Stereoselectivity of Nitrile Oxide Cycloadditions to Chiral Allylic Fluorides: Experiment and Theory

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Abstract: The cycloadditions of nitrile oxides with new and previously studied allylic fluorides were examined. The 1,3-dipolar cycloaddition reactions were also investigated theoretically with density functional theory (B3LYP) based transition-state modelling. The predictions provided reasonable agreement with experiment, indicating that both steric and electronic effects have important influences on the stereoselectivities of these reactions.

Keywords: cycloaddition · density functional calculations · diastereoselectivity · regioselectivity

Introduction

New synthetic methods are sought in fluorine chemistry, due to the growing interest for this element in organic and bioorganic chemistry.[1] Several strategies for the synthesis of allylic fluorides were designed recently to achieve good regio- and stereocontrol in the fluorination step.[2] These methods have been applied to the preparation of analogues of bioactive molecules.[3] In parallel to these synthetic applications it was of interest to establish the relative roles of steric and electronic effects on the reaction stereoselectivities of allylic fluorides, and to provide general rules for the prediction of reaction products.

We recently reported conformational studies of allylic fluorides as well as experimental and theoretical studies of the Diels–Alder reactions of these substituted alkenes.[4] The well-known 1,3-dipolar cycloadditions have a closely related mechanism.[5] However, the latter reactions are more complex due especially to the presence of heteroatoms on the 1,3-dipoles and their possible interactions with the allylic fluorine atom. In order to understand how the steric and electronic factors control cycloadditions to allylic fluorides, we have extended the previous studies to nitrile oxide cycloadditions. These 1,3-dipoles were selected as models because detailed studies have been already performed on their reactions with allylic ethers leading to the discovery of a inside alkoxy effect.[6] A direct comparison of fluorine with OR was made experimentally and at the level of the calculated transition state structures.

Synthesis of allylic fluorides and cycloadditions with nitrile oxides: Three allylic fluorides **2, 3**, and **4** were selected for these studies (Figure 1). The fluoride **2** was obtained by hydrogenation (Lindlar's catalyst, 84% yield) of the known propargylic fluoride **1**;[7] the derivatives **3** and **4** have been described previously.[4]

The 1,3-dipolar cycloadditions of propionitrile oxide have been performed starting from nitropropane and using Mukaiyama's procedure.[8] The cycloaddition to **2** yielded a 1:2 ratio of the two adducts **5** and **6** (Scheme 1). A careful NMR monitoring (using ^{19}F, ^{13}C and ^{1}H) of the crude reaction mixture excluded the presence of the other regioisomers.

The diastereoisomers **5** and **6** were separated by chromatography, and their structures were established by NMR (Table 1). From literature data it is clearly established that for this type of isoxazolines, the C_4 carbon signals appear

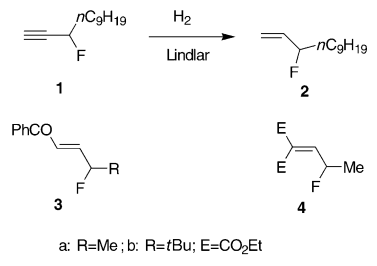

Figure 1.

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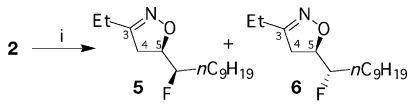
Table 1. Characteristic NMR data for isoxazolines **5** and **6**.

	H_4H_5	H_5H_6	H_5F	H_6F	C_3	C_4	C_5	C_6
5	7.8	3.6	21.6	47.7	159.7	38.2	79.7	93.6
	11.2				$J_{CF}=0$ Hz	$J_{CF}=5.6$ Hz	$J_{CF}=20.9$ Hz	$J_{CF}=176.5$ Hz
6	6.8	5.9	12.8	48.8	159.1	38.8	81.2	94.0
	10.5				$J_{CF}=0$ Hz	$J_{CF}=4.0$ Hz	$J_{CF}=24.1$ Hz	$J_{CF}=175.1$ Hz



Scheme 1. i) PhNCO added during 3 h into **2**, $C_3H_7NO_2$, NEt_3, toluene at rt then 50 °C for 2.5 h, **5** (22 %) and **6** (57 %).

around 40 ppm while the C_5 signals are close to 80 ppm.[9] Therefore, 2D correlation experiments have easily demonstrated that the CH_2 was on the C_4 carbon (38.16 ppm for **5** and 38.82 ppm for **6**) while the H_5 was connected to the C_5 (79.72 ppm for **5** and 81.22 ppm for **6**). Then the stereochemistry was deduced from the coupling constants: the *syn*-adduct **5** had a small $^3J_{HH}$ (3.6 Hz) and a large $^3J_{HF}$ (21.6 Hz) while the *anti*-derivative **6** had medium range values for both $^3J_{HH}$ (5.6 Hz) and $^3J_{HF}$ (12.8 Hz). This result is in agreement with the NMR data obtained previously with the Diels–Alder cycloadducts, indicative of conformational preferences around the corresponding C–C bond.[10] Furthermore, computational studies on the conformations and coupling constants of similar isoxazolines are in qualitative agreement and are discussed later.

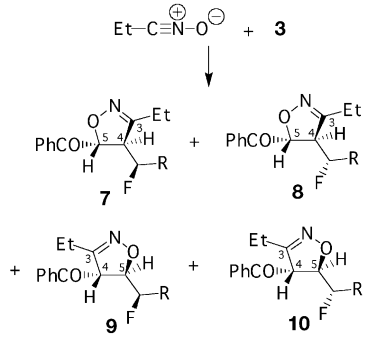
The reaction of the nitrile oxide with allylic fluorides **3** yielded a complex mixture of cycloadducts (Scheme 2, Table 2).

The ratios of these adducts have been established by ^{19}F NMR spectroscopy on the crude reaction mixtures. Extensive chromatography did not allow a complete separation of these isoxazolines. However, mixtures enriched in each isomer have been obtained, and extensive NMR studies of corresponding samples allowed a complete analysis of the individual data for each compound (Table 3).

The regioselectivity was easily established from the ^{13}C NMR data and using the C–F coupling constants from the C_4 and C_5 carbon atoms: such $^2J_{C,F}$ values are around 20 Hz

Table 2. Ratio of the isoxazolines.

	7	**8**	**9**	**10**
a	41	35	7	17
b	38	32	0	30



Scheme 2. a) R = Me; b) R = *t*Bu.

for the carbon vicinal to the CHFR chain, while the $^3J_{C,F}$ coupling is close to 4 Hz for the carbon in the β position. These data clearly indicate that **7** and **8** have the CHFR chain linked to the C_4 carbon, while **9** and **10** are the C_5 regioisomers. For the stereochemistry the same criteria as before were used with the *syn* derivatives having small $^3J_{H,H}$ (3 Hz) and larger $^3J_{H,F}$ (25 Hz), while the *anti* have $^3J_{H,H}$ values around 6 Hz and $^3J_{H,F}$ values around 12 Hz.

These data led to the conclusion that, for both series (R = Me or *t*Bu), the regioisomer with the fluorine close to C_4 was strongly favoured (70–76 %); for this regioisomer, there was a very small preference for the *syn* isomer. On the contrary for the minor C_5 regioisomers there was a net preference for the *anti* stereoisomer; this becomes exclusive for the *tert*-butyl derivative.

The reaction of the nitrile oxide with the allylic fluoride **4** yielded a mixture of the cycloadducts **11** to **13**, with a small amount of the Michael adduct **14** (Scheme 3).

