KINETICS AND MECHANISM OF BROMINATION OF CYCLIC ACETALS WITH 1,4-DIOXANE DIBROMIDE

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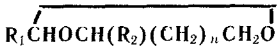
It is shown that the reactivities of cyclic formals in the case of bromination with dioxane dibromide increase in the order 1,3-dioxepane > 1,3-dioxalane ≫ 1,3-dioxane, which is explained not only by steric factors but also by the ease of cleavage of the C_4-O_3 bond of the dioxacyclane ring. The bromination of cyclic acetals takes place through prior enolization of the cyclic acetal with subsequent electrophilic addition of bromine to the double bond.

The bromination of cyclic acetals is not only of practical interest but also may be a convenient model reaction for the study of the reactivities of compounds of this class. The kinetics of bromination of 1,3-dioxacyclanes with 1,4-dioxane dibromide were previously regarded as electrophilic substitution at the acetal carbon atom that proceeds through a four-membered cyclic transition state with the intermediately formed labile 2-bromo-1,3-dioxacyclane [1-3]. In the opinion of the authors of this paper, electron-donor substituents are capable of stabilizing the positive charge on the secondary carbon atom of the cyclic acetal and facilitate the formation of α-bromoacetals. Since the bromination of formals leads to ring opening, whereas the bromination of acetals (ketals) leads to 2-(α-bromoalkyl)-1,3-dioxacyclanes, the data obtained in [1-3] actually pertain to two different types of reactions and cannot be interpreted from a single point of view. Consequently, the assumption of an intermediately formed 2-bromo-1,3-dioxacyclane can, in our opinion, be regarded as unfounded.

The observed contradictions made it necessary for us to examine the kinetics of bromination of cyclic acetals with dioxane dibromide in order to study the effect of the size of the ring, as well as the character and position of the alkyl substituents on the reactivities of a number of 1,3-dioxacyclanes. We also observed that the character of the solvent has a substantial effect on the correctness of the kinetic parameters determined. Thus a study of the kinetics in benzene [1-3] may be considered to be unsuccessful, since benzene undergoes bromination at an appreciable rate (to give up to 30% bromobenzene) in this case. The bromina-

TABLE 1. Kinetic Parameters of the Bromination of Cyclic Acetals with 1,4-Dioxane Dibromide



$R_1CHOCH(R_2)(CH_2)_nCH_2O$

Compound	n	R_1	R_2	k ·10⁴, liters/mole·sec			lg A	ΔH≠, kcal/mole	−ΔS≠, eu	ΔG≠, kcal/mole
				303 °K	313 °K	323 °K				
I	0	H	H	1,0±0,2	2,1±0,3	3,4±0,7	4,52	11,2±1,0	40,0±1,2	23,7±1,5
II	1	H	H	0,2±0,02	0,4±0,03	0,8±0,05	6,69	15,4±1,2	30,0±1,0	24,7±2,0
III	2	H	H	1,6±0,1	2,8±0,4	4,7±0,7	3,50	9,5±1,0	44,7±1,2	23,5±2,0
IV	0	H	CH_3	8,3±1,0	14,0±2,0	22,4±3,0	3,90	9,0±0,8	42,2±1,0	22,2±1,5
V	1	H	CH_3	3,4±0,5	6,5±0,8	13,4±2,0	6,16	12,7±2,0	32,5±1,0	22,9±2,0
VI	2	H	CH_3	11,7±2,0	17,5±2,5	26,6±3,5	2,84	7,4±0,6	47,6±2,0	22,1±1,6
VII	0	CH_3	H	14,0±2,0	34,0±4,0	72,8±8,0	8,61	15,3±1,0	21,3±0,6	22,0±3,0
VIII	1	CH_3	H	4,8±0,7	11,0±2,5	28,0±3,0	9,07	16,6±1,0	19,2±1,0	22,6±2,0
IX	2	CH_3	H	24,0±3,0	51,0±3,0	110±12	8,11	14,2±0,7	23,8±1,0	21,6±1,5
X	2	C_2H_5	H	43,0±4,0	81,0±10,0	174±19	6,47	13,1±1,0	26,7±1,0	21,5±0,9
XI	2	i-C_3H_7	H	47,0±5,0	89,0±9,0	182±22	5,97	12,3±0,8	29,0±1,1	21,3±1,2

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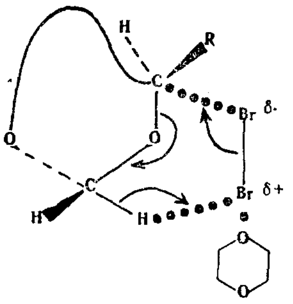
tion of 1,4-dioxane and tetrahydrofuran (THF) proceeds even more rapidly. In this connection, we chose carbon tetrachloride, in which "self-bromination," although it does occur, takes place considerably more slowly than bromination of the investigated 1,3-dioxacyclanes. In each specific case allowance for "self-bromination" was made by means of specially designed "blank" experiments. Since the reaction under consideration is first-order in both dioxane dibromide and the substrate [1-3], the pseudomonomolecular reaction constants were determined in the case of a tenfold excess of the corresponding cyclic acetals. The consumption of dioxane dibromide, in this case up to 60-70% conversion, is described satisfactorily by a first-order equation. The dependence of the biomolecular rate constants for the bromination of the investigated 1,3-dioxacyclanes on the temperature and the corresponding activation parameters are presented in Table 1. Under the examined conditions the bromination of the corresponding ketals proceeds so rapidly that we were unable to determine the kinetic parameters.

