Synthesis of N-acyl sulfamates from fluorosulfonates and potassium trimethylsilyloxy imidates

zhang shuning, Huan Xiong, Fengping Lu, Fei Ma, Yuang Gu, Peixiang Ma, Hongtao Xu, and Guang Yang

J. Org. Chem., Just Accepted Manuscript • DOI: 10.1021/acs.joc.9b02394 • Publication Date (Web): 31 Oct 2019

Downloaded from pubs.acs.org on November 3, 2019

“Just Accepted” manuscripts have been peer-reviewed and accepted for publication. They are posted online prior to technical editing, formatting for publication and author proofing. The American Chemical Society provides “Just Accepted” as a service to the research community to expedite the dissemination of scientific material as soon as possible after acceptance. “Just Accepted” manuscripts appear in full in PDF format accompanied by an HTML abstract. “Just Accepted” manuscripts have been fully peer reviewed, but should not be considered the official version of record. They are citable by the Digital Object Identifier (DOI®). “Just Accepted” is an optional service offered to authors. Therefore, the “Just Accepted” Web site may not include all articles that will be published in the journal. After a manuscript is technically edited and formatted, it will be removed from the “Just Accepted” Web site and published as an ASAP article. Note that technical editing may introduce minor changes to the manuscript text and/or graphics which could affect content, and all legal disclaimers and ethical guidelines that apply to the journal pertain. ACS cannot be held responsible for errors or consequences arising from the use of information contained in these “Just Accepted” manuscripts.
Synthesis of N-acyl sulfamates from fluorosulfonates and potassium trimethylsilyloxyl imidates

Shuning Zhang a,b, Huan Xiong a, Fengping Lu a, Fei Ma a, Yuang Gu a,b, Peixiang Ma a,* Hongtao Xu a,* and Guang Yang a,*

a Shanghai Institute for Advanced Immunochemical Studies, ShanghaiTech University, 201210 Shanghai, China
b School of Life Science and Technology, ShanghaiTech University, 201210 Shanghai, China

ABSTRACT

An efficient and operationally simple method for the synthesis of N-acyl sulfamates from fluorosulfonates and potassium trimethylsilyloxyl imidates as amide precursor is reported. This approach showed broad substrate scope, mild and base free reaction conditions, short reaction time, and high to excellent yields. Notably, we demonstrated the power of this reaction in the rapid late-stage functionalization of three complex phenol-containing bioactive molecules. Given the prevalence of phenol-containing drugs and building blocks, this method is applicable toward a diversity-oriented drug discovery.

INTRODUCTION

Sulfur (S), one of the top-five elements in FDA-approved drugs, is just behind the mainstays of conventional synthetic organic chemistry: carbon (C), hydrogen (H), oxygen (O) and nitrogen (N). sulfonamides and sulfur-containing functional groups play a key role in medicinal chemistry and drug design. Since the discovery of the first sulfonamide containing antibacterial agent prontosil in 1930s, sulfonamides and related sulfur-containing agents have gained significant attention in medicinal chemistry, and there are more than 150 FDA approved drugs bearing sulfur (S) up to now. In view of the prevalence of sulfur-containing therapeutic agents, methods that enable efficient access to sulfonamides, sulfamates and related sulfur-containing functionalities, and especially the late-stage decoration of common sulfur functionalities in the context of complex molecules are of great value in drug discovery.

Among various sulfur-containing functional groups, N-acyl sulfamate is present in a diverse array of biological active compounds covering not only in medicinal chemistry but also in food industry. For example, Avasimibe is an acyl-coenzyme A: cholesterol acyltransferase (ACAT) inhibitor that have reached phase III clinic for the treatment of atherosclerosis and hyperlipidemia (Figure 1); Ascamycin is a natural antibiotic that exerts its antibiotic activity via inhibition of aminoaeryl-tRNA synthetases (aaRSs); Acesulfam-K, an artificial sweetener, is widely used in food industry. Oestrone 3-O-(N-acetylated)-sulphamate (N-Acetylated-EMATE) is an irreversible
inhibitor of oestrogen sulphatase (E1-STS), and it can be used as a molecular probe for the active site of E1-STS in drug discovery. In addition, N-acyl sulfamate could also serve as a valuable bioisoster of phosphate in drug design.

Figure 1. N-Acyl sulfamates containing bioactive molecules.

Despite the importance of N-acyl sulfamates, their chemistry is relatively unexplored, and currently there are only limited synthetic routes available for their synthesis (Scheme 1). Classical methods rely on the use of reactive and toxic chlorosulfonyl isocyanate (Scheme 1, route i) or its unstable derivative, sulfamoyl chloride (Scheme 1, route ii). More recently, the De Borggraeve’s group reported a novel route that involves direct coupling of aryl fluorosulfonates with amides in the presence of sodium hydride to afford N-acyl sulfamates (Scheme 1, route iii). However, this method remains suffer from several major drawbacks: (a) more than two equivalents of strong base (sodium hydride) was needed, (b) lack of N-heterocycles containing substrates, and (c) low yields of some substrates. As a consequence, the development of a mild, efficient and practical synthesis toward N-acyl sulfamates is of great interest.

Scheme 1. Strategies for the synthesis of N-Acyl Sulfamates

Fluorosulfate was first reported in 1990s. It’s chemistry, however, was relatively unexplored until the Sharpless group reported the robust synthesis of (hetero)aryl fluorosulfonates in 2014.
which sparked a surge in investigation of the chemistry of fluorosulfonate for medicinal, biological, and material applications. Currently, as an emerging class of electrophiles, fluorosulfonate have already showed great versatility in various chemical transformation ranging from conventional organic synthesis to bio-compatible click chemistry, i.e. cross-coupling reactions, C-H activation reactions, late-stage drug functionalization, sulfur(VI) fluoride exchange (SuFEx) based click chemistry.

