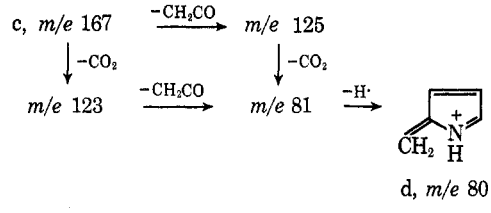
ion a (*m/e* 239) to the base ion c (*m/e* 167) can be pictured as proceeding *via* loss of carbon monoxide to b, followed by loss of acetaldehyde to give c. The presence of metastable ions at *m/e* 186.3 and 132.2 support this sequence. The high-resolution mass spectrum of **2** shows the *m/e* 167 peak to be *m/e* 167.0583 (calcd for $C_8H_9NO_3$, 167.0582); therefore, it does not arise *via* loss of carbon monoxide and carbon dioxide from the parent ion.

The pathways followed in the further decomposition of ion c are sequential variations of a common theme, *i.e.*, decay to the resonance stabilized ion d. The



d, *m/e* 80

m/e 125 ion also proceeds to d by the loss of 45 mass units in a sequence which must involve a one-hydrogen transfer prior to loss of a carboxyl radical. The sequences of decay to ion d are supported by the observation of the required metastable peaks.

Experimental Section[8]

Oxidation of *N*-Acetylactinobolamine.[9]—To a prewarmed 50-ml solution of 8 *N* nitric acid was added 2.339 g (10.3 mmol) of *N*-acetylactinobolamine. The exothermic nature of the reaction rapidly brought the solution to a condition of slow reflux which was maintained for a period of 10 min.[10] The reaction solution was poured into 250 ml of chilled water which was passed onto a column containing 550 ml of chilled Bio-Rad AG 21-K anion-exchange resin (hydroxide form). The column was eluted with 500 ml of water and 1500 ml of acetic acid–water (1:9). The eluents were freeze-dried. The bulk of the material appeared in the first 1000 ml of acetic acid eluent as a tan semisolid which on crystallization from ethyl alcohol gave 734 mg of crude **2**. Recrystallization from ethyl alcohol gave 490 mg of **2** as analytically pure material: mp 241° dec; $[\alpha]^{25}D$ +166° (*c* 6.1%, DMSO); homogenous to tlc (Bio-Sil A,[11a] ethyl acetate–ethyl alcohol, 2:1 v/v, and MN-cellulose,[11b] *n*-butyl alcohol–water–acetic acid, 4:1:5 v/v/v, upper phase). Column chromatography of the crystallization mother liquids (silicic acid[12] eluted with ethyl acetate containing increasing amounts of ethyl alcohol) followed by crystallization from ethyl alcohol gave an additional 155 mg of **2**, mp 241° dec, for a total yield of 645 mg of **2** (2.70 mmol, 26.2%). Pertinent ir and nmr are listed in the text; mass spectrum *m/e* (relative intensity 239 (4), 211 (5), 167 (100), 125 (14), 123 (3), 81 (8), 80 (10), metastable ions at 186.3, 132.2, 93.6, 90.5, 53.3, 52.5, 51.2, 79.0.

Anal. Calcd for $C_{11}H_{13}NO_5$: C, 55.23; H, 5.48; O, 33.44; mol wt, 239.0794. Found: C, 55.48; H, 5.71; O, 33.37; mol wt, 239.0807 (mass spectrum).

(8) Instruments used: Thomas-Hoover capillary melting point apparatus (melting points corrected); Perkin-Elmer Model 237B Infracord spectrometer; Rudolf Model 80 polarimeter; Varian Associates HA-100 spectrometer; Atlas CH-4B mass spectrometer (heated inlet, 19 μA, 70 eV); Atlas SM-1B high-resolution mass spectrometer. Fragmentation sequences and metastable peaks were matched with computer program CMSPKS, written by S. H. Brown of Stanford University. Microanalyses were performed by Midwest Microlab, Inc., Indianapolis, Ind.

