[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Neighboring Carbon and Hydrogen. XXXIII.[1] Reactivities of 3,5-Cyclocholestan-6-yl Derivatives. Strain and Reactivity in Homoallylic Systems[2]

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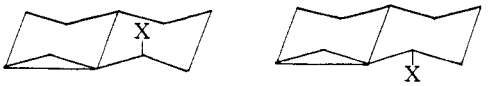
The kinetics of solvolysis of the relatively reactive 3,5-cyclocholestan-6-yl trichloroacetates and chlorides have been studied. In addition, the rates of acid-catalyzed isomerization of the 3,5-cyclocholestan-6-ols and the corresponding acetates to cholesterol or cholesteryl acetate have been measured. A striking feature of the present results is the very high reactivity of the 3,5-cyclocholestan-6β-yl derivatives in solvolysis. In acetic acid or 90% dioxane at 25°, 3,5-cyclocholestan-6β-yl chloride is more reactive than cholesteryl chloride by a factor of $10^{7.4}$. The ratio of 3,5-cyclocholestan-6β-yl chloride to cholesteryl chloride at equilibrium may be estimated from the kinetic data, since the equilibrium constant, K_e, is the product of a reactivity ratio and a partition factor for reaction of the intermediate cation at the two reaction centers. On this basis, K_e is *ca.* $10^{-6.4}$, the difference in molar standard ground state free energies of the two isomers being *ca.* 9000 calories. The important role of ground state free energies in determining the relative reactivity pattern in homoallylic systems is discussed, the 5-norbornenyl system being contrasted with cholesteryl. As we go from one system to the other, ground state free energy factors are responsible for a 10^8 change in relative reactivity of the two isomers. A connection is drawn between the ground state free energy pattern and the magnitude of strain and electron delocalization effects on reactivity of homoallylic isomers. 3,5-Cholestan-6β-yl derivatives are more reactive than the 6α-isomers in the various reactions by factors of 10^1–10^2. The bearing of these results on the question of the nature of the non-classical cation first produced by ionization is discussed. Further consideration is given the general question of plurality of homoallylic cations and the relation between homoallylic and bicyclobutonium cations.

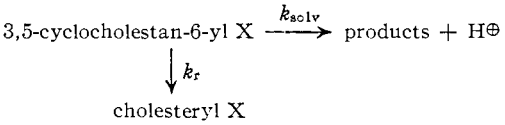
In two previous articles we reported the preparation and solvolysis of trichloroacetates[4] and chlorides[5] derived from the epimeric 3,5-cyclocholestan-6-ols. Because the results were of interest in furthering our understanding of reactivity in homoallylic systems[2,6–9] and the nature of homoallylic cations,[2,6–10] we studied the kinetics of solvolysis of the trichloroacetates and chlorides. Also, the rate of solvolysis of cholesteryl chloride was studied briefly. In addition, the kinetics of the acid-catalyzed isomerization of the 3,5-cyclocholestan-6α- and 6β-ols to cholesterol and that of the corresponding acetates to cholesteryl acetate were examined. The results of this investigation are presented and discussed in the present article.

Results

Trichloroacetates.—The rates of hydrolysis of the epimeric 3,5-cyclocholestan-6-yl trichloroacetates[4] I and II were measured in 90% dioxane. Due to ion pair return[4,11] accompanying the hydrolysis of the trichloroacetates, the amount of acid generated in hydrolysis fell below one equivalent. For example, the infinity acid titer was 83% of theoretical in the hydrolysis of the 3,5-cyclocholestan-6β-yl trichloroacetate I in the absence of any added salts. Good first-order behavior in the solvolysis was observed by treating the disappearance of the trichloroacetates in terms of a first-order solvolysis with a specific reaction rate constant k_{solv} and a first-order rearrangement to inert cholesteryl derivative with a rate constant k_r, according to the scheme



I, X = $OCOCCl_3$ II, X = $OCOCCl_3$
III, X = Cl IV, X = Cl
V, X = OH VI, X = OH
VII, X = OAc VIII, X = OAc



On this basis the integrated kinetic expression to be employed is the one in equation 1, where H_0, H and H_∞ are acid titers at zero time, time t, and infinity, respectively. The first-order reaction rate constant k which is evaluated in this way is actually the sum of k_{solv} and k_r.

$$2.303 \log \left(\frac{H_\infty - H_0}{H_\infty - H} \right) = (k_s + k_r)\, t = kt \quad (1)$$

A representative run, illustrating the first-order kinetics of hydrolysis of 3,5-cyclocholestan-6β-yl trichloroacetate (I) in 90% dioxane is shown in Table I. All the results of the study of the kinetics of hydrolysis of the epimeric 3,5-cyclocholestan-6-yl trichloroacetates are summarized in Table II.

A difficulty in the rate measurements was the tendency for the infinity acid titers to drift downward due to disappearance of trichloroacetic acid. One possible cause of this disappearance is decarboxylation by way of trichloroacetate ion.[12] However, the rate of decomposition of trichloro-

(1)(a) Paper XXX, R. Baird and S. Winstein, THIS JOURNAL, **79**, 4238 (1957); (b) Paper XXXI, S. Winstein and J. Takahashi, *Tetrahedron*, **2**, 316 (1958); (c) Paper XXXII, S. Winstein, F. Gadient, E. T. Stafford and P. E. Klinedinst, Jr., THIS JOURNAL, **80**, 5895 (1958).

(2) Part of the material of this manuscript was presented at the 15th National Organic Chemistry Symposium of the American Chemical Society, Rochester, N. Y., June 17–20, 1957, p. 29 of Abstracts.

(3) Research Fellow of the National Institutes of Health, 1949–1952.

(4) E. M. Kosower and S. Winstein, THIS JOURNAL, **78**, 4347 (1956).

(5) E. M. Kosower and S. Winstein, *ibid.*, **78**, 4354 (1956).

(6) (a) S. Winstein and R. Adams, *ibid.*, **70**, 838 (1948); (b) S. Winstein and A. H. Schlesinger, *ibid.*, **70**, 3528 (1948).

(7) (a) S. Winstein, *Bull. soc. chim. France*, **18**, 55 (1951); (b) S. Winstein, *Experientia Suppl. II*, 137 (1955).

(8) S. Winstein, H. M. Walborsky and K. C. Schreiber, THIS JOURNAL, **72**, 5795 (1950).

(9) (a) S. Winstein, M. Shatavsky, C. Norton and R. B. Woodward, *ibid.*, **77**, 4183 (1955); (b) S. Winstein and M. Shatavsky, *ibid.*, **78**, 592 (1956).

(10) (a) S. Winstein, M. Brown, K. C. Schreiber and A. H. Schlesinger, *ibid.*, **74**, 1140 (1952); (b) M. Simonetta and S. Winstein, *ibid.*, **76**, 18 (1954).

(11) S. Winstein, E. Clippinger, A. H. Fainberg, R. Heck and G. C. Robinson, *ibid.*, **76**, 328 (1956).

(12) F. H. Verhoek, *ibid.*, **56**, 571 (1951).

TABLE I

RATE OF SOLVOLYSIS OF 0.029 *M* 3,5-CYCLOCHOLESTAN-6β-YL TRICHLOROACETATE IN 90% DIOXANE AT 24.9°

Time, sec.	Base,[a] ml.	$10^5 k$, sec.$^{-1}$
...	0.138	
3120	.387	(4.26)
6000	.552	3.85
8100	.643	3.58
11100	.786	3.51
14310	.937	3.55
17580	1.060	3.50
22080	1.256	3.69
27100	1.390	3.61
31090	1.516	3.73
∞	2.146[b]	

Mean 3.63 ± 0.10

[a] Vol. of 0.0559 *N* sodium hydroxide per 5.019-ml. aliquot. [b] 83.2% of theoretical.

