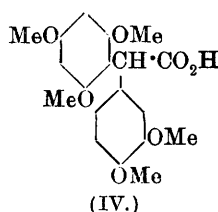
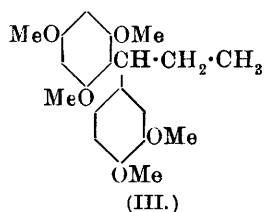
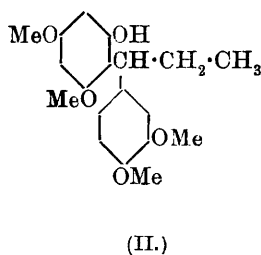
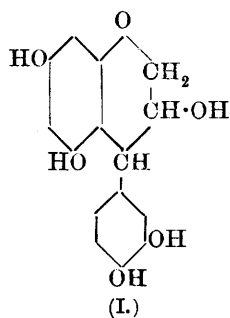


CXXX.—*The Constitution of Catechin. Part II.*

By MAXIMILIAN NIERENSTEIN.

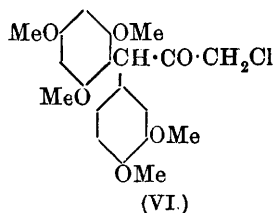
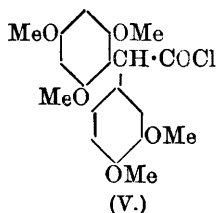
IN the previous communication (this vol., p. 971), provisional formulæ were suggested for catechin (I) and for the methylated reduction product (III) obtained by Kostanecki and Lampe (*Ber.*, 1907, **40**, 720) from catechin tetramethyl ether. At the same time, it was shown that Kostanecki and Lampe's substance may be oxidised to 3:4:2':4':6'-pentamethoxydiphenylacetic acid (IV).



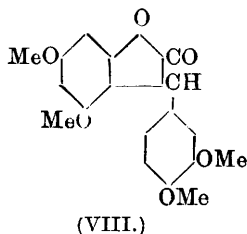
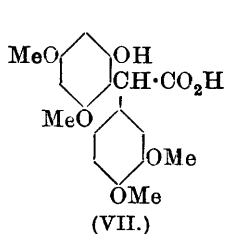
The present communication describes the synthesis of 3:4:2':4':6'-pentamethoxy- α -diphenylpropane (III), which was

1152 NIERENSTEIN: THE CONSTITUTION OF CATECHIN. PART II.

found to be identical in every respect with the methylated reduction product of Kostanecki and Lampe. The synthesis was carried out according to the following scheme: 3:4:2':4':6'-pentamethoxydiphenylacetyl chloride (V), on treatment with diazomethane (compare Clibbens and Nierenstein, T., 1915, **107**, 1491), yielded 3:4:2':4':6'-pentamethoxydiphenylmethyl chloromethyl ketone (VI), which, on reduction with metallic sodium and alcohol, gave 3:4:2':4':6'-pentamethoxy- α -diphenylpropane (III).



The intermediate 2'-hydroxy-3:4:4':6'-tetramethoxy- α -diphenylpropane (II) has previously not been investigated; thus, Kostanecki and Lampe (*loc. cit.*) only refer to it as an oil, without further mention. It has now been obtained as a crystalline substance, which yields on oxidation 2'-hydroxy-3:4:4':6'-tetramethoxydiphenylacetic acid (VII). The latter substance behaves normally towards methyl sulphate, diazomethane, and acetyl chloride and pyridine, yielding the corresponding derivatives. On digestion with acetic anhydride and anhydrous sodium acetate, however, 3:5:3':4'-tetramethoxy-2-phenylcoumaran-1-one* (VIII) is formed, which is also produced when 3:4:2':4':6'-pentamethoxydiphenylacetic acid (IV) is treated with acetyl chloride according to Stoermer and Friderici's method (*Ber.*, 1908, **41**, 340).



* The numbering of the coumaran nucleus is as suggested by Stoermer (*Annalen*, 1900, **312**, 258).

EXPERIMENTAL.

3:4:2':4':6'-Pentamethoxydiphenylacetyl Chloride (V).

Six and a-half grams of 3:4:2':4':6'-pentamethoxydiphenylacetic acid are heated on a water-bath for three hours with 10 grams of thionyl chloride. As much as possible of the unchanged thionyl chloride is distilled off under diminished pressure and the residue dissolved in dry benzene. The solid obtained by evaporating the benzene is left over solid potassium hydroxide in a vacuum for some time, so as to remove the adhering traces of thionyl chloride. The product crystallises from benzene in small clusters of prismatic needles, which melt at 76.5°. The yield is 98 per cent. of the theoretical (Found: Cl=9.6. $C_{19}H_{21}O_6Cl$ requires Cl=9.3 per cent.).

