Sulfur Assisted Tandem Electrophilic Fluorinative Decacylation: Synthesis of α-Fluoro β-Ketosulfides

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ABSTRACT: A successful synthesis of α-fluoro-β-ketosulfides using an electrophilic fluorination method has been reported for the first time. The reaction proceeds via an electrophilic fluorination of α-sulfonyl-β-diketones followed by an unexpected tandem decylation. The resulting products, α-fluoro-β-ketosulfides, are easily oxidized to the corresponding α-fluoro-β-ketosulfones, which can be used for further useful olefination reactions.

INTRODUCTION

Incorporation of fluorine into organic molecules is an active research area in organic synthesis because fluorine containing organic compounds are found in many biologically active compounds, pharmaceuticals, agrochemicals, and materials. A plethora of methods is available in the literature for incorporation of fluorine into organic molecules to obtain a variety of structurally diverse molecular scaffolds. However, controlled monoelectrophilic fluorination at the α-position of an electron withdrawing group still remains a challenge in organic synthesis. This problem becomes compounded when a sulfonyl group is present at α-position to an electron withdrawing moiety. Several attempts toward synthesizing α-fluoro-β-ketosulfides via electrophilic fluorination method by various groups have resulted in the formation of undesired or overfluorinated products (Scheme 1). This is probably due to (i) the strong affinity between sulfur and fluorine to form S–F/S → F bond, which leads to undesired side reactions, and (ii) the presence of a sulfur atom at α-position increases the acidity of C–H bond and results in rapid uncontrolled fluorination. The methods for the formation of α-fluoro-β-ketosulfides are limited to a few β-ketosulfide derivatives that bear the substitution at the α-position.

In contrast to electrophilic fluorination, the controlled nuclease fluorination of β-ketosulfides was successfully achieved by electrochemical methods (eq 1, Scheme 2).

The only chemical method known to obtain α-fluoro-β-ketosulfides is the nuclease fluorination of sulfoxide with DAST (diethyl amino sulfur trifluoride) in the presence of catalytic amount of ZnL2 (eq 2, Scheme 2). However, the nuclease substitution of α-bromofluorocarbonyl compounds with thiol provides the expected α-fluoro-β-ketosulfides (eq 3, Scheme 2).

On the other hand, several reports of deacylation of β-dicarbonyl compounds such as classical acetoacetic ester synthesis are well-documented in the literature. In recent years, the release of trifluoro acetate groups from the fluorinated β-dicarbonyl compounds has been shown as an important reaction in organic synthesis. When the α-position of β-dicarbonyl compounds is substituted with sulfonyl, the deacylation is relatively facile. The deacylation of β-ketoesters is facile in the presence of nucleophilic base at ambient temperature. However, the deacylation of β-diketones generally requires transition-metal catalysts and oxidants, and the reaction is performed at higher temperature. A report for the electrophilic halogenative (+Cl and +Br) deacylation of nonsulfide bearing β-dicarbonyl compounds is known in the literature. Distinct from these reports, the present work involves an unexpected tandem deacylation of α-fluoro sulfonyl β-diketones in mild reaction conditions to synthesize α-fluoro-β-ketosulfides (eq 4, Scheme 2). To the best of our knowledge, to date, (i) a controlled fluorination leading to monoelectrophilic fluorination of β-ketosulfides and (ii) a successful synthesis of α-fluoro-β-ketosulfides via electrophilic fluorination method are unknown.

RESULTS AND DISCUSSION

Optimization Studies. Initially, we performed a fluorination of α-sulfonyl-β-diketone (1a, 1 equiv) using NFSI (N-fluorobenzenesulfonimide, 1.1 equiv) as a fluorinating reagent and K2CO3 (1.2 equiv) as a base in CH3CN (2 mL). The initial reaction furnished a mixture of fluorinated product 2a and the corresponding deacylated product 3a in 54 and 43% yields, respectively (determined by 1H NMR, Table 1, entry 1). Extending the reaction time to 1 h led to the formation of 2a and 3a in 44 and 56% yields, respectively (entry 2).

Further extension to 2 h led to the formation of a mixture of 2a and 3a in 10 and 90% yields, respectively (entry 3). On purification, we were able to isolate exclusively deacylated product 3a in 96% isolated yield (entry 3), indicating that the...
fluorinated product 2a underwent deacylation under the chromatographic conditions (see the Supporting Information, SI3 and 4). Further, reaction of 1a using solvents such as THF and acetone resulted in the formation of a mixture of 2a and 3a (entries 4–6). The reaction of 1a with NFSI in EtOAc (1 h) furnished the products 2a and 3a in 22 and 78% yields, respectively (entry 7). Further, when the reaction was carried out in EtOAc for 2 h, it furnished exclusively deacylated product 3a in almost quantitative yield (entry 8). Reactions with solvents such as CH2Cl2 and toluene led to a mixture of 2a and 3a (entries 9 and 10, respectively). Furthermore, the reaction in MeOH formed a complex mixture, whereas the reaction in H2O was not successful (entries 11 and 12). The reaction performed using Na2CO3 gave 2a and 3a in 59 and 23% yields, respectively (entry 13), whereas the reaction using Cs2CO3 proceeded smoothly to furnish only 3a in quantitative yield (entry 14).

