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Supplementary Information of the manuscript entitled:

Piperazine derivatives of boronic acids - potential bifunctional biologically active compounds.

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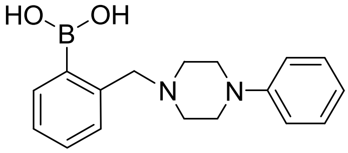

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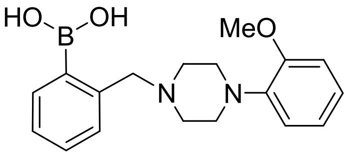

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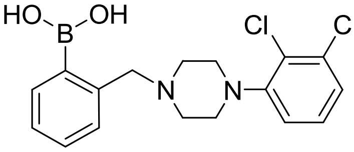

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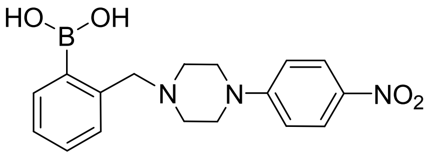

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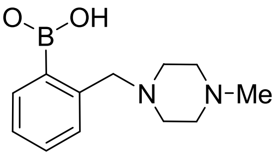

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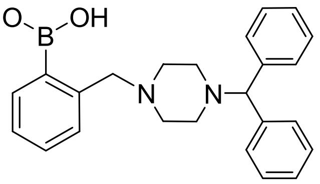

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Figure S1. Studied phenylboronic derivatives of piperazines.

Details on X-ray diffraction studies

The positions of H atoms of the hydroxyl groups were refined freely in the case of **1**, **3** and **4**. The remaining hydrogen atoms were placed in calculated positions with fixed isotropic thermal parameters (U_{iso}(H) = 1.2×U_{eq} (CH and CH_2) or U_{iso}(H) = 1.5×U_{eq}(CH_3) and were included in the structure factor calculations in the final stage of the refinement. Values involving hydrogen atoms in the calculated positions are given in Table 1, Tables S1 and S2 without estimated standard deviations.

The high residual electron density observed during refinement of **2** indicated a presence of a severely disordered or diffused solvent but no satisfactory model could be applied. The calculated total solvent accessible volume per unit cell amounted to 306.5 Å3 (~8.5%). Therefore the solvent mask procedure in OLEX2 was used. The masked region is defined as the solvent accessible region left by the ordered part of the structure. Any atoms in the voids were thus omitted from the structural model. The electron density was estimated to be 12.4 electrons per unit cell, and correction of the Fobs data to remove its contribution resulted in R_1 and wR_2 falling to 3.92% and 10.20%, respectively, and the residual electron density below ~0.3 e/Å3.

In the case of **6** difference Fourier maps, calculated at a late stage of the refinement, indicated disorder of one of the phenyl ring. Final results were obtained with a restraint model in which atoms of the phenyl group were disordered over two sets of positions tilted along C42–C63 bond, with adjusted site occupancy factor for major conformer equals to 0.508(2). Owing to partial overlapping of the atoms of the disordered groups, geometrical restrains were introduced. The distances and anisotropic displacement parameters between complementary atom pairs were restrained to be equal (SADI and EADP command respectively). Atoms in disordered ring were also supposed to lie on a common plane so the FLAT instruction was applied. We also forced the C42 atom to possess the same coordinates by using EXYZ command. The FLACK parameter, *x*,[1] for **2** has refined to the value of –0.1(2) indicating the presence of the inverted twin. Attempts to refine the reverse structure gave the FLACK equal to 1, higher discrepancy factor R_1 and unusual shape of ellipsoids. For the analysis of bond lengths, angles between them and the geometrical parameters of hydrogen bonds the PLATON[2] program was applied. Molecular and packing diagrams were generated using DIAMOND[3] and ORTEP-3 for Windows[4]

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[1] a) H. D. Flack, G. Bernardinelli, *Acta Crystallogr. A*, **1999**, *55*, 908-915, b) H. D. Flack, G. Bernardinelli, *J. Appl. Cryst*., **1999**, *32*, 1143-1148.

[2] L. Spek, *J. Appl. Crystallogr*., **2003**, *36*, 7-13.

[3] K. Brandenburg, Diamond - Crystal and Molecular Structure Visualization, Version 3.2i; Crystal Impact GbR: Bonn, Germany, 2012.

