Face Selection in Claisen Rearrangements

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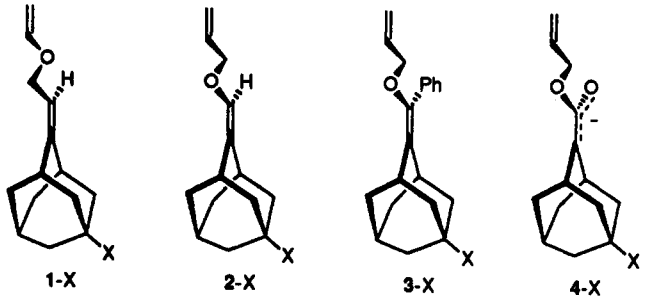
An investigation is reported of the stereochemistry of the Claisen rearrangement of 2-(5-phenyl-2-adamantylidene)ethyl vinyl ether (1-Ph) and of allyl (5-fluoro-2-adamantylidene)methyl ether (2-F). Both ethers undergo the rearrangement principally with the newly forming bond at the *zu* face (*i.e.*, *syn* to the 5-substituent), showing that this bond in the transition state is electron deficient from the standpoint of *both* termini. The two derivatives of the latter ether in which the one remaining hydrogen has been replaced by a phenyl group or an oxide anion function (3-F and 4-F) were also examined. In these two instances as well, the *zu* face of the vinyl terminus is favored; in all four cases, the ratio of stereoisomers is in the range of 1.33 to 1.56. The introduction of a negative charge at this terminus evidently fails to bring about the onset of the type of delocalization envisioned in the Anh model. Taken together with the oxy-Cope and allyl vinyl sulfoxide rearrangements studied earlier, these [3,3] sigmatropic shifts all exhibit a remarkably uniform face selectivity.

As noted in the preceding paper,[1] our studies of the electronic factor involved in the stereochemistry of bond formation (addition) and cleavage (elimination) have taken advantage of two special features characterizing the derivatives of 5-substituted adamantanone used as our probes: their rigidity and their virtually perfect facial equality in the steric domain. A summary of these studies has appeared elsewhere;[2] they include a number of pericyclic reactions[3] such as cycloadditions and -reversions[4] and [3,3] sigmatropic shifts such as the oxy-Cope[5] and allyl vinyl sulfoxide rearrangements.[6] All of the stereochemistry observed has been accounted for by the simple rule that the favored approach is that antiperiplanar to the more electron-rich vicinal bonds: C_1–C_8 and C_3–C_{10} if X is an electron-withdrawing group and C_1–C_9 and C_3–C_4 if it is a σ donor. In particular, we were interested in the questions, first, whether the newly forming bond appears to be electron deficient from the point of view of *both* termini and, secondly, whether the stereochemistry would show a pronounced shift in the direction of the Anh sense[1] if the vinyl terminus is negatively charged. The substrates used in this study were 1–4-X. We originally planned to have X = H and X = F in all four cases; however, we were unable to obtain 1-F and had to settle for 1-Ph instead. Our previous studies[7] show that both fluoro and phenyl behave as electron-withdrawing substituents, so that this discontinuity did not present a serious problem.



Syntheses. Compounds 1-H and 1-Ph were prepared via the route outlined in Scheme 1; the trans-etherification was the step that failed during the attempted formation of 1-F.

Compounds 2-X were prepared as shown in Scheme 2. As in the first step of the previous scheme, two stereoisomers form, presently in the reactions leading to 10-F and 11-F. The *syn* approach products are modestly dominant; however, as we had studied these reactions in detail before,[2] no special effort was made to determine the isomer ratios on the way to the racemic allyl vinyl ethers 1-Ph and 2-F.

The preparation of 3-H and 3-F is given in Scheme 3; again, the isomer ratios in the first step have been studied previously.[1]

Finally, the route to 4-X was the same as that for 2-X except that 11-X was oxidized to acids 16-X prior to the formation of allyl esters 17-X. The esters were treated with sodium hydride to give anions 4-X and rearranged in that form to acids 18-X. Methyl esters 19-X were prepared in the last step to facilitate analysis (see Scheme 4).

Rearrangement Studies. The ^{13}C NMR spectrum of aldehyde 9-H obtained in the Claisen rearrangement of ether 1-H was examined in chloroform solution containing various concentrations of the shift reagent Eu(fod)$_3$. The $C_{4,9}$ and $C_{8,10}$ pairs (readily recognized by means of attached-proton spectra and previous experience) are distinguished by steeply different sensitivities to the shift reagent; the slopes indicating the response of δ to increasing concentrations of the shift reagent differ by almost 50%. Thus the more sensitive carbons are assigned as $C_{8,10}$. The mixture of *E*- and *Z*-9-Ph was investigated similarly. This

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(7) Cheung, C. K.; Tseng, L. T.; Lin, M.-h.; Srivastava, S.; le Noble, W. J. *J. Am. Chem. Soc.* 1986, *108*, 1598; 1987, *109*, 7239. It may at first sight seem surprising that phenyl and fluoro are similar in electron-withdrawing power. We attribute this to the fact that the phenyl group exerts its effect by means of the sp^3–sp^2 bond by which it is held at C5, without any possibility of back-donation via the π orbitals. As pointed out by Adcock and Trout, even *p*-aminophenyl behaves as an electron-withdrawing group in this connection: Adcock, W.; Trout, N. A. *J. Org. Chem.* 1991, *56*, 3229. See also: Li, H.; le Noble, W. J. *Tetrahedron Lett.* 1990, *31*, 4391.

