Solvolysis of [3-^{13}C]-4-Homoadamantyl Tosylate. Limited Degeneracy of 4-Homoadamantyl Cation via Multiple Wagner–Meerwein Rearrangement and Vicinal Hydride Shifts under Solvolytic Conditions

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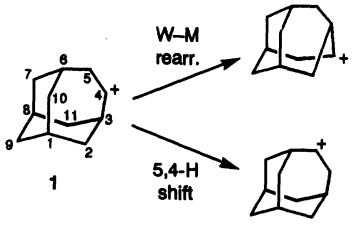
The solvolysis of 4-homoadamantyl tosylate in methanol, acetic acid, and 2,2,2-trifluoroethanol yielded 4-substituted homoadamantane and 4-homoadamantene as major products, together with *exo*-2-substituted homoadamantane and 2,4-dehydrohomoadamantane. The analysis of carbon-13 label distribution in the products from the [3-^{13}C]-labeled reactant, which provided results complementary to those of Nordlander's deuterium label experiments, showed that the 4-homoadamantyl cation is a classical ion that is rapidly rearranging via the degenerate Wagner–Meerwein process (k_w). This equilibrium was more nearly complete in less nucleophilic solvents. Another possible degenerate rearrangement, 5,4-hydride shift (k_h), was shown to be much slower (k_w/k_h = 140–760): most of the 4-substituted product is formed with no more than a single hydride shift. Thus, the potential 11-fold degeneracy of the 4-homoadamantyl cation through the two types of rearrangements is partially restricted by competing solvent attack (k_p). The analysis of the label distribution for the recovered reactant revealed involvement of appreciable ion pair return (k_{-i}). The relative rates of the four possible processes concerning the fate of 4-homoadamantyl cation were determined in acetic acid at 40 °C to be k_p:k_{-i}:k_w:k_h = 1:3.0:9.7:0.068.

Introduction

Multiple degenerate rearrangements of secondary alicyclic carbenium ions often construct systems with complete degeneracy over their entire structures.[1] The 4-homoadamantyl cation (1) potentially undergoes two types of degenerate rearrangements, Wagner–Meerwein rearrangement and 5,4-hydride shift. If both processes take place repeatedly, all 11 carbons of the tricyclic framework become equivalent. Operation of each type of rearrangement can be detected independently by the analysis of the label distribution in the products from an isotopically labeled precursor.



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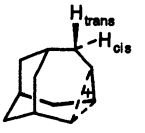

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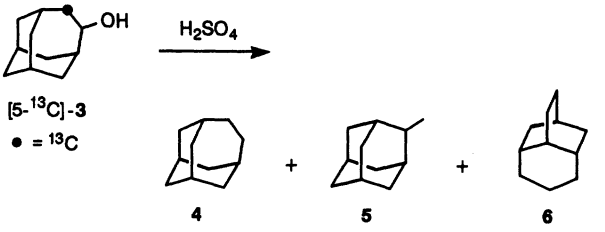
Majerski et al. have reported the ^{13}C label scrambling of the 4-homoadamantyl cation under two contrasting conditions.[2,3] Treatment of [5-^{13}C]-4-homoadamantanol ([5-^{13}C]-3) with sulfuric acid gave homoadamantane (4), 2-methyladamantane (5), and 4-homoisotwistane (6) in a ratio 1:1:2. The label had scrambled over all carbons in each product.[2] On the other hand, $AlBr_3$ in carbon disulfide converted [4-^{13}C]homoadamantene to [^{13}C]-5 as



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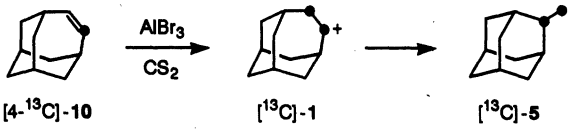
a single major product, in which the majority (~90%) of the label equally distributed at only C-2 and CH_3.[3] This marked difference in the degree of label scrambling was explained in terms of extended lifetime of the 4-homoadamantyl cation in sulfuric acid and its tight ion pairing in carbon disulfide.



[4-^{13}C]-10 [^{13}C]-1 [^{13}C]-5

In addition, the 4-homoadamantyl cation generated under solvolytic conditions was anticipated to show partial degeneracy, since the rearrangements occur in competition with solvent capture.[4,5] Nordlander[4] analyzed the label distribution in the acetolysis products, 4-homoadamantyl acetate (8b) and 4-homoadamantene (10), from deuterium-labeled 4-homoadamantyl tosylates [^{2}H]-7 and showed that the substitution process is accompanied by essentially full Wagner–Meerwein rearrangement of 1 together with its limited rearrangement by 5,4-hydride shift. On the basis of the absence of cis–trans stereoselectivity in the hydride shift, involvement of σ-bridged intermediate 2

• Abstract published in *Advance ACS Abstracts*, December 1, 1993.

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(4) Nordlander, J. E.; Hamilton, J. B., Jr.; Wu, F. Y.-H.; Jindal, S. P.; Gruetzmacher, R. R. *J. Am. Chem. Soc.* **1976**, *98*, 6658.

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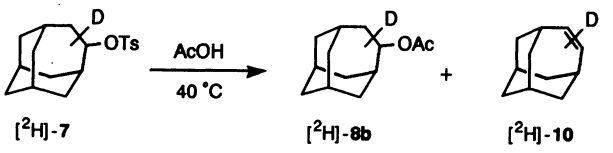
Table I. Rate Constants for the Solvolyses of 4-Homoadamantyl Tosylate 7

solvent	$Y_{2\text{-AdOTs}}$[a]	N_{OTs}[a]	temp (°C)	k_1 (s^{-1})	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$\Delta S^{\ddagger}$ (eu)
EtOH[b]	−1.75	0.00	25.0	1.68×10^{-6} [c]		
MeOH[b]	−0.92	−0.04	25.0	1.05×10^{-5} [c]	24.9	2.1
			40.0	8.23×10^{-5} [c]		
AcOH[d]	−0.61	−2.35	25.0	1.35×10^{-5} [e]	22.7	−4.9
			40.0	8.17×10^{-5} [c]		
80% EtOH[b]	0.00	0.00	25.0	4.50×10^{-5} [c]		
60% EtOH[b]	0.92	−0.08	25.0	3.10×10^{-4} [f]		
50% EtOH[b]	1.29	−0.09	25.0	8.70×10^{-4} [f]		
TFE[b]	1.80	−3.0	25.0	1.74×10^{-3} [f]	19.0	−7.6
			40.0	8.45×10^{-3} [f]		
TFA[g]	4.57	−5.56	25.0	2.26×10^{-1} [e]	10.3	−27.0

[a] Schadt, F. L.; Bentley, T. W.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1976**, *98*, 7667. [b] Buffered with 2,6-lutidine. [c] Determined titrimetrically within an experimental error of ±2%. [d] Buffered with sodium acetate. [e] Calculated from data at other temperatures, ref 4. [f] Determined conductimetrically within an experimental error ±0.5%. [g] Buffered with sodium trifluoroacetate.



was ruled out. However, large kinetic and equilibrium isotope effects by deuterium left the question of how extensively vicinal hydride shifts take place and how rapidly the 4-homoadamantyl cation undergoes Wagner–Meerwein rearrangement relative to hydride shift and to product formation.

