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Asymmetric Nucleophilic Monofluorobenzylation of Allyl and Propargyl Halides Mediated by a Remote Sulfinyl Group: Synthesis of Homoallylic and Homopropargylic Fluorides

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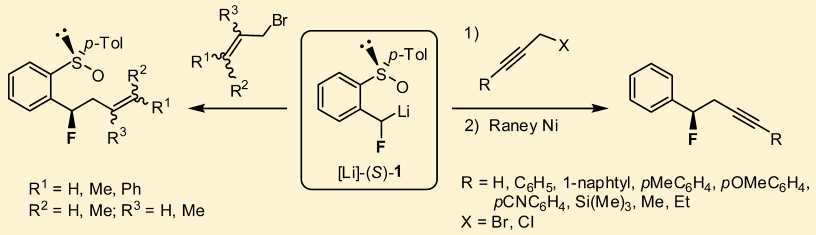
Supporting Information



ABSTRACT: Fluorinated 2-(*p*-tolylsulfinyl)benzyl carbanions react with allyl and propargyl halides in a highly stereoselective way, providing homoallylic and homopropargylic fluorides, respectively, with high optical purity. Theoretical calculations found transition states for these transformations whose relative stabilities are consistent with the experimentally observed stereoselectivity.

INTRODUCTION

Organofluorine compounds are well-recognized as strong candidates for pharmaceutical, agrochemical, and high-performance materials because of the ability of the fluorine atom to modulate molecular characteristics.[1] However, because fluorinated compounds occur extremely rarely in nature,[2] fluorine substituents are generally introduced into molecules through chemical synthesis. The two main strategies that have been developed for preparing monofluorinated molecules are electrophilic fluorination of active methylene compounds and nucleophilic monofluoroalkylation reactions of electrophiles, with their asymmetric versions being notably commendable. The former makes possible the preparation of enantiomerically enriched (ee) α-fluorocarbonyl derivatives and allylic fluorides,[3] whereas the latter, mainly based on the contributions of Olah,[4] Hu,[5] and Shibata and Toru,[6] provide monofluoroalkyl derivatives by using as efficient nucleophilic monofluoromethylating reagents fluoromethyl carbanions stabilized by some electron-withdrawing substituent (normally sulfonyl ones), removal of which produces CH_2F groups, thus excluding the possibility of preparing compounds with the fluorine atom joined to a chiral carbon. Therefore, the stereoselective construction of a fluorinated chiral carbon center still remains an attractive challenging task. In this regard, we have recently reported that the Li carbanion derived from 1-(fluoromethyl)-2-[(*S*)-*p*-tolylsulfinyl]benzene, [Li]-(*S*)-**1**, is efficiently stabilized by the remote *o*-sulfinyl group and can be used as an efficient chiral monofluorinated reagent in its reactions with electrophiles such as (*R*)-*N*-sulfinyl aldimines,[7] prochiral carbonyl compounds,[8] vinyl sulfones, and α,β-unsaturated esters,[9] providing benzylic fluorinated centers with almost complete control of the stereoselectivity (Scheme 1).

With the aim of widening the scope of the nucleophilic monofluorobenzylation reactions with our chiral monofluori-

Scheme 1. Synthesis of Homochiral Benzylic Fluorinated Centers Using [Li]-(*S*)-1

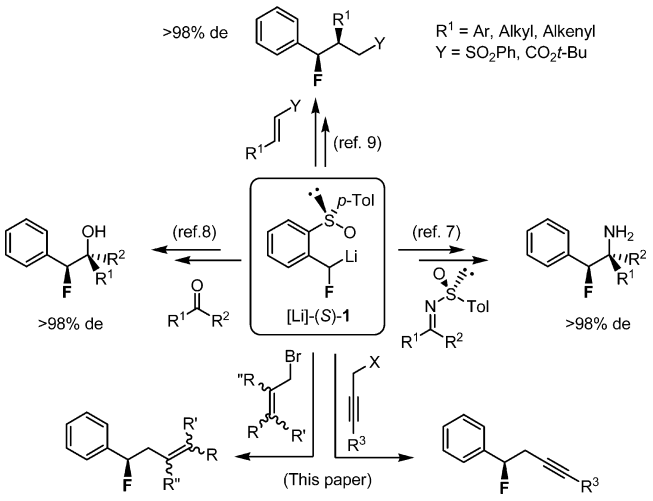


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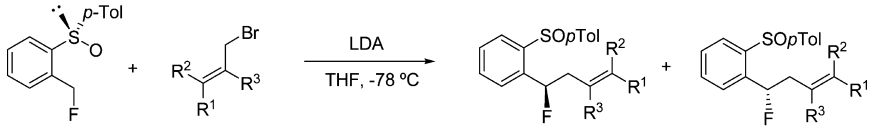
Table 1. Reactions of (*S*)-1 with Allyl Bromides 2a−e

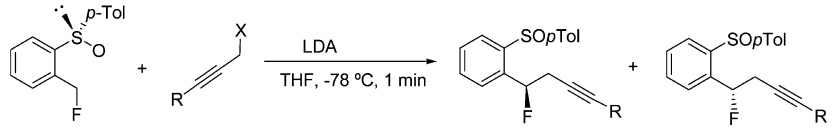


(*S*)-**1** **2a-e** (2 equiv) **3** **3'**

entry	allyl bromide	R^1	R^2	R^3	d.r. (**3**/**3′**)[a]	yield (%)[b]
1	(*S*)-**2a**	H	H	H	78:22	78[c]
2	(*S*)-**2b**	H	H	CH_3	81:19	65
3	(*S*)-**2c**	CH_3	H	H	88:12	78[c]
4	(*S*)-**2d**	CH_3	CH_3	H	85:15	69
5	(*S*)-**2e**	C_6H_5	H	H	80:20	68

[a]Diastereomeric ratios determined by ^{1}H NMR spectroscopy on the crude reaction mixtures. [b]Isolated yields of the major isomers after flash chromatography. [c]Combined yield.

Table 2. Reactions of (*S*)-1 with Propargyl Halides 4a−i



(*S*)-**1** **4a-i** (4 equiv) **5** **5'**

entry	propargyl bromide	R	X	d.r. (**5**/**5′**)[a]	yield (%)[b]
1	**4a**	H	Br	>98:<2	74
2	**4b**	C_6H_5	Cl	96:4	73
3	**4c**	1-naphthyl	Br	96:4	75
4	**4d**	*p*-$CH_3C_6H_4$	Br	96:4	72
5	**4e**	*p*-$OMeC_6H_4$	Br	95:5	75
6	**4f**	*p*-CNC_6H_4	Br	65:35	65[c]
7	**4g**	$Si(Me)_3$	Br	98:2	68
8	**4h**	CH_3	Br	88:12	62
9	**4i**	CH_2CH_3	Br	85:15	60

[a]Diastereomeric ratios determined by ^{1}H NMR spectroscopy on the crude reaction mixtures. [b]Isolated yields of the major isomers after flash chromatography. [c]Combined yield.

nated reagent (*S*)-**1**, we have studied its reactions with allyl and propargyl halides as an easy entry to homoallylic and homopropargylic monofluorides, respectively, bearing the fluorine atom attached to a chiral center (Scheme 1). These compounds constitute important building blocks in the construction of a wide library of chiral fluorinated molecules, taking advantage of the chemical versatility of the easily modifiable double and triple bonds present in their structures.[10] Despite this potential interest, the chemistry of homoallylic and homopropargylic fluorides, in both racemic and enantioenriched forms, remains underexplored because of the absence of reported methods allowing their preparation. Herein we describe the results we have obtained in the asymmetric nucleophilic monofluorobenzylation of allyl and propargyl halides with the α-fluoro-γ-sulfinylbenzyl carbanion derived from (*S*)-**1**, which allows the synthesis of enantioenriched homoallylic and homopropargylic monofluorides with the fluorine atom joined to a chiral benzylic carbon.

