CROATICA CHEMICA ACTA CCACAA **65** (3) 517–538 (1992)

ISSN 0011-1643
UDC 547.67
CCA – 2074

Original Scientific Paper

Solvolysis of 1-(3-Noradamantyl)-2-methylpropyl and 1-(3-Noradamantyl)-2,2-dimethylpropyl Pemsylates*

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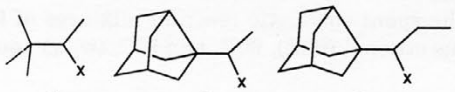
Received March 04, 1992

Rates, *m*-values, α-*d* and β-*d* rate effects are reported for solvolyses of the title esters along with MMX calculations of the strain energies of initial and transition states. These results are compared with those from several lower homologs and related adamantyl carbinyl esters. It is found that the noradamantyl carbinyl ester solvolyses are accelerated up to 10,000-fold by C–C σ-participation; β-branching in the alkyl side-chain reduces this rate effect by as much as 100-fold.

INTRODUCTION

Over twenty years ago it was proposed that pinacolyl (3,3-dimethyl-2-butyl) sulfonates (**1**) solvolyzed by rate-determining ionization without internal return and without participation by solvent or neighboring group.[1] Because this proposal was seen by some as controversial,[2] an effort to further our understanding of structural requirements and experimental manifestations of neighboring carbon σ-participation in solvolysis reactions was begun by studying the influence of the noradamantyl substituent group in the solvolysis of the 1-(3-noradamantyl)ethyl and propyl sulfonate esters, **2** and **3**. The detailed results and conclusions from the study of these compounds are being presented elsewhere.[3]



1 2 3

1-3, X = a sulfonate group; **1a-3a** X = OTs, *p*-toluenesulfonate; **2b & 3b**, X = OPms, pentamethylbenzenesulfonate.

* Dedicated to Professor Dionis E. Sunko on the occasion of his seventieth birthday.
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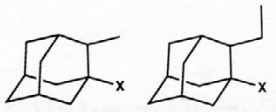
# This work constitutes part of the Ph.D. Thesis of D. T. Stoelting, Indiana University, 1990.

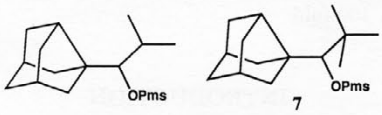
In brief, **2** and **3** were found to solvolyze by a classic k_Δ mechanism complicated by large proportions of concurrent internal isomerization to the tertiary 1-adamantyl sulfonate isomers, **4** and **5**, which also solvolyzed concomitantly with the unrearranged isomers.



4 5

4 & 5, X = a sulfonate group; **4a & 5a**, X = OTs, *p*-toluenesulfonate;
4b & 5b, X = OPms, pentamethylbenzenesulfonate;
5c, X = OHFB, heptafluorobutyrate.

We extended this study of the effects of tying the γ-carbon atoms of pinacolyl sulfonates into the noradamantyl ring system by examining the solvolysis of the two higher homologs, **6** and **7**. Compound **6** is 1-(3-noradamantyl)-2-methylpropyl pentamethylbenzenesulfonate (pemsylate, OPms); **7** is 1-(3-noradamantyl)-2,2-dimethylpropyl pemsylate.



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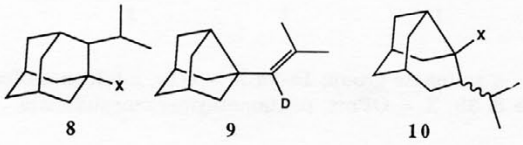
RESULTS AND DISCUSSION

Product Analysis. 1-(3-Noradamantyl)-2-methylpropyl Pemsylate (**6**). Unlike the lower homologs, **2** and **3**, aqueous ethanolyses of 1-(3-noradamantyl)-2-methylpropyl pemsylate (**6**) and its α-d_1 and β-d_1 isotopomers, followed strictly first-order kinetics. If the mechanism for **6** is the same as that proposed for **2** and **3** the solvolysis will be first-order if the rearranged 2-isopropyl-1-adamantyl pemsylate (**8**) is much more reactive than **6**.

Information on the products of the reaction was first obtained from the 55.4-MHz ^{2}H NMR spectra of the spent solvolytic reaction mixtures of the α-d_1 isotopomer of **6** (**6**-α-***d***) in 95% aqueous ethanol (95E), 90E, and 97% (w/w) aqueous 2,2,2-trifluoroetha-



8 9 10

8,10, X = OPms, pentamethylbenzenesulfonate;
8a,10a, X = OH; **8b,10b**, X = OEt or OCH_2CF_3;
8c, X = $OCOC_3F_7$, heptafluorobutyrate.

nol (97T). Like the lower homologs, **6** yielded no *unrearranged* substitution products in these solvents; unlike the lower homologs it yielded, in addition to 1-adamantyl substitution, other rearrangement products and, in ethanolic solvents, ~3% of vinyl-d_1 alkene (**9**).

In order to identify each peak in the ^{2}H NMR spectra, most of the products of solvolysis of **6**-α-**d** in 100E, 97T and 83% aqueous acetone were separated by HPLC and identified from the 300-MHz ^{1}H NMR and 75-MHz ^{13}C NMR spectra of the various fractions. These spectra showed conclusively that the major products of solvolysis in all solvents are 2-isopropyl-1-adamantyl alcohol and ethers (**8a** and **8b**) and that the minor products are 4-isopropyl-3-protoadamantyl alcohol and ethers (**10a** and **10b**). The stereochemistry of **10a** and **10b** was not conclusively established, but our proposed mechanism suggests that the predominant epimer is *endo* which would have the alkyl group in formula **10** oriented down. The 300-MHz ^{1}H NMR spectra of the products from solvolysis of **6** in 100E also showed the following minor products: unrearranged substitution (~ 0.2%), an allyl-d_1 containing compound (~ 0.2%), and the minor epimer of the protoadamantyl ether **10b** (1.1%). There was no evidence of the production of the minor epimer of **10a** or **10b** from solvolysis in 97T or 83% aqueous acetone; thus the rearrangement of **6** to the 3-protoadamantyl ring system is strongly stereoselective.

TABLE I

55.4-MHz ^{2}H NMR Chemical Shifts (δ)[a] of the Solvolysis Products from 1-(3-Noradamantyl)-2-methylpropyl-1-d_1 Pemsylate (6) and 1-(3-noradamantyl)-2,2-dimethylpropyl-1-d Pemsylate (7)

compd	solvent		
	95E	90E	97T
2-isopropyl-1-adamantanol-2-*d*, **8a**	1.791	1.725	1.554
ethyl 2-isopropyl-1-adamantyl-2-*d* ether, **8b**	1.965	1.905	1.691
2-t-butyl-1-adamantanol-2-d, **13a**	2.043	2.000	1.859
ethyl 2-t-butyl-1-adamantyl-2-*d* ether, **13b**	2.118	2.047	1.955
4-isopropyl-3-protoadamantanol-4-*d*, **10a**	2.300	2.268	2.111
ethyl 4-isopropyl-3-protoadamantyl-4-*d* ether, **10b**	2.538	2.453	2.257
4-t-butyl-3-protoadamantol-4-*d*, **14a**	not resolved from 14b below		
ethyl 4-t-butyl-3-protoadamantyl-4-*d* ether, **14b**	2.309	2.247	2.141
1-(3-noradamantyl)-2-methylpropene-1-*d*, **9**	5.881	5.882	
3-(3-noradamantyl)-2-methylbutene-3-*d*, **15**	2.762	2.702	2.563

[a] Peak positions are relative to external $CDCl_3$ in chloroform assigned as 7.25 δ.

Each of the principal products isolated from solvolysis of **6**-α-***d*** and identified as described above, were separately dissolved in 95E and 97T and their 55.4-MHz ^{2}H NMR spectra recorded to allow their identification in the spectra of reaction mixtures. The spectral assignments are shown in Table I and the product compositions from solvolysis of labeled **6**-α-***d*** in 90E, 95E, and 97T, identified by analysis of the 55.4-MHz ^{2}H NMR spectra of the spent buffered reaction mixtures, are presented in Table II. In all solvents used, including aqueous acetone, ethanol, aqueous ethanol, and 97% aqueous trifluoroethanol, 2-isopropyl-1-adamantyl substitution products (**8a** & **8b**) are produced in about 90% combined yield. The balance of ~10% is mainly 4-isopropyl-3-

TABLE II

*Yields of Products from Solvolysis of 1-(3-Noradamantyl)-2-methylpropyl-1-d Pemsylate (**6**-α-d)*[a]

product	solvent				
	100E[b]	95E[c]	90E[c]	83A[b]	97T[d]
8a-2-*d*	0.0	20.0	37.0	89.0	36.0
8b-2-*d*	90.4	66.0	53.0	0.0	53.0
9-3-*d*	2.4	4.0	3.0	0.0	0.0
10a-4-*d*	0.0	4.0	3.0	0.0	7.0
endo-**10b**-4-*d*	6.1	6.0	4.0	11.0	4.0
exo-**10b**-4-*d*	1.1	0.0	0.0	0.0	0.0

[a] In %, errors estimated at ±1–2%. Analyses were done on spent reaction mixtures, originally ~0.1M in reactant and buffered with a slight excess of 2,6-lutidine.
[b] Analyzed by weights of fractions separated by HPLC; **8b** and **10b** from 100E eluted together and their relative amounts were found by integration of the methyl group resonances in the 300-MHz ^{1}H NMR spectra.
[c] Determined from the relative peak heights of characteristic resonances in the ^{2}H NMR spectra of spent solvolysis reaction mixtures.
[d] Overlap of peaks increases the uncertainty of these results which are based on a Gaussian fit

protoadamantyl alcohol and ether (**10a** & **10b**). The only product which appears to be a function of solvent is the alkene (**9**) which is not produced in 97T. Since trifluoroethanol is expected to have lower basicity and/or hydrogen bond accepting ability the lack of **9** in 97T is understandable.

Solvolysis 2-Isopropyl-1-Adamantyl Pemsylate. 2-Isopropyl-1-adamantyl-2-d_1 pemsylate (**8**-β-*d*) was prepared and examined as the putative reactive intermediate formed in the solvolysis of **6**-α-*d*. The 300-MHz ^{1}H NMR spectrum and the 75-MHz ^{13}C (decoupled) NMR spectrum in $CDCl_3$ were consistent with the assigned structure and showed the sample to have excellent purity in spite of its high reactivity. The solvolytic rate constant in 95E was determined conductometrically to be $1466 \pm 16 \times 10^{-5}$ sec^{-1}, 996 times faster than that of **6**. Even if **6**, like its lower homologs, were to rearrange during solvolysis to form the isomer **8**, the near 1000-fold greater reactivity of **8** over **6** would not allow a significant concentration of rearranged ester, **8**, to build up and cause the kinetics of **6** to deviate from first-order behavior. Arguments presented later suggest that **10** should have reactivity similar to **8** and any production of it would also not affect the kinetic behavior of **6**.