**Substrate Scope.** Under the established optimized reaction conditions A (entry 8, Table 1), the scope and limitations of this fluorinative deacylation reaction were explored (Scheme 3). As seen in Scheme 3, a variety of α-benzoxazole-2-sulfenyl acetylactone derivatives bearing alkyl/aryl/halo substitution on benzoxazole ring (1a–1g) and unsubstituted α-benzoxazole-2-sulfonyl acetylactone (1h) underwent smooth electrophilic fluorination followed by deacylation, furnishing products 3a–3h in moderate to excellent yields (96, 92, 80, 93, 69, 44, and 98%, respectively). Further, a facile deacylation was observed even in the case of α-benzoxazole-2-sulfonyl-3,5-heptanediones (1i and 1j), and the expected products 3i and 3j were obtained in good yields (70 and 73%, respectively). Under the optimal conditions, the benzothiazole derivative (1k) furnished the expected product 3k in excellent yield (96%). However, α-benzothiazole-2-sulfonyl 3,5-heptanediones (1l) furnished an inseparable mixture of 2l and 3l in 12 and 77% yields, respectively (based on 1H NMR ratio). The fluorinative deacylation reaction of α-oxazole-2-sulfonyl acetylactone (1m) furnished only 30% of the desired product 3m after column purification. The compound 1n, which has the unsymmetrical diketone moiety, underwent fluorinative deacylation to give the mixture of 2n, 3n, and 3a in a ratio of 40:36:24. The compounds 3n and 3a were isolated in 40 and 35% yields, respectively, whereas

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**Scheme 1. Undesired/Uncontrolled Electrophilic Fluorination**

(i) Electrophilic fluorination by using IF3-pyridine-HF as fluorinating reagent (ref. 4b)

(ii) Electrophilic fluorination by using Selectfluor® as fluorinating reagent (ref. 4c-4d)
compound 2n underwent deacylation on silica gel column. Hence, the increment in the isolated yields of 3n and 3a was observed.

The compound 1o, which preferentially exists in diketone form (due to bulky carbonyl groups) bearing a relatively less acidic proton,7a did not furnish the expected product 3o, and starting material was intact (based on 1H NMR spectrum, Scheme 4). The starting materials 1p and 1q did not furnish the α-alkylthio-β-diketones (Scheme 4).8a Further, when the starting material 1a was allowed to react with NCS/NBS/NIS instead of NFSI, the reaction produced a complex inseparable mixture (Scheme 4).

Optimization for Aryl-Substituted Sulfdes. Under the optimized reaction conditions A, 3-(phenylthio)pentane-2,4-dione (4a) did not undergo complete deacylation and instead furnished a mixture of nondeacylated and deacylated fluorine compounds. Therefore, further optimization study was taken to enhance the deacylation process (entries 1−5, Table 2).

During this optimization study, we found that increasing the concentration of the reaction mixture (0.5 mmol of 4 in 2 mL of CH3CN) in the presence of a strong base (Cs2CO3, 1.2 equiv) resulted in complete deacylation (entry 5, optimized reaction condition B; Table 2).

Substrate Scope. Under the reaction conditions B, α-fluoro-β-ketosulfones are important starting materials in Julia−Kocienski fluoroo-olefination reaction for synthesizing fluoroo-olefins.6b,c,10 Further, the sulfones have great utility in organic synthesis as well as in pharmaceutical chemistry.4b,6b,c,9 The general reaction sequences used for the synthesis of α-fluoro-β-ketosulfones are cumbersome and have multiple problems (eq 1, Scheme 6).6b,c,10a−c Hu et al. reported an...
alternate strategy which avoids the overfluorination (eq 2, Scheme 6). To address these synthetic challenges, we thought that α-fluoro-β-ketosulfides would be suitable substrates for synthesiz-
Table 2. Optimization for Aryl Substituted Sulﬁdes (6a–6i) (Standard Conditions B)

<table>
<thead>
<tr>
<th>entry</th>
<th>4a (mmol)</th>
<th>solvent (mL)</th>
<th>base (equiv)</th>
<th>conversion ratios in crude reaction mixture&lt;sup&gt;b&lt;/sup&gt; 5a:6a</th>
<th>ratios after subjecting to column puriﬁcation&lt;sup&gt;c, d&lt;/sup&gt; 5a:6a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.25</td>
<td>EtOAc (2.0)</td>
<td>K2CO3 (1.2)</td>
<td>68:32</td>
<td>30:70 5a (19%); 6a (60%)</td>
</tr>
<tr>
<td>2</td>
<td>0.5</td>
<td>EtOAc (4.0)</td>
<td>K2CO3 (3.0)</td>
<td>38:62</td>
<td>8:92 5a (6%); 6a (82%)</td>
</tr>
<tr>
<td>3</td>
<td>0.5</td>
<td>EtOAc (2.0)</td>
<td>Cs2CO3 (1.2)</td>
<td>25:75</td>
<td>7:93 5a (5%); 6a (91%)</td>
</tr>
<tr>
<td>4</td>
<td>0.25</td>
<td>CH3CN (2.0)</td>
<td>K2CO3 (1.2)</td>
<td>34:66</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0.5</td>
<td>CH3CN (2.0)</td>
<td>Cs2CO3 (1.2)</td>
<td>3:97</td>
<td>0:100 5a (0%); 6a (88%)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reaction conditions: 4a (1 equiv) and base (x equiv) were prestirred for 2 h; then, NFSI (1.1 equiv) was added, and the reaction mixture was stirred at room temperature for 3 h. <sup>b</sup> 1H NMR ratio of products. <sup>c</sup> 1H NMR ratio of products after silica gel column puriﬁcation. <sup>d</sup> Values in the parentheses are the isolated yield of an inseparable mixture of products 5a and 6a.

Scheme 5. Substrate Scope under the Optimized Reaction Conditions B<sup>a, b</sup>

Scheme 6. Reaction Development for the Synthesis of Fluorosulﬁones
ing α-fluoro-β-ketosulfones (eq 3, Scheme 6). Hence, the compound 6a was chosen as the model substrate for the oxidation, and sulfones 7a, 9a, and 9b were synthesized in good to excellent yields (96, 73, and 68%, respectively Scheme 7) from the starting material 6a under mild reaction conditions using m-CPBA as an oxidant.8b To demonstrate further synthetic utility, both allylation and benzylation of 6a were performed, in which only the products 8a and 8b were obtained from 6a (see the Supporting Information, SI 92 and 96).

