DOI: 10.1002/ejoc.201000851

Highly Enantioselective Addition of 1-Fluoro-1-nitro(phenylsulfonyl)methane to α,β-Unsaturated Aldehydes

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Keywords: Fluorine / Organocatalysis / Aldehydes / Enantioselectivity / Diastereoselectivity / Michael addition

An organocatalytic, highly enantioselective addition of 1-fluoro-1-nitro(phenylsulfonyl)methane to α,β-unsaturated aldehydes is reported. The reaction is simply catalyzed by secondary amines and furnishes the corresponding fluorinated derivatives in good yields, with moderate diastereoselectivities and excellent enantioselectivities. The absolute configuration of the major diastereomers was unambiguously ascertained by X-ray diffraction analysis.

Introduction

The chemistry of fluorinated compounds and materials is a very active field, fostered by the unique physical, chemical, and biological properties often resulting from the presence of fluorine atoms in organic molecules.[1,2] In the case of biologically active molecules, the need for the stereocontrolled introduction of fluorine or of fluorinated moieties is particularly important, and research in this area continues unabated.[3]

In 2009 one of our research groups,[4] concurrently with those of Wang[5] and Córdova,[6] reported a practical and highly enantioselective formal addition of the fluoromethyl anion to α,β-unsaturated aldehydes on the basis of an asymmetric organocatalytic Michael addition of fluorobis(phenylsulfonyl)methane.[7] Very recently, we have also disclosed the first enantioselective addition of 2-fluoromalonates to α,β-unsaturated aldehydes.[8,9] In this context, we turned our attention to the addition of 1-fluoro-1-nitro(phenylsulfonyl)methane (FNSM), readily prepared by electrophilic fluorination of commercially available (phenylsulfonyl)nitromethane, to α,β-unsaturated aldehydes as an easy and versatile entry to interesting products for medicinal chemistry such as building blocks for drug synthesis or of fluoride-labeled natural products. It is worth noting that during the experimental implementation of this concept, Córdova and co-workers[6] described a single example of the catalytic asymmetric addition of FNSM to cinnamaldehyde. We report herein our results on the chiral pyrrolidine-catalyzed addition of this reagent to a range of aromatic and aliphatic enals, as well as on the unambiguous determination of the stereochemical course of this process.

Results and Discussion

In our initial screening we tested the addition of FNSM (**1**) to cinnamyl aldehyde (**2a**) in the presence of several chiral secondary amines (Table 1). To our delight, we found that the reaction was efficiently catalyzed by the well-known TMS-protected diphenylprolinol **I** (Jørgensen–Hayashi catalyst)[10] by using toluene as the solvent at –20 °C. Initially formed Michael adduct **3a** (^{1}H NMR monitoring of the reaction mixture) was not isolated, and in situ reduction with $NaBH_4$ afforded alcohol **4a** in 46% yield (after chromatographic purification). The diastereomeric ratio of intermediate aldehyde **3a**, determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture, was 2:1. The enantiomeric ratios of the major and minor diastereomers of **4a**, determined by chiral HPLC, were 95:5 and 96:4, respectively (Table 1, Entry 1). When the reaction was catalyzed by MacMillan's first generation imidazolidinone **II**,[11] only trace amounts of the final product were detected (Table 1, Entry 2). The reaction was also very poorly catalyzed by prolinol **III** (Table 1, Entry 3). When proline (**IV**) was used as the catalyst, the final reduced Michael adducts were obtained in good yields, but with low enantioselectivi-

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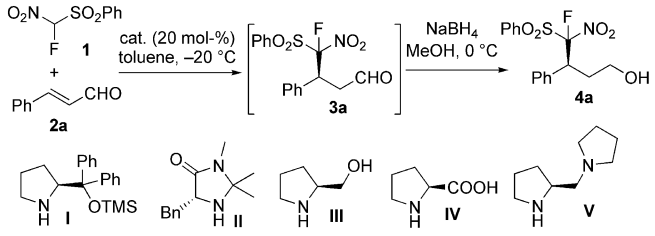
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201000851.

ties (Table 1, Entry 4). Finally, when diamine **V** was used, product **4a** was obtained in moderate yields and in almost racemic form (Table 1, Entry 5).

Table 1. Catalyst screening for the reaction between **1** and **2a**.[a]



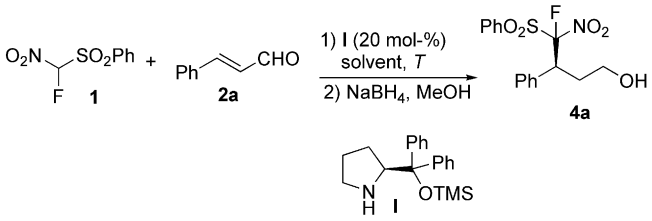
Entry	Catalyst	*dr* (**3a**)[b]	*er* (**4a**)[c]	Yield [%][d]
1	**I**	2:1	96:4/95:5	46
2	**II**	n.d.	n.d.	traces
3	**III**	n.d.	n.d.	traces
4	**IV**	3:1	60:40/50:50	57
5	**V**	3:1	51:49/51:49	64

[a] In a small vial, **1** (0.25 mmol, 1 equiv.) was treated with **2a** (0.5 mmol, 2 equiv.) in toluene (1 mL) in the presence of catalyst **I**–**V** (0.05 mmol, 0.2 equiv.) for 24 h at –20 °C; then, the reaction mixture was subjected to "in situ" reduction to afford **4a**. [b] Determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [c] Determined by chiral HPLC analysis of compound **4a**. [d] Isolated yield of **4a** after column chromatography.

We decided next to test the same reaction in other solvents (Table 2). The addition performed well in several relatively nonpolar solvents such as dichloromethane, chloroform, ethanol, or diethyl ether, but with lower diastereo- and enantioselectivities (Table 2, Entries 1–3 and 7). When the reaction was run in toluene at temperatures higher than –20 °C, the diastereomer ratio was not affected, but the enantioselectivities decreased dramatically (Table 2, Entries 5 and 6).

