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Ranking Relative Hydrogen-Bond Strengths in Hydroxybenzoic Acids for Crystal-Engineering Purposes

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Abstract: Systematic co-crystallizations resulting in a total of six new crystal structures involving either 3-hydroxy- or 4-hydroxybenzoic acid, complemented by calculated molecular electrostatic potential surfaces and existing structural data, have shown that in a competitive molecular recognition situation, the −OH moiety is a more effective hydrogen-bond donor than the −COOH moiety which, in turn, highlights that electrostatic charge can offer more useful guidance than acidity for predicting competitive hydrogen-bond preferences.

Keywords: co-crystals · crystal engineering · hierarchy · hydrogen bonding · intermolecular interactions

Introduction

The deliberate and targeted synthesis of co-crystals[1] with desired stoichiometries and intermolecular connectivities relies on our ability to apply the concepts of tectons[2] and synthons[3] in a rational and reproducible manner. The task of identifying synthons in the first place is facilitated greatly through careful analysis[4] of the structural information contained in the CSD.[5] However, it is not always possible to find enough data to allow a reliable ranking of the relative importance of different synthons, especially in structurally competitive situations. It is undoubtedly highly desirable to establish robust guidelines for supramolecular synthesis, because multicomponent solid-state architectures have found applications in areas involving pharmaceuticals[6], agrochemicals[7], nonlinear optics,[8] explosives[9], and organic semiconductors[10]. In principle, co-crystals can offer a wide selection of solid forms of a particular active ingredient, which, in turn, improves our chances of optimizing physical properties of a solid, without tampering with the chemical nature of the key component.

The reversible nature of intermolecular interactions and the fact that they are relatively weak compared to most covalent bonds means that we will not always be able to produce a strict hierarchy of hydrogen-bond-based supramolecular synthesis that completely avoids "synthon crossover"[11] or "synthon polymorphism".[12] Instead, the goal is to establish guidelines that provide a framework around which synthetic strategies that have a reasonable chance of success can be built.[13]

As a starting point, it is known that certain molecules and functional groups exhibit a higher propensity to form co-crystals than others.[14] The hydrogen-bond-based selectivity found in molecular solids was rationalized by Etter: "The best hydrogen-bond donor and the best hydrogen-bond acceptor will preferentially form hydrogen bonds to one another".[15] A consequence of this statement is that we need to acquire reliable means for ranking hydrogen-bond donor and acceptor groups to develop transferable robust and high-yielding[16] supramolecular design strategies based on hydrogen bonds.

Several approaches have been proposed for quantifying hydrogen-bond strength on a thermodynamic basis,[17,18,19] and, in some systems, a successful ranking has been achieved by using pK_a/pK_b values of the participating components.[20,21] However, it is important to note that the latter quantities can only provide a useful guide when a series of molecules carrying the same chemical functionality is being examined. A more general strategy for ranking and comparing hydrogen-bond donor strength across a broad spectrum of chemical functionalities based on electrostatic charge has been developed by Hunter and co-workers.[22,23] This approach utilizes calculated molecular electrostatic potential surfaces (by using AM1 or DFT) around the molecule, in which potential maxima and minima correspond to hydrogen-bond donor and acceptor sites, respectively.

Herein, we examine two common functional groups, a carboxylic acid and a phenolic moiety in the context of hydrogen-bond strength and their ability to compete for hydrogen-bond acceptors with differing strengths.

