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Structures of 1 : 1 Inclusion Complexes of Cholic Acid with Fluoroethanols; Conformational Analysis of Fluoroethanols in the Host Cavity

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Abstract. The crystal structures of the inclusion complexes of cholic acid (CA) with 2-fluoroethanol (MFEtOH), 2,2-difluoroethanol (DFEtOH) and 2,2,2-trifluoroethanol (TFEtOH) have been determined by X-ray crystallography, which demonstrates that the guest alcohols are accommodated inside the cavity provided by CA molecules in a similar manner to that for the ethanol molecule in the CA-ethanol inclusion complex. As distinct from the ethanol molecule, the methylene C atoms of the fluoroethanols are not disordered; instead, the substituted F atoms are statistically disordered. All the alcohols are hydrogen-bonded to the OH groups of CA. The X-ray study showed that 46% of MFEtOH adopt the *trans-trans* conformer, which is different from the exclusively predominant conformer in the gas and liquid phases, i.e., the *gauche-trans* conformer. The study also showed that the F atoms of DFEtOH are statistically disordered, suggesting the possibility that three conformers exist inside the cavity. Such disorder presumably occurs in order to fill the vacant space around the CH_2F and CHF_2 groups inside the cavity. By contrast, we could not observe any disorder of the F atoms of TFEtOH.

Key words: X-ray crystal structure, multimolecular inclusion complex, cholic acid, fluoroethanol.

1. Introduction

Over the last few years, much attention has been paid to cholic acid (CA) and its derivatives as multimolecular hosts [1]. Several X-ray studies have shown that CA molecules form channel- or cavity-like spaces for a variety of molecules that fit inside the space in the solid state [2–5]. Since most of the wall of the space is dominated by H atoms attached to C atoms, it is relatively hydrophobic; part of the wall consists of several OH groups, which form a hydrogen bond network in the crystal lattice. Thus the nature of the cavity is somewhat analogous to the active site of enzymes. We have used this space as a model system to investigate the structural and dynamic characteristics of organofluorine compounds inside the space and the effect of an F atom on the hydrogen bond network pattern and molecular assembly. In a previous paper [3], we reported that the F atom substitution of aniline forms a second channel and a different hydrogen bond network pattern around the NH_2 group compared with that of the CA-aniline crystal structure.

Previously Johnson *et al.* reported the crystal structure of the CA-ethanol (EtOH) inclusion complex [4] and furthermore Jones *et al.* have recently reported a further refinement of the structure, demonstrating that the EtOH molecule is accommodated within the cavity and the methylene C atom of EtOH is statistically disordered over two sites [5]. Here we report the crystal structures of the inclusion complexes of CA with 2-fluoroethanol (MFEtOH), 2,2-difluoroethanol (DFEtOH) and 2,2,2-trifluoroethanol (TFEtOH), which demonstrate that the fluoroethanols are accommodated within the cavity in a similar manner to that of EtOH. The conformations of the fluoroethanols inside the cavity and the effect of the substituted F atoms on the conformations are discussed, comparing the conformation of EtOH in the cavity and those in the gas phase.

2. Experimental

2.1. PREPARATION OF INCLUSION COMPLEXES

When a soluiton of CA (0.3 g) in fluoroethanol (MFEtOH, DFEtOH or TFEtOH) (2 mL) was kept at room temperature for about 12 h, crystals of the 1 : 1 inclusion complex were obtained as colorless prisms.

2.2. CRYSTAL STRUCTURE DETERMINATION

2.2.1. *X-Ray Data Collection and Processing*

All the crystals are orthorhombic, space group $P2_12_12_1$ (No. 19). Lattice parameters were obtained from a least-squares refinement of diffractometer angles for 25 automatically centered reflections. Z values of the present crystals are 4.

Crystal Data for CA-MFEtOH (measured at 298 K): $C_{24}H_{40}O_5+C_2H_5FO$, $M = 472.64$, $a = 14.585(5)$, $b = 15.319(4)$, $c = 11.792(3)$ Å, $V = 2603(1)$ Å^3, $D_x = 1.206$ g cm^{-3}, crystal dimensions $0.40 \times 0.30 \times 0.40$ mm, $\mu(CuK_\alpha) = 7.22$ cm^{-1}. For CA-DFEtOH (at 298 K): $C_{24}H_{40}O_5+C_2H_4F_2O$, $M = 490.63$, $a = 14.461(5)$, $b = 15.314(5)$, $c = 11.848(5)$ Å, $V = 2623(1)$ Å^3, $D_x = 1.242$ g cm^{-3}, crystal dimensions $0.50 \times 0.30 \times 0.50$ mm, $\mu(CuK_\alpha) = 7.59$ cm^{-1}. For CA-DFEtOH (at 123 K): $C_{24}H_{40}O_5+C_2H_4F_2O$, $M = 490.63$, $a = 14.23(1)$, $b = 15.41(1)$, $c = 11.72(1)$ Å, $V = 2570(3)$ Å^3, $D_x = 1.268$ g cm^{-3}, crystal dimensions $0.30 \times 0.20 \times 0.40$ mm, $\mu(CuK_\alpha) = 7.75$ cm^{-1}. For CA-TFEtOH (at 298 K): $C_{24}H_{40}O_5+C_2H_3F_3O$, $M = 508.62$, $a = 14.562(3)$, $b = 15.269(2)$, $c = 11.894(2)$ Å, $V = 2644.6(5)$ Å^3, $D_x = 1.277$ g cm^{-3}, crystal dimensions $0.40 \times 0.25 \times 0.40$ mm, $\mu(CuK_\alpha) = 8.29$ cm^{-1}.

