

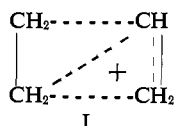
Heat Capacity of Activation for the Hydrolysis of Cyclopropylcarbinyl and Cyclobutyl Chlorides in Water^{1a}

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Abstract: The hydrolyses of cyclopropylcarbinyl and cyclobutyl chlorides have been studied in water. There is no evidence here of a common intermediate being reached by the transition state or of ion-return mechanism. The temperature coefficient of the enthalpy (ΔC_p^*) is large and negative for both reactants, consistent with an S_N1 mechanism.

The solvolytic reactions of cyclopropylcarbinyl and cyclobutyl chlorides and sulfonates have been investigated by several workers in ethanol and in acetic acid.²⁻⁵ Roberts and co-workers proposed the formation of the nonsymmetrical bicyclobutonium structure I⁴ to explain the unusual solvolytic reactivity



and to account for the methylene group rearrangement in the cyclopropylcarbinyl compounds. Other authors^{3,4,6,7} have confirmed both the unusual reactivity of these compounds in solvolytic reactions and evidence of extensive rearrangement. However, the detailed mechanism of these changes remains a matter of continued interest.

The assumption that the transition states for the solvolysis of these two compounds is characterized by the common nonclassical intermediate I, proposed by Roberts and co-workers,⁴ seems to provide an answer to many questions, presented by the unique activity of these compounds. Recently,⁸ the question has been raised as to the exact formulation of the first intermediate in the solvolysis of cyclopropylcarbinyl derivatives. It has been suggested that the postulated nonclassical intermediate cannot fully explain the observed secondary deuterium isotope effects. Another seeming peculiarity in these systems is the apparent insensitivity of the solvolytic rate for the one-ring substituents of cyclopropylarenesulfonates.⁷⁻¹⁰ Further questions are raised by the products in various solvents.

(1) (a) Presented in part at the 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1965, NRC Publication No. 9054; (b) National Research Council Postdoctoral Fellow, 1963-1965.

(2) C. G. Bergstrom and S. Siegel, *J. Am. Chem. Soc.*, **74**, 145 (1952).

(3) M. C. Caserio, W. H. Graham, and J. D. Roberts, *Tetrahedron*, **11**, 171 (1960).

(4) (a) R. H. Mazur, W. N. White, D. A. Semenow, C. C. Lee, M. S. Silver, and J. D. Roberts, *J. Am. Chem. Soc.*, **81**, 4390 (1959); (b) E. F. Cox, M. C. Caserio, M. S. Silver, and J. D. Roberts, *ibid.*, **83**, 2719 (1961).

(5) S. Borčić, M. Nikoletić, and D. E. Sunko, *ibid.*, **84**, 1615 (1962).

(6) S. Borčić and D. E. Sunko, *Croat. Chem. Acta*, **33**, 77 (1961).

(7) D. D. Roberts, *J. Org. Chem.*, **30**, 23 (1965).

(8) M. Nikoletić, S. Borčić, and D. E. Sunko, *Pure Appl. Chem.*, **8**, 441 (1964).

(9) W. B. Kover, Ph.D. Thesis, California Institute of Technology, 1964.

(10) D. D. Roberts, *J. Org. Chem.*, **27**, 3430 (1962); **29**, 294 (1964).

Although the work reported here may contribute a little to our knowledge of the structure of the solute in the transition state for the hydrolysis of cyclopropylcarbinyl and cyclobutyl chlorides, our primary object was to examine the degree and extent of solvent reorganization accompanying such reactions involving such a nonclassical intermediate as indicated by the respective values of the heat capacity of activation, ΔC_p^* . We have shown that the value of ΔC_p^* for the hydrolysis of halides in water can provide a useful indicator of differences in solvent reorganization which appears to depend on whether the reaction follows the S_N1 or S_N2 mechanism.¹¹⁻¹³

The values of ΔC_p^* for the hydrolysis of primary halides normally lie in the range -45 to -55 cal/mole deg, while the few examples available for the corresponding values for the secondary halides tend to fall in the range -55 to -60 cal/mole deg. Nucleophilic interaction is assumed to be necessary in both series, and the difference is tentatively attributed to some difference in the initial state solvation shell.

