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TROPANE ALKALOIDS FROM *SCHIZANTHUS HOOKERI*

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Key Word Index—*Schizanthus hookeri*; Solanaceae; hygrolines; tropine; 3α-senecioyloxytropan-6β-ol; 6β-angeloyloxytropan-3α-ol.

Abstract—Tropine, a pair of diastereoisomeric hygrolines and two new tropane alkaloids; 3α-senecioyloxytropan-6β-ol and 6β-angeloyloxytropan-3α-ol, were isolated from roots of *Schizanthus hookeri*.

INTRODUCTION

The genus *Schizanthus* (Solanaceae, Tribe Salpiglossideae) comprises *ca* 27 species, all indigenous to Chile [1]. The only chemical study reported on this genus is a recent paper describing the structure of two new tropane-derived alkaloids from *Schizanthus pinnatus* [2]. This paper describes the isolation and characterization of five alkaloids present in the roots of *S. hookeri*. Three of these alkaloids were identified as tropine (**1a**) and a pair of diastereoisomeric hygrolines **2**. The other two alkaloids, 3α-senecioyloxytropan-6β-ol, (**1b**) and 6β-angeloyloxytropan-3α-ol, (**1c**), are new.

RESULTS AND DISCUSSION

The alkaloids were isolated from the crude basic extract by a combination of countercurrent distribution and column chromatography. The isolated compounds are described according to their decreasing basicity. The main component in the strongly basic fractions was identified as tropine. The next fractions contained a major compound whose spectroscopic data (see Experimental) indicated that it was a hygroline. However, the ^{1}H NMR spectrum clearly showed that it was a mixture of two diastereoisomers. They were eventually separated by repeated fractional crystallization of appropriate derivatives and characterized as (+)-pseudohygroline (2*R*, 2′*S*) and (−)-hygroline (2*S*, 2′*S*) [3]. This is the first report of the natural occurrence of (+)-pseudohygroline; (−)-hygroline, originally isolated from *Erythroxylum coca*, has also been reported in *Cochlearia artica* [4].*

The fourth compound, **1b**, $C_{13}H_{21}NO_3$(M^+ 239) showed the presence of an OH group (3150 cm^{-1}) and an α,β-unsaturated ester group (1700, 1640 cm^{-1}). The ^{1}H NMR spectrum exhibited the characteristics of a disubstituted tropane nucleus [5,6]: a triplet at δ 4.9 suggested a C-3 α-substitution, whereas a doublet of a doublet centred at δ 4.37 indicated a free β-hydroxyl at C-6. The nature of the ester side chain was also evident from the ^{1}H NMR data: a narrow multiplet at δ 5.58, together with two three-proton doublets at 1.92 and 2.18 (J = 2 Hz) are typical of a senecioyl moiety. These values, the chemical shift of the olefinic proton and its bandwidth (5 Hz), are readily distinguishable from the corresponding values associated to a tigloyl residue: a *qq* at 6.70–6.80, $W_{1/2}$ = 14 Hz [7,8]. The MS of **1b** is in agreement with the suggested structure and the fragmentation pattern confirms the nature and positions of the substituents [6,9]; thus, signals at *m/e* 195 ($M^+ - C_2H_4O$), 140 ($M^+ - C_5H_7O_2$) and 94 (base peak) are consistent with attachment of the ester group at C-3 (senecioyl substitution at C-6 would have shown a strong signal at *m/e* 113: *vide infra*). Basic hydrolysis of **1b** afforded (+)-tropan-3α,6β-diol, whose absolute configuration is known [10]. From these spectral data and this chemical transformation, **1b** was confirmed to be (−)-3α-senecioyloxytropan-6β-ol.

