Role of Hydrogen Bond and Spacial Fitting in the Chiral Recognition by Cyclodextrins. Crystal Structures of Hexakis(2,3,6-tri-*O*-methyl)-α-cyclodextrin Inclusion Complexes with (*R*)- and (*S*)-1-Phenylethanol

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Crystal structures of 1:1 inclusion complexes of hexakis(2,3,6-tri-*O*-methyl)-α-cyclodextrin with (*R*)- and (*S*)-1-phenylethanol have been determined by X-ray analysis and refined to *R*-values of 0.077 and 0.073, respectively. In both isomorphous crystals, host molecules are arranged in a 'head-to-tail' mode which forms a column structure along the *a*-axis and guest molecules are aligned within the column. The phenyl group is inserted into the host molecule from the O(2), O(3) side and is in van der Waals contact with the inside wall of the host cavity. The hydroxyl group of the guests is hydrogen-bonded to an O(2) oxygen atom of the host. Compared with the disposition of the (*S*)-isomer in the host cavity, the (*R*)-isomer is rotated by 12° around an axis normal to the phenyl group. The geometry of the host–guest interaction indicates that the host molecule recognizes the phenyl group by the spacial fitting to the hydrophobic cavity and the hydroxy group by the hydrogen-bond formation.

Cyclodextrins, cyclic oligosaccharides consisting of six or more α-1,4-linked D-glucose units, form diastereoisomeric inclusion complexes with optically active guests. A number of reports have shown that cyclodextrins are effective reagents for the resolution of racemic compounds,[1] especially when utilized in liquid chromatography.[2] As a reagent for selective precipitation from aqueous solution, however, the ability of cyclodextrins for optical resolution has been found to be poor.[3,4] Some X-ray structural studies[5–7] have revealed that such poor ability is ascribed to the round and rigid structure of cyclodextrins. The cavity of cyclodextrins has pseudo C_n symmetry and sometimes includes (*R*)- and (*S*)-isomers equally.

Recently, we have found that permethylated α-cyclodextrin [hexakis(2,3,6-tri-*O*-methyl)-α-cyclodextrin, TM-αCDx] recognizes the chirality of mandelic acid and forms crystalline complexes having a different packing structure for each optical isomer.[8] 1-Phenylethanol is a chiral molecule having a similar structure to mandelic acid and has a methyl group instead of the carboxy group of mandelic acid. The X-ray structure analysis of TM-αCDx complexes with (*R*)- and (*S*)-1-phenylethanol (abbreviated to R-PE and S-PE, respectively) has been undertaken to investigate the effect of shape and size of the guest molecule on the chiral recognition by cyclodextrins.

Experimental

Crystallization and Data Collection.—TM-αCDx complexes with R-PE and S-PE were crystallized at 50 °C by slow evaporation of an aqueous solution containing TM-αCDx and guest with *ca.* 1:1 molar ratio. Crystals, transparent plates, were stable in air but dissolved in mother solution at room temperature. X-Ray experiments were carried out on a four-circle diffractometer, Enraf Nonius CAD4 for the R-PE complex and Nicolet P3/F for the S-PE complex, with graphite-monochromated Cu-K_α radiation at room temperature. Lattice parameters were determined by the least-squares method using 25 reflections for both crystals. Intensity data were measured by using θ-2θ scan mode and 4 099 (R-PE complex, $2\theta \leqslant 136°$) and 4 479 (S-PE complex, $2\theta \leqslant 118°$) reflections with $|F| \geqslant 3\sigma(F)$ were used for structure determination and refinement. No corrections were made for absorption or extinction effects.

Crystal Data.—(**1**) R–PE complex: $C_{54}H_{96}O_{30}\cdot C_8H_{10}O$, $M = 1\,347.5$. Monoclinic, space group $P2_1$, $Z = 2$. $a = 11.604(1)$, $b = 23.669(3)$, $c = 13.824(1)$ Å, $\beta = 106.72(1)°$, $V = 3\,636(1)$ Å^3. $D_x = 1.230$ g cm^{-3} (**2**) S–PE complex: $C_{54}H_{96}O_{30}\cdot C_8H_{10}O\cdot H_2O$, $M = 1\,365.5$. Monoclinic, space group $P2_1$, $Z = 2$. $a = 11.586(3)$, $b = 23.641(6)$, $c = 13.762(3)$ Å, $\beta = 106.45(2)°$, $V = 3\,615(2)$ Å^3. $D_x = 1.254$ g cm^{-3}.

Structure Determination and Refinement.—Crystal structures of both complexes were determined by using a set of atomic co-ordinates of the isomorphous (*R*)-mandelic acid complex,[8] and refined by the least-squares method and successive Fourier and difference-Fourier syntheses. Positions of hydrogen atoms in methine, methylene, and phenyl groups were calculated and included in the least-squares calculation with the temperature factor of bonded carbon atoms. The final block-diagonal least-squares refinement with unit weight for all the reflections achieved *R*-values of 0.077 for the R-PE complex and 0.073 for the S-PE complex. The computation was carried out on a FACOM M-780 computer at the RIPS Computer Center, AIST, Tsukuba. The programs used were those developed in the author's laboratory. Atomic co-ordinates are given in Table 1. Tables of anisotropic temperature factors and atomic parameters of hydrogen atoms, have been deposited with CCDC. See Instructions for Authors in the January issue.

