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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.8b02785 • Publication Date (Web): 24 Dec 2018

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Synthesis of *N*-Acyl Sulfamates from Fluorosulfates and Amides

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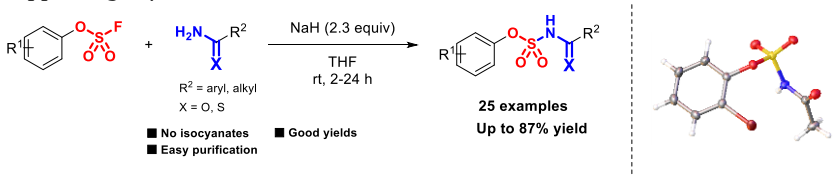
Supporting Information Placeholder



ABSTRACT: A novel synthetic strategy towards *N*-acyl sulfamates was developed. Interestingly, fluorosulfates, a new emerging class of electrophiles, were used to construct the sulfamate core. This precludes handling of chlorosulfonyl isocyanate and sulfamoyl chloride. In combination with amides, a wide and diverse set of *N*-acyl sulfamates was synthesized, including functionalized bioactive compounds. Furthermore, initial results showed that this method is also amenable to access *N*-thioacyl sulfamates.

Sulfur-based functional groups are encountered in numerous biologically relevant molecules.[1] In particular sulfonamides and thioesters are virtually essential in our daily therapeutics.[2] Recently, sulfamates have gained more attention by the scientific community as this functional group has bioactive properties.[3-5]

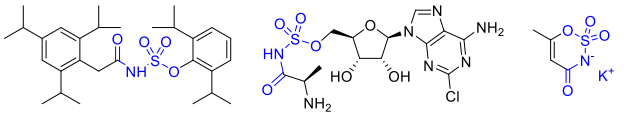
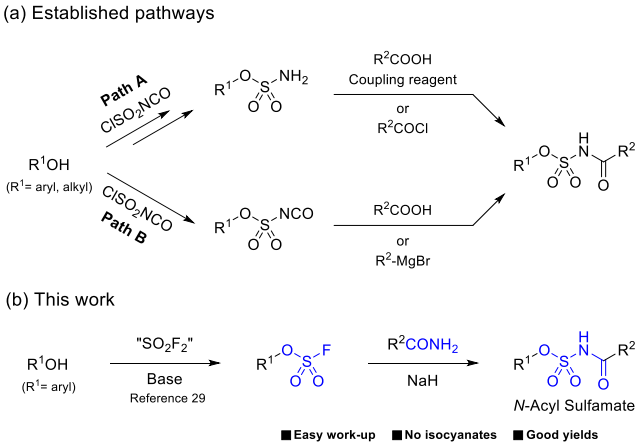


Figure 1. Sulfamate-containing bioactive molecules.

In particular the *N*-acylated sulfamate analogs exhibit interesting biological activities with Avasimibe and Ascamycin as two archetypal examples (Figure 1). The former is an Acyl-coenzyme A:Cholesterol Acyl Transferase (ACAT) inhibitor that reached clinical phase III as an anti-hyperlipidemic and anti-atherosclerotic agent. The latter, Ascamycin, is a natural nucleotide antibiotic produced by *Strepromyces sp.* and is identified as a potent inhibitor of aminoacyl-tRNA synthetases (aaRSs).[6,7] Moreover, the *N*-acyl sulfamate moiety serves as a good bioisoster for the labile acylphosphate functional group.[8-10] *N*-acyl sulfamates are not only endowed with therapeutic applications, *e.g.* Acesulfam-K is a well known artificial sweetener and is widely used in the food industry.[11] Other applications of the *N*-acyl sulfamate functionality can be found in ruthenium catalysis as it acts as an oxidizing directing group.[12]

Despite the presence of *N*-acyl sulfamates in biologically relevant molecules, only limited synthetic methodologies for their synthesis exist (Scheme 1). Current strategies rely on the use of chlorosulfonyl isocyanate or its unstable derivative, sulfamoyl chloride. Syntheses involve highly exothermic reaction procedures that release stoichiometric amounts of carbon monoxide and carbon dioxide.[13-16] Both agents are classified as reactive, toxic and hence require storage at low temperatures. In addition, the established pathways are susceptible to extensive purifications and variable yields.

Scheme 1. Strategies for the synthesis of *N*-acyl sulfamates.

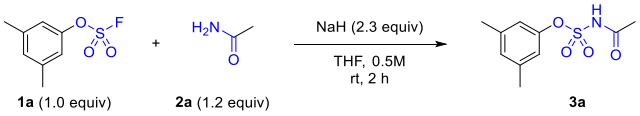


Here, we propose an alternative and straightforward strategy starting from fluorosulfates as the sulfate core. This newly emerging class of electrophiles are excellent substrates for various transformations including Sharpless' click sulfur(VI) fluoride exchange (SuFEx) chemistry[17-19] and cross-coupling reactions.[20-24]

For a long time, fluorosulfates have been rather hard to synthesize given the requirement of using lecture bottles of pressurized SO_2F_2 or inefficient protocols. Recently, these problems have been overcome by the development of general fluorosulfation procedures either by using an *ex situ* SO_2F_2 precursor in a two-chamber reactor[25] or *in situ* surrogates.[26,27] With this methodology at hand we now report on the synthesis of *N*-acyl sulfamates starting from aryl fluorosulfates and amides.

We hypothesized that aryl fluorosulfates are able to react with weak nucleophiles, amides in particular, under strong basic conditions. After a thorough optimization study, the desired *N*-acyl sulfamate **3a** could be isolated in 85% yield (Table 1). The optimized reaction conditions consist of reacting fluorosulfate **1a** (1.0 equiv) and acetamide (1.2 equiv) in the presence of sodium hydride (2.3 equiv) in THF at room temperature for two hours (entry 1). Performing the reaction with less equivalents of sodium hydride (1.5 instead of 2.3 equiv) diminished the yield to 64% (entry 2). This observation was expected as formation of the *N*-acyl sulfamate generates a second acidic proton that consumes the remaining unreacted base. On the other hand, increasing the amount of sodium hydride had no deterring effect on the reaction (entry 3). The reaction also works using a higher boiling, aprotic solvent such as dioxane (entry 4). Next, the applicability of organobases was examined. 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), which is widely used in SuFEx chemistry as a catalytic base, was not able to successfully couple the fluorosulfate with the amide as only trace amounts of the product were observed (entry 6). The more basic 1,5,7-triazabicyclo[4.4.0]dec-5-ene did furnish the desired product, although in only 17% yield (entry 7). Potassium *tert*-butoxide solidified the reaction mixture and hence was not suitable for this reaction (entry 8). Unfortunately, $NaNH_2$ yielded only 24% of the product (entry 9).

Table 1. Optimization of the reaction conditions

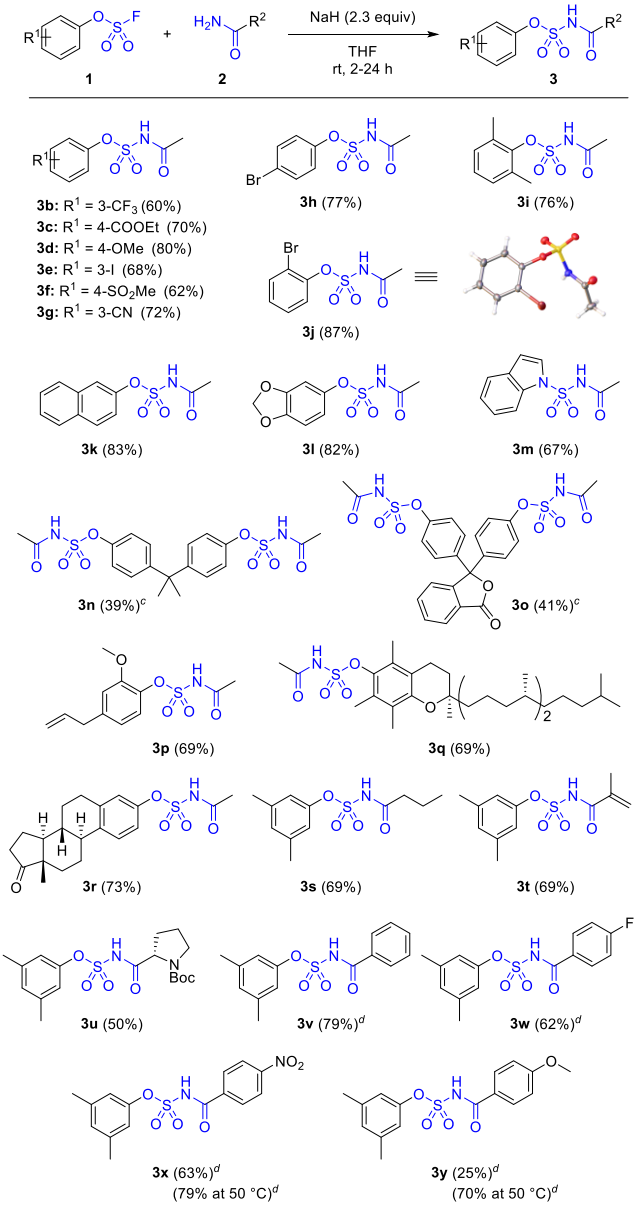


1a (1.0 equiv) **2a** (1.2 equiv) **3a**

entry	Deviation from standard conditions	Yield[a] (%)
1	none	97 (85)[b]
2	1.5 equiv NaH	64
3	3.0 equiv NaH	97
4	30 min reaction time	83
5	Dioxane instead of THF	87
6	2.3 equiv DBU instead of NaH, 24 h	Traces
7	2.3 equiv TBD instead of NaH	17
8	2.3 equiv *t*-BuOK instead of NaH	- [c]
9	2.3 equiv $NaNH_2$ instead of NaH	24

[a]Yield determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. [b]Isolated yield. [c]The reaction mixture instantaneously solidified upon addition of the solvent.

