[Contribution from the Department of Chemistry, Purdue University]

Transmission of Electrical Effects Through Homoallylic Systems. II. Kinetics of Solvolysis of Some 6-Arylcholesteryl p-Toluenesulfonate Esters

By Richard A. Sneen

Received December 16, 1957

The rates of solvolysis in 90 volume per cent. aqueous dioxane of a series of 6-arylcholesteryl p-toluenesulfonate esters have been measured and shown to be correlated by the Hammett free energy relationship, with slope $\rho = -0.96$ and probable error in log $k = 0.06$. 6-Phenylcholesteryl p-toluenesulfonate is shown to solvolyze at a rate approximately 38 times the calculated rate of solvolysis of the saturated cholestanyl p-toluenesulfonate but only 0.32 times the rate of cholesteryl p-toluenesulfonate. The mechanistic implications of these results are discussed briefly.

Since the original suggestion by Winstein and Rowland Adams[1] that sulfonate esters of cholesterol undergo certain unimolecular solvolyses with alkyl–oxygen fission to yield an intermediate cyclocholesteryl cation intermediate I, a considerable amount of new evidence has been offered and older evidence has been interpreted to corroborate this
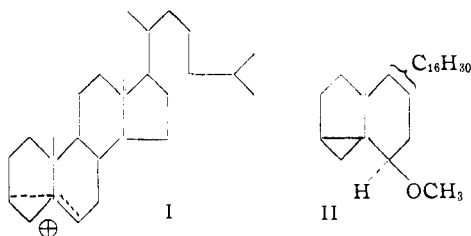

hypothesis. Contemporary with the suggestion of Winstein and Adams was that of Shoppee[2] who noted that cholesteryl chloride, in contrast to the saturated cholestanyl chloride, undergoes acetolysis with essentially complete retention of configuration and was thereby led to postulate that the π-electrons of the C_5–C_6 double bond are capable of holding configuration at the C_3-position during unimolecular substitution. The unimolecular nature of these reactions was demonstrated by Winstein and Adams[1] and recently has been confirmed.[3]

Some of the most convincing arguments for the involvement of the C_5–C_6 π-electrons of cholesteryl systems during solvolysis are of a kinetic nature. Indeed, the original suggestion[1] for the postulated cyclocholesteryl ion (I) came as a result of a comparison between the relative rates for acetolysis of cholesteryl p-toluenesulfonate and of the model secondary ester, cyclohexyl p-toluenesulfonate, the former acetolyzing 119 times as rapidly as the latter.

The postulated intermediacy of the cyclocholesteryl cation in reactions of cholesteryl systems is, of course, not actually demanded by the kinetic evidence referred to in the preceding paragraph; this evidence only requires that the transition states of these ionization reactions be appreciably stabilized by the delocalization energy provided by interaction of the C_5–C_6 π-electron cloud with the incipient positive charge at C_3. However a wealth of data has been accumulated to support the view that, in general, the cyclic ion I is actually in-

volved as a true intermediate in ionization reactions of cholesteryl derivatives. Early work[4] had indicated that one of the primary products of buffered methanolysis of cholesteryl tosylate is the cyclic methyl ether II. More recently, Kosower and Winstein[5] have shown that both cholesteryl p-toluenesulfonate and the trichloroacetate ester of 3,5-cyclocholesterol undergo methanolytic alkyl–oxygen cleavage to yield identical mixtures of products, consisting of $10 \pm 2\%$ cholesteryl and $90 \pm 2\%$ 3,5-cyclocholesteryl methyl ether, thereby suggesting the incurrence of an intermediate common to both reactions and, in particular, of an intermediate capable of giving rise to both cyclic and normal products. Additional evidence is found in the recent elegant studies of salt effects and ion pairs during acetolysis of cholesteryl p-toluenesulfonate carried out by Clippinger and Winstein[6] as well as in the results of molecular-orbital calculations.[7,8] These calculations assign a net stabilization to the cyclocholesteryl cation I of ca. 4–6 kcal., when compared to the classical ion bearing the total positive charge at C_3.[9]

