The effect of substitution of the C–F group for the C–H group in crystal packing as well as thermal behaviour

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The packing motif and/or thermal stability of a crystal is controlled by intermolecular C–F···π interactions.

The C–F group is similar to the C–H group in size. However, when the C–F group is substituted for the C–H group, the crystal structure is generally no longer identical.[1] In a few cases, the change in the packing motif has been explained in terms of C–H···F–C interaction,[2] π–π interaction,[3] *etc.* Here we report the first example of an intermolecular C–F··π interaction which controls the packing motif as well as the thermal stability of the crystal, on the basis of comparison of four crystalline complexes which are composed of triphenylmethanol derivatives, *i.e.* triphenylmethanol (**F0**), (4-fluorophenyl)diphenylmethanol (**F1**), bis(4-fluorophenyl)phenylmethanol (**F2**) and tris(4-fluorophenyl)methanol (**F3**), and MeOH.

By slow evaporation from MeOH solution, **F1** and **F2** afforded 1:1 complexes, as **F1**·MeOH‡ and **F2**·MeOH,‡ respectively, their stoichiometric ratios being the same as that of **F0**.[4] Interestingly, an X-ray analysis revealed that both **F1**·MeOH and **F2**·MeOH are isostructural to **F0**·MeOH;[5] one host and one guest molecule exist in an asymmetric unit, and two hosts and two guest molecules comprise a molecular assembly with the aid of a hydrogen bond (Fig. 1). The fact that none of the fluorine atoms take part in hydrogen bonding with the hydroxy groups is consistent with the reports of Dunitz and Taylor.[6] It is noteworthy that the fluorine atom is disordered in **F1**·MeOH. The disordered fluorines are observed only on two phenyl moieties [*i.e.* plane A and B, in Fig. 1(*a*)], occupancy factors of which are evaluated to be 0.69 and 0.31 for F(A) and F(B), respectively. Disorder of the fluorine atoms is also found in **F2**·MeOH, but it is not identical to that in **F1**·MeOH. The fluorine atoms in **F2**·MeOH are observed on all the three phenyl rings; the occupancy factors are 0.95, 0.80, and 0.25 for F(A), F(B), and F(C), respectively [Fig. 1(*b*)].

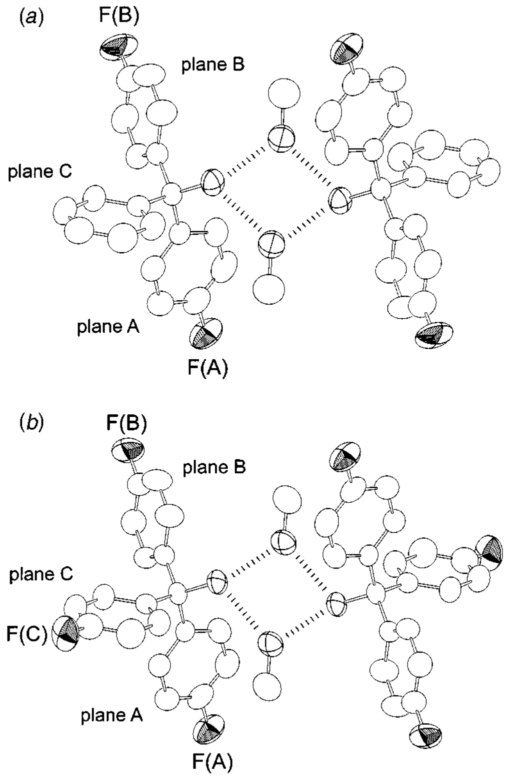

Fig. 1 Perspective views of (*a*) **F1**·MeOH and (*b*) **F2**·MeOH. For clarity, fluorine and oxygen atoms are represented by discriminated ellipsoids, and hydrogen atoms are omitted. Hydrogen bonds are specified by dotted lines.

Despite their isomorphous characteristics, the thermal behaviour of **F0**·MeOH, **F1**·MeOH and **F2**·MeOH upon DSC (differential scanning calorimetry) measurement§ are somewhat different. On heating, the guest molecule in **F0**·MeOH and **F1**·MeOH was lost at very similar temperatures (T_{onset} = 78.5[4] and 76.0 °C, respectively), whereas **F2**·MeOH released the guest at rather lower temperature (T_{onset} = 64.8 °C).

This finding can be explained in terms of C–H··π and C–F··π interactions: Fig. 2 shows that two phenyl rings in **F1**·MeOH, *i.e.* plane C and B, are arranged in an edge-to-face manner. The interplanar angle and centroid-to-centroid distance of the two planes are estimated to be 91.5° and 5.39 Å, respectively. No C–H··π interactions could be observed among the other pairs of phenyl rings. Such a T-shaped arrangement of two benzene rings is known to be energetically favourable.[7] If a fluorine atom is substituted onto plane C in this packing motif, the energetic advantage due to the C–H··π interaction will be lost. This is one of the principal reasons that the disordered fluorine atom in **F1**·MeOH was observed solely on plane A and B. On the other hand, the disordered fluorine atoms, F(A) and F(B), play no role with respect to the thermal stability of the lattice.

