The CF$_3$-DAST-induced deacylative trifluoromethylthiolation of cyclic 1,3-diketones/lactams/lactones and its extension to deacylative pentafluorophenylthiolations

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1. Experimental Section

1.1 General Methods

All reactions were performed in oven-dried glassware under a positive pressure of nitrogen. Solvents were transferred via syringe and were introduced into the reaction vessels though a rubber septum. All reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica-gel (60-F254). The TLC plates were visualized with UV light and 7% phosphomolybdic acid or KMnO₄ in water/heat. Column chromatography was carried out on a column packed with silica-gel 60N spherical neutral size 63-210 μm. The ¹H-NMR (300 MHz), ¹⁹F-NMR (282 MHz), ¹³C-NMR (125.7 MHz) spectra for solution in CDCl₃ were recorded on a Bruker Avance 500, Varian Mercury 300. Chemical shifts (δ) are expressed in ppm downfield from internal TMS (δ = 0.00). The C₆F₆ [δ = −162.2 (CDCl₃)] was used as internal standard for ¹⁹F NMR. High resolution mass spectrometry was recorded on a Waters Synapt G2 HDMS (ESI-MS, EI-MS). Infrared spectra were recorded on a JASCO FT/IR-4100 spectrometer. Melting point were recorded on a BUCHI M-565. All solvents were dried and distilled before use.

DAST [(Diethylamino)sulfur Trifluoride] (Purity: >90.0%) was purchased from Tokyo Chemical Industry Co., Ltd., Japan.
2. Optimization of trifluoromethylthiolation reaction condition;

2.1 Table S1. Optimization of reaction condition.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Temp. (°C)</th>
<th>CF\textsubscript{3}-DAST (equiv.)</th>
<th>CF\textsubscript{3}-DAST (M)</th>
<th>Yield (%)\textsuperscript{b}</th>
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<tr>
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<tr>
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[a] The reaction of 1a with CF$_3$-DAST was carried out in different solvents at different temperatures. [b] The yield was determined by $^{19}$F NMR spectroscopy with an internal standard, C$_6$H$_5$CF$_3$. [c] 1.2 equivalent of base was used for preparation of reagent. [d] 1.2 equivalent of TMSCF$_3$ was used for preparation of reagent.

2.2 Table S2. Optimization of reaction condition.$^a$

<table>
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<tr>
<th>Entry</th>
<th>Solvent</th>
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<th>Yield (%)$^b$</th>
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[a] The reaction of 3a with CF₃-DAST was carried out in different solvents at different temperatures. [b] The yield was determined by ¹⁹F NMR spectroscopy with an internal standard, C₆H₅CF₃. [c] MS 4Å was added to the reaction system. [d] MgSO₄ was added to the reaction system.

3. Typical procedure preparation of Rf-DAST reagents

A flame-dried vessel was charged with diisopropylethylamine (1.2 equivalent) and anhydrous dichloromethane (2 mL, 0.5 M), cooled to −20 °C under the nitrogen atmosphere. The diethylamino sulfur trifluoride (DAST) (1.0 mmol, 1.0 equivalent) was added and stirred for 15 min at the same temperature, then the trimethylsilyl trifluoromethane (TMSCF₃) or trimethyl(perfluorophenyl)silane (TMSC₆F₅) (1.2 mmol, 1.2 equivalent) was added slowly by syringe. The mixture was stirred for two hours under the same reaction temperature. After two hours, the solution was directly used for next step without purification.

A flame-dried vessel was charged with 1,3-diketones 1a—1n (1.0 equivalent) and anhydrous CH₂Cl₂ (0.1 M) under nitrogen gas atmosphere. The solution was cooled to –40 °C and the 0.5 M solution of CF₃-DAST in CH₂Cl₂ (2.0 equivalents taken from the solution above mentioned) was added slowly by syringe. Then the reaction mixture was stirred at –40 °C for overnight, quenched by addition of water, extracted with ethyl acetate, dried over with Na₂SO₄ and then concentrated. The crude product was purified by flash column chromatography to provide the title compound 2a—2n.

4.1 2-((trifluoromethyl)thio)-2,3-dihydro-1H-inden-1-one (2a);

Following the general procedure, using substrate 1a—1d (0.1 mmol, 1.0 equivalent) and CF₃-DAST (2.0 equivalent, 0.5 M solution in CH₂Cl₂) in CH₂Cl₂ (1.0 mL), the reaction mixture was stirred at –40 °C for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 20:1) to provide the title compound 2a as a yellow oil in 44%—72% yield. ¹H NMR (CDCl₃, 300 MHz) δ: 7.82 (d, 1H, J = 7.5 Hz), 7.68 (t, 1H, J = 7.0 Hz), 7.41—7.49 (m, 2H), 4.24 (dd, 1H, J = 8.1 Hz, J = 4.5 Hz), 3.79 (dd, 1H, J = 17.7 Hz, J = 8.1 Hz), 3.37 (dd, 1H, J = 17.7 Hz, J = 4.5 Hz) ppm. ¹⁹F NMR (282 MHz, CDCl₃) δ: -39.99 (s, 3F) ppm. ¹³C NMR (CDCl₃, 125.7 MHz) δ: 199.36, 151.96, 136.19, 134.71, 130.76 (q, J = 307.5 Hz), 128.44, 126.54, 124.93, 47.59, 36.49 ppm. IR (neat): 3079, 2927, 1725, 1606, 1465, 1276, 1112, 748 cm⁻¹. HRMS (ESI): Calcd. for C₁₀H₇F₃NaOS [M+Na]⁺: 255.0067. Found: 255.0062. Spectroscopic data were in agreement with the literature.¹¹

