

## Synthesis of a New Cyclophane Host and Crystal Structures of Its Compounds with Neutral Guests

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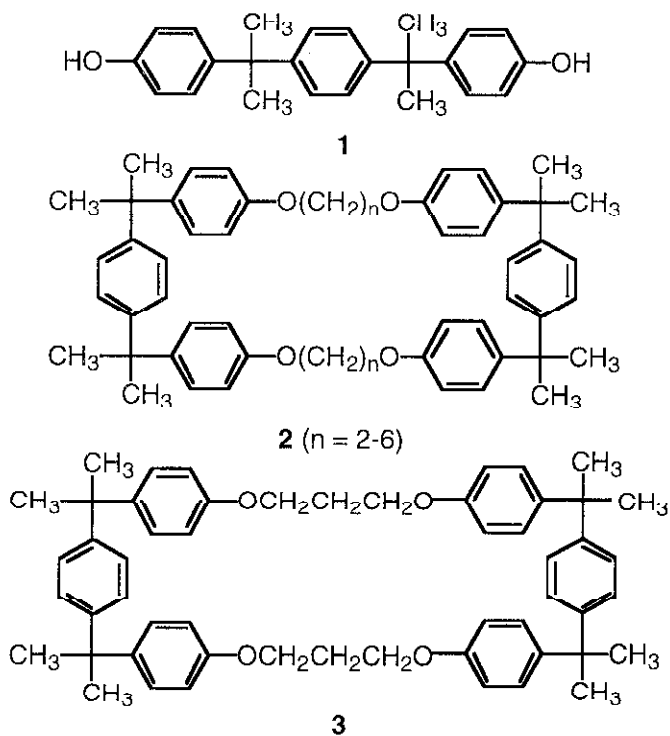
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**Abstract.** A new cyclophane host molecule **3** is prepared by connecting the oxygen atoms of two  $\alpha,\alpha'$ -di(4-hydroxyphenyl)-1,4-diisopropylbenzene units with two trimethylene spacers. Solid-state structures are determined for compounds of **3** with dichloromethane and *p*-xylene guests. The crystals of the two host-guest compounds are isomorphous.

**Key words.** Cyclophane, molecular receptor, inclusion compound, solid-state structure

### 1. Introduction

During the past three decades, a variety of macrocyclic receptors for the complexation of molecular species have been synthesized [1, 2]. Guest species are complexed within the central cavities of the cyclophane host molecules. With the goal of providing a new family of cyclophanes receptors, we are using the relatively unexplored bisphenol **1** [3] as a  $\pi$ -electron rich, hydrophobic unit for the construction of hosts **2** in which the dimensions of the central cavity can be systematically varied by changing the length of the multi-methylene spacers. It was envisioned that due to their rigidity, the  $\alpha,\alpha'$ -di(4-oxyphenyl)-1,4-diisopropylbenzene units would provide an open cavity in which  $\pi$ -interactions would encourage the complexation of aromatic guest species. Since the aromatic guests would be contained within the central cavities of the receptors, the cyclophane hosts **2** are termed "corrals". We now report the synthesis of cyclophane **3**, the first member of this family of new host molecules and the solid-state structures for compounds of this corral with dichloromethane and *p*-xylene guests.



## 2. Experimental

IR spectra were taken with a Perkin Elmer Model 1600 spectrophotometer.  $^1H$  NMR spectra were recorded with IBM AF-200 and Varian Gemini 200 MHz spectrometers and chemical shifts are reported in parts per million ( $\delta$ ) downfield from TMS. Combustion analysis was performed by Desert Analytics Laboratories of Tucson, Arizona. All X-ray data were obtained using a Siemens R3m/V automated diffractometer with Mo,  $K\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ). Programs used for solving, refining and displaying these structures are contained in the SHELXTL-PLUS program package [4].

### 2.1. MATERIALS

Unless specified otherwise, reagent grade reactants and solvents were used as received from chemical suppliers. Bisphenol **1** and cesium carbonate were obtained from TCI America and Chemetall GMBH (marketed in the U.S.A. by CM Chemical Products, Inc. of Berkeley Heights, New Jersey), respectively. DMF was distilled from calcium hydride.

