1976

Structural studies of naturally occurring toxicogenic compounds

James Patrick Springer
Iowa State University

Structural studies of naturally occurring toxicogenic compounds

by

James Patrick Springer

A Dissertation Submitted to the
Graduate Faculty in Partial Fulfillment of
The Requirements for the Degree of
DOCTOR OF PHILOSOPHY

Department: Chemistry
Major: Physical Chemistry

Approved:

Signature was redacted for privacy.

In Charge of Major Work

Signature was redacted for privacy.

For the Major Department

Signature was redacted for privacy.

For the Graduate College

Iowa State University
Ames, Iowa

1976

TABLE OF CONTENTS

INTRODUCTION

Toxins have long been of interest and of use to man in rather nefarious ways. Reports from the beginning of recorded history document man's fascination with these substances. No doubt this fascination was concerned more with the outcome rather than the mechanism of toxicity. The fact that man, who is able to ingest and metabolize an extremely diverse array of plant and animal life, should suffer such devastating effects from minuscule amounts of certain plant and animal extracts has elicited some scientific inquiry. Currently, considerable interest exists in understanding the mode of action of toxins at a molecular level.

A number of naturally occurring compounds originally isolated and characterized because of their toxicity have been found to possess important beneficial medicinal properties at sub-lethal concentrations. A large percentage of the clinically useful drugs available today including analgesics, tranquilizers, stimulants, etc. are modified and simplified forms of natural compounds. The whole philosophy of chemotherapy in treating some forms of cancer is based upon the fact that certain compounds are more toxic to fast growing cancerous cells than to normal cells. Most antibiotics and all anticancer compounds can also be classified as toxins.

Traditionally, most of the more potent toxins, i.e., those producing the most acute effects with the smallest

amount of material have been plant extracts. However, in recent times more attention has been placed on discovering the long term or chronic effects of the broad spectrum of chemicals both from natural as well as from synthetic sources to which modern man is exposed. It is of seminal importance to completely characterize a toxin in terms of its chemical structure if one wishes to understand its mode of action in the physiological system. Traditionally, it was necessary to degrade an incompletely characterized molecule into smaller, more manageable fragments in order to establish its chemical constitution. Consequently, the synthesis of a new organic compound was necessary to completely confirm the proposed structure derived from degradative experiments. However, considerable resources in terms of time and money could be spent in this effort since compounds produced by nature are noted for their diversity and complexity. However, in recent years physical methods have been used with growing success to determine the chemical configurations of increasingly complex molecules. The singular technique of single crystal X-ray diffraction offers one the possibility of rapidly determining the structure of a complex molecule using limited amounts of material ($<<1$/mg) in the absence of prior chemical information. This technique proved to be pivotal in completely determining the structure of the compounds described in this dissertation.

SAXITOXIN

Background

Paralytic shellfish poisoning has been, even in recent times, a serious economic and health problem. Early references may be found in the book of Exodus (1) and American Indian folklore. Outbreaks of this poisoning have been reported in such widespread locations as the northern Pacific and northern Atlantic coasts of the United States, the North Sea, and in the coastal areas of Japan and South Africa. In general, these regions are greater than 30° north or south latitude. The outbreak in New England in 1972 and each subsequent year has been particularly menacing. The danger from shellfish poisoning lies in the suddenness in which the shellfish becomes toxic and the uncertainty of detection. Shellfish from a specific location can be perfectly safe one week and lethal the next with no visible warning. The classic red coloration of the sea is an inadequate warning signal by two orders of magnitude. The first symptoms of poisoning occur within 30 minutes after the ingestion of a lethal amount of toxic shellfish. A lethal dose can be as little as 1/4 of a shellfish. Numbness in the lips and fingertips is followed by progressive paralysis leading to death from respiratory failure in 2 to 12 hours. If a victim is able to survive for 24 hours his prognosis is good. No proven antidotes to shellfish poisoning exist, however, certain

salts such as NaCl and alcohols such as ethanol reduce the effects to a certain extent. Artificial respiration has proved to be helpful in marginal cases. Toxicity, however, is not destroyed by heating or by washing of the shellfish (2).

In 1937, Sommer and coworkers (3) were able to show that the dinoflagellate Gonyaulax catenella contained a poison which produced identical symptoms in mice as toxic extracts from the California sea mussel (Mytilus californianus). Subsequently, it was shown that the toxin produced by G. catenella in axenic cultures was chemically and physically identical to the purified toxin from mussels (4). In 1947, Needler (5) proposed that the paralytic poison in scallops (Pecten grandis) was due to the dinoflagellate Gonyaulax tamerenis. This theory was substantiated in 1963 by Prakash (6). A paralytic poison identical with that found in mussels has also been found in the Alaska butter clam (Saxidomus giganteus); however, the source of this toxin has remained obscure (7). The name of saxitoxin has been proposed for the paralytic shellfish poison found in G. catenella, M. californianus, and S. giganteus (8).

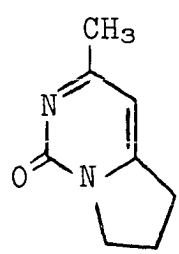
Chemical characterization of saxitoxin has been severely hindered by its nonvolatile, noncrystalline, hygroscopic, and highly polar nature. The best reported purifications have been carried out by Schantz and co-

workers (9) by extracting toxic clam and mussel tissue with acidified aqueous ethanol followed by ion exchange fractionation on carboxylic acid resins and then subsequent chromatography on acid washed alumina columns. The white amorphous solid isolated by this procedure had a specific toxicity of 5500 $\pm$ 500 mouse units per milligram. A mouse unit is defined as the amount of toxin that will kill a 20 gram mouse in 15 minutes (10). The molecular formula determined by elemental analysis was $C_{10}H_{17}N_7O_4 \cdot 2HCl$ (9). Saxitoxin possessed a specific rotation of 130 $\pm$ 5° and had a diffusion constant of 4.9 $\pm$ .2 x 10^{-6} cm^2/sec which corresponded well to the molecular weight of 372 g/mole. The toxin was found to be very soluble in water and methanol, somewhat soluble in acetic acid and ethanol, and insoluble in other common less polar organic solvents. No u.v. absorption was observed above 220 nm (11) and titrations with base revealed two acidic groups with pKa values of 8.3 and 11.5.

Oxidation by potassium permanganate and periodic acid followed by acid hydrolysis yielded the identifiable fragments of urea, guanidine, ammonia, guanidioproprionic acid, and carbon dioxide. Saxitoxin was reduced under aqueous neutral, acid, and alkaline solutions using 1 atmosphere of hydrogen and a platinum catalyst and found to consume 1 equivalent of hydrogen. A weak ir absorption at 1770 cm^{-1}

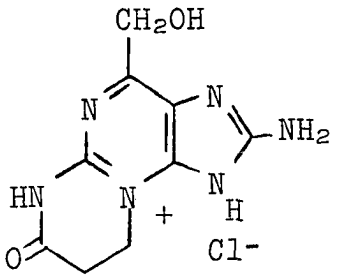
disappeared indicating that a >C=O had been reduced. The reduced material possessed essentially no toxicity (< 1% that of saxitoxin) which is of interest from a physiological viewpoint. It is not yet clear how such a simple change in chemical constitution could drastically reduce the toxicity. Upon countercurrent distribution (12) two components were partially separated which individually returned to the same equilibrium mixture upon standing in the presence of acid. Saxitoxin is heat stable and acid stable but found to decompose in the presence of base.

When saxitoxin was heated with red phosphorus and hydriodic acid in acetic acid, a weakly basic compound was isolated in 57% yield which was the pyrrolopyrimidine 1 (8) containing eight of the ten carbon atoms originally present.



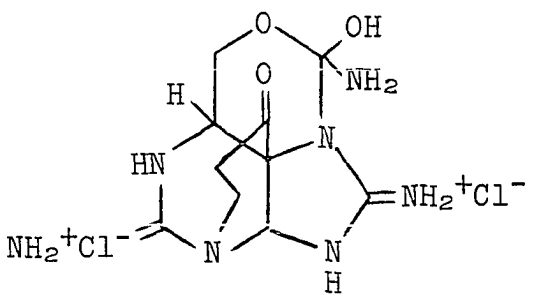
1

Under a variety of mild oxidizing conditions such as treatment of saxitoxin in dilute sodium hydroxide with 8% hydrogen peroxide at 25° gave 2 (13) in 25% yield which retained nine of ten carbon atoms and six of the seven nitrogen atoms initially contained in saxitoxin.



2

Further work indicated that when saxitoxin, $C_{10}H_{17}N_7O_4 \cdot 2HCl$ was dried to constant weight at 110° and 10^{-5} mm it lost a molecule of water to give a compound, $C_{10}H_{15}N_7O_3 \cdot 2HCl$, with retention of biological activity. Two methylene protons (δ2.37 m) underwent reversible but very slow exchange in water at room temperature. On the basis of all the previous work and utilizing proton nuclear magnetic resonance experiments the chemical structure 3 was proposed for saxitoxin (14).



3

While this proposed structure 3 was generally viewed with skepticism, no better model could be put forward. The "urea hydrate" aspect was particularly difficult to reconcile with known chemistry. In 1973, it became clear that this structure did not fit all of the available data. In particular ^{13}C nmr showed all ten carbons of saxitoxin but no resonances appropriate for the $>C=O$ (15). It was elected to reexamine the structure of saxitoxin via X-ray diffraction.

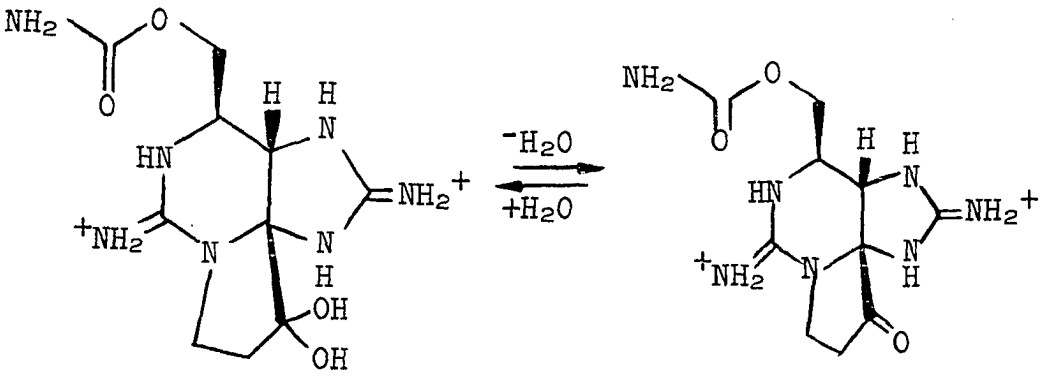
Experimental

Satisfactory crystals of saxitoxin suitable for single crystal X-ray diffraction analysis (16, 17) were obtained by dissolving the purified toxin ($C_{10}H_{17}N_7O_4 \cdot 2HCl$) in water and adding p-bromobenzenesulfonic acid. The crystals which resulted were washed with cold water and recrystallized again from water. The crystals which were used in the diffraction experiments were prepared by V. Ghazarossian and supplied by E.J. Schantz and F.M. Strong. A crystal measuring approximately 0.1 x 0.2 x 0.6 mm was mounted in a Lindemann thin walled capillary, the bottom of the capillary was filled with mother liquor, and the capillary was subsequently sealed. Preliminary diffraction experiments using Polaroid photographs and an automatic diffractometer indicated that the unit cell was orthorhombic. Fifteen strong reflections within a 2θ range of 35°-45° were

centered and upon least-squares analysis gave the unit cell parameters of $\underline{a} = 31.095(4)$, $\underline{b} = 12.180(1)$, and $\underline{c} = 7.8057(9)$ Å. The space group was $P2_12_12_1$ (*vide infra*) and upon structure solution the asymmetric unit contained one unit of $C_{10}H_{17}N_7O_4 \cdot 2C_6H_5BrSO_3$ indicating that each Cl anion had been replaced by a p-bromobenzenesulfonate. The calculated density was 1.74 g/cm^3 for $Z = 4$. All unique reflection data with $\theta \leq 57^\circ$ were collected using an automatic four-circle diffractometer with graphite monochromated CuK_α radiation ($\lambda = 1.5418$Å). Since there was a definite spread in the diffraction maxima it was decided to use an ω-scan technique with a constant ω range of 1° with backgrounds measured at 1° from the center of the calculated angle. Of the total of 2340 reflections, 1895 (81%) were judged observed ($I \geq 3\sigma(I)$) and corrected for Lorentz and polarization effects (18). An examination of the data revealed that reflections h00, $h = 2n + 1$; 0k0, $k = 2n + 1$; and 00ℓ, $\ell = 2n + 1$ were unobserved indicating that the space group was $P2_12_12_1$ which proved to be correct upon structure solution.

Two unique bromine and two unique sulfur atoms were easily located using a combination of Patterson techniques (19) and direct methods (20). Subsequent electron density syntheses revealed the remainder of the 43 nonhydrogen atoms. The correct chemical structure for saxitoxin was

found to be 4. Full matrix least-squares refinements (21) with anisotropic temperature factors lowered the conventional dis-



4 4a

crepancy index (R factor) to 6.3%. Placement of all hydrogens followed by further least-squares refinements lowered the discrepancy index to 5.6%. Inclusion of anomalous scattering contributions for bromine and sulfur, followed by still further least-squares refinements lowered the discrepancy index to 5.2% for the present structure and 5.7% for its mirror image, a statistically significant difference with a probability greater than .995 (22). No absorbtion corrections were made (μ = 59 cm^{-1}). As an additional check the 20 most enantiomorphic sensitive reflections were carefully remeasured and indicated the same absolute configuration. Figure 1 shows a computer generated drawing of the crystalline saxitoxin 4. Tables 1, 2, 3, and 4 contain the final fractional coordinates, bond distances, bond angles, and observed and calculated structure factors respectively.

Figure 1. A computer generated perspective drawing of saxitoxin (4) crystallized as the p-bromobenzenesulfonate. For clarity the hydrogen atoms of the saxitoxin portion and all atoms of the sulfonate are omitted. The absolute configuration is as shown.

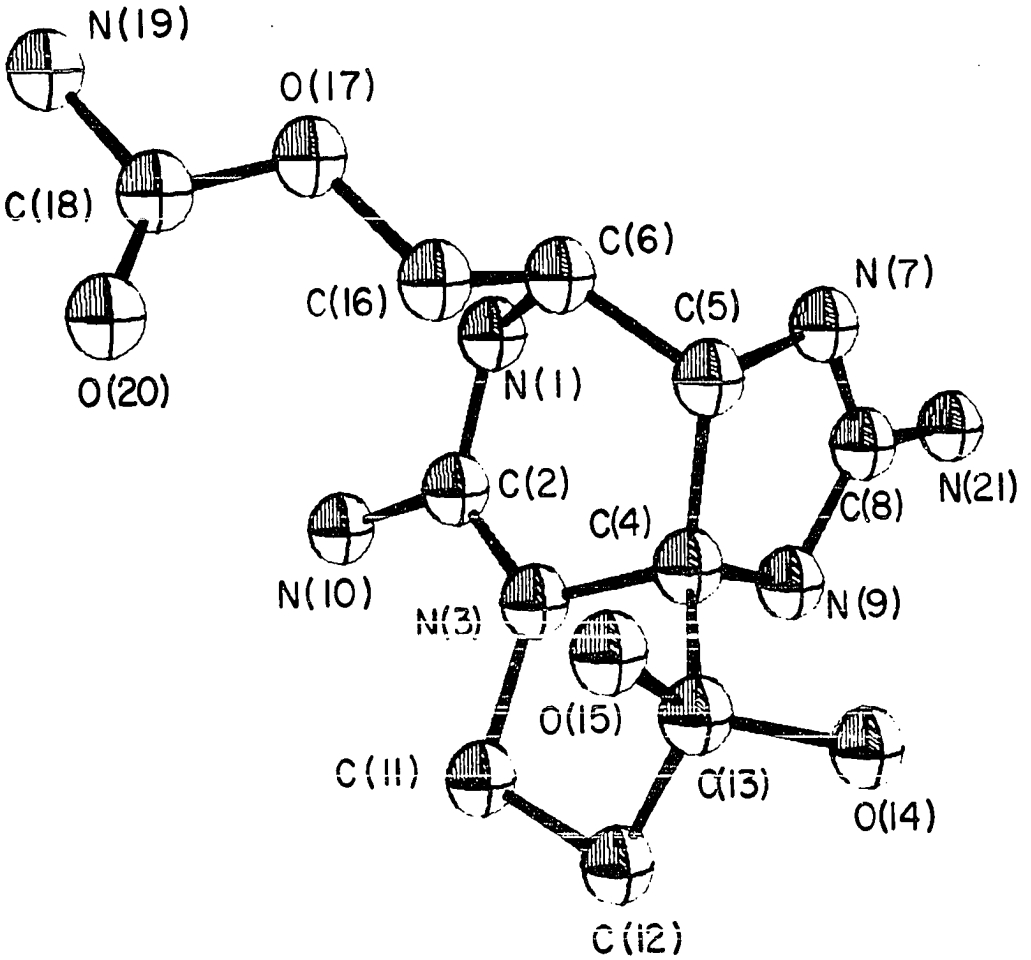

N(19)
O(17)
C(18)
C(6)
C(16)
N(7)
C(5)
O(20)
N(1)
C(2)
C(8)
N(21)
C(4)
N(10)
N(9)
N(3)
O(15)
C(11)
C(13)
O(14)
C(12)

Table 1. Final fractional coordinates for the p-bromobenzenesulfonate derivative of saxitoxin (4). The estimated standard deviation of the least significant figure is given in parentheses. The atoms of the p-bromobenzenesulfonate anions are indicated by primes. Hydrogen atoms are numbered as the heavy atom to which they are attached. The numbering scheme refers to Figure 1.

N(1)	.6016(2)	.7834(5)	.437(1)
C(2)	.6027(2)	.7515(7)	.600(1)
N(3)	.5718(2)	.7891(5)	.7020(9)
C(4)	.5440(2)	.8825(7)	.654(1)
C(5)	.5364(2)	.8927(7)	.458(1)
C(6)	.5594(3)	.8031(7)	.360(1)
N(7)	.5646(2)	.9811(5)	.6974(9)
C(8)	.5703(2)	1.0467(6)	.558(1)
N(9)	.5545(2)	.9983(6)	.421(1)
N(10)	.6322(2)	.6840(6)	.656(1)
C(11)	.5621(3)	.7395(8)	.872(1)
C(12)	.5227(3)	.8093(7)	.929(1)
C(13)	.5037(3)	.8524(8)	.763(1)
O(14)	.4778(2)	.9451(5)	.7833(9)
O(15)	.4826(2)	.7713(6)	.6757(9)
C(16)	.5332(3)	.6957(6)	.348(1)
O(17)	.5566(2)	.6250(5)	.2325(8)
C(18)	.5527(3)	.5180(7)	.259(1)
N(19)	.5570(2)	.4572(6)	.148(1)
O(20)	.5294(2)	.4755(5)	.366(1)
N(21)	.5907(3)	1.1420(6)	.560(1)
Br(1')	.6240(1)	.4011(1)	.5837(2)
C(2')	.6848(3)	.3860(7)	.596(1)
C(3')	.7048(4)	.3097(9)	.493(2)
C(4')	.7502(4)	.2984(8)	.506(2)
C(5')	.7719(3)	.3584(9)	.617(1)
C(6')	.7508(4)	.4359(7)	.720(1)
C(7')	.7067(3)	.4452(8)	.710(1)
S(8')	.8285(1)	.3466(2)	.6383(4)
O(9')	.8397(2)	.3973(9)	.8065(9)
O(10')	.8480(2)	.4137(6)	.500(1)
O(11')	.8390(2)	.2312(7)	.627(2)
Br(1")	.8078(1)	.0470(2)	.1395(3)
C(2")	.7476(3)	.0771(8)	.115(2)

Table 1 (Continued)

C(3")	.7185(4)	.002(1)	.166(2)
C(4")	.6761(3)	.0270(9)	.150(2)
C(5")	.6623(3)	.1213(8)	.084(1)
C(6")	.6919(4)	.1976(8)	.031(2)
C(7")	.7355(4)	.1786(9)	.055(2)
S(8")	.6066(1)	.1513(2)	.0626(3)
O(9")	.5847(2)	.0474(5)	.0574(9)
O(10")	.6024(2)	.2111(5)	-.0956(8)
O(11")	.5942(2)	.2112(5)	.2113(8)
H(1)	.623(5)	.791(9)	.38(1)
H(5)	.507(2)	.910(7)	.44(1)
H(6)	.566(3)	.824(7)	.23(1)
H(7)	.569(3)	1.031(9)	.79(1)
H(9)	.562(3)	1.026(8)	.31(1)
H(10A)	.650(3)	.665(8)	.58(1)
H(10B)	.636(4)	.672(8)	.75(1)
H(11A)	.587(3)	.703(7)	.94(1)
H(11B)	.544(3)	.669(7)	.87(1)
H(12A)	.495(3)	.801(8)	1.01(1)
H(12B)	.536(5)	.846(9)	1.05(1)
H(14)	.456(4)	.935(9)	.85(1)
H(15)	.455(3)	.812(7)	.63(1)
H(16A)	.532(2)	.657(7)	.45(1)
H(16B)	.502(3)	.704(7)	.30(1)
H(19A)	.574(4)	.393(9)	.14(1)
H(19B)	.592(3)	.488(9)	.10(1)
H(3')	.690(3)	.267(9)	.42(1)
H(4')	.764(3)	.224(7)	.46(1)
H(6')	.768(3)	.466(9)	.80(1)
H(7')	.693(5)	.492(9)	.78(1)
H(3")	.728(3)	-.077(7)	.18(1)
H(4")	.656(3)	-.024(7)	.18(1)
H(6")	.683(3)	.261(8)	-.02(1)
H(7")	.757(3)	.212(7)	.00(1)

Table 2. Bond distances in angstroms of the p-bromobenzenesulfonate derivative of saxitoxin (4). The estimated standard deviation of the least significant figure is given in parentheses. The atoms of the p-bromobenzenesulfonate anions are indicated by primes. The numbering scheme refers to Figure 1.

N(1)	- C(2)	1.33(1)	Br(1')	- C(2')	1.902(8)
N(1)	- C(6)	1.46(1)	C(2')	- C(3')	1.38(1)
C(2)	- N(3)	1.33(1)	C(2')	- C(7')	1.34(1)
C(2)	- N(10)	1.33(1)	C(3')	- C(4')	1.42(1)
N(3)	- C(4)	1.48(1)	C(4')	- C(5')	1.32(1)
N(3)	- C(11)	1.49(1)	C(5')	- C(6')	1.40(1)
C(4)	- C(5)	1.55(1)	C(5')	- S(8')	1.775(9)
C(4)	- C(7)	1.40(1)	C(6')	- C(7')	1.40(1)
C(4)	- C(13)	1.56(1)	S(8')	- O(9')	1.493(8)
C(5)	- C(6)	1.51(1)	S(8')	- O(10')	1.486(8)
C(5)	- N(9)	1.43(1)	S(8')	- O(11')	1.442(9)
C(6)	- C(16)	1.54(1)			
N(7)	- C(8)	1.36(1)	Br(1")	- C(2")	1.92(1)
C(8)	- N(9)	1.32(1)	C(2")	- C(3")	1.35(1)
C(8)	- N(21)	1.32(1)	C(2")	- C(7")	1.38(1)
C(11)	- C(12)	1.56(1)	C(3")	- C(4")	1.36(1)
C(12)	- C(13)	1.52(1)	C(4")	- C(5")	1.33(1)
C(13)	- O(14)	1.40(1)	C(5")	- C(6")	1.38(1)
C(13)	- O(15)	1.37(1)	C(5")	- S(8")	1.774(9)
C(16)	- O(17)	1.45(1)	C(6")	- C(7")	1.39(1)
O(17)	- C(18)	1.32(1)	S(8")	- O(9")	1.438(6)
C(18)	- N(19)	1.37(1)	S(8")	- O(10")	1.440(7)
C(18)	- O(20)	1.22(1)	S(8")	- O(11")	1.424(7)

Table 3. Bond angles in degrees of the p-bromobenzenesulfonate of saxitoxin (4). The estimated standard deviation of the least significant figure is given in parentheses. The atoms of the p-bromobenzenesulfonate anions are indicated by primes. The numbering scheme refers to Figure 1.

C(2)	- N(1)	- C(6)	117.6(7)
N(1)	- C(2)	- N(3)	117.1(7)
N(1)	- C(2)	- N(10)	121.0(7)
N(3)	- C(2)	- N(10)	121.9(7)
C(2)	- N(3)	- C(4)	122.3(7)
C(2)	- N(3)	- C(11)	122.9(6)
C(4)	- N(3)	- C(11)	114.8(6)
N(3)	- C(4)	- C(5)	113.7(7)
N(3)	- C(4)	- N(7)	109.1(6)
N(3)	- C(4)	- C(13)	98.6(7)
C(5)	- C(4)	- N(7)	103.9(7)
C(5)	- C(4)	- C(13)	115.9(7)
N(7)	- C(4)	- C(13)	115.7(7)
C(4)	- C(5)	- C(6)	111.7(7)
C(4)	- C(5)	- N(9)	102.2(7)
C(6)	- C(5)	- N(9)	111.1(6)
N(1)	- C(6)	- C(5)	109.6(6)
N(1)	- C(6)	- C(16)	111.0(7)
C(5)	- C(6)	- C(16)	113.0(6)
C(4)	- N(7)	- C(8)	111.5(7)
N(7)	- C(8)	- N(9)	109.7(6)
N(7)	- C(8)	- N(21)	124.5(8)
N(9)	- C(8)	- N(21)	125.7(8)
C(5)	- N(9)	- C(8)	112.7(7)
N(3)	- C(11)	- C(12)	101.2(7)
C(11)	- C(12)	- C(13)	104.6(7)
C(4)	- C(13)	- C(12)	103.6(6)
C(4)	- C(13)	- O(14)	109.5(7)
C(4)	- C(13)	- O(15)	106.3(7)
C(12)	- C(13)	- O(14)	114.2(7)
C(12)	- C(13)	- O(15)	111.3(8)
O(14)	- C(13)	- O(15)	111.3(7)
C(6)	- C(16)	- O(17)	105.9(6)
C(16)	- O(17)	- C(18)	116.1(7)
O(17)	- C(18)	- N(19)	112.5(8)
O(17)	- C(18)	- O(20)	125.5(8)
N(19)	- C(18)	- O(20)	122.0(7)
Br(1')	- C(2')	- C(3')	119.0(8)
Br(1')	- C(2')	- C(7')	119.3(7)

Table 3 (Continued)

C(3') - C(2') - C(7')	121.6(9)
C(2') - C(3') - C(4')	118.3(9)
C(3') - C(4') - C(5')	119.9(9)
C(4') - C(5') - C(6')	120.7(9)
C(4') - C(5') - S(8')	121.6(9)
C(6') - C(5') - S(8')	117.8(8)
C(5') - C(6') - C(7')	119.4(9)
C(2') - C(7') - C(6')	120.0(9)
C(5') - S(8') - O(9')	106.2(5)
C(5') - S(8') - O(10')	106.8(4)
C(5') - S(8') - O(11')	107.4(5)
O(9') - S(8') - O(10')	108.3(5)
O(9') - S(8') - O(11')	114.1(7)
O(10') - S(8') - O(11')	113.6(6)
Br(1") - C(2") - C(3")	119.8(8)
Br(1") - C(2") - C(7")	118.3(7)
C(3") - C(2") - C(7")	121.9(9)
C(2") - C(3") - C(4")	118.1(9)
C(3") - C(4") - C(5")	123.0(9)
C(4") - C(5") - C(6")	118.9(9)
C(4") - C(5") - S(8")	122.0(7)
C(6") - C(5") - S(8")	119.1(8)
C(5") - C(6") - C(7")	120.1(9)
C(2") - C(7") - C(6")	117.7(8)
C(5") - S(8") - O(9")	106.4(4)
C(5") - S(8") - O(10")	105.9(4)
C(5") - S(8") - O(11")	107.0(5)
O(9") - S(8") - O(10")	112.2(4)
O(9") - S(8") - O(11")	110.2(4)
O(10") - S(8") - O(11")	114.5(3)

Table 4. The observed and calculated structure factors for the p-bromobenzenesulfonate of saxitoxin (4).

