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Acid-Catalyzed Hydrothiolation of *gem*-Difluorostyrenes to Access α,α-Difluoroalkylthioethers

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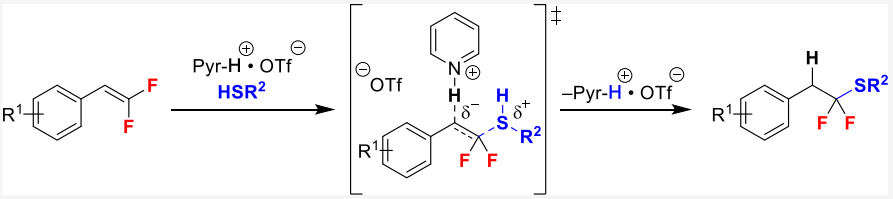

ABSTRACT: The substitution of hydrogen atoms with fluorine in bioactive molecules can greatly impact physicochemical, pharmacokinetic, and pharmacodynamic properties. However, current synthetic methods cannot readily access many fluorinated motifs, which impedes utilization of these groups. Thus, the development of new methods to introduce fluorinated functional groups is critical for developing the next generation of biological probes and therapeutic agents. The synthesis of one such substructure, the α,α-difluoroalkylthioether, typically requires specialized conditions that necessitate early-stage installation. A late-stage and convergent approach to access α,α-difluoroalkylthioethers could involve nucleophilic addition of thiols across *gem*-difluorostyrenes. Unfortunately, under basic conditions, nucleophilic addition to *gem*-difluorostyrenes generates an anionic intermediate that can undergo facile elimination of fluoride to generate α-fluorovinylthioethers. To overcome this decomposition, we herein exploit an acid-based catalyst system to facilitate simultaneous nucleophilic addition and protonation of the unstable intermediate. Ultimately, the optimized mild conditions afford the desired α,α-difluoroalkylthioethers in high selectivity and moderate to excellent yields. These α,α-difluoroalkylthioethers are less nucleophilic and more oxidatively stable relative to nonfluorinated thioethers, suggesting the potential application of this unexplored functional group in biological probes and therapeutic agents.

INTRODUCTION

The substitution of hydrogen atoms with fluorine in bioactive molecules can greatly impact physicochemical, pharmacokinetic, and pharmacodynamic properties.[1−5] Thus, the development of new strategies to access fluorinated functional groups is critical for developing the next generation of biological probes and therapeutic agents.[4,6] From a synthetic standpoint, the incorporation of fluorine onto an organic substrate can perturb standard properties, which enables new and specialized reactivities creating opportunities for accessing drug-like substructures.[5] The synthesis of one such substructure, α,α-difluoroalkylthioether, currently requires specialized conditions that often necessitate early-stage installation.[7−10] Though a recently published general late-stage strategy generates terminal α,α-difluoroalkylthioethers,[11] convergent strategies bringing together two larger fragments remain largely underrepresented.

A late-stage convergent approach to access α,α-difluoroalkylthioethers could involve nucleophilic addition of thiols across *gem*-difluorostyrenes. Unfortunately, under basic conditions, nucleophilic addition to *gem*-difluorostyrenes generates an anionic intermediate that can undergo facile elimination of fluoride to generate α-fluorovinylthioethers (Scheme 1A, a).[12,13] To avoid this elimination, the β-fluoroanionic intermediate can be trapped intramolecularly with an aldehyde or protonated using a base-catalyzed strategy (Scheme 1A, c−d).[14] Alternately, one electron processes add thiyl radicals to *gem*-difluorostyrenes (Scheme 1A, b).[15] However, these strategies only function with thiophenol-derived nucleophiles. In contrast, the corresponding reactions of *gem*-difluorostyrenes with alkylthiol-derived nucleophiles typically also involve elimination of fluoride (Scheme 1A, e).[12,16−18] Herein, we report conditions for a selective synthesis of α,α-difluoroalkylthioethers that involves acid-catalyzed addition of thiols across *gem*-difluorostyrenes. Preliminary studies demonstrate that these fluorinated thioethers are less nucleophilic and more oxidatively stable relative to nonfluorinated thioethers.[1,2]

RESULTS AND DISCUSSION

We initially envisioned that access to alkylthiol-derived α,α-difluoroalkylthioethers could be accomplished using a base-catalyzed strategy that has successfully added phenols and

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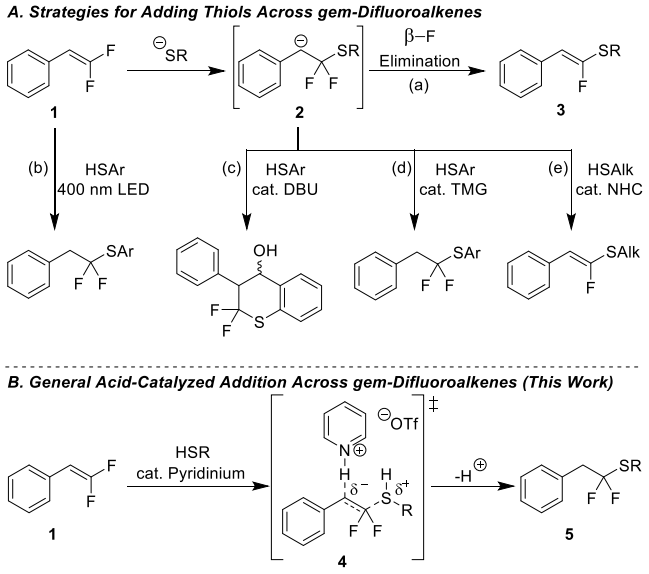
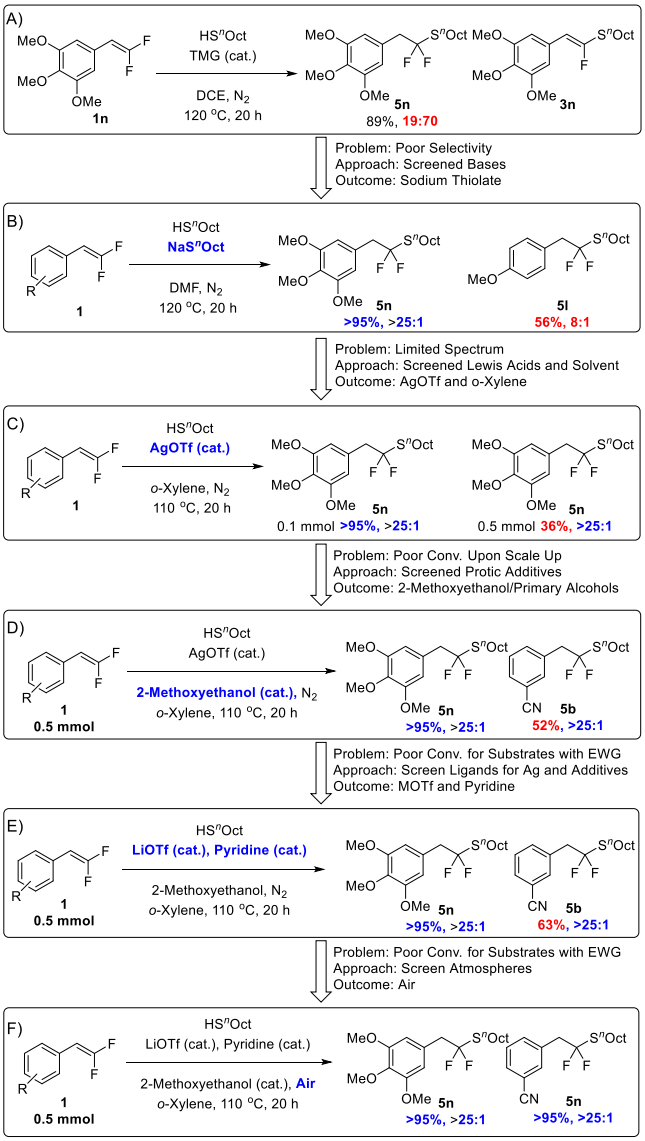
Scheme 1. Strategies for Generating α,α-Difluoroalkylthioethers



thiophenols across fluorostyrenes (Scheme 2A).[14,19] Unfortunately, these initial conditions utilizing 1,1,3,3-tetramethylguanidine (TMG) selectively afforded addition/elimination product **3n** (Scheme 2A). Upon evaluation of alternate bases, use of catalytic amounts of the corresponding sodium thiolate improved selectivity for the desired α,α-difluoroalkylthioether product **5n** (Scheme 2B). However, these conditions did not apply to a variety of *gem*-difluorostyrene substrates. Borrowing inspiration from Ag-mediated addition of fluoride to *gem*-difluorostyrenes,[20] we envisioned that a Ag-based catalyst system might deliver S-based radicals and prevent the elimination of fluoride. In fact, the use of AgOTf in catalytic amounts provided desired product **5n** in excellent selectivity (Scheme 2C). Unfortunately, when scaled to 0.5 mmol, this Ag-catalyzed system suffered from poor conversion, and routine optimization (time, temperature, solvent, and catalyst loading) did not substantially improve the reaction. Considering the proposed mechanism of nucleophilic addition across the alkene, we explored the use of additives that might protonate the presumed unstable intermediate β,β-difluorosytrenyl anion (Scheme 1A, **2**) and deliver the desired product. To this end, the addition of primary alcohols, such as 2-methoxyethanol, improved the selectivity (Scheme 2D). Upon further optimization, the addition of pyridine-derived ligands rendered Ag unnecessary and enabled use of alkali triflate salts (Scheme 2E). Using a system of LiOTf (10 mol %), pyridine (20 mol %), and 2-methoxyethanol (2 equiv.) in *o*-xylene, the use of an atmosphere of air improved the rate of reaction relative to an atmosphere of N_2 (Scheme 2F). However, when run under a pure O_2 atmosphere, this optimized system only generated trace amounts of the desired product, presumably from extensive oxidative degradation of the thiol nucleophile (see Supporting Information; Figure S1).

A range of *gem*-difluorostyrene substrates reacted with alkylthiols to deliver α,α-difluoroalkylthioethers in high selectivity over α-fluorovinylthioether side products (typically >25:1; Scheme 3). Electron-deficient difluorostyrenes containing nitrile, nitro, or trifluoromethyl groups reacted smoothly giving excellent yields (**5b**–**5f**; 72–92%). *gem*-Difluorostyrenes bearing halogens and pseudohalogens were compatible and

Scheme 2. Optimization Workflow of Selective Hydrofunctionalization of *gem*-Difluorostyrenes



afforded products in good yields (**5g**–**5k**; 61–82%). Additionally, amides were compatible with this reaction giving the desired product in moderate yield (**5u**; 63%). Interestingly, a substrate bearing a competing secondary electrophilic site, such as an α,β-unsaturated ester, produced α,α-difluoroalkylthioether product (**5t**; 76%) in high selectivity. Substrates containing electron-donating groups afforded respectable yields of the anticipated products (**5l**–**5q**; 62–95%). Unfortunately, a *gem*-difluorostyrene bearing a free phenol suffered from low overall conversion and poor yields (**5v**; 22%), though reactions of protected phenols proceeded smoothly under the optimized conditions (**5w**–**5x**; 50–87%). Substrates containing dibenzothiophene or pyrazole were also compatible with this system (**5y**–**5z**; 53–72%). However, other heterocycle scaffolds including pyridine, tryptophan, thiazole, and phenothiazines did not couple. Furthermore, a substrate with a fully substituted alkene reacted well under the standard conditions to generate the desired product (**5aa**; 73%). However, no desired products were obtained when nonstyrene-derived *gem*-difluoroalkenes were used.

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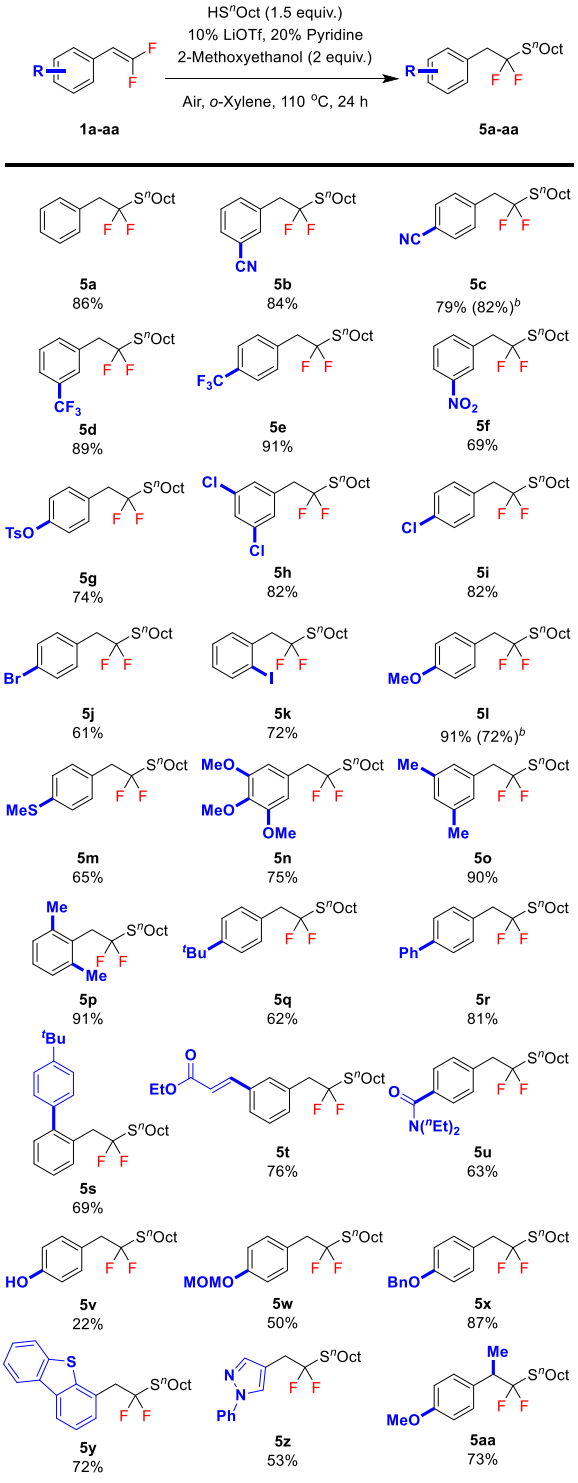
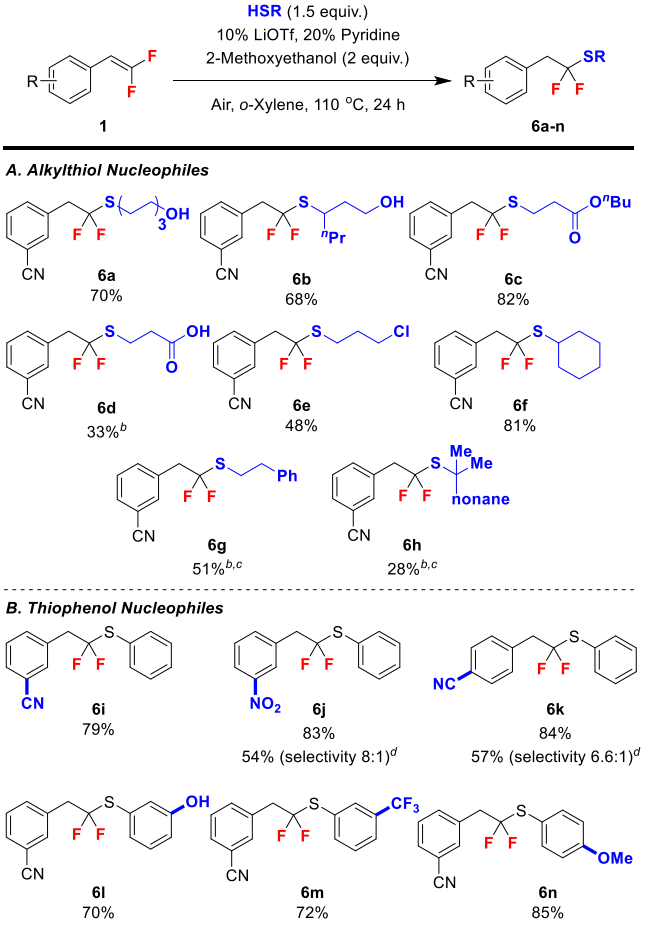
Scheme 3. Scope of *gem*-Difluorostyrenes[a]



