Magna Scientia Advanced Research and Reviews

eISSN: 2582-9394

Cross Ref DOI: 10.30574/msarr

Journal homepage: https://magnascientiapub.com/journals/msarr/

(RESEARCH ARTICLE)

On the chemistry of creatinine detection via oxaziridine intermediate

Francisco Sánchez-Viesca * and Reina Gómez Gómez

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

Magna Scientia Advanced Research and Reviews, 2025, 13(02), 058-061

Publication history: Received on 09 February 2025; revised on 02 April 2025; accepted on 05 April 2025

Article DOI: https://doi.org/10.30574/msarr.2025.13.2.0044

Abstract

In this communication the chemistry of the interaction of creatinine with mercuric cyanide in alkaline medium is described. The separation of elemental mercury is idoneous for a chemical test and also is a hint of what is happening at least in one step. The separation of mercury was taken in advantage by Snapp for his test. Its chemistry is as follows: a hydroxide is added to the imino group present in one of the two tautomeric forms of creatinine. After hydrion transfer an amino group and an alkoxide are formed. The last ion reacts with mercury cyanide eliminating a cyanide ion. The resultant organometallic intermediate is prone to cyclisation because besides the electrodotic effect of the amino group, the δ^- in the cyano group produces a δ^+ in the mercury atom. The last two joined effects facilitate the withdrawal of cyanide ion and elemental mercury, this being equivalent to a good leaving group which is necessary for oxaziridine formation (imine oxide). Finally, isomerisation via ring opening of the oxaziridine gives 2-hydoxylamino-creatinine.

Keywords: Electrodotic effect; Elemental mercury; Hydrion transfer; Imine oxide; Mercuric cyanide; Organometallic intermediate; Oxaziridine

1. Introduction

Serum creatinine, a blood measurement, is an important indicator of kidney function. Creatinine is a byproduct of muscle metabolism that is excreted by the kidneys. It is removed from the blood by the kidneys. If filtration in the kidney is deficient, blood creatinine concentrations rise, [1]. Figure 1.

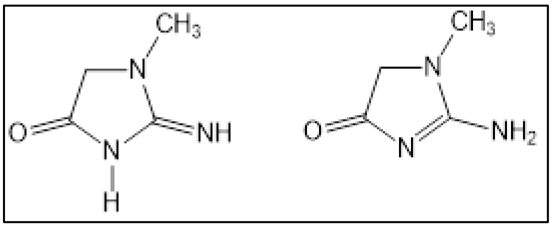

Figure 1 Tautomeric structures of creatinine

A normal blood serum creatinine level for adults is 0.7 – 1.3 mg/dL for men; and 0.6 – 1.1 mg/dL for women, [2].

A normal creatinine level in urine is 930 – 2,955 mg/24 hour for males; and 601 – 1,781 mg/24 hour for females, [3].

* Corresponding author: Francisco Sánchez-Viesca

Knapp test for creatinine is based on the reduction of mercuric cyanide to elemental mercury in alkaline medium, [4]. In this communication the reaction mechanism of this test is provided. It is a follow up of our studies on reaction mechanism, [5-9].

2. Study Method and Process

This is a Theoretical Study involving both Organic and Inorganic Chemistry. It is based on the chemical deportment of reagent and substrate. All is in accordance with the reaction medium and the nature of the oxidizer employed. The steps leading to the final product are entirely commented, as well as the reaction mechanism.

3. Antecedents

The test under study is due to Professor K. Knapp and it is as follows: dissolve 10 g of mercury cyanide with 100 ml of sodium hydroxide solution (D = l.145) in enough water to make a litre. This reagent is reduced upon warming with creatinine, metallic mercury precipitating.

Some remarks on the reagent. Mercuric cyanide is an odourless, poisonous, white powder. It is highly soluble in polar solvents such as water, alcohol, and ammonia. $Hg(CN)_2$ molecules are linear, both in the solid state as in aqueous solution, [10]. Mercuric cyanide is formed from aqueous hydrogen cyanide and mercuric oxide, [11]. It rapidly decomposes in acid to give off hydrogen cyanide. It is used in germicidal soaps, photography, and making cyanogen gas.

The electronic configuration of mercury is $[Xe]4f^{14}5d^{10}6s^2$, [12].

4. Discussion

In this test, the initial reaction site is the imine, more reactive than the lactam, a cyclic amide. Figure 2.

