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CHROMANS FROM *HELIANTHELLA QUINQUENERVIS*

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Key Word Index—*Helianthella quinquenervis*; Compositae; Heliantheae; *p*-hydroxyacetophenone derivatives; encecalin; 3,4-chromanediols.

Abstract—Investigation of *Helianthella quinquenervis* afforded, in addition to several known 6-acetylchromenes, 3-prenyl-4-hydroxyphenone and the benzofuran encecalin, *cis*- and *trans*-2,2-dimethyl-3,4,7-trihydroxy-6-acetylchroman.

INTRODUCTION

Helianthella is a small genus of helianthoid composites indigenous to the western United States and adjacent Canada and Mexico [1]. Transitionally it is included in subtribe Verbesininae (or Helianthinae) as defined by Stuessy [2], while a recent revision of the tribe has placed it in a redefined subtribe Ecliptinae [3]. Chemical reports on the genus seem to be limited to the roots of *H. uniflora* (Nutt.) T. & G. [4]. The present report describes the results of our examination of the aerial parts of *H. quinquenervis* (Hook.) Gray.

RESULTS AND DISCUSSION

Chloroform extraction of *H. quinquenervis* furnished the known chromenes **1a**–**1c** and the related known compounds **2** and **3**. Substances **1a**, **1b**, **2** and **3** were previously isolated from the roots of *H. uniflora* [4] and **1c** (encecalin) from the aerial parts of *Encelia californica* [5]. Two new isomeric diols **4a** and **5a**, $C_{13}H_{16}O_5$, were obtained in small amounts from the polar fraction. The ^{1}H NMR spectrum of **4a** exhibited signals of mutually coupled protons at δ4.77 and 3.73, shifted to δ6.59 and 5.77 on conversion of **4a** to dibenzoate **4b** and hence obviously due to two hydrogens under vicinal hydroxyl groups. This, in conjunction with the other signals in the ^{1}H NMR spectrum (see Experimental), led to formulation of the diol as **4a**, the *cis*-stereochemistry of the hydroxyl groups being based on the value of $J_{3,4}$ (4 Hz). This was confirmed by partial synthesis of **4a** by oxidation of **1a** with osmium tetroxide.

The isomeric diol exhibited mutually coupled signals at δ4.50 and 3.53 (J = 9 Hz) which moved downfield to δ6.44 and 5.75 on dibenzoylation to **5b**; hence it was the *trans*-isomer **5a**. Attempts to synthesize **5a** from **1a** by the Prévost reaction gave the *trans*-iodoacetates **6a** and **6b**, but no diacetate. The facile iodination of the aromatic ring under these conditions is surprising; that C-5 was unsubstituted was shown by the chemical shift of the remaining aromatic proton signal which is allylically coupled to H-4. Prévost reaction on **1d** afforded only **6c**; base treatment of the latter resulted in the formation of **7** rather than hydrolysis to **5a**, thus establishing the location of the non-aromatic iodine atom in **6a**–**6c**.

Kis and coworkers [6] have isolated similar diols, the 3,4-*cis*- and 3,4-*trans*-dihydroxy-6-methoxy-2,2-dimethylchromans **8** and **9**, from the basidomycete *Panus rudis* Fr. The absolute configurations shown in formulae **8** and **9** were established by CD spectrometry of the corresponding dibenzoates. Our diols were optically inactive.*

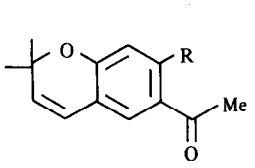
From a chemical point of view, the root extract of *H. uniflora* and the extract of the herb of *H. quinquenervis* do not differ significantly. Further work is necessary to establish whether the occurrence of isopentenylacetophenones is characteristic of the genus. Some other representatives of genera are included in Ecliptinae as redefined [3] elaborate similar compounds, but the chemistry of the subtribe as a whole is not uniform [7].

EXPERIMENTAL

Isolation of H. quinquenervis *constituents.* Above-ground parts (1.3 kg) of *Helianthella quinquenervis* (Hook.) Gray, collected by Dr. B. H. Braun in Boulder County, Colorado in summer 1960, were extracted with $CHCl_3$ and worked up in the usual fashion [8]. The crude gum (22 g) was adsorbed on 30 g silicic acid (Mallinckrodt 100 mesh) and chromatographed over 400 g of the same adsorbent packed in hexane, 500 ml fractions of eluant being collected as follows: fractions 1–4 (hexane), 5–10 (hexane–EtOAc, 19:1), 11–16 (hexane–EtOAc, 9:1), 17–22 (hexane–EtOAc, 4:1), 23–28 (hexane–EtOAc, 3:2), 29–32 (hexane–EtOAc, 2:3), 33–36 (hexane–EtOAc, 1:4), 37–38 (EtOAc), 39–40 (EtOAc–MeOH, 99:1) 41–42 (EtOAc–MeOH, 49:1), 43–44 (EtOAc–MeOH, 19:1) and 45–46 (EtOAc–MeOH, 9:1).

