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Inclusion Compounds from a Host Mixture: A Cautionary Tale

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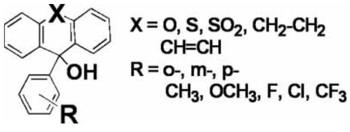
The inclusion properties of a dibenzocycloheptenol host with a variety of volatile guests have been analysed. The packing and intermolecular interactions of the inclusion compounds have been examined. Unexpected structures arising from impurities in the host, termed the 'host mixture', have been elucidated.

INTRODUCTION

We have embarked on a study of the inclusion properties of a series of hydroxyl hosts of general formula described in Scheme 1.

Many of these compounds form good hosts which complex a variety of aliphatic and aromatic guests. They conform to Weber's rules for host design [1] in that they are bulky, rigid and have hydroxyl moieties that act as hydrogen-bond donors, and in some cases have electronegative moieties at X, which act as hydrogen-bond acceptors.

We have studied the inclusion compounds of a number of xylenols (X=O) and have characterized their inclusion compounds with a variety of guests. With the host 9-(3-chlorophenyl)-9H-xanthen-9-ol we elucidated the structures of its clathrates with benzene, toluene, *p*-xylene and pyridine, measured the desolvation kinetics of the *p*-xylene inclusion compound, and analysed the process of guest exchange of this compound with benzene and toluene vapour [2]. The related host 9-(4-methoxyphenyl)-9H-xanthen-9-ol yields a series of isostructural clathrates with benzene and the isomers of xylene and their activation energies of desolvation have been established [3]. The dioxane clathrate of 9-(1-naphthyl)-9H-xanthen-9-ol has been characterized, its thermal stability measured, and its kinetics of desolvation modelled with the Avrami-Erofeev law, yielding an activation energy of desolvation of 111(2) kJ mol^{-1} [4].



SCHEME 1 General formula of our hydroxyl Hosts.

In this work we present the results of the inclusion of properties of the host 5-(1-naphthyl),5H-dibenzo[a,d]cyclohepten-5-ol, A with 1,4-dioxane, dimethylsulfoxide and pyridine, as well as the structures of the related compounds, which were part of the 'host mixture', details of which are discussed later.

RESULTS AND DISCUSSION

Synthesis

The host compound, A, was synthesized via a Grignard reaction as shown in Scheme 2.

However, the reaction was incomplete and some of the starting compound B, 5H-dibenzo[a,d]cyclohepten-5-one, remained as part of the product, which was kept in a sealed vial at room temperature for two years. During this time, compound B dimerized to the photosynthetic product C, 4b,4c, 13b,13c-tetrahydro-tetrabenzo[c,c′,f,f]cyclobuta[1,2-a:3,4-a′]dicycloheptene-9,18-dione. (A + B + C) therefore comprised the 'Host mixture'.

The reaction scheme of the three compounds when the host mixture was dissolved in various liquid guests is shown in Scheme 3.

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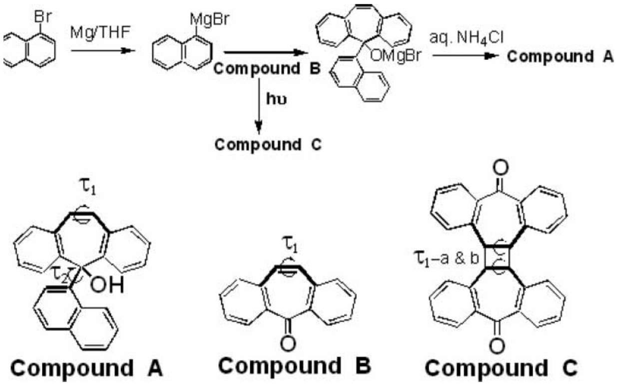


SCHEME 2 Synthetic route leading to compound A.

Structures

Crystal data and refinement parameters are given in Table I.

