

# Separation of xylenols by inclusion

Mino R. Caira,<sup>1</sup> Luigi R. Nassimbeni,<sup>1\*</sup> Dejana Vujovic<sup>1</sup> and Fumio Toda<sup>2</sup>

<sup>1</sup>Department of Chemistry, University of Cape Town, Rondebosch 7701, South Africa

<sup>2</sup>Department of Applied Chemistry, Faculty of Engineering, Ehime University, Matsuyama, Ehime 790-8577, Japan

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**ABSTRACT:** The host 1,1-bis(4-hydroxyphenyl)cyclohexane, **H**, forms 1:1 inclusion compounds with 2,3-xyleneol, **H**·**23X**, and with 3,5-xyleneol, **H**·**35X**. Competition experiments were conducted to determine the host selectivity toward three xyleneol isomers, 2,3-, 3,5- and 2,6-xyleneol. The structure of the solid formed between **H** and a mixture of **23X** and **35X** was elucidated. Copyright © 2000 John Wiley & Sons, Ltd.

**KEYWORDS:** Xyleneol separation; inclusion

## INTRODUCTION

The process of molecular recognition lies at the heart of host–guest chemistry. Thus the formation and stability of a particular inclusion compound depend on the strengths and directions of the various intermolecular forces impinging on the multi-component system. This can be exploited to carry out selective enclathration, whereby a given host molecule is exposed to a mixture of possible guests, and preferentially forms an inclusion compound with only one guest, thus enacting a perfect separation. In practice this is seldom achieved in a single cycle, particularly when we seek to separate close isomers, where the differences between guests may be subtle. Nevertheless, we have used the host 1,1-bis(4-hydroxyphenyl)cyclohexane (**H**) to separate the isomers of the phenylenediamines,<sup>1</sup> the benzenediols<sup>2</sup> and the picolines.<sup>3</sup> This host also forms inclusion compounds with phenol and the cresols and their structures have been elucidated.<sup>4</sup> We now present the results of competition experiments between this host and three isomers of xyleneol: 2,3-xyleneol (**23X**), 3,5-xyleneol (**35X**) and 2,6-xyleneol (**26X**), and discuss the formation of a solid solution formed between the host, **H**, and a mixture of **23X** and **35X**.

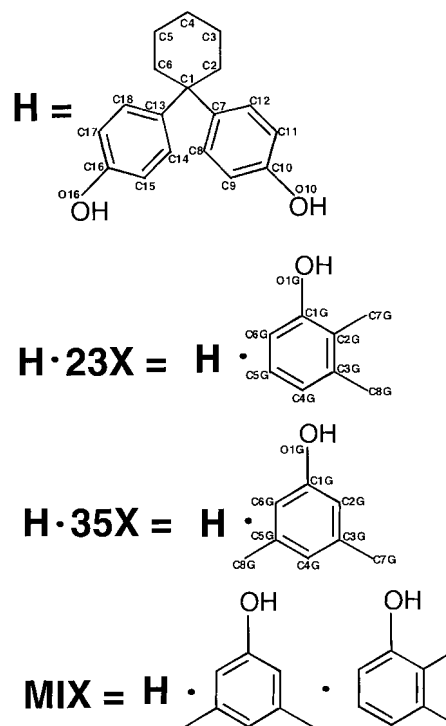
## EXPERIMENTAL

Suitable crystals of **H**·**23X** and **H**·**35X** were obtained by slow cooling of the host–guest mixture in ethyl acetate over a period of 12 h. Stoichiometric quantities of the

host compound (**H**) and the guest (**23X** and **35X**) were dissolved in a minimum amount of ethyl acetate.

Numerous attempts to obtain suitable crystals of the host with 2,6-xyleneol were unsuccessful and therefore the structure of this complex cannot be reported.

Preliminary cell dimensions and space group symmetry were determined photographically and the unit cell data were subsequently refined by standard procedures on a Nonius Kappa CCD diffractometer. Relevant crystal and experimental data are given in Table 1. Both structures were solved by direct methods using



Scheme 1

\*Correspondence to: L. R. Nassimbeni, Department of Chemistry, University of Cape Town, Rondebosch 7701, South Africa.  
E-mail: xrayluig@psipsy.uct.ac.za

