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A NOVEL PHENOLIC GLYCOSIDE FROM *MONDIA WHYTEI* SKEELS

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ABSTRACT. A novel phenolic glycoside, was isolated from *Mondia whytei*. The aglycone, 2-hydroxy-4-methoxybenzaldehyde is linked to glucose, which is in turn connected to a xylopranose residue.

INTRODUCTION

In Eastern, Southern and Central Africa, the powdered tubers of *Mondia whytei* (Hook.f.) Skeels (Asclepiadaceae - milkweed family) are added to porridge, beer, soup or tea and taken orally as an aphrodisiac and also to treat anorexia, schistosomiasis, constipation and gonorrhoea [1]. We report the isolation and characterization of a novel phenolic glycoside **1** from the MeOH extract of the tubers. The stucture of compound **1** was determined by spectroscopic method and synthesis of the aglycone. This is the first report on the chemistry of this plant.

RESULTS AND DISCUSSION

Compound **1** gave positive test to 2,4-DNPH and had the relative mass of 444 as determined by its FABMS. The IR spectrum showed a strong carbonyl absorption band at 1710 cm^{-1} and the UV spectrum displayed absorption maxima at 296, 272, 226 and 202 nm. The ^{13}C NMR spectrum (in d_5-Py DEPT Table 1) showed the presence of 19 carbon atoms and suggested the presence of three tertiary and three quaternary aromatic C atoms. In addition the presence of an OCH_3, an aldehyde functionality, a glucopyranose and a xylopyranose was evident from the spectrum.

The ^1H NMR spectrum showed an ABX pattern at δ 7.98 (1H, d, J=8.7 Hz) 6.65 (1H, dd, J=8.7, 2.2 Hz) and 7.34 (1H, d, J=2.2 Hz) attributable to H-6, H-5 and H-3, respectively. The singlets at δ 3.79 and 10.82 are assignable to C-8 OMe and C-7 CHO, respectively. The anomeric protons of xylopyranose and glucopyranose resonated at δ 4.93 (1H, d, J=7.1 Hz) and 5.62 (1H, d, J=7.3 Hz), respectively. The remaining 11H multiplet at δ 4.00-4.39 is assignable to the rest of the sugar protons. Furthermore, the substitution pattern on the aromatic ring was established by an nOe difference experiment. Irradiation of the aldehydic proton resonance at δ 10.82 resulted in an enhancement of the H-3 signal only whereas irradiation of the $-OCH_3$ signal affected the H-4 and H-6 resonances. Thus the -CHO and $-OCH_3$ groups are *para* to each other with the CHO group *ortho* to the sugar moiety linked at the phenolic OH group at C-2. The aromatic protons are therefore located at C-3, C-4 and C-6, respectively.

Further fragmentation peaks in the MS spectrum at m/z 312 (glucose + xylose + H) and 153 (aglycone + H) became useful in the structural elucidation. Particularly the ion peak at 312 suggested that xylose was a terminal sugar

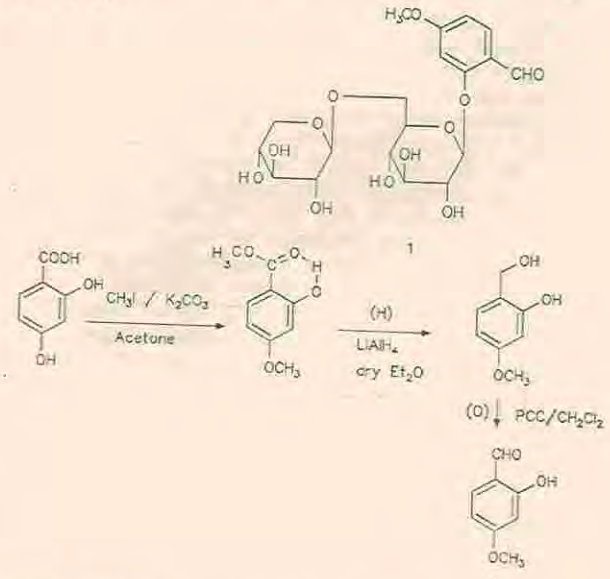
Table 1. ^1H NMR and ^{13}C NMR of phenolic glycoside 1 (500 and 75 MHz, pyridine -d_5)

	^{13}C NMR		^1H NMR	
	C	1	H	1
aglycone C -	1	120.2		
	2	166.6		
	3	109.5	C-3	7.34 (d, J=2.2 Hz)
	4	162.9		
	5	102.6	C-5	6.65 (dd, J=8.7, 2.2 Hz)
	6	129.6	C-6	7.98 (d, J=8.7 Hz)
	7	188.4		
			C-7	10.82 (s)
	8	55.9	C-8	3.79 (s)
glucose	1'	102.5	C-1	5.62 (d, J=7.3 Hz)
	2'	75.1		
	3'	77.7		
	4'	71.4		4.00 - 4.39 multiplet
	5'	78.4		
	6'	70.5		
xylose	1"	106.3	C-1"	4.93 (d, J=7.1 Hz)
	2"	74.8		
	3"	78.5		4.00 - 4.39 multiplet
	4"	71.1		
	5"	67.2		

J (Hz) in parentheses

(M^+ - xylose - H; 446-133 → 313-H). From the MS and ^{13}C NMR spectral data, it was therefore evident that the aglycone, 2-hydroxy-4-methoxybenzaldehyde, was linked to glucose which was further attached to xylose in a 1→6 linkage. Thus, compound 1, was assigned the molecular formula $C_{19}H_{26}O_{12}$ and its structure was established as 2-hydroxy-4-methoxybenzaldelyde-2-O-β-D-glucopyranose-1→6-O-β-D-xylopyranoside (**1**).

