acetonitrile was preelectrolyzed at −2.16 V *vs.* Ag/Ag$^+$ until the current dropped to a constant 400 μA. A solution of 545.3 μmol of (−)-1-iodo-1-methyl-2,2-diphenylcyclopropane (**2**) ($[\alpha]^{26}_{5461}$ −199°) in a minimum amount of acetonitrile was injected into the cathode compartment and electrolyzed at −2.16 V *vs.* Ag/Ag$^+$. The current was initially 26 mA, requiring 19 V across the cell, and dropped nonexponentially (similar to Figure 1) to a constant 100 μA after 141 min. Calculations from coulometer readings gave an *n* value of 1.57 F/mole. The catholyte was concentrated and applied to a 40 × 20 × 0.2 cm preparative tlc plate and developed with $CHCl_3$–hexane 15:85. The two bands of material visible under 2540 Å uv were collected to yield 0.0740 g of R_2Hg (**3**) and 0.0635 g of RH. Analysis of (glpc) of the hydrocarbon fraction showed it contained 3.5 % of $Ph_2C{=}CMe_2$. The hydrocarbon fraction was applied to a 20 × 20 × 0.2 cm preparative tlc plate and developed with *n*-hexane. The RH band was collected to yield a colorless oil which was distilled in a micromolecular still yielding a pure sample of RH $[\alpha]^{26}_{5461}$ +5.9° (*c* 0.484, $CHCl_3$) (3.9% optically pure) with a glpc retention time and the infrared spectrum identical with those of an authentic sample. The R_2Hg (**3**) sample gave $[\alpha]^{26}_{5461}$ 0.0° (*c* 1.4800, $CHCl_3$), mp 198–200°. The infrared spectrum, nmr spectrum, and tlc R_f value were identical with those of an authentic sample: yields–1,1-diphenyl-2,2-dimethylethylene, 10.5 μmol, 1.9%; RH, 294.3 μmol, 54%; R_2Hg (**3**) 120.4 μmol, 44%.

The R_2Hg (**3**) sample (0.0740 g, 120.4 μmol) was dissolved in refluxing CCl_4 and bromine added until the color of the latter persisted. The reaction mixture was concentrated, applied to a 20 × 10 × 0.2 cm preparative tlc plate, and developed with *n*-hexane. The RBr (**1**) band was collected, eluted, concentrated and crystallized from methanol to give 0.033 g (48%) of RBr (**1**), mp 80–81°, and an infrared and nmr spectrum identical with those of an authentic sample.

A sample of 564.5 μmol of RI (**2**) ($[\alpha]^{26}_{5461}$ −199°) was electrolyzed at −2.80 V *vs.* Ag/Ag$^+$ and worked up by exactly the same procedure as given above to yield 0.0881 g (423.0 μmol, 75%) of RH $[\alpha]^{25}_{5461}$ +5.1°, 3.4% optically pure; 0.0027 g (12.9 μmol, 2.3%) of 1,1-diphenyl-2,2-dimethylethylene; 0.0291 g (47.3 μmol, 17%) of R_2Hg (**3**) $[\alpha]^{25}_{5461}$ 0.0°.

Mercury Analyses of RI (2) Reduction Products. Samples of RI (**2**) (103.9 μmol) were electrolyzed by the procedure described above at −2.10, −2.17, −2.37, −2.47, −2.50, and −2.90 V *vs.* Ag/Ag$^+$. The catholyte was concentrated and exhaustively oxidized with a mixture of concentrated sulfuric and nitric acid. The resulting solutions were treated with dithizone and the concentration of mercury was determined by colorimetric analysis.

Carbonium Ion Rearrangements in the Deltacyclane Ring System[1]

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Abstract: The acetolyses of *exo*- and *endo*-8-deltacyclyl brosylate, a mixture of *exo*- and *endo*-8-deltacyclyl chloride, as well as deamination of 8-deltacyclylamine in acetic acid, all lead to *exo*-8-deltacyclyl acetate (less than 0.4% *endo* epimer). Chlorodecarboxylation of deltacyclane-8-carboxylic acid with lead(IV) acetate and lithium chloride yields *exo*-8-deltacyclyl acetate (less than 0.4% *endo* epimer) and a mixture of *exo*- and *endo*-8-chlorodeltacyclane (the *exo*:*endo* ratio varies from 70:30 to 83:17). The rates of acetolysis of *exo*- and *endo*-8-deltacyclyl brosylate at 25.68° are 2.61 ± 0.09 × 10^{-4} and 4.62 ± 0.06 × 10^{-6} sec^{-1}, respectively. Acetolysis of *exo*-8-deuterio-*endo*-8-deltacyclyl brosylate yields *exo*-8-deltacyclyl acetate with deuterium scrambled between the *endo*-C-8 and C-4 positions, with deuteration predominating at the *endo*-C-8 position, while acetolysis of *endo*-8-deltacyclyl brosylate (69% deuteration at the C-9 positions) generates *exo*-8-acetate with 45% rearrangement of the deuterium to the C-5 positions. Acetolysis of *endo*-8-deuterio-*exo*-8-deltacyclyl brosylate results in *exo*-8-acetate in which the deuterium is scrambled between the *endo*-C-8 and C-4 positions, while acetolysis of *exo*-9-deuterio-*exo*-8-deltacyclyl brosylate produces *exo*-8-acetate in which 50% of the deuterium content has been scrambled into the C-5 position. The nmr spectra of fluorosulfonic acid–sulfur dioxide solutions of *exo*- and *endo*-8-deltacyclanol were measured and found to be identical, exhibiting absorptions at τ 4.83, 7.08, 7.50, 7.83, and 8.23 in the ratio of 2:2:2:1:4. An analysis of the acetolysis of optically active *endo*-8-brosylate reveals that *exo*-8-acetate is formed with 57% racemization, while acetolysis of optically active *exo*-8-brosylate produces *exo*-8-acetate with 99% retention of optical activity. The mechanistic implications of these results are discussed.

At the time this work was initiated, the deltacyclane (tetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]nonane)[3] ring system, which serves as the basic structural unit for the mixture of nitrile epimers (**1**-CN, **2**-CN) obtained in the homo-Diels–Alder condensation of acrylonitrile with norbornadiene, had not been extensively studied due to the low yields previously encountered in the synthesis of useful intermediates.[4] It was felt that if a good synthetic scheme could be developed for the syntheses of suitable *exo*- and *endo*-8-substituted deltacyclane substrates (**1** and **2**), an investigation of their solvolytic properties would be an especially interesting problem. The deltacyclane ring system incorporates both the nortricyclene (carbons 1, 2, 4, 3, 7, 6, and 5) and norbornane (carbons 1, 2, 3, 7, 8, 9, and 6) ring systems, and, due to this unique skeletal structure, a double norbornonium ion **4**, as well as the more traditional norbornonium ions **3**, are possible intermediates to be expected in ionization reactions of substrates **1** and **2**. Our study of the deltacyclane ring system was facilitated by the development of a method for achieving the syntheses of addition products, which conceptually are the result of Diels–

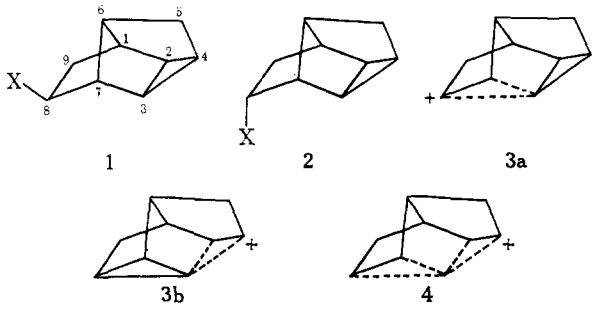
(1) Previously published in part in preliminary form: P. K. Freeman and D. M. Balls, *Tetrahedron Lett.*, 437 (1967).

(2) Address all correspondence to this author at the Department of Chemistry, Oregon State University, Corvallis, Oregon.

(3) The name deltacyclane has been suggested for tetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]nonane and deltacyclene for the related olefin tetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]non-8-ene (**16**) by A. Nickon, private communication; A. Nickon, G. D. Pandit, and R. O. Williams, *Tetrahedron Lett.*, 2851 (1967); and H. R. Kwasnik, Ph.D. Thesis, Johns Hopkins University, 1966.

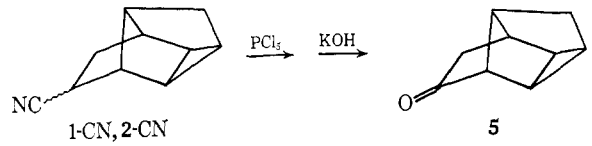
(4) H. K. Hall, Jr., *J. Org. Chem.*, **25**, 42 (1960).