(9) Performed with Mr. Chidambar L. Kulkarni.

(10) A preliminary thin layer (Bio-Sil A,[11a] ethyl acetate–ethyl alcohol, 2:1 v/v) chromatographic assay of the fate of *N*-acetylactinobolamine (**1b**) and **2** in refluxing nitric acid demonstrated the need for a short contact time.

(11) (a) Bio-Sil A, 10–30 μ with 5% binder, purchased from Bio-Rad Laboratories, Richmond, Calif.; (b) MN-cellulose powder 300G distributed by Brinkman Instruments, Great Neck, N. Y.

(12) Bio-Sil A, 100–200 mesh, purchased from Bio-Rad Laboratories.

Registry No.—**1b**, 31729-81-4; **2**, 31729-82-5.

Acknowledgments.—Special thanks are due to Dr. T. H. Haskell of Parke, Davis and Co., who performed the initial nitric acid oxidation of *N*-acetylactinobolamine, to Professor J. Kutney, University of British Columbia, and W. C. Jankowski, Varian Associates, for nmr spectra, and to Professor P. Brown, Arizona State University, for helpful discussions of the mass spectra. We are indebted to the National Science Foundation for funds to purchase the Atlas CH-4B (Grant GB 4939) and Atlas SM-1B (NSF Grant No. GP-6979).

Polarity Effects in the Solvolysis of Steroid Derivatives. The Synthesis and Acetolysis of 6α-Tosyloxy-3α- and -3β-chloro-5α-cholestane[1]

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Transmission of electrical effects from remote dipolar substituents to a reaction site has been long under investigation.[3] The phenomenon is usually regarded as a manifestation of either an inductive effect operative through the bonds or a field effect operative through space or solvent. In an elegant study of the dissociation constants of 4-substituted bicyclo[2.2.2]octane- and bicyclo[2.2.1]heptane-1-carboxylic acids, Wilcox and Leung[3] found that the ΔpK_a's were best correlated by the field effect model. Recently we reported studies on the influence of polar substituents upon the rate of solvolysis of esters of substituted cyclohexanols[4] and *trans*-1-decalols.[5] In all cases investigated we found that the solvolysis rates are most satisfactorily explained on the basis of a field effect. In this connection it became of interest to us to extend these studies to other conformationally rigid molecules. Because of its established conformational integrity, the steroid nucleus seemed well suited for our purpose. To this end we wish to report the synthesis and acetolysis of the *p*-toluenesulfonate esters of 3α-chloro-5α-chloestan-6α-ol (**4b**) and 3β-chloro-5α-cholestan-6α-ol (**2b**).

Synthetic Method.—Synthetic routes are summarized in Scheme I. Entry into the desired cholestan-6α-ol systems was accomplished smoothly *via* oxidative hydroboration of an appropriate cholesteryl derivative using a modification of the method reported by Shoppee, *et al.*[6] The expected least highly substituted alcohols were obtained in good yield. Stereochemically, the stanol products were exclusively equatorial (6α). This is presumably a result of steric hindrance by the

(1) This research was supported in part by Research Grant GP-6133X from the National Science Foundation.

(2) Postdoctoral Research Associate, 1966–1967. Lecturer in chemistry, 1967–1968.

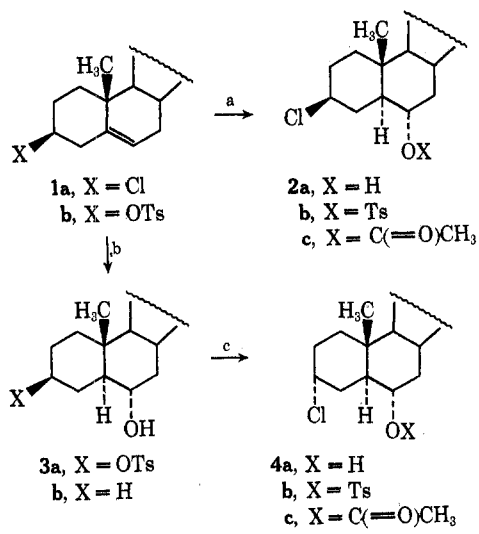
(3) C. F. Wilcox and C. Leung, *J. Amer. Chem. Soc.*, **90**, 336 (1968), and references therein.

