Complexation with diol host compounds. Part 32.† Separation of lutidine isomers by 1,1,6,6-tetraphenylhexa-2,4-diyne-1,6-diol

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Received (in Cambridge, UK) 5th August 1999, Accepted 27th September 1999

The title host compound forms inclusion compounds with 2,4-, 3,5- and 2,6-lutidine. In each case the host : guest ratio is 1 : 2 and the structures are stabilised by (Host)O–H · · · N(Guest) hydrogen bonds. Competition experiments show that the host selects the guests in order of preference of 3,5-lutidine > 2,6-lutidine > 2,4-lutidine. These results are in general agreement with the lattice energy calculations.

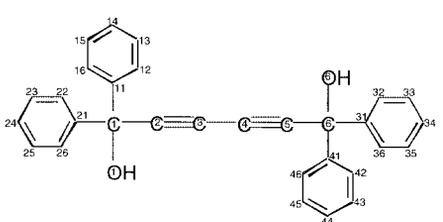
Introduction

The compound 1,1,6,6-tetraphenylhexa-2,4-diyne-1,6-diol, which was synthesized by Toda in 1968, is an example of a "wheel-and-axle" host compound.[1] It conforms to the principles of directed host design as formulated by Weber,[2] in that it is bulky and rigid so that, when crystallised, it packs inefficiently, leaving suitable cavities which can accommodate guest molecules. In addition it contains two hydroxy moieties which are efficient hydrogen-bond donors, and thus forms a variety of inclusion compounds that may be regarded as "coordinatoclathrates".

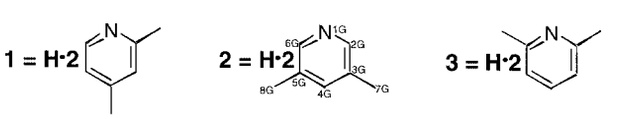
The solid state reactions between this host and a variety of guests have been studied,[3] while the kinetics of the reaction with acetone (solid–gas) and with benzophenone (solid–solid), have been analysed.[4]

The inclusion compounds formed with methyl ethyl ketone, diethyl ketone and acetophenone, including their thermal decomposition, have been studied.[5]

In this work we present the results of the competition experiments carried out with the title host and three lutidine isomers: 2,4-lutidine, 3,5-lutidine and 2,6-lutidine, as shown in Scheme 1, which also shows the atomic numbering scheme.



1,1,6,6-tetraphenylhexa-2,4-diyne-1,6-diol (**H**)



2,4-lutidine 3,5-lutidine 2,6-lutidine

Scheme 1

The selectivity is discussed in terms of the interaction from the crystal structures of the three inclusion compounds.

Experimental

The inclusion compounds **1**, **2** and **3** were obtained by dissolving the host compound **H** in the liquid guest, and crystals of suitable quality appeared by slow evaporation over a period of 2 hours. Preliminary cell dimensions and space group symmetry were determined photographically and subsequently refined on a Nonius Kappa CCD diffractometer using graphite-monochromated Mo Kα radiation. The strategy for the data collection was evaluated using the COLLECT[6] software. The detector to crystal distance for **1**, **2** and **3** was 35, 30 and 40 mm respectively. For all three structures data were collected by the standard φ scan and ω scan techniques. For each structure all sets of data were scaled and reduced using DENZO-SMN.[7] The important crystal and experimental data are given in Table 1. All three structures were solved by direct methods using SHELX-86[8] and refined employing full-matrix least-squares with the program SHELX-93[9] refining on F^2.

Competition experiments

Competition experiments were carried out between pairs of guests as follows: A series of 11 vials was made up with mixtures of two guests such that the mole fraction of a given guest varied from 0 to 1. Host compound was added to each mixture, keeping the ratio of host : total guest at 1 : 70, and allowed to dissolve by warming. The vials were allowed to cool slowly. The resulting crystalline inclusion compounds were filtered, dried and placed in vials with silicone seals. The latter were heated to release the guest mixtures, which were then analysed by gas chromatography.

The experiment was extended to analyse simultaneous competition by all three isomers. Initial mixtures of all three guests were selected on an inner triangle drawn on a triangular diagram representing the competition of the isomers as shown in Fig. 1. The equi-mixture of the guests, with mole fraction 1/3 each, representing the centre of the inner triangle, was also analysed. The crystalline inclusion compounds obtained were analysed as before.

