

# Hydrogen-bond patterns and the structures of 1,4-cyclohexanediol: 2:1 *cis:trans*-1,4-cyclohexanediol

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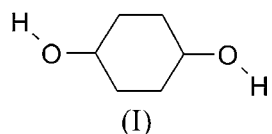
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The structure of a co-crystal with both *trans* and *cis* isomers of 1,4-cyclohexanediol (1,4-CHD) is reported. The intermolecular hydrogen-bond patterns are described and compared with those of the all *trans* structure, using the graph-set model. A second crystal with possible *cis/trans* disorder is also described. The results of molecular modeling of the simple isomers and conformers are compared with the known structures.

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## 1. Introduction

The title compound is a deceptively simple molecule, and when we started looking at it more than a decade ago we were surprised that there were no structures of it reported in the Cambridge Structural Database (CSD; Allen, 2002). In preparing this report, we found that our original surprise at not finding 1,4-CHD in the CSD was not due to lack of interest in the compound. Crystallographic investigations in the 1930s by Patterson & White (1931), White (1931), Halmöy & Hassel (1932), and later by Furberg & Hassel (1950) show that studies of these compounds by crystallographic methods were of significant interest but limited by the technology available at the time. These authors were clearly interested in these same structures and their prior work should be acknowledged.



The 1,4-CHD molecules have an unusual set of features that make them unique and valuable candidates for exploring the relationships between molecular geometry, hydrogen bonding and the resulting crystal structures. Since the organic backbone is a cyclohexane ring, the molecules are expected to be most stable in either a chair or a boat conformation.

A simple analysis shows that there are six distinct isomers/conformers (abbreviated to isocons hereafter) if we consider the pure chair and boat forms of the cyclohexane ring, with the substituents at the bow and stern of the boat. However, if we bisect these six molecules midway between the hydroxyls, there are only two distinguishable fragments, differing solely in whether the C—O bond is approximately perpendicular to, or parallel with, the cleaved C—C bonds. Fig. 1 shows that we only need to specify which two fragments are used and whether the second also has the kink at C4 up (boat) or inverted (chair, indicated by a bar over the second symbol, *i.e.*  $\bar{a}$  or  $\bar{b}$ ).

We became interested in this compound in connection with our study of alcohol–amine co-crystals (Loehlin *et al.*, 1998)

**Table 1**

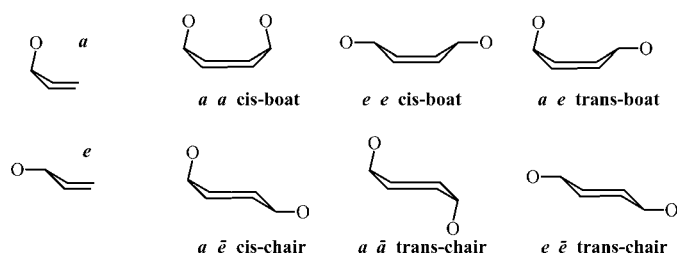
Hydrogen-bond lengths (O...O), angles (O—H...O) and GS motifs for 1,4-cyclohexane diols.

Donor > acceptor	POVSEY	POVSEY01	(I)	(II)
$a > e$	2.714 Å, 173.0° $D_2^2(10)$	2.722 Å	2.701 Å, 177.4° $C(7)$	2.734 Å
$e > e$	2.729 Å, 175.7° $C(7)$	2.738 Å	2.726 Å, 175.4° $D_2^2(8)$	2.780 Å
$e > a$	2.748 Å, 175.6° $D_2^2(8)$	2.754 Å	2.719 Å, 171.8° $D_2^2(10)$	2.781 Å

where we were looking for diols with the C—O orientation of hydroxyls antiparallel. We found that mixed-isomer 1,4-CHD was available from Aldrich. As our primary interest was in the *trans* isomer, we attempted to separate the isomers by vacuum sublimation at ~ 343 K. Nice looking crystals resulted and we set out to determine which isomer we had by collecting a single-crystal dataset. Although many crystals appeared twinned, we found one that was not and the structure was readily solved. To our surprise it showed a mixed-isomer crystal with  $e \bar{e}$  (*trans*) isomers at centers of inversion and  $a \bar{e}$  (*cis*) isomers in general positions. Refinement, however, did not converge to a satisfactory model, and close inspection indicated disorder of the molecules at general positions. In addition, since this route clearly did not assist in separating the isomers, we put the data aside, only to come back to it again as structure (II) below.

