Conformations of Allylic Fluorides and Stereoselectivities of Their Diels−Alder Cycloadditions

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The preparations of new allylic fluorides from the corresponding alcohols are reported. Conformational analysis is achieved by comparison of experimental NMR measurements with theoretical (B3LYP) calculations of relative energies of conformers and $J_{H,H}$ and $J_{H,F}$ coupling constants. The Diels−Alder reactions of allylic fluorides are investigated experimentally and theoretically. The stereoselectivities of the reactions were determined by NMR analysis and, in one case, by X-ray crystallography. Theoretical predictions of stereoselectivity based upon transition state modeling provided good agreement with experiment. Theoretical models for allylic fluorides and transition state conformations are reported.

Introduction

The stereoselectivities of additions to chiral alkenes are of wide interest, both from a mechanistic and synthetic point of view.[1] Introduction of fluorine in organic molecules induces significant modifications of their physical, chemical, and biological properties due to the small size and very high electronegativity of this atom.[2] However, very little is known about the influence of allylic fluorines on addition stereoselectivities. For relatively simple systems suitable for modeling studies, we have found literature reports on the stereoselectivity of an osmylation of a compound containing allylic fluoride[3] and an interesting experimental and theoretical study of epoxidation.[4] General rules to predict the stereochemical outcome of reactions of allylic fluorides would be useful. The lack of regiocontrolled synthetic methods for the preparation of allylic fluorides probably accounts for the surprising lack of information about such systems.

We report here the preparation of new electrophilic alkenes, **1** and **2**, selected as prototypes of allylic fluorides. By use of experiment and quantum mechanical methods, we have explored the conformations of these molecules and the stereoselectivities of their Diels−Alder cycloaddition reactions. These results establish the relative roles of steric and electronic effects on the reaction stereoselectivities of allylic fluorides and provide general rules for the prediction.

Synthesis

The new allylic fluorides, **1** and **2**, were prepared by direct fluorination of corresponding allylic alcohols, as outlined in Schemes 1 and 2. Derivatives **4a**, **4b**,[5] and **4c** are easily obtained in two steps from protected lactaldehyde **3**,[6] while **1d** was prepared from diol **5**.[7] Fluorination of allylic alcohols, **4a**−**4c**, by diethylamino sulfur trifluoride (DAST)[8] is completely regio- and stereocontrolled giving only the *E* isomers **1**, as established by NMR. No allylic transposition was observed.[9] Fluorina-

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(1) See recent *Chemical Reviews* issue for diastereoselection: *Chem. Rev.* **1999**, *5*.

(2) (a) *Chemistry of Organic Fluorine Compounds II*; Hudlicky, M., Pavlath, A. E., Eds.; ACS Monograph 187; American Chemical Society: Washington, DC, 1995. (b) *Experimental Methods in Organic Fluorine Chemistry*; Katazume, T., Yamazaki, T., Eds.; Kodansha: Tokyo, 1998. (c) *Biomedicinal Aspects of Fluorine Chemistry*; Filler, R., Kobayashi, Y., Eds.; Elsevier: Amsterdam, 1982. (d) Mann, J. *J. Chem. Soc.* **1987**, *16*, 381. (e) Welch, J. T. *Tetrahedron* **1987**, 43, 3123. (f) Welch, J. T. *Selective Fluorination in Organic and Bioorganic Chemistry*; ACS Symposium Series 456; American Chemical Society: Washington, DC, 1991. (g) Ojima, I.; McCarthy, J. R.; Welch, J. T. *Biomedical Frontiers of Fluorine Chemistry*; ACS Symposium Series 639; American Chemical Society: Washington, DC. **1996**.

(3) Davis, F. A.; Qi, H.; Sundarababu, G. *Tetrahedron Lett.* **1996**, 37, 4345.

(4) Fujita, M.; Ishizuka, H.; Ogura, K. *Tetrahedron Lett.* **1991**, 32, 6355.

(5) For another synthesis of **4b** see: Busque, P.; De March, P.; Figueredo, M.; Font, J.; Monsalvatde, M.; Virgili, A.; Alvarez-Larena, A.; Piniella, J. F. *J. Org. Chem.* **1996**, *61*, 8578.

(6) Massad, S. K.; Hawkins, L. D.; Baker, D. C. *J. Org. Chem.* **1983**, *48*, 5180.

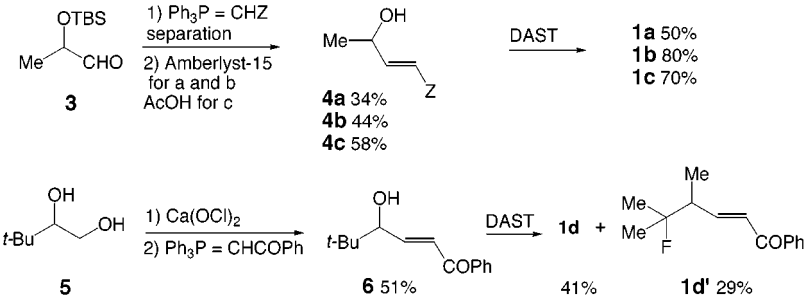
(7) Inokuchi, T.; Matsumoto, S.; Nishiyama, T.; Torii, S. *J. Org. Chem.* **1990**, *55*, 462.

(8) Middleton, W. J. *J. Org. Chem.* **1975**, *40*, 575−578. Hudlicky, M. *Org. React.* **1988**, *35*, 513.

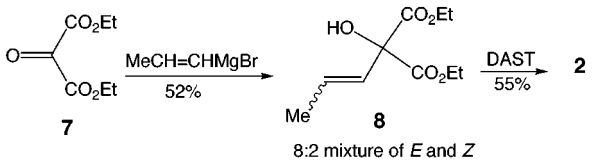
(9) For results on phenyl substituted and polyunsaturated systems, see: Boukerb, A.; Gree, D.; Laabassi, M.; Gree, R. *J. Fluorine Chem.* **1998**, *88*, 23.

10.1021/jo0016024 CCC: $20.00
Published on Web 03/09/2001

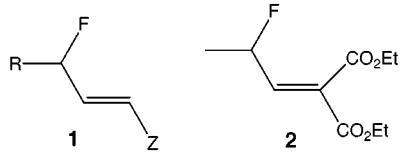
Scheme 1



Scheme 2



tion of **6** gave not only **1d** (41% yield) but also **1d′** (29%) resulting from a methyl migration in a carbocation intermediate. These derivatives were separated by chromatography. Methylenemalonate derivative **2** was prepared in two steps from diethyl mesoxalate **7** (Scheme 2). It is worth noting that, in that case, fluorination of **8** occurs with a complete allylic transposition. In fluorination of allylic alcohols with DAST, competition between the reaction with and without transposition (formal S_N and S_N', respectively) is frequently observed.[8] The reactions of **4**, **6**, and **7** gave only the most conjugated, and probably the most stable, compounds **1** and **2**.[10]



a: R = Me; Z = CN
b: R = Me; Z = CO_2Me
c: R = Me; Z = COPh
d: R = *t*-Bu; Z = COPh

Ground State Conformational Studies. Previous studies[11] dealing with the conformational properties of allylic fluorides predicted a very low preference (0.5−0.7 kcal/mol) for eclipsing of the C−F linkage with the double bond. Exceptions occur only for systems with an electron-withdrawing group at the β position: for **1a**, the calculated energy difference between the ground state (CF eclipsed) and higher energy conformer (CH eclipsed) was reported to be 1.8 kcal/mol.[11]

Computational studies were performed here to confirm these results and to extend them to other type **1** *E* and *Z* allylic alkenes. Hybrid density functional theory with the B3LYP/6-31G* basis[12] set was used for optimizations of 3-fluoro-1-butene and its 1-substituted derivatives.