[a]Unless otherwise stated, all reactions were carried out with **1** (0.5 mmol), 1-octanethiol (0.75 mmol), LiOTf (10 mol%), pyridine (20 mol%), and 2-methoxyethanol (1.0 mmol) in *o*-xylene heated at 110 °C for 24 h under an atmosphere of air. [b]Reaction was carried out with **1** (1.0 mmol), 1-octanethiol (1.50 mmol), LiOTf (10 mol%), pyridine (20 mol%), and 2-methoxyethanol (2.0 mmol) in *o*-xylene heated at 110 °C for 24 h under an atmosphere of air. Isolated yields have >25:1 selectivity, and represent an average of two independent reactions.

Under the optimized conditions, primary aliphatic thiols reacted efficiently in high selectivity (>25:1), though secondary

Scheme 4. Scope of Thiol Nucleophiles[a]



[a]Unless otherwise stated, all reactions were carried out with **1** (0.5 mmol), thiol (0.75 mmol), LiOTf (10 mol%), pyridine (20 mol%), and 2-methoxyethanol (1.0 mmol) in *o*-xylene heated at 110 °C for 24 h under an atmosphere of air. Isolated yields have >25:1 selectivity and represent an average of two independent reactions. [b]Pyridine (200 mol%) was used. [c]Reaction heated to 120 °C. [d]**8** (0.5 mmol), PhSH (1.5 mmol), TMG (5 mol%) in DCE heated to 100 °C for 20 h under an atmosphere of N_2.

and tertiary thiols reacted sluggishly (Scheme 4A). While cyclohexanethiol reacted smoothly (**6f**; 81%), increasing steric bulk near sulfur (e.g., tertiary or phenethyl thiols) decreased both conversion and yields (**6h**–**6i**; 28–56%) and required more forcing conditions (120 °C, 200 mol % pyridine) to generate product. Unfortunately, further increasing the temperature, equivalents of the nucleophile, or reaction times did not improve the reactivity of these hindered substrates. Alkyl thiols bearing carbonyl groups, including esters, were well tolerated (**6c**; 88%). Free carboxylic acids were compatible, though this reaction required the addition of excess pyridine (**6d**; 33%). The reaction of substrates bearing an alcohol and a thiol selectively reacted at the thiol (**6a**–**6b**; 68–73%). Interestingly, a substrate containing a primary halogen did not undergo intramolecular cyclization but instead generated the linear haloalkane product in moderate yield (**6e**; 48%). Furthermore, the use of cysteine and its protected equivalents was unsuccessful, which in its current form, discourages application of the method toward

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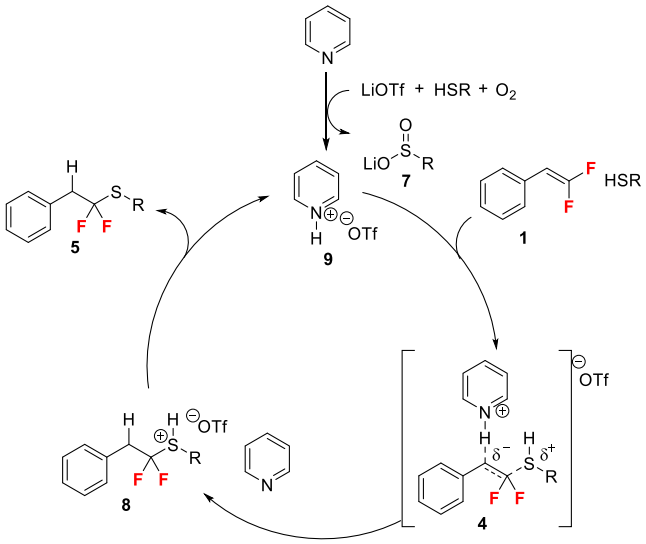
peptide and protein bioconjugation reactions. Additionally, initial attempts to adapt the reaction to aqueous biocompatible conditions did not provide appreciable quantities of difluorinated products.

In addition to alkylthiols, the optimized conditions effectively added thiophenol nucleophiles across the *gem*-difluorostyrenes (Scheme 4B). In fact, the reaction effectively coupled thiophenols with electron-deficient *gem*-difluorostyrenes (**6i**–**6k**; 79–84%), which could not be effectively coupled using our previous base-catalyzed conditions (5 mol % tetramethylguanidine, 1,2-dichlorobenzene, and 100 °C).[14]

Preliminary mechanistic studies support a general acid-catalyzed process involving concurrent nucleophilic attack of the *gem*-difluorostyrene (**1**) by the thiol and protonation by pyridinium (**9**) to generate thionium intermediate **8** (Scheme 5). Thionium **8** is then deprotonated to furnish the desired

Scheme 5. Plausible Mechanism

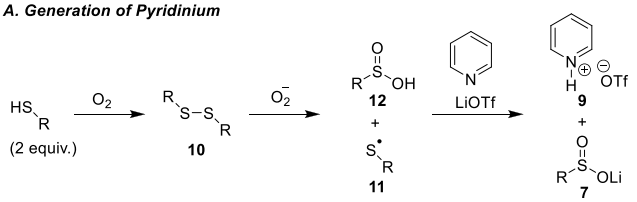


product (**5**) and regenerate pyridinium **9**. Such concerted hydrothiolation reactions of nonfluorinated alkenes has been previously suggested, though minimal experimental support exists for this mechanistic proposal.[21,22] Notably, this mechanism does not involve a β-F anionic intermediate that would typically decompose to deliver fluorovinylether side products.

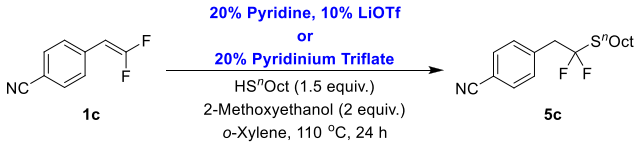
Mechanistically, both literature and probing experiments indicate that pyridine might serve as a precursor to an acid-based catalyst system. First, considering pK_as, pyridine (3.4 in DMSO) is insufficiently basic to deprotonate HS–alkyl (17 in DMSO),[23] which disfavors mechanisms that would involve deprotonation of the thiol prior to attacking the difluorostyrene.[23,24] This discrepancy in pK_a requires the formation of a more acidic species to protonate pyridine, presumably a sulfinic acid formed via oxidation of the thiol (Scheme 6A).[25−27] This initial oxidation was previously shown to generate an equivalent of superoxide,[28] which can further oxidize disulfides to sulfinic and sulfonic acids.[26] Supporting this activation sequence, under our reaction conditions, trace quantities of sulfinic and sulfonic acids were observed by LCMS (Figure S2). To probe whether oxidized sulfur-based acids could protonate pyridine and serve as a catalyst, direct use of octanesulfonic acid might eliminate the need to run the reaction in an atmosphere of air. In fact, addition of 1 mol % octanesulfonic acid under N_2 enabled the reaction of **1c** with octanethiol to proceed at the same initial rate as the

Scheme 6. Pyridinium Serves as the Active Catalyst

A. Generation of Pyridinium



B. Pyridinium is a Competent Catalyst Under N_2



Entry	Conditions	Additive	Atm.	Average Product μmol/min
1	*Pyridine + LiOTf*	-	*Air*	2.2
2	*Pyridine + LiOTf*	-	N_2	0.1
3	*Pyridine + LiOTf*	*1% Octanesulfonic Acid*	N_2	2.3
4	*Pyridinium Triflate*	-	N_2	2.5

standard reaction conditions using Pyr under air (2.3 vs 2.2 μmol/min). Furthermore, direct use of a pyridinium surrogate (e.g., Pyr–H$^+$OTf$^-$) under N_2 proceeded at a similar rate (2.5 μmol/min). Combined, these reactions support the proposed oxidative activation sequence (Scheme 6B).

Support for a two-electron process derives from a combination of linear free energy relationship and KIE studies. Specifically, a correlation with σ^- (p = −0.41, R^2 = 0.92) implicated partial anionic character at the benzylic position at the transition state (Scheme 7A). Moreover, poor correlation with $\sigma^\bullet$ (R^2 = 0.02) and σ^+ (p = −0.43, R^2 = 0.74) discounted processes that might proceed through benzyl radical or cation intermediates (see Supporting Information, Figures S3 and S4). During the course of the reaction, homocoupled nucleophile, an intermediate capable of homolytical cleavage to generate $^\bullet$SR, did form (15%, Scheme 7B); however, performing the reaction using pregenerated disulfide did not generate product **5b**, thus discounting RSSR serving as an *in situ* generated substrate (Scheme 7C). Furthermore, both competitive and parallel systems demonstrated a primary KIE, supporting a concerted general acid-catalyzed addition, rather than sequential thiol addition and subsequent proton transfer (Scheme 7D,E).

α,α-Difluorinated thioethers display decreased nucleophilicity and increased oxidative stability relative to nonfluorinated analogs. To assess nucleophilicity, compounds **13** and **5a** were subjected to standard alkylation conditions with MeI [dimethyl formamide (DMF), rt]. The nonfluorinated analog (**13**) reacted in 66% conversion over 18 h, while the corresponding α,α-difluorinated analog (**5a**) remained unreacted (Scheme 8A). These data suggest that fluorination α to S in bioactive compounds might decrease metabolic alkylation by *S*-methyltransferases and related enzymes.[29] Furthermore, upon exposure to common chemical oxidants (NaOCl, $KMnO_4$, H_2O_2, and *m*-CPBA), the nonfluorinated analog (**13**) decomposed substantially within 1 h, while the α,α-difluorinated analog (**5a**) did not degrade under extended exposure to chemical oxidants (Scheme 8B, see Supporting Information, Figure S12). When exposed to *m*-CPBA, a stronger oxidant, both the fluorinated and nonfluorinated analogs were completely oxidized. These experiments suggest that fluorination α to S might disfavor

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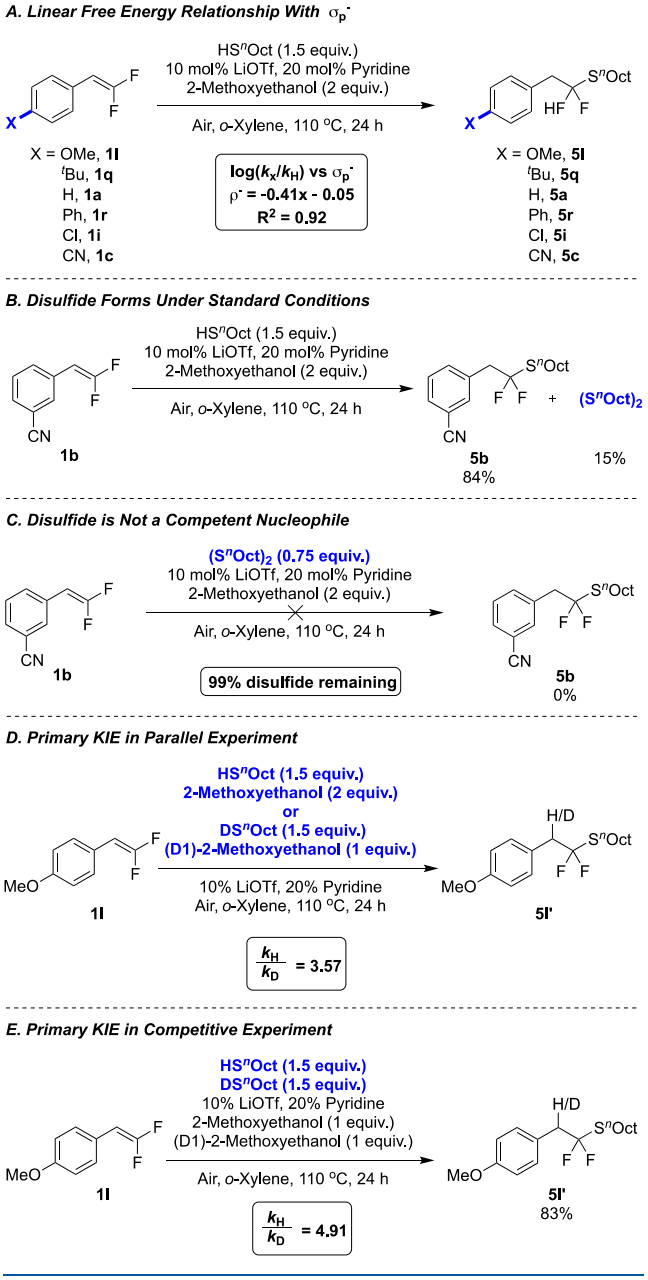
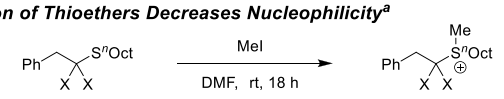
Scheme 7. Mechanistic Studies



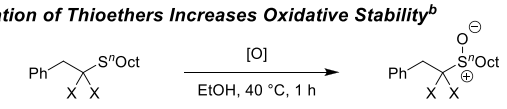
nonenzymatic oxidation, as experienced in lysosomes and peroxisomes,[30] which again highlights the potential utility of this fluorinated motif toward developing biologically active small molecules.