If one considers the most important canonical resonance forms for the cyclocholesteryl cation (I), it becomes apparent that an appreciable electron
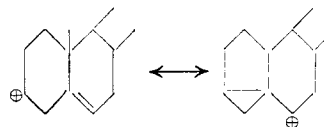
deficiency should exist not only at C_3 but also at C_6. An appropriately constituted alkyl or aryl substituent at a positive center might be expected to stabilize that positive center. Thus it seemed of interest to study the effects of aryl substituents at C_6 in stabilizing the transition states of ionizations leading, presumably, to the corresponding cyclocholesteryl cations. This communication reports the results of a study of the kinetics of solvolysis of a series of 6-arylcholesteryl p-toluenesulfonate esters. The synthesis of 6-phenyl-, 6-p-anisyl-, 6-p-tolyl-, 6-p-chlorophenyl- and 6-p-nitrophenylcholesterol and of the corresponding

(1) S. Winstein and R. Adams, This Journal, 70, 838 (1948).

(2) C. W. Shoppee, J. Chem. Soc., 1147 (1946); cf. E. Bergmann, This Journal, 60, 1997 (1938).

(3) C. W. Shoppee and D. T. Westcott, J. Chem. Soc., 1891 (1955).

(4) See ref. 1 for earlier references.

(5) E. M. Kosower and S. Winstein, This Journal, 78, 4347 (1956).

(6) S. Winstein and E. Clippinger, ibid., 78, 2784 (1956).

(7) M. Simonetta and S. Winstein, ibid., 76, 18 (1954).

(8) C. W. Shoppee and D. F. Williams, J. Chem. Soc., 2488 (1956).

(9) The classical cyclocholesteryl cation with the entire positive charge resident at C_6 would be expected to be several orders of magnitude less stable than a classical normal cholesteryl ion; see ref. 5.

p-toluenesulfonate esters has been reported in a preceding paper.[10]

Kinetic Results.—The results of the kinetic studies are summarized in Table I. Each of the 6-arylcholesteryl p-toluenesulfonates was allowed to solvolyze in 90 volume per cent. aqueous dioxane containing a slight molar excess of lithium acetate. The rates were determined by measuring the amount of acid formed titrimetrically with aqueous standard potassium hydroxide to the phenolphthalein end-point. In general the rates were followed to 80–90% reaction. In the case of p-chlorophenylcholesteryl tosylate, the rate constant of reaction also was determined polarimetrically and found to agree, within experimental error, with the titrimetric rate constant. The readily available p-toluenesulfonate of cholesterol also was solvolyzed under these conditions, both as a check on the techniques employed as well as to provide a basis for comparison of the determined rates of the arylcholesteryl p-toluenesulfonates. These results are assembled also in Table I.

TABLE I

SOLVOLYSIS OF 6-ARYLCHOLESTERYL p-TOLUENESULFONATES
IN 9:1 DIOXANE–WATER (VOLUME)

Cholesteryl p-tosylate	[ROTs][a] × 10²	[LiOAc][a] × 10²	k, sec.$^{-1}$ × 10⁶	Method[b]	Reaction, %	Temp., °C.
Parent	1.26	1.50	18.0 ± 0.2	T	8.8–89	50.00
	1.53	1.71	18.3 ± .4	T	4.9–83	50.00
	1.46	1.72	18.3 ± .3	T	4.2–92	49.97
Phenyl.[c]	1.09	1.18	5.79 ± .10	T	4.9–94	50.00
	1.49	1.67	73.7 ± 1.7	T	6.4–81	75.10
p-Anisyl-	1.05	1.32	14.4 ± 0.3	T	6.1–91	50.00
	1.52	1.82	14.0 ± .7	T	3.9–68	49.95
	0.867	1.38	13.4 ± .4	T	5.9–89	49.98
p-Chlorophenyl-	0.916	2.08	2.81 ± .16	T	5.7–87	49.98
	1.50	1.96	2.77 ± .33	P		49.98
p-Tolyl-	1.53	1.66	8.34 ± .22	T	3.7–78	49.95
p-Nitrophenyl-	1.10	1.72	1.26 ± .09[d]	T	5.0–70	49.98

