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FLAVONOIDS OF *ANDROGRAPHIS PANICULATA*

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Key Word Index—*Andrographis paniculata*, Acanthaceae, roots, 5-hydroxy-7,8-dimethoxyflavanone, 3,7,8,2′-tetramethoxyflavone

Abstract—Chromatographic separation of the petrol extract of *Andrographis paniculata* roots resulted in the isolation and characterization of two new flavonoids, 5-hydroxy-7,8-dimethoxyflavanone and 5-hydroxy-3,7,8,2′-tetramethoxyflavone, as well as the known flavonoid 5-hydroxy-7,8-dimethoxyflavone

INTRODUCTION

Andrographis paniculata Nees is widely known for its medicinal value [1] Earlier reports on its chemical constituents include flavonoids, sesquiterpene lactones and other compounds [2–8] In this paper we report the isolation and characterization of two new flavonoids, (±)-5-hydroxy-7,8-dimethoxyflavanone and 5-hydroxy-3,7,8,2′-tetramethoxyflavone, from the roots In addition, 5-hydroxy-7,8-dimethoxyflavone (7-*O*-methylwogonin) is also reported for the first time from this species

RESULTS AND DISCUSSION

When subjected to column chromatography, the petrol extract resulted in the isolation of compounds **1**–**3** (Fig 1) Compound **1**, mp 98–99° was assigned the structure (±)-5-hydroxy-7,8-dimethoxyflavanone on the basis of the following data It analysed for $C_{17}H_{16}O_5$ The UV spectrum gave bands at 288 and 342 nm and UV shifts with diagnostic reagents ascertained the presence of a 5-hydroxyl group The ^{1}H NMR spectrum ($CDCl_3$) gave a multiplet centred at δ3 0 assigned to C-3 methylenes, besides signals for two methoxyls A double doublet at δ5 33 (J = 5 and 10 Hz) identified the C-2 proton The C-6 proton was located at δ6 13 and a broad singlet was observed at δ7 46 for the aromatic protons of ring B Acetylation gave the monoacetate, mp 130–132° In the ^{1}H NMR spectrum of this acetate the signal for C-6 shifted to δ6 33, other signals remained practically at their original positions With diazomethane under normal conditions, no methylation was observed However, when methylated with DMS, a monomethyl ether, mp 156–158°, was formed This confirms that the only hydroxyl group present is at C-5, which is chelated Oxidation with $KMnO_4$ in acetone gave an acid which was identified as benzoic acid, confirming the unsubstituted ring B Mass fragmentation fully supported the assigned structure Therefore, **1** is (±)-5-hydroxy-7,8-dimethoxyflavanone Flavanones of the same structural formula with 5,7,8- and 5,6,7-substitution patterns are known synthetically [9, 10] Compound **1** agrees closely with the physical data of the 5,7,8-substituted synthetic compound, which is reported to have mp 98–99°, the other isomer having mp 148–149° This is the first report of **1** as a natural substance

Compound **2**, mp 209–211°, analysed for $C_{19}H_{18}O_7$ The UV spectrum in methanol showed strong absorptions at 272, 362 and an inflexion at 302 nm, and a shift with $AlCl_3$–HCl indicated the presence of a 5-hydroxyl group The ^{1}H NMR spectrum (60 MHz, $CDCl_3$), gave, besides the signals for four methoxyl groups, a sharp singlet at δ6 46 for the C-6 proton and a multiplet centred at δ7 10 for the 3′, 4′, 5′ protons C-6′ was located separately as a multiplet at δ7 60 Acetylation resulted in the formation of the monoacetate, mp 158–159°, in the ^{1}H NMR of which, C-6 shifted to δ6 7, other signals remained practically at their original positions Methylation gave a monomethyl ether, mp 152–154° On the basis of the above data, **2** must be 5-hydroxy-3,7,8,2′-tetramethoxyflavone The 5,7,8-substitution pattern of ring A in **2** was further confirmed when the chemical shift values of the C-6 proton of **2** were compared with dechlorochloroflavonin [11], a metabolite from cultures of *A candicans*, which is reported to have the same substitution pattern The ring B substitution pattern was confirmed when the methyl ether was oxidized with $KMnO_4$ in acetone One of the products was an acid (mp 99–100°), which was identified as methylsalicylic acid This establishes the structure of **2** conclusively