Thermal analysis

Thermogravimetry (TG) and differential scanning calorimetry (DSC) were carried out on a Perkin-Elmer PC7-Series system. TG analyses were performed to ascertain accurate host : guest ratios, while DSC was used to determine onset temperatures of guest release and to monitor any phase changes occurring in structures upon heating. These experiments were performed over a temperature range of 30–300 °C at a heating rate of 10 °C min^{-1} with a purge of dry nitrogen flowing at 30 ml min^{-1}. The samples were crushed, blotted dry and placed in

† For Part 31 see ref. 18.

Table 1 Crystal data, experimental and refinement parameters

Inclusion compound	**1**	**2**	**3**
Molecular formula	$C_{30}H_{22}O_2{\cdot}2C_7H_9N$	$C_{30}H_{22}O_2{\cdot}2C_7H_9N$	$C_{30}H_{22}O_2{\cdot}2C_7H_9N$
M_r/g mol^{-1}	628.78	628.78	628.78
T/K	293(2)	293(2)	293(2)
Crystal system	triclinic	triclinic	monoclinic
Space group	$P\bar{1}$	$P\bar{1}$	$P2_1/n$
a/Å	10.313(1)	8.407(1)	10.502(1)
b/Å	11.917(1)	10.569(1)	8.368(1)
c/Å	16.752(1)	11.442(1)	20.216(1)
α/°	99.64(1)	109.38(1)	90
β/°	101.47(1)	110.45(1)	96.14(1)
γ/°	114.15(1)	91.39(1)	90
V/Å^3	1768.5(3)	887.2(2)	1766.4(3)
Z	2	1	2
No. reflections collected/observed	6431/4519	4956/2178	9481/3141
No. parameters	445	239	240
R_1	0.0648	0.0795	0.0720
$R(int)$	0.034	0.100	0.068

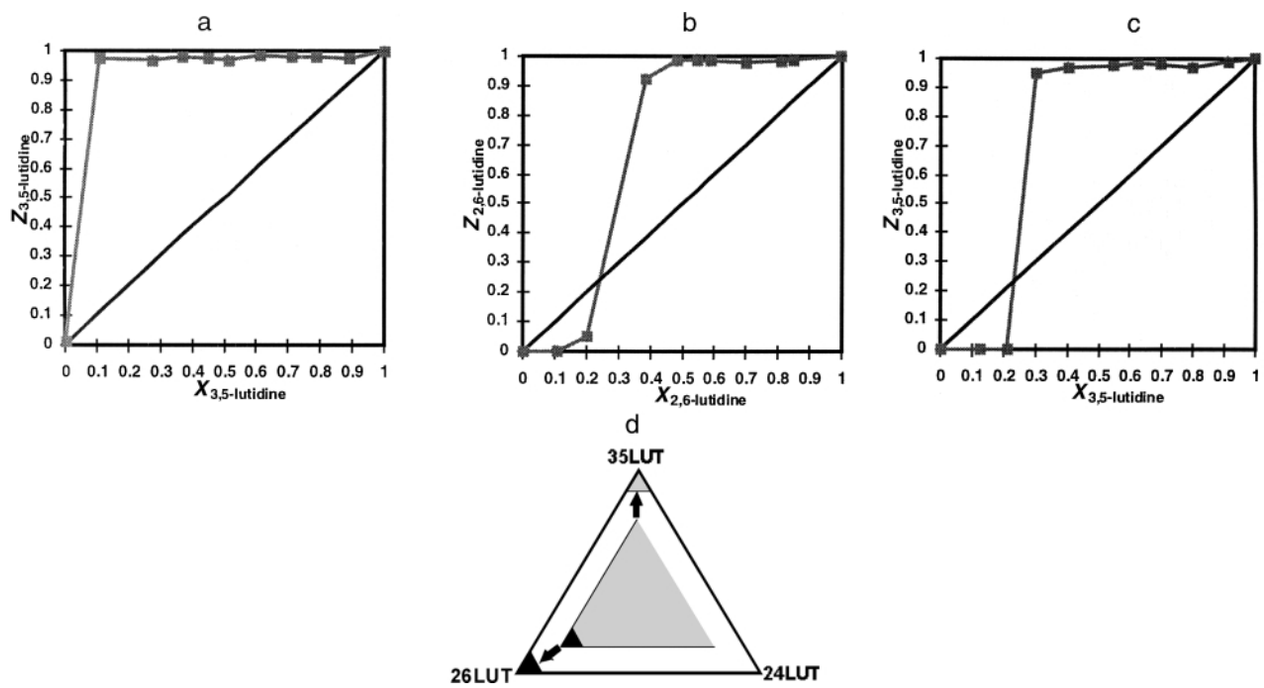


Fig. 1 Results of the competition experiments: a) 2,4- *versus* 3,5-lutidine; b) 2,4- *versus* 2,6-lutidine; c) 2,6- *versus* 3,5-lutidine; d) three-component competition.

open platinum pans for TG experiments and in crimped but vented aluminium pans for DSC.