Alder or homo-Diels–Alder addition of ketene.[5] The synthesis of the required intermediate in this case,



1 2 3a 3b 4

8-deltacyclanone (**5**), provides a good illustration of this new synthetic scheme. The mixture of nitrile epimers (**1**-CN, **2**-CN) obtained by homo-Diels–Alder condensation of acrylonitrile with norbornadiene was chlorinated with phosphorus pentachloride in refluxing carbon tetrachloride. The α-chloronitriles so obtained were then converted to ketone **5** by treatment with potassium hydroxide in dimethyl sulfoxide (40% yield based on nitriles **1**-CN and **2**-CN).

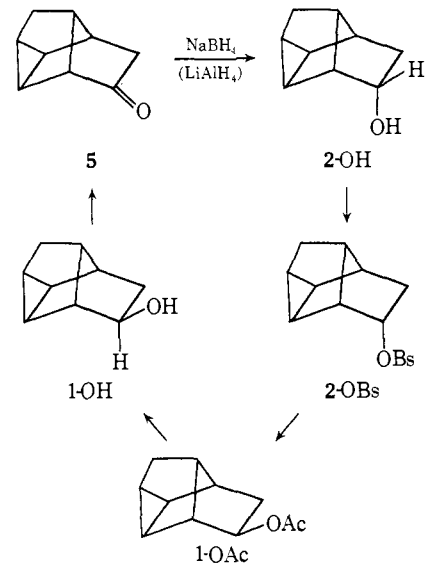


1-CN, 2-CN 5

With a facile synthesis of 8-deltacyclanone in hand the syntheses of *exo*- and *endo*-8-deltacyclanol, as well as the related brosylates, were relatively straightforward. Metal hydride reduction of **5** gave predominantly *endo*-**2**-OH, with sodium borohydride generating an 86:14 *endo*:*exo* ratio and lithium aluminum hydride producing an 88:12 *endo*:*exo* ratio. Treatment of this mixture of alcohol epimers with *p*-bromobenzenesulfonyl chloride in pyridine gave a mixture of esters from which *endo*-**2**-OBs could be obtained by fractional crystallization. Acetolysis of **2**-OBs in acetic acid–sodium acetate gave a single acetate product, which upon saponification yielded an alcohol which was identical with the minor component obtained in the metal hydride reduction. The epimeric nature of the alcohol obtained by the acetolysis–saponification of **2**-OBs and the major alcohol component of the metal hydride reduction was reinforced by oxidation of the former with chromium trioxide in pyridine to **5**, as outlined in Scheme I. The assignment of structure to the epimeric alcohols **2**-OH and **1**-OH obtained by this sequence is based upon the expected predominance of *endo* alcohol in the metal hydride reductions and upon the splitting patterns exhibited by the protons α to hydroxyl. In **1**-OH the C-8 proton is split into a doublet of doublets ($J_{8n,9x}$ = 2.0, $J_{8n,9n}$ = 6.6 Hz) at τ 5.99, while the analogous proton in **2**-OH appears as a complex multiplet at τ 5.60.[6]

Since it is generally useful to generate carbonium ions of interest from several different types of carbonium ion precursors, an epimeric mixture of 8-deltacyclylamines was synthesized by a modified Hoffmann rearrangement (treatment with sodium methoxide in methanol, bromine, followed by hydrolysis of the urethan intermediate)[7] of amides **1**-$CONH_2$ and **2**-$CONH_2$, which were, in turn, prepared by selective hydrolysis of nitriles **1**-CN and **2**-CN. The mixture of *exo*- and *endo*-8-cyanodeltacyclanes was prepared by homo-Diels–Alder addition of acrylonitrile to norbornadiene.[8] Vigorous base catalyzed hydrolysis of amides **1**-$CONH_2$ and **2**-$CONH_2$ gave a mixture of epimeric carboxylic acids **1**-CO_2H and **2**-CO_2H, which, in turn, was subjected to halodecarboxylation by treatment with lead tetraacetate in the presence of lithium chloride, according to the procedure of Kochi.[9] A single acetate, *exo*-8-deltacyclyl acetate (**1**-OAc) was formed, accompanied by an epimeric mixture of 8-chlorides (**1**-Cl and **2**-Cl), which varied in *exo*:*endo* ratio from 70:30 to 83:17 in several runs. A consideration of the work of Kochi[9,10] on the decarboxylation of lead(IV) carboxylate salts and related work on norbornyl carboxylate salts,[11] suggests that the product composition obtained in the present case can best be rationalized as arising *via* the 8-deltacyclyl free radical. In this instance the rates of oxidative decarboxylation (electron transfer) leading to the 8-deltacyclyl carbonium ion and to acetate product and halodecarboxylation (chlorine transfer to the radical) are much more evenly balanced than in the examples cited by Kochi. This view is reinforced by a consideration of product stereochemistry, since Kooyman[12] found that free-radical chlorination of norbornane yields a 70:25 *exo*:*endo* ratio of 2-norbornyl chlorides and the 8-deltacyclyl carbonium ion produces *exo*-8 products exclusively (*vide infra*). Subsequent to our investigation of the Kochi decarboxylation of **1**-CO_2H and **2**-CO_2H, we learned that Slee has decarboxylated the epimeric 8-acids with lead tetraacetate in benzene–pyridine to obtain the *exo*-8-acetate as the sole product.[13] In four additional solvolytic experiments, acetolysis of

Scheme I



5 2-OH 1-OH 2-OBs 1-OAc

(5) P. K. Freeman, D. M. Balls, and D. J. Brown, *J. Org. Chem.*, **33**, 2211 (1968).

(6) P. Lazzlo and P. v. R. Schleyer, *J. Am. Chem. Soc.*, **86**, 1171 (1964). *exo,exo*-Tricyclo[3.2.1.$0^{2,4}$]octan-6-ol exhibits J_{6n7n} = 7.4 and J_{6n7x} = 2 Hz for the proton α to hydroxyl: J. N. Blazevich, unpublished work.

(7) H. Stetter, H. Held, and J. Mayer, *Ann.*, **658**, 151 (1962).

(8) G. N. Schrauzer and P. Glockner, *Chem. Ber.*, **97**, 2451 (1964); G. N. Schrauzer and S. Eichler, *ibid.*, **95**, 2764 (1962).

(9) J. K. Kochi, *J. Am. Chem. Soc.*, **87**, 2500 (1965); *J. Org. Chem.*, 30, 3265 (1965).

(10) J. K. Kochi, *J. Am. Chem. Soc.*, **87**, 1811, 3609 (1965).

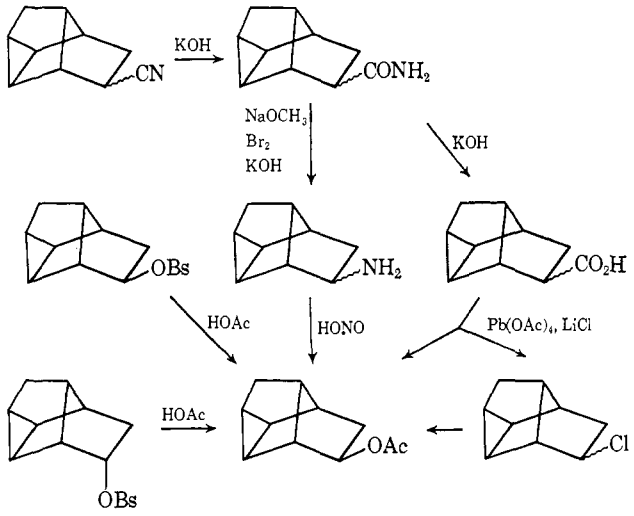
(11) G. E. Gream and D. Wege, *Tetrahedron Lett.*, 503 (1967); E. J. Corey and J. Casanova, Jr., *J. Am. Chem. Soc.*, **85**, 165 (1963); D. I. Davies and C. Waring, *Chem. Commun.*, 263 (1965).

(12) E. C. Kooyman and G. C. Vegter, *Tetrahedron*, **4**, 382 (1958).

(13) J. D. Slee, M. S. Thesis, Michigan State University, 1966.

a mixture of epimeric chlorides **1**-Cl and **2**-Cl, deamination of a mixture of amines **1**-NH_2 and **2**-NH_2 with nitrous acid in acetic acid, and acetolyses of **1**-OBs and **2**-OBs all resulted in the production of a single product, *exo*-8-acetate (**1**-OAc), as summarized in Scheme II.