The structures and yields of solvolysis products of **8** in 95E, 90E, and 97T were determined *in situ* from the 55.4–MHz ^{2}H NMR spectra of the crude reaction mixtures.

TABLE III

*Yields of Solvolysis Products from 1-Isopropyl-1-Adamantyl-2-d Pemsylate (**8**-β-d)*[a,b].

product	solvent		
	95E	90E	97T[d]
8a-2-*d*	26.0	42.0	27.0
8b-2-*d*	74.0	58.0	73.0

[a,b,d] See footnotes to Table I.

The peaks were at the positions expected for 2-isopropyl-1-adamantyl-2-d_1 substitution, **8a** and **8b**, as indicated in Table I. The yields, given in Table III, show that these two products are formed in near the same proportions in 95E and 90E from both **6** and **8** as expected if both reactions share a common intermediate. The different ratios found in 97T may be due to analytical difficulties caused by the poor separation of the NMR peaks in that solvent. The relative molar reactivity of water and alcohol in capturing the tertiary carbenium ion, k_a/k_e values, were calculated to be 2.1 (95E), 2.0 (90E), and 2.2 (97T) in line with other 2-alkyl-1-adamantyl substitution selectivities observed.[3] Since **8** does not give any rearranged protoadamantyl products it can be concluded that rearrangement from **6** is irreversible.

TABLE IV

*Solvolysis Rate Constants and m-Values for 2-Isopropyl-1-Adamantyl- (**8c**) and Related Heptafluorobutyrates*

compd	$k/10^{-5}$ s^{-1}		*m*-value[a]
	50E	60E	
2-isopropyl-1-adamantyl OHFB, **8c**	2.623	0.9453	0.9786
2-ethyl-1-adamantyl OHFB, **5c**	0.04087	0.01316	1.0757
2,2-dimethyl-1-adamantyl OHFB	0.06205		
t-Butyl OHFB	2.527	1.053	0.818[a]

[a] Calculated by linear least-squares fit of the data points of log k of compound *vs.* log k 2-adamantyl tosylate (Y_{OTs}); 2-Adamantyl tosylate rate constants were determined in this laboratory.[16] The 80E and 60E k values for *t*-butyl OHFB were determined by F. P. Wilgis.[8]

The rate of solvolysis of **8** is also enhanced relative to 2-ethyl-1-adamantyl pemsylate (**5b**) which reacts 120 times more slowly.[3] This acceleration is caused by the relief of initial state strain between the leaving group and the one of methyl groups of the isopropyl substituent (F strain[4]). In order to obtain a better assessment of the reactivity and kinetics of the 2-isopropyl-1-adamantyl system the less reactive heptafluorobutyrate ester (**8c**) was prepared and its solvolysis examined.[5] Solvolysis of the 2-ethyl-1-adamantyl esters in 80E gave a OPms/OHFB leaving group ratio of 10^5. Table IV presents the rate constants and Grunwald-Winstein *m*-values found for **8c**, **5c**, and two other tertiary heptafluorobutyrates, 2,2-dimethyl-1-adamantyl OHFB and *tert*-butyl OHFB. The *m*-value for **8c** is similar in magnitude to that for the other 1-adamantyl esters and does not suggest any unusual mechanistic complications. The *m*-value for *tert*-Butyl OHFB is considerably lower and indicates the relative effects of ethanol and water in solvating the smaller transition state. The solvolysis of **8c** gave strictly first-order kinetics; the rate constants showed the expected steric acceleration relative to the 2-ethyl and 2,2-dimethyl analogs with the result that **8c** reacts at about the same rate as *tert*-butyl OHFB. The contribution of strain to the acceleration of **8c** over 2-ethyl-1-admantyl OHFB (**5c**) is estimated from the changes in strain energy (ΔSE, carbonium ion minus alcohol) calculated using PCMODEL.[6] The results suggest that for **8c** ΔSE is 4.00 kcal/mole but for **5c** ΔSE was 6.83 kcal/mole. The lower ΔSE for **8a** is shown by the calculations to be due to a larger increase in strain energy for the initial state (3.71 kcal/mole) than for the carbonium ion (0.89 kcal/mole) upon γ-methyl substitution. The predicted relative rate, then, is 118 which is in fair agreement with the relative rate (72) calculated from the 60E data reported in Table IV.

Reactivity of the 3-Protoadamantyl Esters. As indicated above, it is likely that 3-protoadamantyl pemsylate (**10**) is produced along with **8** by internal return from a tight ion pair produced by rearrangement of **6**. If this is so there are two likely alternative reactivities for **10** which can account for the observed first-order kinetics found for **6**. These two possible alternatives are (1) that **10** solvolyzes faster than **6** by a factor of ~1000 or (2) that **10** solvolyzes more slowly by a factor of 100 or more. Molecular mechanics calculations using PCMODEL indicate that 3-protoadamantyl bromide should solvolyze near the rate of 1-adamantyl bromide[7] and that the same steric acceleration due to the relief of F strain should be operative in the solvolysis of **10**. In fact **10** is estimated to react only 2.6 times more slowly than **8**. The second alternative can be ruled out experimentally since we found that the parameters calculated to fit the solvolytic kinetics give a value for acid concentration at the end of the reaction which is actually a few percent greater than that predicted from the weights of the reactant and solvent for two conductometric experiments with **6** in 95E. If an *unreactive* sulfonate was produced, the calculated values of acid concentration at infinite time would be too low. The slightly high infinity values were in the range expected from experimental error. This result is, of course, consistent with the molecular mechanics calculations which indicate that **8** and **10** react at approximately the same rate.

TABLE V

Solvolysis Rates of Pemsylate Esters, 25 °C

compd	solvents	$k/10^{-5}$ s^{-1}	k/k(**6**)
1-(3-noradamantyl)ethyl pemsylate (**2**-OPms)	95E	3.214	2.183
	90E	6.818	2.438
	80E	19.48	2.800
1-(3-noradamantyl)propyl pemsylate (**3**-OPms)	95E	7.255	4.929
	90E	14.448	5.167
	80E	39.97	5.457
1-(3-noradamantyl)-2-methylpropyl pemsylate (**6**)	95E	1.472	1.000
	90E	2.796	1.000
	80E	6.958	1.000
	70E	14.19	1.000
	60E	27.74	1.000
1-(3-noradamantyl)-2,2-dimethylpropyl pemsylate (**7**)	95E	1.214	0.8247
	90E	2.305	0.8244
	80E	5.869	0.8435
	70E	12.30	0.8668
	60E	25.28	0.9113
1-(1-adamantyl)-2-methylpropyl pemsylate	80E	0.1217	0.01745
	70E	0.2620	0.01846
	60E	0.5519	0.01990
1-(1-adamantyl)-2,2-dimethylpropyl pemsylate	95E	0.1955	0.1328
	90E	0.3803	0.1360
	80E	1.0247	0.1473
	70E	2.235	0.1575
	60E	4.679	0.1687
2,2-dimethyl-3-pentyl pemsylate	80E	0.0583	0.00838
	60E	0.3152	0.01136

[a] Rate constants determined conductometrically.

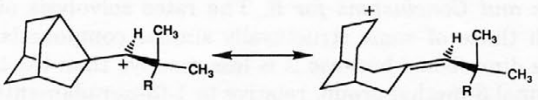
Kinetic Results and Conclusions for 6. The rates solvolysis of **6** are reported in Table V along with those of some structurally similar compounds. Anchimeric assistance appears to be diminished because it is less reactive than the lower homologs, **2b** and **3b**. The additional β-methyl group, relative to 1-(3-noradamantyl)propyl pemsylate (**3b**), is expected to accelerate the rate by a factor of at least 2 if the mechanism is the same and if steric effects such as B-strain are not significant. Because **6** solvolyzes ~5 times more slowly than **3b**, anchimeric assistance is apparently decreased relative to **3** by a factor of ~10. On the other hand, **6** is still accelerated, by a factor of 57 in 80E, relative to 1-(1-adamantyl)-2-methylpropyl pemsylate, a close structural relative with similar inductive effects which has much less strain in the tricyclic ring. As much as 50% of this acceleration could be due to the elimination of all internal return in solvolysis of **6** by rapid Wagner-Meerwein rearrangement in the tight ion-pair since it is known that internal return slows the solvolysis of the 1-(1-adamantyl) analogs;[1,8] however, MMX model calculations[9] of strain effects suggest that ionization of **6** without participation would be 4.2 times slower than 1-(1-adamantyl)-2-methylpropyl pemsylate. Thus, it appears that anchimeric assistance, assuming the absence of internal return, causes the solvolysis of **6** to be accelerated by a factor of about 240 (4.2/0.0175). In comparison with the participating lower homolog **3**, one expects that the additional methyl group would cause **6**, in the absence of steric effects, to react two times faster than **3** or ten times faster than observed. This reduction in rate could be the result of lower transition state σ-bonding between γ- and α-carbons associated with steric hindrance around the isopropyl group.

If the mechanism of solvolysis of **6** is similar to that proposed for **2** and **3** with acceleration caused by participation and rearrangement to the less strained adamantyl cation, the concurrent formation of protoadamantyl substitution and unrearranged alkene products presents a problem. How can the formation of these products, which do not have lower strain energies than the reactant, be competitive? If the reaction is strongly accelerated due to the direct formation of the rearranged 2-isopropyl-1-adamantyl cation how are the products which do not have this ring system formed? There are several possible explanations, including the following:

1. Perhaps the expected accelerations estimated above are too large and the formation of an unrearranged cation from **6** *can* occur, in a conformation having one of the C–C bonds of the six-membered ring anti-periplanar to the leaving group, at a competitive albeit slower rate. This would be more likely if the strain of the noradamantyl ring system causes sufficient bending of the bonds in the *six-membered ring* to enhance hyperconjugation which would accelerate the formation of the unrearranged cation from **6**.

2. Perhaps the reaction proceeds by participation of the most strained bond to form a bridged ion which, under subsequent solvent attack, can give the various products. The bridged intermediate can be represented by the resonance structures **11a** and **11b** (R = H). Such an intermediate might allow rotation of the exocyclic C–C bond followed by a 1,2-shift to form the 3-protoadamantyl cation or elimination or migration of a β proton. 3-Protoadamantyl substitution products are also formed in solvolysis of **2** and **3**, although in considerably smaller amounts (2–3%). Since the production of the minor products is inversely proportional to the change in the reaction rates in the series, a simple explanation involving independent competitive pathway, such as 1 above, looks attractive.