Scheme 2. Synthesis of *N*-acyl sulfamates from fluorosulfates and amides using sodium hydride as base.[a, b]



[a]Reaction conditions: 1.0 mmol of **1**, 1.2 mmol of amide **2**, 2.3 mmol NaH, 2 mL THF (dry) under argon atmosphere. [b]Isolated yield. [c]0.5 mmol instead of 1.0 mmol fluorosulfate. [d]Reaction was stirred for 24 hours.

Other bases such as sodium bis(trimethylsilyl)amide (NaHMDS) and lithium bis(trimethylsilyl)amide (LiHMDS) were evaluated as well but resulted in very complex reaction mixtures with poor yields (results not shown). It is clear that the use of sodium hydride is mandatory to convert the fluorosulfate smoothly into the *N*-acyl sulfamate. Noteworthy is the ease of purification of this reaction; extraction with 10% $NaHCO_3$ and subsequent acidification using 4 M HCl provided the desired product in high purity. Throughout the optimization study, one main side product was regularly observed and identified as the phenol of the corresponding fluorosulfate. It is hypothesized that traces of water might be able to hydrolyze either the fluorosulfate or the *N*-acyl sulfamate during the progress of the reaction.

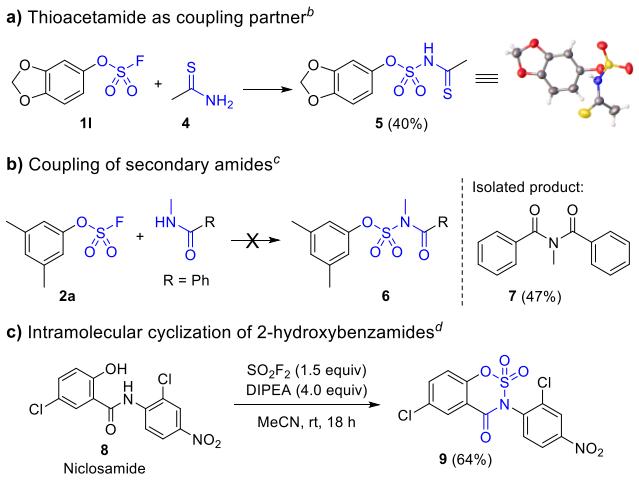
Next, the scope and functional group tolerance of the reaction were investigated (Scheme 2). First, several mono-substituted

fluorosulfates (including halide, ester and nitrile substituents) were coupled and isolated in moderate to very good yields (**3b-3j**). Gratifyingly, both the ester and nitrile group were tolerated under the optimized reaction conditions (**3c** and **3g**). Additionally, ortho-substituents did not dramatically hamper the reaction as seen with compounds **3i** and **3j**. Moreover, the structure of **3j** was confirmed *via* X-ray analysis. Bicyclic compounds **3k** and **3l** were obtained successfully from their corresponding fluorosulfates. The fluorosulfonyl analog of indole (-NSO_2F) produced the corresponding sulfonylacetamide in comparable yield (**3m**) suggesting similar reactivity compared to fluorosulfates (-OSO_2F). Substrates containing two fluorosulfate groups formed the bifunctional *N*-acylderivatives in fair yields (**3n-3o**). Next, it was investigated whether naturally occurring phenols could be derivatized with the *N*-acetyl sulfamate group. First, eugenol and D-α-tocopherol were fluorosulfated in excellent yields (see SI) and subsequently converted into the *N*-acyl sulfamate derivative (**3p** and **3q**). Interestingly, the developed procedure was amenable to the synthesis of the *N*-acetylated sulfamate analog of estrone (**3r**), a known bioactive compound that has been subject to biological studies on the mechanism of irreversible estrone sulphatase inhibitors.[28]

We also briefly investigated the scope of various amides as coupling partners. Both butyramide as well as methylacrylamide provided **3s** and **3t** in good yields. In addition, Boc-prolinamide was successfully converted into **3u**. Benzamide proved to be less reactive than alkylamides; after 24 hours of reaction, **3v** was isolated in 79% yield. When evaluating para-substituted benzamides, however, the products **3w**-**3y** were furnished in significantly lower yield. We speculate that this can be explained by the poor solubility of these benzamides. Fortunately, performing the reaction at elevated temperatures (50 °C) improved the yield significantly.

A few additional experiments were performed to further investigate the scope and limitations of the developed procedure. Since thioamides are well-known isosters of amides, we wondered if they could be used in this transformation.[29]

Scheme 3. Additional experiments[a]



[a]Isolated yield. [b]Reaction conditions: 1.0 mmol of **1l**, 1.2 mmol of thioamide **4**, 2.3 mmol NaH, 2 mL THF (dry) under argon atmosphere. [c]1.3 mmol NaH was used. [d]The reaction was conducted in a two-chamber reactor, see Experimental Section for details.

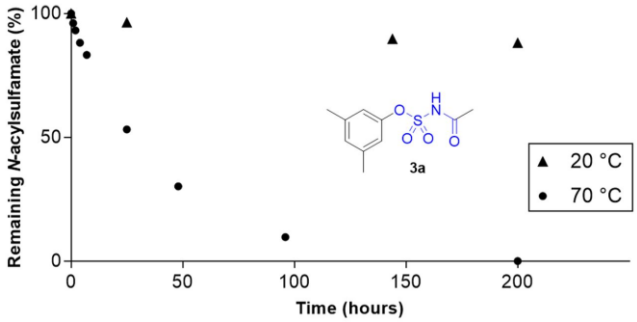


Figure 2. Experimental plot of the decomposition of **3a** in a pH 13 aqueous solution at 20 and 70 °C.

Gratifyingly, reaction of the fluorosulfated analog of sesamol with thioacetamide yielded the desired compound (**5**); the structure was confirmed *via* X-ray analysis (Scheme 3a). To the best of our knowledge, this is the first method to synthesize acyclic *N*-thioacyl sulfamates.

Next, we were interested if secondary amides performed equally well in the above outlined reaction. Unfortunately, when reacting *N*-methyl benzamide with fluorosulfate **2a**, the *N*-substituted *N*-acyl sulfamate **6** was not formed (Scheme 3b). Instead, the symmetric imide **7** derived from benzamide was isolated. We hypothesize that the *N*-substituted *N*-acyl sulfamate is formed *in situ* but instantaneously reacts with a second equivalent of benzamide under the basic conditions. These findings were not observed for the free *N*-acyl sulfamate; here the remainder of the base directly deprotonates the newly created acidic proton thus decreasing its reactivity towards an attack on the carbonyl functionality.

