## SUPPLEMENTARY NOTE

**General Information.** Commercial reagents were obtained from reputable suppliers and used as received. All solvents were purchased in septum-sealed bottles stored under an inert atmosphere. All reactions were sealed with septa through which a nitrogen atmosphere was introduced unless otherwise noted. Reactions were conducted in round-bottomed flasks or septum-capped crimp-top vials containing Teflon-coated magnetic stir bars. Heating of reactions was accomplished with a silicon oil bath or an aluminum reaction block on top of a stirring hotplate equipped with an electronic contact thermometer to maintain the indicated temperatures.

Reactions were monitored by thin layer chromatography (TLC) on precoated TLC glass plates (silica gel 60 $F_{254}$, 250 µm thickness) or by LC/MS (Phenomenex Kinetex 2.1 mm × 30 mm 2.6 µm C18 column; 5 µL injection; 5–98% MeCN/$H_2O$, linear gradient, with constant 0.1% v/v $HCO_2H$ additive; 6 min run; 0.5 mL/min flow; ESI; positive ion mode). TLC chromatograms were visualized by UV illumination or developed with anisaldehyde, ceric ammonium molybdate, or $KMnO_4$ stain. Reaction products were purified by flash chromatography on an automated purification system using pre-packed silica gel columns or by preparative HPLC (Phenomenex Gemini–NX 30 × 150 mm 5 µm C18 column). Analytical HPLC analysis was performed with an Agilent Eclipse XDB 4.6 × 150 mm 5 µm C18 column under the indicated conditions. High-resolution mass spectrometry was performed by the Mass Spectrometry Center in the Department of Medicinal Chemistry at the University of Washington and the High Resolution Mass Spectrometry Facility at the University of Iowa.

NMR spectra were recorded on a 400 MHz spectrometer. $^1H$ and $^{13}C$ chemical shifts (δ) were referenced to TMS or residual solvent peaks, and $^{19}F$ chemical shifts (δ) were referenced to $CFCl_3$. Data for $^1H$ NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet), coupling constant (Hz), integration. Data for $^{13}C$ NMR spectra are reported by chemical shift (δ ppm) with hydrogen multiplicity (C, CH, $CH_2$, $CH_3$) information obtained from DEPT spectra.

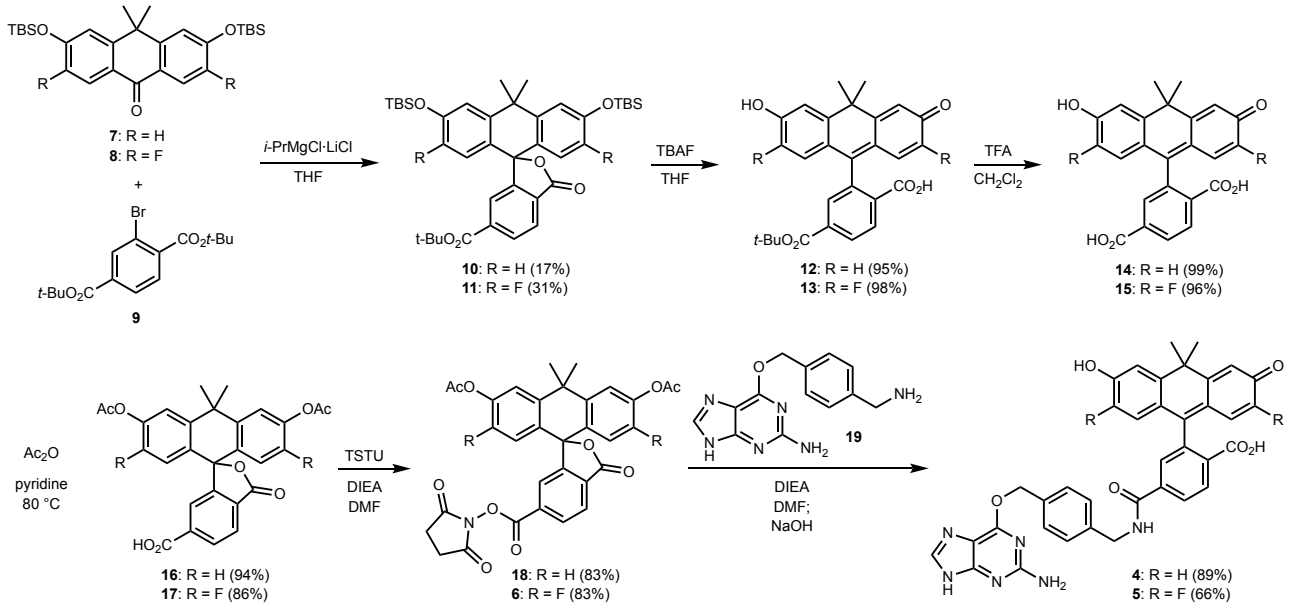
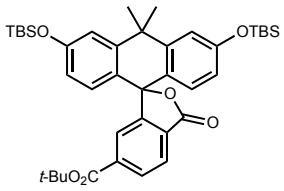
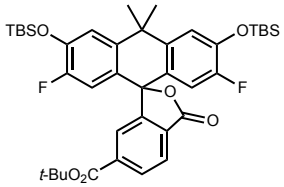



