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Optimized Monofluoromethylsulfonium Reagents for Fluoromethylene-Transfer Chemistry

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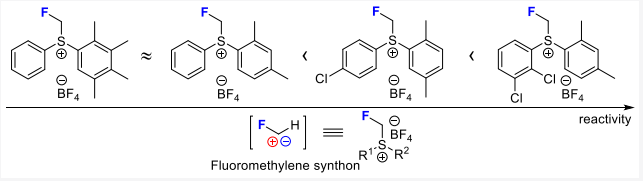
ABSTRACT: An investigation of the properties and reactivity of fluoromethylsulfonium salts resulted in the redesign of the reagents for fluoromethylene transfer chemistry. The model reaction, fluorocyclopropanation of nitrostyrene, turned out to be a suitable platform for the discovery of more streamlined fluoromethylene transfer reagents. The incorporation of halides on one aryl ring increased the reactivity, and 2,4-dimethyl substitution on the other aryl ring provided a balance between the reactivity/crystallinity of the reagent as well as the atom economy. The utility of new reagents was demonstrated by the development of an efficient fluorocyclopropanation protocol to access a range of monofluorinated cyclopropane derivatives.



INTRODUCTION

Large endeavors in the field of fluorine chemistry have resulted in many efficient new synthetic technologies to incorporate fluorine atoms into a synthetic target.[1] This situation is mainly driven by the fact that a plethora of pharmaceutical drugs,[2] agrochemicals[3] and materials[4] contain fluorine atoms in their chemical structure. One can distinguish two major approaches to accessing monofluorinated organic products: reactions that accommodate the formation of carbon−fluorine bonds or direct fluorination methodologies[5] and the use of preformed fluorinated building blocks.[6] Notably, significantly less investigated is the merger between these two approaches, an application of fluorocarbene precursors, the simplest of the fluoroorganic building blocks, allowing one fluorine and one carbon modification.[7] Fluoromethylation has recently been investigated, offering a single attachment point for the target substrate.[8] However, fluoromethylene group transfer[9−11] formally offers two connection points, giving access to monofluorinated 3-membered rings.[11d] Along this line, we have recently reported on fluoromethylene transfer[12] from *S*-monofluoromethyl-*S*-phenyl-2,3,4,5-tetramethylphenylsulfonium tetrafluoroborate (**2a**) (Figure 1) via ylide intermediate as an alternative to freon ($CHFX_2$) chemistry[7] to access monofluorinated cyclopropane[12b,c] and epoxide[12a] derivatives. Reagent **2a**, originally developed[13] for monofluoromethylation, turned out to be efficient; however, it was not an optimal reagent for fluoromethylene transfer chemistry.[12c]

In the context of global health challenges and threats due to the limited arsenal humanity possesses to combat viral infections,[14] it is notable that multiple cyclopropane rings are present in many known antiviral agents, such as glaveprevir, boceprevir, simeprevir (HCV protease (serine protease) inhibitors), odanacatib (cathepsin and calpain protease (cysteine protease) inhibitors), and others.[15] The bioisosteric

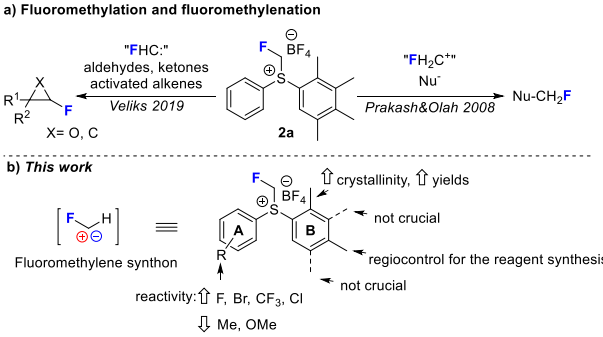


Figure 1. Diarylfluoromethyl sulfonium reagents: (a) fluoromethylation and fluoromethylenation; (b) identification of structural parameters for fluoromethylene-transfer applications.

replacement of hydrogen atoms with fluorine[16] is routine in medicinal chemistry programs; however, access to fluorocyclopropanes[17] is somewhat limited, and fluorocyclopropyl analogues of the aforementioned pharmaceuticals have not been reported.[18] In this endeavor, well-designed reagents as well as handy synthetic methods are of high priority. In our pursuit of developing new fluoromethylene transfer technologies, we have identified several problems of the currently employed fluoromethylsulfonium salts: (i) there is a high cost for the starting material 1,2,3,4-tetramethylbenzene for **2a**

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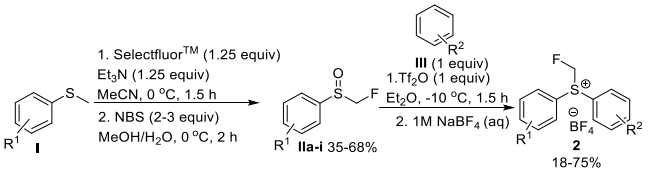
synthesis; (ii) all known monofluoromethylsulfonium salts were reported to be sticky oils, with some exceptions bearing bulky substituents (such as **2a**)[19]—not a favorable property for a practical reagent; (iii) some substrate classes underperformed using **2a**,[12c] for example, nitroalkenes; and (iv) there is a lack of reports of the structure influence on the reagent performance. Therefore, we opted to investigate the properties of sulfonium salts of type **2** to develop a new design of reagents specifically allocated for fluoromethylene transfer purposes.

RESULTS AND DISCUSSION

The synthetic studies initially started with optimization of the synthetic route to obtain fluoromethylene transfer reagents of type **2**. We have modified the existing synthetic routes to obtain sulfonium salts **2**, which typically involve overnight reactions and notorious reagents. We streamlined the process by the replacement of freon chemistry,[13] sluggish nucleophilic substitution[20] with fluoride, or potentially explosive DAST[19] with more user-friendly Selectfluor via a fast fluoro-Pummerer rearrangement process[21] allowing the synthesis of fluoromethylsulfonium reagents **2** within 1 day (Scheme 1). The fast

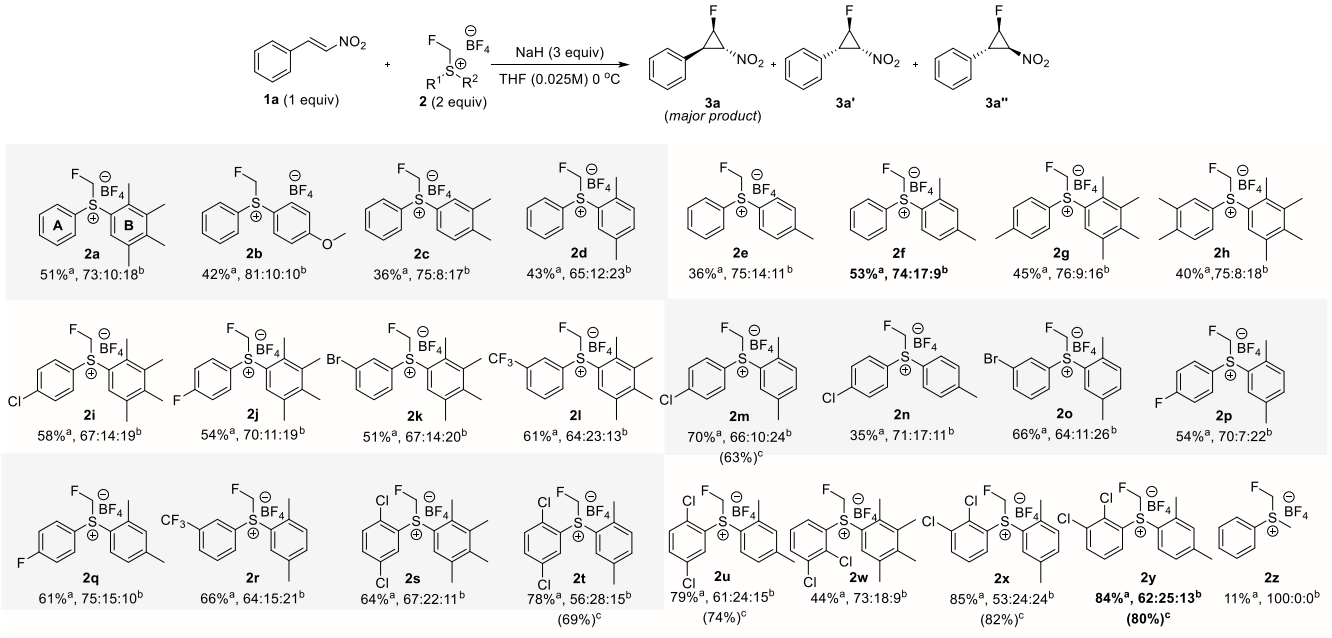
Scheme 1. Synthesis of Diarylfluoromethyl Sulfonium Salts 2



access to the collection of >20 novel reagents **2** allowed the identification of several key structural motifs of the sulfonium salt influencing the reactivity and properties. To investigate the efficiency of the reagents, we selected previously unreported monofluorocyclopropanation of *β*-nitrostyrene as a model reaction. Nitrostyrenes gave only moderate yields of the corresponding fluorocyclopropanes **3** when using reagent **2a**, a deliberately chosen platform for the detection of changes in reagent performance.

Our model reaction (Scheme 2) allowed us to uncover the reactivity profile of various fluoromethylsulfonium salts. For illustration purposes, we arbitrarily labeled the aryl rings with A and B denotations. The sulfonium salts **2** were arranged according to their substitution pattern in the aryl rings A and B and tested in the fluorocyclopropanation reaction with the aim of improving the F-cyclopropane **3** outcome. Performing the reaction with sulfonium salts **2a**–**f**, ring A remains unsubstituted, but ring B is decorated with methyl or methoxy groups at various positions, giving similar product **3a** yields. However, comparing the prices of the starting materials *m*-xylene (23 eur/mol, Alfa Aesar) and 1,2,3,4-tetramethylbenzene (3382 eur/mol, Alfa Aesar),[22] the comparable performance of the previously unreported reagent **2f** is clearly advantageous over the original tetramethyl-substituted sulfonium salt **2a**. The *o*-methyl group in ring B allows the maintenance of the crystallinity of the corresponding salts, as in our hands, reagents **2** lacking this substitution turned out to be a sticky oil and displayed significantly lower yields of **3a**. The yield of product **3a**, compared to the original reagent **2a**, is slightly decreased if additional methyl groups are introduced in the A ring (compounds **2g**–**h**). However, a slight improvement can be observed when the A ring is decorated with halogen or trifluoromethyl groups (**2i** and **2l**). Furthermore, reagent **2m**, with a decreased number of methyl groups at ring B and a preserved *p*-Cl substituent, gives product **3a** in a good 70% yield. This trend can also be observed for sulfonium salts **2o**, **2q**, and **2r**, but as mentioned above, the removal of *o*-methyl from ring B, as for **2n**, gives a drop in the yield of the desired fluorocyclopropane **3a**. Additional improvements can

Scheme 2. Probing Reagent 2 for Fluorocyclopropanation of Nitrostyrene 1a*



*Reaction conditions: **1a** (0.067 mmol), **2** (0.134 mmol), THF (2.7 mL), and NaH (0.201 mmol). [a]^{1}H NMR yield determined using EtOAc as an internal standard. [b]dr (**3a**/**3a′**/**3a″**) determined by ^{1}H NMR. [c]Isolated yields for the mixture of diastereomers of **3a**.

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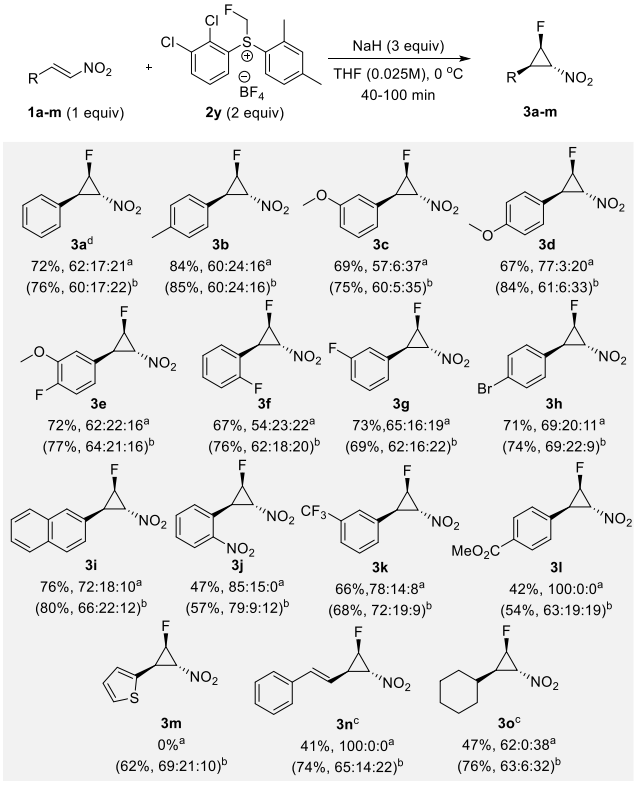
be achieved by the introduction of two halogens in the aryl system (**2t**,**u**). The modification of halogens at various positions of the benzene ring allowed a significant improvement in the product **3a** yield. The sulfonium salts **2x** and **2y** efficiently afforded **3a** in very good yields and moderate diastereoselectivity. Alkyl-substituted sulfonium salt **2z** performed poorly in the fluorocyclopropanation of nitrostyrene **1a**. Slow diffusion of Et_2O vapor into an acetonitrile solution of sulfonium salts **2a**,**d**,**i**,**p**,**s**,**w** resulted in the formation of monocrystals, which allowed us to obtain crystal structures (for more details on the solid structure of **2a**, see the SI). Out of the collection of fluoromethylsulfonium salts **2**, reagent **2f** stands out as the most affordable and **2y** as the most reactive. With improved reagent **2y** in hand, we investigated the substrate scope for the fluorocyclopropanation of nitroalkenes (Scheme 3). The nitrofluorocyclopropanes are formed with

Scheme 3. Fluorocyclopropanation of Nitroalkenes 1*



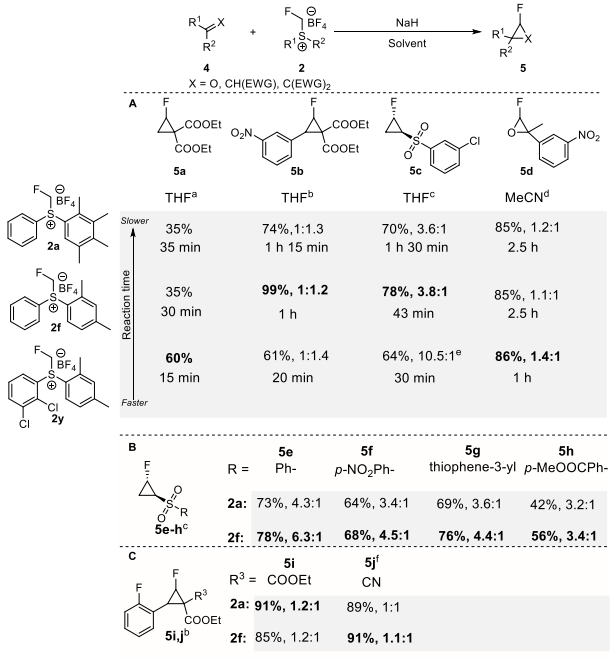
*Reaction conditions: nitroalkene **1** (0.201 mmol, 1 equiv), sulfonium salt **2y** (2 equiv), NaH (3 equiv), THF (0.025 M), 0 °C, 40−100 min. [a]Isolated yield for a mixture of diastereomers **3**/**3′**/**3″**, dr determined by ^{1}H or ^{19}F NMR. [b]Crude product yield determined by ^{1}H NMR using EtOAc as an internal standard, dr determined by ^{1}H or ^{19}F NMR. [c]Three equivalents of **2y** and 4.5 equiv of NaH were used. [d]The reaction was repeated on a 1 mmol scale of **1a**. Isolated yield of **3a** 75%, dr = 68:21:11, ^{1}H NMR yield of crude (72%, dr = 60:21:19).

moderate to very good yields with moderate diastereoselectivities. The aryl- and alkyl-substituted nitroalkenes participate in the reaction, providing a range of fluorocyclopropane **3** derivatives.

Various substituents at the aryl ring are tolerated, such as electron-donating groups (alkyl- **1b**, alkoxy- **1c**−**e**), halogen **1e**−**h**, and electron-accepting groups (nitro **1j**, trifluoromethyl- **1k**, and ester **1l**). Nitro- and ester-substituted substrates **1j**,**l** give fluorocyclopropanes **3j** and **3l** in moderate yield, but the *p*-methyl substituent gives product **3b** in the highest yield. The thiophene **1m**, conjugated diene **1n**, and **1o** alicyclic participate in the fluorocyclopropanation reaction as well, affording corresponding products **3m**, **3n**, and **3o**. The thiophene **3m** forms in rather good yield, as detected by ^{1}H NMR of a crude product; however, the product displayed instability upon chromatographic purification. All other nitrofluorocyclopropanes **3** were obtained as stable, chromatographically isolable products. Conjugated nitroalkene **1n** and cyclohexyl-substituted alkene **1o** gave products in moderate yields. The diastereomers can be readily separated by silica gel chromatography. Most of the nitrofluorocyclopropanes **3** are air-stable oils with naphthyl-substituted product **3i** as an exception, which is a solid. The relative configurations of all three isolated diastereomers of **3a** were assigned by analysis of J_{H-F} and J_{H-H} values in ^{1}H and ^{19}F NMR spectra and additionally supported by NOESY NMR (see the Experimental Section and SI). In order to demonstrate the Johnson−Corey−Chaykovsky[23,12] fluorocyclopropanation of nitroalkenes as a synthetic tool, the upscale of the reaction was performed on a 1 mmol scale, giving comparable results to those of the small-scale reaction.

Furthermore, we probed reagents **2a**, **2f**, and **2y** with other substrate classes (Scheme 4). The 2,4-dimethyl-substituted **2f** reagent performed similarly or slightly better than the original tetramethyl reagent **2a**.[12] For the fast-reacting substrate ethyl methylidene malonate (**4a**), 2,3-dichloro reagent **2y** significantly improved both the reaction time and the yield of product **5a**; however, for the slower reacting substrates **4b** and

Scheme 4. Comparison of Reagents 2a, 2f, and 2y for Different Substrate Classes*



*Isolated yields of **5** reported, dr determined by ^{1}H or ^{19}F NMR of crude product. Reaction conditions: alkene **4** (1 equiv), (a) sulfonium salt **2** (2 equiv), NaH (9.5 equiv), THF (0.0085 M), 0 °C; (b) sulfonium salt **2** (1.6 equiv), NaH (4 equiv), THF (0.07 M), rt; (c) sulfonium salt **2** (2 equiv), NaH (4 equiv), THF (0.1 M), rt; (d) sulfonium salt **2** (1.5 equiv), NaH (1.6 equiv), MeCN (0.05 M), 0 °C; (e) MeCN; (f) 1,4-dioxane used as a solvent.

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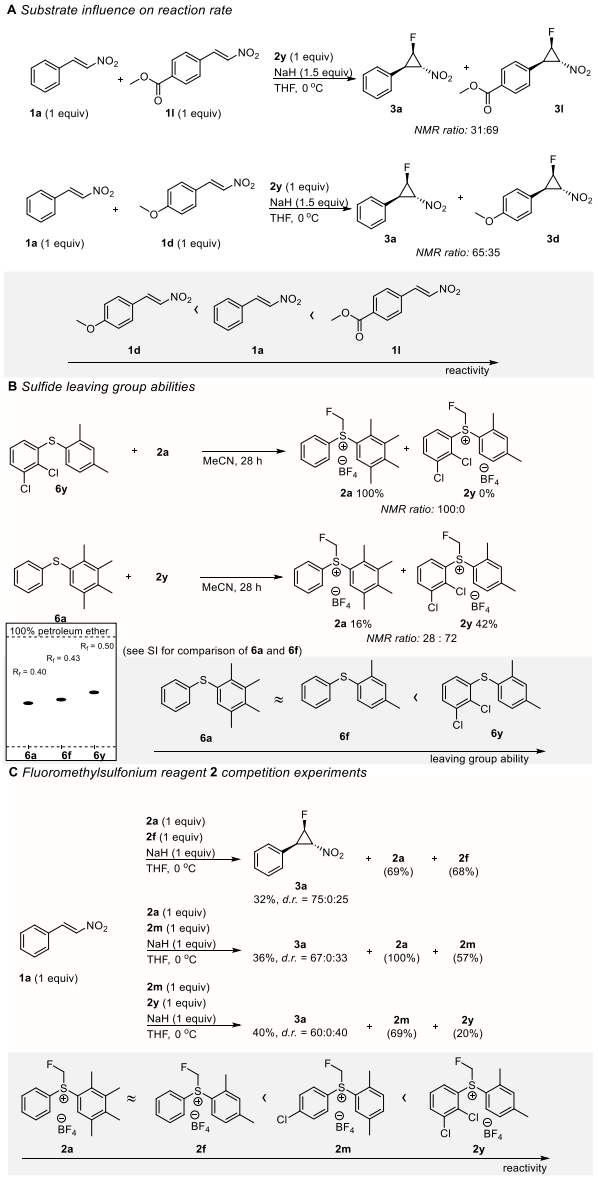
4c, the very reactive reagent **2y** gave lower yields. The prolonged reaction time resulted in competing polymerization of THF,[24] suggesting that **2y** may also act as a strong Lewis acid if not consumed by the substrate. Thus, **2f** is more suitable for Michael acceptors bearing sulfone groups or arylidene malonates. However, the fluoromethylene transfer to ketone **4d**,[12a] which takes 2.5 h with reagent **2a** in MeCN, proceeds in just 1 h when **2y** is used, giving fluoroepoxide **5y** in comparable yield to that of reagents **2a** and **2f**.

Several control experiments allowed us to draw the landscape of some reaction parameters (Scheme 5). The more electron-deficient substrate **1** (with EWG groups) reacts faster than the one with EDG (Scheme 5A). The leaving group capability of the corresponding diaryl sulfides **6** was probed by substitution reaction experiments with reagent **2** (Scheme 5B). Sulfide **6a** partially replaced **6y** in reagent **2y**; in contrast, **6y** was not capable of outcompeting **6a** from fluoromethylsulfonium salt **2a**. Compounds **6f** and **6a** have comparable leaving group abilities. In this context, it is worth mentioning the chromatographic behavior of diaryl sulfides—**6y** is less polar on silica gel than **6f** and **6a**. This is a favorable property of **6y** for purification purposes, diminishing the possibility of its coelution with products, which typically are more polar than sulfides **6**.