Scheme II

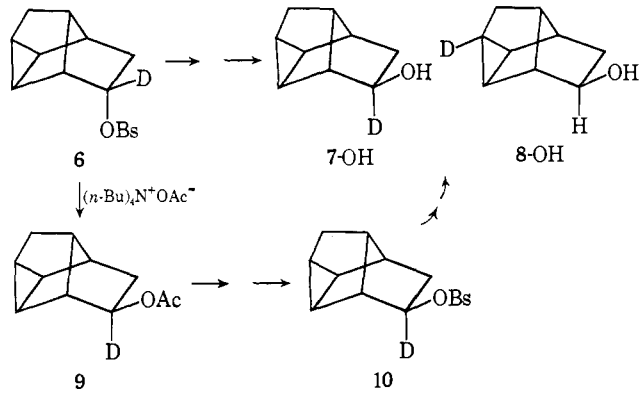


The degree of stereoselectivity in each acetolysis was determined by saponification of product acetate to 8-deltacyclanol and vapor phase chromatographic analysis on a 21-ft QF-1 column. No *endo*-8-alcohol was detectable by this method and thus no *endo*-8-acetate was produced in any of the five solvolyses. The use of standard mixtures of **1**-OH and **2**-OH demonstrated that as much as 0.4% **2**-OH could have been detected.

Having established the stereospecificity of the solvolysis of *endo*- and *exo*-8-deltacyclyl substrates, we turned our attention to a kinetic analysis of the solvolyses of *exo*- and *endo*-8-brosylates (**1**-OBs and **2**-OBs). Solvolysis in acetic acid–sodium acetate gave good first-order behavior and rate constants for **1**-OBs and **2**-OBs at 25.68° of $2.61 \pm 0.09 \times 10^{-4}$ and $4.62 \pm 0.06 \times 10^{-6}$ sec^{-1}, respectively. Using the method of Schleyer[14] to calculate nonassisted acetolysis rates, the rate of *exo*-brosylate **1**-OBs appears to be enhanced by $10^{5.3}$, while the rate of the *endo* epimer **2**-OBs is apparently enhanced by a factor of $10^{3.1}$. A similar pattern emerges for the *exo,exo*- and *exo,endo*-tricyclo[3.2.1.$0^{2,4}$]octan-6-yl brosylates studied by Wiberg and Wenzinger[15] and Colter and Musso,[16] with an estimation of rate enhancement of $10^{4.2}$ for the *exo,exo*-brosylate and $10^{0.7}$ for the *exo,endo*-brosylate.[17,18]

Since product analyses in the solvolytic experiments revealed no skeletal transformations, yet the rates of solvolysis of both **1**-OBs and **2**-OBs suggest anchimeric assistance, it seemed logical to provide further characterization of the carbonium ion intermediates generated through deuterium tracer experiments. *exo*-8-Deuterio-*endo*-8-brosylate **6** was prepared by reduction of 8-deltacyclanone with lithium aluminum deuteride, followed by conversion to brosylate ester in the usual manner. Acetolysis of **6** gave labeled *exo*-8-deltacyclyl acetate, which exhibited an absorption in the infrared at 3067 cm^{-1} (cyclopropane C–H stretch) which was diminished in intensity by a ratio of 5.0:6.0 relative to that of unlabeled *exo*-8-deltacyclyl acetate. This corresponds to rearrangement of deuterium into the cyclopropane ring to an extent of approximately 50%. In this first run the extent of loss of deuterium from C-8 was measured by integration of the *endo*-C-8 proton in the mixture of labeled *exo*-8-deltacyclanols formed upon saponification of product acetate. Hydrogen was present to an extent of 44% at the *endo*-C-8 position, which corresponds to 44% rearrangement. In a second run the mixture of labeled alcohols **7**-OH and **8**-OH, obtained after saponification of product acetate, was analyzed by 100-MHz nmr, which provides satisfactory resolution of the C-4 hydrogen at τ 8.89 and the *exo*-C-9 proton (a doublet of triplets centered at τ 8.59). Integration revealed an absorption due to the C-8 proton at 5.99 of 0.40 H and an absorption due to the C-4 hydrogen at 8.89 of 0.59 H (Table I).

Scheme III



With the pattern of scrambling established as C-8 to C-4 in the case of *endo*-brosylate **6**, we wished to provide additional evidence bearing on the extent of this scrambling, since the nmr evidence clearly suggests that **7**-OH predominates over **8**-OH in the mixture of labeled alcohol products (Scheme III). The C-9 protons of ketone **5** were exchanged by treatment with deuterium oxide and potassium deuteroxide in pyridine. Seven successive portions of deuterium oxide were used, with each spent fraction of deuterium oxide being removed by azeotropic distillation. Deuterated ketone **11** was reduced with lithium aluminum hydride and converted to *endo*-brosylate **12**. Acetolysis of **12** gave *exo*-acetate **13** with scrambled deuterium label. Acetate **13** was saponified to the corresponding alcohol and then oxidized to labeled 8-deltacyclanone. The deuterium content at C-9 in the 8-deltacyclanone, at this stage, was then removed by base-catalyzed exchange to yield **14** (Scheme IV). Mass spectral analysis of scrambled acetate **13** and the related ketone **14** revealed that 45% of the label had migrated from the C-9 position (Table II), which is in good agreement with the nmr data on the acetolysis of **6**, reinforcing the conclusion that **7**-OH predominates over **8**-OH.

(14) The carbonyl stretching frequency for ketone **5** is 1756 cm^{-1}, measured in dilute CCl_4 and calibrated against a polystyrene spectrum. Nonbonded interaction strain was taken as an average of that for *endo*-2-norbornenyl and *endo*-2-norbornyl tosylate (0.9 kcal): P. v. R. Schleyer, *J. Am. Chem. Soc.*, **86**, 1854, 1856 (1964); C. S. Foote, *ibid.*, 86, 1853 (1964).

(15) K. B. Wiberg and G. R. Wenzinger, *J. Org. Chem.*, 30, 2278 (1965).

(16) A. K. Colter and R. C. Musso, *ibid.*, **30**, 2462 (1965).

(17) The carbonyl stretching frequency for the related ketone is 1757 cm^{-1}.

(18) The rate enhancements calculated for **1**-OBs, **2**-OBs, and the tricyclo[3.2.1.$0^{2,4}$]octan-6-yl brosylates are slightly lower than previously reported, ref 1, due to an error, but the pattern of enhancement remains the same.

Table I. Nmr Analysis of Deuterium Distribution Patterns of the Alcohols Derived from Labeled Brosylates **6**, **10**, and **18**

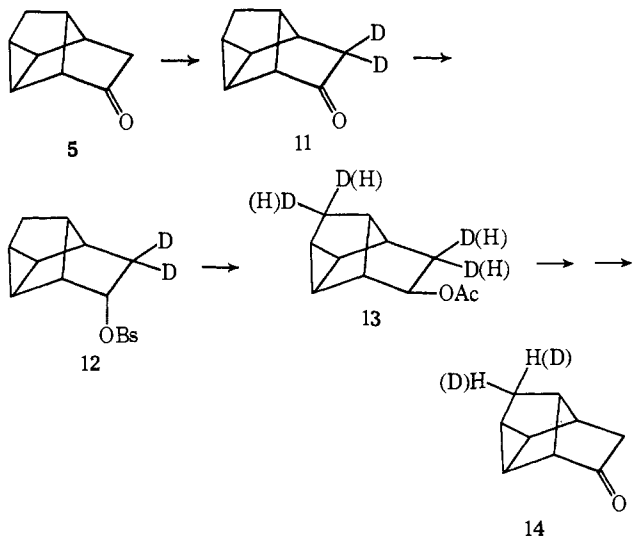
Source	OH	*H*COH τ 5.99	*endo*-C-9, C-1, C-6, C-7 (7.98–8.09)	C-5 (8.47)	*exo*-C-9 (8.59)	C-4 (8.89)	C-2, C-3 (9.21–9.27)
exo-Alcohol from **6**[a]		0.40 H	4.07	3.01		0.59	1.91
exo-Alcohol from **10**[a]	0.98 H	0.49	3.95	2.99		0.56	2.02
exo-Alcohol from **18**[b]	0.96 H	0.96	3.96	1.54	0.52	1.02	2.04

[a] 100 MHz, solvent CCl_4. [b] 220 MHz, solvent CCl_4.