Diffraction measurements were made on a Rigaku AFC7R diffractometer with graphite monochromated CuK_α radiation at 298 and/or 123 K. The integrated intensities were collected in the ω-2ϑ scan mode with an ω rate of 16.0 deg

TABLE I. Positional parameters and temperature factors $[B_{(eq)}]$ for non-hydrogen atoms of CA-MFEtOH (at 298 K).

atom	x	y	z	$B_{(eq)}$[a]
F(33A)[b]	−0.596(2)	−0.358(1)	−0.091(2)	17(1)
F(33B)[c]	−0.580(2)	−0.251(2)	−0.080(3)	23(1)
O(25)	−0.8254(4)	−0.1346(3)	−0.0729(4)	6.7(1)
O(26)	−0.6791(2)	0.1952(2)	−0.3507(3)	4.18(8)
O(27)	−0.3700(4)	0.5779(4)	−0.3290(4)	7.5(1)
O(28)	−0.3932(3)	0.6338(4)	−0.5011(4)	6.8(1)
O(29)	−0.7734(2)	0.1813(3)	0.0405(3)	4.34(8)
O(32)	−0.7079(6)	−0.2010(5)	−0.2278(5)	9.9(2)
C(1)	−0.9514(4)	0.0284(4)	−0.2507(4)	4.4(1)
C(2)	−0.8816(4)	−0.0432(3)	−0.2205(4)	4.5(1)
C(3)	−0.8920(5)	−0.0681(4)	−0.0980(4)	4.8(1)
C(4)	−0.8815(4)	0.0116(4)	−0.0226(4)	4.2(1)
C(5)	−0.9489(3)	0.0843(4)	−0.0502(4)	4.1(1)
C(6)	−0.9399(4)	0.1647(4)	0.0271(5)	4.4(1)
C(7)	−0.8564(3)	0.2222(3)	0.0039(4)	3.7(1)
C(8)	−0.8482(3)	0.2465(3)	−0.1219(4)	3.4(1)
C(9)	−0.8564(3)	0.1666(3)	−0.1999(4)	3.08(9)
C(10)	−0.9460(3)	0.1133(3)	−0.1790(4)	3.8(1)
C(11)	−0.8457(4)	0.1931(3)	−0.3252(4)	3.9(1)
C(12)	−0.7604(3)	0.2479(3)	−0.3507(4)	3.4(1)
C(13)	−0.7536(3)	0.3290(3)	−0.2727(4)	3.3(1)
C(14)	−0.7601(3)	0.2965(3)	−0.1493(4)	3.20(9)
C(15)	−0.7343(4)	0.3770(4)	−0.0778(5)	4.3(1)
C(16)	−0.6655(4)	0.4268(3)	−0.1535(5)	4.2(1)
C(17)	−0.6604(3)	0.3796(3)	−0.2686(4)	3.4(1)
C(18)	−0.8309(3)	0.3936(3)	−0.3020(5)	4.2(1)
C(19)	−1.0324(3)	0.1663(4)	−0.2083(5)	5.0(1)
C(20)	−0.6330(4)	0.4393(3)	−0.3660(4)	4.1(1)
C(21)	−0.6360(5)	0.3943(5)	−0.4824(5)	6.1(2)
C(22)	−0.5366(4)	0.4781(4)	−0.3429(5)	5.1(1)
C(23)	−0.5106(4)	0.5496(5)	−0.4262(6)	5.8(1)
C(24)	−0.4190(4)	0.5876(4)	−0.4130(5)	4.6(1)
C(30)	−0.584(1)	−0.292(1)	−0.163(2)	12.5(5)
C(31)	−0.681(1)	−0.286(1)	−0.195(1)	11.1(4)

[a] $B_{(eq)} = (8/3)\pi^2\{U_{11}(aa^*)^2 + U_{22}(bb^*)^2 + U_{33}(bb^*)^2 + 2U_{12}aa^*bb^* \cos\gamma + 2U_{13}aa^*cc^* \cos\beta + 2U_{23}bb^*cc^* \cos\alpha\}$.
[b,c] Occupancies for F(33A) and F(33B) are 0.46(3) and 0.54(5), respectively.

min^{-1} to a maximum 2ϑ value of 120.1°, ω scan width $= [1.37 + 0.30\tan\vartheta]°$, $[1.10 + 0.30\tan\vartheta]°$, $[1.05 + 0.30\tan\vartheta]°$ and $[1.15 + 0.30\tan\vartheta]°$ for CA-MFEtOH,

CA-DFEtOH (298 K), CA-DFEtOH (123 K) and CA-TFEtOH, respectively. Three reference reflections were measured every 150 reflections. The data were corrected for Lorentz and polarization effects. An empirical absorption correction based on azimuthal scans of several reflections was applied to CA-MFEtOH and CA-DFEtOH (298 K) and an empirical absorption correction using the program DIFABS [6] was applied to CA-DFEtOH (123 K) and CA-TFEtOH. A correction for secondary extinction was applied.

2.2.2. *Structure Analysis and Refinement*

The structures were solved by the direct methods SIR88 [7] and DIRDIF92 [8] for CA-MFEtOH, SHELXS86 [9] and DIRDIF92 for CA-DFEtOH (298, 123 K), MULTAN88 [10] and DIRDIF92 for CA-TFEtOH. Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares refinement was based on 1857, 2048, 1812 and 1960 observed reflections $[I > 3\sigma(I)]$ for CA-MFEtOH, CA-DFEtOH (298 K), CA-DFEtOH (123 K) and CA-TFEtOH, respectively; the function minimized was $\Sigma w(|F_o|^2 - |F_c|^2)^2$. Goodness of fit indicators were 2.12, 2.10, 1.47 and 1.42 for CA-MFEtOH, CA-DFEtOH (298 K), CA-DFEtOH (123 K) and CA-TFEtOH, respectively. The weighting scheme used was $w = 1/\sigma^2(F_o) = 4F_o^2/\sigma^2(F_o^2)$. The final R and R_w values are as follows: CA-MFEtOH 0.061 and 0.095, CA-DFEtOH (298 K) 0.062 and 0.102, CA-DFEtOH (123 K) 0.040 and 0.051, CA-TFEtOH 0.052 and 0.088. The absolute configurations were conformed to that of CA reported previously [2]. All the calculations were performed using the TEXSAN crystallographic software package of Molecular Structure Corporation [11].

3. Results and Discussion

3.1. CRYSTAL STRUCTURE OF INCLUSION COMPLEXES

The positional parameters and temperature factors for non-hydrogen atoms are given in Tables I, II, III and IV for CA-MFEtOH, CA-DFEtOH (298 K), CA-DFEtOH (123 K) and CA-TFEtOH, respectively. Figure 1 shows *ORTEP* [12] drawing of CA in the CA-TFEtOH inclusion complex. A notable difference in the side chain conformation, which is the most mobile moiety in CA, is not observed among the four crystal structures. For example, the C(17)-C(20)-C(22)-C(23) torsion angles are $-170.7(5)$, $-170.2(4)$, $-166.4(3)$ and $-171.5(4)°$ for CA-MFEtOH, CA-DFEtOH (298 K), CA-DFEtOH (123 K) and CA-TFEtOH, respectively, all of which correspond to the *anti* configuration, whereas the corresponding torsion angle for CA-EtOH is $-169.9(6)°$ [5]. Thus the substitution of F atoms scarcely affects the conformation of the CA molecule.

