

Structures of Two Polymorphic Forms of Cyclohexylammonium Phosphoenolpyruvate

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Abstract. Cyclohexylammonium 1-carboxyethenyl hydrogen phosphate, $C_6H_{14}N^+ \cdot C_3H_4O_6P^-$, $M_r = 267.22$, crystallizes in two different crystalline forms: (I) orthorhombic, $P2_12_12_1$, $a = 5.892$ (4), $b = 12.22$ (1), $c = 18.12$ (2) Å, $V = 1305$ (2) Å³, $Z = 4$, $D_m = 1.36$, $D_x = 1.36$ Mg m⁻³, Mo $K\alpha$, $\lambda = 0.71069$ Å, $\mu = 0.233$ mm⁻¹, $F(000) = 568$, $T = 303$ (1) K, final $R = 0.0357$ for 3546 observed data including both hkl and $\bar{h}\bar{k}l$ reflections; (II) monoclinic, $P2_1/c$, $a = 13.48$ (1), $b = 8.104$ (6), $c = 12.98$ (1) Å, $\beta = 112.81$ (6)°, $V = 1307$ (2) Å³, $Z = 4$, $D_m = 1.36$, $D_x = 1.36$ Mg m⁻³, Mo $K\alpha$, $\mu = 0.233$ mm⁻¹, $F(000) = 568$, $T = 301$ (2) K, final $R = 0.0445$ for 2440 observed reflections. The phosphate groups display different orientations with respect to the enolpyruvate moieties in the two forms. The carboxylic hydroxyl group is *trans* to the ester O atom in (I) but *cis* in (II). The length of the P–O(ester) bond is 1.610 (2) Å in (I) and 1.604 (2) Å in (II).

Introduction. This work is a continuation of our investigations of organic phosphates (Weichsel & Lis, 1989). Although the structure of the monoclinic form of cyclohexylammonium phosphoenolpyruvate (PEPCHA) has been reported by Watson & Kennard (1973) on the basis of photographic data we decided to reinvestigate this structure in order to obtain more accurate atomic parameters. However, as we later observed, the compound crystallizes in two different forms: orthorhombic (I) and monoclinic (II). The form isolated strongly depends on the crystallization conditions. The molecular and crystal structures of both forms are presented in this paper. The structure of another salt of phosphoenolpyruvic acid, bis(cyclohexylammonium) phosphoenolpyruvate methanol solvate (1/0.5), will be published later.

Experimental. Orthorhombic crystals (I) were obtained as needles from water solution. Monoclinic crystals (II) were grown as oblique parallelepipeds from methanol solution by diffusion of diethyl ether through the vapor phase in the desiccator. It was found that the kind of crystals obtained strongly depended on the solvent no matter what kind of seed was used for crystallization. D_m by flotation in $CH_2Cl_2/CHCl_3$ for both crystals. Systematic absences on Weissenberg photographs

uniquely indicated the space groups. Specimens $0.8 \times 0.7 \times 0.7$ mm for (I) and $0.45 \times 0.6 \times 0.6$ for (II) were cut from large crystals and mounted in capillaries. Syntex $P2_1$ diffractometer, Mo $K\alpha$ radiation for lattice parameters [15 reflections in the range $21 < 2\theta < 28^\circ$ for (I) and $20 < 2\theta < 28^\circ$ for (II)] and intensity measurements; ω – 2θ scan technique. 5085 reflections below $2\theta = 65^\circ$ for (I) ($0 \leq h \leq 8$, $0 \leq k \leq 18$, $-27 \leq l \leq 27$); 4388 reflections below $2\theta = 58^\circ$ for (II) ($-18 \leq h \leq 18$, $0 \leq k \leq 10$, $-16 \leq l \leq 16$). After every 50 reflections two standards were measured, variation $\pm 5\%$ for (I) and $\pm 10\%$ for (II). After averaging, 3546 data for (I) and 2440 for (II) with $I > 3\sigma(I)$ were used in calculations; R_{merge} was 0.0248 for (I) and 0.0205 for (II). Neutral-atom scattering factors from *International Tables for X-ray Crystallography* (1974); real and imaginary components of anomalous dispersion included for all non-H atoms. Structure of (I) solved by direct methods using *SHELXS* program (Sheldrick, 1986); H atoms were located from difference Fourier synthesis. Refinement, *SHELX76* (Sheldrick, 1976), based on F values with $w = 1/\sigma^2(F_o)$; (P, N, C, O anisotropic, H isotropic). The positional parameters of the H atoms in both structures were refined with constraints $d(C-H) = 1.08$, $d(N-H) = 1.00$ and $d(O-H) = 0.96$ Å. For (I) the refinement based on hkl and $\bar{h}\bar{k}l$ reflections gave final $R = 0.0357$, and $wR = 0.0345$ (refinement of the inverted structure gave $R = 0.0362$ and $wR = 0.0349$). For (II) preliminary examination of unit-cell parameters suggested the same crystal modification as that described by Watson & Kennard (1973). However, our values for a [13.48 (1) Å] and β [112.81 (6)°] differ significantly from those reported by Watson & Kennard (1973) [$a = 13.218$ (5) Å and $\beta = 109^\circ 54$ (1)'], although practically the same unit-cell volume was obtained in each investigation. Watson & Kennard determined the unit-cell parameters by measurement of the 2θ values of axial reflections with a Picker automatic four-circle diffractometer. The refinement for (II) was started with the published coordinates of Watson & Kennard (1973). Full-matrix refinement with $w = 1/\sigma^2(F_o)$ gave final $R = 0.0445$ and $wR = 0.0435$. Max. Δ/σ was 0.07 for (I) and 0.06 for (II). Residual electron density within -0.40 and 0.44 e Å⁻³ for (I) and -0.33 and 0.31 e Å⁻³ for (II).