Scheme 5. Control Experiments



The reactivity of sulfonium reagent **2** was investigated by performing several competition experiments, which allowed ranking the selected reagents **2a**,**f**,**m**,**y** (Scheme 5C). The increased number of halogens increases the reactivity of **2**, which correlates well with a higher leaving group capability for halogenated reagents as well as faster reactions (Scheme 4) and improved performance (Scheme 2).

CONCLUSIONS

In conclusion, we have redesigned fluoromethylsulfonium salts for fluoromethylene transfer purposes. To investigate the reactivity of various diaryl fluoromethylsulfonium reagents using fluorocyclopropanation of nitroalkenes as the model reaction, we selected the best reagents for this purpose. (i) 2,4-dimethyl-substituted reagent **2f** offers a cheaper, simpler, and more efficient replacement for the known reagent **2a**; (ii) dichlorinated reagent **2y** turns out to be the most reactive reagent, offering superior performance for previously challenging substrates—nitroalkenes; and (iii) reagent **2f** followed by **2y** would be a rational protocol to search for the best conditions for fluoromethylene transfer chemistry. The reactivity of fluoromethylsulfonium salts increases upon decreasing electron density of the aryl ring. Halogen substituents increase reactivity, but methyl or methoxy substituents decrease reactivity. The *o*-methyl substituent on the aryl ring of reagent **2** provides crystallinity and maintains performance.

EXPERIMENTAL SECTION

General Information. Reagents and starting materials were obtained from commercial sources and used as received. Starting materials and dry solvents (1,4-dioxane, MeCN, DMF, DMSO) were purchased from Fluorochem, SigmaAldrich, Acros, or AlfaAeser and used as received. Anhydrous THF, Et_2O, and DCM were obtained from dry solvent still. Flash column chromatography was carried out using Kieselgel silica gel (35−70 and 60−200 μm). Thin-layer chromatography (TLC) was performed on silica gel using Merck TLC silca gel 60 F254 Aluminum sheets and was visualized by UV lamp, staining with $KMnO_4$. Preparative TLC was carrier out on 20 × 20 cm Merck TLC silca gel 60 F254 aluminum sheets. NMR spectra were recorded on 300 or 400 MHz Bruker spectrometers with chemical shift values (δ) in parts per million using the residual solvent signal as an internal reference. HRMS analyses were performed on a hybrid quadrupole time-of-flight mass spectrometer equipped with an electrospray ion source. Elemental analyses were performed by analytical service of LIOS. X-ray structures were investigated on a Rigaku, XtaLAB Synergy, Dualflex, or HyPix diffractometer. The X-ray structures were deposited with the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures. The compound names were generated using the ChemDraw structure to name convertor.

General Procedure A for the Synthesis of Sulfoxides IIa-i. Selectfluor (20.00 g, 56.46 mmol, 1.25 equiv) was suspended in anhydrous MeCN (85 mL) under argon atmosphere and cooled to 0 °C. To the suspension was added thioanisole (**Ia**) (5.30 mL, 45.2 mmol, 1 equiv) solution in anhydrous MeCN (10 mL) dropwise over 10 min at 0 °C. The reaction mixture was stirred for 1 h at the same temperature and then to the mixture was slowly added Et_3N (7.87 mL, 56.5 mmol, 1.25 equiv). After 30 min, the reaction mixture was poured on water (500 mL), and the aqueous phase was extracted with petroleum ether (3 × 150 mL). The combined organic phases were

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dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude (fluoromethyl)(phenyl)sulfane intermediate was dissolved in a mixture of MeOH (80 mL) and H_2O (7 mL) and cooled to 0 °C. To the solution was added NBS (16.08 g, 90.33 mmol, 2.00 equiv), and the reaction mixture was stirred at the same temperature until full conversion (TLC control PE/EtOAc 1:1) (~2 h). The reaction mixture was quenched with 10% Na_2SO_3 (~50 mL), and saturated $NaHCO_3$ was added to the mixture until pH = 8. Then MeOH was partly evaporated under reduced pressure, and the suspension was extracted with DCM (3 × 100 mL). The combined organic phases were dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The crude sulfoxide **IIa** was purified by silica gel column chromatography (eluent gradient PE/EtOAc 5:1 to PE/EtOAc 1:1). The ((fluoromethyl)sulfinyl)benzene **IIa**[13] (2.74 g, 17.3 mmol, 38%) was obtained as a yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73−7.63 (m, 2H), 7.63−7.52 (m, 3H), 5.10 (dd, J = 48.1, 8.1 Hz, 1H), 5.07 (dd, J = 47.6, 8.2 Hz, 1H).

*1-Chloro-4-((fluoromethyl)sulfinyl)benzene (**IIb**).* The product was obtained following general procedure A using 4-chlorothioanisole (**Ib**) (2.00 g, 12.6 mmol, 1.00 equiv), Selectfluor (5.58 g, 15.8 mmol, 1.25 equiv), Et_3N (2.20 mL, 15.8 mmol, 1.25 equiv), MeCN (24 mL), NBS (4.49 g, 25.2 mmol 2.00 equiv), MeOH (23 mL), and H_2O (2 mL). The product **IIb** (1.36 g, 7.07 mmol, 56%) was obtained as a white solid. Mp: 66−69 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65−7.60 (m, 2H), 7.58−7.53 (m, 2H), 5.11 (dd, J = 47.9, 8.2 Hz, 1H), 5.06 (dd, J = 47.4, 8.2 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 138.7, 137.4 (C−F, d, $^3J_{C-F}$ = 6.1 Hz), 130.1, 126.3, 97.8 (C−F, d, $^1J_{C-F}$ = 222.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −212.52 (t, J = 47.7 Hz).HRMS (ESI) m/z: [M + H]$^+$ calcd for C_7H_7OSClF 192.9890, found 192.9898.

*1,2-Dichloro-3-((fluoromethyl)sulfinyl)benzene (**IIc**).* The product was obtained following general procedure A, using 2,3-dichlorothioanisole (**Ic**) (1.000 g, 5.179 mmol, 1.00 equiv), Selectfluor (0.2293 g, 6.474 mmol, 1.25 equiv), Et_3N (0.90 mL, 6.5 mmol, 1.25 equiv), MeCN (26 mL), NBS (1.844 g, 10.36 mmol, 2.00 equiv), MeOH (22 mL), and H_2O (3 mL). The product **IIc** (0.4870 g, 2.145 mmol, 41%) was obtained as a white solid. Mp: 61−63 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88−7.81 (m, 1H), 7.68−7.64 (m, 1H), 7.55−7.49 (m, 1H), 5.46 (dd, J = 47.5, 8.5 Hz, 1H), 5.12 (dd, J = 48.1, 8.5 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 138.8 (C−F, d, $^3J_{C-F}$ = 8.4 Hz), 134.1, 133.6, 128.9, 128.6, 125.7, 97.2 (C−F, d, $^1J_{C-F}$ = 223.4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −214.45 (t, J = 47.7 Hz). HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_7H_6OSCl_2F$ 226.9500, found 226.9510.

*1-Bromo-3-((fluoromethyl)sulfinyl)benzene (**IId**).* The product was obtained following general procedure A, using 3-bromothioanisole (**Id**) (0.8400 g, 4.136 mmol, 1.00 equiv), Selectfluor (1.832 g, 5.170 mmol, 1.25 equiv), Et_3N (0.72 mL, 5.2 mmol, 1.25 equiv), MeCN (13 mL), NBS (1.472 g, 8.272 mmol, 2.00 equiv), MeOH (11 mL), and H_2O (1 mL). The product **IId** (0.4220 g, 1.780 mmol, 43%) was obtained as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (t, J = 1.8 Hz, 1H), 7.70 (ddd, J = 7.9, 1.9, 1.0 Hz, 1H), 7.58 (dt, J = 7.8, 1.1 Hz, 1H), 7.44 (t, J = 7.9 Hz, 1H), 5.12 (dd, J = 47.8, 8.2 Hz, 1H), 5.09 (dd, J = 47.5, 8.2 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 141.2 (C−F, d, $^3J_{C-F}$ = 6.1 Hz), 135.3, 131.1, 127.7 (C−F, d, $^4J_{C-F}$ = 0.6 Hz), 124.0, 123.4 (C−F, d, $^4J_{C-F}$ = 0.8 Hz), 98.0 (C−F, d, $^1J_{C-F}$ = 222.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −212.46 (t, J = 47.6 Hz). HRMS (ESI) m/z: [M + H]$^+$ calcd for C_7H_7OFSBr 236.9385, found 236.9389.

*1-Fluoro-4-((fluoromethyl)sulfinyl)benzene (**IIe**).* The product was obtained following general procedure A, using 4-fluorothioanisole (**Ie**) (2.57 mL, 21.1 mmol, 1.00 equiv), Selectfluor (6.880 g, 26.37 mmol, 1.25 equiv), Et_3N (3.68 mL, 26.4 mmol, 1.25 equiv), MeCN (40 mL), NBS (7.510 g, 42.20 mmol, 2.50 equiv), MeOH (37 mL), and H_2O (3 mL). The product **IIe** (3.717 g, 9.715 mmol, 46%) was obtained as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72−7.66 (m, 2H), 7.30−7.24 (m, 2H), 5.09 (dd, J = 48.0, 8.2 Hz, 1H), 5.04 (dd, J = 47.4, 8.2 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 165.2 (C−F, d, $^1J_{C-F}$ = 253.0 Hz), 134.3 (C−F, dd, $^{3,4}J_{C-F}$ = 6.1, 3.1 Hz), 127.3 (C−F, dd, $^{3,4}J_{C-F}$ = 9.2, 0.9 Hz), 117.2 (C−F, d, $^2J_{C-F}$ = 22.7 Hz), 97.8 (C−F, dd, $^{1,6}J_{C-F}$ = 222.3, 1.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −106.59 to −106.68 (m), −212.40 (t, J = 47.7 Hz). HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_7H_7OF_2S$ 177.0186, found 177.0194.

*1-((Fluoromethyl)sulfinyl)-4-methylbenzene (**IIf**).*[19a] The product was obtained following general procedure A, using 4-methylthioanisole (**If**) (2.500 g, 18.09 mmol, 1.00 equiv), Selectfluor (8.009 g, 22.61 mmol, 1.25 equiv), Et_3N (3.15 mL, 22.6 mmol, 1.25 equiv), MeCN (50 mL), NBS (6.438 g, 36.17 mmol, 2.00 equiv), MeOH (60 mL), and H_2O (5 mL). The product **IIf** (1.096 g, 6.364 mmol, 35%) was obtained as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58−7.54 (m, 2H), 7.39−7.35 (m, 2H), 5.07 (dd, J = 48.3, 8.2 Hz, 1H), 5.03 (dd, J = 47.5, 8.2 Hz, 1H), 2.43 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −211.47 (t, J = 48.1 Hz).

*1-((Fluoromethyl)sulfinyl)-3-(trifluoromethyl)benzene (**IIg**).* The product was obtained following general procedure A, using 3-trifluoromethylthioanisole (**Ig**) (0.6900 g, 3.590 mmol, 1.00 equiv), Selectfluor (2.226 g, 6.283 mmol, 1.75 equiv), Et_3N (0.88 mL, 6.3 mmol, 1.75 equiv), MeCN (9.8 mL), NBS (1.917 g, 10.770 mmol, 3.00 equiv), MeOH (9 mL), and H_2O (1 mL). The product **IIg** (0.3662 g, 1.619 mmol, 45%) was obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00−7.95 (m, 1H), 7.91−7.81 (m, 2H), 7.73 (tq, J = 7.7, 0.7 Hz, 1H), 5.16 (dd, J = 47.7, 8.2 Hz, 1H), 5.12 (dd, J = 47.4, 8.2 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 140.7 (C−F, d, $^3J_{C-F}$ = 6.1 Hz), 132.5 (C−F, q, $^2J_{C-F}$ = 33.5 Hz), 130.3, 129.0 (C−F, q, $^3J_{C-F}$ = 3.6 Hz), 128.2 (C−F, p, $^{4,5}J_{C-F}$ = 1.2 Hz), 123.1 (C−F, q, $^1J_{C-F}$ = 272.9 Hz), 121.9 (C−F, qd, $^{3,4}J_{C-F}$ = 3.8, 1.0 Hz) 97.6 (C−F, d, $^1J_{C-F}$ = 223.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −62.86, −213.12 (t, J = 47.3 Hz). HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_8H_7OF_4S$ 227.0154, found 227.0161.

*4-((Fluoromethyl)sulfinyl)-1,2-dimethylbenzene (**IIh**).* The product was obtained following general procedure A, using 3,4-dimethylthioanisole (**Ih**) (1.000 g, 6.568 mmol, 1.00 equiv), Selectfluor (2.908 g, 8.210 mmol, 1.25 equiv), Et_3N (1.14 mL, 8.21 mmol, 1.25 equiv), MeCN (12 mL), NBS (2.338 g, 13.14 mmol, 2.00 equiv), MeOH (10 mL), and H_2O (1 mL). The product **IIh** (0.4600 g, 2.470 mmol, 38%) was obtained as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (s, 1H), 7.38 (dd, J = 7.9, 1.9 Hz, 1H), 7.31 (d, J = 7.9 Hz, 1H), 5.06 (dd, J = 48.4, 8.2 Hz, 1H), 5.03 (dd, J = 47.5, 8.2 Hz, 1H), 2.34 (s, 3H), 2.33 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 141.7, 138.7, 135.6 (C−F, d, $^3J_{C-F}$ = 6.3 Hz), 130.8, 125.6, 122.4, 98.5 (C−F, d, $^1J_{C-F}$ = 220.4 Hz), 20.0, 20.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ −211.15 (t, J = 47.9 Hz). HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_9H_{12}OFS$ 187.0593, found 187.0600.

*1,4-Dichloro-2-((fluoromethyl)sulfinyl)benzene (**IIi**).* The product was obtained following general procedure A, using 2,5-dichlorothioanisole (**Ii**) (3.000 g, 15.54 mmol, 1.00 equiv), Selectfluor (6.880 g, 19.42 mmol, 1.25 equiv), Et_3N (2.71 mL, 19.4 mmol, 1.25 equiv), MeCN (60 mL), NBS (6.913 g, 38.84 mmol, 2.50 equiv), MeOH (56 mL), and H_2O (6 mL). The product **IIi** (2.930 g, 10.53 mmol, 68%) was obtained as a white solid. Mp: 97−100 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (t, J = 2.2 Hz, 1H), 7.47 (ddd, J = 8.5, 2.5, 1.0 Hz, 1H), 7.38 (d, J = 8.5 Hz, 1H), 5.45 (dd, J = 47.5, 8.5 Hz, 1H), 5.14 (dd, J = 48.1, 8.5 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 138.2 (C−F, d, $^3J_{C-F}$ = 8.5 Hz), 135.3, 133.3, 131.3, 128.7, 127.5, 97.1 (C−F, d, $^1J_{C-F}$ = 223.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −214.58 (t, J = 47.7 Hz). HRMS (ESI) m/z: [M + H]$^+$ calcd for $C_7H_6OFSCl_2$ 226.9500, found 226.9501.

General Procedure B for the Synthesis of Diaryl Fluoromethyl Sulfonium Salts 2a−y.[13,19] ((Fluoromethyl)sulfinyl)-benzene (**IIa**) (2.7400 g, 17.321 mmol, 1 equiv) under argon atmosphere was dissolved in anhydrous Et_2O (80 mL), and to the solution was added 1,2,3,4-tetramethylbenzene (2.77 mL, 17.3 mmol, 1 equiv). To the obtained solution was added trifluoromethanesulfonic anhydride (2.84 mL, 17.3 mmol, 1 equiv) dropwise over 10 min at −10 °C. Upon addition, a solid formed and the resulting suspension was stirred until full conversion of the starting material **IIa** (TLC control PE/EtOAc 1:1) (~2 h). The formed solid was filtered and washed with Et_2O (3 × 20 mL). Then the solid was dissolved in DCM (20 mL) and washed with a 1 M $NaBF_4$ (6 × 30 mL) aqueous

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solution. The organic phase was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was triturated with Et_2O (3 × 40 mL) to afford product **2a**[13] (4.689 g, 12.96 mmol, 75%) as a gray solid. Mp: 118−121 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (m, 2H), 7.76−7.69 (m, 1H), 7.66 (m, 2H), 7.43 (s, 1H), 6.55 (dd, *J* = 46.6, 9.6 Hz, 1H), 6.42 (dd, *J* = 45.6, 9.5 Hz, 1H), 2.49 (s, 3H), 2.38 (s, 3H), 2.30 (s, 3H), 2.28 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −151.45, −151.51, −207.18 (t, *J* = 46.4 Hz). Slow Et_2O vapor diffusion into an acetonitrile solution of **2a** gave suitable crystals for a single crystal XRD (CCDC 2032388).

*(Fluoromethyl)(4-methoxyphenyl)(phenyl)sulfonium Tetrafluoroborate (**2b**).* The product was obtained following general procedure B, using ((fluoromethyl)sulfinyl)benzene (**IIa**) (750 mg, 4.74 mmol, 1.00 equiv), methoxybenzene (0.52 mL, 4.7 mmol, 1.00 equiv), trifluoromethanesulfonic anhydride (0.78 mL, 3.2 mmol, 1.00 equiv), and Et_2O (25 mL). After addition of trifluoromethanesulfonic anhydride, a triflate salt formed as an oil. Upon completion of the reaction the formed Et_2O layer was decanted from the product. After anion exchange as described in procedure B the obtained oil was treated with PE, then PE/Et_2O 1:1 and Et_2O. The product **2b** (800 mg, 2.38 mmol, 50%) was obtained as a dark brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90−7.79 (m, 4H), 7.77−7.71 (m, 1H), 7.70−7.64 (m, 2H), 7.21−7.15 (m, 2H), 6.54 (dd, *J* = 46.3, 9.3 Hz, 1H), 6.43 (dd, *J* = 46.1, 9.3 Hz, 1H), 3.90 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −150.72, −150.78, −207.88 (t, *J* = 46.2 Hz). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 165.3, 134.5, 134.4 (C−F, d, $^4J_{C-F}$ = 1.8 Hz), 131.5, 130.7, 122.1 (C−F, d, $^3J_{C-F}$ = 2.1 Hz), 117.3, 109.4 (C−F, d, $^3J_{C-F}$ = 1.7 Hz), 90.5 (C−F, d, $^1J_{C-F}$ = 241.2 Hz), 56.2. HRMS (ESI) *m*/*z*: [M]$^+$ calcd for $C_{14}H_{14}FOS^+$ 249.0744, found: 249.0753.

*(3,4-Dimethylphenyl)(fluoromethyl)(phenyl)sulfonium Tetrafluoroborate (**2c**).*[19a] The product was obtained following the modified general procedure B, using ((fluoromethyl)sulfinyl)benzene (**IIa**) (500.0 mg, 3.161 mmol, 1.00 equiv), 1,2-dimethylbenzene (0.38 mL, 3.2 mmol, 1.00 equiv), trifluoromethanesulfonic anhydride (0.52 mL, 3.2 mmol, 1.00 equiv) and Et_2O (6.7 mL). After addition of trifluoromethanesulfonic anhydride, triflate salt formed as an oil. Upon completion of the reaction the formed Et_2O layer was decanted from the product. The anion exchanged was performed as described in procedure B. The product **2c** (693.0 mg, 2.074 mmol, 66%) was obtained as a dark brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88−7.81 (m, 2H), 7.80−7.71 (m, 1H), 7.71−7.67 (m, 2H), 7.67−7.64 (m, 1H), 7.59 (dd, *J* = 8.1, 2.1 Hz, 1H), 7.44 (d, *J* = 8.2 Hz, 1H), 6.55 (dd, *J* = 46.3, 9.3 Hz, 1H), 6.49 (dd, *J* = 46.2, 9.3 Hz, 1H), 2.36 (s, 6H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −150.70, −150.75, −207.53 (t, *J* = 46.2 Hz).

*(2,5-Dimethylphenyl)(fluoromethyl)(phenyl)sulfonium Tetrafluoroborate (**2d**).*[19a] The product was obtained following the modified general procedure B, using ((fluoromethyl)sulfinyl)benzene (**IIa**) (500.0 mg, 3.161 mmol, 1.00 equiv), 1,4-dimethylbenzene (0.39 mL, 3.2 mmol, 1.00 equiv), trifluoromethanesulfonic anhydride (0.52 mL, 3.2 mmol, 1.00 equiv) and Et_2O (6.5 mL). After addition of trifluoromethanesulfonic anhydride, triflate salt formed as an oil. Upon completion of the reaction the formed Et_2O layer was decanted from the product. After anion exchange as described in procedure B the obtained oil was crystallized by treatment with PE, then PE/Et_2O 1:1 and Et_2O. The product **2d** (550.0 mg, 1.646 mmol, 52%) was obtained as a yellow solid. Mp: 94−96 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84−7.75 (m, 2H), 7.78−7.72 (m, 1H), 7.72−7.64 (m, 2H), 7.63 (s, 1H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.37 (d, *J* = 7.9 Hz, 1H), 6.57 (d, *J* = 46.4 Hz, 2H), 2.52 (s, 3H), 2.46 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −150.99, −151.04, −206.95 (t, *J* = 46.3 Hz). Slow Et_2O vapor diffusion into acetonitrile solution of **2d** gave suitable crystals for a single crystal XRD[CCDC 2032000].

*(Fluoromethyl)(phenyl)(p-tolyl)sulfonium Tetrafluoroborate (**2e**).* The product was obtained following the modified general procedure B, using ((fluoromethyl)sulfinyl)benzene (**IIa**) (500 mg, 3.16 mmol, 1.00 equiv), toulene (0.33 mL, 3.2 mmol, 1.00 equiv), trifluoromethanesulfonic anhydride (0.52 mL, 3.2 mmol, 1.00 equiv) and Et_2O (6.5 mL). After addition of trifluoromethanesulfonic anhydride, triflate salt formed as an oil. Upon completion of the reaction the formed Et_2O layer was decanted from the product. After anion exchange as described in procedure B the obtained oil treated with PE, then PE/Et_2O 1:1 and Et_2O. The product **2e** (340 mg, 1.06 mmol, 34%) was obtained as a dark brown oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87−7.83 (m, 2H), 7.80−7.72 (m, 3H), 7.70−7.64 (m, 2H), 7.51−7.47 (m, 2H), 6.55 (dd, *J* = 46.2, 9.4 Hz, 1H), 6.50 (dd, *J* = 46.1, 9.4 Hz, 1H), 2.47 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 146.9, 134.8, 132.4, 131.8 (C−F, d, $^4J_{C-F}$ = 1.6 Hz), 131.6, 131.3 (C−F, d, $^4J_{C-F}$ = 1.2 Hz), 121.4 (C−F, d, $^3J_{C-F}$ = 1.9 Hz), 117.1 (C−F, d, $^3J_{C-F}$ = 1.5 Hz), 90.4 (C−F, d, $^1J_{C-F}$ = 242.4 Hz), 21.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ −150.47, −150.53, −207.79 (t, *J* = 46.3 Hz). HRMS (ESI) *m*/*z*: [M]$^+$ calcd for $C_{14}H_{14}FS^+$ 233.0795, found 233.0811.