4.2 6-methyl-2-((trifluoromethyl)thio)-2,3-dihydro-1H-inden-1-one (2e);
Following the general procedure, using 2-acetyl-6-methyl-2,3-dihydro-1H-inden-1-one 1e (0.1 mmol, 1.0 equivalent) and CF₃-DAST (2.0 equivalent, 0.5 M solution in CH₂Cl₂) in CH₂Cl₂ (1.0 mL), the reaction mixture was stirred at −40 °C for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 20:1) to provide the title compound 2e as a white solid in 73% yield. Mp: 51.7—52.9 °C. ¹H NMR (CDCl₃, 300 MHz) δ: 7.62 (s, 1H), 7.50 (d, 1H, J = 7.8 Hz), 7.37 (d, 1H, J = 7.8 Hz), 4.23 (dd, 1H, J = 8.1 Hz, J = 4.5 Hz) 3.74 (dd, 1H, J = 17.4 Hz, J = 8.1 Hz), 3.32 (dd, 1H, J = 17.4 Hz, J = 4.2 Hz), 2.42 (s, 3H) ppm. ¹⁹F NMR (282 MHz, CDCl₃) δ: -40.00 (s, 3F) ppm. ¹³C NMR (CDCl₃, 125.7 MHz) δ: 199.42, 149.25, 138.55, 137.46, 134.81, 130.78 (q, J = 306.7 Hz), 126.18, 124.75, 47.90, 36.16, 21.24 ppm. IR (KBr): 3419, 2925, 1722, 1614, 1488, 1282, 1116, 755 cm⁻¹. HRMS (ESI): Calcd. for C₁₁H₀F₃NaOS [M+Na]⁺: 269.0224. Found: 269.0224.

4.3 6-bromo-2-((trifluoromethyl)thio)-2,3-dihydro-1H-inden-1-one (2f);

Following the general procedure, using 2-acetyl-6-bromo-2,3-dihydro-1H-inden-1-one 1f (0.1 mmol, 1.0 equivalent) and CF₃-DAST (2.0 equivalent, 0.5 M solution in CH₂Cl₂) in CH₂Cl₂ (1.0 mL), the reaction mixture was stirred at −40 °C for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 25:1) to provide the title compound 2f as a yellow oil in 41% yield. ¹H NMR (CDCl₃, 300 MHz) δ: 7.94 (d, 1H, J = 1.0 Hz), 7.77 (dd, 1H, J = 8.1 Hz, J = 1.8 Hz), 7.37 (d, 1H, J = 8.1 Hz), 4.25
(dd, 1H, $J = 8.1$ Hz, $J = 4.5$ Hz), 3.74 (dd, 1H, $J = 17.7$ Hz, $J = 8.1$ Hz), 3.30 (dd, 1H, $J = 17.7$ Hz, $J = 4.5$ Hz) ppm. $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$: -39.91 (s, 3F) ppm. $^{13}$C NMR (CDCl$_3$, 125.7 MHz) $\delta$: 197.7, 150.28, 138.94, 136.43, 130.58 (q, $J = 306.7$ Hz), 128.06, 127.80, 122.67, 47.65, 36.05 ppm. IR (neat): 3405, 3068, 2927, 1708, 1592, 1430, 1255, 1112, 707 cm$^{-1}$. HRMS (ESI): Calcd. for C$_{10}$H$_6$BrF$_3$NaOS [M+Na]$^+$: 332.9173. Found: 332.9178.

4.4 5-fluoro-2-((trifluoromethyl)thio)-2,3-dihydro-1H-inden-1-one (2g);

Following the general procedure, using 2-acetyl-5-fluoro-2,3-dihydro-1H-inden-1-one 1g (0.1 mmol, 1.0 equivalent) and CF$_3$-DAST (2.0 equivalent, 0.5 M solution in CH$_2$Cl$_2$) in CH$_2$Cl$_2$ (1.0 mL), the reaction mixture was stirred at $-40$ °C for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 20:1) to provide the title compound 2g as a yellow oil in 82% yield. $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$: 7.85—7.81 (m, 1H), 7.17—7.11 (m, 2H), 4.25 (dd, 1H, $J = 8.1$ Hz, $J = 4.5$ Hz), 3.78 (dd, 1H, $J = 18.0$ Hz, $J = 8.1$ Hz), 3.36 (dd, 1H, $J = 18.0$ Hz, $J = 3.9$ Hz) ppm. $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$: -39.96 (s, 3F), -100.33 (s, 1F) ppm. $^{13}$C NMR (CDCl$_3$, 125.7 MHz) $\delta$: 197.40, 168.04 (d, $J = 258.9$ Hz), 154.76 (d, $J = 10.1$ Hz), 131.12, 130.65 (q, $J = 306.7$ Hz) 127.40 (d, $J = 11.3$ Hz), 116.92 (d, $J = 23.9$ Hz), 113.32 (d, $J = 22.6$ Hz), 47.61, 36.35 ppm. IR (neat): 3062, 2929, 1724, 1616, 1592, 1257, 1112, 836 cm$^{-1}$. HRMS (ESI): Calcd. for C$_{10}$H$_6$F$_4$NaOS [M+Na]$^+$: 272.9973. Found: 272.9980.