**Table 1.** Crystal data, experimental and refinement parameters

Guest compound	2, 3-Xylenol ( <b>23X</b> )	3, 5-Xylenol ( <b>35X</b> )	2, 3-Xylenol + 3, 5-xyleneol <b>MIX</b>
Inclusion compound	<b>H·23X</b>	<b>H·35X</b>	
Molecular formula	C <sub>18</sub> H <sub>20</sub> O <sub>2</sub> ·C <sub>8</sub> H <sub>10</sub> O	C <sub>18</sub> H <sub>20</sub> O <sub>2</sub> ·C <sub>8</sub> H <sub>10</sub> O	C <sub>18</sub> H <sub>20</sub> O <sub>2</sub> · <b>23X</b> · <b>35X</b>
<i>M<sub>r</sub></i> (g mol <sup>-1</sup> )	390.50	390.50	390.50
<i>T</i> (K)	293(2)	293(2)	293(2)
$\lambda$ (Å)	0.71069	0.71069	0.71069
Crystal system	Triclinic	Triclinic	Triclinic
Space group	<i>P</i> $\bar{1}$	<i>P</i> $\bar{1}$	<i>P</i> $\bar{1}$
<i>a</i> (Å)	6.266(1)	6.279(1)	6.291(1)
<i>b</i> (Å)	10.815(2)	10.758(1)	10.783(1)
<i>c</i> (Å)	16.263(4)	16.651(1)	16.679(1)
$\alpha$ (°)	95.59(1)	98.46(1)	98.33(1)
$\beta$ (°)	94.00(1)	99.21(1)	99.07(1)
$\gamma$ (°)	100.58(1)	97.99(1)	98.10(1)
<i>V</i> (Å <sup>3</sup> )	1073.9(4)	1082.9(2)	1089.9(2)
<i>Z</i>	2	2	2
<i>D<sub>c</sub></i> (Mg/m <sup>-3</sup> )	1.208	1.198	1.165
$\mu$ (Mo K $\alpha$ ) (cm <sup>-1</sup> )	0.77	0.77	0.75
<i>F</i> (000)	420	420	420
Crystal size (mm)	0.45 × 0.40 × 0.30	0.40 × 0.40 × 0.25	0.45 × 0.45 × 0.30
Range scanned, $\theta$ (°)	1.26–26.37	1.26–26.46	1.25–24.98
Range of indices	<i>h</i> 0–7, <i>k</i> ± 11, <i>l</i> ± 20	<i>h</i> 0–7, <i>k</i> ± 13, <i>l</i> ± 20	<i>h</i> ± 7, <i>k</i> ± 12, <i>l</i> 0–19
No of reflections collected	3867	4405	3975
No of reflections observed	2425	3203	1406
No of parameters	264	281	271
<i>S</i>	1.101	1.104	1.115
<i>R</i> <sub>1</sub>	0.0585	0.0485	0.0798
<i>wR</i> <sub>2</sub>	0.1650	0.1466	0.1999
$\Delta\rho$ excursions (e Å <sup>-3</sup> )	0.413; –0.413	0.188; –0.182	0.606; –0.262

SHELX-86<sup>5</sup> and refined employing full matrix least-squares using SHELX-93,<sup>6</sup> refining on *F*<sup>2</sup>. The numbering scheme is shown in Scheme 1. For both structures all non-hydrogen atoms were treated anisotropically except for methyl carbons of **H·23X**. The aromatic and methylene hydrogens were geometrically constrained and refined with common isotropic temperature factors. The hydroxy hydrogens were located in difference electron density maps and refined with independent temperature factors and with simple bond length constraints.

We also grew single crystals of the host with a mixture of **23X** and **35X**. We concentrated on obtaining relatively large single crystals (typically 3 × 4 × 10 mm) so that we could cut such a single crystal into portions and carry out crystal structure analysis, differential scanning calorimetry (DSC) and gas chromatography (GC) on the same single crystal. This is an important point, because inclusion compounds in general, and those with mixed guests in particular, are notoriously non-stoichiometric. We have experience of growing batches of single crystals from mixed guests where the ratio of the included guests varies not only from batch to batch but also within the same batch of crystals.

Competition experiments were conducted between pairs of xylenols as follows. A series of 11 vials were made up with mixtures of the two guests (in ethyl acetate), varying the mole fraction of the guests from 0 to 1 in the series, but keeping the host:guest ratio at 1:20 in

each vial. Crystals were obtained by slow evaporation, filtered from the mother liquor and dissolved in ethyl acetate. The relative composition of the included guests and mother liquors with which they were in equilibrium were determined by GC, using a Carlo Erba Fractovap 4200 instrument equipped with a Carbowax capillary column (25 m × 0.25 mm i.d.) and a Spectra-Physics SP4290 integrator.