**Control Experiments.** To understand the effect of sulfur on deacylation reaction, the compound 10a was fluorinated under optimized reaction conditions B, which furnished only the nondeacylated product 11a in 42% yield (eq 1, Scheme 8, see SI 106 and SI 107). This result clearly indicates the necessity of the sulfur moiety for deacylation of α-fluoro-β-diketones. Earlier, we reported a reaction in which the active methine position of 1a is substituted (allylation and benzylation reactions) to form the nondeacylated products (eq 2, Scheme 8).7a This result clearly suggests the necessity of fluorine moiety for deacylation of α-sulfenyl β-diketones. Hence, these two results clearly indicate that the presence of both sulfur and fluorine at α-position of β-dicarbonyl is essential for facile deacylation. On the basis of these observations, a tentative mechanism has been proposed (Scheme 8). Fluorine being the most electronegative element, its

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**Scheme 7. Synthetic Application**

![Scheme 7](image_url)

**Scheme 8. Establishment of Mechanism**

![Scheme 8](image_url)
substitution at α-position of β-dicarbonyl enhances the electrophilicity of the carbonyl carbons, thereby facilitating a even weak nucleophile to attack carbonyl carbons.\(^{1,4a}\) On the other hand, the vacant d-orbital of sulfur stabilizes the adjacent carbanion\(^{11b,c}\) (Scheme 8), thereby favoring the deacylation.

Therefore, the electronegativity factor as well as carbаниon stabilization operate together, causing the deacylation. Further, the residue that forms after the reaction has been identified as the potassium/cesium salt of benzenesulfonimide, and that of 4a was found to be cesium salt of benzenesulfonimide (compound 13, determined by \(^1\)H NMR in D₂O, Scheme 8). This indicates that the anion of benzenesulfonimide has probably no role in deacylation. Further, in addressing the substrate scope of the present work, the inherent instability of α-sulfinyl-β-dicarbonyl to undergo deacylation limits the substrate scope as synthesizing the anion of benzenesulfonimide has probably no role in deacylation. The starting materials is cumbersome. α-Sulfinyl-β-ketoesters are especially prone to undergo deacylation and decompose during isolation. However, we believe that the significance of the present fluorinative deacylation methodology and the application of α-fluoro β-ketosulfides overcomes the limitation of the substrate scope.

**CONCLUSION**

In conclusion, we developed an unprecedented tandem electrophilic fluorinative deacylation method for synthesizing α-fluoro-β-keto sulfides under mild basic reaction conditions at room temperature. The unexpected deacylation upon fluorination of α-sulfinyl β-dicarbons is the salient feature of this method. The synthetic potential of the methodology has been demonstrated by synthesizing a series of sulfones which can be used for synthesizing fluoro olefins.

**EXPERIMENTAL SECTION**

**General Experimental.** All of the reactions were carried out using commercially available AR grade solvents without further distillation. Unless otherwise noted, starting materials and solvents obtained from commercial suppliers were used without further purification. Reactions were monitored by using precoated silica TLC plates. Column chromatography was performed on silica gel 100–200 mesh. Distilled petroleum ether was used for column chromatography. The starting materials α-sulfinyl β-diketones (1a–1n) were prepared as described in our earlier reports,\(^{3,12}\) and α-sulfinyl-β-diketones (3a–3h) were prepared as described in the literature\(^ 3\) with necessary modifications (see the given procedure and note 1). NMR spectra were recorded at 400 MHz using CDCl₃. For the spectra recorded in CDCl₃, TMS (tetramethylsilane) or residual CHCl₃ served as internal standard for \(^1\)H NMR (0.00 ppm or 7.26), and solvent signal was used as reference signal for \(^1\)C NMR (77.00 ppm). IR spectra were measured using an FT-IR spectrometer. Mass spectra were measured using Q-TOF (ESI-HRMS).

**Experimental Procedures for the Synthesis of Starting Materials.**

**Typical Experimental Procedure for the Synthesis of (E)-3-(Ethylthio)-4-hydroxypent-3-en-2-one (1p).** To a well-stirred, ice cold mixture of ethyl thiol (10 mmol) and α-chloro acetylacetone (10 mmol) was added pyridine slowly (11 mmol) for a period of 1 min. The reaction mixture was stirred vigorously at room temperature for 12 h. Then, diethyl ether (15 mL) was added to the reaction mixture, and crude compound was filtered through sintered funnel, and the filtrate containing crude compound was adsorbed on silica gel (100–200 mesh size) and purified on a silica gel column using EtOAc:petroleum ether (0:100–4:96) as eluent to obtain the expected α-sulfinyl β-diketone 1p.

**Note 1:** When thiols are liquid, no solvent was used in the reaction. When thiols are solid, the reaction was performed in diethyl ether (15 mL); i.e., pyridine was added to the ice cold solution of thiol and α-chloro acetylacetone in diethyl ether.

**Typical Experimental Procedure for the Synthesis of Starting Material 4j.** To a well-stirred, ice cold mixture of thiophenol (10 mmol) and α-chloro methyl acetoacetate (10 mmol) was added pyridine slowly (11 mmol) for a period of 1 min. The reaction mixture was stirred vigorously at room temperature for 12 h. Then, the diethyl ether (15 mL) was added to the reaction mixture; crude compound was filtered through sintered funnel, and the filtrate containing crude compound was adsorbed on silica gel (100–200 mesh size) and purified on a silica gel column using EtOAc:petroleum ether (0:100–4:96) as eluent to obtain the expected product 4j.