To achieve the goal of facile synthesis of N-Acyl sulfamates, the key is to employ a reactive, and easy-to-handle equivalent of amide in the reaction with fluorosulfonate. In 2000, Merchant and coworkers reported that heating of a nitrile with potassium trimethylsilanolate (TMSOK) in tetrahydrofuran or toluene could generate a trimethylsilyloxy iminium salt. Due to its insolubility in most aprotic solvents, it can be purified by simply washing to remove all impurities. Thus, potassium trimethylsilyloxy imidate represents a useful precursor for the synthesis of amide. Since it is in the form of potassium, we envisioned that the N-acylation of sulfamates could be achieved under base free conditions. In view of the electronic properties of fluorosulfonates (electrophilic) and potassium trimethylsilyloxy imidates (nucleophilic), we hypothesized that the negative charge residing on the nitrogen of 2a1 was strong enough to allow the reaction to proceed. Nucleophilic attack of iminium ion 2a1 at the activated electrophilic sulfur center of 1a1 to yield intermediate 3ai (Scheme 2), and simultaneously release a charged fluoride ion that could further react with intermediate 3ai to afford intermediate 3aii and the volatile fluorotrimethylsilane (TMSF) whose boiling point is 16 °C at 1 atm, and the release of TMSF would be another driving force of the reaction. Finally, protonation of intermediate 3aii to give N-acyl sulfamate 3a1.

Scheme 2. Proposed reaction mechanism.

RESULTS AND DISCUSSION

To test our hypothesis, we commenced our investigation using 1a1 and 2a1 as the model substrates (Table 1). To our gratification, when we added 1a1 into a stirring solution of 2a1 in
anhydrous tetrahydrofuran at room temperature, the desired N-acyl sulfamates 3a1 was obtained in a surprisingly excellent yield of 92%. We next evaluated the influences of various solvent on the conversation. Delightfully, all the tested solvents showed little influence on the transformation and offered excellent >90% yields in general, except for dichloromethane, which afforded a moderated yield of 52% (45% unreacted 1a1). We speculate that this is probably due to the poor solubility of the 2a1 in dichloromethane. Finally, we investigated the effect of reaction time and found 20 min to be the optimal.

Table 1. Optimization of reaction conditions

<table>
<thead>
<tr>
<th>entry</th>
<th>reaction conditions</th>
<th>yieldsb (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1,4-Dioxane, r.t., 30 min</td>
<td>71</td>
</tr>
<tr>
<td>2</td>
<td>DCM, r.t., 30 min</td>
<td>52</td>
</tr>
<tr>
<td>3</td>
<td>DMSO, r.t., 30 min</td>
<td>95</td>
</tr>
<tr>
<td>4</td>
<td>CH3CN, r.t., 30 min</td>
<td>90</td>
</tr>
<tr>
<td>5</td>
<td>THF, r.t., 30 min</td>
<td>92</td>
</tr>
<tr>
<td>6</td>
<td>DMF, r.t., 30 min</td>
<td>93</td>
</tr>
<tr>
<td>7</td>
<td>DMF, r.t., 20 min</td>
<td>95 (86)c</td>
</tr>
<tr>
<td>8</td>
<td>DMF, r.t., 10 min</td>
<td>92</td>
</tr>
</tbody>
</table>

aReactions performed using 1a1 (1 mmol) 2a1 (1.2 mmol). bYield determined by 1H NMR analysis of the crude reaction mixture with 1,3,5-trimethylbenzene as the internal standard. cYield determined by the purified 3a1.

With the optimized reaction conditions in hand, we examined the scope and generality in terms of functional groups on aryl fluorosulfonates. Results are summarized in Scheme 3. Generally, aryl fluorosulfonates with a broad scope of functional groups at various position could be accommodated and showed high to excellent yields. Both electron donating (3a1, 3b2, 3b3, 3b4, and 3c1) and withdrawing (3a4, 3a5, 3a6, 3b2 and 3c2) substituents on the aromatic ring gave the expected N-acylation products in excellent yields with short reaction time (20 min). Gratifyingly, the sensitive nitrile groups (3a6, 3b2 and 3c2) were also well tolerated under the optimized reaction conditions. Moreover, ortho-substituents (3c1-3c3 and 3d) did not dramatically hamper the reaction, even for the highly stericly hindered tertiary butyl (3c1, 85%). What’s more, hetero aromatic fluorosulfonates containing pyridine (3e) and quinoline (3f) moiety were all worked well in the reaction to give the corresponding N-acylation products with satisfactory yields.

We also investigated the scope of potassium trimethylsilyloxy imidates. Both electron donating (3g) and withdrawing (3h and 3i) substituents on the aromatic ring gave the expected N-acylation products in excellent yields with short reaction time (20 min). In addition, the hetero aromatic (3j and 3k) and alkyl (3l) substituted imidates also works well under the optimized reaction conditions. Notably, fluorosulfonyl analogs containing either -NSO2F (3m and 3n) or -CO2F (3o and 3p)
could also produce the corresponding N-acyl sulfonylacetamide in high to excellent yields (79-89%) suggesting a compatible reactivity to fluorosulfates (−OSO₂F).

**Scheme 3.** Synthesis of N-Acyl Sulfamates from Fluorosulfonates and trimethylsilyloxy imidates

![Scheme 3]

3a1: R¹ = Ph (86%)  
3a2: R¹ = Me (91%)  
3a3: R¹ = OMe (92%)  
3a4: R¹ = Cl (89%)  
3a5: R¹ = I (85%)  
3a6: R¹ = CN (90%)

3b1: R² = OMe (88%)  
3b2: R² = CN (82%)

3c1: R³ = t-Bu (85%)  
3c2: R³ = CN (91%)  
3c3: R³ = Br (85%)

3d (86%)  
3e (78%)  
3f (87%)  
3g (91%)  
3h (89%)

3i (85%)  
3j (81%)  
3k (83%)  
3l (80%)  
3m (82%)  
3n (89%)  
3o (79%)  
3p (84%)

4a

3q (70-85%, Scheme 4)

**a**Reaction conditions: 0.5 mmol of 1, 0.6 mmol of 2, 1 mL DMF (dry) at room temperature.

To demonstrate the practicality of this method, we sought to investigate whether the established methodology could efficiently decorate N-acyl sulfamates on complex molecules such as natural products (NPs) and approved drugs in a late-stage functionalization. First, 17-β-estrone, fulvestrant, and (-)-arctigenin were converted to their corresponding fluorosulfonates 2q, 2r, and 2s in good to excellent yields (see supporting information). Subsequently, under the established reaction conditions, we were pleased to obtain the desired N-acyl sulfamates 3q, 3r, and 3s in good yields (70-85%, Scheme 4). These results further emphasized the application of this novel methodology on the late-stage functionalization of bioactive molecules. The evaluation of biological activities of these new N-acyl sulfamates derivatives are ongoing, and will be disclosed in due course.
**Scheme 4.** Late-stage functionalization of natural products and/or approved drugs.

