Open Access Research Journal of
Chemistry and Pharmacy
Journals home page: https://oarjpublication/journals/oarjcp/
ISSN: 2783-0276 (Online)

OARJ OPEN ACCESS RESEARCH JOURNALS

(RESEARCH ARTICLE)

Check for updates

The reaction of Codeine with ammonium peroxodisulphate in acidic medium

Francisco Sánchez-Viesca * and Reina Gómez

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

Open Access Research Journal of Chemistry and Pharmacy, 2025, 07(01), 001-004

Publication history: Received on 01 June 2025; revised on 10 July 2025; accepted on 12 July 2025

Article DOI: https://doi.org/10.53022/oarjcp.2025.7.1.0014

Abstract

The analytical chemistry of medicinal products is very important. In this communication the reactions occurring between the analyte codeine with ammonium persulphate in sulphuric acid are provided, as well the reaction mechanism. This colour reaction was devised by Orlow and Horst, codeine giving orange colour in this assay. The analytical procedure is interesting since it is a double variant of the Elbs persulphate oxidation which employs monophenols in alkaline medium that are oxidised to hydroxy phenols. The Orlow-Horst test uses a phenolic methyl ether instead of the free phenol, and the reaction medium is acid, not alkaline. There is sulfation at C-2, hydrion removal and aromatization, followed by protonation of the oxygen at C-2. This oxonium ion produces a δ+ on the sulphur atom plus a similar effect due to the sulphonyl group, facilitating addition of water and separation of 2-hydroxy-codeine. This compound forms a hydrogen bond in a five-member ring.

Finally, a hydrion transfer in the inorganic intermediate gives sulphuric acid.

Keywords: Ammonium persulphate; Codeine; Elbs persulphate oxidation; Orlow-Horst test; Phenolic ethers; Reaction and mechanistic variations

1. Introduction

Codeine is the phenolic methyl ether of morphine. Figure 1. It was first isolated by the French chemist Pierre Robiquet in 1832. He used the mother liquor after the extraction of morphine, [1, 2]. Codeine dissolution in boiling water and cooling forms white, silky clusters with two equivalents of water. It is a strong base and is used for cough control.

Orlow and Horst devised a colour test for alkaloids that gives different colour when ammonium persulphate in sulphuric acid are used, [3, 4].

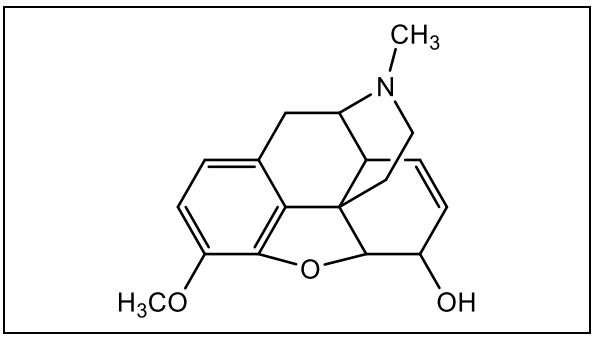


Figure 1 Chemical structure of codeine

* Corresponding author: Francisco Sánchez-Viesca

In the present communication we present the reactions that occur in this assay when codeine is used as substrate. This is a follow up of our studies on reaction mechanism, [5-9].

2. Antecedents

There are other tests for codeine: Mecke colour test employs selenious acid in sulphuric acid, [10, 11]. The organoselenium chemistry of this test produces with codeine blue colour, changing to emerald green, plus separation of elemental selenium.

Anderson employed nitric acid in different concentrations. Codeine in concentrated nitric acid is heated at the water bath to dryness and then warming with soda lye evolves methyl amine, which is identified, [12] This process involves many steps, including rearrangement to apomorphine and degradation, [13].

In the test under study an admixture of codeine in sulphuric acid affords orange colour on addition of ammonium persulphate, see Introduction.

Ammonium persulphate, $(NH_4)_2S_2O_8$, is a colourless salt that is highly soluble in water. It is a powerful oxidizing agent. It was first described in 1891 by Hugh Marshall (1868-1913) working at the University of Edinburgh, [14]. Ammonium peroxydisulphate is obtained by the process of electrolysis with a cold concentrated solution of ammonium bisulphate or ammonium sulphate in sulphuric acid, [15].

