Structures of Paraensidimerins B, E, F, and G, Four New Dimeric Quinolinone Alkaloids from *Euxylophora paraensis*

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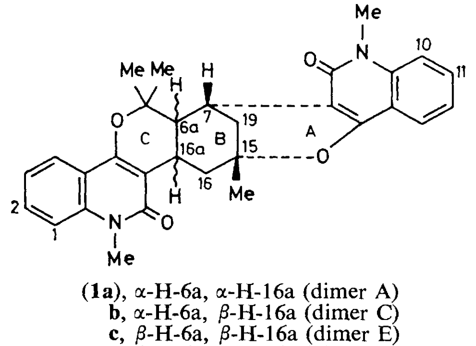
Paraensidimerins E and F, two new alkaloids from the heartwood of *Euxylophora paraensis* (Rutaceae), have been shown to be the heptacyclic bis-quinolin-2-one derivatives (**1c**) and (**1d**); they are stereoisomers of paraensidimerins A (**1a**) and C (**1b**) which have previously been isolated from the same plant, and form part of a new group of alkaloids isolated from this plant, the other two members of which are paraensidimerins G (**2**) and B (**3**).

We have recently reported[1] that the heartwood of the Brazilian tree, *Euxylophora paraensis* (Rutaceae), contains *N*-methylflindersine and a related hexacyclic bis-quinolin-2-one alkaloid, paraensidimerin D. More recently two other dimers, A and C, both of which are racemic and isomeric with D, have been identified by *X*-ray analysis as the heptacyclic bis-quinolin-2-ones (**1a**) and (**1b**), respectively.[2] These dimers differ in the configuration at C-16a and have the same stereochemistry as vepridimerines A and B, two racemic bis-quinolin-2-one compounds[3] isolated at about the same time from the bark of the West African species *Vepris louisii*, and shown to be the 1,2,10,11-tetramethoxy derivatives of (**1a**) and (**1b**). The ABC ring system of dimers of type (**1**) has been found[4] previously in only one other alkaloid, namely afilaramine, an optically inactive hordenine derivative from *Zanthoxylum punctatum*.

In these compounds the AB ring junction must of necessity be *cis*, although the BC ring fusion may be *cis* or *trans*.[5] Thus, dimers with the gross structural features of (**1**) may theoretically exist as four racemates. Further work on the separation of *Euxylophora* constituents has now produced a number of new monomeric and dimeric quinolinone alkaloids, including two racemic dimers, E and F, which have been identified as the stereoisomers (**1c**) and (**1d**), respectively. All four possible stereoisomeric racemates, therefore, have now been isolated from the same plant source. Two other new dimers, G and B, have also been identified. Dimer G is an unsaturated derivative (**2**) of dimers A and C, and dimer B is the tertiary alcohol (**3**) which may be formed by addition of water to the exocyclic double bond[1] of paraensidimerin D. These structures were assigned on the basis of ^{1}H and ^{13}C n.m.r. spectral measurements, which established that dimers E, F, and G, like dimers A and C, have three *C*-methyl, two methylene, and three methine groups. Dimer B, on the other hand, has four *C*-methyl groups like dimer D. In the spectra[†] of these new dimers the aromatic H-4 and H-13 proton signals appear at about δ 8.0 and the carbonyl carbon at about 162 p.p.m. showing[6] that they are quinolin-2-one, and not quinolin-4-one, derivatives.

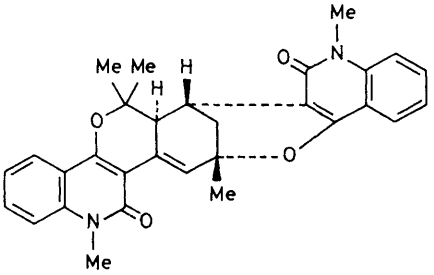


(**1a**), α-H-6a, α-H-16a (dimer A)
b, α-H-6a, β-H-16a (dimer C)
c, β-H-6a, β-H-16a (dimer E)
d, β-H-6a, α-H-16a (dimer F)