TABLE II

RATE CONSTANTS FOR HYDROLYSIS OF 3,5-CYCLOCHOLESTAN-6-YL TRICHLOROACETATES IN 90% DIOXANE

Isomer	Concn. $10^2 M$	Other solute	Concn. $10^2 M$	Temp., °C.	% ∞	$10^6 k$, sec.$^{-1}$
β	2.9	.....	..	24.9	84	36.3
β	3.1	.....	..	24.9	83	33.6
β	3.1	LiOAc	4.2	24.9	83[a]	25.4
β	2.9	$LiClO_4$	3.0	24.9	89	52.3
β	3.0	LiTCA[b]	3.1	24.9	82	36.8
β	2.9	.....	..	50.0	81	654
α	2.8	.....	..	24.9	82[c]	3.86
α	3.1	.....	..	24.9	84[c]	3.80
α	2.8	$LiClO_4$	3.0	24.9	82[c]	4.38
α	2.0	.....	..	75.0	81[c]	899

[a] Estimated graphically from plot of titration data. [b] Lithium trichloroacetate. [c] Estimated roughly from decrease of apparent ∞ titer with time.

acetic acid decreases[13] rapidly in dioxane–water solutions with dioxane content greater than 62%, and it is relatively negligible in 90% dioxane. In the presence of added salts, ionization of trichloroacetic acid is increased and loss of acidity from this cause is more serious. Loss of acidity was the most serious when the added salt was lithium trichloroacetate. Another reason for disappearance of trichloroacetic acid is the slow consumption of trichloroacetic acid by the hydrolysis product[4] 3,5-cyclocholestan-6β-ol V with resultant formation of cholesteryl trichloroacetate.

Where the drift in the infinity acid titer warranted it, corrected values of H_∞, estimated empirically, were employed in evaluating rate constants with the aid of equation 1. Thus, some of the infinity titers listed in Table II and the corresponding rate constants are relatively inaccurate. Nevertheless, the rate constants show that common ion rate effects[11] from added lithium trichloroacetate are negligible, for the added common-ion salt neither depresses rate nor increases the formation of cholesteryl trichloroacetate which accompanies hydrolysis.

Chlorides.—The rates of solvolysis of the various chlorides were studied in acetic acid and 90% dioxane as solvents. Since solvolysis of cholesteryl chloride is relatively slow, it was studied at 100°. In acetic acid, even with lithium acetate included, and in aqueous dioxane, first-order solvolysis rate constants drifted down badly. This is illustrated in Table III. A similar behavior has been noted by Shoppee and his co-workers[14] in acetolysis of

TABLE III

RATE OF SOLVOLYSIS OF 0.0247 *M* CHOLESTERYL CHLORIDE WITH 0.0380 *M* LITHIUM ACETATE IN ACETIC ACID AT 99.8°

Time, min.	KCNS, ml.	$10^4 k$, min.$^{-1}$
...	5.052	
212	4.793	2.48
725	4.317	2.19
1016	4.012	2.28
1730	3.636	1.91
1994	3.504	1.84
2622	3.381	1.54
3385	3.160	1.39
4722	2.807	1.25
6105	2.476	1.17
8380	2.270	0.96
15772	1.270	0.91
∞	0.093 (Calcd.)	

cholesteryl bromide. The downward drift is evidently due to the fact that solvolysis of cholesteryl chloride gives rise to 3,5-cyclocholestanyl derivatives which are not stable under the reaction conditions. In acetic acid containing lithium chloride, or in aqueous dioxane containing hydrogen chloride, the 3,5-cyclocholestanyl derivatives re-ionize and yield a certain proportion of cholesteryl chloride. This reconversion to cholesteryl chloride becomes more and more serious as the reaction progresses, so that first-order rate constants drift down in a run. The rate constants listed for cholesteryl chloride in Table V, which summarizes the data for the several chlorides, are estimated initial values.

TABLE IV

SOLVOLYSIS OF 0.019 *M* 3,5-CYCLOCHOLESTAN-6β-YL CHLORIDE (83.6% "ACTIVE") IN 90% DIOXANE AT 25.0°

Time, sec.	Base, ml.	$10^3 k$, sec.$^{-1}$
...	0.371	
95	1.085	1.45
195	1.689	1.39
285	2.297	1.49
360	2.670	1.48
480	3.383	1.63
645	3.834	1.51
885	4.636	1.65
5805	5.427[a]	
10945	4.945	
49800	3.198	

Mean 1.51 ± 0.07

[a] Correction of this figure by +0.5 ml. leads to 68% infinity acid titer.

Solvolysis of 3,5-cyclocholestan-6β-yl chlorides III followed first-order kinetics quite satisfactorily in 90% dioxane or 50% acetic acid–dioxane at 25°, a sample run in 90% dioxane being shown in Table IV. However, the infinity hydrogen chloride titer in 90% dioxane tended to drift down due to con-

(13) E. J. Salmi and R. Korte, *Annales Acad. Scient. Fennicae (Finland)*, **A54**, No. 10 (1940).

(14) R. H. Davies, S. Meecham and C. W. Shoppee, *J. Chem. Soc.*, 679 (1955).

TABLE V

RATE CONSTANTS OF SOLVOLYSIS OF CHOLESTERYL AND 3,5-CYCLOCHOLESTAN-6-YL CHLORIDES

Isomer	Solvent	Concn. 10^2M	Other solute	Concn. 10^2M	Temp. °C.	% ∞[a]	10^5k, sec.$^{-1}$
3β	AcOH[b]	2.5	LiOAc	3.8	99.8		0.0042[c]
3β	90% dioxane	4.0	....	..	99.7		.0002[c]
6β	90% dioxane	1.2[d]	....	..	25.0	69	1.64[e]
6β	90% dioxane	1.9[f]	....	..	25.0	68	1.51
6β	90% dioxane	1.3[f]	LiCl	1.9	25.0	80	1.44
6β	90% dioxane	1.1[f]	LiBr	1.4	24.9	71	1.79[g]
6β	90% dioxane	1.1[f]	$LiClO_4$	1.2	24.9	77	2.30
6β	90% dioxane	2.7[f]	LiOAc	3.9	24.9	76	1.47
6β	50% AcOH–dioxane[h]	4.4[f]	LiOAc	3.4	24.9	20	0.61

[a] % of "active chloride" appearing as chloride ion. [b] 0.01 M in Ac_2O. [c] Estimated initial rate constants. [d] Molarity of RCl, 72.4% of which was "active chloride"; sample prepared with pyridine. [e] Less accurate procedure employed in this run. [f] Molarity of RCl, 83.6% of which was "active chloride." [g] Rate constant drifted upward in run from 1.55 to 1.96. [h] Run carried out by Dr. Arnold Fainberg.

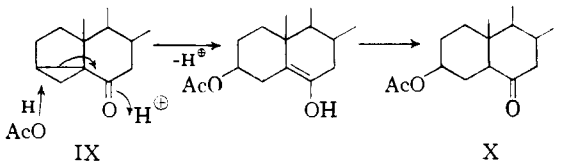
version of 3,5-cyclocholestan-6β-ol (V) to cholesteryl chloride. For this reason, it was necessary to make a small correction for the drift in choosing an H_∞-value to be employed in calculating the first-order rate constant by means of equation 1.

Ion pair return accompanied the solvolysis of 3,5-cyclocholestan-6β-yl chloride to a very considerable extent.[5] This was most serious in 50% acetic acid–dioxane containing lithium acetate. In this case the titratable chloride ion which was produced was only 20% of the theoretical value. Ion pair return was less serious in 90% dioxane, 68% of the theoretical acid titer being obtained. Added salts tended to decrease ion pair return, this being reflected in somewhat higher infinity acid titers listed in Table V. Added lithium bromide had a more complicated action, since the rate constant rose during the run, suggesting that 3,5-cyclocholestan-6β-yl bromide was being formed.

As reported previously,[5] the product from the action of thionyl chloride on 3,5-cyclocholestan-6α-ol (VI) contained an "active chloride," presumably 3,5-cyclocholestan-6α-yl chloride (IV), somewhat less reactive than 3,5-cyclocholestan-6β-yl chloride (III). Therefore, the chloride mixture displayed a drifting first-order rate constant of hydrolysis in 90% dioxane. From an analysis of the data described in the Experimental section, a value of 1.6 ± 0.3 was obtained for 10^4k for hydrolysis of the less reactive chloride in 90% dioxane at 25°.