**Figure SN1.** Synthesis of CFI and VO derivatives.

**Experimentals and characterization data for all compounds**



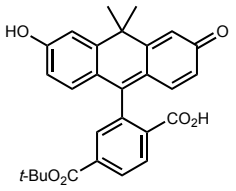

**$TBS_2$-CFl-6-$CO_2$*t*-Bu (10):** A vial was charged with di-*tert*-butyl 2-bromoterephthalate (**9**; 1.48 g, 4.14 mmol, 2 eq), sealed, and flushed with nitrogen. After dissolving the bromide in THF (7 mL) and cooling the reaction to −15 °C, *i*PrMgCl·LiCl (1.3 M in THF, 3.19 mL, 4.14 mmol, 2 eq) was added. The reaction was warmed to −10 °C and stirred for 4 h. A solution of 3,6-bis((*tert*-butyldimethylsilyl)oxy)-10,10-dimethylanthracen-9(10*H*)-one[1] (**7**; 1.00 g, 2.07 mmol) in THF (4 mL) was then added dropwise. The reaction mixture was warmed to room temperature and stirred for 2 h. It was subsequently quenched with saturated $NH_4Cl$, diluted with water, and extracted with EtOAc (2×). The combined organics were washed with brine, dried over anhydrous $MgSO_4$, filtered, and evaporated. Silica gel chromatography (0–10% $Et_2O$/hexanes, linear gradient) provided 245 mg (17%) of **10** as a colorless solid. $^1$H NMR ($CDCl_3$, 400 MHz) δ 8.16 (dd, *J* = 8.0, 1.3 Hz, 1H), 8.02 (dd, *J* = 8.0, 0.6 Hz, 1H), 7.63 – 7.59 (m, 1H), 7.09 – 7.05 (m, 2H), 6.64 – 6.57 (m, 4H), 1.81 (s, 3H), 1.72 (s, 3H), 1.54 (s, 9H), 0.99 (s, 18H), 0.22 (s, 12H); $^{13}$C NMR ($CDCl_3$, 101 MHz) δ 169.9 (C), 164.4 (C), 156.5 (C), 155.5 (C), 147.0 (C), 138.1 (C), 130.3 (CH), 129.7 (C), 129.3 (CH), 125.1 (CH), 125.0 (CH), 124.0 (C), 119.2 (CH), 117.8 (CH), 87.0 (C), 82.5 (C), 38.2 (C), 35.0 ($CH_3$), 33.2 ($CH_3$), 28.2 ($CH_3$), 25.8 ($CH_3$), 18.4 (C), -4.17 ($CH_3$), -4.19 ($CH_3$); HRMS (ESI) calcd for $C_{40}H_{55}O_6Si_2$ $[M+H]^+$ 687.3537, found 687.3533.



