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The Chemistry of Hager's Test for Brucine

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Abstract

The purpose of the article is clear up what is happening in the test tube during the Hager's test for brucine, that is, throughout the interaction of brucine with manganese dioxide in acidic medium. The paper is a Theoretical Organic Chemistry Study based on the chemical deportment of reagent and substrate, in accordance with the reaction medium. A series of reactions occur during the test: electrophilic attack to double bond, acidolysis of organometallic intermediates, oxidation of secondary alcohol to ketone, acid catalysed hydration, reaction of enol, epoxide formation, ring opening, selective reaction of diol, and ring cleavage of seven-member ring. A yellowish-red to blood-red colour is observed after filtering residual black manganese dioxide. This is due to halochromism, present in acidic medium, since there are no chromogenic groupings.

1. Introduction

Brucine is an alkaloid found in the *Strychnos nux vomica* tree and in St. Ignatius bean (*Strychnos ignatii*). It is 2,3-dimethoxy strychnine and possesses wide pharmacological activities, such as antitumor, anti-inflammatory, and analgesic. Brucine has also effects on cardiovascular- and nervous systems, [1].

Brucine is a weak alkaline indole alkaloid that crystallises as white needles from acetone-water. Figure 1. In China *Nux-vomica* is used for treatment of dyspepsia, nervous system diseases and chronic rheumatism, [2].

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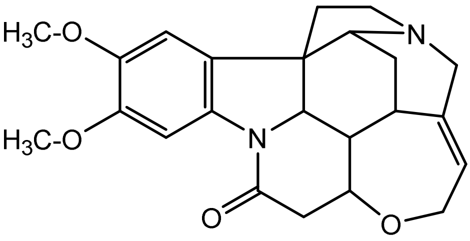

Figure 1. Structure of brucine.

When heated, brucine emits highly toxic fumes of nitrogen oxides. Brucine produces nausea, vomiting, restlessness. Convulsions can be controlled with diazepam or with phenobarbital. The content of brucine is 1% in both seeds, but the bark of S. nux-vomica contains 2.4% of brucine, [3].

Hager devised a test for brucine with peroxide of manganese (manganese dioxide) and sulphuric acid. Manganese dioxide is a black solid that occurs naturally as pyrolusite, and is an oxidant in organic synthesis, [4].

The effectiveness of the reagent depends on the method of preparation, [5]. Usually the reagent is generated in situ by treatment of an aqueous solution of potassium permanganate with a manganese(II) salt, [6]:

$$2\ KMnO_4 + 3\ MnSO_4 + 2\ H_2O \rightarrow 5\ MnO_2 + K_2SO_4 + 2\ H_2SO_4$$

Manganese dioxide oxidises primary alcohols to aldehydes, and secondary alcohols to ketones, [7].

The present communication is a follow up of our studies on reaction mechanism, [8-12].

2. Antecedents

Other test for brucine is due to Flückiger [13-15], he employed a brucine salt and mercurous nitrate. A carmine colour is produced after heating on a water bath. Strychnine, the alkaloids of opium and cinchona, veratrin, caffeine, and piperine are not coloured under the same circumstances.

If a solution of mercury(I) nitrate is boiled, it disproportionate into elemental mercury and mercury(II) nitrate, [16].

The test under study is due to Herman Hager (1816-1897). A yellowish-red to blood-red colour develops on adding dilute sulphuric acid and manganese dioxide to a solution of brucine and let stay some hours at room temperature, with frequent shake, and then filtering, [17]. The test was registered in books of tests [18-20].

3. Discussion

In the Hager's test for brucine, the reactive species is protonated manganese dioxide which reacts with the carbon-carbon double bond (electrophilic attack), Figure 2, a.

