Phytochemistry, 1975, Vol. 14, pp. 2522–2523. Pergamon Press. Printed in England.

TWO OXOAPORPHINE ALKALOIDS OF *STEPHANIA JAPONICA**

YASUO WATANABE, MATAO MATSUI, MAYUMI IIBUCHI and SACHIE HIROE

Daiichi College of Pharmaceutical Sciences, Minami-ku, Fukuoka 815, Japan

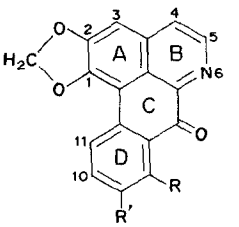
(*Received* 21 *April* 1975)

Key Word Index—*Stephania japonica*; Menispermaceae; new oxoaporphine alkaloid; oxostephanine; 1,2-methylenedioxy-8-methoxyoxoaporphine; lanuginosine.

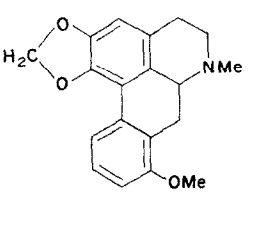
In a previous paper [1] we reported that non-quaternary bases, tentatively named base-S, base-X, and base-P† were isolated from the "weak base fraction" [1] of *Stephania japonica* Miers (Menispermaceae) collected in Kagoshima Prefecture, the south-west part of Japan. Further investigation of these bases led to the conclusion that base-S was a new oxoaporphine alkaloid, named oxostephanine (**1**) and base-X was identical to lanuginosine (**2**) [2,3] by direct comparison.

Oxostephanine (**1**) was obtained as yellow pillars from $CHCl_3$ mp 270–272°, $C_{18}H_{11}O_4N$, $[\alpha]_D \pm 0°$. It was nearly insoluble in organic solvents but readily dissolved in acid solution. The $CHCl_3$ soln showed a green–yellow fluorescence in visible light and the acid soln showed a red color. Its UV spectrum underwent a bathochromic shift in acid (see Experimental). Its IR spectrum showed absorption bands at 1660 and 1592 cm^{-1} assignable to conjugated ketone and $\nu_{C=C}$ of aromatic ring, respectively. The above spectral arguments coupled with the formula ($C_{18}H_{11}O_4N$), of which proportion of the hydrogens to the carbons was extremely low, disclosed that oxostephanine (**1**) was highly conjugated and contained a carbonyl group. Additionally, the characteristic yellow color of crystals and physical properties of oxostephanine (**1**) suggested that it was a congener of the oxoaporphine series.

Its NMR spectrum exhibited signals for a methoxyl group at δ 4·22, a methylenedioxy group at δ 6·67, and six aromatic protons in the region of δ 7·60–8·76 but showed no signals for *N*-methyl and N-H group (see Experimental). The signal patterns due to the methylenedioxy, ring-A, and ring-B protons showed a resemblance to



(**1**) R = OMe, R' = H
(**2**) R = H, R' = OMe



(**3**)

those reported for 1,2-methylenedioxyoxoaporphines [4,5], whereas those for the ring-D protons were clearly different. The coupling constant values of the signals for the ring-D protons, δ 7·42 (double doublet, J 8·5 and 1·2 Hz), δ 8·08 (triplet, J 8·5 Hz), and δ 8·59 (double doublet, J 8·5 and 1·2 Hz) corresponded to those for *ortho* and *meta* coupling, indicating that the three hydrogens should be situated at adjacent positions one another. Further, the downfield signal (δ 8·59) was found to be indicative of C-11 proton by well known facts that in the spectra of oxoaporphine series the C-11 proton appears the farthest downfield [4,5]. The methoxyl group, therefore, must be located at C-8 position. Although the above spectral evidence showed that oxostephanine (**1**) is 1,2-methylenedioxy-8-methoxyoxoaporphine, this structure was further supported by the following chemical transformation. Reduction with

* Part 264 of the series "Studies on the Alkaloids of Menispermaceous Plants". Part 263: Matsui, M. Watanabe, Y., Ibuka, T. and Tanaka, K., (1975) *Chem. Pharm. Bull.* (Tokyo) **23**, 1323.

† The structure of this base will be reported in forthcoming paper.

Zn-HCl followed by *N*-methylation with formic acid-formalin gave (±)-stephanine (**3**), mp 136–137°, which was identical with (−)-stephanine [6] isolated from this plant in IR($CHCl_3$) and NMR($CDCl_3$) spectra except for optical rotation. The structure of oxostephanine was thus substantiated as **1**.

The other oxoaporphine, base-X was found to be identical with lanuginosine (**2**) which has been isolated from *Michelia lanuginosa* [2] (Magnoliaceae), *Stephania abyssinica* [3] (Menispermaceae), *Xylopia brasiliensis* [7] (Anonaceae), and *Magnolia campbellii* [8] (Magnoliaceae).

EXPERIMENTAL

General procedures. Mp's were uncorrected. NMR spectra were recorded with TMS as an internal standard. Column chromatography was carried out on Brockmann neutral alumina (act. II–III) (E. Merck).

