Supporting information

A Direct Approach to Decoration of Bioactive Compounds via C–H Amination Reaction

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1. **Reagents:** Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. Column chromatography purifications were performed using 200–300 mesh silica gel.

2. **Instruments:** NMR spectra were recorded on Varian Inova–400 MHz, Inova–300 MHz, Bruker DRX–400 or Bruker DRX–500 instruments and calibrated using residual solvent peaks as internal reference. Multiplicities are recorded as: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet. HRMS analysis were carried out using a Bruker micro TOF–Q instrument or a TOF–MS instrument.

3. **Optimization of Reaction Conditions**

\[ \text{Catalyst (5 mol%), AgSbF}_6 \text{(20 mol%), Base (20 mol%) in solvent (1.5 mL) for 18 h under nitrogen in a sealed tube.} \]

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<th>solvent</th>
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<th>yield(%)</th>
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°1a (0.20 mmol), 2a (0.4 mmol), catalyst (5 mol %), AgSbF\text{$_6$} (20 mol %), Base (20 mol %) in solvent (1.5 mL) for 18 h under nitrogen in a sealed tube. °[Cp*IrCl]_2 (2.5 mol %), AgSbF\text{$_6$} (10 mol %). °AgOAc instead of AgSbF\text{$_6$}. °°AgOAc instead of AgSbF\text{$_6$}. Yield of isolated product.
4. General Procedure for C-H Amidation

4.1 General procedures for Cross-coupling Two Bioactive Molecules

**General procedures for 3**: A mixture of 1 (0.2 mmol, 1.0 equiv), 2a (0.3 mmol, 1.5 equiv), [Cp*IrCl₂](8.0 mg, 0.010 mmol, 0.050 equiv), AgSbF₆ (13.8 mg, 0.04 mmol, 0.02 equiv), NaOAc (3.4 mg, 0.04 mmol, 0.02 equiv) and 1,2-DCE (1.5 mL) in a 15 mL glass vial sealed under air atmosphere was heated at 140 °C for 18 hours. The reaction mixture cooled to room temperature and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel (PE : EA = 4 : 1) to give the product 3.

4.2 General procedures for Aminating Reagents in C–H Amination Reactions

**General procedures for 6**: A mixture of 4 (0.2 mmol, 1.0 equiv), 5 (0.4 mmol, 2.0 equiv), [Cp*IrCl₂] (8.0 mg, 0.010 mmol, 0.050 equiv), AgSbF₆ (13.8 mg, 0.04 mmol, 0.02 equiv), NaOAc (3.4 mg, 0.04 mmol, 0.02 equiv) and 1,2-DCE (1.5 mL) in a 15 mL glass vial sealed under air atmosphere was heated at 140 °C for 18 hours. The reaction mixture cooled to room temperature and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel (PE : EA = 4 : 1) to give the product 6.

5 General Procedure for Synthesis Materials

**General Procedure A**: 1) To a solution of the carboxylic acid (3.0 mmol, 1.0 eq.) in dry CH₂Cl₂ (10 mL) at 0 °C under Ar was added dropwise oxalyl chloride (0.34 mL, 3.6 mmol, 1.2 eq.) followed by a catalytic amount of dry DMF (2 drops). The reaction was allowed to stir at rt until completion (typically 4 h). The solvent was then removed under reduce pressure to afford the corresponding crude acid chloride.
2) Methoxyamine hydrochloride (301.0 mg, 3.6 mmol, 1.2 eq.) was added to a biphasic mixture of K₂CO₃ (829.0 mg, 6.0 mmol, 2.0 eq.) in a 2:1 mixture of EtOAc (24 mL) and H₂O (12 mL). The resulting solution was cooled to 0°C followed by dropwise addition of the unpurified acid chloride dissolved in a minimum amount of EtOAc. The flask containing the acid chloride was then rinsed with additional EtOAc. The reaction was allowed to stir for 4h while reaching rt. Afterwards, the phases were separated and the aqueous phase was extracted twice with EtOAc. The combined organic layers were dried over MgSO₄, filtered, and evaporated under reduced pressure. The crude was purified via silica gel chromatography (80:20/Hexane:EtOAc) to obtain the desired product.

General Procedure B: 1) To a solution of carboxylic acid (3.0 mmol, 1.0 eq.) in dichloromethane (3 ml) was added thionyl chloride (2 ml) and the reaction mixture was stirred at 80 °C for 4 h. The mixture was allowed to cool and the solvent was removed in vacuo. The crude acid chloride was used directly in the coupling step without further purification.

2) Methoxyamine hydrochloride (301.0 mg, 3.6 mmol, 1.2 eq.) was added to a biphasic mixture of K₂CO₃ (829.0 mg, 6.0 mmol, 2.0 eq.) in a 2:1 mixture of EtOAc (24 mL) and H₂O (12 mL). The resulting solution was cooled to 0°C followed by dropwise addition of the unpurified acid chloride dissolved in a minimum amount of EtOAc. The flask containing the acid chloride was then rinsed with additional EtOAc. The reaction was allowed to stir for 4h while reaching rt. Afterwards, the phases were separated and the aqueous phase was extracted twice with EtOAc. The combined organic layers were dried over MgSO₄, filtered, and evaporated under reduced pressure. The crude was purified via silica gel chromatography (80:20/Hexane:EtOAc) to obtain the desired product.

General Procedure C: To a stirring solution of acid (10.0 mmol, 1.0 equiv) and Methoxyamine hydrochloride (1.03g, 10.5 mmol, 1.05 equiv) in DCM (30.0 mL) at 0°C was added Et₃N (2.8 mL, 20.0 mmol, 2.0 equiv), 4-DMAP (61 mg, 0.5 mmol, 0.05 equiv) and DCC (2.18 g, 10.5 mmol, 1.05 equiv). The reaction was allowed to stir overnight while warming to room temperature. The reaction was diluted with DCM and quenched with water. The layers were separated and the aqueous layer was extracted once with DCM (100 mL). The combined organic layers were washed with saturated NaHCO₃, water, brine, dried over MgSO₄, filtered and concentrated under reduced pressure. The crude was purified via silica gel chromatography (80:20/Hexane:EtOAc) to obtain the desired product.
General Procedure D:

1) In RBF fitted with Dean-stark apparatus and a reflux condenser, phthalic acid anhydride (8.14 g, 55 mmol) and appropriate amino acids (50 mmol) were refluxed in toluene in the presence of 0.1 mL triethylamine for 3 hours (in an oil bath). The organic solvents were removed under reduced pressure to get a sticky oily mass. Water was added to this oily mass and the mixture was acidified with hydrochloric acid, and stirred for 30 min to get a product. This product was filtered off, washed with water, and dried to get a target compound. The crude product was used in the next step without any purification.

2) To a 250 mL round-bottom flask were added the acid (50 mmol, 1 equiv), DCM (100 mL), and 0.05 mL DMF, oxalyl chloride (100 mmol, 8.5 mL, 2 equiv) was added slowly to the mixture, the above mixture were reacted for 3 h at room temperature. Then, the excess of oxalyl chloride and DCM were removed in vacuo, and the crude acid chloride in DCM (60 mL) was added slowly to a vigorously stirring solution of H₂NOMe•HCl (60 mmol, 5.0 g, 1.2 equiv) and NaHCO₃ (120 mmol, 2.4 equiv), in DCM (60 mL) and water (60 mL) in ice cooled bath. The reaction mixture was stirred for 3 h at 0 °C (monitored by TLC), after which H₂O and DCM was added to the reaction mixture. The aqueous layer was then extracted with DCM (3 × 20 ml) and the combined organics were washed with brine, dried over Na₂SO₄, filtered and concentrated. The product was recrystallized in DCM/hexanes to give the pure amide (over 90% yield).

