Supporting Information

Title: Exploring the structural landscape of 2-aminopyrazines *via* co-crystallizations

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Table S1. IR stretch for carbonyl group of acids in all solids resulting from combinations of acids **A1-A30** and **B1-B3**.

	NAME	B1	B2	B3
		C=O	C=O	C=O
A1	4-Aminobenzoic acid	-	-	-
A2	4-Hydroxybenzoic acid	1666	1686	-
A3	3,5-Dihydroxybenzoic acid	1706	-	-
A4	2,4-Dimethoxybenzoic acid	1672	-	-
A5	3,4-Dihydroxybenzoic acid	1646	-	-
A6	2,3-Dihydroxybenzoic acid	-	-	-
A7	2,5-Dihydroxybenzoic acid	-	-	1690

A8	2,3-Dimethylbenzoic acid	1646	-	-
A9	2,5-Dimethylbenzoic acid	-	1706	-
A10	Benzoic acid	1672	-	-
A11	4-Nitrobenzoic acid	1695	-	-
A12	4-Fluorobenozoic acid	1646	-	-
A13	Pentafluorobenzoic acid	1679	-	1695
A14	3,5-Dinitrobenzoic acid	1672	1706	1619
A15	2,4-Dinitrobenzoic acid	1664	1716	-
A16	3-Nitrobenzoic acid	1699	1706	1701
A17	2-Chloro-6-fluorobenzoic acid	-	1699	1699
A18	2,6-Difluorobenzoic acid	1712	-	-
A19	3-Fluorobenzoic acid	1653	-	-
A29	4-Cyanobenzoic acid	1654	1700	-
A21	Oxalic acid	1729	1685	1697
A22	Malonic acid	1724	-	-
A23	Succinic acid	1679, 1633	1710	-
A24	Glutaric acid	1697, 1676	1703	-
A25	Adipic acid	1673, 1643	-	-
A26	Pimelic acid	1674, 1633	1717, 1694	-
A27	Suberic acid	1683, 1643	1711	-
A28	Azelaic acid	1673, 1636	-	-
A29	Sebacic acid	1685, 1650	-	-
A30	Dodecanedioic acid	1687, 1645	-	-

Table S2. Results from IR spectroscopy arranged in order of decreasing charge on hydrogen of carboxylic acids. Empty boxes represent 'no reaction' and filled boxes represent a 'reaction'.

Acids	**Label**	**Charge on COOH(kJ/mol)***	**B1**	**B2**	**B3**
Malonic acid	**A22**	177			
3,5-Dinitrobenzoic acid	**A14**	168			
Oxalic acid	**A21**	158			
2,3-Dihydroxybenzoic acid	**A6**	151			

Pentafluorobenzoic acid	**A13**	148			
4-Nitrobenzoic acid	**A11**	147			
2,5-Dihydroxybenzoic acid	**A7**	140			
3-Nitrobenzoic acid	**A16**	139			
Glutaric acid	**A24**	139			
Adipic acid	**A25**	139			
Sebacic acid	**A29**	138			
2,4-Dinitrobenzoic acid	**A15**	136			
Succinic acid	**A23**	136			
Suberic acid	**A27**	135			
Pimelic acid	**A26**	134			
Dodecanedioic acid	**A30**	133			
Azelaic acid	**A28**	132			
4-Fluorobenozoic acid	**A12**	128			
3,4-Dihydroxybenzoic acid	**A5**	124			
3-Fluorobenzoic acid	**A19**	124			
Benzoic acid	**A10**	118			
3,5-Dihydroxybenzoic acid	**A3**	116			
2,5-Dimethylbenzoic acid	**A9**	115			
2,6-Difluorobenzoic acid	**A18**	114			
4-Cyanobenzoic acid	**A20**	113			
2,3-Dimethylbenzoic acid	**A8**	112			
2-Chloro-6-fluorobenzoic acid	**A17**	111			
2,4-Dimethoxybenzoic acid	**A4**	107			
4-Hydroxybenzoic acid	**A2**	106			
4-Aminobenzoic acid	**A1**	105			

X-ray crystallography

Data sets were collected on Bruker Kappa APEX II system (**B1·A11**, **B1·A14**, **B1·A23**, **B3·A14**, **B3·A18**) or a SMART APEX II system (**B1·A16**, **B1·A24**, **B1·A26**, **B1·A27**, **B1·A29**, **B3·A13**, **B3·A7**), at 120 K using APEX2 software.[a] An Oxford Croystream 700 low-temperature device was used to control temperature. MoKα radiation was used. Initial cell constants were found by small widely separated "matrix" runs. Data collection strategies were determined using COSMO.[b] Scan speeds and scan widths were chosen based on scattering power and peak rocking curves.

Unit cell constants and orientation matrices were improved by least-squares refinement of reflections thresholded from the entire dataset. Integrations were performed with SAINT,[c] using these improved unit cells as a starting point. Precise unit cell constants were calculated in SAINT from the final merged datasets. Lorenz and polarization corrections were applied. Absorption corrections was applied using SADABS[d] (**B1.A16**, **B3·A13**, **B3.A14**, **B3·A18**) or TWINABS[e] (**B1·A14**, **B3·A7**).

