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Synthesis of α-Trifluoromethyl-*β*-lactams and Esters of *β*-Amino Acids via 1,3-Dipolar Cycloaddition of Nitrones to Fluoroalkenes†

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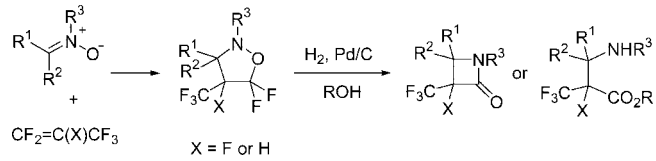

Nitrones derived from aromatic or aliphatic aldehydes or ketones react with hexafluoropropene (HFP) or 2*H*-pentafluoropropene (PFP) to give the respective fluorinated isoxazolidine derivatives in good yields with complete regioselectivity and moderate diastereoselectivity. Catalytic hydrogenolysis of the N−O bond under ambient pressure and temperature leads to fluorides of *β*-amino acids that undergo cyclization to α-trifluoromethylated *β*-lactams or, under acidic conditions, form esters of α-trifluoromethylated *β*-amino acids.

Introduction

Fluorinated analogues of biologically relevant compounds are increasingly important as modern pharmaceutical and plant protection agents.[1,2] In particular, there is a growing interest in new methods of selective introduction of a trifluoromethyl group into the desired position in the molecule.[1,3] While a similar size of fluorine and hydrogen allows the biological activity to be retained,[4] the special properties of perfluoroalkyl groups, like the high energy of C−F bonds, low polarizability, and high lipophilicity,[1,5] often provide an increased metabolic stability and improved bioavailability to the resulting modified molecule. High electronegativity of fluorine also has a significant influence on the electronic character of the neighboring functional groups, for example, it can strongly decrease basicity of amine functions.[6]

In this paper we wish to report a novel approach to α-trifluoromethylated *β*-lactams and *β*-amino acids. In spite of very wide application of pharmaceuticals containing a *β*-lactam moiety[7] only a few examples of the synthesis of their trifluoromethylated derivatives have been reported so far.[6,8] Such compounds can be obtained via [2 + 2] cycloaddition of fluoroalkylketenes to imines and diimides.[9,10] Formation of α-trifluoromethylated *β*-lactams as side products of the diastereoselective synthesis of α-trifluoromethyl-*β*-amino acids from imines and benzyl 2-bromoperfluoropropionate was reported by Ishihara and co-workers.[11] [2 + 2] cycloaddition of perfluoroisobutene to benzanilide and hydrolysis of the CF_2−N ring fragment to amide group provided an α,α-bis(trifluoromethylated) *β*-lactam.[12] A multistep synthesis of α-methyl-α-trifluoromethyl *β*-lactam was described.[13] 4-Trifluoromethyl-2-azetidin-2-one was used in the synthesis of derivatives of 4-trifluoromethylazetidine.[6]

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† This paper is dedicated to Professor Dieter Seebach on the occasion of his 70th birthday.

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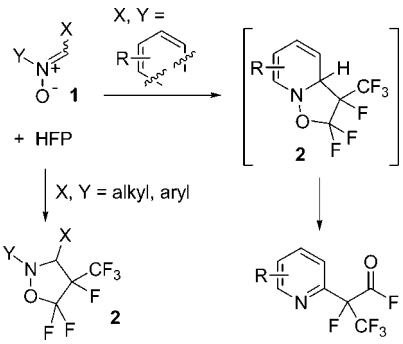
SCHEME 1. 1,3-Dipolar Cycloaddition of Azines *N*-Oxides and Nitrones to HFP

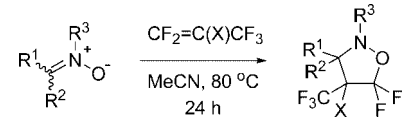


In the course of our research focused on new methods of selective introduction of fluoroalkyl groups into organic compounds we investigated a reaction of aromatic *N*-oxides with hexa- or 2*H*-pentafluoropropene (HFP or PFP). Isoxazolidines, the initial products of 1,3-dipolar cycloaddition, are unstable and undergo spontaneous ring opening leading to a wide range of derivatives of 2-heteroarylperfluoropropionic acids.[14] Herein we report our results concerning an analogous reaction of 1,3-dipolar cycloaddition of nitrones to fluorinated alkenes (Scheme 1).[15] The obtained isoxazolidines are stable but can be further transformed under reductive conditions into α-trifluoromethyl-β-lactams and esters of β-amino acids.

The synthesis of β-lactams via ring contraction of adducts of nitrones to alkenes and alkynes containing peculiar substituents has several precedents. The Kinugasa reaction is a well-established way of accessing azetidinone rings from nitrones and copper acetylides.[16] Syntheses of β-lactams from adducts of nitrones and 2-nitroacrylonitrile[17] or trimethylsilylacetylene were described.[18] Cordero and co-workers reported the formation of β-lactams by ethylene extrusion from spirocyclopropane isoxazolidines, prepared from nitrones and methylenecyclopropanes.[19] Another example, more closely related with our work, is formation of a trifluoromethylated β-lactam by ring contraction of an isoxazolidine obtained from a nitrone and 1-nitro-3,3,3-trifluoropropene.[20]

The outcome of the reaction of HFP with compounds of the general structure **1** containing a X−C=N$^+$(Y)−O$^-$ moiety depends on whether this fragment is or is not a part of an aromatic ring. For aromatic azine *N*-oxides, rearomatization of the heterocyclic ring provides the driving force for the N−O bond scission in the transient 4,5,5-trifluoro-4-trifluoromethyl-isoxazolidines **2** which usually cannot be isolated.[21] Instead, they are spontaneously transformed into acyl fluorides of 2-heteroarylperfluoropropionic acids with elimination of HF as described by us before.[14] In the case of nitrones the adducts are expected to be stable compounds. This reaction pathway was only scarcely investigated and only a few examples of adducts of HFP and perfluoroisobutene to nitrones prepared under harsh conditions (autoclave) were described in a single report by Knunyants and co-workers.[22]

TABLE 1. Cycloaddition of Nitrones to HFP and PFP



alkene	nitrone (R^1, R^2, R^3)	product[a]
HFP (X = F)	**1a** (*p*-MeC$_6$H$_4$, H, Me)	**2a** (85%; 2.8:1)
	1b (Ph, H, Me)	**2b** (60%; 3.5:1)
	1c (*p*-MeOC$_6$H$_4$, H, Me)	**2c** (87%; 2.1:1)
	1d (2-thienyl, H, Me)	**2d** (63%; 4.0:1)
	1e (3-Py, H, Me)	**2e** (73%; 1.2:1)[b]
	1f (Ph, Ph, Me)	**2f** (68%)
	1g (Ph, H, −(CH$_2$)$_3$OH)	**2g** (63%; 1.4:1)
	1h, 3,4-dihydro-6,7-dimethoxyisoquinoline *N*-oxide	**2h** (75%; 1:3.7)
	1i, 2-methoxycarbonyl-pyrroline *N*-oxide	**2i** (31%; 1:4.5)
	1j, 3,4,5,6-tetrahydropyridine *N*-oxide	**2j** (86%; 1:3.4)[c]
PFP (X = H)	**1a** (*p*-MeC6H4, H, Me)	**3a** (68%; 2.0:1)
	1c (*p*-MeOC$_6$H$_4$, H, Me)	**3c** (88%; 2.0:1)
	1d (2-thienyl, H, Me)	**3d** (65%; >9:1)[d]

[a] Yields and diastereoisomers ratios given in parentheses. [b] Reaction at rt for 7 days; [c] Reaction at rt. [d] 4 days.