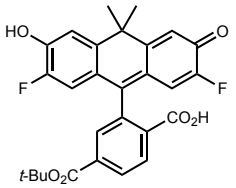

**$TBS_2$-VO-6-$CO_2$*t*-Bu (11):** A vial was charged with di-*tert*-butyl 2-bromoterephthalate (**9**; 1.03 g, 2.89 mmol, 1.5 eq), sealed, and flushed with nitrogen. After dissolving the bromide in THF (5 mL) and cooling the reaction to −50 °C, *i*-PrMgCl·LiCl (1.3 M in THF, 2.22 mL, 2.89 mmol, 1.5 eq) was added. The reaction was stirred at −40 °C for 4 h. A solution of 3,6-bis((*tert*-butyldimethylsilyl)oxy)-2,7-difluoro-10,10-dimethylanthracen-9(10*H*)-one[2] (**8**; 1.00 g, 1.93 mmol) in THF (5 mL) was then added dropwise. The reaction mixture was warmed to room temperature and stirred for 2 h. It was subsequently quenched with saturated $NH_4Cl$, diluted with water, and extracted with EtOAc (2×). The combined organics were washed with brine, dried over anhydrous $MgSO_4$, filtered, and evaporated. Silica gel chromatography (0–10% $Et_2O$/hexanes, linear gradient) provided 439 mg (31%) of **11** as a white solid. $^1$H NMR ($CDCl_3$, 400 MHz) δ 8.20 (dd, *J* = 8.0, 1.3 Hz, 1H), 8.05 (dd, *J* = 8.0, 0.6 Hz, 1H), 7.65 – 7.60 (m, 1H), 7.12 (d, *J* = 8.3 Hz, 2H), 6.36 (d, *J* = 11.3 Hz, 2H), 1.77 (s, 3H), 1.68 (s, 3H), 1.56 (s, 9H), 1.01 (s, 18H), 0.21 (s, 12H); $^{19}$F NMR ($CDCl_3$, 376 MHz) δ -133.17 – -133.27 (m); $^{13}$C NMR ($CDCl_3$, 101 MHz) δ 169.3 (C), 164.2 (C), 154.6 (C), 152.8 (d, $^1J_{CF}$ = 245.8 Hz, C), 144.6 (d, $^2J_{CF}$ = 12.7 Hz, C), 141.6 (d, $^4J_{CF}$ = 3.4 Hz, C), 138.5 (C), 130.9 (CH), 129.2 (C), 125.5

[1] Grimm, J. B.; Sung, A. J.; Legant, W. R.; Hulamm, P.; Matlosz, S. M.; Betzig, E.; Lavis, L. D. *ACS Chem. Biol.* **2013**, *8*, 1303–1310.
[2] Grimm, J. B.; Gruber, T. D.; Ortiz, G.; Brown, T. A.; Lavis, L. D. *Bioconjugate Chem.* **2016**, *27*, 474–480.

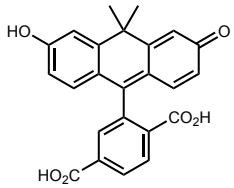
(CH), 124.8 (CH), 124.4 (d, $^3J_{CF}$ = 5.5 Hz, C), 120.3 (d, $^3J_{CF}$ = 1.9 Hz, CH), 115.0 (d, $^2J_{CF}$ = 20.1 Hz, CH), 85.7 (C), 82.7 (C), 37.6 (C), 35.1 ($CH_3$), 33.6 ($CH_3$), 28.2 ($CH_3$), 25.7 ($CH_3$), 18.5 (C), -4.5 ($CH_3$); HRMS (ESI) calcd for $C_{40}H_{53}F_2O_6Si_2$ $[M+H]^+$ 723.3343, found 723.3352.



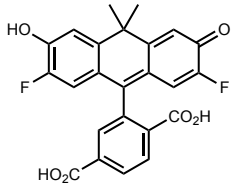

**CFl-6-$CO_2$*t*-Bu (12):** A solution of **10** (215 mg, 0.313 mmol) in THF (5 mL) was cooled to 0 °C, and TBAF (1.0 M in THF, 1.25 mL, 1.25 mmol, 4 eq) was added. The reaction was warmed to room temperature and stirred for 1 h. It was subsequently diluted with saturated $NH_4Cl$ and extracted with EtOAc (2×). The organic extracts were washed with brine, dried over anhydrous $MgSO_4$, filtered, and evaporated. Flash chromatography (10–100% EtOAc/hexanes, linear gradient) yielded **12** (137 mg, 95%) as a pale orange solid. $^1$H NMR (DMSO-$d_6$, 400 MHz) δ 9.74 (s, 2H), 8.14 (dd, $J$ = 8.0, 1.2 Hz, 1H), 8.10 (dd, $J$ = 8.0, 0.6 Hz, 1H), 7.40 – 7.36 (m, 1H), 7.10 (d, $J$ = 2.4 Hz, 2H), 6.63 (dd, $J$ = 8.6, 2.4 Hz, 2H), 6.51 (d, $J$ = 8.6 Hz, 2H), 1.74 (s, 3H), 1.65 (s, 3H), 1.48 (s, 9H); $^{13}$C NMR (DMSO-$d_6$, 101 MHz) δ 168.8 (C), 163.5 (C), 158.1 (C), 155.2 (C), 146.5 (C), 137.3 (C), 130.1 (CH), 128.9 (C), 128.8 (CH), 125.4 (CH), 123.4 (CH), 121.0 (C), 115.1 (CH), 112.7 (CH), 86.5 (C), 82.2 (C), 37.6 (C), 34.3 ($CH_3$), 33.3 ($CH_3$), 27.5 ($CH_3$); HRMS (ESI) calcd for $C_{28}H_{27}O_6$ $[M+H]^+$ 459.1802, found 459.1818.



