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(RESEARCH ARTICLE)

On the mechanism of the interaction of uric acid with Fehling reagent

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Abstract

That uric acid gives a positive test with Fehling's reagent for aliphatic aldehydes is unexpected. In this communication we give the mechanism of the interaction of uric acid with Fehling' reagent. There is an electron transfer from the imidate at N-1 to a cupric ion, and the remaining free radical couples with an electron from the double bond. A five-member ring is formed in companion with an aziridinone. Alkaline hydrolysis gives a carboxylate and the remaining free radical is captured by a cupric ion, forming a carbonium ion which is neutralised by water. Basic hydrolysis of the pseudo hemiaminal gives a ureido chain at C-5 and a carbonyl group at C-4, which enhances decarboxylation. This way, the final product, 5-ureido-2,4-dioxo-imidazolidine, is formed.

Keywords: Acetilenediurea; Aziridinone; Electron transfer; Fehling's reagent; Free radical coupling; 5-Ureido-2,4-dioxo-imidazolidine

1. Introduction

The oxidation of uric acid has been achieved with different oxidizers, and in acid or in alkaline medium. Although the oxidation product is generally known, that is not the case with the reaction route, and less with the mechanisms involved in the whole process.

In this communication we provide the reaction route and give the mechanism for each step occurring during the interaction of uric acid with Fehling's reagent. Although this reagent is well known for identification of aliphatic aldehydes and reducing carbohydrates, the reaction with a very different substrate such as uric acid is a novelty.

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

2. Antecedents

The reaction under study was discovered by Babo, [6]. White cupric urate is formed first, which on heating gives red cuprous oxide.

Fehling's reagent comprises two solutions. I: 25 g of CuSO4-5 H2O are dissolved in 500 ml of water. Solution II: 175 g of sodium potassium tartrate (Rochelle salt) and 50 g of NaOH are dissolved in 500 ml of water. Equal volumes of solutions are mixed shortly before use, [7]. More concentrated solutions are also described, [8].

The mixed solutions give a complex that maintain copper in alkaline solution not precipitating the hydroxide. Cupric ion can have two ligands [9, 10] or four ligands [11], as in the case of tetraaminocupric sulphate, [12]. Figure 1.

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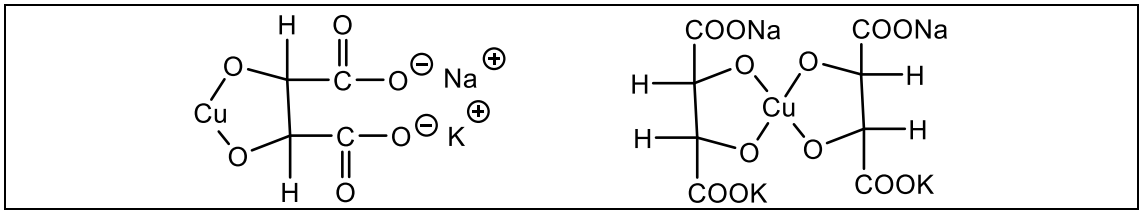

Figure 1 Cupric tartrate complexes

3. Discussion

The hydrogen atom in the imido group present in the uric acid molecule, is acidic. Thus, the imidate is formed in alkaline medium. This negatively charged nitrogen atom can transfer an electron to a cupric ion (redox step), forming unstable cuprous hydroxide. Two molecules of the latter afford red cuprous oxide after rapid dehydration. Figure 2.

