504. *The Indole Alkaloids. Part III.* The Isolation of Diaboline, and Three New Alkaloids, Henningsamine, Henningsoline, and Rindline from* Strychnos henningsii *Gilg.*

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Strychnos henningsii Gilg. is extracted to give diaboline, the alkaloid, m. p. 214—215°, now designated rindline, as well as two new alkaloids, henningsamine and henningsoline.

The bark of *Strychnos henningsii* Gilg. was first shown to contain alkaloids by Andrews.[1] Rindl [2] obtained from a weakly basic solution a phenolic base, m. p. 280—282°, and later, with Sapiro,[3] isolated two different crystalline bases, namely prisms, $C_{22}H_{24}N_2O_3(OCH_3)_2$, m. p. 214—215°, and needles (unanalysed) m. p. 191—194°, the latter considered by them to be impure.

The extraction has been reinvestigated and on no occasion have we isolated a phenolic alkaloid, m. p. 280—282°. The weakly basic fraction gave the alkaloid, m. p. 214—215°, which is now named rindline. The strongly basic fraction has been separated to give a phenolic alkaloid, henningsoline, $C_{22}H_{26}N_2O_5$, m. p. 208—210°, and the non-phenolic fraction gave the main alkaloid as diaboline, m. p. 190°, and in small quantity another alkaloid, henningsamine, $C_{23}H_{26}N_2O_4$, m. p. 205—206°, further characterised as its picrate, m. p. 229—231°, and its methiodide, m. p. 231—233°.

Diaboline, only obtained pure by way of its picrate, gave the hydrochloride, $C_{21}H_{25}ClN_2O_3,2H_2O$, m. p. 238—240° (the hydrate and hemihydrate only have been previously reported [4]), the picrate, and the *O*-methyldiaboline methiodide, $C_{23}H_{29}IN_2O_3$, m. p. 171° [the last-named previously reported [4] as the hydrates ($2{\cdot}5H_2O$), m. p. 290 and 200—220°]. Diaboline was finally characterised by hydrolysis to the Wieland–Gumlich aldehyde and the preparation of its oxime.

Experimental

All extractions were carried to completion as shown by Mayer's Test. Solutions were kept cool during any change of pH. Paper chromatography, using butanol–water–acetic acid (5 : 2·2 : 1), was used to check the homogeneity of alkaloid fractions. Analytical samples were dried at 125°/0·01 mm. unless otherwise stated. All molecular weights were by mass spectrometry kindly determined by Professor K. Biemann.

Extraction.—The dried bark (1500 g.) of *S. henningsii* was boiled with 1% acetic acid in ethanol (8 × 2 l.). The extracts were flash evaporated at 50°/30 mm. to 1 l., steam-distilled, cooled, acidified with acetic acid, and extracted with ether (5 × 1 l.), and then with chloroform. The dried (K_2CO_3) chloroform extract yielded a weakly basic alkaloid mixture (WB) (22 g.).

The aqueous solution, basified with ammonia and decanted from the precipitated gummy bases, was extracted with chloroform. The chloroform extract was extracted with 4% sodium hydroxide solution (extract P) (3 × 500 ml.), washed with sodium chloride solution and dried (Na_2SO_4) to give a strongly basic, non-phenolic alkaloid extract (SB) as a pale yellow foam (20 g.). The precipitated gummy bases, similarly extracted with sodium hydroxide solution (extract P), gave a further quantity of strongly basic, non-phenolic alkaloid mixture (SB) (114 g.).

Mixture WB (22 g.) in 0·5N-hydrochloric acid (100 ml.) was filtered, treated with ammonia to pH 7, and extracted with ether to remove non-alkaloidal material, to pH 8 and extracted with chloroform (extract WBA), and to pH 11 and re-extracted with chloroform (extract WBB).

Extract WBA (5·5 g.) in benzene was chromatographed over alumina (80 g.) and eluted with different solvents into fractions (25 ml.): 10% ethyl acetate in benzene (fractions 1—16);

* Part II, B. O. G. Schuler, A. A. Verbeck, and F. L. Warren, *J.*, 1958, 4776.

[1] A. E. Andrews, *Bull. Imp. Inst.*, 1915, **13**, 30.
[2] M. M. Rindl, *S. African J. Sci.*, 1929, **26**, 50; *Trans. Roy. Soc. S. Africa*, 1932, **20**, 59.
[3] M. M. Rindl and M. L. Sapiro, *Trans. Roy. Soc. S. Africa*, 1936, **23**, 361.
[4] H. King, *J.*, 1949, 955.

