

Supplementary Information for:
Molecular Docking, MM/GBSA, FEP/MD, and
DFT/MM MD Studies on Predicting Binding
Affinity of Carbonic Anhydrase II Inhibitors

Ryoma Shimizu, Yu Takano, Toru Saito*

Department of Biomedical Information Sciences, Graduate School of Information Sciences,
Hiroshima City University, 3-4-1 Ozuka-Higashi, Asa-Minami-Ku, Hiroshima 731-3194 Japan

*Corresponding author: tsaito@hiroshima-cu.ac.jp

Contents

Section 1: Figure S1

Section 2: Figure S2

Section 3: Figure S3

Section 4: Figure S4

Section 5: Figure S5

Section 6: Figure S6

Section 7: Figure S7

Section 8: Topology and parameter files for zinc active site and sulfonamide core.

Section 1: Figure S1

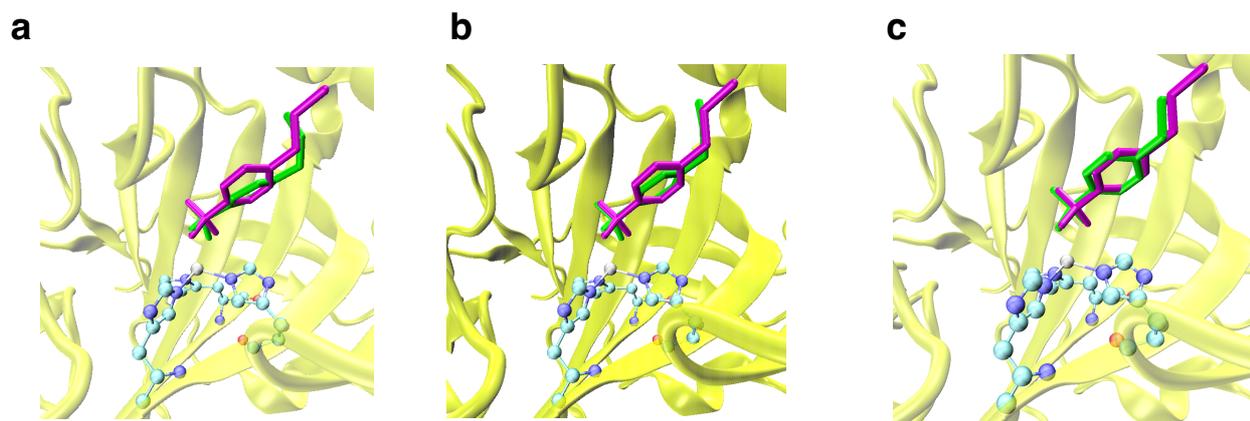


Figure S1. Overlay of the best docked pose (green) with respect to the X-ray crystallographic structure (magenta) obtained with (a) AutoDock Vina, (b) AutoDock4, and (c) GOLD simulations.