With these optimized conditions in hand, we decided to study the scope of the reaction with different α,β-unsaturated aldehydes **2a**–**i** (Table 3). The addition can be performed both with both aromatic and aliphatic α,β-unsaturated aldehydes and tolerates different functional groups such as halogens, nitro, or nitriles. As before, initial Michael adducts **3a**–**i** were not isolated but were reduced in situ to afford corresponding alcohols **4a**–**i**, which were more stable and easier to purify. The diastereoselectivity of the reaction is somewhat dependent of the nature of the substituent in the aromatic ring. For example, when electron-withdrawing groups were placed in the *para* position, the diastereoselectivity decreased (Table 3, Entries 2 and 3). On the opposite hand, when halogen or electron-donating groups were placed in the aromatic rings, the diastereoselectivity increased up to 2.5:1 (Table 3, Entry 5). It is noteworthy that the yields are higher with aliphatic aldehydes, and surprisingly the diastereoselectivity decreased when the steric bulk of the aliphatic group increased. For example, crotonaldehyde (**2g**) afforded Michael adduct **3g** in 4:1 *dr* (Table 3, Entry 7), whereas 2-pentenaldehyde (**2h**) afforded compound **3h** in 3:1 *dr* (Table 3, Entry 8). In all of the examples, the enantioselectivities were good to excellent, up to 99:1 *er* for the major diastereomer of **4e**. The diastereomers of final alcohols **4a**–**i** could be separated by careful chromatographic purification.

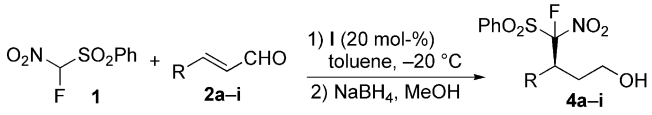
Table 2. Solvent and temperature screening for the reaction between **1** and **2a**.[a]



Entry	Solvent	*T* [°C]	*dr* (**3a**)[b]	*er* (**4a**)[c]	Yield[d] [%]
1	CH_2Cl_2	–20	1:1	84:16/85:15	51
2	$CHCl_3$	–20	3:2	92:8/84:16	43
3	Et_2O	–20	2:3	91:9/95:5	16
4	toluene	–20	2:1	96:4/95:5	46
5	toluene	0	2:1	88:12/79:21	51
6	toluene	r.t.	2:1	75:25/55:45	53
7	EtOH	0	1:1	87:13/80:20	53

[a] In a small vial, **1** (0.25 mmol, 1 equiv.) was treated with **2a** (0.5 mmol, 2 equiv.) for 24 h in the solvent and at the temperature specified in the presence of **I** (0.05 mmol, 0.2 equiv.) at –20 °C; then, the reaction mixture was subjected to "in situ" reduction to afford **4a**. [b] Determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [c] Determined by chiral HPLC analysis of compound **4a**. [d] Isolated yield of **4a** after column chromatography.

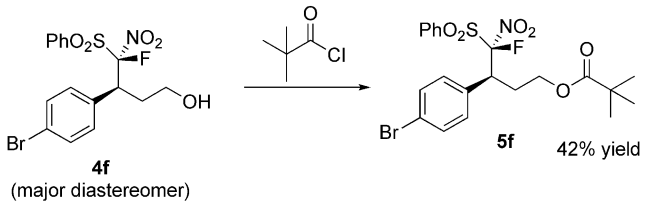
Table 3. Scope of the organocatalytic FSNM additions.[a]



Entry	R	Product	*dr* (**3a**)[b]	*er* (**4a**)[c]	Yield [%][d]
1	Ph	**4a**	2:1	96:4/95:5	46
2	*p*-$NO_2C_6H_4$	**4b**	1:1	96:4/95:5	80
3	*p*-CNC_6H_4	**4c**	3:2	87:13/n.d.	36
4	naphthyl	**4d**	3:1	91:9/81:19	20
5	*p*-ClC_6H_4	**4e**	5:2	99:1/98:2	45
6	*p*-BrC_6H_4	**4f**	2:1	95:5/93:7	42
7	Me	**4g**	4:1	96:4/n.d.	77
8	Et	**4h**	3.3:1	96:4/95:5	70
9	Pr	**4i**	3:1	96:4/95:5	73

[a] In a small vial, **1** (0.25 mmol, 1 equiv.) and **2a**–**i** (0.5 mmol, 2 equiv.) were added in toluene (1 mL) in the presence of **I** (0.05 mmol, 0.2 equiv.) at –20 °C; then, the reaction was subjected to "in situ" reduction to afford **4**. [b] Determined by ^{1}H NMR spectroscopic analysis of the crude reaction mixture. [c] Determined by chiral HPLC analysis of compound **4a**–**i**. [d] Isolated yield of **4a**–**i** after column chromatography.

To ascertain the absolute configuration of the adducts, we performed an anomalous X-ray diffraction analysis of compound **5f**, obtained from the major diastereomer of **4f** after pivaloylation (Scheme 1).



Scheme 1. Synthesis of compound **5f**.

As shown in Figure 1, both stereogenic centers (C3 and C4) have an (*S*) absolute configuration. We assume that all of adducts (both diastereomers) have the same absolute configuration at C3 [(*S*) for cinnamaldehyde derivatives **4a**–**f** and (*R*) for **4g**–**i**] and that at least for the aromatic enal adducts, the major diastereomer has a (4*S*) configuration.

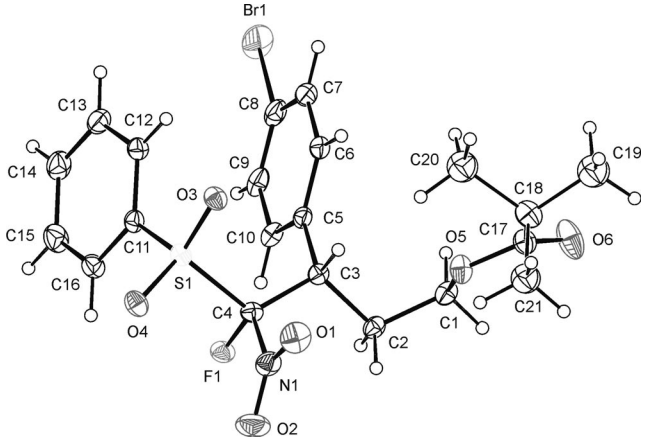
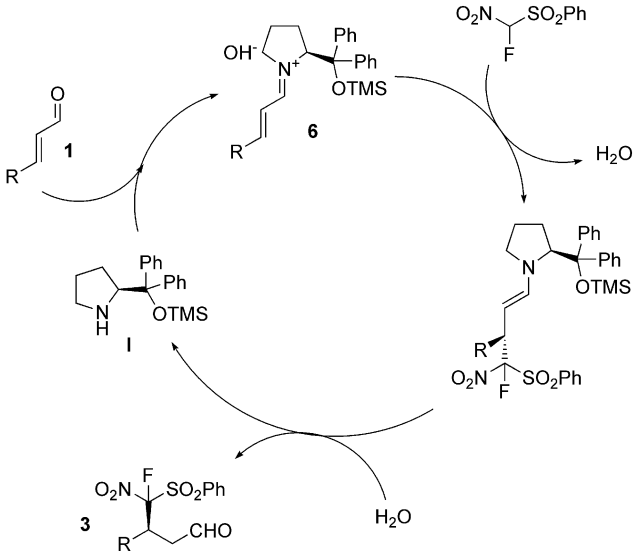


Figure 1. Molecular structure (anomalous X-ray diffraction analysis) of **5f**.[12] The displacement ellipsoids are drawn at the 30% probability level. Only the most populated positions of atoms in the disordered *tert*-butyl moiety are shown for clarity.