The experiment was extended to analyse simultaneous competition by three xylenol isomers: **23X**, **35X** and **26X**. Initial mixtures of the three guests were selected and were represented on a triangular diagram as shown in Fig. 1. The relative compositions of the included guests and mother liquors were analysed as before.

DSC and thermogravimetry (TG) were performed on a Perkin-Elmer PC7 instrument. Fine powdered specimens, obtained by crushing crystals immersed in mother liquor, were dried in air on filter-paper and placed on open platinum pans for TG experiments and in crimped, vented aluminium sample pans for DSC experiments. Sample masses in each case were 3–7 mg and the samples were purged by a stream of nitrogen flowing at 30 ml min<sup>-1</sup>.

## RESULTS AND DISCUSSION

Both **H·23X** and **H·35X** crystallize in the space group *P* $\bar{1}$  and have similar cell dimensions. Their packing is characterized by double ribbons of host molecules

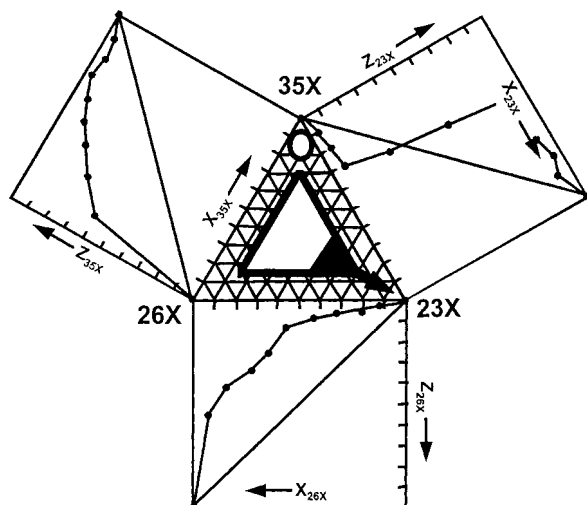


Figure 1. Results of the competition experiments

running parallel to [010] which are interleaved by channels containing the guest molecules. This is shown in Fig. 2, where the structure is projected along [100]. The structures are characterized by extensive host–host and host–guest hydrogen bonding, which is detailed in Table 2. In both **H·23X** and **H·35X** the hydrogen bonding network forms a helix parallel to the *x*-axis.

The results of competition experiments are shown in Fig. 1. Each two-component result shows the mole ratio *X* of the initial solution *versus* *Z* included by the host. For the **26X–35X** competition the latter is strongly favoured even in mixtures containing only 10% of **35X**. The **23X** is also preferred to **26X** in all mixtures but not as strongly. The **23X–35X** competition experiment is concentration dependent: **23X** is preferentially included when the **35X** concentration is <40%, whereas **35X** is favoured for initial concentrations >50%. When the starting solution is made of 40% **35X** and 60% **23X**, the preferential inclusion of either isomer is random and varies in different batches.

The three-component experiment is shown on the equilateral triangle. The starting solutions were located on the sides of the inner triangle. The results obtained

Table 2. Hydrogen bonding parameters

Compound	Donor (D)	Acceptor (A)	D...H (Å)	D...A (Å)	D...H—A (°)
<b>H·23X</b>	O16	O10	0.97(3)	2.71(3)	166(2)
	O10	O1G	0.97(3)	2.74(4)	161(3)
	O1G	O16	0.97(3)	2.74(3)	166(2)
<b>H·35X</b>	O10	O16	0.97(3)	2.69(3)	160(3)
	O16	O1G	0.97(2)	2.71(3)	166(2)
	O1G	O10	0.97(3)	2.67(3)	174(2)
<b>MIX</b>	O16	O10	0.97(4)	2.71(4)	161(3)
	O10	O1G	0.97(4)	2.69(4)	161(3)
	O1G	O16	0.97(3)	2.70(3)	173(2)

