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NORTILIACORININE-A AND NORTILIACORINE-A FROM *TILIACORA FUNIFERA*

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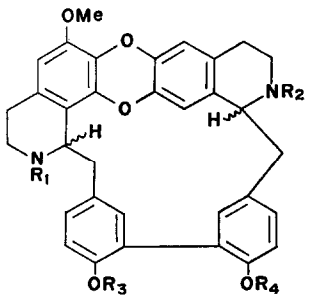
Key Word Index—*Tiliacora funifera*; Menispermaceae; dibenzo-1,4-dioxin alkaloids; nortiliacorinine-A; nortiliacorine-A.

Abstract—Pseudotiliarine, a base of *Tiliacora funifera*, has been identified as nortiliacorinine-A. Isotiliarine, another alkaloid of *T. funifera*, has been shown to be the first nortiliacorine and has been renamed nortiliacorine-A.

Tiliacora funifera (*T. warneckei*) Engl. ex Diels (Menispermaceae) is a stout spreading undershrub or woody climber native to Ghana and other parts of West Africa.[1] It is often found in grassy regions and thickets along coastal areas. The plant is used as a tie for securing firewood bundles and roofs[1] and for the treatment of gastric fevers, strangulated hernia and various menstrual irregularities.[2] The isolation of a number of alkaloids of *T. funifera* has been reported earlier.[3,4] Two of these bases, pseudotiliarine and isotiliarine, were only partially characterized. This paper reports the identification of pseudotiliarine as nortiliacorinine-A (III), a base of *T. racemosa*,[5] and proposes the structure of isotiliarine as a nortiliacorine. In agreement with previously published nomenclature,[5] we propose the name nortiliacorine-A for isotiliarine.



(I) $R_1 = R_2 = R_3 = Me$; $R_4 = H$
(II) $R_1 = R_2 = R_4 = Me$; $R_3 = H$
(III) R_1, R_2 = Me, H or vice versa
R_3, R_4 = Me, H or vice versa

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Pseudotiliarine, m.p. 252–254° dec. (Abs. EtOH), $[\alpha]_D^{28}$ +325° (*c* 2·0, $CHCl_3$); λ_{max}^{MeOH} 212 nm (log ε 4·75), 236 (sh) (4·67) and 292 (3·99); λ_{min}^{MeOH} 263 nm (log ε 3·59); was obtained as colorless crystals by chromatography of the crude bases of *T. funifera* in EtOAc over a column of alumina.[4] The NMR spectrum indicated the presence of one *N*-methyl group at δ 2·30 (3H), two *O*-methyl groups at δ 3·80 (3H) and 3·92 (3H) and nine aromatic protons at δ 6·26–8·08 (9H). The MS fragmentation pattern was characteristic of a dibenzo-1,4-dioxin alkaloid[6–8] and showed a molecular ion (M^+) and base peak at *m/e* 562 for $C_{35}H_{34}N_2O_5$ and other important fragments at *m/e* 336 (36%), 335 (89), 321 (22), and 168 (40). These data were suggestive of a tiliacorine [(I) or (II)] like structure. Pseudotiliarine was subsequently found to be identical with nortiliacorinine A (III) by direct comparison (IR, UV, MS, m.p., m.m.p.).

