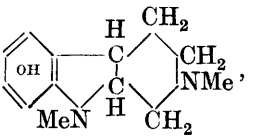
XCIX.—*A New Degradation Product of Physostigmine.*

By Edgar Stedman.

In the course of an investigation of the constitution of physostigmine, an attempt was made to prepare the methyl ether of eseroline methiodide by the action of methyl iodide and sodium ethoxide

on eseroline methiodide, $C_{14}H_{21}ON_2I$. In place of the expected ether, a compound of the composition $C_{10}H_{17}ON_2I$ was obtained; the molecule has therefore suffered an at present inexplicable nett loss of C_4H_4. (If one methyl group were added, C_5H_6 has been eliminated from the original molecule.) Straus (*Annalen*, 1913, **401**, 358) has suggested the following provisional constitution for eseroline:



but it is difficult to conceive how such a compound could lose four or five carbon atoms and still retain two nitrogen atoms. The carbon atoms cannot come from the benzene ring, for the new iodide, $C_{10}H_{17}ON_2I$, still gives an indole derivative on distillation; and if the piperidine ring were broken down, its nitrogen would be eliminated. It is not inconceivable that eseroline (and physostigmine) do not contain a preformed pyrrole ring at all, but possibly a heterocyclic ring with two nitrogen atoms, which survives the gentle treatment with alcoholic sodium ethoxide and methyl iodide, but is broken down on heating eseroline methiodide at a much higher temperature (the second way in which Straus obtained physostigmol, an indole derivative). Max and Michel Polonovski (*Bull. Soc. chim.*, 1918, [iv], **23**, 336) are convinced that eserolinium hydroxide (Straus's first method) does not undergo simple fission into dimethylamine and physostigmol, but that it is formed by a complete disintegration of the molecule.

It is thought that the methiodide now obtained will be a suitable starting-point for further investigation of the constitution of the alkaloid. Experiments are also in progress to elucidate the mechanism of its formation.

Experimental.

Preparation of the Compound $C_{10}H_{17}ON_2I$.—The following is an example of several similar experiments: Thirteen c.c. of a solution of 0·5 gram of sodium in 50 c.c. of ethyl alcohol were placed in a flask fitted with a reflux condenser and the air was displaced from the apparatus by means of a current of hydrogen. One gram of eseroline methiodide, prepared by Straus's modification of Salway's method (*Annalen*, 1913, **401**, 350), was then added. When solution had taken place, excess of methyl iodide was added through the condenser and the flask heated on the water-bath for one and a

half hours, a slow stream of hydrogen being passed through the apparatus continuously. During this period a crystalline solid separated. The solution was now cooled in ice, causing a further separation of crystals, and filtered (yield 0·3 gram). When recrystallised from methyl alcohol, the substance formed plates which commenced to darken at about 210° and melted at 235° with decomposition and evolution of a gas (Found: C=39·08; H=5·51; N=9·02 *; I=41·74, 42·19. $C_{10}H_{17}ON_2I$ requires C=38·96; H=5·52; N=9·09; I=41·23 per cent.).

Estimation of Methoxy- and N-*Methyl Groups.*—A methoxyl estimation by Zeisel's method on 0·1111 gram of substance gave a negative result, but when the temperature was raised for the estimation of *N*-methyl groups by Herzig and Meyer's method a separation of silver iodide began at 160°, and on a second distillation a further separation occurred at 250°. A third distillation, during which the temperature was finally raised to 300°, produced no result (Found: Me=14·04. 3Me in $C_{10}H_{17}ON_2I$ requires Me=14·61 per cent.).

As methyl iodide began to be given off at as low a temperature as 160°, it is as yet not quite certain whether all three methyl groups are attached to nitrogen or whether one methoxy-group is present.

Attempted Degradation of the Compound.—The iodine was readily removed by treating an aqueous solution of 0·3 gram of the compound with moist silver oxide. After filtration, the solution was evaporated under diminished pressure, leaving the quaternary hydroxide as a brown syrup. This was distilled under diminished pressure. Decomposition commenced at about 160°/12 mm., a volatile amine being evolved, and at 220°/12 mm. an almost colourless syrup was collected. On admission of air into the apparatus, however, this appeared to polymerise partly. The remainder was dissolved in ether, but decomposed on evaporation on the water-bath, and was evidently very unstable. So far, the volatile amine has not been collected in sufficient quantity to identify it.

The substance $C_{10}H_{17}ON_2I$ itself does not give any indole reactions, but when it is heated above its melting point under atmospheric pressure gases and an oily distillate are formed, giving an indole reaction with *p*-dimethylaminobenzaldehyde. The vapours formed give the pinewood reaction.

In conclusion, the author desires to express his thanks to Prof. G. Barger, F.R.S., for his advice and assistance during the course

* Micro-Dumas according to Dubsky. 12·334 mg. gave 0·980 c.c. N at 16° and 757 mm.

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DEPARTMENT OF MEDICAL CHEMISTRY,
UNIVERSITY OF EDINBURGH. [*Received, May 12th*, 1921.]