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The characterization and structures of aknadilactam and steporphine from Stephania Sasakii HAYATA

Jun-ichi Kunitomo, Yasuko Okamoto, Etsuko Yuge, and Yoshiko Nagai

Faculty of Pharmaceutical Sciences, Mukogawa Women's University, Nishinomiya, Japan.

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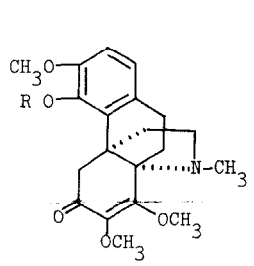
Recently, two new alkaloids have been isolated from Stephania Sasakii HAYATA[1] with 4-desmethylhasubanonine (aknadinine)[2] (I) etc., and named aknadilactam and steporphine, respectively. This communication described the characterization and structures of these two new alkaloids.

Aknadilactam(III) was obtained from the weakly basic fraction as an amorphous powder showing a single spot on TLC. It's cryptophenolic base and positive with Gibbs' reagent, $[\alpha]_D$ -212° ($CHCl_3$). The U.V. spectrum [λ_{max}^{EtOH} 232mμ(sh)(log ε 3.84), 267(3.98)] exhibits a bathochromic shift in alkaline ethanol solution. Its I.R. spectrum (in $CHCl_3$) shows conjugated ketone, five-membered lactam at 1680 cm^{-1}(very strong), 1612 cm^{-1}, and hydroxyl group (at 3500 cm^{-1}). Its N.M.R. spectrum (in $CDCl_3$) reveals an N-methyl group (7.04τ), three methoxyl groups (5.89, 6.16, 6.31τ), two aromatic protons (3.27, 3.46τ, 2×doublet, J=8.5 cps) and one hydroxyl group (1H, s., 3.80τ). These data are quite similar to those of 4-desmethylhasubanonine(aknadinine)(I) with the exception of chemical shift value of N-methyl group in the N.M.R. spectrum[3] and intensity at 1680 cm^{-1} on the I.R. spectrum, which suggests that aknadilactam (III) has the same skeletal structure as aknadinine (I) and contains the five-membered lactam system in its molecule.

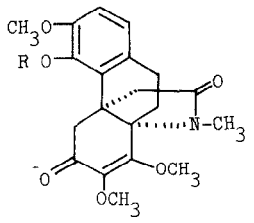
On the basis of these evidences, presume the formula (III) for aknadilactam. In addition, evidence for the structure of this alkaloid was given by the correlation with aknadinine (I) as following method. Treatment of aknadinine (I) with acetic anhydride and pyridine gave an O-acetylaknadinine (II), which shows acetyl group at 1768 cm^{-1} in the I.R.(in $CHCl_3$) and is negative with Gibbs' reagent. Subsequently, oxidation of (II) with potassium permanganate in the presence of magnesium sulfate yielded a lactam (IV). I.R.(in $CHCl_3$) of (IV) shows acetyl group (at 1714 cm^{-1}), conjugated ketone and five-membered lactam (at 1684 cm^{-1}). Mild hydrolysis of this product (acetylaknadilactam)(IV) with sodium bicarbonate afforded a phenolic compound (III), which was identified with natural aknadilactam (III) by comparison with I.R. spectrum (in $CHCl_3$), T.L.C. and specific rotation; $[\alpha]_D$ -189°($CHCl_3$).

Steporphine (VI) was crystallized from acetone-ether in light yellowish needles, m.p. 177-179°, $[\alpha]_D$ -90.6° (MeOH), shows the molecular ion peak at m/e 295 in the mass spectrum