[a] Initial concentrations. [b] T = titrimetric; P = polarimetric. [c] $\Delta H\ddagger$ = 22.0 kcal; $\Delta S\ddagger$ = −14.7 e.u. [d] Calculated using theoretical infinity.

All of the tosylates studied showed fair to good first-order kinetics.[11] The more slowly solvolyzing compounds, p-chlorophenyl- and p-nitrophenylcholesteryl p-toluenesulfonate, displayed somewhat erratic kinetic behavior; however, neither compound showed any tendency to drift.

A comparison of the solvolysis rates of the arylcholesteryl p-toluenesulfonates with the saturated cholestanyl p-toluenesulfonate is of interest. Cholesteryl p-toluenesulfonate has been shown to acetolyze at a rate 117 times that of cholestanyl tosylate[12] and 119 times that of the model compound, cyclohexyl p-toluenesulfonate[1] at 50°. If one extrapolates this ratio to the solvent system used in the present work, 9:1 dioxane–water, a rate constant of ca. 1.54×10^{-7} sec.$^{-1}$ can be estimated for the solvolysis of cholestanyl tosylate at 50° in this solvent. In Table II are assembled

rates for cholesteryl and the arylcholesteryl tosylates relative to this estimated rate for cholestanyl tosylate.

TABLE II

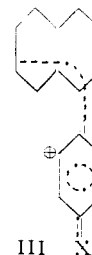RELATIVE RATES OF SOLVOLYSIS IN 9:1 DIOXANE : WATER
AT 50°

p-Toluenesulfonate	Relative rate
Cholestanyl[a]	1.00
p-Nitrophenylcholesteryl	8.2
p-Chlorophenylcholesteryl	18.2
Phenylcholesteryl	37.6
p-Tolylcholesteryl	54.0
p-Anisylcholesteryl	91
Cholesteryl	118

[a] Extrapolated from acetolysis data; see ref. 12.

The rates of solvolysis of the arylcholesteryl tosylates cover a rather small range of 11, a p-methoxyl substituent enhancing the rate of the unsubstituted phenyl compound by a factor of 2.4, and the p-nitrophenyl group diminishing it by a factor of 4.6.

In attempting to analyze the rates of solvolysis of the arylcholesteryl tosylates it would be desirable, of course, to have available a reliable rate value for the unassisted portion (k_s) of ionization of the arylcholesteryl tosylates.[13] Unfortunately, in the present case this is quantitatively impossible. A phenyl group is well known to exhibit a -I effect[14] and various authors[15,16] have ascribed a rate-retarding factor of 8–10 to this depressive effect for β-phenyl substituents. The systems under investigation are obviously not amenable to this treatment; the aryl substituents are here removed to the δ-position and a double bond (-I effect) intervenes between the reaction site and these aryl groups. However, it is fairly safe to say that, in the absence of unusual steric effects, unassisted ionization of the arylcholesteryl tosylates would be expected to proceed at a rate considerably slower than that of the saturated cholestanyl tosylate.

As can be seen from Table II, even the slowest of the arylcholesteryl tosylates, the p-nitrophenyl compound, solvolyzes at a rate 8.2 times that of the extrapolated rate of cholestanyl tosylate whereas p-anisylcholesteryl tosylate is 91 times as fast. It seems reasonably certain that all of the 6-arylcholesteryl tosylates undergo largely anchimerically-assisted ionization by way of a transition state resembling at least to some degree a cyclocholesteryl ion (III).