15% ethyl acetate in benzene (fractions 17—23, 70 mg.; fractions 24—29, 200 mg.); ethyl acetate (fractions 30—40, 200 mg.); chloroform (fractions 41—43, nothing extracted); 10% methanol in chloroform (fractions 44—48, 500 mg.). Fractions 19—23 gave rindline, fractions 30—40 gave henningsamine, and fractions 44—48 and extract WBB gave diaboline.

Rindline.—Fractions 19—23 crystallised twice from ether to give rindline, m. p. 214—216° (lit.,[3] 214°), $[\alpha]_D^{19}$ +194° (*c* 1 in chloroform), R_F 0·77, $\lambda_{max.}$ 222, 253, 290 mμ (log ε 4·4, 3·9, 3·55) (Found: C, 67·9; H, 7·0%; *M*, 426. Calc. for $C_{24}H_{30}N_2O_5$: C, 67·6; H, 7·1%; *M*, 426). The *picrate* crystallised from ethanol as yellow prisms, m. p. 224° (decomp.) (Found: C, 55·2; H, 5·0; N, 10·2. $C_{30}H_{33}N_5O_{12}$ requires C, 55·0; H, 5·1; N, 10·7%).

Henningsoline.—The combined sodium hydroxide extracts (extracts P) were acidified with hydrochloric acid, rebasified with ammonia, and extracted with chloroform (4 × 200 ml.). The chloroform extract, washed with sodium chloride solution and dried (Na_2SO_4), gave a yellow solid (10·5 g.) which was homogeneous. Crystallisation of the solid from acetone gave henningsoline as prisms, m. p. 207—209°, $[\alpha]_D^{20}$ −200° (*c* 1 in chloroform), R_F 0·60, pK_a 7·1, $\lambda_{max.}$ 223, 256 mμ (log ε 4·42, 3·84), $\lambda_{infl.}$ 285 mμ (log ε 2·9); λ (KBr), 2·85 (aliphatic OH), 6·12 (hydrogen-bonded amide CO), 7·28 (Me of NAc), 8·0 (aromatic OMe), 12·50 μ (aromatic ring, 2 adjacent hydrogens) (Found: C, 65·4, 65·1; H, 6·5, 6·8; N, 7·2; O, 21·1; OMe, 7·5; Ac, 10·7%; Equiv., 390; *M*, 398. $C_{22}H_{26}N_2O_5,\frac{1}{4}H_2O$ requires C, 65·6; H, 6·6; N, 7·0; O, 20·8; OMe, 7·7; Ac, 10·7%; *M*, 398. Found, after drying only at 96°/0·01 mm.: C, 64·3; H, 6·7. $C_{22}H_{26}N_2O_5,\frac{3}{4}H_2O$ requires C, 64·15; H, 6·7%).

Henningsoline picrate crystallised from aqueous methanol as prisms, m. p. 167—168° (Found, after drying at 75°/0·01 mm.: C, 52·2; H, 4·8. $C_{28}H_{29}N_5O_{12},H_2O$ requires C, 52·1; H, 4·85%).

Henningsoline methiodide crystallised from methanol–acetone as colourless prisms, m. p. 223—224° (Found: C, 47·9; H, 6·3; OMe, 5·6; *N*-Me, 6·8. $C_{23}H_{29}IN_2O_5,2H_2O$ requires C, 47·9; H, 5·8; OMe, 5·4; *N*-Me, 5·0%).

Henningsoline hydroreineckate crystallised twice by diluting an acetone solution with warm water, separated as needles, decomposing above 220° (Found, after drying at 25°/0·01 mm.: C, 42·4; H, 4·9; Cr, 7·3; OMe, 4·8. $C_{26}H_{33}CrN_8O_5S_4,H_2O$ requires C, 42·4; H, 4·8; Cr, 7·1; OMe, 4·2%).

Henningsoline hydroperchlorate crystallised from methanol as prisms, m. p. 253—254° (decomp.) (Found: C, 53·1, 53·1; H, 5·3, 5·6; OMe, 6·5. $C_{22}H_{27}ClN_2O_9$ requires C, 53·0; H, 5·45; OMe, 6·2%).

