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Articles

Solvolyses of Bicyclo[2.2.2]oct-1-yl and 1-Adamantyl Systems Containing an Ethylidene Substituent on the 2-Position: Typical Examples of Rate Enhancements Ascribed to Relief of F-Strain

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The first typical examples are described on the solvolysis rate enhancements ascribed to the relief of F-strain between an alkyl group and the leaving group atom directly attached to the reaction center. The rates and products of solvolyses in ethanol were studied for 2-methylene- and (*Z*)- and (*E*)-2-ethylidenebicyclo[2.2.2]oct-1-yl triflates. Solvolyses were also conducted in ethanol and 2,2,2-trifluoroethanol (TFE) on 2-methylene- and (*Z*)- and (*E*)-2-ethylidene-1-adamantyl compounds having OMs, F, Cl, Br, or I as a leaving group. All the substrates gave the corresponding bridgehead substitution products as kinetic control products. The *Z*:*E* rate ratios at 25 °C were 217 ± 6 for 2-ethylidenebicyclo[2.2.2]oct-1-yl triflates (ethanol) and 109 ± 11 (ethanol) and 117 ± 1 (TFE) for 2-ethylidene-1-adamantyl mesylates. ^{18}O scrambling studies on the ethanolyses of (*Z*)- and (*E*)-2-ethylidene-1-adamantyl mesylates showed that the titrimetrically determined *Z*:*E* rate ratios can be used as a measure of the rate ratios for the ionization step. The *Z*:*E* rate ratio in TFE at 25 °C for 2-ethylidene-1-adamantyl halides varied in the sequence F (ca. 70), Cl (1020 ± 160), Br (2230 ± 90), and I (9500 ± 280). The significant increases in the rate ratio with the increase in the atomic size of halogen were explained in terms of the presence of F-strain in the *Z* substrates and its essential absence in the *E* substrates. Linear correlations were found in a plot of $1.36 \times \log[k_Z/k_E]$ against the MM2 steric energy difference between the *Z* and *E* isomers (slope 1.0) and against Hansch's Es, demonstrating the significance of F-strain effect in the enhanced rates of the (*Z*)-2-ethylidene-1-adamantyl system. These correlations showed an intercept of 0.8 kcal mol^{-1}, which suggested the greater stability of the (*Z*)-2-ethylidene-1-adamantyl cation than the corresponding *E* cation by this amount. Ab initio calculations (RHF/6-31G**) showed that the *Z* cation is more stable than the *E* cation by 1.0 kcal mol^{-1}, and that the large *Z*:*E* rate ratios are in part ascribed to the difference in the cation stability.

Quantitative understanding of steric effects on the behavior of organic compounds has been one of major subjects in physical organic chemistry.[1] Such quantitative treatments have been most extensively done on the formation and breaking of chemical bonds, for example, coordination of amines with alkylboranes,[2] ester hydrolysis,[1a,3] solvolysis,[4] and carbon—carbon σ bond breaking.[5] Recent progress in molecular mechanics calculations has allowed for the explanation of various experimental data on a steric basis, and classic theories based on experiments are now being reassessed by calculations.[6] However, even now typical experimental data are not sufficient to generalize proposed theories.

The back strain (B-strain) and front strain (F-strain) theories were originally proposed by Brown in the 1950s to explain the enormous steric effects on the heat of coordination of amines with alkylboranes.[2] These theories have played an important role in rationalizing markedly enhanced rates of S_N1 solvolyses.[7] In the transition state of ionization of crowded molecule R_3CX, both B-strain among the three alkyl groups (R) and F-strain between the leaving group and the alkyl groups (R) are partially relieved, resulting in enhancement of solvolysis rates (Scheme 1). Hitherto, many examples of the rate enhancement ascribable to the B-strain effect have been reported[1c,d,7] and rationalized by molecular mechanics calculations.[4b,8] However, it is not necessarily easy to evaluate the B- and F-strain effects separately, because increasing the bulkiness of the R groups to assess the B-strain effect inevitably increases the F-strain effect

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(1) For example, see: (a) *Steric Effects in Organic Chemistry*; Newman, M. S., Ed.; Wiley: New York, 1956. (b) Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. *Conformational Analysis*; Wiley: New York, 1965. (c) Tidwell, T. T. *Tetrahedron* **1978**, *34*, 1855. (d) Stirling, C. J. M. *Ibid.* **1985**, *41*, 1613.

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(7) Brown, H. C. (with comments by Schleyer, P. v. R.) *Nonclassical Ion Problem*; Plenum: New York, 1977.

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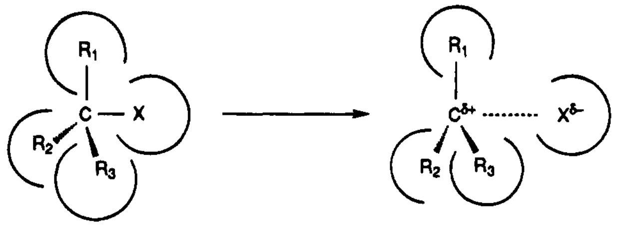
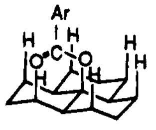
0022-3263/94/1959-4056$04.50/0

Scheme 1

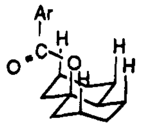


between the R groups and the leaving group X.[9] To our knowledge, only three studies seem to be useful as supporting evidence for the F-strain effect in solvolysis.

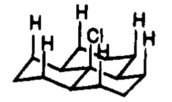
The most unambiguous example is the work reported by Schleyer and Brown.[10] They found that *trans,trans,trans*-perhydro-9b-phenalyl *p*-nitrobenzoate (**1-OPNB**) solvolyzes 2860 times faster than *trans*-9-decalyl *p*-nitrobenzoate (**2-OPNB**) in 80% acetone at 25 °C.[10] Since the rate enhancement essentially vanishes in the chloride (**1-Cl**), the major F-strain effect of **1-OPNB** was attributed to the repulsion between the carbonyl group (and/or aryl group) and the ring system, and the F-strain effect of a leaving group atom directly attached to the reaction center was taken as unimportant.[10] This notion was supported by molecular mechanics calculations.[4b] A similar example was provided by Dubois and his coworkers, who compared the *t*-Bu/Me rate ratios of solvolysis by changing the leaving group of 2-alkyl-2-adamantyl system **3**.[11b,c] The large *t*-Bu/Me rate ratio at 25 °C of 225 000 for *p*-nitrobenzoate solvolyses[11a] as compared with 1820 for alcohol dehydration[11b,c] was ascribed to the greater F-strain effect for the *p*-nitrobenzoate than for the protonated alcohol.



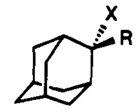
1-OPNB



2-OPNB



1-Cl



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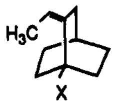
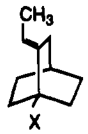
R = *t*-Bu or Me
X = OPNB or OH⁺

The F-strain effect exerted by *the leaving group atom directly attached to the reaction center* was evaluated by Brown and Stern.[12] They reported that the *t*-Bu/Me rate ratio in the solvolysis of RMe_2CX (X = halogen) increases with the bulkiness of X in the manner 1.21 (X = Cl), 1.68 (X = Br), and 2.84 (X = I) in 80% ethanol at 25 °C.[12] These results show a small but definite trend supporting the leaving group strain effect. However, it appeared to the present authors that the changes were too small to warrant detailed analyses.

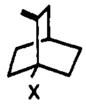
Consequently, we wished to design an appropriate system for evaluation of the F-strain effect of *the leaving group atom which is directly attached to the reaction center*. As such systems, we selected the bicyclo[2.2.2]oct-1-yl and 1-adamantyl systems having a (*Z*)-ethylidene substituent on the 2-position.[13,14] Since allylic conjugation in their carbocations had been shown to be insignificant,[15] the solvolysis rate ratios between the *Z* and *E* substrates were thought to afford a good measure of F-strain effect in the *Z* substrates with the B-strain effect being kept essentially constant. This paper describes the details of the solvolyses of various bicyclo[2.2.2]oct-1-yl (**4**, **5**) and 1-adamantyl (**6**–**8**) derivatives.[13] The leaving group was variously changed, and a methylene, a (*Z*)-ethylidene, or an (*E*)-ethylidene substituent was placed on the 2-position. The rate data and molecular mechanics calculations clearly showed a dramatic F-strain effect in the solvolyses of the (*Z*)-2-ethylidene substrates and its essential vanishing in the 2-methylene and (*E*)-2-ethylidene substrates.



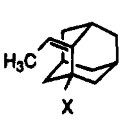
(*Z*)-4-X



(*E*)-4-X

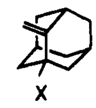


5-X

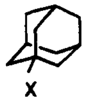


(*Z*)-6-X

(*E*)-6-X



7-X



8-X

Results

Synthesis. The triflate (*Z*)-**4-OTf** was prepared from the previously reported alcohol (*Z*)-**4-OH**.[15c] Mesylate **7-OMs** was derived from the corresponding known alcohol **7-OH**[15a,b] which was provided by the Wittig methylenation of the *tert*-butyldimethylsilyl ether of 1-hydroxy-2-adamantanone. 2-Ethylidene-1-adamantanols [(*Z*)- and (*E*)-**6-OH**] were prepared by the previously reported method[14] and their stereochemistry was determined by ^{1}H NMR NOE difference experiments (see Experimental Section). These alcohols were converted to 2-ethylidene-1-adamantyl chlorides [(*Z*)- and (*E*)-**6-Cl**] or bromides [(*Z*)- and (*E*)-**6-Br**] by treatment with thionyl chloride or thionyl bromide, respectively, in the presence of pyridine.

A new route which had been developed for the synthesis of 2-methylene-1-adamantyl iodide (**7-I**) and 2-ethylidene-1-adamantyl iodides [(*Z*)- and (*E*)-**6-I**][14] was applied to the preparation of the other 2-methylene-1-adamantyl halides (**7-Cl** and **7-Br**) and 2-ethylidene-1-adamantyl fluorides [(*Z*)- and (*E*)-**6-F**] as shown in Scheme 2. Acylative ring expansion of noradamantane-

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(9) Cheng, P.-T.; Nyburg, S. C.; Thankachan, C.; Tidwell, T. T. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 654.

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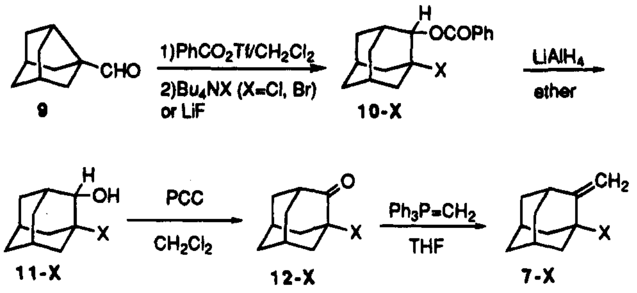
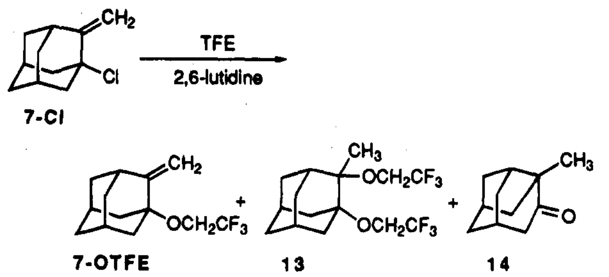
Scheme 2



Scheme 3



3-carbaldehyde (**9**) with benzoyl triflate[16] in CH_2Cl_2 followed by treatment with Bu_4NX (X = Cl or Br) or finely powdered LiF gave 1-halo-2-adamantyl benzoates (**10-X**).[17] Reduction of **10-X** with $LiAlH_4$ followed by oxidation with pyridinium chlorochromate afforded 1-halo-2-adamantanones[18] (**12-X**). The Wittig methylenation of **12-X** with methylenetriphenylphosphorane in THF gave **7-X**. Ethylidenation of 1-fluoro-2-adamantanone (**12-F**) in THF gave a mixture of (*Z*)- and (*E*)-2-ethylidene-1-adamantyl fluorides, which were separated from each other by means of MPLC (SiO_2) in yields of 45 and 41%, respectively.

The determination of the *Z* or *E* stereochemistry of **6-F**'s and **6-I**'s rests upon comparisons of their ^{13}C NMR chemical shift data with those of **6-Cl**'s and **6-Br**'s whose stereochemistry has been unambiguously established.[20] Two general characteristics are that the methyl and C(3) carbons of the *Z* compounds resonate at 1.5 ± 0.2 and 11.8 ± 1.5 ppm lower field than those of the *E* ones, respectively. It is also worth mentioning that the ^{13}C chemical shift difference (ppm) between the *Z* and *E* compounds with respect to the C(1) carbon decreases in the sequence **6-F** (2.9), **6-Cl** (−1.5), **6-Br** (−5.5), and **6-I** (−13.1), presumably because of increasing steric compression between the (*Z*)-methyl and the halogen atom.

