

molecules are included in this cavity. The high anisotropic thermal parameter for β_{33} of O(2') [14.0 (6) Å² for (1); 13.9 (3) Å² for (2)] may be an indication of disordering of O(2') effected by the disorder of the solvent molecules. O(2') is linked by an O—H...O hydrogen bond to O(2A). O(1W) donates another O—H...O hydrogen bond to O(2)(x, y, 1+z). Furthermore, O(1W) is linked by an O—H...O hydrogen bond to O(2W) [O...O 3.02 (7) Å for (1), and 2.94 (4) Å for (2)]. Any one of the three H atoms [one H of O(1W) and two H of O(2W)] may participate in this hydrogen bond. However, the probability of participation of each H atom could not be determined. Such solvent inclusion as found in the present crystals has been observed in some β -truxinic acid type photodimers by UV and IR spectroscopy and differential scanning calorimetry (Nakanishi, Nakanishi, Tsuchiya & Hasegawa, 1976).

The authors thank the Research Center for Protein Engineering, Institute for Protein Research, Osaka University, for the use of their facility, and Dr Masaru Kimura of Okayama University for the elemental analysis.

References

- ALLINGER, N. L. & YUH, Y. H. (1985). *MM2*. Program for molecular-mechanics calculation. Quantum Chemistry Program Exchange, Indiana Univ., Indiana, USA.
- ASHIDA, T. (1973). *HBLS-V* and *DAPH*. *The Universal Crystallographic Computing System, Osaka*. The Computation Center, Osaka Univ., Japan.
- BOWEN, J. P., REDDY, V. V., PATTERSON, D. G. JR & ALLINGER, N. L. (1988). *J. Org. Chem.* **53**, 5471–5475.
- COHEN, M. D. & SCHMIDT, G. M. J. (1964). *J. Chem. Soc.* pp. 1996–2000.
- COHEN, M. D., SCHMIDT, G. M. J. & SONNTAG, F. I. (1964). *J. Chem. Soc.* pp. 2000–2013.
- FUJII, S. (1979). *MOLCON*. *The Universal Crystallographic Computing System, Osaka*. The Computation Center, Osaka Univ., Japan.
- IWAMOTO, T., KASHINO, S. & HAISA, M. (1989). *Acta Cryst.* **C45**, 1753–1758.
- JOHNSON, C. K. (1971). *ORTEPII*. Report ORNL-3794, revised. Oak Ridge National Laboratory, Tennessee, USA.
- KANAO, S., KASHINO, S. & HAISA, M. (1990). *Acta Cryst.* **C46**, 2436–2438.
- KASHINO, S., OKA, H. & HAISA, M. (1989). *Acta Cryst.* **C45**, 154–157.
- NAKANISHI, F., NAKANISHI, H., TSUCHIYA, M. & HASEGAWA, M. (1976). *Bull. Chem. Soc. Jpn.* **49**, 3096–3099.
- SCHMIDT, G. M. J. (1964). *J. Chem. Soc.* pp. 2014–2021.
- TAKUSAGAWA, F. (1982). *CRLS*. Tech. Rep. ICR-1982-0001-0002-001. The Institute for Cancer Research, Philadelphia, USA.

Acta Cryst. (1990). **C46**, 2442–2445

Crystal Structure of Cholic Acid with No Guest Molecules

BY KUNIO MIKI* AND NOBUTAMI KASAI

Department of Applied Chemistry, Faculty of Engineering, Osaka University, Yamadaoka, Suita, Osaka 565, Japan

MOTONARI SHIBAKAMI, SUWABUN CHIRACHANCHAI AND KIICHI TAKEMOTO

Department of Applied Fine Chemistry, Faculty of Engineering, Osaka University, Yamadaoka, Suita, Osaka 565, Japan

AND MIKIJI MIYATA*

Department of Applied Chemistry, Faculty of Engineering, Gifu University, Yanagido, Gifu, Gifu 501–11, Japan

(Received 27 March 1990; accepted 25 April 1990)

Abstract. Cholic acid, C₂₄H₄₀O₅, $M_r = 408.58$, orthorhombic, $P2_12_12_1$, $a = 16.477$ (4), $b = 8.394$ (3), $c = 16.993$ (3) Å, $V = 2350.3$ (9) Å³, $Z = 4$, $D_x = 1.155$ g cm⁻³, $\lambda(\text{Mo } K\alpha) = 0.71069$ Å, $\mu = 0.851$ cm⁻¹, $F(000) = 896$, $T = 295$ K, $R = 0.057$ for 1807 observed reflections. The crystal structure of

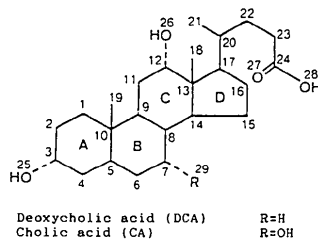
cholic acid containing no guest organic molecules has been found from recrystallization from acetone. The hydrogen-bond network is rigidly formed between four OH and one C=O groups of cholic acid molecules in the crystal structure.