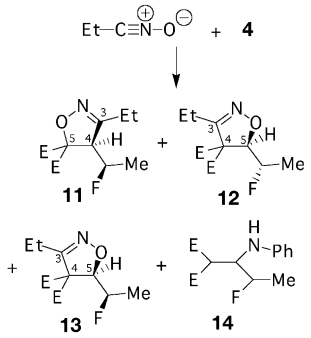
The relative ratios of the cycloadducts have been established by ^{19}F NMR on the crude reaction mixture: **11** (50 %), **12** (29 %) and **13** (21 %). By chromatography (silica gel) it was possible to isolate **11** and obtain mixtures enriched in **12** or **13** for NMR analysis. Compound **14** was identified by comparison with an authentic sample made by addition of aniline on **4**. The characteristic NMR data of **11**–**13** are given in Table 4.

Table 3. Characteristic NMR data for isoxazolines **7, 8, 9** and **10**.

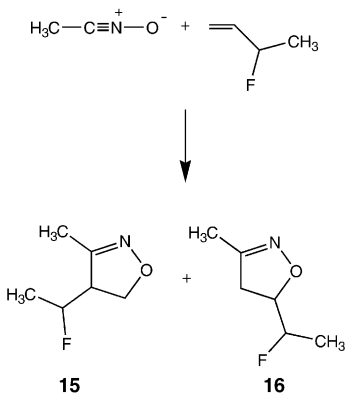
	H_4H_5	H_4H_6 (**7, 8**) H_5H_6 (**9, 10**)	H_4F (**7, 8**) H_5F (**9, 10**)	H_6F	C_3	C_4	C_5	C_6
7	7.4	2.7	28.8	47.2	159.6, $J_{CF}=1.1$ Hz	56.1, $J_{CF}=21.3$ Hz	81.2, $J_{CF}=3.5$ Hz	86.8, $J_{CF}=174.2$ Hz
8	5.4	6.2	11.6	46.6	160.0, $J_{CF}=4.9$ Hz	55.6, $J_{CF}=22.3$ Hz	81.9, $J_{CF}=3.7$ Hz	88.4, $J_{CF}=173.4$ Hz
9	7.4	2.8	21.6	46.9	158.0, $J_{CF}=0$ Hz	58.6, $J_{CF}=3.6$ Hz	84.9, $J_{CF}=20.8$ Hz	89.1, $J_{CF}=175.2$ Hz
10	6.1	6.2	12.7	49.6	158.1, $J_{CF}=0$ Hz	59.0, $J_{CF}=2.4$ Hz	86.0, $J_{CF}=23.0$ Hz	89.1, $J_{CF}=173.0$ Hz

Table 4. Characteristic NMR data for isoxazolines **11, 12** and **13**.

	H_4H_6 (**11a**) H_5H_6 (**12, 13**)	H_4F (**11**) H_5F (**12, 13**)	C_3	C_4	C_5	C_6
11	3.8	24.5	159.7, $J_{CF}=2.8$ Hz	59.8, $J_{CF}=22.1$ Hz	89.3, $J_{CF}=1.8$ Hz	86.3, $J_{CF}=173.0$ Hz
12	8.1	8.1	157.3, $J_{CF}=0$ Hz	72.8, $J_{CF}=0$ Hz	86.5, $J_{CF}=26.1$ Hz	86.0, $J_{CF}=171.1$ Hz
13	1.7	28.3	156.4, $J_{CF}=0$ Hz	71.5, $J_{CF}=0$ Hz	87.0, $J_{CF}=17.7$ Hz	86.6, $J_{CF}=0$ Hz



Scheme 3.



Scheme 4.

The regiochemistry and stereochemistry were established using the same criteria as in the previous cases: particulary relevant are the $^3J_{H,H}$ and $^3J_{H,F}$ data (for example, see **12** and **13**). This led to the conclusion that, in the case of this highly electrophilic allylic fluoride, equal amounts of the two regioisomers were obtained. Only the *syn* derivative was isolated in the case of the C_4 regioisomer while for the C_5 there was a slight preference for the *anti* compound.

Theoretical studies of adduct conformations and coupling constants: For each regioisomer **15** and **16**, optimizations of the two possible diastereomeric products (Scheme 4) were carried out using B3LYP/6-31G* to confirm the preferred conformations of the allylic substituents. The *anti* and *syn* diastereomers of **15**, shown in Figure 3, are higher in energy than **16** (Figure 2). The relative energies of structures **A**–**L** are given in Table 5.

The three staggered conformations of both regioisomers are described in Figure 4. Figure 2 shows that, for the more stable 5-substituted isoxazoline **16**, the conformations with the highest energies place the fluorine in position 2. When the fluorine occupies position 3 the electrostatic repulsion with the oxygen is minimized. The methyl substituent shows a strong preference for position 2 to minimize steric repulsions with adjacent methylene hydrogens. Similarly, the fluorine shows a slight preference for position 2 (structures **H** and **K**), while the methyl adopts either position 1 or 3 to minimize steric interactions.

A Boltzmann distribution based on the relative energies of the conformations of each product predicted the percentage of each rotamer present at equilibrium (Table 5). Using the Karplus–Altona equation, the J_{HH} and J_{HF} values for the major regioisomer **16** were calculated and compared to experimental values.[12] The predicted J_{HH} for the *anti* diastereomer of **16** is large (7.3 Hz) since, in the most stable conformation, the dihedral angle is 177°. The smaller J_{HH} value for the *syn* diastereomer (4.6 Hz) is consistent with the dihedral angles of the two most stable conformations (56° and −65°, respectively). The calculated J_{HF} values also reflect the dihedral angles of the more stable conformations. These

Table 5. Predicted relative energies [kcal mol^{-1}] for each rotamer of both diastereomeric products obtained for the reaction in Scheme 4 using B3LYP/6-31G*. The calculated J_{HH} and J_{HF} values are compared to experimental values for the reaction in Scheme 1 (given in parenthesis).

Regioisomer	Diastereomer	Structure	E_{rel}	% rotamer	J_{HH} [Hz]	J_{HF} [Hz]
16	*anti*	**A**	0.0	85		
		B	2.2	2	7.3 (5.6)	11.5 (12.8)
		C	1.1	13		
	syn	**D**	0.8	67	4.6 (3.6)	35.5(21.6)
		E	2.5	4		
		F	1.3	29		
15	*anti*	**G**	5.1	7		
		H	3.8	62	3.1	12.6
		I	4.2	31		
	syn	**J**	5.5	4		
		K	3.8	73	8.4	6.5
		L	4.5	22		

