



The chemistry of Mandelin's test for strychnine

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Abstract

Strychnine reacts with Mandelin's reagent giving a violet-blue colouration which changes to orange-red and finally to yellow. The chromic acid test for strychnine was surpassed by Mandelin's assay due to better reagent stability, lower detection limits and fewer false positives. The reagent is ammonium metavanadate in sulphuric acid. In this communication we provide the reaction route and the mechanism of each step, from the alkaloid to the complex final oxidation product. Several oxidations take place and the vanadic acid formed in situ is reduced to vanadous acid. Some information related to vanadium and vanadium compounds is given in order to understand the reactivity of the involved compound.

Keywords: Ammonium metavanadate; Reaction mechanism; Reactive intermediates; Redox reactions; Vanadium electron shells; Electron configuration; Oxidation states

1. Introduction

Strychnine is a basic alkaloid and can be extracted from the seeds of the strychnos plant as an odourless, bitter-tasting white crystalline material. The fatal dose of this poisonous compound is about 30 to 50 mg for strychnine and 1 to 3 grams for strychnos seeds, [1].

Thus the detection of this alkaloid is very important. In this Theoretical Organic Chemistry communication we provide for the first time the route and mechanism of the reactions taking place in the Mandelin's test for strychnine in order to know what is happening in the test tube.

This paper is a follow up of our studies on reaction mechanism, [2-6].

2. Antecedents

Mandelin's reagent is composed of a mixture of ammonium metavanadate and concentrated sulphuric acid. The United States Department of Justice method for producing the reagent is the addition of 100 ml of concentrated sulphuric acid to 0.5–1 g of ammonium metavanadate. The reagent was invented by the German pharmacologist Karl Friedrich Mandelin (1854-1906), [7]. When strychnine is treated with Mandelin's reagent a violet-blue colouration results, which soon changes to an orange-red, and finally to a yellow. This test was proposed in 1883 in several German journals, [8]. The test was registered in Germany [9], and in the United States [10].

Vanadium is a transition metal. It is in the third column, that is, in the 5-B subgroup. Vanadium shows all possible valencies up to five. Their highest oxides are anhydrides of not very strong acids, [11]. Vanadium has atomic number 23. Its electrons are in the K, L, M, N shells: 2, 8, 11, 2. The electron configuration is: 2/2, 6/2, 6, 3/2, [11, 12]. It readily

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exists in four different oxidation states: +5, +4, +3 and +2, corresponding to the d^0 , d^1 , d^2 and d^3 electron configurations, (M shell), [13].

The price of vanadium is 1000 times higher than that for iron, and more than 3 times for silver [14].

Vanadium (+5) compounds are oxidizing agents [15]. When sodium vanadate solution is acidified with sulphuric acid, vanadic acid is precipitated. Sodium vanadate is reduced to vanadyl sulphate, $VOSO_4$, by the action of sulphur dioxide in the presence of sulphuric acid, [16]. The VO^{2+} ion is blue, [14]. Ammonium metavanadate is NH_4VO_3 , [17].

3. Discussion

The strychnine molecule has the following functional groups: a lactam, a cyclic ether, a double bond, and a tertiary amine, Figure 1.

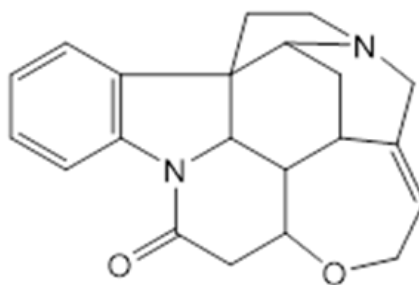


Figure 1 Strychnine structure

The product isolated from potassium permanganate oxidation exhibits a carbonyl group vicinal to the tertiary nitrogen, that is, a new lactam group. There are also a ketone and a carboxylic acid. An uptake of four oxygen atoms and loss of two hydrogen atoms has occurred, [18]. Since vanadium (+5) compounds are oxidants, ammonium metavanadate will accomplish the described oxidations to the final product. In as much as the resulting functional groups are in the higher oxidation state, there will not be further oxidation.

The reaction takes place as follows, Figure 2. There is electrophilic attack to the strychnine double bond by the VO_2^+ ion resulting by dehydration of metavanadic acid formed in situ, a. Insertion of a VO_2 group affords a tertiary carbonium ion, b.

Neutralization by proton elimination yields an enamine with orbital overlap between the electron pair on nitrogen and the π -electrons of the double bond, Cf. [19], c. This explains exocyclic double bond instead of an endocyclic one not linked to the nitrogen atom.

Protonation of the dioxo-vanadium group originates a 6-member concerted mechanism including the electrodotic [20] properties of the enamine group, c. Vanadous acid is formed, the double bond is regenerated and the resulting iminium ion, d, is hydrated to a carbinol amine, e, which is oxidized to carbonyl, f. Vanadic acid is added to the conjugated system (I,4 addition), f. Protonation of the vanadic ester, g, yields vanadous acid, an epoxide and a lactam, h. The oxirane ring is opened by protonation affording an alcohol and a carbocation which is neutralized by vanadic acid, i. Protonation of the vanadic ester produces vanadous acid, opening of the 7-member ring, an aldehyde and a keto group, j. Finally the aldehyde is oxidized to carboxyl, k. As it can be seen, four oxygen atoms have been added to the strychnine molecule, and there is loss of two hydrogen atoms vicinal to the nitrogen atom.

