

Medicinal Au(I) compounds targeting urease as prospective antimicrobial agents: unveiling the structural basis for enzyme inhibition

SUPPLEMENTARY INFORMATION

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Table 1-SI. Data collection, processing and refinement statistics for the X-ray crystal structures of SPU co-crystallized in the presence of Au(PEt₃)I (**3**, PDB code 7P7N) and Au(PEt₃)₂Cl (**4**, PDB code 7P7O).

Data collection	7P7N Au(PEt ₃)I (3)	7P7O Au(PEt ₃) ₂ Cl (4)
Wavelength (Å)	0.9762	
Detector	DECTRIS PILATUS 6M	
Crystal-to-Detector distance (mm)	269.4	
Oscillation angle (degrees)	0.100	
Number of images	1800	
Space group	P6 ₃ 22	
Unit cell (<i>a</i> , <i>b</i> , <i>c</i> , Å)	131.6 131.6 189.2	131.8, 131.8, 189.4
Resolution range (Å) ^a	114.0–1.80 (1.83–1.80)	114.1–1.87 (1.90–1.87)
Total number of reflections ^a	1180987 (61039)	1400616 (79653)
Unique reflections ^a	89759 (4534)	80498 (4557)
Multiplicity ^a	13.2 (13.5)	17.4 (17.5)
Completeness ^a (%)	100.0 (100.0)	100.0 (100.0)
R _{sym} ^{a,b} (%)	14.2 (230.0)	15.8 (300.1)
R _{pim} ^{a,c} (%)	5.8 (93.1)	5.0 (108.0)
Mean I half-set correlation CC(1/2) ^a	0.999 (0.694)	0.999 (0.744)
Mean I/σ(I) ^a	17.0 (1.5)	17.9 (1.5)
Refinement statistics		
Number of monomers in the asymmetric unit	3 (αβγ)	3 (αβγ)
R _{factor} ^d (%)	14.7	16.3
R _{free} ^d (%)	17.7	20.4
Cruickshank's DPI for coordinate error ^e based on R _{factor} (Å) ^e	0.093	0.116
Wilson plot B-factor (Å ²)	25.3	26.9
Average all atom B-factor ^f (Å ²)	31.7	38.9
B-factor ^f for the Ni atoms (Å ²)	31.6; 30.3	36.1; 36.7
RMS (bonds) ^d	0.01	0.01
RMS (angles) ^d	1.69	1.63
Total number of atoms	6937	6879
Total number of water molecules	549	469
Solvent content (%)	53.2	53.6
Matthews Coefficient (Å ³ /Da)	2.63	2.65
Ramachandran plot^d		
Favored regions (%)	95.5	95.6
Additionally allowed regions (%)	3.7	3.7
Disallowed regions (%)	0.8	0.7

^a Highest resolution bin in parentheses;

$$R_{sym} = \frac{\sum_{hkl} \sum_j |I_j - \langle I \rangle|}{\sum_{hkl} \sum_j I_j}, \text{ where } I \text{ is the intensity of a reflection, and } \langle I \rangle \text{ is the mean intensity of all symmetry related reflections } j; ^c$$

$$R_{p.i.m.} = \frac{\sum_{hkl} \left\{ [1/(N-1)]^{1/2} \sum_j |I_j - \langle I \rangle| \right\}}{\sum_{hkl} \sum_j I_j}, \text{ where } I \text{ is the intensity of a reflection, and } \langle I \rangle \text{ is the mean intensity of all symmetry related reflections } j, \text{ and } N \text{ is the multiplicity}^{[13]};$$

^d Taken from REFMAC; R_{free} is calculated using 5% of the total reflections that were randomly selected and excluded from refinement;

^e $DPI = R_{factor} \cdot D_{max} \cdot compl^{-1/3} \sqrt{\frac{N_{atoms}}{(N_{refl} - N_{params})}}$, where *N*_{atoms} is the number of the atoms included in the refinement, *N*_{refl} is the number of the reflections included in the refinement, *D*_{max} is the maximum resolution of reflections included in the refinement, *compl* is the completeness of the observed data, and for isotropic refinement, *N*_{params} ≈ 4*N*_{atoms};

^f Taken from BAVEGAGE.