Carboxylic acids are frequently assumed to be "better" or more effective hydrogen-bond donors than phenols. When considering 4-hydroxybenzoic acid, for example, pK_a values alone would suggest that the −COOH group ($pK_a = 4.48$) is a far superior hydrogen-bond donor to the −OH group

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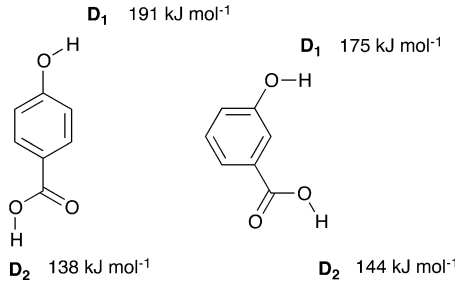
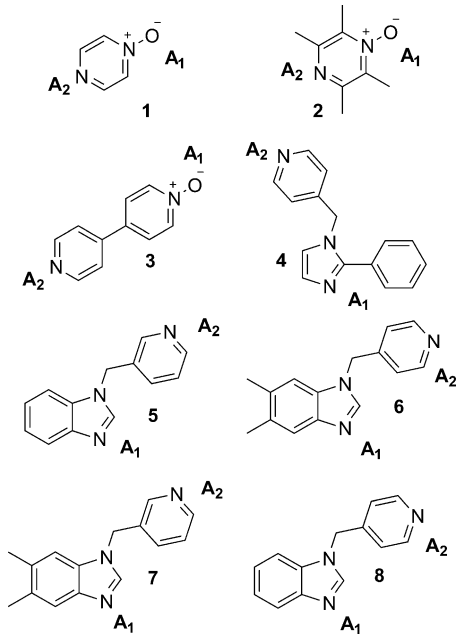
($pK_a = 9.32$). Molecular electrostatic potential calculations on the other hand, show that the −OH group could be viewed as a highly competitive, or possibly even better donor compared to the −COOH group (Scheme 1). One



Scheme 1. MEP surface calculations show the −OH group to be the best donor **D1** and the −COOH moiety to be the second-best donor **D2**.

way to probe the practical consequences of intermolecular interactions is to perform systematic co-crystallizations, in which molecules carrying specific functional groups are confronted with a variety of potential "partners". By examining binding preferences by using crystallographic data, it may be possible to begin to formulate guidelines that will allow us to predict which synthons are most likely to form in a competitive situation. To determine how to rank the relative hydrogen-bond capability of −OH and −COOH groups when they are attached to the same molecular backbone, 3-hydroxybenzoic acid, **3-HBA**, and 4-hydroxybenzic acid, **4-HBA**, was co-crystallized with a series of ditopic molecules each containing two hydrogen-bond acceptor sites of different strength, Scheme 2. The fundamental question that we want to address is whether a ranking based on charge or on



Scheme 2. **A1** and **A2** are assigned based on calculated AM1 charges and refer to best- and second-best acceptor, respectively.

acidity offer a better method for predicting synthon preference in this family of ditopic hydrogen-bond donors.

Results and Discussion

Formation of a co-crystal was readily determined by IR spectroscopy through the appearance of an O−H···N stretch or by shifts to the carbonyl band. The data listed in Table 1

Table 1. Relevant IR spectroscopic data from all 16 solids obtained in this study.

Acceptor	3-HBA		4-HBA	
	O−H···N	C=O	O−H···N	C=O
	–	1681	–	1669
1	–	1698	–	1691
2	1932	1692	1904	1681
3	1935	1687	1940	1666
4	1920	1665	1877	1686
5	1928	1693	1864	1666
6	1926	1694	1929	1667
7	1935	1692	1912	1667
8	1932	1693	1912	1671

indicate that a co-crystal was formed in each of the sixteen cases. Although vibrational spectroscopy offers an unambiguous assessment of reaction outcome, it is not possible to elucidate the precise binding modes and the presence of specific synthons in this family of compounds; this required single-crystal diffraction data, which were obtained for six compounds.

Despite considerable efforts, we were unable to grow suitable single crystals for any additional co-crystals; the **3-HBA** based co-crystals were particularly troublesome, because most of them produced oils upon re-crystallization.

The crystal structure determination of **4-HBA:1** shows that in the resulting 1:1 co-crystal the best donor (as was determined by MEP values), the −OH moiety, forms a hydrogen bond to the *N*-oxide oxygen atom, the best acceptor, (O24···O11 2.6442(11) Å, O24−H24···O11 1.763(17) Å), and the second-best donor, the carboxylic moiety, engages in a hydrogen bond with the pyridyl nitrogen atom, the second-best acceptor (O21···N14 2.7203(11) Å, O21−H21···N14 1.756(16) Å; Figure 1).