Table II. Mass Spectral Analysis of the Deuterium Distribution in the Solvolyses of Brosylates **12** and **18**

Compd	d_0	d_1	d_2	Av no. of deuterium atoms per molecule
13	3.5	55.2	41.2	1.38
14	56.8	24.5	18.7	0.62
% deuterium retained		44.4	45.4	45
19	5.0	95		
20	42.5	47.5		
% deuterium retained		50		

Scheme IV

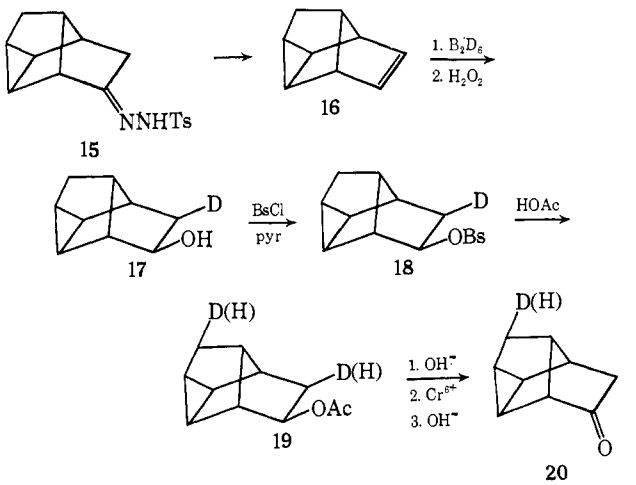


The pattern and extent of deuterium scrambling in the case of the solvolysis of labeled *exo*-8-deltacyclyl brosylate were determined in experiments on two additional substrates. *endo*-8-Deuterio-*exo*-8-deltacyclyl brosylate (**10**) was prepared from *exo*-8-acetate **9**, which was synthesized from **6** by SN2 displacement of brosylate ion with acetate, using the tetra-*n*-butylammonium acetate procedure of Winstein and coworkers[19] (Scheme III). Solvolysis of labeled *exo*-brosylate **10** in acetic acid–sodium acetate, followed by saponification, gave a mixture of labeled *exo*-8-deltacyclanols (**7**-OH and **8**-OH) as evidenced by the 100-MHz nmr spectrum, which exhibited absorption multiplets which integrated to 0.49 for the C-8 proton and 0.56 H for the C-4 proton, with appropriate integral values for all other absorption bands (Table I).

(19) S. Winstein, E. C. Friedrick, R. Baker, and Yang-L-Lin, *Tetrahedron Suppl.*, **8**, 621 (1966).

In an analysis using a second substrate, the extent of rearrangement in the solvolysis of *exo*-8-brosylate was determined by nmr and mass spectral analysis of products derived from *exo*-9-deuterio-*exo*-8-deltacyclyl brosylate **18**. The key starting material, deltacyclene (**16**), was synthesized by carbenoid decomposition of the tosylhydrazone of 8-deltacyclanone (**15**).[20] Deuteroboration of deltacyclene followed by oxidation yielded 97% *exo*-9-deuterio-*exo*-8-deltacyclanol (hydrogen α to hydroxyl appears in the nmr spectrum as a doublet centered at τ 5.99, J = 6.6 Hz) and 3% 9-deuterio-*endo*-8-deltacyclanol (the stereochemistry of the C-9 deuterium was not determined). Solvolysis of *exo*-brosylate **18**, prepared from *exo*-alcohol **17**, in acetic acid–sodium acetate gave scrambled *exo*-acetate **19**, which was, in turn, converted to scrambled *exo*-alcohol. The nmr analysis of the deuterium distribution pattern in this alcohol was complicated by the fact that at 100 MHz the downfield half of the doublet of triplets absorption for the *exo*-C-9 proton (τ 8.59, J_s = 13.0, *ca.* 2 Hz) overlaps with the anticipated migration terminus at C-5 (τ 8.47). This problem was solved by analysis at 220 MHz, which neatly resolved the *exo*-C-9 proton from the absorption for the C-5 protons and demonstrated that 0.46 deuteron had migrated to C-5, leaving 0.48 deuteron at *exo*-C-9 (Table I). Oxidation of the scrambled *exo*-8-alcohol followed by removal of the deuterium content at C-9 by exchange with aqueous, methanolic potassium hydroxide yielded ketone **20** (Scheme V). Mass spectral analysis of the deuterium content of scrambled *exo*-acetate **19** and ketone **20**, summarized in Table II, revealed that 50 ± 1% rearrangement had occurred.

Scheme V

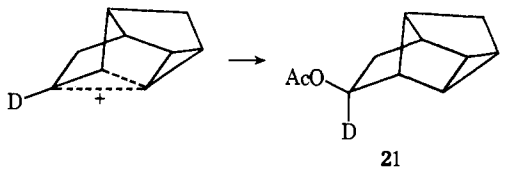


(20) P. K. Freeman and D. M. Balls, *J. Org. Chem.*, **32**, 2354 (1967).

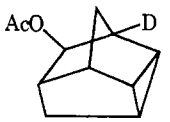
The recent nmr studies of Schleyer, Olah and coworkers[21] on relatively stable solutions of the 2-norbornyl cation in super acid media provided the necessary impetus to attempt to characterize the 8-deltacyclyl carbonium ion in an analogous fashion. Chloroform solutions of **1**-OH and **2**-OH were shaken with fluorosulfonic acid–sulfur dioxide solvent at −60 to −30°. The nmr spectra of the two alcohols in this solvent pair were identical and underwent no significant changes as the solution was warmed from −55 to −10°. The spectrum obtained in this range is characteistic of a carbonium ion,[21] showing absorptions at τ 4.83, 7.08, 7.50, 7.83, and 8.23 (internal reference, $CHCl_3$) in the ratio 2:2:2:1:4, respectively. Neutralization of either nmr sample in aqueous potassium hydroxide yields **1**-OH.

Discussion

The stereochemical course observed in the solvolytic experiments combined with the results of the deuterium scrambling experiments, provides a clearcut case against norbornonium ion **3a** as the single product determining intermediate in solvolyses of substrates **1** and **2**, since deuterium at C-8 is scrambled between C-8 and C-4 in the deltacyclane system and not between C-8 in the deltacyclane system and the bridgehead position indicated in the Wagner–Meerwein rearrangement product **22**. Although the results of the deuterium scrambling experiments would be consistent with the postulation of



21

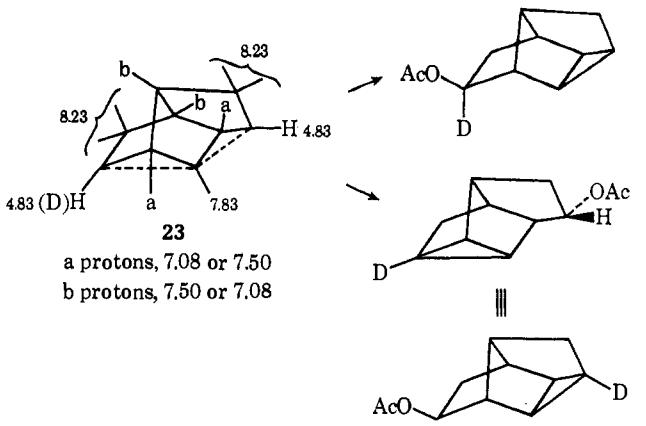


22

a double norbornonium ion **4** or a rapid equilibrium of equivalent norbornonium ions **3a** and **3b**, the nmr spectrum obtained by dissolution of either **1**-OH or **2**-OH in FSO_3H–SO_2 suggests that both these possibilities can be ruled out, since in either case a four-proton absorption would be anticipated downfield, rather than the two-proton band observed at τ 4.83. The nmr spectrum is, instead, consistent with a moderately rapid equilibrium of norbornonium ions **3a** and **3b** $k_{equil} < 30\ sec^{-1}$ and a fourth possibility, which is represented by structure **23**. Carbonium ion **23** is preferred over a moderately rapid equilibrium of norbornonium ions, since no Wagner–Meerwein rearrangement was observed, and the relatively simple nmr spectrum is more consistent with that anticipated for **23** than for **3a** or **3b**. Owing to the C_2 symmetry of ion **23**, it possesses five pairs of equivalent protons and one unique proton and the assignments can be made as indicated in **23**, whereas carbonium ion **3** has no equivalent protons and would be expected to exhibit a more complex spectrum. The deuterium scrambling between C-8 and C-4 is nicely explained in terms of the generation of ion **23** as outlined in Scheme VI.

(21) P. v. R. Schleyer, W. E. Watts, R. C. Fort, Jr., M. B. Comisarow, and G. A. Olah, *J. Am. Chem. Soc.*, **86**, 5679 (1964); M. Saunders, P. v. R. Schleyer, and G. A. Olah, *ibid.*, **86**, 5680 (1964).