Fractions 5 and 6 were combined; recrystallization gave 3.4 g of **1a**, mp 81–82°, lit. mp 77° [4]. Purification of fractions 5 and 6 by TLC (C_6H_6–EtOAc 19:1, multiple developments) afforded gummy **1b** (0.355 g) and **1c** (0.557 g). Fraction 12 had mainly one constituent; purification by TLC (C_6H_6–EtOAc, 19:1) yielded **2** (1.3 g); fraction 11 also gave 0.230 g **2**. Purification of fraction 17 by TLC (C_6H_6–EtOAc 19:1, 2 developments) gave **3** (89 mg), mp 89–91° (Et_2O–hexane), lit. mp 93–94° [4]. Fraction 25 on standing in EtOAc deposited 84 mg of a 1:1 mixture of **4a** and **5a**.

*The slight rotation exhibited by **5a** (see Experimental) can be ascribed to an impurity as the rotation of **5b**, like that of **4b**, was 0° and as the CD curves of **4b** and **5b** were transparent.



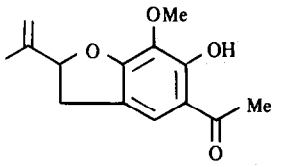
R

1a OH

1b H

1c OMe

1d OAc



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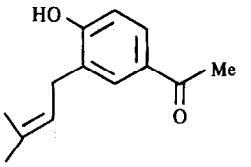

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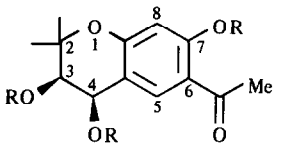
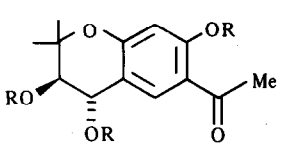


R

4a H

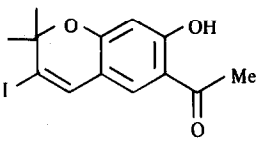
4b COPh



R

5a H

5b COPh



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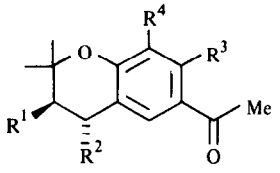
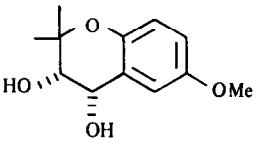


6a $R^1, R^4 = I; R^2 = OAc; R^3 = OH$

6b $R^1 = I; R^2 = OAc; R^3 = OH; R^4 = H$

6c $R^1 = I; R^2, R^3 = OAc; R^4 = H$



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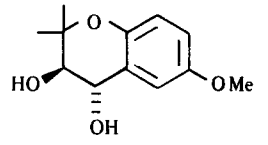

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Purification of 45 g of the mixture by TLC ($CHCl_3$–MeOH–EtOAc, 18:1:1, 2 developments) yielded spectroscopically pure **4a** (14 mg) and **5a** (18 mg).

Diol **4a**, mp 220–221° (MeOH) had IR bands (KBr) at 3470, 3400, 1650 and 1610 cm^{-1}; ^1H NMR spectrum (270 MHz, $CDCl_3$ and 3 drops of DMSO-d_6–D_2O): δ7.97 (*d*, J = 1 Hz, H-5), 6.34 (H-8), 4.77 (*dd*, J = 4, 1 Hz, H-4), 3.73 (*d*, J = 4 Hz, H-3), 2.58 (3H, H-9), 1.50 and 1.31 (*br*, each 3H, H-10 and H-11), and 12.42 (7-OH). [Calc. for $C_{13}H_{16}O_5$: MW, 252.0999. Found: MW(MS), 252.1013.]

Diol **5a** had mp 170–172° ($CHCl_3$–MeOH), $[\alpha]_D$ −6°, IR bands (KBr) at 3470, 3400, 1650 and 1610 cm^{-1}; ^1H NMR spectra (270 MHz, $CDCl_3$–3 drops of DMSO-d_6): δ12.41 (7-OH), 7.96 (*d*, J = 1 Hz, H-5), 6.25 (H-8), 4.91 (*d*, J = 5 Hz, 4-OH), 4.82 (*d*, J = 4 Hz, 3-OH), 4.49 (*ddd*, J = 9, 5, 1 Hz, H-4), 3.52 (*dd*, J = 9, 4 Hz, H-3), 2.58 (3H, H-9), 1.49 and 1.24 (*br*, each 3H, H-10 and H-11) (addition of D_2O caused disappearance of the –OH signals and simplification of the H-3 and H-4 signals); [Calc. for $C_{13}H_{16}O_5$: MW, 252.0999. Found: MW(MS), 252.0986].

