The Chemistry of Protoadamantane. IV. Preparation and Solvolysis of Secondary 4-Protoadamantyl Esters. The Relationship to the Solvolysis of 2-Adamantyl Derivatives[1]

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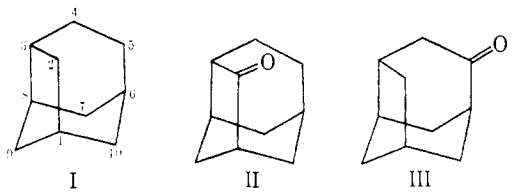
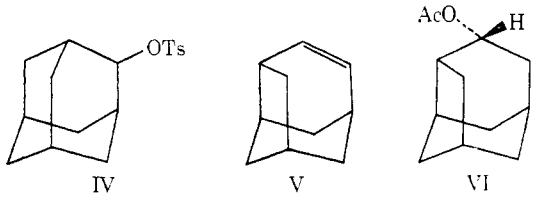
Abstract: The synthesis of 4-protoadamantyl derivatives, the determination of their configuration and conformation, and their cationic rearrangements and solvolytic behavior are described. Nitrous acid deamination of 2-amino-1-adamantanol (VIII) gave 4-protoadamantanone (VII) in high yield; reduction of this ketone gave a mixture of exo (X) and endo (XI) alcohols from which other derivatives could be prepared. Alternatively, oxymercuration–reduction of protoadamantene (V) affords a good route to 4-*exo*-protoadamantanol (X). Protonic acids add to protoadamantene (V) to give only 2-adamantyl products. Spectral evidence and computer conformational analysis calculations on a variety of protoadamantane derivatives indicate that the two-carbon (C-4,5) bridge is twisted, with a dihedral angle of ~25–30° between the 4-exo and 5-exo positions, and ~145–150° between the 4-exo and 5-endo positions. 4-*exo*-Protoadamantyl derivatives are much more reactive than their endo counterparts due to their direct conversion to the 2-adamantyl system with relief of ring strain. Under conditions of kinetic control, acetolysis of 2-adamantyl tosylate (IV) gives 0.4% of 4-*exo*-protoadamantyl acetate, showing the interrelationship between the two systems. A highly unsymmetrical, weakly bridged intermediate (XIX) is consistent with this behavior. Our previous conclusion that the 2-adamantyl system is essentially a limiting k_c-type system is essentially unaltered by this possibility of very weak bridging. The 4-*endo*-protoadamantyl system undergoes a degenerate rearrangement, as shown by deuterium scrambling, more rapidly than "leakage" to 2-adamantyl products which, of course, are thermodynamically much more stable. Another bridged ion, XX, is a possible intermediate, but its propensity toward leakage indicates that it is not a very stable species. Many rearrangements apparently involve such 4-protoadamantyl–4-protoadamantyl interconversion steps, *e.g.*, the sulfuric acid catalyzed rearrangement of 4-protoadamantanone (VII) to adamantanone (IX). With $AlBr_3$, protoadamantane (I) is easily converted to adamantane.

Despite its close structural and mechanistic relationship to adamantane,[3] tricyclo[4.3.1.0^{3,8}]decane (I) and its derivatives remained unreported until 1968. By means of a Favorskii ring contraction of a dibromohomoadamantanedione, followed by removal of functional groups, Vogt first synthesized the parent hydrocarbon (I) for which the trivial name "isoadamantane" was proposed.[4] Sulfuric acid rearrangement of 2-anisyl-2-twistanol gave an isomeric tertiary alcohol which could be oxidized to tricyclo[4.3.1.0^{3,8}]decan-2-one (II).[5] The corresponding 5-one (III) was prepared by reduction of dehydroadamantanone;[6] Wolff–Kischner reduction of either of these ketones gave I.[5] Noting that I was the penultimate tricyclic $C_{10}H_{16}$ isomer on the rearrangement graph leading to adamantane, Whitlock and Siefken proposed the trivial name "protoadamantane" for I.[5] Since many "isoadamantanes" are possible,[5] the more specific protoadamantane designation seems to us preferable for I.



I II III

Although the adamantane skeleton was long regarded as being practically inviolate,[3,5] Sinnot, Storesund, and Whiting discovered that buffered acetolysis of 2-adamantyl tosylate (IV) gave a small amount (0.3–0.5%) of one of the epimeric 4-protoadamantyl acetates; a larger amount of this ester as well as protoadamantene (V) were produced on deamination.[7] We have confirmed and extended these observations; Whiting's ester proves to have the exo configuration (VI).[1a,2b] This subject is treated at length in the present paper.



IV V VI

More recently, a number of routes to protoadamantane derivatives have been developed.[1a,8–13] In fact, 4-

(1) (a) Preliminary accounts of this work were presented at the 159th National Meeting of the American Chemical Society, Houston, Texas, Feb 1970, Abstract PETR-040, and were published as the first paper of this series: D. Lenoir and P. v. R. Schleyer, *Chem. Commun.*, 941 (1970). (b) Paper II: D. Lenoir, P. v. R. Schleyer, C. A. Cupas, and W. E. Heyd, *ibid.*, 26 (1971). (c) Paper III: D. Lenoir, R. Glaser, P. Mison, and P. v. R. Schleyer, *J. Org. Chem.*, **36**, 1821 (1971).

(2) (a) National Institutes of Health International Postdoctoral Fellow, 1969–1970; (b) A.B. Thesis, Princeton University, 1970.

(3) Reviews: R. C. Fort, Jr., and P. v. R. Schleyer, *Chem. Rev.*, **64**, 277 (1964); R. C. Bingham, Ph.D. Thesis, Princeton University, 1970; R. C. Bingham and P. v. R. Schleyer, *Fortschr. Chem. Forsch.*, **18**, 1 (1971); E. M. Engler and P. v. R. Schleyer, *MTP (Med. Tech. Publ. Co.) Int. Rev. Sci., Org. Chem., Ser. 1*, **5**, 239 (1973).

(4) B. R. Vogt, *Tetrahedron Lett.*, 1575 (1968).

(5) H. W. Whitlock, Jr., and M. W. Siefken, *J. Amer. Chem. Soc.*, **90**, 4929 (1968). A more detailed analysis of the adamantane rearrangement, following the graphical method outlined in this paper, is now available: E. M. Engler, M. Farcasiu, A. Sevin, J. M. Cense, and P. v. R. Schleyer, *ibid.*, **95**, 5769 (1973).

(6) J. E. Baldwin and W. D. Foglesong, *J. Amer. Chem. Soc.*, **90**, 4303 (1968).

(7) M. S. Sinnot, H. J. Storesund, and M. C. Whiting, *Chem. Commun.*, 1000 (1969).

(8) J. R. Alford and M. A. McKervey, *Chem. Commun.*, 615 (1970).

protoadamantanone (VII)[1a,8,9,12] and protoadamantene (V)[9,10,13] have become such readily available compounds that they can be used to prepare 1,2- and 2,4-disubstituted adamantanes by routes involving rearrangements.[1b,c,13,14] Protoadamantyl intermediates have also been implicated recently in the rearrangement of 2-methyl to 1-methyladamantane,[15] in the automerization of adamantane,[16] in the bromination of 2-methyladamantane,[17a] in the rearrangement of 2,2-dimethyladamantanols in sulfuric acid,[17b,c] and in the chlorination of adamantylidene adamantane.[17d] Solvolysis of 4-twistyl tosylate gives 10-protoadamantyl derivatives.[18b] Study of the substitution chemistry of protoadamantane has begun.[18a]

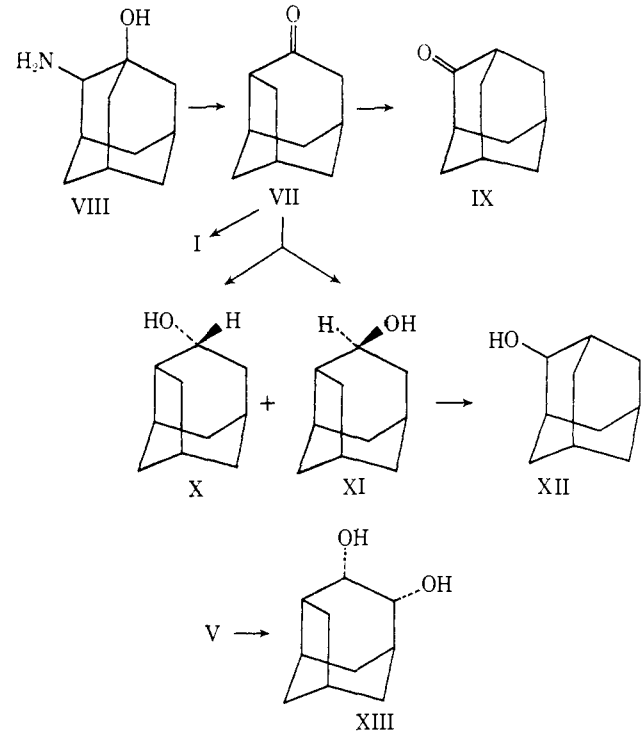
The present paper describes the synthesis of 4-protoadamantyl derivatives, the determination of their configuration and conformation, and their behavior toward solvolysis and other carbonium ion processes. 2-Adamantyl tosylate (IV) has been proposed as a model for limiting (k_c-type) solvolysis in secondary systems.[19] The 2-adamantyl and the 4-protoadamantyl cations are intimately related. This relationship, and the possibility of σ participation during secondary solvolysis of 2-adamantyl and 4-protoadamantyl systems, are analyzed here. The accompanying papers deal with the response of these systems to methyl and polymethyl substitution and provide an especially clear example of nonclassical carbonium ion theory to be compared and contrasted with 2-norbornyl behavior.[20]

Results

Synthesis of 4-Protoadamantanone (VII) and Its Derivatives.

Scheme I summarizes the preparative

Scheme I



methods we have employed. Our route to 4-protoadamantanone (VII)—the nitrous acid semipinacolic deamination of 2-amino-1-adamantanol (VIII)[21]—was straightforward and proceeded in high yield. The structure of this ketone, identical with samples prepared by other routes,[8,9,12] was confirmed by the following experiments. Wolff–Kischner reduction gave protoadamantane (I),[4,5] thus establishing the carbon skeleton. Exchange under mild conditions introduced two deuterium atoms into the ketone, a result which should only be possible with 4- and 5-protoadamantanone (VII and III, respectively) but not with the four other possible protoadamantanones. The reported properties of 5-protoadamantanone (III)[5,13] differ from those of our semipinacolic deamination product, 4-protoadamantanone (VII).

Lithium aluminum hydride reduction of ketone VII gave a 2:1 mixture of the epimeric 4-protoadamantanols, XI and X, respectively. The configuration of these alcohols was assigned on the basis of their nmr spectra and their chemical behavior: of the two, the minor exo epimer X (as well as its derivatives) rearranges much more rapidly to 2-adamantyl products (XII). Both these lines of evidence are discussed in detail below. Silica gel chromatography separated X and XI. 4-*exo*-Protoadamantanol (X), the minor product from $LiAlH_4$ reduction, eluted first.