Optimization of 3-fluoro-1-butene gave three conformers, **A**, **B**, and **C**, shown in Figure 1. Conformation **A**, in which the fluorine is eclipsed with the double bond, is lowest in energy. In conformations **B** and **C** the fluorine is skew to the double bond, and either H or Me is eclipsed.

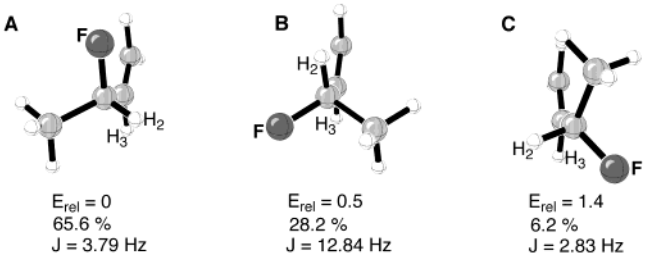


Figure 1. B3LYP/6-31G* optimized geometries of 3-fluoro-1-butene. Energies are in kcal/mol; populations were calculated using the Boltzmann distribution at 298 K; coupling constants for H2−H3 were calculated using the Karplus relationship ($^3J_{HH} = 7 - 1\cos\alpha + 5\cos 2\alpha$).

These conformers were found to be higher in energy than **A** by 0.5 and 1.4 kcal/mol, respectively. In conformation **C** there is steric repulsion between the CH_3 and the CH_2 group. From the relative energies of the conformers, their percentages at 25 °C were calculated using a Boltzmann distribution to be 65.6%, 28.2%, and 6.2% for **A**, **B**, and **C** respectively. Using the Karplus relationship ($^3J_{HH} = 7 - 1\cos\alpha + 5\cos 2\alpha$)[13] a $^3J_{H_2H_3}$ coupling of 6.3 Hz was predicted for compound **1a** at room temperature. Experimentally, a value of 6.4 Hz was measured. Calculated relative energies for the three conformations of 4-fluoro-*trans*-2-pentene, the compound with a *trans*-methyl group added, were similar. In this case, a $J_{H_3H_9}$ coupling of 6.1 Hz was predicted, while a value of 6.7 Hz was measured.

Electron withdrawing groups at the β position have a dramatic effect on the relative energies of various conformers and, consequently, on the coupling constant. Calculations for *trans*-1-cyano-3-fluoro-butene (**1a**) gave three conformations, **D**, **E**, and **F**, shown in Figure 2. Calculations predict a large preference for **D**, which has the fluorine eclipsed with the double bond. Conformers **E** and **F** are now higher in energy by 1.8 and 2.7 kcal/mol, respectively. This is consistent with the earlier results from Kahn et al.[11] In **D,** there is maximum electron donation from the CH and CC bonding orbitals into the electron-deficient cyanoalkene π^* orbital. In the other conformers, there is less opportunity for donation

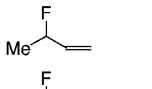
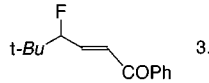
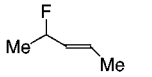
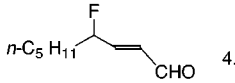
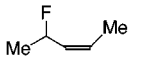
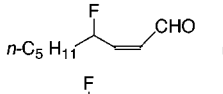
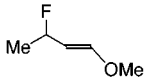
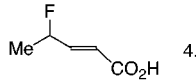
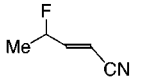
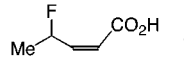
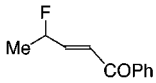
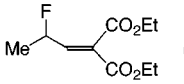
(10) For another example, see: Li, Y.; Luthman, K.; Hacksell, U. *Tetrahedron Lett.* **1992**, *43*, 4487.

(11) Kahn, S. D.; Pau, C. F.; Chamberlin, A. R.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 650 and references therein.

(12) All calculations used Gaussian 94 (Revision A.1). Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T. A.; Peterson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. *Gaussian 94*, revision A.1; Gaussian, Inc.: Pittsburgh, PA, 1995.

(13) Macomber, S. R. *A Complete Introduction to NMR Spectroscopy*; Wiley: New York, 1998.

Table 1.

Structure	Measured J_{HH}	E_{rel} F eclipsed H eclipsed Me eclipsed	Calculated J_{HH}	Structure	Measured J_{HH}	E_{rel} F eclipsed H eclipsed Me eclipsed	Calculated J_{HH}
	6.4	0.0 0.5 1.4	6.3		3.7		
	6.7	0.4 0.0 1.5	6.1		4.0	0.0 1.2 1.8	3.3[d]
	8.6[a]	0.4 0.0 0.4			6.5		
	-b	0.3 0.0 1.5	9.2		4.0[c]	0.0; 0.8 1.6; 2.2 2.4; 3.0	4.3
	3.5	0 1.8 2.5	4.1		-e	2.7 0.0 ----	9.2
	3.5				6.6	1.2; 1.2 0.0 ----	9.3

Coupling constants are in Hz. Energies are in kcal/mol. a: ^3J value for Z-9-fluoro-2-methyloctadec-7-ene. b: unknown compound: DAST fluorination of corresponding allylic alcohol leads only to decomposition products. c: J value for the methyl ester derivative. d: Calculations were performed on the methyl not pentyl derivatives. e: unknown derivative.

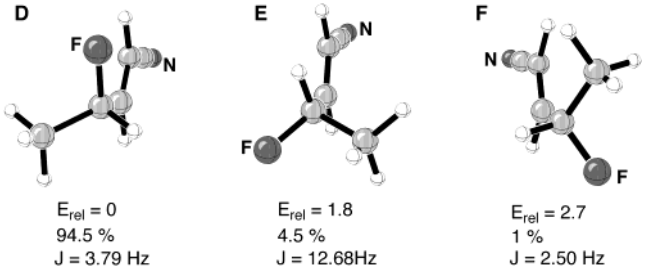


Figure 2. B3LYP/6-31G* optimized geometries for *trans*-1-cyano-3-fluoro-1-butene.

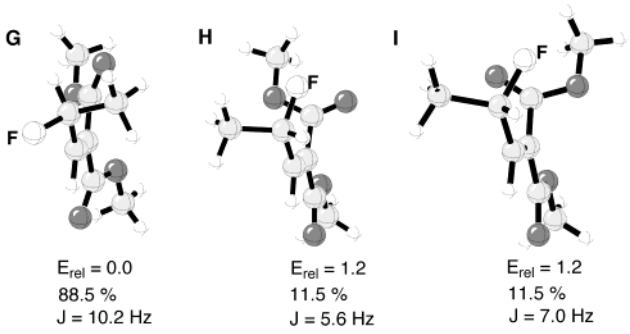


Figure 3. B3LYP/6-31G* optimized geometries for the methyl ester of **2**.

into the π^* orbital. Because the allylic CH is skew in the highly populated **D**, the predicted coupling constant drops to 4.2 Hz, compared to a measured value of 3.5 Hz. The microwave spectrum of 1-cyano-3-fluoro-1-butene was recently reported.[14] The conformation with the allylic CF eclipsed with the alkene was found to be the predominant structure.