Datasets were reduced with SHELXTL.[f] The structures were solved by direct methods without incident. Unless noted below, coordinates for all carboxylic acid, amine, ammonium, and phenol hydrogens were allowed to refine. All other hydrogens were assigned to idealized positions and were allowed to ride. Isotropic thermal parameters for the hydrogen atoms were constrained to be 1.5x (methyl) / 1.2x (all other) that of the connected atom.

B1·A11 The carboxylic acid was protonated at both oxygens; hydrogens (H17 & H18) were given idealized coordinates and were assigned half occupancy. The amine was disordered over an inversion center and was assigned half occupancy. Overall stoichiometry was therefore 2 : 1 acid : amine.

B1·A14 The crystal was a nonmerohedral twin and data were processed with TWINABS.[e] Proton transfer from carboxylic acid to pyridine nitrogen was observed.

B1·A16 The amine was located on an inversion center. The $-NH_2$ group which broke symmetry was assigned half occupancy. Overall stoichiometry was therefore 2 : 1 acid : amine.

B1·A23 The dicarboxylic acid was located on an inversion center. Overall stoichiometry was therefore 1 : 2 acid : amine.

B1·A24, B1·A26, B1·A27, B1·A29 - The dicarboxylic acid and amine were both located on inversion centers. The $-NH_2$ group which broke symmetry was assigned half occupancy. Overall stoichiometry was therefore 1 : 2 acid : amine.

B3·A7- The crystal was a nonmerohedral twin and data were processed with TWINABS.[e] Coordinates of acid proton H27, phenol proton H22, and amine protons H12A & H12B were allowed to refine. The phenol proton H25 was disordered over two in-plane sites. The two sites (H25A & H25B) were assigned half occupancy and were located in idealized positions.

B3·A13, **B3·A14, B3·A18, T**he unit cell contained two acid / amine pairs. These pairs were assigned to two residues.

Table S3. Hydrogen-bond Geometries for **B3, B1·A11, B1·A14, B1·A16, B1·A23, B1·A24, B1·A26, B1·A27, B1·A29, B3·A7, B3·A13, B3·A14** and **B3·A18**

Structure	D-H···A	d(D-H)/Å	d(H···A)/Å	d(D···A)/Å	<(DHA)/°
B1·A11[i]	O(17)-H(17)...N(21)	0.82	1.95	2.744(6)	163.9
	O(18)-H(18)...N(24)#1	0.82	1.89	2.704(5)	171.1
	N(22)-H(22A)...O(18)	0.92(6)	2.11(7)	3.006(10)	164(5)
	N(22)-H(22B)...O(17)#2	0.92(6)	2.28(6)	3.194(11)	175(6)
B1·A14[ii]	N(11)-H(11)...O(21)	0.97(4)	1.61(4)	2.573(4)	169(4)
	N(12)-H(12A)...O(22)	0.84(5)	1.95(5)	2.790(4)	178(4)
	N(12)-H(12B)...O(25)#1	0.92(5)	2.39(4)	3.096(4)	133(3)
	N(12)-H(12B)...O(26)#1	0.92(5)	2.29(5)	3.187(5)	166(4)
B1·A16[iii]	O(11)-H(11)...N(21)	0.965(17)	1.660(17)	2.6174(14)	170.7(14)
	N(22)-H(22A)...O(12)	0.86(3)	2.12(3)	2.967(2)	167(3)
	N(22)-H(22B)...O(14)#2	0.85(3)	2.22(3)	3.027(2)	158(3)
B1·A23[iv]	O(21)-H(21)...N(14)	0.93(4)	1.72(4)	2.643(4)	168(4)
	N(12)-H(12A)...N(11)#2	0.85(5)	2.19(5)	3.036(4)	176(4)
	N(12)-H(12B)...O(22)#3	0.86(4)	2.17(5)	3.018(4)	168(4)
B1·A24[v]	N(12)-H(12A)...O(22)	0.906(19)	2.261(19)	3.1366(16)	162.3(15)
	N(12)-H(12B)...O(26)#1	0.835(19)	2.21(2)	3.0153(15)	161.5(18)
	O(21)-H(21)...N(11)	0.91(2)	1.77(2)	2.6792(13)	173.7(19)
	O(25)-H(25)...N(14)#2	0.956(19)	1.72(2)	2.6551(13)	166.7(17)
B1·A26[vi]	O(21)-H(21)...N(11)	0.947(19)	1.721(19)	2.6588(11)	170.0(17)
	N(12)-H(12A)...O(22)	0.925(16)	2.140(16)	3.0459(12)	166.2(13)