*(2,4-Dimethylphenyl)(fluoromethyl)(phenyl)sulfonium Tetrafluoroborate (**2f**).* The product was obtained following general procedure B, using ((fluoromethyl)sulfinyl)benzene (**IIa**) (0.2420 g, 1.530 mmol, 1.00 equiv), 1,3-dimethylbenzene (0.19 mL, 1.5 mmol, 1.0 equiv), trifluoromethanesulfonic anhydride (0.25 mL, 1.5 mmol, 1.0 equiv) and Et_2O (6 mL). The formed sulfonium triflate was washed with 0.5 M $NaBF_4$ aqueous solution for anion exchange. The product **2f** (0.2928 g, 0.8762 mmol, 57%) was obtained as a beige solid. Mp 93−95 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80−7.75 (m, 2H), 7.75−7.70 (m, 2H), 7.68−7.63 (m, 2H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.30 (s, 1H), 6.53 (dd, *J* = 46.5, 9.4 Hz, 1H), 6.50 (dd, *J* = 45.9, 9.4 Hz, 1H), 2.52 (s, 3H), 2.42 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −151.01 to −151.16 (m), −207.30 (t, *J* = 46.2 Hz). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 146.8, 141.9, 134.7, 134.0, 131.6, 131.1, 130.8 (C−F, d, $^4J_{C-F}$ = 4.5 Hz), 130.3, 120.8 (C−F, d, $^3J_{C-F}$ = 2.6 Hz), 116.3, 89.6 (C−F, d, $^1J_{C-F}$ = 241.9 Hz), 21.6, 19.9. HRMS (ESI) *m*/*z*: [M]$^+$ calcd for $C_{15}H_{16}FS^+$ 247.0957, found 247.0964.

*(Fluoromethyl)(2,3,4,5-tetramethylphenyl)(p-tolyl)sulfonium Tetrafluoroborate (**2g**).*[19a] The product was obtained following general procedure B, using 1-((fluoromethyl)sulfinyl)-4-methylbenzene (**IIf**) (1.096 g, 6.364 mmol, 1.00 equiv), 1,2,3,4-tetramethylbenzene (1.02 mL, 6.36 mmol, 1.00 equiv), trifluoromethanesulfonic anhydride (1.04 mL, 0.874 mmol, 1.00 equiv) and Et_2O (40 mL). The product **2g** (1.870 g, 4.970 mmol, 78%) was obtained as a beige amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69−7.64 (m, 2H), 7.48−7.43 (m, 2H), 7.41 (s, 1H), 6.49 (dd, *J* = 47.1, 9.6 Hz, 1H), 6.43 (dd, *J* = 46.2, 9.6 Hz, 1H), 2.49 (s, 3H), 2.46 (s, 3H), 2.38 (s, 3H), 2.30 (s, 3H), 2.28 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −151.67, −151.73, −207.41 (t, *J* = 46.4 Hz).

*(3,4-Dimethylphenyl)(fluoromethyl)(2,3,4,5-tetramethylphenyl)sulfonium Tetrafluoroborate (**2h**).* The product was obtained following general procedure B, using 4-((fluoromethyl)sulfinyl)-1,2-dimethylbenzene (**IIh**) (0.1560 g, 0.8376 mmol, 1.00 equiv), 1,2,3,4-tetramethylbenzene (0.12 mL, 0.84 mmol, 1.00 equiv), trifluoromethanesulfonic anhydride (0.14 mL, 0.87 mmol, 1.00 equiv) and Et_2O (5 mL). The formed sulfonium triflate was washed with 0.5 M $NaBF_4$ aqueous solution for anion exchange as described in procedure B. After anion exchange the obtained oil was crystallized by treatment with PE, then PE/Et_2O 1:1, and Et_2O. The product **2h** (0.1250 g, 0.3203 mmol, 38%) was obtained as a beige solid. Mp: >110 dec °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 2.2 Hz, 1H), 7.45 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.42−7.37 (m, 2H), 6.46 (dd, *J* = 46.8, 9.4 Hz, 1H), 6.42 (dd, *J* = 46.0, 9.4 Hz, 1H), 2.48 (s, 3H), 2.37 (s, 3H), 2.34 (s, 6H), 2.29 (s, 3H), 2.27 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 144.9, 143.8, 141.1, 139.4, 138.2, 137.2, 132.5, 131.5, 128.5, 128.3 (C−F, d, $^4J_{C-F}$ = 4.2 Hz), 117.4 (C−F, d, $^3J_{C-F}$ = 2.4 Hz), 116.8, 89.6 (C−F, d, $^1J_{C-F}$ = 240.7 Hz), 21.2, 20.2, 20.0, 17.7, 17.0, 16.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ −151.61, −151.66, −207.23 (t, *J* = 46.4 Hz). HRMS (ESI) *m*/*z*: [M]$^+$ calcd for $C_{19}H_{24}FS^+$ 303.1583, found 303.1592.

*(4-Chlorophenyl)(fluoromethyl)(2,3,4,5-tetramethylphenyl)sulfonium Tetrafluoroborate (**2i**).* The product was obtained following general procedure B, using 1-chloro-4-((fluoromethyl)sulfinyl)benzene (**IIb**) (0.5000 g, 2.596 mmol, 1.00 equiv), 1,2,3,4-tetramethylbenzene (0.42 mL, 2.6 mmol, 1.00 equiv), trifluorome-

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thanesulfonic anhydride (0.43 mL, 2.6 mmol, 1.0 equiv), and Et_2O (12 mL). The product **2i** (0.5830 g, 1.470 mmol, 57%) was obtained as a gray solid. Mp: 115−120 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.79−7.70 (m, 2H), 7.65−7.60 (m, 2H), 6.57 (dd, *J* = 46.9, 9.5 Hz, 1H), 6.44 (dd, *J* = 45.9, 9.5 Hz, 1H), 2.48 (s, 3H), 2.38 (s, 3H), 2.30 (s, 3H), 2.28 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −150.98, −151.03, −207.14 (t, *J* = 46.4 Hz). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 144.3, 141.7, 139.7, 138.6, 137.6, 132.5 (C−F, d, $^4J_{C-F}$ = 1.0 Hz), 131.8, 128.4 (C−F, d, $^4J_{C-F}$ = 4.7 Hz), 119.6 (C−F, d, $^3J_{C-F}$ = 2.9 Hz), 116.2, 89.8 (C−F, d, $^1J_{C-F}$ = 242.2 Hz), 21.3, 17.9, 17.1, 17.0. HRMS (ESI) *m*/*z*: $[M]^+$ calcd for $C_{17}H_{19}ClFS^+$ 309.0875, found 309.0886. Slow Et_2O vapor diffusion into acetonitrile solution of **2i** gave suitable crystals for a single crystal XRD (CCDC 2032001).

*(Fluoromethyl)(4-fluorophenyl)(2,3,4,5-tetramethylphenyl)-sulfonium Tetrafluoroborate (**2j**).* The product was obtained following general procedure B, using 1-fluoro-4-((fluoromethyl)-sulfinyl)benzene (**IIe**) (0.3000 g, 1.703 mmol, 1.00 equiv), 1,2,3,4-tetramethylbenzene (0.28 mL, 1.7 mmol, 1.0 equiv), trifluoromethanesulfonic anhydride (0.28 mL, 1.7 mmol, 1.0 equiv), and Et_2O (7.5 mL). The formed sulfonium triflate was washed with 0.5 M $NaBF_4$ aqueous solution for anion exchange as described in procedure B. The product **2j** (0.4995 g, 1.314 mmol, 77%) was obtained as a gray solid. Mp: 80−82 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.89−7.83 (m, 2H), 7.46 (s, 1H), 7.39−7.29 (m, 2H), 6.53 (dd, *J* = 46.6, 9.2 Hz, 1H), 6.48 (dd, *J* = 45.5, 9.2 Hz, 1H), 2.46 (s, 3H), 2.38 (s, 3H), 2.29 (s, 3H), 2.27 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 166.3 (C−F, d, $^1J_{C-F}$ = 259.1 Hz), 144.2, 139.6, 138.6, 137.3, 134.1 (C−F, d, $^3J_{C-F}$ = 9.7 Hz), 128.2 (C−F, d, $^3J_{C-F}$ = 4.2 Hz), 119.1 (C−F, d, $^2J_{C-F}$ = 23.2 Hz), 116.5, 116.4 (C−F, t, $^{3,4}J_{C-F}$ = 3.1 Hz), 89.6 (C−F, d, $^1J_{C-F}$ = 241.2 Hz), 21.2, 17.7, 17.0, 16.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ −101.04 to −101.13 (m), −150.93, −150.99, −207.12 (t, *J* = 46.1 Hz). HRMS (ESI) *m*/*z*: $[M]^+$ calcd for $C_{17}H_{19}F_2S^+$ 293.1176, found 293.1186.

*(3-Bromophenyl)(fluoromethyl)(2,3,4,5-tetramethylphenyl)-sulfonium Tetrafluoroborate (**2k**).* The product was obtained following general procedure B, using 1-bromo-3-((fluoromethyl)-sulfinyl)benzene (**IId**) (0.2000 g, 0.8436 mmol, 1.00 equiv), 1,2,3,4-tetramethylbenzene (0.14 mL, 0.84 mmol, 1.00 equiv), trifluoromethanesulfonic anhydride (0.14 mL, 0.84 mmol, 1.00 equiv) and Et_2O (5 mL). After anion exchange as described in procedure B the obtained oil was crystallized by treatment with PE, then PE/Et_2O 1:1 and Et_2O. The product **2k** (0.2500 g, 0.5668 mmol, 67%) was obtained as a gray solid. Mp: >130 dec °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.88−7.80 (m, 2H), 7.74 (t, *J* = 1.9 Hz, 1H), 7.58 (t, *J* = 8.1 Hz, 1H), 7.42 (s, 1H), 6.57 (dd, *J* = 46.9, 9.5 Hz, 1H), 6.49 (dd, *J* = 45.7, 9.6 Hz, 1H), 2.49 (s, 3H), 2.39 (s, 3H), 2.31 (s, 3H), 2.29 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 144.5, 139.7, 138.6, 137.9, 137.7, 133.0, 132.9, 129.8, 128.5 (C−F, d, $^4J_{C-F}$ = 4.9 Hz), 124.9, 123.3 (C−F, d, $^3J_{C-F}$ = 2.9 Hz), 115.7, 89.9 (C−F, d, $^1J_{C-F}$ = 243.2 Hz), 21.3, 17.9, 17.1, 17.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ −151.00, −151.05, −206.63 (t, *J* = 46.2 Hz). HRMS (ESI) *m*/*z*: $[M]^+$ calcd for $C_{17}H_{19}BrFS^+$ 353.0369, found 353.0386.

*(Fluoromethyl)(2,3,4,5-tetramethylphenyl)(3-(trifluoromethyl)-phenyl)sulfonium Tetrafluoroborate (**2l**).* The product was obtained following general procedure B, using 1-((fluoromethyl)sulfinyl)-3-(trifluoromethyl)benzene (**IIg**) (153.0 mg, 0.6764 mmol, 1.00 equiv), 1,2,3,4-tetramethylbenzene (0.11 mL, 0.68 mmol, 1.0 equiv), trifluoromethanesulfonic anhydride (0.11 mL, 0.68 mmol, 1.0 equiv), and Et_2O (4 mL). After addition of trifluoromethanesulfonic anhydride, triflate salt formed as an oil. Upon completion of the reaction the formed Et_2O layer was decanted from the product. After anion exchange as described in procedure B the obtained oil was crystallized by treatment with PE, then PE/Et_2O 1:1 and Et_2O. The product **2l** (136.0 mg, 0.3161 mmol, 47%) was obtained as a beige solid. Mp: 96−99 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, *J* = 8.2 Hz, 1H), 7.96 (d, *J* = 7.9 Hz, 1H), 7.91−7.85 (m, 2H), 7.43 (s, 1H), 6.63 (dd, *J* = 46.8, 9.4 Hz, 1H), 6.55 (dd, *J* = 45.5, 9.4 Hz, 1H), 2.50 (s, 3H), 2.38 (s, 3H), 2.31 (s, 3H), 2.29 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 144.7, 139.8, 138.8, 138.0, 134.6, 133.6 (C−F, q, $^2J_{C-F}$ = 34.1 Hz), 132.5, 131.1 (C−F, q, $^3J_{C-F}$ = 3.3 Hz), 128.5 (C−F, d, $^4J_{C-F}$ = 4.6 Hz), 127.5 (C−F, d, $^3J_{C-F}$ = 3.8 Hz), 123.3 (C−F, d, $^3J_{C-F}$ = 3.0 Hz), 122.7 (C−F, q, $^1J_{C-F}$ = 273.9 Hz), 115.5, 89.9 (C−F, d, $^1J_{C-F}$ = 242.9 Hz), 21.2, 17.9, 17.1, 17.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ −62.93, −150.71, −150.76, −206.76 (t, *J* = 46.2 Hz). HRMS (ESI) *m*/*z*: $[M]^+$ calcd for $C_{18}H_{19}F_4S^+$ 343.1144, found: 343.1143.

*(4-Chlorophenyl)(2,5-dimethylphenyl)(fluoromethyl)sulfonium Tetrafluoroborate (**2m**).* The product was obtained following general procedure B, using 1-chloro-4-((fluoromethyl)sulfinyl)benzene (**IIb**) (0.3000 g, 1.557 mmol, 1.00 equiv), 1,4-dimethylbenzene (0.19 mL, 1.6 mmol, 1.0 equiv), trifluoromethanesulfonic anhydride (0.26 mL, 1.6 mmol, 1.00 equiv), and Et_2O (7.2 mL). After addition of trifluoromethanesulfonic anhydride, triflate salt formed as an oil. Upon completion of the reaction the formed Et_2O layer was decanted from the product. The anion exchange performed as described in procedure B. The product **2m** (0.1320 g, 0.3581 mmol, 23%) was obtained as a brown solid. Mp: 82−84 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.82−7.74 (m, 2H), 7.66−7.59 (m, 3H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 7.9 Hz, 1H), 6.68−6.49 (m, 2H), 2.49 (s, 3H), 2.45 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 142.0, 140.2, 138.9, 136.3, 133.1, 132.8, 131.9, 130.5 (C−F, d, $^4J_{C-F}$ = 4.4 Hz), 119.6, 118.8 (C−F, d, $^3J_{C-F}$ = 2.8 Hz), 89.5 (C−F, d, $^1J_{C-F}$ = 242.2 Hz), 21.2, 19.5. ^{19}F NMR (376 MHz, $CDCl_3$): δ −150.47, −150.52, −206.88 (t, *J* = 45.8 Hz). HRMS (ESI) *m*/*z*: $[M]^+$ calcd for $C_{15}H_{15}ClFS^+$ 281.0562, found 281.0580.

*(4-Chlorophenyl)(fluoromethyl)(p-tolyl)sulfonium Tetrafluoroborate (**2n**).* The product was obtained following general procedure B, using 1-chloro-4-((fluoromethyl)sulfinyl)benzene (**IIb**) (0.4000 g, 2.076 mmol, 1.00 equiv), toluene (0.22 g, 2.1 mmol, 1.00 equiv), trifluoromethanesulfonic anhydride (0.34 mL, 2.1 mmol, 1.00 equiv), and Et_2O (4.3 mL). After addition of trifluoromethanesulfonic anhydride, triflate salt formed as an oil. Upon completion of the reaction the formed Et_2O layer was decanted from the product. After anion exchange as described in procedure B the obtained oil was treated with PE, then PE/Et_2O 1:1 and Et_2O. The product **2n** (0.1300 g, 0.3666 mmol, 18%) was obtained as a brown oil. ^1H NMR (400 MHz, $CDCl_3$): δ 7.84−7.80 (m, 2H), 7.79−7.74 (m, 2H), 7.65−7.60 (m, 2H), 7.51−7.46 (m, 2H), 6.57 (dd, *J* = 46.1, 9.5 Hz, 1H), 6.45 (dd, *J* = 46.0, 9.3 Hz, 1H), 2.46 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 147.0, 141.9, 132.7 (C−F, d, $^4J_{C-F}$ = 1.5 Hz), 132.5, 131.8, 131.7 (d, *J* = 2.0 Hz), 119.8 (C−F, d, $^4J_{C-F}$ = 2.2 Hz), 117.0 (C−F, d, $^3J_{C-F}$ = 1.5 Hz), 90.3 (C−F, d, $^1J_{C-F}$ = 242.5 Hz), 21.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ −149.92, −149.97, −207.97 (t, *J* = 46.1 Hz). HRMS (ESI) *m*/*z*: $[M]^+$ calcd for $C_{14}H_{13}ClFS^+$ 267.0405, found 267.0422.

*(3-Bromophenyl)(2,5-dimethylphenyl)(fluoromethyl)sulfonium Tetrafluoroborate (**2o**).* The product was obtained following general procedure B, using 1-bromo-3-((fluoromethyl)sulfinyl)benzene (**IId**) (190 mg, 0.801 mmol, 1.00 equiv), 1,4-dimethylbenzene (0.10 mL, 0.80 mmol, 1.0 equiv), trifluoromethanesulfonic anhydride (0.13 mL, 0.80 mmol, 1.00 equiv), and Et_2O (5 mL). After addition of trifluoromethanesulfonic anhydride, triflate salt formed as an oil. Upon completion of the reaction the formed Et_2O layer was decanted from the product. The formed sulfonium triflate was washed with 0.5 M $NaBF_4$ aqueous solution for anion exchange as described in procedure B. After anion exchange the obtained oil was crystallized by treatment with PE, then PE/Et_2O 1:1 and Et_2O. The product **2o** (95.0 mg, 0.230 mmol, 29%) was obtained as a brown solid. Mp: 85−90 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.89−7.85 (m, 2H), 7.76 (t, *J* = 1.9 Hz, 1H), 7.62 (s, 1H), 7.59 (t, *J* = 8.1 Hz, 1H), 7.51 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.39 (d, *J* = 7.9 Hz, 1H), 6.62 (dd, *J* = 45.8, 9.6 Hz, 1H), 6.59 (dd, *J* = 46.7, 9.6 Hz, 1H), 2.52 (s, 3H), 2.47 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 140.3, 139.2, 138.0, 136.6, 133.3, 133.3, 132.9, 130.7 (C−F, d, $^4J_{C-F}$ = 4.8 Hz), 130.1, 125.0, 122.5 (C−F, d, $^3J_{C-F}$ = 2.9 Hz), 119.2, 89.8 (C−F, d, $^1J_{C-F}$ = 243.5 Hz), 21.3, 19.7. ^{19}F NMR (376 MHz, $CDCl_3$): δ −150.50, −150.55, −206.40 (t, *J* = 46.3 Hz). HRMS (ESI) *m*/*z*: $[M]^+$ calcd for $C_{15}H_{15}BrFS+$ 325.0056, found 325.0074.

*(2,5-Dimethylphenyl)(fluoromethyl)(4-fluorophenyl)sulfonium Tetrafluoroborate (**2p**).* The product was obtained following general

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procedure B, using 1-fluoro-4-((fluoromethyl)sulfinyl)benzene (**IIe**) (0.4000 g, 2.270 mmol, 1.00 equiv), 1,4-dimethylbenzene (0.28 mL, 2.3 mmol, 1.0 equiv), trifluoromethanesulfonic anhydride (0.37 mL, 2.3 mmol, 1.00 equiv), and Et_2O (10 mL). After addition of trifluoromethanesulfonic anhydride, triflate salt formed as an oil. Upon completion of the reaction the formed Et_2O layer was decanted from the product. The formed sulfonium triflate was washed with 0.5 M $NaBF_4$ aqueous solution for anion exchange as described in procedure B. The product **2p** (0.1850 g, 0.5254 mmol, 23%) was obtained as a gray solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93−7.83 (m, 2H), 7.66 (s, 1H), 7.47 (d, J = 7.9 Hz, 1H), 7.41−7.31 (m, 3H), 6.57 (dd, J = 45.5, 9.3 Hz, 1H), 6.54 (dd, J = 46.4, 9.3 Hz, 1H), 2.48 (s, 3H), 2.45 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 166.5 (C−F, d, $^1J_{C-F}$ = 259.8 Hz), 140.2, 138.6, 136.2, 134.5 (C−F, d, $^3J_{C-F}$ = 9.9 Hz), 133.1, 130.3 (C−F, d, $^4J_{C-F}$ = 4.2 Hz), 119.9, 119.3 (C−F, d, $^2J_{C-F}$ = 23.3 Hz), 115.5 (C−F, t, $^{3,4}J_{C-F}$ = 3.1 Hz), 89.4 (C−F, d, $^1J_{C-F}$ = 241.5 Hz), 21.2, 19.5. ^{19}F NMR (376 MHz, $CDCl_3$): δ −100.42 to −100.55 (m), −150.50, −150.56, −207.02 (t, J = 45.8 Hz). HRMS (ESI) m/z: $[M]^+$ calcd for $C_{15}H_{15}F_2S^+$ 265.0863, found 265.0871. Slow Et_2O vapor diffusion in **2p** acetonitrile solution gave suitable crystals for a single crystal XRD (CCDC 2032003).

*(2,4-Dimethylphenyl)(fluoromethyl)(4-fluorophenyl)sulfonium Tetrafluoroborate (**2q**).* The product was obtained following general procedure B, using 1-fluoro-4-((fluoromethyl)sulfinyl)benzene (**IIe**) (0.4000 g, 2.270 mmol, 1.00 equiv), 1,3-dimethylbenzene (0.28 mL, 2.3 mmol, 1.00 equiv), trifluoromethanesulfonic anhydride (0.37 mL, 2.3 mmol, 1.00 equiv), and Et_2O (10 mL). After addition of trifluoromethanesulfonic anhydride, triflate salt formed as an oil. Upon completion of the reaction the formed Et_2O layer was decanted from the product. The formed sulfonium triflate was washed with 0.5 M $NaBF_4$ aqueous solution for anion exchange as described in procedure B. The product **2q** (0.4640 g, 1.318 mmol, 58%) was obtained as a gray solid. Mp: 53−55 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (m, 2H), 7.77 (d, J = 8.3 Hz, 1H), 7.40−7.32 (m, 3H), 7.29 (s, 1H), 6.52 (d, J = 46.0 Hz, 2H), 2.51 (s, 3H), 2.42 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 166.4 (C−F, d, $^1J_{C-F}$ = 259.6 Hz), 146.9, 141.7, 134.3 (C−F, d, $^3J_{C-F}$ = 9.9 Hz), 134.0, 130.5 (C−F, d, $^4J_{C-F}$ = 4.4 Hz), 130.4, 119.2 (C−F, d, $^2J_{C-F}$ = 23.3 Hz), 116.6, 115.9 (C−F, d, $^{3,4}J_{C-F}$ = 3.2 Hz), 89.7 (C−F, d, $^1J_{C-F}$ = 241.6 Hz), 21.6, 19.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ −100.71 to −100.79 (m), −150.68, −150.73, −207.33 (t, J = 45.9 Hz). HRMS (ESI) m/z: $[M]^+$ calcd for $C_{15}H_{15}F_2S^+$ 265.0863, found 265.0870.

