green–yellow crystals (300 mg, 0.006%) mp 306°, $M^+$ 326. (Found: C, 62.55; H, 3.02. $C_{17}H_{10}O_7$, requires: C, 62.58: H, 3.06%). The monoacetate (**1c**) crystallized from MeOH as colourless crystals (40 mg), mp 262°, $M^+$ 368. (Found: C, 61.92; H, 3.23. $C_{19}H_{12}O_8$ requires: C, 61.95; H, 3.26%). UV $\lambda_{max}^{MeOH}$ nm (log ε): 245 (4.79), 285 (4.47), 315 (4.13), 355 (4.34), IR $\nu_{max}^{KBr}$: $cm^{-1}$: 1760, 1740, 1255, 933. The monomethyl ether **1b** crystallized from MeOH, mp 245° (decomp.), $M^+$ 340. (Found: C, 63.51; H, 3.5. $C_{18}H_{12}O_7$ requires: C, 63.53; H, 3.53%). UV $\lambda_{max}^{MeOH}$ nm (log ε): 250 (4.55), 285 (4.0), 315 (3.77), 355 (4.15); IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1720, 1260, 925.

*Synthesis.* 6-7-Dimethoxy-4-hydroxycoumarin [10] (1 g) and catechol (0.6 g) were dissolved in aq. $Me_2CO$ (10 ml; 1:1) containing NaOAc (3 g). Addition of a soln of $K_3Fe(CN)_6$ (3 g) and NaOAc (3 g) in $H_2O$ (20 ml) to the above soln yielded **2**, a brown ppt. which crystallized from MeOH as pale yellow crystals, mp > 300° (decomp.) (0.8 g). (Found: C, 62.12; H, 3.6. $C_{17}H_{12}O_7$ requires: C, 62.19; H, 3.66%). A mixture of **2** (0.5 g) and $CH_2I_2$ (5 ml) was refluxed in $Me_2CO$ (120 ml)–$K_2CO_3$ (10 g) for 8 hr and worked up as usual. The product on crystallization from MeOH gave a pale yellow crystalline compound, mp 245° (decomp.) (0.4 g), identical with **1b**.

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# EHRETININE, A NOVEL PYRROLIZIDINE ALKALOID FROM *EHRETIA ASPERA*

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**Key Word Index**—*Ehretia aspera;* Boraginaceae; pyrrolizidine; retronecanol; *p*-methoxybenzoic acid.

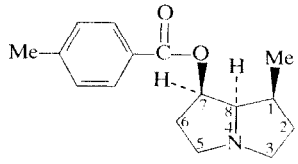
**Abstract**—The structure for ehretinine, 7-*O*-(*p*-methoxybenzoyl)-retronecanol, a new pyrrolizidine alkaloid isolated from leaves of *Ehretia aspera* has been established by a combination of spectroscopic and chemical methods. To our knowledge this constitutes the first report of the natural occurrence of a retronecanol ester.

## INTRODUCTION

*Ehretia aspera* Willd. [1], a tree growing in Deccan peninsula extending northwards to Uttarpradesh and Punjab has not been chemically investigated. Present investigations on the alkaloids from the leaves of this species have resulted in the isolation and identification of a retronecanol ester of *p*-methoxybenzoic acid.

## RESULTS AND DISCUSSION

The $^1H$ NMR ($CDCl_3$) spectrum of ehretinine (**1**) exhibits characteristic signals of a pyrrolizidine nucleus [2] at δ 2.4 (*m*, H-2 and H-6), 2.8 (*m*, H-5), 3.8 (*m*, H-3) and 5.8 (*m*, H-7). The usual position of the H-7 signal in pyrrolizidine secondary esters is *ca* δ 5, this peculiar downfield shift could only be explained after