In conclusion, we developed a new catalytic general acid-catalyzed strategy to generate α,α-difluoroalkylthioethers in high selectivity via the addition of thiol- and thiophenol-derived nucleophiles across *gem*-difluorostyrenes. This reaction circumvents unstable anionic intermediates through a concerted acid-mediated hydrothiolation step. Additionally, these α,α-difluoroalkylthioethers are less nucleophilic and more oxidatively stable than their nonfluorinated counterparts, which should enable the strategic use of this underexplored functional group in biological probes and therapeutic agents.

Scheme 8. α,α-Difluoroalkylthioethers Resist Alkylation and Oxidation[a]



Entry	X,X	% Remaining
1	H,H (**13**)	34
2	F,F (**5a**)	>95



Entry	X,X	[O]	E^0 (V)	% Remaining
1	H,H (**13**)	NaOCl	0.94	4
2	F,F (**5a**)	NaOCl	0.94	>95
3	H,H (**13**)	$KMnO_4$	1.70	62
4	F,F (**5a**)	$KMnO_4$	1.70	>95
5	H,H (**13**)	H_2O_2	1.78	54
6	F,F (**5a**)	H_2O_2	1.78	>95
7	H,H (**13**)	mCPBA	1.96	<5
8	F,F (**5a**)	mCPBA	1.96	<5

[a]% remaining is represented by an average of two independent reactions monitored by GC-FID. [b]Thioether (0.1 mmol) and MeI (1 equiv) stirred at rt in DMF (1 mL) for 18 h. [c]Thioether (0.1 mmol) and [O] (2 equiv) heated at 40 °C in EtOH (1 mL) for 1 h.

EXPERIMENTAL SECTION

General Information. Air- and moisture-sensitive reactions were carried out in oven-dried one-dram vials sealed with a polytetrafluoroethylene (PTFE)-lined septum or glassware sealed with a rubber septum under an atmosphere of dry nitrogen. PTFE syringes equipped with stainless-steel needles were used to transfer air- and moisture-sensitive liquid reagents. Reactions were stirred using teflon-coated magnetic stir bars. Elevated temperatures were maintained using thermostat-controlled heating mantles. Organic solutions were concentrated using a rotary evaporator with a diaphragm vacuum pump. Thin-layer chromatography was performed on silica gel UNIPLATE Silica Gel HLF UV254 plates, and spots were visualized by quenching ultraviolet light (λ = 254 nm). Purification of products was accomplished by automated flash column chromatography on silica gel (VWR Common Silica Gel 60 Å, 40−60 μm). Unless otherwise noted, reagents and solvents were purchased from various commercial sources and used as received.

NMR spectra were recorded on a Bruker DRX 500 MHz (^{1}H at 500 MHz, ^{19}F at 471 MHz), Bruker AVIIIHD 400 MHz (^{13}C at 126 MHz) or AVIII 800 MHz (^{13}C at 201 MHz) nuclear magnetic resonance spectrometer. ^{1}H NMR spectra were calibrated against residual $CHCl_3$ in the solvent (7.26 ppm). ^{19}F NMR spectra were calibrated against the internal standard $CFCl_3$ (0.00 ppm). $^{13}C\{^1H\}$ NMR spectra were calibrated against the peak of the residual $CHCl_3$ in the solvent (77.2 ppm). NMR data are represented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, and m = multiplet), coupling constant in hertz (Hz), and integration. GC analysis was performed on an Agilent Technologies 7890A instrument equipped with J&W HP-5 GC Column (30 m, 0.32 mm, 0.25 μm and 7 in. cage) and a FID detector using helium as the carrier gas. High-resolution mass determination was carried out either by electrospray ionization (ESI) on a Waters LCT Premier mass spectrometer where samples were dissolved in MeOH and MeOH was used as the ionization solvent or by atmospheric-pressure chemical ionization (APCI-hexanes/PhMe) on a Waters Q-Tof Premier, where samples were dissolved in hexanes, and hexanes or PhMe/hexanes were used as the ionization solvent. Infrared spectra were measured on a

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PerkinElmer Spectrum Two Fourier Transform Infrared Spectrometer by loading samples on a diamond ATR sample base plate. Uncorrected melting points were measured on a Thomas Hoover UNI-MELT Capillary Melting Point apparatus.

General Procedure A for the Preparation of *gem*-Difluorostyrenes. An oven-dried three-neck round-bottomed flask equipped with an addition funnel and a magnetic stir bar was charged with aryl aldehyde (1.0 equiv) and PPh_3 (1.5 equiv). The system was sealed with three rubber septa, and subsequently evacuated and backfilled with dry N_2 three times. Dry DMF was added via a syringe and the system was immersed in an oil bath preheated to 90 °C. A solution of KO_2CCF_2Br (1.8 equiv) in DMF was added dropwise using an addition funnel over 0.5 h, with the rate of addition controlling the evolution of the CO_2 gas. Once all of the KO_2CCF_2Br was added, the solution was allowed to stir for 0.5 h at 90 °C. Upon completion, the reaction was cooled to 0 °C and then quenched with H_2O. Subsequently, Et_2O was added to the mixture, and the organic layer was washed with H_2O (three times) and then an aqueous solution of LiCl (10% in H_2O; one time). Subsequently, MeI (1.5 equiv) was added to the organic layer, and the mixture stirred at room temperature for 30 min to methylate the residual PPh_3. The organic layer was washed with H_2O (three times) then brine, and then dried over Na_2SO_4. The crude material was eluted through a pad of silica gel with Et_2O/pentane (1:1). The solution was concentrated, and the resulting residue was subjected to normal phase flash chromatography using EtOAc and hexanes.

General Procedure B for the Preparation of *gem*-Difluorostyrenes. An oven-dried three-neck round-bottomed flask equipped with a magnetic stir bar was charged with aryl aldehyde (1.0 equiv) and PPh_3 (1.5 equiv). The system was sealed with three rubber septa, and subsequently evacuated and backfilled with dry N_2 three times. Dry DMF was added via a syringe, and the system was immersed in an oil bath preheated to 90 °C. KO_2CCF_2Br (1.8 equiv) was added portion wise over 0.5 h, with the rate of addition controlling the evolution of CO_2 gas. Once all of KO_2CCF_2Br was added, the solution was allowed to stir for 0.5 h at 90 °C. Upon completion, the reaction was cooled to 0 °C and then quenched with H_2O. Subsequently, Et_2O was added to the mixture, and the organic layer was washed with H_2O (three times) then an aqueous solution of LiCl (10% in H_2O; one time). Subsequently, H_2O_2 (30% in H_2O) was added to the mother liquor, and the mixture was allowed to react for 30 min to oxidize the residual PPh_3. Solid additions of $Na_2S_2O_5$ were then added iteratively to quench excess H_2O_2, and the quenching process was monitored for completion using peroxide strips. The organic layer was washed with H_2O (three times) then brine and dried over Na_2SO_4. The crude material was then eluted through a pad of silica gel with Et_2O/pentane (1:1) to remove PPh_3O. The solution was then concentrated, and the resulting residue was subjected to normal phase flash chromatography using EtOAc and hexanes.

*(2,2-Difluorovinyl)benzene (**1a**).* Following general procedure A, a solution of KO_2CCF_2Br (9.6 g, 45 mmol) in 20 mL of DMF was added dropwise to a mixture of benzaldehyde (2.50 mL, 25.0 mmol) and PPh_3 (9.80 g, 37.5 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 2.99 g (85% yield) of desired product **1a** as a colorless oil. ^{1}H NMR spectra match the previous reports.[31]

*3-(2,2-Difluorovinyl)benzonitrile (**1b**).* Following general procedure A, a solution of KO_2CCF_2Br (18.6 g, 90 mmol) in 20 mL of DMF was added dropwise to a mixture of 3-formylbenzonitrile (6.56 mL, 50.0 mmol) and PPh_3 (18.6 g, 75 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 3.60 g (44% yield) of desired product **1b** as a colorless solid. ^{1}H NMR spectra match previous reports.[32]

*4-(2,2-Difluorovinyl)benzonitrile (**1c**).* Following general procedure A, a solution of KO_2CCF_2Br (19.2 g, 90 mmol) in 20 mL of DMF was added dropwise to a mixture of 4-formylbenzonitrile (6.55 mL, 50.0 mmol) and PPh_3 (19.6 g, 75 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 6.10 g (74% yield) of desired product **1c** as a colorless solid. ^{1}H NMR spectra match previous reports.[31]

*1-(2,2-Difluorovinyl)-3-(trifluoromethyl)benzene (**1d**).* Following general procedure A, a solution of KO_2CCF_2Br (9.6 g, 45 mmol) in 20 mL of DMF was added dropwise to a mixture of 3-(trifluoromethyl)-benzaldehyde (3.35 mL, 25.0 mmol) and PPh_3 (9.80 g, 37.5 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 2.80 g (55% yield) of desired product **1d** as a colorless oil. ^{1}H NMR spectra match previous reports.[32]

*1-(2,2-Difluorovinyl)-4-(trifluoromethyl)benzene (**1e**).* Following general procedure A, a solution of KO_2CCF_2Br (9.6 g, 45 mmol) in 20 mL of DMF was added dropwise to a mixture of 4-(trifluoromethyl)-benzaldehyde (3.4 mL, 25.0 mmol) and PPh_3 (9.80 g, 37.5 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 2.5 g (49% yield) of desired product **1e** as a colorless oil. ^{1}H NMR spectra match previous reports.[31]

*1-(2,2-Difluorovinyl)-3-nitrobenzene (**1f**).* Following general procedure A, a solution of KO_2CCF_2Br (9.6 g, 45 mmol) in 20 mL of DMF was added dropwise to a mixture of 3-nitrobenzaldehyde (3.78 g, 25.0 mmol) and PPh_3 (9.80 g, 37.5 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 0.69 g (15% yield) of desired product **1f** as a pale yellow solid. ^{1}H NMR spectra match previous reports.[32]

*4-(2,2-Difluorovinyl)phenyl 4-Methylbenzenesulfonate (**1g**).* Following general procedure A, a solution of KO_2CCF_2Br (4.80 g, 22.5 mmol) in 10 mL of DMF was added dropwise to a mixture of 4-formylphenyl 4-methylbenzenesulfonate (3.50 g, 25.0 mmol) and PPh_3 (4.90 g, 18.8 mmol) in 25 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 1.93 g (50% yield) of desired product **1g** as a colorless solid. ^{1}H NMR spectra match previous reports.[32]

*1,3-Dichloro-5-(2,2-difluorovinyl)benzene (**1h**).* Following general procedure A, a solution of KO_2CCF_2Br (9.6 g, 45 mmol) in 20 mL of DMF was added dropwise to a mixture of 4-chlorobenzaldehyde (5.38 g, 25.0 mmol) and PPh_3 (9.80 g, 37.5 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 2.5 g (48% yield) of desired product **1i** as a colorless oil. ^{1}H NMR spectra match previous reports.[32]

*1-Chloro-4-(2,2-difluorovinyl)benzene (**1i**).* Following general procedure A, a solution of KO_2CCF_2Br (9.6 g, 45 mmol) in 20 mL of DMF was added dropwise to a mixture of 4-chlorobenzaldehyde (3.5 mL, 25.0 mmol) and PPh_3 (9.80 g, 37.5 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 2.8 g (65% yield) of desired product **1i** as a colorless oil. ^{1}H NMR spectra match previous reports.[31]

*1-Bromo-4-(2,2-difluorovinyl)benzene (**1j**).* Following general procedure A, a solution of KO_2CCF_2Br (15.4 g, 72 mmol) in 20 mL of DMF was added dropwise to a mixture of 4-bromobenzaldehyde (7.4 g, 40.0 mmol) and PPh_3 (12.6 g, 48.0 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 6.02 g (69% yield) of desired product **1j** as a colorless oil. ^{1}H NMR spectra match previous reports.[32]

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*1-(2,2-Difluorovinyl)-4-methoxybenzene (**1l**).* Following general procedure A, a solution of KO_2CCF_2Br (9.6 g, 45 mmol) in 20 mL of DMF was added dropwise to a mixture of 4-methoxybenzaldehyde (3.05 mL, 25.0 mmol) and PPh_3 (9.80 g, 37.5 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 3.63 g (85% yield) of desired product **1l** as a colorless oil. ^{1}H NMR spectra match previous reports.[32]

*(4-(2,2-Difluorovinyl)phenyl)(methyl)sulfane (**1m**).* Following general procedure B, KO_2CCF_2Br (28.8 g, 135 mmol) was added portion wise to a mixture of 4-(methylthio)benzaldehyde (10.0 mL, 75.0 mmol) and PPh_3 (29.5 g, 110 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 9.27 g (67% yield) of desired product **1m** as a colorless solid. ^{1}H NMR spectra match previous reports.[32]

*5-(2,2-Difluorovinyl)-1,2,3-trimethoxybenzene (**1n**).* Following general procedure B, KO_2CCF_2Br (39.1 g, 180 mmol) was added portion wise to a mixture of 3,4,5-trimethoxybenzaldehyde (20 g, 100.0 mmol) and PPh_3 (40.1 g, 150 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 13.9 g (60% yield) of desired product **1n** as a colorless solid. ^{1}H NMR spectra match previous reports.[32]

*1-(tert-Butyl)-4-(2,2-difluorovinyl)benzene (**1q**).* Following general procedure A, a solution of KO_2CCF_2Br (2.3 g, 10.8 mmol) in 5 mL of DMF was added dropwise to a mixture of 4-(*tert*-butyl)benzaldehyde (1.0 mL, 6.0 mmol) and PPh_3 (2.4 g, 9 mmol) in 10 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 380 mg (32% yield) of desired product **1q** as a colorless oil. ^{1}H NMR spectra match previous reports.[32]

*4-(2,2-Difluorovinyl)-1,1′-biphenyl (**1r**).* Following general procedure A, a solution of KO_2CCF_2Br (9.6 g, 45 mmol) in 20 mL of DMF was added dropwise to a mixture of [1,1′-biphenyl]-4-carbaldehyde (4.56 mL, 25.0 mmol) and PPh_3 (9.80 g, 37.5 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 3.67 g (68% yield) of desired product **1r** as a colorless solid. ^{1}H NMR spectra match previous reports.[31]