As expected, the stereochemical course of the Michael addition at C3 is coherent with the hypothesis that the mechanism and transition states (TSs) are similar to those described for other organocatalytic Michael additions catalyzed by diphenylprolinol derivatives reported in the literature.[4,13] Thus, efficient shielding of the *Si* face of chiral iminium intermediate **6** by the bulky aryl groups of chiral pyrrolidine **I** leads to the stereoselective *Re* facial nucleophilic conjugate addition by the FNSM anion, as shown in Scheme 2.

Previous reports on the addition of FNSM to different electrophiles can also account for the diastereoselectivity of the reaction.[3k] As previously reported, the stereoselectivity at C4 (α-fluoro carbon) does not originate from the stereoselective deprotonation of FNMS by the secondary amine. The stereoselectivity is actually derived from the interaction between the FNSM anion and the iminium ion. Figure 2 shows clearly that TSs **A** and **D** minimize the steric interaction between the bulky phenylsulfonyl moiety and the unsaturated iminium ion. Moreover, TS **D**, leading to the (4*S*) diastereomer, should be slightly more stable than TS **A** due



Scheme 2. Proposed mechanism for the chiral pyrrolidine-catalyzed addition of 1-fluoro-1-nitro(phenylsulfonyl)methane to enals.

to the *anti* disposition of the phenyl and nitro groups. This small difference should explain the diastereoselection observed in the reaction.

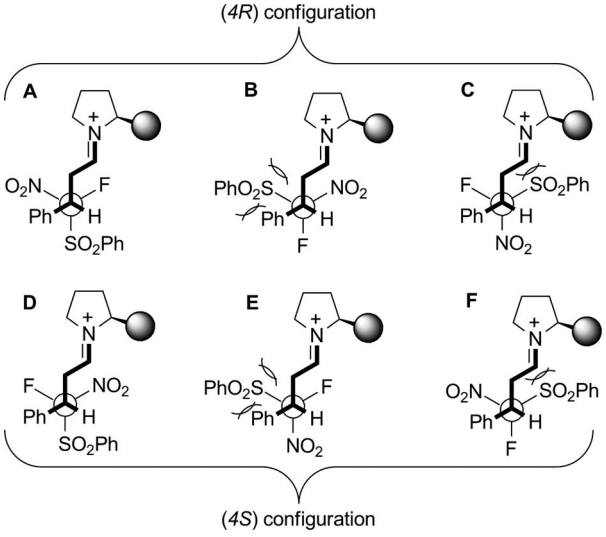


Figure 2. Transition states suggested for the FNMS addition to unsaturated aldehydes.

Conclusions

In summary, we have reported the asymmetric organocatalytic Michael addition of 1-fluoro-1-nitro(phenylsulfonyl)methane (FNSM) to aromatic or aliphatic α,β-unsaturated aldehydes. The reaction is efficiently catalyzed by commercially available chiral pyrrolidine derivatives and gives the corresponding adducts in moderate to good yields, with moderate to good diastereoselectivities and with excellent enantioselectivities (up to 99:1 *er*). Mechanistic studies

and synthetic applications of this new methodology, as well as the discovery of new reactions based on this concept, are currently ongoing in our laboratories.

Experimental Section

General Methods: Chemicals and solvents were either purchased (puriss p.A.) from commercial suppliers or purified by standard techniques. For thin-layer chromatography (TLC), silica gel plates Merck 60 F254 were used, and compounds were visualized by irradiation with UV light and/or by treatment with a solution of phosphomolybdic acid (25 g), $Ce(SO_4)_2{\cdot}H_2O$ (10 g), concd. H_2SO_4 (60 mL), and H_2O (940 mL) followed by heating or by treatment with a solution of *p*-anisaldehyde (23 mL), concd. H_2SO_4 (35 mL), acetic acid (10 mL), and ethanol (900 mL) followed by heating. Flash chromatography was performed by using silica gel Merck 60 (particle size 0.040–0.063 mm). ^1H, ^{19}F and ^{13}C NMR spectra were recorded with Varian AS 400 or Bruker 300 instruments. Chemical shifts are given in ppm relative to tetramethylsilane (TMS), and coupling constants *J* are given in Hz. The spectra were recorded in $CDCl_3$ as solvent at room temperature. TMS served as internal standard (δ = 0 ppm) for ^1H NMR, $CDCl_3$ was used as internal standard (δ = 77.0 ppm) for ^{13}C NMR, and TFA was used as external standard for ^{19}F NMR. High-resolution mass spectra were recorded with a Bruker MicrOTOF spectrometer. Chiral HPLC was carried out by using an LCP 5020 Ignos liquid chromatography pump with LCD 5000 spectrophotometric detector.

General Procedure for the Formation of 3-Substituted-4-fluoro-4-nitro-4-(phenylsulfonyl)butanal Derivatives 3a–i: To a sample vial equipped with a magnetic stirring bar was added toluene (1 mL), catalyst **I** (16 mg, 20 mol-%, 0.05 mmol), α,β-unsaturated aldehyde **2a**–**i** (0.5 mmol, 2 equiv.), and [fluoro(nitro)methylsulfonyl]benzene (**1**; 55 mg, 0.25 mmol, 1 equiv.) at –20 °C. The reaction mixture was stirred at –20 °C for 24 h and purified by column chromatography (hexane/EtOAc, 5:1) to afford aldehydes **3a**–**i**.