The crystal structures drawn by *CHARON* [13] of CA-MFEtOH, CA-DFEtOH (298 K), CA-DFEtOH (123 K) and CA-TFEtOH are depicted in Figure 2. A num-

TABLE II. Positional parameters and temperature factors $[B_{(eq)}]$ for non-hydrogen atoms of CA-DFEtOH (at 298 K).

atom	x	y	z	$B_{(eq)}{}^a$
F(33)[b]	−0.9251(7)	−0.8654(4)	−0.3871(7)	13.2(3)
F(34)[c]	−0.9280(7)	−0.7393(6)	−0.4358(6)	8.6(2)
F(35)[d]	−0.9620(9)	−0.774(1)	−0.272(1)	12.2(5)
O(25)	−0.6790(3)	−0.6321(2)	−0.4282(3)	6.2(1)
O(26)	−0.8215(2)	−0.3050(2)	−0.1497(3)	4.02(7)
O(27)	−1.1294(3)	0.0778(3)	−0.1702(4)	6.8(1)
O(28)	−1.1035(3)	0.1334(3)	−0.0011(3)	6.6(1)
O(29)	−0.7275(2)	−0.3189(2)	−0.5401(2)	3.93(7)
O(32)	−0.7931(5)	−0.6957(4)	−0.2711(4)	8.9(2)
C(1)	−0.5497(3)	−0.4727(3)	−0.2513(4)	4.1(1)
C(2)	−0.6207(4)	−0.5421(3)	−0.2791(3)	4.2(1)
C(3)	−0.6097(4)	−0.5673(3)	−0.4040(4)	4.5(1)
C(4)	−0.6210(4)	−0.4878(3)	−0.4790(4)	4.1(1)
C(5)	−0.5512(3)	−0.4173(3)	−0.4502(4)	3.86(9)
C(6)	−0.5595(3)	−0.3369(3)	−0.5280(4)	3.81(9)
C(7)	−0.6423(3)	−0.2792(3)	−0.5036(4)	3.51(8)
C(8)	−0.6505(3)	−0.2552(2)	−0.3791(4)	3.19(8)
C(9)	−0.6433(3)	−0.3352(2)	−0.3011(3)	2.89(7)
C(10)	−0.5537(3)	−0.3887(3)	−0.3225(4)	3.62(9)
C(11)	−0.6531(3)	−0.3077(3)	−0.1751(3)	3.59(9)
C(12)	−0.7382(3)	−0.2531(3)	−0.1507(3)	3.24(8)
C(13)	−0.7455(3)	−0.1729(2)	−0.2287(3)	2.90(7)
C(14)	−0.7391(3)	−0.2057(2)	−0.3514(3)	2.96(7)
C(15)	−0.7638(3)	−0.1247(3)	−0.4219(4)	4.1(1)
C(16)	−0.8328(3)	−0.0755(3)	−0.3489(4)	3.73(8)
C(17)	−0.8386(3)	−0.1228(3)	−0.2317(3)	3.08(8)
C(18)	−0.6662(3)	−0.1105(3)	−0.1996(4)	3.94(9)
C(19)	−0.4665(3)	−0.3369(3)	−0.2949(5)	4.7(1)
C(20)	−0.8644(3)	−0.0627(3)	−0.1346(4)	3.83(9)
C(21)	−0.8614(4)	−0.1080(4)	−0.0203(4)	5.5(1)
C(22)	−0.9621(3)	−0.0230(3)	−0.1575(4)	4.3(1)
C(23)	−0.9862(3)	0.0483(4)	−0.0766(5)	5.3(1)
C(24)	−1.0794(3)	0.0873(3)	−0.0884(4)	4.3(1)
C(30)	−0.9102(7)	−0.7873(5)	−0.3460(7)	7.6(2)
C(31)	−0.8166(7)	−0.7843(7)	−0.3057(6)	8.6(2)

[a] $B_{(eq)} = (8/3)\pi^2\{U_{11}(aa^*)^2 + U_{22}(bb^*)^2 + U_{33}(bb^*)^2 + 2U_{12}aa^*bb^* \cos \gamma + 2U_{13}aa^*cc^* \cos \beta + 2U_{23}bb^*cc^* \cos \alpha\}$.

[b,c,d] Occupancies for F(33), F(34) and F(35) are 0.94(2), 0.55(1) and 0.51(2), respectively.
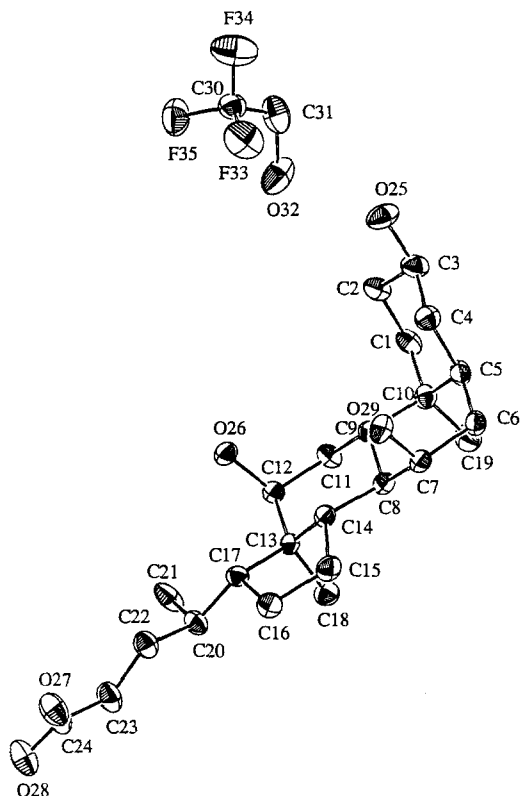
Fig. 1. *ORTEP* drawing of the molecular structures of CA and TFEtOH in the CA-TFEtOH inclusion complex. All the atoms are represented by thermal ellipsoids with 30% probability levels. H atoms are omitted for clarity.

ber of CA molecules are arranged to form a non-layered structure. The present arrangements are essentially the same as that of the CA-EtOH inclusion complex, which indicates that the substitution of F atoms virtually does not affect the crystal packing pattern. In each crystal, the cyclic hydrogen bond network plays an important role in stabilizing the molecular assembly and the formation of the cavity; five kinds of hydrogen bonds form a hydrogen bond network with the common cyclic sequence of -O(26)-H···O(27)=C(24)-O(28)-H···O(29)-H···O(32)-H···O(25)-H···O(26). The O···O distances are tabulated in Table V. It is noteworthy that the O(32)···O(25) distance tends to shorten with the increase in the number of the substituted F atoms. This tendency is partly because the substituted F atoms increase the acidity of the alcohols.