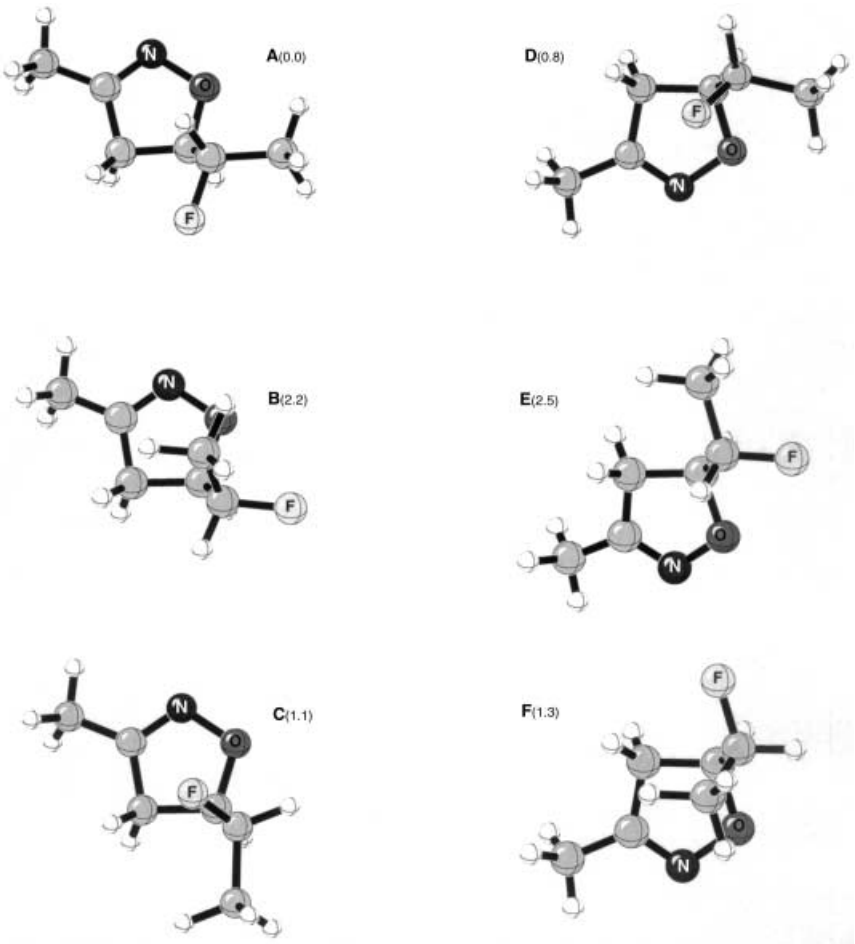


Figure 2. Optimized geometries of 5-substituted isoxazoline products (B3LYP/6-31G*). Structure **A**–**C** are the three conformations of the *anti* diastereomer. Structures **D**–**F** are the three conformations of the *syn* diastereomer. Relative energies are given in kcal mol^{-1}.

calculated J_{HH} and J_{HF} values are in qualitative agreement with the experimental values, thus confirming the conformational preferences around the corresponding C–C bond described above.

Theoretical studies of transition states and stereoselectivities: The reaction between acetonitrile oxide and 3-fluoro-1-butene (Scheme 4) may proceed through twelve possible transition structures: two regioisomers, *Re* or *Si* attack on the alkene, and three staggered transition structures for each case. These twelve structures were optimized using B3LYP/6-31G*. Figure 5 shows the optimized transition structures **M**–**O** leading to the three conformations of the *anti* 5-substituted 2-isoxazoline product and transition structures **P**–**R** which give the *syn* 5-substituted isoxazolines. The transition structures leading to the *anti* and *syn* 4-substituted 2-isoxazoline are given in Figure 6. The relative energies of the transition structures are also shown.

Transition structure **M** (Figure 5), where the fluorine is inside and the methyl is *anti* with respect to the forming C–C bonds is lowest in energy. This agrees with previous conclusions based on nitrile oxide cycloadditions with 3-alkoxy-1-butenes.[6] Structure **P** is the second lowest in energy and is 0.5 kcal mol^{-1} higher since the outside methyl is in a more crowded environment. In structures **N** and **Q** the fluorine is either *anti* or outside resulting in energies 0.9 and 1.8 kcal mol^{-1} higher than structure **M**. The methyl group occupies the inside position in structures **O** and **R**, forcing the fluorine to adopt either the outside or the *anti* position. Structures **O** and **R** are 2.0 and 1.3 kcal mol^{-1} higher in energy than structure **M**. These results are fully consistent with calculated results for allylic ethers: the alkyl group prefers *anti* and the halide (or alkoxy) prefers inside.

The computational studies of the reaction between acetonitrile oxide and 3-methoxy-1-butene showed that the stereoselectivity of the cycloaddition is determined by the inside alkoxy effect.[6] The methoxy group favors the inside position in the transition state, and the methyl group favors the sterically least crowded *anti* position. Similarly, the results of this investigation show that the allylic fluorine substituent prefers the inside over the outside position to minimize lone pair-lone pair electron repulsions with the nitrile oxide oxygen. In both cases, the *anti* position is avoided in order to minimize electron withdrawal from the already electron deficient transition state.

The second best transition structure, **P**, leads to the *syn* product. In this conformation, the fluorine is inside but the methyl is outside. In contrast, the second best transition structure for the cycloaddition with 3-methoxy-1-butene has the methoxy outside and the methyl *anti*. Thus, these calculations predict that the repulsion between the nitrile oxide oxygen and the fluorine is greater than the repulsion between the nitrile oxide oxygen and the methoxy group. Since fluorine is more electronegative than oxygen, there is more electron density around the fluorine substituent, which increases the repulsion between the fluorine and the oxygen relative to that of the methoxy group. Unlike the methoxy case, where the steric hindrance of the methyl favors the *anti* position even in the minor product, the repulsion between the nitrile oxide oxygen and the fluorine is more significant than the steric repulsion of the methyl group.

There is quite a powerful preference for the fluorine to adopt the inside position in the transition state. The calculated product ratio is primarily a result of this and the more fa-

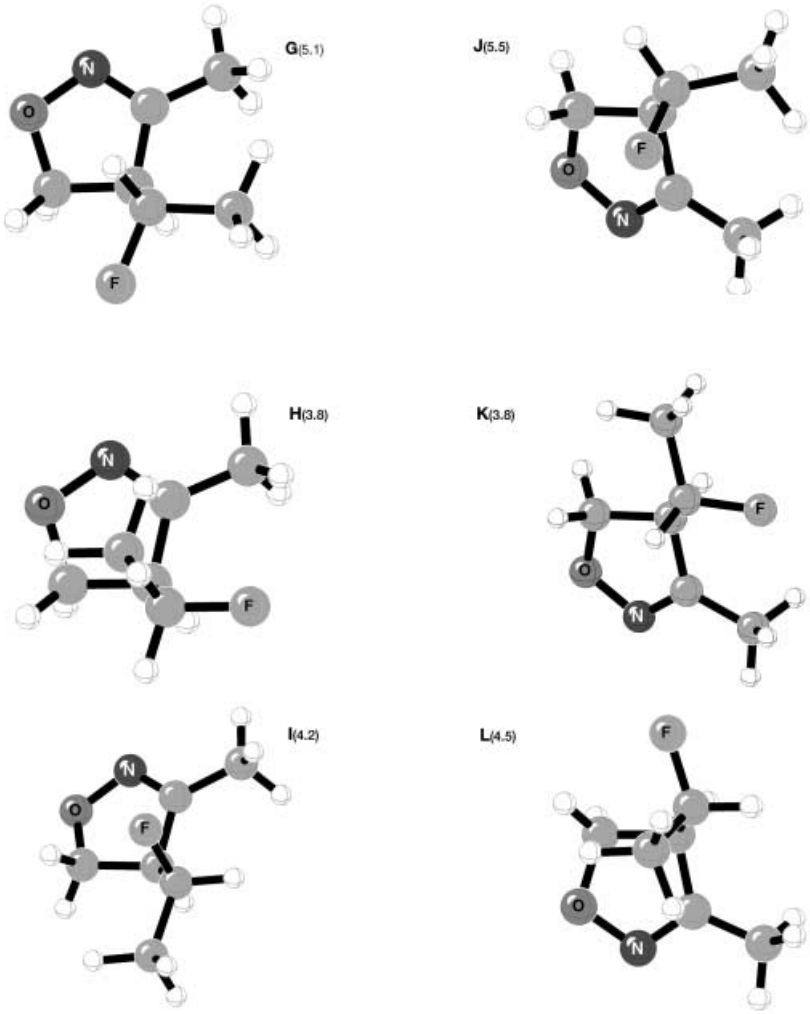


Figure 3. Optimized geometries of 4-substituted isoxazoline products (B3LYP/6-31G*). Structure **G–I** are the three conformations of the *anti* diastereomer. Structures **J–L** are the three conformations of the *syn* diastereomer. Relative energies are given in kcal mol^{-1}.

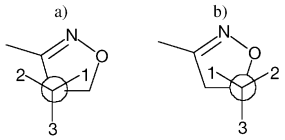


Figure 4. Relative positions of substituents on both *anti* and *syn* a) 4-substituted isoxazolines and b) 5-substituted isoxazolines. Positions 1, 2, and 3 are also referred to as inside, outside, and *anti*, respectively.

vorable *anti* arrangement of the methyl group. This preference for the fluorine to adopt the inside position, while the bulky methyl occupies the *anti* position in the transition state was also observed experimentally in the epoxidation of chiral allylic fluorides.[13] Table 6 shows the predicted product ratios for both diastereomers of each regioisomer.