Karl Elbs (1858-1933), working at the University of Freiburg, carried on the oxidation of monophenols to hydroxy-phenols with ammonium persulphate in alkaline medium, [16-18].

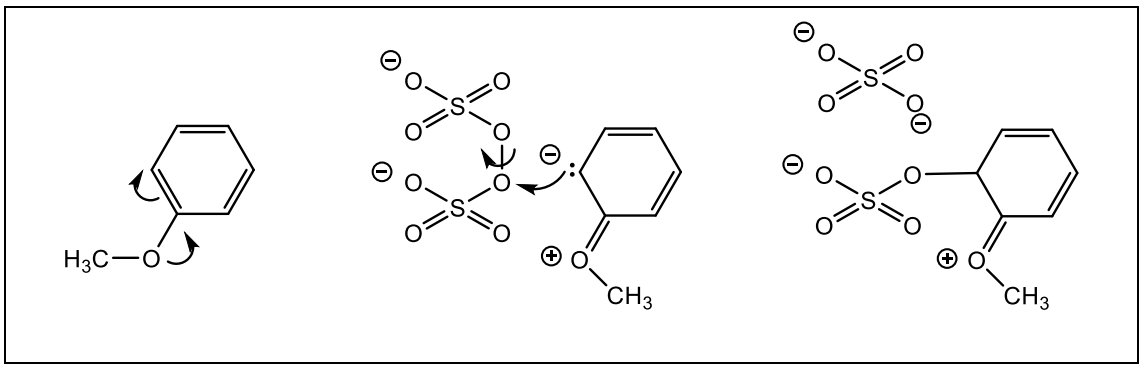
The chemical structures of morphine and codeine were proposed in England by J. M. Gulland and R. Robinson in 1925, [19, 20].

3. Discussion

The electrodotic property [21, 22] of the methoxy group in codeine is the driving force for reaction with the persulphate anion. Being occupied the para-position in codeine, reaction occurs at ortho-position, C-2. Figure 2.

The oxygen atoms in the peroxo group act in similar manner as the chlorine atoms in the chlorine molecule, that is, as a chloronium-chloride pair, [23, 24]. One oxygen receives the electrons formed at C-2, occurring sulfation, and the other oxygen from the peroxo group is eliminated as sulphate ion.

Hydrion elimination from C-2 restores aromaticity and the positive charge at oxygen is neutralised. The next step is acid hydrolysis of the sulphate at C-2. Protonation of the oxygen linked to the aromatic ring produces a δ+ at the sulphur atom in union with the effect of the sulphonyl group. This enhances addition of water and separation of 2-hydroxy-codeine. Hydrion interchange in the inorganic moiety eliminates the oxonium ion and gives sulphuric acid. The observed orange colour in the test is due to halochromism, (25).



