Electronic Supporting Information

Development of sulfonyl fluoride chemical probes to advance the discovery of cereblon modulators

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Contents

<table>
<thead>
<tr>
<th>Contents</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellular CRBN NanoBRET engagement assay</td>
<td>S2</td>
</tr>
<tr>
<td>Cellular IKZF1 HiBiT degradation assay</td>
<td>S3</td>
</tr>
<tr>
<td>MS Proteomics</td>
<td>S4</td>
</tr>
<tr>
<td>Hazards</td>
<td>S5</td>
</tr>
<tr>
<td>Compound Syntheses</td>
<td>S5</td>
</tr>
<tr>
<td>NMR Spectra</td>
<td>S27</td>
</tr>
<tr>
<td>References</td>
<td>S37</td>
</tr>
</tbody>
</table>
Cellular CRBN NanoBRET engagement assay

HEK293T cells were transduced with lentivirus and put under puromycin selection (5 μg/mL) for two weeks to produce a cell line stably expressing CRBN with N-terminally fused NanoLuc luciferase (NanoLuc-CRBN). After antibiotic selection, cells were cultured in DMEM (Gibco, Life Technologies) supplemented with 10% FBS and 1 μg/mL puromycin to maintain stable NanoLuc-CRBN expression. To run the assay, cells were cultured to confluency in 10 cm² tissue culture treated plates (Corning, 430165), washed with PBS and trypsinized at room temperature to detach from the cell culture plate. After 3-4 min, the trypsin was quenched with 5x volume DMEM media (Gibco, Life Technologies) with 10% FBS and cells were collected by centrifugation (1000 rpm, 5 min). The supernatant was removed by vacuum aspiration and the pellet was then resuspended in Opti-MEM without phenol red. The density of this cell suspension was determined by diluting the cells 1:1 with trypan blue and counting using a Countess II (Thermo Fischer Scientific). The required volume of the cell suspension was prepared at 2 x 10⁵ viable cells/mL in Opti-MEM I (Gibco, Life Technologies). To this suspension was added the CRBN engagement tracer (stock at 10 μM in 31.25% PEG-400, 12.5 mM HEPES, pH 7.5, filtered using a 0.22 μm nitrocellulose membrane; final concentration in cell suspension for assay at 250 nM). Cells were then plated in a white/opaque cell culture treated 384-well plate (Corning, 3570) at volume of 50 μL/well. After plating, the assay plate was centrifuged (500 x g, 5 min) and covered in aluminum foil. Compounds for testing were added to the plate using a D300e Digital Dispenser (HP) in duplicate 12-pt titrations from a 10 mM stock in DMSO, with DMSO normalized to 1% total volume. The plate was then placed in an incubator at 37 °C, 5% CO₂ for two hours. After incubation, the plate was removed and set on the bench to cool to room temperature (~10-15 min). The NanoLuc substrate (500X solution) and extracellular inhibitor (1500X solution) were diluted in Opti-MEM I (Gibco, Life Technologies) to prepare a 3X solution. This was then added to each well (25 μL/well). The plate was read on a Pherastar FSX microplate reader with simultaneous dual emission capabilities to read 384-well plates at 450 and 520 nm. The NanoBRET ratio was calculated by dividing the signal at 520 nm by the signal at 450 nm for each sample. Duplicate points were averaged and plotted against [compound, M] to generate an EC₅₀ curve. The Nluc substrate and extracellular inhibitor were purchased as a kit from Promega Corporation and used as is from the box - Promega NanoBRET Nano-Glo Substrate/Inhibitor; Promega Catalog number N2161 for 10,000 assay kit. Compound data are shown in Figure S1.
Figure S1. NanoBRET CRBN engagement assay. Compounds were dispensed in duplicate 11-point dose response (N=2). IC\textsubscript{50} values were determined with Prism 9 Variable Slope model and are shown as IC\textsubscript{50} ± standard error.

**Cellular IKZF1 HiBiT degradation assay**

Previously described HiBiT-IKZF1 MOLT4 cells were used in the assay.\(^2\) To run the assay, compounds were first dispensed ranging from 10 \(\mu\text{M}\) in 3-fold dilution into 384-well white flat bottom TC-treated plates (Corning, 3570). Then 4000 cells per well in 50 \(\mu\text{L}\) of media were plated. Cells were mixed, centrifuged at 500 rpm for 1 min, and incubated for 24h at 37\(^\circ\)C, 5\% CO\(_2\). Before reading, plates were equilibrated to room temperature, while HiBiT lytic reagent was prepared according to manufacturer’s instructions (Promega): for 10 mL of reagent, dilute 200 \(\mu\text{L}\) HiBiT substrate and 100 \(\mu\text{L}\) of LgBiT protein in 10 mL of lytic buffer. 12.5 \(\mu\text{L}\) of prepared reagent was added to each well (1:4 dilution). Plates were shaken at room temperature for 10 min under aluminum foil cover, then read on an EnVision plate reader (Perkin Elmer). For data analysis, DMSO-treated samples were averaged, and %DMSO treated was calculated for each test sample. Data were analyzed using GraphPad Prism 9 and dose response curves were fitted using Variable Slope equation model.
Mass spectrometry proteomics

Broad degradation capacity of key compounds was performed using quantitative MS proteomics. Assessment of EM364 was performed in MOLT4 cells using a previously reported procedure. The ability for EM12 and CPD-2743 to degrade SALL4 was assessed using Kelly cells (which do not express IKZF1) using a previously reported procedure (pomalidomide and CC-220 were used as positive SALL4 degrader controls in the experiment). All compounds were run at 1 μM concentration for 6 hours to avoid any indirect protein downregulation effects.

Figure S2. MS proteomics for key compounds EM364-SF (MOLT4 cells), and EM12, CPD-2743, CC-220 (iberdomide) and pomalidomide (Kelly cells).
Hazards

All IMiD derivative compounds are teratogenicity risks. Follow additional guidance in safety data sheets.

