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IDENTIFICATION OF SESQUITERPENES FROM *PEREZIA TURBINATA*

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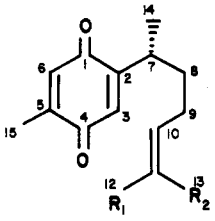
ABSTRACT.—Three new and four known sesquiterpenes have been isolated from the roots of *Perezia turbinata*. The new sesquiterpenes are 2-(*Z*-1,5-dimethyl-6-oxo-4-hexenyl)-5-methyl *p*-benzoquinone [**1**], 13-acetoxyxanthorrhizol [**2**], and parvifolinone [**4**]. The known compounds are parvifoline [**3**], α,β pipitzols, isovalerate of curcuquinol, and isoparvifolinone. The structure of **1** was confirmed by correlation with that of glandulone A [**5**] and the structure of **2** by transformation to **1**.

The genus *Perezia* (Compositae) consists of more than 40 species spread throughout North America. Thirty-seven species are recorded in Mexico (1). In the traditional Mexican system of medicine, indigenous Mexicans have used *Perezia* species as antiphlogistic agents, as fever remedies, etc. (2). Biological studies of some of these compounds have been reported (3,4). We have completed the phytochemical investigation of *Perezia turbinata* LaLlave & Lexarza, which provides new compounds which will be probed as antimicrobials.

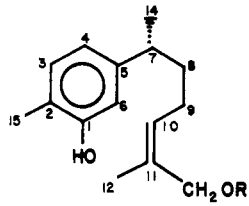
RESULTS AND DISCUSSION

In a continuation of studies on the constituents of the genus *Perezia*, we have isolated and characterized several sesquiterpenes from *P. turbinata*. Parvifoline [**3**] (5) and α,β pipitzoles (6) were crystallized from hexane extracts of the roots and identified by direct comparison with authentic samples.

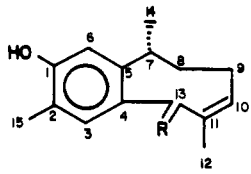
The mother liquors left after crystallization were chromatographed repeatedly. The less polar fraction gave a colorless oil characterized as the isovalerate of curcuquinol (7) by spectral data (ir, H and ^{13}C nmr) and comparison with an authentic sample.



1 R_1=Me, R_2=CHO
5 R_1=CHO, R_2=Me
6 R_1=R_2=Me
7 R_1=Me, R_2=CH_2OH



2 R=Ac
8 R=H



3 R=H_2
4 R=O

Further chromatography gave a mixture which by successive chromatography gave **1** and **2**. The less polar compound **1**, $[\alpha]_D$ −115.3°, was a pale yellow oil, the ^{1}H-nmr spectrum of which showed signals due to an aldehyde proton (δ 6.61, q, J=1.5) and 6.60 (d, J=1.0), a vinylic proton at δ 6.48, and other signals assigned to methyl and methylene groups (Table 1). The structure of compound **1** was deduced from ^{1}H- and ^{13}C-nmr spectra by means of COSY and ^{13}C APT experiments. The configuration at C-7 was assigned as *R*, since double bond isomerization (8) yielded (−)-glandulone [**5**] (9), $[\alpha]$ −139.7°, which was also obtained by SeO_2 oxidation (10) of (−)-*R*-curcuquinone [**6**] (11).

Compound **2** was obtained as a colorless oil: $C_{17}H_{24}O_3$ (based on hrms). The nature of the oxygen atoms was defined after inspection of the ir spectrum. Absorption at 3500 cm^{-1} is attributed to a hydroxyl group, and the band at 1750 cm^{-1} corresponds to a nonconjugated ester. The nature of the hydroxyl group was deduced by a positive $FeCl_3$ test and inspection of the ^{1}H- and ^{13}C-nmr spectra data, which in addition gave further structural information. The aromatic ring was evident from a ^{13}C oxygen-bearing singlet at δ 154.27, singlets at δ 146.39 and 121.67, and three doublets at 130.9, 119.20, and 113.68 and from ^{1}H-nmr signals for three aromatic protons at positions 1, 2, and 4 (δ 6.61, 6.60, and 7.03). The remaining sp^2 ^{13}C signals were assigned to a carbonyl (δ 171.43) and to a double bond which shows signals at δ 129.77 and 130.89. One of the substituents of the double bond is a methyl group (δ 1.72) and the other is a methylene at δ 4.53 which is bonded to an acetoxy group. When compound **2** was hydrolyzed, the methylene group was shifted to δ 3.89. The *Z* stereochemistry of the double bond and the *R* configuration of C-7 in compound **2** were confirmed when alcohol **8** (obtained by hydrolysis of **2**) was treated with Fremy's salt to afford quinone **7**. Subsequent allylic alcohol oxidation (DDQ) yielded a yellow oil, which was shown to be identical in all respects with **1**.

Compound **2** is of special interest, since Bohlmann suggested than 13-hydroxyxanthorrizol could be a biogenetic precursor of parvifoline [**3**] (12,13).