We tested for internal return by allowing **6**, labeled with 80% ether ^{18}O, to react in 95E for about one half-life. The partially solvolyzed ester was recovered and the α-



11a 11b

^{13}C resonances in the 125-MHz ^{13}C spectrum indicated that no scrambling occurred.[10] This is consistent with a mechanism in which ionization to a tight ion pair is assisted by hyperconjugation of the bent bond of the noradamantyl ring system and is followed by rapid rearrangement which allows no return to covalent substrate.

TABLE VI

Deuterium Isotope Effects in Solvolysis[a]

Compound	Solvent	$k_H/k_{\alpha\text{-d}}$	$k_H/k_{\beta\text{-d}}$
1-(3-noradamantyl)-2-methylpropyl pemsylate (**6**)	95E	1.192	1.065
	90E	1.188	
	80E	1.189	1.064
1-(3-noradamantyl(-2,2-dimethyl-propyl pemsylate (**7**)	95E	1.191	
	90E	1.187	
	80E	1.191	
	70E	1.193	

[a] The rate constants for each H and D compound are the averages of 3 to 9 determinations. Errors are ±0.001–0.002.

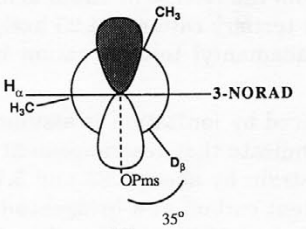
The α-d_1 and β-d_1 kinetic isotope effects found for **6** are reported in Table VI. These isotope effects are consistent with the mechanism suggested by the relative rate and product data. The α-d_1 effects are 1.7% larger than those for 1-(3-noradamantyl)propyl pemsylate (**3b**), which in turn are larger than those expected for simple ionization (15–16%) but smaller than those expected for rate-determining separation of the ion pairs (22–23%).[8] We suggest that these larger α-d effects reflect larger degrees of π- and smaller degrees of σ-bonding from the γ-carbon to the α-carbon in the transition state as illustrated in resonance contributing form **11b**; α-d effects are reduced by sigma but not by pi bonding. The larger steric influence of the isopropyl group could act to stretch the C_α–C_γ partial bond in the transition state. The β-d_1 effect is only eight-tenths of a percent lower than the square root of the β-d_2 effect (1.152) found for **3b**. The Sunko, Szele, and Hehre equation,[11]

$$\log k(\mathrm{H/D})_\theta = \frac{2}{3}\cos^2(\theta)\,[\log k(\mathrm{CH_3/CD_3}) - 3\log 0.999] + \log 0.999$$

shows that the experimental β-d_1 effect of 1.065 is consistent with a dihedral angle of 35° and an inductive effect of 0.990; the transition state conformation according to this model is represented by structure **12**.

The m-values for solvolysis of **6** and structurally similar reactants are shown in Table VII. Just as **3b** is less sensitive to ionizing power than **2b**, **6** is also less sensitive than **3b**. This is consistent with the mechanism for **6** being not much different since the m-value might be expected to increase if a major change in mechanism occurred.

The difference between the *m*-values for **6** and 1-(1-adamantyl)-2-methylpropyl pemsylate over the same range of solvents is only 0.06 but the latter pemsylate has α-d_1 kie values of 1.23±0.01, 1.22±0.01, 1.211±0.003 in 70E, 60E, and 97T respectively, indicating that it has a larger degree of ion separation in the transition state as expected for a reaction which involves internal return.[8]



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MMX calculations were used, along with solvolysis rates, to estimate the relative energies of all the important transition structures and reactants in the solvolysis of 1-(3-noradamantyl)-2-methylpropyl pemsylate in 95E. For simplicity, alcohols were used as models for the initial states. The strain energies of the initial state for **6** were included in the calculation as the average energy over all nine possible rotamers. The relative energies found are: 2-isopropyl-1-adamantol, 0 (reference); 1-(3-noradamantyl)-2-methylpropanol 9.81; *endo*-4-isopropyl-3-protoadamantanol, 8.48; *exo*-4-isopropyl-3-protoadamantanol, 12.09; transition state (TS) for ionization of the 2-isopropyl-1-adamantyl ester 19.96; TS for ionization of the 1-(3-noradamantyl)-2-methylpropyl ester, 33.87

TABLE VII

*Winstein-Grunwald m-Values for 1-(3-Noradamantyl)-2-methylpropyl Pemsylate (**6**), 1-(3-Noradamantyl)-2,2-dimethylpropyl Pemsylate (**7**) and Several Analogues.*[a,b]

compd	*m*-value	solvents
1-(3-noradamantyl)ethyl pemsylate, **2b**	0.674±0.002	80E, 90E, 95E
1-(3-noradamantyl)ethyl tosylate, **2a**	0.731±0.003	80E, 90E, 95E
1-(3-noradamantyl)propyl pemsylate, **3b**	0.618±0.002	80E, 90E, 95E
1-(3-noradamantyl)propyl tosylate, **3a**	0.683±0.003	80E, 90E, 95E
1-(3-noradamantyl)-2-methylpropyl pemsylate, **6**	0.581±0.003	80E, 90E, 95E
	0.674±0.004	60E, 70E, 80E
1-(3-noradamantyl)-2,2-dimethylpropyl pemsylate, **7**	0.590±0.006	80E, 90E, 95E
	0.711±0.009	60E, 70E, 80E
pinacolyl tosylate	0.936±0.006	50E, 60E, 70E
2,2-dimethyl-3-pentyl pemsylate	0.827±0.002	50E, 60E, 80E
2,2-dimethyl-3-pentyl tosylate	0.914±0.004	50E, 60E, 70E, 80E
1-(1-adamantyl)-2-methylpropyl pemsylate	0.738±0.008	60E, 70E, 80E
1-(1-adamantyl)-2,2-dimethylpropyl pemsylate	0.621±0.008	80E, 90E, 95E
	0.740±0.006	60E, 70E, 80E
1-(1-adamantyl)-2,2-dimethylpropyl tosylate	0.690±0.005	80E, 90E, 95E
	0.821±0.011	60E, 70E, 80E

[a] Slopes (*m*-values) determined by linear least-squares calculation on data points of log *k* for compound and log *k* for 2-adamantyl tosylate in the solvents shwon. All rate constants, including those for 2-adamantyl tosylate, were determined conductometrically in this laboratory.[16]

kcal/mole; TS for ionization of *endo*-4-isopropyl-3-protoadamantyl pemsylate, 28.92; TS for ionization of *exo*-4-isopropyl-3-protoadamantyl pemsylate, 31.13; the last two values were estimated with the assumption that the energies were different from that of the TS for ionization of the 2-isopropyladamantyl ester only by the differences in the strain energies of the cations. Thus we find that the TS for formation of the 1-adamantyl cation is 13.91 kcal/mole lower in energy than the TS formed from **6**. The contribution to this energy from the release of strain is 5.42. The TS for the formation of the *endo*-3-protoadamantyl tertiary cation is 4.95 kcal/mole lower, and that for the formation of the *exo*-3-protoadamantyl tertiary cation is 2.74 kcal/mole lower, than the TS for ionization of **6**.

If the intermediate produced by ionization is assumed to have a structure like **11** (R = H), MMX calculations indicate that rearrangement to the *endo* and *exo* 3-protoadamantyl cations *increases* strain by about 3.63 and 5.75 kcal/mole respectively, because of placement of a trivalent carbon at a bridgehead position.[12] When one carries out the same analysis with the unsubstituted homolog, 1-(3-noradamantyl)ethyl pemsylate, the rearrangement to the 1-adamantyl cation releases 11.5 kcal/mole while the rearrangement to the 3-protoadamantyl cation releases only 1.96 kcal/mole. Thus, as expected, the estimated transition state energies indicate that the products of solvolysis of **2**, **3** and **6**, should be 1-adamantyl substitution not 3-protoadamantyl substitution. The lower yield of 1-adamantyl substitution products from **6** than from **2** and **3** is probably caused a reduction in the C_α–C_γ σ-bonding, which is a requirement for the rearrangement of **6**, owing to the steric influence of the β-methyl groups of the isopropyl substituent; *i.e.* the rearrangements are governed by kinetic factors not directly related to product stability. This steric effect is the same one mentioned above to account for the relative rates and the α-d_1 and β-d_1 kinetic isotope effects; it is analogous to the steric hindrance of β-methyl substituents to S_N2 attack by external nucleophiles. In the bridged-ion explanation, the solvolysis products of **6** would be determined by how quickly the intermediate **11** (R = H) could rearrange through an early transition state to the 1-adamantyl cation, eliminate to the alkene, or rotate the bond to allow rearrangement to the 3-protoadamantyl cation. Since these three transition states are still unrearranged cations they will not differ greatly in energy and so the stability of the products would not control the reaction. This explanation for the observed products and their yields is consistent with the formation of intermediate **11** (R = H); since the rotamer of **11** (R = H) which is expected to rearrange to the *endo* 3-protoadamantyl cation is found to be 1.43 kcal/mole less strained than the rotamer which rearranges to the *exo* epimer one expects the *endo* protoadamantyl epimer to be formed in larger yield than the *exo*.

Conclusions from the Study of **6**. The conclusions from this study are: (1) substitution of two β-methyl groups in the 1-(3-noradamantyl)ethyl ester introduces strain in the solvolytic transition state which reduces C_α-C_γ bonding and slows the rate; (2) the α-d_1 effect is larger than that for the 1-(3-noradamantyl)propyl ester (by 1.7%) because of the reduced TS σ-bonding and a concomitant increase in π-type bonding to the reaction center; (3) ionization may proceed either, a) to a single bridged secondary carbonium ion intermediate, which gives all products, or b) to a rearranged 1-adamantyl cation and at least one other secondary ion which produces some unrearranged and some protoadamantyl products.

Product Studies. 1-(3-Noradamantyl)-2,2-dimethylpropyl Pemsylate (**7**). The next higher homolog of the 1-(3-noradamantyl)ethyl sulfonate ester series, 1-(3-noradaman-

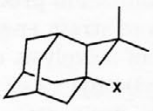
TABLE VIII

Yields of Products from Solvolysis of 1-(3-Noradamantyl)-2,2-dimethylpropyl-2-d Pemsylate (7-α-d)[a]

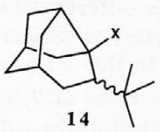
product	solvent			
	100E[b]	95E[c]	90E[c]	97T[c]
13a-2-*d*	0.0	11.0	29.0	28.0
13b-4-*d*	67.1	61.0	45.0	52.0
14a-2-*d* + **14b**-2-*d*	28.3	23.0	21.0	15.0
15-3-*d*	4.6	5.0	5.0	5.0

[a] In %, errors estimated at ±1–2%. Analyses were done on spent reaction mixtures, originally ~0.1M in reactant and buffered with a slight excess of 2,6-lutidine.
[b] Analyzed by areas of peaks in HPLC chromatogram.
[c] Determined from the relative peak heights of characteristic resonances in the ^2H NMR spectra of spent solvolysis reaction mixtures.