4.5 5-chloro-2-((trifluoromethyl)thio)-2,3-dihydro-1H-inden-1-one (2h);
Following the general procedure, using 2-acetyl-5-chloro-2,3-dihydro-1H-inden-1-one 1h (0.1 mmol, 1.0 equivalent) and CF₃-DAST (2.0 equivalent, 0.5 M solution in CH₂Cl₂) in CH₂Cl₂ (1.0 mL), the reaction mixture was stirred at −40 °C for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 20:1) to provide the title compound 2h as a white solid in 51% yield. Mp: 69.7—70.3 °C. ¹H NMR (CDCl₃, 300 MHz) δ: 7.75 (d, 1H, J = 8.1 Hz), 7.48 (s, 1H), 7.42 (d, 1H, J = 8.7 Hz), 4.24 (dd, 1H, J = 8.1 Hz, J = 4.8 Hz), 3.77 (dd, 1H, J = 17.7 Hz, J = 8.1 Hz), 3.35 (dd, 1H, J = 18.0 Hz, J = 4.5 Hz) ppm. ¹⁹F NMR (282 MHz, CDCl₃) δ: -39.92 (s, 3F) ppm. ¹³C NMR (CDCl₃, 125.7 MHz) δ: 197.88, 153.19, 142.93, 133.13, 130.61 (q, J = 307.9 Hz), 129.33, 126.75, 126.02, 47.50, 36.12 ppm. IR (KBr): 3413, 2925, 1714, 1600, 1428, 1319, 1118, 781 cm⁻¹. HRMS (ESI): Calcd. for C₁₀H₆ClF₃NaOS [M+Na]⁺: 288.9678. Found: 288.9676.

4.6 5-bromo-2-((trifluoromethyl)thio)-2,3-dihydro-1H-inden-1-one (2i);

Following the general procedure, using 2-acetyl-5-bromo-2,3-dihydro-1H-inden-1-one 1i (0.1 mmol, 1.0 equivalent) and CF₃-DAST (2.0 equivalent, 0.5 M solution in CH₂Cl₂) in CH₂Cl₂ (1.0 mL), the reaction mixture was stirred at −40 °C for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 20:1) to provide
the title compound 2i as a yellow solid in 52% yield. Mp: 81.6—83.3 °C. $^1$H NMR (CDCl$_3$, 300 MHz) δ: 7.94 (s, 1H), 7.76 (d, 1H, $J = 8.1$ Hz), 7.37 (d, 1H, $J = 8.1$ Hz), 4.24 (dd, 1H, $J = 8.1$ Hz, $J = 4.5$ Hz), 3.74 (dd, 1H, $J = 17.7$ Hz, $J = 8.1$ Hz), 3.30 (dd, 1H, $J = 17.7$ Hz, $J = 4.5$ Hz) ppm. $^{19}$F NMR (282 MHz, CDCl$_3$) δ: -39.91 (s, 3F) ppm. $^{13}$C NMR (CDCl$_3$, 125.7 MHz) δ 197.85, 150.15, 138.82, 136.31, 130.45 (q, $J = 307.9$ Hz), 127.93, 127.67, 122.54, 47.52, 35.92 ppm. IR (KBr): 3401, 3068, 2923, 1708, 1592, 1432, 1255, 1112, 707 cm$^{-1}$. HRMS (ESI): Calcd. for C$_{10}$H$_6$BrF$_3$NaOS [M+Na]$^+$: 332.9173. Found: 332.9176.

4.7 5,6-dimethoxy-2-((trifluoromethyl)thio)-2,3-dihydro-1H-inden-1-one (2j);

