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Supramolecular synthons in the co-crystal structures of 2-aminopyrimidine with diols and carboxylic acids

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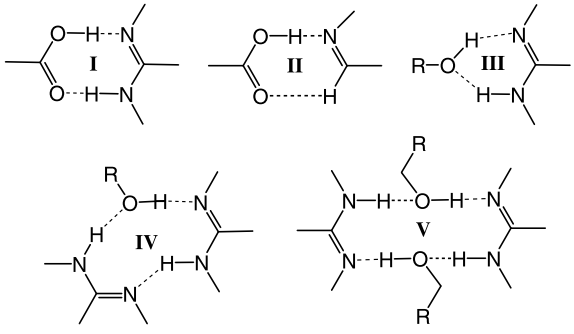
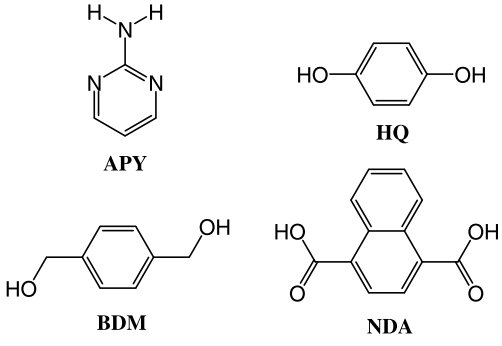
Abstract—The co-crystal structures of 2-aminopyrimidine (**APY**) with diols have been analysed and poly-component hydrogen bond arrangements have been found. In addition, a novel supramolecular synthon has been identified and rationalised in the co-crystal structure of **APY** and 1,4-naphthalenedicarboxylic acid (**NDA**).

The role of hydrogen bonding in crystal engineering and the creation of desired supramolecular structures is well established.[1–4] So-called strong hydrogen bonds, such as O–H···O, N–H···O and O–H···N interactions,[5] play a particularly important structure-directing role. Furthermore, those supramolecular arrangements that possess proportionally more strong hydrogen bonds are likely to be favoured amongst possible alternative arrangements. When designing supramolecular tapes involving carboxylic acids and *N*-heterocycles, therefore, synthon **I** is likely to be preferred to synthon **II**—synthon **I** creating two strong hydrogen bonds whereas synthon **II** is composed of one weak (C–H···O) and one strong hydrogen bond.

In the Cambridge Structural Database (CSD),[6] 22 structures have been reported to date for co-crystals involving 2-aminopyrimidine (**APY**). Of these, 21 involve **APY** co-crystallised with molecules possessing at least one carboxylic acid group and in each structure, synthon **I** is observed.[7] Thus, from the existing crystallographic data, it is possible to predict with reasonable confidence at least the local supramolecular arrangement in carboxylic acid/**APY** co-crystals, i.e. interaction via synthon **I**. Despite the abundance of carboxylic acid/**APY** co-crystals within the CSD, there is little information concerning the types of synthons or supramolecular structures that **APY** will form with other types of functional groups. Diols, for example, are of interest from the viewpoint of crystal engineering because they can be considered as being derived from carboxylic acids with the carbonyl group (C=O) omitted. The carbonyl group is clearly essential in the formation of synthon **I**. In the absence of appropriate crystal structures, a possible new synthon (synthon **III**), which retains the original O–H···N interaction in synthon **I** and creates a new N–H···O interaction, might be predicted as the likely hydrogen bond arrangement in diol/**APY** co-crystals (Schemes 1 and 2).



Scheme 1.



Scheme 2.

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To investigate this hypothesis, two representative diols, hydroquinone (**HQ**) and 1,4-benzenedimethanol (**BDM**),[8] were co-crystallised with **APY**. Two co-crystals in the molar ratio 1:2 (**HQ·2APY** and **BDM·2APY**)[9] were obtained by slow evaporation at room temperature from a 1:1 diol/**APY** solution in ethanol.

