STRUCTURAL BASIS FOR THE BROAD-SPECTRUM INHIBITION OF METALLO-β-LACTAMASES BY THIOLS

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SUPPORTING INFORMATION

I. Crystallographic data

Table S1. Data collection and refinement statistics

Metallo-β-Lactamase Inhibitor	CphA **2**	L1 **5a**
Data collection		
Wavelength (Å)	0.93100	1.54179
Resolution (Å) [a]	39.5 - 1.66 (1.70 - 1.66)	26.55 - 2.00 (2.11 - 2.00)
Total Observations	220003	292187
Unique Observations	30263	21311
Space group	$C222_1$	$P6_422$
Unit cell		
(Å)	43.0 101.0 116.8	105.3 105.3 98.0
(°)	90.0 90.0 90.0	90.0 90.0 120.0
Completeness (%) [a]	99.1 (99.1)	96.5 (94.2)
Multiplicity [a]	5.7 (3.2)	13.7 (11.0)
R merge (%) [a, b]	8.1 (22.2)	8.4 (40.4)
$<I / \delta (I)>$ [a]	17.1(4.4)	28.1 (5.5)
Refinement statistics		
R factor / R free (%) [c, d]	14.8 / 17.0	17.0 / 19.2
R. m. s. deviations		
Bond lengths (Å)	0.010	0.013
Bond angles (°)	1.28	1.40
Number of atoms (non-H)		
Zn	1	2
Inhibitor [e]	1 × 14	1 × 11
Sulfate [e]	4 × 5	2 × 5
Glycerol [e]	2 × 6	–
Water	202	235
Average B-factor ($Å^2$)	12.0	30.5

[a] Number in parentheses refer to the highest resolution shell.
[b] $R_{merge} = \sum_{khl} \sum_i | I_i - <I> | / \sum_{khl} \sum_i I_i$.
[c] $R_{fact} = \sum_{khl} | F_o (hkl) – F_c (hkl) | / \sum_{khl} | F_o (hkl) |$.
[d] R_{free} was calculated based on 5% of the total data omitted during structure refinement
[e] Number of molecules × number of atoms