## 2.2. SYNTHESIS OF HOST 3

### 2.2.1. Preparation of $\alpha,\alpha'$ -Di[(3-bromo-1-propoxy)phenyl]-1,4-diisopropylbenzene

A mixture of bisphenol **1** (1.73 g, 5.0 mmol), 1,3-dibromopropane (20.19 g, 0.10 mol), and 5.0 g of freshly ground potassium carbonate in 50 mL of DMF was stirred at room temperature for 15 hours. The mixture was filtered, the filtrate was evaporated *in vacuo*, and the residue was dissolved in dichloromethane. The solution was washed twice with water and evaporated *in vacuo*. The residue was chromatographed on silica gel with dichloromethane (1:1) as eluent to give 2.32 g (79%) of the title compound which was contaminated with a small amount of the monoallyl monobromo elimination product. Since attempts to remove this contaminant by chromatography were unsuccessful, the slightly impure compound was used for the next step.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.62 (s, 12H), 2.84 (q, 4H), 3.58 (t, 4H,  $J = 6.4$  Hz), 4.06 (t, 4H,  $J = 5.4$  Hz), 6.79 and 7.14 (dd, 8H,  $J = 8.8$  Hz), 7.09 (s, 4H).

### 2.2.2. Preparation of Cyclophane 3

A mixture of the dibromide prepared above (0.59 g, 1.0 mmol), bisphenol **1** (0.35 g, 1.0 mmol), and 2.15 g of pulverized cesium carbonate in 500 mL of DMF was stirred at 50-70 °C under nitrogen for 7 days. After the DMF was removed under *in vacuo*, water and dichloromethane were added to the residue. The organic layer was separated, washed with water, dried over magnesium sulfate, and evaporated *in vacuo*. The residue was chromatographed on silica gel with dichloromethane hexane (1:1) as eluent to give 0.15 g (40%) of white solid with mp = 268-270 °C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  1.62 (s, 24H), 2.19 (q, 4H), 4.07 (t, 8H), 6.75 and 7.07 (dd, 16H,  $J = 8.8$  Hz), 7.09 (s, 8H). IR (KBr) 3036, 2966, 2919, 2872, 1601, 1507, 1467, 1402, 1384, 1361, 1290, 1249, 1184, 1061, 1014, 826, 755, 591  $\text{cm}^{-1}$ . *Anal. Calcd.* for  $\text{C}_{54}\text{H}_{60}\text{O}_4 \cdot 0.5\text{H}_2\text{O}$ : C, 82.93; H, 7.86. *Found*: C, 82.63; H, 7.80.

## 2.3. PREPARATION OF HOST-GUEST COMPOUNDS

Crystallization of **3** from dichloromethane and from *p*-xylene gave the **3**-dichloromethane (**3**-DCM) and **3**-*p*-xylene (**3**-XYL) compounds, respectively.

## 2.4. STRUCTURE DETERMINATIONS

The lattice parameters and the orientation matrix of each crystal were obtained using a least-squares procedure with an appropriate number of carefully centered reflections. The crystal data and experimental details for the two compounds are listed in Table I. The lattice parameters for the two compounds are similar which suggested that the two crystals were isomorphous. Because the host molecule contains a different guest in the two compounds, each structure was solved by direct methods. When symmetry transformations were applied to the atomic coordinates obtained from the refinement of **3**-XYL, it was apparent that chemically identical atoms of the