General Procedure for Formation of 3-Aryl-4-fluoro-4-nitro-4-(phenylsulfonyl)butanol (4a–i): To a sample vial equipped with a magnetic stirring bar was added toluene (1 mL), catalyst **I** (16 mg, 20 mol-%, 0.05 mmol), α,β-unsaturated aldehyde **2a**–**i** (0.5 mmol, 2 equiv.), and [fluoro(nitro)methylsulfonyl]benzene (**1**; 55 mg, 0.25 mmol, 1 equiv.) at –20 °C. The reaction mixture was stirred at –20 °C for 24 h, poured into cold (–20 °C) MeOH (4 mL). Next, the reaction mixture was treated with $NaBH_4$ (1.5 mmol, 3 equiv.) and after 15 min at 0 °C was poured over a solution EtOAc (40 mL)/HCl (1 M, 4 mL) at 0 °C. The reaction mixture was warmed to room temperature, and the organic layer was separated, dried with anhydrous magnesium(II) sulfate, and filtered. The solvent were removed in vacuo, and the crude mixture was purified by column chromatography (silica gel; hexane/EtOAc, 4:1) to afford alcohols **4a**–**i**.

3a: Mixture of diastereomers **3a**/**3a′** (*dr* = 2:1), pale-yellow oil. IR (KBr): ṽ = 3065, 3035, 2960, 2923, 2846, 2736, 1970, 1906, 1725, 1576, 1449, 1353, 1185, 1158, 1082, 977, 754, 716, 699, 684, 599, 561, 540, 446.74 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{14}O_5NFSNa$ $[M + Na]^+$ 374.0474; found 374.0468.

3a (Major Diastereomer): ^1H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 9.60 (br. s, 1 H, CHO), 7.90–7.22 (m, 10 H, Ar), 4.94 (ddd, *J* = 31.6 Hz, *J* = 10.9 Hz, *J* = 2.9 Hz, 1 H, CH), 3.73 (dd, *J* = 18.4 Hz, *J* = 3.0 Hz, 1 H, CH_2), 3.26 (ddd, *J* = 18.4 Hz, *J* = 10.9 Hz, *J* = 1.6 Hz, 1 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 196.36 (d, *J* = 3.3 Hz), 136.64–129.00 (m, 12 C), 124.85 (d, *J* = 289.7 Hz), 43.73 (br. s), 41.59 (d, *J* = 16.5 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$, 25 °C): δ = –67.39 (d, *J* = 31.6 Hz) ppm.

3a′ (Minor Diastereomer): ^1H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 9.49 (t, *J* = 1.3 Hz, 1 H, CHO), 7.90–7.22 (m, 10 H, Ar), 4.88 (ddd, *J* = 26.2 Hz, *J* = 10.8 Hz, *J* = 2.9 Hz, 1 H, CH), 3.18 (ddd, *J* = 17.9 Hz, *J* = 10.7 Hz, *J* = 1.5 Hz, 1 H, CH_2), 2.90 (dd, *J* = 18.0 Hz, *J* = 2.9 Hz, 1 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 195.8 (d, *J* = 3.2 Hz), 136–129 (m, 12 C), 124.6 (d, *J* = 287.8 Hz), 44.0 (d, *J* = 2.2 Hz), 42.4 (d, *J* = 17.6 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$, 25 °C): δ = –60.02 (d, *J* = 25.4 Hz) ppm.

4a: Yield: 40 mg (46%), mixture of diastereomers, pale-yellow oil. IR (KBr): ṽ = 3584.27, 3346.14, 3053.05, 2958.15, 3884.88, 1577.21, 1493.81, 1447.48, 1346.58, 1314.67, 1158.17, 1081.98, 788.32, 753.47, 715.31, 683.79, 603.73 cm^{-1}. $[\alpha]_D$ = +24.8 (*c* = 1.5, $CHCl_3$). HRMS (ESI): calcd. for $C_{16}H_{16}O_5NFS$ $[M - H]^-$ 352.0655; found 352.0663.

4a (Major Diastereomer): ^1H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 7.92–7.21 (m, 10 H, Ar), 4.55 (ddd, *J* = 12.3 Hz, *J* = 13.1 Hz, *J* = 13.4 Hz, 1 H, CH), 3.64 (ddd, *J* = 10.7 Hz, *J* = 6.1 Hz, *J* = 3.5 Hz, 1 H, CH_2OH), 3.27 (ddd, *J* = 10.1 Hz, *J* = 10.1 Hz, *J* = 4.7 Hz, 1 H, CH_2OH), 2.83 (dddd, *J* = 13.9 Hz, *J* = 7.5 Hz, *J* = 6.1 Hz, *J* = 3.1 Hz, 1 H, CH_2), 2.13 (dddd, *J* = 14 Hz, *J* = 12.1 Hz, *J* = 3.7 Hz, *J* = 3.7 Hz, 1 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 136–128 (m, 12 C), 126.4 (d, *J* = 290.6 Hz), 58.4 (s), 44.9 (d, *J* = 16.4 Hz), 32.1 (s) ppm. ^{19}F NMR (375 MHz, $CDCl_3$, 25 °C): δ = –63.5 (d, *J* = 31.06 Hz) ppm. Enantiomeric excess was determined by HPLC with an IC chiral column (*n*-heptane/*i*PrOH = 92:8, λ = 230 nm, 1 mL/min): t_R = 72.83 (major), 50.22 (minor) min.

4a′ (Minor Diastereomer): ^1H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 7.92–7.21 (m, 10 H, Ar), 4.51 (td, *J* = 12.5 Hz, *J* = 3.1 Hz, 1 H, CH), 3.5 (ddd, *J* = 10.8 Hz, *J* = 6.0 Hz, *J* = 3.6 Hz, 1 H, CH_2OH), 3.15 (ddd, *J* = 10.8 Hz, *J* = 9.8 Hz, *J* = 3.6 Hz, 1 H, CH_2OH), 1.99 (dddd, *J* = 13.7 Hz, *J* = 12.0 Hz, *J* = 4.6 Hz, *J* = 3.7 Hz, 1 H, CH_2), 1.77 (dddd, *J* = 12.9 Hz, *J* = 9.4 Hz, *J* = 6.1 Hz, *J* = 3.1 Hz, 1 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 136–128 (m, 12 C), 125.9 (d, *J* = 290.7 Hz), 59.2 (s), 44.7 (d, *J* = 16.8 Hz), 32.8 (s) ppm. ^{19}F NMR (375 MHz, $CDCl_3$, 25 °C): δ = –67.9 (d, *J* = 31.6 Hz) ppm. Enantiomeric excess was determined by HPLC with an IC chiral column (*n*-heptane/*i*PrOH = 92:8, λ = 230 nm, 1 mL/min): t_R = 27.44 (major), 24.75 (minor) min.

