TWO NEW 4,5-DIOXOAPORPHINE ALKALOIDS ISOLATED FROM *Aristolochia tuberosa*

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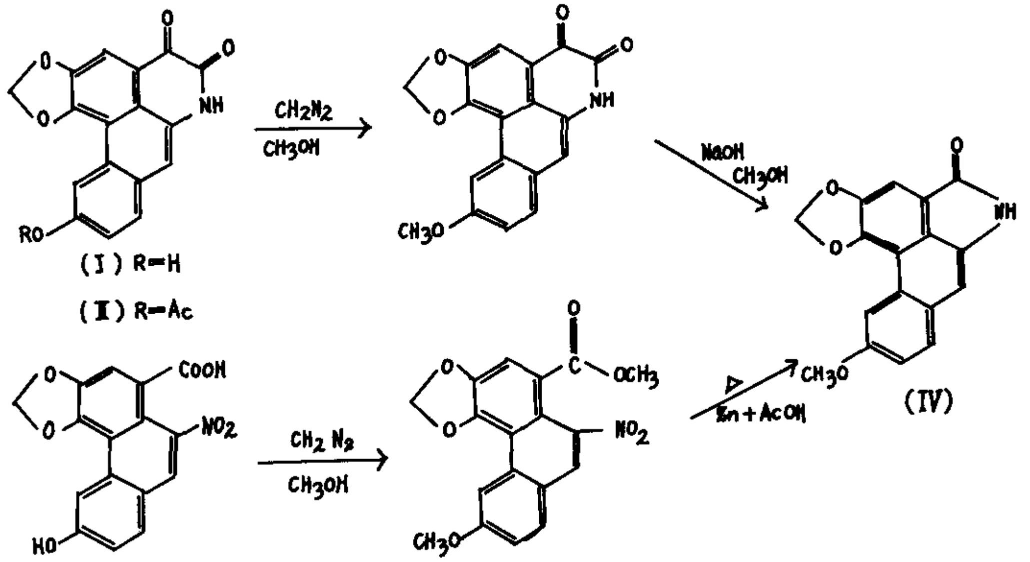
Abstract— From the roots of *Aristolochia tuberosa* C. F. Liong *et* S. M. Hwang, two new oxoaporphine alkaloids, tuberosinone and tuberosinone-N-β-D-glucoside, were isolated, structures of which can be described as (I) and (II).

Aristolochia tuberosa (Aristolochiaceae) is distributed in south China and widely used for the treatment of sore throat, venomous snake bites and tuberculosis in folk medicine. This paper will report the structural elucidation of two new 4,5-dioxoaporphine alkaloids, tuberosinone and tuberosinone-N-β-D-glucoside, isolated from this plant.

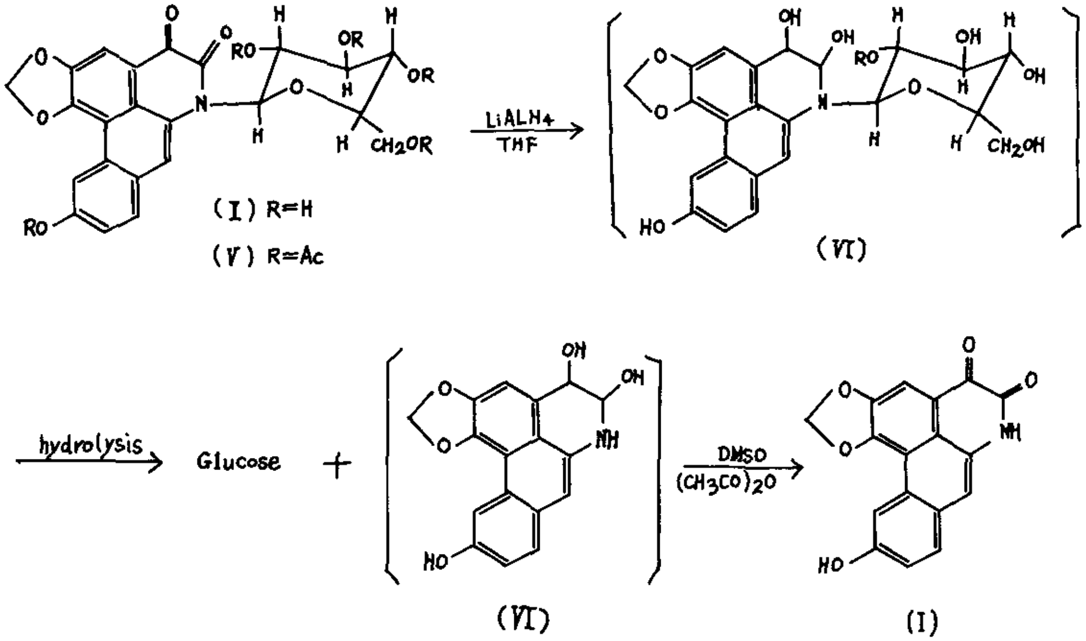
Tuberosinone (I), red needles, mp 340°C, $C_{17}H_9O_5N$. IR ν_{max}^{KBr} cm^{-1}; 3400(OH), 3100(NH), 1690, 1655(C=O). UV λ_{max}^{EtOH} nm (log ε): 238(4.57), 277(4.12), 286(4.15), 318(4.05), 330(4.16), 372(3.91), 390(3.94), 476(4.22). The NMR spectrum (DMSO-d_6) showed a signal of methylenedioxy group at δ 6.50(2H, s), three signals of ABX system of aromatic protons at δ 7.14 (1H, dd, J=8, 2 Hz), 7.74(1H, d, J=8 Hz), 8.12(1H, d, J=2 Hz), two singlets at δ 8.05(1H, s), 7.63(1H, s), NH signal at δ ca.12(1H, br) and OH signal at δ ca.10(1H, br). Mass spectrum: m/e 307(M^+), *the fragment pattern showed to have two characteristic peaks of consecutive loss* of C=O; m/e 279, 251. Acetate (III) of tuberosinone crystallized as yellow needles, mp 340°C, $C_{19}H_{11}O_6N$, M^+ 349. UV λ_{max}^{EtOH} nm (log ε): 238(4.01), 284(3.94), 305(4.04), 316(4.08), 382 (3.74), 450(4.02). NMR (DMSO-d_6): δ 2.38(3H, s, $COCH_3$), 6.62(2H, s, $\begin{smallmatrix}-O\\-O\end{smallmatrix}\!>CH_2$), 7.58(1H, dd, J=8, 2 Hz), 7.63(1H, s), 8.05(1H, s), 8.10(1H, d, J=8 Hz), 8.67(1H, d, J=2 Hz) and ca.12(1H, br). On the basis of these data compound (I) might be suggested to be 1,2-methylenedioxy-4,5-dioxo-10-hydroxyaporphine.

