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On the Dimerization of Morphine by Tetraaminocupric Sulphate

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Abstract

Lindo proposed an assay for identification of morphine using copper sulphate and aqueous ammonia. In the presence of morphine an emerald-green colour is obtained.

In this communication the chemistry of this test is provided. The principal reaction site in morphine is the phenol at C-3 which forms the phenolate in alkaline medium. This anion is in resonance with a carbanion at C-2. This is less stable and therefore more reactive. The cupric ion accepts four ligands, in this case four NH3 molecules. Copper (II) is an electron acceptor passing to cuprous ion. Thus, the electrodotic carbanion transfers one electron to the metal (redox step). The remaining free electron in the organic molecule couples with another similar species. The dimer obtained is transoid in order to eliminate steric hindrance between the two dienones.

Finally, aromaticity is restored by enolization and 2,2'bimorphine is obtained. The observed colour in the test is due to halochromism, not to an inorganic product.

Keywords: Carbanion; Cuprammonium Sulphate; Electron Acceptor; Electron Coupling; Electron Donor; Halochromism

1 Introduction

Lindo proposed an assay for morphine identification based on the use of copper sulphate in aqueous ammonia. Figure 1.

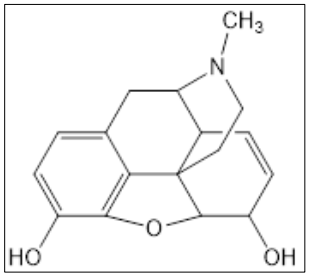

Figure 1 Morphine chemical structure

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The formation of the reagent used in this study is as follows: if a concentrated ammonia solution is added to a solution of copper sulphate the hydroxide is first precipitated, but this quickly dissolves to give a clear purple-blue solution owing to the formation of a complex. The coordination number of the cupric ion is four, that is, the number of ligands that can be added. In the complex, four ammonia molecules take place of the four water molecules associated with the cupric ion, giving tetraaminocupric sulphate (cuprammonium sulphate). If alcohol be added to the deep purple-blue solution, crystals of the same colour separate, [1].

In the present communication the chemistry of Lindo test for morphine is described. It is a follow up of our studies on reaction mechanism, [2-6].

2 Study Method and Process

This is an Organic Chemistry Theoretical Study. It is based on the chemical deportment of reagent and substrate. All is in accordance with the reaction medium and the catalyst present. The several steps leading to the final product are fully commented and the electron flow is also given.

3 Antecedents

The test under study is due to Professor Lindo and is as follows: solution of ammonio-cupric sulphate is prepared from 1 part sulphate of copper in 10 parts of water and add sufficient ammonia till clear. This reagent in the presence of morphia gives emerald green colour. The test was published in Germany and it is registered in three books on analytical tests, [7-9].

Some remarks on the substrate and reagent. Morphine is an opiate analgesic drug derived from opium known for its efficacy in pain management. It acts on the spinal cord to provide analgesia by activating specific channels, and its dosage varies based on factors like age and type of pain, [10].

Intravenous morphine at a dose equivalent to 20% of the basal oral dose is safe and effective in the majority of patients experiencing pain exacerbation. This treatment is inexpensive and can be used at little risk to patients, [11].

In 1831, William Gregory, a physician and chemist in Edinburgh discovered a cheap method of isolating and purifying morphine salts for widespread pharmaceutical usage, [12, 13].

Now let's see the electronic configuration of Cu, Cu^{+}, Cu^{2+}, and cuprammonium complex. The shells (orbits) of copper are: 1^{2}, 2^{8}, 3^{18}, 4^{1}, [14].

The expected electron configuration for copper will be; $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 4s^2\ 3d^9$

However, the electron configuration of copper is: $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 3d^{10}\ 4s^1$

For the Cu^{+}: $3d^{10}$. For $Cu2^{+}$: $3d^9$, [15].

For tetraaminocupric sulphate: $3d^8$, dsp^2 hybridization, $4p^1$ (according to Pauling).

Idem, $3d^9$, sp^2d hybridization (according to Huggins). The last four orbitals are in shell 4, [16].

4 Discussion

The phenol group in morphine is responsible of many oxidation reactions. [17].

The first step in Lindo test is the formation of the phenolate in alkaline medium followed by resonance to carbanion at C-2. Cupric ions are electron acceptors [18], passing to cuprous ions (reduction step). Figure 2.