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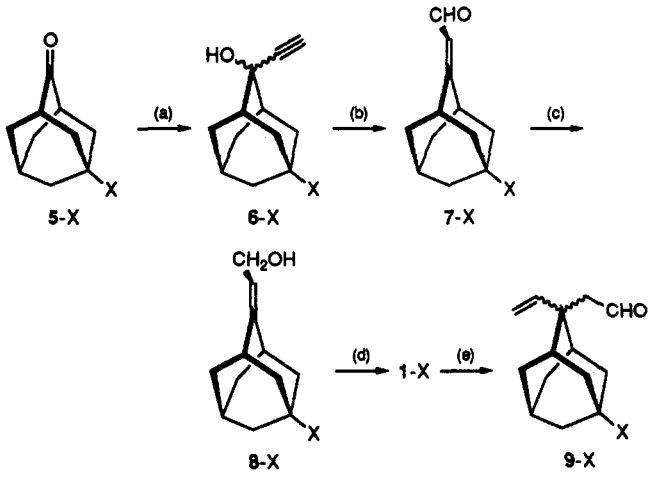
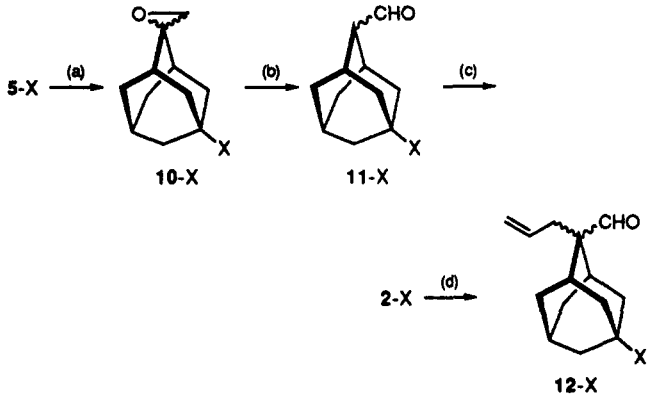
Scheme 1[a]



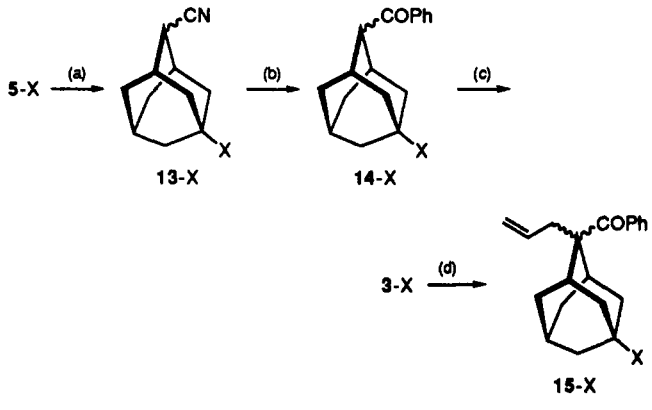
[a] (a) C_2H_2 and $NaNH_2$ in NH_3 (l); (b) refluxing in moist HCOOH; (c) $NaBH_4$; (d) $EtOCH{=}CH_2$ and $Hg(OAc)_2$; (e) neat, 150 °C, 5 h.

Scheme 2[a]



[a] (a) $Me_3SO^+I^-$, NaOH; (b) $BF_3{\cdot}OEt_2$, C_6H_6; (c) NaH, DMF, allyl bromide; (d) 170 °C, 2.5 h.

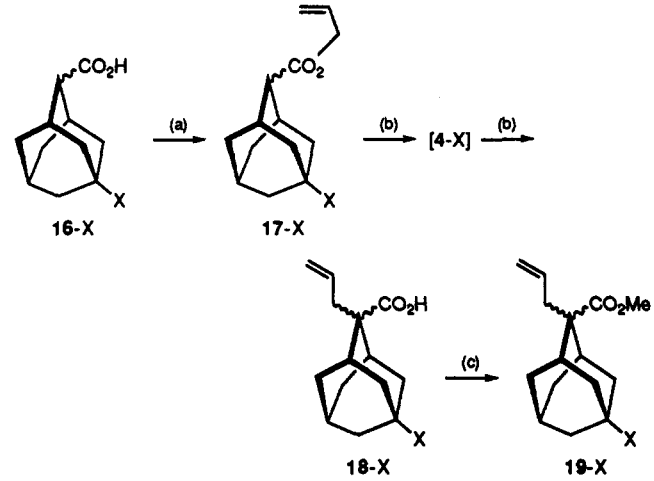
Scheme 3[a]



[a] (a) $TosCH_2NC$, *t*-BuOK, DME; (b) PhLi in Et_2O; (c) NaH, DMF, allyl bromide; (d) 170 °C, 0.5 h.

mixture exhibited four peaks of which two responded more strongly than the other two to the shift reagent. The sensitive pair must be $C_{4,9}$ of one isomer (*E*) and $C_{8,10}$ of the other (*Z*), whereas the relatively insensitive pair represents $C_{8,10}$ in the former isomer and $C_{4,9}$ in the latter. Integration of these four peaks with 10-s pulse delays showed the isomers to be present in the *E*/*Z* ratio of 57:43. In further confirmation of the assignment, the chemical shifts of these two signals in both isomers were calculated

Scheme 4[a]



[a] (a) NaH, DMF, allyl bromide; (b) NaH, PhMe, 110 °C, 24 h; (c) CH_2N_2, Et_2O.

from the corresponding signals in 9-H, 1-phenyladamantane, and adamantane itself, and excellent agreement was found.

The analysis of the mixture of *E*- and *Z*-12-F differed in that the ratio of isomers was based on the integration of the two signals seen in the ^{19}F spectrum; a pulse delay of 30 s was employed. The result was 61:39 (*E*:*Z*). The assignment was based on a shift reagent analysis of the ^{13}C NMR spectra as before; the fact that the $C_{4,9}$ signals are strongly split by the nearby ^{19}F was very helpful in this assignment. The analysis of the mixture of *E*- and *Z*-15-F was entirely similar and gave a result of 59:41, respectively; the mixture of *E*- and *Z*-acids 18-F was also carried out in this manner, and gave a result of 58:42.