A similar $LiAlH_4$ reduction of the deuterated ketone, VII-*5*-d_2, and reduction of VII by $LiAlD_4$ gave the corresponding deuterium-labeled alcohols, X-*5*-d_2, XI-*5*-d_2, X-*4*-*d*, and XI-*4*-*d* needed for spectral and mechanistic purposes.

While both alcohols X and XI could easily be converted to their acetate and 3,5-dinitrobenzoate esters, only endo tosylate (XI-OTs) could be prepared. 4-*exo*-Protoadamantyl tosylate (X-OTs) could not be

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(10) C. A. Cupas, W. Schumann, and W. E. Heyd, *J. Amer. Chem. Soc.*, 92, 3237 (1970).
(11) (a) L. A. Spurlock and K. P. Clark, *J. Amer. Chem. Soc.*, 92, 3829 (1970); (b) *ibid.*, 94, 5349 (1972).
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(13) (a) J. Boyd and K. H. Overton, *Chem. Commun.*, 211 (1971); (b) *J. Chem. Soc., Perkin Trans. 1*, 2533 (1972).
(14) (a) B. D. Cuddy, D. Grant, and M. A. McKervey, *Chem. Commun.*, 27 (1971); (b) *J. Chem. Soc. C*, 3173 (1971).
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(16) Z. Majerski, S. H. Liggero, P. v. R. Schleyer, and A. P. Wolf, *Chem. Commun.*, 1596 (1970).
(17) (a) J. R. Alford, D. Grant, and M. A. McKervey, *J. Chem. Soc. C*, 880 (1971); (b) B. D. Cuddy, D. Grant, A. Karim, and M. A. McKervey, *ibid.*, 2701 (1972); (c) F. Blaney, D. Faulkner, M. A. McKervey, and G. Step, *ibid.*, 2697 (1972); (d) J. H. Wieringa, J. Strating, and H. Wynberg, *Tetrahedron Lett.*, 4579 (1970).
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(20) (a) D. Lenoir, D. J. Raber, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, 96, 2149 (1974); (b) D. Lenoir, P. Mison, E. Hyson, P. v. R. Schleyer, P. Vogel, L. Telkowski, and M. Saunders, *ibid.*, 96, 2157 (1974).
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isolated from any of the three procedures[22] tried. For example, tosylation of X in pyridine[22a] gave only the rearranged 2-adamantyl tosylate (IV). Such rearrangements during tosylation are known,[23] but they tend to take place only with highly reactive systems. This qualitative observation thus provided an early indication of the greater reactivity of 4-*exo*- over 4-*endo*-protoadamantyl systems. Since we could not prepare X-OTs, the corresponding 3,5-dinitrobenzoate was used for solvolysis studies.

In order to ascertain their relative thermodynamic stability, 4-*exo*- and 4-*endo*-protoadamantanol (X and XI) were equilibrated by the aluminum isopropoxide method.[24] Unfortunately, at 150° equilibration was incomplete, while at 190° extensive dehydration and rearrangement to 2-adamantanol (XII-OH) occurred.[25] The data, although imperfect, nevertheless indicate that X and XI do not differ very much in stability; the equilibrium appears to be somewhat in favor of 4-*endo*-protoadamantanol (XI). The relative stabilities of all *exo*- and *endo*-protoadamantyl substituents were probed more precisely by molecular mechanics calculations (see below).

Additions to Protoadamantene (V). All reagents which we[1] and others[13,14,17a] have investigated have been found to add preferentially from the exo side of protoadamantene (V). An example is osmylation, which gives exo diol XIII.[1c] These results are expected on steric grounds. High regioselectivity is usually also exhibited.[1,14,17a] Only hydroboration–oxidation of V gave slightly more of the 4-protoadamantanols (X and XI) than their 5 isomers.[13] In contrast, oxymercuration–reduction[26] of V in our hands and in the literature[13b,14] gave 4-*exo*-protoadamantanol (X) quite cleanly.

The addition of protonic acids to protoadamantene (V) is complicated by the possibility of rearrangement to 2-adamantyl products (XII). For example, V with HBr at reflux in $CHCl_3$ solution gave 2-adamantyl bromide (XII-Br)[27] in 77% yield as the only detectable product. Similarly, the strong acid-catalyzed addition of acetic acid to V gave only 2-adamantyl acetate (XII-OAc). These results undoubtedly are the result of thermodynamic, rather than kinetic control. Neither 4-*exo*- nor 4-*endo*-protoadamantyl acetate is stable to the action of acid catalyzed, refluxing acetic acid. However, at 51° 4-*exo*-adamantyl acetate (X-OAc) is known to rearrange selectively to 2-adamantyl acetate (XII-OAc).[28] In the absence of a strong acid catalyst, refluxing acetic acid adds to protoadamantene (V) to give a 2:1 mixture of 2-adamantyl acetate (XII-OAc) and 4-*endo*-protoadamantyl acetate (XI-OAc). The exo isomer (X-OAc) would not survive these conditions.

Table I. Analysis of Nmr Data for Protoadamantane Derivatives

Coupling	Approx. dihedral angles, deg: Set I (E)[a]	Set II	Obsd coupling constants, Hz: XIII[b]	X[c]	X-5-d_2	XI[d]	XI-5-d_2
H_3-H_4-exo	65 (59)	30				3.4[e]	~3.2[f]
H_3-H_4-endo	55 (59)	90	3.5	4.0[e]	~4[e]		
H_4-exo-H_5-exo	30 (29)	30				8.0[e]	
H_4-exo-H_5-endo	150 (144)	90				8.4[e]	
H_4-endo-H_5-exo	90 (88)	150		~0[g]			
H_4-endo-H_5-endo	30 (27)	30	7.5	7.6[e]			
H_5-exo-H_6	30 (34)	65					
H_5-endo-H_6	90 (82)	55	~0[g]				

[a] Values in parentheses from molecualr mechanics calculations on I (Engler force field). [b] The same coupling constants are found in the acetonide of XIII.[1c] [c] X-ODNB gives coupling constants of ~7 and ~3.5 Hz. [d] The coupling constants (Hz) for derivatives are: XI-ODNB, ~3.2, ~8.5, ~8.5; XI-OAc, ~3.5, ~8.5, ~8.5; XI-OTs, 3.5, 8.0, 8.0. [e] Determined at 220 MHz; the other values are at 60 MHz. [f] Broad peak, W_h = 6.4 Hz. [g] Small value, not measured accurately.

Spectral Evidence for Configuration and Conformations. The high symmetry of adamantane (T_d point group) facilitates analysis of the nmr spectra of its derivatives.[29] In contrast, protoadamantane (I) is a chiral molecule (C_1 point group) with no symmetry element; all 16 hydrogens are different! An analysis of the nmr spectra of 4- and 5-protoadamantanols using the Eu(dpm)$_3$ shift technique has been reported.[13b] We obtained nmr structural evidence independently from analysis of the CHX signals of protoadamantane derivatives.

Framework models indicate that the ethylene bridge (C_4–C_5) of protoadamantane might reasonably assume a range of conformations. Dreiding models, which tend to overweigh angle strain effects, indicate that a single conformation of I should be favored strongly. It turned out that this Dreiding conformation (set I, Table I) proved to be consistent with the ir, nmr, and chemical data, as well as with refined molecular mechanics calculations (see below). These calculations indicate the conformation represented by set II (Table I) to be less stable by about 6 kcal/mol. We desired detailed structural information independent of these calculations. Cis diol XIII provided the key indication that the C-4,5 ethylene bridge assumes a conformation with an approximately 30° dihedral angle between both 4-endo-5-endo and 4-exo-5-exo groupings. This conclusion was based on the intramolecular hydrogen bonding ir spectral shift, 80 cm^{-1},[30] and the

(22) (a) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley, New York, N. Y., 1967, p 1180; (b) procedure developed by W. J. Hammar; see H. C. Brown, R. Bernheimer, C. J. Kim, and S. E. Schappele, *J. Amer. Chem. Soc.*, **89**, 370 (1967); (c) R. M. Coates and J. P. Chen, *Tetrahedron Lett.*, 2705 (1969).

(23) For example, see P. v. R. Schleyer, W. E. Watts, and C. Cupas, *J. Amer. Chem. Soc.*, **86**, 2722 (1964); E. C. Friedrich and S. Winstein, *ibid.*, **86**, 2721 (1964).

(24) See C. F. Wilcox, Jr., M. Sexton, and M. F. Wilcox, *J. Org. Chem.*, **28**, 1079 (1963).

(25) Boyd and Overton report failure in their attempts to equilibrate the 5-protoadamantanols.[13b] Equilibration of the 2-protoadamantanols was also difficult to achieve.[11b]

(26) H. C. Brown and P. Geoghegan, Jr., *J. Amer. Chem. Soc.*, **89**, 1522 (1967); H. C. Brown and W. J. Hammar, *ibid.*, **89**, 1525 (1967); H. C. Brown, J. H. Kawakami, and S. Ikegami, *ibid.*, **89**, 1526 (1967).

(27) W. Hoek, J. Strating, and H. Wynberg, *Recl. Trav. Chim. Pays-Bas*, **85**, 1045 (1966).

(28) Professor M. C. Whiting (private communication) has found that 4-*exo*-protoadamantyl acetate (X-OAc) rearranges to 2-adamantyl acetate (XII-OAc) at 51° in acetic acid in the presence of 0.15 *M* toluenesulfonic acid with a pseudo-first-order rate constant of 1.84×10^{-4} sec^{-1}. 4-*endo*-Protoadamantyl acetate (XI-OAc) is stable under these conditions.

(29) (a) R. C. Fort, Jr., and P. v. R. Schleyer, *J. Org. Chem.*, **30**, 789 (1965); (b) F. W. van Deursen and P. K. Korver, *Tetrahedron Lett.*, 3923 (1967); (c) F. W. van Deursen and A. C. Udding, *Recl. Trav. Chim. Pays-Bas*, **11**, 1243 (1968).

(30) According to F. V. Brutcher, Jr., and W. Bauer, Jr. [*J. Amer. Chem. Soc.*, **84**, 2236 (1962)], a $\Delta\nu$ of 80 cm^{-1} corresponds to a dihedral angle of about 27°. M. Tichý and L. Kniezo [*Tetrahedron Lett.*, 1665 (1971)] showed that *cis*-4,5-twistane diol, with an assumed dihedral angle of 30°, gave $\Delta\nu$ = 78 cm^{-1}. *Cf.* T. M. Gorrie, E. M. Engler, R. C. Bingham, and P. v. R. Schleyer, *Tetrahedron Lett.*, 3039 (1972).