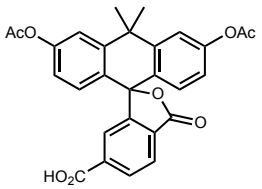

**VO-6-$CO_2$*t*-Bu (13):** To a solution of **11** (300 mg, 0.415 mmol) in THF (5 mL) was added TBAF (1.0 M in THF, 1.66 mL, 1.66 mmol, 4 eq). The reaction was stirred at room temperature for 30 min. It was subsequently acidified with 1 N HCl, diluted with water, and extracted with EtOAc (2×). The organic extracts were dried over anhydrous $MgSO_4$, filtered, and evaporated. Flash chromatography (0–30% EtOAc/toluene, linear gradient) afforded **13** (201 mg, 98%) as a yellow-orange solid. $^1$H NMR (DMSO-$d_6$, 400 MHz) δ 10.28 (s, 2H), 8.16 (dd, $J$ = 8.0, 1.3 Hz, 1H), 8.11 (dd, $J$ = 8.0, 0.7 Hz, 1H), 7.44 – 7.40 (m, 1H), 7.29 (d, $^4J_{HF}$ = 8.8 Hz, 2H), 6.41 (d, $^3J_{HF}$ = 11.9 Hz, 2H), 1.73 (s, 3H), 1.63 (s, 3H), 1.48 (s, 9H); $^{19}$F NMR (DMSO-$d_6$, 376 MHz) δ -136.55 (dd, $J_{FH}$ = 11.8, 8.9 Hz); $^{13}$C NMR (DMSO-$d_6$, 101 MHz) δ 168.4 (C), 163.5 (C), 154.2 (C), 149.8 (d, $^1J_{CF}$ = 242.7 Hz, C), 146.2 (d, $^2J_{CF}$ = 12.5 Hz, C), 141.5 (d, $^4J_{CF}$ = 3.0 Hz, C), 137.5 (C), 130.5 (CH), 128.5 (C), 125.9 (CH), 123.2 (CH), 121.3 (d, $^3J_{CF}$ = 5.3 Hz, C), 115.7 (d, $^3J_{CF}$ = 2.7 Hz, CH), 113.9 (d, $^2J_{CF}$ = 18.8 Hz, CH), 85.0 (C), 82.2 (C), 37.1 (C), 34.2 ($CH_3$), 33.7 ($CH_3$), 27.5 ($CH_3$); HRMS (ESI) calcd for $C_{28}H_{25}F_2O_6$ $[M+H]^+$ 495.1614, found 495.1625.




**CFl-6-$CO_2H$ (14):** Ester **12** (75 mg, 0.164 mmol) was taken up in $CH_2Cl_2$ (3 mL), and trifluoroacetic acid (0.6 mL) was added. The reaction was stirred at room temperature for 6 h. Toluene (3 mL) was added; the reaction mixture was concentrated to dryness and then azeotroped with MeOH three times to provide **14** as a red solid (65 mg, 99%). Analytical HPLC and NMR indicated that the material was >95% pure and did not require further purification. $^1$H NMR (DMSO-$d_6$, 400 MHz) δ 13.57 (s, 1H), 9.74 (s, 2H), 8.17 (dd, $J$ = 8.0, 1.3 Hz, 1H), 8.09 (dd, $J$ = 8.0, 0.7 Hz, 1H), 7.44 (dd, $J$ = 1.2, 0.8 Hz, 1H), 7.09 (d, $J$ = 2.5 Hz, 2H), 6.62 (dd, $J$ = 8.6, 2.5 Hz, 2H), 6.50 (d, $J$ = 8.6 Hz, 2H), 1.74 (s, 3H), 1.64 (s, 3H); $^{13}$C NMR (DMSO-$d_6$, 101 MHz) δ 168.9 (C), 166.0 (C), 158.1 (C), 155.2 (C), 146.6 (C), 137.1 (C), 130.3 (CH), 128.92 (C), 128.90 (CH), 125.3 (CH), 123.9 (CH), 121.0 (C), 115.0 (CH), 112.7 (CH), 86.5 (C), 37.6 (C), 34.4 ($CH_3$), 33.2 ($CH_3$); HRMS (ESI) calcd for $C_{24}H_{17}O_6$ $[M-H]^-$ 401.1031, found 401.1037.