For the 4-substituted regioisomer, the results are quite different. The lowest energy transition structures leading to the 4-substituted product are structures **U** and **W** (Figure 6), which have the fluorine outside and the methyl either inside or *anti* (the latter is slightly better). The calculated transition structures for the 4-substituted product show a strong preference for the fluorine to occupy the outside position in order to minimize electronic repulsion with the nitrile oxide oxygen. Contrary to the 5-substituted case, the structures where the fluorine is inside are highest in energy. However, the methyl still favors the *anti* position which minimizes steric repulsions. The outside position is more sterically hindered in the 4-substituted case since it is in close proximity to the acetonitrile oxide methyl group.

Figures 5 and 6 also show the calculated bond lengths for the forming C–C and C–O bonds. In the transition structures leading to the major 5-substituted regioisomer, the forming C–C bonds are about 2.2 Å and the forming C–O bonds are closer to 2.4 Å. However, in the minor regioisomer, leading to the 4-substituted product, both the C–C and the C–O forming bond lengths are approximately equal (between 2.25 and 2.30 Å).

The differences in transition state bond lengths can be rationalized by FMO arguments. These reactions are dipole LUMO controlled, and the major product arises from the union of the electrophilic nitrile oxide C (the site with the largest LUMO coefficient) with the unsubstituted alkene terminus. This is the nucleophilic site with the largest HOMO coefficient. The relatively short C–C bond in the transition state for the major, 5-substituted product, occurs due to the stronger bonding at the site of large coefficients.[5]

In contrast, the transition state leading to the 4-substituted adduct has non-ideal HOMO–LUMO alignment and similar bond lengths at both sites.

Examination of the calculated dipole moments for the gas phase transition structures demonstrates the importance of electrostatic effects (Table 7). For the structures leading to the 5-substituted product (**M-R**), the increase in dipole moments parallels the increase in relative energies. In the

Table 6. Predicted Product Percentages for reaction in Scheme 4.

Product	% Product	% Product (toluene)
anti-4-substituted (**A–C**)	6.3	4.3
syn-4-substituted (**D–F**)	17.1	15.0
anti-5-substituted (**G–I**)	52.3	53.3
syn-5-substituted (**J–L**)	24.4	27.4

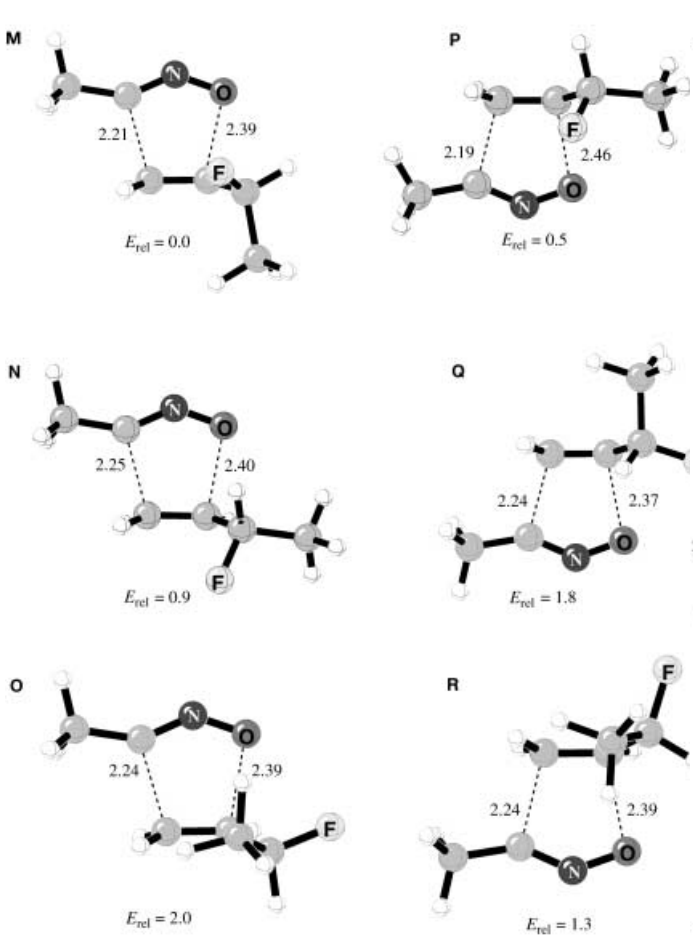


Figure 5. B3LYP/6-31G(d) transition states for the cycloaddition of acetonitrile oxide with (*S*)-3-fluorobutene leading to the 5-substituted 2-isoxazoline. Structures **M, N**, and **O** lead to the *anti* isomer and **P, Q**, and **R** lead to the *syn* isomer. Relative energies are given in kcal mol^{-1}. Distances are in Ångstroms.

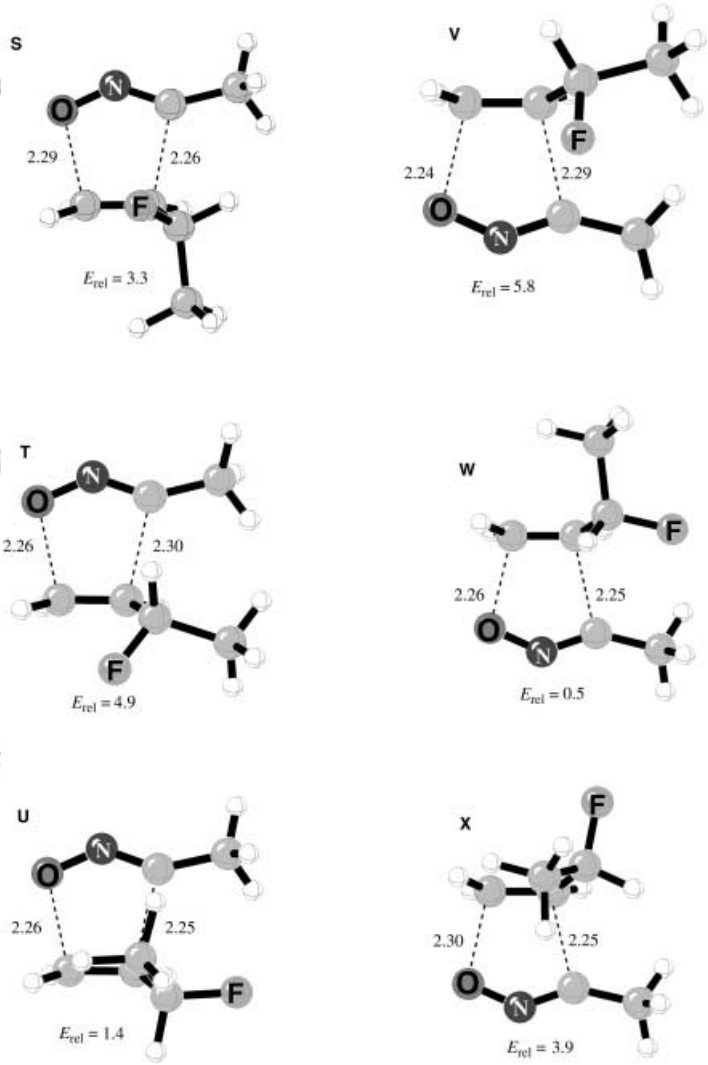


Figure 6. B3LYP/6-31G* transition states for the cycloaddition of acetonitrile oxide with (*S*)-3-fluorobutene leading to the 4-substituted 2-isoxazoline. Structures **S, T**, and **U** lead to the *anti* isomer and **V, W**, and **Z** lead to the *syn* isomer. Relative energies are given in kcal mol^{-1}. Distances are in Ångstroms.