3:4:2':4':6'-Pentamethoxydiphenylmethyl Chloromethyl Ketone (VI).

To a solution of 6 grams of the acyl chloride in dry ether (according to Grignard), an ethereal solution of freshly prepared diazomethane from 30 c.c. of nitrosomethylurethane is added. When the evolution of nitrogen ceases, the same amount of diazomethane is again added, and the solution allowed to remain for several days, moisture being excluded. The ether, which contains an excess of diazomethane, is distilled off, and the residue crystallised from benzene. Large, glistening plates separate, which melt at 102° and have the characteristic odour of the chloromethyl ketones. The yield is 94 per cent. of the theoretical (Found*: C=60.6; H=5.9; Cl=8.9. $C_{20}H_{23}O_6Cl$ requires C=60.9; H=5.8; Cl=9.0 per cent.).

3:4:2':4':6'-Pentamethoxy-*aa*-diphenylpropane (III).

A solution of 6 grams of the ketone in about 200 c.c. alcohol is heated on a water-bath with 20 grams of metallic sodium until the latter disappears. The solution is subsequently reduced to about 50 c.c. and diluted with water. The precipitate crystallises from alcohol in small needles, which melt at 83—84°. This melting point is not depressed when mixed with the methylated reduction product of Kostanecki and Lampe (Found*: C=69.2; H=7.7. Calc.: C=69.3; H=7.5 per cent.).

* Dried over paraffin in a vacuum.

2'-Hydroxy-3:4:4':6'-tetramethoxy- α -diphenylpropane (II).

By distilling Kostanecki and Lampe's reduction product (deoxyhydrocatechin tetramethyl ether) under diminished pressure, the greater proportion is obtained as an oil boiling at 235—238°/10—11 mm. After remaining on ice for a short time, it readily solidifies. A few crystals of this substance are sufficient to cause the oil of other preparations to become semi-solid without previous distillation. Prepared by this method, any adhering oil may be removed by washing with light petroleum and subsequent drying on a porous plate. Three preparations from 10 grams of catechin tetramethyl ether gave 7.8, 6.2, and 8.1 grams, respectively, of the solid.* It crystallises from alcohol in rectangular plates, which feel oily and melt at 106°. The substance is soluble in the usual organic solvents, with the exception of light petroleum in the cold. The alcoholic solution turns violet with ferric chloride (Found †: C=68.5; H=7.4. $C_{19}H_{24}O_5$ requires C=68.7; H=7.2 per cent.).

On treatment with methyl sulphate, the theoretical yield of 3:4:2':4':6'-pentamethoxy- α -diphenylpropane (III) is obtained. It melts at 83—84°, and this melting point is not depressed when mixed with the methylated reduction product of Kostanecki and Lampe.

2'-Hydroxy-3:4:4':6'-tetramethoxydiphenylacetic Acid (VII).

Nine grams of 2'-hydroxy-3:4:4':6'-tetramethoxy- α -diphenylpropane suspended in 300 c.c. of a 20 per cent. solution of potassium hydroxide in water are oxidised on a boiling-water bath for four hours with 9 grams of potassium permanganate dissolved in 200 c.c. of water. The solution is filtered while hot, and, after cooling, acidified with dilute sulphuric acid. The dark-coloured precipitate is not filtered, but the solution extracted several times with ether, in which the precipitate dissolves. The ethereal extract, dried over anhydrous sodium sulphate, leaves a solid on evaporation, which, after several crystallisations from water,

* The reduction of catechin tetramethyl ether according to the method of Kostanecki and Lampe (*loc. cit.*) is apparently accompanied by some decomposition, since the crude reduction product has an odour of acetic acid. Several attempts were made to isolate some of the disintegration products by extracting the porous plate with alcohol. A small crop of needles was obtained from the alcoholic extract. They melted at 178—180°, which is the melting point given for veratric acid, but there was not enough material to establish their identity.

† Dried over paraffin in a vacuum

animal charcoal being used, yields long, prismatic needles melting at 168—169°, carbon dioxide being evolved. By prolonged drying over phosphoric oxide in a vacuum, or heating at 110°, one molecule of water is lost (Found*: $\text{H}_2\text{O}=5.0$. Calc.: $\text{H}_2\text{O}=4.9$ per cent.). The anhydrous product is powdery in appearance and melts at 172—173°, carbon dioxide being evolved. The substance is also soluble in alcohol or ethyl acetate, but insoluble in benzene or toluene. Both the aqueous and alcoholic solutions turn bluish-violet with ferric chloride. The yield is 78 per cent. of the theoretical (Found*: $\text{C}=62.2$; $\text{H}=5.9$. $\text{C}_{18}\text{H}_{20}\text{O}_7$ requires $\text{C}=62.1$; $\text{H}=5.7$ per cent.).

