31.5 mg product was obtained from 36.0 mg of 8. Mp: 81–82 °C. MS (m/z): 316 (M + 2, 5.3), 315 (M + 1, 44.0), 299 (M − CH_3, 53.1), 165 ($SnMe_3$, 100.0). IR (cm^{-1}): 2909 (s), 2839 (w), 1712 (s), 766 (m), 526 (s), 464 (w). ^1H NMR ($CDCl_3$): δ 2.55–1.94 (b m, 13 H), −0.005 (s, 9 H). ^{13}C NMR ($CDCl_3$): δ 218.1, 48.33, 44.36, 40.66, 39.04, 28.07, 26.79, −12.67. Anal. Calcd for $C_{13}H_{22}OSn$: C, 49.90; H, 7.09. Found: C, 50.12; H, 7.20.

5-(Trimethylstannyl)adamatan-2-ol (9). The procedure used was similar to that described for 2; 70 mg of 9 was obtained in quantitative yield. After flash chromatography, we obtained Z-9, mp 109 °C. MS (m/z): 316 (M, 0.7), 151 (M − $SnMe_3$, 57), 165 ($SnMe_3$, 43). IR (cm^{-1}): 1446 (w), 1057 (m), 1027 (w), 766 (s), 522 (s), 510 (w). ^1H NMR ($CDCl_3$): δ 3.91 (b, 1 H), 2.27–1.70 (m, 14 H), −0.048 (s, 9 H). ^{13}C NMR ($CDCl_3$): δ 74.64, 41.99, 36.57, 35.27, 27.80, 27.03, −13.05. Anal. Calcd for $C_{13}H_{24}OSn$: C, 49.56; H, 7.68. Found: C, 49.71; H, 7.74. E-9: mp 138–140 °C. ^1H NMR ($CDCl_3$): δ 3.87 (b, 1 H), 2.17–1.25 (m, 14 H), −0.036 (s, 9 H). ^{13}C NMR ($CDCl_3$): δ 74.54, 41.93, 40.98, 35.33, 31.07, 28.34, 26.22, −12.95. Anal. Calcd for $C_{13}H_{24}OSn$: C, 49.56; H, 7.68. Found: C, 49.39; H, 7.83.

2-Methyl-5-(trimethylstannyl)adamantan-2-ol (10). An ethyl ether solution of methyllithium (1.5 M, 1 mL) was injected slowly into a solution of 1-$SnMe_3$ (106 mg, 0.34 mmol) in 5 mL of anhydrous ether at 0 °C. The mixture was allowed to react for 3 h at 0 °C, quenched with saturated aqueous ammonium chloride, and extracted with ether (3 × 50 mL). The combined extract was washed with saturated aqueous sodium chloride, dried ($MgSO_4$), and evaporated, giving a mixture of the isomers of 10 in quantitative yield. They were separated by flash chromatography (85% hexane, 15% ethyl acetate). Z-10: mp 83 °C. MS (m/z): high resolution, 330.1006 (calcd 330.1006); 330 (M, 4.1), 165 ($SnMe_3$, M − $SnMe_3$, 100). IR (cm^{-1}): 3356 (m), 2884 (s), 1121 (m), 920 (w), 761 (w), 522 (m). ^1H NMR ($CDCl_3$): δ 2.37–2.33 (d, b, 2 H), 1.92–1.64 (m, b, 11 H), 1.39 (s, 1 H), 1.33 (s, 3 H), −0.04 (s, 9 H). ^{13}C NMR δ 73.81, 42.72, 39.88, 37.25, 35.17, 28.32, 27.66, 26.29, −12.94. E-10: mp 93 °C. ^1H NMR: δ 2.22–2.19 (d, b, 2 H), 2.01–1.59 (m, b, 11 H), 1.51 (s, 1 H), 1.32 (s, 3 H), −0.04 (s, 9 H). ^{13}C NMR: δ 73.65, 42.63, 39.84, 39.51, 33.00, 27.85, 27.21, 26.51, −13.01.