III

(10) R. A. Sneen, THIS JOURNAL, **80**, 3971 (1958).

(11) Since the concentration of lithium acetate varied in the course of reaction, often by factors of 4 or 5, any second-order reaction involving the concentration of lithium acetate should have resulted in downward-drifting rate constants.

(12) Private communication from S. Winstein.

(13) For nomenclature, see S. Winstein, C. R. Lindegren, H. Marshall and L. L. Ingraham, THIS JOURNAL, **75**, 147 (1953).

(14) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 68.

(15) S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber and J. Corse, THIS JOURNAL, **74**, 1113 (1952).

(16) A. Streitwieser, Jr., Chem. Revs., **56**, 718 (1956).

Consideration of the solvolytic rates of the 6-arylcholesteryl tosylates relative to that of the unsaturated reference compound, cholesteryl tosylate, is also of interest. It will be seen from the data compiled in Table II that even p-anisylcholesteryl tosylate, the most reactive of the aryl compounds, is only 0.77 times as reactive as its 6-hydrogen analog.[17]

With solvolytic rate data for five arylcholesteryl p-toluenesulfonates available, it seemed of interest to attempt to correlate them by means of the Hammett equation[18]

$$\log (k/k^0) = \rho\sigma$$

The reaction series under discussion differs in several respects from the usual types of reaction series which have been successfully correlated by the Hammett equation. In the first place, the reaction studied would be expected to have relatively great electron demands. Further, there exists, to the author's knowledge, no published example of an attempt to apply the Hammett free energy equation to a reaction in which the reaction center is conjugated with the aromatic substituent through a homoallylic system. Finally, the reaction center, C_3, is separated from the aromatic substituent by seven carbon atoms.

However, the Hammett-type analysis of the solvolytic data reported in this paper was fairly successful. A plot of log k vs. σ for this reaction series appears in Fig. 1. It will be seen that the points roughly define a line of slope, $\rho = -0.96$, determined by the least squares method. The fit is, by Jaffé's[19] standards, satisfactory, with correlation coefficient, $r = 0.979$, and standard deviation, $s = 0.095$. This corresponds to a probable error in log k of 0.064.

Since the Hammett substituent constants, σ, are assumed to represent an average blend of inductive and resonance effects of these substituents, they cannot be expected to fit all reaction series indiscriminately. Okamoto and Brown[20] have recently shown that strongly electron-demanding reactions are, in general, better correlated by a new set of substituent constants, which they have designated σ^+ constants. Accordingly, an attempt has been made to fit our data with this new set of substituent constants.

In Fig. 1, a line of slope $\rho = -0.71$, defined by the least squares method, has been drawn through a plot of log k vs. σ^+. The correlation coefficient is $r = 0.977$ and the standard deviation $s = 0.10$.

As summarized in Table III, there seems to be little choice between the correlations effected by σ and σ^+. As would be expected the σ^+ treatment improves the fit for the p-anisyl compound; however, the p-tolyl-, p-chlorophenyl- and phenyl compounds are better correlated by the log k vs. σ plot.

One factor mentioned above as a possible source of interference with a Hammett analysis of the data

(17) Some possible implications of these findings will be discussed in a succeeding publication; R. A. Sneen, THIS JOURNAL, **80**, 3982 (1958).

(18) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, pp. 184 et seq.

(19) H. H. Jaffé, Chem. Revs., **53**, 233 (1953).