Introduction. Many crystal structures have been reported for the typical steroidal bile acid deoxy-

* To whom correspondence should be addressed.

cholic acid ($3\alpha,12\alpha$ -dihydroxy- 5β -cholan-24-oic acid; DCA) and it is well known that DCA provides tunnel-like spaces, usually called 'channels', in which a wide variety of organic molecules can be accommodated (Giglio, 1984). However, only a few crystal structures are known for cholic acid ($3\alpha,7\alpha,12\alpha$ -trihydroxy- 5β -cholan-24-oic acid; CA) which has only one additional OH group to DCA in its molecular structure. In addition to two known CA crystal structures containing ethanol (Johnson & Schaefer, 1972) and water (Lessinger, 1982), we have recently obtained the first evidence for a channel-like inclusion ability of CA in the crystal structure with acetophenone as a guest molecule (Miki, Masui, Kasai, Miyata, Shibakami & Takemoto, 1988). However, only crystal structures including guest molecules have ever been found for CA and also for the widely studied DCA.

Here, we report the first crystal structure of a steroidal bile acid which consists of the CA molecule without organic guest molecules. The present structure was reported in part by Miyata, Shibakami, Chirachanchai, Takemoto, Kasai & Miki (1990).



Experimental. CA crystals with no guest molecules were grown as colorless prisms from acetone solution. A well shaped crystal with dimensions $0.20 \times 0.30 \times 0.40$ mm was mounted on a Rigaku automated four-circle diffractometer with graphite-monochromatized Mo $K\alpha$ radiation. Unit-cell parameters were determined by least-squares refinement of 2θ values of 25 reflections in the range 20.1 – 30.5° . Intensities were measured by the θ – 2θ scan technique with a scan rate of 4° min^{-1} in 2θ and scan width $\Delta(2\theta) = (2.0 + 0.70 \tan \theta)^\circ$. Background intensities were measured for 5 s at each end of a scan. Four standard reflections (240, 440, 10,0,0, 0,0,12) were remeasured every 60 reflections, no significant loss in intensities being observed. 2429 reflections were collected with 2θ up to 50.5° ($\sin \theta / \lambda = 0.600 \text{ \AA}^{-1}$) and index range $h = 0$ to 19, $k = 0$ to 10, $l = 0$ to 20. Corrections for Lorentz and polarization effects, but no correction for absorption or extinction.

Direct methods using *SHELXS86* (Sheldrick, 1986) were employed for the structure solution, which found all 29 non-H atoms. The structure was

Table 1. Fractional atomic coordinates and equivalent isotropic thermal parameters of non-H atoms with e.s.d.'s in parentheses

