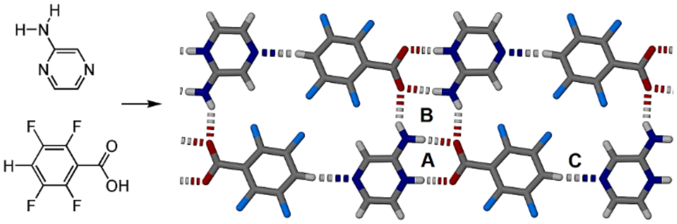
Cooperative Strong Charge Assisted N-H---O Hydrogen Bonding and Weaker Nonconventional C-H---N Hydrogen Bonding in the Formation of Extended Hydrogen Bonded Networks with 2,3,5,6-Tetrafluorobenzoic Acid

Eric Bosch*,† and Nathan P. Bowling‡

†Department of Chemistry, Missouri State University, Springfield, Missouri 65897, USA

‡Department of Chemistry, University of Wisconsin-Stevens Point, 2001 Fourth Avenue, Stevens Point, WI, 54481, USA



Abstract

Cooperative strong charge assisted hydrogen bonding and weaker nonconventional hydrogen bonding is probed through cocrystals formed between 2,3,5,6-tetrafluorobenzoic acid and three 2-aminopyrazines. In each of these cocrystals cooperative nonconventional hydrogen bonding and charge assisted hydrogen bonding results in the formation of hydrogen bonded supramolecular networks. A charge assisted cyclic hydrogen bonded motif, $R_2^2(8)$, is formed between the 2-aminopyrazinium cation and the carboxylate anion along with a nonconventional C-H---N hydrogen bond between the phenyl hydrogen and second ring N in the pyrazine. Secondary hydrogen bonding interactions result in the formation of a double stranded linear polymer, a planar 2D polymer or an interconnected 3D network dependent on secondary substitution of the 2-aminopyrazine. The related formation of both 1:1 and 2:1 cocrystals between 4-pyrrolidinopyridine and 2,3,5,6-tetrafluorobenzoic acid is also reported.

Introduction

The assembly of supramolecular polymers using non-covalent intermolecular interactions such as hydrogen bonding is well established.[1,2] The role of weaker non-conventional hydrogen bonding, involving either a C-H---N or a CH---O interaction, is generally observed as an important cooperative intermolecular interaction in the solid state but is seldom considered a dominant non-covalent interaction for the formation of supramolecular polymers.[3] We have, however, demonstrated that acidic aromatic hydrogen atoms, for example on octafluorobiphenyl, may also be exploited in the formation of supramolecular polymers on cocrystallization with bipyridines.[4] Furthermore several other researchers have also noted nonconventional hydrogen bonding to protons on polyfluorobenzenes.[5,6,7] Recently we reported the formation of one dimensional supramolecular polymers through cooperative halogen bonding and weaker non-conventional C-H---N hydrogen bonding.[8] We further reasoned that 2,3,5,6-tetrafluoro benzoic acid could be employed as a multitasking supramolecular tecton through the ability to form cooperative conventional hydrogen bonds, possibly charge assisted, through the carboxylic acid moiety and non-conventional hydrogen bonds through the activated C-H moiety. The observation that Bis and Zaworotko[9] clearly demonstrated that 2-aminopyridines predominantly form charge assisted hydrogen bonds to benzoic acids led us to choose 2-aminopyrazines as cocrystallization partners with 2,3,5,6-tetrafluorobenzoic acid. Our expectation was that the pyrazine nitrogen atom flanked by the amino group would form hydrogen bonds to the carboxyl group while the second pyrazine N would form a non-conventional C-H---N hydrogen bond to the activated phenyl hydrogen resulting in the formation of supramolecular polymers as shown in Figure 1. This proposal was supported by Aakeröy's report establishing 2-aminopyrazines as multitasking tectons capable of concomitant conventional hydrogen bonding and halogen bonding.[10]

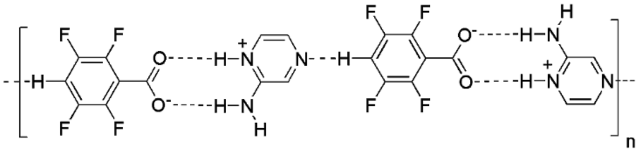


Figure 1. Proposed hydrogen bonding interactions in the formation of supramolecular polymers on cocrystallization of 2,3,5,6-tetrafluorobenzoic acid and 2-aminopyrazine.

We chose to cocrystallize the commercially available 2-aminopyrazine and the isomeric 3-, 5- and 6-methyl substituted pyrazin-2-amines with 2,3,5,6-tetrafluorobenzoic acid as we reasoned that the methyl substituent would demonstrate the flexibility of the approach without either diminishing the basicity of the pyrazine nitrogen atoms or introducing significant steric hinderance. To further explore the cooperative conventional and non-conventional hydrogen bonding we also attempted to form 2:1 cocrystals between 4-pyrrolidino pyridine and 2,3,5,6-tetrafluorobenzoic acid.

Experimental Section

Chemicals. All chemicals are commercially available and were used as received. 2-Amino pyrazine was purchased from Alfa Aesar, 4-pyrrolidinopyridine from Sigma-Aldrich, and 2,3,5,6-tetrafluorobenzoic acid was purchased from Matrix Scientific. The substituted pyrazines 3-methylpyrazin-2-amine, 5-methylpyrazin-2-amine and 6-methylpyrazin-2-amine were purchased from Arctom Chemicals.