Section 2: Figure S2

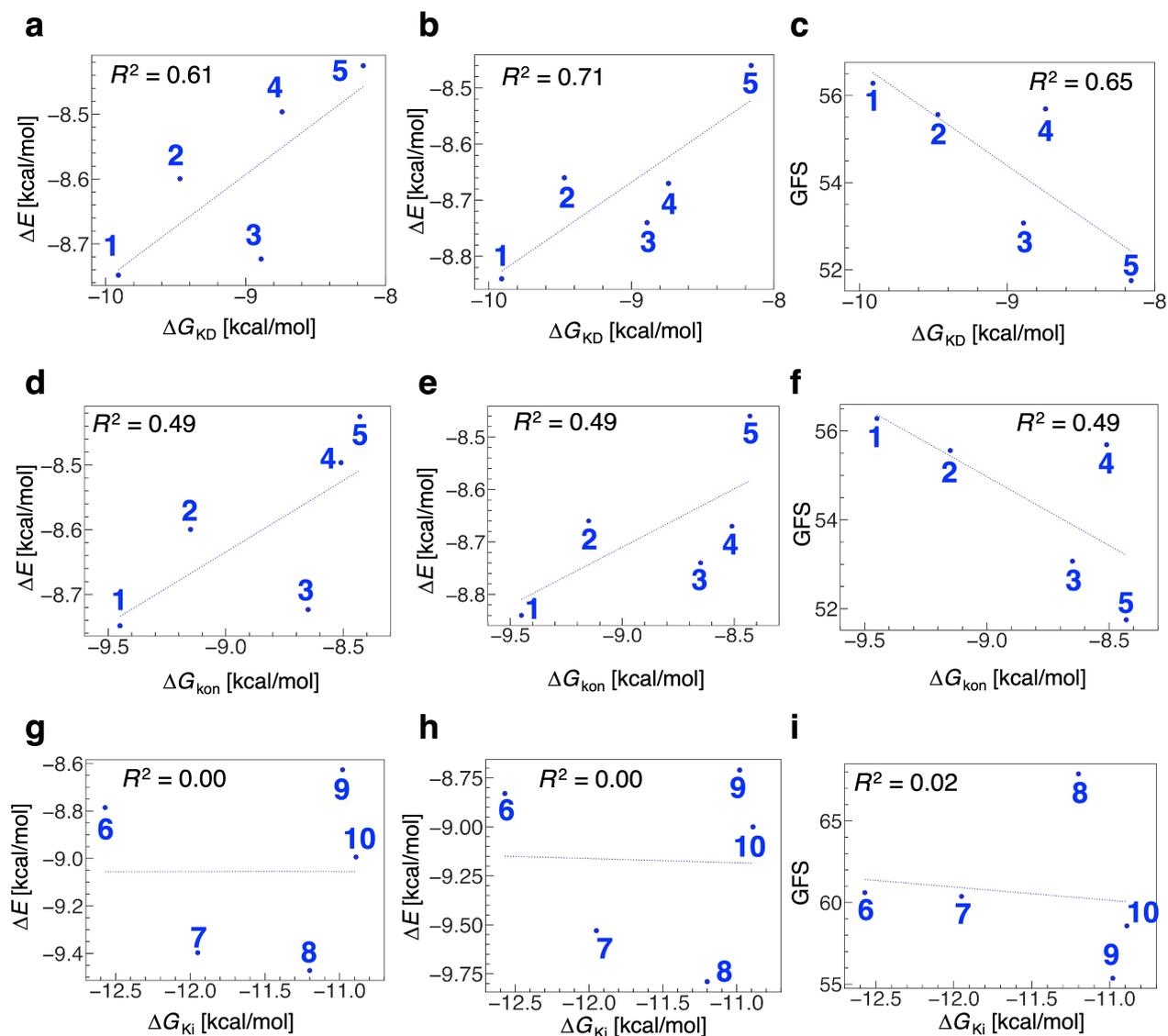


Figure S2. Comparison of binding free energies (ΔG_{KD} , ΔG_{kon} , ΔG_{Ki}) between the experimental and calculated results obtained by (a, d, g) AutoDock Vina, (b, e, h) AutoDock4, and (c, f, i) GOLD calculations.

Section 3: Figure S3

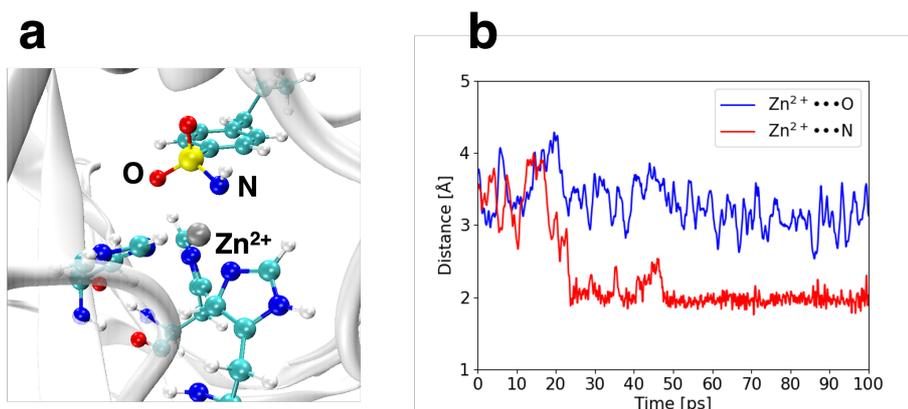


Figure S3. (a) Representative snapshot of the zinc active site and (b) evolutions of the Zn•••O and Zn•••N distances during a 100 ps QM/MM metadynamics simulation.

Section 4: Figure S4

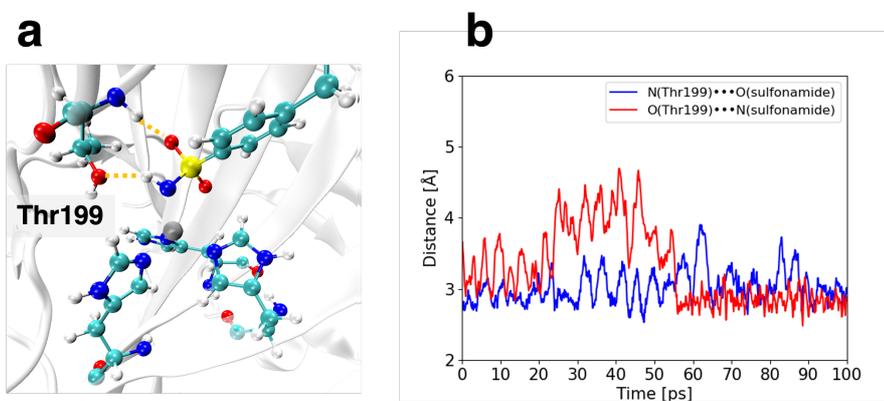


Figure S4. (a) Representative snapshot of the zinc active site and Thr199 and (b) evolutions of the N(Thr199)•••O(sulfonamide) and O(Thr199)•••N(sulfonamide) distances during a 100 ps QM/MM metadynamics simulation.

