Reactivities Involved in the Seliwanoff Reaction

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Abstract: The Seliwanoff Reaction, a well-known colour reaction for ketoses, is based in the fact that ketoses are dehydrated more rapidly than aldoses to give a furfural derivative. Further condensation with resorcinol in dilute hydrochloric acid gives the colour product. But a problem has remained unsolved for many years: why the ketoses are dehydrated faster than aldoses? Based on recent experimental results, as well as in ab initio methodology on the chemistry of aldoses and ketoses, we studied the reactivities involved in dehydrations and isomerizations of these compounds and propose an explanation of why ketose require less reaction time in the Seliwanoff Test.

Keywords: Aldoses, Especial Reactivities, Ketoses, Reaction Mechanisms, Reactive Intermediates

1. Introduction

Fructose is an important and interesting ketose. It is well-tolerated by diabetics [1]. Unlike glucose, fructose does not stimulate a substantial insulin release. Fructose glycemic index is only 19, compared to 100 for glucose or 65 for table sugar [2].

Fructosuria is a rare disorder from liver malfunction. Fructose in urine can be detected by the Seliwanoff’s Test [3, 4].

Continuing our studies on fructose [5-7], we have turned our attention to the Seliwanoff’s Reaction. It is a colour test for ketose identification, giving a cherry-red or Burgundy-red colour with resorcinol in dilute HCl.

This test showed that fructose reacts faster than glucose in order to give a positive result: patent with fructose and slightly pink with glucose. When the test was extended to ketoses and aldoses the same chemical deportment was observed.

This indicates that ketoses are dehydrated more rapidly than aldoses to give a furan derivative that finally reacts with the reagent producing the observed colouration.

However, a question has remained unanswered until now: why ketoses react faster than aldoses in the same reaction conditions?

In order to clear-up this interesting academic theme we reviewed the recent advances in Carbohydrate Chemistry related with the monosaccharides, especially dehydrations and isomerizations. Experimental results as well as ab initio theoretical studies were examined. So, on the basis of the new information we propose a theoretical explanation on the subject.

2. The Seliwanoff Reaction

The Seliwanoff colour reaction for fructose is due to the Russian chemist Feodor Feodorovich Seliwanov (Russian transliteration), and known as Theodor Seliwanoff (German phonetics) [8]. A memorial article is available [9].

The test, 0.1% resorcinol in 4M HCl, has been extended to ketohexoses which also give the deep cherry-red colour. Ketopentoses can also been identified since they provide bluish-green solutions [10].

The reaction consists in the triple dehydration of the monosaccharide to 5-hydroxymethylfurfural (ketohexoses) or to furfural (ketopentoses). Finally, the furan derivative reacts with resorcinol to give the coloured condensation product. Figure 1.
Several structures have been proposed for the red compound. The most simple has been given in Ukraine, a two ring semiquinone structure [11]. Figure 2a.

Other structure involves two resorcinol molecules, affording a three ring derivative [12]. Figure 2b.

An interesting work with a cognate reagent, 4-ethyl-resorcinol, permitted isolate the reaction product. The structure assigned is of xanthene type [13]. Figure 2c is for the classical reaction [14].

In the ketohexoses the bathochromic shift (red shift) is due to the 5-hydroxymethyl group present in the furan derivative.

A method has been described for the colorimetric determination of fructose in fermentation media by the use of Seliwanoff’s colour reaction [15].

In a related reaction for fructose identification, fructose in glacial acetic acid is treated with phenol in the same solvent containing sulphuric acid. A green colour is developed after heating in a boiling water bath. The test is also positive for those substances yielding fructose on hydrolysis [16].

A very different chemical deportment is observed in the condensation of resorcinol with other aldehydes yielding resorcinarenes, macrocycles formed from four units of each reactant [17].

3. The Involved Mechanisms

Looking for an explanation why the ketohexoses are dehydrated more readily than the aldohexoses, molecular level understanding of acid-catalyzed conversion of sugar molecules into hydroxymethylfurfural (HMF) and furfural is essential.

Several reaction mechanisms have been proposed through the years. In the obtention of furfural the reaction was believed to start from the open structure of the pentoses. Paquette [18] dehydrates an aldopentose to the α-keto-aldehyde via the enol. A second dehydration affords an α, β-unsaturated ketone.
Finally, acid catalyzed cyclization and dehydration gives furfural. Figure 4.

This point of view had been mentioned earlier [19], though not cited, and it is faulty. First, it is improbable since the percentage of open chain structure is very low. The mechanism is faulty since there is no hydroxide evolution to the proton, but hydroxyl protonation affording the oxonium ion, followed by water elimination. Besides the proposed double bond would yield a trans-product which is not prone to cyclization. These errors are still online from industrial sources, not academic [20].

