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CONSTITUENTS OF THAI MEDICINAL PLANTS - IV

NEW NITROGENOUS COMPOUNDS - ODORINE AND ODORINOL

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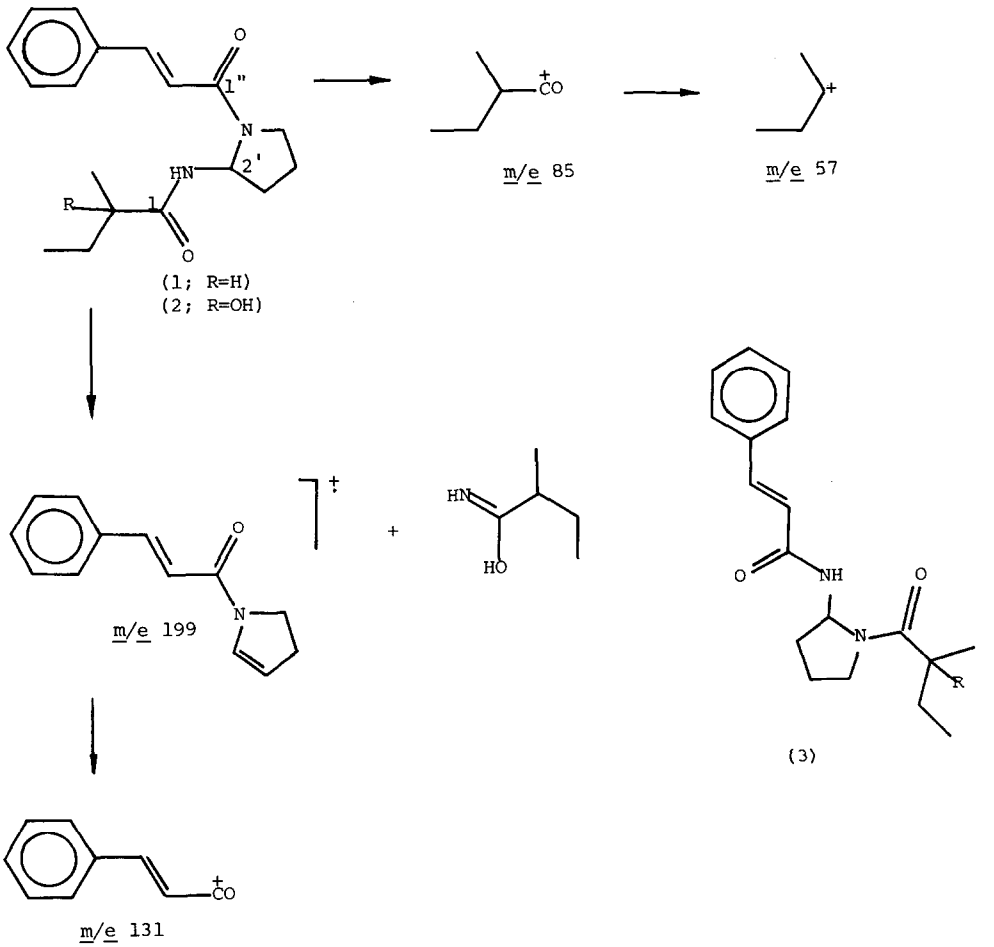
Two new nitrogenous compounds were isolated from the leaves of Aglaia odorata. Their structures were elucidated by spectral evidences as odorine (1) and odorinol (2).

The structures of several new tetracyclic triterpenes, isolated from the extracts of the leaves of Aglaia odorata Lour., were reported in earlier papers.[1] Further investigation of the leaf extracts, using chromatography on alumina, led to the isolation of two new nitrogenous compounds, named odorine (1) and odorinol (2). Their structures possess an unusual bisamide moiety with both nitrogen atoms attached to a chiral centre.

2-Methyl-N-[1'-(1"-oxo-3"-phenylprop-2"-enyl)pyrrolidin-2'-yl]butanamide (odorine, 1), m.p. 218-219° (needles from benzene), $[\alpha]_D^{25}$ + 72.6° (C 0.03, $CHCl_3$) has the formula $C_{18}H_{24}N_2O_2$.[2] Absorptions in the infrared spectrum, characteristic of the amide group, were present at ν_{max} (KBr disc) 3245, 1670, 1650, 1535 and 1320 cm^{-1}. The ultraviolet spectrum [λ_{max}(ethanol) 283 nm, log ε 4.20] was compatible with that expected for a cinnamide derivative. ^1H n.m.r. δ ($CDCl_3$) 0.7 [3H, t, J 6Hz, $(H4)_3$], 1.05 (3H, d, J 6Hz, 2-CH_3), 1.4 [2H, m, J 6Hz, $(H3)_2$], 1.6-2.2 [5H,m, $(H3')_2$, $(H4')_2$ and H2], 3.0-3.8 [2H,m, $(H5')_2$], 5.8 [2H, m (becomes a doublet, J 3Hz on D_2O exchange), H2' and NH], 6.6 (1H, d, J 15Hz, H2"), 6.8-7.2 (5H, m, phenyl), 7.3 (1H, d, J 15Hz, H3"). ^{13}C n.m.r. δ ($CDCl_3$) 11.8 (q,C4), 17.4, 21.8, 27.1, 34.6, 43.3 (d,C2), 46.1 (t, C5'), 62.8 (d, C2') 118.2 (d, C3"), 128.2 (d, 2 x m-aromatic), 128.8 (d, 2 x o-aromatic), 129.8 (d, p-aromatic), 135.4 (s, aromatic), 143.0 (d, C2"), 166.2 (s, C1"), 175.9 (s, C1). m/e 300 (M^+), 215, 199, 169, 131, 103, 85, 57.



