LETTER

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Polymorphism of an *o*-anisaldehyde: a novel example of channel-type organization sustained by weak C–H···O and C–H···N hydrogen bonds†

Jarugu Narasimha Moorthy,*[a] Ramalingam Natarajan,[a] Prasenjit Mal[a] and Paloth Venugopalan*[b]

[a] *Department of Chemistry, Indian Institute of Technology, Kanpur, 208 016 India. E-mail: moorthy@iitk.ac.in; Fax: +91 512 2597436; Tel: +91 512 2597438*
[b] *Department of Chemistry, Panjab University, Chandigarh, 160 014 India. E-mail: venu@pu.ac.in*

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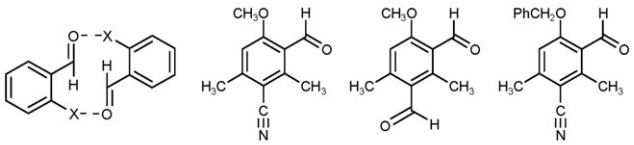
The aldehyde 1 exhibits dimorphic behaviour; one of the modifications results from a novel helical self-assembly of the aldehyde into a channel-type organization sustained entirely by C–H···O and C–H···N hydrogen bonds.

Molecular self-assembly based on strong and highly directional noncovalent metal coordination[1] and hydrogen bonds[2] to construct predetermined architectures with well-defined functions is of contemporary interest. Although strong hydrogen bonds are reliable in controlling molecular packing,[3] it is becoming increasingly evident that the weak, but strongly anisotropic intermolecular interactions such as C–H···O, C–H···N, *etc*., can be decisive in molecular assembly.[4] Indeed, it has been found that the crystal packing based on supramolecular synthons[5] constituted by strong hydrogen bonds is not necessarily observed in molecules endowed with groups that are capable of interacting *via* strong (*e.g*., O–H···O) as well as weak (*e.g*., C–H···X) intermolecular hydrogen bonds.[6] Thus, the understanding of how the latter contribute to the overall crystal packing is important in supramolecular chemistry, and this also concerns one of the challenges today.[7]

Formyl compounds, namely aldehydes, represent an important class of organic molecules with widespread utility in fine chemicals and fragrances. Incidentally, the noncovalent supramolecular interactions associated with the formyl group have been explored only little, if at all.[8] In the course of our studies on the solid-state photochemistry of *o*-tolualdehydes,[9] we recently uncovered a unique supramolecular synthon I, which controls the crystal packing of *o*-halobenzaldehydes.[10] The anticipation that *o*-methoxybenzaldehydes would similarly exploit weak C–H···O hydrogen bonds, by virtue of the presence of hydrogen bond acceptor oxygens and donor formyl and methyl hydrogens, in their crystal packing prompted us to undertake the structural studies of some crystalline *o*-anisaldehydes. In this endeavor, we discovered that the cyano derivative **1** exhibits polymorphism in that it crystallizes in two distinct modifications. As the polymorphs exhibit distinct differences in their properties, the phenomenon of polymorphism has elicited current interest.[11] In particular, the properties of drugs, dyes and explosives are crucially dependent on a particular type of modification. Thus, the understanding of factors that are responsible for polymorphism is very important. The substituents and their substitution pattern in aldehyde **1** appear to lend themselves to a modification in which the aldehyde **1** undergoes a hitherto unprecedented self-assembly to generate channels that are sustained entirely by C–H···O and C–H···N hydrogen bonds.

The needle-like crystals of **1** obtained from dichloromethane–pentane mixture corresponded to the orthorhombic crystal system (**1*o***, space group: *Pba*2), as revealed by X-ray analysis. On the other hand, crystallization from CH_2Cl_2 or from other solvents invariably led to clusters of tiny rectangular crystals corresponding to the triclinic crystal system (**1*t***, space group: $P\bar{1}$).[12]