In order to answer these questions, we carried out the solvolysis of [3-^{13}C]-4-homoadamantyl tosylate ([3-^{13}C]-7). Carbon-13 was used as an isotopic label instead of deuterium to minimize the influence of isotope effect. The lifetime of the cationic intermediate was varied by using solvents with different nucleophilicities. This paper describes the results of the label distribution analyses over all ring carbons of the products and the recovered reactant by quantitative ^{13}C NMR measurements.

Results

Synthesis. Lithium aluminum hydride reduction of 4-homoadamantanone, obtained by acylative ring expansion[6] of 1-adamantanecarbaldehyde, gave 4-homoadamantanol. The alcohol was converted to tosylate **7** in the usual manner.[7] Carbon-13 label was introduced by following the same procedure starting with 1-adamantane-[^{13}C]carbaldehyde.[6] ^{13}C NMR analysis of the [3-^{13}C]-4-homoadamantanol obtained in this way indicated that the label was located exclusively at C-3 with a ^{13}C content of 96.8 ± 0.1%.

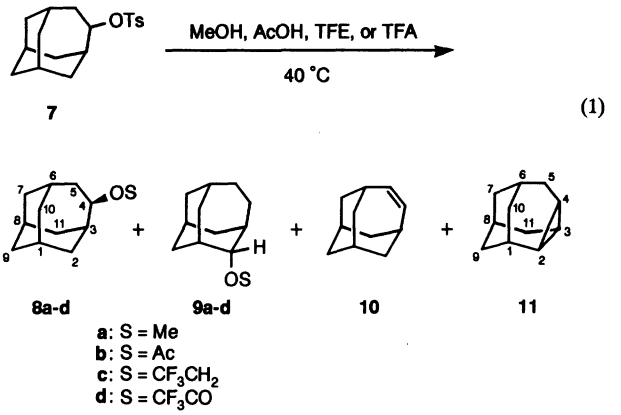
Solvolysis Rates. The rates of solvolysis of unlabeled 4-homoadamantyl tosylate (**7**) were determined by titrimetric or conductimetric methods in MeOH, 2,2,2-trifluoroethanol (TFE), EtOH, and aqueous EtOH in the presence of excess 2,6-lutidine. Good first-order plots ($r > 0.9997$) were obtained in all cases. The rate data are summarized in Table I, together with those reported[4] for acetolysis and trifluoroacetolysis of **7**.

Table II. Products of Solvolyses of 4-Homoadamantyl Tosylate 7[a]

substrate	solvent	temp (°C)	product distribution (%) 8a-d	9a-d	10	11
7	MeOH[b]	25.0	70	1	25	4
	AcOH[c]	25.0	61	2	33	4
	TFE[b]	25.0	75	6	17	2
	TFA[d]	25.0	72	28	0	
[3-^{13}C]-7	MeOH[b]	40.0	69	1	26	4
	AcOH[c]	40.0	63	3	31	3
	TFE[b]	40.0	73	7	18	2

[a] Relative yields determined by GC. [b] Buffered with 2,6-lutidine. [c] Buffered with sodium acetate. [d] Buffered with sodium trifluoroacetate, ref 4.

Product Studies. For the product study the buffered solvolysis of labeled and unlabeled **7** was carried out in MeOH, AcOH, and TFE at 25 °C (10 half-lives) and at 40 °C (20 half-lives). Analysis of the reaction mixture by GC indicated the presence of four compounds, which were identified as 4-substituted homoadamantanes (**8a-c**), *exo*-2-substituted homoadamantanes (**9a-c**), 4-homoadamantene (**10**), and 2,4-dehydrohomoadamantane (**11**, tetracyclo[5.3.1.0^{3,5}0^{4,9}]undecane). Compounds **8a**, **8b**, **9a**, **9b**, **10**, and **11** were synthesized via independent routes for the comparison purposes. Trifluoroethyl ethers **8c** and **9c** were identified by the NMR spectra of the trifluoroethanolysis products. Control experiments showed that each product was stable under the solvolysis conditions. The product distributions were determined by GC and listed in Table II.[8]



^{13}C Label Distribution in Solvolysis Products. The chemical shifts of some homoadamantane derivatives are summarized in Table III. Signals were assigned based on chemical shifts, signal intensities, and off-resonance decoupling or the DEPT measurements. Additional information about assignment was obtained on the basis of the ^{13}C–^{13}C coupling observed for labeled products. All the products and the recovered tosylate were found to contain more than 90% of the label at two adjacent positions, which were assigned to C-3 and C-4, in approximately 1:1 ratios. C-2, -5, and -11 were readily distinguished from other carbons by the line splitting caused by C-3 and C-4.

C-2 and C-10 were differentiated from C-11 and C-7, respectively, with the assumption that these carbons are

(6) Takeuchi, K.; Yoshida, M.; Nishida, M.; Kohama, A.; Kitagawa, T. *Synthesis* **1991**, 37.

(7) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; John Wiley and Sons: New York, 1967; Vol. 1, p 1179.

(8) It was shown by Nordlander that the addition of TFA to 4-homoadamantene (**10**) is not involved in the trifluoroacetolysis of **7**.[4] However, **8d** and **9d** may have been formed partly through 2,4-dehydrohomoadamantane (**11**), since rapid addition of TFA was observed to this compound at 25 °C to yield **8d** and **9d** in a ratio of 75:25.

Table III. ^{13}C NMR Chemical Shifts of Homoadamantane Derivatives

	chemical shift/ppm[a]										
compd	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11
4	27.5	38.2	31.8	33.8	33.8	31.8	38.2	27.5	36.3	38.2	38.2
7[b]	26.5*	29.7	37.6	88.3	41.5	29.0	39.5	26.7*	35.4†	35.8†	34.9
8a[c]	26.8*	29.8	34.9	86.1	41.8	29.4	40.0	27.3*	35.9†	36.5†	35.9
8b[d]	26.9*	30.4	36.7	78.9	41.0	29.4	39.8	27.0*	35.6†	36.1†	35.4
8c[e]	26.9*	29.6	35.6	86.5	41.4	29.3	39.8	27.2*	35.6†	36.3†	35.8
9c[f]	30.7*	87.3	36.1	29.1	33.2†	30.4*	39.0§	26.7	29.1	33.1§	32.8†
10	29.8	33.9	32.3	138.0	138.0	32.3	33.9	29.8	37.0	33.9	33.9
11	21.2	12.6	10.0	10.0	28.3	26.4	38.6	26.4	32.2	32.2	28.3

[a] Measured at 67.8 MHz in $CDCl_3$. The ring carbons are numbered as indicated in eq 1. Chemical shifts marked with *, †, and § may be interchanged. [b] Tosylate group: 144.2, 134.7, 129.6, 127.5, and 21.5 ppm. [c] Methoxy group: 56.3 ppm. [d] Acetyl group: 170.0 and 21.3 ppm. [e] Trifluoroethyl group: 124.2 and 66.3 ppm. [f] Trifluoroethyl group: 124.3 and 66.3 ppm.