It transpires that synthon **III** is found in neither of the two diol/**APY** co-crystals, and instead larger cyclic hydrogen-bonded motifs are formed. In the structure of **HQ·2APY** (Fig. 1) molecules assemble in an $R_3^3(10)$ trimer arrangement (synthon **IV**) involving N–H···N, N–H···O and O–H···N hydrogen bonds [N···N, H···N, N–H···N ($-x$, $y-0.5$, $-z+0.5$): 3.06, 2.18 Å, 144°; N···O, H···O, N–H···O ($-x$, $y+0.5$, $-z+0.5$): 3.00, 2.13 Å, 144°; O···N, H···N, O–H···N: 2.76, 1.78 Å, 174°].[10,11] This supramolecular hydrogen-bonded ring adopts an 'envelope' conformation similar to that for cyclopentane, and results in a noticeable non-linear arrangement for the N donor hydrogen bond. Infinite supramolecular sheets are formed exclusively using synthon **IV**.

In the structure of **BDM·2APY** (Fig. 2), an $R_4^4(12)$ hydrogen-bonded cyclic synthon exists (synthon **V**) involving two **APY** molecules and two **BDM** molecules. An inversion centre exists within the ring and a *boat-like* conformation is adopted, in which a pair of O–H···N and N–H···O hydrogen bonds exist [N···O, H···O, N–H···O: 2.91, 2.03 Å, 143°; O···N, H···N, O–H···N ($-x+1$, $-y+2$, $-z+1$): 2.83, 1.86 Å, 173°]. Again supramolecular sheets are formed, in which molecules are linked by synthon **V** as well as **APY** $R_2^2(8)$ dimers with C_i symmetry [N···N, H···N, N–H···N ($-x$, $-y+2$, $-z$): 3.03, 2.04 Å, 168°].

The absence of synthon **III** in these two diol/**APY** structures may be rationalised in part by the poor directionality of the N–H···O hydrogen bond (theoretically ca. 130°) that would exist within such a synthon—especially when considered in competition with more geometrically favourable synthons such as **IV** and **V**. Similarly, it is noteworthy that in the presence of carboxyl groups (C=O), synthon **I** is more preferable than synthon **IV** and **V** in the molecular assemblies of carboxylic acid/**APY** co-crystals.

As part of a more general study, we have also been interested in co-crystals formed with 1,4-naphthalenedicarboxylic acid (**NDA**).[12] On the basis of existing crystallographic data, we would predict that synthon **I** would be the *only* direct hydrogen bond arrangement between the carboxylic acid group and **APY** in **NDA·APY** co-crystals. Interestingly, when co-crystals of **APY** and **NDA**[9] are obtained from slow evaporation at room temperature from a 1:1 (acid:base) molar ratio in *N*,*N*-dimethylformamide, synthon **III** is observed [N···O, H···O, N–H···O: 3.17, 2.42 Å, 130°; O···N, H···N, O–H···N ($-x-1$, $-y+1$, $-z+3$): 2.65, 1.67 Å, 159°]. As shown in Fig. 3, supramolecular sheets are

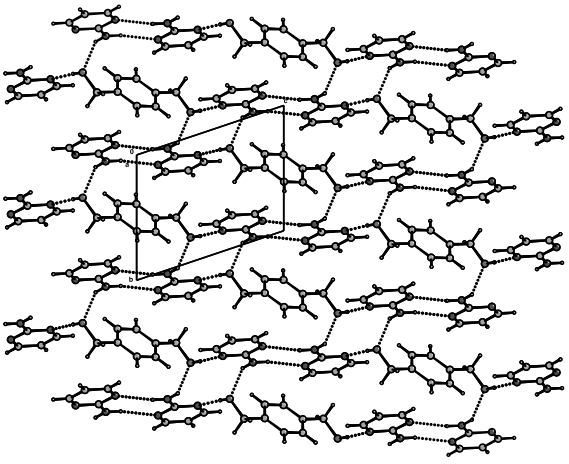

Figure 2. The supramolecular sheet in the co-crystal structure of **BDM·2APY** involving synthon **V**.

