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LETTERS

Design and Synthesis of Host-Guest Complexes through Non-Covalent Bonds

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Abstract: 3,5-Dinitro-4-methylbenzoic acid functions as a host accommodating guest molecules in cavities created due to the coupling of six neighbouring molecules through hydrogen bonding. 2,6-Dimethylnaphthalene is encapsulated within the cavity unlike naphthalene. It is thought that the latter is not able to effectively fill the cavity.

Both the design of materials with novel and tailor-made properties as well as the development of methods for purifying mixtures are topics which make use of host-guest chemistry.[1] Examples have appeared in the recent literature illustrating various types of host-guest complexes.[1-3] In all cases, the critical factor in the successful preparation of a complex is the identification of an appropriate host. One approach to the design of suitable host molecules is through conventional organic synthetic routes and is illustrated by the study of crown-ethers.[4] An alternative is the use of specific intermolecular interactions, such as hydrogen bonds, to construct a non-covalent network as part of the recognition process.[5]

Several reported crystal structures, such as trimesic acid, **1** possess large two-dimensional voids.[6,7] However, these voids are not apparent or are reduced in the size, in the overall three dimensional arrangement as a result of catenation or interweaving of adjacent layers. Nevertheless, if the two-dimensional layers remain intact such compounds could act as hosts for guest molecules of dimension equivalent to the voids present in the layers. In other words, co-crystallisation of a host in the presence of guest molecules may perturb the catenation of layers in the host. Indeed a recent study by Zimmerman *et al.* is an example of such an effect.[8] Nevertheless, the voids that are seen in the acid **1**, are unusually large and it will be difficult to incorporate single molecules of sufficient size. Our interest, therefore, is in the identification of novel host(s) with reduced cavities for smaller guests. In this regard, systematic modification of acid **1** by replacing -COOH groups with -NO_2 groups (the NO_2 group is known for its ability to form various types of hydrogen bonds[9]) has resulted in the

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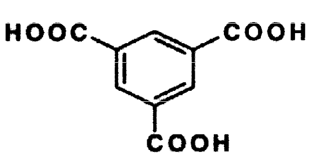
identification of 3,5-dinitro-4-methylbenzoic acid, **2**, as a possible host. The results described here illustrate co-crystal formation of **2** with 2,6 dimethylnaphthlene.



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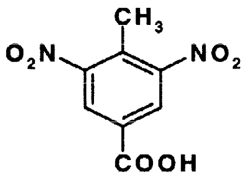

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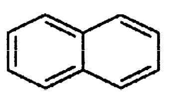

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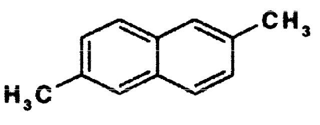

4

Crystallographic information for **2**[10] was available from Cambridge Structural Database.[6] We re-determined the structure, however, to be confident of the H-bond geometry as the R-factor of the reported structure was high at 14%. Acid, **2**, forms a layered structure[11] with elliptical voids of 7 x 13Å dimension as shown in Figure 1.

These voids are filled by groups of atoms from the adjacent layers. It is known from Figure 1 that the voids are formed as a result of coupling of each of six molecules of acid **2** through O-H...O hydrogen bonds (H...O, 1.83Å) and C-H...O (H...O 2.66, 2.78Å). These structural features encouraged us to attempt to co-crystallise **2** with molecules such as naphthalene, **3** and 2,6-dimethylnaphthalene, **4**.[12]

