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THE STRUCTURES OF VEPRIDIMERINES A-D, FOUR NEW DIMERIC PRENYLATED QUINOLONE ALKALOIDS FROM VEPRIS LOUISII AND ORICIA RENIERI (RUTACEAE)

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Summary. Four new isomeric dimeric prenylated quinolone alkaloids, vepridimerines A-D, have been isolated from the bark of Vepris louisii and Oricia renieri (Rutaceae) and have been assigned structures (2)-(5) respectively on the basis of spectroscopic evidence, in particular ^{1}H and ^{13}C n.m.r. data.

Previous investigations of the bark of Vepris louisii from Cameroon[1,2] and Oricia renieri from Rwanda[3] have yielded 2-quinolone, furoquinoline, acridone and pyrano-2-quinolone alkaloids, including veprisine (1) from both species. Further work has now resulted in the isolation of three isomeric dimeric prenylated quinolone alkaloids, vepridimerines A-C, from V. louisii. Two of these, vepridimerines B and C, have also been obtained from O. renieri together with a fourth dimer, vepridimerine D. Mass measurements of all four alkaloids show that they have the molecular formula $C_{34}H_{38}N_2O_8$. Structures (2)-(5) are assigned to vepridimerines A-D respectively on the basis of the following spectroscopic evidence.

Vepridimerine A (2), m.p. 343-5°, has spectroscopic properties[4] consistent with the presence of two 2-quinolone units with the same substitution pattern as veprisine (1). These two units are joined by a C_{10} moiety which consists of three tertiary methyls (δ_C 24.77, 28.59, 29.05; δ_H 1.49, 1.50, 1.81), two methylenes (δ_C 32.23, 39.48), three methines (δ_C 26.20, 27.55, 43.55) and two fully substituted carbons bearing oxygen (δ_C 76.83, 78.95). Decoupling experiments at 360 MHz established the assignment of the coupling constants between the protons shown in (6) (chemical shifts in parentheses) and led to structure (2) for vepridimerine A. The relative stereochemistry shown is consistent with the coupling information in (6) which reveals, in particular, the cis relationship of H_d and H_e (^3J 6.1 Hz). Inspection of models shows that, with the cyclohexane ring in a chair conformation, H_f and H_a have an ideal W relationship for the observed ^4J coupling (2.2 Hz) and that the positions of H_f and H_c relative to the carbonyl groups account for their lowfield chemical shifts (δ_H 3.10 and 3.61 respectively).

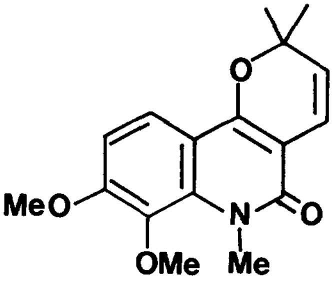
Vepridimerine B (3), m.p. 278-9°, has the same gross structural features as A (2) but differs in stereochemistry. The chemical shifts and coupling constants of the protons are recorded in diagram (7). The large value of the coupling constant between H_d and H_e (^3J 12.5 Hz) indicates that they have a <u>trans</u> relationship. The coupling information is consistent with the stereochemistry of vepridimerine B as in (3). It is clear from models that in (3) the cyclohexane ring must adopt a boat conformation thus excluding the possibility of the ^4J coupling observed with vepridimerine A (2). The alternative <u>trans</u> arrangement permits a chair conformation of the cyclohexane and the observation of a long range coupling would have been expected. Deshielding by the carbonyl groups again accounts for the lowfield chemical shifts of H_g (δ_H 3.80) and H_c (δ_H 3.20).

It is readily apparent from the spectroscopic properties of the third dimer vepridimerine C (4), m.p. 272°, that it contains a 4-quinolone unit as well as a 2-quinolone. Thus one of the H-5 resonances (δ_H 8.06) and one of the carbonyl carbon resonances (δ_C 176.29) exhibit the large downfield shifts expected for a 4-quinolone [the corresponding 2-quinolone shifts in vepridimerine A (2) are δ_H 7.69 and δ_C 164.33]. The remaining chemical shifts and coupling constants [as in (8)] are virtually identical to those of vepridimerine A (2) indicating that vepridimerine C has structure (4) with the same stereochemistry as A (2). The small chemical shift differences (<u>ca</u> 0.2 p.p.m.) of H_e and of H_f between (2) and (4) show that the 4-quinolone is on the left.

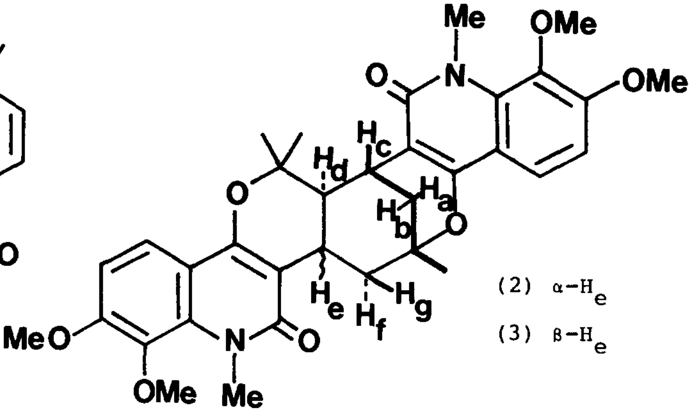
A similar argument leads to structure (5) for vepridimerine D which corresponds to B (3) with the left hand unit converted to a 4-quinolone. The appropriate chemical shifts and coupling constants are recorded in diagram (9).