Section 5: Figure S5

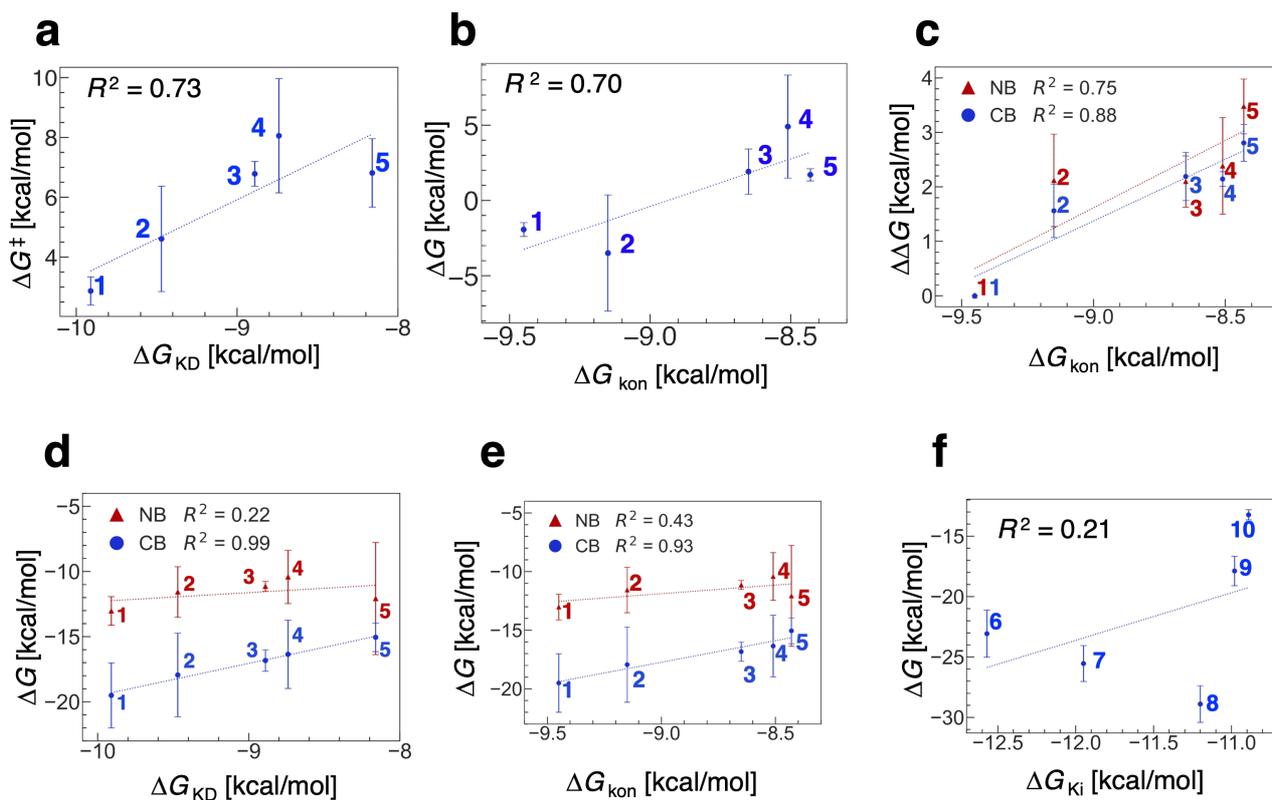


Figure S5. Comparison of binding free energies (ΔG_{KD} , ΔG_{kon} , and ΔG_{Ki}) between the experimental and calculated results obtained by (a, b) QM(B3LYP)/MM(CHARMM) MD for 1–5, (c) FEP/MD for 1–5, (d, e) MM/GBSA for 1–5, and (f) MM/GBSA for 6–10.

