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proportion of nitrous acid (or nitrogen peroxide) by means of the *m*-phenylenediamine reaction, doubtless owing to some secondary reaction.

Summary.

Nitric acid of 96 per cent. and sulphuric acid of 98 per cent. concentration show definitely marked characteristics, analogous, although not in all cases strictly parallel, as regards certain properties, more especially density, contraction, and electrical conductivity; also in the case of the former, refractive indices, as investigated by ourselves, and in the case of the latter chemical reactivity, boiling point, vapour pressure, and, to a less degree, viscosity and capillarity, as investigated by Knietzsch.

The precise constitution of acids having these critical concentrations remains at present a matter for further inquiry.

C.—The Alkylation of Sugars.

By THOMAS PURDIE, F.R.S., and JAMES C. IRVINE, Ph.D., D.Sc.

IN the course of the earlier researches on the synthesis of glucosides, attempts were no doubt frequently made to prepare alkyl ethers of the sugars. Berthelot (*Ann. Chim. Phys.*, 1860, [iii], 60, 103), by heating cane sugar with caustic potash and ethyl bromide, obtained a substance which he describes as a diethylglucosan ether. Practically, however, the only methods of alkylating sugars at present known are those of Fischer (*Ber.*, 1893, 26, 2400; 1895, 28, 1145) and of Koenigs and Knorr (*Ber.*, 1901, 34, 957); in the former process, the alkylation is effected by the direct action of alcohol on the sugar in the presence of hydrochloric acid, whilst the latter is due to the interaction of alcohol and the acetohalogen or acetonitro-derivative, and subsequent removal of the acetyl groups by hydrolysis with alkali. By these methods, as is well known, only one of the carbinol groups of the sugar is etherified, and the products are of a glucosidic nature. Alkyl ethers of the sugars in the stricter sense of the term, that is to say, ethers which retain the aldehydic or ketonic properties of the parent sugar and resist the action of hydrolysing agents, are, however, so far unknown. The main purpose of the following research was the preparation and investigation of compounds of this class.

In alkylating the esters of optically active hydroxy-acids, we found that the object could be attained, when other methods had failed, as in the case of malic, lactic, and tartaric esters (*Trans.*, 1899, 75, 153, 483; 1901, 79, 957) and of mandelicesters (McKenzie, *Trans.*, 1899, 75, 753),

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by employing dry silver oxide and alkyl iodide, and the application of this method has been much extended since then by G. D. Lander (Trans., 1903, 83, 414, and earlier papers). Provided the oxidising effect of the silver oxide could be obviated, it seemed not improbable that the sugars might lend themselves to this reaction, and that we might thus obtain alkyl ethers of the above-mentioned class. Alkylated sugars should be compounds of considerable interest. A completely alkylated hexose, such as pentamethyl glucose, should be capable of existing, like penta-acetylglucose, in three stable forms. Of these, two should be glucosidic in structure and stereoisomeric, corresponding with the well-known penta-acetylglucoses (m. p. 112° and 131°), the relations of which as α - and β -derivatives, in the sense of Fischer's nomenclature of the glucosides, have been recently established by Koenigs and Knorr (*loc. cit.*) and by Fischer and Armstrong (*Ber.*, 1901, 34, 2885). The third isomeride, structurally different from the other two, should possess the properties of an ordinary aldehyde. Among the penta-acetylglucoses, Tanret's compound (*Bull. Soc. chim.*, 1895, [iii], 13, 268), melting at 86°, probably represents this form, although its aldehydic properties do not so far appear to have been definitely proved.

In their behaviour towards hydrolytic agents, however, the alkylated sugars should differ from the corresponding acyl derivatives. The penta-acyl glucoses are readily hydrolysed with production of the parent sugar. The pentamethyl glucose of aldehydic structure, on the other hand, should resist the action of these agents, whilst the corresponding glucosidic isomerides should lose on hydrolysis only one methyl group and yield a tetramethyl glucose ether. It seemed to us interesting to ascertain how far a sugar derivative of this kind exhibits the properties of an aldose. Adopting Fischer's view of the structure of the alkylglucosides, the derivative referred to might possibly possess a stable constitution represented by one or other of the following formulæ :



or, like the parent glucose, the substance might be tautomeric and exhibit the functions of both forms. Few acyl derivatives of this class appeared to have been prepared, and on account of their ready hydrolysis they would not be convenient for investigation. A further interest attaches to the tetra-alkyl aldose and ketose ethers of the above type. It is not improbable that they might lend themselves to the synthesis of alkylated disaccharides, a study of which might throw some light on the constitution of the common natural sugars of this class.