Preparation of amino pyrazine-tetrafluorobenzoic acid co-crystals. In a typical experiment 3-methylpyrazin-2-amine (17.6 mg, 0.16 mmol) and 2,3,5,6-tetrafluorobenzoic acid (32.6 mg, 0.17

mmol) were weighed into a vial. Absolute ethanol (3 mL) was added and the mixture vortexed to form a homogeneous solution. Slow evaporation yielded a homogeneous mass of thin rod-shaped cocrystals **(3)** suitable for X-ray analysis. Similar combinations of 2-amino pyrazine with 2,3,5,6-tetrafluorobenzoic acid and 6-methylpyrazin-2-amine with 2,3,5,6-tetrafluorobenzoic acid yielded cocrystals (**1**) and (**2**) while a homogeneous mass of fine hair-like crystals unsuitable for X-ray analysis was obtained from solutions of 5-methylpyrazin-2-amine and 2,3,5,6-tetrafluorobenzoic acid.

Preparation of 4-pyrrolidinopyridine-tetrafluorobenzoic acid co-crystals. 4-Pyrrolidinopyridine (17.3 mg, 0.12 mmol) and 2,3,5,6-Tetrafluorobenzoic acid (21.3 mg, 0.11 mmol) were weighed into a vial and 1.5 mL of absolute ethanol added. The mixture was vortexed to form a homogeneous solution. Slow evaporation yielded a mass of block shaped cocrystals **(5)** suitable for X-ray analysis. Similar reaction with a 2:1 ratio of components yielded plate shaped cocrystal **(4)**.

Structure solution. For each co-crystal a single crystal was mounted on a Kryoloop using viscous hydrocarbon oil. Data were collected using a Bruker Apex 2 CCD diffractometer equipped with Mo Kα radiation with $\lambda = 0.71073$ Å. Data collection at low temperature was facilitated by use of a Kryoflex system with an accuracy of ±1 K. Initial data processing was carried out using the Apex 3 software suite.[11] Structures were solved by direct methods using SHELXT-2018[12] and refined against F^2 using SHELXL-2018.[13] The program X-Seed was used as a graphical interface.[14] All H atoms were located in the difference maps. For each cocrystal the acidic proton was located between the carboxyl O and the pyrazine N significantly closer to the N atom. For example, during refinement of the data corresponding to cocrystal **(1)** the residual peak between the O and N atoms was located at distances of 0.969 and 1.679 Å from the

N and O atoms respectively. Hydrogen atoms on N were restrained in the refinement with N−H = 0.87 (2) Å with $U_{iso}(H) = 1.2U_{eq}(N)$. The H---H distance of the amine hydrogen atoms was restrained to 1.50 (2) Å. Hydrogen atoms on O were restrained in the refinement with O−H = 0.84 (2) Å with $U_{iso}(H) = 1.2U_{eq}(O)$. The phenyl hydrogen atoms involved in C-H---N hydrogen-bonding interactions were restrained in the refinement with C−H = 0.95 (2) Å and with $U_{iso}(H) = 1.2U_{eq}(C)$. All other hydrogen atoms were treated as riding atoms in geometrically idealized positions with C—H = 0.95 Å and $U_{iso}(H) = 1.2U_{eq}(C)$ for aryl protons, C—H = 0.99 Å and $U_{iso}(H) = 1.2U_{eq}(C)$ for methylene protons and C—H = 0.98 Å and $U_{iso}(H) = 1.5U_{eq}(C)$ for methyl protons. For cocrystal **(1)** the program SQUEEZE was used through the Platon interface to ameliorate the effect of a disordered solvent molecule on the refinement.[15] The solvent accessible volume of 29 Å^3 and 12 electrons found in the solvent accessible volume suggests the possible disorder of an adventitious water molecule. This is reasonable since the channel in which the disordered solvent resides is flanked by carboxylate groups. For cocrystal **(4)** one of the pyrrolidine rings was disordered over two positions and was modelled and refined as such with the aid of a free variable that refined to 0.51 indicating essentially equal occupancy of the two positions. The crystallographic data are collected in Table 1.

Results and Discussion.

Aminopyrazine-tetrafluorobenzoic acid cocrystal formation and analysis. Rod-shaped colorless crystals formed from an equimolar ethanol solution of 2,3,5,6-tetrafluorobenzoic acid and 2-aminopyrazine. The cocrystal **(1)** crystallized in the triclinic space group P-1 with one molecule of each of the components in the asymmetric unit. Proton transfer between the components was evident by the location of the acidic proton on N, as noted in the experimental section, and the

C11-O1 and C12-O2 bond distances of 1.259 and 1.239 respectively.

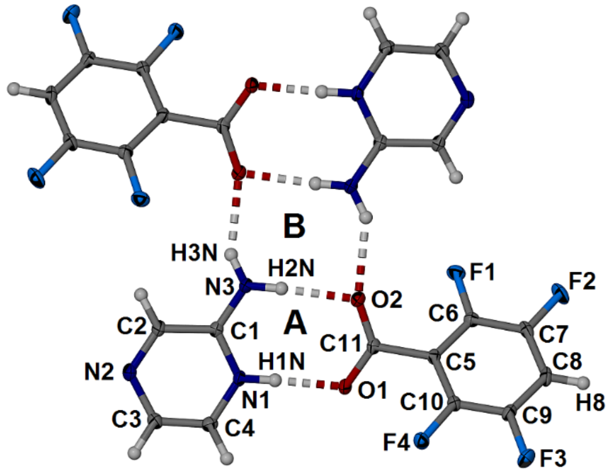


Figure 2. Labelled asymmetric unit of the cocrystal **(1)** showing the self-complementary dimeric unit formed by two cyclic hydrogen bonded networks **A** and **B**.