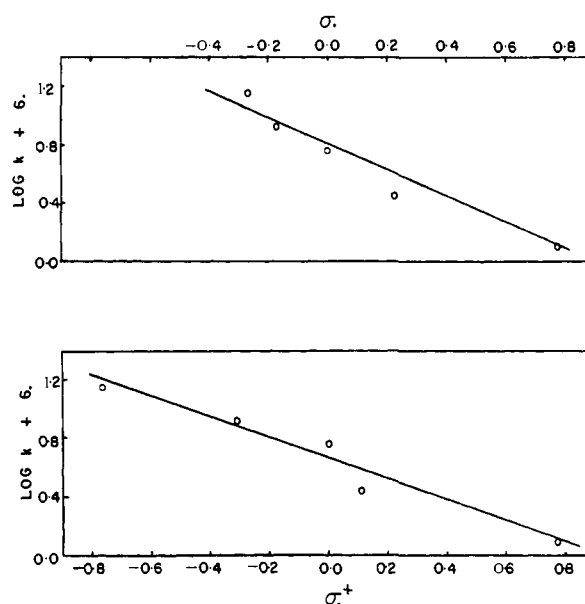(20) Y. Okamoto and H. C. Brown, J. Org. Chem., **22**, 485 (1957).

Fig. 1.—Correlation of rates of solvolysis of 6-arylcholesteryl p-toluenesulfonate esters in 9:1 dioxane–water at 50.0°.

reported in this communication is the extensive nature of the resonating system, the activating substituent being removed from the site of bond-breaking, C_3, by seven carbon atoms. One would expect any inductive contribution to a σ-constant to decrease rapidly with increasing distance. The resonance contribution, on the other hand, would be expected to be much less sensitive to distance.

TABLE III

Substituent constant	log k^0	ρ	r	s
σ	−5.2128	−0.962	0.979	0.095
σ^{+a}	−5.3499	−0.705	0.977	0.10

^{a} See reference 20.

That problems of this nature would not be of great importance had already been suggested by work on other extended systems, notable among which is an investigation of the pK_a values of the m- and p-substituted biphenylcarboxylic acids by Berliner and Blommers.[21] Attempts on our part to analyze discrepancies in our data from this standpoint were completely unsuccessful.

It is of some interest to compare the value of the constant ρ obtained in the present work with ρ values obtained in similar reactions. This constant is usually considered a measure of the sensitivity of a given reaction to electronic influences. In ionization reactions of the type under discussion, it has generally been assumed a measure of the degree of bond-breaking in the transition state.

Kochi and Hammond[22] have investigated the kinetics of solvolysis of a series of substituted benzyl tosylates in 76.6 mole per cent. aqueous acetone at 25.3°. Their data (exclusive of the p-methyl and p-methoxyl compounds) defines a Hammett plot with $\rho = -2.20 \pm 0.07$. This

(21) E. Berliner and E. A. Blommers, THIS JOURNAL, **73**, 2479 (1951).

(22) J. K. Kochi and G. S. Hammond, ibid., **75**, 3445 (1953).

TABLE IV

Cholesteryl tosylate	α_∞	$\alpha_\infty - \alpha_0{}^a$	$\dfrac{mg.}{100\ ml.}$	$\dfrac{Mol.\ wt._{alcy.}}{Mol.\ wt._{tos.}}$	$\dfrac{\Delta\alpha \times 100}{g. \times (mol.\ wt._{alcy.})/mol.\ wt._{tos}} = A$	$\dfrac{A \times mol.\ wt.\ alcy.}{100}$	$M_{D\ alcy.}{}^b$ in $CHCl_3$
p-Anisyl	354.71	−0.11	420	0.76	−34.3	−169	−214
p-Tolyl	354.62	− .20	665	.76	−39.8	−190	−219
Phenyl	354.57	− .25	717	.75	−46.4	−215	−203
p-Chlorophenyl	354.60	− .22	581	.76	··49.6	−247	−198 −195ᶜ
p-Nitrophenyl	354.33	− .49	729	.77	−87.3	−447	−195

^{a} α_0 = 354.82. ^{b} See ref. 10. ^{c} Measured in 9:1 dioxane–water.

means that the free energy of activation differences between members of the benzyl series are approximately 2.1 times as large as those between the corresponding arylcholesteryl tosylates. The somewhat lesser degree of sensitivity to substituents observed with the arylcholesteryl tosylates is consistent with the finding that all of the latter compounds solvolyze more slowly than does cholesteryl tosylate. Undoubtedly the same factors which decrease the rates of solvolysis contribute to the reduction in sensitivity to substituents.[23]

Products.—Only a preliminary examination of the products of solvolysis of the various 6-arylcholesteryl tosylates has been made. However, since some of the results of these early experiments have mechanistic implications, they will be discussed briefly in this communication.