![Scheme 4](image)

17β-Estradiol

**a)**

\[
\text{HO} \quad \rightarrow \quad \text{O} \quad \rightarrow \quad 1q \quad \rightarrow \quad 3q \quad (85\%)
\]

**b)**

![Fulvestrant](image)

\[
\text{HO} \quad \rightarrow \quad \text{OF} \quad \rightarrow \quad 1r \quad (70\%)
\]

**c)**

![(-)-Arctigenin](image)

\[
\text{OH} \quad \rightarrow \quad \text{S} \quad \rightarrow \quad 3s \quad (75\%)
\]

Reaction conditions: a) SO\(_2\)F\(_2\), TEA (2 equiv), r.t.; b) trimethylsilyloxyl imidates 2a1 (1.2 equiv), r.t., 20 min.

Encouraged by the wide substrate scope and high efficiency of N-acyl sulfamates from fluorosulfonates and potassium trimethylsilyloxyl imidates, we next evaluated the feasibility of one-pot synthesis of N-acyl sulfamates from phenols via arylsulfonates generated in the presence of sulfuryl fluoride (SO\(_2\)F\(_2\)) and triethyl amine. As shown in Scheme 5, reaction of phenol s1 with sulfuryl fluoride (SO\(_2\)F\(_2\)) in anhydrous N,N-Dimethylformamide (DMF) in the presence of triethyl amine for 3h produced 1a1 in nearly quantitative yield (determined by LC-MS). Without further purification, 1a1 was reacted with 2a1 at room temperature for 20 min to generate 3a1 in excellent yield (90%).

**Scheme 5.** One-pot phenol fluorosulfation/N-acylation

![Scheme 5](image)

\[\text{Ph} \quad \rightarrow \quad \text{S} \quad \rightarrow \quad 3a1\]

\(^{a}\)Reaction conditions: a mixture of phenol (s1, 1 mmol), Et\(_3\)N (2 mmol, 2.0 eq.) and DMF (1 mL) charged with a SO\(_2\)F\(_2\) balloon was stirred at room temperature for 3 hours before 2a1 (1.2 mmol, 1.2 eq.) were added and then the mixture reacted at room temperature for an additional 20 min.
CONCLUSION

In summary, we describe an operationally simple methodology for the synthesis of $N$-acyl sulfamates from fluorosulfonates and potassium trimethylsilyloxyl imidates. Notable merits of this method include high yields, mild reaction conditions, short reaction times, and broad substrate scope, which make it an attractive alternative to existing methods. Under the optimized reaction conditions, various fluorosulfates converted well providing the $N$-acyl sulfamates in good yields, and especially in the context of steric and spatial complex molecules. Overall, such method provides a powerful tool in the late-stage functionalization (LSF) tool-box of natural products and/or other bioactive molecules.

EXPERIMENT SECTION

General Information. All commercially available organic compounds were purchased from Sigma-Aldrich and adamas-beta in China. Unless otherwise noted, all commercial reagents and solvents were used without additional purification. NMR spectrums were recorded on Bruker AM-500 instruments and/or Bruker AM-600 instruments. Chemical shifts are reported in $\delta$ (ppm) referenced to TMS as an internal standard for $^1$H NMR and CDCl$_3$ ($\delta$ 77.0) for $^{13}$C NMR. High-resolution mass spectra (HRMS-ESI) were obtained on an Agilent Technologies 6230 Accurate Mass TOF LC/MS instrument or an AB Sciex 4600 QTOF MS instrument or Finnigan MAT-95 mass spectrometer.

General procedure for the synthesis of fluorosulfonates:

A 100 mL flask equipped with a magnetic stir bar was charged with the relative phenol or amine (1 mmol, 1 equiv.). DCM (5 mL) was added, followed by triethylamine (0.28 mL, 2 mmol, 2 equiv.). Sealed with a rubber septum, the flask was evacuated to low vacuum, and backfilled with sulfuryl fluoride gas by a balloon. The resulting mixture was stirred at room temperature for 12 h. Upon completion, volatiles were removed in vacuo. The crude product was purified by flash chromatography on silica gel (Reverse phase silica gel; Mobile phase (gradient elution): 10 to 90% solvent B (Acetonitrile) in solvent A (Water) over 20 minutes) to give the desired fluorosulfonates.

$[1,1'$-Biphenyl]-4-yl sulfurofluoridate (1a1), white solid, (227 mg, 90%), $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.67 (d, $J = 8.8$ Hz, 2H), 7.56 (d, $J = 8.1$ Hz, 2H), 7.48 (t, $J = 7.5$ Hz, 2H), 7.41 (t, $J = 7.6$ Hz, 3H). These data are in agreement with literature data.$^{45}$

p-Tolyl sulfurofluoridate (1a2) colorless oil (175 mg, 85%), $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.33 – 7.17 (m, 4H), 2.40 (s, 3H). These data are in agreement with literature data.$^{50}$

4-Methoxyphenyl sulfurofluoridate (1a3), colorless oil (190 mg, 92%), 1H NMR (500 MHz, CDCl$_3$) $\delta$ 7.26 (dd, $J = 9.3$, 1.1 Hz, 1H), 6.94 (d, $J = 9.2$ Hz, 1H), 3.82 (s, 2H). These data are in agreement with literature data.$^{43}$
**4-Chlorophenyl sulfurofluoridate (1a4)**, colorless oil (177 mg, 84%), $^1$H NMR (500 MHz, CDCl$_3$) δ 7.47 – 7.42 (m, 1H), 7.33 – 7.27 (m, 1H). These data are in agreement with literature data.\(^{26}\)

**4-Iodophenyl sulfurofluoridate (1a5)**, colorless oil (272 mg, 90%), $^1$H NMR (500 MHz, CDCl$_3$) δ 7.80 (d, $J = 8.8$ Hz, 1H), 7.10 (d, $J = 8.5$ Hz, 1H). These data are in agreement with literature data.\(^{26}\)

**4-Cyanophenyl sulfurofluoridate (1a6)**, colorless oil (185 mg, 92%), $^1$H NMR (500 MHz, CDCl$_3$) δ 7.82 (d, $J = 8.9$ Hz, 1H), 7.50 (dd, $J = 9.0$, 0.9 Hz, 1H). These data are in agreement with literature data.\(^{38}\)

**3-Methoxyphenyl sulfurofluoridate (1b1)**, colorless oil (184 mg, 89%), $^1$H NMR (500 MHz, CDCl$_3$) δ 7.14 (t, $J = 8.1$ Hz, 1H), 6.52 (ddd, $J = 8.2$, 2.3, 0.9 Hz, 1H), 6.48 – 6.42 (m, 2H), 3.78 (s, 3H). These data are in agreement with literature data.\(^{43}\)