The last three compounds isolated from the roots were characterized as taraxasterol (14), isoparvifolinone (15), previously isolated from this genus, and parvifolinone [**4**]. The structure of **4** was established from its spectral data (summarized in the Experimental) and by its being obtained from SeO_2 oxidation of parvifoline [**3**] (7). Parvifolinone [**4**] has not previously been isolated from a natural source.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points are uncorrected, ir spectra and optical rotations were determined in $CHCl_3$ solution, and nmr spectra were obtained in $CDCl_3$.

EXTRACTIONS OF *P. TURBINATA*.—The roots of *P. turbinata* were collected at Jacona, Michoacán México, and voucher samples (UMEB 92-896) were deposited at Escuela de Biología, Universidad Michoacana, Morelia, Michoacán México, where Prof. Xavier Madrigal kindly classified the material. The dried and ground roots (5 kg) were extracted with hexane under reflux for 6 h. The combined extracts were evaporated to a small volume and left overnight at 4°. After crystallization, the oily material was decanted. Chromatography and recrystallization (Et_2O) of the amorphous solid gave parvifoline [**4**] and α and β pipitzols, identified by direct comparison with authentic samples. The mother liquors from isolation of parvifoline and the pipitzols were evaporated to dryness and chromatographed over Si gel. Five main fractions were separated: A (hexane), B (hexane/C_6H_6), C, D, and E (hexane/EtOAc in ascending polarity).

Curcuquinol monoisovalerate.—Fraction A, rechromatographed over SiO_2 (hexane), gave a colorless oil identified by ^{1}H and ^{13}C nmr and by direct comparison with an authentic sample (7).

2-(Z-1,5-dimethyl-6-oxo-4-hexenyl)-5-methyl p-*benzoquinone* [**1**].—Fraction B, rechromatographed over SiO_2 in increasing polarity (hexane, hexane/C_6H_6), gave two compounds. The less polar compound **1** was a pale yellow oil: $[\alpha]_D$ −115.3° ($CHCl_3$, c=0.93); ir 2720 and 1685 (O-H and C=O, α,β-unsaturated aldehyde), 1650 (C=C-C=O, quinone); ^{1}H and ^{13}C nmr see Table 1; hrms *m/z* 246.1243 (calcd for $C_{15}H_{18}O_3$, 246.1256).

TABLE 1. ^{1}H- (200 MHz) and ^{13}C-nmr Data of Compound **1**.[a]

Position	^{1}H	^{13}C
1	—	187.72[b]
2	6.61 q (J=1.5)	131.84[c]
3	—	145.90
4	—	188.74[b]
5	6.60 d (J=1.0)	134.23
6	—	136.86[c]
7	2.92 brq (J=7.0)	31.55
8	1.66—1.75 m	25.04
9	2.5 m	36.19
10	6.48 (J=7.2, 1)	153.61
11	—	154.08
12	1.76 d (J=1)	19.64
13	10.08 s	191.42
14	1.61 d (J=7.0)	11.43
15	2.05 d (J=1.5)	14.54

[a]Assignment with HETCOR.
[b,c]Assignments interchangeable.

13-Acetoxyxanthorrhizol [**2**].—The last compound isolated by rechromatography of fraction B was obtained as a colorless oil identified as **2**: $[\alpha]_D$ −76.5° ($CHCl_3$; c=0.52); ir 3500 and 1750 (OH phenol and C=O acetate); ^{1}H nmr (200 MHz) 7.04 and 6.65 (1H each, d), 6.60 (1H, s), 6.1 (1H, br, s, D_2O exchangeable), 5.37 (1H, t, with further couplings, J=7 Hz), 4.56 and 4.53 (2H, A-B system J=11, CH_2O), 2.56 (1H, sext, J=7 Hz, CH), 2.20 (3H, s, ArMe), 2.07 (3H s, acetate), 1.96 (2H, m, CH_2-), 1.72 (3H, s, Me), 1.58 (2H, m, CH_2), 1.19 (3H, d, J=7 Hz, *Me*CH); ^{13}C nmr 171.43 (C=O), 154.27, 146.39, 129.77, and 121.67 (C-1, -2, -11, and -5), 130.95, 113.68, and 119.20 (C-3, -10, -4, and -16), 63.57 (C-13), 38.20 (C-8), 32.95 (C-7), 25.76 (C-9), 22.67 (C-14), 21.34 (C-12), 21.67 (C-Ac), 15.5 (C-15); hrms m/z 276.1730 (calcd for $C_{17}H_{24}O_3$, 276.1726).

(−)-Glandulone A [**5**].—Curcuquinone [**6**] (250 mg) was obtained by the reported method (11). Compound **6** was treated with SeO_2 in EtOH (9), and after Se elimination and purification yielded (−)-glandulone A [**5**] (180 mg). Spectroscopic constants of the product were the same as those reported earlier for (+)-glandulone (10) except for the sign of optical rotation: $[\alpha]_D$ −139.7 (c=0.79, $CHCl_3$). The same compound **5** was, obtained by isomerization of compound **1** (100 mg) and dioxane (50 ml) with alkaline alumina in an N_2 atmosphere (16).

