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GUAIANOLIDES FROM *TRICHOLEPIS GLABERRIMA*

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Key Word Index—*Tricholepis glaberrima*; Compositae; sesquiterpene lactones; guaianolides.

Abstract—Cynaropicrin and 11,13-dihydrodesacylcynaropicrin were isolated from *Tricholepis glaberrima*.

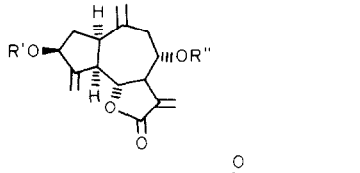
INTRODUCTION

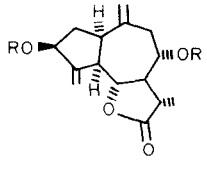
Tricholepis (tribe Carduineae, subtribe Centaureinae) [1] is a relatively small genus of India and adjacent Afghanistan. Knowledge of its chemistry appears to be limited to *Tricholepis glaberrima* DC., in whose petrol extract various plant sterols, triterpenes, alkanes, alkanols and quercetin-3-rutinoside have been identified [2–5]. We now report on the isolation of the sesquiterpene lactones cynaropicrin (**1a**) and 11,13-dihydrodesacylcynaropicrin (**2a**) from the $CHCl_3$ extract of the aerial parts of this species.

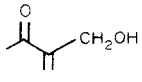
RESULTS AND DISCUSSION

The less polar noncrystalline lactone constituent of *T. glaberrima* was identified as cynaropicrin (**1a**) [6, 7] by comparison of its IR and ^1H NMR spectra with those of authentic **1a** and by hydrolysis (MeOH–K_2CO_3) to the known crystalline compound **3a** [8].

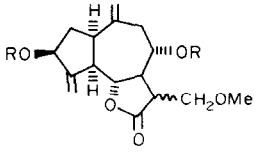
A more polar lactone, $C_{15}H_{20}O_4$, $[\alpha]_D$ +79.1°, was shown to be the diol **2a** by analysis of its 270-MHz ^1H NMR spectrum. This was very similar to that of **1a** except for (a) the replacement of the typical narrowly split doublets of H-13a, b of **1a** at δ 6.20 and 5.60 by a methyl doublet at δ 1.42, and (b) the absence of the signals of the hydroxymethacroyl ester side-chain of **1a** and upfield shift of the H-8 multiplet from δ 5.12 to 3.78. Acetylation of **2a** to **2b** resulted in the introduction of two acetyl groups and the expected paramagnetic shifts of the H-3 and the H-8 signals. The coupling constants for **1a**, **2a** and **2b** were essentially identical, thus leading to the stereochemistry at C-1, C-3, and C-5 to C-8 shown in formula **2a**. The stereochemistry at C-11 appeared to be α because of the value of $J_{7,11}$ (10 Hz). A crystalline substance, mp 136–137°, $[\alpha]_D^{25}$ 72.8°, to which this stereochemistry has been assigned was obtained [9] by hydrolysis of cynaropicrin (**1a**) and its analogues to **1b** followed by $NaBH_4$ reduction of the conjugated methylene group. To confirm the identity of our material which was semisolid we repeated the hydrolysis of **1a** and its subsequent reduction with $NaBH_4$. The product remained non-crystalline and was identical in all respects (NMR, IR, TLC, MS) with **2a** obtained directly from the plant.





1a R'=H, R"= 
1b R', R"=H
1c R', R"=Ac

2a R=H
2b R=Ac



3a R=H
3b R=Ac

EXPERIMENTAL

Isolation of lactones. Aerial parts (1 kg) of *T. glaberrima* collected in the Dehradoon Hills of Uttar Pradesh, India, on 4 Feb. 1979 were extracted with $CHCl_3$ for 8 hr. Evaporation of the solvent at reduced pressure yielded 12.0 g of residue which was dissolved in 500 ml 10% aq. MeOH and left overnight. After removal of insoluble material, the soln was washed with petrol (bp 60–80°) until the washings were almost colourless. Most of the MeOH was removed at reduced pressure, the residue was extracted with $CHCl_3$ (6 × 200 ml), the washed and dried extract was evaporated at reduced pressure, and the residue was chromatographed over 300 g Si gel, 200-ml fractions being collected as follows: Fractions 1–3 (C_6H_6), 4–7 (C_6H_6–EtOAc 9:1), 8–13 (C_6H_6–EtOAc, 4:1), 13–15 (C_6H_6–EtOAc, 1:1), 16–20 (C_6H_6–EtOAc, 1:2), 21–25 (C_6H_6–EtOAc, 1:9), 26–30 (EtOAc, 31–40 (EtOAc–MeOH, 49:1) and 41–50 (EtOAc–MeOH, 9:1).

