

Acetic Acid Complex of 3-Amino-1,4-dimethyl-5*H*-pyrido[4,3-*b*]indole (Trp-P-1); A Potent Mutagenic Product from the Dry Distillation of Tryptophan

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Abstract. C₁₃H₁₄N₃⁺. C₂H₃O₂⁻, monoclinic, *P*2₁/*a*, *Z* = 4, *a* = 12.687 (6), *b* = 11.146 (6), *c* = 10.104 (5) Å, $\beta = 103.19 (7)^\circ$. The final *R* value was 0.04 including H atoms. The present study established the chemical and molecular structure of Trp-P-1, a small amount of which had been extracted from the pyrolysis products of tryptophan.

Introduction. It was recently shown that the charred material in the surface layer of broiled fish and meat exhibits a high mutagenic activity (Nagao, Honda, Seino, Yahagi, Kawachi & Sugimura, 1977; Sugimura, Nagao, Kawachi, Honda, Yahagi, Seino, Matsushima, Shirai, Sawamura, Sato, Matsumoto & Matsukura, 1977) and a certain mutagenic principle has been extracted from the pyrolysis products of DL-tryptophan and DL-phenylalanine.

A small amount of the principle obtained from DL-tryptophan has been used for the present X-ray diffraction study to elucidate the chemical structure. Papers describing the extraction, purification and structure of the principle have been published (Sugimura, Kawachi, Nagao, Yahagi, Seino, Okamoto, Shudo, Kosuge, Tsuji, Wakabayashi, Iitaka & Itai, 1977; Kosuge *et al.*, 1978).

The lattice constants and intensity data were obtained from the measurements on a Philips PW 1100 diffractometer using Cu *K* α radiation monochromated by a graphite plate. Intensities were measured by the θ - 2θ scan method with a scanning speed of 2° min⁻¹ in θ . The scans were repeated twice when the total counts during the single scan were less than 2000. Background was measured at each end of the scan range for half the total scan time. 1823 reflexions were measured within a 2θ angle of 130°; 176 of these were excluded as unobserved reflexions since their intensities were below the 2 σ level. Intensities were then corrected for Lorentz and polarization factors. The *R* value for 154 equivalent observed structure factors was 0.027. The data of 1493 independent reflexions were used for the subsequent analysis. The crystal structure was determined by the direct method using *MULTAN* (Main, Woolfson & Germain, 1971) and refined by the block-diagonal least-squares method using the program *HBL5* IV (Okaya & Ashida, 1967). The final *R* value

Table 1. Fractional atomic coordinates ($\times 10^4$ for non-hydrogen atoms and $\times 10^3$ for hydrogen atoms)

Estimated standard deviations are given in parentheses.

| | <i>x</i> | <i>y</i> | <i>z</i> |
|----------|-----------|----------|----------|
| C(1) | 1636 (2) | 291 (2) | 5293 (2) |
| C(2) | 2209 (2) | -594 (2) | 6107 (3) |
| C(3) | 2083 (2) | -678 (3) | 7430 (3) |
| C(4) | 1389 (2) | 92 (3) | 7905 (3) |
| C(5) | 820 (2) | 982 (2) | 7093 (3) |
| C(6) | 948 (2) | 1102 (2) | 5761 (2) |
| C(7) | 533 (2) | 1912 (2) | 4630 (2) |
| C(8) | 982 (2) | 1523 (2) | 3530 (2) |
| C(9) | 760 (2) | 2070 (2) | 2268 (3) |
| C(10) | 96 (2) | 3082 (2) | 2138 (3) |
| C(11) | -136 (2) | 2885 (2) | 4438 (2) |
| C(12) | 1164 (2) | 1577 (3) | 1097 (3) |
| C(13) | -693 (2) | 3388 (3) | 5469 (3) |
| C(14) | -1845 (2) | 6023 (2) | 1784 (3) |
| C(15) | -2819 (3) | 6848 (3) | 1474 (3) |
| N(1) | 1630 (2) | 550 (2) | 3945 (2) |
| N(2) | -326 (2) | 3445 (2) | 3213 (2) |
| N(3) | -189 (2) | 3737 (2) | 993 (2) |
| O(1) | -1159 (2) | 6085 (2) | 1087 (2) |
| O(2) | -1773 (1) | 5308 (2) | 2768 (2) |
| H(C2) | 269 (2) | -115 (2) | 568 (3) |
| H(C3) | 248 (2) | -131 (3) | 805 (3) |
| H(C4) | 129 (3) | 1 (3) | 889 (3) |
| H(C5) | 35 (2) | 155 (2) | 743 (3) |
| H(C12) | 139 (2) | 217 (3) | 58 (3) |
| H'(C12) | 193 (3) | 118 (3) | 140 (3) |
| H''(C12) | 68 (3) | 130 (3) | 43 (3) |
| H(C13) | -100 (2) | 414 (3) | 518 (3) |
| H'(C13) | -20 (3) | 351 (3) | 633 (3) |
| H''(C13) | -120 (3) | 282 (3) | 568 (3) |
| H(C15) | -345 (3) | 654 (3) | 181 (3) |
| H'(C15) | -320 (3) | 680 (3) | 47 (3) |
| H''(C15) | -268 (3) | 762 (3) | 157 (3) |
| H(N1) | 211 (3) | 17 (3) | 341 (3) |
| H(N2) | -81 (2) | 411 (3) | 300 (3) |
| H(N3) | 18 (3) | 364 (3) | 36 (3) |
| H'(N3) | -58 (3) | 450 (3) | 100 (3) |

was 0.04 including H atoms. The weighting scheme was: $\sqrt{w} = 0.8$ when $F_o \leq 2$; $\sqrt{w} = 1.0$ when $2 < F_o \leq 18$; and $\sqrt{w} = 18/F_o$ when $F_o > 18$. The atomic scattering factors for C, N and O atoms were those given in *International Tables for X-ray Crystallography* (1962) as SX-6, SX-7 and SX-8, and for H

atoms those given by Stewart, Davidson & Simpson (1965). The final atomic coordinates are listed in Table 1.*