Results and Discussion

In the preliminary experiments of dipolar cycloaddition between nitrones and fluoroalkenes we found that this reaction is rather slow at room temperature and under moderate pressure (glass pressure tube). However, after a short search for optimal reaction conditions for the reaction of *C*-*p*-methylphenyl-*N*-methyl nitrone **1a** with HFP we found that at elevated temperature (80 °C) in MeCN the respective isoxazolidine **2a** is formed in good 85% yield.

We then performed a series of reactions of HFP and PFP with nitrones (Table 1), obtained from condensation of aliphatic and aromatic aldehydes and ketones with *N*-substituted hydroxylamines or by oxidation of the respective secondary amines. In the cases where the nitrone double bond was conjugated with an aromatic ring or an ester group, the conditions similar to that established for **1a** allowed the expected adducts **2** and **3** to be obtained in good to high yields. In the case of aliphatic nitrone **1j**, owing to its higher nucleophilicity and its nature of a cyclic nitrone, which blocks the *E* configuration, the reaction proceeded satisfactorily already at room temperature.

In all cases the fluorinated isoxazolidines were obtained with complete regioselectivity. Dipolar cycloaddition of nitrones to electron-deficient alkenes like HFP or PFP is probably a type I cycloaddition and is controlled by the interaction of HOMO of the dipole and LUMO of the alkene.[23] The CF_2 end of

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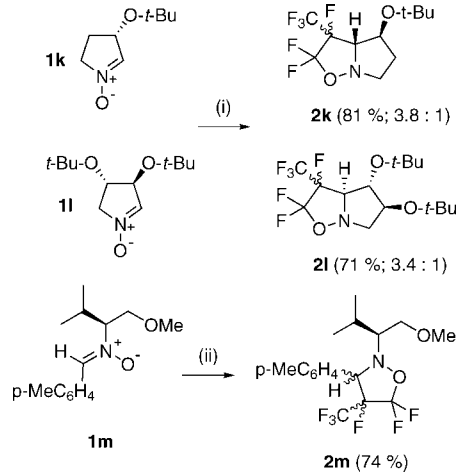
SCHEME 2. Reactions of Chiral Nitrones with HFP[a]



[a] Reagents and conditions: (i) HFP, MeCN, rt, 25 h; (ii) MeCN, 80 °C, 72 h.

fluoroalkenes is particularly prone to undergo nucleophilic adddition[1] and it preferentially reacts with the negative end of the dipole.

The formation of **2** and **3** proceeded with only modest cis/trans diastereoselectivity. In the case of **2** the two diastereoisomers could not be separated and their ratio was determined by using ^{1}H and ^{19}F NMR spectra, whereas isomers of compounds **3** were readily separable by chromatography. However, assignment of the relative stereochemistry was impossible on the basis of the ^{1}H and ^{19}F NMR spectra. In each case the vicinal $^3J_{HF}$ coupling constant for the major product was in the range 22−23 Hz, and for the minor one 28−30 Hz (except for **2h** and **2j**). For the only example of isoxazolidine described by Knunyants for which stereochemical assignment was made, the coupling constant value was 26 Hz for the trans isomer.[22]

In the reactions of chiral cyclic nitrones **1k**,***l*** with HFP only two of the four possible diastereoisomers were obtained. The values of $^3J_{HH}$ and $^3J_{HF}$ coupling constants of the bridgehead protons and their NOE interactions with *O*-*t*Bu groups indicate that the configuration of the products **2k**,***l*** is the one shown in Scheme 2 and is in agreement with the outcome of cycloaddition of **1*l*** to dimethyl maleate reported by Goti, Brandi, and coworkers.[24] Acyclic nitrone **1m** gave a 15.7:4.2:2.8:1 mixture of diastereoisomers, the first and third of which exhibited a smaller $^3J_{HF}$ value.

We then investigated the possibility of N−O bond scission in adducts **2** and **3**. First we attempted to cleave the heterocyclic ring in the process analogous to the one shown in Scheme 1 for aromatic *N*-oxides. Although in the case of **2** and **3** there is no driving force like rearomatization, we expected that the elimination reaction and formation of the C=N double bond could be induced by a sufficiently strong base. Unfortunately, upon the action of bases of varied strength (pyridine, DBU, LDA, *n*-BuLi) and at various temperatures isoxazolidines **2** remained unchanged or underwent decomposition.

We thus turned to the possibility of reductive cleavage of the N−O bond. It is a widely applied strategy for the synthesis of γ-amino alcohols etc. from the primary adducts of nitrones to alkenes.[25] We expected that the primary reduction products would eliminate HF to provide acyl fluorides (Scheme 3). This reaction pathway seemed very attractive as such fluorides could react with nucleophiles similarly to the ones generated in the reactions of *N*-oxides with fluoroalkenes (see Scheme 1).[14] In particular, an intramolecular reaction with the amine group would provide fluorinated β-lactams. A literature precedent supporting this assumption was reported by Tada and Toda, who obtained small amounts of 3-fluoro-3-trifluoromethyl-1,4-diphenylazetidin-2-one after heating *C*,*N*-diphenylnitrone with HFP (without isolating the intermediate cycloadduct).[26,15a] Two examples of a reaction similar to the one envisaged by us, but with isoxazolidines derived from $(PhS)_2C{=}CF_2$ as the dipolarophile, were also described.[27]

SCHEME 3. Reductive Cleavage of the N−O Bond in 4,5,5-Trifluoro-4-trifluoromethylisoxazolines

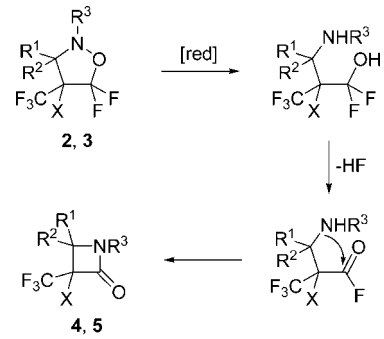
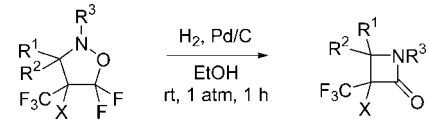