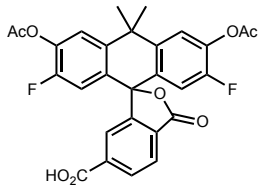



**VO-6-$CO_2H$ (15):** Ester **13** (185 mg, 0.374 mmol) was taken up in $CH_2Cl_2$ (5 mL), and trifluoroacetic acid (1 mL) was added. The reaction was stirred at room temperature for 8 h. Toluene (3 mL) was added; the reaction mixture was concentrated to dryness and then azeotroped with MeOH three times to provide acid **15** as an orange solid (158 mg, 96%). Analytical HPLC and NMR indicated that the material was >95% pure and did not require further purification. $^1$H NMR (DMSO-$d_6$, 400 MHz) δ 13.58 (s, 1H), 10.27 (s, 2H), 8.20 (dd, $J$ = 8.0, 1.3 Hz, 1H), 8.11 (dd, $J$ = 8.0, 0.5 Hz, 1H), 7.50 – 7.46 (m, 1H), 7.29 (d, $^4J_{HF}$ = 8.8 Hz, 2H), 6.40 (d, $^3J_{HF}$ = 11.9 Hz, 2H), 1.73 (s, 3H), 1.63 (s, 3H); $^{19}$F NMR (DMSO-$d_6$, 376 MHz) δ -136.63 (dd, $J_{FH}$ = 11.8, 8.9 Hz); $^{13}$C NMR (DMSO-$d_6$, 101 MHz) δ 168.5 (C), 165.9 (C), 154.2 (C), 149.8 (d, $^2J_{CF}$ = 242.6 Hz, C), 146.2 (d, $^2J_{CF}$ = 12.5 Hz, C), 141.6 (d, $^4J_{CF}$ = 3.0 Hz, C), 137.3 (C), 130.7 (CH), 128.6 (C), 125.9 (CH), 123.6 (CH), 121.4 (d, $^3J_{CF}$ = 5.2 Hz, C), 115.6 (d, $^3J_{CF}$ = 2.8 Hz, CH), 114.0 (d, $^2J_{CF}$ = 18.9 Hz, CH), 85.1 (C), 37.2 (C), 34.4 ($CH_3$), 33.5 ($CH_3$); HRMS (ESI) calcd for $C_{24}H_{15}F_2O_6$ $[M-H]^-$ 437.0842, found 437.0853.

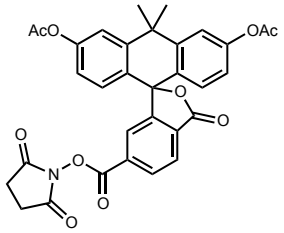



**$Ac_2$-CFl-6-$CO_2H$ (16):** Dye **14** (90 mg, 0.224 mmol), pyridine (90 μL, 1.12 mmol, 5 eq), and acetic anhydride (2 mL) were combined in a vial and stirred at 80 °C for 1 h. The reaction was cooled to room temperature, concentrated *in vacuo*, diluted with 1 N HCl, and extracted with EtOAc (2×). The organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, deposited onto silica gel, and evaporated. The residue was purified by flash chromatography

(20–100% EtOAc/hexanes, linear gradient, with constant 1% v/v AcOH; dry load with silica gel) to afford 102 mg (94%) of **16** as a white foam. $^{1}$H NMR ($CDCl_3$, 400 MHz) δ 8.29 (dd, $J$ = 8.0, 1.2 Hz, 1H), 8.11 (dd, $J$ = 8.0, 0.5 Hz, 1H), 7.75 – 7.71 (m, 1H), 7.38 (d, $J$ = 2.3 Hz, 2H), 6.91 (dd, $J$ = 8.7, 2.4 Hz, 2H), 6.75 (d, $J$ = 8.7 Hz, 2H), 2.31 (s, 6H), 1.86 (s, 3H), 1.75 (s, 3H); $^{13}$C NMR ($CDCl_3$, 101 MHz) δ 169.6 (C), 169.23 (C), 169.15 (C), 154.9 (C), 151.6 (C), 146.8 (C), 135.6 (C), 131.5 (CH), 130.4 (C), 129.2 (CH), 128.2 (C), 125.8 (CH), 125.7 (CH), 120.8 (CH), 119.7 (CH), 85.8 (C), 38.7 (C), 35.0 ($CH_3$), 33.0 ($CH_3$), 21.3 ($CH_3$); HRMS (ESI) calcd for $C_{28}H_{21}O_8$ $[M-H]^-$ 485.1242, found 485.1235.

