

Supporting Information for

**Benzylaminoethyureido-tailed benzenesulfonamides: Design, synthesis, kinetic and X-ray investigations on human Carbonic anhydrases**

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**Statistics on data collection, processing and structure determination**

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	18	19	24	26	29	34
<b>Data collection</b>						
Cell parameters (a, b, c, Å)	62.56, 71.66, 121.83	62.60, 71.65, 121.69	62.07, 70.89, 121.51	62.84, 70.98, 120.80	62.51, 70.85, 121.56	62.57, 71.38, 121.40
Resolution (Å)	62.56 – 1.53 (1.57 – 1.53)	62.60 – 1.54 (1.58 – 1.54)	61.22 – 1.44 (1.48 – 1.44)	62.85 – 1.55 (1.59 – 1.55)	62.51 – 1.66 (1.70 – 1.66)	61.5 – 1.37 (1.41-1.37)
Completeness (%)	100.0 (100.0)	100.0 (100.0)	100.0 (100.0)	100.0 (100.0)	100.0 (100.0)	99.9 (98.3)
Unique reflections	83442 (6072)	81860 (5955)	97700 (7186)	79244 (5757)	64678 (4718)	114640 (8252)
Multiplicity	13.3 (13.6)	13.2 (13.4)	13.2 (12.4)	13.1 (13.4)	13.2 (13.4)	12.5 (7.4)
Rmerge	0.091 (1.899)	0.103 (1.981)	0.148 (2.455)	0.083 (1.793)	0.144 (1.945)	0.063 (1.25)
Rpim	0.027 (0.556)	0.029 (0.557)	0.043 (0.735)	0.025(0.526)	0.042 (0.57)	0.019 (0.522)
<math>\langle I/\sigma(I) \rangle</math>	12.5 (1.2)	11.4 (1.2)	9.7 (1.1)	12.2 (1.1)	8.6 (1.2)	14.6 (1.0)
<b>Refinement</b>						
Rcryst/Rfree	0.1962/0.2184	0.1901/0.2141	0.1862/0.2213	0.2002 / 0.2241	0.1855 / 0.2209	0.1978/0.2184
Protein atoms/ligand / solvent atoms	4031/52/680	4031/52/718	4031/28/849	4031/50/610	4031/52/700	4031/54/739
<b>Geometry</b>						
Ramachandran favored/outliers (%)	96.86/0.0	96.47/0.0	97.06/0.0	96.86 /0.0	96.67/0.0	96.67/0.0
Rotamer outliers (%) /Overall score	0.0 / 1.24	0.00/1.24	0.22/1.20	0.22/1.24	0.22/1.23	0.22/1.32

r.m.s.d. on bond length (Å), angles (°)	0.008 / 0.99	0.009, 0.84	0.005, 0.96	0.007/0.85	0.006, 0.89	0.005, 0.84
<b>Ligand validation</b>						
Isotropic B value	41.1 (A) 38.8 (B)	41.0 (A) 36.5 (B)	31.6	37.8 (A) 31.5 (B)	39.0 (A) 34.8 (B)	31.7 (A) 47.0 (B)
Real-space Correlation Coefficient (RSCC)	0.92 (A) 0.96 (B)	0.95 (A) 0.96 (B)	0.913	0.95 (A) 0.97 (B)	0.93 (A) 0.97 (B)	0.94 (A) 0.83 (B)

**Table S1. Statistics on data collection, processing and structure determination.** In all cases, a rotation of 360° was applied, with a rotation/frame of 0.1°. The wavelength used was 0.97624 Å. Number in parentheses refer to the high-resolution shell. Data were kept at the maximum resolution compatible with a  $\langle I/\sigma(I) \rangle$  larger or equal to 1.