A better alternative would be cyclization before any double bond, then hemiketal dehydration to the dihydrofuran ring and finally dehydration to 2-furaldehyde. This way the resulting double bonds are Z. Figure 5. However, this sequence is also based in the open chain structure.

Recently, the formation of furfural from a pentose is considered to take place starting from the pyranose form of the pentose, by protonation at O-2 of the pyranose ring. Water elimination is followed by ring contraction, then neutralization of the resulting carbocation yields an enol that isomerizes to the aldehyde. This tetrahydrofuran derivative is a 2, 5-anhydride, the pair of locants identifying the two hydroxy groups involved in the formation of the intramolecular ether. A second dehydration gives the α, β-unsaturated compound and the third water loss affords furfural [21]. An example with xylose is in Figure 6.

Since glucose reacts much slower than fructose as observed in the Seliwanoff’s Test, we thought that this delay could be attributed to a previous isomerization of glucose to fructose. Thus, we looked for the current trends on this isomerization. We found that there is evidence for a C-2 to C-1 intramolecular hydrogen-transfer during the acid-catalized isomerization of D-glucose to D-fructose [22]. The reaction from β-D-glucopyranose to α-D-fructofuranose is depicted in Figure 7, from a novel method of direct degradation of cellulose in to 5-hydroxymethylfurfural with sodium or potassium salts of acidic salts (sulphates and phosphates), a green HMF production [23].

Other isomerization of glucose to fructose by means of Lewis acid involves the same hydride transfer from C-2 to C-1 [24].

The dehydration of fructose to 5-hydroxymethylfurfural occurs through the fructofuranose form. This can be originated either by glucose isomerization to fructose or more directly from the fructopyranose form. Dehydration starts at
the hemiketal, and the intermediate enol rearranges to the aldehyde. The second dehydration gives the α, β-unsaturated derivative. A third water loss affords hydroxymethylfurural [25], Figure 8.

![Figure 8. Dehydration steps from fructose to HMF.](image)

The route of glucose to 5-hydroxymethylfurural has been studied recently using high-level *ab initio* methods (G4MP2 along with SMD solvation model), [26]. The reaction mechanism confirms the previous one described for pentoses to furfural, such as xylose [21], i.e., protonation at O-2, water elimination, ring contraction, neutralization, deprotonation, and two more dehydrations.

*Other ab initio* study using density functional and two-layer ONIOM calculations found that no dehydration pathway of open-chain glucose is favoured over its isomerization to β-glucopyranose or to fructose. The chair conformers are given in the ring contraction mechanism to 5-hydroxymethylfurural [27], Figure 9.

![Figure 9. Oxygen-assisted ring-contraction.](image)

4. Conclusion

Since 5-hydroxymethylfurural is the key intermediate that reacts with resorcinol to give the coloured xanthenoïd, and the fact that ketoses react faster than the aldoses in the Seliwanoff Test, prompted us to direct our attention to the HMF formation in order to clear-up the theoretical core that permits an explanation of the reaction rates involved in the formation of the key intermediate.

We reviewed the actual information regarding the formation of furfural and hydroxymethylfurural from aldopentoses, aldohexoses and ketohexoses. The isomerization of glucose to fructose was also revised. All this has been detailed in the previous section.

If we look at the reactivities involved from fructose to hydroxymethylfurural we observe that dehydration is initiated by protonation of the more reactive OH, the anomeric, which can be stabilized by resonance, previously to vicinal deprotonation. Then a tautomerism occurs and two simple dehydrations of a tetrahydrofuran derivative yield hydroxymethylfurural. The first dehydration can be visualized as an α, β-conjugation but also, prior to tautomerism, as a very rapid dehydration of the allylic OH, supported by the enolic electron donation.

On the contrary, in glucose to 5-hydroxymethylfurural, the starting protonation does not occur at the most basic OH but at O-2. Then a cationic rearrangement contraction provides the five-member ring intermediate. Two further dehydrations afford HMF. In this route we observe two not common reactivities, the starting point and the ring contraction.

The isomerization of glucose to fructose, another route to HMF, also presents an uncommon reactivity, a hydride shift. Besides, the total course implies more steps to HMF and obviously more reaction time.

— Thus, in the Seliwanoff’s Test ketoses react via a diverse reaction mechanism than aldoses, being significative differences at molecular level.

— Fructose presents common reactivities in the synthesis of hydroxymethylfurural, this not being the case with glucose or glucose isomerization to fructose. This explains the different reaction times observed in the test and it’s utility for ketose identification. Slower reactions resulted in accord with less common reaction steps, i.e., with especial reactivities.

— The theory of the Seliwanoff’s Reaction has been cleared-up. This is important because generally aldehydes react faster than ketones but now we are not dealing with isolated functional groups but with polyfunctional molecules with mixed groups.

References


