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(−)-*O*-ACETYLSUKHODIANINE AND OXOSTEPHANOSINE: TWO NEW APORPHINOIDS FROM *STEPHANIA VENOSA*

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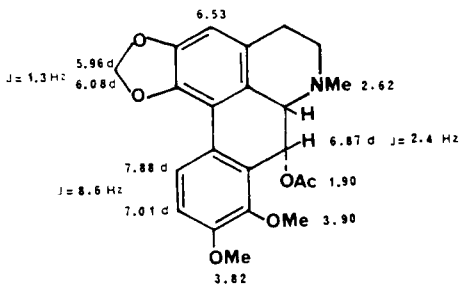
The vine *Stephania venosa* Spreng. (Menispermaceae) is commonly known in Thailand under the name of "sabu-lead" or blood-soap, due to the red color of its latex, and is often used as a bitter tonic. Previous studies on the rhizomes of this plant have indicated the presence of the new oxoaporphinium salts, uthongine and thailandine (1), and the 7-hydroxylated aporphines, ayuthianine and sukhodianine (2).

We have presently studied the alkaloidal content of the leaves from which we have isolated two new alkaloids, namely the aporphine (−)-*O*-acetylsukhodianine (**1**) and the oxoaporphine oxostephanosine (**2**).

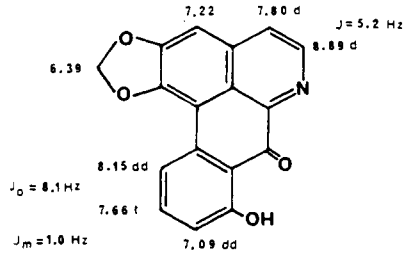


1

The 200 MHz ^{1}H-nmr spectrum of (−)-*O*-acetylsukhodianine in $CDCl_3$ is presented around expression **1**. Special features of this spectrum included the three-proton singlet at δ 1.90 due to the *O*-acetyl group and the one-proton doublet at δ 6.87 (J=2.4 Hz) representing H-7. Absorptions for an *N*-methyl function, two methoxyls, and one methylenedioxy group were also in evidence. One-proton doublets at δ 7.88 and 7.01 (J=8.6 Hz) represented H-11 and H-10, respectively.

The mass spectrum showed a small molecular ion *m/z* 397 ($C_{22}H_{23}NO_6$). The base peak, *m/z* 337, was due to the loss of 60 mass units, corresponding to the elements of HOAc, from the molecular ion.

Since (−)-sukhodianine, which is the C-7 alcohol corresponding to **1**, was presently reisolated from the leaves, the biogenetic relationship between the two alkaloids was clearly evident. Indeed, *O*-acetylation of (−)-sukhodianine (2) using Ac_2O in pyridine provided (−)-*O*-acetylsukhodianine, identical with alkaloid **1**. (−)-*O*-Acetylsukhodianine is the first known example of a naturally occurring 7-acetoxylated aporphine.



2

Our second new alkaloid is the yellow oxostephanosine whose $CDCl_3$ ^{1}H-nmr spectrum at 200 MHz has been summarized around expression **2**. A methylenedioxy absorption was present at δ 6.39, while the H-3 singlet was located at δ 7.22. A significant trait of the spectrum was the set of peaks stretching from δ 7.09 to 8.15 due to H-9, H-10, and H-11; while the aromatic H-4 and H-5 absorptions appeared as doublets at δ 7.80 and 8.89 with a typical small coupling constant of 5.2 Hz.

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The mass spectrum displayed a strong molecular ion *m/z* 291 ($C_{17}H_9NO_4$) and a base peak *m/z* 263 due to loss of CO from the molecular ion.

Final proof of structure was provided by *O*-methylation of **2** using CH_2N_2 to generate the known oxostephanine (≡ 1,2-methylenedioxy-8-methoxyoxoaporphine) which significantly is the most abundant alkaloid in the leaves (3).

There is a possibility that the phenolic oxostephanosine could have been formed from oxostephanine by *O*-demethylation during chromatography. It is also true, however, that *O*-methylated alkaloids are generally formed in vivo by *O*-methylation of phenolic precursors.

Known alkaloids also obtained were (−)-crebanine, dehydrocrebanine, (−)-tetrahydropalmatine, (−)-kikemanine, liriodenine, oxocrebanine, and (−)-ushinsunine, besides the aforementioned oxostephanine and (−)-sukhodianine.

EXPERIMENTAL

GENERAL ISOLATION PROCEDURE.—The dried powdered leaves of *S. venosa* (5.5 kg) were first defatted with petroleum ether and extracted with cold EtOH. The ethanolic extracts were concentrated to a syrup (750 g) which was extracted with 5% HCl. The acidic aqueous layer was extracted with $CHCl_3$; the organic layer separated, and the solvent evaporated. The residue, Fraction A, weighed 7 g.

The acidic aqueous mother liquor was basified with NH_4OH and extracted with $CHCl_3$. Separation and evaporation of the organic layer left a residue, Fraction B, weighing 14 g.

Fractions A and B were placed separately on silica gel columns. Elution was with $CHCl_3$ containing increasing amounts of MeOH. Further purification was by tlc on silica gel plates.

Fraction A provided (−)-crebanine (340 mg), dehydrocrebanine (4 mg), (−)-*O*-acetylsukhodianine (2 mg), (−)-tetrahydropalmatine (25 mg), and (−)-kikemanine (49 mg).

Fraction B gave oxostephanine (5.35 g), liriodenine (10 mg), oxocrebanine (2 mg), dehydrocrebanine (45 mg), (−)-ushinsunine (48 mg), (−)-sukhodianine (44 mg), (−)-kikemanine (380 mg), and oxostephanosine (4 mg).

All alkaloids which had previously been reported in the literature were characterized spectrally or by comparison with authentic samples (3).

(−)-O-*Acetylsukhodianine* (**1**): *m/z* 397 (M^+) (1), 396 (1.4), 355 (19), 354 (85), 337 (100), 322 (40), 279 (13); λ max (MeOH) 214, 280, 296 sh nm (log ε 4.35, 4.14, 3.73); ν max ($CHCl_3$) 1730 cm^{-1}; $[\alpha]^{25}D$ −68° (c 0.06, $CHCl_3$).

Acetylation of (−)-Sukhodianine: (−)-Sukhodianine (3 mg) was dissolved in 1 ml dry pyridine containing two drops Ac_2O. The solution was allowed to stand overnight. Work-up provided (−)-*O*-acetylsukhodianine (**1**).

Oxostephanosine (**2**): *m/z* 291 (M^+) (85), 263 (100), 234 (17), 205 (31), 177 (17), 150 (19); λ max (MeOH) 215, 245, 275, 320, 364, 448 nm (log ε 3.90, 3.75, 3.66, 3.13, 3.21, 3.48); λ max ($MeOH+H^+$) 257, 292, 344, 381, 496 nm (log ε 3.76, 3.65, 3.06, 3.27, 3.17); ν max ($CHCl_3$) 1662, 3540 cm^{-1}.

O-Methylation of **2** *to Oxostephanine:* Oxostephanosine (2 mg) was dissolved in MeOH (2 ml) and freshly distilled ethereal CH_2N_2 (3 ml) added. The mixture was retained in a refrigerator overnight. Workup furnished oxostephanine, identical with authentic material.

ACKNOWLEDGMENTS

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3. For a listing of the aporphinoids see H. Guinaudeau, M. Leboeuf, and A. Cavé, *J. Nat. Prod.*, **46**, 761 (1983); and references cited therein.

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