Supporting Information

Derivatives of 3-amino-2-methylpyridine as BAZ2B Bromodomain Ligands: *in silico* Discovery and *in crystallo* Validation

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Table S1. Data Collection and Refinement Statistics

	Cmpd **1**	Cmpd **2**	Cmpd **3**	Cmpd **4**	Cmpd **5**	Cmpd **6**
Data Collection						
Space group	$C222_1$	$C222_1$	$C222_1$	$C222_1$	$C222_1$	$C222_1$
Unit-cell parameters (Å)	a = 81.88 b = 96.81 c = 57.90	a = 80.83 b = 96.38 c = 57.66	a = 81.81 b = 96.72 c = 57.64	a = 80.50 b = 96.39 c = 57.61	a = 81.31, b = 96.81, c = 57.72	a = 82.01, b = 96.84, c = 57.79
Resolution (Å)	42.48-2.15 (2.22-2.15)	48.19-1.85 (1.89-1.85)	48.36-2.05 (2.11-2.05)	48.20-2.26 (2.34-2.26)	48.41-1.85 (1.89-1.85)	48.42-2.00 (2.05-2.00)
R_{merge} (%)	6.9 (43.5)	4.5 (82.4)	8.7 (68.2)	6.8 (43.8)	5.9 (87.4)	7.6 (89.3)
R_{meas} (%)	7.6 (48.2)	4.9 (90.5)	9.5 (74.3)	7.5 (47.9)	6.5 (95.9)	8.3 (97.0)
R_{pim} (%)	3.2 (20.2)	1.9 (36.7)	3.7 (29.0)	3.0 (19.0)	2.5 (38.9)	3.3 (37.5)
$\langle I/\sigma(I)\rangle$	13.0 (3.1)	21.3 (2.3)	14.1 (2.8)	17.0 (3.6)	17.1 (2.5)	14.3 (2.1)
Completeness (%)	99.3 (99.7)	99.6 (99.8)	99.8 (99.6)	99.7 (98.5)	99.9 (99.9)	99.9 (100.0)
Multiplicity	5.1 (5.3)	6.4 (6.1)	6.3 (6.5)	6.1 (6.1)	6.3 (6.0)	6.2 (6.6)
Refinement						
Resolution (Å)	33.43-2.15	48.19-1.85	48.36-2.05	48.20-2.26	48.41-1.85	48.42-2.00
R_{work}/R_{free} (%)	19.0/22.8	18.8/20.9	18.3/21.1	20.4/23.4	17.3/19.2	17.7/20.4
R.m.s. deviations						
Bond lengths (Å)	0.005	0.006	0.007	0.007	0.007	0.007
Bond angles (°)	1.0	1.1	1.1	1.1	1.0	1.0
PDB entry	5L96	5L8T	5L97	5L98	5L8U	5L99

Figure S1. Inactive molecules in the AlphaScreen assay. (A) Compounds **10-15** originate from the first docking campaign, (B) **16-18** originate from the pharmacophore search, and (C) **19**-**20** from the substructure search. Compound **20** was selected as a negative control, and as representative of the 2,6-dimethylpyridine family of purchasable compounds.