Results and Discussion

Structure of TM-αCDx.—The structure, with atomic numbering of the R-PE complex is shown in Figure 1. The host TM-αCDx molecule in both crystals is in the shape of an elliptically distorted bucket. All 2,3,6-tri-*O*-methylglucose units have a pyranose ring with the $^4C_1$ chair conformation. Methyl groups attached to O(2) point away from the centre of the macrocycle, while the methyl groups bonded to O(3) are oriented towards the inside of the macrocyclic ring. The C(6)–O(6) bond in G1, G2, G3, and G5 units is *gauche* to the C(5)–O(5) bond and *trans* to the C(4)–C(5) bond. The methyl groups attached to O(6) of G1 points towards the inside of the macrocycle. The other O(6)CH_3 groups are *trans* to the C(5)–C(6) bond.

Table 1. Atomic co-ordinates.

	x	*y*	*z*
(*R*)-Phenylethanol complex			
C(1,G1)	0.115 4(11)	0.475 7(5)	0.339 1(8)
C(2,G1)	0.203 3(11)	0.489 1(5)	0.442 1(9)
C(3,G1)	0.236 3(11)	0.437 5(5)	0.510 0(8)
C(4,G1)	0.129 1(11)	0.400 7(5)	0.511 9(8)
C(5,G1)	0.040 6(10)	0.394 7(5)	0.406 0(8)
C(6,G1)	−0.084 9(12)	0.372 4(7)	0.412 7(11)
C(7,G1)	0.301 8(15)	0.573 1(6)	0.412 0(13)
C(8,G1)	0.416 6(14)	0.467 0(8)	0.644 5(12)
C(9,G1)	−0.144 0(19)	0.302 5(8)	0.280 2(13)
O(2,G1)	0.310 4(8)	0.513 6(4)	0.433 6(7)
O(3,G1)	0.289 9(9)	0.455 2(4)	0.614 7(6)
O(4,G1)	0.173 9(7)	0.346 2(3)	0.547 9(5)
O(5,G1)	0.012 8(6)	0.448 8(3)	0.358 2(5)
O(6,G1)	−0.162 8(9)	0.359 4(5)	0.318 0(8)
C(1,G2)	0.132 1(10)	0.390 8(9)	−0.008 8(8)
C(2,G2)	0.229 1(11)	0.434 5(5)	0.034 1(9)
C(3,G2)	0.254 4(10)	0.437 5(5)	0.149 0(8)
C(4,G2)	0.138 4(10)	0.449 6(5)	0.175 4(8)
C(5,G2)	0.033 1(9)	0.411 2(4)	0.117 0(8)
C(6,G2)	−0.090 5(11)	0.434 7(5)	0.120 5(9)
C(7,G2)	0.361 9(18)	0.459 7(11)	−0.058 5(18)
C(8,G2)	0.447 9(12)	0.462 8(8)	0.258 6(12)
C(9,G2)	−0.295 2(12)	0.416 0(7)	0.071 9(13)
O(2,G2)	0.335 1(8)	0.422 4(4)	0.007 8(7)
O(3,G2)	0.335 4(7)	0.481 7(4)	0.186 1(6)
O(4,G2)	0.167 7(6)	0.440 0(3)	0.283 4(5)
O(5,G2)	0.026 5(6)	0.408 8(3)	0.012 9(5)
O(6,G2)	−0.180 3(7)	0.397 1(4)	0.070 5(7)
C(1,G3)	0.138 6(13)	0.164 8(5)	−0.041 1(9)
C(2,G3)	0.262 3(13)	0.196 4(6)	−0.036 5(10)
C(3,G3)	0.269 6(11)	0.251 9(6)	0.017 8(10)
C(4,G3)	0.157 2(11)	0.288 2(5)	−0.025 5(8)
C(5,G3)	0.046 2(11)	0.254 4(5)	−0.026 2(9)
C(6,G3)	−0.072 7(13)	0.285 6(5)	−0.087 2(13)
C(7,G3)	0.444 0(17)	0.150 2(11)	−0.039 3(16)
C(8,G3)	0.458 8(14)	0.295 5(9)	0.108 7(16)
C(9,G3)	−0.275 8(17)	0.279 1(9)	−0.081 2(23)
O(2,G3)	0.359 0(9)	0.160 6(4)	0.011 3(8)
O(3,G3)	0.375 8(8)	0.281 0(4)	0.009 6(8)
O(4,G3)	0.169 6(6)	0.337 2(3)	0.036 5(5)
O(5,G3)	0.043 2(8)	0.202 9(3)	−0.083 7(6)
O(6,G3)	−0.174 0(9)	0.254 0(4)	−0.068 5(11)
C(1,G4)	0.041 9(11)	0.022 2(5)	0.219 3(9)
C(2,G4)	0.138 7(11)	0.005 2(5)	0.170 8(9)
C(3,G4)	0.188 1(11)	0.056 6(5)	0.132 8(8)
C(4,G4)	0.086 6(11)	0.093 4(5)	0.064 4(8)
C(5,G4)	−0.018 3(10)	0.102 6(5)	0.110 2(8)
C(6,G4)	−0.133 8(14)	0.126 2(6)	0.036 3(10)
C(7,G4)	0.209 4(17)	−0.081 9(6)	0.250 3(15)
C(8,G4)	0.396 2(13)	0.056 5(9)	0.132 7(14)
C(9,G4)	−0.282 3(14)	0.110 6(8)	−0.117 5(11)
O(2,G4)	0.231 3(8)	−0.024 3(3)	0.238 9(6)
O(3,G4)	0.265 9(8)	0.041 8(4)	0.074 3(7)
O(4,G4)	0.139 0(6)	0.148 1(3)	0.055 5(5)
O(5,G4)	−0.052 1(7)	0.049 7(3)	0.143 8(6)
O(6,G4)	−0.166 3(8)	0.090 4(4)	−0.048 9(7)
C(1,G5)	0.069 0(11)	0.113 0(5)	0.579 9(9)
C(2,G5)	0.144 8(12)	0.059 7(5)	0.580 4(9)
C(3,G5)	0.171 1(11)	0.051 9(5)	0.477 7(8)