Both the p.m.r. and c.m.r. spectra of odorine (1) indicated the presence of a monosubstituted benzene ring and a disubstituted double bond; the coupling constant, $J_{2",3"}$ 15Hz, showed that the double bond was trans-disubstituted. The c.m.r. spectrum also supported the presence of two amide carbonyl carbon atoms in the molecule, one of which (δ 166.2 ppm) was α, β-unsaturated. Together with the occurrence of a fragment ion at m/e 131 in the mass spectrum, this information suggested the presence of a cinnamide moiety in the molecule. Confirmation of this was obtained from the acid hydrolysis of odorine (1), which gave cinnamic acid.

The high-field proton resonances indicated the presence of both an ethyl and a methyl group in the molecule, and these were shown by spin-decoupling experiments to be coupled to

a common C-H (H2). The presence of a 2-substituted butane was therefore established.

The major mass-spectral fragmentation of the molecule consists of successive losses of mass units of 101 and 68 from the molecular ion to give the cinnamoyl cation, which then undergoes the normal mass-spectral decomposition. As a minor fragmentation pathway, the simple cleavage of the molecular ion to give an ion with m/e 85 was observed. From the observation that this ion subsequently loses carbon monoxide to yield an ion with m/e 57, it is possible to conclude that the second carbonyl is attached to the butane chain.

Therefore, there remained only the elucidation of the nature of the remaining C_4H_8N moiety to be determined. The p.m.r. spectrum of odorine (1) had shown that there was only one deuterium-exchangeable proton, and, because it exchanged slowly, it was probably an amide proton. Also, the low-field non-olefinic resonance at δ 5.8 together with a carbon resonance at δ 62.8 suggested the presence of a N-CH-N moiety in the molecule, incorporating a pyrrolidine ring

It was possible to exclude structure (3) because the major fragmentation of the molecule (m/e 300 → m/e 199) corresponds to the McLafferty rearrangement.[3] This process cannot be accommodated by structure (3). Confirmation of the structure of odorine as (1) came from acid hydrolysis of odorine which gave 2-methylbutanoic acid, in addition to cinnamic acid.

Catalytic hydrogenation of odorine, in the presence of PtO_2 or Pd/C in ethanol, gave dihydroodorine, m.p. 110-112°, $C_{18}H_{26}N_2O_2$ (M^+ at m/e 302).

The second naturally occurring compound, 2-hydroxy-2-methyl-N-[1'-(1"-oxo-3"-phenylprop-2"-enyl)pyrrolidin-2'-yl]butanamide (odorinol, 2) has an extra oxygen atom in the formula, $C_{18}H_{24}N_2O_3$, m.p. 166-168° (needles from light petroleum-benzene), $[\alpha]_D^{25}$ + 40.5° (C 0.01 $CHCl_3$). ν_{max} (KBr disc) 3480, 3295, 1655, 1542, 1340 cm^{-1}. λ_{max}(ethanol) 283 nm, log ε 4.25. ^1H n.m.r. δ ($CDCl_3$) 0.9[3H, t, J 7Hz, $(H4)_3$], 1.4 (3H, s, C2-CH_3), 1.6 [2H, q, J 7 Hz, $(H3)_2$], 1.5-24 (4H, m), 3.2-3.9 [2H, brm, $(H5')_2$], 3.5 (1H, s, exch. D_2O, OH), 6.2 (1H, brm, H2'), 6.9 (1H, d, J 15Hz, H2"), 7.2-7.7 (6H, m, aromatic and NH), 7.6 (1H, d, J 15Hz, H3"). m/e 316 (M^+), 244, 215, 201, 200, 199, 185, 131, 103, 85.

The spectra of odorinol (2) are in general very similar to those of odorine (1), the most significant differences occurring in the p.m.r. spectrum. In the spectrum of (2) the resonance corresponding to the multiplet at δ 1.4 p.p.m. in odorine (1) is a quartet, and

the methyl group (C2-CH_3) appears as a singlet instead of a doublet as in odorine (1). An additional deuterium-exchangeable resonance, which undergoes rapid exchange on the addition of D_2O, is consistent with the presence of an hydroxyl group. It was concluded that it must be tertiary and is located at C2. Confirmation of the structure as (2) came from acid hydrolysis of odorinol which gave cinnamic acid and 2-hydroxy-2-methylbutanoic acid.

The biosynthetic origin of the pyrrolidine ring is not clear but it could arise from a basic amino acid such as ornithine. The absolute configuration and the synthesis of odorine (1) are being studied and will be reported soon.

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