Results and discussion

The results of the competition experiments are illustrated in Fig. 1. Each two-component experiment shows the mole fraction X of a given guest in the initial solution *versus* the mole fraction Z of the guest that is included by the host.

We note that 3,5-lutidine is strongly favoured over 2,4-lutidine (Fig. 1a), but the results of the other two-component experiments are concentration dependent. Thus in the 2,4- *versus* 2,6-lutidine the latter is selected when X(2,6-lutidine) > 0.2 (Fig. 1b) and in the 2,6- *versus* 3,5-lutidine the latter is also preferred when X(3,5-lutidine) > 0.2 (Fig. 1c).

The three-component experiment is shown on the equilateral triangle, the three apices of which represent the pure component lutidines (Fig. 1d). We selected starting mixtures represented by the inner shaded area, and the resulting mixtures are indicated by the arrows. We see that for most starting mixtures there is a pronounced migration towards the 3,5-lutidine but that if the initial mixture has a mole fraction X(2,6-lutidine) > 0.7, then the latter is enriched.

For **1**, the space group is $P\bar{1}$, with $Z = 2$. Two independent host molecules are each located on centres of inversion at Wyckoff[10] positions *b* and *e*, while the 2,4-lutidine guests are located in general positions. Similar structural patterns occur with the other two structures: in **2**, the space group is $P\bar{1}$ with $Z = 1$ requiring the host to be located at Wyckoff[10] position *h* with the two 3,5-lutidine guests in general positions, while in **3**, the structure adopts the space group $P2_1/n$ with $Z = 2$ and the host is on a centre of inversion at Wyckoff[11] position *d*, with the guests again located in general positions.

For all three structures symmetry requires that the host hydroxy moieties hold the *trans*-configuration, and the guest molecules are each hydrogen bonded *via* (**H**)–O–H · · · N(**G**) hydrogen bonds. These are detailed in Table 2. The packing of all three structures is shown as projections in Fig. 2, while Fig. 3 shows a space-filled representation of **2** with the guest molecules removed,[12] showing that these are located in channels. We have analysed the topology of these channels which run in the [100] direction using the program SECTION,[13] and have meas-

Table 2 Hydrogen-bonding parameters

Compound	Donor (D)	Acceptor (A)	D–H/Å	D···A/Å	D···H–A/°
1	O1	N1GA	0.970(3)	2.733(5)	172(4)
	O1	N1GB	0.970(3)	2.835(5)	170(4)
2	O1	N1G	0.970(3)	2.763(3)	153(4)
3	O1	N1G	0.970(3)	2.789(2)	164(3)

