A Refinement of the Crystal Structure of Quinolinic Acid at 100 K with Neutron Diffraction Data*

By Fusao Takusagawa and Thomas F. Koetzle†

Chemistry Department, Brookhaven National Laboratory, Upton, New York 11973, USA

The crystal structure of quinolinic acid (pyridine-2,3-dicarboxylic acid: $C_7H_5NO_4$) has been refined, based upon neutron diffraction data measured at 100 K. Crystal data: space group $P2_1/c$; $a = 7.415$ (5), $b = 12.396$ (9), $c = 7.826$ (6) Å, $\beta = 117.05$ (4)°, $Z = 4$. The final unweighted R value based on F^2 is 0.048 for all 1643 unique reflections, and bond distances have been determined with precision better than 0.003 Å. The major temperature dependence in the cell constants is observed for the b axis, which is perpendicular to the molecular planes. Rigid-body analyses of the thermal parameters determined here at 100 K and those found in a prior study at 297 K indicate that the translational motion changes with temperature more along the b axis than in other directions. Significant differences between the structure at 100 and 297 K are observed in the intramolecular $O\cdots H\cdots O$ hydrogen bond, where the H atom shifts towards the midpoint of the bond when the crystal is cooled. This temperature effect is discussed in the light of results of the rigid-body thermal-motion analyses.

Introduction

The general features of the crystal structure of quinolinic acid with a very short asymmetric intramolecular hydrogen bond have been elucidated from X-ray photographic data by Takusagawa, Hirotsu & Shimada (1973). Positions of the H atoms, including that in the short hydrogen bond, $O\cdots O$ 2.398 (3) Å, have been confirmed by neutron diffraction techniques at room temperature by Kvick, Koetzle, Thomas & Takusagawa (1974). We have now refined the structure and determined accurate atomic positions and thermal parameters from single-crystal neutron diffraction data measured at 100 K. This work has been undertaken as part of a study of the charge-density distribution in quinolinic acid by combined X-ray and neutron diffraction techniques.

Data collection

The sample of quinolinic acid used in this work was recrystallized from aqueous solution and had a volume of 7.53 mm³. The crystal was mounted on an aluminum pin, the end of which was hollow to reduce the amount of metal in the neutron beam, and was oriented along the crystallographic c axis. The sample was placed in a specially constructed closed-cycle helium refrigerator‡ and mounted on an automated four-circle diffractometer (Dimmler, Greenlaw, Kelley, Potter, Rankowitz & Stubblefield, 1976; McMullan, Andrews, Koetzle, Reidinger, Thomas & Williams, 1976) at the Brookhaven High Flux Beam Reactor, with a crystal-monochromated neutron beam of wavelength 1.047 Å (based upon KBr, $a = 6.600$ Å). The temperature of the sample during data collection was 100 ± 1 K. Cell dimensions refined by a least-squares procedure based on setting angles of 29 reflections are listed in Table 1. Intensities were measured for

‡ Air Products and Chemicals, Inc. DISPLEX® Model CS-202.

Table 1. *Crystal data for quinolinic acid (pyridine-2,3-dicarboxylic acid:* $C_7H_5NO_4$)

	100 K	297 K*	Δ
a	7.415 (5) Å	7.422 (1) Å	0.007 Å
b	12.396 (9)	12.705 (2)	0.309
c	7.826 (6)	7.834 (1)	0.008
β	117.05 (4)°	116.95 (1)°	−0.10°
V	640.6 Å³	658.5 Å³	17.9 Å³
D_n	1.733 g cm⁻³	1.686 g cm⁻³	
Space group	$P2_1/c$		
μ†	1.247 cm⁻¹	1.227 cm⁻¹	

* Unit-cell parameters determined from X-ray powder diffraction data (Kvick *et al.*, 1974).

† Mass absorption coefficients of C, N and O were obtained from *International Tables for X-ray Crystallography* (1962). For H, 23.9 cm² g⁻¹ was used for the effective mass absorption coefficient due to incoherent scattering, corresponding to an incoherent cross-section of 40 barn.

reflections in four octants of reciprocal space (hkl, $\bar{h}kl$, $h\bar{k}l$, $hk\bar{l}$), of which the $h\bar{k}l$ and $\bar{h}kl$ octants were not complete, with $2\theta \leq 90°$, employing a $\theta/2\theta$ step-scan technique. The scan range was varied according to $\Delta 2\theta = 1.596(1.0 + 4.785 \tan \theta)°$ for the high-angle data ($50° \leq 2\theta \leq 90°$) and $\Delta 2\theta = 4.5°$ for the low-angle data, and the step size was adjusted to give approximately 60 steps in each scan. As a general check on experimental stability, the intensities of two standard reflections were remeasured every 100 reflections. These did not vary to any significant degree during the entire period of data collection.