Compound Syntheses

Synthesis of 3-oxo-2-(6-oxopiperidin-3-yl)isoindoline-5-sulfonyl fluoride (CPD-2130)

6-bromo-2-(6-oxopiperidin-3-yl)isoindolin-1-one To a solution of methyl 5-bromo-2-(bromomethyl) benzoate (1.8 g, 5.84 mmol, 1 eq) in NMP (10 mL) was added DIEA (2.27 g, 17.53 mmol, 3 mL, 3 eq) and 5-aminopiperidin-2-one (880 mg, 5.84 mmol, 1 eq, HCl). The mixture was stirred at 100 °C for 2 h. The reaction mixture was poured into H₂O (20 mL), while yellow solid formed. The solid was filtered and washed by H₂O (5 mL x 2). The filter cake was collected and dried under reduced pressure to give a residue. The crude product was triturated with PE/EtOAc (4/1, 20 mL) to afford the title compound (150 mg, 8% yield) as a yellow solid. ¹H NMR (400 MHz, DMSO-d₆) δ = 7.75-7.87 (m, 2H), 7.50-7.65 (m, 2H), 4.50 (d, J = 3.13 Hz, 2H), 4.32-4.42 (m, 1H), 3.21-3.32 (m, 2H), 2.26-2.49 (m, 2H), 2.05-2.17 (m, 1H), 1.88-1.98 (m, 1H).
6-(benzylthio)-2-(6-oxopiperidin-3-yl)isoindolin-1-one A mixture of 6-bromo-2-(6-oxo-3-piperidyl)isoindolin-1-one (0.15 g, 485 umol, 1 eq), phenylmethanethiol (72 mg, 582 umol, 68 uL, 1.2 eq), Pd$_2$(dba)$_3$ (22 mg, 24 umol, 0.05 eq), Xantphos (28 mg, 48 umol, 0.1 eq) and DIEA (125 mg, 970 umol, 169 uL, 2 eq) in dioxane (5 mL) was degassed and purged with N$_2$ for 3 times, and then the mixture was stirred at 110 °C for 12 h under N$_2$ atmosphere. The mixture was filtered through the celite and washed by EtOAc (50 mL x 3). The filtrate was concentrated under reduced pressure to give a residue. The residue was triturated by PE/EtOAc (4/1, 100 mL) to afford the title compound (0.15 g, 88% yield) as a yellow solid.

![3-oxo-2-(6-oxopiperidin-3-yl)isoindoline-5-sulfonyl chloride](image)

3-oxo-2-(6-oxopiperidin-3-yl)isoindoline-5-sulfonyl chloride To a solution of 6-benzylsulfanyl-2-(6-oxo-3-piperidyl)isoindolin-1-one (0.15 g, 425 umol, 1 eq) in AcOH (1.8 mL) and H$_2$O (0.2 mL) was added NCS (113 mg, 851 umol, 2 eq). The mixture was stirred at 20 °C for 2 h. The reaction mixture was concentrated under reduced pressure to afford the title compound (0.12 g, crude) as yellow oil.

![3-oxo-2-(6-oxopiperidin-3-yl)isoindoline-5-sulfonyl fluoride (CPD-2130)](image)

3-oxo-2-(6-oxopiperidin-3-yl)isoindoline-5-sulfonyl fluoride (CPD-2130) To a solution of 3-oxo-2-(6-oxo-3-piperidyl)isoindoline-5-sulfonyl chloride (0.12 g, 365 umol, 1 eq) in THF (2 mL) and H$_2$O (0.1 mL) was added KF (63 mg, 1.09 mmol, 25 uL, 3 eq). The mixture was stirred at 20 °C for 1 h. The reaction mixture was concentrated under reduced pressure to give a residue. The residue was purified by prep-HPLC to afford the title compound (19 mg, 16% yield, 98.3% HPLC purity) as a white solid. MS (M+H$^+$): 312.9. $^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ = 8.38 (dd, J = 1.69, 8.07 Hz, 1H), 8.28 (d, J = 1.38 Hz, 1H), 8.06 (d, J = 8.00 Hz, 1H), 7.66 (br s, 1H), 4.74 (d, J = 3.25 Hz, 2H), 4.37-4.50 (m, 1H), 3.22-3.43 (m, 2H), 2.28-2.49 (m, 2H), 2.06-2.22 (m, 1H), 1.93-2.06 (m, 1H). $^{19}$F NMR: (376 MHz, DMSO-d$_6$) $\delta$ = 66.89 (s, 1F). HRMS (m/z) for C$_{13}$H$_{14}$FN$_2$O$_4$S$^+$ [M + H$^+$]: calcd, 313.0653; found, 313.0657.
Synthesis of 2-(2,6-dioxopiperidin-3-yl)isoindoline-5-sulfonyl fluoride (CPD-2158)

3-(5-bromoisoindolin-2-yl)piperidine-2,6-dione

To a solution of 3-bromopiperidine-2,6-dione (818 mg, 4.26 mmol, 1 eq) and 5-bromoisoindoline (1g, 4.26 mmol, 1 eq, HCl) in DMF (10 mL) was added DIEA (1.65 g, 12.79 mmol, 2.2 mL, 3 eq). The mixture was stirred at 25 °C for 12 h and 60 °C for 1 h. The reaction mixture was poured into H$_2$O (100 mL), and extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine (50 mL x 2), dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure to give a residue. The residue was purified by column chromatography to afford the title compound (740 mg, 56% yield) as a gray solid. $^1$H NMR (400 MHz, DMSO-$_d$6) $\delta$ = 10.75 (s, 1H), 7.47 (s, 1H), 7.39 (dd, $J$ = 1.75, 8.00 Hz, 1H), 7.22 (d, $J$ = 8.00 Hz, 1H), 3.99-4.18 (m, 4H), 3.65 (dd, $J$ = 5.00, 8.50 Hz, 1H), 2.58 (t, $J$ = 6.44 Hz, 2H), 1.97-2.12 (m, 2H)

3-(5-(benzylthio)isoindolin-2-yl)piperidine-2,6-dione

A mixture of 3-(5-bromoisoindolin-2-yl)piperidine-2,6-dione (350 mg, 1.13 mmol, 1 eq), phenylmethanethiol (168 mg, 1.36 mmol, 159 uL, 1.2 eq), Pd$_2$(dba)$_3$ (52 mg, 56 umol, 0.05 eq), Xantphos (65 mg, 113 umol, 0.1 eq) and DIEA
(292 mg, 2.26 mmol, 394 uL, 2 eq) in dioxane (6 mL) was degassed and purged with N₂ for 3 times, and then the mixture was stirred at 110 °C for 12 h under N₂ atmosphere. The reaction mixture was poured into H₂O (30 mL), and extracted with EtOAc (20 mL x 3). The combined organic layers were washed with brine (30 mL x 2), dried over Na₂SO₄, filtered and concentrated under reduced pressure to give a residue. The residue was purified by column chromatography to afford the title compound (330 mg, 83% yield) as a black oil. ¹H NMR (400 MHz, DMSO-d₆) δ = 10.74 (s, 1H), 7.28-7.35 (m, 4H), 7.19-7.25 (m, 2H), 7.14-7.18 (m, 2H), 4.21 (s, 2H), 3.99-4.11 (m, 4H), 3.62 (dd, J = 4.75, 8.38 Hz, 1H), 2.57 (t, J = 6.38 Hz, 2H), 2.01-2.09 (m, 2H)