Shift Reagent Studies. Eu(fod)$_3$ was dried in a vacuum Büchi GKR-50 desiccator over P_2O_5 for 12 h. $CDCl_3$, which was stored over activated molecular sieves (4A), was used to dissolve the Eu(fod)$_3$ and the alcohols. Typically, 0.5 mL of 0.8 M alcohol solution and 0.3 mL of 0.2 M Eu(fod)$_3$ solution were prepared separately. ^{13}C NMR spectra were measured in the presence of varying amounts of the shift reagent solution: 0.015, 0.030, 0.045, 0.060, 0.075, and 0.090 mL. The assignment was based on the fact that the carbon atoms on the syn side of hydroxy group are shifted downfield more than the carbon atoms on the anti side.

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Effects of Two Oppositely Polarizing, Distant Substituents on the Rate and Stereochemistry of Solvolysis of 2-Adamantyl Tosylate[1]

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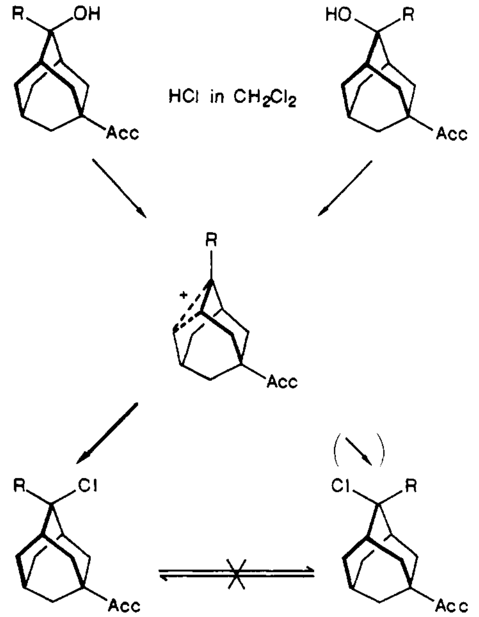
The hydrolysis rates are reported of (*E*)- and (*Z*)-5-fluoro- and -(trimethylstannyl)adamant-2-yl tosylate as well as of the parent ester. The fluoro derivatives react 4–6 orders of magnitude more slowly than the parent, while the tin compounds do so about the 10 times more rapidly. The (*Z*)-fluoro ester and the (*E*)-tin ester react with complete retention; the (*E*)-fluoro ester and (*Z*)-tin compound undergo significant inversion. The epimeric rate ratios (*E*/*Z*) are about 0.005 for the fluoro pair and 0.7 for the tin pair.

In 1970, the Schleyer group reported[2-4] solvolysis rates for 2-adamantyl esters under a variety of conditions and drew the conclusion that these reactions were remarkably free of solvent assistance and neighboring-group participation.[5] These results proved to be very stimulating, and 2-adamantyl solvolysis became a durable mainstay among the physical organic chemist's interests. In the subsequent literature, an important place must be accorded to a paper by Whiting[6] in which it was shown that if a 5-methyl group is present, both secondary and tertiary derivatives of 2-adamantanol hydrolyze to give primarily the alcohols from which they were derived, i.e., with retention of configuration. Another landmark paper was that by Bunnett,[7] who showed that ion pairing must be an important feature of the reaction since oxygen scrambling occurs in the tosylate during solvolysis. The interest in the adamantyl

Scheme I



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[1] This work was done by M.X. in partial fulfillment of the requirement for the M.S. degree.