Table 1. Final atomic parameters for the orthorhombic form (I)

$$U_{eq} = \frac{1}{3}(U_{11} + U_{22} + U_{33}).$$

| | x | y | z | $U_{eq}/U_{iso}(\text{\AA}^2)$ |
|-------|--------------|--------------|--------------|--------------------------------|
| P | 0.93406 (8) | 0.38494 (4) | 0.37333 (2) | 0.0292 (2) |
| O(1) | 0.94260 (25) | 0.30594 (11) | 0.30228 (7) | 0.0412 (4) |
| O(2) | 0.75493 (26) | 0.47608 (10) | 0.35569 (8) | 0.0408 (5) |
| O(3) | 1.16885 (22) | 0.43216 (10) | 0.37706 (7) | 0.0355 (4) |
| O(4) | 0.85116 (25) | 0.32307 (10) | 0.43845 (7) | 0.0389 (5) |
| O(21) | 0.69042 (27) | 0.09938 (13) | 0.19564 (9) | 0.0541 (6) |
| O(22) | 1.04710 (27) | 0.12162 (13) | 0.23463 (9) | 0.0534 (5) |
| N | 0.4369 (4) | 0.38339 (14) | 0.50125 (8) | 0.0367 (5) |
| C(1) | 0.7630 (4) | 0.24429 (16) | 0.27698 (10) | 0.0369 (6) |
| C(2) | 0.8500 (4) | 0.14847 (16) | 0.23338 (11) | 0.0374 (6) |
| C(3) | 0.5458 (4) | 0.26075 (20) | 0.28939 (13) | 0.0494 (7) |
| C(4) | 0.4153 (5) | 0.47270 (17) | 0.55736 (11) | 0.0426 (7) |
| C(5) | 0.1697 (5) | 0.48219 (22) | 0.58056 (15) | 0.0605 (10) |
| C(6) | 0.1379 (7) | 0.57635 (27) | 0.63609 (18) | 0.0794 (13) |
| C(7) | 0.2272 (8) | 0.68236 (25) | 0.60507 (18) | 0.0879 (15) |
| C(8) | 0.4735 (8) | 0.67214 (28) | 0.58211 (21) | 0.0944 (16) |
| C(9) | 0.5058 (6) | 0.57893 (22) | 0.52644 (16) | 0.0687 (11) |
| H(2) | 0.808 (5) | 0.5296 (17) | 0.3209 (12) | 0.101 (12) |
| H(21) | 0.741 (5) | 0.0380 (13) | 0.1671 (11) | 0.076 (9) |
| H(11) | 0.340 (4) | 0.3884 (23) | 0.4562 (9) | 0.082 (9) |
| H(12) | 0.597 (2) | 0.3786 (21) | 0.4829 (11) | 0.058 (7) |
| H(13) | 0.394 (5) | 0.3113 (9) | 0.5234 (11) | 0.056 (7) |