Isotiliarine, m.p. 258–260°; $[\alpha]_D$ +194·5° (*c* 0·77, $CHCl_3$); λ_{max}^{MeOH} 215 nm (log ε 4·80) 235 (sh) (4·69) and 293 (4·00); λ_{min}^{EtOH} 263 nm (log ε 3·64), was obtained as colorless crystals by chromatography of the crude bases of *T. funifera* in EtOAc followed by MeOH over a column of alumina.[4] The NMR spectrum indicated the presence of one *N*-methyl group at δ 2·28 (3H), two *O*-methyl groups at δ 3·81 (3H) and 3·91 (3H) and nine aromatic protons at δ 6·26–7·95 (9H). The MS was nearly identical to that of nortiliacorinine A and showed a molecular ion (M^+) at *m/e* 562 (69%) and other important fragments at *m/e* 366 (35), 335 (100), 321 (24) and 168 (42). Treatment of isotiliarine with acetic anhydride in pyridine afforded the *O,N*-diacetyl derivative, m.p. 249–252 dec. The MS of the diacetate showed a molecular ion (M^+) and base peak at *m/e* 646 (100%) for $C_{39}H_{38}N_2O_7$ and other intense peaks at *m/e* 335 (97%) and 168 (37). Treatment of isotiliarine with formaldehyde and sodium borohydride afforded tiliacorine, identified by direct comparison (IR, UV, NMR, MS, m.p., m.m.p.) with an authentic sample. Thus, isotiliarine, is a *N*-demethyltiliacorine and we propose the name nortiliacorine-A for isotiliarine. It has been shown that tiliacorine and tiliacorinine, bases of *T. racemosa*,[5] are diasteromers of either I or II by two-stage Hofmann degradation of their respective *O*-ethyl ether dimethiodides. It has further been demonstrated that two minor alkaloids of *T. racemosa*,[5] nortiliacorinine A and nortiliacorinine-B, are isomeric *N*-demethyltiliacorinines of structure III. Therefore, anticipating the future isolation of a second isomeric *N*-demethyltiliacorine, we propose the name of nortiliacorine-A for isotiliarine and assign it structure III.

EXPERIMENTAL

M.ps were determined in capillaries and are uncorrected. IR were recorded in KBr pellets; UV in MeOH or EtOH; optical rotation in $CHCl_3$ on a Rudolph polarimeter; NMR in $CDCl_3$ with TMS as internal standard on a M.P.C. Corporation 100 MHz spectrometer; MS on a LKB-9000 mass spectrometer.

Isolation of the bases. The detailed isolation procedure and physical properties of nortiliacorinine-A (pseudotiliarine) and nortiliacorine-A (isotiliarine), as well as other alkaloids of *T. funifera* have been reported earlier.[4]

Acetylation of nortiliacorine-A (isotiliarine) (III). To nortiliacorine-A (15 mg) in pyridine (1·0 ml) was added Ac_2O (0·3 ml). The resulting solution was maintained at 40° for 20 hr, poured into H_2O (5 ml), basified with NH_4OH to pH 9 and extracted 2× with $CHCl_3$ (50 ml). The $CHCl_3$ extracts were washed, dried and evaporated to leave a crystalline residue (19 mg). Treatment of this residue with petrol.–EtOAc

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afforded needles of *O,N*-diacetylnortiliacorine-A, m.p. 249–252° dec; λ_{max}^{MeOH} 208 nm (log ϵ 4·79), 233 (sh) (4·65) and 291 (3·77); λ_{min}^{MeOH} 266 nm (log ϵ 3·58); ν_{max}^{KBr} 1765 cm^{-1} (ArOCOMe) and 1625 (NCOMe); MS M^+ 646 (100%) for $C_{39}H_{38}N_2O_7$, 631 (16), 604 (13), 603 (13), 378 (16), 377 (18), 336 (22), 335 (97), 333 (24), 281 (6), 211 (5) and 168 (37).

N-*Methylation of nortiliacorine-A* (*isotiliarine*) (III). To nortiliacorine-A (18 mg) in MeOH (30 ml) was added formalin (37% CH_2O) (0·3 ml) dropwise with stirring. After stirring for an additional 60 min, the resulting solution was cooled in an ice bath, $NaBH_4$ (60 mg) added slowly, and stirring continued another 60 min at room temp. The solution was evaporated to dryness and the residue dissolved in HCl (1%) (20 ml) and extracted with $CHCl_3$ (20 ml). The acidic layer was separated, basified with NH_4OH to pH 9 and extracted 2× with $CHCl_3$ (75 ml). The $CHCl_3$ extracts were dried and the solvent removed to afford a crystalline residue (32 mg). Crystallization from hot MOH afforded tiliacorine as cubes, m.p. 248 dec, identical with a reference sample by direct comparison (IR, UV, NMR, MS, m.p., m.m.p.).

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