Table I. Crystal data and experimental details

|  | 3-DCM   | 3-XYL   |
|--|---|---|
| Formula  | $C_{54}H_{60}O_4 \cdot CH_2Cl_2$                          | $C_{54}H_{60}O_4 \cdot C_8H_{10}$                         |
| Formula weight                                     | 857.9   | 879.2   |
| F(000)   | 458   | 474   |
| Crystal size, mm                                   | 0.18x0.20x0.40  | 0.20x0.30x0.50  |
| $\mu$ , mm <sup>-1</sup>                           | 0.173   | 0.071   |
| Temperature, °C                                    | 20  | 20  |
| Crystal system                                     | triclinic   | triclinic   |
| Space group  | $P \bar{1}$   | $P \bar{1}$   |
| a, Å   | 5.965(2)  | 6.007(2)  |
| b, Å   | 13.066(4)   | 13.091(3)   |
| c, Å   | 16.670(4)   | 16.576(5)   |
| $\alpha$ , °                                       | 99.65(2)  | 101.58(2)   |
| $\beta$ , °  | 92.83(2)  | 90.80(2)  |
| $\gamma$ , °                                       | 101.74(2)   | 101.28(2)   |
| V, Å <sup>3</sup>                                  | 1249.3  | 1250.4  |
| Z  | 1   | 1   |
| $\rho$ , kg/m <sup>3</sup>                         | 1.14  | 1.17  |
| Max $2\theta$ , °                                  | 45  | 45  |
| Total data   | 3665  | 3657  |
| Unique data  | 3287( $R_{int}=2.23\%$ )                                  | 3284( $R_{int}=1.13\%$ )                                  |
| Observed data                                      | 1382( $F>4.0\sigma(F)$ )                                  | 1819( $F>6.0\sigma(F)$ )                                  |
| R  | 7.89%   | 9.56%   |
| $R_w$  | 7.79%   | 10.05%  |
| Data/parameter                                     | 4.9/1   | 6.0/1   |
| Goodness of fit                                    | 1.47  | 1.49  |
| Largest peak, $\Delta\mu_{map}$ , eÅ <sup>-3</sup> | 0.41  | 0.32  |
| Largest hole, $\Delta\mu_{map}$ , eÅ <sup>-3</sup> | -0.24   | -0.22   |
| Index range  | $0 \leq h \leq 6, -14 \leq k \leq 13, -17 \leq l \leq 17$ | $0 \leq h \leq 6, -14 \leq k \leq 13, -17 \leq l \leq 17$ |

hosts were situated in nearly identical positions in the two compounds. The host molecule in each structure is located about the center of inversion at 1/2,1/2,1/2. The non-hydrogen atoms of both host molecules were refined anisotropically with the exception of O26', a disordered oxygen atom in 3-XYL.

#### 2.4.1. Structure of 3-Dichloromethane (3-DCM)

It was not anticipated that the **3** crystallized from dichloromethane would contain a solvent molecule. However, the peaks in the difference map indicated that a dichloromethane molecule was present. This was later confirmed by  $^1\text{H}$  NMR spectroscopy of a solution of **3**-DCM in deuteriochloroform. The structure of the compound is shown in Figure 1. There are no short interatomic distances between the chlorine atoms of the guest and an atom of the host. The shortest distance, 3.812 Å, is between Cl(1) and C2. These long distances indicate that there are weak or no interactions between the guest and the host, which explains the large thermal parameters of the non-hydrogen atoms of the guest. The absence of short contact distances between the guest and the host indicates that even though the dichloromethane molecule is encapsulated in the host (see Table IV), **3** is not distorted by the guest. Therefore, the conformation of the host in **3**-DCM may be assumed to be that of uncomplexed **3** for comparison purposes. Positions of the hydrogen atoms bonded to the carbon atoms in **3** and C30 of the guest were calculated. These hydrogen atoms were allowed to ride on their neighboring carbon atoms during the refinement and were assigned isotropic thermal parameters which were not refined.

#### 2.4.2. Structure of 3-Xylene (3-XYL)

The *p*-xylene guest in **3**-XYL was evident in the E-map and the carbon atoms of the guest were also refined anisotropically. The structure of the complex is shown in Figure 3. The *p*-xylene molecule is located about the same center of symmetry as the host. Disorder of O26 in the host was resolved using difference maps. The occupancy factors for the atom sites were initially estimated from peak heights in the difference maps, and then refined with O26 having an occupancy of 0.93 and O26' an occupancy factor of 0.07. The bond lengths involving O26 and O26' were constrained to have normal values during the refinement. The O26 in **3**-XYL refined to a position similar to that of O26 in **3**-DCM. The positional parameters of all hydrogen atoms of **3**-XYL were calculated and isotropic thermal parameters were assigned to those atoms. The methyl group of the *p*-xylene guest was refined as a rigid body.

### 3. Results and Discussion

#### 3.1. SYNTHESIS OF CYCLOPHANE **3** AND ITS COMPLEXES

The new molecular receptor **3** was prepared in two steps from commercially available  $\alpha,\alpha'$ -di(4-hydroxyphenyl)-1,4-diisopropylbenzene (**1**). Reaction of **1** with 10 equivalents of 1,3-dibromopropane and potassium carbonate in DMF gave  $\alpha,\alpha'$ -di[(3-bromo-1-propoxy)phenyl]-1,4-diisopropylbenzene. Cyclization of equivalent amounts of this dibromide and bisphenol **1** with cesium carbonate in DMF gave a 40% yield of corral **3** whose structure was verified by NMR and IR spectroscopy and by combustion analysis.