Sometime after this, Steiner & Saenger (1998) published two very interesting structures with *trans*-1,4-CHD: POVSEY, which contains both the  $a \bar{a}$  and the  $e \bar{e}$  conformers, and POVSIC, with an  $a \bar{a}$  conformer in a co-crystal. The CSD (January 2008) now has two more structures containing this isomer: POVSEY01 (Chambers *et al.*, 2000), a duplicate determination, and JEGZAX (Tanaka *et al.*, 2006), a co-crystalline complex with  $e \bar{e}$  conformation. No structures of the other four 1,4-CHD isocons are yet in the CSD.

After the publication of POVSEY, we made further attempts to obtain an ordered crystal and/or to separate the isomers. Recrystallization from solution in methylene chloride appeared to produce at least two morphologies, larger prisms with fine needle-like clumps of fuzz. Physical separation followed by recrystallization of the needle-like fuzz led to a poorly diffracting crystal of POVSEY. Recrystallization of the prisms produced nice crystals that gas chromatographic



**Figure 1**

The half molecular fragments and the six isocons of 1,4-CHD. H atoms are omitted for clarity.

analysis of individual crystals showed to be 2:1 *cis:trans* [duplicate analyses of separate solutions of two crystals gave 33.7 (6)% *trans*; another gave 35.7 (5)%]. Although most appeared twinned, a portion cleaved from one gave the satisfactory structure, (I), reported here.

## 2. Hydrogen-bond patterns

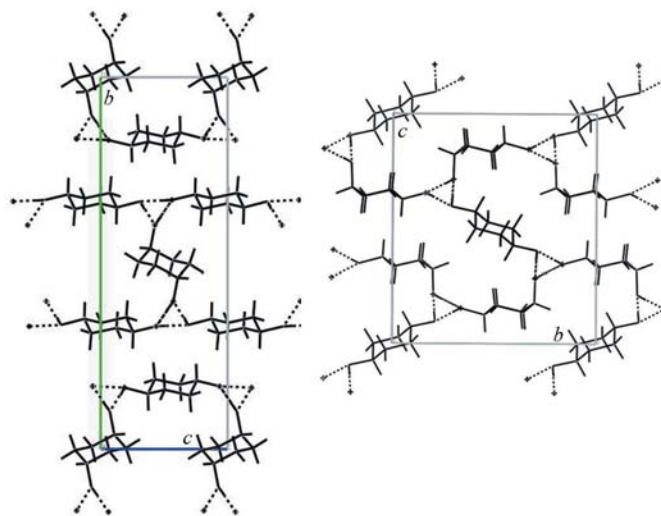
### 2.1. Ladders and brick walls

The striking feature of the structures of both POVSEY and (I) are the hydrogen-bond patterns in the two. The projections along the  $a$  axis are shown in Fig. 2. Each pure CHD structure has three distinct hydrogen bonds as shown in Table 1. Since the asymmetric unit in each structure has one axial and two equatorial hydroxyls, the hydroxyl orientation is used to identify the bonds. In all cases, the axial donor is the shortest of the three hydrogen bonds. The intramolecular O—O distances for POVSEY01 and for (II) are included for comparison.

An analysis of these patterns using the Etter graph-set (GS) model (Etter, 1990; Etter *et al.*, 1990), as further developed by Bernstein *et al.* (1995), shows that each structure has the same three motifs.  $N_1 = D_2^2(8) C(7) D_2^2(10)$  and  $N_1 = D_2^2(8) D_2^2(10) C(7)$  for POVSEY and (I), respectively. The most obvious hydrogen-bond pattern which occurs at the third level is an OH...OH...OH  $C(2)$  chain forming a triangular helix in each of the two structures. It is at the  $N_2$  level that the differences between the patterns appear. It is also at this level that the GS assignment becomes a problem.