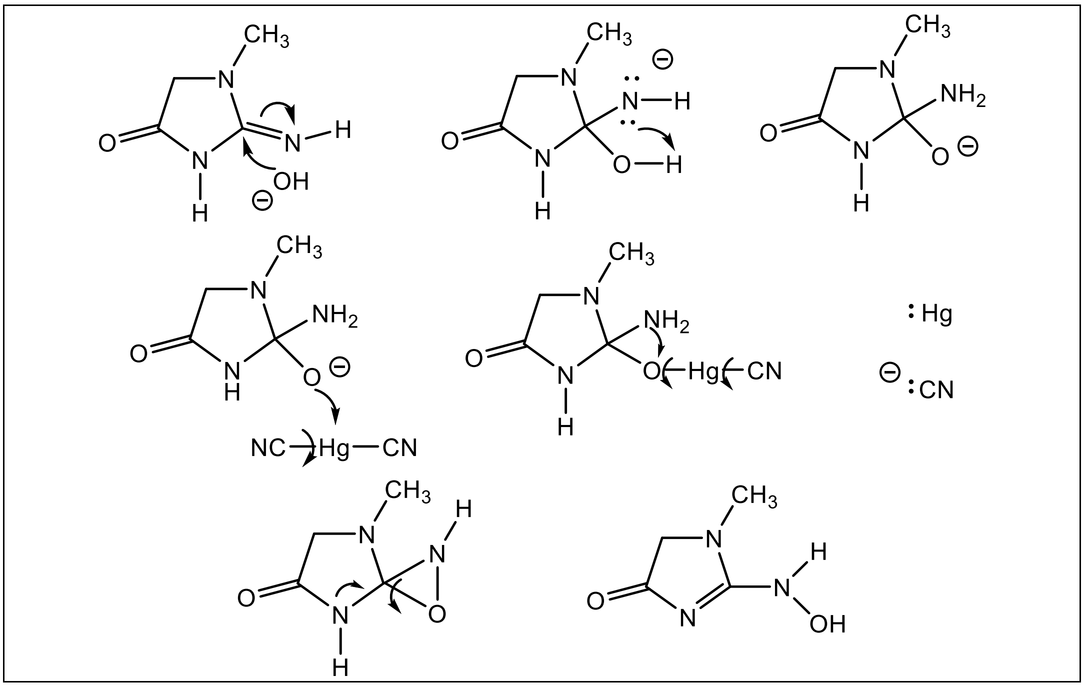

Figure 2 Reaction of creatinine with mercury cyanide in alkaline medium

The hydroxide adds to the imino group and there is hydrion interchange to amino and alkoxide groups. The last one, not being able to eliminate a negative NH_2^- reacts with mercury cyanide, displacing one CN group. In this organometallic intermediate there is formation of a three-member ring, an oxaziridine. Thus, an imine oxide has been formed (oxidation step). This reaction has been possible due to the existence of a good leaving group that forms elemental mercury and a cyanide anion.

Finally, the free electron pair of the N-3 nitrogen forms a double bond with simultaneous ring opening to a hydroxylamine. This way 2-hydroxylamino-1-methyl-imidazoline-4-one has been formed.

This reaction sequence is similar to imine oxidation employing peracid, [13]. The imine is protonated at the nitrogen and the per-carboxylate is added to the carbonium ion. The electrodotic property of the nitrogen [14, 15] forms the small ring oxaziridine by elimination of a carboxylate.

Most of the products obtained have a substituent at nitrogen, and anhydrous peracetic acid has been used, [16].

There are four important differences in the chemistry of the studied test. First, the involved nitrogen has no substituent. This is relevant because the inductive effect of the substituent was not necessary. Second, the reaction conditions were not anhydrous, but watery. Third, the reaction medium was not acidic, but alkaline. Fourth, there is a leaving mercury atom and a leaving cyanide anion, instead of a single leaving group. So, the chemistry of the Knapp test for creatinine is very interesting.

5. Conclusion

The chemistry of Knapp's test for creatinine has been cleared. It is an oxido-reduction process in which the imino group present in one tautomeric form of the compound is oxidized to imino oxide, that is, to an oxaziridine. This transformation occurs via an organometallic intermediate that loses elemental mercury and a cyanide ion (reduction step). Finally, there is isomerization to the 2-hydroxylamino derivative after ring opening.

Compliance with ethical standards

Acknowledgments

Many thanks are given to Luz Clarita.

Disclosure of conflict of interest

There is no conflict of interest to declare.

References

[1] Creatinine. https://en.wikipedia.org/wiki/Creatinine

[2] Blood creatinine level. See: serum creatinine, mayo clinic.

[3] Creatinine in urine: Creatinine, 24 Hour, Urine-Mayo Clinic.

[4] Cohn AI. Tests and Reagents. New York, J. Wiley & Sons, 1903; 158.

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

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

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

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

[9] Sánchez-Viesca F, Gómez R. On the Chemistry of Beckurt´s test for physostigmine: A novel hydride transfer. Magna Scientia Adv. Res. and Rev. 2023; 08(02): 022-025.

[10] Aylett BJ. Mercury (II) Pseudohalides. Comprehensive Inorganic Chemistry, vol. 3: 304-6. Oxford, Pergamon, 1973.

[11] Brauer G. ed. Handbook of Preparative Inorganic Chemistry, 2nd ed. vol. 2, p. 1021. New York, Academic Press, 1963.

[12] Lee JD. Concise Inorganic Chemistry. London, Van Nostrand, 1964; 192.

[13] Williamson KS, Michaelis DJ, Yoon TP. Advances in the chemistry of oxaziridines. Chem. Rev. 2014; 114(16): 8016-8036.

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

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

[16] Acheson RM. An Introduction to the Chemistry of Heterocyclic Compounds 3rd ed. New York, Wiley, 1976; 46