(4) D. S. Noyce, B. N. Bastian, P. T. S. Lau, R. S. Monson, and B. Weinstein, *J. Org. Chem.*, **34**, 1247 (1969).

(5) D. S. Noyce and B. E. Johnston, *ibid.*, **34**, 1252 (1969).

(6) C. W. Shoppee, R. Lack, and B. McLean, *J. Chem. Soc.*, 4996 (1964).

SCHEME I[a]



[a] a, X = Cl, B_2H_6, NaOH, 30% H_2O_2; b, X = OTs, B_2H_6, 30% H_2O_2; c, X = OTs, $Et_4N^+Cl^-$, K_2CO_3, DMF.

19-angular methyl group to the diborane approach on the β side of the molecule. Thus **2a** was obtained directly by hydroboration of **1a**.

The synthesis of **4a** by an indirect route (eight steps from cholesterol) has been reported.[6] In addition to low yield, **4a** (and **4c**) could not be induced to crystallize due to contamination. We were able to prepare crystalline **4a** from cholesterol in three steps by taking advantage of the fact that cholestanyl tosylates undergo bimolecular nucleophilic displacement with inversion when treated with chloride ion in refluxing DMF.[7] Treatment of 3β-tosyloxy-5α-cholestan-6α-ol (**3a**) with excess tetraethylammonium chloride in refluxing DMF containing 1 equiv of potassium carbonate gave **4a** in 65% yield.

The *p*-toluenesulfonates of **2a** and **4a** were prepared by standard methods. The conformational assignments of the epimeric chlorides are based upon the synthetic design and are supported by the observation that the carbon–chlorine infrared stretching frequencies are in agreement with those reported earlier.[6]

Kinetic Results.—The first-order rate constants for the acetolyses are summarized in Table I, with the

TABLE I

RATES OF ACETOLYSIS OF 3-SUBSTITUTED 6α-TOSYLOXY-5α-CHOLESTANES

Compd	Concn of sulfonate, M[a]	Temp,[b] °C	10^5k, sec^{-1}
2b	0.002	75.00	0.343 ± 0.018
	0.002	90.00	2.08 ± 0.05
	0.002	110.00	18.5 ± 0.60
4b	0.002	75.00	0.616 ± 0.012
	0.002	90.00	3.49 ± 0.13
	0.002	110.00	28.6 ± 1.2
3b-OTs[c]	0.01	75.00	2.25 ± 0.02

[a] All solvolyses were carried out in acetic acid with added acetic anhydride and sodium acetate, both at twice the concentration of the sulfonate. [b] Temperatures all within ±0.05°. [c] Reference 8.

derived thermodynamic parameters in Table II. The acetolysis rate of the unsubstituted 6α-tosyloxy-5α-cholestane (**3b**-OTs) has been reported elsewhere[8] and is also listed in Table I.

(7) G. A. Selter and K. D. Mc Michael, *J. Org. Chem.*, **32**, 2546 (1967).

TABLE II

ACTIVATION PARAMETERS

Compd	$\Delta H^{\ddagger}$, kcal	$\Delta S^{\ddagger}$, eu
2b	29.5 ± 0.2	0.8 ± 0.4
4b	28.3 ± 0.2	−1.3 ± 0.4

The rates of solvolysis in the present study are lower than for the parent compound **3b**-OTs by a factor of four- to sevenfold as is expected for molecules bearing electron-withdrawing substituents. More important are the relative rates for the isomeric compounds. Compound **4b** is the more reactive; at 75.00° k_{4b}/k_{2b} is 1.8, and at 110° it is 1.54. The observed ratios show that there is a significant difference in the solvolysis rates due to the change in orientation of the substituent dipole. As in the earlier studies,[4,5] these results are consistent with the field effect model in that the more reactive epimer **4b** is the one in which the negative end of the dipolar substituent lies closer to the reaction center. The data cannot be explained solely on the basis of an inductive effect, since that model is insensitive to changes in orientation of a dipole at a given position.