Section 6: Figure S6

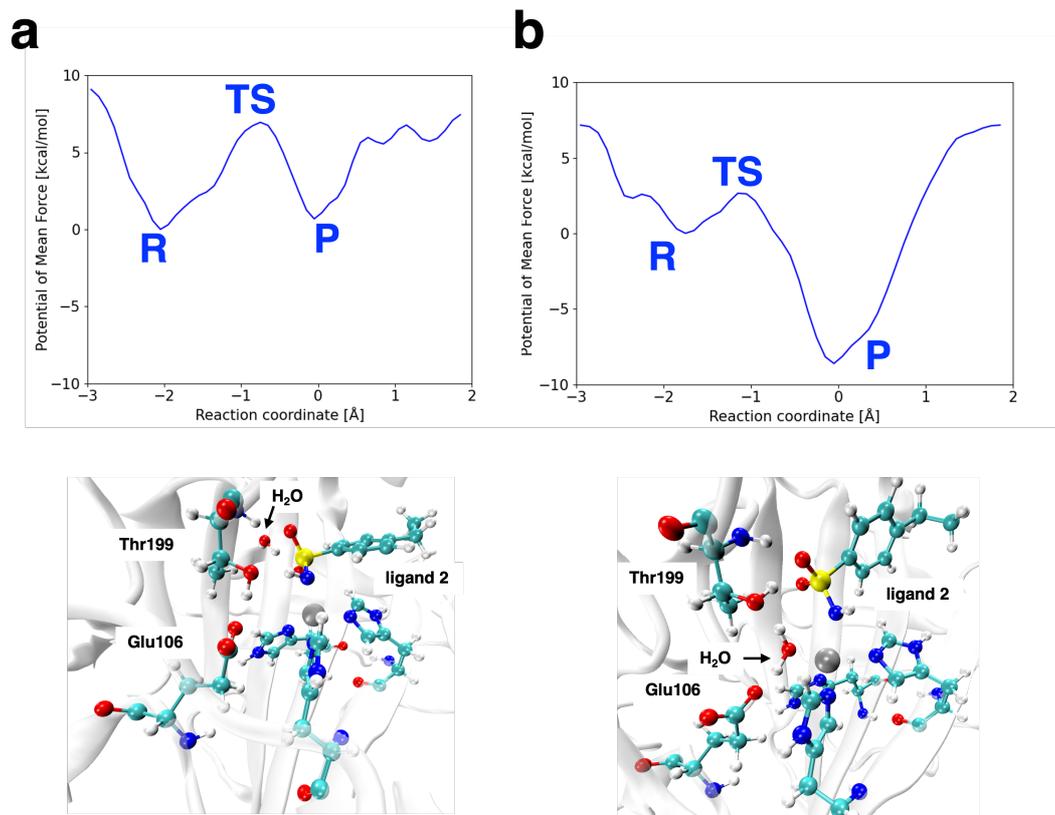


Figure S6. One-dimensional potentials of mean force (1D-PMF) from the reactant (R) to product (P) state via transition state (TS) for the formation of (a) water-free and (b) water-coordinate complexes for ligand 2, together with their representative snapshots in P taken from the 100-ps-long QM(B3LYP)/MM(CHARMM) metadynamics simulations.

Section 7: Figure S7

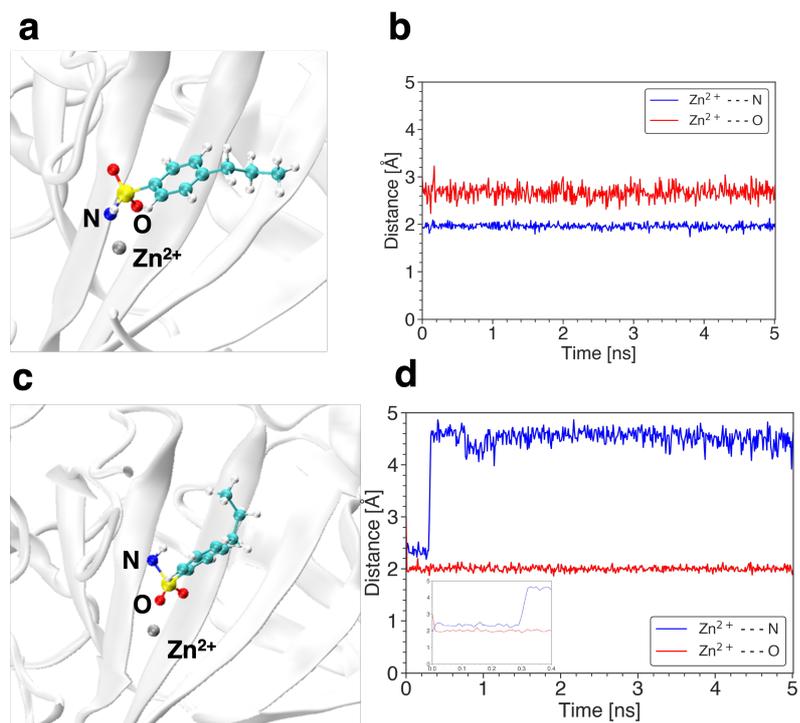


Figure S7. (a) Representative snapshot of the zinc active site taken from the 5-ns-long equilibration and (b) evolutions of the Zn²⁺•••O and Zn²⁺•••N distances with the CB model. (c) and (d) represents those obtained with the NB model.

Section 8: Topology and parameter files for zinc active site and sulfonamide core.

! Topology file for the Zn(His)₃ active site

```

RESI ZN1          0.39
GROUP
ATOM ZN   ZN     0.39
PATCHING FIRST NONE LAST NONE

RESI MH1          0.33
GROUP
ATOM N     NH1   -0.42 !      |           HD1   HE1
ATOM HN    H     0.33 !      |           |           /
ATOM CA    CT1   0.02 !      |           |           |
ATOM HA    HB1   0.10 !      |           |           |
ATOM ND1   NR1  -0.29 !      |           |           |
ATOM HD1   H     0.37 !      |           |           |
ATOM CG    CPH1  0.23 !      |           |           |
ATOM CB    CT2  -0.35 !      |           |           |
ATOM HB1   HA2   0.14 !      |           |           |
ATOM HB2   HA2   0.14         |           |           |
ATOM NE2   L1    -0.03         |           |           |
ATOM CD2   CPH1  -0.31         |           |           |
ATOM HD2   HR3   0.19         |           |           |
ATOM CE1   CPH2  0.02         |           |           |
ATOM HE1   HR1   0.16         |           |           |
ATOM C     C     0.60         |           |           |
ATOM O     O    -0.57         |           |           |
BOND CB   CA    CG    CB    ND1 CG    CE1 ND1
BOND NE2  CD2   N     HN    N     CA
BOND C    CA    C     +N    CA    HA    CB    HB1
BOND CB   HB2   ND1  HD1   CD2  HD2   CE1  HE1
DOUBLE O   C     CG    CD2   CE1  NE2
IMPR ND1  CG    CE1  HD1   CD2  CG    NE2  HD2   CE1  ND1  NE2  HE1
IMPR ND1  CE1  CG    HD1   CD2  NE2  CG    HD2   CE1  NE2  ND1  HE1
IMPR N    -C   CA    HN    C     CA    +N    O
CMAP -C   N    CA    C     N     CA    C     +N
DONOR HN  N
DONOR HD1 ND1
ACCEPTOR NE2
ACCEPTOR O C
IC -C    CA    *N    HN     1.3475 123.2700 180.0000 115.2100 0.9988
IC -C    N     CA    C      1.3475 123.2700 180.0000 107.7000 1.5166
IC N     CA    C     +N     1.4521 107.7000 180.0000 117.5700 1.3509
IC +N    CA    *C    O      1.3509 117.5700 180.0000 120.2400 1.2273
IC CA    C     +N    +CA    1.5166 117.5700 180.0000 123.7200 1.4545
IC N     C     *CA   CB     1.4521 107.7000 122.4600 109.9900 1.5519
IC N     C     *CA   HA     1.4521 107.7000 -117.4900 107.3700 1.0830
IC N     CA    CB    CG     1.4521 112.1200 180.0000 114.0500 1.5041
IC CG    CA    *CB   HB1    1.5041 114.0500 121.1700 109.0100 1.1118
IC CG    CA    *CB   HB2    1.5041 114.0500 -122.3600 109.5300 1.1121

