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)

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The chemistry of the Wender's test for Dulcin

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Open Access Research Journal of Chemistry and Pharmacy, 2023, 04(01), 001–004

Publication history: Received on 10 May 2023; revised on 25 June 2023; accepted on 28 June 2023

Article DOI: https://doi.org/10.53022/oarjcp.2023.4.1.0066

Abstract

The reaction route of Wender's test for Dulcin, p-phenetolecarbamide, is disclosed in this article. The many steps in this interesting oxido-degradation process are fully commented and the electron flow is given. Wender used fuming nitric acid as reagent. A violent reaction takes place; however, the test is safe due to the minute quantity employed of this sweetener. Further addition of phenol solution and sulphuric acid gives a blood-red colour. The reactions that occur are as follows: nitration of the ureido group, nitrous acid removal, nitrate formation, elimination of nitrous acid, nitroso group formation, separation of nitric acid and carbon monoxide, free radical degradation to p-benzoquinone imine, hydrolysis, and formation of red phenoquinone, the colour observed in the test.

Keywords: P-Benzoquinone imine; Free radicals; Nitrourea; Oxido-degradation; P-Phenetolecarbamide; Phenoquinone

1. Introduction

Dulcin is an artificial sweetener about 250 times sweeter than sugar, discovered in 1883 by the Polish chemist Jósef Berlinerblau (1859-1935), [1]. Dulcin is p-phenetolcarbamide, Figure 1.

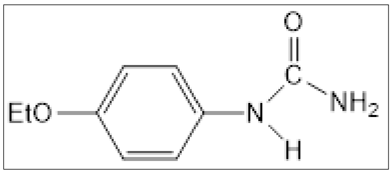

Figure 1 Chemical structure of Dulcin

Dulcin can be prepared by the addition of potassium cyanate to p-phenetidine hydrochloride in aqueous solution at room temperature. Other way is by refluxing an aqueous solution of p-phenetidine hydrochloride with urea during 6 hours, [2].

p-Phenetidine is prepared by reduction of p-nitrophenetole with iron fillings and hydrochloric acid. p-Nitrophenetole is obtained by reaction of p-nitrophenol sodium salt with ethyl chloride in an autoclave, [3].

There is an interesting study about Dulcin, [4]. This compound on treatment with water is hydrolysed to p-phenetidine which reacts with unchanged Dulcin to give the disubstituted product, di-p-phenetole-carbamide. This substance can be converted into the simple carbamide, Dulcin, by heating with urea at 160° under pressure.

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N. Wender found that Dulcin reacts violently by heating it with fuming nitric acid. The residue gives an intense red colour with aqueous phenol and sulphuric acid. In this communication we provide the reaction route of this test, giving the electron flow in each step, explaining why occurs a violent reaction and clearing up the nature of the red colour observed.

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

2. Antecedents

The test under study is due to the German chemist N. Wender. He published his test in 1894 in an analytical journal, [10]. His assay was recorded in a book on tests, in the United States [11], and in a similar book in Germany, [12].

The test is as follows: Treat a trace of Dulcin, one or two crystals, with a few drops of fuming nitric acid in a porcelain evaporating dish, a violent reaction takes place, and an orange-yellow substance result. On evaporating to dryness in the water bath, the residue is varnish-like, orange-yellow, and soluble in alcohol, ether, or chloroform. Treat the residue with 2 drops of phenol solution and 2 drops of concentrated sulphuric acid, a blood-red colour is developed.

Being Dulcin an ureido, the chemical deportment of urea with nitric acid was revised. The reaction of urea with warm dilute nitric acid affords urea nitrate, [13]. Nitrourea is an explosive compound synthesised by. dehydration of dry, powdered, urea nitrate by concentrated sulphuric at -3° C, [14]. Nitrourea appears as a colourless to white crystalline powder, midly sensitive to heat and shock. It is an extremely powerful explosive. Decomposes to emit toxic nitrogen oxide.

There is a Patent for production of nitrourea, [15]. The invention involves the nitration of a sulphuric acid solution of urea. To 425 parts of conc. H_2SO_4 at 0° C, 60 parts of urea were added in small portions and 100 parts of conc. HNO_3 at 0° C were added dropwise with stirring, and continued 30 min. The reaction solution was poured into 525 parts of ice. Nitro urea precipitated, yield 60%.

Nitrous acid is formed in nitric acid oxidations. It decomposes into nitrogen dioxide, nitric oxide, and water. Nitrogen dioxide is a bent molecule that can be represented as a dipolar ion with a free radical at nitrogen or as a free radical at oxygen with no electrical charges. Both structures are resonant, [16]. This light brown-red gas is heavier than air and has a pungent odour.

Nitric oxide is a colourless gas, it is a free radical, very toxic by inhalation.

The successive steps that take place in the reaction of Dulcin with fuming nitric acid are disclosed in the next section.

3. Discussion

The Wender test for Dulcin is carried out at room temperature, without any cooling.

The addition of concentrated nitric acid to an ureido produces a strong exothermic reaction. Thus, addition of fuming nitric acid at room temperature instead of cooling gives rise to a violent reaction that goes farther than substituted nitrourea formation. Figure 2, a, b. The test is safe due to the minute quantity of Dulcin employed.

Nitrous acid is evolved by reaction of the nitro compound with more nitric acid, c (first oxidation step). The resulting positive charged nitrogen at the chain combines with a nitrate anion, d, e. Protonation of the nitrate eliminates nitrous acid with concomitant formation of a nitroso group, f, g (second oxidation step). The high temperature splits off nitric oxide and carbon monoxide, Figure 3 g, h (degradation steps).