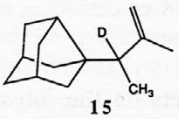
tyl)-2,2-dimethylpropyl pemsylate (**7**) also solvolyzes by strictly first-order kinetics. The ethyl ethers, **13b** and **14b**, recovered from solvolysis of **7**-α-*d* in ethanol and purified by HPLC were identified from their ^1H and ^{13}C NMR spectra. Their 55-MHz ^2H NMR chemical shifts observed in separate solutions in 95E enabled the unambiguous assignment of peaks in the ^2H NMR spectra of the spent reaction mixtures from solvolysis of **7**-α-*d* in 95E, 90E, and 97T. Product yields from analysis of these spectra are presented in Table VIII. The alkene product **15** is suggested in these spectra since there is a peak with a relative area of ~5% in each solvent at a position characteristic of an allyl-d_1 resonance. The products are ~75% 1-adamantyl **13** and ~20% 3-protoadamantyl **14** alcohols and ethers, ~ 5% alkene which probably results from β-methyl group migration; the similarity of products produced by **7** and **6** suggests that they react *via* similar pathways.



13



14



15

13 & **14**, X = OPms, pentamethylbenzenesulfonate;
13a & **14a** X = OH; **13b** & **14b**, X = OEt or OTFE

Table VIII shows that the yield of the minor alkene product is the same in all solvents used. However, the yield of 3-protoadamantyl substitution products **14** is smaller in 97T (15%) than in the ethanol-water solvents; 29% in 100E; 23% in 95E; and 21% in 90E. Since it is generally found that trifluoroethanol-water solvents, relative to ethanol-water solvents, promote participation over non-participating reactions[8] this result favors the idea that the adamantyl products are produced *via* participation and the protoadamantyl ones are not; that is, that the expansion of the five membered ring accompanies ionization, but the expansion of the six membered ring occurs after ionization.

Kinetic Results and Conclusions for **7**. Table V gives the relative rates for **7** and a number of analogs. It is clear that participation in the solvolysis of **7** is reduced from that in solvolysis of **2** since the solvolysis rate of **7** is slower even though the additional β-methyl groups would exert an inductive effect to accelerate the rate. It would appear that the best way to estimate the acceleration due to participation in the noradamantyl carbinyl derivatives **2b** and **7** is to compare them in each case with the closely related but much less strained adamantyl carbinyl analogs. These comparisons are especially appropriate since (1) the inductive effects in each comparison should be the same and (2) the 1-(1-adamantyl)ethyl brosylate solvolyses have been shown in an earlier study to proceed without anchimeric assistance and the fractions of internal return have been estimated.[8] Thus the brosylate ester analog of **2** has been found to solvolyze in 95E 2141 times faster than 1-(1-adamantyl)ethyl brosylate;[13] since the latter ester ionizes about 2.83 (80E value) times faster than it solvolyzes[8] but has three equivalent reactive conformations while **2b** has only one the corrected acceleration factor is about 2,270. MMX calculations of the differential effects of the release of steric strain on ionization of the two esters increases the estimated acceleration factor to ~ 10,000. On the other hand, Table V shows that **7** solvolyzes only six times faster than the nonparticipating analog, 1-(1-adamantyl)-2,2-dimethylpropyl pemsylate.[14] The same corrections used above for conformational degeneracy and internal return gives a corrected ratio of ionization rates of 6.58, while correction for differential steric effects on ionization, from MMX calculations, gives a final corrected ratio of ~100. Thus participation is estimated to accelerate the solvolysis of **2b** by a factor of $\sim 10^4$ and **7** by $\sim 10^2$. The *tert*-butyl group of **7** apparently reduces participation by interfering with the approach of C_γ to C_α causing a reduction in C_γ–C_α σ-bonding in the transition state and a reduction of anchimeric acceleration. This result clearly indicates that the structural changes on activation of **2b** are like those expected from participation. The fact that the yield of protoadamantyl products is increased indicates that the *tert*-butyl group causes less of this kind of strain in the transition state involved in their formation than it does in the transition state for the formation of adamantyl products and lends support to the idea that there may be at least two ionization processes. It should be noted that MMX calculations of the differential effects of strain energy release provide a good estimate (285x) of the observed acceleration of solvolysis of 1-(1-adamantyl)-2,2-dimethylpropyl ester relative to the 1(1-adamantyl)ethyl ester (271x).[15]

The α-d_1 effects on the solvolysis rates of **7**, given in Table VI, are 1.190 ± 0.002 in 80E, 90E, and 95E, essentially identical to the values for **6**-α-*d* even though the yield of 3-protoadamantyl substitution from **7** is ~10% greater. This hints that 3-protoadamantyl substitution and 1-adamantyl substitution may share the same rate-determining step; however, if there were two different rate-determining steps, the change in product yields would be expected to change the isotope effects by only a few tenths of a percent at most.

Table VII shows that there are only small differences between the Grunwald-Winstein *m*-values for **7** and those for its close relatives; for the same series of solvents the *m*-value for **6** is only 0.04 larger than the one for **7** which is only 0.03 larger than the one for 1-(1-adamantyl)-2,2-dimethylpropyl pemsylate even though participation should be involved in the solvolysis of the first two compounds and not in the last one. The trend, even though it may not be outside of experimental error, is consistent with decreasing degrees of participation in the order cited.

The relative energies of reactants and transitions states for the solvolysis of 1-(3-noradamantyl)-2,2-methylpropyl pemsylate in 95E at 25 °C estimated as described above for **6** are: 2-*tert*-butyl-1-adamantanol, 0 (reference); 1-(3-noradamantyl)-2,2-dimethylpropanol (average over all three conformers), 6.3; transition state (TS) for ionization of the 2-*tert*-butyl-1-adamantyl pemsylate 21.7; TS for ionization of 1-(3-noradamantyl)-2,2-dimethylpropyl pemsylate, 29.8; TS for formation of *endo*-4-*tert*-butyl-3-protoadamantyl cation, 27.3; TS for formation of *exo*-4-*tert*-butyl-3-protoadamantyl cation 30.0; the last two values were estimated with the assumption that the energies were different from that of the TS for ionization of the 2-*tert*-butyladamantyl ester only by the differences in the strain energies of the cations. Thus we find that energy of the TS for formation of the tertiary 1-adamantyl cations is ~8.0 kcal/mol lower than the energy of the TS for formation of the 1-(3-noradamantyl)-2,2-dimethylpropyl cation. The portion of this energy that is due to the release of steric strain is ~ 3.0 kcal/mol, assuming that the TS for ionization of **7** is similar to **11** (R =CH_3). The TS for the formation of endo 3-protoadamantyl tertiary cation is 2.5 kcal/mole lower than the TS for formation of 1-(3-noradamantyl)-2,2-dimethylpropyl cation. The TS for the formation of *exo*-3-protoadamantyl tertiary cation is 0.23 kcal/mole higher than the TS formed by ionization of **7**. If the TS for ionization of **7** is similar to **11** (R = CH_3), MMX calculations estimate that rearrangement to the *endo* and *exo* 4-*tert*-butyl-3-protoadamantyl cations actually increases strain by about 2.86 and 5.6 kcal/mole, respectively, because of placement of a trivalent carbon at a bridgehead position. These energy differences suggest that the transition states for product formation can have progressed only a little way towards product because product stability obviously strongly favors the exclusive formation of the rearranged 1-adamantyl cation over the 3-protoadamantyl cation.

Conclusions from the Study of **7**. The main conclusions reached from the study of the solvolysis of **7** are: (1) the similarity of α-d_1 isotope effects on solvolysis of **6** and **7** suggests that very similar mechanisms involving C–C σ-participation are operative in both cases, (2) the slower solvolysis rates and larger yields of protoadamantyl substitution products for **7** relative to **6** both indicate that steric hindrance from β-methyl groups reduces participation by the CC bond of the five-membered rings and makes ionization in an alternative conformation without participation slightly more competitive.

EXPERIMENTAL

Boiling points are uncorrected. Melting points are corrected. Combustion analysis was performed by Galbraith Laboratories, Inc. NMR spectra were recorded on Varian Associates T-60, EM390, and XL-300; Nicolet 360; and Bruker 500 spectrometers. Chemical shifts are recorded in parts per million (δ) from tetramethylsilane (TMS) for ^1H spectra, from $CDCl_3$ (δ 77.1) for ^{13}C spectra, and from external $CDCl_3$ in chloroform solvent for ^2H spectra. Infrared spectra were recorded on a Perkin-Elmer 298 spectrometer. Gravity column chromatography was conducted with Kieselgel 60 (70–230 mesh) (E. Merck No. 7734). High-performance liquid chromatography separations were performed on a Rainin HP Rabbit instrument equipped with a semi-preparative 10mm ID × 25 cm L or preparative 21.4 mm ID × 25 cm L prepacked silica (8 μm) gel, stainless steel column and connected to a KNAUER Differential-Refractometer and a strip-chart recorder. This experimental is a shortened version of the one in reference 16.

Product Determination. The procedure utilizing ^2H NMR has been described in reference 17.

Conductance Kinetic Procedure. This is described in references 18 and 19.

Solvent Preparation. The procedures employed can be found through the citations given in reference 8.

3-Noradamantanecarboxaldehyde was prepared according to a general procedure[20] with a modification obtained from Coope.[21] In a 2000-mL round-bottom flask fitted with a reflux condenser, pyridinium chlorochromate (PCC) (58.83 g, 0.2730 mol) was suspended in anhydrous dichloromethane (364 mL). A volume of celite equal to the volume of PCC used was added. 3-Noradamantylmethanol (27.70 g, 0.1820 mol) which was made in the manner reported in Ref. 3 was washed in with some dry dichloromethane. After 2 h, dry diethyl ether (364 mL) was added and the supernatant liquid was decanted. The insoluble residue was washed with dry diethyl ether (3 × 88 mL). The combined organic solution was passed through a short pad of Fluorisil several times to remove the color. The solvent was removed by rotary evaporation under reduced pressure leaving a greenish oil which weighted 26.4 g (96.6% yield). The aldehyde was used in the next step without any attempt at further purification.