An inspection of the crystal packing diagram of **1*o*** reveals an intriguing molecular packing with the formation of channels down the *c* axis (Fig. 1). The overall molecular organization may be best described as follows: first, the noncovalent linkage of two 2-fold symmetry-related molecules of **1*o*** (a and b, Fig. 2) *via* two C–H···O hydrogen bonds [$d_{C–H···O}$ = 2.766(1) Å; $\theta_{C–H···O}$ = 155.58(1)°] involving the formyl hydrogen and the methoxy oxygen leads to the formation of a dimer.[13] The aldehyde 'b' of the dimer interacts through its phenyl hydrogen with the cyano nitrogen of molecule 'c' *via* a C–H···N hydrogen bond, while the cyano nitrogen of aldehyde 'a' hydrogen bonds in a similar manner with phenyl hydrogen of the aldehyde d; the geometrical parameters for this interaction are: $d_{C–H···N}$ = 2.611(1) Å; $\theta_{C–H···N}$ = 163.17(1)°. The aldehydes c and 'd' further hydrogen bond (C–H···N) to the dimeric aldehydes as shown in Fig. 2. The C_2-symmetry-related molecules of the hydrogen-bonded dimer are found to be inclined with respect to each other by an angle of *ca*. 54.04°. Indeed, it is this inclination of planes of the molecules that appears to facilitate the construction of a helix as shown in Fig. 2. The repeat distance of an aldehyde (c or d) at the turn of the helix is 15.819 Å, and each turn typically consists of six aldehydes. Given that the translational unit cell (*c* axis) dimension is 3.955 Å, each channel in Fig. 1 may be construed as

† Electronic supplementary information (ESI) available: optical micrographs of crystals of **1*o*** and **1*t***; DSC scans of two modifications of **1**; crystal packing diagram of **3**. See http://www.rsc.org/suppdata/nj/b4/b407199a/

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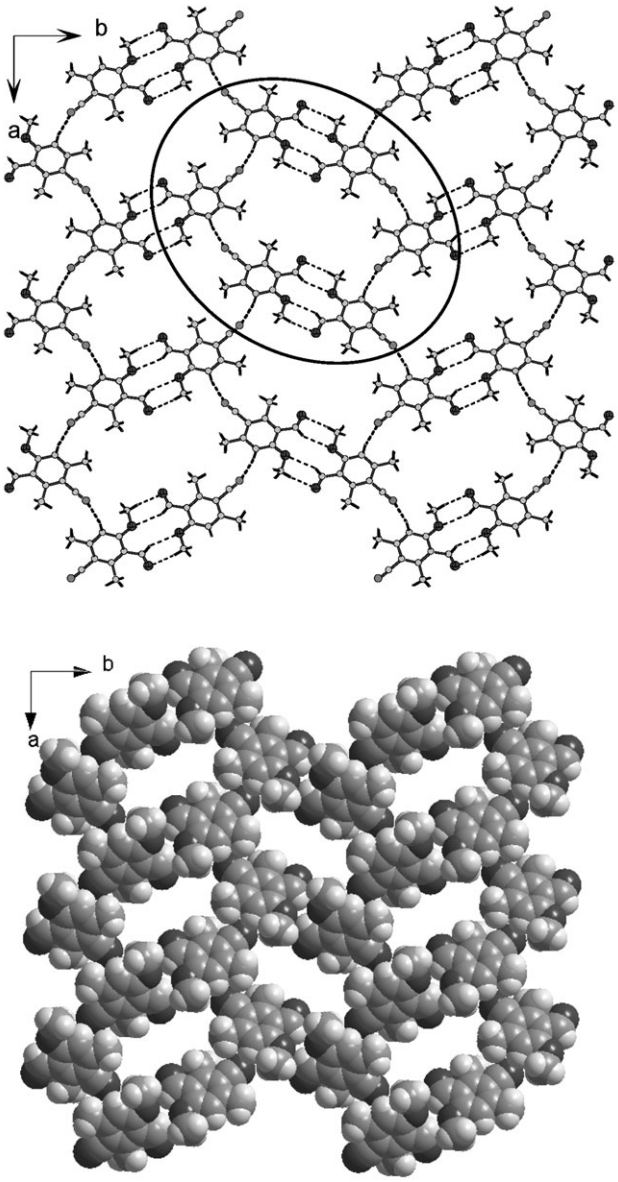

Fig. 1 Top: The crystal packing of **1*o*** viewed down the *c* axis. The disordered solvent molecules have been removed for clarity. The molecular organization responsible for the formation of channels is shown in a circle. Bottom: The space-filling CPK diagram, which reveals the empty channels.

