TABLE I[a]

Compound	Rate, k_1 Sec.$^{-1}$		
	50.0 ± 0.1°	75.0 ± 0.1°	100.0 ± 0.1°
4,4-Dimethylcholesteryl p-toluenesulfonate	9.13×10^{-5}	1.26×10^{-3}	1.10×10^{-2}[b]
Cholesteryl p-toluenesulfonate	2.27×10^{-5}	3.24×10^{-4}	2.72×10^{-3}
4,4-Dimethylcholestanyl p-toluenesulfonate			6.10×10^{-5}
Cholestanyl p-toluenesulfonate			4.64×10^{-5}

[a] The values given are the averages of several determinations. [b] Extrapolated from the values at the lower temperatures.

axial C-4 methyl group, and in order to relieve this interaction the A-ring might become somewhat distorted, resulting in a geometry in which less effective overlap of the π-orbitals of the double bond with the developing empty p-orbital at C-3 during ionization might occur.

In conclusion it may be said that 4,4-dimethylcholesteryl p-toluenesulfonate reacts predominantly *via* C-5:C-6 double bond participation. Further work is called for to determine the path followed in the solvolysis of 4,4-dimethylcholestanyl p-toluenesulfonate.

EXPERIMENTAL[5]

4,4-Dimethylcholesteryl p-toluenesulfonate (I).[2a]

Cholesteryl p-toluenesulfonate (IV). Cholesterol and p-toluenesulfonyl chloride were allowed to react in pyridine according to the procedure utilized for the preparation of I to give IV (69%), m.p. 131.5–133°; reported 131.5–132.5°.[6]

4,4-Dimethylcholestanyl p-toluenesulfonate (VII). 4,4-Dimethylcholestanol and p-toluenesulfonyl chloride were treated in pyridine at room temperature for 18 hr. After this period the reaction mixture was poured into ice water, stirred, and then extracted with ether three times. The combined organic layers were washed successively with cold 1:1 hydrochloric acid and water, dried, and filtered. Treatment with decolorizing charcoal followed by filtration and crystallization yielded VII (65%), m.p. 108–109°.

Anal. Calcd. for $C_{36}H_{58}O_3S$: C, 75.74; H, 10.24. Found: C, 75.51; H, 10.20.

Cholestanyl p-toluenesulfonate (VIII). Cholestanol and p-toluenesulfonyl chloride were allowed to react in pyridine as in the preparation of VII above. Crystallization from ether yielded VIII (34%), m.p. 132.5–133.5°; reported 134–135°.[7]

Anal. Calcd. for $C_{34}H_{54}O_3S$: C, 75.23; H, 10.03; S, 5.90. Found: C, 75.09; H, 9.91; S, 5.76.

Determination of the rates of hydrolysis. The rates of hydrolysis were followed by titration of aliquots (in sealed ampoules) of the approximately $1 \times 10^{-2}M$ ester solutions with standard base after appropriate time intervals. In the cases of cholesteryl p-toluenesulfonate and 4,4-dimethylcholesteryl p-toluenesulfonate, the theoretical infinity titration volumes were used in the calculation of the rate.

Acknowledgment. It is a pleasure to acknowledge the participation of C. J. Heller and W. V. Cox in certain aspects of this investigation.

PRINCETON, N. J.

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[5] Melting points (capillary) are uncorrected; analyses by George Robertson, Florham Park, N. J., and Schwarzkopf Microanalytical Laboratory, Woodside 77, N. Y.

[6] E. S. Wallis, E. Fernholz, and F. T. Gephard, *J. Am. Chem. Soc.*, **59**, 137 (1937).

[7] A. Stoll, *Z. physiol. chem.*, **207**, 147 (1932).

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Thermodynamic Properties of Activation for *cis*- and *trans*-Deoxymercuration[1]

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Entropies (ΔS^*) and enthalpies (ΔH^*) of activation have been measured for four additional deoxymercuration reactions induced by nonhalogen acids. These have been compared with values previously obtained for cyclohexane derivatives and with each other. Variations in ΔH^* and ΔS^* are semiquantitatively predicted by theory if the curve of potential energy *vs.* θ has deep minima at *both* 0° and 180° and maxima at 90° and 270°. (The angle between the carbon-carbon-oxygen plane and the carbon-carbon-mercury plane is θ.) This is a reasonable result in view of the likely mechanism for deoxymercuration.