Although benzoin (Lander, *loc. cit.*) and salicylaldehyde (Irvine,

Trans., 1901, 79, 668) can be etherified, the latter almost quantitatively, by means of silver oxide and alkyl iodide, the method proved inapplicable to the reducing sugars. When silver oxide was added to a mixture of glucose, dissolved in methyl alcohol and methyl iodide, a vigorous reaction ensued, and when a large excess of the alkylating agent was used a product soluble in ether but having an acid reaction was obtained. On attempting to distil this, much decomposition occurred, and the only substance isolated was methyl oxalate. When ethyl iodide was employed in a similar reaction, the product was also acid, and an analysis of the silver residues showed that only 45 per cent. of the silver oxide taken was converted into iodide, the remainder having been reduced to the metallic state. The reaction was evidently a complex one. An attempt to alkylate levulose by this method was also unsuccessful.

To avoid oxidation, it was evidently requisite that the aldehydic or ketonic group of the sugar should be masked, and instead of glucose, therefore, we used Fischer's easily accessible α -methylglucoside. Methyl iodide was employed throughout our experiments, as previous experience with tartaric esters had shown that the slower action of the higher iodides gave scope for the occurrence of oxidation which resulted in the production of oxalates in considerable quantity.

The methylglucoside in methyl alcoholic solution reacted readily with methyl iodide in the presence of silver oxide, and was found to be nearly proof against the oxidising action of the latter. The product, consisting of a mixture of methyl ethers of the glucoside, was a neutral, viscid syrup, soluble in ether, having no action on Fehling's solution and distilling without decomposition in a vacuum. The solubility in organic solvents and the volatility of these compounds, as was to be expected, increase with the number of the methoxyl groups present in the molecule, and it was found possible, therefore, to isolate the main constituent of the mixture by fractional distillation. This substance, which proved to be a trimethyl methylglucoside, boils at 167—170° under 17 mm. pressure and is readily hydrolysed by dilute hydrochloric acid, giving a syrup which reduces Fehling's solution vigorously. It is shown in the succeeding paper that three of the four methoxyl groups are retained throughout the hydrolysis, the product being a trimethyl glucose. Attempts to obtain a hydrazone or osazone from this compound having failed, evidence of its aldose nature was sought by oxidising it with bromine water according to Kiliari's method. The process gave an almost neutral syrup, an analysis of which after distillation gave figures approximating to those for trimethylgluconolactone. The lactonic nature of the compound was confirmed by titration with alkali and by the gradual change in the optical rotation of its solution.

As stated above, the main product of the methylation when it is

carried out in methyl alcohol is a trimethyl methylglucoside. The last remaining hydroxyl, probably that of the terminal primary carbinol group of the chain, alkylates more slowly than the others. Even when the alkylating agent was used in considerable excess, the tetramethyl derivative was produced in very small quantity. This is partly due to the fact, which is evident from the abundant production of dimethyl ether in the course of the process, that the alkylation extends to the solvent alcohol, and that much of the alkylating agent is thus lost. Complete alkylation of the glucoside can, however, be effected by taking advantage of the fact that the trimethyl methylglucoside is readily soluble in methyl iodide. Such a solution reacts readily with silver oxide, and under these conditions tetramethyl methylglucoside is obtained as a neutral, comparatively mobile liquid boiling at 144—145° under 17 mm. pressure and showing no action on Fehling's solution.

On hydrolysing this compound with dilute hydrochloric acid, the glucosidic methoxyl only is removed, and a tetramethylated glucose is produced, which distils without decomposition at 182—185° under 20 mm. pressure and gradually solidifies; by recrystallising from warm ligroin, it is obtained in long needles melting at 81—83°. The compound reduces both Fehling's solution and ammoniacal silver nitrate on warming, and has undoubtedly the structure of an aldose. To indicate this and to distinguish it from the isomeric trimethyl methylglucoside referred to above, it may be named tetramethyl glucose.

Although the substance reacted with phenylhydrazine, attempts to procure from it an osazone or crystallised hydrazone were not successful, but evidence of its nature was procured, as before, by Kiliani's process of oxidising aldoses to aldonic acids. The product was an acid oil, soluble in ether, but dissolving completely in water only on heating. Analysis of the substance dried at 100° in a vacuum showed it to be tetramethyl gluconolactone. This conclusion was confirmed by the analysis of a barium salt prepared from it, also by its behaviour on neutralisation, and by the gradual diminution in specific rotation shown by its aqueous alcoholic solution.

Tetramethyl glucose was obtained, as stated, by hydrolysing tetramethyl α -methylglucoside. With the idea of ascertaining whether the methyl group lost in hydrolysis could be re-introduced by our method of alkylation, and, if so, whether this would result in the reproduction of the initial compound or an isomeride, the crystalline tetramethyl glucose was dissolved in methyl iodide and treated with silver oxide.

The product was a neutral oil distilling without decomposition at 124—127° under 8 mm. pressure, which, after 3 months, deposited crystals melting at 42—43°. Analysis of the crystalline substance showed it to be a pentamethylated glucose; it reduced ammoniacal

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