Lastly, we investigated whether the reaction could occur intramolecularly and if we could hence cyclize ortho-amidesubstituted fluorosulfates, forming a 6-membered ring. Such cyclizations are interesting in *e.g.* late-stage functionalization of active pharmaceutical ingredients (API's). Niclosamide, an anthelmintic agent, was chosen as substrate. To our surprise, the intramolecular cyclization already occurred during the fluorosulfation reaction; compound **9** was furnished in 64% yield by reacting Niclosamide **8** with SO_2F_2 under basic conditions (Scheme 3c). A similar observation was reported earlier by Hedayatullah.[30]

The stability of the *N*-acyl sulfamate functionality towards hydrolytic cleavage was assessed in basic medium. Compound **3a** was dissolved in an aqueous solution at pH 13 and stored at both 20 and 70 °C (Figure 2). The sample stored at 20 °C showed slow degradation towards the corresponding phenol with 88% of the *N*-acyl sulfamate still intact after an incubation time of 200 hours (or approximately 8 days). In contrast, at higher temperatures, **3a** is more prone towards degradation: already 50% of the starting material is hydrolyzed after 24 hours. After 200 hours, no remaining *N*-acyl sulfamate was detected in the sample. The acidic stability had been assessed in earlier work and *N*-acyl sulfamates showed higher lability under those conditions with half-life values in the range of 0.6-1.5 hours at 70 °C.[31]

In summary, we describe a novel route towards biologically interesting *N*-acyl sulfamates. After a detailed optimization study, it was found that sodium hydride exhibits a privileged performance for the direct coupling of aryl fluorosulfates with amides to afford *N*-acyl sulfamates. Interestingly, the developed method relies on fluorosulfates, a newly emerging class of elec-

trophiles and thereby omits the use of chlorosulfonyl isocyanate. Various fluorosulfates were prepared, including several analogs of bioactive molecules, and subsequently coupled with a variety of amides. Moreover, initial results suggest that this method can be extended towards the synthesis of unpreceded acyclic *N*-thioacyl sulfamates.

EXPERIMENTAL SECTION

General Experimental Information. All reagents were obtained from commercially available sources and were used as purchased without further purification. 1,1'-Sulfonyldiimidazole (SDI) was in house prepared using the procedure described by Veryser *et al.*[25] Chromatography solvents were distilled prior to use. All moisture-sensitive reactions were carried out under nitrogen atmosphere and in flame-dried glassware. Reactions were magnetically stirred and monitored by using Macherey-Nagel SIL G-25 UV254 0.25 mm UV254 pre-coated silica gel glass-supported TLC plates. Compounds were visualized by UV irradiation (254 nm). Column chromatography was performed using either a MPLC apparatus or via standard column chromatography. Silica gel for MPLC: ACROS Silica gel, for column chromatography, ultra pure, 40-60 µm, average pore diameter of 60 Å. Silica gel for standard column chromatography: ACROS Silica gel, for column chromatography, 60-200 µm, average pore diameter of 60 Å. The MPLC device is a Buchi Sepacore™ flash apparatus, consisting of a C-660 Buchi fraction collector, C-615 Pump manager, C-635 UV-photometer, two C-605 pump modules and a Linseis D120S plotter. Solvents were evaporated with a rotavapor at a temperature of 50 °C. ^{1}H NMR spectra were recorded on Bruker Avance 400 (400 MHz) and Bruker Avance II^{+} 600 (600 MHz) spectrometers. Samples were dissolved in $CDCl_3$ (7.26 ppm, singlet) or DMSO-d_6 (2.50 ppm, quintet) and tetramethylsilane was used as an internal standard. ^{13}C-NMR spectra were recorded on Bruker Avance 400 (working at 101 MHz) and Bruker Avance II^{+} 600 (working at 151 MHz) spectrometers. The deuterated solvents were used as internal standard ($CDCl_3$: 77.16 ppm, triplet; DMSO-d_6: 39.52 ppm, quintet). ^{19}F NMR spectra were recorded on Bruker Avance 400 (working at 376 MHz) and Bruker Avance II^{+} 600 (working at 565 MHz) spectrometers. Samples were dissolved in $CDCl_3$ or DMSO-d_6. All δ-values are expressed in ppm. HR-MS spectra were acquired on a quadrupole orthogonal acceleration time-of-flight mass spectrometer (Synapt G2 HDMS, Waters, Milford, MA). Samples were dissolved in a mixtrue of 1:1 (v/v) acetonitrile:water and infused at 3uL/min. Spectra were obtained in negative ionization mode with a resolution of 15000 (FWHM) using leucine enkephalin as lock mass. Infrared spectra were recorded on a Bruker Alpha-T FT-IR spectrometer with universal sampling module and data was processed using the Opus software. Melting/decomposition points were determined on a Mettler-Toledo DSC1 instrument, using a heating rate of 15 °C min^{-1} under helium atmosphere. CHN (carbon, hydrogen, nitrogen) elemental analyses were obtained with the aid of a Thermo Scientific Interscience Flash 2000 Elemental analyser. Crystal structures for **3j** and **5** (CCDC 1868893 and 1868894) were determined on an Agilent SuperNova diffractometer (single source at offset, Eos detector).

General procedure A for the synthesis of fluorosulfates. Chamber A of a flame-dried medium-sized two-chamber reactor (Figure S1) was filled with 1,1'-sulfonyldiimidazole (SDI, 1.487 g, 7.5 mmol, 1.5 eq.) and potassium fluoride (KF, 1.162 g, 20.0 mmol, 4.0 equiv). Next, chamber B was charged with the appropriate aryl alcohol (5.0 mmol), triethylamine (1.394 mL, 10.0 mmol, 2.0 eq.) and dichloromethane (DCM, 4 mL). Finally, 15 mL of a trifluoroacetic acid (TFA)/water mixture (1/1, v/v) was added by injection through the septum in chamber A and instant gas formation was observed. After 18 hours stirring at room temperature, one of the caps was carefully removed to release the residual pressure. As sulfuryl fluoride is a toxic gas, the reaction was stirred for another 15 minutes to ensure that all sulfuryl fluoride was extracted out of the fume hood. Next, the content of chamber B was transferred to a 100 mL round-bottomed flask. Chamber B was rinsed five times with 10 mL of dichloromethane and these fractions were added to the same flask. After the addition of Celite®545, the solvent was removed under reduced pressure. The crude product was dry-loaded on a silica gel column for purification.

General procedure B for the synthesis of fluorosulfates. Identical to general procedure A, except that *N*,*N*-diisopropylethylamine (DIPEA, 2.67 mL, 15.0 mmol, 3.0 eq.) was used as base in chamber A and acetonitrile (MeCN, 10 mL) as solvent in chamber B.

*3,5-dimethylphenyl sulfurofluoridate (**1a**)*: General procedure A was followed using 611 mg of 3,5-dimethylphenol (99 wt%, 5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 98/2 as the eluent). The title compound was obtained as a white solid (930 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (s, 1H), 6.94 (s, 2H), 2.36 (s, 6H); ^{19}F{^{1}H, ^{13}C} NMR (377 MHz, $CDCl_3$) δ 37.52; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 150.1, 140.6, 130.2, 118.2, 21.2; FT-IR (neat, cm^{-1}): 3080, 2929, 1618, 1588, 1437, 1222; CHN Anal. Calcd for $C_8H_9FO_3S$: C, 47.05; H, 4.44; N, 0.00. Found: C, 46.73; H, 4.42; N, 0.00. Melting point: 43-46 °C

*3-(trifluoromethyl)phenyl sulfurofluoridate (**1b**)*: General procedure A was followed using 827 mg of 3-(trifluoromethyl)phenol (98 wt%, 5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 98/2 as the eluent). The title compound was obtained as a colorless oil (1010 mg, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.68 (m, 1H), 7.67 – 7.60 (m, 2H), 7.58 – 7.54 (m, 1H); ^{19}F{^{1}H, ^{13}C} NMR (377 MHz, $CDCl_3$) δ 38.13, -63.10; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 149.8 (s), 133.2 (q, J = 33.8 Hz), 131.3 (s), 125.6 (q, J = 3.6 Hz), 124.5 (s), 123.2 (q, J = 272.7 Hz), 118.4 (q, J = 3.6 Hz); FT-IR (neat, cm^{-1}): 3105, 2979, 2918, 1685, 1324, 1127; CHN Anal. Calcd for $C_7H_4F_4O_3S$: C, 34.44; H, 1.65; N, 0.00. Found: C, 34.24; H, 1.88; N, 0.00.

