Bull. Chem. Soc. Ethiop. **2000**, 14(2), 155-159.
Printed in Ethiopia

ISSN 1011-3294

PHENOLIC METABOLITES FROM THE SEEDS OF *CANARIUM SCHWEINFURTHII*

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(Received October 2, 2000; revised November 28, 2000)

ABSTRACT. The seeds of *Canarium schweinfurthii* yielded a new phenylpropanoid, schweinfurthinol, characterized as 1-(4-hydroxyphenyl)-2,3-dihydroxypropan-1-one. *p*-hydroxybenzaldehyde, *p*-hydroxybenzoic acid, 3-(4-hydroxyphenyl)-prop-2-enal (p-hydroxycinnamaldehyde), 3-(3-methoxy-4-hydroxyphenyl)-prop-2-enal (coniferaldehyde), ligballinol and amentoflavone were also identified. Structures were established by spectroscopic analysis and comparison with published information.

INTRODUCTION

Canarium (Burseraceae) is a genus of 77 species [1]. There are only two species in Africa: *C. schweinfurthii* and *C. madagascariens*, the latter found only in the island of Madagascar. *C. schweinfurthii* Engl. is a big tree up to 40 m high with a massive straight cylindrical trunk and widely spreading branches [1]. It has edible fruits and seeds and it is believed that the spread and wide occurrence of this species is brought about by primates and birds, especially hornbills who appear to be fond of the fruits. The fruits are sold in West African markets and the natural area of distribution may have been considerably extended by humans. As part of our ongoing program to study the chemical constituents of African marketed plants [2-5], we have investigated the dichloromethane/methanol extract of the seeds of *C. schweinfurthii*. The present paper describes the isolation and structural elucidation of a new phenylpropanoid derivative (**1**), for which the name schweinfurthinol is proposed, as well as the known *p*-hydroxybenzaldehyde [6], *p*-hydroxybenzoic acid [6], 3-(4-hydroxyphenyl)-prop-2-enal (p-hydroxycinnamaldehyde) [7, 8], 3-(3-methoxy-4-hydroxyphenyl)-prop-2-enal (coniferaldehyde) [6, 9], ligballinol [6] and amentoflavone [10, 11].

RESULTS AND DISCUSSION

The CH_2Cl_2/MeOH extract of the seeds of *C. schweinfurthii* was subjected to vacuum liquid chromatography followed by repeated silica gel column chromatography and preparative TLC separations (see Experimental) to give *p*-hydroxybenzaldehyde [6], *p*-hydroxybenzoic acid [6], *p*-hydroxycinnamaldehyde [7, 8] and compounds **1**-**4**.

Compound **1** was obtained as brown powder and its molecular formula was determined as $C_9H_{10}O_4$ from the EIMS and NMR spectral measurements. The ^{1}H NMR of **1** (Table 1) showed two *ortho* and *meta* coupled signals at δ 7.93 and 6.88 (2H each J = 8.8 Hz) characteristic of a *p*-disubstituted benzene ring; the downfield chemical shift of the former

signal indicating the presence of an electron-withdrawing group attached to the benzene. The electron withdrawing group was finally assigned to a carbonyl since the ^{13}C NMR displayed a downfield signal at δ 198.5. In the ^{1}H NMR spectrum an ABX system at δ 3.75 (*dd*, J = 11.7, 5.1 Hz), 3.90 (*dd*, J = 11.9, 3.7 Hz) and 5.11 (*dd*, J = 5.1, 3.7 Hz) was also observed. The foregoing data are suggestive of a propanoyl moiety attached to the *para* position of a phenol. It is also clear that the ABX system belongs to the propanoyl moiety and from analyses of the ^{13}C NMR and HMQC the 2,3-dihydroxypropan-1-one structure of the substituent was unequivocally established. Compound **1** was, thus, identified as 1-(4-hydroxyphenyl)-2,3-dihydroxypropan-1-one for which the name schweinfurthinol is proposed. The ^{13}C NMR signals (Table 1) were fully assigned using DEPT, HMQC and HMBC spectra. The IR spectrum of schweinfurthinol showed absorption bands at ν_{max} 3400 and 1675 cm^{-1} characteristic of hydroxyl and carbonyl groups, respectively. Furthermore the structure of schweinfurthinol was supported by the UV spectra which showed bathochromic shift (see Experimental) in the presence of aluminium chloride and which was reversed upon addition of HCl. C-Veratroylglycol, a 3'-methoxyl derivative of schweinfurthinol, has been isolated from the bark wood of *Endospermum diadenum* (Euphorbiaceae) [11].