Host A, Apohost

Pure crystals of the apohost, A, could not be crystallized directly, using a variety of solvents. Therefore we prepared the 1:1 dioxane inclusion compound, which we then isolated and desorbed by heating to 80°C under vacuum for 3 h. We monitored the desorption by mass loss (measured 22.3%, calculated 20.0%) as well as by X-ray powder diffraction. The resulting powder was then recrystallized from ethanol, yielding satisfactory crystals of A. By monitoring the mass yields we established that the 'host mixture' contained 59.5% of A and 40.5% of (B + C) by mass.

The apohost crystallizes in the space group Pccn with $Z = 8$ with all the molecules in general positions. In the final refinement model, all the non-hydrogen atoms were treated anisotropically and the hydrogen atoms were found in difference electron density maps and their positions and isotropic factors were refined independently.

The hydroxyl hydrogens, located in a difference electron density map, are disordered over two positions, and the structure is stabilized by a very weak hydrogen bond, O–H···O(H) with a d O···O = 3.346(2) Å, which lies across a center of inversion at Wyckoff position a. This is shown in Fig. 1.

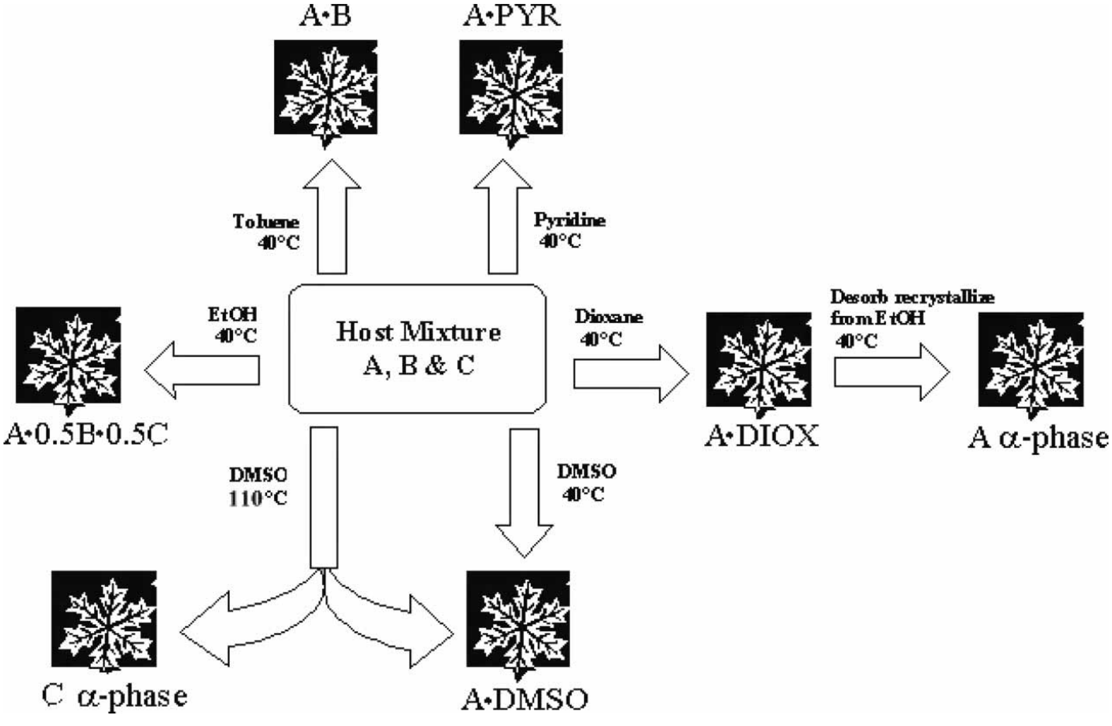
A similar refinement procedure was adopted for the other structure determinations.

A·DIOX Structure

A·DIOX crystallizes in the space group P-1 with $Z = 2$ and both host and guest molecules are in general position. There is a (host) O–H···O (guest) hydrogen bond, d O···O = 2.762(2) Å. The packing of the structure is shown in Fig. 2, in which the host is represented with Van der Waals radii and the dioxane as sticks.

