Electronic and Steric Influences on Face Selection during the Oxy-Cope Rearrangement of an α-Allyl-α-vinylbenzyl Alcohol

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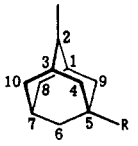
The racemic *RR,SS* and *RS,SR* diastereomers of 5-(5-fluoroadamant-2-ylidene)-4-hydroxy-4-phenyl-1-pentene (**1-F**) have been synthesized. Their configurations have been determined by means of ^{13}C NMR as well as by way of an X-ray diffraction study of the acetate of the former alcohol. Both alcohols undergo the oxy-Cope rearrangement to give mixtures of the (*E*) and (*Z*)-2-allyl-2-benzoyl-5-fluoroadamantanes (**5-F**). Analysis of these mixtures allows the conclusions to be drawn that the preferred site of the phenyl group in the chair transition states is the quasi-equatorial one, and that the electronically preferred face of the adamantyl terminus is that *syn* to the fluorine (*zu* face). These preferences amount to factors of 2.75 and 1.54, respectively. Hyperconjugation involving the incipient σ* orbital can account for the electronic preference observed. Pyramidalization of C_2 in the acetate of **1-F** was not detectible in the X-ray diffraction study.

Introduction

The oxy-Cope rearrangement is one of the most useful [3,3] sigmatropic shifts to have been discovered.[1] *Chemical Abstracts* has listed nearly 100 entries under this heading up to now; the large majority of these represent recent papers describing the application of the reaction to the synthesis of neutral products and of ring systems otherwise not easily accessible. The principle that conversions of sp^3 to sp^2 carbon should be promoted by the presence of an α-oxide function might be expected to be general, and, indeed, extensions of the reaction have appeared that include 1,3-shifts,[2] 1,5-shifts,[3] and retro-Diels–Alder reactions.[4] The mechanism of the reaction has been investigated;[5] it is clear now that the reaction is concerted[6] and that the transition state has a quasi-chair shape.[7]

Our research of the reaction[8] evolved from an interest in the electronic factor in face selection: the stereochemical aspect accompanying all interconversions of trigonal and tetragonal carbon. In the case of the oxy-Cope rearrangement, an investigation of the face selection appeared to be quite challenging to us. First of all, in all previous instances in which the face selected in this reaction can in principle be identified, it is so because cyclic or polycyclic features in the carbon skeleton enforce one option. Secondly, there is a choice of face at both ends of open-chain 1,5-hexadienes, and the choice at one terminus may affect that at the other. Fortunately, previous research[6,7] that has established the chair-shaped transition state in this reaction now limits the selection to two pairs of faces, since the other two involve boats.

The probe we have employed in previous studies of face selection such as it occurs with carbonyl compounds[9] and carbocations[10] vis-à-vis nucleophiles, with olefins[11] vis-à-vis electrophiles, and in cycloadditions[12] consists of a 5-substituted adamantane nucleus with a trigonal center at C_2.



The substituent R serves simultaneously to render the two faces of C_2 diastereotopic and to polarize the flanking vicinal bonds into two electronically distinct pairs. To date, all of our results can be generalized by the statement that, when R is electron withdrawing, all reagents—whether nucleophilic or electrophilic in nature—preferentially bond at the *zu* (or *syn* or *ci*) face, and, when R is an electron donor, they predominantly approach the *en* (or *anti* or *tr*) face of C_2. We base our interpretation of these facts on the notion that the transition state may be stabilized by delocalization of antiperiplanar σ electrons into the incipient σ* orbital.

This idea was first offered by Cieplak[13] to explain the well-known predilection of nucleophiles for axial approach to the carbonyl group in rigid cyclohexanones. We regard it is an extension of Winstein's proposal of σ participation to account for retentive solvolysis in many instances.[14] The virtues of our probe include the facts that the two faces of C_2 are sterically essentially the same, that the results are not subject to conformational doubts, that the products are generally obtained in high yields and are easily purified, and that only two products form, both of them achiral.

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(1) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 4765.
(2) Zoeckler, M. T.; Carpenter, B. K. *J. Am. Chem. Soc.* **1981**, *103*, 7661.
(3) Battye, P. J.; Jones, D. W. *J. Chem. Soc., Chem. Commun.* **1984**, 990.
(4) RajanBabu, T. V.; Eaton, D. F.; Fukunaga, T. *J. Org. Chem.* **1983**, *48*, 652.
(5) Rozeboom, M. D.; Kiplinger, J. P.; Bartness, J. E. *J. Am. Chem. Soc.* **1984**, *106*, 1025 and literature quoted there.
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(7) Evans, D. A.; Nelson, J. V. *J. Am. Chem. Soc.* **1980**, *102*, 774.
(8) Preliminary communication: Lin, M.-h.; le Noble, W. J. *J. Org. Chem.* **1989**, *54*, 997.
(9) Cheung, C. K.; Tseng, L. T.; Lin, M.-h.; Srivastava, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 1598.
(10) Lin, M.-h.; Cheung, C. K.; le Noble, W. J. *J. Am. Chem. Soc.* **1988**, *110*, 6562.
(11) Srivastava, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 5874.
(12) Chung, W.-S.; Turro, N. J.; Srivastava, S.; Li, H.; le Noble, W. J. *J. Am. Chem. Soc.* **1988**, *110*, 7882.
(13) Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540.
(14) Winstein, S.; Trifan, D. *J. Am. Chem. Soc.* **1952**, *74*, 1147, 1154.

