



## The oxidation mechanism of Morphine with Antimony trichloride

Francisco Sánchez-Viesca \* and Reina Gómez

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

World Journal of Chemical and Pharmaceutical Sciences, 2024, 04(01), 007–010

Publication history: Received on 05 December 2023; revised on 28 January 2024; accepted on 31 January 2024

Article DOI: <https://doi.org/10.53346/wjcps.2024.4.1.0021>

### Abstract

In this communication the oxidation route of morphine with antimony trichloride is provided. The deliquescent reagent is partially hydrolysed to antimonyl chloride with concomitant release of hydrogen chloride. The reactive species is obtained by protonation of the oxychloride. The electro donor phenol group in morphine forms an organometallic ester of gem-chlorohydrin type which eliminates hydrogen chloride. Protonation of the oxo-antimonite creates a  $\delta^+$  at the aryl oxygen, favouring a nucleophilic reaction at ortho-position. Reaction of dichloro-hydroxy-antimony at this site produces a ketone and separation of antimony mono-hydroxide (Redox step). Aromaticity is recovered by enolization and the electro donor phenol gives rise to an ortho-quinone with separation of antimony mono-chloride and a chloride ion (Second redox step). Another cyclic reaction mechanism can operate involving five atoms. Finally, a bimolecular electron transfer yields two atoms of elemental antimony.

**Keywords:** Antimonyl chloride; Dichloro-hydroxy-antimony; Gem-chlorohydrin; Organometallic ester; Oxo-antimonite; Reactive intermediates

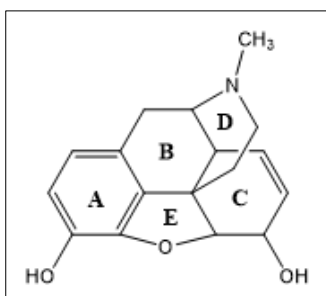
### 1 Introduction

Between 1805 and 1816 Friedrich Wilhelm Sertürner isolated a yellowish-white crystalline compound from crude opium after immersing it in ammoniated hot water. He tested this compound on a few dogs which died. Then he tested smaller doses on himself and some boys. The effects were pain relief and euphoria. He also noted that high doses of the drug could lead to psychiatric effects, nausea, vomiting, depression of the cough, constipation and slowed breathing. Pain relief was ten times that experienced with opium use, [1].

The commercially available forms of morphine are the hydrochloride and the sulphate. These are around 300 times more water-soluble than morphine hydrate. These salts are much more acidic, with pH around 5, than the saturated morphine hydrate solution which has a pH of 8.5. The salts are therefore neutralized with small amounts of sodium hydroxide to make them suitable for injection, [2]. Figure 1.

In this communication we provide the oxidation route of morphine by means of antimony trichloride. This is a follow up of our studies on reaction mechanism, [3-7].

\* Corresponding author: Francisco Sánchez-Viesca



**Figure 1** Morphine structure

## 2 Antecedents

The mechanism of the oxidation of morphine with antimony trichloride, Smith reagent [8], is provided.

Antimony has atomic number 51. It is in fourth row of group 5A (the nitrogen family), IUPAC group 15, and is classified as a metalloid. Its electronic structure is: [Kr] 4d<sup>10</sup> 5s<sup>2</sup>5p<sup>3</sup>, [9]. Antimony displays four oxidation states: -3, 0, +3, +5, [10].

Antimony trichloride, antimonous chloride, in the air it attracts water and deliquesces. It dissolves unchanged in water acidified with hydrochloric acid, [11]. SbCl<sub>3</sub> is readily hydrolysed: SbCl<sub>3</sub> + H<sub>2</sub>O = 2 HCl + Cl-Sb=O, giving hydrochloric acid and antimony oxychloride, antimonyl chloride, [12].