General Procedure E:

Following a reported procedure, commercially available (2R,3R,4S,5R)-2-(6-chloro-9H-purin-9-yl)-5-(hydroxymethyl)tetrahydrofuran-3,4-diol (573.0 mg, 2.0 mmol, 1.0 equiv) was suspended in MeCN (12.5 mL, 0.15 M). Then Triethylamine (2.9 mL, 20.0 mmol, 10.0 equiv) and Acetic Anhydride (1.1 mL, 12.0 mmol, 6.0 equiv) were added at 0°C. After stirring for 1h at room temperature, the mixture was refluxed for 5 hours. The resulting solution was evaporated to dryness and EtOAc (30 mL) and water (30 mL) were added. The organic layer was separated, dried over Na₂SO₄, filtered and concentrated under reduced pressure to give a light brown oil, which was recrystallized from EtOAc/Ether to give product.
Subsequently, to a solution of 4c (500 mg, 1.2 mmol) in a mixture of 4/1 toluene (12 mL, 0.1 M) was added K$_2$CO$_3$ (218 mg, 1.6 mmol, 1.3 equiv.) followed by Pd(PPh$_3$)$_4$ (42.0 mg, 30.0 μmol, 3 mol %) and phenylboronic acid (192 mg, 1.58 mmol, 1.30 equiv.) under argon atmosphere in a 20 mL two-necked flask. The reaction mixture was refluxed for 12 h in an oil bath, and then cooled to room temperature. To the reaction mixture was added sat. aqueous NH$_4$Cl (15.0 mL), then the mixture was extracted by EtOAc (3 x 5 mL). The combined organic extracts were dried over MgSO$_4$, filtered and concentrated in vacuo. The resulting crude product was purified by flash chromatography (PE : EA = 4 : 1) to afford product.

**General Procedure F**

Based upon a procedure by Fu and co-workers, triethylamine (1.1 eq) was added to a stirred solution of the required 5-pyrazolin-3-one (1 eq) in THF (0.5 - 0.8 M) at 0ºC, followed by addition of the required chloroformate (1.1 eq) after 15 min. The mixture was stirred at ambient temperature overnight. The resulting solution was poured into water and the aqueous phase extracted with diethyl ether (x 3). The combined organic layers were washed with 1 M hydrochloric acid solution, sodiumhydrogen carbonate solution, brine, dried MgSO$_4$, filtered and concentrated in vacuo. The resulting crude product was purified by flash chromatography (PE : EA = 5 : 1) to afford product (80% yield).

**General Procedure G**

To a solution of DCC (210.0 mg, 1 mmol, 1.0 equiv) in DCM (15 mL) at 0ºC was added DMAP (150.0 mg, 1.2 mmol, 1.2 equiv) and Ataluren (PTC124) (284 mg, 1 mmol, 1.0 equiv). To the resulting suspension was then added methanol (64.0 mg, 2.0 mmol, 2.0 equiv). The reaction mixture was allowed to stir while slowly warming to room temperature over 15 h. The reaction was concentrated in vacuo, washed with ether, filtered through Celite, washed again with NaOH (aq, 20 mL), washed with saturated NH$_4$Cl (aq, 20 mL), dried over sodium sulfate, and concentrated in vacuo. The crude mixture was purified by column chromatography on silica gel (PE : EA = 8 : 1) to give the corresponding products (75% yield).
General Procedure H:

A mixture of celecoxib (4.1 mmol), benzyl bromide (10.3 mmol) and anhydrous K₂CO₃ (3g) in anhydrous 2-Butanone (20.0 mL) in the presence of catalytic amount of NaI was refluxed for 12 h in an oil bath. After cooling, the mixture was filtered (Celite) and the solvent was concentrated in vacuo. The crude product was recrystallized in DCM/hexanes to give the pure product (90% yield).

General Procedure I:

1) To a stirred solution of 9 (6.6 g, 36 mmol) PPh₃ (12.3 g, 47.0 mmol, 1.3 equiv) and PhthNOH (7.0 g, 43.2 mmol, 1.2 equiv) in THF (100 ml) was added DIAD (9.5 g, 47.0 mmol, 1.3 equiv) dropwise over 30 min. The mixture was stirred at r.t. for 6 h. TLC showed without of starting material. The reaction mixture was concentrated and then the residue was dissolved in ethanol (30 ml) to get 9a as a solid. The solid was washed with ethanol to afford a pure 9a in 93% yield as a solid. The crude product 9a was dissolved in ethanol (8 mL) and hydrazine monohydrate (2.0 equiv) was added. The reaction was refluxed for 2 h and filtered. Ethanol was removed under reduced pressure. The crude product was purified by flash column chromatography (PE : EA = 4 : 1) on silica gel.

2) To a stirring solution of 9a (10 mmol, 1.0 eq), Et₃N (1.5 mL, 11 mmol) in EtOAc (50 mL), was added trimethylacetyl chloride (1.5 mL, 20 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 10 minutes. Then, the reaction mixture was stirred at room temperature overnight. After that, the reaction mixture was extracted with EtOAc, washed with brine and dried over anhydrous Na₂SO₄. Then, the extract was concentrated in vacuo and purified by flash column chromatography (PE : EA = 5: 1) on silica gel to give the product 8, yield 65 % as white solid.

General Procedure B: white solid. R_f = 0.43 (hexane /ethyl acetate, 1/1).

^1H NMR (400 MHz, CDCl₃) δ 9.06 (s, 1H), 8.26 (s, 1H), 7.98 (s, 1H), 7.91 (d, J = 6.0 Hz, 2H), 7.78 (d,
$J = 8.4 \text{ Hz, } 2\text{H}$), 7.59 (s, 1H), 7.52 (d, $J = 8.1 \text{ Hz, } 1\text{H}$), 6.99 (d, $J = 8.3 \text{ Hz, } 1\text{H}$), 3.94 (s, 3H), 3.90 (s, 3H), 2.18 (s, 6H), 2.10 (s, 2H), 1.80 (s, 7H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 159.1, 141.3, 139.2, 135.6, 132.6, 131.4, 129.4, 128.9, 128.6, 128.1, 127.7, 126.9, 126.1, 125.8, 124.9, 123.8, 112.2, 64.9, 55.3, 40.7, 37.4, 37.3, 29.2.

HRMS Calcd for C$_{29}$H$_{30}$O$_3$ [M+Na$^+$]: 449.2093, Found: 449.2074.

General Procedure B: white solid. R$_f$ = 0.52 (hexane/ethyl acetate, 1/1).

$^{1}$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 12.02 (s, 1H), 8.46 (s, 1H), 8.24 – 8.21 (m, 2H), 7.98 (d, $J = 7.7 \text{ Hz, } 1\text{H}$), 7.81 – 7.76 (m, 1H), 7.72 – 7.68 (m, 1H), 7.61 – 7.42 (m, 2H), 3.76 (s, 3H).

$^{13}$C NMR (101 MHz, DMSO-d$_6$) $\delta$ 172.7 (d, $J_{C-F} = 4.1 \text{ Hz}$), 167.5, 161.3, 158.7, 135.8 (d, $J_{C-F} = 8.9 \text{ Hz}$), 133.3, 130.9, 130.1, 129.7, 127.8, 126.3, 125.9, 125.5 (d, $J_{C-F} = 3.4 \text{ Hz}$), 117.4 (d, $J_{C-F} = 20.6 \text{ Hz}$), 111.7 (d, $J_{C-F} = 11.2 \text{ Hz}$), 63.4.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -104.62 (s).

HRMS Calcd for C$_{16}$H$_{11}$FN$_2$O$_3$ [M+Na$^+$]: 336.0760, Found: 336.0756.

General Procedure C: white solid. R$_f$ = 0.40 (petroleum ester/ethyl acetate, 2/1).

$^{1}$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.44 (s, 1H), 7.37 (s, 5H), 4.89 (s, 2H), 2.02 (s, 2H), 1.67 – 1.48 (m, 2H), 1.25 (s, 28H), 0.87 (t, $J = 6.8 \text{ Hz, } 3\text{H}$).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 171.2, 135.6, 129.3, 128.8, 128.7, 33.4, 32.0, 29.8, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 25.5, 22.8, 14.2.

HRMS Calcd for C$_{25}$H$_{43}$NO$_2$ [M+Na$^+$]: 412.3191, Found: 412.3206.

General Procedure B: white solid. R$_f$ = 0.53 (hexane/ethyl acetate, 1/1).