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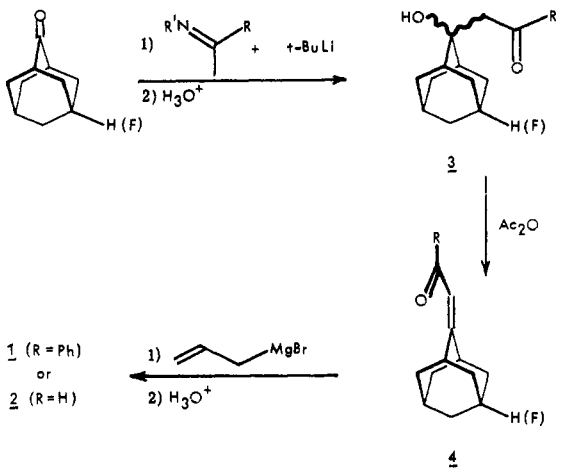
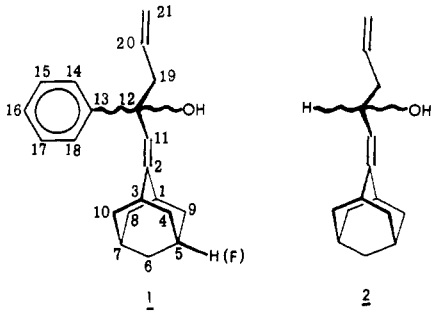
Scheme I



In all of our previous studies, the probe itself has had no stereoisomers; however, that could not be the case in the present study. Thus, 3-hydroxyhexa-1,5-dienes are necessarily chiral, and attaching a 5-substituted adamantane at one end unavoidably leads to two diastereomeric pairs. Since fluoro is the ideal 5-substituent (sterically the most innocuous and electronically the most strongly polarizing), we settled on the diastereomers implied by **1**-F as the probes with which to pursue our study. We began with an investigation of the parent racemic pair **1**-H as well as of the secondary alcohol **2** for explorative and comparative purposes.



1 2

Results and Discussion

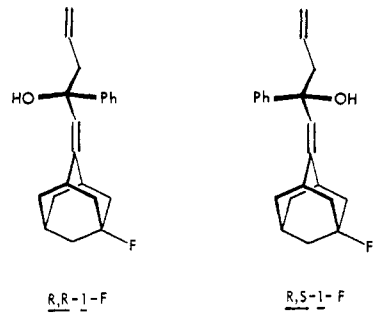
Alcohols **1** and **2** were prepared by the route shown in Scheme I. To obtain the α,β-unsaturated aldehyde required to prepare **2** we used Meyers' procedure[15] based on acetaldehyde *N-tert*-butylimine and lithium diisopropylamide; however, this approach led to considerable amounts (up to 40%) of adamantan-2-ol. Furthermore, we found that **2** is unreactive under the typical oxy-Cope conditions, and hence this part of the study was abandoned.

On the way to **1**, we fared better by using the *N*-cyclohexylimine of acetophenone[16] and *tert*-butyllithium. The intermediate ketols **3** could be isolated; in the case of **3**-F, the yield was 96%. The *E*/*Z* isomer ratio in that case was 56:44, in keeping with all of our previous experience in the alkylation of 5-substituted adamantanones to the effect that nucleophiles preferably approach the carbonyl carbon from the side anti to the more electron-rich vicinal bonds. The analysis was based on the intensities of the C_2 peaks in the ^{13}C NMR spectrum; these two peaks could be assigned on the basis of the analogous signal of the parent **3**-H and application of the additivity rule.[17] The mixture was not separated but dehydrated with acetic anhydride to yield racemic enone **4**-F; reaction with allylmagnesium bromide completed the preparation of **1**-F as a mixture of two diastereomers[18] *RR*,*SS* and *RS*,*SR* in 97% combined yield. These diastereomers (hereafter referred to as *RR* and *RS*, respectively) could be separated quantitatively by means of flash chromatography, which produced 175 mg of one ("major") isomer and 168 mg of the "minor" one.

Table I. Compounds 1: ^{13}C Chemical Shifts (ppm) and ^{19}F Coupling Constants (Hz)

C_n	δ (parent) (1-H)[a]	δ ((*RR*)-1-F)	$J^{19}F$	δ ((*RS*)-1-F)	$J^{19}F$
1	40.59	42.43	9.8	42.56	9.9
2	153.93	149.87		149.71	
3	33.06	34.60	9.9	34.74	9.9
4	36.97	41.19	17.8	42.74	17.6
5	27.86	91.86	184.6	91.95	184.1
6	38.84	43.74	18.6	43.75	17.1
7	28.00	31.18	8.9	31.05	9.3
8	39.82	38.09		38.15	
9	39.75	42.15	16.9	42.16	17.0
10	37.03	37.11		35.50	
11	123.19	125.19		125.16	
12	74.78	74.61		74.60	
19	58.89	50.76		50.63	
20	133.70	133.24		133.23	
21	119.03	119.78		119.79	
(13)	147.99	147.35		147.52	
(14, 18)	125.58	125.37		125.47	
(15, 17)	127.55	127.80		127.76	
(16)	126.11	126.46		126.33	

[a] In the parent compound, C_4 and C_{10} may have been interchanged, as may C_8 and C_9, and C_5 and C_7.



R,R-1-F R,S-1-F

The tentative assignment of the major isomer as *RR*, as reported in the preliminary report,[8] was based on ^{13}C NMR. It involved the assumption that the hydroxy group rather than allyl or phenyl is closest to the adamantyl bridgehead carbon C_3, for steric reasons. In such a conformation, the phenyl group would be directly above C_4 in the *RR* configuration, or above C_{10} in the *RS* isomer. Indeed, in the major isomer, the C_4 signal is shifted upfield by 1.6 ppm compared to the minor one, whereas in the minor isomer, the C_{10} signal is shifted upfield by 1.6 ppm compared to the major one. C_8 and C_{10} signals are of course readily distinguished from C_4 and C_9 by the fluorine splittings; see Table I.