4b: Yield: 80 mg (80%), mixture of diastereomers, colorless oil. ^1H NMR (400 MHz, $CDCl_3$, TMS_{int}, diastereomer 1): δ = 8.17 (d, *J* = 8.8 Hz, 2 H, Ar), 7.69 (t, *J* = 6.8 Hz, 1 H, Ar), 7.61 (d, *J* = 8.2 Hz, 2 H, Ar), 7.56 (d, *J* = 8.2 Hz, 2 H, Ar), 7.45 (t, *J* = 7.6 Hz, 2 H, Ar), 4.78 (ddd, *J* = 3.0 Hz, *J* = 11.6 Hz, *J* = 30.5 Hz, 1 H, CH), 3.63–3.58 (m, 1 H, CH_2OH), 315–3.10 (m, 1 H, CH_2OH), 2.08–2.00 (m, 1 H, CH_2), 1.88–1.80 (m, 1 H, CH_2) ppm. ^1H NMR (400 MHz, $CDCl_3$, TMS_{int}, diastereomer 2): δ = 8.17 (d, *J* = 9.3 Hz, 2 H, Ar), 7.93 (d, *J* = 7.1 Hz, 2 H, Ar), 7.79 (t, *J* = 7.2 Hz, 1 H, Ar), 7.61 (d, *J* = 8.2 Hz, 2 H, Ar), 7.46 (t, *J* = 8.2 Hz, 2 H, Ar), 5.02–4.91 (m, 1 H, CH), 3.77–3.72 (m, 1 H, CH_2OH), 323–3.17 (m, 1 H, CH_2OH), 1.97–1.89 (m, 2 H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, diastereomer 1): δ = 131.9, 130.8, 128.1, 125.3, 125.2, 64.3, 59.8, 33.2, 30.8, 30.8 ppm. ^{13}C NMR (100 MHz, $CDCl_3$, diastereomer 2): δ = 128.3, 127.3, 125.9, 123.0, 122.8, 62.1, 56.8, 29.9, 28.7, 28.4 ppm. ^{19}F NMR (375 MHz, $CDCl_3$, diastereomer 1): δ = –127.95 (d, *J* = 30.5 Hz) ppm, ^{19}F NMR (375 MHz, $CDCl_3$, diastereomer 2): δ = –130.63 (d, *J* = 29.8 Hz) ppm. HRMS (ESI): calcd. for $C_{16}H_{16}FN_2O_7S$ $[M + H]^+$ 399.0657; found 399.0660. HPLC (Chiralpak® IC, *n*-hexane/*i*PrOH = 90:10, λ = 254 nm, 1 mL/min): t_{R1} = 36.919 and 50.895 min, t_{R2} = 28.024

and 31.838 min. $[\alpha]_D^{25}$ (diastereomer 1) = –6.0 (c = 0.74, $CHCl_3$, 28%*ee*), $[\alpha]_D^{25}$ (diastereomer 2) = +8.1 (c = 0.84, $CHCl_3$, 92%*ee*).

4c: Yield: 34 mg (36%), mixture of diastereomers, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, TMS_{int}): δ = 7.92 (d, J = 7.2 Hz, 2 H, Ar), 7.78 (t, J = 7.5 Hz, 1 H, Ar), 7.63–7.59 (m, 4 H, Ar), 7.39 (d, J = 7.2 Hz, 2 H, Ar), 4.72 (ddd, J = 3.0 Hz, J = 11.8 Hz, J = 31.7 Hz, 1 H, CH), 3.75–3.70 (m, 1 H, CH_2OH), 3.20 (td, J = 3.6 Hz, J = 10.4 Hz, 1 H, CH_2OH), 2.95–2.87 (m, 1 H, CH_2), 2.15–2.07 (m, 1 H, CH_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.1, 133.6, 132.4, 131.6, 130.5, 59.0, 45.8, 45.6, 33.5, 32.1, 30.9 ppm. ^{19}FNMR (375 MHz, $CDCl_3$): δ = –127.25 (J = 31.7 Hz) ppm. HRMS (ESI): calcd. for $[C_{17}H_{19}FN_3O_5S]^+$ $[M + NH_4]^+$ 396.1026; found 396.1022. HPLC (Chiralpak® IB, *n*-hexane/*i*PrOH = 90:10, λ = 254 nm, 1 mL/min): t_R = 30.582, 32.699 min. $[\alpha]_D^{25}$ = +12.9 (c = 1.00, $CHCl_3$, 74%*ee*).

3d: Mixture of diastereomers, pale-yellow oil. IR (KBr): $\tilde{\nu}$ = 3061, 2923, 2841, 2733, 1726, 1577, 1448, 1352, 1274, 1158, 1081, 998, 816, 753, 716, 684, 618, 584, 541, 477 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{16}O_5NFS$ $[M + Na]^+$ 424.0631; found 424.0624.

3d (Main Diastereomer): ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 9.63 (br. s, 1 H, CHO), 7.95–7.10 (m, 12 H, Ar), 5.13 (ddd, J = 31.6 Hz, J = 10.9 Hz, J = 2.9 Hz, 1 H, CH), 3.81 (ddd, J = 18.4 Hz, J = 10.9 Hz, J = 1.4 Hz, 1 H, CH_2), 3.38 (dd, J = 18.4 Hz, J = 2.9 Hz, 1 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 196.3 (s), 136–123 (m, 16 C), 43.9 (s), 41.7 (d, J = 16.8 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$, 25 °C): δ = –67.0 (d, J = 31.5 Hz) ppm.

3d′ (Minor Diastereomer): ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 9.51 (br. s, 1 H, CHO), 7.92–7.10 (m, 12 H, Ar), 5.05 (ddd, J = 26.8 Hz, J = 10.9 Hz, J = 2.9 Hz, 1 H, CH), 3.28 (ddd, J = 18.0 Hz, J = 10.8 Hz, J = 1.4 Hz, 1 H, CH_2), 2.94 (dd, J = 18.1 Hz, J = 2.9 Hz, 1 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 195.7 (s), 136–123 (m, 18 C), 44.1 (s), 42.6 (d, J = 17.0 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$, 25 °C): δ = –60.0 (d, J = 27.0 Hz) ppm.

4d: Yield: 20 mg, 20%, mixture of diastereomers, pale-yellow oil. IR (KBr): $\tilde{\nu}$ = 3296, 3059, 2957, 2925, 2854, 1716, 1578, 1448, 1350, 1158, 1081, 817, 757, 683, 590, 514, 478 cm^{-1}. $[\alpha]_D^{25}$ = +6.5 (c = 0.31, $CDCl_3$). HRMS (ESI): calcd. for $C_{20}H_{18}O_5NFS$ $[M + Na]^+$ 426.0787; found 426.0782.