Acid-catalyzed Rearrangements of 3,5-Cyclocholestan-6-yl Derivatives.—The acid-catalyzed isomerization of 3,5-cyclocholestan-6-β-ol (V) to cholesterol and analogous isomerizations of various derivatives of the alcohol are well known. Also, Wallis[15] has reported virtually quantitative conversion of 3,5-cyclocholestan-6α-ol[16] (VI) into cholesterol by treatment with sulfuric acid in acetic acid and subsequent hydrolysis. The kinetics of the sulfuric acid-catalyzed rearrangement of the 6α-alcohol[16] VI in dry dioxane have been reported by Wolff and Wallis.[17]

The rates of acid-catalyzed isomerization of the epimeric 3,5-cyclocholestan-6-ols V and VI to cholesterol in 90% dioxane, and also that of the corresponding acetates VII and VIII to cholesteryl acetate in acetic acid solvent, were measured. For comparison, one measurement was made of the rate of the somewhat related acid-catalyzed conversion of 3,5-cyclocholestan-6-one (IX) to the 3β-acetoxycholestan-6-one[18] (X) in acetic acid solvent. Rates of acid-catalyzed isomerizations were followed polarimetrically, the data being treated by means of equation 2, where α_0, α and α_∞ represent optical rotations at zero time, time t and infinity, respectively. Fairly satisfactory



IX X

$$2.303 \log \left[\frac{\alpha_\infty - \alpha_0}{\alpha_\infty - \alpha}\right] = kt \qquad (2)$$

first-order kinetics were observed, sample runs for 3,5-cyclocholestan-6β-ol (V) and the α-epimer VI with perchloric acid as catalyst being summarized in Tables VI and VII. An over-all summary of the rates of the acid-catalyzed rearrangements is given in Table VIII.

TABLE VI

REARRANGEMENT OF 0.038 M 3,5-CYCLOCHOLESTAN-6β-OL WITH 0.0301 N PERCHLORIC ACID IN 90% DIOXANE AT 24.5°

Time, sec.	Obsd. α, °	10^5k, sec.$^{-1}$
...	+0.652	
810	.568	9.27
1980	.502	6.97
3150	.378	8.55
4380	.274	8.99
5700	.178	9.20
7185	.090	9.22
9390	−0.037	9.57
11610	.120	9.39
48510[a]	.510	
		Mean 9.17 ± 0.23

[a] 6.4 Reaction half-lives.

In the perchloric acid-catalyzed isomerization of 3,5-cyclocholestan-6β-ol (V), the isomerization rate was nearly linear in perchloric acid over a 10-fold

(15) A. F. Wagner, N. E. Wolff and E. S. Wallis, *J. Org. Chem.*, **17**, 529 (1952).

(16) This epimer was designated β by Wallis; see ref. 4.

(17) N. E. Wolff and E. S. Wallis, *J. Org. Chem.*, **17**, 1361 (1952).

(18) K. Ladenburg, P. N. Chakravorty and E. S. Wallis, THIS JOURNAL, **61**, 3483 (1939).

TABLE VII

REARRANGEMENT OF 0.036 *M* 3,5-CYCLOCHOLESTAN-6α-OL WITH 0.0301 *N* PERCHLORIC ACID IN 90% DIOXANE AT 75.2°

Time, min.	Obsd. α, °	10^3k, min.$^{-1}$
..	+0.843	
15	.682	9.03
30	.565	8.27
47	.446	7.98
87	.220	7.76
110	.082	8.31
149	−0.070	8.54
200	.190	8.40
1200(∞)	.426	
	Mean	8.33 ± 0.28

in solvolysis. A comparison of reactivities of 3,5-cyclocholestan-6β-yl chloride (III) and cholesteryl chloride (XI) in acetic acid, summarized in Table IX, may be made by extrapolating the observed rate of cholesteryl chloride at 100° down to 25°. While the necessary activation energy was not directly observed, there is available the activation energy for acetolysis of cholesteryl bromide from the work of Shoppee and his co-workers.[14] These authors studied the acetolysis of the bromide in lieu of the chloride, which they noted was too slow for convenient measurement. From the reported activation energy of 26.5 kcal./mole for acetolysis of the bromide, a value of 27.4 kcal./mole may be estimated for cholesteryl chloride, since 0.9 kcal./mole is the average difference in energies of activation between chloride and bromide in several systems[20], namely, *t*-Bu, α-phenylethyl, neophyl and benzhydryl.

TABLE VIII

RATES OF ACID-CATALYZED REARRANGEMENTS OF 3,5-CYCLOCHOLESTAN-6-YL DERIVATIVES

Compound	Solvent	Concn. 10^2 *M*	Acid	Concn. 10^2 *M*	Temp., °C.	10^5k, sec.$^{-1}$	$10^3k/(HX)$
6β-OH	90% dioxane	6.2	$HClO_4$	0.32	25.0	0.67	2.1
6β-OH	90% dioxane	3.8	$HClO_4$	3.01	24.5	9.2	3.1
6β-OH	90% dioxane	4.1	$HClO_4$	3.01	24.5	10.3	3.4
			$LiClO_4$	3.4			
6β-OH	90% dioxane	4.1	HTCA[a]	2.35	24.4	0.032	0.014
6β-OH	90% dioxane	4.2	HTCA	2.35	25.0	0.46	0.20
			$LiClO_4$	2.4			
6α-OH	90% dioxane	5.6	$HClO_4$	0.32	25.0	0.001	0.0031
6α-OH	90% dioxane	3.6	$HClO_4$	3.01	75.2	14	4.7
6α-OH	90% dioxane	3.6	$HClO_4$	3.01	99.7	190	63
6β-OAc	AcOH	3.9	$HClO_4$	0.0464	24.8	45	970
6α-OAc	AcOH	3.9	$HClO_4$	0.0464	24.8	10	220
6-Ketone	AcOH	5.3	$HClO_4$	4.66	20.0	12	2.6

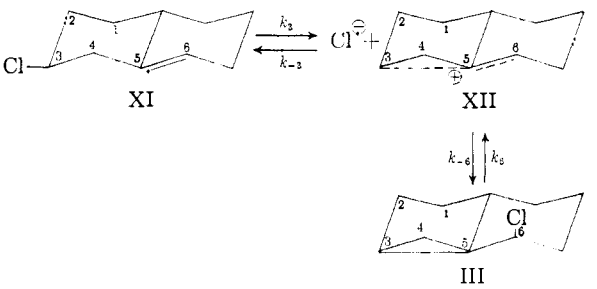
[a] Trichloroacetic acid.

change in perchloric acid concentration, this being evident from the second-order rate constant, $[10^3k/(HX)]$, in Table VIII. Further, inclusion of lithium perchlorate produced only a very small rise in isomerization rate. Trichloroacetic acid produced much lower rates of isomerization than did perchloric acid, and this rate was increased by a factor of approximately 15 by the inclusion of 0.024 *M* lithium perchlorate.[19] Trichloroacetic acid is a weak acid in 90% dioxane, and ionization is obviously very much facilitated by inclusion of salt. While these effects are of some interest in themselves, the main interest of the present investigation was in relative reactivity of isomeric materials, and these observations were not pursued further.

From comparison of rates of reaction given in Table VIII, allowing for the difference in concentrations of perchloric acid catalyst employed, the conversion of 3,5-cyclocholestan-6-one (IX) to 3β-acetoxycholestan-6-one (X) appears to be slower than the acid-catalyzed rearrangement of 3,5-cyclocholestan-6β-yl acetate (VII) in acetic acid by approximately two powers of ten.

Discussion

3,5-Cyclocholestan-6β-yl Reactivity.—A striking feature of the present results is the very high reactivity of the 3,5-cyclocholestan-6β-yl derivatives



The derived factor between the 3,5-cyclocholestan-6β-yl and cholesteryl chlorides in acetic acid is $10^{7.4}$. A similar factor may be estimated in 90% dioxane (Table IX). The derived reactivity ratio between the 3,5-cyclocholestan-6β-yl and cholesteryl chlorides is on the conservative side as an estimate of relative rates of ionization. This is because the measured rate constants for both chlorides are lower than ionization rate constants due to ion pair return. Judging by the relative reactivities[4,5] of the intermediate cation XII at carbon atoms C_3 and C_6, correction for ion pair return would revise the measured rate constant upwards

(19) Qualitative indication of this effect of lithium perchlorate was observed previously.[4] Whereas the product of hydrolysis of 3,5-cyclocholestan-6β-yl trichloroacetate (I) in 90% dioxane contains a large proportion of the 6β-alcohol V, it contains predominantly cholesterol when lithium perchlorate is included in the hydrolysis medium.

