Anal. Calcd for $C_{17}H_{15}N_5O_5$: C, 55.29; H, 4.09; N, 18.96. Found: C, 55.56; H, 4.19; N, 18.89.

3-(2-Carboxy-4-methoxyphenyl)propionic Acid (9). Method A. The cyanoaldehyde **8** (0.50 g) was oxidized in acetone solution by Jones' reagent and the product was obtained in ether, then extracted into sodium carbonate solution. This solution was acidified and the product was extracted into ether which was washed, dried, and evaporated to leave 80 mg of nitrile acid: $\lambda\lambda^{\mathrm{KBr}}$ 2.8–4.0 (-COOH), 4.48 (-CN), 5.80 μm (-COOH).

The nitrile acid was hydrolyzed by 24 hr boiling in 25 ml of 10% sodium hydroxide. An ether extract of the acidified reaction solution was washed, dried, filtered, and evaporated to leave a pale yellow solid, mp 193–194°. This was sublimed at 160° (1 mm), then recrystallized from acetone to give colorless, very fine crystals, mp 195.5–196.9°. The melting point was not depressed on admixture with a sample prepared as described in method B, and the infrared spectra of the two samples were identical.

Method B. 7-Methoxytetralone (2.00 g) was converted into its enol acetate by the action of isopropenyl acetate and toluenesulfonic acid. The crude product was distilled at 100° (0.1 mm) to give 0.91 g of colorless enol acetate **10**: $\lambda\lambda^{\mathrm{neat}}$ 5.65 (carbonyl) and 12.50 μm (trisubstituted olefin).

1-Acetoxy-3,4-dihydro-7-methoxynaphthalene (**10**, 910 mg) was oxidized at 0° in acetone solution by the slow addition of 1.74 g (22% excess) of finely powdered potassium permanganate. The dark residue resulting on removal of the acetone was dissolved in 10% sulfuric acid, bleached with sodium sulfite, and extracted with ether. The ether extract was extracted with saturated sodium bicarbonate which was acidified and again extracted with ether. The dried ether solution yielded 308 mg of diacid, purified as described in method A. The analytical sample, mp 196–197°, was recrystallized from dioxane–water.

Anal. Calcd for $C_{11}H_{12}O_5$: C, 58.93; H, 5.39. Found: C, 59.06; H, 5.68.

Methyl *p*-Toluenethiolsulfonate. Sodium thiotosylate (sharp decomposition at 308°, vacuum) in methanol was methylated by dimethyl sulfate. The product (51% based on starting tosyl chloride) after two recrystallizations from benzene was large, colorless prisms: mp 57.5–58.5° (lit.[30] mp 58°); $\delta^{\mathrm{CHCl_3}}$ 2.46 (sharp singlet, C*Me*), 2.51 (sharper singlet, S*Me*), 7.55 ppm (quartet, aromatic *H*'s).

2-Chloro-1,1,2-trifluorotriethylamine (12). The addition of diethylamine to chlorotrifluoroethylene was conducted essentially as described by Yarovenko and Raksha.[31] It was distilled at 35° (11 mm) and for best results was used immediately after preparation. It deteriorated at an appreciable rate even on storage at −80°.

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(30) D. T. Gibson, *J. Chem. Soc.*, 2637 (1931).

(31) N. N. Yarovenko and M. A. Raksha, *Zh. Obshch. Khim.*, **29**, 2159 (1959).

The Tricyclo[4.4.0.0^{3,8}]decane to Adamantane Rearrangement

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Contribution from the Department of Chemistry, University of Wisconsin, Madison, Wisconsin. *Received February 9, 1968*

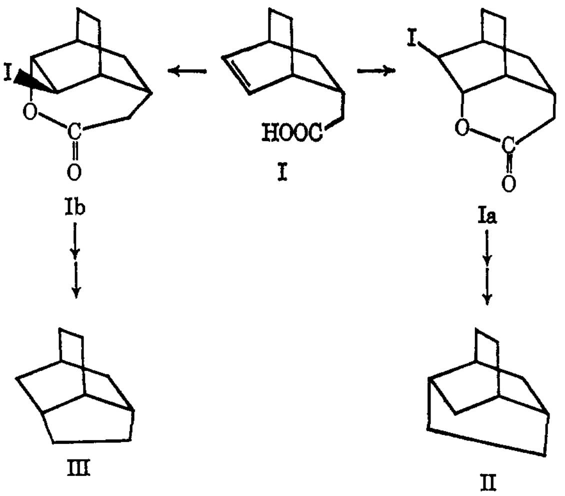
Abstract: Synthesis of the tricyclo[4.4.0.0^{3,8}]decane ring system is detailed and its behavior in carbonium ion rearrangements is investigated. A scheme for the formalization of complex rearrangements is advanced and discussed.

The work of Schleyer and others[1-3] over the past several years has led to the recognition that the combination of the thermodynamic stability of the adamantane carbon skeleton with the protean phenomena accompanying aluminum halide catalyzed alkane isomerizations results in the facile, often high-yield formation of adamantane and substituted adamantanes from (usually) isomeric hydrocarbons. This paper is concerned with the synthesis and chemistry of tricyclo[4.4.0.0^{3,8}]decane (twistane)[4] and its derivatives, and particularly with the systematics of their rearrangement to the adamantane carbon skeleton.

Synthesis

The synthesis of twistane and its simple functionalized derivatives is basically as communicated several years ago[5] and is detailed in the Experimental Section. Several points concerning the synthesis should be mentioned.

A possible ambiguity in the synthesis of twistane lies in the direction of iodolactonization of acid I which is formally capable of either δ lactonization (Ia) (and hence to twistane (II)) or ω lactonization (Ib) with ultimate formation of tricyclo[4.3.1.0^{3,7}]decane (III) (eq 1). Formation of an analogous pair of isomeric iodolactones from *endo*-bicyclo[2.2.2]oct-2-ene-5-carboxylic acid has



(1)

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(1) M. Nomura, P. von R. Schleyer, and A. A. Arz, *J. Amer. Chem. Soc.*, **89**, 3657 (1967), and earlier references.

(2) R. C. Fort, Jr., and P. von R. Schleyer, *Chem. Rev.*, **64**, 277 (1964).

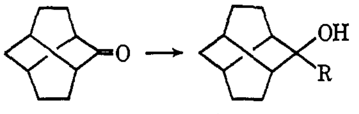
(3) A. Schneider, R. W. Warren, and E. J. Janoski, *J. Org. Chem.*, **31**, 1617 (1966).

(4) The best justification of the use of short "pet" names such as twistane and protoadamantane as is done here lies in the cumbersomeness of their systematic alternatives.

(5) H. W. Whitlock, Jr., *J. Amer. Chem. Soc.*, **84**, 3412 (1962).

been reported.[6] We are confident that the iodolactonization proceeded as expected since (1) Ia could be degraded to *endo,endo*-2-hydroxybicyclo[2.2.2]octane-5-carboxylic acid lactone by successive hydrogenolysis, condensation with ethyl formate, and ozonization; (2) twistane has been synthesized by an alternate route[7] that does not suffer from this ambiguity; (3) hydrocarbon III has been synthesized[8] and is clearly different from twistane, and (4) the structure of twistane has been confirmed by electron-diffraction studies.[9]

Twistanone (IV) was reduced by Wolff–Kishner reduction to II and was converted to alcohols Va–d by reaction with lithium aluminum hydride, lithium aluminum deuteride, *p*-methoxyphenyllithium, and methyllithium, respectively (eq 2). The nmr spectrum of Va offers further confirmation of the proposed structure. Absorption due to the carbinol hydrogen appears as a doublet, $J = 4.8$ cps, at δ 3.85 which is consistent with the dihedral angles between this hydrogen and its immediate two nonequivalent neighbors.



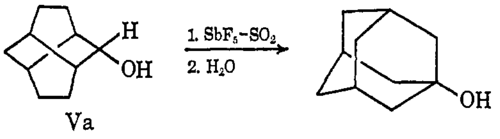
(2)

IV

Va, R = H
b, R = D
c, R = *p*-anisyl
d, R = CH$_3$

Carbonium Ion Rearrangements of the Twistane Skeleton. Rearrangement of Twistane. As expected, twistane may be rearranged to adamantane on treatment with aluminum chloride or bromide. The smoothness of this reaction contrasts markedly with the adamantanization of tetrahydrodicyclopentadiene. An 85% yield of adamantane could be isolated from the former reaction and the isomerization could be carried out at 60° in hexane solution. No apparent intermediates were involved since glpc monitoring of the reaction mixture showed only twistane and adamantane to be present at intermediate times.

Rearrangement of 2-Twistanol. Addition of the Lewis acids antimony pentafluoride or antimony pentafluoride–fluorosulfonic acid mixtures[10] to sulfur dioxide solutions of 2-twistanol (Va) at −80° followed by quenching led to high (∼80%) yields of 1-adamantanol (eq 3). We have not directly observed formation of the



(3)

Va

adamantyl cation by action of these acids on Va but on the basis of the following pair of observations are confident that it is present as the primary product under these reaction conditions. Quenching of the reaction mixture by addition to methanol produced a high yield of 1-adamantyl methyl ether. Also, varying the aqueous quenching technique produced adamantanol as the sole low molecular weight product, although the yield of it varied with the quenching technique. The highest yield of adamantanol was obtained by slow addition of a cold sulfur dioxide solution of the reaction mixture to vigorously stirred ice water.[11] Slow addition of water to the reaction mixture at −80° produced mainly gummy material, although here too adamantanol was the only isolable low molecular weight product.

Particularly interesting are the results of rearranging 2-twistanol-2-d_1 (Vb). Typical results are shown in Table I.

Table I. Isomerization of 2-Twistanol-2-d_1[a] to 1-Adamantanol-d_x

			Adamantanol				
Entry	Temp, °C	Time, hr	d_0	d_1	d_2	d_3	d_4
1[b]	−80	0.05	20	64	15	1	...
2[b]	−80	1.5	24	57	16	2	1
3[b,c]	−10	5.0	20	65	14	1	...
4[d]	−80	0.5	24	58	16	2	...
5[e]	Random (calcd)		37.1	38.0	18.2	5.4	1.1

[a] The Vb was 95.9% d_1, 4.1% d_0 by low-voltage mass spectrometry. All quoted results are derived from quenching the reaction mixture by addition of it to water. The reverse procedure gave the same results within experimental error. [b] By addition of antimony pentafluoride to liquid sulfur dioxide solutions of the alcohol at the temperature shown. [c] At the reflux temperature of sulfur dioxide. [d] As in footnote *b* except at 4:1 mixture of fluorosulfonic acid and antimony pentafluoride was used. [e] Calculated for complete randomization of $C_{10}H_{14.04}D_{0.96}$.

