The Crystal and Molecular Structure of 1-(2-Amino-4-pyrimidinyl)-β-carboline**

Yoshinobu YOKOMORI,* Kiyotane SEKIDO, Tian-Shung WU,†
Hsien-Jun TIEN,†† and Sakutaro HIROKAWA

Department of Chemistry, The National Defense Academy, Hashirimizu, Yokosuka 239
† *Chia-Nan Junior College of Pharmacy, Tainan, Taiwan, R.O.C.*
†† *Department of Chemistry, National Cheng Kung University, Tainan, Taiwan, R.O.C.*

(Received October 2, 1981)

An alkaloid extracted from a small evergreen tree, *Annona montata*, was identified as 1-(2-amino-4-pyrimidinyl)-β-carboline monohydrate by the X-ray method. The crystal data are; $a=20.699$, $b=4.453$, $c=15.720$ Å, and $\beta=112.16°$; space group, $P2_1/c$; $Z=4$. The structure was solved by the direct method and refined by the least-squares method to the final R value of 0.109 for 1451 independent reflections. The water molecule is connected to four nitrogen atoms by hydrogen bonds. Two of them are in different groups; one is in the five-membered ring of the β-carboline skelton, and the other is in the pyridine of the β-carboline skelton. The fifth hydrogen bond connects two nitrogen atoms, one of which is in the amino group, and the other, in the pyrimidine skelton.

As a part of studies of Formosan folk-medicines, the constituents of small evergreen tree, *Annona montana* Macf., have been investigated by several workers. Yang *et al.*[1] isolated seven species of alkaloids from this plant. The present report will describe the molecular and crystal structure of one of them, annomurine, which has thus been designated by us. This substance was identified as 1-(2-amino-4-pyrimidinyl)-β-carboline by this work.

Experimental

The EtOH extract of the stem bark was triturated with 3% AcOH, and the filtrate was shaken with $CHCl_3$ to separate a $CHCl_3$-soluble fraction and an aqueous fraction. Crystals were obtained from the $CHCl_3$-soluble fraction in the form of light yellow plates. They were recrystallized by slow evaporation from an aqueous solution of MeOH. The result of the structure analysis showed that they were monohydrates.

The cell dimensions were determined by the least-squares method using various sets of high-angle reflections on a diffractometer. The crystal data are given in Table 1. The crystal (0.31, 0.03, 1.86 mm) was mounted on a four-circle diffractometer (Rigaku AFC III), with Mo $K\alpha$ ($\lambda=0.7107$ Å) from a graphite monochromator. The intensities were collected for the independent 1759 reflections within $2\theta<60°$, using the ω-2θ scan technique with a scanning speed of 4° min^{-1} in 2θ, while 344 reflections with $|F_o|<3\sigma(F)$ were designated as unobserved. Corrections for the background and the Lorentz-polarization factor were made, but not for the absorption or the extinction.

Table 1. Crystallographic data for 1-(2-amino-4-pyrimidinyl)-β-carboline monohydrate

$C_{15}H_{11}N_5 \cdot H_2O$, space group $P2_1/c$, $Mr=279.2$	
$a=20.699(7)$ Å	$D_m=1.396$ g cm^{-3} (flotation; $CHCl_3/CH_3C_6H_5$)
$b=4.453(2)$ Å	$D_x=1.439$ g cm^{-3} ($Z=4$)
$c=15.720(5)$ Å	μ (Mo $K\alpha$) $=0.856$ cm^{-1}
$\beta=112.16(2)°$	
$V=1341.8$ Å^3	

All the numerical calculations were carried out on a NEAC 2200 MODEL 575 computer at the Computing Center of the National Defense Academy with programs of the Universal Crystallographic Computing System.[2] The phase problem was solved without difficulty by the use of MULTAN.[3] The initial residual index was 0.44 for the trial structure. The structure was refined by a block-diagonal least-squares procedure. Five cycles of refinement reduced the R value to 0.201. Further refinements were made using anisotropic thermal parameters for the non-hydrogen atoms, together with isotropic B values of the hydrogen atoms, which were fixed assuming the angle of 120° for each carbon atom and a bond length of 1.09 Å for each C–H bond. The hydrogen positions of water were deduced from a difference Fourier synthesis. The R value at this stage was 0.109. The atomic scattering factors were taken from International Tables for X-Ray Crystallography.[4] The final atomic coordinates, together with B_{eq}, are given in Table 2.†††

Discussion

The R value did not decrease to less than 0.109, partly because attempts to obtain good-shaped single crystals suitable for X-ray analysis were not successful. The mean standard deviations are 0.02 Å for the interatomic distance and 0.9° for the angle. These values may be sufficient to discuss the molecular geometry and the packing of the molecules in the unit cell, especially the role the hydrogen bonds play in the crystal.