Following the general procedure, using 2-acetyl-5,6-dimethoxy-2,3-dihydro-1H-inden-1-one 1j (0.1 mmol, 1.0 equivalent) and CF$_3$-DAST (2.0 equivalent, 0.5 M solution in CH$_2$Cl$_2$) in CH$_2$Cl$_2$ (1.0 mL), the reaction mixture was stirred at −40 °C for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 10:1) to provide the title compound 2j as a white solid in 71% yield. Mp: 106.2—107.0 °C. $^1$H NMR (CDCl$_3$, 300 MHz) δ: 7.20 (s, 1H), 6.87 (s, 1H), 4.22 (dd, 1H, $J = 7.5$ Hz, $J = 3.9$ Hz), 3.98 (s, 3H), 3.91 (s, 3H), 3.69 (dd, 1H, $J = 17.4$ Hz, $J = 7.5$ Hz), 3.28 (dd, 1H, $J = 17.4$ Hz, $J = 3.6$ Hz) ppm. $^{19}$F NMR (282 MHz, CDCl$_3$) δ: -40.04 (s, 3F) ppm. $^{13}$C NMR (CDCl$_3$, 125.7 MHz) δ: 197.68, 156.78, 150.18, 147.55, 130.84 (q, $J = 307.9$ Hz), 127.50, 107.19, 104.98, 56.54, 56.32, 47.78, 36.38 ppm. IR (KBr): 3409, 3075, 2942, 2910, 1714, 1596, 1467, 1251, 1120, 750 cm$^{-1}$. HRMS (ESI): Calcd. for C$_{12}$H$_{11}$F$_3$NaO$_3$S [M+Na]$^+$:
Following the general procedure, using 2-acetylcyclopentanone 1k (0.5 mmol, 1.0 equivalent) and CF₃-DAST (2.0 equivalent, 0.5 M solution in CH₂Cl₂) in CH₂Cl₂ (5.0 mL), the reaction mixture was stirred at −40 °C for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 50:1) to provide the title compound 2k as a colorless oil in 21% yield. ¹H NMR (CDCl₃, 300 MHz) δ: 3.14—3.07 (m, 1H), 2.54 (s, 3H), 2.44—2.40 (m, 1H), 2.18—2.09 (m, 1H), 2.04—1.91 (m, 1H) ppm. ¹⁹F NMR (282 MHz, CDCl₃) δ: -37.76 (s, 3F), -42.63 (trace) ppm. ¹³C NMR (CDCl₃, 125.7 MHz) δ: 208.36, 198.65, 129.77 (q, J = 307.9 Hz), 70.89, 37.07, 34.25, 25.71, 20.26 ppm. IR (neat): 2958, 2931, 1747, 1718, 1263, 1114, 736 cm⁻¹. HRMS (EI): Calcd. for C₆H₇F₃OS [M]⁺: 184.0170. Found: 184.0170.

Following the general procedure, using 2-acetyl-3,4-dihydonaphthalen-1(2H)-one 1l (0.2 mmol, 1.0 equivalent) and CF₃-DAST (2.0 equivalent, 0.5 M solution in CH₂Cl₂) in CH₂Cl₂ (2.0 mL), the reaction mixture was stirred at −40 °C for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 30:1) to provide the title compound 2l as a yellow oil in 15% yield. ¹H NMR (CDCl₃, 300 MHz) δ: 8.04
(d, 1H, J = 7.8 Hz), 7.52 (t, 1H, J = 7.5 Hz), 7.37—7.27 (m, 2H), 4.36 (dd, 1H, J = 10.8 Hz, J = 4.2 Hz), 3.15—3.11 (m, 2H), 2.74—2.65 (m, 1H), 2.46—2.33 (m, 1H) ppm. ^19^F NMR (282 MHz, CDCl$_3$) δ: -39.21 (s, 3F), -41.98 (trace) ppm. ^13^C NMR (CDCl$_3$, 125.7 MHz) δ: 192.25, 142.98, 134.34, 131.10, 130.76 (q, J = 306.7 Hz), 128.78, 128.21, 127.22, 51.77, 31.24, 28.21 ppm. IR (neat): 3062, 2931, 2861, 1687, 1600, 1455, 1288, 1141, 746 cm$^{-1}$. HRMS (ESI): Calcd. for C$_{11}$H$_9$F$_3$NaOS [M+Na]$^+$: 269.0224. Found: 269.0219. Spectroscopic data were in agreement with the literature.$^{[2]}$

4.10 6-((trifluoromethyl)thio)-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one (2m);

Following the general procedure, using 6-acetyl-6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-one 1m (0.2 mmol, 1.0 equivalent) and CF$_3$-DAST (2.0 equivalent, 0.5 M solution in CH$_2$Cl$_2$) in CH$_2$Cl$_2$ (2.0 mL), the reaction mixture was stirred at −40 °C for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 30:1) to provide the title compound 2m as a yellow oil in 13% yield. $^1$H NMR (CDCl$_3$, 300 MHz) δ: 7.71 (d, 1H, J = 7.8 Hz), 7.45 (t, 1H, J = 7.5 Hz), 7.35—7.24 (m, 2H), 4.50 (dd, 1H, J = 10.2 Hz, J = 6.0 Hz), 3.06—3.02 (m, 2H), 2.49—2.39 (m, 1H), 2.24—2.04 (m, 2H), 1.83—1.77 (m, 1H) ppm. $^{19}$F NMR (282 MHz, CDCl$_3$) δ: -40.33 (s, 3F) ppm. $^{13}$C NMR (CDCl$_3$, 125.7 MHz) δ: 199.86, 141.91, 137.46, 132.51, 130.81 (q, J = 306.7 Hz), 130.36, 129.49, 126.98, 53.68, 33.82, 32.25, 25.31 ppm. IR (neat): 2931, 2861, 1735, 1681, 1455, 1263, 1116, 736 cm$^{-1}$. HRMS (EI): Calcd. for C$_{12}$H$_{11}$F$_3$OS [M]$^+$: 260.0483. Found: 260.0486.