```

IC CA	CB	CG	ND1	1.5519	114.0500	90.0000	124.1000	1.3783
IC ND1	CB	*CG	CD2	1.3783	124.1000	-171.2900	129.6000	1.3597
IC CB	CG	ND1	CE1	1.5041	124.1000	-173.2100	107.0300	1.3549
IC CB	CG	CD2	NE2	1.5041	129.6000	171.9900	110.0300	1.3817
IC NE2	ND1	*CE1	HE1	1.3166	111.6300	-179.6300	123.8900	1.0932
IC CE1	CG	*ND1	HD1	1.3549	107.0300	-174.6500	126.2600	1.0005
IC NE2	CG	*CD2	HD2	1.3817	110.0300	-177.8500	129.6300	1.0834

RESI MH2 0.38
GROUP

ATOM N	NH1	-0.42	!			HD1	HE1
ATOM HN	H	0.31	!	HN-N			/
ATOM CA	CT1	0.02	!		HB1	ND1-----CE1	
ATOM HA	HB1	0.08	!			/	
ATOM ND1	NR1	-0.20	!	HA-CA--CB---CG			
ATOM HD1	H	0.35	!			CD2-----NE2	
ATOM CG	CPH1	-0.12	!		HB2		
ATOM CB	CT2	0.18	!	O=C			
ATOM HB1	HA2	0.03	!			HD2	
ATOM HB2	HA2	0.03					
ATOM NE2	L2	-0.06					
ATOM CD2	CPH1	-0.15					
ATOM HD2	HR3	0.13					
ATOM CE1	CPH2	-0.01					
ATOM HE1	HR1	0.18					
ATOM C	C	0.60					
ATOM O	O	-0.57					

BOND CB CA CG CB ND1 CG CE1 ND1

BOND NE2 CD2 N HN N CA

BOND C CA C +N CA HA CB HB1

BOND CB HB2 ND1 HD1 CD2 HD2 CE1 HE1

DOUBLE O C CG CD2 CE1 NE2

IMPR ND1 CG CE1 HD1 CD2 CG NE2 HD2 CE1 ND1 NE2 HE1

IMPR ND1 CE1 CG HD1 CD2 NE2 CG HD2 CE1 NE2 ND1 HE1

IMPR N -C CA HN C CA +N O

CMAP -C N CA C N CA C +N

DONOR HN N

DONOR HD1 ND1

ACCEPTOR NE2

ACCEPTOR O C

IC -C CA *N HN 1.3475 123.2700 180.0000 115.2100 0.9988

IC -C N CA C 1.3475 123.2700 180.0000 107.7000 1.5166

IC N CA C +N 1.4521 107.7000 180.0000 117.5700 1.3509

IC +N CA *C O 1.3509 117.5700 180.0000 120.2400 1.2273

IC CA C +N +CA 1.5166 117.5700 180.0000 123.7200 1.4545

IC N C *CA CB 1.4521 107.7000 122.4600 109.9900 1.5519

IC N C *CA HA 1.4521 107.7000 -117.4900 107.3700 1.0830

IC N CA CB CG 1.4521 112.1200 180.0000 114.0500 1.5041

IC CG CA *CB HB1 1.5041 114.0500 121.1700 109.0100 1.1118

IC CG CA *CB HB2 1.5041 114.0500 -122.3600 109.5300 1.1121

IC CA CB CG ND1 1.5519 114.0500 90.0000 124.1000 1.3783

IC ND1 CB *CG CD2 1.3783 124.1000 -171.2900 129.6000 1.3597

IC CB	CG	ND1	CE1	1.5041	124.1000	-173.2100	107.0300	1.3549
IC CB	CG	CD2	NE2	1.5041	129.6000	171.9900	110.0300	1.3817
IC NE2	ND1	*CE1	HE1	1.3166	111.6300	-179.6300	123.8900	1.0932
IC CE1	CG	*ND1	HD1	1.3549	107.0300	-174.6500	126.2600	1.0005
IC NE2	CG	*CD2	HD2	1.3817	110.0300	-177.8500	129.6300	1.0834

RESI MH3 0.44

GROUP

ATOM N	NH1	-0.42	!					HE1
ATOM HN	H	0.31	!	HN-N				/
ATOM CA	CT1	-0.06	!		HB1	ND1-----	CE1	
ATOM HA	HB1	0.13	!			/		
ATOM NE2	NR1	-0.21	!	HA-CA---	CB---	CG		
ATOM HE2	H	0.35	!			\		
ATOM CD2	CPH1	-0.09	!		HB2	CD2-----	NE2	
ATOM HD2	HR3	0.17	!	O=C			\	
ATOM ND1	L3	0.12	!			HD2	HE2	
ATOM CG	CPH1	-0.14						
ATOM CE1	CPH2	-0.10						
ATOM HE1	HR1	0.18						
ATOM CB	CT2	0.05						
ATOM HB1	HA2	0.06						
ATOM HB2	HA2	0.06						
ATOM C	C	0.60						
ATOM O	O	-0.57						