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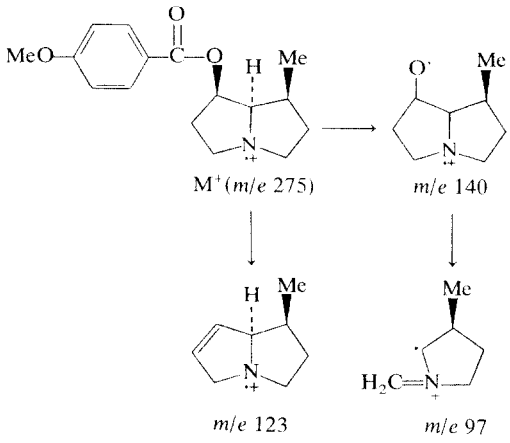
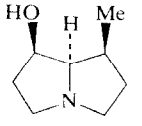
the study of molecular models which clearly showed that H-7 falls in a deshielding cone area of the ester carbonyl. The $^1$H NMR spectrum also showed a —OMe signal at $\delta$ 3.9 and signals for a *para*-substituted benzoyl group in the form of an $A_2B_2$ system at $\delta$ 7.0 and 8.0 ($J$ = 8.5 Hz). The most upfield signal in the spectrum, a doublet at $\delta$ 1.2 ($J$ = 6.5 Hz), was assigned to a $CH_3$–CH group. $D_2O$ exchange revealed the absence of any exchangeable proton.



Scheme 1.

The MS of the alkaloid (Scheme 1) showed prominent peaks at *m/e* 275 ($M^+$, supported molecular formula $C_{16}H_{21}NO_3$ as derived from elemental analysis), with a base peak at *m/e* 140 representing the fragment after cleavage of the ester function. Other diagnostic fragments were recorded at *m/e* 123 ($C_8H_{13}N$) and 97 ($C_6H_{11}N$). Hydrolysis of ehretinine with 2N NaOH (MeOH) yielded retronecanol (**2**) (picrate mp 207°) and an acid mp 183°, which was identified as anisic acid (**3**) by $^1$H NMR, mmp and superimposable IR with authentic sample.



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Ehretinine may, therefore, be structurally represented as 7-*O*-(*p*-methoxybenzoyl)-retronecanol. The assigned structure was supported by a partial synthesis of the alkaloid.

## EXPERIMENTAL

Mps are uncorr. $^1$H NMR spectra were recorded at 60 MHz using TMS as internal ref. in $CDCl_3$ or TFA. $R_f$ values recorded are on Si gel plates.

*Extraction of alkaloids.* Dried and powdered leaves (5 kg) containing 0.002% tertiary bases were extracted with 95% EtOH. The EtOH extract on processing by the method of ref. [3] yielded a mixture of alkaloids which on column chromatography over neutral $Al_2O_3$ or Si gel failed to yield any pure constituent. However, extraction of partially impure fractions with hot EtOAc, treatment with charcoal and concn of the EtOAc soln to a small vol. yielded crystalline alkaloid after standing overnight at room temp. The crystalline alkaloid, yield 65 mg, named as ehretinine, mp 187–188°, $R_f$ 0.48 (cf. monocrotaline 0.50; $CHCl_3$–MeOH–$NH_4OH$, 85:14:1), $C_{16}H_{21}NO_3$ ($M^+$ 275); (Found: C, 69.7; H, 7.68; N, 5.1%; $C_{16}H_{21}NO_3$ requires C, 69.82; H, 7.64; N, 5.09%); $[\alpha]_D^{25}$ − 108° (*c* 1% MeOH); $\nu_{max}^{film}$ cm$^{-1}$ 1710 (aromatic ester CO), 1605 (C—C ring stretch), 1255 (C—O—C stretching band of alkyl aryl ethers).

*Alkaline hydrolysis.* Ehretinine (55 mg) was treated with 2 M NaOH (MeOH) and the soln allowed to stand at room temp. for 2 hr. MeOH was distilled off under red. pres., the residue dissolved in 0.5 N HCl and the acid soln extracted with $Et_2O$ to give necic acid, mp and mmp with authentic *p*-methoxybenzoic acid 183°. The aq. residue was made alkaline with NaOH and extracted with $CHCl_3$ to yield impure necine which was characterized as its picrate, mp 207°, mmp with authentic retronecanol picrate undepressed.

*Synthesis of ehretinine.* Retronecanol (25 mg) was treated with anisoyl chloride and heated at 100° under dry conditions for *ca* 2 hr. The reaction mixture on usual processing and purification by column chromatography yielded pure ehretinine, as supported by co-TLC, undepressed mmp and superimposable IR.

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