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FURTHER EVIDENCE FOR THE STRUCTURE OF VATICAFFINOL AND A REVISION OF ITS STEREOCHEMISTRY

SUBRAMANIAM SOTHEESWARAN,* M. N. CHAMPIKA DIYASENA,† A. A. LESLIE GUNATILAKA,† MICHAEL BOKEL‡ and WOLFGANG KRAUS‡

School of Pure and Applied Sciences, University of the South Pacific, Suva, Fiji; † Department of Chemistry, University of Peradeniya, Peradeniya, Sri Lanka; ‡ Institut für Chemie, Universität Hohenheim, 7000 Stuttgart 70, F.R.G.

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Key Word Index—*Stemonoporus canaliculatus*; Dipterocarpaceae; vaticaffinol; stereochemistry; resveratrol tetramer.

Abstract—The resveratrol tetramer, vaticaffinol, has been isolated from the bark of *Stemonoporus canaliculatus*. Further evidence has been obtained to support its structure. Its stereochemistry has been revised on the results of NOE and ^{1}H NMR homodecoupling experiments.

INTRODUCTION

Polyphenols from *Stemonoporus* species have been reported by Samaraweera *et al.* [1]. They studied six *Stemonoporus* species and reported the isolation of stemonoporol (1) from four species and vaticaffinol (2) from two species. In our study of a new *Stemonoporus* species, namely, *S. canaliculatus*, we isolated a polyphenol and identified it as vaticaffinol. However, we analysed the decaacetate, octamethyl ether, decamethyl ether and the polyphenol more closely using homodecoupling studies and NOE techniques and found that the stereochemistry of H-7 and H-8 (see Fig. 1) in vaticaffinol should be *cis* and not *trans* as reported [2, 3]. Also, the stereochemistry of H-2 and H-3 should be *cis* and not *trans* [2, 3].

RESULTS AND DISCUSSION

The bark of *S. canaliculatus* was extracted with cold acetone. The acetone extract showed antifungal activity against the fungus *Cladosporium cladosporioides*. Column chromatographic separation followed by preparative TLC on silica gel gave the pure polyphenol which showed antifungal activity against *C. cladosporioides*. Its properties were similar to those of vaticaffinol isolated by Surendrakumar and co-workers [2, 3]. Acetylation (acetic anhydride–pyridine) gave a decaacetate, mp 165–169°, $[\alpha]_D$ − 32.5°. Methylation with dimethyl sulphate gave an octamethyl ether, mp 119–122°, $[\alpha]_D$ + 25°, and a decamethyl ether, mp 154–160°, $[\alpha]_D$ + 20.5°. There were eight aliphatic protons as shown by the ^{1}H NMR data of the polyphenol, acetate and the methyl ether. The chemical shifts of these protons have been assigned as follows. The protons have been numbered with respect to the partial structure given in Fig. 1. Polyphenol: δ_H 5.67 (1H, *d*, *J* = 11.8 Hz, 1-H), 4.34 (1H, *d*, *J* = 11.8 Hz, 2-H), 5.10 (1H, *m*, 3-H), 3.15 (1H, *m*, 4-H), 4.10 (1H, *m*, 5-H), 4.44 (1H, *m*, 6-H), 4.62 (1H, *d*, *J* = 5.1 Hz, 7-H) and 5.26 (1H, *d*, *J* = 5.10 Hz, 8-H).

Homodecoupling at δ_H 5.67 resulted in the doublet at δ_H 4.34 becoming a singlet and vice versa; decoupling at δ_H 3.15 changed the multiplet at δ_H 4.10 to a doublet and the multiplet at δ_H 5.10 to a singlet; decoupling at δ_H 4.10 resulted in the multiplet at δ_H 3.15 becoming a broad singlet; irradiation at δ_H 5.26 resulted in the doublet at δ_H 4.62 becoming a singlet.

Decaacetate: δ_H 5.90 (1H, *d*, *J* = 11.8 Hz, 1-H), 4.28 (1H, *d*, *J* = 11.8 Hz, 2-H), 4.51 (1H, *d*, *J* = 2.7 Hz, 3-H), 3.67 (1H, *dd*, *J* = 11.5 and 2.7 Hz, 4-H), 4.08 (1H, *t*, *J* = 11.3 Hz, 5-H), 4.22 (1H, *d*, *J* = 11.3 Hz, 6-H), 4.58 (1H, *d*, *J* = 5.8 Hz, 7-H) and 5.52 (1H, *d*, *J* = 5.3 Hz, 8-H).

