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Oxindole alkaloids of Strychnos burteri Solered (Loganiaceae) (**)

SUMMARY. — From leaves of *Strychnos burteri* Solered (West Africa) three known indole alkaloids, 10-hydroxynigritanin, 18-dehydro-10-hydroxynigritanin and 18-dehydronigritanin, and two new oxindole alkaloids, burterine and 10-hydroxyburterine, were isolated. The structures of the alkaloids were assigned on the basis of spectroscopic data (UV, IR, NMR, ORD and MS). Spiro carbon C(7) has *R* configuration.

RIASSUNTO. — Dalle foglie di *Strychnos burteri* Solered (Africa Occidentale) sono stati isolati tre alcaloidi indolici noti, 10-idroxinigritanina, 18-deidro-10-idroxinigritanina e 18-deidronigritanina, e due alcaloidi ossindolici nuovi, la burterina e la 10-idrossiburterina. Le strutture dei nuovi alcaloidi sono state assegnate in base ai dati spettroscopici (UV, IR, RMN, DOR e di massa). L'atomo di carbonio spiranico C(7) ha la configurazione R.

Strychnos burteri Solered (Loganiaceae) is a large liane, found mostly on river banks in the rain forest of West Africa [1, 2].

Tertiary alkaloids were isolated with good yield (0.8%) from leaves of *S. burteri* Solered collected in the State of Anambra (Nigeria).

The separation of the alkaloids was performed by counter current distribution (CCD) between $CHCl_3$ and buffer solution at discontinuously decreasing pH [3] and made possible the isolation of five compounds (*1-5*, fig. 1). Three of them, 18-dehydro-10-hydroxynigritanin *1*, $C_{20}H_{22}N_2O$ ($K_1K_5 = 1.8 \times 10^{-4}$), 18-dehydronigritanin *2*, $C_{20}H_{24}N_2$ ($K_1K_5 = 1.4 \times 10^{-10}$) and 10-hydroxynigritanin *3*, $C_{20}H_{24}N_2O$ ($K_1K_5 = 7.3 \times 10^{-5}$) (isolated in much smaller amounts than *1* and *2*), were previously identified in leaves of *S. nigritana* Bak [4]; whereas *4* ($K_1K_5 = 1 \times 10^{-8}$) and *5* ($K_1K_5 = 3.2 \times 10^{-5}$), present in very low amounts, are new alkaloids, which were further purified by preparative TLC (silica gel, $CHCl_3$: MeOH 8:2 v/v).

Alkaloids *1*, *2* and *3* were identified by comparison (TLC, NMR spectra and rotatory powers) with authentic samples.

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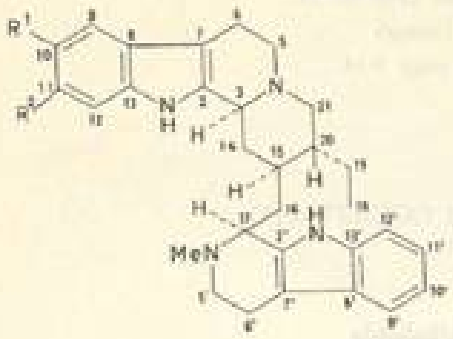

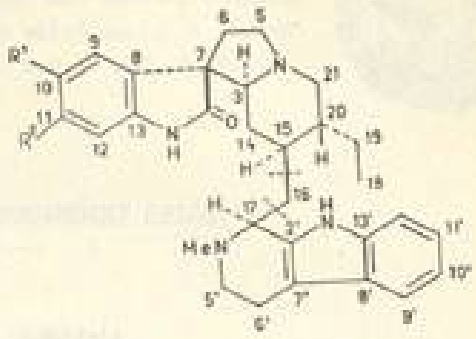

		R'	R²				R'	R²	
1	18-dehydro-10-hydroxynigritanin	OH	H	Δ[18]	*4*	10-hydroxybarterine	OH	H	
2	18-dehydronigritanin	H	H	Δ[18]	*5*	barterine	H	H	
3	10-hydroxynigritanin	OH	H		*6*	strychnofoline	H	OH	7(S)
8	11-hydroxyusambarine	H	OH		*7*	isostrychnofoline	H	OH	7(R)

Dashed lines indicate the mass fragmentation

FIG. 1

Alkaloid *5* named barterine, m.p. 166-8° C (from AcOEt and *n-hexane*), $C_{38}H_{36}N_4O$, $[\alpha]_D^{25} = +58.1$ (c 0.7, EtOH), UV_{MeOH} (λ_{max}, log ε): 218 (4.70), 269 (4.22), 288 (4.09) nm, is an isomer of 18-dehydro-10-hydroxynigritanin *1*, but unlike it [4], *5* reduced neither the Fehling's solution nor the ammoniacal silver nitrate and its UV spectrum did not show any bathochromic shift with alkali.

