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(RESEARCH ARTICLE)

The chemistry of Marchand's test for strychnine identification

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Abstract

The chemistry of a spot test for identification of a substance with biological activity is important. Besides the academic interest of knowing what is going on in the test, the study reveals the chemical deportment of the active compound, and this is related to biochemistry. This result can be used to enhance, or on the contrary, deter the activity of the compound. In this communication we provide the chemistry involved in the spot test for strychnine identification by means of lead dioxide (Marchand's test). The electron flow, step by step, is given from the alkaloid to the complex oxidation product. Thus, this toxicological assay has been up-dated.

Keywords: Allylic oxidation; Lactam formation; 1,4-Addition; Epoxidation; Ring opening; Alcohol and aldehyde oxidation.

1. Introduction

The Marchand's test for strychnine identification gives a colour series after reaction of the alkaloid with 'peroxide of lead' (lead dioxide) in the presence of sulphuric acid containing one percent nitric acid. The reaction is very sensitive and minute quantities of strychnine can be detected.

The reaction is very important since it has been used extensively in legal procedures as a toxicological test. This assay is based in the oxidation of strychnine and gave rise to other tests based on the same principle but using a different oxidizer. This will be commented in the next section.

The course of the reaction has not been described; in this communication we provide the electron flow, from the alkaloid to the complex oxidation product whose structure was elucidated much later.

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

2. Antecedents

The test for strychnine identification using lead dioxide and sulphuric acid with one percent nitric acid is due to Eugene Marchand (1816-1895), [6]. His French communication was reviewed in the United States: 'the new test for strychnine by E. Marchand is so sensible as to give a very appreciable reaction, even when you operate upon an imponderable quantity of sulphate of strychnine. When you triturate a very small portion of strychnine with a few drops of concentrated sulphuric acid containing a hundredth of its weight of nitric acid, the strychnine disappears without giving rise to any perceptible phenomenon, but if you add to the mixture a minute quantity of peroxide of lead, it immediately develops a magnificent blue color, which rapidly passes to violet, then gradually to red, and finishes lastly, after several hours, by turning to canary yellow. This reaction is characteristic for strychnine'. [7].

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This spot test induced other workers to try other oxidizers. Mack's study was reviewed in London: 'I tried whether other readily de-oxidisable substances would also effect the same changes of colour as the peroxide of lead. I mixed some nitrate of strychnine, which was obtained by dissolving pure strychnine in dilute nitric acid, with a little finely powdered manganese peroxide, and then added a few drops of concentrated sulphuric acid to the mixture: at once was observed a deep blue colour, which shortly passed into violet, and finely became a rose red tint; in 24 hours the liquid assumed a yellow colour', [8].

Marchand's response to substitutions and omission of the nitric acid was mentioned in the Chemical Gazette, in London: 'several chemists have examined this reaction, and M. Herzog has proposed to omit the nitric acid as useless; another chemist proposes to substitute peroxide of manganese for peroxide of lead, and M. Otto prefers bichromate of potash to these oxides, which, according to him, gives rise to a much finer violet colour, and to a certain extent this is certainly the case. Marchand proposes objections to all this. The nitric acid is not useless, for by its influence the series of colours is produced much more readily and sensible than when it is omitted. Besides, it is almost impossible to perceive the red and the yellow colours. The manganese salts sometimes possess a red colour, there can be no certainty since one of the reagents employed may itself give rise to one of the colours indicated. The bichromate in sulphuric acid produces a yellow or green colour, so the series of colours is diminished by at least one colour, and sometimes by two, the yellow and the red', [9].

As said previously, Otto used potassium dichromate [10, 11]. The employment of manganese dioxide is known as Allen's test [12, 13]. However, Allen in a note in the Analyst states: 'my method of procedure has no claim to novelty. There is considerable choice in the oxidizing agent employed', [14]. He only preferred the use of manganese dioxide, despite the black colour of the reagent that may obscure the violet colour. The Mack test is 32 years earlier.

The use of potassium permanganate and sulphuric acid is the Wenzell test [15]. Other test for strychnine is due to Mandelin. He used as reagent a solution of sodium vanadate in sulphuric acid [16].

The colour changes in the chromic acid test and with the vanadium reagent have been considered recently as due to changes in the oxidation states of chromium and vanadium [17]. This is a misconception since the colour changes are the same when reagents with other elements are used, such as lead, manganese and iron. These have very different oxidation states, and ions of different colours are produced.

Other example that gives the colours proper of strychnine is the Sonnenschein test [18]. He used the oxide Ce_3O_4. This has been named ceroceric oxide, [19]. That is ($2CeO.CeO_2$), similar to Pb_3O_4.

The observed colours in the tests for strychnine are due to halochromism, proper of a substance in strong acidic medium [20]. The colour changes come from different cations formed as the oxidation reaction proceeds.

We looked for Organic Chemistry information on strychnine oxidation and see if a reaction mechanism had been advanced or not. This point will be treated in the next section.

3. Discussion

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

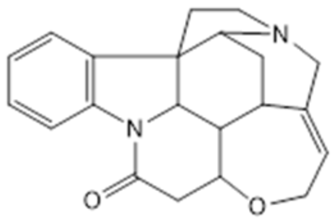

Figure 1 Strychnine structure

The oxidation 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, [21]. We must bear in mind that the Marchand and the Wenzell test ($KMnO4/H2SO4$) gave the same colour sequence, that is, the same reaction.