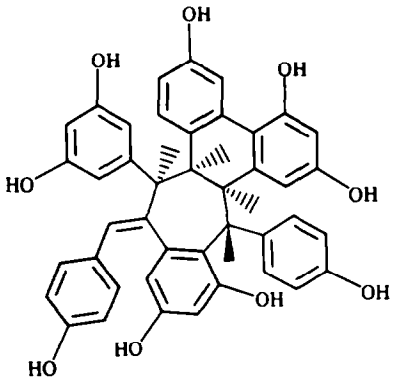
Homodecoupling at δ_H 5.90 resulted in the doublet at δ_H 4.28 becoming a singlet; irradiation at δ_H 4.51 resulted in the double doublet at δ_H 3.67 becoming a doublet; irradiation at δ_H 3.67 changed the multiplicity of the triplet at δ_H 4.08 and the doublet at δ_H 4.51 became a singlet; irradiation at δ_H 4.08 resulted in the doublet at δ_H 4.22 becoming a singlet and the double doublet at δ_H 3.67 becoming a broad singlet; decoupling at δ_H 4.58 changed the doublet at δ_H 5.52 to a singlet.

NOE difference experiment by saturation of the signal at δ4.51 led to a slight enhancement of the signals at δ_H 3.67 and 4.28. Saturation of the proton at δ_H 3.67 showed NOEs of the proton signal at δ_H4.51. The relative configurations of the protons H-2, H-3 and H-4 are established as *cis* on the basis of the above NOE experiments. Saturation of the proton at δ_H 4.58 showed NOEs of the proton signals at δ_H 4.22, 5.52, 6.10 and 6.80. These establish the configuration of the protons H-6, H-7 and H-8 as *cis*. Saturation of the proton at δ_H 4.08 showed no NOE on the aliphatic protons but showed a NOE of the aromatic proton signal at δ_H 6.60. Thus H-5 is *trans* with respect to the H-4 and H-6. Saturation of the proton at δ_H 5.90 showed no NOE on the aliphatic protons confirming a *trans* orientation of H-1 and H-2.

Octamethylether: δ_H 5.84 (1H, *d*, *J* = 11.9 Hz, 1-H), 4.43 (1H, *d*, *J* = 11.9 Hz, 2-H), 5.09 (1H, *d*, *J* = 2.7 Hz, 3-H), 3.50 (1H, under OMe signals, 4-H), 4.08 (1H, *t*, *J* = 11.0 Hz, 5-H), 4.23 (1H, *d*, *J* = 11.0 Hz, 6-H), 4.49 (1H, *d*, *J* = 4.5 Hz, 7-H), 5.38 (1H, *d*, *J* = 4.5 Hz, 8-H).

Decoupling at δ_H 5.84 caused the doublet at 4.43 to collapse to a singlet and vice versa; irradiation at δ_H 5.38

* To whom correspondence should be addressed.



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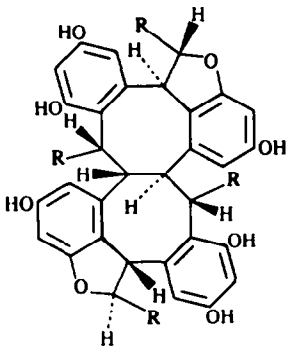

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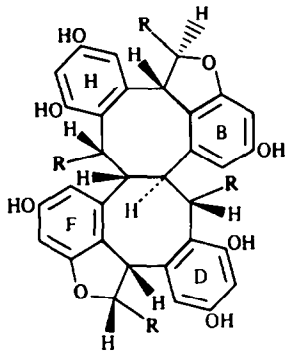

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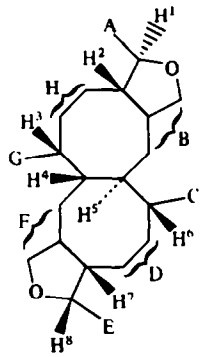

A = C = E = G = R = p-C_6H_4OH
B = D = F = H = aromatic ring
(see structure 3)

Fig. 1.

caused the doublet at δ_H 4.49 to collapse to a singlet and vice versa; irradiation at δ_H 4.23 changed the multiplicity of the triplet at δ_H 4.08; irradiation at δ_H 4.08 changed the doublet at δ_H 4.23 to a singlet. No noticeable change in the spectrum could be seen when the decoupling was done at δ_H 5.09.

The coupling constant data and homodecoupling studies as shown above for the polyphenol, decaacetate and octamethyl ether clearly show that H-1 and H-2 should be *trans* (J = 11.8 Hz) and in agreement with the published structure (2) for vaticaffinol. However from the NOE studies, H-7 and H-8 should be *cis*-oriented (J = 5–6 Hz) as in structure 3 and not *trans* as in 2. The correct stereochemistry of the methine protons for vaticaffinol should therefore be as shown in 3. This therefore constitutes the first report of a *cis*-2-aryl-2,3-dihydrobenzofuran system in plants.

Attempts to prepare a crystalline derivative to obtain X-ray crystallographic data for vaticaffinol were not successful.

EXPERIMENTAL

The bark of *S. canaliculatus* was collected from Kanneliya forest in the South of Sri Lanka. It (3 kg) was successively extracted with petrol and cold Me_2CO. The Me_2CO extract (150 g) contained the polyphenol.