	x	y	z	$B_{\text{eq}}^*(\text{\AA}^2)$
C(1)	0.9149 (3)	–0.2429 (6)	0.9104 (3)	3.24
C(2)	0.9875 (3)	–0.2340 (6)	0.8548 (3)	3.41
C(3)	1.0245 (3)	–0.0684 (6)	0.8585 (3)	3.41
C(4)	0.9614 (3)	0.0542 (6)	0.8359 (3)	3.29
C(5)	0.8850 (3)	0.0470 (6)	0.8879 (3)	3.41
C(6)	0.8227 (3)	0.1743 (6)	0.8645 (3)	3.70
C(7)	0.7733 (3)	0.1373 (5)	0.7907 (3)	3.22
C(8)	0.7390 (3)	–0.0331 (5)	0.7923 (3)	2.60
C(9)	0.8049 (3)	–0.1574 (6)	0.8107 (3)	2.74
C(10)	0.8465 (3)	–0.1227 (6)	0.8917 (3)	2.95
C(11)	0.7712 (3)	–0.3285 (6)	0.8054 (3)	2.84
C(12)	0.7234 (3)	–0.3665 (5)	0.7297 (3)	2.71
C(13)	0.6558 (3)	–0.2433 (5)	0.7164 (3)	2.50
C(14)	0.6950 (3)	–0.0756 (5)	0.7163 (3)	2.46
C(15)	0.6267 (3)	0.0349 (6)	0.6891 (3)	3.14
C(16)	0.5743 (3)	–0.0690 (6)	0.6336 (3)	3.10
C(17)	0.6125 (3)	–0.2399 (5)	0.6342 (3)	2.43
C(18)	0.5924 (3)	–0.2644 (6)	0.7822 (3)	3.29
C(19)	0.7857 (3)	–0.1313 (7)	0.9599 (3)	4.11
C(20)	0.5492 (3)	–0.3711 (6)	0.6154 (3)	2.97
C(21)	0.5865 (4)	–0.5367 (6)	0.6153 (3)	4.52
C(22)	0.5065 (3)	–0.3373 (6)	0.5367 (3)	3.44
C(23)	0.4312 (3)	–0.4405 (7)	0.5238 (3)	4.49
C(24)	0.3841 (3)	–0.3881 (6)	0.4520 (3)	4.03
O(25)	1.0920 (2)	–0.0540 (4)	0.8049 (2)	4.03
O(26)	0.7768 (2)	–0.3680 (4)	0.6628 (2)	3.19
O(27)	0.3873 (3)	–0.4477 (6)	0.3896 (3)	9.48
O(28)	0.3377 (3)	–0.2644 (5)	0.4647 (2)	5.26
O(29)	0.8213 (2)	0.1678 (4)	0.7215 (2)	3.82

* As defined by Hamilton (1959).

refined by the block-diagonal least-squares procedure with the program *HBL5-V* (Ashida, 1979) using 1807 observed reflections [$|F_o| \geq 3\sigma(|F_o|)$] except for reflections 110 and 002 which were strongly affected by the extinction effects. On the difference Fourier maps all the H atoms were found at the expected positions. The H-atom positional parameters were further refined, whereas their temperature factors were fixed to the B_{eq} values of connecting C and O atoms. The function minimized was $\sum w(|F_o| - |F_c|)^2$, where $w = [\sigma(F_o)^2 + 0.0030|F_o| + 0.0012|F_o|^2]^{-1}$. The number of observations per refined parameter is $1807/423 = 4.27$ and $S = 1.13$. The final R and wR are 0.057 and 0.061, respectively. The $(\Delta/\sigma)_{\text{max}}$ of non-H atoms in the final refinement cycle is 0.28. The peaks in the final $\Delta\rho$ map were between 0.19 and -0.23 e \AA^{-3} . The atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974, Vol. IV). The final atomic parameters are listed in Table 1.* All computations were performed on an ACOS 930 computer at the Crystallographic Research Center, Institute for Protein Research, Osaka University.

* Lists of structure factors, anisotropic thermal parameters and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53221 (11 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Discussion. The molecular structure of CA as drawn by ORTEP (Johnson, 1976) is presented in Fig. 1. The molecular conformation is essentially the same as that found in the CA crystals containing ethanol (Johnson & Schaefer, 1972). Bond distances and angles are listed in Table 2, all of which show the normal values for the standard steroidal compounds within experimental errors.

The crystal packing diagram is presented in Fig. 2. The arrangement of the molecules is also somewhat similar to that in the crystal structure with ethanol (Johnson & Schaefer, 1972), which also belongs to the orthorhombic space group $P2_12_12_1$ with $a = 14.661$, $b = 11.759$, $c = 15.066$ Å. The a and c axes are about 11% shorter but the b axis is 40% longer than those of the present no-guest crystals due to the addition of ethanol. The hydrogen-bond networks in the present no-guest and the ethanol-including crystals are shown in Fig. 3. In both crystals, the hydrogen bonds are extended along the crystallographic b axis. In the no-guest crystals, four kinds of hydrogen bonds are formed between five CA molecules; $O(28)-H(x,y,z)\cdots O(26)-H(-\frac{1}{2}+x, -\frac{1}{2}-y, 1-z)$

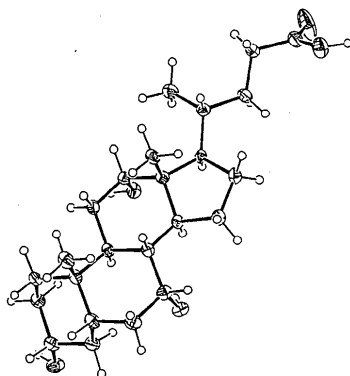


Fig. 1. ORTEP drawing (Johnson, 1976) of the CA molecular structure. Non-H atoms are represented by thermal ellipsoids with 30% probability levels, whereas H atoms are drawn by a sphere with $B = 1.0 \text{ \AA}^2$.