Additional calculations are summarized in Table 1. Calculations for a *trans*-β-formyl and the *trans*-carboxylic acid also predict a large preference for the eclipsed conformation. Here coupling constants are predicted to be 4.3 and 3.3 Hz for the acid and aldehyde, respectively. Experimentally, a value of 4.0 Hz is measured for both 4-fluoro-2-*trans*-pentenal and *trans*-4-fluoro-2-pentenoate.

With a donor substituent on the alkene, there is little preference for the fluoride to be eclipsed or staggered with the double bond. Calculations predict a 0.3 kcal/mol preference for the CH eclipsed over the CF eclipsed, since there is a favorable interaction between the electron-rich alkene π orbital and the out of plane σ^* CF. A $^3J_{HH}$ coupling constant of 9.2 Hz is predicted.

Figure 3 shows three calculated low energy conformations for the methyl ester of **2.** There is a 1.2 kcal/mol preference for **G** in which the fluorine is anti to the double bond, over **H**, and in which it is syn. In **G** the electronegative fluorine is far away from the oxygens of the ester. The calculated J_{HH} coupling constant for the methyl ester is 9.3 Hz compared to the measured value of 6.6 Hz for **2**.

The pattern of conformations of these allylic fluorides is readily understandable, and the calculations reproduce the experimental coupling constants, except in this last case.

Diels Alder Cycloadditions of Allylic Fluorides. The reaction of 2,3-dimethyl-1,3-butadiene with **1c** at 60 °C proceeded to give a 76:24 mixture of adducts **9c** and **9c′** in 85% overall yield (Scheme 3). These derivatives were separated by chromatography. Neither reversibility nor epimerization was observed when each stereoisomer was heated separately under the reaction conditions. The stereochemistry of **9c** could be confirmed unambiguously in the following way: epoxidation of **9c** gave a 2:1 mixture of **10c** and **10c′**, which was separated by chromatography. The epoxide **10c′** gave crystals suitable for X-ray diffraction studies. The X-ray structure establishes the stereochemical relationships shown in **10c′**.

(14) Kassi, S.; Grée, D.; Grée, R.; Duflot, D.; Petitprez, D.; Wlodarczak, G. *J. Mol. Spectrosc.* **2000**, *202*, 19.

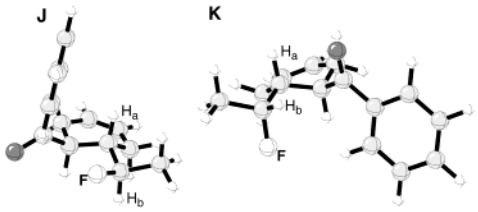
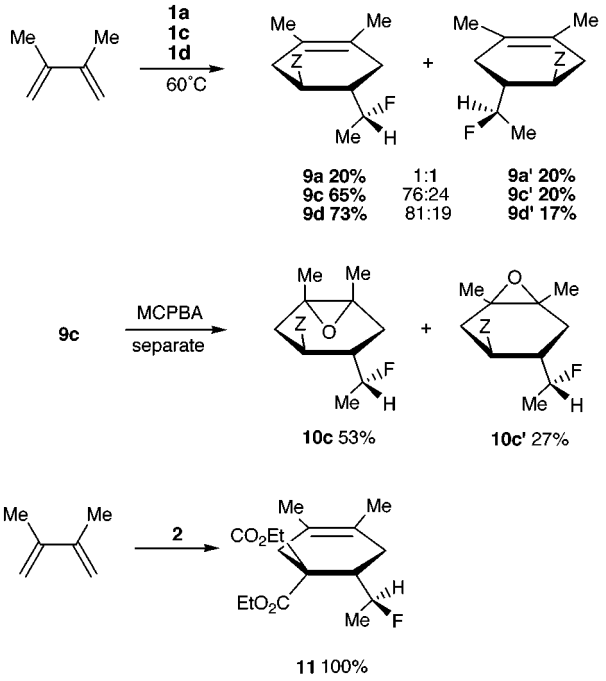


Figure 4. PM3 optimized geometries for **9c** (**J**) and **9c′** (**K**).

Scheme 3



The product stereochemistries were supported by NMR data, which allowed identification of products from related reactions. Isomer **9c′** has a very low $^3J_{H_aH_b}$ coupling constant (2.0 Hz) and a high $^3J_{H_aF}$ (30.0 Hz), while isomer **9c** has opposite trends: $^3J_{H_aH_b} = 7.7$ Hz and $^3J_{H_aF} = 8.0$ Hz. Here H_a and H_b refer to the H geminal to F and the methine vicinal to F. The conformations that are consistent with these assignments are shown in Figure 4. The minor product **9c′** (**K**) has the CF bond anti to the ring CH bond and consequently a large $^3J_{HF} = 30$ Hz. The CH bonds are gauche and have a small coupling. This conformer is found to place the CH near the COPh substituent and to place the Me in the least crowded position. The major product **9c** (**J**), has the Me in the least crowded position, while it places the CF bond near the COPh substituent. Consequently the $^3J_{HH}$ is large, a result of the antiperiplanar arrangement.

The cycloaddition of **1d** gave similar results. An 81:19 ratio of adducts **9d** and **9d′** was obtained in 90% yield. The NMR spectra (see experimental) are very similar to **9c** and **9c′** and could be used for isomer identification.

Cycloaddition with **1a** proved to be slow (only 40% reaction after 10 days) leading to a 1:1 mixture of **9a** and **9a′**. The stereochemistries of these adducts were established using NMR, by analogy with **9c** and **9c′**. No Diels–Alder reaction was observed with ester **1b**; only starting material was recovered in that case.

Under similar reaction conditions, the cycloaddition of the doubly activated **2** is complete in 3 days, and a single adduct, **11**, is obtained (NMR control of the crude reaction mixture). It is isolated in 49% yield. The stereochemistry of **11** was deduced from the NMR data which showed a low $^3J_{H_aH_b}$ (3.1 Hz) and a high $^3J_{H_aF}$ (23.4 Hz).

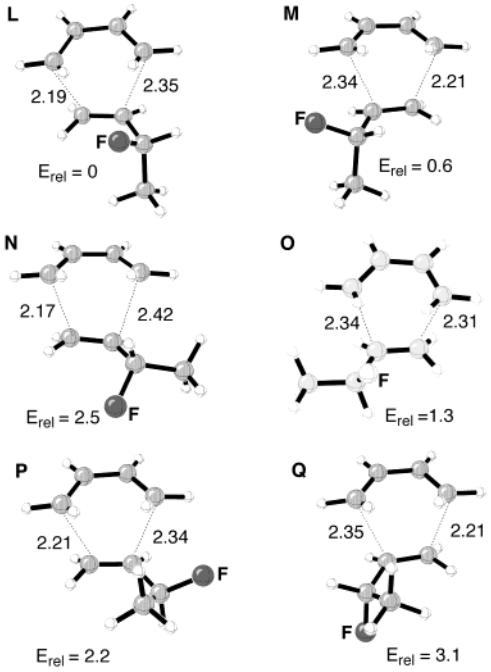


Figure 5. B3LYP/6-31G* TS for the reaction of butadiene with 3-fluorobutene.