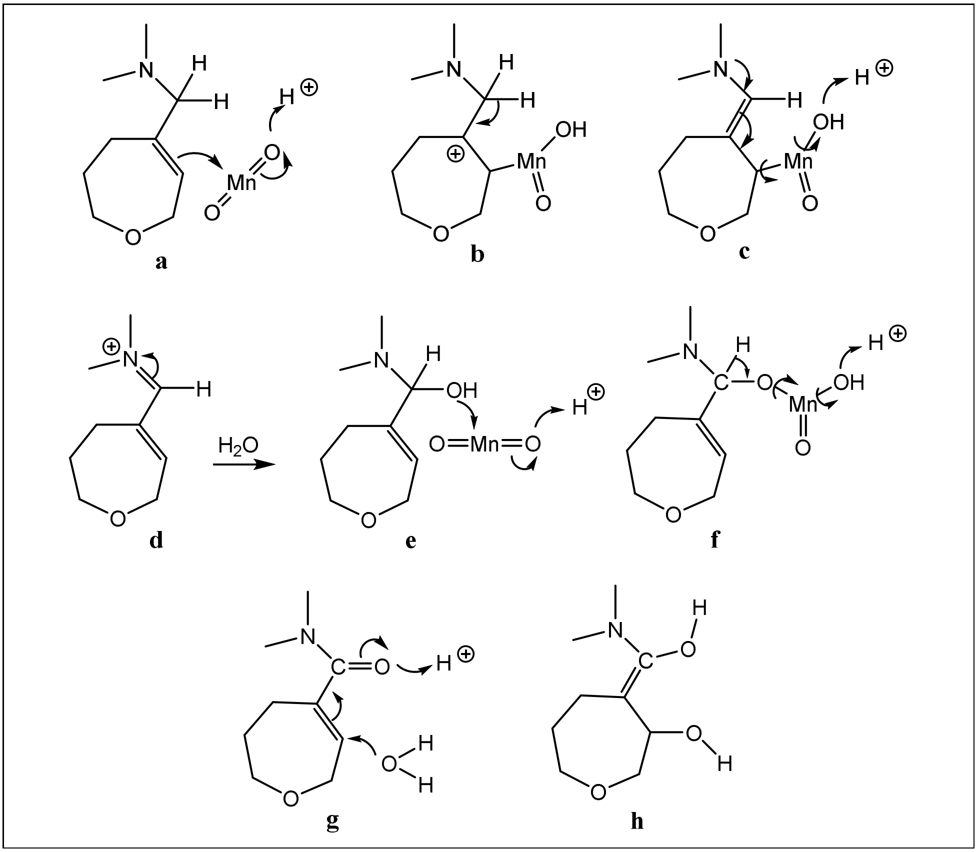

Figure 2. First and second oxidation steps of brucine and hydration.

The tertiary carbonium ion is neutralized by deprotonation, b. The organometallic intermediate breaks down by a concerted mechanism initiated by protonation of the manganese hydroxy group, c. Manganese(II) oxide is formed, the double bond is restored, and an iminium ion results, d. The last ion is neutralized by reaction with water, yielding a hemiaminal, e, which is oxidized to lactam, f, g. The α,β-unsaturated system is hydrated by acid catalysis, h.

The resulting enol reacts with protonated manganese dioxide, Figure 3, h. Protolysis of the intermediate manganite produces a synchronous mechanism with four electron shifts, i, and an epoxide vicinal to the lactam is formed, j. Opening of the oxirane and reaction with water gives rise to a diol, k, l. Reaction of the less hindered alcohol with protonated MnO_2, m, yields an aldehyde and a ketone, n, via opening of the seven-member ring.

The observed colour is due to halochromism, [21, 22].

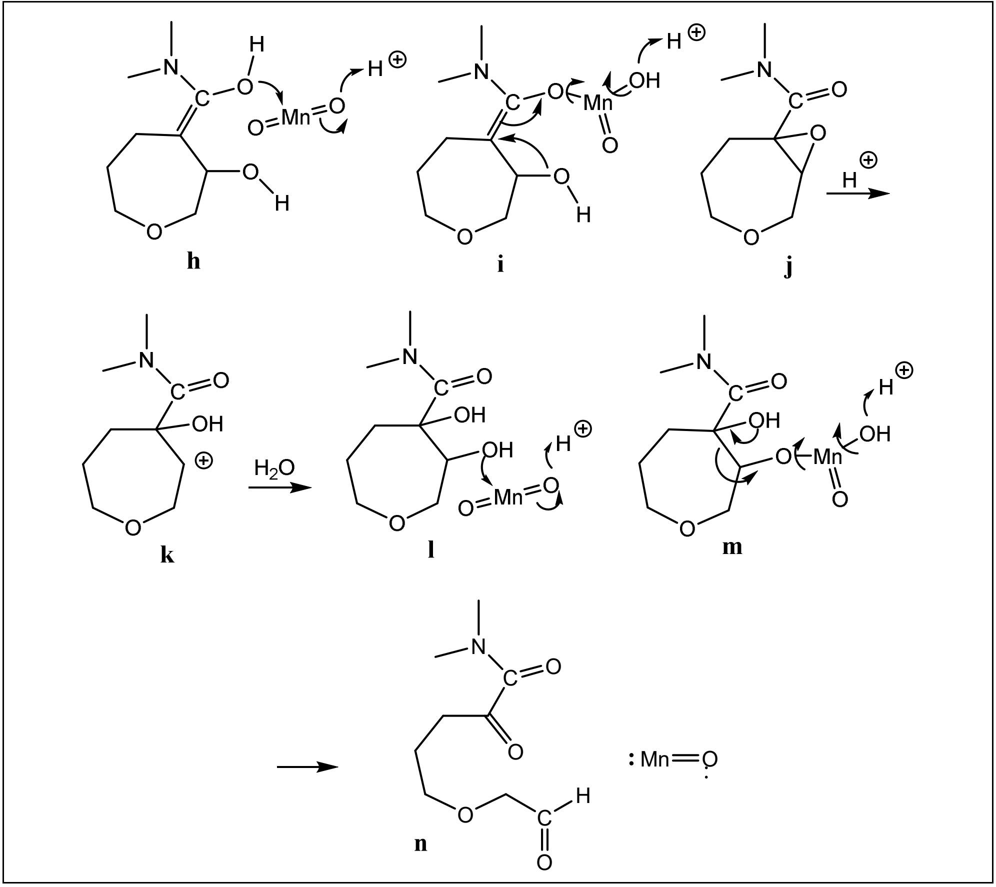

Figure 3. Manganite intermediate, epoxide and diol formation and final oxidation.

4. Conclusion

A carbonium ion can react with a hydroxylated oxidizer, forming an organometallic ester. When an oxide is used instead of an acid, the carbocation is neutralized by water, if present. This is the case with manganese dioxide and it is corroborated experimentally since in the test under study there is plenty of water because diluted sulphuric acid and a brucine solution are employed. Then protonated manganese dioxide can react with the alcohol and form a mixed ester. Acidolysis of this intermediate gives rise to the oxidation product.

Other difference with manganese dioxide is its lesser oxidizing power compared to potassium dichromate, potassium permanganate and other strong oxidants. Manganese dioxide does not oxide aldehydes to carboxylic acid.

The reaction mechanism proposed in the 'Discussion' is in accordance with the above facts and with the chemical deportment of reagent and substrate in acidic medium.

Conflicts of Interest

There are no conflicts to declare.

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