RESULTS AND DISCUSSION

Optically pure (*S*)-**1** was successfully prepared in a three-step sequence (sulfinylation, tosylation, and fluorination with CsF) starting from 2-bromobenzylic alcohol according to the procedure previously reported by us.[7] Allyl and propargyl halides were commercially available except for alkynes **4d−f**, which were prepared by Sonogashira coupling of the propargylic alcohol with the appropriate aryl iodide followed by a mesylation/bromination protocol.[11]

We first studied the behavior of (*S*)-**1** with allyl bromides **2a−e**. The alkylation reactions were performed in THF using 1.2 equiv of LDA (generated in situ at −78 °C), to which were added 1 equiv of (*S*)-**1** and, after 10 min of stirring, 2 equiv of allyl bromide **2**. In all cases, the reactions were complete in less than 1 min. As summarized in Table 1, this process provided a mixture of two diastereomers **3** and **3′** differing in the configuration at the newly created stereogenic center. The reaction of Li-(*S*)-**1** and **2a**, with no substituents on the olefinic fragment, led to a 78:22 mixture of **3a** and **3′a**, which are epimers at the benzylic carbon (entry 1). A slight improvement in the stereoselectivity was observed in the reactions with substituted allyl bromides **2b−e**. Thus, the β-methyl-substituted allyl bromide **2b** yielded an 81:19 distereoisomeric mixture of **3b** and **3′b** (entry 2). The reaction with (*E*)-1-bromobut-2-ene (**2c**) proceeded with better diatereoselectivity (76% de; entry 3), which is very similar to that obtained in the reaction with the γ-disubstituted allyl bromide **2d** (**3d**/**3′d** = 85:15; entry 4). Alkylation of cinamyl bromide (**2e**) was also tested. Once again, only moderate stereoselectivity was achieved (**3e**/**3′e** = 80:20) but the major isomer **3e** was isolated as a pure compound in 68% isolated yield (entry 5). These results suggest that the sulfinyl group is not able to exert complete control over the stereoselectivity of the process,

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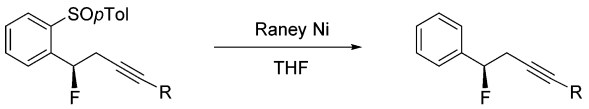
which contrasts with the results obtained in all of the other reactions with (*S*)-**1** studied to date[7−9] (see Scheme 1).

Next, we considered the addition of our fluorinated benzyllithium derivative [Li]-(*S*)-**1** to propargyl halides **4** to get the corresponding homopropargylic fluorides. Two main complications in the preparation of these compounds are the lower reactivities of propargylic substrates in comparison with allylic ones [determining incomplete conversions of (*S*)-**1**] and the difficulties associated with control of the regioselectivity (S_N2 vs S_N2'). We found that the optimal conditions involved the addition of 4 molar equiv of propargyl bromides **4** to [Li]-(*S*)-**1**. Under these conditions, quantitative conversions and completely regioselective processes were obtained, giving the S_N2 products, in most cases as mixtures of two diastereomers, **5** and **5′** (epimers at the benzylic position), which were readily separated by flash chromatography.

The reaction starting from propargyl bromide (**4a**) gave the desired homopropargylic fluoride **5a** in 74% yield with complete diastereoselectivity (>98% de; Table 2, entry 1). This result proves that the sulfinyl group completely controls the configuration at the newly created stereogenic fluorinated carbon. The reaction with γ-phenylpropargyl chloride (**4b**) evolved with high diastereoselectivity, furnishing a 96:4 mixture of **5b** and **5′b**. Other γ-arylpropargyl bromides bearing a 1-naphthyl group (**4c**) or a phenyl ring with an electron-donating group such as *p*-Me (**4d**) or *p*-MeO (**4e**) afforded similar results (about 92% de; entries 3−5). In contrast, the presence of an electron-withdrawing group on the benzene ring of the propargyl bromide, such as *p*-CN (**4f**), strongly decreased the stereoselectivity (entry 6).[12] These results suggested a significant role of electronic factors in the stereochemical course of the reaction. We also studied the reaction with TMS-propargyl bromide (**4g**), which proceeded with almost complete diastereoselectivity (96% de; entry 7). Finally, reactions of γ-alkylpropargyl bromides (**4h** and **4i**) evolved with high but incomplete stereoselectivity, giving easily separable 7:1 mixtures of diastereomers **5** and **5′** in good isolated yields (entries 8 and 9).

Removal of the chiral auxiliary from the major monofluorinated homopropargyl derivatives could be successfully performed with Raney Ni.[13] We checked the efficiency of this procedure in the cases of **5d** and **5i** (Scheme 2). The corresponding monofluorinated homopropargylic compounds **6d** and **6i** were obtained in good yields as pure compounds.

Scheme 2. Desulfinylation of 5d and 5i with Raney Ni

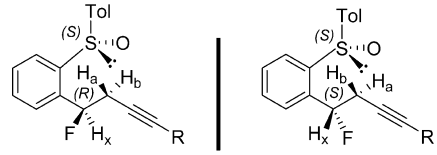


5d (R = *p*Tol)
5i (R = Et)

6d (75 %)
6i (70 %)

Initially, the configurational assignments of diastereomers **3** and **3′** (Table 1) as well as **5** and **5′** (Table 2) were based on the assumption that these reactions would follow the same stereochemical course that has been demonstrated for all of the other previously studied reactions of electrophiles with (*S*)-**1**[7−9] and other γ-sulfinylbenzyl carbanions.[14] According to this, we tentatively assigned the *R* configuration at the fluorinated carbon atom for the major compounds **3** and **5** and the *S* configuration for the minor ones **3′** and **5′**. The impossibility of obtaining good crystals from any of the synthesized allylic and homopropargylic fluorides or their sulfonyl derivatives prevented us from unequivocally assigning their absolute configurations by X-ray analysis. However, a detailed study of the NMR spectra of the diastereomers **5** and **5′** revealed that there were systematic differences in their chemical shifts, allowing the unequivocal differentiation of the epimers at the benzylic carbon (see the Supporting Information). Focusing our attention on protons H_a, H_b, and H_x (Table 3), we observed that the major isomers **5** always showed δ_H values lower (by ∼0.1−0.2 ppm) than those of the corresponding minor isomers **5′** (Table 3).

Table 3. Chemical Shifts (in ppm) of Compounds 5 and 5′ That Are Significant for Their Configurational Assignment



5 (major) **5'** (minor)

	5			5′		
R	δ_{H_a}	δ_{H_b}	δ_{H_x}	δ_{H_a}	δ_{H_b}	δ_{H_x}
C_6H_5	2.90	2.82	6.06	3.13	3.07	6.23
1-naphthyl	3.17	2.99	6.18	3.17 (2H)		6.23
p-MeC_6H_4	2.87	2.71	5.97	3.03	2.98	6.13
p-$OMeC_6H_4$	2.94	2.78	6.03	3.10	3.05	6.20
p-CNC_6H_4	2.99	2.88	6.09	3.12 (2H)		6.29
Me	2.47−2.70 (2H)		5.93	2.71−2.90 (2H)		6.09
Et	2.68	2.50	5.90	2.76−2.87 (2H)		6.06
Me[a]	2.49	2.43	6.02	3.05	2.89	6.33

[a]Estimated by theoretical calculations of model compounds in which a phenyl group was used as a simplified model for tolyl one.

