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(RESEARCH ARTICLE)

The chemistry of Husemann's test for morphine

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Abstract

In this article is cleared up what is happening in the test tube during the Husemann's test for morphine. According to different experimental conditions, morphine in sulphuric acid is heated during half an hour, boiled, or heated at 150° during brief time, previously to the addition of an oxidant. The heating of morphine in sulphuric acid produces the transformation of morphine into apomorphine. A blue-violet to red-violet colour results on addition of chlorine water. The sensibility is one eighteenth of milligram. Reaction of chlorine with water forms a complex that reacts with the external hydroxyl group in apomorphine. An unstable organic hypochlorite gives rise to a concerted mechanism and a new hypochlorite is formed in ortho position. Enolization recovers aromatization and the electro-donor properties of the phenol group form an o-quinone via three electron-shifts.

Keywords: Apomorphine; Chlorine water; Reaction mechanism; Reactive intermediates; Rearrangement; Redox reactions

1 Introduction

Opium is extracted from *Papaverum somniferum.* In 1805 the German pharmacist Friedrich Sertuerner isolated from opium the sleeping agent in crystalline form and named it morphine. This psychoactive alkaloid is classified as a depressant.

Morphine is used in medicine as narcotic analgesic in the form of hydrochloride or other salts, being of use in the treatment of pain in cancer and in other severe conditions, [1, 2].

The morphine molecule compresses five rings: phenolic ring, cyclohexane, piperidine, cyclohexenol and dihydrofuran, Figure 1.

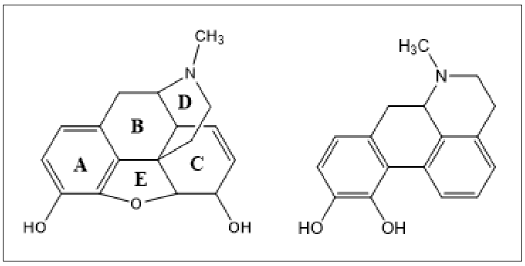

Figure 1 Morphine and apomorphine structures

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Morphine is readily oxidized and this property is responsible of the several colour reactions for its identification, [3].

In this communication we provide the reactions that take place during the interaction of morphine with chlorine water in acidic medium (Husemann test).

This paper is a follow up of our studies on reaction mechanism, [4-8].

2 Antecedents

In the Wellcome test for morphine a red colour is produced when chlorinated lime is added to a solution of morphine, [9]. A related test is due to August Husemann (1833-1877). He employed a previously heated morphine solution in concentrated sulphuric acid to which chlorine water is added after cooling. A blue colour changing to red-violet is obtained. However, the reaction mechanism of these two apparently similar oxidations is entirely different. Moreover, in the Husemann test reaction goes via previously formed apomorphine and then occur the oxidation steps, as it will be seen forwards.

In the Wellcome test, the phenol group reacts with the hypochlorite anion via a 4+2 sigma complex (electrostatic arrangement) and an α chloro-ketone is formed. Subsequent enolization gives o-chlorophenol.

A second halogenation in the ipso carbon atom followed by reaction with a hydroxide ion gives rise to a gem-halohydrin and the to an o-quinone, [10].

The change of reaction medium to acid provokes an entirely different reaction mechanism as it is discussed in the next section.

3 Discussion

In the Huseman's test, morphine is heated for half an hour with sulphuric acid [11], boiled [12], or heated at 150° for a few moments [13, 14], not just warmed [15]. After cooling, and addition of chlorine water, sodium hypochlorite or potassium chlorate, a blue to violet-red colour appears.

In the first step, heating with sulphuric acid, occurs the transformation of morphine to apomorphine, [16, 17]. The mechanism of the morphine-apomorphine rearrangement has been cleared recently, [18].

Chlorine reacts with water yielding hydrochloric acid and hypochlorous acid via a cationic complex, [19, 20]. This reactive species reacts with the less hindered, external phenolic group in apomorphine and an organic hypochlorite is formed, with concomitant water loosening, Figure 2.

The chlorine atom in the intermediate hypochlorite is labile, separation as chloride ion (inductive effect) produces ketone formation (first oxidation step) and Umpolung at ortho-position which favours reaction with hypochlorous acid (nucleophilic addition).

Aromatization is recovered via enolization, this step cannot occur if there is reaction at the other phenol group. The electrodotic properties [21] of the phenol group gives rise to an ortho quinone and hydrochloric acid, via a concerted mechanism involving three electron-shifts, with elimination of a chloride ion from the new organic hypochlorite (second oxidation step).

The redox reactions that occur during the test have been explained. Ortho-quinones are red [22]. Quinones of all types form vividly coloured oxonium salts in concentrated sulphuric acid, [23]. Thus, the blue and red-violet colours observed in the test are due to halochromism, [24].

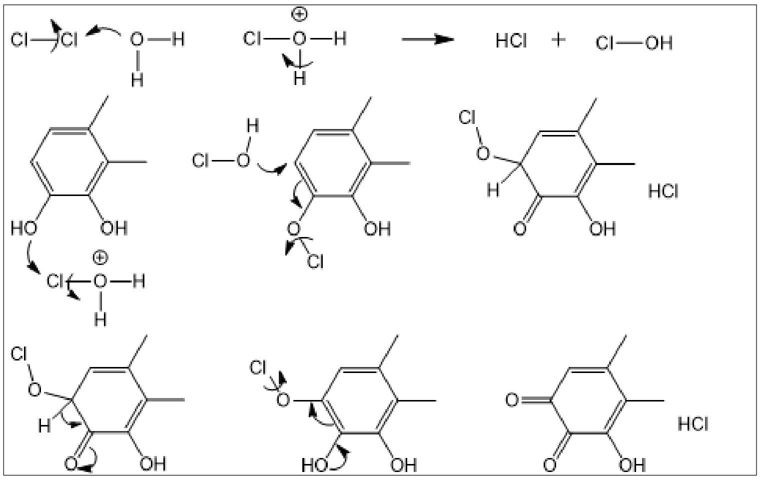

Figure 2 Reaction mechanism of the Husemann's test for morphine

4 Conclusion

The Husemann test for morphine involves a previous heating of morphine in sulphuric acid. This experimental datum is very important since during this process occurs the transformation to apomorphine, not mentioned in the test. Addition of chlorine water after cooling produces a blue- to violet-red colour. The reaction goes through an unstable hypochlorite giving a ketone and a new hypochlorite at ortho position via Umpolung. Enolization produces a phenol whose electron-donor property gives rise to an o-quinone and hydrogen chloride, via a concerted mechanism involving three electron-shifts.

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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