SUPPORTING INFORMATION

Table S1. Nonbonded distances (Å) between cofactor carboxylates and other atoms in the active site of the MD (standard deviations in parentheses) averaged (2000–3000 ps) and crystal structures.

Nonbonded distances	X-ray	**A**	**B**	**C**
O2A···NH1(Arg408)	3.71	3.85 (±0.28)*	3.63 (±0.22)*	3.87 (±0.25)*
O2B···NH1(Arg408)	3.03	2.79 (±0.14)*	2.71 (±0.10)**	2.71 (±0.10)*
O2A···NH2(Arg408)	2.77	2.81 (±0.16)*	2.76 (±0.12)*	2.87 (±0.17)*
O2B···NH2(Arg408)	3.52	3.20 (±0.20)**	3.35 (±0.20)*	3.20 (±0.20)**
O2B···NE2(Gln231)	3.06	2.88 (±0.14)*	2.92 (±0.18)*	3.00 (±0.28)*
O7A···OG1(Thr348)	2.84	2.74 (±0.10)*	2.79 (±0.13)*	2.67 (±0.09)*
O7B···NZ(Lys377)	2.64	2.66 (±0.09)*	2.63 (±0.08)*	2.72 (±0.11)*
O7A···O(TIP3P)	___	____	____	2.78 (±0.12)
O9A···OH(Tyr343)	4.91	4.20 (±0.49)	5.92 (±1.25)	2.63 (±0.10)
O9A···NH1(Arg406)	2.80	2.81 (±0.13)*	2.80 (±0.16)*	3.30 (±0.35)
O9A···NH2(Arg406)	3.58	3.21 (±0.25)**	3.44 (±0.39)*	3.24 (±0.41)**
O9B···NH2(Arg406)	2.90	2.77 (±0.11)*	2.76 (±0.22)*	2.91 (±0.25)*

Values within *0.25 Å and **0.26–0.45 Å different than the crystal structure

Table S2. Nonbonded distances (Å) between various atoms in the active site of the MD (standard deviations in parentheses) averaged (2000–3000 ps) and crystal structures.

Nonbonded distances	X-ray	**A**	**B**	**C**
C5···NE2(His144)	4.71	4.89 (±0.23)*	4.88 (±0.21)*	4.54 (±0.25)*
O5···NE2(His144)	4.40	4.76 (±0.24)**	4.79 (±0.24)**	3.83 (±0.28)
H5···NE2(His144)	___	____	5.64 (±0.21)	4.82 (±0.25)
O5···NE2(Gln168)	5.86	6.60 (±0.38)	7.57 (±0.61)	4.84 (±0.45)
O5···NH1(Arg228)	2.83	2.82 (±0.12)*	2.62 (±0.08)*	3.75 (±0.25)
O5···NH2(Arg228)	3.37	3.44 (±0.25)*	2.86 (±0.23)	2.97 (±0.18)**
C5···OE1(Gln246)	4.25	3.25 (±0.19)	3.88 (±0.34)**	3.54 (±0.23)
H5···OE1(Gln246)	___	____	3.11 (±0.46)	3.27 (±0.28)
H5···O(Gly247)	___	____	4.63 (±0.21)	3.40 (±0.17)
C5···NE2(Gln246)	2.95	4.51 (±0.24)	[a]4.25 (±0.38)	4.92 (±0.33)
H5···NE2(Gln246)	___	____	[a]3.26 (±0.38)	4.99 (±0.34)
H5···O4	___	____	2.88 (±0.10)	2.55 (±0.08)
NE2(His144)···NH2(Arg228)	3.50	3.46 (±0.21)*	3.40 (±0.23)*	3.21 (±0.18)**
NE2(His144)···OD1(Asp163)	2.62	[b]3.04 (±0.59)**	2.62 (±0.07)*	3.14 (±0.69)
NE2(His144)···OD2(Asp163)	4.01	[c]2.70 (±0.09)	4.13 (±0.22)*	3.81 (±0.69)*
O4···NE2(His144)	3.30	3.62 (±0.27)**	3.05 (±0.23)*	3.59 (±0.28)**
O4···HE2(His144)	___	____	2.75 (±0.42)	____
O4···ND1(His144)	5.03	5.12 (±0.23)*	4.49 (±0.23)	4.93 (±0.26)*
O4···NH1(Arg228)	3.37	3.37 (±0.20)*	3.42 (±0.19)*	2.94 (±0.15)**
O4···NH2(Arg228)	4.58	4.54 (±0.30)*	3.78 (±0.36)	3.94 (±0.25)
O4···ND2(Asn229)	3.02	2.90 (±0.15)*	3.09 (±0.31)*	2.94 (±0.16)*
OG(Ser146)···OD1(Asn229)	2.62	2.74 (±0.13)*	2.73 (±0.12)*	2.72 (±0.12)*

Values within *0.25 Å and **0.26–0.45 Å different than the crystal structure

Values averaged from [a]2250–3000 ps, [b]2751–3000 ps and [c]2000–2750 ps

Table S3. Nonbonded distances (Å) between waters and atoms in the active site of the MD (standard deviations in parentheses) averaged (2000–3000 ps) and crystal structures.

