Crystal Structure of 7-Methoxy-4-[(E)-oct-1-enyl]pyrrolo[1,2-a]quinoxaline

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The X-ray crystal structure of the antileishmanial 7-methoxy-4-[(E)-oct-1-enyl]pyrrolo[1,2-a]quinoxaline was established. It crystallizes in the monoclinic space group $P2_1/c$. Solid-state data could be used to clarify the mechanism of action implicating this new antileishmanial 4-(E)-alkenylpyrrolo[1,2-a]quinoxaline.

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Leishmaniasis is caused by different species belonging to the genus *Leishmania*, a protozoan that is transmitted to humans by the bite of an insect vector, phlebotomine sandfly. Leishmaniasis has an overwhelming impact on global public health, and is endemic in many tropical and subtropical regions of the world. It affects around 12 million people of the world, and 350 million are estimated to be prone to the disease, of which around 1.7 million people will be infected each year. The infection by various strains of *Leishmania* causes a wide spectrum of disease in humans, with many different clinical manifestations, that is, cutaneous, mucocutaneous and visceral.¹

In the course of our work on the synthesis of new

antileishmanial drugs, we have focused our interest in the synthesis of 4-(E)-alkenylpyrrolo[1,2-a]quinoxalines,^{2,3} new structural analogues of alkaloid chamanine B.⁴ These 4-(E)-alkenylpyrrolo[1,2-a]quinoxalines were synthesized in good yields using efficient palladium(0)-catalyzed Suzuki-Miyaura cross-coupling reactions.³

Fig. 1 Chemical structure of 7-methoxy-4-[(E)-oct-1-enyl]pyrrolo[1,2-a]quinoxaline.

Table 2 Final atomic coordinates and equivalent isotropic thermal parameters ($U_{eq}(\text{\AA}^2)$)

Atom	<i>x</i>	<i>y</i>	<i>z</i>	U_{eq}
C(1)	0.2028(3)	0.1364(1)	-0.2072(2)	0.0081(1)
C(2)	0.1493(3)	0.2113(1)	-0.2446(2)	0.0066(1)
C(3)	0.2028(3)	0.2655(1)	-0.1491(2)	0.0058(1)
C(4)	0.1455(3)	0.3399(1)	-0.1875(2)	0.0057(1)
C(5)	0.1945(3)	0.3972(1)	-0.0963(2)	0.0057(1)
C(6)	0.1311(3)	0.4693(1)	-0.1451(2)	0.0061(1)
C(7)	0.1746(3)	0.5318(1)	-0.0669(2)	0.0058(1)
C(8)	0.2760(3)	0.5348(1)	0.0382(2)	0.0058(1)
C(9)	0.3098(2)	0.6004(1)	0.1064(2)	0.0054(1)
N(10)	0.2536(2)	0.6602(1)	0.0553(1)	0.0055(1)
C(11)	0.2835(2)	0.7220(1)	0.1212(2)	0.0050(1)
C(12)	0.3713(2)	0.7236(1)	0.2386(2)	0.0051(1)
N(13)	0.4336(2)	0.6588(1)	0.2891(2)	0.0052(1)
C(14)	0.4034(2)	0.5965(1)	0.2253(1)	0.0054(1)
C(15)	0.4801(3)	0.5424(1)	0.2987(2)	0.0066(1)
C(16)	0.5575(3)	0.5724(1)	0.4061(2)	0.0070(1)
C(17)	0.5280(3)	0.6434(1)	0.3988(2)	0.0063(1)
C(18)	0.2215(3)	0.7858(1)	0.0655(1)	0.0055(1)
C(19)	0.2467(3)	0.8486(1)	0.1257(2)	0.0057(1)
C(20)	0.3312(3)	0.8486(1)	0.2434(2)	0.0062(1)
C(21)	0.3924(3)	0.7871(1)	0.2992(2)	0.0059(1)
O(22)	0.1925(2)	0.9135(1)	0.0795(2)	0.0074(1)
C(23)	0.1035(3)	0.9158(1)	-0.0398(2)	0.0078(1)

$$U_{eq} = (1/3)\sum_i \sum_j U_{ij}(a_i^* a_j^*)(a_i a_j).$$

We report herein the structural characterization of one of them, *i.e.* the 7-methoxy-4-[(*E*)-oct-1-enyl]pyrrolo[1,2-*a*]quinoxaline (Fig. 1), which shows antileishmanial activity *in vitro* upon the *Leishmania amazonensis* (IC₅₀ = 2 μM) and *Leishmania infantum* strains (IC₅₀ = 1.2 μM).

Pale-yellow crystals suitable for X-ray analysis were obtained by slow crystallization from an ethanol solution at 0°C. The structure of 7-methoxy-4-[(*E*)-oct-1-enyl]pyrrolo[1,2-*a*]quinoxaline is illustrated in Fig. 2. Crystal and experimental data are given in Table 1.

The 3D spatial structure of the 4-octenylpyrrolo[1,2-*a*]quinoxaline showed the (*E*)-isomerism of the 4-lateral C₈ α-unsaturated alkenyl chain in the solid state, as anticipated based on ¹H NMR data.³ The *trans* C(8)–C(7) octenyl double bond was noticed at 1.308(3) Å, as typically observed for C=C double bonds.

The pyrrolo[1,2-*a*]quinoxaline moiety is almost planar, and the maximum deviation from planarity is found for C(21) lying –0.0414(2) Å from the plane defined by the hetero-tricyclic

Table 3 Hydrogen-bonding geometry (Å, °)

C–H...A	H–A	C–A	N–H...A
C(7)–H(7)...N(10)	2.46	2.820(3)	103

system. The 4-(*E*)-octenyl chain was also found to be quite planar; a deviation of the C(5) atom was noticed at –0.0586(2) Å from the least-square plane defined by the other atoms of the alkenyl group. The angle between the least-squares planes, defined by the pyrroloquinoxaline moiety and the alkenyl chain, was approximately 4.18(1)°. The final atomic coordinates and the equivalent isotropic thermal parameters are listed in Table 2.

The alkenyl chain substituted at position 4 adopts a quite regular conformation, described by the torsion angles C(1)–C(2)–C(3)–C(4), C(2)–C(3)–C(4)–C(5), C(3)–C(4)–C(5)–C(6), C(4)–C(5)–C(6)–C(7) and C(6)–C(7)–C(8)–C(9), which are –179.0(2), 180.0(2), 179.7(2), –177.9(2) and 179.4(2)°, respectively. However, the C(5)–C(6)–C(7)–C(8) angle was noticed at 6.9(3)°, involving such a conformation of this 4-lateral chain through rotation around the C(6)–C(7) bond.

There are no solvent accessible voids in the crystal lattice of the 4-(*E*)-octenylpyrrolo[1,2-*a*]quinoxaline. The structure exhibits an intramolecular hydrogen bond of the type C–H...N (Table 3).

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