Supporting Information

Structure-based drug design of novel Aurora kinase A inhibitors: Structural basis for potency and specificity

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Contents

1. HPLC purity determination:

The percentage purity of compounds were determined by an Agilent 1100 series HPLC system and were reported using two different columns.

Elution conditions: Mobile phase A-Acetonitrile; Mobile phase B-Water containing 0.1% formic acid + 10 mmol NH_4OAc. The flow-rate was 0.2 ml/min and the injection volume was 5 µl. The system operated at 25°C. Peaks were detected at 210 nm.

Table 1. Elution condition

Time (min)	Mobile Phase A (ratio)	Mobile Phase B (ratio)
0	10	90
45	90	10
50	10	90
60	10	90

Table 2. Purity of compounds **8a, 12a-c,e,p,w.**

Column A: Agilent ZORBAX Eclipse XDB-C18 5 μm. 4.6 mm × 150 mm column.

Column B: Agilent ZORBAX Eclipse XDB-C8 5 μm. 3.0 mm × 150 mm column.

Compound	Column A		Column B	
	Retention time (min)	% Purity	Retention time (min)	% Purity
8a	30.49	98.96	22.24	96.79
12a	36.55	92.99	28.44	95.30
12b	29.89	96.96	23.62	97.13
12c	31.27	92.84	24.98	95.53
12e	29.98	98.59	23.41	97.82
12p	29.84	96.32	23.41	93.79
12w	24.05	98.09	18.74	97.64

Table 3. Purity of compounds **8b,d,f,g,h,i and 12j,n,q.**

Column A: Agilent ZORBAX Eclipse XDB-C18 5 μm. 4.6 mm × 150 mm column.

Column B: Waters SunFire-C8 5 μm. 4.6 mm × 150 mm column.

Compound	Column A		Column B	
	Retention time (min)	% Purity	Retention time (min)	% Purity
8b	30.29	99.76	30.41	99.38
8d	31.10	98.25	31.19	98.74
8f	18.75	96.30	17.77	97.55
8g	29.28	99.00	29.72	98.95
8h	29.22	98.21	29.54	98.4
8i	32.81	95.40	32.12	95.08
12j	30.51	96.70	30.92	95.82
12n	31.01	99.12	31.02	97.81
12q	31.13	94.70	31.29	98.98

2. X-ray structure refinement statistics:

Table 4. X-ray data collection and structure refinement statistics of compounds **8a**, **12a-e,w**.

Parameter	8a	12a	12b	12c	12d	12e	12w
resolution (Å) Unit cell *P6122(α=β=90°,γ=120°)*	30-2.45	30-2.90	30-2.15	30-2.6	30-2.5	30-2.3	30-1.9
a, Å	83.093	83.578	81.553	83.499	83.351	82.277	81.613
b, Å	83.093	83.578	81.553	83.499	83.351	82.277	81.613
c, Å	171.852	172.324	169.689	171.242	171.282	169.734	169.145
total reflections observed	446656	298230	604575	845250	639061	295764	480714
unique reflections	13607	8511	18996	11563	12908	15828	27121
multiplicity	32.83	35.04	31.83	73.1	49.51	18.69	17.72
R_{merge}, % (outer shell)	4.8 (38.5)	5.0 (39.0)	4.8 (43.3)	5 (40)	4.2 (40.5)	7.1 (43.3)	3.5 (46.7)
<I/σ(I)>(outer shell)	44.5 (6.91)	40.49 (5.20)	29.54 (4.27)	34.79 (7.4)	43.08 (7.67)	19.1 (3.65)	28.94 (2.56)
completeness, %	99.6	93.8	99.6	96.8	98.3	96.9	98.0
(outer shell)	93.3	89.3	97.9	90.8	92.2	92.2	93.7
R_{work}, %	24.1	19.9	24.3	22.5	24.2	23.4	22.8
R_{free}, %	29.6	33.2	29.5	29.3	29.7	28.5	28.7
RMS[a] bonds, Å	0.013	0.013	0.010	0.014	0.012	0.012	0.012
RMS[a] angles, deg	1.484	1.589	1.395	1.568	1.45	1.461	1.413

[a] RMS = Root-mean-square deviation