13-Hydroxyxanthorrhizol [**8**].—To a solution of acetate **2** (300 mg) in dioxane under N_2 was added 10% K_2CO_3 (2 ml), and the mixture was stirred at 45° for 3 h. After neutralization, the product was extracted and concentrated. Its ^{1}H nmr showed δ 3.89 due to a CH_2OH group in addition to other signals typical of the molecule (13); hrms m/z 234.1625 (calcd for $C_{15}H_{22}O_2$, 234.1620.

CHEMICAL CORRELATION OF **2** WITH **1**.—A $CHCl_3$ solution of **8** (200 mg), obtained by hydrolysis of **2**, was treated with an Na_2HPO_4/NaH_2PO_4 buffered solution (pH 6) of Fremy's salt (3 molar excess) with stirring for 1 h at room temperature. The organic phase was washed with H_2O, dried, and concentrated. The residue **7** (yellow oil) without purification was dissolved in CCl_4 (10 ml), and 250 mg of DDQ was added. After 3 h of stirring at room temperature, DDQH formed and was filtered, and evaporation of the solvent yielded 80 mg of **1** identical in all respects with natural **1**.

Parvifolinone [**4**].—Fraction E [hexane-EtOAc (8:2)] rechromatographed over SiO_2 [hexane-EtOAc (9.5:0.5)] afforded white needles: mp 184–185°; ir ($CHCl_3$) ν max 3500 and 1600 cm^{-1} (OH and C=C-C=O); ^{1}H nmr (100 MHz, $CDCl_3$) δ 7.42 (1H, s, br, H-6), 6.65 (1H, s, H-3), 6.47 (1H, t, with further unresolved couplings, J_t=7 Hz, H-10), 4.51 (1H, s, lost on addition of D_2O, OH), 3.12 (1H, m, H-7), 2.24 (3H, s, Ar-Me), 3.04 (3H, d, vinyl Me), 1.3 (3H, d, J=7 Hz, secondary Me), remaining four protons (H_a-8, H_b-8, H_a-9, and H_b-9) in the 1.5–2.1 region; ^{13}C nmr 195.30 (c=O), 157.09, 143.36, 140.98, 135.17, and 121.62 (C-1, -2, -4, -5, and -11), 139.24, 132.75 and 110.11 (C-6, -3, and -10), 39.18 and 25.55 (C-8 and -9), 31.40 (C-7), 21.21, 18.15, and 15.17 (C-12, -14, and -15).

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LITERATURE CITED

1. R. Bacigalupi, "A monograph of the genus *Perezia* Section Acourtia," Contr. Gray Herbarium of Harvard, **97**: 1-81, Cambridge, 1931.
2. J.L. Diaz, in: "Usos de las Plantas Medicinales de México." Ed. by Libros de Mexico S.A., IMEPLAM, México D.F., 1976.
3. M. Perusquia, R. Ibañez, and G. Alcántara, *Med. Sci. Res.*, **19**, 857 (1991).
4. X. García, L. Cano, L. Herréra, N.R. Magaña, G. Alcántara, and E. Gijon, *Proc. West. Pharmacol. Sci.*, **35**, 93 (1992).
5. E. García G., V. Mendoza, and J.A. Guzmán B., *J. Nat. Prod.*, **51**, 150 (1988).
6. F. Walls, J. Padilla, P. Joseph-Nathan, F. Giral, and J. Romo, *Tetrahedron Lett.*, 1577 (1965).
7. P. Joseph-Nathan, J.D. Hernández, L.U&. Román, E. García G., and V. Mendoza, *Phytochemistry*, **21**, 669 (1982).
8. A.J. Hubert and H. Reimlinger, *Synthesis*, 97 (1969).
9. O. Spring, U. Rodon, and F.A. Macias, *Phytochemistry*, **31**, 1541 (1992).
10. P. Joseph-Nathan, V. Mendoza, and E. García G., *Tetrahedron*, **33**, 1573 (1977).
11. E. García G., V. Mendoza, and A. Guzmán B., *J. Nat. Prod.*, **50**, 1055 (1987).
12. F. Bohlmann and C. Zdero, *Chem. Ber.*, **110**, 468 (1977).
13. W. Krause and F. Bohlmann, *Tetrahedron Lett.*, **28**, 2575 (1987).
14. L.R. Angeles, O. Lock de U., I.C. Salkeld, and P. Joseph-Nathan, *Phytochemistry*, **23**, 2094 (1984).
15. P. Joseph-Nathan, J.D. Hernández, L.U. Román, E. García G., V. Mendoza, and S. Mendoza, *Phytochemistry*, **21**, 1129 (1982).
16. H. Zimmer, D.C. Lankin, and S.W. Horgan, *Chem. Rev.*, **71**, 2229 (1971).

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