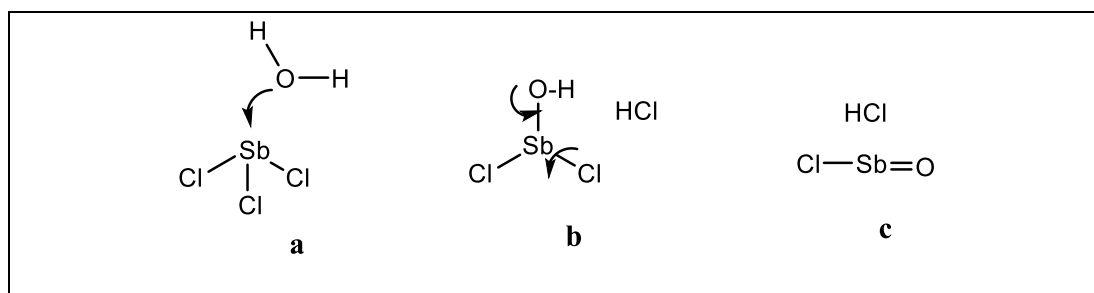
Antimony trichloride is a strong oxidizing agent. Contact can irritate and burn the skin and eyes with possible eye damage, [13]. Its preparation from antimony sulphide has been described in detail, [14, 15].

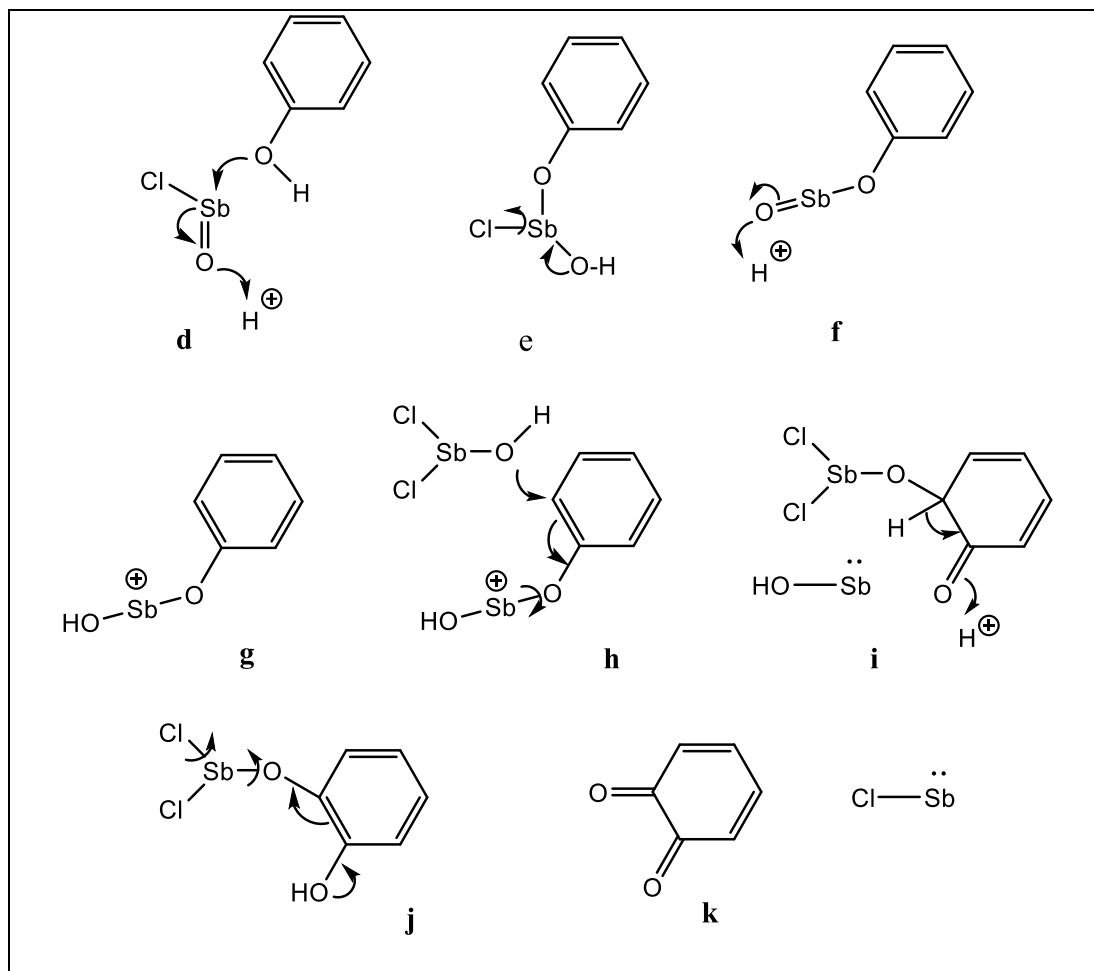
There is a very complete book on the plant alkaloids including the alkaloids of opium, [16]. Dr. Ludwig David from Szeged University, Hungary, studied the colour reactions given by 13 opioids with 2% basic magnesium hypochlorite in acetic acid and sulphuric acid as catalyst: 5 mg of the alkaloid are dissolved in 3 ml of the reagent and carefully layered on 3 ml of concentrated sulphuric acid. The produced colours are observed at intervals until 22 hrs. and given in a table, [17]. There is a review on the principal chemical tests for morphine, [18].