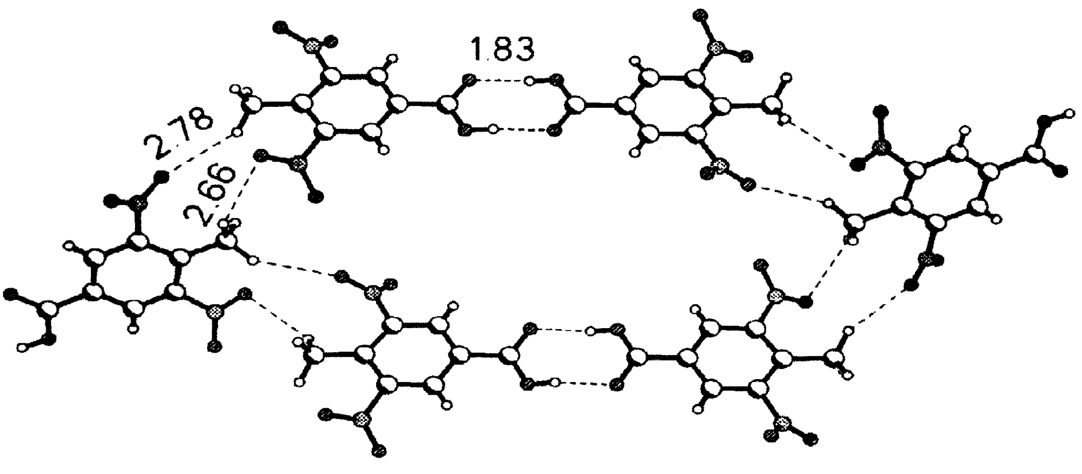

Figure 1: A two-dimensional arrangement of molecules of 3,5-dinitro-4-methylbenzoic acid, **2**. Notice the mutual coupling of six molecules through O-H...O and C-H...O hydrogen bonds. Unique hydrogen bond distances, H...O, are quoted.

Acid **2** did not yield co-crystals with **3** but single crystals were readily obtained with **4** from a methanol solution. Crystal structure determination[13] reveals that acid **2** and **4** co-crystallise in a 2:1 ratio. The packing analysis of the co-crystal indicates that acid **2** retains a motif, with a little topological distortion,[14] similar to that in pure **2**, forming again two-dimensional sheets as shown in Figure 2.

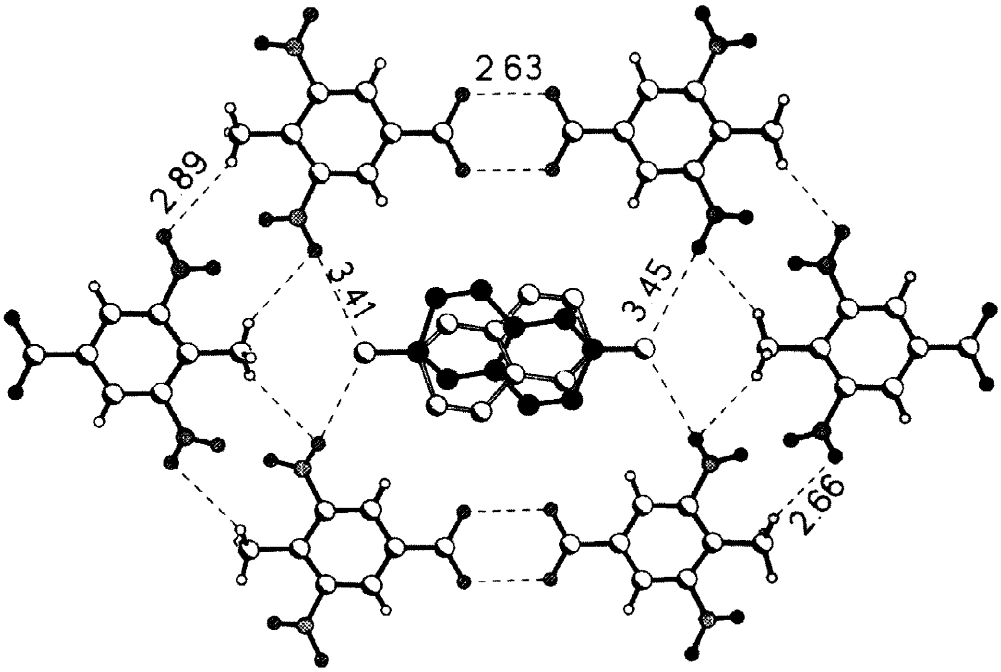

Figure 2: Arrangement of molecules of 3,5-dinitro-4-methylbenzoic acid, **2** and 2,6-dimethyl-naphthalene, **4** in a host-guest pattern. The dashed lines represent O...O distance between carboxyl groups, H...O distances between nitro and methyl groups and C...O distances between host and guest.

Further, it is evident from Figure 2 that molecules of **4** are clearly encapsulated in the voids formed by each of six molecules of acid, **2**. In particular, the host **2** and guest molecules interact through C-H...O hydrogen bonds, with C...O distances in the range of 3.41 - 3.45Å, formed between methyl and NO_2 groups. It is, furthermore, interesting to note that with **4** the co-crystal is disordered. The two different orientations have been represented in Figure 2 in open and solid patterns. The disordered nature of **4** in the co-crystal results from the need for effective filling of void space. This observation explains why naphthalene, being smaller than **4**, is not able to form co-crystals and be incorporated in the cavities of the acid **2**.