H = 0				8	6	21	22	3	6	35	37	11	4	10	8
K	L	FO	FC	9	1	25	25	3	7	31	27	12	0	42	38
0	2	44	32	9	2	19	20	3	8	19	20	12	1	10	12
0	4	145	130	9	3	32	35	4	0	116	123	12	2	33	32
0	6	40	38	9	4	86	87	4	1	23	25	12	3	14	16
0	8	15	16	9	5	11	6	4	2	64	68	13	0	11	5
1	1	27	31	9	6	14	12	4	3	65	67				
1	2	39	68	10	0	11	13	4	4	81	86	H = 2			
1	3	70	68	10	1	14	11	4	5	11	10	K	L	FO	FC
1	4	35	37	10	2	20	22	5	0	140	147	0	0	45	47
1	5	13	17	10	3	30	30	5	1	60	64	0	1	84	81
1	7	20	16	11	2	38	40	5	3	26	32	0	2	71	70
1	8	13	14	11	3	40	41	5	4	26	28	0	3	57	57
2	0	37	45	11	4	34	32	5	5	55	57	0	4	36	37
2	1	262	323	12	0	17	20	5	6	22	24	0	5	15	17
2	2	68	79	12	2	9	11	5	7	17	16	0	6	33	33
2	3	69	76	12	3	13	11	6	0	40	40	0	8	12	15
2	4	15	16	13	1	20	22	6	1	77	70	1	0	16	13
2	5	22	23					6	2	37	40	1	1	78	74
3	1	65	69	H = 1				6	3	67	68	1	2	129	124
3	2	99	107	K	L	FO	FC	6	4	15	14	1	3	98	100
3	4	13	18	0	1	35	34	6	5	30	30	1	4	30	33
3	6	45	46	0	2	399	372	7	1	55	56	1	5	61	63
3	7	25	27	0	4	15	17	7	2	35	33	1	6	45	46
4	1	92	107	0	5	15	14	7	3	48	51	1	7	12	13
4	2	75	78	0	7	10	11	7	4	26	30	1	8	22	23
4	3	30	28	1	0	30	31	7	5	11	11	2	0	69	69
4	4	15	15	1	1	45	45	8	0	71	71	2	1	99	99
4	5	9	12	1	2	66	64	8	1	16	20	2	2	80	80
4	6	29	27	1	3	21	24	8	2	52	52	2	3	100	102
4	7	16	15	1	4	84	93	8	3	33	31	2	4	59	52
5	1	47	52	1	5	20	20	8	4	21	24	2	5	35	37
5	2	65	82	1	6	30	33	8	5	17	16	2	6	19	21
5	3	70	68	1	7	20	24	8	6	24	22	2	7	13	15
5	6	18	20	1	8	12	13	9	0	13	13	2	8	9	12
5	7	16	14	2	0	34	37	9	2	41	44	3	0	124	126
6	0	21	13	2	1	245	281	9	3	23	22	3	1	63	66
6	2	10	3	2	2	104	106	9	4	19	14	3	2	113	117
6	3	84	81	2	3	37	36	9	5	18	18	3	3	83	87
6	4	11	1	2	4	25	29	9	6	17	16	3	4	59	61
6	7	18	18	2	5	35	38	10	0	15	12	3	5	25	27
7	1	81	81	2	6	12	12	10	2	22	23	3	6	52	52
7	3	24	21	3	0	110	106	10	3	33	35	3	8	13	15
7	4	52	51	3	1	65	71	10	4	11	10	4	0	58	55
7	5	24	24	3	2	77	89	11	0	35	36	4	1	87	93
7	6	13	13	3	3	26	29	11	1	21	20	4	2	131	146
8	0	33	17	3	4	76	82	11	2	24	23	4	3	9	6
8	0	28	17	3	5	37	39	11	3	27	27	4	4	35	35

Table 4 (Continued)

4	5	16	16	12	0	14	17	5	2	31	31		H =	4	
5	0	22	24	12	2	37	34	5	3	43	41	K	L	FO	FC
5	1	39	40					5	4	24	26	0	0	117	119
5	2	51	54		H =	3		5	5	36	35	0	1	54	55
5	3	70	76	K	L	FO	FC	5	6	27	27	0	2	134	134
5	4	35	36	0	1	14	11	5	7	16	15	0	3	20	20
5	5	33	32	0	2	9	5	6	0	28	20	0	4	55	56
5	6	21	23	0	3	68	70	6	1	46	49	0	6	44	46
5	7	27	26	0	4	30	33	6	2	27	27	0	7	11	9
6	0	23	22	0	6	52	52	6	3	51	54	0	8	21	22
6	1	70	71	0	7	13	16	6	4	18	21	1	0	7	5
6	2	21	23	0	8	11	11	6	5	14	11	1	1	21	23
6	3	12	19	1	0	26	27	6	6	21	22	1	2	86	80
6	4	27	26	1	1	44	45	7	0	12	18	1	3	70	66
6	5	35	38	1	2	70	65	7	1	29	31	1	4	36	37
6	6	17	18	1	3	66	58	7	2	84	88	1	5	22	20
6	7	15	15	1	4	58	57	7	3	33	31	1	6	44	44
7	0	25	29	1	5	14	16	7	4	35	36	1	7	24	26
7	1	48	47	1	6	37	38	7	5	23	23	2	0	68	66
7	2	35	34	1	7	31	32	7	7	14	12	2	1	41	42
7	3	11	7	1	8	26	28	8	0	60	59	2	2	75	69
7	4	35	36	2	0	90	92	8	1	52	51	2	3	102	101
7	5	15	13	2	1	119	118	8	2	20	20	2	4	36	35
7	6	20	19	2	2	22	22	8	3	22	23	2	5	35	32
7	7	9	6	2	3	77	79	8	4	30	30	2	6	34	34
8	0	41	39	2	4	50	47	8	5	39	38	2	7	19	21
8	1	29	29	2	5	19	19	8	6	13	11	3	0	147	149
8	2	81	85	2	6	20	20	9	0	18	15	3	1	131	131
8	3	29	28	2	7	30	30	9	1	65	63	3	2	43	42
8	4	56	54	3	0	123	122	9	2	26	25	3	3	52	52
8	5	36	35	3	1	93	96	9	3	65	67	3	4	47	45
9	0	18	19	3	2	52	56	9	5	12	16	3	5	51	51
9	1	27	25	3	3	22	23	9	6	18	19	3	6	22	23
9	2	17	16	3	4	52	50	10	1	39	41	4	0	108	110
9	3	47	46	3	5	11	14	10	2	10	12	4	1	29	30
9	4	30	28	3	6	11	7	10	3	34	32	4	2	89	93
9	5	11	9	3	7	14	15	10	4	30	33	4	3	82	85
10	0	12	12	3	8	10	11	10	5	10	9	4	4	19	19
10	1	65	64	4	0	135	139	11	0	48	47	4	5	12	13
10	2	17	20	4	1	26	27	11	1	18	21	4	6	10	15
10	3	34	29	4	2	86	88	11	2	41	38	4	7	28	28
10	4	18	21	4	3	59	58	11	3	27	27	4	8	17	14
10	5	22	19	4	4	79	82	12	0	24	23	5	0	72	69
11	0	18	13	4	5	25	24	12	3	11	11	5	1	18	17
11	1	24	22	4	6	10	14	13	0	14	10	5	2	16	15
11	2	21	19	4	7	15	14	13	1	13	16	5	3	18	20
11	3	23	22	5	0	119	125					5	4	36	36
11	4	25	22	5	1	38	38					5	5	11	8

Table 4 (Continued)

5	7	13	15	0	6	47	47	7	3	34	32	1	8	8	4
6	0	62	57	0	8	9	11	7	4	11	12	2	0	39	41
6	1	66	71	1	0	112	107	7	5	10	8	2	1	111	111
6	2	54	57	1	1	94	90	7	6	21	20	2	2	20	18
6	3	83	84	1	2	150	149	8	0	70	71	2	3	63	57
6	4	10	11	1	3	48	47	8	1	30	30	2	4	59	56
6	5	17	17	1	4	31	31	8	2	42	45	2	5	38	37
6	6	26	27	1	5	54	51	8	3	21	22	3	0	175	166
6	7	9	12	1	8	18	19	8	4	28	26	3	1	43	40
7	0	64	66	2	0	106	103	8	5	10	7	3	2	98	100
7	1	87	91	2	1	97	93	8	6	30	29	3	3	42	43
7	2	45	45	2	2	50	54	9	0	29	27	3	4	40	40
7	3	28	26	2	3	52	47	9	1	12	9	3	5	34	33
7	4	58	60	2	4	51	49	9	2	26	25	3	6	21	22
7	6	12	11	2	5	61	60	9	3	13	11	3	7	23	21
8	0	35	38	2	6	15	15	9	5	34	33	4	0	73	65
8	1	37	33	2	8	15	17	10	0	15	13	4	1	55	55
8	2	19	19	3	0	93	88	10	1	35	35	4	2	7	9
8	3	18	14	3	1	11	7	10	2	22	23	4	3	42	39
8	4	28	28	3	2	134	133	10	3	22	24	4	4	42	42
8	5	10	11	3	3	68	67	10	4	29	28	4	5	13	13
8	6	16	14	3	4	71	70	10	5	20	20	4	7	13	14
9	0	37	38	3	5	33	28	11	0	48	47	5	0	57	52
9	1	57	54	3	6	26	27	11	2	12	16	5	1	24	24
9	2	45	44	3	8	11	11	11	4	9	13	5	2	26	22
9	4	34	33	4	0	23	20	12	0	39	38	5	3	64	64
9	5	30	25	4	1	61	62	12	1	22	19	5	4	29	35
10	0	17	18	4	2	33	33	12	2	19	18	5	5	11	10
10	1	18	20	4	3	39	38	13	1	21	23	5	6	26	26
10	2	17	22	4	4	42	42					5	7	14	14
10	4	9	11	4	5	14	12		H =	6		6	0	15	13
11	0	53	53	4	6	24	24	K	L	FO	FC	6	1	62	58
11	1	17	14	5	0	72	80	0	0	42	44	6	2	44	48
11	2	37	37	5	1	86	87	0	1	34	33	6	3	28	29
11	3	11	7	5	2	63	63	0	2	51	59	6	4	36	37
11	4	18	16	5	3	22	25	0	3	38	36	6	5	34	34
12	0	17	14	5	4	30	29	0	4	41	42	6	7	20	17
12	1	17	18	5	5	10	10	0	5	32	31	7	0	57	56
12	3	14	7	5	6	17	16	0	6	46	47	7	1	18	20
13	1	34	34	6	0	85	94	0	8	21	21	7	2	50	50
				6	1	47	48	1	0	160	150	7	3	20	23
	H =	5		6	2	9	14	1	1	161	160	7	4	12	9
K	L	FO	FC	6	3	47	46	1	2	23	28	7	5	12	11
0	1	44	43	6	4	35	37	1	3	98	92	7	7	8	7
0	2	152	157	6	5	41	41	1	4	63	61	8	1	30	31
0	3	75	74	6	7	10	12	1	5	22	23	8	2	56	58
0	4	75	74	7	1	36	38	1	6	39	39	8	3	20	20
0	5	22	22	7	2	10	18	1	7	11	15	8	4	38	39

Table 4 (Continued)

8	5	23	22	3	0	139	140	10	2	27	27	5	5	15	20
8	6	9	10	3	1	77	72	10	3	36	36	6	0	85	76
9	1	16	14	3	2	102	100	10	4	19	20	6	1	50	49
9	2	31	31	3	3	33	34	11	0	45	45	6	2	27	28
9	3	15	17	3	4	44	45	11	1	20	17	6	3	34	37
9	4	40	42	3	5	40	38	11	2	24	24	6	5	18	17
9	5	13	8	3	6	10	8	11	3	41	42	6	6	16	15
10	1	33	34	3	7	10	10	12	2	24	20	7	0	21	25
10	2	36	36	3	8	10	11					7	1	36	35
10	3	26	23	4	1	75	76		H =	8		7	2	62	64
10	5	9	12	4	2	39	40	K	L	FO	FC	7	3	36	36
11	0	23	23	4	3	25	27	0	0	108	109	7	4	25	27
11	1	12	15	4	4	66	63	0	2	102	103	7	5	25	22
11	2	9	13	4	5	12	15	0	3	26	22	7	6	14	13
11	3	13	12	4	6	29	28	0	4	38	38	8	1	44	43
11	4	9	11	4	7	14	14	0	5	8	6	8	2	24	22
12	1	14	15	5	0	83	81	0	6	42	42	8	3	32	32
12	2	27	27	5	1	61	62	0	7	14	12	8	4	39	38
12	3	19	20	5	2	19	17	0	8	13	15	8	5	23	22
13	0	11	15	5	3	53	52	1	0	195	185	8	6	18	20
				5	4	25	27	1	1	29	31	9	1	37	36
	H =	7		5	5	18	19	1	2	139	133	9	2	28	27
K	L	FO	FC	5	6	20	18	1	5	13	11	9	3	31	30
0	1	35	34	5	7	13	10	2	0	143	139	9	4	21	21
0	2	54	53	6	0	55	51	2	1	59	54	9	5	14	14
0	3	17	17	6	1	17	16	2	2	8	11	10	0	33	36
0	4	77	78	6	2	30	29	2	3	70	71	10	1	20	21
0	5	45	46	6	3	16	20	2	4	31	30	10	2	19	20
0	6	42	41	6	4	15	16	2	5	59	56	10	3	28	26
0	7	11	11	6	6	20	20	2	6	32	29	10	4	24	25
1	0	41	41	7	0	44	43	2	8	9	10	11	1	45	44
1	1	137	137	7	2	44	45	3	0	46	50	11	2	17	17
1	2	23	24	7	3	35	35	3	1	131	131	11	3	9	8
1	3	106	94	7	4	29	29	3	2	60	59	12	0	29	32
1	4	52	48	7	5	14	15	3	3	64	64	12	2	11	9
1	5	28	26	8	0	27	28	3	4	28	26				
1	6	15	12	8	1	52	52	3	5	28	28		H =	9	
1	7	16	17	8	3	60	59	4	0	139	135	K	L	FO	FC
1	8	15	16	8	4	38	39	4	1	9	10	0	1	133	133
2	0	29	25	8	5	16	18	4	2	42	44	0	2	121	125
2	1	38	41	9	0	37	37	4	3	18	17	0	3	26	27
2	2	52	50	9	1	31	29	4	4	25	23	0	4	37	39
2	3	63	59	9	2	43	43	4	6	24	26	0	5	10	12
2	4	58	55	9	3	27	25	5	0	85	79	0	6	10	9
2	5	28	28	9	4	17	16	5	1	67	65	0	7	31	31
2	6	49	49	9	5	27	26	5	2	29	30	0	8	9	10
2	7	41	41	10	0	17	15	5	3	51	49	1	0	256	254
2	8	8	6	10	1	24	21	5	4	40	39	1	1	165	165

Table 4 (Continued)

1	2	51	54	7	6	9	10	3	0	76	76	11	1	15	15
1	3	27	27	8	0	34	34	3	1	18	16	11	3	18	17
1	4	39	38	8	1	31	33	3	2	24	21	11	4	9	9
1	6	30	30	8	2	51	53	3	3	34	35	12	1	12	11
1	7	16	14	8	3	15	14	3	4	19	15	12	2	8	8
2	0	93	88	8	5	27	28	3	5	14	12				
2	1	22	20	8	6	16	15	3	6	30	29		H = 11		
2	2	81	81	9	0	16	9	3	7	14	15	K	L	FO	FC
2	3	54	54	9	4	12	11	4	0	48	43	0	1	29	31
2	4	13	9	9	5	10	6	4	1	47	47	0	2	15	15
2	5	39	38	10	2	31	33	4	2	27	27	0	3	26	29
2	6	23	21	10	3	42	43	4	3	43	43	0	4	24	24
2	8	16	18	10	4	21	23	4	4	45	46	0	7	19	19
3	0	27	25	10	5	24	24	4	5	16	16	0	8	9	8
3	1	77	76	11	1	18	19	4	6	38	36	1	0	11	10
3	2	75	70	11	2	13	12	5	0	31	26	1	1	50	49
3	3	52	51	11	4	11	10	5	1	71	72	1	2	33	37
3	4	30	28	12	0	18	13	5	2	42	41	1	3	54	59
3	5	16	15	12	1	17	15	5	3	69	70	1	4	12	11
3	6	16	16	12	2	23	26	5	4	11	10	1	5	19	19
4	0	92	91					5	5	20	21	1	6	33	34
4	1	85	84		H = 10			5	7	9	13	1	7	14	13
4	2	84	81	K	L	FO	FC	6	1	78	76	1	8	8	8
4	3	27	23	0	0	57	53	6	2	57	60	2	0	54	53
4	4	15	14	0	1	92	90	6	3	28	28	2	1	89	90
4	6	23	21	0	2	45	45	6	4	19	23	2	2	93	91
4	7	11	8	0	3	16	20	6	5	33	33	2	4	20	22
5	0	45	41	0	4	27	26	6	6	10	10	2	5	21	19
5	1	108	105	0	5	26	26	6	7	24	25	2	7	27	24
5	2	55	59	0	6	27	26	7	0	43	44	3	0	61	55
5	3	29	28	0	7	18	19	7	1	19	22	3	1	17	15
5	4	26	24	0	8	17	18	7	2	38	39	3	2	26	25
5	5	24	23	1	0	115	107	7	4	43	43	3	3	55	53
5	6	18	18	1	1	155	155	8	0	33	31	3	4	18	16
6	0	47	46	1	2	59	59	8	1	17	15	3	5	22	21
6	1	90	89	1	3	36	37	8	2	27	27	3	6	17	20
6	2	55	53	1	4	33	35	8	3	24	27	3	7	9	12
6	3	48	47	1	5	12	13	8	4	25	23	4	0	20	22
6	4	27	25	1	7	15	16	8	5	18	18	4	1	70	68
6	5	24	27	2	0	27	28	9	1	24	25	4	2	50	48
6	6	9	4	2	1	26	26	9	2	32	33	4	3	98	99
6	7	11	11	2	2	49	50	9	3	16	18	4	4	19	20
7	0	68	71	2	3	28	28	9	5	26	26	4	5	20	17
7	1	9	9	2	4	59	56	10	0	41	40	4	6	25	25
7	2	18	19	2	5	9	8	10	1	26	29	5	1	47	45
7	3	26	26	2	6	38	36	10	2	16	18	5	2	67	65
7	4	9	13	2	7	16	15	10	3	25	25	5	3	10	8
7	5	14	14	2	8	14	13	10	4	10	12	5	4	26	24

Table 4 (Continued)

5	5	16	18	1	5	52	52	8	3	42	42	4	0	164	163
5	6	34	33	1	6	27	29	8	4	12	15	4	1	33	32
5	7	11	13	1	7	28	26	8	5	13	15	4	2	13	13
6	0	53	54	2	0	84	81	8	6	9	11	4	3	18	14
6	2	40	42	2	1	59	55	9	1	28	28	4	4	27	26
6	3	18	20	2	2	26	25	9	2	37	37	4	5	15	14
6	4	31	30	2	3	83	81	9	3	19	16	4	7	10	6
6	5	20	22	2	4	22	24	9	5	13	15	5	0	49	45
6	6	18	18	2	5	21	18	10	0	65	65	5	1	33	32
6	7	13	10	2	6	30	32	10	2	25	27	5	2	63	66
7	0	47	48	3	0	23	22	10	3	23	23	5	3	29	28
7	1	28	27	3	1	75	72	10	4	25	26	5	4	29	29
7	2	20	22	3	2	26	24	11	1	24	22	5	5	41	40
7	3	61	63	3	3	33	31	11	2	30	31	5	7	12	6
7	4	29	29	3	4	37	35	11	3	13	9	6	0	16	11
7	6	12	12	3	5	32	34	12	0	12	11	6	1	61	61
8	0	18	19	3	6	26	24	12	1	14	14	6	2	33	34
8	2	11	13	4	0	48	43					6	3	34	35
8	4	28	29	4	1	64	66		H = 13			6	4	31	30
8	5	22	21	4	2	71	67	K	L	FO	FC	6	5	14	13
9	0	35	36	4	3	15	13	0	1	121	125	6	6	11	7
9	1	30	32	4	4	11	13	0	2	10	9	7	0	22	23
9	2	23	22	4	5	23	24	0	3	78	78	7	1	13	11
9	3	38	42	4	6	13	16	0	4	17	15	7	2	55	54
9	4	30	30	5	0	33	31	0	5	49	49	7	4	40	40
10	2	16	13	5	1	47	48	0	6	16	15	8	0	35	34
10	4	9	4	5	2	69	71	0	7	21	20	8	1	47	47
11	0	28	28	5	3	50	52	1	0	42	42	8	2	15	16
11	1	20	19	5	4	46	47	1	1	40	40	8	3	22	21
11	3	23	20	5	5	12	14	1	2	66	62	8	4	19	17
12	0	8	6	5	6	15	18	1	3	39	39	8	5	14	15
12	1	9	8	5	7	14	15	1	4	32	34	9	0	26	26
12	2	21	19	6	0	29	29	1	5	47	48	9	1	10	10
				6	1	59	60	1	6	32	35	9	2	24	26
	H = 12			6	2	23	24	1	7	14	15	9	5	14	13
K	L	FO	FC	6	3	18	17	2	0	163	159	10	2	47	48
0	0	8	8	6	4	25	24	2	1	80	78	10	3	22	23
0	1	48	47	6	5	22	21	2	2	50	47	10	4	16	18
0	2	26	26	6	6	13	12	2	3	28	27	11	1	23	21
0	3	30	31	7	0	26	23	2	4	38	38	11	2	9	3
0	4	24	25	7	1	37	40	2	5	18	16	12	0	21	21
0	5	20	19	7	2	41	41	3	0	90	89	12	1	24	25
0	6	9	12	7	3	18	20	3	1	86	81				
0	7	27	29	7	4	20	16	3	2	37	37		H = 14		
1	0	119	118	7	5	18	16	3	3	56	58	K	L	FO	FC
1	2	45	43	8	0	13	16	3	4	54	53	0	0	134	128
1	3	49	50	8	1	28	26	3	5	26	26	0	1	223	220
1	4	63	64	8	2	15	17	3	6	33	35	0	2	64	62

Table 4 (Continued)

0	3	75	77	7	2	22	20	3	1	59	55	0	2	19	18
0	4	59	62	7	3	10	13	3	2	16	16	0	3	37	36
0	5	45	46	7	4	40	42	3	3	49	48	0	4	30	31
0	6	20	19	7	6	20	22	3	4	27	25	1	0	30	27
1	0	12	12	8	1	17	14	3	5	15	14	1	1	39	39
1	1	62	62	8	2	19	17	3	7	23	20	1	2	29	30
1	2	73	71	8	3	29	29	4	2	62	57	1	3	51	51
1	3	60	65	8	4	16	15	4	3	67	65	1	4	34	35
1	5	19	20	8	5	9	10	4	4	24	23	1	5	15	14
1	6	16	18	9	0	44	45	4	5	26	26	1	6	22	20
1	7	15	18	9	1	9	10	4	6	12	11	1	7	20	20
2	0	38	36	9	2	13	17	4	7	10	7	2	0	87	90
2	1	88	85	9	3	33	35	5	0	41	41	2	1	58	58
2	2	132	133	9	5	14	13	5	1	74	69	2	2	48	47
2	3	62	62	10	0	13	10	5	2	20	21	2	3	53	52
2	4	55	55	10	1	31	30	5	3	25	25	2	4	33	34
2	5	25	27	10	2	16	10	5	4	52	52	2	5	20	21
2	6	11	14	10	3	10	10	5	5	29	27	2	6	22	23
3	0	11	10	11	1	23	24	5	6	23	21	3	1	39	39
3	1	71	66	11	2	20	20	6	0	17	12	3	2	58	60
3	2	24	25	11	3	18	18	6	1	15	10	3	3	27	27
3	3	41	41	12	0	10	13	6	2	51	51	3	4	18	19
3	4	16	14					6	4	9	7	3	5	62	61
3	5	23	20	H = 15				6	5	12	12	3	7	22	19
3	6	29	25	K	L	FO	FC	6	6	18	21	4	0	21	21
4	0	42	42	0	1	182	179	7	1	11	9	4	1	78	75
4	1	35	35	0	2	91	97	7	2	44	47	4	3	38	40
4	2	63	65	0	3	82	85	7	3	45	46	4	4	34	32
4	3	19	19	0	4	15	14	7	4	9	11	4	5	32	31
4	4	20	19	0	5	12	7	7	5	14	15	4	6	19	19
4	5	33	32	0	6	10	11	7	6	10	15	4	7	11	12
4	6	13	16	0	7	13	16	8	0	20	20	5	0	16	13
4	7	15	14	1	0	21	22	8	1	13	16	5	1	23	20
5	0	69	69	1	1	34	33	8	3	17	14	5	2	41	39
5	1	37	36	1	2	18	20	8	5	12	10	5	3	31	29
5	2	26	25	1	3	51	53	9	0	26	26	5	4	45	45
5	3	31	29	1	4	19	19	9	1	28	31	5	6	27	25
5	4	26	26	1	5	11	13	9	3	36	36	6	0	31	31
5	5	22	20	1	6	48	49	9	4	18	17	6	1	48	49
5	6	14	14	1	7	12	12	10	2	11	13	6	2	25	24
5	7	15	15	2	0	173	168	10	4	15	14	6	4	43	44
6	1	30	31	2	1	122	117	11	0	17	17	6	5	28	28
6	2	28	27	2	2	32	32	11	1	21	23	6	6	10	11
6	3	15	14	2	3	53	50					7	1	61	63
6	4	31	29	2	4	44	44	H = 16				7	3	29	28
6	6	13	11	2	5	33	34	K	L	FO	FC	7	4	16	14
7	0	88	90	2	6	24	25	0	0	103	98	7	5	30	30
7	1	16	19	3	0	63	61	0	1	57	53	8	2	46	46

Table 4 (Continued)

8	3	44	46	5	5	18	17	2	6	15	15		H =	19	
8	4	12	13	5	6	29	29	3	0	75	72	K	L	FO	FC
8	5	23	22	6	0	16	16	3	1	35	35	0	1	79	80
9	0	28	27	6	1	36	36	3	2	33	31	0	2	18	20
9	1	15	17	6	2	34	34	3	3	20	17	0	3	45	43
9	2	34	33	6	3	59	61	3	4	38	39	0	4	31	32
9	3	12	14	6	4	22	23	3	5	23	20	0	5	35	35
9	4	16	15	6	5	13	13	3	6	10	9	1	0	90	87
10	0	30	30	6	6	9	11	4	0	45	47	1	1	58	56
10	1	29	30	7	1	42	43	4	1	50	50	1	2	14	14
10	2	20	20	7	2	34	34	4	2	51	52	1	3	29	30
11	1	15	16	7	3	32	33	4	3	22	21	1	4	51	49
11	2	25	26	7	4	12	10	4	4	18	16	1	5	23	26
				7	5	17	18	4	5	27	28	1	6	9	8
	H =	17		8	0	63	64	4	6	23	21	2	0	94	92
K	L	FO	FC	8	1	27	29	5	0	36	40	2	1	21	22
0	1	14	12	8	2	35	36	5	1	59	58	2	2	22	21
0	2	80	78	8	4	27	28	5	2	15	17	2	3	13	12
0	3	27	27	8	5	9	11	5	3	30	29	2	5	29	27
1	0	7	8	9	0	45	45	5	5	19	18	2	6	23	24
1	1	37	37	9	1	20	23	6	0	35	34	3	0	30	31
1	2	32	33	9	2	23	27	6	1	73	73	3	1	50	49
1	3	26	26	9	4	20	20	6	2	25	25	3	3	60	57
1	4	28	26	10	1	20	22	6	3	27	30	3	4	13	13
1	5	30	30	10	2	30	30	6	4	42	40	3	5	12	9
1	6	17	16	10	3	15	15	6	5	19	17	4	0	60	59
2	1	12	9	11	1	14	14	7	0	78	78	4	1	23	24
2	2	90	94	11	2	14	14	7	1	15	16	4	2	46	45
2	3	41	43					7	2	24	23	4	3	49	50
2	6	15	13		H =	18		7	3	20	22	4	4	26	26
3	0	80	79	K	L	FO	FC	7	4	21	21	4	5	13	12
3	1	21	20	0	0	15	13	8	0	67	67	4	6	16	15
3	2	45	45	0	1	48	51	8	1	30	29	5	0	66	67
3	3	43	43	0	3	9	9	8	2	27	28	5	1	22	20
3	4	28	28	0	5	15	15	8	3	14	13	5	2	12	13
3	5	33	34	0	6	25	27	8	4	10	11	5	3	16	19
3	6	17	15	0	7	20	21	9	0	24	24	5	4	28	27
3	7	25	25	1	0	19	19	9	1	19	19	5	5	9	11
4	0	24	25	1	2	70	68	9	2	17	19	6	0	28	27
4	1	66	65	1	3	53	55	9	3	31	32	6	1	54	53
4	2	57	57	1	6	27	27	10	1	20	21	6	2	39	39
4	3	47	49	1	7	23	22	10	2	9	11	6	4	31	30
4	4	12	14	2	0	71	68	10	3	18	22	6	5	18	20
4	5	26	25	2	1	50	49	11	0	25	21	7	1	15	16
5	0	22	20	2	2	38	37	11	1	20	19	7	2	34	35
5	1	77	78	2	3	12	12					7	3	16	15
5	2	30	29	2	4	64	64					7	4	12	8
5	3	40	39	2	5	17	18					7	5	8	7

Table 4 (Continued)

8	0	13	12	6	4	13	12	6	0	17	16	5	3	37	38
8	3	9	9	6	5	13	11	6	1	33	34	5	4	35	35
8	4	13	3	7	0	14	13	6	2	27	29	5	5	16	16
9	0	11	7	7	1	27	25	6	3	24	24	6	0	28	27
9	1	28	29	7	2	15	12	6	4	15	17	6	1	26	27
9	2	12	13	7	3	12	12	7	0	20	22	6	2	29	29
9	4	13	19	7	5	21	20	7	1	20	19	6	3	25	23
10	0	21	20	8	1	34	34	7	2	15	15	6	4	16	14
10	1	16	15	8	2	22	20	7	3	25	25	6	5	9	10
10	2	14	13	8	3	29	30	7	4	10	11	7	0	21	21
				9	1	12	10	8	0	46	45	7	1	13	13
H = 20				10	0	19	16	8	1	13	17	7	2	26	27
K	L	FO	FC	10	1	14	13	8	3	9	7	7	3	31	32
0	0	12	7					8	4	16	16	8	0	19	19
0	1	55	55	H = 21				9	1	19	20	8	1	15	13
0	3	30	33	K	L	FO	FC	9	2	19	16	8	2	38	40
0	4	39	40	0	1	19	19	9	3	9	12	9	1	18	20
0	5	23	23	0	2	40	41	10	1	23	22	9	2	15	15
1	1	75	73	0	3	9	12								
1	2	69	69	0	5	57	55	H = 22				H = 23			
1	3	36	36	0	6	17	17	K	L	FO	FC	K	L	FO	FC
1	4	18	16	1	0	47	47	0	0	44	44	0	1	42	42
1	5	50	50	1	1	61	63	0	1	18	21	0	2	24	25
2	0	22	22	1	2	23	25	0	3	47	47	0	3	10	12
2	1	11	10	1	3	54	54	1	0	13	13	0	4	18	18
2	2	40	40	1	4	47	47	1	1	51	51	0	5	34	34
2	3	52	52	1	5	17	17	1	3	16	16	1	0	72	71
2	6	14	14	2	0	18	18	1	6	13	13	1	1	42	41
3	0	42	41	2	1	14	19	2	1	29	28	1	3	24	22
3	1	60	59	2	2	24	24	2	2	24	23	1	4	29	29
3	2	41	41	2	4	29	28	2	3	35	34	2	0	12	7
3	3	27	26	2	5	20	21	2	4	30	30	2	1	33	31
3	4	33	34	2	6	14	15	2	5	17	15	2	2	39	38
3	5	20	19	3	0	51	50	2	6	16	16	2	3	10	11
4	0	41	40	3	1	20	23	3	0	98	96	2	4	26	23
4	1	39	38	3	2	70	71	3	1	41	40	2	6	18	21
4	2	28	26	3	3	57	56	3	2	24	23	3	1	55	56
4	3	18	17	3	4	24	23	3	3	18	18	3	2	32	34
4	4	28	28	3	6	12	13	3	4	11	14	3	3	21	22
4	5	24	23	4	0	13	16	3	5	16	15	3	4	20	19
4	6	13	15	4	1	39	37	4	0	16	17	3	5	12	14
5	0	17	16	4	2	13	14	4	1	61	60	4	1	52	52
5	2	65	64	4	3	32	31	4	2	23	22	4	2	13	13
5	4	22	22	4	4	12	10	4	3	26	21	4	3	25	24
6	0	9	12	5	1	46	45	4	5	13	11	4	5	22	21
6	1	14	13	5	2	46	46	5	0	84	86	5	1	15	20
6	2	21	22	5	3	32	33	5	1	48	50	5	2	53	53
6	3	20	19	5	5	17	17	5	2	12	15	5	3	28	27