2-(2,6-dioxopiperidin-3-yl)isoindoline-5-sulfonyl chloride To a solution of 3-(5-benzylsulfanylisoindolin-2-yl)piperidine-2,6-dione (100 mg, 283 umol, 1 eq) in AcOH (2.7 mL) and H₂O (0.3 mL) was added NCS (113 mg, 851 umol, 3 eq). The mixture was stirred at 20 °C for 2 h to afford the title compound (90 mg, crude) as a yellow oil. It was used directly into next step without further purification.

2-(2,6-dioxopiperidin-3-yl)isoindoline-5-sulfonyl fluoride To a solution of 2-(2,6-dioxo-3-piperidyl)isoindoline-5-sulfonyl chloride (60 mg, 182 umol, 1 eq) in THF (0.6 mL) was added KF (32 mg, 547 umol, 13 uL, 3 eq). The mixture was stirred at 25 °C for 1 h. The residue was purified by prep-HPLC to afford the title compound (40 mg, 70% yield, 99.4% HPLC purity) as a white solid. MS (M+H⁺): 312.9. ¹H NMR (400 MHz, DMSO-d₆) δ = 11.29 (br s, 1H), 8.21 (s, 1H), 8.14 (br d, J = 8.03 Hz, 1H), 7.79 (br d, J=8.28 Hz, 1H), 4.62-4.95 (m, 5H), 2.63-2.69 (m, 2H), 2.13-2.26 (m, 2H). ¹⁹F NMR: (376 MHz, DMSO-d₆) δ = 66.71 (s, 1F). HRMS (m/z) for C₁₃H₁₄FN₂O₄S⁺ [M + H]⁺: calcd, 313.0653; found, 313.0656.
Synthesis of 2-(1-methyl-2,6-dioxopiperidin-3-yl)-3-oxoisooindoline-5-sulfonfyl fluoride (CPD-2129)

3-(6-bromo-1-oxoisooindolin-2-yl)-1-methylpiperidine-2,6-dione To a solution of 3-(6-bromo-1-oxoisooindolin-2-yl)piperidine-2,6-dione (1 g, 3.09 mmol, 1 eq) in DMF (10 mL) was added K$_2$CO$_3$ (855 mg, 6.19 mmol, 2 eq) and CH$_3$I (790 mg, 5.57 mmol, 346 uL, 1.8 eq). The mixture was stirred at 20 °C for 12 h. It was filtered and concentrated under reduced pressure to give a residue. Then the reaction mixture was poured into H$_2$O (20 mL), and extracted with EtOAc (20 mL x 3). The combined organic layers were washed with brine (20 mL x 2), dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure to afford the title compound (1 g, 96% yield) as a white solid. $^1$H NMR (400 MHz, DMSO-d$_6$) δ = 7.88 (d, J = 1.63 Hz, 1H), 7.82 (br d, J = 1.88 Hz, 1H), 7.59-7.63 (m, 1H), 5.19 (dd, J = 5.07, 13.45 Hz, 1H), 4.42-4.49 (m, 1H), 4.28-4.36 (m, 1H), 3.01 (s, 3H), 2.93-3.00 (m, 1H), 2.73-2.81 (m, 1H), 2.34-2.46 (m, 1H), 2.00-2.08 (m, 1H).

3-(6-(benzylthio)-1-oxoisooindolin-2-yl)-1-methylpiperidine-2,6-dione A mixture of 3-(6-bromo-1-oxoisooindolin-2-yl)-1-methyl-piperidine-2,6-dione (0.5 g, 1.48 mmol, 1 eq), phenylmethanethiol (221 mg, 1.78 mmol, 208 uL, 1.2 eq), Pd$_2$(dba)$_3$ (68 mg, 74 umol, 0.05 eq), Xantphos (86 mg, 148 umol, 0.1 eq) and DIEA (383 mg, 2.97 mmol, 516 uL, 2 eq) in dioxane (5
mL) was degassed and purged with N₂ for 3 times, and then the mixture was stirred at 110 °C for 3 h under N₂ atmosphere. The mixture was filtered through the celite, and washed by EtOAc (20 mL x 3). The filtrate was concentrated under reduced pressure to give a residue. The residue was purified by column chromatography to afford the title compound (0.5 g, 88% yield) as a yellow solid. 

\[ \text{1H NMR (400 MHz, DMSO-}d_6) \delta = 7.60-7.62 \text{ (m, 1H), 7.56 (br d, J = 1.75 Hz, 1H), 7.48 (s, 1H), 7.31-7.36 (m, 2H), 7.24-7.29 (m, 2H), 7.17-7.22 (m, 1H), 5.10-5.16 (m, 1H), 4.34-4.43 (m, 1H), 4.29-4.32 (m, 2H), 4.20-4.28 (m, 1H), 2.96 (s, 3H), 2.89-2.95 (m, 1H), 2.68-2.76 (m, 1H), 2.27-2.41 (m, 1H), 1.93-2.02 (m, 1H).} \]

![Chemical structure](image)

**2-(1-methyl-2,6-dioxopiperidin-3-yl)-3-oxoisoindoline-5-sulfonyl chloride** To a solution of 3-(6-benzylsulfanyl-1-oxo-isoindolin-2-yl)-1-methyl-piperidine-2,6-dione (0.2 g, 525 umol, 1 eq) in AcOH (7 mL) and H₂O (0.8 mL) was added NCS (210 mg, 1.58 mmol, 3 eq). The mixture was stirred at 20 °C for 2 h to afford the title compound (180 mg, crude) as a yellow oil. It was used directly into next step without further purification.

