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# A NEW PYRROLIZIDINE ALKALOID FROM *CACCINIA GLAUCA*

MUSHTAQ A. SIDDIQI, KRISHAN A. SURI, OM P. SURI and CHAND K. ATAL
Regional Research Laboratory (C.S.I.R.), Jammu-Tawi, India

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**Key Word Index**—*Caccinia glauca*; Boraginaceae; flowers; pyrrolizidine alkaloids; retronecine-7:9-dibenzoate; retronecanol; benzoic acid.

**Abstract**—An alkaloid CG-I, isolated from flowers of *Caccinia glauca* Savi (Gule-Gaozaban) has been shown by spectroscopy and chemical evidence to be a diester of retronecine and benzoic acid.

## INTRODUCTION

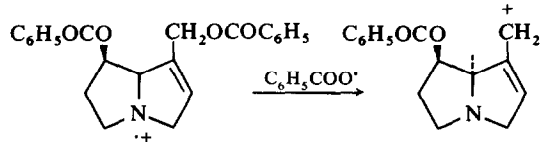
*Caccinia glauca* Savi, a plant with violet flowers grows in Baluchistan and is used in medicine [1]. Earlier workers have reported the isolation of a glycoside [2] and a triterpenoid saponin [3] from the plant. However, our investigations on the alkaloids from the flowers of this species has shown the presence of a new aromatic ester of retronecine.

## RESULTS AND DISCUSSION

The PMR spectrum of CG-I, exhibits the characteristic signals of a pyrrolizidine nucleus [4] at $\delta$ 2.3 (*m*, C-6), 2.7 (*m*, C-5), 3.45 (*m*, C-3), 5.02 (*bs*, C-9) and 6.05 (*bs*, C-2). A multiplet centred at $\delta$7.5 integrated for 6 protons and two double doublets centred at $\delta$ 8.05 ($J$ = 7 Hz, *ortho* coupling and $J$ = 3 Hz, *meta* coupling) integrated for 4 protons, in the vicinity of carbonyl functions, accounted for the aromatic protons. $D_2O$ exchange showed the absence of any exchangeable protons.

The MS of CG-I showed characteristic peaks at *m/e* 93, 94, 119 and 136 showing it to be an ester of a retronecine type aminoalcohol [5]. The $M^+$ at *m/e* 363 assigned it a molecular formula of $C_{22}H_{21}NO_4$. Another significant peak at *m/e* 242 was assigned to the ion obtained after loss of a benzoate group attached to allylic carbon atom (Scheme 1).

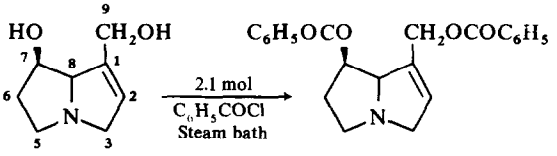
Scheme 1




*m/e* 363 (2%) *m/e* 242 (63%)

The alkaloid on hydrogenation (Adams catalyst) gave an acid and a necine. The acid was identified as benzoic acid by direct comparison with authentic sample, mmp, IR and co-TLC. The PMR of the necine part showed a doublet at $\delta$ 0.92 (*d*, $J$ = 7 Hz, $CH_3$-CH), in addition to characteristic signals for aromatic protons integrating for 5 protons. The necine was identified as 7-*O*-benzoyl retronecanol by comparison with the 7-ester obtained by benzoylation of retronecanol. Hydrolysis of the 7-ester by NaOH (2N in MeOH) gave retronecanol (mp 95°) and benzoic acid (mp 122°) identified by mmp, co-TLC and IR.

Scheme 2




Final proof as to the structure of the alkaloid was provided by its unequivocal synthesis from retronecine (Scheme 2).

## EXPERIMENTAL

Mps are uncorr. PMR spectra were recorded in $CDCl_3$ using TMS as internal reference.

*Extraction of alkaloids from the flowers of* C. glauca. Powdered flowers (3 kg) containing 0.04% tertiary bases were extracted with EtOH. The extract on further processing [6] yielded the total alkaloids.

*Separation.* Total alkaloids on TLC ($CHCl_3$–MeOH, 17:3) showed one major spot $R_f$ 0.83. The alkaloid was obtained in pure form by CC over neutral $Al_2O_3$ (grade-I BDH). Attempts to crystallize the alkaloid proved futile but its picrate was crystallized from EtOH: mp 136–137°. (Found: C, 58.20; H, 4.10; N, 9.40; $C_{28}H_{24}N_4O_{10}$ requires: C, 58.33; H, 4.11; N, 9.72%) $\nu_{max}^{film}$ $cm^{-1}$: 1750 (ester CO) and 1725 (aryl CO).

*Hydrogenation.* The base (300 mg) was hydrogenated in EtOH (Raney Ni). 2 moles of $H_2$ were absorbed in 2 hr. Work up of the reaction mixture afforded necic acid (80 mg) and the 7-ester (150 mg). The necic acid on TLC ($C_6H_6$–MeOH–HOAc, 20:4:3) showed a single spot, $R_f$ 0.57, which corresponded to benzoic acid. Crystallization of the acid from hot $H_2O$ afforded shining needles mp, mmp 122°. The 7-ester was crystallized as its picrate (EtOH) mp 222–224°, (Found: C, 54.9; H, 4.7; N, 12.1; $C_{21}H_{22}N_4O_8$ requires: C, 55.02; H, 4.8; N, 12.2%).

*Benzoylation of retronecanol.* Retronecanol (100 mg) was heated at 100° for 2 hr when TLC showed completion of the reaction. Work up of the reaction mixture afforded a crude alkaloid which was purified by CC over neutral $Al_2O_3$. Pure alkaloid was neutralized with ethanolic picric acid and crystallized, mp 222–223° undepressed on admixture with the 7-ester picrate obtained by hydrogenation of CG-I.

*Hydrolysis of the 7-ester.* The compound (120 mg) was dissolved in 2 N methanolic NaOH (6 ml) at room temp., the reaction was complete after 3 hr. MeOH was removed under red. pres. and the residue taken in dil. HCl and filtered. The filtrate on extraction with $Et_2O$ afforded a necic acid, mp 122° (hot $H_2O$). The aq. part was basified with $NH_4OH$ and extrac-

tion with $Et_2O$ afforded retronecanol ($Et_2O$–petrol) mp, mmp 93–94°.

*Acid hydrolysis of alkaloid.* The base (100 mg) was heated with 12% HCl (6 ml) at 100° for 12 hr. Usual work up of the reaction mixture gave necic acid, mp 122°, mmp with benzoic acid undepressed. Necine–HCl separated by evapn of the aq. extract in a vacuum desiccator was identified as retronecine HCl by mmp (163°), co-TIC and IR.

*Synthesis of alkaloid CG-I.* Retronecine (200 mg) was heated with benzoyl chloride (2.1 mol) at 100° for 2 hr under anhydrous conditions. The reaction mixture was cooled and taken up in 5% aq. HCl. The acid extract was extracted with $Et_2O$ to remove excess benzoic acid. The aq. layer was basified with $NH_4OH$ and extracted with $Et_2O$. The $Et_2O$ extract on concn afforded a crude alkaloid which was purified by chromatography over neutral $Al_2O_3$. The alkaloid was identical to CG-I by co-TLC. IR, NMR and mmp of picrates, 136°.

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