

193. Strychnine. Part II.

By G. R. CLEMO and R. RAPER.

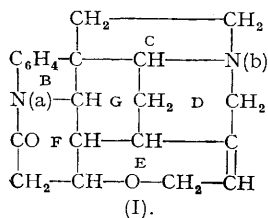
The catalytic reduction of strychnine with Raney nickel at 220° and 150 atmospheres results in the production of a base, $C_{21}H_{26}O_2N_2$, in which one of the rings is broken, a second base, m. p. 190°, and small quantities of dihydrostrychnine, trimethylamine, and a neutral product.

In Part I (*J.*, 1936, 1695) certain degradation products of strychnine were described, including 4-methyl-3-ethylpyridine and a bicyclic base, $C_{10}H_{11}N$, whose constitution has not yet been established. Recently further work on strychnine has been carried out and in particular its reduction with hydrogen in the presence of Raney nickel has been examined. In this reaction the main product is a base "D," $C_{21}H_{26}O_2N_2$, of m. p. 252°, and amongst the other products are a trace of dihydrostrychnine, a base "E," m. p. 190°, and small amounts of trimethylamine and a non-basic material which has not yet been identified.

Base "D" gives the usual strychnine colour reactions, and on electrolytic reduction a base $C_{21}H_{28}ON_2$ of the strychnidine type is formed, so that in "D" the $-N(a)-CO-$ system remains intact. The fact that in the catalytic reduction four hydrogen atoms have been added on (two presumably to the double bond) indicates that at any rate one ring has been opened. In "D," N(b) appears to be tertiary as in strychnine—it gives no nitroso-derivative—and since sparteine, which contains *m*-bridged nitrogen ring systems (*J.*, 1933, 644) is unaffected by hydrogenation under the conditions used in this work it is unlikely that either of the rings containing N(b) or ring G has been opened. "D" does not contain an alkoxy-group but gives an acetyl derivative, although the Zerewitinoff determination in xylene is negative (cf. quinol, which gives a negative result in amyl ether, although resorcinol behaves normally. Houben-Weyl, "Methoden der organischen Chemie," 2nd Ed., IV, 793). The electrolytic reduction product of "D," however, gives results agreeing with one hydroxyl group.

We infer, therefore, that the 7-membered oxygen containing ring E has been opened to give either a primary or secondary alcohol. If, as we believe, ring "D" is six-membered as it is in the structure now advanced by Robinson (I) (*Experientia*, 1946, II, 38; compare also Prelog and Szpilfogel, *Helv. Chim. Acta*, 1945, 28, 1669) the production of 4-methyl-3-ethylpyridine is easily explained.

Further work on the above lines is in progress, but it seems desirable that these results should be recorded at this stage.



EXPERIMENTAL.

Base "D," $C_{21}H_{26}O_2N_2$.—Strychnine (10 g.), methanol (130 c.c.), and Raney nickel (3 g.) were heated and stirred with hydrogen during 4 hours at 100 atm. pressure, the temperature rising to 220° and the pressure to 150 atm. The heating and stirring were continued at these conditions during a further 4 hours* and the autoclave allowed to cool overnight. The resulting methanol solution, which smelled strongly of trimethylamine, was filtered and evaporated (residue A). The distillate of methanol and volatile products was acidified and evaporated to dryness, and the residue basified and extracted with ether. The extract gave, with alcoholic picric acid, a picrate, m. p. 214°, not depressed by admixture with trimethylamine picrate. The colourless solid (residue A) was digested first with warm ether and then with acetone (extracts B and C below), leaving a colourless solid (8.6 g., m. p. 250°) which crystallised from alcohol in well-formed prisms, m. p. 252° (Found: C, 74.3, 74.6; H, 7.7, 7.6; N, 8.5. $C_{21}H_{26}O_2N_2$ requires C, 74.5; H, 7.7; N, 8.3%). The substance gives no precipitate with alcoholic silver nitrate in the micro-Zeisel determination.

Acetyl "D."—When base "D" (0.2 g.) was refluxed during six hours with acetic anhydride (1 c.c.) it was converted into an acetyl derivative which crystallised from ethyl acetate in well-formed prisms, m. p. 194° (Found: C, 72.4; H, 7.3; N, 7.4. $C_{23}H_{28}O_3N_2$ requires C, 72.6; H, 7.4; N, 7.4%). The base was recovered largely unchanged if the heating only lasted one hour, indicating the possibly secondary alcoholic nature of "D."

Electrolytic Reduction of "D."—Base "D" (1.5 g.) in sulphuric acid (50 c.c., 30%) was placed in the cathode compartment of an electrolytic cell (J., 1918, 764) and 5 amps. passed for 16 hours, the temperature being kept below 45° by external cooling. Basification of the cathode liquor gave a solid (1.2 g.) which crystallised from benzene or a little alcohol in colourless prisms, m. p. 217° (Found: C, 77.2; H, 8.6; N, 8.25; active hydrogen, 1.1. $C_{21}H_{28}ON_2$ requires C, 77.8; H, 8.6; N, 8.6%; active hydrogen, 1). We are indebted to Mr. C. G. Moore for the Zerewitinoff determinations. The pink solution of this base in dilute sulphuric acid is changed to intense red on the addition of a trace of chromic acid, whilst an alcoholic solution of the base and *p*-dimethylaminobenzaldehyde acidified with hydrochloric acid becomes dark green on warming.

Ethereal Extract B.—In some experiments this deposited a small amount of material which formed well-defined prisms from acetone, m. p. 219° (Found: C, 74.6; H, 7.05; N, 8.3. Calc. for dihydrostrychnine, $C_{21}H_{24}O_2N_2$: C, 75.0; H, 7.1; N, 8.3%). The major part of the extract (usually 0.8 to 1.1 g.) was a resin from which a picrate, stout yellow prisms, m. p. 264° (decomp.), was obtained by adding picric acid in alcohol and recrystallising from glacial acetic acid. The acetone extract C gave the same picrate (Found: C, 52.4; H, 4.7%). The picrolonate, m. p. 206°, was crystallised from alcohol (Found: C, 62.0; H, 5.85%). The picrate was not decomposed by cold hydrochloric acid (1:1), but, after it had been ground with 2*N*-sodium hydroxide, ether extracted a base which crystallised from light petroleum (b. p. 60–80°) in colourless prisms, m. p. 190° [Found: (Weiler and Strauss) C, 76.4, 76.8; H, 7.5, 7.75; N, 8.6, 8.9%. (W. A. Campbell) C, 76.75; H, 7.05%; *M*, 325. It is impossible to deduce any definite formula from these analyses. The hydrogen and nitrogen and molecular weight values, however, all indicate $C_{21}H_{24}ON_2$, which requires C, 78.7; H, 7.5; N, 8.7%; *M*, 320. $C_{21}H_{24}ON_2, C_6H_3O_7N_3$ requires C, 55.0; H, 4.9. $C_{21}H_{24}ON_2, C_{16}H_8O_5N_4$ requires C, 63.7; H, 5.5%]. This difficulty may be due to the presence of an alkyl group on a quaternary carbon atom, as has been occasionally found in the terpene series.

UNIVERSITY OF DURHAM, KING'S COLLEGE, NEWCASTLE-UPON-TYNE.

[Received, March 30th, 1946.]

* In one experiment the temperature accidentally rose to 270° during the second 4-hour period, and the pressure to well over 600 atms. The heating was immediately discontinued to avoid a burst, and after cooling the gases were found to contain 80% of methane, clearly formed by reduction of the methanol.