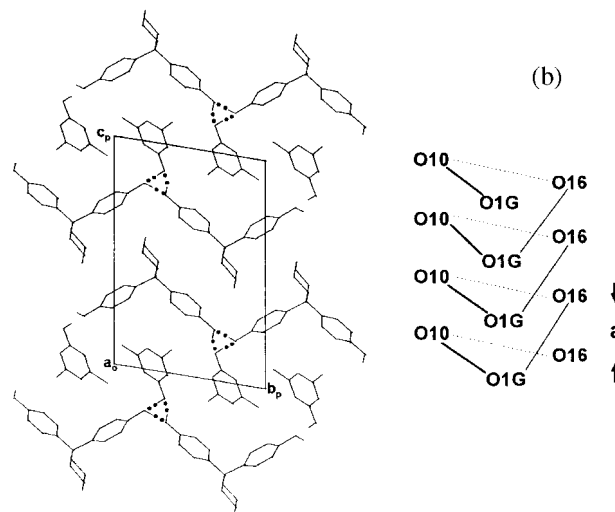
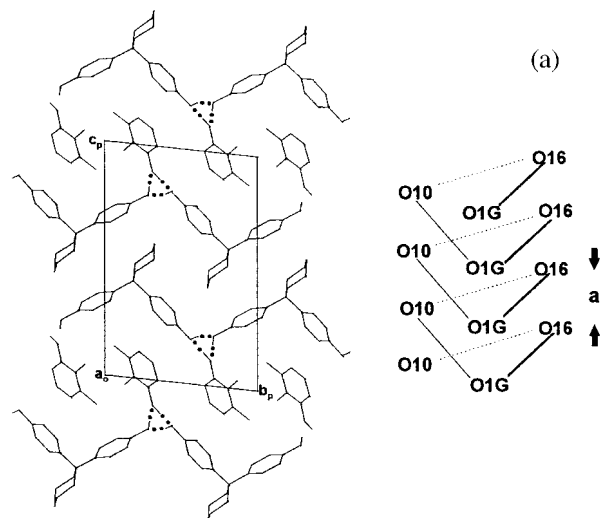
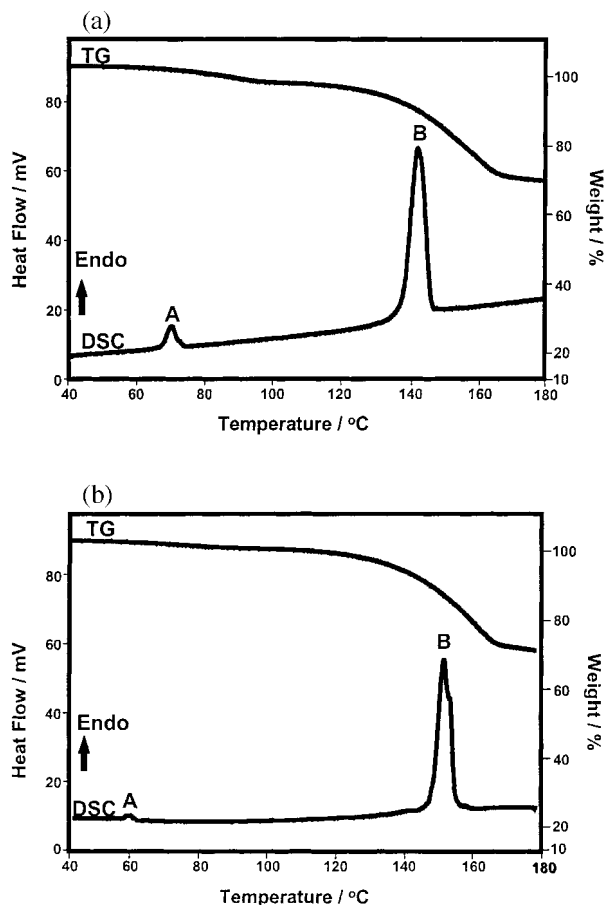


Figure 2. (a) Projection of the **H·23X** structure viewed along [100] and schematic H-bonding viewed in elevation. (b) Projection of the **H·35X** structure viewed along [100] and schematic H-bonding viewed in elevation

agree with those of the two-component experiments: **35X** is strongly favoured in all cases except when **23X** is present at initial concentrations higher than 60% and is preferentially included; **26X** is the least favoured isomer for complexation with the host. Hence the starting solutions represented by the white part of the inner triangle migrate to the white ellipse near the **35X** apex. In contrast, the starting solutions, initially rich in **23X** and represented by the darkened part of the inner triangle, move towards the **23X** apex.

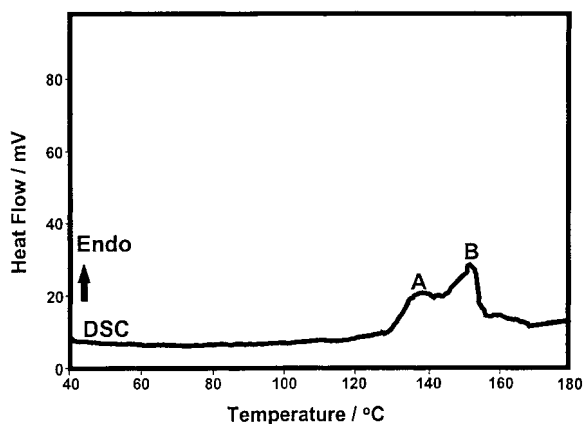
The results of thermal analyses are shown in Fig. 3. For both **23X** and **35X** the endotherm A corresponds to the loss of surface ethyl acetate while endotherm B represents the guest loss. The TG curves show two-step mass losses corresponding to endotherms A and B. The thermal results are summarized in Table 3.