Transition States and Stereoselectivity Models. The reaction of butadiene with 3-fluoro-1-butene was used as a model reaction to explore these Diels–Alder reactions theoretically. For this reaction there are twelve possible transition structures; each of the three staggered conformers of the allylic fluoride can add to butadiene exo or endo and to the top or bottom of the diene. Figure 5 shows B3LYP/6-31G* exo transition structures. Structures on the left column give the products similar to **9a**–**9d**; while those on the right column produce **9a′**–**9d′**. Configuration of the stereogenic center in the drawings of 3-fluoro-1-butene in Figure 5 are the opposite of the products in Figure 4. The reactants used experimentally were racemic.

Transition structure conformation **L**, in which the fluorine is inside and methyl is anti, has the lowest energy. The second lowest in energy is **M**, by 0.6 kcal/mol. In **M** the fluorine is outside and the methyl is anti. Calculations predict a small preference for the formation of the product from F-inside, and Me-anti, in accord with the experiment. In conformations **N** and **O** the fluorine is anti or inside with respect to the double bond, and the methyl is in the more crowded outside position. Structures **N** and **O** are 2.5 and 1.3 kcal/mol, respectively, higher in energy than **L**. In conformations **P** and **Q** the methyl is inside, this places the fluorine either outside or anti and perpendicular to the double bond. Structures **P** and **Q** are 2.2 and 3.1 kcal/mol, respectively, higher in energy than **L**.

Figure 6 shows four exo B3LYP/6-31G* transition states for the cycloaddition of 4-fluoropent-2-en-1-al, a model system for reactions of **1c** and **1d**, with 2,3-dimethyl-1,3-butadiene. Structures on the left column give the diastereomeric products similar to **9a**–**9d** while those on the right column produce **9a′**–**9d′**. Conformation **R,** in which the fluorine is inside, has the lowest energy.

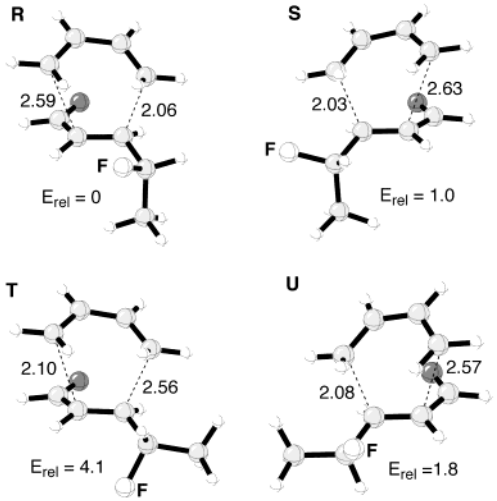


Figure 6. B3LYP/6-31G* TS for the cycloaddition of butadiene with 4-fluoropen-2-en-1-al.

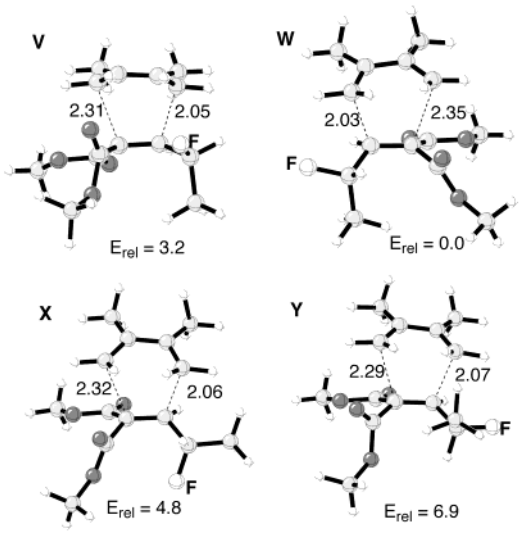


Figure 7. B3LYP/6-31G*//PM3 TS for the reaction of **2** with 2,3-dimethyl-1,3-butadiene.

The TS is more asynchronous compared to 3-fluorobutene with the longer forming bond to the carbon alpha to the carbonyl. Transition state **S** is second lowest in energy by 1.0 kcal/mol. In both cases, the methyl adopts the anti position. In **R** the fluorine is inside, and in **S** the fluorine is outside. There is now a larger preference for formation of the F-inside, Me-anti transition state. In **T** and **U** the methyl is in the more crowded outside position, and fluorine is anti (**T**, 4.1 kcal/mol) or inside (**U**, 1.8 kcal/mol).

Figure 7 shows four exo B3LYP/6-31G*//PM3 transition states for the highly stereoselective cycloaddition of the diester, **2**, with 2,3-dimethyl-1,3-butadiene. The lowest energy transition structure, **W**, has the methyl anti as usual, but now the fluorine is outside. This transition structure leads to the product **11**. Structure **V** is 3.2 kcal/mol higher in energy and gives the unobserved isomer. Calculations predict a large preference for formation of isomer **11** in accord with the experiment. The higher energy of **V** is due to repulsions between the carbonyl oxygen with the inside fluorine. Placing the methyl group on the inside gives **Y**, which is 6.9 kcal/mol higher in energy than **W**. This energy difference is a result of steric crowding between the methyl substituent and an ester substituent. Structure **X** shows anti attack when the fluorine is perpendicular to the double bond. Structure **X** is 4.8 kcal/mol higher in energy than **W**.

Conclusion

We have presented experimental and theoretical results on the simple formation of chiral, allylic fluorides from their corresponding alcohols and their stereoselective Diels−Alder reactions. We have shown that the B3LYP/6-31G* level accurately reproduces geometries and Diels−Alder transition structures for allylic fluorides in accord with our experimental stereochemical data. In chiral *E* allylic fluorides, with an electron-withdrawing group at the β position, the fluorine has a large preference to be eclipsed with the double bond.

In Diels−Alder transition states, there is a significant preference for the alkyl group at the stereogenic center to be anti with respect to the forming bond and the fluorine to be *inside*. A cis substituent on the double bond produces a reversal in selectivity, since the fluorine now adopts the outside position. Earlier studies with allylic ethers found anti alkyl and inside alkoxy preferred,[15] and the same preference is found here with the fluorine adopting the role of the "inside-alkoxy" group. Indeed, the overal stereochemical features are nearly the same for the corresponding allylic ethers and fluorides.

Experimental Section

General Procedures. All dry solvents were freshly distilled under nitrogen from the recommended drying agent. Toluene was distilled from sodium, ether and THF were distilled from sodium benzophenone ketyl, and dichloromethane was distilled from CaH_2. Pentane or low boiling (bp < 60 °C) petroleum ether were used for chromatography. Other reagents and solvents were used as received from the commercial suppliers. All reactions were performed with dry solvents and under a dry nitrogen atmosphere unless specified. External bath temperatures are reported. Melting points are uncorrected. FTIR was recorded on NaCl plates as thin film. Elemental analyses were done at the Service de Microanalyse (ICSN, Gif-sur-Yvette, France). MS was performed by the Centre Régional de Mesures Physiques de l'Ouest (Rennes). ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded in the specified solvent.

Allylic Fluorides 1a to 1c. Wittig Reactions of 3. A solution of protected lactaldehyde[6] (**3**) (2.4 g, 12 mmol) and corresponding phosphorane (18 mmol, 1.5 equiv) in toluene (40 mL) was heated under stirring at 70 °C for 3 h (derivatives **1a** and **1b**) or for 5 h (**1c**). After evaporation of toluene, ether was added to the reaction mixture. After filtration of Ph_3PO and evaporation of the solvent the olefins were obtained, as a 1:1 mixture of the *E* and *Z* isomers for derivative **a**, as a 7:3 mixture of *E* and *Z* isomers for compound **1b** and as a single *E* isomer in the case of **1c**. All these isomers were separated by flash chromatography on silica gel using as eluent a 15:85 mixture of ether and petroleum ether.