The crystal structure determination of **4-HBA:3** showed that the outcome is a 1:1 co-crystal, in which the −OH moiety forms a hydrogen bond to the *N*-oxide site, the best acceptor (O34···O21 2.590 Å, O34−H34···O21 1.703 Å). This

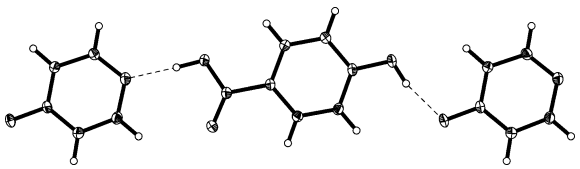


Figure 1. Primary hydrogen-bond interactions in the crystal structure of **4-HBA:1**.

leaves the second-best donor, the −COOH group, free to form a hydrogen bond with the second-best acceptor, the pyridyl nitrogen atom (O31···N11 2.616(3) Å, O31−H31···N11 1.57(3) Å; Figure 2).

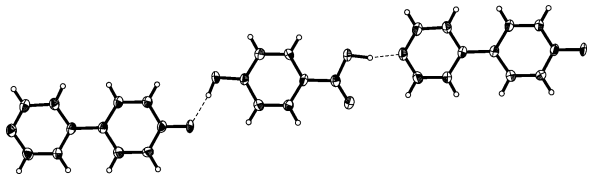


Figure 2. Primary hydrogen-bond interactions in the crystal structure of **4-HBA:3**.

The structure determination of **4-HBA:5** revealed a 1:1 co-crystal, in which the −OH moiety forms a hydrogen bond to the benzimidazole site (O34···N13 2.7238(13) Å, O34−H34···N13 1.819(18) Å). Similar to the previous two structures, the −COOH group forms a hydrogen bond to the second-best acceptor, the pyridyl nitrogen atom (O31···N21 2.6627(13) Å, O31−H31···N21 1.748(17) Å; Figure 3).

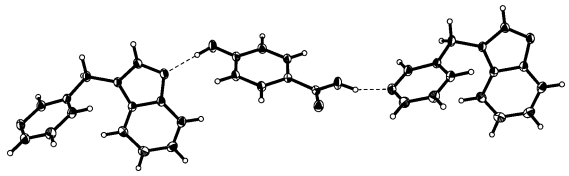


Figure 3. Primary hydrogen-bond interactions in the crystal structure of **4-HBA:5**.

Changing the donor molecule from 4-HBA to 3-HBA while keeping the acceptor **5** the same also gave a 1:1 co-crystal, in which the −OH moiety forms a hydrogen bond to the benzimidazole site (O33···N13 2.6778(16) Å, O33-H33···N13 1.77(2) Å), and the −COOH engages in a hydrogen bond with the pyridyl nitrogen atom (O31···N21 2.6266(17) Å, O31−H31···N21 1.65(2) Å; Figure 4).

In the crystal structure of **3-HBA:7**·CH_3CN·H_2O, the two principle components present in a 1:1 ratio are joined by water and acetonitrile molecules. Despite the potentially disruptive influence that included solvent molecules can have (especially, water molecules), the best donor on **3-HBA**, the −OH group, forms a hydrogen bond to the benzimidazole

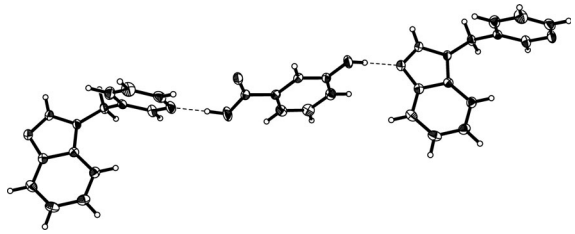


Figure 4. Primary hydrogen-bond interactions in the crystal structure of **3-HBA:5**.

nitrogen atom (O43···N13 2.746(2) Å) and the second-best donor −COOH forms a hydrogen bond with the pyridyl nitrogen atom, the second-best acceptor (O48···N31 2.683(3) Å; Figure 5).