BOND CB CA CG CB ND1 CG
 BOND NE2 CD2 N HN N CA
 BOND C CA C +N NE2 CE1 CA HA CB HB1
 BOND CB HB2 NE2 HE2 CD2 HD2 CE1 HE1
 DOUBLE O C CD2 CG CE1 ND1
 IMPR NE2 CD2 CE1 HE2 CD2 CG NE2 HD2 CE1 ND1 NE2 HE1
 IMPR NE2 CE1 CD2 HE2 CD2 NE2 CG HD2 CE1 NE2 ND1 HE1
 IMPR N -C CA HN C CA +N O
 CMAP -C N CA C N CA C +N

DONOR HN N

DONOR HE2 NE2

ACCEPTOR ND1

ACCEPTOR O C

IC -C	CA	*N	HN	1.3472	124.1600	180.0000	114.3600	0.9991
IC -C	N	CA	C	1.3472	124.1600	180.0000	106.4300	1.5166
IC N	CA	C	+N	1.4532	106.4300	180.0000	116.9700	1.3446
IC +N	CA	*C	O	1.3446	116.9700	180.0000	120.6800	1.2290
IC CA	C	+N	+CA	1.5166	116.9700	180.0000	124.9500	1.4505
IC N	C	*CA	CB	1.4532	106.4300	123.5200	111.6700	1.5578
IC N	C	*CA	HA	1.4532	106.4300	-116.4900	107.0800	1.0833
IC N	CA	CB	CG	1.4532	112.8200	180.0000	116.9400	1.5109
IC CG	CA	*CB	HB1	1.5109	116.9400	119.8000	107.9100	1.1114
IC CG	CA	*CB	HB2	1.5109	116.9400	-124.0400	109.5000	1.1101
IC CA	CB	CG	ND1	1.5578	116.9400	90.0000	120.1700	1.3859
IC ND1	CB	*CG	CD2	1.3859	120.1700	-178.2600	129.7100	1.3596
IC CB	CG	ND1	CE1	1.5109	120.1700	-179.2000	105.2000	1.3170
IC CB	CG	CD2	NE2	1.5109	129.7100	178.6600	105.8000	1.3782

IC NE2	ND1	*CE1 HE1	1.3539	111.7600	179.6900	124.5800	1.0929
IC CE1	CD2	*NE2 HE2	1.3539	107.1500	-178.6900	125.8600	0.9996
IC NE2	CG	*CD2 HD2	1.3782	105.8000	-179.3500	129.8900	1.0809

PRES ZH1 0.00
 BOND 1NE2 2ZN
 ANGLE 1CE1 1NE2 2ZN 1CD2 1NE2 2ZN

PRES ZH2 0.00
 BOND 1NE2 2ZN
 ANGLE 1CE1 1NE2 2ZN 1CD2 1NE2 2ZN

PRES ZH3 0.00
 BOND 1ND1 2ZN
 ANGLE 1CE1 1ND1 2ZN 1CG 1ND1 2ZN

PRES ZNL 0.00
 BOND 1N 2ZN
 ANGLE 1S 1N 2ZN 1H7 1N 2ZN

! Parameter file for Zn(His)₃ active site

ATOMS

MASS	1	L1	14.01000	! His94
MASS	2	L2	14.01000	! His96
MASS	3	L3	14.01000	! His119
MASS	4	L4	14.01000	! sulfonamide
MASS	5	SG3O1	32.06000	! sulfonamide
MASS	6	OG2P1	15.99900	! sulfonamide
MASS	7	CG2R61	12.01100	! sulfonamide
MASS	8	HGP1	1.00800	! sulfonamide

BOND

ZN	L1	73.30	2.0219
ZN	L2	51.70	2.0790
ZN	L3	64.00	2.0408
CPH1	L3	410.00	1.3940
CPH2	L1	488.00	1.3350
CPH2	L2	488.00	1.3350
CPH1	L1	410.00	1.3940
CPH1	L2	410.00	1.3940
CPH2	L3	488.00	1.3350
L4	ZN	100.20	1.9653
SG3O1	L4	454.10	1.5440
HGP1	L4	385.60	1.0230