It is clear that considerable intermolecular hydrogen scrambling has occurred. The amount of scrambling, however, is considerably less than that expected on the basis of complete randomization (entry 5, Table I). Moreover the scrambling which is occurring must be occurring *during* and not after the rearrangement of the adamantyl carbonium ion. This follows from entries 1 and 3 in Table I which gave basically the same scrambling result. The manner in which intermolecular hydrogen scrambling occurs is not clear. It must not be occurring by a protonation–deprotonation sequence involving intermediate olefins since carrying out the isomerization in the presence of fluorosulfonic acid did not lead to dilution of deuterium content in the derived adamantanol. The presence of hydrogen fluoride in the reaction mixture also led to no isotope dilution. We favor as an explanation hydrogen exchange *via* hydride transfers catalyzed by small amounts of probably polymeric hydrocarbons. Transient disproportionation of two adamantyl cations is not likely. Rigorous purification of reagents led to no noticeable change in the label distribution of the adamantanol and attempted trapping of intermediate carbonium ions by carrying out the isomerization in the presence of triphenylmethane led to complete destruction of the reaction product. Only small amounts of diphenylmethane could be isolated.

We are therefore left with the idea that the amount of scrambling accompanying this rearrangement is that occurring *during* the course of rearrangement only and that the adamantyl cation once formed is stable toward further hydrogen exchange. That this is not a com-

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(6) W. Boehme, E. Schipper, W. G. Scharpf, and J. Nichols, *J. Amer. Chem. Soc.*, 80, 5488 (1958).

(7) J. Gauthier and P. Deslongchamps, *Can. J. Chem.*, **45**, 297 (1967).

(8) W. von E. Doering and A. Krantz, private communication.

(9) O. Bastiansen and B. Andersen, private communication.

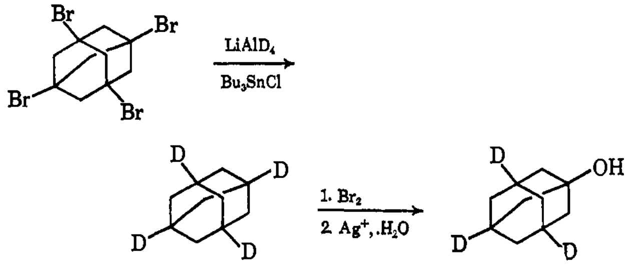
(10) G. A. Olah, M. B. Comisarow, C. A. Cupas, and C. U. Pittman, Jr., *J. Amer. Chem. Soc.*, 87, 2997 (1965).

(11) G. A. Olah, E. B. Baker, J. C. Evans, W. S, Tolgyesi, J. S. McIntyre, and I. J. Bastien, *ibid.*, **86**, 1360 (1964).

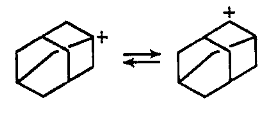
pletely accurate picture of the processes involved, however, is seen from the experiments now discussed that show that, although the adamantyl cation as a whole is stable toward hydrogen randomization, there is rapid intermolecular exchange of its bridgehead hydrogens.

Adamantanol-3,5,7-d_3 was synthesized as shown in Scheme I.[12,13] Mass spectrometry (96.8% d_3, 3.2% d_2), essentially complete disappearance of absorption of the signal at δ 2.1 in its nmr spectrum attributed to the bridgehead hydrogens,[14] and mixture melting point all point to the assigned structure.[15-17]

Scheme I



Subjection of adamantanol-d_3 to the standard reaction conditions at −78° for 30 min led to recovery on quenching of unchanged material. The mass spectrum showed the deuterium distribution to be 96.8% d_3, 3.2% d_2, compared to 97.8% d_3, 2.2% d_2 in the starting material. In addition examination of the nmr spectrum of the product showed that the bridgehead positions were still occupied exclusively by deuterium. Accordingly one may conclude that under these strongly acidic conditions the equilibrium between 1- and 2-adamantyl carbonium ions is kinetically inaccessible (eq 4) as this process must lead to scrambling between bridgehead and methylene hydrogens regardless of whether it occurs by an intramolecular or intermolecular route. This is not to say of course that this equilibrium cannot be attained as is amply illustrated by the oxidation[18] of 1-adamantanol to adamantanone by sulfuric acid at 75°. The two sets of conditions are of course quite different. Also the more or less equal distribution of deuterium between bridgehead and methylene positions (the sensitivity of the nmr technique is quite low) in adamantanol produced from Vb must be a phenomenon associated with the rearrangement and not with the adamantyl cation itself. A more interesting result was obtained when a 1:1 mixture of 1-adamantanol-3,5,7-d_3 and adamantanol-d_0 was subjected to the standard ionization conditions. The recovered adamantanol had an average deuterium content of 1.5 D/molecule as expected and the nmr spectrum of the material showed that deuterium was still exclusively at the bridgehead. The mass spectrum, however, showed that the deuterium was completely randomized between the bridgehead positions (Table II).



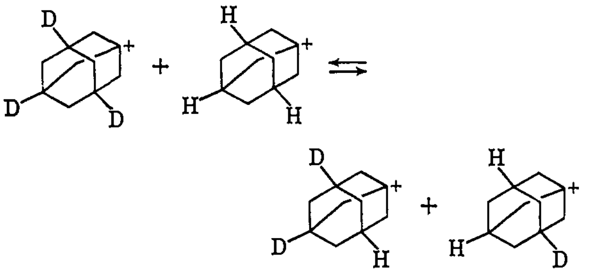
(4)

Table II[a]

Entry	d_0	d_1	d_2	d_3	d_4
1[b]	13.4	38.2	36.5	11.9	...
2[c]	14.2	38.3	36.0	11.5	...
Random (bridgehead)[d]	13.3	38.2	36.7	11.8	...
Random (complete)[e]	21.3	34.7	26.4	12.4	4.0

[a] Analyses as in Table I. [b] A mixture of 20.0 mg of adamantanol-d_0 and 20.4 mg of adamantanol-d_3 (97.8% d_3, 2.2% d_1). [c] Repeat of run 1. [d] Calculated randomization among bridgehead positions only. [e] Calculated randomization among all positions on the adamantane nucleus.

The net result of this then is that one may refine one's ideas as to the stability of the adamantyl cation in liquid SO_2 *vis-à-vis* hydrogen exchange to include the equilibrium in eq 5. The numbers in Table I are thus an *upper limit* on the amount of hydrogen–deuterium exchange accompanying the adamantanization of 2-twistanol-2-d_1.



(5)

Rearrangement of 2-Methyl-2-twistanol. When 2-methyl-2-twistanol (Vd) was subjected to the standard ionization conditions, 2-methyl-2-adamantanol was obtained in good yield as the *sole* product after quenching. 3-Methyl-1-adamantanol could not be detected.

Since the 2-methyladamantan-2-yl cation (VI) is surely more stable than 3-methyladamantan-1-yl cation (VII), it is not immediately clear that the above result reflects a kinetic feature of the reaction and not that one is merely detecting the more stable of an equilibrating pair of methyladamantyl cations. When 3-methyl-1-adamantanol was subjected to these reaction conditions it could be recovered on quenching essentially unchanged. Glpc examination of the recovered alcohol showed the presence of 2–3% of a contaminant having the same retention time as 2-methyl-2-adamantanol. When a 1:1 mixture of Vd and 1-methyl-3-adamantanol was subjected to the rearrangement conditions the recovered methyladamantanol was a 41:59 mixture of 2-methyl-2-adamantanol and 3-methyl-1-adamantanol. We ac-

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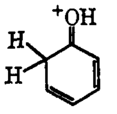
(12) E. Müller and U. Trense, *Tetrahedron Lett.*, **49**, 4979 (1967).

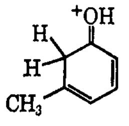
(13) H. G. Kuivila and L. Menapace, *J. Org. Chem.*, **28**, 2165 (1963).

(14) R. C. Fort, Jr., and P. von R. Schleyer, *ibid.*, 30, 789 (1965).

(15) Fragments at m/e 95 (i) and 109 (ii) in the mass spectrum of adamantanol-d_0 are shifted to m/e 97 and 110, respectively, in the mass spectrum of adamantanol-d_3. This result speaks for both even distribution of the deuterium about the threefold axis of adamantanol and the correctness of the standard rationalization of this type of fragmentation[16,17] of cyclohexanols.



i



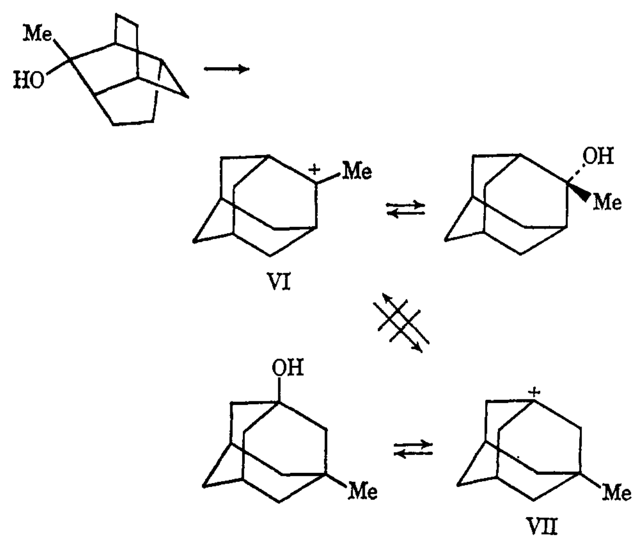
ii

(16) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden Day, Inc., San Francisco, Calif., 1967, p 107.

(17) For a recent study of the fragmentation behavior of substituted adamantances, see Z. Dolejsek, S. Hala, V. Hanus, and S. Landa, *Collect. Czech. Chem. Commun.*, **31**, 425 (1966).