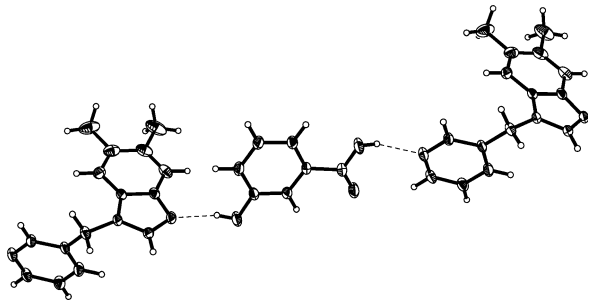


Figure 5. Primary hydrogen-bond interactions in the crystal structure of **3-HBA:7.$CH_3CN.H_2O$**.

Finally, the structure determination of **4-HBA:6** showed a 1:1 monohydrate co-crystal, in which the −OH moiety forms a hydrogen bond to the benzimidazole site (O44···N13 2.683(3) Å, O44−H44···N13 1.78(3) Å), and the −COOH group interacts with the pyridyl nitrogen atom (O41···N31 2.659(3) Å, O41−H41···N31 1.66(3) Å; Figure 6). The water molecule does not interfere with any of the postulated primary O−H···N interactions, which is quite unusual in hydrates.[24]

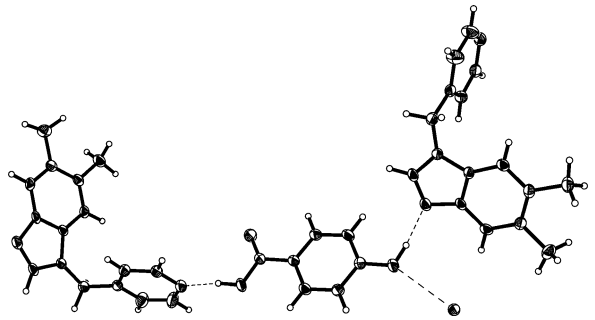


Figure 6. Primary hydrogen-bond interactions in the crystal structure of **4-HBA:6.H_2O**.

In all six of the crystal structures that were obtained from this series of co-crystallizations, the −OH group formed a hydrogen bond with the acceptor atom associated with the highest negative electrostatic potential, leaving the carboxylic acid to bind to the second-best acceptor (ranking determined by charge). If the −OH and −COOH groups had been ranked according to acidity (which would reverse **D1** and **D2**), then the commonly observed "best donor/best acceptor" behavior in hydrogen-bonded molecular solids would not have held up in a single case. To place our observations in the context of other structural data, we also examined relevant crystallographic information from the existing literature.

A previously reported structure of **4-HBA:4**[28] exhibits the same behavior: the −OH group forms a hydrogen bond to the best acceptor, the imidazole moiety, and the −COOH group interacts with the pyridine nitrogen atom (Figure 7).

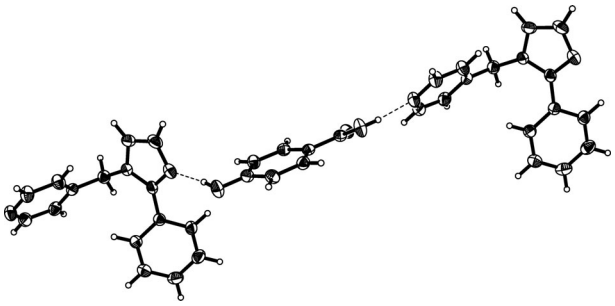


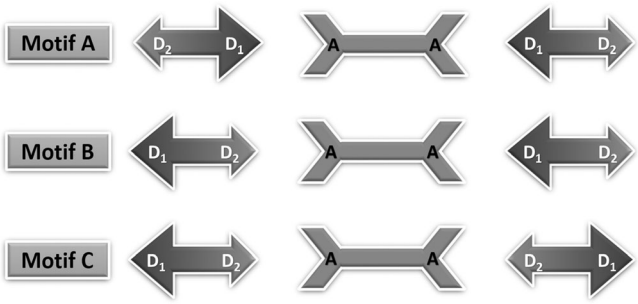
Figure 7. Primary hydrogen-bond interactions in the crystal structure of **4-HBA:4**.[28]