**Experimental Procedures for the Synthesis of the Products.**

**General Experimental Procedure for the Synthesis of α-Fluoro β-Ketosulfides (3a–3n).** To a well-stirred solution of α-sulfinyl-β-diketone (1.0, 0.25 mmol) in EtOAc (2 mL) was added anhydrous K₂CO₃ (1.2 equiv). The reaction mixture was stirred at room temperature until it turned into a white turbid heterogeneous reaction mixture (generally 60–90 min). The round-bottom flask was then placed under the ice bath, and NFSI (1.1 equiv) was added slowly to the cold reaction mixture. After 5 min of complete addition of NFSI, the ice bath was removed, and stirring was continued at room temperature for 3 h. Then, the crude compound was filtered through sintered funnel, and the residue was washed with EtOAc (5 mL × 2). The filtrate was adsorbed on silica gel (100–200 mesh size) and purified on silica gel (100–200 mesh size) column by using EtOAc:petroleum ether (0:100–5:95) as the eluent to obtain the expected α-fluoro-β-ketosulfides (3a–3n).

**General Experimental Procedure for the Synthesis of α-Fluoro β-Ketosulfides (6a–6l).** To a well-stirred solution of α-sulfinyl β-diketone (4, 0.5 mmol) in CH₃CN (2.0 mL) was added anhydrous Cs₂CO₃ (1.2 equiv). The reaction mixture was stirred at room temperature until it turned into a white turbid heterogeneous reaction mixture (generally 2 h). The round-bottom flask was then placed under the ice bath, and NFSI (1.1 equiv) was added slowly to the cold reaction mixture. After 5 min of complete addition of NFSI, the ice bath was removed, and stirring was continued at room temperature for 3 h. Then, the crude compound was filtered through sintered funnel, and the residue was washed with EtOAc (5 mL × 2). The filtrate was adsorbed on silica gel (100–200 mesh size) and purified on silica gel (100–200 mesh size) column by using EtOAc:petroleum ether (0:100–5:95) as the eluent to obtain the expected α-fluoro-β-ketosulfides (6a–6l).

Note 2: For optimization studies, the following workup procedure was followed: The crude compound in EtOAc (10 mL) was taken in separating funnel; water (10 mL) was added, and then the mixture was shaken well to form white turbid mixture. To this white turbid mixture was added the brine solution (3–5 mL) to obtain a clear biaery of organic and aqueous mixture. The organic layer was separated, and the aqueous layer was washed with EtOAc (5 mL × 2). The combined organic fraction was dried over anhydrous Na₂SO₄, and \(^1\)H NMR yield was determined by using terephthaldehyde as internal standard.

Note 3: Other than in the reaction medium, we also observed the deacylation process on silica gel column. Under the standard reaction
conditions, in some cases the complete monodeacylation of fluorinated compound did not occur. Therefore, retaining a small amount of nondeacylated compounds, i.e., α,α-fluoro sulfinyl β-diketones, was observed after the workup (found by 1H and 19F NMR). However, such nondeacylated fluorinated compounds (2 or 5) underwent deacylation on silica gel column during purification to give an additional amount of expected product. As we observed, the α,α-fluoro sulfinyl β-diketones containing heteroaryl sulfinyl moiety showed a high propensity to undergo deacylation. In these cases, irrespective of the ratio of deacylated and nondeacylated products obtained from the reaction media, the complete monodeacylated compounds were obtained after silica gel column chromatography. However, α,α-fluoro sulfinyl β-diketones containing aryl sulfinyl moiety showed less propensity to undergo deacylation on the silica gel column.

Note 4: As silica gel also influenced the deacylation process, 100−200 mesh sized silica gel columns with fixed size of 5 × 20 cm² were preferred for purification of all the crude compounds.

Typical Experimental Procedure for the Synthesis of 1-Fluoro-1-(phenylsulfonyl)propan-2-one (7a)⁶⁻⁹c To a well-stirred solution of 1-fluoro-1-(phenylthio)hex-5-en-2-one (0.1 mmol) in CH₂Cl₂ (1 mL) was added mCPBA (55−70%, 4 equiv) at room temperature, and the reaction mixture was stirred at room temperature for 6 h. Then, the saturated aqueous sodium sulfite solution was added to the reaction mixture, and stirring was continued at room temperature for further 2 h. The crude compound was extracted into CH₂Cl₂ (10 mL × 3) and dried over anhydrous Na₂SO₄. The crude compound in CH₂Cl₂ and then adsorbed on silica gel (100−200 mesh size) and purified on silica gel column chromatography by using EtOAc:petroleum ether (2:98−5:95) as eluent to obtain only the nondeacylated product 9a in 68% yield.

Note 7: For synthesis of sulfones, mCPBA was dried under reduced pressure (4−5 h) before being used in the reaction.

Typical Experimental Procedure for the Synthesis of 3-Benzyl-3-fluoropentane-2,4-dione (11a). To a well-stirred solution of 3-benzylpentane-2,4-dione (7a, 0.25 mmol) in CH₂CN (1.5 mL) was added anhydrous Cs₂CO₃ (1.2 equiv). The reaction mixture was stirred at room temperature until it turned into a white turbid heterogeneous reaction mixture (4−5 h). The round-bottom flask was then placed under the ice bath, and NFSI (1.1 equiv) was added slowly to the cold reaction mixture. After 5 min of complete addition of NFSI, the ice bath was removed, and stirring was continued at room temperature for 8 h. Then, the crude compound was filtered through a sintered funnel, and the residue was washed with EtOAc (5 mL × 3). The filtrate was then adsorbed on silica gel (100−200 mesh size) and purified on silica gel (100−200 mesh size) column by using EtOAc:petroleum ether (2:98−5:95) as the eluent to obtain only the nondeacylated product 11a in 42%.

Note 8: The 1H NMR and 19F NMR (single peak) of the crude compound showed only the presence of 11a.