TABLE 2. Synthesis of α-Trifluoromethyl-β-lactams via Reductive Cleavage of Isoxazolidines 2 and 3



X	isoxazolidine	product[a]
F	**2a**	**4a** (90%; 3.1:1)
	2c	**4c** (70%; 1.5:1)
	2d	**4d** (62%; 7.3:1)
	2e	**4e** (66%; 1.1:1)[b]
	2f	**4f** (95%)
	2g	**4g** (55%; 2.0:1)[b,c]
	2h	**4h** (77%; 1:3.2)
	2i	**4i** (50%; 1:10)
	2j	**4j** (51%; 1:7.3)
	2m	**4m** (64%; 16.7:7.2:6.0:1)
H	**3a**	**5a** (85%)
	3c	**5c** (76%)
	3d	**5d** (97%)

[a] Yields and diastereoisomers ratios given in parentheses; the first diasteroisomer is the one with the 3-X, 4-H trans configuration. [b] Reaction performed for 20 h. [c] 11% of the ethyl ester of the respective β-amino acid **6g** (single diastereoisomer) was isolated.

Reductive cleavage of isoxazolidines **2** and **3** proved to be a very facile process. Under atmospheric pressure of hydrogen and in the presence of Pd/C catalyst they underwent smooth transformation into the α-trifluoromethyl β-lactam derivatives **4** and **5** (Table 2). Compounds **4** were obtained from diastereoisomeric mixtures of **2** as mixtures of cis/trans diastereoisomers which could be separated only in the case of **4a**. The isoxazo-

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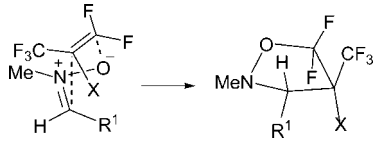
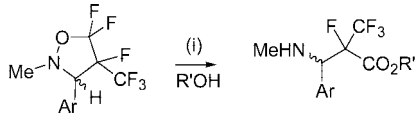
SCHEME 4. *Endo* Transition State Leading to the Major Diastereoisomers of 2 and 3



SCHEME 5. Preparation of Esters of α-Trifluoromethyl-β-amino Acids by Reduction of Isoxazolidines under Acidic Conditions[a]



Ar = p-MeC$_6$H$_4$ **6a** (74 %; 1.7:1 *threo*:*erythro*)
p-MeOC$_6$H$_4$ **6c** (60 %, only *threo* isolated)
2-thienyl **6d** (29 %; 1.6:1 *threo*:*erythro*)

[a] Reagents and conditions: (i) H_2, Pd/C, H_2SO_4, EtOH, then Na_2CO_3 for **6a**; H_2, Pd/C, 2.5 M HCl/Et_2O, MeOH, then Na_2CO_3 for **6c**; H_2, Pd/C, 37% $HCl_{(aq)}$, EtOH, then Na_2CO_3 for **6d**.

lidines **3** were subjected to hydrogenation as pure major diastereoisomers and thus lactams **5** were obtained as single diastereoisomers as well.

Owing to the rigid nature of the four-membered ring of **4** the coupling constants $^3J_{HF}$ differ significantly for cis and trans diastereoisomers. In the cis diastereoisomers (the ones having the 3-F atom and the R^1 substituent in relative cis configuration) the dihedral angle between the C−F and C−H bonds is close to 90°. This configuration should then be assigned to the β-lactam isomers which were formed as the major ones for **4a**,**c**−**g**,**m** and as minor ones for **4h**,**i**,**j**; they all exhibit $^3J_{HF}$ values around 3 Hz. For the other isomer in each case the coupling constant was in the range 11−13 Hz, a value expected for the cis arrangement of C−F and C−H bonds, which refers to trans configuration of the molecule. Since no bonds at the stereogenic centers are broken during the reduction step, the same stereochemical assignment holds for the isoxazolidines **2**. A similar analysis of the $^3J_{HH}$ values in the β-lactams **5** indicates that *trans*-isoxazolidines (with CF_3 and R^1 groups trans) are major products of the cycloaddition of acyclic nitrones to PFP. The cycloaddition of nitrones to fluoroalkenes is thus preferentially an *endo* addition—in all cases of isoxazolidines derived from acyclic nitrones the CF_3 group and the substituent at the C terminus of the nitrone are in a trans relationship in the predominating diastereoisomers of the resulting cycloadducts (Scheme 4). The cyclic nitrones are locked in the opposite *E* configuration and thus give opposite diastereoselectivity.

According to Scheme 3, protonation of the amino group prior to its intramolecular acylation should prevent formation of the β-lactam and provide a simple access to another group of biologically interesting building blocks, that is β-amino acids derivatives.[28] Indeed, hydrogenation of **2a** in dry EtOH acidified with concentrated H_2SO_4 gave ethyl ester **6a** in good yield (Scheme 5). Similar reactions were observed for **2c** and **2d** in MeOH or EtOH containing concentrated aqueous HCl or better dry ∼1 M HCl/Et_2O. The presence of water in the reaction mixture has a strongly deteriorating effect on the yield of the ester. When the hydrogenolysis reaction is performed, for example, in a solvent containing diluted aqueous HCl and EtOH, the starting isoxazolidine is consumed but the ethyl ester of the type **6** is formed only in trace amounts. Instead we observed formation of a white, very poorly soluble residue that we believe contains free α-trifluoromethyl-β-amino acid formed by hydrolysis (instead of alcoholysis) of the intermediate acyl fluoride.

Formation of side product ester **6g** from reduction of **2g** (see Table 2) may result from intramolecular hydrogen bonding of the nitrogen atom by the free hydroxy group.

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Conclusions

In conclusion, we established that 1,3-dipolar cycloaddition of nitrones to fluorinated alkenes yields the respective fluorinated isoxazolidine derivatives in preparatively useful yields and with complete regioselectivity. Under very mild conditions these products undergo a reductive N−O bond cleavage. This two-step process provides a novel and general entry to β-lactams and esters of β-amino acids containing a trifluoromethyl group.