Data reduction and refinements

Background corrections were made by the program *PEAK* (Takusagawa, 1977) written for a PDP-11/40 computer with interactive graphics display (Bernstein *et al.*, 1974; Vector General, Inc., 1973). Initially, a linear background function was fitted by least-squares calculations to the flat portion of each profile. Reflections with weak net intensity or unusual backgrounds were displayed and the most suitable background corrections estimated manually. Absorption corrections for observed intensities were made by a semi-empirical method (North, Phillips & Mathews, 1968) based on ψ-scan intensity data for several reflections.* The standard deviation of each reflection was estimated as follows:

$$\sigma^2(I) = T + B + [0.025(T - B)]^2 + (0.025B)^2,$$

where T and B are total and background counts, respectively, and the factor 0.025 represents an

---

* A semi-empirical absorption correction was employed, because the sample was irregular in shape. An attempt was made to describe the crystal by eight rational boundary planes, and analytical absorption corrections were calculated based on this description. Refinements based on the analytically corrected data gave results which agreed to within experimental error with those based on the empirical correction which are reported here.

estimate of non-statistical errors. Squared observed structure factors were obtained as $F_o^2 = I \sin 2\theta$ and averaged for symmetry-related reflections. The agreement factor obtained on averaging is

$$R_c = \Sigma \left(\sum_{i=1}^{n} |\langle F_o^2 \rangle - F_{oi}^2| \right) / \Sigma n \langle F_o^2 \rangle = 0.034.$$

The atomic coordinates from the neutron diffraction study of Kvick *et al.* (1974) were used as initial values for a full-matrix least-squares refinement minimizing $\Sigma w(F_o^2 - k^2 F_c^2)^2$ and using *FLINUS*, a local version of *ORFLS* (Busing, Martin & Levy, 1962). Weights were chosen as $w = 1/\sigma^2(F_o^2) = 1/[\sigma^2(I) \sin^2 2\theta]$. A scale factor, k, the coherent neutron scattering length of nitrogen and a Zachariasen isotropic extinction parameter, g (Zachariasen, 1967), were varied together with positional and anisotropic thermal parameters for all atoms. The extinction correction, applied to F_c^2, is given by

$$y = [1 + (2\bar{T}F_c^2 g/\bar{V} \sin 2\theta)]^{-1/2}$$

where $\bar{T}$ is the effective mean path length approximated from the calculated absorption A, by $\bar{T} \simeq -\ln A/\mu$, and $\bar{V} = V^2/\lambda^3$. The smallest y value was calculated to be 0.84 for the reflection 040, and the value of g is 0.041×10^{-4}. Finally a correction was applied for the effects of a small number of neutrons in the incident beam with wavelength $\lambda/2$, by means of a least-squares procedure, minimizing

$$L = \Sigma w[F_o^2(hkl) - F_c^2(hkl) - k' F_c^2(2h2k2l)]^2.$$

The value of k' obtained is 0.0023 (4). The data collection and structure refinement procedures are summarized in Table 2. Final positional parameters for

Table 2. *Experimental and refinement parameters*

Crystal weight	0.0127 g
Crystal volume (room temperature)	7.53 mm³
Number of faces	8
Number of reflections measured	2950
Number of independent reflections	1643
Number of reflections with $F_o^2 > 3\sigma(F_o^2)$	1315
$R = \Sigma |F_o^2 - k^2 F_c^2|/\Sigma F_o^2$ (all reflections)	0.048
$R = \Sigma |F_o^2 - k^2 F_c^2|/\Sigma F_o^2$ [reflections with $F_o^2 > 3\sigma(F_o^2)$]	0.044
$Rw = (\Sigma w|F_o^2 - k^2 F_c^2|^2/\Sigma wF_o^4)^{1/2}$ (all reflections)	0.074
$Rw = (\Sigma w|F_o^2 - k^2 F_c^2|^2/\Sigma wF_o^4)^{1/2}$ [reflections with $F_o^2 > 3\sigma(F_o^2)$]	0.067
$S = [\Sigma w(F_o^2 - k^2 F_c^2)^2/(m - n)]^{1/2}$ (all reflections)*	1.703
$S = [\Sigma w(F_o^2 - k^2 F_c^2)^2/(m - n)]^{1/2}$ [reflections with $F_o^2 > 3\sigma(F_o^2)$]	1.744

* m is the number of reflections and n the number of parameters.

