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NOTE

Rapid Bromination Study of Nucleobase-Uracil in Aqueous Medium by Hydrodynamic Voltammetry

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The kinetics and mechanism of the rapid bromination of the nucleobase uracil, by molecular bromine in aqueous medium at pH 7 has been studied employing hydrodynamic voltammetry, NMR and FTIR. The formation of the mono-bromo derivative is found to be a second order rapid reaction. The rate constant, energy of activation and frequency factor for the reaction have been determined and a probable mechanism for the reaction has been proposed.

Keywords: Bromo-uracil, Hydrodynamic voltammetry, Saturated calomel electrode, Rotating platinum electrode.

Uracil, is one of the three pyrimidine nucleobases present in nucleic acids. It is a heterocyclic molecule having a pyrimidine ring. Its importance lies in its role as a constituent of genetic material. C-5 substitution in uracil by a halogen atom possesses various biological and synthetic properties and is also used in direct displacement reactions with nucleophiles [1-3]. 5-Bromouracil is one of the vastly studied derivatives of uracil because of its role in mismatch pairing with thiamine in DNA base pairing and as a substituent in anti-cancer and antiviral drugs [4-6]. The bromination of uracil has been studied by various researchers using various brominating agents in acidic medium. The overall mechanism of bromination of uracil by Br_2 in aqueous medium was proposed first by Wang [4,7].

Presently we have studied the kinetics of bromination of uracil in aqueous medium at 7 pH using Br_2. The electrophilic attack is focused at 5 position in aqueous medium because this position is the least electron deficient position [4]. The reaction under study is found to be rapid and of the second order. The technique-hydrodynamic voltammetry, employed to study this reaction uses a rotating platinum electrode to observe the fall in concentration of Br_2 in the reaction [8,9].

Uracil was purchased from Himedia India, disodium hydrogen phosphate from Merck, sodium thiosulphate and citric acid from Fischer Scientific. Aqueous bromine was prepared in the laboratory by dissolving liquid bromine in doubly distilled water and its concentration was determined by iodometry. A.R. grade KNO_3 was used as the supporting electrolyte. A platinum electrode rotating at 600 rpm, a moving coil galvanometer, a shunt and a potentiometer were used. The saturated calomel electrode (SCE) was the negative electrode.

Measurement of the diffusion current: The diffusion current due to unreacted Br_2 in the reaction was observed in terms of the galvanometer deflection. Calibration of the diffusion current was obtained by preparing different concentrations of Br_2 in doubly distilled water and recording their deflections.

Kinetic measurement: 2×10^{-5} M 50 mL each of Br_2 and uracil containing buffers to maintain 7 pH and 100 fold KNO_3 as the supporting electrolyte were maintained in a thermostat in different flasks. 50 mL solution of Br_2 was transferred to the reaction vessel of 200 mL capacity the reading on the scale was adjusted to around 40 cm using a shunt. The potential applied to the solution was 0.1 V and the electrodes were rotating platinum electrode and saturated calomel electrode. Then 50 mL solution of uracil was added and a stopwatch was started immediately. The readings on the scale were recorded at every 10 s. This procedure was carried out at different temperatures and the plot obtained between $[Br_2]^{-1}$ *versus* time was linear. Hence the reaction was inferred to be of the second order. The kinetic and related thermodynamic parameters were evaluated.

The plot of $[Br_2]^{-1}$ *versus* time is a straight line the slope of which is the specific reaction rate, unlike a first order reaction, Hence the reaction studied is concluded to follow

second order kinetics. The results of the bromination of uracil by Br_2 in aqueous solutions at pH 7 are shown in Tables 1-3 and Figs. 1 and 2. The energy of activation was obtained from the Arrhenius plot.