### 2.2. POVSEY structure

The POVSEY structure has ladder patterns at the binary level. Nguyen *et al.* (2001) have analyzed hydrogen-bonded diol ladders, but their set of examples shows only one-

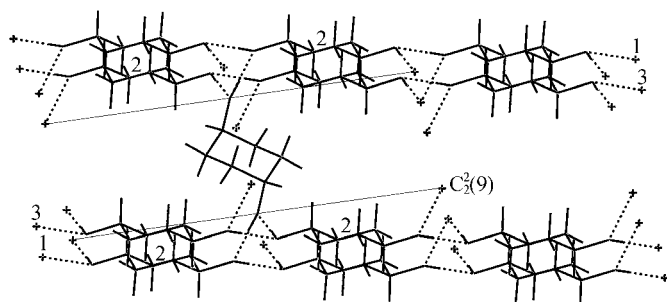


**Figure 2**

The unit cells of POVSEY (left) and (I), looking along the  $a$  axis and the triangular helical  $C(2)$  hydrogen-bond chain.

dimensional molecular ladders, with molecular chains forming the rails which are interlinked with hydrogen bonds supplying the rungs. They are not the intersecting ladders which form the two- and three-dimensional structures observed with 1,4-CHD, which in addition have molecules acting as rungs to link the molecular chain rails. Hydrogen-bonded ladders have not been addressed in any authoritative way to allow a simple graph-set assignment. In an earlier work (Loehlin *et al.*, 1998) we made some suggestions on how to assign graph sets to ladders. In POVSEY (see Fig. 3) the centrosymmetric biaxial diols form the rungs of the ladders. The rails for two of the ladders (1 and 3) are the  $C(7)$  chains running in the  $c$  direction. The rungs act as donors in one ladder (1) and as acceptors in the other (3). The third ladder (2) is formed by the rungs, utilizing both donor and acceptor hydrogen bonds at each end, linking the biequatorial molecules so that the OH groups of the rung diol are part of the rails. The rails in this case are  $C_2^2(9)$ , diagonally intersecting adjacent  $C(7)$  chains. Using our earlier designation for the ladder graph sets,  $N_2 = 2C(7)[R_6^6(32)] 2C_2^2(9)[R_4^4(28)] 2C(7)[R_6^6(32)]$ , where the three ladders are each designated by two rails consisting of chains, linking a series of rings formed from the rails and adjacent rungs. The end result is a two-dimensional, bilayered sheet structure, with sheets linked by the centrosymmetric biaxial, ladder rungs, with only weak forces between adjacent bilayers.

As the crystal contains both  $a \bar{a}$  and  $e \bar{e}$  conformers, Steiner and Saenger suggest that POVSEY can almost be considered a co-crystal. This designation should probably be reserved for materials where the species do not interconvert during the time needed for crystal growth. The structures of two 1,4-disubstituted-1,4-CHDs, CEMQOA and CEMQOA01 (Bilton *et al.*, 1999), also have *trans*, mixed axial and equatorial conformers, and the authors address the question of nomenclature of crystals of this type. In these, the three motifs are  $C_2^2(14)$  chains along different axial directions. At the binary level they interconnect all the molecules in the crystals. There are  $C(2)$  helices of direct  $\text{OH} \cdots \text{O}$  hydrogen bonds at the ternary level, similar to POVSEY, (I) and (II). Structure (I) is a co-crystal since the molecules making up the crystal are not merely different conformations of the same molecule, but separate *cis* and *trans* isomers which cannot be interconverted without breaking chemical bonds.