Although all four of the reactions studied produced within the usual error limits of 1–2% the same result of 1.43 ± 0.07, there are two noteworthy aspects of this finding. One of these is related to the fact that 1 and 2 have the adamantylidene reporter placed at opposite ends of the 1,5-diene system, and in that way they furnish information about the electronic nature of the incipient bond at both termini. A contrary indication would have been very difficult to square with the view that transition-state hyperconjugation, whether in the Anh or Cieplak sense, is responsible for the observed stereochemistry. While a great deal of work has been devoted to the stereochemistry of pericyclic reactions in many laboratories, little information is as yet available on precisely this question (*i.e.*, the relative electron demands at the two termini). The Diels–Alder reaction is perhaps the only exception.[4]

The other conclusion that can be drawn from this work is that when neutral and anionic Claisen rearrangements are compared, reversal of stereochemistry is not observed. As discussed in the preceding paper, such a reversal would be anticipated if a high charge density at the terminus were to determine whether hyperconjugation in the Anh direction might overshadow that in the Cieplak sense in that case. In fact, the isomer ratios are virtually the same. We conclude from this finding and others such as those detailed in the preceding paper that newly forming bonds are apparently always electron deficient and stabilized through hyperconjugative participation by antiperiplanar vicinal bonds.

Experimental Section

2-(2-Adamantylidene)ethyl Vinyl Ether (1-H). 2-Adamantylideneacetaldehyde (7-H) was prepared as described:[8] white solid, mp 56.5–57.5 °C (lit.[8] mp 55–57 °C); ^{1}H NMR ($CDCl_3$) δ 10.02 (bs, 1H), 5.81 (bs, 1H), 3.64 (s, 1H), 2.55 (s, 1H), 2.0–1.9 (m, 12H). This material (1.6 g, 9 mmol) was reduced in 99% yield with sodium borohydride (0.7 g, 18 mmol) in 2-propanol to give 2-adamantylideneethanol (8-H) as a colorless liquid: MS, *m/z* (rel intensity) 178 (M^+, 16), 160 (10), 149 (61), 135 (56), 91 (65), 79 (100); ^{1}H NMR ($CDCl_3$) δ 5.18 (t, 1H, *J* = 6.6 Hz), 3.99 (d, 2H, *J* = 7.2 Hz), 3.51 (bs, 1H), 2.73 (s, 1H), 2.24 (s, 1H), 1.82–1.63 (m, 14H); ^{13}C NMR ($CDCl_3$) δ 150.55, 115.54, 57.18, 39.96, 39.23, 38.56, 36.76, 31.94, 28.12. The alcohol was converted into the title compound 1-H by the method of Church.[9] In preparation, ethyl vinyl ether was washed free of stabilizer with cold 2 N hydrochloric acid and extracted with 2 N sodium hydroxide. After drying over anhydrous sodium carbonate, it was distilled over sodium and stored in the dark at 0 °C until use.[10] The ether was then used to dissolve mercuric acetate (1.5 g, recrystallized from ethanol containing 0.02% glacial acetic acid) and 8-H (1.0 g, 5.6 mmol). The solution was heated under reflux in a nitrogen atmosphere for 16 h, cooled, and treated with glacial acetic acid (0.2 mL). After stirring (3 h) at room temperature, the reaction mixture was diluted with an equal volume of petroleum ether (30–60 °C), washed with 5% aqueous sodium hydroxide (15 mL), and dried over anhydrous potassium carbonate. After removal of the solvent, the residue was chromatographed with alumina and light petroleum ether to give 1-H (0.9 g, 78%) as a colorless, mobile liquid: MS, *m/z* (rel intensity) 204 (M^+, 4), 191 (3), 175 (15), 161 (100), 135 (45), 91 (81), 84 (100); ^{1}H NMR ($CDCl_3$) δ 6.48 (dd, 1H, *J* = 6.6, 10.8 Hz), 5.29 (t, 1H, *J* = 6.9 Hz), 4.24–4.18 (m, 3H), 4.00 (d, 1H, *J* = 6.9 Hz), 2.84 (s, 1H), 2.41 (s, 1H), 1.96–1.72 (m, 12H); ^{13}C NMR ($CDCl_3$) δ 154.92, 151.72, 111.37, 86.56, 63.84, 40.42, 39.65, 38.98, 37.11, 32.62, 28.41.

(2-Vinyladamant-2-yl)acetaldehyde (9-H). Ether 1-H (50 mg) was heated in a sealed tube under nitrogen to 150 °C for 5 h. The light yellow liquid product was chromatographed with Florisil and light petroleum ether to give a small amount of unreacted 1-H; further elution with the same solvent containing 10% ether afforded 9-H (35 mg, 70%) as a colorless, mobile liquid: MS, *m/z* (rel intensity) 204 (M^+, 6) 175 (M^+ – CHO, 10), 161 (34), 148 (15), 135 (39), 105 (35), 91 (79), 79 (100); ^{1}H NMR ($CDCl_3$) δ 9.70 (t, 1H, *J* = 3.0 Hz), 5.89 (dd, 1H, *J* = 11.1, 18.0 Hz), 5.39 (d, 1H, *J* = 11.1 Hz), 5.08 (d, 1H, *J* = 18.0 Hz), 2.61 (d, 2H, *J* = 2.7 Hz), 2.10–1.54 (m, 14H); ^{13}C NMR ($CDCl_3$) δ 203.84, 145.69, 114.44, 50.85, 44.21, 38.74, 34.67, 33.16, 32.37, 27.74, 27.50.

2-Ethynyl-5-fluoroadamantan-2-ol (6-F). This compound was prepared in 70% yield by ethynylation of the adamantanone (5-F)[7] in the same way as the parent ketone: mp 106–108 °C; MS, *m/z* (rel intensity) 194 (M^+, 1), 168 (33), 168 (33), 166 (42), 151 (22), 137 (26), 110 (58), 97 (100).

