction mixtures containing uronic acid, alkali and an excess of oxidant (BAT or BAB) were kept at 30°C for 24 hours. The unconsumed oxidant was determined iodometrically. From these data, the amount of the oxidant consumed per mole of the uronic acid was found to be 1 mole to form the corresponding dicarboxylic acid. The reaction can be represented as follows,

$$C_6H_{10}O_7 + RNBr^- + H_2O \longrightarrow C_6H_{10}O_8 + RNH_2 + Br^-$$

where $R = -CH_3C_6H_4SO_2$ for BAT and $R = -C_6H_5SO_2$ for BAB.

The reaction product, *p*-toluenesulfonamide was detected by paper chromatography using benzyl alcohol saturated with water as solvent with 0.5% vanillin in 1% HCl in ethanol as spray reagent ($R_f = 0.905$), and benzenesulfonamide was detected by TLC using light petroleum–chloroform–1-butanol (2:2:1 v/v) as the solvent and iodine for detection ($R_f = 0.88$). The uronic acid oxidation products were extracted with ether, the residual solution was then concentrated and analyzed by paper chromatography using 1-butanol–acetic acid–water (4:1:5 v/v) and detected with *p*-anisidine hydrochloride. The product is found to contain D-glucaric acid ($R_f = 0.19$) and D-galactaric acid ($R_f = 0.16$).

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