***tert*-Butyldimethylsilyl Ethers: Olefin a (*E*).** 950 mg (38%), Rf = 0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.68 (dd, 1H, J = 16.0, J = 3.0); 5.56 (dd, 1H, J = 16.0, J = 2.2); 4.30 (bm, 1H); 1.19 (d, 3H, J = 6.7); 0.84 (s, 9H); 0.02 (s, 3H); 0.01 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 158.1; 117.6; 97.7; 67.6; 25.7; 23.4; 18.1; −4.8; −5.0. IR (film): 2957; 2932; 2890; 2860; 2223 cm^{-1}.

(15) (a) Houk, K. N.; Moses, S. R.; Wu, Y,; Rondan, N. G.; Jager, V.; Schohe, R. Fronczek, F. R. *J. Am. Chem. Soc.* **1984**, *106*, 3880. (b) Haller, J.; Niwayama, S.; Duh, H.; Houk, K. N. *J. Org. Chem.* **1997**, *62*, 5728 and references therein.

Olefin a (*Z*). 950 mg (38%), Rf = 0.6. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.34 (dd, 1H, J = 11.2, J = 8.1); 5.17 (dd, 1H, J = 11.2, J = 1.0); 4.62 (bm, 1H); 1.19 (d, 3H, J = 6.4); 0.80 (s, 9H); 0.0 (s, 3H); −0.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 158.1; 115.3; 97.1; 67.8; 25.8; 23.7; 18.1; −4.8; −5.0. IR (film): identical to (*E*) isomer.

Olefin b (*E*). 1.74 g (60%), Rf = 0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.87 (dd, 1H, J = 15.8, J = 4.0); 5.94 (dd, 1H, J = 15.8, J = 1.5); 4.39 (bm, 1H); 3.67 (s, 3H); 1.18 (d, 3H, J = 6.6); 0.84 (s, 9H); 0.07 (s, 3H); 0.06 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.2; 152.2; 118.5; 67.6; 51.4; 25.7; 23.5; 18.2; −4.9. IR (film): 2956; 2932; 2890; 2859; 1729; 1650 cm^{-1}.

Olefin b (*Z*). 750 mg (25%), Rf = 0.7. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.19 (dd, 1H, J = 11.7, J = 7.6); 5.63 (dd, 1H, J = 11.7, J = 1.6); 5.41 (dqd, 1H, J = 7.6, J = 6.1, J = 1.6); 3.68 (s, 3H); 1.22 (d, 3H, J = 6.1); 0.87 (s, 9H); 0.05 (s, 3H); 0.04 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.1; 155.1; 116.3; 65.5; 51.2; 25.8; 23.5; 18.1; −4.7; −4.8. IR (film): identical to (*E*) isomer.

Olefin c. 2.56 g (78%), Rf = 0.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.0−7.90 (m, 2H); 7.60−7.52 (m, 1H); 7.50−7.42 (m, 2H); 7.14 (dd, 1H, J = 15.3, J = 1.5); 7.04 (dd, 1H, J = 15.3, J = 3.0); 4.58 (qdd, 1H, J = 6.6, J = 3.0, J = 1.5); 1.32 (d, 3H, J = 6.6); 0.96 (s, 9H); 0.11 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 190.8; 152.1; 137.9; 132.7; 128.5; 128.4; 122.7; 68.1; 25.8; 23.5; 18.2; −4.8; −4.9. IR (film): 2956; 2890; 2858; 1820; 1673; 1622 cm^{-1}.

Allylic Alcohols 4a and 4b (Desilylation). To the preceding olefin **a** or **b** (3 mmol of pure *E* isomer) in acetone (8 mL) was added Amberlyst 15 (0.7 g) and H_2O (0.2 g). The reaction mixture was stirred for 3 h at 60 °C (for derivative **a**) and at 40 °C (in the case of **1b**), then it was filtered and solid Na_2CO_3 was added. After filtration and evaporation of solvents, the allylic alcohols were purified by chromatography on silica gel using a 50:50 mixture of ether and petroleum ether as eluent.

4a. 260 mg (90%), Rf = 0.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.77 (dd, 1H, J = 16.1, J = 4.0); 5.67 (dd, 1H, J = 16.1, J = 2.0); 4.48 (m, 1H); 2.20 (d, 1H, J = 4.5); 1.34 (d, 3H, J = 6.6). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 157.5; 117.3; 98.2; 67.0; 22.4. IR (film): 3420; 2979; 2228; 1635 cm^{-1}.

4b. 292 mg (75%). The spectroscopical data were in agreement with literature.[5]

Allylic Alcohol 4c. To the preceding silyl ether (478 mg, 1.74 mmol) in THF (3 mL) were added acetic acid (9 mL) and water (3 mL). The reaction mixture was stirred at room temperature for 48 h. After addition of a saturated Na_2CO_3 solution and extraction with ether, the organic phase was dried ($MgSO_4$) and evaporated. The allylic alcohol **4c** was purified by flash chromatography on silica gel using a 50:50 mixture of ether and petroleum ether as eluent.

4c. 230 mg (75%), Rf = 0.2. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00−7.90 (m, 2H); 7.60−7.40 (m, 3H); 7.13 (dd, 1H, J = 15.3, J = 1.0); 7.05 (dd, 1H, J = 15.3, J = 4.1); 4.60 (bm, 1H); 2.99 (bs, 1H); 1.38 (d, 3H, J = 6.6). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.0; 151.5; 137.4; 132.9; 128.53; 128.49; 123.0; 67.4; 22.7. IR (film): 3422; 2975; 1667; 1623; 1598 cm^{-1}. HRMS(EI) for $C_{11}H_{12}O_2$ (M^+) calcd 176.0837, found 176.0831.

Fluorination of 4a−4c. To a solution of DAST (0.19 mL, 1.2 mmol) in CH_2Cl_2 (2 mL) was added, under nitrogen at room temperature, a solution of allylic alcohol **4a−4c** (1 mmol) in CH_2Cl_2 (2 mL). After the mixture was stirred for 10 min, solid Na_2CO_3 (250 mg) was added first. After filtration, the organic phase was washed with a saturated Na_2CO_3 solution and dried ($MgSO_4$). The solvent was removed by distillation at atmospheric pressure, and the allylic fluorides were purified by flash chromatography on silica gel using as eluent a 10:90 mixture of ether and pentane.

1a. 50 mg (50%), Rf = 0.4 (ether/petroleum ether 2:8). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.72 (ddd, 1H, J_{HF} = 19.8, J = 16.3, J = 3.4); 5.67 (ddd, 1H, J = 16.3, J = 1.9, J_{HF} = 1.7); 5.23 (dqdd, 1H, J_{HF} = 47.4, J = 6.7, J = 3.5, J = 2.0); 1.47 (dd, 3H, J_{HF} = 23.7, J = 6.7). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.2 (J_{CF} = 17.9); 116.5; 99.6 (J_{CF} = 15.2); 87.4 (J_{CF} = 174.9); 20.3 (J_{CF} = 22.5). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −180.2. IR (film): 2990; 2927; 2858; 2228; 1705; 1642 cm^{-1}. HRMS(EI) for C_5H_6NF (M^+) calcd 99.0484, found 99.0487.