Potassium or Cesium Salt of Benzensulfonamide (13a or 13b). These compounds are the residues obtained by filtration of the crude reaction mixture of the fluorinative deacylation reaction of 1 or 4 under the respective optimized reaction conditions.

Experimental Data for Starting Materials. (E)-3-(Ethylthio)-4-hydroxypent-3-en-2-one (1p).¹ 13 Yellow viscous liquid; yield: 82% (1.7 g); R₅ (Pet ether) 0.2; IR (KBr, cm⁻¹): 1729, 1674, 1587, 1477, 1407, 1255, 1081, 1014; 1H NMR (400 MHz, CDCl₃): δ 179.5, 140.4, 130.4, 124.5, 14.1; ESI-HRMS (m/z): calcd for C₆H₆O₂SNa⁺ (M + Na⁺): 183.0456, found (M + Na⁺): 183.0453.

(E)-4-Hydroxy-3-isopropylpent-3-en-2-one (1q).¹² 13 Yellow liquid; yield: 24% (417 mg); R₅ (5% EtoAc/Pet ether) 0.6; IR (Neat, cm⁻¹): 3494, 3206, 2335, 1628, 1466, 1180, 1128, 1020; 1H NMR (400 MHz, CDCl₃): δ 17.26 (brs, 1H), 7.29–7.25 (m, 2H), 7.13–7.08 (m, 3H), 2.35 (s, 6H); 13C NMR (100 MHz, CDCl₃): δ 197.9, 194.2, 34.9, 24.7, 24.6; ESI-HRMS (m/z): calcd for C₅H₁₁O₂SNa⁺ (M + Na⁺): 197.0612, found (M + Na⁺): 197.0614.

(E)-4-Hydroxy-3-(phenylthio)pent-3-en-2-one (1r).¹³ 13 Yellow liquid; yield: 82% (1.7 g); R₅ (Pet ether) 0.2; IR (Neat, cm⁻¹): 1782, 1477, 1404, 1255, 1081, 1018, 909; 1H NMR (400 MHz, CDCl₃): δ 17.26 (brs, 1H), 7.29–7.25 (m, 2H), 7.13–7.08 (m, 3H), 2.35 (s, 6H); 13C NMR (100 MHz, CDCl₃): δ 198.3, 135.7, 129.2, 125.1, 124.6, 101.8, 24.3, ESI-HRMS (m/z): calcd for C₆H₅O₂SNa⁺ (M + Na⁺): 213.0456, found (M + Na⁺): 231.0459.

(E)-4-Hydroxy-3-(tolylthio)pent-3-en-2-one (1s).⁴ ¹² White solid; yield: 80% (1.78 g); mp: 67–69 °C; R₅ (Pet ether) 0.2; IR (KBr, cm⁻¹): 1573, 1458, 1386, 1255, 1044, 1003, 748; 1H NMR (400 MHz, CDCl₃): δ 6.75–7.10 (m, 2H), 7.06–7.02 (m, 1H), 6.83 (d, J = 6.7 Hz, 1H), 2.38 (s, 3H), 2.30 (s, 6H); 13C NMR (100 MHz, CDCl₃): δ 198.3, 135.6, 134.3, 130.3, 126.7, 124.7, 122.7, 100.7, 24.2, 19.6; ESI-HRMS (m/z): calcd for C₁₂H₁₀O₂SNa⁺ (M + Na⁺): 245.0612, found (M + Na⁺): 245.0612.

(E)-4-Hydroxy-3-(phenylthio)pent-3-en-2-one (1t).¹⁴,¹⁵ Low melting yellow crystalline solid; yield: 82% (1.82 g); R₅ (Pet ether) 0.25; IR (Neat, cm⁻¹): 1729, 1674, 1589, 1492, 1413, 1376, 1252, 1014; 1H NMR (400 MHz, CDCl₃): δ 7.09 (d, J = 7.2 Hz, 2H), 6.99 (dd, J₁ = 7.2 Hz, J₂ = 1.6 Hz, 2H), 2.34 (s, 6H), 2.30 (s, 3H); 13C NMR (100 MHz, CDCl₃): δ 157.9, 145.8, 1386, 1255, 1044, 1003, 748; 1H NMR (400 MHz, CDCl₃): δ 6.75–7.10 (m, 2H), 7.06–7.02 (m, 1H), 6.83 (d, J = 6.7 Hz, 1H), 2.38 (s, 3H), 2.30 (s, 6H); 13C NMR (100 MHz, CDCl₃): δ 198.3, 135.6, 134.3, 130.3, 126.7, 124.7, 122.7, 100.7, 24.2, 19.6; ESI-HRMS (m/z): calcd for C₁₂H₁₀O₂SNa⁺ (M + Na⁺): 245.0612, found (M + Na⁺): 245.0612.

Typical Experimental Procedure for the Synthesis of 3-Fluoro-phenylsulfonyl)butan-2-one (9b). To a well-stirred solution of 1-fluoro-1-(phenylthio)propan-2-one (8b, 0.4 mmol) in CH₂Cl₂ (5 mL) was added mCPBA (55−70%, 4 equiv) at room temperature, and the reaction mixture was stirred at room temperature for 6 h. Then, the saturated aqueous sodium sulfite solution was added to the reaction mixture, and stirring was continued at room temperature for further 2 h. The crude compound was extracted into CH₂Cl₂ (10 mL × 3) and dried over anhydrous Na₂SO₄. The crude compound in CH₂Cl₂ was then adsorbed on silica gel (100−200 mesh size) column chromatography by using EtOAc:petroleum ether (20:80–40:60) as eluent to obtain the α-fluoro-β-ketosulfone 9b in 68% yield.