Experimental Section

General Procedure for Reactions of Nitrones with Fluoroalkenes: Synthesis of Fluorinated Isoxazolidines 2 and 3. Fluoroalkene (ca. 0.5 mL, 4 mmol) was condensed in a glass pressure tube at −78 °C under argon atmosphere. MeCN (2.8 mL) and nitrone (0.95 mmol) were introduced and the pressure tube was closed with a Teflon valve. The contents of the tube were stirred vigorously at 80 °C for 24 h (or in some cases at room temperature and/or for a different period of time—see main text, Table 1 and Scheme 2). After opening the tube the reaction mixture was poured into water (10 mL) and the products were extracted with CH_2Cl_2 (3 × 5 mL). Combined organic layers were washed with water (5 × 10 mL), dried over anhydrous Na_2SO_4, and concentrated. The products were purified by column chromatography on silica gel, using 10:1 or 5:1 mixtures of hexanes/AcOEt or hexanes/Et_2O as eluent. All products were obtained as colorless or pale yellow oils.

2-Methyl-3-*p*-methylphenyl-4,5,5-trifluoro-4-trifluoromethylisoxazolidine (2a). IR (film, ν_{max}/cm^{-1}) 2929, 2887, 1517, 1309, 1284, 1238, 1211, 1164, 1128, 1035, 1006, 787, 738. Major diasteroisomer: ^{1}H NMR δ 2.37 (3H, s), 2.78 (3H, d, $^5J_{HF}$ = 1.4 Hz), 4.12 (1H, dd, $^3J_{HF}$ = 23.4 Hz, $^4J_{HF}$ = 3.0 Hz), 7.18 − 7.23 (2H, m); ^{13}C NMR δ 21.2, 43.8, 75.2 (d, $^2J_{CF}$ = 19.0 Hz), 96.1 (dm, $^1J_{CF}$ = 220.7 Hz, $^2J_{CF}$ = 31.9 Hz), 120.3 (qdm, $^1J_{CF}$ = 283.6 Hz, $^2J_{CF}$ = 30.2 Hz), 122.8 (ddd, $^1J_{CF}$ = 280.2, 260.4 Hz, $^2J_{CF}$ = 23.3 Hz), 125.3 (d, $^3J_{CF}$ = 2.6 Hz), 129.5, 129.7 (d, $^4J_{CF}$ = 1.7 Hz), 140.4; ^{19}F NMR δ −183.55 (1F, m), −85.13 (1F, dm, $^2J_{FF}$ = 145.0 Hz, $^4J_{FF}$ = 13.7 Hz), −82.12 (1F, d, $^2J_{FF}$ = 145.0 Hz), −76.75 (3F, m). Minor diastereoisomer: ^{1}H NMR δ 2.37 (3H, s), 2.84 (3H, d, $^5J_{HF}$ = 1.4 Hz), 4.21 (1H, dd, $^3J_{HF}$ = 30.0 Hz, $^4J_{HF}$ = 1.4 Hz), 7.18−7.23 (2H, m); ^{13}C NMR δ 21.2, 44.0, 79.2 (d, $^2J_{CF}$ = 26.7 Hz), 96.1 (dm, $^1J_{CF}$ = 220.7, $^2J_{CF}$ = 31.9 Hz), 120.0 (qdm, $^1J_{CF}$ = 284.5 Hz, $^2J_{CF}$ = ca. 30 Hz), 122.8 (ddd, $^1J_{CF}$ = 279.3, 264.7 Hz, $^2J_{CF}$ = 22.4 Hz), 126.1 (d, $^3J_{CF}$ = 1.7 Hz), 128.5, 129.6, 140.0; ^{19}F NMR δ −165.83 (1F, dm, $^3J_{FH}$ = 29.0 Hz, $^3J_{FF}$ = 7.6 H), −86.90 (1F, d, $^2J_{FF}$ = 145.0 Hz), −81.64 (1F, d, $^2J_{FF}$ = 145.0 Hz, $^4J_{FF}$ = 16.8 Hz), −74.31 (3F, dm, $^4J_{FF}$ = 16.9 Hz, $^3J_{FF}$ = 7.6 Hz); MS (EI 70 eV, *m*/*z*, %) 299 (M^+, 96), 280 (10), 148 (66), 132 (100); HRMS (EI) calcd for $C_{12}H_{11}NOF_6$ (M^+) 299.0745, found 299.0738. Anal. Calcd for $C_{12}H_{11}NOF_6$: C, 48.17; H, 3.71; N, 4.68; F, 38.10. Found: C, 47.98; H, 3.70; N, 4.77; F, 38.02.

2-Methyl-3,3-diphenyl-4,5,5-trifluoro-4-trifluoromethylisoxazolidine (2f). IR (film, ν_{max}/cm^{-1}) 3064, 2949, 1449, 1309, 1275, 1220, 1151, 1114, 1050, 999, 870, 737, 701; ^{1}H NMR δ 2.60 (3H, d, $^5J_{HF}$ = 0.9 Hz), 7.10−7.70 (10H, m); ^{13}C NMR δ 41.2 (d, $^4J_{CF}$ = 2.6 Hz), 80.8 (d, $^2J_{CF}$ = 19.0 Hz), 101.4 (dtq, $^1J_{CF}$ = 224.2 Hz, $^2J_{CF}$ = 31.0, 22.4 Hz), 120.4 (qd, $^1J_{CF}$ = 285.4 Hz, $^2J_{CF}$ = 31.0 Hz), 125.5 (td, $^1J_{CF}$ = 273.3 Hz, $^2J_{CF}$ = 21.6 Hz), 127.5, 127.9,

128.7, 128.7, 130.7, 130.7, 135.0, 135.9; ^{19}F NMR δ −166.22 (1F, m), −80.15 (1F, $^2J_{FF}$ = 146.2 Hz), −76.20 (1F, m), −71.18 (3F, dd, J_{FF} = 19.1 Hz, 5.1 Hz); MS (EI 70 eV, *m*/*z*, %) 361 (M^+, 39), 284 (33), 210 (87), 194 (100), 165 (23), 127 (23), 118 (78); HRMS (EI) calcd for $C_{17}H_{13}NOF_6$ (M^+) 361.0901, found 361.0908. Anal. Calcd for $C_{17}H_{13}NOF_6$: C, 56.51; H, 3.63; N, 3.88; F, 31.55. Found: C, 56.51; H, 3.61; N, 3.85; F, 31.51.