Configuration of the Molecule. The numbering scheme of the nonhydrogen atoms and four molecular planes (A, B, C, D) is presented in Fig. 1.[5] The numbering scheme of the hydrogen atoms is shown in Table 2. The mean atomic deviations were ±0.007 Å for the A plane, ±0.005 Å for B, ±0.007 Å for C, and ±0.014 Å for D. The dihedral angle between A and B is 1.1°, while that between B and C is 1.0°. The value of the indole nucleus is 2.1°.[6] The two six-membered rings (A and C) make an angle of 1.9°.

** A preliminary report was presented at the 42nd National Meeting of the Chemical Society of Japan, Sendai, September 1980.

††† The complete tables of the anisotropic thermal parameters, the F_o-F_c data, and the torsion angles are deposited as Document No. 8226 at the Office of the Editor of the Bulletin, the Chemical Society of Japan.

Table 2. Final fractional atomic coordinates and their standard deviations (in parentheses)

Atom	x	y	z	B_{eq}/Å^2
C1	0.2692(4)	0.2985(18)	0.1557(5)	3.23
N2	0.2535(3)	0.4153(15)	0.0717(4)	3.45
C3	0.1919(4)	0.3438(20)	0.0042(4)	4.29
C4	0.1432(3)	0.1547(19)	0.0149(4)	3.69
C5	0.0560(4)	−0.3087(17)	0.1037(5)	3.56
C6	0.0377(4)	−0.4917(20)	0.1603(6)	4.19
C7	0.0819(4)	−0.5430(19)	0.2518(5)	3.69
C8	0.1467(4)	−0.4013(19)	0.2880(5)	3.51
N9	0.2264(3)	−0.0533(14)	0.2496(3)	3.32
C10	0.2233(3)	0.0991(16)	0.1725(4)	2.73
C11	0.1582(3)	0.0320(16)	0.1006(4)	2.70
C12	0.1660(3)	−0.2218(17)	0.2307(5)	3.23
C13	0.1224(3)	−0.1678(17)	0.1382(4)	3.10
C14	0.3360(3)	0.3878(18)	0.2291(5)	3.40
N15	0.3474(3)	0.2755(15)	0.3119(4)	3.94
C16	0.4059(4)	0.3670(19)	0.3802(5)	4.02
N17	0.4530(3)	0.5605(18)	0.3726(4)	4.76
C18	0.4395(4)	0.6637(23)	0.2885(5)	4.93
C19	0.3817(4)	0.5975(22)	0.2133(5)	4.35
N20	0.4154(3)	0.2643(19)	0.4654(4)	6.05
O21	0.3109(3)	−0.2111(16)	0.4583(4)	5.25
H1(C3)	0.180	0.443	−0.062	0.36
H2(C4)	0.095	0.106	−0.042	4.12
H3(C5)	0.021	−0.269	0.034	2.50
H4(C6)	−0.012	−0.602	0.134	1.25
H5(C7)	0.066	−0.694	0.294	4.45
H6(C8)	0.181	−0.429	0.359	4.27
H7(N9)	0.269	−0.046	0.315	2.95
H8(C18)	0.476	0.814	0.279	2.48
H9(C19)	0.372	0.678	0.146	3.71
H10(N20)	0.390	0.078	0.469	0.35
H11(N20)	0.452	0.267	0.509	8.23
H12(O21)	0.332	−0.386	0.471	5.57
H13(O21)	0.294	−0.170	0.513	5.90

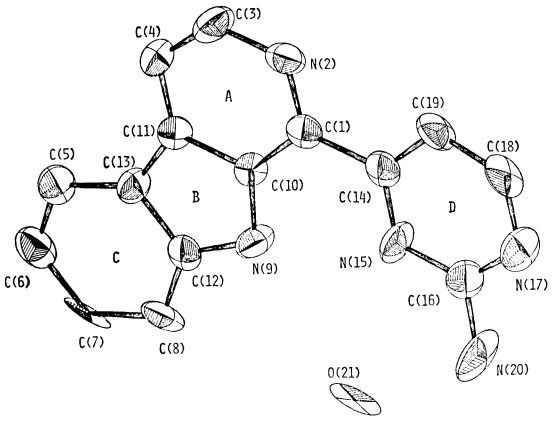

Fig. 1. Thermal ellipsoids representation of the molecule and water. The ellipsoids enclose 50 per cent probability.