arising from four helices (a tetruplex) running in parallel with an interhelix distance of 3.955 Å. The channels are stabilized by interhelical C–H···O hydrogen bonds; the inclination of molecular planes of the aldehydes 'a' and 'b' leads to C–H···O hydrogen bond formation [($d_{C-H\cdots O}$ = 2.55(1) Å; $\theta_{C-H\cdots O}$ = 166.06(1)°] between a methoxy hydrogen of an aldehyde of one helix and the carbonyl oxygen of another aldehyde of a parallel helix. The entire crystal packing may thus be understood based on further self-assembly of the aldehydes responsible for the formation of channels (Fig. 1) *via* the sites of the molecules that were nonbonded.

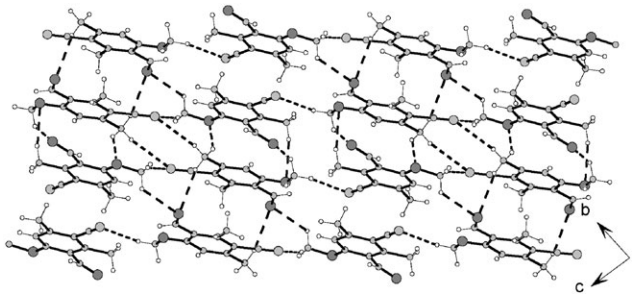

Fig. 3 The crystal packing diagram of the triclinic modification of *o*-anisaldehyde **1*t***. The C–H···O and C–H···N hydrogen bonds responsible for the crystal packing are shown with dashed lines.

The X-ray diffraction analysis of **1*o*** at 100 K revealed the presence of highly disordered solvent molecules in the channels.[14] From the analysis of the difference Fourier electron density map, the possibility of the solvent being dichloromethane was ruled out. The residual electron density was best modelled for *n*-pentane. As the crystallization of the orthorhombic modification **1*o*** occurs only in the presence of *n*-pentane in CH_2Cl_2, the former presumably templates the crystal growth. A perusal of Fig. 2 also shows that the nature of the interior of the channels is highly hydrophobic with the methyl and methoxy methyl groups pointing inside, which justifies the inclusion of a hydrophobic guest such as *n*-pentane.

In contrast to the crystal packing of the orthorhombic modification **1*o***, that of the triclinic one **1*t*** is quite ordinary. In this case, the crystal lattice is stabilized by aromatic stacking interactions and C–H···O/N hydrogen bonds (Fig. 3); the centroid-to-centroid and plane-to-plane perpendicular distances between the aromatic rings are 3.66 and 3.59 Å, respectively.

To determine if the dimeric association of the C_2-symmetry-related aldehydes in **1*o*** is observable in analogous compounds, we synthesized the aldehydes **2** and **3**, and carried out X-ray crystallographic analyses. Fig. 4 shows the crystal packing of the dialdehyde **2** (space group: *C*2). As can be seen, the aldehydes related by 2-fold symmetry associate *via* two hydrogen bonds involving the formyl hydrogens and the methoxy oxygens, while their methoxy methyl hydrogens participate in