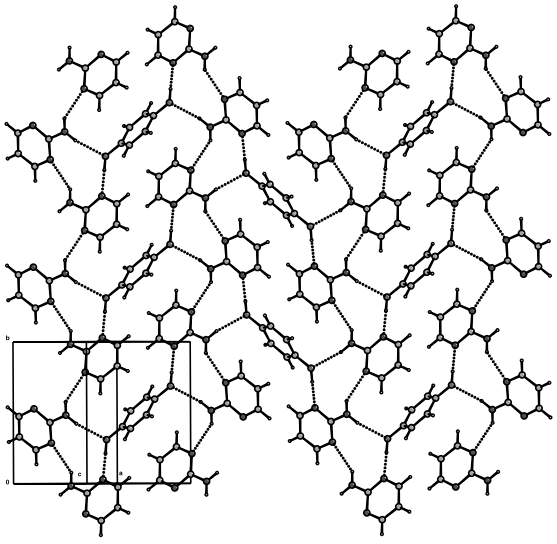

Figure 1. The supramolecular sheet in the co-crystal structure of **HQ·2APY** involving synthon **IV**.

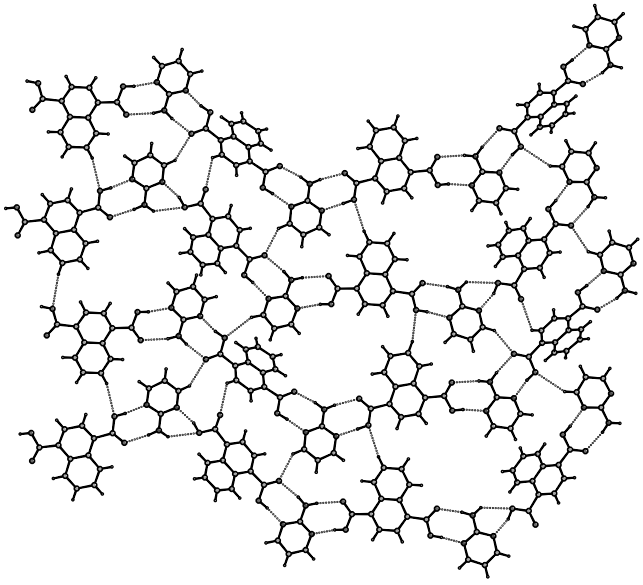

Figure 3. The supramolecular sheet in the co-crystal structure of **NDA·APY** involving synthon **I** and synthon **III**.

formed by the alternate packing of two distinct tapes, one of them formed entirely by synthon **I** while the other tape involves both synthon **I** and **III**. Tapes interact via C–H···O interactions to form supramolecular sheets.

The structure of the terephthalic acid (**TA**)/**APY** co-crystal reported in the CSD allows us to rationalise the existence of synthon **III** in **NDA·APY**. In **TA·APY**,[13] supramolecular tapes are formed via synthon **I**. In addition, tapes assemble via inter-tape C–H···O interactions to create supramolecular sheets (Fig. 4). In **NDA·APY**, however, supramolecular tapes formed *only* by synthon **I** cannot, unlike **TA**, pack efficiently because of the asymmetry created by the naphthalene ring on **NDA**. Synthon **III** is then utilised as an alternative choice for close packing. Additionally, the existence of synthon **III** may result from the presence of the carboxyl group, which may prevent the formation of other geometrically more favourable synthons such as synthons **IV** and **V**. Clearly therefore, under appropriate conditions synthon **III** becomes viable.

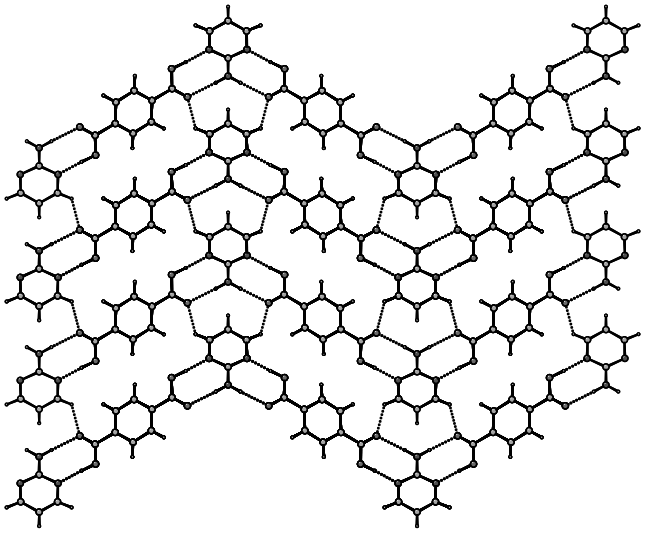

Figure 4. Projection of the supramolecular sheet in the co-crystal structure of **TA·APY** involving synthon **I**.