In previous papers[2-4] the mechanism of the acid induced deoxymercuration reaction (Equation 1) has been discussed, and it has been shown that the preferred conformation of the transition state is *trans*.[3] It is possible, however, to prepare five- and six-membered cyclic oxymercurials in

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[1] This research was supported in part by the Air Force Office of Scientific Research through Contract No. AF 49(638)711 and in part by the National Science Foundation through Grant No. NSF G-8179. Reproduction is permitted for any purpose of the United States Government.

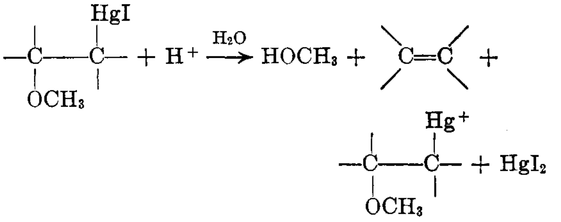
[2] M. M. Kreevoy, *J. Am. Chem. Soc.*, **81**, 1099 (1959).

[3] M. M. Kreevoy and F. R. Kowitt, *J. Am. Chem. Soc.*, **82**, 739 (1960).

[4] M. M. Kreevoy, L. L. Schaleger, and J. C. Wave, unpublished work.

[5] J. Romeyn and G. F. Wright, *J. Am. Chem. Soc.*, **69**, 697 (1947); it is assumed that the structures assigned in ref. 3 are correct.

which the oxygen and the mercury are on the same side of the ring.[5] These cannot utilize the reaction coordinate described for the *trans* isomers[3] because


(1)

it would involve unacceptable distortions of the bond angles of the ring. A slightly different reaction coordinate was suggested for these,[3] also leading to the mercury-olefin π-complex as the product of the rate determining step.

In the present paper enthalpies (ΔH^*) and entropies (ΔS^*) of activation are presented for deoxymercuration of three cyclic and one open chain oxymercurial by nonhalogen acids. Two ΔH^*'s and two ΔS^*'s previously measured[3] are also considered. Three of these compounds are able to assume the *trans*-conformation without undue strain and three are not. It is shown that the previously suggested reaction coordinates[3] are consistent with the data and the most plausible alternatives are unlikely.

RESULTS

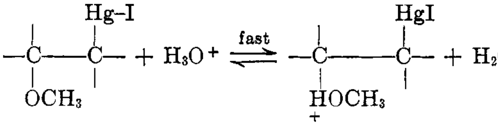
Rates were measured by previously described methods.[2,3] Slower reactions were studied with dilute perchloric acid, faster reactions with acetic acid–sodium acetate buffers. The reproducibility of individual rates was about ±5% in all cases except those obtained with 1-*exo*-iodomercuri-2-*exo*-methoxy[2.2.1]bicycloheptane. In that case reproducibility was about ±10% because of the limited water solubility of the compound. Rates obtained with the two acid systems were identical within experimental uncertainty in comparable experiments. In no case was any systematic trend observed which could be attributed to catalysis by molecular acetic acid. In all cases plots of log (k_2/T) *vs.* $1/T$ were linear, and the deviations from the correlation line were of about the magnitude of the reproducibility of individual rate constants. The table shows the compounds studies, the number of experiments, the temperature range, and the resulting values of ΔH^* and ΔS^*. The values of ΔH^* shown were obtained from Equation 2 by the

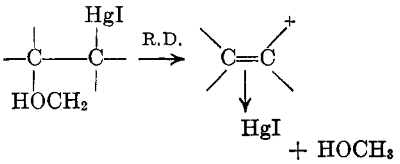
$$R \ln (k_2/T) = -\Delta H^*/T + [\Delta H^*/T_0 - R \ln(T_0/k_0)] \quad (2)$$