Confirmation by means of X-ray diffraction became possible when we succeeded in preparing the acetate ester of the major isomer of **1**-F by means of a reaction that takes place with retention; the tentatively identified *RR* diastereomer did indeed have that configuration. It may

(15) Meyers, A. I.; Tomioka, K.; Fleming, M. P. *J. Org. Chem.* **1978**, *43*, 3788.
(16) Norton, D. G.; Haury, V. E.; Davis, F. C.; Mitchell, L. J.; Ballard, S. A. *J. Org. Chem.* **1954**, *19*, 1054.
(17) Srivastava, S.; Cheung, C. K.; le Noble, W. J. *Magn. Reson. Chem.* **1985**, *23*, 232.
(18) The first letter in *RR* etc., designates the configuration of the adamantyl moiety, and the second that of the benzyl alcohol carbon. The chiral compounds described in this study are all understood to be racemic.

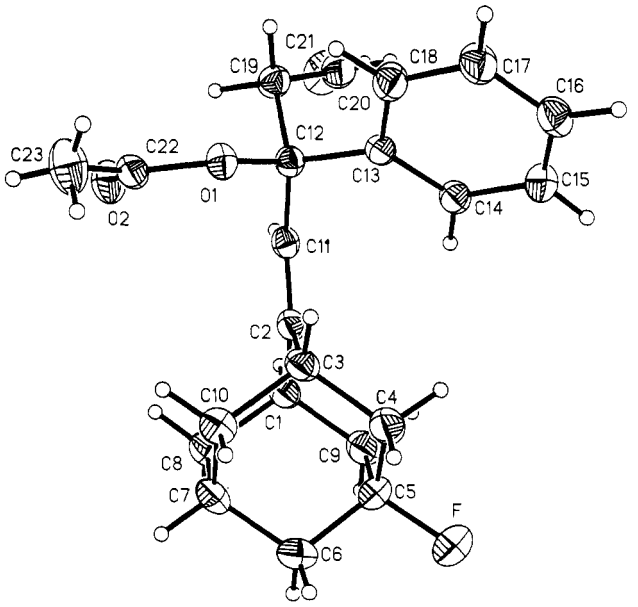
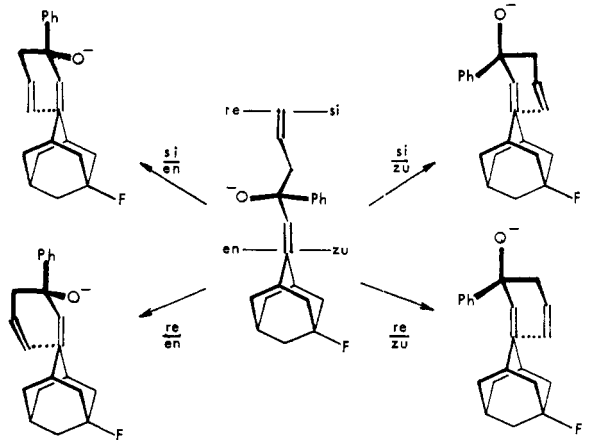


Figure 1. ORTEP of 1-F acetate.

Scheme II



be noted that the phenyl group location directly above C_4 is confirmed (see Figure 1 and further discussion of the X-ray structure below).

Knowledge of the configurations tempts us to comment on the product distribution in the allylation of ketone 4-F. We recently published evidence that face selection in the formation of allylic cations is subject to control by orbital symmetry;[19] in principle, the same phenomenon may be detectible in α,β-unsaturated carbonyl compounds. Thus, approach anti to the fluorine atom might in the present case be preferred in the allylation. There does seem to be a very slight preference (51% *RR*); however, the small excess of this isomer and the need, however reasonable, to assume an s-cis conformation of ketone 4-F render any more emphatic claims unprofitable.

Four combinations of face selection are possible for the reaction of either diastereomer of 1-F; they are listed in Table II and, for the *RR* isomer, illustrated in Scheme II.

As noted in the Introduction, previous research[6,7] had already ruled out the intervention of boat transition states. Inspection of the chair transition states in Table II shows that (*RR*)-1-F and (*RS*)-1-F differ in that in one isomer

(19) Lin, M.-h.; le Noble, W. J. *J. Am. Chem. Soc.* **1989**, *111*, 8746.
(20) For the stereo designations used, see: (a) Hanson, K. R. *J. Am. Chem. Soc.* **1966**, *88*, 2731. (b) Eliel, E. L. *J. Chem. Educ.* **1971**, *48*, 163. (c) Kaloustian, S. A.; Kaloustian, M. K. *J. Chem. Educ.* **1975**, *52*, 56.

Table II. Possible Face Selections in Racemic (*RR*)- and (*RS*)-1-F

isomer	moiety	face selected[a]	transition-state shape	eq gp	ax gp	product[b]
RR	Ad[c]	*zu, si*	chair	O^-	Ph	*E*
	Al	*si, si*				
	Ad	*en, re*	chair	Ph	O^-	*Z*
	Al	*re, re*				
	Ad	*zu, si*	boat	O^-	Ph	*E*
	Al	*re, re*				
	Ad	*en, re*	boat	Ph	O^-	*Z*
	Al	*si, si*				
RS	Ad	*zu, si*	chair	Ph	O^-	*E*
	Al	*si, si*				
	Ad	*en, re*	chair	O^-	Ph	*Z*
	Al	*re, re*				
	Ad	*zu, si*	boat	Ph	O^-	*E*
	Al	*re, re*				
	Ad	*en, re*	boat	O^-	Ph	*Z*
	Al	*si, si*				

[a] For review of the descriptors used in this column, see ref 20. [b] Note that attack on the face syn to the fluorine gives *E* product while anti approach gives *Z*. [c] Ad = adamantyl, Al = allyl.