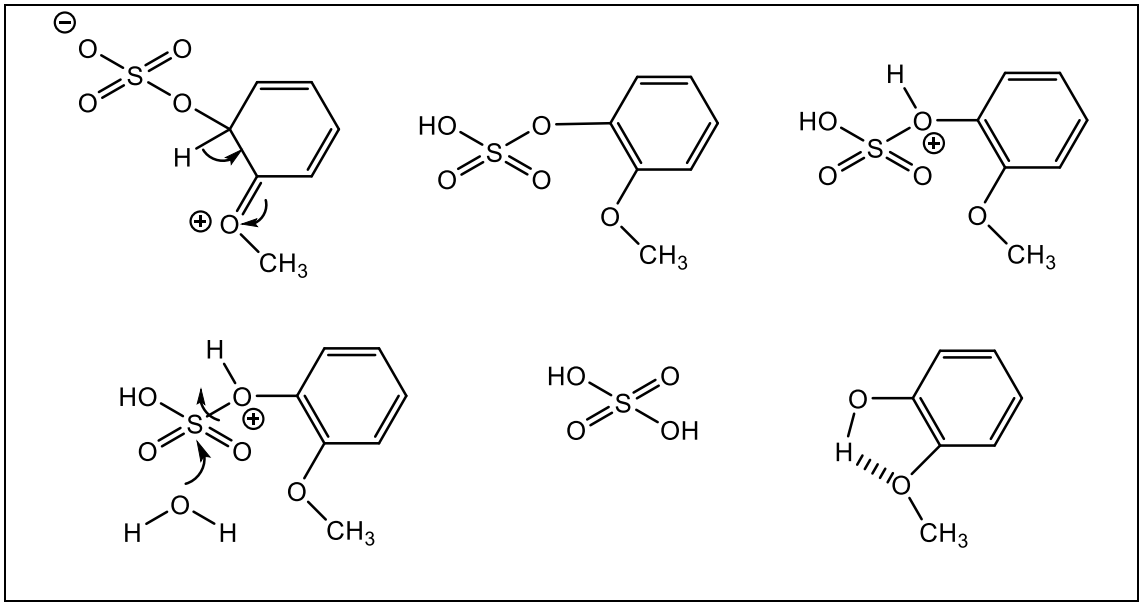


Figure 2 Interaction of codeine with ammonium persulphate in acid medium

4. Conclusion

The chemistry of the Orlow-Horst test for codeine has been cleared. It is a double variation of the Elbs reaction, using a phenol ether and acidic medium instead of the free phenol and alkaline medium. There is sulfation at ortho position because para position is occupied. Finally, there is acid hydrolysis of the sulphate at C-2. The observed orange colour in the test is due to halochromism.

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] Robiquet PJ. New Observations on the Principal Products of Opium. Chapter IV. Ann. de Chim. et de Phys. 1832; 51(2): 261-264.

[2] Wisniak J. Pierre Robiquet. Chemical Education. Mexico, 2013; 24(51): 139-149.

[3] Merck E. Merck´s List of reagents. Springer, Darmstadt, 1903; 107.

[4] Cohn AI. Test and Reagents. J. Wiley & Sons. New York, 1903; 222.

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

[6] Sánchez-Viesca F, Gómez R. On apomorphine detection by colour reactions. J. Chem. Biol. and Phys. Sci. 2024; 15(1): 001-005.

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

[8] Sánchez-Viesca F, Gómez R. Mechanism of the interaction of alkaline tungstate with uric acid. J. Chem. Biol. and Phys. Sci. 2024; 14(4): 311-315.

[9] Sánchez-Viesca F, Gómez R. The mechanism of Frabot test for uric acid. Earthline J. Chem. Sci. 2023; 10(1); 125-130.

[10] Merck E. Merck´s List of reagents. Springer, Darmstadt, 1903; 97.

[11] Cohn AI. Test and Reagents, J. Wiley & Sons. New York, 1903; 202.

[12] Anderson Th. On the constitution of codeine and its product of decomposition. IV. Action of nitric acid, Trans. Royal Soc. Edinb. 1853; 20(1): 69-70.

[13] Sánchez-Viesca F, Gómez R. The chemistry of Anderson´s test for codeine. Int. J. of Scholarly Res. in Chem. and Pharm. 2023; 03(01): 01-04.

[14] Marshall H. Contributions from the Chemical Laboratory of the University of Edinburg. J. Chem. Soc., Trans. 1891; 59: 771-786.

[15] Ammonium peroxydisulphate. https://byjus.com>chemistry>ammonium-persulfate

[16] Gowan JE, Wheeler TS. Name Index of Organic Reactions. Longmans, London, 1960; 79.

[17] Surrey AR. Name Reactions in Organic Chemistry, 2nd ed. Academic Press, New York, 1961; 88.

[18] Hassner A, Namboothiri I, Golan M. Organic Synthesis Based on Name Reactions, 4th ed. Amsterdam, Elsevier, 2025.

[19] Gulland JM, Robinson R. Morphine structure. Chem. Abstr. 1926; 20, 765.

[20] Holleman AF. Wibaut JP. Organic Chemistry, Elsevier, New York, 1951; 617-620.

[21] Luder WF, Zuffanti S. The Electronic Theory of Acids and Bases, 2nd ed. Dover, New York, 1961; 71.

[22] Merriam Webster Dictionary, electrodotic, meaning. Springfield, Mass, 2024.

[23] Packer J, Vaughan J. A Modern Approach to Organic Chemistry. Clarendon, Oxford, 1958; 56.

[24] Baker JW. Electronic Theories of Organic Chemistry. Clarendon, Oxford, 1958; 210.

[25] Pesez M, Poirier P. Methods and Reactions of Organic Analysis. Masson, Paris, 1954; 3, 227.