Table IV. ^{13}C Distributions in the 4-Substituted Homoadamantanes (8a-c)[a] and *exo*-2-(Trifluoroethoxy)homoadamantane (9c) from the Solvolysis of [3-^{13}C]-7

		^{13}C distribution[b] (%)										
solvent	product	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11
MeOH	**8a**	0.2*	0.4	54.7	43.9	0.4	0.4	0.0	0.0*	0.0	0.0	0.0
AcOH	**8b**	1.0*	0.9	49.2	44.4	1.8	1.8	0.0	0.5*	0.1†	0.0†	0.3
TFE	**8c**	1.5*	1.5	46.6[c]	45.6	1.6	1.6	0.0	0.6*		0.2[d]	0.8
TFE	**9c**	0.4*	0.4	47.8	46.0[e]	1.6†	1.6*	0.0	1.2		0.0	1.0†

[a] The ring carbons of **8a-c** are numbered as indicated in eq 1. [b] Numbers marked with * and † may be interchanged. [c] C-3 + (C-9 or C-10). [d] C-9 or C-10. [e] C-4 + C-9.

Table V. ^{13}C Distributions in the 4-Homoadamantane (10) from the Solvolysis of [3-^{13}C]-7

	^{13}C distribution (%) in **10**				
solvent	C-1,8	C-2,7,10,11	C-3,6	C-4,5	C-9
MeOH	0.1	0.0	62.3	37.6	0.0
AcOH	0.8	0.6	56.8	41.8	0.0
TFE	1.2	0.8	55.4	42.4	0.2

more shielded than the former owing to the oxygen atom attached to C-4.[9] The assignments of C-1 and C-8 and those of C-9 and C-10, however, remained interchangeable with this procedure. The spectrum of **9c** was analyzed in the same way, but the assignments were only partially successful. The signals of **10** and **11** obtained from the labeled tosylate were assigned unambiguously with the assumption that the label was located mainly at C-3 and C-4.

For the determination of label distribution, proton-decoupled ^{13}C NMR spectra were measured in the presence of a relaxation reagent Fe(acac)$_3$[10] (0.05 M) by the gated decoupling method. The ^{13}C content at the nth carbon (x_n, n = 1–11) was calculated from peak integrations (A_n) by the following equation.

$$x_n\,(\%) = (96.8 + 10(1.108))A_n/\sum A_n \qquad (2)$$

To obtain label distribution, these values were subtracted by the natural abundance of ^{13}C (1.108%) and normalized in such a way that the total is 100%. The resulting data are given in Tables IV–VI. Generally, uncertainty limit for the label percent is estimated to be ±0.5% at C-3 and C-4 and ±0.2% at other positions. In the case of 2,4-dehydrohomoadamantane (**11**), however, greater errors were observed for some carbons (Table VI), owing to significant overlap of signals. Yields of **9a** and **9b** were so low that the low singal-to-noise ratios did not allow integrations with sufficient precision.

Table VI. ^{13}C Distributions in the 2,4-Dehydrohomoadamantane (11)[a] from the Solvolysis of [3-^{13}C]-7

	^{13}C distribution (%) in **11**						
solvent	C-1	C-2	C-3,4	C-5,11	C-6,8	C-7	C-9,10
MeOH	0.0	0.1	98.7	0.2	0.4	0.0	0.6 ± 1.0
AcOH	0.2	0.1	93.8	1.8	2.4	0.0	1.7 ± 1.0
TFE	1.0	0.7	93.5	1.9	1.6	0.8	0.5 ± 1.0

[a] The ring carbons of **11** are numbered as indicated in eq 1.

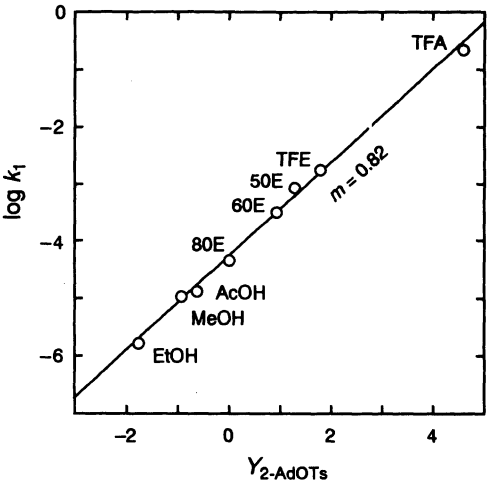


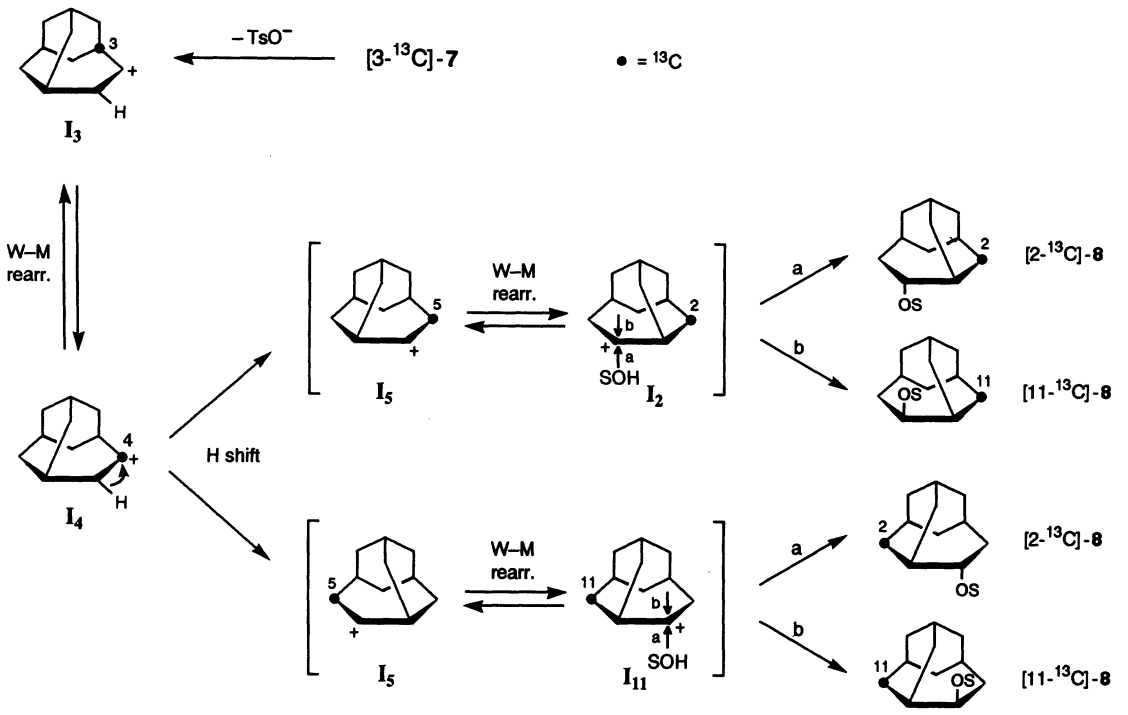
Figure 1. Plot of log k_1 for solvolysis of 4-homoadamantyl tosylate at 25 °C vs $Y_{2\text{-AdOTs}}$.