6.96 (d, \(J\) = 8.8 Hz, 2 H), 3.78 (s, 3 H), 2.36 (s, 6 H); 13C NMR (100 MHz, CDCl3): \(\delta 198.0, 157.4, 147.9, 142.3, 135.9, 125.8, 120.1, 119.4, 108.6, 55.4, 24.2\); ESI-HRMS (m/z): calc for C11H12O3SNa (M + Na): 261.0561, found (M + Na): 261.0562.

(E)-2-(Fluorophenylthio)-4-hydroxy-3-phenyl-3-one (4e). Pale yellow crystalline solid; mp: 54–56 °C; yield: 70% (1.58 g); R\(_f\) (Pet ether) 0.2; IR (KBr cm\(^{-1}\)): 1573, 1460, 1403, 1256, 1113, 1073, 1016, 910; 1H NMR (400 MHz, CDCl3),\(\delta 7.20\) (t, \(J = 8.0\) Hz, 1H), 7.10 (d, \(J = 8.0\) Hz, 1H), 7.04 (s, 1H), 6.96 (d, \(J = 7.6\) Hz, 2H), 2.48 (s, 3H); 13C NMR (100 MHz, CDCl3): \(\delta 198.3, 159.3\) (d, \(J = 249.2\) Hz), 126.82 (d, \(J = 251.8\) Hz, 1H), 121.3 (d, \(J = 188.0\) Hz, 1H), 121.49 (d, \(J = 161.0\) Hz), 127.45 (d, \(J = 5.8\) Hz, 1H), 116.9 (d, \(J = 21.7\) Hz), 97.4, 23.4; ES-MSI-HRMS (m/z): calc for C11H10O2SNa (M + Na): 265.0066, found (M + Na): 265.0066.

(E)-3-(4-Chlorophenylthio)-4-hydroxy-3-phenyl-3-one (4g).\(^{13}\) White solid; yield: 83% (2.0 g); R\(_f\) (Pet ether) 0.25; IR (KBr cm\(^{-1}\)): 1554, 1468, 1388, 1081, 1001, 907; 1H NMR (400 MHz, CDCl3),\(\delta 17.27\) (birs, 1H), 7.47 (d, \(J = 8.8\) Hz, 2H), 7.17 (d, \(J = 8.8\) Hz, 2H), 2.32 (s, 3H); 13C NMR (100 MHz, CDCl3): \(\delta 198.3, 136.4, 131.1, 129.3, 125.9, 101.3, 24.3\); ESI-HRMS (m/z): calc for C11H9ClO2SNa (M + Na): 265.0066, found (M + Na): 265.0065.

(E)-3-(4-Bromophenylthio)-4-hydroxy-3-phenyl-3-one (4h).\(^{13,14}\) White crystalline solid; yield: 87% (2.5 g); R\(_f\) (Pet ether) 0.25; IR (KBr cm\(^{-1}\)): 1548, 1465, 1379, 1244, 1079, 997, 905, 803; 1H NMR (400 MHz, CDCl3),\(\delta 7.37\) (d, \(J = 8.4\) Hz, 2H), 6.96 (dd, \(J = 8.8\) Hz, \(J = 2.0\) Hz, 1H), 2.32 (s, 3H); 13C NMR (100 MHz, CDCl3): \(\delta 198.2, 137.9, 132.1, 126.1, 118.7, 101.1, 24.3\); ES-MSI-HRMS (m/z): calc for C11H9BrO2SNa (M + Na): 280.9561, found (M + Na): 280.9562, (M + 2 + Na): 310.9602.

(E)-4-Hydroxy-3-(naphthalen-1-ylthio)-3-phenyl-3-one (4i).\(^{13}\) Brown liquid; yield: 40% (896 mg); R\(_f\) (EtOAc/Pet ether) 0.55; IR (KBr cm\(^{-1}\)): 1633, 1589, 1441, 1328, 1254, 1070; 1H NMR (400 MHz, CDCl3),\(\delta 13.80\) (birs, 1H), 7.27–7.24 (m, 2H), 7.13–7.09 (m, 3H), 3.76 (s, 3H), 2.34 (s, 3H); 13C NMR (100 MHz, CDCl3): \(\delta 185.2, 173.4, 137.9, 134.2, 128.9, 125.1, 91.5, 52.7, 20.9\); ESI-HRMS (m/z): calc for C11H9NO2SNa (M + Na): 281.0612, found (M + Na): 281.0612.

(E)-4-Hydroxy-3-(phenylthio)-3-phenyl-3-one (4j).\(^{13}\) Colorless liquid; yield: 98% (35 mg); R\(_f\) (EtOAc/hexane) 0.25; IR (KBr cm\(^{-1}\)): 1778, 1735, 1509, 1481, 1452, 1383, 1159; 1H NMR (400 MHz, CDCl3),\(\delta 7.45\) (s, 1H), 7.11 (d, \(J = 8.0\) Hz, 1H), 6.78 (d, \(J = 259.4\) Hz, 1H), 2.49 (d, \(J = 259.4\) Hz, 3H), 2.32 (s, 3H); 13C NMR (100 MHz, CDCl3),\(\delta 198.9\) (d, \(J = 259.4\) Hz); 1H NMR (400 MHz, CDCl3),\(\delta 198.9\) (d, \(J = 259.4\) Hz); 1H NMR (400 MHz, CDCl3),\(\delta 198.9\) (d, \(J = 259.4\) Hz); 1H NMR (400 MHz, CDCl3),\(\delta 198.9\) (d, \(J = 259.4\) Hz).
C10H8NO2FSNa (M + Na): 248.0157, found (M + Na): 248.0157.

(s, 3H), 1.18 (t, J = 7.2 Hz, 3H). 3C NMR (100 MHz, CDCl3): δ 198.6 (d, J = 169.2 Hz, 1), 163.5, 153.7, 136.8, 125.8, 124.0, 121.2, 97.2 (d, J = 237.8 Hz), 76.3; 13C NMR (377 MHz, CDCl3): δ 163.6; calculated for C7H8NO,FSCN (M + Na): 263.9924, found (M + Na): 263.9920.