A·PYR Structure

A·PYR also crystallizes in P-1, but with $Z = 4$ and there are two host and two guest molecules in the



SCHEME 3 Details of the crystals obtained from the 'host mixture'.

TABLE I Crystal data and refinement parameters

	A(α)	A·DIOX	A·DMSO	A·PYR	A·B	A·0.5B·0.5C	C(α)
Molecular formula	$C_{25}H_{18}O$	$C_{25}H_{18}O\cdot C_4H_8O_2$	$C_{25}H_{18}O\cdot C_2H_6OS$	$C_{25}H_{18}O\cdot C_5H_5N$	$C_{25}H_{18}O\cdot C_{15}H_{10}O$	$C_{25}H_{18}O\cdot 0.5(C_{15}H_{10}O)\cdot 0.5(C_{30}H_{20}O_2)$	$C_{30}H_{20}O_2$
Molar ratios	–	1:1	1:1	1:1	1:1	1:0.5:0.5	–
Molecular mass	334.39	422.50	412.54	413.49	540.62	643.78	412.46
Temperature, K	173	173	173	173	173	173	173
λ, Å	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073
Crystal system	Orthorhombic	Triclinic	Orthorhombic	Triclinic	Triclinic	Triclinic	Monoclinic
Space group	Pccn	P-1	P2(1)2(1)2(1)	P-1	P-1	P-1	P2(1)/c
a, Å	14.940(3)	8.8664(18)	8.4314(17)	8.3226(17)	8.7963(18)	8.8707(18)	10.357(2)
b, Å	19.311(4)	9.4792(19)	14.684(3)	8.7665(18)	9.3907(19)	9.4432(19)	10.655(2)
c, Å	11.928(2)	14.188(3)	16.887(3)	31.766(6)	17.241(3)	19.206(4)	18.881(4)
α, °	90	103.71(3)	90	84.58(3)	77.46(3)	95.51(3)	90
β, °	90	105.96(3)	90	88.71(3)	89.32(3)	94.00(3)	99.24(3)
γ, °	90	97.92(3)	90	69.48(3)	77.26(3)	101.98(3)	90
V, Å^3	3441.3(11)	1087.2(5)	2090.7(7)	2160.8(9)	1355.0(5)	1559.9(6)	2056.6(7)
Z	8	2	4	4	2	2	4
D_c, mg m^{-3}	1.291	1.291	1.291	1.271	1.325	1.360	1.332
μ mm^{-1}	0.077	0.082	0.176	0.076	0.080	0.083	0.082
F(000)	1408	448	848	872	568	672	864
Approx. crystal size, mm	0.1 × 0.1 × 0.2	0.1 × 0.2 × 0.2	0.1 × 0.15 × 0.15	0.1 × 0.1 × 0.1	0.15 × 0.2 × 0.2	0.1 × 0.15 × 0.2	0.1 × 0.1 × 0.2
θ_{max} for collected data, deg	27.5	27.6	26.3	27.0	27.5	27.1	26.8
Index ranges min/max h,k,l	−18/18; −24/24; −15/15	0/11; −12/12; −18/17	−10/10; −18/18; −20/21	−10/10; −10/11; −40/39	−11/11; −12/11; −22/22	−11/11; −12/12; −24/24	−13/13; −13/13; −23/23
Reflections collected	7265	4959	4212	15583	10723	12483	33531
Independent reflections	3882	4959	4212	8934	6118	6769	4366
R_{int}	0.025	–	–	0.038	0.040	0.015	0.092
Data/parameters refined	3882/303	4959/289	4212/256	8934/753	6118/491	6769/447	4366/369
R (F) [$I > 2\sigma(I)$]	0.0405	0.0432	0.0654	0.0440	0.0443	0.0717	0.0409
No. of reflections with $I > 2\sigma(I)$	2912	3763	3386	5731	3807	5492	3228
WR (all F^2)	0.1126	0.1123	0.1738	0.1370	0.0994	0.2157	0.1039
Largest diff. Peak and hole, e/Å^{-3}	−0.41 and 0.35	−0.39 and 0.40	−0.58 and 0.63	−0.21 and 0.22	−0.23 and 0.20	−0.77 and 0.58	−0.25 and 0.15