## 3 Discussion

Antimony trichloride is a strong oxidizer as was mentioned in 'Antecedents'. However, this chloride cannot oxidize as such. Nevertheless, this compound is extremely hygroscopic and is easily hydrolysed to antimony oxychloride with release of hydrogen chloride. Figure 2 a, b, c. Now there is an oxygenated intermediate and acid catalysis.

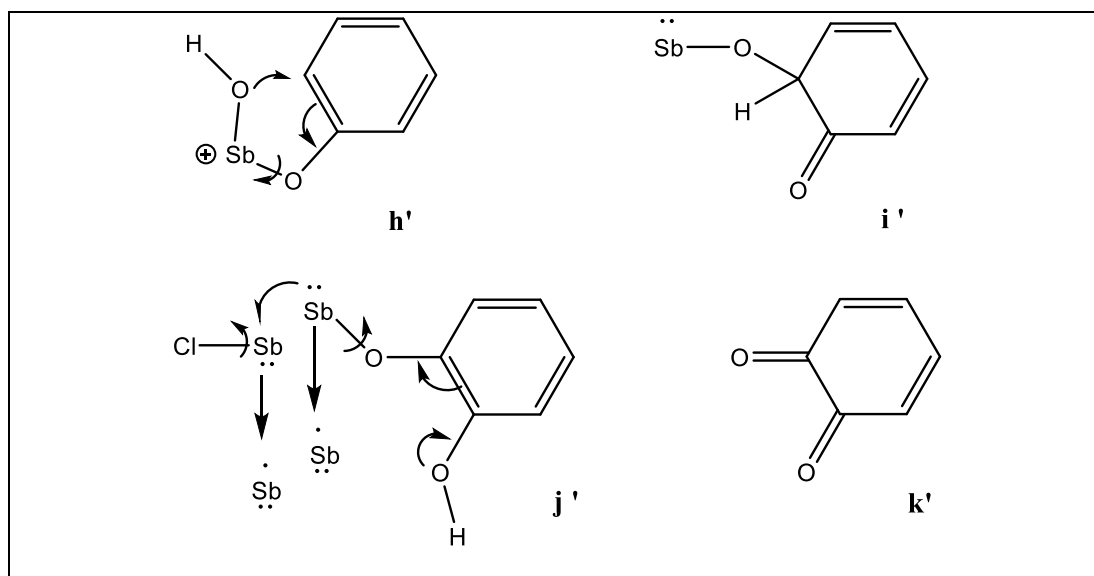
Protonation of this reactive intermediate enhances reaction with the phenolic group in morphine, d. The resulting organometallic gem-chlorohydrin loses hydrogen chloride, e, yielding a mixed antimonite whose protonation gives rise to a δ<sup>+</sup> at the phenoxy group. f, g, h. This fact originates Umpolung in the ortho-position, favouring reaction with dichloro-hydroxy-antimony. This way neutral hydroxy antimony(I) is formed. Enolization of the intermediate ketone restores aromaticity, j. The electrodotic property [19] of the phenol affords an ortho-benzoquinone via four electron-shifts in a concerted mechanism, and antimony monochloride, k.





