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Supplementary material for

B–H···π and C–H···π Interactions in Protein–Ligand Complexes: Carbonic Anhydrase II Inhibition by Carborane Sulfonamides

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Results

Table S1: Diffraction data processing and refinement statistics.

CAII in complex with		
	2	**3**
Data collection statistics		
Wavelength (Å)	0.91841	0.91841
Space group	$P2_1$	$P2_1$
Cell parameters (Å, °)	42.4 41.6 72.5 90.0 104.3 90.0	42.3 41.7 72.4 90.0 104.3 90.0
Resolution range (Å)	50-1.09 (1.22-1.15)	50.0-1.15 (1.22-1.15)
Number of unique reflection	86327 (13506)	86320 (13658)
Multiplicity	3.6(3.5)	6.3 (5.9)
Completeness (%)	98.4 (95.8)	98.8 (97.3)
R_{merge}[a]	0.044 (1.07)	0.052 (1.12)
$CC_{(1/2)}$ (%)	99.9 (53.0)	99.9 (63.2)
Average I/σ(I)	12.5 (1.2)	14.3 (1.33)
Wilson B (Å^2)q	18.7	18.8
Refinement statistics		
Resolution range (Å)	40.9-1.09 (1.18-1.15)	41.0-1.15 (1.18-1.15)
No. of reflection in working set	83156(6102)	81812 (5987)
No. of reflection in the test set	2098(146)	4306 (315)
R_{work} value (%)[b]	16.1 (38.0)	15.3 (27.1)
R_{free} value (%)[c]	18.0 (40.8)	18.3 (25.7)
RMSD bond length (Å)	0.010	0.010
RMSD angle (°)	1.6	1.7
Mean ADP value (Å^2)	21.2	19.1
Ramachandran plot statistics		
Residues in favored regions (%)	96.1	96.5
Residues in allowed regions (%)	3.9	3.5
PDB code	8AA6	8AAE

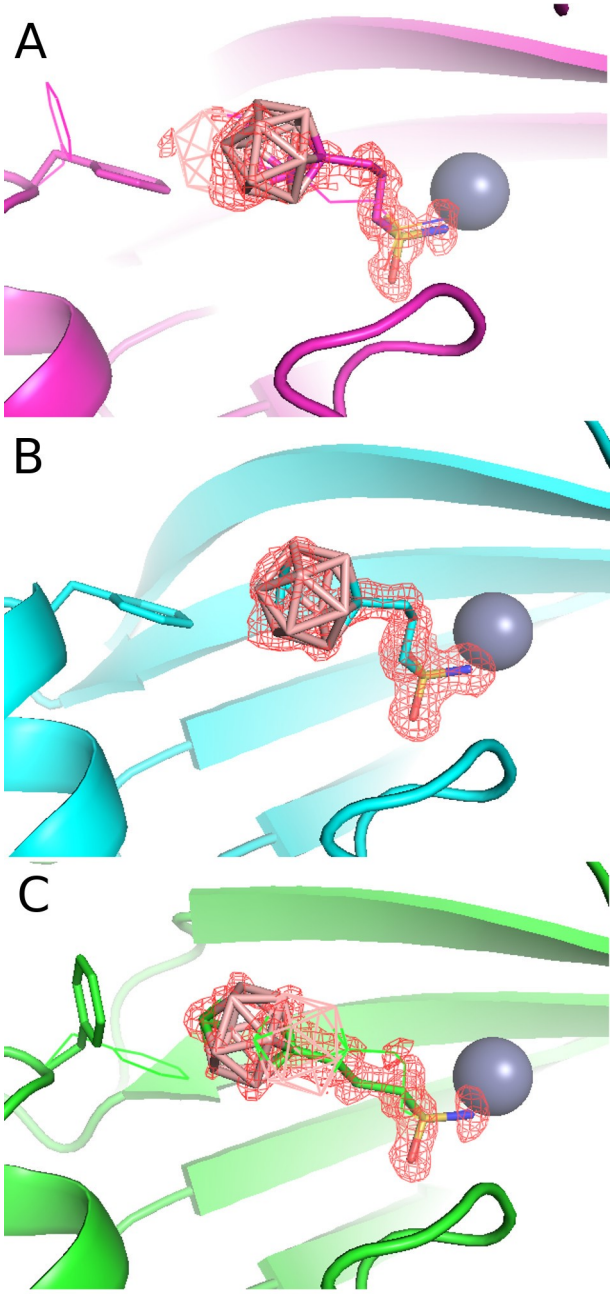
The data in parentheses refer to the highest-resolution shell.

[a] $R_{merge} = (|I_{hkl} - \langle I \rangle|)/I_{hkl}$, where the average intensity $\langle I \rangle$ is taken over all symmetry equivalent measurements and I_{hkl} is the measured intensity for any given reflection.

[b] R-value = $||F_o| - |F_c||/|F_o|$, where F_o and F_c are the observed and calculated structure factors, respectively.

[c] R_{free} is equivalent to the R-value but is calculated for 5% of the reflections chosen at random and omitted from the refinement process.

Figure S1. 1 (A), **2** (B) and **3** (C) OMIT difference maps displaying the inhibitor electron density calculated with a 3 sigma cutoff.



Molecular modeling. The **1** inhibitor is bound in two alternative conformations (pose I and II). Moreover *ortho* carborane of **1** has five rotamers that are distinguished only by the positions of the BH and CH groups. All rotamers were modeled and their stabilities are shown in Table S2.

Table S2. Relative 'free' energies of **1**:CA II in kcal mol^{-1}. The dihedral angle (φ) of 0 degrees corresponds to the C position in the X-ray structure.

Orientation	φ	ΔG'
I	-144	1.9
	-72	2.8
	0	4.7
	72	5.2
	144	2.0
II	-144	2.8
	-72	0.0
	0	1.0
	72	4.2
	+144	4.0

Inhibitor **2** is only bound in a single conformation (Pose I). Position of the CH vertex in the crystal structure agrees with position of the most stable rotamer in the QM/MM model (see Table S3).

Table S3. Relative 'free' energies of **2**:CA II in kcal/mol. The dihedral angle (φ) of 0 degrees corresponds to the C position in the X-ray structure.

φ	ΔG'
-144	1.4
-72	1.6
0	0.0
+72	3.1
+144	2.2