From the buffered solvolysis of 6-phenylcholesteryl p-toluenesulfonate was obtained a crystalline mixture which on chromatography furnished 6-phenylcholesterol in 73% of the theoretical yield.[24] No other reaction products have been obtained in a crystalline state. That the alcohol of retained configuration is a primary product of the reaction is made probable by the observation that the polarimetric rate of solvolysis of 6-p-chlorophenylcholesteryl tosylate showed fairly good first-order kinetics, the polarimetric rate constant being within experimental error of the titrimetric rate constant (see Table I). Except for a coincidental near-equality of the optical rotation values of an initial product and its rearrangement products, the instability of an initially formed product should reveal itself in a drifting polarimetric rate constant.

An alternative explanation, not incompatible with the data, must be considered. Thus, if the initially-formed products are extremely unstable and rearranged at a rate very fast compared to the rate-determining solvolysis step, the observed equality of polarimetric and titrimetric rate constants could be explained. In view of the known formation in 70–90% yields of 3,5-cyclocholestan-6β-ol and its derivatives in solvolyses of cholesteryl p-toluenesulfonate[5] and the ease with which these cyclic compounds undergo rearrangement to the corresponding Δ^5-cholestene-3β-yl derivatives, the initial formation of the 6β-aryl-3,5-cyclocholestan-6β-ols and their rapid isomerization to the corresponding 6-arylcholesterols cannot be ruled out.

(23) See ref. 18 for a discussion of this point.

(24) That at least some of this alcohol is present in the reaction mixture prior to chromatography was shown by the isolation of 6-p-chlorophenylcholesterol in 48% of the theoretical yield by direct recrystallization of the solid, crystalline material obtained by quenching a small sample of a kinetic run in cold water.

We have, as yet, been unable to isolate any of the cyclic aryl alcohols needed to run the obvious controls.

Some interesting conclusions can be drawn from the isolation of 6-phenylcholesterol as a product of the solvolysis of the corresponding p-toluenesulfonate. In the first place, in addition to confirming the unimolecular nature of the reaction,[1,3] the observed retention of configuration complements the kinetic data already discussed, in implying the intervention of Δ^5-π-electrons in the transition state, and thus, indirectly, the probable intermediacy of the 6-arylcyclocholesteryl cations.

An interesting correlation can be seen to exist for the data collected in Table IV. Here the optical rotations of the 6-arylcholesteryl tosylate solvolysis mixtures after at least ten half-lives have been recorded. In calculating the "specific rotations" and "molecular rotations" for these mixtures, it has been assumed that the products have molecular weights equal to those of the corresponding 6-arylcholesterols. It would seem that the error introduced by making this assumption is smaller than the experimental error in reading the optical rotations. Also included in Table IV are the molecular rotations of these 6-arylcholesterols as measured in chloroform.[10,25]

It can be seen from Table IV that there exists a qualitative relationship between the "molecular rotation" of the solvolysis products and the reactivity of the corresponding 6-arylcholesteryl p-toluenesulfonate. These data require that, in addition to the 6-arylcholesterols, at least two other types of products must be formed from the spectrum of tosylates, since the two fastest-solvolyzing tosylates (p-anisyl- and p-tolyl-) yield products with a "molecular rotation" more positive than the corresponding 6-arylcholesterols, whereas the three slower tosylates furnish products more levorotatory than the corresponding alcohol.