Table II. Calculated Protoadamantane Bond Lengths and Angles[a]

Bond	Bond length, Å A	Bond length, Å E	Angle	Bond angle, deg A	Bond angle, deg E
C_1C_2	1.527	1.527	$C_1C_2C_3$	103.1	104.0
C_1C_9	1.527	1.525	$C_1C_9C_8$	99.6	100.6
C_1C_{10}	1.533	1.544	$C_1C_{10}C_6$	114.4	114.6
C_2C_3	1.535	1.535	$C_2C_3C_4$	111.1	110.3
C_3C_4	1.526	1.535	$C_2C_1C_9$	101.3	99.9
C_3C_8	1.540	1.546	$C_2C_1C_{10}$	111.3	112.1
C_4C_5	1.534	1.540	$C_2C_3C_8$	106.0	105.3
C_5C_6	1.536	1.541	$C_3C_4C_5$	109.8	112.2
C_6C_7	1.526	1.533	$C_3C_8C_7$	111.2	111.7
C_6C_{10}	1.539	1.547	$C_3C_8C_9$	103.2	103.2
C_7C_8	1.530	1.539	$C_4C_5C_6$	111.8	112.6
C_8C_9	1.530	1.528	$C_4C_3C_8$	111.8	112.2
			$C_5C_6C_7$	108.1	107.9
			$C_6C_6C_{10}$	115.0	113.0
			$C_6C_7C_8$	107.4	108.5
			$C_7C_8C_9$	108.5	107.1
			$C_7C_6C_{10}$	109.1	109.6
			$C_9C_1C_{10}$	109.4	110.0

[a] A, Allinger force field;[33b] E, Engler force field.[33c]

the configurations and conformations assigned these molecules.[1,13,32]

The conformation indicated for the protoadamantane skeleton (set I, Table I) is significant: antiperiplanar arrangements are found between the C_4-exo bond and C_2–C_3 (179° by molecular mechanics calculations on I) and between the C_4-endo bond and C_3–C_8 (177°). With leaving groups at C_4, a potentially participating anti C–C bond is present in either configuration.

Computer Conformational Analysis of Protoadamantane (I) and Derivatives. Quantitative computer conformational analysis (molecular mechanics) in its present state of refinement can rival experiment in favorable instances (*e.g.*, alkanes) for the determination of the precise structures and energies of molecules.[33] To reduce the possibility of error, our standard procedure is now to compare the results of two independent calculations employing quite different force fields with full energy minimization ("Allinger" (A)[33b] and "Engler" (E)[33c]). When the results agree, as is generally the case,[33c] confidence in their accuracy is enhanced. Because of its structural complexity, protoadamantane (I) provides an excellent test of this procedure. Table II summarizes the C–C bond lengths and C–C–C bond angles predicted by the two force fields. Dihedral angles are in similar agreement; values for C-3,4,5,6 are listed in Table III.

Table III. Molecular Mechanics Calculations[a,b]

Compound	$-\Delta H_f°$, kcal/mol A	$-\Delta H_f°$, kcal/mol E	Strain, kcal/mol A	Strain, kcal/mol E	C-3,4,5,6 dihedral angle, deg A	C-3,4,5,6 dihedral angle, deg E
Protoadamantane	22.63	21.13	17.13	18.29	29.6	25.2
1-Methylprotoadamantane		30.54		17.03		26.7
2-*exo*-Methylprotoadamantane	28.71	27.43	18.00	19.07	28.3	26.2
2-*endo*-Methylprotoadamantane	25.58	24.66	21.13	21.84	22.6	22.1
3-Methylprotoadamantane		30.15		17.46		27.3
4-*exo*-Methylprotoadamantane	27.19	26.31	19.52	20.19	22.4	19.9
4-*endo*-Methylprotoadamantane	29.13	27.81	17.58	18.69	31.0	29.8
5-*exo*-Methylprotoadamantane	29.41	28.27	17.30	18.23	29.4	28.3
5-*endo*-Methylprotoadamantane	26.77	25.88	19.94	20.62	21.8	19.1
6-Methylprotoadamantane		30.11		17.50		27.4
7-*exo*-Methylprotoadamantane	27.45	28.26	19.26	20.44	23.6	22.4
7-*endo*-Methylprotoadamantane	26.27	25.16	20.44	21.34	28.0	26.2
8-Methylprotoadamantane		30.64		16.97		26.7
9-*exo*-Methylprotoadamantane	28.54	26.90	18.17	19.60	29.2	26.9
9-*endo*-Methylprotoadamantane	27.04	25.67	19.67	20.83	29.0	26.5
10-*exo*-Methylprotoadamantane	27.85	26.47	18.86	20.03	27.8	25.4
10-*endo*-Methylprotoadamantane	28.08	26.98	18.03	19.52	28.4	25.3
4,4-Dimethylprotoadamantane	33.42	31.73	21.40	22.96	22.5	21.8
4,5-*exo*-Methyleneprotoadamantane	(78.97)[c]	(44.82)[c]	(117.85)[c]	(82.19)[c]	13.0	12.7
4,5-*endo*-Methyleneprotoadamantane	(80.94)[c]	(42.88)[c]	(119.82)[c]	(83.42)[c]	10.5	10.5

[a] A, Allinger force field.[33b] [b] E, Engler force field.[33c] [c] Values to be used only for exo–endo comparisons. The force fields (especially of ref 33b) are not appropriate to obtain absolute energies of cyclopropane derivatives.

The chemistry of protoadamantane is developing rapidly. As a guide to experimentalists, we probed the "conformational surface" of I by calculating all 16 possible monomethyl derivatives as well as 4,4-dimethylprotoadamantane and the 4,5-*exo*- and -*endo*-cyclopropanes (XIV) (Table III).

Each of the four faces of protoadamantane are different and approximate twist-chair cycloheptane, distorted chair cyclohexane, twist-boat cyclohexane, and half-chair (C_2) cyclopentane conformations; views A–D, Figure 1, emphasize different perspectives. In

magnitude of the H_4–H_5 pmr coupling constant, 7.5 Hz,[31] and would be independent of a cis-endo- or a cis-exo assignment to diol XIII. Assuming that this ~30° dihedral angle pertains to other protoadamantane derivatives, the problem is reduced to two sets of possible values (Table I). Only the first of these two sets is consistent with all of the nmr data listed in Table I.[13,32] All available evidence—chemical, spectroscopic, and computational[33]—is in agreement regarding

(31) We assume the Karplus relationship holds roughly. See L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy to Organic Chemistry," 2nd ed, Pergamon Press, Elmsford, N. Y., 1969, p 280 f.

(32) Similar conclusions have been reached by Alford and McKervey[8] for the related 4,8-protoadamantanediols on the basis of a similar nmr coupling constant analysis. The main $LiAlH_4$ reduction product of 8-hydroxy-4-protoadamantanone was also the endo isomer.

(33) (a) Review: J. D. Williams, P. J. Stang, and P. v. R. Schleyer, *Annu. Rev. Phys. Chem.*, **19**, 531 (1968); (b) N. L. Allinger, M. T. Tribble, M. A. Miller, and D. W. Wertz, *J. Amer. Chem. Soc.*, **93**, 1637 (1971); (c) E. M. Engler, J. Andose, and P. v. R. Schleyer, *ibid.*, **95**, 8005 (1973).

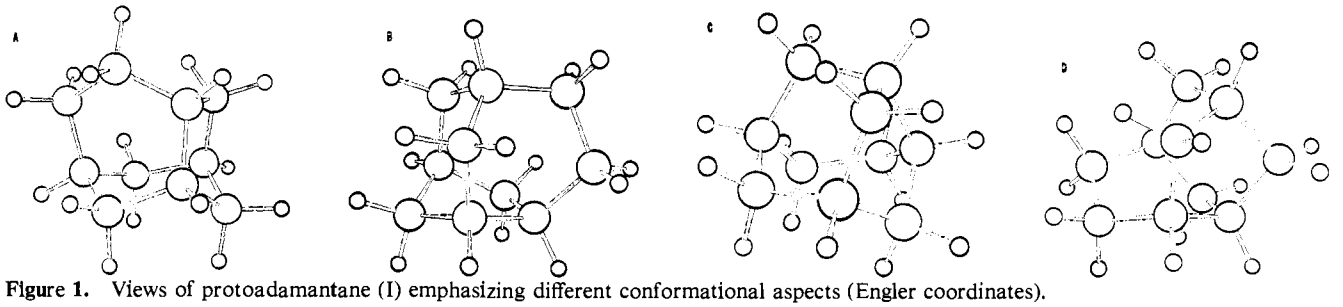
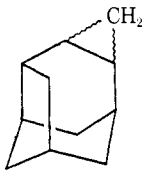
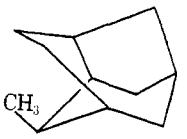


Figure 1. Views of protoadamantane (I) emphasizing different conformational aspects (Engler coordinates).



XIV endo and exo



XV

addition, if C-2 and C-7 are omitted, a distorted boat–chair cyclooctane is seen.

The structure of protoadamantane, like many cage molecules, is largely determined by its connectivity. While angle strain is chiefly responsible for the conformation of the C-4,5 ethylene bridge, torsional, and nonbonded strains are indicated by both force fields to contribute comparably to the overall strain energy of protoadamantane. The average C–C–C–C torsional angles around 8 out of the 12 C–C bonds are in the range 60 ± 20°; only two are <20° (C-3,8 av ~15°; C-5,6 av ~18°). The C-3,4,5,6 dihedral angle discussed in the preceding section is of chief interest. Table II summarizes values of these angles calculated for protoadamantane and its methyl derivatives. The range including both force fields is only 12° (19.1–31.0°). Only the methyl groups attached to and directed toward the C-4,5 ethylene bridge influence the C-3,4,5,6 dihedral angle significantly; the effects are small and are in the directions expected from repulsive steric effects.

A nomenclature problem arises when describing protoadamantane derivatives. We designate a substituent "endo" when it is oriented toward the *larger* ring; its epimer, facing the smaller ring, is "exo." This rule can be applied without ambiguity to five of the six methylenes of protoadamantane, only C-7 requires the further designation that boat cyclohexanes take precedence over chairs. Thus, XV is 7-*endo*-methylprotoadamantane.

The largest epimeric methyl energy difference (~3 kcal/mol, Table IV) favors the 2-exo over the 2-endo position. Equilibration of the 2-protoadamantanols agrees qualitatively.[11b] Exo isomers are also found to be more stable at the 5 (~2.5 kcal/mol) and 9 (~1.4 kcal/mol) positions; the same is true of C-7 (~1.0 kcal/mol) where both epimers are uncomfortably crowded. As suggested by our qualitative 4-protoadamantanol equilibration experiments, the equatorial-like 4-*endo*-methyl group is more stable than its exo isomer by ~1.7 kcal/mol. The smallest difference, 0.7 kcal/mol, is found at the 10 position, also favoring the endo isomer, but both epimers are quite strained. The 7-*exo*-, 9-*endo*-, and 10-*endo*-methyl groups are axial to the chair cyclohexane, all contribute 1.7–2.6 kcal/mol to the total strain; the value for 2-methyladamantane is 2.7 kcal/mol.[33c]

Table IV. Change in Strain Due to Substitution, 25°, kcal/mol

	Δ strain (from protoadamantane I)				Exo → endo	
	—Exo[a]—		—Endo[a]—		$\Delta H°$ isomerization[a]	
Substituents	A	E	A	E	A	E
2-Methyl	0.87	0.78	4.00	3.45	3.13	2.77
4-Methyl	2.39	1.90	0.45	0.40	−1.94	−1.50
5-Methyl	0.17	−0.06	2.81	2.33	2.64	2.39
7-Methyl	2.13	2.15	3.31	3.05	1.18	0.90
9-Methyl	1.04	1.31	2.54	2.54	1.50	1.23
10-Methyl	1.73	1.74	0.90	1.23	−0.83	−0.51
4,5-Methylene	*b*	*b*	*b*	*b*	1.97	1.94
	A	E				
4,4-Dimethyl	4.27	4.67				
1-Methyl		−1.23				
3-Methyl		−0.83				
6-Methyl		−0.79				
8-Methyl		−1.32				

[a] A, Allinger force field;[33b,c] E, Engler force field.[33c] [b] See footnote *c*, Table III.

