

## The Structure of Bipolaramide, a Novel Dioxopiperazine from *Bipolaris sorokiniana*

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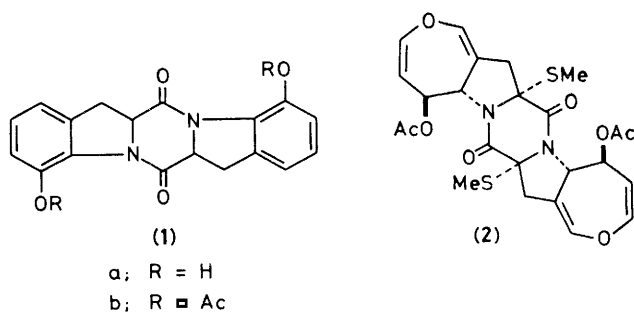
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The structure of bipolaramide, a new dioxopiperazine from cultures of *Bipolaris sorokiniana*, is based on the X-ray crystallographic study of this substance.

In the course of previous studies<sup>1</sup> on a toxigenic strain of a *Bipolaris* sp. (IMI 115076), curvularin, bipolarin, and the carcinogen sterigmatocystin were identified. We now report the structure elucidation of a new dioxopiperazine, bipolaramide (**1a**), isolated from whole maize cultures of a toxigenic strain of *Bipolaris sorokiniana* (Saccardo in Sorok) Shoem. (MRC 93). This strain was isolated in the Karroo from an indigenous weed *Tribulus terrestris*; its toxigenicity was also attributed to the production of sterigmatocystin.

Bipolaramide (**1a**) crystallized from acetone as colourless needle-shaped crystals, m.p. 296–297 °C, and analysed for C<sub>18</sub>H<sub>14</sub>N<sub>2</sub>O<sub>4</sub> (*M*<sup>+</sup>, 322); it had [α]<sub>D</sub><sup>20</sup> –210° (*c* 1.0, acetone); λ<sub>max</sub> (MeOH) 218, 260, and 294 nm (log ε 4.65, 4.17, and 3.88, respectively); ν<sub>max</sub> (KBr) 1645 (amide CO) and 1610 cm<sup>-1</sup>; δ<sub>H</sub> (acetone) 7.15 (1H, t, *J* 7.5 Hz), 6.87 (1H, dd, *J* 7.5, 2.8 Hz), 6.80 (1H, dd, *J* 7.5, 2.8 Hz), 5.53 (1H, t, *J* 9.8 Hz), 3.78 (1H, dd, *J* 17.3, 9.8 Hz), 3.51 (1H, dd, *J* 17.3, 9.8 Hz), and 11.40 (D<sub>2</sub>O-removable hydroxy-group); and δ<sub>C</sub> [(CD<sub>3</sub>)<sub>2</sub>CO] 164.5(s), 145.1(s), 132.4(d), 127.5(d), 126.3(d), 116.4(d), 115.4(d), 61.4(d), and 30.3 p.p.m. (t). These data indicated the presence of three contiguous aromatic protons and of an ABX aliphatic system. The vicinal coupling constants (*J* 9.8 Hz) observed for the ABX system are in accordance with the dihedral angular relationship obtained from X-ray crystallography viz. 149.8 and 31.6° for H(3)–C(3)–C(4)–H(4A) and H(3)–C(3)–C(4)–H(4B), respectively.



Bipolaramide is a symmetrical dimer as indicated by its physical characteristics and molecular weight (*M*<sup>+</sup>, 322 and a fragment peak at *m/e* 161). Acetylation of bipolaramide gave di-*O*-acetylbipolaramide (**1b**), C<sub>22</sub>H<sub>18</sub>N<sub>2</sub>O<sub>6</sub>, m.p. 240–242 °C (acetone).