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References and Notes:

1) (a) Lehn, J. M. in Supramolecular Chemistry: Concepts and Perspectives, VCH Verlag, Weinheim, 1995. (b) Vogtle, F. Supramolecular Chemistry, Wiley, Chichester, 1971. (c) Inclusion Compounds, Vol. 2 and 3, Eds. Atwood, J. L., Davies, J. E. and MacNicol, D. D. Academic Press, London, 1984. (d) Desiraju, G. R. in Crystal Engineering: The Design of Organic Solids, Elsevier, New York, 1989.

2) (a) Pedireddi, V. R.; Chatterjee, S.; Ranganathan, A.; Rao, C. N. R. J. Am. Chem. Soc., 1997, **119**, 10867.

3) Hollingsworth, M. D.; Harris, K. D. M.; Jones, W.; Thomas, J. J. Inclusion Phenom., 1987, **5**, 273.

4) Lehn, J. -M. Science, 1986, **225**, 849. b) Cram, D. J. Science, 1983, **219**, 1

5) (a) Whitesides, G. M.; Simanek, E. E.; Mathias, J. P.; Seto, C. T.; Chin, D. N.; Mammen, M.; Gordon, D.M. Acc. Chem. Res., 1995, **28**, 37. (b) Geib, S. J.; vicent, C.; Fan, E.; Hamilton, A. D. Angew. Chem. Int. Ed. Engl. 1993, **32**, 119.

6) Allen, F. H.; Kennard, O. Chemical Design Automation News 1993, **8(1)**, 31.

7) a) Duchamp, D. J.; Marsh, R. E. Acta Cryst. 1969, **B25**, 5. b) Herbstein, F. H.; Kapon, M.; Reisner, G. M. Acta Cryst., 1985, **B41**, 348.

8) Kolotuchin, S. V.; Fenlon, E. E.; Wilson, S. R.; Loweth, C. J.; Zimmerman, S. C. Angew. Chem. Int. Ed. Engl. 1995, **34**, 2654.

9) (a) Pedireddi, V. R.; Jones, W.; Chorlton, A. P.; Docherty, R. Chem. Commun., 1996, 987. (b) Pedireddi, V. R.; Jones, W.; Chorlton, A. P.; Docherty, R. Chem. Commun. 1996, 997.

10) Grant, D. F.; Richards, J. P. G. Acta Cryst. 1969, **B25**, 564.

11) Crystal Data for acid, **2**: $C_8H_6N_2O_6$, M=226.15, monoclinic, space group $P2_1/c$, a=8.896(2), b=8.893(2), c=12.255(2)Å, β=110.82(3)°, V=906.2(3)$Å^3$, Z=4, ρ_{calcd}=1.658, $\mu(MoK_\alpha)$=0.146mm^{-1}, F(000)=464, λ=0.71073, Enraf-Nonius CAD-4, The structure was solved by direct methods (SHELXTL-PLUS) and refined by full-matrix least squares on F^2 (SHELX-93; G. M. Sheldrick, Gottengen, 1993) to R_1=0.043 and wR_2=0.094. Residual density, min/max -0.161/0.193e.$Å^{-3}$.

12) The choice of **3** and **4** lies with the fact that the higher analogue, anthracene, perturbs the host structure while forming a complex with **2**.[9a]

13) Crystal Data for complex of **2** and **4**: $2(C_8H_6N_2O_6)$: $(C_{12}H_{12})$, M=608.51, monoclinic, space group $P2_1/m$, a=10.822(2), b=12.615(3), c=11.290(2)Å, β=116.02(3)°, V=1385.1(5)$Å^3$, Z=2, ρ_{calcd}=1.459, $\mu(MoK_\alpha)$=0.116 mm^{-1}, F(000)=636, λ=0.71073, Enraf-Nonius CAD-4, R_1=0.061 and wR_2=0.194, SHELXTL- PLUS. Hydrogen atoms corresponding to **4** and carboxylic hydrogen atom of **2** were not taken into account. Residual density, min/max -0.261/0.363e.$Å^{-3}$

14) The distortion of six-molecules ring noted in the crystal structure of co-crystals of **2**:**4** from that of observed in the crystal structure of acid **2** could be accounted for the efficient close-packing of two-dimensional sheets through π-π interaction in the co-crystals.