Table 3. *Atomic coordinates of quinolinic acid at 100 K*

	x	y	z
N(1)	0.93855 (11)	0.12256 (7)	0.10843 (10)
C(2)	0.73551 (16)	0.12461 (9)	−0.00157 (14)
C(3)	0.61223 (15)	0.12613 (9)	0.09093 (14)
C(4)	0.70694 (16)	0.12206 (9)	0.29186 (15)
C(5)	0.91604 (16)	0.12158 (10)	0.39775 (15)
C(6)	1.03156 (16)	0.12224 (10)	0.29951 (15)
C(7)	0.68297 (17)	0.12097 (10)	−0.21579 (15)
C(8)	0.38208 (15)	0.13385 (9)	−0.00503 (15)
O(1)	0.82623 (21)	0.10664 (13)	−0.25163 (19)
O(2)	0.49928 (20)	0.13474 (12)	−0.33812 (18)
O(3)	0.28614 (20)	0.15526 (12)	−0.18371 (20)
O(4)	0.29860 (20)	0.11964 (12)	0.09746 (19)
H(1)	0.61272 (38)	0.12072 (25)	0.36461 (35)
H(2)	0.98737 (40)	0.12084 (26)	0.55342 (34)
H(3)	1.19675 (35)	0.12212 (25)	0.36698 (35)
H(4)	1.03038 (37)	0.12049 (23)	0.04022 (34)
H(5)	0.39003 (42)	0.14979 (24)	−0.26071 (39)

all atoms are listed in Table 3.* Neutron scattering lengths used are $b_C = 0.665 \times 10^{-12}$ (Bacon, 1972), $b_H = -0.374 \times 10^{-12}$, $b_O = 0.580 \times 10^{-12}$ (Shull, 1972), $b_N = 0.941$ (5) $\times 10^{-12}$ cm. This value of b_N is slightly larger than those obtained in a number of recent structure refinements (Kvick et al., 1974), where values ranged from 0.904 (6) to 0.931 (3) $\times 10^{-12}$ cm.

Discussion

The crystal structure has been discussed in detail in earlier papers (Takusagawa et al., 1973; Kvick et al., 1974). The discussion here will mainly be restricted to those aspects of the structure which are observed to change when the temperature of the crystal is lowered.

---

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33106 (31 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

The molecular structure of quinolinic acid in the crystalline state determined by neutron diffraction at 100 and 297 K is illustrated in Fig. 1 (Johnson, 1976), and bond distances and angles found at 100 K are shown in Fig. 2. Differences in bond distances and angles determined at 297 and 100 K are presented in Fig. 3. The difference thermal ellipsoids are illustrated in Fig. 4 and results of rigid-body thermal-motion analyses are summarized in Table 4.

Unit-cell dimensions determined at 100 K are compared in Table 1 with those found at room temperature. The major change is observed in the crystallographic b axis, which is perpendicular to the molecular planes. There is no hydrogen bond between these molecular sheets as has been noted earlier (Takusagawa et al., 1973; Kvick et al., 1974). The sheets interact only by means of van der Waals forces. Rigid-body thermal-motion analyses carried out by the method of Schomaker & Trueblood (1968) indicate that the largest translation tensor component is perpendicular to the molecular planes (T_Z). All trans-
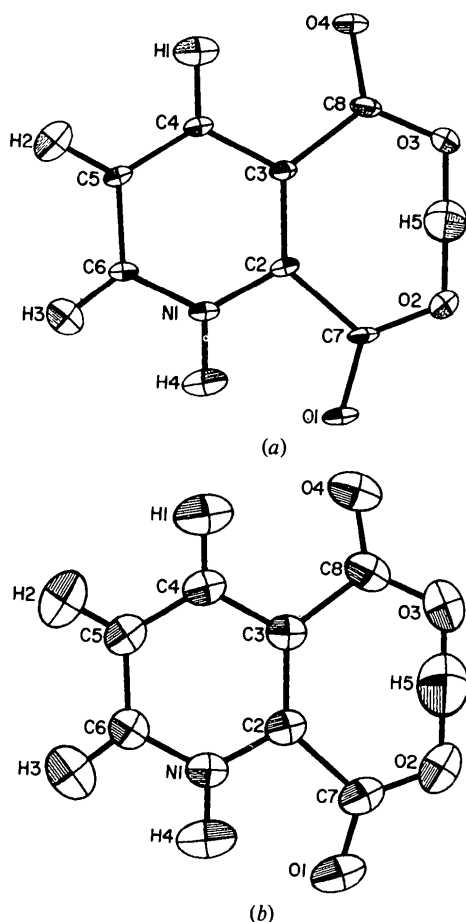

