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STRUCTURE OF PHYLLANTIDINE

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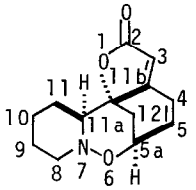
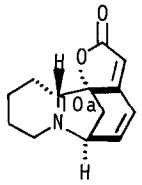
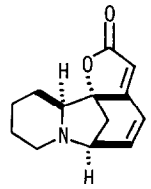
Phyllantidine, $C_{13}H_{15}O_3N$ (M^+ 233), m.p. 169-170°, $[\alpha]_D$ -450° ($CHCl_3$, c=0.33), λ_{max}^{EtOH} 258 nm (log ε 4.20), $\nu_{max}^{CCl_4}$ 1785, 1775 cm^{-1}, was first isolated from Phyllanthus discoides Muell. Arg. by one of us (J. P.) (1) and reported to have the structure of an oxidized derivative of securinine (II) (2) or allosecurinine (III) (3) but the chemical function including the oxygen atom was not defined (1). The same alkaloid was now also isolated from the root barks of Securinega suffruticosa Rehd. grown in Formosa and the structure I was assigned to this alkaloid.



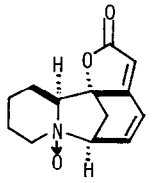
(I)



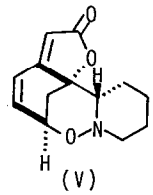
(II)



(III)



(IV)



(V)

Phyllantidine was obtained from allosecurinine (III) in excellent yield by the oxidation with hydrogen peroxide in chloroform-methanol (4). As the

molecular formula of phyllantidine implies the addition of one oxygen atom to III, the most possible structure of phyllantidine would be the N-oxide (IV). The structure N-oxide (IV) for phyllantidine, however, was excluded by its very low solubility in water, higher Rf-value than III in thin-layer chromatography, NMR and mass spectra.

The peaks, M^+ -16, M^+ -17 and M^+ -18, generally observed for aliphatic N-oxides (5), did not appear clearly in the mass spectrum of phyllantidine. The intensive peaks, m/e 100 (base peak) and m/e 83, could be interpreted as shown below and suggested the presence of the tetrahydro-1,2-oxazine ring in I.

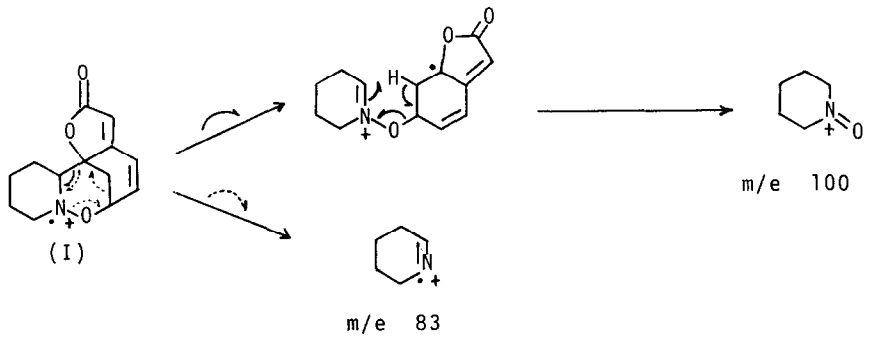


Table. NMR data of I in $CDCl_3$ at 60 Mc.

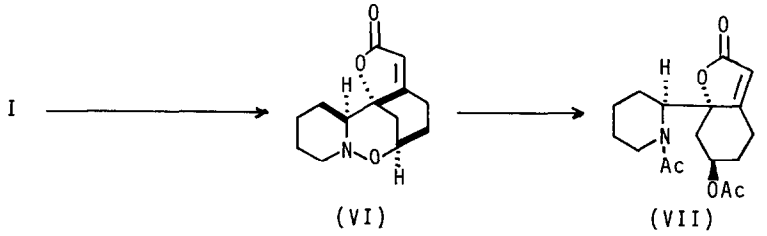
Proton	Chemical Shift δ in ppm	Coupling Constant J in Hz
H_4	6.88 d	9.5
H_5	6.28 d-d	9.5; 5.5
H_3	5.85 s	——
H_{5a}	4.73 d-t	5.5; ca. 3.0
H_{12}	2.53 d-d	11.5; 3.5
$H_{12'}$	2.00 d-d	11.5; 2.5

The NMR spectrum of I was summarized in Table. The proton H_{5a} appeared at very lower field than the corresponding proton of allosecurinine (δ 3.90 ppm). The paramagnetic shift of this proton was caused by the introduction of oxygen in place of nitrogen on the allylic carbon. If phyllantidine has the N-oxide

structure, the downfield shifts should be observed not only in proton H_{5a} but also in protons attached to carbons neighbouring N-oxide. The proton H_{10a} of allosecurinine appeared at 3.67 ppm, but there are no other corresponding signals at lower field than 3.2 ppm in the NMR spectrum of phyllantidine.

On the other hand, T. Nakano et al. obtained two products by the oxidation of virosecurinine (6) with monoperphthalic acid and assigned the minor product as V (7), the spectral data of which were very similar to those of phyllantidine.

The presence of the tetrahydro-1,2-oxazine ring in phyllantidine was proved finally by the chemical degradation of I. Catalytic hydrogenation of I over 10% palladium on charcoal gave dihydrophyllantidine (VI). Hydrogenolysis of VI with zinc in 15% hydrochloric acid, followed by acetylation with acetic anhydride in pyridine gave the N, O-diacetyl derivative (VII), $C_{17}H_{23}O_5N$ (M^+ 321), $\nu_{max}^{CHCl_3}$ 1745, 1635 cm^{-1}, δ 2.12 s, 2.03 s ppm.



As the absolute stereochemistry of allosecurinine was already established (8), the structure I represented also the absolute stereochemistry of phyllantidine. Phyllantidine is a very rare alkaloid having tetrahydro-1,2-oxazine ring as geneserine (9).

The UV spectrum of allosecurinine showed two absorption maxima (256 and 307 nm) (10), the longer wave-length maximum of which was attributed to the homoconjugation of the nitrogen with the conjugated diene system (8,11). It is very interesting that the corresponding maximum disappeared in the UV spectrum of phyllantidine.

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