Table 4 (Continued)

5	5	14	14	6	1	23	22		H = 26			1	3	14	11
6	0	72	72	6	2	28	29	K	L	FO	FC	1	5	10	9
6	1	29	27	7	0	12	10	0	1	28	28	2	1	24	22
6	2	26	28	7	1	17	20	0	2	18	17	2	2	30	31
6	4	14	13	7	2	10	8	0	3	11	13	2	3	12	11
7	0	21	21	8	1	20	20	0	4	11	10	3	0	16	15
7	1	30	33	8	2	8	5	0	5	11	10	3	1	15	14
7	2	17	13	8	3	29	29	1	0	20	22	3	2	21	21
7	3	12	16					1	1	16	17	3	3	18	18
7	4	24	25		H = 25			1	2	37	38	4	1	37	39
8	0	28	29	K	L	FO	FC	1	3	27	28	4	2	10	9
8	1	24	23	0	1	20	20	2	0	47	45	4	3	22	21
9	1	25	23	0	3	12	10	2	2	27	28	4	4	12	11
9	2	14	16	1	0	63	64	2	3	19	18	5	0	20	21
				1	1	29	30	2	4	37	36	5	1	22	23
	H = 24			1	2	10	12	3	0	14	15	5	2	24	25
K	L	FO	FC	1	3	23	25	3	1	15	16	6	1	10	10
0	0	10	12	1	4	11	12	3	2	25	25	6	2	27	27
0	1	17	17	1	5	12	11	3	3	29	29	7	1	29	29
0	2	11	12	2	0	48	47	3	5	9	10	7	2	11	9
0	3	49	50	2	1	19	19	4	0	13	12				
0	5	10	12	2	2	20	21	4	1	37	36		H = 28		
1	1	61	59	2	3	20	19	4	2	14	14	K	L	FC	FC
1	2	53	53	2	4	11	11	4	3	12	13	0	0	44	43
1	3	10	11	2	5	13	11	5	0	18	20	0	1	9	12
1	5	22	21	3	0	24	23	5	2	19	20	0	3	16	18
2	0	12	12	3	1	31	29	5	3	20	21	0	4	13	12
2	1	28	28	3	2	34	34	5	4	19	19	1	0	12	13
2	2	36	37	3	3	21	20	6	0	23	23	1	1	29	30
2	3	18	18	3	4	17	19	6	1	11	7	1	4	24	26
2	4	28	30	4	0	17	18	6	2	14	12	2	0	33	32
2	5	14	11	4	1	21	23	6	3	12	14	2	1	22	24
3	1	27	26	4	2	31	30	7	0	25	25	2	2	34	35
3	2	17	13	4	3	22	21	7	1	24	24	2	3	21	21
3	3	31	31	4	4	16	16	7	2	11	12	3	0	28	26
3	4	18	17	5	1	17	17	7	3	16	17	3	1	15	15
3	5	15	14	5	3	19	16	8	0	9	9	3	2	11	12
4	0	70	71	5	4	14	12	8	1	15	13	3	3	17	15
4	1	17	12	6	0	21	19					4	0	13	11
4	3	20	21	6	1	13	11		H = 27			4	1	35	35
4	4	27	25	6	2	10	8	K	L	FO	FC	4	2	12	10
4	5	26	23	6	3	24	22	0	1	11	9	4	3	24	23
5	0	32	33	6	4	21	21	0	2	45	46	4	4	10	8
5	1	27	28	7	1	16	15	0	3	18	18	5	0	9	12
5	2	25	23	7	2	17	16	0	4	22	23	5	1	17	17
5	3	20	21	8	0	11	10	0	5	9	10	5	2	18	18
5	4	29	29	8	1	12	13	1	1	22	22	6	0	28	29
6	0	27	27					1	2	19	18	7	0	9	4

Table 4 (Continued)

7	1	30	31

H = 29

K	L	FO	FC
0	1	30	31
0	3	48	48
1	0	12	12
1	1	13	13
1	2	9	7
2	0	47	46
2	1	14	14
2	2	15	12
2	4	34	34
3	0	20	17
3	1	10	12
3	2	10	8
3	3	16	14
4	0	12	15
4	1	18	20
4	2	11	11
4	3	28	29
5	0	27	27
5	1	24	25
5	2	13	14
6	2	13	13

H = 30

K	L	FO	FC
0	0	20	18
0	1	45	46
0	3	24	23
2	0	28	28
2	1	24	24
2	2	37	36
2	3	20	20
3	1	24	24
3	2	18	19
4	1	26	25
4	2	23	24
5	0	22	21
5	1	12	5
6	0	15	17

H = 31

K	L	FC	FC
0	1	21	22
0	3	15	17
1	0	23	23
1	1	10	14
1	2	9	9
2	0	27	25
2	1	23	23
2	2	21	22
3	0	14	16
3	1	20	21
3	2	15	14
4	0	25	24
4	1	32	35
5	0	27	27

H = 32

K	L	FO	FC
0	0	32	35
1	0	16	20
1	1	28	30
1	2	8	9
2	0	23	24
2	1	11	10
3	0	16	18
3	1	15	17
4	0	9	4
4	1	23	23

H = 33

K	L	FO	FC
1	0	20	22
1	1	21	21
2	0	23	23
2	1	16	16

Discussion

Saxitoxin 4 is a tricyclic compound and can be conveniently described as a 3,4,6-trialkyltetrahydropurine. The 3 and 4 positions of the purine are bridged by a three carbon fragment to form the third ring containing a hydrated ketone. The 2 and 8 positions of the purine system contain $-NH_2$ groups as substituents which form the two guanidinium moieties of saxitoxin 4 (14). Position 6 is substituted by a CH_2OCONH_2 moiety which adopts a pseudo-axial conformation in the crystalline state. The crystal structure reveals 13 possible hydrogen bonds but none of these appears to be intramolecular.

The five-membered ring containing a guanidinium group is planar with a maximum deviation from the least-squares plane of 0.001Å. In contrast, the other five-membered ring exists in an envelope conformation with N(3), C(4), C(11), and C(12) forming a plane having a maximum deviation of 0.01Å with C(13) being 0.62Å from this plane. The six-membered ring also contains a four atom plane (N(3), C(4), C(5), and C(6)) with a maximum deviation of 0.001Å. N(1) and C(2) are on the same side of this plane and are 0.87Å and 0.57Å respectively away from it. The guanidinium moiety (N(1), C(2), N(3), and N(10)) is planar with a maximum deviation of 0.003Å. All the C...N bonds of both guanidiniums are the same within experimental error (1.32(1)Å except for

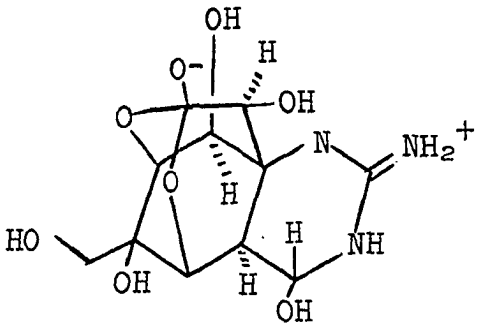
C(8)-N(9) which is 1.36(1)Å. All intramolecular distances and angles are in agreement with previously determined values (23).

The structure presented for saxitoxin 4 is compatible with all of the previously published chemical and spectral data if an equilibrium exists in solution between 4 and its keto form 4a. The ketone hydrates readily in saxitoxin 4 because of the electron withdrawing effects of the guanidinium groups. The keto form is reduced (H_2-PtO_2 or $NaBH_4$) which eliminates the ketone ir absorption at 1770 cm^{-1} and detoxifies saxitoxin (11). Also under rigorous drying conditions (110°C at 10^{-5} mm to constant weight) the ketone hydrate loses one molecule of water to reconcile the proposed molecular formulas (14). Only one atom of ^{18}O can be incorporated when the keto form is dissolved in $H_2{}^{18}O$. This ^{18}O is subsequently lost on vigorous drying. Thus, the same O enters and leaves to form the ketone hydrate. The keto form also explains the deuterium exchange at the C(12) methylene. The nmr (14) spectral assignments are now δ4.27 (1H, q, J = 11, 9 Hz) and δ4.05 (1H, q, J = 11, 5 Hz) to the two hydrogens on C(16), δ3.87 (1H, d of q, J = 9, 5, 1 Hz) to the lone hydrogen on C(6) and δ4.77 (1H, d, J = 1 Hz) to the bridgehead H on C(5). The dihedral angle of 72° between these last two hydrogens in the crystalline state explains their relatively small coupling. The protons on

C(11) are responsible for the resonances at δ3.85 and δ3.57 and the δ2.37 multiplet is attributed to the protons on C(12).

An interesting point which is still not fully explained by structure 4 is the observed pKa values of 8.3 and 11.5 in water (4) and the shift of the lower one to 9.05 in a solution of 50% ethanol and water (14). The shift to a higher pKa on decreasing polarity of the solvent is normally characteristic of a proton dissociating from an oxygen atom rather than from a nitrogen atom (24). This result was used to rationalize the erroneous structure 3. In view of the structure 4 it would appear that both pKa values must be associated with the two guanidinium groups for the hydrated ketone cannot be responsible since reduced saxitoxin has the same pKa values as saxitoxin (11). One explanation for the observed phenomenon is that the carbamate group could intramolecularly stabilize one of the guanidinium groups in the less polar environment of 50% ethanol and 50% water.

The pharmacological actions of saxitoxin 4 and tetrodotoxin 5 (25), a neurotoxin isolated from the puffer fish in Japan and from egg clusters of the California newt, are very similar. Both have been found to specifically block the sodium ion membrane channel over the potassium ion channel in axonic nerve transmission (26). Theories of the



5

mode of action and schematics of the sodium pore have been postulated (27, 28, 29) on the basis of the known structures of the two neurotoxins. As a further tool in studying the structure of the sodium channel, modifications of the native saxitoxin 4 could be made to determine what structural elements are necessary to retain the high toxicity. It would be of particular interest to know the structure of the inactive hydrogenated saxitoxin. Recently Ghazarossian and coworkers (30) were able to generate decarbamaylated saxitoxin by acid hydrolysis of the native material. The hydrolyzed compound retained 60% of the activity of saxitoxin.

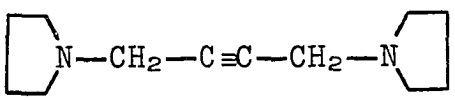
In addition to its usefulness in studying the structure and mechanism of the sodium ion membrane channel it is hoped that the knowledge of the structure of saxitoxin will enable a better monitoring system for toxic shellfish to be found. The present monitoring system uses a mouse bioassay, but this method has some disadvantages in that the

bioassay is not as sensitive or as selective as would be liked. Possibly a rapid, on site chemical method could be developed to measure minute amounts of saxitoxin in contaminated shellfish. Recently, a report has been published of a chemical assay which claims to be more sensitive than the mouse bioassay (31).

PAXILLINE, PASPALINE, AND PASPALICINE

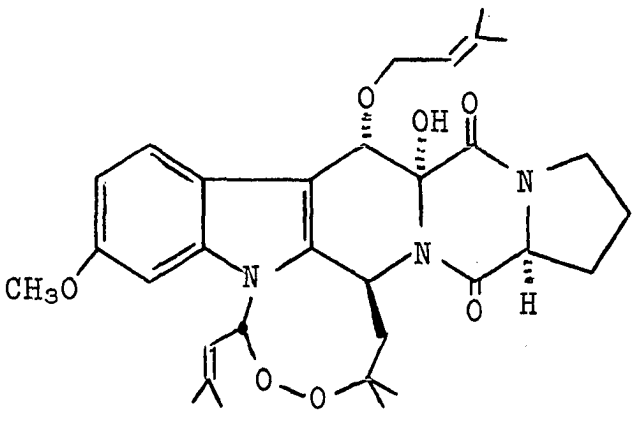
General Introduction

Reports of compounds capable of producing sustained tremors have been quite rare in the scientific literature. Everett and coworkers (32) have reported that out of 10,000 compounds tested only 10 were tremorgenic. The most potent of these was tremorine 6 which produced tremors when injected into mice at the dosage of 20 mg/kg bodyweight. Tremorgens are of scientific interest since elucidation of



6

their mode of action would increase man's understanding of the physiology and chemistry of nerve mechanism. Also they can be used to induce reproducible tremors in test animals providing a biological screen for anti-tremorgenic compounds such as those useful in treating Parkinson's disease. Recently, reports have described a number of tremorgens produced by various species of Penicillium and Aspergillus fungi (33). Those for which chemical structures have been determined can biogenetically be formally derived from 6-methoxytryptophan, proline and a number of mevalonic acid units. A typical example is fumitremorgen A 7 (34) isolated from Aspergillus fumigatus.

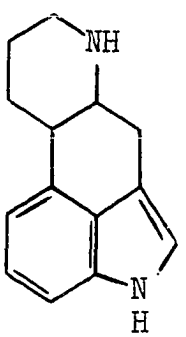


7

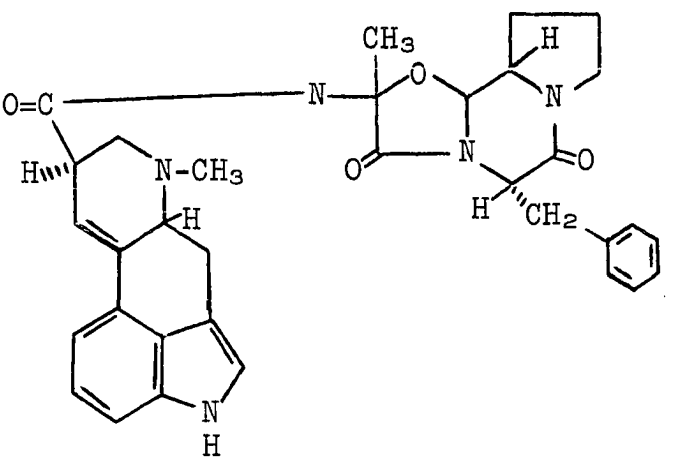
Naturally occurring compounds formally derived from the amino acid tryptophan and containing five-carbon structural units derived from mevalonic acid can be grouped in a relatively small number of categories based on their structural features as well as their biogenesis. One such large, homogeneous class is the ergot alkaloids, principally found as metabolic products from various species of parasitic fungi belonging to the genus Claviceps. Ingestion of bread and other products made from rye flour contaminated with the principal ergot fungus Claviceps purpurea resulted in the mass poisoning and death of thousands of people in the Middle Ages in Europe. A number of the naturally occurring ergot alkaloids have been shown to possess significant psychotomimetic activity. However, semi-synthetic lysergic acid diethylamide (LSD) is perhaps best known and has led to the development of the field of psychopharmacology.

Poisoning from ergot has been variously known as "holy fire" and "St. Anthony's fire" and has recently been attributed to have caused the strange action of "witches" in Salem, Massachusetts in 1692 (35).

The structural characteristic of the ergot alkaloids is the ergoline ring system 8 which is evident in ergotamine 9 (36). The ergoline ring system is formed biosyn-

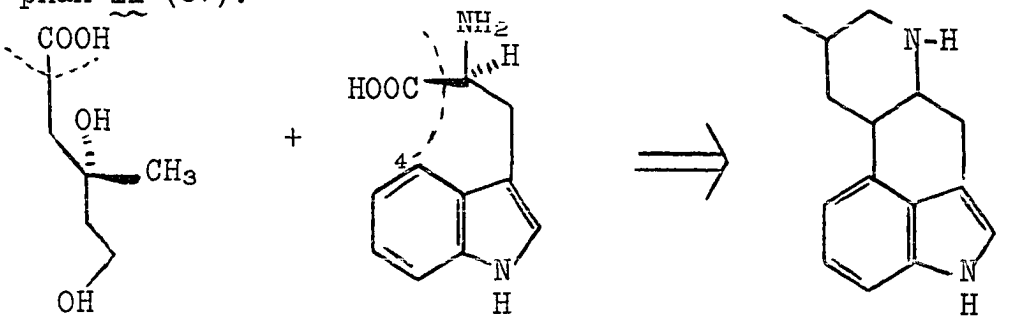


8



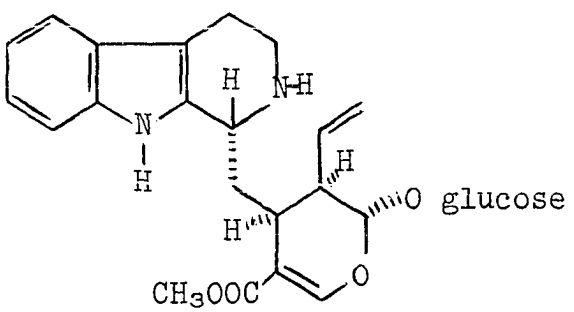
9

thetically from a five-carbon moiety derived from mevalonic acid 10 attached to position 4 of the amino acid tryptophan 11 (37).



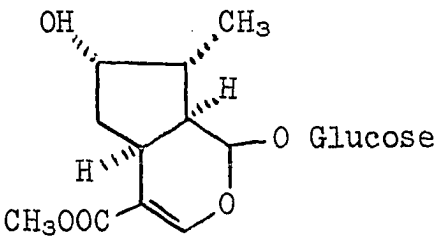
10 11

Another broad, omnifarious class of compounds found in higher plants of the families Apocynaceae, Loganiaceae, and Pubiaceae is also composed of compounds of mixed mevalonate - tryptophan origin. Some of the first compounds characterized in this group have historically been known to produce unusual physiological effects. In fact, a number of new structural classes of natural products have been opened up by the characterization of compounds originally isolated because of their biological activity. Examples of this group which are known for their activities are strychnine-noted for its toxicity, reserpine-used as one of the first tranquilizers, quinine-used in the treatment of malaria, and leurocristine-used in therapeutically treating certain types of leukemia. A typical structural example of one of the simpler members of this large class is vincoside 12 (38) which has been shown to be derived biosynthetically in Vinca rosea from



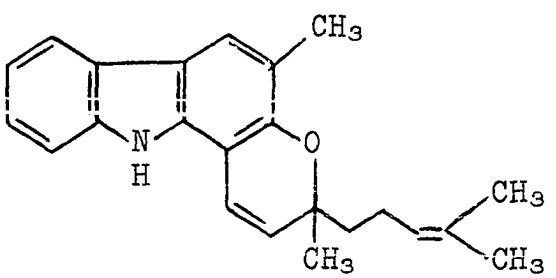
12

tryptophan 11 as well as from the mevalonate derived monoterpene loganin 13 (39).



13

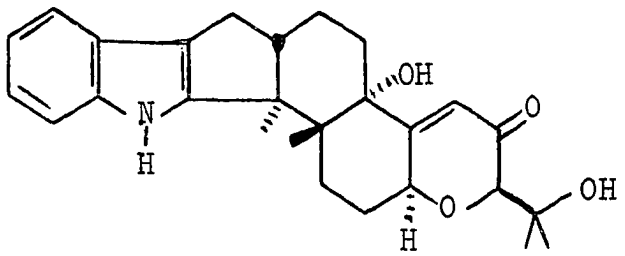
An example of a compound which contains an indole moiety as well as a fifteen-carbon terpenoid chain is mahanimbin 14 (40).



14

Background - Paxilline

Several preliminary reports of new compounds containing a 2,3 disubstituted indole functionality as well as possibly being of mevalonoid origin had appeared (41, 42) prior to the inception of this work, however, no complete chemical structures had been published. A tremorgenic compound was isolated from the fungus Penicillium paxilli. The ED_{50} (effective dose) for producing severe tremors in mice was 25 mg/kg, however the LD_{50} (lethal dose) was quite a bit larger at 150 mg/kg. Preliminary investigation (42) of its chemical and physical properties indicated a number of salient structural features. The u.v. spectrum λ_{max}^{MeOH} 230 ($\epsilon = 41,500$) and 281 nm ($\epsilon = 8,000$) was indicative of a 2,3 substituted indole unit with no conjugation into the indole ring system. The mass spectrum and elemental analysis indicated a molecular formula of $C_{27}H_{33}NO_4$. Additional evidence from ir and nmr measurements indicated that paxilline contained an α,β-unsaturated ketone, a tertiary hydroxyl group, a gem-dimethyl group as well as two additional methyl groups. X-Ray diffraction experiments were subsequently carried out to delineate the stereostructure of paxilline 15 (43).



15

Experimental - Paxilline

A sample of paxilline 15 supplied by R.J. Cole was recrystallized from acetone-heptane mixtures to give large, clear cubes. Preliminary oscillation, Weissenberg, and precession photographs revealed that paxilline crystallized in the common orthorhombic space group $P2_12_12_1$ with a = 31.009(3), b = 11.522(1), and c = 7.707(1) Å. A total of 2186 reflections were measured with $2\theta \leq 120^\circ$ on an automatic four-circle diffractometer using CuK_α (λ = 1.5418 Å) and graphite monochromation. Background corrections were applied and the 1840 (84%) reflections judged observed ($I \geq 3\sigma(I)$) were further corrected for Lorentz and polarization effects (18). The structure was elucidated using a multiple solution tangent formula approach employing a tangent formula recycling procedure (20, 44). Nitrogen and oxygen atoms were assigned on the basis of temperature parameters, bond distances, and bond angles (21). When all 32 nonhydrogen atoms had been located, a difference map (19) was calculated

which indicated the presence of a solvent molecule of acetone tightly hydrogen bonded to the indole nitrogen's hydrogen. This was included in further least-squares refinements. Positions for the hydrogen atoms were found and concluding full matrix least-squares refinements using anisotropic temperature parameters for the nonhydrogen atoms and isotropic temperature parameters for the hydrogen atoms lowered the unweighted residual index to 4.0%. Figure 2 contains a computer generated perspective drawing of paxilline 15 with the correct absolute configuration (vide infra). Tables 5, 6, 7, and 8 contain the fractional coordinates, bond distances, bond angles, and observed and calculated structure factors for paxilline 15.

Discussion - Paxilline

As can be seen from Figure 2, paxilline 15 possesses a nonlinear array of six fused rings. The planar bicyclic indole moiety is fused at C(2) and C(18) to a cyclopentane ring which is itself fused in a trans fashion to a cyclohexane ring to form a linear tetracyclic arrangement of rings. The cyclohexane ring exists in a chair conformation with H(16) and C(25) at the bridgehead positions possessing a diaxial arrangement. An additional fused cyclohexane ring at C(4) and C(13) produces a bend in the molecule which is completed by a fused (at C(7) and C(12)) six-membered oxygen heterocyclic ring containing an α,β-unsaturated ketone.

Figure 2. A computer generated perspective drawing of paxilline (15). Hydrogens are not shown for clarity.

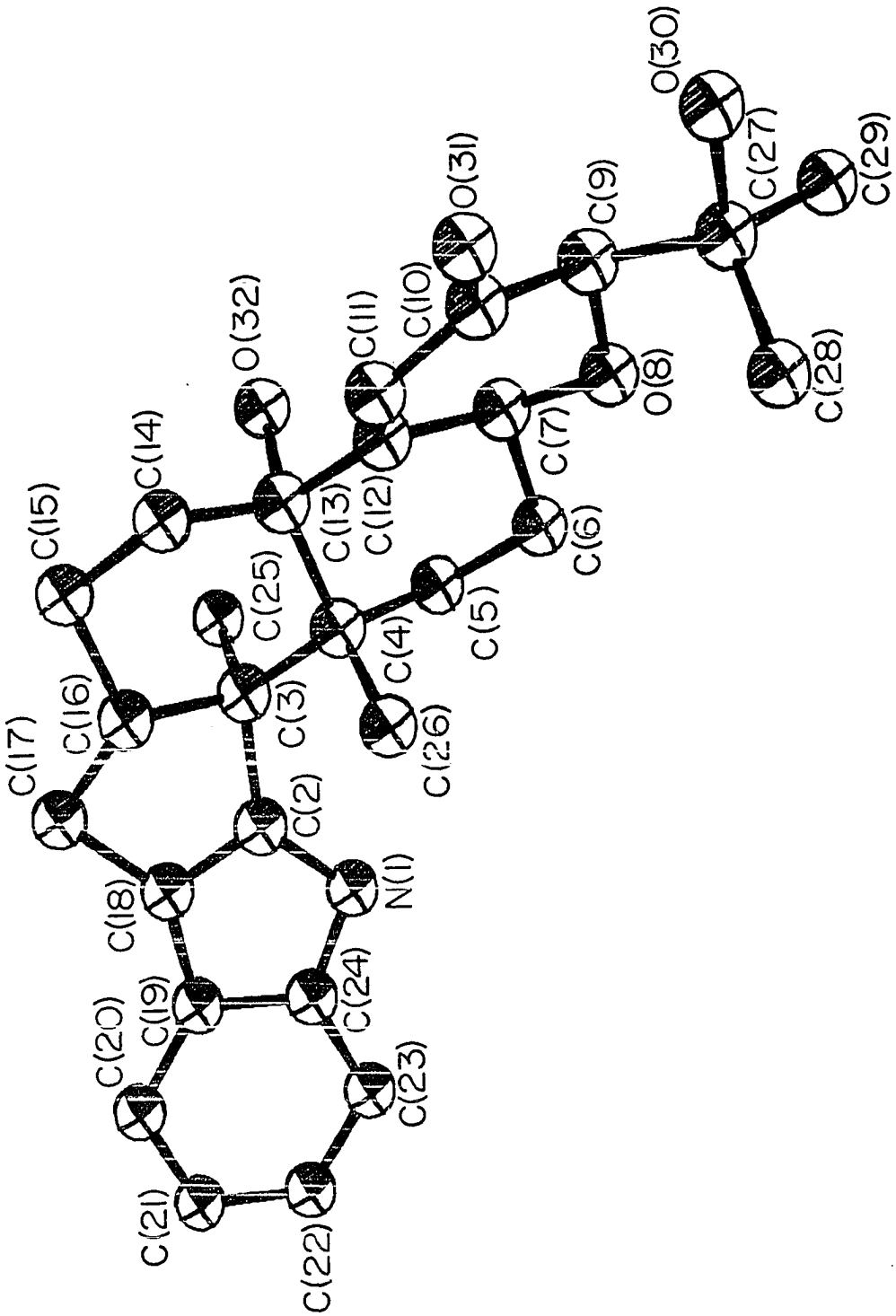

O(30)
O(31)
C(9)
C(27)
C(29)
O(32)
C(11)
C(10)
O(8)
C(28)
C(14)
C(7)
C(15)
C(13)
C(12)
C(6)
C(25)
C(5)
C(4)
C(16)
C(3)
C(26)
C(17)
C(2)
N(1)
C(18)
C(24)
C(20)
C(19)
C(23)
C(21)
C(22)

Table 5. Final fractional coordinates for paxilline (15). The estimated standard deviation of the least significant figure is given in parentheses. The numbering scheme refers to Figure 2.

N(1)	.0582(1)	.4318(2)	.4645(4)
C(2)	.0970(1)	.4707(3)	.5244(4)
C(3)	.1399(1)	.4181(3)	.5670(4)
C(4)	.1405(1)	.3069(3)	.6824(4)
C(5)	.1288(1)	.1955(3)	.5797(5)
C(6)	.1273(1)	.0882(3)	.6910(5)
C(7)	.1693(1)	.0700(3)	.7936(4)
O(8)	.1592(1)	-.0165(2)	.9176(3)
C(9)	.1920(1)	-.0430(3)	1.0389(4)
C(10)	.2044(1)	.0691(3)	1.1337(4)
C(11)	.1997(1)	.1776(3)	1.0415(5)
C(12)	.1853(1)	.1805(3)	.8771(4)
C(13)	.1869(1)	.2860(3)	.7571(4)
C(14)	.2060(1)	.3954(3)	.8425(5)
C(15)	.2057(1)	.5011(3)	.7217(7)
C(16)	.1586(1)	.5213(3)	.6694(5)
C(17)	.1430(1)	.6315(3)	.5758(6)
C(18)	.0985(1)	.5894(3)	.5208(5)
C(19)	.0571(1)	.6293(3)	.4638(5)
C(20)	.0366(1)	.7371(3)	.4384(5)
C(21)	-.0053(1)	.7407(4)	.3850(6)
C(22)	-.0294(1)	.6396(4)	.3602(6)
C(23)	-.0101(1)	.5312(4)	.3812(6)
C(24)	.0322(1)	.5285(3)	.4321(4)
C(25)	.1634(1)	.4031(4)	.3900(6)
C(26)	.1082(1)	.3193(3)	.8319(5)
C(27)	.1759(1)	-.1404(3)	1.1544(5)
C(28)	.1351(1)	-.1037(5)	1.2523(7)
C(29)	.1690(1)	-.2480(4)	1.0480(8)
O(30)	.2094(1)	-.1690(2)	1.2752(3)
O(31)	.2200(1)	.0645(2)	1.2811(3)
O(32)	.2149(1)	.2525(2)	.6182(3)
H(1)	.047(1)	.365(3)	.495(5)
H(5A)	.150(1)	.191(4)	.477(7)
H(5B)	.098(1)	.205(2)	.526(4)
H(6A)	.123(1)	.017(3)	.611(6)
H(6B)	.100(1)	.087(4)	.794(6)
H(7)	.192(1)	.027(2)	.714(4)
H(9)	.217(1)	-.071(3)	.988(4)
H(11)	.211(1)	.245(3)	1.101(5)

Table 5 (Continued)

H(14A)	.234(1)	.377(3)	.875(5)
H(14B)	.189(1)	.416(2)	.947(4)
H(15A)	.219(1)	.575(3)	.780(4)
H(15B)	.221(1)	.489(4)	.629(8)
H(16)	.144(1)	.528(3)	.786(5)
H(17A)	.143(1)	.698(4)	.668(7)
H(17B)	.160(1)	.662(3)	.474(6)
H(20)	.051(1)	.809(4)	.441(6)
H(21)	-.020(1)	.814(4)	.362(6)
H(22)	-.060(1)	.643(2)	.326(4)
H(23)	-.027(1)	.464(4)	.355(6)
H(25A)	.167(1)	.486(3)	.332(5)
H(25B)	.150(1)	.357(4)	.318(7)
H(25C)	.192(1)	.363(4)	.397(6)
H(26A)	.115(1)	.376(3)	.909(6)
H(26B)	.078(1)	.308(3)	.779(6)
H(26C)	.110(1)	.246(4)	.919(6)
H(28A)	.125(2)	-.165(5)	1.338(9)
H(28B)	.115(1)	-.080(3)	1.164(5)
H(28C)	.138(1)	-.021(5)	1.334(8)
H(29A)	.146(1)	-.235(4)	.955(6)
H(29B)	.196(1)	-.269(3)	.976(6)
H(29C)	.158(2)	-.309(6)	1.121(9)
H(30)	.214(1)	-.111(3)	1.330(5)
H(32)	.239(1)	.226(3)	.680(5)
C(1')[a]	-.0108(1)	.1510(4)	.5835(6)
C(2')	-.0552(2)	.1769(9)	.5459(9)
C(3')	.0016(3)	.0315(6)	.6288(9)
O(4')	.0166(1)	.2234(3)	.5840(8)
H(2'A)	-.065(2)	.131(5)	.443(9)
H(2'B)	-.068(2)	.155(5)	.680(9)
H(2'C)	-.058(2)	.270(5)	.473(9)
H(3'A)	.003(3)	.009(8)	.748(9)
H(3'B)	.027(3)	.013(9)	.552(9)
H(3'C)	-.028(4)	.009(9)	.506(9)

[a]Acetone of crystallization.