A portion of the Me_2CO extract (30 g) was separated on a column of silica gel which was eluted with C_6H_6 to remove less polar materials. Elution with C_6H_6–Me_2CO (1:1) gave the crude polyphenol (5 g). Purification of this by preparative TLC using silica gel as adsorbent gave the analytically pure polyphenol which was identified as vaticaffinol. Mps (Kofler apparatus): uncorr; ^{1}H NMR and ^{13}C NMR: 250 MHz; Optical rotations: 27°, conc. 3 mg/10 ml.

Vaticaffinol. Mp 285° (dec.), $[\alpha]_D$ −22° (MeOH), lit. [3] mp 280–282°, $[\alpha]_D$ −22.5°; ^{1}H NMR: δ_H (CD_3OD) 7.15 (8H, *s*, ArH), 6.75 (2H, *d*, J = 8.6 Hz), 6.73 (2H, *d*, J = 8.6 Hz), 6.68 (2H, *d*, J = 8.6 Hz), 6.45 (2H, ArH), 6.2 (4H, *m*, ArH), 6.08 (4H, *m*, ArH). See Results and Discussion for chemical shifts of aliphatic protons.

Vaticaffinol decaacetate. The polyphenol (200 mg) was acetylated using Ac_2O (1.0 ml) and C_5H_5N (2 ml) at room temp. for 24 hr. After work-up and purification by preparative TLC, analytically pure decaacetate (150 mg) was obtained, mp 165–169°, $[\alpha]_D$ − 32.5° ($CHCl_3$, lit. [3] mp 154–156°, $[\alpha]_D$ − 33.9°. ^{1}H NMR: δ_H ($CDCl_3$) 6.80–7.40 (*m*, ArH), 6.60 (1H, *s*, ArH), 6.30, 1H, *s*, ArH), 2.30 (30H, *s*, 10–OAc). For the chemical shift data of the rest of the protons, see Results and Discussion. ^{13}C NMR: δ_C($CDCl_3$) 169.73, 169.41, 169.66, 168.79, 168.65, 168.54, 160.35, 152.50, 151.31, 150.83, 150.56, 149.59, 149.36, 147.26, 145.54, 142.83, 140.99, 140.39, 140.08, 138.45, 135.16, 134.72, 134.53, 129.54, 129.10, 128.48, 126.22, 125.99, 125.68, 122.14, 121.94, 121.86, 121.70, 120.56, 117.01, 115.16, 114.42, 113.47, 102.63, 92.52, 60.03, 55.87, 51.55, 49.66, 47.40.

Vaticaffinol octamethyl ether. The polyphenol (200 mg) was refluxed Me_2SO_4 (0.5 ml) in dry Me_2CO (15 ml) and K_2CO_3 (750 mg) for 24 hr. The product was worked up in the usual way to give a mixture which was purified by preparative TLC using silica gel to give analytically pure methyl ether, which was identified as the octamethyl ether, mp 119–122°, $[\alpha]_D$ + 25° ($CHCl_3$), ^{1}H NMR: δ_H ($CDCl_3$) 7.26 (*ortho*-coupled protons under solvent peak), 7.15 (1H, *d*, J = 8.6 Hz), 6.87 (2H, *d*, J = 8.8 Hz), 6.84 (2H, *d*, J = 8.8 Hz), 6.71 (2H, *d*, J = 8.80 Hz), 6.58 (1H, *d*, J = 8.8 Hz), 6.48–6.50 (*meta*-coupled ArH), 6.41 (1H, *d*, J = 2.0 Hz), 6.33 (1H, *d*, J = 2.3 Hz), 6.16 (1H, *d*, J = 2.3 Hz), 6.13 (ArH), 3.62, 3.77, 3.78, 3.57, 3.15 (integrated for 8 OMe, *s*). For chemical shift data for the rest of the protons, see Results and Discussion.

Vaticaffinol decamethyl ether. The second major product obtained in the above expt was purified twice by preparative TLC and was identified as the decamethyl ether of vaticaffinol, mp 154–160°, $[\alpha]_D$ + 20.5° ($CHCl_3$), lit. [3] mp 160–162°, $[\alpha]_D$ + 20.9° by comparison with an authentic sample.

TLC bioassay of polyphenol for antifungal activity. A TLC plate (silica gel) was spotted with the polyphenol and run in MeOH–CH_2Cl_2 (17:83). The plate was dried in air overnight, sprayed with *Cladosporium cladosporioides* in Czapex-Dox nutrient soln and incubated in a moist chamber at room temp. for 48 hr. The region in which fungal growth was inhibited appeared light-coloured against the mycelium background.

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REFERENCES

1. Samaraweera, S., Sotheeswaran, S. and Sultanbawa, M. U. S. (1982) *Phytochemistry* **21**, 2585.
2. Sultanbawa, M. U. S., Surendrakumar, S., Wazeer, M. I. M. W. and Bladon, P. (1981) *J. Chem. Soc. Chem. Commun.* 1204.
3. Sotheeswaran, S., Sultanbawa, M. U. S., Surendrakumar, S., Balasubramaniam, S. and Bladon, P. (1985) *J. Chem. Soc. Perkin Trans.* 1, 159.