(18) H. W. Geluk and J. L. M. A. Schlatmann, *Chem. Commun.*, **9**, 426 (1967).

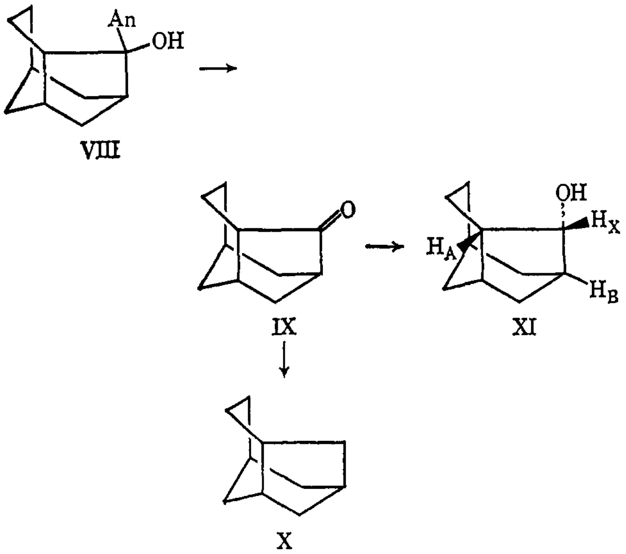
Scheme II



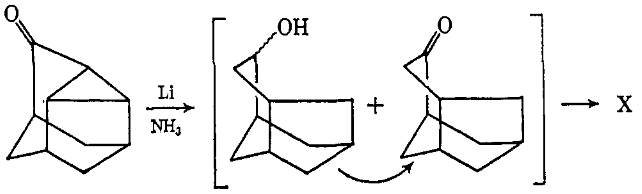
cordingly conclude that its presumed greater stability notwithstanding, VI is the initial product of the reaction (Scheme II).

Rearrangement of 2-Anisyl-2-twistanol. Alcohol Vc was destroyed by the action of antimony pentafluoride in sulfur dioxide but ionization could be affected quite smoothly by dissolving it in 96% sulfuric acid—the procedure of Bartlett, *et al.*[19] The absorption spectrum of the ion thus produced, $\lambda_{max}^{H_2SO_4}$ 381 mμ (ϵ 45,000), was in good agreement with those reported for similar ions.[19,20] Quenching the sulfuric acid solution led to a 77% yield of an alcohol isomeric with Vc to which is tentatively assigned the structure VIII (Scheme III) on which is based the following discussion. Oxidation of VIII with chromic acid afforded in good yield a ketone IX, $\lambda_{max}^{CCl_4}$ 5.75 μ. Wolff–Kishner reduction of IX afforded a single hydrocarbon that was identified as protoadamantane (X), by comparison with a sample synthesized from dehydroadamantanone[21] (most kindly supplied by Messrs. Baldwin and Foglesong) as depicted in Scheme IV.

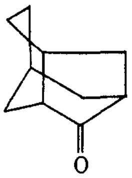
Scheme III

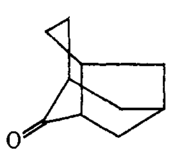


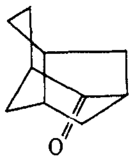
Scheme IV



Attempted base-catalyzed hydrogen–deuterium exchange on IX led to no incorporation of deuterium into the molecule under conditions that camphor exchanged both α hydrogens. Reduction of IX with lithium aluminum hydride afforded a single alcohol, XI. The nmr spectrum of XI showed absorption due to the carbinol hydrogen as the X portion of an ABX pattern at δ 4.22 with J_{AX} = 9.0 cps, J_{BX} = 4.5 cps. The calculated[22] values for dihedral angles of 10 and 40° between H_X and H_A and H_B, respectively, are 8 and 4.7 cps, respectively. The splitting values calculated for the alcohols derived by reduction of the other possible ketones, XII, XIII, and XIV, making the standard "steric approach control" assumption for product stereochemistry, are not in agreement with those observed. The carbonyl stretching frequency is consistent with the assigned structure but does not rule out structures XII–XIV.[23]


XII


XIII


XIV

Solvolysis of 2-twistanol toluenesulfonate in buffered acetic acid afforded a mixture containing six principal components. Capillary glpc demonstrated the *absence* of twistyl acetate, 1- and 2-adamantyl acetates, and the acetate of XI. None of the products were identified.

Discussion

One is able to draw two qualitative conclusions from the above results. First, the simplest pathway[24] between the adamantane and twistane skeletons, that involving spinning of a one-carbon bridge of twistane and the intermediacy of the protoadamantane skeleton (eq 6), suffices remarkably well to explain our experimental results. Initial production of the 2-methyladamantyl skeleton from methyltwistanol (Vd) is predicted. In the rearrangement of Vc, the protoadamantane skeleton is in fact detected and the suggested

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[19] P. D. Bartlett, E. R. Webster, C. E. Dills, and H. G. Richey, Jr., *Ann.*, **623**, 217 (1959); N. C. Deno, P. T. Groves, J. J. Jaruzelski, and M. N. Lugasch, *J. Amer. Chem. Soc.*, **82**, 4719 (1960).

[20] P. von R. Schleyer, D. C. Kleinfelter, and H. G. Richey, Jr., *ibid.*, **85**, 479 (1963); N. C. Deno, P. von R. Schleyer, and D. C. Kleinfelter, *Tetrahedron Lett.*, 414 (1961).

[21] J. E. Baldwin and W. D. Foglesong, *ibid.*, **34**, 4089 (1966).

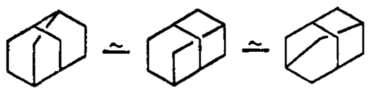
[22] M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).

[23] A. C. Cope, J. M. Grisar, and P. E. Peterson, *J. Amer. Chem. Soc.*, **82**, 4299 (1960).

[24] By pathway we mean a particular sequential interconversion of carbon skeletons, each of which is a set of carbonium ions and parent

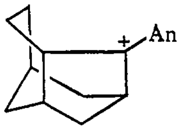
$$\begin{bmatrix} R^+ \\ \updownarrow \\ RH \end{bmatrix} \rightleftharpoons \begin{bmatrix} R_1^+ \\ \updownarrow \\ R_1H \end{bmatrix} \rightleftharpoons \begin{bmatrix} R_2^+ \\ \updownarrow \\ R_2H \end{bmatrix} \rightleftharpoons \begin{bmatrix} R_3^+ \\ \updownarrow \\ R_3H \end{bmatrix}$$

hydrocarbon and which is not encountered more than once in the sequence.



(6)

structure for the rearranged cation, XV, is that in which the anisyl-bearing carbon is the spinning one.



XV

It is important to recognize, however, that eq 6 is a disembodied representation of a very lively situation and offers in itself no answers to the problem of reconciling such mutual discrepancies as the observation of substantial intermolecular hydrogen scrambling in the rearrangement of Vb coupled with the *lack* of positional isomerism of the methyl group in the isomerization of Vd and the inability of Vc to get past the protoadamantane stage XV. Equation 6 does, however, serve as the basis on which various rational if speculative answers to these problems may be constructed. More importantly it emphasizes the principal point of interest in complex carbonium ion rearrangements of this type; namely, that one is interested in changes associated with labeling groups only to the extent that they reflect changes of the parent carbon skeleton. That is, the question of a mechanistic pathway is the question of the fate of the carbon frameworks involved.

Secondly, one is left with the distinct if qualitative impression that rearrangement of the twistane skeleton to the adamantane skeleton is a much more facile process than that of tetrahydrodicyclopentadiene (THDCP). Adamantanization of twistane *via* aluminum chloride in hexane is a facile and high-yield process while THDCP merely undergoes *end–oexo* isomerism under similar conditions.[25] The deuterium scrambling results (Table I) also imply the availability of a relatively straightforward route from the twistyl to the adamantyl cation. The quantitative interpretation that one may place on the numerical values of scrambling is limited, however, because of the inability to unravel the relative contribution of things such as the site of deuterium on the extent to which it scrambles, the role of 2-adamantyl cations (those initially produced) in intermolecular hydrogen scrambling, the ability of the adamantyl cation to exchange hydrogens with various rearranging species, etc. In one method of treating the data of Table I, ignoring subsequent exchange of the adamantyl cation and interpreting the exchange seen in terms of competitive completely intramolecular and completely randomizing rearrangements, between one-quarter and one-half of the molecules must rearrange in an intramolecular manner; twistyl-d_1 → adamantyl-d_1. This analysis is of course only exemplary but does emphasize the initial impression.

The problem of defining the relationship of twistane and THDCP to adamantane, particularly the fact that the evidence available suggests that twistane is "nearer" adamantane than is THDCP, is not a simple one. In rearrangements as complicated as these it does not necessarily follow, for example, that the shortest pathway between two skeletons should be particularly relevant to the actual pathway traversed.[26,27] Our proposal is that the sheer complexity of rearrangements of this type[27,28] allows one to classify and interpret them in terms of random rearrangement processes. The particular series in question is especially amenable to this type of analysis in that adamantane may be conceived of as a bottomless pit into which rearranging molecules may irreversibly fall. Our interpretation is contained in the following list of proposals.

(1) One may define a basis set of rearranging structures and an operation or operations relating them. In the simplest case (that one considered here) a single operation (cationic 1,2 shifts) is defined. (2) Application of the operation to the basis set results in definition of an undirected graph.[29] The nodes of the graph represent members of the basis set of structures while an edge connecting two nodes represents the ability to the two associated structures to interconvert by a single application of the operation. (3) This graph or one of its more mathematically tractable matrix representations constitutes a complete formal description (or map) of the rearranging system in question, and such graph theoretic ideas as diameter, radius, flow properties, distance between nodes, etc., may be exploited to clarify the relationships between members of the set. For example, the idea of nearness mentioned above is simply defined. (4) Within the limitation of the assumptions made one may translate the formal relationships into chemical predictions. Arguments may be developed to equate distance between nodes with rate and yield of interconversion of the members of the set.[30] One very important feature of this analysis is that it may be simply programmed on digital computers, since analysis of a basis set of structures as large as that of the adamantane isomers involves a substantial number of repetitive and very fatiguing operations.