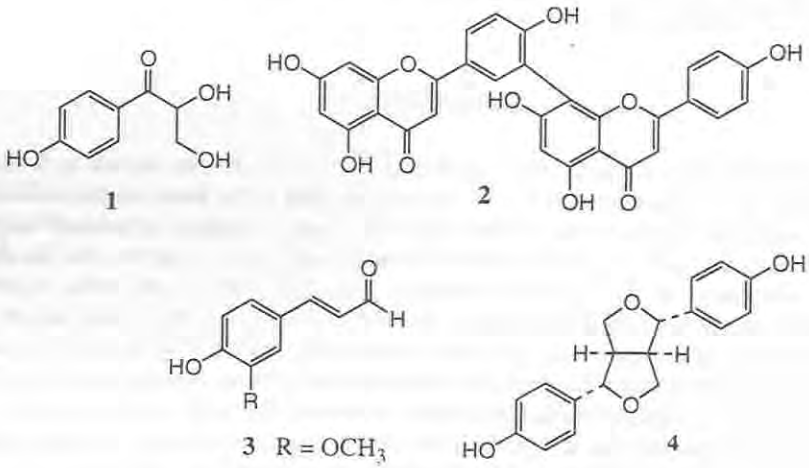

Table 1. NMR assignments of schweinfurthinol **1** and ^{2}J, ^{3}J gradient HMBC correlations in CD_3OD; chemical schifts (δ) are given in ppm; multiplicities and coupling constant J (parentheses) in Hz.

C/H	δC	δH	^{2}J and ^{3}J correlated C
1	198.5 (*s*)	--	--
2	74 .5 (*d*)	5. 11 (*dd*, J = 5.1, 3.7)	198.5 (C- 1), 65.1 (C-3)
3a	65. 1 (*t*)	3.90 (*dd*, J = 11. 9, 3.7)	198.5 (C-1), 74.5 (C-2)
3b	65. 1 (*d*)	3.75 (*dd*, J = 11.7, 5.1)	198.5 (C-1), 74.5 (C-2)
1'	126.7 (*s*)	--	--
2'/6'	13 1.4 (*d*)	7.93 (*d*, J= 8.8)	198.5 (C-1), 163.2 (C-4')
3'/5'	115.4 (*d*)	6.88 (*d*, J= 8.8)	163.3 (C-4'), 126.7 (C-1')
4'	163.2 (*s*)	--	--

The NMR spectra of compound **2** showed signals for two chelated hydroxyl groups at δ 12.98 and 13.11, two carbonyls at δ 182.6 and 183.0 and two proton singlets at δ 6.41 and 6.80. The IR, UV and NMR of **2** were consistent with its formulation as *bis*-5-hydroxyflavone. This compound appears to be identical with a *bis* flavone previously reported from *Rhus succedanea* (Anacardiaceae) and named amentoflavone [10]. The chemical shifts of the ^{13}C NMR spectrum of this compound in (DMSO-d_6) were compared (Table 2) with those published by Chari *et al.* [10] for amentoflavone measured in the same solvent. We noticed that all the chemical shifts recorded by us were shifted downfield by *ca* 0.6 ppm. The two compounds should be identical and this discrepancy can be due to solvent reference calibration.