Additionally, ^{1}H chemical shifts of model compounds for **5h** and **5′h** (R = Me; Ph instead of Tol) were estimated by means of DFT calculations.[15] The calculated chemical shifts correspond to conformationally averaged values from the most relevant conformers (eight structures in each case) according to a Boltzmann analysis.[16] The most stable structures showed a favored *anti* arrangement of the S−O and C−F bonds, minimizing the dipole moments. In the case of **5h**, this arrangement locates H_a, H_b, and H_x under the shielding effect of the *p*-tolylsulfinyl group, which could explain the slightly lower chemical shifts calculated for these protons, in good agreement with experimentally observed values, thus supporting the configurational assignment.

On the other hand, we were interested in understanding the origin of the diastereoselectivity observed in these processes as well as its dependence on electronic factors. To this end, we carried out a theoretical study of the possible transition states that would afford compounds **5b**, **5f**, and **5h** and their corresponding diastereomers **5′b**, **5′f**, and **5′h**. The different configurations of these compounds are determined during the C−C bond formation by the approach of the electrophile to either the *Re* or *Si* face of the benzylic position of carbanion **1**. Since our previous theoretical studies on the structure of this carbanion[7] indicated similar contributions of conformations with the fluorine and sulfinyl groups in *syn* or *anti* arrangements, which would afford different configurations for the approach of the electrophile to the same face of the carbanion plane, several transition states varying the approach

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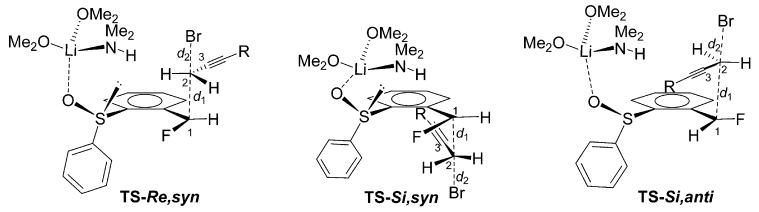
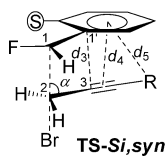


R	ΔG_{relat}	d_1	d_2	τ	ΔG_{relat}	d_1	d_2	τ	ΔG_{relat}	d_1	d_2	τ
C_6H_5	0	2.61	2.21	177.7	2.3	2.57	2.31	143.1	2.4	2.56	2.24	-130.4
p-CNC_6H_4	0	2.62	2.19	179.0	0.7	2.55	2.29	145.9	2.9	2.56	2.23	-115.5
CH_3	0	2.61	2.23	179.0	4.1	2.60	2.30	128.5	1.3	2.55	2.25	-127.8

Figure 1. Calculated structures [$CPCM_{(THF)}$/wB97xd/6-311G(d,p) (C,H,N,O,F) and SDB-cc-pVTZ (Br)//6-31G(d) (C,H,N,O,F) and LANL2DZ* (Br)] of some possible transition states involved in the reaction of propargyl bromides **4** with [Li]-(*S*)-**1**.[18] Values of the relative Gibbs free energy (ΔG_{relat}, kcal·mol^{-1}), representative distances (d_1 and d_2, in Å), and the F−C1−C2−C3 torsion angle (τ, in deg) are indicated.

of the electrophile to both faces of the benzylic position as well as to both faces of the carbanion plane were studied. The most relevant results are summarized in Figure 1.[17]

The most stable transition state in all cases was **TS-*Re,syn***, which would afford products showing the *R* configuration at the benzylic position. In this transition state, the F−C1−C2−C3 dihedral angle (τ) is almost 180°, indicating that the triple bond adopts an antiperiplanar arrangement with respect to the fluorine atom, thus minimizing the steric interactions and the electronic repulsion of the lone electron pairs on fluorine with the π electrons of the triple bond. The other two TSs (**TS-*Si,syn*** and **TS-*Si,anti***) would afford the *S* diastereomer. They are sterically less stable because the triple bond adopts an almost eclipsed arrangement with respect to one of the benzylic hydrogens (τ close to 120°). In the case of **TS-*Si,anti***, this arrangement minimizes the interactions of the R−C≡C and SOPh moieties (strongly repulsive for the antiperiplanar arrangement between F and R−C≡C) and is less destabilizing when R = Me (ΔG_{relat} = 1.3 kcal/mol). By contrast, deviations of the antiperiplanar arrangement between F and R−C≡C in **TS-*Si,syn*** must be attributed to a stabilizing π−π-stacking interaction between the aryl group and the triple bond. As the relative Gibbs free energy (ΔG_{relat}) varies in the order *p*-CNC_6H_4 < C_6H_5 < Me (Figure 1), we conclude that the presence of the aryl ring on the triple bond reinforce this π−π-stacking interaction, mainly for deactivated rings. These electronic effects translate into certain structure parameters of **TS-*Si,syn*** that are shown in Figure 2. Thus, the C1−C2−C3



R	ΔG_{relat}	d_3	d_4	d_5	α
C_6H_5	2.3	3.01	3.45	4.40	91.9
p-CNC_6H_4	0.7	2.99	3.45	4.29	89.3
CH_3	4.1	3.05	3.48	---	91.8

Figure 2. Calculated structures [$CPCM_{(THF)}$/wB97xd/6-311G(d,p) (C,H,N,O,F) and SDB-cc-pVTZ (Br)//6-31G(d) (C,H,N,O,F) and LANL2DZ* (Br)] of **TS-*Si,syn***. Values of the relative Gibbs free energy (ΔG_{relat}, kcal·mol^{-1}), representative distances (d_3, d_4, and d_5, in Å), and the C1−C2−C3 bond angle (α in deg) are indicated.

angle (α) and the C1′−C3 distance (d_3) decrease as π−π-stacking interactions increase. The distances between the centroid of the aromatic ring on the nucleophile and the triple bond of the electrophile (d_4) are the same for aromatic R groups, but d_4 is slightly longer for R = Me.[19] Moreover, a shorter distance between the aromatic rings (d_5) in the case of the *p*-CN group is observed, indicating a stronger interaction in this case.

The results provided by the theoretical calculations are in perfect concordance with the experimental ones. Thus, in the reaction of **4b** (R = Ph), **TS-*Re,syn*** is more stable than **TS-*Si,syn*** (2.3 kcal/mol) and **TS-*Si,anti*** (2.4 kcal/mol), allowing the prediction of a 98:2 diastereomeric ratio (96:4 was determined by NMR analysis; Table 2, entry 2). However, **TS-*Si,syn*** becomes much more stable for **4f** (R = *p*-CNC_6H_4, ΔG_{relat} = 0.7 kcal/mol), and the model predicts a 77:23 ratio of **5f** and **5′f**, very similar to the 65:35 ratio obtained experimentally (Table 2, entry 6). Finally, in the case of **4h** (R = Me), **TS-*Si,anti*** is only 1.3 kcal/mol less stable than **TS-*Re,syn***, affording a calculated distereomeric ratio of 90:10, in good agreement with the experimentally observed selectivity of 88:12 (Table 2, entry 8).

■ CONCLUSION

We have studied the asymmetric nucleophilic monofluorobenzylation of allyl and propargyl halides with 2-(*p*-tolylsulfinyl)-benzyl fluorides in the presence of LDA. The evolution of the fluorinated benzylcarbanions stabilized by a remote sulfinyl group is highly stereoselective, which allows the synthesis of homoallylic and homopropargylic fluorides with high optical purity. The course of the reaction has been studied by theoretical calculations, which provide results that are in an excellent agreement with the experimental data.