**3-Cyanophenyl sulfurofluoridate (1b2)**, colorless oil (161 mg, 80%), $^1$H NMR (500 MHz, CDCl$_3$) δ 7.75 (dt, $J = 7.2$, 1.5 Hz, 1H), 7.68 – 7.60 (m, 3H). These data are in agreement with literature data.\(^{38}\)

**2-(tert-Butyl)phenyl sulfurofluoridate (1c1)**, Following the general procedure, 1c1 was obtained as a colorless oil (200 mg, 86% yield), $^1$H NMR (500 MHz, CDCl$_3$) δ 7.38 – 7.29 (m, 1H), 7.23 (d, $J = 7.2$ Hz, 1H), 7.12 (dt, $J = 11.6$, 5.7 Hz, 2H), 1.29 (d, $J = 9.6$ Hz, 9H); $^{13}$C{$^1$H} NMR (126 MHz, CDCl$_3$) δ 150.1, 141.0, 128.7, 128.1, 128.0, 120.2, 34.8, 30.3; HRMS (ESI) calcd for [M+H]$^+$ [C$_{10}$H$_{14}$FO$_3$S]$^+$ 233.0648, found 233.0663.

**2-Cyanophenyl sulfurofluoridate (1c2)**, colorless oil (181 mg, 90%), $^1$H NMR (500 MHz, CDCl$_3$) δ 7.87 – 7.73 (m, 2H), 7.63 – 7.53 (m, 2H). These data are in agreement with literature data.\(^{26}\)

**2-Bromophenyl sulfurofluoridate (1c3)**, colorless oil (224 mg, 88%), $^1$H NMR (500 MHz, CDCl$_3$) δ 7.47 (dd, $J = 8.0$, 1.6 Hz, 1H), 7.23 (dd, $J = 8.1$, 1.5 Hz, 1H), 7.04 (dd, $J = 8.2$, 1.5 Hz, 1H), 6.82 (ddd, $J = 8.0$, 1.5 Hz, 1H), 7.75 (mq, $J = 8.3$, 1.5 Hz, 1H). These data are in agreement with literature data.\(^{17}\)

**2,6-Dimethylphenyl sulfurofluoridate (1d)**, colorless oil (165 mg, 81%), $^1$H NMR (500 MHz, CDCl$_3$) δ 7.18 (dd, $J = 8.6$, 6.2 Hz, 1H), 7.16 – 7.10 (m, 2H), 2.39 (s, 6H). These data are in agreement with literature data.\(^{17}\)

**Pyridin-3-yl sulfurofluoridate (1e)**, colorless oil (138 mg, 78%), $^1$H NMR (500 MHz, CDCl$_3$) δ 8.71 – 8.64 (m, 1H), 7.75 – 7.64 (m, 1H), 7.51 – 7.41 (m, 1H). These data are in agreement with literature data.\(^{44}\)

**Quinolin-8-yl sulfurofluoridate (1f)**, colorless oil (216 mg, 95%), $^1$H NMR (500 MHz, Chloroform-$d$) δ 9.06 (dd, $J = 4.2$, 1.7 Hz, 1H), 8.24 (dd, $J = 8.3$, 1.7 Hz, 1H), 7.90 (dd, $J = 8.3$, 1.3 Hz, 1H), 7.75 (dt, $J = 7.7$, 1.2 Hz, 1H), 7.61 – 7.57 (m, 1H), 7.55 (dd, $J = 8.3$, 4.2 Hz, 1H). These data are in agreement with literature data.\(^{44}\)
4-(4-methoxyphenyl)piperazine-1-sulfonyl fluoride (1m) Following the general procedure, 1m was obtained as a white solid (263 mg, 96% yield). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.00 – 6.80 (m, 4H), 3.77 (d, $J = 1.7$ Hz, 3H), 3.59 (t, $J = 5.1$ Hz, 4H), 3.14 (t, $J = 5.1$ Hz, 4H); $^{13}$C($^1$H) (126 MHz, CDCl$_3$) $\delta$ 154.9, 144.6, 119.5, 114.6, 55.6, 50.2, 47.2; HRMS (ESI) calcd for [M+H]$^+$ [C$_{11}$H$_{16}$FN$_2$O$_3$S]$^+$ 275.0866, found 275.0881.

5-Methoxy-1H-indole-1-sulfonyl fluoride (1n) Following the general procedure, 1n was obtained as a white solid (218 mg, 95% yield). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.75 (dd, $J = 9.0$, 1.8 Hz, 1H), 7.41 – 7.33 (m, 1H), 7.09 – 6.97 (m, 2H), 6.74 – 6.68 (m, 1H), 3.84 (d, $J = 2.0$ Hz, 3H); $^{13}$C($^1$H) NMR (126 MHz, CDCl$_3$) $\delta$ 157.42, 131.46, 129.31, 126.75, 114.58, 114.30, 111.14, 104.42, 55.71; HRMS (ESI) calcd for [M+H]$^+$ [C$_9$H$_9$FNO$_3$S]$^+$ 230.0287, found 230.0298.

(8R,9S,13S,14S,17S)-17-hydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[alphenanthren-3-yl sulfooxiduridate (1q), white solid, (298 mg, 84%), $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.36 (dd, $J = 8.7$, 1.1 Hz, 1H), 7.09 (dd, $J = 8.6$, 2.6 Hz, 1H), 7.03 (dd, $J = 2.6$, 1.1 Hz, 1H), 3.75 (dd, $J = 9.0$, 8.1 Hz, 1H), 2.95 – 2.87 (m, 2H), 2.33 (ddt, $J = 13.4$, 4.3, 2.8 Hz, 1H), 2.27 – 2.19 (m, 1H), 2.13 (dtd, $J = 13.2$, 9.3, 5.7 Hz, 1H), 2.02 – 1.95 (m, 1H), 1.95 – 1.89 (m, 1H), 1.76 – 1.67 (m, 1H), 1.60 – 1.44 (m, 3H), 1.44 – 1.26 (m, 1H), 1.21 (ddd, $J = 12.2$, 10.9, 7.3 Hz, 1H), 0.79 (s, 3H). These data are in agreement with literature data.