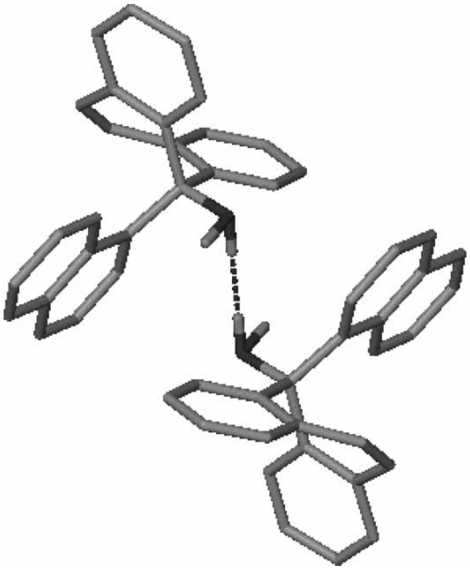


FIGURE 1 Hydrogen-bonded dimer formed by the apohost, A.

asymmetric unit. The structure is stabilized by (host)-O–H···N (Pyr) hydrogen bonds d O···N = 2.882(2) and 2.863(2) Å. The pyridine guests are in channels located parallel to a, as shown in Fig. 3.

The metrics of these hydrogen bonds, as well as those occurring in the other structures, are shown in Table III.

A·DMSO Structure

When the host mixture is dissolved in dimethylsulfoxide under mild conditions (40°C), the ensuing crystals are of the inclusion compound A·DMSO. This compound crystallizes in the space group $P2_12_12_1$, with $Z = 4$. The DMSO guest is disordered with the sulphur atom distributed over two positions, with site occupancies of 0.62 and 0.38.

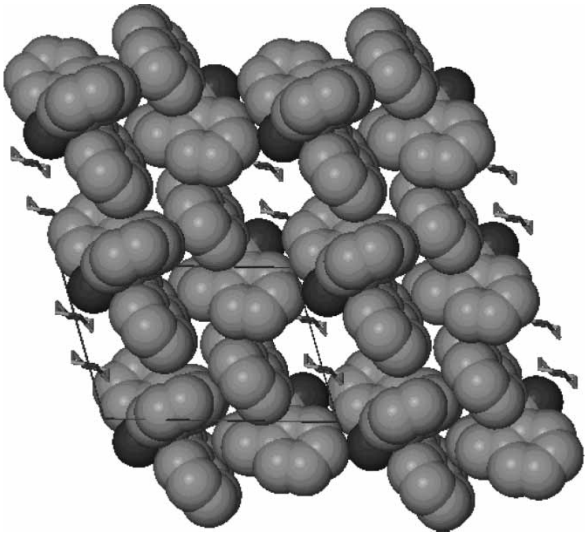


FIGURE 2 Packing of A·DIOX along [100] showing channels in which the dioxane guests are located.

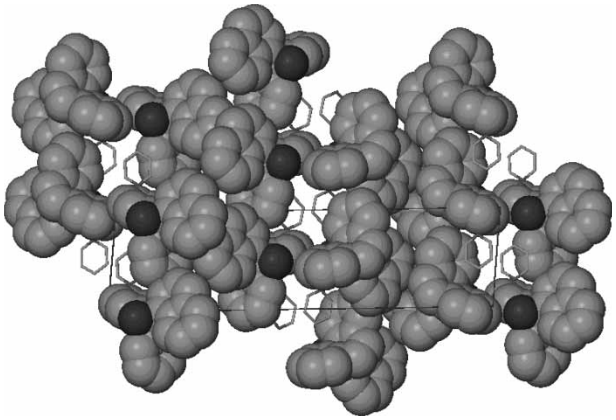


FIGURE 3 Packing of A·PYR along [100].