[4] L. J Farrugia., *J. Appl. Crystallogr*., **1997**, *30*, 565-565.

Table S1. Geometrical parameters for studied compounds.

Compound	**1**	**2**	**3**	**4**	**5**	**6A***	**6B**[a]
				bond lengths, Å			
B1–O1	1.364(1)	1.360(2)	1.359(2)	1.343(2)	1.362(2)	1.356(2)	1.362(2)
B1–O2	1.360(1)	1.361(2)	1.354(2)	1.371(2)	1.356(3)	1.362(2)	1.360(2)
B1–C1	1.587(1)	1.585(3)	1.593(3)	1.599(2)	1.592(3)	1.585(2)	1.580(2)
C1–C2	1.413(1)	1.415(2)	1.414(2)	1.416(2)	1.402(3)	1.415(2)	1.411(2)
C1–C6	1.401(1)	1.401(2)	1.404(3)	1.402(2)	1.410(3)	1.401(2)	1.400(2)
C2–C7	1.513(1)	1.514(2)	1.518(2)	1.514(2)	1.523(3)	1.516(2)	1.513(2)
N1–C7	1.478(1)	1.471(2)	1.480(2)	1.473(2)	1.477(2)	1.476(1)	1.478(2)
N1–C8	1.460(1)	1.471(2)	1.474(2)	1.464(2)	1.476(2)	1.475(1)	1.474(1)
N1–C11	1.466(1)	1.478(2)	1.464(2)	1.465(2)	1.469(2)	1.471(1)	1.471(1)
N2–C9	1.457(1)	1.463(2)	1.472(2)	1.469(2)	1.472(2)	1.466(1)	1.466(1)
N2–C10	1.461(1)	1.467(2)	1.464(2)	1.469(2)	1.466(2)	1.465(1)	1.463(1)
N2–C12	1.412(1)	1.416(2)	1.408(2)	1.377(2)	1.470(2)	1.476(1)	1.474(2)
B1…N1	3.299(1)	3.248(2)	3.269(3)	3.254(2)	3.287(3)	3.244(3)	3.267(3)
				bond angles, °			
O1–B1–O2	119.5(1)	119.9(2)	120.1(2)	119.9(1)	120.1(2)	119.8(1)	120.2(1)
O1–B1–C1	123.3(1)	123.0(1)	122.5(2)	124.9(1)	123.2(2)	123.3(1)	122.9(1)
O2–B1– C1	117.2(1)	117.1(1)	117.3(2)	115.2(1)	116.6(2)	116.9(1)	116.9(1)
B1–C1–C2	126.1(1)	125.3(1)	125.9(2)	126.7(1)	126.6(2)	125.6(1)	125.3(1)
B1–C1–C6	116.9(1)	117.3(1)	116.8(2)	116.0(1)	115.8(2)	117.3(1)	117.4(1)
C7–N1–C8	109.4(1)	109.9(1)	110.1(1)	109.2(1)	110.5(2)	110.1(1)	109.9(1)
C7–N1–C11	112.4(1)	110.2(1)	111.2(1)	112.5(1)	112.3(1)	111.1(1)	110.3(1)
C8–N1–C11	108.5(1)	109.0(1)	109.9(1)	107.6(1)	108.8(1)	108.9(1)	109.2(1)
C9–N2–C10	110.8(1)	109.1(1)	109.4(1)	114.2(1)	109.8(1)	107.4(1)	107.3(1)
C9–N2–C12	117.8(1)	116.7(1)	115.8(1)	117.1(1)	110.8(2)	111.3(1)	110.5(1)
C10–N2–C12	118.4(1)	115.0(1)	116.7(1)	118.6(1)	110.2(2)	112.3(1)	113.2(1)
				torsion angles, °			
O1-B1-C1-C2	17.1(2)	26.0(2)	-21.7(3)	-20.8(2)	-24.8(3)	-18.7(2)	25.4(2)
O1-B1-C1-C6	-161.8(1)	-155.4(1)	155.2(2)	158.3(1)	152.8(2)	160.4(1)	-152.7(1)
O2-B1-C1-C2	-165.0(1)	-154.4(1)	162.4(2)	161.8(1)	157.6(2)	162.9(1)	-156.9(1)
O2-B1-C1-C6	16.1(1)	24.3(2)	-20.8(2)	-19.1(2)	-24.8(2)	-18.0(2)	25.0(2)
C1-C2-C7-N1	-64.4(1)	-63.2(2)	66.5(2)	60.4(2)	61.8(2)	61.6(1)	-66.5(1)
C2-C7-N1-C8	178.5(1)	177.6(1)	-168.6(1)	-172.5(1)	179.0(1)	-176.3(1)	178.1(1)
C2-C7-N1-C11	-61.0(1)	-62.3(1)	69.5(2)	68.0(1)	57.3(2)	63.0(1)	-61.5(1)
twist angle, °[b]	16.76(5)	25.05(8)	23.0(1)	20.13(7)	26.68 (1)	18.45(6)	25.74(7)
fold angle, °[c]	81.17(3)	75.06(4)	71.59(7)	81.25(4)	83.39(4)	80.80(3)	73.92(3)
pyr_N1, Å[d]	0.474(2)	0.485(1)	0.468(2)	0.481(1)	0.465(2)	0.478(1)	0.483(1)
pyr_N21, Å[d]	0.305(1)	0.373(1)	0.360(2)	0.268(1)	0.471(2)	0.468(1)	0.467(1)

