

# The Mechanism of Nylander's Test for Glucose in Urine

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**Abstract** The Nylander's test for glucose detection in urine is based on the reduction of bismuth subnitrate to elemental bismuth in alkaline medium and in the presence a Seignette's salt. However the reaction route and the mechanisms have not been advanced. In this communication both of them are provided, each step being fully commented. Since Nylander's assay is a top test not surpassed in sensitivity by other method it is interesting know the series of steps from the reagents to the final elemental bismuth separation that occurs via a one electron transfer in a bimolecular reaction. That is, through the bismuth tartrate complex and several organometallic intermediates. This Theoretical Organic Chemistry Study is important since glucose is an analyte.

**Keywords** Bismuth subnitrate, Glucose, Potassium sodium tartrate, Reaction mechanism, Reactive intermediates, Redox reactions

## 1. Introduction

The Nylander's test is an optimum assay for glucose detection in urine not overtaken by any other method.

The test is based on the reduction of bismuth subnitrate by glucose in alkaline medium in the presence of Rochelle salt. The reaction route has not been provided, and less the mechanism. In this communication we supply both of them in accordance with the experimental procedure since the addition order of the reagents is of utmost importance.

This paper is a follow up of our studies on reaction mechanism [1-5].

## 2. Antecedents

The test under study is due to Emil Nylander. He published his test in an analytical journal [6] and in a journal of physiological chemistry [7]. His test was recorded in Germany [8,9] and in the United States [10].

The test is as follows: Dissolve 4 g of sodium tartrate in 100 ml of a 10% NaOH solution. Then add 2 g of bismuth subnitrate. Heat the mixture to 50°C and filter after cooling. Preserving the reagent, even for months, leaves it unaltered. Boil 10 ml of urine with 1 ml of the reagent for 2 min. When sugar is present there is a brown to black colouration of the fluid where metallic bismuth settles down. If the dark colouration occurs as the fluid is cooling down, it does not prove the presence of sugar. The reaction takes place when the proportion of sugar in the urine is 0.1%. If the test is

negative there is no need to do any further test, [11]. Potassium sodium tartrate (Rochelle salt) is also used [12].

Bismuth is a post transition metal having 83 electrons in six shells, [13]. The electron configuration of ground state gaseous neutral bismuth is: [Xe] 4f<sup>14</sup> 5d<sup>10</sup> 6s<sup>2</sup> 6p<sup>3</sup>, [14]. Thus bismuth is trivalent.

## 3. Discussion

The activation of the glucose molecule takes place in alkaline medium since this aldose is a carbon acid and forms a reactive enolate in basic conditions. On the other hand the reagent, bismuth subnitrate, forms insoluble bismuth hydroxide with sodium or potassium hydroxide, [15, 16]. In order to avoid this reaction and maintain bismuth in solution even in basic medium it must be taken as tartrate complex.

The nitrate and one hydroxyl group in bismuth subnitrate are displaced by carboxylate and the vicinal alkoxide in tartrate anion. Besides the 5 member heterocyclic ring there remains a carboxylate for solubility, Figure 1.

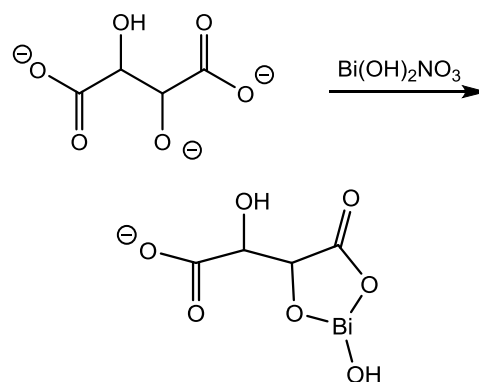


Figure 1. Formation of bismuth tartrate complex

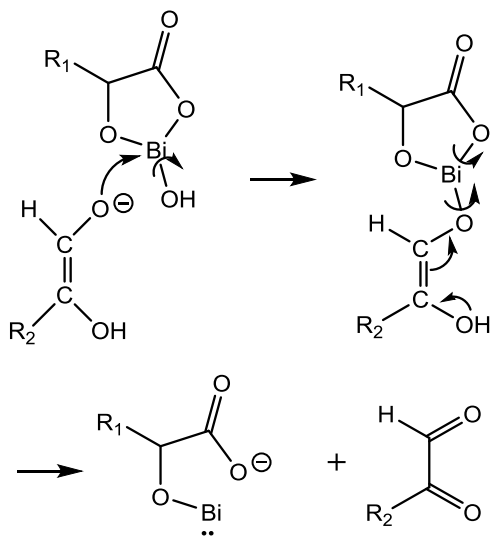
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Received: Nov. 1, 2022; Accepted: Nov. 19, 2022; Published: Dec. 28, 2022