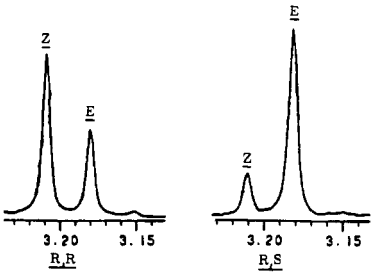
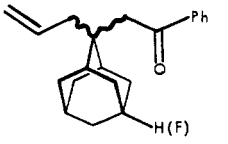


Figure 2. ^1H NMR analysis of mixtures of (*E*)- and (*Z*)-5 obtained from (*RR*)- and (*RS*)-1-F.

the electronic preference (approach syn or anti to the fluorine) and the steric preference (equatorial phenyl or oxide anion) will be working in the same direction; in the other isomer, these factors will be opposed. The product ratio *E* to *Z* 5-F will therefore differ from unity most when



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the two factors act in unison. Our expectation was that the *RS* isomer would be the one showing the effect of collaborating factors, since it would form the new bond at the site antiperiplanar to the more electron-rich vicinal bonds and since that same transition state would have the phenyl group in the pseudo-equatorial position. However, this last supposition is not supportable by simply comparing the *A* values of phenyl and hydroxyl groups. The oxide anion site is doubtlessly paired with a counterion, and both will be solvated; thus, its steric requirements are unknown.

The product mixtures of both reactions were flash chromatographed to remove some extraneous material. ^1H NMR spectra showed that the $-CH_2CO-$region was unaffected by this purification; both crude and purified mixtures gave the same 81 to 19 and 36 to 64 ratios for the mixtures derived from the *RS* and *RR* substrates, respectively (see Figure 2). Comparison of the ^{13}C spectra with the chemical shifts calculated[17] for both compounds from those of the parent compound **5**-H, 1-fluoro-

Table III. Carbon-13 Chemical Shift (ppm) Assignment of (*E*)-, (*Z*)-5-F (Adamantane Skeleton Only)[a]

compound	C-1,3	C-2	C-4,9	C-5	C-6	C-7	C-8,10
(*E*)-5-F calc	36.54	39.71	37.47	91.87	44.61	30.85	31.39
(*Z*)-5-F calc	36.54	39.71	38.27	91.97	44.61	30.74	30.59
(*E*)-5-F obs	36.62	40.59	37.56	92.04	44.48	30.56	31.61
(*Z*)-5-F obs	36.73	40.65	38.31	92.21	44.48	30.52	30.87
ΔE, corr	0.08	0.88	0.09	0.17	−0.13	−0.29	0.22
ΔZ, corr	0.19	0.94	0.04	0.24	−0.13	−0.22	0.28
ΔE, inc	0.19	0.94	0.84	0.34	−0.13	−0.33	−0.52
ΔZ, inc	0.08	0.88	−0.71	0.07	−0.13	−0.18	1.02
[ΔE + ΔZ]corr	0.27	1.82	0.13	0.41	0.26	0.51	0.50
[ΔE + ΔZ]inc	0.27	1.82	1.55	0.41	0.26	0.51	1.54

[a] The spectral assignments are based on the effects of $Eu(fod)_3$ on the ^{13}C chemical shifts of 5-H. Note that the atoms in the $C_1C_2C_3$ plane have the same calculated values in both epimers and hence are of no use; the C_4C_9 and C_8C_{10} pairs furnish the principal basis for the *E* and *Z* assignment. Symbols (for example): ΔE, corr is the error in ppm when the observed and calculated values are compared; the calculation has been described in ref 17.

adamantane, and adamantane itself (Table III) shows clearly that the product provided in substantial excess by the *RS* substrate had the *E* configuration. The main product provided by the *RR,SS* pair of 1-F was the *Z* isomer. Based on these results, simple arithmetic shows that the preference for equatorial phenyl alone amounts to a factor of 2.75, whereas the preference for approach syn to fluorine alone gives a factor of 1.54. In the absence of the steric factor, the syn preference would give 61% *E* product; in the absence of the electronic effect, the equatorial phenyl preference would lead to 73% *Z* product. The steric factor is less pronounced than we had feared (had it been much larger, the electronic factor would have been swamped). Evidently, the solvated/paired oxide anion has a steric requirement not drastically smaller than that of phenyl. So far as the electronic factor is concerned, the oxy-Cope reaction clearly obeys the general rule we have observed in all of our previous investigations; the face selected is that antiperiplanar to the more electron-rich vicinal bonds.

The origin of this effect has been subject to controversy. As noted above, we attribute it to hyperconjugation in the transition state, as Cieplak[13] did to explain the stereochemistry of cyclohexanone reduction. Initially, this idea depended on the assumption that CH bonds are better π donors than CC bonds, in other words, that these bonds follow the Baker–Nathan order. This notion is itself somewhat controversial, as Cieplak noted; however, the adamantyl probe offers only a choice of CC bonds which would be identical but for the C_5 substitutent, and hence that objection does not apply here. The strength of the hyperconjugation argument is that it explains the similarity so often observed in stereochemistry in the formation and capture of carbocations, on the one hand, and the reactions of nucleophiles with the isostructural ketones on the other. This similarity, we believe, is the result of a common factor enforcing stereochemistry in both. In cations, the reason is now generally accepted to be Winstein's σ delocalization into an empty p orbital; in ketones, it would be σ delocalization of the same bonds into the σ^* orbital of the newly forming bond in the addition process. Several comments, both pro[21] and con,[22] have appeared in the recent literature concerning the validity of this model; however, these have been based on observations made with systems in which either steric differences between the two faces or conformational factors complicate the picture. Even where such differences and factors are absent and an electronic factor is clearly operating, the resulting selectivities have been interpreted variously.[23] One of the possibilities sometimes mentioned is that the sp^2-hybridized C_2 atom may be subject to significant pyramidalization. Our previous efforts to get an insight into this by means of X-ray studies have all been frustrated by disordered crystals; this was the case with 5-fluoro-, 5-bromo- and 5-phenyladamantan-2-ones. From this point of view, the crystal structure data for the acetate of (*RR*)-1-F are of special interest (see Table IV). The three bond angles at C_2 add up to 359.9 ± 0.1°, and we conclude that pyramidalization cannot be a factor in the selectivity observed in the oxy-Cope rearrangement.[24] While we believe

