

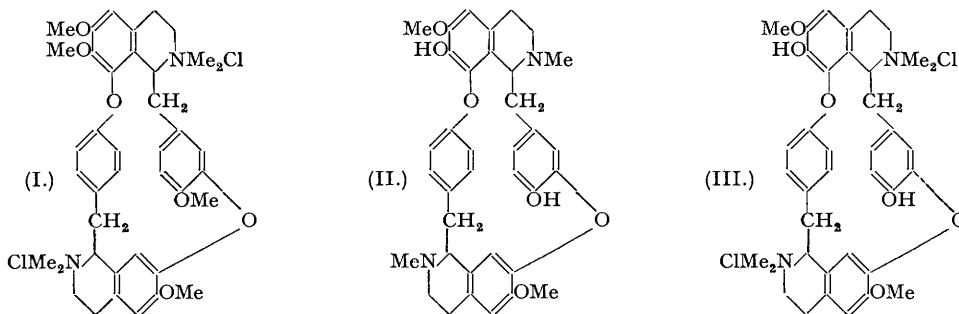
64. *Curare Alkaloids. Part VII. Constitution of
dextroTubocurarine Chloride.*

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The aim of the present investigation was the determination of the constitution of *dextro*tubocurarine chloride. This has been accomplished by *O*-ethylation followed by a two-stage Hofmann degradation to *O*-ethylbebeerilene, the nitrogen-free substance previously obtained from bebeerine. *dextro*Tubocurarine chloride and bebeerine have therefore the same distribution of methoxy- and phenolic groups, and their particular orientation is known since the structure of bebeerine has previously been completely elucidated.

It was shown in Part I (King, *J.*, 1935, 1381) that *dextro*bebeerine when methylated on its phenolic groups and on its tertiary nitrogen atoms gave a substance, *O*-methylbebeerine methochloride, isomeric with the product obtained by methylation of the phenolic groups of *dextro*tubocurarine chloride. Furthermore, these two completely methylated quaternary alkaloids gave, when submitted to a two-stage Hofmann degradation, one and the same nitrogen-free substance, *O*-methylbebeerilene. The difference between the two completely methylated alkaloids was thus due to diastereoisomerism.

In Part II (King, *J.*, 1936, 1276) the constitution of *O*-methylbebeerine methochloride and *O*-methyltubocurarine chloride was shown to be (I), the difference in these completely methylated



bases residing in the asymmetric centres. In Part IV (King, *J.*, 1939, 1157) it was demonstrated by degradation experiments on *O*-ethylated bebeerine that bebeerine had the constitution (II). It was also pointed out at the same time that the quaternary alkaloid *dextro*tubocurarine chloride might have a similar distribution of phenolic groups.

Through the generosity of the Wellcome Foundation Ltd., who presented me with a supply of the valuable alkaloid, *dextro*tubocurarine chloride, it has been possible to determine the orientation of the phenolic groups in this quaternary salt. On *O*-ethylation it gave amorphous *O*-ethyltubocurarine chloride which when submitted to a two-stage Hofmann degradation gave the nitrogen-free *O*-ethylbebeerilene identical in properties with the substance obtained from bebeerine. *dextro*Tubocurarine chloride must accordingly have the structure (III). The evidence supplied by observations on the optical rotations of the methines obtained from *O*-methylbebeerine methochloride and *O*-methyltubocurarine chloride (Part I, *loc. cit.*) suggests that in *dextro*bebeerine both asymmetric centres are dextrorotatory whilst in *dextro*tubocurarine chloride one is dextro- and one lævo-rotatory.

EXPERIMENTAL.

Anhydrous *dextro*tubocurarine chloride (0.97 g.), absolute alcohol (10 c.c.), 0.5*N*-alcoholic potash (5.6 c.c.; 2 mols.), and ethyl iodide (1 c.c.) were boiled for 7 hours, a second portion of 0.5*N*-alcoholic potash (2.8 c.c.) and ethyl iodide (1 c.c.) being added after 3 hours' boiling. The solvents having been removed, water was added and sufficient alcohol to dissolve the precipitated gum, followed by excess of freshly precipitated silver chloride. After thorough mixing by shaking for a few minutes, the solution was filtered and evaporated to dryness. The non-crystalline residue mixed with some sodium chloride was treated with water (20 c.c.) and sodium hydroxide (4 g.), and boiled for 75 minutes. On cooling, the gum was extracted with chloroform, the solvent removed, and the residue boiled with methyl alcohol (10 c.c.) and methyl iodide (2 c.c.) for 8 hours. The solvent having been removed, the residue was dissolved in aqueous alcohol and freed from iodide by addition of silver chloride. The filtered solution was evaporated to dryness, the residue treated with water (20 c.c.) and sodium hydroxide (4 g.), and the solution boiled for 90 minutes. The gum which had separated was taken up in chloroform, the solvent removed, and the residue (0.45 g.) moistened with glacial acetic acid. A crystalline solid rapidly separated (0.14 g.), and on repeated crystallisation from 10 parts of glacial acetic acid retained a melting point of 167—168° and when mixed with authentic *O*-ethylbebeerilene showed no depression of melting point. Both ethers crystallised from acetic acid in sheaves of elongated plates which on drying in the oven at 95° effloresced and lost their transparent appearance. Both when added to concentrated sulphuric acid gave a cherry-red solution (Found: C, 77.0; H, 6.2. Calc. for C₃₈H₃₈O₆: C, 77.5; H, 6.2%).