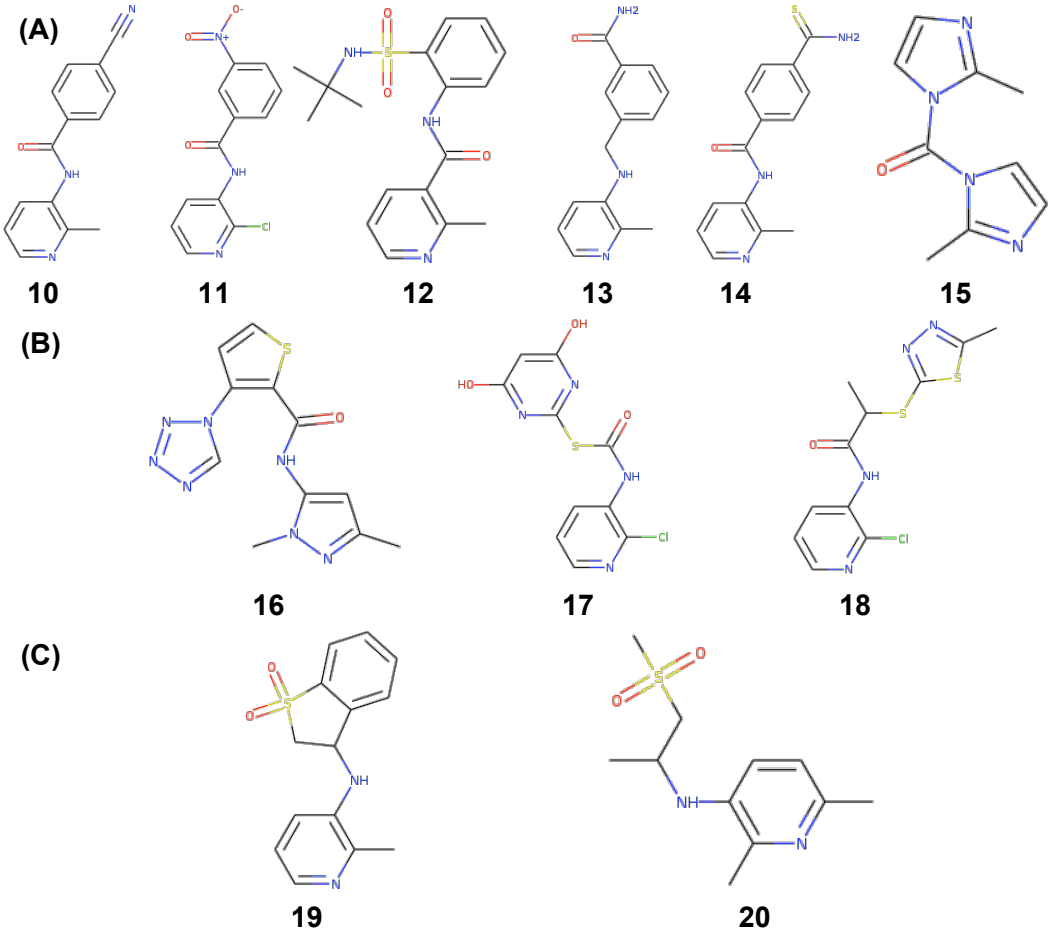

Figure S2. Comparison of binding modes of compounds **1** (salmon sticks), **2** (green sticks), and **3** (orange sticks). (A, B) Two different orientations of the complexes are shown. The protein backbone is represented in cartoons (gray), interacting residues and ligands **1-3** by sticks (green). Binding mode of compounds (C) **1**, (D) **2**, (E) **3**, (F) **4**, (G) **5**, and (H) **6**.