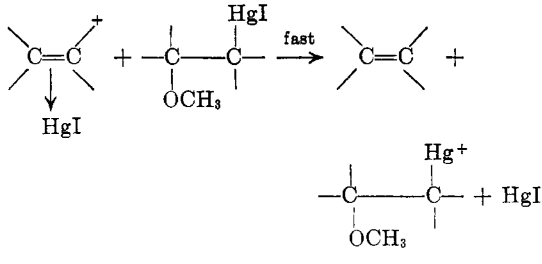
method of least squares.[6,7] The uncertainties given with ΔH^* and ΔS^* are 50% confidence limits.[7]

DISCUSSION

The following mechanism has been established for the deoxymercuration of open chain and *trans*-cyclic oxymercurials in aqueous, nonhalogen acids[2,3]


$$-\underset{OCH_3}{\overset{|}{\underset{|}{C}}}-\overset{HgI}{\underset{|}{\overset{|}{C}}}- + H_3O^+ \underset{}{\overset{fast}{\rightleftharpoons}} -\underset{\underset{+}{HOCH_3}}{\overset{|}{\underset{|}{C}}}-\overset{HgI}{\underset{|}{\overset{|}{C}}}- + H_2O \quad (3)$$


(4)


(5)

Equation 5 represents processes that follow the rate determining step and may well actually take place in a number of steps. The transition state for the reaction represented by Equation 4 is the over-all transition state. In a plot of potential energy *vs.* angle made by the carbon-carbon-oxygen plane with the carbon-carbon-mercury plane (θ) there is a deep well corresponding to the *trans* conformation ($\theta = 180°$) because that conformation permits the formation of the mercury-olefin π-bond to be well coordinated with the cleavage of the carbon-oxygen bond. On the other hand, the favored configuration of the starting state is very probably that in which the oxygen atom and the mercury atom are gauche ($\theta = 60°$).[4]

The present results for 2-methoxyethylmercuric iodide (I), *trans*-2-methoxycyclopentylmercuric iodide (II), and *trans*-2-methoxycyclohexylmercuric iodide (III) are in general accord with these ideas and, therefore, strengthen them. Both I and II are, likely, more flexible than III.[8,9] Both, therefore, give more negative entropies of activation than III following the general rule that a loss in internal freedom accompanies the formation of a polar transition state from a relatively nonpolar starting state.[10] A good deal of the freedom lost is probably rotational freedom about the carbon-carbon single bond which is becoming a double

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(6) Equation 2 appears in ref. 3 with an error in the sign of the first term following the equality.

(7) C. A. Bennett and N. L. Franklin, *Statistical Analysis in Chemistry and the Chemical Industry*, John Wiley and Sons, Inc., New York, 1954, pp. 36–40.

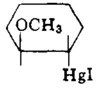
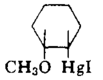
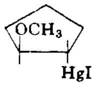
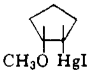
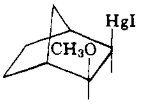
(8) J. G. Aston, in *Determination of Organic Structures by Physical Methods*, E. A. Braude, and F. C. Nachod, eds., Academic Press, Inc., New York, 1955, p. 546.

(9) K. S. Pitzer and W. E. Donath, *J. Am. Chem. Soc.*, **81**, 3213 (1959).

(10) F. P. Price, Jr., and L. P. Hammett, *J. Am. Chem. Soc.*, **63**, 2387 (1941).

TABLE I

ENTHALPIES AND ENTROPIES OF ACTIVATION

Compound	Temp. Range	No. of Expts.	ΔH^*, Kcal. Mole^{-1}	ΔS^*, Cal. Mole^{-1} Deg.$^{-1}$
$CH_3OCH_2CH_2HgI$	0–60	14	19.5 ± 0.7	0.1 ± 2.0
	0–60	6	17.75 ± 0.19	4.6 ± 0.6
	15–75	6	26.2 ± 0.7	4.5 ± 2.0
	0–60	13	15.01 ± 0.06	−3.0 ± 0.2
	0–60	15	19.96 ± 0.04	−4.0 ± 0.1
	5–72	24	21.08 ± 0.24	2.8 ± 0.7