Table 2. Final atomic parameters for the monoclinic form (II)

$$U_{eq} = \frac{1}{3} \sum_i \sum_j U_{ij} a_i^* a_j^* (\mathbf{a}_i \cdot \mathbf{a}_j).$$

| | x | y | z | $U_{eq}/U_{iso}(\text{\AA}^2)$ |
|-------|---------------|--------------|--------------|--------------------------------|
| P | 0.06818 (5) | 0.17404 (8) | 0.21047 (5) | 0.0325 (2) |
| O(1) | 0.16785 (14) | 0.29106 (22) | 0.27949 (13) | 0.0420 (7) |
| O(2) | -0.01482 (15) | 0.30525 (23) | 0.13940 (14) | 0.0485 (8) |
| O(3) | 0.09651 (14) | 0.06548 (22) | 0.13306 (14) | 0.0432 (7) |
| O(4) | 0.03263 (13) | 0.08678 (21) | 0.29210 (13) | 0.0385 (6) |
| O(21) | 0.14153 (15) | 0.36216 (27) | 0.46349 (14) | 0.0497 (7) |
| O(22) | 0.28613 (19) | 0.2217 (4) | 0.57254 (18) | 0.0874 (12) |
| N | -0.09778 (16) | 0.22933 (28) | 0.39295 (17) | 0.0375 (8) |
| C(1) | 0.24602 (18) | 0.2360 (4) | 0.37789 (21) | 0.0433 (10) |
| C(2) | 0.22672 (20) | 0.2709 (4) | 0.48127 (21) | 0.0468 (10) |
| C(3) | 0.33463 (25) | 0.1650 (6) | 0.3799 (4) | 0.0717 (15) |
| C(4) | -0.21123 (19) | 0.1660 (4) | 0.34116 (21) | 0.0406 (9) |
| C(5) | -0.25496 (24) | 0.1949 (5) | 0.21690 (25) | 0.0576 (12) |
| C(6) | -0.3723 (4) | 0.1386 (7) | 0.1642 (4) | 0.0853 (18) |
| C(7) | -0.44042 (27) | 0.2221 (7) | 0.2193 (4) | 0.0917 (20) |
| C(8) | -0.39534 (27) | 0.1927 (7) | 0.3429 (4) | 0.0845 (19) |
| C(9) | -0.27784 (24) | 0.2491 (6) | 0.3975 (3) | 0.0648 (14) |
| H(2) | -0.031 (3) | 0.406 (3) | 0.169 (3) | 0.073 (11) |
| H(21) | 0.127 (4) | 0.369 (8) | 0.530 (3) | 0.184 (23) |
| H(11) | -0.043 (2) | 0.177 (4) | 0.370 (3) | 0.067 (10) |
| H(12) | -0.061 (3) | 0.218 (5) | 0.476 (1) | 0.087 (12) |
| H(13) | -0.091 (3) | 0.351 (1) | 0.385 (3) | 0.056 (9) |

The final atomic parameters are given in Table 1 for (I) and in Table 2 for (II).*

Discussion. Both crystals investigated consist of phosphoenolpyruvate monoanions and cyclohexylammonium cations. The principal bond lengths, bond

Table 3. Principal interatomic distances (\AA), bond angles ($^\circ$) and torsion angles ($^\circ$) in both crystalline forms