*(2,5-Dimethylphenyl)(fluoromethyl)(3-(trifluoromethyl)phenyl)-sulfonium Tetrafluoroborate (**2r**).* The product was obtained following general procedure B, using 1-((fluoromethyl)sulfinyl)-3-(trifluoromethyl)benzene (**IIg**) (0.1800 g, 0.7958 mmol, 1.00 equiv), 1,4-dimethylbenzene (0.11 mL, 0.68 mmol, 1.0 equiv), trifluoromethanesulfonic anhydride (0.10 mL, 0.80 mmol, 1.0 equiv), and Et_2O (5 mL). After addition of trifluoromethanesulfonic anhydride, triflate salt formed as an oil. Upon completion of the reaction the formed Et_2O layer was decanted from the product. After anion exchange as described in procedure B the obtained oil was treated with PE, then PE/Et_2O 1:1 and Et_2O. The product **2r** (65.0 mg, 0.161 mmol, 20%) was obtained as a brown amorphous solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, J = 8.1 Hz, 1H), 8.05−7.96 (m, 1H), 7.92−7.84 (m, 2H), 7.63 (s, 1H), 7.53 (d, J = 7.9 Hz, 1H), 7.41 (d, J = 7.9 Hz, 1H), 6.67 (dd, J = 46.7, 9.7 Hz, 1H), 6.64 (dd, J = 45.9, 9.7 Hz, 1H), 2.54 (s, 3H), 2.48 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 140.4, 139.4, 136.8, 135.0, 133.0 (C−F, q, $^2J_{C-F}$ = 34.3 Hz), 133.4, 132.5, 131.5 (C−F, q, $^3J_{C-F}$ = 3.2 Hz), 130.7 (C−F, d, $^4J_{C-F}$ = 5.0 Hz), 127.8 (C−F, d, $^3J_{C-F}$ = 3.7 Hz), 122.6 (C−F, q, $^1J_{C-F}$ = 273.7 Hz), 122.5 (C−F, d, $^3J_{C-F}$ = 2.9 Hz), 119.0, 90.0 (C−F, d, $^1J_{C-F}$ = 243.8 Hz), 21.3, 19.7. ^{19}F NMR (376 MHz, $CDCl_3$): δ −62.99, −150.09, −150.15, −206.44 (t, J = 46.4 Hz). HRMS (ESI) m/z: $[M]^+$ calcd for $C_{16}H_{15}SF_4^+$ 315.0831, found 315.0835.

*(2,5-Dichlorophenyl)(fluoromethyl)(2,3,4,5-tetramethylphenyl)-sulfonium Tetrafluoroborate (**2s**).* The product was obtained following general procedure B, using 1,4-dichloro-2-((fluoromethyl)-sulfinyl)benzene (**IIi**) (0.3000 g, 1.321 mmol, 1.00 equiv), 1,2,3,4-tetramethylbenzene (0.21 mL, 1.3 mmol, 1.00 equiv), trifluoromethanesulfonic anhydride (0.22 mL, 1.3 mmol, 1.00 equiv), and Et_2O (24 mL). The formed sulfonium triflate was washed with 0.5 M $NaBF_4$ aqueous solution for anion exchange as described in procedure B. The product **2s** (0.2109 g, 0.4892 mmol, 37%) was obtained as a beige solid. Product decomposition is observed in deuterated chloroform and deuterated acetonitrile solvent system. Mp: 178−182 °C. ^{1}H NMR (400 MHz, $CDCl_3$+ 10% MeCN - d_3): δ 7.64 (dd, J = 8.6, 2.2 Hz, 1H), 7.58 (s, 1H), 7.57−7.53 (m, 1H), 7.06 (s, 1H), 6.49 (dd, J = 45.9, 9.3 Hz, 1H), 6.32 (dd, J = 45.1, 9.3 Hz, 1H), 2.46 (s, 3H), 2.22 (s, 3H), 2.21 (s, 3H), 2.20 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$+ 10% MeCN - d_3): δ 144.6, 139.4, 138.4, 137.5, 135.9, 135.4, 133.5, 132.8, 130.9 (C−F, d, $^4J_{C-F}$ = 3.1 Hz), 128.4 (C−F, d, $^4J_{C-F}$ = 3.0 Hz), 122.1 (C−F, d, $^3J_{C-F}$ = 2.0 Hz), 113.9, 88.0 (C−F, d, $^1J_{C-F}$ = 243.2 Hz), 20.5, 17.3, 16.6, 16.5. ^{19}F NMR (376 MHz, $CDCl_3$+ 10% MeCN-d_3): δ −146.76, −146.82, −200.62 (t, J = 45.7 Hz). HRMS (ESI) m/z: $[M]^+$ calcd for $C_{17}H_{18}FSCl_2^+$ 343.0490, found 343.0496. Slow Et_2O vapor diffusion into acetonitrile solution of **2s** gave suitable crystals for a single crystal XRD (CCDC 2031999).

*(2,5-Dichlorophenyl)(2,5-dimethylphenyl)(fluoromethyl)-sulfonium Tetrafluoroborate (**2t**).* The product was obtained following general procedure B, using 1,4-dichloro-2-((fluoromethyl)-sulfinyl)benzene (**IIi**) (0.5000 g, 2.202 mmol, 1.00 equiv), 1,4-dimethylbenzene (0.27 mL, 2.2 mmol, 1.00 equiv), trifluoromethanesulfonic anhydride (0.36 mL, 2.2 mmol, 1.00 equiv), and Et_2O (40 mL). The formed sulfonium triflate was washed with 0.5 M $NaBF_4$ aqueous solution for anion exchange as described in procedure B. The product **2t** (0.2533 g, 0.6285 mmol, 29%) was obtained as a brown solid. Product decomposition was observed in chloroform-*d*. Mp: >95 °C dec. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (dd, J = 8.6, 2.2 Hz, 1H), 7.65 (d, J = 8.6 Hz, 1H), 7.56 (d, J = 2.2 Hz, 1H), 7.52 (d, J = 7.3 Hz, 1H), 7.43 (d, J = 7.9 Hz, 1H), 7.35 (s, 1H), 6.74 (dd, J = 46.9, 9.8 Hz, 1H), 6.61 (dd, J = 45.9, 9.8 Hz, 1H), 2.65 (s, 3H), 2.44 (s, 3H). ^{13}C{^{1}H} NMR spectra was not obtained due to the product instability. ^{19}F NMR (376 MHz, $CDCl_3$): δ −151.34, −204.96 (t, J = 46.3 Hz). HRMS (ESI) m/z: $[M]^+$ calcd for $C_{15}H_{14}FSCl_2$ + 315.0177, found 315.0190.

*(2,5-Dichlorophenyl)(2,4-dimethylphenyl)(fluoromethyl)-sulfonium Tetrafluoroborate (**2u**).* The product was obtained following general procedure B, using 1,4-dichloro-2-((fluoromethyl)-sulfinyl)benzene (**IIi**) (0.5000 g, 2.202 mmol, 1.00 equiv), 1,3-dimethylbenzene (0.27 mL, 2.2 mmol, 1.0 equiv), trifluoromethanesulfonic anhydride (0.36 mL, 2.2 mmol, 1.0 equiv), and Et_2O (40 mL). The formed sulfonium triflate was washed with 0.5 M $NaBF_4$ aqueous solution for anion exchange as described in procedure B. The product **2u** (0.3277 g, 0.8131 mmol, 37%) was obtained as a gray solid. Product decomposition is observed in chloroform-*d*. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (dd, J = 8.6, 2.2 Hz, 1H), 7.64 (d, J = 8.6 Hz, 1H), 7.60 (d, J = 2.2 Hz, 1H), 7.47 (d, J = 7.8 Hz, 1H), 7.38−7.30 (m, 2H), 6.70 (dd, J = 46.6, 9.6 Hz, 1H), 6.56 (dd, J = 45.9, 9.7 Hz, 1H), 2.65 (s, 3H), 2.44 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 147.5, 142.7, 136.1, 136.0, 134.2, 134.0, 133.2, 131.4 (C−F, d, $^4J_{C-F}$ = 3.5 Hz), 131.3 (C−F, d, $^4J_{C-F}$ = 3.3 Hz), 130.6, 122.4 (C−F, d, $^3J_{C-F}$ = 2.0 Hz), 114.8, 88.8 (C−F, d, $^1J_{C-F}$ = 243.8 Hz), 21.8, 19.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ −151.31, −205.63 (t, J = 46.2 Hz). HRMS (ESI) m/z: $[M]^+$ calcd for $C_{15}H_{14}FSCl_2^+$ 315.0177, found 315.0189.

*(2,3-Dichlorophenyl)(fluoromethyl)(2,3,4,5-tetramethylphenyl)-sulfonium Tetrafluoroborate (**2w**).* The product was obtained following general procedure B, using 1,2-dichloro-3-((fluoromethyl)-sulfinyl)benzene (**IIc**) (0.2000 g, 0.8807 mmol, 1.00 equiv), 1,2,3,4-tetramethylbenzene (0.14 mL, 0.88 mmol, 1.00 equiv), trifluoromethanesulfonic anhydride (0.14 mL, 0.88 mmol, 1.00 equiv), and Et_2O (5 mL). The product **2w** (0.2560 g, 0.5938 mmol, 67%) was obtained as a brown solid. Mp: 114−117 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86−7.82 (m, 2H), 7.67 (t, J = 8.1 Hz, 1H), 7.14 (s, 1H), 6.67 (dd, J = 45.9, 9.2 Hz, 1H), 6.55 (dd, J = 45.7, 9.2 Hz, 1H), 2.63 (s, 3H), 2.31 (s, 3H), 2.30 (s, 3H), 2.28 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 144.7, 139.6, 138.8, 138.2, 136.3, 136.2, 133.6, 130.6, 130.5 (C−F, d, $^4J_{C-F}$ = 3.1 Hz), 128.9 (C−F, d, $^4J_{C-F}$ = 2.7 Hz), 123.5 (C−F, d, $^3J_{C-F}$ = 1.2 Hz), 115.0, 88.8 (C−F, d, $^1J_{C-F}$ = 241.8

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Hz), 21.1, 17.8, 17.1, 17.1. ^{19}F NMR (376 MHz, $CDCl_3$): δ −151.41, −151.46, −205.56 (t, J = 45.8 Hz). HRMS (ESI) m/z: $[M]^+$ calcd for $C_{17}H_{18}SCl_2F$+ 343.0490, found 343.0500. Slow Et_2O vapor diffusion in **2w** acetonitrile solution gave suitable crystals for a single crystal XRD (CCDC 2032002).

*(2,3-Dichlorophenyl)(2,5-dimethylphenyl)(fluoromethyl)-sulfonium Tetrafluoroborate (**2x**).* The product was obtained following general procedure B, using 1,2-dichloro-3-((fluoromethyl)-sulfinyl)benzene (**IIc**) (0.3000 g, 1.321 mmol, 1.00 equiv), 1,4-dimethylbenzene (0.16 mL, 1.3 mmol, 1.00 equiv), trifluoromethanesulfonic anhydride (0.22 mL, 1.3 mmol, 1.00 equiv), and Et_2O (10 mL). The formed sulfonium triflate was washed with 0.5 M $NaBF_4$ aqueous solution for anion exchange as described in procedure B. The product **2x** (0.3140 g, 0.7791 mmol, 59%) was obtained as a white solid. Product decomposition is observed in chloroform-*d*. Mp: 84−88 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90−7.81 (m, 2H), 7.73−7.63 (m, 1H), 7.47 (dd, J = 7.9, 1.7 Hz, 1H), 7.40 (d, J = 8.0 Hz, 1H), 7.30 (s, 1H), 6.71 (dd, J = 45.6, 9.2 Hz, 1H), 6.57 (dd, J = 45.5, 9.2 Hz, 1H), 2.67 (s, 3H), 2.37 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 140.4, 139.7, 136.7, 136.5, 136.4, 133.7, 133.0, 131.2 (C−F, d, $^4J_{C-F}$ = 2.6 Hz), 130.8, 130.6 (C−F, d, $^4J_{C-F}$ = 3.1 Hz), 122.8, 118.3, 88.6 (C−F, d, $^1J_{C-F}$ = 242.7 Hz), 21.1, 19.5. ^{19}F NMR (376 MHz, $CDCl_3$): δ −150.88, −205.72 (t, J = 45.4 Hz). HRMS (ESI) m/z: $[M]^+$ calcd for $C_{15}H_{14}FSCl_2^+$ 315.0177, found 315.0188.

*(2,3-Dichlorophenyl)(2,4-dimethylphenyl)(fluoromethyl)-sulfonium Tetrafluoroborate (**2y**).* The product was obtained following general procedure B, using 1,2-dichloro-3-((fluoromethyl)-sulfinyl)benzene (**IIc**) (0.3000 g, 1.321 mmol, 1.00 equiv), 1,3-dimethylbenzene (0.16 mL, 1.3 mmol, 1.00 equiv), trifluoromethanesulfonic anhydride (0.22 mL, 1.3 mmol, 1.00 equiv), and Et_2O (10 mL). The formed sulfonium triflate was washed with 0.5 M $NaBF_4$ aqueous solution for anion exchange as described in procedure B. The product **2y** (0.3630 g, 0.9006 mmol, 68%) was obtained as a white solid. Product decomposition is observed in deuterated chloroform. Mp: 111−112 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88−7.78 (m, 2H), 7.66 (t, J = 8.2 Hz, 1H), 7.44−7.37 (m, 1H), 7.34−7.32 (m, 1H), 7.30 (dd, J = 8.3, 2.0 Hz, 1H), 6.70 (dd, J = 45.8, 9.3 Hz, 1H), 6.53 (dd, J = 45.6, 9.3 Hz, 1H), 2.68 (s, 3H), 2.41 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −151.05, −206.04 (t, J = 45.8 Hz). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 147.4, 142.6, 136.4, 136.3, 133.9, 133.6, 131.5 (C−F, d, $^4J_{C-F}$ = 2.7 Hz), 130.6, 130.6, 130.5 (C−F, d, $^4J_{C-F}$ = 3.3 Hz), 123.1 (C−F, d, $^3J_{C-F}$ = 1.4 Hz), 115.0, 88.7 (C−F, d, $^1J_{C-F}$ = 242.8 Hz), 21.7, 19.9. HRMS (ESI) m/z: $[M]^+$ calcd for $C_{15}H_{14}FSCl_2^+$ 315.0177, found 315.0184.

*(Fluoromethyl)(methyl)(phenyl)sulfonium Tetrafluoroborate (**2z**).* (Fluoromethyl)(phenyl)(2,3,4,5-tetramethylphenyl)sulfonium tetrafluoroborate (**2b**) (200.0 mg, 0.5522 mmol) was added to thioanisole (2 mL) under argon atmosphere. The resulting suspension was stirred for 3 days at room temperature. To the reaction mixture petroleum ether (2 mL) was added, and the obtained suspension was carefully decanted from precipitate; addition of petroleum ether and decantation were repeated two more times. Precipitate was then washed with Et_2O (3 mL x 5). The product **2z** (118.6 mg, 0.4860 mmol, 88%) was obtained as a brown solid. Mp: 88−91 °C. ^{1}H NMR (300 MHz, MeCN- d_3): δ 7.92 (d, J = 7.6 Hz, 2H), 7.89−7.80 (m, 1H), 7.80−7.69 (m, 2H), 6.04 (dd, J = 46.0, 8.8 Hz, 1H), 5.97 (dd, J = 45.3, 8.4 Hz, 1H), 3.29 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$+ MeCN-d_3): δ 135.5, 131.4, 131.3, 120.2, 89.4 (C−F, d, $^1J_{C-F}$ = 238.9 Hz), 21.1 (C−F, d, $^3J_{C-F}$ = 5.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$ + MeCN-d_3): δ −145.87, −145.92, −209.15 (t, J = 46.1 Hz). HRMS: $[M]^+$ calcd for $C_8H_{10}FS^+$ 157.0487, found 157.0493.

Synthesis of α,β-Unsaturated Nitroalkenes 1a−o. The compounds **1a−l**,[25] **1m**,[26] **1n**,[27] and **1o**[28] were prepared following the literature procedures.

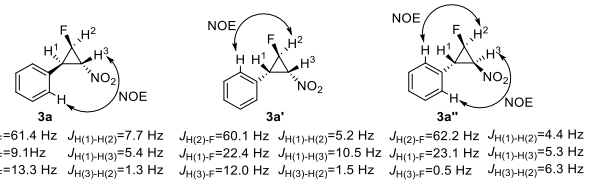
General Procedure for the Reagent 2 Performance Assessment in Fluorocyclopropanation of Nitrostyrene 1a. A mixture of nitrostyrene **1a** (0.067 mmol) and sulfonium salt **2** (0.1341 mmol) in anhydrous THF (2.7 mL) under Ar atmosphere was cooled to 0 °C. To the mixture was added NaH (0.2013 mmol). The reaction mixture was stirred at the same temperature until full conversion (determined by TLC using eluent PE/EtOAc) or for 6 h if full conversion was not achieved. To the reaction mixture was added Et_2O (5 mL), and the resulting suspension was filtered and the solid on the filter was washed with Et_2O (3 × 2 mL). The filtrate was evaporated under reduced pressure. To the residue were added $CDCl_3$ (0.6 mL) and an internal standard EtOAc (1 equiv). For the ^{1}H or ^{19}F NMR analysis the solution was transferred to an NMR tube.

General Procedure C for the Synthesis of Monofluorinated Nitrocyclopropanes 3a−m. (*E*)-(2-Nitrovinyl)benzene (**1a**) (30.0 mg, 0.201 mmol, 1 equiv) was dissolved in anhydrous THF (8 mL), and the formed solution was cooled to 0 °C. Then (2,3-dichlorophenyl)(2,4-dimethylphenyl)(fluoromethyl)sulfonium tetrafluoroborate (**2y**) (162.1 mg, 0.4023 mmol, 2 equiv) was added to the solution followed by immediate addition of NaH (60% dispersion in mineral oil, 24.1 mg, 0.604 mmol, 3 equiv). The reaction mixture was stirred at 0 °C until full conversion of nitroalkene **1a** (TLC control, PE/EtOAc 10:1) (~60 min). Et_2O (12 mL) was added to the reaction mixture, and after stirring for 10 min the resulting suspension was filtered. The filtrate was evaporated under reduced pressure to give a crude product **3a** (76%, dr = 60:17:22, determined by ^{1}H NMR, using EtOAc as an internal standard). The crude product was purified by silica gel column chromatography (eluent gradient PE/EtOAc 100:0 to PE/EtOAc 10:1). The product **3a** (26.2 mg, 0.145 mmol, 72%, dr = 62:17:21) was obtained as a yellow oil. The diastereomers can be separated using preparative TLC (PE/Et_2O 7:1). Three separate diastereomers were obtained.

((1R,2R*,3R*)-2-Fluoro-3-nitrocyclopropyl)benzene (**3a**).* First fraction (14.2 mg, 0.0784 mmol, 39%) a slightly yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42−7.35 (m, 3H), 7.31−7.27 (m, 2H), 5.47 (ddd, J = 61.4, 7.7, 1.3 Hz, 1H), 4.87 (ddd, J = 13.3, 5.4, 1.3 Hz, 1H), 3.47 (ddd, J = 9.1, 7.7, 5.4 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 129.9 (C−F, d, $^3J_{C-F}$ = 2.6 Hz), 129.0, 128.8 (C−F, d, $^4J_{C-F}$ = 1.1 Hz), 128.5, 75.8 (C−F, d, $^1J_{C-F}$ = 242.2 Hz), 63.5 (C−F, d, $^2J_{C-F}$ = 13.3 Hz), 35.3 (C−F, d, $^2J_{C-F}$ = 9.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −216.48 (ddd, J = 61.3, 13.3, 9.1 Hz). Anal. Calcd for $C_9H_8FNO_2$: C, 59.67; H, 4.45; N, 7.73. Found: C, 59.59; H, 4.45; N 7.73.

((1S,2R*,3R*)-2-Fluoro-3-nitrocyclopropyl)benzene (**3a′**).* Second fraction (3.2 mg, 0.018 mmol, 9%) a slightly yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39−7.32 (m, 3H), 7.29−7.26 (m, 2H), 5.73 (ddd, J = 60.0, 5.2, 1.5 Hz, 1H), 4.97 (ddd, J = 12.0, 10.4, 1.5 Hz, 1H), 3.48 (ddd, J = 22.3, 10.5, 5.3 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 129.1, 129.0 (C−F, d, $^4J_{C-F}$ = 1.2 Hz), 128.9, 128.9 (C−F, d, $^3J_{C-F}$ = 2.4 Hz), 75.0 (C−F, d, $^1J_{C-F}$ = 238.7 Hz), 63.8 (C−F, d, $^2J_{C-F}$ = 13.5 Hz), 36.7 (C−F, d, $^2J_{C-F}$ = 10.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −206.65 (ddd, J = 60.1, 22.4, 12.0 Hz).

((1S,2R*,3S*)-2-Fluoro-3-nitrocyclopropyl)benzene (**3a′′**).* Third fraction (4.3 mg, 0.024 mmol, 12%) a slightly yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39−7.32 (m, 3H), 7.16−7.12 (m, 2H), 4.95 (ddd, J = 61.8, 6.3, 4.4 Hz, 1H), 4.58 (ddd, J = 6.2, 5.3, 0.5 Hz, 1H), 3.95 (dt, J = 23.1, 4.8 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 132.5 (C−F, d, $^3J_{C-F}$ = 1.2 Hz), 129.3, 128.5, 127.3, 74.8 (C−F, d, $^1J_{C-F}$ = 247.3 Hz), 63.8 (C−F, d, $^2J_{C-F}$ = 10.5 Hz), 32.2 (C−F, d, $^2J_{C-F}$ = 10.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −215.54 (dd, J = 62.2, 23.1 Hz).