(a)

(b)

Fig. 1. (a) Molecular view of quinolinic acid at 100 K. Thermal ellipsoids are drawn at the 74% probability level. (b) Molecular view of quinolinic acid at 297 K. Thermal ellipsoids are drawn as in (a).
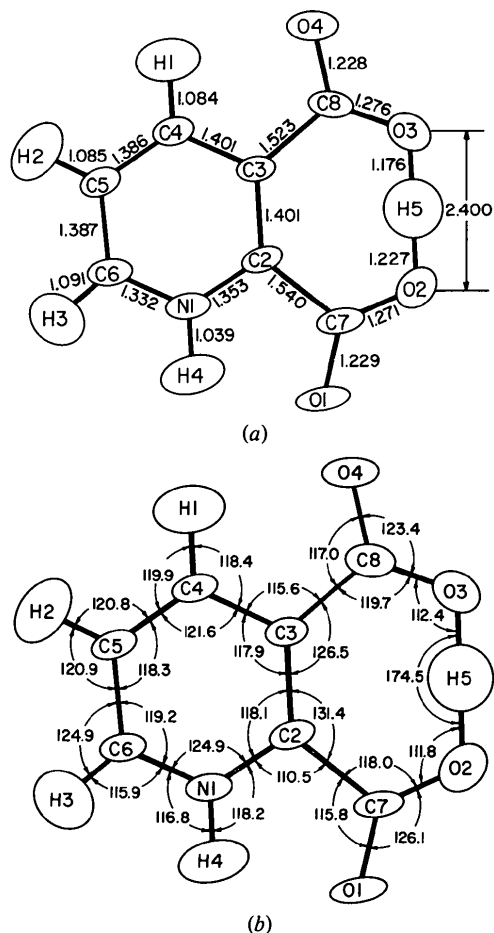

(a)

(b)

Fig. 2. (a) Bond distances at 100 K. Estimated standard deviations are in the range 0.001 to 0.003 Å. (b) Bond angles at 100 K. Estimated standard deviations are 0.1 to 0.2° except 0.3° for O(2)–H(5)–O(3).

Table 4. *Summary of rigid-body thermal-motion analyses*

The units for mean square amplitude of translational vibration (T), librational vibration (L), and root-mean-square fit, $\langle \Delta U^2 \rangle^{1/2}$, are 0·0001 Å², 0·0001 square radian, and 0·0001 Å² respectively.

Model*	Temperature	T_X	T_Y	T_Z	L_X	L_Y	L_Z	$\langle \Delta U^2 \rangle^{1/2}$
	100 K	110	39	101	17	9	2	5
	297 K	223	149	321	46	32	11	6
	Diff¹	113	110	220	29	23	9	–
	Diff²	113	110	215	28	21	8	6
	100 K	135	35	37	52	26	12	30
	297 K	256	138	249	87	50	23	36
	Diff¹	121	103	212	35	24	11	–
	Diff²	121	103	210	32	22	10	11
	100 K	123	39	60	30	28	11	32
	297 K	239	154	278	70	56	23	47
	Diff¹	116	115	218	40	28	12	–
	Diff²	116	115	217	37	26	12	35
	100 K	73	74	113	57	20	12	7
	297 K	177	204	344	214	61	36	7
	Diff¹	104	130	231	157	41	24	–
	Diff²	103	131	226	150	40	24	7
	100 K	89	63	106	86	15	9	7
	297 K	198	185	345	233	51	32	10
	Diff¹	109	122	239	147	36	23	–
	Diff²	109	122	235	141	34	23	6

Diff¹: difference between values calculated at 297 K and 100 K.
Diff²: T, L, and$\langle \Delta U^2 \rangle^{1/2}$are calculated from difference thermal parameters [*i.e.* β_{ij}(Diff) = β_{ij}(297 K) – β_{ij}(100 K)].