On methylation with methyl sulphate, 3:4:2':4':6'-penta-methoxydiphenylacetic acid (IV), melting at 150—151°, is formed. Diazomethane converts 2'-hydroxy-3:4:4':6'-tetramethoxydiphenylacetic acid quantitatively into the corresponding methyl ester, which melts at 119°. Neither of these melting points is depressed when the compounds are mixed with the corresponding substances previously described (*loc. cit.*, p. 879).

The *acetyl* derivative is prepared by the action of acetyl chloride (3 grams) and pyridine (30 grams) on the anhydrous acid (3 grams). It crystallises from alcohol in prismatic needles, which melt at 183—184°, carbon dioxide being evolved (Found*: $\text{C}=61.5$; $\text{H}=5.7$. $\text{C}_{20}\text{H}_{22}\text{O}_8$ requires $\text{C}=61.5$; $\text{H}=5.6$ per cent.).

3:5:3':4'-Tetramethoxy-2-phenylcoumaran-1-one (VIII).

One gram of 2'-hydroxy-3:4:4':6'-tetramethoxydiphenylacetic acid is digested with 30 c.c. of acetic anhydride and 3 grams of anhydrous sodium acetate, and the mixture subsequently diluted with water. The precipitate obtained in this way crystallises from absolute alcohol in stout, prismatic needles, which melt at 117°. The yield is 85 per cent. of the theoretical (Found†: $\text{C}=65.4$; $\text{H}=5.5$. $\text{C}_{18}\text{H}_{18}\text{O}_6$ requires $\text{C}=65.5$; $\text{H}=5.4$ per cent.). The same product is also obtained when 3 grams of 3:4:2':4':6'-penta-methoxydiphenylacetic acid, dissolved in 20 c.c. of glacial acetic acid, are kept at the ordinary temperature for forty-eight hours with 50.4 c.c. of a solution of 100 c.c. glacial acetic acid and 2.12 grams of acetyl chloride (1 mol. of acetyl chloride). The greater part of the acetic acid is removed under diminished pressure and the residue precipitated with water. The product crystallises from absolute alcohol in stout, prismatic needles, which melt at 117°.

* Dried at 110°.

† Dried over paraffin in a vacuum.

1156 NIERENSTEIN: THE CONSTITUTION OF CATECHIN. PART II.

and this melting point is not altered on mixing with the previous preparation. The yield is 91 per cent. of the theoretical.

The author is indebted to the Colston Society of the University of Bristol for a grant which has covered the expenses of this research.

BIOCHEMICAL LABORATORY,
CHEMICAL DEPARTMENT,
UNIVERSITY OF BRISTOL.

[Received, September 9th, 1920.]

Note added October 1st, 1920.—Since this communication was submitted, a paper by Freudenberg (*Ber.*, 1920, **53**, [B], 1416) has appeared, in which he describes 3:4:2':4':6'-pentamethoxy- $\alpha\gamma$ -diphenylpropane as melting at 87—88°, which is the melting point given by the author (this vol., p. 972) for this substance. Freudenberg states, further, that Kostanecki and Lampe's methylated reduction product also melts at 87—88°, which is not correct. This substance melts at 83—84°, as given by Kostanecki and Lampe (*Ber.*, 1902, **40**, 720). The author has on five separate occasions prepared this product, and has always found it to melt at 83—84°. No difference of the melting point has been recorded by Ryan and Walsh (*Sci. Proc. Roy. Dublin Soc.*, 1916, **15**, 120), who have also prepared Kostanecki and Lampe's product. In view of Freudenberg's assumption that Kostanecki and Lampe's methylated reduction product is identical with 3:4:2':4':6'-pentamethoxy- $\alpha\gamma$ -diphenylpropane, the following mixed melting points were taken. They clearly disprove his contentions. (1) Kostanecki and Lampe's methylated reduction product (m. p. 83—84°) and 3:4:2':4':6'-pentamethoxy- $\alpha\gamma$ -diphenylpropane (m. p. 87—88°) giving a depression of 9 to 11 degrees. Similar results were obtained (August 11th, 1919) when three mixed melting points of these two substances were taken. (2) On the other hand, a mixture of Kostanecki and Lampe's product (m. p. 83—84°) with 3:4:2':4':6'-pentamethoxy- $\alpha\alpha$ -diphenylpropane (m. p. 83—84°), described in the present communication, melted at 83—84° without the slightest depression, as already observed (April 26th, 1920), when two mixed melting points of these substances were taken.