bond in the rate determining step. Other tortional modes in II also may have increased restrictions placed on them. Restriction of internal freedom would change ΔH^* very little because of the substantial cancellation of the zero-point vibrational term and the partition function terms in Equation 6.[11] (The notation of Equation 6 is the same as that

$$\Delta H^* = \Delta E_p + \Delta E_s + RT^2 \frac{d}{dT} \times \left[\ln\left(\frac{f^* f_{H_2O}}{f_S f_{H_3O^+}}\right)\right] \quad (6)$$

of ref. 11.) If a tortional oscillation is considered to be harmonic in both the starting state and the transition state and its frequency goes from 25 cm.$^{-1}$ in the starting state to 200 cm.$^{-1}$ in the transition state, it will make a contribution of −4.1 cal. mole^{-1} to ΔS^* and 0.07 kcal. mole^{-1} to ΔH^*. The former is of the proper magnitude to explain the entropy changes if one such degree of freedom is involved in I and about two in II. The starting state for III can assume a "perfect" conformation, with all bonds staggered and all bond angles tetrahedral. The transition state for III cannot, nor can the starting state for II assume such a conformation. This may account for the difference between ΔH^* for III and that for II. It is not likely that changes in solvation are responsible since the change in ΔS^* is reasonably accounted for by intramolecular considerations. The origin of the change in ΔH^* on going from III to I is probably inductive.[12]

The results for the deoxymercuration of the *cis* compounds are predictable if it is assumed that they also use the mechanism shown in Equations 3–5. The only change required is that the mercury atom and the oxygen atom are now on the same side of the molecule. Mercury-olefin π-complex formation is again coordinated with the carbon-oxygen bond cleavage and coplanarity is again required for the oxygen atom, the mercury atom, and the two carbon atoms involved. The ΔH^* values for the *cis* compounds are generally higher than those for comparable *trans* compounds because of higher nonbonded atom repulsions.[3] The conformation in which the two carbon atoms, the oxygen and the mercury are coplanar and the latter are *cis* corresponds to one of the stable conformations of the five-membered ring (C_S),[9] but this arrangement requires a boat form for the six-membered ring. The starting state for *cis*-2-methoxycyclohexylmercuric iodide (IV) would be a chair form and the conversion from the chair to the boat form of the cyclohexane ring requires about 5 kcal. mole.$^{-1}$ [13] This is a good approximation to the difference between ΔH^* for IV and that for *cis*-2-methoxycyclopentylmercuric iodide (V). The bridge in 1-*exo*-iodomercuri-2-*exo*-methoxy[2.2.1]-bicycloheptane (VI) confines it to the boat form in both the starting state and the transition state so its ΔH^* is less than that of IV by the 5 kcal. mole^{-1} required to convert the chair to the boat in the latter.

If the transition states for the deoxymercuration of IV and V are about as rigid as those for II and III, it would plainly be predicted that ΔS^* for IV would be comparable to that for III, since the starting states would also be comparably rigid. Similarly ΔS^* for II and V should be comparable because their starting states would both incorporate the relative flexibility of the five-membered ring. Since the bicyclic system in VI is rigid, its ΔS^*

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[11] L. P. Hammett, *Physical Organic Chemistry*, McGraw Hill Book Co., New York, 1940, p. 77.

[12] L. L. Schaleger, Ph.D. thesis, University of Minnesota, 1961, p. 43.

[13] W. S. Johnson, J. L. Margrove, V. J. Bauer, M. A. Frisch, L. J. Dreger, and W. N. Hubbard, *J. Am. Chem. Soc.*, **82**, 1255 (1960).

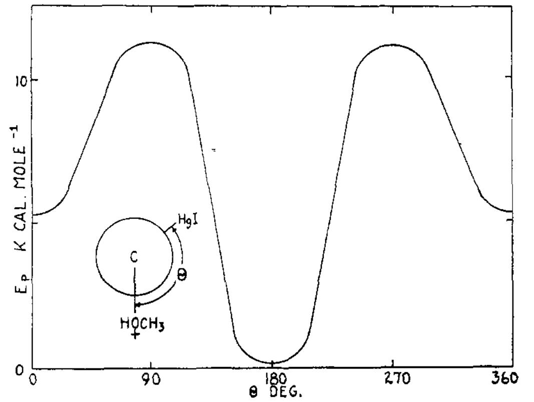

Fig. 1. The potential energy of the deoxymercuration transition state as a function of the dihedral angle, θ

should be comparable to that of III and IV. These predictions are amply borne out by the results.