Table IV. Bond Angles (Deg) and Lengths (Å) for (*RR*)-1-F-OA$_c$

C(2)–C(1)–C(8)	108.5 (3)	C(2)–C(1)–C(9)	109.7 (3)
C(8)–C(1)–C(9)	109.4 (3)	C(1)–C(2)–C(3)	111.7 (3)
C(1)–C(2)–C(11)	122.1 (3)	C(3)–C(2)–C(11)	126.1 (3)
C(2)–C(3)–C(4)	109.1 (3)	C(2)–C(3)–C(10)	108.4 (3)
C(4)–C(3)–C(10)	108.0 (3)	C(3)–C(4)–C(5)	109.3 (3)
C(4)–C(5)–F	108.1 (3)	C(4)–C(5)–C(6)	110.2 (3)
F–C(5)–C(6)	108.6 (3)	C(4)–C(5)–C(9)	111.2 (3)
F–C(5)–C(9)	108.0 (3)	C(6)–C(5)–C(9)	110.7 (3)
C(5)–C(6)–C(7)	108.2 (3)	C(6)–C(7)–C(8)	109.8 (3)
C(6)–C(7)–C(10)	109.6 (3)	C(8)–C(7)–C(10)	109.1 (3)
C(1)–C(8)–C(7)	109.3 (3)	C(1)–C(9)–C(5)	108.1 (3)
C(3)–C(10)–C(7)	110.1 (3)	C(2)–C(11)–C(12)	128.9 (3)
C(11)–C(12)–C(13)	114.5 (3)	C(11)–C(12)–C(19)	110.8 (3)
C(13)–C(12)–C(19)	108.8 (3)	C(11)–C(12)–O(1)	111.7 (3)
C(13)–C(12)–O(1)	102.4 (2)	C(19)–C(12)–O(1)	108.2 (3)
C(12)–C(13)–C(14)	121.5 (1)	C(12)–C(13)–C(18)	118.5 (1)
C(12)–C(19)–C(20)	113.8 (3)	C(19)–C(20)–C(21)	126.5 (4)
C(12)–O(1)–C(22)	120.2 (3)	O(1)–C(22)–O(2)	124.3 (4)
O(1)–C(22)–C(23)	110.4 (3)	O(2)–C(22)–C(23)	125.2 (4)

C(1)–C(2)	1.501 (5)	C(1)–C(8)	1.538 (6)
C(1)–C(9)	1.537 (5)	C(2)–C(3)	1.509 (5)
C(2)–C(11)	1.320 (5)	C(3)–C(4)	1.537 (5)
C(3)–C(10)	1.537 (5)	C(4)–C(5)	1.503 (5)
C(5)–F	1.413 (4)	C(5)–C(6)	1.517 (6)
C(5)–C(9)	1.511 (6)	C(6)–C(7)	1.531 (5)
C(7)–C(8)	1.525 (6)	C(7)–C(10)	1.517 (5)
C(11)–C(12)	1.510 (5)	C(12)–C(13)	1.537 (4)
C(12)–C(19)	1.534 (5)	C(12)–O(1)	1.481 (4)
C(19)–C(20)	1.484 (6)	C(20)–C(21)	1.294 (6)
O(1)–C(22)	1.354 (4)	C(22)–O(2)	1.192 (5)
C(22)–C(23)	1.494 (6)		

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that transition-state σ delocalization provides a satisfying basis for all of the selectivities we have observed with the adamantyl probe, it is not yet clear how strong a contribution this factor can make. thus, the tuning substituent is quite distant from the site of reaction, and we do not know whether placing it nearer that site will reinforce it or whether direct involvement of unshared electrons will alter the outcome. Similarly, it is not yet clear what changes will occur when all vicinal bonds in a position to participate are electron poor. Anh[25] years ago proposed a net electron movement in the opposite direction, from σ^* to the σ^* orbitals of flanking vicinal bonds. Thus, for now the possibility must be kept in mind that selectivities may be reversed if an appropriate probe with electron-poor vicinal bonds can be designed. Perhaps Meyers' recently observed "anti Cieplak" reaction[22a] can be understood on that basis.

Experimental Section

Acetophenone Cyclohexylimine.[16] A solution of acetophenone (12 g, 0.1 mol) and cyclohexylamine (9.9 g, 0.1 mol) in 10 mL of benzene was allowed to reflux overnight, a Dean-Stark trap being used to collect the water formed; 2 mL was collected. Vacuum distillation at 3.5 Torr gave a product boiling at 140–3 °C with a yield of 60% (12.2 g): ^{1}H NMR δ 1.3–1.8 (m, 10), 2.15 (s, 3), 3.44 (m, 1), 7.26 (m, 3), 7.73 (m, 2); ^{13}C NMR δ 14.35, 24.30, 25.36, 33.09, 59.18, 126.07, 127.45, 128.47, 141.16, 161.27.

2-(Benzoylmethyl)adamantan-2-ol (3-H). This solid was prepared from the imine and adamantanone in 56% yield by means of Meyers' procedure;[15] 40% of 2-adamantanol was also formed: ^{13}C NMR δ 27.09 and 27.21 ($C_{5,7}$), 32.44 and 34.63 (C_4, C_{8-10}), 37.19 ($C_{1,3}$), 38.16 (C_6), 43.86 (C_{11}), 74.80 (C_2), 127.92 and 128.52 ($C_{o,m}$), 133.35 (C_p), 137.53 (C_i), 202.08 (CO).