Rate Studies. The solvolyses of (*E*)-**4-OTf**,[15c] **5-OTf**,[15c] (*Z*)- and (*E*)-**6-OMs**,[14] and (*Z*)- and (*E*)-**6-I**[14] were reported previously. All the substrates, except for (*Z*)-**4-OTf**, were purified by means of MPLC (SiO_2) and subsequent recrystallization. (*Z*)-**4-OTf** was very unstable to water and column chromatography. Therefore, the crude substrate which was essentially pure (>97%) on the basis of ^{13}C NMR was used for solvolysis without further purification; the sole impurity, if any, was the starting alcohol that did not influence the solvolysis rates. Except for the fluorides (*Z*)- and (*E*)-**6-F** and **8-F**, the solvolysis rates were measured either titrimetrically or conductimetrically in the presence of 2,6-lutidine to give good first-order kinetics (r > 0.997) over 80−90% of the reactions.

Initially, the rate measurement for 1-adamantyl fluoride (**8-F**) was attempted by using the titrimetric method, but it turned out that the produced HF was consumed, most probably owing to the reaction with glass, the material of the Pyrex ampules. Therefore, the rates of the fluorides were determined by following the substrate: product ratio by GLC (PEG 20M). Since the fluorides solvolyzed very slowly even in TFE, the reactions were followed over 4−16% at 100 and 125 °C. All the fluorides followed fairly good first-order kinetics within an experimental error of 1−7% for the rate constants at a 95% confidence limit. However, because of long extrapolations from data at 125 and 100 °C, the estimated rates of (*Z*)- and (*E*)-**6-F** at 25 °C are considered to include an error of ca. ±40%. All the first-order rate constants are summarized in Table 1 together with previously reported data for (*Z*)- and (*E*)-**6-OMs**[14] and (*Z*)- and (*E*)-**6-I**.[14]

The *Z*:*E* rate ratio in EtOH at 25 °C was 217 ± 6 for **4-OTf** and 109 ± 11 for **6-OMs**. Since the *Z*:*E* rate ratio for **6-OMs** in TFE (117 ± 1 at 25 °C) was very close to that in EtOH, the effect of changing the solvent on the rate ratio is small. The *Z*:*E* rate ratio for **6-X** (X = halogen) in TFE at 25 °C increased in the order **6-F** (ca. 70 or 28−160), **6-Cl** (1020 ± 160), **6-Br** (2230 ± 90), and **6-I** (9500 ± 280).

Product Studies. The solvolyses were carried out in ethanol and TFE on 0.040 M substrate solutions containing 0.050 M 2,6-lutidine at convenient temperatures for 10 half-lives or longer periods. Solvolysis products were identified by ^{13}C NMR and GLC (PEG 20M). The substrates gave solely the corresponding bridgehead ethers, except for **7-Cl** in TFE and **7-OMs** in ethanol. **7-Cl** afforded a mixture of bridgehead trifluoroethyl ether **7-OTFE** (71%), 1,2-bis(2,2,2-trifluoroethoxy)-2-methyladamantane (**13**) (20%), and 2-methyl-4-protoadamantanone (**14**) (9%) after 10 half-lives at 125 °C (Scheme 3). These products were separated by MPLC (SiO_2), and trifluoroethyl ether **7-OTFE** and **13** were identified by ^{13}C and ^1H NMR. The identification of **14** was conducted by comparing its spectral and GLC data with those of authentic **14** that was synthesized by the pinacol rearrangement of 2-methyl-1,2-adamantanediol. The ethanolysis of **7-OMs** also gave a mixture of **7-OEt**, 1,2-diethoxy-2-methyladamantane, and ketone **14**.

In order to elucidate the route to **13** and **14**, the product distribution in the trifluoroethanolysis of **7-Cl** was followed by GLC: the results are summarized in Table 2. The data of Table 2 clearly show that both **13** and **14** were formed from normal substitution product **7-OTFE** and not directly from the substrate. Since the solvolyses of **7-Cl** in TFE and of **7-OMs** in ethanol were conducted at 125 °C because of their slow rates, once-formed products **7-OTFE** and **7-OEt** presumably underwent acid-catalyzed addition of the solvent molecule to the double bond to give 1,2-dialkoxy-2-methyladamantane even in the presence of excess 2,6-lutidine. Although we were unable to detect diethyl ether or bis(trifluoroethyl) ether, the ketone **14** is presumed to have been formed through the reaction of protoadamantyl cation **15** with the solvent molecule (Scheme 4). Previously, the forma-

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[16] Takeuchi, K.; Kitagawa, I.; Akiyama, F.; Shibata, T.; Kato, M.; Okamoto, K. *Synthesis* **1987**, 612.

[17] The use of a commercially available THF solution of Bu_4NF was unsuccessful because of difficulties in preparing an anhydrous solution.

[18] **12-F**,[19a] **12-Cl**,[19b] and **12-Br**[19c] have been reported, but the synthetic methods employed in the literature are not appropriate for preparative-scale syntheses.

[19] (a) Tabushi, I.; Aoyama, Y. *J. Org. Chem.* **1973**, *38*, 3447. (b) Hirsl-Starcevic, S.; Majerski, Z. *J. Org. Chem.* **1982**, *47*, 2520. (c) Tabushi, I.; Aoyama, Y.; Yoshida, Z. *J. Am. Chem. Soc.* **1971**, *93*, 2077.

[20] For ^{13}C NMR data of (*Z*)- and (*E*)-**6-I**, see ref 14.

Table 1. Rate Data of Solvolysis of 2-Ethylidene, 2-Methylene, or Parent Bridgehead Compounds

compound	solvent	temp (°C)	k (s^{-1})	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$\Delta S^{\ddagger}$ (eu)	relative rate	
(*Z*)-**4-OTf**	EtOH	25.0	$(4.04 \pm 0.04) \times 10^{-4}$ [a]	23.8 ± 0.3	5.6 ± 0.8	1370 ± 100	217 ± 6
		40.0	$(2.89 \pm 0.03) \times 10^{-3}$ [a]				
(*E*)-**4-OTf**	EtOH	25.0	$(1.86 \pm 0.03) \times 10^{-6}$ [b,c]	26.8 ± 0.2	5.1 ± 0.8	6.3 ± 0.5	1
		50.0	$(6.65 \pm 0.10) \times 10^{-5}$ [b,c]				
5-OTf	EtOH	25.0	$(2.95 \pm 0.18) \times 10^{-7}$ [c,d]	27.1 ± 0.3	2.3 ± 1.0	1	
		50.0	$(1.09 \pm 0.04) \times 10^{-5}$ [b,c]				
		75.0	$(2.40 \pm 0.04) \times 10^{-4}$ [b,c]				
(*Z*)-**6-OMs**	EtOH	25.0	$(2.28 \pm 0.03) \times 10^{-6}$ [b]	25.8 ± 0.2	2.0 ± 0.7	745 ± 90	109 ± 11
		50.0	$(7.11 \pm 0.11) \times 10^{-5}$ [b]				
(*E*)-**6-OMs**	EtOH	25.0	$(2.09 \pm 0.17) \times 10^{-8}$ [d]	26.8 ± 0.3	-3.9 ± 0.8	6.8 ± 1.3	1
		75.0	$(1.59 \pm 0.02) \times 10^{-5}$ [b]				
		100.0	$(2.25 \pm 0.03) \times 10^{-4}$ [b]				
7-OMs	EtOH	25.0	$(3.06 \pm 0.30) \times 10^{-9}$ [d]	27.0 ± 0.4	-7.2 ± 1.1	1	
		75.0	$(2.42 \pm 0.04) \times 10^{-6}$ [b]				
		100.0	$(3.84 \pm 0.05) \times 10^{-5}$ [b]				
(*Z*)-**6-OMs**	TFE	4.1	$(4.04 \pm 0.04) \times 10^{-3}$ [e]				
		25.0	$(4.65 \pm 0.02) \times 10^{-2}$ [e,f]	18.6 ± 0.1	-2.2 ± 0.4	1340 ± 30	117 ± 1
(*E*)-**6-OMs**	TFE	25.0	$(3.96 \pm 0.02) \times 10^{-4}$ [e,f]	19.4 ± 0.2	-9.1 ± 0.6	11.4 ± 0.3	1
		40.0	$(1.99 \pm 0.02) \times 10^{-3}$ [e]				
7-OMs	TFE	25.0	$(3.46 \pm 0.05) \times 10^{-5}$ [b]	21.7 ± 0.2	-6.3 ± 0.7	1	
		50.0	$(6.32 \pm 0.09) \times 10^{-4}$ [b]				
(*Z*)-**6-F**	TFE	25.0	$(6.0 \pm 2.5) \times 10^{-11}$ [d]	20.1 ± 1.4	-38.0 ± 3.7		ca. 70 (28–160)
		100.0	$(6.63 \pm 0.42) \times 10^{-8}$ [g]				
		125.0	$(3.82 \pm 0.22) \times 10^{-7}$ [g]				
(*E*)-**6-F**	TFE	25.0	$(8.8 \pm 3.4) \times 10^{-13}$ [d]	25.6 ± 1.4	-28.0 ± 3.5		1
		100.0	$(6.30 \pm 0.28) \times 10^{-9}$ [g]				
		125.0	$(5.77 \pm 0.39) \times 10^{-8}$ [g]				
8-F	TFE	25.0	$(7.08 \pm 0.53) \times 10^{-9}$ [d]	18.7 ± 0.3	-33.0 ± 0.7		
		75.0	$(7.57 \pm 0.11) \times 10^{-7}$ [g]				
		100.0	$(5.09 \pm 0.15) \times 10^{-6}$ [g]				
		125.0	$(2.52 \pm 0.08) \times 10^{-5}$ [g]				
(*Z*)-**6-Cl**	TFE	25.0	$(3.95 \pm 0.21) \times 10^{-6}$ [d]	19.5 ± 0.3	-17.8 ± 0.8	6690 ± 1530	1020 ± 160
		50.0	$(5.46 \pm 0.08) \times 10^{-6}$ [b]				
		75.0	$(5.17 \pm 0.08) \times 10^{-4}$ [b]				
(*E*)-**6-Cl**	TFE	25.0	$(3.86 \pm 0.36) \times 10^{-9}$ [d]	23.4 ± 0.7	-18.5 ± 0.9	6.5 ± 1.8	1
		75.0	$(1.30 \pm 0.02) \times 10^{-6}$ [b]				
		100.0	$(1.33 \pm 0.02) \times 10^{-5}$ [b]				
7-Cl	TFE	25.0	$(5.90 \pm 0.84) \times 10^{-10}$ [d]	22.2 ± 0.4	-26.3 ± 0.9	1	
		100.0	$(1.35 \pm 0.02) \times 10^{-6}$ [b]				
		125.0	$(9.31 \pm 0.14) \times 10^{-6}$ [b]				
(*Z*)-**6-Br**	TFE	25.0	$(2.50 \pm 0.03) \times 10^{-4}$ [e]	18.5 ± 0.2	-13.0 ± 0.8	29980 ± 3490	2230 ± 90
		40.0	$(1.17 \pm 0.01) \times 10^{-3}$ [e]				
(*E*)-**6-Br**	TFE	25.0	$(1.12 \pm 0.03) \times 10^{-7}$ [d]	22.5 ± 0.2	-15.1 ± 0.4	13.4 ± 1.8	1
		75.0	$(2.99 \pm 0.04) \times 10^{-5}$ [b]				
		100.0	$(2.75 \pm 0.04) \times 10^{-4}$ [b]				
7-Br	TFE	25.0	$(8.34 \pm 0.78) \times 10^{-9}$ [d]	23.3 ± 0.3	-17.6 ± 0.9	1	
		75.0	$(2.68 \pm 0.04) \times 10^{-6}$ [b]				
		100.0	$(2.69 \pm 0.04) \times 10^{-5}$ [b]				
(*Z*)-**6-I**	TFE	25.0	$(9.78 \pm 0.10) \times 10^{-4}$ [e]	19.6 ± 0.2	-6.5 ± 0.5	136200 ± 16350	9500 ± 280
		40.0	$(5.26 \pm 0.05) \times 10^{-3}$ [e]				
		50.0	$(1.36 \pm 0.01) \times 10^{-2}$ [f]				
(*E*)-**6-I**	TFE	25.0	$(1.03 \pm 0.02) \times 10^{-7}$ [d]	24.1 ± 0.1	-9.9 ± 0.3	14.3 ± 1.9	1
		50.0	$(2.51 \pm 0.02) \times 10^{-6}$ [b,f]				
		75.0	$(4.19 \pm 0.06) \times 10^{-5}$ [b]				
		100.0	$(4.27 \pm 0.06) \times 10^{-4}$ [b]				
7-I	TFE	25.0	$(7.18 \pm 0.71) \times 10^{-9}$ [d]	24.7 ± 0.4	-13.2 ± 1.0	1	
		75.0	$(3.25 \pm 0.05) \times 10^{-6}$ [b]				
		100.0	$(3.74 \pm 0.07) \times 10^{-5}$ [b]				

[a] Determined conductimetrically for 0.00020 M substrate in the presence of 0.025 M 2,6-lutidine within an experimental error of ±1.0%. [b] Determined titrimetrically for 0.020 M substrate in the presence of 0.025 M 2,6-lutidine within an experimental error of ±1.5%. [c] Reference 15c. [d] Extrapolated from data at other temperatures. [e] Determined conductimetrically for 0.00074 M substrate in the presence of 0.00119 M 2,6-lutidine within an experimental error of ±1.0%. [f] Reference 14. [g] Determined by GLC method within the given experimental error at 95% confidence limit.

tion of an unidentified compound was reported for the acetolysis of **7-OTs**.[15b] It is now highly probable that the unidentified product was **14**.