| | (I) | (II) |
|----------------------|------------|-----------|
| P—O(1) | 1.610 (2) | 1.604 (2) |
| P—O(2) | 1.567 (2) | 1.560 (2) |
| P—O(3) | 1.500 (2) | 1.492 (2) |
| P—O(4) | 1.484 (2) | 1.499 (2) |
| O(1)—C(1) | 1.377 (3) | 1.377 (3) |
| C(1)—C(2) | 1.503 (3) | 1.490 (4) |
| C(1)—C(3) | 1.315 (3) | 1.317 (5) |
| C(2)—O(21) | 1.308 (3) | 1.309 (4) |
| C(2)—O(22) | 1.207 (3) | 1.212 (4) |
| N—C(4) | 1.497 (3) | 1.502 (4) |
| C(4)—C(5) | 1.511 (4) | 1.506 (4) |
| C(5)—C(6) | 1.540 (4) | 1.530 (6) |
| C(6)—C(7) | 1.507 (5) | 1.524 (7) |
| C(7)—C(8) | 1.515 (7) | 1.499 (7) |
| C(8)—C(9) | 1.533 (5) | 1.533 (6) |
| C(9)—C(4) | 1.511 (4) | 1.518 (5) |
| O(1)—P—O(2) | 106.5 (1) | 100.4 (1) |
| O(1)—P—O(3) | 103.8 (2) | 110.3 (1) |
| O(1)—P—O(4) | 109.9 (1) | 108.2 (1) |
| O(2)—P—O(3) | 110.9 (1) | 108.4 (2) |
| O(2)—P—O(4) | 107.6 (1) | 112.8 (2) |
| O(3)—P—O(4) | 117.6 (1) | 115.7 (2) |
| P—O(1)—C(1) | 124.8 (2) | 120.0 (2) |
| O(1)—C(1)—C(2) | 109.8 (2) | 115.8 (3) |
| O(1)—C(1)—C(3) | 127.4 (2) | 121.4 (3) |
| C(2)—C(1)—C(3) | 122.8 (2) | 122.6 (3) |
| C(1)—C(2)—O(21) | 112.8 (2) | 113.3 (3) |
| C(1)—C(2)—O(22) | 122.0 (2) | 122.6 (3) |
| O(21)—C(2)—O(22) | 125.2 (2) | 124.1 (3) |
| O(2)—P—O(1)—C(1) | -62.9 (6) | 158.9 (4) |
| O(3)—P—O(1)—C(1) | 180.0 (6) | -86.9 (4) |
| O(4)—P—O(1)—C(1) | 53.4 (6) | 40.5 (4) |
| P—O(1)—C(1)—C(2) | -155.8 (6) | -89.7 (5) |
| P—O(1)—C(1)—C(3) | 22.1 (8) | 93.7 (6) |
| C(3)—C(1)—C(2)—O(21) | 14.9 (6) | 171.0 (6) |
| C(3)—C(1)—C(2)—O(22) | -164.8 (6) | -7.5 (6) |

angles and torsion angles are summarized in Table 3. Views of the phosphoenolpyruvate anions in (I) and (II) are shown in Fig. 1. The enolpyruvate moiety is non-planar in both structures but the departure from planarity is more marked in (II): the angle between the carboxyl group and the plane through O(1), C(1), C(3) is $7.8(9)^\circ$ in (I) and $13.9(9)^\circ$ in (II). In (I) the carboxylic hydroxyl group is *trans* planar to the ester O atom as was earlier observed in the Na (Katti, Hosur & Viswamitra, 1981) and K (Lis, 1987) PEP salts. This is in contrast to the *cis* planar orientation in (II). The orientation of the phosphate group with respect to the enolpyruvate moiety is very different in the two forms. In (II) the torsion angle C(2)—C(1)—O(1)—P is $-89.7(5)^\circ$ and the phosphate group sticks out of the plane of the enolpyruvate system. In (I) the P atom is situated *trans* to C(2) and the torsion angle C(2)—C(1)—O(1)—P is $-155.8(7)^\circ$. It is now evident that the orientation both of the phosphate group relative to the enolpyruvate system and also of the carboxylic $-\text{CO}_2\text{H}$ group relative to the ester O atom O(1) in phosphoenolpyruvate monoanions depends upon the cation and upon the polarity and nature of the solvent from which the crystal was grown.

* 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 51778 (39 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

The respective C—C and C—O bond lengths are similar in both crystals and compare well with values found in PEPK and PEPNa. The short C(1)—O(1) distance of 1.377 (3) Å in both (I) and (II) suggests partial double-bond character for this enolic bond. The phosphate ester bond lengths are 1.610 (2) and 1.604 (2) Å for (I) and (II) respectively and are similar to those found in high- as well as in low-energy mono-ionized mono-esterified phosphates.

The geometry of cyclohexylammonium cations is normal and similar to that found in other crystals containing this cation, e.g. bis(cyclohexylammonium) D-glucose 3-phosphate (Weichsel & Lis, 1989). Both cyclohexyl rings adopt chair conformations.

In both (I) and (II) the hydrogen-bonding scheme (Table 4) involves all O- and N-bonded H atoms. The N atoms in both forms are utilized in N—H...O bonds with the phosphate O atoms only. In (I) the crystal structure is stabilized by a three-dimensional hydrogen-bonding network (Fig. 2). In (II) contacts between two-dimensional nets parallel to the (100) plane involve only hydrophobic cyclohexyl and methylene groups (Fig. 3).