C(4,G5)	0.052 1(11)	0.055 0(5)	0.390 1(8)
C(5,G5)	−0.021 2(10)	0.105 8(5)	0.400 6(8)
C(6,G5)	−0.154 2(12)	0.100 0(7)	0.327 5(9)
C(7,G5)	0.255 4(15)	0.042 7(10)	0.750 2(10)
C(8,G5)	0.353 5(13)	0.000 3(8)	0.481 5(12)
C(9,G5)	−0.335 0(15)	0.150 8(11)	0.257 6(17)
O(2,G5)	0.255 4(7)	0.062 9(4)	0.656 2(6)
O(3,G5)	0.223 6(9)	−0.002 0(4)	0.474 9(7)
O(4,G5)	0.089 3(7)	0.059 5(3)	0.301 0(5)
O(5,G5)	−0.038 4(7)	0.107 7(4)	0.498 4(6)
O(6,G5)	−0.208 8(10)	0.153 0(5)	0.324 3(9)
C(1,G6)	0.167 7(11)	0.331 4(5)	0.645 6(8)
C(2,G6)	0.274 5(11)	0.293 4(5)	0.696 6(8)
C(3,G6)	0.266 2(10)	0.235 2(5)	0.645 0(8)
C(4,G6)	0.140 4(11)	0.209 5(5)	0.628 3(8)
C(5,G6)	0.039 2(10)	0.250 9(5)	0.577 6(8)
C(6,G6)	−0.088 7(11)	0.233 1(6)	0.569 4(10)
C(7,G6)	0.458 5(18)	0.332 9(11)	0.792 0(13)
C(8,G6)	0.435 9(13)	0.172 3(8)	0.665 4(13)
G(9,G6)	−0.214 1(15)	0.214 6(10)	0.671 5(14)
O(2,G6)	0.384 6(8)	0.318 3(4)	0.697 6(6)
O(3,G6)	0.352 3(8)	0.198 6(4)	0.706 9(6)
O(4,G6)	0.134 2(7)	0.161 5(3)	0.562 8(5)
O(5,G6)	0.058 4(7)	0.303 3(4)	0.638 2(6)
O(6,G6)	−0.093 8(9)	0.212 5(5)	0.663 5(7)
C(1,RP)	0.429 0(14)	0.270 2(6)	0.416 8(12)
C(2,RP)	0.439 7(21)	0.214 9(9)	0.404 4(15)
C(3,RP)	0.352 1(24)	0.181 5(9)	0.349 4(14)
C(4,RP)	0.245 2(19)	0.207 2(10)	0.301 0(15)
C(5,RP)	0.226 0(15)	0.264 2(11)	0.306 3(14)
C(6,RP)	0.324 3(16)	0.296 4(7)	0.367 5(13)
C(7,RP)	0.539 5(17)	0.303 8(8)	0.482 1(20)
C(8,RP)	0.611 6(17)	0.327 6(11)	0.420 8(21)
O(1,RP)	0.496 0(12)	0.346 3(6)	0.541 6(10)
(*S*)-Phenylethanol complex			
C(1,G1)	0.116 5(7)	0.474 6(4)	0.340 1(6)
C(2,G1)	0.204 0(8)	0.488 1(4)	0.440 7(7)
C(3,G1)	0.234 3(8)	0.436 9(4)	0.512 2(6)
C(4,G1)	0.125 4(8)	0.400 9(4)	0.510 8(6)
C(5,G1)	0.038 9(8)	0.395 0(4)	0.407 8(7)
C(6,G1)	−0.084 3(8)	0.373 5(5)	0.412 0(8)
C(7,G1)	0.310 4(12)	0.568 8(5)	0.414 6(10)
C(8,G1)	0.414 4(11)	0.461 5(6)	0.645 3(10)
C(9,G1)	−0.140 9(15)	0.303 6(6)	0.282 3(11)
O(2,G1)	0.316 0(6)	0.510 9(3)	0.434 0(5)
O(3,G1)	0.286 6(7)	0.453 5(3)	0.615 5(5)
O(4,G1)	0.171 1(5)	0.346 1(3)	0.547 3(4)
O(5,G1)	0.014 5(5)	0.449 4(3)	0.357 9(5)
O(6,G1)	−0.160 7(7)	0.359 4(4)	0.318 3(6)
C(1,G2)	0.133 1(8)	0.389 8(4)	−0.010 9(7)
C(2,G2)	0.228 5(8)	0.435 0(4)	0.031 0(7)
C(3,G2)	0.255 1(8)	0.438 2(4)	0.145 4(7)
C(4,G2)	0.138 2(7)	0.450 0(4)	0.174 7(6)
C(5,G2)	0.033 4(7)	0.411 3(4)	0.116 9(6)
C(6,G2)	−0.086 0(8)	0.434 5(4)	0.120 0(7)
C(7,G2)	0.361 9(15)	0.461 1(8)	−0.056 7(15)
C(8,G2)	0.451 2(9)	0.464 1(6)	0.250 0(10)
C(9,G2)	−0.293 1(10)	0.415 3(6)	0.072 5(10)
O(2,G2)	0.334 9(6)	0.422 2(3)	0.003 2(6)
O(3,G2)	0.336 4(6)	0.482 6(3)	0.182 6(5)
O(4,G2)	0.169 7(5)	0.439 7(2)	0.282 3(4)
O(5,G2)	0.026 5(5)	0.408 5(3)	0.011 7(5)
O(6,G2)	−0.175 5(6)	0.395 7(3)	0.070 4(6)
C(1,G3)	0.148 1(9)	0.166 1(4)	−0.037 5(6)
C(2,G3)	0.267 6(9)	0.195 5(5)	−0.030 4(7)
C(3,G3)	0.274 4(8)	0.253 0(4)	0.024 8(8)
C(4,G3)	0.161 9(8)	0.288 2(3)	−0.025 6(6)
C(5,G3)	0.048 0(8)	0.253 8(4)	−0.028 6(7)
C(6,G3)	−0.062 6(9)	0.284 4(4)	−0.087 3(9)
C(7,G3)	0.457 8(13)	0.154 0(8)	−0.026 8(13)
C(8,G3)	0.461 7(12)	0.296 6(6)	0.112 7(11)
C(9,G3)	−0.263 8(14)	0.279 6(7)	−0.091 2(17)
O(2,G3)	0.365 1(6)	0.160 8(3)	0.020 2(6)
O(3,G3)	0.379 6(6)	0.281 8(3)	0.015 7(6)
O(4,G3)	0.171 6(5)	0.337 1(2)	0.036 1(4)
O(5,G3)	0.052 5(6)	0.202 5(3)	−0.083 4(4)
O(6,G3)	−0.163 5(6)	0.253 3(3)	−0.078 6(8)
C(1,G4)	0.040 5(9)	0.022 7(4)	0.220 0(7)
C(2,G4)	0.137 3(9)	0.005 2(4)	0.172 2(7)
C(3,G4)	0.190 4(8)	0.058 0(4)	0.135 4(6)