III. NMR

III.1 Effect of the titration of **5a/5b** to BcII followed by 1H-NMR

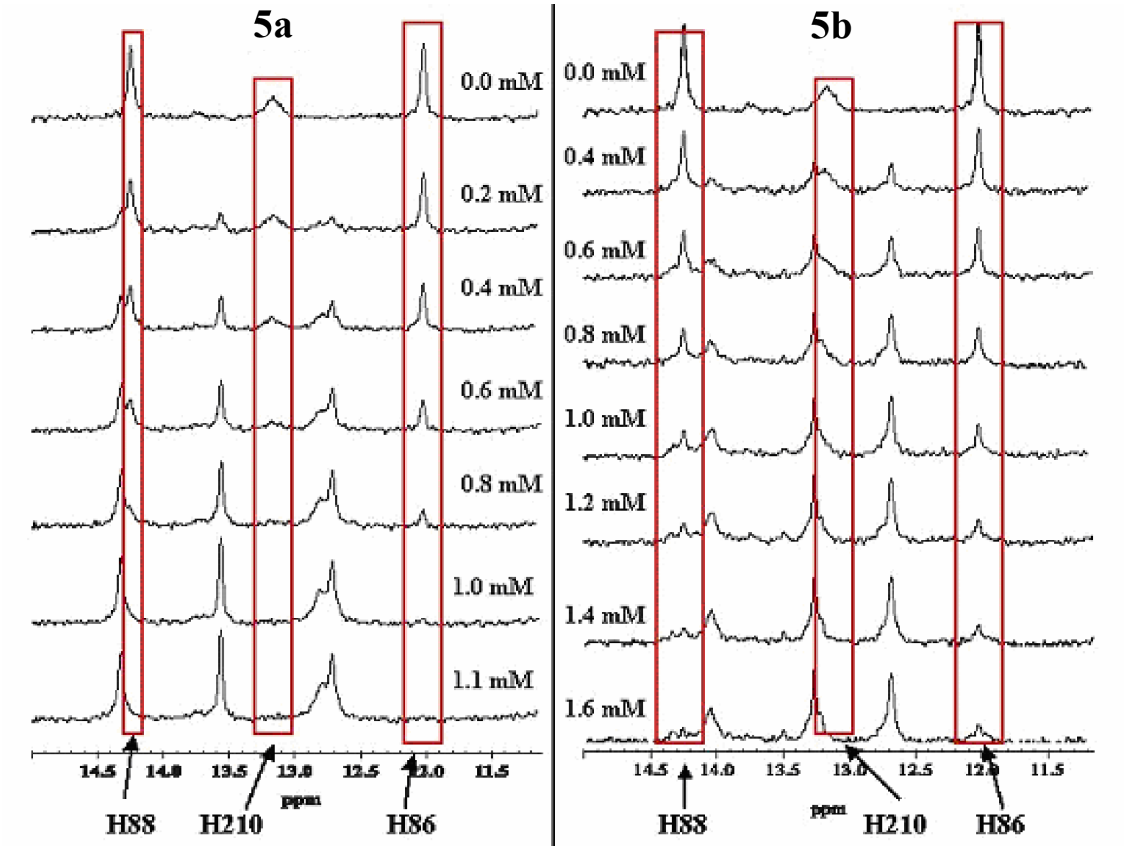

Figure S1. Selected region of the ^{1}H NMR spectra of the BcII MBL from *Bacillus cereus* showing the observed changes in the imidazole NH resonance signals of the metal binding histidine residues (His86, His88 and His210) during the titration of **5a** (left panel) and **5b** (right panel).

III.2 ^{1}H-^{15}N HMQC spectra

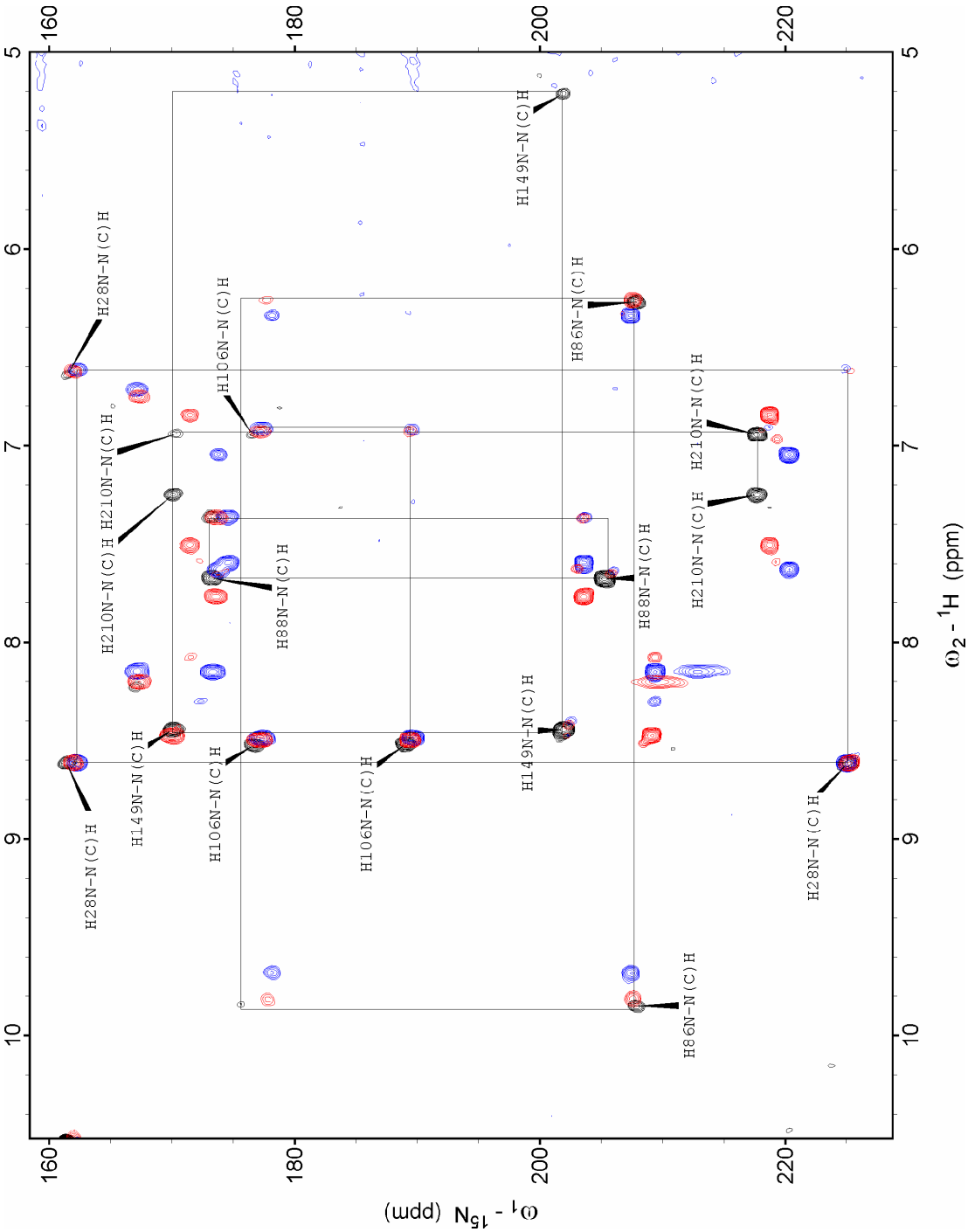

Figure S2. ^{1}H-^{15}N HMQC spectrum optimized for the detection of long-range ^{1}H-^{15}N couplings in the imidazole ring depicting the imidazole resonances. Cross peaks corresponding to the imidazole spin systems for BcII:Zn_2 are in black (connected by black lines), BcII:Zn_2:**5a** in red and BcII:Zn_2:**5b** in blue. Assigned spin systems are labelled by the individual cross peaks for the BcII:Zn_2 peaks only.