Izoxazolidine 2i. IR (film, ν_{max}/cm^{-1}) 2964, 1756, 1440, 1318, 1254, 1215, 1169, 1122, 1076, 1044, 966, 916, 866, 745, 706. Major diasteroisomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.94 (1H, m), 2.24 (1H, m, $^3J_{HH}$ = 8.4, 4.4 Hz, $^4J_{HF}$ = 1.1 Hz), 2.46 (1H, ddd, $^2J_{HH}$ = 13.5 Hz, $^3J_{HH}$ = 8.4, 4.3 Hz), 2.58 (1H, m), 3.45 (1H, m), 3.61 (1H, m), 3.85 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.1, 29.4 (q, $^4J_{CF}$ = 3.0 Hz), 53.7, 56.2, 82.8 (d, $^2J_{CF}$ = 19.4 Hz), 97.5 (dm, $^1J_{CF}$ = 217.5 Hz), 119.8 (qd, $^1J_{CF}$ = 284.7 Hz, $^2J_{CF}$ = 30.6 Hz), 123.1 (ddd, $^1J_{CF}$ = 280.0, 263.4 Hz, $^2J_{CF}$ = 23.3 Hz), 165.6 (d, $^3J_{CF}$ = 4.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −168.64 (1F, m, $^3J_{FF}$ = 6.5 Hz), −82.86 (1F, d, $^2J_{FF}$ = 145.8 Hz), −79.26 (1F, dqd, $^2J_{FF}$ = 145.8 Hz, $^4J_{FF}$ = 14.3 Hz, $^3J_{FF}$ = 3.4 Hz), −73.14 (3F, ddd, $^4J_{FF}$ = 13.6, 2.7 Hz, $^3J_{FF}$ = 6.8 Hz). Minor diasteroisomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.94 (1H, m), 2.14 (1H, m, $^3J_{HH}$ = 7.7 Hz), 2.39 (1H, m), 2.68 (1H, dddd, $^2J_{HH}$ = 15.7 Hz, $^3J_{HH}$ = 9.5 Hz, 6.1 Hz, $^4J_{HF}$ = 2.3 Hz), 3.38 (1H, dd, $^2J_{HH}$ = 13.4 Hz, $^3J_{HH}$ = 7.7 Hz, 3.4 Hz), 3.61 (1H, m), 3.84 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.5, 30.2 (d, $^3J_{CF}$ = 12.5 Hz), 53.7, 57.5, 80.8 (d, $^2J_{CF}$ = 21.5 Hz), 97.5 (dm, $^1J_{CF}$ = 217.5 Hz), 113−128 (m), 167.0 (d, $^3J_{CF}$ = 4.7 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ −170.51 (1F, m), −85.32 (1F, ddm, $^2J_{FF}$ = 145.1 Hz, $^3J_{FF}$ = 10.2 Hz, $^4J_{FF}$ = 2.7 Hz), −79.80 (1F, dq, $^2J_{FF}$ = 145.1 Hz, $^4J_{FF}$ = 16.3 Hz), −75.17 (3F, ddd, $^4J_{FF}$ = 16.3, 2.7 Hz, $^3J_{FF}$ = 8.2 Hz); MS (EI 70 eV, *m*/*z*, %) 293 (M^+, <1), 234 (100); HRMS (EI) calcd for $C_9H_9NO_3F_6$ (M^+) 293.0487, found 293.0499. Anal. Calcd for $C_9H_9NO_3F_6$: C, 36.87; H, 3.09; N, 4.78; F, 38.88. Found: C, 36.88; H, 3.12; N, 4.88; F, 38.01.

Izoxazolidine 2k. IR (film, ν_{max}/cm^{-1}) 2982, 1476, 1445, 1394, 1368, 1347, 1328, 1271, 1210, 1163, 1131, 1109, 1080, 1064, 1026, 913, 837, 781, 714. Major diasteroisomer: ^{1}H NMR δ 1.20 (9H, s), 1.80−1.95 (1H, m), 2.20−2.38 (1H, m), 3.32−3.50 (1H, m), 3.55−3.70 (1H, m), 3.97 (1H, dm, $^3J_{HF}$ = 21.3 Hz), 4.60 (1H, s); ^{13}C NMR δ 28.4, 34.4, 56.5, 71.1 (m), 75.0, 80.7 (d, $^2J_{CF}$ = 19.8 Hz), ∼98 (dm, $^1J_{CF}$ = 208.6 Hz), 115−127 (m); ^{19}F NMR δ −163.50 (1F, m), −87.40 (1F, dm, $^2J_{FF}$ = 146.1 Hz), −80.87 (1F, dq, $^2J_{FF}$ = 146.1 Hz, $^4J_{FF}$ = 15.0 Hz), −74.16 (3F, ddd, $^4J_{FF}$ = 14.4, 2.0 Hz, $^3J_{FF}$ = 7.8 Hz). Minor diasteroisomer: ^{1}H NMR δ 1.20 (9H, s), 1.80−1.95 (1H, m), 2.20−2.38 (1H, m), 3.32−3.50 (1H, m, NCH_2), 3.55−3.70 (1H, m, NCH_2), 4.11 (1H, dd, $^3J_{HF}$ = 16.1 Hz, $^3J_{HH}$ = 2.1 Hz, CHCF), 4.55 (1H, m); ^{13}C NMR δ 28.0, 34.4, 56.8, 71.1 (m), 75.1, 77.0 (d, $^2J_{CF}$ = 37.1), ∼98 (dm, $^1J_{CF}$ = 210.0 Hz), 115−127 (m); ^{19}F NMR δ −177.20 (1F, m), −93.00 (1F, ddm, $^2J_{FF}$ = 146.7 Hz, $^3J_{FF}$ = 11.1 Hz), −82.45 (1F, dq, $^2J_{FF}$ = 146.7 Hz, $^4J_{FF}$ = 14.4 Hz), −78.33 (3F, ddd, $^4J_{FF}$ = 15.0, 2.6 Hz, $^3J_{FF}$ = 8.5 Hz); MS (EI 70 eV, *m*/*z*, %) 292 (2), 234 (10), 185 (10), 57 (100). Anal. Calcd for $C_{11}H_{15}NO_2F_6$: C, 43.00; H, 4.92; N, 4.56; F, 37.10. Found: C, 42.83; H, 4.97; N, 4.35; F, 37.15.

***trans*-2-Methyl-3-*p*-methylphenyl-5,5-difluoro-4-trifluoromethylisoxazolidine (*trans*-3a).** IR (film, ν_{max}/cm^{-1}) 3008, 2977, 2928, 2884, 1516, 1391, 1301, 1247, 1218, 1149, 1133, 1086, 1052, 840, 811, 709, 509; ^{1}H NMR δ 2.37 (3H, s), 2.71 (3H, d, $^5J_{HF}$ = 1.1 Hz), 3.63 (1H, m, $^3J_{HH}$ = 10.1 Hz, $^3J_{HF}$ = 7.7 Hz), 4.01 (1H, d, $^3J_{HH}$ = 10.6 Hz), 7.19−7.24 (2H, m), 7.26−7.30 (2H, m); ^{13}C NMR δ 21.2, 43.2, 59.9 (m), 73.6, 122.8 (qd, $^1J_{CF}$ = 278.0 Hz, $^2J_{CF}$ = 3.0 Hz), 125.1 (ddm, $^1J_{CF}$ = 268.1 Hz, 259.1 Hz), 127.8, 129.9, 130.1, 139.8; ^{19}F NMR δ −81.70 (1F, dm, $^2J_{FF}$ = 145.2 Hz), −66.83 (3F, ddd, $^4J_{FF}$ = 11.9, 3.3 Hz, $^3J_{FH}$ = 7.7 Hz), −62.85 (1F, d, $^2J_{FF}$ = 145.2 Hz); MS (EI 70 eV, *m*/*z*, %) 281 (M^+, 48), 262(4), 235 (8), 215 (14), 190 (18), 148 (100), 132 (35), 91 (25); HRMS (EI) calcd for $C_{12}H_{12}NOF_5$ (M^+) 281.0839, found 281.0851. Anal. Calcd for $C_{12}H_{12}NOF_5$: C, 51.25; H, 4.30; N, 4.98; F, 33.78. Found: C, 51.01; H, 4.26; N, 5.00; F, 33.77.