* Coordinate systems used in these calculations are indicated by arrows →X and →Y. The Z coordinate is taken in the direction perpendicular to the page.

lational and librational tensor components are markedly lower at 100 than at 297 K, as expected. In particular, the large decrease in T_Z reduces the effective 'thickness' of the molecules. This allows shorter van der Waals contacts between the molecular planes and is in turn related to the large temperature coefficient of b mentioned above. The effects of cooling on thermal motions of individual atoms are illustrated in Fig. 4. Ellipsoids calculated by β_{ij}(Diff) = β_{ij}(297 K) − β_{ij}(100 K) show the reduction in thermal motion of each atom. These β_{ij}(Diff) have been subjected to rigid-body thermal-motion analyses, and results of these
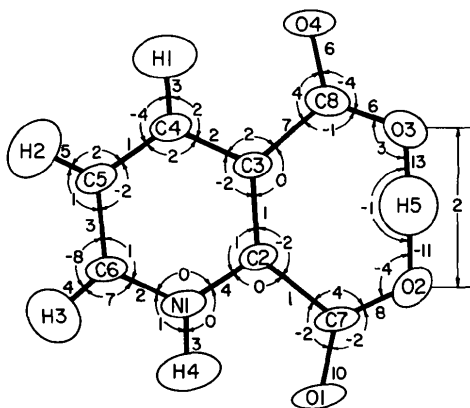

Fig. 3. Differences in bond distances and angles between the structures determined at 297 and 100 K. The units for bond distances and angles are 0·001 Å and 0·1° respectively.
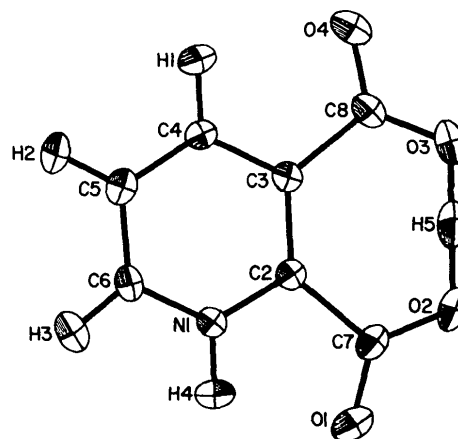

Fig. 4. Difference thermal ellipsoids which are calculated by β_{ij}(Diff) = β_{ij}(297 K) − β_{ij}(100 K). Ellipsoids are drawn as in Fig. 1.

calculations are listed in Table 4. The T and L values calculated based on β_{ij}(Diff) are in good agreement with the difference between corresponding tensor components calculated at 297 and 100 K. The difference thermal motions in Fig. 4 are quite reasonable for all atoms except H(5), which is involved in the short O$\cdots$H$\cdots$O hydrogen bond. The motion of this atom will be discussed below.

The observed differences in bond distances, shown in Fig. 3, are quite reasonable in the light of the temperature effects except for the short hydrogen bond. Bond distances corrected for effects of rigid-body libration (Schomaker & Trueblood, 1968) are given in Table 5. No significant change with temperature is found in bond angles. Displacements from the least-squares plane through the six non-hydrogen atoms of the pyridine ring are shown in Fig. 5, along with the changes in these displacements between 297 and 100 K. Significant changes are observed in the carboxyl groups and in H(4), which are involved in hydrogen bonding.

In the case of the intermolecular hydrogen bond N(1)—H(4)$\cdots$O(4), the H(4)$\cdots$O(4) distance is reduced by 0·016 Å upon cooling [100 K: 1·829 (4) Å, 297 K: 1·845 (4) Å]. This decrease may partly be due to a change in the dihedral angle of the C(8) carboxyl group. But the N(1)—H(4)$\cdots$O(4) angle does not change to any significant degree [100 K: 140·2 (2)°, 297 K: 140·5°].