A pair of charge assisted hydrogen bonds, formed on proton transfer, form the hydrogen bonded aminopyrazinium benzoate core with a hydrogen bonded net with graph set notation $R^{2}_{2}(8)$ shown as **A** in Figure 2.[16] The charge assisted hydrogen bonds have N1---O1 and N3---O2 distances of 2.6470(13) and 2.8094(14) Å respectively and N1-H1N---O1 and N3-H2N---O2 angles of 175(2) and 176.1(2)° respectively. The pyrazine and benzene rings are not coplanar with a dihedral angle of 26.08(4)° while the hydrogen bonded net is essentially planar with all 8 atoms within 0.142(5) Å of the least squares plane defined by the 8 atoms. Two pyrazinium benzoates then form a self-complementary dimeric unit through cyclic hydrogen bonded motif **B** with graph set notation $R^{2}_{4}(8)$ where the carboxylate oxygen atom O2 accepts two hydrogen bonds. The hydrogen bond unique to **B** has N3---O2 distance 2.8278(14) Å and N3-H3N---O2 angle 148.8(15)°. The hydrogen bonded network, **B**, is also essentially planar with a maximum deviation from the plane of 0.015(13) Å. The angle between the planes defined by networks **A** and **B** is 11.6(4)°. The self-complementary dimeric units shown in Figure 2 are linked together through the non-conventional hydrogen bond, shown as **C** in Figure 3, to form a duplex linear supramolecular polymer. The H8---N2 and C8---N2 distances are 2.4395(16) and 3.3496(16) Å respectively with a C8-H8---N2 angle of 163.9(16)°. This N···H distance is 89.7% of the sum of the van der Waals radii and only marginally longer than the H···N distances observed in the cocrystals formed between octafluorobiphenyl and three bipyridines where the average H···N distance was 2.293 Å (84.3% the sum of the van der Waals radii).[4]

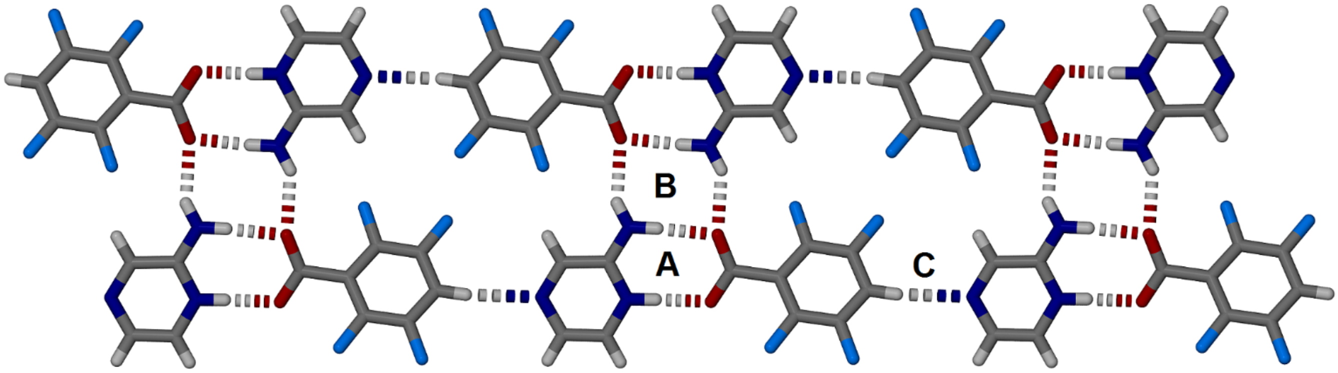


Figure 3. Portion of the structure of cocrystal **(1)** showing the duplex supramolecular polymer.

The cocrystal **(2)** formed between 2,3,5,6-tetrafluorobenzoic acid and 2-amino-6-methylpyrazine crystallized in the monoclinic space group P21/n with one molecule of each of the components in the asymmetric unit. The charge assisted hydrogen bonds have N1---O1 and N3---O2 distances of 2.620(3) and 2.822(3) Å respectively and N1-H1N---O1 and N3-H2N---O2 angles of 176(3) and 175(3)° respectively and form a similar hydrogen bonded net with graph set notation R_2^2 (8), **A** in Figure 4. The pyrazine and benzene rings are not coplanar with a torsional angle of 28.01(9)°. Similar to cocrystal **(1)** two pyrazinium benzoates moieties form a self-complementary dimeric unit through the cyclic hydrogen bonded $R_4^2(8)$ motif shown as **B** in Figure 4. The hydrogen bond unique to **B** has N3---O2 distance 2.774(3) Å and N3-H3N---O2 angle 145(3)°. In common with cocrystal **(1)** both cyclic hydrogen bonded nets are essentially planar with maximum deviations from the least squares planes of 0.073(9) and 0.152(12) Å for **A** and **B** respectively. Indeed the extended hydrogen bonded network **A**-**B**-**A** is essentially planar with an angle between the planes **A** and **B** of only 1.6(6)°.