Table 6. Bond distances in angstroms of paxilline (15). The estimated standard deviation of the least significant figure is given in parentheses. The numbering scheme refers to Figure 2.

N(1)	- C(2)	1.364(5)	C(11)	- C(12)	1.345(5)
N(1)	- C(24)	1.397(5)	C(12)	- C(13)	1.528(5)
C(2)	- C(3)	1.499(5)	C(13)	- C(14)	1.540(5)
C(2)	- C(18)	1.369(5)	C(13)	- O(32)	1.430(4)
C(3)	- C(4)	1.559(5)	C(14)	- C(15)	1.533(6)
C(3)	- C(16)	1.541(5)	C(15)	- C(16)	1.534(5)
C(3)	- C(25)	1.555(6)	C(16)	- C(17)	1.537(6)
C(4)	- C(5)	1.551(5)	C(17)	- C(18)	1.523(6)
C(4)	- C(13)	1.569(5)	C(18)	- C(19)	1.432(6)
C(4)	- C(26)	1.532(5)	C(19)	- C(20)	1.408(6)
C(5)	- C(6)	1.505(6)	C(19)	- C(24)	1.416(6)
C(6)	- C(7)	1.536(5)	C(20)	- C(21)	1.368(7)
C(7)	- O(8)	1.417(4)	C(21)	- C(22)	1.396(7)
C(7)	- C(12)	1.510(5)	C(22)	- C(23)	1.393(6)
O(8)	- C(9)	1.415(4)	C(23)	- C(24)	1.372(6)
C(9)	- C(10)	1.534(5)	C(27)	- C(28)	1.530(6)
C(9)	- C(27)	1.518(5)	C(27)	- C(29)	1.501(7)
C(10)	- C(11)	1.445(6)	C(27)	- O(30)	1.433(4)
C(10)	- O(31)	1.236(4)			

Table 7. Bond angles in degrees of paxilline (15). Estimated standard deviation of the least significant figure is given in parentheses. The numbering scheme refers to Figure 2.

C(2)	- N(1)	- C(24)	107.9(3)
N(1)	- C(2)	- C(3)	136.4(3)
N(1)	- C(2)	- C(18)	110.6(3)
C(3)	- C(2)	- C(18)	112.2(3)
C(2)	- C(3)	- C(4)	117.9(3)
C(2)	- C(3)	- C(16)	97.7(3)
C(2)	- C(3)	- C(25)	105.6(3)
C(4)	- C(3)	- C(16)	109.7(3)
C(4)	- C(3)	- C(25)	113.8(3)
C(16)	- C(3)	- C(25)	111.0(3)
C(3)	- C(4)	- C(5)	112.7(3)
C(3)	- C(4)	- C(13)	110.3(3)
C(3)	- C(4)	- C(26)	110.2(3)
C(5)	- C(4)	- C(13)	105.9(3)
C(5)	- C(4)	- C(26)	107.9(3)
C(13)	- C(4)	- C(26)	109.7(3)
C(4)	- C(5)	- C(6)	113.3(3)
C(5)	- C(6)	- C(7)	112.3(3)
C(6)	- C(7)	- O(8)	104.8(3)
C(6)	- C(7)	- C(12)	112.4(3)
O(8)	- C(7)	- C(12)	112.2(3)
C(7)	- O(8)	- C(9)	116.0(3)
O(8)	- C(9)	- C(10)	108.3(3)
O(8)	- C(9)	- C(27)	108.0(3)
C(10)	- C(9)	- C(27)	115.3(3)
C(9)	- C(10)	- C(11)	118.0(3)
C(9)	- C(10)	- O(31)	120.0(4)
C(11)	- C(10)	- O(31)	121.9(4)
C(10)	- C(11)	- C(12)	121.2(4)
C(7)	- C(12)	- C(11)	119.4(4)
C(7)	- C(12)	- C(13)	115.1(3)
C(11)	- C(12)	- C(13)	125.3(3)
C(4)	- C(13)	- C(12)	108.3(3)
C(4)	- C(13)	- C(14)	112.6(3)
C(4)	- C(13)	- O(32)	108.8(3)
C(12)	- C(13)	- C(14)	113.9(3)
C(12)	- C(13)	- O(32)	105.0(3)
C(14)	- C(13)	- O(32)	107.9(3)
C(13)	- C(14)	- C(15)	112.9(3)
C(14)	- C(15)	- C(16)	106.6(3)
C(3)	- C(16)	- C(15)	112.1(3)
C(3)	- C(16)	- C(17)	106.2(3)

Table 7 (Continued)

C(15) - C(16) - C(17)	123.2(3)
C(16) - C(17) - C(18)	98.8(3)
C(2) - C(18) - C(17)	110.1(3)
C(2) - C(18) - C(19)	107.2(3)
C(17) - C(18) - C(19)	142.7(3)
C(18) - C(19) - C(20)	136.8(4)
C(18) - C(19) - C(24)	106.2(3)
C(20) - C(19) - C(24)	117.0(3)
C(19) - C(20) - C(21)	119.9(4)
C(20) - C(21) - C(22)	121.7(4)
C(21) - C(22) - C(23)	120.1(4)
C(22) - C(23) - C(24)	117.7(4)
N(1) - C(24) - C(19)	107.9(3)
N(1) - C(24) - C(23)	128.5(4)
C(19) - C(24) - C(23)	123.5(4)
C(9) - C(27) - C(28)	110.9(4)
C(9) - C(27) - C(29)	109.7(3)
C(9) - C(27) - O(30)	108.1(3)
C(28) - C(27) - C(29)	112.3(4)
C(28) - C(27) - O(30)	109.9(3)
C(29) - C(27) - O(30)	105.6(3)

Table 8. The observed and calculated structure factors for paxilline (15).

H = 0			
K	L	FO	FC
0	2	54	53
0	4	22	22
0	6	13	13
0	8	5	5
1	1	33	34
1	2	73	76
1	3	17	18
1	4	20	22
1	5	10	10
1	6	16	16
1	7	3	4
1	8	10	10
2	0	19	19
2	1	46	50
2	2	21	18
2	4	19	19
2	5	11	11
2	6	6	6
2	7	4	5
2	8	2	3
3	1	11	10
3	2	46	49
3	3	11	11
3	4	9	8
3	5	5	6
3	6	8	8
3	7	6	7
3	8	3	3
4	0	37	36
4	1	4	3
4	2	23	23
4	3	34	34
4	4	10	10
4	5	3	4
4	6	10	10
4	7	15	15
5	1	58	59
5	2	17	15
5	3	14	14
5	4	26	28
5	5	6	5
5	6	7	7
6	0	13	14
6	1	20	19
6	2	10	10
6	3	4	5
6	4	4	5
6	5	5	4
6	7	4	5
7	1	7	6
7	2	8	8
7	3	20	20
7	4	10	10
7	5	3	3
7	6	3	0
8	1	6	6
8	2	13	13
8	3	10	10
8	4	12	12
8	5	4	5
8	6	3	4
9	3	3	2
9	4	6	7
10	1	4	5
10	2	10	9
10	3	3	3
10	4	3	2
10	5	7	6
11	2	8	8
11	4	3	2
12	0	7	7

H = 1			
K	L	FO	FC
0	1	44	46
0	2	33	36
0	3	3	0
0	4	25	25
0	8	11	12
1	0	21	22
1	2	83	88
1	3	25	24
1	4	30	29
1	5	3	3
1	6	7	7
2	0	70	74
2	1	7	7
2	2	50	48
2	3	9	9
2	4	18	18
2	5	8	7
2	6	4	3
2	7	3	4
2	8	5	5
3	0	10	11
3	1	58	59
3	2	31	30
3	3	25	23
3	4	13	13
3	5	4	4
3	6	4	3
3	7	12	13
3	8	4	2
4	0	17	18
4	1	27	26
4	2	73	72
4	3	14	14
4	4	11	11
4	5	15	14
4	6	10	11
5	0	7	8
5	1	32	31
5	2	75	71
5	3	27	27
5	4	16	16
5	5	14	13
5	6	13	14
6	0	6	5
6	1	10	11
6	2	14	15
6	3	15	16
6	4	20	20
6	5	4	4
6	6	9	8
6	7	5	6
7	0	10	10
7	1	6	5
7	2	12	12
7	3	9	8
7	4	10	9
8	0	4	5
8	1	11	12
8	2	8	7
8	3	4	3
8	4	14	14
8	5	7	7
8	6	5	5
9	0	28	27
9	1	11	10
9	2	16	16
9	3	6	6
9	4	10	9
10	0	13	14
10	1	19	18
10	2	7	8
10	3	6	6
10	4	7	6
11	1	4	4
11	2	3	3
11	3	3	3
11	4	3	3
12	0	4	3

H = 2			
K	L	FO	FC
0	0	45	46
0	1	61	61
0	3	20	20
0	4	16	16
0	5	13	13
0	7	8	8
0	8	3	4
1	0	63	66
1	1	63	65
1	2	82	84
1	3	21	21
1	4	26	28
1	5	7	7
1	6	9	9
1	7	9	9
1	8	8	8
2	0	19	18
2	1	33	35
2	2	45	45
2	3	13	14
2	5	17	17
2	7	4	5
2	8	3	4
3	0	10	9
3	1	48	51
3	2	6	5
3	3	13	14
3	4	6	5
3	5	6	5
3	6	3	1
3	7	4	5
3	8	3	3
4	0	15	15
4	1	32	32
4	2	6	6

Table 8 (Continued)

4	3	33	33		H = 3			6	2	16	16	1	6	6	7
4	4	16	16	K	L	FO	FC	6	3	17	17	1	7	10	10
4	5	12	13	0	2	7	6	6	4	7	7	1	8	4	4
4	6	12	11	0	3	36	37	6	5	14	13	2	0	30	31
4	7	8	8	0	4	32	32	6	6	12	12	2	1	64	65
5	0	25	25	0	5	5	3	6	7	4	5	2	2	29	28
5	1	40	40	0	6	3	3	7	0	9	10	2	3	11	11
5	2	47	47	0	8	5	5	7	1	10	9	2	4	16	16
5	3	36	34	1	1	89	93	7	2	3	3	2	5	4	4
5	4	8	8	1	2	113	119	7	3	10	9	2	6	4	3
5	5	11	11	1	3	6	5	7	4	8	8	3	0	3	3
5	6	10	10	1	4	33	32	7	5	6	6	3	1	8	8
5	7	12	12	1	5	14	15	7	6	6	5	3	2	26	25
6	0	5	6	1	6	7	8	8	0	7	8	3	3	22	23
6	1	27	28	1	7	8	8	8	1	8	8	3	4	3	2
6	2	6	5	2	1	16	14	8	2	7	8	3	5	17	17
6	3	6	5	2	2	20	20	8	3	10	10	3	7	4	4
6	4	11	12	2	3	14	14	8	5	4	5	4	0	61	59
6	5	8	8	2	4	15	15	8	6	4	3	4	1	65	66
7	0	11	11	2	5	18	18	9	0	23	23	4	2	19	18
7	1	19	20	2	6	4	4	9	1	12	12	4	3	41	39
7	2	13	12	2	7	7	7	9	2	23	23	4	4	17	16
7	4	11	10	2	8	3	3	9	4	6	7	4	5	10	10
7	5	3	5	3	0	32	34	9	5	6	7	4	6	26	27
7	6	4	5	3	1	34	33	10	0	26	26	4	7	8	8
8	0	14	14	3	2	25	28	10	1	11	11	5	0	11	11
8	1	15	16	3	3	24	25	10	2	9	9	5	1	23	23
8	2	3	2	3	4	19	19	10	3	6	5	5	2	60	59
8	3	3	4	3	5	11	11	10	4	5	3	5	3	31	31
8	4	5	4	3	7	8	7	11	1	4	4	5	4	14	14
8	5	3	2	3	8	3	1	11	3	4	4	5	5	16	15
9	0	42	43	4	0	18	19	12	1	3	2	5	7	4	4
9	1	19	20	4	1	63	64	12	2	3	2	6	0	4	4
9	3	7	7	4	2	78	78					6	1	14	14
9	4	8	9	4	3	9	9		H = 4			6	2	3	3
9	5	4	4	4	4	18	18	K	L	FO	FC	6	3	3	3
10	0	8	9	4	5	5	5	0	0	4	5	6	4	16	16
10	1	7	7	4	6	11	11	0	3	80	81	6	5	19	18
10	2	3	2	4	7	10	10	0	4	24	24	6	6	5	6
10	3	10	10	5	1	26	26	0	6	10	10	6	7	4	4
10	5	4	4	5	2	28	28	0	7	4	4	7	0	25	26
11	0	4	4	5	3	13	13	0	8	10	11	7	1	9	9
11	2	4	4	5	4	5	6	1	0	76	76	7	2	6	6
11	3	3	3	5	5	11	10	1	1	69	70	7	3	15	16
12	0	5	6	5	6	15	15	1	2	82	84	7	4	6	5
12	2	4	5	5	7	4	4	1	3	15	14	7	5	5	6
				6	0	5	6	1	4	40	41	7	6	3	3
				6	1	3	4	1	5	14	14	8	0	15	15

Table 8 (Continued)

8	1	11	12	3	1	33	34	11	2	8	7	5	1	8	7
8	3	3	2	3	2	37	39	11	3	7	7	5	2	33	33
8	4	10	10	3	3	17	17					5	3	20	20
8	5	3	3	3	4	8	8		H =	6		5	4	12	12
8	6	8	8	3	5	6	6	K	L	FO	FC	5	5	34	34
9	0	23	23	3	6	8	8	0	1	73	73	5	6	6	6
9	1	4	4	3	7	9	9	0	2	10	11	5	7	4	4
9	2	4	5	3	8	2	3	0	3	11	10	6	0	14	14
9	3	7	8	4	0	11	10	0	4	59	60	6	1	14	14
9	4	6	3	4	1	37	37	0	5	7	6	6	2	9	8
9	5	6	3	4	2	47	46	0	6	16	17	6	3	14	14
10	0	23	23	4	3	15	15	0	7	9	9	6	4	5	5
10	1	6	6	4	4	15	14	1	0	11	11	6	5	11	10
10	2	9	9	4	5	8	9	1	1	70	69	6	7	4	5
10	3	5	5	4	6	11	10	1	2	20	20	7	0	24	24
10	4	5	4	4	7	8	8	1	3	28	27	7	1	14	14
11	1	5	5	5	0	3	2	1	4	21	21	7	2	6	6
11	2	7	7	5	1	34	33	1	5	13	13	7	3	9	9
11	3	6	6	5	2	47	44	1	6	7	7	7	4	9	8
12	2	4	5	5	3	14	15	1	7	4	4	8	0	14	13
				5	4	19	19	1	8	12	12	8	1	17	17
	H =	5		5	5	17	17	2	0	6	5	8	2	10	10
K	L	FO	FC	5	6	29	29	2	1	56	56	8	3	3	3
0	1	39	39	6	0	48	49	2	2	27	25	8	4	7	7
0	2	38	36	6	1	7	6	2	3	10	11	8	5	5	5
0	3	32	30	6	2	3	3	2	4	25	24	9	2	12	12
0	4	24	24	6	3	14	15	2	5	9	8	9	4	11	11
0	5	11	12	6	4	17	17	2	6	4	4	9	5	6	6
0	6	32	31	6	5	4	4	2	7	9	8	10	1	8	8
0	7	16	16	6	6	12	13	2	8	4	4	10	2	6	6
0	8	7	7	6	7	3	3	3	0	31	28	10	3	6	6
1	0	49	48	7	3	9	9	3	1	6	7	10	4	12	12
1	1	57	57	7	4	9	9	3	2	14	14	11	0	5	4
1	2	66	65	7	5	6	5	3	3	4	5	11	2	10	10
1	3	34	35	7	6	3	4	3	4	8	7				
1	4	23	24	8	0	19	20	3	5	17	17		H =	7	
1	5	15	15	8	1	23	23	3	6	4	3	K	L	FO	FC
1	6	4	5	8	2	5	7	3	7	4	4	0	1	53	53
1	7	3	4	8	3	7	5	3	8	4	2	0	2	20	19
2	0	29	28	9	1	22	22	4	0	53	52	0	3	29	29
2	1	29	29	9	2	15	15	4	1	51	51	0	4	36	35
2	2	12	10	9	3	8	8	4	2	19	19	0	5	31	30
2	3	21	21	9	5	9	8	4	3	39	40	0	6	14	14
2	4	20	20	10	1	7	7	4	4	19	19	0	7	14	15
2	6	4	4	10	2	4	3	4	5	14	13	0	8	8	8
2	7	5	5	10	3	9	9	4	6	16	16	1	0	28	27
2	8	3	4	10	4	8	7	4	7	3	3	1	1	6	6
3	0	21	20	11	1	6	7	5	0	29	29	1	2	25	24

Table 8 (Continued)

1	3	40	39	8	1	29	29	3	4	7	7		H =	9	
1	4	10	10	8	3	7	5	3	5	9	8	K	L	FO	FC
1	5	15	15	8	4	5	5	4	0	12	11	0	1	8	9
1	6	8	8	8	5	4	6	4	1	32	30	0	2	44	42
1	7	8	8	9	0	15	15	4	2	22	21	0	3	69	65
2	0	13	15	9	1	9	9	4	3	19	17	0	4	35	38
2	1	52	51	9	2	10	10	4	4	21	21	0	6	5	6
2	2	18	19	9	3	7	6	4	5	32	32	0	7	11	12
2	3	32	32	9	5	6	5	4	6	10	10	0	8	6	6
2	4	15	15	10	0	13	12	5	0	42	40	1	0	3	5
2	5	6	5	10	1	22	22	5	1	23	23	1	1	70	71
2	6	5	6	10	2	8	8	5	2	36	34	1	2	66	67
3	0	12	12	10	3	4	6	5	3	23	24	1	3	44	43
3	1	22	24	10	4	7	6	5	4	15	14	1	4	14	13
3	2	36	35	11	2	6	5	5	5	18	18	1	5	10	10
3	3	22	21					5	6	7	8	1	6	9	9
3	4	19	19		H =	8		6	0	7	6	1	7	13	14
3	5	17	17	K	L	FO	FC	6	1	11	11	1	8	7	7
3	6	13	12	0	0	34	37	6	2	9	10	2	0	15	16
3	7	5	5	0	1	11	12	6	3	8	7	2	1	29	29
4	0	11	11	0	2	29	29	6	4	5	5	2	2	31	29
4	1	29	29	0	3	3	4	6	5	11	11	2	3	24	24
4	2	22	21	0	4	32	33	6	7	6	6	2	4	9	9
4	3	11	11	0	5	8	9	7	0	4	5	2	5	10	10
4	5	11	12	0	6	5	6	7	1	15	16	2	6	7	7
4	6	20	20	0	7	4	2	7	2	11	12	2	7	5	5
5	0	20	21	0	8	5	4	7	3	4	4	3	0	28	28
5	1	14	13	1	0	51	52	7	4	17	9	3	1	22	21
5	2	20	19	1	1	68	66	7	5	8	8	3	2	6	5
5	3	4	5	1	2	27	27	8	0	4	4	3	3	24	24
5	4	14	13	1	3	15	15	8	1	16	17	3	4	9	9
5	5	16	16	1	4	34	33	8	2	6	7	3	7	6	5
5	6	14	14	1	5	20	20	8	3	7	7	4	0	54	54
6	0	16	15	1	6	10	10	8	4	3	2	4	1	32	29
6	1	19	19	1	7	8	8	8	6	4	4	4	2	27	25
6	2	15	15	1	8	9	10	9	0	31	31	4	3	24	23
6	3	14	15	2	1	13	12	9	1	12	12	4	4	10	10
6	4	16	16	2	2	16	15	9	2	15	14	4	5	9	9
6	6	6	6	2	3	15	15	9	3	14	14	4	6	8	8
6	7	4	5	2	4	11	10	9	4	4	4	4	7	5	4
7	0	6	7	2	5	16	16	10	0	7	7	5	0	8	7
7	1	12	12	2	6	9	9	10	1	9	8	5	1	21	21
7	2	13	13	2	7	7	7	10	2	13	13	5	2	31	30
7	3	9	9	2	8	6	5	10	3	10	11	5	3	11	12
7	4	10	9	3	0	15	15	10	4	4	3	5	4	4	3
7	5	5	5	3	1	11	10	11	0	3	4	5	5	8	8
7	6	6	6	3	2	37	35	11	1	7	7	5	6	11	11
8	0	12	12		3	28	29					6	0	23	22

Table 8 (Continued)

6	1	23	22	1	3	19	19	8	3	5	5	4	5	13	13
6	2	8	6	1	4	25	25	8	5	4	4	4	6	6	5
6	3	21	21	1	5	12	11	9	0	4	5	4	7	6	6
6	4	5	4	1	6	15	15	9	1	29	29	5	0	8	8
6	5	9	9	1	7	8	8	9	3	4	4	5	1	13	12
6	6	10	10	2	0	16	16	9	4	4	4	5	2	5	5
6	7	3	3	2	1	40	40	9	5	3	3	5	3	34	33
7	0	4	4	2	2	36	37	10	0	3	3	5	4	13	13
7	1	9	9	2	3	5	4	10	3	4	5	5	5	15	15
7	2	3	4	2	4	20	20	10	4	7	7	5	6	9	9
7	3	4	4	2	5	11	12	11	0	3	1	5	7	3	3
7	4	4	4	2	6	11	11	11	1	6	6	6	0	4	2
7	5	10	10	2	7	5	6	11	3	4	5	6	1	13	12
7	6	5	4	3	0	15	16					6	2	12	13
8	0	12	12	3	1	18	17		H = 11			6	3	14	14
8	1	16	16	3	2	24	23	K	L	FO	FC	6	4	21	20
8	2	8	9	3	3	7	6	0	1	22	22	6	5	8	8
8	3	4	6	3	4	7	7	0	2	46	45	6	6	9	10
8	4	9	9	3	5	9	10	0	3	42	41	7	0	16	16
8	6	3	2	3	6	8	7	0	4	37	36	7	1	5	4
9	0	22	22	3	7	6	6	0	5	22	22	7	2	6	6
9	1	12	12	4	0	32	32	0	7	4	5	7	4	6	7
9	2	9	8	4	1	47	46	1	0	47	48	7	5	8	7
9	3	11	12	4	2	27	26	1	1	39	41	7	6	4	4
9	4	5	5	4	3	13	13	1	2	48	47	8	0	6	6
9	5	7	6	4	4	14	14	1	3	13	13	8	1	21	21
10	1	5	5	4	5	19	19	1	4	7	6	8	2	12	12
10	2	13	13	5	0	20	19	1	5	15	14	8	3	7	7
10	3	8	8	5	1	13	13	1	6	8	8	8	4	8	7
10	4	5	5	5	2	14	14	1	7	6	6	8	5	5	4
11	2	6	6	5	3	12	12	2	1	18	18	9	0	12	12
11	3	6	7	5	4	5	4	2	2	17	18	9	1	4	5
12	0	3	4	5	5	21	20	2	3	9	9	9	2	11	11
				5	6	8	8	2	4	3	3	9	4	6	5
	H = 10			6	0	5	4	2	5	9	8	10	0	14	15
K	L	FO	FC	6	1	5	5	2	6	8	8	10	1	6	6
0	0	57	59	6	2	9	8	2	7	4	4	10	2	9	9
0	1	72	72	6	3	5	6	3	0	48	48	10	3	3	3
0	2	35	37	6	4	15	15	3	1	10	10	10	4	6	5
0	3	19	19	6	5	8	8	3	2	14	15	11	0	3	3
0	4	5	5	6	6	6	6	3	4	12	13	11	1	9	9
0	5	4	3	7	0	7	7	3	5	10	10				
0	6	7	7	7	3	9	9	3	6	13	14		H = 12		
0	7	17	17	7	4	9	10	3	7	5	5	K	L	FO	FC
0	8	12	12	7	5	7	6	4	0	4	5	0	0	73	74
1	0	62	63	8	0	10	10	4	1	20	21	0	1	74	73
1	1	71	71	8	1	8	9	4	2	23	23	0	2	22	21
1	2	56	53	8	2	4	4	4	3	8	7	0	3	50	48

Table 8 (Continued)

0	4	21	19	7	3	4	3	3	3	6	6	0	4	6	6
0	6	3	3	7	4	8	9	3	4	21	21	0	5	4	4
1	0	44	45	7	6	5	4	3	5	10	10	0	6	8	8
1	1	22	23	8	0	13	13	3	6	14	14	0	7	13	13
1	2	24	24	8	1	8	8	4	0	8	9	1	0	7	7
1	3	31	31	8	2	11	12	4	1	8	6	1	1	27	28
1	4	10	10	8	3	4	4	4	2	9	8	1	2	15	15
1	6	7	7	8	4	8	8	4	3	25	26	1	3	12	12
1	7	8	9	8	5	5	4	4	4	9	10	1	4	4	4
2	0	29	29	9	0	10	11	4	5	19	19	1	5	4	5
2	1	24	23	9	1	12	12	4	7	5	5	1	6	8	8
2	2	11	11	9	2	7	8	5	1	12	13	1	7	4	4
2	3	26	26	9	3	8	7	5	2	14	14	2	0	8	9
2	4	13	13	9	4	3	3	5	3	15	15	2	1	2	2
2	5	14	14	9	5	3	3	5	4	11	10	2	2	17	17
2	6	5	6	10	0	7	6	5	5	14	14	2	3	9	9
2	7	4	4	10	1	6	6	6	1	18	18	2	4	11	10
3	0	24	24	10	2	5	6	6	2	15	16	2	5	8	9
3	1	8	10	10	3	5	5	6	3	3	2	2	6	5	6
3	2	16	15	11	0	9	9	6	4	11	11	2	7	5	5
3	3	24	23	11	1	3	4	6	5	5	4	3	0	6	7
3	4	9	9	11	2	5	4	6	6	7	6	3	1	6	6
3	5	26	26					7	0	8	7	3	2	18	18
3	6	4	3	H = 13				7	1	6	6	3	3	23	22
3	7	8	8	K	L	FO	FC	7	2	6	6	3	4	18	17
4	0	29	30	0	1	4	4	7	3	8	7	3	5	8	8
4	1	40	41	0	2	16	16	8	0	7	7	3	6	8	8
4	2	10	11	0	3	45	42	8	1	11	11	3	7	6	7
4	3	7	6	0	5	7	7	8	2	8	8	4	1	22	22
4	5	5	5	0	6	11	11	8	3	14	14	4	2	11	11
4	6	11	11	0	7	11	10	8	4	4	5	4	3	7	7
4	7	6	6	1	0	10	9	9	0	7	7	4	4	23	23
5	0	28	28	1	1	18	18	9	1	7	7	4	5	12	12
5	1	10	10	1	2	15	15	9	2	3	2	4	6	6	6
5	2	19	19	1	3	16	15	9	4	3	2	5	0	3	0
5	3	26	26	1	4	16	17	10	0	6	5	5	1	15	14
5	4	26	26	1	5	3	4	10	1	11	11	5	2	6	7
5	5	14	14	1	6	8	8	10	2	5	5	5	3	4	3
5	6	3	2	1	7	4	5	10	3	8	8	5	4	11	12
5	7	5	4	2	1	21	20	11	0	6	7	5	5	16	16
6	0	5	6	2	2	15	15	11	1	5	7	5	6	7	6
6	2	5	6	2	3	26	25	11	2	4	3	6	0	10	10
6	3	14	15	2	4	9	10					6	1	4	6
6	4	19	19	2	5	7	7	H = 14				6	2	5	5
6	6	6	6	2	7	3	3	K	L	FO	FC	6	3	8	8
7	0	13	13	3	0	3	2	0	0	61	62	6	4	19	20
7	1	7	7	3	1	6	7	0	2	27	28	6	5	8	9
7	2	7	6	3	2	24	23	0	3	9	9	6	6	5	4

Table 8 (Continued)