Acknowledgements

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6. CCDC, The Cambridge Structural Database, ConQuest 1.3, Cambridge, UK, 2001.
7. Among these, five contain synthon **I** but with proton transfer between the carboxylic acid group and the aromatic N atom on the pyrimidine ring.
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9. X-Ray diffraction data (Mo-K_α $\lambda=0.7107$ Å) were collected at 180(2) K using a Nonius Kappa CCD diffractometer equipped with an Oxford Cryosystems cryostream. Data reduction and cell refinement were performed with the programs DENZO (University of Texas, Southwestern Medical Center at Dallas, HKL Denzo and Scalepack, USA, 1997) and COLLECT (Nonius, B. V. Delft, The Netherlands, 1998) and multi-scan absorption corrections were applied with the program *SORTAV* (Blessing, R. H. *Acta Crystallogr.* **1995**, *A51*, 33–38). Structures were solved by direct methods using SHELXS-97 (University of Göttingen, Germany, 1997) and refined on F^2 against all data using SHELXL-97 (University of Göttingen, Germany, 1997). All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms bonded to C or N atoms were placed geometrically and were allowed to ride during subsequent refinement with an isotropic displacement parameter fixed at 1.2 times U_{eq} for the atoms to which they were attached. Hydrogen atoms bonded to O were located in difference Fourier maps and refined isotropically without restraint.
Crystal data for **HQ·APY**: $C_7H_8N_3O$, $M=150.16$, colourless block, monoclinic, space group $P2_1/c$, $a=7.3831(5)$, $b=8.8495(6)$, $c=10.8365(4)$ Å, $\beta=93.621(4)°$, $V=706.61(7)$ Å^3, $Z=4$, $D_c=1.412$ Mg/m^3, $\mu=0.100$ mm^{-1}, $F(000)=316$, crystal size $0.39\times0.23\times0.23$ mm^3, 4984 reflections collected, 1576 independent reflections ($R_{int}=0.0387$), $R_1=0.0397$, $wR_2=0.0984$ for $I>2\sigma(I)$, $R_1=0.0485$, $wR_2=0.1046$ for all data, extinction coefficient 0.108(10).
Crystal data for **BDM·APY**: $C_8H_{10}N_3O$, $M=164.19$, colourless block, triclinic, space group P-1, $a=6.5880(5)$, $b=7.4197(6)$, $c=9.3465(6)$ Å, $\alpha=103.588(4)$, $\beta=107.958(4)$, $\gamma=102.109(3)°$, $V=402.29(5)$ Å^3, $Z=2$, $D_c=1.355$ Mg/m^3, $\mu=0.094$ mm^{-1}, $F(000)=174$, crystal size $0.35\times0.23\times0.09$ mm^3, 3981 reflections collected, 1822 independent reflections ($R_{int}=0.0376$), $R_1=0.0429$, $wR_2=0.1075$ for $I>2\sigma(I)$, $R_1=0.0563$, $wR_2=0.1160$ for all data.
Crystal data for **NDA·APY**: $C_{16}H_{13}N_3O_4$, $M=311.29$, yellow block, monoclinic, space group $P2_1/n$, $a=11.7912(3)$, $b=17.7583(6)$, $c=27.8061(8)$ Å, $\beta=98.430(2)°$, $V=5759.5(3)$ Å^3, $Z=16$, $D_c=1.436$ Mg/m^3, $\mu=0.106$ mm^{-1}, $F(000)=2592$, crystal size $0.23\times0.18\times0.18$ mm^3, 25986 reflections collected, 9846 independent reflections ($R_{int}=0.0607$), $R_1=0.0509$, $wR_2=0.1167$ for $I>2\sigma(I)$, $R_1=0.1023$, $wR_2=0.1389$ for all data.

Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 176101–176103. Copies of these data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

10. Bond distances and angles to H atoms were normalised to standard neutron-derived distances along the bond vectors derived from the X-ray results.
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