[a] Independent molecules of **6** are named A and B. The numbers for molecule B are derived from these for A by adding a value of 30.

[b] Twist angle: a dihedral angle between the plane containing $B(OH)_2$ moiety and the plane defined by the phenyl ring of boronic acid fragment.

[c] Fold angle: a dihedral angle between the plane containing boronic fragment and the plane containing heavy atoms of piperazine moiety.

[d] Pyramidallization of N1 and N2 atoms: the distance from the atom in question to the plane defined by three directly bonding atoms.

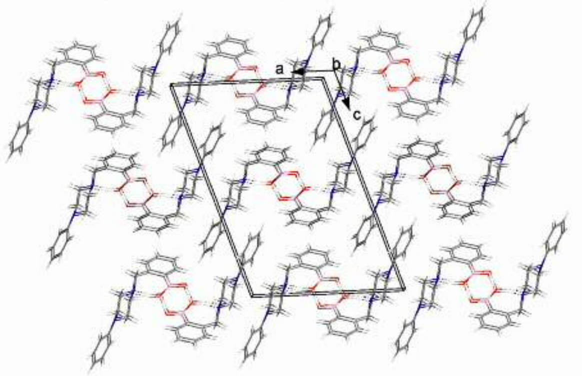
Table S2. Geometrical parameters of weak intermolecular interactions.

	H…A, Å	**D…A, Å**	**D–H…A, º**
1			
C15–H15…O2^{i}	2.49	3.437(1)	175
C4–H4…cg1^{ii}	2.71	3.535(1)	145
C17–H17…cg2^{iii}	2.97	3.581(1)	123
2			
C11–H11B…O3^{iv}	2.49	3.233(2)	132
C3–H3…cg2^{iv}	2.96	3.849(2)	156
C9–H9B…cg1^{v}	2.83	3.676(2)	144
3			
C4–H4…cg2^{vi}	2.79	3.542(2)	137
C7–H7B…cg1^{vii}	2.64	3.425(2)	136
C16–H16…cg1^{viii}	2.97	3.808(2)	147
4			
C5–H5…O4^{ix}	2.49	3.158(2)	127
C13–H13…O2^{x}	2.50	3.406(1)	160
C14–H14…O3^{xi}	2.56	3.429(2)	153
C8–H8A…cg1^{x}	2.59	3.507(1)	154
C17–H17…cg1^{xii}	2.91	3.778(1)	152
5			
C4–H4…O3^{xiii}	2.50	3.239(3)	135
C8–H8A…cg1^{xiv}	2.62	3.550(2)	157
6			
C42–H42A…O5	2.58	3.572(2)	171
C55–H55C…O4^{xv}	2.59	3.563(2)	171
C8–H8A…cg2a^{vii}	2.98	3.955(1)	169
C8–H8B…cg2b^{xvi}	2.77	3.752(1)	173
C11–H11A…cg2a^{xvi}	2.82	3.642(1)	137
C37–H37A…cg2c^{xv}	2.95	3.901(4)	162
C57–H57C…cg1a^{xvii}	2.87	3.606(2)	132