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Table I. Rate Constants and Products in the Hydrolysis of 5-X-2-AdOTs

5-X	config	solvent	H_2O, vol %	*t*, °C	k_1, s^{-1}	corr *C*	$k/k_{X=H}$	ret/inv
F	*E*	MeCN	10	75.0	4.73×10^{-6}	0.9998	2.5×10^{-6}	52/48
F	*Z*	MeCN	10	75.0	9.80×10^{-4}	0.9999	5×10^{-4}	100/0
H	–	MeCN	10	50.0	1.69×10^{-3}	0.9996	–	–
H	–	MeCN	10	42.2	2.32×10^{-4}	0.9984	–	–
H	–	Me_2CO	50	50.0	7.45×10^{-6}	0.9997	–	–
$SnMe_3$	*E*	Me_2CO	50	50.0	7.81×10^{-5}	0.9994	10	100/0
$SnMe_3$	*Z*	Me_2CO	50	50.0	1.12×10^{-4}	0.9999	15	9/91

system derives in part from the fact that steric factors cannot cloud any σ delocalization that might occur in the generation and capture of such ions, in stark contrast to the controversial 2-norbornyl ion.

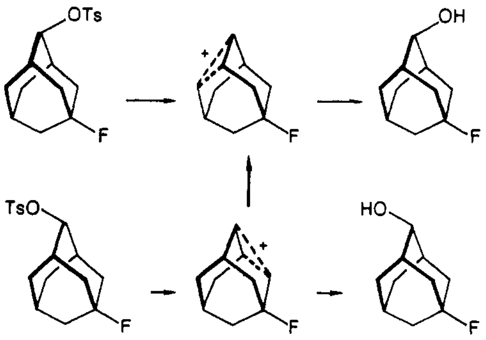
Our own initial work in this area, published[8] in 1986, confirmed by means of a 5-deuterio label[9,10] that 2-adamantyl tosylate solvolyzes with retention; furthermore, since tertiary 2-adamantyl cations with an acceptor group as substituent in the 5-position capture nucleophiles preferentially on the side syn to the acceptor regardless of which epimeric alcohol preceded the cation, we were able to rule out solvent-separated ion pairs as the only remaining alternative explanation to σ participation (see Scheme I). One important opportunity afforded by this conclusion was that it allowed us to expose an important source of confusion that had long permeated the discussions of the norbornyl ion, namely the assumption that cation stabilizing α-substituents should level the need for σ participation.[11] It was found, however, that tertiary ions such as 2-anisyl- and 2-methoxy-2-adamantyl capture borohydride with undiminished preference for that face which is anti to the more electron-rich C–C bonds.[12]

The σ delocalization occurring in these cations also affects the transition states of reduction of 5-substituted adamantanones;[8] the operation of this effect had been advocated by Cieplak in 1981 to explain the preferred axial approach of nucleophiles to locked cyclohexanones.[13] Confirming results with 5-donor-substituted adamantanones were described in the preceding paper; presently, we wish to present our solvolysis results with epimeric pairs of both 5-donor- and 5-acceptor-substituted 2-adamantyl tosylates.

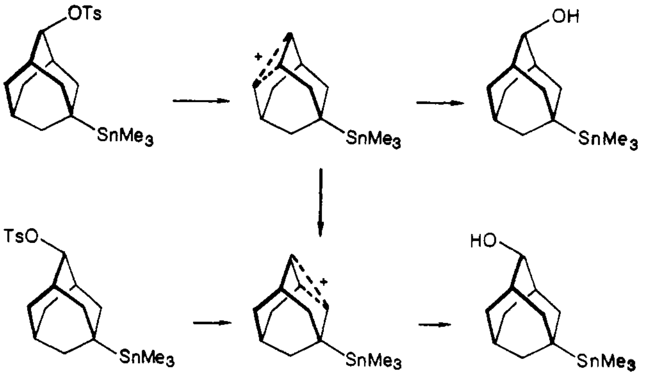
Result and Discussion

The original plan had been to generate the tertiary cations derivable from the 2-methyladamantan-2-ols and study their capture as mentioned above; however, we found that the tin–carbon bonds are protiolyzed under these conditions. As an alternative, we decided to study the solvolysis rates of the secondary tosylates. The 5-(trimethylstannyl)adamantan-2-ols used were described in the preceding paper; the 5-fluoro analogues were still available from previous work.[8] The rates were obtained by means of conductance measurements[14] over several half-lives and by means of Guggenheim plots.[15] The tin-substituted pair was measured in aqueous acetone. The rates of the 5-fluoro analogues were sufficiently slow that a faster solvent was needed (aqueous acetonitrile); we were able to extrapolate the data so as to allow comparisons of the two pairs with the parent 2-adamantyl tosylate. The alcohol products were analyzed by means of GC and ^1H NMR. The result are shown in Table I.