1b. Bp: 70°/20 mmHg. 105 mg (80%), Rf = 0.45 (ether/petroleum ether 2:8). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.91 (ddd, 1H, J_{HF} = 19.8, J = 15.8, J = 4.0); 6.04 (dt, 1H, J = 15.8, J_{HH} = J_{HF} = 1.5); 5.29 (dqdd, 1H, J_{HF} = 47.9, J = 6.6, J = 4.0, J = 1.5); 3.75 (s, 3H); 1.44 (dd, 3H, J_{HF} = 23.6, J = 6.6). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.5; 146.3 (J_{CF} = 18.7); 120.2 (J_{CF} = 11.1); 87.8 (J_{CF} = 170.5); 51.8; 20.6 (J_{CF} = 22.9). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −177.6 (dqd J_{HF} = 48.0, J_{HF} = 23.6, J_{HF} = 20.0). Anal. Calcd for $C_6H_9O_2F$: C, 54.54, H, 6.82. Found: C, 54.36; H, 6.71.

1c. 125 mg (70%), Rf = 0.5 (ether/petroleum ether 3/7). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00−7.95 (m, 2H); 7.60−7.44 (m, 3H); 7.19 (ddd, 1H, J = 15.5, J = 1.7, J_{HF} = 0.9); 7.02 (ddd, 1H, J_{HF} = 20.7, J = 15.5, J = 3.6); 5.39 (dqdd, 1H, J_{HF} = 48.0, J = 6.7, J = 3.6, J = 1.7); 1.55 (dd, 3H, J_{HF} = 23.6, J = 6.7). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 189.9; 145.8 (J_{CF} = 17.6); 137.4; 133.1; 128.7; 128.6; 123.5 (J_{CF} = 9.2); 88.4 (J_{CF} = 171.4); 20.8 (J_{CF} = 22.9). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −177.3. IR (film): 3064; 2986; 2934; 1677; 1633; 1598; 1580; 1449 cm^{-1}. HRMS-(EI) for $C_{11}H_{11}OF$ (M^+) calcd 178.0794, found 178.0799.

Allylic Fluoride 1d. Allylic Alcohol 6. 3,3-Dimethyl-1,2-butanediol **(5)** (25 mmol) was oxidized following Torii's procedure[7], using Ca $(OCl)_2$ as oxidant. The reaction yielded 3 g of crude hydroxyaldehyde, directly used for the next step.

Starting from this crude aldehyde, the Wittig reaction was done under previous conditions (toluene, 70 °C, 3h). After a flash chromatography on silica gel using a 50:50 mixture of ether and petroleum ether as eluent, allylic alcohol **6** was isolated as a viscous oil which crystallized slowly in the refrigerator.

6. F = 74 °C (hexane). 2.8 g (51% overall yield, 2 steps), Rf = 0.35. ^{1}H NMR (400 MHz, C_6D_6) δ: 8.08−8.05 (m, 2H); 7.39 (dd, 1H, J = 15.3, J = 4.8); 7.30−7.15 (m, 4H); 3.9 (d, 1H, J = 4.8); 1.0 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 190.6; 148.1; 137.7; 132.9; 128.6; 125.5; 79.4; 35.8; 25.7. Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.06; H, 8.25. Found: C, 76.86; H, 8.27.

Fluorination of 6. To a solution of DAST (0.16 mL, 1.2 mmol) in a mixture of pentane (3 mL) and toluene (1 mL) was added, at room temperature under nitrogen, allylic alcohol **6** (220 mg, 1 mmol) in small portions. After 10 min stirring, the same Na_2CO_3 work up as in the preceding cases was applied. The fluorides **1d** and **1d′** were separated by flash chromatography on silica gel using a 10:90 mixture of ether and pentane as eluent.

1d. 92 mg (41%), Rf = 0.64 (ether/petroleum ether: 20/80). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02−7.70 (m, 5H); 7.21 (dd, 1H, J = 15.5, J = 1.5); 7.10 (ddd, 1H, J_{HF} = 22.2, J = 15.5, J = 3.7); 4.87 (ddd, 1H, J_{HF} = 47.3, J = 3.7, J = 1.5); 1.04 (d, 9H, J_{HF} = 1.3). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 189.6; 142.7 (J_{CF} = 18.3); 137.4; 133.0; 128.6; 125.5 (J_{CF} = 10.3); 98.5 (J_{CF} = 180.6); 35.6 (J_{CF} = 19.3); 25.2 (J_{CF} = 4.5). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −189.8 (dd, J_{HF} = 47.3, J_{HF} = 20.5). HRMS-(EI) for $C_{14}H_{17}OF$ (M^+) calcd 220.1263, found 220.1247.

1d′. 64 mg (29%), Rf = 0.53 (ether/petroleum ether: 20/80). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.98−7.47 (m, 5H); 7.03 (dd, 1H, J = 15.6, J = 8.0); 6.94 (d, 1H, J = 15.6); 2.70 (dqt, 1H, J_{HF} = 13.6, J = 6.9); 1.40 (d, 6H, J_{HF} = 21.7); 1.20 (d, 3H, J = 6.9). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 190.7; 149.2 (J_{CF} = 6.2); 137.7; 132.7; 128.6; 126.6; 96.4 (J_{CF} = 171.1); 46.6 (J_{CF} = 23.0); 24.9 (J_{CF} = 24.5); 24.5 (J_{CF} = 24.6); 141 (J_{CF} = 5.5). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −140.8 (d sept., J_{HF} = 21.3, J_{HF} = 12.5). HRMS(EI) for $C_{14}H_{17}OF$ (M^+) calcd 220.1263, found 220.1267.

Allylic Fluoride 2. Allylic Alcohol 8. To a solution of ethyl mesoxalate **(7)** (2 g, 11.5 mmol) in dry THF (10 mL) was added, dropwise under nitrogen at −50 °C, propenylmagnesium bromide (18 mL of a 1 M solution in THF, 1.5 equiv). The reaction mixture was stirred for 30 min at −40 °C before addition, at this temperature, of a saturated NH_4Cl solution (20 mL). After extraction with ether, the organic phase was washed, dried ($MgSO_4$), and evaporated. Alcohol **8** (80:20 mixture of *E* and *Z* isomers) was isolated by flash chromatography on silica gel using a 50:50 mixture of ether and petroleum ether as eluent.

8. (4:1 *E*/*Z* mixture) 1.3 g (52%), Rf = 0.43. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.07 (dq, 1H *E*, J = 15.3, J = 6.6); 5.93 (d, 1H *Z* +*E*, J (*Z*) = 11.5); 5.84 (dq, 1H, *Z*, J = 11.5, J = 7.1); 4.28 (q, 4H, *Z* +*E*, J = 7.1); 3.96 (bs, 1H, *Z*); 3.90 (bs, 1H, *E*); 1.80−1.75 (m, 3H, *Z* +*E*); 1.30 (t, 3H, *Z* +*E*, J = 7.1). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.2; 132.4 (*Z*); 128.4 (*E*); 125.4 (*E*); 124.7 (*Z*); 62.8; 17.7; 14.3; 14.0. IR (film): 3482; 2984; 2920; 1739; 1658; 1632 cm^{-1}. HRMS(EI) for $C_{10}H_{16}O_5$ (M^+) calcd 216.0997, found 216.1007.

Fluorination of 8. Starting from **8** the same DAST fluorination procedure as before was used. It gave allylic fluoride **2** together with a small amount (around 15−20%) of unidentified, nonfluorinated byproducts. Derivative **2** was isolated by flash chromatography on silica gel using a 98:2 mixture of toluene and ether as eluent.