![Chemical structure](image)

**2-(1-methyl-2,6-dioxopiperidin-3-yl)-3-oxoisoindoline-5-sulfonyl fluoride** To a solution of 2-(1-methyl-2,6-dioxo-3-piperidyl)-3-oxo-isoindoline-5-sulfonyl chloride (0.18 g, 504 umol, 1 eq) in acetone (1 mL) and H₂O (1 mL) was added KF (439 mg, 7.57 mmol, 177 uL, 15 eq). The mixture was stirred at 20 °C for 1 h. The reaction was concentrated by vacuum. The residue was purified by prep-HPLC to afford the title compound (2 mg, 1% yield, 98.7% purity) as a white solid. MS (M+H⁺): 341.0. 

\[ \text{1H NMR (400 MHz, DMSO-}d_6) \delta = 8.39-8.43 \text{ (m, 1H), 8.31-8.35 (m, 1H), 8.04-8.09 (m, 1H), 5.21-5.28 (m, 1H), 4.65-4.72 (m, 1H), 4.51-4.58 (m, 1H), 3.00-3.02 (m, 3H), 2.74-2.82 (m, 1H), 2.53-2.58 (m, 1H), 2.40-2.46 (m, 1H), 2.02-2.10 (m, 1H).} \]

\[ \text{19F NMR (376 MHz,} \]
DMSO-d6): δ = 66.87 (s, 1F). HRMS (m/z) for C_{14}H_{14}FN_{2}O_{5}S^{+} [M + H]^+: calcd, 341.0602; found, 341.0603.

**Synthesis of 3-(4-((4-(morpholinomethyl)benzyl)oxy)isoindolin-2-yl)piperidine-2,6-dione (CPD-2743)**

**tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoindoline-2-carboxylate**

A mixture of tert-butyl 4-bromoisoindoline-2-carboxylate (1.7 g, 5.70 mmol, 1 eq) and BPD (1.74 g, 6.84 mmol, 1.2 eq) in dioxane (17 mL) was added KOAc (1.12 g, 11.40 mmol, 2 eq) and stirred at 20 °C for 15 min under N_{2} atmosphere. Then Pd(dppf)Cl_{2} (417 mg, 570 umol, 0.1 eq) was added to solution. The mixture was stirred at 110 °C for 12h. The reaction mixture was poured into H_{2}O.
(50 mL), and extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine (50 mL x 2), dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure to give a residue. The residue was purified by column chromatography to afford the title compound (1.85 g, 94% yield) as a white solid. $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta = 7.59-7.70$ (m, 1H), 7.46-7.56 (m, 1H), 7.29-7.39 (m, 1H), 4.57-4.79 (m, 4H), 1.46-1.57 (m, 9H), 1.33-1.44 (m, 12H).

**tert-butyl 4-hydroxyisoindoline-2-carboxylate**

To a solution of tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)isoindoline-2-carboxylate (1.65 g, 4.78 mmol, 1 eq) in THF (33 mL) and H$_2$O (16.5 mL) was added NaBO$_3$ (2.50 g, 16.25 mmol, 3 mL, 3.4 eq). The mixture was stirred at 20 °C for 16 h. The reaction mixture was poured into H$_2$O (50 mL), and extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine (50 mL x 2), dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure to give a residue. The residue was purified by column chromatography to afford the title compound (1 g, 89% yield) as a white solid. $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta = 9.59-9.66$ (m, 1H), 7.05-7.13 (m, 1H), 6.71-6.78 (m, 1H), 6.63-6.70 (m, 1H), 4.51-4.58 (m, 2H), 4.41-4.50 (m, 2H), 1.43-1.48 (m, 9H).

**tert-butyl 4-((4-(morpholinomethyl)phenyl)methyl)oxy)isoindoline-2-carboxylate**

To a solution of tert-butyl 4-hydroxyisoindoline-2-carboxylate (0.2 g, 850 umol, 1 eq) and 4-[(4-chloromethyl)phenyl)methyl]morpholine (178 mg, 680 umol, 0.8 eq, HCl) in DMF (4 mL) was added K$_2$CO$_3$ (235 mg, 1.70 mmol, 2 eq). The mixture was stirred at 50 °C for 12 h. The reaction mixture was poured into H$_2$O (50 mL), and extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine (50 mL x 2), dried over Na$_2$SO$_4$, filtered and concentrated.
under reduced pressure to give a residue. The residue was purified by column chromatography to afford the title compound (0.19 g, 53% yield) as a yellow oil. \(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \(\delta = 7.43-7.48\) (m, 2H), 7.36-7.40 (m, 2H), 7.30 (t, \(J=7.84\) Hz, 1H), 7.01 (br d, \(J=8.28\) Hz, 1H), 6.96 (dd, \(J=3.58, 7.47\) Hz, 1H), 5.20 (s, 2H), 4.63 (br d, \(J=11.42\) Hz, 2H), 4.56 (br s, 2H), 3.58-3.65 (m, 4H), 3.51 (s, 2H), 2.40 (br s, 4H), 1.51 (s, 9H).

4-(4-(((isoindolin-4-yloxy)methyl)benzyl)morpholine The solution of tert-butyl 4-[[4-(morpholinomethyl)phenyl]methoxy]isoindoline -2-carboxylate (0.19 g, 447 umol, 1 eq) in HCl/EtOAc (5 mL) was stirred at 20 °C for 2 h. The mixture was concentrated in vacuum to afford the title compound (0.14 g, crude) as a white solid. It was used directly into next step without further purification.

3-(4-((4-(morpholinomethyl)benzyl)oxy)isoindolin-2-yl)piperidine-2,6-dione To a solution of 4-[[4-(isoindolin-4-yl oxy)methyl]phenyl)methyl]morpholine (0.11 g, 305 umol, 1 eq, HCl) and 3-bromopiperidine-2,6-dione (70 mg, 366 umol, 1.2 eq) in DMF (2 mL) was added NaHCO\(_3\) (77 mg, 914 umol, 35 uL, 3 eq). The mixture was stirred at 80 °C for 6 h. The mixture was added HCl/EtOAc (3mL) and removed the solvent by \(N_2\) flow. The residue was purified by prep-HPLC.
to afford the title compound (27 mg, 20% yield, 99.4% HPLC purity) as a white solid. MS (M+H\(^+\)): 436.2. \(^1\)H NMR (400 MHz, DMSO-\(d_6\)) \(\delta = 10.77\) (s, 1H), 8.20 (s, 1H), 7.42-7.47 (m, 2H), 7.35-7.39 (m, 2H), 7.22 (t, J = 7.82 Hz, 1H), 6.95 (d, J = 8.13 Hz, 1H), 6.89 (d, J = 7.38 Hz, 1H), 5.16 (s, 2H), 4.05-4.21 (m, 4H), 3.69 (dd, J = 4.25, 9.13 Hz, 1H), 3.59-3.65 (m, 4H), 2.62 (br t, J = 6.38 Hz, 2H), 2.56-2.57 (m, 2H), 2.34-2.43 (m, 4H), 2.02-2.19 (m, 2H). HRMS (\(m/z\)) for C\(_{25}\)H\(_{30}\)N\(_3\)O\(_4\)\(^+\)[M + H\(^+\)]: calcd, 436.2231; found, 436.2229.