Benzoylation of the diols. The 1:1 mixture of **4a** and **5a** (30 mg) in 0.5 ml pyridine was stirred with 0.2 ml benzoyl chloride overnight at room temp. The usual work-up and purification of the product by TLC (C_6H_6–EtOAc, 39:1) afforded 31 mg **4b** and 26 mg **5b**. Dibenzoate **4b** had mp 168–170° (Et_2O–hexane), $[\alpha]_D$ 0°; ^1H NMR spectrum (270 MHz, $CDCl_3$): δ8.26–7.30 (*m*, 16H, aromatic H and H-5), 6.84 (H-8), 6.59 (*dd*, J = 4, 1 Hz, H-4), 5.77 (*d*, J = 4 Hz, H-3), 2.45 (3H, H-9) and 1.57 (*br*, 6H, H-10 and H-11). Dibenzoate **5b** had mp 191–191.5° (Et_2O–hexane), $[\alpha]_D$ 0°; ^1H NMR spectrum (270 MHz, $CDCl_3$): δ8.27–7.74 and 7.76–7.38 (*m*, 16H, aromatic H and H-5), 6.83 (H-8), 6.44 (*dbr*, J = 5.8 Hz, H-4), 5.67 (*d*, J = 5.8 Hz, H-3), 2.44 (3H, H-9), 1.61 and 1.54 (*br*, each 3H, H-10 and H-11).

Reactions of **1a**. (A) A soln of 0.250 g **1a** in 3 ml pyridine was stirred with 0.250 g O_5O_4 at room temp. for 24 hr. After addition of 0.450 g $NaHSO_3$ in 8 ml H_2O and 5 ml pyridine, stirring was continued for 15 min. The mixture was extracted with $CHCl_3$. The washed and dried organic layer on evapn gave a product identical in all respects with **4a**.

(B) A soln of 0.400 g **1a** in 15 ml C_6H_6 was stirred with 0.80 g AgOAc in N_2 while 0.60 g I_2 was added in portions during a 10 min period. The mixture was refluxed for 2 hr, filtered while hot and evapd. TLC (C_6H_6–EtOAc, 39:1, 3 developments) of the residue yielded 0.120 g **6a** and 0.210 g of a mixture of **6a** and **6b**. The low resolution MS of **6a** had peaks at *m/z* (rel. int.) 530 (M^+, $C_{15}H_{16}O_5I_2$), 488 (2), 470 (19), 455 (46), 360 (73), 343 (100) and 328 (93); ^{1}H NMR spectrum (270 MHz, $CDCl_3$): δ13.54 (7-OH), 7.61 (*br*, H-5), 6.33 (*dbr*, J = 7.5 Hz, H-4), 4.42 (*d*, J = 7.5 Hz, H-3), 2.56 (3H, H-9), 2.22 (3H, Ac), 1.76 and 1.63 (*br*, each 3H, H-10 and H-11); ^{1}H NMR spectrum of **6b** (from that of the mixture, 270 MHz, $CDCl_3$): δ12.44 (7-OH), 7.59 (*br*, H-5), 6.38 (H-8), 6.29 (*dbr*, J = 7.5 Hz, H-4), 4.43 (*d*, J = 7.5 Hz, H-3), 2.52 (3H, H-9), 2.21 (3H, Ac), 1.67 and 1.57 (each 3H, H-10 and H-11).

(C) Acetylation of **1a** furnished monoacetate **1d** [4]. Repetition of the AgOAc–I_2 reaction with **1d** (0.340 g) gave 0.240 g **6c**; ^{1}H NMR spectrum (270 MHz, $CDCl_3$): δ7.70 (*br*, H-5), 6.60 (H-8), 6.35 (*dbr*, J = 7.5 Hz, H-4), 4.24 (*d*, J = 7.5 Hz, H-3), 2.48 (3H, H-9), 2.34 and 2.21 (each 3H, Ac), 1.68 and 1.59 (*br*, each 3H, H-10 and H-11). A soln of 60 mg **6c** in 3.5 ml THF and 6 ml MeOH was stirred with 2 ml 1 N NaOH for 3 hr at room temp. Removal of the solvent gave 34 mg **7**, ^{1}H NMR spectrum (270 MHz, $CDCl_3$): δ12.73 (7-OH), 7.27 (H-5), 6.95 (H-4), 6.35 (H-8), 2.53 (3H, H-9) and 1.59 (6H, H-10 and H-11).

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