It is apparent from Table 1 that formals I-VI can be arranged in the order of 1,3-dioxepane > 1,3-dioxalane ≫ 1,3-dioxane with respect to increasing reactivity. The introduction of a methyl group in the 4 position of the 1,3-dioxacyclane ring leads to a certain decrease in the activation parameters, which may indicate participation of this carbon atom in the transition state.* The large negative activation entropies evidently indicate that the bromination of cyclic formals proceeds through an extremely ordered transition state, which can be represented as:



From steric considerations, this transition state is more likely in the case of 1,3-dioxanes II and V, for which a chair conformation is primarily realized, and less likely for 1,3-dioxalanes I and IV and particularly 1,3-dioxepanes III and VI, which exist primarily in envelope and twist-chair conformations, respectively [5-7]. In addition, the order of reactivities of cyclic acetals presented above is in good agreement with the well-known assumptions [8, 9] regarding the stability of rings of this sort in heterolytic reactions. The latter is demonstrated quite successfully by the character of the change in the $\Delta H^{\neq}$ values as a function of the size of the ring.

Thus the reactivities of cyclic formals in the reaction with dioxane dibromide are determined not only by steric factors but also by the ease of cleavage of the C_4-O_3 bond of the 1,3-dioxacyclane ring, which proceeds more readily in the case of 1,3-dioxalanes and particularly 1,3-dioxepanes as compared with 1,3-dioxanes; this is in good agreement with the experimental data.

In light of our results, one can hardly agree with the assumption expressed in [3] that the increased reactivities of 4-substituted 1,3-dioxacyclanes are associated with significant (!) transmission of the electronic effect of the substituent through the group, $-\overset{|}{C}H-O-$ since the methyl group has vurtually no polar effect on the acetal carbon atom, the increase in the reactivity of compounds of this sort in the reaction with dioxane dibromide, in conformity with our proposed mechanism, is most likely associated with activation of the reaction center (the C_4 atom), which participates in a reaction of the S_N2 type (particuarly in the case of 4-Ph [3]). Moreover, according to the data in [3], a phenyl

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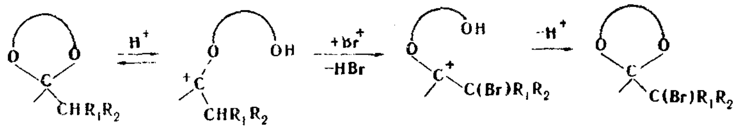
*We carried out a preparative experiment, as a resuult of which we demonstrated unambiguously that the bromination of these compounds takes place with cleavage of the C_4-O_3 bond to give the corresponding bromoalkyl formates $HCOOCH_2(CH_2)_nCH(CH_3)Br$, where $n = 0, 1, 2$. The alternative esters were not detected in the reaction products.

group in the 4 position has a considerably greater (by an order of magnitude) accelerating effect than the same substituent in the 2 position, which is not in agreement with the ideas of the authors of the cited paper regarding the mechanism of this reaction.

The character of the kinetic parameters of the bromination of acetals VII-XI differs appreciably from that observed for formals I-VI (see Table 1). Thus the $\Delta H^{\neq}$ and $\Delta S^{\neq}$ values for VII-IX remain virtually unchanged, regardless of the size of the ring, although a certain tendency for an increase in the order 1,3-dioxane < 1,3-dioxalane < 1,3-dioxepane for the rate constant occurs. At the same time, an appreciable change occurs in the kinetic parameters for IX-XI as the character of the alkyl substituent in the 2 position changes: IX < X < XI. In this connection, the fact of the increase in the activation energies and the pre-exponential functions on passing from 2-methyl- to 2-isopropyl-substituted 1,3-dioxanes is incomprehensible [3].

In [10] on the basis of an examination of the bromination of 2-methyl-substituted 1,3-dioxalanes with pyridinium dibromide perbromide it was assumed that the formation of the corresponding 2-bromomethyl derivatives proceeds through a preliminary step involving the enolization of the cyclic acetal with subsequent electrophilic addition of bromine to the double bond:



If the scheme presented above is correct, the above-noted change in the rate constants in the VII-IX series and the appreciable effect on the kinetic parameters of the number of methyl groups attached to the reaction center in the IX-XI series become understandable.

However, there is no doubt that a more rigorous interpretation of the possible mechanism of the reaction under consideration can be given on the basis of additional experimental data.

EXPERIMENTAL

Compounds I-XI were obtained and purified as in [11]. The benzene, 1,4-dioxane, THF, and carbon tetrachloride were purified as in [12, 13]. 1,4-Dioxane dibromide was prepared by the method in [14] and was stored in an argon atmosphere at 0°C.

The kinetic measurements were made in a glass thermostattable reactor equipped with a stirrer and a reflux condenser at 30-50°C.

A solution of the cyclic acetal in carbon tetrachloride was placed in the reactor. After thermostatting for 30 min, a freshly prepared solution of 1,4-dioxane dibromide in carbon tetrachloride (a solution of the necessary concentration was prepared prior to each new kinetic study) was added. The consumption of dioxane dibromide was monitored iodometrically [15]. A "blank" experiment in which the same amount of solvent was used in place of a solution of the cyclic acetal was carried out simultaneously. The amount of dioxane dibromide consumed was determined as the difference between its total consumption and the consumption in the "blank" experiment for the same time intervals.

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