[2-(5-Fluoroadamantylidene)]acetaldehyde (7-F). This compound, obtained by the same route as the parent compound, was sublimed to give a white pasty solid in 76% yield: MS, *m/z* (rel intensity) 194 (M^+, 6), 174 (15), 134 (100), 120 (37), 105 (75), 95 (71); ^{1}H NMR ($CDCl_3$) δ 9.91 (d, 1H, *J* = 8.1 Hz), 5.80 (d, 1H, *J* = 8.1 Hz), 3.76–1.70 (m, 13H).

[2-(5-Fluoroadamantylidene)]ethanol (8-F). This compound was obtained as a colorless liquid in 86% yield by reduction of 7-F with sodium borohydride in 2-propanol. ^{1}H NMR $CDCl_3$ δ 5.31 (t, 1H, *J* = 7.0 Hz), 4.12–3.88 (m, 3H), 3.00 (s, 1H), 2.53 (s, 1H), 2.19–1.16 (m, 11H).

Attempted Preparation of 2-[2-(5-Fluoroadamantylidene)]ethyl Vinyl Ether (1-F). Application of the procedure used for the parent compound 1-H completely consumed alcohol 8-F but none of the spectra of the product(s) gave any hint of the presence of 1-F.

[2-(5-Phenyladamantylidene)]acetaldehyde (7-Ph). This compound was obtained in 77% yield by hydration of the previously described ethynol[11] in 98% formic acid as detailed for the parent aldehyde. Sublimation gave white solid 7-Ph in 83% yield: mp 94 °C; MS, *m/z* (rel intensity) 252 (M^+, 6), 226 (3), 155 (18), 134 (100), 105 (80), 91 (87); ^{1}H NMR ($CDCl_3$) δ 10.09 (d, 1H, *J* = 8.4 Hz), 7.37–7.23 (m, 5H), 5.92 (d, 1H, *J* = 8.1 Hz), 3.82 (s, 1H), 2.75 (s, 1H), 2.30–2.00 (m, 11H).

2-[2-(5-Phenyladamantylidene)]ethanol (8-Ph). This colorless liquid was obtained in 98% yield by reduction of 7-Ph with sodium borohydride in 2-propanol: MS, *m/z* (rel intensity) 254 (M^+, 5), 238 (14), 167 (12), 155 (28), 107 (47), 91 (100); ^{1}H NMR ($CDCl_3$) δ 7.40–7.23 (m, 5H), 5.46 (t, 1H, *J* = 7.2 Hz), 4.23 (d, 2H, *J* = 7.2 Hz), 3.11 (bs, 1H), 2.62 (bs, 1H), 2.11–1.93 (m, 11H); ^{13}C NMR ($CDCl_3$) δ 128.16, 125.73, 124.79, 116.06, 58.26, 53.40, 44.91, 44.37, 42.49, 40.61, 38.82, 38.26, 32.64, 29.09 (quaternary carbon not observed).

2-[2-(5-Phenyladamantylidene)]ethyl Vinyl Ether (1-Ph). The preparation was the same as for the parent ether 1-H; it gave a mobile liquid in 67% yield after chromatography with neutral alumina and light petroleum ether: MS, *m/z* (rel intensity) 280 (M^+, 1), 254 (19), 155 (53), 117 (33), 91 (100); ^{1}H NMR ($CDCl_3$) δ 7.40–7.22 (m, 5H), 6.53 (dd, 1H, *J* = 14.4, 6.9 Hz), 5.41 (t, 1H, *J* = 6.9 Hz), 4.32–4.23 (m, 3H), 4.06 (d, 1H, *J* = 6.9 Hz), 3.05 (s, 1H), 2.63 (s, 1H), 2.23–1.85 (m, 11H); ^{13}C NMR ($CDCl_3$) δ 152.33, 151.66, 149.88, 128.16, 125.70, 124.78, 112.13, 86.69, 63.86, 44.91, 44.26, 42.55, 40.68, 38.82, 38.12, 36.59, 32.93, 29.12.

[2-(5-Phenyl-2-vinyladamantyl)]acetaldehyde (9-Ph). Vinyl ether 1-Ph (80 mg) was sealed in a tube under nitrogen and heated to 150 °C for 5 h. The light yellow product was chromatographed with Florisil and light petroleum ether to give a trace of the unreacted starting material. Further elution with the same solvent containing 10% ether afforded a 94% yield of a mixture of *E*- and *Z*-aldehydes 9-Ph as a colorless, mobile liquid: MS, *m/z* (rel intensity) 280 (M^+, 6), 251 (3), 238 (33), 224 (4), 195 (4), 167 (12), 155 (25), 115 (25), 91 (100); ^{1}H NMR ($CDCl_3$) δ 10.28 and 10.25 (2s, 1H), 7.92–7.71 (m, 5H), 6.55–6.41 (m, 1H), 5.91–5.64 (m, 2H), 3.22–3.18 (m, 2H), 2.84–1.79 (m, 13H); ^{13}C NMR ($CDCl_3$) δ 203.42, 150.27, 150.07, 145.32, 145.03, 128.22, 128.13, 125.82, 125.70, 114.94, 114.87, 50.88, 50.53, 44.62, 44.29, 43.59, 43.53, 38.65, 37.84, 35.99, 35.95, 35.45, 35.28, 32.35, 31.57, 28.39, 28.14.