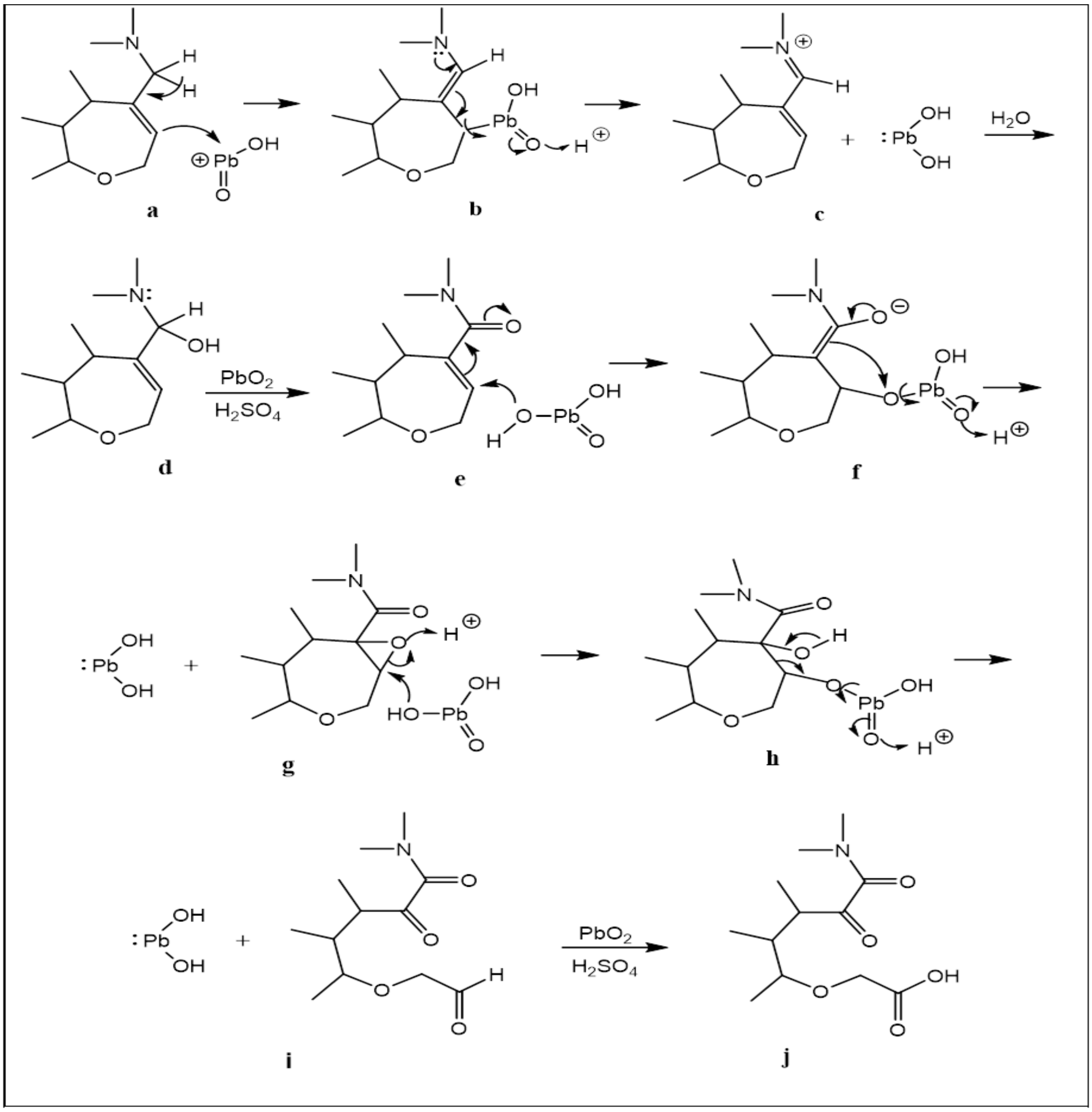

Figure 2 Sequence of strychnine reaction with PbO_2/H_2SO_4.

The initial reactive species is protonated lead dioxide and the first reaction is electrophilic attack to the double bond. Figure 2, **a**. A transient carbonium ion is formed which is neutralized by proton elimination, being enamine formation, **b**.

The organometallic intermediate is broken by protonation at the oxygen which is double bonded to the lead. Lead (II) hydroxide is formed and reaction with sulphuric acid yields lead sulphate and two water molecules.

The initial double bond is regenerated and an iminium ion is formed, **c.** This intermediate is neutralized by reaction with water, affording a carbinolamine, **d.** Oxidation by the reagent gives a new lactam.

Reaction of protonated lead dioxide with water yields hydrated lead dioxide which adds to the conjugated system, **e.** The lactam is reformed by another protolysis, and an epoxide results, **f**, **g.** The inorganic chemistry is repeated as above.

Protonation of the epoxide and ring opening forms a carbocation that reacts with hydrated lead dioxide, **g.** Protolysis breaks down the organometallic intermediate by a concerted reaction mechanism, **h.** An aldehyde and a ketone are formed via opening of the seven member ring, **i**. The last step of this sequence of reactions is oxidation of the aldehyde to carboxylic acid, **j**.

4. Conclusion

The Marchand test for strychnine identification, using lead dioxide and sulphuric acid with one percent nitric acid, inspired half a dozen of other chemists to try other oxidizers for the same purpose. This way many cognate tests are registered under the name of the proposer, such as the test of Mack, Otto, Wenzell, Mandelin, Sonnenschein, Allen, etc.These tests are only variations of the original test by Marchand.

Being strychnine potent venom not difficult to obtain, it has been used in many murders. Thus, this toxicological test for strychnine identification has been very useful in legal chemistry.

In this communication we provide the chemistry involved in this test, giving the theoretical basis of the procedure. This reveals strychnine chemical deportment, as well as role of the oxidizer, giving to toxicology a scientific basis, not only the experimental result of a spot test.

Compliance with ethical standards

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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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