(20) (a) S. Winstein and A. H. Fainberg, THIS JOURNAL, **79**, 5937 (1957); (b) A. H. Fainberg and S. Winstein, *ibid.*, **79**, 1597 (1957); (c) A. H. Fainberg and S. Winstein, *ibid.*, **79**, 1602 (1957); (d) A. H. Fainberg and S. Winstein, *ibid.*, **79**, 1608 (1957); (e) S. Winstein, A. H. Fainberg and E. Grunwald, *ibid.*, **79**, 4146 (1957).

TABLE IX

COMPARISON OF SOLVOLYTIC REACTIVITIES OF 3,5-CYCLOCHOLESTAN-6β-YL AND CHOLEST-5-EN-3β-YL CHLORIDES AT 25°

Solvent	AcOH	90% dioxane
6β-Cl; 10^3k, sec.$^{-1}$	9.2[a]	1.5
3β-Cl; $10^{10}k$, sec.$^{-1}$	3.8[b]	0.60[c]
6β/3β ratio	$10^{7.4}$	$10^{7.4}$

[a] Observed k in 50% AcOH–dioxane multiplied by 15, the factor observed for norbornyl p-bromobenzenesulfonate between AcOH and 50% AcOH–dioxane.[21] [b] Extrapolated from 100° with an activation energy of 27.4 kcal./mole. [c] Extrapolated from 100° with an activation energy of 23.9 kcal./mole, lower than the 27.4 kcal./mole figure for acetic acid solvent by 3.5 kcal./mole. The latter figure is the average difference between activation energies for solvolysis in acetic acid and 90% dioxane observed[20] with t-butyl, α-phenylethyl and benzhydryl chlorides.

by more in the case of the 3,5-cyclocholestan-6β-yl chloride than for cholesteryl chloride.

As large as the derived reactivity factor is, it still does not fully represent the high reactivity of the 3,5-cyclocholestan-6β-yl chloride, since solvolysis of cholesteryl derivatives are anchimerically accelerated[6a] by a factor of the order of 10^2.

Free Energy, Strain and Reactivity.—It is very instructive for our understanding of reactivities in homoallylic systems to consider first the equilibrium between two homoallylic isomers. In the present instance, the equilibrium is between cholesteryl and 3,5-cyclocholestan-6β-yl chlorides, XI and III, respectively, and it may be visualized by way of the unsymmetrical homoallylic cation XII. For our present purposes, it will be sufficient to employ only one homoallylic cation and to formulate the equilibrium by way of a dissociated cation rather than ion pairs. The corresponding equilibrium constant K_e may be expressed in the form of equation 3 as the product of two ratios, a reactivity ratio, (k_3/k_6), and a partition factor (k_{-6}/k_{-3}). The latter, symbolized P_6, is the ratio of reactivities of the cation XII toward chloride ion at its two reaction centers, C_6 and C_3.

$$K_e = \frac{[6\beta\text{-Cl}]}{[3\beta\text{-Cl}]} = \left(\frac{k_3}{k_6}\right)\left(\frac{k_{-6}}{k_{-3}}\right) = \left(\frac{k_3}{k_6}\right) P_6 \qquad (3)$$

Reactivity ratio Partition factor

$$(k_6/k_3) = (1/K_e)P_6 \qquad (4)$$

Equation 3 may be rewritten in the form of expression 5 for $\Delta F°$, the difference in molar standard free energies of the two homoallylic isomers. This is given as the difference between two quantities, $(\Delta F^*_3 - \Delta F^*_6)$, the difference in free energies of activation for ionization of the two homoallylic isomers, and $(\Delta F^*_{-3} - \Delta F^*_{-6})$, the difference

$$\Delta F^0 = -RT \ln K_e = (\Delta F^*_3 - \Delta F^*_6) - (\Delta F^*_{-3} - \Delta F^*_{-6}) \qquad (5)$$

$$(\Delta F^*_3 - \Delta F^*_6) = \Delta F^0 + (\Delta F^*_{-3} - \Delta F^*_{-6}) \qquad (6)$$

in free energies of activation for reaction of the homoallylic cation at the two reaction centers. The various quantities are indicated in Fig. 1 which presents a free energy diagram helpful in visualizing the thermodynamic situation.

(21) B. Clippinger, unpublished work.

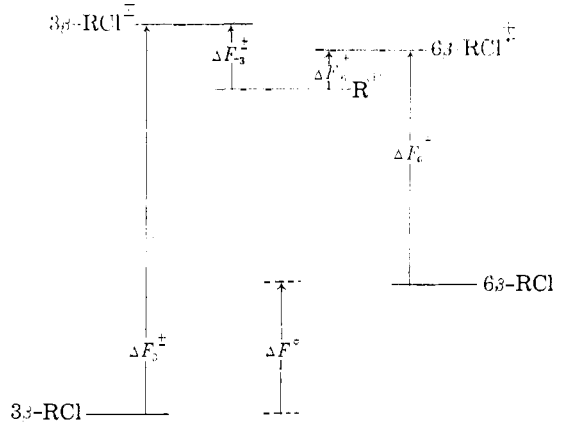
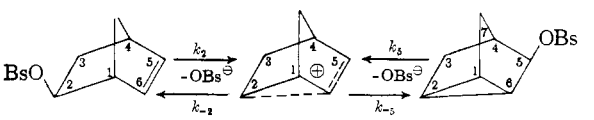


Fig. 1.—Free energy diagram for equilibrium between cholesteryl and 3,5-cyclocholestan-6β-yl chlorides.

Applying equation 3, we see that K_e is equal to $10^{-7.4}P_6$. The partition factor, P_6, for chloride ion as nucleophile is at least 5, and more probably higher than this.[5] The value is more nearly 10 for methanol and water as nucleophiles.[4,5] In any case, a value of 10^1 for P_6 to be employed in equation 3 is sufficiently accurate for our purposes. On this basis, K_e is estimated as $10^{-6.4}$, $\Delta F°$, the difference in molar standard free energies of the two homoallylic isomers, being *ca.* 9,000 cal./mole. Obviously, cholesteryl chloride is very much more stable than its homoallylic isomer.

For a discussion of relative reactivity of the homoallylic isomers, it is convenient to rewrite equations 3 and 5 in the form of equations 4 and 6. From these, it is clear that the (k_6/k_3) ratio of $10^{7.4}$ for the relative reactivity of the two homoallylic isomers is mainly due to the large ground state free energy difference, $\Delta F°$. Making up *ca.* 10,000 cal./mole difference in free energies of activation for ionization of the two homoallylic chlorides is *ca.* 9,000 cal./mole ground state free energy difference and *ca.* 1,000 cal./mole difference in free energies of activation for reaction of the homoallylic cation at its two reaction centers. That the latter quantity is so small is not surprising, in view of the fact that the intermediate cation is a very reactive species, and the transition states for its reactions at one or the other of its reaction centers may be expected to resemble the cation closely.[22] Thus, the difference between ΔF^*_{-3} and ΔF^*_{-6} is inevitably small. To a first approximation, therefore, $(\Delta F^*_3 - \Delta F^*_6)$, the difference in free energies of activation for ionization of the two homoallylic isomers, may be taken equal to $\Delta F°$, the difference in ground state free energies.