Table 7. Relative energies and dipole moments for transition structures of the reaction between acetonitrile oxide and 3-fluoro-1-butene (Scheme 4).

Transition structure	Relative E [kcal mol^{-1}]	Dipole moment [D]
M	0.0	2.6
N	0.9	3.8
O	2.0	4.8
P	0.5	2.6
Q	1.8	4.7
R	1.3	4.3
S	3.3	3.9
T	4.9	3.9
U	1.2	1.8
V	5.8	4.2
W	0.5	2.1
X	3.9	3.0

lowest energy transition structures (**M, P** and **N**), the C–F bond dipole points in a direction that partially cancels the dipole created by the nitrile oxide. The highest energy structures (**O** and **Q**), where the fluorine is outside, have high dipole moments since the C–F bond dipole is essentially parallel to the nitrile oxide N–O dipole. The steric effect is most pronounced when comparing structures **N** and **R**. In structure **R**, the methyl group is in the sterically crowded inside position which causes the C–C bond to rotate leading to an increase in the net dipole moment. Consequently, the relative energy for structure **R** is higher than structure **N**.

In the transition structures leading to the minor 4-substituted regioisomer, the lowest energy conformations **W** and **U** have small dipole moments. Structure **W** is the lowest energy structure leading to the minor regioisomer, but structure **U** has a smaller dipole moment. The steric hindrance of the methyl group in the inside position in structure **W** leads to a higher relative energy despite the small dipole moment. Also, structures **S** and **T** have similar dipole moments but structure **T** is higher in energy (by 1.6 kcal mol^{-1}) due to the steric interactions of the methyl in the outside position. The highest energy conformer **V** has both a large net dipole and unfavorable steric interactions.

The theoretical studies on the model reaction between acetonitrile oxide and 3-fluoro-1-butene predict a 4:1 ratio of the 5-substituted regioisomer to the 4-substituted regioisomer in toluene. For the major 5-substituted adduct, the *anti* is favored over the *syn* 2:1. The *syn* is favored over the *anti* by 3:1 for the 4-substituted product. Although these results correctly predict the *anti* to *syn* ratio for the major regioisomer, the experiments conducted on the reaction with **2** to yield **5** and **6** did not produce any detectable amount of the 4-substituted regioisomer. This discrepancy could be due, at least in part, to the steric effect of the alkyl groups present both on the 1,3-dipole and on the alkene. Furthermore, it is interesting to note that experiments conducted on the more electrophilic allylic fluorides **3** and **4** did show a preference for the *syn* product in accordance with our calculations even though the presence of such electron withdrawing groups will induce further steric and electronic effects.

Conclusion

We have presented experimental and theoretical results on the stereoselectivity of nitrile oxide cycloadditions to chiral allylic fluorides. We have shown that the role of the allylic fluorine parallels the role of allylic ethers.[6] That is, the diastereoselectivity of the 5-substituted regioisomer is determined by the preference for the alkyl group at the stereogenic center to be *anti* with respect to the forming bond and the fluorine to be inside. The fluorine adopts the role of the inside-alkoxy group, but has a larger inside preference. This effect was also seen in the Diels–Alder reactions with chiral allylic fluorides.[3] We further established the preference for the fluorine to adopt the outside position in the 4-substituted regioisomer, leading to the formation of the *syn* product.

The experimental and theoretical studies on the cycloadditions with chiral alkenes have determined that the diastereoselectivity of the reactions are influenced by the electronegativity and steric bulk of the allylic substituents. In general, small, electronegative atoms like fluorine or oxygen (alkoxy) will position themselves to avoid electrostatic interactions and to minimize the net dipole of the transition state. Analyzing the possible transition states of cycloadditions to chiral alkenes to minimize steric and electrostatic interactions with allylic substituents will predict the stereochemical outcome of the reaction.

Experimental Section

General: All reactions were carried out in flame-dried glassware under an atmosphere of nitrogen with magnetic stirring. Thin-layer chromatography (TLC) was done on Merck (Art. 1.05554) precoated silica gel 60 F_{254} aluminium sheets (layer thickness 0.2 mm) and developed in the indicated eluent systems. Visualisation was effected with a UV lamp (254 nm) and/or either by staining with *p*-anisaldehyde/H_2SO_4 solution or by staining with $KMnO_4$ solution. Flash column chromatography was performed using silica gel 60 (Geduran, 40–63 μm, Merck). Solvents were purified as follows: tetrahydrofuran was freshly distilled from sodium/benzophenone under N_2. Diethyl ether and dichloromethane were distilled from P_2O_5 and stored over 3 Å molecular sieves. Triethylamine was distilled from CaH_2. The petroleum ether used had a boiling range of 30–60 °C. NMR spectra were recorded on a Bruker ARX 400 MHz spectrometer. All chemical shifts are reported in parts per million (δ). ^{1}H NMR (400 MHz) spectra were recorded at room temperature in $CDCl_3$ or C_6D_6 solutions and referenced to residual $CHCl_3$ (7.27 ppm) or C_6H_6 (7.16 ppm). Fully decoupled ^{13}C NMR (100 MHz) spectra were recorded in $CDCl_3$ or C_6D_6 solutions. The center peaks of $CDCl_3$ (77.0 ppm) and C_6D_6 (128.7 ppm) were used as the internal reference. ^{19}F NMR (376.5 MHz) spectra were recorded in $CDCl_3$ or C_6D_6 solutions using $CFCl_3$ as internal reference. Elemental analyses were performed by the department of microanalyses (C.R.M.P.O.) in Rennes (France). Mass spectra were carried out on a VARIAN MAT 311 spectrometer at the C.R.M.P.O. in Rennes (France).

3-Fluoro-1-ene-dodecane (2): Lindlar catalyst (30 mg, 20% weight) was added to a solution of propargylic fluorinated compound **1** (150 mg, 0.8 mmol, 1.0 equiv) and pyridine (66 μL, 0.8 mmol, 1.0 equiv) in pentane (5 mL) at room temperature. The black suspension was stirred under a hydrogen atmosphere during 15 h. When analysis of an aliquot by ^{19}F NMR showed no more starting material (signal at −175.45 ppm), the reaction mixture was filtered through Celite and concentrated at reduced pressure. Purification by flash chromatography (pentane) gave the title compound **2** (126 mg, 84%) as a colorless oil. R_f = 0.58 (pentane); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.89 (dddd, J = 17.3 Hz, J_{HF} = 13.9 Hz, J = 10.6 Hz, J = 6.0 Hz, 1H, H_2), 5.31 (ddt, J = 17.3 Hz, J_{HF} = 3.6 Hz, J = 1.3 Hz, 1H, H_{1trans}), 5.22 (dt, J = 10.6 Hz, J = 1.3 Hz, 1H, H_{1cis}), 4.87 (dqt, J_{HF} = 48.7 Hz, J = 6.0 Hz, J = 1.3 Hz, 1H, H_3), 1.80–1.53 (m, 2H, H_4), 1.50–1.22 (m, 14H, H_{5-11}), 0.89 (t, J = 6.7 Hz, 3H, H_{12}); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 136.80 (d, J = 19.5 Hz, C_2), 116.69 (d, J = 11.8 Hz, C_1), 93.75 (d, J = 166.6 Hz, C_3), 35.22 (d, J = 22.1 Hz, C_4), 31.88 (C), 29.51 (2C), 29.38 (C), 29.31 (C), 24.66 (d, J = 4.6 Hz, C_5), 22.68 (C), 14.10 (C_{12}); ^{19}F NMR ($CDCl_3$, 376.5 MHz): δ = −177.22 (ddddd, J = 48.1 Hz, J = 26.3 Hz, J = 17.6 Hz, J = 14.0 Hz, J = 3.5 Hz); MS (EI, 70 eV): m/z (%): 166 (1.3) $[M-HF]^+$, 138 (3.0) $[M-Et-F]^+$, 137 (1.2) $[M-Et-HF]^+$, 43 (100.0) $[C_3H_7]^+$; HRMS (EI, 70 eV): calcd for $C_{12}H_{22}$: 166.1722 $[M-HF]^+$; found: 166.172; calcd for $C_{10}H_{18}$: 138.1409 $[M-Et-F]^+$; found: 138.141; calcd for $C_{10}H_{17}$: 137.1330 $[M-Et-HF]^+$; found: 137.132.