Realization of the above proposals was accomplished as follows. The basis set of structures was defined as all possible ten-carbon tricyclic frameworks possessing all carbons in rings (no alkyl groups) and having no three- or four-membered rings, and is pictured in Figure 1.[31] This set was in turn derived from the set of all tricyclic graphs (Figure 2) whose nodes are of degree three or four by considering nodes to be bridgehead carbons and edges to be chains of methylene groups. The interconverting operation as programmed was chosen to represent the process in eq 7, each member of the basis set being rearranged in all possible ways *via* 1,2 shifts involving secondary and tertiary

$$R_1H \rightleftharpoons R_1^{\oplus} \rightleftharpoons R_2^{\oplus} \rightleftharpoons R_2H \qquad (7)$$

carbonium ions only. A particular structure (i) in the

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[25] P. von R. Schleyer and M. M. Donaldson, *J. Amer. Chem. Soc.*, **82**, 4645 (1960).

[26] J. D. Roberts, R. E. McMahon, and J. S. Hine, *ibid.*, **72**, 4237 (1950).

[27] F. E. Condon in "Catalysis," Vol. VI, P. H. Emmett, Ed., Reinhold Publishing Corp., New York, N. Y., 1958.

[28] N. C. Deno, *Progr. Phys. Org. Chem.*, **2**, 129 (1964).

[29] R. G. Busacker and T. L. Saaty, "Finite Graphs and Networks," McGraw-Hill Book Co., Inc., New York, N. Y., 1965.

[30] A similar but more generalized and mathematical graph approach to rearranging sets has been investigated by A. T. Balaban, D. Farcasiu, and R. Banica, *Rev. Roum. Chim.*, **11**, 1205 (1966).

[31] Stereoisomers of the structures were not distinguished. Note that those structures capable of existing as stereoisomers (**1**, **4**, **13**, and **14**) should be readily equilibrated with their stereoisomer under reversible carbonium ion forming conditions.

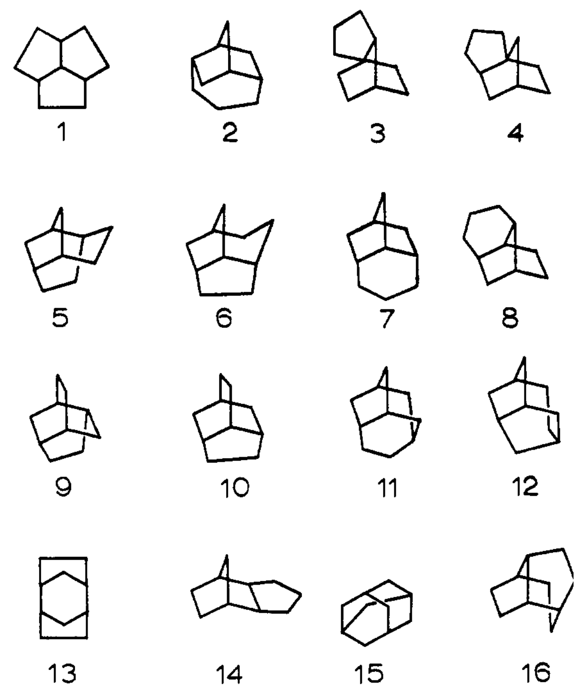

Figure 1. The basis set of C-10 tricyclic structures that contain all ten carbons within rings (no alkyl groups) and no three- or four-membered rings. Some of the structures (**1**, **4**, **13**, **14**) are stereoisomerically degenerate.

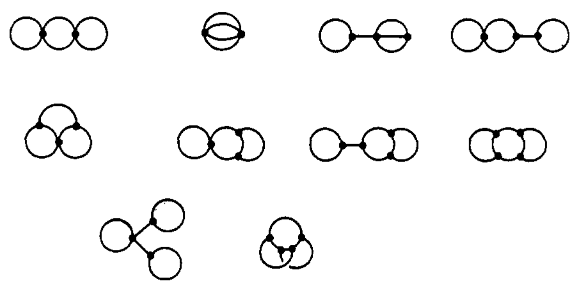

Figure 2. The set of tricyclic graphs whose nodes (bridgehead carbons) are of degree 3 or 4. Construction of Figure 1 from Figure 2 was accomplished by replacing edges in the graphs by chains of methylene groups.

basis set was converted[32] into a carbonium ion. The carbonium ion was then subjected to a 1,2 shift and the result of the shift, structure j, was inspected to see if it was a secondary or tertiary (not a primary) carbonium ion and, if so, if the generated structure was a member (j) of the basis set. If so, the adjacency matrix[29] elements were defined; $a_{ij} = a_{ji} = 1$. Repetition of this process over *all* 1,2 shifts of *all* carbonium ions of *all* structures of the basis set completely defines the rearrangement possibilities. The result of applying this to the adamantane set of structures wherein *no bridgehead carbonium ion restrictions* were imposed is pictured in Figure 3.

To what extent is this analysis anything more than a convenient summary of the rearrangement possibilities? This is an important question to answer since one wishes to relate such things as rates and yields of reactions to the graph. The assumptions implicit in the graph as presently defined, translated into kinetic and

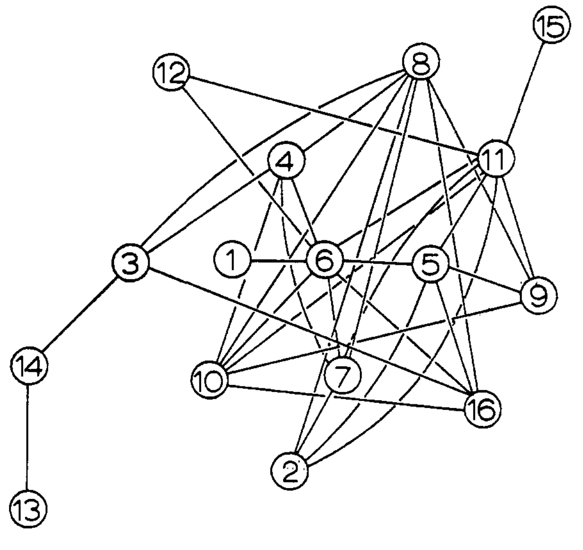

Figure 3. The bridgehead-free map of interconversions of the C-10 tricyclic carbon skeletons. The numbered nodes represent structures in Figure 1 and edges represent the ability of the two associated structures to interconvert by a single 1,2 shift. The lengths of the edges are of no significance.

thermodynamic terms, are that all rate constants are equal and that all structures are of equal energy. Energy differences between species and energy barriers separating them are ignored. The analysis also does not allow of the existence of well-established equilibria that proceed with the formal intermediacy of primary carbonium ions, such as that relating methylcyclopentane and cyclohexane. On the other hand, the basis set and the interconverting operation *do* seem to be reasonable models of the processes involved in aluminum chloride catalyzed isomerization of hydrocarbons and of rearranging carbonium ions in strongly acidic media. Processes involving or simulating primary carbonium ions[33,34] are probably not normally competitive in rate with those involving secondary and tertiary carbonium ions. One can, moreover, nicely rationalize our results on the basis of graphs of this type, and our inclination at present is to conclude that traversal of the graph's paths by a rearranging molecule presents sufficient problems, just from the point of view of surviving the journey, that the distance properties of the graph are of an importance comparable to considerations such as unequal rates of interconversion and unequal energies of species involved.

Consider the graph in Figure 3. One sees that certain of the structures such as adamantane (**15**) and **13** lie on the periphery while other such as **4** and **8** are more centrally located.[35] Twistane (**9**) is nearer adamantane (**15**) (two steps) than is tetrahydrodicyclopentadiene (**14**) (five steps). Adamantane and **13** are the two

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[32] "Converting" the structure into a carbonium ion merely involves designation of a secondary or tertiary carbon of the structure as being the site of reactivity.

[33] G. J. Karabatsos and F. M. Vane, *J. Amer. Chem. Soc.*, **85**, 729 (1963).

[34] G. A. Olah, J. M. Bollinger, C. A. Cupas, and J. Lukas, *ibid.*, **89**, 2692 (1967).

[35] The diameter of an undirected graph is defined (ref 29, p 56) as the greatest distance between any two nodes, distance being in turn defined as the minimum number of edges connecting them. The radius of a graph is the minimum maximum distance between any two nodes and the centers of the graph are those nodes whose maximum separation from other nodes is the radius. The diameter of the graph in Figure 4 is 6, its radius is 3, and its centers are structures **4** and **8**.

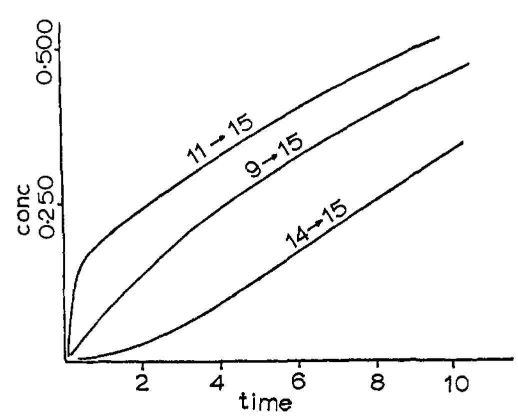


Figure 4. Formal time–concentration plot for reversible movement of structures across the map to admantane. The kinetic assumptions are in the text. The relatively efficient initial conversion of protoadamantane (**11** → **15**) arises from the initial partitioning of the protoadamantane skeleton between **2**, **5**, **6**, **7**, **9**, **10**, **12**, and (irreversibly) **15**.

skeletons farthest apart, being separated by the diameter of the graph.

The difficulties in considering a shortest pathway between **14** and **15** (for example, **14** → **3** → **4** → **7** → **11** → **15**) to be of physical significance are apparent. There are by count 2897 different pathways[24] between **14** and **15**, of which this particular pathway is but one. Not only might the conversion proceed by other pathways (there are nine other five-step paths between **14** and **15**) but one has every reason to expect it to do so. The per cent contribution of any one path to the over-all transformation should then be very small when the nodes are this far apart. When the path length is small, as in the conversion of **9** to adamantane, it should be of more importance in defining the actual course of the isomerization, but even here the 2196 other possible paths should as a whole contribute predominantly to this isomerization. On a random walk basis, the probability of the path **9** → **11** → **15** is only $^1/_{32}$.