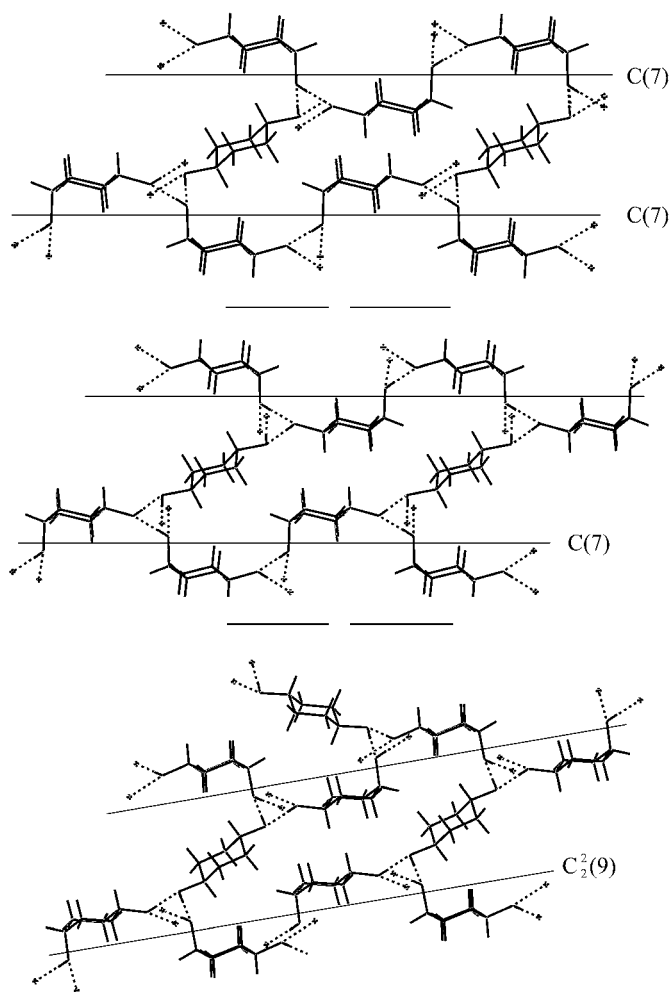


**Figure 3**  
POVSEY ladders utilizing a single  $a \bar{a}$  rung. The four parallel  $C(7)$  rails belong to ladders 1 and 3. Ladder 2 with  $C_2^2(9)$  rails uses the molecules labeled 2.

### 2.3. Structure (I)

As pointed out above, it is at the binary level that the GS assignment in (I) is more complicated.  $C(7)$  ladder rails are still present, formed by *cis* isomers related to adjacent ones by  $2_1$  symmetry, but now the 'rungs' project from alternate sides of each rail. Thus, in the place of ladders, we have a two-dimensional sheet with a 'brick-wall' arrangement, where hydrogen bonds of the 'mortar' hold the sheet together at the intersections of the 'bricks'. The sheets formed by pairs of hydrogen bonds intersect each other as did the ladders in POVSEY, now linking them together at the ternary level into a three-dimensional network connecting all of the molecules in the crystal. Fig. 4 shows each of the sheets in a projection similar to that of POVSEY ladders in Fig. 3.

The replacement of the simple rails in POVSEY with rails having  $2_1$  symmetry in (I) suggests that we designate each graph set by replacing the 2 for a simple ladder with a  $2_1$  to indicate the alternating 'rung' directions. [We use  $2_1$  with the  $C_2^2(9)$  chains although the adjacent rail links involve a translation as well as the  $2_1$  operation.] Thus, we obtain the



**Figure 4**  
The three binary GS networks of (I). The viewpoints of the three are slightly different to make clear the hydrogen bonds not utilized in that pattern. Straight lines have been drawn to show the chain directions.