Diaboline.—Extract WBA (fractions 44—48) and extract WBB were worked up separately. The base (1 mol.) treated with dilute hydrochloric acid (1 mol.) and evaporated to dryness at 20°, was crystallised from ethanol–ether to give diaboline hydrochloride monohydrate as needles, m. p. 240—245° (decomp.), $[\alpha]_D^{20}$ +130° ± 3° (*c* 1 in water) (Found: C, 62·4, 62·2; H, 6·4, 6·8; Cl, 8·8; N, 6·4. Calc. for $C_{21}H_{25}ClN_2O_3,H_2O$: C, 62·0; H, 6·7; Cl, 8·7; N, 6·9%). King [4] refers to the hydrochloride or monohydrate or hemihydrate, of no definite m. p., but shrinking and turning brown *ca.* 260°, and gives $[\alpha]_{5461}^{20}$ +184° (water) for the anhydrous salt. Badar *et al.*[5] give m. p. >360° for the unanalysed salt. *Diaboline hydrochloride dihydrate* crystallised slowly from water at 0° as hexagonal plates, m. p. 238—240°, $[\alpha]_D^{20}$ +110·5° (*c* 1 in water) (Found: C, 58·8; H, 7·15; Cl, 8·0. $C_{21}H_{25}ClN_2O_3,2H_2O$ requires C, 59·35; H, 6·9; Cl, 8·4%).

The picrate crystallised from methanol or ethanol as yellow needles or rods, respectively, m. p. 238—240° (decomp.) [lit., 244° (decomp.),[4] 235—240° (decomp.)[5]] (Found: C, 55·5; H, 4·5; N, 11·8. Calc. for $C_{27}H_{27}N_5O_{10}$: C, 55·7; H, 4·7; N, 12·0%). Diaboline, regenerated from the picrate, crystallised slowly from methanol in bipyramidal crystals, m. p. 190°, $[\alpha]_D^{27}$ +44·8° (*c* 1 in ethanol) {lit., m. p. 187°,[4] 187—189°,[5] $[\alpha]_D^{22}$ +38° (chloroform) [6]} (Found: C, 70·15; H, 7·0. Calc. for $C_{21}H_{24}N_2O_3,\frac{1}{2}H_2O$: C, 69·8; H, 7·0%). Diaboline, refluxed with methyl iodide and methanol for 3 hr., and the product crystallised from methanol, gave *O-methyldiaboline methiodide* as needles, m. p. 258—260°, $[\alpha]_D^{27}$ +119°, which recrystallised from methanol as colourless silky needles, m. p. 171°, $[\alpha]_D^{27}$ +60·3° (*c* 1 in water) [King [4] refers to *O*-methyldiaboline methiodides as hydrates (2·5H_2O), m. p. 290° and 200—220, $[\alpha]_D$ for anhydrous salts +42 and +143°, all respectively] (Found: C, 54·75; H, 5·8. $C_{23}H_{29}IN_2O_3$ requires C, 54·3; H, 5·75%).

Diaboline hydrochloride was hydrolysed and the product crystallised from acetone–methanol to give the Wieland–Gumlich aldehyde as crystals, m. p. 204—205·5°, $[\alpha]_D^{19}$ −130·4° (*c* 1 in

[5] F. E. Bader, E. Schlittler, and H. Schwarz, *Helv. Chim. Acta*, 1953, **36**, 1256.
[6] J. A. Deyrup, H. Schmid, and P. Karrer, *Helv. Chim. Acta*, 1962, **45**, 2266.

methanol) [lit., m. p. 217°,[7] 197—198°,[5] 213—214°, $[\alpha]_D$ −134·5° (methanol) [8]] (Found: C, 73·3; H, 7·1; N, 8·5. Calc. for $C_{19}H_{22}N_2O_2$: C, 73·5; H, 7·1; N, 9·0%). The oxime had m. p. 245° (decomp.) [lit.,[7] 245° (decomp.)] (Found: C, 69·8; H, 7·3. Calc. for $C_{19}H_{23}N_3O_2$: C, 70·1; H, 7·1%).

Henningsamine.—Extract WBA (fractions 30—40) crystallised from ethyl acetate–light petroleum to give henningsamine as needles, m. p. 205—206°, $[\alpha]_D^{19}$ −43·9° (*c* 1 in chloroform), R_F 0·69 (Found: C, 69·95; H, 6·95; N, 6·6%; *M*, 394. $C_{23}H_{26}N_2O_4$ requires C, 70·0; H, 6·6; N, 7·1%; *M*, 394). The *picrate* crystallised from methanol as needles, m. p. 229—231° (Found: C, 55·5; H, 4·8. $C_{29}H_{29}N_5O_{11}$ requires C, 55·9; H, 4·65%). The *methiodide* crystallised from methanol–ether as needles, m. p. 231—233° (Found: C, 52·3; H, 5·8. $C_{24}H_{29}IN_2O_4,H_2O$ requires C, 52·1; H, 5·6%).

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[7] H. Wieland and K. Kaziro, *Annalen*, 1933, **506**, 60.
[8] K. Bernauer, S. K. Pavanaram, W. von Philipsborn, H. Schmid, and P. Karrer, *Helv. Chim. Acta*, 1958, **41**, 1405.