Scheme VI

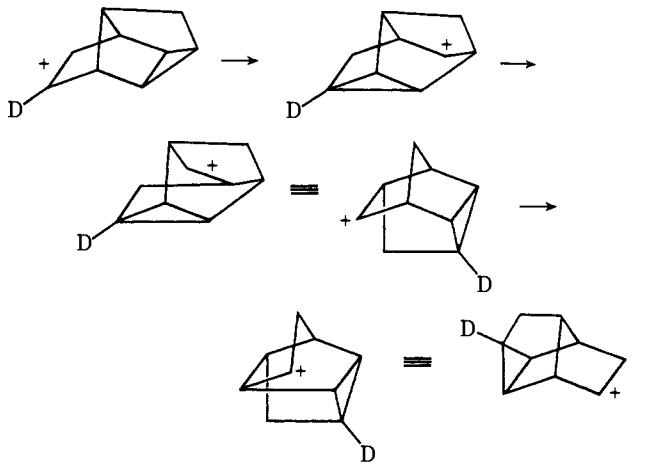


23

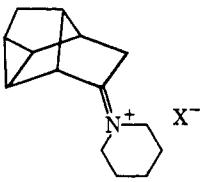
a protons, 7.08 or 7.50
b protons, 7.50 or 7.08

The deuterium scrambling found in the solvolyses of labeled **1**-OBs and **2**-OBs, although nicely accommodated by reaction *via* **23**, might also be rationalized by the sequence of alkyl shifts illustrated in Scheme VII. The significant difference in the two reaction pathways for deuterium scrambling is that migration of deuterium from C-8 to C-4 *via* ion **23** occurs with retention of configuration, while C-8 to C-4 migration, according to the sequence of alkyl shifts in Scheme VII, occurs with inversion. Since a simple test of these alternatives required the synthesis of optically active solvolytic precursors, the method of Chapman for the resolution of ketones[22] was used for partial resolution of 8-deltacyclanone (**5**). A diastereomeric mixture of iminium *d*-camphor-10-sulfonate salts (one diastereomer represented in

Scheme VII



24b) was prepared by treatment of the corresponding iminium perchlorate salt (**24a**) with potassium *d*-camphor-10-sulfonate. The iminium perchlorate salt was prepared by allowing ketone **5** to react with a solution of pyrrolidinium perchlorate in ethanol. Partial resolution of the *d*-camphor-10-sulfonate salts was achieved

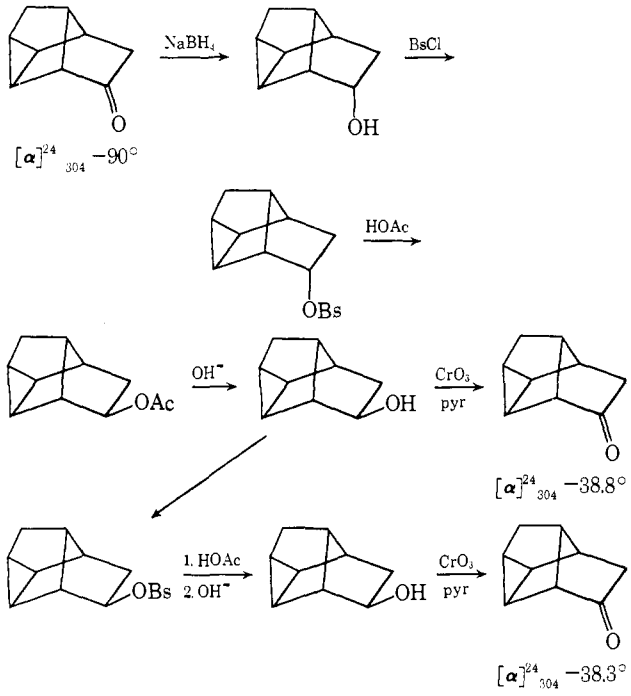


24a, X = ClO_4
b, X = *d*-camphor-10-sulfonate

(22) O. L. Chapman, W. R. Adams, J. B. Sieja, and W. J. Welstead, Jr., *ibid.*, 88, 162 (1966).

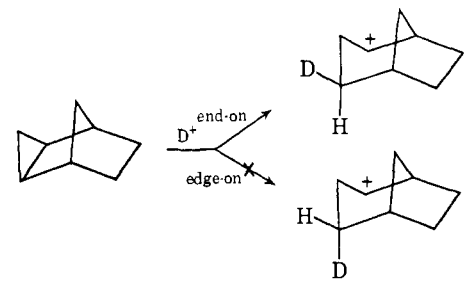
by fractional crystallization, and a selected fraction so obtained yielded, after mild alkaline hydrolysis and steam distillation, ketone **5**, $[\alpha]^{24}_{304}$ −90 ± 1° (*c* 0.05 methanol). Standard reduction and esterification procedures were used to prepare **2**-OBs from this optically active 8-deltacyclanone fraction. Solvolysis in acetic acid–sodium acetate gave **1**-OAc, which was saponified to yield **1**-OH. The *exo*-8-deltacyclanol obtained in this fashion was divided into two portions. The first portion was oxidized back to 8-deltacyclanone using chromium trioxide–pyridine, while the second portion was converted to *exo*-8-brosylate and subjected to solvolysis in acetic acid–sodium acetate. The **1**-OAc obtained was saponified to **1**-OH, which, in turn, was oxidized to 8-deltacyclanone. The two ketone fractions obtained in this manner had $[\alpha]^{24}_{304}$ −38.8 and −38.3° (*c* 0.05, methanol), respectively, as outlined in Scheme VIII. Thus the loss of optical activity during solvolysis

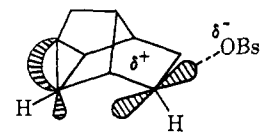
Scheme VIII



of the *endo*-brosylate was 57%, while the *exo*-brosylate solvolyzes with 99% retention of optical activity.

In the case of the solvolysis of **1**-OBs, it is clear that the sequence of alkyl shifts pictured in Scheme VII does not occur. In view of this and the other data discussed above on the stereochemical course of the reaction, the rate enhancement, the deuterium scrambling, and the nmr spectrum of the stable carbonium ion, the simplest rationalization which can be put forward is to suggest that the solvolytic reactions of the *exo*-8-deltacyclyl substrates proceed directly through a delocalized cyclopropylethyl carbonium ion of structure similar to ion **23**.[23] One might raise the question as to why the C-3–C-4 cyclopropane bond participates and the transannular C-2–C-3 bond does not. Electrophilic addition of hydrogen to cyclopropanols[24–26] and cyclopropanes[27,28] generally proceeds with predominant retention (edge-on attack) in acid solution. In contrast electrophilic addition of bromine occurs with inversion (end-on attack).[24] Our case is perhaps most similar to that investigated by LaLonde and coworkers,[29] who found that electrophilic addition to the cyclopropane ring of *exo*-tricyclo[3.2.1.$0^{2,4}$]octane proceeds by end-on addition to the cyclopropane bond, rather than by edge-on attack from the hindered *endo* side. In the case of the solvolytic reactions of *exo*-8-deltacyclyl substrates the electrophilic attack route also appears to be governed by steric considerations. A sketch of the transition state for ionization (**25**) reveals that the developing p orbital at C-8 is well aligned for end-on attack on the C-3–C-4 cyclopropane bond, cannot attack the transannular C-2–C-3 cyclopropane bond in an end-on fashion, and, further, does not appear to be located favorably for edge-on attack on the transannular bond.





25

While the rate enhancement calculated for the *exo*-8-deltacyclyl brosylate seems to provide relatively strong support for anchimeric assistance by the cyclopropane ring, the anchimeric assistance calculated for the *endo*-8 epimer is less convincing, especially when viewed with the data on the degree of racemization, the extent of deuterium scrambling and the uncertainties concerning steric retardation of *endo* epimers.[30] The 57% racemi-

(23) For related studies on 2-cyclopropylethyl carbonium ion systems, see (a) S. Winstein and J. Sonnenberg, *J. Am. Chem. Soc.*, **83**, 3235 (1961); **83**, 3244 (1961); S. Winstein, *ibid.*, **81**, 6524 (1959); S. Winstein, J. Sonnenberg, and L. de Vries, *ibid.*, **81**, 6523 (1959); (b) J. S. Haywood-Farmer and R. E. Pincock, *ibid.*, **91**, 3020 (1969); J. S. Haywood-Farmer, R. E. Pincock, and J. I. Wells, *Tetrahedron*, **22**, 2007 (1966); M. A. Battiste, C. L. Deyrup, R. E. Pincock, and J. Haywood-Farmer, *J. Am. Chem. Soc.*, **89**, 1954 (1967); H. Tanida, T. Tsuji, and T. Irie, *ibid.*, **89**, 1953 (1967); (c) R. R. Sauers, J. A. Beisler, and H. Freilich, *J. Org. Chem.*, **32**, 569 (1967); R. R. Sauers and J. A. Beisler, *Tetrahedron Lett.*, 2181 (1964); (d) B. C. Henshaw, D. W. Rome, and B. L. Johnson, *ibid.*, 6049 (1968); (e) M. J. S. Dewar and J. M. Harris, *J. Am. Chem. Soc.*, **90**, 4468 (1968); Y. E. Rhodes and T. Takino, *ibid.*, **90**, 4469 (1968); R. R. Sauers and R. W. Ubersax, *J. Org. Chem.*, 31, 495 (1966); G. E. Cartier and S. C. Bunce, *J. Am. Chem. Soc.*, **85**, 932 (1963); (f) C. F. Wilcox, Jr., and R. G. Jesaitis, *Tetrahedron Lett.*, 2567 (1967); (g) S. Winstein, P. Bruck, P. Radlick, and R. Baker, *J. Am. Chem. Soc.*, **86**, 1866 (1964); (h) A. C. Cope, S. Moon, and C. H. Park, *ibid.*, **84**, 4850 (1962); and ref 15, 16, and 19.