We subsequently carried out a search of the Cambridge Structural Database (CSD) on all co-crystals of **3-HBA** and **4-HBA** with geometrically unbiased acceptors and obtained a total of 28 hits and analyzed them in the context of a best donor/best acceptor approach (Table 2). The results can be split into three different outcomes. In the first case, the −OH "wins" the competition for the donor (motif A in Scheme 3). In the second case, both the −COOH and the −OH moiety form hydrogen bonds to equivalent acceptor sites (motif B in Scheme 3). In the third case, the −COOH moiety wins the competition for the hydrogen-bond acceptor (motif C in Scheme 3).

Table 2. Analysis of 28 co-crystals of **3-HBA** and **4-HBA** with geometrically unbiased hydrogen-bond acceptors.

−OH "wins"	Both groups bind	−COOH "wins"
9:28	14:28	5:28
32%	50%	18%

In the majority of cases, both donors engage in hydrogen bonding to equivalent acceptor sites, which indicates that these two moieties are comparable strength and ability when it comes to finding an acceptor in a competitive chemical system. In the remaining cases (motif A and motif C in Scheme 3; 14:28) when a preference can be unambiguously established, there is about a 2:1 advantage in favor of the −OH group.



Scheme 3. Three plausible outcomes when forming co-crystals of **3-HBA** or **4-HBA** with symmetric ditopic acceptors.

If the two donors, −OH versus −COOH, are ranked by using a pK_a-based argument (in which the former is 10^5 times weaker), one should expect a far higher "winning percentage" for the −COOH than what is actually observed. If the results from our current study are added to the structures found in the CSD, the bias is even more strongly in favor of the −OH being a more effective hydrogen-bond donor than the −COOH moiety in hydroxybenzoic acids (Table 3).

Table 3. Combined results from current study and the CSD.

−OH "wins"	Both groups bind	−COOH "wins"
15:34	14:34	5:34
44%	41%	15%

The combined data show that when ditopic asymmetric acceptors are employed, the −OH group binds to the best acceptor, and the −COOH group binds to the second-best acceptor in all seven cases. When symmetric ditopic acceptors are employed (19 structures), the −OH group formed hydrogen bonds with both acceptor groups (motif A) on 4:19 occasions. In 11:19 cases, both donor groups formed hydrogen bonds with the acceptor groups (motif B). Finally, in 4:19 cases, the −COOH group formed hydrogen bonds with both acceptors (motif C; Scheme 3).

In the eight known co-crystals of **3-HBA** and **4-HBA** with monotopic acceptors, the −OH group wins four times, the −COOH moiety wins once, and in the three remaining cases, the result is a 2:1 co-crystal with both donors participating in an O−H···N hydrogen bond.

A closer examination of the distribution of outcomes with symmetric ditopic donors as a function of donor molecule, shows that for **3-HBA**, both moieties bind to the available equivalent acceptors in 8:9 cases (Table 4). However, in the ten known co-crystals of **4-HBA**, there are four instances of (motif A) and three each of motif B and motif C, respectively (Table 4).

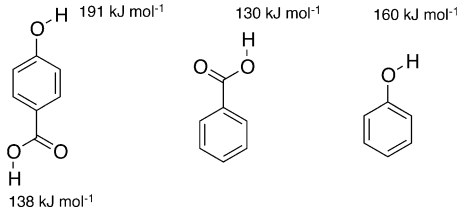
The fact that the two probe molecules, **3-HBA** and **4-HBA**, display somewhat different pattern preferences may be attributed to the difference in donor strengths of the two donors in each molecule. As shown in Scheme 1, the difference in molecular electrostatic potential (MEP) values between the two hydrogen-bond donor sites of **4-HBA** (53 kJ mol^{-1}) is much greater than in the case of **3-HBA** (31 kJ mol^{-1}). It is therefore reasonable to infer that the difference in charge between the two donors of 3-hydroxybenzoic acid is not sufficiently high to impart a more pro-

Table 4. Distribution of outcomes with symmetric ditopic acceptors.

