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Prenylated flavonoids from *Tephrosia apollinea*

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Abstract

In continuation of our chemical investigation on some medicinal plants of the genus *Tephrosia*, re-investigation of the methylenechloride/methanol (1:1) extract of the air-dried aerial part of *Tephrosia apollinea* afforded a new prenylated flavonoid **1**, in addition to an aromatic ester, a sesquiterpene, a lignan and several known prenylated flavonoids. The structures were established by (^{1}H NMR, ^{13}C NMR, DEPT, ^{1}H–^{1}H COSY, HMQC, HMBC, NOESY and HRMS). Relative configurations of **9** and **10** were confirmed by X-ray analysis.

Keywords: *Tephrosia apollinea*; Leguminosae; Prenylated flavonoids

The genus *Tephrosia* (Leguminosae; subfamily Papilionoideae; tribe *Tephrosieae*) includes about 400 species [1]. Extracts of some species have been reported to possess antibacterial and antifungal [2] and antiviral activities [3]. The extract of the whole flowering and fruiting parts of *T. purpurea* Pers. induced quinine reductase (QR) activity on cultured Hepa 1c1c7 (mouse hepatoma) cells [4,5]. Previously phytochemical investigation on *Tephrosia apollinea* gave prenylated flavonoids as the main constituent [6]. *T. purpurea* have revealed the presence of rotenoids, isoflavones, flavanones, flavanols, flavones [7] with chemotaxonomic importance in genus [8]. Re-investigation of *T. apollinea* afforded a new 8-prenylated flavonoid **1**, in addition to nine known compounds.

Column chromatography was carried out on kieslgel 60 (Merck; 230–400 mesh) and Sephadex LH-20 (Pharmacia Co. Tokyo, Japan). TLC was performed on silica gel 60 F_{254} plated (0.25 mm, Merck Co.), and spots were detected under UV light and coloured by spraying with 10% H_2SO4 solution followed by heating. The aerial part of *T. apollinea* was collected in spring of 2002, Aswan Island, Aswan, South of Egypt. A voucher specimen has been deposited in the Herbarium of the Department of Botany, Faculty of Science, South Valley University, Aswan, Egypt.

Air-dried aerial part (600 g) was extracted with CH_2Cl_2\methanol at room temperature. The extract was concentrated *in vacuo* to give a residue (50 g), which was chromatographed by using flash column chromatography on a silica gel eluted with *n*-hexane (2 L) followed by a gradient of *n*-hexane–CH_2Cl_2 up to CH_2Cl_2 and CH_2Cl_2–MeOH up to 15% MeOH (2 L each of the solvent mixture). The *n*-hexane–CH_2Cl_2 fraction (1:3) was carefully chromatographed on a Sephadex LH-20 column eluted with *n*-hexane–CH_2Cl_2–MeOH (7:4:0.25) with increasing the

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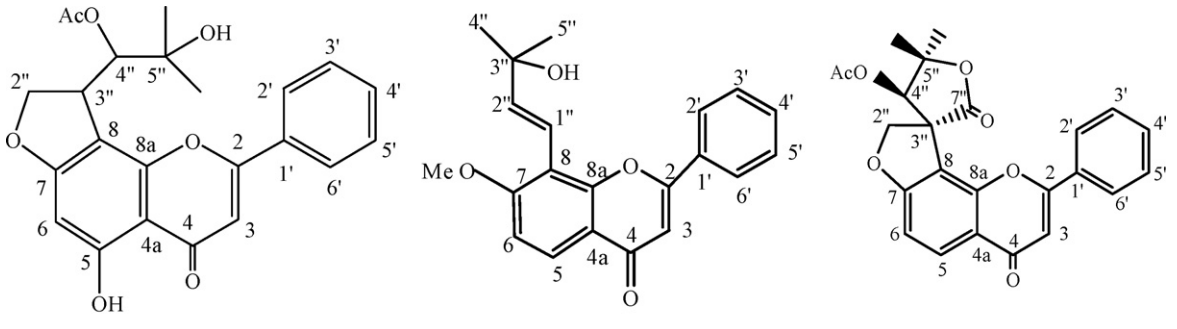
polarity to give compound **2** (12 mg), compound **3** (5 mg), compound **4** (15 mg), compound **5** (10 mg) and compound **9** (30 mg). The CH_2Cl_2 fraction (100%) was chromatographed on a Sephadex LH-20 column eluted with *n*-hexane–CH_2Cl_2–MeOH (7:4:0.5) afforded compound **1** (20 mg), compound **6** (15 mg), compound **7** (18 mg), compound **8** (7 mg), and compound **10** (35 mg). Here, we describe the isolation and identification of the new compound **1**, in addition to the X-ray structures of compounds **9** and **10**.

