The Mechanism of the Davy Test for Strychnine

.

ABSTRACT

The chemistry of a spot test for identification of a bioactive compound is important the more if the substance is strychnine. This converts the test in a toxicological assay with forensic application. The Davy test is based on the oxidation of strychnine by means of potassium ferricyanide in the presence of sulphuric acid. This Theoretical Organic Chemistry study reveals the reaction series that occurs during the test, the electron flow is provided step by step. The process is an electron-transfer oxidation, from the alkaloid to the multi-functional final product having two lactams, a ketone and a carboxylic acid. The involved reactions are electrophilic attack to double bond, hydrogen elimination, free radical subtraction, isomerization, alcohol oxidation, epoxide formation, hydrolysis, concerted reaction mechanism to ketone and aldehyde via carbon-carbon fission, and oxidation of aldehyde to carboxylic acid. All is in accordance with the chemical deportment of the involved compounds and is supported by the references.

Keywords: 1,4-addition, epoxidation, lactam formation, ring opening, alcohol and aldehyde oxidation

1. INTRODUCTION

The Davy test for strychnine identification, based on the colours produced by means of potassium ferricyanide and sulphuric acid, is a very sensitive reaction. It has advantages over the test that employs potassium dichromate/sulphuric acid; notwithstanding, the latter has got a good reception.

It is important ascertain what is happening in a spot test, the more if a violent poison as strychnine is involved. It is used to exterminate undesirable animals.

The reaction series occurs via radical-ion mechanism due to the one-electron abstracting property of potassium ferricyanide.

This communication is a follow up of our studies on reaction mechanism, [1-5].

2. ANTECEDENTS

The test under study is due to the Irish chemist Edmund William Davy (1826-1898), Professor of Forensic Medicine in Dublin, [6]. He published his test in a Dublin medical journal [7]. This communication was reproduced in London [8,] and in Philadelphia, USA [9]. This indicates the importance conceded to his work. The test is also mentioned in analytical records [10-12].

The test is as follows: to a little of strychnine in powder or small crystals a drop of undiluted sulphuric acid is added, and a minute particle of potassium ferricyanide should then be dropped. A magnificent violet colour is developed, of considerable permanence and very intense. This gradually passes to a brick-red (crimson), then to a scarlet-red which remains for a number of hours.

The violet colour is less fleeting than in the Lefort test: potassium dichromate/sulphuric acid, [13-14], and the test is equal in delicacy to the latter. Besides, the new test is less affected by organic matter, that is, the presence of a little alcohol, ether or sugar with strychnine. In

* Tel.: +xx xx 265xxxxx; fax: +xx aa 462xxxxx.
E-mail address: xyz@abc.com.

the Lefort test these substances destroy the test and instead of the violet colour, a green is produced. However, the dichromate test has gained acceptance [15-16].
There is an interesting commentary on the colour tests for strychnine, [17].
Now let's see the reagent, potassium ferricyanide, formerly called red prussiate of potash. There are many examples of reactions employing it but in alkaline medium, [18]. In the reaction of potassium ferricyanide with sulphuric acid alone hydrogen cyanide is evolved, [19]. There is a book about the chemistry of the cyano complexes of the transition metals, [20], as well as general information [21].

3. DISCUSSION

The strychnine molecule has the following functional groups: a lactam, a cyclic ether, a double bond, and a tertiary amine, Fig. 1.

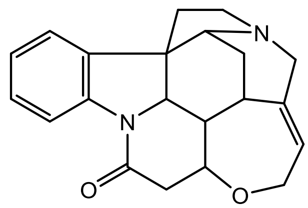

Fig. 1 Structure of strychnine

The oxidation product isolated from potassium permanganate oxidation exhibits a carbonyl group vicinal to the tertiary nitrogen, that is, a new lactam group. There are also a ketone and a carboxylic acid. An uptake of four oxygen atoms and loss of two hydrogen atoms has occurred, [22]. Since ferric compounds are powerful oxidants, potassium ferricyanide, a one electron abstracting reagent [23] will accomplish the described oxidations to the final product. On the other hand, the functional groups obtained are in the higher oxidation state, so there will be no further oxidation.
The reaction goes as follows, Fig. 2**:** electrophilic attack of the ferricyanide anion to the strychnine double bond, **a**, affords a tertiary carbonium ion and a free radical, **b**. Neutralization by proton elimination yields an enamine, **c** with orbital overlap between the electron pair on nitrogen and the π-electrons of the double bond, compare [24]. This is why the exocyclic double bond is preferred to an endocyclic one, more distant to the nitrogen atom.
The remaining electron is captured by Fe3+ and the resulting carbocation **d** is neutralized by the enamine. The iminium group is neutralized by water, **e**: a carbinol amine is formed, **f** and oxidized to carbonyl, a conjugated lactam being formed, **g**. Acid catalyzed hydration of this system yields an allylic alcohol **h**, whose oxidation gives rise to an epoxide, **i, j, k**, compare a similar mechanism [25].
Ring opening of the oxirane affords a vicinal diol, **l**. Oxidation of the less hindered alcohol leads to a positive charged oxygen atom, **m** that promotes a concerted mechanism. A ketone and an aldehyde are formed via C-C fission, **n**. Finally, the aldehyde is oxidized to carboxylic acid, **o**.
Being strychnine potent venom not difficult to obtain, it has been used in many murders. Thus, a toxicological test for strychnine identification is very useful in legal chemistry.