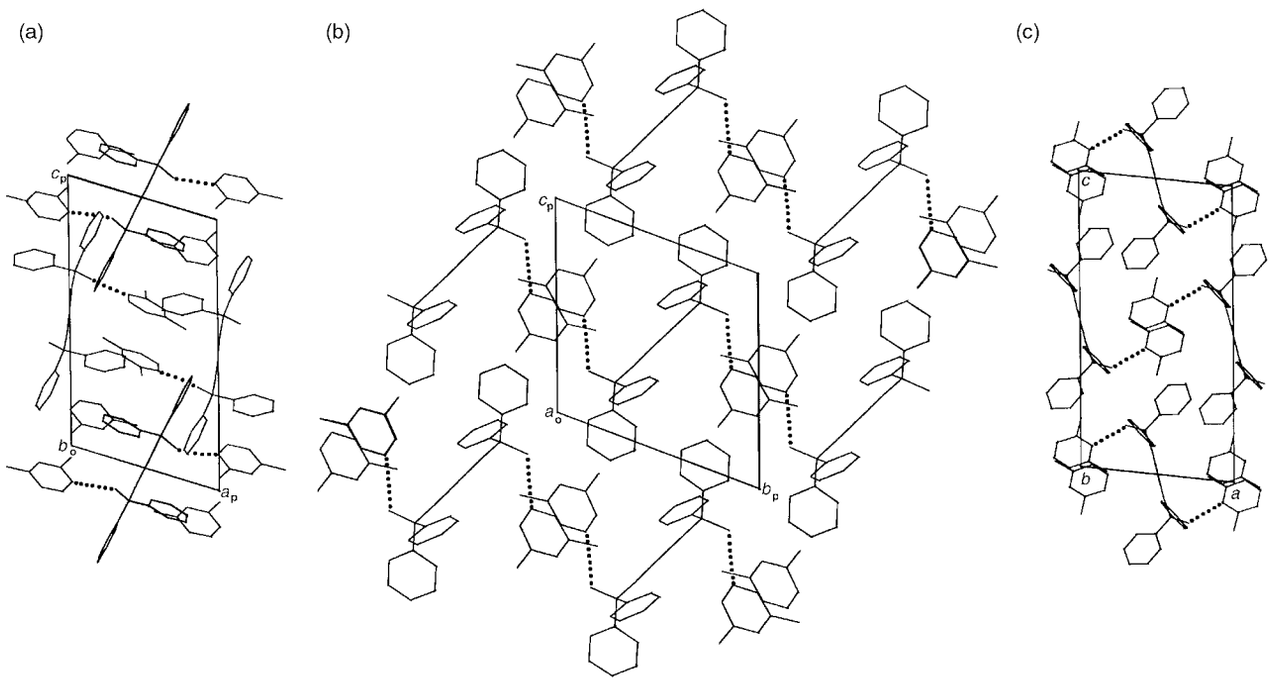


Fig. 2 a) Projection of **1** along [010]; b) projection of **2** along [100]; c) projection of **3** along [010].

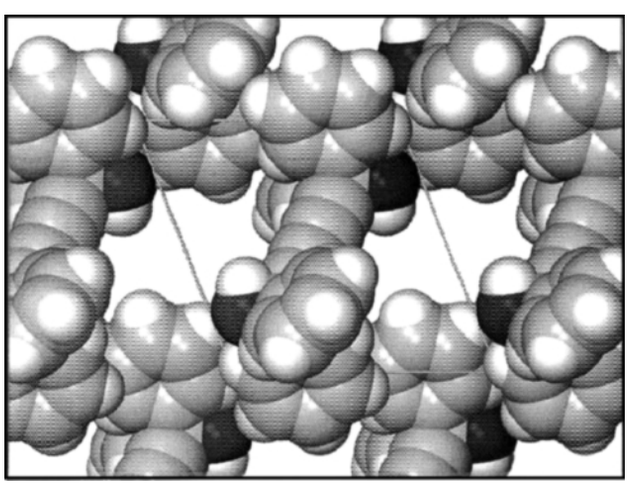


Fig. 3 Space-filling projection of **2** along [100] with guest-molecules omitted, showing the open channels.

ured their cross sectional area, which varies from 9.1 × 7.2 to 8.7 × 4.5 Å. Similar analyses were carried out for the other two structures. For **1**, the channels run in the [111] direction and are best described as hour-glass shaped, with dimensions varying from 8.3 × 14.5 Å to constrictions of 5.0 × 10.4 Å. For **3**, the channels run along [010], and vary in cross section from 10.8 × 6.7 to 6.4 × 4.9 Å.

Lattice energy calculations were performed for all three structures using the atom–atom potential method. We employed the program HEENY,[14] using a force field of the type given by eqn. (1), where r is the interatomic distance and the coefficients

$$V(r) = a \exp(-br) - c/r^6 \qquad (1)$$

a, b and c are those given by Gavezzotti.[15] We incorporated a hydrogen bonding potential which is a simplified version of that given by Vedani and Dunitz[16] and is formulated as eqn. (2),

$$V(\text{H-bond}) = (A/R^{12} - C/R^{10})\cos^2\theta \qquad (2)$$

where R is the distance between the hydroxy hydrogen and the N acceptor. θ is the O–H···N angle, and the $\cos^2\theta$ term is the energy penalty paid by the bond to take non-linearity into account. We selected a representative host–guest pair and carried out appropriate summations of all host···host, host···guest and guest···guest interactions. We obtained the following values for the lattice energies: **1**, −320.8 kJ mol^{-1}; **2**, −452.5 kJ mol^{-1} and **3**, −441.4 kJ mol^{-1}. This outcome is gratifying, in that it shows that the stabilities of the inclusion complexes are in the order **2** > **3** > **1**. This is in agreement with the major results obtained in the three-component competition experiments, in that in the three-component system 2,4-lutidine is always disfavoured and the majority of starting mixtures migrate towards 3,5-lutidine.

