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NOVEL CYANOMACLURIN ANALOGUE FROM *PELTOPHORUM AFRICANUM*

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Key Word Index—*Peltophorum africanum*; Leguminosae, heartwood metabolites, flavanoids, (6*R* 12*R* 13*S*)-12,13-*cis*-6,13-*cis*-2,3,9,13-tetrahydroxy-6,12-metano-6H,12H-dibenzo [*b*, *f*] [1, 5] dioxocin

Abstract—Several unusual condensed flavanoids and an affluence of familiar pyrano [3, 2-*c*] [2] benzopyran-6-(2H)-ones are accompanied in the heartwood of *Peltophorum africanum* Sond. by a novel 6,12-metano-6H,12H-dibenzo [b, f] [1, 5] dioxocin related to cyanomaclurin

INTRODUCTION

Peltophorum africanum represents the only species of this genus with a widespread distribution in Southern Africa [1]. Commonly known as Weeping wattle or African-wattle it is valued by several local tribes for its gum which although poisonous, is reputed to possess remedial properties [1, 2] Its red heartwood divulged a metabolic pool composed of divergent compound types comprising several unusual monomeric as well as condensed flavanoids, pyrano [3, 2-*c*] [2]-benzopyran-6-(2H)-ones and dibenzo [*b*, *d*]pyrones* of heterodimeric nature, similar to those from *Umtiza listerana* [3]

RESULTS AND DISCUSSION

[2*R*-(2α,3β,4α,10bβ)]-3,4,4a,10b-Tetrahydro-3,4,8,10-tetrahydroxy-2-(hydroxymethy)-9-methoxypyrano-[3, 2-*c*] [2] benzopyran-6(2H)-one (bergenin) [4] occurs at exceptionally high concentration (34% of total phenolic content) and was isolated from the heartwood together with its 11-*O*-galloyl ester [5] as the *O*-acetyl derivatives following acetylation. Coexisting flavanoids include (4α, 6)-bis-(−)-fisetinidol and its (4β, 6)-isomer with a natural distribution hitherto confined to *Colophospermum mopane* [6, 7], the 2,3-*trans*-3,4-*cis*: 2′,3′-*trans*-3′,4′, *cis*- and 2,3-*trans*-3,4-*trans*. 2′,3′-*trans*-3′,4′-*cis*-[3,4′ 3′,4]-*O*,*O*-linked-bis-(3,4,7-trihydroxyflavans) isolated previously only from *Acacia mearnsii* [8, 9], (−)-fisetinidol and fisetin. These are accompanied by a pair of unknown 4-arylflavan-3-ols,† a related δ-lactone† and the cyanomaclurin analogue (6*R*·12*R*:13*S*)-12,13-*cis*-6,13-*cis*-2,3,9,13-tetrahydroxy-6,12-metano-6H,12H-dibenzo[*b*, *f*] [1, 5] dioxocin (**1**). Compound **1** represents the first natural 6,12-metano-6H,12H-dibenzo[*b*, *f*] [1, 5] dioxocin displaying 1,2,4-oxygenation of the B-ring, the significance of which is augmented by the previous restriction of the natural occurrence of this class of compounds to a single example, cyanomaclurin (**2**) [10–12] Acetylation affords the tetraacetate (**3**, $[M]^+$ *m/z* 456). This gives rise to a ^{1}H NMR spectrum in which the A-ring protons resonate as an ABX-system typically compatible with resorcinol-type rings, but are accompanied by two singlets (δ6 68, 7 16, H-4, 1, respectively) as opposed to the AB-system (δ6 54, 6 59, $J_{2,4}$ 2 3 Hz, H-2, 4) displayed by the B-ring protons of an authentic cyanomaclurin tetraacetate sample (**4**). In correspondence to the latter however, both H-6 and H-12 are manifested by a doublet-of-doublets (δ5 32, 5 49, J = 2 0, 3.0 Hz × 2, H-6, 12, respectively), the smaller coupling originating from a pronounced *W*-effect [13] resulting from the rigid half-chair conformations adopted by both the C- and D-rings As anticipated H-13 occurs as a doublet-of-doublets (δ5 42, J = 3 0, 3 0 Hz) while ^{1}H NMR (singlets, δ2.02, 2 19, 2 20, 2 22) as well as mass spectrometry [*m/z* 456 $[M]^+$ −60 *m/z* 396 −42 (× 3) *m/z* 270] are consistent with the presence of a single aliphatic and three aromatic acetoxy groups Ambiguity regarding the relative positions of rings A and B is eliminated by ^{1}H NOE difference spectroscopy indicating association of H-12 with the low-field singlet (δ7 16, H-1, 4 4%) and H-6 with the doublet (δ7 34, J = 8 5 Hz, H-7, 1 8%) CD of the acetate (**3**) exhibits Cotton effects similar to those of the cyanomaclurin derivative (**4**) thus indicating the same (6*R*, 12*R*)-configuration at the benzylic chiral centres This *cis*-juncture between rings C and D is also evident from ^{1}H NMR coupling constants ($J_{6,13}$ = 3 0 Hz and $J_{12,13}$ = 3.0 Hz) and Dreiding models [14] Although the lack of evidence precludes unambiguous assignment of the chirality at C-13, conclusions resulting from a structural investigation of the cyanomaclurins [11] [δ(H-12)–δ(H-6) < 0.15 for (6*R*.12*R*.13*S*) and δ (H-12) (H-6) > 0 43 for (6*R*·12*R* 13*R*)] tentatively indicate a 13*S*-configuration [δ(H-12)–(H-6) = 0 17] and hence an absolute configuration of (6*R* 12*R* 13*S*) for (**3**)

