

## The mechanism of Mecke's test for opioids

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, 2023, 02(01), 023–027

Publication history: Received on 12 December 2022; revised on 25 January 2023; accepted on 27 January 2023

Article DOI: <https://doi.org/10.53346/wjcps.2023.2.1.0014>

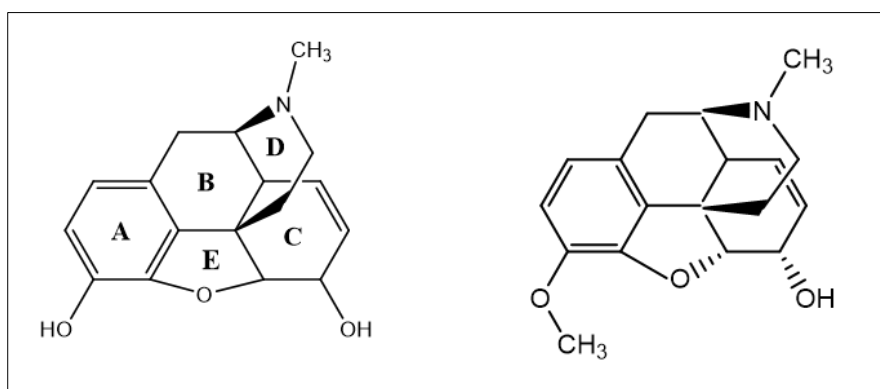
### Abstract

Mecke colour test is an official assay for opioids, either for opium or for purified compounds. It employs a solution of selenious acid in sulphuric acid. However, organoselenium chemistry was misunderstood for many years. The reaction mechanism involving selenium (IV) compounds was explained by way of electron back donation, which is a theoretical contravention. In this communication we provide the reactions that take place during this test. Each step is fully commented and the electron flow is given. The reaction proceeds by way of an enol selenite. Acidolysis gives rise to a reduced selenium (II) intermediate and an activated ketone at C-2, that is, a redox reaction with polarity inversion. Addition of selenious acid and further electron shifts affords morphine ortho-quinone and elemental selenium.

**Keywords:** Electron back donation; Polarity inversion; Reaction mechanism; Reactive intermediates; Redox reactions; Selenious acid

### 1 Introduction

Mecke's colour test for opium alkaloids is based in organoselenium chemistry. The reagent is a solution of selenious acid in sulphuric acid which produces characteristic colours with alkaloids. This assay is used for identification of drugs of abuse and therefore is important in forensic science. However, there are opioids used in medicine like codeine, a cough suppressant, that can give positive tests for opiates, [1, 2].



**Figure 1** Morphine and codeine structures

\*Corresponding author: Francisco Sánchez-Viesca

Poppy seed ingestion is a contributing factor to opiate-positive urinalysis results [3]. Patients should abstain from consuming poppy seeds for 3 days prior to a urine drug test, [4]. Colorimetric assays offer simple visual readouts and do not require instruments for the analysis.

This communication is a follow up of our studies on reaction mechanism, [5-9].

---

## 2 Antecedents

Mecke observed the colours produced on the addition of a 0.5% solution of selenious acid in concentrated sulphuric acid to the opium alkaloids and recommended this solution as a reagent for the identification of minute quantities of these compounds, [10, 11]. Mecke's modified reagent is 1% solution instead of 0.5%.

Selenious acid,  $\text{H}_2\text{SeO}_3$ , a diprotic acid moderately oxidizing in nature, is used for drug checking. A green to blue-green is produced by opium [12], and a blue to green colour with morphine, [13]. Initial rearrangement to apomorphine is discarded since this compound affords dark bluish-violet colour with Mecke reagent. The mechanism for the morphine-apomorphine rearrangement has been cleared out recently, [14].

Selenium dioxide, the anhydride of selenious acid and an oxidizer by itself, has been prepared by hydrogen peroxide oxidation of selenium, [15].

The organoselenium chemistry has not always been understood. The selenium dioxide oxidation, Riley oxidation [16], has been explained by a mechanism involving electron back donation [17] that is, inverting the normal polarization of a functional group. This is a theoretical contravention. The electronegative values (Pauling) of oxygen and selenium are 3.5 and 2.4, respectively [18]. Thus the selenium-oxygen double bond is polarized outwards, not inwards, selenium is electrophilic, not the oxygen atom.

A later mechanism proceeds by way of an intermediate enol selenite, but the next step involves electron back donation [19]. Finally, there is a mechanism with correct electron shifts [20], with oxygen as electrodotic [21] atom.

A mechanism employing  $\text{SeO}_2$  instead of selenious acid has been advanced [22]. For general information on the Riley oxidation see references [23, 24].

