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NOVEL PYRROLIZIDINE ALKALOID FROM *CROTALARIA NANA**

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Key Word Index—*Crotalaria nana*; Leguminosae; pyrrolizidine; crotananine; retronecine; crotananic acid; nine carbon acid.

Abstract—Crotananine, isolated from the seeds of *Crotalaria nana* has been shown by spectroscopy and chemical evidence to be the macrocyclic diester of retronecine and a new C_9 necic acid, crotananic acid.

INTRODUCTION

The chemical composition of *Crotalaria nana* Burm, an annual growing in the western peninsula and Ceylon [1] has not been studied previously but the plant has recently been shown to be responsible for liver ascites in the Surguja district of M.P. (India). Present investigations on the alkaloids from the seeds of this species have resulted in the identification of a retronecine macrocyclic diester with a new C_9 necic acid as the esterifying acid.

RESULTS AND DISCUSSION

Structure of crotananine (**1**)

The PMR spectrum ($CDCl_3$) of the alkaloid showed signals at δ 1.18 (*d*, J = 7 Hz, 2 × $C\underline{H}_3$—CH—), 1.28 (*d*, J = 6.5 Hz, CH_3—C(=O)—C—O), 2.4 (*m*, C-6 and OH), 4.3 and 5.2 (ABq, J = 12 Hz, C-9), 4.98 (*m*, C-7) and 6.01 (*m*, C-2). The ΔH-9 value of 0.9 ppm is a good evidence for macrocyclic ring [2]. D_2O exchange showed the presence of an exchangeable proton at δ 2.4.

In the MS, the presence of significant ions at *m/e* 80, 93, 95, 119, 120, 121, 136 and 138 strongly suggests it to be an ester of a retronecine type aminoalcohol. The sequence of various substituents in the macrocyclic ring is supported by the fragmentation pattern of crotananine (Scheme 1). The compound exhibits an M^+–17 (4%) fragment attributable to the loss of an OH group which must be at C-12 because those alkaloids having an OH group at positions other than C-12, e.g. floricaline and floridanine, do not show this peak [3]. Other prominent peaks in the MS are at *m/e* 279 (48%), 278 (55%), 250 (48%) and 206 (80%).

Ba $(OH)_2$ hydrolysis of crotananine afforded retronecine HCl mp 163–164° and an acid (**3**) mp 142–143°. PMR (TFA) of the acid showed signals at δ 0.67 (*d*, J = 7 Hz, $C\underline{H}_3$—C—C—COOH), 0.88 (*d*, J = 7 Hz, $C\underline{H}_3$—C—C—OH), 1.1 (*d*, J = 6.5 Hz, $C\underline{H}_3$—C—COOH) and *ca* 2.3 (*m*, —C$\underline{H}$—C$\underline{H}$—C$\underline{H}$—). A single proton signal at δ 4.8 accounted for the proton attached to the carbon carrying the OH and COOH groups.

Crotananine on acid hydrolysis gave retronecine HCl and an acid lactone (**4**) mp 146–147°. The MS (M^+ *m/e* 186) of the acid lactone is in good agreement with its proposed structure (Scheme 2). The base peak *m/e* 68 is due to the formation of a furanium ion.

The structure of crotananic acid may, therefore, be represented as 2-hydroxy-3,4,5-trimethyl adipic acid and that of crotananine as (**1**)(12-hydroxy-13,14,15-trimethyl-senec-1-enine).

EXPERIMENTAL

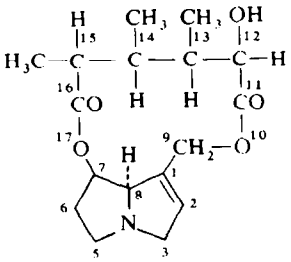
Mps are uncorr. PMR spectra were recorded at 60 MHz using TMS as internal reference in $CDCl_3$ or TFA. R_f values recorded are on Si gel G. Botanical verification of the plant was carried out by R. R. L. Jammu (Plant Survey Discipline) Accession Nos. 15511–15514.

Extraction of alkaloids. Powdered seeds (1.3 kg) containing 2.5% tertiary bases and 0.07% of *N*-oxides were defatted with *n*-hexane and subsequently extracted with 95% EtOH. The EtOH extract on further processing [4] yielded a mixture of alkaloids. The $CHCl_3$ soln of the mixture of crude alkaloids was treated with charcoal and the filtrate evapd to dryness under red. pres. Fractional crystallization of the dried mixture from EtOAc afforded a crystalline mass which on repeated crystallization from hot EtOAc afforded needle shaped crystals, mp 174–175°, R_f 0.61 ($CHCl_3$–MeOH–NH_3, 85:14:1); $C_{17}H_{25}NO_5$ (M^+ 323); (Found: C, 62.94; H, 7.65; N, 4.30. Calc. for $C_{17}H_{25}NO_5$: C, 63.15; H, 7.73; N, 4.33%); $[\alpha]_D^{23}$ −80° (*c*, 1.02 MeOH); λ_{max}^{MeOH} 218 nm; ν_{max}^{film} cm^{-1}: 3320 (OH), 1750 (ester CO).