(7R,8R,9S,13S,14S,17S)-17-hydroxy-13-methyl-7-(9-((4,4,5,5,5-pentafluoropentyl)sulfinyl)nonyl)-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[alphenanthren-3-yl sulfooxiduridate (1r), white solid, (496 mg, 72%), $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.39 (d, $J = 8.2$ Hz, 1H), 7.11 (d, $J = 8.3$ Hz, 1H), 3.79 (t, $J = 12.4$ Hz, 1H), 2.95 (dd, $J = 16.2$, 8.5 Hz, 1H), 2.85-2.62 (m, 5H), 2.42 - 2.12 (m, 7H), 1.98 (d, $J = 12.3$ Hz, 1H), 1.84-1.73 (m, 3H), 1.64-1.58 (m, 4H), 1.57-1.21 (m, 17H), 0.99 (brs, 1H), 0.79 (s, 3H); These data are in agreement with literature data.

4-(((3R,4R)-4-(3,4-dimethoxybenzyl)-2-oxotetrahydrofuran-3-yl)methyl)-2-methoxyphenyl sulfurofluoridate (1s) Following the general procedure, 1s was obtained as a white solid (409 mg, 90% yield). $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.20 (d, $J = 8.3$ Hz, 1H), 6.82 (d, $J = 1.9$ Hz, 1H), 6.77 (d, $J = 8.0$ Hz, 1H), 6.69 (dd, $J = 8.2$, 2.1 Hz, 1H), 6.58 – 6.49 (m, 2H), 4.22 (t, $J = 8.4$ Hz, 1H), 3.91 (t, $J = 8.7$ Hz, 1H), 3.87 – 3.79 (m, 9H), 3.01 – 2.92 (m, 2H), 2.64 (h, $J = 6.6$ Hz, 3H), 2.47 (p, $J = 7.8$ Hz, 1H); $^{13}$C($^1$H) NMR (126 MHz, CDCl$_3$) $\delta$ 178.3, 151.1, 149.1, 148.0, 140.0, 137.8, 130.1, 122.1, 121.6, 120.6, 114.4, 111.9, 111.4, 71.2, 56.2, 55.9, 55.9, 46.3, 41.1, 38.0, 34.4; HRMS (ESI) calcd for [M+H]$^+$ [C$_{21}$H$_{24}$FO$_3$S]$^+$ 455.1176, found 455.1187.

**General procedure for the synthesis of N-acyl sulfamates:**

A 100 mL flask equipped with a magnetic stir bar was charged with potassium trimethylsilanolate (513 mg, 4 mmol, 2 equiv.). Then anhydrous tetrahydrofuran (THF) or benzotrifluoride (10 mL) was added, followed by aromatic nitrile (using THF as solvent) or aliphatic
nitrile (using benzotrifluoride as solvent) (2 mmol, 1 equiv.). Then the reaction mixture was heated to reflux until the nitrile was consumed and the solid was filtered, and washed with anhydrous solvent (THF or benzotrifluoride), dried under reduced pressure to give the desired trimethylsilyloxy imidate, which without purification was used for the next step reaction.

A 10 mL flask equipped with a magnetic stir bar was charged with trimethylsilyloxyl imidate, (0.6 mmol, 1.2 equiv.). Then anhydrous DMF (1 mL) was added, followed by fluorosulfate (0.5 mmol, 1 equiv.) at room temperature. After stirring at room temperature for 10 to 20 min, the solvent was removed under reduced pressure and the crude product was purified by flash chromatography on silica gel (Reverse phase silica gel; Mobile phase (gradient elution): 10% to 90% solvent B (Acetonitrile) in solvent A (Water) over 20 minutes) to give the desired product.

**1,1'-Biphenyl-4-yl benzoylsulfamate (3a1)** Following the general procedure, 3a1 was obtained as a white solid (152 mg, 86% yield), ¹H NMR (500 MHz, CDCl₃) δ 7.87 – 7.79 (m, 2H), 7.60 (t, J = 7.5 Hz, 1H), 7.48 (ddt, J = 13.0, 7.9, 7.3, 3.0 Hz, 6H), 7.40 (t, J = 7.6 Hz, 2H), 7.37 – 7.30 (m, 3H); ¹³C¹H NMR (126 MHz, CDCl₃) δ 164.1, 149.2, 141.1, 139.6, 134.1, 130.6, 129.2, 128.9, 128.7, 128.1, 127.9, 127.1, 122.2; HRMS (ESI) calcd for [M+H]+ [C₁₉H₁₄NO₃S]+ 354.0800, found 354.0804.

**p-Tolyl benzoylsulfamate (3a2)** Following the general procedure, 3a2 was obtained as a white solid (133 mg, 91% yield), ¹H NMR (500 MHz, CDCl₃) δ 7.85 – 7.79 (m, 2H), 7.53 – 7.45 (m, 2H), 7.25 – 7.13 (m, 4H), 2.31 (s, 3H); ¹³C¹H NMR (126 MHz, CDCl₃) δ 166.3, 148.1, 137.6, 133.3, 131.6, 130.1, 128.5, 128.0, 121.3, 19.5; HRMS (ESI) calcd for [M+H]+ [C₁₉H₁₄NO₃S]+ 292.0644, found 292.0651.

**4-Methoxyphenyl benzoylsulfamate (3a3)**: Following the general procedure, 3a3 was obtained as a white solid (141 mg, 92% yield), ¹H NMR (500 MHz, CDCl₃) δ 8.22 (dd, J = 8.4, 1.4 Hz, 2H), 7.66 – 7.59 (m, 1H), 7.53 – 7.45 (m, 2H), 7.25 – 7.13 (m, 4H), 2.31 (s, 3H); ¹³C¹H NMR (126 MHz, CDCl₃) δ 166.3, 158.9, 143.5, 133.3, 131.6, 128.6, 128.1, 122.6, 114.5, 54.8; HRMS (ESI) calcd for [M+H]+ [C₁₉H₁₄NO₃S]+ 312.0099, found 312.0097.

**4-Chlorophenyl benzoylsulfamate (3a4)** Following the general procedure, 3a4 was obtained as a white solid (129 mg, 89% yield), ¹H NMR (500 MHz, CDCl₃) δ 7.86 – 7.78 (m, 2H), 7.62 (t, J = 7.4 Hz, 1H), 7.52 – 7.45 (m, 2H), 7.26 – 7.19 (m, 2H), 6.96 – 6.88 (m, 2H), 3.75 (s, 3H); ¹³C¹H NMR (126 MHz, CDCl₃) δ 166.3, 158.9, 143.5, 133.3, 131.6, 128.6, 128.1, 122.6, 114.5, 54.8; HRMS (ESI) calcd for [M+H]+ [C₁₉H₁₄NO₃S]+ 308.0593, found 308.0580.