Oxostephanine (**1**). Yellow pillars; mp 270–272° ($CHCl_3$); $[\alpha]_D^{25}$ ±0°. (c = 0·1, $CHCl_3$). UV: λ_{max}^{MeOH} (ε) 248(17000), 270(14000), 308(800), 356(2600) nm; $\lambda_{max}^{MeOH-1\,N\,HCl}$ (ε) (258(20000), 287(13700), 324(1300) nm; IR: ν_{max}^{Nujol} 1660, 1592, 1573, 1495, 1406, 1365, 1308, 1283, 1270, 1250, 1232, 1193, 1130, 1045, 1016 cm^{-1}; NMR(CF_3COOH): δ 4·22(3H, *s*, OMe), 6·67(2H, *s*, O–CH_2–O), 7·42(1H, *dd*, *J* 8·5 and 1·2 Hz, C-9H), 7·60(1H, *s*, C-3H), 8·08(1H, *t*, *J* 8·5 Hz, C-10H), 8·45(1H, *d*, *J* 6·0 Hz, C-4H), 8·59(1H, *dd*, *J* 8·5 and 1·2 Hz, C-11H), 8·76(1H, *d*, *J* 6·0 Hz, C-5H); MS: *m/e* 305(M^+, 100%), 276(M^+ - CHO, 96%). (Found: C, 70·70; H, 3·81; N, 4·59 $C_{18}H_{11}O_4N$ requires: C, 70·81; H, 3·62; N, 4·59%).

Reduction of oxostephanine (**1**). To a soln of **1** (96 mg) in AcOH–H_2O (2:1) was added zinc dust (13·1 g) and 10N HCl (26 ml). The mixture was heated under mechanical stirring at 100° for 9 hr, after which time Zn dust (13·1 g) and 10N HCl (14 ml) were added again and continuously heated with stirring at 100° for an additional 24 hr. After cooling, the mixture was filtered and residual Zn dust was washed with 10N HCl then the combined filtrate was made alkaline with NH_4OH and extracted with $CHCl_3$. The extract, after being washed with H_2O and dried, was evaporated to give a brown residue (83 mg), which was used for the following reaction without further purification.

(±)-*Stephanine* (**3**). The mixture of the above product (83 mg), formic acid (0·5 ml), and formalin (0·5 ml) was heated for 4 hr on a water bath. The reaction mixture was made alkaline and extracted with CH_2Cl_2. The extract was washed with H_2O and dried; after removal of solvent, the brown residue (76 mg) dissolved in C_6H_6 was chromatographed over alumina column (0·9 × 6 cm). Elution with C_6H_6 gave a pale yellow solid. Recrystallization from Me_2CO gave (±)-stephanine (**3**) (32 mg) as colorless prisms, mp 136–137°. $[\alpha]_D^{23}$ ±0° (c = 0·3, $CHCl_3$); UV: λ_{max}^{MeOH} (ε) 272(16000), 281(13600), 301(4700) nm; IR: $\nu_{max}^{CHCl_3}$ 1585, 1502, 1485, 1420, 1390, 1150, 990, 945 cm^{-1}; MS: *m/e* 309(M^+, 63%), 308(M^+-1, 100%); NMR($CDCl_3$): δ 2·57(3H, *s*, NMe), 3·84(3H, *s*, OMe), 5·87(1H, *d*, *J* 1·4 Hz, O–CH–O), 6·25(1H, *d*, *J* 1·4 Hz, O–CH–O), 6·52–7·80 (4H, aromatic H). (Found: C, 73·59; H, 6·01; N, 4·55. Calc. for $C_{19}H_{19}O_3N$: C, 73·76; H, 6·19; N, 4·53%). The IR and NMR spectra of this product were superimposable with those for an authentic sample of (−)-stephanine.

Lanuginosine (**2**). Orange–yellow prisms, mp 316–318° (decomp.) ($CHCl_3$). $[\alpha]_D^{23}$ ±0° (c = 0·32, $CHCl_3$); MS *m/e* 305(M^+, 100%). (Found: C, 70·85; H, 3·81; N, 4·63. Calc. for $C_{18}H_{11}O_4N$: C, 70·81; H, 3·63; N, 4·59%). This compound was identical with lanuginosine (**2**) by m.m.p. and by direct comparison of IR spectra and TLC behavior.

Acknowledgements—The authors are grateful to Emeritus Professor M. Tomita, Kyoto University, for his hearty encouragement. Sincere thanks are also due to Professor S. M. Kupchan, University of Virginia, U.S.A. and Dr. S. K. Talapatra, University College of Science, Culcutta, India for their kind identification and valuable communications. Thanks are also due to Mr. T. Nishiyori of this college for elemental analyses and to Mr. M. Tajimi, Japan Electron Optics Laboratory Co., Ltd. for MS measurements.

REFERENCES

1. Matsui, M., Watanabe, Y., Ibuka, T. and Tanaka, K. (1975) *Chem. Pharm. Bull. (Tokyo)* **23**, 1323.
2. Talapatra, S. K., Patra, A. and Talapatra, B. (1969) *Chem. Ind. (London)* 1056.
3. Kupchan, S. M., Suffness, M. I. and Gordon, E. M. (1970) *J. Org. Chem.* **35**, 1682.
4. Shamma, M. (1972) *The Isoquinoline Alkaloids, pp.* 250–251, Academic Press, New York.
5. Shamma, M. and Castenson, R. L. (1973) *The Alkaloids* (Manske, R. H. F., ed.), Vol XIV, pp. 254–257, Academic Press, New York.
6. Tomita, M. and Shirai, T. (1942) *J. Pharm. Soc. Japan* **62**, 381; Shirai, H. (1944) *Ibid.* **64B**, 208; Shirai, H. and Oda, N. (1956) *J. Pharm. Soc. Japan* **76**, 1287.
7. Casagrande, C. and Merotti, G. (1970) *Farmaco. Ed. Sci.* **25**, 799.
8. Talapatra, B., Mukhopadhyay, P. and Dutta, L. N. (1975) *Phytochemistry* **14**, 589.