The interesting part of the competition experiment lay



**Figure 3.** TG and DSC traces for (a) **H·23X** and (b) **H·35X**

in our analysis of the large mixed-guest crystal which we grew with composition **H·32% 23X·68% 35X** (**MIX**). The analysis of this crystal, **MIX**, showed the presence of both **23X** and **35X** in the complex endotherm exhibited by the DSC in Fig. 4. The GC analysis yielded two peaks corresponding to 32% **23X** and 68% **35X**. The results of the x-ray diffraction study show that the structure is practically isomorphous with the two parent compounds,



**Figure 4.** DSC trace for **MIX**

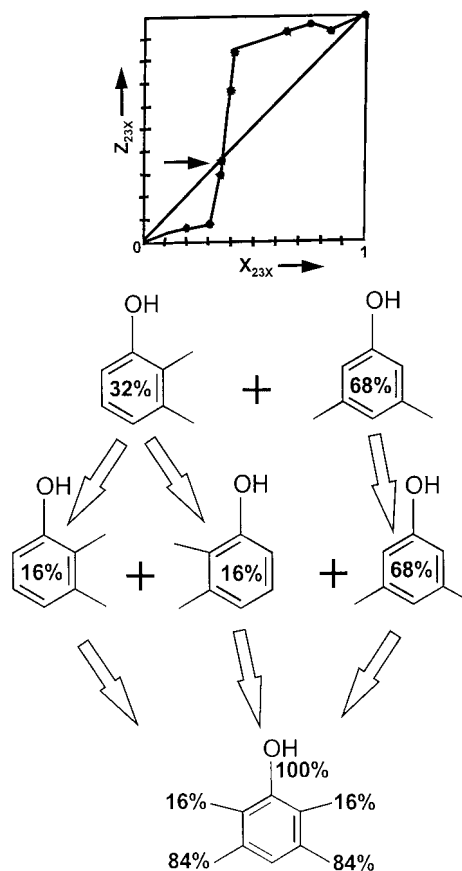
**Table 3.** Thermal analysis data

Parameter	<b>H·23X</b>	<b>H·35X</b>	<b>MIX</b>
H:G ratio	1:1	1:1	1:1
TG Results:			
Calc. mass loss (%)	31.28	31.28	—
Exp. mass loss (%)	31.12	31.03	—
DSC Results:			
Peak A: $T_{on}$ (°C)	63.7	54.4	127.0
Peak B: $T_{on}$ (°C)	129.9	146.7	139.0

having similar unit cell parameters and crystallizing in the same space group  $P\bar{1}$ .

The direct method solution yielded the positions of all the host non-hydrogen atoms, and when these were allowed to refine, the positions of the mixed guest appeared in a difference electron density map.

We noted that there were six peaks in a regular hexagon corresponding to the phenyl carbon atoms, and the oxygen peak was readily identified by its magnitude and by its distance of 2.698 Å from the host O16 corresponding to the hydrogen bond. The other four



**Figure 5.** Competition experiment with the arrow showing the composition of **MIX**. Rationale for assignment of hydroxy and methylene carbon site occupancy factors for the 'averaged' guest molecule of **MIX**

peaks could be rationalized in terms of the scheme shown in Fig. 5. We reasoned that the difference electron density map corresponded to a superposition of the disordered **23X** ( $2 \times 16\%$ ) plus the **35X** (68%). These four carbon atoms were therefore refined with site occupancies of 0.16 and 0.84, without imposing any bond length constraints. Attempts to model the methyl hydrogens on these carbons (C7G, C8G, C9G and C10G) proved unsuccessful, but the final model had reasonable isotropic temperature factors.

We have therefore successfully elucidated the structure of a solid solution of mixed guests in a matrix made up of the host compound. Although the final parameters of the mixed guests are clearly not as well refined as in the two parent compounds, we are confident that we have demonstrated the existence of the 'average structure' of

the two guests, which has been clearly found in the result of the DSC and GC analyses.

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