General procedure for formation of isoxazolines by Mukaiyama's method:[8] A solution of phenyl isocyanate in dry toluene was added dropwise over 3 h to a mixture of alkene, nitro compound and triethylamine in dry toluene at room temperature. After a few minutes, evolution of CO_2 began and diphenylurea separated out. At the end of the addition, the mixture was heated for 2 h at 50 °C, and then was allowed to cool to room temperature. The reaction mixture was stirred for an additional hour with water (1 mL) and filtered. The filtrate was dried over $MgSO_4$, concentrated under reduced pressure and the isoxazolines were purified by chromatography.

(5*RS*)-[(1*RS*)-Fluorodecyl]-3-ethyl-2-isoxazoline (*syn*-5) and (5*RS*)-5-[(1*SR*)-1-fluorodecyl]-3-ethyl-2-isoxazoline (*anti*-6): Starting from phenyl isocyanate (63 μL, 0.6 mmol, 2 equiv), alkene **2** (53 mg, 0.3 mmol, 1 equiv), nitropropane (26 μL, 0.3 mmol, 1 equiv) and triethylamine (four drops) in a total amount of 150 μL dry toluene, a *syn*/*anti* mixture of the title compounds was obtained in a 3:7 ratio (as determined by ^{19}F NMR). The two diastereomers were separated by silica gel column chromatography (pentane/Et_2O 8:2) affording pure ***syn*-5** (16 mg, 22%) and pure ***anti*-6** (42 mg, 57%) as white powders.

***syn*-5**: R_f = 0.28 (P/E 8:2); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 4.59 (dddd, J_{HF} = 21.6 Hz, J = 11.2 Hz, J = 7.8 Hz, J = 3.6 Hz, 1H, H_5), 4.43 (ddt, J_{HF} = 47.7 Hz, J = 9.2 Hz, J = 3.6 Hz, 1H, H_6), AB System: $\tilde{\nu}_A$ = 3.01 (dd, J = 17.0 Hz, J = 11.2 Hz, 1H, H_4) and $\tilde{\nu}_B$ = 2.89 (dd, J = 17.0 Hz, J = 7.8 Hz, 1H, H_4), 2.37 (q, J = 7.6 Hz, 2H, H_2), 1.87–1.73 (m, 2H, H_7), 1.59–1.22 (m, 14H, H_{8-14}), 1.18 (t, J = 7.5 Hz, 3H, H_1), 0.89 (t, J = 6.4 Hz, 3H, H_{15}); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 159.69 (C_3), 93.63 (d, J = 176.48 Hz, C_6), 79.72 (d, J = 20.9 Hz, C_5), 38.16 (d, J = 5.6 Hz, C_4), 31.84 (C), 30.55 (d, J = 21.1 Hz, C_7), 29.46 (C), 29.42 (C), 29.33 (C), 29.25 (C), 25.09 (d, J = 4.0 Hz, C_8), 22.64 (C), 21.13 (C_2), 14.09 (C_{15}), 10.84 (C_1); ^{19}F NMR ($CDCl_3$, 376.5 MHz): δ = −196.59 (dddd, J = 47.7 Hz, J = 35.0 Hz, J = 21.0 Hz, J = 14.0 Hz); HRMS (EI, 70 eV): calcd for $C_{15}H_{28}NOF$: 257.2155 $[M]^+$; found: 257.217 (4 ppm); elemental analysis (%) calcd for $C_{15}H_{28}FNO$: C 70.00, H 10.97; found: C 69.15, H 10.75.

***anti*-6**: R_f=0.38 (P/E 8:2); ^{1}H NMR (C_6D_6, 400 MHz): δ=4.29 (ddt, J_{HF}=48.8 Hz, J=7.4 Hz, J=5.9 Hz, 1H, H_6), 4.21 (dddd, J_{HF}=12.8 Hz, J=10.5 Hz, J=6.8 Hz, J=5.9 Hz, 1H, H_5), AB system: $\tilde{\nu}_A$=2.50 (dd, J=17.0 Hz, J=6.8 Hz, 1H, H_4) and $\tilde{\nu}_B$=2.29 (dd, J=17.0 Hz, J=10.5 Hz, 1H, H_4), 1.93 (q, J=7.5 Hz, 2H, H_2), 1.57–1.43 (m, 2H, H_7), 1.36–1.17 (m, 14H, H_{8-14}), 0.92 (t, J=7.5 Hz, 3H, H_{15}), 0.88 (t, J=7.5 Hz, 3H, H_1); ^{13}C NMR (C_6D_6, 100 MHz): δ = 159.12 (C_3), 94.01 (d, J=175.1 Hz, C_6), 81.22 (d, J=24.1 Hz, C_5), 38.82 (d, J=4.0 Hz, C_4), 33.01 (d, J=20.3 Hz, C_7), 32.96 (C), 30.60 (C), 30.55 (C), 30.45 (C), 30.41 (C), 25.96 (d, J=3.2 Hz, C_8), 23.77 (C), 21.86 (C_2), 15.03 (C_{15}), 11.57 (C_1); ^{19}F NMR (C_6D_6, 376.5 MHz): δ = −193.87 (m); HRMS (EI, 70 eV): calcd for $C_{15}H_{28}NOF$: 257.2155 $[M]^+$; found: 257.215 (2 ppm); elemental analysis (%) calcd for $C_{15}H_{28}FNO$: C 70.00, H 10.97; found: C 70.35, H 10.86.

5(*SR*)-5-Benzoyl-(4*RS*)-4-[(1*RS*)-1-fluoroethyl]-3-ethyl-2-isoxazoline (*syn*-7a), (5*SR*)-5-benzoyl-(4*RS*)-4-[(1*SR*)-1-fluoroethyl]-3-ethyl-2-isoxazoline (*anti*-8a), (5*SR*)-5-[(1*SR*)-1-fluoroethyl]-(4*RS*)-4-benzoyl-3-ethyl-2-isoxazoline (*syn*-9a) and (5*SR*)-5-[(1*RS*)-1-fluoroethyl]-(4*RS*)-4-benzoyl-3-ethyl-2-isoxazoline (*anti*-10a): Starting from phenyl isocyanate (220 μL, 1.98 mmol, 1.8 equiv), alkene **3a** (200 mg, 1.12 mmol, 1 equiv), nitropropane (100 μL, 1.1 mmol, 1 equiv) and triethylamine (four drops) in a total amount of 2 mL dry toluene, 240 mg (overall yield 85%) of a mixture ***syn*-7a**/***anti*-8a**/***syn*-9a**/***anti*-10a** of the four title compounds were obtained in a ratio 41:35:7:17 (as determined by ^{19}F NMR). Different mixtures enriched in the individual diastereomers were obtained using silica gel column chromatography (petroleum ether/Et_2O 9:1). Extensive NMR studies on these mixtures allowed to characterize each isomer.