Similar to EtOH in the CA-EtOH inclusion complex, all the fluoroethanol molecules are hydrogen-bonded to the CA molecules. Figure 3 shows a stereo drawing of the cavity formed by eight CA molecules and included TFEtOH. It is noteworthy that the methylene C atom of the fluoroethanol molecule is not disordered, different from that of EtOH. The F atoms have statistically disordered

TABLE III. Positional parameters and temperature factors $[B_{(eq)}]$ for non-hydrogen atoms of CA-DFEtOH (at 123 K).

atom	x	y	z	$B_{(eq)}$ [a]
F(33)[b]	−0.0665(3)	−0.3728(2)	−0.6245(3)	5.8(1)
F(34)[c]	−0.0632(2)	−0.2442(2)	−0.5592(3)	4.14(9)
F(35)[d]	−0.0305(8)	−0.2780(8)	−0.731(1)	5.2(4)
O(25)	−0.8149(2)	−0.3696(2)	−0.4304(2)	3.03(7)
O(26)	−0.6762(2)	−0.6965(2)	−0.1501(2)	2.03(6)
O(27)	−0.3687(2)	−1.0789(2)	−0.1706(2)	3.14(7)
O(28)	−0.3975(2)	−1.1373(2)	0.0003(3)	2.95(7)
O(29)	−0.7743(2)	−0.6815(2)	−0.5431(2)	2.01(6)
O(32)	−0.1944(2)	−0.1901(2)	−0.7262(2)	3.64(8)
C(1)	−0.9484(3)	−0.5251(2)	−0.2482(3)	2.14(8)
C(2)	−0.8753(3)	−0.4577(2)	−0.2794(3)	2.14(8)
C(3)	−0.8856(3)	−0.4316(3)	−0.4027(3)	2.29(9)
C(4)	−0.8783(3)	−0.5110(3)	−0.4795(3)	2.12(8)
C(5)	−0.9506(3)	−0.5803(3)	−0.4491(3)	1.94(8)
C(6)	−0.9451(3)	−0.6596(3)	−0.5277(3)	2.25(9)
C(7)	−0.8623(3)	−0.7194(2)	−0.5048(3)	1.81(8)
C(8)	−0.8531(2)	−0.7434(2)	−0.3788(3)	1.64(7)
C(9)	−0.8580(3)	−0.6635(2)	−0.3002(3)	1.58(7)
C(10)	−0.9483(3)	−0.6077(2)	−0.3215(3)	1.96(8)
C(11)	−0.8474(3)	−0.6912(2)	−0.1754(3)	1.87(8)
C(12)	−0.7625(3)	−0.7469(2)	−0.1489(3)	1.59(7)
C(13)	−0.7571(2)	−0.8266(2)	−0.2281(3)	1.50(7)
C(14)	−0.7634(3)	−0.7939(2)	−0.3532(3)	1.69(7)
C(15)	−0.7398(3)	−0.8738(3)	−0.4229(3)	1.99(8)
C(16)	−0.6702(3)	−0.9252(2)	−0.3495(3)	2.16(8)
C(17)	−0.6634(3)	−0.8774(2)	−0.2329(3)	1.74(8)
C(18)	−0.8379(3)	−0.8882(2)	−0.1982(3)	2.02(8)
C(19)	−1.0381(3)	−0.6577(3)	−0.2919(4)	2.36(9)
C(20)	−0.6364(3)	−0.9382(2)	−0.1348(3)	2.00(8)
C(21)	−0.6422(3)	−0.8956(3)	−0.0178(4)	2.6(1)
C(22)	−0.5374(3)	−0.9753(2)	−0.1550(3)	2.05(8)
C(23)	−0.5160(3)	−1.0510(3)	−0.0775(4)	2.6(1)
C(24)	−0.4201(3)	−1.0888(3)	−0.0886(4)	2.18(9)
C(30)	−0.0799(4)	−0.2887(3)	−0.6550(4)	3.2(1)
C(31)	−0.1789(4)	−0.2775(3)	−0.6952(4)	3.2(1)

[a] $B_{(eq)} = (8/3)\pi^2 \{U_{11}(aa^*)^2 + U_{22}(bb^*)^2 + U_{33}(bb^*)^2 + 2U_{12}aa^*bb^* \cos\gamma + 2U_{13}aa^*cc^* \cos\beta + 2U_{23}bb^*cc^* \cos\alpha\}$.
[b,c,d] Occupancies for F(33), F(34) and F(35) are 0.96(1), 0.81(1) and 0.23(1), respectively.
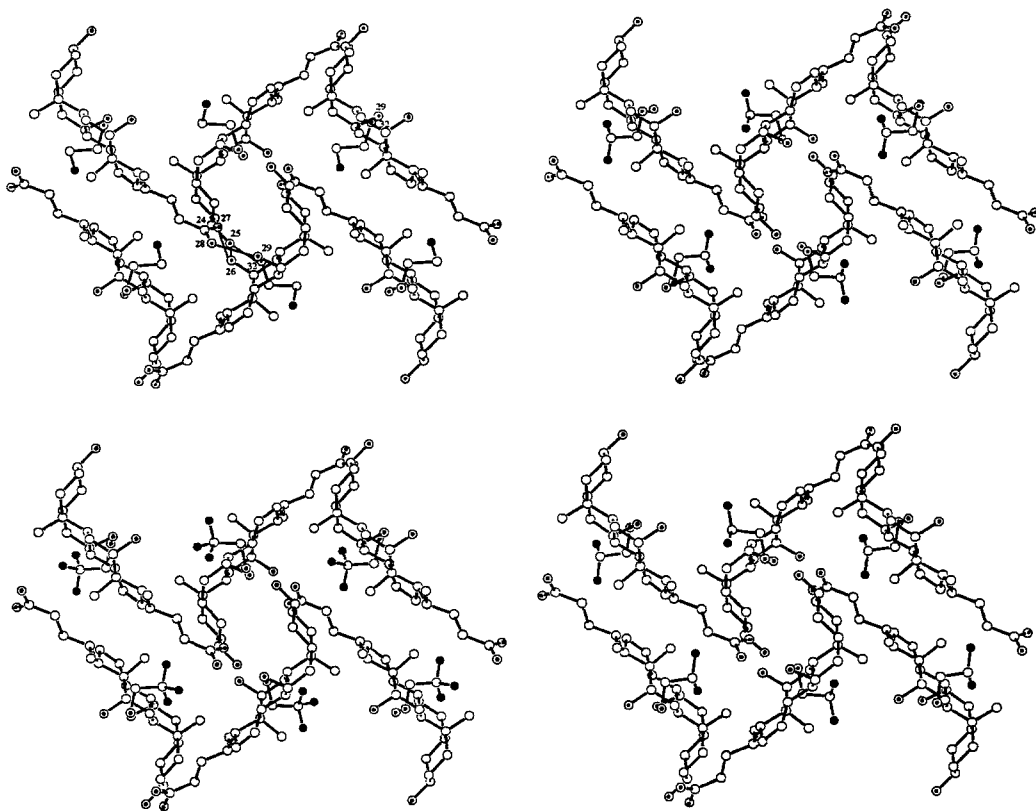
Fig. 2. *CHARON* drawings of the packing diagrams of the CA inclusion complexes as viewed along the *c* axis. Clockwise from top left: CA-MFEtOH (at 298 K), CA-DFEtOH (at 298 K), CA-DFEtOH (at 123 K), CA-TFEtOH (at 298 K). The hydrogen bond network, together with the numbering scheme of atoms concerned is shown by solid lines only in the CA-MFEtOH drawing. C, O and F atoms are represented by empty, half-filled and filled circles, respectively. H atoms are omitted for clarity.