7	0	6	6	4	0	21	21	1	0	33	33	8	2	8	7
7	1	4	3	4	1	4	4	1	1	48	46	8	3	10	10
7	2	5	6	4	2	28	28	1	2	43	44	8	4	6	7
7	3	9	10	4	3	17	17	1	3	14	13	8	5	6	7
7	4	9	9	4	4	17	18	1	4	11	11	9	1	4	4
7	5	4	3	4	5	18	19	1	5	11	10	9	2	5	5
7	6	5	5	4	6	6	6	1	6	17	17	9	3	4	5
8	1	10	10	5	0	7	7	1	7	4	4	10	2	8	9
8	2	4	4	5	1	6	5	2	0	33	31	10	3	4	3
8	3	7	7	5	2	6	6	2	1	31	31	11	0	3	2
8	4	7	7	5	3	24	25	2	2	19	19				
8	5	3	3	5	4	10	11	2	3	14	14		H = 17		
9	0	11	11	5	5	14	14	2	4	7	7	K	L	FO	FC
9	1	8	8	5	6	10	10	2	5	4	3	0	1	4	6
9	2	8	8	6	1	4	4	2	6	5	4	0	2	40	40
9	4	5	5	6	2	5	5	2	7	4	4	0	3	15	14
10	1	6	6	6	3	7	7	3	0	20	20	0	4	6	5
10	2	10	10	6	4	16	17	3	1	23	23	0	5	4	2
10	3	5	6	6	5	5	3	3	2	18	18	0	6	11	11
11	1	3	4	7	0	11	11	3	3	9	9	0	7	5	6
11	2	7	7	7	1	11	11	3	4	11	12	1	0	27	28
				7	2	3	3	3	5	8	8	1	1	22	22
	H = 15			7	3	11	10	3	6	9	9	1	2	28	26
K	L	FO	FC	7	4	14	14	3	7	3	3	1	3	13	13
0	1	9	10	7	5	8	8	4	0	24	24	1	4	3	4
0	2	41	40	8	0	12	13	4	1	12	13	1	5	8	8
0	3	12	12	8	1	8	8	4	2	14	14	1	6	11	11
0	4	13	13	8	2	5	5	4	3	12	12	2	0	4	4
0	5	5	4	8	3	3	3	4	4	21	21	2	1	13	12
0	6	8	9	8	4	4	5	4	5	15	15	2	2	22	23
0	7	7	7	8	5	3	2	4	6	5	5	2	3	5	5
1	1	32	30	9	1	9	10	5	0	20	21	2	4	10	10
1	2	38	37	9	2	10	10	5	1	3	2	2	5	11	11
1	3	19	19	9	3	7	7	5	2	7	8	2	6	4	5
1	4	7	8	9	4	3	4	5	3	17	17	3	1	17	18
1	6	6	6	10	0	3	5	5	4	14	13	3	2	6	7
2	0	4	4	10	1	5	5	5	5	4	4	3	3	10	10
2	1	13	11	10	3	3	2	5	6	8	8	3	4	8	8
2	2	35	34	11	0	4	5	6	2	5	5	3	6	3	4
2	3	25	26					6	3	23	23	4	1	9	9
2	4	22	22		H = 16			6	4	9	9	4	3	10	9
2	5	5	4	K	L	FO	FC	6	5	11	11	4	4	12	12
2	7	4	4	0	0	19	18	7	0	9	9	4	5	6	6
3	1	28	27	0	2	6	5	7	1	4	3	5	0	9	9
3	2	9	9	0	3	29	29	7	2	3	2	5	1	15	15
3	3	10	9	0	4	3	4	7	3	4	3	5	2	10	9
3	4	26	26	0	5	8	7	7	5	6	6	5	3	4	5
3	5	4	4	0	7	10	10	8	0	13	13	5	4	21	22

Table 8 (Continued)

5	5	9	9	3	0	11	11	1	2	12	12				
5	6	6	7	3	1	3	3	1	3	10	10		H = 20		
6	1	3	2	3	2	21	21	1	4	5	5	K	L	FO	FC
6	2	6	6	3	3	14	14	1	6	4	4	0	0	30	30
6	3	20	21	3	4	5	5	2	0	6	6	0	1	17	17
6	4	8	7	3	5	4	4	2	1	25	24	0	2	27	27
6	5	4	5	4	0	9	9	2	2	18	18	0	4	7	7
7	0	6	6	4	1	3	3	2	3	9	9	0	5	7	7
7	1	3	4	4	2	3	4	2	4	13	13	0	6	5	6
7	2	14	14	4	3	15	15	2	5	12	13	1	1	20	21
7	3	5	5	4	4	14	15	2	6	4	4	1	2	8	8
7	4	7	7	4	5	6	6	3	0	9	9	1	3	13	12
8	1	14	14	5	0	13	13	3	1	16	16	1	4	11	11
8	2	7	8	5	2	7	6	3	2	14	14	1	5	14	14
8	3	11	11	5	3	5	5	3	3	24	25	1	6	4	4
8	4	6	6	5	4	23	22	3	4	7	7	2	0	17	16
9	0	3	2	5	6	4	3	3	5	7	7	2	1	14	14
9	1	8	9	6	0	12	13	3	6	4	4	2	2	20	20
9	2	5	5	6	2	12	13	4	0	15	16	2	3	5	4
9	3	7	6	6	3	16	15	4	1	15	15	2	4	4	3
10	0	3	3	6	4	5	4	4	2	20	20	2	5	12	13
10	1	4	4	6	5	6	7	4	3	13	13	2	6	3	3
10	2	9	8	7	0	9	9	4	4	18	18	3	0	12	11
				7	1	3	3	4	5	6	7	3	1	4	4
	H = 18			7	2	7	8	5	1	7	7	3	2	13	13
K	L	FO	FC	7	3	11	10	5	2	4	3	3	3	12	12
0	0	15	15	7	4	10	10	5	3	10	10	3	4	11	10
0	1	30	29	7	5	4	5	5	4	5	5	3	5	4	4
0	2	4	0	8	0	8	9	5	5	8	8	3	6	4	4
0	3	5	5	8	1	7	6	5	6	9	9	4	0	7	7
0	4	6	6	8	2	8	9	6	1	6	6	4	1	5	4
0	5	6	5	8	4	4	5	6	2	15	15	4	2	13	14
0	6	6	5	9	0	4	3	6	3	7	6	4	3	9	9
1	0	16	16	9	1	6	6	6	4	3	3	4	4	22	22
1	1	28	29	9	3	5	4	7	0	6	5	4	5	6	6
1	2	6	6	10	0	9	9	7	1	6	7	5	0	30	31
1	3	9	9	10	1	6	6	7	4	5	5	5	1	12	12
1	4	9	10	10	2	4	4	8	0	4	4	5	2	8	8
1	5	9	8					8	1	14	14	5	3	12	12
1	6	10	10		H = 19			8	2	9	9	5	4	3	2
1	7	7	7	K	L	FO	FC	8	3	3	3	5	5	5	5
2	0	8	8	0	2	5	5	8	4	5	5	6	0	7	7
2	1	6	7	0	3	6	7	9	0	7	8	6	2	20	20
2	2	24	25	0	4	7	8	9	1	6	5	6	3	6	6
2	3	9	10	0	5	6	5	9	2	11	11	6	4	12	12
2	4	4	4	0	6	13	13	9	3	3	3	6	5	5	3
2	5	8	8	1	0	27	26	10	0	4	4	7	0	15	15
2	6	3	2	1	1	14	14	10	1	4	4	7	1	12	12

Table 8 (Continued)

7	2	8	7
7	3	8	7
7	4	7	7
8	1	5	5
8	3	7	7
9	0	4	4
9	1	8	7
9	2	4	3
9	3	3	3

H = 21

K	L	FO	FC
0	1	11	11
0	2	8	8
0	5	4	4
0	6	3	3
1	0	22	22
1	1	19	19
1	2	13	13
1	3	21	21
1	4	7	8
1	5	9	8
1	6	8	9
2	1	14	14
2	2	9	9
2	3	13	13
2	4	12	12
3	0	20	21
3	1	11	12
3	2	15	15
3	3	13	13
3	4	18	18
3	5	4	3
3	6	3	3
4	0	14	15
4	1	10	10
4	2	22	22
4	3	15	15
4	4	6	6
4	5	4	4
5	0	22	22
5	1	9	9
5	2	6	6
5	3	7	7
5	4	5	6
6	0	18	19
6	1	11	12
6	2	5	4
6	3	8	9
6	4	6	6
6	5	4	4
7	0	8	8
7	1	6	5
7	2	3	3
7	3	11	11
7	4	8	8
8	0	3	3
8	1	6	5
8	2	9	9
9	2	3	4

H = 22

K	L	FO	FC
0	0	7	7
0	1	8	9
0	2	3	3
0	3	12	11
0	4	9	10
0	5	10	10
0	6	3	3
1	0	6	6
1	1	10	10
1	2	10	9
1	3	17	17
1	4	6	7
1	5	11	11
2	0	15	15
2	1	13	12
2	2	7	7
2	3	10	10
2	4	9	9
2	5	7	7
2	6	3	2
3	0	17	18
3	1	10	10
3	2	20	20
3	3	9	8
3	4	6	7
3	5	3	2
3	6	3	2
4	0	8	8
4	1	17	16
4	2	4	4
4	3	9	9
4	5	5	4
5	0	4	4
5	1	7	7
5	2	18	19
5	3	5	6
5	4	3	2
6	0	14	14
6	1	13	13
6	2	6	6
6	3	9	9
6	4	9	9
7	0	12	12
7	1	11	10
7	2	10	9
7	3	4	3
7	4	3	3
8	1	4	4
8	3	6	5
9	1	3	3

H = 23

K	L	FO	FC
0	1	9	9
0	2	10	10
0	3	9	10
0	4	4	4
1	0	14	15
1	1	12	13
1	2	20	20
1	3	4	4
1	4	6	5
1	5	5	4
2	1	3	3
2	2	10	10
2	4	16	16
2	5	3	3
3	0	21	21
3	1	7	6
3	2	10	10
3	3	14	14
3	4	8	8
4	0	14	14
4	2	4	4
4	3	6	6
4	4	10	10
4	5	5	4
5	2	13	13
5	3	6	6
5	4	5	5
5	5	2	3
6	0	11	11
6	1	17	17
6	2	5	4
6	3	4	4
6	4	4	3
7	0	4	4
7	1	4	3
7	2	8	7
7	3	3	4
8	1	4	5
8	2	5	5
8	3	4	4
9	0	6	5
9	1	3	3

H = 24

K	L	FO	FC
0	0	5	5
0	1	21	21
0	2	16	16
0	3	7	7
0	4	9	10
0	5	5	5
1	0	4	1
1	1	6	7
1	2	6	5
1	3	5	6
1	4	5	4
1	5	9	9
2	0	5	5
2	1	12	11
2	2	27	26
2	3	17	16
2	4	7	7
3	0	7	8
3	1	5	5
3	2	9	9
3	3	9	9
3	4	7	6
3	5	4	4
4	0	9	9
4	1	7	8
4	2	11	11
4	4	4	4
5	0	36	37
5	1	11	11
5	2	10	9
5	3	5	5

Table 8 (Continued)

5	4	5	4
6	0	8	7
6	1	6	6
6	2	4	3
6	3	7	7
6	4	11	11
7	0	9	9
7	2	4	5
7	3	6	6
8	0	9	9
8	1	4	3
8	2	4	3

H = 25

K	L	FO	FC
0	2	12	12
0	3	17	17
1	0	5	6
1	1	6	7
1	2	12	12
1	3	9	8
1	4	4	5
2	1	21	21
2	2	11	11
2	3	6	5
3	0	9	9
3	1	11	12
3	2	9	9
3	3	19	19
3	4	11	10
4	0	3	2
4	1	9	9
4	2	15	15
4	3	4	3
4	4	7	7
5	0	6	7
5	1	12	12
5	3	7	7
6	0	11	12
6	1	9	9
6	2	3	3
6	3	6	6
7	0	8	8
7	1	7	8
7	2	5	4
7	3	6	5
8	1	7	7

H = 26

K	L	FO	FC
0	0	27	27
0	1	15	15
0	3	6	6
0	4	6	6
0	5	4	5
1	0	5	5
1	1	15	14
1	2	8	8
1	3	3	3
1	5	5	5
2	1	11	11
2	2	12	12
2	3	5	5
2	4	6	5
2	5	6	6
3	0	15	14
3	1	14	14
3	2	6	6
3	4	4	4
4	0	16	16
4	1	8	7
4	2	6	5
4	3	5	4
4	4	3	2
5	0	5	5
5	1	8	7
5	3	3	3
5	4	7	6
6	0	9	9
6	1	3	2
6	2	12	12
6	3	8	8
7	0	8	8
7	1	6	5
7	2	5	5

H = 27

K	L	FO	FC
0	2	6	6
0	4	7	6
1	0	12	12
1	1	15	14
1	2	18	18
1	3	3	3
2	0	4	4
2	1	13	13
2	2	8	8
2	3	8	8
2	4	6	5
3	0	12	13
3	1	8	8
3	3	8	7
4	0	7	6
4	1	9	8
4	2	7	7
4	3	7	7
4	4	3	3
5	0	8	7
5	1	4	4
5	2	7	7
5	3	6	5
6	0	6	6
6	1	8	7
6	2	4	4
7	0	6	6

H = 28

K	L	FO	FC
0	0	4	5
0	1	14	14
0	2	11	12
0	3	8	9
0	4	6	5
1	0	4	4
1	1	5	5
1	2	7	6
1	4	5	5
2	0	15	15
2	1	7	7
2	2	9	9
2	3	11	11
2	4	3	4
3	0	13	14
3	1	5	5
3	2	9	8
3	4	8	7
4	1	3	2
4	3	4	4
5	0	5	4
5	1	3	3
5	2	3	4
5	3	6	6
6	0	3	3
6	1	7	7
6	2	6	6

H = 29

K	L	FO	FC
0	1	5	6
0	4	3	3
1	1	7	7
1	2	4	4
1	4	3	2
2	0	7	7
2	1	5	5
2	2	8	8
2	4	6	5
3	0	8	8
3	1	5	5
3	3	3	3
4	0	10	10
4	2	3	4
4	3	7	7
5	0	4	4
5	1	3	3
5	1	3	3
5	2	7	7
6	0	4	4
6	1	2	2

H = 30

K	L	FO	FC
0	0	12	12
0	2	4	4
0	3	6	5
1	1	13	13
1	2	5	5
1	3	7	6
2	0	11	11
2	3	8	8
3	0	3	3
3	1	8	8
3	2	4	5
4	1	6	5
4	2	3	4
5	0	9	10

H = 31

K	L	FO	FC
0	2	5	5
0	3	5	5
1	1	8	9

Table 8 (Continued)

1	3	5	5
2	0	9	8
2	1	4	4
2	2	5	5
2	3	5	5
3	0	4	3
3	1	8	8
4	0	5	6
4	1	3	3

H = 32

K	L	FO	FC
0	2	6	6
1	1	3	2
2	1	3	2
2	2	7	6
3	1	3	3

H = 33

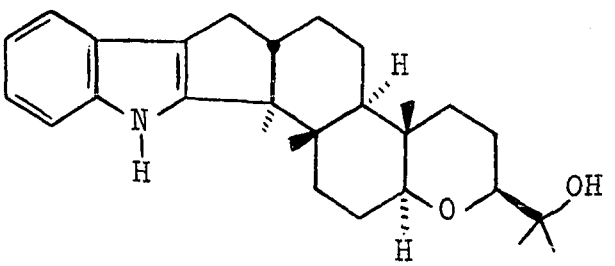
K	L	FC	FC
1	0	5	5
2	0	3	3

The second cyclohexane ring again exists in a chair conformation with C(26) and O(32) at the bridgehead positions existing in a trans diaxial arrangement. The heterocyclic ring exists in a twisted conformation with H(10) in a pseudo-axial position and C(27) being pseudo-equatorial. Inspection of Dreiding models indicates that the whole molecule with the exception of the isopropyl alcohol moiety is extremely rigid. A hydrogen bond exists between the indole nitrogen's hydrogen H(1) and oxygen atom of the acetone of crystallization with distances N(1) - H(1) .88Å, H(1) - O(4') 2.00Å, and N(1) - O(4') 2.88Å and with the N(1) - H(1) - O(4') angle being 173°. Also present in the crystal structure are two additional hydrogen bonds. One intramolecular one between H(30) and O(31) has distances O(30) - H(30) .80Å, H(30) - O(31) 2.06Å, and O(30) - O(31) 2.71Å with the angle delineated by O(30) - H(30) - O(31) being 137°. The other intermolecular bond between H(32) and O(30) has distances O(32) - H(32) .94Å, H(32) - O(30) 1.88Å, and O(30) - O(32) 2.81Å with an angle of 172° for O(32) - H(32) - O(30). There are no other abnormally short intermolecular contacts and all bond distances and angles agree well with generally accepted values (23).

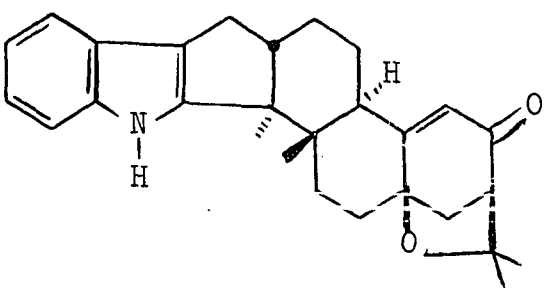
The chemical structure as determined by X-ray diffraction analysis is consistent with the physical data previously reported (42) (vide supra). More detailed 100 MHz

pmr experiments were carried out with acetone-d_6 as solvent and TMS as an internal standard at δ0.00. Assignments of the absorptions listed below are made with reference to Fig. 2. The spectrum showed absorptions at δ1.04, s, 3H, CH_3 (26); 1.22, s, 6H, CH_3 (28, 29); 1.40, s, 3H, CH_3 (25); 1.7-2.95, bm, CH, CH_2 (5, 6, 14, 15, 16, 17); 3.70, d, J = 2 Hz, 1H, CH (9); 4.05, s, 1H, OH (32); 4.08, s, 1H, OH (30); 4.94, m, 1H, CH (7); 5.85, d, J = 2 Hz, 1H, CH (11); 6.95, m, 2H, CH (21, 22); 7.30, m, 2H, CH (20, 23); 9.82, s, 1H, NH (1). Irradiation of the multiplet at δ4.94 collapsed the doublets at δ3.70 and δ5.85 to singlets. Irradiation at δ1.85 sharpened the multiplet at δ4.94 to a broad singlet. Addition of D_2O to the sample caused the disappearance of absorptions at δ4.05, 4.08 and 9.82. The δ1.40 resonance was assigned to CH_3 (25) on the basis of the expected deshielding by the neighboring hydroxyl and proximity to the aromatic ring. Addition of $Eu(fod)_3$ caused a shift of the δ4.08 peak to lower field at the same time the isopropyl moiety was affected to approximately the same extent while the protons on the NH and the other hydroxyl were relatively unaffected. In addition, the CD spectrum showed positive Cotton effects for two bands ($[\theta]_{335nm}$ + 5.0 x 10^3; $[\theta]_{300nm}$ + 1.09 x 10^4) while a third band at shorter wavelength appeared to give a negative Cotton effect but only part of this band was observed. The significance of the CD

spectrum to the absolute configuration of paxilline 15 will be discussed in the next part of the dissertation when the absolute configurations of paspaline 16 and paspalicine 17 are considered.



16



17

Background - Paspaline and Paspalicine

The fungal metabolites paspaline 16 and paspalicine 17 were isolated from Claviceps paspali Stammes and their chemical constitutions determined (41, 45, 46). The relative as well as the absolute configurations of five of the seven asymmetric centers in paspaline 16 were determined by chemical and physical methods, however, no comment was made about the stereostructure of the closely related paspalicine 17. Single crystal X-ray diffraction experiments were carried out to determine the configuration of the last two chiral centers in paspaline 16 as well as to establish the stereostructure of paspalicine 17. It was also of interest to determine how closely the configurations of these two metabolites corresponded to paxilline 15.

Experimental - Paspaline

Crystals of paspaline 16, $C_{28}H_{39}NO_2$, were grown from methanol and crystallized in the orthorhombic space group $P2_12_12$ with $a = 49.388(5)$, $b = 6.527(1)$, and $c = 7.891(1)$ Å. The crystallographic unit cell contained 4 molecules of paspaline 16 and 2 molecules of methanol (vide infra) for a calculated density of 1.14 g/cc. Data were collected using graphite monochromated CuK_α radiation ($\lambda = 1.5418$ Å) and an automated four-circle diffractometer. Of the 2088 reflections measured with $2\theta \leq 114°$, 1535 (74%) were considered observed ($I \geq 3\sigma(I)$) after correction for background

effects. Lorentz and polarization corrections were subsequently applied (18). Systematic absences of h00 ($h \neq 2n$) and 0k0 ($k \neq 2n$) strongly indicated the space group $P2_12_12$. Structure solution was carried out using a multi-solution direct methods approach (20). Subsequent least-squares refinements (21) and difference maps indicated that methanol was present in the crystal structure. Inclusion of the methanol with further least-squares refinements using anisotropic temperature factors for the non-hydrogen atoms and isotropic temperature factors for the hydrogen atoms lowered the conventional unweighted R factor to its present value of 3.8% (19, 21). Tables 9, 10, 11 and 12 contain the fractional coordinates, bond distances, bond angles and observed and calculated structure factors.

Discussion - Paspaline

The X-ray structure determination confirmed the relative stereochemical details as have been previously determined (45), i.e., the configurations around C(4), C(7), C(9), C(12), and C(13). In addition the methyl group at C(3) is trans to both the methyl at C(4) and the hydrogen at C(16). This information consequently completes the absolute configuration of paspaline 16. Paspaline 16, thus, possesses the same basic hexacyclic array as paxilline 15 previously described. The major structural differences are that paspaline 16 does not

Figure 3. A computer generated perspective drawing from the crystal structure of paspaline (16) with hydrogens and the molecule of methanol omitted for clarity.

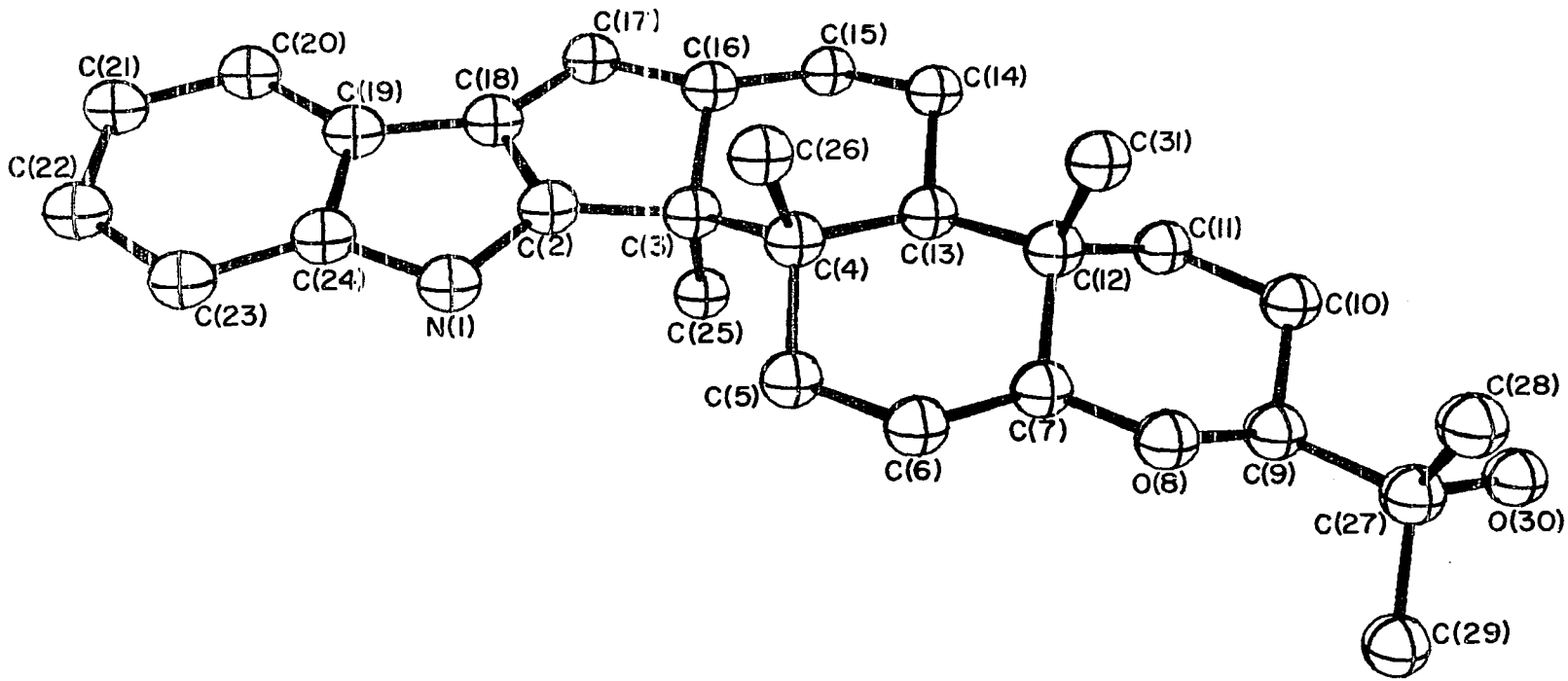

C(17)
C(20)
C(16)
C(15)
C(21)
C(19)
C(18)
C(14)
C(26)
C(31)
C(22)
C(11)
C(2)
C(3)
C(13)
C(24)
C(4)
C(12)
C(10)
C(23)
N(1)
C(25)
C(28)
C(5)
C(7)
C(6)
O(8)
C(9)
C(27)
O(30)
C(29)

Table 9. Final fractional coordinates for paspaline (16) with the estimated standard deviation of the least significant figure given in parentheses. The numbering scheme refers to Figure 3 with the primed numbers refering to the solvent molecule of methanol.

N(1)	.71462(5)	.4338(4)	-.0890(3)
C(2)	.69341(5)	.3346(5)	-.1648(4)
C(3)	.66279(5)	.3566(5)	-.1668(3)
C(4)	.64680(5)	.3578(5)	.0060(4)
C(5)	.65068(6)	.5600(6)	.1004(5)
C(6)	.63211(6)	.5840(6)	.2547(4)
C(7)	.60305(5)	.5652(5)	.1992(4)
O(8)	.58586(4)	.5995(3)	.3429(3)
C(9)	.55805(6)	.6262(6)	.2966(4)
C(10)	.54741(6)	.4479(7)	.1930(5)
C(11)	.56676(6)	.3914(7)	.0480(4)
C(12)	.59615(5)	.3614(5)	.1122(4)
C(13)	.61582(5)	.3357(5)	-.0402(4)
C(14)	.60977(7)	.1448(6)	-.1506(4)
C(15)	.62696(6)	.1361(7)	-.3128(4)
C(16)	.65621(6)	.1508(6)	-.2603(4)
C(17)	.67964(6)	.1188(7)	-.3889(4)
C(18)	.70277(6)	.2101(5)	-.2897(4)
C(19)	.73161(6)	.2237(5)	-.2918(4)
C(20)	.75233(6)	.1329(6)	-.3852(4)
C(21)	.77874(6)	.1836(5)	-.3529(4)
C(22)	.78502(6)	.3269(5)	-.2274(4)
C(23)	.76512(6)	.4183(5)	-.1291(4)
C(24)	.73841(5)	.3671(4)	-.1636(4)
C(25)	.65710(8)	.5445(6)	-.2782(5)
C(26)	.65824(7)	.1839(6)	.1176(4)
C(27)	.54241(6)	.6667(6)	.4626(4)
C(28)	.54586(8)	.4934(8)	.5886(6)
C(29)	.55069(9)	.8690(9)	.5372(7)
O(30)	.51407(4)	.6812(4)	.4194(3)
C(31)	.59635(8)	.1802(6)	.2361(5)
H(1)	.7135(5)	.508(5)	-.002(4)
H(5A)	.6703(6)	.556(5)	.140(4)
H(5B)	.6456(5)	.668(5)	.016(4)
H(6A)	.6355(5)	.484(4)	.345(4)
H(6B)	.6340(6)	.731(5)	.302(4)
H(7)	5992(5)	.671(4)	.117(4)
H(9)	.5576(5)	.758(4)	.227(3)
H(10A)	.5457(5)	.336(5)	.277(4)
H(10B)	.5296(7)	.482(5)	.138(4)

Table 9 (Continued)

H(11A)	.5606(6)	.265(5)	-.004(4)
H(11B)	.5670(6)	.505(6)	-.046(4)
H(13)	.6120(5)	.464(4)	-.119(4)
H(14A)	.6139(5)	.011(5)	-.076(4)
H(14B)	.5911(6)	.137(5)	-.172(4)
H(15A)	.6235(7)	.002(7)	-.376(6)
H(15B)	.6224(7)	.247(6)	-.390(6)
H(16)	.6609(5)	.040(4)	-.171(4)
H(17A)	.6824(6)	-.033(6)	-.420(4)
H(17B)	.6771(6)	.185(5)	-.500(4)
H(20)	.7477(6)	.035(5)	-.469(4)
H(21)	.7943(7)	.112(6)	-.417(5)
H(22)	.8046(6)	.378(5)	-.210(4)
H(23)	.7694(5)	.521(5)	-.037(4)
H(25A)	.6636(6)	.517(5)	-.396(5)
H(25B)	.6382(6)	.577(4)	-.291(3)
H(25C)	.6673(7)	.664(6)	-.230(5)
H(26A)	.6781(8)	.173(7)	.103(5)
H(26B)	.6543(6)	.221(5)	.232(4)
H(26C)	.6514(6)	.046(6)	.086(5)
H(28A)	.5656(8)	.491(6)	.621(5)
H(28B)	.5351(8)	.534(7)	.700(6)
H(29A)	.5471(9)	.989(8)	.458(6)
H(29B)	.5397(7)	.915(6)	.639(6)
H(29C)	.5703(7)	.882(6)	.562(4)
H(31A)	.5848(6)	.215(5)	.340(5)
H(31B)	.5870(9)	.052(8)	.170(6)
H(31C)	.6129(8)	.157(6)	.285(5)
C(1')	.5000	1.0000	.034(1)
O(2')	.5000	1.0000	.2138(8)

Table 10. Bond distances in angstroms of paspaline (16) with the estimated standard deviation of the least significant figure given in parentheses. The primed numbers refer to the solvent molecule of methanol.

N(1) - C(2)	1.369(4)
N(1) - C(24)	1.384(4)
C(2) - C(3)	1.519(4)
C(2) - C(18)	1.359(4)
C(3) - C(4)	1.576(4)
C(3) - C(16)	1.567(5)
C(3) - C(25)	1.535(5)
C(4) - C(5)	1.527(5)
C(4) - C(13)	1.579(3)
C(4) - C(26)	1.544(5)
C(5) - C(6)	1.533(5)
C(6) - C(7)	1.506(4)
C(7) - O(8)	1.434(4)
C(7) - C(12)	1.536(4)
O(8) - C(9)	1.432(3)
C(9) - C(10)	1.516(5)
C(9) - C(27)	1.543(4)
C(10) - C(11)	1.536(5)
C(11) - C(12)	1.550(4)
C(12) - C(13)	1.555(4)
C(12) - C(31)	1.535(5)
C(13) - C(14)	1.549(5)
C(14) - C(15)	1.537(5)
C(15) - C(16)	1.506(4)
C(16) - C(17)	1.553(4)
C(17) - C(18)	1.508(4)
C(18) - C(19)	1.427(4)
C(19) - C(20)	1.393(4)
C(19) - C(24)	1.419(4)
C(20) - C(21)	1.370(4)
C(21) - C(22)	1.397(5)
C(22) - C(23)	1.387(5)
C(23) - C(24)	1.388(4)
C(27) - C(28)	1.516(6)
C(27) - C(29)	1.502(6)
C(27) - O(30)	1.443(3)
C(1') - O(2')	1.42(1)

Table 11. Important bond angles in degrees of paspaline (16). Estimated standard deviations of the least significant figures are given in parentheses. The numbering scheme refers to Figure 3.