Discussion. The present determination elucidated the structure of Trp-P-1 as 3-amino-1,4-dimethyl-5H-pyrido[4,3-*b*]indole as shown in Fig. 1, which also gives the bond lengths and valency angles. The standard deviations are estimated as: $\sigma(\text{C}-\text{C}) = 0.004$, $\sigma(\text{C}-\text{H}) = 0.03$ Å and $\sigma(\text{C}-\text{C}-\text{C}) = 0.2$, $\sigma(\text{C}-\text{C}-\text{H}) = 2.0$, $\sigma(\text{H}-\text{C}-\text{H}) = 3.0^\circ$. As can be seen in Fig. 1, the three fused rings form a conjugated system with $\text{C}=\text{C}$ lengths ranging from 1.363 to 1.458 Å, and $\text{C}=\text{N}$ from 1.358 to 1.391 Å. These values are close to those found in pyridoindole hydrobromide (Kumagai, Naganawa, Aoyagi, Umezawa, Nakamura & Iitaka, 1975). The maximum and the mean differences in the corresponding bond lengths in these two compounds taken for the same kind of bonds are 0.04 and 0.02 Å respectively.

The planarity of the Trp-P-1 cation and the deviations of the atoms from the plane are shown in Table 2. The most significant deviations are shown by C(12) and N(3); these deviations seem to be caused by mutual repulsion between these substituent atoms which are *ortho* to each other. The acetate anion is also planar (except for the H atoms) and is strongly bound to the cation by two $\text{N}-\text{H}\cdots\text{O}$ hydrogen bonds of

* Lists of structure factors and thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 33726 (8 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

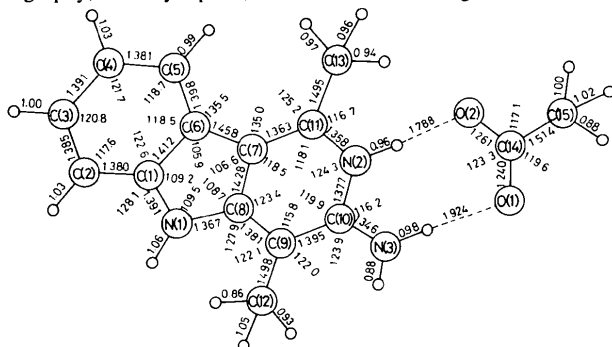


Fig. 1. Bond lengths (Å) and valency angles ($^\circ$) of the Trp-P-1 and acetate ions.

Table 2. Deviations (Å) of the atoms from the least-squares planes

| | | | |
|---------------|--------|-------|--------|
| Trp-P-1 plane | | | |
| C(1) | 0.008 | C(6) | -0.023 |
| C(2) | 0.051 | C(7) | -0.011 |
| C(3) | 0.051 | C(8) | -0.001 |
| C(4) | -0.012 | C(9) | -0.005 |
| C(5) | -0.047 | C(10) | 0.044 |
| | | C(11) | -0.002 |
| | | N(1) | 0.000 |
| | | N(2) | 0.038 |
| | | C(12) | -0.116 |
| | | C(13) | -0.045 |
| | | N(3) | 0.070 |
| Acetate plane | | | |
| C(14) | 0.004 | O(1) | -0.002 |
| C(15) | -0.001 | O(2) | -0.001 |

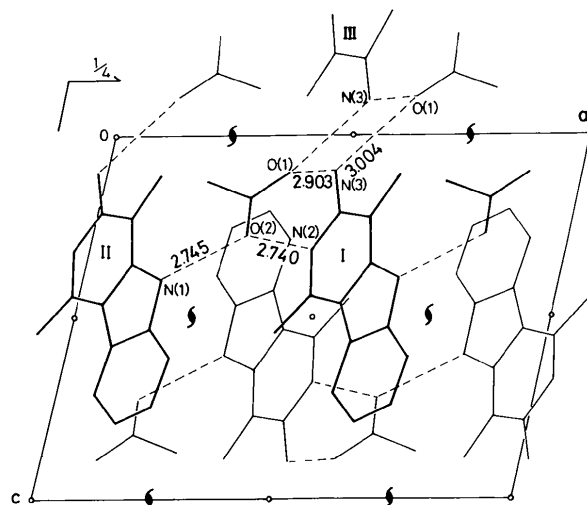


Fig. 2. Projection of the crystal structure along the *b* axis. Hydrogen bonds are shown by broken lines. Symmetry operations for the molecules are: (I) $\frac{1}{2} + x, \frac{1}{2} - y, z$; (II) x, y, z ; (III) $\frac{1}{2} - x, \frac{1}{2} + y, -z$.

2.740 and 2.903 Å. The planes of these two residues make a dihedral angle of 28.2° . The *b*-axis projection of the crystal structure is shown in Fig. 2. The Trp-P-1 residues stack along the *b* axis face to face with perpendicular distances of 3.256 and 3.501 Å. Besides the above-mentioned hydrogen bonds, the protonated indole atom N(1) and the amino atom N(3) form hydrogen bonds (2.745 and 3.004 Å) to the acetate O atoms.

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