Oxygen-18 Scrambling Study. Any rate of S_N1 solvolysis as determined by following the rate of product formation is intrinsically slower than that of the ionization step because such an overall rate additionally includes those of product formation and ion-pair return steps. In the present objective in which the F-strain effect on the ionization step is to be investigated, we should determine the rate of ionization. At present, however, there is no method available to precisely measure the rates of ionization in solvolysis reactions. One approach is to measure the rate of oxygen scrambling of a sulfonate leaving group, which is much closer to the rate of the ionization step than a titrimetrically or conductimetrically determined one. Consequently, we followed the rates of oxygen scrambling of (*Z*)- and (*E*)-2-ethylidene-1-adamantyl mesylates labeled with a 10% excess of ^{18}O on the ether oxygen of the methanesulfonyloxyl moiety by means of mass spectrometric analysis.

The two ^{18}O-labeled mesylates ([^{18}O]-(*Z*)-2-ethylidene-

Table 2. Product Distribution in the Trifluoroethanolysis of 7-Cl at 125.0 °C Determined by GLC

compound	0.1 × $t_{1/2}$	0.3 × $t_{1/2}$	$t_{1/2}$	2 × $t_{1/2}$	10 × $t_{1/2}$	11.5 × $t_{1/2}$
7-Cl	91	83	52	27	0	0 (0[a])
7-OTFE	9	17	48	73	71	60 (56[a])
13	0	0	0	0	20	27 (29[a])
14	0	0	0	0	9	13 (14[a])

[a] Isolated yield.

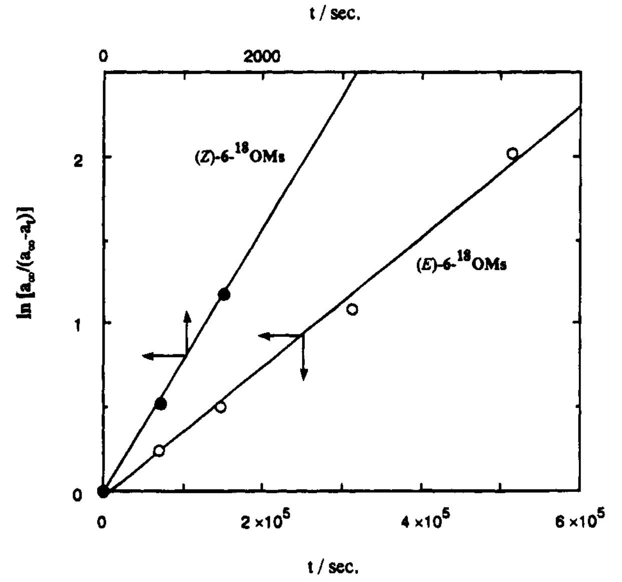
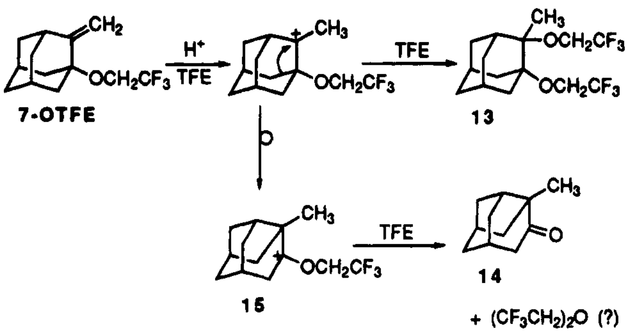


Figure 1. First-order plot of ^{18}O-scrambling study for (*Z*)- and (*E*)-**6-^{18}OMs** in ethanol at 50 °C. a_∞ and a_t denote the decrease of ^{18}O content on the ether site at $t_{1/2}$ × 10 and *t*, respectively.

Scheme 4



1-adamantyl and [^{18}O]-(*E*)-2-ethylidene-1-adamantyl [$^{18}O_1$]-mesylates) were prepared by hydrolyzing unlabeled mesylates in 90% THF–10% $H_2{}^{18}O$ (10 excess atom %) in the presence of excess 2,6-lutidine. The resulting 2-ethylidene-1-adamantanols were found to contain 10.9 ± 0.1% ^{18}O as determined by comparing the intensities of the mass spectral peaks at M (178) and M + 2 (180). Lithiation of the alcohols with BuLi in THF and subsequent treatment with methanesulfonyl chloride (MsCl) gave the desired labeled mesylates.

The solvolysis was carried out in ethanol on 0.040 M substrate in the presence of 0.050 M 2,6-lutidine at 50.0 °C. At intervals aliquots were worked up in the usual manner and the unchanged mesylate was recovered by MPLC (SiO_2) at −40 °C. The recovered mesylate was cleaved to the alcohol by treatment with *t*-BuOK in DMSO.[21] Control experiments showed that oxygen scrambling did not occur throughout the overall treatment within an absolute error of ±0.5% (or relative error of ±5%). The first-order plots are shown in Figure 1, and the first-order rate constants of ^{18}O scrambling (k_{sc}) are summarized in Table 3 along with titrimetric ones (k_t). Because of a relative error of ±5% in each ^{18}O scrambling determination, the k_{sc} values include ±(16–21)% errors. It was found that k_{sc} was greater than k_t by 9–13 times for (*Z*)-**6-OMs** and 4.6–6.3 times for (*E*)-**6-OMs**. The *Z*/*E* rate ratios were 95 ± 5 for k_t and 190 ± 80 for k_{sc} at 50 °C.

Table 3. Rate Constants for Solvolysis (k_t) and Oxygen Scrambling (k_{sc}) for Ethanolysis of 2-Ethylidene-1-adamantyl Mesylates at 50.0 °C

	(*Z*)-**6-OMs**	(*E*)-**6-OMs**	*Z*/*E*
k_t	(7.11 ± 0.11) × 10^{-5}	(7.46 ± 0.31) × 10^{-7}	95 ± 5
k_{sc}	(7.86 ± 1.46) × 10^{-4} [a]	(4.06 ± 0.64) × 10^{-6} [a]	190 ± 80

[a] Error is expressed as a standard deviation at 95% confidence limit.

Discussion

Essential Absence of Solvent Effects on the *Z*:*E* Rate Ratios. Ethanol and TFE are two extreme solvents in S_N1 solvolysis although their dielectric constants are very similar (24.32 and 26.14, respectively, at 25 °C).[22] The Y_{OTs} (= $Y_{2\text{-AdOTs}}$) values of ethanol and TFE are −1.75 and 1.80, and the respective N_{OTs} values are 0.00 and −3.0.[23] These values show that TFE is much more ionizing and much less nucleophilic than ethanol. Despite these marked dissimilarities, the *Z*:*E* rate ratios for **6-OMs** are almost identical, 109 ± 11 in EtOH and 117 ± 1 in TFE at 25 °C (Table 1). Interestingly, the (*Z*)-methyl group does not appear to affect the magnitude of electrophilic solvation by the protic solvents toward the leaving group in the transition state. This reasoning may be supported by two-point $mY_{1\text{-AdOMs}}$ relations by using the ethanol and TFE data.[24] The approximate *m* values are calculated to be 1.1 for (*Z*)-**6-OMs** and 1.0 for (*E*)-**6-OMs** and **7-OMs**. These results suggest that we can safely discuss the *Z*:*E* rate ratios on the basis of the shape of the molecules without much worrying about the solvation effects.

Origin of the Large *Z*:*E* Rate Ratios. Previously, the groups of Martin[15a] and Schleyer[15b] independently reported that the allylic conjugation is essentially prohibited in the incipient carbocation from **7-OTs** because of perpendicular relation between the developing cationic p orbital and the methylene π system. We also reported that it is also the case for **5-OTf** and (*E*)-**4-OTf**.[15c] The faster rates of (*E*)-**4-OTf** than **5-OTf** and of (*E*)-**6-OMs** than **6-OMs** by respective factors of 6.3 (= 1.86 × 10^{-6}/2.95 × 10^{-7} in EtOH) and 11.4 (= 3.96 × 10^{-4}/3.46 × 10^{-5} in TFE) at 25 °C may be principally attributed to the electron-donating character (inductive and hyperconjugative) of the (*E*)-methyl substituent.

The variation of the leaving group of (*Z*)- and (*E*)-**6-X** significantly influenced the *Z*:*E* rate ratio, which increased in the order F (ca. 70 or 28–160), OMs (117 ± 1), Cl (1020 ± 160), Br (2230 ± 90), and I (9500 ± 280) in TFE at 25 °C (Table 1). As discussed below, the large *Z*:*E* rate ratios cannot wholly be ascribed to steric origin.

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[21] Chang, F.-C. *Tetrahedron Lett.* **1964**, 305.

[22] Mukherjee, L. M.; Grunwald, E. *J. Phys. Chem.* **1958**, *62*, 1311.

[23] Schadt, F. L.; Bentley, T. W.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1976**, *98*, 7667.

[24] Takeuchi, K.; Ikai, K.; Shibata, T.; Tsugeno, A. *J. Org. Chem.* **1988**, *53*, 2852.

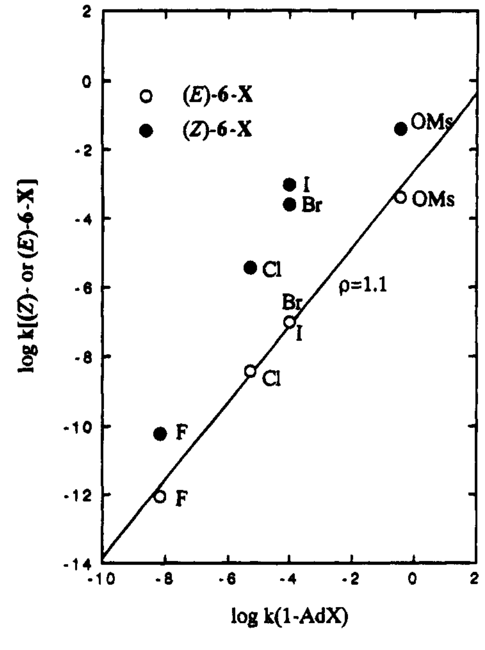

Figure 2. Plot of log k for (Z)- and (E)-**6-X** in 100% TFE against log k for **8-X** in 97% or 100% TFE at 25 °C.

However, they strongly suggest that in (Z)-**6-X** the F-strain between the (Z)-methyl group and the leaving group atom directly attached to the reaction center increases in the above sequence of atomic size, whereas in (E)-**6-X** there would be no serious F-strain between the hydrogen atom in the Z position and the leaving group. Figure 2 gives a plot of log k values for **6-X**'s against those for the corresponding parent 1-adamantyl compounds **8-X** (X = OMs,[25a] F,[26] Cl,[25b] Br,[25b] I[25c]) in 97% TFE. A good linear correlation with a slope of 1.1 for (E)-**6-X**'s indicates the essential absence of an extra F-strain effect. In contrast, the points for (Z)-**6-X**'s scatter, supporting the development of F-strain.

The present result is in striking contrast to the solvolysis of *trans,trans,trans*-perhydro-9b-phenalyl system **1** where the marked F-strain in the *p*-nitrobenzoate **1-OPNB** completely vanishes in the chloride **1-Cl**.[10] Our previous work on the deuterium kinetic isotope effect on the Z:E rate ratios by using methyl-d_3 compounds of (Z)- and (E)-**6-X** showed a large steric isotope effect in the (Z)-iodide but its marked decrease in the (Z)-mesylate.[14]

Z:E Rate Ratios Based on ^{18}O Scrambling. The internal return in the solvolysis of 1-adamantyl derivatives has only recently been disclosed. Kevill and his coworkers reported that 1-adamantyl chloroformate in hydroxylic solvents reacts with loss of carbon dioxide to give solvolysis product (**1-AdOS**) and decomposition product (**1-AdCl**).[27a] The fraction of the decomposition product, which was 20−72.5% in several solvents, was regarded as a minimum fraction of internal return during solvolysis of 1-adamantyl chloride. Recently, Stoelting and Shiner examined the ^{18}O scrambling of 2-methyl- and 2,2-dimethyl-1-adamantyl pentamethylbenzenesulfonates (pemsylates) in 95% ethanol and found respective minimum fractions of internal return of 81% and 89%.[27b] Our data of Table 3 provide the values $(100 \times k_{sc}/(k_{sc} + k_t))$[27b] of 92% and 84% for (Z)- and (E)-**6-OMs**, respectively.