**Table 2**  
Experimental details.

	CHDct (I)	CHDdis (II)
Crystal data		
Chemical formula	<i>cis</i> -C <sub>6</sub> H <sub>12</sub> O <sub>2</sub> – <i>trans</i> -C <sub>6</sub> H <sub>12</sub> O <sub>2</sub> (2/1)	<i>cis</i> -C <sub>6</sub> H <sub>12</sub> O <sub>2</sub> / <i>trans</i> -C <sub>6</sub> H <sub>12</sub> O <sub>2</sub> (2/1)
<i>M<sub>r</sub></i>	348.47	348.47
Cell setting, space group	Monoclinic, <i>P</i> <sub>2</sub> <sub>1</sub> / <i>c</i>	Monoclinic, <i>P</i> <sub>2</sub> <sub>1</sub> / <i>c</i>
Temperature (K)	193	293
<i>a</i> , <i>b</i> , <i>c</i> (Å)	6.453 (2), 11.678 (4), 13.396 (4)	6.5263 (3), 11.527 (1), 14.2082 (3)
$\beta$ (°)	101.378 (6)	100.123 (6)
<i>V</i> (Å <sup>3</sup> )	989.7 (6)	1052.22 (11)
<i>Z</i>	2	2
<i>D<sub>x</sub></i> (Mg m <sup>-3</sup> )	1.169	1.100
Radiation type	Mo <i>K</i> $\alpha$	Mo <i>K</i> $\alpha$
$\mu$ (mm <sup>-1</sup> )	0.09	0.08
Crystal form, color	Narrow plate, colorless	Prism, colorless
Crystal size (mm)	0.20 × 0.14 × 0.12	0.50 × 0.35 × 0.22
Data collection		
Diffractometer	Bruker SMART CCD	Siemens P4
Data collection method	$\omega/2\theta$	$\omega/2\theta$
Absorption correction	None	None
No. of measured, independent and observed reflections	6517, 2331, 1407	6016, 2042, 675
Criterion for observed reflections	<i>I</i> > 3.00 <i>u</i> ( <i>I</i> )	<i>I</i> > 2.00 <i>u</i> ( <i>I</i> )
<i>R</i> <sub>int</sub>	0.07	0.03
$\theta_{\max}$ (°)	27.9	26.3
Refinement		
Refinement on	<i>F</i> <sup>2</sup>	<i>F</i> <sup>2</sup>
<i>R</i> [ <i>F</i> <sup>2</sup> > 2 $\sigma$ ( <i>F</i> <sup>2</sup> )], <i>wR</i> ( <i>F</i> <sup>2</sup> ), <i>S</i>	0.048, 0.119, 1.02	0.068, 0.150, 0.91
No. of reflections	1407	675
No. of parameters	122	118
H-atom treatment	Mixture†	Mixture†
Weighting scheme	Method = Prince modified Chebychev polynomial (Watkin, 1994); <i>W</i> = [weight] * [1 – ( $\delta F/6\sigma F$ ) <sup>2</sup> ] <sup>2</sup> 24.1 37.9 18.5 4.67	Method = Prince modified Chebychev polynomial (Watkin, 1994); <i>W</i> = [weight] * [1 – ( $\delta F/6\sigma F$ ) <sup>2</sup> ] <sup>2</sup> 21.1 30.8 13.7 2.59
( $\Delta/\sigma$ ) <sub>max</sub>	< 0.0001	0.004
$\Delta\rho_{\max}$ , $\Delta\rho_{\min}$ (e Å <sup>-3</sup> )	0.24, –0.22	0.36, –0.14

Computer programs used: omega scans 0.3deg/frame, 1271 frames, *XSCANS* (Siemens, 1993), *SMART*, *SAINTE*, *SIR92*, *SIR97* (Altomare *et al.*, 1994), *CRYSTALS* (Watkin *et al.*, 2001), *CAMERON* (Watkin *et al.*, 1996), *MERCURY* (Bruno *et al.*, 2002). † Mixture of independent and constrained refinement.

binary GS designation, in the standard increasing order of priority, *N*<sub>2</sub> = 2<sub>1</sub>*C*<sub>2</sub><sup>2</sup>(9)[*R*<sub>8</sub><sup>8</sup>(46)] 2<sub>1</sub>*C*(7)[*R*<sub>8</sub><sup>8</sup>(46)] 2<sub>1</sub>*C*(7)[*R*<sub>8</sub><sup>8</sup>(46)].

The 1,6-cyclododecane diols are in a number of ways similar to 1,4-CHD. Structures of pure *trans*, CDECOL11 (Ermer *et al.*, 1973), pure *cis*, VENIX, along with a 2:1 *cis:trans* co-crystal VENZOD (Ermer *et al.*, 1989) have been determined. VENZOD and a co-crystal formed by hydroquinone and an unrelated diol, UHAZOS (Yue *et al.*, 2002), have similar linkage patterns to that observed in (I).