To appreciate further the role of ground state free energy in controlling reactivity of homoallylic isomers, it is instructive to consider the system of dehydronorbornyl and nortricyclyl bromobenzene-



XIII XIV XV

(22) G. S. Hammond, THIS JOURNAL, **77**, 334 (1955).

sulfonates[2,7,8,23] XIII and XV. Using the indicated numbering system, the analogs of equations 3 and 4 are 7 and 8, respectively.

$$K_e = \frac{[\text{nortricyclyl OBs}]}{[\text{norbornenyl OBs}]} = \left(\frac{k_2}{k_5}\right)\left(\frac{k_{-5}}{k_{-2}}\right) = \left(\frac{k_2}{k_5}\right) P_5 \quad (7)$$

$$(k_5/k_2) = (1/K_e)P_5 \quad (8)$$

Applying equation 7 to the dehydronorbornyl and nortricyclyl bromobenzenesulfonates XIII and XV, (k_2/k_5) is *ca.* 5 for acetolysis[8,23] and 2–3 for hydrolysis[23] in 75% acetone at 25°. The partition factor, P_5, is *ca.* 15 in acetolysis[8,23] and *ca.* 6 in hydrolysis[23]; if these values are used as approximations to P_5 for bromobenzenesulfonate ion, the estimated K_e is in the range of 12–75. In actual fact, while side reactions preclude an accurate determination of K_e by direct equilibration, attempts to equilibrate the two isomers in nitrobenzene at 75° do show[23] that the equilibrium proportion of dehydronorbornyl bromobenzenesulfonate XIII is less than 10%. In this homoallylic system, the isomer containing the cyclopropane ring is the more stable one,[2,24] in contrast with the relationship which exists between cholesteryl and 3,5-cyclocholestanyl isomers.

Using equations 4 and 8 to contrast the relative reactivities of the homoallylic isomers in the norbornenyl and cholesteryl systems, we have already seen that (k_5/k_2) in the norbornenyl system is less than unity, whereas (k_6/k_3) in the cholesteryl system is $10^{7.4}$. The partition factors P_5 and P_6 are approximately equal in the two systems. Therefore, the difference between (k_5/k_2) and (k_6/k_3) is to be sought in the $(1/K_e)$ factor. In other words, ground state free energy factors are responsible for a 10^8 change in relative reactivity of the homoallylic isomers from one system to another. Since there is no reason to expect the above two systems to be extremes, there may arise even more extreme examples.

Strain and Electron Delocalization.—Without regard for the role of ground state free energies in controlling reactivity of homoallylic derivatives, one can be misled regarding the importance of electron delocalization in stabilizing homoallylic cations. To make this point clear, it may be helpful to consider the cholesteryl–cyclocholestanyl chloride system further, focusing attention on the homoallylic cation rather than on transition states, since we have already seen that the latter resemble the intermediate cation quite closely. As portrayed in Fig. 2, ionization of cholesteryl chloride is assisted by electron delocalization, which more than compensates for strain introduced in the cation.[10b] Equation 9 expresses the standard free energy of ionization of cholesteryl chloride, ΔF^0_3, as ΔF^0_{in}, the value in the absence of strain and electron delocalization, modified by a positive strain free energy, ΔF°_{s3} and a negative term due to electron delocalization, ΔF°_{e3}.

$$\Delta F^0_3 = \Delta F^0_{in} + \Delta F^0_{s3} + \Delta F^0_{e3} \quad (9)$$

$$\Delta F^0_6 = \Delta F^0_{in} + \Delta F^0_{s6} + \Delta F^0_{e6} \quad (10)$$

$$\Delta F^0 = \Delta F^0_{s3} - \Delta F^0_{s6} \quad (11)$$

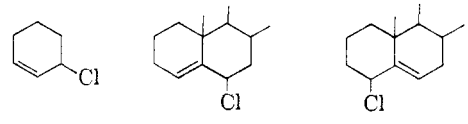
(23) H. J. Schmid, unpublished work.

(24) P. Schleyer, THIS JOURNAL, **80**, 1700 (1958), has reported equilibration of the parent hydrocarbons, norbornene and nortricyclene; nortricyclene is favored over norbornene at equilibrium by a factor of *ca.* 3 at reflux temperature.

Equation 10, analogous to equation 9, expresses the standard free energy of ionization of cyclocholestanyl chloride, ΔF^0_6, as ΔF^0_{in}, the value in the absence of strain and electron delocalization effects, modified by strain and electron delocalization free energies, ΔF^0_{s6} and ΔF^0_{e6}, respectively. Since the situation is idealized, the same ΔF^0_{in} is used in equations 9 and 10, differences due to inductive effects, repulsions between non-bonded atoms, etc., being neglected.

Both bond energies and strain energies are logically involved in a discussion of the thermochemistry of an equilibrium between olefinic chloride XI and cyclocholestanyl chloride III. However, we can choose to have the term "strain" include changes in both bond and strain energies. On this basis, ΔF° may be called the strain free energy difference between the homoallylic isomers XI and III. Since ΔF° is the difference between the strain free energies of ionization of the two isomers, ΔF^0_{s3} and ΔF^0_{s6}, repectively, we can write equation 11. From this, it is clear that ΔF^0_{s6} has a negative value, ionization of cyclocholestanyl chloride III being attended by relief of strain. This conclusion may be reached from structural considerations, also.

As brought out above and illustrated in Fig. 2, the high reactivity of cyclocholestanyl chloride III is to be ascribed partly to strain relief and partly to electron delocalization. If strain relief on ionization were ignored, and the whole rate enhancement of this homoallylic derivative were taken as an indication of stabilization of a cationic intermediate by electron delocalization, this might appear so high as to call for a unique explanation. For example, cyclocholestanyl chloride III is more reactive in solvolysis than the classically allylic compounds, cyclohexenyl chloride XVI, studied by Goering,[25] and 6β-chlorocholest-4-ene (XVII) and 4β-chlorocholest-5-ene (XVIII), studied by W. G. Young and his co-workers[26] in these laboratories.



XVI XVII XVIII

Depending on the case, insufficient consideration of the role of ground state free energies in solvolysis of α-cyclopropylalkyl derivatives may lead one either to overestimate or underestimate the conjugative accelerative effect of the cyclopropane ring. For example, cyclopropylcarbinyl derivatives are more reactive in solvolysis than the allyl analogs,[27] and this was part of the basis for the suggestion of the "tricyclobutonium" structure[27b,28] XIX for the cationic intermediate. The apparently greater conjugative acceleration of rate by α-cyclopropyl compared to α-vinyl was thus accounted for by the increased resonance energy[27b] due to the threefold

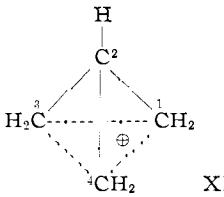
(25) H. L. Goering, T. D. Nevitt and E. F. Silversmith, THIS JOURNAL, **77**, 5026 (1955).

(26) R. E. Ireland, T. I. Wrigley and W. G. Young, *ibid.*, **80**, 4604 (1958).

(27) (a) J. D. Roberts and R. H. Mazur, *ibid.*, **73**, 2509 (1951); (b) C. G. Bergstrom and S. Siegel, *ibid.*, **74**, 145 (1952).

(28) J. D. Roberts and R. H. Mazur, *ibid.*, **73**, 3542 (1951).

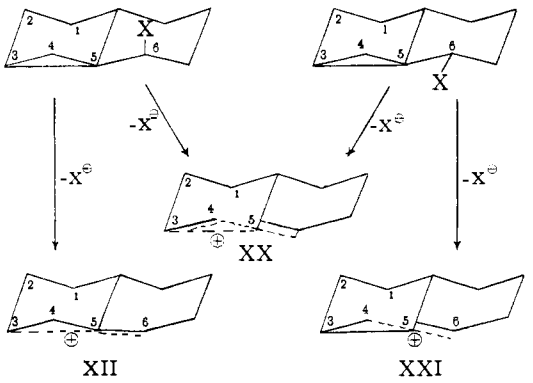
symmetry of XIX. Actually, such a structure was not required to explain the rate, nor was it demanded by any of the other facts.[27-29] Instead of XIX, bicyclobutonium ions, discussed in a later section of this article, are now being invoked by Roberts and co-workers.[30]



XIX

In the norbornenyl–nortricyclyl homoallylic system (XIII and XV), the relatively low rate of the nortricyclyl isomer, already commented on, has been taken as an indication of relatively poor electron release by the cyclopropane ring and ascribed[31] to "steric inhibition of hyperconjugation." Actually, we believe it is the ground state free energy picture which accounts mainly for the relatively low rate of the nortricyclyl derivative, and not steric inhibition of conjugation.

