

Short Communications

The Structures of Alkaloids from
Pedicularis olgae Regel
(Scrophulariaceae) and *Plantago*
indica (*P. ramosa*, Plantaginaceae)

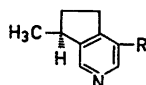
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Three alkaloids have been isolated from *Plantago indica*: plantagonine, $C_{19}H_{11}O_2N$, m.p. 218–220°, $[\alpha]_D = +30.8^\circ$, indicaine, $C_{19}H_{11}ON$, and indicamine, $C_{14}H_{23}ON$.¹ Indicaine, which has an aldehyde function, could be oxidized to plantagonine by silver oxide.² The two alkaloids were also found in *Pedicularis olgae*.³ The physical data given for indicaine from the two sources were different but in both cases plantagonine was obtained on oxidation. A structure based upon a pyridine nucleus was proposed;⁴ the substitution pattern given is, however, highly improbable. The structure given in *The Alkaloids*, X,⁵ is also incorrect.

The molecular composition indicates a monoterpenoid origin suggestive of a series of alkaloids of actinidine type,^{6,7} I, that is wide-spread in the plant kingdom. The UV data⁴ for plantagonine, $\lambda_{max} 270 m\mu$, $\log \epsilon$ 3.12, are in agreement with the data for Ia, $\lambda_{max} 263 m\mu$, $\log \epsilon$ 3.15,⁶ and Id, $\lambda_{max} 270 m\mu$, $\log \epsilon$ 3.38.⁸ The ethyl ester of plantagonine has m.p. 43–4° and $[\alpha]_D = +30.7^\circ$.^{2,3} Optical active Id, m.p. 44°, happened to be prepared recently as an intermediate in the synthesis of D-(+)-teocostidine.⁹ The mass spectra of plantagonine and indicaine⁴ have characteristic features in common with spectra of actinidine⁷ and monoterpenoid alkaloids from *Valeriana officinalis*,⁷ *Jasminum* and *Ligustrum* species.⁸ It seems therefore

justified to propose that the structures of plantagonine and indicaine in fact are represented by Ic and Ib, respectively.



Ia R = CH₃
Ib R = CHO
Ic R = COOH
Id R = COOC₂H₅

Prof. A. V. Danilova very kindly provided us with a small sample of plantagonine. The NMR spectrum showed the presence of only two aromatic protons as singlets at δ 9.15 and 8.64 (CDCl₃, recorded 137 times), in excellent agreement with the expected positions of the 2 and 6 protons of structure Ic. The corresponding pairs of protons of, e.g., nicotinic acid and jasminine⁸ are located at δ 9.17, 8.85, and δ 9.01, 8.57, respectively. The C-methyl group appears as a doublet at δ 1.32, J 6.9 cps, which agrees well with the data for the CHCH₃-system of the major alkaloid of *Valeriana officinalis*,⁷ δ 1.23, J 6.9 cps. The other aliphatic ring protons appear around δ 2.5–3.5 but are unfortunately masked by the background.

Thus the NMR data in combination with the evidence presented above give convincing support for the structures Ib and Ic for indicaine and plantagonine.

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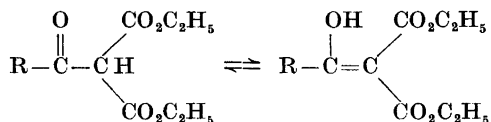
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Enol-Keto Tautomerism in Diethyl Acylmalonates Studied by NMR

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During our investigation of (1-alkyl-sulfinylalkylidene)-malonic acids at these laboratories¹ we prepared a number of diethyl acylmalonates by the method of Lund.² We have now determined the enol content of these compounds and the results are given in Table I. At the same time we should like to report the chemical shifts for the various protons.



The enol-keto equilibrium positions for the three first compounds in Table I have been determined earlier by Meyer³ and by Auwers and Jacobsen,⁴ who titrated the enol with bromine at about 0°C. They found the enol content to be 64 %³ and 70 %⁴ respectively, for R=CH₃. For R=C₂H₅ and R=(CH₃)₂CH, Auwers and Jacobsen give the values 43 % and 47 %, respec-

tively.⁴ These determinations agree rather well with ours.

From Table I one can see that the enol content is greater in III than in II, but is reduced to zero in IV where steric interactions destabilize the enol. It is easily appreciated that an ethoxycarbonyl- and a *tert.*-butyl group *cis* to a double bond will produce a rather unfavourable system. Similar effects have also been noted by Campbell and Gilow in their studies on β -diketones.⁵ Even in diethyl benzoylmalonate (V) steric effects are of importance diminishing the enol content as compared with diethyl acetylmalonate, in spite of the conjugated system which is formed in the enol of V. Insertion of a benzyl group in place of the phenyl group reduces the steric interaction and gives rise to more enol tautomer.

The enol form is also more favored in newly distilled compounds. A freshly distilled sample of diethyl benzoylmalonate held 18 % enol but after storing for a week only 7 %.

The position of the OH-proton signal does not vary appreciably among the compounds studied and occurs at very low applied fields. This depends upon the presence of intramolecular hydrogen bonds in the enols, which are not as strong as those in the β -diketones studied by Burdett and Rogers,⁶ but stronger than those in the β -ketoesters investigated by the same authors. Even for the α -protons the chemical shift does not vary very much, but in the series I-IV the protons will be more deshielded the bulkier the acyl group, due to electronic effects from the acyl groups which increase the electron density at the α -carbon in this way.

The ester groups of the enol form of the compounds are not magnetically equivalent and are also different from the keto tautomer. In compound V, however, the equilibrium is unfavourable for the enol form and when the resolution was insufficiently high, the signals from the enol disappeared under those from the keto form, since the shift difference is small. This small shift difference has also given rise to some uncertainty in the determination of the chemical shift, especially for diethyl propionylmalonate, where an ethyl group is present also in the acyl part of the molecule.

Experimental. Proton magnetic resonance spectra were obtained on the Varian A 60