It is interesting to note that vepridimerines A-D are racemic. Their formation can be rationalised in terms of Diels Alder dimerisations of the diene (10) followed by addition of 2- or 4-hydroxyl groups to the residual double bonds. A discussion of the stereochemical details of these dimerisations will be given in our full paper. Recently it has been shown[5] that compounds similar to veprisine (1) are excellent dienophiles. The <u>cis</u> compound vepridimerine A (2) could also arise by a Diels Alder reaction involving veprisine (1) and the diene (10) but the formation of vepridimerine C (4) is not easily rationalised by this route.

The vepridimerines are new additions to a small group of dimeric quinolone alkaloids found, to date, only in the Rutaceae and which includes pteledimerine and pteledimeridine from <u>Ptelea trifoliata</u>,[6,7] and paraensidimerine D from <u>Euxylophora paraensis</u>.[8] The vepridimerines represent a different mode of dimerisation to those involved in the formation of the other quinolone dimers

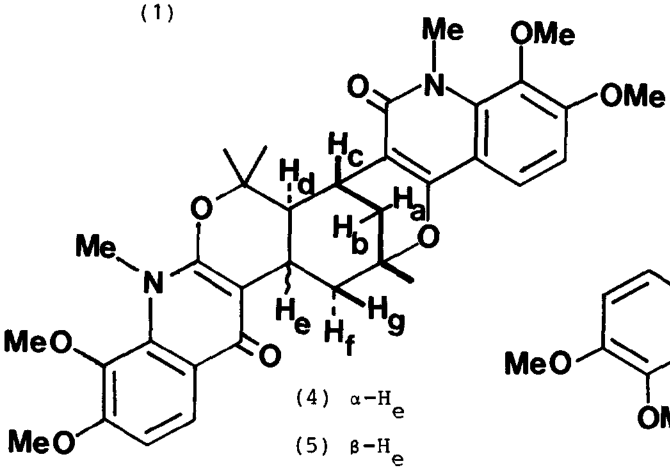


(1)



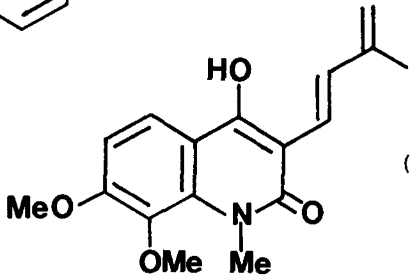
(2) α-H_e

(3) β-H_e

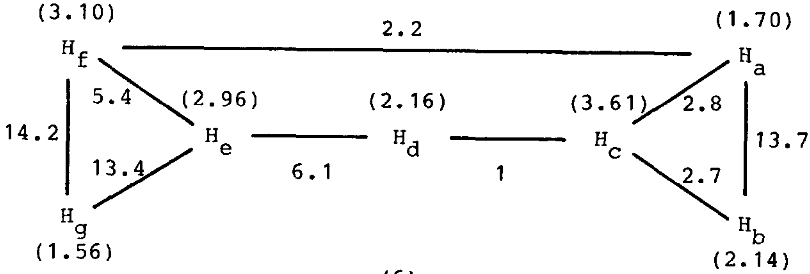


(4) α-H_e

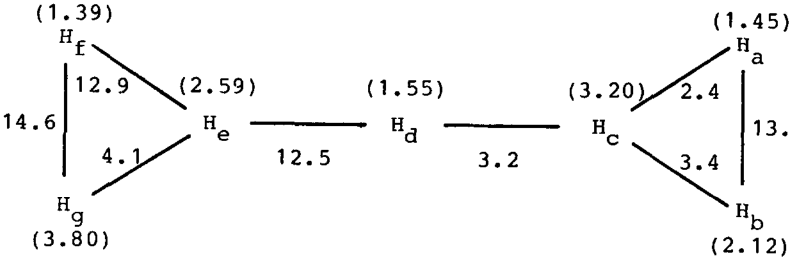
(5) β-H_e



(10)



(6)



(7)

but may arise by a similar route to that for the dimeric prenylated β-phenylethylamine alkaloid alfileramine from *Zanthoxylum punctatum*,[9] another member of the Rutaceae.

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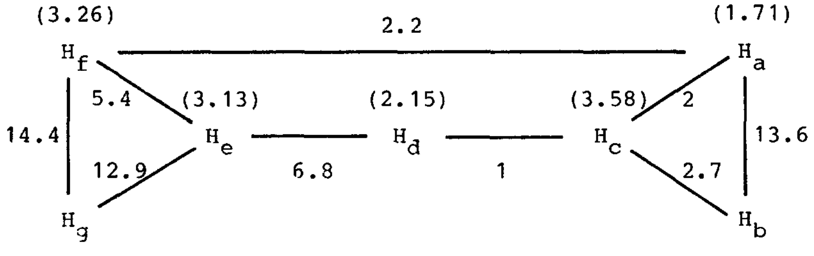

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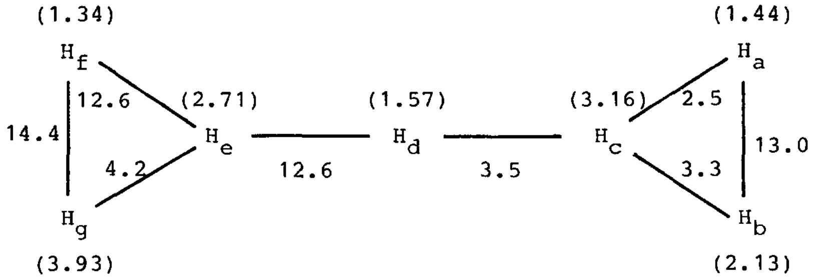

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