Nonbonded distances	X-ray	**A**	**B**	**C**
N6···O(Wat55)	3.01	3.24 (±0.13)*	3.51 (±0.15)**	3.00 (±0.11)*
O7A···O(Wat55)	3.28	3.03 (±0.12)*	2.83 (±0.16)**	2.91 (±0.12)**
O5···O(Wat55)	3.17	3.06 (±0.14)*	3.27 (±0.16)*	5.14 (±0.19)
C5···O(Wat55)	3.55	3.54 (±0.14)*	3.76 (±0.21)**	4.16 (±0.18)
H5···O(Wat55)	___	____	3.43 (±0.30)	3.39 (±0.20)
OE1(Gln246)···O(Wat55)	4.98	2.82 (±0.20)	5.38 (±1.36)**	2.98 (±0.41)
NE2(Gln246)···O(Wat55)	2.75	5.04 (±0.19)	5.45 (±0.44)*	5.10 (±0.39)
O(Gly247)···O(Wat55)	3.11	2.90 (±0.12)*	2.98 (±0.15)*	2.80 (±0.11)**
N(Gly247)···O(Wat55)	3.78	3.56 (±0.17)*	3.54 (±0.20)*	3.49 (±0.17)**
OD1(Asp252)···O(Wat55)	2.69	2.65 (±0.09)*	2.63 (±0.09)*	2.65 (±0.09)*
N6···O(Wat89)	3.33	2.99 (±0.11)**	3.13 (±0.17)*	3.19 (±0.13)*
O7A···O(Wat89)	3.37	3.65 (±0.15)**	3.47 (±0.24)*	4.21 (±0.10)
O5···O(Wat89)	3.49	2.91 (±0.14)	3.14 (±0.18)**	2.80 (±0.16)
C5···O(Wat89)	3.98	3.61 (±0.14)**	4.03 (±0.22)*	3.22 (±0.13)
H5···O(Wat89)	___	____	4.86 (±0.18)	2.74 (±0.19)
NH2(Arg228)···O(Wat89)	3.19	3.33 (±0.22)*	3.23 (±0.24)*	3.05 (±0.14)
O(Pro247)···O(Wat89)	3.92	3.44 (±0.16)**	3.23 (±0.28)	2.87 (±0.14)
O(Pro248)···O(Wat89)	3.17	2.88 (±0.13)**	2.83 (±0.19)**	3.17 (±0.16)*

Values within *0.25 Å and **0.26–0.45 Å different than the crystal structure

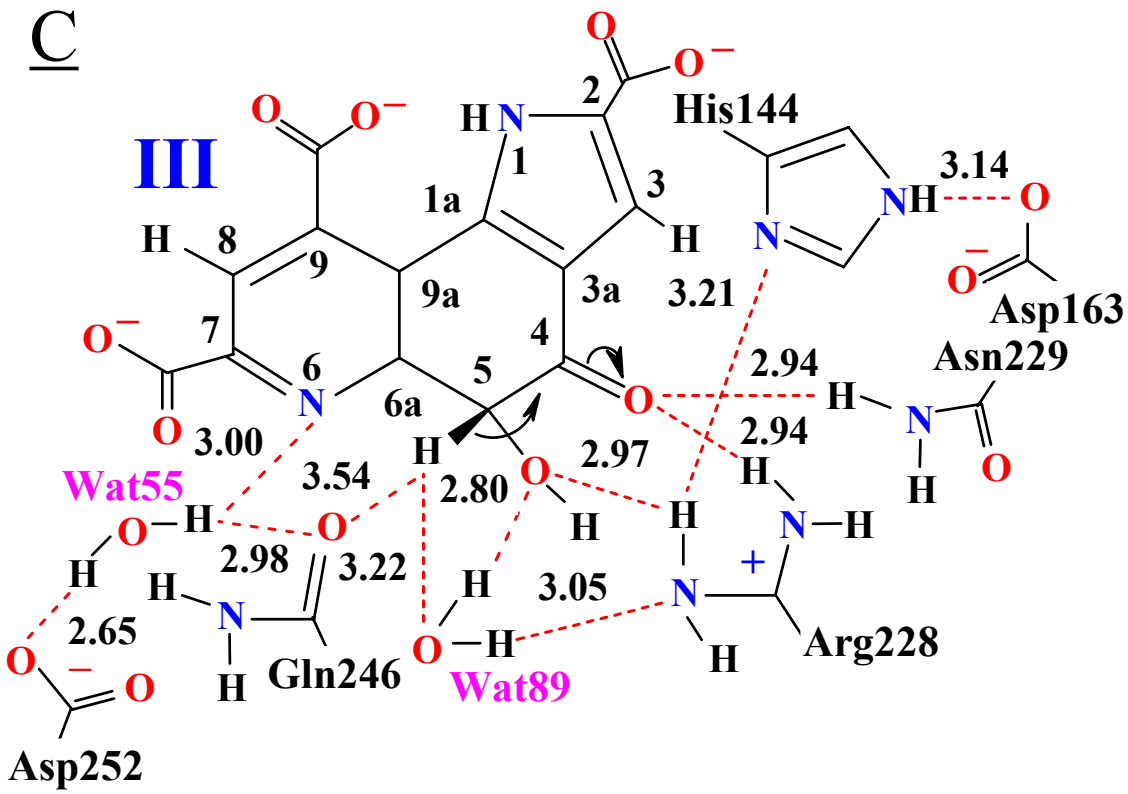

Figure S1. Active site residues of the MD averaged (2000–3000 ps) structure **C**. Ca^{2+} is omitted for clarity. Nonbonded interactions are in red and distances (Å) between the heavy atoms are given in black.