The observed colours come from halochromism [21, 22], and are due to cationic intermediates proper of strychnine.

Since strychnine has been used in many murders, a toxicological test like Mandelin's is very useful in legal chemistry.

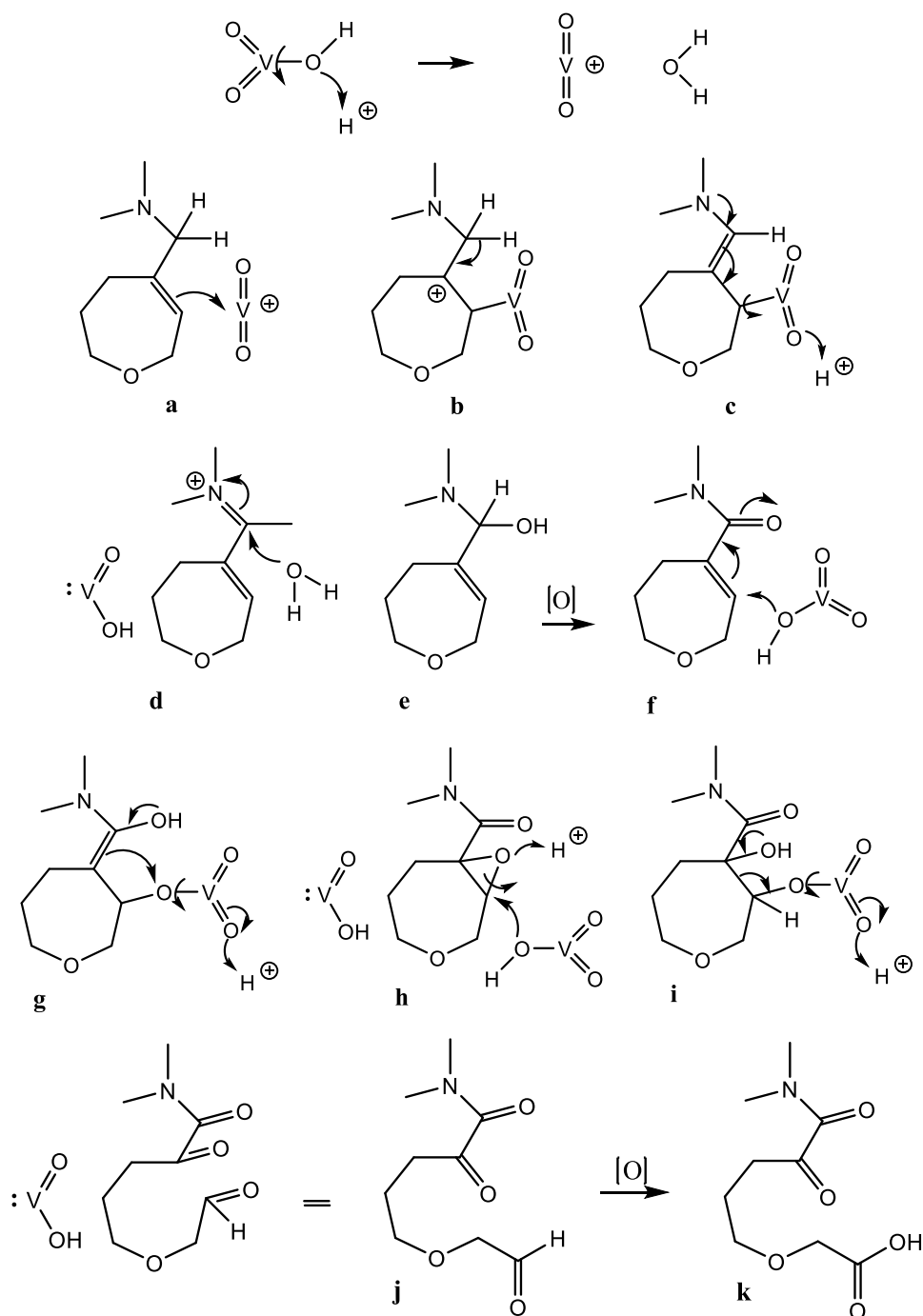


Figure 2 Reaction route from strychnine to the complex final product

4. Conclusion

The mechanism of Mandelin's test for strychnine has been cleared up. It is an ionic mechanism involving VO_2^+ ions and directed by protons due to the presence of sulphuric acid. The vanadic acid formed in situ intervenes as such and also as the dehydrated ion. The organometallic intermediates are oxidized via protonations and concerted mechanisms with concomitant formation of vanadous acid. There are several redox reactions. The observed colours are due to halochromism and are proper of strychnine cationic intermediates.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

There is no conflict of interest among the authors or any other person.

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