1-(3-Noradamantyl)-2-methylpropanol. The aldehyde of the previous step (26.4 g) was taken up in dry diethyl ether (~ 300 mL). To a 50% molar excess of isopropylmagnesium chloride (150 mL, 2.0 M *i*-PrMgCl/diethyl ether) purchased from Aldrich Chemical Co., the aldehyde solution was added dropwise. After addition the reaction was left stirring for 12 h and then the magnesium salt was decomposed with 2N aq H_2SO_4 at 0 °C. The organic solution was dried over $MgSO_4$; the drying agent was removed by suction filtration through a bed consisting of a layer of celite below a layer of fluorisil. Evaporation of the solvent left the alcohol in 77% yield (26.4 g) from the aldehyde. This crude product which contains 3-noradamantylmethanol was rapidly purified by column chromatography on Kieselgel 60 (70-230 mesh) with 95% hexane-5% ethyl acetate as the mobile phase. Further purification was accomplished by high-performance liquid chromatography (HPLC) on a prepacked silica gel column with 95% hexane-5% ethyl acetate as mobile phase. Mp 58–59 °C. Sublimated material was submitted for combustion analysis. *Anal.* Calc for $C_{13}H_{22}O$: C 80.35, H 11.41; found: C 80.65, H 11.16.

1-(3-Noradamantyl)-2-methylpropanone was first prepared by oxidation of the alcohol by a method obtained from Coope[21] who cites a general published procedure.[22] 1-(3-Noradamantyl)-2-methylpropanol (7.82 g, 0.04026 mol) was dissolved in CH_2Cl_2 (118 mL) and diethyl ether (32 mL) in a 1000-mL three-necked round-bottom flask. Celite (8.0 g) was added and the mixture was magnetically stirred at 0 °C. Chromium trioxide (8.05 g, 0.0805 mol) was added in several portions. After 1 h, celite (8 g) and diethyl ether (128 mL) were added and the mixture was stirred for an additional 20 min. The mixture was filtered through silica gel and Fluorisil (1:1) and then the solvent was evaporated under reduced pressure to obtain the crude, clear yellow, liquid ketone in 70.4% yield (5.45 g). Simple distillation (0.2 torr, 55–60 °C) gave a clear liquid (4.81 g, 62%). IR (film): $\nu_{C=O}$ 1698 cm^{-1}. The ketone was also made by oxidation of the alcohol with pyridinium chlorochromate in the manner reported above for the synthesis of 3-noradamantanecarboxaldehyde. The latter method of oxidation is better because incomplete oxidation was not a problem. The product was purified by HPLC on a 10mm ID × 25cm L prepacked silica gel column with 95% hexane-5% ethyl acetate as mobile phase. 300-MHz ^1H NMR ($CDCl_3$): δ 1.074 (d, 6H), 1.55–1.85 (m, 9H), 2.02–2.1 (m, 2H), 2.32 (m, 2H), 2.62 (m, 1H), 2.95 (septet, 1H), 75-MHz ^{13}C NMR ($CDCl_3$): δ 218.045, 61.367, 45.881, 43.712, 42.184, 37.250, 36.042, 34.849, 19.712.

1-(3-Noradamantyl)-2-methylpropanol-1-d_1. 1-(3-Noradamantyl)-2-methylpropanone (1.5 g, 0.00780 mol) was reduced in the usual manner with LAH (0.2 g) in dry diethyl ether (200 mL). The reaction mixture was refluxed for 24 h before isolation of the alcohol. The product was a white solid obtained in nearly 100% yield (1.61 g). The alcohol was purified by HPLC on a 10mm ID × 25cm L prepacked silica gel column with 95% hexane-5% ethyl acetate as mobile phase. Mp 57–62 °C. 300-MHz ^1H NMR ($CDCl_3$): δ 0.93 (d, 3H), 1.015 (d, 3H), 1.356 (s, 1H), 1.5–1.85 (m, 10H), 1.870 (septet, 1H), 2.25 (m, 3H).

1-(3-Noradamantyl)-2-methylpropyl-1-d_1 Pemsylate. The modified Kochi-Hammond procedure was used. The α-d_1 alcohol (1.21 g, 0.006197 mol) from the previous synthesis was dissolved in anhydrous ether (7 mL) and the solution was placed in a 250 mL four-necked round-bottom bantamware flask under argon. One neck was equipped with a serum stopper and the others with glass stoppers. At 0 °C methyllithium (4.43 mL, 1.4 M CH_3Li/diethyl ether) was added via syringe. The reaction mixture was stirred for 30 min at room temperature before *N,N'*-dimethylpropylene urea (4 mL DMPU) was added via syringe. At 0°C pemsyl chloride (1.53 g) in diethyl

ether (15 mL) was added via syringe. The reaction mixture was warmed to room temperature and left stirring for 2 h before being rinsed with diethyl ether into a separatory funnel containing diethyl ether (300 mL) and H_2O (70 mL). After separation the organic layer was extracted in succession with 2N aq H_2SO_4 (70 mL), saturated aq $NaHCO_3$ (70 mL), and H_2O (70 mL). The organic solution was dried over $MgSO_4$ and decolorized with carbon; the solid was removed by suction filtration through a fritted funnel containing a bed of celite. Evaporation of the diethyl ether left a white solid in 86% yield (2.17 g). The solid was dissolved in a boiling mixture of hexane (70 mL) and ethyl acetate (5 mL) and recrystallized at below 0 °C. The white crystals so obtained were rinsed with hexane and dried under reduced pressure to afford the pemsylate in 59.8% yield (1.5 g). Additional pemsylate was made from alcohol not purified by HPLC to provide material for product studies. Mp 114–118 °C. 300-MHz ^1H NMR ($CDCl_3$): δ 0.913 (d, 3H), 0.945 (d, 3H), 1.3–1.71 (m, 9H), 1.82 (m, 1H) 2.2 (septet, 1H), 2.1–2.3 (m, 3H), 2.232 (s, 6H), 2.267 (s, 3H), 2.624 (s, 6H). 75-MHz ^{13}C NMR ($CDCl_3$): δ 139.337, 136.426, 134.489, 133.489, 93.246 (triplet), 53.541, 47.052, 45.167, 43.372, 43.051, 42.923, 37.472, 37.331, 35.497, 30.432, 21.827, 18.941, 17.736, 17.338, 16.979.

1-(3-Noradamantyl)-2-methylpropyl Pemsylate. A modified Kochi-Hammond procedure was used. In the same manner described for the synthesis of 1-(3-noradamantyl)-2-methylpropyl-1-*d* pemsylate, the alcohol (0.65 g, 0.003346 mol) was converted to the pemsylate in 44% yield (0.6 g) after isolation and recrystallization from hexane. There was a first-crop of 0.38 g and a second-crop of 0.22 g which were put into the same vial. The alcohol had been purified by HPLC. The pemsylate was also made from alcohol not HPLC purified to provide material for non-kinetic purposes but kinetics done with it are indistinguishable from the kinetics done with pemsylate made from HPLC purified alcohol. Mp 118–123 °C. 300-MHz ^1H NMR ($CDCl_3$): δ 0.989 (d, 3H), 0.961 (d, 3H), 1.3–1.75 (m, 9H), 1.83 (m, 1H), 2.2 (m, 1H), 2.1–2.3 (m, 3H), 2.246 (s, 6H), 2.283 (s, 3H), 2.637 (s, 6H), 4.91 (d, 1H, J = 2.1 Hz). 75-MHz ^{13}C NMR ($CDCl_3$): δ 139.5, 136.5, 134.5, 133.5, 93.7, 53.541, 46.975, 45.064, 43.243, 42.948, 42.781, 37.357, 37.215, 35.382, 30.419, 21.724, 18.800, 17.607, 17.235, 16.876. In each spectrum there are a number of small resonance peaks which are not visible in the spectra of the deuterated isotopomer. The impurity or impurities produced no effect on the conductometric error plots from first-order fit of the data.

Isolation and Identification of the Solvolysis Products of 1-(3-Noradamantyl)-2-methylpropyl-1-d_1 Pemsylate in 100% Ethanol. 1-(3-Noradamantyl)-2-methylpropyl-1-d_1 pemsylate (1.48 g, 0.003649 mol) with 5.8% d_0 impurity was allowed to react for 10 half-lives in 100 ml of conductivity ethanol containing 1.1 equivalents of lutidine. The reaction temperature was room temperature and the reaction solution was magnetically stirred. Most ethanol was removed by rotary evaporation with application of heat from a hot water bath. The solid residue was dissolved in diethyl ether which was then decanted into a separatory funnel. The organic solution was extracted in succession with 2N aq H_2SO_4, saturated aq $NaHCO_3$, and water. The organic extract was dried over $MgSO_4$; the drying agent was removed by suction filtration. Evaporation of the diethyl ether by rotary evaporation under reduced pressure left a clear liquid product in 99% yield (0.8 g). This product mixture was purified by HPLC on a prepacked silica gel column (10mm ID) with 95% hexane-5% ethyl acetate as the mobile phase. The two major products eluted together and accounted for 96% (0.67 g) of the total yield. Integration of the methyl groups of the isopropyl groups shows the 1-adamantyl isomer to compromise 94.4%. The other peaks in the chromatogram corresponded to compounds which eluted before and after latter two ethers and accounted for approximately 4% (30 mg) of the total yield. NMR data for *ethyl 2-isopropyl-1-adamantyl-3-d_1 ether:* 300-MHz ^1H NMR ($CDCl_3$): δ 0.9 (d, 3H), 1.158 (d, 3H), 1.139 (t, 3H), 1.34–1.43 (m, 1H), 1.55–1.84 (m, 8H), 1.86–2.15 (m, 5H), 3.42 (m, 2H). 75-MHz ^{13}C (decoupled) NMR ($CDCl_3$): δ 74.561, 54.401, 52.631 (s, β-carbon attached to *t*-butyl group of the d_0 impurity), 52.054 (triplet of β carbon attached to *t*-butyl group and to deuterium), 42.705, 38.537, 37.267, 36.972, 31.996, 31.432, 30.381, 29.932, 26.854, 24.327, 21.506, 15.658. 75-MHz ^{13}C (coupled) NMR ($CDCl_3$): δ 74.560 (singlet), 54.349 (triplet), 15.664 (quartet). 55.4-MHz ^2H NMR (95E): δ 1.95. NMR data for *ethyl 4-isopropyl-3-protoadamantyl-4-d_1 ether*: 300-MHz ^1H NMR ($CDCl_3$): δ 0.938 (d, 3H), 0.962 (d, 3H), 75-MHz ^{13}C (decoupled) NMR ($CDCl_3$): δ 86.500, 56.889, 40.653, 39.601, 38.832, 35.741, 33.279, 28.123, 27.931, 26.636, 22.417, 18.146, 15.927. 75-MHz ^{13}C