Table 2-SI. Selected distances (Å) and angles (°) around the Ni(II) ions in the crystal structures of SPU co-crystallized in the presence of Au(PEt₃)I (**3**, PDB code 7P7N) and Au(PEt₃)₂Cl (**4**, PDB code 7P7O). The same parameters reported for the structures of native (PDB 4CEU) and Au(I)-bound SPU (PDB code 6I9Y) are reported for comparison.

	7P7N Au(PEt ₃)I (3)	7P7O Au(PEt ₃) ₂ Cl (4)	4CEU Native	6I9Y Au(I)-SPU
Ni - L Distances (Å)				
Ni(1) - αLys220* Oθ1	2.0	2.0	1.9	2.0
Ni(1) - O _B ^a	2.1	2.1	2.1	1.9
Ni(1) - O ₁	2.2	2.1	2.2	2.2
Ni(1) - αHis249 Nδ	2.0	2.1	2.0	2.1
Ni(1) - αHis275 Nε	2.1	2.0	2.0	2.2
Ni(2) - αLys220* Oθ2	2.0	2.1	2.1	2.1
Ni(2) - O _B	2.1	2.2	2.1	2.2
Ni(2) - O ₂	2.3	2.3	2.1	2.6
Ni(2) - αHis137 Nε	2.1	2.1	2.1	2.1
Ni(2) - αHis139 Nε	2.1	2.1	2.1	2.2
Ni(2) - αAsp363 Oδ1	2.1	2.1	2.1	2.2
Ni(1) ••• Ni(2)	3.6	3.7	3.7	3.6
O ₁ ••• O ₂	2.1	2.0	2.4	2.2
L - Ni - L Angles (°)				
αLys220* Oθ1 - Ni(1) - αHis249 Nδ	108.3	103.7	100.4	103.2
αLys220* Oθ1 - Ni(1) - αHis275 Nε	102.5	103.2	107.2	104.0
αLys220* Oθ1 - Ni(1) - O _B	93.8	96.4	96.6	91.2
αLys220* Oθ1 - Ni(1) - O ₁	107.0	101.6	108.2	110.8
αHis249 Nδ - Ni(1) - αHis275 Nε	97.1	98.5	98.6	91.9
αHis275 Nε - Ni(1) - O _B	95.1	96.1	94.6	93.2
O _B - Ni(1) - O ₁	63.0	61.2	67.0	80.2
O ₁ - Ni(1) - αHis249 Nδ	93.2	94.9	89.3	86.4
αHis249 Nδ - Ni(1) - O _B	151.9	151.6	154.2	163.1
αHis275 Nε - Ni(1) - O ₁	143.8	148.1	141.6	144.7
αLys220* Oθ2 - Ni(2) - αHis137 Nε	95.1	93.5	90.8	90.9
αLys220* Oθ2 - Ni(2) - αHis139 Nε	93.4	92.3	91.7	91.2
αLys220* Oθ2 - Ni(2) - O ₂	91.2	88.6	92.9	93.5
αLys220* Oθ2 - Ni(2) - O _B	95.8	95.1	95.6	91.7
αAsp363 Oδ1 - Ni(2) - αHis137 Nε	84.4	83.5	82.8	83.6
αAsp363 Oδ1 - Ni(2) - αHis139 Nε	81.7	85.0	86.4	87.2
αAsp363 Oδ1 - Ni(2) - O ₂	91.6	94.8	94.5	93.1
αAsp363 Oδ1 - Ni(2) - O _B	90.0	90.2	89.1	92.3
O ₂ - Ni(2) - O _B	61.3	61.3	67.7	68.8
O _B - Ni(2) - αHis137 Nε	94.8	95.8	95.0	90.1
αHis137 Nε - Ni(2) - αHis139 Nε	114.4	113.4	108.5	112.8
αHis139 Nε - Ni(2) - O ₂	88.5	89.3	88.4	88.0
αLys220* Oθ2 - Ni(2) - αAsp363 Oδ1	174.3	174.5	172.4	173.1
O _B - Ni(2) - αHis139 Nε	148.5	149.3	155.3	156.8
O ₂ - Ni(2) - αHis137 Nε	155.8	157.1	162.6	158.6
Ni(1) - O _B - Ni(2)	119.0	117.8	122.1	125.8