Treatment of methyl ether of tuberosinone with sodium hydroxide[1] in methanol gave a yellow fluorescent compound (IV) which was identified as aristololactam by direct comparison of the mixed mp and IR spectrum with the authentic sample derived from O-methylaristolochic acid C methyl ester by Zn-AcOH reduction.[2] This evidence supports the above suggestion.



Tuberosinone-N-β-D-glucoside (II): red needles, mp 235-237°C, $C_{23}H_{19}O_{10}N$ MS: m/e 469(M^+), 307, 278, 251. Its UV spectrum λ_{max}^{EtOH} nm (log ε) 227(4.59), 240(4.63), 285(4.08), 330(4.09), 370(3.72), 388(3.72), 477(4.14) resembled that of tuberosinone. The IR spectrum showed broad peaks at 3400(OH) and 1650, 1645(C=O), but the absorption attributable to NH stretching was absent. The NMR (DMSO-d_6) showed δ 6.54(2H, s $\begin{matrix}-O\\-O\end{matrix}\!>CH_2$), 7.16(1H, dd, J=8 2 Hz), 7.78(1H, d, J=8 Hz), 7.89(1H, s), 8.28(1H, d, J=2 Hz), 8.27(1H, s), ca.10(1H, br, OH), and the other eleven protons appeared at δ 6.20(1H, d, J=9 Hz), 5.80(3H, m), 4.46(1H, m), 3-4(6H, m). The five protons at δ ca.10, 5.80, 4.64 disappeared by the addition of D_2O. The proton of NH of low field (δ ca.12) as tuberosinone (I) was absent. Hence (II) probably contained sugar moiety, and it could be considered to be attached at the nitrogen. Acetylation of (II) gave the pentaacetate (V), mp 290-292°C, MS: m/e 679(M^+), 637, 559, 349, 307, 279, 274, 251; UV λ_{max}^{EtOH} nm (log ε): 228(4.66), 280(4.02), 306(4.19), 318(4.17), 387(3.82), 442(4.42). The NMR spectrum showed five signals assignable to acetate: δ 1.70, 1.94, 2.08, 2.12, 2.40 (each 3H, s).

Compound (II) was resistant to mineral acid hydrolysis and this property was similar to the behavior of N-glycosides of the pyrimidine nucleoside group.[3] Therefore, reduction of (II) with lithium aluminium hydride in tetrahydrofuran yielded (VI), which was readily hydrolyzed *to yield glucose and (VII). Characterization of the glucose was carried out by parallel paper* chromatography with authentic glucose samples in four solvent systems. Oxidation of the aglycone moiety (VII) with dimethylsulfoxide and acetic anhydride gave red needles, which was proved to be identical with tuberosinone (I) by direct comparison of R_f and IR spectrum. The large coupling constant (J=9 Hz) of C-1' anomeric proton in the NMR spectrum of (II) suggests a β-anomeric linkage in (II). The specific rotation of (II) was -39°, compared with the specific rotation of -14° for aristololactam- -D-glucoside.[3] Hence the D configuration is indicated for the glucose moiety in (II). The combined evidence supports the assignment of the tuberosinone-N-β-D-glucoside structure.



It is for the first time to isolate the tuberosinone and tuberosinone-N- -D-glucoside with 4,5-dioxoaporphine type compound from the plant of Aristolochiaceae. Since aporphine alkaloids have been postulated as *precursors of aristololactams and aristolochic acid in plants,* 4,5-dioxoaporphines may be considered as possible intermediates. These facts are very interesting from the point of view of biogenesis.

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