In the NMR spectrum ($CDCl_3$) of *5*, the signals of 8 aromatic protons (δ 6.3-7.3), one vinyl (5.2-5.7) and one MeN (2.42) were present. The above data and a strong absorption band at 1710 cm^{-1} in the IR spectrum of *5* suggested an oxindole structure with a C(7) spiro carbon atom.

In several plants the simultaneous occurrence of indole alkaloids and their corresponding oxindoles was already ascertained, *e.g.* from leaves of *S. usambarensis* Gilg, strychnofoline *6* and isostrychnofoline *7* [5], two oxindole alkaloids epimer at C(7), were isolated together with 11-hydroxyusambarine *8*.

In the MS spectrum of barterine *5*, complementary peaks at m/e 199 and 267 and at m/e 185 and 281, corresponding to the fragmentations of fig. 1, are present. The peaks due to the oxindole moiety of *5* are in low percentage on account of hydrogen change rearrangements and output of near mass peaks. Moreover, S configuration of chiral centres C(3) and C(17) (as in 18-dehydronigritanin *2*) and R configuration for spiro carbon atom C(7) were attributed on the basis of the positive Cotton effect, as for isostrychnofoline *7* [5]. The configuration H-α for C(15) was suggested from known monoterpene unit biogenesis [6], whereas the configuration H-β of C(20) was inferred by analogy with alkaloids *1*, *2*, *3*. Therefore barterine *5* is the 7 (R) oxindole alkaloid correspondent of 18-dehydronigritanin *2*.

For alkaloid *4*, m.p. 189-92° C (from AcOEt and *n*-hexane), $C_{20}H_{20}N_2O_3$, $[\alpha]_D^{20} = -9.5$ (*c* 1, EtOH), UV_{EtOH} (λ_{max}, log ε): 218 (4.71), 270 (4.24), 289 (4.09), UV_{OH^-} (λ_{max}, log ε): 278 (4.26), 291 (4.18), 310 (3.76) nm, an oxindole structure could be suggested, as for barterine *5*, on the basis of NMR data (7 aromatic protons, δ 6.3-7.3, one vinyl group, δ 5.2-5.7, and one MeN group, δ 2.33) and IR band at 1710 cm^{-1}.

In the MS spectrum of *4*, complementary peaks at m/e 199 and 283 and at m/e 185 and 297 (see fragmentaton lines in fig. 1) localized the phenolic hydroxy group (whose presence was inferred from the UV spectrum) in the oxindole moiety of the molecule.

The 10 position for the hydroxy group in *4* was suggested, as for sarpagine [7], by the reduction of Fehling's solution and ammoniacal silver nitrate. However, as reported for *1* and *3* [4], the NMR spectrum of *4* in $CDCl_3$ resulted unintelligible, because of the presence of the hydroxy group in 10 position.

S configuration for chiral centers C(3) and C(17) and R configuration for spiro carbon atom C(7) were assigned to alkaloid *4* on the basis of its positive Cotton effect, as for barterine *5*. The configuration H-α for C(15) and H-β for C(20) were assigned as for barterine.

Therefore alkaloid *4*, 10-hydroxybarterine, is the 7(R) oxindole alkaloid correspondent to 18-dehydro-10-hydroxynigritanin *1*.

As partial confirmation of the *4* structure, the MS spectrum of 10-hydroxybarterine is practically identical to those of its isomers strychnofoline *6* and isostrychnofoline *7* [5].

Experimental

UV spectra were recorded with an Ultrascan Hilgher & Watts, NMR spectra with a Varian T 60 ($CDCl_3$, TMS as internal reference), MS spectra with an LKB 9000 S and ORD curves with a Cary 60 spectropolarimeter.

Material - *S. barteri* Solered leaves were collected in the State of Anambra (Nigeria); the plant was identified by A. Ozioko. A voucher sample is deposited in the Herbarium of the University of Nigeria.

Extraction - The leaves (1600 g) were dried, powdered, extracted with petroleum ether 40-60° C in a Soxhlet for 40 h and then eluted with 2% aqueous AcOH until negative Dragendorff reaction occurred. The pooled percolation liquids were made alkaline with $NaHCO_3$ and then extracted twice with $CHCl_3$. The pooled extracts were dried over Na_2SO_4 and evaporated *in vacuo* to give a residue, which amounted to *ca.* 0.8% of the starting material. In the aqueous phase quaternary alkaloids were precipitated after neutralization with HCl by adding the Reinecke salt and they will be object of future communication.