Figure 1-SI. Per residue C α RMSD calculated between the α , β and γ subunits (coloured red, magenta and blue, respectively) of SPU co-crystallized in the presence of Au(PEt₃)I (**3**, PDB code P7PN) (upper panel) and Au(PEt₃)₂Cl (**4**, PDB code P7PO) (bottom panel) with respect to native SPU (PDB code 4CEU).

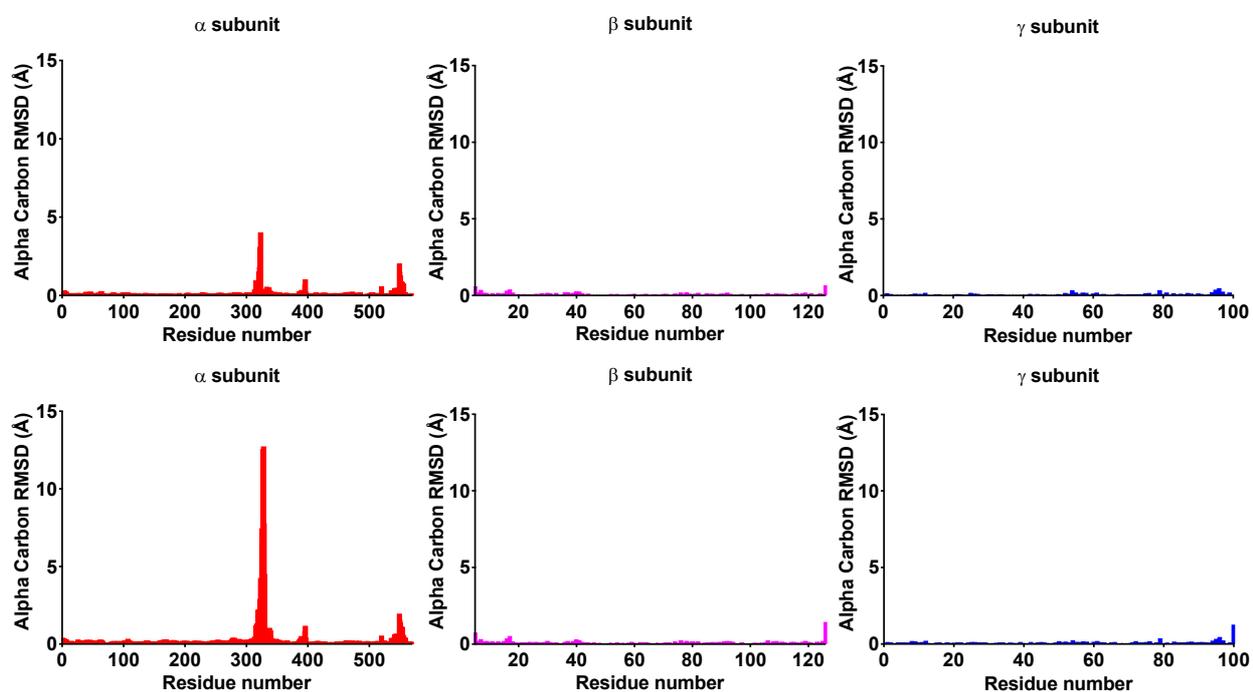


Figure 2-SI. Per residue C α RMSD calculated between the α , β and γ subunits (coloured black, dark grey and grey, respectively) of SPU co-crystallized in the presence of Au(PEt₃)I (**3**, PDB code 7P7N) (upper panel) and Au(PEt₃)₂Cl (**4**, PDB code 7P7O) (bottom panel) with respect to Au(I)-inhibited SPU (PDB code 6I9Y).