---

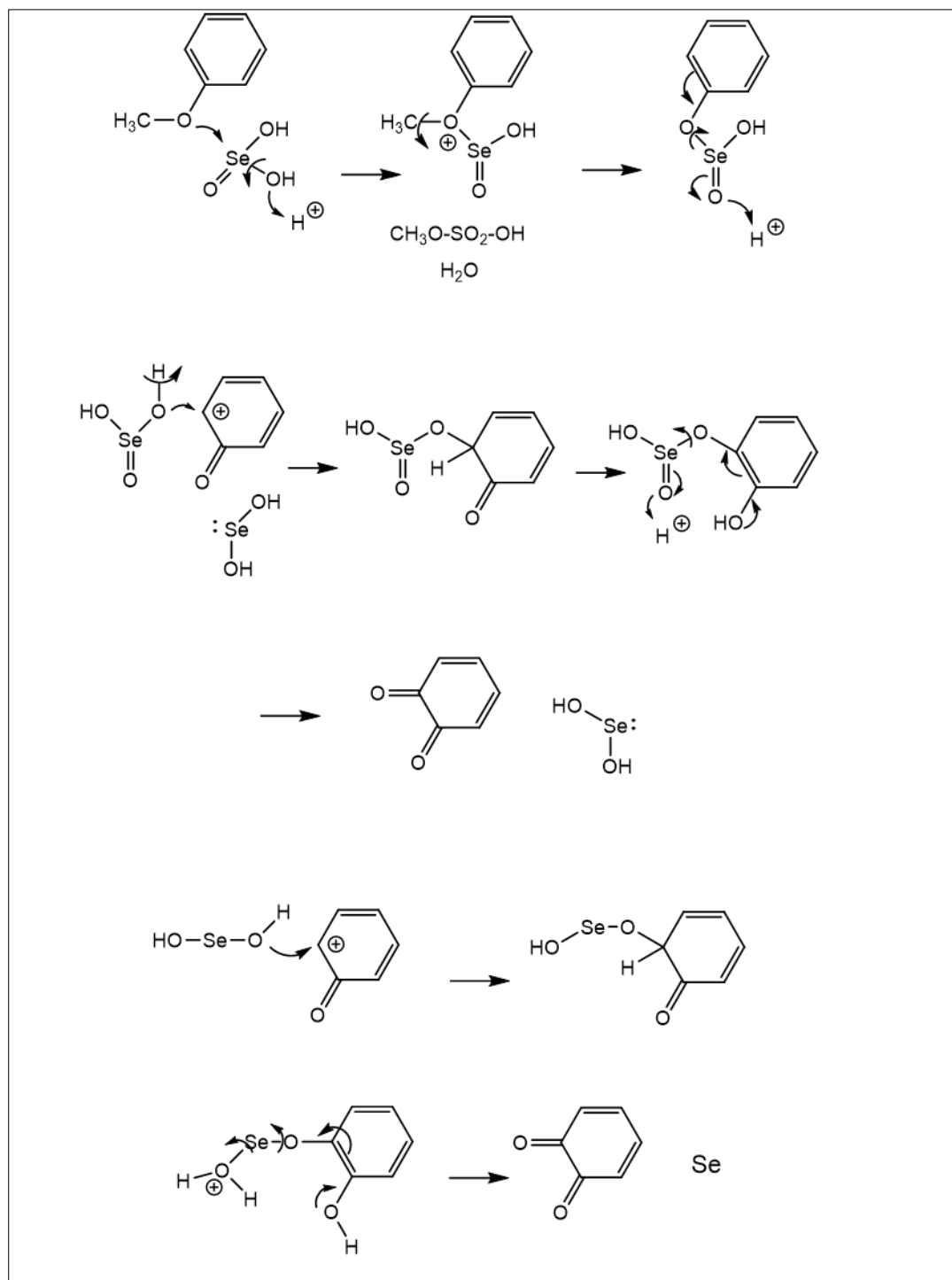
## 3 Discussion

The Marquis and Mecke reagents give a violet colour in the presence of opiates including morphine, codeine, and heroin, [25]. This indicates that codeine, phenolic ether (3-methyl-morphine), must be demethylated during the test. This is confirmed experimentally since Levine observed the colour reactions of phenols and phenolic ethers with selenious acid-sulphuric acid reagent, [26]. This is interesting since the Zeisel method for the determination of methoxy and ethoxy groups employs boiling hydriodic acid, [27, 28].

Thus codeine was selected to exemplify the mechanism of the reaction of an opioid with selenious acid in sulphuric medium. The first step is reaction of protonated selenious acid with the methoxy group. A selenite ester is formed with elimination of a methyl carbocation, giving hydrogen methyl sulphate and water.

Protonation of the selenium-oxygen double bond of the ester separates selenium (II) hydroxide, a keto group is formed and a transient carbonium ion is neutralized by addition of selenious acid. There has been Umpolung at C-2. Aromatization can be accomplished and protonation of the selenium-oxygen double bond produces a 6-member concerted mechanism. An ortho-quinone is formed and the selenium (II) intermediate can be reduced to elemental selenium by reaction with the incipient carbonium ion in other molecule. A same mechanism as before yields selenium and morphine o-quinone.

A five-member concerted mechanism previous to aromatization can be postulated between the ester  $\alpha$ -to ketone and the active hydrogen atom.