Separation - The extract (4 g) was separated by CCD between $CHCl_3$ and phosphate-citric acid buffer (mobile phase) at discontinuously decreasing pH in

a Craig Post apparatus (200 stages, 10:10 ml, upper and lower phase). The separation was followed by TLC on Silica gel $HF_{254+366}$ (solvent: benzene, AcOEt, $NHEt_2$ 5:4:1). Alkaloids were extracted with $CHCl_3$ from the aqueous phase after alkalinization with $NaHCO_3$.

These alkaloids give sparingly soluble salts (chlorides, sulphates, phosphates) as reported for ochrolifuanines [8]. For this reason buffer at pH 7 was used and only subsequently at pH 5.6, which is the necessary value for separating alkaloids *1*, *3*, *4* and *5*. After 185 transfers at pH 5.6 the following alkaloids were eluted separately: 10-hydroxybarterine *4*, 42 mg, $K_1K_5 = 1 \times 10^{-1}$; 10-hydroxynigritanin *3*, 110 mg, $K_1K_5 = 7.3 \times 10^{-1}$; barterine *5*, 36 mg, $K_1K_5 = 3.2 \times 10^{-8}$; 18-dehydro-10-hydroxynigritanin *1*, 1.4 g, $K_1K_5 = 1.8 \times 10^{-8}$; successively at pH 4.4 after 200 transfers 18-dehydronigritanin *2*, 1.1 g, $K_1K_5 = 1.4 \times 10^{-10}$, was eluted. Alkaloids *4* and *5* were subjected to final further purification by preparative TLC (Silica gel, $CHCl_3$, MeOH 8:2 v/v).

18-dehydro-10-hydroxynigritanin 1 - Crystals from AcOEt and *n*-hexane, m.p. 174-6° C; Rf value, $[\alpha]_D^{20}$ and NMR spectrum are identical with those of an authentic sample.

18-dehydronigritanin 2 - Crystals from AcOEt and *n*-hexane, m.p. 226-8° C; Rf value, $[\alpha]_D^{20}$ and NMR spectrum are identical to those of an authentic sample.

10-hydroxynigritanin 3 - Crystals from AcOEt, m.p. 181-3° C; Rf value, $[\alpha]_D^{20}$ and NMR spectrum are identical to those of an authentic sample.

10-hydroxybarterine 4 - Crystals from AcOEt and *n*-hexane, m.p. 189-92° C; *elem. anal.*, found (%) (calcd. for $C_{28}H_{34}N_4O_2$): C 74.72 (74.66); H 6.95 (7.10); N 11.49 (11.61); $[\alpha]_D^{20} = -9.5$ (c 0.5, EtOH); NMR, δ : 2.33 (3H, s, MeN), 5.20-5.70 (3H, $CH_2 = CH$ —), 6.3-7.3 (7H, aromatic); MS, m/e (%): 482 (48), 467 (2), 439 (1), 438 (1), 321 (2), 320 (1), 307 (1), 297 (4), 296 (9), 295 (10), 294 (4), 284 (10), 283 (7), 282 (22), 277 (1), 265 (2), 255 (2), 225 (5), 223 (7), 199 (3), 198 (3), 186 (16), 185 (100); UV_{EtOH} (λ_{max}, log ε) 218 (4.71), 270 (4.24), 289 (4.09), $UV_{0.1N}$ (λ_{max}, log ε) 278 (4.26), 291 (4.18), 310 (3.76); IR ($CHCl_3$) 3400 and 1710 cm^{-1}; $[\Phi]_{MeOH}$ (λ_{max}, nm): + 4000 (300). — 8000 (280).

barterine 5 - Crystals from AcOEt and *n*-hexane, m.p. 166-8° C; *elem. anal.*, found (%) (calcd. for $C_{28}H_{34}N_4O$): C 77.30 (77.22); H 7.24 (7.35); N 12.13 (12.01); $[\alpha]_D^{20} = + 58.1$ (c 1, EtOH); NMR, δ : 2.42 (3H, s, MeN), 5.20-5.7 (3H, $CH_2 = CH$ —), 6.3-7.3 (8H, aromatic); MS, m/e (%): 466 (21), 451 (3), 423 (1), 422 (1), 338 (18), 296 (17), 281 (3), 280 (2), 279 (6), 278 (3), 268 (5), 267 (6), 266 (9), 241 (18), 199 (33), 198 (12), 186 (31), 185 (100); UV_{EtOH} (λ_{max}, log ε) 218 (4.70), 269 (4.22), 288 (4.09); IR ($CHCl_3$) 1710 cm^{-1}; $[\Phi]_{MeOH}$ (λ_{max}, nm): + 5600 (296), —15000 (278).

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