$^{1}$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.13 (s, 1H), 7.42 (d, $J = 1.8 \text{ Hz, } 1\text{H}$), 7.30 (dd, $J = 8.3, 1.8 \text{ Hz, } 1\text{H}$), 7.12 (d, $J = 8.3 \text{ Hz, } 1\text{H}$), 6.68 (t, $J = 75.0 \text{ Hz, } 1\text{H}$), 3.86 (d, $J = 7.0 \text{ Hz, } 2\text{H}$), 3.81 (s, 2H), 1.31 – 1.20 (m, 1H), 0.62 (q, $J = 5.8 \text{ Hz, } 1\text{H}$), 0.31 (q, $J = 4.8 \text{ Hz, } 1\text{H}$).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 165.2, 150.6, 143.1 (t, $J = 3.0 \text{ Hz}$), 129.9, 122.1, 119.7, 115.8 (t, $J = 261.9 \text{ Hz}$), 113.5, 74.1, 64.3, 10.1, 3.3.

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19F NMR (376 MHz, CDCl$_3$) $\delta$ -81.99 (d, $J = 75.0$ Hz).

HRMS Calcd for C$_{13}$H$_{15}$F$_2$NO$_4$ [M+Na$^+$]: 310.0867, Found: 310.0878.

General Procedure G: white solid. R$_f$ = 0.56 (petroleum ester/ethyl acetate, 5/1).

1H NMR (400 MHz, CDCl$_3$) $\delta$ 8.82 (s, 1H), 8.35 (d, $J = 7.8$ Hz, 1H), 8.24 – 8.16 (m, 2H), 7.66 – 7.54 (m, 2H), 7.36 – 7.28 (m, 2H), 3.98 (s, 3H).

13C NMR (101 MHz, CDCl$_3$) $\delta$ 173.1 (d, $J = 4.3$ Hz), 168.1, 166.4, 160.9 (d, $J = 260.6$ Hz), 134.8 (d, $J = 8.7$ Hz), 132.3, 131.8, 131.1, 129.1, 128.8, 127.3, 124.8 (d, $J = 3.7$ Hz), 117.3 (d, $J = 20.9$ Hz), 112.8 (d, $J = 11.3$ Hz), 52.48.

19F NMR (376 MHz, CDCl$_3$) $\delta$ -108.17 (s).


General Procedure D: white solid. R$_f$ = 0.40 (hexane/ethyl acetate, 1/1).

1H NMR (400 MHz, DMSO-d$_6$) $\delta$ 11.10 (s, 1H), 7.87 – 7.78 (m, 4H), 3.78 (t, $J = 7.0$ Hz, 2H), 3.51 (s, 3H), 2.32 (t, $J = 7.0$ Hz, 2H).

13C NMR (101 MHz, DMSO-d$_6$) $\delta$ 167.6, 166.5, 134.4, 131.7, 123.0, 63.1, 34.1, 31.4.

HRMS Calcd for C$_{12}$H$_{12}$N$_2$O$_4$ [M+Na$^+$]: 217.0695, Found: 217.0685.

General Procedure D: white solid. R$_f$ = 0.8 (hexane/ethyl acetate, 1/1).

1H NMR (400 MHz, CDCl$_3$) $\delta$ 9.66 (s, 1H), 7.78 – 7.72 (m, 2H), 7.66 – 7.62 (m, 2H), 3.78 – 3.59 (m, 5H), 2.11 (t, $J = 6.4$ Hz, 2H), 2.02 – 1.84 (m, 2H).

13C NMR (101 MHz, CDCl$_3$) $\delta$ 170.0, 168.6, 134.1, 131.9, 123.3, 64.2, 37.2, 30.4, 24.7.

HRMS Calcd for C$_{13}$H$_{14}$N$_2$O$_4$ [M+Na$^+$]: 351.1033, Found: 351.1037.

General Procedure D: white solid. R$_f$ = 0.36 (hexane/ethyl acetate, 1/1).

1H NMR (400 MHz, CDCl$_3$) $\delta$ 9.52 (s, 1H), 7.77 – 7.72 (m, 2H), 7.66 – 7.62 (m, 2H), 4.85 – 4.78 (m, 1H), 3.58 (s, 3H), 2.86 (dd, $J = 14.1$, 9.6 Hz, 1H), 2.61 (dd, $J = 14.2$, 6.0 Hz, 1H), 1.45 (d, $J = 6.4$ Hz, 3H).

13C NMR (101 MHz, CDCl$_3$) $\delta$ 168.3, 167.9, 134.0, 131.9, 123.2, 64.1, 44.2, 36.8, 18.7.
HRMS Calcd for C_{13}H_{14}N_{2}O_{4} [M+Na^+]: 285.0851, Found: 285.0852.

General Procedure B: white solid. R_f = 0.43 (hexane/ethyl acetate, 1/1).

^1H NMR (400 MHz, DMSO-d_6) δ 11.83 (s, 1H), 7.72 (d, J = 1.6 Hz, 1H), 7.65 (dd, J = 8.4, 1.7 Hz, 1H), 7.49 (d, J = 8.4 Hz, 1H), 3.71 (s, 3H).

^13C NMR (101 MHz, DMSO-d_6) δ 162.5, 144.9, 142.8, 131.2 (t, J_{C:F} = 255.0 Hz), 129.0, 124.2, 110.1, 109.0, 63.3.

^19F NMR (377 MHz, DMSO-d_6) δ -49.06 (s).

HRMS Calcd for C_{9}H_{7}F_{2}NO_{4} [M+Na^+]: 254.0241, Found: 254.0239.

HRMS Calcd for C_{40}H_{42}N_{6}O_{10} [M+Na^+]: 789.2860, Found: 789.2894.

HRMS Calcd for C_{41}H_{42}N_{6}O_{10} [M+Na^+]: 789.2860, Found: 789.2894.
4.44 (m, 2H), 4.40 (dd, $J = 12.0, 4.4$ Hz, 1H), 3.24 – 2.98 (m, 4H), 2.16 (s, 3H), 2.12 (s, 3H), 2.09 (s, 3H), 1.61 – 1.48 (m, 4H), 0.88 (t, $J = 7.4$ Hz, 6H).

$^1$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.4, 169.7, 169.5, 164.3, 156.4, 152.2, 150.6, 143.2, 143.1, 139.5, 139.3, 133.6, 132.6, 131.7, 128.2, 127.5, 123.9, 121.6, 121.4, 86.9, 80.5, 73.2, 70.6, 63.1, 50.1, 22.1, 20.9, 20.6, 20.5, 11.3.

HRMS Calcd for C$_{35}$H$_{40}$N$_{6}$O$_{10}$S [M+Na$^+$]: 759.2424, Found: 759.2435.

White solid, 55.1 mg, 91%. See general Procedure I, $R_f = 0.30$ (petroleum ester/ethyl acetate, 1/1).

$^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 13.66 (s, 1H), 9.26 (s, 1H), 9.12 (d, $J = 7.9$ Hz, 1H), 9.01 (s, 1H), 8.69 (d, $J = 8.3$ Hz, 1H), 8.19 (d, $J = 8.2$ Hz, 2H), 8.06 (d, $J = 8.1$ Hz, 2H), 7.61 (t, $J = 7.6$ Hz, 1H), 7.37 (t, $J = 7.5$ Hz, 1H), 6.14 (d, $J = 5.3$ Hz, 1H), 5.59 (d, $J = 5.8$ Hz, 1H), 5.30 (d, $J = 4.9$ Hz, 1H), 5.15 (t, $J = 5.2$ Hz, 1H), 4.67 (dd, $J = 10.4, 5.1$ Hz, 1H), 4.24 (d, $J = 4.1$ Hz, 1H), 4.03 (d, $J = 3.4$ Hz, 1H), 3.86 – 3.59 (m, 2H), 3.14 – 2.92 (m, 4H), 1.50 (dd, $J = 14.5, 7.3$ Hz, 4H), 0.83 (t, $J = 7.3$ Hz, 4H).

$^1$C NMR (101 MHz, DMSO-d$_6$) $\delta$ 163.3, 154.3, 152.3, 150.8, 145.2, 142.3, 138.7, 138.1, 133.2, 131.8, 130.9, 128.2, 127.6, 123.7, 122.2, 121.4, 87.8, 85.8, 73.9, 70.3, 61.2, 49.7, 21.7, 11.0.