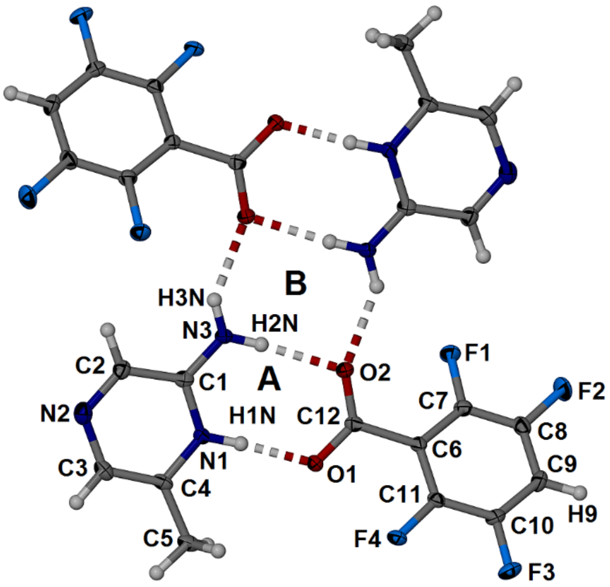


Figure 4. Labelled asymmetric unit of the cocrystal **(2)** showing the self-complementary dimeric pyrazinium benzoate unit formed by the two cyclic hydrogen bonded networks **A** and **B**.

The dimeric pyrazinium benzoate units are similarly connected by the non-conventional hydrogen bond (**C** in Figure 5) with H9···N2 and C9---N2 distances of 2.47(2) and 3.369(4) Å respectively and C9-H9---N2 angle of 158(3)°. The methyl substituent, however, results in a different arrangement than in **(1)** and in cocrystal **(2)** adjacent dimeric units are flipped resulting in a two-dimensional corrugated supramolecular polymer for **(2)** rather than the double stranded one-dimensional supramolecular polymer formed in **(1)**.

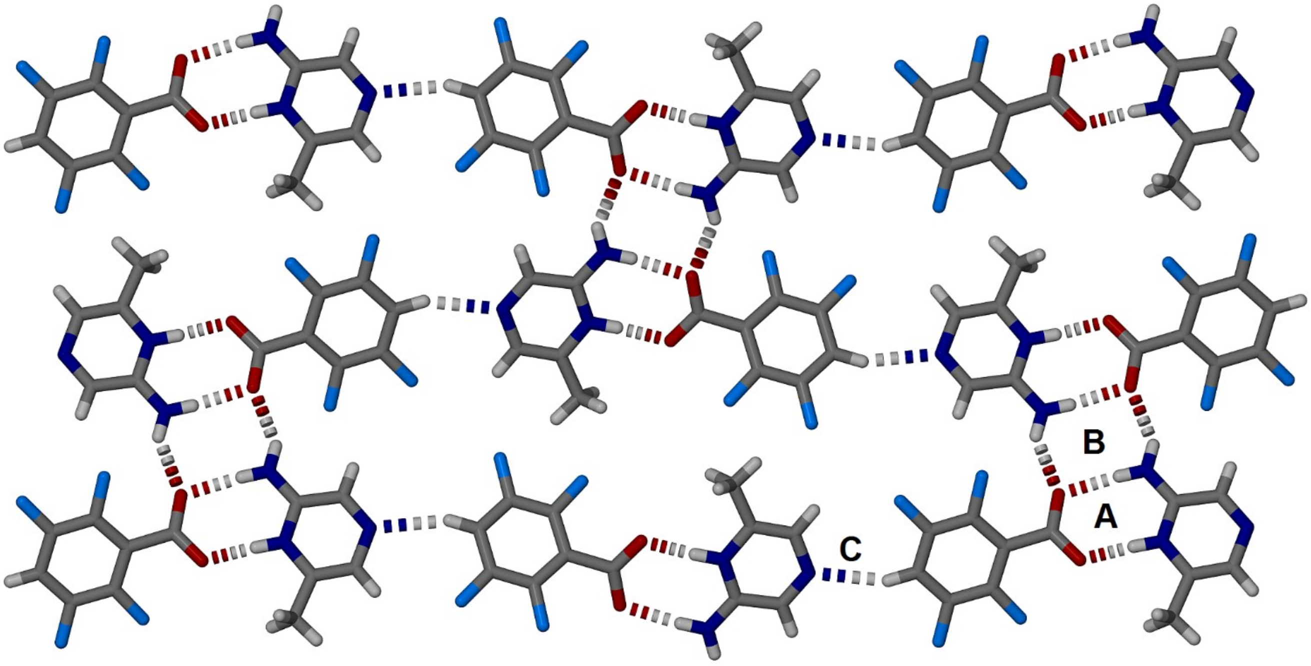


Figure 5. Portion of the structure of the cocrystal **(2)**, showing the charge assisted hydrogen bonding motifs **A** and **B** and the non-conventional hydrogen bond, **C**, that result in a two dimensional supramolecular polymer.