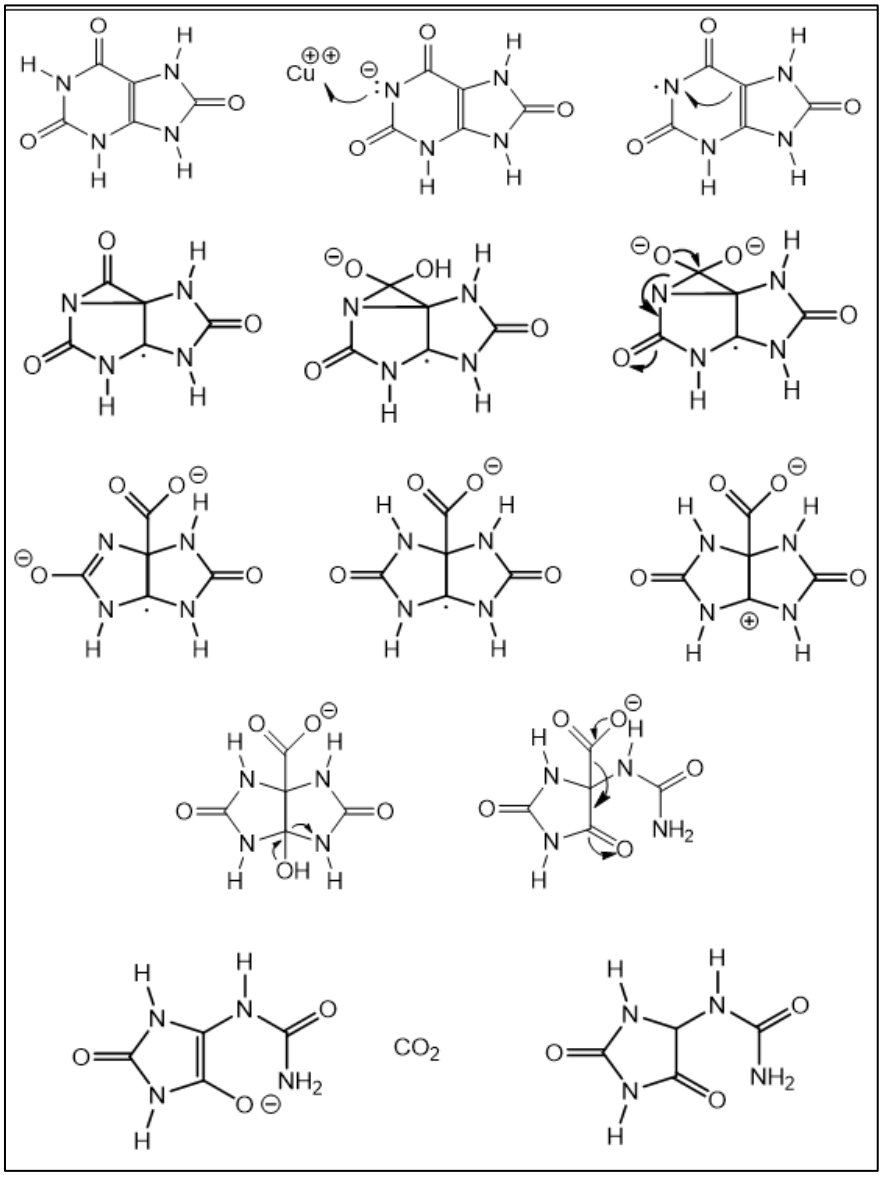

Figure 2 Oxidation and transformation of uric acid by cupric tartrate complex

The remaining free radical on nitrogen couples with an electron from the double bond forming a five-member ring and an aziridinone. This α-lactam presents high ring strain and unique reactivity. Basic hydrolysis of this lactam occurs via dianion [13] since via monoanion the loss of the hydroxyl is the thermodynamical preferred route and there is no

hydrolysis, [14]. A symmetric intermediate with a carboxylate and a free radical, both in interanular positions, is obtained. Electron transfer to a cupric ion left a carbonium ion which is neutralised by water. A carboxy-hydroxy-acetilene-diurea results. Ring opening of the pseudo hemiaminal lefts a carbonyl at C-4, β-to the carboxylate, enhancing decarboxylation to 5-ureido-2,4-dioxo-imidazolidine (5-ureido hydantoin, allantoin). This route is in accordance with the observation that uric acid oxidations in alkaline medium yield allantoin, [15, 16] This compound is also produced in the oxidation of uric acid with alkaline hydrogen peroxide, [17].

The structure of sodium urate at C-2 with cross conjugation has been proposed [18] as well at C-8, from the 7-8 lactim (in gout crystals), [19]. It is interesting to note that in this case the salt has the structure of the imidazole ring. That the lactimic hydrogens at 2 and 8 positions are ionizable was commented earlier, [20].

4. Conclusion

The chemistry of the interaction of uric acid with Fehling's reagent has been provided. There is salt formation, electron transfer to cupric ion, free radical coupling, basic hydrolysis, electron transfer to cupric ion, hydration of carbonium ion, alkaline rupture of pseudo carbinolamine and decarboxylation to the final product, 5-ureido-hydantoin.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

There is no conflict of interest to declare.

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