C(2)	- N(1)	- C(24)	108.4(2)
N(1)	- C(2)	- C(3)	136.2(3)
N(1)	- C(2)	- C(18)	109.8(2)
C(3)	- C(2)	- C(18)	112.8(2)
C(2)	- C(3)	- C(4)	119.4(2)
C(2)	- C(3)	- C(16)	97.5(2)
C(2)	- C(3)	- C(25)	105.3(2)
C(4)	- C(3)	- C(16)	107.9(2)
C(4)	- C(3)	- C(25)	113.6(3)
C(16)	- C(3)	- C(25)	112.2(2)
C(3)	- C(4)	- C(5)	111.3(2)
C(3)	- C(4)	- C(13)	106.6(2)
C(3)	- C(4)	- C(26)	107.8(2)
C(5)	- C(4)	- C(13)	108.2(2)
C(5)	- C(4)	- C(26)	108.1(2)
C(13)	- C(4)	- C(26)	114.8(2)
C(4)	- C(5)	- C(6)	113.6(3)
C(5)	- C(6)	- C(7)	109.3(3)
C(6)	- C(7)	- C(8)	108.7(2)
C(6)	- C(7)	- C(12)	114.3(3)
O(8)	- C(7)	- C(12)	110.9(2)
C(7)	- O(8)	- C(9)	112.6(2)
O(8)	- C(9)	- C(10)	112.1(2)
O(8)	- C(9)	- C(27)	106.5(2)
C(10)	- C(9)	- C(27)	114.5(3)
C(9)	- C(10)	- C(11)	111.7(3)
C(10)	- C(11)	- C(12)	111.7(3)
C(7)	- C(12)	- C(11)	104.1(2)
C(7)	- C(12)	- C(13)	107.5(2)
C(7)	- C(12)	- C(31)	112.4(3)
C(11)	- C(12)	- C(13)	110.2(2)
C(11)	- C(12)	- C(31)	108.2(3)
C(13)	- C(12)	- C(31)	113.9(3)
C(4)	- C(13)	- C(12)	114.6(2)
C(4)	- C(13)	- C(14)	112.9(2)
C(12)	- C(13)	- C(14)	113.6(2)
C(13)	- C(14)	- C(15)	113.0(3)
C(14)	- C(15)	- C(16)	107.4(3)
C(3)	- C(16)	- C(15)	112.5(3)
C(3)	- C(16)	- C(17)	105.6(3)
C(15)	- C(16)	- C(17)	121.8(3)

Table 11 (Continued)

C(16) - C(17) - C(18)	99.9(3)
C(2) - C(18) - C(17)	110.8(2)
C(2) - C(18) - C(19)	108.1(3)
C(17) - C(18) - C(19)	140.8(3)
C(18) - C(19) - C(20)	135.4(3)
C(18) - C(19) - C(24)	105.6(3)
C(20) - C(19) - C(24)	118.9(3)
C(19) - C(20) - C(21)	119.9(3)
C(20) - C(21) - C(22)	120.3(3)
C(21) - C(22) - C(23)	121.8(3)
C(22) - C(23) - C(24)	117.4(3)
N(1) - C(24) - C(19)	108.0(2)
N(1) - C(24) - C(23)	130.4(3)
C(19) - C(24) - C(23)	121.6(2)
C(9) - C(27) - C(28)	111.9(3)
C(9) - C(27) - C(29)	110.3(3)
C(9) - C(27) - O(30)	107.3(3)
C(28) - C(27) - C(29)	111.6(4)
C(28) - C(27) - O(30)	108.2(3)
C(29) - C(27) - O(30)	107.4(3)

Table 12. The observed and calculated structure factors for paspaline (16).

H = 0			
K	L	FO	FC
0	1	49	49
0	2	93	95
0	4	21	21
0	7	16	16
1	1	60	57
1	2	80	81
1	3	6	4
1	4	8	9
1	5	5	4
2	0	9	7
2	1	33	31
2	2	16	15
2	3	14	13
2	4	14	14
2	7	9	9
3	1	40	38
3	2	86	85
3	3	27	27
3	4	22	23
3	5	11	11
3	6	15	16
3	7	4	5
4	0	75	74
4	1	11	11
4	4	9	9
4	6	9	9
5	1	16	16
5	6	8	8
6	0	20	19
6	3	4	4
7	1	4	4

H = 1			
K	L	FO	FC
0	1	87	85
0	2	33	35
0	3	6	6
0	5	9	8
0	6	6	6
0	8	16	16
1	0	113	121
1	1	155	161
1	2	23	22
1	3	17	17
1	4	11	10
1	5	15	15
1	7	7	7
1	8	11	12
2	0	47	45
2	1	95	94
2	2	66	64
2	3	56	56
2	5	15	15
2	6	17	16
2	7	9	9
3	0	13	12
3	1	38	38
3	2	47	44
3	3	26	26
3	4	9	10
3	5	13	13
3	6	6	8
3	7	6	7
4	0	7	7
4	1	10	10
4	2	11	12
4	3	9	9
4	4	15	16
4	5	15	14
5	0	12	11
5	1	19	19
5	2	18	18
5	3	6	8
5	4	10	11
5	5	7	6
6	0	13	13
6	1	10	10
6	2	6	4
6	4	4	4

H = 2			
K	L	FO	FC
0	0	34	48
0	1	68	74
0	2	69	70
0	3	3	4
0	4	30	30
0	5	18	18
0	7	7	7
1	0	109	116
1	1	103	109
1	2	73	76
1	3	11	9
1	4	7	7
1	5	7	7
1	6	12	12
1	7	15	15
2	0	48	47
2	1	28	26
2	2	46	47
2	3	19	18
2	4	12	12
2	5	6	6
2	6	8	9
2	7	7	7
2	8	6	7
3	0	20	21
3	1	36	34
3	2	37	36
3	3	20	19
3	4	30	30
3	5	10	11
3	7	6	7
4	0	11	11
4	1	12	12
4	3	15	15
4	4	14	15
4	5	21	21
5	0	36	37
5	1	27	27
5	2	9	8
5	3	5	5
5	4	12	11
6	2	11	10
6	3	9	9

H = 3			
K	L	FO	FC
0	1	107	108
0	2	27	25
0	3	15	14
0	4	7	6
0	5	4	5
0	7	17	17
0	8	19	19
1	0	30	27
1	1	95	97
1	2	18	18
1	4	12	12
1	5	5	6
1	7	9	10
2	0	61	62
2	1	12	12
2	2	83	83
2	3	34	34
2	4	6	6
2	5	11	11
2	6	9	9
2	8	5	6
3	0	45	45
3	1	35	34
3	2	46	44
3	3	36	37
3	4	15	15
3	5	20	20
3	6	20	19
4	0	18	18
4	1	12	12
4	3	19	19
4	4	12	11
4	5	11	12
5	0	12	13
5	1	5	4
5	3	6	5
5	4	12	12
5	6	9	9
6	1	8	9
6	2	12	12
6	4	4	5
7	1	7	6

H = 4			
K	L	FO	FC
0	0	45	60
0	1	99	107
0	2	49	47
0	3	22	22
0	4	18	19
0	5	15	14
0	6	5	4
0	8	6	6
1	0	83	89
1	1	90	91
1	2	63	63
1	3	4	6
1	4	8	8
1	5	14	14
1	6	10	10
1	7	14	14
1	8	6	5

Table 12 (Continued)

2	1	58	55	2	3	46	46	2	3	34	34	2	0	17	17
2	2	102	102	2	4	7	6	2	4	13	14	2	1	15	14
2	3	37	35	2	5	18	18	2	5	15	15	2	2	45	43
2	5	21	21	2	6	21	21	2	6	20	20	2	3	10	10
3	0	5	5	2	8	6	6	2	7	7	7	2	4	5	4
3	1	26	26	3	0	15	16	3	0	12	13	2	5	19	19
3	2	22	23	3	1	25	25	3	1	16	16	2	6	19	19
3	3	27	27	3	2	19	18	3	2	23	22	2	7	10	10
3	4	7	6	3	3	25	24	3	3	28	29	2	8	9	10
3	5	11	12	3	4	9	8	3	4	8	8	3	0	11	11
3	6	10	10	3	5	19	20	3	5	28	28	3	1	31	31
3	7	8	7	3	6	10	11	3	6	14	14	3	2	15	17
4	0	28	29	4	0	43	43	3	7	12	12	3	3	8	8
4	1	18	18	4	1	12	12	4	0	22	22	3	4	21	22
4	2	10	9	4	2	9	9	4	1	11	10	3	5	25	25
4	3	11	11	4	3	7	7	4	3	8	8	4	0	11	10
4	4	13	13	4	6	7	6	4	4	23	23	4	1	32	33
4	5	23	23	5	0	10	11	4	5	13	13	4	2	13	13
5	0	16	16	5	1	10	9	4	7	4	5	4	3	5	5
5	1	23	23	5	3	6	5	5	0	45	45	4	4	17	17
5	3	6	7	5	4	10	9	5	2	13	13	5	0	11	10
5	4	5	6	5	5	7	8	5	3	6	5	5	1	15	15
5	6	6	7	6	0	6	5	5	4	7	8	5	2	7	6
6	1	13	14	6	1	11	11	5	5	6	6	5	3	15	15
6	2	5	6	6	2	6	6	5	6	4	5	5	4	8	9
6	3	5	5	6	4	4	5	6	0	10	11	5	5	5	4
7	1	4	5					6	1	12	12	6	1	6	6
				H = 6				6	3	8	8	6	4	6	6
H = 5				K	L	FO	FC	7	0	5	4	7	0	7	7
K	L	FO	FC	0	0	25	36								
0	1	71	79	0	1	4	3	H = 7				H = 8			
0	2	9	8	0	2	14	13	K	L	FO	FC	K	L	FO	FC
0	3	35	34	0	3	11	13	0	1	39	45	0	0	28	21
0	4	20	20	0	4	21	21	0	2	31	35	0	1	50	53
0	5	6	7	0	5	6	7	0	3	50	51	0	2	15	17
0	6	5	5	0	6	13	13	0	4	15	15	0	3	14	13
0	7	5	4	0	7	14	14	0	5	12	13	0	8	7	7
1	0	44	42	0	8	6	5	0	6	14	15	1	0	24	24
1	1	33	32	1	0	73	76	0	7	11	11	1	1	10	10
1	2	29	29	1	1	54	55	1	0	42	42	1	2	25	25
1	3	27	26	1	2	29	30	1	1	26	25	1	3	10	11
1	4	14	13	1	3	13	13	1	2	14	15	1	4	14	14
1	5	11	10	1	4	9	8	1	3	16	17	1	5	19	19
1	6	11	11	1	5	11	11	1	4	29	29	1	6	13	12
1	7	7	7	1	7	11	11	1	5	13	13	1	7	11	11
2	0	62	61	2	0	8	7	1	6	8	8	1	8	6	6
2	1	40	41	2	1	6	7	1	7	11	11	2	1	26	25
2	2	33	33	2	2	39	39	1	8	6	7	2	2	45	43

Table 12 (Continued)

2	3	36	34	3	1	10	11	3	2	40	38	3	3	12	11
2	4	20	20	3	2	36	36	3	3	18	18	3	4	11	11
2	5	9	8	3	3	9	8	3	4	8	8	3	5	15	16
2	6	24	23	3	4	18	18	3	5	26	26	3	6	8	7
3	0	9	9	3	5	6	6	3	6	10	9	3	7	4	4
3	1	26	26	3	6	12	14	4	0	13	14	4	0	9	9
3	2	26	25	3	7	5	4	4	1	11	10	4	1	15	15
3	3	14	13	4	0	9	9	4	2	17	17	4	2	7	6
3	4	14	14	4	1	16	15	4	3	16	16	4	3	8	7
3	5	22	23	4	3	11	11	4	4	13	14	4	4	8	7
3	6	12	12	4	4	17	17	5	0	11	12	4	5	8	9
4	1	24	24	4	5	7	8	5	1	6	5	5	0	6	5
4	4	7	8	4	6	7	7	5	2	9	9	5	1	9	9
4	5	5	5	5	0	5	6	5	3	7	7	5	3	10	11
4	6	5	4	5	1	11	11	5	4	9	8	6	0	5	4
5	0	10	10	5	2	11	10	5	5	5	5	6	1	14	13
5	1	5	7	5	4	7	8	6	0	5	3	6	2	5	5
5	2	7	7	6	1	7	8	6	1	7	7	6	3	9	8
5	3	19	19	6	2	5	5	6	2	6	6				
5	4	5	4					6	3	6	5		H = 12		
5	5	9	9		H = 10							K	L	FO	FC
6	2	10	10	K	L	FO	FC		H = 11			0	0	4	0
6	3	9	9	0	0	65	78	K	L	FO	FC	0	1	32	34
				0	1	35	36	0	1	22	21	0	2	11	12
	H =	9		0	2	31	32	0	2	25	23	0	3	6	7
K	L	FO	FC	0	3	5	4	0	3	11	10	0	4	38	38
0	1	50	49	0	4	18	18	0	4	17	17	0	5	11	11
0	2	76	79	0	5	9	8	0	5	4	4	0	8	12	11
0	3	20	20	0	7	16	16	0	6	5	4	1	0	29	32
0	4	58	57	0	8	5	5	1	0	65	66	1	1	27	28
0	6	17	17	1	0	37	38	1	1	37	35	1	2	36	35
0	7	16	16	1	1	18	17	1	2	10	11	1	3	52	51
1	0	54	56	1	2	23	23	1	3	26	26	1	4	17	16
1	1	31	29	1	3	34	33	1	4	14	14	1	5	7	7
1	2	36	36	1	4	14	14	1	5	20	20	1	6	11	11
1	3	19	18	1	5	30	31	1	6	12	12	1	7	10	11
1	4	15	15	1	6	12	12	1	7	7	6	1	8	6	5
1	5	16	16	1	8	10	9	2	1	5	5	2	0	7	7
1	6	7	8	2	0	35	37	2	2	13	13	2	2	10	9
1	7	12	12	2	1	20	20	2	3	21	21	2	3	27	27
2	0	22	23	2	2	17	17	2	4	7	7	2	4	11	11
2	1	23	22	2	3	28	28	2	5	17	16	2	5	19	19
2	2	10	10	2	4	4	4	2	6	19	19	2	6	15	15
2	3	16	15	2	5	25	25	2	7	8	8	2	7	7	7
2	5	14	14	2	6	16	15	2	8	7	7	3	0	13	12
2	6	22	22	2	7	9	9	3	0	18	18	3	1	12	12
2	8	8	8	3	0	5	5	3	1	12	12	3	2	5	4
3	0	22	24	3	1	5	7	3	2	17	17	3	3	5	5

Table 12 (Continued)

3	4	11	11
3	5	19	19
3	6	17	17
3	7	9	10
4	0	13	13
4	4	20	20
4	5	14	15
5	0	9	9
5	1	7	7
5	2	8	8
5	3	6	6
5	4	9	9
5	5	4	5
6	1	12	11
6	2	5	3
6	3	6	6
6	4	6	6

H = 13

K	L	FO	FC
0	1	48	47
0	3	90	88
0	4	26	26
0	5	19	19
0	6	9	8
1	0	12	13
1	1	32	33
1	2	17	17
1	3	58	58
1	4	36	36
1	5	16	16
1	6	15	14
1	7	7	7
1	8	7	8
2	0	56	56
2	1	13	13
2	2	26	26
2	3	10	10
2	5	27	28
2	6	10	10
2	7	12	12
3	0	17	17
3	1	18	18
3	2	7	7
3	4	17	16
3	5	21	21
3	6	17	17
3	7	7	8
4	1	8	6
4	2	6	5
4	3	9	9
4	4	16	16
4	5	6	6
4	6	10	9
5	0	20	21
5	3	11	12
6	0	6	6
6	1	7	8
6	2	7	7
6	3	10	9

H = 14

K	L	FO	FC
0	0	13	10
0	1	50	53
0	2	8	8
0	3	72	72
0	4	32	32
0	5	23	23
0	6	8	8
1	0	5	7
1	1	26	25
1	2	30	29
1	3	34	33
1	4	28	28
1	5	11	11
1	6	7	7
1	7	7	7
1	8	8	8
2	0	6	6
2	1	35	35
2	2	17	17
2	3	13	13
2	5	27	26
2	6	13	14
2	7	6	7
3	0	17	16
3	1	17	17
3	2	13	12
3	3	15	15
3	4	19	19
3	5	6	7
3	6	6	6
3	7	10	9
4	0	13	14
4	1	8	8
4	2	7	7
4	3	12	12
4	4	13	14
4	6	7	7
5	0	17	17
5	1	8	7
5	2	11	10
5	3	13	13

H = 15

K	L	FO	FC
0	1	8	7
0	2	20	19
0	3	27	27
0	5	17	17
0	6	7	8
0	8	16	16
1	0	12	11
1	1	17	18
1	2	34	32
1	3	18	17
1	4	6	6
1	5	10	10
1	6	8	8
1	7	4	3
1	8	11	10
2	0	22	22
2	1	16	16
2	2	14	13
2	3	4	3
2	4	5	4
2	5	8	8
3	0	14	15
3	1	8	9
3	2	21	20
3	3	7	7
3	4	11	11
3	5	5	5
3	6	7	7
4	0	5	4
4	2	10	10
4	3	7	6
4	4	6	6
4	6	7	7
5	1	7	6
5	2	13	13
5	3	17	17
5	5	5	6
6	0	15	15
6	3	5	5

H = 16

K	L	FO	FC
0	0	52	58
0	1	43	43
0	2	33	33
0	3	25	25
0	4	7	6
0	5	19	20
0	6	7	7
0	7	4	4
0	8	9	9
1	0	41	39
1	1	18	19
1	2	33	31
1	3	5	4
1	4	17	17
1	5	16	16
1	6	5	4
1	8	5	5
2	0	8	8
2	1	12	13
2	2	14	12
2	3	12	12
2	4	10	11
2	5	14	14
2	7	12	13
3	1	11	12
3	2	14	14
3	3	5	5
3	4	11	11
3	6	6	6
4	1	17	17
4	2	8	8
4	3	8	9
4	4	7	8
4	6	4	2
5	0	6	6
5	1	8	8
5	2	5	6
5	3	9	9
5	4	9	9
6	0	4	4
6	2	5	6

Table 12 (Continued)

H = 17

K	L	FC	FC
0	1	32	33
0	2	10	9
0	3	37	36
0	4	7	8
0	5	12	12
0	6	6	6
1	0	59	58
1	1	20	20
1	2	27	26
1	3	11	11
1	4	21	21
1	5	11	12
1	6	5	5
1	7	8	8
1	8	5	6
2	0	12	12
2	1	32	33
2	2	19	18
2	3	13	14
2	4	7	8
2	5	8	7
2	6	6	5
3	0	20	21
3	1	16	16
3	2	33	33
3	3	14	14
3	4	9	9
3	6	7	7
4	0	12	12
4	1	13	12
4	2	6	6
4	3	8	8
4	4	7	6
4	5	10	10
5	0	11	11
5	3	12	13
5	5	4	5
6	0	8	8
6	2	9	9
6	3	5	5

H = 18

K	L	FO	FC
0	0	82	83
0	1	36	37
0	3	27	27
0	4	7	7
0	6	7	6
0	8	6	5
1	0	13	12
1	1	27	27
1	2	19	19
1	3	19	19
1	4	18	18
1	5	4	4
1	6	12	12
1	7	10	10
2	0	5	6
2	1	12	12
2	3	30	29
2	4	10	10
2	5	8	7
3	0	9	8
3	1	17	17
3	2	6	6
3	3	6	6
3	6	8	8
4	0	5	5
4	1	9	9
4	2	10	10
4	3	19	19
4	4	5	5
4	5	7	7
5	2	8	8
5	5	6	6
6	0	8	8
6	2	11	11

H = 19

K	L	FO	FC
0	1	19	18
0	2	15	16
0	3	15	14
0	4	14	14
0	5	8	8
0	6	7	7
0	8	5	5
1	0	30	30
1	1	31	30
1	2	12	11
1	4	15	16
1	6	5	4
2	0	7	5
2	1	21	21
2	2	5	6
2	3	7	7
2	4	13	14
2	6	12	12
2	7	14	13
3	0	30	30
3	1	4	6
3	2	21	21
3	3	20	20
3	6	11	10
4	0	13	14
4	2	9	8
4	3	5	5
4	4	16	17
4	5	6	4
5	0	7	8
5	1	11	10
5	3	6	6
5	4	5	5
6	0	5	4
6	1	7	7
6	2	4	4

H = 20

K	L	FO	FC
0	0	93	94
0	1	25	26
0	2	13	13
0	3	45	45
0	4	12	12
0	5	6	6
0	7	8	8
1	1	31	31
1	2	40	40
1	3	8	8
1	4	7	7
1	5	13	13
2	0	16	16
2	1	11	12
2	2	7	7
2	3	29	28
2	4	8	7
2	5	5	6
2	6	4	4
2	7	5	5
3	0	26	26
3	1	5	4
3	2	5	5
3	3	6	7
3	4	6	6
3	5	13	14
3	6	6	6
3	7	5	4
4	0	6	6
4	2	19	20
4	3	7	8
4	4	9	8
5	1	7	6
5	3	5	4
5	4	6	6
6	0	8	9

H = 21

K	L	FC	FC
0	1	47	47
0	2	42	43
0	3	7	6
0	4	15	15
1	0	9	9
1	1	16	15
1	2	25	26
1	3	8	9
1	4	15	15
1	5	10	10
1	6	6	6
2	1	32	32
2	2	25	25
2	3	20	21
2	5	8	9
2	6	14	14
2	7	6	6
3	0	17	17
3	1	16	16
3	2	16	16
3	3	8	8
3	4	7	8
3	5	7	7
3	6	4	5
3	7	4	5
4	1	10	9
4	2	5	5
4	3	6	6
4	4	7	6
4	6	5	6
5	1	7	7
5	2	5	7

Table 12 (Continued)

5	3	9	9
6	0	8	8
6	1	5	5
6	3	4	2

H = 22

K	L	FO	FC
0	0	12	12
0	1	56	56
0	2	8	8
0	5	6	6
0	6	5	5
0	7	7	8
1	0	17	18
1	1	30	29
1	2	26	27
1	3	8	8
1	4	13	13
1	5	8	8
1	6	9	9
1	7	4	4
2	0	21	21
2	1	15	15
2	2	10	10
2	3	12	12
2	4	19	19
2	5	9	9
2	7	4	4
3	0	19	19
3	1	8	7
3	2	9	9
3	3	22	21
3	5	12	12
3	6	5	4
4	0	5	5
4	1	13	13
4	4	5	4
4	5	7	7
5	0	16	16
5	1	19	20
5	2	6	7
5	3	14	14
5	4	4	4
6	0	6	7
6	2	6	6

H = 23

K	L	FO	FC
0	1	51	51
0	2	4	3
0	3	53	55
0	4	10	10
0	5	6	5
0	7	10	11
1	0	4	3
1	1	17	16
1	2	15	15
1	3	6	5
1	4	12	13
1	5	11	11
1	6	6	6
2	1	15	14
2	2	9	9
2	3	10	11
2	5	9	9
2	6	4	3
2	7	5	5
3	0	9	10
3	1	7	8
3	2	11	11
3	3	8	9
3	5	16	16
4	0	7	6
4	1	6	6
4	2	6	7
4	4	11	12
4	5	6	7
5	1	12	12
5	3	5	4
6	0	5	4
6	1	8	8
6	2	12	11

H = 24

K	L	FO	FC
0	0	11	12
0	1	51	50
0	2	13	13
0	7	8	7
1	0	69	69
1	1	7	7
1	2	28	28
1	3	13	13
1	4	8	7
1	5	9	9
1	6	9	8
1	7	9	9
2	0	18	18
2	1	13	14
2	2	26	27
2	3	15	15
2	4	10	10
2	5	16	17
2	6	7	7
3	0	14	14
3	1	5	4
3	2	11	12
3	4	14	13
3	5	6	6
3	6	7	7
4	1	15	15
4	2	20	21
4	5	5	4
5	0	24	24
5	1	11	11
5	2	8	7
5	3	8	7
6	1	7	7
6	2	5	3

H = 25

K	L	FO	FC
0	1	65	64
0	3	34	34
0	5	10	10
0	7	7	7
1	0	13	12
1	1	26	27
1	2	32	32
1	3	8	8
1	4	7	8
1	5	15	14
1	6	6	6
2	0	25	25
2	1	25	25
2	2	7	7
2	3	28	29
2	4	7	7
2	5	10	10
2	6	7	7
3	1	9	10
3	2	20	21
3	3	20	20
3	4	16	16
3	5	16	16
3	6	5	6
4	0	10	10
4	1	11	11
4	2	22	23
4	3	6	7
5	1	8	8
5	2	5	5
5	3	5	5
5	4	7	7
6	0	9	9
6	1	9	9

H = 26

K	L	FO	FC
0	0	9	9
0	1	31	32
0	2	6	8
0	3	8	8
0	5	5	5
0	6	14	14
0	7	10	10
1	1	32	32
1	2	41	42
1	3	8	8
1	5	7	7
1	6	4	4
2	0	4	4
2	1	11	12
2	3	22	22
2	4	13	13
2	5	6	6
2	6	7	7
2	7	5	4
3	0	20	20
3	2	12	13
3	3	34	35
3	5	13	13
4	0	10	10
4	1	12	13
4	2	23	23
4	3	10	10
4	4	15	15
5	1	8	8
5	2	9	8
5	3	9	8

Table 12 (Continued)

5	4	5	4
6	0	4	4
6	1	12	11

H = 27

K	L	FO	FC
0	1	10	10
0	3	9	8
0	7	12	12
1	0	10	10
1	1	20	19
1	2	22	21
1	3	7	8
1	4	10	10
1	5	5	5
1	6	6	5
1	7	9	9
2	0	5	5
2	1	5	6
2	2	13	13
2	3	20	21
2	4	7	6
2	5	19	19
2	6	10	10
3	1	8	8
3	2	11	11
3	3	22	22
3	4	17	17
3	5	7	7
4	0	6	6
4	1	12	12
4	2	7	8
4	3	7	7
4	4	6	6
5	0	10	10
5	1	11	11
5	2	14	13
6	0	6	6
6	1	6	4

H = 28

K	L	FC	FC
0	0	35	35
0	1	23	23
0	2	44	44
0	5	20	19
0	6	7	7
0	7	15	14
1	0	15	14
1	1	21	20
1	2	16	15
1	3	9	10
1	4	18	18
1	5	10	10
2	0	21	21
2	1	7	8
2	3	34	35
2	4	15	15
2	5	5	5
3	0	6	7
3	2	27	27
3	3	15	15
3	4	13	12
3	5	16	15
4	1	8	8
4	2	11	11
4	3	9	10
4	5	7	6
5	1	5	5
5	3	10	10
5	4	5	5

H = 29

K	L	FO	FC
0	2	15	14
0	3	15	15
0	5	21	21
0	6	5	4
1	0	9	10
1	1	9	9
1	2	5	4
1	3	33	33
1	4	11	11
1	5	8	8
1	6	10	10
1	7	10	10
2	1	14	14
2	2	17	17
2	3	25	26
2	4	36	36
2	5	6	6
2	6	5	5
3	1	6	5
3	3	16	16
3	4	10	10
3	5	7	5
3	6	5	5
4	1	7	8
4	2	7	8
4	3	7	8
4	4	6	6
4	5	8	8
5	0	9	8
5	1	5	5

H = 30

K	L	FO	FC
0	0	26	26
0	1	27	27
0	2	39	39
0	3	17	17
0	4	11	11
0	5	12	11
0	6	4	4
0	7	8	8
1	0	14	14
1	1	12	12
1	2	9	9
1	3	18	17
1	4	12	12
1	5	15	15
2	1	8	9
2	2	7	7
2	4	7	6
2	5	15	15
3	0	12	11
3	1	7	7
3	2	16	15
3	3	7	8
3	4	15	15
3	5	5	6
4	0	8	9
4	1	13	14
4	2	10	10
4	3	14	14
4	4	7	5
5	0	8	7
5	2	6	5
5	3	4	4

H = 31

K	L	FC	FC
0	2	23	23
0	3	17	17
0	4	7	7
0	5	8	8
0	7	10	10
1	0	10	9
1	2	13	13
1	3	8	8
1	4	13	13
1	6	13	13
2	0	13	13
2	1	5	4
2	2	13	12
2	3	13	13
2	4	15	16
2	5	5	6
2	6	4	4
3	1	10	11
3	2	14	14
3	3	18	18
3	4	20	21
4	0	10	11
4	2	8	8
4	3	5	5
5	0	7	7
5	1	9	9
5	2	9	8
5	3	12	12

H = 32

K	L	FO	FC
0	0	11	11
0	1	20	20
0	2	18	18
0	3	17	17
0	5	11	11
0	6	11	10
1	0	5	5
1	2	20	20
1	3	12	11
1	4	9	11
1	5	10	11
2	2	5	4
2	3	16	16
2	4	27	27
2	5	9	9
2	6	4	4
3	1	5	5
3	2	7	6
3	3	9	9

Table 12 (Continued)