This structure is also stabilized by a (host)–O–H···O–(guest) hydrogen bond (d O···O = 2.715(5) Å) and the DMSO guests are located in cavities as shown in Fig. 4.

Structure of C

When the host mixture was dissolved in dimethylsulphoxide at the elevated temperature of 110°C and subsequently cooled, we obtained a mixture of crystals of both C and A·DMSO.

Compound C is the dimerized form of the ketone B used as a starting material in the synthesis of the host A. It crystallizes in the space group $P2_1/c$ with $Z = 4$. A perspective view of the molecule is given in Fig. 5.

Of interest is the central four-membered ring in which the bond angles are all less than 90°, showing that the molecule is strained. The conformation of this ring is described in Table II, which gives the metrics of interest to compound C.

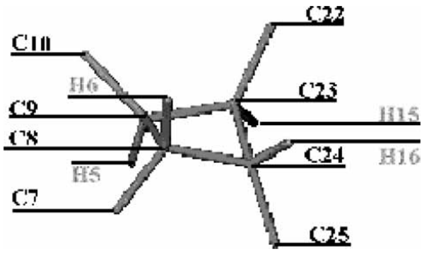
Structure of A·B

When the host mixture was recrystallized from toluene at 40°C we obtained the 1:1 molecular complex A·B, which crystallized in the space group P-1 with $Z = 2$. Thus the asymmetric unit consists of one molecule of the host A which is hydrogen-bonded to the ketone B with (A)–O–H···O–(B) with d O···O = 2.779(2) Å shown in Fig. 6.

Structure of A·0.5B·0.5C

Crystals of this compound were obtained by recrystallizing the host mixture from ethanol (mild condition: 40°C), and they give rise to a complicated but interesting structure. The space group is P-1 with $Z = 2$. In the unit cell there are two molecules of A in general positions, one of B located in a center of

TABLE II Metrics of the four-membered ring in compound C

	Inner bond length (Å)	Angles (°)	Torsion angles (°)
	C8–C9: 1.560(2) C9–C23: 1.556(2) C23–C24: 1.589(2) C24–C8: 1.557(2)	C8–C9–C23: 88.54(10) C9–C23–C24: 87.77(10) C23–C24–C8: 87.45(10) C24–C8–C9: 88.78(10)	C7–C8–C9–C10: 85.02(16) C22–C23–C24-C25: 135.38(12) C10–C9–C23–C22: 35.19(18) C7–C8–C24–C25: 30.82 (17)

inversion at Wyckoff position e, and one molecule of C. The latter is disordered with the molecular centroid located near the origin and repeating along the *x*-axis.

The peaks from the electron density map are shown in Fig. 7, in which the molecular structure of B is picked out in bold lines.

Molecular Conformations

The important conformation parameters for molecules A, B and C are defined in Scheme 1 and presented in Tables III and IV. The result shows that the conformations are remarkably consistent, with a modest variation in the torsion angles τ_1 and τ_2 for compound A.

CONCLUSION

This work is an example of the complications that arise when inclusion compounds are grown from an impure host. The 'host mixture' gave rise to a serendipitous series of interesting results, in which compounds related to the target host formed crystalline products of unexpected molecular complexes as

TABLE III Metrics of the hydrogen bond in the crystal structures

	A(α)	A·DIOX	A·DMSO	A·PYR		A·B	A·0.5B·0.5C
d (host) O···acceptor atom (guest) Å	3.346(2)	2.762(2)	2.717(4)	2.882(3)	2.862(3)	2.779(2)	2.860(2)
d (guest) acceptor atom···H(O) (host) Å	2.54(4)	1.97(4)	1.89(4)	2.04(4)	1.87(4)	1.876(19)	1.94(4)
Angle (°) (host) O–H···acceptor atom (guest)	172(4)	157(2)	168(2)	176(2)	177(2)	160.6(18)	174(3)