■ EXPERIMENTAL SECTION

General Methods. Dry solvents and liquid reagents were distilled under argon just prior to use; THF and CH_2Cl_2 were dried over activated 4 Å molecular sieves, and diisopropylamine was dried over KOH. *n*-BuLi (2.5 M solution in hexane) was purchased from a commercial supplier and used as received. Reactions were carried out in flame- or oven-dried glassware under an inert Ar atmosphere. NMR spectra were acquired on a 400 MHz spectrometer running at 400, 100, and 375 MHz for ^{1}H, ^{13}C, and ^{19}F, respectively. Chemical shifts (δ) are reported in parts per million relative to residual solvent signals ($CDCl_3$, 7.26 ppm for ^{1}H NMR spectra and 77.0 ppm for ^{13}C NMR spectra), and coupling constants (J) are given in hertz. ^{13}C NMR spectra were acquired in broadband-decoupled mode. Mass spectra were measured by electron impact (EI, 70 eV) or fast atom bombardment (FAB). Analytical thin-layer chromatography (TLC) was performed using precoated aluminum-backed plates and visualized by UV irradiation or phosphomolybdic acid solution. Purification of reaction products was carried out by flash chromatography (FC) using silica gel and an SCX column. Diastereoisomeric ratios were determined from integration of well-separated signals in the ^{1}H NMR and ^{19}F spectra of the crude reaction mixtures (H−C1 for

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compounds **3**/**3′** and **5**/**5′**). Melting points were measured in open capillary tubes and are uncorrected. The optical rotation was measured at room temperature using a polarimeter (concentration *c* given in g/100 mL).

Allyl bromides **2a**−**e** and propargyl bromides **4a**−**c** and **4g**−**i** were commercially available. Propargyl bromides **4d**−**f** were prepared by Sonogashira coupling of the propargylic alcohol with the appropriate aryl iodide followed by a mesylation/bromination protocol.[11]

General Procedure for the Reactions Summarized in Table 1. A solution of *n*-BuLi (0.6 mmol, 2.3 M in hexane) was added to *i*Pr$_2$NH (0.9 mmol) in THF (3 mL) at 0 °C. After 10 min of stirring, the mixture was cooled to −78 °C, and then a solution of the compound (*S*)-**1** (0.5 mmol) in THF (2 mL) was added. After 30 min of stirring, the corresponding allyl halide **2a**−**e**, (1 mmol) in THF (2 mL) was added at −78 °C. When the reaction was completed (15 min), the mixture was hydrolyzed at that temperature with saturated aqueous NH_4Cl solution (2 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography.

*1-[(R/S)-1-Fluorobut-3-enyl]-2-[(S)-p-tolylsulfinyl]benzene (**3a**/**3′a**).* These compounds were obtained as an inseparable mixture of diastereomers (78:22) from allyl bromide **2a** and (*S*)-**1**. Eluent for chromatography hexane/AcOEt 5:1; yield 78% (113 mg); colorless oil. *Major diastereomer*: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.08−2.20 (m, 1H), 2.35 (s, 3H), 2.48−2.66 (m, 1H), 4.96−5.11 (m, 2H), 5.67−5.83 (m, 1H), 5.81 (ddd, 1H, *J* = 3.8, 8.8, 47.7 Hz), 7.22 and 7.46 (AA′BB′ system, 4H), 7.36−7.62 (m, 3H), 8.04 (d, 1H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 40.1 (d, J_{C-F} = 24.0 Hz), 90.6 (d, J_{C-F} = 173.3 Hz), 124.7 (d, J_{C-F} = 3.8 Hz), 125.9, 126.0, 127.0, 127.9, 129.5 (d, J_{C-F} = 7.5 Hz), 130.0, 131.2, 138.3 (d, J_{C-F} = 21.0 Hz), 141.9, 142.5 (d, J_{C-F} = 3.5 Hz); ^{19}F NMR (375 MHz, $CDCl_3$) δ −170.7 (ddd, 1F, *J* = 17.4, 31.4, 47.7 Hz). *Minor diastereomer*: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.20−2.27 (m, 1H), 2.35 (s, 3H), 2.66−2.79 (m, 1H), 5.12−5.20 (m, 2H), 5.67−5.83 (m, 1H), 6.00 (ddd, 1H, *J* = 4.7, 7.9, 46.8 Hz), 7.23 and 7.47 (AA′BB′ system, 4H), 7.36−7.62 (m, 3H), 7.90 (t, 1H, *J* = 4.4 Hz); ^{19}F NMR (375 MHz, $CDCl_3$) δ −174.6 (ddd, 1F, *J* = 18.1, 28.8, 46.8 Hz). HRMS calcd for $C_{17}H_{17}FOSNa$ (TOF/ESI+) ([M + Na]$^+$) 311.0876, found 311.0862.

*1-[(R)-1-Fluoro-3-methylbut-3-enyl]-2-[(S)-p-tolylsulfinyl]benzene (**3b**).* Compound **3b** was obtained as the major diastereomer from allyl bromide **2b** and (*S*)-**1**. Eluent for chromatography hexane/CH_2Cl_2/AcOEt 3:2:1; yield 65% (100 mg); white syrup; $[\alpha]_D^{20}$ = +26.0 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.72 (s, 3H), 2.08 (ddd, 1H, *J* = 3.2, 15.2, 36.3 Hz), 2.35 (s, 3H), 2.58 (qd, 1H, *J* = 9.6, 15.2 Hz), 4.76 (s, 1H), 4.86 (s, 1H), 5.93 (ddd, 1H, *J* = 3.2, 9.6, 47.2 Hz), 7.23 and 7.49 (AA′BB′ system, 4H), 7.46−7.57 (m, 3H), 8.03 (d, 1H, *J* = 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 22.7, 45.0 (d, J_{C-F} = 24.3 Hz), 89.3 (d, J_{C-F} = 175.0 Hz), 113.8, 125.6, 126.1, 126.9 (d, J_{C-F} = 7.2 Hz), 129.6, 130.1, 131.4, 138.6 (d, J_{C-F} = 27.9 Hz), 138.8, 140.6, 141.8, 142.2 (d, J_{C-F} = 3.5 Hz); ^{19}F NMR (375 MHz, $CDCl_3$) δ −169.9 (ddd, 1F, *J* = 15.2, 36.3, 47.2 Hz); HRMS calcd for $C_{18}H_{19}FOSNa$ (TOF/ESI+) ([M + Na]$^+$) 325.1032, found 325.1021.

*1-[(S)-1-Fluoro-3-methylbut-3-enyl]-2-[(S)-p-tolylsulfinyl]benzene (**3′b**).* Compound **3′b** was obtained as the minor diastereomer from allyl bromide **2b** and (*S*)-**1**, and it was characterized from a mixture of diastereomers **3b** and **3′b**. Eluent for chromatography hexane/CH_2Cl_2/AcOEt 3:2:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.82 (s, 3H), 1.97−2.21 (m, 1H), 2.35 (s, 3H), 2.47−2.74 (m, 1H), 4.82 (s, 1H), 4.90 (s, 1H), 6.09 (ddd, 1H, *J* = 4.3, 8.6, 48.5 Hz), 7.24 and 7.50 (AA′BB′ system, 4H), 7.39−7.58 (m, 3H), 7.90 (dd, 1H, *J* = 3.6, 5.4 Hz); ^{19}F NMR (375 MHz, $CDCl_3$) δ −174.6 (ddd, 1F, *J* = 17.1, 32.9, 48.5 Hz).