Fractions 32–35 showed a single spot on TLC (C_6H_6–EtOAc, 1 : 1) and were combined to give 3 g cynaropicrin (**1a**) as a gum. IR ν_{max}^{film} cm^{-1}: 3450, 1770, 1715; ^1H NMR (270 MHz, $CDCl_3$, not spin decoupled, probable assignments): δ 2.98 (*m*, H-1), 2.22 [*dd*, J = 13, 7 Hz H-2a], 1.73 (*ddd*, J = 13, 11, 7 Hz, H-2b), 4.50 [*t*(*br*), J = 7 Hz, H-3], 2.82 [*t*(*br*), J = 10.5 Hz, H-5], 4.25 (*dd*, J = 10.5, 9 Hz, H-6), 3.18 (*m*, H-7), 5.12 (*dt*, 9, 4.5 Hz, H-8), 2.70 (*dd*, 15, 4.5 Hz, H-9a), 2.38 (*dd*, J = 15, 4 Hz, H-9b), 6.70 (*d*, J = 3 Hz) and 5.60 (*d*, J = 3 Hz, H-13), 5.14 (*br*) and 4.93 (*br*, H-14), 5.48 (*t*) and 5.35 (*t*, J = 1 Hz, H-15), 4.37 (2p, H-3'), 6.36 (*br*) and 5.96 (*br*, H-4'); MS *m/z*: 346 $[M]^+$, 262, 244 and 226. IR and ^1H NMR spectra identical with those of authentic cynaropicrin. Hydrolysis of 50 mg of **1a** in 10 ml MeOH with 100 mg K_2CO_3 in 2 ml of H_2O at room temp. (N_2 atmosphere) for 4 hr, acidification with HOAc, extraction with $CHCl_3$ and evaporation of the washed and dried extract furnished 25 mg **3a**, mp 156–157° (lit. mp 156–157° [8]). IR ν_{max}^{film} cm^{-1}: 3500, 1765 and 1640; ^1H NMR (270 MHz, $CDCl_3$): δ 2.93 (*m*, H-1), 2.25 (*m*, H-2a), 1.75 (*m*, H-2b), 4.53 [*t*(*br*), J = 7 Hz, H-3], 2.80 [*t*(*br*), J = 10 Hz, H-5], 4.13 (*t*, J = 10 Hz, H-6), 2.78 (*m*, H-7), 3.69 (*ddd*, H-8), 2.68 (*dd*, J = 15, 4.5 Hz, H-9a), 2.25 (*m*, H-9b), 2.78 (*m*, H-11), 3.34 (*dd*, partly obscured) and 3.80 (*dd*, J = 10, 3 Hz, H-13), 5.08 (*br*) and 5.03 (*br*, H-14), 5.38 (*t*) and 5.33 (*t*, J = 1 Hz, H-15), 3.34 (OMe); MS *m/z*: 294 $[M]^+$, 276, 263, 258 and 214. Acetylation of 20 mg **3a** (Ac_2O–pyridine, 12 hr, room temp.) yielded 25 mg non-crystalline gave 20 mg **3b** which remained non-crystalline and had IR ν_{max}^{film} cm^{-1}: 1770, 1735 and 1650; ^1H NMR (270 MHz, $CDCl_3$): δ 2.90 (*m*, H-1), 2.20 (*m*, H-2a), 2.80 (*m*, H-5), 4.06 (*t*, J = 10 Hz, H-6), 2.80 (*m*, H-7), 4.91 (*m*, H-8), 2.80 (*m*, H-9a), 2.47 (*m*, H-9b), 2.58 (*dt*, J = 10.5, 2Hz, H-11), 3.80 (*dd*) and 3.51 (*dd*, J = 10, 3 Hz, H-13), 5.09 (*br*) and 5.00 (*br*, H-14), 5.43 (*t*) and 5.29 (*t*, J = 1 Hz, H-15), 3.37 (OMe), 2.09 (two Ac); MS *m/z*: 378 $[M]^+$, 336, 318, 305, 294, 280, 258 and 213.