6β:6α-Comparison.—Solvolysis product studies[4,5] have shown that the intermediates which give rise to products are the same, whether the derivative being solvolyzed is cholesteryl, 3,5-cyclocholestan-6β-yl or 3,5-cyclocholestan-6α-yl. Further information on the nature of the first cationic intermediates produced by ionization of the 3,5-cyclo-6β- and 6α-steroids could conceivably come from a comparison of reactivities of 6β- and 6α-derivatives. A study of crude models suggests that, if ionization of the 6β- and 6α-derivatives proceeds stereospecifically to unsymmetrical homoallylic ions[4] XII and XXI, respectively, that geometry is much more favorable for participation of the 3,5-bonding electron pair in the 6β-derivative than the 4,5-bonding pair in the 6α-derivative. Since we might expect,[4] further, that XII is more stable than XXI, a large 6β:6α rate factor would be anticipated on this basis.



XII XXI

Models suggest that the stereoelectronic situation is quite favorable in a symmetrical[4,7,10] homoallylic ion XX. In a chair B ring, the plane of a cationic C_6 center is only slightly away from perpendicular to the plane of the cyclopropane ring, which wave-mechanical considerations[32] suggest is the best arrangement for conjugation. If ionization of both 6β- and 6α- derivatives were to a symmetrical homoallylic ion XX, and the transition states corresponded to a high degree of ionization, the reactivity ratio between 6β- and 6α-derivatives would not be expected to be large.

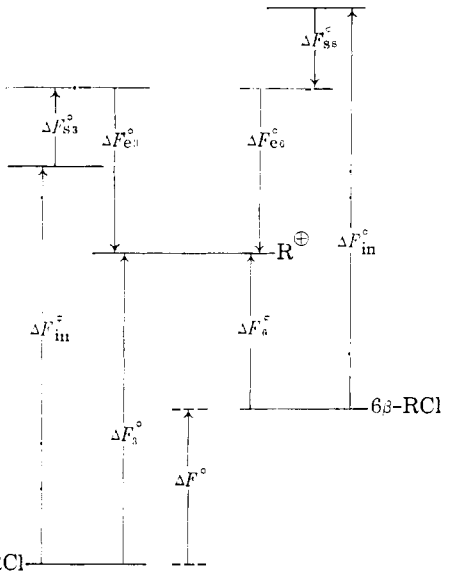


Fig. 2.—Free energy diagram representing strain and electron delocalization effects in ionization of cholesteryl and 3,5-cyclocholestan-6-yl chlorides.

A comparison of relative reactivities of the 6β- and 6α-derivatives in the various reactions studied is summarized in Table X. From the table, it

TABLE X

RELATIVE REACTIVITIES OF 3,5-CYCLOCHOLESTAN-6-YL DERIVATIVES AT 25°

Reaction	6β/6α rate ratio
$ROCOCCl_3$, 90% dioxane	8.7
$ROCOCCl_3$, 90% dioxane, 0.03 M $LiClO_4$	11.9
RCl, 90% dioxane	10
ROH, 90% dioxane, $HClO_4$	670[a]
ROAc, AcOH, $HClO_4$	4.5

[a] This figure, for 0.32×10^{-2} M $HClO_4$, is relatively rough because of the low rate of the 6α-alcohol at 25°. Extrapolation of the 99.7° and 75.2° values for the 6α-alcohol at 3.01×10^{-2} M $HClO_4$ down to 24.5° and comparison with the value for the 6β-alcohol leads to a value of 540.

is clear that the 6β:6α-ratio is of the order of only 10^1 or 10^2, a small factor compared to 10^9 or 10^{10}, the factor by which 3,5-cyclocholestan-6β-yl derivatives are accelerated over cholestan-3β-yl analogs. The variation in the 6β:6α-ratios for the various reactions is considerable, and this feature is being studied further. One of the disturbances which affects the apparent 6β:6α-ratio is due to ion pair return. For this reason, the rate constants evaluated by means of equation 1 for the 6β-derivatives are lower than ionization rate

(29) (a) A. Streitwieser, Jr., *Chem. Revs.*, **56**, 710 (1956); (b) H. Hart, J. M. Sandri and D. P. Wyman, American Chemical Society, Miami, Florida, April 7–12, 1957, Abstracts, p. 65-O.

(30) R. H. Mazur, W. N. White, D. A. Semenow, C. C. Lee, M. S. Silver and J. D. Roberts, THIS JOURNAL, **81**, 4390 (1959).

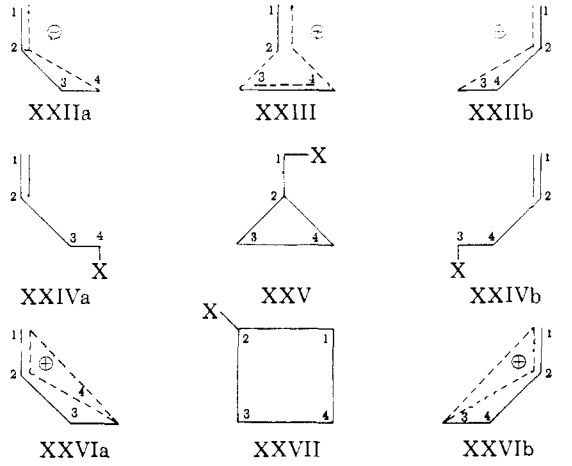
(31) J. D. Roberts, W. Bennett and R. Armstrong, *ibid.*, **72**, 3329 (1950); see also J. D. Roberts and W. Bennett, *ibid.*, **76**, 4623 (1954), and ref. 30.

(32) (a) A. D. Walsh, *Trans. Faraday Soc.*, **45**, 179 (1949); (b) C. A. Coulson and W. E. Moffitt, *Phil. Mag.*, [7] **40**, 1 (1949).

constants. Similarly, the rates of the acid-catalyzed reactions of the 6β-derivatives are lower than ionization rate constants by a factor of *ca.* 10^1 due to the tendency for the cationic intermediate to return to 6β-derivative instead of yielding the cholesteryl product. The same kinds of return must occur in the reactions of the 6α-derivatives, so a certain steady-state proportion of more reactive 6β-derivative must appear relatively early in a run and then be reacting along with the 6α-derivative during the main part of the rate run. However, the kinetic studies were not sufficiently thorough to disclose this disturbance.

The important point established by the 6β:6α-comparison is that there is actually not a very large difference in reactivities of the 6β- and 6α-derivatives. This is especially noteworthy when we allow further for the fact that ionization of the 6β-derivatives might be expected to be sterically accelerated compared to the 6α-analogs due to the 6β-X,10-CH_3 interaction in the 6β-derivative. All the facts are probably best accommodated by supposing that ionization of the 3,5-cyclocholestan-6α-yl derivatives first yields the symmetrical homoallylic cation XX. This would allow us to understand, not only rate, but the indication that some 6α-chloride is formed along with 6β- by the action of thionyl chloride on 3,5-cyclocholestan-6α-ol. In the case of ionization of the 3,5-cyclocholestan-6β-yl derivatives, the rate data could be accommodated by formation of either the symmetrical cation XX or unsymmetrical XII, as far as our present information goes. We hope to study this matter further.

Homoallylic and Bicyclobutonium Ions.—With certain systems, homoallylic rearrangements become intertwined with Wagner–Meerwein rearrangements involving 3 → 4 ring expansion or 4 → 3 ring contraction. For example, cyclopropylcarbinyl derivatives XXV are related, not only to



allylcarbinyl XXIV, but to cyclobutyl analogs XXVII as well. This is clearest from the elegant work of J. D. Roberts and co-workers[27a,28,30] in recent years. The number and the structures of electron-deficient cationic intermediates involved in homoallylic and Wagner–Meerwein rearrangements of the sort being considered represent difficult questions, the answers to which are still in a state of flux. Either explicitly, or from the kind of resonance structures envisioned, the cation from a cyclopropylcarbinyl derivative XXV has at various times been formulated as an unsymmetrical homoallylic ion[27a,29a] XXII, symmetrical homoallylic ion[27b] XXIII, symmetrical tricyclobutonium ion[27b,28] XIX, or unsymmetrical bicyclobutonium ion[30] XXVI. It is necessary to note the differences between these formulations.