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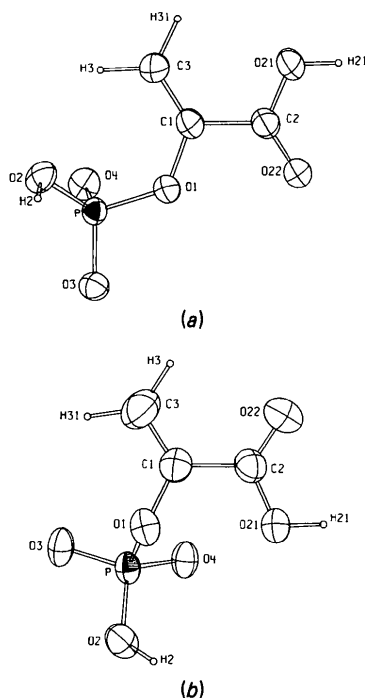


Fig. 1. Molecular geometry and numbering scheme of phosphoenolpyruvate monoanion (a) in (I) and (b) in (II).

Table 4. Geometry (Å and °) of the hydrogen bonds for crystalline forms (I) and (II)

| X—H...O | X...O | H...O | X—H...O |
|--|-----------|----------|---------|
| (I) | | | |
| O(2)—H(2)...O(22 ^b) | 2.684 (3) | 1.74 (3) | 169 (3) |
| O(21)—H(21)...O(3 ^{ll}) | 2.569 (3) | 1.61 (2) | 177 (3) |
| N—H(11)...O(3 ^{lll}) | 2.813 (3) | 1.83 (2) | 167 (2) |
| N—H(12)...O(4) | 2.792 (3) | 1.83 (2) | 160 (2) |
| N—H(13)...O(4 ^{iv}) | 2.795 (3) | 1.80 (2) | 173 (2) |
| Symmetry code: (i) 2-x, 0.5+y, 0.5-z; (ii) 2-x, y-0.5, 0.5-z; (iii) x-1, y, z; (iv) x-0.5, 0.5-y, 1-z. | | | |
| (II) | | | |
| O(2)—H(2)...O(4 ^b) | 2.494 (3) | 1.56 (2) | 164 (3) |
| O(21)—H(21)...O(3 ^{ll}) | 2.568 (3) | 1.63 (4) | 164 (5) |
| N—H(11)...O(4) | 2.815 (3) | 1.84 (3) | 166 (3) |
| N—H(12)...O(2 ^b) | 2.965 (3) | 1.98 (3) | 169 (3) |
| N—H(13)...O(3 ^b) | 2.746 (3) | 1.75 (3) | 173 (3) |

Symmetry code: (i) -x, 0.5+y, 0.5-z; (ii) x, 0.5-y, 0.5+z.

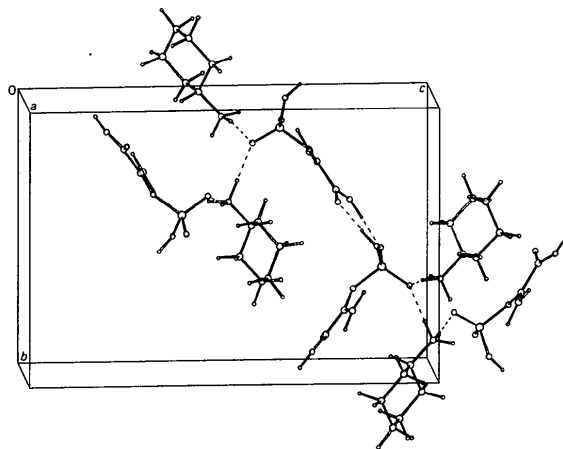


Fig. 2. Packing arrangement and hydrogen bonds in orthorhombic form.

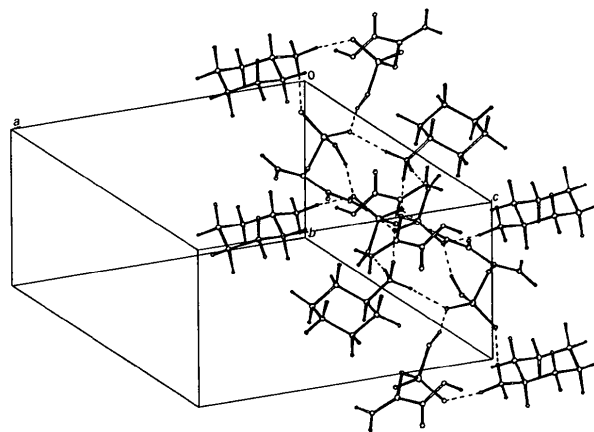


Fig. 3. Packing arrangement and hydrogen bonds in monoclinic form.