*4′-(tert-Butyl)-2-(2,2-difluorovinyl)-1,1′-biphenyl (**1s**).* Following general procedure B, KO_2CCF_2Br (13.2 g, 61.0 mmol) was added portion wise to a mixture of 4′-(*tert*-butyl)-[1,1′-biphenyl]-2-carbaldehyde (8.01 g, 36.4 mmol) and PPh_3 (13.2 g, 50.0 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 4.67 g (80% yield) of desired product **1s** as a colorless oil. ^{1}H NMR spectra match previous reports.[32]

*Ethyl (E)-3-(3-(2,2-Difluorovinyl)phenyl)acrylate (**1t**).* Following general procedure B, KO_2CCF_2Br (0.9 g, 4.3 mmol) was added portion wise to a mixture of ethyl (*E*)-3-(3-formylphenyl)acrylate (0.50 g, 2.5 mmol) and PPh_3 (0.95 g, 3.6 mmol) in 5 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 499 mg (84% yield) of desired product **1t** as a colorless solid. ^{1}H NMR spectra match previous reports.[32]

*4-(2,2-Difluorovinyl)-N,N-diethylbenzamide (**1u**).* Following general procedure A, a solution of KO_2CCF_2Br (9.6 g, 45 mmol) in 20 mL of DMF was added dropwise to a mixture of *N*,*N*-diethyl-4-formylbenzamide (5.13 mL, 25.0 mmol) and PPh_3 (9.80 g, 37.5 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 1.49 g (25% yield) of desired product **1u** as a colorless solid. ^{1}H NMR spectra match previous reports.[33]

*1-(2,2-Difluorovinyl)-4-(methoxymethoxy)benzene (**1w**).* Following general procedure A, a solution of KO_2CCF_2Br (9.6 g, 45 mmol) in 20 mL of DMF was added dropwise to a mixture of 4-(methoxymethoxy)benzaldehyde (4.15 mL, 25.0 mmol) and PPh_3 (9.80 g, 37.5 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 2.8 g (56% yield) of desired product **1w** as a colorless oil. ^{1}H NMR spectra match previous reports.[33]

*1-(Benzyloxy)-4-(2,2-difluorovinyl)benzene (**1x**).* Following general procedure A, a solution of KO_2CCF_2Br (9.6 g, 45 mmol) in 20 mL of DMF was added dropwise to a mixture of 4-(benzyloxy)-benzaldehyde (5.3 mL, 25.0 mmol) and PPh_3 (9.80 g, 37.5 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 2.56 g (42% yield) of desired product **1x** as a colorless solid. ^{1}H NMR spectra match previous reports.[33]

*4-(2,2-Difluorovinyl)dibenzo[b,d]thiophene (**1y**).* Following general procedure B, KO_2CCF_2Br (2.3 g, 11 mmol) was added portion wise to a mixture of dibenzo[*b*,*d*]thiophene-4-carbaldehyde (1.3 g, 6.0 mmol) and PPh_3 (2.3 g, 9.0 mmol) in 20 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 0.68 g (46% yield) of desired product **1s** as a pale yellow solid. ^{1}H NMR spectra match previous reports.[32]

*4-(2,2-Difluorovinyl)-1-phenyl-1H-pyrazole (**1z**).* Following general procedure B, KO_2CCF_2Br (8.05 g, 38.0 mmol) was added portion wise to a mixture of 1-phenyl-1*H*-pyrazole-4-carbaldehyde (3.65 g, 21.0 mmol) and PPh_3 (8.33 g, 3.80 mmol) in 50 mL of DMF heated in a 90 °C oil bath and stirred for 1 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:20) to furnish 1.5 g (32% yield) of desired product **1s** as a colorless solid. ^{1}H NMR spectra match previous reports.[32]

*1-(2,2-Difluorovinyl)-2-iodobenzene (**1k**).* Compound **1k** was prepared according to a previous report.[14]

*1-(2,2-Difluorovinyl)-3,5-dimethylbenzene (**1o**).* Compound **1o** was prepared according to a previous report.[32]

*2-(2,2-Difluorovinyl)-1,3-dimethylbenzene (**1p**).* Compound **1p** was prepared according to a previous report.[32]

*4-(2,2-Difluorovinyl)phenol (**1v**).* Compound **1v** was prepared according to a previous report.[33]

Synthesis of Compound 1aa. An oven-dried round-bottomed flask equipped with magnetic stir bar was charged with aryl 1-(4-methoxyphenyl)ethan-1-one (0.30 g, 2.0 mmol) and 2,2-difluoro-2-(tris(dimethylamino)phosphonio)acetate (1.0 g, 4.0 mmol). The system was sealed with a rubber septa, and subsequently evacuated and backfilled with dry N_2 three times. Dry PhMe (3 mL) and DMA (1 mL) were added via a syringe, and the system was immersed in an oil bath preheated to 100 °C for 3 h. Upon completion, the reaction was cooled to 0 °C and then quenched with H_2O. Subsequently, Et_2O was added to the mixture, and the organic layer was washed with H_2O (three times) and then an aqueous solution of LiCl (10% in H_2O; one time). The crude material was then eluted through a pad of silica gel with Et_2O/pentane (1:1). The solution was then concentrated and subjected to normal phase flash chromatography using 0 to 20% EtOAc in hexane furnishing 0.17 g (46% yield) of desired product **1a** as a colorless oil. ^{1}H NMR spectra match previous reports.[34]

General Procedure A for the Triflate-Catalyzed Addition of Alkylthiols to *gem*-Difluorostyrenes. An oven-dried one-dram vial equipped with a magnetic stir bar was charged with *gem*-difluorostyrene (1.0 equiv) and LiOTf (1.5 equiv). Dry *o*-xylene (0.33 M), pyridine (0.2 equiv), 2-methoxyethanol (2.0 equiv), and alkylthiol (1.5 equiv) were added via a syringe and the vial was sealed with a screw-top cap containing a PTFE-lined septum. The vial was then connected to a

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balloon filled with air using a 16-gauge needle, then stirred in a heating mantle to 110 °C for 24 h. Upon completion, the reaction was cooled to rt, concentrated onto SiO_2, and purified by normal-phase flash chromatography using EtOAc and hexanes to provide the desired product in >95% purity.

General Procedure B for the Triflate-Catalyzed Addition of Alkylthiols to *gem*-Difluorostyrenes. An oven-dried one-dram vial equipped with a magnetic stir bar was charged with *gem*-difluorostyrene (1.0 equiv) and LiOTf (1.5 equiv). Dry *o*-xylene (0.33 M), pyridine (1.0 equiv), 2-methoxyethanol (2.0 equiv), and alkylthiol (1.5 equiv) were added via a syringe and the vial was sealed with a screw-top cap containing a PTFE-lined septum. The vial was then connected to a balloon filled with air using a 16-gauge needle, then stirred in a heating mantle to 110 °C for 24 h. Upon completion, the reaction was cooled to rt, concentrated onto SiO_2, and purified by normal-phase flash chromatography using EtOAc and hexanes to provide the desired product in >95% purity.

General Procedure C for the Triflate-Catalyzed Addition of Alkylthiols to *gem*-Difluorostyrenes. An oven-dried one-dram vial equipped with a magnetic stir bar was charged with *gem*-difluorostyrene (1.0 equiv) and LiOTf (1.5 equiv). Dry *o*-xylene (0.33 M), pyridine (1.0 equiv), 2-methoxyethanol (2.0 equiv), and alkylthiol (1.5 equiv) were added via a syringe and the vial was sealed with a screw-top cap containing a PTFE-lined septum. The vial was then connected to a balloon filled with air using a 16-gauge needle, then stirred in a heating mantle to 120 °C for 24 h. Upon completion, the reaction was cooled to rt, concentrated onto SiO_2 and purified by normal-phase flash chromatography using EtOAc and hexanes to provide the desired product in >95% purity.

*(1,1-Difluoro-2-phenylethyl) (octyl)sulfane (**5a**).* Following general procedure A, compound **1a** (0.070 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.010 mL, 0.100 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.123 g (86% yield) of desired product **5a** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.38−7.28 (m, 5H), 3.41 (t, J = 14.6 Hz, 2H), 2.82 (t, J = 7.5 Hz, 2H), 1.63 (p, J = 7.5 Hz, 2H), 1.44−1.33 (m, 2H), 1.30 (m, 8H), 0.90 (t, J = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 132.3 (t, $^3J_{C-F_2}$ = 4.0 Hz), 130.5, 130.1 (t, $^1J_{C-F_2}$ = 277.0 Hz), 128.4, 127.7, 46.3 (t, $^2J_{C-F_2}$ = 42.4 Hz), 31.8, 29.8, 29.1, 29.0, 28.8, 27.9 (t, $^3J_{C-F_2}$ = 3.6 Hz), 22.6, 14.1. ^{19}F NMR (471 MHz, chloroform-*d*): δ −73.04 (t, J = 14.6 Hz). IR (film): 3034, 2925, 2855, 1455, 1265, 1153, 1006, 988, 740, 725, 698 cm^{-1}. HRMS (APCI)$^+$ m/z: calcd $C_{16}H_{24}F_2S$ [M + H]$^+$, 287.1640; found, 287.1649.

*3-(2,2-Difluoro-2-(octylthio)ethyl)benzonitrile (**5b**).* Following general procedure A, compound **1b** (0.082 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.130 g (84% yield) of desired product **5b** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.64 (d, J = 8.3 Hz, 1H), 7.62 (s, 1H), 7.56 (d, J = 7.8 Hz, 1H), 7.47 (t, J = 7.7 Hz, 1H), 3.44 (t, J = 14.2 Hz, 2H), 2.84 (t, J = 7.5 Hz, 2H), 1.64 (p, J = 7.4 Hz, 2H), 1.37 (m, 2H), 1.30 (m, 8H), 0.90 (t, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 135.0, 134.0, 133.7 (t, $^3J_{C-F_2}$ = 3.9 Hz), 131.4, 129.4 (t, $^1J_{C-F_2}$ = 276.7 Hz), 129.3, 118.56, 112.7, 45.7 (t, $^2J_{C-F_2}$ = 25.2 Hz), 31.8, 29.7, 29.1, 29.0, 28.8, 28.1 (t, $^3J_{C-F_2}$ = 3.6 Hz), 22.6, 14.1. ^{19}F NMR (471 MHz, chloroform-*d*): δ −73.3 (t, J = 14.3 Hz). IR (film): 2926, 2855, 2231, 1353, 1258, 1187, 1151, 1017, 995, 882, 798, 687 cm^{-1}. HRMS (APCI)$^+$ m/z: calcd $C_{17}H_{23}F_2NS$ [M + H]$^+$, 312.1598; found, 312.1587.

*4-(2,2-Difluoro-2-(octylthio)ethyl)benzonitrile (**5c**).* Following general procedure A, compound **1c** (0.082 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.123 g (79% yield) of desired product **5c** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.66 (d, J = 7.8 Hz, 2H), 7.44 (d, J = 7.8 Hz, 2H), 3.48 (t, J = 14.2 Hz, 2H), 2.84 (t, J = 7.4 Hz, 2H), 1.64 (p, J = 7.3 Hz, 2H), 1.36 (m, 2H), 1.29 (m, 8H), 0.90 (t, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 137.8, 132.2, 131.3, 128.3 (t, $^1J_{C-F_2}$ = 278.0 Hz), 118.6, 111.8, 45.5 (t, $^2J_{C-F_2}$ = 25.2 Hz), 29.7, 29.1, 29.0, 28.8, 28.1 (t, $^3J_{C-F_2}$ = 3.7 Hz), 22.6, 14.1. ^{19}F NMR (471 MHz, chloroform-*d*): δ −72.9 (t, J = 14.2 Hz). IR (film): 2927, 2856, 2231, 1509, 1464, 1265, 1013, 993, 740, 705 cm^{-1}. HRMS (APCI)$^+$ m/z: calcd $C_{17}H_{24}F_2NS$ [M + H]$^+$ 312.1598; found, 312.1592.

General Procedure for a 1 mmol Scale Reaction to Synthesize (5c). An oven-dried one-dram vial equipped with a magnetic stir bar was charged with **1c** (0.165 g, 1.0 mmol) and LiOTf (0.016 g, 0.100 mmol). Dry *o*-xylene (3 mL, 0.33 M), pyridine (0.02 mL, 0.20 mmol), 2-methoxyethanol (0.160 mL, 2.00 mmol), and 1-octanethiol (0.260 mL, 1.5 mmol) were added via a syringe and the vial was sealed with a screw-top cap containing a PTFE-lined septum. The vial was then connected to a balloon filled with air using a 16-gauge needle, then stirred using a heating mantle to 110 °C for 24 h. Upon completion, the reaction was cooled to rt, concentrated onto SiO_2 and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.254 g (82% yield) of desired product **5c** as a colorless oil.

*(1,1-Difluoro-2-(3-(trifluoromethyl)phenyl)ethyl)(octyl)sulfane (**5d**).* Following general procedure A, compound **1d** (0.104 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.164 g (89% yield) of desired product **5d** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.62−7.56 (m, 2H), 7.54−7.46 (m, 2H), 3.47 (t, J = 14.4 Hz, 2H), 2.84 (t, J = 7.5 Hz, 2H), 1.65 (p, J = 7.4 Hz, 2H), 1.38 (m, 2H), 1.29 (m, 8H), 0.91 (t, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 133.9, 133.6 (t, $^3J_{C-F_2}$ = 3.7 Hz), 129.6 (t, $^1J_{C-F_2}$ = 277.6 Hz), 128.9, 127.3 (q, $^3J_{C-F_3}$ = 4.0 Hz), 125.1, 124.6 (q, $^3J_{C-F_3}$ = 4.3 Hz), 122.9, 45.4 (t, $^2J_{C-F_2}$ = 25.2 Hz), 31.8, 29.8, 29.1, 29.0, 28.8, 28.0 (t, $^3J_{C-F_2}$ = 3.6 Hz), 22.6, 14.1. ^{19}F NMR (471 MHz, chloroform-*d*): δ −62.7, −72.8 (t, J = 14.4 Hz). IR (film) 2927, 2856, 1420, 1323, 1164, 1126, 1112, 1067, 1020, 992, 851, 748 cm^{-1}. HRMS (APCI)$^+$ m/z: calcd $C_{17}H_{23}F_5S$ [M + H]$^+$, 355.1519; found, 355.1509.