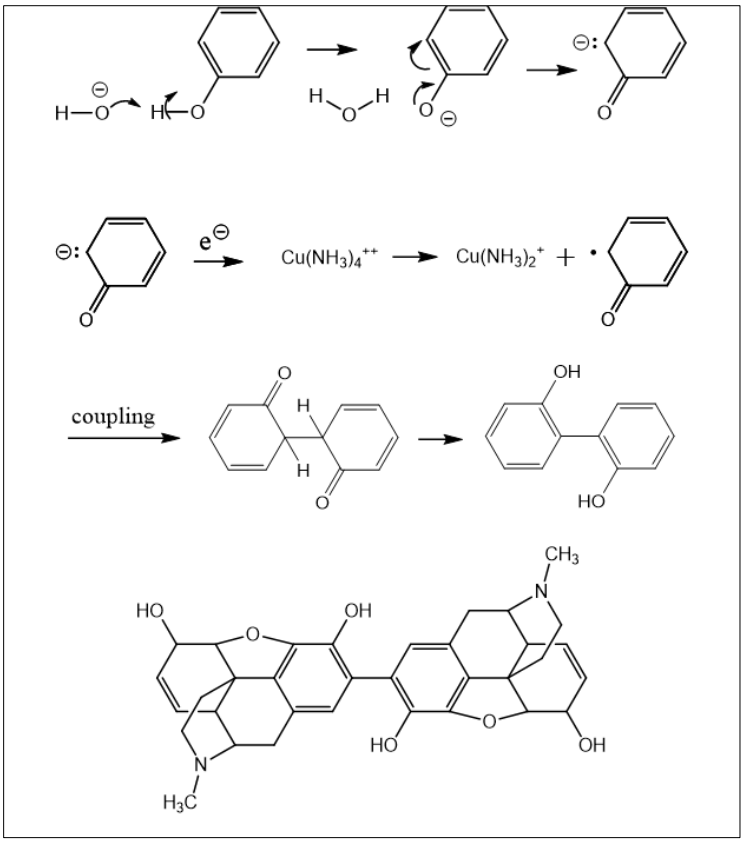

Figure 2 Morphine dimerization by means of cuprammonium sulphate

The organic molecule is oxidized, leaving a free radical at C-2. These radicals are stabilized by coupling yielding a dimerization intermediate which is transoid in order to eliminate steric hindrance between the two carbonyls. Finally, the two dienones isomerize to aromatic rings. This way 2,2'-bimorphine is obtained. There is an interesting article on this compound also known as pseudomorphine, [19]. The structure of pseudomorphine was published in England, [20].

In Lindo test for morphine an emerald green colour result. So, we revised the colour of the reduced copper complex. The diamine copper (I) ion is colourless [21] so, the green colour could not be attributed to the reduced product and must be due to halochromism, [22].

4 Conclusion

The Lindo test for morphine has been cleared. It is a redox process in which the complex cupric ion is reduced to cuprous ion. The assay is based on the electrodotic property of the phenolate formed in situ. There is electron transfer and coupling reaction followed by isomerization.

Compliance with ethical standards

Acknowledgments

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Disclosure of conflict of interest

There is no conflict of interest to declare.

References

[1] J. H. White. Inorganic Chemistry, 2nd ed. London, University of London Press, 1964, 205.

[2] F. Sánchez-Viesca and R. Gómez. On the chemistry of creatinine detection via oxaziridine intermediate. Magna Scientia Adv. Res. & Rev., vol. 13(02), pp. 058-061, 2025.

[3] F. Sánchez-Viesca and R. Gómez. On the chemistry of Jorissen test for morphine. Int. J. of Chem. & Pharm. Res. Updates., vol. 04(02), pp. 001-004, 2025.

[4] F. Sánchez-Viesca and R. Gómez. On apomorphine detection by colour reactions. J. Chem. Biol. & Phys. Sc., vol. 15(1), pp. 001-005, 2024.

[5] F. Sánchez-Viesca and R. Gómez. A novel transamination reaction in a murexide-like sequence for caffeine detection. Earthline J. of Chem. Sci., vol. 11(1), pp. 437-444, 2024.

[6] F. Sánchez-Viesca and R. Gómez. A complete and sustained organic/inorganic reaction mechanism of Baeyer´s test. World J. of Chem. & Pharm., vol. 4(2), pp. 1-5, 2024.

[7] H. Wilder. List of Tests (Reagents) Arranged in Alphabetical Order according to the Names of the Originators, test 468, p. 46. New York, P. W. Bedford, 1885.

[8] A. I. Cohn. Tests and Reagents. New York. J. Wiley & Sons, 1903, 181.

[9] E. Merck. Merck´s Reagentien-Verzeichnis, Darmstadt, Springer, 1903, 88.

[10] Morphine. https://sciencedirect.com/topics/neuroscience/morphine

[11] Intravenous morphine. J. of Pain & Symptom management, 27(4), 352-359, 2004.

[12] W. Gregory. On a Process for Preparing Economically the Muriate of Morphine. Edinb. Med. Surg. J. 35(107), 331-338, 1831.

[13] G. B. Stefano. Reciprocal Evolution of Opiate Science. Nat. Institutes of Health (NIH), (gov). 2017.

[14] The electron configuration of copper. Chemical Book. Direct access.

[15] Electron configuration for copper. University of Maryland. Direct access.

[16] J. D. Lee. Concise Inorganic Chemistry, London, Van Nostrand, 1964, 190.

[17] C. Hidalgo. Chemical Pharmacy, Madrid, Alhambra, 1969, 370.

[18] S. Patai. Glossary of Organic Chemistry, New York, Interscience, 1962, 69.

[19] J. Donath, O. Hesse and K. Polstorff. On dehydromorphine (Oxydimorphine, Pseudomorphine). Zeits. für anal. Chem. vol. 26, pp. 743-746, 1887.

[20] K. W. Bentley and S. F. Dyke. The structure of pseudomorphine. J. Chem. Soc. (London),1959 pp. 2574-2577.

[21] D. A. Brown. Comparative Inorganic Chemistry, London, McGraw-Hill, 1967, 317.

[22] M. Pesez and P. Poirier. Methods and Reactions of Organic Analysis, vol. 3, p. 227. Paris, Masson, 1954.