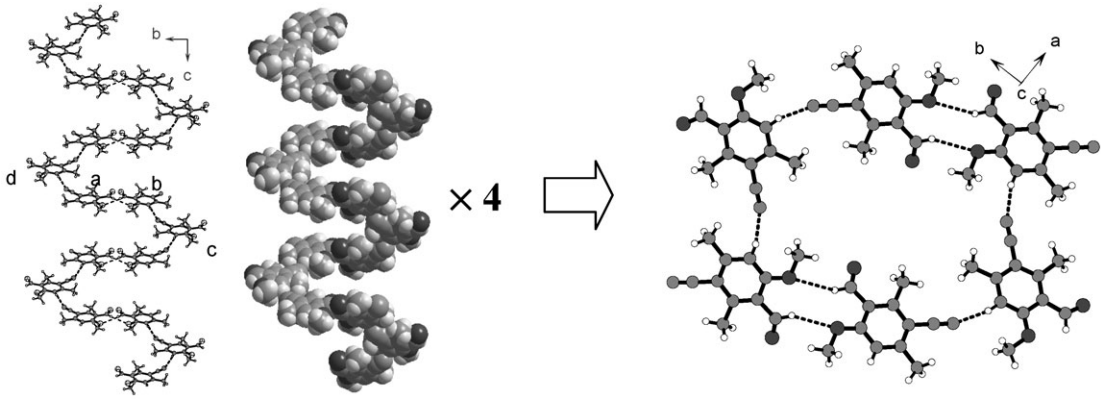

Fig. 2 Propagation of a helix *via* C–H···O and C–H···N hydrogen bonds and the formation of a channel *via* the self-assembly of four such helices. The molecular organization responsible for the formation of channels undergoes further self-assembly to make up the crystal lattice.

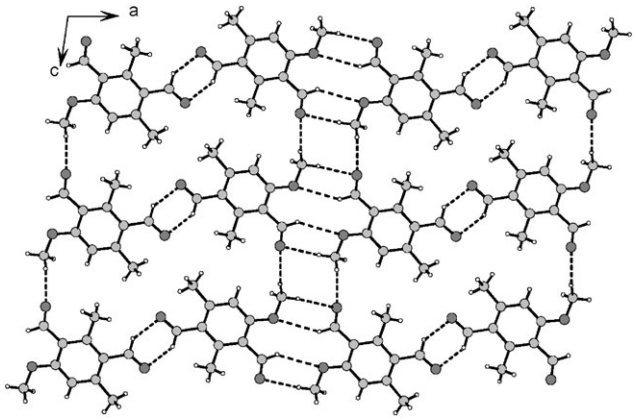

Fig. 4 The crystal packing of the diformyl derivative **2**. Observe the dimeric pattern between the 2-fold symmetry related aldehydes. Note that the *meta*-formyl groups also self-assemble about the 2-fold axis.

hydrogen bonding with carbonyl oxygens of the symmetry-related aldehydes. The angle of inclination of the aromatic planes in this instance is *ca.* 53.2°. However, the crystal packing of the benzyl derivative **3** is found to be devoid of such a dimeric motif (*cf.* Electronic Supplementary Information). It appears that factors such as (i) the ability of the benzylic hydrogens to competitively participate in C–H···O/N hydrogen bonding and (ii) the steric bulk associated with the benzyl groups preclude the dimeric association as in **1*o*** and **2**. Thus, the dimeric association appears to be limited to *o*-anisaldehydes.

In light of the above discussion and the fact that both the phenyl hydrogen and the cyano group interact *via* C–H···N hydrogen bonds,[15] the *o*-anisaldehyde **1** can be represented as a 3-connecting molecular node. The crystal packing observed with the metastable orthorhombic modification **1*o*** is a result of the self-assembly of such a molecular system with unique substituents and substitution pattern. It also emerges from the crystal packing of **1*o*** that the connectivity at one site with inclination of planes induces helicity.[16] The fact that such a crystal packing is not a thermodynamically preferred one and that the aldehyde **1** crystallizes in the alternative triclinic modification by exploiting edge-to-face aromatic stacking interactions in combination with C–H···O/N hydrogen bonds suggests the following: substrates endowed with functional groups that can interact only *via* weaker hydrogen bonds may explore alternative packing modes (*e.g.*, based on aromatic stacking interactions) in addition to the expected pattern of self-assembly. The isolation of the crystals of aldehyde **1** with incorporation of the solvent in the crystal lattice was fortuitous, and one can *a priori* have no idea as to the attributes of an appropriate guest. This indeed is a serious problem associated with polymorphism.[11]

The crystal packing of **1*o*** constitutes a novel example of a channel-type organization sustained entirely by C–H···O/N hydrogen bonds. Given the current interest in helical organizations,[17] the results observed with aldehyde **1** are significant, and further emphasize the importance of weak interactions in the construction of novel structures.

Experimental

X-Ray crystallography

The crystals of **1*o*** were obtained by slow evaporation of the solution of **1** in CH_2Cl_2–*n*-pentane over 3–4 days. A similar procedure using CH_2Cl_2 or CH_2Cl_2–toluene yielded triclinic crystals **1*t***. The crystals of **2** and **3** were obtained by slow evaporation of their solutions in CH_2Cl_2–CH_3OH.