3a	3a'	3a''
$J_{H(2)-F}$=61.4 Hz	$J_{H(2)-F}$=60.1 Hz	$J_{H(2)-F}$=62.2 Hz
$J_{H(1)-H(2)}$=7.7 Hz	$J_{H(1)-H(2)}$=5.2 Hz	$J_{H(1)-H(2)}$=4.4 Hz
$J_{H(1)-F}$=9.1Hz	$J_{H(1)-F}$=22.4 Hz	$J_{H(1)-F}$=23.1 Hz
$J_{H(1)-H(3)}$=5.4 Hz	$J_{H(1)-H(3)}$=10.5 Hz	$J_{H(1)-H(3)}$=5.3 Hz
$J_{H(3)-F}$=13.3 Hz	$J_{H(3)-F}$=12.0 Hz	$J_{H(3)-F}$=0.5 Hz
$J_{H(3)-H(2)}$=1.3 Hz	$J_{H(3)-H(2)}$=1.5 Hz	$J_{H(3)-H(2)}$=6.3 Hz

Upscale Reaction for the Synthesis of 2-Fluoro-3-nitrocyclopropyl)benzene (3a). The reaction was performed following general procedure C on a 1 mmol scale of (*E*)-(2-nitrovinyl)benzene **1a**. Crude **3a** (72%, *d.r.* = 60:21:19, determined by ^{1}H NMR, using EtOAc as an internal standard). Isolated yield of **3a** (75%, 0.7524 mmol, dr = 68:21:11).

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*1-(2-Fluoro-3-nitrocyclopropyl)-4-methylbenzene (**3b**).* The product was obtained following general procedure C, using (*E*)-1-methyl-4-(2-nitrovinyl)benzene (**1b**) (32.8 mg, 0.201 mmol, 1 equiv), (2,3-dichlorophenyl)(2,4-dimethylphenyl)(fluoromethyl)sulfonium tetrafluoroborate (**2y**) (162.1 mg, 0.4023 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 24.1 mg, 0.6036 mmol, 3 equiv), and THF (8 mL) to give the crude product **3b** (85%, dr = 60:24:16, determined by ^{1}H NMR, using EtOAc as an internal standard). After purification, **3b** (32.8 mg, 0.168 mmol, 84%, dr = 60:24:16) was obtained as a yellow oil. For separation of diastereomers a preparative TLC was used, eluting with PE/Et_2O 7:1. Three separate diastereomers were obtained.

1-((1R,2R*,3R*)-2-Fluoro-3-nitrocyclopropyl)-4-methylbenzene (**3b**).* First fraction (17.5 mg, 0.0897 mmol, 45%) a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21−7.15 (m, 4H), 5.44 (ddd, J = 61.4, 7.7, 1.2 Hz, 1H), 4.83 (ddd, J = 13.3, 5.3, 1.3 Hz, 1H), 3.43 (ddd, J = 8.7, 7.8, 5.4 Hz, 1H), 2.36 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 138.4, 129.7, 128.7 (C−F, d, $^4J_{C-F}$ = 1.4 Hz), 126.8 (C−F, d, $^3J_{C-F}$ = 2.7 Hz), 75.8 (C−F, d, $^1J_{C-F}$ = 241.9 Hz), 63.6 (C−F, d, $^2J_{C-F}$ = 13.5 Hz), 35.2 (C−F, d, $^2J_{C-F}$ = 9.3 Hz), 21.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ −216.50 (ddd, J = 61.3, 13.1, 9.0 Hz). Anal. Calcd for $C_{10}H_{10}FNO_2$: C, 61.53; H, 5.16; N, 7.18. Found: C, 62.37; H, 5.49; N 6.75.

1-((1S,2R*,3R*)-2-Fluoro-3-nitrocyclopropyl)-4-methylbenzene (**3b′**).* Second fraction (7.2 mg, 0.037 mmol, 18%) a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15 (m, 4H), 5.70 (ddd, J = 60.0, 5.2, 1.5 Hz, 1H), 4.94 (ddd, J = 12.0, 10.4, 1.5 Hz, 1H), 3.44 (ddd, J = 22.5, 10.4, 5.2 Hz, 1H), 2.33 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 138.8, 129.8, 128.8 (C−F, d, $^4J_{C-F}$ = 1.0 Hz), 125.7, 75.1 (C−F, d, $^1J_{C-F}$ = 238.2 Hz), 63.8 (C−F, d, $^2J_{C-F}$ = 13.9 Hz), 36.6 (C−F, d, $^2J_{C-F}$ = 10.7 Hz), 21.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ −206.61 (ddd, J = 60.1, 22.4, 12.1 Hz).

1-((1S,2R*,3S*)-2-Fluoro-3-nitrocyclopropyl)-4-methylbenzene (**3b″**).* Third fraction (5.1 mg, 0.026 mmol, 13%) a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18−7.14 (m, 2H), 7.06−7.01 (m, 2H), 4.92 (ddd, J = 61.9, 6.3, 4.4 Hz, 1H), 4.54 (ddd, J = 6.3, 5.3, 0.6 Hz, 1H), 3.91 (dt, J = 23.1, 4.8 Hz, 1H), 2.34 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 138.4, 130.0, 129.4 (C−F, d, $^3J_{C-F}$ = 1.1 Hz), 127.1, 74.9 (C−F, d, $^1J_{C-F}$ = 247.1 Hz), 63.8 (C−F, d, $^2J_{C-F}$ = 10.7 Hz), 32.0 (C−F, d, $^2J_{C-F}$ = 9.9 Hz), 21.2. ^{19}F NMR (376 MHz, $CDCl_3$): δ −215.67 (dd, J = 61.5, 22.9 Hz).

*1-(2-Fluoro-3-nitrocyclopropyl)-3-methoxybenzene (**3c**).* The product was obtained following general procedure C, using (*E*)-1-methoxy-3-(2-nitrovinyl)benzene (**3c**) (36.0 mg, 0.201 mmol, 1 equiv), (2,3-dichlorophenyl)(2,4-dimethylphenyl)(fluoromethyl)-sulfonium tetrafluoroborate (**2y**) (162.1 mg, 0.4023 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 24.1 mg, 0.604 mmol, 3 equiv), and THF (8 mL) to give the crude product **3c** (75%, dr = 60:5:35, determined by ^{1}H NMR, using EtOAc as an internal standard). After purification, **3c** (29.2 mg, 0.138 mmol, 69%, dr = 57:6:37) was obtained as a yellow oil. For separation of diastereomers a preparative TLC was used, eluting with PE/Et_2O 7:1. Two separate diastereomers were obtained.

1-((1R,2R*,3R*)-2-Fluoro-3-nitrocyclopropyl)-3-methoxybenzene (**3c**).* First fraction (13.9 mg, 0.0658 mmol, 33%) a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (t, J = 8.0 Hz, 1H), 6.92−6.83 (m, 2H), 6.81 (m, 1H), 5.45 (ddd, J = 61.4, 7.7, 1.3 Hz, 1H), 4.85 (ddd, J = 13.4, 5.4, 1.3 Hz, 1H), 3.81 (s, 3H), 3.44 (ddd, J = 9.1, 7.7, 5.4 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 160.0, 131.3 (C−F, d, $^3J_{C-F}$ = 2.6 Hz), 130.1, 121.1 (C−F, d, $^2J_{C-F}$ = 1.3 Hz), 114.8 (C−F, d, $^2J_{C-F}$ = 1.2 Hz), 113.8, 75.8 (C−F, d, $^1J_{C-F}$ = 242.5 Hz), 63.5 (C−F, d, $^2J_{C-F}$ = 13.5 Hz), 55.5, 35.2 (C−F, d, $^2J_{C-F}$ = 9.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −216.37 (ddd, J = 61.4, 13.7, 9.1 Hz). HRMS calcd for $[M + H]^+$: $C_{10}H_{11}NO_3F$ 212.0723, found 212.0719.

1-((1S,2R*,3S*)-2-Fluoro-3-nitrocyclopropyl)-3-methoxybenzene (**3c′′**).* Third fraction (8.6 mg, 0.041 mmol, 20%) a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (t, J = 7.9 Hz, 1H), 6.86 (ddd, J = 8.3, 2.5, 0.9 Hz, 1H), 6.71−6.66 (m, 2H), 4.94 (ddd, J = 61.8, 6.3, 4.4 Hz, 1H), 4.57 (td, J = 6.0, 5.4, 0.6 Hz, 1H), 3.92 (dt, J = 23.0, 4.8 Hz, 1H), 3.81 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 160.3, 133.9 (C−F, d, $^3J_{C-F}$ = 1.2 Hz), 130.4, 119.2, 113.7, 113.3, 74.7 (C−F, d, $^1J_{C-F}$ = 247.3 Hz), 63.8 (C−F, d, $^2J_{C-F}$ = 11.0 Hz), 55.5, 32.2 (C−F, d, $^2J_{C-F}$ = 10.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −215.45 (dd, J = 61.8, 23.0 Hz).

*1-(2-Fluoro-3-nitrocyclopropyl)-4-methoxybenzene (**3d**).* The product was obtained following general procedure C, using (*E*)-1-methoxy-4-(2-nitrovinyl)benzene (**1d**) (36.0 mg, 0.201 mmol, 1 equiv), (2,3-dichlorophenyl)(2,4-dimethylphenyl)(fluoromethyl)-sulfonium tetrafluoroborate (**2y**) (162.1 mg, 0.4023 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 24.1 mg, 0.604 mmol, 3 equiv), and THF (8 mL) to give the crude product **3d** (84%, dr = 61:6:33, determined by ^{1}H NMR, using EtOAc as an internal standard). After purification, **3d** (28.6 mg, 0.135 mmol, 67%, dr = 77:3:20) was obtained as a yellow oil. For separation of the major diastereomer a preparative TLC was used, eluting with PE/Et_2O 7:1.

1-((1R,2R*,3R*)-2-Fluoro-3-nitrocyclopropyl)-4-methoxybenzene (**3d**).* First fraction (17.7 mg, 0.0838 mmol, 42%) a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23−7.18 (m, 2H), 6.93−6.88 (m, 2H), 5.44 (ddd, J = 61.4, 7.7, 1.3 Hz, 1H), 4.79 (ddd, J = 13.3, 5.3, 1.3 Hz, 1H), 3.81 (s, 3H), 3.41 (ddd, J = 9.0, 7.7, 5.3 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 159.7, 130.0 (C−F, d, $^4J_{C-F}$ = 1.2 Hz), 121.8 (C−F, d, $^3J_{C-F}$ = 2.9 Hz), 114.5, 75.9 (C−F, d, $^1J_{C-F}$ = 241.6 Hz), 63.7 (C−F, d, $^2J_{C-F}$ = 13.4 Hz), 55.5, 34.9 (C−F, d, $^2J_{C-F}$ = 9.4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −216.56 (ddd, J = 61.4, 13.3, 8.9 Hz). HRMS calcd for $[M + H]^+$: $C_{10}H_{11}NO_3F$ 212.0723, found 212.0726.

*1-Fluoro-4-(2-fluoro-3-nitrocyclopropyl)-2-methoxybenzene (**3e**).* The product was obtained following general procedure C, using (*E*)-1-fluoro-2-methoxy-4-(2-nitrovinyl)benzene (**1e**) (39.7 mg, 0.201 mmol, 1 equiv), (2,3-dichlorophenyl)(2,4-dimethylphenyl)-(fluoromethyl)sulfonium tetrafluoroborate (**2y**) (162.1 mg, 0.402 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 24.1 mg, 0.6036 mmol, 3 equiv) and THF (8 mL) to give the crude product **3e** (77%, dr = 64:21:16, determined by ^{1}H NMR, using EtOAc as an internal standard). After purification, **3e** (38.6 mg, 0.168 mmol, 72%, dr = 62:22:16) was obtained as a yellow oil. For separation of the major diastereomer a preparative TLC was used, eluting with PE/Et_2O 5:1.

1-Fluoro-4-((1R,2R*,3R*)-2-fluoro-3-nitrocyclopropyl)-2-methoxybenzene (**3e**).* First fraction (12.2 mg, 0.0532 mmol, 27%) a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.07 (dd, J = 11.0, 8.3 Hz, 1H), 6.87 (dd, J = 7.8, 2.2 Hz, 1H), 6.87−6.79 (m, 1H), 5.45 (ddd, J = 61.3, 7.7, 1.3 Hz, 1H), 4.81 (ddd, J = 13.4, 5.4, 1.3 Hz, 1H), 3.90 (s, 3H), 3.43 (ddd, J = 8.8, 7.8, 5.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 152.5 (C−F, d, $^1J_{C-F}$ = 247.9 Hz), 148.1 (C−F, d, $^2J_{C-F}$ = 11.0 Hz), 126.1 (C−F, dd, $^{3,4}J_{C-F}$ = 3.8, 2.7 Hz), 121.4 (C−F, dd, $^{3,4}J_{C-F}$ = 7.0, 1.5 Hz), 116.6 (C−F, d, $^2J_{C-F}$ = 18.8 Hz), 114.2, 74.5, 63.6 (C−F, d, $^2J_{C-F}$ = 13.5 Hz), 56.5, 34.7 (d, J = 9.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −134.70 (ddd, J = 11.1, 7.6, 4.0 Hz), −216.39 (ddd, J = 61.2, 13.1, 8.8 Hz). HRMS calcd for $[M + H]^+$: $C_{10}H_{10}NO_3F_2$ 230.0629, found 230.0624.

*1-Fluoro-2-(2-fluoro-3-nitrocyclopropyl)benzene (**3f**).* The product was obtained following general procedure C, using (*E*)-1-fluoro-2-(2-nitrovinyl)benzene (**1f**) (33.6 mg, 0.201 mmol, 1 equiv), (2,3-dichlorophenyl)(2,4-dimethylphenyl)(fluoromethyl)sulfonium tetrafluoroborate (**2y**) (162.1 mg, 0.4023 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 24.1 mg, 0.604 mmol, 3 equiv), and THF (8 mL) to give the crude product **3f** (76%, dr = 62:18:20, determined by ^{1}H NMR, using EtOAc as an internal standard). After purification, **3f** (26.7 mg, 0.134 mmol, 67%, dr = 54:23:22) was obtained as a yellow oil. For separation of diastereomers a preparative TLC was used, eluting with PE/Et_2O 7:1. Three separate diastereomers were obtained.

1-Fluoro-2-((1R,2R*,3R*)-2-fluoro-3-nitrocyclopropyl)benzene (**3f**).* First fraction (12.9 mg, 0.0648 mmol, 32%) a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.30 (m, 1H), 7.29−7.21 (m, 1H), 7.19−7.08 (m, 2H), 5.50 (ddd, J = 61.3, 7.8, 1.4 Hz, 1H), 4.86 (ddd, J = 13.3, 5.5, 1.3 Hz, 1H), 3.52 (ddd, J = 8.8, 7.7, 5.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 161.9 (C−F, d, $^1J_{C-F}$ = 248.7 Hz), 130.4 (C−F, d, $^3J_{C-F}$ = 8.3 Hz), 129.9 (C−F, t, $^3J_{C-F}$ = 2.5 Hz), 124.5 (C−F, d, $^4J_{C-F}$ = 3.7 Hz), 117.3 (C−F, dd, $^{2,3}J_{C-F}$ = 14.3, 3.0 Hz), 116.0

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(C−F, d, $^{2}J_{C-F}$ = 21.2 Hz), 75.2 (C−F, d, $^{1}J_{C-F}$ = 242.5 Hz), 62.6 (C−F, d, $^{2}J_{C-F}$ = 13.7 Hz), 29.2 (C−F, dd, $^{2,3}J_{C-F}$ = 9.2, 4.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −115.52 to −115.64 (m), −216.02 (dddd, J = 61.1, 13.3, 8.8, 2.6 Hz). Anal. Calcd for $C_9H_7F_2NO_2$: C, 54.28; H, 3.54; N, 7.03. Found: C, 55.26; H, 3.77; N 6.60.

1-Fluoro-2-((1S,2R*,3R*)-2-fluoro-3-nitrocyclopropyl)benzene (**3f′**).* Second fraction (5.5 mg, 0.028 mmol, 14%) a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.27 (m, 2H), 7.16 (td, J = 7.6, 1.3 Hz, 1H), 7.07 (ddd, J = 9.5, 8.4, 1.1 Hz, 1H), 5.69 (ddd, J = 59.6, 5.2, 1.4, 0.5 Hz, 2H), 5.03 (ddd, J = 11.9, 10.2, 1.5 Hz, 1H), 3.40 (ddd, J = 21.8, 10.2, 5.3 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 161.9 (C−F, dd, $^{1,4}J_{C-F}$ = 248.4, 1.6 Hz), 130.7 (C−F, d, $^{3}J_{C-F}$ = 8.2 Hz), 130.5 (C−F, d, $^{3}J_{C-F}$ = 2.8 Hz), 124.6 (C−F, d, $^{4}J_{C-F}$ = 3.8 Hz), 116.5 (C−F, d, $^{2}J_{C-F}$ = 14.4 Hz), 116.0 (C−F, d, $^{2}J_{C-F}$ = 21.0 Hz), 74.8 (C−F, dd, $^{1,4}J_{C-F}$ = 239.8, 2.5 Hz), 63.1−62.9 (C−F, m), 31.2 (C−F, dd, $^{2,3}J_{C-F}$ = 11.6, 2.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −115.64 to −115.72 (m), −205.91 (ddd, J = 60.1, 21.8, 12.1 Hz).

1-Fluoro-2-((1S,2R*,3S*)-2-fluoro-3-nitrocyclopropyl)benzene (**3f″**).* Third fraction (4.6 mg, 0.023 mmol, 12%) a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36−7.28 (m, 1H), 7.18−7.06 (m, 3H), 5.09 (ddd, J = 61.7, 6.2, 4.5 Hz, 1H), 4.69 (ddd, J = 6.2, 5.5, 0.6 Hz, 1H), 3.93 (ddd, J = 23.1, 5.5, 4.5 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 161.3 (C−F, d, $^{1}J_{C-F}$ = 247.5 Hz), 130.3 (C−F, d, $^{3}J_{C-F}$ = 8.3 Hz), 129.2 (C−F, d, $^{3}J_{C-F}$ = 3.4 Hz), 124.8 (C−F, d, $^{4}J_{C-F}$ = 3.8 Hz), 119.9 (C−F, dd, $^{2,3}J_{C-F}$ = 13.8, 1.1 Hz), 116.3 (C−F, d, $^{2}J_{C-F}$ = 21.1 Hz), 74.1 (C−F, dd, $^{1,4}J_{C-F}$ = 247.0, 4.0 Hz), 63.2 (C−F, d, $^{2}J_{C-F}$ = 6.1 Hz), 27.7 (C−F, dd, $^{2,3}J_{C-F}$ = 11.5, 2.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −117.21 to −117.31 (m), −215.82 (ddd, J = 62.2, 23.1, 1.5 Hz).

*1-Fluoro-3-(2-fluoro-3-nitrocyclopropyl)benzene (**3g**).* The product was obtained following general procedure C, using (*E*)-1-fluoro-3-(2-nitrovinyl)benzene (**1g**) (33.6 mg, 0.201 mmol, 1 equiv), (2,3-dichlorophenyl)(2,4-dimethylphenyl)(fluoromethyl)sulfonium tetrafluoroborate (**2y**) (162.1 mg, 0.4023 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 24.1 mg, 0.604 mmol, 3 equiv) and THF (8 mL) to give the crude product **3g** (69%, dr = 62:16:22, determined by ^{1}H NMR, using EtOAc as an internal standard). After purification, **3g** (29.3 mg, 0.147 mmol, 73%, dr = 65:16:19) was obtained as a slightly yellow oil. For separation of diastereomers a preparative TLC was used, eluting with PE/Et_2O 7:1. Three separate diastereomers were obtained.

1-Fluoro-3-((1R,2R*,3*)-2-fluoro-3-nitrocyclopropyl)benzene (**3g**).* First fraction (16.7 mg, 0.0838 mmol, 42%) a slightly yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35 (td, J = 8.0, 6.0 Hz, 1H), 7.12−7.05 (m, 1H), 7.08−7.01 (m, 1H), 7.02−6.98 (m, 1H), 5.46 (ddd, J = 61.1, 7.7, 1.3 Hz, 1H), 4.84 (ddd, J = 13.4, 5.4, 1.3 Hz, 1H), 3.45 (td, J = 8.8, 7.7, 5.5 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 162.9 (C−F, d, $^{1}J_{C-F}$ = 247.5 Hz), 132.2 (C−F, dd, $^{3,3}J_{C-F}$ = 8.2, 2.8 Hz), 130.6 (C−F, d, $^{3}J_{C-F}$ = 8.4 Hz), 124.7 (C−F, dd, $^{4,4}J_{C-F}$ = 3.1, 1.4 Hz), 116.0 (C−F, dd, $^{2,4}J_{C-F}$ = 22.8, 1.7 Hz), 115.6 (C−F, d, $^{2}J_{C-F}$ = 21.0 Hz), 75.5 (C−F, d, $^{1}J_{C-F}$ = 242.8 Hz), 63.4 (C−F, d, $^{2}J_{C-F}$ = 13.5 Hz), 34.6 (C−F, d, $^{2,4}J_{C-F}$ = 9.2, 2.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −111.81 (td, J = 9.0, 6.0 Hz), −216.63 (ddd, J = 61.2, 13.1, 8.9 Hz). HRMS calcd for $[M + H]^+$: $C_9H_8NO_2F_2$ 200.0523, found 200.0511.

1-Fluoro-3-((1S,2R*,3R*)-2-fluoro-3-nitrocyclopropyl)benzene (**3g′**).* Second fraction (4.4 mg, 0.0221 mmol, 11%) a slightly yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (td, J = 8.0, 5.9 Hz, 1H), 7.08−7.04 (m, 1H), 7.04−6.98 (m, 2H), 5.70 (ddd, J = 59.8, 5.2, 1.5 Hz, 1H), 4.97 (ddd, J = 11.9, 10.4, 1.5 Hz, 1H), 3.45 (ddd, J = 21.9, 10.4, 5.2 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 163.0 (C−F, d, $^{1}J_{C-F}$ = 247.7 Hz), 131.2 (C−F, d, $^{3}J_{C-F}$ = 8.0 Hz), 130.7 (C−F, d, $^{3}J_{C-F}$ = 8.4 Hz), 124.7 (C−F, dd, $^{4,4}J_{C-F}$ = 3.0, 1.2 Hz), 116.2 (C−F, dd, $^{2,4}J_{C-F}$ = 22.5, 1.0 Hz), 116.1 (C−F, d, $^{2}J_{C-F}$ = 21.0 Hz), 74.7 (C−F, d, $^{1}J_{C-F}$ = 239.4 Hz), 63.7 (C−F, d, $^{2}J_{C-F}$ = 13.7 Hz), 36.0 (C−F, d, $^{2,4}J_{C-F}$ = 11.1, 2.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −111.73 to −111.84 (m), −206.67 (ddd, J = 59.9, 21.9, 12.0 Hz).