In connection with participation of a β-olefinic group in solvolysis, an unsymmetrical homoallylic cation XII was first proposed for the cholesteryl system by Winstein and Adams[6a] and almost simultaneously by Dodson and Riegel.[33] This formation of the unsymmetrical homoallylic cation may be symbolized in the general case by XXIVa→XXIIa. The cation from cyclopropylcarbinyl derivatives XXV subsequently was formulated in this fashion.[27a,29a]

Further electron delocalization and change in geometry of XXIIa may be visualized[7,10] to give rise to the symmetrical homoallylic ion XXIII and finally the second unsymmetrical homoallylic ion XXIIb. These may be considered[7,10] as possible discrete species which accommodate homoallylic rearrangement, as well as Wagner–Meerwein rearrangement of the vinyl group between atoms 3 and 4. The symmetrical homoallylic ion XXIII, considered as a possible discrete intermediate in the conversion of one unsymmetrical homoallylic ion to the other, is presumed to involve conjugation of the cyclopropane ring with a cationic center at C_1, the plane of the cationic carbon atom being perpendicular to the plane of the cyclopropane ring. Species XXIII can be visualized to give rise to homoallyl derivative XXIVa, cyclopropane derivative XXV, and homoallyl derivative XXIVb, species XXIIa to the first two of these products, and species XXIIb to the latter two. However, the actual products and their proportions from reaction of $X^{\ominus}$ with each species are related by the principle of microscopic reversibility to the nature and the relative timing of formation of the various cationic species involved in equilibrating homoallylic and cyclopropane-ring-containing isomers XXIVa, XXIVb and XXV.

The norbornenyl system XIII is one for which both unsymmetrical[31,34] and symmetrical[7b,35] homoallylic cations were visualized early.[36] The highly accelerated rate[8] of solvolysis of the *exo*-norbornenyl ester XIII and the results of Roberts and his coworkers[35] on ^{14}C-scrambling in the norbornenyl product of solvolysis of ^{14}C-labeled norbornenyl bromobenzenesulfonate show that (i) an unsymmetrical homoallylic cation XIV, leading to some unrearranged norbornenyl solvolysis product, is formed first by ionization of norbornenyl bromobenzenesulfonate, and (ii) at least one additional intermediate cation is required. The investigation

(33) R. M. Dodson and B. M. Riegel, *J. Org. Chem.*, **13**, 424 (1948).

(34) J. D. Roberts, Symposium on Organic Reaction Mechanisms, 75th Anniversary Meeting of the American Chemical Society, Sept. 7, 1951.

(35) J. D. Roberts, C. C. Lee and W. H. Saunders, Jr., THIS JOURNAL, **77**, 3034 (1955).

(36) S. Winstein, Symposium on Organic Reaction Mechanisms, 75th Anniversary Meeting of the American Chemical Society, Sept. 7, 1951.

of Schmid[7b,23] has shown that the percentage of unsaturated component in the solvolysis product is definitely lower from nortricyclyl than from the norbornenyl bromobenzenesulfonate. This suggests that solvolysis product does not arise from only unsymmetrical homoallylic cations, otherwise nortricyclyl and norbornenyl starting materials would give solvolysis products with the same proportion of unsaturated component. Although a stereochemical study would be desirable, the available facts suggest that all three unsymmetrical and symmetrical homoallylic cations are involved in solvolysis of the bromobenzenesulfonates, the norbornenyl ester first ionizing to an unsymmetrical ion, the nortricyclyl ester to a symmetrical one.[7b,37] For the symmetrical cation, the geometry of the nortricyclyl skeleton is perfect, the plane of a cationic center at C_5 being exactly perpendicular to the plane of the cyclopropane ring.

In the cholesteryl system there are no clear indications of the occurrence of all three conceivable homoallylic cations XII, XX and XXI. However, with 4,4-dimethylcholesteryl toluenesulfonate, the rate of solvolysis is similar to that of cholesteryl toluenesulfonate, but the predominant products are ring-contracted.[38] The 4,4-dimethylcholesteryl cation, with the 4,4-methyl groups favoring the change, apparently does pass through the structure of the second unsymmetrical homoallylic cation analogous to XXI.

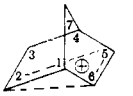
In carbonium ion reactions of the simplest α-cyclopropylalkyl derivatives, namely, cyclopropylcarbinyl XXV, the products contain[27a] cyclobutyl materials XXVII and display a considerable degree of approach to equivalence[28,30] of carbon atoms C_1, C_3 and C_4. J. D. Roberts and co-workers[30] now explain this behavior with the aid of bicyclobutonium ions of the type of XXVI, which tend to equilibrate C_1, C_3 and C_4 possibly by way of XIX.[39] The bicyclobutonium ion XXVI presumably is formed by ionization of either cyclopropylcarbinyl or cyclobutyl derivatives XXV or XXVII, and it reacts with nucleophiles to yield the allylcarbinyl, cyclopropylcarbinyl and cyclobutyl products XXIV, XXV and XXVII, respectively.

The geometry and orbital description which have been suggested[30] for the unsymmetrical bicyclobutonium ion XXVI are very similar to those visualized by Simonetta and Winstein[10b] in their treatment of the unsymmetrical homoallylic ion XXII. However, in the unsymmetrical bicyclobutonium ion XXVI, a C_4–C_1 interaction is explicitly considered along with C_4–C_2, and some rotation of the C_4-methylene group about the C_3–C_4 bond is visualized[30] for improved overlap of the p-orbital on C_4 with the p-orbital on C_1.

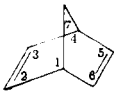
In principle, it can be argued that the 1,4-interaction should never be omitted and that all homoallylic cations have some "bicyclobutonium" character. For example, the unsymmetrical homoallylic norbornenyl cation XIV could be rewritten as XXVIII. However, it is common practice to limit any treatment to the more important interactions and omit a generally less important one until the latter becomes necessary to understand a specific situation. The usual treatment of an allyl cation includes 1,2- and omits 1,3-interactions, while the treatment of Simonetta and Winstein[10b] of the unsymmetrical homoallylic cation includes 1,3- and omits 1,4-interactions.

In systems such as cholesteryl (XII) and norbornenyl (XIV), the constraints of the ring systems favor 1,3-interactions more than 1,4-interactions and "bicyclobutonium" character in the cations. For ion XIV, this can be illustrated with the results of calculations[40] which have been carried out for bicycloheptadiene XXIX. In this hydrocarbon, the 2,6-overlap integral, S_{26}, is greater than S_{25} by a factor of 2.2. Depending on the treatment[40] the exchange integral, β_{26}, is greater than β_{25} by factors of 2–9. Inspection of crude models suggests further that deformation of ions XII and XIV to increase 1,4-bonding would be attended by unusually large strain energies. There is one noteworthy cation where the distinction between 1,3- and 1,4-interactions has vanished, namely, the 7-norbornenyl cation XXX, discovered by Winstein, Shatavsky, Norton and Woodward.[9a] The equivalent overlap of the C_7-p orbital with C_2- and C_3-p orbitals in XXX has been emphasized[9,41] and the cation has been called both homoallylic[9] and "bis-homocyclopropenyl."[41]

Where homoallylic rearrangements do become intertwined with 3→4 and 4→3 ring changes, it seems to us not yet clear[10b] how many non-classical cations are actually involved. It proved[30] impossible to maintain economy of non-classical intermediates at one symmetrical tricyclobutonium ion[27,28] XIX in the interpretation of reactions of cyclopropylcarbinyl derivatives XXV, and the question still remains whether bicyclobutonium ions

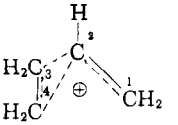


XXVIII



XXIX

XXX



XXXI

(37) If this is correct, the principle of microscopic reversibility leads to the conclusion that reaction of bromobenzenesulfonate ion with the symmetrical cation yields only nortricyclyl ester, while reaction with the unsymmetrical ion yields only norbornenyl ester. By analogy, reaction with solvent would be formulated similarly. On this basis, the behavior of the homoallylic cations toward nucleophiles differs from that visualized previously.[7b,35]

Since, on this basis, two homoallylic cations are involved in equilibration of norbornenyl and nortricyclyl bromobenzenesulfonates, equation 7 for the equilibrium constant, K_e, becomes $K_e = (k_3/k_5)(k_{-5}/k_{-3})(k^u/k^s)$. A third ratio, (k^u/k^s), the relative rate constants for conversion of unsymmetrical and symmetrical cations into each other, is thus added to the right-hand side of equation 7. The counterpart of this change is necessary in free energy diagrams of the type in Figs. 1 and 2. Two cations at similar free energy levels need to be introduced in place of the one intermediate.

