Phytochemistry, Vol. 25, No. 6, pp. 1498–1500, 1986.
Printed in Great Britain.

0031–9422/86 $3.00 + 0.00

ANOTHER ANTIBACTERIAL POLYPHENOL, COPALLIFEROL B, FROM *VATERIA COPALLIFERA* (DIPTEROCARPACEAE)

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(*Received* 8 *October* 1985)

Key Word Index—*Vateria copallifera*; Dipterocarpaceae; bark; copalliferol B; copalliferol A; resveratrol; antibacterial activity.

Abstract—Another new resveratrol trimer, copalliferol B, isolated from *Vateria copallifera*, has been characterized on the basis of chemical, spectroscopic and biogenetic evidence.

INTRODUCTION

The isolation of a new polyphenol, copalliferol A (1), from *Vateria copallifera* was the subject of an earlier communication [1]. In this paper, we report the isolation of yet another polyphenol named copalliferol B (2) which is isomeric with copalliferol A (1).

RESULTS AND DISCUSSION

The cold acetone extracts of the bark of *Vateria copallifera* yielded two polyphenols both of which were found to have antibacterial properties. The structure of one, copalliferol A, was reported earlier [1] as the resveratrol trimer, 1. The second polyphenol, mp 300° (decomp.), $[\alpha]_D$ −186°, $[M]^+$ 680.1948 ($C_{42}H_{32}O_9$) was named copalliferol B. It gave a nonamethyl ether, mp 114°, $[\alpha]_D$ −128° $[M]^+$ 806.3474 ($C_{51}H_{50}O_9$) and a nona-acetate, mp 158°, $[\alpha]_D$ −170° indicating that all the oxygen atoms in copalliferol B are present as hydroxyl groups. The UV absorption, λ_{max} 283 (log ε 3.43) nm suggests the presence of phenolic chromaphores and the spectrum remained unchanged on addition of sodium acetate–boric acid showing the absence of *ortho*-dihydroxy groups. The IR spectrum showed strong absorptions at 3200 (OH), 1600 (aromatic C=C) and a prominent band at 830 cm^{-1} indicating a 1,4-disubstituted aromatic system. The ^{13}C NMR spectra of the nonamethyl ether had four doublets (δ_C 34–64) due to aliphatic carbon atoms, nine methyl carbons (OMe) (δ_C 55–56.8), nine singlets (δ_C 157–161) due to the aromatic carbon atoms containing the methoxy groups, ten singlets for quaternary carbon atoms (δ_C 118–147) and twelve doublets for nineteen aromatic carbon atoms.

The above data and the molecular formula of copalliferol B showed that the polyphenol is probably a trimer of 3,5,4′-trihydroxystilbene (resveratrol) like [1] copalliferol A (1). It is probable that copalliferol B is biogenetically formed by the phenol oxidative coupling of three resveratrol units. The presence of four doublets in the ^{13}C NMR spectrum due to four aliphatic carbon atoms suggests that these four carbon atoms in the resveratrol trimer are saturated carrying, in each case, a single proton. The carbon signals at δ_C 123 and 129 were singlets indicating that the two olefinic carbon atoms present were fully substituted. Copalliferol B thus contains a total of six aliphatic carbon atoms which could have arisen from the six olefinic carbon atoms of the three resveratrol units (Scheme 1). Copalliferol B probably has these six aliphatic carbon atoms in a tetrahydroazulene system as shown in Fig. 1 and the biosynthetic scheme (1). The ^1H NMR spectrum of the nona-methyl ether showed resonances for only four methine protons (δ_H 3.94–4.75) confirming the presence of a tetrahydroazulene system in copalliferol B. Decoupling studies on the methine signals revealed that two of the four methine protons were coupled to give doublets and double-doublets at δ_H 4.75 (J = 11.0 Hz) and 4.60 (J = 11.0 Hz and 0.5 Hz) respectively. The two methine protons at δ_H 4.43 and 3.94 appeared as singlets indicating that these protons were either in an isolated environment or that the torsional angle between the vicinal protons is at about 90°. The chemical shifts of the methine protons and their coupling constants are what would be expected from the proposed stereochemistry (Fig. 1) with the seven membered ring in the half-chair conformation and the tetrahydroazulene ring containing the two fused benzene rings in a *cis-trans-transoid* configuration. The chemical shift assignments of the aliphatic protons are given in Fig. 1. Though, there are five possible ways of locating the double bond in the tetrahydroazulene ring, its assignment at C-2/C-3 (Fig. 1) was prompted by the following observations. Copalliferol B had an intense fluorescence under UV light indicating the presence of a stilbene system and this reduced the possibilities for the positions of the double bond to four. The two structures with the tetrahydroazulene ring having the double bond in conjugation with three benzene rings will have too many vicinal protons and the singlets at δ_H 4.43 and 3.94 will be difficult to explain. The structure assigned to