Compound **3**, mp 180–181°, was identified as 5-hydroxy-7,8-dimethoxyflavone (lit mp 173–175° [12]) from its spectral data and derivatives There appear to be some inaccuracies in the published spectral data for this compound, so spectral details are being presented here

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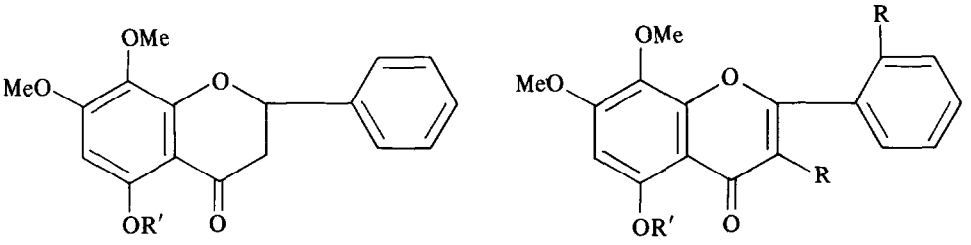

1 R′ = H
1a R′ = Ac
1b R′ = Me

2 R = OMe, R′ = H
2a R = OMe, R′ = Ac
2b R = OMe, R′ = Me
3 R = R′ = H
3a R = H, R′ = Ac
3b R = H, R′ = Me

Fig 1

EXPERIMENTAL

All the mps are uncorr Roots of *Andrographis paniculata* (1 kg) were extracted first with petrol (bp 60–80°), followed by EtOH The petrol extract was concd and kept at 0° A solid mass (700 mg) separated, which was subjected to CC over Si gel (50 g) using C_6H_6, EtOAc and MeOH in different proportions

Compound **1** was isolated from the C_6H_6 fractions, crystallized from Me_2CO–petrol as cream plates (80 mg), mp 98–99°, analysed for $C_{17}H_{16}O_5$ Found C, 68 07, H, 5 29 Requires C, 68 0; H, 5 33% UV λ_{max}^{MeOH} nm 288, 342, + NaOMe 286, 360, + $AlCl_3$ 310, 364, + $AlCl_3$–HCl 310, 364, + NaOAc 288, 342 IR cm^{-1} 3435 (OH), 1650 (C = O) MS *m/z* (rel int) 300 (M^+, 100), 299 (16 58), 285 (27 77), 257 (6 80), 223 (32 86), 197 (21 99), 196 (100), 181 (100), 168 (49 44), 167 (28 47), 153 (95), 104 (23 96) and 103 (28 20) Fragments 196 and 104 occurred due to retro-Diels–Alder fragmentation of *m/z* 300 The monoacetate crystallized from MeOH as yellow crystals, mp 130–132°, analysed for $C_{19}H_{18}O_6$ ^1H NMR (60 MHz, $CDCl_3$) δ 2 4 (3H, *s*, -OCOMe), 3 0 (2H, *m*, 3-H), 3 85 and 3 95 (2 × 3H, 2*s*, 7,8-OMe), 5 53 (1H, *dd*, *J* = 5 and 10 Hz, 2-H), 6 36 (1H, *s*, 6-H), 7 46 (5H, *s*, 2′,3′,4′,5′,6′-H) The methyl ether crystallized from MeOH as yellow crystals, mp 156–158°, analysed for $C_{18}H_{18}O_5$ ^1H NMR (60 MHz, $CDCl_3$) δ 3 0 (2H, *m*, 3-H), 3 75, 3 85 and 3 9 (3 × 3H, 3*s*, 5,7,8-OMe), 5 53 (1H, *dd*, *J* = 5 and 10 Hz, 2-H), 6 15 (1H, *s*, 6-H), 7 46 (5H, *s*, 2′,3′,4′,5′,6′-H)