(coupled) NMR ($CDCl_3$): δ 86.50 (singlet), 56.889 (triplet), 16.2 (quartet). 55.4-MHz ^2H NMR (95E): δ 2.537. The 300-MHz ^1H spectrum of the products (2.4% of the total yield) which eluted just before the ethers which gave the largest peak in the chromatogram indicated mostly 1-(3-noradamantyl)-2-methylpropene-1-d_1 (73%), some ethyl 1-(3-noradamantyl)-2-methylpropyl-1-d_1 ether (9%), and some alkene product(s) (18%) which could not be positively identified. The 300-MHz ^1H spectrum of the product (1.1% of the total yield) which the chromatogram shows to elute just after the large peak indicated the epimer of the 3-protoadamantyl ether. 300-MHz ^1H NMR ($CDCl_3$) data for *1-(3-noradamantyl)-2-methylpropene-1-d_1*: δ 1.48–1.65 (m, 5H), 1.7 (s, 3H), 1.7 (s, 3H), 1.73–1.9 (m, 5H), 2.15–2.25 (m, 2H), 2.28 (t of t, 1H). 300-MHz ^1H NMR ($CDCl_3$) data for *ethyl 1-(3-noradamantyl)-2-methylpropyl-1-d_1 ether*: δ 0.94 (d, 3H), 1.01 (d, 3H), 1.18 (t, 3H), 3.52–3.74 (m, 2H). 300-MHz ^1H NMR ($CDCl_3$) data for the epimeric *ethyl 4-isopropyl-3-protoadamantyl-4-d_1 ether*: δ 0.881 (d, 3H), 1.12 (d, 3H), 1.135 (t, 3H), 1.3–1.4 (m, 1H), 1.5–2.23 (m, 14H), 3.33–3.52 (m, 2H).

Isolation and Identification of the Solvolysis Products of 1-(3-Noradamantyl)-2-methylpropyl-2-d_1 Pemsylate in 83% Aqueous Acetone. 1-(3-Noradamantyl)-2-methylpropyl-1-d_1 pemsylate (1.77 g, 0.004364 mol) was placed in a 500-mL round-bottom flask to which was added conductometric grade acetone (100 mL), lutidine (0.51 g, 1.1 equiv.), and distilled water (20 mL). The solution was refluxed for 2 days and 19 h. Most of the volatile material was removed by rotary evaporation under reduced pressure. The residue was dissolved in diethyl ether and then the solution was extracted in succession with 2N aq H_2SO_4, aq saturated $NaHCO_3$, and water. The organic extract was dried over $MgSO_4$ and the drying agent was removed by suction filtration. Evaporation of the solvent left a white solid (0.76 g, 89%). The solid mixture was purified by HPLC on a prepacked silica gel column (10 mm ID) with 95% hexane-5% ethyl acetate as the mobile phase. The compound with the lower retention time was also produced in greater yield (0.64 g, 93% yield). This product must be the adamantyl isomer, *2-isopropyl-1-adamantol-2-d_1*, because the α-^{13}C resonance is at position typical of 1-adamantyl alcohols. Mp 105–106 °C. 300-MHz ^1H NMR ($CDCl_3$): δ 0.872 (d, 3H), 1.146 (d, 3H), 1.232 (s, 1H), 1.3–1.5 (m, 2H), 1.5–1.76 (m 7H), 1.89 (septet, 1H), 1.96–2.12 (m, 4H), 75-MHz ^{13}C NMR ($CDCl_3$): δ 71.739, 55.824 (triplet), 48.924, 40.383, 38.536, 36.754, 32.368, 31.303, 30.932, 30.239, 26.905, 25.635, 21.518. 55.4-MHz ^2H NMR (95E): δ 1.791, (97T): δ 1.554. *4-Isopropyl-3-Protoadamantyl-4-d_1* was a minor product (0.0503 g, 7.3% of products) of the solvolysis of the pemsylate. Mp 87–89 °C. 300-MHz ^1H NMR ($CDCl_3$): δ 0.93 (d, 3H), 0.99 (d, 3H), 1.12–1.5 (m, 6H), 1.6–1.92 (m, 5H), 2.1 (septet, 1H), 2.0 (m,1H), 2.16–2.26 (m, 2H). 75-MHz ^{13}C NMR ($CDCl_3$): δ 82.730, 47.552, 44.346, 43.474 (triplet), 39.396, 38.601, 37.100, 33.253, 29.123, 28.636, 27.546, 22.942, 18.902. 55.4-MHz ^2H NMR (95E): δ 2.326, (97T): 2.093.

2-Isopropyl-1-Adamantyl-2-d_1 Pemsylate. A modified Kochi-Hammond procedure was used (see the procedure for the preparation of 1-(3-noradamantyl)-2-methylpropyl-1-d_1 pemsylate). 2-Isopropyl-1-adamantol-3-d_1 (0.59 g, 0.00302 mol), methyllithium (2.16 mL, 1.4 M CH_3Li/diethyl ether), DMPU (2 mL), and pemsyl chloride (0.75 g) in diethyl ether were used. Isolation of the product gave a greenish oil in 82% yield (1.0 g). A white solid (0.51 g) was isolated by crystallization from petroleum ether (bp 30–60 °C) in 42% yield at the temperature of a Dry Ice-acetone bath. Since the 300-MHz spectrum showed impurities to be present the compound was recrystallized at room temperature from hexane (30 mL). In this manner pure pemsylate was obtained which weighed 220 mg. Mp 140–150 °C. 300-MHz ^1H NMR ($CDCl_3$): δ 0.911 (d, 3H), 1.021 (d, 3H), 1.34–1.45 (m, 1H), 1.5–1.8 (m, 5H), 2.04 (septet. 1H), 2.1–2.55 (m, 7H), 2.235 (s, 6H), 2.272 (s, 3H), 2.595 (s, 6H), 75-MHz ^{13}C NMR ($CDCl_3$): δ 139.632, 137.272, 134.553, 134.104, 95.657, 54.785 (triplet), 44.808. 38.524, 38.011, 36.254, 33.522, 31.586, 31.175, 31.137, 27.123, 25.058, 21.480, 19.095,17.825,17.017.

2-Isopropyl-1-Adamantanol and 4-Isopropyl-3-Protoadamantanol. 1-(3-Noradamantyl)-2-methylpropyl pemsylate (4.38 g, 0.01083 mol) was mixed with acetone (170 mL), water (41 mL), and lutidine (1.3 g, 0.0121 mol) in a 500-mL round-bottom flask. The reaction solution was gently refluxed for three days. The product was isolated in the manner described in the 2-isopropyl-1-adamantanol-2-*d* preparation above to obtain a white solid product in 100% yield (2.17 g). The solid mixture was purified by HPLC (10mm ID) on a prepacked silica gel column with 90%

hexane-10% ethyl acetate as the mobile phase to obtain the adamantanol (1.64 g) and the protoadamantanol (0.16 g). Mp (Protodamantanol) 83–86 °C. Mp (Adamantanol) 104–106 °C.

2-Isopropyl-1-Adamantyl Heptafluorobutyrate (OHFB) was prepared in the manner of Farcasiu *et. al.*[6]. 2-Isopropyl-1-adamantanol (0.27 g, 0.00139 mol) was dissolved in pyridine (1 mL, dried by distillation from NaOH and stored over molecular sieves) and placed under argon in a 50-mL round-bottom flask equipped with a magnetic stirring bar and a rubber serum stopper. The flask was cooled to 0 °C. Heptafluorobutyryl chloride (HFBCl) (0.59 g, 0.00254 mol) in CH_2Cl_2 (1.8 mL, dried over molecular sieves) was added *via* a 10-mL syringe. An additional amount of CH_2Cl_2 (1 mL) was used to rinse the flask from which the HFBCl solution had been removed. After stirring for 19 min the flask was placed in a freezer for 24 h. The reaction mixture was poured into a separatory funnel containing diethyl ether (250 mL). The reaction flask was rinsed out with methylene chloride (25 mL). Next, the organic layer was extracted in succession with 25-mL portions of cold 2N aq H_2SO_4, cold aq saturated $NaHCO_3$, and cold water. The organic extract was dried over $MgSO_4$; the drying agent was removed by suction filtration. Evaporation of the solvent left a clear green liquid (0.4883 g, 90%). This compound was purified by gravity column chromatography on silica gel with hexane as the mobile phase. The solvent was removed and the compound was transferred to a small vial. The compound was then placed under partial vacuum (1 torr) for 2.5 h to leave a clear liquid in 45% yield (242 mg). The liquid was purified by HPLC with a prepacked silica gel column (10mm ID × 25 cm L) and with hexane as the mobile phase. After evaporation of most of the hexane any residual solvent was removed under low pressure (2 torr) for about 2 hr. IR (film): $\nu_{C=O}$ 1768 cm^{-1}. 300-MHz ^1H NMR ($CDCl_3$): δ 0.97 (d, 3H), 1.03 (d, 3H), 1.4–1.5 (m, 1H), 1.7–1.9 (m, 5H), 1.9–2.3 (m, 8H), 2.4–2.5 (m, 1H). 75-MHz ^{13}C NMR ($CDCl_3$): δ 156.749 (triplet), 100–122 (multiplets), 92.014, 53.196, 42.053, 37.987, 36.705, 36.410, 33.396, 31.178, 31.037, 30.883, 27.485, 23.227, 21.765.

1-(3-Noradamantyl)-1-methylethyl Heptafluorobutyrate was prepared in the manner used to synthesize the 2-isopropyl-1-adamantyl OHFB. 1-(3-Noradamantyl)-1-methylethanol (4.0 g) was allowed to react with heptafluorobutyryl chloride to obtain the heptafluorobutyrate in 82% yield (6.82 g). The liquid product was purified by simple distillation (55–60 °C/0.06 torr). Both the ^1H and ^{13}C spectra indicated that the clear liquid consisted of ~18% of the isomer, 2,2-dimethyl-1-adamantyl heptafluorobutyrate and 82% of the desired unrearranged ester. 300-MHz ^1H NMR ($CDCl_3$): ratio of unrearranged to rearranged ester was indicated from the peak intensities of the rearranged methyl-group protons and the unrearranged bridgehead protons to be 4.5. 75-MHz ^{13}C (decoupled) NMR ($CDCl_3$): ratio of the carbinyl carbons at δ 93.9 and 92.4 was 4.3. IR (film): $\nu_{C=O}$ 1775 cm^{-1}.

