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Phytochemistry, 1980, Vol. 19, pp. 1882–1883. © Pergamon Press Ltd. Printed in England. 0031-9422/80/0801-1882 $02.00/0

ISOLATION OF FUNIFERINE DIMETHIODIDE AND OBLONGINE FROM *TILIACORA FUNIFERA*

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(*Received* 19 *November* 1979)

Key Word Index—*Tiliacora funifera*; Menispermaceae; benzylisoquinoline; alkaloids; funiferine dimethiodide; oblongine.

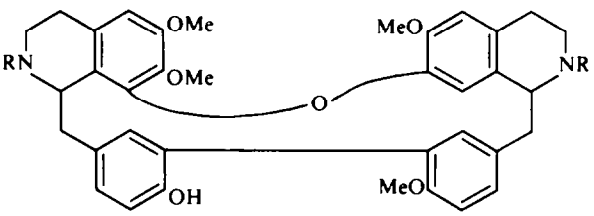
In previous papers [1–5] we have reported the isolation of various dimeric benzylisoquinoline alkaloids from the roots and leaves of *Tilicora funifera* Engl. ex Diels (Menispermaceae). In this paper we wish to present the isolation and identification of funiferine dimethiodide (**2**) and the novel quaternary benzylisoquinoline monomer oblongine (**3**) from the water-soluble alkaloid fraction of an extract of the roots of *T. funifera*.

The identity of funiferine dimethiodide (**2**) was established by a comparison of its physical and spectral properties with those of funiferine (**1**). The identity was confirmed by direct comparison of the properties of the isolated **2** with those of a specimen prepared by treating funiferine (**1**) with methyl iodide in acetone.

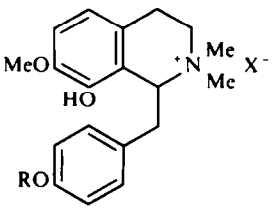
The ^{1}H NMR and MS of oblongine (**3**) suggested that it was a quaternary benzylisoquinoline alkaloid of the petaline type (**4**) [6]. That the isolated compound was oblongine (**3**) was indicated by a comparison of its spectral data with those published for oblongine (**3**) [7, 8]. The identity was confirmed by a direct comparison of the properties of the isolated compound with a synthetic racemic sample prepared by an unambiguous route [8].

Funiferine dimethiodide (**2**) is a new natural product that, to our knowledge, has not been reported previously. This is also the first report of a naturally-occurring quaternary bisbenzylisoquinoline biphenyl alkaloid. Funiferine dimethiodide (**2**) has previously been shown to be a slightly more potent muscle-relaxing agent than (+)-tubocurarine chloride [9].

Oblongine (**3**) has been found previously in *Berberis oblonga* [7] and another *Tiliacora* species, *T. dinklagei* [7].



1 R = Me
2 R = diMe; I^-



3 R = H; X = I
4 R = Me

Part XXIV in the series "Constituents of West African Medicinal Plants". For Part XXIII see (1979) *J. Nat. Prod.* **42**, 116.

The occurrence in the genus *Tiliacora* of a monomeric benzylisoquinoline alkaloid with this unusual oxygenation pattern is of interest since dimeric alkaloids that appear to arise from this type precursor have not to date been discovered in the genus.

EXPERIMENTAL

General. Mps are uncorr. UV spectra were obtained in EtOH and IR spectra in KBr discs. ^{1}H NMR spectra were recorded in the solvents noted with TMS as int. standard. All reagents were analytical grade unless otherwise noted and all evapns were conducted *in vacuo* at 40°.

Extraction and purification. Root material used in this study was collected in Ghana and authenticated by Mr. K. Obeng-Darko, Faculty of Agriculture, University of Science and Technology, Kumasi, Ghana. Voucher specimens are on file at the Center for Scientific and Industrial Research, Accra, Ghana. Oven-dried, powdered roots of *Tiliacora funifera* Engl. ex Diels (Menispermaceae) (1 kg) were extracted by percolation with EtOH (16 l.). Evapn of the EtOH afforded a sirupy extract (224 g) which was dissolved in 3 l. 10% aq. HOAc. The acidic soln was diluted with 10 l. H_2O, filtered and the filtrate rendered alkaline (pH *ca* 8) with conc NH_4OH. The alkaline soln was extracted with $CHCl_3$ (4 × 1 l.) and then re-acidified (pH *ca* 3) with conc HOAc. To the acidic solution was added 1.35 l. of Mayer's reagent [10] and the alkaloidal ppt. recovered by filtration. The ppt. was suspended in 1 l. of H_2O and the suspension stirred for 24 hr with 500 ml Amberlite IRA-401S anion exchange resin (I^- form). The mixture was filtered, the resin washed once with 500 ml H_2O and the washings combined with the filtrate. Evapn of this soln left a residue of crude alkaloidal iodides (16 g).