### 3. Experimental

Most of the experimental details of the two structures reported here are shown in Table 2<sup>1</sup> and packing diagrams are shown in Fig. 5.

<sup>1</sup> Supplementary data for this paper are available from the IUCr electronic archives (Reference: BK5075). Services for accessing these data are described at the back of the journal.

The same atomic numbering scheme was used for both (I) and (II). The bonding in the individual molecules and the individual hydrogen bonds linking the molecules together show no unusual bond lengths or angles.

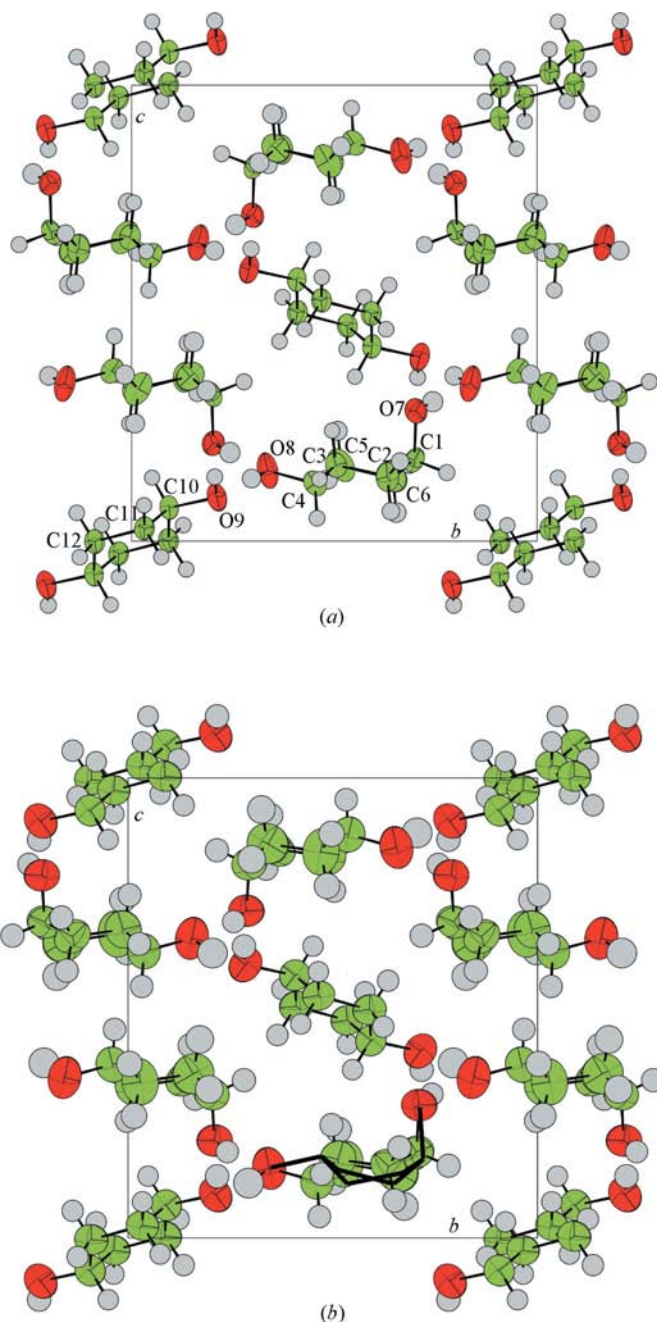
#### 3.1. Discussion of disorder in (II)