In our opinion the best method of picturing distance relationships between nodes is in terms of rate processes. Letting all edges except that one leading to **15** represent reversible reactions with all rate constants unity, letting edge **11**–**15** represent an irreversible conversion to **15** with unit rate constant and starting with unit concentration of the starting material in question, the conversion of starting material into **15** may be expressed as a formal time–concentration plot and a time for half-reaction may be derived. Rate plots of this type for **9**, **11**, and **14** going to adamantane are in Figure 4 and the kinetic distance between these and **15**, **14** > **9** > **11**, is apparent. The half-times for formation of **15** from **14**, **9**, and **11** are 15.4, 11.3, and 9.1, respectively. The relatively small difference between these values is due to the difficulty of getting out of the central maze once a molecule has entered it.

Introduction of the idea of bridgehead carbonium ions into the interrelating operation produces a remarkable result. When the carbons circled in Figure 5 are not permitted to serve as carbonium ion sites, the adamantane graph is split into two (Figure 6). Edges **3**–**8**, **3**–**16**, **4**–**8**, **4**–**6**, **4**–**7**, and **4**–**10** are eliminated[36] so

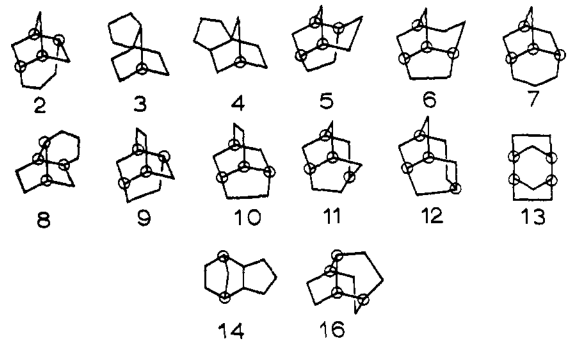


Figure 5. Bridgehead sites.

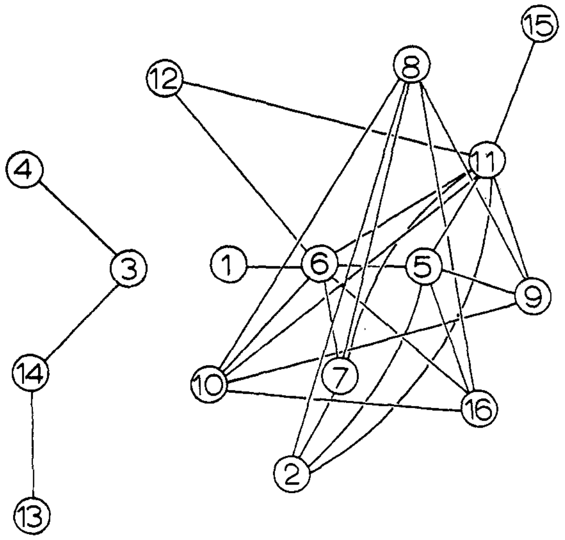
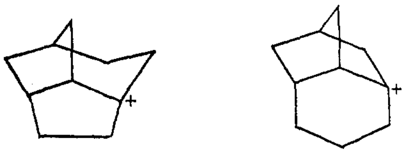


Figure 6. The modified map of adamantaneland wherein carbonium ions on sites circled in Figure 5 are *not* permitted. The effect of this restriction is to split Figure 3 into the two graphs shown. Interconversion of structures between these two sets can occur *only via* bridgehead carbonium ions.

that nodes **3**, **4**, **13**, and **14** define one graph and the remaining 12 nodes define another. One cannot, accordingly, get from **14** to adamantane without involving a bridgehead carbonium ion, whereas the twistane–adamantane interconversion does not suffer from this disability. This, of course, offers a ready and physically much more convincing explanation of the difference in ease of adamantanization of **9** and **14** than does Figure 3. If one eases the restrictions somewhat, permitting ions **6a** and **7a**[37] (Scheme V) that seem to be relatively acceptable bridgehead carbonium ions, edge **4**–**7** is reestablished as in (Scheme VI) and the graphs are rejoined. The same consider-

Scheme V



6a **7a**

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(36) These edges constitute a proper cut set, being the minimal number of edges required to separate nodes **3**, **4**, **13**, and **14** from the remainder.

(37) E. J. Corey and R. S. Glass, *J. Amer. Chem. Soc.*, **89**, 2600 (1967).

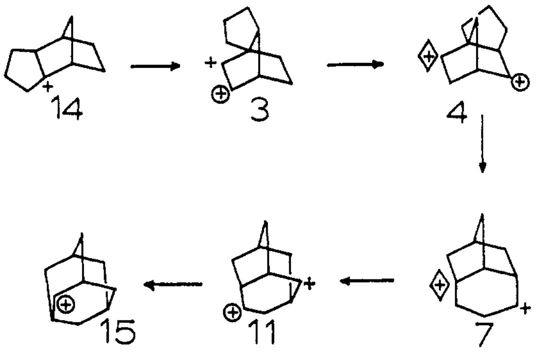
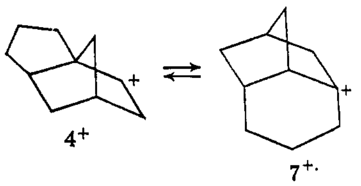


Figure 7. Shortest pathway between tetrahydrodicyclopentadiene and adamantane *via* 1,2 shifts. The carbonium ions involved in linking adjacent structures are of the same designation; *e.g.*, the last two structures are interconverted by way of the circled carbonium ions, the first two structures by uncircled, etc.

ations hold as above as far as distance between nodes is concerned, and one is left with the shortest pathway between THDCP and adamantane being **14–3–4–7–11–15** (Figure 7). The chemical interpretation of the intervention of bridgehead carbonium ions is apparent and the conclusion that twistane is closer to adamantane than is tetrahydrodicyclopentadiene is reinforced.

Scheme VI



It is interesting to compare this pathway with that suggested by Schleyer and Donaldson.[25] Their suggestion, **14** → **2** → **11** → **15,** suffered, as the authors pointed out, from a 1,3 alkyl shift (**14** → **2**). The contortions that the molecules must undergo to achieve this effect by 1,2 shifts is seen in the sequence **14** → **3** → **4** → **7** → **2** (Figure 8) now derivable from Figure 6. Given structure **2,** their proposed route in the shortest to adamantane.

Experimental Section[38]

5-Carbethoxybicyclo[2.2.2]oct-2-ene.[39] A mixture of 100 g (1.25 mol) of 1,3-cyclohexadiene,[40] 1 g of hydroquinone, and 130 g (1.3 mol) of freshly distilled ethyl acrylate were heated in a sealed tube at 150° for 16 hr. Distillation afforded 178 g (77% yield) of I: bp 107–110° (16 mm) (lit.[1] bp 105–107° (16–17 mm)); $n^{25}\mathrm{D}$ 1.4767 (lit.[41] 1.4772).

5-Hydroxymethylbicyclo[2.2.2]oct-2-ene. To a solution of 19 g of lithium aluminum hydride in 1 l. of ether in a 2-l., three-necked flask fitted with stirrer and condenser was added dropwise a solution of 150 g (0.83 mol) of the above ester in 200 ml of ether. After refluxing overnight the reaction mixture was hydrolyzed and worked up using Rochelle salts to afford 114 g (99% yield) of product, bp 45° (0.03 mm), 110–111 (10 mm).

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.11; H, 10.16.

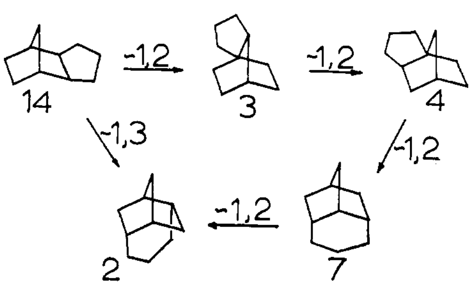


Figure 8. Comparison of the molecular change affected by Schleyer's 1,3 shift[25] and the rearrangements necessary to accomplish this result by a series of sequential 1,2 shifts.

5-Mesyloxymethylbicyclo[2.2.2]oct-2-ene. To a solution of 27.6 g (0.2 mol) of the above alcohol in 50 ml of dry pyridine at 0° was added with stirring 25.1 g (0.22 mol, 16.9 ml) of methanesulfonyl chloride. The reaction mixture was allowed to come to room temperature and stand there for 4 hr. After addition of 10 ml of water the reaction mixture was poured into water and extracted with ether. The ether extracts were washed with cold dilute hydrochloric acid, water, and saturated salt solution, dried over anhydrous sodium sulfate, and evaporated. Evaporative distillation at 70° (0.03 mm) gave 34 g (79%) of the methanesulfonate as a pale pink oil.

Anal. Calcd for $C_{10}H_{16}O_3S$: C, 55.54; H, 7.46; S, 14.80. Found: C, 55.63; H, 7.44; S, 14.71.

5-Cyanomethylbicyclo[2.2.2]oct-2-ene. The crude methanesulfonate from 62 g (0.45 mol) of 5-hydroxymethylbicyclo[2.2.2]-oct-2-ene was dissolved in 200 ml of dimethylformamide, 49 g (1 mol) of sodium cyanide and 1 g of sodium iodide were added, and the mixture was heated at 110° with stirring for 14 hr. The cooled reaction mixture was poured into water and the aqueous phase was extracted with hexane. The combined hexane extracts were washed with water and saturated salt solution, dried over anhydrous sodium sulfate, evaporated, and distilled to afford 53 g (80%) of nitrile, bp 114–119° (10 mm), $n^{24.3}\mathrm{D}$ 1.4953.

Anal. Calcd for $C_{16}H_{13}N$: C, 81.58; H, 8.90; N, 9.52. Found: C, 81.40; H, 9.08; N, 9.72.

5-Carboxymethylbicyclo[2.2.2]oct-2-ene (I). A mixture of 20.0 g (0.14 mol) of nitrile and 15 g of potassium hydroxide in 75 ml of ethylene glycol was heated with stirring under nitrogen to 155°. At this temperature ammonia evolution commenced and the nitrile dissolved. After stirring at 155° for 2 hr, the reaction mixture was cooled, diluted with 200 ml of water, and extracted once with ether. The aqueous layer was acidified and repeatedly extracted with ether. The combined ether extracts from the acidified aqueous phase were washed with water and saturated salt solution, dried over anhydrous sodium sulfate, and evaporated to afford 20.8 g (92% yield) of acid as mushy needles. Repeated recrystallization from pentane at −40° afforded a pure sample of the presumably *endo* isomer, mp 39.0–40.8°. The crude acid was used for iodolactonization.