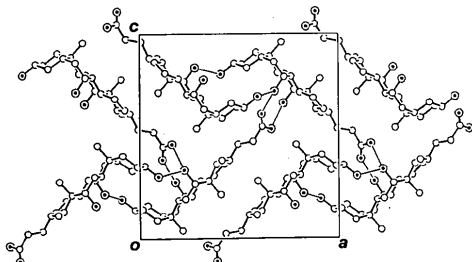


Fig. 2. ORTEP drawing (Johnson, 1976) of the packing diagram of the CA crystal with 'no guest' as viewed along the b axis. C and O atoms are represented by empty and half-filled circles, respectively. H-atoms are omitted for clarity. The hydrogen-bond network is shown by thin lines.

Table 2. Bond distances (Å), bond angles ($^\circ$) for non-H atoms and hydrogen-bond parameters (Å, $^\circ$) with e.s.d.'s in parentheses

C(1)—C(2)	1.526 (7)	C(1)—C(10)	1.546 (7)
C(2)—C(3)	1.519 (7)	C(3)—C(4)	1.513 (7)
C(3)—O(25)	1.443 (6)	C(4)—C(5)	1.539 (7)
C(5)—C(6)	1.534 (7)	C(5)—C(10)	1.561 (7)
C(6)—C(7)	1.526 (7)	C(7)—C(8)	1.538 (7)
C(7)—O(29)	1.441 (6)	C(8)—C(9)	1.539 (6)
C(8)—C(14)	1.523 (6)	C(9)—C(10)	1.566 (7)
C(9)—C(11)	1.542 (7)	C(10)—C(19)	1.534 (7)
C(11)—C(12)	1.542 (6)	C(12)—C(13)	1.536 (6)
C(12)—O(26)	1.437 (5)	C(13)—C(14)	1.549 (6)
C(13)—C(17)	1.569 (6)	C(13)—C(18)	1.541 (7)
C(14)—C(15)	1.531 (6)	C(15)—C(16)	1.548 (7)
C(16)—C(17)	1.568 (7)	C(17)—C(20)	1.550 (7)
C(20)—C(21)	1.520 (7)	C(20)—C(22)	1.538 (7)
C(22)—C(23)	1.529 (8)	C(23)—C(24)	1.512 (8)
C(24)—O(27)	1.174 (7)	C(24)—O(28)	1.307 (7)
C(2)—C(1)—C(10)	114.4 (4)	C(1)—C(2)—C(3)	109.5 (4)
C(2)—C(3)—C(4)	109.7 (4)	C(2)—C(3)—O(25)	111.1 (4)
C(4)—C(3)—O(25)	108.2 (4)	C(3)—C(4)—C(5)	112.9 (4)
C(4)—C(5)—C(6)	111.8 (4)	C(4)—C(5)—C(10)	113.1 (4)
C(6)—C(5)—C(10)	112.0 (4)	C(5)—C(6)—C(7)	115.3 (4)
C(6)—C(7)—C(8)	111.8 (4)	C(6)—C(7)—O(29)	110.0 (4)
C(8)—C(7)—O(29)	112.4 (4)	C(7)—C(8)—C(9)	112.0 (4)
C(7)—C(8)—C(14)	112.2 (4)	C(9)—C(8)—C(14)	110.4 (4)
C(8)—C(9)—C(10)	111.2 (4)	C(8)—C(9)—C(11)	111.4 (4)
C(10)—C(9)—C(11)	112.5 (4)	C(1)—C(10)—C(5)	108.0 (4)
C(1)—C(10)—C(9)	112.2 (4)	C(1)—C(10)—C(19)	106.9 (4)
C(5)—C(10)—C(9)	108.1 (4)	C(5)—C(10)—C(19)	109.9 (4)
C(9)—C(10)—C(19)	111.7 (4)	C(9)—C(11)—C(12)	115.2 (4)
C(11)—C(12)—C(13)	110.7 (4)	C(11)—C(12)—O(26)	110.4 (4)
C(13)—C(12)—O(26)	109.5 (4)	C(12)—C(13)—C(14)	108.1 (4)
C(12)—C(13)—C(17)	118.2 (4)	C(12)—C(13)—C(18)	107.9 (4)
C(14)—C(13)—C(17)	99.9 (4)	C(14)—C(13)—C(18)	112.9 (4)
C(17)—C(13)—C(18)	109.9 (4)	C(8)—C(14)—C(13)	114.2 (4)
C(8)—C(14)—C(15)	117.6 (4)	C(13)—C(14)—C(15)	104.1 (4)
C(14)—C(15)—C(16)	104.7 (4)	C(15)—C(16)—C(17)	106.7 (4)
C(13)—C(17)—C(16)	101.8 (4)	C(13)—C(17)—C(20)	118.4 (4)
C(16)—C(17)—C(20)	112.2 (4)	C(17)—C(20)—C(21)	112.2 (4)
C(17)—C(20)—C(22)	110.8 (4)	C(21)—C(20)—C(22)	110.7 (4)
C(20)—C(22)—C(23)	113.1 (4)	C(22)—C(23)—C(24)	111.6 (5)
C(23)—C(24)—O(27)	125.6 (5)	C(23)—C(24)—O(28)	113.4 (5)
O(27)—C(24)—O(28)	121.0 (5)		
O—H \cdots O		O \cdots O	O—H
O(28)—H(28) ⁱ \cdots O(26) ⁱⁱ	2.634 (5)	0.96 (5)	1.68 (5)
O(26)—H(26) ⁱⁱⁱ \cdots O(25) ⁱⁱⁱ	2.723 (5)	0.91 (5)	1.81 (5)
O(25)—H(25) ⁱⁱⁱ \cdots O(29) ^{iv}	2.774 (5)	0.90 (5)	1.88 (5)
O(29)—H(29) ^{iv} \cdots O(27) ^v	2.856 (6)	0.89 (6)	1.98 (6)
		H \cdots O	O—H \cdots O
		1.81 (5)	174 (5)
		1.88 (5)	171 (5)
		1.98 (6)	169 (6)