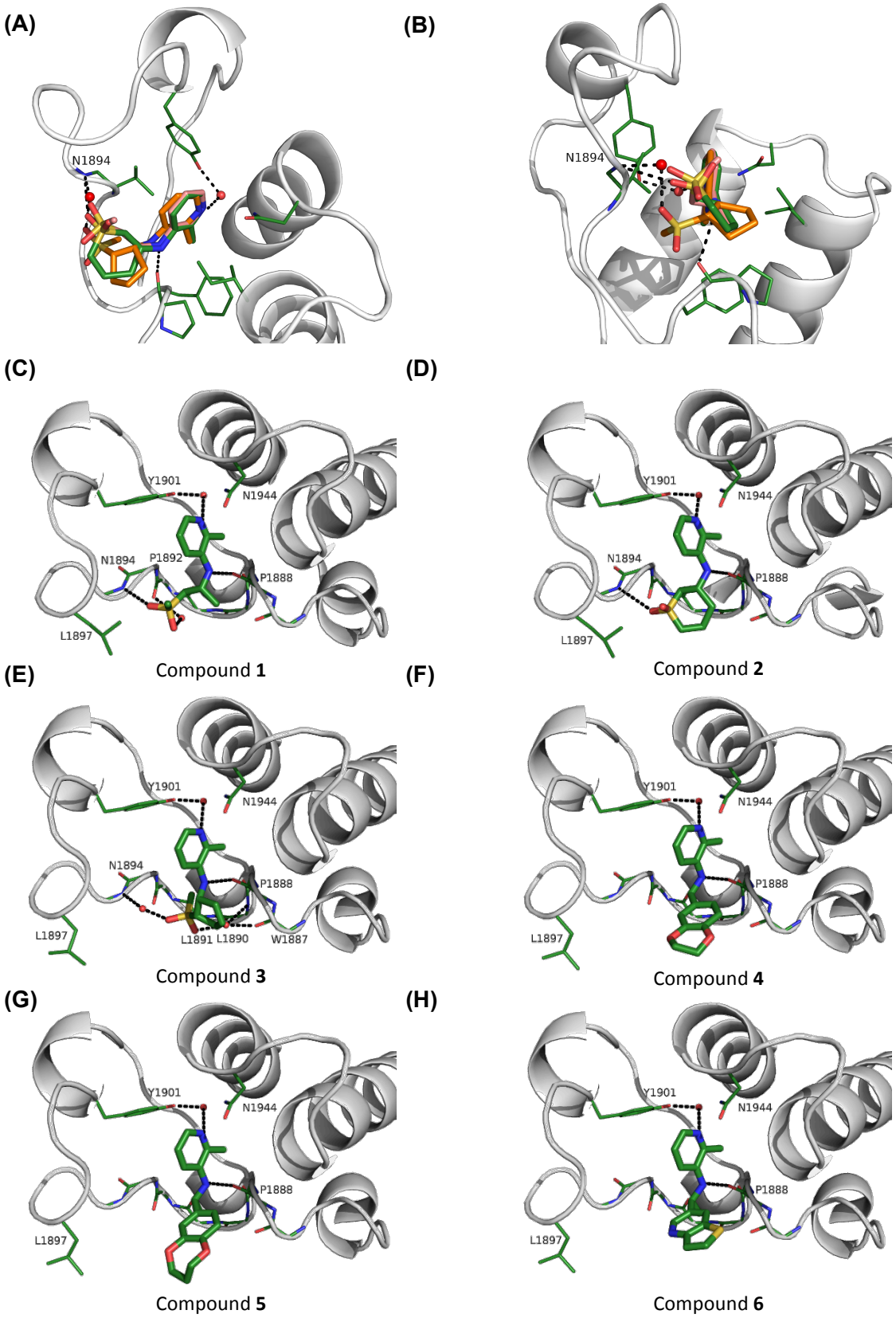

Figure S3. Comparison between compound **2** (in green sticks) and acetylated histone peptides (in salmon sticks) (A) H3K14ac (PDB code 4QC1) and (B) H4K8acK12ac (PDB code 4QC3).

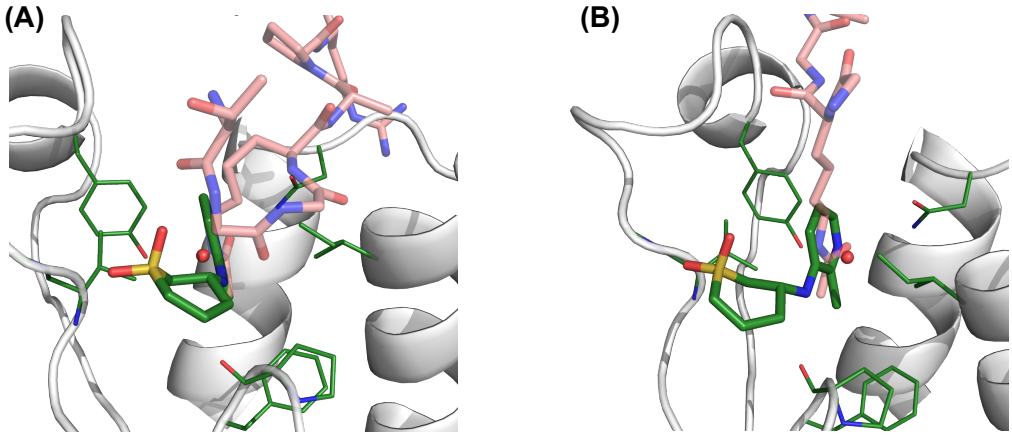

Figure S4. Alphascreen dose response curves for compounds **2** (a), **4** and **6** (b), and the positive control GSK2801 (c). These experiments were carried out at Reaction Biology Inc.

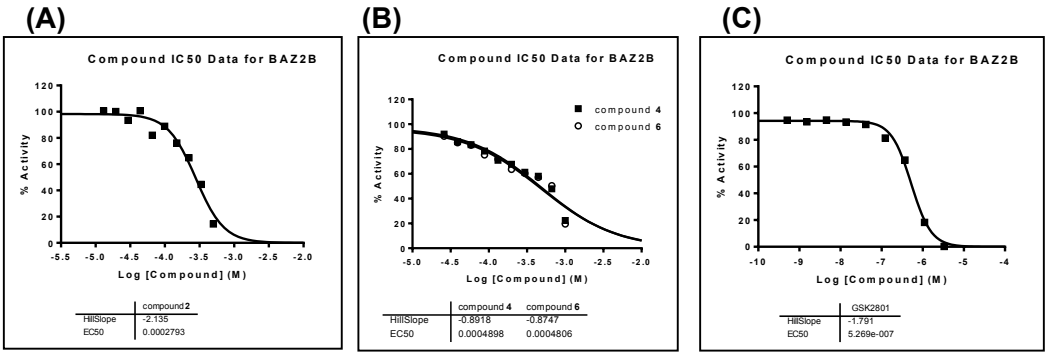

Figure S5. Properties of the 493 molecules of the library which was assembled manually on the basis of our previously discovered fragment binders to the BAZ2B bromodomain.