In the case of **F2**·MeOH, the disordered fluorine atoms are observed on the plane C as well. It causes the loss of the energetically favorable C–H··π interaction as well as introducing an electrostatic repulsion between the electronegative fluorine atom and the π-electrons. In addition to these, a steric

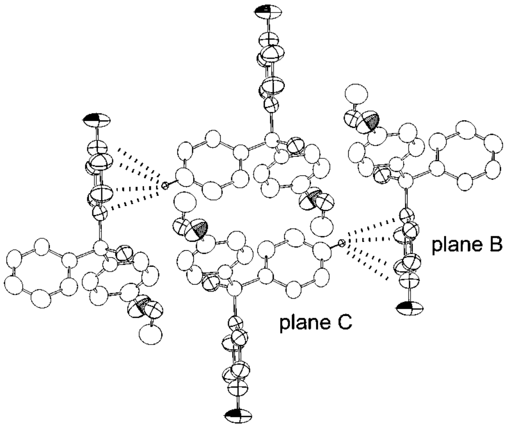

Fig. 2 Projection of the host–guest structure of **F1**·MeOH. Dashed lines represent CH–π interactions.

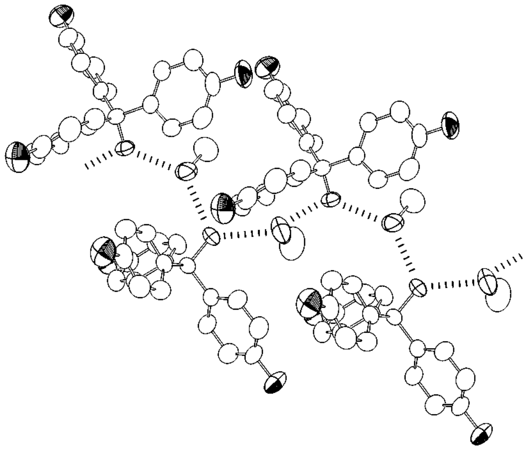

Fig. 3 Perspective view of **F3**·MeOH. For clarity, fluorine and oxygen atoms are represented by discriminated ellipsoids, and hydrogen atoms are omitted. Hydrogen bonds are specified by dotted lines.

repulsion arises, since the distance from the fluorine to the plane B is calculated to be 2.87 Å, which is significantly shorter than the sum of van der Waals radii's of each moiety (F = 1.47, C_{ar} = 1.77 Å).[8] The sum of these factors should lead the instability of the lattice of **F2**·MeOH, so that the guest MeOH is lost more readily than that of **F0**·MeOH and **F1**·MeOH.

Although **F3** also afforded 1:1 complex with MeOH, the crystal structure of **F3**·MeOH‡ is quite different from those of the others. The hydrogen-bonded cyclic network (H–G–H–G) is found in the other complexes, whilst the –H–G–H–G– sequence of an infinite chain of hydrogen bonding is observed in **F3**·MeOH (Fig. 3). Among the four MeOH complexes described here, **F3**·MeOH is thermally most unstable: the guest MeOH was released just at 48.3 °C (onset). The exceptional packing motif of **F3**·MeOH is ascribable to the unfavorable C–F··π interaction again. The C–F··π interaction is not critical in **F2**·MeOH with respect to the packing motif, because only one fourth of the *para* positions of plane C are substituted by fluorine atoms. However, complete occupation would make it too disadvantageous in energy for **F3** to adopt a similar packing motif to the other complexes, so that **F3**·MeOH crystallized in a distinct manner.

These results demonstrate new aspects of a fluorine in crystalline chemistry as well as in medicinal and biological chemistry. Further investigations on the effect of fluorine on crystal structure as well as thermal behaviour are currently underway.

Notes and References

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‡ *Crystal data* for **F1**·MeOH: $C_{20}H_{19}F_1O_2$, M = 310.36, triclinic, $P\bar{1}$ (no.2), a = 9.348(4), b = 11.756(5), c = 8.537(3) Å, α = 98.93(4), β = 114.31(3), γ = 77.66(4)°, V = 832.8(6) Å^3, T = 298 K, Z = 2, μ(Mo-Kα) = 0.86 cm^{-1}, refined using 1438 reflections R = 0.066. For **F2**·MeOH: $C_{20}H_{18}F_2O_2$, M = 328.34, triclinic, $P\bar{1}$ (no.2), a = 9.489(3), b = 11.698(3), c = 8.595(3) Å, α = 99.35(2), β = 113.47(2), γ = 77.68(2)°, V = 851.8(4) Å^3, T = 298 K, Z = 2, μ(Mo-Kα) = 0.96 cm^{-1}, refined using 1427 reflections, R = 0.047. For **F3**·MeOH: $C_{20}H_{17}F_3O_2$, M = 346.32, monoclinic, Cc (no.9), a = 10.402(2), b = 23.251(4), c = 8.170(1) Å, β = 115.79(1)°, V = 1779.1(6) Å^3, T = 288 K, Z = 4, μ(Mo-Kα) = 1.03 cm^{-1}, refined using 1616 reflections, R = 0.045. All the structures were solved by direct methods and refined on teXsan (ref. 9). CCDC 182/948.

§ DSC analysis was performed as follows: crystals were removed from the mother liquor, blotted dry on filter paper and crushed before analysis. Sample weight in each case was 7–10 mg. The temperature range was from ambient temperature to 200 °C at a heating rate of 10 °C min^{-1}.

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