*1-[(R/S,E)-1-Fluoropent-3-enyl]-2-[(S)-p-tolylsulfinyl]benzene (**3c**/**3′c**).* These compounds were obtained as an inseparable mixture of diastereomers (88:12) from allyl bromide **2c** and (*S*)-**1**. Eluent for chromatography hexane/AcOEt 5:1; yield 78% (127 mg); colorless oil. *Major diastereomer*: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.63 (d, 3H, *J* = 6.0 Hz), 2.14 (dddd, 1H, *J* = 4.3, 6.2, 14.6, 31.0 Hz), 2.35 (s, 3H), 2.43−2.58 (m, 1H), 5.26−5.61 (m, 3H), 7.22 and 7.45 (AA′BB′ system, 4H), 7.39−7.56 (m, 3H), 8.02 (dd, 1H, *J* = 1.2, 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.0, 21.4, 40.1 (d, J_{C-F} = 24.3 Hz), 90.6 (d, J_{C-F} = 174.7 Hz), 124.7 (d, J_{C-F} = 3.8 Hz), 125.3, 126.1, 127.0, 127.9, 129.5 (d, J_{C-F} = 7.6 Hz), 130.1, 131.2, 138.3 (d, J_{C-F} = 21.0 Hz), 142.0, 142.5 (d, J_{C-F} = 2.6 Hz); ^{19}F NMR (375 MHz, $CDCl_3$) δ −169.8 (ddd, 1F, *J* = 17.3, 31.0, 47.3 Hz). *Minor diastereomer*: ^{1}H NMR δ 1.45 (d, 3H, *J* = 6.8 Hz), 2.23−2.40 (m, 1H), 2.34 (s, 3H), 2.56−2.70 (m, 1H), 5.72 (ddd, 1H, *J* = 7.0, 8.5, 46.7 Hz), 5.79−6.03 (m, 2H), 7.21−7.46 (AA′BB′ system, 4H), 7.39−7.56 (m, 3H), 7.87−7.92 (m, 1H); ^{19}F NMR (375 MHz, $CDCl_3$) δ −174.0 (ddd, 1F, *J* = 17.8, 28.2, 46.7 Hz). HRMS calcd for $C_{18}H_{19}FOSNa$ (TOF/ESI+) ([M + Na]$^+$) 325.1032, found 325.1045.

*1-[(R)-1-Fluoro-4-methylpent-3-enyl]-2-[(S)-p-tolylsulfinyl]-benzene (**3d**).* Compound **3d** was obtained as the major diastereomer from allyl bromide **2d** and (*S*)-**1**. Eluent for chromatography hexane/CH_2Cl_2/AcOEt 3:2:1; yield 69% (108 mg); white syrup; $[\alpha]_D^{20}$ = −57.8 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 3H), 1.67 (s, 3H), 2.15−2.31 (m, 1H), 2.34 (s, 3H), 2.58 (qd, 1H, *J* = 8.2, 15.8 Hz), 5.03−5.13 (m, 1H), 5.77 (ddd, 1H, *J* = 4.6, 8.2, 46.8 Hz), 7.21 and 7.46 (AA′BB′ system, 4H), 7.37−7.56 (m, 3H), 8.01 (d, 1H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.8, 21.4, 25.7, 35.8 (d, J_{C-F} = 24.4 Hz), 90.9 (d, J_{C-F} = 174.7 Hz), 117.6 (d, 4.0 Hz), 125.4, 125.9, 126.9 (d, J_{C-F} = 7.5 Hz), 129.5, 130.0, 131.1, 135.8, 138.8 (d, J_{C-F} = 20.6 Hz), 141.6, 142.0, 142.6 (d, J_{C-F} = 2.3 Hz); ^{19}F NMR (375 MHz, $CDCl_3$) δ −168.8 (ddd, 1F, *J* = 15.8, 29.0, 46.8 Hz); HRMS calcd for $C_{19}H_{21}FOSNa$ (TOF/ESI+) ([M + Na]$^+$) 339.1189, found 339.1178.

*1-[(S)-1-Fluoro-4-methylpent-3-enyl]-2-[(S)-p-tolylsulfinyl]-benzene (**3′d**).* Compound **3′d** was obtained as the minor diastereomer from allyl bromide **2d** and (*S*)-**1**, and it was characterized from a mixture of diastereomers **3d** and **3′d**. Eluent for chromatography hexane/CH_2Cl_2/AcOEt 3:2:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.56 (s, 3H), 1.71 (s, 3H), 2.16−2.41 (m, 1H), 2.34 (s, 3H), 2.60−2.78 (m, 1H), 5.13−5.20 (m, 1H), 5.91 (ddd, 1H, *J* = 5.6, 7.6, 47.2 Hz), 7.22 and 7.47 (AA′BB′ system, 4H), 7.39−7.56 (m, 3H), 7.89 (dd, 1H, *J* = 3.6, 5.3 Hz); ^{19}F NMR (375 MHz, $CDCl_3$) δ −173.9 (ddd, 1F, *J* = 19.2, 28.4, 47.2 Hz).

*1-[(R)-1-Fluoro-4-phenylbut-3-enyl]-2-[(S)-p-tolylsulfinyl]benzene (**3e**).* Compound **3e** was obtained as the major diastereomer from allyl bromide **2e** and (*S*)-**1**. Eluent for chromatography hexane/CH_2Cl_2/AcOEt 3:1:1; yield 68% (124 mg); white syrup; $[\alpha]_D^{20}$ = −85.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.29−2.41 (m, 1H), 2.34 (s, 3H), 2.74 (dddd, 1H, *J* = 6.7, 8.4, 15.1, 19.3 Hz), 5.89 (ddd, 1H, *J* = 4.2, 8.5, 47.7 Hz), 6.10 (ddd, 1H, *J* = 6.7, 7.4, 16.6 Hz), 6.31 (d, 1H, *J* = 16.6 Hz), 7.19 and 7.46 (AA′BB′ system, 4H), 7.21−7.30 (m, 4H), 7.47−7.60 (m, 4H), 8.04 (dt, 1H, *J* = 1.3, 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 40.5 (d, J_{C-F} = 24.5 Hz), 90.0 (d, J_{C-F} = 175.1 Hz), 123.6 (d, J_{C-F} = 4.0 Hz), 125.5, 126.1, 126.2, 127.0 (d, J_{C-F} = 7.2 Hz), 127.5, 128.5, 130.0, 130.1, 131.3, 133.7, 136.9, 138.0 (d, J_{C-F} = 21.1 Hz), 141.7, 141.8, 142.3; ^{19}F NMR (375 MHz, $CDCl_3$) δ −175.2 (ddd, 1F, *J* = 19.3, 29.0, 47.7 Hz); HMRS calcd $C_{23}H_{21}FS$ ([M − O]$^+$) 348.1348, found 348.1332.

*1-[(S)-1-Fluoro-4-phenylbut-3-enyl]-2-[(S)-p-tolylsulfinyl]benzene (**3′e**).* Compound **3′e** was obtained as the minor diastereomer from allyl bromide **2e** and (*S*)-**1**, and it was characterized from a mixture of diastereomers **3e** and **3′e**. Eluent for chromatography hexane/CH_2Cl_2/AcOEt 3:1:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.30−2.42 (m, 1H), 2.35 (s, 3H), 2.78−2.92 (m, 1H), 6.07 (ddd, 1H, *J* = 4.4, 8.0, 47.0 Hz), 6.21 (dt, 1H, *J* = 7.1, 15.9 Hz), 6.48 (d, 1H, *J* = 15.9 Hz), 7.20−7.36 (m, 7H), 7.45−7.57 (m, 5H), 7.90 (dd, 1H, *J* = 3.6, 6.0 Hz); ^{19}F NMR δ −169.8 (ddd, 1F, *J* = 17.0, 30.2, 47.0 Hz).

General Procedure for the Reactions Summarized in Table 2. A solution of *n*-BuLi (0.6 mmol, 2.3 M in hexane) was added to *i*Pr$_2$NH (0.9 mmol) in THF (3 mL) at 0 °C. After 10 min of stirring, the mixture was cooled to −78 °C, and then a solution of the compound (*S*)-**1** (0.5 mmol) in THF (2 mL) was added. After 30 min of stirring, the corresponding propargyl compound **4a**−**j** (2.0 mmol) in THF (1 mL) was added at −78 °C. When the reaction was completed (5 min), the mixture was hydrolyzed at that temperature with saturated aqueous NH_4Cl solution (2 mL) and extracted with

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CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography.