2,2-Dimethyl-2-Adamantyl Heptafluorobutyrate. This compound was made by rearrangement of 1-(3-noradamantyl)-1-methylethyl heptafluorobutyrate by passing it through a column of silica gel with hexane as the mobile phase. Evaporation of the solvent in vacuo left the clear, liquid ester. 300-MHz ^1H NMR ($CDCl_3$): δ 1.140 (s, 6H), 1.45–1.7 (m, 5H), 2.0–2.3 (m, 6H), 2.55–2.65 (m, 2H). 75-MHz ^{13}C (decoupled) NMR ($CDCl_3$): δ 157 (triplet), 124-102 (multiplets), 92.412, 41.974, 40.730, 37.588, 35.587, 32.099, 31.624, 22.916.

2-Ethyl-1-Adamantyl Heptafluorobutyrate. 2-Ethyl-1-adamantanol (1.0 g, 0.05546 mol) was treated in the usual manner to produce the heptafluorobutyrate. The isolated product was purified by *vacuum* transfer with a short path still. Next, the compound was purified further by column chromatography (hexane). Evaporation of the hexane *in vacuo* left the heptafluorobutyrate in 79.7% yield (1.64 g). 300-MHz ^1H NMR ($CDCl_3$): δ 0.903 (t, 3H), 1.2–1.9 (m, 8H), 2.0–2.4 (m, 8H). 75-MHz ^{13}C (decoupled) NMR ($CDCl_3$): δ 156.496 (triplet), 124–103 (multiplets), 90.720, 49.168, 31.435, 37.665, 36.549, 36.075, 32.201, 31.406, 30.881, 29.919, 19.274, 11.849.

Isolation and Identification of the Solvolysis Products of 1-(3-Noradamantyl)-2-methylpropyl-1-d_1 Pemsylate in 97% Aqueous 2,2,2-Trifluoroethanol. 1-(3-Noradamantyl)-2-methylpropyl-1-d_1 pemsylate (1.26 g, 3.106 mmol) was added to 97T (45 mL) containing lutidine (0.3983 g). After the solvolysis reaction was allowed to go to completion, the solvent was removed in vacuo. Diethyl ether was used to extract the substitution products from the lutidinium salt. The diethyl ether solution (250 mL) was extracted in succession with H_2O, 2N aq H_2SO_4, and saturated aq $NaHCO_3$. The diethyl ether solution was dried over $MgSO_4$; the drying agent was removed by

suction filtration. Evaporation of the ether under reduced pressure left a greenish oil which weighed 0.89 g. Crystals began to precipitate from the oil to make it a whitish mass. This was dissolved in 95% hexane-5% ethyl acetate which was then filtered through a nylon HPLC filter. The filtrate was concentrated (3.2 mL). Next, the trifluoroethyl ethers were isolated by HPLC purification on a prepacked silica gel column (10 mm ID × 25 cmL) and 95% hexane-5% ethyl acetate as the mobile phase to obtain a greenish liquid which weighed 0.491 g. *2,2,2-Trifluoroethyl 2-isopropyl-1-adamantyl-2-d_1 Ether:* 300-MHz ^{1}H NMR ($CDCl_3$): δ 3.69–3.83 (m, 2H), 2.08–2.2 (m, 3H), 1.5–2.0 (m, 10H), 1.35–1.45 (m, 1H), 1.123 (d, 3H), 0.896 (d, 3H). 75-MHz ^{13}C NMR ($CDCl_3$): δ 249.427 (quartet, J = 279.2 Hz), 77.493, 58.685 (quartet, J = 33.7 Hz), 53.773 (triplet), 42.301, 38.473, 36.839, 35.794, 32.419, 31.503, 30.705, 30.163, 27.147, 24.801, 21.642. 55.4-MHz ^{2}H NMR (97T): δ 1.688. *2,2,2,-Trifluoroethyl 4-isopropyl-3-protoadamantyl-4-d_1 ether:* 300-MHz ^{1}H NMR ($CDCl_3$): δ 0.9455 (two superimposed doublets, 6H), 75-MHz ^{13}C NMR ($CDCl_3$): δ 89.0, 61.346 (quartet, J = 33.9 Hz), 40.356, 39.592, 39.092, 36.038, 33.512, 30.898, 30.343, 28.348, 28.237, 22.504, 18.484. 55.4-MHz ^{2}H NMR (97T): δ 2.250. The corresponding alcohols were isolated also and the ^{1}H and ^{13}C NMR spectra were identical to the ones found previously.

1-(3-Noradamantyl)-2-methylpropanone-2-d_1. The β-deuteration of the ketone (1.33 g) was accomplished in the manner reported in Ref. 23. For the first exchange, 1-(3-noradamantyl)-2-methylpropanone was added to a solution of dioxane-D_2O which had been used previously and contained Na_2CO_3 in a 100-mL round-bottom flask equipped with a condenser with an inlet where N_2 was pumped through to provide an indifferent atmosphere. Sodium (100 mg) was added to the magnetically stirred mixture. After heating the mixture under slow reflux for 26 h the cooled mixture was poured into a separatory funnel containing pentane (500 mL). The organic solution was washed with five 250-mL portions of ice-water. The pentane solution was dried over $MgSO_4$; the drying agent was removed by suction filtration. The pentane was evaporated under reduced pressure. The 500-MHz ^{1}H spectrum showed that the ketone was 40–50% deuterated. Two more exchanges were performed in a mixture of dioxane (25 mL) which had been distilled from LAH, pure D_2O (25 mL), and sodium. The sodium had been weighed into a tared vial containing hexane (108.2 mg for the first exchange and 164.7 mg for the second). The mixture was heated under slow reflux for 3 and 2.4 days for the second and third exchanges, respectively. After the second exchange the 90-MHz ^{1}H spectrum indicated almost complete β deuteration. After the third exchange no β hydrogen was apparent and the ketone was obtained in 100% yield (1.3 g). 90-MHz ^{1}H NMR ($CDCl_3$): the changes from the spectrum of the hydrogen isotopomer are the following: no resonance at δ 2.95 and a singlet for the six protons of the two methyl groups at δ 1.05.

1-(3-Noradamantyl)-2-methylpropanol-2-d_1. The ketone (1.3 g) from the previous synthesis was reduced in the usual manner with LAH to yield the alcohol in 91% yield. The 90-MHz ^{1}H NMR ($CDCl_3$) spectrum showed the expected changes relative to the undeuterated compound: δ 0.9 (s, 3H), 1.0 (s, 3H), 3.42 (s, 1H). The alcohol was purified by HPLC on a prepacked silica gel column (21.4 mm ID × 25 cmL) with 95% hexane-5% ethyl acetate as the mobile phase. Removal of the solvent afforded the alcohol in 79% yield (1.03 g).

1-(3-Noradamantyl)-2-methylpropyl-2-d_1 Pemsylate. The alcohol (1.03 g) from the previous synthesis was caused to react with pemsyl chloride in the same manner employed to synthesize 1-(3-noradamantyl)-2-methylpropyl-1-d_1 pemsylate. Pure pemsylate was isolated by recrystallization from a boiling mixture of hexane (60 mL) and ethyl acetate (10 mL) in 53% yield (1.13 g). The 500-MHz ^{1}H NMR and 125.7-MHz ^{13}C NMR spectra were consistent with the assigned structure and indicated good purity. 500-MHz ^{1}H NMR ($CDCl_3$): δ 0.904 (s, 3H), 0.936 (s, 3H), no resonances for the β hydrogen between 1.85 and 2.1, 4.89 (s, 1H), 125.7-MHz ^{13}C NMR ($CDCl_3$): δ 30.2885, 30.1376, and 29.9872 (three resonances from C–D coupling), 30.5396 (small peak which indicates a couple percent d_0 impurity).

1-(3-Noradamantyl)-2-methylpropanone-^{18}O. The ketone (2.57 g, 0.0134 mol) reacted in benzene (60 mL) with ethylene glycol (0.912 g) and *p*-toluenesulfonic acid (0.10 g) to yield the dioxolane (2.46 g) and some unchanged ketone (0.47 g). The mixture of dioxolane and ketone were introduced into a flame-dried, 10-mL round-bottom flask. $H_2{}^{18}O$ (0.4 mL) was added *via* syringe

and a catalytic amount of *p*-toluenesulfonic acid (50 mg) was added. The mixture was magnetically stirred for 24 h. Methanolic NaOMe (220 mg Na, 7 mL MeOH) was added and the reaction solution was rinsed with diethyl ether into a separatory funnel. The ether solution was washed with cold water (4 × 40 mL). The organic extract was dried over $MgSO_4$; the drying agent was removed by suction filtration. Evaporation of the solvent under reduced pressure left a liquid (2.27 g). The IR spectrum indicated ^{18}O incorporation because of the single carbonyl stretch at 1668 cm^{-1} but it also indicated unchanged ketal to be present.

1-(3-Noradamantyl)-2-methylpropanol-^{18}O. The mixture of ketal and ketone from the previous preparation was allowed to react in the usual manner with LAH (0.18 g). After the standard work-up procedure, a liquid (2.28 g) was obtained which was purified by HPLC on a preparative column prepacked with silica (90% hexane-10% ethyl acetate) to furnish the alcohol (0.42 g) and unaltered dioxolane (1.66 g).

1-(3-Noradamantyl)-2-methylpropyl-ether-^{18}O Pemsylate. The alcohol (0.420 g) from the previous synthesis was caused to react with pemsyl chloride (0.54 g, 8 mL diethyl ether) in the same manner employed to synthesize 1-(3-noradamantyl)-2-methylpropyl-1-d_1 pemsylate. *n*-Butyllithium (2.5 M *n*BuLi/hexanes, 0.86 mL) was used instead of methylithium. After the conventional work-up, the pemsylate was crystallized from petroleum ether by slow evaporation of the solvent under reduced pressure on a rotary evaporator to obtain the product in 44% yield (0.38 g). 125-MHz ^1H NMR ($CDCl_3$): δ 93.714 and 93.665 (α-^{13}C absorptions); 79.55% ether-^{18}O incorporation after integration by the cut and weigh technique. The 90-MHz ^1H NMR ($CDCl_3$) was virtually indistinguishable from previous 90-MHz spectra of the ether-^{16}O pemsylate.