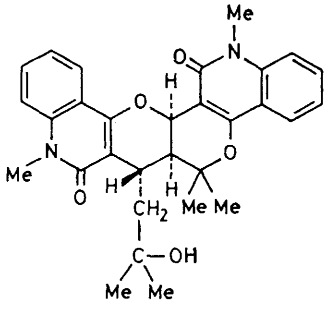
Paraensidimerin F, $C_{30}H_{30}N_2O_4$, crystallizes from chloroform–methanol as rhombic crystals, m.p. 308—309 °C. The observation of a large (12 Hz) coupling between H-6a and H-16a, and of long-range coupling (2.5 Hz) between H-16(*eq*) and H-19(*eq*) is in accord with structure (**1d**) in which ring B is in the chair form.

Paraensidimerin E (**1c**), $C_{30}H_{30}N_2O_4$, crystallizes from pyridine–methanol as colourless needles, m.p. 289—290 °C. This fourth remaining racemate has a *trans*-axial–equatorial BC ring junction, and the B ring has been twisted so that carbons 6a, 16a, 16, 15, and 19 are approximately co-planar.

Paraensidimerin G (**2**), $C_{30}H_{28}N_2O_4$, m.p. 280—281 °C, differs from dimer A and C by the loss of two hydrogens with formation of a cyclohexene ring. This was shown by the appearance of only five B-ring protons, one at low field in the ^{1}H n.m.r. spectrum (δ 1.80, 1.99, 2.65, 3.63, and 7.60), and by the appearance in the ^{13}C n.m.r. spectrum of a quaternary carbon signal at δ 130.4 p.p.m. and a methine carbon signal at δ 128.1 p.p.m. (with loss of two carbon signals at about



(**2**)
(paraensidimerin G)



(**3**)
(paraensidimerin B)

[†] Unless otherwise stated all ^{1}H and ^{13}C n.m.r. spectra were measured in $CDCl_3$, using tetramethylsilane as internal standard. Full details of n.m.r. and other spectroscopic and analytical data will be published elsewhere.

δ 26—32 p.p.m.). The double bond must be located at 16–16a, since a double bond at 7–19 does not allow an AB ring junction at 7–15. The observed coupling between H-6a (δ 2.65) and H-7 (δ 3.63) is near zero, suggesting that H-6a has a *trans*-orientation relative to H-7 with a dihedral angle of about 90°. This was confirmed by the conversion of both dimers A and C into dimer G by oxidation with dichlorodicyanobenzoquinone in benzene.

Paraensidimerin B (3), $C_{30}H_{32}N_2O_5$, crystallizes from chloroform–methanol as colourless needles, m.p. 286—287 °C, ν_{max} 3450 and 1635 cm^{-1} (mineral oil). The presence of four aliphatic methyls at δ 1.22, 1.32, 1.39, and 1.79 in the ^1H n.m.r. spectrum shows that this dimer is related to dimer D.[1] However, signals of an exocyclic olefinic group do not appear in the ^1H and ^{13}C n.m.r. spectra, indicating that dimer B may be derived by addition of water to the ethylenic double bond of D. This was confirmed by the presence of a methylene group (proton signals at δ 1.97 and 1.82 and a carbon signal at δ 52.5 p.p.m.) and an oxygen-linked carbon at δ 70.0 p.p.m. These signals do not appear in the corresponding spectrum of paraensidimerin D.

Dimeric quinolinone alkaloids may be formed biosynthetically by cycloaddition reactions of *N*-methylflindersine[1,7] with related quinolinone quinone methides or by dimerization[3] of a quinolone diene. The wide variety of racemic dimers from *Euxylophola paraensis* suggests that if these reactions do occur they are not under enzymic control. Since mixtures of the dimers rapidly crystallize from concentrated low-boiling petroleum extracts during the initial wood extraction process, these dimeric alkaloids are not artifacts formed from monomeric quinolinones by long standing of wood extracts in air and sunlight.

Received, 26th August 1982; Com. 1034

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