***cis*-2-Methyl-3-*p*-methylphenyl-5,5-difluoro-4-trifluoromethylisoxazolidine (*cis*-3a).** IR (film, ν_{max}/cm^{-1}) 3010, 2978, 2928, 2885, 1516, 1392, 1299, 1195, 1162, 1132, 1071, 1039, 851, 813, 756, 667, 504; ^{1}H NMR δ 2.36 (3H, s), 2.79 (3H, s), 3.66 (1H, m), 4.30 (1H, d, $^3J_{HH}$ = 8.2 Hz), 7.15−7.21 (2H, m), 7.25−7.30 (2H, m); ^{13}C NMR δ 21.2, 44.1, 56.8 (m, $^2J_{CF}$ = 27.6 Hz), 72.7, 122.6 (qd, $^1J_{CF}$ = 279.8 Hz, $^2J_{CF}$ = 3.0 Hz), 125.7 (ddm, $^1J_{CF}$ = 276.7, 255.2 Hz), 128.2, 128.4, 129.4, 139.2; ^{19}F NMR δ −76.29 (1F, dm, $^2J_{FF}$ = 145.4 Hz), −68.30 (1F, d, $^2J_{FF}$ = 146.3 Hz), −63.06 (3F, dd, $^4J_{FF}$ = 14.4 Hz, $^3J_{FH}$ = 9.4 Hz); MS (EI 70 eV, *m*/*z*, %) 281 (M^+, 68), 262 (4), 235 (11), 215 (19), 190 (23), 148 (100), 132 (36), 91 (21); HRMS (EI) calcd for $C_{12}H_{12}NOF_5$ (M^+) 281.0839, found 281.0843. Anal. Calcd for $C_{12}H_{12}NOF_5$: C, 51.25; H, 4.30; N, 4.98; F, 33.78. Found: C, 50.93; H, 4.15; N, 4.92; F, 33.52.

Hydrogenolysis of Isoxazolidines 2 and 3: Preparation of α-Trifluoromethyl-β-lactams 4 and 5. Under Ar atmosphere, palladium on charcoal (10%, 400 mg) was added to a solution of substrate (1.0 mmol) in EtOH (10 mL) in a round-bottomed flask. Argon was then replaced by hydrogen and the reaction mixture was stirred vigorously at room temperature at 1 atm of H_2 for 1 h (or longer, see Table 2 in the main text). The flask was again filled with argon and the reaction mixture was filtered through a pad of celite under reduced pressure (**Caution**: the dry catalyst on the celite may start burning). After evaporation of EtOH the products were purified by using column chromatography on silica gel with hexanes/AcOEt or hexanes/Et_2O 2:1 or 1:1 mixtures as eluents. All products with the exception of **4f** were colorless or pale yellow oils.

***cis*-1-Methyl-4-*p*-methylphenyl-3-fluoro-3-trifluoromethyl-2-azetidinone (*cis*-4a).** IR (CH_2Cl_2, ν_{max}/cm^{-1}) 2926, 1794, 1333, 1274, 1183, 1055, 993, 879, 812; ^{1}H NMR δ 2.40 (3H, s), 2.92 (3H, d, $^5J_{HF}$ = 1.6 Hz), 4.86 (1H, d, $^3J_{HF}$ = 3.3 Hz), 7.23 (4H, AB, J = 8.1 Hz). ^{13}C NMR δ 21.3, 27.0, 63.1 (d, $^2J_{CF}$ = 24.1 Hz), 97.5 (m), 120.8 (qd, $^1J_{CF}$ = 281.9 Hz, $^2J_{CF}$ = 31.0 Hz), 126.6, 127.9, 129.9, 140.2, 158.8 (dm, $^2J_{CF}$ = 23.5 Hz); ^{19}F NMR δ −187.24 (1F, m), −79.33 (3F, d, $^3J_{FF}$ = 10.5 Hz); MS (EI 70 eV, *m*/*z*, %) 261 (M^+, 17), 246 (49), 204 (100), 177 (13), 135 (34); HRMS (EI) calcd for $C_{12}H_{11}NOF_4$ (M^+) 261.0777, found 261.0781. Anal. Calcd for $C_{12}H_{11}NOF_4$: C, 55.18; H, 4.24; N, 5.36; F, 29.09. Found: C, 55.08; H, 4.25; N, 5.46; F, 28.31.

***trans*-1-Methyl-4-*p*-methylphenyl-3-fluoro-3-trifluoromethyl-2-azetidinone (*trans*-4a).** IR (KBr, ν_{max}/cm^{-1}) 2929, 1770, 1430, 1331, 1192, 1062, 1003, 821; ^{1}H NMR δ 2.38 (3H, s), 3.00 (3H, d, $^5J_{HF}$ = 0.9 Hz), 4.93 (1H, d, $^3J_{HF}$ = 12.6 Hz), 7.22 (4H, AB, J = 8.1 Hz); ^{13}C NMR δ 21.2, 27.8, 66.6 (d, $^2J_{CF}$ = 24.9 Hz), 97.5 (dq, $^1J_{CF}$ = 231.0 Hz, $^2J_{CF}$ = 34.5 Hz), 119.9 (qd, $^1J_{CF}$ = 281.9 Hz, $^2J_{CF}$ = 31.0 Hz), 126.3, 127.4, 129.6, 139.8, 158.9 (dq, $^2J_{CF}$ = 23.3 Hz, $^3J_{CF}$ = 1.7 Hz); ^{19}F NMR δ −174.12 (1F, dq, $^3J_{FH}$ = 12.6 Hz, $^3J_{FF}$ = 9.8 Hz), −74.95 (3F, d, $^3J_{FF}$ = 9.8 Hz); MS (EI 70 eV, *m*/*z*, %) 261 (M^+, 31), 246 (68), 204 (100), 177 (18), 135 (42); HRMS (EI) calcd for $C_{12}H_{11}NOF_4$ (M^+) 261.0777, found 261.0770. Anal. Calcd for $C_{12}H_{11}NOF_4$: C, 55.18; H, 4.24; N, 5.36; F, 29.09. Found: C, 55.12; H, 4.20; N, 5.24; F, 29.06.