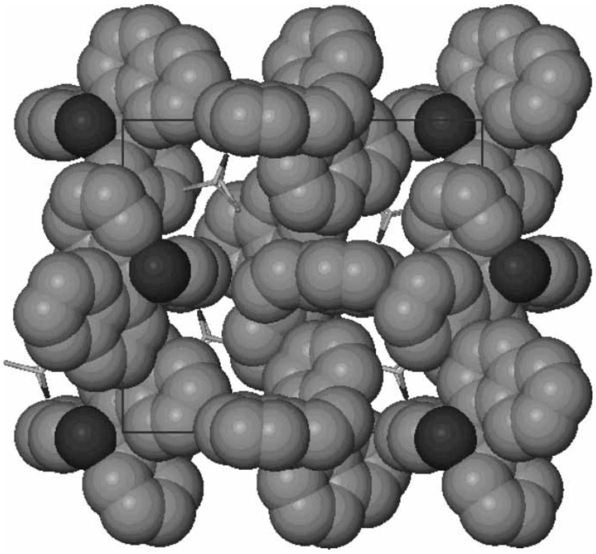


FIGURE 4 Packing of the A·DMSO along [100] showing the DMSO molecules trapped in pockets.

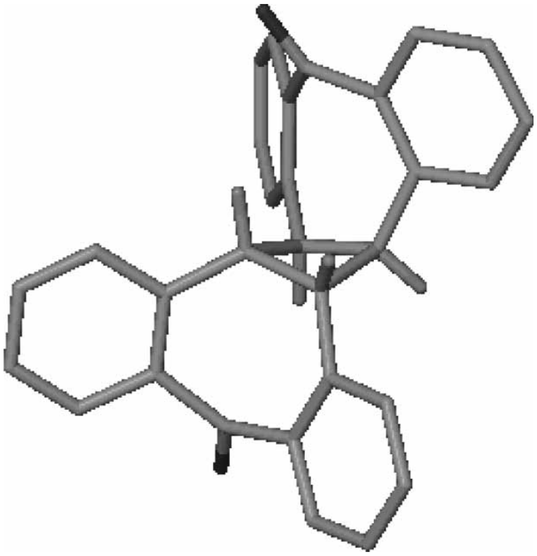


FIGURE 5 Scheme of compound C showing the hydrogen atoms only on the four-membered ring.

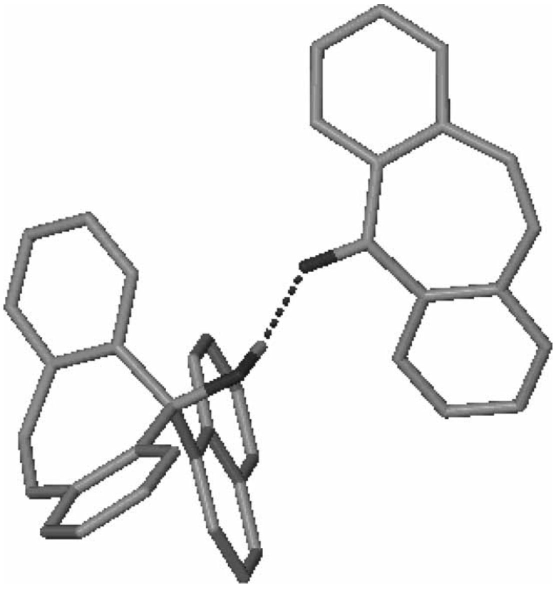


FIGURE 6 Scheme of the hydrogen-bond in the complex formed by A and B.

well as the desired host-guest compounds. It serves as a warning to check the purity of the starting host compound, particularly when the latter is labile.

EXPERIMENTAL

Crystal Structures

Crystals were obtained by crystallizing saturated solutions of the 'host mixture' in the respective solvent: Dioxane, Pyridine, DMSO, Ethanol and Toluene at 25°C.