*(1,1-Difluoro-2-(4-(trifluoromethyl)phenyl)ethyl)(octyl)sulfane (**5e**).* Following general procedure A, compound **1e** (0.104 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.161 g (91% yield) of desired product **5e** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.52 (d, J = 8.1 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 3.37 (t, J = 14.3 Hz, 2H), 2.89 (t, J = 7.3 Hz, 2H), 1.54 (p, J = 7.4 Hz, 2H), 1.35−1.22 (m, 2H), 1.20 (m, 8H), 0.80 (t, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 136.8−136.0 (m), 131.0, 130.2 (q, $^2J_{C-F_2}$ = 32.4 Hz), 129.9, 129.77 (t, $^1J_{C-F_2}$ = 276.7 Hz), 125.4 (q, $^3J_{C-F_2}$ = 4.0 Hz), 45.9 (t, $^2J_{C-F_2}$ = 25.8 Hz), 31.9, 29.9, 29.2, 29.1, 28.9, 28.1 (t, $^3J_{C-F_2}$ = 3.6 Hz), 22.7, 14.2. ^{19}F NMR (471 MHz,

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chloroform-*d*): δ −63.15, −73.06 (t, *J* = 14.3 Hz). IR (film): 2927, 2856, 1690, 1621, 1323, 1164, 1126, 1112, 1067, 1020, 992, 851, 748 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{17}H_{23}F_5S$ [M + H]$^+$, 355.1519; found, 355.1512.

*(1,1-Difluoro-2-(3-nitrophenyl)ethyl)(octyl)sulfane (**5f**).* Following general procedure A, compound **1f** (0.092 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.114 g (69% yield) of desired product **5f** as a yellow oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 8.21 (d, *J* = 3.9 Hz, 1H), 8.21 (s, 1H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.55 (dd, *J* = 9.0, 7.6 Hz, 1H), 3.52 (t, *J* = 14.1 Hz, 2H), 2.85 (t, *J* = 7.5 Hz, 2H), 1.65 (p, *J* = 7.5 Hz, 2H), 1.42−1.35 (m, 2H), 1.30 (dd, *J* = 11.3, 5.5 Hz, 8H), 0.90 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 148.3, 136.6, 134.2 (t, $^3J_{C-F_2}$ = 3.7 Hz), 129.4 (t, $^1J_{C-F_2}$ = 278.0 Hz), 129.4, 125.7, 122.9, 45.1 (t, $^2J_{C-F_2}$ = 25.3 Hz), 31.8, 29.7, 29.1, 29.0, 28.8, 28.1 (t, $^3J_{C-F_2}$ = 3.5 Hz), 22.6, 14.1. ^{19}F NMR (471 MHz, chloroform-*d*): δ −73.3 (t, *J* = 14.1 Hz). IR (film): 3075, 2926, 2855, 1728, 1531, 1349, 1017, 995, 821, 805, 736, 727 cm^{-1}. MS (APCI)$^+$ *m*/*z*: calcd $C_{16}H_{24}F_2NO_2S$ [M + H]$^+$, 332.1496; found, 332.1482.

*4-(2,2-Difluoro-2-(octylthio)ethyl)phenyl 4-Methylbenzenesulfane (**5g**).* Following general procedure A, compound **1g** (0.155 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.167 g (74% yield) of desired product **5g** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.70 (d, *J* = 8.1 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 1H), 7.20 (d, *J* = 8.3 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 3.34 (t, *J* = 14.4 Hz, 1H), 2.79 (t, *J* = 7.5 Hz, 1H), 2.45 (s, 2H), 1.61 (p, *J* = 7.5 Hz, 1H), 1.34 (m, *J* = 6.9, 4.3 Hz, 1H), 1.31−1.22 (m, 4H), 0.87 (t, *J* = 6.8 Hz, 2H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 149.3, 145.4, 132.5, 131.8, 131.3 (t, $^3J_{C-F_2}$ = 3.8 Hz), 129.8, 129.8 (t, $^1J_{C-F_2}$ = 282 Hz), 128.6, 122.4, 45.1 (t, $^2J_{C-F_2}$ = 24.4 Hz), 31.9, 29.9, 29.2, 29.1, 28.9, 28.1 (t, $^3J_{C-F_2}$ = 3.6 Hz), 22.7, 21.8, 14.2. ^{19}F NMR (470 MHz, chloroform-*d*): δ −72.79 (t, *J* = 14.5 Hz). IR (film): 2926, 2855, 1503, 1375, 1199, 1178, 1152, 1093, 1019, 866, 737, 705 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{23}H_{31}F_2O_3S_2$ [M + H]$^+$, 457.1677; found, 457.1694.

*(2-(3,5-Dichlorophenyl)-1,1-difluoroethyl)(octyl)sulfane (**5h**).* Following general procedure A, compound **1h** (0.104 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.130 g (73% yield) of desired product **5h** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.34 (t, *J* = 1.9 Hz, 1H), 7.21 (d, *J* = 1.9 Hz, 2H), 3.35 (t, *J* = 14.2 Hz, 2H), 2.89−2.73 (t, *J* = 7.4, 2H), 1.65 (p, *J* = 7.4 Hz, 2H), 1.39 (m, 2H), 1.29 (m, 8H), 0.90 (t, *J* = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 135.4 (t, $^3J_{C-F_2}$ = 3.7 Hz), 135.0, 129.4 (t, $^1J_{C-F_2}$ = 277.9 Hz), 129.1, 128.1, 44.9 (t, $^2J_{C-F_2}$ = 25.4 Hz), 31.9, 29.8, 29.2, 29.1, 28.9, 28.2 (t, $^3J_{C-F_2}$ = 3.6 Hz), 22.7, 14.2. ^{19}F NMR (471 MHz, chloroform-*d*): δ −73.1 (t, *J* = 14.2 Hz). IR (film): 2955, 2925, 2854, 1569, 1434, 1212, 1018, 997, 798, 743 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{16}H_{22}Cl_2F_2S$ [M + H]$^+$, 355.0866; found, 355.0858.

*(2-(4-Chlorophenyl)-1,1-difluoroethyl)(octyl)sulfane (**5i**).* Following general procedure A, compound **1i** (0.082 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.131 g (82% yield) of desired product **5i** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.22 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 8.2 Hz, 2H), 3.27 (t, *J* = 14.4 Hz, 2H), 2.72 (t, *J* = 7.5 Hz, 2H), 1.53 (p, *J* = 7.5 Hz, 2H), 1.31−1.24 (m, 2H), 1.20 (m, 8H), 0.80 (t, *J* = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 133.8, 131.8, 130.8 (t, $^3J_{C-F_2}$ = 4.1 Hz), 129.8 (t, $^1J_{C-F_2}$ = 277.8 Hz), 128.6, 45.6 (t, $^2J_{C-F_2}$ = 25.0 Hz), 31.7, 29.7, 29.1, 29.0, 28.8, 27.9 (t, $^3J_{C-F_2}$ = 3.6 Hz), 22.6, 14.0. ^{19}F NMR (471 MHz, chloroform-*d*): δ −73.22 (t, *J* = 14.4 Hz). IR (film): 3006, 2989, 2839, 1591, 1494, 1275, 1259, 1222, 1097, 1028, 764, 750 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{16}H_{23}ClF_2S$ [M + H]$^+$, 321.1250; found, 321.1246.

*(2-(4-Bromophenyl)-1,1-difluoroethyl)(octyl)sulfane (**5j**).* Following general procedure A, compound **1j** (0.110 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.115 g (63% yield) of desired product **5j** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.49 (d, *J* = 8.3 Hz, 2H), 7.19 (d, *J* = 8.1 Hz, 2H), 3.37 (t, *J* = 14.4 Hz, 2H), 2.83 (t, *J* = 7.5 Hz, 2H), 1.64 (p, *J* = 7.4 Hz, 2H), 1.41−1.35 (m, 2H), 1.29 (m, 8H), 0.91 (t, *J* = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 132.2, 131.6, 131.2 (t, $^3J_{C-F_2}$ = 3.8 Hz), 128.6 (t, $^1J_{C-F_2}$ = 277.5 Hz), 122.0, 45.0 (t, $^2J_{C-F_2}$ = 25.1 Hz), 31.8, 29.8, 29.1, 29.0, 28.8, 28.0 (t, $^3J_{C-F_2}$ = 3.6 Hz), 22.6, 14.1. ^{19}F NMR (471 MHz, chloroform-*d*): δ −73.19 (t, *J* = 14.4 Hz). IR (film): 2955, 2926, 2854, 1489, 1464, 1264, 1012, 764, 738, 705 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{16}H_{24}BrF_2S$ [M + H]$^+$, 365.0750; found, 365.0755.

*(1,1-Difluoro-2-(2-iodophenyl)ethyl)(octyl)sulfane (**5k**).* Following general procedure A, compound **1k** (0.132 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.134 g (65% yield) of desired product **5k** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.88 (d, *J* = 7.8 Hz, 1H), 7.41 (d, *J* = 7.5 Hz, 1H), 7.33 (d, *J* = 7.6 Hz, 1H), 6.98 (td, *J* = 7.7, 1.7 Hz, 1H), 3.66 (t, *J* = 14.5 Hz, 2H), 2.83 (t, *J* = 7.4 Hz, 2H), 1.64 (p, *J* = 8.4, 7.6 Hz, 2H), 1.36 (p, *J* = 6.9 Hz, 2H), 1.31−1.19 (m, 8H), 0.88 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 139.9, 135.8 (t, $^3J_{C-F_2}$ = 3.3 Hz), 131.5, 130.0 (t, $^1J_{C-F_2}$ = 279.1 Hz), 129.4, 128.2, 102.2, 49.2 (t, $^2J_{C-F_2}$ = 24.6 Hz), 31.8, 29.8, 29.1, 29.0, 28.9, 28.2 (t, $^3J_{C-F_2}$ = 3.7 Hz), 22.6, 14.1. ^{19}F NMR (470 MHz, chloroform-*d*): δ −72.1 (t, *J* = 14.5 Hz). IR (film): 2955, 2926, 2854, 1464, 1436, 1378, 1264, 1020, 742, 705 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{16}H_{23}F_2IS$ [M + H]$^+$, 413.0612; found, 413.0624.

*(1,1-Difluoro-2-(4-methoxyphenyl)ethyl)(octyl)sulfane (**5l**).* Following general procedure A, compound **1l** (0.085 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.144 g (91% yield) of desired product **5l** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.25 (d, *J* = 8.2 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 3.83 (s, 3H), 3.37 (t, *J* = 14.5 Hz, 2H), 2.83 (t, *J* = 7.5 Hz, 2H), 1.65 (p, *J* = 7.5 Hz, 2H), 1.47−1.36 (m, 2H), 1.32−1.29 (m, 8H), 0.92 (t, *J* = 6.8

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Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, chloroform-*d*): δ 159.2, 131.5, 129.3 (t, $^1J_{C-F_2}$ = 277.1 Hz), 124.3 (t, $^3J_{C-F_2}$ = 3.8 Hz), 113.8, 55.2, 44.8 (t, $^2J_{C-F_2}$ = 24.8 Hz), 31.8, 29.8, 29.1, 29.1, 28.9, 27.9 (t, $^3J_{C-F_2}$ = 3.8 Hz), 22.7, 14.1. ^{19}F NMR (471 MHz, chloroform-*d*): δ −72.8 (t, *J* = 14.5 Hz). IR (film): 2955, 2924, 2854, 1489, 1464, 1264, 1012, 990, 764, 741 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{17}H_{27}F_2OS$ [M + H]$^+$, 317.1751; found, 317.1741.

*General Procedure for a 1 mmol Scale Reaction to Synthesize (**5l**).* An oven-dried one-dram vial equipped with a magnetic stir bar was charged with **1l** (0.170 g, 1.0 mmol) and LiOTf (0.016 g, 0.100 mmol). Dry *o*-xylene (3 mL, 0.33 M), pyridine (0.02 mL, 0.20 mmol), 2-methoxyethanol (0.160 mL, 2.00 mmol), and 1-octanethiol (0.260 mL, 1.5 mmol) were added via a syringe and the vial was sealed with a screw-top cap containing a PTFE-lined septum. The vial was then connected to a balloon filled with air using a 16-gauge needle, then stirred using a heating mantle to 110 °C for 24 h. Upon completion, the reaction was cooled to rt, concentrated onto SiO_2 and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.228 g (72% yield) of desired product **5c** as a colorless oil.

*(1,1-Difluoro-2-(4-(methylthio)phenyl)ethyl)(octyl)sulfane (**5m**).* Following general procedure A, compound **1m** (0.093 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.108 g (65% yield) of desired product **5m** as a colorless oil. ^1H NMR (500 MHz, chloroform-*d*): δ 7.14 (s, 4H), 3.27 (t, *J* = 14.5 Hz, 2H), 2.72 (t, *J* = 7.5 Hz, 2H), 2.40 (s, 3H), 1.54 (p, *J* = 7.4 Hz, 2H), 1.34−1.22 (m, 2H), 1.19 (m, 8H), 0.80 (t, *J* = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, chloroform-*d*): δ 138.1, 130.9, 130.1 (t, $^1J_{C-F_2}$ = 278.4 Hz), 128.9 (t, $^3J_{C-F_2}$ = 4.0 Hz), 126.5, 45.0 (t, $^2J_{C-F_2}$ = 24.8 Hz), 31.8, 29.8, 29.1, 29.0, 28.8, 27.9 (t, $^3J_{C-F_2}$ = 3.6 Hz), 22.6, 15.7, 14.1. ^{19}F NMR (471 MHz, chloroform-*d*): δ −73.13 (t, *J* = 14.5 Hz). IR (film): 2923, 2854, 1495, 1437, 1264, 1152, 1009, 989, 870, 766, 740 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{17}H_{26}F_2S_2$ [M + H]$^+$, 333.1517; found, 333.1519.