(24) C. H. De Puy, *Accounts Chem. Res.*, **1**, 33 (1968).

(25) A. Nickon, J. L. Lambert, R. O. Williams, and N. H. Werstink, *J. Am. Chem. Soc.*, **88**, 3354 (1966); A. Nickon, J. H. Hammons, J. L. Lambert, and R. O. Williams, *ibid.*, **85**, 3713 (1963).

(26) P. S. Wharton and T. I. Blair, *J. Org. Chem.*, **31**, 2480 (1966).

(27) J. H. Hammons, E. K. Probasco, L. A. Sanders, and E. J. Whalen, *ibid.*, **33**, 4493 (1968).

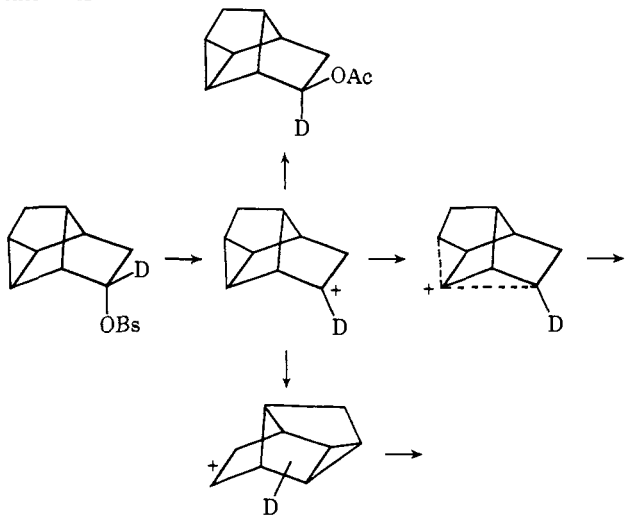
(28) J. M. Brown and M. C. McIvov, *Chem. Commun.*, 238 (1969).

(29) R. T. LaLonde, J. Ding, and M. A. Tobias, *J. Am. Chem. Soc.*, **89**, 6651 (1967).

(30) H. C. Brown and S. Ikegami, *ibid.*, **90**, 7122 (1968); S. Ikegami, D. L. Vander Jagt, and H. C. Brown, *ibid.*, **90**, 7124 (1968); H. C. Brown, I. Rothberg, P. v. R. Schleyer, M. M. Donaldson, and I. J. Harper, *Proc. Nat. Acad. Sci. U. S.*, **56**, 1653 (1966); H. C. Brown and W. J. Hammar, *J. Am. Chem. Soc.*, **89**, 6378 (1967); H. C. Brown,

zation found in the solvolysis of active *endo*-8-deltacyclyl brosylate might be explained, initially, by C-9 to C-8 hydride ion migration in a first-formed classical carbonium ion intermediate or by the sequence of alkyl shifts outlined in Scheme VII (or a closely related variation). The first racemization route may be ruled out on the basis of the deuterium scrambling pattern found in the solvolysis of *exo*-8-deuterio-*endo*-8-deltacyclyl brosylate. We have, therefore, settled on the overall view of the racemization and deuterium scrambling for *endo*-brosylate pictured in Scheme IX. Acetolysis of labeled

Scheme IX



endo-brosylate generates a classical 8-deltacyclyl carbonium ion, which has three choices: (a) reaction with solvent to give *exo*-acetate with retention and no deuterium migration, (b) leakage to a nonclassical ion of type **23** which generates *exo*-acetate with retention and 50–50 deuterium scrambling between C-4 and C-8, and (c) rearrangement by a series of alkyl shifts to an ion of inverted configuration. The sequence of shifts might well be closely related to the sequence of Scheme VII; however, a consideration of reasonable variations on sequence VII suggests that the inversion mechanism might proceed with distribution of the deuterium between C-4 and C-8 or with no migration of deuterium label. An additional facet is that the first step of the inversion process of VII might actually involve a two-bond shift; a Wagner–Meerwein shift of the C-3–C-7 bond, followed by a shift of the bond originally labeled as C-2–C-3 accomplishes an identical transformation. Our data at the present time do not allow us to choose among these interesting variations. Additional work on the complexities of the solvolytic route for the ionization of *endo*-8-deltacyclyl substrates is in progress.

Experimental Section

Melting points are uncorrected. The nmr spectra were recorded with a Varian Associates A-60 or HA100 nmr spectrometer, using tetramethylsilane as an internal standard except as noted. Infrared spectra were recorded with a Perkin-Elmer Model 137 infrared spectrometer and were calibrated with a polystyrene spike at 1601.4 cm^{-1}. Gas–liquid partition chromatographic analyses were performed on an F & M Model 609 chromatograph equipped with a flame ionization detector and an Aerograph Model A90P chromatograph equipped with a thermal conductivity detector. The following columns were used: column A, 14 ft × 0.25 in., 15% Carbowax 20M on 70/80 mesh Anakrom AS, and column B, 21 ft × 0.25 in., 12% QF-1 on 70/80 mesh Anakrom AS. Mass spectra were recorded using a Hitachi–Perkin-Elmer Model RMU-6E mass spectrometer. Ultraviolet spectra were run using a Cary Model 14 spectrometer, while optical rotatory dispersion curves were determined on a Jasco Model ORD/UV-5 spectrometer. Fractional distillations were accomplished on an 18 × 0.25 in. Nester-Faust semimicro, spinning-band, distillation column. Elemental analyses were performed by Max Bernhardt, Microanalytisches Laboratorium, Max-Planck Institute, Mulheim, Germany; Galbraith Microanalytical Laboratories, Knoxville, Tenn.; and B. E. Landberg, Oregon State University.

Preparation of Deltacyclane-8-carboxamide. A mixture of nitriles **1**-CN and **2**-CN[8] (145 g, 1.0 mol) was refluxed in 400 ml of isopropyl alcohol containing 60 ml of water and 98.6 g (1.5 mol) of 85% potassium hydroxide for 12 hr. After the reaction mixture had cooled to room temperature, 124 ml (1.5 mol) of concentrated hydrochloric acid was cautiously added. Filtration of the cooled solution gave 125 g (77%) of amide: mp 170–171°; ir (Nujol mull) 3450, 3250 (amide NH_2), 3100 (cyclopropyl CH), 1670, 1630 (amide C=O), and 795 cm^{-1} (nortricyclene ring); nmr (pyridine internal reference and solvent) τ 6.03 (s, 2 H, $CONH_2$), 6.83–7.50 (m, 1 H, $CHCONH_2$), 7.57–8.40 (m, 5 H), 8.57 (s, 2 H), and 8.84–9.33 (m, 3 H, tertiary cyclopropyl).

Anal. Calcd for $C_{10}H_{13}NO$: C, 73.57; H, 8.03. Found: C, 73.35; H, 7.98.

Preparation of 8-Deltacyclylamine. Deltacyclane-8-carboxamide (35.2 g, 0.21 mol) was added to a solution of sodium methoxide prepared by allowing 10.5 g (0.45 g-atom) of sodium metal to react with 400 ml of anhydrous methanol. After cooling in an ice bath, bromine (35.2 g, 0.22 mol) was added to the slurry. When the addition was complete the resulting clear solution was allowed to warm to 55° and held at that temperature for 90 min. Potassium hydroxide (85%, 66 g, 1 mol) in 200 ml of water was added, and the reaction mixture was heated at reflux for 24 hr. Removal of the methanol by fractional distillation, extraction of the aqueous phase twice with ether, drying ($MgSO_4$), and fractional distillation gave 12.1 g (42% overall) of 8-deltacyclylamine: bp 70–71° (6 mm); ir (neat) 3420, 3340 (NH_2 stretch), 3100 (cyclopropyl CH) and 1600 cm^{-1} (NH_2 deformation); nmr (CF_3CO_2H, internal reference $CHCl_3$) τ 2.90 (broad, 3 H, CNH_3^+), 5.94–6.62 (m, 1 H, $-CHNH_3^+$), 7.52–8.17 (m, 4 H), 8.42 (s, 3 H), 8.63–9.28 (m, 3 H).

Anal. Calcd for $C_9H_{13}N$: C, 79.95; H, 9.69. Found: C, 79.81; H, 9.54.