*1-[(R)-1-Fluoro-3-butynyl]-2-[(S)-p-tolylsulfinyl]benzene (**5a**).* Compound **5a** was obtained as a unique diastereomer from propargyl bromide **4a** and (*S*)-**1**. Eluent for chromatography hexane/Et_2O 1:2; yield 74% (106 mg); colorless oil; $[\alpha]_D^{20}$ = −102.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.01 (t, 1H, *J* = 2.6 Hz), 2.35 (s, 3H), 2.49 (dddd, 1H, *J* = 2.6, 4.6, 17.3, 24.4 Hz), 2.70 (dddd, 1H, *J* = 2.6, 7.2, 17.3, 19.2 Hz), 5.94 (ddd, 1H, *J* = 4.6, 7.2, 46.0 Hz), 7.23 (part of AA′BB′ system, 2H), 7.43−7.58 (m, 5H), 8.00 (d, 1H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 27.0 (d, J_{C-F} = 27.0 Hz), 71.3, 78.3, 88.2 (d, J_{C-F} = 182.0 Hz), 125.6, 125.8, 127.2 (d, J_{C-F} = 7.9 Hz), 129.9, 130.1, 131.3, 141.5, 141.8, 142.4; ^{19}F NMR (375 MHz, $CDCl_3$) δ −169.8 (ddd, 1F, *J* = 19.2, 24.4, 46.0 Hz); HMRS calcd for $C_{17}H_{15}FS$ ($[M - O]^+$) 270.0878, found 270.0889.

*1-[(R)-1-Fluoro-4-phenyl-3-butynyl]-2-[(S)-p-tolylsulfinyl]benzene (**5b**).* Compound **5b** was obtained as the major diastereomer from propargyl chloride **4b** and (*S*)-**1**. Eluent for chromatography hexane/Et_2O 1:2; yield 73% (133 mg); white syrup; $[\alpha]_D^{20}$ = −55.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (s, 3H), 2.82 (ddd, 1H, *J* = 5.0, 17.1, 22.0 Hz), 2.90 (ddd, 1H, *J* = 6.7, 17.1, 27.7 Hz), 6.06 (ddd, 1H, *J* = 5.0, 6.7, 45.9 Hz), 7.21−7.37 (m, 6H), 7.50−7.60 (m, 2H), 7.52 and 7.58 (AA′BB′ system, 4H), 8.03 (dd, 1H, *J* = 1.8, 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 28.2 (d, J_{C-F} = 27.2 Hz), 83.6, 83.9, 88.7 (d, J_{C-F} = 179.4 Hz), 125.9, 126.0, 127.5 (d, J_{C-F} = 7.8 Hz), 128.3, 128.4, 130.2, 130.3, 131.5, 131.8, 137.3 (d, J_{C-F} = 21.0 Hz), 141.9, 142.0, 142.9; ^{19}F NMR (375 MHz, $CDCl_3$) δ −169.1 (ddd, 1F, *J* = 22.0, 27.7, 45.9 Hz); HMRS calcd for $C_{23}H_{20}FOS$ (M^+ + 1) 363.1213, found 363.1216.

*1-[(S)-1-Fluoro-4-phenyl-3-butynyl]-2-[(S)-p-tolylsulfinyl]benzene (**5′b**).* Compound **5′b** was obtained as the minor diastereomer from propargyl bromide **4b** and (*S*)-**1**, and it was characterized from a mixture of diastereomers **5b** and **5′b**. Eluent for chromatography hexane/Et_2O 1:2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 3.07 (ddd, 1H, *J* = 6.4, 20.1, 21.8 Hz), 3.13 (ddd, 1H, *J* = 6.1, 18.6, 21.8 Hz), 6.23 (ddd, 1H, *J* = 6.1, 6.4, 46.0 Hz), 7.14 (part of AA′BB′ system, 2H), 7.22−7.42 (m, 4H), 7.49−7.75 (m, 6H), 7.88−7.90 (m, 1H); ^{19}F NMR (375 MHz, $CDCl_3$) δ −172.5 (ddd, 1F, *J* = 18.6, 20.1, 46.0 Hz).

*1-[(R)-1-Fluoro-4-naphthyl-3-butynyl]-2-[(S)-p-tolylsulfinyl]-benzene (**5c**).* Compound **5c** was obtained as the major diastereomer from propargyl bromide **4c** and (*S*)-**1**. Eluent for chromatography hexane/Et_2O 1:1; yield 75% (155 mg); white syrup; $[\alpha]_D^{20}$ = −59.0 (*c* 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 3H), 2.99 (ddd, 1H, *J* = 5.2, 17.2, 22.0 Hz), 3.17 (ddd, 1H, *J* = 6.7, 18.5, 22.0 Hz), 6.18 (ddd, 1H, *J* = 5.2, 6.7, 46.0 Hz), 7.14 and 7.41 (AA′BB′ system, 4H), 7.38−7.70 (m, 8H), 7.71−7.79 (m, 2H), 8.06 (d, 1H, *J* = 7.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 28.1 (d, J_{C-F} = 28.0 Hz), 81.5, 88.3, (d, J_{C-F} = 178.7.4 Hz), 89.4, 125.1, 125.6, 125.7, 126.0, 126.3, 126.6, 127.4 (d, J_{C-F} = 7.5 Hz), 128.1, 128.5, 130.0, 130.1, 130.3, 131.3, 133.0, 133.3, 137.0 (d, J_{C-F} = 20.8 Hz), 141.4, 141.7, 142.6; ^{19}F NMR (375 MHz, $CDCl_3$) δ −168.5 (ddd, 1F, *J* = 17.2, 18.5, 46.0 Hz); HMRS calcd for $C_{27}H_{21}FS$ ($[M - O]^+$) 396.1353, found 396.1336.

*1-[(S)-1-Fluoro-4-naphthyl-3-butynyl]-2-[(S)-p-tolylsulfinyl]-benzene (**5′c**).* Compound **5′c** was obtained as the minor diastereomer from propargyl bromide **4c** and (*S*)-**1**, and it was characterized from a mixture of diastereomers **5c** and **5′c**. Eluent for chromatography hexane/Et_2O 1:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28 (s, 3H), 3.19 (dd, 2H, *J* = 6.0, 20.0 Hz), 6.23 (td, 1H, *J* = 6.0, 46.0 Hz), 7.10 (part of AA′BB′ system, 2H), 7.15−7.21 (m, 2H), 7.26−7.67 (m, 9H), 7.96−8.01 (m, 1H), 8.10−8.18 (m, 1H); ^{19}F NMR (375 MHz, $CDCl_3$) δ −168.1 (td, 1F, *J* = 20.0, 46.0 Hz).

*1-[(R)-1-Fluoro-4-tolyl-3-butynyl]-2-[(S)-p-tolylsulfinyl]benzene (**5d**).* Compound **5d** was obtained as the major diastereomer from propargyl bromide **4d** and (*S*)-**1**. Eluent for chromatography hexane/CH_2Cl_2/AcOEt 3:1:1; yield 72% (136 mg); white syrup; $[\alpha]_D^{20}$ = +96.0 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26 and 2.27 (two s, 6H), 2.71 (ddd, 1H, *J* = 5.0, 17.3, 22.2 Hz), 2.87 (ddd, 1H, *J* = 6.8, 17.3, 19.5 Hz), 5.97 (ddd, 1H, *J* = 5.0, 6.8, 46.0 Hz), 7.01, 7.14, 7.15, and 7.42 (two AA′BB′ systems, 8H), 7.39−7.53 (m, 3H), 7.94 (dd, 1H, *J* = 2.0, 6.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 21.5, 28.0 (d, J_{C-F} = 27.3 Hz), 82.9, 83.4, 88.6 (d, J_{C-F} = 177.5 Hz), 119.9, 125.5, 125.8, 127.3 (d, J_{C-F} = 7.7 Hz), 128.9, 130.1, 131.2, 131.5, 137.0 (d, J_{C-F} = 20.9 Hz), 138.2, 141.5, 141.8, 142.5; ^{19}F NMR (375 MHz, $CDCl_3$) δ −168.7 (ddd, 1F, *J* = 19.5, 22.2, 46.0 Hz); HMRS calcd for $C_{24}H_{21}FS$ ($[M - O]^+$) 360.1348, found 360.1365.

