

# APORPHINE ALKALOIDS OXYGENATED AT C-7

HÉLÈNE GUINAUDEAU<sup>1</sup> and MAURICE SHAMMA\*

*Department of Chemistry, The Pennsylvania State University,  
University Park, Pennsylvania 16802*

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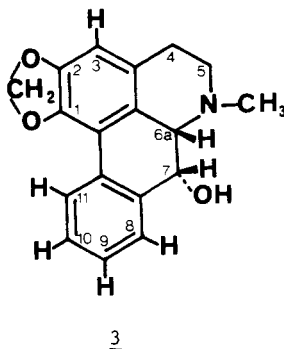
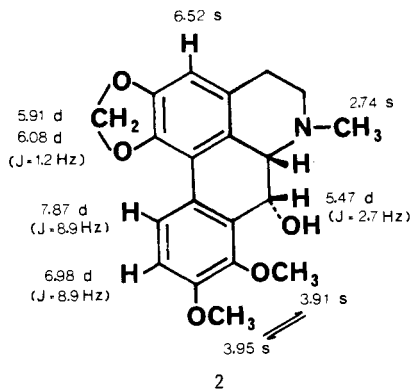
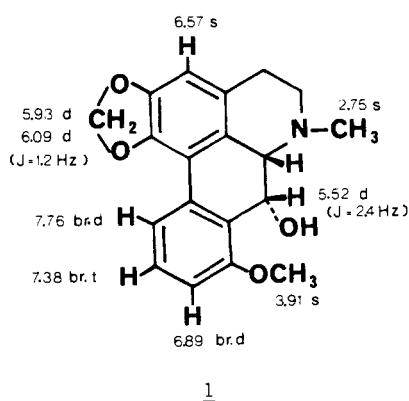
BAMRUNG TANTISEWIE and KALAYA PHARADAI

*Department of Pharmacognosy, Chulalongkorn University, Bangkok 5, Thailand*

**ABSTRACT.**—*Stephania venosa* Spreng. (Menispermaceae) is a source of the new 7-hydroxylated aporphine alkaloids ayuthianine (1) and sukhodianine (2). Generalizations have been drawn concerning the stereochemistry and occurrence of aporphines oxygenated at C-7. Such compounds always belong to the C-6a *R* configuration. The trans relationship between H-6a and H-7 is found only among alkaloids of the Annonaceae. Similarly, it is solely the Annonaceae that produce aporphines bearing a C-7 methoxyl group. The occurrence of C-7 oxygenated aporphines is limited to the four families Annonaceae, Menispermaceae, Magnoliaceae and Lauraceae.

As part of an investigation of the flora of Thailand for its alkaloid content, we found that the polar alkaloid fraction from the dried tuberous root powder of *Stephania venosa* Spreng. (= *S. rotunda* Lour.) (Menispermaceae) yielded two new 7-hydroxylated aporphines.

The first, ayuthianine (1), C<sub>19</sub>H<sub>19</sub>O<sub>4</sub>N; ms *m/z* 325 (M<sup>+</sup>, 100), 324 (63), 307 (46), 292 (60) and 267 (45); λ max (MeOH) 218, 270 and 302 (log ε 4.40, 4.05 and 3.76); has an nmr spectrum (360 MHz, CDCl<sub>3</sub>) showing H-7 as a doublet at δ5.52 (*J*=



<sup>1</sup>Permanent address: Faculté de Médecine et de Pharmacie, Université de Limoges, 87032 Limoges Cedex, France; and E.R.A. 317, U.E.R. de Chimie Thérapeutique, Centre d'Etudes Pharmaceutiques, 92290 Chatenay-Malabry, France.

2.4 Hz), pointing to a *cis* relationship between H-6a and H-7. The second, sukhodianine (2), C<sub>20</sub>H<sub>21</sub>O<sub>5</sub>N; ms *m/z* 355 (M<sup>+</sup>, 22), 337 (87), 322 (100), 297 (12) and 279 (46); λ max (MeOH) 216 and 280 nm (log ε 4.42 and 4.18); must also incorporate a *cis* relationship between H-6a and H-7 since the latter proton appears in the nmr spectrum (200 MHz, CDCl<sub>3</sub>) as a doublet at δ5.47 (*J* = 2.7 Hz). Ayuthianine (1) and sukhodianine (2) possess the *R* configuration at C-6a as indicated by their CD curves, Δε<sub>nm</sub> (MeOH) +4.0<sub>274</sub> and -23.9<sub>236</sub>; and +4.5<sub>276</sub> and -28.3<sub>237</sub>, respectively (1). A small quantity of the known alkaloid (-)-ushinsunine (3) was also found.