Chlorodecarboxylation of Deltacyclane-8-carboxylic Acid. Deltacyclane-8-carboxylic acid was prepared from a mixture of **1**-CN and **2**-CN in a 62% yield by the method of Hall[4] except that 20% aqueous isopropyl alcohol was used for the solvent and heating at reflux was carried out over a 7-day period. The chlorodecarboxylation was patterened after Kochi's procedure.[10] Deltacyclane-8-carboxylic acid (82 g, 0.50 mol) was dissolved in a solution of 600 ml of benzene containing lead(IV) acetate (120 g, 0.25 mol, 90% purity). Nitrogen was passed through the flask while the heterogeneous mixture was refluxed. Lithium chloride (21.2 g, 0.5 mol) was added *slowly via* a solids addition apparatus. After a short time the solution foamed vigorously. On completion of the addition 300 ml of water was added and the solution was filtered. Washing with 10% potassium carbonate solution and fractionating part of the benzene off gave about 150 ml of solution which was distilled on a semimicro, spinning-band, distillation column to give two main fractions: 18 g, bp 80–83° (40 mm), and 6 g, bp 78–80° (1 mm).

Analysis of these two samples by vpc (column A) showed that the second fraction contained one component. Spectral examination confirmed that the second fraction was identical with acetate **1**-OAc prepared by solvolyzing brosylates **1**-OBs and **2**-OBs or chlorides **1**-Cl and **2**-Cl. The first fraction contained two components as indicated by vpc analysis. In several preparations the ratio of these components varied from 70:30 to 83:17 (in order of increasing retention time) and proved to be *exo*- and *endo*-8-chlorodeltacyclane. The structure of the major component of this fraction is assigned the *exo* configuration on the basis of nmr spectral comparison with other 8-substituted derivatives in this system (alcohols **1**-OH and **2**-OH, acetate **1**-OAc, and brosylates **1**-OBs and **2**-OBs, for example). Spectral data for the chlorides **1**-Cl and **2**-Cl are ir (neat) 3100 (cyclopropyl CH) and 803 cm^{-1}, no absorbance from 2800 to 1460 cm^{-1}; nmr (CCl_4) τ 5.63 (complex multiplet, *endo*-chloride, $CHCl$), 5.85 (doublet of doublets, J = 3 Hz, 8 Hz, *exo*-chloride, $CHCl$), 7.39–9.42 (complex absorptions, ratio of area relative to absorbance at 5.63 and 5.85 is 10:1).

I. I. Rothberg, and D. L. Vander Jagt, *J. Am. Chem. Soc.*, **89**, 6380 (1967); H. C. Brown, W. J. Hammar, J. H. Kawalkami, I. Rothberg, and D. L. Vander Jagt, *ibid.*, **89**, 6381 (1967).

Anal. Calcd for $C_9H_{11}Cl$: C, 74.13; H, 7.92. Found: C, 74.29; H, 7.81.

Deamination of 8-Deltacyclylamine in Acetic Acid. 8-Deltacyclylamine (1.35 g, 0.010 mol) was dissolved in 100 ml of glacial acetic acid. Sodium nitrite (1.1 g, 0.016 mol) was added in several small portions over a period of 1 hr. The solution was added to 500 ml of water and extracted three times with 100-ml portions of ether. The ether extracts were washed with 10% aqueous sodium carbonate, dried ($MgSO_4$), and evaporated to give 1.72 g of crude acetate **1**-OAc. Vpc analysis of this material on column B showed it to be homogeneous. Purification by preparative vpc on this same column and subsequent ir and nmr analysis showed this acetate to be identical with the acetates obtained by acetolysis of brosylates **1**-OBs or **2**-OBs or of chlorides **1**-Cl and **2**-Cl and the acetate obtained by chlorodecarboxylation of deltacyclane-8-carboxylic acid.

Saponification of Acetate 1-OAc. Acetate **1**-OAc (17.8 g, 0.10 mol), methanol (200 ml), and potassium hydroxide (10.5 g, 0.15 mol, 85% purity) were mixed and heated at reflux for 18–24 hr. Distillation of this solution on an 18-in. semimicro spinning-band column yielded 11.0 g (81%) of alcohol **1**-OH: bp 76–78° (3 mm); mp 33–33.5°; ir (neat) 3400 (OH), 3100 (cyclopropyl CH), 805 cm^{-1} (nortricyclene ring); nmr ($CHCl_3$) τ 5.72 (doublet of doublets, J = 2, 6.6 Hz, 1 H, C*H*OH), 6.80 (s, 1 H, CHO*H*), 8.03 (m, 4 H), 8.45 (s, 2 H), 8.58–9.33 (complex m, 3 H).

Anal. Calcd for $C_9H_{12}O$: C, 79.37; H, 8.88. Found: C, 79.25; H, 8.80.

Analysis of alcohol **1**-OH on column B showed it to be composed of only the *exo* isomer. No peak having the retention time of *endo*-alcohol **2**-OH could be observed under conditions where more than 0.4% could be detected. This analysis was applied to each acetate obtained from brosylate or chloride acetolysis, amine deamination or acid chlorodecarboxylation with the same results; no (<0.4%) *endo*-alcohol could be detected.

Reduction of 8-Deltacyclanone (5) with Sodium Borohydride. Ketone **5** (134 g, 1.0 mol) was added to a solution of sodium borohydride (14.2 g, 0.60 mol) and sodium hydroxide (14.2 g, 0.10 mol) in 400 ml of 80% aqueous tetrahydrofuran. The resulting two-phase solution was stirred vigorously for 12 hr. Ir analysis of the organic layer at this time revealed that no more carbonyl was present (no 1750 cm^{-1} absorption). The product was isolated by extracting three times with 300-ml portions of ether, drying the extracts ($MgSO_4$), evaporation of the ether, and distillation to give alcohols **1**-OH and **2**-OH (129 g, 95%): bp 76–78° (3 mm); mp 40–41°; ir (neat) 3400 (OH), 3100 (cyclopropyl CH), 796 cm^{-1} (nortricyclene ring); nmr ($CHCl_3$) τ 5.60 (complex multiplet), 5.99 (doublet of doublets, J = 2, 6.6 Hz), 7.51 (s, 1 H, O*H*), 7.72–8.34 (complex m, 5 H), 8.48 (m, 2 H), 8.88 (s, 3 H). Total relative area of the 5.60 and 5.99 peaks was equivalent to one proton. These absorption bands are assigned to the proton α to hydroxyl for *endo* and *exo* isomers, respectively. Of several vpc columns tested, column B was unique in its ability to separate alcohols **1**-OH and **2**-OH. The ratio of isomers found using column B was 84:16 for *endo* and *exo*, respectively, in order of increasing retention time.

Anal. Calcd for $C_9H_{10}O$: C, 79.37; H, 8.88. Found: C, 79.74; H, 9.01.

Reduction of 8-Deltacyclanone (5) with Lithium Aluminum Hydride. Ketone **5** (13.4 g, 0.10 mol) was reduced using an ether–lithium aluminum hydride slurry and worked up in the usual manner to give 11.4 g (86%) of alcohols **1**-OH and **2**-OH. Physical and spectral properties of these alcohols were essentially the same as the alcohols obtained from sodium borohydride reduction of ketone **5**. Analysis of these alcohols by vpc (column B) showed the ratio of isomers (*endo*:*exo*) to be 88:12 in order of increasing retention time.

Reduction of 8-Deltacyclanone (5) with Lithium Aluminum Deuteride. Ketone **5** (5.0 g, 37.3 mmol) in 20 ml of anhydrous tetrahydrofuran was added to a slurry of 0.50 g (12.0 mmol) of lithium aluminum deuteride in anhydrous tetrahydrofuran (30 ml) under a nitrogen atmosphere. After 8 hr, 10% hydrochloric acid was cautiously added until the slurry turned to a clear two-phase system. Extraction of this solution four times with 30-ml portions of ether, drying the extracts, and distillation on an 18-in. semimicro spinning-band column gave 4.2 g (87%) of 8-deuterio-8-deltacyclanol.

Deuterioboration–Oxidation of Deltacyclene (16). Deltacyclene (4.3 g, 27.9 mmol) was placed in a flask fitted with a stirrer, provision for a nitrogen atmosphere, and a syringe septum. A 0.17 M solution of perdeuteriodiborane (70 ml) in tetrahydrofuran (obtained from Ventron Corp.) was injected into the reaction vessel by means of a syringe and the resulting solution was stirred for 12 hr. At this time a solution of 10 ml of 10% aqueous hydrogen peroxide and 0.5 g sodium hydroxide was slowly added and the resulting reaction mixture stirred for 1 hr. Extraction of the reaction mixture three times with ether, drying ($MgSO_4$) the ether extracts, and distillation afforded 3.1 g (81%) of alcohol **17**. The nmr spectrum of this material showed a doublet (J = 6.6 Hz) for the C*H*O proton at τ 5.99 (CCl_4). The remainder of the spectrum was similar to the nmr spectrum of unlabeled alcohol **1**-OH. The infrared spectrum of **17** had a C–D absorption at 2175 cm^{-1} and an OH absorption at 3330 cm^{-1}. Analysis of this material by vpc on column B indicated that it was composed of 97% *exo* and 3% *endo* epimers.