Buttressing is found in 4,4-dimethylprotoadamantane; the total substituent strain (4.5 kcal/mol) exceeds the sum of the individual strain contributions from 4-endo and 4-exo groups by 2.0 kcal/mol.

All bridgehead positions are uncrowded; methyl substitution actually reduces the total strain relative to I. A cyclopropane group is 2.0 kcal/mol more stable 4,5-exo than 4,5-endo, a magnitude and direction consistent with the generally more favorable exo attack on 4-protoadamantene.[1,13,14,17a]

Solvolysis Rates and Products. The qualitative indications that 4-*exo*-protoadamantyl derivatives are more reactive than their 4-endo epimers were confirmed by quantitative measurements (Table V). Solvolysis of 4-*endo*-protoadamantyl tosylate (XI-OTs) was studied kinetically in both acetic acid and 60% acetone; the latter solvent was used for 4-*exo*-protoadamantyl 3,5-dinitrobenzoate (X-ODNB). Solvolysis was followed for *ca.* 6 half-lives and clean first-order kinetics were uniformly observed, but the behavior of X-ODNB was complicated by return: about 80% of the product was 2-adamantyl 3,5-dinitrobenzoate (XII-ODNB), inert under the reaction conditions. Solvolysis (to give 2-adamantanol (XII)) thus comprised only about 20% of the reaction of X-ODNB in the presence of 0.01 *M* lutidine buffer.

Since the same leaving groups were not used, the 4-exo/4-endo rate comparison had to be made indirectly. This can be done in several ways (Table VI).

Table V. Solvolysis Rates for 2-Adamantyl Tosylate and Epimeric 4-Protoadamantyl Esters

Compound	Solvent	Temp, °C	k_1, sec^{-1} [a]	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
2-Adamantyl tosylate (IV)	60% acetone	75.1	$(6.01 \pm 0.1) \times 10^{-5}$	25.3	−5.5
		100.2	$(7.52 \pm 0.1) \times 10^{-4}$		
		25.0	1.11×10^{-7} [b]		
	Acetic acid	25.0	5.94×10^{-9} [c]		
4-*endo*-Protoadamantyl tosylate (XI-OTs)	60% acetone	50.5	$(6.42 \pm 0.1) \times 10^{-5}$	24.8	−4.4
		75.1	$(9.42 \pm 0.1) \times 10^{-4}$		
		25.0	2.50×10^{-6} [b]		
		100.0	1.00×10^{-2} [b]		
	Acetic acid	75.0	$(2.44 \pm 0.1) \times 10^{-4}$	26.1	−0.3
		99.7	$(3.20 \pm 0.1) \times 10^{-3}$		
		25.0	3.67×10^{-7} [b]		
4-*exo*-Protoadamantyl 3,5-dinitrobenzoate (X-ODNB)	60% acetone	100.15	$(4.4 \pm 0.2) \times 10^{-6}$	(21.0)[d]	(−27)[d]
		(124.5	$(2.65 \pm 0.15) \times 10^{-5}$)[d]		
		(25.0	2.8×10^{-9}) [b,d]		

[a] Rate constants determined conductometrically; average of two runs. [b] Calculated from values at other temperatures. [c] See ref 19c. [d] These values are provisional because of possible inaccuracies in conductivity measurements at 125°.

Table VI. Relative Reactivity of 4-Protoadamantyl and 2-Adamantyl Derivatives

Tosylate	Rel rate comparisons: HOAc, 25°	60% acetone, 100°
2-Adamantyl (IV)	1.0	1.0
4-*endo*-Protoadamantyl (XI-OTs)	60	14
4-*exo*-Protoadamantyl (X-OTs)	3.6×10^5 [a]	1.2×10^5 [b]

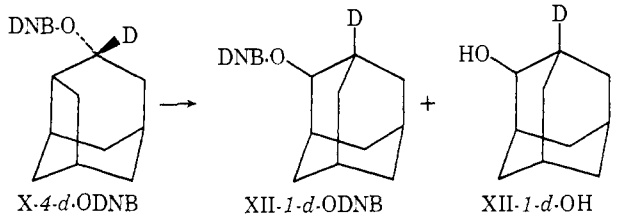
[a] Estimate based on the rate of X-ODNB in 60% acetone at 100° and the conversion factor of 490.[34] [b] Calculated using a k_{OTs}/k_{ODNB} conversion factor of 2×10^7 at 100° in 60% acetone.[35]

Baldwin and Foglesong[34] have shown that a tosylate in acetic acid at 25° is expected to react about 490 times faster than the corresponding 3,5-dinitrobenzoate in 60% acetone at 100°. Another comparison is available from data on cyclopropylcarbinyl derivatives[35] which permit the estimation of an OTs/ODNB leaving group ratio of 2×10^7 for 60% acetone at 100°. On either basis (Table VI), the 4-*exo*-protoadamantyl system is ~10^4 more reactive than the 4-endo. Both 4-protoadamantyl isomers are more reactive than 2-adamantyl (Table VI).

Solvolysis of 4-*endo* tosylate (XI-OTs) in KOAc buffered acetic acid at 100° gave only (±1%) 2-adamantyl acetate (XII-OAc), but in 60% acetone (lutidine buffer) a 4:1 mixture of 2-adamantanol (XII) and 4-*endo*-protoadamantanol (XI) was obtained. In the latter case, no 4-*exo*-protoadamantanol (X) was detected by glc; if any were present, it must have been less than 0.5%.

The acetolysis of 2-adamantyl tosylate (IV) was studied very carefully in order to check independently the results reported by Whiting, *et al.*,[7] and to establish the configuration of the 4-protoadamantyl product. In unbuffered acetic acid, only 2-adamantyl acetate (XII-OAc) was found, but other possible products are unstable under these conditions.[27] In buffered acetic acid at 100°, when IV was solvolyzed for ~10 half-lives, 0.4% of a second product, identified as 4-*exo*-protoadamantyl acetate (X-OAc), was detected along with 0.03% of a material whose structure could not be established, but which was not 4-*endo*-protoadamantyl acetate (XI-OAc), 1-adamantyl acetate, or 7-acetoxymethylene-2-bicyclo[3.3.1]nonene.[36] The analysis of the solvolysis product mixture was best carried out by $LiAlH_4$ reduction, followed by trimethylsilylation and gas chromatography. The trimethylsilyl ethers of 4-*exo*- and 4-*endo*-protoadamantanol and of 2-adamantanol are glc stable and have very distinctive retention times on all columns used. 2-Adamantyl-*2-d* tosylate (IV-*2-d*) was allowed to react for a week at 25° with trifluoroacetic acid (more than 100 half-lives). After conversion of the product to alcohol (XII), nmr showed no detectable C*H*OH proton signal. Within 5%, no detectable 1,2-, 1,3-, or intermolecular hydride shifts[37] were observed under these conditions.[38]

Solvolysis of D-Labeled 4-Protoadamantyl Derivatives. Mechanistic insight was provided by solvolysis of deuterium-labeled 4-protoadamantanes, and the behavior of the exo system was straightforward. 4-*exo*-Protoadamantyl-*4-d* dinitrobenzoate (X-*4-d*-ODNB) gave in 60% acetone at 125° a mixture of 2-adamantanol-*1-d* (XII-*1-d*), and the corresponding return product, 2-adamantyl-*1-d* dinitrobenzoate (XII-*1-d*-ODNB).



X-*4-d*-ODNB XII-*1-d*-ODNB XII-*1-d*-OH

(34) J. E. Baldwin and W. D. Foglesong, *J. Amer. Chem. Soc.*, **90**, 4303 (1968).

(35) Cyclopropylcarbinyl 3,5-dinitrobenzoate; P. v. R. Schleyer and F. W. Van Dine, *J. Amer. Chem. Soc.*, **88**, 2321 (1966). Data for cyclopropylcarbinyl tosylate (K. B. Wiberg and A. J. Ashe, *ibid.*, **90**, 63 (1968); D. D. Roberts, *J. Org. Chem.*, **29**, 294 (1964)) were converted to 60% acetone at 100° by reasonable temperature and solvent extrapolations, the latter using the mY treatment.

(36) Prepared from the corresponding alcohol by treatment with acetic anhydride in pyridine: A. C. Udding, H. Wynberg, and J. Strating, *Tetrahedron Lett.*, 5719 (1968).

(37) *Cf.* P. v. R. Schleyer, L. K. M. Lam, D. J. Raber, J. L. Fry, M. A. McKervey, J. R. Alford, B. D. Cuddy, V. G. Keizer, H. W. Geluk, and J. L. M. A. Schlatmann, *J. Amer. Chem. Soc.*, 92, 5246 (1970); P. Vogel, M. Saunders, W. Thielecke, and P. v. R. Schleyer, *Tetrahedron Lett.*, 1429 (1971). This conclusion contrasts with a report of a 1,3-hydride shift in a more complex adamantane system: E. Boelma, J. H. Wieringa, H. Wynberg, and J. Strating, *ibid.*, 2377 (1973).

(38) Similar conclusions have been reached for acetolysis: M. C. Whiting, private communication. J. Slutsky (unpublished observations) has subjected 2-adamantanol-*2-d* to the action of trifluoroacetic acid at 150° for 48 hr. Although some decomposition occurs, no detectable C*H*–OR signal appears.

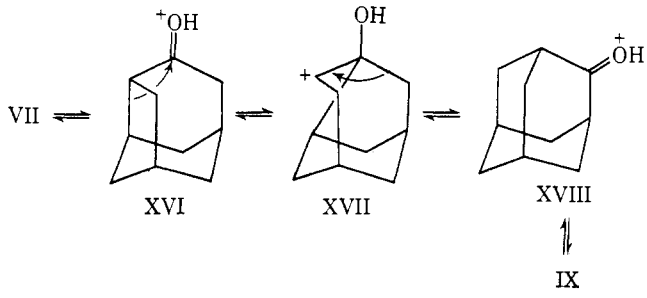
Within the limits of nmr detectability, the deuterium labels in these products were only at the 1 positions. This was indicated by the doublet nature of the CHO signals and the fact that these signals integrated for 1.0 ± 0.05 proton.

In contrast, deuterium scrambling occurred during solvolysis of 4-*endo*-protoadamanty-l4-*d* tosylate (XI-4-*d*-OTs). The crude product from solvolysis in 60% acetone, consisting of a mixture of 4-*endo*-protoadamantanol (XI) and 2-adamantanol (XII), gave a combined C*H*OH signal integrating for 0.48 ± 0.05 proton. This showed that the degenerate 4-protoadamantyl ⇌ 4-protoadamantyl rearrangement had occurred, distributing the deuterium approximately equally between two positions. A search was made to find conditions under which deuterium scrambling could be demonstrated in the 4-*endo*-protoadamantyl tosylate recovered after partial solvolysis. This did not prove to be easy; no C*H*OTs pmr signal was detected in tosylate (XI-4-*d*-OTs) recovered from 60% acetone and from acetic acid. However, use of a solvent system, 90% dioxane–10% formic acid, known to favor internal return strongly,[39] succeeded. Even then, tosylate (XI-*d*-OTs), recovered after ~1 half-life, showed only 8% deuterium scrambling.