***syn*-7a**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.15–8.05 (m, 2H, $H_{10,11}$), 7.70–7.50 (m, 3H, H_{12-14}), 5.54 (d, J=5.4 Hz, 1H, H_5), 4.95 (dquint, J_{HF}=46.6 Hz, J=6.4 Hz, 1H, H_6), 4.25 (ddd, J_{HF}=11.6 Hz, J=6.2 Hz, J=5.5 Hz, 1H, H_4), 2.55 (dq, J=15.0 Hz, J=7.4 Hz, 1H, H_2), 2.36 (dq, J=15.0 Hz, J=7.4 Hz, 1H, H_2), 1.42 (dd, J_{HF}=24.0 Hz, J=6.3 Hz, 3H, H_7), 1.25 (t, J=7.2 Hz, 3H, H_1); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 193.2, 159.9 (d, J_{CF}=4.9 Hz), 134.4, 134.1, 129.8, 128.6, 88.6 (d, J_{CF}=173.4 Hz), 81.9 (d, J_{CF}=3.7 Hz), 55.6 (d, J_{CF}=22.4 Hz), 21.0 (d, J_{CF}=1.8 Hz), 18.0 (d, J_{CF}=22.8 Hz), 10.7; ^{19}F NMR ($CDCl_3$, 376.5 MHz): δ = −176.2 (dqd, J=47.7 Hz, J=24.0 Hz, J=11.5 Hz).

***anti*-8a**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.15–8.05 (m, 2H, $H_{10,11}$), 7.70–7.50 (m, 3H, H_{12-14}), 5.58 (d, J=7.4 Hz, 1H, H_5), 5.09 (dqd, J_{HF}=47.2 Hz, J=6.4 Hz, J=2.7 Hz, 1H, H_6), 4.15 (ddd, J_{HF}=28.8 Hz, J=7.3 Hz, J=2.7 Hz, 1H, H_4), 2.57 (dq, J=15.0 Hz, J=7.4 Hz, 1H, H_2), 2.37 (dq, J=15.0 Hz, J=7.4 Hz, 1H, H_2), 1.42 (dd, J_{HF}=24.0 Hz, J=6.3 Hz, 3H, H_7), 1.25 (t, J=7.2 Hz, 3H, H_1); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 193.6, 159.5 (d, J_{CF}=1.0 Hz), 134.5, 134.1, 129.9, 128.8, 86.8 (d, J_{CF}=174.2 Hz), 81.2 (d, J_{CF}=3.5 Hz), 56.1 (d, J_{CF}=21.3 Hz), 20.1, 18.9 (d, J_{CF}=22.4 Hz), 10.6; ^{19}F NMR ($CDCl_3$, 376.5 MHz): δ = −180.40 (ddq, J=47.2 Hz, J=28.4 Hz, J=23.6 Hz); HRMS (EI, 70 eV): calcd for $C_{14}H_{16}NO_2F$: 249.1165 $[M]^+$; found: 249.116.

***syn*-9a**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.04–8.00 (m, 2H, $H_{10,11}$), 7.70–7.40 (m, 3H, H_{12-14}), 5.07 (d, J=7.4 Hz, 1H, H_4), 4.85 (ddd, J_{HF}=21.6 Hz, J=7.4 Hz, J=2.8 Hz, 1H, H_5), 2.50–2.20 (m, 2H, H_2), 1.49 (dd, J_{HF}=24.0 Hz, J=6.4 Hz, 3H, H_7), 1.20 (t, J=7.4 Hz, 3H, H_1); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 195.0, 158.0, 134.5, 133.8, 129.7, 129.1, 89.1 (d, J_{CF}=175.2 Hz), 84.9 (d, J_{CF}=20.8 Hz), 58.6 (d, J_{CF}=3.6 Hz), 21.0, 16.3 (d, J_{CF}=22.7 Hz), 10.8; ^{19}F NMR ($CDCl_3$, 376.5 MHz): δ = −189.50 (dquint, J=46.5 Hz, J=24.1 Hz).

***anti*-10a**: ^{1}H NMR (C_6D_6, 400 MHz): δ = 7.90–7.80 (m, 2H, $H_{10,11}$), 7.10–6.95 (m, 3H, H_{12-14}), 4.81 (d, J=6.6 Hz, 1H, H_4), 4.76 (dt, J_{HF}=12.7 Hz, J=6.2 Hz, 1H, H_5), 4.40 (dquint, J_{HF}=48.6 Hz, J=6.2 Hz, 1H, H_6), 1.97 (dq, J=16.6 Hz, J=7.4 Hz, 1H, H_2), 1.81 (dq, J=16.6 Hz, J=7.4 Hz, 1H, H_2), 0.96 (dd, J_{HF}=24.3 Hz, J=6.3 Hz, 3H, H_7), 0.90 (t, J=7.4 Hz, 3H, H_1); ^{13}C NMR (C_6D_6, 100 MHz): δ = 194.7, 157.2, 136.1, 133.9, 133.6, 129.0, 89.2 (d, J_{CF}=173.3 Hz), 86.3 (d, J_{CF}=22.5 Hz), 59.2 (d, J_{CF}=2.3 Hz), 21.2, 17.9 (d, J_{CF}=21.6 Hz), 10.7; ^{19}F NMR (C_6D_6, 376.5 MHz): δ = −184.80 (dqd, J=48.7 Hz, J=24.5 Hz, J=12.7 Hz).

(5*SR*)-5-Benzoyl-(4*RS*)-4-[(1*RS*)-1-fluoro-2,2-dimethyl-propyl]-3-ethyl-2-isoxazoline (*syn*-7b), (5*SR*)-5-benzoyl-(4*RS*)-4-[(1*SR*)-1-fluoro-2,2-dimethyl-propyl]-3-ethyl-2-isoxazoline (*anti*-8b) and (5*SR*)-5-[(1*RS*)-1-fluoro-2,2-dimethyl-propyl]-(4*RS*)-4-benzoyl-3-ethyl-2-isoxazoline (*anti*-10b): Starting from phenyl isocyanate (100 μL, 0.90 mmol, 2.2 equiv), alkene **3b** (90 mg, 0.41 mmol, 1 equiv), nitropropane (50 μL, 0.55 mmol, 1.3 equiv) and triethylamine (two drops) in a total amount of 0.5 mL dry toluene, 95 mg (overall yield 80%) of a mixture ***syn*-7b**/***anti*-8b**/***anti*-10b** of the three title compounds were obtained in a ratio 38:32:30 (as determined by ^{19}F NMR). Different mixtures enriched in the individual diastereomers were obtained using silica gel column chromatography (petroleum ether/Et_2O 95:5). Extensive NMR studies on these mixtures allowed to characterize each isomer.

***syn*-7b**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.20–8.00 (m, 2H, $H_{13,14}$), 7.80–7.40 (m, 3H, H_{15-17}), 5.38 (d, J=3.5 Hz, 1H, H_5), 4.36 (dd, J_{HF}=48.4 Hz, J=9.4 Hz, 1H, H_6), 4.35 (dd, J=9.4 Hz, J=3.5 Hz, 1H, H_4), 2.59 (dq, J=15.2 Hz, J=7.4 Hz, 1H, H_2), 2.36 (dq, J=15.3 Hz, J=7.4 Hz, 1H, H_2), 1.18 (t, J=7.5 Hz, 3H, H_1), 1.00 (d, J_{HF}=1.3 Hz, 9H, H_{8-10}); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 193.5 (d, J_{CF}=1.0 Hz), 162.4 (d, J_{CF}=4.0 Hz), 134.2, 134.0, 129.9, 128.7, 99.9 (d, J_{CF}=181.7 Hz), 84.6 (d, J_{CF}=7.1 Hz), 49.5 (d, J_{CF}=22.0 Hz), 35.9 (d, J_{CF}=20.1 Hz), 25.3 (d, J_{CF}=5.2 Hz), 22.1 (d, J_{CF}=7.5 Hz), 11.2; ^{19}F NMR ($CDCl_3$, 376.5 MHz): δ = −185.80 (d, J=48.6 Hz).