Table 4. Pertinent Bond Lengths and Steric Energies for (Z)- and (E)-2-Ethylidene-1-adamantyl Substrates (6-X) Calculated by MM2(87)

	bond length,[a] Å				steric energy, kcal mol^{-1}
compound	X−C$_\alpha$	C$_\alpha$−C$_\beta$	C$_\beta$=C$_\gamma$	C$_\gamma$−CH$_3$	
(Z)-**6-OH**[b]	1.426	1.519	1.346	1.505	20.4
(E)-**6-OH**[b]	1.429	1.520	1.346	1.507	18.1
Δ	−0.003	−0.001	0.000	−0.002	2.3
(Z)-**6-F**	1.395	1.518	1.345	1.504	20.8
(E)-**6-F**	1.397	1.520	1.345	1.507	19.3
Δ	−0.002	−0.002	0.000	−0.003	1.5
(Z)-**6-Cl**	1.810	1.526	1.347	1.504	24.8
(E)-**6-Cl**	1.815	1.527	1.347	1.508	21.6
Δ	−0.005	−0.001	0.000	−0.004	3.2
(Z)-**6-Br**	1.979	1.530	1.348	1.504	26.7
(E)-**6-Br**	1.985	1.530	1.347	1.508	22.8
Δ	−0.006	0.000	0.001	−0.004	3.9
(Z)-**6-I**	2.186	1.531	1.348	1.503	27.5
(E)-**6-I**	2.191	1.531	1.347	1.508	22.9
Δ	−0.005	0.000	0.001	−0.005	4.6

[a] $C_\alpha-C_\beta$ and $C_\beta=C_\gamma$ denote the bonds in the allylic part $X-C_\alpha-C_\beta=C_\gamma-CH_3$ with C_α being the bridgehead carbon. [b] Surrogate of mesylate.

Despite significant internal return in the present solvolyses, the Z/E rate ratio for k_{sc} is 190 ± 80 in ethanol at 50 °C, which is only twice as large as the Z/E rate ratio 95 ± 5 for k_t. Consequently, it has been shown that the Z/E rate ratios determined from k_t can be used as a measure of the F-strain effect on the ionization step.

Molecular Mechanics (MM2) Calculations. In order to obtain information on geometries and steric energies in the ground state, MM2(87) calculations were performed on (Z)- and (E)-2-ethylidene-1-adamantyl substrates.[28] From the lack of parameters of sulfonates, the calculations for mesylates were carried out on the corresponding alcohols as surrogates. As pertinent data, the bond lengths included in the $X-C_\alpha-C_\beta=C_\gamma-CH_3$ part (where C_α denotes the bridgehead carbon) were compared between the Z and E substrates; however, the effect of changing the leaving group X on the geometry was very small.[29] On the other hand, steric energies significantly changed depending on the leaving group (Table 4).

The data of Table 4 show that the difference in steric energy between the Z and E isomers ($SE_Z - SE_E$, kcal mol^{-1}) increases in the sequence of the leaving group, F (1.5), OH (2.3), Cl (3.2), Br (3.9), and I (4.6). Figure 3 shows a plot of $1.36 \times \log[k_Z/k_E]$ values against $SE_Z - SE_E$ for 2-ethylidene-1-adamantyl halides and mesylates. A linear correlation with a slope of 1.0 indicates that a change in $SE_Z - SE_E$ on changing the leaving group is exactly reflected to the change in the $\Delta G^\ddagger$ difference between the two isomers. The intercept value of 0.8 kcal mol^{-1} should be taken as meaningful and not due to inherent errors in MM2 calculations. The value suggests that the hypothetical heterolysis of 2-ethylideneadamantane (**16**) (Scheme 5) would be more favorable by 0.8 kcal

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(25) (a) Bentley, T. W.; Carter, G. E. *J. Org. Chem.* **1983**, *48*, 579. (b) Bentley, T. W.; Carter, G. E. *J. Am. Chem. Soc.* **1982**, *104*, 5741. (c) Bentley, T. W.; Carter, G. E.; Roberts, K. *J. Org. Chem.* **1984**, *49*, 5183.

(26) This work; the rate in 100% TFE.

(27) (a) Kevill, D. N.; Kyong, J. B.; Weitl, F. L. *J. Org. Chem.* **1990**, *55*, 4304. (b) Stoelting, D. T.; Shiner, V. J., Jr. *J. Am. Chem. Soc.* **1993**, *115*, 1695.

(28) The MM2(87) program was obtained from QCPE. In calculations on (Z)- and (E)-**6-OH**, lone pair electrons were placed on the oxygen atom. In both cases smaller steric energy was obtained for the conformation that involves the O−H between C(8)−C(1)−C(2) than between C(8)−C(1)−C(9). The MM2 calculations on (Z)- and (E)-**4-OH** as surrogates of triflates were briefly reported in ref 13a.

(29) For a recent article describing the importance of F-strain in structural organic chemistry, see: Knorr, R.; von Roman, Th.; Nöth, H.; Böck, S. *J. Chem. Soc., Perkin Trans. 2* **1992**, 127. The X-ray structural study of some of the present substrates is underway in this laboratory.

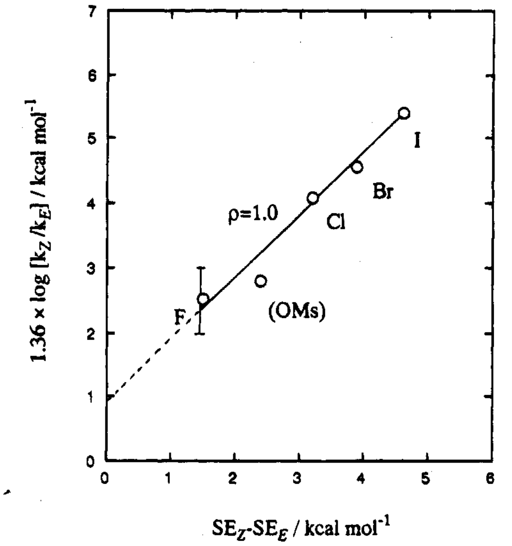
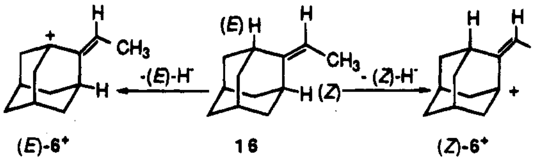


Figure 3. Plot of 1.36 × log[k_Z/k_E] against steric energy difference between (*Z*)-**6-X** and (*E*)-**6-X** calculated by MM2.

Scheme 5



mol^{-1} for the bridgehead hydrogen at the *Z* position than that at the *E* position. In other words, it is suggested that the transition state from (*Z*)-**6-X** is more stable than that from (*E*)-**6-X** by 0.8 kcal mol^{-1}. MM2 calculations on 2-ethylideneadamantane (**16**) have indicated that the van der Waals repulsion between the methyl group and the (*Z*) hydrogen is greater than that between the vinylic hydrogen and the (*E*) hydrogen by 0.6 kcal mol^{-1}. This value can account for 75% of the intercept value. As shown below, ab initio (RHF/6-31G**) calculations showed that the (*Z*) cation [(*Z*)-**6**$^+$] is more stable than the (*E*) cation [(*E*)-**6**$^+$] by 1.0 kcal mol^{-1}.

Correlation with Hansch's Es. Kutter and Hansch improved Taft's steric parameters Es by using average van der Waals radii of various substituents.[30] By employing Hansch's Es as an empirical parameter, we evaluated the *Z*:*E* rate ratios. Figure 4 shows a plot of 1.36 × log[k_Z/k_E] values against Hansch's Es. The nicely linear plot reinforces the conclusion reached by MM2 calculations that the major origin of the large *Z*:*E* rate ratios is F-strain between the (*Z*)-methyl group and the leaving group atom directly attached to the reaction center. Furthermore, the intercept that corresponds to the value for the hydride leaving group (Es = 0) is 1.1 kcal mol^{-1}, which is comparable with the intercept obtained in Figure 3.

Ab Initio (RHF/6-31G) Calculations on 2-Ethylidene-1-adamantyl Cations.** With a view to seeing the structure and energies of the cations, we optimized (*Z*)- and (*E*)-**6**$^+$ by applying the Gaussian 90 program. We assumed here a C_s symmetry in which the external double bond and the methyl carbon have been placed in the symmetry plane. The calculated total energies of (*Z*) and (*E*) cations were −464.0842945 and −464.0826948 au, respectively, at the RHF/6-31G** level, suggesting that the former cation is more stable than the latter one by 1.0 kcal mol^{-1}. Notably, this value is in very good agreement with the intercept values of 0.8 and 1.1 kcal mol^{-1} which were obtained in the plots of Figures 3 and 4. It is now almost certain that the *Z*:*E* rate ratios in the 2-ethylidene-1-adamantyl solvolyses include a rate factor of approximately 5 coming from the greater stability of (*Z*)-**6**$^+$ than (*E*)-**6**$^+$ by 0.8−1.1 kcal mol^{-1}. If allowances are made for the observed rate ratios by this factor, the net *Z*:*E* rate ratios ascribed solely to the F-strain effect in the trifluoroethanolysis of **6-X** are 23 (**6-OMs**), ca. 14 (**6-F**), 200 (**6-Cl**), 450 (**6-Br**), and 1900 (**6-I**) at 25 °C.

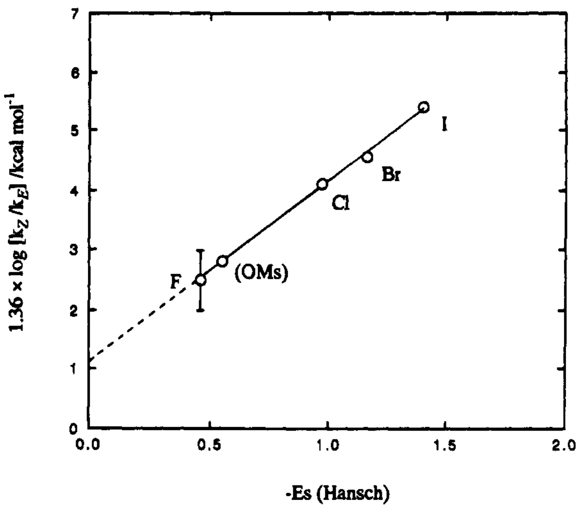


Figure 4. Plot of 1.36 × log[k_Z/k_E] against Hansch's Es.

As shown in Figure 5, the cationic center has the arrangement of bonds that is close to an sp^2-hybridized carbon, the C—C$^+$—C bond angles being 116.9−117.1°. The bond length between the cationic center and the adjacent sp^2 carbon is seen to be almost the same as those between the cationic center and the adjacent sp^3 carbons. This is natural because the 2pπ atomic orbital of the cationic center is not allowed to conjugate with the double bond in these configurations. Having an sp^2-like cationic center in an adamantyl cage, two sp^3 carbon—carbon bonds are seen to be stretched to have an unusually long length of 1.611 Å. These geometric data are very close to those of 3,5,7-trimethyl-1-adamantyl cation which were determined by X-ray structural analysis of the $Sb_2F_{11}^-$ salt.[32] The 3,5,7-trimethyl-1-adamantyl cation was found to have the C—C$^+$—C angles of 116°, 118°, and 120° and a C(2)—C(3) bond of 1.62 Å.

Experimental Section

Melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer 1640 spectrophotometer. ^{1}H NMR spectra were recorded on a Hitachi R-24 (60 MHz), JEOL FX90A (89.55 MHz), or JEOL GSX270 (270.05 MHz) spectrometer. ^{13}C NMR spectra were recorded on a JEOL FX90A (22.5 MHz) or JEOL GSX270 (67.8 MHz) spectrometer. In all NMR

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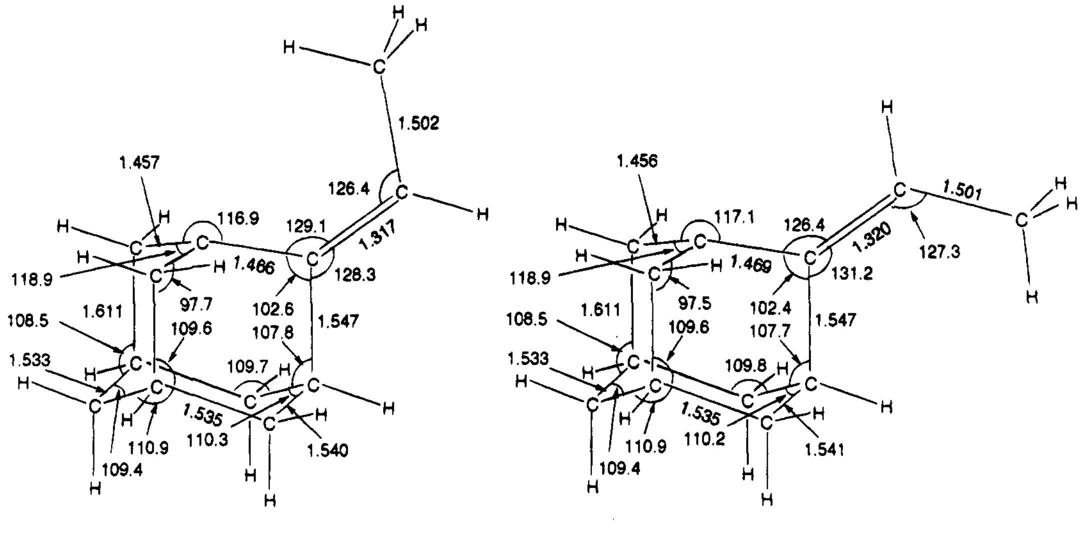
(30) Kutter, E.; Hansch, C. *J. Med. Chem.* **1969**, *12*, 647. Unger, S. H.; Hansch, C. Quantitative Models of Steric Effects. In *Progress in Physical Organic Chemistry*; Taft, R. W., Ed.; Wiley-Interscience: New York, 1976; 12, pp 91–118. The Es value of the ethoxy group was employed for the methanesulfonyloxy group.