positions in MFEtOH and DFEtOH. While such disorder cannot be observed in TFEtOH, let the replacement of F atoms change the disorder pattern inside the cavity according to the number of F atoms.

3.2. CONFORMATIONS OF ALCOHOLS

The guest alcohols are surrounded by the wall of the cavity, so that the molecular geometries should differ somewhat from those observed in the gas and liquid phases. The geometries for guest alcohols are given in Table VI.
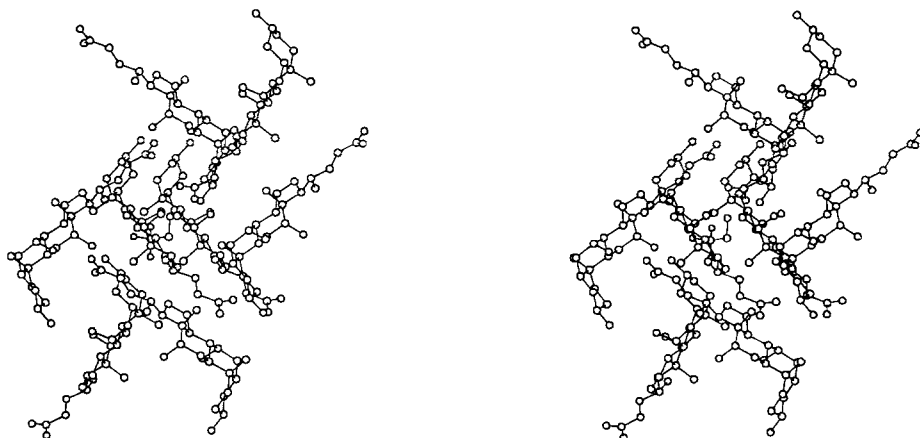
Fig. 3. Stereo drawing of the CA-TFEtOH inclusion complex. H atoms are omitted for clarity.

3.2.1. *Conformation of MFEtOH*

From the structural result of CA-MFEtOH, we found that the F atom is statistically disordered over two sites [F(33A) and F(33B)] with a ratio of 46 : 54. The torsion angles of F(33A)-C(30)-C(31)-O(32) and F(33B)-C(30)-C(31)-O(32) are 151(1) and 68(1)°, respectively. Intermolecular hydrogen bonds are formed between H(32)$\cdots$O(25) and H(32)$\cdots$O(29). One conformer of MFEtOH, F(33B), is approximately *gauche-trans* (GT), where the first letter is the conformation about the C-C bond and the second is the conformation about the C-O bond. Another conformer, F(33A), nearly corresponds to *trans-trans* (TT). It is noteworthy that the occupancies show that 46% of MFEtOH molecules adopt the TT conformer inside the cavity; approximately half of the conformation about the C-C bond is *trans*. Thus far several theoretical and experimental studies have indicated that the '*gauche* effect', i.e., "a tendency to adopt that structure which has the maximum number of *gauche* interactions between the adjacent electron pairs and/or polar bonds" [14], stabilizes the GG conformer [15–17]. The archetypical example of the *gauche* effect has been observed in the conformation of 1,2-difluoroethane (DFE). For instance, Brunvoll has reported that at room temperature gas phase samples of DFE contain 85–96% *gauche* molecules [18]. Fernholt *et al.* used electron diffraction to discover that 91% of DFE molecules adopt the *gauche* form at 298 K [19]. Hirano *et al.* have estimated that the conformational energy difference between the *gauche* and *trans* forms of DFE in the gas phase is about −0.8 kcal mol^{-1} using ^{19}F- and ^{1}H-NMR spectroscopy [20]. By contrast, the *gauche* effect does not work effectively in the present case.

This statistical disorder is probably because the volume of the CH$_2$F group is somewhat smaller than that of the space accommodating this group. As shown in

TABLE IV. Positional parameters and temperature factors $[B_{(eq)}]$ for non-hydrogen atoms of CA-TFEtOH (at 298 K).