*1-[(S)-1-Fluoro-4-tolyl-3-butynyl]-2-[(S)-p-tolylsulfinyl]benzene (**5′d**).* Compound **5′d** was obtained as the minor diastereomer from propargyl bromide **4d** and (*S*)-**1**, and it was characterized from a mixture of diastereomers **5d** and **5′d**. Eluent for chromatography hexane/CH_2Cl_2/AcOEt 3:1:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.26 and 2.30 (two s, 6H), 2.98 (ddd, 1H, *J* = 6.0, 18.4, 22.2 Hz), 3.03 (ddd, 1H, *J* = 6.4, 20.4, 22.2 Hz), 6.13 (ddd, 1H, *J* = 6.0, 6.4, 46.4 Hz), 7.02 (part of AA′BB′ system, 2H), 7.11−7.22 (m, 4H), 7.41−7.52 (m, 4H), 7.57 (dd, 1H, *J* = 4.6, 6.4 Hz), 7.87 (dd, 1H, *J* = 5.0, 6.8 Hz); ^{19}F NMR (375 MHz, $CDCl_3$) δ −171.9 (ddd, 1F, *J* = 18.4, 20.4, 46.4 Hz).

*1-[(R)-1-Fluoro-4-(4-methoxyphenyl)-3-butynyl]-2-[(S)-p-tolylsulfinyl]benzene (**5e**).* Compound **5e** was obtained as the major diastereomer from propargyl bromide **4e** and (*S*)-**1**. Eluent for chromatography hexane/AcOEt 2:1; yield 75% (147 mg); white syrup; $[\alpha]_D^{20}$ = −63.4 (*c* 0.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 and 3.80 (two s, 6H), 2.78 (ddd, 1H, *J* = 5.0, 17.3, 22.3 Hz), 2.94 (ddd, 1H, *J* = 6.8, 17.3, 19.4 Hz), 6.03 (ddd, 1H, *J* = 5.0, 6.8, 46.0 Hz), 6.81, 7.21, 7.28, and 7.50 (two AA′BB′ systems, 8H), 7.48−7.59 (m, 3H), 8.03 (d, 1H, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 28.0 (d, J_{C-F} = 27.6 Hz), 55.2, 82.1, 83.3, 88.6 (d, J_{C-F} = 177.0 Hz), 113.8, 115.1, 125.6, 125.7, 127.3 (d, J_{C-F} = 7.7 Hz), 129.9, 130.0, 130.1, 131.2, 133.0, 137.1 (d, J_{C-F} = 21.0 Hz), 141.6, 141.7, 142.6, 159.4; ^{19}F NMR (375 MHz, $CDCl_3$) δ −168.5 (ddd, 1F, *J* = 19.4, 22.3, 46.0 Hz); HMRS calcd for $C_{24}H_{21}FOS$ ($[M - O]^+$) 376.1297, found 376.1283.

*1-[(S)-1-Fluoro-4-(4-methoxyphenyl)-3-butynyl]-2-[(S)-p-tolylsulfinyl]benzene (**5′e**).* Compound **5′e** was obtained as the minor diastereomer from propargyl bromide **4e** and (*S*)-**1**, and it was characterized from a mixture of diastereomers **5e** and **5′e.** Eluent for chromatography hexane/AcOEt 2:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 and 3.79 (two s, 6H), 3.05 (ddd, 1H, *J* = 6.4, 20.0, 25.0 Hz), 3.10 (ddd, 1H, *J* = 6.0, 18.0, 25.0 Hz), 6.20 (ddd, 1H, *J* = 6.0, 6.4, 46.4 Hz), 6.81, 7.28, 7.32, and 7.53 (two AA′BB′ systems, 8H), 7.43−7.66 (m, 3H), 7.91−7.96 (m, 1H); ^{19}F NMR (375 MHz, $CDCl_3$) δ −171.9 (ddd, 1F, *J* = 18.0, 20.0, 46.4 Hz).

*1-[(R/S)-1-Fluoro-4-(4-cyanophenyl)-3-butynyl]-2-[(S)-p-tolylsulfinyl]benzene (**5f/5′f**).* This compound was obtained as an inseparable mixture of diastereomers (65:35) from propargyl bromide **5f** and (*S*)-**1**. Eluent for chromatography hexane/Et_2O 1:1; yield 65% (126 mg); colorless syrup. *Major diastereomer*: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (s, 3H), 2.88 (ddd, 1H, *J* = 6.6, 15.0, 21.0 Hz), 2.99 (ddd, 1H, *J* = 6.9, 21.0, 24.0 Hz), 6.09 (ddd, 1H, *J* = 6.6, 6.9, 45.9 Hz), 7.23 and 7.27 (AA′BB′ system, 4H), 7.42−7.60 (m, 7H), 8.04 (d, 1H, *J* = 7.1 Hz); ^{19}F NMR (375 MHz, $CDCl_3$) δ −170.1 (ddd, 1F, *J* = 15.0, 24.0, 45.9 Hz). *Minor diastereomer*: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 3.12 (td, 2H, *J* = 6.3, 21.0 Hz), 6.29 (td, 1H, *J* = 6.3, 46.0 Hz), 7.33−7.62 (m, 10H), 7.68−7.72 (m, 1H), 7.88−7.92 (m, 1H); ^{19}F NMR (375 MHz, $CDCl_3$) δ −173.1 (ddd, 1F, *J* = 17.5, 20.0, 46.0 Hz). HMRS calcd for $C_{24}H_{18}FNS$ ($[M - O]^+$) 371.1144, found 371.1128.

*1-[(R)-1-Fluoro-4-(trimethylsilyl)-3-butynyl]-2-[(S)-p-tolylsulfinyl]-benzene (**5g**).* Compound **5g** was obtained as the major diastereomer from propargyl bromide **4g** and (*S*)-**1**. Eluent for chromatography hexane/Et_2O 1:1; yield 68% (122 mg); colorless oil; $[\alpha]_D^{20}$ = +60.0 (*c* 2.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.14 (s, 9H), 2.38 (s, 3H), 2.59 (ddd, 1H, *J* = 4.8, 17.4, 22.4 Hz), 2.76 (ddd, 1H, *J* = 6.7, 17.4, 21.0 Hz), 5.93 (ddd, 1H, *J* = 4.8, 6.7, 45.7 Hz), 7.25 and 7.49 (AA′BB′ system, 4H), 7.48−7.60 (m, 3H), 8.01 (dd, 1H, *J* = 1.0, 7.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 0.1, 21.4, 28.4 (d, J_{C-F} = 26.7 Hz), 88.3, 88.6 (d, J_{C-F} = 178.9 Hz), 100.4, 125.5, 125.7, 127.5 (d, J_{C-F} = 8.1 Hz), 129.9, 130.1, 131.0, 136.7 (d, J_{C-F} = 21.1 Hz), 141.6, 141.7, 142.3; ^{19}F NMR (375 MHz, $CDCl_3$) δ −170.0 (ddd, 1F, *J* = 21.0, 22.4,

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45.7 Hz); HMRS calcd for $C_{20}H_{23}FSSi$ ([M − O]$^+$) 342.1274, found 342.1285.