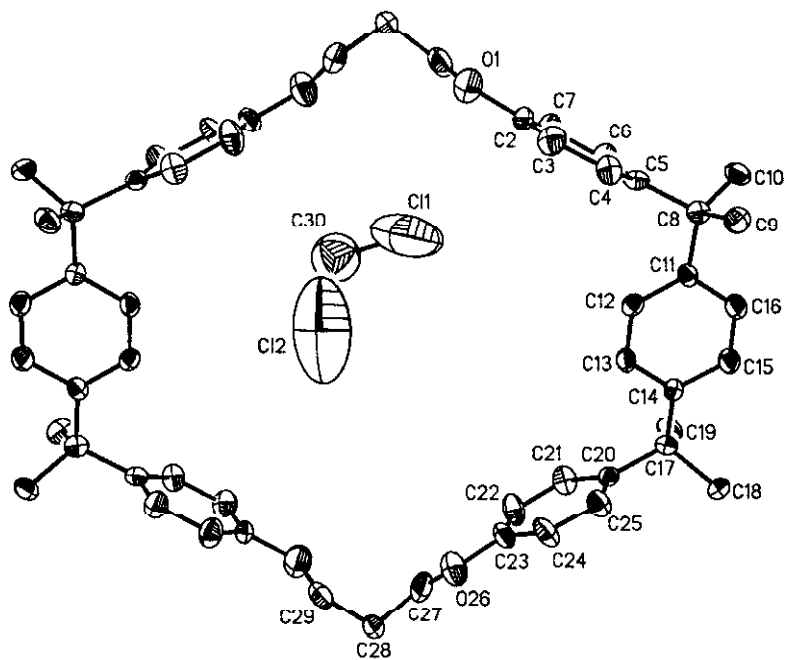


Figure 1. A computer drawing of the crystal structure of 3-DCM with the thermal ellipsoids drawn at the 25% probability level. Hydrogen atoms are omitted for clarity.

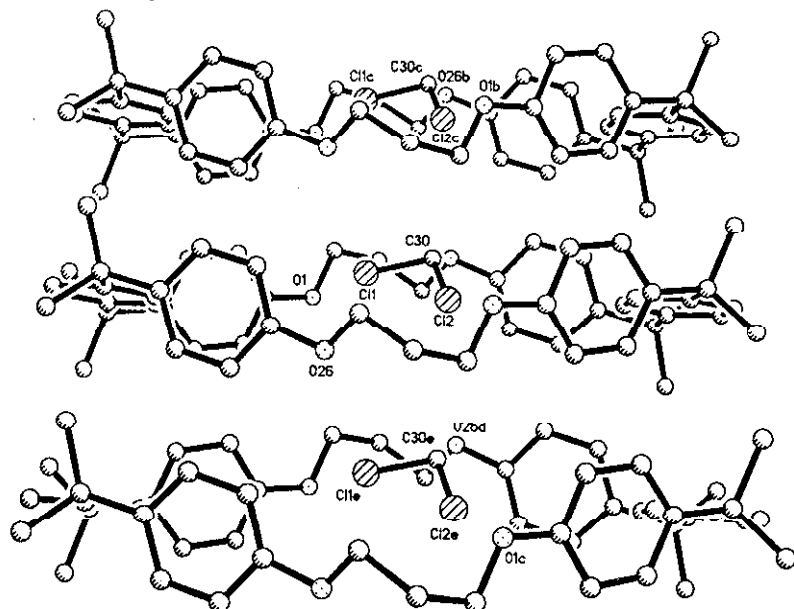


Figure 2. A stacking drawing of 3-DCM which illustrates the one-to-one stoichiometry of the compound.

Crystallization of corral **3** from dichloromethane and *p*-xylene gave **3**-dichloromethane (**3**-DCM) and **3**-*p*-xylene (**3**-XYL), respectively.