1-Fluoro-3-((1S,2R*,3S*)-2-fluoro-3-nitrocyclopropyl)benzene (**3g″**).* Third fraction (5.8 mg, 0.029 mmol, 15%) a slightly yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 (td, J = 8.1, 5.9 Hz, 1H), 7.03 (tdd, J = 8.4, 2.6, 0.9 Hz, 1H), 6.93 (ddt, J = 7.7, 1.7, 0.8 Hz, 1H), 6.86 (dt, J = 9.3, 2.2 Hz, 1H), 4.94 (ddd, J = 61.5, 6.4, 4.4 Hz, 1H), 4.58 (ddd, J = 6.2, 5.3, 0.7 Hz, 1H), 3.94 (dt, J = 22.7, 4.8 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 163.2 (C−F, d, $^{1}J_{C-F}$ = 248.3 Hz), 134.8 (C−F, dd, $^{3,3}J_{C-F}$ = 7.7, 1.1 Hz), 131.1 (C−F, d, $^{3}J_{C-F}$ = 8.4 Hz), 123.0 (C−F, d, $^{4}J_{C-F}$ = 3.1 Hz), 115.6 (C−F, d, $^{2}J_{C-F}$ = 21.0 Hz), 114.5 (C−F, d, $^{2}J_{C-F}$ = 22.5 Hz), 74.4 (C−F, d, $^{1}J_{C-F}$ = 247.9 Hz), 63.7 (C−F, d, $^{2}J_{C-F}$ = 10.7 Hz), 31.7 (C−F, dd, $^{2,4}J_{C-F}$ = 10.4, 2.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −111.26 (td, J = 8.9, 6.0 Hz), −215.38 (dd, J = 61.5, 22.8 Hz).

*1-Bromo-4-(2-fluoro-3-nitrocyclopropyl)benzene (**3h**).* The product was obtained following general procedure C, using (*E*)-1-bromo-4-(2-nitrovinyl)benzene(**1h**) (45.9 mg, 0.201 mmol, 1 equiv), (2,3-dichlorophenyl)(2,4-dimethylphenyl)(fluoromethyl)sulfonium tetrafluoroborate (**2y**) (162.1 mg, 0.4023 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 24.1 mg, 0.604 mmol, 3 equiv), and THF (8 mL) to give the crude product **3h** (74%, dr = 69:22:9, determined by ^{1}H NMR, using EtOAc as an internal standard). After purification, **3h** (36.9 mg, 0.142 mmol, 71%, dr = 69:20:11) was obtained as a yellow oil. For separation of diastereomers a preparative TLC was used, eluting with PE/Et_2O 7:1.

1-Bromo-4-((1R,2R*,3R*)-2-fluoro-3-nitrocyclopropyl)benzene (**3h**).* First fraction (24.5 mg, 0.0942 mmol, 47%) a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53−7.49 (m, 2H), 7.18−7.14 (m, 2H), 5.46 (ddd, J = 61.2, 7.7, 1.3 Hz, 1H), 4.82 (ddd, J = 13.3, 5.4, 1.3 Hz, 1H), 3.41 (ddd, J = 8.8, 7.6, 5.4 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 132.2, 130.5 (C−F, d, $^{4}J_{C-F}$ = 1.5 Hz), 128.9 (C−F, d, $^{3}J_{C-F}$ = 2.7 Hz), 122.7, 75.5 (C−F, d, $^{1}J_{C-F}$ = 242.5 Hz), 63.3 (C−F, d, $^{2}J_{C-F}$ = 13.4 Hz), 34.5 (C−F, d, $^{2}J_{C-F}$ = 9.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −216.55 (ddd, J = 61.2, 13.2, 9.0 Hz). Anal. Calcd for $C_9H_7BrFNO_2$: C, 41.57; H, 2.71; N, 5.39. Found: C, 42.97; H, 3.08; N 4.87.

1-Bromo-4-((1S,2R*)-2-fluoro-3-nitrocyclopropyl)benzene (**3h′+3h″**).* Second fraction (10.7 mg, 0.0411 mmol, 21%, dr = 67:33) a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53−7.45 (m, 4H), 7.18−7.13 (m, 2H), 7.06−6.99 (m, 2H), 5.68 (ddd, J = 59.8, 5.2, 1.5 Hz, 1H), 4.96 (ddd, J = 11.9, 10.4, 1.5 Hz, 1H), 4.92 (ddd, J = 61.5, 6.3, 4.4 Hz, 1H), 4.55 (ddd, J = 6.2, 5.3, 0.5 Hz, 1H), 3.90 (dt, J = 22.7, 4.8 Hz, 1H), 3.40 (ddd, J = 22.0, 10.4, 5.2 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 132.5, 132.3, 131.4 (C−F, d, $^{3}J_{C-F}$ = 1.0 Hz), 130.6 (C−F, d, $^{4}J_{C-F}$ = 1.3 Hz), 129.0 (C−F, d, $^{4}J_{C-F}$ = 0.6 Hz), 127.9, 123.1, 122.6, 74.7 (C−F, d, $^{1}J_{C-F}$ = 239.4 Hz), 74.4 (C−F, d, $^{1}J_{C-F}$ = 247.9 Hz), 63.9−63.4 (C−F, m), 36.0 (C−F, d, $^{2}J_{C-F}$ = 11.1 Hz), 31.6 (C−F, d, $^{2}J_{C-F}$ = 10.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −206.60 (ddd, J = 59.9, 22.0, 12.2 Hz), −215.45 (dd, J = 61.5, 22.4 Hz).

*2-(2-Fluoro-3-nitrocyclopropyl)naphthalene (**3i**).* The product was obtained following general procedure C, using (*E*)-2-(2-nitrovinyl)naphthalene (**1i**) (40.1 mg, 0.201 mmol, 1 equiv), (2,3-dichlorophenyl)(2,4-dimethylphenyl)(fluoromethyl)sulfonium tetrafluoroborate (**2y**) (162.1 mg, 0.4023 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 24.1 mg, 0.604 mmol, 3 equiv), and THF (8 mL) to give the crude product **3i** (80%, dr = 66:22:12, determined by ^{1}H NMR, using EtOAc as an internal standard). After purification, **3i** (35.5 mg, 0.154 mmol, 76%, dr = 72:18:10) was obtained as a slightly yellow oil. For separation of the major diastereomer a silica gel column chromatography was used, eluting with PE/EtOAc 10:1.

2-((1R,2R*,3R*)-2-Fluoro-3-nitrocyclopropyl)naphthalene (**3i**).* First fraction (12.8 mg, 0.0554 mmol, 28%) white solid. Mp: 107−109 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88−7.81 (m, 3H), 7.78 (s, 1H), 7.57−7.47 (m, 2H), 7.36 (dd, J = 8.5, 1.9 Hz, 1H), 5.54 (ddd, J = 61.3, 7.7, 1.3 Hz, 1H), 4.98 (ddd, J = 13.3, 5.4, 1.3 Hz, 1H), 3.63 (ddd, J = 9.0, 7.6, 5.2 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 133.3, 133.0, 128.9, 128.2 (C−F, d, $^{4}J_{C-F}$ = 1.5 Hz), 127.9, 127.9, 127.2 (C−F, d, $^{3}J_{C-F}$ = 2.6 Hz), 126.9, 126.8, 126.2 (C−F, d, $^{4}J_{C-F}$ = 1.2 Hz), 75.9 (C−F, d, $^{1}J_{C-F}$ = 242.5 Hz), 63.6 (C−F, d, $^{2}J_{C-F}$ = 13.5 Hz), 35.5 (C−F, d, $^{2}J_{C-F}$ = 9.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −216.14 (ddd, J = 61.3, 13.1, 9.0 Hz). HRMS calcd for $[M + H]^+$: $C_{13}H_{11}NO_2F$ 232.0778, found 232.0774.

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1-((1R,2R*,3R*)-2-Fluoro-3-nitrocyclopropyl)-2-nitrobenzene (**3j**).* The product was obtained following general procedure C, using (*E*)-1-nitro-2-(2-nitrovinyl)benzene (**1j**) (32.2 mg, 0.166 mmol, 1 equiv), (2,3-dichlorophenyl)(2,4-dimethylphenyl)(fluoromethyl)-sulfonium tetrafluoroborate (**2y**) (133.7 mg, 0.3317 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 19.9 mg, 0.604 mmol, 3 equiv), and THF (6.6 mL) to give the crude product **3j** (57%, *dr* = 79:9:12, determined by ^{1}H NMR, using EtOAc as an internal standard). After purification, **3j** (17.6 mg, 0.0778 mmol, 47%, dr = 85:15:0) was obtained as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (major diastereomer) 8.15 (dd, J = 8.4, 1.4 Hz, 1H), 7.71−7.66 (m, 1H), 7.61−7.54 (m, 2H), 5.55 (ddd, J = 60.6, 7.6, 1.2 Hz, 1H), 4.77 (ddd, J = 13.7, 5.8, 1.2 Hz, 1H), 3.93 (ddd, J = 8.7, 7.7, 5.5 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ (major diastereomer) 149.8, 134.0, 132.0 (C−F, d, $^4J_{C-F}$ = 1.8 Hz), 130.0, 125.7, 125.2 (C−F, d, $^3J_{C-F}$ = 3.3 Hz), 75.4 (C−F, d, $^1J_{C-F}$ = 241.8 Hz), 63.5 (C−F, d, $^2J_{C-F}$ = 13.7 Hz), 33.1 (C−F, d, $^2J_{C-F}$ = 8.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ (major diastereomer) −213.54 (ddd, J = 60.3, 13.3, 8.2 Hz). Anal. Calcd for $C_9H_7FN_2O_4$: C, 47.80; H, 3.12; N, 12.39. Found: C, 48.40; H, 3.28; N, 11.86.

*1-(2-Fluoro-3-nitrocyclopropyl)-3-(trifluoromethyl)benzene (**3k**).* The product was obtained following general procedure C, using (*E*)-1-(2-nitrovinyl)-3-(trifluoromethyl)benzene (**1k**) (43.7 mg, 0.201 mmol, 1 equiv), (2,3-dichlorophenyl)(2,4-dimethylphenyl)-(fluoromethyl)sulfonium tetrafluoroborate (**2y**) (162.1 mg, 0.4023 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 24.1 mg, 0.604 mmol, 3 equiv) and THF (8 mL) to give the crude product **3k** (68%, *dr* = 72:19:9, determined by ^{1}H NMR, using EtOAc as an internal standard). After purification, **3k** (32.8 mg, 0.132 mmol, 66%, dr = 78:14:8 obtained as a yellow oil. For separation of the major diastereomer a preparative TLC was used, eluting with PE/Et_2O 7:1.

1-((1R,2R*,3R*)-2-Fluoro-3-nitrocyclopropyl)-3-(trifluoromethyl)benzene (**3k**).* First fraction (22.9 mg, 0.0919 mmol, 46%) a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66−7.60 (m, 1H), 7.57−7.46 (m, 3H), 5.50 (ddd, J = 61.1, 7.7, 1.3 Hz, 1H), 4.89 (ddd, J = 13.4, 5.4, 1.3 Hz, 1H), 3.52 (ddd, J = 8.8, 7.7, 5.4 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 132.2 (C−F, p, $^{4,5}J_{C-F}$ = 1.2 Hz), 131.6 (C−F, d, $^2J_{C-F}$ = 32.6 Hz), 131.0 (C−F, d, $^3J_{C-F}$ = 2.7 Hz), 129.6, 125.8 (C−F, d, $^{3,4}J_{C-F}$ = 3.8, 1.3 Hz), 125.4 (C−F, d, $^3J_{C-F}$ = 3.7 Hz), 123.8 (C−F, d, $^1J_{C-F}$ = 272.5 Hz), 75.4 (C−F, d, $^1J_{C-F}$ = 242.7 Hz), 63.2 (C−F, d, $^2J_{C-F}$ = 13.6 Hz), 34.4 (C−F, d, $^2J_{C-F}$ = 9.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −62.83, −216.49 (ddd, J = 61.0, 13.5, 8.8 Hz). Unstable under HRMS conditions.

Methyl 4-((1R,2R*,3R*)-2-Fluoro-3-nitrocyclopropyl)benzoate (**3l**).* The product was obtained following general procedure C, using methyl (*E*)-4-(2-nitrovinyl)benzoate (**1l**) (41.6 mg, 0.201 mmol, 1 equiv), (2,3-dichlorophenyl)(2,4-dimethylphenyl)-(fluoromethyl)sulfonium tetrafluoroborate (**2y**) (162.1 mg, 0.4023 mmol, 2 equiv), NaH (60% dispersion in mineral oil, 24.1 mg, 0.604 mmol, 3 equiv), and THF (8 mL) to give the crude product **3l** (54%, dr = 63:19:19, determined by ^{1}H NMR, using EtOAc as an internal standard). After purification, with silica gel column chromatography and preparative TLC (PE/Et_2O 5:1) main diastereomer **3l** (20.2 mg, 0.0844 mmol, 42%) was obtained as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07−8.00 (m, 2H), 7.39−7.32 (m, 2H), 5.49 (ddd, J = 61.2, 7.7, 1.4 Hz, 1H), 4.90 (ddd, J = 13.4, 5.4, 1.4 Hz, 1H), 3.92 (s, 3H), 3.49 (ddd, J = 8.8, 7.7, 5.6 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 166.5, 134.9 (C−F, d, $^3J_{C-F}$ = 2.4 Hz), 130.3, 130.2, 128.9 (C−F, d, $^4J_{C-F}$ = 1.3 Hz), 75.6 (C−F, d, $^1J_{C-F}$ = 242.9 Hz), 63.4 (C−F, d, $^2J_{C-F}$ = 13.4 Hz), 52.4, 34.8 (C−F, d, $^2J_{C-F}$ = 9.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −216.47 (ddd, J = 61.2, 13.1, 9.0 Hz). HRMS calcd for $[M + H]^+$: $C_{11}H_{11}NO_4F$ 240.0672, found: 240.0671.

((E)-2-((1R,2R*,3R*)-2-Fluoro-3-nitrocyclopropyl)vinyl)benzene (**3n**).* The product was obtained following a modified general procedure C, where ((1*E*,3*E*)-4-nitrobuta-1,3-dien-1-yl)benzene (**1n**) (38.0 mg, 0.217 mmol, 1 equiv) was dissolved in THF (8.7 mL) and at 0 °C (2,3-dichlorophenyl)(2,4-dimethylphenyl)-(fluoromethyl)sulfonium tetrafluoroborate (**2y**) (174.9 mg, 0.4339 mmol, 2 equiv) and NaH (60% dispersion in mineral oil, 26.0 mg, 0.651 mmol, 3 equiv) were added. After 1 h, an additional portion of (2,3-dichlorophenyl)(2,4-dimethylphenyl)(fluoromethyl)sulfonium tetrafluoroborate (**2y**) (87.5 mg, 0.217 mmol, 1 equiv) and NaH (60% dispersion in mineral oil, 13.0 mg, 0.325 mmol, 1.5 equiv) was added, and the mixture was stirred for another 60 min to give the crude product **3n** (74%, dr = 65:14:22, determined by ^{1}H NMR, using EtOAc as an internal standard). After purification by silica gel column chromatography and preparative TLC (PE/Et_2O 7:1) main diastereomer **3n** (18.3 mg, 0.0883 mmol, 41%) was obtained as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.26 (m, 5H), 6.80 (d, J = 15.9 Hz, 1H), 5.94 (dd, J = 15.9, 8.9 Hz, 1H), 5.40 (ddd, J = 60.4, 7.4, 1.2 Hz, 1H), 4.62 (ddd, J = 13.7, 4.7, 1.3 Hz, 1H), 3.09 (dddd, J = 9.0, 8.2, 4.7, 0.9 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 136.7, 135.9, 128.9, 128.6, 126.5, 117.3 (C−F, d, $^3J_{C-F}$ = 7.4 Hz), 75.8 (C−F, d, $^1J_{C-F}$ = 240.3 Hz), 63.4 (C−F, d, $^2J_{C-F}$ = 14.2 Hz), 34.9 (C−F, d, $^2J_{C-F}$ = 9.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −216.47 (ddd, J = 60.3, 13.7, 8.2 Hz). HRMS calcd for $[M + H]^+$: $C_{11}H_{11}FNO_2$ 208.0774, found: 208.0772.

*(2-Fluoro-3-nitrocyclopropyl)cyclohexane (**3o**).* The product was obtained following a modified general procedure C, where (*E*)-(2-nitrovinyl)cyclohexane (**1o**) (26.2 mg, 0.169 mmol, 1 equiv) was dissolved in THF (8.7 mL) and at 0 °C (2,3-dichlorophenyl)(2,4-dimethylphenyl)(fluoromethyl)sulfonium tetrafluoroborate (**2y**) (136.1 mg, 0.3377 mmol, 2 equiv) and NaH (60% dispersion in mineral oil, 20.3 mg, 0.507 mmol, 3 equiv) were added. After 1 h, an additional portion of (2,3-dichlorophenyl)(2,4-dimethylphenyl)-(fluoromethyl)sulfonium tetrafluoroborate (**2y**) (68 mg, 0.17 mmol, 1 equiv) and NaH (60% dispersion in mineral oil, 10.1 mg, 0.253 mmol, 1.5 equiv) was added and the mixture was stirred for another 40 min to give the crude product **3o** (76% dr = 63:6:32, determined by ^{1}H NMR, using EtOAc as an internal standard). After purification with silica gel column chromatography and preparative TLC (PE/EtOAc 30:1) two diastereomers were obtained.

((1R,2R*,3R*)-2-Fluoro-3-nitrocyclopropyl)cyclohexane (**3o**).* First fraction (9.1 mg, 0.049 mmol, 29%) a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.27 (ddd, J = 61.8, 7.5, 0.9 Hz, 1H), 4.31 (ddd, J = 13.4, 4.9, 0.9 Hz, 1H), 2.09 (dddd, J = 10.4, 9.2, 7.5, 5.0 Hz, 1H), 1.90−1.63 (m, 6H), 1.28−1.20 (m, 5H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 76.5 (C−F, d, $^1J_{C-F}$ = 238.2 Hz), 62.1 (C−F, d, $^2J_{C-F}$ = 13.4 Hz), 38.1 (C−F, d, $^2J_{C-F}$ = 9.4 Hz), 33.9 (C−F, d, $^3J_{C-F}$ = 4.4 Hz), 32.5, 32.4, 26.0, 25.9, 25.7. ^{19}F NMR (376 MHz, $CDCl_3$): δ −219.16 (ddd, J = 62.0, 13.4, 9.2 Hz).

((1S,2R*,3S*)-2-Fluoro-3-nitrocyclopropyl)cyclohexane (**3o′′**).* Third fraction (5.8 mg, 0.031 mmol, 18%) a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.58 (ddd, J = 62.7, 6.3, 4.4 Hz, 1H), 4.14 (dd, J = 6.3, 5.1 Hz, 1H), 2.62 (ddd, J = 24.0, 9.5, 4.8 Hz, 1H), 1.85−1.62 (m, 5H), 1.31−1.02 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 74.2 (C−F, d, $^1J_{C-F}$ = 243.7 Hz), 61.6 (C−F, d, $^2J_{C-F}$ = 11.2 Hz), 36.4, 34.4 (C−F, d, $^2J_{C-F}$ = 6.8 Hz), 31.5, 31.0, 26.0, 25.7, 25.7. ^{19}F NMR (376 MHz, $CDCl_3$): δ −216.35 (dd, J = 63.0, 24.0 Hz). HRMS calcd for $[M + H]^+$: $C_9H_{15}NO_2F$ 188.1087, found: 188.1081.

Synthesis of other Fluorocyclopropanes 5a−j. *Diethyl 2-Fluorocyclopropane-1,1-dicarboxylate (**5a**).*[12c] To a solution of diethyl 2-methylenemalonate (**4a**) (30 mg, 0.17 mmol, 1.0 equiv) in anhydrous THF (20 mL) cooled in ice bath under Ar atmosphere was added sulfonium salt **2y** (140.5 mg, 0.349 mmol, 2.0 equiv) followed by NaH (60% dispersion in mineral oil, 66 mg, 1.7 mmol, 9.5 equiv). The reaction mixture was stirred for 15 min at 0 °C. The color of the reaction mixture changed from pale gray turbid to light brown. A TLC control (PE/Et_2O 3:1) indicated full conversion of the starting material **4a** (R_f 0.25, staining with $KMnO_4$ TLC stain, color appears without heating) after 10 min. While still cold, the solvent was evaporated under reduced pressure (do not immerse the flask in a heating bath!). The resulting brown residue was suspended in petroleum ether (PE) (~2 mL), and directly transferred to a Pasteur pipet equipped with a cotton plug and silica gel (H 45 mm, W 6 mm). The residue was eluted with 100% PE until all (2,3-dichlorophenyl)-(2,4-dimethylphenyl)sulfane (**6y**) was collected (R_f 0.64 PE/Et_2O 3:1), and then the eluent was switched to PE/Et_2O 3:1 (fraction volume ~0.6 mL) to collect the desired fluorocyclopropane **5a** (R_f

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0.35 PE/Et_2O 3:1). After solvent evaporation (do not immerse in the heating bath! Product could be volatile) the desired product **5a** (21.4 mg, 60%) was obtained as a colorless oil.

Under the same conditions, the reagents **2a** and **2f** showed full conversion of the starting material **4a** in 35 and 30 min correspondingly. The corresponding isolated yields of **5a** (12.5 mg, 35%) for the reagent **2a** and **5a** (12.5 mg, 35%) for the reagent **2f**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.06 (ddd, J = 64.4, 6.1, 4.2 Hz, 1H), 4.37−4.09 (m, 4H), 2.21−2.09 (m, 1H), 1.63−1.53 (m, 1H), 1.30 (t, J = 7.1 Hz, 3H), 1.27 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 168.0, 164.7 (C−F, d, $^3J_{C-F}$ = 3.3 Hz), 75.0 (C−F, d, $^1J_{C-F}$ = 234.6 Hz), 62.2, 62.0, 34.6 (C−F, d, $^2J_{C-F}$ = 12.3 Hz), 20.1 (C−F, d, $^2J_{C-F}$ = 9.1 Hz), 14.2, 14.2. ^{19}F NMR (376 MHz, $CDCl_3$): δ −212.50 (ddd, J = 64.3, 22.2, 14.2 Hz).