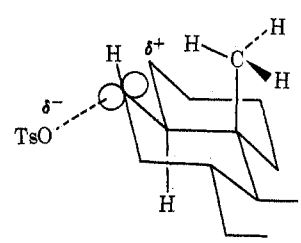
Product Study.—The acetolysis products are listed in Table III. Although excess inversion is usually observed in the substitution products,[4,9] it should be noted that the acetates **2c** and **4c** are exclusively those of retained stereochemistry. Upon inspection it appears that the stereochemistry of the products reflects the steric environment of the incipient carbonium ions. The β side of the developing p orbital of the cation (structure I) is precluded from significant solvation due

TABLE III

PRODUCTS FROM THE ACETOLYSIS OF 6α-TOSYLOXY-3α- AND -3β-CHLORO-5α-CHOLESTANE

Compd solvolyzed	Products formed,[a] mol % A	B	C	D
2b	51.5	48.5	N.D.[b]	N.D.
4b	25.3	53.1	21.6	N.D.

[a] Products formed: A = 5-ene; B = 6α-acetate; C = 6α-alcohol; D = 6β-acetate. Relative yields reported; total recovery *ca.* 96%. [b] N.D. = none detected.



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to shielding by the 19-angular methyl group. On the other hand, the α side of the cation is relatively unhindered, enabling solvent to either capture it (affording **2c** or **4c**) or allowing solvent to remove the 5α proton (producing olefin).

Formation of the 6α-stanol **4a** is probably the result of ester hydrolysis during the work-up or chromato-

(8) S. Nishida, *J. Amer. Chem. Soc.*, **82**, 4290 (1960).

(9) N. C. G. Campbell, D. M. Muir, R. R. Hill, J. H. Parish, R. M. Southam, and M. C. Whiting, *J. Chem. Soc., B*, 355 (1968).

graphic separation. This conclusion is supported by the fact that no alcohols were detected in the solvolysis products of **2b** even though the same solvent was used in each case.

Experimental Section[10]

3β-Chloro-5α-cholestan-6α-ol (2a).—To a solution of cholesteryl chloride[11] (**1a**) (24.3 g, 60 mmol) in 300 ml of THF was added sodium borohydride (10 g). The mixture was cooled to 0° and stirred under nitrogen as a solution of boron trifluoride etherate (50 ml) in THF (50 ml) was added dropwise over 45 min. After stirring at 25° for 12 hr, the mixture was cooled to 0° and 100 ml of 12% NaOH was added cautiously during 1 hr followed by 75 ml of 30% hydrogen peroxide over 20 min. The mixture was stirred at 25° for 1 hr, diluted with water, and extracted with ether (two times). The combined ether extracts were washed with water (two times), 5% $NaHSO_3$ (two times), and water, dried ($MgSO_4$), and filtered. Ether evaporation under reduced pressure gave a colorless syrup which crystallized from aqueous acetone containing methanol. Three crystallizations from aqueous acetone gave 11.2 g (40%) of the stanol **2a**: mp 101–102° and 110–110.5°; $[\alpha]^{23}D$ +50° (lit.[6] mp 116–118°; $[\alpha]^{23}D$ +52°); ir (CS_2) 3625 (OH), 758 cm^{-1} (equatorial CCl). Treatment of **2a** with acetic anhydride afforded the acetate **2c** which crystallized from acetone–methanol (1:1), mp 97–99°, $[\alpha]^{23}D$ +59° (lit.[6,12] mp 97–99°).