HRMS Calcd for C$_{29}$H$_{34}$N$_{6}$O$_{7}$S [M+Na$^+$]: 663.2107, Found: 663.2097.

White solid, 97.1 mg, 64%. $R_f = 0.53$ (petroleum ester/ethyl acetate, 1/1).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 12.98 (s, 1H), 9.11 (dd, $J = 9.0, 6.6$ Hz, 1H), 9.02 (s, 1H), 8.32 (s, 1H), 8.17 (d, $J = 12.1, 2.7$ Hz, 1H), 7.64 – 7.59 (m, 2H), 7.57 – 7.50 (m, 2H), 6.86 – 6.77 (m, 1H), 6.32 (d, $J = 5.3$ Hz, 1H), 6.01 (t, $J = 5.4$ Hz, 1H), 5.70 (t, $J = 5.0$ Hz, 1H), 4.53 – 4.46 (m, 2H), 4.42 (dd, $J = 12.4, 4.7$ Hz, 1H), 3.75 – 3.65 (m, 1H), 3.65 – 3.60 (m, 1H), 2.85 – 2.71 (m, 1H), 2.64 – 2.29 (m, 3H), 2.17 (s, 2H), 2.15 (s, 3H), 2.10 (s, 3H), 1.78 (dt, $J = 13.4, 6.7$ Hz, 1H), 1.30 (t, $J = 7.2$ Hz, 2H), 0.96 (d, $J = 6.5$ Hz, 3H), 0.93 (d, $J = 6.5$ Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.8, 170.4, 169.7, 169.5, 168.7, 164.64 (d, $J_{C-F} = 251.4$ Hz), 155.8, 152.0, 150.9, 142.7, 141.8 (d, $J_{C-F} = 12.5$ Hz), 135.3 (d, $J_{C-F} = 10.2$ Hz), 133.9, 131.9, 131.2, 123.1, 116.6, 110.9 (d, $J_{C-F} = 22.0$ Hz), 107.9 (d, $J_{C-F} = 27.9$ Hz), 86.7, 80.6, 73.2, 70.7, 63.2, 42.6, 42.4, 32.8, 25.5, 22.9, 22.6, 20.9, 20.7, 20.5.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -105.02 – -105.11 (m).
**HRMS** Calcd for C₁₃H₁₉FN₆O₆ [M+Na⁺]: 781.2609, Found: 781.2611.

![Diagram of 3d]

White solid, 78.4 mg, 52%. Rₜ = 0.56 (petroleum ester/ethyl acetate, 1/1).

**¹H NMR** (400 MHz, CDCl₃) δ 14.23 (s, 1H), 9.38 (dd, J = 9.0, 6.5 Hz, 1H), 8.99 (s, 1H), 8.75 (dd, J = 8.4 Hz, 2H), 7.98 (d, J = 8.4 Hz, 2H), 7.18 – 6.92 (m, 1H), 6.30 (d, J = 5.0 Hz, 1H), 6.00 (t, J = 5.3 Hz, 1H), 5.68 (t, J = 5.1 Hz, 1H), 4.53 – 4.50 (m, 1H), 4.49 – 4.39 (m, 2H), 3.19 – 3.08 (m, 4H), 2.18 (s, 3H), 2.14 (s, 3H), 2.11 (s, 3H), 1.61 – 1.53 (m, 4H), 0.89 (t, J = 7.4 Hz, 6H).

**¹³C NMR** (101 MHz, CDCl₃) δ 170.4, 169.8, 169.6, 164.6, 163.8, 155.7, 152.2, 150.6, 143.5, 143.0, 142.1 (d, J₁-C₂F = 12.2 Hz), 139.0, 135.9 (d, J₁-C₂F = 10.6 Hz), 131.4, 128.3, 127.6, 117.3, 111.1 (d, J₁-C₂F = 21.9 Hz), 108.7 (d, J₁-C₂F = 27.6 Hz), 86.9, 80.6, 73.3, 70.7, 63.2, 50.2, 22.1, 20.9, 20.7, 20.6, 11.3.

**¹⁹F NMR** (377 MHz, CDCl₃) δ -94.50 – -111.96 (m).

**HRMS** Calcd for C₁₃H₁₉FN₆O₆S [M+Na⁺]: 777.2330, Found: 777.2317.

White solid, 107.8 mg, 70%. Rₜ = 0.48 (petroleum ester/ethyl acetate, 1/1).

**¹H NMR** (400 MHz, CDCl₃) δ 12.99 (s, 1H), 9.15 (dd, J = 8.8, 6.7 Hz, 1H), 8.91 (s, 1H), 8.49 (dd, J = 12.0, 2.4 Hz, 1H), 8.32 (s, 1H), 7.80 – 7.75 (m, 2H), 7.72 – 7.67 (m, 2H), 7.00 – 6.81 (m, 1H), 6.28 (d, J = 5.0 Hz, 1H), 6.00 (t, J = 5.3 Hz, 1H), 5.69 (t, J = 5.1 Hz, 1H), 4.50 – 4.44 (m, 2H), 4.39 (dd, J = 12.3, 4.7 Hz, 1H), 3.87 (s, 2H), 2.54 (s, 2H), 2.16 (s, 3H), 2.12 (s, 3H), 2.09 (s, 3H), 1.76 (d, J = 9.7 Hz, 2H), 1.65 (s, 2H), 1.57 – 1.40 (m, 5H), 1.24 (s, 1H).

**¹³C NMR** (101 MHz, CDCl₃) δ 170.4, 170.3, 169.7, 169.5, 169.3, 163.6, 155.8, 151.9, 150.8, 142.8, 141.9 (d, J₁-C₂F = 12.4 Hz), 135.4 (d, J₁-C₂F = 9.8 Hz), 134.1, 132.1, 131.3, 123.3, 116.8 (d, J₁-C₂F = 2.9 Hz), 110.2 (d, J₁-C₂F = 22.5 Hz), 108.4 (d, J₁-C₂F = 28.1 Hz), 86.8, 80.5, 73.2, 70.6, 63.1, 46.2, 44.8, 39.3, 33.8, 25.8, 21.9, 20.9, 20.6, 20.5.

**¹⁹F NMR** (376 MHz, CDCl₃) δ -94.05 – -117.39 (m).

**HRMS** Calcd for C₁₃H₁₉FN₆O₅ [M+Na⁺]: 667.3392, Found: 667.2297.
Yellow liquid, 69.2 mg, 53%. RF = 0.53 (petroleum ester/ethyl acetate, 1/1).

**1H NMR** (400 MHz, CDCl₃) δ 12.99 (s, 1H), 9.19 (dd, J = 9.0, 6.6 Hz, 1H), 8.97 (s, 1H), 8.58 (dd, J = 12.0, 2.6 Hz, 1H), 8.31 (s, 1H), 7.06 – 6.84 (m, 1H), 6.29 (d, J = 5.1 Hz, 1H), 6.01 (t, J = 5.3 Hz, 1H), 5.85 – 5.73 (m, 1H), 5.69 (t, J = 5.1 Hz, 1H), 5.12 – 4.81 (m, 2H), 4.53 – 4.48 (m, 1H), 4.48 – 4.38 (m, 2H), 2.47 (t, J = 7.6 Hz, 2H), 2.17 (s, 3H), 2.14 (s, 3H), 2.10 (s, 3H), 2.05 – 1.98 (m, 2H), 1.83 – 1.73 (m, 2H), 1.42 – 1.32 (m, 5H), 1.30 – 1.25 (m, 5H).

**13C NMR** (101 MHz, CDCl₃) δ 172.4, 170.4, 169.7, 169.5, 165.0 (d, J_C–F = 251.6 Hz), 156.0, 152.0, 150.7, 142.8, 142.2 (d, J_C–F = 12.5 Hz), 139.3, 135.5 (d, J_C–F = 10.3 Hz), 131.4, 116.8 (d, J_C–F = 2.8 Hz), 114.3 (s), 110.3 (d, J_C–F = 22.2 Hz), 108.5 (d, J_C–F = 27.9 Hz), 86.8, 80.6, 73.2, 70.7, 63.2, 39.0, 33.9, 29.5, 29.5, 29.4, 29.2, 29.0, 25.7, 20.9, 20.7, 20.6.

