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On the mechanism of the Tattersall test for morphine

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Abstract

Being morphine a restricted drug, a rapid colour test for its detection is very useful. Tattersall employed as reagent trisodium ortho-arsenate in sulphuric acid. However, the more common disodiumhydrogen ortho-arsenate heptahydrate can be used also because both salts yield the same reactive species, that is, protonated arsenic acid and a cation with arsenic(IV). An arsenate is formed with the phenolic group in morphine. Dehydration of this organometallic ester yields a cationic intermediate that induces reaction with arsenic acid at ortho-position (electromeric effect), and a concerted mechanism takes place. A dienone is formed and there is elimination of meta-arsenous acid. Aromatization followed by acidolysis of the new arsenate gives water, meta-arsenous acid, and morphine ortho-quinone, via a six-member concerted mechanism. The colours observed in the test are due to halochromism.

Keywords: Electromeric effect; Meta-arsenous acid; Organic arsenical; Reaction mechanism; Reactive intermediates; Redox reactions; Trisodium arsenate

1. Introduction

Opium and its components have been used from long time as medicine as well as abuse drugs. Thus, a rapid analysis of opioids is desirable. Several tests have been proposed for this purpose**;** however, several issues must be taken into account like the price and availability of the reagent.

The Tattersall colour test employs sodium arsenate in sulphuric acid, giving a grayish-violet that turns dark sea-green on heating. Besides the usefulness of the assay, it is interesting to know what is happening at molecular level during the test.

In this communication we provide the reaction route and the electron flow in each step. This article is a follow up of our studies on reaction mechanism, [1-5].

2. Study Method and Process

This is a Theoretical Organic Chemistry Study. It is based on the chemical deportment of reagents and substrate. All is in accordance with the reaction medium, the nature of the oxidizer and catalyst employed. The several steps leading to morphine ortho-quinone and meta-arsenous acid are fully commented and the electron flow is given in each step.

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3. Antecedents

The test under study is due to T. Tattersall. He published his reaction in England [6], and in Germany, [7]. His test was registered in analytical records in the United States [8], and in Germany [9].

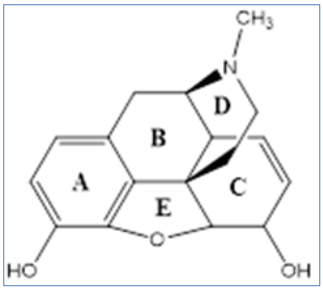

Figure 1 Morphine structure

The test is as follows: Morphine if mixed with concentrated sulphuric acid and a crystal of Na_3AsO_4, gives first a grayish-violet colour, becoming on heating dark sea-green, when acid vapours escape a rather fugitive dark gray colour appears.

Ortho-arsenic acid presents different sodium salts, the most common is disodium hydrogen arsenate heptahydrate. It is a colourless to white crystalline solid soluble in water forming weakly acidic solutions. When heated to decomposition it emits toxic fumes of arsenic. This salt is toxic by ingestion**;** there is high mortality rate due to acute poisoning usually within 48 hours. It is a weak oxidizing agent and may react with strong or weak reducing compounds, [10].

Besides the secondary sodium arsenate there is trisodium arsenate, the salt employed by Tattersall in his test. This dodecahydrate is very soluble in water, 38.9 gr per 100 g H_2O, [11]. This tertiary arsenate is prepared by oxidation of sodium orthoarsenite, Na_3AsO_3, with iodine and sodium bicarbonate, [12]. It can also be prepared by oxidation of arsenic by means of sodium hypochlorite and sodium hydroxide [13].

Now some notes about the substrate. Apart from morphine taken as medicine [14], or as abuse drug, ingestion of bakery products containing poppy seeds can also cause morphine to be excreted in urine. These nutritious oilseeds have pleasant nutty taste. The morphine content is 18.6 mg/kg and 2.3 mg/kg of codeine, [15, 16].

On the other hand, commercial morphine sulphate is the form most employed in instances of poisoning, [17].

4. Discussion

Disodium or trisodium ortho-arsenate in sulphuric acid forms ortho-arsenic acid and sodium sulphate. Further protonation of arsenic acid yields an active species which on reaction with an electrodotic group [18] like a phenol gives rise to an organometallic ester and water, Figure 2, a, b.

Being sulphuric acid a potent dehydrating agent it can eliminate water from arsenic acid and yield other reactive species, a cation with arsenic(IV). This ion can react with a phenol if present or form meta-arsenic acid by proton elimination. This step is reversible and the arsenic cation can result again by reaction with a hydrion.