***anti*-8b**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.20–8.00 (m, 2H, $H_{13,14}$), 7.80–7.40 (m, 3H, H_{15-17}), 5.84 (d, J=6.6 Hz, 1H, H_5), 4.50 (d, J_{HF}=46.2 Hz, 1H, H_6), 4.37 (dd, J_{HF}=34.5 Hz, J=6.6 Hz, 1H, H_4), 2.60 (dq, J=15.1 Hz, J=7.4 Hz, 1H, H_2), 2.38 (dq, J=15.1 Hz, J=7.4 Hz, 1H, H_2), 1.23 (t, J=7.4 Hz, 3H, H_1), 0.96 (s, 9H, H_{8-10}); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 193.2, 160.0, 134.8, 134.1, 130.0, 128.8, 96.1 (d, J_{CF}=184.6 Hz), 80.1 (d, J_{CF}=5.6 Hz), 50.5 (d, J_{CF}=20.8 Hz), 35.4 (d, J_{CF}=19.0 Hz), 25.6 (d, J_{CF}=4.3 Hz), 19.5, 10.8; ^{19}F NMR ($CDCl_3$, 376.5 MHz): δ = −195.50 (dd, J=46.0 Hz, J=34.0 Hz); HRMS (EI, 70 eV): calcd for $C_{17}H_{22}NO_2F$: 291.1634 $[M]^+$; found: 291.164.

***anti*-10b**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.20–8.00 (m, 2H, $H_{13,14}$), 7.80–7.40 (m, 3H, H_{15-17}), 5.22 (d, J=7.0 Hz, 1H, H_4), 5.11 (ddd, J_{HF}=11.3 Hz, J=7.0 Hz, J=6.0 Hz, 1H, H_5), 4.31 (dd, J_{HF}=46.7 Hz, J=6.0 Hz, 1H, H_6), 2.70–2.15 (m, 2H, H_2), 1.37 (t, J=7.5 Hz, 3H, H_1), 0.98 (d, J_{HF}=1.4 Hz, 9H, H_{8-10}); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 195.3, 157.8, 134.3, 134.1, 129.8, 128.8, 99.0 (d, J_{CF}=180.8 Hz), 82.9 (d, J_{CF}=23.9 Hz), 59.2 (d, J_{CF}=5.9 Hz), 34.3 (d, J_{CF}=19.0 Hz), 25.5 (d, J_{CF}=5.1 Hz), 21.2, 10.7; ^{19}F NMR ($CDCl_3$, 376.5 MHz): δ = −192.80 (dd, J=48.6 Hz, J=11.3 Hz).

5,5-Diethoxycarbonyl-(4*RS*)-4-[(1*RS*)-1-fluoroethyl]-3-ethyl-2-isoxazoline (*syn*-11), (5*SR*)-5-[(1*RS*)-1-fluoroethyl]-4,4-diethoxycarbonyl-3-ethyl-2-isoxazoline (*anti*-12), (5*SR*)-5-[(1*SR*)-1-fluoroethyl]-4,4-diethoxycarbonyl-3-ethyl-2-isoxazoline (*syn*-13) and fluorinated amine 14: Starting from phenyl isocyanate (660 μL, 5.95 mmol, 2.2 equiv), alkene **4** (600 mg, 2.75 mmol, 1 equiv), nitropropane (300 μL, 3.29 mmol, 1.2 equiv) and triethylamine (five drops) in a total amount of 6 mL dry toluene, a mixture ***syn*-11**/***anti*-12**/***syn*-13**/**amine** of the four title compounds was obtained in a ratio 31:19:10:40 (as determined by ^{19}F NMR: a ratio of 52:31:17 is calculated for the mixture ***syn*-11**/***anti*-12**/***syn*-13**). Using silica gel column chromatography (petroleum ether/Et_2O 9:1) it was possible to isolate ***syn*-11** and several mixtures enriched in ***anti*-12** and ***syn*-13** which allowed to characterize each of them by NMR.

***syn*-11**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.02 (dqd, J_{HF}=47.0 Hz, J=6.6 Hz, J=3.9 Hz, 1H, H_6), 4.40–4.23 (m, 4H, $H_{8,10}$), 4.17 (dd, J_{HF}=24.5 Hz, J=3.9 Hz, 1H, H_4), 2.61 (dq, J=14.8 Hz, J=7.4 Hz, 1H, H_2), 2.39 (dq, J=14.8 Hz, J=7.4 Hz, 1H, H_2), 1.55 (dd, J_{HF}=23.7 Hz, J=6.6 Hz, 3H, H_7), 1.33 (t, J=7.1 Hz, 6H, $H_{9,11}$), 1.24 (t, J=7.4 Hz, 3H, H_1); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 167.0, 166.2, 159.7 (d, J_{CF}=2.8 Hz), 89.3 (d, J_{CF}=1.8 Hz), 86.3 (d, J_{CF}=172.9 Hz), 63.2, 62.9, 59.8 (d, J_{CF}=22.1 Hz), 22.0 (d, J_{CF}=2.2 Hz), 19.7 (d, J_{CF}=22.7 Hz), 13.96, 13.92, 10.8; ^{19}F NMR ($CDCl_3$, 376.5 MHz): δ = −179.90 (dquint, J=47.2 Hz, J=23.9 Hz); HRMS (EI, 70 eV): calcd for $C_{13}H_{20}NO_5F$: 189.1325 $[M]^+$; found: 289.133.

***anti*-12**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.18 (t, J_{HF}=J_{HH}=8.1 Hz, 1H, H_5), 4.75 (ddq, J_{HF}=47.1 Hz, J=8.1 Hz, J=6.2 Hz, 1H, H_6), 4.35–4.20 (m, 4H, $H_{8,10}$), 2.55 (q, J=7.4 Hz, 2H, H_2), 1.50 (dd, J_{HF}=25.0 Hz, J=6.2 Hz, 3H, H_7), 1.26 (t, J=7.4 Hz, 3H, H_1), 1.15 (t, J=7.2 Hz, 6H, $H_{9,11}$); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 165.5, 165.4, 157.3, 86.5 (d, J_{CF}=26.1 Hz), 86.0 (d, J_{CF}=171.1 Hz), 72.8, 63.0, 62.8, 20.7, 18.1 (d, J_{CF}=21.3 Hz), 13.9, 13.8, 10.8; ^{19}F NMR ($CDCl_3$, 376.5 MHz): δ = −182.30 (dqd, J=50.1 Hz, J=25.1 Hz, J=8.0 Hz).

***syn*-13**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.06 (dd, J_{HF}=28.3 Hz, J=1.7 Hz, 1H, H_5), 5.01 (dqd, J_{HF}=46.4 Hz, J=6.6 Hz, J=1.7 Hz, 1H, H_6),

4.38–4.22 (m, 4H, $H_{8,10}$), 2.50–2.30 (m, 2H, H_2), 1.55 (dd, $J_{HF}=23.9$ Hz, $J=6.6$ Hz, 3H, H_7), 1.32 (t, $J=7.1$ Hz, 6H, $H_{9,11}$), 1.27 (t, $J=6.1$ Hz, 3H, H_1); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 165.7, 156.4, 87.0 (d, $J_{CF}=17.7$ Hz), 86.7 (d, $J_{CF}=176.3$ Hz), 71.5, 63.2, 62.8, 20.8, 17.9 (d, $J_{CF}=23.1$ Hz), 14.0, 13.9, 11.1; ^{19}F NMR ($CDCl_3$, 376.5 MHz): δ = −189.30 (ddq, $J=$ 47.7 Hz, $J=28.3$ Hz, $J=23.9$ Hz).

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[1] See for instance: a) *Fluorine in Bioorganic Chemistry* (Eds.: J. T. Welch, S. Eswarakrishnan), Wiley-Interscience, New York, **1991**; b) *Experimental Methods in Organic Fluorine Chemistry* (Eds.: T. Kitazume, T. Yamazaki), Gordon and Breach Science Publishers, Tokyo, **1998**; c) *Enantiocontrolled Synthesis of Fluoro-Organic Compounds* (Ed.: V. A. Soloshonok), Wiley, Chichester, **1999**, and references therein.

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