**4-Iodophenyl benzoylsulfamate (3a5)** Following the general procedure, 3a5 was obtained as a white solid (171 mg, 85% yield), ¹H NMR (500 MHz, CDCl₃) δ 8.97 (s, 1H), 7.82 (dd, J = 8.0, 1.5 Hz, 2H), 7.72 – 7.58 (m, 3H), 7.50 (t, J = 7.8 Hz, 2H), 7.12 – 6.99 (m, 2H); ¹³C¹H NMR (126 MHz, CDCl₃) δ 164.0, 149.7, 139.2, 134.2, 130.4, 129.2, 128.0, 124.0, 92.7; HRMS (ESI) calcd for [M+H]+ [C₁₉H₁₁ClNO₃S] 403.9453, found 403.9455.
4-Cyanophenyl benzoylsulfamate (3a6) Following the general procedure, 3a6 was obtained as a white solid (136 mg, 90% yield), 1H NMR (500 MHz, CD3OD) δ 7.88 – 7.81 (m, 4H), 7.66 – 7.62 (m, 1H), 7.55 – 7.48 (m, 4H); 13C{1H} NMR (126 MHz, CD3OD) δ 166.3, 153.1, 134.1, 133.4, 131.5, 128.6, 128.2, 123.0, 117.3, 111.2; HRMS (ESI) caleed for [M+H]+ [C14H11N2O6S]+ 303.0440, found 303.0445.

3-Methoxyphenyl benzoylsulfamate (3b1) Following the general procedure, 3b1 was obtained as a white solid (135 mg, 88% yield), 1H NMR (500 MHz, CD3OD) δ 7.85 – 7.80 (m, 2H), 7.67 – 7.60 (m, 1H), 7.53 – 7.46 (m, 2H), 7.31 (t, J = 8.2 Hz, 1H), 6.93 – 6.85 (m, 3H), 3.73 (s, 3H); 13C{1H} NMR (126 MHz, CD3OD) δ 166.4, 160.9, 151.0, 133.3, 131.6, 130.0, 128.5, 128.0, 113.5, 113.2, 107.4, 54.6; HRMS (ESI) caleed for [M+H]+ [C14H11O4S]+ 308.0593, found 308.0599.

3-Cyanophenyl benzoylsulfamate (3b2) Following the general procedure, 3b2 was obtained as a white solid (124 mg, 82% yield), 1H NMR (500 MHz, CD3OD) δ 7.87 – 7.83 (m, 2H), 7.76 – 7.71 (m, 2H), 7.68 – 7.61 (m, 3H), 7.51 (t, J = 7.7 Hz, 2H); 13C{1H} NMR (126 MHz, CD3OD) δ 166.1, 150.1, 133.5, 131.3, 131.2, 131.2, 128.6, 128.1, 126.8, 125.6, 116.9, 113.6; HRMS (ESI) caleed for [M+H]+ [C14H11N2O6S]+ 303.0440, found 303.0438.

2-(tert-Butyl)phenyl benzoylsulfamate (3c1) Following the general procedure, 3c1 was obtained as a white solid (142 mg, 85% yield), 1H NMR (500 MHz, CD3OD) δ 7.90 (dd, J = 8.4, 1.4 Hz, 2H), 7.64 (d, J = 7.5 Hz, 1H), 7.56 – 7.49 (m, 3H), 7.49 – 7.43 (m, 1H), 7.22 (ddd, J = 9.0, 7.5, 1.8 Hz, 2H), 1.43 (s, 9H); 13C{1H} NMR (126 MHz, CDCl3) δ 150.1, 141.0, 128.7, 128.1, 128.0, 120.2, 134.8, 30.3; HRMS (ESI) caleed for [M+H]+ [C17H23NO4S]+ 334.1113, found 334.1103.

2-Cyanophenyl benzoylsulfamate (3c2) Following the general procedure, 3c2 was obtained as a white solid (138 mg, 91% yield), 1H NMR (500 MHz, CD3OD) δ 7.90 – 7.86 (m, 2H), 7.81 (dd, J = 7.8, 1.7 Hz, 1H), 7.76 (ddd, J = 9.1, 7.5, 1.7 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.60 (ddd, J = 8.5, 1.1 Hz, 1H), 7.54 – 7.49 (m, 3H); 13C{1H} NMR (126 MHz, CD3OD) δ 166.1, 151.0, 134.6, 133.9, 133.4, 131.6, 128.6, 128.3, 127.8, 123.2, 114.3, 107.2; HRMS (ESI) caleed for [M+H]+ [C14H11N2O6S]+ 303.0440, found 303.0438.

2-Bromophenyl benzoylsulfamate (3c3) Following the general procedure, 3c3 was obtained as a yellow solid (151 mg, 85% yield), 1H NMR (500 MHz, DMSO-d6) δ 7.97 – 7.93 (m, 2H), 7.60 (ddd, J = 8.2, 3.8, 1.6 Hz, 2H), 7.45 – 7.41 (m, 1H), 7.39 – 7.34 (m, 2H), 7.31 (ddd, J = 8.3, 7.4, 1.6 Hz, 1H), 7.08 – 7.02 (m, 1H); 13C{1H} NMR (126 MHz, DMSO-d6) δ 170.7, 150.0, 138.8, 133.4, 130.9, 128.9, 128.8, 128.1, 126.1, 123.0, 115.5; HRMS (ESI) caleed for [M+H]+ [C14H11BrNO4S]+ 355.9592, found 355.9600.

2,6-Dimethylphenyl benzoylsulfamate (3d) Following the general procedure, 3d was obtained as a white solid (131 mg, 86% yield), 1H NMR (500 MHz, CDCl3) δ 7.83 (dt, J = 7.3, 1.3 Hz, 2H), 7.68 – 7.61 (m, 1H), 7.50 (t, J = 7.9 Hz, 2H), 7.12 – 7.01 (m, 3H), 7.08 (dd, J = 8.6, 6.0 Hz, 1H), 7.04 (d, J = 8.6, 2H), 2.37 (s, 6H); 13C{1H} NMR (126 MHz, CDCl3) δ 163.8, 148.0, 133.9, 131.9, 130.9, 129.5, 129.3, 127.9, 127.3, 17.2; HRMS (ESI) caleed for [M+H]+ [C15H12NO4S]+ 306.0800, found 306.0809.
**Pyridin-3-yl benzoysulfamate (3e)** Following the general procedure, 3e was obtained as a white solid (109 mg, 78% yield). $^1$H NMR (500 MHz, DMSO-$d_6$) δ 8.77 (d, $J = 2.6$ Hz, 1H), 8.65 (dd, $J = 5.3, 1.3$ Hz, 1H), 8.20 (ddd, $J = 8.6, 2.7, 1.3$ Hz, 1H), 7.95 – 7.89 (m, 2H), 7.85 (dd, $J = 8.6, 5.2$ Hz, 1H), 7.55 – 7.50 (m, 1H), 7.46 – 7.40 (m, 2H); $^{13}$C ($^1$H) NMR (126 MHz, DMSO-$d_6$) δ 169.1, 149.9, 142.7, 139.3, 135.7, 135.2, 132.4, 129.0, 128.6, 127.1; HRMS (ESI) calcd for [M+H]$^+$ [C$_2$H$_3$N$_2$O$_3$S]$^+$ 279.0440, found 279.0445.