*Although the dibenzo [*b*, *d*] pyrones could be typified by comparative NMR, confirmation regarding the substitution patterns was precluded by the lack of sufficient material–these are consequently not presently discussed

†Details to be included in an impending publication

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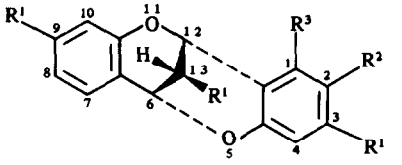

1 $R^1 = R^2 = OH$, $R^3 = H$
2 $R^1 = R^3 = OH$, $R^2 = H$
3 $R^1 = R^2 = OAc$, $R^3 = H$
4 $R^1 = R^3 = OAc$, $R^2 = H$

EXPERIMENTAL

Unless otherwise stated sepns were carried out by prep. TLC on Kieselgel PF_{254} (1 mm × 20 × 20 cm) or CC utilizing Sephadex LH-20 with EtOH as eluant Known compounds were identified by comparison of published physical data (mp, $[\alpha]_D$, CD, MS and ^1H NMR). Heartwood drillings (2.78 kg) from *P africanum* Sond were consecutively extd with EtOAc (3 × 12 l), Me_2CO (5 × 12 l) and MeOH (4 × 12 l) at room temp to yield crude material (28.2, 98.9 and 104.9 g, respectively) Bergenin (2 95 g) was crystallized (EtOH) from the EtOAc–extract following purification by CC (EtOH–MeOH gradient elution) and was characterized as its penta-*O*-acetyl derivative [15]. Supplementary extns by Soxhlet (EtOAc) of composites (1 . 1) of both the Me_2CO- and MeOH-exts with purified sand were respectively succeeded by Craig countercurrent procedures (20 tubes, H_2O–hexane–butan-2-ol, 5 2 3) to yield in total five fractions, A-D (from MeOH-extract) and E (from Me_2CO-extract) Secondary fractionation of A (3.4 g) by CC produced five subfractions (A1–A5 in order of increasing R_f) while fractions B–E were refined by the same method (CC).

TLC (C_6H_6–Me_2CO, 6 4, × 3) of fraction A3 (110 mg) gave two components (R_f 0 11 and 0.39) which were acetylated and respectively purified by TLC (hexane–Me_2CO–EtOAc, 11·6:3, R_f 0 30 and C_6H_6–Me_2CO, 9.1, R_f 0 40) to yield hepta-*O*-acetyl-11-*O*-galloylbergenin (9.6 mg) [5] and the hexa-acetate of a 2,3-*trans*-3,4-*trans*-4-aryl-flavan-3-ol (3.6 mg) * The 2,3-*trans*-3,4-*cis*-isomer (3.5 mg)* of the latter was obtained from fraction A2 (30 mg) following purification (TLC, C_6H_6–MeOH, 3 1, R_f 0.32), acetylation and repurification by TLC (C_6H_6–Me_2CO, 9:1, R_f 0.26). These are accompanied in fraction A4 (123 mg) by the related δ-lactone which was isolated as the Me ether derivative (21 mg)* by TLC (C_6H_6–Me_2CO, 19.1, R_f 0.19)