After obtaining structure (I) we decided to compare it with the previously obtained data for (II). The two sets of data were collected at different temperatures, but the anisotropic variation of the cell parameters may not be a purely thermal effect. There is also a qualitative difference in the atomic displacement parameters for the molecules in general positions, with ellipsoids of the ring atoms at the *e* side of the molecule appearing elongated normal to the ring. Even though the data do not allow much confidence in the numerical values of these parameters, they and the locations of residuals during refinement appeared to be consistent with chair/boat disorder of the cyclohexane ring of the molecules in general positions. As the reported *cis/trans* percentage in the starting material was 56/43, implying that about 15% of it was excess *trans* isomer above the 2:1 *cis/trans* ratio observed in (I), a possible *trans*-for-*cis* disorder seemed plausible. Models suggest that *trans* isomers in the boat configuration might have a similar

shape and hydrogen-bonding geometry to the *cis* chair. Transformation of isomers from one conformation to another is supported by the two different conformations found in POVSEY. Thus, if one of the free, excess *trans* molecules formed one hydrogen bond at what should be a *cis* site on the growing surface, and could readily change its conformation to approximate a *cis* molecule, the formation of a disordered crystal would appear logical. In addition, since the crystals of (II) were grown by sublimation, kinetic factors should play a larger part than thermodynamic ones relative to growth from solution.

To further test this hypothesis, we used molecular mechanics to model the expected geometry of the individual isocons. We used *SPARTAN* (Wavefunction Inc., 2004) and constructed each isocon individually and then allowed minimization using Hartree–Fock 3-21G(\*). The *aa* isocon gave separate minima depending on whether or not intramolecular hydrogen bonding occurred. All isocon models relaxed to

reasonable conformations. Boat conformations tended to be twisted, while chairs were close to ideal. For intercomparison, we used the C1–C4 line to represent the ring and calculated the C–O angles to this line. These angles and the intramolecular O–O distance allow comparisons among different isocons and between models and actual structures where they are known. These measurements are shown in Table 3. Manipulation of the *trans*-boat *a e* isocon shows that it is more



**Figure 5**  
The structures of (I) and (II). The atomic numbering scheme is given for structure (I) in (a). The same scheme was used in (b) for (II) which has the heavy atom outline for the *a e* isocon from the SPARTAN model superimposed. All displacement ellipsoids are at 50% probability.

**Table 3**

Calculated intramolecular O–O distances (Å), the C–O–O' angles (°), and the energies (kJ mol<sup>-1</sup>) from molecular modeling (SPARTAN, Wavefunction Inc., 2004) for all 1,4-CHD isocons.

Measured values from CSD and this study are included unless identical by crystal symmetry.

		O...O	O–C...O'	O'–C'–O	Energy
<i>cis</i> -boat	<i>a a</i>				
SPARTAN	Hydrogen bonded	2.72	62.5	59.5	39.2
SPARTAN		4.84	114.7	114.6	38.1
<i>cis</i> -boat	<i>e e</i>				
SPARTAN		5.56	165.1	164.1	52.8
<i>trans</i> -boat	<i>a e</i>				
SPARTAN		4.44	165.0	90.2	48.0
<i>cis</i> -chair	<i>a ē</i>				
(I)		4.62	129.3	96.1	
(II)		4.64	145.4	111.1	
SPARTAN		4.57	126.8	93.9	24.3
<i>trans</i> -chair	<i>a ā</i>				
POVSEY		4.55	125.8		
POVSEY01		4.57	125.9		
POVSIC		4.48	131.7	118.1	
SPARTAN		4.55	125.8	20.8	
<i>trans</i> -chair	<i>e ē</i>				
POVSEY		5.60	160.5	159.9	
POVSEY01		5.62	160.4	160.1	
(I)		5.60	160.3		
(II)		5.64	150.3		
JEGZAX		5.63	159.8		
SPARTAN		5.58	158.5	28.7	

flexible than the chair conformers. Not only can the cyclohexane ring twist in either direction, but also the O–O distance may vary by >20% in conjunction with the degree of twist. Superposition of the heavy atom skeleton of the minimized *a e* model at the same scale as the crystal structure of (II) is shown in Fig. 5(b).

#### 4. Discussion and conclusions

Clearly our dataset for (II) is inadequate for more than indicating the plausibility of this model. Testing this hypothesis will probably require samples of pure isomers to adjust the composition of starting materials. Perhaps some other investigator can obtain the necessary materials and investigate this system more thoroughly. The data in Table 3 also suggest that the *e e* isocon just might be induced to substitute for the *e ē* one in some other mixed-isomer growth situation.

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