2-(Benzoylmethylidene)adamantane (4-H). Dehydration of this alcohol gave the enone as follows: 775 mg (2.87 mmol) in 15 mL of a mixture of acetic acid and acetic anhydride (85/15) was treated with a 1% solution of sulfuric acid in acetic acid (3 mL) at room temperature;[26] the reaction was complete in 30 min. After workup and silica gel chromatography (CH_2Cl_2), the enone was obtained in 56% yield (as well as a substantial amount of the acetate of the starting alcohol): ^{1}H NMR δ 1.8–2.1 (m), 2.54 (bs, 1, H_3), 3.93 (bs, 1), 6.60 (s, 1, vinyl H), 7.4 (m, 3, $H_{m,p}$), 7.9 (m, 2, H_o); ^{13}C NMR δ 27.93, 33.53, 36.82, 39.33, 40.36 and 41.84 (C_1, C_{3-6}, and C_9), 114.25 (C_{11}), 128.19 and 128.27 ($C_{o,m}$), 132.12 (C_p), 139.42 (C_i), 171.72 (C_2), 192.24 (CO).

5-(Adamant-2-ylidene)-4-hydroxy-4-phenyl-1-pentene (1-H). The enone 4-H (400 mg, 1.59 mmol) was dissolved in THF (27 mL) and cooled to −78 °C. Allylmagnesium bromide in ether was added slowly under nitrogen. Quenching with aqueous ammonium chloride (2 mL) followed 2 h later. The usual workup gave a residue that was flash chromatographed (CH_2Cl_2 – petroleum ether, 30/70) to give 1-H in 94% yield: ^{1}H NMR δ 1.2–2.0 (m), 2.1 (s, 1, OH), 2.4 (bs, 1, H_1), 2.55 (d, 2, H_{13}), 2.75 (bs, 1, H_3), 5.1–5.2 (m, 2, H_{15}), 5.7–5.8 (m, 2, H_{11}, H_{14}), 7.2–7.5 (m, 5, C_6H_5); ^{13}C NMR, see Table I. Mass spectrum: M^+ calcd 294.1984, found 294.1980.

2-Allyl-2-(benzoylmethyl)adamantane (5-H). A 35% oil dispersion of potassium hydride was washed[27] with dry THF (3 × 3 mL) under nitrogen by means of a syringe; after vacuum drying, 150 mg of dry KH was left. Dry THF (2 mL) was added, followed by 80 mg of the hexadiene 1-H in 3 mL of THF. The mixture was stirred for 3 h at 67 °C, quenched with 5% aqueous ammonium chloride, and extracted with petroleum ether (100 mL). Washing with brine and drying over Na_2CO_3 led to a 42% yield of rearrangement product while 37% of starting material was recovered. A sample of the product was made to undergo the entire procedure once again and quantitatively recovered: ^{13}C NMR δ 27.70 (C_5), 27.80 (C_7), 32.56 ($C_{4,9}$), 33.36 ($C_{8,10}$), 33.49 ($C_{1,3}$), 37.24 (C_{12}), 39.70 (C_6), 41.09 (C_{11}), 41.68 (C_2), 117.37 (C_{21}), 127.58 (C_o), 128.32 (C_m), 132.35 (C_p), 134.89 (C_{20}), 138.85 (C_i), 200.44 (C_{12}). The assignments were based on shift changes upon the addition of Eu(fod)$_3$ ranging from 2 to 24 mol %. Mass spectrum: M^+ calcd 294.1984, found 294.1988.

2-(Benzoylmethyl)-5-fluoroadamantan-2-ols (3-F). To a solution of acetophenone cyclohexylimine (1.14 g, 5.67 mmol) in dry THF (15 mL) under nitrogen, 3.5 mL (6 mmol) of *tert*-butyllithium solution was added slowly by syringe at −78 °C. After being stirred for 20 min, the mixture was allowed 30 min to reach room temperature, then recooled to −78 °C; 5-fluoroadamantan-2-one (160 mg, 0.95 mmol) in dry THF (5 mL) was added. Again, the temperature was allowed to rise to ambient; stirring was continued for 40 h. Oxalic acid (1.13 g, 12.5 mmol) in water and benzene (20 mL each) were added; after 24 h of additional stirring, extraction with ether (3 × 60 mL), successive washings with dilute oxalic acid, sodium bicarbonate, and brine, drying over potassium carbonate, and flash evaporation, the residue was chromatographed (silica gel, 10–30% ethyl acetate in hexane) to give 250 mg (96%) of solid 3-F. ^{13}C NMR showed the C_2 peaks of *E* and *Z* to be in the ratio of 56:44. The NMR peaks were assigned on the basis of their intensities in the case of ^{1}H and of their calculated shifts in the case of ^{13}C. *E* isomer: ^{1}H NMR δ 1.4–2.4 (m, 13), 3.42 (s, 2, H_{11}), 4.41 (s, 1, OH), 7.45 (m, 2, H_m), 7.65 (m, 1, H_p), 7.95 (m, 2, H_o); ^{13}C NMR δ 29.97 (C_7, J_{CF} = 10.6 Hz), 30.74 ($C_{8,10}$), 39.06 ($C_{4,9}$, J_{CF} = 18.6 Hz), 39.65 ($C_{1,3}$, J_{CF} = 9.9 Hz), 43.17 (C_6, J_{CF} = 16.5 Hz), 43.43 (C_{11}), 73.43 (C_2), 91.70 (C_5, J_{CF} = 184.2 Hz), 127.89 (C_o), 128.56 (C_m), 133.57 (C_p), 137.09 (C_i), 201.57 (CO). *Z* isomer: ^{1}H NMR δ 1.6–2.7 (m, 13), 3.36 (s, 2, H_{11}), 4.44 (s, 1, OH), 7.5 (m, 2, H_m), 7.7 (m, 1, H_p), 7.95 (m, 2, H_o); ^{13}C NMR δ 30.08 (C_7, J_{CF} = 9.6 Hz), 32.91 ($C_{8,10}$), 37.34 ($C_{4,9}$, J_{CF} = 18.7 Hz), 40.11 ($C_{1,3}$, J_{CF} = 9.9 Hz), 42.90 (C_{11}), 43.07 (C_6, J_{CF} = 19.4 Hz), 73.06 (C_2), 91.48 (C_5, J_{CF} = 182.8 Hz), 127.94 (C_o), 128.67 (C_m), 133.69 (C_p), 137.17 (C_i), 201.73 (CO).