(2S)-\(N\)-[(3-bromophenyl)methyl]-5-oxo-pyrrolidine-2-carboxamide To a solution of (2S)-5-oxopyrrolidine-2-carboxylic acid (1 g, 7.75 mmol, 1 eq), HOBt (1.15 g, 8.52 mmol, 1.1 eq), EDCI (1.63 g, 8.52 mmol, 1.1 eq) and DIEA (2.00 g, 15.5 mmol, 2.7 mL, 2 eq) in DCM (20 mL) was added (3-bromophenyl)methanamine (1.59 g, 8.52 mmol, 1.1 eq). The mixture was stirred at 20 °C for 12 h. After completion of the reaction, the mixture was poured into H\(_2\)O (50 mL), and
extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine (50 mL x 2), dried over Na₂SO₄, filtered and concentrated under reduced pressure to give a residue. The residue was purified by column chromatography to afford the title compound (1 g, 41% yield, 93.4% purity, 100% ee) as a yellow solid. 

\[ ^1H \text{NMR (400 MHz, DMSO-}d_6\text{)} \delta = 8.57 \text{ (t, J = 6.0 Hz, 1H), } 7.80 \text{ (s, 1H), } 7.48-7.40 \text{ (m, 2H), } 7.33-7.27 \text{ (m, 2H), } 4.30 \text{ (d, J = 6.0 Hz, 1H), } 4.07-4.04 \text{ (m, 2H), } 2.35-2.28 \text{ (m, 1H), } 2.23-2.05 \text{ (m, 2H), } 1.92-1.89 \text{ (m, 1H).} \]

(2S)-N-[(3-benzylsulfanylphenyl)methyl]-5-oxo-pyrrolidine-2-carboxamide To a solution of (2S)-N-[(3-bromophenyl)methyl]-5-oxo-pyrrolidine-2-carboxamide (0.5 g, 1.68 mmol, 1 eq) and phenylmethanethiol (229 mg, 1.85 mmol, 216 uL, 1.1 eq) in dioxane (5 mL) was added DIEA (434 mg, 3.37 mmol, 586 uL, 2 eq) and Pd₂(dba)₃ (92 mg, 101 umol, 0.06 eq) and Xantphos (116 mg, 201 umol, 0.12 eq). The mixture was stirred at 120 °C for 5 h. After completion of the reaction, the mixture was poured into H₂O (50 mL), and extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine (50 mL x 2), dried over Na₂SO₄, filtered and concentrated under reduced pressure to give a residue. The residue was purified by column chromatography to afford the title compound (250 mg, 43% yield) as a yellow oil. 

\[ ^1H \text{NMR (400 MHz, DMSO-}d_6\text{)} \delta = 8.57 \text{ (t, J = 6.0 Hz, 1H), } 7.80 \text{ (s, 1H), } 7.48-7.40 \text{ (m, 2H), } 7.37-7.30 \text{ (m, 2H), } 7.28-7.22 \text{ (m, 4H), } 7.11-7.05 \text{ (m, 1H), } 4.33-4.21 \text{ (m, 4H), } 4.07-4.04 \text{ (m, 1H), } 2.31-2.15 \text{ (m, 1H), } 2.13-2.10 \text{ (m, 2H), } 1.92-1.89 \text{ (m, 1H).} \]
(S)-3-((5-oxopyrrolidine-2-carboxamido)methyl)benzenesulfonyl chloride To a solution of (2S)-N-[(3-benzylsulfanylphenyl)methyl]-5-oxo-pyrrolidine-2-carboxamide (200 mg, 587 umol, 1 eq) in AcOH (2.7 mL) and H2O (0.3 mL) was added NCS (94 mg, 704 umol, 1.2 eq). The mixture was stirred at 40 °C for 6 h. After completion of the reaction, the title compound as a black solution in AcOH/H2O was used into the next step without further purification.


To a solution of 3-[[[(2S)-5-oxopyrrolidine-2-carbonyl]amino]methyl]benzenesulfonyl chloride (200 mg, 631 umol, 1 eq) in H2O (4 mL) and acetone (4 mL) was added KF (550 mg, 9.47 mmol, 221 uL, 15 eq). The mixture was stirred at 20 °C for 1 h. After completion of the reaction, the reaction was diluted with ACN (2 mL), and used for purification directly without further work-up. The residue was purified by prep-HPLC to afford title compound (68 mg, 35% yield, 97.3% HPLC purity, 100% ee) as a white solid. MS (M+H+): 301.0. 1H NMR (400 MHz, DMSO-d6) δ = 8.68 (t, J = 6.0 Hz, 1H), 8.04-8.02 (m, 2H), 7.95 (s, 1H), 7.86-7.84 (m, 1H), 7.80-7.76 (m, 1H), 4.37 (d, J = 6.0 Hz, 2H), 4.09-4.02 (m, 1H), 2.34-2.29 (m, 1H), 2.18-2.13 (m, 2H), 1.98-1.80 (m, 1H). HRMS (m/z) for C12H14FN2O4S+ [M + H]+: calcd, 301.0653; found, 301.0656.