Discussion

Solvent Effect on Solvolysis Rates. A plot of log k_1 at 25 °C against $Y_{2\text{-AdOTs}}$ of the solvent showed a linear correlation with a slope of 0.82 (Figure 1, r = 0.998). The linear plot over a wide range of solvent ionizing power with a slope close to unity indicates that 4-homoadamantyl tosylate practically undergoes a limiting k_c process. This result supports the previous conclusion given by Nordlander[4] that the 4-homoadamantyl tosylate is highly resistant to backside nucleophilic assistance by solvent

(9) Duddeck, H.; Wolff, P. *Org. Magn. Reson.* **1977**, *9*, 528.
(10) Martin, M. L.; Martin, G. J.; Delpuech, J.-J. *Practical NMR Spectroscopy*, Heyden and Sons: London, 1980; Chapter 10, Section 3.

Scheme I



owing to steric limitations similar to those observed for the solvolysis of the 2-adamantyl systems.

Structure of 4-Homoadamantyl Cation. The result of the label analysis for the 4-substituted products, 8a-c (Table IV), provided detailed information on the structure and the reactivity of the 4-homoadamantyl cation intermediate.

The unequal label distributions on C-3 and C-4 indicate that the 3,4-methylene shift equilibrium is not completely established prior to product formation. The observed ratios of 3-^{13}C/4-^{13}C, 1.25 ± 0.03 (MeOH), 1.11 ± 0.02 (AcOH), and 1.02 ± 0.02 (TFE), show distinct deviation from those expected from primary carbon-13 isotope effect on the carbenium ion stability. Saunders et al.[11] have reported that 2,3-dimethyl[2-^{13}C]-2-butyl cation in SbF_5/SO_2ClF favors the positive charge on the labeled carbon with equilibrium constants ($^{12}C^+/^{13}C^+$) ranging between 0.9840 (-108 °C) and 0.9884 (-61 °C). A similar isotope effect, $^{12}C^+/^{13}C^+ = 0.9833$, has been reported by Kresge et al.[12] for ionization of triphenyl[^{13}C]methyl chloride in SO_2 at 0 °C.

The greater extent of C-3–C-4 scrambling in a less nucleophilic solvent is taken as evidence against the symmetrical, σ-bridged structure and is interpreted as indicating that the 4-homoadamantyl cation is a classical ion that is rapidly rearranging via the degenerate Wagner–Meerwein process. The contribution of nucleophilic solvent assistance is considered unlikely, based on the result of the rate study, as well as on the greater extent of C-3–C-4 label scrambling in substitution than in elimination (*vide infra*).

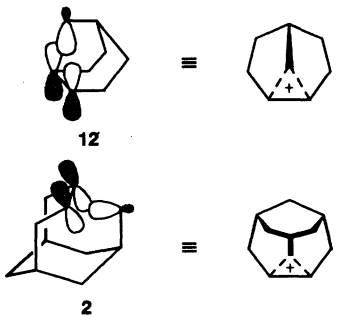
More convincing evidence for the classical nature of 4-homoadamantyl cation is provided by inspecting the 4-substituted homoadamantanes (8a-c) produced from unsymmetrically labeled intermediates, e.g., [2-^{13}C]- and [11-^{13}C]-4-homoadamantyl cations (I_2 and I_{11}, the subscript represents the position of the label[13]), which are potential precursors of both [2-^{13}C]-8 and [11-^{13}C]-8 (Scheme I). If these cations had σ-bridged structures I_5

$I_5 \leftrightarrow I_2$ $I_5 \leftrightarrow I_{11}$

$\leftrightarrow I_2$ and $I_5 \leftrightarrow I_{11}$, respectively, attack of the solvent molecule from the frontside of the bridge would be strictly prohibited. This should result in exclusive formation of [2-^{13}C]-8 rather than [11-^{13}C]-8. Therefore, the observed formation of a significant amount of [11-^{13}C]-8 (2-^{13}C: 11-^{13}C ≃ 2:1, Table IV) is strong evidence for the absence of σ-bridging. This conclusion is in accord with the absence of cis–trans stereospecificity in the 5,4-hydride shift of the 4-homoadamantyl cation reported by Nordlander.[4] Since the equilibrating ions $I_5 \rightleftarrows I_2$ and $I_5 \rightleftarrows I_{11}$ are supposed to have lost contact relationship with the tosylate anion after the preceding hydride shift,[4] the steric effect by the counterion may not be the source of the stereoselectivity. The preferred formation of [2-^{13}C]-8 is rather ascribed to the steric inhibition of the solvent attack from the direction cis to the migrating carbon.

These results are in contrast to that reported for bicyclo[3.2.1]oct-2-yl cation. Goering[14] proposed a σ-bridged structure 12 based on the fact that acetolysis of *endo*-bicyclo[3.2.1]oct-2-yl tosylate proceeds with complete retention of configuration. Appropriate orbital overlap for a symmetrically bridged structure appears much more encumbered in the homoadamantyl cation (2) than in 12, although both cations are analogous in that positively charged carbons belong to a seven-membered ring. A similar geometric restriction has been suggested by Ber-

(11) Saunders, M.; Cline, G. W. *J. Am. Chem. Soc.* **1990**, *112*, 3955.
(12) Kresge, A. J.; Lichtin, N. N.; Rao, K. N.; Weston, R. E., Jr. *J. Am. Chem. Soc.* **1965**, *87*, 437.
(13) The ring carbons of the 4-homoadamantyl cation are numbered as indicated in structural formula 1.
(14) Goering, H. L.; Sloan, M. F. *J. Am. Chem. Soc.* **1961**, *83*, 1397.