	Motif A	Motif B	Motif C
3-HBA	0	8	1
4-HBA	4	3	3

nounced "winner" resulting in a higher percentage for motif B in co-crystals involving **3-HBA**.

In this study, we have focused exclusively on molecules that contain hydroxylic and carboxylic groups attached to the same backbone. Because the two moieties are present on a single conjugated frame, there is a cooperative effect in place that attenuates the charge advantage that the −OH group has over the −COOH moiety (Scheme 4).



Scheme 4. Effect on electrostatic potentials of −OH and −COOH moieties when both are attached to the same aromatic scaffolding.

The interdependence of charge on different functionalities on the same backbone also means that the results may be slightly different if a molecular-recognition competition is arranged, in which the −OH and −COOH moieties are located on different molecules or on one backbone that precludes electrostatic cooperation.

Because hydrogen bonds are relatively weak and reversible, one should not expect that supramolecular guidelines can offer any guarantees as far the specific structural outcome of any co-crystallization goes, as was evidenced by conventional polymorphism and synthon crossover. However, it may be useful to employ a MEP-based view of hydrogen-bond interactions to rationalize somewhat unexpected structural behavior. For example, the four symmetric ditopic acceptors in Table 5 are known to exhibit synthon crossover.[12a,25] The charges on the carbonyl group on **4-HBA** and **3-HBA** are −285 and −267 kJ mol^{-1}, respectively, and are comparable or in some cases greater than the charges of the acceptors in Table 5, and this could explain the appearance of the alternate synthon, in which the −OH group binds to the carbonyl group on the acid.

Table 5. Symmetric hydrogen-bond acceptors known to display synthon crossover.

Acceptor	MEP-AM1 [kJ mol^{-1}]
1,2-bi(4-pyridyl)ethane	−285
2,3,5,6-tetramethylpyrazine	−273
4,4′-bipyridine	−269
pyrazine	−224

Conclusion

Our results emphasize first of all that a reliable ranking of hydrogen-bond donor strength can be achieved by using molecular electrostatic potential surfaces obtained by using low-level semi-empirical methods. Furthermore, this approach indicates that a hydroxylic group is a highly competitive, and in the majority of cases, a more dominant hydrogen-bond donor than a carboxylic moiety, as long as both groups are attached to the same conjugated backbone. If the two components are competing for two hydrogen-bond acceptor sites of different strengths (again ranked based on MEPs values), the −OH group is more likely to bind to the best acceptor, leaving the −COOH group to bind to the second-best acceptor. This means that the −OH group is a more effective hydrogen-bond donor for crystal-engineering purposes than is the carboxylic acid group in co-crystals of hydroxybenzoic acids. This study has focused on geometrically unbiased acceptors, because there is no doubt that steric factors could influence the outcome. If a potential acceptor site also contained an auxiliary group that could act as a powerful hydrogen-bond donor for the C=O moiety of the acid, then the −COOH group is favored to win. For example, 2-aminopyridine is more likely to bind to a carboxylic acid through a pair of O−H···N/N−H···O=C hydrogen bonds than to opt for a phenol through a single O−H···N interaction.