Additional Protoadamantyl–Adamantyl Rearrangements. The examples already presented indicate that protoadamantyl derivatives have a high propensity toward rearrangement to adamantyl products. This is not surprising. According to the best estimates available,[20a,33c] protoadamantane (I) is ~11 kcal/mol more strained than adamantane. Thermodynamically controlled reactions allowing interconversion of these isomers would thus give essentially only adamantyl products.

As would be predicted,[5] protoadamantane (I) rearranges very readily to adamantane in the presence of $AlBr_3$ catalyst. When the reaction was carried out in CS_2 solution at 25°, a 71% yield of adamantane was obtained. No intermediates could be detected. Presumably the 4-protoadamantyl cation is generated by hydride abstraction.

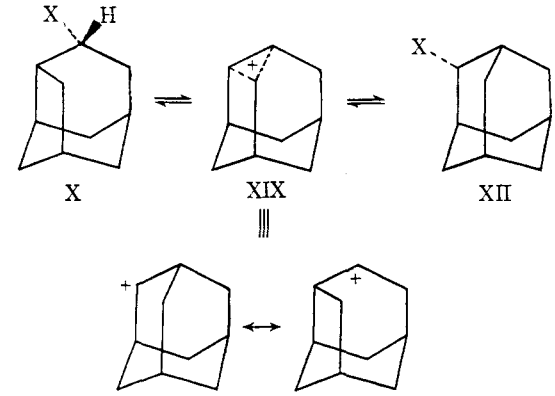
Rearrangements less direct mechanistically can also be effected. Concentrated sulfuric acid at 125° converts 4-protoadamantanone (VII) to 2-adamantanone (IX).[40] Due to charring, the yield is only 28%; less destructive protonic or Lewis acid catalysts might well give better results. The possible mechanism



shown involves 4-protoadamantyl → 4-protoadamantyl (XVI → XVII) and 4-protoadamantyl → 2-adamantyl (XVII → XVIII) rearrangement steps. Similar mechanisms have already been postulated;[1a,15–18] supporting evidence for steps of this type is presented below.

Discussion

While both 4-*exo*- and 4-*endo*-protoadamantyl derivatives tend to give 2-adamantyl products, the two epimers behave quite differently. Noteworthy is the large exo/endo reactivity ratio, ~10^4 (Table V). Since the ground-state energies are nearly the same, this high ratio and the fast absolute rate constants of the 4-exo derivatives demonstrate that considerable anchimeric assistance is present. The ready rearrangement of 4-*exo*-protoadamantyl derivatives to 2-adamantyl products, and the observation of a small amount of 4-*exo*-protoadamantyl products from 2-adamantyl precursors under kinetic conditions, establishes the relationship between these two systems. Thus, delocalization of the C_2–C_3 bond electrons is occurring during ionization of 4-*exo*-protoadamantyl derivatives. The transition state is partially bridged. Of course, the driving force is provided by rearrangement during reaction to the more stable adamantyl system. Whether or not the intermediate formed either from X or XII precursors is also partially bridged (*i.e.*, XIX), is more difficult to establish with certainty.



major contributor minor contributor

We have detailed much evidence which shows that the solvolyses of 2-adamantyl derivatives are limiting (k_c) or nearly so, at least with respect to nucleophilic solvent participation.[19] However, some evidence is consistent with a weakly bridged intermediate: (1) the formation of a small amount of 4-*exo*-protoadamantyl product, but no detectable amount of the endo epimer; (2) the estimated observation of from 64 to 84% *retention* of configuration during solvolysis of 2-adamantyl derivatives in protic media.[19e] Alternative explanations not involving the postulate of a bridged intermediate can also account for these results. A very small amount of the classical 4-protoadamantyl cation may be present in equilibrium with the 2-adamantyl cation and may be, for steric or other reasons, attacked exo by solvent more rapidly than the 2-adamantyl cation. Retention of configuration in the 2-adamantyl products, inferred from the behavior of methyl-substituted derivatives,[19e] might be due to collapse of an external ion pair, $R^+\cdots O(S)H\cdots X^- \rightarrow ROS + HX$.[19h] It may be significant that the only nonprotic solvent in-

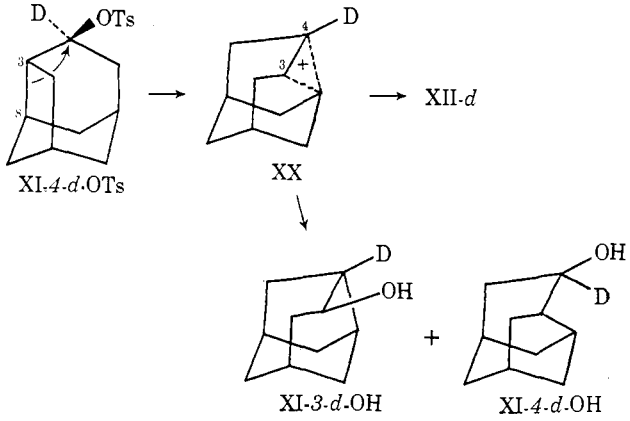
(39) S. Winstein and G. S. Robinson, *J. Amer. Chem. Soc.*, 79, 2533 (1957).

(40) About 0.05% of 4-protoadamantanone (VII) could be detected gas chromatographically in both a commercial (Aldrich) sample of 2-adamantanone and a sample prepared by sulfuric acid oxidation of adamantane at 70°.[38] Under these conditions, 4-protoadamantanone (VII) does not rearrange to adamantanone; the presence of VII is evidently due to kinetic control.

vestigated by Bone and Whiting[19e] gave net inversion of configuration; such a nonprotic solvent could not form such a hydrogen-bonded external ion pair complex.

Even if the intermediate is bridged, the bridging should be weak and it must be unsymmetrical, *i.e.*, the bridging carbon C_2 should be unsymmetrically located with regard to C_3 and C_4.[41] The carbon skeleton of the 2-adamantyl cation is much more stable than that of the 4-protoadamantyl cation; any tendency of the 2-adamantyl cation to bridge must be offset, at least in part, by an increase in skeletal ring strain. This matter is discussed at greater length in the following papers, where additional evidence is presented.[20]

The 4-*endo*-protoadamantyl tosylate (XI-OTs) also shows a modest rate enhancement when compared to 2-adamantyl tosylate (IV); see Table VI. While this rate enhancement, of course, could be due to conformational effects [γ_{CO} (VII) 1712 and 1719 cm^{-1}, but γ_{CO} (IX) 1727 cm^{-1}], anchimeric assistance also may be responsible.[42] The C_3–C_8 bond is stereochemically well situated for participation; the symmetrical bridged 4-*endo*-protoadamantyl cation (XX) (or a rapidly equilibrating degenerate pair of partially bridged cations) is a possible intermediate. Degenerate 4-protoadamantyl–4-protoadamantyl rearrangements, consistent with the intervention of XX, are demonstrated by our deuterium scrambling results and have been implicated previously many times.[15–18] However, XX cannot be a very stable species, since "leakage" to the 2-adamantyl system (XII) occurs so readily.



Only the more nucleophilic solvents like 60% acetone permit the capture of some 4-*endo*-protoadamantyl products, and an extremely favorable solvent system, 90% dioxane–10% formic acid, is needed to detect any internal return in recovered deuterated 4-*endo*-protoadamantyl tosylate. Nevertheless, 4-protoadamantyl–4-protoadamantyl rearrangements occur readily, more rapidly than leakage to 2-adamantyl products, as is indicated by the approximately 50% deuterium scrambling found in the product mixture obtained from solvolysis of 4-*endo*-protoadamantyl-*4-d* tosylate.

(41) Experimental and theoretical evidence for unsymmetrically bridged structures has been published recently: G. A. Olah, A. M. White, J. R. DeMember, A. Commeyras, and C. Y. Lui, *J. Amer. Chem. Soc.*, **92**, 4627 (1970); G. A. Olah, J. R. DeMember, C. Y. Lui, and R. D. Porter, *ibid.*, **93**, 1442 (1971); L. Radom, J. A. Pople, V. Buss, and P. v. R. Schleyer, *ibid.*, **93**, 1813 (1971); G. A. Olah, G. D. Mateescu, and T. L. Riemenschneider, *ibid.*, **94**, 2529 (1972); P. C. Hariharan, L. Radom, J. A. Pople, and P. v. R. Schleyer, *ibid.*, **96**, 601 (1974).

(42) (a) C. S. Foote, *J. Amer. Chem. Soc.*, **86**, 1853 (1964); (b) P. v. R. Schleyer, *ibid.*, **86**, 1854, 1856 (1964). The C_3–C_4–C_5 angle in I is indicated by the conformation analysis calculations to be 112.2°.

Experimental Section

General. Melting points were determined on a Mettler FPI apparatus in sealed capillaries, and are uncorrected. Elemental analyses were performed by G. Robertson, Florham Park, N. J. Unless otherwise stated, pmr spectra were determined in $CDCl_3$ solution (TMS internal standards), on Varian A-60 A spectrometers. The 220-MHz pmr spectra were taken on a Varian instrument through the courtesy of Professor Adam Allerhand, University of Indiana. Mass spectra were determined on a AEI MS-9 spectrometer at 150° and 70 eV with $(C_4F_9)_3N$ as reference. High-resolution molecular weight determinations were performed on the parent peaks of some compounds.[43] The deuterium contents of the labeled compounds were calculated from the parent peak ratios of their mass spectra.

1-Hydroxy-2-aminoadamantane (VIII). 1-Hydroxy-2-aminoadamantane hydrochloride[21] (4 g) was dissolved in 150 ml of 2 *M* sodium hydroxide solution and the free amine (VIII) was extracted six times with 30 ml of chloroform. The combined organic phases were washed with water, dried over anhydrous sodium sulfate and evaporated *in vacuo* to give 3.2 g of crude 1-hydroxy-2-aminoadamantane (VIII). This product was used directly for the deamination. A sample of VIII was sublimed *in vacuo:* mp 268–270°; nmr τ 7.8–8.8 (m, 16, adamantyl H + NH_2), 7.22 (d, 1, C*H*NH_2); mass spectrum *m/e* (rel intensity) 167 (52, M^+), 167.1310 (calcd. for $C_{10}H_{17}NO$, 167.1310), 166 (63), 149 (100), 138 (19), 107 (32), 95 (68), 79 (24), 70 (51), 56 (31).