NMR Analyses of 9-H and the Mixture of 9-Ph. A solution of 0.164 g of Eu(fod)$_3$ in $CDCl_3$ (1 mL) was prepared and 250-mL portions of this solution were added to an NMR tube containing 35 mg of 9-H, also in $CDCl_3$. After each addition, nitrogen was passed into the tube to reduce the level of the liquid to its original position. This process was repeated four times. ^{1}H and ^{13}C NMR spectra were taken after each such treatment. The chemical shifts observed were plotted against the amount of shift reagent added. The slope of the signal at δ 33.16 is about 50% smaller than that at δ 32.37; the former is therefore assigned to $C_{4,9}$ (*syn* to vinyl) and the latter to $C_{8,10}$. A similar study with a mixture of the two isomers of 9-Ph showed that among the peaks at δ 38.65, 37.84, 32.35, and 31.57, the first and last had nearly identical slopes about 50% larger than those of the second and third peaks which were nearly identical to each other. The first two must therefore correspond to the methylene carbons "underneath" the aldehyde carbon, and the other pair represents the methylene carbons "underneath" the vinyl group. When these results are matched with the calculated values, we conclude that the four peaks represent $C_{4,9}$ in *Z*- and *E*-9-Ph, and $C_{8,10}$ in *E*- and *Z*-9-Ph, respectively. The average agreement between observed and calculated chemical shifts equals about 0.13 ppm; no other combination of assignments comes close to this conformity (thus, if the assignments of $C_{4,9}$ and $C_{8,10}$ had been reversed in both 9-H and 9-Ph, the average agreement would have amounted to almost 1 ppm). Finally, a 40-mg sample of unpurified mixed 9-Ph was used for quantitative analysis by means of heteronuclear inverse gated decoupling and a 10-s pulse delay; all four of the above-mentioned peaks were integrated to give an *E*/*Z* ratio of 57:43.

Adamantanespirooxirane (10-H).[6] A solution of adamantanone (1.0 g, 6.6 mmol), trimethylsulfoxonium iodide (2.4 g, 10.9 mmol), and sodium hydroxide (1.0 g, 25.0 mmol) in 2-propanol (5 mL) was refluxed for 1 h, cooled, diluted with water (15 mL), filtered, and extracted with hexane. Chromatography with silica

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gel and 3% ethyl acetate in hexane gave the title compound in 85% yield: mp 175–7 °C, lit.[12] mp 179–82 °C; ^{1}H NMR ($CDCl_3$) δ 2.59 (s, 2H), 2.0–1.3 (m, 14H); ^{13}C NMR ($CDCl_3$) δ 64.50, 54.68, 36.93, 36.71, 35.74, 34.93, 26.99, 26.86.

Adamantane-2-carboxaldehyde (11-H).[6] Freshly distilled boron trifluoride etherate (0.304 g, 2.13 mmol) was added to a solution of 10-H (0.55 g, 3.35 mmol) in dry benzene (6.5 mL) in a separatory funnel; the solution was shaken vigorously for 1 min and worked up immediately with water (20 mL) and benzene (5 mL). The aldehyde is not stable and was used in the next step without purification: ^{1}H NMR ($CDCl_3$) δ 9.71 (s, 1H), 2.4–1.5 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 205.83, 56.48, 37.70, 36.90, 33.42, 28.05, 27.81, 27.40.

Adamantylidenemethyl Allyl Ether (2-H). A solution of 11-H (0.10 g, 0.60 mmol) in dry DMF was added dropwise to a suspension of sodium hydride (0.1 g, 4.34 mmol) in the same solvent (5 mL) with stirring. After 4 h, allyl bromide was added dropwise; the mixture was stirred overnight, quenched with water (5 mL), extracted with ether (50 mL), dried over anhydrous magnesium sulfate, and reduced to small volume. After chromatography (silica gel, 5% ethyl acetate in hexane), 2-H was obtained as a colorless liquid in 72% yield: ^{1}H NMR ($CDCl_3$) δ 6.0–5.9 (m, 1H), 5.81 (s, 1H), 5.30–5.17 (dd, 2H), 4.17 (d, 2H), 3.02 (s, 1H), 2.22 (s, 1H), 2.0–1.6 (m, 12H); ^{13}C NMR ($CDCl_3$) δ 135.90, 134.38, 132.99, 116.56, 72.17, 39.74, 38.27, 37.27, 33.97, 29.05, 28.69.

2-Allyladamantane-2-carboxaldehyde (12-H). Ether 2-H (70 mg) was heated under nitrogen to 170 °C for 2.5 h; it rearranged completely to colorless oil 12-H during this period: ^{1}H NMR ($CDCl_3$) δ 9.44 (s, 1H), 5.70–5.50 (m, 1H), 5.10–5.00 (d, 2H), 2.37 (d, 2H), 2.20–1.40 (m, 14H); ^{13}C NMR ($CDCl_3$) δ 207.57, 131.98, 118.07, 54.05, 38.04, 36.66, 34.56, 31.76, 30.55, 27.55.

[2-(5-Fluoroadamantane)]spirooxetane (10-F). The preparation of this compound, starting with 5-F, was the same as that of 10-H; it was obtained in 88% yield as a white solid mixture which was not separated or analyzed: ^{1}H NMR ($CDCl_3$) δ 2.65 (s, 2H), 2.63 (s, 2H), 2.25 (s, 2H), 2.16 (s, 2H), 2.10–1.57 (m, 22H); ^{13}C NMR ($CDCl_3$) δ 90.95 (d, J = 183.5 Hz), 62.79, 62.32, 54.76, 54.02, 42.24 (d, J = 16.6 Hz), 42.13 (d, 16.7 Hz), 41.14 (d, J = 19.6 Hz), 39.83 (d, J = 18.9 Hz), 38.42 (d, J = 8.31 Hz), 37.63 (d, J = 9.3 Hz), 35.04, 33.34, 30.01 (d, J = 10.2 Hz), 29.86 (d, J = 12.0 Hz).

5-Fluoroadamantane-2-carboxaldehyde (11-F).[6] The isomerization of oxirane 10-F was carried out in the same way as that of 10-H; the mixture of E- and Z-11-F was obtained in 60% yield but not purified or analyzed: ^{1}H NMR ($CDCl_3$) δ 9.67 (s, 1H), 9.65 (s, 1H), 2.63 (bs, 2H), 2.32 (s, 2H), 2.01–1.50 (m, 22H).