Oxidative degradation of **1** The methyl ether of **1** (30 mg) was subjected to oxidative degradation by $KMnO_4$ in Me_2CO Among other products, a compound crystallized from boiling H_2O (4 0 mg), mp 122°, analysed for $C_7H_6O_2$ and was identified as benzoic acid by co-TLC, mmp and superimposable IR **2** was isolated from C_6H_6–EtOAc (95 5) fractions, crystallized from MeOH as yellow plates, mp 209–211° (100 mg), analysed for $C_{19}H_{18}O_7$ Found C, 63 73, H, 5 01 Requires C, 63 69, H, 5 02% UV λ_{max}^{MeOH} nm 272, 302 inf, 362, + NaOMe 272, 360, + NaOMe 272, 360; + $AlCl_3$ 278, 362, + $AlCl_3$–HCl 278, 362, + NaOAc 272, 358 IR ν^{KBr} cm^{-1} 3440 (OH), 1660 (C = O), 1600, 1580, 1500, 1370, 1235, 850 MS *m/z* (rel int) 358 (M^+, 90), 343 (100), 328 (9 01), 313 (25 60), 285 (4 18), 181 (20 21), 162 (2 31), 153 (34 38), 147 (5 45) and 125 (12 14) The monoacetate crystallized from MeOH, mp 158–159°, analysed for $C_{21}H_{20}O_8$ ^1H NMR (60 MHz, $CDCl_3$) δ 2 53 (3H, *s*, -OCOMe), 3 87, 3 9, 4 0, 4 03 (3H each, 4*s*, 3,7,8,2′-OMe), 6 7 (1H, *s*, 6-H), 7 10 (3H, *s*, 3′,4′,5′-H), 7 60 (1H, *s*, 6′-H) The methyl ether was obtained as dark-coloured plates from Me_2CO, mp 152–154°, analysed for $C_{20}H_{20}O_7$ ^1H NMR (60 MHz, $CDCl_3$) δ 3 96 (15H, *m*, 3,5,7,8,2′-OMe), 6 46 (1H, *s*, 6-H), 7 10 (3H, *m*, 3′,4′,5′-H), 7 60 (1H, *s*, 6′-H)

Oxidative degradation The methyl ether of **2** (40 mg) was subjected to oxidative degradation by $KMnO_4$ in Me_2CO Among other products, a compound crystallized from boiling H_2O (6 0 mg), mp 99–100°, analysed for $C_8H_8O_3$ and was identified as methylsalicylic acid by co-TLC, mmp and superimposable IR **3** was isolated from later benzene fractions, crystallized from MeOH, yellow needles, mp 180–181° (120 mg) and analysed for $C_{17}H_{14}O_4$ Found C, 68 46, H, 4 70 Requires C, 68 45, H, 4 69% UV λ_{max}^{MeOH} nm 274, 346, + NaOMe 274, 346, + $AlCl_3$ 280, 362, + $AlCl_3$–HCl 280, 362, + NaOAc 274, 344 IR ν^{KBr} cm^{-1} 3440 (OH), 1665 (C = O) ^1H NMR (60 MHz, $CDCl_3$) δ 3 97 (6H, *s*, 7,8-OMe), 6 43 (1H, *s*, 6-H), 6 66 (1H, *s*, 3-H), 7 45–7 60 (3H, *m*, 3′,4′,5′-H), 7 85–8 0 (2H, *m*, 2′,6′-H), 12 30 (1H, *s*,-OH), which disappeared on D_2O exchange MS *m/z* (rel int) 298 (M^+, 90), 283 (100), 255 (10 03), 181, (25 12), 153 (55 85), 125 (19 71), 102 (14 40) The monoacetate, crystallized from MeOH as yellow crystals, mp 228–229°, and analysed for $C_{19}H_{16}O_6$ ^1H NMR (60 MHz, $CDCl_3$) δ 3 42 (3H, *s*, OCOMe), 4 0, 4 03 (3H each, 2*s*, 7,8-OMe), 6 66 (1H, *s*, 3-H), 6 70 (1H, *s*, 6-H), 7 45–7 60 (3H, *m*, 3′,4′,5′-H), 7 85–8 0 (2H, *m*, 2′,6′-H) The methyl ether was obtained as yellow plates from MeOH, mp 161–163°, analysed for $C_{18}H_{16}O_5$ ^1H NMR (60 MHz, $CDCl_3$) δ 4 0 (9H, *s* (*br*), 5,7,8-OMe), 6 45 (1H, *s*, 6-H), 6 70 (1H, *s*, 3-H), 7 45–7 60 (3H, *m*, 3′,4′,5′-H), 7 85–8 0 (2H, *m*, 2′,6′-H)

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