The cocrystal (**3)** formed between 2,3,5,6-tetrafluorobenzoic acid and 2-amino-3-methylpyrazine crystallized in the monoclinic space group P21 and similarly contained one molecule of each of the components in the asymmetric unit. Similar to cocrystals **(1)** and **(2)** the charge assisted hydrogen bonds have N1---O1 and N3---O2 distances of 2.633(2) and 2.788(2) Å respectively and N1-H1N---O1 and N3-H2N---O2 angles of 177(3) and 179(3)° respectively and form a similar hydrogen bonded net with graph set notation R_2^2 (8), **A** shown in Figure 6. The hydrogen bonded net is essentially planar with a maximum deviation from the least squares planes of 0.031(11) Å for all 8 atoms. The pyrazine and benzene rings are not coplanar with a torsional angle of 14.54(11)°. The one dimensional supramolecular polymers exhibit a weak C-H---N interaction between the phenyl hydrogen and the second pyrazine N with H9---N2 and C9---N2 distances are 2.80(3) and 3.745(3) Å respectively with a C9-H9---N2 angle of 173(2)°. The longer N···H distance is possibly due to the steric effect of the methyl group flanking the N atom. Even though the N---H is slightly larger than of the sum of the van der Waals radii of 2.75Å the almost linear arrangement of the atoms suggests that this is indeed a weak non-conventional hydrogen bond (**C** in Figure 6). Adjacent pyrazinium benzoates, in contrast to cocrystals **(1)** and **(2)**, are almost orthogonal with a single hydrogen bonding interaction shown as b in Figure 6. This orthogonal arrangement is likely a result of a steric interaction between the 3-methyl group and fluorine atoms on the tetrafluorobenzoate.

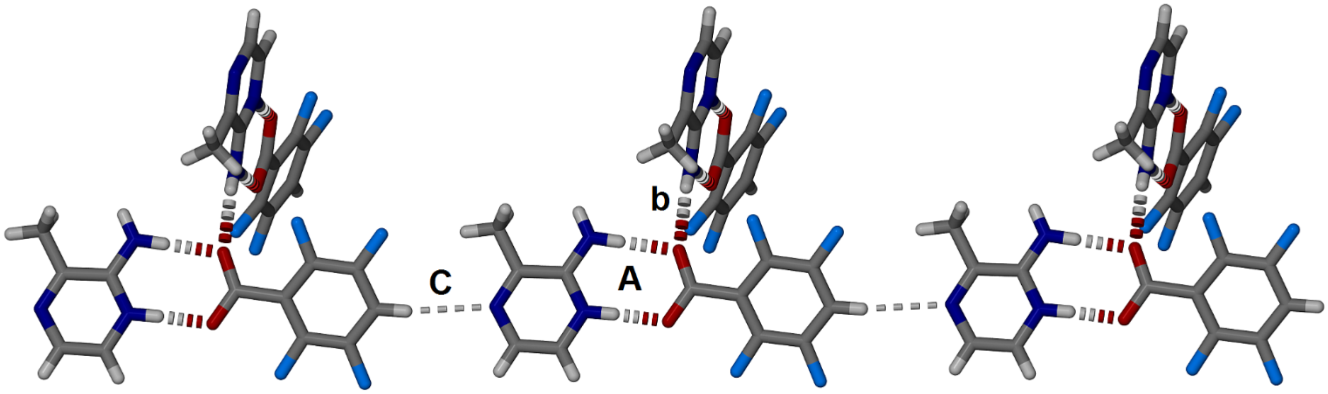


Figure 6. Portion of the structure of the cocrystal **(3)**, showing the charge assisted hydrogen bonding motif **A,** the C-H---N interaction **C,** and the interstrand hydrogen bond, **b**, that results in a complex three dimensional hydrogen bonded supramolecular network.

Comparative analysis of the pyrazinium-tetrafluorobenzoate cocrystals.

Each of the three cocrystals exist as an ion-pair resulting from proton transfer. There are three strong charge-assisted hydrogen bonds: one involving the pyrazinium proton and two involving the amino protons and are shown in Figure 8.

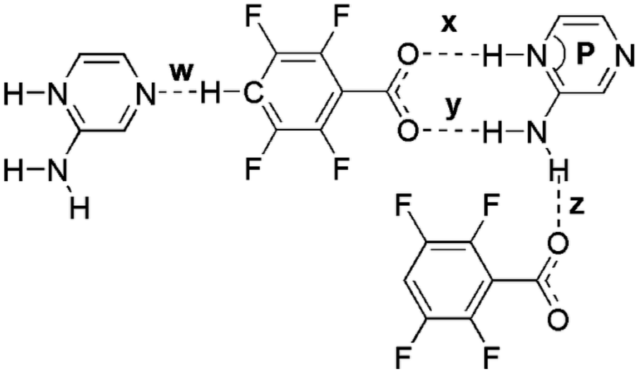


Figure 7. Labelled hydrogen bonds and bond angles in pyrazinium-tetrafluorobenzoate cocrystals.

The distances and angles related to these three hydrogen bonds are collected in Table 2. The pyrazinium hydrogen bond (x) is consistently the shortest with N-H---O distances averaging 1.74 Å with the second ion pair hydrogen bond N-H---O distance averaging 1.93 Å while the hydrogen bond between ion pairs has an average N-H---O distance of 2.06 Å. In order to place these results in context we searched the Cambridge Structural Database Version 5.41[17] using Conquest Version 2.0.4[18] for crystals that included both the 2-aminopyrazine and a carboxyl group. Closer examination of the crude results allowed us to group them into ion-pair cocrystals, the result of proton transfer, and neutral cocrystals in which the carboxylic acid proton was intact. The C-N-C angle indicated as P in Figure 8 was extracted for each of these groups. For those cocrystals that did not include proton transfer the average of angle C-N-C is 117.1° while for those ion-pair cocrystals in which the pyrazine N is protonated the average of angle C-N-C is

121.3°. The angle C-N-C for cocrystals **(1)**, **(2)** and **(3)** are 121.53(10), 121,7(2) and 121.04(18)° respectively. For the group of neutral cocrystals the C-O distances were distinctive with the carbonyl and hydroxy C---O distances averaging 1.31 and 1.21 Å while the C---O distances for the group of ion pair crystals averages 1.25 Å ranging from 1.22 to 1.27 Å. These observations serve to confirm the proton transfer observed in cocrystals **(1)**, **(2)** and **(3)**.