4d (Major Diastereomer): ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 7.95–7.33 (m, 16 H, Ar), 4.74 (ddd, J = 31.9 Hz, J = 12.0 Hz, J = 3.0 Hz, 1 H, CH), 3.65 (m, 1 H, CH_2OH), 3.27 (td, J = 10.4 Hz, J = 4.5 Hz, 1 H, CH_2OH), 2.91 (m, 1 H, CH_2), 2.25 (m, 1 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 130.42 (d, J = 26.5 Hz), 136–123 (m, 16 C), 59.2 (s), 44.8 (s), 32.1 (s) ppm. ^{19}F NMR (375 MHz, $CDCl_3$, 25 °C): δ = –67.6 (d, J = 31.9 Hz) ppm. Enantiomeric excess was determined by HPLC with an IC chiral column (*n*-heptane/*i*PrOH = 92:8, λ = 230 nm, 1 mL/min): t_R = 62.87 (major), 54.11 (minor) min.

4d′ (Minor Diastereomer): Enantiomeric excess was determined by HPLC with an IC chiral column (*n*-heptane/*i*PrOH = 92:8, λ = 230 nm, 1 mL/min): t_R = 223.70 (major), 134.20 (minor) min.

3e: Mixture of diastereomers, pale-yellow oil. IR (KBr): $\tilde{\nu}$ = 3095, 3066, 2959, 2922, 2844, 2735, 1726, 1579, 1497, 1448, 1413, 1355, 1158, 1094, 1013, 757, 719, 684, 626, 572, 542 cm^{-1}. HRMS (ESI): calcd. for $C_{16}H_{13}O_5NClFS$ $[M + Na]^+$ 408.0085; found 408.0080.

3e (Major Diastereomer): ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 9.65 (t, J = 1.1 Hz, 1 H, CHO), 7.93 –7.21 (m, 9 H, Ar), 4.99 (ddd, J = 31.4 Hz, J = 10.9 Hz, J = 2.8 Hz, 1 H, CH), 3.80 (dd, J = 18.6 Hz, J = 2.9 Hz, 1 H, CH_2), 3.26 (ddd, J = 18.6 Hz, J = 11.0 Hz, J = 1.3 Hz, 1 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 195.9 (s), 136–129 (m, 12 C), 124.3 (d, J = 289.9 Hz), 43.7 (s), 40.9 (d, J = 16.8 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$, 25 °C): δ = –67.5 (d, J = 31.4 Hz) ppm.

3e′ (Minor Diastereomer): ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 9.54 (t, J = 1.3 Hz, 1 H, CHO), 7.93 –7.21 (m, 9 H, Ar), 4.92 (ddd, J = 26.5 Hz, J = 10.9 Hz, J = 2.8 Hz, 1 H, CH), 3.19 (ddd, J = 18.2 Hz, J = 10.9 Hz, J = 1.47 Hz, 1 H, CH_2), 2.92 (dd, J = 18.2 Hz, J = 2.8 Hz, 1 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 195.0 (s), 136–129 (m, 12 C), 124.5 (d, J = 287.6 Hz), 43.9 (s), 41.7 (d, J = 17.3 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$, 25 °C): δ = –60.6 (d, J = 25.98 Hz) ppm.

4e: Yield: 44 mg (45%), mixture of diastereomers, pale-yellow oil. IR (KBr): $\tilde{\nu}$ = 3586, 3315, 3095, 3065, 2956, 2925, 2854, 1714, 1579, 1492, 1446, 1415, 1349, 1158, 1092, 1016, 843, 756, 722, 685, 577, 542 cm^{-1}. $[\alpha]_D^{25}$ = +79.5 (c = 1.075, $CHCl_3$). HRMS (ESI): calcd. for $C_{16}H_{15}O_5NClFS$ $[M + Na]^+$ 410.0241; found 410.0236.

4e (Major diastereomer): ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 7.91–7.12 (m, 9 H, Ar), 4.59 (ddd, J = 16.4 Hz, J = 12.1 Hz, J = 3.0 Hz, 1 H, CH), 3.66 (ddd, J = 10.6 Hz, J = 6.5 Hz, J = 4.1 Hz, 1 H, CH_2OH), 3.24 (td, J = 10.3 Hz, J = 4.3 Hz, 1 H, CH_2OH), 2.86 (m, 1 H, CH_2), 2.07 (m, 1 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 136–129 (m, 12 C), 125.5 (d, J = 290.9 Hz), 58.9 (s), 44.1 (s), 32.0 (s) ppm. ^{19}F NMR (375 MHz, $CDCl_3$, 25 °C): δ = –68.1 (d, J = 31.3 Hz) ppm. Enantiomeric excess was determined by HPLC with an IC chiral column (*n*-heptane/*i*PrOH = 92:8, λ = 230 nm, 1 mL/min): t_R = 41.96 (major), 32.85 (minor) min.

4e′ (Minor Diastereomer): ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 7.91–7.12 (m, 9 H, Ar), 4.53 (ddd, J = 16.1 Hz, J = 11.9 Hz, J = 3.0 Hz, 1 H, CH), 3.53 (ddd, J = 9.9 Hz, J = 5.6 Hz, J = 3.3 Hz, 1 H, CH_2OH), 3.12 (td, J = 10.3 Hz, J = 4.3 Hz, 1 H, CH_2OH), 1.92 (m, 1 H, CH_2), 1.75 (m, 1 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 136–129 (m, 12 C), 126.1 (d, J = 290.4 Hz), 58.1 (s), 44.4 (s), 32.5 (s) ppm. ^{19}F NMR (375 MHz, $CDCl_3$, 25 °C): δ = –64.2 (d, J = 31.1 Hz) ppm. Enantiomeric excess was determined by HPLC with an IC chiral column (*n*-heptane/*i*PrOH = 92:8, λ = 230 nm, 1 mL/min): t_R = 136.50 (major), 89.37 (minor) min.

3f: Mixture of diastereomers, pale-yellow. IR (KBr): $\tilde{\nu}$ = 3094, 3067, 2918, 2843, 2734, 1726, 1579, 1488, 1447, 1410, 1354, 1157, 1082, 1012, 755, 719, 683, 613, 564, 541 cm^{-1}. HRMS (EI): calcd. for $C_{16}H_{13}NO_5FSBr$ $[M]^+$ 428.9682; found 428.9690.