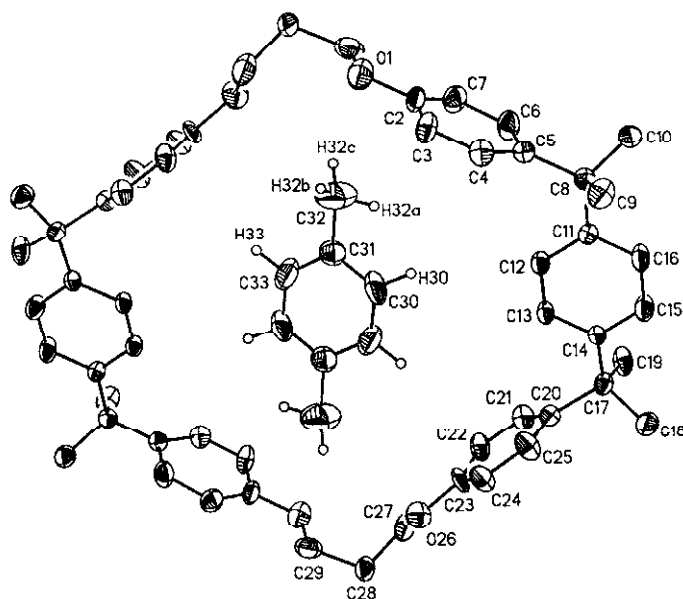


Figure 5. A computer drawing of the crystal structure of **3**-XYL with the thermal ellipsoids drawn at the 25% probability level. Hydrogen atoms of the host and the disordered oxygen O26' are omitted for clarity.

### 3.2 STRUCTURE DETERMINATIONS

Positional parameters and the equivalent isotropic displacement coefficients of the atoms of **3**-DCM and **3**-XYL are listed in Tables II and III, respectively. The isomorphism of the hosts in the two compounds is apparent from a comparison of the positional parameters for atoms of the host. Computer drawings of **3**-DCM and **3**-XYL are displayed in Figures 1 and 3, respectively. The similarity of the structures is readily apparent from the figures. The only significant difference in the two compounds is the different guest molecules present. Rigidity caused by the two  $\alpha,\alpha'$ -di(4-oxyphenyl)-1,4-diisopropylbenzene units in the host is a major causative factor for the similarity of the host structures in the two compounds.

In both compounds, the host molecule lies about a center of inversion at  $1/2, 1/2, 1/2$ . In **3**-XYL, the guest molecule also lies about the same center of inversion. The non-hydrogen atoms of the guest in **3**-DCM are planar and lie near the  $1/2, 1/2, 1/2$  center of symmetry.

Least-squares planes were calculated for the host in the two molecules. In each case O1, C8, C17, O26 and their symmetry related atoms were used to calculate the plane. Least-squares planes were also calculated for the guests of the **3**-DCM and **3**-XYL molecules using all of the non-hydrogen atoms of

Table II. Atomic coordinates ( $\times 10^4$ ) and equivalent isotropic displacement coefficients ( $\text{\AA}^2 \times 10^3$ ) for the non-hydrogen atoms of 3-DCM.

|       | x         | y        | z        | U(eq) <sup>a</sup>   |
|-------|-----------|----------|----------|----------------------|
| O1    | -489(15)  | 6777(7)  | 2738(5)  | 96(4)                |
| C2    | -166(21)  | 5851(9)  | 2244(7)  | 65(5)                |
| C3    | 1684(21)  | 5971(8)  | 1802(7)  | 72(5)                |
| C4    | 2077(17)  | 5138(8)  | 1264(6)  | 59(4)                |
| C5    | 718(15)   | 4127(7)  | 1155(6)  | 45(4)                |
| C6    | -1103(17) | 4013(8)  | 1633(6)  | 68(5)                |
| C7    | -1573(19) | 4858(9)  | 2181(6)  | 77(5)                |
| C8    | 1092(15)  | 3170(7)  | 553(5)   | 45(4)                |
| C9    | 2886(17)  | 3553(8)  | -51(6)   | 67(5)                |
| C10   | -1187(15) | 2593(7)  | 48(6)    | 63(4)                |
| C11   | 2101(15)  | 2402(8)  | 1000(6)  | 44(4)                |
| C12   | 3031(14)  | 2659(7)  | 1796(6)  | 46(4)                |
| C13   | 3992(16)  | 1965(7)  | 2171(5)  | 50(4)                |
| C14   | 4012(15)  | 950(7)   | 1768(5)  | 39(3)                |
| C15   | 3091(17)  | 681(7)   | 953(6)   | 58(4)                |
| C16   | 2148(17)  | 1383(8)  | 593(6)   | 59(4)                |
| C17   | 4882(15)  | 116(7)   | 2184(5)  | 45(4)                |
| C18   | 6356(17)  | -483(8)  | 1609(6)  | 69(5)                |
| C19   | 2767(15)  | -708(7)  | 2324(6)  | 63(4)                |
| C20   | 6364(16)  | 642(7)   | 2980(5)  | 43(4)                |
| C21   | 5679(19)  | 494(8)   | 3737(6)  | 68(5)                |
| C22   | 7094(22)  | 937(9)   | 4458(6)  | 80(5)                |
| C23   | 9191(20)  | 1548(8)  | 4428(6)  | 62(5)                |
| C24   | 9893(18)  | 1734(8)  | 3686(6)  | 80(5)                |
| C25   | 8522(17)  | 1278(10) | 2978(6)  | 66(5)                |
| O26   | 10773(14) | 2034(7)  | 5090(5)  | 96(4)                |
| C27   | 10475(23) | 1647(10) | 5802(7)  | 101(7)               |
| C28   | 12511(21) | 2175(9)  | 6417(7)  | 92(6)                |
| C29   | 12361(19) | 3297(10) | 6812(7)  | 83(6)                |
| Cl(1) | 2070(39)  | 5448(25) | 4325(19) | 478(25)              |
| Cl(2) | 5627(43)  | 5627(18) | 5694(11) | 555(23)              |
| C30   | 2521(58)  | 5774(41) | 5391(19) | 243(24) <sup>b</sup> |