3	4	14	14	1	2	10	10	4	3	9	9	3	2	20	20
3	5	6	6	1	3	6	6	4	4	9	9	4	0	9	8
4	0	8	9	1	4	11	11	5	1	14	14	4	1	8	8
4	1	7	7	1	5	6	6	5	2	9	7	4	2	11	11
4	2	10	9	1	6	6	6					4	3	5	6
4	3	10	11	2	2	14	13	H = 36				5	0	5	4
5	1	13	13	2	3	7	7	K	L	FO	FC	5	1	5	4
5	2	11	11	2	4	16	17	0	0	30	30				
5	3	7	7	2	5	6	5	0	2	8	8	H = 38			
				2	6	4	2	0	3	8	8	K	L	FO	FC
H = 33				3	0	14	14	0	4	4	4	0	0	8	8
K	L	FO	FC	3	2	13	13	0	5	6	6	0	1	8	7
0	1	5	6	3	3	17	17	0	6	15	16	0	2	35	35
0	2	10	10	3	5	8	8	1	0	12	12	0	3	18	18
0	4	8	9	4	2	10	9	1	1	4	4	0	5	9	9
0	5	10	10	4	3	9	8	1	2	8	8	1	0	16	16
0	6	7	6	5	0	8	8	1	3	13	12	1	1	13	13
1	0	6	7	5	2	8	8	1	4	17	18	1	2	21	22
1	1	19	20					1	5	8	8	1	3	30	30
1	2	20	20	H = 35				2	1	10	9	1	4	8	8
1	3	12	12	K	L	FO	FC	2	2	10	11	1	5	6	5
1	4	16	16	0	1	5	5	2	3	10	10	2	0	18	18
1	5	19	19	0	2	14	14	2	4	9	9	2	1	23	23
1	6	7	6	0	3	5	4	3	0	8	8	2	2	7	6
2	0	12	13	0	4	15	15	3	2	6	6	2	4	13	13
2	1	11	12	0	5	12	11	3	3	8	7	2	5	10	10
2	2	12	12	1	0	17	18	3	4	7	7	3	0	5	5
2	3	18	17	1	1	8	8	3	5	10	9	3	1	9	8
2	4	11	11	1	2	10	10	4	1	5	4	3	3	14	15
2	5	6	6	1	3	17	17	4	2	6	7	3	4	6	6
3	0	5	5	1	4	7	6	5	1	5	5	4	2	10	9
3	1	8	7	1	5	6	5	5	2	14	12	4	3	7	6
3	3	14	14	1	6	8	9								
3	5	7	7	2	0	5	4	H = 37				H = 39			
4	2	15	15	2	1	24	24	K	L	FO	FC	K	L	FO	FC
4	3	9	9	2	2	9	10	0	2	33	33	0	1	7	7
5	0	11	11	2	3	11	10	0	3	30	30	0	2	49	49
5	2	10	9	2	4	6	5	0	4	13	14	0	4	9	9
				2	5	5	4	0	6	4	4	0	5	6	7
H = 34				2	6	6	6	1	1	6	6	1	0	23	23
K	L	FO	FC	3	0	14	13	1	2	21	20	1	1	17	17
0	0	18	18	3	1	12	13	1	3	9	8	1	2	18	18
0	1	24	24	3	2	11	10	1	5	6	6	1	3	14	14
0	2	9	9	3	3	11	11	2	1	9	9	1	4	6	6
0	3	29	29	3	4	10	10	2	2	5	5	2	0	7	6
0	5	11	11	3	5	5	5	2	4	21	20	2	1	16	16
0	6	5	6	4	1	5	6	3	0	6	6	2	3	12	12
1	0	10	10	4	2	11	11	3	1	5	5	2	4	6	6

Table 12 (Continued)

2	5	6	5
3	0	33	33
3	1	16	16
3	2	6	7
4	0	5	6
4	1	14	13
4	2	11	11
4	3	4	4

H = 40

K	L	FO	FC
0	0	11	11
0	1	7	7
0	4	8	7
1	1	24	24
1	2	19	19
1	5	5	5
2	2	5	6
2	3	11	10
2	4	5	4
2	5	7	6
3	0	22	21
3	1	9	10
3	2	7	6
4	0	6	7
4	1	11	11
4	2	7	6
4	3	7	6

H = 41

K	L	FO	FC
0	1	9	9
0	2	11	10
0	3	12	13
1	0	6	7
1	1	16	16
1	2	13	13
1	3	12	12
1	4	16	16
1	5	5	4
2	0	39	39
2	1	16	17
2	2	14	14
2	4	9	8
3	0	8	9
3	1	12	11
3	4	4	3
4	0	5	4
4	2	6	6

H = 42

K	L	FO	FC
0	1	27	27
0	2	14	14
0	3	23	23
0	5	8	7
1	0	7	8
1	1	25	25
1	2	8	7
1	3	5	4
2	1	7	8
2	2	6	7
2	4	4	5
3	1	21	20
3	2	6	6
3	3	11	11
4	1	11	10
4	2	9	9

H = 43

K	L	FO	FC
0	1	11	11
0	2	12	12
1	1	7	7
1	2	19	19
1	5	6	6
2	0	41	42
2	2	5	6
2	3	5	5
2	4	7	6
3	1	11	10
3	2	8	8
3	3	4	4
4	0	8	7

H = 44

K	L	FO	FC
0	0	5	4
0	1	10	10
1	0	16	16
1	1	5	4
1	2	5	6
1	3	4	4
2	1	9	9
3	0	5	6
3	1	7	7
4	0	4	5

H = 45

K	L	FO	FC
0	4	5	4
1	0	5	4
1	1	18	18
1	2	6	6
1	3	5	5
1	4	6	6
2	0	7	7
2	1	5	4
3	0	8	9
3	1	12	13
3	2	5	5

H = 46

K	L	FO	FC
0	0	19	18
0	1	7	6
1	0	13	13
1	3	7	6
1	4	5	4
2	0	11	12
2	1	8	8
3	0	6	5

H = 47

K	L	FO	FC
0	3	4	3
1	0	10	9
1	2	9	8
2	0	9	8
2	1	9	9

H = 48

K	L	FO	FC
0	0	9	8
0	1	7	5
0	2	6	5
0	3	6	6
1	1	7	7
2	1	6	6

H = 49

K	L	FO	FC
0	3	6	4
1	1	5	5

H = 50

K	L	FC	FC
0	1	4	3
0	2	4	4
1	1	7	6
1	2	6	5
2	0	7	6

H = 51

K	L	FC	FC
2	1	6	6

H = 52

K	L	FC	FC
0	1	5	5

contain the α,β-unsaturated ketone functionality nor the hydroxyl group at C(13), but instead possesses a tertiary methyl group at C(12) which is trans to the hydrogen at C(7). The relative configurations of the 6 corresponding stereochemical centers of paspaline 16 and paxilline 15 are identical. Bond distances and angles of paspaline 16 are normal (23) and correspond quite closely to those found in paxilline 15. The methanol that co-crystallizes is found in the special position b (0, 1/2, z; 1/2, 0, -z) on a twofold axis along z. This allows for a special hydrogen bonding arrangement. The O(30) hydroxyl group forms an intermolecular hydrogen bond with O(30) of another molecule related by a two-fold rotation around z with an O(30) - O(30') distance of 2.74 Å. A hydrogen bond also exists between O(30) and the hydroxyl group of the solvent methanol with an interatomic distance of 2.73 Å. Because of the twofold rotation axis difficulty was experienced in the determination of the correct positions for the hydrogen atoms of the hydroxyl groups as well as the methyl hydrogens of the methanol. No other abnormally close intermolecular contacts were found in the crystal structure. Paspaline 16 was tested as has been previously described (42) but found to possess neither toxic nor tremorgenic activity. A study of the biosynthesis of paspaline 16 as well as paspalicine 17 is currently in progress in Professor Arigoni's laboratories at the ETH in Zürich.

Experimental - Paspalicine

Paspalicine 17, $C_{27}H_{31}NO_3$, was originally crystallized from methanol in the monoclinic space group $P2_1$ with $\underset{\sim}{a}$ = 13.439(2), $\underset{\sim}{b}$ = 11.740(1), $\underset{\sim}{c}$ = 15.295(2) Å and β = 97.38(1)° with Z = 4. After a number of unsuccessful attempts to solve the crystal structure using direct methods, paspalicine 17 was crystallized from acetone to form large needles, mp. ~240 (dec.). The space group of the recrystallized material was $P2_12_12_1$ with $\underset{\sim}{a}$ = 9.706(1), $\underset{\sim}{b}$ = 10.670(1), and $\underset{\sim}{c}$ = 21.775(2) Å for a calculated density of 1.23g/cc for Z = 4. Data were taken as previously described and of the 1787 reflections measured 1583 (89%) were considered observed ($I \geq 3\sigma(I)$) and then corrected for Lorentz and polarization effects (18). Structure solution was again successfully accomplished through the use of a multi-solution tangent formula approach (20). All 31 nonhydrogen atoms were found in the E-map giving the highest combined figure of merit. Subsequent full matrix least-squares refinements (19, 21) lowered the unweighted residual index (R factor) to 3.3% using anisotropic temperature factors for the nonhydrogen atoms and isotropic temperature factors for the hydrogen atoms. Figure 4 is a computer generated perspective drawing of paspalicine 17. Tables 13, 14, 15, and 16 contain the fractional coordinates, bond distances, bond angles, and observed and calculated structure factors.

Figure 4. A computer generated perspective drawing from the crystal structure of paspalicine (17) with hydrogens omitted for clarity.

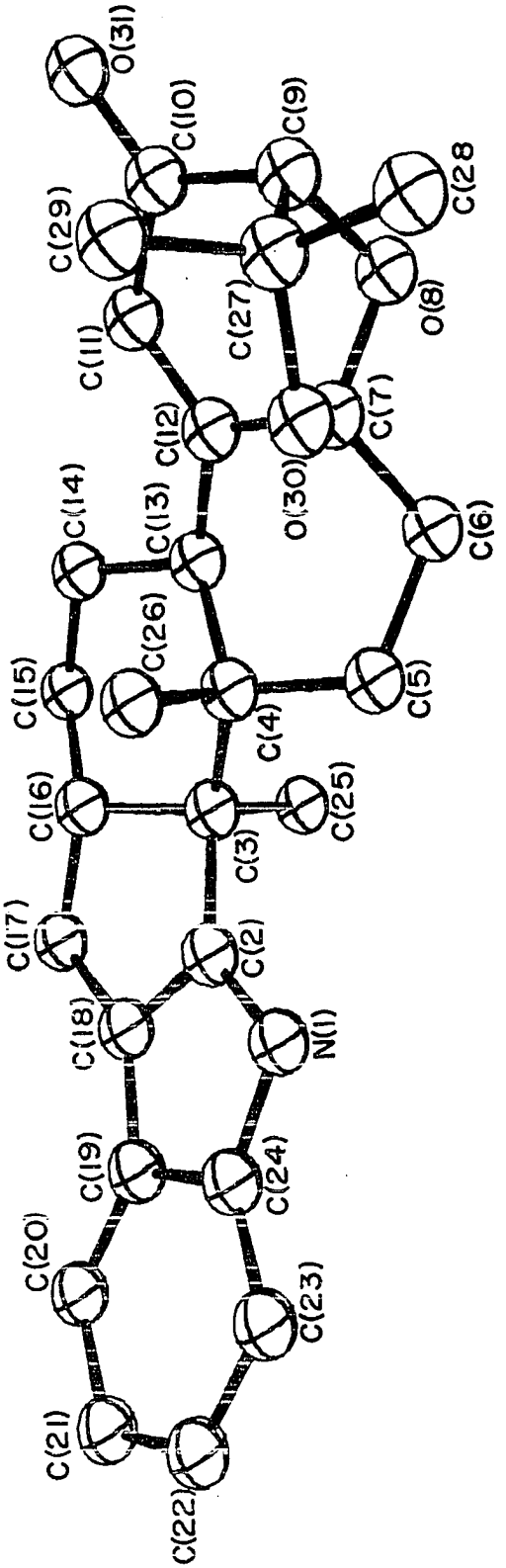

O(31)
C(10)
C(9)
C(28)
C(29)
C(27)
O(8)
C(11)
C(12)
C(7)
O(30)
C(6)
C(14)
C(13)
C(26)
C(15)
C(4)
C(5)
C(16)
C(3)
C(25)
C(17)
C(2)
C(18)
N(1)
C(19)
C(24)
C(20)
C(23)
C(21)
C(22)

Table 13. Final fractional coordinates for paspalicine (17) with the estimated standard deviation of the least significant figure given in parentheses. The numbering scheme refers to Figure 4.

N(1)	.2842(2)	.4915(2)	.8308(1)
C(2)	.1810(2)	.5554(2)	.8015(1)
C(3)	.0533(2)	.6266(2)	.8201(1)
C(4)	-.0387(2)	.5703(2)	.8720(1)
C(5)	.0301(3)	.5830(3)	.9365(1)
C(6)	-.0680(3)	.6240(3)	.9883(1)
C(7)	-.2061(2)	.5622(2)	.9821(1)
O(8)	-.2982(2)	.5991(2)	1.0294(1)
C(9)	-.4028(2)	.5048(2)	1.0241(1)
C(10)	-.4859(2)	.5252(2)	.9663(1)
C(11)	-.4089(2)	.5774(2)	.9150(1)
C(12)	-.2725(2)	.5934(2)	.9203(1)
C(13)	-.1785(2)	.6442(2)	.8714(1)
C(14)	-.2466(2)	.6553(2)	.8078(1)
C(15)	-.1507(3)	.7013(2)	.7570(1)
C(16)	-.0241(2)	.6178(2)	.7575(1)
C(17)	.0896(3)	.6252(2)	.7074(1)
C(18)	.2044(2)	.5583(2)	.7398(1)
C(19)	.3319(2)	.4948(2)	.7286(1)
C(20)	.4119(3)	.4676(2)	.6765(1)
C(21)	.5287(3)	.3954(3)	.6829(1)
C(22)	.5676(3)	.5480(3)	.7599(1)
C(23)	.4925(3)	.3754(3)	.7924(1)
C(24)	.3770(2)	.4516(2)	.7864(1)
C(25)	.0974(3)	.7636(2)	.8339(1)
C(26)	-.0664(2)	.4313(2)	.8592(1)
C(27)	-.3152(3)	.3838(2)	1.0210(1)
C(28)	-.2725(4)	.3406(4)	1.0847(1)
C(29)	-.3754(4)	.2768(3)	.9838(1)
O(30)	-.1925(2)	.4293(1)	.9900(1)
O(31)	-.6074(2)	.4944(2)	.9636(1)
H(1)	.299(3)	.480(2)	.868(1)
H(5A)	.103(3)	.642(3)	.936(1)
H(5B)	.069(3)	.493(3)	.946(1)
H(6A)	-.080(3)	.718(3)	.989(1)
H(6B)	-.031(3)	.600(3)	1.027(1)
H(9)	-.461(3)	.511(3)	1.059(1)
H(11)	-.465(3)	.595(2)	.877(1)
H(13)	-.158(2)	.735(2)	.886(1)
H(14A)	-.326(3)	.710(2)	.809(1)
H(14B)	-.286(2)	.570(2)	.797(1)

Table 13 (Continued)

H(15A)	-.122(3)	.792(3)	.766(1)
H(15B)	-.195(3)	.700(2)	.719(1)
H(16)	-.058(2)	.529(2)	.756(1)
H(17A)	.105(3)	.717(2)	.697(1)
H(17B)	.057(3)	.582(3)	.668(1)
H(20)	.383(3)	.493(3)	.636(1)
H(21)	.589(3)	.373(3)	.646(1)
H(22)	.650(3)	.294(3)	.745(1)
H(23)	.516(3)	.341(3)	.832(1)
H(25A)	.173(3)	.765(3)	.867(1)
H(25B)	.019(3)	.814(3)	.848(1)
H(25C)	.131(3)	.802(3)	.796(1)
H(26A)	-.140(3)	.416(3)	.826(1)
H(26B)	-.105(3)	.388(2)	.893(1)
H(26C)	.021(3)	.390(2)	.845(1)
H(28A)	-.197(4)	.270(3)	1.083(1)
H(28B)	-.351(4)	.307(3)	1.104(1)
H(28C)	-.233(4)	.419(4)	1.109(2)
H(29A)	-.389(3)	.303(3)	.938(1)
H(29B)	-.464(4)	.250(4)	.997(2)
H(29C)	-.309(4)	.206(3)	.985(1)

Table 14. Bond distances in angstroms for paspalicine (17) with the estimated standard deviation of the least significant figure given in parentheses. The numbering scheme refers to Figure 4.

N(1) - C(2)	1.370(3)
N(1) - C(24)	1.388(3)
C(2) - C(3)	1.509(3)
C(2) - C(18)	1.363(3)
C(3) - C(4)	1.560(3)
C(3) - C(16)	1.560(3)
C(3) - C(25)	1.552(3)
C(4) - C(5)	1.561(3)
C(4) - C(13)	1.570(3)
C(4) - C(26)	1.532(3)
C(5) - C(6)	1.540(3)
C(6) - C(7)	1.500(4)
C(7) - O(8)	1.420(2)
C(7) - C(12)	1.529(3)
C(7) - O(30)	1.434(3)
O(8) - C(9)	1.434(3)
C(9) - C(10)	1.510(3)
C(9) - C(27)	1.547(4)
C(10) - C(11)	1.456(3)
C(10) - O(31)	1.227(3)
C(11) - C(12)	1.340(3)
C(12) - C(13)	1.503(3)
C(13) - C(14)	1.538(3)
C(14) - C(15)	1.528(3)
C(15) - C(16)	1.518(3)
C(16) - C(17)	1.555(3)
C(17) - C(18)	1.501(3)
C(18) - C(19)	1.431(3)
C(19) - C(20)	1.404(3)
C(19) - C(24)	1.411(3)
C(20) - C(21)	1.378(4)
C(21) - C(22)	1.392(4)
C(22) - C(23)	1.388(4)
C(23) - C(24)	1.390(4)
C(27) - C(28)	1.519(3)
C(27) - C(29)	1.516(4)
C(27) - O(30)	1.452(3)

Table 15. Bond angles in degrees of paspalicine (17). Estimated standard deviations of the least significant figures are given in parentheses. The numbering scheme refers to Figure 4.

C(2)	- N(1)	- C(24)	107.6(2)
N(1)	- C(2)	- C(3)	136.6(2)
N(1)	- C(2)	- C(18)	110.4(2)
C(3)	- C(2)	- C(18)	113.0(2)
C(2)	- C(3)	- C(4)	118.0(2)
C(2)	- C(3)	- C(16)	97.5(2)
C(2)	- C(3)	- C(25)	107.4(2)
C(4)	- C(3)	- C(16)	109.5(2)
C(4)	- C(3)	- C(25)	112.4(2)
C(16)	- C(3)	- C(25)	111.0(2)
C(3)	- C(4)	- C(5)	111.9(2)
C(3)	- C(4)	- C(13)	107.1(2)
C(3)	- C(4)	- C(26)	110.1(2)
C(5)	- C(4)	- C(13)	109.5(2)
C(5)	- C(4)	- C(26)	108.8(2)
C(13)	- C(4)	- C(26)	109.4(2)
C(4)	- C(5)	- C(6)	114.8(2)
C(5)	- C(6)	- C(7)	111.2(2)
C(6)	- C(7)	- C(8)	112.0(2)
C(6)	- C(7)	- C(12)	111.1(2)
C(6)	- C(7)	- O(30)	109.9(2)
O(8)	- C(7)	- C(12)	108.3(2)
O(8)	- C(7)	- O(30)	104.2(2)
C(12)	- C(7)	- O(30)	111.1(2)
C(7)	- O(8)	- C(9)	101.0(2)
O(8)	- C(9)	- C(10)	110.1(2)
O(8)	- C(9)	- C(27)	101.6(2)
C(10)	- C(9)	- C(27)	112.1(2)
C(9)	- C(10)	- C(11)	114.9(2)
C(9)	- C(10)	- O(31)	121.1(2)
C(11)	- C(10)	- O(31)	123.9(2)
C(10)	- C(11)	- C(12)	119.3(2)
C(7)	- C(12)	- C(11)	117.7(2)
C(7)	- C(12)	- C(13)	116.5(2)
C(11)	- C(12)	- C(13)	125.8(2)
C(4)	- C(13)	- C(12)	109.7(2)
C(4)	- C(13)	- C(14)	114.7(2)
C(12)	- C(13)	- C(14)	113.8(2)
C(13)	- C(14)	- C(15)	114.6(2)
C(14)	- C(15)	- C(16)	107.4(2)
C(3)	- C(16)	- C(15)	111.2(2)
C(3)	- C(16)	- C(17)	105.6(2)

Table 15 (Continued)

C(15) - C(16) - C(17)	122.6(2)
C(16) - C(17) - C(18)	99.9(2)
C(2) - C(18) - C(17)	110.5(2)
C(2) - C(18) - C(19)	107.6(2)
C(17) - C(18) - C(19)	141.8(2)
C(18) - C(19) - C(20)	135.6(2)
C(18) - C(19) - C(24)	105.7(2)
C(20) - C(19) - C(24)	118.7(2)
C(19) - C(20) - C(21)	119.3(2)
C(20) - C(21) - C(22)	121.1(2)
C(21) - C(22) - C(23)	121.0(2)
C(22) - C(23) - C(24)	118.0(2)
N(1) - C(24) - C(19)	108.7(2)
N(1) - C(24) - C(23)	129.6(2)
C(19) - C(24) - C(23)	121.6(2)
C(9) - C(27) - C(28)	111.3(2)
C(9) - C(27) - C(29)	116.1(2)
C(9) - C(27) - O(30)	101.0(2)
C(28) - C(27) - C(29)	111.4(2)
C(28) - C(27) - O(30)	107.6(2)
C(29) - C(27) - O(30)	108.6(2)
C(7) - O(30) - C(27)	108.1(2)

Table 16. The observed and calculated structure factors for paspalicine (17).

H = 0				2	16	13	14	5	8	37	38	8	0	13	13
K	L	FO	FC	2	17	35	35	5	9	17	17	8	1	4	5
0	2	19	20	2	18	7	6	5	10	11	12	8	2	5	5
0	4	149	173	2	20	14	14	5	11	10	10	8	3	4	4
0	6	82	85	2	21	2	0	5	12	21	21	8	4	7	8
0	8	21	21	2	23	3	4	5	13	9	9	8	5	10	10
0	10	14	14	3	1	81	84	5	14	4	4	8	6	15	15
0	12	21	21	3	2	18	18	5	15	4	3	8	7	18	18
0	14	20	20	3	3	40	40	5	16	16	16	8	8	11	11
0	16	5	5	3	4	33	33	5	17	17	17	8	9	9	9
0	18	38	38	3	5	15	14	5	18	16	16	8	11	18	19
0	20	25	25	3	6	20	20	5	19	4	4	8	14	15	14
0	22	8	8	3	7	20	19	5	21	13	13	8	16	10	10
1	1	43	44	3	8	21	21	6	0	33	32	9	2	11	12
1	2	108	129	3	9	23	22	6	1	17	17	9	3	6	6
1	3	66	70	3	10	3	2	6	2	31	31	9	4	10	9
1	4	19	18	3	11	21	21	6	3	8	8	9	5	12	12
1	5	7	8	3	12	6	6	6	4	7	6	9	6	7	7
1	6	12	12	3	13	20	20	6	5	19	19	9	7	19	19
1	8	19	19	3	14	5	5	6	6	9	8	9	8	4	4
1	9	31	30	3	15	5	5	6	7	16	16	9	10	14	14
1	12	2	3	3	16	8	7	6	8	8	8	9	12	8	8
1	13	10	10	3	18	24	24	6	9	4	5	9	14	8	8
1	14	20	19	3	19	29	28	6	10	11	11	10	1	5	5
1	15	9	9	3	20	5	5	6	12	9	9	10	2	12	12
1	16	28	28	3	21	5	5	6	13	3	3	10	3	5	6
1	17	20	21	3	22	12	12	6	14	17	16	10	4	6	7
1	18	6	6	4	0	50	50	6	15	7	7	10	6	6	6
1	19	24	24	4	2	14	14	6	16	5	5	10	8	4	4
1	20	5	6	4	3	14	14	6	18	6	6	10	9	10	10
1	21	4	4	4	4	6	5	6	19	11	11	10	10	7	7
1	23	3	3	4	5	32	32	7	1	12	12	10	11	4	5
2	0	144	181	4	6	20	20	7	2	11	10	10	12	6	7
2	1	70	74	4	7	25	25	7	3	2	2	11	3	4	5
2	2	41	42	4	10	34	33	7	4	20	20	11	4	6	6
2	3	47	49	4	11	12	11	7	5	13	13	11	5	3	4
2	4	44	43	4	14	14	15	7	6	4	4	11	6	7	7
2	5	44	46	4	16	20	20	7	8	17	17				
2	6	34	35	4	17	7	7	7	9	9	9	H = 1			
2	7	43	42	4	18	20	21	7	10	18	18	K	L	FO	FC
2	8	12	12	4	20	3	3	7	11	3	3	0	1	40	42
2	9	29	29	4	21	4	4	7	12	5	5	0	3	24	23
2	10	9	9	5	1	8	8	7	13	16	15	0	4	17	16
2	11	5	5	5	2	33	30	7	14	11	11	0	5	25	26
2	12	22	21	5	3	2	2	7	15	5	5	0	6	31	30
2	13	7	7	5	5	19	18	7	16	25	25	0	7	18	17
2	14	7	8	5	6	22	22	7	17	8	8	0	8	44	45
2	15	4	5	5	7	24	24	7	18	4	5	0	9	47	46

Table 16 (Continued)

0	10	24	25	2	13	13	13	4	17	11	11	7	2	18	18
0	11	8	8	2	14	20	20	4	18	11	11	7	3	8	8
0	12	15	15	2	15	7	7	4	19	8	8	7	4	8	8
0	14	5	5	2	16	26	27	4	20	5	6	7	5	5	5
0	16	15	15	2	17	22	22	4	21	9	9	7	6	13	13
0	17	32	32	2	18	11	11	4	22	7	7	7	7	19	20
0	18	29	30	2	19	14	14	5	0	55	55	7	8	11	10
0	19	10	10	2	21	12	12	5	1	52	50	7	10	3	2
0	20	3	3	2	22	7	7	5	2	39	37	7	11	12	12
0	21	17	17	2	23	6	5	5	3	9	9	7	12	13	12
0	22	17	17	3	0	129	144	5	4	6	5	7	13	10	10
0	23	4	4	3	1	34	34	5	5	18	18	7	14	7	7
1	0	60	65	3	2	50	53	5	6	20	21	7	15	11	11
1	1	23	24	3	3	60	60	5	7	29	28	7	16	11	11
1	2	134	162	3	4	18	17	5	8	11	11	7	17	9	9
1	3	78	83	3	5	18	18	5	9	19	19	7	18	10	9
1	4	13	13	3	6	13	13	5	10	7	7	8	0	6	6
1	5	13	13	3	7	9	9	5	11	5	5	8	1	3	3
1	6	24	24	3	8	18	18	5	12	6	6	8	2	15	15
1	7	56	57	3	9	18	18	5	13	7	7	8	3	3	3
1	8	58	58	3	10	16	15	5	14	6	6	8	4	11	11
1	9	23	22	3	11	9	10	5	16	13	13	8	5	10	10
1	10	30	30	3	12	11	11	5	17	17	17	8	7	11	11
1	11	11	12	3	13	7	7	5	18	5	5	8	8	24	24
1	12	13	13	3	14	27	27	5	19	10	9	8	9	10	10
1	13	19	20	3	15	24	24	5	20	16	16	8	11	6	6
1	14	9	9	3	16	4	2	5	21	4	4	8	12	10	9
1	15	22	23	3	17	4	3	6	0	32	31	8	13	13	13
1	16	2	2	3	18	8	9	6	1	28	28	8	14	17	17
1	17	42	42	3	19	15	16	6	2	13	13	8	15	6	6
1	18	29	29	3	20	9	9	6	4	28	28	8	16	4	4
1	19	10	9	3	21	7	7	6	5	4	4	8	17	4	4
1	20	10	10	4	1	30	28	6	6	12	12	9	1	12	12
1	21	14	15	4	2	45	45	6	7	8	7	9	2	5	6
1	22	3	3	4	3	32	32	6	8	5	5	9	3	3	2
2	0	139	163	4	4	19	20	6	9	24	25	9	4	10	10
2	1	47	49	4	5	33	33	6	10	7	7	9	5	5	6
2	2	82	87	4	6	14	13	6	11	7	7	9	6	6	6
2	3	29	31	4	7	32	32	6	12	3	3	9	7	13	13
2	4	67	68	4	8	26	26	6	13	7	6	9	9	7	7
2	5	16	15	4	9	24	25	6	14	20	20	9	10	4	4
2	6	35	34	4	10	17	17	6	15	17	17	9	11	9	9
2	7	30	30	4	11	14	14	6	16	8	8	9	13	7	6
2	8	32	30	4	12	11	11	6	17	4	4	9	14	6	6
2	9	20	19	4	13	12	12	6	18	7	7	10	0	16	16
2	10	10	11	4	14	13	13	6	19	2	2	10	2	8	9
2	11	24	24	4	15	16	16	7	0	27	27	10	3	6	5
2	12	21	21	4	16	11	11	7	1	19	19	10	4	7	7

Table 16 (Continued)

10	5	10	10	1	9	82	82	3	12	18	17	5	17	11	10
10	6	4	4	1	10	46	46	3	13	9	9	5	18	5	6
10	7	4	4	1	11	38	38	3	14	20	20	5	19	3	3
10	8	16	16	1	12	27	27	3	15	6	6	6	0	6	7
10	10	10	10	1	13	27	28	3	16	7	6	6	1	10	10
11	0	4	3	1	14	7	7	3	17	32	32	6	2	32	32
11	1	5	5	1	15	19	20	3	18	7	7	6	3	19	18
11	2	3	3	1	16	15	15	3	19	8	8	6	4	39	40
11	3	7	7	1	17	18	18	3	20	12	13	6	5	12	12
11	4	2	3	1	18	7	6	3	21	10	10	6	7	7	7
11	5	4	4	1	19	14	15	4	0	22	22	6	8	15	15
11	6	5	6	1	20	13	12	4	1	16	15	6	9	18	18
11	7	4	4	1	21	6	5	4	2	85	85	6	10	12	12
				1	22	3	2	4	3	35	35	6	11	9	9
	H =	2		1	23	3	3	4	4	5	6	6	12	4	4
K	L	FO	FC	2	0	4	2	4	5	26	27	6	13	12	12
0	0	11	11	2	1	64	64	4	6	12	12	6	14	15	15
0	1	19	20	2	2	33	33	4	7	14	14	6	15	6	6
0	2	41	43	2	3	20	20	4	8	8	8	6	16	18	18
0	3	20	22	2	4	32	32	4	9	23	23	6	17	7	7
0	4	21	21	2	5	28	28	4	10	3	3	6	18	16	15
0	5	12	11	2	6	21	22	4	11	4	4	7	0	5	5
0	6	7	6	2	7	40	40	4	12	14	14	7	1	4	4
0	7	24	23	2	8	20	20	4	13	8	8	7	2	11	11
0	8	16	16	2	9	35	34	4	14	5	5	7	3	14	14
0	9	50	49	2	10	32	31	4	15	8	8	7	4	10	10
0	10	32	32	2	12	23	23	4	16	21	21	7	5	16	16
0	11	42	42	2	13	4	4	4	17	5	5	7	6	21	21
0	12	18	17	2	15	7	7	4	18	16	16	7	7	6	6
0	13	4	4	2	16	6	7	4	20	6	6	7	8	3	3
0	15	15	16	2	17	6	6	4	21	3	3	7	10	5	5
0	16	13	13	2	18	12	11	5	0	66	67	7	11	7	7
0	17	9	10	2	19	15	16	5	1	41	41	7	12	14	15
0	18	9	9	2	20	3	3	5	2	28	27	7	13	5	5
0	19	9	9	2	21	4	4	5	3	18	17	7	14	14	14
0	20	5	5	2	22	4	3	5	4	12	12	7	15	4	4
0	21	10	11	3	0	85	87	5	5	9	9	7	16	3	4
0	22	4	4	3	1	46	46	5	6	4	4	7	17	9	9
0	23	4	4	3	2	11	10	5	7	3	3	7	18	3	1
1	0	3	4	3	3	17	16	5	8	17	17	8	0	19	19
1	1	47	48	3	4	34	32	5	9	19	19	8	1	10	11
1	2	28	30	3	5	15	15	5	10	5	6	8	2	9	9
1	3	34	33	3	6	16	15	5	11	17	17	8	4	31	32
1	4	75	79	3	7	40	39	5	12	8	8	8	5	11	11
1	5	15	15	3	8	17	17	5	13	7	7	8	6	9	8
1	6	23	22	3	9	6	6	5	14	3	4	8	7	13	13
1	7	43	44	3	10	24	24	5	15	9	10	8	8	3	2
1	8	66	65	3	11	9	10	5	16	7	7	8	9	6	6