**Quinolin-8-yl benzoysulfamate (3f)** Following the general procedure, 3f was obtained as a white solid (143 mg, 87% yield). $^1$H NMR (500 MHz, DMSO-$d_6$) δ 9.43 (dd, $J = 5.2, 1.5$ Hz, 1H), 9.18 (dd, $J = 8.4, 1.4$ Hz, 1H), 8.26 (dd, $J = 8.2, 1.3$ Hz, 1H), 8.16 – 8.09 (m, 3H), 8.00 (dd, $J = 7.7, 1.3$ Hz, 1H), 7.95 (t, $J = 7.9$ Hz, 1H), 7.63 – 7.56 (m, 1H), 7.50 (dd, $J = 8.3, 7.0$ Hz, 2H); $^{13}$C ($^1$H) NMR (126 MHz, DMSO-$d_6$) δ 172.7, 147.2, 145.4, 142.7, 136.1, 134.9, 132.6, 130.3, 129.9, 129.3, 128.7, 127.1, 126.4, 123.4; HRMS (ESI) calcd for [M+H]$^+$ [C$_{14}$H$_{13}$N$_2$O$_3$S]$^+$ 329.0596, found 329.0591.

**p-Tolyl (4-methoxybenzoyl)sulfamate (3g)** Following the general procedure, 3g was obtained as a white solid (146 mg, 91% yield). $^1$H NMR (500 MHz, DMSO-$d_6$) δ 7.87 – 7.82 (m, 2H), 7.07 (s, 4H), 6.88 – 6.83 (m, 2H), 3.77 (s, 3H), 2.23 (s, 3H); $^{13}$C ($^1$H) NMR (126 MHz, DMSO-$d_6$) δ 170.1, 161.4, 150.5, 133.8, 131.7, 130.6, 129.7, 122.1, 113.2, 55.6, 20.8; HRMS (ESI) calcd for [M+H]$^+$ [C$_{15}$H$_{14}$NO$_5$S]$^+$ 322.0749, found 322.0735.

**p-Tolyl (4-bromobenzoyl)sulfamate (3h)** Following the general procedure, 3h was obtained as a yellow solid (165 mg, 89% yield). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.69 (d, $J = 8.3$ Hz, 2H), 7.62 (d, $J = 8.3$ Hz, 2H), 7.14 (s, 4H), 2.32 (s, 3H); $^{13}$C ($^1$H) NMR (126 MHz, CDCl$_3$) δ 163.5, 147.7, 138.0, 132.4, 130.5, 129.6, 129.5, 129.2, 121.5, 20.9; HRMS (ESI) calcd for [M+H]$^+$ [C$_{16}$H$_{13}$BrNO$_5$S]$^+$ 369.9749, found 369.9743.

**p-Tolyl (4-( trifluoromethyl)benzoyl)sulfamate (3i)** Following the general procedure, 3i was obtained as a white solid (153 mg, 85% yield). $^1$H NMR (500 MHz, DMSO-$d_6$) δ 8.09 (d, $J = 8.1$ Hz, 2H), 7.89 (d, $J = 8.2$ Hz, 2H), 7.25 (d, $J = 8.2$ Hz, 2H), 7.22 – 7.14 (m, 2H), 2.29 (s, 3H); $^{13}$C ($^1$H) NMR (126 MHz, DMSO-$d_6$) δ 165.6, 148.2, 137.4, 136.5, 133.02 (q, $J_{C,F} = 32.1$ Hz), 130.9, 129.9, 125.99 (q, $J_{C,F} = 3.8$ Hz), 124.15 (q, $J_{C,F} = 272.6$ Hz); 121.9, 20.8; HRMS (ESI) calcd for [M+H]$^+$ [C$_{17}$H$_{12}$F$_3$NO$_5$S]$^+$ 360.0517, found 360.0513.

**p-Tolyl benzoysulfamate (3j)** Following the general procedure, 3j was obtained as a white solid (118 mg, 81% yield). $^1$H NMR (500 MHz, DMSO-$d_6$) δ 8.63 – 8.58 (m, 2H), 7.77 – 7.74 (m, 2H), 7.11 (s, 4H), 2.25 (s, 3H); $^{13}$C ($^1$H) NMR (126 MHz, DMSO-$d_6$) δ 168.9, 150.2, 150.1, 146.1, 134.4, 129.9, 122.8, 122.1, 20.8; HRMS (ESI) calcd for [M+H]$^+$ [C$_{16}$H$_{13}$NO$_4$S]$^+$ 293.0596, found 293.0607.

**p-Tolyl (thiophene-2-carbonyl)sulfamate (3k)** Following the general procedure, 3k was obtained as a white solid (123 mg, 83% yield). $^1$H NMR (500 MHz, DMSO-$d_6$) δ 7.53 (d, $J = 5.0$ Hz, 1H), 7.45 (dd, $J = 3.6, 1.3$ Hz, 1H), 7.10 (d, $J = 1.6$ Hz, 4H), 7.01 (dd, $J = 5.0, 3.6, 1.1$ Hz, 1H), 2.25 (s, 3H); $^{13}$C ($^1$H) NMR (126 MHz, DMSO-$d_6$) δ 166.1, 150.2, 145.2, 134.3, 130.0, 129.8,
N-(4-(4-methoxyphenyl)piperazin-1-yl)sulfonyl)benzamide (3n) Following the general procedure, 3n was obtained as a yellow solid (149 mg, 84% yield), 1H NMR (500 MHz, DMSO-d6) δ 8.07 (d, J = 8.5 Hz, 1H), 7.91 – 7.85 (m, 2H), 7.62 (d, J = 7.4 Hz, 1H), 7.53 – 7.46 (m, 2H); 13C {1H} NMR (126 MHz, DMSO-d6) δ 165.7, 151.7, 134.8, 133.7, 131.9, 131.8, 131.2, 129.3, 129.2, 129.1, 128.95, 128.78, 124.2, 118.7, 115.8, 45.6; HRMS (ESI) calcld for [M+H]+ [C16H25N2O4S]2+ 355.1116, found 355.1103.