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.98; H, 8.57.

***exo*-2-Iodo-*endo*-3-hydroxybicyclo[2.2.2]octane-*endo*-5-acetic Acid Lactone (Ia).**[42] The crude stereoisomeric mixture of acids (52.3 g) from 46.3 g of nitrile was suspended in 150 ml of water and dissolved by dropwise addition of 50% aqueous sodium hydroxide. Solid $NaHCO_3$ was added to saturation and a solution of 125 g (0.5 mol) of iodine and 120 g of potassium iodide in 400 ml of water was added. After stirring at 25° for 2 hr, the reaction mixture was decolorized by adding solid sodium bisulfite and extracted with ethyl acetate. The combined organic extracts were washed, dried, and evaporated. One recrystallization of the residue from ethyl acetate gave 62 g (68% yield from the nitrile) of iodolactone Ia, mp 127–129°. The analytical sample was obtained by repeated recrystallization from ethyl acetate as rods, mp 127–129°.

Anal. Calcd for $C_{10}H_{13}O_2I$: C, 41.11; H, 4.48; I, 43.44. Found: C, 41.31; H, 4.49; I, 42.85.

Application to bicyclo[2.2.2]oct-2-ene-5-carboxylic acid gave the corresponding γ-iodolactone, mp 80–81°.[43]

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(38) Nmr spectra were determined in deuteriochloroform solution and are referred to internal tetramethylsilane as δ 0 ppm. Mass spectra were determined at 150–250° on a CEC-103C mass spectrometer equipped with heated glass inlet system and modified for low-voltage spectra determination.

(39) W. R. Boehme and J. Nichols, U. S. Patent 2,942,026 (1960); *Chem. Abstr.*, **54,** 24464*i* (1960).

(40) C. A. Grob, H. Kny, and A. Gagneux, *Helv. Chim. Acta,* **40,** 130 (1957).

(41) R. Seka and O. Tramposch, *Ber.*, **75,** 1379 (1942).

(42) C. D. Ver Nooy and C. S. Rondestvedt, Jr., *J. Amer. Chem. Soc.*, 77, 3583 (1955).

(43) W. Boehme, E. Schepper, and W. E. Scharpf, *ibid.*, **80,** 5488 (1958).

***endo*-2-Hydroxybicyclo[2.2.2]octane-*endo*-6-acetic Acid Lactone.** A mixture of 29.2 g (0.1 mol) of iodolactone Ia, 10.0 g (14.4 ml, 0.1 mol) of triethylamine, and 1 g of platinum oxide in 500 ml of ethyl acetate in a Parr shaker under 40 psi of hydrogen rapidly (0.5 hr) took up 1 equiv of hydrogen. The reaction mixture was filtered and the filtrate was washed with dilute hydrochloric acid, saturated sodium bicarbonate solution, and saturated salt solution, dried over anhydrous sodium sulfate, and evaporated. One recrystallization of the residue from hexane–ethyl acetate gave 13.1 g (79% yield) of the lactone as rancid flakes, mp 58.5–64°. The analytical sample was prepared by repeated recrystallization from hexane–ethyl acetate as flakes, mp 67–69°.

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.13; H, 8.69.

Hydrogenolysis of the γ-iodolactone gave the γ-lactone, *endo*,-*endo*-2-hydroxybicyclo[2.2.2]octane-6-carboxylic acid lactone, mp 205–206°.

Anal. Calcd for $C_9H_{12}O_2$: C, 71.02; H, 7.95. Found: C, 71.32; H, 8.06.

***endo*,*endo*-2-Hydroxybicyclo[2.2.2]octane-6-carboxylic Acid Lactone.** A solution of 1.66 g (0.01 mol) of the δ-lactone in 25 ml of freshly distilled ethyl formate was added to a stirred slurry of 0.288 g (12 mmol, as suspension in oil) of sodium hydride in 25 ml of ether. The reaction mixture was heated at reflux for 2 hr and allowed to stir at 25° for 24 hr. Water was added and the organic layer was separated and washed with water. The combined aqueous layer was extracted with ether and acidified. The precipitated solid was taken up in ether and the ether solution was washed, dried, and evaporated to afford 1.55 g (80% yield) of the hydroxymethylene δ-lactone as leaflets, mp 106–110°. The analytical sample was prepared by repeated recrystallization from hexane–ethyl acetate as leaflets, mp 109–110°.

Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 68.14; H, 7.42.

A solution of 900 mg (4.64 mmol) of the hydroxymethylene lactone in 50 ml of acetic acid and 10 ml of acetic anhydride was ozonized, 5 ml of 30% hydrogen peroxide was added, and the mixture was allowed to stand at 25° for 14 hr. A pinch of 5% palladium on charcoal was added and solvents were removed at 40° under reduced pressure. The residue was diluted with ether and filtered, and the filtrate was concentrated to afford 502 mg (71% yield) of the desired lactone, mp 199–203°. One recrystallization from hexane–ethyl acetate gave 140 mg, mp 204.5–205.5° (sealed capillary). A mixture melting point with an authentic sample of the γ-lactone of mp 205–206.5° as prepared by hydrogenation of the iodolactone was 205.5–206.5°, and their infrared spectra were identical.

***endo*,*endo*-2-Hydroxy-6-(2-hydroxyethyl)bicyclo[2.2.2]octane.** Reduction of 1.95 g (11.7 mmol) of the δ-lactone with lithium aluminum hydride in refluxing ether gave on working up with Rochelle salt and after one recrystallization from hexane–ethyl acetate 1.73 g (87% yield) of diol, mp 79–82°. The analytical sample was prepared as plates, mp 82.2–83.1°.

Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.77; H, 10.66.

2-Oxo-6-*endo*-(2-mesyloxyethyl)bicyclo[2.2.2]octane. To a solution of 6.43 g (37.9 mmol) of the above diol in 25 ml of dry pyridine at 5° was added dropwise with stirring 4.79 g (42 mmol, 3.24 ml) of methanesulfonyl chloride. The mixture was allowed to stand at 3° for 14 hr, 10 ml of water was added, and the mixture was stirred at 0° for 0.5 hr. The mixture was poured into ice–dilute hydrochloric acid and the aqueous layer was extracted with five 100-ml portions of ether. The ether extracts were washed with water and brine, dried over anhydrous sodium sulfate, and concentrated under reduced pressure at 0° to 100 ml. While the ether was stirred at 25° a solution of 3.98 g of sodium dichromate dihydrate and 2.98 ml of concentrated sulfuric acid in 20 ml of water[44] was added over 0.5 hr. The green-brown two-phase system was stirred at 25° for 14 hr. The ether layer was separated, washed, dried, and evaporated to afford 8.1 g (87% yield from diol) of yellow crystals, mp 50–59°. The analytical sample was prepared by recrystallization from hexane–ethyl acetate as sheaves of spears, mp 62.8–64.3°.

Anal. Calcd for $C_{11}H_{18}O_4S$: C, 53.64; H, 7.36; S, 13.02. Found: C, 53.81; H, 6.97; S, 13.11.

Twistanone. A mixture of 7.4 g (55 mmol) of ketomesylate and 2.5 g of sodium hydride in 100 ml of dimethylformamide were heated at 60° under nitrogen with stirring for 8 hr. The unreacted sodium hydride was destroyed by dropwise addition of methanol and the reaction mixture was poured into 600 ml of water. The aqueous layer was extracted with pentane and the combined pentane extracts were washed with cold 5% hydrochloric acid and saturated salt solution, dried over anhydrous sodium sulfate, and evaporated to afford 3.57 g of crystals, mp 187–194°. Continuous extraction of the aqueous layer with pentane for 14 hr gave an additional 452 mg (total yield 89%) of yellow crystals. One recrystallization from pentane at −70° raised the melting point to 193–197°. The analytical sample was prepared by repeated recrystallization from pentane at −70° and sublimation as waxy needles, mp 198–199.5°.

Anal. Calcd for $C_{10}H_{14}O$: C, 79.95; H, 9.39. Found: C, 79.79; H, 9.56.

Reaction of 53 mg of twistanone with 2,4-dinitrophenylhydrazine reagent for 2 days at 25° gave 103 mg of dinitrophenylhydrazone as flakes, mp 183.5–184°, raised to 186–187° on recrystallization from ethyl acetate.

Anal. Calcd for $C_{16}H_{18}O_4N_4$: C, 58.17; H, 5.49; N, 16.96. Found: C, 58.06; H, 5.38; N, 16.95.

Twistane. A mixture of 0.300 g (1.98 mol) of twistanone, 1.0 ml (20 mmol) of anhydrous hydrazine, and six drops of acetic acid in 10 ml of diethylene glycol was heated under nitrogen at 90° for 24 hr. Potassium hydroxide (1 g) was then added and with stirring the temperature was raised to 190° (oil bath) for 6 hr and 210° for 4 hr. Considerable amounts of white solid sublimed into the cooler upper parts of the apparatus but no effort was made to remove it while heating. After cooling the reaction mixture was poured into water and the apparatus and aqueous layer were washed and extracted, respectively, with pentane. The combined pentane washes were washed with saturated salt solution, dried over anhydrous sodium sulfate, and concentrated by distillation through a spinning-band column. Final removal of solvent was effected by distillation at −78° (0.1 mm). The residue was sublimed (40° (0.760 mm)) to afford 139 mg (52% yield) of twistane as fluffy needles, mp 162–165°. Repeated sublimation afforded the analytical sample, mp 163–164.5°.

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 87.92; H, 12.00.

Isomerization of Twistane to Adamantane. A mixture of 50 mg of aluminum chloride and a solution of 5 mg of twistane in 1.0 ml of purified hexane in a sealed tube under nitrogen was held at 70° for 2 hr. Quantitative glpc analysis indicated an 85% yield of adamantane and a 5% yield of twistane to be present. Repetition on a 50-mg scale and trapping of the glpc peak which corresponded in retention time to adamantane afforded this hydrocarbon, mp 267–269° (mmp 267–269°), having an identical infrared spectrum with the authentic material. Except for an unidentified short retention time peak (2 min *vs.* 13 min for adamantane) only adamantane and unreacted twistane could be identified in this isomerization.