(31) Frisch, M. J.; Head-Gordon, M.; Trucks, G. W.; Foresman, J. B.; Schlegel, H. B.; Raghavachari, K.; Robb, M. A.; Binkley, J. S.; Gonzales, C.; Defrees, D. J.; Fox, D. J.; Whiteside, R. A.; Seeger, R.; Melius, C. F.; Baker, J.; Martin, R. L.; Kahn, L. R.; Stewart, J. J. P.; Topiol, S.; Pople, J. A. *GAUSSIAN 90*; Gaussian Inc.: Pittsburgh, PA, 1990.

(32) Laube, T. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 349.



(*Z*)-**6**$^+$ (*E*)-**6**$^+$

Figure 5. Opitmized geometries of (*Z*)-**6**$^+$ and (*E*)-**6**$^+$ at RHF/6-31G**.

measurements TMS was used as an internal standard. Mass spectra were recorded on a Hitachi M-80 GC-MS spectrometer equipped with a Hitachi M-003 data processor. Elemental analyses were performed by the Microanalytical Center, Kyoto University, Kyoto. (*Z*)-**4-OH**,[15c] (*E*)-**4-OTf**,[15c] **5-OTf**,[15c] (*Z*)- and (*E*)-**6-OMs**,[14] and (*Z*)- and (*E*)-**6-I**[14] were described previously. **8-F** was prepared by following a literature method.[33] Ethanol was refluxed over magnesium ethoxide and distilled. 2,2,2-Trifluoroethanol (TFE) was stored over 5A molecular sieves and distilled. Benzoyl triflate was prepared by the method of Brown and Koreeda.[34] Commercially available methyl- and ethyltriphenylphosphonium bromides were dried at 95−100 °C in vacuo for 1 h before use. Bu_4NBr, Bu_4NCl, and LiF were dried at 100−120 °C in vacuo for longer than 6 h before use. All anhydrous solvents used for synthetic work were purified by standard procedures. Other commercially available reagents were of a reagent-grade quality and used as received. Medium-pressure liquid chromatography (MPLC) was conducted on Merck silica gel 60 (230−400 mesh).

(*Z*)-2-Ethylidenebicyclo[2.2.2]oct-1-yl Triflate ((*Z*)-4-OTf). To a solution of (*Z*)-**4-OH**[15c] (0.152 g, 1.00 mmol) and pyridine (0.156 g, 1.97 mmol) in CH_2Cl_2 (1.2 mL) was added a solution of triflic anhydride (0.369 g, 1.31 mmol) in CH_2Cl_2 with stirring at 0 °C over 5 min, and then stirring continued for 1.5 h. After having been stored in a freezer overnight, the reaction mixture was diluted with CH_2Cl_2 (10 mL), washed at 0 °C with water (2 × 8 mL), 10% aqueous HCl (2 × 8 mL), 10% aqueous NaCl (8 mL), saturated aqueous $NaHCO_3$ (8 mL) and 10% aqueous NaCl (8 mL), and dried ($MgSO_4$). Evaporation of solvent with a rotary evaporator afforded (*Z*)-**4-OTf** (0.214 g, 75%) as an unstable brown oil, which was used for solvolysis studies without further purification: ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 135.0, 102.9 (C); 119.0, 25.4 (CH); 39.2, 31.4, 27.5 (CH_2); 13.3 (CH_3); 118.0 (q, CF_3, J = 319.2 Hz).

2-Methylene-1-adamantyl Mesylate (7-OMs). To a solution of **7-OH** (0.200 g, 1.22 mmol) in THF (2.4 mL) was added dropwise 1.6 M BuLi in hexane (0.78 mL) at −40 °C over 3 min. After the mixture was stirred at −40 °C for 1.5 h, methanesulfonyl chloride (0.140 g, 1.22 mmol) in THF (2.4 mL) was added and stirring continued for 4.5 h; then the solution was allowed to warm slowly to 10 °C over 2 h. After most of the solvent had been removed with a rotary evaporator, hexane was added. An insoluble white precipitate was removed by filtration. Evaporation of solvent followed by MPLC (SiO_2, hexane−ether (9:1)) afforded **7-OMs** (0.112 g, 38%) and **7-OH** (0.052 g, 26%) in this sequence. **7-OMs**: mp 58.0−59.0 °C (from hexane); IR (CCl_4) 2927, 2858, 1657, 1454, 1331, 1174, 1042, 931, 910, 846 cm^{-1}; ^1H NMR (89.55 MHz, $CDCl_3$) δ 1.67−2.89 (m, 13 H), 3.06 (s, 3 H), 4.76 (br s, 1 H), 4.86 (br s, 1 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 152.7, 92.0 (C), 42.0, 31.5 (CH), 102.1, 44.2, 38.0, 35.2 (CH_2), 40.9 (CH_3). Anal. Calcd for $C_{12}H_{18}O_3S$: C, 59.48; H, 7.49. Found: C, 59.37; H, 7.73.

(*Z*)-2-Ethylidene-1-chloroadamantane ((*Z*)-6-Cl). To a solution of $SOCl_2$ (0.163 g, 1.37 mmol) in benzene (1.0 mL) was added a solution of (*Z*)-**6-OH**[14] (0.050 g, 0.28 mmol) and pyridine (0.225 g, 2.84 mmol) in benzene (1.0 mL) at room temperature over 6 min. The reaction mixture was stirred at room temperature for 22 h. The reaction mixture was poured into ice−water (10 mL) and extracted with ether (3 × 10 mL). The combined extracts were washed with 10% aqueous HCl (2 × 10 mL) and saturated aqueous $NaHCO_3$ (2 × 10 mL) and dried ($MgSO_4$). Evaporation of solvent gave (*Z*)-**6-Cl** (0.049 g, 89%) as colorless crystals: mp 60.0 °C (from pentane); IR (CCl_4) 3063, 2928, 2855, 1661, 1449, 1299, 1206, 1042, 880 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 1.57−2.50 (m, 13 H), 1.96 (d, 3 H, J = 7.4 Hz), 5.31 (q, 1 H, J = 7.3 Hz); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 143.6, 72.9 (C), 115.5, 46.1, 31.5 (CH), 50.8, 38.4, 35.5 (CH_2), 13.9 (CH_3). Anal. Calcd for $C_{12}H_{17}Cl$: C, 73.27; H, 8.71; Cl, 18.02. Found: C, 72.98; H, 8.92; Cl, 18.00.

(*E*)-2-Ethylidene-1-chloroadamantane ((*E*)-6-Cl). To a solution of $SOCl_2$ (0.163 g, 1.37 mmol) in benzene (0.5 mL) was added a solution of (*E*)-**6-OH**[14] (0.050 g, 0.28 mmol) and pyridine (0.225 g, 2.84 mmol) in benzene (1.0 mL) at room temperature over 5 min. The reaction mixture was stirred at room temperature for 30 min and then at 50 °C for 3 h. The reaction mixture was worked up as described for the preparation of (*Z*)-**6-Cl** and the crude product subjected to MPLC (SiO_2, hexane) to give (*E*)-**6-Cl** (0.039 g, 71%) as pale yellow crystals: mp 43.0−43.5 °C (from pentane); IR (CCl_4) 2926, 2854, 1671, 1449, 1380, 1338, 1289, 1107, 1034, 997, 899 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 1.25−2.40 (m, 12 H), 1.59 (d, 3 H, J = 6.8 Hz), 3.10 (s, 1 H), 5.47 (q, 1 H, J = 7.0 Hz); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 144.7, 73.6 (C), 113.0, 34.1, 29.7 (CH), 50.2, 37.3, 35.3(CH_2), 12.2 (CH_3). Anal. Calcd for $C_{12}H_{17}Cl$: C, 73.27; H, 8.71; Cl, 18.02. Found: C, 73.01; H, 8.82; Cl, 17.89.

(*Z*)-2-Ethylidene-1-bromoadamantane ((*Z*)-6-Br). To a solution of $SOBr_2$ (0.697 g, 3.35 mmol) in benzene (3.0 mL) was added a solution of (*Z*)-**6-OH**[14] (0.300 g, 1.68 mmol) and pyridine (0.538 g, 6.80 mmol) in benzene (6.0 mL) at 0 °C over 5 min. The reaction mixture was stirred at 0 °C for 45 min and then poured into ice−water (30 mL) and extracted with ether (3 × 30 mL). The combined extracts were washed with 10% aqueous HCl (3 × 30 mL) and saturated aqueous $NaHCO_3$ (3 × 30 mL) and dried ($MgSO_4$). Evaporation of solvent

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(34) Brown, J.; Koreeda, M. *J. Org. Chem.* **1984**, *49*. 3875.

followed by MPLC (SiO_2, hexane) afforded (*Z*)-**6-Br** (0.341 g, 84%) as colorless crystals: mp 58.5–59.0 °C (from hexane); IR (CCl_4) 3061, 2929, 2855, 1450, 1402, 1292, 1206, 1039 cm^{-1}; ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.81–2.98 (m, 13 H), 2.02 (d, 3 H, J = 7.0 Hz), 5.43 (q, 1 H, J = 7.0 Hz); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 143.7, 67.3 (C), 116.1, 47.1, 32.3 (CH), 52.6, 38.4, 35.2 (CH_2), 14.0 (CH_3). Anal. Calcd for $C_{12}H_{17}Br$: C, 59.76; H, 7.10; Br, 33.13. Found: C, 59.46; H, 7.18; Br, 32.92.

(*E*)-2-Ethylidene-1-bromoadamantane ((*E*)-6-Br). To a solution of $SOBr_2$ (0.697 g, 3.35 mmol) in benzene (3.0 mL) was added a solution of (*E*)-**6-OH**[14] (0.300 g, 1.68 mmol) and pyridine (0.538 g, 6.80 mmol) in benzene (6.0 mL) at 0 °C over 5 min. The reaction mixture was stirred at 0 °C for 30 min and at 30 °C for 5 h and then poured into ice–water (30 mL) and extracted with ether (3 × 30 mL). The combined extracts were washed with 10% aqueous HCl (3 × 30 mL) and saturated aqueous $NaHCO_3$ (3 × 30 mL) and dried ($MgSO_4$). Evaporation of solvent followed by MPLC (SiO_2, hexane) afforded (*E*)-**6-Br** (0.277 g, 68%) as colorless crystals: mp 27.0–27.5 °C (from hexane); IR (CCl_4) 3055, 2930, 2856, 1450, 1379, 1288, 1029, 893 cm^{-1}; ^{1}H NMR (60 MHz, $CDCl_3$) δ 1.63 (d, 3 H, J = 6.6 Hz), 1.82–2.47 (m, 12 H), 3.19 (s, 1 H), 5.43 (q, 1 H, J = 7.0 Hz); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 144.9, 72.8 (C), 115.7, 34.6, 32.4 (CH), 51.8, 37.3, 35.2 (CH_2), 12.4 (CH_3). Anal. Calcd for $C_{12}H_{17}Br$: C, 59.76; H, 7.10; Br, 33.13. Found: C, 59.92; H, 7.10; Br, 33.29.

1-Chloro-2-adamantyl Benzoate (10-Cl). To a solution of benzoyl triflate (10.57 g, 41.6 mmol) in CH_2Cl_2 (40 mL) was added a solution of **9** (5.20 g, 34.6 mmol) in CH_2Cl_2 (40 mL) over 14 min under N_2, while the temperature was kept below 8 °C in an ice–water bath. After the mixture was stirred for 10 min, Bu_4NCl (14.0 g, 50.4 mmol) was added. The mixture was stirred at room temperature for 17 h. The reaction mixture was poured into ice–water (80 mL) and extracted with ether (3 × 80 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (2 × 70 mL) and saturated aqueous NaCl (2 × 70 mL) and dried ($MgSO_4$). Evaporation of solvent followed by MPLC (SiO_2, hexane–ether (95:5)) afforded **10-Cl** (6.18 g, 61%) as colorless crystals: mp 86.0–87.0 °C (from hexane); IR (CCl_4) 3071, 2936, 2923, 2860, 1724, 1603, 1452, 1275, 1112, 709 cm^{-1}; ^{1}H NMR (89.55 MHz, $CDCl_3$) δ 1.46–2.73 (m, 13 H), 5.30 (d, 1 H, J = 3.62 Hz), 7.34–8.20 (m, 5 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 165.4, 130.4, 68.4 (C), 132.9, 129.6, 128.3, 79.5, 35.4, 30.7, 30.7 (CH), 47.0, 42.3, 35.2, 35.1, 30.1 (CH_2). Anal. Calcd for $C_{17}H_{19}O_2Cl$: C, 70.22; H, 6.59; Cl, 12.19. Found: C, 70.21; H, 6.61; Cl, 11.98.