Allyl [2-(5-Fluoroadamantylidene)]methyl Ether (2-F). This liquid was prepared from the mixture 11-F in 75% yield with conditions the same as those used for the parent compound 2-H: MS, m/z (rel intensity) 222.14 (M^+, 100), 181 (54), 166 (25), 163 (28), 153 (42), 143 (22), 109 (32), 105 (28); HRMS calcd 222.1420, obsd 222.1418; ^{1}H NMR ($CDCl_3$) δ 6.0–5.8 (m, 1H), 5.81 (s, 1H), 5.40–5.15 (m, 2H), 4.20–4.17 (d, 2H), 3.29 (s, 1H), 2.51 (s, 1H), 2.31 (s, 1H), 2.0–1.5 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 141.45, 134.53, 134.27, 116.98, 90.18 (d, J = 182.5 Hz), 72.47, 44.27 (d, J = 16.7 Hz), 42.61 (d, J = 17.0 Hz), 38.28, 36.77, 36.30 (d, J = 10.7 Hz), 31.92 (d, J = 10.5 Hz), 31.21 (d, J = 9.9 Hz).

2-Allyl-5-fluoroadamantane-2-carboxaldehyde (12-F). A solution of 2-F (75 mg) in toluene (10 mL) was heated to reflux under nitrogen for 48 h. After removal of the solvent, 12-F was obtained as a mixture of two colorless oils: ^{1}H NMR ($CDCl_3$) δ 9.45 (s, 1H), 9.42 (s, 1H), 5.65–5.45 (m, 2H), 5.2–5.0 (m, 4H), 2.5–1.4 (m, 32H); ^{13}C NMR ($CDCl_3$) δ 205.88, 205.28, 131.41, 131.04, 118.80, 118.62, 90.17 (d, J = 183 Hz), 43.06 (d, J = 17.0 Hz), 39.50 (d, J = 18.6 Hz), 36.88 (d, J = 18.5 Hz), 36.55, 35.86, 33.76 (d, J = 10.0 Hz), 33.21 (d, J = 10.2 Hz), 32.86, 30.98 (d, J = 10.5 Hz), 30.87 (d, J = 10.2 Hz), 30.12. By means of experiments such as those described above involving the use of the shift reagent Eu(fod)$_3$, it was established that the E-isomer's $C_{4,9}$ and $C_{8,10}$ signals are those at δ 36.88 and 32.86, respectively, and that the corresponding carbons of the Z-isomer appear at δ 39.50 and 30.12. Both ^{13}C and ^{19}F NMR signal integration (the latter with 30-s pulse delay) showed that the product ratio was 61:39, with the E-isomer in excess.

α-(2-Adamantylidene)benzyl Allyl Ether (3-H). 2-Cyanoadamantane (13-H) was prepared as described:[13] mp 180–2 °C, lit.[13] mp 181–2 °C; ^{1}H NMR ($CDCl_3$) δ 2.90 (s, 1H), 2.25–1.75 (m, 14H); ^{13}C NMR ($CDCl_3$) δ 122.26, 36.99, 36.68, 36.60, 33.05, 30.35, 26.87, 26.72. This compound was converted into 2-adamantyl phenyl ketone (14-H) as described:[14] mp 91–3 °C, lit.[14] mp 92–4 °C; ^{1}H NMR ($CDCl_3$) δ 7.9–7.2 (m, 5H), 3.35 (s, 1H), 2.6–1.3 (m, 14H); ^{13}C NMR ($CDCl_3$) δ 204.5, 137.16, 131.99, 128.31, 127.93, 52.03, 38.74, 37.37, 32.69, 30.25, 27.89, 27.47. The ketone was converted into the title ether in the same way as was compound 2-H; the liquid product was obtained in 70% yield: ^{1}H NMR ($CDCl_3$) δ 7.24–7.20 (m, 5H), 6.0–5.8 (m, 1H), 5.2–5.0 (m, 2H), 3.88 (d, 2H), 3.25 (s, 1H), 2.59 (s, 1H), 2.0–1.6 (m, 12H); ^{13}C NMR ($CDCl_3$) δ 142.0, 135.61, 134.74, 132.15, 129.39, 127.92, 127.31, 116.97, 70.22, 39.24, 38.95, 37.22, 32.31, 30.29, 28.33.

2-Allyl-2-benzoyladamantane (15-H). Ether 3-H was heated in neat form at 170 °C for 30 min to give colorless liquid product 15-H: ^{1}H NMR ($CDCl_3$) δ 7.8–7.2 (m, 5H), 5.8–5.6 (dd, 2H), 2.78 (d, 2H), 2.42 (d, 2H), 2.2–1.4 (m, 12H); ^{13}C NMR ($CDCl_3$) δ 202.70, 139.92, 133.26, 130.73, 127.95, 127.72, 117.35, 57.35, 38.85, 35.02, 32.40, 32.24, 27.55, 26.85.

2-Cyano-5-fluoroadamantane (13-F). This compound was prepared from ketone 5-F[7] by the van Leusen reaction.[13] A 78% yield was realized; the product was a white solid mixture of E- and Z-isomers which was not separated or analyzed: ^{1}H NMR ($CDCl_3$) δ 3.0–1.4 (m); ^{13}C NMR ($CDCl_3$) δ 120.80, 120.68, 89.95 (d, J = 184.1 Hz), 89.69 (d, J = 183.8 Hz), 41.18 (d, J = 19.3 Hz), 38.18 (d, J = 19.2 Hz), 35.22, 34.99, 34.47, 33.58 (d, J = 9.8 Hz), 33.28 (d, J = 10.3 Hz), 31.18, 29.85 (d, J = 9.6 Hz), 29.63 (d, J = 9.6 Hz).