The structure of the fifth alkaloid, **1c** was readily deduced by comparison of its spectral data with that of **1b**. The ^{1}H NMR spectrum of **1c** displayed a broad one-proton quartet at δ 6.05 and two broad three-proton multiplets at 1.93 and 2.03 which are characteristics of an angeloyl moiety [7,8]. A one-proton doublet of a doublet at 5.65 and a one-proton multiplet at 5.40 were assigned to H-6 and H-3, respectively. The base peak in the MS of **1c** at *m/e* 113, together with prominent signals at *m/e* 156($M^+ - C_5H_7O$) and 94 confirm the attachment of the ester function at C-6 and the free hydroxyl at C-3 of the tropane nucleus. Hydrolysis of **1c** also gave (+)-tropan-3α,6β-diol. On the basis of these data, **1c** corresponds to (−)-6β-angeloyloxytropan-3α-ol.

Although many genera of the Solanaceae, particularly *Datura*, *Atropa* and *Duboisia*, elaborate tropane alkaloids esterified by tiglic and or other C_5 or aromatic acids [5], so far there have been no reports of the occurrence of tropanol esterified by senecioic or angelic acids.† Our finding, together with the isolation of other senecioyl esters of tropanol in *Schizanthus pinnatus* [2], may be of chemotaxonomic interest.

* Our evidence (see Experimental) suggests that this mixture of diastereoisomers is not due to epimerization during work-up; hence, these compounds do appear to occur naturally in the plant.

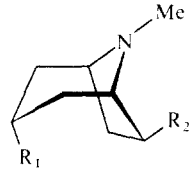
†Dioscorine, which had been regarded as a senecioyl ester of tropine, has been shown to be an isoquinuclidine [11].

EXPERIMENTAL

Mps are uncorr. Optical rotations were measured on a PE-141 polarimeter. ^{1}H NMR spectra were recorded at 60 MHz in $CDCl_3$ soln with TMS as int. standard. MS (70 eV direct inlet). *Schizanthus hookeri* Gill collected in El Volcan (Santiago) in January, was identified by Prof. R. Rodriguez (Univ. de Concepción); voucher specimens are deposited at U.C.

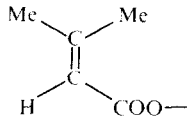
Isolation of alkaloids. The methanolic extract of ground roots of *S. hookeri* (3 kg) was partitioned between acid and base in the usual manner to yield 14 g of basic material. This residue was subjected to a countercurrent distribution, in 12 funnels, between $CHCl_3$ (moving phase) and McIlvaine buffer pH 8.0. The fractions so obtained were regrouped into four new fractions according to their chromatographic behaviour. Fraction A (strong bases) (2 g), contained one major component which was readily identified as tropine (**1a**) by comparison (TLC, IR, NMR, MS) with an authentic sample. Fractions B and C (3.5 g) contained varying amounts of two liquid bases.

(2R, 2'S)-*Hygroline* (**2**). Colourless oil, $[\alpha]_D^{25}$ + 73.13 (*c*. 1.68, EtOH) (ref. [3] + 84.4°). *O*-Acetylpicrate, mp 163° (MeOH) (ref. [3] 165°). *N*-Methyliodide, mp 118° (MeOH) (ref. [3] 118–120°). IR ν_{max}^{film} cm^{-1}: 3200, 2850, 1460, 1180. ^{1}H NMR: δ 1.20 (3 H, *d*, *J* = 6 Hz), 2.33 (3 H, *s*), 3.9 (1 H, *m*). MS: *m/e* (rel. int.) 143.1296 ($C_8H_{17}NO$, 1.5% calc. 143.1306), 115 (1.3), 114 (10), 84 (100), 82 (7), 70 (5), 57 (4), 42 (9). (2S, 2'S)-*Hygroline* (**2**). Colourless oil, $[\alpha]_D^{25}$ − 28.5° (ref. [3] −31.4°). *O*-Benzoyl-HPtCl$_6$, mp 152° ($CHCl_3$–Et_2O) (ref. [4] 150–152°). IR and MS same as above. ^{1}H NMR: 1.15 (3 H, *d*, *J* = 6 Hz), 2.38 (3 H, *s*), 4.1 (1 H, *m*).