<sup>a</sup>Equivalent isotropic U defined as one third of the trace of the orthogonalized  $U_{ij}$  tensor.

<sup>b</sup>Isotropic U value.



Table III. Atomic coordinates ( $\times 10^4$ ) and equivalent isotropic displacement coefficients ( $\text{\AA}^2 \times 10^3$ ) for the non-hydrogen atoms of 3-XYL.

|      | x         | y        | z       | U(eq) <sup>a</sup>  |
|------|-----------|----------|---------|---------------------|
| O1   | -661(14)  | 6891(6)  | 2703(4) | 91(4)               |
| C2   | -329(20)  | 5950(7)  | 2189(6) | 66(4)               |
| C3   | 1553(20)  | 6023(7)  | 1777(6) | 75(5)               |
| C4   | 2007(16)  | 5149(7)  | 1251(5) | 64(4)               |
| C5   | 649(14)   | 4152(6)  | 1146(5) | 47(3)               |
| C6   | -1207(17) | 4095(8)  | 1597(6) | 78(4)               |
| C7   | -1723(17) | 4993(8)  | 2138(6) | 75(5)               |
| C8   | 1135(14)  | 3182(6)  | 546(5)  | 49(3)               |
| C9   | 2875(17)  | 3502(7)  | -63(5)  | 75(4)               |
| C10  | -1084(16) | 2599(7)  | 55(6)   | 71(4)               |
| C11  | 2063(13)  | 2426(6)  | 999(5)  | 44(3)               |
| C12  | 2981(14)  | 2731(6)  | 1803(5) | 49(3)               |
| C13  | 3932(14)  | 2052(6)  | 2177(5) | 48(3)               |
| C14  | 3972(13)  | 1009(6)  | 1786(5) | 46(3)               |
| C15  | 3064(17)  | 717(7)   | 978(5)  | 70(4)               |
| C16  | 2144(17)  | 1410(7)  | 600(5)  | 67(4)               |
| C17  | 4800(15)  | 198(6)   | 2197(5) | 51(3)               |
| C18  | 6266(17)  | -408(8)  | 1632(6) | 79(5)               |
| C19  | 2715(16)  | -586(6)  | 2350(5) | 71(4)               |
| C20  | 6227(14)  | 733(6)   | 3001(5) | 47(3)               |
| C21  | 5569(17)  | 585(7)   | 3768(6) | 64(4)               |
| C22  | 6971(19)  | 988(7)   | 4470(5) | 68(4)               |
| C23  | 9074(18)  | 1524(7)  | 4434(5) | 63(4)               |
| C24  | 9744(17)  | 1751(8)  | 3689(6) | 78(5)               |
| C25  | 8357(16)  | 1344(8)  | 2994(6) | 76(4)               |
| O26  | 10721(15) | 1947(6)  | 5072(4) | 83(4)               |
| O26' | 8945(106) | 1880(58) | 5271(6) | 57(35) <sup>b</sup> |
| C27  | 10431(23) | 1565(8)  | 5768(7) | 100(6)              |
| C28  | 12497(19) | 2002(8)  | 6359(6) | 81(5)               |
| C29  | 12545(18) | 3162(9)  | 6843(7) | 90(5)               |
| C30  | 4134(24)  | 4505(10) | 4249(7) | 102(6)              |
| C31  | 3411(20)  | 5400(10) | 4600(8) | 89(6)               |
| C32  | 1634(26)  | 5810(13) | 4225(9) | 178(11)             |
| C33  | 4236(26)  | 5849(9)  | 5367(9) | 144(7)              |