1-(5-Chlorobenzo[d]thiazol-2-ylthio)-1-fluorobutan-2-one (3J). Colorless liquid: yield: 75% (30 mg). Rf (5% EtOAc/hexane) 0.3; IR (Neat, cm\(^{-1}\)): 1735, 1647, 1437, 1307, 1107, 1045; 1H NMR (400 MHz, CDCl3): δ 7.92 (d, J = 8.0 Hz, 1H), 7.24 (d, J = 8.0 Hz, 1H); 1.84 (d, J = 7.2 Hz, 3H). 13C NMR (100 MHz, CDCl3): δ 198.6 (d, J = 170.0 Hz, 1), 163.5, 153.9, 147.8, 133.1, 131.5, 125.5, 124.0, 121.2, 97.2 (d, J = 237.8 Hz), 76.2; 13C NMR (377 MHz, CDCl3): δ 163.7; calculated for C7H8NO,FSCN (M + Na): 263.9924, found (M + Na): 263.9920.

Mixtures of 4-(Benzo[d]thiazol-2-ylthio)-4-fluorothiophene-3,5-dione (2l) and 1-(Benzo[d]thiazol-2-ylthio)-1-fluorobutan-2-one (3K). Colorless liquid; yield: 98% (50 mg). Rf (5% EtOAc/hexane) 0.2; IR (Neat, cm\(^{-1}\)): 1738, 1647, 1437, 1307, 1107, 1045; 1H NMR (400 MHz, CDCl3): δ 7.92 (d, J = 8.0 Hz, 1H), 7.24 (d, J = 8.0 Hz, 1H); 1.82 (d, J = 7.2 Hz, 3H). 13C NMR (100 MHz, CDCl3): δ 198.6 (d, J = 170.0 Hz, 1), 163.5, 153.9, 147.8, 133.1, 131.5, 125.5, 124.0, 121.2, 97.2 (d, J = 237.8 Hz), 76.2; 13C NMR (377 MHz, CDCl3): δ 163.7; calculated for C7H8NO,FSCN (M + Na): 263.9924, found (M + Na): 263.9920.

1-(5-Chlorobenzo[d]thiazol-2-ylthio)-1-fluorobutan-2-one (3K). Colorless liquid; yield: 98% (50 mg). Rf (5% EtOAc/hexane) 0.2; IR (Neat, cm\(^{-1}\)): 1738, 1647, 1437, 1307, 1107, 1045; 1H NMR (400 MHz, CDCl3): δ 7.92 (d, J = 8.0 Hz, 1H), 7.24 (d, J = 8.0 Hz, 1H); 1.82 (d, J = 7.2 Hz, 3H). 13C NMR (100 MHz, CDCl3): δ 198.6 (d, J = 170.0 Hz, 1), 163.5, 153.9, 147.8, 133.1, 131.5, 125.5, 124.0, 121.2, 97.2 (d, J = 237.8 Hz), 76.2; 13C NMR (377 MHz, CDCl3): δ 163.7; calculated for C7H8NO,FSCN (M + Na): 263.9924, found (M + Na): 263.9920.

1-(5-Chlorobenzo[d]thiazol-2-ylthio)-1-fluorobutan-2-one (3M). Colorless liquid; yield: 30% (14 mg). Rf (5% EtOAc/hexane) 0.1; IR (Neat, cm\(^{-1}\)): 1642, 1499, 1365, 1284, 1156, 1019, 1H NMR (400 MHz, CDCl3): δ 7.74 (d, J = 8.0 Hz, 1H), 7.19–7.44 (m, 4H), 7.00 (t, J = 7.2 Hz, 3H). 13C NMR (100 MHz, CDCl3): δ 202.1 (d, J = 24.0 Hz), 159.7, 152.6, 156.1, 126.5, 125.3, 122.4, 121.2, 97.2 (d, J = 237.8 Hz), 73.2, 73.0; 13C NMR (377 MHz, CDCl3): δ 163.6; calculated for C7H8NO,FSCN (M + Na): 263.9924, found (M + Na): 278.0086; calculated for C7H8NO,FSCN (M + Na): 278.0086.

1-(Fluorobenzoyl)[(o-tolyl)]-1-fluorobutan-2-one (6d). Pale yellow liquid; yield: 78% (85 mg). Rf (5% EtOAc/hexane) 0.25; IR (Neat, cm\(^{-1}\)): 1734, 1570, 1462, 1404, 1359, 1233, 1118, 1041; 1H NMR (400 MHz, CDCl3): δ 7.54–7.53 (m, 1H), 7.42 (d, J = 7.6 Hz, 1H), 7.37–7.36 (m, 1H), 7.30 (d, J = 8.0 Hz, 1H), 6.02 (d, J = 7.6 Hz, 1H), 2.18 (d, J = 7.6 Hz, 1H); 13C NMR (100 MHz, CDCl3): δ 198.82 (d, J = 260.0 Hz), 134.9, 133.215 (d, J = 1.0 Hz), 131.7, 131.3, 130.4, 129.6, 99.21 (d, J = 250.0 Hz), 26.1; 13C NMR (377 MHz, CDCl3): δ 161.8; calculated for C7H8NO,FSCN (M + Na): 225.0162, found (M + Na): 225.0162.