*(1,1-Difluoro-2-(3,4,5-trimethoxyphenyl)ethyl)(octyl)sulfane (**5n**).* Following general procedure A, compound **1n** (0.115 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:5) to furnish 0.141 g (75% yield) of desired product **5n** as a colorless oil. ^1H NMR (500 MHz, chloroform-*d*): δ 6.52 (s, 2H), 3.88 (s, 6H), 3.87 (s, 3H), 3.35 (t, *J* = 14.5, 2H), 2.84 (t, *J* = 7.3, 2H), 1.66 (p, *J* = 7.4, 2H), 1.38 (m, 2H), 1.29 (m, 8H), 0.91 (t, *J* = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, chloroform-*d*): δ 153.0, 137.6, 130.1 (t, $^1J_{C-F_2}$ = 276.8 Hz), 127.7 (t, $^3J_{C-F_2}$ = 3.9 Hz), 107.6, 60.9, 56.1, 31.8, 29.8, 29.1, 29.0, 28.9, 27.9 (t, $^3J_{C-F_2}$ = 3.8 Hz), 22.6, 14.1. ^{19}F NMR (471 MHz, chloroform-*d*): δ −73.0 (t, *J* = 14.5 Hz). IR (film): 2927, 2855, 1730, 1589, 1508, 1459, 1421, 1244, 1127, 1007, 737 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{19}H_{30}F_2O_3S$ [M + H]$^+$, 377.1962; found, 377.1952.

*(2-(3,5-Dimethylphenyl)-1,1-difluoroethyl)(octyl)sulfane (**5o**).* Following general procedure A, compound **1o** (0.084 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.142 g (90% yield) of desired product **5o** as a colorless oil. ^1H NMR (500 MHz, chloroform-*d*): δ 6.95 (s, 1H), 6.91 (s, 2H), 3.31 (t, *J* = 14.7 Hz, 2H), 2.80 (t, *J* = 7.5 Hz, 2H), 2.31 (s, 6H), 1.62 (p, *J* = 7.4 Hz, 2H), 1.39−1.33 (m, 2H), 1.32−1.16 (m, 8H), 0.88 (t, *J* = 6.9 Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, chloroform-*d*): δ 137.9, 132.0 (t, $^3J_{C-F_2}$ = 3.7 Hz), 130.2 (t, $^1J_{C-F_2}$ = 277.3 Hz), 129.4, 128.3, 45.5 (t, $^2J_{C-F_2}$ = 25.2 Hz), 31.8, 29.8, 29.12, 29.0, 28.9, 28.0 (t, $^3J_{C-F_2}$ = 3.7 Hz), 22.6, 21.3, 14.1. ^{19}F NMR (470 MHz, chloroform-*d*): δ −72.9 (t, *J* = 14.8 Hz). IR (film): 2955, 2924, 2854, 1463, 1264, 1152, 1022, 742, 714 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{18}H_{29}F_2S$ [M + H]$^+$, 315.1958; found, 315.1948.

*(2-(2,6-Dimethylphenyl)-1,1-difluoroethyl)(octyl)sulfane (**5p**).* Following general procedure A, compound **1p** (0.084 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.143 g (91% yield) of desired product **5p** as a colorless oil. ^1H NMR (500 MHz, chloroform-*d*): δ 7.10 (dd, *J* = 8.5, 6.4 Hz, 1H), 7.05 (d, *J* = 7.4 Hz, 2H), 3.54 (t, *J* = 15.4 Hz, 2H), 2.83 (t, *J* = 7.6 Hz, 2H), 2.38 (s, 6H), 1.64 (p, *J* = 7.5 Hz, 2H), 1.37 (p, *J* = 7.5 Hz, 2H), 1.30−1.24 (m, 8H), 0.88 (t, *J* = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, chloroform-*d*): δ 138.5, 132.1 (t, $^1J_{C-F_2}$ = 278.4 Hz), 129.6 (t, $^3J_{C-F_2}$ = 2.3 Hz), 128.3, 127.5, 39.0 (t, $^2J_{C-F_2}$ = 24.6 Hz), 31.8, 29.8, 29.1, 29.0, 28.9, 28.1 (t, $^3J_{C-F_2}$ = 3.6 Hz), 22.6, 20.8 (t, *J* = 3.1 Hz), 14.1. ^{19}F NMR (470 MHz, chloroform-*d*): δ −70.9 (t, *J* = 15.5 Hz). IR (film): 2956, 2926, 2855, 1467, 1264, 986, 766, 743, 708 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{18}H_{29}F_2S$ [M + H]$^+$, 315.1958; found, 315.1947.

*(2-(4-(tert-Butyl)phenyl)-1,1-difluoroethyl)(octyl)sulfane (**5q**).* Following general procedure A, compound **1q** (0.098 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.107 g (62% yield) of desired product **5q** as a colorless oil. ^1H NMR (500 MHz, chloroform-*d*): δ 7.27 (d, *J* = 8.1 Hz, 2H), 7.14 (d, *J* = 7.9 Hz, 2H), 3.28 (t, *J* = 14.7 Hz, 2H), 2.72 (t, *J* = 7.5 Hz, 2H), 1.54 (p, *J* = 7.4 Hz, 2H), 1.27 (s, 9H), 1.26−1.23 (m, 2H), 1.18 (m, 8H), 0.80 (t, *J* = 6.7 Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, chloroform-*d*): δ 150.5, 130.2 (t, $^1J_{C-F_2}$ = 276.6 Hz), 130.1, 129.1 (t, $^3J_{C-F_2}$ = 3.8 Hz), 125.3, 45.8 (t, $^2J_{C-F_2}$ = 25.4 Hz), 39.2, 34.5, 31.8, 31.3, 29.8, 29.1, 29.0, 28.8, 27.9 (t, $^3J_{C-F_2}$ = 3.6 Hz), 22.6, 14.0. ^{19}F NMR (471 MHz, chloroform-*d*): δ −73.14 (t, *J* = 14.7 Hz). IR (film): 2957, 2925, 2855, 1464, 1153, 1027, 1007, 989, 764, 749 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{20}H_{33}F_2S$ [M + H]$^+$, 343.2271; found, 343.2258.

*(2-([1,1′-Biphenyl]-4-yl)-1,1-difluoroethyl)(octyl)sulfane (**5r**).* Following general procedure A, compound **1r** (0.108 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.147 g (81% yield) of desired product **5r** as a colorless solid. ^1H NMR (500 MHz, chloroform-*d*): δ 7.59 (d, *J* = 7.8 Hz, 2H), 7.57 (d, *J* = 8.1 Hz, 2H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.37 (d, *J* = 8.2 Hz, 2H), 7.34 (t, *J* = 7.1 Hz, 1H), 3.43 (t, *J* = 14.5 Hz, 2H), 2.82 (t, *J* = 7.5 Hz, 2H), 1.63 (p, *J* = 7.4 Hz, 2H), 1.40−1.32 (m, 2H), 1.27 (m, 8H), 0.87 (t, *J* = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz, chloroform-*d*): δ 140.7, 140.6, 131.2, 130.9 (t, $^1J_{C-F_2}$ = 275.7 Hz), 130.1, 128.7, 127.3, 127.1, 127.1, 45.3 (t, $^2J_{C-F_2}$ = 24.8 Hz), 31.7, 29.7, 29.1, 29.0, 28.8, 28.0 (t, $^3J_{C-F_2}$ = 3.7 Hz), 22.3, 14.0. ^{19}F NMR (471 MHz, chloroform-*d*): δ −72.99 (t, *J* = 14.6 Hz). mp 43−45 °C. IR (film): 2955, 2921, 2871, 2851, 1488, 1379, 1275, 1260, 1119, 1075, 989, 764, 749, 724 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{22}H_{28}F_2S$ [M + H]$^+$, 363.1953; found, 363.1953.

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*(2-(4′-(tert-Butyl)-[1,1′-biphenyl]-2-yl)-1,1-difluoroethyl)(octyl)-sulfane (**5s**).* Following general procedure A, compound **1s** (0.136 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.144 g (69% yield) of desired product **5s** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.58−7.51 (m, 4H), 7.48 (d, J = 8.3 Hz, 2H), 7.40 (t, J = 7.6 Hz, 1H), 7.26 (d, J = 9.0 Hz, 1H), 3.46 (t, J = 14.5 Hz, 2H), 2.81 (t, J = 7.5 Hz, 2H), 1.62 (p, J = 7.4 Hz, 2H), 1.37 (s, 9H), 1.36 (s, 2H), 1.31−1.23 (m, 9H), 0.88 (t, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 150.3, 141.1, 132.5, 130.0 (t, $^1J_{C-F_2}$ = 277.4 Hz), 129.2, 129.0, 126.8, 126.3, 125.6, 45.7 (t, $^2J_{C-F_2}$ = 24.5 Hz), 31.7, 31.3, 29.7, 29.0, 28.9, 28.7, 27.9, 22.5, 14.0. ^{19}F NMR (471 MHz, chloroform-*d*): δ −73.85 (t, J = 14.5 Hz). IR (film): 2957, 2926, 2855, 1728, 1483, 1267, 1191, 1152, 1008, 835, 766, 750, 703 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{26}H_{36}F_2S$ [M + H]$^+$, 419.2586; found, 419.2586.

*Ethyl (E)-3-(3-(2,2-Difluoro-2-(octylthio)ethyl)phenyl)acrylate (**5t**).* Following general procedure A, compound **1t** (0.119 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.146 g (76% yield) of desired product **5t** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.68 (d, J = 16.0 Hz, 1H), 7.48 (d, J = 7.6 Hz, 1H), 7.45 (s, 1H), 7.36 (t, J = 7.6 Hz, 1H), 7.31 (d, J = 7.6 Hz, 1H), 6.45 (d, J = 16.0 Hz, 1H), 4.27 (q, J = 7.1 Hz, 2H), 3.40 (t, J = 14.4 Hz, 2H), 2.80 (t, J = 7.5 Hz, 2H), 1.61 (p, J = 14.0, 6.9 Hz, 2H), 1.35 (m, 2H), 1.34 (t, J = 7.1 Hz, 3H), 1.27 (m, 8H), 0.87 (t, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 166.9, 144.2, 134.7, 133.0, 132.3, 130.2, 129.9 (t, $^1J_{C-F_2}$ = 276.8 Hz), 128.9, 127.3, 118.7, 60.5, 46.4 (t, $^2J_{C-F_2}$ = 24.9 Hz), 31.8, 29.8, 29.1, 29.0, 28.8, 28.0 (t, $^3J_{C-F_2}$ = 3.5 Hz), 22.6, 14.3, 14.1. ^{19}F NMR (471 MHz, chloroform-*d*): δ −73.03 (t, J = 14.4 Hz). IR (film): 2925, 2854, 1712, 1639, 1309, 1177, 1161, 1129, 992, 864 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{21}H_{30}F_2O_2S$ [M + H]$^+$, 385.2007; found, 385.1962.

*4-(2,2-Difluoro-2-(octylthio)ethyl)-N,N-diethylbenzamide (**5u**).* Following general procedure A, compound **1t** (0.120 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:5) to furnish 0.121 g (63% yield) of desired product **5t** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.27 (d, J = 15.0 Hz, 2H), 7.25 (d, J = 15.0 Hz, 2H), 3.48 (s, 2H), 3.33 (t, J = 14.5 Hz, 2H), 3.20 (s, 2H), 2.74 (t, J = 7.5 Hz, 2H), 1.55 (p, J = 7.5 Hz, 2H), 1.31−1.25 (m, 2H), 1.19 (s, 8H), 1.05 (s, 6H), 0.80 (t, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR(126 MHz, chloroform-*d*): δ 170.9, 136.5, 133.2 (t, $^3J_{C-F_2}$ = 3.6 Hz), 130.5, 129.8 (t, $^1J_{C-F_2}$ = 277.3 Hz), 126.4, 45.4 (t, $^2J_{C-F_2}$ = 25.0 Hz), 43.3, 39.2, 31.7, 29.7, 29.1, 29.0, 28.8, 27.9 (t, $^3J_{C-F_2}$ = 3.5 Hz), 22.6, 14.1. ^{19}F NMR (471 MHz, chloroform-*d*): δ −73.11 (t, J = 14.5 Hz). IR (film): 2925, 2854, 1630, 1457, 1425, 1285, 1219, 1094, 1011, 990, 784, 744 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{21}H_{33}F_2NOSNa$ [M + Na]$^+$, 408.2149; found, 408.2137.

*4-(2,2-Difluoro-2-(octylthio)ethyl)phenol (**5v**).* Following general procedure A, compound **1v** (0.078 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.033 g (22% yield) of desired product **5v** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.16 (d, J = 8.3 Hz, 2H), 6.80 (d, J = 8.4 Hz, 2H), 4.89 (s, 1H), 3.32 (t, J = 14.5 Hz, 2H), 2.83−2.74 (t, J = 7.5 Hz, 2H), 1.61 (p, J = 7.4 Hz, 2H), 1.42−1.18 (m, 10H), 0.88 (t, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 155.1, 131.8, 130.3 (t, $^1J_{C-F_2}$ = 277.7 Hz), 124.5 (t, $^3J_{C-F_2}$ = 4.0 Hz), 115.3, 44.7 (t, $^2J_{C-F_2}$ = 24.8 Hz), 31.8, 29.8, 29.1, 29.0, 28.8, 27.9 (t, $^3J_{C-F_2}$ = 3.6 Hz), 22.6, 14.1. ^{19}F NMR (471 MHz, chloroform-*d*): δ −72.83 (t, J = 14.6 Hz). IR (film): 3381, 2953, 2920, 2875, 2851, 1516, 1453, 1257, 1153, 998, 785, 766, 749, 707 cm^{-1}. HRMS (ESI)$^-$ *m*/*z*: calcd $C_{16}H_{23}F_2OS$ [M − H]$^-$, 301.1432; found, 301.1436.

*(1,1-Difluoro-2-(4-(methoxymethoxy)phenyl)ethyl)(octyl)sulfane (**5w**).* Following general procedure A, compound **1w** (0.100 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.086 g (50% yield) of desired product **6w** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.24 (d, J = 8.5 Hz, 2H), 7.03 (d, J = 8.6 Hz, 2H), 5.20 (s, 2H), 3.51 (s, 3H), 3.36 (t, J = 14.6 Hz, 3H), 2.83 (t, J = 7.5 Hz, 3H), 1.65 (p, J = 14.8, 7.3 Hz, 2H), 1.45−1.18 (m, 11H), 0.91 (t, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 156.9, 131.6, 130.2 (t, $^1J_{C-F_2}$ = 278.5 Hz), 125.5 (t, $^3J_{C-F_2}$ = 4.3 Hz), 116.1, 94.4, 56.0, 44.8 (t, $^2J_{C-F_2}$ = 24.8 Hz), 31.8, 29.8, 29.1, 29.1, 28.9, 27.9 (t, $^3J_{C-F_2}$ = 3.6 Hz), 22.7, 14.1. ^{19}F NMR (471 MHz, chloroform-*d*) −72.80 (t, J = 14.6 Hz). IR (film): 2961, 2926, 2855, 151, 1236, 1151, 1079, 1003, 779, 722, 652 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{18}H_{29}F_2O_2S$ [M + H]$^+$, 346.1773; found, 346.1780.