Compound (**1**) was isolated as colourless material; $[\alpha]_D^{25}$ +2.13 (1.90, $CHCl_3$). The structure of compound **1** was established from ^{1}H-NMR, ^{13}C-NMR, DEPT, ^{1}H–^{1}H COSY, ^{1}H–^{13}C COSY, HMBC, EIMS and HREIMS. The EIMS spectrum showed the molecular ion peak at *m*/*z* = 410 (23%) in agreement with the molecular formula $C_{23}H_{22}O_7$. The base peak at *m*/*z* = 279 (100%) was attributed to cleavage of side chain (2-hydroxy-2-methyl-propyl acetate). Exact mass determination of the molecular ion established the elemental composition $C_{23}H_{22}O_7$, exp. 410.1354, (calcd. 410.1353). The ^{1}H-NMR spectrum of compound (**1**) showed three singlet signals at δ_H 1.25 (3H, s), 1.29 (3H, s) and 1.92 (3H, s) were assigned to the *gem*-Me_2 group adjacent to an oxygen function and the methyl of the secondary acetate group. Furthermore, it revealed the presence of three singlet signals at δ_H = 6.63 (1H), 6.26 (1H), and 5.61 (1H), were assigned to H-3, H-6 and H-4″, respectively. Additionally the ^{1}H-NMR spectrum showed a triplet signal at δ_H = 4.73 (*J* = 19.0 Hz) and a doublet of doublets appeared at δ_H = 5.11 (*J* = 10.2, 19.0 Hz), showed correlations in ^{1}H–^{13}C COSY with one carbon signal at δ_C = 73.7, C-2″. The later protons showed clear correlations in ^{1}H–^{1}H COSY with a doublet of doublets at δ_C = 4.26 (*J* = 10.2, 19.0 Hz), H-3″. Meanwhile, the ^{13}C-NMR spectrum with the aid of DEPT experimental displayed 23 carbon signals, of them 2 carbonyls, 1 methylene, 3 methyls, 8 quaternary, and 9 methines. The large amount of this compound allowed us to run HMBC experiment, which gave clear correlations between H-3 with C-2, C-1′, C-4a; H-6 with C-5, C-7, C-8, C-4a; H-2″ with C-7, C-4″; H-3″ with C-7, C-8 and H-4″ with C-8, carbonyl carbon of acetate. Therefore, compound (**1**) was identified as 5-hydroxytephroapollin F, a new natural product.

The structures of known compounds, 2-propenoic acid, 3-(4-(acetyloxy)-3-methoxypheny)-3(4-actyloxy)-3-methoxyphenyl)-2-propenyl ester **2** [9], 4-isopropyl-1,8-dimethyldecahydroazulene-5,8,9-triol. **3** [10], pinoresino **4**



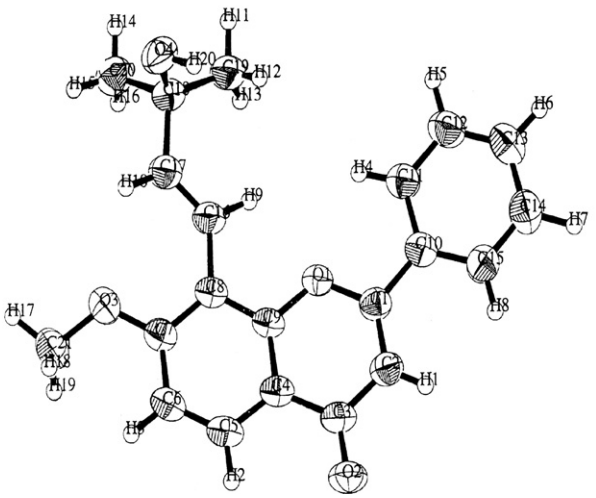


Fig. 1. ORTEP diagram of the X-ray structure of compound **9**.

[11], pseudosemiglabrin **5**; (−)-semiglabrin **6**; (−)-semiglabrinol **7** and (+)-tephroglabrin **8** [8] have been deduced by comparison of their spectral data with those in literature.

1. X-ray crystallography of compound *9*

Single crystal X-ray analysis established the complete structure and relative stereochemistry of compound (**9**) (Fig. 1) and the crystal data summarized as follows: $C_{21}H_{20}O_4$, formula wt 336.39, monoclinic, space group $P2_1$-c (# 14) $a = 7.3500$ (4) Å, $b = 11.3130$ (4) Å, $c = 20.571$ (1) Å, $V = 1710.49$ (1) Å^3, $Z = 4$, $D = 1.369$ g cm^{-3}. All measurements were made on a MacScience DIP2030 imaging plate area detector with graphite monochromated Mo Kα radiation. The structure was solves by direct methods [12], and expanded using Fourier techniques [13]. By comparing the data of compound **9** with those isolated before [14], all the data were in complete agreement with those reported for lanceolatin-A.