General Procedure for the Synthesis of Vinyl Sulfones 4c,e−h. The vinylsulfones **4c,e−h** were synthesized following the literature procedure.[12b]

General Procedure E for the Synthesis of Fluorocyclopropyl Sulfones 5c,e−h. To a solution of 1-chloro-3-(vinylsulfonyl)-benzene (**4c**) (21.1 mg, 0.10 mmol, 1 equiv) in anhydrous THF (1 mL) under argon atmosphere was added (2,4-dimethylphenyl)-(fluoromethyl)(phenyl)sulfonium tetrafluoroborate (**2f**) (69.6 mg, 0.21 mmol, 2 equiv) at room temperature. To the reaction mixture was added NaH (60% dispersion in mineral oil, 16.7 mg, 0.42 mmol, 4 equiv). The reaction mixture was stirred at room temperature until completion (30−40 min) (TLC control). The reaction mixture was filtered through a cotton plug, and the collected precipitate on the plug was washed with THF (3 × 2 mL). The filtrate was evaporated under reduced pressure (*trans*/*cis* dr = 3.8:1 of crude by ^{19}F NMR). The crude product was purified by prep. TLC (eluent: PE, PE/EtOAc, 3/1). After chromatography the *trans* product **5c** 19.0 mg (78%) was obtained as a yellowish oil.

Under the same conditions using sulfonium salt **2a** the reaction time was 1 h 30 min and the product yield 70% (for crude *trans*:*cis* dr = 3.6:1).[12b]

General Procedure F for the Synthesis of Fluorocyclopropyl Sulfone 5c in THF. To a solution of 1-chloro-3-(vinylsulfonyl)-benzene (**4c**) (20.7 mg, 0.10 mmol, 1 equiv) in anhydrous THF (1 mL) under argon atmosphere was added (2,3-dichlorophenyl)(2,4-dimethylphenyl)(fluoromethyl)sulfonium tetrafluoroborate (**2y**) (82.3 mg, 0.20 mmol, 2 equiv) at 0 °C. To the reaction mixture was added NaH (60% dispersion in mineral oil, 16.34 mg, 0.41 mmol, 4 equiv). The reaction mixture was stirred at 0 °C for 2 h. Then the reaction mixture was filtered through a cotton plug and the collected precipitate on the plug was washed with THF (3 × 2 mL). The filtrate was evaporated under reduced pressure (*trans*:*cis* dr = 2.8:1 of crude by ^{19}F NMR). The crude product was purified by prep. TLC (eluent: PE, PE/EtOAc, 4/1, 3/1). After chromatography the *trans* product **5c** 11.4 mg (48%) was obtained as a yellowish oil.

General Procedure G for the Synthesis of Fluorocyclopropylsulfone 5c in MeCN. To a solution of 1-chloro-3-(vinylsulfonyl)-benzene (**4c**) (22.0 mg, 0.11 mmol, 1 equiv) in anhydrous MeCN (1 mL) under argon atmosphere was added (2,3-dichlorophenyl)(2,4-dimethylphenyl)(fluoromethyl)sulfonium tetrafluoroborate (**2y**) (87.5 mg, 0.22 mmol, 2 equiv) at room temperature. To the reaction mixture was added NaH (60% dispersion in mineral oil, 17.4 mg, 0.43 mmol, 4 equiv). The reaction mixture was stirred at room temperature for 30 min. Then the reaction mixture was filtered through a cotton plug, and the collected precipitate on the plug was washed with MeCN (3 × 2 mL). The filtrate was evaporated under reduced pressure. The crude product was purified by preparative TLC (eluent: PE, PE/EtOAc, 3/1). (^{19}F NMR of crude *trans*:*cis* dr = 10.5:1). After chromatography, the *trans* product **5c** 16.4 mg (64%) was obtained as a yellowish oil.

*trans-1-Chloro-3-((2-fluorocyclopropyl)sulfonyl)benzene (**5c**).*[12b] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (t, J = 1.8 Hz, 1H), 7.82−7.76 (m, 1H), 7.65 (ddd, J = 8.0, 2.0, 1.0 Hz, 1H), 7.54 (t, J = 7.9 Hz, 1H), 5.03 (dddd, J = 62.9, 6.3, 4.3, 1.8 Hz, 1H), 2.95−2.85 (m, 1H), 1.77−1.64 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 141.8, 136.2, 134.6, 131.3, 128.2, 126.2, 71.2 (C−F, d, $^1J_{C-F}$ = 234.6 Hz), 38.3 (C−F, d, $^2J_{C-F}$ = 11.2 Hz), 13.9 (C−F, d, $^2J_{C-F}$ = 10.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −209.69 (dq, J = 63.0, 16.4 Hz).

*trans-1-((2-Fluorocyclopropyl)sulfonyl)benzene (**5e**).*[12b] The product was obtained following general procedure E from phenyl vinyl sulfone (**4e**) (17.4 mg, 0.10 mmol, 1 equiv) using (2,4-dimethylphenyl)(fluoromethyl)(phenyl)sulfonium tetrafluoroborate (**2f**) (68.3 mg, 0.20 mmol, 2 equiv) and NaH (60% dispersion in mineral oil, 16.3 mg, 0.41 mmol, 4 equiv). (^{19}F NMR of crude *trans*:*cis* dr = 6.3:1). After chromatography the *trans* product **3m** 16.1 mg (78%) was obtained as a colorless oil. Under the same conditions using sulfonium salt **2a** product yield was 73% (for crude *trans*:*cis* dr = 4.3:1).[12b] ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93−7.88 (m, 2H), 7.71−7.66 (m, 1H), 7.62−7.56 (m, 2H), 5.03 (dddd, J = 63.1, 6.7, 3.9, 1.7 Hz, 1H), 2.89 (dddd, J = 15.5, 10.4, 7.1, 1.8 Hz, 1H), 1.76−1.60 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 139.9, 134.1, 129.6, 127.8, 71.0 (C−F, d, $^1J_{C-F}$ = 233.8 Hz), 38.1 (C−F, d, $^2J_{C-F}$ = 10.9 Hz), 13.4 (C−F, d, $^2J_{C-F}$ = 10.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −209.99 (dddd, J = 63.2, 19.1, 15.5, 12.1 Hz).

*trans-1-((2-Fluorocyclopropyl)sulfonyl)-4-nitrobenzene (**5f**).*[12b] The product was obtained following general procedure E from 1-nitro-4-(vinylsulfonyl)benzene (**4f**) (21.5 mg, 0.10 mmol, 1 equiv) using (2,4-dimethylphenyl)(fluoromethyl)(phenyl)sulfonium tetrafluoroborate (**2f**) (67.4 mg, 0.20 mmol, 2 equiv) and NaH (60% dispersion in mineral oil, 16.1 mg, 0.40 mmol, 4 equiv). (^{19}F NMR of crude *trans*:*cis* dr = 4.5:1). After chromatography the *trans* product **5f** 16.7 mg (68%) was obtained as a yellow oil. Under the same conditions using sulfonium salt **2a**[12b] product yield was 64% (for crude *trans*:*cis* dr = 3.4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47−8.40 (m, 2H), 8.15−8.07 (m, 2H), 5.17−4.95 (m, 1H), 2.99−2.87 (m, 1H), 1.83−1.69 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 151.1, 145.3, 129.3, 124.9, 70.8 (C−F, d, $^1J_{C-F}$ = 235.4 Hz), 37.9 (C−F, d, $^2J_{C-F}$ = 11.5 Hz), 13.8 (C−F, d, $^2J_{C-F}$ = 10.4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −209.5 (dm, J = 62.7 Hz).

*trans-3-((2-Fluorocyclopropyl)sulfonyl)thiophene (**5g**).*[12b] The product was obtained following general procedure E from 3-(vinylsulfonyl)thiophene (**4g**) (17.8 mg, 0.10 mmol, 1 equiv) using (2,4-dimethylphenyl)(fluoromethyl)(phenyl)sulfonium tetrafluoroborate (**2f**) (68.3 mg, 0.20 mmol, 2 equiv) and NaH (60% dispersion in mineral oil, 16.3 mg, 0.41 mmol, 4 equiv). (^{19}F NMR of crude *trans*:*cis* dr = 4.4:1). After chromatography the *trans* product **5g** 15.9 mg (76%) was obtained as a yellowish oil. Under the same conditions using sulfonium salt **2a** product yield was 69% (for crude *trans*:*cis* dr = 3.6:1).[12b] ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (dd, J = 3.1, 1.3 Hz, 1H), 7.50 (dd, J = 5.1, 3.1 Hz, 1H), 7.41 (dd, J = 5.2, 1.3 Hz, 1H), 5.13−4.92 (m, 1H), 3.00−2.88 (m, 1H), 1.76−1.63 (m, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 140.0, 132.3, 128.7, 125.6, 70.8 (C−F, d, $^1J_{C-F}$ = 234.0 Hz), 38.1 (C−F, d, $^2J_{C-F}$ = 11.1 Hz), 13.3 (C−F, d, $^2J_{C-F}$ = 10.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −209.90 (dq, J = 63.2, 15.9 Hz).

*Methyl trans-4-((2-Fluorocyclopropyl)sulfonyl)benzoate (**5h**).*[12b] The product was obtained following general procedure E from methyl 4-(vinylsulfonyl)benzoate (**4h**) (23.8 mg, 0.11 mmol, 1 equiv) using (2,4-dimethylphenyl)(fluoromethyl)(phenyl)sulfonium tetrafluoroborate (**2f**) (84.8 mg, 0.25 mmol, 2.4 equiv) and NaH (60% dispersion in mineral oil, 16.8 mg, 0.42 mmol, 4 equiv). (^{19}F NMR of crude *trans*:*cis* dr = 3.4:1). After chromatography the *trans* product **5h** 15.2 mg (56%) was obtained as a yellowish oil. Under the same conditions using sulfonium salt **2a** product yield was 42% (for crude *trans*:*cis* dr = 3.2:1).[12b] ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28−8.20 (m, 2H), 8.02−7.94 (m, 2H), 5.16−4.92 (m, 1H), 3.97 (s, 3H), 2.97−2.84 (m, 1H), 1.78−1.63 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 165.5, 143.6, 135.2, 130.8, 127.8, 70.9 (C−F, d, $^1J_{C-F}$ = 234.6 Hz), 52.9, 37.9 (C−F, d, $^2J_{C-F}$ = 11.4 Hz), 13.6 (C−F, d, $^2J_{C-F}$ = 10.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −209.77 (dddd, J = 63.0, 18.9, 15.7, 13.4 Hz).

General Procedure H for Fluorocyclopropanation of Double-Activated Alkenes. *Diethyl 2-Fluoro-3-(2-fluorophenyl)-cyclopropane-1,1-dicarboxylate (**5i**).*[12c] Diethyl 2-(2-fluorobenzylidene)malonate (**4i**) (130 mg, 0.488 mmol, 1 equiv) and (2,4-dimethylphenyl)(fluoromethyl)(phenyl)sulfonium tetra-

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fluoroborate (**2f**) (261 mg, 0.781 mmol, 1.6 equiv) were suspended in anhydrous THF (7 mL) under argon atmosphere. To the suspension was added NaH (60% dispersion in mineral oil, 78 mg, 1.95 mmol, 4 equiv), and the mixture was stirred at room temperature until completion (TLC control). Afterwards, the solvent was evaporated under reduced pressure (*the flask kept above the heating bath). The crude material was suspended in PE/Et_2O (40:7) and filtered through a cotton plug. The filtrate was concentrated under reduced pressure (*). The crude product was dissolved in $CDCl_3$ (1 mL) and an internal standard (EtOAc 1 equiv) was added. NMR yield 94%, dr 1:0.85. The crude product was purified by silica gel column chromatography (PE/EtOAc 100:0 to 80:20). Product **5i** was obtained as a light yellow oil as a mixture of (2*R**,3*R**)- and (2*S**,3*R**)-diastereomers (124 mg, 85%, dr 1:1). ^{1}H NMR corresponds to the reported spectra in literature. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32−7.22 (m, 1H), 7.41−7.10 (m, 1H), 7.11−7.00 (m, 2H), 5.56 (dd, J = 63.2, 4.7 Hz, 1H)^{2R*,3R*}, 5.25 (dd, J = 63.4, 6.4 Hz, 1H)^{2S*,3R*}, 4.40−4.22 (m, 4H), 4.09−3.99 (m, 2H), 3.94 (q, J = 7.1 Hz, 2H), 3.85 (dd, J = 22.0, 4.7 Hz, 1H)^{2R*,3R*}, 3.03 (dd, J = 11.2, 6.4 Hz, 1H)^{2S*,3R*}, 1.33 (t, J = 7.1 Hz, 3H), 1.31 (t, J = 7.1 Hz, 3H), 1.02 (t, J = 7.2 Hz, 3H), 0.95 (t, J = 7.1 Hz, 3H).

*Diethyl 2-Fluoro-3-(3-nitrophenyl)cyclopropane-1,1-dicarboxylate (**5b**).*[12c] The product was obtained following general procedure H, using diethyl 2-(3-nitrobenzylidene)malonate (**4b**) (60 mg, 0.20 mmol, 1 equiv), (2,4-dimethylphenyl)(fluoromethyl)(phenyl)-sulfonium tetrafluoroborate (**2f**) (109 mg, 0.327 mmol, 1.6 equiv), and NaH (60% dispersion in mineral oil, 33 mg, 0.82 mmol, 4 equiv). The reaction mixture was stirred in anhydrous THF (4.3 mL) for 1 h. NMR yield 99%, dr 1:1.2. Product was purified by silica gel column chromatography (PE/EtOAc 100:0 to 80:20). Product **5b** was obtained as a yellow oil as a mixture of (2*R**,3*R**)- and (2*S**,3*R**)-diastereomers (66 mg, 99%, dr = 1:1.29).

General Procedure I for Cyclopropanation of Double-Activated Alkenes. *Diethyl 2-Fluoro-3-(3-nitrophenyl)-cyclopropane-1,1-dicarboxylate (**5b**).*[12c] Diethyl 2-(3-nitrobenzylidene)malonate (**4b**) (41 mg, 0.17 mmol, 1 equiv) was dissolved in anhydrous THF (2.8 mL) and cooled to 0 °C. (2,3-Dichlorophenyl)(2,4-dimethylphenyl)(fluoromethyl)sulfonium tetrafluoroborate (**2y**) (113 mg, 0.280, 2 equiv) and NaH (60% dispersion in mineral oil, 17 mg, 0.42 mmol, 3 equiv) were subsequently added. The reaction mixture was stirred at the same temperature for 20 min (TLC control). Then the solvent was evaporated under reduced pressure. The crude material was suspended in ether and filtered through a cotton plug. The obtained filtrate was concentrated under reduced pressure. The crude product was dissolved in $CHCl_3$ (1 mL) and an internal standard (1 equiv EtOAc) was added. NMR yield 76%, dr 1:1.4. The crude product was purified via column chromatography (PE/EtOAc 100:0 to 80:20). Product **5b** was obtained as a light yellow oil (27.8 mg, 61%, dr 1:1.2). ^{1}H NMR corresponds to the reported spectra in literature.[12c] ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27−8.22 (m, 1H), 8.18−8.08 (m, 3H), 7.72−7.67 (m, 1H), 7.60−7.54 (m, 1H), 7.52−7.45 (m, 2H), 5.58 (dd, J = 62.2, 4.6 Hz, 1H)^{2R*,3S*}, 5.20 (dd, J = 63.4, 6.4 Hz, 1H)^{2S*,3S*}, 4.43−4.23 (m, 4H), 4.09 (q, J = 7.1 Hz, 2H), 4.01−3.86 (m, 3H), 3.08 (dd, J = 10.6, 6.0 Hz, 1H)^{2S*,3S*}, 1.33 (t, J = 6.92, 3H), 1.31 (t, J = 7.24 Hz, 3H), 1.09 (t, J = 7.1 Hz, 3H), 1.00 (t, J = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$): δ −213.19 (dd, J = 62.2, 21.2 Hz), −219.40 (dd, J = 63.6, 10.6 Hz). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 167.5, 164.3, 163.8 (C−F, d, $^3J_{C-F}$ = 3.3 Hz), 162.6 (C−F, d, $^3J_{C-F}$ = 2.1 Hz), 148.3, 148.0, 136.2 (C−F, d, $^4J_{C-F}$ = 3.5 Hz), 134.8, 133.9, 133.1 (C−F, d, $^3J_{C-F}$ = 1.9 Hz), 129.6, 129.3, 129.0, 125.7, 125.3 (C−F, d, $^4J_{C-F}$ = 3.3 Hz), 123.7, 123.0, 122.6, 76.7 (C−F, d, $^1J_{C-F}$ = 238.9 Hz), 76.1 (C−F, d, $^1J_{C-F}$ = 225.8 Hz), 62.8, 62.7, 62.0, 61.9, 43.6 (C−F, d, $^2J_{C-F}$ = 12.7 Hz), 38.3 (C−F, d, $^2J_{C-F}$ = 9.7 Hz), 35.1 (C−F, d, $^2J_{C-F}$ = 11.6 Hz), 32.3 (C−F, d, $^2J_{C-F}$ = 6.8 Hz), 14.1, 14.0, 13.8, 13.8.

*Ethyl 1-Cyano-2-fluoro-3-(2-fluorophenyl)cyclopropane-1-carboxylate (**5j**).*[12c] The product was obtained following general procedure H using ethyl 2-cyano-2-((2-fluorophenyl)methylidene)-acetate (**4j**) (48 mg, 0.22 mmol, 1 equiv), (2,4-dimethylphenyl)-(fluoromethyl)(phenyl)sulfonium tetrafluoroborate (**2f**) (117 mg, 0.350 mmol, 1.6 equiv), and NaH (60% dispersion in mineral oil, 35 mg, 0.88 mmol, 4 equiv), and anhydrous 1,4-dioxane (3.2 mL) was used as a solvent. The reaction mixture was stirred for 40 min. NMR yield −97%,dr 1.07:1. Product **5j** was obtained as a colorless oil as a mixture of 2*R**,3*R** and 2*S**,3*R** diastereomers (50 mg, 91%, dr 1.14:1). ^{1}H NMR corresponds to the reported spectra in literature. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50−7.42 (m, 1H), 7.42−7.33 (m, 1H), 7.28−7.10 (m, 2H), 5.38 (dd, J = 61.0, 5.3 Hz, 1H)^{2R*,3R*}, 5.34 (dd, J = 61.8, 6.2 Hz, 1H)^{2S*,3R*}, 4.38 (q, J = 7.23 Hz, 2H), 4.34 (q, J = 7.18 Hz, 2H) 3.97 (dd, J = 21.06, 5.38 Hz 1H), 3.29 (dd, J = 11.8, 5.8 Hz, 1H), 1.38 (t, J = 7.2 Hz, 3H), 1.38 (t, J = 7.1 Hz, 3H).

General Procedure J for Synthesis of Monofluorinated Epoxides.[12a] To *m*-nitroacetophenone (**4d**) (22.8 mg, 1.0 equiv, 0.138 mmol) in anhydrous MeCN (2.8 mL) under argon atmosphere was added (2,4-dimethylphenyl)(fluoromethyl)(phenyl)sulfonium tetrafluoroborate (**2f**) (69.2 mg, 1.5 equiv, 0.207 mmol) immediately followed by NaH (60% dispersion in mineral oil, 8.84 mg, 1.60 equiv, 0.221 mmol) at 0 °C. The reaction mixture was stirred at this temperature for 2 h 30 min. After completion (TLC control), the reaction mixture was evaporated. The solid residue was suspended in Et_2O (2 × 2 mL) and filtered through a cotton plug. The solvent was evaporated. The ^{1}H NMR yield for the crude product was determined using EtOAc (1 equiv) as an internal standard (100%, dr 1:1.). The crude product was purified by silica gel (pretreated with 2% Et_3N in PE) column chromatography (Pasteur pipet) eluting with PE then switched to PE/EtOAc 10:1 to give the desired product **5d** (23.2 mg, 85%, dr 1.1:1) as a colorless oil.

Under the same conditions, the reagent **2a** (75.0 mg, 0.207 mmol, 1.5 equiv) gave full conversion in 2.5 h and the desired product **5d** (23.2 mg, 86%, dr 1.2:1) was obtained as a colorless oil.

Under the same conditions, the reagent **2y** (83.4 mg, 1.5 equiv, 0.207 mmol) gave full conversion in 1 h and the desired product **5d** (23.5 mg, 86%, dr 1.4:1) was obtained as a colorless oil.

*3-Fluoro-2-methyl-2-(3-nitrophenyl)oxirane (**5d**).*[12a] ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (ddt, J = 2.2, 1.7, 0.5 Hz, 1H), 8.22−8.16 (m, 3H)^{trans,cis}, 7.79−7.74 (m, 1H), 7.66−7.61 (m, 1H), 7.60−7.53 (m, 2H)$^{trans,\ cis}$, 5.60 (d, J = 87.5 Hz, 1H)^{cis}, 5.38 (dq, J = 87.4, 0.5 Hz, 1H)^{trans}, 1.87 (dd, J = 1.2, 0.5 Hz, 3H)^{trans}, 1.70 (d, J = 2.8 Hz, 3H)^{cis}. ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 148.6, 148.4, 140.1 (C−F, d, $^3J_{C-F}$ = 3.9 Hz), 138.2 (C−F, d, $^3J_{C-F}$ = 4.4 Hz), 133.0, 131.6, 129.9, 129.5, 123.5, 123.4, 122.2, 120.9, 93.3 (C−F, d, $^1J_{C-F}$ = 276.9 Hz), 93.2 (C−F, d, $^1J_{C-F}$ = 271.4 Hz), 62.0 (C−F, d, $^2J_{C-F}$ = 17.1 Hz), 60.8 (C−F, d, $^2J_{C-F}$ = 17.0 Hz), 20.2 (C−F, d, $^3J_{C-F}$ = 4.4 Hz), 16.2 (C−F, d, $^3J_{C-F}$ = 3.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ −150.71 (d, J = 87.4 Hz)^{trans}, −154.44 (dq, J = 87.8, 2.7 Hz)^{cis}.

Procedure for Obtaining Diaryl Sulfides 6. *Phenyl(2,3,4,5-tetramethylphenyl)sulfane (**6a**).* The side product **6a** was isolated from the reactions using the reagent **2a**. Isolation by silica gel column chromatography, eluted with 100% petroleum ether (R_f 0.40). **6a** obtained as a white solid. Mp: 64−65 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25−7.19 (m, 3H), 7.15−7.04 (m, 3H), 2.38 (s, 3H), 2.27 (s, 3H), 2.25 (s, 3H), 2.24 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 138.5, 137.3, 136.5, 136.3, 134.8, 134.1, 129.0, 128.8, 127.7, 125.4, 20.7, 17.9, 17.1, 2. Due to poor ionization under HRMS conditions a molecular ion cannot be detected.