1-(Fluorobenzoyl)[(o-tolyl)]-1-fluorobutan-2-one (6d). Pale yellow liquid; yield: 98% (96 mg). Rf (5% EtOAc/hexane) 0.8; IR (Neat, cm\(^{-1}\)): 1734, 1570, 1462, 1404, 1359, 1233, 1118, 1041; 1H NMR (400 MHz, CDCl3): δ 7.54–7.53 (m, 1H), 7.42 (d, J = 7.6 Hz, 1H), 7.37–7.36 (m, 1H), 7.30 (d, J = 8.0 Hz, 1H), 6.02 (d, J = 7.6 Hz, 1H), 2.18 (d, J = 7.6 Hz, 1H); 13C NMR (100 MHz, CDCl3): δ 198.82 (d, J = 260.0 Hz), 134.9, 133.215 (d, J = 1.0 Hz), 131.7, 131.3, 130.4, 129.6, 99.21 (d, J = 250.0 Hz), 26.1; 13C NMR (377 MHz, CDCl3): δ 161.8; calculated for C7H8NO,FSCN (M + Na): 225.0162, found (M + Na): 225.0162.
1-(4-Bromophenylthio)-1-fluoropropan-2-one (6h). Colorless liquid; yield: 82% (96 mg); Rf (5% EtOAc/hexane) 0.4; IR (Neat, cm−1): 1727, 1556, 1499, 1420, 1357, 1223, 1040, 952; 1H NMR (400 MHz, CDCl3): δ 8.08 (s, 1 H), 7.84–7.80 (m, 3 H), 7.57 (dd, J = 7.2 Hz, 2 H, J3 = 1.2 Hz, H1), 7.54–7.50 (m, 2 H), 6.66 (d, J = 19.0 Hz, CH–F = 52 Hz, H1), 7.25 (d, J = 19.0 Hz, CH–F = 2.8 Hz, 3 H); 13C NMR (100 MHz, CDCl3): δ 199.56 (d, J = 20.0 Hz, C); yield: 94% (104 mg) IR (Neat, cm−1): 1739, 1448, 1335, 1214, 1153, 1076; 1H NMR (400 MHz, CDCl3): δ 7.90 (d, J = 8.0 Hz, 2 H), 7.73 (t, J = 7.4 Hz, 1 H, J3 = 7.4 Hz, H1), 7.59 (t, J = 7.8 Hz, 2 H), 5.50 (d, J = 19.0 Hz, CH–F = 48 Hz, CH3), 2.32 (d, J = 19.0 Hz, CH–F = 4.0 Hz, 3 H); 13C NMR (100 MHz, CDCl3): δ 195.51 (d, J = 21.0 Hz, C), 133.5, 134.7, 129.50, 129.47, 101.26 (d, J = 233.0 Hz, C), 27.42; 19F NMR (377 MHz, CDCl3): δ −158.5; ESIMS (m/z): for C16H15OFSNa (M + Na): 257.0412, found (M + Na): 257.0414.

1-Fluoro-1-(naphthalen-1-ylthio)propan-2-one (6i). Colorless liquid; yield: 82% (96 mg); Rf (3% EtOAc/hexane) 0.4; IR (Neat, cm−1): 1737, 1586, 1499, 1420, 1357, 1223, 1040, 952; 1H NMR (400 MHz, CDCl3): δ 8.08 (s, 1 H), 7.84–7.80 (m, 3 H), 7.57 (dd, J = 7.2 Hz, 2 H, J3 = 1.2 Hz, H1), 7.54–7.50 (m, 2 H), 6.66 (d, J = 19.0 Hz, CH–F = 52 Hz, H1), 7.25 (d, J = 19.0 Hz, CH–F = 2.8 Hz, 3 H); 13C NMR (100 MHz, CDCl3): δ 199.56 (d, J = 20.0 Hz, C); yield: 94% (104 mg) IR (Neat, cm−1): 1739, 1448, 1335, 1214, 1153, 1076; 1H NMR (400 MHz, CDCl3): δ 7.90 (d, J = 8.0 Hz, 2 H), 7.73 (t, J = 7.4 Hz, 1 H, J3 = 7.4 Hz, H1), 7.59 (t, J = 7.8 Hz, 2 H), 5.50 (d, J = 19.0 Hz, CH–F = 48 Hz, CH3), 2.32 (d, J = 19.0 Hz, CH–F = 4.0 Hz, 3 H); 13C NMR (100 MHz, CDCl3): δ 195.51 (d, J = 21.0 Hz, C), 133.5, 134.7, 129.50, 129.47, 101.26 (d, J = 233.0 Hz, C), 27.42; 19F NMR (377 MHz, CDCl3): δ −158.5; ESIMS (m/z): for C16H15OFSNa (M + Na): 257.0412, found (M + Na): 257.0414.

Cesium Salt of Bis(phenylsulfonyl)amide (13b). White solid; mp: 208–210°C; yield: 99% (106 mg); 1H NMR (400 MHz, D2O): δ 231.0 (m, 2 H), 228.0; 19F NMR (377 MHz, CDCl3): δ −28.0; 19F NMR (377 MHz, CDCl3): δ −28.0; 19F NMR (377 MHz, CDCl3): δ −28.0; 19F NMR (377 MHz, CDCl3): δ −28.0; 19F NMR (377 MHz, CDCl3): δ −28.0; 19F NMR (377 MHz, CDCl3): δ −28.0; 19F NMR (377 MHz, CDCl3): δ −28.0; 19F NMR (377 MHz, CDCl3): δ −28.0; 19F NMR (377 MHz, CDCl3): δ −28.0. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.7b01547.
REFERENCES


(8) (a) The products 3p and 3q seem to be low boiling liquids such as starting materials; hence, the isolation was not successful for small scale synthesis... (b) While m-CPBA is a widely used reagent for the oxidation of sulides, our attempts to oxidize the α-fluoro-β-ketosulones 3a or 3k were not successful using m-CPBA as the oxidant. However, the methodology for oxidation of the α-fluoro-β-ketosulides containing heteroaryl moiety is already disclosed with various other oxidizing agents (ref 6b and 6c).