2. 120 mg (55%), Rf = 0.8 (ether/petroleum ether: 1/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.96 (dd, 1H, J_{HF} = 17.9, J = 6.6); 5.50 (dqt, 1H, J_{HF} = 49.1, J = 6.6); 4.35−4.20 (m, 4H); 1.52 (dd, 3H, J_{HF} = 23.7, J = 6.6); 1.33 (t, 3H, J = 7.1); 1.31 (t, 3H, J = 7.1). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.4; 163.4; 146.3 (J_{CF} = 24.9); 128.1 (J_{CF} = 8.8); 86.9 (J_{CF} = 165.7); 61.8; 61.7; 20.5 (J_{CF} = 23.5); 14.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −173.2 (dqd, J_{HF} = 47.5; J_{HF} = 23.7; J_{HF} = 17.8). HRMS(EI) for $C_{10}H_{15}O_4F$ (M^+) calcd 218.0954, found 218.0958.

Diels−Alder Cycloadditions. The representative procedure was as follows: a solution of **1c** (0.150 g, 0.84 mmol) in dimethylbutadiene (4 mL) was heated at 60 °C for 19 h. A control using ^{19}F NMR established that the reaction was complete and gave a 76:24 ratio of **9c** and **9c′**. After evaporation of excess diene, the two cycloadducts were separated by flash chromatography on silica gel using 20:80 mixture of ether and petroleum ether as eluent.

9c. 142 mg (65%), Rf = 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02−7.45 (m, 5H); 4.62(ddq, 1H, J_{HF} = 47.7, J = 7.7, J = 6.2); 3.64 (td, 1H, J = 8.8, J = 5.7); 2.49 (m, 1H, J_{HF} = 8.0, J = 8.8; J = 7.7; J = 5.8); 2.29 (dd, 1H, J = 17.1, J = 8.8); 2.18 (dd, 1H, J = 17.1, J = 5.4); 2.09 (dd, 1H, J = 17.2, J = 5.8); 1.85 (dd, 1H, J = 17.1, J = 8.2); 1.66 (bs, 6H); 1.28 (dd, 3H, J_{HF} = 24.9, J = 6.2). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 203.5; 136.9 (J_{CF} = 1.2); 132.8; 128.6; 128.2; 124.2; 123.2 (J_{CF} = 0.6); 92.5 (J_{CF} = 168.0); 43.0 (J_{CF} = 5.1); 41.6 (J_{CF} = 18.5); 34.5; 31.5 (J_{CF} = 6.9); 18.9; 18.6; 18.3 (J_{CF} = 23.3). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −171.4 (dqd, J = 47.7; 24.9; 8.0). IR (film): 2983; 2915; 2859; 1680; 1596; 1580 cm^{-1}. HRMS(EI) for $C_{17}H_{21}OF$ (M^+) calcd 260.1576, found 260.1579.

9c′. 44 mg (20%), Rf = 0.5. ^{1}H NMR (400 MHz, C_6D_6) δ: 8.06−7.10 (m, 5H); 4.85 (dqd, 1H, J_{HF} = 49.3, J = 6.1, J = 2.0); 3.80 (td, 1H, J = 11.2, J = 5.1); 2.40−2.30 (m, 2H); 2.35−2.20 (m, 1H, J_{HF} = 30.0, J = 11.2, J = 5.3, J = 2.0); 2.04−1.88 (m, 2H); 1.60 (s, 3H); 1.50 (s, 3H); 1.05 (dd, 3H, J_{HF} = 23.9, J = 6.1). ^{13}C NMR (100 MHz, C_6D_6) δ: 203.8; 137.8; 133.0; 128.8; 128.7; 124.7; 124.1; 89.9 (J_{CF} = 168.3); 43.4 (J_{CF} = 3.1); 41.2 (J_{CF} = 19.2); 36.9; 29.3 (J_{CF} = 3.4); 19.0; 18.6; 18.1 (J_{CF} = 22.8). ^{19}F NMR (376 MHz, C_6D_6) δ: −190.9 (ddq, J_{HF} = 49.3, J_{HF} = 30.0, J_{HF} = 23.9). IR (film): 2984; 2912; 2860; 1678; 1596; 1580 cm^{-1} Anal. Calcd for $C_{17}H_{21}OF$: C, 78.39; H, 8.07. Found: C, 78.42; H, 8.13.

The same reaction starting from **1d** (0.250 g, 1.14 mmol) gave, after 48 h, a 80:20 mixture (NMR control) of **9d** and **9d′**; they were separated by flash chromatography on silica gel using a 10:90 mixture of ether and petroleum ether as eluent.

9d. F = 92°. 190 mg (55%), Rf = 0.60. ^{1}H NMR (400 MHz, C_6D_6) δ: 8.13−8.09 (m, 2H); 7.27−7.21 (m, 3H); 3.94 (dd, 1H, J_{HF} = 48.6, J = 7.9); 3.72 (td, 1H, J = 9.4, J = 5.7); 2.87 (m, 1H, J_{HF} = 2.5); 2.33 (dd, 1H, J = 16.5, J = 2.2); 2.18 (dd, 1H, J = 16.5, J = 5.1); 2.13 (dd, 1H, J = 16.8, J = 5.4); 1.83 (dd, 1H, J = 16.8, J = 8.7); 1.64 (s, 3H); 1.60 (s, 3H); 1.00 (d, 9H, J_{HF} = 1.4). ^{13}C NMR (100 MHz, C_6D_6) δ: 202.3 (J_{CF} = 2.9); 137.7 (J_{CF} = 2.5); 132.2; 128.6; 128.5; 124.6; 123.1 (J_{CF} = 1.8); 105.7 (J_{CF} = 181.2);43.0 (J_{CF} = 12.1); 38.0 (J_{CF} = 6.0); 37.2 (J_{CF} = 18.1); 35.4; 35.2 (J_{CF} = 20.5);25.9 (J_{CF} = 5.5); 18.9; 18.6. ^{19}F NMR (376 MHz, C_6D_6) δ: −176.1 (d, J_{HF} = 48.5). Anal. Calcd for $C_{20}H_{27}OF$: C, 79.47; H, 8.94. found: C, 79.39; H, 8.84.

9d′. 50 mg (15%), Rf = 0.65. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05−8.01 (m, 2H); 7.60−7.47 (m, 3H); 4.08 (dd, 1H, J_{HF} = 47.4, J = 0.7); 3.82 (td, 1H, J = 10.8, J = 5.4); 2.52 (dtdd, 1H, J_{HF} = 30.2, J = 11.0, J = 5.8, J = 0.7); 2.36 (m, 1H); 2.15 (m, 3H); 1.69 (s, 3H); 1.62 (s, 3H); 0.99 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 205.3; 137.5; 133.2; 128.7; 128.3; 125.1; 123.3; 100.4 (J_{CF} = 178.8); 44.7 (J_{CF} = 1.4); 37.2 (J_{CF} = 19.9); 36.8; 35.5 (J_{CF} = 19.2); 30.8 (J_{CF}= 7.4); 26.8 (J_{CF} = 4.8); 19.1; 18.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −204.0 (dd, J_{HF} = 47.4, J_{HF} = 30.2). HRMS(EI) for $C_{20}H_{27}OF$ (M^+) calcd 302.2046, found 302.2051.

The same reaction applied to **2** (75 mg, 0.34 mmol) gave, after 72 h, a single adduct **11** (NMR control 80% reaction with 20% remaining **2**), purified by flash chromatography on silica gel using a 20:80 mixture of ether and petroleum ether as eluent.