**19F NMR** (376 MHz, CDCl₃) δ -104.70 (s).

**HRMS** Calcd for C₃₃H₄₀FN₅O₈ [M+Na⁺]: 676.2759, Found: 676.2757.

Colorless liquid, 88.8 mg, 59%. RF = 0.52 (petroleum ester/ethyl acetate, 1/1).

**1H NMR** (400 MHz, CDCl₃) δ 12.98 (s, 1H), 9.19 (dd, J = 9.0, 6.6 Hz, 1H), 8.97 (s, 1H), 8.59 (dd, J = 12.1, 2.7 Hz, 1H), 8.31 (s, 1H), 6.98 – 6.90 (m, 1H), 6.29 (d, J = 5.2 Hz, 1H), 6.01 (t, J = 5.4 Hz, 1H), 5.69 (t, J = 5.1 Hz, 1H), 4.52 – 4.48 (m, 2H), 4.41 (dd, J = 12.2, 4.6 Hz, 1H), 2.47 (t, J = 7.6 Hz, 2H), 2.17 (s, 3H), 2.14 (s, 3H), 2.10 (s, 3H), 1.83 – 1.73 (m, 2H), 1.24 (s, 28H), 0.87 (t, J = 6.8 Hz, 3H).

**13C NMR** (101 MHz, CDCl₃) δ 172.4, 170.4, 169.7, 169.5, 165.0 (d, J_C–F = 251.5 Hz), 156.0, 152.0, 150.7, 142.8, 142.2 (d, J_C–F = 12.5 Hz), 135.5 (d, J_C–F = 10.2 Hz), 131.4, 116.8 (d, J_C–F = 3.1 Hz), 110.3 (d, J_C–F = 22.2 Hz), 108.5 (d, J_C–F = 27.8 Hz), 86.6, 80.6, 73.2, 70.7, 63.2, 39.0, 32.1, 29.8, 29.8, 29.8, 29.7, 29.6, 29.5, 29.4, 25.7, 22.8, 20.9, 20.7, 20.6, 14.3.

**19F NMR** (376 MHz, CDCl₃) δ -104.67 (s).

**HRMS** Calcd for C₄₀H₅₆FN₅O₈ [M+Na⁺]: 776.4011, Found: 776.4034.
White solid, 71.2 mg, 49%. R<sub>f</sub> = 0.45 (petroleum ester/ethyl acetate, 1/1).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 14.01 (s, 1H), 9.33 (dd, <i>J</i> = 9.0, 6.5 Hz, 1H), 9.00 (s, 1H), 8.74 (dd, <i>J</i> = 12.0, 2.7 Hz, 1H), 8.33 (s, 1H), 7.72 (d, <i>J</i> = 2.0 Hz, 1H), 7.62 (dd, <i>J</i> = 8.3, 2.0 Hz, 1H), 7.32 (d, <i>J</i> = 8.3 Hz, 1H), 7.06 – 6.95 (m, 1H), 6.75 (t, <i>J</i> = 75.0 Hz, 1H), 6.29 (d, <i>J</i> = 5.0 Hz, 1H), 6.00 (t, <i>J</i> = 5.3 Hz, 1H), 5.69 (t, <i>J</i> = 5.2 Hz, 1H), 4.54 – 4.48 (m, 1H), 4.49 – 4.37 (m, 2H), 4.00 (d, <i>J</i> = 6.9 Hz, 2H), 2.18 (s, 3H), 2.14 (s, 3H), 2.11 (s, 3H), 1.33 – 1.22 (m, 1H), 0.75 – 0.61 (m, 2H), 0.43 – 0.35 (m, 2H).

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 170.4, 169.7, 169.6, 166.3 (d, <i>J</i><sub>C-F</sub> = 253.0 Hz), 165.1, 155.9, 152.1, 150.9, 150.6, 143.3 (t, <i>J</i><sub>C-F</sub> = 3.0 Hz), 143.0, 142.4 (d, <i>J</i><sub>C-F</sub> = 12.4 Hz), 135.8 (d, <i>J</i><sub>C-F</sub> = 9.8 Hz), 133.9, 131.4, 122.2, 119.4, 117.2 (d, <i>J</i><sub>C-F</sub> = 2.8 Hz), 116.0 (t, <i>J</i><sub>C-F</sub> = 261.7 Hz), 114.5, 110.8 (d, <i>J</i><sub>C-F</sub> = 22.0 Hz), 108.6 (d, <i>J</i><sub>C-F</sub> = 28.1 Hz), 86.9, 80.6, 74.3, 73.3, 70.7, 20.7, 20.6, 10.2, 3.4.

**<sup>19</sup>F NMR** (376 MHz, CDCl<sub>3</sub>) δ -81.80 (s), -104.18 (s).

**HRMS** Calcd for C<sub>34</sub>H<sub>32</sub>F<sub>3</sub>N<sub>5</sub>O<sub>10</sub> [M+Na<sup>+</sup>]: 750.1999, Found: 750.1997.

White solid, 93.2 mg, 54%. R<sub>f</sub> = 0.40 (petroleum ester/ethyl acetate, 1/1).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 13.82 (s, 1H), 9.17 (dd, <i>J</i> = 8.0, 1.5 Hz, 1H), 9.10 (s, 1H), 8.96 (dd, <i>J</i> = 8.4, 0.9 Hz, 1H), 8.60 (s, 1H), 8.35 (s, 1H), 8.14 (dd, <i>J</i> = 8.6, 1.7 Hz, 1H), 8.03 (t, <i>J</i> = 8.5 Hz, 3H), 7.84 (dd, <i>J</i> = 8.5, 1.7 Hz, 1H), 7.67 – 7.55 (m, 3H), 7.35 – 7.28 (m, 1H), 7.01 (d, <i>J</i> = 8.5 Hz, 1H), 6.31 (d, <i>J</i> = 5.1 Hz, 1H), 6.04 (t, <i>J</i> = 5.3 Hz, 1H), 5.72 (t, <i>J</i> = 5.2 Hz, 1H), 4.53 – 4.48 (m, 1H), 4.48 – 4.38 (m, 2H), 3.91 (s, 3H), 2.21 – 2.16 (m, 11H), 2.13 (s, 3H), 2.10 (s, 3H), 1.82 (s, 7H).

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 169.9, 169.1, 168.9, 165.4, 158.4, 156.2, 151.6, 150.2, 142.4, 140.5, 139.5, 138.5, 134.9, 133.0, 132.2, 132.0, 131.2, 131.1, 129.0, 128.2, 127.4, 126.2, 125.5, 125.3, 124.3, 123.8 122.8, 121.1, 120.7, 111.7, 86.2, 80.0, 72.6, 70.1, 62.6, 54.7, 40.1, 36.7, 36.7, 28.7, 20.3, 20.1, 19.9.

**HRMS** Calcd for C<sub>50</sub>H<sub>49</sub>N<sub>5</sub>O<sub>9</sub> [M+Na<sup>+</sup>]: 886.3428, Found: 886.3463.
White solid, 88.2 mg, 60%. R<sub>f</sub> = 0.44 (petroleum ester/ethyl acetate, 1/1).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 14.06 (s, 1H), 9.46 (s, 1H), 9.19 (d, J = 8.0 Hz, 1H), 8.99 (s, 1H), 8.92 (d, J = 8.3 Hz, 1H), 8.48 – 8.22 (m, 4H), 7.73 – 7.52 (m, 3H), 7.44 – 7.28 (m, 3H), 6.34 (d, J = 5.4 Hz, 1H), 6.02 (t, J = 5.5 Hz, 1H), 5.65 (t, J = 5.4 Hz, 1H), 4.50 – 4.46 (m, 1H), 4.44 – 4.36 (m, 2H), 2.16 (s, 3H), 2.13 (s, 3H), 2.07 (s, 3H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 173.2 (d, J<sub>C-F</sub> = 4.4 Hz), 170.4, 169.7, 169.5, 168.4, 164.5, 162.2, 159.7, 156.4, 152.3, 151.6, 142.8, 139.9, 136.1, 134.9 (d, J<sub>C-F</sub> = 8.6 Hz), 133.6, 132.5, 131.6, 131.5, 131.1, 130.8, 129.7, 127.2, 125.4, 124.9 (d, J<sub>C-F</sub> = 3.7 Hz), 123.6, 121.6 (d, J<sub>C-F</sub> = 17.4 Hz), 117.4 (d, J<sub>C-F</sub> = 20.9 Hz), 112.9 (d, J<sub>C-F</sub> = 11.3 Hz), 86.5, 80.7, 73.2, 70.8, 63.1, 20.9, 20.7, 20.5.