4.11 4-phenyl-3-((trifluoromethyl)thio)butan-2-one (2n);
Following the general procedure, using 3-benzylpentane-2,4-dione 1n (0.2mmol, 1.0 equivalent) and CF$_3$-DAST (2.0 equivalent, 0.5 M solution in CH$_2$Cl$_2$) in CH$_2$Cl$_2$ (2.0 mL), the reaction mixture was stirred at –40 °C for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 50:1) to provide the title compound 2n as a yellow oil in 12% yield. $^1$H NMR (CDCl$_3$, 300 MHz) δ: 7.34—7.28 (m, 2H), 7.23—7.13 (m, 3H), 4.02 (dd, 1H, $J = 8.4$ Hz, $J = 6.6$ Hz), 3.25 (dd, 1H, $J = 14.1$ Hz, $J = 9.0$ Hz), 3.07 (dd, 1H, $J = 14.1$ Hz, $J = 6.6$ Hz), 2.18 (s, 3H) ppm. $^{19}$F NMR (282 MHz, CDCl$_3$) δ: -40.39 (s, 3F) ppm. MS (ESI): Calcd. for C$_{11}$H$_{11}$F$_3$OS [M-H] $^-$: 247. Found: 247. Spectroscopic data were in agreement with the literature.$^{[3]}$

5. General procedure and product characterization data for Scheme 3.

A flame-dried vessel was charged with β-keto esters 3a—3i (1.0 equivalent) and anhydrous CH$_3$CN (0.1 M) under nitrogen gas atmosphere. The 0.5 M solution of CF$_3$-DAST in CH$_2$Cl$_2$ (2.0 equivalents taken from the solution above mentioned) was added slowly by syringe. Then the reaction mixture was stirred at room temperature for overnight, quenched by addition of water, extracted with ethyl acetate, dried over with Na$_2$SO$_4$ and then concentrated. The crude product was purified by flash column chromatography to provide the title compound 4a—4i.

5.1 tert-butyl 2-oxo-3-((trifluoromethyl)thio)pyrrolidine-1-carboxylate (4a);
Following the general procedure, using substrate 3a—3c (0.1 mmol, 1.0 equivalent) and CF$_3$-DAST (2.0 equivalent, 0.5 M solution in CH$_2$Cl$_2$) in CH$_3$CN (1.0 mL, 0.1 M), the reaction mixture was stirred at room temperature for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 20:1) to provide the title compound 4a as a white solid in 80—84% yield. Mp: 68.5—69.3 °C. $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$: 4.17 (dd, 1H, $J = 10.0$ Hz, $J = 8.4$ Hz), 3.93—3.85 (m, 1H), 3.73—3.64 (m, 1H), 2.67—2.57 (m, 1H), 2.28—2.14 (m, 1H), 1.53 (s, 9H) ppm. $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$: -40.18 (s, 3F) ppm. $^{13}$C NMR (CDCl$_3$, 125.7 MHz) $\delta$: 168.60, 149.79, 130.35 (q, $J = 306.7$ Hz), 84.16, 46.21, 44.41, 28.07, 27.67 ppm. IR (KBr): 2989, 2938, 1774, 1378, 1319, 1120, 846, 779 cm$^{-1}$. HRMS (ESI): Calcd. for C$_{10}$H$_{14}$F$_3$NNaO$_3$S [M+Na]$^+$: 308.0544. Found: 308.0550.

5.2 1-tosyl-3-((trifluoromethyl)thio)pyrrolidin-2-one (4d);

Following the general procedure, using 3-benzoyl-1-tosylpyrrolidin-2-one 3d (0.1 mmol, 1.0 equivalent) and CF$_3$-DAST (2.0 equivalent, 0.5 M solution in CH$_2$Cl$_2$) in CH$_3$CN (1.0 mL, 0.1 M), the reaction mixture was stirred at room temperature for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 10:1) to provide the title compound 4d as a white solid in 61% yield. Mp: 101.6—102.7 °C. $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$: 7.92 (d, 1H, $J = 8.1$ Hz), 7.35 (d, 1H, $J = 8.4$ Hz), 4.07—3.99 (m, 2H), 3.87—3.79 (m, 1H), 2.73—2.62 (m, 1H), 2.45 (s, 3H), 2.31—2.18 (m, 1H) ppm. $^{19}$F
NMR (282 MHz, CDCl$_3$) $\delta$: -40.05 (s, 3F) ppm. $^{13}$C NMR (CDCl$_3$, 125.7 MHz) $\delta$: 168.18, 146.05, 134.34, 130.00 (q, $J = 307.9$ Hz), 130.02, 128.41, 45.17, 28.09, 21.90 ppm. IR (KBr): 2983, 2927, 1743, 1363, 1232, 1122, 811, 661 cm$^{-1}$. HRMS (ESI): Calcd. for C$_{12}$H$_{12}$F$_3$NNaO$_3$S$_2$ [M+Na]$^+$: 362.0108. Found: 362.0105.