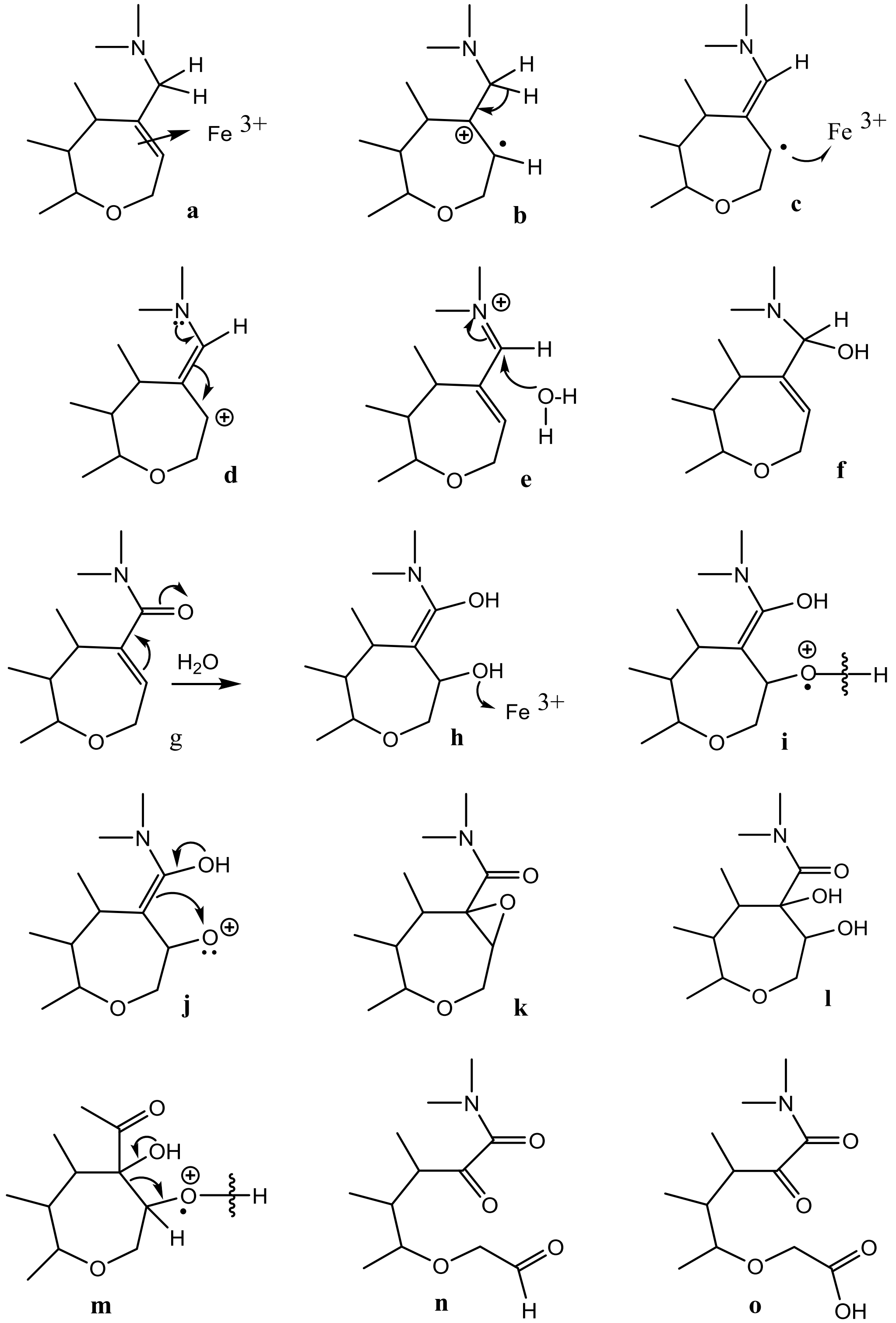

Fig. 2 Reaction route of the successive oxidations of strychnine in Davy test

4. CONCLUSION

Davy employed potassium ferricyanide for strychnine identification. Being the reagent a potent oxidizer, strychnine undergoes successive oxidations, gaining four oxygen atoms and losing two hydrogen atoms. The reactions go through radical-ion mechanism due to the one-electron abstracting property of the ferricyanide anion. The reaction course is electrophilic attack to the double bond, enamine formation, electron subtraction, isomerization, hydration, oxidation, epoxide formation, hydrolysis and a concerted 4-member mechanism involving C-C fission.