Table 1 (*continued*)

	x	*y*	*z*
C(4,G4)	0.088 8(8)	0.093 9(4)	0.067 9(6)
C(5,G4)	−0.014 7(8)	0.103.0(4)	0.111.0(7)
C(6,G4)	−0.122 8(9)	0.128 4(4)	0.038 5(7)
C(7,G4)	0.204 3(16)	−0.081 8(5)	0.254 0(12)
C(8,G4)	0.397 2(11)	0.045 1(8)	0.132 6(12)
C(9,G4)	−0.279 5(10)	0.110 5(6)	−0.111 7(9)
O(2,G4)	0.231 4(6)	−0.024 0(3)	0.239 6(5)
O(3,G4)	0.268 7(7)	0.042 9(3)	0.075 8(6)
O(4,G4)	0.143 3(5)	0.148 8(2)	0.058 8(4)
O(5,G4)	−0.050 9(5)	0.050 4(3)	0.146 0(4)
O(6,G4)	−0.162 4(6)	0.093 5(3)	−0.047 1(5)
C(1,G5)	0.065 1(8)	0.112 2(4)	0.582 3(7)
C(2,G5)	0.144 2(8)	0.059 6(4)	0.582 2(7)
C(3,G5)	0.167 8(9)	0.051 6(4)	0.479 6(7)
C(4,G5)	0.053 0(8)	0.055 2(4)	0.393 0(7)
C(5,G5)	−0.025 1(8)	0.104 7(4)	0.402 1(7)
C(6,G5)	−0.151 5(8)	0.099 5(5)	0.329 0(8)
C(7,G5)	0.251 1(12)	0.047 0(8)	0.755 3(8)
C(8,G5)	0.352 8(10)	0.002 1(6)	0.479 4(10)
C(9,G5)	−0.334 5(13)	0.153 1(8)	0.272 1(15)
O(2,G5)	0.255 6(6)	0.062 4(3)	0.658 1(5)
O(3,G5)	0.224 2(7)	−0.001 9(3)	0.477 7(5)
O(4,G5)	0.089 8(6)	0.059 2(3)	0.303 0(4)
O(5,G5)	−0.040 3(5)	0.106 8(3)	0.503 4(5)
O(6,G5)	−0.206 8(7)	0.152 1(4)	0.329 1(7)
C(1,G6)	0.165 2(9)	0.330 9(4)	0.647 3(6)
C(2,G6)	0.267 2(8)	0.292 2(4)	0.698 8(7)
C(3,G6)	0.258 8(8)	0.234 3(4)	0.647 4(6)
C(4,G6)	0.136 2(8)	0.209 2(4)	0.631 2(6)
C(5,G6)	0.037 1(8)	0.251 5(4)	0.580 1(7)
C(6,G6)	−0.090 2(9)	0.232 5(5)	0.567 4(8)
C(7,G6)	0.452 3(16)	0.333 5(9)	0.793 1(11)
C(8,G6)	0.434 7(9)	0.172 9(5)	0.672 9(10)
C(9,G6)	−0.228 3(10)	0.216 2(7)	0.657 1(10)
O(2,G6)	0.379 2(6)	0.318 5(3)	0.698 2(5)
O(3,G6)	0.347 9(6)	0.198 8(3)	0.713 2(5)
O(4,G6)	0.132 7(5)	0.161 0(3)	0.566 0(4)
O(5,G6)	0.054 3(5)	0.302 4(3)	0.640 0(4)
O(6,G6)	−0.104 1(6)	0.214 7(4)	0.660 0(5)
C(1,SP)	0.410 8(9)	0.283 8(5)	0.408 3(8)
C(2,SP)	0.446 4(12)	0.227 5(6)	0.416 7(10)
C(3,SP)	0.360 1(16)	0.185 3(6)	0.366 5(11)
C(4,SP)	0.250 8(13)	0.200 9(8)	0.314 6(11)
C(5,SP)	0.219 9(12)	0.255 7(8)	0.303 2(11)
C(6,SP)	0.296 2(11)	0.298 1(6)	0.347 5(10)
C(7,SP)	0.498 6(11)	0.330 3(5)	0.458 5(10)
C(8,SP)	0.611 2(11)	0.332 8(7)	0.423 4(11)
O(1,SP)	0.0535 1(7)	0.320 6(4)	0.567 2(7)
O(W1)	−0.053 5(11)	0.105 1(5)	0.783 6(8)

Table 2. Geometrical data of TM-α-CDx complex with R-PE (1) and *S*-PE (2).