Twistanol (Va). A solution of 200 mg of lithium aluminum hydride and 400 mg of twistanone in 50 ml of dry ether was refluxed for 5 hr and worked up with Rochelle salts to afford, after sublimation (60° (15 mm)), 350 mg (86% yield) of twistanol, mp 214–216°. In the nmr spectrum (CCl_4) the *CHOH* appeared as a doublet, *J* = 4.8 cps, at δ 3.85. The analytical sample was prepared by recrystallization from pentane–ether as needles, mp 214.4–216.4°.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.90; H, 10.67.

Reduction of 553 mg of twistanone in 10 ml of absolute ethanol by portionwise addition of 2 g of sodium gave, after one recrystallization from pentane, 400 mg (72% yield) of twistanol, mp 212.5–214.5, mmp 212–214°. Recrystallization of the mother liquors afforded an additional 35 mg (6% yield) of alcohol, mp 210–213°.

Reduction of twistanone with lithium aluminum deuteride gave α-deuteriotwistanol (Vb) in 71% yield, mp 214–216°. Its structure was confirmed by nmr and its mass spectrum.

Attempted Detection of Twistane in the Mother Liquors from the Preparation of Adamantane from Tetrahydrodicyclopentadiene. Examination by glpc on packed columns of the mother liquors resulting from the Schleyer synthesis of adamantane[25] revealed that there was a small peak, eluted shortly after adamantane and *endo*-tetrahydrodicyclopentadiene, that corresponded exactly in retention time on several columns (SE-30, 110°; Apiezon L, 112°; SF-96, 132°) to twistane. Resolution was sufficient to detect approximately 20 discrete peaks in the adamantane mother liquors. Sufficient material was trapped, using the latter column, to permit rechromatography on a capillary column (150 ft, Ucon Polar, 50°). Under these conditions the retention time was clearly distinct from

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[44] H. C. Brown and C. P. Garg, *J. Amer. Chem. Soc.*, 83, 2952 (1961).

that of twistane. Furthermore examination of the adamantane mother liquors with capillary vpc showed no detectable peak corresponding in retention time to twistane. The peak trapped from the column was identified by mass spectrometry and glpc as 1-methyladamantane: mass spectrum, *m/e* 150 (parent), 135 (P − CH_3, base), 93 ($C_7H_9^+$).

Isomerization of Twistanol to Adamantanol in Antimony Pentafluoride–Sulfur Dioxide. In a typical reaction 30 mg (0.2 mmol) of twistanol was placed in a dry three-necked flask fitted with a Dry Ice–acetone condenser with drying tube, gas inlet, magnetic stirring bar, and rubber septum, and cooled in a Dry Ice–acetone bath. Sulfur dioxide (10 ml) was distilled in, the apparatus was placed under a positive pressure of nitrogen, and with stirring 0.8 ml of antimony pentafluoride was injected over a 2-min period. The reaction mixture was stirred at −78° for 1 min and then poured into 50 ml of ice water that was being vigorously agitated with a "vibromischer."[45] After stirring for 30 min solid sodium carbonate was added to neutrality and the mixture was extracted with four 50-ml portions of ether. The combined ether extracts were washed with saturated salt solution, dried over anhydrous sodium sulfate, and concentrated by distillation. Glpc analysis showed 1-adamantanol to be the only volatile product present (92% yield). Recrystallization of the crude product from hexane afforded 1-adamantanol, mp 282–284°, mmp 282–284°. The infrared spectrum ($CHCl_3$) was identical with that of an authentic sample.

In a typical reaction with deuterated substrate 150 mg (1.0 mmol) of twistanol-*d* (95.9% d_1, 4.1% d_0) was stirred with 1.5 ml of antimony pentafluoride in 25 ml of sulfur dioxide at −78° for 20 min. Work-up as above afforded after sublimation 122 mg (81% yield) of 1-adamantanol-d_x, mp 282–284°: 23.8% d_0, 59.0% d_1, 15.5% d_2, 1.5% d_3, 0.3% d_4; total deuterium content, 0.95 D/molecule.

Isomerization of Twistanol-d_1 in Antimony Pentafluoride–Fluorosulfonic Acid in Sulfur Dioxide. A solution of 30 mg (0.20 mmol) of twistanol-d_1 (95.9% d_1, 4.1% d_0) in 10 ml of sulfur dioxide was added to a mixture of 2.4 ml of fluorosulfonic acid and 0.8 ml of antimony pentafluoride (both freshly distilled) cooled to −78°. The resulting solution was stirred at −78° for 30 min and then poured into 50 ml of ice water with vigorous stirring. Conventional work-up afforded 90% yield of adamantanol-*d* whose deuterium content was 23.9% d_0, 57.7% d_1, 16.3% d_2, 1.7% d_3, 0.4% d_4.

Lithium Aluminum Hydride–Tributyltin Chloride Reduction of 1,3,5,7-Tetrabromoadamantane. To a slurry of 400 mg (11 mg equiv) of lithium aluminum deuteride (putative 98.5% deuterium content) in 35 ml of dry ether was added a solution of 1.2 g (3.2 mmol) of tributyltin chloride in 5 ml of ether. To this was then added in one portion 2 g (4.4 mmol) of tetrabromoadamantane and the resulting mixture was stirred and heated under reflux under nitrogen for 24 hr. After standing at room temperature for an additional 10 hr, vpc analysis showed adamantane and tributyltin hydride as the only volatile products other than solvent. Deuterium oxide (4 ml) was added slowly to the reaction mixture, the mixture was poured into 30 ml of water, and the aqueous layer was extracted with four 40-ml portions of pentane. The combined pentane extracts were washed with saturated salt solution, dried over anhydrous sodium sulfate, and concentrated by distillation on a spinning-band column (~30 theoretical plates). The concentrate was adsorbed on a column of 50 g of alumina and eluted with hexane to afford 568 mg (92% yield) of adamantane-d_4 (95.4% d_4, 4.6% d_3 by low-voltage mass spectrometry), mp 265–267.5°. The nmr spectrum showed a single at δ 1.75.

The adamantane-d_4 from above, 568 mg, was brominated according to the procedure of Stetter.[46] The crude product, 810 mg (92% yield), was adsorbed on a column of 50 g of alumina and eluted with hexane to afford 692 mg (78.5% yield) of 1-bromoadamantane-d_3, mp 114–116°. This (617 mg) was dissolved in 3 ml of dioxane in a 25-ml, round-bottomed flask, 1 ml of water and 0.5 g of silver nitrate were added, and the resulting mixture was heated under reflux with stirring for 3 hr. The reaction mixture was worked up to afford directly 408 mg (93% yield) of 1-adamantanol-d_3, mp 283–284°. A low-voltage mass spectrum showed its deuterium content to be 96.8% d_3, 3.2% d_2. Its nmr spectrum showed absorption at δ 1.71, 1.62, and 1.44 but very little at δ 2.1 (bridgehead methine).

Ionization of Adamantanol-d_3. To a solution of 30 mg of 1-adamantanol-d_3 (97.8% d_3) in 10 ml of sulfur dioxide at −78° was added 2.4 ml of fluorosulfonic acid and 0.8 ml of antimony trifluoride. After stirring at −78° for 30 min the reaction mixture was poured into ice water with vigorous stirring and worked up to afford, after sublimation, 25 mg (83% yield) of adamantanol-d_x, mp 282–283°. Mass spectral analysis showed its deuterium content to be 96.8% d_3 and 3.2% d_2. Examination of its nmr spectrum showed the intensity of the absorbtion in the region of δ 2.1 to be negligible.

Ionization of a Mixture of Adamantanol-d_3 and Adamantanol-d_0. To a solution of 20 mg of adamantanol-d_0 and 20.4 mg of adamantanol-d_3 (97.8% d_3) in 10 ml of sulfur dioxide was added, with stirring at −78°, 2.4 ml of fluorosulfonic acid and 0.8 ml of antimony pentafluoride. After stirring at −78° for 30 min the reaction mixture was poured into ice water and worked up as above to afford after sublimation 30 mg (75% yield) of adamantanol, mp 282–283°. Low-voltage mass spectral analysis of the alcohol showed its deuterium content to be 13.4% d_0, 38.2% d_1, 36.5% d_2, 11.9% d_3. The nmr spectrum of the alcohol showed absorption at δ 2.13 in an intensity corresponding to 1.5 hydrogen relative to intensity corresponding to 13 hydrogens at higher field.

2-*p*-Anisyltricyclo[4.4.0.0^{3,8}]decan-2-ol (Anisyltwistanol (Vc)). To a solution of 4.3 ml (34 mmol) of *p*-bromoanisole in 15 ml of ether contained in a 50-ml, round-bottomed flask fitted with a condenser with nitrogen inlet, dropping funnel, and rubber septum was added dropwise 15 ml (34 mmol) of a solution of *n*-butyllithium in hexane (2.24 *M*). After stirring at 0° for 30 min a solution of 500 mg (3.3 mmol) of twistanone in 10 ml of ether was added dropwise over a period of 10 min. The reaction mixture was then stirred at room temperature for 45 min, poured into water, and worked up. The crude product was adsorbed on a column of 50 g of alumina and eluted with hexane. After initial elution of the excess *p*-bromoanisole there was eluted 793 mg (92% yield) of anisyltwistanol, mp 133–135°. The analytical sample was prepared by repeated recrystallization from ethyl acetate–hexane, mp 137–138.5°.

Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 78.74; H, 8.43.

Oxidation of Anisyltwistanol Protoadamantanone (IX). To a mixture of 6 ml of glacial acetic acid, 0.6 ml of concentrated sulfuric acid, and 1 ml of water at 0° was added 400 mg of anisyltwistanol (Vc). After stirring for 5 min at 0°, 600 mg of sodium dichromate dihydrate was added in one portion. The resulting dark solution was stirred at 25° for 20 min, 20 ml of water was added, and the aqueous layer was extracted with three 30-ml portions of ether. The combined ether extracts were washed successively with 5% sodium hydroxide solution and saturated salt solution, dried over anhydrous sodium sulfate, and evaporated. Sublimation of the residue afforded 77 mg (33% yield) of a camphoraceous solid (IX), mp 239–241°. Recrystallization from hexane at −78° raised the mp to 241–243°. The ketone was homogeneous by capillary glpc (Ucon Polar column, 150 ft, 130°) and readily separable under these conditions from twistanone. Its infrared spectrum (Perkin-Elmer Model 421 grating spectrophotometer) exhibited $\lambda_{max}^{CCl_4}$ 5.75 μ, its nmr spectrum exhibited broad absorption in the region τ 7.5–9.0, and its mass spectrum showed a parent ion at *m/e* 150. The analytical sample, mp 241–243°, was prepared by repeated sublimation.