2-(5-Fluoroadamantyl) Phenyl Ketone (14-F). A 1.8 M solution (2 mL) of phenyllithium was added dropwise to a solution of 13-F (0.20 g, 1.2 mmol) in dry ether (5 mL) over a 15-min period. Stirring was continued for 4 h, 2.5 mL each of acetone and concentrated hydrochloric acid were added, and the mixture was heated to reflux for 4 h. Aqueous workup gave a liquid mixture of the two isomers of 14-F in 78% yield; it was not separated or analyzed: ^{1}H NMR ($CDCl_3$) δ 8.0–7.0 (m, 10H), 3.36 (s, 1H), 3.23 (s, 1H), 2.7–1.0 (m, 26H); ^{13}C NMR ($CDCl_3$) δ 202.50, 140.50, 132.43, 128.67, 128.52, 128.00, 127.91, 127.16, 127.07, 91.92 (d, J = 183.4 Hz), 50.59, 50.34, 43.38 (d, J = 18.9 Hz), 42.56 (d, J = 18.9 Hz), 42.56 (d, J = 16.1 Hz), 42.54 (d, J = 16.7 Hz), 38.2 (d, J = 18.2 Hz), 36.94, 33.79 (d, J = 9.1 Hz), 33.12 (d, J = 10.4 Hz), 31.18 (d, J = 8.8 Hz), 31.12, 30.63 (d, J = 9.0 Hz).

Allyl α-[2-(5-Fluoroadamantylidene)]benzyl Ether (3-F). This compound was prepared from 14-F in the same way as ether 2-H. The yield of this colorless liquid was 65%: MS, m/z (rel intensity) 298 (M^+, 38), 257 (6), 229 (53), 143 (14), 105 (100), 91 (28), 77 (42); HRMS calcd 298.1733, obsd 228.1740; ^{1}H NMR ($CDCl_3$) δ 7.5–7.0 (m, 5H), 5.81 (m, 1H), 5.09 (d, 2H), 3.87 (d, 2H), 3.52 (s, 1H), 2.81 (d, 1H), 2.28 (d, 1H), 1.9–1.5 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 7.5–7.0 (m, 5H), 5.81 (m, 1H), 5.09 (d, 2H), 3.87 (d, 2H), 3.52 (s, 1H), 2.81 (d, 1H), 2.28 (d, 1H), 1.9–1.5 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 142.00, 134.70, 134.53, 133.50, 129.38, 128.12, 127.82, 117.16, 91.51 (d, J = 183.1 Hz), 70.09, 56.25, 56.06, 43.56 (d, J = 19.0 Hz), 43.32 (d, J = 17.9 Hz), 42.48 (d, J = 17.0 Hz), 37.72, 37.37, 34.85 (d, J = 10.1 Hz), 32.56 (d, J = 9.9 Hz), 31.76 (d, J = 9.3 Hz).

2-Allyl-2-benzoyl-5-fluoroadamantane (15-F). Ether 3-F (70 mg) was dissolved in toluene (10 mL) and the solution was heated to reflux for 48 h, during which time it rearranged completely to 15-F as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 7.9–7.1 (m, 10H), 5.75–5.5 (m, 2H), 5.2–5.0 (m, 4H), 2.9–2.7 (m, 8H), 2.4–1.4 (m, 22H); ^{13}C NMR ($CDCl_3$) δ 202.70, 139.29, 138.98, 134.35, 132.70, 132.32, 131.21, 128.16, 127.74, 118.12, 117.91, 91.01 (d, J = 180.0 Hz), 56.25, 56.06, 43.22 (d, J = 17.6 Hz), 39.95 (d, J = 17.7 Hz), 38.74, 38.06, 37.35 (d, J = 17.8 Hz), 35.28 (d, J = 9.9 Hz), 35.09 (d, J = 9.5 Hz), 33.35, 30.75, 30.38 (d, J = 8.9 Hz), 29.94 (d, J = 10.2 Hz). The assignments of configuration were

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based on a shift reagent study as in the case of 12-F and the result was confirmed by means of an additivity calculation; quantitative analyses based on ^{13}C and ^{19}F NMR proceded also exactly as in the case of 12-F. The E/Z ratio equals 59:41 in the present instance.

2-Adamantanecarboxylic Acid (16-H). The acid was prepared by oxidation of aldehyde 11-H with Jones reagent in 80% yield: mp 140–1 °C, lit.[2] mp 140–1 °C; ^1H NMR ($CDCl_3$) δ 2.66 (s, 1H), 2.35 (s, 2H), 1.9–1.6 (m, 12H); ^{13}C NMR ($CDCl_3$) δ 181.57, 49.37, 38.00, 37.26, 33.49, 29.25, 27.33.

Allyl 2-Adamantanecarboxylate (17-H). Allyl bromide (1 mL, 0.83 mmol) was added dropwise to a solution of 16-H (0.20 g, 1.1 mmol) and diisopropylamine (0.25 mL, 2.5 mmol) in a mixture of DMF (3 mL) and HMPA (3 mL), and the mixture was stirred at 35–40 °C overnight. After normal aqueous workup, a colorless liquid product was obtained that was purified by means of chromatography (silica and 3% ethyl acetate in hexane); the yield was 79%: ^1H NMR ($CDCl_3$) δ 6.0–5.8 (m, 1H), 5.4–5.2 (dd, 2H), 4.65–4.55 (d, 2H), 2.61 (s, 1H), 2.33 (s, 1H), 2.0–1.5 (m, 12H); ^{13}C NMR ($CDCl_3$) δ 174.08, 132.48, 117.70, 64.55, 49.49, 38.03, 37.28, 33.44, 29.47, 27.39, 27.33.