Scheme II



Scheme III



The temperature interval over which the parent tosylate was measured in the aqueous acetonitrile was small because of a combination of solubility limitations and inconveniently rapid rates; the apparent rate change seems unreasonably large (about seven times over an 8° temperature change). Thus, the ratio F to H may not be very accurate; but it is clear that the inductive retardation of heterolysis by fluorine is quite potent even when it is in the δ position, through three intervening carbon–carbon single bonds. The *ratio* of the two fluoro derivatives (which is *not* subject to the same reservation) is remarkably large; it strongly supports that the heterolysis is assisted by the antiperiplanar carbon–carbon bonds. When these bonds are deactivated by nearby fluorine, the rate is about 200 times slower than when the fluorine is one position farther away from them. The product stereochemistry is also informative. We recall that 5-deuterioadamant-2-yl tosylate hydrolyzes with 65–92% retention depending on the solvent; the fact that retention is complete in the (*Z*)-fluoro tosylate clearly supports σ assistance. Assistance is much weaker in the *E* isomer, but it still occurs; the first intermediate to some degree "leaks" into the more favored

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Table II. ^{13}C NMR Signals and Melting Points of 2-Adamantyl Tosylates

C	5-H	(*E*)-5-F	(*Z*)-5-F	(*E*)-5-Sn	(*Z*)-5-Sn
1, 3	32.56	34.75	36.19	33.41	33.15
2	86.19	83.11	82.75	86.51	86.64
4, 9	30.98	40.44[c]	36.42[b]	40.86	35.37
5	26.70	90.32[e]	90.61[d]	25.49	25.95
6	36.97	42.19[g]	42.13[f]	41.44	41.54
7	26.45	29.76[i]	29.65[h]	27.54	27.18
8, 10	36.27	29.45	34.60	31.15	36.45
CMe_3	–	–	–	−12.92	−12.95
C_i	134.83	134.19	134.48	135.03	134.95
C_o	127.35	127.39	127.39	127.47	127.46
C_m	129.61	129.73	129.77	129.68	129.68
C_p	144.16	144.54	144.57	144.17	144.20
p-Me	21.50	21.49	21.58	21.61	21.60
mp, °C	82[a]	89	57	82	108

[a] Lit.[19] mp 82.7–83.7 α. [b] J_{CF} = 19.8 Hz. [c] J_{CF} = 19.4 Hz. [d] J_{CF} = 185.2 Hz. [e] J_{CF} = 185.5 Hz. [f,g] J_{CF} = 17.7 Hz. [h] J_{CF} = 9.5 Hz. [i] J_{CF} = 9.8 Hz.

structure[16] to give a significant amount of inverted product (Scheme II).

The effect of trimethylstannyl substitution is much more modest, at roughly a factor of 10. Extremely large accelerations by tin in a position β to the leaving group have been reported by Lambert[17] recently. These authors concluded that most of this effect is ascribable to hyperconjugation rather than to induction. What is especially revealing in our data is the contrast in stereochemistry; whereas with 5-fluoro substitution, complete retention is observed with the *Z* isomer and cross-over with the *E* epimer, with 5-trimethylstannyl substitution, the *E* isomer hydrolyzes with complete retention, and very substantial cross-over (>90%) is noted with the *Z* isomer (Scheme III).