With the constitution of these other products which accompany the formation of the 6-arylcholesterols as yet unknown, attempts to attach theoretical significance to the correlation discussed above have been unsuccessful. Qualitatively, the correlation is not unexpected. The distribution of charge in the postulated intermediates, the 6-arylcyclocholestanyl cations, would be expected to depend on the *para* activating substituent. A detailed discussion of this point must await a more thorough investigation.

(25) That these data can be safely extrapolated from chloroform to the solvent system used in this work, 9:1 dioxane–water, was shown explicitly for the case of p-chlorophenylcholesterol.

Experimental

Preparation of Rate Solutions.—The solvent used in the present work, 90 volume per cent. aqueous dioxane, was prepared by adding one volume of distilled carbonate-free water to nine volumes of dioxane, purified by the method described by Fieser.[26] Anhydrous lithium acetate was weighed into a volumetric flask and dissolved to volume in the dioxane–water solution. The reaction mixtures were in general 0.01–0.02 M in lithium acetate.

The lithium acetate solution was in turn added to a weighed amount of the p-toluenesulfonate ester. The rates of solution of the esters in this solvent were fairly slow and it was found expedient to filter the solution when most of the ester had dissolved. Approximately 7–8-ml. portions of this solution were introduced into glass ampoules, sealed under nitrogen, and immersed in a constant temperature bath accurate to ±0.1°.

Kinetic Measurements. A. Titrimetric Rates.—At appropriate time intervals the sealed ampoules were removed and cooled rapidly with tap water to room temperature. An aliquot (ca. 5 ml.) was pipetted into ca. 8 ml. of carbonate-free water and titrated with dilute aqueous potassium hydroxide (ca. 1.7×10^{-2} M) to the phenolphthalein endpoint. Infinity titers were measured after approximately ten half-lives (99.9%). In several instances infinity titers were also measured after 20 or more half-lives and found to be essentially unchanged. In general, the rate constants reported in Table I were calculated from 8–13 experimental points. A typical kinetic run is illustrated in Table V.

TABLE V

SOLVOLYSIS OF 1.09×10^{-2} M 6-PHENYLCHOLESTERYL p-TOLUENESULFONATE IN 90 VOLUME PER CENT. AQUEOUS DIOXANE AT 50.00°

[LiOAc]$_{initial}$ = 1.18×10^{-2} M; [KOH] = 1.698×10^{-2} M

Time, sec.	KOH, ml.	k_1, sec.$^{-1} \times 10^6$
0	0.160	..
42360	0.840	5.77
56040	1.037	5.85
70920	1.200	5.68
99240	1.503	5.64
129960	1.790	5.64
155460	2.050	5.92
223200	2.462	5.91
310260	2.789	5.87
∞	3.297	

Average 5.79 ± 0.10

B. Polarimetric Rate.—The polarimetric rate of solvolysis of p-chlorophenylcholesteryl p-toluenesulfonate was determined simultaneously with a titrimetric rate run. A portion of the contents of each ampoule was placed in a 1-dm. polarimetry tube and the optical rotation, at 27° using the sodium D line, was measured. The integrated, first-order polarimetric rate constant was evaluated from the expression

$$k_1 = 2.303 \log (\alpha_\infty - \alpha_0/\alpha_\infty - \alpha_t)$$

where α_∞ represents the observed rotation at 10 half-lives, α_0 the rotation at zero time, and α_t the rotation at any time t. The data are illustrated in Table VI.

Lithium Acetate.—This salt was prepared by neutralizing lithium carbonate with a slight excess of aqueous acetic acid. The resulting solution was filtered through a cotton plug and water was removed in vacuo until crystallization ensued. The hydrated crystals of lithium acetate were dried in vacuo at 140° to constant weight.

Cholesteryl p-toluenesulfonate was prepared according to the published procedure,[27] recrystallization being accom-

(26) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1941, p. 369.