	N(12)-H(12B)...O(28)#1	0.901(19)	2.10(2)	2.9616(13)	160.9(16)
	O(27)-H(27)...N(14)#2	0.98(2)	1.68(2)	2.6544(11)	170(2)
B1·A27[vii]	N(12)-H(12A)...O(22)	0.84(4)	2.06(4)	2.883(3)	167(3)
	N(12)-H(12B)...O(29)#1	0.86(4)	2.13(4)	2.966(3)	164(3)
	N(15)-H(15B)...O(22)#2	0.86	2.50	3.289(16)	153.3
	N(15)-H(15A)...O(29)#3	0.86	2.13	2.962(14)	162.2
	O(21)-H(21)...N(11)	0.95(3)	1.80(3)	2.741(2)	172(3)
	O(28)-H(28)...N(14)#4	0.96(4)	1.74(4)	2.689(2)	168(3)
B1A29 [viii]	O(21)-H(21)...N(11)	0.905(17)	1.809(17)	2.6939(11)	165.2(14)
	N(12)-H(12A)...O(22)	0.85(3)	1.97(3)	2.8120(18)	177(3)
	N(12)-H(12B)...O(22)#3	0.81(3)	2.05(3)	2.7437(18)	144(3)
B3·A7[ix]	O(27)-H(27)...N(14)	0.80(4)	1.91(4)	2.704(3)	174(4)
	N(13)-H(13A)...O(28)	0.88	2.02	2.891(3)	167.9
	N(13)-H(13B)...O(22)#1	0.88	2.35	2.944(3)	125.4
	O(22)-H(22)...O(28)	0.78(4)	1.87(4)	2.574(3)	149(4)
	O(25)-H(25A)...O(25)#2	0.84	1.96	2.762(4)	159.5
B3·A13[x]	O(21)-H(21)...N(11)	0.76(2)	1.84(2)	2.5892(19)	172(3)
	N(12)-H(12A)...O(22)	0.86(2)	2.17(2)	3.0174(19)	169(2)
	N(12)-H(12B)...O(22)#1	0.82(2)	2.37(2)	3.074(2)	144(2)
B3·A14[xi]	O(21)-H(21)...N(11)	0.73(2)	1.94(2)	2.6728(17)	176(2)
	N(12)-H(12A)...O(25)#1	0.76(2)	2.38(2)	3.031(2)	145(2)
	N(12)-H(12B)...O(23)#2	0.88(2)	2.32(2)	3.165(2)	162(2)
B3·A18[xii]	O(21)-H(21)...N(11)	0.81(3)	1.88(3)	2.685(2)	171(2)
	N(12)-H(12A)...O(22)	0.81(3)	2.17(3)	2.976(3)	174(2)
	N(12)-H(12B)...F(26)#1	0.82(3)	2.68(3)	3.335(2)	138(2)

Symmetry transformations used to generate equivalent atoms:

i) #1 -x+1,-y+1,-z+1 #2 x,-y+3/2,z+1/2 ii) #1 x-1,y,z+1 iii) #1 -x+1,-y,-z+1 #2 x,y-1,z iv) #1 -x+1,-y+1,-z+1 #2 -x+1,-y,-z+1 #3 x-1,-y+1/2,z-1/2 v) #1 -x+2,-y+1,-z+1 #2 -x+1,y-1/2,-z+1/2 vi) #1 -x+2,-y+1,-z+1 #2 -x+1,y+1/2,-z+1/2 vii) #1 -x,y+1/2,-z #2 -x+1,y-1/2,-z+1 #3 x+1,y,z+2 #4 x-1,y,z-2 viii) #1 -x+2,-y+2,-z+2 #2 -x,-y+1,-z #3 -

x+2,-y+2,-z+1 ix) #1 -x+1,-y+1,-z #2 -x+2,-y,-z+1 x) #1 -x+3/2,y-1/2,-z+1/2 xi) #1 -x+2,-y,-z+1 #2 x+1,y+1,z-1 xii) #1 -x+1,-y+2,-z+1

Table S4. The CSD analysis showing binding preference of carboxylic acid when both 2-aminopyridine and pyridine binding sites are available.

Refcode	*2-Aminopyridine end*	*Pyridine end*
COWHOM	COOH	N-H
COWHUS	COOH	I
COWJAA	COOH	I
COWJOO	COOH	NA
OCATUH	homodimer	COOH
PEQPAD	COOH	NH
PEQPEH	COOH	NA
PEQPIL	COOH	OH
PEQPOR	COOH	NA
PEQPUX	COOH	NA
PEQQAE	COOH	NH
PEQQEI	COOH	CH
PEQQIM	COOH	NA
PEQQOS	COOH	NH

References:

(a) APEXII v2009. 5-1, © 2009, Bruker Analytical X-ray Systems, Madison, WI.

(b) COSMO v1. 60, © 1999 - 2009, Bruker Analytical X-ray Systems, Madison, WI.

(c) SAINT v7. 60a, © 1997 - 2008, Bruker Analytical X-ray Systems, Madison, WI.

(d) SADABS v2008/1, © 2008, , Bruker Analytical X-ray Systems, Madison, WI.

(e) TWINABS v2008/4, © 2008, , Bruker Analytical X-ray Systems, Madison, WI.

(f) SHELXTL v2008/4, © 2008, , Bruker Analytical X-ray Systems, Madison, WI.