Dehydration of the arsenical ester, c, gives a reactive intermediate, d, that produces polarity inversion at ortho-position, that is, a δ+ charge that induces reaction with another arsenic acid molecule, electromeric effect, [19]. A concerted mechanism yields a new arsenate and there is ketone formation and elimination of meta**–**arsenous acid, e, (first redox reaction). This process, d, is in accordance with the reaction given for the reduction of arsenic acid to meta-arsenous acid:

$$H_3AsO_4 + 2\ H^+ + 2\ e^- \longrightarrow HAsO_2 + 2\ H_2O \qquad [20].$$

In organoselenium chemistry a cyclic five-member mechanism has been proposed, yielding elemental selenium, [21]. However, sodium arsenate is reduced only to arsenite. Besides, a cationic group is not electrodotic, even having a hydroxyl group because there is an inductive effect from the oxygen towards the positive charged atom and then the

oxygen atom is not suitable as electron donor, and it is presumed that it will not react at ortho position. Therefore, the mechanism involving two molecules of arsenic acid is preferable.

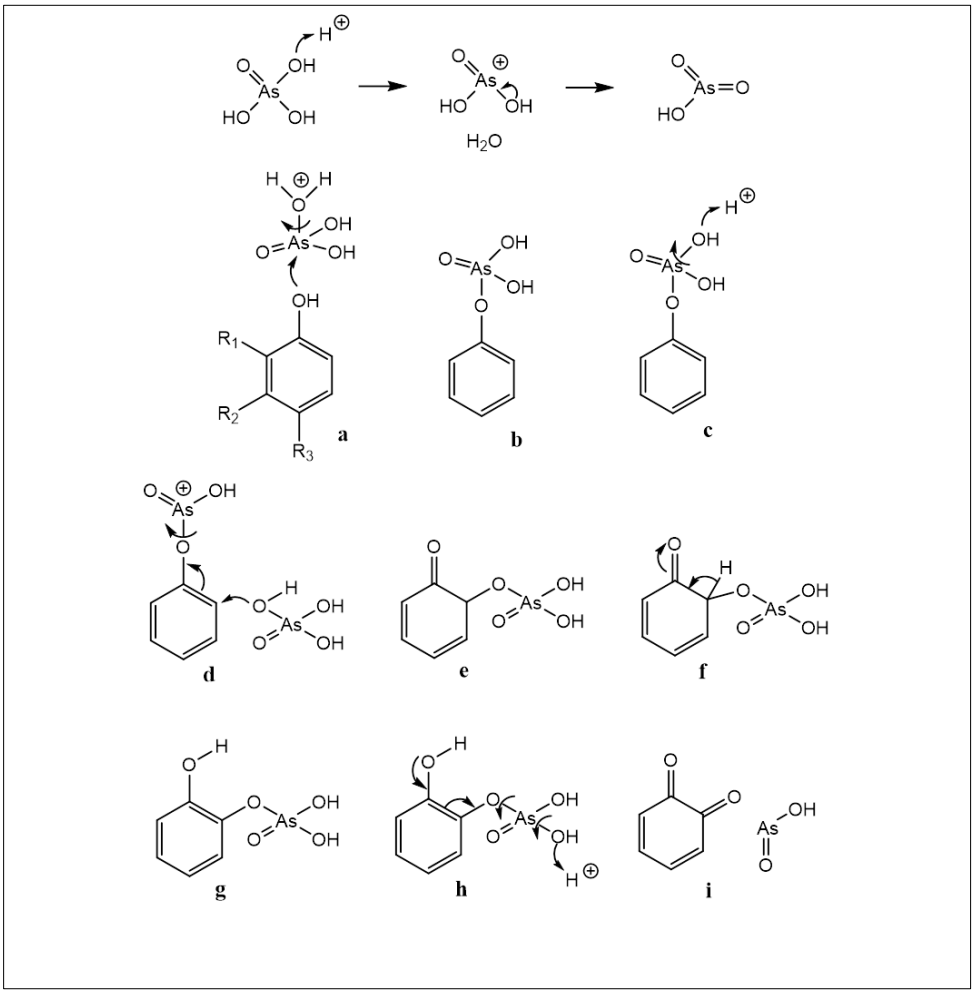

Figure 2 Oxidation of morphine via arsenical ester, electromeric effect, and 6-member concerted mechanism

Isomerization of the obtained dienone to the enolic form restores aromaticity, f, g. Acidolysis of the arsenate produces a six-member concerted mechanism, h. There is concomitant formation of water, meta-arsenous acid, and morphine ortho-quinone, i, (second redox reaction). This way the chemistry of the Tattersall test has been explained. The observed colours in the test are due to halochromism, [22, 23].

5. Conclusion

The chemistry of the Tattersall test for morphine has been cleared up. The reaction mechanism of the series of steps that take place has been provided. The formation of two reactive species is discussed. The first reaction is formation of an organometallic ester whose dehydration gives rise to an electromeric effect. Reaction with arsenic acid at ortho position yields a new arsenate, a dienone and meta-arsenous acid. Aromatization followed by protonation of a hydroxyl group at the arsenical gives water, meta-arsenous acid, and morphine ortho-quinone, via a concerted six-member mechanism.

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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