2-(Benzoylmethylidene)-5-fluoroadamantane (4-F). The mixture of alcohols obtained above (375 mg, 1.30 mmol) was treated with a 1% solution of sulfuric acid in acetic acid (2 mL) followed by 6 mL of a mixture of acetic acid and acetic anhydride (85/15). Dissolution occurred within a few minutes; TLC indicated the reaction to be complete in 1 h. Dilution with petroleum ether (100 mL) followed by aqueous workup gave 375 mg of a residue which was chromatographed over silica gel with CH_2Cl_2; the enone was obtained in 81% yield (283 mg). (The acetate of 3-F was isolated in 3% yield (12 mg).) ^{1}H NMR δ 1.8–2.1 (m, 10), 2.35 (bs, 1, H_7), 2.79 (bs, 1, H_3), 4.13 (bs, 1, H_1), 6.63 (s, 1, H_{11}), 7.4 (m, 3, $H_{m,p}$), 7.93 (m, 2, H_o); ^{13}C NMR δ 31.17 (C_7, J_{CF} = 10.1 Hz), 34.85 (C_3, J_{CF} = 10.3 Hz), 37.81 (C_{10}), 38.84 (C_8), 41.92 (C_4, J_{CF} = 16.9 Hz), 42.80 (C_9, J_{CF} = 18.6 Hz), 43.36 (C_1, J_{CF} = 10.6 Hz), 43.69 (C_6, J_{CF} = 18.5 Hz), 91.16 (C_5, J_{CF} = 184.7 Hz), 115.75 (C_{11}), 128.19 and 128.38 ($C_{o,m}$), 132.48 (C_p), 138.84 (C_i), 165.77 (C_2), 191.91 (CO).

5-(5-Fluoroadamant-2-ylidene)-4-hydroxy-4-phenyl-1-pentene (1-F). The enone (305 mg, 1.13 mmol) was converted into 1-F in exactly the same way as the parent compound described earlier. Chromatography gave two liquid isomers in amounts of 175 and 168 mg, respectively (overall yield 97%). Major isomer (*RR*): ^{1}H NMR δ 1.3–2.0 (m, 10), 2.12 (s, 1, OH), 2.26 (bs, 1, H_7), 2.57 (d, 2, H_{13}, J_{HH} = 7.24 Hz), 2.63 (bs, 1, H_1), 3.02 (bs, 1, H_3), 5.1 (m, 2, H_{15}), 5.71 (s, 1, H_{11}, 7.2–7.4 (m, 5, H_{Ph}); ^{13}C NMR, see Table I. Minor isomer (*RS*): ^{1}H NMR δ 1.1–1.3 (m, 2, H_{10}), 1.6–2.2 (m, 9), 2.12 (s, 1, OH), 2.15 (bs, 1, H_7), 2.58 (d, 2, H_{13}, J_{HH} = 7.29 Hz), 2.62 (bs, 1, H_1), 3.07 (bs, 1, H_3), 5.1 (m, 2, H_{15}), 5.7 (m, 1, H_{14}), 5.70 (s, 1, H_{11}), 7.2–7.4 (m, 5, Ph); ^{13}C NMR, see Table I.

Acetylation of Major Alcohol 1-F. A solution was made of the major isomer of 1-F (56 mg, 0.19 mmol) and 4-(dimethylamino)pyridine (30 mg, 0.24 mmol) in 2 mL of triethylamine, and 0.15 mL of acetic anhydride was added at room temperature under nitrogen. TLC indicated formation of the acetate ester to the extent of about 30% in 2 days, and about 60% in 9 days. After concentration to small volume, the residue was chromatographed on a small silica gel column with 2–4% ethyl acetate in hexane. A triene (6 mg) was obtained, followed by the acetate (15 mg, white

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solid) and starting alcohol (20 mg). The ester was further purified by chromatography over aluminum oxide gel with 5% ethyl acetate in hexane. Slow crystallization from benzene yielded crystals suitable for X-ray diffraction: ^{1}H NMR δ 1.2–2.2 (m), 2.21 s, 3, H_{Ac}), 2.65 (bs, 2, H_{13}), 2.76 (dd, 1, H_{13}, J_{gem} = 13.7 Hz, $J_{H^{13}-H^{14}}$ = 6.6 Hz), 3.17 (dd, 1, H_{13}, J_{gem} = 13.7 Hz, $J_{H^{13}-H^{14}}$ = 7.8 Hz), 4.90 (m, 2, H_{15}), 5.30 (m, 1, H_{14}), 5.81 (s, 1, H_{11}), 7.2–7.3 (m, 5, Ph); ^{13}C NMR δ 21.94 (C_{CH_3}), 31.15 (C_7, J_{CF} = 8.92 Hz), 34.84 (C_3, J_{CF} = 11.1 Hz), 36.70 (C_{10}), 38.04 (C_8), 40.77 (C_4, J_{CF} = 18.4 Hz), 42.05 (C_1, J_{CF} = 11.5 Hz), 42.07 (C_9, J_{CF} = 15.8 Hz), 43.46 (C_6, J_{CF} = 17.4 Hz), 45.94 (C_{19}), 83.39 (C_{12}), 91.76 (C_5, J_{CF} = 183.7 Hz), 118.62 (C_{21}), 123.53 (C_{11}), 125.84 (C_o), 126.87 (C_p), 127.69 (C_m), 132.28 (C_{20}), 144.00 (C_i), 147.96 (C_2), 168.60 (CO).