5.3 1-benzyl-3-((trifluoromethyl)thio)pyrrolidin-2-one (4e);

Following the general procedure, using 3-benzoyl-1-benzylpyrrolidin-2-one 3e (0.1 mmol, 1.0 equivalent) and CF$_3$-DAST (2.0 equivalent, 0.5 M solution in CH$_2$Cl$_2$) in CH$_3$CN (1.0 mL, 0.1 M), the reaction mixture was stirred at room temperature for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 20:1) to provide the title compound 4e as a yellow oil in 26% yield. $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$: 7.38—7.28 (m, 3H), 7.27—7.22 (m, 2H), 4.54—4.44 (m, 2H), 4.15 (t, 1H, $J = 8.4$ Hz), 3.36—3.22 (m, 2H), 2.67—2.56 (m, 1H), 2.30—2.17 (m, 1H) ppm. $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$: -40.22 (s, 3F) ppm. $^{13}$C NMR (CDCl$_3$, 125.7 MHz) $\delta$: 169.38, 135.60, 130.64 (q, $J = 306.7$ Hz), 129.01, 128.36, 128.12, 47.55, 44.94, 44.65, 28.49 ppm. IR (neat): 3058, 2929, 1695, 1486, 1434, 1282, 1116, 700 cm$^{-1}$. HRMS (ESI): Calcd. for C$_{12}$H$_{12}$F$_3$NNaOS [M+Na]$^+$: 298.0489. Found: 298.0488.

5.4 tert-butyl 2-oxo-3-((trifluoromethyl)thio)piperidine-1-carboxylate (4f);

Following the general procedure, using tert-butyl 3-benzoyl-2-oxopiperidine-1-
Following the general procedure, using tert-butyl 3-benzoyl-2-oxoazepane-1-carboxylate 3g (0.2 mmol, 1.0 equivalent) and CF₃-DAST (2.0 equivalent, 0.5 M solution in CH₂Cl₂) in CH₃CN (2.0 mL, 0.1 M), the reaction mixture was stirred at room temperature for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 20:1) to provide the title compound 4g as a yellow oil in 15% yield. ¹H NMR (CDCl₃, 300 MHz) δ: 4.43 (dd, 1H, J = 10.8 Hz, J = 2.4 Hz), 4.27—4.21 (m, 1H), 3.36—3.29 (m, 1H), 2.37—2.31 (m, 1H), 2.10—1.87 (m, 4H), 1.79—1.66 (m, 1H), 1.52 (s, 9H) ppm. ¹⁹F NMR (282 MHz, CDCl₃) δ: -40.33 (s, 3F) ppm. ¹³C NMR (CDCl₃, 125.7 MHz) δ: 171.23, 152.65, 130.93 (q, J = 306.7 Hz), 84.19, 52.62, 45.95, 33.48, 28.06, 27.94, 27.86 ppm. IR (neat): 2977, 2935, 1768, 1725, 1459, 1257, 1116, 734 cm⁻¹. HRMS (ESI): Calcd. for C₃₁H₂₆F₉NaO₅S: [M+Na]⁺: 622.0703. Found: 622.0703.
C_{12}H_{18}F_{3}NNaO_{3}S [M+Na]^+: 336.0857. Found: 336.0860.

5.6 3-((trifluoromethyl)thio)dihydrofuran-2(3H)-one (4h);

Following the general procedure, using 3-acetyldihydrofuran-2(3H)-one 3h (0.1 mmol, 1.0 equivalent) and CF_{3}-DAST (2.0 equivalent, 0.5 M solution in CH_{2}Cl_{2}) in CH_{3}CN (1.0 mL, 0.1 M), the reaction mixture was stirred at room temperature for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 40:1) to provide the title compound 4h as a yellow oil in 80% yield. \(^1\)H NMR (CDCl_{3}, 300 MHz) \(\delta\): 4.54—4.47 (m, 1H), 4.39—4.31 (m, 1H), 4.21—4.15 (m, 1H), 2.91—2.80 (m, 1H), 2.57—2.44 (m, 1H) ppm. \(^19\)F NMR (282 MHz, CDCl_{3}) \(\delta\): -40.16 (s, 3F) ppm. \(^{13}\)C NMR (CDCl_{3}, 125.7 MHz) \(\delta\): 172.30, 130.03 (q, \(J = 307.9\) Hz), 66.90, 41.31, 32.03 ppm. IR (neat): 2925, 2856, 1781, 1257, 1112, 734 cm\(^{-1}\). HRMS (EI): Calcd. for C_{5}H_{5}F_{3}O_{2}S [M]^+: 185.9962. Found: 185.9972.

