CLXX.—*Studies of the Glucosides. Part IV. Aesculin.*

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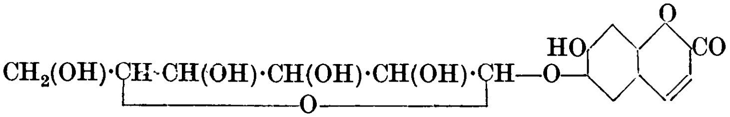
THE study of the constitution of this glucoside was undertaken some time ago, and although the work has not yet been completed the results obtained are now communicated on account of the appearance of the paper by Head and Robertson (J., 1930, 2434). The main purpose of the research was to determine the position of the sugar residue in the glucoside, to ascertain the nature of the glucose present, and to support the structure by orientation of the methylcoumarin obtained, and by synthesis of methylaesculin. The structure of the glucoside was established, and the results were presented as part of the Liversidge Research Lecture in the University of Sydney (June 6th, 1930). It was shown that aesculin was 6-glucosidoxy-7-hydroxycoumarin, the sugar being present in the amylene-oxide form linked as a β-glucose residue. This is in agreement with the evidence of the activity of the 6-hydroxyl group in the formation of scopoletin as a plant product, and supports the conclusions of Head and Robertson as to the position of the sugar residue. Aesculin is accordingly shown to possess the structure



EXPERIMENTAL.

Methylation of Aesculin. 7-O-*Methylaesculin.*—(a) Aesculin (5 g.) in methyl alcohol (100 c.c.) containing the equivalent amount of potassium hydroxide was refluxed (10 hours) with excess of methyl iodide until the solution was neutral. Solvents were then distilled off and the residue was recrystallised from boiling water. (b) Aesculin (10 g.), suspended in dry methyl alcohol, was treated at intervals with an ethereal solution of diazomethane. After 3 days the excess of diazomethane and the solvents were distilled off and the residue was recrystallised from methyl alcohol or boiling water. 7-*O*-Methylaesculin separated as a dihydrate in long, white, feathery needles (from water), m. p. 229° (Found : C, 49·2; H, 5·5. Calc. for $C_{16}H_{18}O_9,2H_2O$: C, 49·2; H, 5·6%. Found in material dried at 120° : OMe, 7·9. Calc. : OMe, 8·8%). The methylaesculin did not reduce Fehling's solution, was hydrolysed by emulsin, and its solutions exhibited a feeble fluorescence in ultra-violet light or sunlight. It had $[\alpha]_D$ −98° (*c*, 0·0812) in water and − 131° (*c*, 0·0532) in methyl alcohol; the aqueous solution deposited crystals of the methylglucoside after 2 days.

Hydrolysis of 7-O-*Methylaesculin.*—This was accomplished by emulsin or by refluxing the ether (0·9 g.) with 2% sulphuric acid (100 c.c.) for 30 minutes. Methylaesculetin separated as small spherules of fine needles on cooling, which later coalesced to form a mass. After recrystallisation from methyl alcohol it had m. p. 185°, which was not depressed by admixture with methylaesculetin prepared according to Tiemann and Will (*Ber.*, 1882, **15**, 2072). The structure is therefore that established by Moore (J., 1911, **99**, 1043).

Complete Methylation of Aesculin.—The methylation of the sugar residue in the glucoside is laborious on account of the low solubility of methylaesculin in organic media. It was carried out, however, by the repeated application of the Purdie reaction. Methylaesculin (6 g.) was added to a large excess of equal parts of methyl alcohol and methyl iodide, and silver oxide was added in 10-g. lots at intervals of 8 hours while the mixture was gently refluxed for several days. The residue after removal of solvents was thoroughly extracted with methyl alcohol, and subjected to reaction afresh. (Little methyl alcohol is required when the methoxyl content reaches 25%, and none when the value exceeds 28%.) The progress of the methylation is shown in the following summary :

	Extraneous solvent.	Time.	% Methoxyl.	Yield, g.
1	MeOH, 50%	15 days	19·3	6·3
2	„ 40 „	12 hours	24·6	6·0
3	„ 10 „	12 „	27·5	5·6
4	„ „ „	12 „	28·5	5·3
5—10	Nil	12 „	37·0	4·7

The product was isolated as a yellow-brown glass, readily soluble in methyl alcohol, methyl iodide, and ethyl acetate. It could not be crystallised, but before hydrolysis it was refluxed with light petroleum to remove some of the coloured impurities.

Simultaneous Hydrolysis and Condensation of Pentamethylaesculin.—This was carried out on 3 g. of the fully methylated glucoside by the action of methyl alcohol containing hydrogen chloride (1%)

as described in previous papers (J., 1922, **121**, 1666; 1923, **123**, 723). The resulting syrup, b. p. 110°/0·5 mm. (Found: OMe, 59·8. Calc. for tetramethyl glucose: OMe, 62·0%), was subjected to a Purdie reaction to methylate traces of tetramethyl glucose which had escaped glucoside formation, and the product showed the characteristic properties of the normal form of tetramethyl methylglucoside. On hydrolysis by 8% hydrochloric acid, tetramethyl glucose was obtained which after several crystallisations from light petroleum had m. p. 94° and rotation of + 91° which on mutarotation fell to + 83·2°. The amylene-oxide form of glucose is therefore present in the original glucoside. We were not successful in isolating methylaesculin from the hydrolytic product.

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