In the intramolecular hydrogen bond, the distances O(2)—H(5) and O(3)—H(5) are significantly changed in comparison with the corresponding values at 297 K. At 100 K, the hydrogen atom H(5) moves closer to the midpoint between O(2) and O(3). The rigid-body thermal-motion analyses of the carboxyl groups at 297 K show that very large librations are observed around the bond C(2)—C(7) and C(3)—C(8). At 100 K, these librations are greatly reduced, but are still larger than those about other axes, as shown in Table 4. The motion of H(5) probably includes substantial anhar-
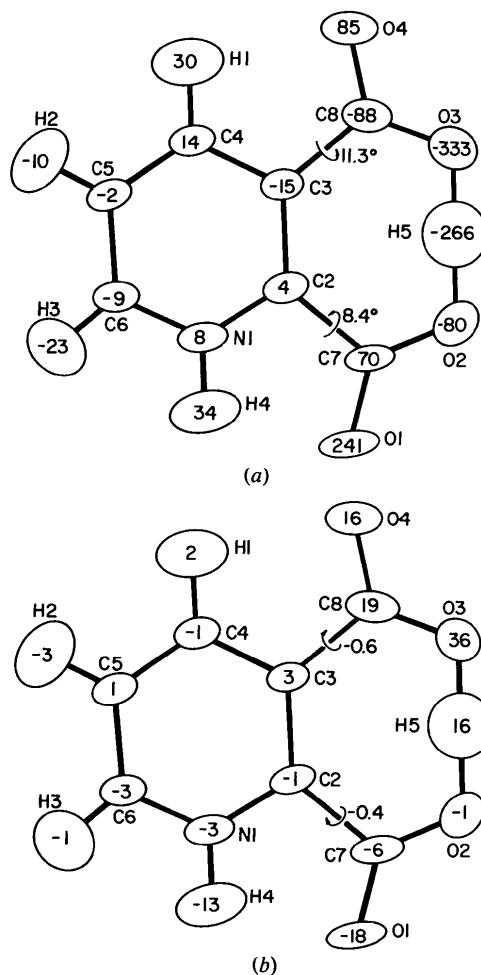

(a)

(b)

Fig. 5. (a) Displacements from the least-squares plane through the six non-hydrogen atoms of the pyridine ring as determined at 100 K. Units are 0·001 Å. Arrows indicate the directions of dihedral angles between the pyridine ring and carboxyl groups. (b) Changes in displacements between the structures determined at 297 and 100 K. Units are 0·001 Å.

monic contributions at 297 K, and cannot properly be approximated as an ellipsoid. Anharmonicity of the potential energy surface governing H(5) could explain the displacement in its refined position toward the midpoint of the hydrogen bond when the crystal is cooled. The O(2)$\cdots$O(3) distances determined at 100 and 297 K are nearly identical [2·400 (2) vs 2·398 (3) Å]. However, if these distances are corrected for effects of thermal motion, assuming that the carboxyl group torsional motions are exactly out of phase, the corrected distances are 2·433 Å at 100 K and 2·466 Å at 297 K. These latter values should be regarded as upper bounds to the true distances (r_0).

Table 5. *Bond distances* (Å) *corrected for effects of thermal motion at* 100 *and* 297 K

The entire quinolinic acid molecule except H(5) is assumed as a rigid-body.

	100 K	297 K*		100 K	297 K*
N(1)—C(2)	1·355	1·353	C(4)—H(1)	1·086	1·090
N(1)—C(6)	1·334	1·333	C(5)—C(6)	1·390	1·388
N(1)—H(4)	1·041	1·039	C(5)—H(2)	1·087	1·083
C(2)—C(3)	1·403	1·404	C(6)—H(3)	1·093	1·098
C(2)—C(7)	1·543	1·545	C(7)—O(1)	1·231	1·222
C(3)—C(4)	1·404	1·403	C(7)—O(2)	1·273	1·266
C(3)—C(8)	1·526	1·521	C(8)—O(3)	1·278	1·273
C(4)—C(5)	1·389	1·389	C(8)—O(4)	1·230	1·226

* Kvick *et al.* (1974).

References

BACON, G. E. (for NEUTRON DIFFRACTION COMMISSION) (1972). *Acta Cryst.* A28, 357–358.

BERNSTEIN, H. J., ANDREWS, L. C., BERMAN, H. M., BERNSTEIN, F. C., CAMPBELL, G. H., CARRELL, H. L., CHIANG, H. B., HAMILTON, W. C., JONES, D. D., KLUNK, D., KOETZLE, T. F., MEYER, E. F., MORIMOTO, C. N., SEVIAN, S. S., STODOLA, R. K., STRONGSON, M. M. & WILLOUGHBY, T. V. (1974). Second Annual AEC Scientific Computer Information Exchange Meeting, Proceedings of the Technical Program, pp. 148–158. Report BNL 18803. Brookhaven National Laboratory, Upton, NY.