4-Protoadamantanone (VII). 1-Hydroxy-2-aminoadamantane (VIII) (3 g, 0.0179 mol) was dissolved in a mixture of 50 ml of acetic acid and 100 ml of water. After the solution was cooled in an ice bath, a solution of 3 g of sodium nitrite in 5 ml of H_2O was added with stirring. Stirring was continued for 10 hr at 0°. Solid sodium bicarbonate was added to neutralize the acetic acid, and the solution was extracted six times with 30-ml portions of carbon tetrachloride. The combined extracts were washed with 10% sodium bicarbonate solution, and with water. After drying over anhydrous sodium sulfate and evaporation *in vacuo*, 2.5 g of a crude product was obtained; sublimation *in vacuo* gave 2.15 g (77%) of quite pure 4-protoadamantanone (VII): mp 208–210° (lit.[7,9] 212–214°); ir (CCl_4) 1712 (sh) and 1719 cm^{-1}; nmr complex pattern of signals at τ 8.12, 7.6, and 7.28; mass spectrum *m/e* (rel intensity) 150 (100 M^+), 150.1043 (calcd for $C_{10}H_{14}O$, 150.2092), 135 (6), 132 (2), 122 (11), 121 (12), 117 (6), 108 (27), 107 (28), 106 (19), 95 (75), 93 (37), 91 (23), 80 (55), 79 (68), 67 (67), 66 (71).

Anal. Calcd for $C_{10}H_{14}O$: C, 79.95; H, 9.39. Found: C, 79.63; H, 9.60.

Protoadamantane (I). 4-Protoadamantanone (VII) (450 mg, 3 mmol) was heated in a solution of 300 mg of powdered potassium hydroxide, 10 ml of triethylene glycol, and 5 ml of hydrazine hydrate to 120° for 2 hr. The mixture was heated to 210° for 5 hr while removing the water which distilled by means of a Dean–Stark separator. After the mixture was cooled, the reaction product was extracted three times with 25 ml of ether. The ether phase was washed with water, dried over sodium sulfate, and evaporated *in vacuo* to give 320 mg of a crude product. Sublimation gave 280 mg (69%) of a white solid, mp 205–212°; a band at 3600 cm^{-1} in the ir spectrum indicated alcoholic contamination. The analytical sample of protoadamantane (I) was obtained by preparative glc on a Carbowax 20M column: mp 210–212° (lit.[5] 210.5–212°); nmr complex pattern of signals centered at τ 8.8, 8.45, and 8.15, mass spectrum *m/e* (rel intensity) 136 (100, M^+) 136.2248 (calcd for $C_{10}H_{16}$, 136.1251), 121 (11), 108 (6), 107 (8), 95 (25), 94 (19), 93 (18), 81 (9), 80 (14), 79 (20), 67 (11), 41 (8). This mass spectrum of I is virtually indistinguishable from that of adamantane.

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.01; H, 11.72.

Reduction of 4-Protoadamantanone (2) with $LiAlH_4$. 4-Protoadamantanone (VII) (500 mg, 3.33 mmol) was dissolved in 25 ml of absolute ether and a slurry of 90 mg of lithium aluminum hydride was added. The mixture was refluxed for 15 hr. The usual work-up procedure[44] gave 480 mg (96%) of a crude mixture which was shown by analytical glc on Carbowax 20M column to consist of two products in the ratio of 1:2. The major component was later

(43) See T. H. Beynon and A. E. Williams, "Mass and Abundance Tables for Use in Mass Spectrometry," Elsevier, Amsterdam, 1963.

(44) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley, New York, N. Y., 1967, p 584.

shown to be 4-*endo*-protoadamantanol (XI) while the minor one proved to be the exo epimer (X).

Separation of 4-Epimeric Protoadamantanol Mixture. The crude reduction mixture (200 mg) was chromatographed on a silica gel column (200 g), using the following eluents: 500 ml of benzene, 500 ml of benzene with 1% ether, and 500 ml of benzene with 2% ether. Fractions of 50 ml were taken, evaporated *in vacuo*, and analyzed by glc. Products were eluted by the ether containing solvents.

(a) **4-*exo*-Protoadamantanol (X)**, the less polar isomer, was obtained in quite pure form. Sublimation gave 55 mg (27%) of substance: mp 204–206°; nmr complex pattern of signals centered at τ 8.75, 8.6, 8.1, and 7.7, and broad signal at 5.62 (C_4-H) resolved in the 220-MHz nmr spectrum into four lines with $J_{4\text{-endo-5-endo}}$ = 7.6 Hz and $J_{3\text{-4-endo}}$ = 4.0 Hz; mass spectrum *m/e* (rel intensity) 152 (13, M^+), 152.1201 (calcd for $C_{10}H_{16}O$, 152.1201), 150 (19), 134 (100), 119 (14), 108 (9), 106 (9), 105 (14), 95 (24), 92 (61), 80 (38), 79 (55), 67 (31).

Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.60. Found: C, 78.59; H, 10.40.

(b) **4-*endo*-Protoadamantanol (XI)**, the more polar compound, was eluted in pure form after 30 mg of a mixture was collected. Sublimation gave 110 mg (55%) of XI: mp 214–216°; nmr complex pattern of signals centered at τ 8.5, 8.25, and 7.7, six-line pattern at 5.95 (4-exo-H), and the 220-MHz nmr spectrum for this resonance gave $J_{4\text{-exo-5-exo}}$ = 8.0 Hz and $J_{4\text{-exo-3}}$ = 3.4 Hz; mass spectrum *m/e* (rel intensity) 152 (48, M^+), 152.1203 (calcd for $C_{10}H_{16}O$, 152.1201), 150 (22), 134 (100), 119 (8), 108 (5), 106 (4), 105 (6), 95 (11), 92 (21), 80 (13), 79 (19), 67 (11), 66 (12).

Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.60. Found: C, 78.97; H, 10.40.

4-*exo*-Protoadamantyl Acetate (X-OAc). 4-*exo*-Protoadamantanol (X) (30 mg) was esterified by using 0.2 ml of pyridine and 0.2 ml of acetic anhydride; 28 mg of a bright yellow oil was obtained, which showed a single peak in the glc and was distinguishable in retention time from 4-*endo*-protoadamantyl acetate (XI-OAc) and from 2-adamantyl acetate. The nmr of X-OAc showed a complex pattern of signals centered at τ 8.72 and 8.12, singlet at 8.08 (acetate CH_3), and multiplet at 4.92 (C_4-H).

4-*exo*-Protoadamantyl 3,5-Dinitrobenzoate (X-ODNB). 4-*exo*-Protoadamantanol (X) (120 mg, 0.79 mmol) was converted in 2 ml of absolute pyridine with 220 mg of 3,5-dinitrobenzoyl chloride[45] into 230 mg of a crude X-ODNB, which was recrystallized from carbon tetrachloride to give 201 mg (73%) of white plates, mp 142–144°. The nmr spectrum of X-ODNB showed a complex pattern of signals centered at τ 8.4–8.7 and 7.88, a multiplet at 4.40 (C_4-H), and the aromatic pattern centered at 1.28.

Anal. Calcd for $C_{17}H_{18}O_6N_2$: C, 58.96; H, 5.24; N, 8.09. Found: C, 58.56; H, 5.21; N, 7.98.

4-*exo*-Protoadamantyl Trimethylsilyl Ether (X-OSi$(CH_3)_3$). 4-*exo*-Protoadamantanol (X) (5 mg) was placed in a small ampoule, and by means of a syringe 0.2 ml of hexamethyl disilazane and 0.2 ml of trimethylchlorosilane were added. The ampoule was sealed and heated at 75° for 8 hr. The resulting product was used for gas chromatographic analyses.

4-*endo*-Protoadamantyl Acetate (XI-OAc). 4-*endo*-Protoadamantanol (XI) (30 mg) was converted with 0.2 ml of pyridine and 0.2 ml of acetic anhydride into its acetate; 26 mg (68%) of an oil was obtained. The nmr spectrum of IX showed complex pattern of signals centered at τ 8.5, 8.3, 7.9, and 7.7, a singlet at 8.15 (acetate CH_3), and a multiplet at 5.2 (C_4-H).

4-*endo*-Protoadamantyl Tosylate (XI-OTs). 4-*endo*-Protoadamantanol (XI) (84 mg, 0.56 mmol) was converted to tosylate by the standard pyridine method.[22a] The crude product was recrystallized from *n*-pentane to give 124 mg (72%) of a white compound, mp 74–75°. The nmr spectrum of XI-OTs showed a complex pattern of signals centered at τ 8.5, 8.2, 7.9, and 7.55, a singlet at 7.50 (tolyl CH_3), and the AB pattern of the benzene ring centered at 2.1 and 2.6. Mass spectrum *m/e* (rel intensity) 306 (3, M^+), 306.1281 (calcd for $C_{17}H_{22}O_3S$, 306.1285), 225 (1), 172 (1), 155 (3), 151 (43), 135 (29), 134 (100), 119 (8), 107 (5), 106 (5), 105 (8), 93 (24), 92 (50), 91 (38), 79 (27), 67 (19).

4-*endo*-Protoadamantyl Trimethylsilyl Ether (XI-OSi$(CH_3)_3$). 4-*endo*-Protoadamantanol (XI) (5 mg) was converted into its trimethylsilyl ether by the same method described for X-OSi$(CH_3)_3$.

4-*endo*-Protoadamantyl 3,5-Dinitrobenzoate (XI-ODNB). 4-*endo*-Protoadamantanol (XI) (20 mg) was converted into its 3,5-dinitrobenzoate by the method described above. After recrystallization from aqueous acetone, 31 mg of white plates was obtained: mp 150.5–152.0°; nmr complex pattern of signals centered at τ 8.45, 8.15, 7.75, and 7.45, and a six-line pattern for C_4-H at 4.60.

4-Protoadamantanone-*5,5-d*$_2$ (VII-*d*$_2$). 4-Protoadamantanone (VII) (500 mg) was refluxed for 12 hr in a solution of 5 ml of absolute dioxane and 3 ml of deuterium oxide, followed by evaporation to dryness *in vacuo*. The same procedure was repeated two more times. The residue was dissolved in carbon tetrachloride; evaporation *in vacuo* gave 410 mg of crude substance; sublimation yielded to 380 mg (76%) of pure 4-protoadamantanone-*5,5-d*$_2$ (VII-*d*$_2$), mp 207–210° (not depressed by mixing with 4-protoadamantanone (VII)). The deuterium content (by mass spectrometry) was 93% d_2, 4% d_1, and 3% d_0.

4-*exo*-Protoadamantanol-*5,5-d*$_2$ (X-*d*$_2$). Ketone VII-*d*$_2$ (250 mg) was reduced with 50 mg of lithium aluminum hydride in 20 ml of absolute ether. The resulting mixture was chromatographed on 220 g of silica gel to give 85 mg of 4-*exo*-protoadamantanol-5,5-*d*$_2$(X-*d*$_2$), mp 204–206° after sublimation, no mixture melting point depression with 4-*exo*-protoadamantanol (X); nmr complex pattern of signals centered at τ 8.8, 8.6, 8.5, 8.05, 7.8, and 7.7; both 60-MHz and 220-MHz spectra gave a doublet at τ 5.83 (C_4-H) with $J_{3\text{-4-endo}}$ = 3–4 Hz.

4-*endo*-Protoadamantanol-*5,5-d*$_2$ (XI-*d*$_2$). The less polar component (103 mg) from silica gel chromatography of the reduction mixture from VII-*d*$_2$ was XI-*d*$_2$, mp 213–216° after sublimation, no mixture melting point depression with 4-*endo*-protoadamantanol (XI); nmr complex pattern of signals centered at τ 8.7, 8.5, 8.35, 8.05, and 7.75, and a broad signal at τ 6.05 (C_4-H) with a 7 Hz half-width.