Methylation of fraction A5 (40 mg) followed by TLC (C_6H_6–Me_2CO, 4:1, R_f 0.25) gave (4α,6)-*bis*-(−)-fisetinidol hexamethyl ether which yielded the diacetate (8.4 mg) [6, 7] on acetylation. Similar treatment of fraction D (56 mg) (TLC, C_6H_6–Me_2CO, 9·1, R_f 0 06) produced the (4β, 6)-epimer (6 6 mg) [6, 7]. The closely related [3,4′·3′,4]-*O*-*O*-linked-2,3-*trans*-3,4-*trans* 2′,3′-*trans*-3′,4′-*cis*-profisetinidin and its 2,3-*trans*-3,4-*cis*-analogue were isolated from fraction C (43 mg) as the hexamethyl ethers (1.1 and 4.2 mg) [8] following methylation to facilitate sepn by TLC (C_6H_6–Me_2CO, 19:1, R_f 0 61 and 0 62).

Fraction E (207 mg) was acetylated to yield tetra-*O*-acetylfisetin (9 6 mg) by TLC (CH_2ClCH_2Cl–Me_2CO, 19:1) This is accompanied by the analogous (−)-fisetinidol in fraction B (305 mg) which was obtained as the trimethyl ether acetate (51 mg) succeeding methylation, purification (TLC, C_6H_6–Me_2CO, 7 3, R_f 0 29) and acetylation

[6R 12R·13S]-12,13-cis-13,6-cis-2,3,9,13-*Tetra-acetoxy*-6,12-*metano*-6H,12H-*dibenzo*[b, f] [1, 5]*dioxocin* (**3**). TLC (C_6H_6–MeOH, 3 1, R_f 0 42) of fraction A1 gave the phenol (**1**) Acetylation followed by TLC purification (C_6H_6–Me_2CO, 9 1, R_f 0 37) gave the tetra-acetate (**3**) (5.1 mg) as a colourless amorphous solid. (Found $[M]^+$ *m/z* 456 10713. $C_{23}H_{20}O_{10}$ requires 456.10565) MS *m/z* (rel. int) 456 $[M]^+$ (23), 414 (51), 396 (27), 372 (68), 354 (76), 330 (67), 312 (100), 288 (28), 287 (26), 270 (78), 178 (59). ^1H NMR (300 MHz, $CDCl_3$). δ2 08 (*s*, OAc-7), 2.27, 2.28, 2 30 (3 × *s*, OAc-2,3,9), 5.15 (*dd*, *J* = 2 0, 3.0 Hz, H-12), 5.32–5 35 (*m*, H-6, 13), 6 63 (*d*, *J* = 2 0 Hz, H-10), 6 68 (*s*, H-4), 6.73 (*dd*, *J* = 2 0, 8.5 Hz, H-8), 7.16 (*s*, H-1), 7 34 (*d*, *J* = 8.5 Hz, H-7), (300 MHz, CD_3COCD_3) δ2.02 (*s*, OAc-13), 2.19, 2 20, 2.22 (3 × *s*, OAc-2,3,9), 5 32 (*dd*, *J* = 2 0, 3 0 Hz, H-6), 5 42 (*dd*, *J* = 3 0, 3.0 Hz, H-13), 5 49 (*dd*, *J* = 2 0, 3 0 Hz, H-12), 6 65 (*d*, *J* = 2.0 Hz, H-10), 6.73 (*s*, H-4), 6 75 (*dd*, *J* = 2.0, 8.5 Hz, H-8), 7 32 (*s*, H-1), 7 47 (*d*, *J* = 8 5 Hz, H-7). CD (MeOH)· $[\theta]_{301}$ O, $[\theta]_{284} + 1.920 \times 10^4$, $[\theta]_{275}$ O, $[\theta]_{265} - 1\,391 \times 10^4$, $[\theta]_{242} - 0.251 \times 10^4$, $[\theta]_{228} - 0\,785 \times 10^4$, $[\theta]_{223}$ O, $[\theta]_{210} + 6\,953 \times 10^4$.

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