12 2

son[15] for the bicyclo[3.2.2]non-2-yl cation to explain the difficulty in attaining a σ-bridged structure.

Relative Rates of Wagner–Meerwein Rearrangement and Vicinal Hydride Shift. If the absence of frontside–backside stereospecificity with respect to the leaving group is assumed for both methylene and hydride migration, a diagram involving all the possible transformations among labeled 4-homoadamantyl cations $\mathbf{I}_n$ (n = 1–11) can be drawn as Scheme II.

The major distribution of the label at C-3 and C-4, but not at C-3 and C-6, with approximately equal populations clearly demonstrates predominant Wagner–Meerwein rearrangement (k_w) over 5,4-hydride shift (k_h). The formation of 4-substituted products **8a-c** labeled at positions other than C-3 or C-4 requires at least one hydride shift. The low total yields of such products, 1.4% (MeOH), 6.4% (AcOH),[16] and 7.8% (TFE), reflect the sluggishness of hydride shift compared to product formation. In particular, the negligible yields of **8a-c** labeled at C-7, -9, and -10, for which a second hydride shift is required, indicate that only the first hydride shift is significant. Further hydride shifts can then be ignored, thereby allowing simplification of the mechanistic model as illustrated in Scheme III.[17] $\mathbf{R}_n$ and $\mathbf{P}_n$ represent, respectively, the tosylate **7** and the 4-substituted product **8** labeled at the nth carbon. Rate constants k_i, k_{-i}, and k_p correspond to ionization, ion pair return, and product formation, respectively.

Steady-state treatment with respect to $\mathbf{I}_3$ and $\mathbf{I}_4$ results in the following rate expressions for tosylate consumption and product distribution

$$[\mathbf{R}_3] + [\mathbf{R}_4] = C_0 \exp\left(-\frac{k_i(k_p + k_h)}{k_{-i} + k_p + k_h}t\right) \quad (3)$$

$$[\mathbf{R}_3] - [\mathbf{R}_4] = C_0 \exp\left(-\frac{k_i(k_p + 2k_w + k_h)}{k_{-i} + k_p + 2k_w + k_h}t\right) \quad (4)$$

$$([\mathbf{P}_3] + [\mathbf{P}_4])_{t=\infty} = \frac{k_p}{k_p + k_h}C_0 \quad (5)$$

$$([\mathbf{P}_3] - [\mathbf{P}_4])_{t=\infty} = \frac{k_p}{k_p + 2k_w + k_h}C_0 \quad (6)$$

where C_0 is the initial concentration of the substrate [3-^{13}C]-**7**. Equations 5 and 6 afford expressions for the rates of Wagner–Meerwein rearrangement and vicinal hydride shift relative to solvent capture:

$$k_h/k_p = C_0/([\mathbf{P}_3] + [\mathbf{P}_4])_{t=\infty} - 1 \quad (7)$$

$$k_w/k_p = 0.5[C_0/([\mathbf{P}_3] - [\mathbf{P}_4])_{t=\infty} - (k_h/k_p) - 1] \quad (8)$$

From the fraction of **8a-c** labeled at C-3 and C-4 (Table IV), values for these rate ratios were calculated as listed in Table VII. This result allows evaluation of the rate of Wagner–Meerwein rearrangement relative to vicinal hydride shift: k_w/k_h = 340 ± 140 (MeOH), 140 ± 20 (AcOH), and 760 ± 340 (TFE).[18]

Ion Pair Return. The rates of ionization (k_i) and ion pair return (k_{-i}) in eqs 3 and 4 are related to two phenomenological rate constants, k_1 and k_{sc}.

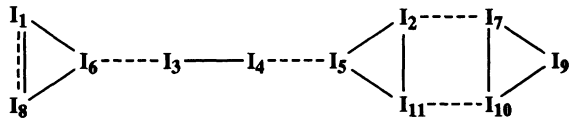
$$k_1 = \frac{k_i(k_p + k_h)}{k_{-i} + k_p + k_h} \quad (9)$$

$$k_{sc} = \frac{k_i(k_p + 2k_w + k_h)}{k_{-i} + k_p + 2k_w + k_h} \quad (10)$$

The rate of tosylate scrambling, k_{sc}, can be derived from eq 4 using the data from acetolysis of [3-^{13}C]-**7** over 1.0 half-life (141 min). The recovered tosylate had retained 54.1 ± 0.5% label at C-3, and 44.1 ± 0.5% of the label was found at C-4. This result, which corresponds to k_{sc} = (2.72 ± 0.06) × 10^{-4} s^{-1}, indicates involvement of appreciable ion pair return through the Wagner–Meerwein process.

With this value for k_{sc} and the values for k_1, k_w/k_p, and k_h/k_p (Tables I and VII), eqs 9 and 10 are solved simultaneously with respect to k_1 and k_{-i}/k_p, yielding k_i = 3.1 × 10^{-4} s^{-1} and k_{-i}/k_p = 3.0. The fractional conversion

Scheme II



Wagner-Meerwein equilibrium (k_w)
vicinal hydride shift equilibrium (k_h)

Scheme III

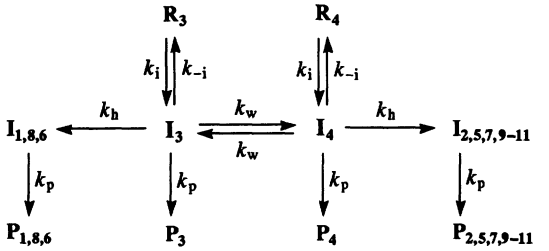


Table VII. Rate Constants of the Wagner–Meerwein Rearrangement (k_w) and 5,4-Hydride Shift (k_h) Relative to Solvent Capture (k_p) for the 4-Homoadamantyl Cation at 40 °C

solvent	k_w/k_p[a]	k_h/k_p
MeOH	4.1 ± 0.2	0.014 ± 0.005
AcOH	9.7 ± 0.8	0.068 ± 0.006
TFE	66 ± 33	0.085 ± 0.006

[a] See ref 18.

(15) Berson, J. A.; Luibrand, R. T.; Kundu, N. G.; Morris, D. G. *J. Am. Chem. Soc.* **1971**, *93*, 3075.

(16) Nordlander[4] reported that 18.6% of **8b** was formed with hydride shift in the acetolysis of [4-^{2}H]-**7**. As he pointed out, however, this number is an overestimation due to a large isotope effect by deuterium.