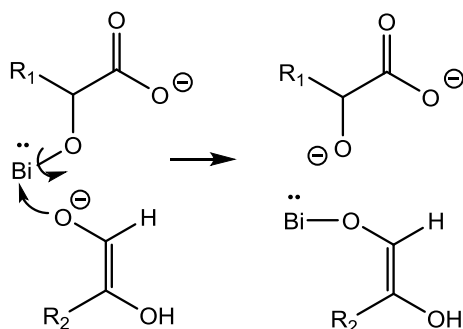
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Glucose enolate displaces the hydroxyl group linked to bismuth giving an organometallic ester. The electrophilic enolate in the glucose moiety originates a 6 member concerted mechanism. Keto-glucose (D-glucosone) is formed and bismuth is reduced to Bi(I) which can be coordinated by negative oxygen atom, Figure 2.



**Figure 2.** First redox reaction to Bi-I complex and keto glucose

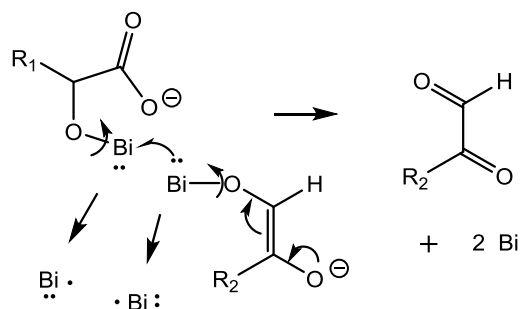
A second glucose unit as enolate reacts with the Bi(I) atom and the tartrate anion is regenerated. Reaction of the enolate in this mixed ester would yield negative charged bismuth (monomolecular step), Figure 3.



**Figure 3.** Formation of one key intermediate

However, a bimolecular reaction involving a second complexed Bi(I) affords two atoms of elemental bismuth via a one electron transfer from the transient electron-rich bismuth atom formed by the enolate, to the Bi(I) in the tartrate complex, Figure 4.

As it can be seen three glucose molecules and two tartrate complexes give two Bi atoms and three molecules of keto-glucose (redox reactions). The latter compound gives gluconic acid via alkaline isomerization (internal Cannizzaro reaction). This can occur through the aldehyde hydrate or directly by reaction with sodium hydroxide forming the alkoxide of the hydrate. Carboxyl formation produces hydride migration to the vicinal carbonyl group and the resulting alkoxide is neutralized by water.



**Figure 4.** Bimolecular reaction via one-electron transfer between two key intermediates

This way the chemistry and the mechanism of Nylander's test for glucose in urine have been cleared out.

## 4. Conclusions

In Nylander's test for glucose bismuth subnitrate in the presence of Rochelle salt is reduced by glucose in alkaline medium to elemental bismuth. This brief experimental account of a top test deserves the study of what is happening in the test tube.

Bismuth must be as tartrate complex in order to avoid formation of insoluble hydroxide in alkaline medium. The latter is necessary to activate the glucose molecule. Several organometallic intermediates are formed. Finally a bimolecular reaction between two different bismuth-I intermediates produces two atoms of elemental bismuth via a one-electron transfer.

Glucose is oxidized to keto-glucose (D-glucosone) and isomerized to gluconic acid by an internal Cannizzaro reaction. Three molecules of glucose and two molecules of bismuth tartrate complex produce two atoms of elemental bismuth and three molecules of keto-glucose.

The present Theoretical Organic Chemistry Study has cleared out completely the reaction route and the mechanism of Nylander's test for glucose in urine.

## ACKNOWLEDGEMENTS

Thanks are given to Martha Berros for support.

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