11. 51 mg (49%), Rf = 0.7. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.90 (dqd, 1H, J_{HF} = 48.3, J = 6.6, J = 3.0); 4.25−4.12 (m, 4H); 2.60 (d, 1H, J = 16.8); 2.48 (dtd, 1H, J_{HF} = 23.4, J = 7.1; J = 3.0); 2.39 (d, 1H, J = 16.8); 2.27 (dd, 1H, J = 18.3, J = 7.1); 2.11 (dd, 1H, J = 18.3, J = 7.1); 1.63 (s, 3H); 1.61 (s, 3H); 1.37 (dd, 3H, J_{HF} = 23.9, J = 6.6); 1.24 (t, 6H, J = 7.1). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.5; 170.3; 124.1 (J_{CF} = 0.8); 122.2; 90.6 (J_{CF} = 169.7) 61.3; 61.2; 56.7 (J_{CF} = 1.5); 42.8 (J_{CF} = 19.8); 36.7 (J_{CF} = 1.5); 29.0 (J_{CF} = 8.8); 20.3; (J_{CF} = 23.7); 18.7; 18;5; 13.90; 13.89. ^{19}F NMR (376 MHz, $CDCl_3$) δ: −181.3 (dqt, J_{HF} = 48.3, J_{HF} = 23.9). IR (film): 2984; 2920; 2861; 1731 cm^{-1}. HRMS(EI) for $C_{16}H_{25}O_4F$ (M^+) calcd 300.1737, found 300.1745.

The same reaction conditions applied to **1a** gave, after 10 days, only 40% cycloaddition with a 1:1 mixture of stereoisomers **8a** and **9a** (NMR control on the crude reaction mixture). These derivatives could not be completely separated by flash chromatography on silica gel; only mixtures enriched in each stereoisomer could be obtained.

8a + **9a.** 31%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.03 (dqd, 1H syn, J_{HF} = 48.3, J = 6.1, J = 2.0); 4.60 (dqt, 1H anti, J_{HF} = 47.8, J = 6.6); 2.81 (td, 1H anti, J = 6.6, J = 6.1); 2.68 (ddd, 1H syn, J = 11.2, J = 9.7, J = 7.6); 2.40−1.68 (m, 5H); 1.56 and 1.52 (bs, 6H); 1.31 (dd, 3H, J_{HF} = 23.9, J = 6.6). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 125.1 and 124.2; 122.7 and 122.5; 122.0 and 121.4; 90;3 (anti, J_{CF} = 169.3); 89.6 (syn, J_{CF} = 170.3) 41.4 (d, syn, J_{CF} = 20.0); 40.9 (anti, J_{CF} = 19.8); 35.1 (syn); 32.8 (anti); 30.4 (syn, J_{CF} = 5.8); 28.7 (syn, J_{CF} = 3.6); 28.6 (anti, J_{CF} = 3.4); 26.6 (anti, J_{CF} = 8.2); 19.1 (anti); 19.0 (syn); 18.7 (anti); 18.5 (syn); 18.1 (anti, J_{CF} = 23.2); 18.0 (syn, J_{CF} = 22.6). ^{19}F NMR (376 MHz, $CDCl_3$) anti δ, −178.3 (dqd, J_{HF} = 48.1, J_{HF} = 24.1, J_{HF} = 7.3); syn δ, −191.3 (ddq, J_{HF} = 48.3, J_{HF} = 29.0, J_{HF} = 23.6). HRMS(EI) for $C_{11}H_{16}NF$ (M^+) (mixture of **8a** + **9a**) calcd 181.1267, found 181.1268.

Epoxides 10c and 10c′. To a solution of **9c** (30 mg, 0.16 mmol) in CH_2Cl_2 (2 mL) was added a solution of metachloroperbenzoic acid (60 mg, 0.48 mmol) in CH_2Cl_2 (2 mL) and anhydrous Na_2CO_3 (10 mg). The reaction mixture was stirred at room temperature for 1.5 h. After filtration, the organic phase was washed with a saturated Na_2CO_3 solution and then with water and dried ($MgSO_4$). After evaporation of the solvent, the diastereoisomeric epoxides (2:1 mixture, NMR control) were separated by flash chromatography on silica gel using a 40:60 mixture of ether and petroleum ether as eluent.

10c. 16 mg (50%), Rf = 0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00−7.90 (m, 2H); 7.60−7.40 (m, 3H); 4.56 (dqt, 1H, J_{HF} = 47.1, J = 6.3); 3.32 (td, 1H, J = 10.3, J = 7.0); 2.56 (qdd, 1H, J_{HF} = J = 11.1, J = 6.4, J = 4.7); 2.19 (dd, 1H, J = 14.8, J = 4.7); 2.17 (dd, 1H, J = 15.5, J = 10.2); 2.06 (dd, 1H, J = 15.5, J = 7.1); 1.64 (dd, 1H, J = 14.8, J =11.2); 1.40 (s, 3H); 1.33 (s, 3H); 1.21 (dd, 3H, J_{HF} = 24.8, J = 6.3). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.7; 137.0; 132.9; 128.7; 128.1; 92.1 (J_{CF} = 169.1); 61.9 (J_{CF} = 0.7); 60.9; 42.7 (J_{CF} = 5.3); 38.4 (J_{CF} = 19.0); 34.6; 32.4 (J_{CF} = 5.5); 20.7; 19.6; 18.0 (J_{CF} = 23.4). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −172.9 (dqd, J_{HF} = 48.0, J_{HF} = 24.0; J_{HF} = 11.9). IR (film): 3440; 2982; 2956; 2929; 2854; 2380; 1677; 1596; 1580 cm^{-1}. HRMS(EI) for $C_{17}H_{21}O_2F$ (M^+) calcd 276.1525, found 276.1525.

10c. F = 65 °C (ether + pentane). 10 mg (31%), Rf = 0.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00−7.90 (m, 2H); 7.60−7.45 (m, 3H); 4.68 (dqt, 1H, J_{HF} = 47.8, J = 6.3); 3.67 (td, 1H, J = 9.1, J = 4.7); 2.34 (b sext, 1H, J_{HF} = J = 8.1); 2.16 (dd, 1H, J = 15.0, J = 4.7); 1.94 (dd, 1H, J = 15.0, J = 9.2); 1.89 (dd, 1H,

J = 15.8, J = 7.3); 1.77 (dd, 1H, J = 15.8, J =8.6); 1.39 (s, 3H); 1.33 (s, 3H); 1.22 (dd, 3H, J_{HF} = 24.8, J = 6.3). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 203.0; 136.2; 133.2; 128.7; 128.3; 92.0 (J_{CF} = 167.4); 62.1; 61.2 (J_{CF} = 0.6); 40.5 (J_{CF} = 19.2); 40.0 (J_{CF} = 5.1); 34.1; 30.1 (J_{CF} = 6.8); 20.7; 19.5; 17.7 (J_{CF} = 23.0). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −170.2 (dqd, J_{HF} = 47.8, J_{HF} = 24.8; J_{HF} = 8.0). IR (film): 3450; 3061; 2986; 2928; 2854; 1680; 1596; 1580 cm^{-1}. Anal. Calcd for $C_{17}H_{21}O_2F$: C, 73.98; H, 7.87; found: C, 73.88; H, 7.66. HRMS(EI) for $C_{17}H_{22}O_2F$ ($M + H^+$) calcd 277.1604, found 277.1604.

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