

the alcoholic solution of which deposits a precipitate rapidly at 0°. Heating, therefore, whether by causing a rearrangement or an alteration in colloidal properties, destroys some of the differences between types I and II.

To explain the existing phenomena it will be necessary to obtain a more definite understanding of the mechanism of the reaction and side reactions which take place when the nitro group is reduced and the processes which may occur when the by-products undergo the subsequent reactions. This work is well under way at the present time.

### Summary

Certain chemical and biological differences between high sulfur, highly toxic arsphenamine obtained from the nitro acid and arsphenamine prepared by the reduction of mixtures of the amino acid and its 5-sulfonic acid have been pointed out. Two suggestions have been made regarding the cause of these differences and work has been started to study the mechanism by which the sulfur compounds are formed as a result of hydrosulfite reduction of the nitric acid.

I wish to thank Dr. Reid Hunt for determining the toxicity of the specimens employed in this work.

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[CONTRIBUTION FROM THE LABORATORY OF PLANT CHEMISTRY OF THE DEPARTMENT OF BOTANY, UNIVERSITY OF MICHIGAN]

## THE CATALYTIC HYDROGENATION OF DEXTRO GLUCOSE. PRELIMINARY NOTICE

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In view of all the recent work in the field of catalytic hydrogenation, it is remarkable that there are no accounts in the literature of the catalytic reduction of the sugars to the sugar-alcohols. It would be surmised that in such a reactive molecule as a straight chain hydroxy-aldehyde or hydroxy-ketone, the aldehyde or ketone group would readily lend itself to reduction by hydrogen in the presence of a catalyst.

The behavior of the sugars in neutral and acid solutions is such as to lead to the conclusion that they are not, for the most part, in a straight chain form, but that they exist in a  $\gamma$ -oxide ring form, in which the molecule does not contain an active aldehyde or ketone group. It is usually considered that the two forms are in equilibrium, and that the equilibrium point is far over to the  $\gamma$ -oxide ring side.

In alkaline solution, on the other hand, it seems as though there is quite an appreciable amount of the straight-chain forms present, either, in the case of the aldoses, as the aldehyde hydrate or, what is more likely, as the aldehyde itself in equilibrium with the aldehyde hydrate, together

with a number of enolic forms. This supposition is especially confirmed by the fact that in alkaline solution the simple sugars are known to change over into some of the isomeric forms. *d*-Glucose, for example, is partially converted in alkaline solution into *d*-mannose and *d*-fructose, and it is possible to conceive of the formation of many other sugars as well, in the same solution. The change is supposed to take place through the breaking of the ring with the intermediate formation of the aldehydrol and the enolic forms. In the formation of the first enol from the aldehydrol by loss of water, the  $\alpha$ -carbon atom loses its asymmetry and, conversely, when this enol adds water again, the  $\alpha$ -carbon atom becomes asymmetric, with the consequent formation of two stereo-isomeric aldehydrols, one a derivative of *d*-mannose and the other a derivative of *d*-glucose. These aldehydrols on loss of water are converted into the respective sugars.

The interconvertibility of the sugars in alkaline solution shows that in such solutions there exists an appreciable amount of straight-chain forms, and one would therefore expect the greatest success in catalytic reduction to be not in neutral or acid solutions, but in alkaline.

Should this supposition prove correct, *d*-glucose should yield on reduction the corresponding sugar alcohol *d*-sorbitol. Furthermore, other stereo-isomeric alcohols might be produced because of the transformation of glucose into its isomers. If in alkaline solution *d*-mannose and *d*-fructose are formed from the *d*-glucose aldehydrol, we should expect to find *d*-mannitol also as a reduction product, in addition to *d*-sorbitol. The determining factor for the proportion of *d*-mannitol in the alcohols resulting from the reduction of *d*-glucose would probably be the rate of hydrogenation. If the reduction were carried on fast enough to use up all the aldehyde as fast as formed from the ring form, then we should expect to find only *d*-sorbitol as a reduction product of *d*-glucose, even in alkaline solution. Of course, if it were possible to carry out this reduction in neutral or acid solution, *d*-sorbitol would then be the only product regardless of the rate of hydrogenation.