In all cases the host-guest ratios were confirmed by Thermal Gravimetry (TG) and details of the crystal data, intensity data collections and refinements are contained in Table I. Cell dimensions were established from the intensity data measurements on a Nonius Kappa CCD diffractometer using graphite-monochromated Mo-$K\alpha$ radiation. The strategy for the data collections was evaluated using COLLECT software [5]. For all structures, data were collected by the standard phi- and omega-scan techniques, and were scaled and reduced using DENZO-SMN software [6]. The structures were solved by direct methods using SHELX-86 [7] and refined by least squares with SHELX-97 [8] refining on F^2. The program X-Seed [9,10] was used as a graphical interface for the structure solution and refinement using SHELX, as well as to produce the packing diagrams.

In each of the structures the positions of all non-hydrogen host atoms were obtained by direct methods and the non-hydrogen guest atoms were located in difference electron density maps. All non-hydrogen atoms were refined with anisotropic temperature factors. Hydrogen atoms were found in difference electron density maps and their positions and isotropic factors were refined independently. All structures were determined at low temperature (173 K).

CCDC-274559–CCDC-274565 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing :data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

Thermal Analysis

Differential scanning calorimetry (DSC) was performed on a Perkin-Elmer PC7 series system and Thermal gravimetry (TG) on a Mettler Toledo TGA/SDTA 851^e system. Finely powdered, air-dried specimens (2–5 mg) were placed in crimped,

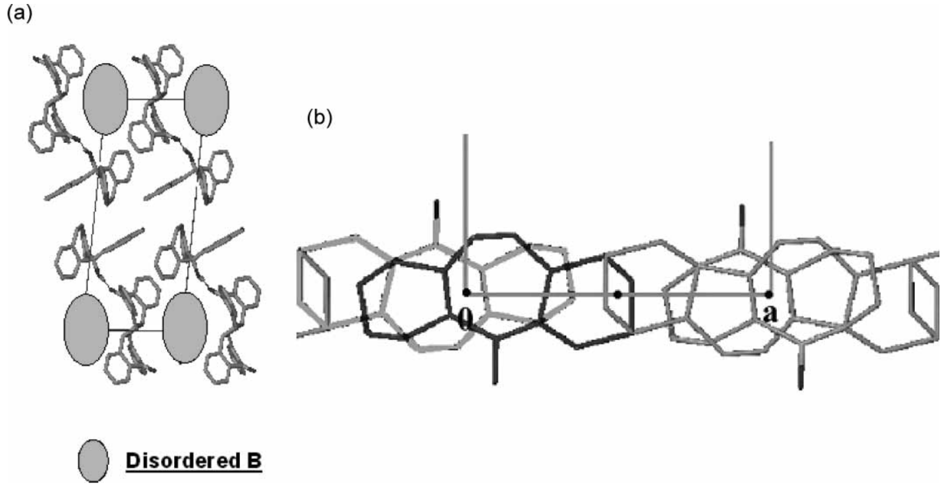


FIGURE 7 (a) Packing of A·05B·05C along [100] showing the hydrogen-bond between A and C and disordered B at the origin; (b) Detail of disordered B (grey ribbon) along axis a and one of its solved disordered position (in black).

TABLE IV Metrics of the torsion angles in the crystal structures

	A(α)	A·DIOX	A·DMSO	A·PYR		A·B	A·0.5B·0.5C	C(α)	
				Pair1	Pair2				
τ_1 (A) °	4.7(3)	3.0(2)	0.4(6)	2.2(4)	1.7(4)	2.8(2)	1.8(4)	–	–
τ_2 (A) °	103.90(18)	119.12(13)	90.9(3)	99.6(3)	96.7(2)	88.28(15)	93.1(2)	–	–
τ_1 (B) °	–	–	–	–	–	0.3(3)	4.7(2)	–	–
τ_1 (C) °	–	–	–	–	–	–		a: 30.82(17)	b: 35.19(18)

vented aluminium DSC pans or open aluminium TG sample pans. Dinitrogen was used as purging gas at a flow rate of 30 ml/min. All experiments were carried out over temperature ranges of 30–300°C for DSC and 30–350°C for the TG experiments at a constant heating rate of 20°C/min.

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