The possibility that differences in nucleophilic requirements alter ΔC_p^* cannot be excluded, though this is assumed to be small,¹¹ ~ -10 cal/mole deg.

Solvolytic displacement of a halide from a tertiary carbon is normally assumed to occur by an S_N1 mechanism, and in keeping with earlier observations that such reactions involve more extensive solvent reorganization, so too a more negative temperature coefficient for the enthalpy (ΔC_p^*) would be anticipated,¹⁴ and was found.^{12,13}

Since there was no reason to doubt that cyclopropylcarbinyl and cyclobutyl chlorides would hydrolyze in water by an S_N1 mechanism, it was of interest to discover whether ΔC_p^* for such reactions would reflect the characteristics of a primary and secondary halide, respectively, or the more negative values which characterize the hydrolysis of a halide by the S_N1 mechanism.

Experimental Section

Cyclopropylcarbinol was prepared by the standard method,¹⁵ by the reduction of cyclopropanecarboxylic acid with LiAlH₄,

(11) R. E. Robertson, *Can. J. Chem.*, **42**, 1707 (1964).

(12) E. A. Moelwyn-Hughes, R. E. Robertson, and S. Sugamori, *J. Chem. Soc.*, 1965 (1965).

(13) K. T. Leffek, R. E. Robertson, and S. Sugamori, *J. Am. Chem. Soc.*, **87**, 2097 (1965).

(14) If it is accepted that work had to be done in the activation process in water to break down the initial state solvation shell.¹¹

(15) J. D. Roberts and R. H. Mazur, *J. Am. Chem. Soc.*, **73**, 2509 (1951).

Table I. Solvolysis Products in Various Solvents

Solvent	Products (%)	Solvent	Products (%)
Cyclopropylcarbinyl chloride		Cyclopropylcarbinyl tosylate ^a	
H ₂ O	▷CH ₂ OH (50), □OH (50)	CH ₃ COOH	▷CH ₂ OH (71), □OH (24)
CH ₃ COOH ^b	▷CH ₂ OAc (72), □OAc (28)	90% acetone	▷CH ₂ OH (84), □OH (16)
	□Cl (63), □_Cl (37)	DMSO	▷CH ₂ OH (100)
Cyclobutyl chloride		CH ₃ OH	▷CH ₂ OCH ₃ (100)
H ₂ O	▷CH ₂ OH (50), □OH (50)		

^a See ref 7. ^b See ref 3.

Table II. Empirical Constants^a for Temperature and Rate Eq 1

Chloride	A	B	C	Temp, °C	n ^b	δ ^c
Cyclopropylcarbinyl	-10,585.48	-39.702	130.456	15-45	38	0.0015
Cyclobutyl	-12,970.22	-52.832	169.409	35-60	42	0.0014

^a These constants were determined using 18-digit accuracy in the calculation but arbitrarily rounded, consistent with experimental reproducibility. ^b n = the number of individual rates. ^c δ = $\sqrt{\sum(\log k_{\text{calcd}} - \log k_{\text{obsd}})^2/(n-1)}$.

and was converted to the chloride by reaction with thionyl chloride in ether in the presence of tri-*n*-butylamine.

Purification was accomplished using an Aerograph Prep-Column, 10 ft 30% silicone-gum rubber on Chromosorb P at 60°. Cyclobutyl chloride was prepared by treating the 2:1 mixture of cyclopropylcarbinyl and cyclobutyl chlorides (which was the product of the reaction of thionyl chloride on cyclopropylcarbinol) with ZnCl₂. It was purified by gas chromatography using the same conditions as specified above. In both cases the products were identified by nmr, boiling point, single peak on vapor phase chromatography, and strict first-order kinetics on hydrolysis.