3f (Major Diastereomer): ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 9.61 (t, J = 1.3 Hz, 1 H, CHO), 7.88–7.11 (m, 9 H, Ar), 4.93 (ddd, J = 31.4 Hz, J = 10.9 Hz, J = 2.8 Hz, 1 H, CH), 3.75 (dd, J = 18.5 Hz, J = 2.8 Hz, 1 H, CH_2), 3.22 (ddd, J = 18.6 Hz, J = 10.9 Hz, J = 1.3 Hz, 1 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 195.9 (s), 136–129 (m, 12 C), 124.5 (d, J = 290.1 Hz), 43.7 (s), 41.0 (d, J = 16.7 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$, 25 °C): δ = –67.4 (d, J = 31.5 Hz) ppm.

3f′ (Minor Diastereomer): ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 9.50 (t, J = 1.3 Hz, 1 H, CHO), 7.88–7.11 (m, 9 H, Ar), 4.86 (ddd, J = 24.1 Hz, J = 10.9 Hz, J = 2.6 Hz, 1 H, CH), 3.14 (ddd, J = 18.2 Hz, J = 10.8 Hz, J = 1.3 Hz, 1 H, CH_2), 2.87 (dd, J = 18.3 Hz, J = 2.8 Hz, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 195.3 (s), 136–129 (m, 12 C), 124.4 (d, J = 287.2 Hz), 43.9 (s), 41.6 (d, J = 17.2 Hz) ppm. ^{19}F NMR (600 MHz, $CDCl_3$, 25 °C): δ = –60.7 (d, J = 26.8 Hz) ppm.

4f: Yield: 45 mg (42%), mixture of diastereomers, pale-yellow oil. IR (KBr): $\tilde{\nu}$ = 3588, 3313, 3093, 3064, 2955, 2926, 2888, 2855, 1713,

1577, 1488, 1447, 1410, 1349, 1158, 1081, 1012, 840, 756, 719, 685, 623, 572, 541 cm^{-1}. $[\alpha]_D^{25}$ = +10.5 (*c* = 0.43, $CHCl_3$). HRMS (ESI): calcd. for $C_{16}H_{14}O_5NBrFS$ $[M]^-$ 429.9760; found 429.9767.

4f (Major Diastereomer): ^1H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 7.90 (br. d, *J* = 7.6 Hz, 2 H, Ar), 7.74 (m, 1 H, Ar), 7.57 (m, 2 H, Ar), 7.40 (br. d, *J* = 8.5 Hz, 2 H, Ar), 7.10 (br. d, *J* = 8.2 Hz, 2 H, Ar), 4.56 (ddd, *J* = 31.6 Hz, *J* = 12.0 Hz, *J* = 3.0 Hz, 1 H, CH), 3.67 (ddd, *J* = 10.7 Hz, *J* = 5.9 Hz, *J* = 3.4 Hz, 1 H, CH_2OH), 3.23 (td, *J* = 10.4 Hz, *J* = 4.4 Hz, 1 H, CH_2OH), 2.83 (m, 1 H, CH_2OH), 2.07 (m, 1 H, CH_2) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 136.2 (s), 132.2 (s, 2 C), 132.1 (s), 132.0 (s), 130.8 (s, 2 C), 130.6 (s, 2 C), 129.5 (s, 2 C), 125.5 (d, *J* = 289.1 Hz), 123.2 (s), 58.9 (s), 44.1 (d, *J* = 17.1 Hz), 32.0 (s) ppm. ^{19}F NMR (375 MHz, $CDCl_3$, 25 °C): δ = –68.1 (d, *J* = 31.7 Hz) ppm. Enantiomeric excess was determined by HPLC with an IC chiral column (*n*-heptane/*i*PrOH = 92:8, λ = 230 nm, 1 mL/min): t_R = 41.96 (major), 32.85 (minor) min.

4f′ (Minor Diastereomer): Enantiomeric excess was determined by HPLC with an IC chiral column (*n*-heptane/*i*PrOH = 92:8, λ = 230 nm, 1 mL/min): t_R = 136.50 (major), 89.37 (minor) min.

4g: Yield: 56 mg (77%), colorless oil. ^1H NMR (400 MHz, $CDCl_3$, TMS_{int}): δ = 7.91 (d, *J* = 7.9 Hz, 2 H, Ar), 7.77 (t, *J* = 7.3 Hz, 1 H, Ar), 7.60 (t, *J* = 7.9 Hz, 2 H, Ar), 4.07–4.0 (m, 1 H, CH), 3.81–3.63 (m, 1 H, CH_2OH), 3.45–3.27 (m, 1 H, CH_2OH), 1.74–1.50 (m, 2 H, CH_2), 1.40 (d, *J* = 6.1 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.0, 131.6, 130.4, 60.0, 35.0, 34.8. 33.7, 30.6, 13.8 ppm. $^{19}FNMR$ (375 MHz, $CDCl_3$): δ = –130.3 (d, *J* = 27.2 Hz) ppm. HRMS (ESI): calcd. for $C_{11}H_{14}FNNaO_5S$ $[M + Na]^+$ 314.0467; found 314.0469. HPLC: (Chiralpak® IC, *n*-hexane/*i*PrOH = 90:10, λ = 254 nm, 1 mL/min): t_R = 31.017, 36.460 min. $[\alpha]_D^{25}$ = +3.2 (*c* = 1.13, $CHCl_3$, 92%*ee*).

4h: Yield: 53 mg (70%), mixture of diastereomers, colorless oil. ^1H NMR (400 MHz, $CDCl_3$, TMS_{int}, major diastereomer): δ = 7.90 (d, *J* = 7.9 Hz, 2 H, Ar), 7.77 (t, *J* = 7.3 Hz, 1 H, Ar), 7.60 (t, *J* = 7.9 Hz, 2 H, Ar), 3.74–3.61 (m, 2 H, CH, CH_2OH), 3.26–3.14 (m, 1 H, CH_2OH), 2.01–1.99 (m, 1 H, CH_2), 1.87–1.67 (m, 3 H, CH_2), 1.06 (td, *J* = 1.3, *J* = 7.5 Hz 3 H, CH_3) ppm. ^1H NMR (400 MHz, $CDCl_3$, TMS_{int}, minor diastereomer): δ = 7.90 (d, *J* = 7.6 Hz, 2 H, Ar), 7.77 (t, *J* = 7.7 Hz, 1 H, Ar), 7.60 (t, *J* = 7.6 Hz, 2 H, Ar), 3.93–3.75 (m, 2 H, CH, CH_2OH), 3.29–3.16 (m, 1 H, CH_2OH), 2.43–2.33 (m, 1 H, CH_2), 2.05–1.95 (m, 1 H, CH_2), 1.45–1.38 (m, 2 H, CH_2), 0.96 (td, *J* = 1.0, *J* = 7.6 Hz 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, major diastereomer): δ = 136.9, 131.6, 130.4, 60.5, 40.2, 40.0, 31.2, 30.6, 21.9, 11.5 ppm. ^{13}C NMR (100 MHz, $CDCl_3$, minor diastereomer): δ = 136.0, 130.7, 129.5, 59.7, 38.9, 31.4, 30.9, 30.2, 21.7, 10.6 ppm. ^{19}F NMR (375 MHz, $CDCl_3$, major diastereomer): δ = –124.87 (d, *J* = 30.5 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$, minor diastereomer): δ = –126.35 (d, *J* = 29.8 Hz) ppm. HRMS (ESI): calcd. for $C_{12}H_{15}FN_3O_4S$ $[M + H]^+$ 288.0703; found 288.0700. HPLC (Chiralpak® IC, *n*-hexane/*i*PrOH = 95:5, λ = 254 nm, 1 mL/min): t_{major} = 28.588 and 34.130 min, t_{minor} = 26.088 and 30.874 min. $[\alpha]_D^{25}$ (major) = –6.8 (*c* = 1.00, $CHCl_3$, 89%*ee*), $[\alpha]_D^{25}$ (minor) = +1.8 (*c* = 0.67, $CHCl_3$, 90%*ee*).