Reduction of 4-Protoadamantanone (VII) with Lithium Aluminum Deuteride. 4-Protoadamantanone (VII) (250 mg) was reduced with 50 mg of lithium aluminum deuteride in 20 ml of absolute ether. After the usual work-up, 232 mg of a mixture of the epimeric alcohols was obtained. This mixture was separated as described above by chromatography on 220 g of silica gel to give 61 mg of **4-*exo*-protoadamantanol-*4-d*** (**X-*d***), gas chromatographically identical with X (by coinjection). The exact deuterium content of X-*d* could not be determined from its mass spectrum because of complications introduced by the strong (M − 1) and (M − 2) peaks. The nmr spectrum of X-*d* showed no C_4-H signal at τ 5.6 indicating a deuterium content >95%.

Also obtained from silica gel chromatography was 115 mg of **4-*endo*-protoadamantanol-*4-d*** (**XI-*4-d***) shown to be gas chromatographically identical with XI by coinjection. The nmr spectrum of the product showed no signal at τ 5.95 indicating a deuterium content >95%.

4-*exo*-Protoadamantyl-*4-d* 3,5-Dinitrobenzoate (X-*4-d*-ODNB). 4-*exo*-Protoadamantanol-*4-d* (X-*d*) (60 mg) was converted into its 3,5-dinitrobenzoate as described above; 99 mg (72%) of X-*4-d*-ODNB was obtained, mp 142–147°; no mixture melting point depression with X-ODNB was observed.

4-*endo*-Protoadamantyl-*4-d* Tosylate (XI-*4-d*-OTs). 4-*endo*-Protoadamantanol-*4-d* (XI-*d*) (110 mg) dissolved in 3 ml of absolute pyridine was converted into its tosylate by treatment with 280 mg of tosyl chloride; 151 mg of 4-*endo*-protoadamantyl-*4-d* tosylate (XI-*4-d*-OTs) was obtained, mp 73–75°, which exhibited no mixture melting point depression with XI-OTs.

Oxymercuration of Protoadamantene (V). Mercuric acetate (638 mg, 0.002 mol) was dissolved in a mixture of 5 ml of H_2O and 5 ml of tetrahydrofuran and 268 mg (0.002 mol) of protoadamantene (V) was added. After the mixture was stirred for 15 min, 2.5 ml of a solution of 0.5 g of $NaBH_4$ in 10% sodium hydroxide and an additional 2.5 ml of 10% sodium hydroxide solution were added. After 10 min, mercury had precipitated; about 0.5 g of sodium chloride was then added. The organic phase was separated and the water phase was extracted twice with 10 ml of tetrahydrofuran. The combined organic phases were dried over sodium sulfate and evaporated *in vacuo*. The crude product remaining was chromatographed on 100 g of silica gel with benzene–2% ether as eluent to give 258 mg (86%) of 4-*exo*-protoadamantanol, mp 203–206°. After sublimation, the nmr spectrum was superimposable on X, prepared by the reduction of ketone VII; glc coinjection gave a single peak.

Reaction of Protoadamantene (V) with HBr in $CHCl_3$. Protoadamantene (V) (67 mg, 0.5 mmol), dissolved in 5 ml of CCl_4, was refluxed for 2 hr under an HBr atmosphere. The solvent was evaporated *in vacuo* and the crude product was sublimed to give 82 mg (77%) of 2-adamantyl bromide, shown by its melting point

(45) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," Wiley, New York, N. Y., 1964, p 247.

(117–119°), mixture melting point, and by glc coinjection with authentic material.

Reaction of Protoadamantene (V) with Acetic Acid. Protoadamantene (V) (67 mg, 0.5 mmol) was dissolved in 10 ml of acetic acid and 1 drop of concentrated hydrochloric acid was added. The mixture was refluxed for 24 hr. The solvent was evaporated *in vacuo* and the residue was dissolved in 20 ml of ether. The ether solution was washed with 10% potassium bicarbonate solution and water, and dried over sodium sulfate. After vacuum evaporation, 63 mg (65%) of a yellow oil was obtained, shown to be gas chromatographically identical with an authentic sample of 2-adamantyl acetate. The nmr spectra (signals between τ 7.5 and 8.8, broad triplet at τ 5.15 (C_2–H)) were also identical.

Reaction of Protoadamantene (V) with Acetic Acid. Protoadamantene (V) (67 mg, 0.5 mmol) was refluxed in 10 ml of acetic acid without strong acid catalyst for 48 hr and the mixture was worked by the same procedure described above. Glc of the crude reaction product showed, besides the starting material, two peaks in the ratio of 3:1. By coinjection, the major product was shown to be 2-adamantyl acetate, the minor one was 4-*endo*-protoadamantyl acetate (XI-OAc).

2-Adamantyl Acetate. 2-Adamantanol (152 mg, 1 mmol) was converted to acetate by 5 ml of pyridine and 5 ml of acetic anhydride; 162 mg (83%) of crude product was obtained; nmr τ 7.50–8.8 (14 H) and 5.15 (CH-OAc).

2-Adamantyl 3,5-Dinitrobenzoate. 2-Adamantanol (760 mg, 5 mmol) was esterified by 10 ml of absolute pyridine and 1380 mg of 3,5-dinitrobenzoyl chloride. The crude product was crystallized rom aqu eous acetone to give 1371 mg (80%) of 2-adamantyl 3,5-dinitrobenzoate as white plates: mp 158.0–159.5°; nmr broad signals at τ 8.38, 8.10, and 7.82, broad triplet at 4.73 (C*H*-ODNB, J = 3 Hz), and three aromatic protons at 0.91.

Anal. Calcd for $C_{17}H_{18}O_6N_2$: C, 58.96; H, 5.24; N, 8.09. Found: C, 58.81; H, 5.21; N, 8.01.

Attempts to Prepare 4-*exo*-Protoadamantyl Tosylate. (a) By the Tosyl Chloride–Pyridine Method.[22a] 4-*exo*-Protoadamantanol (X) (35 mg) dissolved in 2 ml of pyridine was treated with 100 mg of *p*-tosyl chloride. After work-up and crystallization from *n*-pentane, 47 mg of a white crystalline product was obtained, mp 81–82°, which proved to be identical with 2-adamantyl tosylate (IV) shown by the lack of mixture melting point depression with authentic material, and by its nmr spectrum: τ 8.49, 8.23, and 7.90 broad lines, 5.35 (C*H*-OTs), broad triplet.

(b) By the Methyllithium–Tosyl Chloride Method.[22b] 4-*exo*-Protoadamantanol (X) (70 mg) was dissolved in 10 ml of absolute ether and 0.6 ml of a 1 *M* solution of methyllithium in ether was added under a nitrogen atmosphere at 0°. After the mixture was stirred for 15 min, 177 mg of tosyl chloride in 5 ml of absolute ether was added gradually; stirring at 0° was continued for 2 hr. Work-up gave a crude product (62 mg) whose nmr spectrum was shown to be identical with that of 2-adamantanol.

(c) By the Sulfinate Method.[22c] A 1:2 mixture (110 mg) of 4-*exo*-protoadamantanol (X) and its endo isomer (XI) (the unseparated $LiAlH_4$ ketone VII reduction product) was dissolved in 5 ml of absolute ether and 57 mg of absolute pyridine was added. After the mixture was cooled to 0°, 120 mg of freshly distilled *p*-toluenesulfinyl chloride[46] was added which resulted in an immediate precipitation of pyridine hydrochloride. After 10 min the precipitate was filtered off and the crude sulfinate mixture was oxidized at 0° by adding 150 mg of *m*-chloroperoxybenzoic acid dissolved in 5 ml of CH_2Cl_2. After stirring this solution at 0° for 3 hr, it was chromatographed on a 10-g alumina column, using methylene chloride as eluent. Evaporation gave *ca.* 125 mg of an amorphous solid. The possible presence of 4-*exo*-protoadamantyl tosylate was tested by the following solvolysis experiment: 5 mg of the crude product was dissolved in 25 ml of 60% acetone at 0°. The solution was quickly transferred into a conductance cell and the conductance was measured at 0°. No measurable change conductance was found, indicating the absence of 4-*exo*-protoadamantyl tosylate, which should react at a moderate rate under these conditions. The cell was then placed in a 75° bath; the measurable change of conductance observed gave a rate constant of 9.2×10^{-4} sec^{-1}, identical with the value for 4-*endo*-protoadamantyl tosylate (XI-OTs), apparently the only tosylate in the reaction product.

Equilibration of 4-*exo*- and 4-*endo*-Protoadamantanol (X and XI). The aluminum isopropoxide in 2-propanol equilibration method used follows that reported for the 2-norbornanols.[25] The reactions were carried out in the following way: 10 mg of each alcohol (4-*exo*- or 4-*endo*-protoadamantanol (X or XI)) was heated in a sealed ampoule together with 30 mg of aluminum isopropoxide, 0.0005 ml of acetone, and 0.2 ml of 2-propanol. After the desired reaction time, the ampoule was chilled in ice and broken; 3 *M* HCl was added dropwise until the pH was about 5. The reaction product was extracted three times with 1 ml of ether, performed by shaking the ampoule and pipeting the ether phase. The ether phase was dried over sodium sulfate and injected directly into the gas chromatograph. On a 10-ft Carbowax 20M column, the products, 2-adamantanol, 4-*exo*-protoadamantanol (X), and 4-*endo*-protoadamantanol (XI), could be distinguished by their different retention times.

The reaction conditions investigated were: (a) at 100° for 48 hr, neither X nor XI reacted; (b) after 6 days at 150°, 4-*exo*-protoadamantanol (X) gave 48% 4-*exo*-protoadamantanol (X), 50% 4-*endo*-protoadamantanol (XI), and *ca.* 2% 2-adamantanol while 4-*endo*-protoadamantanol (XI) gave 16% 4-*exo*-protoadamantanol, 82% 4-*endo*-protoadamantanol, and *ca.* 2% 2-adamantanol; (c) after 3 days at 190° 4-*endo*-protoadamantanol (XI) gave, besides olefin, *ca.* 80% 2-adamantanol, *ca.* 5% 4-*exo*-protoadamantanol (X), and *ca.* 15% 4-*endo*-protoadamantanol (XI). The true equilibrium of XI and X could not be determined, but roughly, a 3:1 mixture was indicated from these experiments.

Rearrangement of Protoadamantane (I) to Adamantane. Protoadamantane (I) (67 mg, 0.5 mmol) was dissolved in 5 ml of carbon disulfide and 15 mg of anhydrous aluminum bromide was added. The mixture was stirred for 30 min at room temperature; after this time the gas chromatogram indicated rearrangement to adamantane to be complete. The solution was shaken with H_2O, dried over sodium sulfate, and evaporated *in vacuo*. After sublimation 48 mg (71%) of adamantane was obtained, mp 264–268°, gas chromatographically identical with authentic adamantane, as shown by coinjection.

Rearrangement of 4-Protoadamantanone (VII) to Adamantanone IX. 4-Protoadamantanone (VII) (50 mg, 0.33 mmol) was dissolved in 10 ml of 96.5% sulfuric acid and heated to 125° for 18 hr. At the end of this time the black solution was cooled and poured onto ice. The reaction product was extracted six times with 5 ml of methylene chloride. The combined organic extracts were washed with 10% sodium bicarbonate solution and water. After drying over sodium sulfate and vacuum evaporation, 14 mg (28%) of crude ketone was obtained, chromatographically identical with authentic 2-adamantanone as was shown by coinjection. The sublimed product, mp 279–283°, gave no melting point depression when mixed with authentic 2-adamantanone.