2. X-ray crystallography of compound *10*

Single crystal X-ray analysis established the complete structure and relative stereochemistry of compound (**10**) (Fig. 2) and the crystal data summarized as follows: $C_{24}H_{20}O_7$, formula wt 420.42, Orthorhombic, space group $P2_12_12_1$, $a = 14.6740$ (4) Å, $b = 7.1040$ (2) Å, $c = 19.9460$ (5) Å, $V = 2079.25$ (8) Å^3, $Z = 4$, $D = 1.343$ g cm^{-3}. All diagrams and calculations were performed using maXus (Brucker Nonius, Delft & Mac Science, Japan), using graphite monochromated Mo Kα radiation (λ = 0.71069 Å). The structures were refined by full matrix least squares on F^2 using Brucker SHELEXL-97 [15]. The final R and R_w were 0.045 and 0.060, respectively. By comparison the spectral data of compound **10** with those isolated before [16,17], compound **10** was identified as (+)-glabratephrin.

Spectral data of compound **1**: IR, $\tilde{\nu}$/cm^{-1}: 3450 (OH), 1744 ($CH_3\underline{CO}$), 1685 (C=O), 1600 (C=C). ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm): 6.63 (s, 1H, CH, H-3), 6.26 (s, 1H, CH, H-6), 7.88 (m, 2H, CH, H-2′, 6′), 7.55 (m, 3H, CH, H-3′, 5′, H-4′), 4.73 (t, 1H, CH, H-2″a), 5.11 (dd, 1H, CH, H-2″b), 4.26 (dd, 1H, CH, H-3″), 5.61 (s, 1H, CH, H-4″), 1.25 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.92 (s, 3H, $\underline{CH_3}$ CO), 13.06 (s, 1H, phenolic OH). ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm): 163.4 (C-2), 106.3 (C-3), 182.2 (C-4), 105.4 (C-4a), 163.6 (C-5), 94.2 (C-6), 167.0 (C-7), 103.5 (C-8), 153.3 (C-8a), 131.7 (C-1′), 126.2 (C-2′, 6′), 129.1 (C-3′, 5′), 131.7 (C-4′), 73.7 (C-2″), 40.1 (C-3″), 76.8 (C-4″), 72.7 (C-5″), 27.1, 27.5 (*gem*-Me_2), 20.5 ($\underline{CH_3}CO$), 170.0 ($CH_3\underline{CO}$). MS, *m*/*z* (I_r/%): 410 (23) (M^+), 279 (100), 256 (25), 105 (30), 57 (45): calcd. For $C_{23}H_{22}O_7$, 410.1353; found 410.1354.

Spectral data of compound **10**: Colourless crystals, $[\alpha]_D^{25}$ +14.55 (3.12, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$, δ ppm): 6.78 (s, 1H, CH, H-3), 8.21 (d, 1H, CH, H-5), 6.98 (d, 1H, CH, H-6), 7.89 (m, 2H, CH, H-2′, 6′), 7.53 (m, 3H, CH, H-3′, 5′, H-4′), 4.99 (dd, 1H, CH, H-2″), 5.42 (s, 1H, CH, H-4″), 1.49 (s, 3H, CH_3), 1.54 (s, 3H, CH_3), 1.61 (s, 3H,

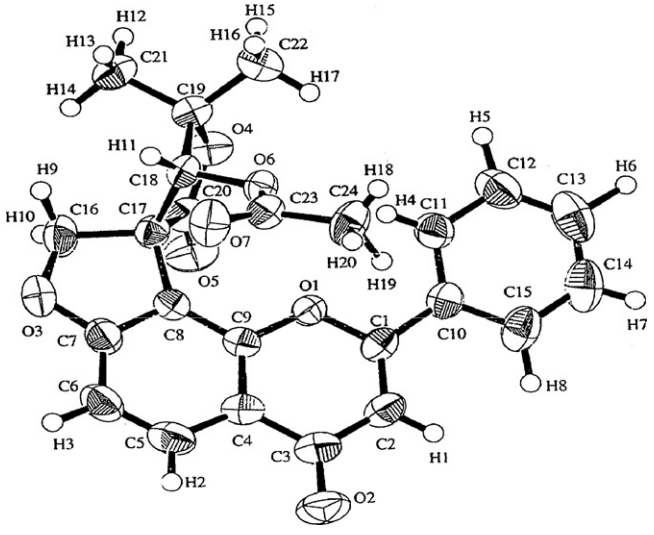


Fig. 2. ORTEP diagram of the X-ray structure of compound **10**.

$\underline{CH_3}$ CO). ^{13}C NMR (125 MHz, $CDCl_3$, δ ppm): 162.5 (C-2), 107.3 (C-3), 177.1 (C-4), 118.6 (C-4a), 130.1 (C-5), 109.2 (C-6), 165.2 (C-7), 111.8 (C-8), 153.7 (C-8a), 131.5 (C-1′), 126.2 (C-2′, 6′), 129.1 (C-3′, 5′), 131.7 (C-4′), 81.4 (C-2″), 58.8 (C-3″), 80.2 (C-4″), 85.3 (C-5″), 174.3 (C-7″), 28.6, 22.2 (*gem*-Me_2), 19.8 ($\underline{CH_3}CO$), 168.8 ($CH_3\underline{CO}$). MS, *m*/*z* (I_r/%): 420 (80) (M^+), 317 (100), 291 (30), 263 (50), 83 (28).

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