Table 2. ^{13}C NMR (75 MHz) assignments of amentoflavone in DMSO-d_6; chemical shifts are given in ppm.

C	Ref. 12	2	C	Ref. 12	2
2	164.0[a]	164.7	2	164.3[a]	165.0
3	103.2[h]	103.8	3	102.8[h]	103.5
4	181.8[c]	182.6	4	182.2[c]	183.0
5	161.6	162.3	5	160.8	161.9
6	98.9[d]	99.5	6	99.1[d]	99.7
7	163.9[e]	164.5	7	162.0[e]	162.7
8	93.9	94.9	8	104.1	104.8
9	157.6	158.2	9	154.7	155.3
10	104.0	104.6	10	104.0	104.5
1'	121.3[f]	121.8	1'	120.3[f]	120.8
2'	127.9	128.7	2'	128.3	129.1
3'	121.6[g]	122.3	3'	116.0	116.6
4'	159.6	160.4	4'	161.1	161.4
5'	116.4	117.0	5'	116.0	116.6
6'	131.6	132.3	6'	128.3	129.1

Chemical shifts with the same subscript are interchangeable.

The ^1H NMR spectrum of **3** was found to be consistent with coniferaldehyde (ferulaldehyde) previously isolated from several species *Acer saccharinum* (Aceraceae), *Juglans cinerea* (Juglandaceae), *Senna incana* (Fabaceae) [12]. Coniferaldehyde has been reported as prostaglandin synthase inhibitor and antifungal agent [12].

The spectroscopic data generated for **4** (NMR, EIMS, IR) were found to be similar to those reported for ligballinol, a lignan, which was reported as stress metabolite from cell cultures of the legume *Vigna angularis* [12].

p-Hydroxybenzaldehyde and the corresponding acids were obtained from the flash chromatography fraction eluted with 10% ethyl acetate in hexane. They were easily identified on the basis of their NMR data and by direct comparison of authentic materials from our own laboratories.

EXPERIMENTAL

General. Melting points were obtained on a micro-melting point apparatus and are uncorrected. UV spectra were taken in methanol solution on Shimadzu UV-210 IPC UV-Vis

Scanning spectrophotometer. IR spectra were measured as KBr disk. ^{1}H and ^{13}C NMR were recorded in $CDCl_3$, CD_3OD, DMSO-d_6 on a Bruker Spectrometer operating at frequencies of 300 and 75 MHz, respectively, with the residual solvent peaks as internal references. HMQC, HMBC and selective NOESY experiments were performed with gradient enhancements. EIMS were recorded by direct inlet (70 eV) on a Finnigan SSQ-7000 Single Quadrupole Mass Spectrometer.

Plant material. The seeds of *Canarium schweinfurthii* were purchased from a vendor in Yaounde, Central Province of Cameroon. The identity of the plant was established by Mr P. Mizili from the National Herbarium at Yaounde where a voucher specimen (No 16929) is kept.

Extraction, isolation and characterization. The air-dried and powdered seeds of *Canarium schweinfurthii* (5 kg), were soaked in the mixture of CH_2Cl_2/MEOH (1:1) for 24 h, followed by MeOH for 4 h. Concentration of the combined organic extracts under reduced pressure yielded a brown residue (200 g) which was extracted with EtOAc. Removal of the solvent left 50 g of residue, which was subjected to flash CC using hexane and introducing an EtOAc gradient and subsequently MeOH gradient in EtOAc. Frs were monitored by TLC and ^{1}H NMR and similar frs combined. Frs 1-5 (3 g) contained mainly mixture of hydrocarbons and were not investigated further. Frs 6-15 (4.8 g) examined on TLC (hexane-EtOAc 3:1) contained two major compounds and were passed through a CC to give *p*-hydroxybenzaldehyde (15 mg) and *p*-hydroxybenzoic acid (35 mg). Frs 16-25 (7.4 g) were subjected successively to CC and PTLC to yield (**3**, 10 mg) and *p*-coumaraldehyde (15 mg). Frs 26-40 (20 g) gave crystals in hexane EtOAc (**2**, 120 mg). The filtrate was passed through repeated CC and PTLC to yield **2** (45 mg), **1** (15 mg), and **4** (30 mg). Known compounds were identified from spectroscopic and physical data and comparison with published information.

