I. Bait 1

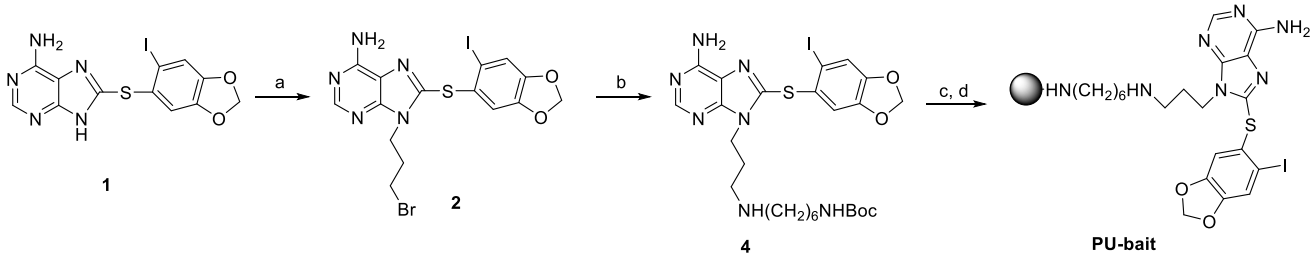
1. Protocols for PU-bait and control bait chemical syntheses

General Methods

^{1}H spectra were recorded on a Bruker 500 or 600 MHz instrument. Chemical shifts are reported in δ values in ppm downfield from TMS as the internal standard. ^{1}H data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constant (Hz), integration. Low resolution mass spectra were obtained on a Waters Acquity Ultra Performance LC with electrospray ionization and SQ detector. High-performance liquid chromatography analyses were performed on a Waters Autopurification system with PDA, MicroMass ZQ and ELSD detector and a reversed phase column (Waters X-Bridge C18, 4.6 x 150 mm, 5 µm) using a gradient of (a) H_2O + 0.1% TFA and (b) CH_3CN + 0.1% TFA, 5 to 95% b over 13 minutes at 1.2 mL/min. Column chromatography was performed using 230-400 mesh silica gel (EMD). Affi-Gel® 10 beads were purchased from Bio-Rad (Hercules, CA).

A. Synthesis of PU-bait[1]

Scheme 1. Synthesis of PU-bait



Reagents and conditions: (a) Cs_2CO_3, 1,3-dibromopropane, DMF, rt; (b) $NH_2(CH_2)_6NHBoc$ (**3**), DMF, rt; (c) TFA, CH_2Cl_2, rt; (d) Affi-Gel® 10, DIEA, DMAP, DMF.

9-(3-Bromopropyl)-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl) adenine (2).[2] In a 250 mL RBF flushed with argon wrapped in aluminum foil, Cs_2CO_3 (4.73 g, 14.5 mmol, 1.2 eq.) and 1,3-dibromopropane (12.2 g, 6.2 mL 60.5 mmol, 5 eq.) was added to a solution of **1**[2] (5.0 g, 12.1 mmol) in anhydrous DMF (150 mL) at rt. After stirring for 45 min. additional Cs_2CO_3 (0.788 g, 2.42 mmol, 0.2 eq.) was added and it was stirred for an additional 45 min. Then the reaction mixture was filtered and DMF was removed under high vacuum (at or below 30 °C). The residue was purified by silica gel chromatography (CH_2Cl_2:MeOH:AcOH, 120:1:0.5 to 90:1:0.5). Fractions containing product were combined, concentrated under reduced pressure, then dried under high vacuum to a solid. This was evaporated from MeOH several times to give **2** (2.38 g, 37%). ^{1}H NMR (500 MHz, $CDCl_3$/MeOH-d_4) 8.24 (s, 1H); 7.38 (s, 1H), 7.04 (s, 1H), 6.05 (s, 2H), 4.37 (t, J = 7.1 Hz, 2H), 3.45 (t, J = 6.6 Hz, 2H), 2.41 (quin, J = 6.9 Hz, 2H); MS (ESI): *m*/*z* 533.9/535.9 $[M+H]^+$.