	Tilt angle (°)[a]		O(4) angle (°)		Planarity (Å)[b]	
	(1)	(2)	(1)	(2)	(1)	(2)
G1	30.6	30.8	116	116	−0.142	−0.131
G2	22.1	23.3	118	117	0.147	0.136
G3	2.7	1.4	120	119	−0.030	−0.019
G4	21.4	22.8	117	118	−0.067	−0.081
G5	26.2	26.9	120	121	0.267	0.268
G6	1.6	1.7	117	117	−0.070	−0.075

[a] The tilt-angle is defined as: $\Phi = |\varphi[C(1)\text{–}C(2)]| + |\varphi[C(2)\text{–}C(3)]| + |\varphi[C(5)\text{–}O(5)]| + |\varphi[O(5)\text{–}C(1)]| - |\varphi[C(3)\text{–}C(4)]| - |\varphi[C(4)\text{–}C(5)]|$, where φ[C(1)–C(2)] is the torsion angle of O(5)–C(1)–C(2)–C(3). [b] The rms deviation of each O(4) atom from the least-squares plane of six O(4) atoms.

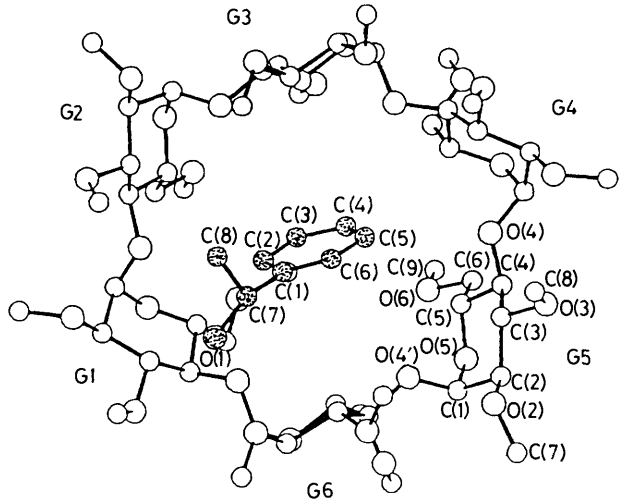

Figure 1. Structure of TM-αCDx–R-PE complex with atomic numbering. R-PE is shown by shaded circles.

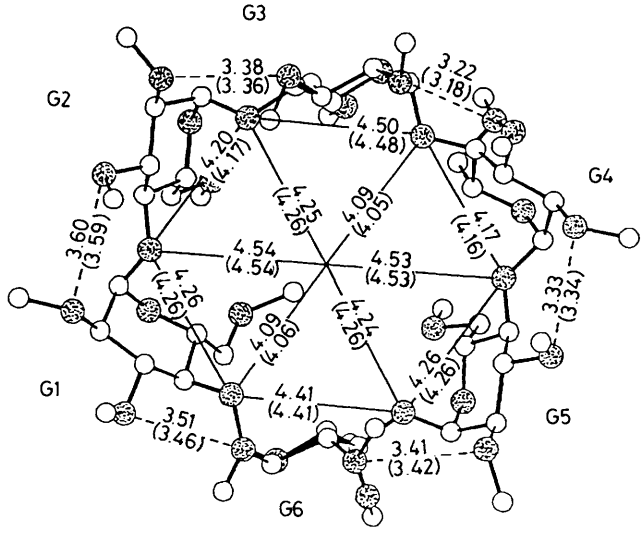

Figure 2. Geometrical parameters of TM-αCDx. Those in the S-PE complex are given in parentheses. Oxygen atoms are shown by shaded circles.

The geometrical data for the host macrocycle are shown in Figure 2 and given in Table 2. (See also Table 3 for bond distances and angles in the complex.) In spite of the considerable distortion of the macrocyclic ring, six O(4) atoms are almost coplanar. The radius of the hexagon composed of O(4) atoms is in the range 4.05–4.54 Å and the side length is 4.16–4.50 Å. As indicated by the tilt angle, G3 and G6 units are almost perpendicular to the O(4) hexagon. The other four units having tilt angles of 21.4–30.8° incline with their O(6) side towards the inside of the macrocycle. In α-cyclodextrin,[5] the degree of inclination of glucose units is less than that of TM-αCDx, since the intramolecular hydrogen bonds between O(2)H and O(3)H of the next glucose unit impose restriction on the inclination of glucose units and maintain the macrocyclic ring rigid and symmetrical. The methylation of O(2)H and O(3)H hydroxy groups makes the formation of intramolecular hydrogen bonds impossible, and as a result, the macrocyclic ring becomes free from the conformational restriction imposed by hydrogen bonds. Moreover, methyl groups attached to O(3) are located adjacent to two O(2) atoms and cause steric hindrance between

Table 3. Bond distances and angles in TM-αCDx.