(38) G. Just and R. Sneen, unpublished work.

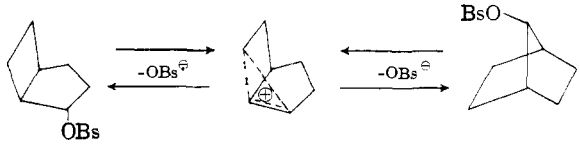
(39) The orbital hybridization and geometry about each of the three methylene groups are quite different from those in the original[28] XIX.

(40) C. Wilcox, unpublished work.

(41) W. G. Woods, R. A. Carboni and J. D. Roberts, THIS JOURNAL, **78**, 5653 (1956).

of the XXVI type are sufficient. For example, one could inquire whether the symmetrical homoallylic ion XXIII (or XXXI) is involved.

The question raised is essentially one of distinction between homoallylic and bicyclobutonium cations. It would seem that bicyclobutonium ions suffice if no energy barrier occurs between classical cyclobutyl and unsymmetrical homoallylic cations, and between classical cyclobutyl and symmetrical homoallylic cations.[42] Models suggest that this state of affairs may not be equally probable in the two cases.



Experimental

Materials and Solvents.—The 3,5-cyclocholestan-6β- and 6α-trichloroacetates and the corresponding alcohols were those described previously.[4] The 3,5-cyclocholestan-6-yl chloride specimens were also those described previously.[5]

Cholesteryl chloride was prepared by an improved procedure. Cholesterol (200 g.) was mixed with 148 ml. of thionyl chloride (240 g.), and the mixture was allowed to stand for 24 hours. The partially solid reaction mixture was poured onto ice and potassium carbonate, and the chloride was filtered off and washed with water. The wet solid was transferred to a beaker and warmed with 2 liters of redistilled petr. ether, b.p. 36–41°. The water layer was removed with a pipet, and the solution was poured through an alumina column (10 × 33 cm., *ca.* 1.6 kg.). Petroleum ether was added until the total volume of eluate had reached 3 liters. The solvent was distilled off on the steam-bath, and 800 ml. of acetone was added to the very light yellow oil. The chloride crystallized almost immediately, and it was filtered off to yield a material, m.p. 96–97°. Concentration of the filtrate yielded an additional amount of product, m.p. 95.5–96.5°. The total yield was 201.5 g. (95.6%).

Dioxane, b.p. 100.5–101.0°, was tested frequently for peroxide, and it was usually refluxed over sodium and distilled prior to use. The 90% dioxane solvent was prepared by mixing nine volumes of dioxane with one volume of water. Acetic acid solvent, approximately 0.03 *M* in acetic anhydride, was prepared in the usual way.[43]

Lithium trichloroacetate, in the form of a white powder, rather soluble in polar solvents, and decomposing on heating at about 270°, was prepared by addition of trichloroacetic acid to an equivalent amount of lithium carbonate suspended in ether. The solid was filtered off, washed with cold ether, dissolved in boiling ether and precipitated by cooling. The final product was obtained by filtration and drying under vacuum. Lithium perchlorate trihydrate, m.p. 94–95°, was kindly supplied by Dr. K. C. Schreiber.

Rate Measurements.—Acid-catalyzed isomerization of the 3,5-cyclocholestan-6α- and 6β-ols and acetates was followed polarimetrically.[44] Fast rates were measured in a jacketed polarimeter tube with temperature maintained by oil pumped from a constant temperature bath through the tube. At intervals, a reading was made as rapidly as possible and the time recorded immediately afterwards. Slow rates were followed by withdrawing samples from solutions maintained at constant temperature, placing the solution in a 1-dcm. polarimeter tube, measuring the rotation, and recording the time immediately after reading the rotation. For runs at 75 and 100°, 1.2–1.5 ml. aliquots were sealed into small ampoules, times taken as the instant of quenching in ice, and the rotations measured as usual.

In following solvolysis of the trichloroacetates, aliquots were removed with a calibrated automatic pipet and quenched in 25 ml. of water. The time used was the instant of opening the pipet to release the sample, except for runs at higher temperatures where the time used was that of cooling the ampoule in ice. The ampoule was warmed to room temperature and sampled as before. The aqueous solution was titrated with standard sodium hydroxide using phenolphthalein as indicator, the solutions showing no drift in end-point. Especially in the case of solvolysis in the presence of added lithium acetate, it was not possible to obtain a reliable infinity titer, and this was estimated graphically.

In following solvolysis of the chlorides, samples were quenched in 50-ml. glass-stoppered flasks containing 25 ml. of pentane and 10 ml. of water. A well-greased stopper was placed in the mouth of the flask, and the whole was shaken vigorously 25 times.[43] The water layer was separated, a boiling chip was added, and the solution was boiled on a hotplate for 2–3 minutes. Then it was allowed to cool, protected from the atmosphere by an ascarite tube, and the acid was titrated with standard base, using the green color of brom thymol blue as end-point. The aqueous solutions derived from the run with lithium acetate were titrated for chloride by the usual Volhard procedure, nitrobenzene being used to protect the silver chloride.

In solvolysis of the chloride prepared from 6α-alcohol and thionyl chloride,[5] a 211-mg. quantity of material (78.6% "active") was dissolved in 63 ml. of pure dioxane and mixed with 7 ml. of water. The solution was thermostatted at 25.0°, and 5.049-ml. aliquots were removed and analyzed for acid. The results obtained are

Time, sec.	Base,[a] ml.	10^3k, sec.$^{-1}$	Time, sec.	Base,[a] ml.	10^3k, sec.$^{-1}$
..	0.142		780	1.211	1.07
90	.339	1.22	4080	1.770	0.48
180	.535	1.29	7920	1.927	.36
285	.684	1.19	15180	2.036	
360	.780	1.14	22380	2.000	
450	.916	1.17		2.072[b]	
540	1.007	1.13			

[a] Ml. 0.00959 *N* base per aliquot. [b] Corrected infinity titer; 67% of theoretical value.

From the measured rate constant for the 6β-chloride and the development of acidity during the first 7 minutes, due essentially entirely to solvolysis of 6β-chloride, the initial concentration of 6β-chloride was estimated. The remainder of the "active" chloride was a slower reacting material. From the initial amount of this chloride and the remaining "active" chloride at 7920 sec. a rate constant of 1.3×10^{-4} sec.$^{-1}$ may be estimated for this chloride. From a plot of log $(a - x)$ *vs.* time, a rate constant of 1.9×10^{-4} sec.$^{-1}$ is estimated for the slower "active" chloride from the straight line through the late points. Correcting the residual "active" chloride concentrations at each of the earlier points for the amount of slower "active" chloride, a good straight line plot is obtained for log $(a - x)$ of the 6β-chloride *vs.* time. From this plot, 1.7×10^{-3} sec.$^{-1}$ is obtained as the rate constant of the 6β-chloride.

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(42) Some analogy exists for the occurrence of only one potential energy minimum in carbonium ion conversions involving 3 ⇄ 4 ring changes. For example, a non-classical tricycloheptonium ion intervenes for the 4 ⇄ 5 ring changes in reactions of the highly strained 2-bicyclo[3.2.0]heptyl and 7-bicyclo[2.2.1]heptyl arenesulfonates.[1c]

(43) A. H. Fainberg and S. Winstein, THIS JOURNAL, **78**, 2770 (1956).

(44) S. Winstein and D. Trifan, *ibid.*, **74**, 1147 (1952).