The fact that proton transfer does not always occur between 2-aminopyrazine and carboxylic acids appears to be related to the relative acidity of the carboxylic acid. Thus, proton transfer was observed with tartaric acid and 3,5-dinitrobenzoic acid with $pK_a = 2.9$ and 2.77 respectively, while proton transfer was not observed with butane-, pentane-, heptane- and octanedioic acids with pK_a greater than 4.5 and 4-nitrobenzoic acid with pK_a 3.41. Since tetrafluorobezoic acid has pK_a 2.71 this is consistent with previous observations. In accord with this Aakeroy reported that the basicity of 2-aminopyrazine was diminished on bromination and a neutral cocrystal was formed between 3,5-dibromopyrazine and 3,5-dinitrobenzoic acid.[19]

Pyrrolidino pyridine-tetrafluorobenzoic acid cocrystal formation and analysis.

Given the results with cocrystals **(1)** to **(3)** we attempted the formation of 2:1 cocrystals between the strong base 4-pyrrolidinopyridine and 2,3,5,6-tetrafluorobenzoic acid. The 2:1 cocrystal **(4)** that formed from a 2:1 molar mixture of the components in ethanol contained one pyridinium moiety hydrogen bonded to the tetrafluorobenzoate and a second pyrridinopyridine forming a weak non-conventional hydrogen bond to the phenyl proton of the tetrafluorobenzoate (Figure 6). The pyridinium benzoate along with a cooperative C-H···O interaction form a $R_2^2(7)$ hydrogen bonded net. The nonconventional hydrogen bond has H15···N3 and C15···N3 distances of 2.473(19) and 3.395(2) Å respectively with a C15-H15···N3 angle of 163.1(15)°.

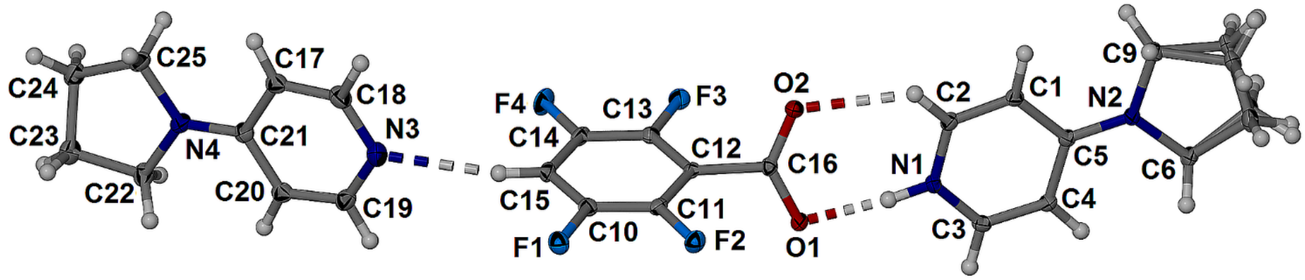


Figure 7. Asymmetric unit of the 2:1 cocrystal, **(4)**, formed between 4-pyrrolidinopyridine and tetrafluorobenzoic acid with displacement ellipsoids of non-hydrogen atoms drawn at the 50% level while H atoms are shown as circles of arbitrary size.

Slow evaporation from an equimolar ethanol solution of 4-pyrrolidinopyridine and tetrafluorobenzoic acid yielded block shaped cocrystal **(5)** that crystallized in the triclinic space group P-1 with two pyridinium cations and two tetrafluorobenzoate anions in the asymmetric unit along with a single adventitious water molecule. The asymmetric unit is shown using displacement ellipsoids in Figure 8 along with the tetrafluorobenzoate and pyrrolidino pyridine molecules that are also hydrogen bonded to the water. Both pyridinium benzoates feature cooperative N-H---O and C-H---O hydrogen bonds and the water molecule effectively bridges the two pyridinium benzoate moieties with two hydrogen bonds to an oxygen atom of each unique carboxylate, O1W-H1W---O2 and O1W-H2W---O4 (Figure 8). The pyridinium and benzoate rings in each pair are close to orthogonal with dihedral angles of 86.45(5) and 79.43(4)°. In contrast the two $R_2^2(7)$ nets are almost planar with root mean square deviations of 0.05 and 0.12 Å respectively and are almost coplanar with the pyridinium rings in both cases with dihedral angles of 5.18(13) and 10.05(14)°. Both hydrogen bonded nets feature short almost linear charge assisted N-H---O hydrogen bonds and a weaker C-H---O hydrogen bond. It is interesting to note that the included water molecule forms a hydrogen bond to one of the activated phenyl hydrogens (H2 in Figure 8) and a weaker hydrogen bond to a pyrrolidine proton with H---O distances of 2.202(14) and 2.49 Å, C---O distances of 3.1128(18) and 3.387(2) Å and C-H---O angles of 164.5(16) and 151.0° respectively.