This way the route from the alkaloid to the penta-functional final product has been provided. Each step is fully commented and the electron flow is given.

The observed colours come from the alkaloid (halochromism) not from the inorganic reagents since the colours are the same in the dichromate test and in the ferricyanide test. In the latter the first colour is not Prussian blue because it turns to crimson and then to scarlet.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Sánchez-Viesca F, Gómez R. The chemistry of the Weyl-Salkowski test for creatinine. Am. J. Chem. 2021; 11(1): 18-21.
2. Sánchez-Viesca F, Gómez R. On the formation mechanism of indigo blue and indigo red from vegetable source. Modern Chemistry. 2021; 9(4): 88-91.
3. Sánchez-Viesca F, Gómez R. On the oxido-degradation of emetine. Magna Scientia Adv. Res. & Rev. 2021; 02(01): 045-049.
4. Sánchez-Viesca F, Gómez R. The chemistry of van de Moer test for cytisine. Earthline J. Chem. Sci. 2021; 6(1): 15-22.
5. Sánchez-Viesca F, Gómez R. The chemistry of Crismer's test for glucose in urine. OAR J. Chem. & Pharm. 2021.; 01(02): 005-008.
6. Mollun Ch. It's part of what we are. Science and Irish Culture. Vol. 1, p 148. Dublin: Royal Dublin Society; 2007.
7. Davy EW. On a new method of detecting strychnia and its salts. Dublin Quart. J. Med. Sci. 1853; 15: 494-495.
8. Davy EW. On a new method of detecting strychnia and its salts. The Chemist: J. Chem. Phil., London. 1852-1853; New Series, 4: 396-397.
9. Davy EW. A new mode of detecting strychnia and its salts. Am. J. Pharm., Philadelphia. 1853; 25: 414-415.
10. Davy E. Strychnine as a poison. Northwestern Med. & Surg. J., Chicago. 1855; 12: 77.
11. Strychnine, Chemistry of and tests for. Index-Catalogue of the Library of the Surgeon-General's Office. U,S, Army. Vol. 13, p. 835. Washington: Government Printing Office; 1892.
12. Cohn AI. Tests and Reagents. New York: J. Wiley & Sons, 1903; 54.
13. Wilder HM. List of tests (reagents) arranged in alphabetical order according to the names of the originators. New York: P. W. Bedford, 1885; test 444.
14. Cohn AI. Tests and Reagents. New York: J. Wiley & Sons, 1903; 175.
15. Paech K, Tracey MB, Eds. Modern Methods of Plant Analysis, vol. 4.Cromwell BT. The Alkaloids. III, the detection of strychnine. 2. Colour tests, p.483. Berlin: Springer; 1980.
16. Johnson CA, Jones ADTh. Drug Identification. London: The Pharmaceutical Press, 1966; 49.

17. Guy WA, Cantab MB. On the colour tests for strychnia. Pharm. Journal & Trans., London. 1862; Second Series, 3: 12.
18. Fieser LF, Fieser M. Reagents for Organic Synthesis. New York: J. Wiley & Sons, 1967: 929-933.
19. Bassett H, Corbet AS. The hydrolysis of potassium ferricyanide by sulphuric acid. J. Chem. Soc., Trans., 1924; pp 1358-1366.
20. Sharpe AG. The Chemistry of Cyano Complexes of the Transition Metals. London: Academic Press; 1976.
21. Kwong HL. Potassium Ferricyanide, in Paquette L, Ed. Encyclopedia of Reagents for Organic Synthesis. New York: J. Wiley & Sons; 2004.
22. Hoffmann RW. Classical Methods in Structure Elucidation of Natural Products. Zürich: Wiley-VCH, 2018; 19: 193-197.
23. Waters WA. Mechanism of Oxidation of Organic Compounds. London: Methuen & Co, 1964; 87.
24. Packer J, Vaughan J. A Modern Approach to Organic Chemistry. Oxford: Clarendon Press, 1958; 616-617.
25. Sánchez-Viesca F, Gómez R. On the mechanism of uric acid oxidation with lead dioxide and with alkaline hydrogen peroxide. Indian J. of Adv. in Chem. Sci. 2020; 8(3): 78-80.

APPENDIX