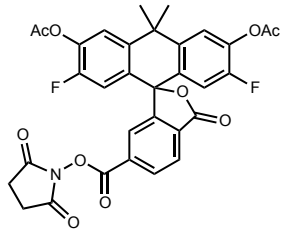



**$Ac_2$-VO-6-$CO_2$H (17):** Dye **15** (125 mg, 0.285 mmol), pyridine (115 µL, 1.43 mmol, 5 eq), and acetic anhydride (2.5 mL) were combined in a vial and stirred at 80 °C for 1 h. The reaction was cooled to room temperature, diluted with 1 N HCl, and extracted with EtOAc (2×). The organic layers were washed with brine, dried over anhydrous $MgSO_4$, filtered, and evaporated. The residue was purified by flash chromatography (10–100% EtOAc/hexanes, linear gradient, with constant 1% v/v AcOH) to afford 128 mg (86%) of **17** as an off-white solid. $^{1}$H NMR (DMSO-$d_6$, 400 MHz) δ 13.62 (s, 1H), 8.23 (dd, $J$ = 8.0, 1.3 Hz, 1H), 8.16 (dd, $J$ = 8.0, 0.7 Hz, 1H), 7.84 (d, $^{4}J_{HF}$ = 7.7 Hz, 2H), 7.60 – 7.55 (m, 1H), 6.76 (d, $^{3}J_{HF}$ = 11.0 Hz, 2H), 2.34 (s, 6H), 1.81 (s, 3H), 1.70 (s, 3H); $^{19}$F NMR (DMSO-$d_6$, 376 MHz) δ -129.33 (dd, $J_{FH}$ = 11.0, 7.7 Hz); $^{13}$C NMR (DMSO-$d_6$, 101 MHz) δ 168.1 (C), 168.0 (C), 165.9 (C), 152.2 (d, $^{1}J_{CF}$ = 248.1 Hz, C), 141.6 (d, $^{4}J_{CF}$ = 3.3 Hz, C), 138.9 (d, $^{2}J_{CF}$ = 13.2 Hz, C), 137.7 (C), 131.1 (CH), 129.2 (d, $^{3}J_{CF}$ = 5.9 Hz, C), 128.3 (C), 126.4 (CH), 123.6 (CH), 123.2 (CH), 114.6 (d, $^{2}J_{CF}$ = 19.7 Hz, CH), 83.6 (C), 37.8 (C), 33.9 ($CH_3$), 33.4 ($CH_3$), 20.2 ($CH_3$); HRMS (ESI) calcd for $C_{28}H_{19}F_2O_8$ $[M-H]^-$ 521.1053, found 521.1050.

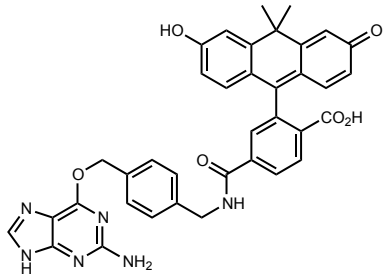



**$Ac_2$-CFl-6-NHS (18):** To a solution of acid **16** (30 mg, 0.0617 mmol) and TSTU (37 mg, 0.123 mmol, 2 eq) in DMF (1.5 mL) was added DIEA (54 µL, 0.309 mmol, 5 eq). The reaction was stirred at room temperature for 2. It was subsequently diluted with 10% w/v citric acid and extracted with EtOAc (2×). The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, filtered, deposited onto silica gel, and concentrated *in vacuo*. Silica gel chromatography (25–100% EtOAc/hexanes, linear gradient; dry load with silica gel) yielded 30 mg (83%) of **18** as an off-white solid. $^{1}$H NMR ($CDCl_3$, 400 MHz) δ 8.37 (dd, $J$ = 8.0, 1.4 Hz, 1H), 8.17 (dd, $J$ = 8.0, 0.7 Hz, 1H), 7.80 (dd, $J$ = 1.3, 0.8 Hz, 1H), 7.41 (d, $J$ = 2.3 Hz, 2H), 6.94 (dd, $J$ = 8.7, 2.4 Hz, 2H), 6.73 (d, $J$ = 8.7 Hz, 2H), 2.87 (s, 4H), 2.31 (s, 6H), 1.86 (s, 3H), 1.75 (s, 3H); $^{13}$C NMR ($CDCl_3$, 101 MHz) δ 169.1 (C), 168.8 (C), 168.5 (C), 160.7 (C), 154.8 (C), 151.8 (C), 147.0 (C), 131.8 (CH), 131.7 (C), 131.4 (C), 129.3 (CH), 127.9 (C), 126.3 (CH), 126.1 (CH), 120.9 (CH),