References

- International Tables for X-ray Crystallography* (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)
 KATTI, S. K., HOSUR, M. V. & VISWAMITRA, M. A. (1981). *Acta Cryst.* B37, 834–838.
 LIS, T. (1987). *Acta Cryst.* C43, 1898–1900.

- SHELDRIK, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.
 SHELDRIK, G. M. (1986). *SHELXS86*. Program for crystal structure solution. Univ. of Göttingen, Federal Republic of Germany.
 WATSON, D. G. & KENNARD, O. (1973). *Acta Cryst.* B29, 2358–2364.
 WEICHSEL, A. & LIS, T. (1989). *Pol. J. Chem.* In the press.

Acta Cryst. (1989). C45, 1180–1181

Stereochemistry of Rings. XVI.* Indole Derivatives. 1. 2,3-Dimethyl-5-nitroindole

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Abstract. C₁₀H₁₀N₂O₂, *M_r* = 190.2, monoclinic, *P*2₁/*n*, *a* = 14.345 (2), *b* = 8.518 (2), *c* = 7.741 (2) Å, β = 95.23 (3)°, *V* = 941.9 Å³, *Z* = 4, *D_x* = 1.34 g cm⁻³, λ(Cu Kα) = 1.5418 Å, μ = 7.50 cm⁻¹, *F*(000) = 400, room temperature. The structure was solved by direct methods and refined by full-matrix least squares to a final *R* = 0.048 for 1519 observed reflections. The molecule as a whole is nearly planar and the methyl groups are both equatorial. A partial π delocalization is observed.

Introduction. As a continuation of our systematic conformational studies on the deformation of rings with different substituents, we report in this paper a structural investigation of an indole derivative. The greatly increasing importance of a number of indole-based biological compounds suggests further conformational analysis on this kind of molecule.

Experimental. Red prismatic crystal (0.31 × 0.42 × 0.64 mm), obtained by slow evaporation of an ethanolic solution, room temperature, Siemens AED single-crystal diffractometer controlled by an IBM PS/2 M30 computer. Cell parameters obtained from setting angles of 27 reflections (12 ≤ θ ≤ 36°) automatically well centered on the diffractometer. Intensities collected with Cu Kα radiation in the 3 ≤ θ ≤ 70° range, *h* −17→17, *k* 0→10, *l* 0→9, with a modified version (Belletti, Cantoni & Pasquinelli, 1988) of the Lehmann & Larsen (1974) procedure, 1794 independent reflections (*R*_{int} = 0.007), 1519 with *I* ≥ 2σ(*I*) classed as observed, one check reflection monitored every 50

reflections, its variation was within counting statistics, Lorentz–polarization corrections applied but none for absorption.

The structure was solved by direct methods using *SHELX76* (Sheldrick, 1976). All the non-H atoms were located from the best *E* map. A few cycles of isotropic refinement converged to *R* = 15.8%, those performed with anisotropic thermal parameters gave *R* = 6.86%, all H atoms localized from Fourier difference map and refined freely giving a final *R* value of 0.048 and *wR* = 0.063 with *w* = 1.0/(σ²*F* + 0.0283*F*²). The function minimized during refinement was Σ*w*(Δ*F*)², 167 parameters refined. At the end of the refinement the maximum shift-to-e.s.d. ratio was 0.24 for the *z*(O1) variable, while the maximum peak in the final Δ*F* map was 0.26 e Å⁻³.

Scattering factors for heavy atoms from *International Tables for X-ray Crystallography* (1974) and from Stewart, Davidson & Simpson (1965) for H atoms. Positional parameters of atoms are in Table 1.†

All the calculations were performed on an IBM PS/2 M80 computer with the *CRYSRULER* package (Rizzoli, Sangermano, Calestani & Andreotti, 1987).

Discussion. The geometrical features of the molecule, depicted in Fig. 1, are detailed in Table 2.

The indole skeleton is nearly planar, the dihedral angle formed by the aromatic and pyrrole mean ring

† Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51811 (11 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

* Part XV: Bocelli & Grenier-Loustalot (1984).