There is a further possibility of the mechanism of the reduction of the simple sugars in alkaline solution that must be considered. The various enolic forms present in such solutions all contain a double bond between two carbon atoms, to each of which a hydroxyl group is attached. It is possible to conceive that the reduction occurs at this point by the addition of two atoms of hydrogen. In this event we should always expect to find more than one alcohol as the reduction product of any sugar, since either one or two carbon atoms are rendered asymmetric, depending upon the particular enol in question.

### Experimental Part

In order to test these points, 200 cc. of a 25% solution of *d*-glucose in 0.5 *N* potassium hydroxide solution was treated with hydrogen in the presence of about 3 g. of platinum

black. The hydrogen was introduced rapidly enough to keep the liquid in considerable agitation and the platinum thoroughly stirred. After 18 hours the solution had lost all of its reducing action on Fehling's solution. When the platinum had settled, the clear colorless liquid was siphoned off, and from it *d*-sorbitol and *d*-mannitol were obtained, using the procedure outlined by Fischer<sup>1</sup> in separating the products of reduction of *d*-fructose by sodium amalgam. The solution was first neutralized with dil. sulfuric acid and then concentrated on a water-bath until most of the potassium sulfate separated from the solution. To this was added 8 times the volume of boiling absolute alcohol, and the precipitated potassium sulfate removed by filtration. After concentrating a little the solution was cooled, whereupon the mannitol separated in the form of fine needle-like crystals, which after purification by recrystallization from 70% alcohol melted at 166°.

The combined filtrates from the recrystallization of the mannitol, and from the original mannitol precipitation, were concentrated on a water-bath, with the addition of water from time to time, until the alcohol was removed, and finally evaporated to a volume of about 50 cc. From this solution the sorbitol was recovered according to the directions of Meunier.<sup>2</sup> After cooling to 0°, an equal volume of 60% sulfuric acid was added, and then the acid solution was shaken with 35 cc. of benzaldehyde. On standing overnight at 0°, there separated a large quantity of the white amorphous dibenzal derivative of sorbitol. This was filtered, washed with a little water and ether, and then hydrolyzed with boiling 5% sulfuric acid. After cooling the liberated benzaldehyde was shaken out with ether, and the sulfuric acid just neutralized with a solution of barium hydroxide. The resulting solution was filtered and concentrated to a thick sirup, to which was added on cooling a little 95% alcohol. The sirup soon solidified and was dried by pressing between filter paper. This was now dissolved in a little hot 90% alcohol and, on standing, the solution soon deposited the sorbitol in the form of colorless clusters. These were filtered, washed with a little alcohol and finally dried in a vacuum desiccator over conc. sulfuric acid. The sorbitol so obtained melted at 73-75°.

Work is now being conducted in this laboratory on the catalytic hydrogenation of the several sugars, under the influence of various catalysts and various conditions of acidity and alkalinity, temperature and pressure. It is expected to show what alcohols result from the sugars under these varying conditions and in what proportions they are formed.

Up to the present, all attempts to reduce *d*-glucose in neutral solution have proved futile. However, if the hydrogenation is conducted under pressure or in the presence of more active catalysts, it may prove possible to do this.

The platinum black used as the catalyst was prepared by a slight modification of the method of Willstätter and Waldschmidt-Leitz,<sup>3</sup> in which dry potassium chloroplatinate suspended in a 20% formaldehyde was reduced, instead of starting with an acid solution of chloroplatinic acid.

## Summary

Preliminary notice of the catalytic hydrogenation of the sugars is given.

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<sup>1</sup> Fischer, *Ber.*, **23**, 3684 (1890).

<sup>2</sup> Meunier, *Compt. rend.*, **110**, 579 (1890). *Ann. chim. phys.*, [6] **22**, 412 (1891).

<sup>3</sup> Willstätter and Waldschmidt-Leitz, *Ber.*, **54**, 113 (1921).