6α-Tosyloxy-3β-chloro-5α-cholestane (2b) was prepared in 97% yield from **2a** in the usual manner. Two crystallizations from acetone gave pure material: mp 162.5–163°; $[\alpha]^{23}D$ +54°; ir (CS_2) 1180 and 1165 (sym S=O), 758 cm^{-1} (equatorial CCl).

Anal. Calcd for $C_{34}H_{53}ClO_3S$: C, 70.73; H, 9.25; Cl, 6.14. Found: C, 70.79; H, 9.40; Cl, 6.25.

3β-Toyloxy-5α-cholestan-6α-ol (3a).—Cholesteryl tosylate[13] (**1b**) (81.1 g, 150 mmol) in THF (700 ml) was hydroborated with sodium borohydride (10 g) and boron trifluoride etherate (30 ml in 25 ml of THF) according to the procedure for **2a**. Subsequent treatment with 12% NaOH (100 ml) and 30% hydrogen peroxide (50 ml) followed by the usual work-up and crystallization from ethanol afforded **3a** (64.7 g, 80%) as colorless crystals: mp 135–135.3°; $[\alpha]^{23}D$ +23°; ir ($CHCl_3$) 3625 (OH), 1188 and 1175 cm^{-1} (sym S=O).

Anal. Calcd for $C_{34}H_{54}O_4S$: C, 73.07; H, 9.73; S, 5.73. Found: C, 72.76; H, 9.96; S, 5.74.

3α-Chloro-5α-cholestan-6α-ol.—A mixture of **3a** (560 mg, 1 mmol), tetraethylammonium chloride (331 mg, 2 mmol), and potassium carbonate (138 mg, 1 mmol) in 30 ml of DMF was refluxed for 25 min. After cooling to 25°, water was added and a white solid was obtained upon additional cooling to 0°. The solid was taken up in ether and filtered to remove the inorganic salts, and the ether was evaporated to give a colorless syrup which was crystallized twice from methanol affording 275 mg (65%) of the stanol **4a**: mp 156–157°; $[\alpha]^{23}D$ +36°; ir (CS_2) 3625 (OH), 720 cm^{-1} (axial CCl). Treatment of **4a** with acetic anhydride gave the acetate **4c**, which crystallized from methanol: mp 100–100.8°; $[\alpha]^{23}D$ +45°; ir (CS_2) 1735 (ester C=O), 1243 (ester CO), 720 cm^{-1} (axial CCl).

6α-Tosyloxy-3α-chloro-5α-cholestane (4b) was prepared in 83% yield from **4a** in the usual manner. The analytical sample was obtained after two crystallizations from 90% aqueous acetone: mp 139–139.5°; $[\alpha]^{23}D$ +28°; ir (CS_2) 1182 and 1162 (sym S=O), 720 cm^{-1} (axial CCl).

Anal. Calcd for $C_{34}H_{53}ClO_3S$: C, 70.73; H, 9.25; Cl, 6.14. Found: C, 70.92; H, 9.12; Cl, 6.33.

Product Analysis.—The products resulting from the solvolysis of both **2b** and **4b** at 90° in acetic acid solutions containing 0.04 *M* sulfonate, 0.08 *M* sodium acetate, and 0.08 *M* acetic anhydride were isolated by the usual ether extraction technique followed by chromatography over 70–325 mesh silicic acid.[7] Products were identified by comparison of their melting points and infrared spectra with those of authentic samples. The results obtained are listed in Table III.

(10) Experimental details have been given elsewhere.[5]

(11) O. Diels and P. Blumberg, *Ber.*, **44**, 2847 (1911).

(12) Professor Shoppee has kindly informed us that the originally reported rotation is in error, and that a new determination gives $[\alpha]D$ +63°, in chloroform. A mixture melting point with a sample generously supplied by Professor Shoppee showed no depression.

(13) E. S. Wallis, E. Fernholz, and F. T. Gephart, *J. Amer. Chem. Soc.*, **59**, 137 (1937).