$Ba(OH)_2$ *hydrolysis.* Crotananine (200 mg) was treated with $Ba(OH)_2$ (500 mg) in H_2O (7 ml). The mixture was heated at 100° for 1 hr. Excess baryta was precipitated using CO_2 and the soln filtered. The filtrate was acidified with dil HCl and extracted with Et_2O to give necic acid, mp 142–143°. The acid responded to the $FeCl_3$ test for α-hydroxy acids. The aq. residue was evapd to dryness in a vacuum desiccator and extracted with EtOH to afford retronecine HCl, mp 163°, mmp with authentic sample undepressed.

Acid hydrolysis. Crotananine (300 mg) was heated with 18% HCl (8 ml) at 100° for 6 hr. Working up of the reaction mixture afforded necic acid (120 mg) and necine HCl (106 mg). The necic acid on TLC (C_6H_6–MeOH–HOAc, 20:4:3) showed two spots having R_f values 0.7 (major) and 0.63 (minor), indicating it to be a mixture of a lactone acid and a diacid. The mixture was heated at 100° with a few drops of HCl so as to effect complete lactonization. The lactone acid crystallized from petrol (40–60°), mp 146–147°; $C_9H_{14}O_4$ (M^+ 186): it did not respond to the $FeCl_3$ test. IR ν_{max}^{film} cm^{-1}: 3500 (OH), 1735 (lactone), 1710 (COOH). The necine HCl was identified by mmp and IR.

*Part 33 in the series, "*Genus Crotalaria*." For Part 32 see Siddiqi, M. A., Suri, K. A., Suri, O. P. and Atal, C. K., Indian Pharmaceutical Congress (Held at Waltair 28–31 December 1977).



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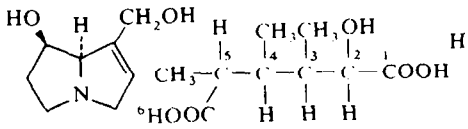

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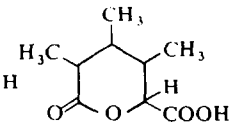

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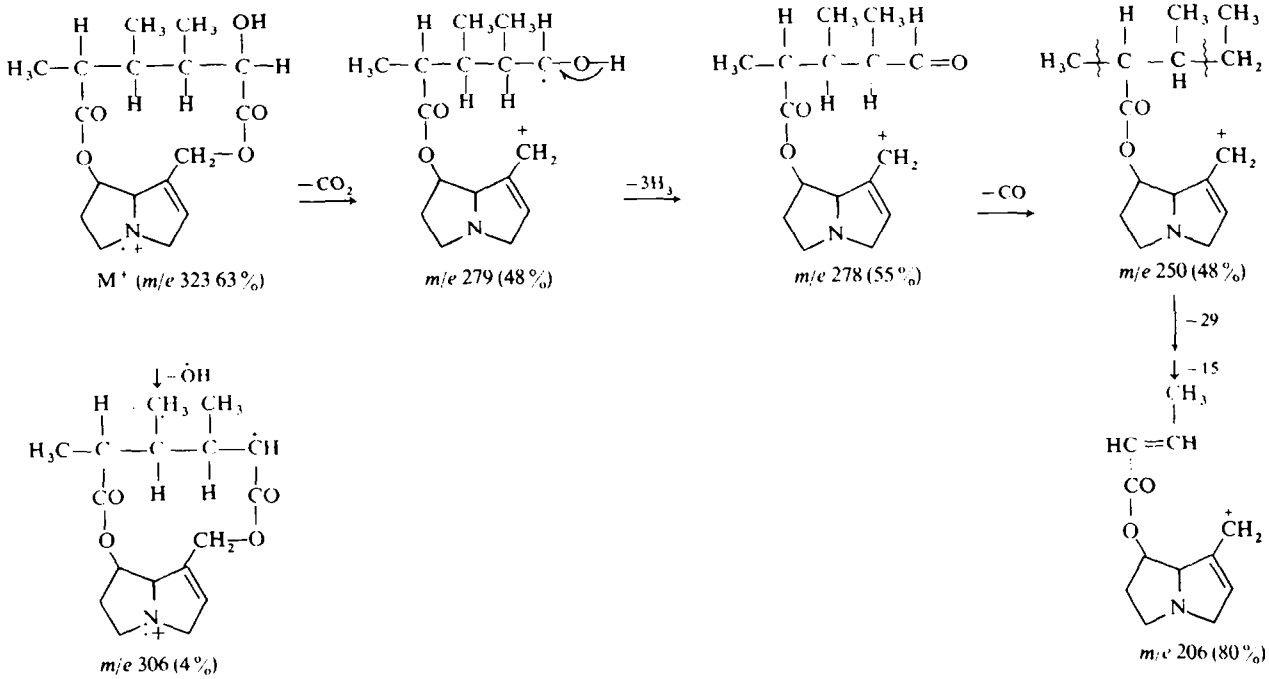
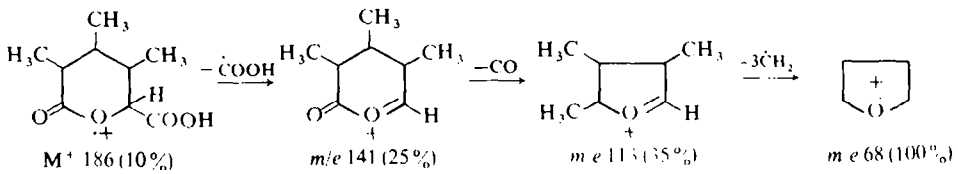


Scheme 1



Scheme 2

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