Kinetics and Mechanism of the Cyclization of Substituted Alkylnitroguanidines. II. 1-β-Bromoethyl-2-nitroguanidine; The Effect of Common Ion[1]

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In an earlier paper[1] the kinetics of the isomerization of some β- and γ-substituted 1-alkyl-2-nitroguanidines to 1-nitro-2-amino-1,3-diazacyclo-2-pentene and -hexene salts, respectively, have been reported. Based on the relative rates of reaction, an internal S_N2 mechanism was deduced. Confirmatory evidence for this mechanism can be obtained by studying the effect of excess anion on the reaction rate. This paper reports such data. Rate measurements have also been made on the cyclization of 1-β-bromoethyl-2-nitroguanidine.

EXPERIMENTAL

1-β-Chloroethyl- and 1-β-bromoethyl-2-nitroguanidine were synthesized according to the method of McKay and Milks.[2] The chloro compound was recrystallized as described in the previous paper. A microgravimetric determination[3] of chloride ion (carried out so as to minimize cyclization during the analysis[1]) showed none present. The bromo compound was not crystallized because it cyclizes too readily.[1] It was not readily soluble in water, and its aqueous solution did not give a positive test for bromide ion with silver nitrate solution. A portion of the bromo compound was converted to its cyclic isomer, 1-nitro-2-amino-1,3-diazacyclopentene-2-bromide, by dry heating at 65° for a few days. A portion of the chloro compound was converted to the analogous chloride salt by dry heating at 75° for 1 week. Microgravimetric determinations on the cyclic compounds showed 37.8% Br^- and 21.5% Cl^- (theoretical 37.9 and 21.3%, respectively).

The cyclization rate measurements in aqueous solution were carried out by the conductimetric technique with the apparatus previously used. The linear relationship expected between conductance and concentration of cyclic isomer (up to 200 mg./l.) in 0.00360*M* sodium chloride solution was found to hold. This concentration of sodium chloride is about the maximum that can be used without completely obscuring the effect of degree of cyclization on conductance. Rate measurements were made on 0.001235*M* 1-β-chloroethyl-2-nitroguanidine in this sodium chloride solution at 30.00° and on 0.000924*M* 1-β-bromoethyl-2-nitroguanidine in conductance water at 30.00 and 40.00°. Duplicate runs were made in each case. Rate constants were determined by the standard least squares procedure.

RESULTS AND DISCUSSION

Plots of the rate data based on conductance measurements show the expected first order linearity. The rate constant for the chloro compound in the presence of added chloride ion was computed using only data from the first 50 hr. (60% cyclized) of the run to eliminate effects of hydrolysis of the cyclic compound. The rate constant obtained, $4.69 \pm .04 \times 10^{-6}$ sec.$^{-1}$, when compared to that previously found in the absence of excess chloride ion (4.75×10^{-6} sec.$^{-1}$), shows that there is no common ion effect on the rate of cyclization. This is to be expected in the case of an S_N2 mechanism.

With the bromo compound, apparent deviations (due to hydrolysis) from the first order linearity of the reaction are noticeable only after the cyclization reaction is 80 to 85% complete. Because of the relatively rapid cyclization and the practice of allowing the solution to stand 0.5 hr. in the constant temperature bath before the initial reading, 35% of the linear compound at 30° and 55% at 40° had been cyclized before the first reading was taken. The kinetic data obtained were: $k_{30.00}$, $1.03 \pm .02 \times 10^{-4}$ sec.$^{-1}$; $k_{40.00}$, $3.645 \pm .005 \times 10^{-4}$ sec.$^{-1}$; energy of activation, E_a, $23.84 \pm .38$ kcal.; frequency factor, 1.59×10^{13} sec.$^{-1}$; entropy of activation, ΔS^*_{40}, -0.2 ± 1.2 e.u. Deviation measures are computed by the formulas of Purlee, Taft, and DeFazio.[4]

The rate of cyclization in aqueous solution of the bromo compound at 30° is 22 times that of the corresponding chloro compound.[1] Relative rates of this order of magnitude are in accordance with those expected from similar data on the rates of hydrolysis of *tert*-butyl, *tert*-amyl, and *sec*-octyl halides reported by Hughes and co-workers.[5-7] The lower energy of activation for the bromo as compared to the chloro compound[1] reflects the difference in bond energy between the C-Br and C-Cl links.

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