Bond	G1	G2	G3	G4	G5	G6	Angle	G1	G2	G3	G4	G5	G6
(*R*)-Phenylethanol complex													
C(1)–C(2)	1.53(2)	1.52(2)	1.60(2)	1.52(2)	1.54(2)	1.53(2)	C(2)–C(1)–O(5)	107(1)	108(1)	108(1)	108(1)	107(1)	110(1)
C(1)–O(5)	1.44(1)	1.41(1)	1.42(2)	1.43(1)	1.43(2)	1.41(2)	C(2)–C(1)–O(4′)	111(1)	110(1)	110(1)	111(1)	109(1)	109(1)
C(1)–O(4′)	1.39(1)	1.41(1)	1.42(2)	1.43(1)	1.43(2)	1.41(2)	O(5)–C(1)–O(4′)	110(1)	110(1)	111(1)	110(1)	109(1)	110(1)
C(2)–C(3)	1.52(2)	1.53(2)	1.50(2)	1.50(2)	1.55(2)	1.54(2)	C(1)–C(2)–C(3)	113(1)	110(1)	110(1)	110(1)	111(1)	112(1)
C(2)–O(2)	1.41(2)	1.41(2)	1.41(2)	1.40(2)	1.41(2)	1.40(2)	C(1)–C(2)–O(2)	112(1)	111(1)	109(1)	111(1)	111(1)	112(1)
C(3)–C(4)	1.52(2)	1.52(2)	1.53(2)	1.55(2)	1.55(2)	1.54(2)	C(3)–C(2)–O(2)	108(1)	111(1)	112(1)	110(1)	108(1)	108(1)
C(3)–O(3)	1.46(2)	1.40(2)	1.45(2)	1.42(2)	1.42(2)	1.41(2)	C(2)–C(3)–C(4)	114(1)	110(1)	112(1)	112(1)	110(1)	111(1)
C(4)–C(5)	1.53(2)	1.55(2)	1.51(2)	1.54(2)	1.51(2)	1.54(2)	C(2)–C(3)–O(3)	110(1)	109(1)	108(1)	112(1)	109(1)	109(1)
C(4)–O(4)	1.43(1)	1.45(1)	1.42(1)	1.45(1)	1.42(1)	1.44(1)	C(4)–C(3)–O(3)	105(1)	109(1)	111(1)	107(1)	108(1)	109(1)
C(5)–C(6)	1.58(2)	1.55(2)	1.58(2)	1.54(2)	1.59(2)	1.52(2)	C(3)–C(4)–C(5)	111(1)	113(1)	110(1)	112(1)	111(1)	113(1)
C(5)–O(5)	1.44(1)	1.42(1)	1.45(2)	1.43(1)	1.42(1)	1.48(1)	C(3)–C(4)–O(4)	108(1)	105(1)	107(1)	107(1)	105(1)	106(1)
C(6)–O(6)	1.39(2)	1.39(2)	1.48(2)	1.41(2)	1.40(2)	1.41(2)	C(5)–C(4)–O(4)	109(1)	111(1)	112(1)	108(1)	110(1)	109(1)
C(7)–O(2)	1.44(2)	1.37(2)	1.39(2)	1.40(2)	1.38(2)	1.39(2)	C(4)–C(5)–C(6)	111(1)	112(1)	112(1)	115(1)	110(1)	117(1)
C(8)–O(3)	1.44(2)	1.47(2)	1.47(2)	1.50(2)	1.49(2)	1.41(2)	C(4)–C(5)–O(5)	104(1)	105(1)	103(1)	105(1)	103(1)	105(1)
C(9)–O(6)	1.48(2)	1.41(2)	1.29(3)	1.49(2)	1.49(2)	1.43(2)	C(5)–C(6)–O(6)	112(1)	109(1)	107(1)	108(1)	107(1)	109(1)
							C(2)–O(2)–C(7)	114(1)	115(1)	117(1)	116(1)	116(1)	115(1)
							C(3)–O(3)–C(8)	117(1)	113(1)	113(1)	113(1)	114(1)	118(1)
							C(4)–O(4)–C(1′)	116(1)	118(1)	120(1)	117(1)	120(1)	117(1)
							C(5)–O(5)–C(1)	113(1)	116(1)	115(1)	114(1)	115(1)	115(1)
							C(6)–O(6)–C(9)	114(1)	111(1)	119(2)	108(1)	110(1)	111(1)
(*S*)-Phenylethanol complex													
C(1)–C(2)	1.50(1)	1.53(1)	1.53(1)	1.51(1)	1.55(1)	1.50(1)	C(2)–C(1)–O(5)	108(1)	106(1)	110(1)	108(1)	109(1)	108(1)
C(1)–O(5)	1.41(1)	1.42(1)	1.40(1)	1.41(1)	1.39(1)	1.43(1)	C(2)–C(1)–O(4′)	111(1)	110(1)	111(1)	110(1)	107(1)	111(1)
C(1)–O(4′)	1.40(1)	1.42(1)	1.40(1)	1.42(1)	1.45(1)	1.44(1)	O(5)–C(1)–O(4′)	112(1)	111(1)	112(1)	111(1)	110(1)	110(1)
C(2)–C(3)	1.54(1)	1.52(1)	1.55(1)	1.54(1)	1.52(1)	1.53(1)	C(1)–C(2)–C(3)	113(1)	110(1)	110(1)	110(1)	111(1)	113(1)
C(2)–O(2)	1.43(1)	1.42(1)	1.41(1)	1.40(1)	1.41(1)	1.44(1)	C(1)–C(2)–O(2)	114(1)	110(1)	111(1)	112(1)	112(1)	109(1)
C(3)–C(4)	1.52(1)	1.54(1)	1.54(1)	1.53(1)	1.52(1)	1.50(1)	C(3)–C(2)–O(2)	107(1)	111(1)	110(1)	108(1)	109(1)	109(1)
C(3)–O(3)	1.43(1)	1.41(1)	1.43(1)	1.43(1)	1.43(1)	1.44(1)	C(2)–C(3)–C(4)	113(1)	110(1)	110(1)	110(1)	112(1)	111(1)
C(4)–C(5)	1.49(1)	1.55(1)	1.54(1)	1.50(1)	1.51(1)	1.54(1)	C(2)–C(3)–O(3)	112(1)	110(1)	108(1)	111(1)	109(1)	107(1)
C(4)–O(4)	1.44(1)	1.44(1)	1.42(1)	1.46(1)	1.42(1)	1.44(1)	C(4)–C(3)–O(3)	106(1)	108(1)	110(1)	107(1)	110(1)	110(1)
C(5)–C(6)	1.53(1)	1.50(1)	1.50(1)	1.49(1)	1.53(1)	1.50(1)	C(3)–C(4)–C(5)	113(1)	112(1)	110(1)	114(1)	113(1)	111(1)
C(5)–O(5)	1.45(1)	1.43(1)	1.44(1)	1.44(1)	1.45(1)	1.44(1)	C(3)–C(4)–O(4)	106(1)	105(1)	105(1)	105(1)	106(1)	105(1)
C(6)–O(6)	1.38(1)	1.41(1)	1.41(1)	1.40(1)	1.40(1)	1.39(1)	C(5)–C(4)–O(4)	109(1)	111(1)	112(1)	109(1)	111(1)	110(1)
C(7)–O(2)	1.39(2)	1.33(2)	1.41(2)	1.43(2)	1.40(2)	1.39(2)	C(4)–C(5)–C(6)	112(1)	111(1)	111(1)	114(1)	112(1)	116(1)
C(8)–O(3)	1.43(2)	1.46(1)	1.45(2)	1.47(2)	1.49(2)	1.42(1)	C(4)–C(5)–O(5)	111(1)	111(1)	108(1)	111(1)	110(1)	109(1)
C(9)–O(6)	1.45(2)	1.45(2)	1.29(2)	1.45(2)	1.47(2)	1.43(2)	C(6)–C(5)–O(5)	105(1)	105(1)	106(1)	108(1)	106(1)	107(1)
							C(5)–C(6)–O(6)	114(1)	108(1)	108(1)	110(1)	106(1)	110(1)
							C(2)–O(2)–C(7)	113(1)	113(1)	117(1)	114(1)	115(1)	115(1)
							C(3)–O(3)–C(8)	116(1)	114(1)	113(1)	113(1)	114(1)	118(1)
							C(4)–O(4)–C(1′)	116(1)	117(1)	119(1)	118(1)	121(1)	117(1)
							C(5)–O(5)–C(1)	114(1)	116(1)	115(1)	114(1)	116(1)	114(1)
							C(6)–O(6)–C(9)	115(1)	110(1)	118(1)	112(1)	114(1)	110(1)