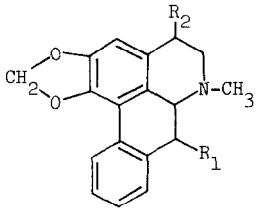
(I) R = H

(II) R = Ac



(III) R = H

(IV) R = Ac



(V) R_1 = OH, R_2 = H

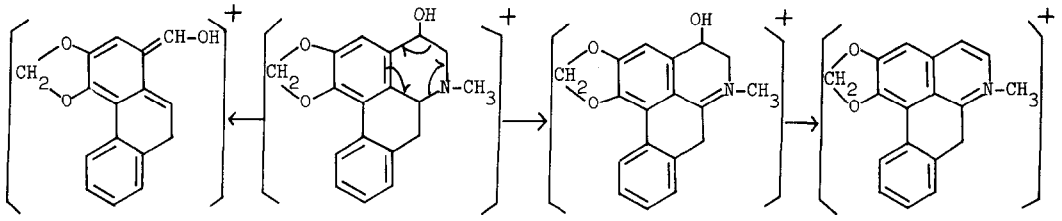
(VI) R_1 = H, R_2 = OH

(VII) R_1 = H, R_2 = OAc

($C_{18}H_{17}O_3N$, M.W. 295). This base is not phenolic and its U.V. spectrum [λ_{max}^{EtOH} 238 mμ(log ε 4.25), 273(4.25), 293(3.87) and 312(3.55)] exhibited characteristic to 1,2-disubstituted aporphine alkaloids. Its I.R. spectrum (in $CHCl_3$) shows a hydroxyl group (at 3360-3500 cm^{-1}), methylenedioxy group (at 1395, 1345, 1050, 940), and its N.M.R. spectrum (in $CDCl_3$) reveals an N-methyl group (at 7.42τ), methylenedioxyl group (at 3.88, 4.05τ, 2×doublet, J=2 cps), five aromatic protons [at 3.16τ(1H, s., C-3), 1.78-2.80τ(4H)] and one proton (at 5.53τ, triplet, J=2.5 cps) which can be ascribed to a hydrogen geminal to a hydroxyl group. These data are close similar to those of ushinsunine (V) which was isolated from a few Michelia species[4], in most of the properties described above. However, in their N.M.R. spectrum some remarkable differences are observed between them: i.e., in the N.M.R. spectrum of steporphine (VI) the aromatic proton at C-3 appears at remarkably lower field than that of ushinsunine (V)[5] and the signal due to -CH(OH)- grouping is observed broad triplet, while doublet in case of ushinsunine (V).

O-acetylation of steporphine (VI) with acetic anhydride and pyridine gave an monoacetate(VII), which shows an acetyl group at 1730 cm^{-1} in the I.R. spectrum ($CHCl_3$). Its N.M.R.($CDCl_3$)[7.83τ (3H, CH_3CO-), 7.44τ(3H, NCH_3), 3.88, 4.03τ(2H, 2×doublet, J=2 cps,-OCH_2O-), 3.21τ(1H, s., C-3), 1.78-2.80τ(4H, aromatic proton) and 4.14τ(1H, triplet, J=2.5 cps, -CH(OAc)-)] suggests the existence of a secondary hydroxyl group and that this hydroxyl group must be located at C-4 or C-5, since the N.M.R. spectrum of (VII) shows one proton triplet due to -CH(OAc)-.

In the mass spectrum of steporphine(VI) appear the characteristic peaks at m/e 294 (M-1, a), 276(b) and 252 (base ion peak) besides the molecular ion peak. The base ion peak at m/e 252 could be depicted by the formula (c), derived from the molecular ion by retro-Diels-Alder type fragmentation, which could not be derived from the formula having a hydroxyl group at C-5.



(c) m/e 252 (VI) m/e 295 (a) m/e 294 (b) m/e 276

This fact strongly suggests that the hydroxyl group must situate at C-4 position.

Thus, the formula (VI) should be proposed for steporphine.

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REFERENCES

1) J. Kunitomo, Y. Okamoto, E. Yuge and Y. Nagai, Yakugaku Zasshi, in press.

2) Aknadinine was identical with 4-desmethylhasubanonine(I) on the I.R.(Nujol), T.L.C. and mix. mp. by the authors. S.M.Kupchan, M.I.Suffness, D.N.J.White, A.T.McPhail, and G.A.Sim, J. Org. Chem. 33, 4529 (1968).

The authors are indebted to Prof. S.M.Kupchan, University of Wisconsin, for a gift of authentic 4-desmethylhasubanonine(I).

3) The N-methyl group of 4-desmethylhasubanonine(aknadinine)(I) in the N.M.R. spectrum ($CDCl_3$) reveals at 7.46τ.

4) T-H, Yang, Yakugaku Zasshi 82, 794, 811(1962), M. Tomita, H. Furukawa, ibid., 82, 925(1962).

5) In the N.M.R. spectrum of ushinsunine(V) appears the C-3 aromatic proton at 3.45τ and the signal due to -CH(OH)- at 5.15 (1H, d., J=2.5 cps). T-H, Yang, Yakugaku Zasshi 82, 804 (1962).