III.3 ^{1}H-^{15}N HSQC spectra

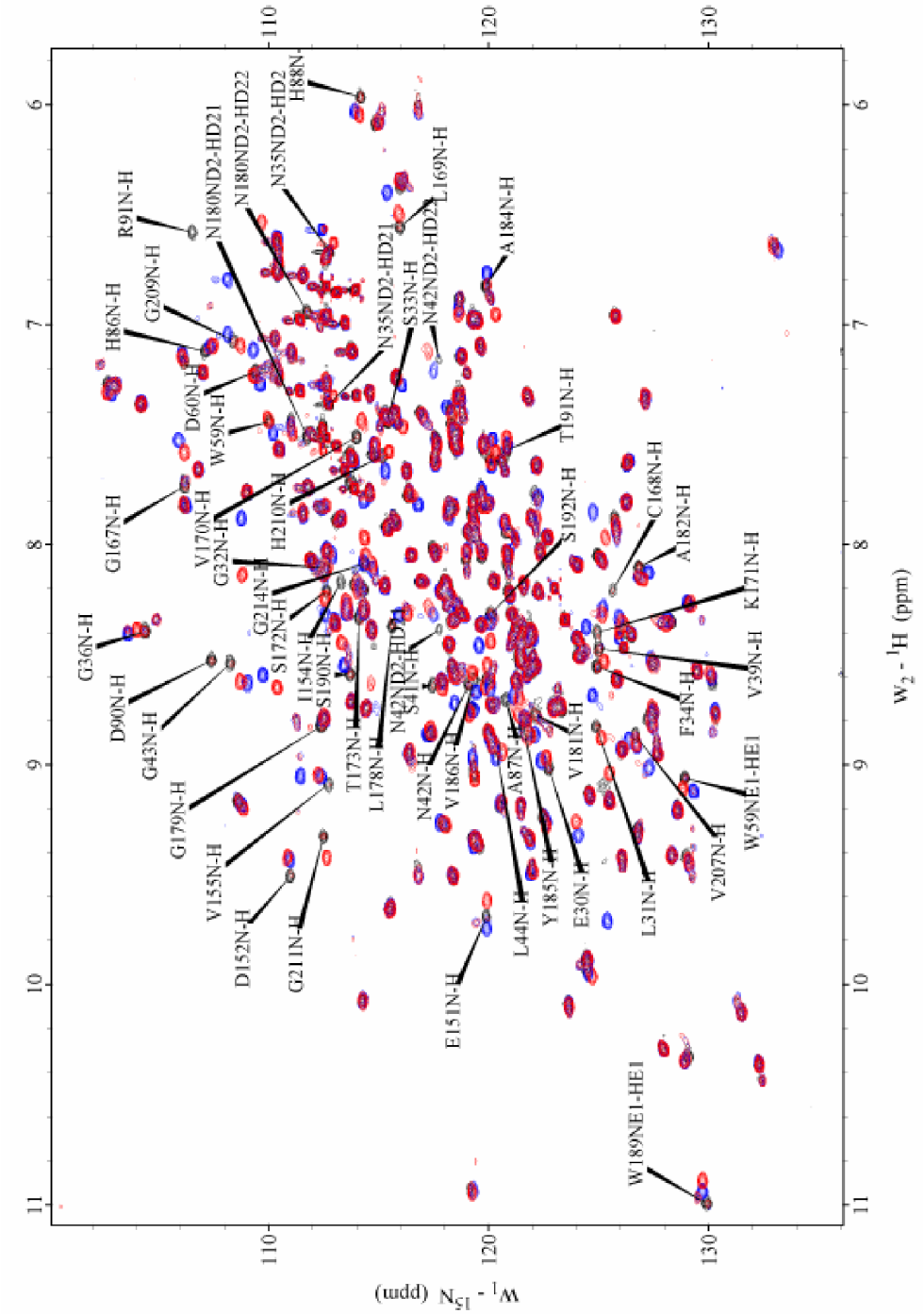

Figure S3. Superposition of ^{1}H-^{15}N HSQC spectra of BcII:Zn_2 in the absence of inhibitors (black), in the presence of **5a** (red) and in the presence of **5b** (blue). The resonance assignments for the most affected backbone, side chain amide and tryptophan indole NH resonances during inhibitor binding are shown.