We note however that the lattice energies of **2** (3,5-lutidine) and **3** (2,6-lutidine) are close; they only differ by 11.1 kJ mol^{-1} (2.6 kcal mol^{-1}) and we believe that this, together with the kinetic effects, is responsible for the concentration dependence of some of the competition experiments.

The results of the thermal analysis are shown in Fig. 4, and the thermal decomposition of each compound was also followed by hot stage microscopy (HSM) on a Linkam TH600 with the aid of a Linkam CO600 temperature controller. For **1**, Fig. 4a, the 2,4-lutidine exhibits a one-step desolvation reaction, and the endotherm A is associated with the dissolution of the host in the released guest and includes the contribution due to desolvation. For **2**, Fig. 4b, the endotherm A is followed by a broad exotherm B. Hot stage microscopy revealed an initial

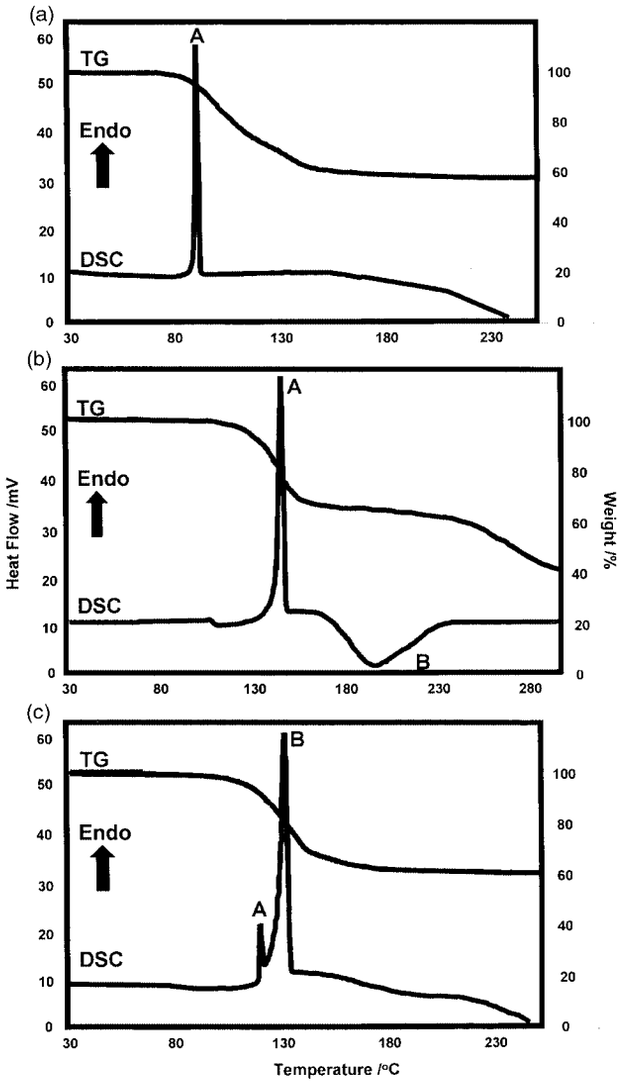


Fig. 4(a to c) TG and DSC results for **1**, **2** and **3**.

bubbling and dissolution (135 °C, endo A), but this was followed by the appearance of new crystals which only dissolved when the temperature was as high as 215 °C. We therefore associate the exotherm B with a phase transition of the host compound. For **3**, Fig. 4c, there are two endotherms A and B. The first endotherm A is associated with a change of colour of the crystals, from colourless to opaque white, followed by a dissolution of the host as the 2,6-lutidine is released, giving rise to endotherm B. Thermal analysis details, for both TG and DSC are given in Table 3.

It is of interest to note the results for this host in comparison with 1,4-bis(9-hydroxyfluoren-9-yl)benzene which has been employed in a similar manner to separate the same three lutidine isomers.[17] The lattice energies of the inclusion compounds obtained with the latter host show the stabilities to be 3,5-lutidine > 2,4-lutidine > 2,6-lutidine. The fluorenyl host proved to be flexible, and the hydroxy moieties adopted the unusual *cis*-configuration in the inclusion compound with 2,6-lutidine.

Table 3 Thermal analysis data

Inclusion compound		**1**	**2**	**3**
H : G ratio		1 : 2	1 : 2	1 : 2
TG results	Calc. % mass loss	34.1	34.1	34.1
	Exp. % mass loss	34.1	34.1	34.1
DSC results	Peak A T_{on}/°C	88.0	150.2	114.9
	Peak B T_{on}/°C	—	168.9	127.2

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Paper 9/06406K