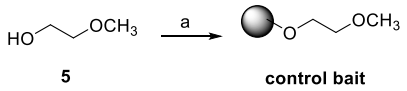
***tert*-Butyl 6-aminohexylcarbamate (3).**[3] 1,6-diaminohexane (10 g, 0.086 mol) and Et_3N (13.05 g, 18.13 mL, 0.129 mol) were suspended in CH_2Cl_2 (300 mL). A solution of di-*tert*-butyl dicarbonate (9.39 g, 0.043 mol) in CH_2Cl_2 (100 mL) was added dropwise over 90 minutes at rt and stirring continued for 18 h. The reaction mixture was added to a separatory funnel and washed with water (100 mL), brine (100 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was chromatographed (CH_2Cl_2:MeOH-NH_3 (7N), 70:1 to 20:1) to give 7.1 g (76%) of **3**. ^{1}H NMR ($CDCl_3$) δ 4.50 (br s, 1H), 3.11 (br s, 2H), 2.68 (t, *J* = 6.6 Hz, 2H), 1.44 (s, 13H), 1.33 (s, 4H); MS (ESI): *m/z* 217.2 $[M+H]^+$.

***tert*-Butyl 6-(3-(6-amino-8-(6-iodobenzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)propylamino)hexylcarbamate (4).**[1] **2** (0.226 g, 0.423 mmol) and **3** (0.915 g, 4.23 mmol) in DMF (7 mL) was stirred at rt for 24 h. The reaction mixture was concentrated and the residue chromatographed ($CHCl_3$:MeOH:MeOH-NH_3 (7N), 100:7:3) to give 0.255 g (90%) of **4**. ^{1}H NMR ($CDCl_3$) δ 8.32 (s, 1H), 7.31 (s, 1H), 6.89 (s, 1H), 5.99 (s, 2H), 5.55 (br s, 2H), 4.57 (br s, 1H), 4.30 (t, *J* = 7.0 Hz, 2H), 3.10 (m, 2H), 2.58 (t, *J* = 6.7 Hz, 2H), 2.52 (t, *J* = 7.2 Hz, 2H), 1.99 (m, 2H), 1.44 (s, 13H), 1.30 (s, 4H); HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{26}H_{37}IN_7O_4S$, 670.1673; found 670.1670; HPLC: t_R = 7.02 min.

PU-H71-Affi-Gel® 10 beads (PU-bait).[1] **4** (0.301 g, 0.45 mmol) was dissolved in 15 mL of CH_2Cl_2:TFA (4:1) and the solution was stirred at rt for 45 min. Solvent was removed under reduced pressure and the residue dried under high vacuum overnight. This was dissolved in DMF (12 mL) and added to 25 mL of Affi-Gel® 10 beads (prewashed, 3 x 50 mL DMF) in a solid phase peptide synthesis vessel. 225 µL of N,N-diisopropylethylamine and several crystals of DMAP were added and this was shaken at rt for 2.5 h. Then 2-methoxyethylamine (0.085 g, 97 µl, 1.13 mmol) was added and shaking was continued for 30 minutes. Then the solvent was removed and the beads washed for 10 minutes each time with CH_2Cl_2:Et_3N (9:1, 4 x 50 mL), DMF (3 x 50 mL), Felts buffer (3 x 50 mL) and *i*-PrOH (3 x 50 mL). The beads (**PU-bait**) were stored in *i*-PrOH (beads: *i*-PrOH (1:2), v/v) at -20°C.

B. Synthesis of control bait[1]

Scheme 2. Synthesis of control bait



Reagents and conditions: (a) Affi-Gel® 10, DIEA, DMAP, DMF.

Control bait.[1] DMF (8.5 mL) was added to 20 mL of Affi-Gel® 10 beads (prewashed, 3 x 40 mL DMF) in a solid phase peptide synthesis vessel. 2-Methoxyethylamine (**5**; 113 mg, 129 µL, 1.5 mmol) and several crystals of DMAP were added and this was shaken at rt for 2.5 h. Then the

solvent was removed and the beads washed for 10 minutes each time with CH_2Cl_2 (4 x 35 mL), DMF (3 x 35 mL), Felts buffer (2 x 35 mL) and *i*-PrOH (4 x 35 mL). The beads were stored in *i*-PrOH (beads: *i*-PrOH (1:2), v/v) at -20°C.

2. Guidelines for PU-bait and control bait storage

The PU-bait and control bait should be stored in *i*-PrOH (beads: *i*-PrOH (1:2), v/v) at -20°C for long-term storage. It is essential to protect the PU-bait from light in a light-protected vial as it is potentially photoreactive. The PU-bait and control bait is stable for over two years when stored at -20°C in a light-protected vial.

References

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3. Hansen, J. B.; Nielsen, M. C.; Ehrbar, U.; Buchardt, O., *Synthesis* **1982**, 404-405.