Symmetry code: (i) x, y, z ; (ii) $-\frac{1}{2}+x, -\frac{1}{2}-y, 1-z$; (iii) $\frac{3}{2}-x, -y, -\frac{1}{2}+z$; (iv) $-\frac{1}{2}+x, \frac{1}{2}-y, 1-z$; (v) $x, 1+y, z$.

$z)\cdots O(25)-H(\frac{3}{2}-x, -y, -\frac{1}{2}+z)\cdots O(29)-H(-\frac{1}{2}+x, \frac{1}{2}-y, 1-z)\cdots O(27) = C(24)-O(28)-H(x, 1+y, z)$. These are in the range for typical hydrogen bonds between oxygen molecules: $O-H\cdots O = 2.63-2.86$ Å and $O-H\cdots O = 169-172^\circ$. The parameters for this hydrogen-bond network are also listed in Table 2. On the other hand, the ethanol molecules are involved in the hydrogen-bond network of the ethanol-including CA crystals, forming five kinds of hydrogen bonds; $O(28)-H(x,y,z)\cdots O(29)-H(\frac{1}{2}-x, 1-y, -\frac{1}{2}+z)\cdots O(\text{ethanol})-H(-\frac{1}{2}+x, \frac{3}{2}-y, -z)\cdots O(25)-H(-\frac{1}{2}+x, \frac{3}{2}-y, -z)\cdots O(26)-H(\frac{1}{2}-x, 2-y, -\frac{1}{2}+z)\cdots O(27) = C(24)-O(28)-H(x, 1+y,$