Enolate Rearrangement of Ester 17-H. A solution of ester 17-H (0.100 g, 0.60 mmol) in toluene (2 mL) was added dropwise to a suspension of sodium hydride (0.1 g, 4.3 mmol) in dry toluene (10 mL) at room temperature over a 2-h period. The solution was then heated to reflux for 40 h before aqueous workup to give white solid 2-allyladamantane-2-carboxylic acid (18-H): ^1H NMR ($CDCl_3$) δ 11.0–10.0 (bs, 1H), 6.0–5.6 (m, 1H), 5.2–5.0 (m, 2H), 2.6–2.4 (m, 2H), 2.1–1.5 (m, 14H); ^{13}C NMR ($CDCl_3$) δ 172.42, 133.27, 117.37, 52.71, 40.14, 38.43, 35.57, 32.13, 31.83, 27.43, 27.06. The acid was at once converted into its methyl ester which was assumed to be more suitable for shift reagent analysis. An ethereal diazomethane solution was first prepared by gently shaking *N*-methyl-*N'*-nitrosoguanidine (300 mg, 2 mmol) in ether (10 mL) with 40% aqueous potassium hydroxide (3 mL) at 0 °C. The resulting yellow ether solution was added dropwise to a solution of acid 18-H (60 mg, 0.2 mmol), also in ether. After 2 h, the mixture was quenched with a few drops of acetic acid. The colorless liquid ester 19-H was obtained in 95% yield after chromatography (silica gel and 10% ethyl acetate in hexane): ^1H NMR ($CDCl_3$) δ 5.8–5.6 (m, 1H), 5.1–4.95 (d, 2H), 3.65 (s, 3H), 2.47–2.44 (d, 2H), 2.1–1.5 (m, 14H); ^{13}C NMR ($CDCl_3$) δ 172.61, 133.68, 52.88, 50.86, 40.27, 38.53, 35.64, 32.23, 32.10, 27.50, 27.18.

5-Fluoroadamantane-2-carboxylic Acid (16-F). Carboxaldehyde 11-F (0.20 g, 1.2 mmol) in acetone (15 mL) was treated with Jones reagent (23 mL) during 30 min at 20 °C with stirring and occasional cooling. After an additional 2 h, the mixture was poured into water and extracted with chloroform. After workup, the residue was extracted with 1 N aqueous sodium hydroxide, which was then acidified and extracted with chloroform again. The resulting mixture (175 mg) of two acids 16-F was not separated: ^1H NMR ($CDCl_3$) δ 11.0–10.0 (bs, 1H), 3.0–1.0 (m, 14H); ^{13}C NMR ($CDCl_3$) δ 179.31, 91.45 (d, J = 185.1 Hz), 42.14, 47.86, 42.71 (d, J = 18.8 Hz), 42.95, 39.11 (d, J = 18.2 Hz), 36.24, 32.83 (d, J = 8.9 Hz), 32.40 (d, J = 10.2 Hz), 31.94, 30.66 (d, J = 9.5 Hz), 30.49 (d, J = 9.9 Hz).

Allyl 5-Fluoroadamantane-2-carboxylate (17-F). The preparation of this ester was the same as that of the parent compound 17-H: ^1H NMR ($CDCl_3$) δ 6.0–5.8 (m, 1H), 5.3–5.1 (dd, 2H), 4.7–4.5 (d, 2H), 3.0–1.4 (m, 14H); ^{13}C NMR ($CDCl_3$) δ 172.88, 172.81, 132.26, 132.20, 118.00, 117.89, 91.22 (d, J = 183.6 Hz), 64.90, 64.84, 48.20, 47.92, 42.75 (d, J = 18.7 Hz), 42.48 (d, J = 17.6 Hz), 39.00 (d, J = 17.6 Hz), 36.30, 33.02 (d, J = 9.6 Hz), 32.57 (d, J = 10.8 Hz), 31.90, 30.74 (d, J = 9.5 Hz), 30.53 (d, J = 9.9 Hz).

Enolate Rearrangement of Ester 17-F. The reaction was carried out in the same manner as that of 17-H. ^{19}F NMR integration of the two peaks of the crude product 18-F gave the isomer ratio as 58:42: ^1H NMR ($CDCl_3$) δ 11.0–10.0 (bs, 1H), 6.0–5.6 (m, 1H), 5.2–5.0 (m, 2H), 2.6–2.4 (m, 2H), 2.1–1.5 (m, 14H); ^{13}C NMR ($CDCl_3$) δ 182.71, 182.06, 132.63, 132.28, 118.06, 118.00, 91.73 (d, J = 180.3 Hz), 91.38 (d, J = 180.7 Hz), 51.73, 51.57, 43.32, 40.51 (d, J = 18.1 Hz), 40.01, 39.21, 37.12 (d, J = 18.7 Hz), 35.29 (d, J = 9.9 Hz), 34.78 (d, J = 10.2 Hz), 33.89, 30.45, 30.19 (d, J = 9.9 Hz), 30.01 (d, J = 11.1 Hz). The mixture was then converted into the methyl esters 19-F as described above: ^1H NMR ($CDCl_3$) δ 5.8–5.6 (m, 1H), 5.1–4.95 (d, 2H), 3.65 (s, 3H), 2.5–1.5 (m, 14H); ^{13}C ($CDCl_3$) δ 175.67, 175.23, 133.04, 132.68, 117.71, 117.51, 93.32 (d, J = 182.9 Hz), 92.81 (d, J = 183.35 Hz), 51.30, 51.27, 43.33, 40.51 (d, J = 18.2 Hz), 40.11, 39.35, 37.16 (d, J = 18.3 Hz), 35.47 (d, J = 9.9 Hz), 34.97 (d, J = 10.2 Hz), 33.89, 30.49, 30.20 (d, J = 9.9 Hz), 30.06 (d, J = 10.5 Hz). The *Z*-isomer's $C_{4,9}$ and $C_{8,10}$ signals were shown to be those at δ 40.51 and 30.49, respectively, and those of the *E*-isomer are at δ 37.16 and 33.89; these assignments rest on a shift reagent study and on additivity calculation as before. Finally, integration of the carbon signals with 10-s delay between pulses confirmed the ratio measured with ^{19}F NMR and showed that the major isomer had been the *E*-isomer.

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Supplementary Material Available: Copies of ^1H and ^{13}C NMR spectra of new compounds (64 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.