ANGLES

CPH1	L1	ZN	52.42	128.19
CPH2	L1	ZN	49.56	125.23
CPH1	L2	ZN	57.73	120.78
CPH2	L2	ZN	57.42	132.88
CPH1	L3	ZN	52.34	130.26
CPH2	L3	ZN	54.44	121.77
L1	ZN	L2	36.80	102.18
L1	ZN	L3	35.96	113.76
L1	ZN	L4	48.02	118.08
L2	ZN	L3	33.11	103.09
L2	ZN	L4	50.07	100.59
L3	ZN	L4	28.80	115.67
SG3O1	L4	ZN	74.13	109.12
HGP1	L4	ZN	42.99	121.59
NR1	CPH2	L1	70.00	120.00
CPH1	CPH1	L1	70.00	120.00
HR3	CPH1	L1	50.00	120.00
HR1	CPH2	L1	50.00	120.00
CPH1	L1	CPH2	70.00	117.00
NR1	CPH2	L2	70.00	120.00
CPH1	CPH1	L2	70.00	120.00
HR3	CPH1	L2	50.00	120.00
HR1	CPH2	L2	50.00	120.00
CPH1	L2	CPH2	70.00	117.00
NR1	CPH2	L3	70.00	120.00
CPH1	CPH1	L3	70.00	120.00
CPH1	L3	CPH2	70.00	117.00
HR1	CPH2	L3	50.00	120.00
CT2	CPH1	L3	70.00	120.00
L4	SG3O1	OG2P1	69.60	123.53
SG3O1	L4	HGP1	48.00	111.17
CG2R61	SG3O1	L4	64.20	103.01

DIHEDRALS

L1	CPH1	CPH1	NR1	14.0000	2	180.00
L1	CPH2	NR1	H	1.0000	2	180.00
CPH2	L1	CPH1	CPH1	14.0000	2	180.00
CT2	CPH1	L1	CPH2	3.0000	2	180.00
HR1	CPH2	L1	CPH1	3.0000	2	180.00
HR3	CPH1	L1	CPH2	3.0000	2	180.00
NR1	CPH2	L1	CPH1	14.0000	2	180.00
L1	CPH1	CPH1	CT2	3.0000	2	180.00
L1	CPH1	CPH1	CT3	3.0000	2	180.00
L1	CPH1	CPH1	HR3	3.0000	2	180.00
L1	CPH1	CT2	CT2	0.1900	3	0.00
L1	CPH1	CT2	CT3	0.1900	3	0.00
L1	CPH1	CT2	HA2	0.1900	3	0.00
L1	CPH1	CT3	HA3	0.1900	3	0.00
L1	CPH2	NR1	CPH1	14.0000	2	180.00
CT1	CT2	CPH1	L1	1.0900	1	0.00
CT1	CT2	CPH1	L1	0.0900	2	0.00

CT1	CT2	CPH1	L1	0.6700	3	180.00		
HR1	NR1	L1	CPH2	0.5000		0	0.0000	
HR1	L1	NR1	CPH2	0.5000		0	0.0000	
HR3	CPH1	L1	CPH1	0.5000		0	0.0000	
HR3	L1	CPH1	CPH1	0.5000		0	0.0000	
HR3	CPH1	L1	CPH1	0.5000		0	0.0000	
L2	CPH1	CPH1	NR1	14.0000	2	180.00		
L2	CPH2	NR1	H	1.0000	2	180.00		
CPH2	L2	CPH1	CPH1	14.0000	2	180.00		
CT2	CPH1	L2	CPH2	3.0000	2	180.00		
HR1	CPH2	L2	CPH1	3.0000	2	180.00		
HR3	CPH1	L2	CPH2	3.0000	2	180.00		
NR1	CPH2	L2	CPH1	14.0000	2	180.00		
L2	CPH1	CPH1	CT2	3.0000	2	180.00		
L2	CPH1	CPH1	CT3	3.0000	2	180.00		
L2	CPH1	CPH1	HR3	3.0000	2	180.00		
L2	CPH1	CT2	CT2	0.1900	3	0.00		
L2	CPH1	CT2	CT3	0.1900	3	0.00		
L2	CPH1	CT2	HA2	0.1900	3	0.00		
L2	CPH1	CT3	HA3	0.1900	3	0.00		
L2	CPH2	NR1	CPH1	14.0000	2	180.00		
CT1	CT2	CPH1	L2	1.0900	1	0.00		
CT1	CT2	CPH1	L2	0.0900	2	0.00		
CT1	CT2	CPH1	L2	0.6700	3	180.00		
HR1	NR1	L2	CPH2	0.5000		0	0.0000	
HR1	L2	NR1	CPH2	0.5000		0	0.0000	
HR3	CPH1	L2	CPH1	0.5000		0	0.0000	
HR3	L2	CPH1	CPH1	0.5000		0	0.0000	
HR3	CPH1	L2	CPH1	0.5000		0	0.0000	
L3	CPH1	CPH1	NR1	14.0000	2	180.00		
L3	CPH2	NR1	H	1.0000	2	180.00		
CPH2	L3	CPH1	CPH1	14.0000	2	180.00		
CT2	CPH1	L3	CPH2	3.0000	2	180.00		
HR1	CPH2	L3	CPH1	3.0000	2	180.00		
HR3	CPH1	L3	CPH2	3.0000	2	180.00		
NR1	CPH2	L3	CPH1	14.0000	2	180.00		
L3	CPH1	CPH1	CT2	3.0000	2	180.00		
L3	CPH1	CPH1	CT3	3.0000	2	180.00		
L3	CPH1	CPH1	HR3	3.0000	2	180.00		
L3	CPH1	CT2	CT2	0.1900	3	0.00		
L3	CPH1	CT2	CT3	0.1900	3	0.00		
L3	CPH1	CT2	HA2	0.1900	3	0.00		
L3	CPH1	CT3	HA3	0.1900	3	0.00		
L3	CPH2	NR1	CPH1	14.0000	2	180.00		
CT1	CT2	CPH1	L3	1.0900	1	0.00		
CT1	CT2	CPH1	L3	0.0900	2	0.00		
CT1	CT2	CPH1	L3	0.6700	3	180.00		
HR1	NR1	L3	CPH2	0.5000		0	0.0000	
HR1	L3	NR1	CPH2	0.5000		0	0.0000	
HR3	CPH1	L3	CPH1	0.5000		0	0.0000	
HR3	L3	CPH1	CPH1	0.5000		0	0.0000	
HR3	CPH1	L3	CPH1	0.5000		0	0.0000	
HR3	L3	CPH1	CPH1	0.5000		0	0.0000	