1-Methyl-3-fluoro-3-trifluoromethyl-4,4-diphenyl-2-azetidinone (4f). Colorless needles, mp 79−80 °C. IR (KBr, ν_{max}/cm^{-1}) 3063, 2938, 1781, 1451, 1312, 1201, 1172, 1064, 729, 704, 696; ^{1}H NMR δ 3.05 (3H, d, $^5J_{HF}$ = 1.0 Hz), 7.28−7.33 (2H, m), 7.33−7.37 (2H, m), 7.40−7.46 (6H, m); ^{13}C NMR δ 27.9, 75.1 (d, $^2J_{CF}$ = 20.7 Hz), 101.2 (dq, $^1J_{CF}$ = 240.5 Hz, $^2J_{CF}$ = 32.8 Hz), 120.3 (qd, $^1J_{CF}$ = 282.8 Hz, $^2J_{CF}$ = 31.9 Hz), 128.3, 128.5, 129.0, 129.0, 129.1, 129.1, 133.2, 134.7, 160.3 (dq, $^2J_{CF}$ = 22.4 Hz, $^3J_{CF}$ = 2.6 Hz); ^{19}F NMR δ −171.30 (1F, q, $^3J_{FF}$ = 10.1 Hz), −73.30 (3F, d, $^3J_{FF}$ = 10.1 Hz); MS (EI 70 eV, *m*/*z*, %) 323 (M^+, 100), 266 (9), 253 (25), 246 (82), 197 (58), 118 (89), 77 (26); HRMS (EI) calcd for $C_{17}H_{13}NOF_4$ (M^+) 323.0933, found 323.0924. Anal. Calcd for $C_{17}H_{13}NOF_4$: C, 63.16; H, 4.09; N, 4.33; F, 23.51. Found: C, 63.19; H, 4.07; N, 4.26; F, 23.56.

***β*-Lactam 4i (Major Diastereoisomer).** ^{1}H NMR δ 2.13 (2H, m), 2.20−2.31 (1H, m), 2.40−2.51 (1H, m), 3.14 (1H, m), 3.87 (3H, s), 3.87−3.93 (1H, m); ^{13}C NMR δ 28.3 (d, $^3J_{CF}$ = 12.1 Hz), 29.7, 46.4, 53.4, 71.2 (d, $^2J_{CF}$ = 23.3 Hz), 97.6 (dq, $^1J_{CF}$ = 244.8 Hz, $^2J_{CF}$ = 36.2 Hz), 120.0 (dq, $^1J_{CF}$ = 282.8 Hz, $^2J_{CF}$ = 30.2 Hz), 161.7 (d,$^3J_{CF}$ = 19.8 Hz), 168.1; ^{19}F NMR δ −172.94 (1F, qd, $^3J_{FF}$ = 8.7 Hz, $^4J_{FH}$ = 4.7 Hz), −75.20 (d,$^3J_{FF}$ = 8.7 Hz); MS (EI 70 eV, *m*/*z*, %) 255 (M^+, <1), 227 (100), 212 (15), 196 (52), 168 (79), 148 (80); HRMS (ESI) calcd for $C_9H_9NO_3F_4Na$ ($M + Na^+$) 278.0411, found 278.0406. Anal. Calcd for $C_9H_9NO_3F_4$: C, 42.36; H, 3.56; N, 5.49; F, 29.78. Found: C, 42.57; H, 3.60; N, 5.42; F, 29.63.

***trans*-1-Methyl-4-*p*-methylphenyl-3-trifluoromethyl-2-azetidinone (*trans*-5a).** IR (CH_2Cl_2, ν_{max}/cm^{-1}) 2925, 1778, 1372, 1261, 1200, 1170, 1121; ^{1}H NMR δ 2.38 (3H, s), 2.82 (3H, d, $^4J_{HH}$ = 0.8 Hz), 3.63 (1H, qm, $^3J_{HH}$ = 9.0 Hz), 4.58 (d, $^3J_{HH}$ = 2.4 Hz), 7.19 (2H, m), 7.25 (2H, m); ^{13}C NMR δ 21.1, 27.3, 56.8 (q, $^3J_{CF}$ = 3.0 Hz), 61.9 (q, $^2J_{CF}$ = 29.7 Hz), 123.4 (q, $^1J_{CF}$ = 277.2 Hz), 126.2, 130.1, 131.9, 139.5, 160.1 (q, $^3J_{CF}$ = 4.8 Hz); ^{19}F NMR δ −68.53 (d, $^3J_{FH}$ = 9.2 Hz); MS (EI 70 eV, *m*/*z*, %) 255 (M^+, 6), 228 (8), 186 (100), 132 (32), 117 (44), 105 (40); HRMS (EI) calcd for $C_{12}H_{12}NOF_3$ (M^+) 243.0871, found 243.0877. Anal. Calcd for $C_{12}H_{12}NOF_3$: C, 59.26; H, 4.97; N, 5.76; F, 23.43. Found: C, 59.08; H, 5.10; N, 5.56; F, 22.14.

Preparation of Ethyl and Methyl Esters of α-Fluoro-α-trifluoromethyl-*β*-amino Acids (6a, 6c, 6d). Isoxazolidine (1 mmol) was dissolved in dry EtOH or MeOH (10 mL). Freshly dried 3 Å molecular sieves and concentrated H_2SO_4 (0.25 mL; **6a**) or concentrated $HCl_{(aq)}$ (0.25 mL; **6d**) or 1 M HCl/Et_2O (1 mL; **6c**) were added and then, under argon atmosphere, 10% Pd/C catalyst (about 100 mg) was introduced. Argon was exchanged for hydrogen and the reaction mixture was vigorously stirred for 1 h at room temperature and ambient pressure of H_2. Hydrogen was then removed and aqueous Na_2CO_3 (6 mL of 1 M solution) was added. After filtration through a pad of celite the mixture was diluted with water and most of the alcohol was removed with a rotary evaporator. The resulting residue was extracted with $CHCl_3$ (3 × 10 mL), the organic phase was dried (Na_2SO_4) and concentrated, and the two diastereoisomers of the product were separatedby using column chromatography (SiO_2, hexanes/AcOEt 5:1).