(17) The rate constant k_h as defined by Scheme III corresponds to half of that used in the kinetic treatment by Nordlander.[4]

(18) The errors in k_w/k_p and k_w/k_h are relatively large for TFE, since the small difference between $[\mathbf{P}_3]$ and $[\mathbf{P}_4]$ is amplified in eq 8.

of intermediates to products is $k_1/k_i = 0.26$, which is in good agreement with the result (0.30) derived from the deuterium scrambling of [4-^{2}H]-7 under the same conditions.[4] The combined data from 1.0 and 20 half-lives provide the relative rates of the four competitive processes concerning the fate of 4-homoadamantyl cation in AcOH at 40 °C: $k_p:k_{-i}:k_w:k_h = 1:3.0:9.7:0.068$. Thus, an unprecedentedly detailed picture of the reactivity was obtained for a secondary alicyclic carbenium ion that is degenerate with respect to both Wagner–Meerwein rearrangement and 1,2-type hydride shifts.

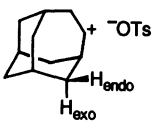
Mechanism of 4,5-Elimination. Nordlander has reported that the acetolytic elimination of 4-homoadamantyl tosylate to produce 4-homoadamantene (**10**) takes place by a syn E1 mechanism in which the effective base is tightly paired tosylate anion.[4] The basicity of the tosylate ion is reduced in a highly ionizing solvent by electrophilic solvation. This accounts for the substantial decrease in the yield of 4-homoadamantene with increasing ionizing power of the solvent (Table II). Similar dependence of elimination/substitution ratio on solvent ionizing power has been observed for the solvolysis of cyclooctyl brosylate.[19]

The ^{13}C label distribution analysis for 4-homoadamantene provided further evidence for the above mechanistic view. First, if elimination is to occur in an earlier ion-pair stage than substitution, a relatively low degree of Wagner–Meerwein equilibration would be attained during the course of 4-homoadamantene formation. Although direct measurement of the label distributions on C-3 and C-4 was not possible owing to the symmetry of the 4-homoadamantene molecule, the ratios C-3,6/C-4,5 = 1.66 ± 0.04 (MeOH), 1.36 ± 0.03 (AcOH), and 1.31 ± 0.03 (TFE) may be good approximations to the extent of C-3–C-4 label scrambling. As expected, comparison of these values with those observed for the 4-substituted products, 1.24 ± 0.03 (MeOH), 1.10 ± 0.02 (AcOH), 1.02 ± 0.02 (TFE), clearly indicates the more limited scrambling in elimination. Secondly, the sum of the label distributions at positions other than C-3, -4, -5, and -6 is a measure of the degree of 5,4-hydride shift: the values 0.1% (MeOH), 1.4% (AcOH), and 2.2% (TFE) were observed for 4-homoadamantene, which are significantly smaller than those observed for 4-substituted products, 0.6% (MeOH), 2.8% (AcOH), and 4.6% (TFE). This finding indicates a smaller degree of 5,4-hydride shift in elimination, and further supports the earlier formation of the olefin relative to the substitution product.

2,4-Hydride Shift. Nordlander et al. have obtained 4-homoadamantyl trifluoroacetate (**8d**) and *exo*-2-homoadamantyl trifluoroacetate (**9d**) in 72% and 28% yields, respectively, from the trifluoroacetolysis of 4-homoadamantyl tosylate.[4] They pointed out the possibility that the 2,4-hydride migration occurs within a σ-bridged cation **2**, which is formed as a second-stage intermediate from localized 4-homoadamantyl cation. Our results, however, indicated a different mechanistic possibility. If the *exo*-2-substituted products **9a-c** were produced via a symmetrically bridged cation **2**, the C-3/C-4 label distribution ratios should be 1 (or smaller if primary ^{13}C isotope effect is taken into account, *vide supra*). The observed ratio for **9c** was 1.04 ± 0.02 (or greater owing to the overlap of C-4 and C-9 signals, Table IV), which is comparable to that observed for **8c** (1.02 ± 0.02). This result suggests that **9c** was formed through direct 2,4-hydride migration from localized 4-homoadamantyl cation.

The fact that the yields of **9a-d** (Table II) increased markedly with decreasing solvent nucleophilicity can be explained by extended lifetimes of the cationic intermediate in weakly nucleophilic solvents. The yields of **9a-c** are similar to the fraction of **8a-c** formed after vicinal hydride shifts (*vide supra*) in each solvent, indicating that 1,2- and 1,3-type hydride shifts occur at comparable rates in the 4-homoadamantyl cation. The exclusive formation of the *exo*-isomer is presumably due to greater steric hindrance of the endo face of the 2-homoadamantyl cation. Similar face selectivity has been observed for the reduction of 2-homoadamantanone with lithium aluminum hydride or sodium borohydride (*exo*-OH:*endo*-OH = 0:100[20] and 5:95,[21] respectively).

2,4-Elimination. Different stereochemistries are expected for 1,3-type elimination to form 2,4-dehydrohomoadamantane (**11**), depending on whether H-2 is abstracted by tightly paired tosylate anion or solvent molecule. *endo*-H-2 should be abstracted selectively in



the former case, whereas in the latter case the abstraction of *exo*-H-2 would be favored by steric reasons. Although the present study does not definitively distinguish between the two possibilities, the latter mechanism seems more reasonable by the following reason. The fraction of **11** formed after vicinal hydride shifts is estimated by the amounts of label at positions other than C-3 and C-4: 1.3% (MeOH), 6.2% (AcOH), and 6.5% (TFE). These numbers are very close to those observed for 4-substituted products **8a-c** in each solvent, 1.4% (MeOH), 6.4% (AcOH), and 7.8% (TFE), indicating that **11** and **8a-c** are formed at essentially the same ion-pair stage. This result contrasts with that for 4-homoadamantene (**10**). As discussed earlier, the formation of **10**, in which the tosylate ion acts as the effective base, is accompanied by much smaller degrees of vicinal hydride shifts.

Experimental Section

Melting points are uncorrected. IR spectra were recorded on a Perkin–Elmer Model 1600 spectrophotometer. NMR spectra were obtained with a JEOL GSX270 instrument (^{1}H, 270 MHz; ^{13}C, 67.8 MHz) and reported in ppm (δ) from TMS. High-resolution mass analyses were perfomed with a JEOL JMS-HX110 mass spectrometer using electron impact ionization. Elemental analyses were performed by the Microanalytical Center, Kyoto University, Kyoto. Gas chromatographic analyses were conducted on a Hitachi 163 instrument equipped with a flame ionization detector and Hitachi Model D-2500 integrator using a PEG-20M column (3 mm × 2 m).

Reagents were of reagent-grade quality except when otherwise noted. Acetic acid was distilled in the presence of 3% acetic anhydride through a 30-cm Dewar column and stored with 1% acetic anhydride. Methanol was refluxed over sodium methoxide and distilled. 2,2,2-Trifluoroethanol was distilled in the presence of P_2O_5 through a 30-cm Dewar column. Ethanol was refluxed

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(20) Yamaguchi, R.; Katsushima, T.; Kawanishi, M. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 2328.