There is one feature in Table I that is rather surprising: while in the 5-trimethyltin pair of epimers, the *E* isomer was expected to react somewhat faster than the *Z*, it did in fact solvolyze 50% more slowly. The quality of the data is such that this cannot be dismissed as the result of experimental error or uncertainty. There are several possible explanations for this. The most probable of them is that the size of the trimethylstannyl and tosylate groups are such that the *Z* substrate is somewhat less stable than its epimer and that this interaction is relieved upon heterolysis. The tight ion pairs are subject to return as Bunnett has shown;[7] the steric factor may also lead to less return in the case of the *Z* pair. Thus, we *have* seen evidence for steric interactions of this sort; for example, both (*E*)- or (*Z*)-2-phenyl-5-fluoroadamantan-2-ol upon treatment with tosyl chloride give the same 3:2 mixture of tosylates;[18] and in the reduction of 5-*tert*-butyladamantan-2-one with lithium aluminum tri-*tert*-butoxyhydride, anti delivery of hydride is favored although a 50/50 mixture is produced with $LiAlH_4$.[8] Still another possible explanation is that the rate-controlling steps may be differently partitioned between ion pairs and free ions in the two cases. Further study will be required to gain a satisfactory understanding of this observation.

Experimental Section

All five tosylates were prepared[19] from the alcohols by means of tosyl chloride in well-dried and previously distilled pyridine. The reactions were stopped after 6 days at room temperature; after aqueous workup, the crude products were purified by means of flash column chromatography. The yields varied 70–87%. The melting points and ^{13}C signals are given in Table II. ^{1}H NMR ($CDCl_3$): 5-H (parent ester) δ 1.49–2.10 (m, 14 H), 2.44 (s, 3 H), 4.68 (s, 1 H), 7.32 (d, 2 H, *J* = 8.1 Hz), 7.80 (d, 2 H, *J* = 8.4 Hz); (*E*)-5-Sn δ −0.054 (s, 9 H), 1.25–2.09 (m, 13 H), 2.44 (s, 3 H), 4.70 (s, 1 H), 7.32 (d, 2 H, *J* = 7.8 Hz), 7.80 (d, 2 H, *J* = 8.1 Hz); (*Z*)-5-Sn δ −0.053 (s, 9 H), 1.60–2.20 (m, 13 H), 2.44 (s, 3 H), 4.70 (s, 1 H), 7.32 (d, 2 H, *J* = 7.8 Hz), 7.80 (d, H, *J* = 8.4 Hz); (*E*)-5-F δ 1.20–2.19 (m, 13 H), 2.44 (s, 3 H), 4.62 (s, 1 H), 7.34 (d, 2 H, *J* = 8.1 Hz), 7.79 (d, 2 H, *J* = 8.4 Hz); (*Z*)-5-F 1.40–2.32 (m, 13 H), 2.46 (s, 3 H), 4.55 (s, 1 H), 7.35 (d, 2 H, *J* = 7.8 Hz), 7.81 (d, 2 H, *J* = 8.4 Hz).

Solvolysis. The tosylate (3.0 mg) was dissolved in 25.0 mL of the appropriate solvent. The solvent was prepared for each experiment by mixing the required amounts of water and of the organic solvent (both predistilled); the organic solvent contained 1.5 equiv of 2,6-di-*tert*-butylpyridine as buffer. The solution was transferred to a conductance cell,[14] which was submerged in a constant temperature oil bath. The resistance of the cell was accurately measured with a Wheatstone Bridge system at regular intervals. The rate constant *k* was calculated by means of the Guggenheim method.[15] After about 10 half-lives, the sample was extracted with methylene chloride and dried over anhydrous sodium sulfate. The products were identified by means of ^{1}H NMR and assayed by GC analysis; in both recordings, the peaks were compared with those of the authentic compounds. The spectra and GC traces showed no evidence of side products. Completely independent duplicate measurements with repurified materials agreed to better than 1%.

Acknowledgment. W. le N. thanks the National Science Foundation and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work.

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