1a R_1 = OH; R_2 = H
1b R_1 = Sen; R_2 = OH
1c R_1 = OH; R_2 = Ang
1d R_1 = OH; R_2 = OH

Sen =



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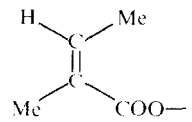

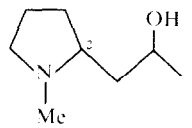

2

A pure sample of **2** (2*R*, 2'*S*) in 5 ml MeOH–H_2O containing 1.0 g of NaOH, was heated under reflux for 6 hr. The ^{1}H NMR of the reisolated alkaloid was identical with that of the starting compound. Also, no evidence of epimerization was obtained after submitting a pure sample of **2** (2*R*, 2'*S*) to the same treatment as described in the work-up of these alkaloids. Fraction D (7.5 g) was subjected to a further countercurrent distribution (pH 6.5). The contents of the last funnels (6.3 g) were chromatographed on Si gel and eluted with solvents of increasing polarity. **1b** and **1c** (1 g) were obtained from the fraction eluted with $CHCl_3$: MeOH (19:1). The remaining fractions were complex mixtures of several components and have not been examined yet.

3α-*Senecioyloxytropan-6β-ol* (**1b**). **1b** was isolated as a solid, mp 79–80° (EtOH Et_2O). $[\alpha]_D$ − 17.6 (*c* 0.08, EtOH). IR ν_{max}^{KBr} cm^{-1}: 3150, 3000–2850, 1700, 1640, 1220, 1160. ^{1}H NMR: δ 1.93 (3 H, *d*, *J* = 2 Hz), 2.18 (3 H, *d*, *J* = 2 Hz), 2.46 (3 H, *s*) 2.82 (1 H, *m*), 3.16 (1 H, *m*), 4.37 (1 H, *dd*, *J* = 9, 2 Hz), 4.85 (1 H, *bt*), 5.58 (1 *H*, *m*, $W_{1/2}$ = 5 Hz). MS: *m/e* (rel. int.): 239 (M$^+$, 42%), 195 (25), 140 (38), 139 (30) 112 (20), 96 (66), 95 (98), 94 (100).

6β-*Angeloyloxytropan-3α-ol* (**1c**). Isolated as an oil. $[\alpha]_D$ − 18 (*c* 0.2, EtOH). Hydrobromide, mp 168–169° (EtOH–Et_2O). IR ν_{max}^{film} cm^{-1}: 3200, 3000–2800, 1705, 1640, 1260, 1190. ^{1}H NMR: δ 1.93 (3 H, *m*), 2.03 (3 H, *m*), 2.50 (3 H, *s*), 3.0–3.4 (2 H, *m*), 4.0 (1 H, *m*), 5.65 (1 H, *dd*, *J* = 7, 2.6), 6.0 (1 H, *bq*, $W_{1/2}$ = 20 Hz). MS: *m/e* (rel. int.): 239 (M$^+$, 38%), 156 (26), 140 (18), 122 (28), 119 (44), 117 (48), 114 (42), 113 (100), 112 (43), 95 (16), 94 (60), 84 (20), 83 (27), 82 (40).

(3R, 6R)-*Tropan-3α,6β-diol* (**1d**). A soln of 45 mg **1b** in 6 ml EtOH–H_2O containing 200 mg $Ba(OH)_2$ was heated under reflux for 7 hr. After cooling, the soln was acidified with H_2SO_4, filtered and washed with Et_2O. The aq. phase, after basification and extraction with $CHCl_3$, was evapd to dryness and the solid residue was sublimed (100°, 10^{-3} mm) affording **1d** (20.3 mg); mp 210° (EtOH–Et_2O), $[\alpha]_D$ +19.3 (*c* 1.03, EtOH) (ref. [10] mp 209–210°, $[\alpha]_D$ +24°, EtOH). Treatment of **1c** under the same conditions also afforded (3*R*, 6*R*)-tropan-3α,6β-diol.

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