Kinetic Measurements.—The usual sealed ampoule technique was used. The concentration of the sulfonate was 0.002 *M* in anhydrous acetic acid containing sodium acetate (0.004 *M*) and acetic anhydride (0.004 *M*). At appropriate time intervals 3-ml aliquots were quenched in ice water and stored at −15°. At the completion of the run the samples were warmed to 25° and transferred to a 1-cm silica cell whereupon the absorbance was determined using a Gilford Model 2000 spectrophotometer at 261 mμ at a slit width of 0.4 mm according to the method of Swain and Morgan.[14] Rate constants were calculated using a nonlinear least-squares program.[15]

Registry No.—**2a**, 1251-93-0; **2b**, 31406-51-6; **3a**, 28398-68-7; **4a**, 1251-94-1; **4b**, 31354-63-9; **4c**, 31354-64-0.

(14) C. G. Swain and C. R. Morgan, *J. Org. Chem.*, **29**, 2097 (1964).

(15) LSKIN2, written by C. E. De Tar and D. F. De Tar, Florida State University, as modified by Dr. H. A. Hammond, University of California.

Synthesis of Adamantane Derivatives. XVII.[1] Facile Synthesis of Bicyclo[3.3.1]non-6-ene-3-aldehyde and -isopropyl alcohol

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Compared with the well-known ring-cleavage reactions of 1,3-disubstituted adamantanes,[2] those of 2,4-disubstituted adamantanes have been reported only recently.[3-5] In a previous publication[5] we reported that facile fragmentation reactions of 4(e)-methylsulfonoxyadamantan-2-one (**1**) with alkali, bromine, and lithium aluminum hydride afforded bicyclo[3.3.1]non-6-ene-3-carboxylic acid, 2(e)-bromo-4-oxahomoadamantan-5-one, and bicyclo[3.3.1]non-6-ene-3-carbinol (**4**), respectively. In this note, we wish to describe the successful application of this type of fragmentation reaction to the preparation of bicyclo[3.3.1]non-6-ene-3-aldehyde (**3**) and -isopropyl alcohol (**5**).

Treatment of **1** with sodium borohydride afforded a mixture of fragmentation products, from which **3** and **4** were isolated in 53 and 41% yields, respectively, both as oils after chromatography on a silica gel column. Aldehyde **3** exhibited ir absorptions (neat) at 2680, 1730, 1720 (sh), and 1645 cm^{-1} and had a M^+ at *m/e* 150. It gave the 2,4-dinitrophenylhydrazone (DNP) derivative, mp 210–211°. Alcohol **4** was identified as bicyclo[3.3.1]non-6-ene-3-carbinol by comparison of ir and nmr spectra and vpc retention time data with those of an authentic sample.[3,5] The

(1) Part XVI: T. Sasaki, S. Eguchi, and T. Toru, *Tetrahedron Lett.*, 1109 (1971).

(2) (a) H. Stetter and P. Tacke, *Angew. Chem.*, **74**, 354 (1962); (b) H. Stetter and P. Tacke, *Chem. Ber.*, **96**, 694 (1963); (c) C. A. Grob and W. W. Schwarz, *Helv. Chim. Acta*, **47**, 1870 (1965); (d) F. N. Stepanov and W. D. Suchowerchow, *Angew. Chem., Int. Ed. Engl.*, **6**, 864 (1967).

(3) For fragmentation of 4(e)-bromoadamantan-2-one with silver perchlorate to bicyclo[3.3.1]non-6-ene-3-carboxylic acid, see A. C. Udding, H. Wynberg, and J. Strating, *Tetrahedron Lett.*, 5719 (1968).

(4) For the Beckmann fission of adamantan-2-one oxime, see J. G. Korsloot and V. G. Keizer, *ibid.*, 3517 (1969).

(5) For the Schmidt fission of adamantan-2-one, see T. Sasaki, S. Eguchi, and T. Toru, *J. Org. Chem.*, **35**, 4109 (1970).