Anal. Calcd for $C_{10}H_{14}O$: C, 79.96; H, 9.39. Found: C, 79.77; H, 9.36.

Oxidation of VIII under the same conditions afforded the same ketone as shown by mixture melting point and comparison of infrared spectra.

Reaction of IX with ethanedithiol in the presence of boron trifluoride etherate afforded a 66% yield of chromatographically pure dithioketal, an oil. Its mass spectrum was uninformative[47] as to the nature of its carbon skeleton, exhibiting intense peaks at *m/e* 226 (P), 198 (P − C_2H_4), and 91 (base).

Heating a mixture of 10 mg of IX, 0.5 ml of deuterium oxide, 0.2 ml of dioxane, and 6 mg of potassium carbonate in a sealed tube at 100° for 12 hr led to no detectable (mass spectrometry) deuterium incorporation into the ketone. Under these conditions camphor was deuterated to the extent of 83% d_2, 17% d_1.

Isomerization of Anisyltwistanol in Sulfuric Acid. To a 25-ml, round-bottomed flask containing 4 ml of 96% sulfuric acid at room temperature was added in one portion 100 mg (0.39 mmol) of anisyltwistanol. The resulting yellow solution was stirred for 15 min and then poured into 25 ml of ice water. To the aqueous layer was added solid sodium carbonate until effervescence ceased,

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(45) Model E-1, A. G. für Chemie-Apparatabau, Zurich, Switzerland.

(46) H. Stetter, M. Schwarz, and A. Hirschhorn, *Chem. Ber.*, 92, 1629 (1959).

(47) G. v. Mutzenbecher, Z. Pelah, D. H. Williams, H. Budzikiewicz, and C. Djerassi, *Steroids*, 2, 475 (1963).

and the aqueous layer was then extracted with three 30-ml portions of methylene chloride. The combined organic extracts were washed with saturated salt solution, dried over anhydrous sodium sulfate, and evaporated to afford 90 mg of an oil that crystallized on standing. This was adsorbed on a column of 50 g of alumina. Elution with hexane afforded 77 mg (77% yield) of isoanisyltwistanol (VIII). Two recrystallizations from hexane afforded 62 mg (62% yield) of VIII, mp 110–112°. The analytical sample was prepared by repeated recrystallization from hexane, mp 110.5–112°.

Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 78.93; H, 8.60.

The nmr spectrum exhibited signals expected for the *p*-anisyl group: an AB quartet centered around δ 7.15 (4 H) and a singlet (methoxy, 3 H) at δ 3.80; and a complex band in the region δ 1.0–2.8 (15 H). The mass spectrum showed peaks at *m/e* 258 (P), 240 ($P - H_2O$), and 121 (methoxytropylium).

Ultraviolet spectra of both Vc and VIII were determined in 96% sulfuric acid. The same absorption curve, λ_{max} 381 mμ, with a shoulder at 366 mμ was found for both alcohols. On standing for several hours the long-wavelength absorbtions decreased and a peak at 230 mμ appeared. The molar extinction coefficients for the 381- and 366-mμ bands, 4.5×10^4 and 3.6×10^4, respectively, were determined by adding dioxane solutions of the alcohols to sulfuric acid to make a resulting 1% (v/v) solution of dioxane in sulfuric acid.

Reduction of Protoadamantanone. Ketone IX, 70 mg (0.46 mmol), was reduced with lithium aluminum hydride to afford after work-up, sublimation, and one recrystallization from hexane 65 mg (92%) of alcohol XI, mp 288–289°. Alcohol XI was homogeneous by glpc. The nmr spectrum (60 and 100 Mc) showed the *C*HOH as the X part of an ABX pattern, a double doublet, $J_{AX} = 9.0$ and $J_{BX} = 4.5$ cps at δ 4.22. The mass spectrum showed strong peaks at *m/e* 152 (P), 134 ($P - H_2O$), and 79 (base). The analytical sample was prepared by repeated recrystallizations from hexane, mp 288–289°.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.74; H, 11.09. Found: C, 78.90; H, 10.59.

Protoadamantane. To a solution of 40 mg (0.27 mmol) of IX in 4 ml of freshly distilled triethylene glycol in a 10-ml, two-necked flask fitted with a condenser and nitrogen inlet was added 0.25 ml (5 mmol) of hydrazine hydrate and four drops of glacial acetic acid. The mixture was then heated at 80–90° under nitrogen for 24 hr. At the end of this time the reflux condenser was replaced by a Claisen head attached to a condenser and a Dry Ice cooled receiving flask, 0.5 g of potassium hydroxide was added, and with stirring the reaction mixture was heated to 190° and held at 190–210° for 6 hr, during which time a white sublimate appeared in the Claisen head. The reaction mixture was cooled and the apparatus was washed with water and pentane. The organic layer was separated and the aqueous layer was further extracted with pentane. The combined pentane washes were washed with saturated salt solution, dried over anhydrous sodium sulfate, and concentrated by careful distillation. Quantitative glpc analysis indicated a single product to have been formed in 74% yield. This product was collected from the glpc column as a white solid, mp 210.5–212°. The mass spectrum showed strong peaks at *m/e* 136 (P), 94 ($P - C_3H_6$), and 79 ($P - C_4H_9$) and the infrared spectrum and vpc retention time were clearly distinguishable from those of adamantane, twistane, and Krantz's hydrocarbon III.[8] The analytical sample was prepared by repeated glpc (SE-30, 110°).

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 87.91; H, 11.86.

Protoadamantane from 8,9-Dehydroadamantan-2-one. To a stirred slurry of 30 mg (4.4 mg-atom) of lithium in 30 ml of refluxing ammonia (distilled from sodium) was added dropwise over 5 min a solution of 48 mg (0.32 mmol) of dehydroadamantanone[21] in 10 ml of ether. The reaction mixture was stirred at reflux for 1 hr and 470 mg of solid ammonium chloride was then added. The ammonia was allowed to evaporate, 50-ml portions each of ether and water were added to the residue, and the layers were separated. The aqueous layer was then extracted with three 40-ml portions of ether and the combined ether extracts were washed with saturated salt solution, dried over anhydrous sodium sulfate, and concentrated by distillation to a volume of 6 ml. Capillary vpc (Ucon Polar, 150 ft, 130°) indicated the absence of starting material, the presence of one peak in the "ketone region" (19.8 min, adamantanone at 18.9 min), and two peaks in the "alcohol region" (30.0 and 32.5 min, 2-adamantanol at 27.4 min). The alcohol:ketone ratio was 64:36. The mixture was oxidized by the procedure of Brown,[44] using 0.16 mol of sodium dichromate dihydrate and 0.04 ml of concentrated sulfuric acid in 0.5 ml of water. Working up the reaction mixture and sublimation (50° (16 mm)) of the crude product afforded 30 mg (62% yield) of a ketone, mp 222–225°. Recrystallization from hexane at −78° raised the melting point to 226–227°. The infrared spectrum showed $\lambda_{max}^{CCl_4}$ 5.82 μ and the mass spectrum showed strong peaks at *m/e* 150 (P) and 79 (base). Reduction of 25 mg of this ketone was carried out exactly as was the reduction of IX to afford a 55% yield (estimated by vpc) of protoadamantane. Repeated glpc and trapping of the peak corresponding to protoadamantane afforded X, mp 210–212°. The infrared spectra of this hydrocarbon and that prepared *via* the anisyltwistanol route were identical as were the nmr spectra, vpc retention times on two capillary columns, and mass spectra. The mixture melting point was 210–212°.

Methyltwistanol (Vd) was prepared by addition of an excess of methyllithium in hexane to a solution of 200 mg of twistanone in ether. Working up and sublimation of the crude product at 50° (15 mm) afforded 180 mg (81% yield) of product, mp 170–173°. Recrystallization at −78° from hexane afforded 140 mg of Vd, mp 174–176°. The mass spectrum showed *m/e* 166 (P), 148 ($P - H_2O$), and 91 (base). The analytical sample was prepared by repeated recrystallization from hexane at −78°, mp 175.5–177°.

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.10; H, 10.58.

Addition of methyllithium to 2-adamantanone afforded in the same manner an 82% yield of 2-methyl-2-adamantanol, mp 210.5–212° (lit.[48] mp 207.8–209°), whose mass spectrum showed intense peaks at *m/e* 166 (P) and 151 ($P - CH_3$).

Isomerization of Vd. A solution of 75 mg (0.45 mmol) of Vd in 10 ml of sulfur dioxide was allowed to react with 0.8 ml of antimony pentafluoride for 30 min at −78°. Sublimation after work-up afforded 30 mg (40% yield) of crude product, mp 175–180°, whose vpc showed it to be primarily a single product. Trapping of the major peak from the glpc (SF-96, 175°) afforded 20 mg (27% yield) of 2-methyl-2-adamantanol, mp (from hexane) 210–212°. The mixture melting point with a sample of 2-methyl-2-adamantanol prepared as above was 210–212°. Their identity was further established by comparison of their infrared (CCl_4), nmr, and mass spectra.

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.15; H, 10.76.

Isomerization of a Mixture of 3-Methyl-1-adamantanol and Methyltwistanol. A solution of 19.5 mg of 3-methyl-1-adamantanol and 16.5 mg of Vd (54:46 ratio) in 10 ml of sulfur dioxide was allowed to react with 0.5 ml of antimony pentafluoride and 1.5 ml of fluorosulfonic acid at −78° for 30 min. The reaction mixture was worked up in the standard manner and analyzed by glpc. The ratio of 3-methyl-1-adamantanol to 2-methyl-2-adamantanol was 59:41.

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[48] P. von R. Schleyer and R. D. Nicholas, *J. Amer. Chem. Soc.*, **83**, 182 (1961).