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On the detection of morphine by formation of Turnbull's Blue

Francisco Sánchez-Viesca * and Reina Gómez Gómez

Department of Organic Chemistry, Faculty of Chemistry, National Autonomous University of Mexico, Mexico City (CDMX), Mexico.

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Abstract

Morphine is a highly efficient analgesic and is still the stronger painkiller today, but also has strong addictive properties. The misuse, due to the euphoria that produces, makes indispensable have at hand a rapid and simple chemical test for morphine identification, like the assay studied in this communication. It employs potassium ferricyanide and ferric chloride as reagents that in contact with morphine gives rise to Turnbull's blue, the blue colour observed in the test. It is based in a redox process that produces ferrous ferricyanide (reduction step) and 2,2'bimorphine (oxidation step), via a free radical mechanism and a coupling reaction.

Keywords: 2,2'-Bimorphine; Ferric chloride; Free radicals; Potassium ferricyanide; Redox reaction; Turnbull's blue

1 Introduction

The test for identification of morphine by formation of a blue colour is attributed to two different authors: Kalbruner and Kieffer. The Merck List of Reagents indicates that Kalbruner test for morphine is the same of Kieffer, without describing the test and gives no reference, [1]. In the Kieffer's entry, the assay is described and there is a reference. At first sight it seems that this is the original test, but the reference is of Kalbruner test and not of Kieffer, [2].

Both assays are mentioned in Cohn's Test and Reagents [3], but without references.

The Kalbruner test is given in Wilder's book [4], whereas Kieffer test is in Schneider's book, [5].

In order to clarify who proposed first this test, the language was observed. In the Wilder account of Kalbruner test there are older terms like morphia, chloride of iron and ferricyanide of potassium, instead of morphine, ferric chloride and potassium ferricyanide. This point favours Kalbruner as the former proponent.

In this communication the reaction route of this test is provided. Each step is fully commented and the electron flow is also given. This paper is a follow up of our studies on reaction mechanism, [6-10].

2 Antecedents

As said before in the Introduction, the test on the detection of morphine by formation of blue colour is attributed to Kalbruner and also to Kieffer. Since there is no date available for Kieffer's test, the priority of this assay was solved by the older chemical language used by Kalbruner. Figure 1. Morphine structure.

The tests are as follows; Kalbruner test for morphia: Add 5 to 6 drops of an aqueous solution of chloride of iron (1:8), then 3 to 4 drops of solution of red ferricyanide of potassium (1:120). Blue colour. In Wilder's book, [4].

* Corresponding author: Francisco Sánchez-Viesca

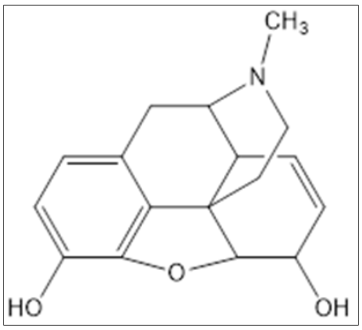

Figure 1 Morphine structure

Kieffer's reaction for morphine: Upon the addition of 5-6 drops of ferric chloride solution (1:8) and 3 drops of a solution of potassium ferricyanide (1:100), a drop of morphine solution will cause a blue colouration or a blue precipitate in consequence of the reduction of the ferricyanide. In Schneider's book, [5].

The chemistry of this test, from morphine to the end products, Turnbull's blue and 2,2'-bimorphine, is given in the next section.

3 Discussion

The reactive group in morphine is the phenol group at C-3. It is responsible of many oxidation reactions of morphine, [11]. In the test under study there is no acid or basic catalyst. In order to form a phenoxide, a basic medium is commonly employed. However, it has been indicated that such a weak base as water can form a hydroxonium ion, promoting the formation of a phenoxide, [12]. Figure 2.

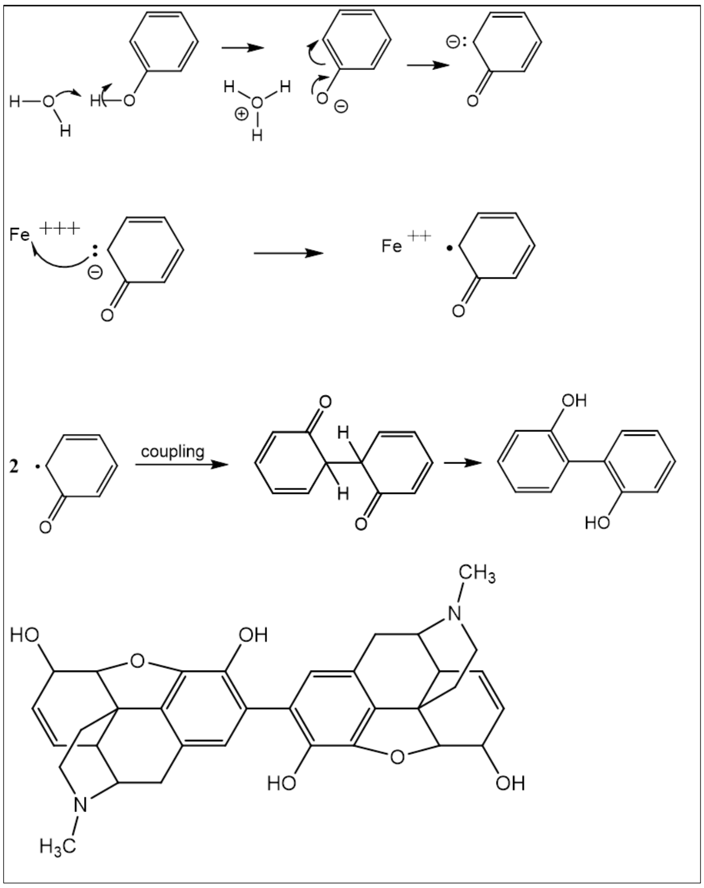

Figure 2 Reaction route from morphine to 2,2'-bimorphine

The electrodotic property [13, 14] of the phenoxide gives rise to a carbanion at C-2 The negative charge on oxygen is more stable than in a carbon atom. Thus, the more unstable carbanion, and therefore more reactive, transfers an electron to a ferric atom in $FeCl_3$ forming ferrous ferricyanide, Turnbull's blue, the colour observed in the test. Cf. [15-17]. This reaction is preferred to addition of an electron to the ferricyanide anion, to give ferric ferrocyanide, Prussian blue.

Now let's see the organic molecule: a free radical is formed at C-2 which is stabilized by combination with another similar reactive intermediate (coupling reaction). This way 2,2'-bimorphine results after enolization of the two intermediate ketones. The dimer is transoid in order to eliminate repulsion between the ketones or the hydroxyls.

Morphine can be oxidized to 2,2'-bimorphine with potassium permanganate [18] and with alkaline ferricyanide, [19]. There is an interesting article on this compound, [20]. See also The Chemistry of the Morphine Group of Alkaloids, [21]

4 Conclusion

The reaction route of Kalbruner test for morphine has been stablished. It is a redox process: ferric ions ($FeCl_3$) are reduced and ferrous ferricyanide is obtained, Turnbull's blue, the colour observed in the test, whereas the organic molecule is oxidized to 2,2'bimorphine via coupling reaction of free radicals.

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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