Three different experiments were done with respect to the product of hydrolysis of cyclopropylcarbinyl chloride. In the first, a 0.1-ml sample of cyclopropylcarbinyl chloride in 0.5 ml of D₂O in a sealed tube was heated at 60° for 5 hr (half-life at this temperature should be less than 1 min in a homogeneous system). Products found were 30% cyclopropylcarbinol and 70% cyclobutanol as indicated by nmr analysis. In the second experiment, a 0.05-ml sample with 0.5 ml of D₂O was agitated at room temperature for 5 days (the half-life at this temperature was about 45 min). The resulting products were 50% cyclopropylcarbinol and the remainder cyclobutanol. Under the same conditions, but in a large amount of solvent, D₂O, 0.05 ml of the chloride was agitated for 6 hr. The product mixture was continuously extracted with ether and analyzed by vapor phase chromatography and nmr to give 55% cyclopropylcarbinol and the remainder cyclobutanol. In a supplementary experiment it was shown that although cyclopropylcarbinol will slowly rearrange into cyclobutanol in the presence of dilute HCl at 60°, rearrangement at room temperature is negligible after 12 hr of agitation. From this we conclude that the hydrolysis of cyclopropylcarbinyl chloride produced an approximately 1:1 mixture of cyclopropylcarbinol and cyclobutanol. No indication of rearrangement was observed in recovered unreacted chloride.

Four experiments were done to determine the products of hydrolysis of cyclobutyl chloride. In the first, a 0.1-ml sample was sealed in a tube with 0.5 ml of D₂O and agitated for 12 hr at 60° (the half-life at 60° is about 1 min). The major product from the hydrolysis solution in D₂O was cyclobutyl alcohol, with less than 5% cyclopropylcarbinol. Recovered chloride was mainly cyclobutyl chloride. In the second experiment, the same reaction conditions were followed, but the reaction was interrupted at 45 min. The product in D₂O solution was a 2:1 mixture of cyclobutanol and cyclopropylcarbinyl chloride. The product of a similar experiment carried out for 4 hr at 50° was a 1:1 mixture of cyclobutanol and cyclopropylcarbinol, the recovered halide fraction being largely the unchanged chloride. A further test was carried out under mild conditions with a large amount of solvent (0.05 ml in 50 ml of D₂O) and stirred at room temperature for 3 days. The aqueous solution was continuously extracted and shown to contain 47% cyclopropylcarbinol and the remainder cyclobutanol. From these experiments we may conclude that the solvolysis of cyclobutyl chloride in water leads to a 1:1 mixture of

cyclopropylcarbinol and cyclobutanol. Prolonged heating under mild acid conditions at 50-60° leads to the conversion of part of the former into cyclobutanol. Since in no case were significant amounts of rearranged chloride found, it was concluded that under the conditions of our experiments internal return *via* ion pair is negligible.

Roberts and co-workers³ reported that acetolysis of both cyclopropylcarbinol chloride and cyclobutyl chloride in acetic acid at 97° give a 2:1 mixture of three- and four-membered ring compounds. It is not surprising to find that the products of hydrolysis in water are slightly different (Table I) from these in acetolysis since water is a much better nucleophile.

Rate Data

Rates of hydrolysis were determined by a conductance method.¹⁶ In the faster runs, the system described by Moelwyn-Hughes, Robertson, and Sugamori,¹² was used, 10 μl of the respective chloride being introduced into 300 ml of water after temperature equilibrium had been established. Repetitive rates were reproducible to better than 0.5% in all cases. The temperature dependence of these rates were summarized adequately by the usual three-constant equation (see Table II).

$$\log k = A/T + B \log T + C \quad (1)$$

By adopting the usual assumptions with regard to the applicability of the transition-state hypothesis and the further assumption that $d\Delta C_p/dT$ is negligible, we can derive the thermodynamic constants shown in Table III.

Discussion

Since strict first-order kinetics within an experimental toleration of less than 0.5% was observed for both compounds over at least 4 half-lives, and since the characterizing constants and reactivity are obviously different, there is no reason to suspect internal-return isomerization over the temperature range investigated, and, obviously, there cannot be equilibrium between the two stabilized intermediates whatever the mode of stabilization. This conclusion from rate studies supplements that from product studies and is the same as

(16) R. L. Heppollette and R. E. Robertson, *J. Am. Chem. Soc.*, **83**, 1834 (1961).