<sup>a</sup>Equivalent isotropic U defined as one third of the trace of the orthogonalized  $U_{ij}$  tensor.<sup>b</sup>Isotropic U value.

the guests. Table IV lists the dihedral angle between the planes of the guest and the host for each compound. Also the maximum distances that an atom of the guest and an atom of the host deviates from the least-squares plane of the host are given. These data establish that in each structure the guest is encapsulated in its host.

Table IV. Comparison of least-squares planes for the host and guest.

| Complex | Dihedral angle between least-squares planes of the host and guest | Largest deviation of a guest atom from the least-squares plane of the host | Largest deviation of a host atom from the least-squares plane of the host* |
|---------|---|--|--|
| 3-DCM   | 42.3°   | 0.95 Å, C30  | 1.48Å, C4  |
| 3-XYL   | 9.2°  | 0.49Å, C32   | 1.44Å, C4  |

\*The methyl carbon atoms of the hosts are not considered in these data.

In 3-DCM, the guest does not contain a center of symmetry and symmetry conditions require that the cavity contain two guest molecules. This is not possible due to the short intermolecular contact distances, as discussed in the Experimental section. The relationship of the guest to the host is shown in Figure 1. The plane of the guest molecule forms a dihedral angle of 42.3° with the least-squares plane of the host, as calculated using atoms O1, C8, C17, O26 and their symmetry related atoms. The chlorine atoms are directed into the cavity of **3**. The short interatomic distance (2.323 Å) between Cl(1) and Cl(2)a, [Cl(2)a being related to Cl(2) by the center of inversion at 1/2,1/2,1/2] establishes that only one dichloromethane molecule can be present in the cavity of the host. To satisfy the condition of a center of symmetry with only one dichloromethane molecule present requires a statistically disordered structure in which half of the guest sites are vacant in an alternating fashion. This is illustrated in the stacking drawing shown in Figure 2. The atoms of the guest molecule were given occupancy factors of 0.50. The two chlorine atoms of the guest were refined anisotropically, while the carbon atom was refined isotropically. The large thermal motion of the guest atoms was discussed earlier. During the refinement process, the C-Cl bonds and Cl-Cl interatomic distance were constrained to values of 1.75 Å and 2.85 Å, respectively. The stoichiometry of the complex is one guest for each host.

Compound 3-XYL is the better characterized structure of the two host-guest compounds of corral **3**. All non-hydrogen atoms of both the host and guest were refined anisotropically. The data in Table IV shows that the guest

is encapsulated in the cavity of the corral host. A comparison of the conformation of **3** in **3**-DCM with that of **3** in **3**-XYL reveals some significant differences in the conformations of the host molecules in the two compounds. The orientation of the *p*-xylene guest in the cavity of the host (see Figure 3)

Table V. Interatomic distances of interest in the complexes

| Complex       | C28...C28a<br>interatomic distance (Å) | C12...C13a<br>interatomic distance (Å) |
|---------------|--|--|
| <b>3</b> -DCM | 13.840                                 | 11.096                                 |
| <b>3</b> -XYL | 14.275                                 | 10.809                                 |

suggests that the host is elongated in the direction of a line joining C28 with C28a and therefore shortened in the direction of a line joining C12 with C13a. These distances are compared for the two compounds in Table V and show that these changes do take place. The changes suggest weak intermolecular forces between the host and guest in **3**-XYL, which are not evident in **3**-DCM.

#### 4. Conclusions

The first member of a new family of molecular receptor cyclophanes called corrals has been synthesized. Corral host **3** forms inclusion compounds with dichloromethane and *p*-xylene guests. The host structures in the two compounds are isomorphous. In **3**-DCM, the guest is not tightly held in the host cavity. However for **3**-XYL, the intermolecular host-guest interactions are sufficiently large to distort the host molecule.

#### Acknowledgment

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