them as suggested from the O(2)–CH_3O(3) distances of 3.0–3.6 Å. To relieve such steric hindrance, the distance between O(2) and O(3) becomes larger. The O(2)–O(3) distance in TM-αCDx, 3.18–3.60 Å, is considerably longer than the corresponding distance 2.81–3.04 Å of the α-cyclodextrin complex with racemic 1-phenylethanol. The elongation of the O(2)–O(3) distance is achieved by making the inclination of 2,3,6-tri-*O*-methylglucose units greater. As a result, the O(2), O(3) side of the host cavity becomes wider and the O(6) side narrower.

Host–Guest Interaction.—In both complexes the guest molecule is included in the same manner as shown in Figures 1 and 3. Figure 4 shows that host molecules are arranged along the *a* axis and form a column structure. The guest molecule is enclosed within the column. Since the C(9)H_3O(6) methoxy group of G1 blocks the O(6) side of the macrocycle, the inner space of the column is not continuous but partitioned at the O(6) side. Therefore, each guest molecule is accommodated in an isolated space. The phenyl group is inserted into the host cavity from the O(2), O(3) side and well-fitted to the elliptically distorted macrocyclic ring. On the inside of the host molecule, C(3)H and C(5)H methine groups, C(6)H_2, methylene groups, and O(4) oxygen atoms constitute the wall of the cylindrical cavity, providing hydrophobic character. Some short contacts between host and guest are observed between the phenyl group and O(4) atoms. The phenyl plane is situated parallel to the O(4,G2)–O(4,G5) diagonal and makes an angle of 72.3° with the plane of O(4) hexagon in the R-PE complex and 72.5° in the S-PE complex. The methyl and hydroxy groups are not inserted into the host cavity but located outside at the O(2), O(3) side of the host molecule. Although the orientation of the hydroxy group differs between R-PE and S-PE, both hydroxy groups are hydrogen-bonded to O(2) of the G1 unit. The space which accommodates the guest is limited in size and shape. To achieve the best fit to the cavity and to form hydrogen bond, the orientation of each guest molecule differs as shown in Figure 5. One isomer is rotated by 12° around the axis perpendicular to the phenyl group against the other isomer.

α-Cyclodextrin forms a crystalline complex with racemic 1-phenylethanol, in which the (*R*)- and (*S*)-isomers are equally included and the difference is found only in the orientation of the hydroxy group. The hydroxy group of the (*S*)-isomer is