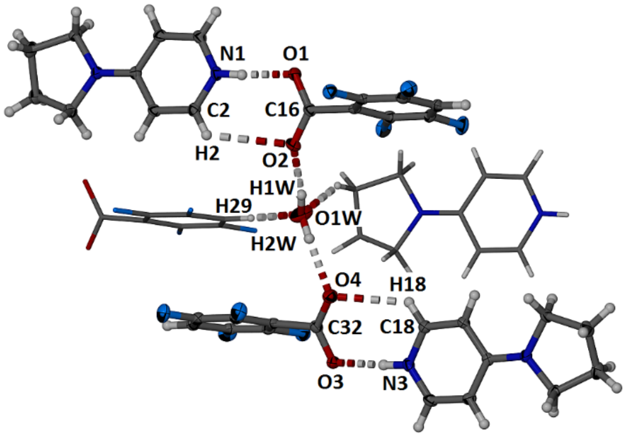


Figure 8.   Partially labelled asymmetric unit of the 1:1 cocrystal, **(5)**, formed between 4-pyrrolidinopyridine and 2,3,5,6-tetrafluorobenzoic acid with displacement ellipsoids of non-hydrogen atoms drawn at the 50% level while H atoms are shown as circles of arbitrary size. Adjacent 4-pyrrolidinopyridine and 2,3,5,6-tetrafluorobenzoic acid molecles hydrogen bonded to the water are shown as stick models.

In conclusion we have demonstrated that 2,3,5,6-tetrafluorobenzoic acid serves as multitasking supramolecular tecton and, in combination with 2-aminopyrazines, froms complex hydrogen bonded networks featuring strong charge assisted pyrazinium carboxylate hydrogen bonds along with weaker nonconventional C-H---N hydrogen bonds. Similarly cocrystallization with pyrrolidinopyridine involves both charge assisted and nonconventional hydrogen bonding. Our future studies will focus on the application of these cooperative interactions to the formation of more complex cocrystals.

Acknowledgements We thank the National Science Foundation for financial support of this research (RUI Grant No. CHE1606556) and the Missouri State University Provost Incentive Fund, which funded the purchase of the X-ray diffractometer.

References

1. Armstrong, G.; Buggy, M. Hydrogen-bonded supramolecular polymers: A literature review. *J. Mater. Sci.,* **2005**, *40*, 547–559.
2. Binder, W. *Hydrogen Bonded Polymers, Advances in Polymer Science*, Springer, Berlin Heidelberg, 2007.
3. Desiraju, G. R.; Steiner, T. *The Weak Hydrogen Bond in Structural Chemistry and Biology, IUCR Monographs on Crystallography 9*, Oxford University Press, New York, 1999.
4. Bosch, E.; Bowling, N. P.; Darko, J. The power of non-conventional phenyl C-H•••N hydrogen bonds: supportive crystal-packing force and dominant supramolecular engineering force. Cryst. Growth Des., 2015, 15, 1634-1641.
5. Prasang, C.; McAllister, L. J.; Whitwood, A. C.; Bruce, D. W. 1 : 1 and 2 : 1 co-crystals of alkoxystilbazoles with tetrafluoroiodobenzenes: halogen bonding, a rare Carene–H···N hydrogen bond and unsymmetric iodine···pyridine interactions. *CrystEngComm*, **2013**, *15*, 8947-8958.

6. Orbach, M.; Choudhury, J.; Lahav, M.; Zenkina, O. V.; Diskin-Posner, Y.; Leitus, G.; Iron, M.A.; van der Boom, M. E. Palladium-Catalyzed Cross-Coupling Reactions with Fluorinated Substrates: Mechanistic Insights into the Undesired Hydrodehalogenation of Aryl Halides. *Organometallics*, **2012**, *31*, 1271-1274.
7. Cole, M. L.; Junk, P. C. *N*,*N*′-Bis(2,6-diisopropylphenyl)formamidinate complexes of the heavy alkaline earths. *New J. Chem.,* **2005**, *29*, 135-140.
8. Bosch, E.; Bowling, N. P. Supramolecular polymer formation featuring cooperative halogen bonding and nonconventional sp^2-CH---N hydrogen-bonding. *Cryst. Growth Des.,* **2019***, published online.*
9. Bis, J. A.; Zaworotko, M. J. The 2-aminopyridinium-carboxylate supramolecular heterosynthon: A robust motif for generation of multiple-component crystals. *Cryst. Growth Des.,* **2005**, *5,* 1169-1179.
10. Aakeroy, C. B.; Chopade, P. D.; Ganser, C.; Desper, J. Facile synthesis and supramolecular chemistry of hydrogen bond/halogen bond-driven multi-tasking tectons. *Chem. Commun.,* **2011,** *47,* 4688-4690.
11. Bruker, Bruker AXS Inc., Madison, Wisconsin, USA, 2014.
12. Sheldrick, G. M. SHELXT – Integrated space-group and crystal-structure determination. *Acta Cryst*., **2015**, *A71*, 3-8.
13. Sheldrick, G. M. Crystal structure refinement with SHELXL *Acta Cryst.* **2015**, *C71*, 3-8.
14. Barbour, L. J. X-Seed - A software tool for supramolecular crystallography. *J. Supramol. Chem*., **2001**, 189-191.
15. Spek, A. L. PLATON SQUEEZE: a tool for the calculation of the disordered solvent contribution to the calculated structure factors. *Acta Cryst.* 2015, *C71*, 9-18.

16. Etter, M. C.; MacDonald, J. C.; Bernstein, J. Graph-Set Analysis of Hydrogen-Bond Patterns in Organic Crystals. *Acta Cryst.* 1990, *B46*, 256-262.

17. C. R. Groom; I. J. Bruno; M. P. Lightfoot; S. C. Ward. The Cambridge Structural Database. *Acta Cryst*. 2016, *B72*, 171-179.

18. I. J. Bruno; J. C. Cole; P. R. Edgington; M. Kessler; C. F. Macrae; P. McCabe; J. Pearson; R. Taylor. New software for searching the Cambridge Structural Database and visualizing crystal structures. *Acta Cryst.,* 2002, *B58*, 389-397.