(27) E. S. Wallis, E. Fernholz and F. T. Gephart, THIS JOURNAL, **59**, 137 (1937).

TABLE VI

SOLVOLYSIS OF 1.50×10^{-2} M 6-p-CHLOROPHENYLCHOLESTERYL p-TOLUENESULFONATE IN 90 VOLUME PER CENT. AQUEOUS DIOXANE AT 50.00°

[LiOAc]$_{initial}$ = $1.96 \times 10^{-2} M$; zero pt.: = 354.73 ± 0.01

Time, sec.	α	k_1, sec.$^{-1} \times 10^6$
0	354.68 ± 0.01	..
61500	354.65 ± .02	2.17
87420	354.62 ± .02	3.30
117360	354.61 ± .01	2.94
165180	354.60 ± .01	2.45
255120	354.56 ± .01	2.72
320580	354.53 ± .02	3.06
1659600 (∞)	354.44 ± .01	
3247880 (∞)	354.47 ± .00	

Average 2.77 ± 0.33 (calcd. from first infinity)

plished from acetone, m.p. 129.5–130.5° (lit.[27] m.p. 131.5–132.5).

6-Arylcholesteryl p-Toluenesulfonates.—The synthesis of these compounds has been described previously.[10]

Products of Buffered Solvolysis of 6-Phenylcholesteryl p-Toluenesulfonate.—A solution containing 1.022 g. ($1.66 \times 10^{-2} M$) of 6-phenylcholesteryl tosylate dissolved in 100 ml. of 90 volume per cent. aqueous dioxane ($2.26 \times 10^{-2} M$ in lithium acetate) was allowed to react at 50.0 ± 0.1° for 7.2 half-lives (>99% reaction). On cooling to room temperature the solution was diluted with a large quantity of ether and washed six times with 50–100-ml. portions of water. The ethereal solution was dried over anhydrous potassium carbonate, filtered and concentrated to about 10 ml. on a steam-bath. The remaining solvent was removed in vacuo without external heating. The crystalline material obtained in this manner was dissolved in ether–ethanol and caused to crystallize by the dropwise addition of water, furnishing 570 mg. (75.8%), m.p. 153–158°, of crude 6-phenylcholesterol. The mother liquor was saved.

Chromatography of the crude alcohol on basic alumina furnished, with ether, 458 mg. (61.0%), m.p. 163–163.5°, of 6-phenylcholesterol. A mixture melting point with the authentic alcohol was undepressed.[10]

Both of the mother liquors as well as the fractions eluted from alumina with solvents less polar than ether were combined, diluted with ether, washed exhaustively with water, dried, filtered and concentrated to dryness as above. The resulting oil was chromatographed on alumina, yielding at least three fractions: a trace of oil with pentane; an apparently different oil with benzene; and 88 mg. (72.7% total yield) of 6-phenylcholesterol from ether, which on recrystallization from ether–ethanol had m.p. 163–164.5°, mixture melting point undepressed. The oils could not be induced to crystallize and were not further investigated.

Products of Buffered Solvolysis of p-Chlorophenylcholesteryl p-Toluenesulfonate.—A 5-ml. aliquot of the kinetic run outlined in Table VI, removed after ca. 6.5 half-lives, was quenched in 8 ml. of water, forming a crystalline solid. After neutralization with aqueous potassium hydroxide the solid material was filtered and recrystallized from ether–ethanol–water, yielding 18 mg. (48%) of 6-p-chlorophenylcholesterol, m.p. 168–177°. A mixture melting point with authentic 6-p-chlorophenylcholesterol[10] was not depressed.

"Molecular Rotations" of Infinity Samples.—An infinity sample (ca. 10 half-lives) of a kinetic run of each of the 6-arylcholesteryl tosylates was placed in a 1-dm. polarimetry tube and the optical rotation at 27°, using the sodium D line, was measured. In several instances it was shown that the optical rotations were essentially unchanged after 20–30 half-lives.