2-Allyl-2-(benzoylmethyl)-5-fluoroadamantanes (5-F). Both isomers were subjected to rearrangement exactly as described for the parent alcohol 1-H; with the major alcohol, 150 mg was used with 265 mg of KH, and with the minor one, 144 mg was employed with 247 mg of KH. The temperature was 67 °C. ^{1}H NMR integration of the (CH_2CO) signals at δ 3.18 and 3.21 showed that the major isomer (*RR*) gave a ratio of 36/64 and the minor one (*RS*) gave a ratio of 81/19. Both mixtures were purified by chromatography (silica gel, 50% methylene chloride in petroleum ether, R_f = 0.33); this did not affect these ratios. ^{1}H NMR δ 1.4–2.3 (m, 2 × 13), 2.59 (d, J_{HH} = 6.6 Hz, 2, $H_{13(Z)}$), 2.62 (d, J_{HH} = 6.6 Hz, 2, $H_{13(E)}$), 3.18 (s, 2, $H_{11(E)}$), 3.21 (s, 2, $H_{11(Z)}$), 4.92 (m, 2 × 2, H_{15}), 5.69 (m, 2 × 1, H_{14}), 7.4–7.9 (m, 2 × 5, Ph); ^{13}C NMR (values in parentheses are those calculated for the adamantyl carbons on the basis of additivity, see text). *E* isomer: δ 30.56 (C_7, 30.85, J_{CF} = 8.7 Hz), 31.61 ($C_{8,10}$, 31.39), 36.62 ($C_{1,3}$, 36.54, J_{CF} = 8.7 Hz), 37.15 (C_{19}), 37.56 ($C_{4,9}$, 37.47, J_{CF} = 17.7 Hz), 40.26 (C_{11}), 40.59 (C_2, 39.71), 44.48 (C_6, 44.61, J_{CF} = 16.8 Hz), 92.04 (C_5, 91.87, J_{CF} = 183.2 Hz), 118.06 (C_{21}), 127.55 (C_o), 128.41 (C_m), 132.59 (C_p), 133.90 (C_{20}), 138.46 (C_i), 199.73 (CO). *Z* isomer: δ 30.52 (C_7, 30.75, J_{CF} = 9.0 Hz), 30.87 ($C_{8,10}$, 30.59), 36.73 ($C_{1,3}$, 36.54, J_{CF} = 8.3 Hz), 36.49 (C_{19}), 38.31 ($C_{4,9}$, 38.27, J_{CF} = 17.7 Hz), 40.86 (C_{11}), 40.65 (C_2, 39.71), 44.48 (C_6, 44.61, J_{CF} = 16.8 Hz), 92.22 (C_5, 91.97, 185.1 Hz), 117.95 (C_{21}), 127.55 (C_o), 128.41 (C_m), 132.59 (C_p), 134.27 (C_{20}), 138.46 (C_i), 199.73 (CO).

X-ray Diffraction Study of Major Acetate. The compound decomposes upon exposure to X-rays and several crystals were required for data collection. The colorless crystals were mounted on a Nicolete R3M/μ update of a $P2_1$ diffractometer. Unit cell dimensions were obtained from a least-squares refinement of 21 low-angle reflections. Crystal decomposition occurred before accurate parameters could be obtained. Crystal data: $C_{23}H_{27}O_2F$; M_r = 354.47, monoclinic; $P2_1/n$; a = 10.706 (4), b = 9.171 (3), c = 19.509 (6) Å; β = 90.32 (3)°; V = 1916 (1) Å^3; Z = 4; D_x = 1.230 g cm^{-3}; μ = 0.90 cm^{-1}; $F(000)$ = 760. Intensity data were collected by the ω-scan technique ($3 \le 2\theta \le 45°$) with a variable scan rate (4 to 29.3° min^{-1}) using graphite-monochromated radiation (Mo Kα, λ = 0.710 73 Å). The various data sets were corrected for decomposition and were scaled together by a least-squares procedure. A total of 2846 reflections yielded 2485 independent reflections (R_{int} = 0.012) of which 1690 had intensities greater than $3\sigma(I)$. Lorentz and polarization corrections were made but no absorption corrections were applied. The structure was solved by direct methods and refined by a block-cascade least-squares technique. The phenyl ring was refined as a rigid body and hydrogen atoms of the phenyl and methyl groups were allowed to ride on the attached atoms. The structure was refined to R = 0.0615 and wR = 0.0560 with 302 parameters and 1690 reflections giving S = 1.451, $(\Delta/\sigma)_{max}$ = 0.025, and the largest peaks in a final difference map of −0.20 and 0.22 e Å^{-3}. The function $\sum w(|F_o| - |F_c|)^2$ was minimized with $w = [\sigma^2(F_o) + 0.00037F_o^2]^{-1}$. All programs were supplied by Nicolet Instrument Corp. for Desktop 30 Microeclipse and Nova 4/C configuration with atomic scattering factors and anomalous dispersion corrections from *International Tables for X-ray Crystallography*.[28]

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Supplementary Material Available: Tables of atomic coordinates, isotropic thermal parameters, and anisotropic thermal parameters for (*RR*)-1-F acetate (3 pages); structure factor tables for (*RR*)-1-F acetate (15 pages). Ordering information is given on any current masthead page.

(28) *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, 1974; Vol. 4 (present distributor Kluwer Academic Publisher: Dordrecht). Nicolet Instrument Corp. (1986), SHELXTL for Desktop (Microeclipse): PN-269-1040340, April.