19. Aakeroy. C. B.; Chopade, P. D.; Ganser, C.; Rajbanshi, A.; Desper, J. Exploring structural landscape of 2-aminopyrazines *via* co-crystallations. *CrystEngComm*, 2012, *14*, 5845-5853.

Table 1. Crystallographic parameters for **(1)** – **(5)**.

Compound	**(1)**	**(2)**	**(3)**	**(4)**	**(5)**
formula	$C_4H_6N_3$•$C_7HF_4O_2$	$C_5H_8N_3$•$C_7HF_4O_2$	$C_4H_6N_3$•$C_7HF_4O_2$	$C_9H_{13}N_2$•$C_7HF_4O_2$•$C_9H_{12}N_2$	2($C_9H_{13}N_2$•$C_7HF_4O_2$)•H_2O
formula mass	289.20	303.22	303.22	490.50	702.60
crystal system	triclinic	monoclinic	monoclinic	monoclinic	triclinic
space group	P-1	P21	P21/n	P21/n	P-1
temperature, K	100	100	100	100	100
a, Å	3.6175(3)	9.6167(7)	3.7684(19)	7.6725(6)	11.3264(6)
b, Å	12.6461(10)	5.1975(4)	13.492(9)	32.427(3)	11.6960(6)
c, Å	12.8223(10)	12.1104(9)	24.238(12)	9.6898(10)	12.9264(7)
α,˚	88.6130(10)	90	90	90	82.2450(10)
β,˚	84.3000(10)	103.3480(10)	93.084(7)	109.0020(10)	73.4910(10)
γ,˚	87.3060(10)	90	90	90	69.2050(10)
V, $Å^3$	582.74(8)	588.96(8)	1230.5(12)	2279.4(3)	1533.75(14)
D, gcm^{-3}	1.648	1.710	1.637	1.429	1.521
Z	2	2	4	4	2
radiation type	Mo Kα	Mo Kα	Mo Kα	Mo Kα	Mo Kα
absorption coefficient, μ/mm^{-1}	0.158	0.0161	0.154	0.115	0.136
reflections measured	2594	2621	2700	5038	20175
independent reflections	2340	2520	2131	4186	6801
R_{int}	0.0120	0.0180	0.0757	0.0442	0.0190
R_1 (I > 2σ(I))	0.0342	0.0298	0.0601	0.0391	0.0427
R_1 (all data)	0.0376	0.0309	0.0772	0.0493	0.0515
wR(F^2) (I > 2σ(I))	0.0893	0.0776	0.1504	0.0932	0.1137
wR(F^2) (all data)	0.0920	0.0788	0.1585	0.0695	0.1222
Goodness-of-fit	1.062	1.054	1.144	1.028	1.050
CCDC	1955975	1955977	1955976	1955978	1955979

Table 2. Hydrogen bond distances (Å) and angles (º) for aminopyrazine-tetrafluorobenzoate cocrystals **(1)-(3)**.

	Pyrazinium-carboxylate (x)[a], N-H---O				Amine-carboxylate (y), N-H---O				Amine-carboxylate (z), N-H---O			
	N-H	H----O	N---O	N-H---O	N-H	H----O	N---O	N-H---O	N-H	H----O	N---O	N-H---O
(1)	0.883(13)	1.766(13)	2.6467(13)	175.3(16)	0.881(12)	1.930(13)	2.8093(14)	176.2(16)	0.858(12)	2.058(14)	2.8280(14)	148.9(14)
(2)	0.887(17)	1.735(18)	2.620(3)	176(3)	0.855(18)	1.969(19)	2.822(3)	175(3)	0.848(18)	2.04(2)	2.774(3)	145(3)
(3)	0.90(2)	1.73(2)	2.633(2)	177(3)	0.91(2)	1.88(2)	2.788(2)	179(2)	0.87(2)	2.08(2)	2.903(2)	157(2)

[a] (x), (y) and (z) are shown in Figure 8.

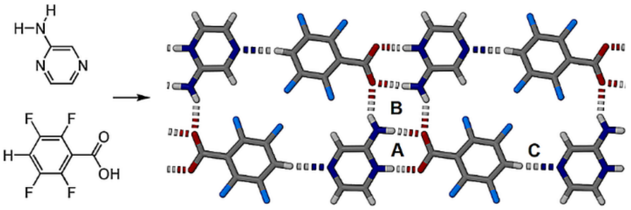
Table 3. Non-conventional C-H---N hydrogen bond distances and angles for cocrystals **(1)-(4)**

Interaction/Cocrystal	**(1)**	**(2)**	**(3)**	**(4)**
C-H	0.936(13)	0.953(18)	0.95(2)	0.952(18)
H---N	2.439(14)	2.47(2)	2.80(2)	2.473
C---N	3.3493(16)	3.369(4)	3.745(3)	3.395(2)
C-H---N	164.1(14)	158(3)	173(2)	163.1(14)

For Table of Contents Entry only

Cooperative Strong Charge Assisted N-H---O Hydrogen Bonding and Weaker Nonconventional C-H---N Hydrogen Bonding in the Formation of Extended Hydrogen Bonded Networks

Eric Bosch and Nathan P. Bowling



Cocrystallization of 2,3,5,6-tetrafluorobenzoic acid and 2-aminopyrazines results in the formation of supramolecular networks that feature cooperative strong, charge assisted, N-H---O hydrogen bonding and weaker