The success of this theory permits the sketching of an approximate potential energy, E_p, of the transition state as a function of θ for an open chain compound such as I. The height of the peaks at θ = 90° and θ = 270° was taken from the estimated rate of unassisted ether cleavage.[14] The plot is shown in Fig. 1.

Two alternative reaction coordinates might be suggested for the *cis* compounds: (1) Carbon-oxygen cleavage might proceed without substantial assistance from any internal rearrangement. In that case the transition state energy would be almost independent of θ. (2) Carbon-oxygen cleavage might be accompanied by the formation of a coordinate bond between mercury and oxygen. In that case the transition state energy would again be minimized when θ = 0.

In the first case similar rates and thermodynamic properties of activation would be predicted for IV and V. In the second case ΔS^* for the *cis* compounds would be consistantly and substantially higher than for the *trans* because less solvent would be immobilized by the *cis* transition states. Since neither of these effects is observed the two alternative reaction coordinates are rejected.

The neglect of solvent in much of this discussion does not imply that it is unimportant. It merely suggests that, within a narrow range of substrate structures, the *change* in solvation on going from the starting state to the transition state, is constant. Even this limited conclusion should be further limited to water as a solvent.

It is noteworthy that no neighboring group participation by carbon[15] needs to be considered to explain the rate, ΔH^*, or ΔS^* for VI. A certain amount of neighboring group participation by carbon is suggested by the formation of VI, rather than its *trans* isomer, in the oxymercuration of norbornene, and the deoxymercuration presumably uses a transition state at least similar to that for oxymercuration. Difficulty in demonstrating neighboring group participation in nonsolvolytic reactions has been previously noted.[16]

EXPERIMENTAL

Kinetic techniques[2,3] and materials[17] used in this investigation have both been previously described.

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[14] C. K. Ingold, *Structure and Mechanism in Organic Chemistry*, Cornell University Press, Ithaca, N. Y., 1953, p. 334.

[15] S. Winstein, *Bull. soc. chim. France*, C59 (1951).

[16] M. M. Kreevoy, C. R. Morgan, and R. W. Taft, Jr., *J. Am. Chem. Soc.*, **82**, 3064 (1960).

[17] M. M. Kreevoy, John W. Gilje, and Richard A. Kretchmer, *J. Am. Chem. Soc.*, **83**, 4205 (1961).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF CORNELL COLLEGE]

Steric Factors in the Hydrolysis Rates of Ketimines[1,2]

J. B. CULBERTSON, DONALD BUTTERFIELD, ORTWIN KOLEWE, AND ROBERT SHAW

Received June 22, 1961

The effects of the different stereoisomeric forms of the cyclohexane ring in 2,6-dimethylcyclohexyl phenyl ketimines on the rates of hydrolysis of these ketimines have been compared. In particular the hydrolysis rates of the *meso-cis-* and the *meso-trans-*2,6-dimethylcyclohexyl phenyl ketimine hydrochlorides have been found to be distinctly slower than where the racemic form of this 2,6-dimethylcyclohexyl ring is involved. For comparison, the hydrolysis rates of the monosubstituted 2-, 3-, and 4-methylcyclohexyl phenyl ketimine hydrochlorides have been obtained.

Previous investigations[3] have revealed great differences in the rates of hydrolysis of variously substituted diphenyl ketimine hydrochlorides: $R{-}C({=}NH_2Cl){-}R' + HOH \rightarrow R{-}CO{-}R' + NH_4Cl$. This difference extends from a half-life (first-order equation)[4] of about two minutes at

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[1] Supported by a grant from the National Science Foundation.

[2] Presented in part at the 137th Meeting of the American Chemical Society in Cleveland, Ohio.

[3] J. B. Culbertson, *J. Am. Chem. Soc.*, **73**, 4818 (1951).

[4] Measurements have been made in 0.01 *M* aqueous solutions.