Although the overall conclusion reached in this systematic structural study may challenge conventional wisdom, it is certainly widely accepted that thiols, which are significantly more acidic than phenols, are inferior hydrogen-bond donors (an observation, which again is consistent with a ranking based upon electrostatic charge). The fact that the charges on the two sites, −OH and −COOH, are quite comparable and that these interactions are weak and reversible mean that we cannot expect these results to hold up under any and all conditions. However, it is unrealistic to expect synthetic strategies based on intermolecular interactions to always lead to a specific outcome that can be traced back to a single molecular property. The mere existence of polymorphism is certainly a manifestation thereof. However, even though the number of data points examined herein is quite small, the combination of new and existing structural data indicate that the balance of intermolecular power is likely to favor −OH over −COOH in hydroxybenzoic acids, especially when facing a molecule with two different binding sites. It is certainly conceivable that with a much larger dataset, an adjustment to these conclusions may be necessary but, in the meantime, we hope that the results presented herein can serve as a starting point for re-examinations of existing structural data, as well as for new studies[26] involving tailor-made molecules that can further advance our ability to rank effective hydrogen-bond strength for crystal-engineering purposes.

Experimental Section

Synthesis of pyrazine mono *N*-oxide (1):[27] A solution of hydrogen peroxide (30 %; 1.42 g, 0.042 mol) in acetic acid (10 mL) was added dropwise by using a drop funnel over a period of 2.5 h to a solution of pyrazine (1.00 g, 0.013 mol) in acetic acid (12.5 mL) at 70–80 °C. Heating was continued for about 5 h. Acetic acid was removed on a rotary evaporator, and then water (10 mL) was added followed by evaporation. The residue

was dissolved in hot chloroform (50 mL) and dried with a mixture of sodium sulfate and sodium carbonate, and the solvent removed on a rotary evaporator. The residue was chromatographed on silica with chloroform/methanol (9:1) as the eluent. Product was isolated as a white powder and recrystallization from methanol gave needle-like crystals (1.2 g, 72%). M.p.: 113–115°C (lit. m.p.: 113–114°C);[11] ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 8.66$ (d, 2H, $J = 4$ Hz), 8.36 ppm (d, 2H, $J = 4$ Hz); ^{13}C NMR (200 MHz, [D$_6$]DMSO): $\delta = 158$, 144 ppm; IR (KBr pellet): $\tilde{\nu} = 3430$, 2914, 1596, 1470, 1433, 1312 (N^+-O^-), 1213, 1005, 861, 540, 477 cm^{-1}.

Synthesis of tetramethylpyrazine mono *N*-oxide (2): 2,3,5,6-Tetramethylpyrazine mono-*N*-oxide was synthesized following the procedure for **1**. Yield: 61%. M.p.: 98–100°C; ^{1}H NMR (200 MHz, [D$_6$]DMSO): $\delta = 2.43$ (d, 6H), 2.32 ppm (d, 6H); ^{13}C NMR (200 MHz, [D$_6$]DMSO): $\delta = 150$, 138, 21, 12 ppm; IR (KBr pellet): $\tilde{\nu} = 3462$, 2914, 1572, 1472, 1320 (N^+-O^-), 1138, 1004, 922, 691 cm^{-1}.

4,4′-Bipyridyl mono *N*-oxide (3): mixture of 4,4′-bipyridine (2.00 g, 12.82 mmol), hydrogen peroxide (30%; 1.33 g, 39 mmol), and glacial acetic acid (8 mL) was stirred in a round-bottom flask for 18 h at 70°C. After cooling the reaction mixture, the solvent was removed by a rotary evaporator and diluted with water (20 mL). The solution was basified with excess sodium carbonate (2 g) and extracted with chloroform (3× 50 mL). The organic layers were combined and then concentrated under reduced pressure by using a rotary evaporator. The product was further purified by column chromatography with an ethyl acetate/methanol mixture (3:1) producing an off-white solid (1.1 g, 52%). M.p.: 170–171°C; ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 8.70$ (d, 2H, $J = 12$ Hz), 8.36 (d, 2H, $J = 12$ Hz), 7.94 (d, 2H, $J = 12$ Hz), 7.83 ppm (d, 2H, $J = 21$ Hz); ^{13}C NMR (400 MHz, [D$_6$]DMSO): $\delta = 150$, 142, 139, 133, 124, 120 ppm; IR (KBr pellet): $\tilde{\nu} = 3222$, 2910, 1600, 1515, 1482, 1410, 1253 (N^+-O^-), 1228, 1191, 1029, 851, 821, 714, 651, 580 cm^{-1}.