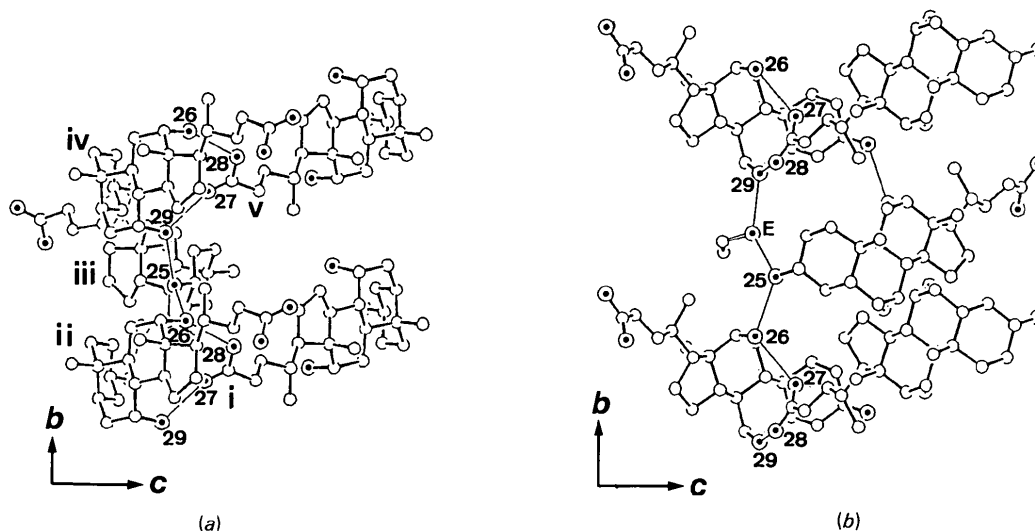


Fig. 3. Hydrogen-bond network extended along the direction of the crystallographic b axis shown by an ORTEP drawing (Johnson, 1976) of the partial packing diagram as viewed along the a axis. (a) The 'no-guest' crystals (this work), (b) the ethanol-including crystal (Johnson & Schaefer, 1972). Atoms are represented as Fig. 2. In (a), the CA molecules of (i)–(v) correspond to those operated by the symmetry codes presented in Table 2. The numbering of the O atoms involved in the hydrogen-bond network is also indicated (E: that of ethanol).

z). It is interesting to compare this hydrogen-bond network with that of the no-guest crystal. The ethanol molecules can be regarded as being inserted between the O(25) and O(29) atoms. It should be noted that this insertion of ethanol molecules induces the change of the direction of donor and acceptor O atoms; this can be understood from Fig. 3, where the O(27) and O(28) atoms change places with each other in the no-guest and ethanol-including CA crystals.

This is the first case where crystals without any guest molecules have been found in CA crystals. It is also noteworthy that such a no-guest crystal form has never been observed in DCA. The crystal structures hitherto known for CA (Johnson & Schaefer, 1972; Lessinger, 1982; Miki, Masui, Kasai, Miyata, Shibakami & Takemoto, 1988) and for DCA (Giglio, 1984) always contain a variety of organic guest molecules; in DCA a crystal form including an organometallic compound, such as ferrocene, has also been obtained (Miki, Kasai, Tsutsumi, Miyata & Takemoto, 1987). The fact that such a no-guest crystal form is found only in CA implies that CA has an ability to adopt a wide variety of molecular arrangements in crystal forms. In fact, we have already found that CA takes several other crystal forms with a variety of guest molecules (Miki *et al.*, unpublished results) other than the crystals with ethanol (Johnson & Schaefer, 1972), water (Lessinger, 1982) and acetophenone (Miki, Masui, Kasai, Miyata, Shibakami & Takemoto, 1988). It should be emphasized that this ability to adopt a variety of crystal forms found only in CA may be of

a quite different nature from that in DCA, because DCA includes various organic guest molecules in a similar molecular arrangement with space group $P2_12_1$. In addition, we have found intercalation phenomena for this CA crystal when soaking in some organic solvents (Miyata, Shibakami, Chirachanchai, Takemoto, Kasai & Miki, 1990). This is also a specific ability observed only in CA crystals.

Part of this work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture.

References

- ASHIDA, T. (1979). HBL5-V. *The Universal Crystallographic Computing System – Osaka*, pp. 53–59. Computation Center, Osaka Univ., Japan.
- GIGLIO, E. (1984). *Inclusion Compounds*, Vol. II, edited by J. L. ATWOOD, J. E. D. DAVIES & D. D. MACNICOL, pp. 207–229. London: Academic Press.
- HAMILTON, W. C. (1959). *Acta Cryst.* **12**, 609–610.
- JOHNSON, C. K. (1976). ORTEPII. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
- JOHNSON, J. N. & SCHAEFER, J. P. (1972). *Acta Cryst.* **B28**, 3083–3088.
- LESSINGER, L. (1982). *Cryst. Struct. Commun.* **11**, 1787–1792.
- MIKI, K., KASAI, N., TSUTSUMI, H., MIYATA, M. & TAKEMOTO, K. (1987). *J. Chem. Soc. Chem. Commun.* pp. 545–546.
- MIKI, K., MASUI, A., KASAI, N., MIYATA, M., SHIBAKAMI, M. & TAKEMOTO, K. (1988). *J. Am. Chem. Soc.* **110**, 6594–6596.
- MIYATA, M., SHIBAKAMI, M., CHIRACHANCHAI, S., TAKEMOTO, K., KASAI, N. & MIKI, K. (1990). *Nature (London)*, **343**, 446–447.
- SHELDRICK, G. M. (1986). SHELXS86. Program for crystal structure determination. Univ. of Göttingen, Federal Republic of Germany.