*ethyl 4-((fluorosulfonyl)oxy)benzoate (**1c**)*: General procedure A was followed using 839 mg of ethyl 4-hydroxybenzoate (99 wt%, 5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 98/2 as the eluent). The title compound was obtained as a colorless oil (1199 mg, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 – 8.05 (m, 2H), 7.46 – 7.35 (m, 2H), 4.40 (q, J = 7.1 Hz, 2H), 1.40 (t, J = 7.1 Hz, 3H); ^{19}F{^{1}H, ^{13}C} NMR (377 MHz, $CDCl_3$) δ 38.66; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.9, 152.8, 132.0, 131.0, 120.9, 61.6, 14.3. These data are in agreement with literature data.[24]

*4-methoxyphenyl sulfurofluoridate (**1d**)*: General procedure A was followed using 627 mg of 4-methoxyphenol (99 wt%, 5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 98/2 as the eluent). The title compound was obtained as a colorless oil (989 mg, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.19 (m, 2H), 6.98 – 6.88 (m, 2H), 3.82 (s, 3H);

$^{19}F\{^{1}H, ^{13}C\}$ NMR (377 MHz, $CDCl_3$) δ 36.37; $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 159.3, 143.6, 122.0, 115.2, 55.8. These data are in agreement with literature data.[24]

*3-iodophenyl sulfurofluoridate (**1e**)*: General procedure A was followed using 1111 mg of 3-iodophenol (99 wt%, 5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 98/2 as the eluent). The title compound was obtained as a colorless oil (1461 mg, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.9 Hz, 1H), 7.70 (s, 1H), 7.34 (dd, *J* = 8.4, 1.5 Hz, 1H), 7.21 (t, *J* = 8.1 Hz, 1H); $^{19}F\{^{1}H, ^{13}C\}$ NMR (377 MHz, $CDCl_3$) δ 38.29; $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 149.7, 137.9, 131.6, 130.0, 120.4, 93.9. These data are in agreement with literature data.[32]

*4-(methylsulfonyl)phenyl sulfurofluoridate (**1f**)*: General procedure A was followed using 888 mg of 4-(methylsulfonyl)phenol (97 wt%, 5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 5/5 as the eluent). The title compound was obtained as white crystals (1177 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 8.5 Hz, 2H), 7.58 (d, J = 8.3 Hz, 2H), 3.10 (s, 3H); $^{19}F\{^{1}H, ^{13}C\}$ NMR (377 MHz, $CDCl_3$) δ 39.38; $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 153.0, 141.1, 130.3, 122.2, 44.5. These data are in agreement with literature data.[24]

*4-cyanophenyl sulfurofluoridate (**1g**)*: General procedure A was followed using 614 mg of 3-hydroxybenzonitrile (97 wt%, 5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 98/2 as the eluent). The title compound was obtained as a colorless oil (980 mg, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.71 (m, 1H), 7.69 – 7.51 (m, 3H); $^{19}F\{^{1}H, ^{13}C\}$ NMR (377 MHz, $CDCl_3$) δ 38.86; $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 149.6, 132.5, 131.6, 125.8, 124.8, 116.6, 114.8. These data are in agreement with literature data.[32]

*4-bromophenyl sulfurofluoridate (**1h**)*: General procedure A was followed using 874 mg of 4-bromophenol (99 wt%, 5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 98/2 as the eluent). The title compound was obtained as a colorless oil (1213 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.56 (m, 2H), 7.29 – 7.19 (m, 2H); $^{19}F\{^{1}H, ^{13}C\}$ NMR (377 MHz, $CDCl_3$) δ 37.80; $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 148.9, 133.6, 122.7, 122.4. These data are in agreement with literature data.[33]

*2,6-dimethylphenyl sulfurofluoridate (**1i**)*: General procedure A was followed using 617 mg of 2,6-dimethylphenyl sulfurofluoridate (99 wt%, 5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 98/2 as the eluent). The title compound was obtained as a colorless oil (718 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 – 7.05 (m, 3H), 2.37 (s, 6H); $^{19}F\{^{1}H, ^{13}C\}$ NMR (377 MHz, $CDCl_3$) δ 43.27; $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 148.8, 131.0, 129.9, 128.2, 16.5; FT-IR (neat, cm^{-1}): 3050, 2969, 2937, 1439, 1267; CHN Anal. Calcd for $C_8H_9FO_3S$: C, 47.05; H, 4.44; N, 0.00. Found C, 47.05; H, 4.48; N, 0.00.

*2-bromophenyl sulfurofluoridate (**1j**)*: General procedure A was followed using 883 mg of 2-bromophenol (98 wt%, 5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 98/2 as the eluent). The title compound was obtained as a colorless oil (1094 mg, 86%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.9 Hz, 1H), 7.47 – 7.40 (m, 2H), 7.32 – 7.25 (m, 1H); $^{19}F\{^{1}H, ^{13}C\}$ NMR (377 MHz, $CDCl_3$) δ 41.45; $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 147.3, 134.6, 129.9, 129.2, 122.6, 115.5. These data are in agreement with literature data.[25]

*naphthalen-2-yl sulfurofluoridate (**1k**)*: General procedure A was followed using 728 mg of naphthalen-2-ol (99 wt%, 5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 98/2 as the eluent). The title compound was obtained as a white solid (1075 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.73 (m, 4H), 7.58 – 7.47 (m, 2H), 7.38 (dd, *J* = 9.0, 2.0 Hz, 1H); $^{19}F\{^{1}H, ^{13}C\}$ NMR (377 MHz, $CDCl_3$) δ 37.80; $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 147.6, 133.3, 132.5, 130.8, 128.1, 128.0, 127.6, 127.3, 119.0, 118.8. These data are in agreement with literature data.[18]

*benzo[d][1,3]dioxol-5-yl sulfurofluoridate (**1l**)*: General procedure A was followed using 705 mg of benzo[*d*][1,3]dioxol-5-ol (98 wt%, 5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 98/2 as the eluent). The title compound was obtained as a colorless oil (1078 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (s, 1H), 6.06 (s, 1H); $^{19}F\{^{1}H, ^{13}C\}$ NMR (377 MHz, $CDCl_3$) δ 36.58; $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 148.6, 147.7, 144.1, 114.0, 108.3, 103.0, 102.5. These data are in agreement with literature data.[18]

*1H-indole-1-sulfonyl fluoride (**1m**)*: General procedure A was followed using 592 mg of 1*H*-indole (99 wt%, 5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 98/2 as the eluent). The title compound was obtained as a colorless oil (366 mg, 37%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.3 Hz, 1H), 7.65 (d, *J* = 7.7 Hz, 1H), 7.52 – 7.31 (m, 3H), 6.81 (d, *J* = 3.7 Hz, 1H); $^{19}F\{^{1}H, ^{13}C\}$ NMR (377 MHz, $CDCl_3$) δ 54.31; $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 134.8, 130.3, 126.1, 125.8, 124.8, 121.9, 113.5, 111.0; FT-IR (neat, cm^{-1}): 3154, 3127, 3060, 2979, 1440, 1262, 1222; CHN Anal. Calcd for $C_8H_6FNO_2S$: C, 48.24; H, 3.04; N, 7.03. Found: C, 47.89; H, 3.10; N, 7.24.

*propane-2,2-diylbis(4,1-phenylene) bis(sulfurofluoridate) (**1n**)*: General procedure A was followed using 588 mg of 4,4'-(propane-2,2-diyl)diphenol (97 wt%, 2.5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 95/5 as the eluent). The title compound was obtained as a white solid (898 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.19 (m, 8H), 1.70 (s, 6H); $^{19}F\{^{1}H, ^{13}C\}$ NMR (377 MHz, $CDCl_3$) δ 37.52; $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 150.4, 148.2, 128.7, 120.6, 42.9, 30.8. These data are in agreement with literature data.[18]

*(3-oxo-1,3-dihydroisobenzofuran-1,1-diyl)bis(4,1-phenylene) bis(sulfurofluoridate)(**1o**)*: General procedure A was followed using 804 mg of (3-oxo-1,3-dihydroisobenzofuran-1,1-diyl)bis(4,1-phenylene) bis(sulfurofluoridate) (99 wt%, 2.5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 5/5 as the eluent). The title compound was obtained as a white solid (1052 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.6 Hz, 1H), 7.79 (t, *J* = 7.5 Hz, 1H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.58 (d, *J* = 7.7 Hz, 1H), 7.47 (d, *J* = 8.8 Hz, 4H), 7.36 (d, *J* = 8.7 Hz, 4H); $^{19}F\{^{1}H, ^{13}C\}$ NMR (377 MHz, $CDCl_3$) δ 38.23; $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 168.6, 150.3, 150.0, 141.0, 134.9, 130.3, 129.2, 126.7, 125.3, 123.9, 121.4, 89.6. These data are in agreement with literature data.[18]

*4-allyl-2-methoxyphenyl sulfurofluoridate (**1p**)*: General procedure A was followed using 829 mg of 4-allyl-2-methoxyphenol (99 wt%, 5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 98/2 as the eluent). The title compound was obtained as a colorless oil (1110 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.3 Hz, 1H), 6.86 (d, *J* = 1.5 Hz, 1H), 6.79 (dd, *J* = 8.3, 1.7 Hz, 1H), 6.03 – 5.82 (m, 1H), 5.21 – 5.01 (m, 2H), 3.87 (s, 3H), 3.38 (d, *J* = 6.7 Hz, 2H); ^{19}F{^{1}H, ^{13}C} NMR (377 MHz, $CDCl_3$) δ 39.32; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 151.0, 142.4, 137.4, 136.3, 122.1, 120.9, 116.9, 113.7, 56.1, 40.1. These data are in agreement with literature data.[18]

