The Structure of Jesaconitine

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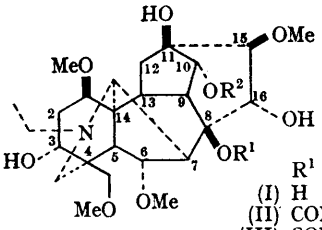
JESACONITINE was first isolated from a variety of tuber (*Aconitum fischeri* Reich) native of Hokkaido[1] and has since been found in other East Asian species, *e.g.*, *A. subcunlatum*, [2,3] *A. sachalinense*,[2,3] *A. yesoense*,[2] and *A. mitakense*.[4] Hydrolysis of jesaconitine affords acetic acid, anisic acid, and the amino-alcohol aconine (I),[3] the latter also being the hydrolysis product of aconitine (II). The absolute stereochemistry of aconine is known from *X*-ray crystallographic studies of one of its derivatives[5] so that the complete structure of jesaconitine follows once the placement of the two ester groups is determined.

There are five hydroxyl groups in aconitine and therefore ten possible isomeric arrangements of the two ester groups. Jesaconitine has been reported to undergo pyrolysis to form a derivative named pyrojesaconitine.[3] Unfortunately, the report did not mention whether acetic acid or anisic acid was eliminated during this reaction, since this pyrolysis is a well characterized reaction for aconitine-type alkaloids which bear an acetoxy-group at C(8).[6] It can be assumed, however, that one of the two ester moieties is located at C(8). An examination of the 100 Mc./sec. spectrum of jesaconitine reveals that the C(10) position is also esterified since the C(10) proton appears at τ 5·38 (doublet, J = 4·5 c./sec.). This signal and coupling constant are characteristic of this proton and have been observed in many of the aconitine-type alkaloids.[7] When not esterified, this proton appears at about τ 5·8, while when esterified with a benzoyloxy- or acetoxy-group it usually appears at about τ 5·1 and 5·2, respectively.[8] Further

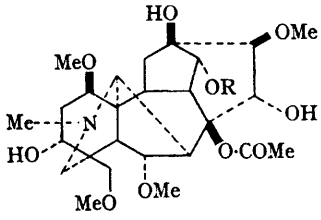
proof of C(8)–C(10) substitution was the highly shielded signal due to the acetoxy-protons (τ 8·64). This has been observed to be characteristic of aconitine-type alkaloids which contain a C(10)-benzoyloxy–C(8)acetoxy substitution pattern and is explained by the diamagnetic anisotropy of the aromatic ring in close proximity to the acetoxy-protons.[7]

The preceding evidence does not exclude the possibility that the aromatic and aliphatic ester moieties in jesaconitine are switched from their usual positions in alkaloids of this type. Accordingly, the n.m.r. spectrum of a solution of 10 mg. of jesaconitine in 0·4 ml. of glycerol containing a trace of D_2SO_4 was monitored at 185° over a two hour period. The τ 8·46 acetoxy signal† slowly disappeared during this time and another signal at τ 7·98 appeared and grew to the approximate height of the signal which had disappeared. Acetic acid in glycerol at 185° gives a signal† at τ 7·98 confirming the elimination of this acid during the pyrolysis. The signals of the 4-methoxybenzoate protons remain unchanged during the pyrolysis. The applicability of this method for the determination of similar C(8)–C(10) aliphatic–aromatic ester substitutions in aconitine-type alkaloids was confirmed by subjecting 10 mg. samples of aconitine (II) and mesaconitine (III) to the pyrolytic conditions described above and monitoring the pyrolyses by n.m.r. spectroscopy. The acetoxy-signals† at τ 8·48 and 8·49 in aconitine and mesaconitine, respectively, were observed to disappear while the corresponding signal of acetic acid (τ 7·98) grew to the approximate size of the former signals.

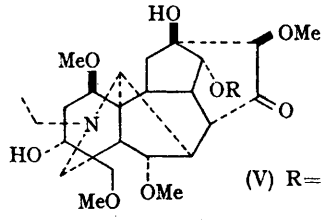
Thus, jesaconitine and pyrojesaconitine may be assigned structures IV and V, respectively. This method of monitoring the pyrolysis by n.m.r. spectroscopy is a convenient way of establishing the presence of certain C(8) ester groups in the aconitine-type skeleton without sacrificing relatively large amounts of material as required for conventional studies of the pyrolytic products of these alkaloids.



	R^1	R^2
(I)	H	H
(II)	COMe	COPh
(III)	COMe	CO·C_6H_4·OMe-p



(III) R=PhCO



(V) R=CO·C_6H_4·OMe-p

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† Relative to sodium 3-(trimethylsilyl)propanesulphonate as an internal standard.

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