(2S)-N-[(3-bromophenyl)methyl]-5-oxo-pyrrolidine-2-carboxamide To a solution of (2R)-5-oxopyrrolidine-2-carboxylic acid (1 g, 7.75 mmol, 1 eq) and (3-bromophenyl)methanamine (1.59 g, 8.53 mmol, 1.1 mL, 1.1 eq) in DCM (12 mL) was added HOBt (1.15 g, 8.53 mmol, 1.1 eq) and EDCI (1.63 g, 8.53 mmol, 1.1 eq) and DIEA (2.00 g, 15.5 mmol, 2.7 mL, 2 eq). The mixture was stirred at 20 °C for 12 h. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure to give a residue. The residue was purified by column chromatography to afford title compound (1.57 g, 66% yield, 97.6% HPLC purity, 100% ee) as a white solid. $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta = 8.55$ (t, J = 6.0 Hz, 1H), 7.87 (s, 1H), 7.46-7.43 (m, 2H), 7.32-7.25 (m, 2H), 4.27 (d, J = 6.0 Hz, 2H), 4.05-4.02 (m, 1H), 2.26-2.10 (m, 3H), 1.89-1.88 (m, 1H).
(2R)-N-[(3-benzylsulfanylphenyl)methyl]-5-oxo-pyrrolidine-2-carboxamide  A mixture of (2R)-N-[(3-bromophenyl)methyl]-5-oxo-pyrrolidine-2-carboxamide (0.77 g, 2.59 mmol, 1 eq), phenylmethanethiol (354 mg, 2.85 mmol, 334 uL, 1.1 eq), DIEA (670 mg, 5.18 mmol, 903 uL, 2 eq), Pd2(dba)3 (142 mg, 155 umol, 0.06 eq) and Xantphos (180 mg, 311 umol, 0.12 eq) in dioxane (16 mL) was degassed and purged with N2 for 3 times, and then the mixture was stirred at 120 °C for 5 h under N2 atmosphere. After the completion of the reaction, the mixture was poured into H2O (30 mL), and extracted with EtOAc (30 mL x 3). The combined organic layers were washed with brine (30 mL x 2), dried over Na2SO4, filtered and concentrated under reduced pressure to give a residue. The residue was purified by column chromatography to afford title compound (0.76 g, 73% yield) as a white solid. 1H NMR (400 MHz, DMSO-d6) δ = 8.55 (t, J = 6.0 Hz, 1H), 7.87 (s, 1H), 7.46-7.30 (m, 9H), 7.10-7.07 (m, 1H), 4.27-4.35 (m, 4H), 4.05-4.02 (m, 1H), 2.35-2.10 (m, 3H), 1.89-1.88 (m, 1H).

3-[[[(2R)-5-oxopyrrolidine-2-carbonyl]amino[methyl]benzenesulfonyl chloride  To a solution of (2R)-N-[(3-benzylsulfanylphenyl)methyl]-5-oxo-pyrrolidine-2-carboxamide (0.3 g, 881 umol, 1 eq) in AcOH (12 mL) and H2O (1.8 mL) was added NCS (353 mg, 2.64 mmol, 3 eq). The mixture was stirred at 20 °C for 12 h. After the completion of the reaction, the mixture was poured into H2O (20 mL), and extracted with EtOAc (20 mL x 3). The combined organic layers were washed with brine (20 mL x 2), dried over Na2SO4, filtered and concentrated under reduced pressure to give a residue to afford title compound (0.34 g, crude) as a white solid.
3-[[[(2R)-5-oxopyrrolidine-2-carbonyl]amino[methyl]benzenesulfonyl fluoride To a solution of 3-[[[(2R)-5-oxopyrrolidine-2-carbonyl]amino[methyl]benzenesulfonyl chloride (340 mg, 1.07 mmol, 1 eq) in acetone (6 mL) and H₂O (6 mL) was added KF (93 mg, 16.10 mmol, 377 uL, 15 eq). The mixture was stirred at 20 °C for 1 h. After the completion of the reaction, the mixture was poured into H₂O (20 mL), and extracted with EtOAc (20 mL x 3). The combined organic layers were washed with brine (20 mL x 2), dried over Na₂SO₄, filtered and concentrated under reduced pressure to give a residue. The residue was purified by prep-HPLC to afford the title compound (82 mg, 25% yield, 97.5% HPLC purity, 99.7% ee) as a white solid. MS (M+H⁺): 301.0. ¹H NMR (400 MHz, DMSO-d₆) δ = 8.71 (t, J = 6.0 Hz, 1H), 8.04-8.02 (m, 2H), 7.90 (s, 1H), 7.86-7.84 (m, 1H), 7.78-7.75 (m 1H), 4.44 (d, J = 6.0 Hz, 2H), 4.08-4.04 (m, 1H), 2.37-2.27 (m, 1H), 2.23-2.07 (m, 2H), 1.92-1.84 (m, 1H). ¹⁹F NMR (400 MHz, DMSO-d₆) δ = 66.29 (s, 1F). HRMS (m/z) for C₁₂H₁₄FN₂O₄S⁺ [M + H]⁺: calcd, 301.0653; found, 301.0658.

(2S)-N-[(4-bromophenyl)methyl]-5-oxopyrrolidine-2-carboxamide To a solution of (2S)-5-oxopyrrolidine-2-carboxylic acid (2 g, 15.49 mmol, 1 eq) and (4-bromophenyl)methanamine (3.17 g, 17.0 mmol, 2.1 mL, 1.1 eq) in DCM (24 mL) was added HOBt (2.30 g, 17.0 mmol, 1.1 eq), EDCI (3.27 g, 17.0 mmol, 1.1 eq) and DIEA (4.0 g, 30.9 mmol, 5.4 mL, 2 eq). The mixture was stirred at 20 °C for 12 h. After completion of the reaction, EtOAc/PE (100 mL, 4/1) was added to reaction mixture, while white solid formed. The solid was collected by filtration and the filter cake was washed by PE (20 mL x 2). The cake was dried under reduced pressure to afford the crude title compound (3.85 g) as a white solid. $^1$H NMR (400 MHz, DMSO- $d_6$) δ = 8.56 (t, $J$ = 6.0 Hz, 1H), 7.86 (s, 1H), 7.51 (d, $J$ = 8.4 Hz, 2H), 7.23 (d, $J$ = 8.4 Hz, 2H), 4.25 (d, $J$ = 6.0 Hz, 2H), 4.05-4.02 (m, 1H), 2.18-2.10 (m, 3H), 1.90-1.86 (m, 1H).
(2S)-N-[(4-benzylsulfanylphenyl)methyl]-5-oxo-pyrrolidine-2-carboxamide To a solution of (2S)-N-[(4-bromophenyl)methyl]-5-oxo-pyrrolidine-2-carboxamide (1 g, 3.37 mmol, 1 eq) in dioxane (20 mL) was added phenylmethanethiol (460 mg, 3.70 mmol, 433 uL, 1.1 eq), DIEA (870 mg, 6.73 mmol, 1.2 mL, 2 eq) and Pd$_2$(dba)$_3$ (185 mg, 201 umol, 0.06 eq) and Xantphos (233 mg, 403 umol, 0.12 eq). The mixture was stirred at 120 °C for 5 h. After the completion of the reaction, the mixture was poured into H$_2$O (50 mL), and extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine (50 mL x 2), dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure to give a residue. The residue was purified by column chromatography to afford title compound (0.87 g, 76% yield) as a light-yellow solid. $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ = 8.52 (t, J = 6.0 Hz, 1H), 7.89 (s, 1H), 7.89-7.22 (m, 9H), 4.30-4.28 (m, 4H), 4.09-4.06 (m, 1H), 2.39-2.14 (m, 3H), 1.95-1.92 (m, 1H).