**Figure 2** Reaction route from codeine to morphine o-quinone and elemental selenium; and five member mechanism to morphine o-quinone and  $\text{Se}(\text{OH})_2$

#### 4 Conclusion

The mechanism of the reaction of codeine with selenious acid-sulfuric acid reagent has been advanced. A selenite ester is formed, as well as methyl hydrogen sulphate and water. Protonation of the ester produces Umpolung at C-2. An incipient carbonium ion is neutralized by addition of selenious acid with concomitant elimination of  $\text{Se}(\text{OH})_2$  and ketone formation. Aromatization followed by protonation of the new selenite gives rise to a 6-member concerted mechanism,  $\text{Se}(\text{OH})_2$  and an ortho-quinone being formed.

The  $\text{Se}(\text{OH})_2$  intermediate can react at an activated C-2 position, as before with selenious acid. In this case elemental selenium results as final product.

Selenium can also be formed prior to aromatization by a 5-member concerted mechanism.

---

## Compliance with ethical standards

### *Acknowledgments*

Thanks are given to Martha Berros for support.

### *Disclosure of conflict of interest*

There is no conflict of interest among the authors or any other person.

---

## References

- [1] Kane BM. (2007). Codeine. Interscience Publishing, New York, USA.
- [2] Codeine (Oral Route) Precautions—Mayo Clinic. <https://www.mayoclinic.org>drugs-2>
- [3] Selavka CM. (1991). Poppy seed ingestion as a contributing factor to opiate-positive urinalysis results. *Journal of Forensic Science*, 36(3), 685-686.
- [4] Poppy seed consumption. <https://arupconsult.com>content>
- [5] Sánchez-Viesca F, and Gómez R. (2023). The chemistry of Mandelin's test for strychnine. *OAR Journal of Chemistry and Pharmacy*, 03(01), 001-004.
- [6] Sánchez-Viesca F, and Gómez R. (2022). The chemistry of the Heller's test for urine indican detection. *Magna Scientia Advanced Research & Reviews*, 05(01), 025-029.
- [7] Sánchez-Viesca F, and Gómez R. (2022). The mechanism of the oxido degradation of the Cinchona alkaloids. *American Journal of Chemistry*, 12(1), 18-21.
- [8] Sánchez-Viesca F, and Gómez R. (2021). The chemistry of Crismer's test for glucose in urine. *OAR Journal of Chemistry & Pharmacy*, 01(02), 005-008.
- [9] Sánchez-Viesca F, and Gómez R. (2021). On the mechanism of the Caro synthesis of methylene blue. *Earthline Journal of Chemical Sciences*, 6(2), 209-214.
- [10] Merck E. (1903). *Merck's Reagentien-Verzeichnis*. Springer, Darmstadt, Germany, 97.
- [11] Cohn AI. (1903). *Tests and Reagents*. J. Wiley & Sons, New York, USA, 202.
- [12] Analytical test for opium. <https://www.org>bulletin>
- [13] *Chemistry and Crime. Narcotics and test reagents*  
<http://www.chem.uwimona.edu.jm/courses/CHEM2402/Crime/Reagent>
- [14] Sánchez-Viesca F, and Gómez R. (2022). The mechanism of the morphine-apomorphine rearrangement. *American Journal of Chemistry* 12(4), 73-75.
- [15] Rossman R, Neptune RW, and Allan BW. (1952). Process for preparing selenium dioxide. US Patent No. 2,616,791.
- [16] Patai S. (1962). *Glossary of Organic Chemistry*. Interscience, London, UK, 188.
- [17] Waters WA. (1964) *Mechanisms of oxidation of organic compounds*. Methuen, London, UK, 94-96.
- [18] Lee JD. (1964). *Concise Inorganic Chemistry*. Van Nostrand, London, UK, 44.
- [19] Isaacs NS. (1974). *Reactive intermediates in Organic Chemistry*. J.Wiley & Sons, London, UK, 453-454.
- [20] House HO. (1972). *Modern Synthetic Reactions*, 2nd ed. W.A. Benjamin, Menlo Park, California, USA, 408.
- [21] Luder WF, and Zuffanti S. (1961). *The electronic theory of acids and bases*, 2nd ed. Dover, New York, USA, 71.
- [22] Selenium dioxide—Riley oxidation. *AdiChemistry*. <https://adichemistry.com>organic>organicroagents>

- [23] Hickinbottom WJ. (1962). *Reactions of Organic Compounds*, 3rd ed. Longmans, London, UK, 247.
- [24] Royals EE. (1961). *Advanced Organic Chemistry*. Prentice-Hall, Englewood Cliffs, NJ, USA, 341, 568.
- [25] Pratiwi R, Noviana E, and Fauziati R. (2021). Analytical methods for codeine determination. *Molecules*, 26, 800.
- [26] Dewey BT, and Gelman AM. (1942). Color reactions of organic nitrogen compounds with selenious acid–sulfuric acid solution. *Industrial & Engineering Chemistry, Analytical Edition*, 14(4), 361-362.
- [27] Patai S. (1962). *Glossary of Organic Chemistry*. Interscience, London, UK, 225.
- [28] Shriner RL, Fuson RC, and Curtin DY. (1958). *The systematic identification of Organic Compounds*, 4th ed. J. Wiley & Sons, New York, USA, 116.