*(2,4-Dimethylphenyl)(phenyl)sulfane (**6f**).* The side product **6f** was isolated from the reactions using the reagent **2f**. Isolation by silica gel column chromatography, eluted with 100% petroleum ether (R_f 0.43). **6f** obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 (d, J = 7.9 Hz, 1H), 7.17−7.12 (m, 2H), 7.09−7.01 (m, 4H), 6.93−6.89 (m, 1H), 2.26 (s, 4H), 2.25 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 141.0, 138.7, 137.5, 134.6, 131.7, 129.4, 129.1, 128.4, 127.7, 125.9, 21.2, 20.7. Due to poor ionization under HRMS conditions a molecular ion cannot be detected.

*(2,3-Dichlorophenyl)(2,4-dimethylphenyl)sulfane (**6y**).* The side-product **6y** was isolated from the reactions using the reagent **2y**. Isolation by silica gel column chromatography, eluted with 100% petroleum ether (R_f 0.50). **6y** obtained as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, J = 7.8 Hz, 1H), 7.20−7.16 (m, 2H), 7.08 (ddt, J = 7.9, 2.2, 0.8 Hz, 1H), 6.94 (t, J = 8.0 Hz, 1H), 6.42 (dd,

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J = 8.1, 1.4 Hz, 1H), 2.38 (s, 3H), 2.33 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 142.9, 140.7, 140.6, 136.8, 133.5, 132.2, 128.9, 128.3, 127.3, 126.5, 126.5, 124.6, 21.4, 20.6. Due to poor ionization under HRMS conditions a molecular ion cannot be detected.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02561.

Experimental procedures for control experiments, X-ray crystallography data, and NMR spectra (PDF)

Accession Codes

CCDC 2031999−2032003 and 2032388 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

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■ REFERENCES

(1) Reviews covering recent progress in fluorine chemistry: (a) Gouverneur, V.; Seppelt, K. Introduction: Fluorine Chemistry. *Chem. Rev.* **2015**, *115* (2), 563−565. (b) Ni, C.; Hu, M.; Hu, J. Good Partnership between Sulfur and Fluorine: Sulfur-Based Fluorination and Fluoroalkylation Reagents for Organic Synthesis. *Chem. Rev.* **2015**, *115* (2), 765−825. (c) Fustero, S.; Sedgwick, D. M.; Román, R.; Barrio, P. Recent Advances in the Synthesis of Functionalised Monofluorinated Compounds. *Chem. Commun.* **2018**, *54* (70), 9706−9725. (d) Ni, C.; Hu, J. The Unique Fluorine Effects in Organic Reactions: Recent Facts and Insights into Fluoroalkylations. *Chem. Soc. Rev.* **2016**, *45* (20), 5441−5454. (e) Preshlock, S.; Tredwell, M.; Gouverneur, V. 18F-Labeling of Arenes and Heteroarenes for Applications in Positron Emission Tomography. *Chem. Rev.* **2016**, *116* (2), 719−766.

(2) For reviews on fluorine containing pharmaceuticals, see: (a) Wang, J.; Sánchez-Roselló, M.; Aceña, J. L.; Pozo, C. D.; Sorochinsky, A. E.; Fustero, S.; Soloshonok, V. A.; Liu, H. Fluorine in Pharmaceutical Industry: Fluorine-Containing Drugs Introduced to the Market in the Last Decade (2001−2011). *Chem. Rev.* **2014**, *114* (4), 2432−2506. (b) Wang, J.; Sánchez-Roselló, M.; Aceña, J. L.; Pozo, C. D.; Sorochinsky, A. E.; Fustero, S.; Soloshonok, V. A.; Liu, H. Fluorine in Pharmaceutical Industry: Fluorine-Containing Drugs Introduced to the Market in the Last Decade (2001−2011). *Chem. Rev.* **2014**, *114* (4), 2432−2506. (c) Zhou, Y.; Wang, J.; Gu, Z.; Wang, S.; Zhu, W.; Aceña, J. L.; Soloshonok, V. A.; Izawa, K.; Liu, H. Next Generation of Fluorine-Containing Pharmaceuticals, Compounds Currently in Phase II-III Clinical Trials of Major Pharmaceutical Companies: New Structural Trends and Therapeutic Areas. *Chem. Rev.* **2016**, *116* (2), 422−518. (d) Mei, H.; Remete, A. M.; Zou, Y.; Moriwaki, H.; Fustero, S.; Kiss, L.; Soloshonok, V. A.; Han, J. Fluorine-Containing Drugs Approved by the FDA in 2019. *Chin. Chem. Lett.* **2020**, *31* (9), 2401−2413.

(3) Fluorine-containing agrochemicals: Fujiwara, T.; O'Hagan, D. Successful Fluorine-Containing Herbicide Agrochemicals. *J. Fluorine Chem.* **2014**, *167*, 16−29.

(4) Organofluorine compounds in materials: Berger, R.; Resnati, G.; Metrangolo, P.; Weber, E.; Hulliger, J. Organic Fluorine Compounds: a Great Opportunity for Enhanced Materials Properties. *Chem. Soc. Rev.* **2011**, *40* (7), 3496.

(5) Campbell, M. G.; Ritter, T. Modern Carbon-Fluorine Bond Forming Reactions for Aryl Fluoride Synthesis. *Chem. Rev.* **2015**, *115* (2), 612−633.

(6) Hiyama, T., Yamamoto, H.Organofluorine Building Blocks. In *Organofluorine Compounds*; Yamamoto, H., Eds.; Springer: Berlin, 2000; DOI: 10.1007/978-3-662-04164-2_3.

(7) For a review on fluorinated carbenes: (a) Brahms, D. L. S.; Dailey, W. P. Fluorinated Carbenes. *Chem. Rev.* **1996**, *96* (5), 1585−1632. (b) Schlosser, M.; Heinz, G. Monofluorocarbene and Itssyn/Anti Selectivity. *Angew. Chem., Int. Ed. Engl.* **1968**, *7* (10), 820−821 For use of $CHFBr_2$ as a reagent for monofluorocarbene generation, see:. Schlosser, M.; Heinz, G. Monofluor-Carben Und Seine syn/Anti-Selektivität. *Angew. Chem.* **1968**, *80* (20), 849−850. (c) Hahnfeld, J. L.; Burton, D. J. Monofluorocarbene: The Synthesis of Fluorocyclopropanes. *Tetrahedron Lett.* **1975**, *16* (22−23), 1819−1822 For $CHFI_2$ as a reagent for monofluorocarbene generation, see:. (d) Kawabata, N.; Tanimoto, M.; Fujiwara, S. Synthesis of Monohalocyclopropane Derivatives from Olefins by the Reaction with Trihalomethanes and Copper. *Tetrahedron* **1979**, *35* (16), 1919−1923. (e) Nishimura, J.; Furukawa, J. The Formation of a Halogenocarbenoid of Zinc. A Novel Synthetic Route to Halogenocyclopropane Derivatives. *J. Chem. Soc. D* **1971**, No. 21, 1375. (f) Beaulieu, L.-P. B.; Schneider, J. F.; Charette, A. B. Highly Enantioselective Simmons-Smith Fluorocyclopropanation of Allylic Alcohols via the Halogen Scrambling Strategy of Zinc Carbenoids. *J. Am. Chem. Soc.* **2013**, *135* (21), 7819−7822. For CHF_2I as a reagent for monofluorocarbenoid generation, see: (g) Navuluri, C.; Charette, A. B. Diastereoselective Fluorocyclopropanation of Chiral Allylic Alcohols Using an α-Fluoroiodomethylzinc Carbenoid. *Org. Lett.* **2015**, *17* (17), 4288−4291.

(8) For reviews covering monofluoromethylation, see: (a) Hu, J.; Zhang, W.; Wang, F. Selective Difluoromethylation and Monofluoromethylation Reactions. *Chem. Commun.* **2009**, No. 48, 7465. (b) Reichel, M.; Karaghiosoff, K. Reagents for Selective Fluoromethylation: A Challenge in Organofluorine Chemistry. *Angew. Chem., Int. Ed.* **2020**, *59* (30), 12268−12281; *Angew. Chem.* **2020**, *132* (30), 12364−12377. (c) For early examples, see: Orr, J. C.; Edwards, J.; Bowers, A. Syntex Corp. US 3080395, 1963. (d) Lesuisse, D.; Gourvest, J. F.; Hartmann, C.; Tric, B.; Benslimane, O.; Philibert, D.; Vevert, J. P. Synthesis and Evaluation of a New Series of Mechanism-Based Aromatase Inhibitors. *J. Med. Chem.* **1992**, *35* (9), 1588−1597. (e) Parisi, G.; Colella, M.; Monticelli, S.; Romanazzi, G.; Holzer, W.;

Langer, T.; Degennaro, L.; Pace, V.; Luisi, R. Exploiting a "Beast" in Carbenoid Chemistry: Development of a Straightforward Direct Nucleophilic Fluoromethylation Strategy. *J. Am. Chem. Soc.* **2017**, *139* (39), 13648−13651 Recent examples of monofluoromethylation:. (f) Liu, Y.; Lu, L.; Shen, Q. Monofluoromethyl-Substituted Sulfonium Ylides: Electrophilic Monofluoromethylating Reagents with Broad Substrate Scopes. *Angew. Chem., Int. Ed.* **2017**, *56* (33), 9930−9934; *Angew. Chem.* **2017**, *129* (33), 10062−10066. (g) Nomura, Y.; Tokunaga, E.; Shibata, N. Inherent Oxygen Preference in Enolate Monofluoromethylation and a Synthetic Entry to Monofluoromethyl Ethers. *Angew. Chem., Int. Ed.* **2011**, *50*, 1885−1889; *Angew. Chem.* **2011**, *123* (8), 1925−1929. (h) Shen, X.; Zhou, M.; Ni, C.; Zhang, W.; Hu, J. Direct Monofluoromethylation of O-, S-, N-, and P-Nucleophiles with $PhSO(NTs)CH_2F$: the Accelerating Effect of α-Fluorine Substitution. *Chem. Sci.* **2014**, *5* (1), 117−122. (i) Senatore, R.; Malik, M.; Spreitzer, M.; Holzer, W.; Pace, V. Direct and Chemoselective Electrophilic Monofluoromethylation of Heteroatoms (O-, S-, N-, P-, Se-) with Fluoroiodomethane. *Org. Lett.* **2020**, *22* (4), 1345−1349.

(9) Indirect methods for the introduction of monofluormethylene synthon. For example, via halofluorocarbene: (a) Oliver, J.; Rao, U.; Emerson, M. Synthesis of Monofluorocyclopropane Derivatives. *Tetrahedron Lett.* **1964**, *5* (46), 3419−3425. (b) Kirihara, M.; Ogata, T.; Itou, A.; Naito, S.; Kishida, M.; Yamazaki, K.; Tabata, H.; Takahashi, H. Synthesis of Monofluoromethylcyclopropanes from Alkenes without Using Freons: Novel Synthesis of Chlorofluoromethyl Phenyl Sulfide and Its Application in Cyclopropanation. *Chem. Lett.* **2013**, *42* (11), 1377−1379 Via chlorofluoromethyl phenyl sulfide:.

(10) Fluorinated sulfoximines for fluoroepoxide synthesis: (a) Zhang, W.; Hu, J. Efficient Synthesis and Ring-Opening Reactions of Monofluorinated Epoxides Derived from α-Fluorosulfoximines. *Adv. Synth. Catal.* **2010**, *352* (16), 2799−2804. (b) Luo, T.; Zhang, R.; Zhang, W.; Shen, X.; Umemoto, T.; Hu, J. Divergent Rearrangements of Cyclopropyl-Substituted Fluoroepoxides Involving C-F Bond Cleavage and Formation. *Org. Lett.* **2014**, *16* (3), 888−891. (c) Luo, T.; Zhang, R.; Shen, X.; Zhang, W.; Ni, C.; Hu, J. Brønsted Acid-Catalyzed 1,2-Fluorine Migration with Fluoroepoxides. *Dalton Trans.* **2015**, *44* (45), 19636−19641. Fluorinated sulfoximines for fluorocyclopropane synthesis: (d) Shen, X.; Zhang, W.; Zhang, L.; Luo, T.; Wan, X.; Gu, Y.; Hu, J. Enantioselective Synthesis of Cyclopropanes That Contain Fluorinated Tertiary Stereogenic Carbon Centers: A Chiral α-Fluoro Carbanion Strategy. *Angew. Chem., Int. Ed.* **2012**, *51* (28), 6966−6970; *Angew. Chem.* **2012**, *124* (28), 7072−7076.

(11) (a) Pons, A.; Tognetti, V.; Joubert, L.; Poisson, T.; Pannecoucke, X.; Charette, A. B.; Jubault, P. Catalytic Enantioselective Cyclopropanation of α-Fluoroacrylates: An Experimental and Theoretical Study. *ACS Catal.* **2019**, *9* (3), 2594−2598. (b) Monticelli, S.; Colella, M.; Pillari, V.; Tota, A.; Langer, T.; Holzer, W.; Degennaro, L.; Luisi, R.; Pace, V. Modular and Chemoselective Strategy for the Direct Access to α-Fluoroepoxides and Aziridines via the Addition of Fluoroiodomethyllithium to Carbonyl-Like Compounds. *Org. Lett.* **2019**, *21* (2), 584−588. (c) Colella, M.; Tota, A.; Großjohann, A.; Carlucci, C.; Aramini, A.; Sheikh, N. S.; Degennaro, L.; Luisi, R. Straightforward Chemo- and Stereoselective Fluorocyclopropanation of Allylic Alcohols: Exploiting the Electrophilic Nature of the Not so Elusive Fluoroiodomethyllithium. *Chem. Commun.* **2019**, *55* (58), 8430−8433. (d) Decaens, J.; Couve-Bonnaire, S.; Charette, A.; Poisson, T.; Jubault, P. Synthesis of Fluoro, Monofluoromethyl, Difluoromethyl and Trifluoromethyl-Substituted Three Membered Rings. *Chem. Eur. J.* **2020**, DOI: 10.1002/chem.202003822.

(12) (a) Veliks, J.; Kazia, A. Fluoromethylene Transfer from Diarylfluoromethylsulfonium Salts: Synthesis of Fluorinated Epoxides. *Chem. - Eur. J.* **2019**, *25* (15), 3786−3789. (b) Melngaile, R.; Sperga, A.; Baldridge, K. K.; Veliks, J. Diastereoselective Monofluorocyclopropanation Using Fluoromethylsulfonium Salts. *Org. Lett.* **2019**, *21* (17), 7174−7178. (c) Kazia, A.; Melngaile, R.; Mishnev, A.; Veliks, J. Johnson-Corey-Chaykovsky Fluorocyclopropanation of Double Activated Alkenes: Scope and Limitations. *Org. Biomol. Chem.* **2020**, *18* (7), 1384−1388.

(13) Prakash, G. K. S.; Ledneczki, I.; Chacko, S.; Olah, G. A. Direct Electrophilic Monofluoromethylation. *Org. Lett.* **2008**, *10* (4), 557−560.

(14) (a) Lo, H. S.; Hui, K. P. Y.; Lai, H.-M.; Khan, K. S.; Kaur, S.; Huang, J.; Li, Z.; Chan, A. K. N.; Cheung, H. H.-Y.; Ng, K.-C.; Ho, J. C. W.; Chen, Y. W.; Ma, B.; Cheung, P. M.-H.; Shin, D.; Wang, K.; Lee, M.-H.; Selisko, B.; Eydoux, C.; Guillemot, J.-C.; Canard, B.; Wu, K.-P.; Liang, P.-H.; Dikic, I.; Zuo, Z.; Chan, F. K. L.; Hui, D. S. C.; Mok, V. C. T.; Wong, K.-B.; Ko, H.; Aik, W. S.; Chan, M. C. W.; Ng, W.-L. Simeprevir Potently Suppresses SARS-CoV-2 Replication and Synergizes with Remdesivir. *bioRxiv* **2020**, DOI: 10.1101/2020.05.26.116020. (b) Ma, C.; Sacco, M. D.; Hurst, B.; Townsend, J. A.; Hu, Y.; Szeto, T.; Zhang, X.; Tarbet, B.; Marty, M. T.; Chen, Y.; Wang, J. Boceprevir, GC-376, and Calpain Inhibitors II, XII Inhibit SARS-CoV-2 Viral Replication by Targeting the Viral Main Protease. *bioRxiv* **2020**, DOI: 10.1101/2020.04.20.051581.

(15) For review on cyclopropane-containing pharmaceuticals, see: Talele, T. T. The "Cyclopropyl Fragment" Is a Versatile Player That Frequently Appears in Preclinical/Clinical Drug Molecules. *J. Med. Chem.* **2016**, *59* (19), 8712−8756.

(16) Meanwell, N. A. Fluorine and Fluorinated Motifs in the Design and Application of Bioisosteres for Drug Design. *J. Med. Chem.* **2018**, *61* (14), 5822−5880.

(17) On fluorocyclopropanes, see: (a) Jubault, P.; Pons, A.; Poisson, T.; Pannecoucke, X.; Charette, A. Synthesis and Applications of Fluorocyclopropanes. *Synthesis* **2016**, *48* (23), 4060−4071. (b) David, E.; Milanole, G.; Ivashkin, P.; Couve-Bonnaire, S.; Jubault, P.; Pannecoucke, X. Syntheses and Applications of Monofluorinated Cyclopropanes. *Chem. - Eur. J.* **2012**, *18* (47), 14904−14917. (c) Thomson, C. J.; Zhang, Q.; Al-Maharik, N.; Bühl, M.; Cordes, D. B.; Slawin, A. M. Z.; O'Hagan, D. Fluorinated Cyclopropanes: Synthesis and Chemistry of the Aryl α,β,β-Trifluorocyclopropane Motif. *Chem. Commun.* **2018**, *54* (60), 8415−8418.

(18) Scifinder search on monofluorocyclopropane analogues of mentioned drug molecules. Recent report on improvements upon incorporation of fluorocyclopropane ring in drug molecule: Veliks, J.; Videja, M.; Kinens, A.; Bobrovs, R.; Priede, M.; Kuka, J. Trans-Fluorine Effect in Cyclopropane: Diastereoselective Synthesis of Fluorocyclopropyl Cabozantinib Analogs. *ACS Med. Chem. Lett.* **2020**, DOI: 10.1021/acsmedchemlett.0c00220.

(19) (a) Leitão, E. P. T. Electrophilic reagents for monohalomethylation, their preparation and their uses. Patent WO2012056201 A2, 2012-03-05. (b) Hong, X.; Liu, Y.; Lu, L.; Shen, Q. Monofluoromethyl-Substituted Sulfonium Ylides: Preparation, Structure-Reactivity Study and Substrate Scope. *Chin. J. Chem.* **2020**, DOI: 10.1002/cjoc.202000206.

(20) Rydzik, A. M.; Leung, I. K. H.; Thalhammer, A.; Kochan, G. T.; Claridge, T. D. W.; Schofield, C. J. Fluoromethylated Derivatives of Carnitine Biosynthesis Intermediates - Synthesis and Applications. *Chem. Commun.* **2014**, *50* (10), 1175−1177.

(21) Lal, G. S. Site-Selective Fluorination of Organic Compounds Using 1-Alkyl-4-Fluoro-1,4-Diazabicyclo[2.2.2]Octane Salts (Selectfluor Reagents). *J. Org. Chem.* **1993**, *58* (10), 2791−2796.

(22) https://www.alfa.com.

(23) For examples of the Johnson−Corey−Chaykovsky reaction, see: (a) Johnson, A. W.; Lacount, R. B. The Chemistry of Ylids. VI. Dimethylsulfonium Fluorenylide—A Synthesis of Epoxides1. *J. Am. Chem. Soc.* **1961**, *83* (2), 417−423. (b) Corey, E. J.; Chaykovsky, M. Dimethyloxosulfonium Methylide ($(CH_3)_2SOCH_2$) and Dimethylsulfonium Methylide ($(CH_3)_2SCH_2$). Formation and Application to Organic Synthesis. *J. Am. Chem. Soc.* **1965**, *87* (6), 1353−1364. (c) Zhurakovskyi, O.; Türkmen, Y. E.; Löffler, L. E.; Moorthie, V. A.; Chen, C. C.; Shaw, M. A.; Crimmin, M. R.; Ferrara, M.; Ahmad, M.; Ostovar, M.; Matlock, J. V.; Aggarwal, V. K. Enantioselective Synthesis of the Cyclopiazonic Acid Family Using Sulfur Ylides. *Angew. Chem., Int. Ed.* **2018**, *57* (5), 1346−1350; *Angew. Chem.* **2018**,

https://dx.doi.org/10.1021/acs.joc.0c02561
J. Org. Chem. 2021, 86, 3196−3212

130, 1360−1364. (d) Hock, K. J.; Hommelsheim, R.; Mertens, L.; Ho, J.; Nguyen, T. V.; Koenigs, R. M. Corey-Chaykovsky Reactions of Nitro Styrenes Enable Cis-Configured Trifluoromethyl Cyclopropanes. *J. Org. Chem.* **2017**, *82* (15), 8220−8227. (e) Duan, Y.; Zhou, B.; Lin, J.-H.; Xiao, J.-C. Diastereoselective Johnson-Corey-Chaykovsky Trifluoroethylidenation. *Chem. Commun.* **2015**, *51* (66), 13127−13130.

(24) Saegusa, T.; Matsumoto, S. Connection of Propagating Species and Rate of Propagation in Cationic Polymerization of Tetrahydrofuran. *Macromolecules* **1968**, *1* (5), 442−445.

(25) Xu, F.; Corley, E.; Zacuto, M.; Conlon, D. A.; Pipik, B.; Humphrey, G.; Murry, J.; Tschaen, D. Asymmetric Synthesis of a Potent, Aminopiperidine-Fused Imidazopyridine Dipeptidyl Peptidase IV Inhibitor. *J. Org. Chem.* **2010**, *75* (5), 1343−1353.

(26) Jalal, S.; Sarkar, S.; Bera, K.; Maiti, S.; Jana, U. Synthesis of Nitroalkenes Involving a Cooperative Catalytic Action of Iron(III) and Piperidine: A One-Pot Synthetic Strategy to 3-Alkylindoles, 2*H*-Chromenes and *N*-Arylpyrrole. *Eur. J. Org. Chem.* **2013**, *2013*, 4823.

(27) Chen, H. Y.; Gou, M.; Wang, J. B. De Novo endo-Functionalized Organic Cages as Cooperative Multi-hydrogen-bond-donating Catalysts. *Chem. Commun.* **2017**, *53*, 3524.

(28) Yu, S.-W.; Zhao, S.-H.; Chen, H.; Xu, X.-Y.; Yuan, W.-C.; Zhang, X.-M. Construction of Novel Kojic Acid Fused Furans by Domino Reactions of a Kojic Acid Derivative with (Z)-Bromonitroalkenes. *Chemistry Select* **2018**, *3*, 4827.

https://dx.doi.org/10.1021/acs.joc.0c02561
J. Org. Chem. 2021, 86, 3196−3212