(21) Murray, R. K., Jr.; Babiak, K. A.; Morgan, T. K., Jr. *J. Org. Chem.* **1975**, *40*, 2463.

over magnesium ethoxide and distilled. Other anhydrous solvents used for synthesis were purified by the standard procedures. 2,6-Lutidine was distilled over CaH_2, bp 139.9–140.1 °C. Sodium acetate was dried at 100 °C under vacuum for 2 h. *p*-Toluenesulfonyl chloride was recrystallized from hexane, mp 71–72 °C. $Fe(acac)_3$ was recrystallized from 95% ethanol, mp 179.5–183.5 °C. $Ba^{13}CO_3$ as the source of $^{13}CO_2$ was purchased from Aldrich (98% ^{13}C) and CEA (90% ^{13}C).

4-Homoadamantanone was synthesized as reported previously[6] via the acylative ring expansion of 1-adamantanecarbaldehyde. [3-^{13}C]-4-Homoadamantanone was synthesized in the same way from 1-adamantane[^{13}C]carbaldehyde, which was obtained by the reaction of 1-adamantylmagnesium bromide with $^{13}CO_2$, followed by lithium aluminum hydride reduction and pyridinium chlorochromate oxidation.

4-Homoadamantanol (3). Reduction of 4-homoadamantanone (442 mg, 2.69 mmol) with lithium aluminum hydride (52 mg, 1.4 mmol) in ether (13 mL) gave 4-homoadamantanol (89% after recrystallization from hexane): colorless crystals, mp 268.5–269 °C (lit.[4] mp 267.0–268.0 °C).

4-Homoadamantyl Tosylate (7). 4-Homoadamantanol (566 mg, 3.40 mmol) was converted to the tosylate with *p*-toluenesulfonyl chloride (650 mg, 3.41 mmol) in dry pyridine (6.8 mL) in the usual manner.[7] Recrystallization from hexane gave pure tosylate (70%) as colorless crystals: mp 74–74.5 °C (lit.[4] mp 73.0–73.5 °C).

[3-^{13}C]-4-Homoadamantyl Tosylate ([3-^{13}C]-7). [3-^{13}C]-4-Homoadamantanone was reduced by lithium aluminum hydride to give the corresponding labeled alcohol: colorless crystals, mp 272–272.5 °C (after recrystallization from hexane). To determine the label content, the ^{13}C NMR spectrum of the undegassed benzene-d_6 solution was measured by the gated decoupling method using a pulse interval of 23 s, which corresponds to five times the T_1 of C-4. The peak integration indicated that the label was located exclusively at position 3 with a ^{13}C content of 96.8 ± 0.1%. Treatment of the labeled alcohol with *p*-toluenesulfonyl chloride in pyridine afforded the labeled tosylate as colorless crystals (mp 74.5–75.5 °C after recrystallization from hexane).

4-Methoxyhomoadamantane (8a). To a stirred solution of 4-homoadamantanol (0.33 g, 2.0 mmol) and methyl iodide (1.14 g, 8.0 mmol) in DMSO (5 mL) was added finely divided KOH (0.45 g, 8.0 mmol). The mixture was stirred at room temperature for 45 min and poured into water (30 mL). The product was extracted with pentane (3 × 10 mL), and the pentane solution was washed with water and dried ($MgSO_4$). Evaporation of the solvent followed by column chromatography (SiO_2, hexane–ether (4:1)) afforded 0.19 g (53%) of **8a** as a colorless oil. The ^{13}C NMR spectral data for **8a** are given in Table III. Other physical properties have been reported in the literature.[22]

4-Homoadamantyl Acetate (8b). Following the method of Nordlander,[4] 4-homoadamantyl acetate was prepared by heating a pyridine solution (3.5 mL) of 4-homoadamantanol (0.21 g, 1.3 mmol) at 100 °C for 3 h in the presence of acetic anhydride (0.51 g, 5.0 mmol). Aqueous workup afforded a yellowish liquid (0.26 g, 99%, lit.[4] 80%), which was used for ^{13}C NMR chemical shift determination (Table III) without further purification.

***exo*-2-Methoxyhomoadamantane (9a).** *exo*-2-Homoadamantanol[20] was prepared by hydrogenation of *exo*-2-hydroxy-4-homoadamantene[20] with 5% Pd–C/H_2. To a DMSO solution (0.9 mL) of this alcohol (48 mg, 0.29 mmol) and methyl iodide (160 mg, 1.1 mmol) was added finely divided KOH (70 mg, 1.2 mmol). The mixture was stirred at room temperature for 1 day and poured into water (10 mL). The product was extracted with ether (3 × 10 mL), and the ether solution was washed with water (3 × 10 mL) and dried ($MgSO_4$). Evaporation of the solvent gave a colorless semisolid, which on MPLC (SiO_2) afforded **9a** (24 mg, 46%, hexane–ether (9:1)) as a colorless oil and the starting alcohol (17 mg, 35%, hexane–ether (3:2)) as a white powder. **9a**: ^{1}H NMR ($CDCl_3$) δ 3.31 (s, 3 H), 3.04 (br d, J = 2.1 Hz, 1 H), 2.19–1.98 (m, 4 H), 1.95–1.80 (m, 4 H), 1.75–1.66 (m, 4 H), 1.47–1.18 (m, 4 H); IR (liquid film) 2920, 1261, 1097, 804 cm^{-1}; HRMS calcd for $C_{12}H_{20}O$ 180.1514, found 180.1514. The ^{13}C NMR spectral data are given in Table III. The analytical data for carbon and hydrogen were ca. 0.9 times the calculated values because of high volatility.

***exo*-2-Homoadamantyl Acetate (9b).** A solution of *exo*-2-homoadamantanol[20] (17 mg, 0.10 mmol) and acetic anhydride (47 mg, 0.46 mmol) in pyridine (1 mL) was stirred for 14 h at room temperature and for a further 1 h at 100 °C. The cooled mixture was poured into water (10 mL) and extracted with ether (3 × 10 mL). The ether solution was washed with 10% HCl, 5% $NaHCO_3$, and saturated NaCl and dried ($MgSO_4$). Evaporation of the solvent afforded 19 mg (89%) of essentially pure **9b**, which was used as an authentic reference for identification of the solvolysis product. The ^{1}H NMR and IR spectral data have been reported in the literature.[21]

4-Homoadamantene (10) and 2,4-Dehydrohomoadamantane (11). Following the method of Kawanishi et al.,[23] 4-homoadamantanol (97 mg, 0.58 mmol) was dissolved in HMPA (0.80 mL) and heated at 235 °C for 5 h. The reaction mixture was poured into water (1 mL) and extracted with pentane (5 × 10 mL). The pentane solution was dried over $MgSO_4$ and filtered through SiO_2 (2 g). Evaporation of the solvent gave a colorless powder, which on MPLC (7% $AgNO_3$ on SiO_2, hexane) gave **11** (6.3 mg, 7.3%) and **10** (43 mg, 50%) in this sequence. **10**: mp 230.5–236.5 °C in a sealed tube (lit.[4] mp 237.5–238.5 °C). **11**: mp 202–204 °C in a sealed tube (lit.[24] mp 226–229 °C).