5.7 1-tert-butyl 2-methyl 5-oxo-4-((trifluoromethyl)thio)pyrrolidine-1,2-dicarboxylate (4i);

Following the general procedure, using (2R)-1-tert-butyl 2-methyl 4-acetyl-5-oxopyrrolidine-1,2-dicarboxylate 3i (0.1 mmol, 1.0 equivalent) and CF_{3}-DAST (2.0 equivalent, 0.5 M solution in CH_{2}Cl_{2}) in CH_{3}CN (1.0 mL, 0.1 M), the reaction mixture was stirred at room temperature for overnight. The crude product was purified by flash
column chromatography (Hex: AcOEt = 20:1) to provide the title compound 4i as a yellow oil in 77% yield (dr; 3:1). $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$: (major) 4.67 (d, 1H, $J = 9.3$ Hz), 4.29 (dd, 1H, $J = 11.4$ Hz, $J = 8.7$ Hz), 3.82 (s, 3H), 2.70—2.62 (m, 1H), 2.54—2.47 (m, 1H), 1.51 (s, 9H). (minor) 4.62—4.58 (m, 1H), 4.16—4.10 (m, 1H), 3.80 (s, 3H), 3.07—2.84 (m, 1H), 2.30—2.23 (m, 1H), 1.48 (s, 9H) ppm. $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$: (major) -40.00 (s, 3F), (minor) -40.76 (s, 3F) ppm. $^{13}$C NMR (CDCl$_3$, 125.7 MHz) $\delta$: (major) 170.97, 167.90, 148.95, 130.19 (q, $J = 307.9$ Hz), 84.98, 56.97, 53.17, 44.38, 31.52, 27.94, 27.91. (minor) 170.73, 167.83, 148.85, 85.01, 57.27, 53.03, 44.37, 30.98, 27.84, 27.80 ppm. IR (neat): 2981, 2938, 1752, 1720, 1648, 1477, 1461, 1316, 1255, 1116, 912, 734 cm$^{-1}$. HRMS (ESI): Calcd. for C$_{12}$H$_{16}$F$_3$NaN$_2$O$_5$S [M+Na]$^+$: 366.0599. Found: 366.0602.


To a solution of 4i (0.27g, 0.8 mmol) in THF (2 mL) at −78 °C was added dropwise a solution of lithium triethylhydroborate (1M in THF, 0.8 mL, 1.0 equivalent). The reaction mixture was stirred at −78 °C for 2 h and it was quenched with aq. NaHCO$_3$ (1 mL). The resulting mixture was then allowed to warm to 0 °C. A solution of hydrogen peroxide (50% in H$_2$O) (0.3 mL, 3.8 mmol) was added dropwise. The mixture was stirred at room temperature for 30 min and concentrated in vacuo to remove THF. The residue was extracted with EtOAc, and the combined organic layers were dried over MgSO$_4$ and concentrated in vacuo. The residue was purified using flash column chromatography to provide the intermediate 5.
To a cooled solution of the intermediate in DCM (3 mL) at –78 °C was added triethylsilane (0.15 mL, 0.88 mmol) followed by BF₃·OEt₂ (0.1 mL, 0.88 mmol). The reaction mixture was stirred at –78 °C for additional 2 h before it was quenched with aq. NaHCO₃ (2.0 mL). The resulting mixture was allowed to warm to room temperature and extracted with DCM. The combined organic layers were dried over MgSO₄, concentrated in vacuo, and purified using flash column chromatography to provide compound 6 in 38% yield (dr, 3:2).

¹H NMR (CDCl₃, 300 MHz) δ: (major and minor) 4.46—4.27 (m, 1.6H), 4.12—3.82 (m, 2.7H), 3.75—3.65 (m, 6.6H), 3.46—3.36 (m, 1.8H), 2.80—2.71 (m, 1H), 2.43—2.26 (m, 1.4H), 2.09—1.99 (m, 1H), 1.45 (s, 7.8H), 1.45 (s, 9H) ppm. ¹⁹F NMR (282 MHz, CDCl₃) δ: (minor) -40.68 (s, 3F), (major) -40.98 (s, 3F) ppm. ¹³C NMR (CDCl₃, 125.7 MHz) δ: (major and minor) 172.65 (d, J = 36.4 Hz), 172.47 (d, J = 38.9 Hz), 153.7 (d, J = 21.3 Hz), 153.1 (d, J = 15.0 Hz), 130.34 (q, J = 306.7 Hz), 130.39 (q, J = 306.7 Hz), 81.00, 80.95, 58.46, 58.29, 58.07, 58.01, 52.61, 52.43, 52.32, 52.25, 39.57 (d, J = 11.3 Hz), 39.02 (d, J = 20.1 Hz), 37.46, 37.38, 36.63, 36.40, 28.44, 28.31 ppm. IR (neat): 2979, 2877, 1751, 1706, 1398, 1257, 1118, 898, 763 cm⁻¹. HRMS (ESI): Calcd. for C₁₂H₁₅F₃NNaO₄S [M+Na]⁺: 352.0806. Found: 352.0802.
7. General procedure and product characterization data for Scheme 5.

7.1 Reaction procedure and product characterization data for 7 and 8;

7.1.1 2-isobutyryl-2-((perfluorophenyl)thio)-2,3-dihydro-1H-inden-1-one (8);

Following the general procedure, using substrate 1c (0.2 mmol, 1.0 equivalent) and C₆F₅-DAST (2.0 equivalent, 0.5 M solution in CH₂Cl₂) in CH₂Cl₂ (2.0 mL), the reaction mixture was stirred at −40 °C for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 50:1) to provide the title compound 7 (trace) and 8 (31% yield) as a yellow oil. ¹H NMR (CDCl₃, 300 MHz) δ: 7.77 (d, 1H, J = 7.8 Hz), 7.64 (t, 1H, J = 7.3 Hz), 7.45—7.41 (m, 2H), 3.93 (d, 1H, J = 17.7 Hz), 3.54—3.45 (m, 1H), 3.26 (d, 1H, J = 17.7 Hz), 1.21 (d, 3H, J = 6.6 Hz), 0.91 (d, 3H, J = 6.6 Hz) ppm.