119.7 (CH), 86.0 (C), 38.8 (C), 35.3 ($CH_3$), 32.6 ($CH_3$), 25.8 ($CH_2$), 21.3 ($CH_3$); HRMS (ESI) calcd for $C_{32}H_{26}NO_{10}$ $[M+H]^+$ 584.1551, found 584.1566.

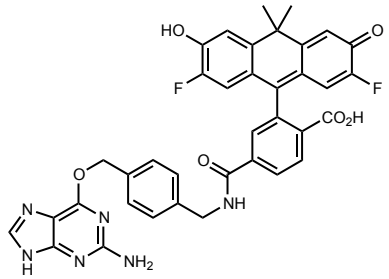



**$Ac_2$-VO-6-NHS (6):** To a solution of acid **17** (53 mg, 0.101 mmol) and TSTU (61 mg, 0.203 mmol, 2 eq) in DMF (2 mL) was added DIEA (44 µL, 0.254 mmol, 2.5 eq). The reaction was stirred at room temperature for 2 h. It was subsequently diluted with 10% w/v citric acid and extracted with EtOAc (2×). The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. Silica gel chromatography (25–100% EtOAc/hexanes, linear gradient) yielded 52 mg (83%) of **6** as a white solid. $^1$H NMR ($CDCl_3$, 400 MHz) δ 8.41 (dd, $J$ = 8.0, 1.3 Hz, 1H), 8.20 (dd, $J$ = 8.0, 0.7 Hz, 1H), 7.83 – 7.78 (m, 1H), 7.44 (d, $^4J_{HF}$ = 7.3 Hz, 2H), 6.50 (d, $^3J_{HF}$ = 10.5 Hz, 2H), 2.88 (s, 4H), 2.34 (s, 6H), 1.82 (s, 3H), 1.73 (s, 3H); $^{19}$F NMR ($CDCl_3$, 376 MHz) δ -128.60 (dd, $J_{FH}$ = 10.4, 7.4 Hz); $^{13}$C NMR ($CDCl_3$, 101 MHz) δ 168.7 (C), 167.9 (C), 160.6 (C), 153.9 (C), 152.8 (d, $^1J_{CF}$ = 251.4 Hz, C), 141.6 (d, $^4J_{CF}$ = 3.6 Hz, C), 139.7 (d, $^2J_{CF}$ = 13.2 Hz, C), 132.3 (CH), 131.8 (C), 130.9 (C), 129.0 (d, $^3J_{CF}$ = 5.8 Hz, C), 126.5 (CH), 126.0 (CH), 122.4 (CH), 115.41 (d, $^2J_{CF}$ = 19.9 Hz, CH), 84.8 (C), 38.2 (C), 35.2 ($CH_3$), 33.4 ($CH_3$), 25.8 ($CH_2$), 20.6 ($CH_3$); HRMS (ESI) calcd for $C_{32}H_{24}F_2NO_{10}$ $[M+H]^+$ 620.1363, found 620.1370.