Table III. Thermodynamic Parameters for Hydrolysis in Water at 25°

Chloride	k_1 , sec ⁻¹	ΔH^* , cal/mole	ΔS^* , cal/mole	ΔC_p^* , cal/mole deg	Ref
Cyclopropyl- carbinyl	5.17×10^{-4}	24,320	8.0	-81	This work
Cyclobutyl	0.1519×10^{-4}	27,450	11.5	-107	This work
<i>t</i> -Butyl	298.9×10^{-4}	22,560	+9.1	-83	12
Benzyl	0.095×10^{-4}	21,400	-4.3	-40	17
Methyl	2.40×10^{-1}	(26,430) ^a	(-4.8)	-52	... ^b

^a Experimental range 50–100°. ^b R. L. Heppollette and R. E. Robertson, *Proc. Roy. Soc. (London)*, **A252**, 273 (1959).

that reported by Wilt and Roberts for the acetolysis of cyclopropylcarbinyl benzenesulfonate.¹⁸ It contrasts with the earlier report of Roberts and co-workers.^{3,4b} These findings do not exclude the formation of a common intermediate *after* the transition state has been passed.

However pertinent to the over-all activation process, these observations are incidental to the question of solvent reorganization which accompanies activation. Whatever the proper terminology, some kind of intermolecular anchimeric assistance seems necessary to account for the solvolytic activity. We assume that under favorable conditions, this will result in charge development on the anion-to-be such that

$$\text{anion-water interaction} = \text{water-water interaction} \quad (2)$$

Granted the initial-state solvation shell possesses a significant degree of structural stability, the assumption is that part of ΔH^* will be the work required to break down this shell in a localized area through competing electrostatic interaction. This abstraction, framed in terms of a static model, is useful in considering quasi-thermodynamic quantities but does not imply the absence of a dynamic equilibrium between solvent molecules in the solvation shell and in bulk solvent. The decrease in the stability of water structure with increasing temperature must necessarily be reflected by a decrease in the structural stability of the solvent shell, and it is this change which we postulate to be the major cause of the negative temperature coefficient of ΔH^* . Reference has been made to the relatively small range covered by the values of ΔC_p^* ¹¹ for primary and secondary halides; hence the conclusion is reached

(17) J. M. W. Scott and R. E. Robertson, *J. Chem. Soc.*, 1596 (1961).

(18) J. W. Wilt and D. D. Roberts, *J. Org. Chem.*, **27**, 3430 (1962).

that similar unit structures of water are involved. The values of ΔC_p^* obtained in this study for a primary and a secondary halide mark exceptions which we associate with a change in mechanism.

Equation 1 does not define the level of charge development corresponding to the transition state for the S_N1 mechanism but rather that for the S_N2 mechanism. In the latter, where overlap has already been established, further charge development will lead to the usual compensating bond making and breaking. For the two compounds investigated here, anion-water interaction will lead to further charge development and presumably further anchimeric interaction, the transition state being reached when

$$\text{cation-water interaction} = \text{water-water interaction adjacent to the cationic moiety} \quad (3)$$

Any further charge development leads to the collapse of the solvent shell in whole or in part about the developing cation, and the reaction goes to completion. The interaction of the water with the anion prior to the transition state may be regarded as electrophilic catalysis by the solvent.

This working hypothesis takes into consideration the evidence for some kind of anchimeric effect and the requirement that the solvent reorganization in the hydrolysis of this primary and secondary halide, as indicated by the ΔC_p^* value, is much more extensive than normal. The values of ΔC_p^* of -87 and -107 cal/mole deg are about the same as for *t*-butyl and *t*-pentyl chloride.^{12,13} Since the latter may be presumed to react by the S_N1 mechanism, the new ΔC_p^* values for cyclopropylcarbinyl and cyclobutyl chlorides may be taken as further evidence that these halides also hydrolyze by the same mechanism in water.