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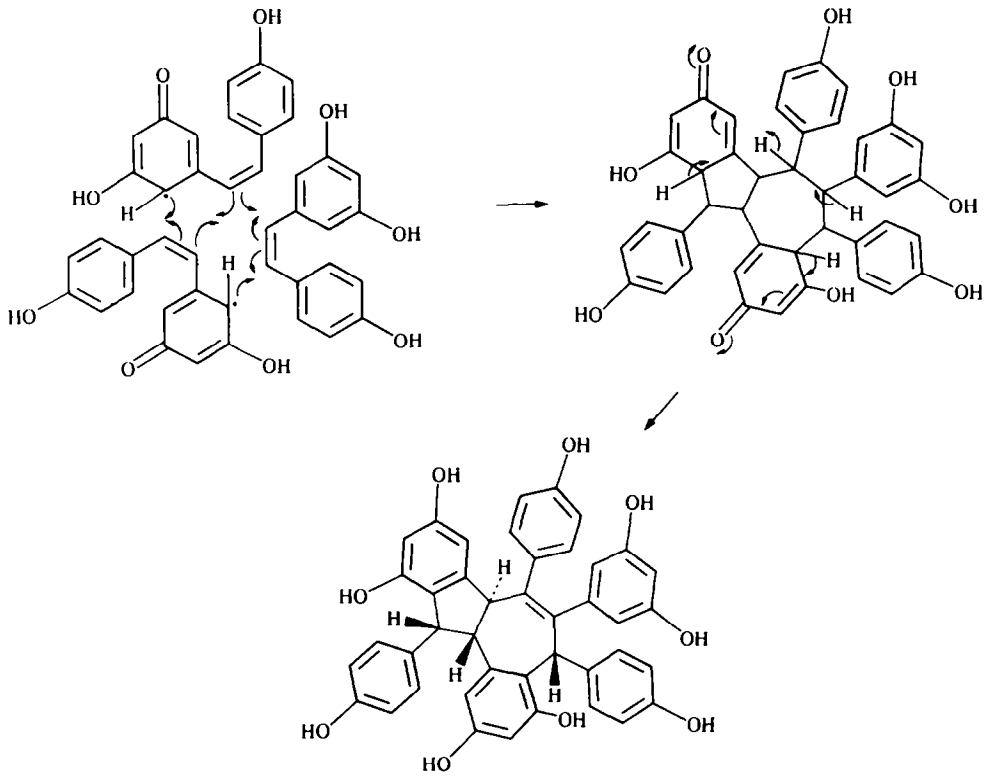


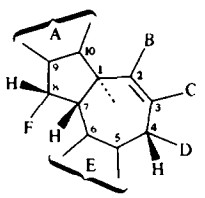
Copalliferol B **2**

Scheme 1.

copalliferol B (2) best explains all the observed spectroscopic data.

Though there are several ways of combining three resveratrol units to give copalliferol A isolated from *Vateria copallifera*, it was argued [1] that the structure best fitting the observed chemical and spectroscopic data was **1**. The isolation of copalliferol B from the same species *V. copallifera* lends further support to structure **2**, assigned to copalliferol B. Copalliferol B showed a pronounced antibacterial activity towards *Oxford staphylococcus* and *E. coli*. The role of stilbenoids in inhibiting fungal and bacterial invasion of wood is well documented in the review of Gorham [2].

The biosynthetic formulation of copalliferol B from three resveratrol units is given in Scheme 1. Figure 2 gives the complete assignment of the ^{13}C NMR shifts of nona-*O*-methylcopalliferol B.



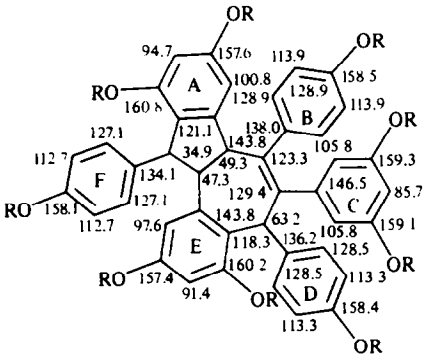
δ_H (90MHz, $CDCl_3$; 4.75 (*d*, H-8), 4.60 (*dd*, H-7), 4.43 (*s*, H-1), 3.94 (*s*, H-4, $J_{7,8}$ = 11.0 Hz, $J_{1,7}$ = 0.5 Hz)

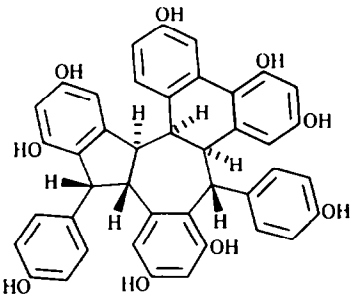
Fig. 1.