Methanolysis of [3-^{13}C]-7. A solution of [3-^{13}C]-7 (257 mg, 0.800 mmol) in methanol (20 mL) containing 0.050 M 2,6-lutidine was heated in a constant temperature water bath (40 °C) for 46 h 57 min (20 half-lives). The solution was subjected to GC analysis, by which product yields were determined. After most of the methanol had been removed at 0 °C under vacuum, the residue was dissolved in ether. This solution was washed with 10% NaCl, 5% HCl, 10% NaCl, 5% $NaHCO_3$, and saturated NaCl and dried ($MgSO_4$). Evaporation of the ether afforded a faintly yellow oil, which on MPLC (SiO_2) afforded a mixture of **10** and **11** (19 mg, hexane) and a mixture of **8a** and **9a** (96 mg, hexane–ether (9:1)).

Acetolysis of [3-^{13}C]-7. (a) 20 Half-lives. A solution of [3-^{13}C]-7 (253 mg, 0.787 mmol) in acetic acid (20 mL) containing 1% acetic anhydride and 0.050 M sodium acetate was heated in a constant temperature water bath (40 °C) for 47 h 12 min (20 half-lives). The solution was poured into water (30 mL) and extracted with ether. The ether solution was washed with water, saturated $NaHCO_3$, and saturated NaCl and dried ($MgSO_4$). Evaporation of ether gave a mixture of faintly yellow oil and colorless solid, for which the product yields were determined by GC. MPLC (SiO_2) afforded a mixture of **10** and **11** (30 mg, hexane) and a mixture of **8b** and **9b** (105 mg, hexane–ether (19:1)).

(b) 1.0 Half-life. The acetolysis of [3-^{13}C]-7 (88.5 mg, 0.275 mmol) was carried out for 141 min (1.0 half-life) in the same way as described above. After quick extraction at 0 °C, the solvent was evaporated under vacuum at 0 °C. Recrystallization of the residue from hexane at 0 °C gave 4-homoadamantyl tosylate (30 mg) as colorless crystals: mp 73.5–74 °C.

Trifluoroethanolysis of [3-^{13}C]-7. A solution of [3-^{13}C]-7 (254 mg, 0.790 mmol) in TFE (20 mL) containing 0.050 M 2,6-lutidine was heated in a constant temperature water bath (40 °C) for 28.1 min (20.6 half-lives). The solution was subjected to GC analysis, by which product yields were determined. After most of the TFE had been removed at 0 °C under vacuum, the residue was dissolved in ether. The solution was washed with 10% NaCl, 5% HCl, 10% NaCl, 5% $NaHCO_3$, and saturated NaCl and dried ($MgSO_4$). Evaporation of the ether afforded a faintly yellow oil, which on MPLC (SiO_2) afforded a mixture of **10** and **11** (12 mg, hexane), **9c** (11 mg, hexane–ether (19:1)), a mixture of **8c** and **9c** (36 mg, hexane–ether (19:1)), and **8c** (94 mg, hexane–ether (19:1)) in this sequence.

Unlabeled **8c** and **9c** were obtained in the same way. **8c**: colorless liquid; ^{1}H NMR ($CDCl_3$) δ 3.86–3.63 (m, 3 H), 2.38 (m, 1 H), 2.19 (m, 1 H), 2.03 (m, 1 H), 1.97–1.79 (m, 6 H), 1.73–1.66 (m, 2 H), 1.55 (s, 3 H), 1.47–1.36 (m, 2 H); IR (liquid film) 2903,

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(24) Yamaguchi, R.; Katsushima, T.; Kawanishi, M. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 2830.

1279, 1159, 1124 cm^{-1}. Anal. Calcd for $C_{13}H_{19}F_3O$: C, 62.89; H, 7.71; F, 22.96; Found: C, 62.68; H, 7.90; F, 23.22. **9c**: colorless liquid; ^1H NMR ($CDCl_3$) δ 3.78 (m, 2 H), 3.30 (m, 1 H), 2.2–1.2 (m, 16 H); IR (liquid film) 2906, 1278, 1157, 1122 cm^{-1}. HRMS calcd for $C_{13}H_{19}F_3O$ 248.1388, found 248.1403. Analysis for C gave a number slightly greater than calculated, since it was difficult to remove the solvent completely owing to high volatility. Anal. Calcd for $C_{13}H_{19}F_3O$: C, 62.89; H, 7.71. Found: C, 63.90; H, 7.84. The ^{13}C NMR spectral data for **8c** and **9c** are listed in Table III.

Quantitative ^{13}C NMR Analysis. The distribution of the ^{13}C label in the solvolysis products was determined from ^{13}C NMR spectra measured for undegassed $CDCl_3$ solutions in the presence of a relaxation reagent, $Fe(acac)_3$ (0.05 M).[10] The influence of the nuclear Overhauser enhancements was eliminated by employing the gated decoupling method. In order to ensure the accuracy of the signal intensity, FID signals were collected with a pulse interval of 3.0 s, which is longer than five times the longest relaxation times (T_1) shown by 4-homoadamantyl acetate. Spectra were recorded with a digital resolution of 0.35–0.52 Hz using an exponential multiplication corresponding to the line broadening of 1.0 Hz. Signals obtained by this procedure consisted of more than 20 points. Basically, signal intensities were obtained by digital integration using the NMR instrument. When two peaks overlap partially, they were resolved by the cut-and-weigh method. Repeated measurements showed that the precision was ca. ±0.5% for C-3 and C-4 and ca. ±0.2% for other carbons.

Kinetic Measurements. The methods for kinetic measurements were described previously.[25] All measurements were conducted in the presence of 0.025 M 2,6-lutidine with substrate concentrations of (1–2) $\times 10^{-2}$ M (titrimetric method) or (2–20) $\times 10^{-4}$ M (conductimetric method). The first-order rate constants were calculated by the least-squares method.

Acknowledgment. We thank Prof. Ryohei Yamaguchi for providing us with *exo*-2-hydroxy-4-homoadamantene.

Supplementary Material Available: ^1H and ^{13}C NMR spectra of **9a** and **9c** (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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