*(2-(4-(Benzyloxy)phenyl)-1,1-difluoroethyl)(octyl)sulfane (**5x**).* Following general procedure A, compound **1x** (0.123 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.171 g (87% yield) of desired product **5x** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.43 (d, J = 7.3 Hz, 2H), 7.39 (t, J = 7.5 Hz, 2H), 7.33 (t, J = 7.2 Hz, 1H), 7.21 (d, J = 8.5 Hz, 2H), 6.95 (d, J = 8.5 Hz, 2H), 5.06 (s, 2H), 3.33 (t, J = 14.5 Hz, 2H), 2.80 (t, J = 7.5 Hz, 2H), 1.62 (p, J = 7.4 Hz, 2H), 1.39−1.32 (m, 2H), 1.32−1.22 (m, 8H), 0.88 (t, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 158.4, 136.9, 131.5, 130.3 (t, $^1J_{C-F_2}$ = 277.1 Hz), 128.6, 127.9, 127.5, 124.5 (t, $^3J_{C-F_2}$ = 4.0 Hz), 114.7, 70.0, 45.7 (t, $^2J_{C-F_2}$ = 24.7 Hz), 31.7, 29.8, 29.1, 29.0, 28.8, 27.9 (t, $^3J_{C-F_2}$ = 3.6 Hz), 22.6, 14.0. ^{19}F NMR (471 MHz, chloroform-*d*): δ −73.31 (t, J = 14.5 Hz). IR (film): 2925, 2854, 1512, 1245, 1220, 1008, 988, 869, 764, 739, 696 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{23}H_{31}F_2OS$ [M + H]$^+$, 393.2064; found, 393.2059.

*4-(2,2-Difluoro-2-(octylthio)ethyl)dibenzo[b,d]thiophene (**5y**).* Following general procedure A, compound **1y** (0.123 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.143 g (72% yield) of desired product **5y** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 8.18−8.09 (m, 2H), 7.91−7.83 (m, 1H), 7.51−7.43 (m, 4H), 3.71 (t, J = 14.4 Hz, 2H), 2.84 (t, J = 7.5 Hz, 2H), 1.63 (p, J = 7.4 Hz, 2H), 1.39−1.32 (m, 2H), 1.32−1.22 (m, 8H), 0.89 (t, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 141.0, 139.0, 136.1, 135.9, 131.4 (t, $^1J_{C-F_2}$ = 278.6 Hz), 129.0, 126.9, 126.8, 124.7, 124.5, 122.7, 121.7, 121.1, 45.8 (t, $^2J_{C-F_2}$ = 25.8 Hz), 31.7, 29.7, 29.1,

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29.0, 28.8, 28.2 (t, $^3J_{C-F_2}$ = 3.5 Hz), 22.6, 14.1. ^{19}F NMR (471 MHz, chloroform-*d*): δ −71.28 (t, *J* = 14.4 Hz). IR (film): 2954, 2924, 2853, 1443, 1403, 1053, 1008, 989, 750, 724, 705 cm^{-1}. HRMS (ESI)$^+$ *m*/*z*: calcd $C_{22}H_{26}F_2S_2$ [M + H]$^+$, 393.1517; found, 393.1513.

*4-(2,2-Difluoro-2-(octylthio)ethyl)-1-phenyl-1H-pyrazole (**5z**).* Following general procedure A, compound **1z** (0.103 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.96 g (53% yield) of desired product **5z** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.88 (s, 1H), 7.68 (d, *J* = 8.1 Hz, 2H), 7.65 (s, 1H), 7.44 (t, *J* = 7.9 Hz, 2H), 7.28 (t, *J* = 7.4 Hz, 1H), 3.35 (t, *J* = 14.4 Hz, 2H), 2.84 (t, *J* = 7.5 Hz, 2H), 1.64 (p, *J* = 7.4 Hz, 2H), 1.41−1.34 (m, 2H), 1.34−1.20 (m, 8H), 0.88 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 141.9, 140.0, 129.8 (t, $^1J_{C-F_2}$ = 276.8 Hz), 129.4, 126.9, 126.5, 119.0, 113.8, 35.2 (t, $^2J_{C-F_2}$ = 26.2 Hz), 31.8, 29.8, 29.1, 29.0, 28.8, 28.0 (t, $^3J_{C-F_2}$ = 3.5 Hz), 22.6, 14.1. ^{19}F NMR (471 MHz, chloroform-*d*): δ −73.84 (t, *J* = 14.4 Hz). IR (film): 2925, 2854, 1601, 1505, 1428, 1400, 1378, 1261, 1073, 1023, 1005, 954, 753, 690 cm^{-1}. HRMS (ESI)$^+$ *m*/*z*: calcd $C_{19}H_{26}F_2N_2S$ [M + H]$^+$, 353.1858; found, 353.1859.

*(1,1-Difluoro-2-(4-methoxyphenyl)propyl)(octyl)sulfane (**5aa**).* Following general procedure A, compound **1aa** (0.097 g, 0.500 mmol) was reacted with 1-octanethiol (0.130 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.110 g (73% yield) of desired product **5aa** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.29 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 3.84 (s, 3H), 3.50−3.32 (m, 1H), 2.85 (t, *J* = 7.6 Hz, 2H), 1.64 (p, *J* = 7.4 Hz, 2H), 1.51 (d, *J* = 7.3 Hz, 2H), 1.41 (m, 2H), 1.32 (m, 8H), 0.93 (t, *J* = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 159.1, 132.5 (t, $^1J_{C-F_2}$ = 277.2 Hz), 130.5, 129.9, 113.7, 55.1, 47.9 (t, $^2J_{C-F_2}$ = 21.8 Hz), 31.8, 29.8, 29.1, 29.0, 28.9, 27.8 (t, $^3J_{C-F_2}$ = 3.9 Hz), 22.6, 15.6, 14.1. ^{19}F NMR (471 MHz, chloroform-*d*): δ −77.68 (dd, *J* = 202.2, 11.3 Hz), −79.98 (dd, *J* = 202.3, 14.5 Hz). IR (film): 2926, 2855, 1514, 1262, 1250, 1180, 1090, 1003, 981, 953, 764, 748, 706 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{18}H_{28}F_2OS$ [M + H]$^+$, 331.1902; found, 331.1892.

*3-(2,2-Difluoro-2-((6-hydroxyhexyl)thio)ethyl)benzonitrile (**6a**).* Following general procedure A, compound **1b** (0.084 g, 0.500 mmol) was reacted with 6-mercaptohexan-1-ol (0.103 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:5) to furnish 0.105 g (70% yield) of desired product **6a** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.62 (d, *J* = 7.7 Hz, 1H), 7.60 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 1H), 3.64 (t, *J* = 6.6 Hz, 2H), 3.42 (t, *J* = 14.2 Hz, 2H), 2.83 (t, *J* = 7.4 Hz, 2H), 1.65 (p, *J* = 7.3 Hz, 2H), 1.56 (p, *J* = 6.7 Hz, 2H), 1.45−1.34 (m, 4H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 135.0, 134.0, 133.7 (t, $^3J_{C-F_2}$ = 3.9 Hz), 131.5, 129.40 (t, $^1J_{C-F_2}$ = 278.1 Hz), 129.3, 115.96, 112.7, 62.8, 45.1 (t, $^2J_{C-F_2}$ = 25.5 Hz), 32.5, 29.7, 28.5, 27.9 (t, $^3J_{C-F_2}$ = 3.7 Hz), 25.2. ^{19}F NMR (470 MHz, chloroform-*d*): δ −73.2 (t, *J* = 14.3 Hz). IR (film): 3353, 2931, 2857, 2231, 1733, 1275, 1260, 1017, 921, 764, 750 cm^{-1}. HRMS (ESI)$^+$ *m*/*z*: calcd $C_{15}H_{19}F_2NOSNa$ [M + Na]$^+$, 322.1053; found, 322.1036.

*3-(2,2-Difluoro-2-((1-hydroxyhexan-3-yl)thio)ethyl)benzonitrile (**6b**).* Following general procedure A, compound **1b** (0.084 g, 0.500 mmol) was reacted with 3-mercaptohexan-1-ol (0.105 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:5) to furnish 0.102 g (68% yield) of desired product **6b** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.61 (d, *J* = 7.7 Hz, 1H), 7.60 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 1H), 3.75 (dtt, *J* = 13.3, 8.0, 4.9 Hz, 2H), 3.43 (t, *J* = 14.3 Hz, 2H), 1.93 (td, *J* = 14.0, 5.8 Hz, 1H), 1.74 (ddt, *J* = 14.5, 9.2, 5.5 Hz, 1H), 1.68−1.53 (m, 3H), 1.50−1.34 (m, 3H), 0.90 (t, *J* = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 134.9, 134.0, 133.6 (t, $^3J_{C-F_2}$ = 3.7 Hz), 131.4, 129.7 (t, $^1J_{C-F_2}$ = 278.4 Hz), 129.2, 118.5, 60.1, 46.5 (t, $^2J_{C-F_2}$ = 24.7 Hz), 41.1, 38.6, 38.3, 19.7, 13.7. ^{19}F NMR (471 MHz, chloroform-*d*): δ −70.61 (dt, *J* = 203.5, 14.4 Hz), −71.43 (dt, *J* = 203.5, 14.2 Hz). IR (film): 3377, 3006, 2959, 2930, 2872, 2231, 1465, 1275, 1260, 1016, 992, 764, 750 cm^{-1}. HRMS (ESI)$^-$ *m*/*zm*/*z*: calcd $C_{15}H_{19}F_2NOS$ [M + Cl]$^-$, 334.0843; found, 334.0860.

*Butyl 3-((2-(3-Cyanophenyl)-1,1-difluoroethyl)thio)propanoate (**6c**).* Following general procedure A, compound **1b** (0.083 g, 0.500 mmol) was reacted with butyl 3-mercaptopropanoate (0.122 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.134 g (82% yield) of desired product **6c** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.62 (d, *J* = 7.7 Hz, 1H), 7.59 (s, 1H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 1H), 4.10 (t, *J* = 6.8 Hz, 2H), 3.42 (t, *J* = 14.3 Hz, 2H), 3.07 (t, *J* = 7.1 Hz, 2H), 2.69 (t, *J* = 7.1 Hz, 3H), 1.70−1.57 (m, 2H), 1.37 (h, *J* = 7.4 Hz, 2H), 0.93 (t, *J* = 7.4 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 171.6, 135.1, 134.1, 133.6 (d, $^3J_{C-F_2}$ = 3.9 Hz), 131.7, 129.6 (t, $^1J_{C-F_2}$ = 278.4 Hz), 129.5, 116.1, 112.9, 64.9, 45.0 (t, $^2J_{C-F_2}$ = 25.0 Hz), 35.5, 30.7, 23.3 (t, $^3J_{C-F_2}$ = 4.1 Hz), 19.2, 13.8. ^{19}F NMR (470 MHz, chloroform-*d*): δ −73.39 (t, *J* = 14.3 Hz). IR (film): 3005, 2988, 2961, 2873, 2231, 1731, 1275, 1260, 1098, 1018, 764, 750 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{16}H_{20}FNO_2S$ [M − F]$^+$, 308.1122; found, 308.1129. The found HRMS corresponds to loss of HF, so GCMS was run to confirm the structure: LRMS (EI)$^+$ *m*/*z*: calcd $C_{16}H_{20}FNO_2S$, 327.1; found, 327.0, 307.1, 254.0, 225.0 166.0, 161.0, 116.0, 105.0, 73.0.

*3-((2-(3-Cyanophenyl)-1,1-difluoroethyl)thio)propanoic Acid (**6d**).* Following general procedure B, compound **1b** (0.083 g, 0.500 mmol) was reacted with 3-mercaptopropionic acid (0.065 mL, 0.750 mmol) in the presence of pyridine (0.10 mL, 1.00 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by reverse-phase flash chromatography using acetonitrile and H_2O containing 0.1% acetic acid (5−95%) to furnish 0.046 g (34% yield) of desired product **6d** as a colorless oil. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.62 (d, *J* = 7.6 Hz, 1H), 7.59 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 1H), 3.43 (t, *J* = 14.3 Hz, 2H), 3.08 (t, *J* = 7.1 Hz, 2H), 2.77 (t, *J* = 7.1 Hz, 2H). ^{13}C{^{1}H} NMR (201 MHz, DMSO): δ 172.9, 136.0, 134.5, 134.4, 131.8, 130.4 (t, $^1J_{C-F_2}$ = 276.7 Hz), 130.0, 119.0, 111.7, 43.7 (t, $^2J_{C-F_2}$ = 24.1 Hz), 31.1, 15.6. ^{19}F NMR (471 MHz, chloroform-*d*): δ −72.74 (t, *J* = 14.4 Hz). IR (film): 3006, 2989, 2925, 2231, 1731, 1705, 1275, 1260, 1027, 919, 754, 750 cm^{-1}. HRMS (ESI)$^-$ *m*/*z*: calcd $C_{12}H_{11}F_2NO_2S$ [M − H]$^-$, 270.0406; found, 270.0424.

*3-(2-((3-Chloropropyl)thio)-2,2-difluoroethyl)benzonitrile (**6e**).* Following general procedure A, compound **1b** (0.083 g, 0.500 mmol) was reacted with 3-chloro-1-propanethiol (0.073 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.066 g (48% yield) of desired product **6e** as a colorless oil. ^{1}H NMR

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(500 MHz, chloroform-*d*): δ 7.62 (d, *J* = 7.7 Hz, 1H), 7.59 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 1H), 3.62 (t, *J* = 6.2 Hz, 2H), 3.43 (t, *J* = 14.3 Hz, 2H), 2.99 (t, *J* = 7.0 Hz, 2H), 2.10 (p, *J* = 6.6 Hz, 2H). $^{13}C\{^1H\}$ NMR (126 MHz, chloroform-*d*): δ 134.9, 133.9, 133.4 (t, $^3J_{C-F_2}$ = 3.6 Hz), 131.5, 129.3 (t, $^1J_{C-F_2}$ = 279.3 Hz), 129.3, 118.4, 44.9 (t, $^2J_{C-F_2}$ = 25.3 Hz), 43.0, 32.5, 25.2 (t, $^3J_{C-F_2}$ = 3.7 Hz). ^{19}F NMR (471 MHz, chloroform-*d*): δ −72.94 (t, *J* = 14.3 Hz). IR (film): 3006, 2989, 2230, 1260, 1275, 1098, 1017, 994, 764, 749, 725 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{12}H_{13}ClF_2NS$ $[M + H]^+$, 276.0420; found, 276.0423.