The following conclusions concerning the C-7 oxygenated aporphines can be drawn from the characterization of the above two new alkaloids, as well as from data culled from currently available literature (2).

- (1) The occurrence of C-7 oxygenated aporphines is limited to the four families Annonaceae, Menispermaceae, Magnoliaceae, and Lauraceae (2).
- (2) Aporphines oxygenated at C-7 inevitably belong to the C-6a *R* configuration. This stands in contrast to aporphines which are not oxygenated at that site, in which case the absolute configuration is usually related to the substitution pattern in ring D.<sup>2</sup> Aporphines of the opposite *S* configuration may also be found in a plant producing 7-hydroxylated aporphines, but the aporphines of the *S* configuration will not be oxygenated at C-7.
- (3) For C-7 oxygenated aporphines, the *trans* configuration between H-6a and H-7 is found only among alkaloids of the Annonaceae. Nevertheless, members of this plant family may also produce C-7 oxygenated aporphines with the corresponding *cis* stereochemistry.<sup>3,4</sup>
- (4) It is solely among the Annonaceae that C-7 methoxylated aporphines occur. In these alkaloids, H-6a and H-7 are *trans* to each other (2).<sup>5</sup>

The above generalizations undoubtedly are a result of the mode of biogenesis of the C-7 oxygenated aporphines. As further aporphines of this type are characterized in the future, it will be of interest to determine exactly to what extent the present trends will need to be modified.

## EXPERIMENTAL

**EXTRACTION AND SEPARATION PROCEDURE.**—The dried and powdered tuberous roots (2.9 g) of *S. venosa* were extracted with ethanol at ambient temperature. A black residue (455 g) was left following evaporation of the solvent. The alkaloid isolation was carried out on about one-sixth of this residue (80 g).

The 80 g fraction of the extracts was treated with dilute acetic acid, and partitioned with ether. The aqueous layer was then brought to pH 7, and extracted with chloroform. Evaporation of the chloroform left a crude alkaloidal residue of 26 g.

The above residue was placed on a silica gel column (Merck II-III). Elution was with chloroform gradually enriched with methanol. The fractions eluting with chloroform-methanol (90:10) provided crude sukhodianine (2) and then crude ayuthianine (1). Further elution with chloroform-methanol (85:15) supplied ushinsunine (3). The aporphines were further purified by tlc on Merck Silica Gel F-254 glass plates by the chloroform-methanol-water (80:20:1) system. Ayuthianine (0.6 mg), sukhodianine (4 mg) and ushinsunine (3.5 mg) were obtained as amorphous materials. Ushinsunine was characterized by comparison with an authentic sample.

<sup>2</sup>Aporphines substituted at both C-10 and C-11, or both C-9 and C-10, are usually dextrorotatory and belong to the *S* series. Aporphines unsubstituted or monosubstituted in ring D can belong either to the *S* or to the *R* series. See M. Shamma and J. L. Moniot, *Isoquinoline Alkaloids Research, 1972-1977*, Plenum Press, New York (1978), p. 146.

<sup>3</sup>Known aporphines hydroxylated at C-7 and with a *trans* relationship between H-6a and H-7 include noroliveroline, oliveroline, oliveroline N-oxide, noroliveridine, oliveridine, oliveridine N-oxide, guatterine, guatterine N-oxide, polyalthine, pachyconfine and duguetine. These alkaloids are found only among the Annonaceae.

<sup>4</sup>Known aporphines hydroxylated at C-7, but with a *cis* relationship between H-6a and H-7 are norushinsunine, ushinsunine, N-methylushinsunine, anaxagoreine, michelanugine, and now ayuthianine and sukhodianine. Aporphines of this stereochemistry may be found in the Annonaceae, Menispermaceae, Magnoliaceae and Lauraceae.

<sup>5</sup>The C-7 methoxylated aporphines are pachypodanthine, N-methylpachypodanthine, N-methylpachypodanthine N-oxide, noroliverine, oliverine, oliverine N-oxide and polysuavine.

## ACKNOWLEDGMENTS

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