BUSING, W. R., MARTIN, K. O. & LEVY, H. A. (1962). *ORFLS*. Report ORNL-TM-305. Oak Ridge National Laboratory, Tennessee.

DIMMLER, D. G., GREENLAW, N., KELLEY, M. A., POTTER, D. W., RANKOWITZ, S. & STUBBLEFIELD, F. W. (1976). *IEEE Trans. Nucl. Sci.* NS-23, 398–405.

International Tables for X-ray Crystallography (1962). Vol. III, pp. 197–200. Birmingham: Kynoch Press.

JOHNSON, C. K. (1976). *ORTEP*-II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee.

KVICK, Å., KOETZLE, T. F., THOMAS, R. & TAKUSAGAWA, F. (1974). *J. Chem. Phys.* 60, 3866–3874.

McMULLAN, R. K., ANDREWS, L. C., KOETZLE, T. F., REIDINGER, F., THOMAS, R. & WILLIAMS, G. J. B. (1976). *NEXDAS. Neutron and X-ray Data Acquisition System.* Unpublished work.

NORTH, A. C. T., PHILLIPS, D. C. & MATHEWS, F. S. (1968). *Acta Cryst.* A24, 351–359.

SCHOMAKER, V. & TRUEBLOOD, K. N. (1968). *Acta Cryst.* B24, 63–76.

SHULL, C. G. (1972). Private communication.

TAKUSAGAWA, F. (1977). Unpublished work.

TAKUSAGAWA, F., HIROTSU, K. & SHIMADA, A. (1973). *Bull. Chem. Soc. Jpn*, 46, 2372–2380.

Vector General, Inc. (1973). *FORTRAN Drawing Package Reference Manual.* 8399 Topanga Canyon Blvd., Canoga Park, Calif. 91304, USA.

ZACHARIASEN, W. H. (1967). *Acta Cryst.* 23, 558–564.

The Crystal and Molecular Structure of Isosteganol

BY S. E. HULL,* L. R. HUGHES, OLGA KENNARD† AND R. A. RAPHAEL

University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, England

As part of the synthetic study of a group of antileukæmic lignans the structure of isosteganol, $C_{22}H_{22}O_8$, a reduction product of an isomer of steganone, was determined. The crystals are triclinic, space group $P\bar{1}$, $a = 7\cdot146$ (1), $b = 9\cdot407$ (1), $c = 14\cdot326$ (2) Å, $\alpha = 79\cdot25$ (1), $\beta = 86\cdot57$ (1), $\gamma = 83\cdot76$ (1)°, $Z = 2$. The structure was solved by direct methods and refined to $R = 0\cdot062$ for the 2583 unique reflexions measured on a diffractometer. The conformation of isosteganol is compared with that of episteganol [Bryan, Gilmore & Restivo (1976), personal communication]. The major difference between the two stereoisomers lies in the conformation of the cyclooctadiene ring which approximates to a distorted crown in isosteganol and a strained tub in episteganol. Apart from the cyclooctadiene ring there is close agreement in the bond length/bond angle values in the two structures.

Introduction

A recent synthetic study of a group of antileukæmic lignans from *Steganotaenia araliacea* Hochst has achieved a total synthesis of the key steganone (I). The approach used resulted in the production of a stereoisomer termed isosteganone, which was found to undergo a smooth thermal rearrangement to give steganone itself. The mild nature of this rearrangement suggested that it might be due to the presence of the

---
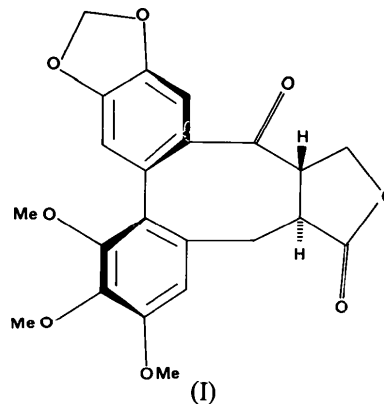
* Present address: Department of Physics, University of York, Heslington, York.

† External Staff, Medical Research Council.

(I)