4i: Yield: 58 mg (73%), mixture of diastereomers, colorless oil. ^1H NMR (400 MHz, $CDCl_3$, TMS_{int}, major diastereomer): δ = 7.90 (d, *J* = 8.0 Hz, 2 H, Ar), 7.77 (t, *J* = 7.6 Hz, 1 H, Ar), 7.60 (t, *J* = 7.9 Hz, 2 H, Ar), 3.74–3.60 (m, 2 H, CH, CH_2OH), 3.27–3.15 (m, 1 H, CH_2OH), 1.99–1.80 (m, 2 H, CH_2), 1.73–1.62 (m, 2 H, CH_2), 1.51–1.39 (m, 2 H, CH_2), 0.96 (t, *J* = 7.2 Hz, 3 H, CH_3) ppm. ^1H NMR (400 MHz, $CDCl_3$, TMS_{int}, minor diastereomer): δ = 7.90 (d, *J* = 8.4 Hz, 2 H, Ar), 7.77 (t, *J* = 7.8 Hz, 1 H, Ar), 7.60 (t, *J* = 7.8 Hz, 2 H, Ar), 3.93–3.74 (m, 2 H, CH, CH_2OH), 3.32–3.18 (m, 1 H, CH_2OH), 2.41–2.32 (m, 1 H, CH_2), 2.06–1.87 (m, 1 H, CH_2), 1.51–1.37 (m, 4 H, CH_2), 0.86 (t, *J* = 7.0 Hz, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, major diastereomer): δ = 136.9, 131.6, 130.4, 60.5, 39.1, 32.0, 31.1, 30.6, 20.5, 15.0 ppm. ^{13}C NMR (100 MHz, $CDCl_3$, minor diastereomer): δ = 136.0, 130.7, 129.5, 59.7, 37.8, 31.4, 30.9, 29.7, 19.6, 13.9 ppm. ^{19}F NMR (375 MHz, $CDCl_3$, major diastereomer): δ = –125.09 (d, *J* = 27.4 Hz) ppm. ^{19}F NMR (375 MHz, $CDCl_3$, minor diastereomer): δ = –126.37 (d, *J* = 30.0 Hz) ppm. HRMS (ESI): calcd. for $C_{13}H_{18}FNNaO_5S$ $[M + Na]^+$ 342.0783; found 342.0782. HPLC (Chiralpak® IC, *n*-hexane/*i*PrOH = 95:5, λ = 254 nm, 1 mL/min): t_{major} = 25.527 and 27.924 min, t_{minor} = 17.470 and 21.643 min. $[\alpha]_D^{25}$ (major) = –5.8 (*c* = 0.98, $CHCl_3$, 87%*ee*), $[\alpha]_D^{25}$ (minor) = +6.7 (*c* = 0.41, $CHCl_3$, 92%*ee*).

5f: Yield: 75 mg (42%), white solid, m.p. 132.3 °C. IR (KBr): $\tilde{\nu}$ = 3097.42, 3064.58, 2974.28, 2932.32, 2905.86, 2871.20, 1729.09, 1584.53, 1478.48, 1348.18, 1284.27, 1159.35, 1076.08, 773.95, 568.66 cm^{-1}. $[\alpha]_D^{25}$ = 69.2 (*c* = 0.46, $CDCl_3$). HRMS (ESI): calcd. for $C_{21}H_{23}BrFNO_6S$ $[M + Na]^+$ 538.0331; found 538.0306. ^1H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 7.66 (br. t, *J* = 7.4 Hz, 1 H, Ar), 7.47 (br. d, *J* = 7.7 Hz, 2 H, Ar), 7.41 (br. t, *J* = 7.8 Hz, 2 H, Ar), 7.39 (br. d, *J* = 8.1 Hz, 2 H, Ar), 7.11 (br. d, *J* = 8.0 Hz, 2 H, Ar), 4.41 (ddd, *J* = 30.8 Hz, *J* = 12.1 Hz, *J* = 2.4 Hz, 1 H, CH), 4.01 (m, 1 H, CH_2OH), 3.50 (td, *J* = 10.9 Hz, *J* = 4.1 Hz, 1 H, CH_2OH), 2.03 (m, 1 H, CH_2), 1.87 (m, 1 H, CH_2), 1.21 (s, 9 H, CH_3) ppm. ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 135.5 (s, 2 C), 132.1 (s), 132.1 (s, 2 C), 131.8 (s, 2 C), 130.5 (s), 130.3 (s, 2 C), 129.1 (s, 2 C), 178.0 (s), 125.6 (d, *J* = 290.4 Hz), 123.5 (s), 59.6 (s), 44.8 (s), 38.9 (s), 29.3 (s), 27.1 (s, 3 C) ppm. ^{19}F NMR (375 MHz, $CDCl_3$, 25 °C): δ = –65.4 (d, *J* = 31.2 Hz) ppm.

Supporting Information (see footnote on the first page of this article): NMR spectra and HPLC traces.

Acknowledgments

We thank the Spanish Ministry of Science and Innovation (MICINN) (Project AYA2009-13920-C02-02), the Ministry of Education of the Czech Republic (Grant No. MSM0021620857), and the Grant Agency of the Czech Republic (Grant No. 203/09/P193) for financial support. A.-N.R.A. is also grateful to the MICINN for a predoctoral fellowship.

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Received: June 14, 2010
Published Online: August 16, 2010