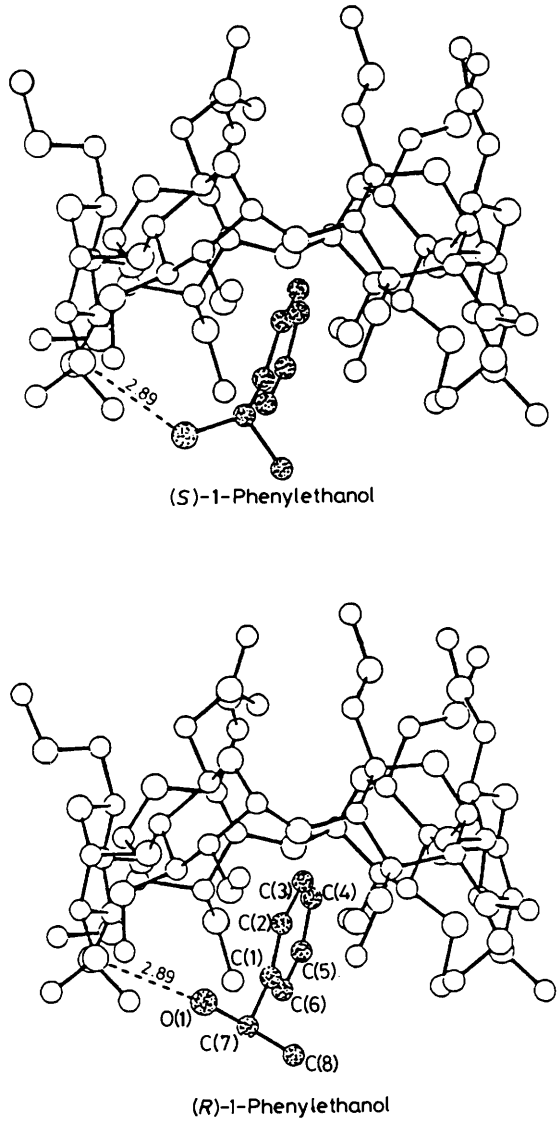

Figure 3. Side view of the inclusion feature. R-PE and S-PE molecules are shaded. The hydrogen bond between the hydroxy group of the guest and an O(2) atom of the host is shown by a dashed line with the oxygen–oxygen distance in Å.

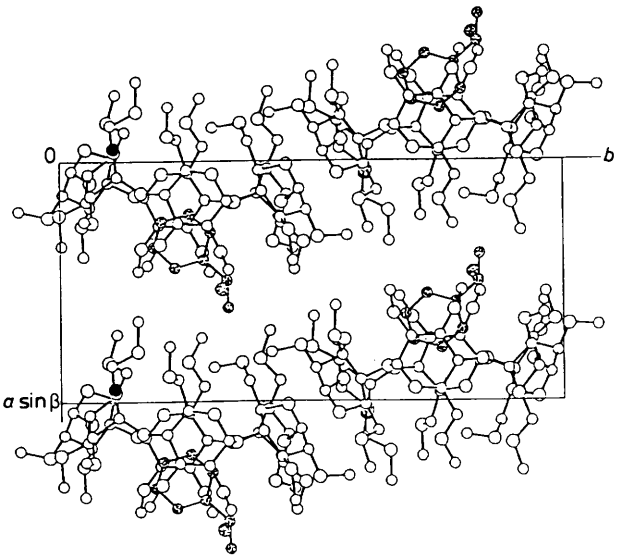

Figure 4. Crystal structure of the R-PE complex viewed along the *c*-axis. R-PE molecules are shaded.

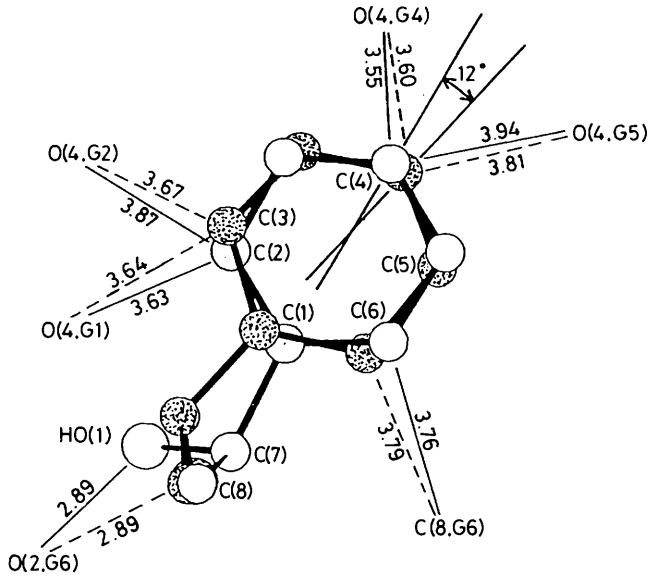

Figure 5. Intermolecular distances between host and guest. Contacts in the complex with S-PE (shaded circles) are shown by dashed lines.

hydrogen-bonded to O(3) and that of the *R*-isomer to O(2). In the TM-αCDx complex, the hydrogen-bond formation with O(3) is blocked by the methyl group bonded to O(3), and, therefore, the hydroxy group of both isomers is obliged to form a hydrogen bond with O(2).

The methyl group has no close contacts with the host molecule and does not seem to play an important role in the host–guest interaction. However, this substituent position becomes important when a bulkier group is introduced. In the TM-αCDx complexes with mandelic acid,[8] the (*R*)-isomer is included in the same manner as found in the 1-phenylethanol complex, but the inclusion feature of the complex with (*S*)-isomer changes. The steric hindrance involving the carboxy group prevents deep penetration of the phenyl group. A comparison of the structures of the 1-phenylethanol complex and the mandelic acid complex suggests that the host molecule should recognize three groups of the guest for the chiral discrimination. In the 1-phenylethanol complex, TM-αCDx recognizes the phenyl group by the inclusion into the cavity and the hydroxy group by the hydrogen-bond formation, but cannot recognize the orientation of the methyl group. However, when the methyl group is replaced by the carboxy group, TM-αCDx recognizes the chirality of the guest and includes each isomer in a different manner. Therefore, cyclodextrins do not recognize the chirality of all the optically active compounds which form inclusion complexes, but have excellent chiral recognition ability for the guests having a specific structure.

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