1-(4-Hydroxyphenyl)-2,3-dihydroxypropan-1-one (1). Brown powder in hexane EtOAc, m.p. 210-212 °C, $[\alpha]_D$ -56.7° (MeOH, c: 0.11); UV λ_{max}^{MeOH} nm log (ε): 201 (4.13), 219 (4.10), 279 (4.25); $\lambda_{max}^{MeOH+AlCl_3}$ nm log (ε): 202 (4.14), 231 (3.91), 322 (4.43); $\lambda_{max}^{MeOH+AlCl_3+HCl}$ nm log (ε): 201 (4.17), 218 (4.13), 280 (4.24); $\lambda_{max}^{MeOH+NaOAc}$ nm, log (ε): 217 (4.52), 329 (4.30); IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 2360, 1675 (C=O), 1585, 1495, 1390, 1270, 1170, 1120, 1060, 960, 820. ^{1}H NMR (300 MHz, CD_3OD): Table 1; ^{13}C NMR (75 MHz, CD_3OD): Table 1; EIMS *m/z* (rel. int.): 182 $[M]^+$ (2), 164 $[M-H_2O]^+$ (4), 151 $[M-CH_3O]^+$ (10), 139 (22), 121 $[M-C_2H_3O_2]^+$ (100), 93 $[121-CO]^+$ (10).

Amenthoflavone (2). UV λ_{max}^{MeOH} nm log (ε): 206 (5.02), 268 (4.89), 332 (4.85); $\lambda_{max}^{MeOH+AlCl_3}$ nm log (ε): 207 (5.07), 277 (4.87), 298 (4.79), 348 (4.88), 386 (4.78); $\lambda_{max}^{MeOH+AlCl_3+HCl}$ nm log (ε): 206 (5.07), 278 (4.88), 346 (4.87), 385 (4.73); $\lambda_{max}^{MeOH+NaOAc}$ nm log (ε): 222 (5.23), 274 (4.99), 375 (4.84); ^{13}C NMR (75 MHz, DMSO-d_6): Table 2.

3-(3-Methoxy-4-hydroxyphenyl)prop-2-enal (coniferaldehyde, 3). Yellow oil; ^{1}H NMR (300 MHz, CD_3OD) δ; 3.91 (3H, *s*, OMe), 6.64 (1H, *dd*, J = 15.7, 7.9 Hz, H-2), 6.85 (1H, *d*, J = 8.2 Hz, H-5'), 7.17 (1H, *dd*, J = 8.2,1.9 Hz, H-6'), 7.25 (1H, d, J = 1.9 Hz, H-2'), 7.59 (1H, *d*, J = 15.7 Hz, H-3), 9.57 (1 H, *d*, J = 7.9 Hz, H-1).

Ligballinol (4). ^{1}H NMR (300 MHz, CD_3OD) δ: 3.13 (1 H, *m*, H-2), 3.83 (1H, *dd*, J = 12.4, 3.7 Hz, H-1a), 4.21 (1H, *m*, H-1b), 4.71 (1 H, *br d*, J= 4.3 Hz, H-3), 6.77 (2H, *dd*, J = 8.4, 1.8 Hz, H-3', 5'), 7.21 (2H, *dd*, J = 8.4, 1.9 Hz, H-2', 6').

ACKNOWLEDGEMENT

BTN is grateful to IPICS for a three-month travel grant to the Department of Chemistry of the University of Botswana under the auspices of NABSA.

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