Moreover, acid hydrolysis of compound **1** gave xylose and glucose, which were identified by comparision with authentic samples on TLC, and the corresponding aglycone, which was identified as 2-hydroxy-4-methoxybenzaldehyde. The ^1H NMR data of the aglycone was identical to that of **2** which was obtained by synthesis (Scheme 1).



Scheme 1. Synthesis of 2-hydroxy-4-methoxybenzaldehyde (2).

This is the first report on the chemical investigation of *Mondia whytei*. Compound **1** is a novel natural product. It is of particular interest because the aglycone has an iso-vanilic substitution pattern. Various biological tests for compound **1** are underway.

EXPERIMENTAL

Mps: uncorr; UV, MeOH; ^1H and ^{13}C NMR, 500 and 75 MHz, respectively, in C_5D_5N, TMS as int. standard.

Plant material. *Mondia whytei* (Hook.F.) Skeels was collected near Ngabu, Malawi, in July 1988 and authenticated by Mr E.A.K. Banda. A voucher specimen (No. 88133) is deposited at the National Herbarium and Botanic Gardens of Malawi in Zomba.

Extraction and seperation. Powdered root tuber (69.53 g) was successively extracted at RT with 3 x 500 ml CH_2Cl_2 (yield, 1.26 g); MeOH (4.88 g) and H_2O (1.24 g) with stirring. The MeOH extract (3.0 g) was separated by DCCC ($CHCl_3$-MeOH-iPrOH-H_2O; 5:6:1:4) descending mode; lower phase as the mobile phase; 254 nm; and also monitored by TLC; $CHCl_3$-MeOH-H_2O; 65:35:5 (Godin spray reagent) to give 17 fractions. Fraction 15 (930 mg) was further separated by sephadex LH-20 (MeOH) to give 4 fractions. Fraction 3 (500 mg) was finally separated on RP-8 MPLC (step gradient solvent system; MeOH-H_2O; 30→50→70→90% MeOH) where Fraction 4 gave a pure compound, **1** (300 mg).

2-hydroxy-4-methoxybenzaldehyde-2-O-β-D-glucopyranosyl-1 → 6-O-β-D-xylopyranoside, 1. (300 mg); Rf. 0.5 ($CHCl_3$-MeOH-H_2O; 65:35:5; Godin); mp 97°C (MeOH); IR$^{\nu}$max (KBr) cm^{-1}: 3400 (OH), 2700, 1710, 1605, 1495, 1450, 1290, 1210, 1085, 805; UV (MeOH) λmax (log ε) nm: 296 sh (4.52), 272 (4.70), 226 (4.78), 202 (4.75); DC/IMS (NH_3) m/z: 464 (M + NH_4), 447 (M + H), 312; ^{13}C NMR (75 MHz, C_5D_5N) see Table 1.

Acid Hydrolysis of compound 1. Compound **1** (21.3 mg) was dissolved in 5% H_2SO_4-EtOH (2 ml) and refluxed with stirring; poured in cold H_2O; extracted with Et_2O and then EtOAc; dried over anhyd. Na_2SO_4 and evaporated to give 2-hydroxy-4-methoxybenzaldehyde (**2**) (10 mg). R_f 0.8 (benzene-EtOAc 1:1); ^1H NMR (500 MHz, d_5-Py): δ7.98 (1H, d, J=8.7 Hz, H-6), 6.65 (1H, dd, J=8.7, 2.2 Hz, H-5), 7.37 (1H, d, J=2.2, Hz, H-3), 3.79 (3H, s, OCH_3), 10.82 (1H, s, CHO), 11.42 (1H, s, OH). The mixture was neutralized with $BaCO_3$, filtered and lypholised to give xylose and glucose, TLC identical with authentic samples (EtOAc - HOAc - MeOH - H_2O, 65:20:15:15, anisidine phthalate).

Sytnesis of the aglycone, 2-hydroxy-4-methoxybenzaldehyde (2). 2,4-Dihydroxybenzoic acid (1 g) in AR acetone (25 ml) was treated with anhyd. K_2CO_3 (0.20 g) and CH_3I (10 ml) and the mixture was refluxed for 2 hr. Usual workup gave 2-hydroxy-4-methoxymethylbenzoate (980 mg) and was used directly in the next step. Reduction with $LiAlH_4$ (0.20 g) in dry Et_2O (20 ml) gave, upon workup, 2-hydroxy-4-methoxy benzyl alcohol (450 mg). Partial oxidation [2] of the primary alcohol (182.1 mg, 0.1 mol) in dry CH_2Cl_2 (1 ml) with pyridiniumchloro chromate (0.40 g, 0.15 mol) in dry CH_2Cl_2 (20 ml) gave 2-hydroxy-4-methoxybenzaldehyde (**2**) (121 mg). For ^1H NMR (in d_5-Py) see Table 1. Compound **2** was identical in all respects to the aglycone obtained after hydrolysis of **1**.

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