A single-crystal X-ray structure determination of bipolaramide (**1a**) was carried out. *Crystal data*: the crystals are orthorhombic, space group *P*2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>, with *a* = 24.55(1), *b* = 8.08(1), *c* = 7.22(1) Å, and *Z* = 4. Intensity measurements were made with Mo-*K*<sub>α</sub> radiation (λ = 0.7107 Å; graphite monochromator) on a modified Hilger and Watts four-circle diffractometer in the ω–2θ mode with 3 ≤ θ ≤ 27°. 1835 reflections were measured of which 105 were

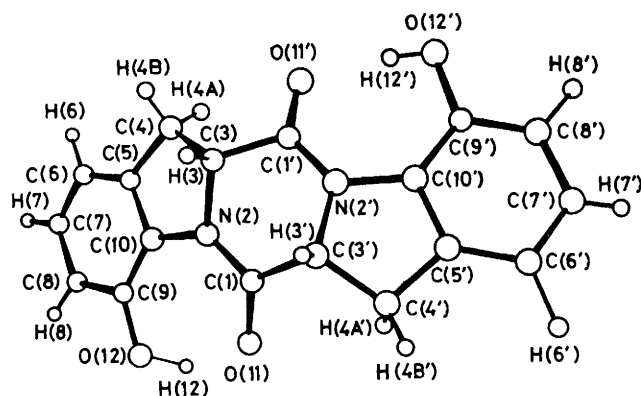


Figure 1. The crystallographic atomic numbering of bipolaramide.

regarded as unobserved with  $I < 2\sigma(I)$ , and the measured intensities were corrected for background and Lorentz-polarization effects only. Accurate cell parameters were obtained by least squares techniques from the setting of 25 reflections. The structure was refined by full-matrix least squares using  $\sigma_F^{-2}$  weights. The final  $R$  factors are  $R = \Sigma|\Delta F|/\Sigma|F_0| = 0.131$  and  $R_w = \Sigma w|\Delta F|/\Sigma w|F_0| = 0.061$ . The SHELX program system was used for all crystallographic computations.<sup>2†</sup>

The atomic numbering scheme is shown in Figure 1. Hydrogen atoms are numbered according to the numbers of the atoms to which they are attached.

In order to identify the conformation of the non-planar rings in the system, their puckering parameters were calculated as described by Cremer and Pople.<sup>3</sup> The schemes by Altona and Sundaralingam<sup>4</sup> and Boeyens<sup>5</sup> were used to deduce the conformations unequivocally from the puckering constants and the results are listed in Table 1.

Strong intramolecular hydrogen bonding exists and the O-H...O distances are 1.783 and 1.781 Å. The molecule

† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

Table 1. Puckering parameters and conformation of the non-planar rings.

Ring	$\phi$	$\theta$	$Q$	Conformation <sup>a</sup>
N(2)-C(3)-C(1')-N(2')-C(3')-C(1)	243.3	88.8	0.54	<sup>2,5</sup> B
N(2)-C(10)-C(5)-C(4)-C(3)	139.8	—	0.17	<sup>5</sup> E + <sup>5</sup> T
N(2')-C(10')-C(5')-C(4')-C(3')	137.6	—	0.17	<sup>5</sup> E + <sup>5</sup> T

<sup>a</sup> The numerical position of a ring atom in the sequences of the first column is used as an identifier in the conformational symbols of the last column, where B, E, and T represent a boat, envelope, and twist-boat conformation, respectively (ref. 5). The symbols  $Q$ ,  $\theta$ , and  $\phi$  represent the amplitude and phase co-ordinates of the puckering geometry (ref. 3).

consists of two identical halves and analysis of the two parts shows no significant differences in the corresponding bond lengths, bond angles, or torsion angles. The puckering analysis shows that both five membered rings have identical conformations, viz. <sup>5</sup>E + <sup>5</sup>T (ca. 70:30). The central six membered ring has a <sup>2,5</sup>B conformation.

Bipolaramide has an interesting biosynthetic and structural resemblance to aranotin and bisdethiobis(methylthio)acetylaranotin (2), metabolites of *Arachniotus aureus*<sup>6</sup> and *Aspergillus terreus*.<sup>7</sup> It seems probable that bipolaramide is formed from *cyclo*(phenylalanylphenylalanyl) which undergoes epoxidation and cyclization during the biosynthesis.

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