Solvolysis Experiments. Solvent Purification. Glacial acetic acid was prepared by refluxing commercial acetic acid with a slight excess of acetic anhydride, and fractional distillation.[47] Analytical reagent grade acetone was refluxed over potassium permanganate for 4 hr; after filtering and drying over calcium sulfate, the acetone was fractionated in a 60-cm Vigreux column, bp 56–57°.[48] Commercial trifluoroacetic acid was distilled twice through a helices-packed column, bp 72.2–72.6°.

Preparative Solvolysis. General. A Perkin-Elmer 810 gas chromatograph with flame ionization detector was used; for glc analyses Carbowax 20M (5% on Chromosorb W) 1/8-in. columns were found to give good results. Typical oven temperatures ranged from 120 to 160°. Generally 1.0 μl samples were injected; retention times were in the order of 20–120 min.

Acetolysis of 2-Adamantyl Tosylate (IV). Carefully purified 2-adamantyl tosylate (IV), mp 81.6–82.1° (1.0 g), was heated at 100° in 50 ml of acetic acid, buffered with 0.15 *M* potassium acetate, for 17 hr. A buffer of 35 g of KOH and 100 g of K_2HPO_4 in 100 ml of water was added after cooling and the resulting solution was extracted three times with 50 ml of ether. The combined ethereal solution was dried over sodium sulfate and evaporated *in vacuo*. The gas chromatogram showed one major peak (99.6%) easily identified as 2-adamantyl acetate. Besides this major component the gas chromatogram showed a peak (0.03%) of shorter retention time and a peak (0.4%) with longer retention time. Neither minor peak corresponded in retention time with 1-adamantyl acetate, 4-*endo*-protoadamantyl acetate (IX), or with bicyclo[3.3.1]non-2-

(46) N. Rabjohn, Ed., "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 937.

(47) S. Winstein, C. Hanson, and E. Grunwald, *J. Amer. Chem. Soc.*, 70, 812 (1948).

(48) Method modified from that described in A. I. Vogel, "A Textbook of Practical Organic Chemistry," Longmans, Green and Co., New York, N. Y., 1961, p 171.

enyl-7-carbinyl acetate prepared from the alcohol by acetylation with acetic anhydride in pyridine. The 0.03% component could not be identified, but the 0.4% peak had the same retention time as 4-*exo*-protoadamantyl acetate. However, since the retention times of 4-*exo*- and 4-*endo*-protoadamantyl acetates (VI and XI-OAc) were nearly identical, even coinjection made conclusive identification somewhat difficult.

Conversion of the Acetolysis Products to Their Trimethylsilyl Ethers. The trimethylsilyl ethers of 2-adamantanol, 4-*exo*-protoadamantanol (X), and 4-*endo*-protoadamantanol (XI) had very different retention times, and were superior to the acetates or alcohols for positive identification. About 0.1 g of the acetolysis product was dissolved in 10 ml of anhydrous ether and a suspension of 0.1 g of lithium aluminum hydride in 10 ml of absolute ether was added. The mixture was refluxed for 15 hr and worked up by the usual procedure. About 80 mg of a solid crude product was obtained; 5 mg of this mixture was converted to trimethylsilyl ethers by method described above. By coinjection on three columns it was shown that the 0.4% peak was chromatographically identical with 4-*exo*-protoadamantyl trimethylsilyl ether (X-OSi$(CH_3)_3$). No 4-*endo*-protoadamantyl trimethylsilyl ether could be chromatographically detected (detection limit *ca.* 0.005%).

Trifluoroacetolysis of 2-Adamantyl-2-*d* Tosylate (IV-*d*). 2-Adamantyl-2-*d* tosylate (IV-2-*d*)[19g] (30 mg) was dissolved in 10 ml of trifluoroacetic acid and allowed to react for a week at 25° (*ca.* 1000 half-lives). The solvent was evaporated *in vacuo* and the product was dissolved in ether. After the usual work-up, the product was analyzed by nmr; no downfield C*H*OH signal was found (detection limit *ca.* 5%) showing that no detectable 1,2-, 1,3-, or intermolecular hydride shifts occurred under these conditions.[38]

Solvolysis of 4-*exo*-Protoadamantyl 3,5-Dinitrobenzoate (X-ODNB) in 60% Acetone. 4-*exo*-Protoadamantyl 3,5-dinitrobenzoate (X-ODNB) (46 mg) was dissolved in 2 ml of 60% acetone (buffered with 0.01 *M* with 2,6-lutidine) and heated to 125° for 8 hr. This resulting solution was injected directly into the gas chromatograph; only one peak gas chromatographically identical with 2-adamantanol was found.

Solvolysis of 4-*exo*-Protoadamantyl-4-*d* 3,5-Dinitrobenzoate (X-*d*-ODNB) in 60% Acetone. 4-*exo*-Protoadamantyl-4-*d* 3,5-dinitrobenzoate (X-*d*-ODNB) (60 mg) was dissolved in 100 ml of acetone buffered with lutidine (0.01 *M*). The solution was heated in a large sealed ampoule at 125° for 42 hr. After cooling, the solution was evaporated *in vacuo* to a small volume and the product was extracted with ether. The ether phase was dried over sodium sulfate and evaporated to give 52 mg of a crude product from which a nmr spectrum was taken in $CDCl_3$ solution. This spectrum showed, besides the complex pattern of aliphatic protons, τ 7.6–8.6, a doublet (J = 2.8 Hz) at τ 4.73 (C*H*-ODNB) indicating the presence of 2-adamantyl-1-*d* 3,5-dinitrobenzoate and a second doublet (J = 3 Hz) at τ 6.12 (C*H*OH) indicating the presence of 2-adamantanol-1-*d*. Integration of both signals at τ 4.73 and 6.12 shows their total combined area to represent 1.00 ± 0.05 protons, based on the assumption of 13 aliphatic protons in the region τ 7.6–8.6. The ratio of the areas at τ 4.73 and at 6.12 indicates a 4:1 mixture of 2-adamantyl-1-*d* 3,5-dinitrobenzoate and 2-adamantanol-1-*d*.

Solvolysis of 4-*endo*-Protoadamantyl Tosylate in 60% Acetone. 4-*endo*-Protoadamantyl tosylate (6 mg) was dissolved in 2 ml of 60% acetone containing 0.01 *M* lutidine buffer and heated to 75° for 20 min. This solution was directly injected into the gas chromatograph. The chromatogram showed two peaks in the ratio of 4:1. The major peak was gas chromatographically identical with 2-adamantanol, the minor one with 4-*endo*-protoadamantanol (XI).

Solvolysis of 4-*endo*-Protoadamantyl Tosylate (XI-OTs) in Acetic Acid. 4-*endo*-Protoadamantyl tosylate (XI-OTs) (18 mg) was dissolved in 1 ml of acetic acid buffered with potassium acetate (0.15 *M*) and heated at 100° for 80 min. After cooling, the solution was diluted with water and the reaction product was extracted with ether. The ether phase was washed with 15% potassium bicarbonate solution and water and dried over sodium sulfate. After evaporation *in vacuo ca.* 12 mg of a crude product was obtained. The nmr spectrum showed this product to be identical with 2-adamantyl acetate; C*H*OAc at τ 5.15.

Solvolysis of 4-*endo*-Protoadamantyl-4-*d* Tosylate (XI-4-*d*-OTs) in 60% Acetone. 4-*endo*-Protoadamantyl-4-*d* tosylate (XI-4-*d*-OTs) (75 mg) was dissolved in 10 ml of 60% acetone containing 0.01 *M* lutidine as buffer and heated at 75° for 1 hr. The mixture was then extracted with ether; the ether phase was washed with 15% potassium bicarbonate solution and water. After the ether phase was dried with sodium sulfate and evaporation *in vacuo*, 41 mg of a crude alcohol product was obtained. Integration of the nmr spectrum showed 0.48 ± 0.05 proton at τ 5.9–6.1, relative to the area of the 13 aliphatic protons at τ 7.8–8.8.

Internal Return Study of the 4-*endo*-Protoadamantyl-4-*d* Tosylate (XI-4-*d*-OTs). (a) In 60% Acetone. 4-*endo*-Protoadamantyl-4-*d* tosylate (XI-4-*d*-OTs) (300 mg) was dissolved in 50 ml of 60% acetone and heated at 75° for 8 min. The solution was evaporated to a volume of *ca.* 20 ml whereupon the unreacted tosylate precipitated. The precipitate was filtered and crystallized from *n*-pentane to give 160 mg of 4-*endo*-protoadamantyl-4-*d* tosylate (XI-4-*d*-OTs, mp 72–74°. The nmr spectrum showed no signal (±0.03) at τ 5.2 indicating that no deuterium scrambling detectable by this method has occurred during solvolysis.

(b) In Acetic Acid. Tosylate (XI-4-*d*-OTs) (160 mg) was dissolved in 30 ml of acetic acid and heated at 75° for 35 min. The solvent was evaporated *in vacuo* and the residue was dissolved in 20 ml of 60% acetone. After standing for 2 days in the refrigerator, the unreacted tosylate precipitated. Filtration and recrystallization from *n*-pentane gave 70 mg of white crystals, mp 71–73°. The nmr spectrum of this product showed no signal at τ 5.2 (±0.03), indicating that no deuterium scrambling has occurred during solvolysis.

(c) In 90% Dioxane–10% Formic Acid. Tosylate XI-4-*d*-OTs (70 mg) in 20 ml of a mixture of 90% dioxane–10% formic acid was heated at 75° for 41 hr. The solvent was then evaporated *in vacuo* and the residue dissolved in 10 ml of 60% acetone. After the mixture stood 2 days in the cold, the unreacted tosylate precipitated. It was filtered and crystallized three times from *n*-pentane to give 20 mg of 4-*endo*-protoadamantyl tosylate (XI-OTs), mp 70–72°. Integration of the nmr spectrum showed a signal at τ 5.2 of area 0.08 ± 0.05 proton (relative to the 13 aliphatic protons) indicating that some deuterium scrambling has occurred during solvolysis. A more precise integration of the signal at τ 5.2 was obtained at 100 MHz; this indicated 0.083 ± 0.005 proton related to the area of the two aromatic protons of the B part of the AB spectrum of the tosylate group.

Kinetic Solvolysis. Rates were determined conductometrically with a Wayne-Kerr Model B 331 Impedence Bridge, capable of 0.1% accuracy. The conductivity cells used had bright platinum electrodes, cell constants of 0.2–0.4, and held approximately 25 ml. In a typical experiment 20 ml of a 10^{-3} *M* solution of the substrate was placed in the conductivity cell. The cell was sealed and equilibrated with shaking for 5 min in the constant-temperature bath. In general 15–18 conductance measurements were taken. The raw conductance data were then fitted to the first-order rate equation by means of a least-squares computer program. All rate constants reported are the result of at least two independent determinations; mean deviations of rate constants of 5% or less were observed. The activation parameters were calculated by a computer program.

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