Isolation of oblongine (**3**). The alkaloidal iodide residue was dissolved in H_2O (1 l.) and the soln concd to *ca* 200 ml by evapn, resulting in the precipitation of some alkaloidal material (117 mg). TLC of this material on Si gel G ($CHCl_3$–MeOH, 7:3) disclosed the presence of one major alkaloidal constituent (R_f 0.35). Chromatography of the mixture over a column of Si gel G (5 g) in $CHCl_3$–MeOH (7:3) afforded a fraction (43 mg) containing oblongine (**3**). Crystallization of this material from hexane–EtOAc afforded oblongine (**3**) (33 mg) in a pure state: mp 150°; $[\alpha]_D^{20}$ 0.70° (MeOH; *c* 1.44); UV λ_{max}^{EtOH} nm: (log ε): 234 (4.08), 284 (3.81) and 362 (3.22); IR ν_{max}^{KBr} cm^{-1}: 3220, 1611, 1590, 1518, 1500 and 1209; ^{1}H NMR (60 MHz, DMSO-d_6): δ 2.92 and 3.00 (each 3 H, *s*, NMe_2), 3.75 (3 H, *s*, OMe), 4.90 (1 H, *s*, C-1), 6.55 (2 H, *d*, *J* = 8 Hz), 6.61 (1 H, *d*, *J* = 8 Hz), 6.90 (1 H, *d*, *J* = 8 Hz), 6.98 (1 H, *d*, *J* = 8 Hz), 9.12 (1 H, *s*, OH) and 9.22 (1 H, *s*, OH); MS (probe) 70 eV *m/e* (rel. int.): 314 [M$^+$] (10), 313 (43), 193 (13), 192 (100), 177 (20), 128 (46), 127 (38), and 107 (11). These data were in good agreement with those reported for oblongine (**3**) [7, 8]. The compound was identical (UV, IR, mp, mmp; NMR and MS) with authentic racemic oblongine [8].

Isolation of funiferine dimethiodide (**2**). An aliquot of the filtrate remaining after the precipitation of the oblongine-containing fraction was evapd and the residue (1.2 g) chromatographed over a column of alumina (Spence H, 36 g). The column was first washed with $CHCl_3$ (1 l.) and then elution was begun with $CHCl_3$–EtOH (9:1) monitored by TLC [Si gel G: MeOH–NH_4OH–H_2O (5:1:2)]. After 1 l. of eluate had passed through the column a fraction containing funiferine dimethiodide (**2**) emerged. Evapn of the fraction left a residue (32 mg). Crystallization of the residue from Me_2CO afforded funiferine methiodide (**2**), 21 mg; mp: 268° $[\alpha]_D^{29}$ + 13.8°; (MeOH; *c* 0.65); UV λ_{max}^{EtOH} nm (log ε): 229 (4.82) and 286 (4.10); IR ν_{max}^{KBr} cm^{-1}: 3420, 2930, 1605, 1500 and 1415; MS (probe) 70 eV *m/e* (rel. int.): 622 [M$^+$ − 2MeI, 100], 395 (95), 381 (35), 379 (17), 198 (68), 142 (70), 128 (5) and 127 (17). The isolated **2** was identical (UV, IR, mp mmp, $[\alpha]_D$ and co-TLC) with a specimen prepared by treating funiferine (**1**) with MeI in Me_2CO.

Acknowledgements—We are grateful to Mr. John Naworal, Graduate School of Public Health, University of Pittsburgh for determining the mass spectra. The mass spectrometry facility was supported by Research grant RR-00273 to the University of Pittsburgh from the National Institutes of Health.

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