*(R)-2,5,7,8-tetramethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chroman-6-yl sulfurofluoridate (**1q**)*: General procedure A was followed using 2220 mg of (*R*)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-ol (97 wt%, 5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 98/2 as the eluent). The title compound was obtained as a colorless oil (2501 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.60 (t, *J* = 6.8 Hz, 2H), 2.23 (s, 3H), 2.20 (s, 3H), 2.10 (s, 3H), 1.89 – 1.72 (m, 2H), 1.60 – 1.00 (m, 24H), 0.90 – 0.80 (m, 12H); ^{19}F{^{1}H, ^{13}C} NMR (377 MHz, $CDCl_3$) δ 41.37; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 151.0, 141.9, 127.5, 126.1, 124.4, 118.4, 75.7, 39.9, 39.4, 37.5, 37.4, 37.3, 32.8, 32.7, 30.8, 28.0, 24.8, 24.4, 23.9, 22.7, 22.6, 21.0, 20.6, 19.8, 19.7, 13.5, 12.7, 11.9. These data are in agreement with literature data.[18]

*(8R,9S,13S,14S)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl sulfurofluoridate (**1r**):* General procedure B was followed using 1366 mg of (8*R*,9*S*,13*S*,14*S*)-3-hydroxy-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (99 wt%, 5 mmol, 1 equiv). The crude reaction mixture was purified by column chromatography on silica gel (mixture of petroleumether/diethylether 5/5 as the eluent). The title compound was obtained as a white solid (1255 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.6 Hz, 1H), 7.14 – 7.03 (m, 2H), 3.02 – 2.88 (m, 2H), 2.52 (dd, *J* = 18.8, 8.6 Hz, 1H), 2.45 – 2.25 (m, 2H), 2.23 – 1.92 (m, 4H), 1.72 – 1.40 (m, 6H), 0.92 (s, 3H); ^{19}F{^{1}H, ^{13}C} NMR (377 MHz, $CDCl_3$) δ 37.42; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 220.5, 148.3, 140.7, 139.6, 127.5, 120.8, 118.0, 50.5, 48.0, 44.2, 37.9, 35.9, 31.6, 29.5, 26.2, 25.8, 21.7, 13.9. These data are in agreement with literature data.[20]

General procedure C for the synthesis of *N*-acylsulfamates. To a flame-dried reaction tube (15 mL) was added subsequently amide (1.2 equiv, 1.3 mmol), fluorosulfate (1.0 equiv, 1 mmol) and sodium hydride (2.3 equiv, 2.3 mmol). Next, the tube was capped with a screw cap fitted with septum and brought under argon atmosphere via three consecutive vacuum-argon cycles using a Schlenk line. 2 mL of THF was added and the reaction was stirred at 1000 rpm at room temperature. After two hours, the reaction was diluted with ethyl acetate and transferred into a separation funnel. The sulfamate was extracted out (4x) towards the aqueous layer using a 10% $NaHCO_3$ solution. The combined aqueous layers were acidified by adding 45 mL of a 4 M HCl solution in small portions and the sulfamate was extracted with DCM. The combined organic layers were dried using sodium sulfate and evaporated *in vacuo* to afford the title compound. **Remark 1:** When the fluorosulfate was a liquid, the fluorosulfate was weighed in a separate flame-dried reaction tube capped with a screw cap fitted with septum and brought under argon atmosphere via three consecutive vacuum-argon cycles using a Schlenk line. Next, the fluorosulfate was dissolved in 2 mL THF (via two portions of 1 mL) and added to the reaction tube (as described above) containing only the amide and sodium hydride. **Remark 2:** In some cases, the fluorosulfate could not be extracted into the aqueous layer. In these cases, the reaction mixture was transferred into a separation funnel and diluted with DCM (the reaction tube was rinsed 3x). 4 M HCl was added and the aqueous layer was extracted 3 times with DCM. The combined DCM fractions were dried on sodium sulfate and Celite® was added to the mixture prior to evaporation. The solid was dry-loaded onto the medium-pressure liquid chromatography system and eluted with the designated solvent system. **Remark 3:** Take care while adding the solvent as H_2 is produced. It is advised to capture the overpressure using a balloon.

*3,5-dimethylphenyl acetylsulfamate (**3a**)*: General procedure C was followed using 204 mg of 3,5-dimethylphenyl sulfurofluoridate (1 mmol, 1 equiv). The title compound was obtained as a white solid (207 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (bs, 1H), 6.96 (s, 1H), 6.86 (s, 2H), 2.31 (s, 6H), 2.20 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.8, 149.6, 140.2, 129.6, 119.1, 23.0, 21.2; FT-IR (neat, cm^{-1}): 3191, 3148, 2921, 2853, 1713, 1466; HR-MS (ESI) *m/z*: calculated for $C_{10}H_{12}NO_4S^-$ 242.0492 [M-H]$^-$, found 242.0474; Decomposition: 95 °C.

*3-(trifluoromethyl)phenyl acetylsulfamate (**3b**)*: General procedure C was followed using 244 mg of 3-(trifluoromethyl)phenyl sulfurofluoridate (1 mmol, 1 equiv). The title compound was obtained as a white solid (170 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (bs, 1H), 7.67 – 7.48 (m, 4H), 2.26 (s, 3H); ^{19}F{^{1}H, ^{13}C} NMR (377 MHz, $CDCl_3$) δ -62.77; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 167.6 (s), 149.6 (s), 132.8 (q, *J* = 33.5 Hz), 130.9 (s), 125.5 (s), 124.8 (q, *J* = 3.7 Hz), 123.0 (q, *J* = 272.7), 119.2 (q, *J* = 3.8 Hz), 23.2 (s); FT-IR (neat, cm^{-1}): 3144, 2914, 2839, 1709, 1461; HR-MS (ESI) *m/z*: calculated for $C_9H_7F_3NO_4S^-$ 282.0053 [M-H]$^-$, found 282.0038; Decomposition: 135 °C.

*ethyl 4-((N-acetylsulfamoyl)oxy)benzoate (**3c**)*: General procedure C was followed using 248 mg of ethyl 4-((fluorosulfonyl)oxy)benzoate (1 mmol, 1 equiv). The title compound was obtained as a white solid (201 mg, 70%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.08 (d, *J* = 8.7 Hz, 2H), 7.41 (d, *J* = 8.7 Hz, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 2.05 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 168.6, 164.7, 152.6, 131.4, 129.1, 122.2, 61.1, 23.3, 14.1; FT-IR (neat, cm^{-1}): 3075, 2990, 2907, 2844, 1711, 1697; HR-MS (ESI) *m/z*: calculated for $C_{11}H_{12}NO_6S^-$ 286.0391 [M-H]$^-$, found 286.0372; Decomposition: 91 °C.

*4-methoxyphenyl acetylsulfamate (**3d**)*: General procedure C was followed using 206 mg of 4-methoxyphenyl sulfurofluoridate (1 mmol, 1 equiv). The title compound was obtained as a white solid (196 mg, 80%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.33 (bs, 1H), 7.18 (d, *J* = 9.0 Hz, 2H), 7.03 (d, *J* = 9.0 Hz, 2H), 3.77 (s, 3H), 2.04 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 168.6, 158.2, 142.8, 122.9, 115.0, 55.6, 23.2; FT-IR (neat, cm^{-1}): 3109, 3014, 2915, 2847, 1710, 1470; HR-MS (ESI) *m/z*: calculated for $C_9H_{10}NO_5S^-$ 244.0285 [M-H]$^-$, found 244.0263; Decomposition: 104 °C.

*3-iodophenyl acetylsulfamate (**3e**)*: General procedure C was followed using 302 mg of 3-iodophenyl sulfurofluoridate (1 mmol, 1 equiv). The title compound was obtained as a white solid (233 mg, 68%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.54 (bs, 1H), 7.79 (d, *J* = 6.8 Hz, 1H), 7.62 (s, 1H), 7.36 – 7.23 (m,

2H), 2.05 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 168.6, 149.5, 136.5, 132.0, 130.3, 121.4, 94.8, 23.3; FT-IR (neat, cm^{-1}): 3239, 2911, 1704, 1459; HR-MS (ESI) *m/z*: calculated for $C_8H_7INO_4S^-$ 339.9148 [M-H]$^-$, found 339.9135; Decomposition: 133 °C.