The free radical at the nitrogen of phenetidine, i, is stabilized by p-benzoquinone imine formation and elimination of ethyl free radical, j.

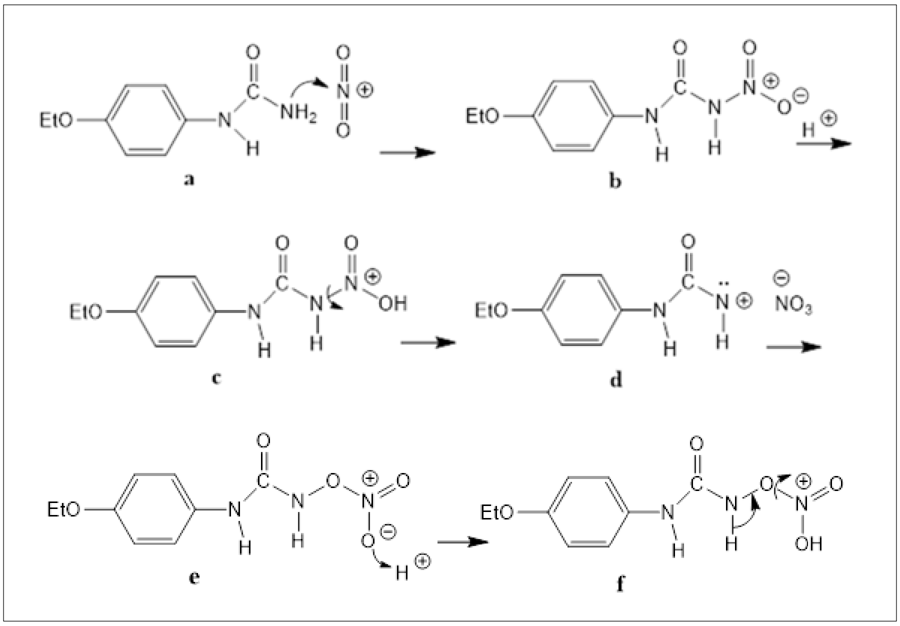

Figure 2 Dulcin oxidation steps

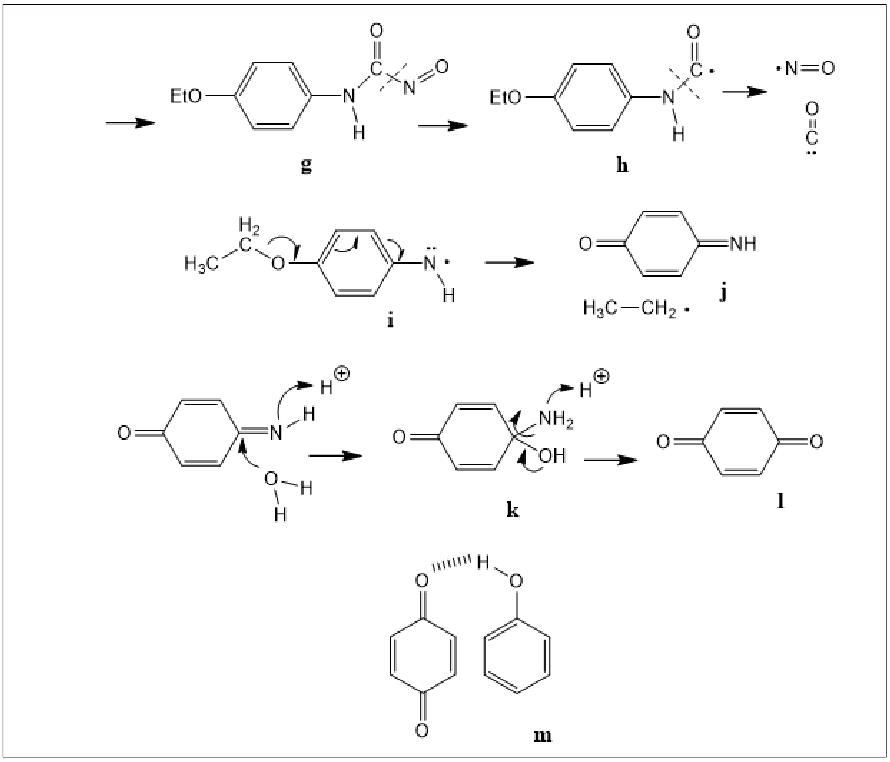

Figure 3 Dulcin degradation steps and red phenoquinone

The second experimental part of the test is addition of a solution of phenol and sulphuric acid to the residue obtained by evaporation to dryness. This produces hydrolysis of the imine to p-benzoquinone, k, l, [17-18], which forms with phenol red phenoquinone, m, [19, 20], that is, the red colour observed in the test.

This way the reaction route of Wender's test for Dulcin has been elucidated, each step is fully commented, and the electron flow has been provided.

4. Conclusion

The mechanism of the Wender test for Dulcin has been cleared up. An oxido-degradation of Dulcin takes place during the assay. Fuming nitric acid not only nitrates the ureido group, but a series of additional reactions also occur. These comprise two steps of nitrous acid elimination, as ell as nitric oxide and carbon monoxide expulsion via homolytic fissions to free radicals. This ´process ends with ethyl radical separation and formation of p-benzoquinone imine. Addition of phenol solution and sulphuric acid hydrolyses the imino group and the resulting phenoquinone is the red product observed in the test.

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.

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