atom	x	y	z	$B_{(eq)}$[a]
F(33)	0.9178(4)	0.7357(3)	0.5728(3)	8.9(1)
F(34)	0.9160(5)	0.8670(3)	0.6142(5)	10.7(1)
F(35)	0.9612(3)	0.7763(3)	0.7355(3)	7.58(9)
O(25)	0.6756(3)	0.6358(2)	0.5731(3)	5.90(9)
O(26)	0.8188(2)	0.3061(2)	0.8519(2)	3.85(6)
O(27)	1.1282(3)	−0.0759(3)	0.8278(3)	5.88(9)
O(28)	1.1028(2)	−0.1330(3)	0.9965(3)	6.23(9)
O(29)	0.7280(2)	0.3221(2)	0.4620(2)	4.10(6)
O(32)	0.7853(4)	0.6990(4)	0.7316(3)	8.2(1)
C(1)	0.5492(3)	0.4734(3)	0.7493(4)	3.99(9)
C(2)	0.6177(4)	0.5439(3)	0.7202(3)	4.13(9)
C(3)	0.6085(4)	0.5696(3)	0.5973(4)	4.6(1)
C(4)	0.6199(3)	0.4904(3)	0.5235(3)	4.11(9)
C(5)	0.5510(3)	0.4181(3)	0.5506(3)	3.68(8)
C(6)	0.5605(3)	0.3393(3)	0.4728(3)	3.70(9)
C(7)	0.6433(3)	0.2814(2)	0.4973(3)	3.35(8)
C(8)	0.6506(3)	0.2563(2)	0.6209(3)	3.26(8)
C(9)	0.6419(3)	0.3367(2)	0.6990(3)	2.94(7)
C(10)	0.5531(3)	0.3903(3)	0.6776(3)	3.64(9)
C(11)	0.6522(3)	0.3083(3)	0.8229(3)	3.52(8)
C(12)	0.7369(3)	0.2539(3)	0.8499(3)	3.17(7)
C(13)	0.7448(2)	0.1741(2)	0.7708(3)	2.90(7)
C(14)	0.7397(3)	0.2071(2)	0.6486(3)	3.10(7)
C(15)	0.7651(3)	0.1276(3)	0.5779(4)	4.19(9)
C(16)	0.8333(3)	0.0768(3)	0.6515(4)	4.00(9)
C(17)	0.8369(3)	0.1247(2)	0.7673(3)	3.15(7)
C(18)	0.6668(3)	0.1095(3)	0.7986(4)	4.04(9)
C(19)	0.4672(3)	0.3362(3)	0.7039(4)	4.8(1)
C(20)	0.8648(3)	0.0626(3)	0.8624(4)	3.83(8)
C(21)	0.8591(4)	0.1066(3)	0.9778(4)	5.4(1)
C(22)	0.9608(3)	0.0256(3)	0.8421(4)	4.39(10)
C(23)	0.9870(4)	−0.0457(3)	0.9227(5)	5.0(1)
C(24)	1.0799(3)	−0.0838(3)	0.9092(4)	4.3(1)
C(30)	0.8999(4)	0.7894(3)	0.6545(4)	5.0(1)
C(31)	0.8039(5)	0.7848(5)	0.6975(5)	6.9(2)

[a] $B_{(eq)} = (8/3)\pi^2\{U_{11}(aa^*)^2 + U_{22}(bb^*)^2 + U_{33}(bb^*)^2 + 2U_{12}aa^*bb^* \cos\gamma + 2U_{13}aa^*cc^* \cos\beta + 2U_{23}bb^*cc^* \cos\alpha\}$.

Figure 4(a), it is obvious that the disordered F atom appreciably fills the space. In addition, it should be noted that the CH_2F group would be loosely included in the cavity unless the group is statistically disordered. Thus MFEtOH prefers filling the

TABLE V. O···O distances in the hydrogen bond network (in Å).

O···O	CA-EtOH (298 K)[a]	CA-MFEtOH (298 K)	CA-DFEtOH (298 K)	CA-DFEtOH (123 K)	CA-TFEtOH (298 K)
O(28)···O(29)	2.584(6)	2.577(5)	2.596(5)	2.587(4)	2.605(4)
O(29)···O(32)	2.714(7)	2.763(7)	2.763(6)	2.745(4)	2.766(5)
O(32)···O(25)	2.720(9)	2.699(7)	2.672(6)	2.675(4)	2.653(5)
O(25)···O(26)	2.765(6)	2.776(5)	2.795(5)	2.773(4)	2.778(4)
O(26)···O(27)	2.847(7)	2.856(6)	2.878(6)	2.847(4)	2.901(5)

[a] Reference 5.

vacant space to exclusively adopting the GT conformer. On the other hand, the GG conformer, which exists exclusively in the gas phase [16], was not found. This is mainly due to the fact that MFEtOH forms an intermolecular hydrogen bond.

As Table VI shows, the C(30)-C(31), C(31)-O(32) and C(30)-F(33A) bond lengths and the C(30)-C(31)-O(32) angle are comparable to those of the gaseous GG conformer, as obtained by electron diffraction [16]: C-C 1.518(6), C-O 1.432(16), C-F 1.398(24) Å, $\angle$ CCO 112.3(14)°. In contrast to these geometries, the F(33A)-C(30)-C(31) and F(33B)-C(30)-C(31) angles are rather smaller than that observed in the gaseous GG conformer, i.e., 108.5(8)°.

3.2.2. Conformation of DFEtOH (at 298 K)

An X-ray crystallographic study of CA-DFEtOH at 298 K showed that two F atoms are statistically disordered over three sites [F(33), F(34) and F(35)] with a ratio of 47 : 28 : 25. The F-C(30)-C(31)-O(32) torsion angles shown in Table VI reveal that the disordered F atoms are positioned at one *anti* and two *gauche* positions. The study also showed that the intermolecular hydrogen bond is formed between H(32) and the OH groups of CA. This geometrical information suggests the possibility that three conformers exist inside the cavity: one GGT and two GTT conformers, where the first and second letters are the conformations of two F atoms about the C-C bond and the third is the conformation about the C-O bond. At the present time, we were not able to determine the ratio of these conformers on account of a lack of information.

This statistical disorder probably occurs in order to fill the vacant space around the CHF_2 group. Figure 4, part (b) shows the sectional view of CA-DFEtOH (at 298 K), which demonstrates that the disordered CHF_2 group is tightly surrounded by the wall of the cavity. In fact, the CHF_2 group is accommodated more loosely than the sectional view shows, since the occupancies of the F atoms are less than 1.
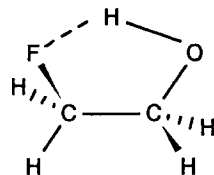
The C-C and C-O bond lengths and F-C-C and C-C-O angles are comparable to MFEtOH geometries obtained in the gas phase [16], but the C-F bond length, especially C(30)-F(35), is too short.
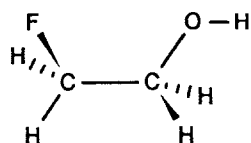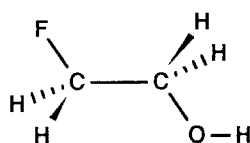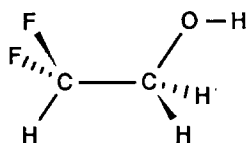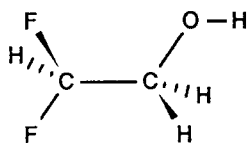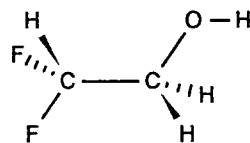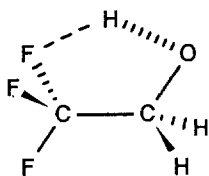
GT **TT** **GG**

GGT **GTT** **GTT**
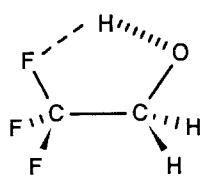
SG **EG**

ST **ET** **S0**
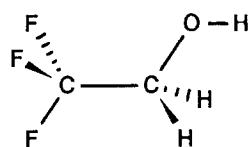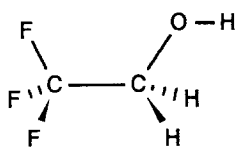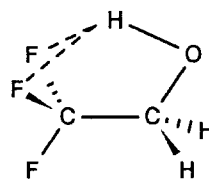
Scheme.