EXPERIMENTAL

The bark of *Vateria copallifera* was collected from the Kanneliya forest in the South of Sri Lanka. The powdered bark was extracted with cold Me_2CO. Evaporation of Me_2CO gave a brown solid which was chromatographed over silica gel. Elution with $CHCl_3$–MeOH (17:3) gave the crude polyphenol. See ref. [3] for other details.

Copalliferol B. Pure copalliferol B was obtained by prep. TLC separation of the crude polyphenol, mp 300° (decomp.), $[\alpha]_D^{25}$ −186° (pyridine), $[M]^+$ 680.1948, $C_{42}H_{32}O_9$ requires $[M]^+$ 680.1736; UV $\lambda_{max}^{95\%\ EtOH}$ nm: (log ε) 283 (3.43); IR ν_{max}^{KBr} cm^{-1}: 3400, 3200, 2900, 1600, 1440, 1320, 1220, 1150, 1000, 830 and 805; ^1H NMR (Me_2CO-d_6, 100 MHz): δ8.12 (3H, *m*, aromatic), 7.9 (1H, *d*, aromatic), 7.4 (1H, *m*, aromatic), 7.08 (2H, *d*, aromatic) 6.95 (2H, *d*, aromatic), 8.8 (1H, *m*, aromatic), 6.7 (1H, *m*, aromatic), 6.5 (1H, *m*, aromatic), 6.4 (3H, *m*, aromatic), 6.28 (2H, *m*, aromatic), 6.1 (2H, *m*, aromatic); MS *m/z* (rel. int.): 680 (6%), 604 (16), 544





1

Fig. 2. ^{13}C NMR chemical shifts.

(43), 531 (26), 505 (48), 492 (41), 368 (24), 354 (54), 331 (11), 318 (75), 285 (30), 232 (25), 107 (100), 94 (37).

Nona-O-methylcopalliferol B. Copalliferol B (500 mg) was refluxed with K_2CO_3 (1.0 g) and dimethyl sulphate (1.0 ml) in dry Me_2CO for 24 hr. The methyl ether was isolated as a pale yellow solid, mp 114°, $[\alpha]_D^{25}$ −128° ($CHCl_3$), $[M]^+$ 806.3474, $C_{51}H_{50}O_9$ requires 806.3513; C, 75.42%, H, 6.31%. Calc. for $C_{51}H_{50}O_9$ C, 75.93%, H, 6.20%; UV $\lambda_{max}^{95\%\ EtOH}$ nm (log ε): 273 (3.79) and 290 (3.60); IR ν_{max}^{KBr} cm^{-1}: 2900, 2840, 1600, 1510, 1460, 1300, 1240, 1200, 1170, 1150, 1080, 1050, 1030, 935 and 825; ^1H NMR ($CDCl_3$, 90 MHz): δ 7.48–5.69 (19H, *m*, aromatic), 4.75 (1H, *d*, *J* = 11.0 Hz), 4.60 (1H, *dd*, *J* = 11.0 and 0.5 Hz), 4.43 (1H, *s*), 4.09 (3H, *s*, OMe), 3.94 (1H, *s*), 3.69 (18H, *s*, 6 × OMe), 3.46 (6H, *s*, 2 × OMe); MS *m/z* (rel. int.): 806 (60%), 579 (8), 556 (15), 388 (13), 151 (11). 149 (20), 121 (100), 109 (11), 108 (9), 97 (15), 95 (54), 83 (21).

Nona-acetate of copalliferol B. Copalliferol B (200 mg) was treated with Ac_2O (3 ml) and pyridine (5.0 ml). The mixture was warmed and was kept at room temp. overnight. The usual work up and prep. TLC separation gave the acetate as an off white solid, mp 158°, $[\alpha]_D^{25}$ −170° ($CHCl_3$); UV $\lambda_{max}^{95\%\ EtOH}$ nm (log ε): 284 (3.99), 313 (3.82); IR ν_{max}^{KBr} cm^{-1}: 2900, 1760, 1755, 1600, 1500, 1470, 1430, 1365, 1200, 1060, 1010, 900 and 840; ^1H NMR ($CDCl_3$, 60 MHz): 7.11–6.58 (17H, *m*, aromatic), 6.44 (1H, *s*, aromatic), 6.28 (1H, *d*, aromatic), 5.93 (1H, *d*), 4.85 (1H, *d*), 4.49 (1H, *s*), 4.33 (1H, *s*), 2.6 (12H, *s*, 4 × OAc), 2.24 (12H, *s*, 4 × OAc), 2.06 (3H, *s*, OAc).

Acknowledgements—We wish to thank the United States Department of Agriculture for a research grant (FG-Ce-107) and the University of Peradeniya, Sri Lanka for a Research Assistantship (Surendrakumar). We also wish to thank Professor S. Balasubramaniam for the provision of plant material.

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