NR1 CPH2 L1 ZN	0.0000	3		0.00		
CPH1 CPH1 L1 ZN	0.0000	3		0.00		
L1 ZN L2 CPH2	0.0000	3		0.00		
L1 ZN L2 CPH1	0.0000	3		0.00		
L1 ZN L3 CPH2	0.0000	3		0.00		
L1 ZN L3 CPH1	0.0000	3		0.00		
L1 ZN L4 HGP1	0.0000	3		0.00		
L1 ZN L4 SG3O1	0.0000	3		0.00		
CPH1 L1 ZN L2	0.0000	3		0.00		
CPH1 L1 ZN L3	0.0000	3		0.00		
CPH1 L1 ZN NG2D	0.0000	3		0.00		
CPH1 L1 ZN L4	0.0000	3		0.00		
X CPH2 L1 X				5.0000	2	180.00
X CPH2 L2 X				5.0000	2	180.00
X CPH1 L3 X				2.4000	2	180.00
X CPH1 L1 X				2.4000	2	180.00
X CPH1 L2 X				2.4000	2	180.00
X CPH2 L3 X				5.0000	2	180.00
CPH2 L1 ZN L2	0.0000	3		0.00		
CPH2 L1 ZN L3	0.0000	3		0.00		
CPH2 L1 ZN L4	0.0000	3		0.00		
HR1 CPH2 L1 ZN	0.0000	3		0.00		
NR1 CPH2 L2 ZN	0.0000	3		0.00		
CPH1 CPH1 L2 ZN	0.0000	3		0.00		
L2 ZN L3 CPH2	0.0000	3		0.00		
L2 ZN L3 CPH1	0.0000	3		0.00		
L2 ZN L4 HGP1	0.0000	3		0.00		
L2 ZN L4 SG3O1	0.0000	3		0.00		
CPH1 L2 ZN L3	0.0000	3		0.00		
CPH1 L2 ZN L4	0.0000	3		0.00		
CPH2 L2 ZN L3	0.0000	3		0.00		
CPH2 L2 ZN L4	0.0000	3		0.00		
HR1 CPH2 L2 ZN	0.0000	3		0.00		
NR1 CPH2 L3 ZN	0.0000	3		0.00		
CPH1 CPH1 L3 ZN	0.0000	3		0.00		
L3 ZN L4 HGP1	0.0000	3		0.00		
L3 ZN L4 SG3O1	0.0000	3		0.00		
CPH1 L3 ZN L4	0.0000	3		0.00		
CPH2 L3 ZN L4	0.0000	3		0.00		
ZN L4 SG3O1 OG2P1	0.0000	3		0.00		
ZN L4 SG3O1 CG2R61	0.0000	3		0.00		
HGP1 L4 SG3O1 CG2R61				0.5000	3	180.00
HGP1 L4 SG3O1 CG2R61				6.8000	1	180.00
CG2R61 CG2R61 SG3O1 L4				1.3000	2	180.00
HGP1 L4 SG3O1 OG2P1				0.5000	3	180.00
HGP1 L4 SG3O1 OG2P1				6.8000	1	180.00

IMPROPER

CPH1 CPH1 L1 HR3	0.5000		0	0.0000 ! ALLOW ARO
CPH1 CPH1 L2 HR3	0.5000		0	0.0000 ! ALLOW ARO
CPH1 CPH1 L3 HR3	0.5000		0	0.0000 ! ALLOW ARO
HR3 CPH1 L1 CPH1	0.5000		0	0.0000 ! ALLOW ARO

HR3	CPH1	L2	CPH1	0.5000	0	0.0000 ! ALLOW ARO
HR3	CPH1	L3	CPH1	0.5000	0	0.0000 ! ALLOW ARO
HR1	L1	NR1	CPH2	0.5000	0	0.0000 ! ALLOW ARO
HR1	L2	NR1	CPH2	0.5000	0	0.0000 ! ALLOW ARO
HR1	L3	NR1	CPH2	0.5000	0	0.0000 ! ALLOW ARO
HR1	NR1	L1	CPH2	0.5000	0	0.0000 ! ALLOW ARO
HR1	NR1	L2	CPH2	0.5000	0	0.0000 ! ALLOW ARO
HR1	NR1	L3	CPH2	0.5000	0	0.0000 ! ALLOW ARO

NONBONDED nbxmod 5 atom cdiel fshift vatom vdistance vswitch -
cutnb 14.0 ctofnb 12.0 ctonnb 10.0 eps 1.0 e14fac 0.8333333333333334 wmin 1.5

L1	0.000000	-0.170000	1.824000	0.000000	-0.085000	1.824000
L2	0.000000	-0.170000	1.824000	0.000000	-0.085000	1.824000
L3	0.000000	-0.170000	1.824000	0.000000	-0.085000	1.824000
L4	0.000000	-0.170000	1.824000	0.000000	-0.085000	1.824000

END