¹⁹F NMR (282 MHz, CDCl₃) δ: -127.41—-127.53 (m, 2F), -147.80—-147.98 (m, 1F), -159.85—160.07 (m, 2F) ppm. ¹³C NMR (CDCl₃, 125.7 MHz) δ: 205.02, 197.29, 150.93, 149.87—149.70 (m), 147.89—147.72 (m), 144.25—144.03 (m), 142.19—141.93 (m), 138.89—138.59 (m), 136.86—136.51 (m), 138.29, 134.41, 128.58, 126.38, 125.14, 105.09—104.72 (m), 69.26, 37.35, 36.55, 20.45, 19.47 ppm. IR (neat): 3585, 2977, 1712, 1513, 1484, 1265, 977, 738, 2927 cm⁻¹. MS (ESI): Calcd. for C₁₉H₁₃F₅NaO₂S [M+Na]⁺ :
423. Found: 423.

7.1.2 2-((perfluorophenyl)thio)-2,3-dihydro-1H-inden-1-one (7);

\[
\text{SC}_{6}F_{5}
\]

(Including addition product) \( ^{1}H \) NMR (CDCl\(_3\), 300 MHz) \( \delta \): 7.76 (d, 1H, \( J = 7.8 \) Hz), 7.67—7.62 (m, 1H), 7.46-7.40 (m, 2H), 4.09—4.07 (m, 1H), 3.62 (dd, 1H, \( J = 18.6 \) Hz, \( J = 6.0 \) Hz), 3.04 (d, 1H, \( J = 17.7 \) Hz) ppm. \( ^{19}F \) NMR (282 MHz, CDCl\(_3\)) \( \delta \): -131.63—

131.71 (m, 2F), -151.39—151.54 (m, 1F), -161.24—161.38 (m, 2F) ppm. MS (ESI): Calcd. for C\(_{15}\)H\(_{7}\)F\(_{5}\)NaOS [M+Na]\(^{+}\) : 353. Found: 353.

7.2 Reaction procedure and product characterization data for 10;

\[
\begin{align*}
\text{Boc} & \quad \text{N} & \quad \text{O} & \quad \text{C}_{6}F_{5}\text{-DAST} \\
\text{3a, R = Ph,} & \quad \text{3c, R = i-Pr} & \quad \text{CH}_{3}\text{CN, rt} & \quad \text{overnight} \\
\end{align*}
\]

7.2.1 tert-butyl 2-oxo-3-((perfluorophenyl)thio)pyrrolidine-1-carboxylate (10);

\[
\text{SC}_{6}F_{5}
\]

Following the general procedure, using tert-butyl 3-benzoyl-2-oxopyrrolidine-1-carboxylate \( \text{3a} \) or \( \text{3c} \) (0.1mmol, 1.0 equivalent) and \( \text{C}_{6}F_{5}\text{-DAST} \) (2.0 equivalent, 0.5 M solution in CH\(_{2}\)Cl\(_{2}\)) in CH\(_{3}\)CN (1.0 mL, 0.1 M), the reaction mixture was stirred at room temperature for overnight. The crude product was purified by flash column chromatography (Hex: AcOEt = 20:1) to provide the title compound \( \text{10} \) as a yellow oil in
67% — 72% yield. $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$: 3.96—3.86 (m, 2H), 3.79—3.71 (m, 1H), 2.49—2.37 (m, 1H), 2.03—1.93 (m, 1H), 1.51 (s, 9H) ppm. $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$: -131.83—-131.94 (m, 2F), -150.96—-151.11 (m, 1F), -161.02—-161.19 (m, 2F) ppm. $^{13}$C NMR (CDCl$_3$, 125.7 MHz) $\delta$: 169.85, 150.01, 149.19—149.07 (m), 147.22—147.11 (m), 143.58—143.34 (m), 141.55—141.25 (m), 138.93—138.65 (m), 136.91—136.64 (m), 106.35—105.98 (m), 83.72, 46.75, 44.29, 28.07, 24.64 ppm. IR (neat): 2981, 2931, 1781, 1724, 1513, 1305, 981, 734 cm$^{-1}$. HRMS (ESI): Calcd. for C$_{15}$H$_{14}$F$_3$NNaO$_3$S [M+Na]$^+$: 406.0512. Found: 406.0508.

8. References;


9. $^1$H NMR, $^{13}$C NMR and $^{19}$F NMR spectra for desired compounds;

9.1 spectra for scheme 2;
9.2 spectra for scheme 3;

\[ \text{Boc} \text{N} \text{SCF}_3 \]
9.3 spectra for scheme 4;
9.4 spectra for scheme 5;