TABLE-1
KINETICS OF BROMINATION OF URACIL BY Br_2 AT pH 7 AND 28 °C IN AQUEOUS SOLUTION

Time (s)	Diffusion current (cm)	$[Br_2]$ (10^{-6} M^{-1})	$[Br_2]^{-1}$ (10^5 M)
10	12.5	6.2	1.61
20	10.5	5.2	1.92
30	9.0	4.5	2.22
40	8.2	4.1	2.44
50	7.4	3.7	2.70
60	6.6	3.3	3.03

TABLE-2
VARIATION OF SPECIFIC REACTION RATES OF BROMINATION OF URACIL IN AQUEOUS MEDIUM AT DIFFERENT TEMPERATURES

Temp. (K)	T^{-1} (10^{-3} K^{-1})	k (M^{-1} s^{-1})	log k
293.15	3.41	1190	3.07
298.15	3.35	2162	3.33
301.15	3.32	3125	3.49
303.15	3.29	3154	3.49

TABLE-3
KINETIC PARAMETERS OF BROMINATION OF URACIL IN AQUEOUS MEDIUM AT 28 °C AND pH 7

Kinetic parameter	Value
Specific reaction rate (M^{-1} s^{-1})	3125
Energy of activation (kJ mol^{-1})	71.11
Frequency factor (M^{-1} s^{-1})	6.94×10^{15}

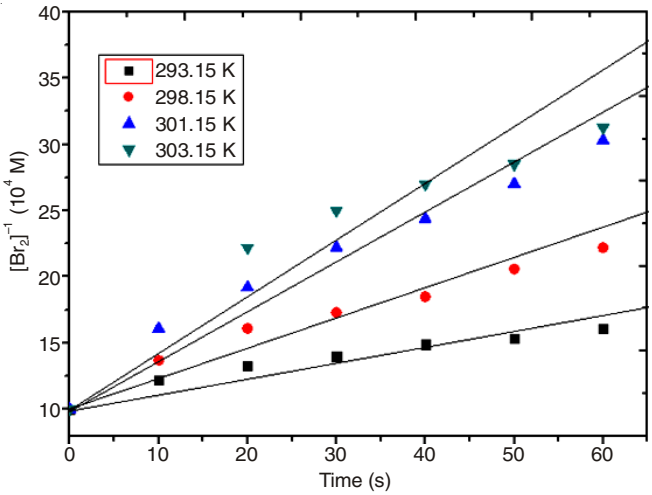


Fig. 1. Kinetics of bromination of uracil at various temperatures and constant pH 7

Bromine is the sole electrophile for the bromination of uracil. The possibility of HOBr or H_2OBr^+ may be ruled out because of their low concentration and negligible reactivity under the reaction conditions [4,7]. Considering this, the mechanism of the reaction may be proposed as follows.

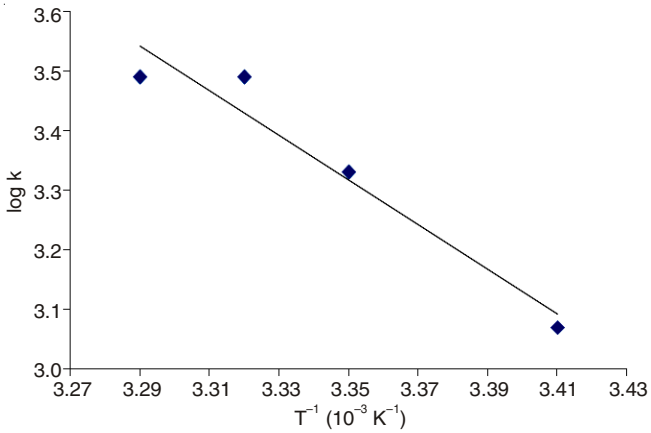
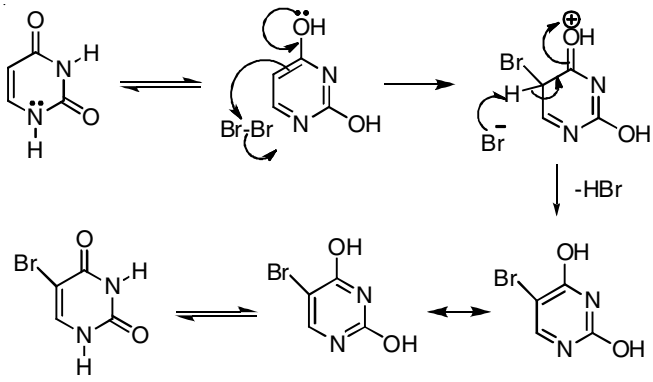


Fig. 2. Kinetics of bromination of uracil (log k *vs.* T^{-1})

Mechanism:



Uracil undergoes tautomerism to form a heterocyclic aromatic compound. The two -OH attached to the ring are electron donating groups and support for aromatic electrophilic substitution. The reaction was performed at different temperatures and the kinetic parameters were calculated.

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