The two benzene rings of carbazole make an angle of 1.6°.[7] The dihedral angle between A and D is 5.6°. The atomic deviations and dihedral angles are given in Table 3.

Table 3. Deviations(l/Å) of atoms from mean planes and dihedral angles(ϕ/°)

Plane A		Plane B		Plane C	
C (1)	0.011	N (9)	0.006	C (5)	0.009
N (2)	−0.003	C (10)	−0.003	C (6)	−0.002
C (3)	−0.002	C (11)	−0.002	C (7)	−0.009
C (4)	−0.002	C (12)	−0.007	C (8)	0.013
C (10)	−0.115	C (13)	0.006	C (12)	−0.006
C (11)	0.011			C (13)	−0.004

Plane D		Dihedral angles	
C (14)	0.009	A-B	1.12
N (15)	−0.012	A-C	1.88
C (16)	−0.025	B-C	1.00
N (17)	−0.009	A-D	5.62
C (18)	−0.001		
C (19)	0.014		
N (20)	0.026		

Table 4. Bond lengths and angles for non hydrogen atoms, with e.s.d.'s in parentheses

Bond length (l/Å)			
C (1)-N (2)	1.341(10)	C (1)-C (10)	1.395(10)
C (1)-C (14)	1.483(11)	N (2)-C (3)	1.355(11)
C (3)-C (4)	1.371(11)	C (4)-C (11)	1.377(10)
C (5)-C (13)	1.421(11)	C (5)-C (6)	1.362(11)
C (6)-C (7)	1.401(12)	C (7)-C (8)	1.394(12)
C (8)-C (12)	1.372(11)	N (9)-C (10)	1.370(9)
N (9)-C (12)	1.390(9)	C (10)-C (11)	1.426(10)
C (11)-C (13)	1.421(10)	C (12)-C (13)	1.412(10)
C (14)-N (15)	1.329(10)	C (14)-C (19)	1.387(11)
N (15)-C (16)	1.343(10)	C (16)-N (17)	1.339(10)
C (16)-N (20)	1.358(11)	N (17)-C (18)	1.325(11)
C (18)-C (19)	1.370(12)		

Bond angle (ϕ/°)			
N(2)-C(1)-C(10)	120.3(7)	N(2)-C(1)-C(14)	118.1(7)
C(10)-C(1)-C(14)	121.7(7)	C(1)-N(2)-C(3)	119.1(7)
N(2)-C(3)-C(4)	124.6(7)	C(3)-C(4)-C(11)	117.3(7)
C(6)-C(5)-C(13)	118.8(7)	C(5)-C(6)-C(7)	122.3(8)
C(6)-C(7)-C(18)	120.0(8)	C(7)-C(8)-C(12)	118.0(8)
C(10)-N(9)-C(12)	109.9(6)	C(1)-C(10)-N(9)	132.4(7)
C(1)-C(10)-C(11)	119.4(6)	N(9)-C(10)-C(11)	108.1(6)
C(4)-C(11)-C(10)	119.3(6)	C(4)-C(11)-C(13)	134.0(7)
C(10)-C(11)-C(13)	106.7(6)	C(8)-C(12)-N(9)	129.4(7)
C(8)-C(12)-C(13)	122.9(7)	N(9)-C(12)-C(13)	107.6(6)
C(5)-C(13)-C(11)	134.4(7)	C(5)-C(13)-C(12)	117.9(7)
C(11)-C(13)-C(12)	107.7(6)	C(1)-C(14)-N(15)	115.4(7)
C(1)-C(14)-C(19)	122.1(7)	N(15)-C(14)-C(19)	122.4(7)
C(14)-N(15)-C(16)	116.2(6)	N(15)-C(16)-N(17)	126.2(7)
N(15)-C(16)-N(20)	115.9(7)	N(17)-C(16)-N(20)	117.7(7)
C(16)-N(17)-C(18)	115.2(7)	N(17)-C(18)-C(19)	124.1(8)
C(18)-C(19)-C(14)	115.9(8)		

Bond Lengths and Bond Angles. The average C–C bond length in the benzene ring is 1.396 Å. The C(5)–C(6) bond (1.362 Å) is significantly shorter than the average value. These results compare well with those found in indole.[6] The C(11)–C(13) bond (1.421 Å) is longer than the standard aromatic C–C bond of 1.395 Å.[8] The mean C–N distance in the five-