<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -97.68 – -130.43 (m).

HRMS Calcd for C<sub>37</sub>H<sub>30</sub>F<sub>7</sub>N<sub>7</sub>O<sub>9</sub> [M+Na<sup>+</sup>]: 758.1987, Found: 759.2015.

Yellow liquid, 80.3 mg, 45%. R<sub>f</sub> = 0.39 (petroleum ester/ethyl acetate, 1/1).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.67 (s, 1H), 9.01 (s, 1H), 8.97 (d, J = 7.7 Hz, 1H), 8.63 (d, J = 8.2 Hz, 1H), 8.33 (s, 1H), 7.54 – 7.49 (m, 1H), 7.29 – 7.25 (m, 1H), 6.30 (d, J = 5.3 Hz, 1H), 6.00 (t, J = 5.4 Hz, 1H), 5.68 (t, J = 5.0 Hz, 1H), 4.51 – 4.38 (m, 3H), 3.08 (t, J = 6.8 Hz, 2H), 2.90 (t, J = 6.9 Hz, 2H), 2.56 (t, J = 6.5 Hz, 2H), 2.15 (d, J = 10.3 Hz, 6H), 2.08 (d, J = 11.7 Hz, 6H), 2.01 (s, 3H), 1.97 (s, 3H), 1.83 – 1.70 (m, 3H), 1.55 – 1.48 (m, 3H), 1.44 – 1.33 (m, 5H), 1.30 – 1.24 (m, 7H), 0.91 – 0.80 (m, 15H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 171.5, 170.4, 169.7, 169.5, 169.5, 156.6, 152.1, 151.0, 149.4, 142.8, 140.6, 139.2, 133.3, 132.3, 132.2, 131.7, 126.8, 125.1, 123.4, 123.0, 121.9, 117.4, 86.6, 80.5, 75.1, 73.2, 70.7, 63.2, 39.5, 37.5, 37.4, 32.9, 32.8, 29.8, 29.2, 28.1, 24.9, 24.5, 22.8, 22.7, 21.1, 20.9, 20.7, 20.6, 20.5, 19.9, 19.8, 13.1, 12.2, 11.9.

HRMS Calcd for C<sub>55</sub>H<sub>75</sub>N<sub>5</sub>O<sub>11</sub> [M+Na<sup>+</sup>]: 1004.5361, Found: 1004.5403.
White solid, 95.3 mg, 60%. R<sub>f</sub> = 0.48 (petroleum ester/ethyl acetate, 2/1).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.83 (d, J = 1.7 Hz, 1H), 8.75 (s, 1H), 7.69 – 7.64 (m, 2H), 7.57 – 7.52 (m, 2H), 7.37 (dd, J = 8.4, 2.0 Hz, 1H), 7.21 – 7.19 (m, 6H), 7.14 – 7.04 (m, 4H), 7.01 (d, J = 8.0 Hz, 2H), 6.91 – 6.89 (m, 3H), 6.81 (s, 1H), 4.93 – 4.76 (m, 1H), 4.32 (s, 4H), 3.21 (dd, J = 15.0, 9.4 Hz, 1H), 2.82 (dd, J = 15.0, 5.7 Hz, 1H), 2.32 (s, 3H), 1.50 (d, J = 6.9 Hz, 3H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 168.5, 168.1, 147.0, 145.0 (q, J<sub>C-F</sub> = 38.8 Hz), 141.6, 140.0, 135.3, 133.9, 133.8, 131.7, 131.2, 129.8, 128.7, 128.5, 128.4, 127.8, 127.6, 124.8, 123.3, 122.7, 122.4, 105.8, 50.7, 44.2, 41.5, 21.4, 19.0.

<sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>) δ -62.43 (s).

HRMS Calcd for C<sub>43</sub>H<sub>36</sub>F<sub>3</sub>N<sub>5</sub>O<sub>5</sub>S [M+Na<sup>+</sup>]: 814.2287, Found: 814.2322.

White solid, 63.5 mg, 37%. R<sub>f</sub> = 0.40 (petroleum ester/ethyl acetate, 2/1).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 9.95 (s, 1H), 9.09 (d, J = 1.7 Hz, 1H), 7.77 – 7.69 (m, 4H), 7.45 (dd, J = 8.3, 1.8 Hz, 1H), 7.25 – 7.21 (m, 6H), 7.18 – 7.09 (m, 8H), 7.01 (d, J = 8.3 Hz, 1H), 6.72 (s, 1H), 4.36 (s, 4H), 3.69 (s, 2H), 2.40 (s, 2H), 2.35 (s, 3H), 1.55 – 1.41 (m, 6H), 1.40 – 1.30 (m, 4H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 167.0, 169.9, 147.7, 144.5 (q, J<sub>C-F</sub> = 38.5 Hz), 141.9, 139.9, 136.0, 135.5, 134.4, 132.2, 131.6, 129.9, 129.0, 128.9, 128.6, 128.3, 127.8, 125.3, 123.5, 122.6(d, J = 12.4 Hz), 105.1, 51.0, 46.6, 43.0, 38.7, 34.2, 25.8, 21.5, 21.4.

<sup>19</sup>F NMR (377 MHz, CDCl<sub>3</sub>) δ -62.49 (s).

HRMS Calcd for C<sub>48</sub>H<sub>44</sub>F<sub>3</sub>N<sub>5</sub>O<sub>5</sub>S [M+Na<sup>+</sup>]: 860.3093, Found: 860.3128.

White solid, 79.2 mg, 51%. R<sub>f</sub> = 0.45 (petroleum ester/ethyl acetate, 2/1).
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.92 (s, 1H), 8.87 (d, $J = 1.5$ Hz, 1H), 7.73 (dd, $J = 5.5, 3.0$ Hz, 2H), 7.64 (dd, $J = 5.5, 3.1$ Hz, 2H), 7.39 (dd, $J = 8.4, 2.0$ Hz, 1H), 7.26 – 7.21 (m, 6H), 7.14 – 7.08 (m, 6H), 7.03 (d, $J = 8.2$ Hz, 2H), 6.91 (d, $J = 8.4$ Hz, 1H), 6.69 (s, 1H), 4.36 (s, 4H), 4.04 (t, $J = 7.0$ Hz, 4H), 4.04 (t, $J = 7.0$ Hz, 2H), 2.75 (t, $J = 7.0$ Hz, 2H), 2.36 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.4, 168.0, 147.1, 144.8 (q, $J = 38.9$ Hz), 141.6, 140.3, 135.5, 134.1, 133.6, 132.0, 131.1, 121.0, 128.8, 128.7, 128.6, 127.9, 125.0, 123.5, 122.7, 105.9, 50.8, 36.4, 34.1, 21.5.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -62.41 (s).

HRMS Calcd for C$_{42}$H$_{34}$F$_3$N$_5$O$_5$S [M+Na$^+$]: 800.2130, Found: 800.2100.

**6d**

White solid, 110.7 mg, 70%. $R_f = 0.52$ (petroleum ester/ethyl acetate, 2/1).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.02 (s, 1H), 8.95 (d, $J = 1.5$ Hz, 1H), 7.82 – 7.75 (m, 2H), 7.73 – 7.65 (m, 2H), 7.40 (dd, $J = 8.4, 2.0$ Hz, 2H), 7.24 – 7.20 (m, 6H), 7.14 – 7.08 (m, 8H), 6.96 (d, $J = 8.4$ Hz, 1H), 6.84 (s, 1H), 4.36 (s, 4H), 3.76 (t, $J = 6.3$ Hz, 2H), 2.50 – 2.29 (m, 5H), 2.22 – 2.02 (m, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 170.5, 168.6, 147.2, 144.6 (q, $J = 38.8$ Hz), 141.6, 140.1, 135.4, 134.3, 134.2, 132.0, 131.1, 129.9, 128.7, 128.5, 127.9, 125.1, 123.3, 122.3 (d, $J = 20.6$ Hz), 105.8, 50.8, 36.9, 34.9, 24.7, 21.4.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -62.42 (s).