Fractions 42–45 showed a single spot on TLC and were combined to give 105 mg of a semicrystalline gum (**2a**) mp $[\alpha]_D^{25}$ +79.1° (MeOH; *c* 1.17b) (lit. mp 136–137°, $[\alpha]_D^{25}$ 72.8° (MeOH; *c* 1.34) [9] IR ν_{max}^{film} cm^{-1}: 3500, 1700 and 1600; ^1H NMR (270 MHz, $CDCl_3$): δ 5.41 (*t*) and 5.32 (*t*, J = 1 Hz, H-15), 5.11 (*br*) and 5.00 (*br*) (H-14), 4.55 [*d*(*br*), J = 8 Hz, H-3], 4.07 (*t*, J = 10 Hz, H-6), 3.78 (*t*, J = 4.5, 9 Hz, H-8), 2.92 (*m*, H-1), 2.85 (*m*, H-5), 2.72 (*dd*, J = 14, 5 Hz, H-9a), 2.58 (*m*, H-11), 2.21 (*dd*, J = 14, 7 Hz, H-9b), partially superimposed on 2.25 (*m*, H-2a), 2.0 (*quint*, J = 10 Hz, H-7), 1.77 (*m*, H-2b), 1.42 (*d*, 3p, J = 7 Hz, H-13); MS *m/z*: 264 $[M]^+$, 246 and 228. (Calculated for $C_{15}H_{20}O_4$: MW, 264.1361. Found: MW (MS), 264.1352.) Acetylation of 25 mg (Ac_2O–Pyridine, 12 hr, room temp.) yielded 25 mg non-crystalline **2b**. IR ν_{max}^{film} cm^{-1}: 1770, 1735 and 1600; ^1H NMR: δ 5.44 (*t*) and 5.31 (*t*, H-15), 5.31 (*br*) and 5.07 (*br*, H-14), 5.54 [*t*(*br*), J = 8 Hz, H-3], 4.92 (*dt*, J = 4.5, 9 Hz, H-8), 4.05 (*t*, J = 10 Hz, H-6), 2.95 (*m*, H-1), 2.85 [*t*(*br*), J = 9.5 Hz, H-5], 2.75 (*dd*, J = 14, 5 Hz, H-9a), 2.48 (*m*, 2p, H-97 and H-11), 2.2 (*m*, H-9b and H-2a), 2.12 and 2.11 (3p each, Ac), 1.81 (*m*, H-2b), 1.31 (*d*, 3p, J = 7 Hz, H-13); MS *m/z*: 306 $[M]^+$, 264, 246 and 228.

Conversion of **1a** to **2a**. A soln of 40 mg **1a** in 10 ml ethylene glycol and 10 ml of 20% aq. KOH was stirred (N_2 atmosphere) for 6 hr at which TLC indicated complete disappearance of starting material. Acidification with HOAc, extraction with EtOAc, evaporation of the washed and dried extract followed by prep. TLC (C_6H_6–EtOAc, 1 : 1) yielded 20 mg **1b** as a gum which could not be induced to crystallize. MS *m/z*: 262 $[M]^+$, 244 and 226. As the substance was relatively insoluble in $CHCl_3$, it was converted (Ac_2O–pyridine, overnight) into the diacetate **1c** whose IR and NMR spectra corresponded to those recorded for **1c** in the literature [8], MS *m/z*: 346 $[M]^+$, 304 and 262. A soln of 25 mg **1b** in 20 ml of MeOH was cooled to 0° and stirred with 150 mg $NaBH_4$ for 10 min, acidified with HOAc and extracted with EtOAc. The washed and dried extract was evaporated; purification of the residue by prep. TLC yielded 20 mg of a gum which was identical in all respects (TLC, IR, NMR, MS) with **2a** from the plant.

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