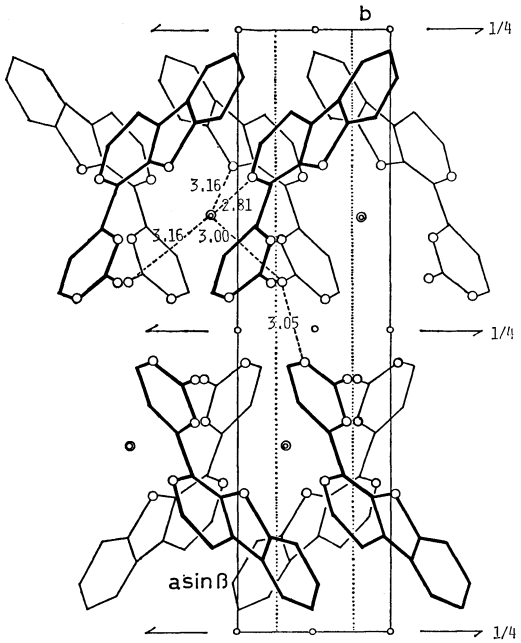

Fig. 2. Packing of the molecules viewed down c. Hydrogen bonds are shown by broken lines with their lengths in Å.

membered ring is 1.381 Å, and the C–C distance is 1.416 Å. The mean bond distances in the pyridine ring are 1.396 Å for C–C and 1.346 Å for C–N. As for the pyrimidine ring, the mean C–N distance is 1.335 Å. The angles at the nitrogen atoms are less than 120° by about 4°, in agreement with the values in similar heterocyclic systems. The angles at the carbon atoms are all greater than 120° [that at C(16) considerably so], with the exception of that at C(19), which is only 115.9°. These results compare well with those found in the structure of pyrimidine.[9]

Environment of the Molecule. Five types of hydrogen bonds can be seen in the structure. The first hydrogen bond connects N(20) with O(21) at a distance of 3.00 Å. The second (3.16 Å) connects N(9) with O(21). The third (2.81 Å) is the O(21)–N′(2) bond, in which N′(2) is equivalent to N(2). The fourth (3.16 Å) connects N″(20), which is equivalent to N(20), with O(21). The fifth hydrogen bond connects N(20) with N‴(17) at a distance of 3.05 Å.

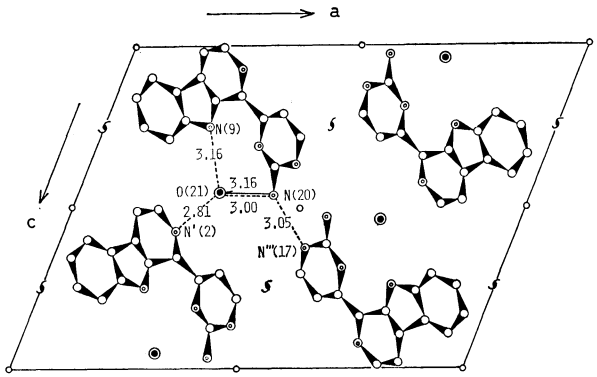

Fig. 3. The packing of the molecules in a unit cell seen along the b axis.

These hydrogen bonds are shown in Figs. 2 and 3.

We wish to thank Mr. Toshio Sato for giving us a chance to cooperate in this work; Professor Daihei Oda, Mr. Osamu Moriya, and Mr. Shigeru Hasegawa for their valuable suggestions, and Dr. Teruo Noguchi and Mr. Jun Ito for plotting the thermal ellipsoids. We also wish to thank Mr. Kazumasa Maruyama for help with the calculations.

References

1) T. H. Yang and M. Chen, *Proc. Natl. Sci. Counc. R. O. C.*, **3**, 63 (1979).
2) "The Universal Crystallographic Computing System," ed by T. Ashida, Library of Programs, Computing Center of Osaka University (1973).
3) G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect. A*, **27**, 368 (1971).
4) "International Tables for X-Ray Crystallography," The Kynoch Press, Birmingham (1959), Vol. III, pp. 201—203.
5) C. K. Johnson, ORTEP, ORNL-3794, Oak Ridge National Laboratory, Tennessee (1965).
6) G. Falkenberg and D. Carlström, *Acta Crystallogr., Sect. B*, **27**, 411 (1971).
7) M. Kurahashi, M. Fukuyo, A. Shimada, A. Furusaki, and I. Nitta, *Bull. Chem. Soc. Jpn.*, **42**, 2174 (1969).
8) K. Chandrasekhal and V. Pattabhi, *Acta Crystallogr., Sect. B*, **36**, 1165 (1980).
9) M. M. Ripoll and H. P. Lorentz, *Acta Crystallogr., Sect. B*, **29**, 2260 (1973).