HRMS Calcd for C$_{43}$H$_{36}$F$_3$N$_5$O$_5$S [M+Na$^+$]: 814.2287, Found: 814.2317.

**6e**

White solid, 47.5 mg, 45%. $R_f = 0.55$ (petroleum ester/ethyl acetate, 2/1).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.75 (s, 1H), 8.93 (d, $J = 2.0$ Hz, 1H), 8.74 (d, $J = 8.9$ Hz, 1H), 8.33 – 8.24 (m, 1H), 8.10 (dd, $J = 8.8, 2.0$ Hz, 1H), 7.79 (dd, $J = 5.4, 3.0$ Hz, 2H), 7.71 – 7.62 (m, 3H), 7.45 – 7.38 (m, 1H), 7.37 – 7.30 (m, 1H), 5.13 – 4.92 (m, 1H), 3.93 (s, 3H), 3.43 (dd, $J = 15.5, 8.9$ Hz, 1H), 3.05 (dd, $J = 15.5, 5.9$ Hz, 1H), 1.59 (d, $J = 7.0$ Hz, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 172.13 (d, $J_{C,F} = 4.8$ Hz), 169.3, 168.3, 167.4, 166.1, 162.4, 159.8, 141.6, 135.5 (d, $J_{C,F} = 8.9$ Hz), 134.0, 133.7, 132.1, 131.2 (d, $J_{C,F} = 8.3$ Hz), 125.2, 125.1, 123.4, 120.5, 117.5 (d, $J_{C,F} = 20.8$ Hz), 113.4, 112.1 (d, $J_{C,F} = 11.0$ Hz), 52.3, 44.0, 41.9, 19.1.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -107.67 (s).

HRMS Calcd for C$_{28}$H$_{21}$FN$_4$O$_6$ [M+Na$^+$]: 551.1343, Found: 551.1313.
White solid, 52.7 mg, 52%. $R_f = 0.56$ (petroleum ester/ethyl acetate, 2/1).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.38 (s, 1H), 8.57 (dd, $J = 8.3$, 1.1 Hz, 1H), 7.68 – 7.56 (m, 2H), 7.43 – 7.34 (m, 4H), 7.34 – 7.30 (m, 3H), 7.19 – 7.08 (m, 2H), 6.19 (s, 1H), 5.19 (s, 2H), 2.40 (s, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 163.3, 150.7, 150.2, 146.3, 146.0, 144.2, 133.9, 133.0, 131.8, 131.4, 129.3, 129.1, 128.9, 128.8, 126.1, 124.8, 124.1, 123.6, 122.5, 109.4, 109.0, 95.6, 71.7, 14.6.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -49.70 (s).

HRMS Calcd for C$_{26}$H$_{19}$F$_2$N$_3$O$_6$ [M+Na$^+$]: 530.1140, Found: 530.1160.

White solid, 52.4 mg, 53%. $R_f = 0.48$ (petroleum ester/ethyl acetate, 2/1).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.49 (s, 1H), 8.66 – 8.62 (m, 2H), 8.36 (d, $J = 7.7$ Hz, 1H), 8.29 – 8.22 (m, 1H), 8.08 (d, $J = 7.8$ Hz, 1H), 7.65 – 7.60 (m, 2H), 7.45 – 7.41 (m, 1H), 7.38 – 7.29 (m, 8H), 7.16 – 7.12 (m, 1H), 6.19 (s, 1H), 5.20 (s, 2H), 2.38 (s, 3H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 173.2 (d, $J = 4.3$ Hz), 168.2, 164.3, 162.2, 159.6, 150.8, 150.6, 145.8, 135.8, 134.9 (d, $J = 8.7$ Hz), 133.9, 133.2, 131.1, 130.9, 130.4, 129.5, 129.2, 129.0, 128.8 (d, $J = 8.1$ Hz), 127.6, 126.3, 126.0, 124.9 (d, $J = 3.9$ Hz), 124.8, 124.1, 122.8, 117.3 (d, $J = 20.9$ Hz), 112.9 (d, $J = 11.4$ Hz), 95.5, 71.6, 14.6.

$^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -93.97 – -110.28 (m).

HRMS Calcd for C$_{33}$H$_{24}$FN$_5$O$_5$ [M+Na$^+$]: 612.1659, Found: 612.1678.

White solid, 70.8 mg, 60%. $R_f = 0.50$ (petroleum ester/ethyl acetate, 2/1).
**1H NMR** (400 MHz, CDCl₃) δ 10.54 (s, 1H), 8.59 (dd, J = 8.3, 1.0 Hz, 1H), 8.00 – 7.94 (m, 2H), 7.92 – 7.86 (m, 2H), 7.45 – 7.39 (m, 1H), 7.38 – 7.30 (m, 6H), 7.15 (td, J = 8.0, 1.4 Hz, 1H), 6.19 (s, 1H), 5.19 (s, 2H), 3.10 (dd, J = 8.6, 6.8 Hz, 4H), 2.39 (s, 3H), 1.61 – 1.50 (m, 4H), 0.88 (t, J = 7.4 Hz, 6H).

**13C NMR** (101 MHz, CDCl₃) δ 163.6, 150.7, 150.2, 145.9, 143.4, 138.4, 133.8, 132.8, 129.3, 129.1, 128.9, 128.8, 128.0, 127.4, 126.2, 124.7, 124.3, 122.5, 95.6, 71.7, 50.1, 22.1, 14.7, 11.3.

**HRMS** Calcd for C₃₁H₃₄N₄O₆ [M+Na⁺]: 613.2097, Found: 613.2069.

White solid, 76.6 mg, 68%. Rₙ = 0.48 (petroleum ester/ethyl acetate, 2/1).

**1H NMR** (400 MHz, CDCl₃) δ 10.19 (s, 1H), 8.57 (d, J = 8.0 Hz, 1H), 7.56 (d, J = 1.7 Hz, 1H), 7.43 – 7.35 (m, 4H), 7.34 – 7.26 (m, 4H), 7.20 (d, J = 8.3 Hz, 1H), 7.12 (t, J = 7.3 Hz, 1H), 6.71 (t, J = 75.1 Hz, 1H), 6.17 (s, 1H), 5.19 (s, 2H), 3.94 (d, J = 7.0 Hz, 2H), 2.38 (s, 3H), 1.35 – 1.25 (m, 1H), 0.66 (q, J = 5.7 Hz, 2H), 0.36 (q, J = 4.9 Hz, 2H).

**13C NMR** (101 MHz, CDCl₃) δ 164.1, 150.8, 150.1, 145.91, 143.2 (t, J_C-F = 3.1 Hz), 133.9, 133.3, 133.2, 129.2, 129.2, 128.9, 128.8, 126.2, 125.0, 124.0, 122.5, 119.3, 116.0 (t, J_C-F = 261.6 Hz) 114.2, 95.5, 74.3, 71.7, 14.7, 10.2, 3.4.

**19F NMR** (376 MHz, CDCl₃) δ -81.82 (s).

**HRMS** Calcd for C₃₀H₂₇F₂N₃O₆ [M+Na⁺]: 586.1766, Found: 586.1789.

White solid, 36.9 mg, 81%. Rₙ = 0.51 (petroleum ester/ethyl acetate, 2/1).

**1H NMR** (400 MHz, CDCl₃) δ 7.85 – 7.79 (m, 4H), 7.43 – 7.31 (m, 5H), 4.94 (s, 2H), 3.43 (s, 3H), 3.15 – 3.01 (m, 4H), 1.58 – 1.52 (m, 4H), 0.87 (t, J = 7.4 Hz, 6H).

**13C NMR** (101 MHz, CDCl₃) δ 168.4, 142.2, 137.9, 136.0, 129.0, 128.9, 128.6, 128.5, 128.2, 126.9, 62.4, 50.10 , 22.1, 11.3, 1.2.