***endo*-8-Deuterio-*exo*-8-deltacyclyl Brosylate (10).** A solution of 11.25 g (0.031 mol) of *exo*-8-deuterio-*endo*-8-deltacyclyl brosylate and 11.5 g (0.04 mol) of tetra-*n*-butylammonium acetate in 500 ml of dry acetone was heated under nitrogen for 20 hr.[19] The solution was concentrated to 35 ml, poured into 10 ml of water, and extracted with three 100-ml portions of ether. The ether extracts were washed with a 10% sodium carbonate solution until effervescence stopped and dried over magnesium sulfate. Distillation gave the epimerized acetate. Hydrolysis of this acetate was accomplished by heating at reflux in potassium hydroxide–methanol to give *endo*-8-deuterio-*exo*-8-deltacyclanol. The 60-MHz nmr spectrum is entirely consistent with this assignment and reveals that the deuteration at *endo*-C-8 is 97%. The desired brosylate **10** was prepared by treating the deuterated precursor alcohol with *p*-bromobenzenesulfonyl chloride in pyridine. The nmr spectrum of the deuterated brosylate **10** (mp 59.5–61°) shows absorption bands at τ 7.77–8.13 (multiplet, 4 H), 8.15–8.52 (multiplet, 3 H), 8.55–9.27 (complex multiplet, 3 H), with an absorption at τ 5.21 indicating 97% deuteration of the *endo*-C-8 position.

Preparation of the Brosylates of *exo*- and *endo*-8-Deltacyclanol. In a typical preparation 0.1 mol of the purified alcohol was dissolved in pyridine (100 g) and the mixture cooled to 10° in an ice–salt bath. *p*-Bromobenzenesulfonyl chloride (0.11 mol) was then added in several portions over a period of 10–20 min. The heterogeneous mixture was vigorously stirred and the temperature not allowed to exceed 10° during this time. Twenty minutes after the addition was complete the mixture was placed in a refrigerator and allowed to remain for 12–18 hr. The entire mixture was then poured into ice water using 200 ml of ether to rinse the flask. Hydrochloric acid (6 N) was then slowly added, with stirring, until the aqueous phase was slightly acid (pH 3–4). Separation of the ether layer, extracting the aqueous phase twice with ether, drying ($MgSO_4$) the ether extracts, and evaporation gave a 60–80% yield of crystalline brosylate. Fractional crystallization from pentane gave *exo*-brosylate, mp 59–60°, and *endo*-brosylate, mp 63–64°.

Anal. Calcd for $C_{15}H_{15}SO_3Br$: C, 50.71; H, 4.25. Found for *exo*-brosylate: C, 50.99; H, 4.42. Found for *endo*-brosylate: C, 51.01; H, 4.27.

Preparative Acetolysis Procedure for Brosylates and Chlorides. In a typical experiment acetic acid which was 0.1 M in brosylate or chloride, 0.12 M in sodium acetate, and 0.01 M in acetic anhydride was placed in a closed container and heated on the steam bath for 24 hr (in the case of the brosylates) or for up to 7 days (in the case of the tetracyclic chlorides). Work-up consisted of pouring the solution into three times its volume of water, extracting three times with ether, washing the extracts with 10% sodium carbonate solution (until effervescence stopped), drying ($MgSO_4$), and evaporating the solvent. The acetate was then fractionally distilled to give 72–86% of the theoretical yield. Vpc analysis of the product from each acetolysis indicated that only one component was present which had physical and spectral properties identical with the acetate produced when 8-deltacyclylamine was deaminated in acetic acid or when deltacyclane-8-carboxylic acid was chlorodecarboxylated. Spectral and physical properties were: bp 78–80° (1.0 mm); nmr (CCl_4) τ 5.02 (m, C*H*O, 1), 7.95 (m, 5), 8.02 (s, COC*H*$_3$, 3), 8.45 (s, 2), 8.85 (d, J = 4 Hz, 1), and 9.10 (d, J = 5 Hz, 1); ir (neat) 3045, 2925, 2850, 1730, 1240, 1025, and 800 cm^{-1}.

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.29; H, 7.81.

Preparation of Iminium Perchlorate Salt 24a. Ketone **5** (134 g, 1 mol), pyrrolidinium perchlorate (171 g, 1.01 mol), and absolute ethanol (100 ml) were heated on a steam bath until a homogeneous solution was obtained. Five drops of pyrrolidine was added and the covered solution was allowed to stand at room temperature for 5 days. During this time large cubic crystals formed. Collection of these crystals and air drying gave 254.8 g (88.6%) of white crystalline **24a**: mp 133–135°; ir (Nujol mull) 1715, 1080, and 796 cm^{-1}; nmr (D_2O) τ 6.10 (broad m, CH_2N, 4 H), 6.83 (s, 1 H), 7.18 (s, 2 H), 7.55 (s, 2 H), 7.80 (m, 4 H), 8.18 (s, 3 H), 8.58 (d, J = 4 Hz, 2 H).

Anal. Calcd for $C_{13}H_{18}NClO_4$: C, 54.24; H, 6.31. Found: C, 54.21; H, 6.24.

Resolution of 8-Deltacyclanone (5). Perchlorate salt **24a** (250 g, 0.87 mol) and potassium *d*-camphor-10-sulfonate (236 g, 0.87 mol) were added to methanol (500 ml) and the mixture was heated to reflux. After cooling the solution in a refrigerator overnight the potassium perchlorate was removed by filtration and the methanol removed on a rotary evaporator. The resulting oil was allowed to stand for 3 months. Crystals finally began to appear at this time. These were removed and the mother liquor was added to 200 ml of tetrahydrofuran. Cooling this solution caused several crops of crystals to be deposited. Recrystallization of these fractions gave products which had melting points ranging from 63 to 108° and optical rotations from +0.19 to +2.94° (1 g/10 ml of methanol, 1-dm cell, sodium D line). After repeated attempts to purify these crystals, the fractions having a rotation of +1.8° and greater were finally combined and hydrolyzed by adding them to a 20% aqueous potassium hydroxide solution. Extraction of these solutions three times with ether, drying ($MgSO_4$), evaporation of the ether, and distillation gave 25 g of tetracyclic ketone **5** having $[\alpha]^{24}_{304}$ −90° (*c* 0.05, methanol).

Kinetic Measurements. The chosen acetolysis conditions and procedures were similar to those of Tanida, *et al.*[31] Rate constants were determined at 25.68 ± 0.02° using a nonlinear least squares curve fitting program (E-2-OSU-CURV FIT). The determination of the rate constant for **1**-OBs, k_{exo} = 2.61 ± 0.09 × 10^{-4} sec^{-1}, is based upon three runs and that for **2**-OBs, k_{endo} = 4.62 ± 0.06 × 10^{-6}, is based upon two runs.

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The Nature of the Hydrogen Migrations in the Cyclization of Squalene Oxide to Lanosterol

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Abstract: The hydrogen migrations that occur during the conversion of squalene to lanosterol have been shown to take place by a sequence of two 1,2-shifts of hydrogen and not as a single 1,3-hydrogen shift. Squalene labeled with tritium at C-14 was converted to lanosterol with a rat liver homogenate; no tritium is located at C-20 of the resultant lanosterol, whereas the anticipated amount of tritium is found at C-17. Thus, the tritium originally at C-14 of squalene becomes attached to C-17 of the lanosterol, as the result of a sequence of two 1,2-shifts of hydrogen.

The conversion of squalene to lanosterol[1-3] has recently been shown to involve oxidation of squalene to 2,3-oxidosqualene and then cyclization of this substance to lanosterol[4-8] with retention of the oxygen of the epoxide function as the C-3 hydroxyl of lanosterol.[9] No cofactor requirements for the cyclase enzyme could be demonstrated.[9,10]

The folding of squalene suggested in 1953[11,12] (Scheme I) and subsequently amplified to include the stereochemical features of triterpene substances[13-15] has been amply confirmed by experiments. In particular, the sequence of 1,2-methyl migrations postulated to occur during the rearrangement of a protosterol cation to lanosterol has been demonstrated.[16-18] However, the nature of the hydrogen migrations are still unsettled. A study of the fate of tritium during the conversion of (4*R*)-mevalonic-4-^{3}H acid to cholesterol has been reported;[19] however, this work does not distinguish between a single 1,3-hydrogen shift, for which there is ample precedence in organic chemistry,[20-24] and a se-

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