**CFl-SNAP-tag ligand (4):** Ester **18** (30 mg, 51.4 µmol) and 6-((4-(aminomethyl)benzyl)oxy)-9*H*-purin-2-amine (BG-$NH_2$, **19**; 18.1 mg, 66.8 µmol, 1.3 eq) were combined in DMF (2 mL). DIEA (17.9 µL, 103 µmol, 2 eq) was added, and the reaction was stirred at room temperature for 2 h. MeOH (1 mL) and 1 N NaOH (200 µL) were then added, and the mixture was stirred at room temperature for an additional 2 h. The reaction was acidified with 1 N HCl (400 µL), diluted with water, and extracted with 15% *i*-PrOH/$CHCl_3$ (2×). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, deposited onto Celite, and concentrated *in vacuo*. The crude product was purified by flash chromatography on silica gel (0–10% MeOH/EtOAc, linear gradient; dry load with Celite) to provide ligand **4** (30 mg, 89%) as an orange solid. $^1$H NMR (MeOD, 400 MHz) δ 8.08 (dd, $J$ = 8.0, 1.4 Hz, 1H), 8.05 (dd, $J$ = 8.0, 0.8 Hz, 1H), 7.82 (s, 1H), 7.48 (dd, $J$ = 1.3, 0.8 Hz, 1H), 7.43 (d, $J$ = 8.2 Hz, 2H), 7.28 (d, $J$ = 8.2 Hz, 2H), 7.10 (d, $J$ = 2.4 Hz, 2H), 6.60 (dd, $J$ = 8.7, 2.5 Hz, 2H), 6.53 (d, $J$ = 8.6 Hz, 2H), 5.50 (s, 2H), 4.48 (s, 2H), 1.80 (s, 3H), 1.70 (s, 3H); $^{13}$C NMR (MeOD, 101 MHz) δ 162.3 (C), 158.8 (C), 152.1 (C), 151.8 (C), 150.0 (C), 147.8 (C), 139.1 (C), 132.7 (C), 130.5 (C), 130.1 (C), 127.4 (C), 120.8 (CH), 120.5 (C), 120.3 (CH), 120.1 (CH), 119.2 (CH), 116.6 (CH), 114.3 (CH), 113.6 (C),

106.4 (CH), 104.3 (CH), 79.7 (C), 59.1 ($CH_2$), 35.0 ($CH_2$), 29.7 (C), 25.9 ($CH_3$), 23.8 ($CH_3$); Analytical HPLC: >99% purity (5 µL injection; 10–95% MeCN/$H_2O$, linear gradient, with constant 0.1% v/v TFA additive; 20 min run; 1 mL/min flow; ESI; positive ion mode; detection at 254 nm); HRMS (ESI) calcd for $C_{37}H_{31}N_6O_6$ $[M+H]^+$ 655.2300, found 655.2306.




**VO-SNAP-tag ligand (5):** Ester **6** (30 mg, 48.4 µmol) and 6-((4-(aminomethyl)benzyl)oxy)-9*H*-purin-2-amine (BG-$NH_2$, **19**; 17.0 mg, 63.0 µmol, 1.3 eq) were combined in DMF (2 mL), and DIEA (16.9 µL, 96.8 µmol, 2 eq) was added. After stirring the reaction for 1 h at room temperature, MeOH (1 mL) and 1 M NaOH (150 µL) were added. The mixture was stirred at room temperature for an additional 1 h. It was then acidified with 1 M HCl (300 µL), diluted with water, and extracted with 15% *i*-PrOH/$CHCl_3$ (2×). The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (0–10% MeOH/EtOAc, linear gradient) to provide 22.1 mg (66%) of ligand **5** as a pink solid. $^1$H NMR (DMSO-$d_6$, 400 MHz) δ 12.38 (s, 1H), 10.26 (s, 2H), 9.25 (t, $J$ = 5.8 Hz, 1H), 8.18 (dd, $J$ = 8.0, 1.3 Hz, 1H), 8.08 (d, $J$ = 7.9 Hz, 1H), 7.78 (s, 1H), 7.54 – 7.48 (m, 1H), 7.42 (d, $J$ = 8.1 Hz, 2H), 7.29 (d, $J$ = 8.1 Hz, 2H), 7.28 (d, $^4J_{HF}$ = 8.9 Hz, 2H), 6.35 (d, $^3J_{HF}$ = 11.9 Hz, 2H), 6.24 (s, 2H), 5.43 (s, 2H), 4.42 (d, $J$ = 5.7 Hz, 2H), 1.73 (s, 3H), 1.62 (s, 3H); $^{19}$F NMR (DMSO-$d_6$, 376 MHz) δ -136.71 (dd, $J_{FH}$ = 11.8, 8.9 Hz); Analytical HPLC: 98.6% purity (5 µL injection; 10–95% $CH_3CN/H_2O$, linear gradient, with constant 0.1% v/v TFA additive; 20 min run; 1 mL/min flow; ESI; positive ion mode; UV detection at 254 nm); HRMS (ESI) calcd for $C_{37}H_{29}F_2N_6O_6$ $[M+H]^+$ 691.2111, found 691.2127.