(8R,9S,13S,14S,17S)-17-Hydroxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decachydro-6H-cyclopenta[al]phenanthren-3-yl benzoysulamate (3q) Following the general procedure, 3q was obtained as a white solid (194 mg, 85% yield), 1H NMR (500 MHz, CD3OD) δ 7.81 (d, J = 7.7 Hz, 2H), 7.63 (s, 1H), 7.51 (d, J = 7.6 Hz, 2H), 7.32 (d, J = 8.6 Hz, 1H), 7.04 (d, J = 8.7 Hz, 1H), 6.99 (s, 1H), 3.65 (t, J = 8.6 Hz, 1H), 2.79 (dd, J = 8.9, 4.2 Hz, 2H), 2.31 (dd, J = 13.7, 3.9 Hz, 1H), 2.23
- 2.15 (m, 1H), 2.07 – 1.92 (m, 2H), 1.87 (dd, J = 11.2, 5.0 Hz, 1H), 1.73 – 1.63 (m, 1H), 1.55 – 1.22 (m, 7H), 1.18 (td, J = 11.5, 7.3 Hz, 1H), 0.75 (s, 3H); $^{13}$C $^{1}$H NMR (126 MHz, CD$_3$OD) δ 166.5, 148.0, 140.0, 138.8, 133.3, 131.8, 128.5, 128.0, 126.6, 121.4, 118.5, 81.0, 49.8, 44.1, 42.9, 38.5, 36.5, 29.3, 29.1, 26.6, 26.0, 22.6, 10.2; HRMS (ESI) calcd for [M+H]$^+$ [C$_{25}$H$_{30}$NO$_5$S]$^+$ 456.1845, found 456.1820.

(7R,9S,13S,14S,17S)-17-Hydroxy-13-methyl-7-(9-((4,4,5,5,5-pentafluoropentyl)sulfinyl)nonyl)-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[al]phenanthren-3-yl benzoylsulfamate (3r) Following the general procedure, 3r was obtained as a white solid (276 mg, 70% yield). $^1$H NMR (600 MHz, DMSO-d$_6$) δ 7.87 (d, J = 7.5 Hz, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.34 (d, J = 8.7 Hz, 1H), 6.99 (dd, J = 8.6, 2.6 Hz, 1H), 2.89 – 2.57 (m, 7H), 2.45 – 2.22 (m, 5H), 1.90 (p, J = 7.5 Hz, 3H), 1.78 (dt, J = 12.5, 3.2 Hz, 1H), 1.70 – 1.39 (m, 17H), 0.89 – 0.77 (m, 1H), 0.65 (s, 3H); $^{13}$C $^{1}$H NMR (126 MHz, DMSO-d$_6$) δ 166.5, 166.4, 166.4, 147.9, 138.3, 137.1, 132.7, 131.2, 129.6, 128.4, 128.4, 128.2, 127.4, 127.4, 122.4, 120.0, 118.8, 116.0, 115.7, 115.5, 112.8, 80.0, 51.0, 49.2, 45.9, 42.8, 41.2, 38.0, 36.7, 33.9, 32.4, 29.8, 29.2, 29.0, 28.8, 28.7, 28.6, 28.5, 28.4, 28.1, 27.3, 26.8, 25.0, 22.2, 22.0, 14.0, 11.3, 11.2; HRMS (ESI) calcd for [M+H]$^+$ [C$_{39}$H$_{53}$F$_5$NO$_6$S$_2$]$^+$ 790.3234, found 790.3233.

4-(((3R,4R)-4-(3,4-dimethoxybenzyl)-2-oxotetrahydrofuran-3-yl)methyl)-2-methoxyphenyl benzoylsulfamate (3s) Following the general procedure, 3s was obtained as a yellow solid (208 mg, 75% yield). $^1$H NMR (500 MHz, DMSO-d$_6$) δ 7.90 (d, J = 7.4 Hz, 2H), 7.59 (d, J = 7.6 Hz, 1H), 7.48 (d, J = 7.7 Hz, 2H), 7.23 (d, J = 8.0 Hz, 1H), 6.94 (s, 1H), 6.80 (dd, J = 15.0, 8.0 Hz, 2H), 6.68 (s, 1H), 6.60 (d, J = 7.9 Hz, 1H), 4.11 (t, J = 7.9 Hz, 1H), 3.90 (s, 1H), 3.69 (d, J = 10.1 Hz, 6H), 3.61 (s, 4H), 2.96 – 2.73 (m, 4H), 1.24 (s, 1H); $^{13}$C $^{1}$H NMR (126 MHz, DMSO-d$_6$) δ 178.8, 178.8, 151.6, 149.1, 147.8, 133.0, 132.9, 131.6, 129.3, 128.9, 128.8, 123.7, 123.4, 121.7, 120.9, 114.8, 112.9, 112.3, 71.2, 56.3, 55.9, 55.8, 45.8, 41.5, 37.2, 34.3; HRMS (ESI) calcd for [M+H]$^+$ [C$_{28}$H$_{30}$NO$_5$S]$^+$ 556.1641, found 556.1622.

ASSOCIATED CONTENT
Supporting information: $^1$H and $^{13}$C NMR of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author
*E-mail: yangguang@shanghaitech.edu.cn (G. Yang), xuht@shanghaitech.edu.cn (H. Xu), mapx@shanghaitech.edu.cn (P. Ma)

ORCID: Hongtao Xu: 0000-0001-5174-9079; Peixiang Ma: 0000-0001-6794-1663

Notes: The authors declare no competing financial interest.
ACKNOWLEDGMENT

This work is supported by the National Natural Science Foundation of China (21977070, and 31500632), and the Science and Technology Commission of Shanghai Municipality (Grant 16DZ1910200).

REFERENCES


Liu, F.; Wang, H.; Li, S.; Bare, G. A. L.; Chen, X.; Wang, C.; Moses, J. E.; Wu, P.; Sharpless, K. B. Biocompatible SuFEx Click Chemistry: Thionyl Tetrafluoride (SOF₄) -Derived