3-(2-(Cyclohexylthio)-2,2-difluoroethyl)benzonitrile (**6f**). Following general procedure A, compound **1b** (0.083 g, 0.500 mmol) was reacted with cyclohexanethiol (0.092 mL, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.114 g (81% yield) of desired product **6f** as a colorless oil. ^1H NMR (500 MHz, chloroform-*d*): δ 7.60 (d, *J* = 9.1 Hz, 2H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 1H), 3.40 (t, *J* = 14.2 Hz, 2H), 3.28 (ddd, *J* = 14.0, 8.5, 3.8 Hz, 1H), 2.05−1.88 (m, 2H), 1.76−1.64 (m, 2H), 1.60−1.53 (m, 1H), 1.39 (ddt, *J* = 34.9, 24.1, 11.2 Hz, 4H), 1.28−1.19 (m, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, chloroform-*d*): δ 134.0, 133.8 (t, $^3J_{C-F_2}$ = 3.9 Hz), 131.3, 129.8 (t, $^1J_{C-F_2}$ = 277.3 Hz), 129.2, 118.6, 45.3 (t, $^2J_{C-F_2}$ = 25.3 Hz), 42.3 (t, $^3J_{C-F_2}$ = 2.3 Hz), 34.5, 25.9, 25.4. ^{19}F NMR (471 MHz, chloroform-*d*): δ −71.27 (t, *J* = 13.6 Hz). IR (film): 3006, 2989, 2931, 2854, 2231, 1449, 1333, 1275, 1260, 1098, 1016, 764, 750 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{15}H_{18}F_2NS$ $[M + H]^+$, 282.1128; found, 282.1124.

3-(2,2-Difluoro-2-(phenethylthio)ethyl)benzonitrile (**6g**). Following general procedure C, compound **1b** (0.083 g, 0.500 mmol) was reacted with 2-phenylethane-1-thiol (0.100 mL, 0.750 mmol) in the presence of pyridine (0.10 mL, 1.00 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 120 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.077 g (51% yield) of desired product **6g** as a colorless oil. ^1H NMR (500 MHz, chloroform-*d*): δ 7.62 (d, *J* = 7.6 Hz, 1H), 7.60 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.30 (t, *J* = 7.5 Hz, 1H), 7.23 (t, *J* = 7.4 Hz, 1H), 7.18 (d, *J* = 6.9 Hz, 2H), 3.43 (t, *J* = 14.2 Hz, 2H), 3.08 (dd, *J* = 9.2, 6.5 Hz, 2H), 2.94 (dd, *J* = 9.1, 6.5 Hz, 2H). $^{13}C\{^1H\}$ NMR (126 MHz, chloroform-*d*): δ 139.6, 134.9, 134.0, 133.6 (t, $^3J_{C-F_2}$ = 3.7 Hz), 131.4, 129.4 (t, $^1J_{C-F_2}$ = 277.0 Hz), 129.2, 128.5, 128.4, 126.6, 118.6, 118.4, 44.9 (t, $^2J_{C-F_2}$ = 25.1 Hz), 36.3, 29.4 (t, $^3J_{C-F_2}$ = 3.4 Hz). ^{19}F NMR (470 MHz, chloroform-*d*): δ −73.1 (t, *J* = 14.3 Hz). IR (film): 2955, 2926, 2854, 2232, 1489, 1264, 1217, 1153, 1012, 990, 764, 738, 764, 705 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{17}H_{16}F_2NS$ $[M + H]^+$, 304.0966; found, 304.0965.

3-(2,2-Difluoro-2-((2-methylundecan-2-yl)thio)ethyl)benzonitrile (**6h**). Following general procedure C, compound **1b** (0.083 g, 0.500 mmol) was reacted with *tert*-dodecylmercaptan (0.176 mL, 0.750 mmol) in the presence of pyridine (0.10 mL, 1.00 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 120 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.051 g (28% yield) of desired product **6h** as a colorless oil. ^1H NMR (500 MHz, chloroform-*d*): δ 7.59 (d, *J* = 5.6 Hz, 2H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 3.37 (t, *J* = 14.3 Hz, 2H), 1.95−1.48 (m, 4H), 1.47−1.04 (m, 10H), 1.05−0.73 (m, 13H). $^{13}C\{^1H\}$ NMR (126 MHz, chloroform-*d*): δ 135.1, 134.1, 131.2 (t, $^3J_{C-F_2}$ = 4.9 Hz), 130.7 (t, $^1J_{C-F_2}$ = 280.8 Hz), 129.9−128.6 (m), 118.6, 112.5 (t, $^3J_{C-F_2}$ = 4.9 Hz), 48.2−43.7 (m), 30.8−28.5 (m), 27.2, 26.7 (d, $^3J_{C-F_2}$ = 3.4 Hz), 25.1, 22.6 (t, $^3J_{C-F_2}$ = 4.3 Hz), 19.2, 15.0−14.2 (m), 14.0, 12.2, 8.7 (d, $^3J_{C-F_2}$ = 3.5 Hz). ^{19}F NMR (471 MHz, chloroform-*d*): δ −66.38−−71.38 (m). IR (film): 3005, 2989, 2872, 2233, 1275, 1260, 1135, 1098, 906, 764, 749 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{21}H_{32}F_2NS$ $[M + H]^+$, 368.2218; found, 368.2223.

3-(2,2-Difluoro-2-(phenylthio)ethyl)benzonitrile (**6i**). Following general procedure A, compound **1b** (0.083 g, 0.500 mmol) was reacted with thiophenol (0.077 g, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.117 g (79% yield) of desired product **6i** as a colorless solid. ^1H NMR (500 MHz, chloroform-*d*): δ 7.63 (d, *J* = 6.5, 1H), 7.58 (s, 2H), 7.56 (s, 1H), 7.53 (d, *J* = 7.4 Hz, 1H), 7.45 (q, *J* = 7.9 Hz, 2H), 7.39 (t, *J* = 8.0 Hz, 2H), 3.45 (t, *J* = 14.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (126 MHz, chloroform-*d*): δ 136.8, 135.0, 134.0, 133.5 (t, $^3J_{C-F_2}$ = 3.6 Hz), 131.5, 130.1, 129.3, 129.2, 128.0 (t, $^1J_{C-F_2}$ = 279.5 Hz), 126.3 (t, $^3J_{C-F_2}$ = 2.6 Hz), 118.5, 112.7, 44.6 (t, $^2J_{C-F_2}$ = 25.1 Hz). ^{19}F NMR (470 MHz, chloroform-*d*): δ −72.6 (t, *J* = 14.6 Hz). mp 33−36 °C. IR (film): 3005, 2989, 2231, 1275, 1260, 1098, 1035, 916, 764, 750, 705 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{15}H_{11}F_2NS$ $[M + H]^+$, 276.0653; found, 276.0659.

(1,1-Difluoro-2-(3-nitrophenyl)ethyl)(phenyl)sulfane (**6j**). Following general procedure A, compound **1e** (0.093 g, 0.500 mmol) was reacted with thiophenol (0.077 g, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.122 g (83% yield) of desired product **6j** as a colorless solid. ^1H NMR spectra match the previously reported spectra.[14]

4-(2,2-Difluoro-2-(phenylthio)ethyl)benzonitrile (**6k**). Following general procedure A, compound **1c** (0.083 g, 0.500 mmol) was reacted with thiophenol (0.077 g, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.116 g (84% yield) of desired product **6k** as a colorless solid. ^1H NMR spectra match the previously reported spectra.[14]

3-(2,2-Difluoro-2-((3-hydroxyphenyl)thio)ethyl)benzonitrile (**6l**). Following general procedure A, compound **1b** (0.082 g, 0.500 mmol) was reacted with 3-hydroxythiophenol (0.095 g, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:5) to furnish 0.102 g (70% yield) of desired product **6l** as a colorless solid. ^1H NMR (500 MHz, chloroform-*d*): δ 7.62 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.57 (s, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 1H), 7.26 (d, *J* = 4.5 Hz, 1H), 7.13 (d, *J* = 7.8 Hz, 1H), 6.91 (dd, *J* = 8.2, 2.7 Hz, 1H), 5.11 (s, 1H), 3.45 (t, *J* = 14.5 Hz, 2H). $^{13}C\{^1H\}$ NMR (126 MHz, chloroform-*d*): δ 155.8, 135.0, 134.1, 133.5 (t, $^3J_{C-F_2}$ = 3.6 Hz), 131.5, 130.2, 129.3, 128.3, 128.0 (t, $^1J_{C-F_2}$ = 280.1 Hz), 127.5 (t, $^3J_{C-F_2}$ = 2.7 Hz), 122.6, 118.5, 117.3, 112.7, 44.6 (t, $^2J_{C-F_2}$ = 24.7 Hz). ^{19}F NMR (470 MHz, chloroform-*d*): δ −72.4 (t, *J* = 14.5 Hz). mp 94−97 °C. IR (film): 3370, 3005, 2989, 2235, 1583, 1275, 1260, 1035, 1017, 886, 764, 750, 689 cm^{-1}. HRMS (ESI)$^-$ *m*/*z*: calcd $C_{15}H_{11}F_2NOS$ $[M - H]^-$, 290.0457; found, 290.0446.

3-(2,2-Difluoro-2-((3-(trifluoromethyl)phenyl)thio)ethyl)-benzonitrile (**6m**). Following general procedure A, compound **1b** (0.083 g, 0.500 mmol) was reacted with 3-trifluoromethylthiophenol (0.134 g, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C

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for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.124 g (72% yield) of desired product **6m** as a colorless solid. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.84 (s, 1H), 7.79 (d, J = 7.8 Hz, 1H), 7.72 (d, J = 7.8 Hz, 1H), 7.67 (d, J = 7.7 Hz, 1H), 7.63 (s, 1H), 7.57 (s, 1H), 7.55 (q, J = 7.9 Hz, 1H), 7.51 (t, J = 7.7 Hz, 1H), 3.52 (t, J = 14.3 Hz, 2H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 139.3, 134.9, 134.0, 133.1 (t, $^3J_{C-F_2}$ = 3.5 Hz), 132.7 (q, $^3J_{C-F_2}$ = 4.4 Hz), 131.8, 131.7, 130.0, 129.6, 129.4, 127.8 (t, $^1J_{C-F_2}$ = 281.7 Hz), 127.5 (t, $^3J_{C-F_2}$ = 2.4 Hz), 126.8 (q, $^3J_{C-F_2}$ = 4.0 Hz), 118.4, 112.9, 44.7 (t, $^2J_{C-F_2}$ = 24.0 Hz). ^{19}F NMR (470 MHz, chloroform-*d*): δ −63.3, −71.9 (t, J = 14.4 Hz). mp 46−49 °C. IR (film): 3006, 2989, 2233, 1303, 1275, 1260, 1085, 764, 750 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{16}H_{11}F_5NS$ [M + H]$^+$, 344.0527; found, 344.0511.

*3-(2,2-Difluoro-2-((4-methoxyphenyl)thio)ethyl)benzonitrile (**6n**).* Following general procedure A, compound **1b** (0.082 g, 0.500 mmol) was reacted with 4-methoxythiophenol (0.105 g, 0.750 mmol) in the presence of pyridine (0.01 mL, 0.10 mmol), LiOTf (0.008 g, 0.050 mmol), and 2-methoxyethanol (0.080 mL, 1.00 mmol) in 1.5 mL of *o*-xylene using a heating mantle at 110 °C for 24 h. The material was worked up according to the general procedure and purified by normal-phase flash chromatography using EtOAc and hexanes (1:10) to furnish 0.130 g (85% yield) of desired product **6n** as a colorless solid. ^{1}H NMR (500 MHz, chloroform-*d*): δ 7.61 (dd, J = 7.7, 1.4 Hz, 1H), 7.57 (s, 1H), 7.53 (d, J = 7.53, 1H), 7.48 (d, J = 7.8 Hz, 2H), 7.44 (t, J = 7.4 Hz, 1H), 6.90 (d, J = 7.72, 2H), 3.83 (s, 3H), 3.42 (t, J = 14.5 Hz, 2H). ^{13}C{^{1}H} NMR (126 MHz, chloroform-*d*): δ 161.3, 138.1, 135.0, 134.0, 133.7 (t, $^3J_{C-F_2}$ = 3.1 Hz), 131.4, 129.3, 127.9 (t, $^1J_{C-F_2}$ = 279.9 Hz), 118.6, 116.7 (t, $^3J_{C-F_2}$ = 2.7 Hz), 114.8, 55.4, 44.3 (t, $^2J_{C-F_2}$ = 25.4 Hz). ^{19}F NMR (470 MHz, chloroform-*d*): δ −73.7 (t, J = 14.5 Hz). mp 73−76 °C. IR (film): 3006, 2989, 2230, 1591, 1275, 1259, 1097, 1028, 985, 764, 750 cm^{-1}. HRMS (APCI)$^+$ *m*/*z*: calcd $C_{16}H_{13}F_2NOS$ [M + H]$^+$, 306.0759; found, 306.0766.

Synthesis of Compound Octane-1-thiol-*d*. An oven-dried 50 mL round bottom flask was charged with octanethiol (2.0 mL, 11 mmol). Then, methanol-d_4 (10.0 mL, 247 mmol) was added and then removed under reduced pressure. Methanol-d_4 (10.0 mL, 247 mmol) was again added to the material and removed under reduced pressure to give a quantitative yield of the desired product (96% deuteration). ^{1}H NMR spectra match the previously reported spectra.[35]

Synthesis of Compound 2-Methoxyethan-1-ol-*d*. 2-Methoxyethan-1-ol-*d* was prepared according to a previous report.[36]

Synthesis of Compound 13. An oven-dried 50 mL round bottom flask equipped with a reflux condenser and a magnetic stir bar was charged with acetonitrile (20 mL). Then, octanethiol (1.5 mL, 8.7 mmol) and styrene (1.0, 8.7 mmol) were added via a syringe. The reaction mixture was then heated to 70 °C and stirred for 24 h. The reaction was then cooled to rt, concentrated onto SiO_2, and purified by normal-phase flash chromatography using hexanes to provide 1.15 g (53% yield) of desired product **13** as a colorless oil. ^{1}H NMR spectra match the previously reported spectra.[37]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02440.

Copies of ^{1}H, ^{13}C{^{1}H}, and ^{19}F spectra for synthesized compounds and data supporting mechanistic investigations (PDF)

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Notes

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