**Figure 2** Oxidation of the phenolic group in morphine to an o-benzoquinone

Other route can take place: a five membered cyclic mechanism, Figure 3 h', followed by a similar intermediate as before, leads to j'. A negative antimony atom cedes an electron to antimony mono-chloride, with elimination of a chloride ion and obtention of two atoms of elemental antimony, each with three electrons, as expected.



**Figure 3** Cyclic mechanism leading to elemental antimony and oxidation to o-quinone

---

## 4 Conclusion

The oxidation of morphine by means of antimony trichloride is initiated by antimony oxychloride formed in situ due to the hygroscopic property of the reagent that hydrolyses it. Two organometallic intermediates lead to a positive charged chain that induces reaction at ortho-position. A new organometallic ester and a ketone are formed, and then an o-benzoquinone results. Other possibility is a cyclic mechanism involving five atoms. Finally, a bimolecular reaction affords two atoms of elemental antimony via one electron transfer.

---

## Compliance with ethical standards

### *Acknowledgments*

Thanks are given to Luz Clarita for support

### *Disclosure of conflict of interest*

There is no conflict of interest to declare

---

## References

- [1] Mandal A. Morphine History, news-medical.net>Morphine-History
- [2] Mandal A. Morphine Chemistry, news-medical.net>Morphine-Chemistry
- [3] Sánchez-Viesca F, and Gómez R (2023). Organometallic intermediates in Böttger test for glucose in urine. *Magna Scientia Adv. Res. & Rev.* 09(02), 051-054.
- [4] Sánchez-Viesca F, and Gómez R (2024). The chemistry of Hager's test for brucine. *Earthline J. of Chemical Sc.* 11(1), 31-37.
- [5] Sánchez-Viesca F, and Gómez R. (2023). The chemistry of Anderson's test for codeine. *Int. J. Scholarly Res. Chem. & Pharm.* 03(01), 001-004.
- [6] Sánchez-Viesca F, and Gómez R. (2023). On Dulcin detection by electron transfer. *World J. Chem. & Pharm.* 03(01), 001-004.
- [7] Sánchez-Viesca F, and Gómez R. (2023). On the chemistry of Beckurt's test for physostigmine: A novel hydride transfer. *Magna Scientia Adv. Res. & Rev.* 08(02), 022-0025.
- [8] Merck E. (1903). **Merck's** Reagentien Verzeichnis. Springer, Darmstadt, 135.
- [9] Lee JD, (1964). *Concise Inorganic Chemistry*, Van Nostrand, London, 94.
- [10] Antimony oxidation states NCBI. Access with the title.
- [11] Richter V, and Klinger H, (1905). *Inorganic Chemistry*, P. Blakiston's Son, Philadelphia, 147.
- [12] Bruni G. (1965). *Inorganic Chemistry*, UTEHA, Barcelona, 194.
- [13] Antimony trichloride. <https://cameochemicals.noaa.gov>antimony-trichloride>
- [14] Riesenfeld EH. (1950). *Practical Inorganic Chemistry*, 2nd ed. Ed. Labor, Barcelona, 248-250.
- [15] Schlessinger G. (1962). *Inorganic Laboratory Preparations*, Chemical Publishing, New York, 111-112.
- [16] Henry Th. A. (1949). *The Plant Alkaloids*, 4th ed. Alkaloids of Opium, p- 175. Blakiston, Philadelphia; [library.sciencemadness.org/library/books/the\\_plant\\_alkaloids](http://library.sciencemadness.org/library/books/the_plant_alkaloids)
- [17] David L. (1925). On the new reactions of some opium alkaloids. *Pharmazeutische Zeitung*, 70. 969-972.
- [18] Fulton Ch. C. (1937). The principal Chemical Tests for Morphine. *Amer- J. Pharm.* 109(5), 219-240.