**HRMS** Calcd for C₂₅H₂₈N₃O₆ [M+Na⁺]: 479.1729, Found: 479.1749.
colorless solid, 72.1 mg, 63%. R<sub>f</sub> = 0.55 (petroleum ester/ethyl acetate, 1/1).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 13.58 (s, 1H), 9.10 (dd, J = 8.0, 1.4 Hz, 1H), 9.02 (s, 1H), 8.94 – 8.83 (m, 1H), 8.33 (s, 1H), 8.08 – 8.04 (m, 2H), 7.61 – 7.53 (m, 3H), 7.54 – 7.48 (m, 1H), 7.48 – 7.48 (m, 1H), 6.29 (d, J = 5.1 Hz, 1H), 6.03 (t, J = 5.3 Hz, 1H), 5.71 (t, J = 5.2 Hz, 1H), 4.63 – 4.29 (m, 3H), 2.16 (s, 3H), 2.12 (s, 3H), 2.09 (s, 3H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 170.4, 169.7, 169.5, 165.9, 156.7, 152.1, 150.8, 143.0, 139.9, 135.8, 133.5, 132.5, 131.8, 131.8, 128.8, 127.5, 123.4, 121.7, 121.4, 86.9, 80.5, 73.2, 70.7, 63.2, 20.9, 20.7, 20.5.

white solid, 22.1 mg, 60%. R<sub>f</sub> = 0.33 (petroleum ester/ethyl acetate, 5/1).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.61 (d, J = 7.9 Hz, 4H), 7.48 – 7.44 (m, 4H), 7.39 – 7.35 (m, 1H), 4.74 (s, 1H), 1.97 (s, 1H).

<sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 140.9, 140.8, 140.0, 128.9, 127.6, 127.4, 124.6, 121.7, 121.4, 86.9, 80.5, 73.2, 70.7, 63.2, 20.9, 20.7, 20.5.

6 Gram scale reaction and further transformation

![Chemical diagram]

**General procedures:** A mixture of 4c (3 mmol, 1.0 equiv), 3ca (6 mol, 2.0 equiv), [Cp*IrCl<sub>2</sub>]<sub>2</sub> (119.4 mg, 0.150 mmol, 0.050 equiv), AgSbF<sub>6</sub> (214.2 mg, 0.6 mmol, 0.02 equiv) and 1,2-DCE (15.0 mL) in a 50 mL glass vial sealed under argon atmosphere was heated at 140 °C for 18 hours in an oil bath. The reaction mixture cooled to room temperature and concentrated in vacuo. The resulting residue was purified by column chromatography on silica gel (PE / EA = 5 / 1) to give the product 6h.

![Chemical diagram]

**General procedures:** A solution of 6h (153.4 mg, 0.26 mol) in absolute methanol (3 mL) was hydrogenated in the presence of 15 % Pd/C (13.0 mg) at room temperature for 12 h. The mixture was filtered (Celite) and washed with methanol. The solvent was and concentrated in vacuo. The crude mixture was purified by column chromatography on silica gel (PE / EA = 5 / 1) to give the corresponding products.
General procedures: To a solution of 3c (0.10 mmol) in methanol (1.5 mL) was added \( \text{K}_2\text{CO}_3 \) (0.006 g, 0.04 mmol). The resulting mixture was stirred under air at room temperature for 10 h. The reaction mixture was then concentrated in vacuo. The crude mixture was purified by silica gel column chromatography (PE / EA = 2 / 1) and the corresponding product 3c’ was white solid (555.6 mg, 91%).

7 Balancing chemical reaction equation\(^{10}\).

General procedures: A mixture of 1b (0.2 mmol, 1.0 equiv), 8 (0.3 mmol, 1.5 equiv), \([\text{Cp}^*\text{IrCl}_2]_2 \) (8.0 mg, 0.010 mmol, 0.050 equiv), AgSbF\(_6\) (13.8 mg, 0.04 mmol, 0.02 equiv) and 1,2-DCE (1.5 mL) in a 15 mL glass vial sealed under argon atmosphere was heated at 140 °C for 18 hours in an oil bath. The reaction mixture cooled to room temperature and concentrated in vacuo. The resulting residue was purified by column chromatography (PE / EA = 5 / 1) on silica gel to give the product 9 (colorless solid, 72.1 mg) and 10 (white solid, 22.1 mg).

8 Control Experiment

General procedures: A mixture of 1b (0.2 mmol, 1.0 equiv), 12 (0.3 mmol, 1.5 equiv), \([\text{Cp}^*\text{IrCl}_2]_2 \) (8.0 mg, 0.010 mmol, 0.050 equiv), AgSbF\(_6\) (13.8 mg, 0.04 mmol, 0.02 equiv), NaOAc (3.8 mg, 0.04 mmol, 0.02 equiv) and 1,2-DCE (1.5 mL) in a 15 mL glass vial sealed under air atmosphere was heated at 140 °C for 18 hours in an oil bath. The reaction mixture cooled to room temperature and concentrated in vacuo. The resulting residue was purified by column chromatography (PE / EA = 5 / 1) on silica gel to give the product 9.
9. References


10. NMR spectra

$^1$H NMR of 2b

$^{13}$C NMR of 2b
$^1$H NMR of 2c

$^{13}$C NMR of 2c
$^1$H NMR of 2d

$^1$F NMR of 2c
$^{13}$C NMR of 2d

$^1$H NMR of 2e
$^{13}$C NMR of 2e

$^{19}$F NMR of 2e
$^1$H NMR of 4a

$^{13}$C NMR of 4a
$^{19}$F NMR of 4a

$^1$H NMR of 4b
$^{13}$C NMR of 4b

$^1$H NMR of 4c
$^{13}$C NMR of 4c

$^1$H NMR of 4d
$^{13}$C NMR of 4d

$^1$H NMR of 4e
$^{13}$C NMR of 4e

$^{19}$F NMR of 4e
1H NMR of 3a

13C NMR of 3a
$^1$H NMR of 3b

$^{13}$C NMR of 3b
$^1$H NMR of 3b’

$^{13}$C NMR of 3b’
$^1$H NMR of 3c

$^{13}$C NMR of 3c
$^{19}F$ NMR of 3c

$^1H$ NMR of 3d
$^{13}$C NMR of 3d

$^{19}$F NMR of 3d
$^1$H NMR of 3e

$^{13}$C NMR of 3e
$^{19}$F NMR of 3e

$^1$H NMR of 3f
$^{13}$C NMR of 3f

$^{19}$F NMR of 3f
$^1$H NMR of 3g

$^{13}$C NMR of 3g
$^{19}$F NMR of 3g

$^1$H NMR of 3h
$^{13}$C NMR of 3h

$^{19}$F NMR of 3h
$^1$H NMR of 3i

$^{13}$C NMR of 3i
$^1$H NMR of 3j

$^{13}$C NMR of 3j
$^1$H NMR of 3k

$^{19}$F NMR of 3j
$^{13}$C NMR of 3k

$^1$H NMR of 6a
$^{13}$C NMR of 6a

$^{19}$F NMR of 6a
$^1$H NMR of 6b

$^{13}$C NMR of 6b
$^1$H NMR of 6c

$^{19}$F NMR of 6b
$^{13}$C NMR of 6c

$^{19}$F NMR of 6c
**$^1$H NMR of 6d**

![H NMR spectrum of 6d]

**$^{13}$C NMR of 6d**

![C NMR spectrum of 6d]
$^{19}$F NMR of 6d

$^1$H NMR of 6e
$^{13}$C NMR of 6e

$^{19}$F NMR of 6e
$^1$H NMR of 6f

$^{13}$C NMR of 6f
$^{19}$F NMR of 6f

$^1$H NMR of 6g
$^{13}$C NMR of 6g

$^{19}$F NMR of 6g
$^1$H NMR of 6h

$^{13}$C NMR of 6h
$^1$H NMR of 6i

$^{13}$C NMR of 6i
$^{19}$F NMR of 6i

$^1$H NMR of 7
$^{13}$C NMR of 7

$^1$H NMR of 9
$^{13}$C NMR of 9

$^1$H NMR of 10
$^{13}$C NMR of 10