3.2.3. *Conformation of DFEtOH (at 123 K)*

As described above, the F atoms of DFEtOH are statistically disordered at room temperature. Next we examined whether the same disorder occurs even at low temperature. X-ray analysis demonstrated that the F atoms are also statistically disordered over three sites [F(33), F(34) and F(35)] with a ratio of 48 : 41 : 11
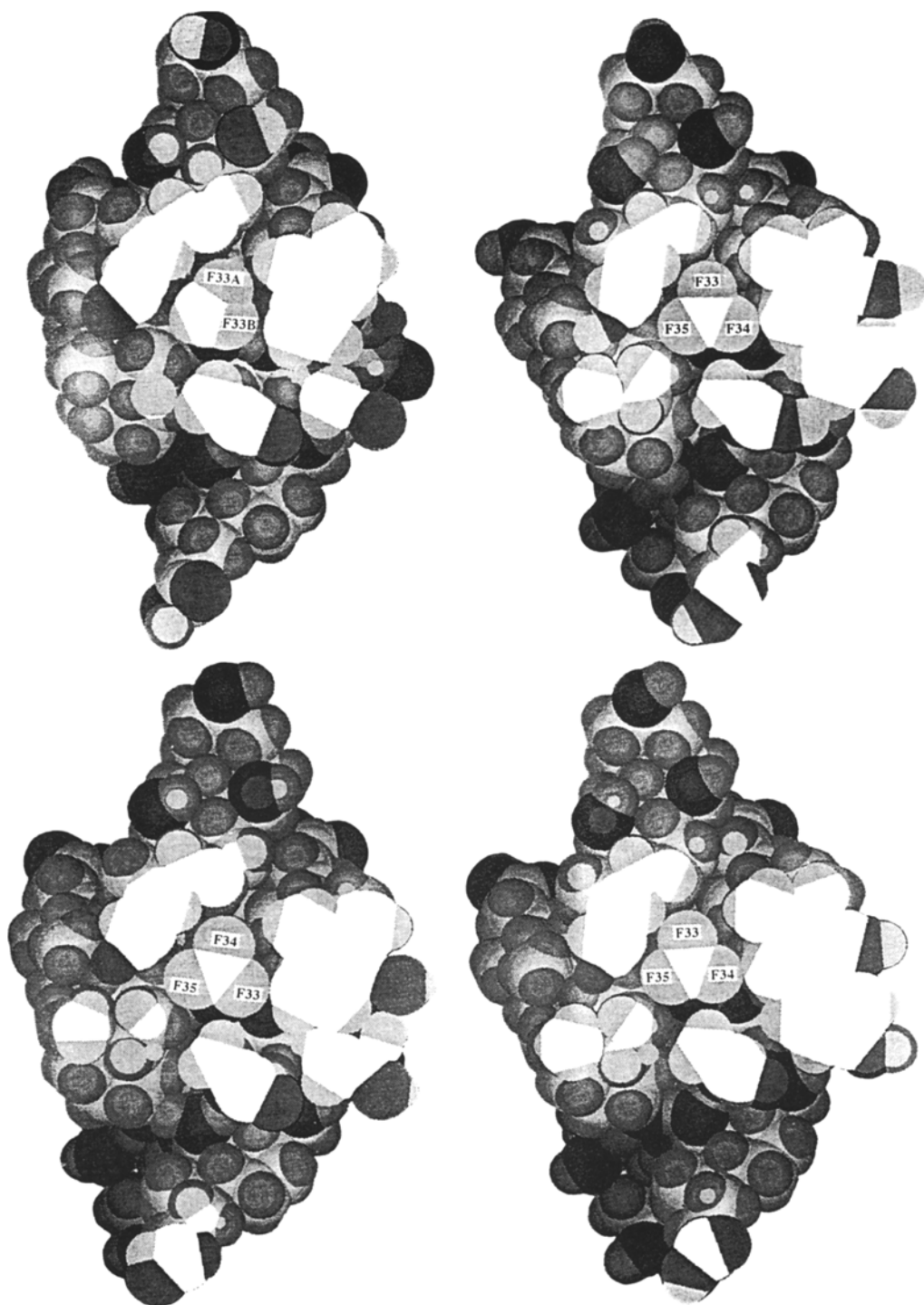
Fig. 4.   Sectional view of the CA cavity and included guest. Clockwise from top left: CA-MFEtOH (at 298 K), CA-DFEtOH (at 298 K), CA-DFEtOH (at 123 K), CA-TFEtOH (at 298 K).

TABLE VI. Geometries for fluoroethanols inside the cavity.[a]

parameters	MFEtOH (298 K)	DFEtOH (298 K)	DFEtOH (123 K)	TFEtOH (298 K)
C(30)-C(31)	1.47(2)	1.44(1)	1.497(7)	1.491(9)
C(31)-O(32)	1.40(2)	1.46(1)	1.412(6)	1.398(9)
C(30)-F(33)[b]	1.33(2)	1.309(9)	1.357(6)	1.298(6)
C(30)-F(34)[c]	1.17(2)	1.319(10)	1.337(6)	1.300(6)
C(30)-F(35)		1.22(1)	1.15(1)	1.328(6)
O(32)-H(32)	0.85	1.07	1.14	1.19
∠ F(33)C(30)C(31)[b]	94(1)	108.0(9)	109.0(4)	114.6(5)
∠ F(34)C(30)C(31)[c]	102(2)	115.7(9)	111.9(4)	106.5(5)
∠ F(35)C(30)C(31)		110.3(9)	108.3(7)	112.0(4)
∠ C(30)C(31)O(32)	112(1)	110.1(8)	109.7(4)	108.9(6)
∠ C(31)O(32)H(32)	71.1	96.2	92.6	95.3
∠ F(33)C(30)C(31)O(32),[b] dh[d]	151(1)	173.4(7)	179.3(4)	56.8(6)
∠ F(34)C(30)C(31)O(32),[c] dh	68(1)	62.2(9)	64.7(5)	175.0(5)
∠ F(35)C(30)C(31)O(32), dh		−66(1)	−67.0(9)	−67.0(6)