The intensity data for the structures **1*o*** and **1*t*** were collected on a Bruker SMART/CCD diffractometer at 100 K and the data for **2** and **3** were collected at 298 K on a Siemens P4 diffractometer using Mo Kα radiation in all cases. The structure solution in each case was achieved by direct methods and the refinement was performed on F^2 with SHELX-97. All the non-hydrogen atoms were refined anisotropically. The hydrogen atoms were included in the ideal positions with fixed isotropic U values and treated as riding on their respective non-hydrogen atoms.‡

Crystal data for 1*o*. 2-Methoxy-4,6-dimethyl-5-cyanobenzaldehyde (pentane solvate), $C_{15}H_{23}NO_2$, M = 261.3, crystal dimensions: 0.41 × 0.36 × 0.29 mm^3, orthorhombic, *Pba*2 (no. 32), a = 12.373(1), b = 24.512(3), c = 3.955(1) Å, U = 1199.4(2) Å^3, ρ_{calcd} = 1.447 g cm^{-3}, T = 100(2) K, μ = 0.094 mm^{-1}, Z = 4, R(int) = 0.0274, 2049 data (θ_{max} = 25.0°) collected of which 1973 are unique, R_1 = 0.0688, wR_2 = 0.1795 [$I > 2\sigma(I)$], GOF = 1.033.

Crystal data for 1*t*. 2-Methoxy-4,6-dimethyl-5-cyanobenzaldehyde, $C_{11}H_{11}NO_2$, M = 189.2, crystal dimensions: 0.33 × 0.27 × 0.21 mm^3, triclinic, *P*$\bar{1}$ (no. 2), a = 7.837(1), b = 10.163(2), c = 12.272(2) Å, α = 82.82(1)°, β = 81.06(1)°, γ = 82.81(3)°, U = 956.7(3) Å^3, ρ_{calcd} = 1.314 g cm^{-3}, T = 100(2) K, μ = 0.091 mm^{-1}, Z = 4, R(int) = 0.0193, 3318 data (θ_{max} = 25.0°) collected of which 2660 are unique, R_1 = 0.0477, wR_2 = 0.0607 [$I > 2\sigma(I)$], GOF = 1.012.

Crystal data for 2. 2-Methoxy-4,6-dimethyl-5-formylbenzaldehyde, $C_{11}H_{12}O_3$, M = 192.2, crystal dimensions: 0.39 × 0.28 × 0.26 mm^3, monoclinic, *C*2 (no. 5), a = 32.676(5), b = 3.964(1), c = 7.502(1) Å, β = 98.47(2)°, U = 961.1(7) Å^3, ρ_{calcd} = 1.328 g cm^{-3}, T = 293(2) K, μ = 0.096 mm^{-1}, Z = 4, R(int) = 0.0227, 906 data (θ_{max} = 24.0°) collected of which 887 are unique, R_1 = 0.0447, wR_2 = 0.1188 [$I > 2\sigma(I)$], GOF = 1.01.

Crystal data for 3. 2-Benzyloxy-4,6-dimethyl-5-cyanobenzaldehyde, $C_{17}H_{15}NO_2$, M = 265.3, crystal dimensions: 0.32 × 0.30 × 0.21 mm^3, triclinic, *P*$\bar{1}$ (no 2), a = 7.574(1), b = 8.315(1), c = 12.782(2) Å, α = 84.56(1)°, β = 79.32(1)°, γ = 63.27(1)°, U = 706.44 (17) Å^3, ρ_{calcd} = 1.247 g cm^{-3}, T = 293 (2) K, μ = 0.082 mm^{-1}, Z = 2, R(int) = 0.0192, 2402 data (θ_{max} = 24.0°) collected of which 2210 are unique, R_1 = 0.0461, wR_2 = 0.1261 [$I > 2\sigma(I)$], GOF = 1.050.

Acknowledgements

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‡ CCDC reference numbers 225291, 225294, 250042, 250043. See http://www.rsc.org/suppdata/nj/b4/b407199a/ for crystallographic data in .cif or other electronic format.

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