4-[[[(2S)-5-oxopyrrolidine-2-carbonyl]amino]methyl]benzenesulfonyl chloride To a solution of (2S)-N-[(4-benzylsulfanylphenyl)methyl]-5-oxo-pyrrolidine-2-carboxamide (400 mg, 1.17 mmol, 1 eq) in AcOH (14 mL) and H$_2$O (1.6 mL) was added NCS (470 mg, 3.52 mmol, 3 eq). The mixture was stirred at 20 °C for 2 h. After the completion of the reaction, the reaction mixture was poured into H$_2$O (30 mL), and extracted with EtOAc (30 mL x 3). The combined organic layers were washed with brine (30 mL x 2), dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure to afford title compound (0.48 g, crude) as brown oil which was used into the next step without further purification.
4-[[[(2S)-5-oxopyrrolidine-2-carbonyl]amino]methyl]benzenesulfonyl fluoride To a solution of 4-[[[(2S)-5-oxopyrrolidine-2-carbonyl]amino]methyl]benzenesulfonyl chloride (200 mg, 631 μmol, 1 eq) in acetone (2.5 mL) and H₂O (2.5 mL) was added KF (550 mg, 9.47 mmol, 222 μL, 15 eq). The mixture was stirred at 20 °C for 1 h. After the completion of the reaction, the mixture was poured into H₂O (10 mL), and extracted with EtOAc (10 mL x 3). The combined organic layers were washed with brine (10 mL x 2), dried over Na₂SO₄, filtered and concentrated under reduced pressure to give a residue. The residue was purified by prep-HPLC to afford title compound (4 mg, 2% yield, 98.9% HPLC purity, 98.2% ee) as a white solid. MS (M+H⁺): 301.0.

¹H NMR (400 MHz, DMSO-d₆) δ = 8.73 (t, J = 6.0 Hz, 1H), 8.10 (d, J = 8.4 Hz, 2H), 7.89 (s, 1H), 7.65 (d, J = 8.4 Hz, 2H), 4.44 (d, J = 6.0 Hz, 2H), 4.08-4.05 (m, 1H), 2.29-2.12 (m, 3H), 1.94-1.93 (m, 1H). ¹⁹F NMR (400 MHz, DMSO-d₆) δ = 66.623 (s, 1F). HRMS (m/z) for C₁₂H₁₄FN₂O₄S⁺ [M + H]⁺: calcd, 301.0653; found, 301.0658.

N-[(4-bromophenyl)methyl]-5-oxo-pyrrolidine-2-carboxamide  To a solution of 5-oxopyrrolidine-2-carboxylic acid (500 mg, 3.87 mmol, 1 eq) and (4-bromophenyl)methanamine (792 mg, 4.26 mmol, 539 uL, 1.1 eq) in DCM (6 mL) was added HOBt (575 mg, 4.26 mmol, 1.1 eq) and EDCI (816 mg, 4.26 mmol, 1.1 eq) and DIEA (1.00 g, 7.75 mmol, 1.3 mL, 2 eq). The mixture was stirred at 20 °C for 12 h. After the completion of the reaction, the mixture was poured into H₂O (20 mL), and extracted with EtOAc (20 mL x 3). The combined organic layers were washed with brine (20 mL x 2), dried over Na₂SO₄, filtered and concentrated under reduced pressure to give a residue. The residue was purified by column chromatography to afford the title compound (0.39 g, 33% yield, 96.8% HPLC purity, 99.1% ee) as a light-yellow solid. ¹H NMR (400 MHz, DMSO-d6) δ = 8.55 (t, J = 6.0 Hz, 1H), 7.86 (s, 1H), 7.52 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 8.4 Hz, 2H), 4.25 (d, J = 6.0 Hz, 2H), 4.05-4.02 (m, 1H), 2.29-2.18 (m, 1H), 2.16-2.10 (m, 2H), 1.91 (m, 1H).
(2R)-N-([4-benzylsulfanylphenyl)methyl]-5-oxo-pyrrolidine-2-carboxamide To a solution of (2R)-N-[(4-bromophenyl)methyl]-5-oxo-pyrrolidine-2-carboxamide (390 mg, 1.31 mmol, 1 eq) and phenylmethanethiol (179 mg, 1.44 mmol, 169 uL, 1.1 eq) in dioxane (8 mL) was added DIEA (339 mg, 2.62 mmol, 457 uL, 2 eq) and Pd$_2$(dba)$_3$ (72 mg, 78 umol, 0.06 eq) and Xantphos (91 mg, 157 umol, 0.12 eq). The mixture was stirred at 120 °C for 5 h. After the completion of the reaction, the reaction mixture was poured into H$_2$O (50 mL), and extracted with EtOAc (50 mL x 3). The combined organic layers were washed with brine (50 mL x 2), dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure to give a residue. The residue was purified by column chromatography to afford title compound (0.34 g, 76% yield) as a white solid. $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ = 8.47 (t, J = 6.0 Hz, 1H), 7.84 (s, 1H), 7.84-7.17 (m, 9H), 4.4-4.22 (m, 4H), 4.04-4.01 (m, 1H), 2.28-2.11 (m, 3H), 2.09-1.88 (m, 1H).