1-Chloro-2-adamantanol (11-Cl). A solution of **10-Cl** (6.18 g, 21.2 mmol) in ether (80 mL) was added dropwise to a solution of $LiAlH_4$ (1.13 g, 29.8 mmol) in ether (100 mL) at room temperature. The reaction mixture was stirred for another 1 h and then worked up in a usual manner. Separation by MPLC (SiO_2, hexane–ether (95:5)) gave **11-Cl** (1.76 g, 44%) as colorless crystals: mp 194.0–195.0 °C (from pentane). The spectral data satisfactorily coincided with the reported data.[19b]

1-Chloro-2-adamantanone (12-Cl). To a suspension of pyridinium chlorochromate (3.89 g, 18.0 mmol) in CH_2Cl_2 (35 mL) was added a solution of **11-Cl** (1.70 g, 9.11 mmol) in CH_2Cl_2 (30 mL), and the resulting mixture was stirred under N_2 at room temperature for 50 h. Ether (35 mL) was added to the reaction mixture, then the solution was passed through a column of Florisil (50 g). Evaporation of solvent followed by MPLC (SiO_2, hexane–ether (95:5)) afforded **12-Cl** (1.54 g, 92%) as colorless crystals: mp 188.0–189.0 °C (from hexane). The spectral data satisfactorily coincided with the reported data.[19b]

1-Chloro-2-methyleneadamantane (7-Cl). To a suspension of methyltriphenylphosphonium bromide (4.10 g, 11.5 mmol) in THF (25 mL) was added dropwise 1.6 M BuLi in hexane (7.2 mL) at room temperature under N_2. After the mixture was stirred for 1 h, a solution of **12-Cl** (0.700 g, 3.79 mmol) in THF (14 mL) was added. The resulting mixture was stirred for another 3 h and then poured into ice–water (60 mL) and extracted with ether (3 × 50 mL). The combined extracts were washed with water (2 × 50 mL) and 10% aqueous NaCl (2 × 50 mL) and dried ($MgSO_4$). Evaporation of solvent followed by MPLC (SiO_2, hexane) afforded **7-Cl** (0.553 g, 80%) as colorless crystals: mp 71.5–72.5 °C (from pentane); IR (CCl_4) 3094, 2996, 2929, 2856, 1810, 1654, 1450, 1034, 903 cm^{-1}; ^{1}H NMR (89.55 MHz, $CDCl_3$) δ 1.76–2.19 (m, 12 H), 2.79 (br s, 1 H), 4.77 (d, 1 H, J = 1.6 Hz), 5.08 (d, 1 H, J = 1.6 Hz); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 154.4, 71.6 (C), 41.7, 31.5 (CH), 104.0, 49.7, 38.1, 35.2 (CH_2). Anal. Calcd for $C_{11}H_{15}Cl$: C, 72.32; H, 8.28; Cl, 19.41. Found: C, 72.19; H, 8.44; Cl, 19.12.

1-Bromo-2-adamantyl Benzoate (10-Br). To a solution of benzoyl triflate (3.96 g, 15.6 mmol) in CH_2Cl_2 (16 mL) was added a solution of **9** (1.95 g, 13.0 mmol) in CH_2Cl_2 (13 mL) over 11 min under N_2, while the temperature was kept below 7 °C in an ice–water bath. After the mixture was stirred for 5 min, Bu_4NBr (5.20 g, 16.1 mmol) was added. The mixture was stirred for 18 h at room temperature. The reaction mixture was poured into ice–water (40 mL) and extracted with ether (3 × 60 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (2 × 60 mL) and saturated aqueous NaCl (2 × 60 mL) and dried ($MgSO_4$). Evaporation of solvent followed by MPLC (SiO_2, hexane–ether (95:5)) afforded **10-Br** (2.57 g, 59%) as colorless crystals: mp 84.5–85.0 °C (from hexane); IR (CCl_4) 3071, 2935, 2861, 1724, 1603, 1452, 1274, 1112, 1027 cm^{-1}; ^{1}H NMR (89.55 MHz, $CDCl_3$) δ 1.42–2.90 (m, 13 H), 5.39 (d, 1 H, J = 3.5 Hz), 7.38–8.19 (m, 5 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 165.1, 130.2, 65.2 (C), 132.8, 129.5, 128.2, 79.8, 35.3, 31.3, 31.2 (CH), 48.3, 43.6, 35.2, 35.0, 29.9 (CH_2). Anal. Calcd for $C_{17}H_{19}O_2Br$: C, 60.91; H, 5.71; Br, 23.83. Found: C, 61.20; H, 5.82; Br, 23.59.

1-Bromo-2-adamantanol (11-Br). A solution of **10-Br** (2.37 g, 7.07 mmol) in ether (30 mL) was added dropwise to $LiAlH_4$ (0.350 g, 9.22 mmol) in ether (40 mL) at room temperature. The reaction mixture was stirred for another 25 min and then worked up in the usual manner. Separation by MPLC (SiO_2, hexane–ether (9:1)) gave **11-Br** (0.993 g, 61%) as colorless crystals: mp 144.5–145.5 °C (from hexane); IR (CCl_4) 3574, 2919, 2859, 1451, 1352, 1058, 1022 cm^{-1}; ^{1}H NMR (89.55 MHz, $CDCl_3$) δ 1.38–2.78 (m, 13 H), 2.59 (s, 1 H), 3.94 (d, 1 H, J = 3.4 Hz); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 74.6 (C), 78.4, 36.3, 32.0, 31.8 (CH), 47.8, 42.8, 35.6, 35.4, 28.9 (CH_2). Anal. Calcd for $C_{10}H_{15}OBr$: C, 51.97; H, 6.54; Br, 34.57. Found: C, 51.83; H, 6.55; Br, 34.59.

1-Bromo-2-adamantanone (12-Br). To a suspension of pyridinium chlorochromate (1.27 g, 5.89 mmol) in CH_2Cl_2 (11 mL) was added a solution of **11-Br** (0.908 g, 3.93 mmol) in CH_2Cl_2 (11 mL), and the resulting mixture was stirred under N_2 at room temperature for 68 h. Ether (15 mL) was added to the reaction mixture; then the solution was passed through a column of Florisil (45 g). Evaporation of solvent afforded **12-Br** (0.832 g, 92%) as colorless crystals: mp 125.0–125.5 °C (from hexane) (lit.[19c] mp 124–125 °C); IR (CCl_4) 2935, 2861, 1743, 1454, 1287, 1052, 1029, 877, 635 cm^{-1}; ^{1}H NMR (89.55 MHz, $CDCl_3$) δ 1.70–2.34 (m, 8 H), 2.47–2.67 (m, 4 H), 2.95 (br s, 1 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 206.0, 70.6 (C), 47.7, 30.8 (CH), 50.6, 38.0, 34.1 (CH_2). Anal. Calcd for $C_{10}H_{13}OBr$: C, 52.42; H, 5.72; Br, 34.87. Found: C, 52.61; H, 5.83; Br, 34.95.

1-Bromo-2-methyleneadamantane (7-Br). To a suspension of methyltriphenylphosphonium bromide (3.90 g, 10.9 mmol) in THF (25 mL) was added dropwise 1.6 M BuLi in hexane (6.8 mL) at room temperature under N_2. After the mixture was stirred for 45 min, a solution of **12-Br** (0.832 g, 3.63 mmol) in THF (14 mL) was added. The resulting mixture was stirred for another 40 min, poured into ice–water (60 mL), and extracted with ether (3 × 50 mL). The combined extracts were washed with water (2 × 50 mL) and 10% aqueous NaCl (2 × 50 mL) and dried ($MgSO_4$). Evaporation of solvent followed by MPLC (SiO_2, hexane) afforded **7-Br** (0.687 g, 83%) as colorless crystals: mp 23.5–24.5 °C (from pentane); IR (CCl_4) 3093, 2995, 2925, 2856, 1652, 1449, 1029, 903 cm^{-1}; ^{1}H NMR (89.55 MHz, $CDCl_3$) δ 1.81–2.83 (m, 13 H), 4.84 (d, 1 H, J = 1.5 Hz), 5.15 (d, 1 H, J = 1.7 Hz); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 154.7, 69.8 (C), 42.0, 32.2 (CH), 106.7, 51.3, 38.2, 35.1 (CH_2). Anal. Calcd for $C_{11}H_{15}Br$: C, 58.17; H, 6.66; Br, 35.18. Found: C, 58.41; H, 6.90; Br, 35.05.

2-Methylene-1-iodoadamantane (7-I). To a suspension of methyltriphenylphosphonium bromide (3.30 g, 9.24 mmol) in THF (21 mL) was added dropwise 1.6 M BuLi in hexane (5.8 mL) at room temperature over 10 min under N_2. After the mixture was stirred for 50 min, a solution of **12-I**[14] (0.852 g, 3.09 mmol) in THF (12 mL) was added. The resulting mixture was stirred another 30 min, poured into ice–water (60 mL), and extracted with ether (3 × 50 mL). The combined extracts were washed with water (2 × 50 mL) and 10% aqueous NaCl (2 × 50 mL) and dried ($MgSO_4$). Evaporation of solvent followed by MPLC (SiO_2, hexane) afforded **7-I** (0.483 g, 57%) as colorless crystals: mp 25.5–26.5 °C (from pentane); IR (CCl_4) 3086, 2990, 2904, 2854, 1648, 1447, 899 cm^{-1}; ^1H NMR (89.55 MHz, $CDCl_3$) δ 1.89 (m, 8 H), 2.51–2.90 (m, 5 H), 4.95 (d, 1 H, J = 1.2 Hz), 5.13 (d, 1 H, J = 1.3 Hz); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 156.1, 56.7 (C), 41.1, 32.7 (CH), 111.2, 54.6, 38.4, 35.2 (CH_2). Anal. Calcd for $C_{11}H_{15}I$: C, 48.19; H, 5.51; I, 46.29. Found: C, 48.47; H, 5.57; I, 46.54.

1-Fluoro-2-adamantyl Benzoate (10-F). To a solution of benzoyl triflate (7.55 g, 29.7 mmol) in CH_2Cl_2 (35 mL) was added a solution of **9** (3.93 g, 26.2 mmol) in CH_2Cl_2 (24 mL) over 12 min under N_2, while the temperature of the solution was kept below 8 °C in an ice–water bath. After 3 min of stirring, LiF (13.0 g, 0.50 mol) was added. The mixture was stirred at room temperature for 16 h, and then ice–water (20 mL) was added. The excess LiF was removed by filtration and the filtrate was extracted with ether (2 × 30 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (2 × 50 mL) and saturated aqueous NaCl (2 × 50 mL) and dried ($MgSO_4$). Evaporation of solvent followed by MPLC (SiO_2, hexane–ether (95:5)) afforded **10-F** (3.58 g, 50%) as colorless crystals: mp 111.5–112.5 °C (from hexane); IR (CCl_4) 3072, 2925, 2859, 1724, 1603, 1452, 1271, 1028 cm^{-1}; ^1H NMR (89.55 MHz, $CDCl_3$) δ 1.43–2.57 (m, 13 H), 5.31 (m, 1 H), 7.30–8.14 (m, 5 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 165.3, 130.3, 91.2 (d, J = 192.8 Hz) (C), 132.7, 129.3, 128.0, 77.1 (d, J = 15.9 Hz), 34.9 (d, J = 8.2 Hz), 30.5 (d, J = 6.6 Hz), 30.1 (d, J = 6.6 Hz) (CH), 41.6 (d, J = 16.5 Hz), 37.1 (d, J = 18.1 Hz), 35.3 (d, J = 2.2 Hz), 34.8 (d, J = 1.1 Hz), 30.2 (d, J = 1.1 Hz) (CH_2). Anal. Calcd for $C_{17}H_{19}O_2F$: C, 74.43; H, 6.98; F, 6.93. Found: C, 74.27; H, 7.04; F, 6.84.

1-Fluoro-2-adamantanol (11-F). A solution of **10-F** (3.58 g, 13.0 mmol) in ether (46 mL) was added dropwise to $LiAlH_4$ (0.600 g, 15.8 mmol) in ether (57 mL) at room temperature over 34 min. The reaction mixture was stirred for 30 min and then worked up in the usual manner. Separation by MPLC (SiO_2, hexane–ether (9:1)) gave **11-F** (2.04 g, 92%) as colorless crystals: mp 224.5 °C (from pentane); IR (CCl_4) 3611, 2917, 2864, 1453, 1355, 1235, 1077 cm^{-1}; ^1H NMR (89.55 MHz, $CDCl_3$) δ 1.29–2.18 (m, 13 H), 2.65 (s, 1 H), 3.87 (dd, 1 H, J = 3.3, 6.6 Hz); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 94.5 (d, J = 185.7 Hz) (C), 75.6 (d, J = 16.0 Hz), 35.9 (d, J = 21.5 Hz), 31.1 (d, J = 9.3 Hz), 30.6 (d, J = 9.9 Hz) (CH), 41.1 (d, J = 21.5 Hz), 36.2 (d, J = 1.6 Hz), 35.8 (d, J = 2.2 Hz), 35.1 (d, J = 2.2 Hz), 29.3 (d, J = 1.7 Hz) (CH_2). Anal. Calcd for $C_{10}H_{15}OF$: C, 70.56; H, 8.88; F, 11.16. Found: C, 70.41; H, 8.85; F, 11.27.