*4-(methylsulfonyl)phenyl acetylsulfamate (**3f**)*: General procedure C was followed using 254 mg of 4-(methylsulfonyl)phenyl sulfurofluoridate (1 mmol, 1 equiv). The title compound was obtained as a white solid (181 mg, 62%). ^1H NMR (400 MHz, DMSO-d_6) δ 8.08 (d, J = 8.7 Hz, 2H), 7.54 (d, J = 8.7 Hz, 2H), 3.27 (s, 3H), 2.07 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 168.8, 152.7, 139.9, 129.6, 123.0, 43.4, 23.4; FT-IR (neat, cm^{-1}): 3195, 3161, 2922, 1695, 1469; HR-MS (ESI) *m/z*: calculated for $C_9H_{10}NO_6S_2^-$ 291.9955 [M-H]$^-$, found 291.9924; Decomposition: 139 °C.

*3-cyanophenyl acetylsulfamate (**3g**)*: General procedure C was followed using 201 mg of 3-cyanophenyl sulfurofluoridate (1 mmol, 1 equiv). The title compound was obtained as a white solid (172 mg, 72%); ^1H NMR (400 MHz, DMSO-d_6) δ 7.91 (d, *J* = 7.6 Hz, 1H), 7.83 (s, 1H), 7.72 (t, *J* = 8.0 Hz, 1H), 7.68 – 7.57 (m, 1H), 2.06 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 168.7, 149.4, 131.7, 131.7, 127.2, 125.6, 117.5, 112.9, 23.4; FT-IR (neat, cm^{-1}): 3136, 2922, 2852, 2230 (C≡N stretch), 1707, 1465; HR-MS (ESI) *m/z*: calculated for $C_9H_7N_2O_4S^-$ 239.0132 [M-H]$^-$, found 239.0112; Decomposition: 97 °C.

*4-bromophenyl acetylsulfamate (**3h**)*: General procedure C was followed using 255 mg of 4-bromophenyl sulfurofluoridate (1 mmol, 1 equiv). The title compound was obtained as a white solid (228 mg, 78%). ^1H NMR (400 MHz, DMSO-d_6) δ 12.50 (bs, 1H), 7.71 (d, *J* = 9.0 Hz, 2H), 7.23 (d, *J* = 9.0 Hz, 2H), 2.05 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 168.6, 148.6, 133.2, 124.1, 120.3, 23.3; FT-IR (neat, cm^{-1}): 3083, 2919, 2851, 1699, 1477; HR-MS (ESI) *m/z*: calculated for $C_8H_7BrNO_4S^-$ 291.9285 [M-H]$^-$, found 291.9268; Decomposition: 140 °C.

*2,6-dimethylphenyl acetylsulfamate (**3i**)*: General procedure C was followed using 204 mg of 2,6-dimethylphenyl acetylsulfamate (1 mmol, 1 equiv). The title compound was obtained as a white solid (184 mg, 76%). ^1H NMR (400 MHz, DMSO-d_6) δ 12.59 (bs, 1H), 7.15 (s, 3H), 2.29 (s, 6H), 2.09 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 168.5, 147.4, 131.5, 129.3, 127.0, 23.4, 16.6; FT-IR (neat, cm^{-1}): 3166, 2929, 2840, 1714, 1468; HR-MS (ESI) *m/z*: calculated for $C_{10}H_{12}NO_4S^-$ 242.0492 [M-H]$^-$, found 242.0466; Decomposition: 100 °C

*2-bromophenyl acetylsulfamate (**3j**)*: General procedure C was followed using 255 mg of 2-bromophenyl sulfurofluoridate (1 mmol, 1 equiv). The title compound was obtained as a white solid (202 mg, 69%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (bs, 1H), 7.65 (d, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 8.2 Hz, 1H), 7.39 (t, *J* = 7.8 Hz, 1H), 7.23 (t, *J* = 7.7 Hz, 1H), 2.34 (s, 3H); $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 168.2, 147.0, 134.2, 129.0, 129.0, 124.1, 115.6, 23.4; FT-IR (neat, cm^{-1}): 3182, 2932, 2850, 1719, 1465; HR-MS (ESI) *m/z*: calculated for $C_8H_7BrNO_4S^-$ 291.9285 [M-H]$^-$, found 291.9267; Decomposition: 138 °C

*naphthalen-2-yl acetylsulfamate (**3k**)*: General procedure C was followed using 226 mg of naphthalen-2-yl sulfurofluoridate (1 mmol, 1 equiv). The title compound was obtained as a white solid (219 mg, 83%). ^1H NMR (400 MHz, DMSO-d_6) δ 12.45 (bs, 1H), 8.12 – 7.96 (m, 3H), 7.84 (d, *J* = 1.6 Hz, 1H), 7.65 – 7.55 (m, 2H), 7.40 (dd, *J* = 8.9, 2.2 Hz, 1H), 2.06 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 168.7, 147.0, 133.1, 131.7, 130.3, 127.9, 127.7, 127.2, 126.7, 120.7, 119.2, 23.3; FT-IR (neat, cm^{-1}): 3213, 3161, 2921, 1716, 1471; HR-MS (ESI) *m/z*: calculated for $C_{12}H_{10}NO_4S^-$ 264.0336 [M-H]$^-$, found 264.0319; Decomposition: 142 °C

*benzo[d][1,3]dioxol-5-yl acetylsulfamate (**3l**)*: General procedure C was followed using 220 mg of benzo[*d*][1,3]dioxol-5-yl sulfurofluoridate (1 mmol, 1 equiv). The title compound was obtained as a white solid (213 mg, 82%). ^1H NMR (400 MHz, DMSO-d_6) δ 12.40 (bs, 1H), 6.99 (d, *J* = 8.5 Hz, 1H), 6.87 (d, *J* = 1.9 Hz, 1H), 6.70 (dd, *J* = 8.4, 1.9 Hz, 1H), 6.10 (s, 2H), 2.04 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 168.6, 147.9, 146.4, 143.5, 114.7, 108.3, 103.7, 102.2, 23.3; FT-IR (neat, cm^{-1}): 3142, 2850, 1703, 1462; HR-MS (ESI) *m/z*: calculated for $C_9H_8NO_6S^-$ 258.0078 [M-H]$^-$, found 258.0062; Decomposition: 101 °C

*N-((1H-indol-1-yl)sulfonyl)acetamide (**3m**)*: General procedure C was followed using 199 mg of 1*H*-indole-1-sulfonyl fluoride (1 mmol, 1 equiv). The title compound was obtained as an off-white solid (158 mg, 67%). ^1H NMR (400 MHz, DMSO-d_6) δ 12.93 (bs, 1H), 7.78 (d, *J* = 8.2 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.60 (d, *J* = 3.6 Hz, 1H), 7.32 (dt, *J* = 33.5, 7.4 Hz, 2H), 6.72 (d, *J* = 3.5 Hz, 1H), 1.91 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 168.7, 133.6, 130.0, 128.4, 124.1, 123.1, 121.5, 112.7, 106.5, 23.1; FT-IR (neat, cm^{-1}): 3115, 2919, 2854, 1705, 1446; HR-MS (ESI) *m/z*: calculated for $C_{10}H_9N_2O_3S^-$ 237.0339 [M-H]$^-$, found 237.0318. Decomposition: 108 °C

*propane-2,2-diylbis(4,1-phenylene) bis(acetylsulfamate) (**3n**)*: General procedure C was followed using 196 mg of propane-2,2-diylbis(4,1-phenylene) bis(sulfurofluoridate) (0.5 mmol, 1 equiv). The title compound was obtained as a white solid (93 mg, 39%). ^1H NMR (400 MHz, DMSO-d_6) δ 12.41 (s, 2H), 7.34 (d, *J* = 8.7 Hz, 4H), 7.18 (d, *J* = 8.7 Hz, 4H), 2.04 (s, 6H), 1.65 (s, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 168.5, 149.2, 147.4, 128.3, 121.5, 42.2, 30.3, 23.3; FT-IR (neat, cm^{-1}): 3207, 3162, 2965, 2918, 1709, 1456; HR-MS (ESI) *m/z*: calculated for $C_{19}H_{21}N_2O_8S_2^-$ 469.0745 [M-H]$^-$, found 469.0732; Decomposition: 175 °C

*(3-oxo-1,3-dihydroisobenzofuran-1,1-diyl)bis(4,1-phenylene) bis(acetylsulfamate) (**3o**)*: General procedure C was followed using 241 mg of (3-oxo-1,3-dihydroisobenzofuran-1,1-diyl)bis(4,1-phenylene) bis(sulfurofluoridate) (0.5 mmol, 1 equiv). The title compound was obtained as white solid (116 mg, 39%). ^1H NMR (400 MHz, DMSO-d_6) δ 12.48 (bs, 2H), 8.03 – 7.89 (m, 3H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 8.7 Hz, 4H), 7.32 (d, *J* = 8.7 Hz, 4H), 2.03 (s, 6H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 168.6, 168.3, 150.6, 149.4, 139.7, 135.5, 130.4, 128.6, 125.9, 124.6, 124.1, 122.4, 89.6, 23.3; FT-IR (neat, cm^{-1}): 3217, 3135, 1776, 1700, 1464; HR-MS (ESI) *m/z*: calculated for $C_{24}H_{19}N_2O_{10}S_2^-$ 559.0486 [M-H]$^-$, found 559.0488; Decomposition: 169 °C