4-[[[(2R)-5-oxopyrrolidine-2-carbonyl]amino[methyl]benzenesulfonyl chloride To a solution of (2R)-N-[(4-benzylsulfanylphenyl)methyl]-5-oxo-pyrrolidine-2-carboxamide (340 mg, 998 umol, 1 eq) in AcOH (12 mL) and H$_2$O (1 mL) was added NCS (400 mg, 3.00 mmol, 3 eq). The mixture was stirred at 20 °C for 2 h. After the completion of the reaction, the mixture was poured into H$_2$O (20 mL), and extracted with EtOAc (20 mL x 3). The combined organic layers were washed with brine (20 mL x 2), dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure to afford title compound (0.31 g, crude) as a white solid.
4-[[[(2R)-5-oxopyrrolidine-2-carbonyl]amino]methyl]benzenesulfonyl fluoride To a solution of 4-[[[(2R)-5-oxopyrrolidine-2-carbonyl]amino]methyl]benzenesulfonyl chloride (310 mg, 978 umol, 1 eq) in acetone (6 mL) and H₂O (6 mL) was added KF (853 mg, 14.68 mmol, 344 uL, 15 eq). The mixture was stirred at 20 °C for 1 h. After the completion of the reaction, the mixture was poured into H₂O (20 mL), and extracted with EtOAc (20 mL x 3). The combined organic layers were washed with brine (20 mL x 2), dried over Na₂SO₄, filtered and concentrated under reduced pressure to give a residue. The residue was purified by prep-HPLC to afford title compound (83 mg, 28% yield, 99.1% HPLC purity) as a white solid. MS (M+H⁺): 301.0.

1H NMR (400 MHz, DMSO-d6) δ = 8.72 (t, J = 6.0 Hz, 1H), 8.10 (d, J = 8.4 Hz, 2H), 7.88 (s, 1H), 7.65 (d, J = 8.4 Hz, 2H), 4.44 (d, J = 6.0 Hz, 2H), 4.09-4.06 (m, 1H), 2.32-2.12 (m, 3H), 1.93-1.92 (m, 1H).

19F NMR (376 MHz, DMSO-d6) δ = 66.63 (s, 1F). HRMS (m/z) for C₁₂H₁₄FN₂O₄S⁺ [M + H⁺]: calcd, 301.0653; found, 301.0658.

Synthesis of 4-(2-((2,6-dioxopiperidin-3-yl)amino)-2-oxoethyl)benzenesulfonyl fluoride (CPD-363)

4-(2-((2,6-dioxopiperidin-3-yl)amino)-2-oxoethyl)benzenesulfonyl fluoride To a solution of 2-(4-(fluorosulfonyl)phenyl)acetic acid (100 mg, 0.4 mmol), 3-aminopiperidine-2,6-dione (120 mg, 0.68 mmol), EDCI (170 mg, 0.9 mmol), HOBT (90 mg, 0.68 mmol), DIEA (300 mg, 2.25 mmol) in DMF (3 ml) was stirred at rt for 16 h. TLC showed the reaction was completed. The solution
was added water, filtered, washed with Et₂O to afford the title compound (84 mg, 56% yield) as a white solid. ESI-MS (EI+, m/z): 329.10. ¹H NMR (400 MHz, DMSO-d₆): δ 10.86 (s, 1H), 8.62 (d, J = 8.2 Hz, 1H), 8.09 (d, J = 8.5 Hz, 2H), 7.69 (d, J = 8.2 Hz, 2H), 4.56 (q, J = 8.5 Hz, 1H), 3.72 (s, 2H), 2.79–2.66 (m, 1H), 1.96–1.90 (m, 2H). HRMS (m/z) for C₁₃H₁₄FN₂O₅S⁺ [M + H]⁺: calcd, 329.0602; found, 329.0606.

**Synthesis of 3-(2-((2,6-dioxopiperidin-3-yl)amino)-2-oxoethyl)benzenesulfonyl fluoride (CPD-362)**

2-(3-(fluorosulfonyl)phenyl)acetic acid 18-crown-6 (10 mg) was added to a mixture of (3-chlorosulfonyl-phenyl)-acetic acid (118 mg, 0.50 mmol) and Potassium hydrogen fluoride (58 mg, 1.0 mmol) in 1.0 mL of acetonitrile, and the mixture was stirred at rt for 16 h. LCMS showed the reaction was completed. The mixture was concentrated to remove the solvents, the residue was purified by prep-TLC to afford the title product (32 mg, 29% yield) as a yellow solid. ¹H NMR (400 MHz, DMSO-d₆): δ 8.07 (d, J = 1.8 Hz, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.85 (d, J = 7.8 Hz, 1H), 7.74 (t, J = 7.8 Hz, 1H), 3.83 (s, 2H).

**3-(2-((2,6-dioxopiperidin-3-yl)amino)-2-oxoethyl)benzenesulfonyl fluoride** Following general procedure of CPD-363 to afford the desired product CPD-362 (15 mg, 50% yield) as a yellow
powder. ESI-MS (EI+, m/z) :329.10. $^1$H NMR (400 MHz, DMSO-$d_6$) δ 10.85 (s, 1H), 8.60 (d, $J = 8.1$ Hz, 1H), 8.08 (br, 1H), 8.02 (d, $J = 7.9$ Hz, 1H), 7.86 (d, $J = 7.7$ Hz, 1H), 7.74 (t, $J = 7.8$ Hz, 1H), 4.62 – 4.49 (m, 1H), 3.72 (s, 2H), 2.70 (dd, $J = 10.8$, 7.8 Hz, 1H), 2.46 (d, $J = 3.5$ Hz, 1H), 2.02 – 1.88 (m, 2H). HRMS (m/z) for C$_{13}$H$_{14}$FN$_2$O$_5$S$^+$ [M + H]$^+$: calcd, 329.0602; found, 329.0611.

**NMR Spectra**

$^1$H NMR trace for CPD-2130.
$^{19}$F NMR trace for CPD-2130.
$^1$H NMR trace for CPD-2158.

$^{19}$F NMR trace for CPD-2158.
$^1$H NMR trace for CPD-2129.
$^{19}$F NMR trace for CPD-2129.

$^1$H NMR trace for CPD-2743.
$^1$H NMR trace for CPD-2005.
$^{19}$F NMR trace for CPD-2004.

$^1$H NMR trace for CPD-1963.
$^{19}$F NMR trace for CPD-1963.
$^{19}$F NMR trace for CPD-1964.
$^1$H NMR trace for CPD-363.
$^1$H NMR trace for CPD-362.

References