1-Fluoro-2-adamantanone (12-F). To a suspension of pyridinium chlorochromate (3.88 g, 18.0 mmol) in CH_2Cl_2 (35 mL) was added a solution of **11-F** (2.04 g, 12.0 mmol) in CH_2Cl_2 (35 mL), and the resulting mixture was stirred under N_2 at room temperature for 19 h. Ether (30 mL) was added to the reaction mixture; then the solution was passed through a column of Florisil (50 g). Evaporation of solvent afforded **12-F** (1.82 g, 90%) as colorless crystals: mp 308.5–309.5 °C (sealed tube, lit.[19a] mp 213–216 °C); ^1H NMR (89.55 MHz, $CDCl_3$) δ 1.85–2.23 (m, 10 H), 2.39 (br s, 2 H), 2.77 (br s, 1 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 209.3 (d, J = 14.0 Hz), 95.0 (d, J = 203.9 Hz) (C), 47.5 (d, J = 1.8 Hz), 30.0 (d, J = 9.2 Hz) (CH), 43.8 (d, J = 17.7 Hz), 37.5 (d, J = 1.2 Hz), 34.1 (d, J = 1.8 Hz) (CH_2). Although the melting point was higher than that reported by ca. 90 °C, the ^{13}C and ^1H NMR spectra were consistent with the structure and analytical data were satisfactory. Anal. Calcd for $C_{10}H_{13}OF$: C, 71.40; H, 7.79; F, 11.29. Found: C, 71.28; H, 8.02; F, 11.41.

(*Z*)- and (*E*)-2-Ethylidene-1-fluoroadamantanes ((*Z*)- and (*E*)-6-F). To a suspension of ethyltriphenylphosphonium bromide (4.46 g, 12.0 mmol) in THF (28 mL) was added dropwise 1.6 M BuLi in hexane (7.5 mL) at room temperature under N_2. After 1 h of stirring, a solution of **12-F** (0.673 g, 4.00 mmol) in THF (17 mL) was added. The resulting mixture was stirred for another 17 h, poured into ice–water (50 mL), and extracted with ether (3 × 40 mL). The combined extracts were washed with water (2 × 40 mL) and 10% aqueous NaCl (2 × 40 mL) and dried ($MgSO_4$). Evaporation of solvent afforded a mixture of (*Z*)- and (*E*)-**6-F**. The mixture was separated by MPLC (SiO_2, hexane–ether (95:5)), the first fraction being pure (*Z*)-**6-F** (0.326 g, 45%) as a colorless liquid, the second being pure (*E*)-**6-F** (0.295 g, 41%) as colorless crystals. **(*Z*)-6-F**: IR (CCl_4) 3068, 2934, 2911, 2854, 1471, 1453, 1392, 1210, 1084 cm^{-1}; ^1H NMR (89.55 MHz, $CDCl_3$) δ 1.66–2.21 (m, 13 H), 1.76 (dd, 3 H, J = 2.9, 7.1 Hz), 5.15 (dq, 1 H, J = 1.7, 7.1 Hz); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 143.7 (d, J = 12.6 Hz), 96.7 (d, J = 192.3 Hz) (C), 112.7, 43.8 (d, J = 6.6 Hz), 31.3 (d, J = 9.9 Hz) (CH), 44.5 (d, J = 18.1 Hz), 38.3 (d, J = 1.6 Hz), 35.4 (d, J = 2.2 Hz) (CH_2), 13.0 (d, J = 11.5 Hz) (CH_3). Anal. Calcd for $C_{12}H_{17}F$: C, 79.96; H, 9.51; F, 10.54. Found: C, 79.82; H, 9.62; F, 10.45. **(*E*)-6-F**: mp 53.0–53.5 °C (from pentane); IR (CCl_4) 3067, 2934, 2920, 2854, 1470, 1451, 1341, 1083 cm^{-1}; ^1H NMR (89.55 MHz, $CDCl_3$) δ 1.60 (d, 3 H, J = 6.9 Hz), 1.69–1.97 (m, 11 H), 2.25 (br s, 1 H), 3.07 (br s, 1 H), 5.37 (q, 1 H, J = 6.8 Hz); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 144.4 (d, J = 12.1 Hz), 93.8 (d, J = 193.4 Hz) (C), 108.4 (d, J = 12.1 Hz), 33.5 (d, J = 3.9 Hz), 31.2 (d, J = 9.9 Hz) (CH), 44.7 (d, J = 18.1 Hz), 37.3 (d, J = 1.7 Hz), 35.5 (d, J = 1.6 Hz) (CH_2), 11.7 (CH_3). Anal. Calcd for $C_{12}H_{17}F$: C, 79.96; H, 9.51; F, 10.54. Found: C, 79.68; H, 9.79; F, 10.48.

Product of Solvolysis of (*Z*)-4-OTf in Ethanol. A solution of (*Z*)-**4-OTf** (0.207 g, 0.73 mmol) in 0.050 M 2,6-lutidine in ethanol (18 mL) was heated in a constant temperature bath (25.0 °C) for 5 h (10 half-lives). GLC analysis (PEG-20M, 3 mm × 2 m) of the reaction mixture exhibited the formation of a single product. After most of solvent had been removed with a rotary evaporator, the residue was diluted with ether (15 mL) and the ether solution was washed with water (15 mL), 10% aqueous HCl (15 mL), saturated aqueous $NaHCO_3$ (15 mL), and saturated aqueous NaCl (15 mL) and dried ($MgSO_4$). Evaporation of solvent afforded 1-ethoxy-(*Z*)-2-ethylidenebicyclo[2.2.2]octane (0.099 g, 76%) as a yellowish brown oil: IR (CCl_4) 2939, 2866, 1732, 1454, 1381, 1317, 1202, 1156, 1115, 1045, 960 cm^{-1}; ^1H NMR (89.55 MHz, $CDCl_3$) δ 1.19 (t, 3 H, J = 7.0 Hz), 1.31–1.89 (m, 9 H), 1.81 (dt, 3 H, J = 7.3, 1.8 Hz), 2.22 (br s, 2 H), 3.44 (q, 2 H, J = 7.0 Hz), 5.21 (qt, 1 H, J = 7.1, 1.9 Hz); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 139.0, 77.8 (C), 117.8, 26.5 (CH), 57.5, 39.2, 31.1, 26.5 (CH_2), 15.7, 13.3 (CH_3).

Product of Solvolysis of (*Z*)-6-OMs in Ethanol. From (*Z*)-**6-OMs** (0.050 g, 0.20 mmol) in 0.050 M 2,6-lutidine in ethanol (4.9 mL) at 50.0 °C for 38 h (13.7 half-lives) was obtained 1-ethoxy-(*Z*)-2-ethylideneadamantane (0.038 g, 95%) as a pale yellow oil: IR (CCl_4) 2928, 2852, 1709, 1450, 1388, 1341, 1211, 1178, 1116, 1095, 1056, 967, 936, 897 cm^{-1}; ^1H NMR (89.55 MHz, $CDCl_3$) δ 1.20 (t, 3 H, J = 6.9 Hz), 1.34–1.97 (m, 10 H), 1.83 (d, 3 H, J = 7.2 Hz), 2.14 (br s, 2 H), 2.43 (br s, 1 H), 3.53 (q, 2 H, J = 6.9 Hz), 5.17 (q, 1 H, J = 7.3 Hz); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 145.6, 78.1 (C), 113.3, 44.5, 30.6 (CH), 56.5, 43.3, 39.1, 36.1 (CH_2), 15.9, 13.4 (CH_3).

Product of Solvolysis of (*E*)-6-OMs in Ethanol. From (*E*)-**6-OMs** (0.035 g, 0.14 mmol) in 0.050 M 2,6-lutidine in ethanol (3.4 mL) at 100.0 °C for 9.5 h (11.3 half-lives) was obtained 1-ethoxy-(*E*)-2-ethylideneadamantane (0.026 g, 93%) as a pale yellow oil: IR (CCl_4) 2927, 2853, 1729, 1449, 1392, 1341, 1295, 1218, 1124, 1093, 1055, 964 cm^{-1}; ^1H NMR (89.55 MHz, $CDCl_3$) δ 1.21 (t, 3 H, J = 7.0 Hz), 1.37–1.90 (m, 10 H), 1.60 (d, 3 H, J = 6.9 Hz), 2.17 (br s, 2 H), 3.03 (br s, 1 H), 3.54 (q, 2 H, J = 7.0 Hz), 5.31 (q, 1 H, J = 6.9 Hz); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 145.5, 75.8 (C), 109.0, 32.9, 30.4 (CH), 56.4, 43.7, 37.9, 36.2 (CH_2), 16.0, 12.0 (CH_3).

Product of Solvolysis of 7-OMs in Ethanol. A solution of **7-OMs** (0.078 g, 0.32 mmol) in 0.050 M 2,6-lutidine in ethanol (8.0 mL) was heated in a constant temperature bath (100.0 °C) for 55 h (11.0 half-lives). After most of solvent had been removed with a rotary evaporator, the residue was diluted with $CHCl_3$ (20 mL). The organic layer was washed with water (10 mL), 10% aqueous HCl (10 mL), saturated aqueous $NaHCO_3$ (10 mL), and water (10 mL) and dried ($MgSO_4$). Evaporation of solvent afforded a mixture of 1-ethoxy-2-methyleneadamantane (**7-OEt**) (94%), 1,2-diethoxy-2-methyladamantane (3%), and 2-methyl-4-protoadamantanone (**14**) (3%). The product distribution was determined by GLC (PEG-20M, 3 mm × 2 m) analysis for crude products. **7-OEt**: ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 155.8, 76.0 (C), 41.3, 30.6 (CH), 100.4, 56.6, 43.9, 38.8, 36.1 (CH_2), 15.9 (CH_3). 1,2-Diethoxy-2-methyladamantane: ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 81.0, 77.2 (C), 37.5, 30.2, 30.1 (CH), 57.7, 55.0, 40.1, 37.4, 35.4, 33.7, 32.1 (CH_2), 16.7, 16.5, 16.2 (CH_3). **14**: The ^{13}C NMR spectral data were consistent with those of authentic **14** that was synthesized by the pinacol rearrangement of 2-methyl-1,2-adamantanediol.

Product of Solvolysis of (*Z*)-6-Cl in TFE. A solution of (*Z*)-**6-Cl** (0.076 g, 0.39 mmol) in 0.050 M 2,6-lutidine in TFE (9.6 mL) was heated in a constant temperature bath (75.0 °C) for 4 h (10.8 half-lives). GLC analysis (PEG-20M, 3 mm × 2 m) of the reaction mixture exhibited the formation of a single product. After most of solvent had been removed with a rotary evaporator, the residue was diluted with ether (20 mL) and the ether solution was washed with water (12 mL), 10% aqueous HCl (15 mL), saturated aqueous $NaHCO_3$ (2 × 15 mL), and water (15 mL) and dried ($MgSO_4$). Evaporation of solvent afforded 1-(trifluoroethoxy)-(*Z*)-2-ethylideneadamantane ((*Z*)-**6-OTFE**)[14] (0.078 g, 77%) as a yellow oil.

Product of Solvolysis of (*E*)-6-Cl in TFE. From (*E*)-**6-Cl** (0.067 g, 0.34 mmol) in 0.050 M 2,6-lutidine in TFE (8.5 mL) at 100.0 °C for 166 h (11.4 half-lives) was obtained 1-(trifluoroethoxy)-(*E*)-2-ethylideneadamantane ((*E*)-**6-OTFE**)[14] (0.083 g, 93%) as a pale yellow oil.