Ligands **4**–**7** were synthesized according to previously published methods.[28,29] *4-((2-Phenyl-1H-imidazol-1-yl)methyl)pyridine* (**4**):[28] m.p. 35–39°C (lit m.p. 33–38°C). *1-(Pyridin-3-ylmethyl)-1H-benzo[d]imidazole* (**5**):[29] m.p. 50–55°C (lit m.p. 48–51°C). *5,6-Dimethyl-1-(pyridin-4-ylmethyl)-1H-benzo[D]imidazole* (**6**):[28] m.p.: 185–190°C (lit. m.p. 182–190°C). *5,6-Dimethyl-1-(pyridin-3-ylmethyl)-1H-benzo[D]imidazole* (**7**):[28] m.p. 147–150°C (lit. m.p. 150–153°C).

Synthesis of 1-(pyridin-4-ylmethyl)-1*H*-benzo[D]imidazole (8): Benzimidazole (0.5 g, 4.23 mmol) was dissolved in acetonitrile (50 mL). Crushed NaOH (0.508 g 12.7 mmol) was added to the solution and was stirred for 3 h. 4-Picolylchloride hydrogen chloride (0.69 g, 4.23 mmol) was dissolved in acetonitrile (50 mL) and added to the benzimidazole solution and stirred for 6 h. Once the absence of the picolyl chloride was confirmed by TLC, the acetonitrile was removed under reduced pressure. The resulting oil was dissolved in ethyl acetate and washed with NaOH (1 N), distilled water, and brine. The solution was dried over $MgSO_4$. Ethyl acetate was removed under reduced pressure to give a brown solid (5.40 g, 69.4%). M.p. 105–110°C; ^{1}H NMR ([D$_6$]DMSO, 400 MHz): $\delta = 8.51$ (d, $J = 6.2$ Hz, 1H), 8.42 (s, 1H), 7.68 (dd, $J = 9.0$, 3.5 Hz, 1H), 7.46 (dd, $J = 9.4$, 3.5 Hz, 1H), 7.21 (dd, $J = 9.0$, 3.5 Hz, 1H), 7.18 (d, $J = 5.5$ Hz, 1H), 5.58 ppm (s, 1H).

Molecular structures for **3-HBA**, **4-HBA**, and **1**–**8** were constructed by using Spartan 06 (Wavefunction, Inc. Irvine, CA). All molecules were optimized by using AM1, with the maxima and minima in the electrostatic potential surface (0.002 e a.u.$^{-1}$ isosurface) determined by using a positive point charge in vacuum as a probe.

Solvent-assisted grinding was carried for combinations of **3-HBA** or **4-HBA** with each of the eight acceptors in a 1:1 ratio with methanol as the solvent. The resulting sixteen solids were characterized by IR spectroscopy, and five of them produced crystals (slow evaporation from methanol) of sufficient quality to enable single-crystal X-ray diffraction analysis to be carried out.

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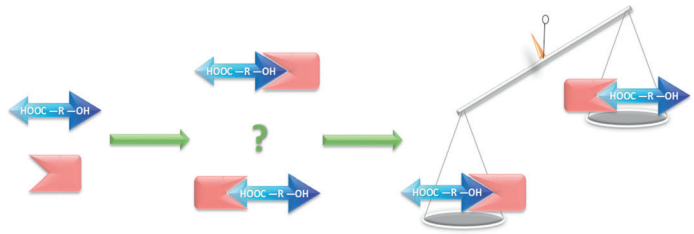

Intermolecular interactions: A ranking based on electrostatic charge and tested against structural data indicate that the −OH moiety is a better hydrogen-bond donor than the −COOH site in hydroxybenzoic acids (see scheme).

Crystal Engineering

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Ranking Relative Hydrogen-Bond Strengths in Hydroxybenzoic Acids for Crystal-Engineering Purposes