*1-[(R)-1-Fluoro-3-pentynyl]-2-[(S)-p-tolylsulfinyl]benzene (**5h**).* Compound **5h** was obtained as the major diastereomer from propargyl bromide **4h** and (*S*)-**1**. Eluent for chromatography hexane/isopropanol 10:1; yield 62% (93 mg); colorless oil; $[\alpha]_D^{20}$ = −44.4 (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.76 (t, 3H, *J* = 2.5 Hz), 2.37 (s, 3H), 2.47−2.70 (m, 2H), 5.93 (ddd, 1H, *J* = 4.8, 7.2, 46.1 Hz), 7.25 and 7.50 (AA′BB′ system, 4H), 7.49−7.59 (m, 3H), 8.03 (dd, 1H, *J* = 1.5, 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.5, 21.4, 27.4 (d, J_{C-F} = 27.1 Hz), 73.2, 78.9, 89.0 (d, J_{C-F} = 177.7 Hz), 123.5, 125.4, 125.7, 127.0 (d, J_{C-F} = 7.6 Hz), 130.0, 131.2, 133.4, 136.2, 137.1 (d, J_{C-F} = 21.2 Hz), 138.8, 142.6; ^{19}F NMR (375 MHz, $CDCl_3$) δ −169.0 (ddd, 1F, *J* = 19.9, 22.5, 46.1 Hz); HMRS calcd for $C_{18}H_{18}FOS$ (M^+ + 1) 301.1056, found 301.1059.

*1-[(S)-1-Fluoro-3-pentynyl]-2-[(S)-p-tolylsulfinyl]benzene (**5′h**).* Compound **5′h** was obtained as the minor diastereomer from propargyl bromide **4h** and (*S*)-**1**, and it was characterized from a mixture of diastereomers **5h** and **5′h**. Eluent for chromatography hexane/isopropanol 10:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.70 (t, 3H, *J* = 2.4 Hz), 2.36 (s, 3H), 2.71−2.90 (m, 2H), 6.09 (td, 1H, *J* = 6.3, 45.8 Hz), 7.25 (part of AA′BB′ system, 2H), 7.49−7.65 (m, 4H), 7.85−7.97 (m, 2H); ^{19}F NMR (375 MHz, $CDCl_3$) δ −171.6 (dd, 1F, *J* = 18.4, 45.8 Hz).

*1-[(R)-1-Fluoro-3-hexynyl]-2-[(S)-p-tolylsulfinyl]benzene (**5i**).* Compound **5i** was obtained as the major diastereomer from propargyl bromide **4i** and (*S*)-**1**. Eluent for chromatography hexane/CH_2Cl_2/AcOEt 3:1:1; yield 60% (95 mg); colorless oil; $[\alpha]_D^{20}$ = −121.8 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (t, 3H, *J* = 7.5 Hz), 2.12 (qd, 2H, *J* = 2.4, 7.5 Hz), 2.35 (s, 3H), 2.50 (dddd, 1H, *J* = 2.4, 4.8, 17.1, 23.5 Hz), 2.68 (dddd, 1H, *J* = 2.4, 7.1, 17.1, 19.5 Hz), 5.90 (ddd, 1H, *J* = 4.8, 7.5, 46.1 Hz), 7.22 and 7.47 (AA′BB′ system, 4H), 7.48−7.57 (m, 3H), 7.99 (d, 1H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 13.9, 21.4, 27.4 (d, J_{C-F} = 27.0 Hz), 73.3, 85.0, 89.1 (d, J_{C-F} = 176.8 Hz), 125.3, 125.4, 125.8, 127.2 (d, J_{C-F} = 7.6 Hz), 129.9, 130.0, 130.1, 131.2, 137.1 (d, J_{C-F} = 21.3 Hz), 141.7; ^{19}F NMR (375 MHz, $CDCl_3$) δ −168.8 (ddd, 1F, *J* = 19.5, 23.5, 46.1 Hz); HMRS calcd for $C_{19}H_{18}OS$ ([M − HF]$^+$) 294.1078, found 294.1105.

*1-[(S)-1-Fluoro-3-hexynyl]-2-[(S)-p-tolylsulfinyl]benzene (**5′i**).* Compound **5′i** was obtained as the minor diastereomer from propargyl bromide **4i** and (*S*)-**1**, and it was characterized from a mixture of diastereomers **5i** and **5′I**. Eluent for chromatography hexane/Et_2O 1.5:1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (t, 3H, *J* = 7.6 Hz), 2.13 (qd, 2H, *J* = 2.4, 7.6 Hz), 2.35 (s, 3H), 2.76−2.88 (m, 2H), 6.06 (td, 1H, *J* = 6.3, 46.4 Hz), 7.26 and 7.47 (AA′BB′ system, 4H), 7.46−7.55 (m, 3H), 7.88−7.91 (m, 1H); ^{19}F NMR (375 MHz, $CDCl_3$) δ −171.4 (ddd, 1F, *J* = 16.3, 19.4, 46.4 Hz).

Representative Procedure for Desulfinylation with Raney Ni. To a stirred solution of the corresponding compound **5d** and **5i** (0.09 mmol) in THF (1 mL) was added activated Raney nickel (0.6 g) in THF (2 mL) at room temperature. When the reaction was completed (1.5 h), the crude was filtered and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography.

*1-[(R)-1-Fluoro-4-tolyl-3-butynyl]benzene (**6d**).* Compound **6d** was obtained as a unique diastereomer from **5d**. Eluent for chromatography hexane/Et_2O 75:1; yield 75% (17 mg); white syrup; $[\alpha]_D^{20}$ = +20.5 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (s, 3H), 2.56−2.67 (m, 2H), 5.43 (ddd, 1H, *J* = 4.3, 8.0, 47.6 Hz), 7.01 and 7.08 (AA′BB′ system, 4H), 7.12−7.25 (m, 1H), 7.27−7.39 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 26.9 (d, J_{C-F} = 4.2 Hz), 79.4, 92.5, 94.5 (d, J_{C-F} = 170.5 Hz), 125.5, 125.6, 128.1 (d, J_{C-F} = 2.0 Hz), 128.2, 128.4, 129.0, 130.0, 130.8, 132.7, 135.2, 138.8, 140.5; ^{19}F NMR (375 MHz, $CDCl_3$) δ −174.5 (ddd, 1F, *J* = 17.1, 28.0, 47.6 Hz); HMRS calcd for $C_{17}H_{14}$ ([M − HF]$^+$) 218.1096, found 218.1083.

*1-[(R)-1-Fluoro-3-hexynyl]benzene (**6i**).* Compound **6i** was obtained as a unique diastereomer from **5i**. Eluent for chromatography hexane/AcOEt 1:2; yield 70% (12 mg); colorless syrup; $[\alpha]_D^{20}$ = +185.0 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 (t, 3H, *J* = 7.5 Hz), 2.12 (qt, 2H, *J* = 2.4, 7.5 Hz), 2.67−2.95 (m, 2H), 5.96 (dt, 1H, *J* = 6.4, 46.4 Hz), 7.33−7.62 (m, 4H), 7.83−7.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.3, 13.5, 28.0 (d, J_{C-F} = 9.5 Hz), 74.9, 80.0, 89.6 (d, J_{C-F} = 164.2 Hz), 128.7, 130.4, 136.6; ^{19}F NMR (375 MHz, $CDCl_3$) δ −176.4 (ddd, 1F, *J* = 14.9, 20.3, 46.7 Hz); HMRS calcd for $C_{12}H_{12}$ ([M − HF]$^+$) 156.0939, found 156.0923.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental and computational details as well as spectroscopic and analytical data for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(16) Up to 10 conformers for **5h** and 12 for **5′h** were optimized, and those with no significant contribution to the conformational equilibrium (less than 1%) were discarded.
(17) Many other transition-state structures were studied and found to be less stable than those collected in Figure 1 (see the Supporting Information).
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