***threo*-6a (Major).** IR (film, ν_{max}/cm^{-1}) 2985, 2878, 2805, 1776, 1751, 1515, 1450, 1372, 1291, 1270, 1207, 1183, 1154, 1101, 853, 783, 665; ^{1}H NMR δ 1.08 (3H, t, $^3J_{HH}$ = 7.2 Hz), 2.26 (3H, s), 2.33 (3H, s), 4.06 (2H, m), 4.21 (1H, d, $^3J_{HF}$ = 27.4 Hz), 7.12−7.21 (4H, m); ^{13}C NMR δ 13.6, 21.1, 33.9, 62.8, 64.4 (d, $^2J_{CF}$ = 18.1 Hz), 95.9 (dq, $^1J_{CF}$ = 208.6 Hz, $^2J_{CF}$ = 29.3 Hz), 121.5 (qd, $^1J_{CF}$ = 286.6 Hz, $^2J_{CF}$ = 29.8 Hz), 128.6 (d, $^4J_{CF}$ = 2.8 Hz), 129.3, 131.7, 138.6, 163.4 (d, $^2J_{CF}$ = 24.6 Hz); ^{19}F NMR δ −188.79 (1F, m), −72.78 (3F, $^3J_{FF}$ = 5.5 Hz); MS (EI 70 eV, *m*/*z*, %) 204 (1), 134 (100); HRMS (ESI) calcd for $C_{14}H_{18}NO_2F_4$ ($M + H^+$) 308.1268, found 308.1263. Anal. Calcd for $C_{14}H_{17}NO_2F_4$: C, 54.72; H, 5.58; N, 4.56; F, 24.73. Found: C, 54.70; H, 5.56; N, 4.52; F, 24.85.

***erythro*-6a (Minor).** IR (CH_2Cl_2, ν_{max}/cm^{-1}) 2940, 1794, 1751, 1516, 1449, 1297, 1259, 1185, 1160, 1100, 1052, 878, 662; ^{1}H NMR δ 1.37 (3H, t, $^3J_{HH}$ = 7.2 Hz), 2.20 (3H, s), 2.36 (3H, s), 4.11 (d, $^3J_{HF}$ = 29.3 Hz), 4.42 (2H, m), 7.19 (4H, m); ^{19}F NMR δ −189.45 (1F, m), −74.08 (3F, d, $^3J_{FF}$ = 7.8 Hz); MS (EI 70 eV, *m*/*z*, %) 246 (6), 204 (16), 134 (100); HRMS (ESI) calcd for $C_{14}H_{17}NO_2F_4Na$ ($M + Na^+$) 330.1088, found 330.1103. Anal. Calcd for $C_{14}H_{17}NO_2F_4$: C, 54.72; H, 5.58; N, 4.56; F, 24.73. Found: C, 54.86; H, 5.45; N, 4.72; F, 24.93.

Ester *threo*-6c. IR (film, ν_{max}/cm^{-1}) 3354, 2959, 2805, 1779, 1755, 1612, 1514, 1442, 1297, 1267, 1209, 1180, 1153, 1101, 1057, 1034, 851,784, 743; ^{1}H NMR δ 2.25 (3H, s), 3.61 (3H, s), 3.80 (3H, s), 4.19 (1H, d, $^3J_{HF}$ = 27.2 Hz), 6.87 (2H, dm, $^3J_{HH}$ = 8.8 Hz), 7.19 (2H, m); ^{13}C NMR δ 33.9, 53.2, 55.2, 64.2 (d, $^2J_{CF}$ = 18.1 Hz), 96.2 (dq, $^1J_{CF}$ = 207.8 Hz, $^2J_{CF}$ = 30.2 Hz), 114.0, 121.4 (qd, $^1J_{CF}$ = 286.2 Hz, $^2J_{CF}$ = 29.3 Hz), 126.8, 129.7, 159.8, 164.0 (d, $^2J_{CF}$ = 25.9 Hz); ^{19}F NMR δ −188.92 (1F, dq, $^3J_{FH}$ = 27.1 Hz, $^3J_{FF}$ = 5.7 Hz), −72.81 (3F, d, $^3J_{FF}$ = 5.7 Hz). Anal. Calcd for $C_{13}H_{15}NO_3F_4$: C, 50.49; H, 4.89; N, 4.53; F, 24.57. Found: C, 50.57; H, 4.63; N, 4.52; F, 24.52.

Ester *threo*-6d (major). IR (CH_2Cl_2, ν_{max}/cm^{-1}) 2924, 1790, 1324, 1193, 1175, 1063, 880; ^{1}H NMR δ 1.14 (3H, t, $^3J_{HH}$ = 7.2 Hz), 2.34 (3H, s), 4.06−4.23 (2H, m), 4.57 (d, $^3J_{HF}$ = 27.2 Hz), 6.98 (1H, dd, $^3J_{HH}$ = 5.0 Hz, 3.5 Hz), 7.02 (1H, m), 7.32 (1H, dm, $^3J_{HH}$ = 5.0 Hz); ^{13}C NMR δ 13.7, 33.9, 60.5 (d, $^2J_{CF}$ = 18.5 Hz), 63.0, 95.7 (m), 121.2 (qd, $^1J_{CF}$ = 286.6 Hz, $^2J_{CF}$ = 29.3 Hz), 126.4, 126.6, 127.9, 163.2 (d, $^2J_{CF}$ = 23.6 Hz); ^{19}F NMR δ −187.93 (1F, m), −72.65 (3F, d, $^3J_{FF}$ = 5.4 Hz). Anal. Calcd for $C_{11}H_{13}NO_2SF_4$: C, 44.14; H, 4.38; N, 4.68; F, 25.39. Found: C, 44.22; H, 4.59; N, 4.24; F, 25.40.

Ester *erythro*-6d (minor). IR (CH_2Cl_2, ν_{max}/cm^{-1}) 3343, 2985, 1775, 1752, 1372, 1269, 1202, 1098, 1054, 780, 709; ^{1}H NMR δ 1.37 (3H, t, $^3J_{HH}$ = 7.2 Hz), 2.29 (3H, s), 4.35−4.47 (2H, m), 4.48 (d, $^3J_{HF}$ = ∼29 Hz), 6.98 (1H, dd, $^3J_{HH}$ = 5.0 Hz, 3.5 Hz), 7.14 (1H, m), 7.35 (1H, dm, $^3J_{HH}$ = 5.1 Hz), 7.54 (1H, m); ^{19}F NMR δ −167.24 (1F, m), −73.84 (3F, d, $^3J_{FF}$ = 8.8 Hz). Anal. Calcd for $C_{11}H_{13}NO_2SF_4$: C, 44.14; H, 4.38; N, 4.68. Found: C, 43.97; H, 4.24; N, 4.38.

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Supporting Information Available: Characterization data for **2b**, **2c**, **2d**, **2e**, **2g**, **2h**, **2j**, **2*l***, **2m**, **3c**, **3d**, **4c**, **4d**, **4e**, **4g**, **6g**, **4h**, **4j**, **4m**, **5c**, and **5d** and copies of the NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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