Symmetry codes: (i) -1+*x*,3/2-*y*,-1/2+*z*; (ii) 1-*x*,1/2+*y*,3/2-*z*; (iii) -*x*,1/2+*y*,1/2-*z*; (iv) 3/2-*x*,*y*,2-*z*; (v) *x*,1/2-*y*,1/2+*z*; (vi) -1+*x*,1+*y*,*z*; (vii) -*x*,1-*y*,1-*z*; (viii) 1-*x*,-*y*,-*z*; (ix) 3/2-*x*,3/2+*y*,1/2-*z*; (x) 1/2-*x*,-1/2+*y*,1/2-*z*; (xi) 1-*x*,-*y*,1-*z*; (xii) 3/2-*x*,-1/2+*y*,1/2-*z*; (xiii) 1/2+*x*,1/2-*y*,*z*; (xiv) -1/2+*x*,3/2-*y*,*z*; (xv) 1-*x*,1-*y*,1-*z*; (xvi) -*x*,1/2+*y*,3/2-*z*; (xvii) 1-*x*,2-*y*,1-*z*.

Figure S2. Packing diagrams of studied compounds **1**-**6**

2-((4-phenylpiperazin-1-yl)methyl)phenylboronic acid (**1**)



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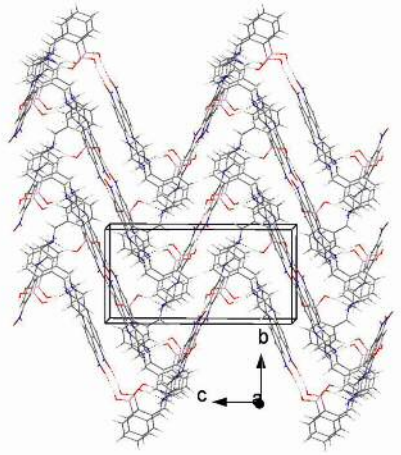

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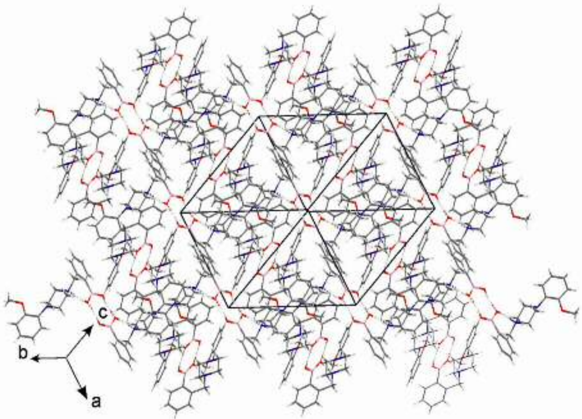
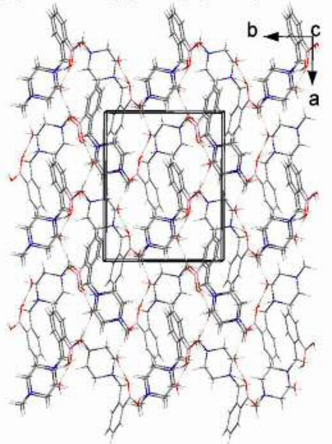


2-((4-methylpiperazin-1-yl)methyl)phenylboronic acid (**5**)



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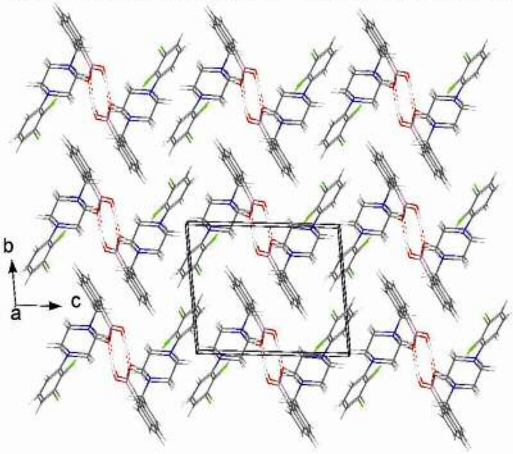

2-((4-benzhydrylpiperazin-1-yl)methyl)phenylboronic acid (**6**)