Oxygen-18 Scrambling Study of 1-(3-Noradamantyl)-2-methylpropyl Pemsylate in 95E. 1-(3-Noradamantyl)-2-methylpropyl-ether-^{18}O pemsylate (0.2071 g, 0.5093 mmol) which had 79.55% ether-^{18}O incorporation was mixed with 95% aqueous ethanol (100 mL) containing lutidine (0.070 g). After the latter mixture was sonicated for 1.72 h and more 95E (51 mL) was added; during that time the pemsylate appeared to be completely dissolved. Next, the reaction solution was kept at 25.000±0.001 °C to complete ~ 1 half-life of reaction (11.5 h). Direct evaporation of the solvent was attempted for 4.22 h with the flask in an ice-bath but was abandoned after only about 90 mL had evaporated. Workup was then attempted by pouring the solution into a separatory funnel which contained diethyl ether (100 mL) and water (100 mL) but this formed a milky-white emulsion with no phase separation. Therefore, the emulsion was extracted several times with chloroform. The combined chloroform extracts were dried over $MgSO_4$; the drying agent was removed by suction filtration. Evaporation of the solvent under reduced pressure left the isolated ester, solvolysis products, and residual lutidine. The 500-MHz ^1H NMR spectrum indicated signals for unsolvolyzed pemsylate at δ 0.945 (d, 3H), 0.912 (d, 3H), 2.622 (s, 6H); for 2-isopropyl-1-adamantyl ether at δ 0.872 (d, 3H), 1.125 (t, 3H), 1.131 (d, 3H) and 3.41 (m, 2H); and 2-isopropyl-1-adamantanol at δ 0.877 (d, 3H), 1.167 (d, 3H). Relative integration of the peaks at 2.62 for the unsolvolyzed ester and at 3.41 for the ether indicated 53% reaction; relative integration of the higher field peaks for the absorptions of the protons of the methyl groups indicated 59% reaction. 125-MHz ^{13}C NMR spectrum taken by Wilgis[8] showed two signals centered at δ 93.364; the signals of the pemsylate ester occur at 93.389 ppm for the ^{13}C–^{16}O resonance peak and at 0.049 ppm upfield from the latter signal for the ^{13}C–^{18}O resonance peak. Cut-and-weigh integration of the latter two peaks indicated 80.90% ether-^{18}O pemsylate and this indicated that no equilibration had occurred.

1-(3-Noradamantyl)-2,2-dimethylpropanol. Into a flask containing a *t*-butyllithium solution (50% excess, 96.3 mL, 1.7 M *t*BuLi/pentane, purchased from Aldrich Chemical Co.) under argon was added 3-noradamantanecarboxaldehyde (16.4 g, 0.1092 mol) in a minimum amount of petroleum ether. The product was isolated in the usual manner (see the preparation of 1-(3-noradamantyl)-2-methylpropanol the next day. A while solid was obtained in 85% yield (19.3 g). The 90-MHz ^1H NMR spectrum indicated that the majority of the product was the desired one. 90-MHz ^1H NMR ($CDCl_3$): δ 3.3 (s, 1H), 2.5–1.2 (m, 13H), 1.33 (s, 1H), 1.0 (s, 9H), a singlet at 3.6 which indicates that 3-noradamantylmethanol (~10%) is present as a by-product.

1-(3-Noradamantyl)-2,2-dimethylpropyl Pemsylate. The alcohol (2.0 g, 0.009603 mol) was allowed to react according to the modified Kochi-Hammond procedure (see the procedure for

preparation of 1-(3-noradamantyl)-2-methylpropyl-1-d_1 pemsylate). Methyllithium (6.86 mL, 1.4 M CH_3Li/diethyl ether, HMPA (4 mL), and PmsCl (2.37 g) in anhydrous ether (50 mL) were used. No precipitate developed in the reaction flask. The product after work-up was a slimy solid which was recrystallized from petroleum ether/hexane in a freezer to obtain the pemsylate in 37.3% yield (1.5 g). The crystals were washed with petroleum ether, dried, and then mashed into a powder with a mortar and pestle. 300-MHz ^1H NMR ($CDCl_3$): δ 4.867 (s, 1H), 2.624 (s, 6H), 2.264 (s, 3H), 2.225 (s, 6H), 0.974 (s, 9H). There were some small unidentified impurity peaks at δ 0.869, 2.590, and 4.06. 75-MHz ^{13}C (decoupled) NMR ($CDCl_3$): δ 139.142, 137.01, 134.506, 133.114, 97.734, 54.61, 48.588, 45.706, 45.576, 42.715, 42.33, 38.265, 37.777, 37.636, 35.465, 28.450, 18.783, 17.731, 17.002. The conductometric kinetics of this compound were good and reproducible but the error plots from first-order fit of the data had small waves to them. Purification of this compound by HPLC on a 20 cm by 1 cm prepacked silica gel column with 95% hexane-5% ethyl acetate as the mobile phase produced a compound which gave linear error plots. Mp 109–112 °C. The impurity which was separated was shown to account for all the impurity peaks mentioned above. Pemsylate which was not purified by HPLC was used for product studies purposes.

1-(3-Noradamantyl)-2,2-dimethylpropanone. This compound was made in the same manner employed to prepare 1-(3-noradamantyl)-2-methylpropanone. The alcohol (6.0 g, 0.02867 mol) was oxidized with PCC (9.27 g). The reaction was carried out for 4 h to yield, after isolation of the product, the desired ketone in 92% yield (5.43 g). IR (CCl_4): 2920 (s), 2864 (m), 1680 (s), 1480 (m), 1460 (m), 1394 (w), 1364 (m), 1300 (w), 1275 (w), 1160 (w), 1118 (w), 1094 (m), 1060 (w), 970 (w), 935 (w), 903 (w), 875 (w).

1-(3-Noradamantyl)-2,2-dimethylpropanol-1-d_1. The ketone (5.43 g) of the previous synthesis was treated in the usual manner with LAD (0.39 g) in anhydrous ether (250 mL). A white solid which weighed 4.7 g (85%) was obtained. 300-MHz ^1H NMR ($CDCl_3$): δ 0.983 (s, 9H), 1.4–2.0 (m, 11H), 2.25 (m, 2H), 2.6 (t of t, 1H).

1-(3-Noradamantyl)-2,2-dimethylpropyl-1-d_1 Pemsylate. The pemsylate was synthesized in the same manner used to prepare the undeuterated isotopomer. Addition of methyllithium to a solution of the alcohol (2.0 g, 0.009558 mol) produced a precipitate. After the pemsyl chloride was added the reaction solution was clear and golden yellow. No precipitate developed during the 2 h reaction time. The crude reaction product was a yellowish slimy solid. Recrystallization from petroleum ether-hexane (75 mL) at sub-zero temperature gave first-crop crystals which weighed 0.67 g. More pemsylate (1.0 g) was recrystallized at below freezing temperature to give a total yield of 41.6%. 300-MHz ^1H NMR ($CDCl_3$): δ 0.973 (s, 9H), 1.21 (m, 2H), 1.42 (m, 1H), 1.62 (m, 2H), 1.6–1.8 (m, 4H), 1.92 (m, 1H), 2.1–2.4 (m, 3H), 2.231 (s, 6H), 2.268 (s, 3H), 2.625 (s, 6H). 75-MHz ^{13}C NMR ($CDCl_3$): δ 139.170, 136.949, 134.521, 133.113, 97.344 (triplet), 54.506, 48.554, 45.697, 45.533, 42.725, 42.321, 38.276, 37.772, 37.548, 35.463, 28.454, 18.827, 17.794, 17.063. Purification of this compound by HPLC on a 20 cm by 1 cm prepacked silica gel column with 95% hexane-5% ethyl acetate as the mobile phase produced compound which gave good first-order solvolytic error plots. Mp 109–112 °C. Pemsylate not purified by HPLC and made from incompletely α-deuterated alcohol was used for product studies.

Isolation and Identification of the Solvolysis Products of 1-(3-Noradamantyl)-2,2-dimethylpropyl-1-d_1 Pemsylate in 100% Ethanol. 1-(3-Noradamantyl)-2,2-dimethylpropyl-1-d_1 pemsylate (1.2 g, 0.00286 mol) with 13% d_0 impurity was allowed to react for 10 half-lives in 100% conductivity ethanol containing 1.1 equivalents of lutidine. The reaction temperature was room temperature and the reaction solution was magnetically stirred. Most ethanol was removed by rotary evaporation with application of heat from a hot water bath. Any remaining ethanol and lutidine was removed at low pressure (~1 torr). The product was taken up in anhydrous ether (100 mL) and any solid was removed by gravity filtration. After removal of the ether by rotary evaporation a liquid was obtained in 93% yield (0.63 g) along with solid which was presumed to be a small amount of lutidinium pemsylate. The product was purified by HPLC on a prepacked silica gel column with hexane as the mobile phase. The second, larger of the two large peaks seen in the chromatogram proved to be *ethyl 2-tert-butyl-1-adamantyl-2-d_1 ether* because of its α-^{13}C resonance. The adamantyl ether was collected in 47% yield (0.32 g). 300-MHz ^1H NMR

($CDCl_3$): δ 1.11 (s, 9H), 1.15 (t, 3H), 1.35–2.3 (multiplets, 13H), 3.45 (m, 2H). 75-MHz ^{13}C (decoupled) NMR ($CDCl_3$): δ 76.326, 56.397 (s, β carbon attached to *t*-butyl group of the d_o impurity), 55.820 (triplet of β carbon attached to *t*-butyl group and to deuterium), 54.615, 44.701, 40.444, 37.468, 36.353, 34.262, 32.916, 32.428, 31.864, 31.095, 30. 338. 75-MHz ^{13}C NMR coupled) ($CDCl_3$): Obvious characteristic peaks are: δ 76.1 (singlet), 54.6 (triplet), 16.1 (quartet). 55.4-MHz ^2H NMR (95E): δ 2.118. *Ethyl 4-tert-butyl-3-protoadamantyl-4-d_1 ether,* the other peak collected, was isolated in 22% yield (0.15 g). 300-MHz ^1H NMR ($CDCl_3$): δ 1.0 (s, 9H), 1.15 (t, 3H), 1.15–2.3 (multiplets, 13H), 3.41 (m, 2H). 75-MHz ^{13}C (decoupled) NMR ($CDCl_3$): δ 88.488, 56.465, 46.296 (s, β carbon attached to *t*-butyl group of the d_o impurity), 45.808 (triplet of β-carbon attached to the *t*-butyl group and to deuterium), 41.525, 40.089. 39.909, 36.059, 36.459, 33.881, 33.702, 31.714, 30. 291, 28.854, 16.248. 75-MHz ^{13}C (coupled) NMR ($CDCl_3$): Obvious characteristic peaks are: δ 88.5 (singlet), 56.5 (triplet), 16.5 (quartet). 55.4-MHz ^2H NMR (95E): δ 2.309.

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SAŽETAK

Solvoliza 1-(3-noradamantil)-2,2,-dimetilpropil-pemsilata

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Izmjerene su brzine te su određene m-vrijednosti i α-d i β-d izotopni efekti za solvolizu naslovnih estera. Za iste su spojeve izračunane i energije napetosti početnog i prijelaznog stanja primjenom metode MMX. Na osnovi usporedbe dobivenih rezultata s onim objavljenim za srodne sustave zaključeno je da se solvoliza razmatranih supstrata bitno ubrzava uslijed C–C σ-participacije.