*4-allyl-2-methoxyphenyl acetylsulfamate (**3p**)*: General procedure C was followed using 246 mg of 4-allyl-2-methoxyphenyl sulfurofluoridate (1 mmol, 1 equiv). The title compound was obtained as an off-white solid (197 mg, 69%). ^1H NMR (400 MHz, DMSO-d_6) δ 12.25 (bs, 1H), 7.16 (d, *J* = 8.2 Hz, 1H), 7.03 (s, 1H), 6.82 (d, *J* = 8.1 Hz, 1H), 5.96 (ddt, *J* = 16.8, 9.9, 6.8 Hz, 1H), 5.20 – 5.00 (m, 2H), 3.78 (s, 3H), 3.38 (d, *J* = 6.7 Hz, 2H), 2.07 (s, 3H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 168.3, 151.3, 140.7, 137.1, 136.2, 123.6, 120.5, 116.3, 113.6, 55.9, 39.2, 23.3; FT-IR (neat, cm^{-1}): 3166, 2976, 1726, 1637, 1461; HR-MS (ESI) *m/z*: calculated for $C_{12}H_{14}NO_5S^-$ 284.0598 [M-H]$^-$, found 284.0576; Decomposition: 143 °C

*(R)-2,5,7,8-tetramethyl-2-((4R,8R)-4,8,12-trimethyltridecyl)chroman-6-yl acetylsulfamate (**3q**)*: General procedure C was followed using 529 mg of (*R*)-2,5,7,8-tetramethyl-2-

((4*R*,8*R*)-4,8,12-trimethyltridecyl)chroman-6-yl sulfurofluoridate (97 wt%, 1 mmol, 1 equiv). Purification was performed according to remark 2. The resulting solid was dry-loaded onto the MPLC system and eluted with following gradient: heptane/ethyl acetate 95/5 - heptane/ethyl acetate 5/5. The title compound was obtained as a pale yellow solid (381 mg, 69%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.40 (bs, 1H), 2.55 (t, *J* = 6.4 Hz, 2H), 2.13 (s, 3H), 2.11 (s, 3H), 2.07 (s, 3H), 2.02 (s, 3H), 1.75 (t, *J* = 6.7 Hz, 2H), 1.54 – 0.98 (m, 24H), 0.88 – 0.78 (m, 12H); ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 168.45, 149.48, 139.98, 128.20, 127.04, 122.62, 117.99, 75.09, 39.27, 38.77, 36.77, 36.76, 36.68, 36.62, 32.08, 31.94, 30.49, 27.37, 24.16, 23.75, 23.43, 23.37, 22.49, 22.40, 20.30, 19.95, 19.55, 19.47, 13.82, 12.96, 11.58; FT-IR (neat, cm^{-1}): 3087, 2925, 2868, 1701, 1460; HR-MS (ESI) *m/z*: calculated for $C_{31}H_{52}NO_5S^-$ 550.3571 [M-H]$^-$, found 550.3571; Decomposition: 74 °C

*(8R,9S,13S,14S)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl acetylsulfamate (**3r**)*: General procedure C was followed using 352 mg of (8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl sulfurofluoridate (1 mmol, 1 equiv). The title compound was obtained as a white solid (285 mg, 73%). ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.36 (bs, 1H), 7.41 (d, *J* = 8.5 Hz, 1H), 7.02 – 6.95 (m, 2H), 2.94 – 2.82 (m, 2H), 2.49 – 2.19 (m, 3H), 2.16 – 1.89 (m, 6H), 1.83 – 1.74 (m, 1H), 1.66 – 1.30 (m, 6H), 0.84 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 220.0, 169.0, 147.8, 139.7, 139.2, 127.6, 122.0, 119.2, 50.0, 47.7, 44.0, 37.8, 35.8, 31.7, 29.3, 26.1, 25.8, 23.7, 21.6, 14.0; FT-IR (neat, cm^{-1}): 3072, 2925, 2839, 1712, 1476; HR-MS (ESI) *m/z*: calculated for $C_{20}H_{24}NO_5S^-$ 390.1381 [M-H]$^-$, found 390.1365; Decomposition: 219 °C

*3,5-dimethylphenyl butyrylsulfamate (**3s**)*: General procedure C was followed using 204 mg of 3,5-dimethylphenyl sulfurofluoridate (1 mmol, 1 equiv) and 106 mg butyramide (99 wt%, 1.2 mmol, 1.2 equiv). Purification was performed according to remark 2. The resulting solid was dry-loaded onto the MPLC system and eluted with following gradient: DCM - DCM/AcOH 98/2. The title compound was obtained as a white solid (187 mg, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (bs, 1H), 6.96 (s, 1H), 6.88 (s, 2H), 2.38 (t, *J* = 7.3 Hz, 2H), 2.31 (s, 6H), 1.76 – 1.60 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 170.7, 149.7, 140.1, 129.5, 119.2, 37.8, 21.2, 17.9, 13.5; FT-IR (neat, cm^{-1}): 3148, 3083, 3017, 2970, 2917, 2875; HR-MS (ESI) *m/z*: calculated for $C_{12}H_{16}NO_4S^-$ 270.0805 [M-H]$^-$, found 270.0786; Decomposition: 94 °C

*3,5-dimethylphenyl methacryloylsulfamate (**3t**)*: General procedure C was followed using 204 mg of 3,5-dimethylphenyl sulfurofluoridate (1 mmol, 1 equiv) and 104 mg methacrylamide (98 wt%, 1.2 mmol, 1.2 equiv). Purification was performed according to remark 2. The resulting solid was dry-loaded onto the MPLC system and eluted with following gradient: DCM - DCM/AcOH 98/2. The title compound was obtained as a white solid (186 mg, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (bs, 1H), 6.95 (s, 1H), 6.89 (s, 2H), 5.77 (s, 1H), 5.65 (d, *J* = 1.3 Hz, 1H), 2.31 (s, 6H), 1.99 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.4, 149.7, 140.0, 138.0, 129.5, 124.0, 119.2, 21.2, 18.2; FT-IR (neat, cm^{-1}): 3193, 2922, 1684, 1453; HR-MS (ESI) *m/z*: calculated for $C_{12}H_{14}NO_4S^-$ 268.0649 [M-H]$^-$, found 268.0625; Decomposition: 104 °C

*tert-butyl (S)-2-(((3,5-dimethylphenoxy)sulfonyl)carbamoyl)pyrrolidine-1-carboxylate (**3u**)*: General procedure C was followed using 204 mg of 3,5-dimethylphenyl sulfurofluoridate (1 mmol, 1 equiv) and 257 mg of *tert*-butyl (*S*)-2-carbamoylpyrrolidine-1-carboxylate (1.2 mmol, 1.2 equiv). The title compound was obtained as a white solid (201 mg, 50%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.99 (bs, 1H), 6.94 (s, 1H), 6.88 (s, 2H), 4.29 (d, *J* = 6.4 Hz, 1H), 3.33 (s, 2H), 2.57 (s, 1H), 2.31 (s, 6H), 1.93 (s, 3H), 1.39 (s, 9H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 168.5, 157.2, 149.9, 139.7, 129.2, 119.2, 82.3, 60.1, 47.3, 28.2, 26.0, 24.5, 21.2; FT-IR (neat, cm^{-1}): 3022, 2984, 2971, 2918, 2883, 2849, 2810, 1743, 1657, 1410; HR-MS (ESI) *m/z*: calculated for $C_{18}H_{25}N_2O_6S^-$ 397.1439 [M-H]$^-$, found 397.1426; Decomposition: 96 °C (thermal decomposition of boc-group) and 173 °C

*3,5-dimethylphenyl benzoylsulfamate (**3v**)*: General procedure C was followed using 204 mg of 3,5-dimethylphenyl sulfurofluoridate (1 mmol, 1 equiv) and 148 mg benzamide (98 wt%, 1.2 mmol, 1.2 equiv). After 24 hours of reaction time, purification was performed according to remark 2. The resulting solid was dry-loaded onto the MPLC system and eluted with following gradient: DCM - DCM/AcOH 98/2. The title compound was obtained as a white solid (242 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (bs, 1H), 7.80 (d, *J* = 7.7 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H), 6.93 (s, 3H), 2.26 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 163.8, 149.8, 140.1, 133.9, 130.9, 129.5, 129.2, 127.8, 119.3, 21.2; FT-IR (neat, cm^{-1}): 3215, 3077, 2919, 1692, 1454. HR-MS (ESI) *m/z*: calculated for $C_{15}H_{14}NO_4S^-$ 304.0649 [M-H]$^-$, found 304.0629; Decomposition: 149 °C