Product of Solvolysis of 7-Cl in TFE. A solution of **7-Cl** (0.066 g, 0.36 mmol) in 0.050 M 2,6-lutidine in TFE (9.0 mL) was heated in a constant temperature bath (125.0 °C) for 237 h (11.5 half-lives). After most of solvent had been removed with a rotary evaporator, the residue was diluted with ether (20 mL) and the ether solution was washed with water (15 mL). The aqueous layer was extracted with ether (2 × 15 mL). The combined extracts were washed with 10% aqueous HCl (15 mL), saturated aqueous $NaHCO_3$ (2 × 15 mL), and water (15 mL) and dried ($MgSO_4$). Evaporation of solvent followed by MPLC (SiO_2, hexane, hexane−ether (9:1)) afforded 1-(trifluoroethoxy)-2-methyleneadamantane (**7-OTFE**) (0.047 g, 56%), 1,2-bis(trifluoroethoxy)-2-methyladamantane (**13**) (0.035 g, 29%), and 2-methyl-4-protoadamantanone (**14**) (0.008 g, 14%) in this sequence. **7-OTFE**: pale yellow oil; IR (CCl_4) 3099, 3000, 2929, 2856, 1654, 1450, 1379, 1356, 1278, 1157, 1128, 977 cm^{-1}; ^1H NMR (89.55 MHz, $CDCl_3$) δ 1.73−1.88 (m, 10 H), 2.25 (br s, 2 H), 2.68 (br s, 1 H), 3.92 (q, 2 H, J = 8.7 Hz), 4.74 (dd, 2 H, J = 5.1, 1.8 Hz); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 154.4, 77.5 (C), 41.4, 30.7 (CH), 101.2, 42.9, 38.5, 35.5 (CH_2), 60.0 (q, OCH_2CF_3, J = 34.1 Hz), 124.3 (q, CF_3, J = 278.0 Hz). **13**: pale yellow oil; ^1H NMR (89.55 MHz, $CDCl_3$) δ 1.26−2.09 (m, 12 H), 1.35 (s, 3 H), 2.52 (m, 1 H), 3.83 (qd, 2 H, J = 8.6, 2.7 Hz), 3.99 (qd, 2 H, J = 8.8, 2.6 Hz); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 83.1, 78.0 (C), 38.3, 30.0, 29.9 (CH), 40.1, 36.8, 34.8, 33.5, 31.5 (CH_2), 61.1 (q, J = 34.2 Hz), 59.8 (q, J = 34.2 Hz) (OCH_2CF_3), 16.2 (CH_3), 124.4 (q, J = 277.2 Hz), 124.3 (q, J = 277.1 Hz) (CF_3). **14**: ^{13}C and ^1H NMR spectral data were consistent with those of authentic **14** that was synthesized by the pinacol rearrangement of 2-methyl-1,2-adamantanediol.

Preparation of 2-Methyl-4-protoadamantanone (14) by the Pinacol Rearrangement of 2-Methyl-1,2-adamantanediol. To a solution of 1-hydroxy-2-adamantanone (0.200 g, 1.20 mmol) in benzene (25 mL) was added dropwise CH_3Li in ether (0.381 M, 19 mL) over 5 min at room temperature under N_2. The reaction mixture was stirred at 70 °C for 23 h and then cold water (10 mL) was added. The resulting mixture was stirred for another 10 min and then extracted with ether (3 × 20 mL) and dried ($MgSO_4$). Evaporation of solvent gave 2-methyl-1,2-adamantanediol (0.218 g, 99%) as pale yellow crystals: mp 269.5−271.5 °C (dec sealed tube, from hexane−benzene); IR (CCl_4) 3599, 3580, 3455, 3014, 2925, 2862, 1449, 1080 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 0.87−2.12 (m, 15 H), 1.33 (s, 3 H); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 76.4, 72.3 (C), 40.9, 30.4, 30.3 (CH), 41.2, 40.8, 36.8, 34.2, 31.7 (CH_2), 22.3 (CH_3). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.21; H, 10.12. A solution of 2-methyl-1,2-adamantanediol (0.658 g, 3.61 mmol) in ether (60 mL) was vigorously stirred with 4 N H_2SO_4 (40 mL) at 45 °C for 118 h. The reaction mixture was extracted with ether (3 × 20 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (3 × 15 mL) and saturated aqueous NaCl (2 × 15 mL) and dried ($MgSO_4$). Evaporation of solvent followed by MPLC (SiO_2, hexane−ether (4:1)) afforded 2-methyl-4-protoadamantanone (**14**) (0.553 g, 93%) as colorless crystals: mp 122.0−122.5 °C (from hexane); IR (CCl_4) 3401, 2925, 2863, 1712, 1458, 1445, 1072 cm^{-1}; ^1H NMR (270.05 MHz, $CDCl_3$) δ 1.10 (s, 3 H), 1.26−2.59 (m, 13 H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 217.0, 52.9 (C), 45.6, 38.9, 29.8 (CH), 45.9, 45.3, 40.1, 37.8, 35.0 (CH_2), 22.8 (CH_3). Analytical data were unsatisfactory presumably because of the sublimating nature. Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 79.84; H, 10.03. HRMS calcd for $C_{11}H_{16}O$ 164.1202, found 164.1198.

Product of Solvolysis of (*Z*)-6-Br in TFE. From (*Z*)-**6-Br** (0.054 g, 0.22 mmol) in 0.050 M 2,6-lutidine in TFE (5.5 mL) at 40.0 °C for 2 h (12.1 half-lives) was obtained 1-(trifluoroethoxy)-(*Z*)-2-ethylideneadamantane ((*Z*)-**6-OTFE**)[14] (0.051 g, 88%) as a pale yellow oil.

Product of Solvolysis of (*E*)-6-Br in TFE. From (*E*)-**6-Br** (0.049 g, 0.20 mmol) in 0.050 M 2,6-lutidine in TFE (5.0 mL) at 100.0 °C for 7.4 h (10.6 half-lives) was obtained 1-(trifluoroethoxy)-(*E*)-2-ethylideneadamantane ((*E*)-**6-OTFE**)[14] (0.051 g, 96%) as a pale yellow oil.

Product of Solvolysis of 7-Br in TFE. From **7-Br** (0.046 g, 0.20 mmol) in 0.050 M 2,6-lutidine in TFE (5.0 mL) at 100.0 °C for 71 h (10 half-lives) was obtained 1-(trifluoroethoxy)-2-methyleneadamantane (**7-OTFE**) (0.043 g, 86%) as a pale yellow oil.

Product of Solvolysis of 7-I in TFE. From **7-I** (0.055 g, 0.20 mmol) in 0.050 M 2,6-lutidine in TFE (5.0 mL) at 100.0 °C for 51.5 h (10 half-lives) was obtained 1-(trifluoroethoxy)-2-methyleneadamantane (**7-OTFE**) (0.048 g, 98%) as a pale yellow oil.

[^{18}O]-(*Z*)-2-Ethylidene-1-adamantanol ((*Z*)-6-^{18}OH). A solution of (*Z*)-**6-OMs** (0.818 g, 3.19 mmol) in 0.50 M 2,6-lutidine in 90% THF−10% $H_2{}^{18}O$ (10 atom % ^{18}O) (8.0 mL) was heated in a constant temperature bath (75.0 °C) for 96 h. After most of solvent had been removed with a rotary evaporator, the residue was extracted with pentane (10 mL + 2 × 4 mL). The combined extracts were washed with 10% aqueous HCl (7 mL), saturated aqueous $NaHCO_3$ (7 mL), and water (7 mL) and dried ($MgSO_4$). Evaporation of solvent afforded (*Z*)-**6-^{18}OH** (0.581 g, 100%). The isotopic composition of the product was determined by analysis of the mass spectral peaks at M (178) and M + 2 (180); the intensity ratio M:(M + 2) was 100:13.8.

[^{18}O]-(*E*)-2-Ethylidene-1-adamantanol ((*E*)-6-^{18}OH). From (*E*)-**6-OMs** (0.923 g, 3.60 mmol) in 0.50 M 2,6-lutidine in 90% THF−10% $H_2{}^{18}O$ (10 atom % ^{18}O) (9.0 mL) at 100.0 °C for 115 h was obtained (*E*)-**6-^{18}OH** (0.640 g, 100%). The isotopic composition of the product was determined by analysis of the mass spectral peaks at M (178) and M + 2 (180); the intensity ratio M:(M + 2) was 100:13.8.

^{18}*O*-(*Z*)-2-Ethylidene-1-adamantyl [$^{18}O_1$]Mesylate ((*Z*)-6-^{18}OMs). To a solution of (*Z*)-**6-^{18}OH** (0.400 g, 2.24 mmol) in THF (5.0 mL) was added dropwise 1.6 M BuLi in hexane (1.4 mL) at −40 °C under N_2. After the mixture was stirred for 50 min, a solution of methanesulfonyl chloride (MsCl) (0.258 g, 2.25 mmol) in THF (5.0 mL) was added. The resulting mixture was stirred at −40 °C for 3 h and then allowed to warm slowly to 10 °C over 2 h. After most of solvent had been removed with a rotary evaporator, hexane was added. An insoluble precipitate was removed by filtration. Evaporation of solvent followed by MPLC at −40 °C (SiO_2, hexane−ether (9:1)) afforded pure (*Z*)-**6-^{18}OMs** (0.396 g, 69%) and a mixture of (*Z*)-**6-^{18}OMs** and (*Z*)-**6-^{18}OH** (0.127 g) in this sequence.

^{18}*O*-(*E*)-2-Ethylidene-1-adamantyl [$^{18}O_1$]Mesylate ((*E*)-6-^{18}OMs). The procedure described for the preparation of (*Z*)-**6-^{18}OMs** was followed. A solution of (*E*)-**6-^{18}OH** (0.400 g, 2.24 mmol) in THF (5.0 mL) was treated with 1.6 M BuLi in hexane (1.4 mL) and then with MsCl (0.252 g, 2.20 mmol) at −40 °C for 4 h. Workup followed by MPLC at −40 °C (SiO_2, hexane−ether (9:1)) afforded (*E*)-**6-^{18}OMs** (0.371 g, 65%) and (*E*)-**6-^{18}OH** (0.120 g, 30%) in this sequence.

NOE Difference Experiments. Nuclear Overhauser enhancement of the C(3) bridgehead proton of (*Z*)- and (*E*)-**6-OH** on irradiation of the olefinic proton was determined at 270.05 MHz by the gated decoupling method using $CDCl_3$ solution degassed under vacuum. An irradiation period of 3.5 times the T_1's of the olefinic proton was employed for NOE generation, followed by a 90° pulse. For spin relaxation, a pulse interval of 3.5 times the T_1's of the olefinic proton was taken before the next pulse. The T_1 values were determined by the inversion recovery method. Irradiation of the olefinic proton of (*Z*)-**6-OH** caused enhancement both of the C(3) bridgehead proton and the methyl protons, 17.0% and 2.6%, respectively. Only the methyl protons showed NOE's (3.4%) when the olefinic proton of (*E*)-**6-OH** was irradiated.

Kinetic Methods. The preparation of solvents and kinetic methods were described previously.[14,24] Titrimetric rates were obtained for solutions containing 0.025 M 2,6-lutidine and 0.020 M substrate in ethanol or TFE, whereas conductimetric rates were determined for solutions containing 2,6-lutidine (0.025 M in ethanol and 0.0012 M in TFE) and 0.0002 M substrate. For the fluorides, the solvolysis rates were determined by GLC as follows. The solvolysis was conducted for TFE solutions containing 0.025 M 2,6-lutidine and 0.020 M substrate, and the concentrations of the substrate and the produced trifluoroethyl ether were determined by GLC (PEG-20M, 3 mm × 2 m) for reaction solutions by using separately determined peak intensity factors. The first-order rate constants were calculated by the least-squares method on a microcomputer.

Oxygen-18 Scrambling Study: Typical Procedure. A solution of (*Z*)-**6-^{18}OMs** (0.090 g, 0.35 mmol) in 0.050 M 2,6-lutidine in ethanol (9.0 mL) was heated at 50.0 °C for 12 min (5% reaction). Evaporation of solvent with an oil pump at 0 °C followed by MPLC at −40 °C (SiO_2, hexane−ether (9:1)) gave (*Z*)-**6-^{18}OMs** (0.070 g, 78%). To a solution of the recovered (*Z*)-**6-^{18}OMs** (0.070 g, 0.27 mmol) in DMSO (4.5 mL) was added 0.5 M *t*-BuOK in DMSO (4.5 mL). The resulting mixture was heated at 50 °C for 40 h. The reaction mixture was poured into ice−water (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined extracts were washed with water (2 × 10 mL) and dried ($MgSO_4$). Evaporation of solvent afforded (*Z*)-**6-^{18}OH** (0.048 g, 98%). The isotopic composition of (*Z*)-**6-^{18}OH** was determined by analysis of the mass spectral peaks at M (178) and M + 2 (180).

Control Experiment for ^{18}O Scrambling Study. A solution of (*E*)-**6-^{18}OH** (0.079 g, 0.44 mmol, M:(M + 2) = 100:7.69) in THF (1.0 mL) was treated with 1.6 M BuLi in hexane (0.28 mL) and then with MsCl (0.050 g, 0.44 mmol) at −40 °C for 5 h. Workup followed by MPLC at −35 °C (SiO_2, hexane−ether (9:1)) afforded (*E*)-**6-^{18}OMs** (0.065 g, 57%) and (*E*)-**6-^{18}OH** (0.021 g, 27%) in this sequence. A solution of the recovered (*E*)-**6-^{18}OMs** (0.065 g, 0.25 mmol) in DMSO (4.3 mL) was treated with 0.5 M *t*-BuOK in DMSO (4.3 mL) at 60 °C for 45 h. The reaction mixture was poured into ice−water (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined extracts were washed with water (2 × 10 mL) and dried ($MgSO_4$). Evaporation of solvent afforded (*E*)-**6-^{18}OH** (0.012 g, 27%). The isotopic composition of the recovered (*E*)-**6-^{18}OH** was determined by analysis of the mass spectral peaks at M (178) and M + 2 (180); the intensity ratio M:(M + 2) was 100:7.75, showing no scrambling of the ether oxygen during MPLC and the cleavage reaction.

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Supplementary Material Available: ^{13}C NMR spectra of new substrates and solvolysis products (27 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.