Table 16 (Continued)

8	10	10	10	0	13	23	23	2	18	3	4	5	0	20	20
8	11	6	6	0	14	6	6	2	19	10	10	5	1	42	42
8	12	8	8	0	15	9	8	2	20	4	4	5	2	14	14
8	13	8	9	0	16	8	8	2	21	7	6	5	3	17	18
8	14	6	6	0	17	16	15	2	22	5	5	5	4	20	20
8	15	8	8	0	18	6	6	3	0	14	14	5	5	14	14
8	16	6	5	0	19	8	8	3	1	17	18	5	6	33	32
9	1	5	5	0	20	3	2	3	2	16	16	5	7	13	13
9	2	15	15	0	21	6	7	3	3	29	30	5	8	9	8
9	3	6	6	0	22	5	5	3	4	35	34	5	9	18	18
9	4	5	4	1	0	18	18	3	5	31	30	5	10	4	4
9	5	13	13	1	1	61	63	3	6	4	4	5	11	14	14
9	6	16	16	1	2	31	31	3	7	8	8	5	12	13	14
9	8	9	9	1	3	11	11	3	8	27	27	5	13	4	4
9	9	10	10	1	4	21	21	3	9	21	20	5	14	5	5
9	10	10	10	1	5	23	22	3	10	14	14	5	15	14	14
9	11	5	6	1	6	13	12	3	11	14	14	5	16	10	10
9	12	9	9	1	7	26	25	3	12	14	14	5	17	6	5
9	13	10	10	1	8	57	55	3	13	15	15	5	18	11	11
9	14	7	6	1	9	41	40	3	14	15	15	5	19	17	17
10	0	3	3	1	10	28	27	3	15	5	6	5	20	8	7
10	1	10	10	1	11	9	9	3	17	3	3	6	0	44	45
10	2	9	8	1	12	21	20	3	18	19	19	6	1	6	5
10	3	9	9	1	14	3	3	3	19	5	5	6	2	28	28
10	4	3	3	1	15	13	14	3	20	7	6	6	3	16	16
10	5	5	4	1	16	8	8	3	21	3	2	6	4	32	33
10	6	3	4	1	17	3	4	4	0	20	20	6	5	10	10
10	9	11	12	1	19	12	12	4	1	23	24	6	6	6	6
10	10	5	5	1	20	5	5	4	2	28	29	6	7	21	21
10	11	10	10	1	21	5	5	4	3	5	5	6	8	9	9
11	0	4	4	2	0	29	27	4	4	37	36	6	9	9	9
11	1	3	3	2	1	44	44	4	5	7	7	6	10	24	24
11	3	7	7	2	2	30	30	4	6	13	12	6	11	8	8
11	4	4	4	2	3	11	13	4	7	19	19	6	12	5	5
11	5	10	10	2	4	65	66	4	8	16	16	6	13	17	17
				2	5	17	17	4	9	17	17	6	14	14	14
	H =	3		2	6	49	48	4	10	33	34	6	15	4	4
K	L	FC	FC	2	7	37	36	4	11	25	25	6	16	4	4
0	1	19	19	2	8	21	21	4	12	13	12	6	17	7	6
0	2	18	18	2	9	40	38	4	13	14	13	6	18	7	8
0	3	7	7	2	10	37	37	4	14	10	10	6	19	4	4
0	5	25	24	2	11	31	30	4	15	15	15	7	0	15	15
0	6	50	50	2	12	12	12	4	16	16	17	7	1	15	16
0	7	30	29	2	13	22	22	4	17	2	3	7	2	16	16
0	8	4	4	2	14	8	8	4	18	13	13	7	3	14	14
0	9	28	26	2	15	7	7	4	19	10	10	7	4	18	18
0	10	2	3	2	16	14	15	4	20	6	6	7	5	18	18
0	11	54	51	2	17	11	11	4	21	5	4	7	6	13	13

Table 16 (Continued)

7	7	11	11					2	8	16	15	4	17	7	7
7	8	6	7	H =	4			2	9	4	3	4	18	10	9
7	9	13	12	K	L	FO	FC	2	10	12	12	4	19	4	4
7	10	4	4	0	0	9	9	2	11	27	26	4	20	2	4
7	11	20	21	0	4	24	23	2	12	19	20	5	0	14	13
7	12	6	6	0	5	16	15	2	13	12	12	5	1	14	14
7	15	5	5	0	6	4	4	2	14	8	8	5	2	10	10
7	16	7	7	0	7	25	24	2	15	6	6	5	3	29	29
7	17	4	4	0	8	24	24	2	16	17	17	5	4	15	15
8	0	27	27	0	9	31	30	2	17	11	11	5	5	10	9
8	1	10	10	0	11	31	31	2	18	3	3	5	6	5	5
8	2	12	12	0	12	8	8	2	20	14	14	5	7	37	37
8	3	26	26	0	13	12	12	2	21	4	4	5	8	13	13
8	5	16	16	0	14	5	5	3	0	25	24	5	9	8	8
8	6	10	10	0	15	7	7	3	1	44	42	5	10	15	15
8	7	6	6	0	16	13	14	3	2	13	13	5	11	24	24
8	8	7	8	0	17	28	28	3	3	11	11	5	12	15	14
8	9	6	6	0	18	8	9	3	4	42	42	5	13	11	12
8	10	7	7	0	19	3	3	3	5	10	10	5	14	5	5
8	11	12	13	0	21	3	3	3	6	16	16	5	15	7	7
8	12	4	4	1	0	9	9	3	7	12	11	5	16	13	13
8	13	17	16	1	1	20	21	3	8	32	30	5	17	8	8
8	14	7	6	1	2	24	23	3	9	10	10	5	18	3	3
8	15	4	4	1	3	21	20	3	11	14	14	5	19	3	4
9	0	3	3	1	4	41	40	3	12	11	10	6	0	11	10
9	1	16	16	1	5	27	27	3	14	19	19	6	1	12	12
9	2	8	8	1	6	7	8	3	15	9	9	6	2	18	18
9	3	9	9	1	7	27	26	3	16	9	8	6	3	21	20
9	4	10	10	1	8	20	19	3	17	13	14	6	4	23	23
9	5	13	13	1	9	3	2	3	18	10	10	6	5	3	2
9	6	12	13	1	11	7	7	3	19	9	9	6	6	11	10
9	7	11	11	1	12	4	4	3	20	2	3	6	7	23	24
9	8	4	3	1	13	22	23	3	21	5	5	6	8	11	11
9	9	6	5	1	14	3	3	4	0	65	64	6	9	10	11
9	10	6	6	1	15	13	13	4	1	35	35	6	10	17	17
9	11	14	14	1	16	3	3	4	2	8	7	6	11	17	17
9	12	7	7	1	17	3	3	4	3	11	10	6	12	11	11
9	13	6	6	1	18	11	12	4	4	30	30	6	13	19	19
10	0	3	4	1	19	16	15	4	5	30	29	6	14	14	14
10	1	9	9	1	20	7	6	4	6	6	6	6	15	10	10
10	2	14	13	2	0	18	19	4	7	14	13	6	16	8	7
10	4	9	9	2	1	24	23	4	8	9	9	6	17	9	8
10	5	4	5	2	2	17	17	4	9	14	14	6	18	4	4
10	6	4	4	2	3	29	30	4	11	10	10	7	0	3	3
10	7	4	4	2	4	2	2	4	12	7	7	7	1	30	31
10	8	4	3	2	5	18	18	4	13	8	8	7	2	15	15
11	1	5	5	2	6	8	9	4	14	13	13	7	3	12	12
11	2	6	6	2	7	15	14	4	15	10	10	7	4	19	19

Table 16 (Continued)

7	5	21	21	0	4	3	3	2	18	7	7	5	12	12	12
7	6	15	16	0	5	50	50	2	19	3	3	5	13	7	7
7	7	11	10	0	7	7	7	2	20	6	6	5	14	3	3
7	8	8	8	0	8	3	2	3	0	10	10	5	15	9	9
7	10	5	5	0	9	35	35	3	1	19	19	5	16	7	7
7	11	8	9	0	10	16	17	3	2	26	26	5	17	12	11
7	12	3	3	0	11	13	13	3	3	38	36	5	18	7	7
7	13	13	13	0	12	9	9	3	4	11	10	6	0	3	3
7	14	5	5	0	13	14	14	3	5	14	13	6	1	4	4
7	15	8	8	0	14	8	8	3	6	4	4	6	2	14	14
8	1	9	9	0	16	22	23	3	7	18	18	6	4	3	2
8	2	14	14	0	17	21	22	3	8	12	12	6	5	19	20
8	3	28	28	0	18	9	9	3	9	18	17	6	6	11	11
8	5	14	14	1	0	44	43	3	10	4	4	6	7	12	13
8	6	6	6	1	1	21	21	3	12	15	15	6	8	7	7
8	7	9	9	1	2	12	12	3	13	8	8	6	9	12	12
8	8	6	6	1	3	26	26	3	14	6	6	6	10	9	9
8	9	17	17	1	4	12	12	3	16	3	4	6	11	13	13
8	10	9	9	1	5	14	14	3	17	13	14	6	12	11	11
8	11	6	6	1	6	17	16	3	18	4	3	6	13	11	11
8	12	5	5	1	7	8	8	3	19	3	3	6	14	7	7
8	13	13	13	1	8	18	18	4	0	5	5	6	15	9	8
9	0	9	9	1	9	27	26	4	1	15	14	6	16	3	4
9	1	15	15	1	10	9	10	4	2	11	11	7	1	14	14
9	2	6	6	1	11	11	11	4	3	11	11	7	2	4	4
9	3	8	9	1	12	12	12	4	4	4	3	7	3	5	4
9	4	6	6	1	14	17	16	4	5	8	8	7	4	27	27
9	5	7	7	1	15	20	20	4	6	11	11	7	5	13	14
9	6	12	12	1	16	6	6	4	8	5	5	7	6	15	15
9	7	7	6	1	17	4	4	4	9	28	28	7	7	18	18
9	8	9	9	1	18	14	13	4	10	9	9	7	8	11	11
9	9	5	5	1	19	4	4	4	11	9	9	7	9	11	11
9	10	6	6	1	20	4	4	4	12	5	4	7	10	14	14
9	11	4	4	2	0	15	15	4	13	18	18	7	11	21	20
10	0	3	2	2	1	24	23	4	14	11	12	7	12	12	12
10	1	6	6	2	2	29	29	4	16	8	8	7	13	4	4
10	2	3	2	2	3	8	7	4	18	8	8	7	14	5	4
10	3	3	3	2	4	20	21	4	19	8	8	7	15	6	6
10	4	6	6	2	5	28	29	5	0	11	10	8	1	20	20
10	5	4	4	2	6	17	17	5	1	10	10	8	2	16	16
10	6	3	3	2	7	9	9	5	3	21	21	8	3	7	7
10	7	3	2	2	9	15	15	5	4	11	11	8	4	13	13
				2	10	15	15	5	5	10	10	8	5	6	5
	H =	5		2	11	9	10	5	6	9	9	8	7	10	9
K	L	FO	FC	2	12	3	4	5	8	11	11	8	8	6	6
0	1	12	11	2	13	4	3	5	9	10	10	8	9	8	8
0	2	4	3	2	16	12	12	5	10	17	17	8	10	5	5
0	3	20	20	2	17	4	4	5	11	11	11	8	11	7	7

Table 16 (Continued)

9	0	8	9	1	13	9	9	4	9	14	14	7	11	13	12
9	1	6	6	1	14	12	12	4	10	19	19	7	12	7	7
9	2	5	4	1	15	13	12	4	11	14	15	7	13	3	4
9	3	4	4	1	17	8	8	4	13	8	8	8	1	7	7
9	4	10	10	1	18	2	2	4	14	10	10	8	2	3	2
9	5	4	5	1	19	7	8	4	15	6	7	8	3	8	8
9	6	6	6	2	2	13	13	4	16	3	3	8	4	6	6
9	7	5	5	2	3	14	14	4	17	3	2	8	6	9	8
9	8	7	7	2	4	13	13	5	0	16	16	8	7	8	8
9	9	3	4	2	6	11	11	5	1	3	3	8	8	4	5
10	0	5	5	2	7	25	24	5	2	7	7	8	9	5	5
10	1	11	11	2	8	5	5	5	3	5	4	8	10	5	5
10	2	3	3	2	9	32	33	5	4	15	15	9	0	7	8
10	3	7	7	2	10	23	23	5	5	21	21	9	1	3	4
10	4	9	9	2	11	13	13	5	6	8	8	9	2	2	2
				2	12	5	4	5	7	3	4	9	3	11	12
	H =	6		2	13	11	11	5	8	13	14	9	4	5	5
K	L	FO	FC	2	14	3	4	5	9	30	30	9	5	11	11
0	0	9	9	2	15	13	13	5	10	8	8	9	6	5	5
0	1	2	2	2	16	4	4	5	11	16	16				
0	2	8	8	2	17	10	10	5	12	12	12		H =	7	
0	3	14	14	2	18	6	6	5	13	8	8	K	L	FC	FC
0	4	22	22	2	19	7	6	5	14	10	9	0	1	10	10
0	5	8	8	3	0	3	4	5	15	6	7	0	3	4	4
0	6	8	8	3	1	4	5	5	16	7	6	0	4	12	11
0	7	45	44	3	2	9	9	6	0	4	4	0	5	12	12
0	8	26	25	3	3	17	16	6	1	19	19	0	6	16	15
0	9	14	15	3	4	5	4	6	2	6	6	0	7	28	27
0	10	5	4	3	5	25	25	6	3	6	6	0	8	11	11
0	11	6	6	3	6	6	7	6	4	15	15	0	9	17	17
0	12	16	15	3	7	6	5	6	5	4	4	0	10	34	34
0	13	15	15	3	8	24	24	6	6	11	12	0	11	32	32
0	14	3	2	3	9	12	13	6	7	21	22	0	12	13	13
0	16	6	7	3	10	10	10	6	8	10	10	0	14	9	9
0	17	16	16	3	11	20	20	6	9	14	14	0	15	14	15
0	18	4	5	3	12	24	24	6	10	7	7	0	16	9	8
0	19	3	4	3	13	10	10	6	11	7	7	0	17	6	5
1	1	12	11	3	15	8	7	6	14	7	6	1	0	19	19
1	2	10	11	3	16	7	7	6	15	2	2	1	2	16	16
1	3	15	14	3	18	3	3	7	1	10	11	1	3	4	4
1	4	14	14	4	0	3	2	7	2	8	8	1	4	9	10
1	5	23	23	4	1	9	10	7	3	10	11	1	5	15	15
1	6	5	5	4	2	9	9	7	4	7	7	1	6	21	21
1	8	4	4	4	4	3	3	7	6	9	9	1	7	15	15
1	9	22	22	4	5	8	8	7	7	9	8	1	8	28	28
1	10	5	5	4	6	19	19	7	8	7	6	1	9	21	21
1	11	18	18	4	7	18	18	7	9	13	13	1	10	6	7
1	12	5	4	4	8	5	6	7	10	5	5	1	11	3	3

Table 16 (Continued)

1	12	14	14	4	9	7	7	0	2	4	4	3	11	3	3
1	13	7	7	4	10	4	4	0	3	8	8	3	13	9	8
1	14	6	7	4	11	7	7	0	4	4	5	4	0	15	15
1	15	11	11	4	12	10	9	0	5	17	17	4	1	12	12
1	16	4	4	4	13	8	8	0	6	15	15	4	2	16	16
2	0	3	3	4	14	13	13	0	8	22	22	4	3	13	13
2	1	8	8	4	15	8	7	0	11	8	7	4	4	8	8
2	2	4	4	5	0	8	8	0	12	8	7	4	5	5	5
2	3	9	9	5	1	8	8	0	14	3	1	4	6	14	14
2	4	8	8	5	3	8	8	1	0	16	16	4	7	5	6
2	5	23	23	5	4	11	11	1	1	6	6	4	8	11	11
2	6	15	16	5	5	11	11	1	2	9	9	4	9	8	8
2	7	17	17	5	6	12	12	1	3	14	14	4	10	5	5
2	8	6	6	5	7	11	11	1	5	5	5	4	11	3	3
2	9	24	24	5	8	16	16	1	6	23	23	5	0	10	9
2	10	28	28	5	9	4	3	1	7	40	40	5	1	7	7
2	11	16	15	5	10	5	4	1	8	10	9	5	2	4	4
2	12	5	5	5	13	9	9	1	9	6	6	5	3	6	6
2	13	3	3	6	0	3	2	1	10	8	8	5	4	6	6
2	14	8	8	6	1	7	7	1	11	9	9	5	5	5	6
2	15	8	8	6	2	5	6	1	12	4	5	5	7	10	9
2	16	5	5	6	3	8	9	1	13	12	12	5	8	4	5
2	17	7	7	6	4	15	14	1	14	5	5	5	11	4	5
3	1	16	15	6	5	5	5	2	0	11	12	6	0	8	9
3	2	15	15	6	6	10	11	2	1	9	9	6	1	5	5
3	3	8	8	6	7	7	7	2	2	3	4	6	2	9	9
3	4	8	8	6	8	5	5	2	3	3	2	6	3	11	10
3	5	7	8	6	9	14	14	2	4	10	10	6	4	5	5
3	6	10	10	6	11	3	3	2	5	11	11	6	5	7	7
3	7	17	18	7	1	7	8	2	6	19	20	6	6	9	9
3	8	25	24	7	2	4	4	2	7	5	6	6	7	5	5
3	9	20	20	7	3	8	8	2	8	11	11	6	9	4	4
3	10	7	7	7	4	4	5	2	9	4	4	7	0	8	7
3	11	6	6	7	5	4	3	2	10	6	6	7	2	3	3
3	12	11	11	7	6	7	7	2	11	11	12	7	3	7	7
3	13	7	7	7	7	10	11	2	12	12	12	7	4	3	3
3	14	3	3	7	8	5	5	2	13	5	5	7	5	3	2
3	15	3	3	7	9	3	2	2	14	7	7				
3	16	5	5	7	10	5	5	3	0	14	14		H =	9	
4	0	7	6	8	0	18	18	3	1	8	9	K	L	FO	FC
4	1	11	12	8	1	3	3	3	2	3	2	0	1	14	14
4	2	15	15	8	3	2	3	3	3	11	11	0	2	3	3
4	3	7	7	8	4	4	4	3	4	6	5	0	3	11	11
4	4	7	7	8	5	10	10	3	5	7	7	0	5	8	8
4	5	13	14					3	6	5	5	0	7	12	12
4	6	29	30		H =	8		3	7	13	13	0	8	10	9
4	7	19	19	K	L	FO	FC	3	8	3	3	0	10	7	7
4	8	6	7	0	0	20	20	3	9	10	10	0	11	5	5

Table 16 (Continued)

0	12	5	5	6	0	7	6
1	1	26	26	6	1	3	4
1	2	22	22				
1	3	14	14		H =	10	
1	4	8	7	K	L	FO	FC
1	5	12	12	0	0	16	16
1	6	5	6	0	1	3	4
1	7	9	10	0	2	13	14
1	8	9	9	0	3	13	13
1	9	3	3	0	4	11	11
1	10	5	5	0	5	14	14
1	11	7	7	0	6	9	9
2	0	8	8	0	7	6	6
2	1	9	10	1	1	5	4
2	2	4	5	1	2	3	2
2	3	11	11	1	3	8	8
2	4	4	5	1	4	3	3
2	5	10	10	1	5	7	7
2	6	4	3	1	6	5	5
2	7	10	10	1	7	5	5
2	8	5	5	2	0	15	14
2	9	5	4	2	1	5	5
2	10	4	4	2	2	7	7
2	11	3	3	2	3	7	7
3	1	7	7	2	4	12	11
3	2	6	6	2	5	8	8
3	3	8	8	2	6	5	4
3	5	6	6	3	1	2	1
3	6	4	5	3	2	8	7
3	7	3	4	3	3	7	8
3	8	2	1	3	4	5	4
3	9	9	9				
3	10	10	9				
4	1	4	5				
4	2	9	10				
4	3	6	6				
4	4	3	3				
4	5	6	6				
4	7	9	8				
4	8	9	9				
4	9	4	3				
5	0	8	9				
5	1	3	2				
5	2	12	12				
5	3	6	6				
5	4	4	4				
5	5	6	6				
5	6	3	4				

Discussion - Paspalicine

The solution of the crystal structure of paspalicine 17 confirms the basic skeleton of the molecule as previously described (46). Paspalicine 17 again possesses a similar, rigid, multi-cyclic system as paspaline 16 and paxilline 15. The differences between paspalicine 17 and paxilline 15 being that the hydroxyl group on C(13) of paxilline 15 has been replaced by a hydrogen and O(30) has bonded to C(7) to form a five-membered ring ketal. All bond lengths and angles are chemically reasonable and no abnormally short intermolecular contacts exist (23). The relative stereochemical configurations of all equivalent asymmetric centers are identical for paspaline 16, paspalicine 17, and paxilline 15 except that the configuration around C(7) is inverted in the formation of the ketal in paspalicine 17. The CD spectrum of paspalicine 17 shows a positive Cotton effect for the band at 348nm with $[\theta] = + 3.9 \times 10^4$. Because the equivalent band in the CD spectrum of paxilline 15 is also strongly positive pazilline 15 most probably corresponds to the same absolute configuration as paspalicine 17. Since the absolute configuration of paspaline 16 is known and paspalicine 17 comes from the same fungal source paspaline 16, paspalicine 17, and paxilline 15 possess the absolute configurations indicated. Limited amounts of paspalicine 17 precluded toxicity or tremorgenic tests.

ACKNOWLEDGMENT

I acknowledge the assistance and encouragement especially provided by my advisor Professor Jon Clardy, as well as other members of the staff and students at Iowa State University.

REFERENCES

1. "...and all the water that was in the Nile turned to blood. And the fish in the Nile died; and the Nile became foul, so that the Egyptians could not drink water from the Nile; and there was blood throughout all the lands of Egypt." Exodus 7:20-21.

2. E.J. Schantz, J. Agr. Food Chem., 17, 413 (1969).

3. H. Sommer, W.F. Whedon, C.A. Kofoid, and R. Stohler, Arch. Pathol., 24, 537 (1937).

4. E.J. Schantz, J.M. Lynch, G. Voyvada, K. Matsumoto, and H. Rapoport, Biochemistry, 5, 1191 (1966).

5. A.B. Needler, J. Fisheries Res. Board Can., 7, 490 (1949).

6. A. Prakash, J. Fisheries Res. Board Can., 20, 983 (1963).

7. E.J. Schantz and H.W. Magnusson, J. Protozool., 11, 239 (1964).

8. W. Schuett and H. Rapoport, J. Amer. Chem. Soc., 84, 2266 (1962).

9. E.J. Schantz, J.D. Mold, D.W. Stanger, J. Shavel, F.J. Riel, J.P. Bowden, J.M. Lynch, R.S. Wyler, B. Riegel, and H. Sommer, J. Amer. Chem. Soc., 79, 5230(1957).

10. H. Sommer and K.F. Meyer, Arch. Pathol., 24, 560 (1937).

11. E.J. Schantz, J.D. Mold, W.L. Howard, J.P. Bowden, D.W. Stanger, J.M. Lynch, O.P. Wintersteiner, J.D. Dutcher, D.R. Walters, and B. Riegel, Can. J. Chem., 39, 2117 (1961).

12. J.D. Mold, J.P. Bowden, D.W. Stanger, J.E. Maurer, J.M. Lynch, R.S. Wyler, E.J. Schantz, and B. Riegel, J. Amer. Chem. Soc., 79, 5235 (1957).

13. J.L. Wong, M.S. Brown, K. Matsumoto, R. Oesterlin, and H. Rapoport, J. Amer. Chem. Soc., 93, 4633 (1971).

14. J.L. Wong, R. Oesterlin, and H. Rapoport, J. Amer. Chem. Soc., 93, 7344 (1971).

15. Private communication from George Büchi.

16. A preliminary report of the present work has been published. E.J. Schantz, V.E. Ghazarossian, H.K. Schoes, F.M. Strong, J.P. Springer, J.O. Pezzanite, and J. Clardy, J. Amer. Chem. Soc., 97, 1238 (1975).

17. Subsequent to the publication of the present work a report appeared of a crystallographic and cmr analysis of saxitoxin ethyl hemiketal dihydrochloride confirming the present structure. J. Bordner, W.E. Thiessen, H.A. Bates, and H. Rapoport, J. Amer. Chem. Soc., 97, 6008 (1975).

18. $|Frel| = (I/Lp)^{1/2}$ with $L = 1/\sin 2\theta$ and $\rho = .5\ (1 + \cos^2 \chi \cos^2 2\theta)/(1 + \cos^2 \chi) + .5\ (1 + \cos \chi \cos^2 2\theta)/(1 + \cos \chi)$ where 2θ is the Bragg angle of the reflection and χ is the angle between the X-ray beam off the target and the X-ray beam off the monochrometer. All X-ray data were collected with a Syntex P_{2_1} diffractometer using 1° ω scans.

19. The following library of crystallographic programs was used: C.R. Hubbard, C.O. Quicksall, and R.A. Jacobson, "The Fast Fourier Algorithm and the programs ALFF, ALFFDP, ALFFPROJ, ALFFT, and FRIEDEL", USAEC Report IS-2625, Iowa State University - Institute for Atomic Research, Ames, Iowa, 1971; W.R. Busing, K.O. Martin, and H.A. Levy, "ORFLS, A Fortran Crystallographic Least-Squares Program", USAEC Report ORNL-TM-305, Oak Ridge National Laboratory, Oak Ridge, Tenn., 1965; C. Johnson, "ORTEP-II, A Fortran Thermal-Ellipsoid Plot Program", USAEC Report ORNL-3794 (2nd Revision with Supplemental Instructions), Oak Ridge National Laboratory, Oak Ridge, Tenn., (1970).

20. G. Germain, P. Main, and M.M. Woolfson, Acta Cryst., B26, 274 (1970).

21. The function minimized was $\Sigma\omega(|F_o|-|F_c|)^2$ with $\omega = 1/(\sigma F_o)^2$ where $\sigma F_o = .5\ \sigma(I)/(LpI)^{1/2}$ x scan rate. The unweighted residual (R factor) is $\Sigma||F_o| - |F_c||/\Sigma|F_o|$. The scattering factors were from H.P. Hanson, F. Herman, J.D. Lea, and S. Skillman, Acta Cryst., 17, 1040 (1960) and from International Tables of X-Ray Crystallography, Vol. II, 2nd ed. (Kynoch Press, Birmingham, England, 1968).

22. W. Hamilton, Acta Cryst., 18, 502 (1965).

23. O. Kennard, D.G. Watson, F.H. Allen, N.W. Isaacs, W.D.S. Motherwell, R.C. Petterson, and W.G. Town, Molecular Structures and Dimensions, Vol. A1 (Crystallographic Data Centre, Cambridge, 1972); International Tables of X-Ray Crystallography, Vol. III, 2nd ed., (Kynoch Press, Birmingham, England, 1968).

24. E. Grunwald and B.J. Berkowitz, J. Amer. Chem. Soc., 73, 4939 (1951); B. Gutbezahl and E. Grunwald, J. Amer. Chem. Soc., 75, 559 (1953).

25. P.J. Scheuer, Chemistry of Marine Natural Products (Academic Press, New York, 1973), p. 149.

26. T. Narahashi, Science, 157, 1441 (1967).

27. C.Y. Kao and A. Nishiyama, J. Physiol. (London), 180, 50 (1965).

28. B. Hille, J. Gen. Physiol., 58, 599 (1971).

29. B. Hille, Biophysical Journal, 15, 615 (1975).

30. V.E. Ghazarossian, E.J. Schantz, H.K. Schoes, and F.M. Strong, Biochem. Biophys. Res. Commun., 68, 776 (1975).

31. H.A. Bates and H. Rapoport, J. Agr. Food Chem., 23, 237 (1975).

32. G.M. Everett, L.E. Blockus, and I.M. Shepperd, Science, 124, 79 (1956).

33. J. Fayos, D. Lokensgard, J. Clardy, R.J. Cole, J.W. Kirksey, J. Amer. Chem. Soc., 96, 6785 (1974) and references cited therein.

34. N. Eickman, J. Clardy, R.J. Cole, and J.W. Kirksey, Tetrahedron Letters, 1051 (1975).

35. L.R. Caporael, Science, 192, 21 (1976).

36. A. Stoll, Helv. Chim. Acta, 28, 1283 (1945).

37. H.G. Floss, Tetrahedron, 32, 873 (1976) and references cited therein.

38. K.C. Mattes, C.R. Hutchinson, J.P. Springer and J. Clardy, J. Amer. Chem. Soc., 97, 6270 (1975).

39. A.R. Battersby, A.R. Burnett, and P.G. Parsons, Chem. Commun., 1282 (1968); A.R. Battersby, A.R. Burnett, and P.G. Parsons, J. Chem. Soc. C, 1193 (1969).

40. N.S. Narasimhan, M.V. Paradkar, and V.P. Chitguppi, Tetrahedron Letters, 5501 (1968).

41. Th. Fehr and W. Acklin, Helv. Chim. Acta, 49, 1907 (1966).

42. R.J. Cole, J.W. Kirksey and J.M. Wells, Can. J. Microbiol., 20, 1159 (1974).

43. A description of the structure of paxilline 15 has been published. J.P. Springer, J. Clardy, J.M. Wells, R.J. Cole, and J.W. Kirksey, Tetrahedron Letters, 2531 (1975).

44. J. Karle, Acta Cryst., B24, 182 (1968).

45. R.P. Gysi, Dissertation No. 4990, Eidgenössischen Technischen Hochschule, Zürich, Switzerland, 1973.

46. A. Leutwiler, Dissertation No. 5163, Eidgenössischen Technischen Hochschule, Zürich, Switzerland, 1973.