*3,5-dimethylphenyl (4-fluorobenzoyl)sulfamate (**3w**)*: General procedure C was followed using 204 mg of 3,5-dimethylphenyl sulfurofluoridate (1 mmol, 1 equiv) and 170 mg 4-fluorobenzamide (98 wt%, 1.2 mmol, 1.2 equiv). After 24 hours of reaction time, purification was performed according to remark 2. The resulting solid was dry-loaded onto the MPLC system and eluted with following gradient: DCM - DCM/AcOH 98/2. The title compound was obtained as a white solid (201 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (bs, 1H), 7.84 (dd, *J* = 8.7, 5.1 Hz, 2H), 7.18 (t, *J* = 8.5 Hz, 2H), 6.94 (s, 1H), 6.91 (s, 2H), 2.26 (s, 6H); ^{19}F{^{1}H, ^{13}C} NMR (377 MHz, $CDCl_3$) δ -103.03; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 167.4 (s), 164.9 (s), 149.7 (s), 140.1 (s), 130.5 (d, *J* = 9.5 Hz), 129.6 (s), 127.0 (s), 119.2 (s), 116.5 (d, *J* = 22.3 Hz), 21.2 (s); FT-IR (neat, cm^{-1}): 3173, 3137, 3085, 2919; HR-MS (ESI) *m/z*: calculated for $C_{15}H_{13}FNO_4S^-$ 322.0555 [M-H]$^-$, found 322.0533; Decomposition: 124 °C

*3,5-dimethylphenyl (4-nitrobenzoyl)sulfamate (**3x**)*: General procedure C was followed using 204 mg of 3,5-dimethylphenyl sulfurofluoridate (1 mmol, 1 equiv) and 203 mg 4-nitrobenzamide (98 wt%, 1.2 mmol, 1.2 equiv). After 24 hours of reaction time, purification was performed according to remark 2. The resulting solid was dry-loaded onto the MPLC system and eluted with following gradient: DCM - DCM/AcOH 98/2. The title compound was obtained as a pale yellow solid (220 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (bs, 1H), 8.33 (d, *J* = 8.7 Hz, 2H), 8.01 (d, *J* = 8.6 Hz, 2H), 6.95 (s, 1H), 6.90 (s, 2H), 2.27 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 162.4, 150.8, 149.7, 140.3, 136.2, 129.7, 129.2, 124.3, 119.1, 21.2; FT-IR (neat, cm^{-1}): 3213, 2918, 2853, 1716, 1523, 1448; HR-MS (ESI) *m/z*: calculated for $C_{15}H_{13}N_2O_6S^-$ 349.0500 [M-H]$^-$, found 349.0480; Decomposition: 163 °C

*3,5-dimethylphenyl (4-methoxybenzoyl)sulfamate (**3y**)*: General procedure C was followed using 204 mg of 3,5-dimethylphenyl sulfurofluoridate (1 mmol, 1 equiv) and 185 mg 4-

methoxybenzamide (98 wt%, 1.2 mmol, 1.2 equiv). After 24 hours of reaction time, purification was performed according to remark 2. The resulting solid was dry-loaded onto the MPLC system and eluted with following gradient: DCM - DCM/AcOH 98/2. The title compound was obtained as a white solid (84 mg, 25%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (bs, 1H), 7.78 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.92 (s, 3H), 3.88 (s, 3H), 2.25 (s, 6H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.2, 163.1, 149.8, 140.0, 130.1, 129.5, 122.8, 119.3, 114.4, 55.6, 21.2; FT-IR (neat, cm^{-1}): 3214, 2916, 2845, 1671, 1436; HR-MS (ESI) *m/z*: calculated for $C_{16}H_{16}NO_5S^-$ 334.0755 [M-H]$^-$, found 334.0734; Decomposition: 97 °C

*benzo[d][1,3]dioxol-5-yl ethanethioylsulfamate (**5**)*: General procedure C was followed using 204 mg of 3,5-dimethylphenyl sulfurofluoridate (1 mmol, 1 equiv) and 90 mg thioacetamide (98 wt%, 1.2 mmol, 1.2 equiv). After 24 hours of reaction time, purification was performed according to remark 2. The resulting solid was dry-loaded onto the MPLC system and eluted with following gradient: DCM - DCM/AcOH 98/2. The title compound was obtained as a yellow solid (110 mg, 40%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (bs, 1H), 6.83 – 6.66 (m, 3H), 6.03 (s, 2H), 2.81 (s, 3H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 205.8, 148.5, 147.3, 143.5, 114.8, 108.3, 103.9, 102.3, 32.6; FT-IR (neat, cm^{-1}): 3191, 3122, 2917, 2851, 1462, 1391; HR-MS (ESI) *m/z*: calculated for $C_9H_8NO_5S_2$ 273.9849 [M-H]$^-$, found 273.9823; Decomposition: 86 °C

*N-benzoyl-N-methylbenzamide (**7**)*: General procedure C was followed using 204 mg of 3,5-dimethylphenyl sulfurofluoridate (1 mmol, 1 equiv). The title compound was obtained as a white liquid after purification via column chromatography (56 mg, 47%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 – 7.44 (m, 4H), 7.33 – 7.27 (m, 2H), 7.20 (tt, *J* = 6.8, 1.6 Hz, 4H), 3.52 (s, 1H). These data are in agreement with literature data.[34]

*6-chloro-3-(2-chloro-4-nitrophenyl)benzo[e][1,2,3]oxathiazin-4(3H)-one 2,2-dioxide (**9**)*: Chamber A of a flame-dried 20 mL two-chamber reactor was filled with 1,1'-sulfonyldiimidazole (SDI, 297 mg, 1.5 mmol, 1.5 equiv) and potassium fluoride (KF, 232 mg, 4 mmol, 4.0 equiv). Next, chamber B was charged with Niclosamide (1 mmol, 1 equiv), DIPEA (0.7 mL, 4 mmol, 4.0 equiv) and acetonitrile (MeCN, 4 mL). Finally, 1 mL of a trifluoroacetic acid (TFA) was added by injection through the septum in chamber A and instant gas formation was observed. After 18 hours stirring at room temperature, one of the caps was carefully removed to release the residual pressure. As sulfuryl fluoride is a toxic gas, the reaction was stirred for another 15 minutes to ensure that all sulfuryl fluoride was extracted out of the fume hood. Next, the content of chamber B was transferred to a 100 mL round-bottomed flask. Chamber B was rinsed five times with 5 mL of dichloromethane and these fractions were added to the same flask. After the addition of Celite®545, the solvent was removed under reduced pressure. The crude product was dry-loaded onto MPLC for purification (mixture of heptane/ethyl acetate 9/1 as the eluent). The title compound was obtained as an off-white solid (249 mg, 64%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (d, *J* = 2.1 Hz, 1H), 8.31 (dd, *J* = 8.7, 2.2 Hz, 1H), 8.18 (d, *J* = 2.3 Hz, 1H), 7.82 – 7.70 (m, 2H), 7.40 (d, *J* = 8.8 Hz, 1H); ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.2, 149.3, 148.8, 137.0, 136.2, 134.9, 133.7, 132.2, 130.5, 126.3, 123.1, 120.3, 118.0. FT-IR (neat, cm^{-1}): 3105, 3083, 2925, 1724, 1530, 1408; CHN Anal. Calcd for $C_{13}H_6Cl_2N_2O_6S$: C, 40.12; H, 1.55; N, 7.20. Found: C, 40.45; H, 1.75; N, 6.99. Decomposition: 190 °C

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Optimization of the reaction conditions, stability study, X-ray analysis data for **3j** and **5** and NMR spectra for all compounds (PDF)

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Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We are grateful to Karel Duerinckx (KU Leuven) for the assistance with NMR measurements and to prof. dr. Jef Rozenski for HR-MS measurements. P.G. and C.V. thank FWO (PhD Fellowship of the Research Foundation - Flanders) for fellowships received. W.M.D.B. thanks KU Leuven for financial support *via* Project OT/14/067. The Hercules Foundation of the Flemish Government is acknowledged for making mass spectrometry possible (grant 20100225-7) and supporting the purchase of a 400 MHz NMR spectrometer through project AKUL1311 and a diffractometer through project AKUL/09/0035.

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