[a] Bond distances in angstroms; bond angles in degrees.
[b],[c] F(33) and F(34) correspond to F(33A) and F(33B) in MFEtOH, respectively.
[d] Symbol dh means dihedral angle.

at 123 K. The change in the ratio compared with the study of DFEtOH at 298 K mentioned above indicates that the C-C rotation is fairly depressed at 123 K. As the F-C-C-O torsion angles and Figures 4(b) and (c) indicate, the F atoms are positioned at almost the same sites as are the F atoms of DFEtOH at 298 K. Thus it seems reasonable to suppose that there are three conformers, i.e., one GGT and two GTT conformers. Similarly to the case of DFEtOH at 298 K, the ratio of these conformers was ambiguous. The ratio of the disordered F atoms, however, suggests that one GTT conformer with the F atoms over the F(33) and F(34) positions slightly predominates over the other conformers. Figure 4(c) shows that the F(33) and F(34) atoms are surrounded more closely by the walls as compared with the F(35) atom, which would lead to this conformer.

The C-C bond length is slightly longer than that of DFEtOH at 298 K, while the C-O bond length is slightly shorter. Nevertheless these geometries as well as the F-C-C and C-C-O angles are comparable to MFEtOH's geometries obtained by electron diffraction [16].

3.2.4. Conformation of TFEtOH

The TFEtOH molecule has a number of possible rotational isomers, in which stable isomers are as follows: SG (staggered-*gauche*), EG (eclipsed-*gauche*), ST (staggered-*trans*), ET (eclipsed-*trans*) and S0(staggered-0°), where the first letter is the rotation of the CF_3 group about the C-C bond and the second is the conformation

(*gauche* or *trans*) about the C-O bond or the C-C-O-H torsion angle. Curtiss *et al.* used *ab initio* calculations to show that the two lowest energy structures are SG and ST; the SG conformer is the most stable due to the internal hydrogen bond [21]. The present X-ray study showed that only the ST conformer exists inside the cavity. This can be explained by the fact that the intermolecular hydrogen bond is formed instead of an internal hydrogen bond; consequently SG could not be formed. The F-C-C-O torsion angles of TFEtOH are not an exact staggered form, which can be explained by the steric hindrance between the TFEtOH molecule and the wall of the cavity. The C-C and C-F bond lengths and the F-C-C and C-C-O angles are comparable to those of gaseous MFEtOH [16]. The C-F bond lengths are relatively short, although the occupancies of the F atoms are 1.

References

1. For example, M. Miyata, M. Shibakami, W. Goonewardena and K. Takemoto: *Chem. Lett* 605 (1987); M. Miyata, M. Shibakami, S. Chirachanchai, K. Takemoto, N. Kasai and K. Miki: *Nature (London)* **343**, 446 (1990); Y. Cheng, D.M. Ho, C.R. Gottlieb and D. Kahne: *J. Am. Chem. Soc.* **114**, 7319 (1992); K. Sada, T. Kondo, M. Miyata, T. Tamada and K. Miki: *J. Chem. Soc., Chem. Commun.* 753 (1993).
2. For example, K. Miki, A. Masui, N. Kasai, M. Miyata, M. Shibakami and K. Takemoto: *J. Am. Chem. Soc.* **110**, 6594 (1988); K. Miki, N. Kasai, M. Shibakami, K. Takemoto and M. Miyata: *J. Chem. Soc., Chem. Commun.* 1757 (1991); M.R. Caira, L.R. Nassimbeni and J.L. Scott: *ibid.* 612 (1993).
3. M. Shibakami and A. Sekiya: *ibid.* 429 (1994).
4. P.L. Johnson and J.P. Schaefer: *Acta Crystallogr., Sect. B* **28**, 3083 (1972).
5. E.L. Jones and L.R. Nassimbeni: *ibid.* **46**, 399 (1990).
6. N. Walker and D. Stuart: DIFABS, An empirical absorption correction program, *Acta Crystallogr., Sect. A* **39**, 158 (1983).
7. M.C. Burla, M. Camalli, G. Cascarano, C. Giacovazzo, G. Polidori, R. Spagna and D. Viterbo: SIR88, *J. Appl. Crystallogr.* **22**, 389 (1989).
8. P.T. Beurskens, G. Admiraal, G. Beurskens, W.P. Bosman, S. Garcia-Granada, R.O. Gould, J.M.M. Smits and C. Smykalla: DIRDIF92, *Technical Report of the Crystallography Laboratory*, University of Nijmegen, The Netherlands (1992).
9. G.M. Sheldrick: SHELXS86 in *Crystallographic Computing* 3, eds. G.M. Sheldrick, C. Cruger and R. Goddard, Oxford University Press, pp. 175–189 (1985).
10. T. Debaerdemaeker, G. Germain, P. Main, L.S. Refaat, C. Tate and M.M. Woolfson: MULTAN88, Computer programs for the automatic solution of crystal structures from X-ray diffraction data, University of York, U.K. (1988).
11. Molecular Structure Corporation: TEXSAN. TEXRAY Structure Analysis Package. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA (1985).
12. C.K. Johnson: *ORTEP* II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA (1976).
13. J.W. Lauher: *CHARON*. A Graphics Program for Postscript Printers, The Research Foundation of the State University of New York (1989).
14. S. Wolfe: *Acc. Chem. Res.* **5**, 102 (1972).
15. For example, K. Buckton and R.G. Azrak: *J. Chem. Phys.* **52**, 5652 (1970); K. Hagen and K. Hedberg: *J. Am. Chem. Soc.* **95**, 8263 (1973).
16. J. Huang and K. Hedberg: *ibid.* **111**, 6909 (1989).
17. D.A. Dixon and B.E. Smart: *J. Phys. Chem.* **95**, 1609 (1991).
18. J. Brunvoll: Thesis, University of Trondheim (1962).
19. L. Fernholt and K. Kveseth: *Acta Chem. Scand.* **A34**, 163 (1980).

20. T. Hirano, S. Nonoyama, T. Miyajima, Y. Kurita, T. Kawamura and H. Sato: *J. Chem. Soc.,*
    Chem. Commun. 606 (1986).
21. L.A. Curtiss, D.J. Frurip and M. Blander: *J. Am. Chem. Soc.* **100**, 79 (1978).