

## On the Interaction of Noscapine (Narcotine) with Ammonium Tellurate in Sulphuric Acid

Francisco Sánchez-Viesca<sup>1,\*</sup> and Reina Gómez<sup>2</sup>

<sup>1</sup>Organic Chemistry Department, Faculty of Chemistry, National Autonomous University of Mexico, Mexico City (CDMX), Mexico; e-mail: franviesca@yahoo.com

<sup>2</sup>Organic Chemistry Department, Faculty of Chemistry, National Autonomous University of Mexico, Mexico City (CDMX), Mexico; e-mail: reinagomezg@yahoo.com.mx

### Abstract

The purpose of this study is to clear up what is happening in the test tube during the interaction of ammonium tellurate with noscapine in sulphuric acid (Brociner test). The approach is a Theoretical Organic Chemistry Study based on the chemical department of reagent and substrate, the reaction medium, and experimental conditions. This point out that a redox process is going up, with the following results: meta-telluric acid is formed in situ whose protonation yields the reactive species. Reaction with the methylenedioxy group present in noscapine affords an oxonium salt. Reaction proceeds when a water molecule forms a hemiacetal and an organometallic ester, a tellurate. Acidolysis of the latter gives rise to a concerted mechanism involving five electron-shifts. This way the following compounds are formed: tellurous acid, an ortho-benzoquinone, and formaldehyde. Tellurium dioxide results by acid catalyzed dehydration of tellurous acid.

### 1. Introduction

Noscapine, also known as narcotine, is the second opioid alkaloid according to its density in raw *Papaver somniferum*, was first isolated by Robiquet in 1817. It is used to suppress cough frequency and intensity in bronchial asthma and pulmonary emphysema, similar to codeine, [1].

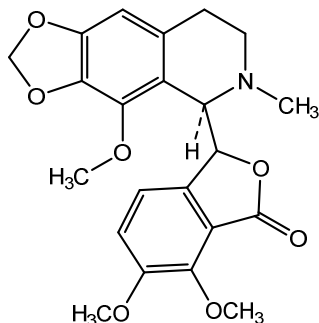
In 1831 Robiquet published a note about narcotine where he remarked that this substance, although perfectly neutral, has the property of combining with acids, largely neutralizing them and forming crystallizable salts, [2, 3].

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\*Corresponding author

It is the first alkaloid to appear in the poppy plant, and may be detected three days after the seeds have sprouted. The mother liquors from morphine production contain narcotine in considerable quantities. It crystallizes from alcohol in colourless prisms, and melts at 175°. Narcotine has no effect on litmus and may be extracted by organic solvents from strongly acid solutions, [4]. Figure 1.



**Figure 1.** The structure of noscapine

In this communication we provide the reaction route of the interaction of noscapine with ammonium tellurate in sulphuric acid.

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

## 2. Antecedents

The test under study is due to Professor Alphonse Brociner, working at the Pharmacy School in Bucharest. He dissolved 1g of ammonium tellurate in 20 ml of concentrated sulphuric acid, choosing the clear solution and leaving the insoluble part. Some salt is decomposed due to the action of the acid, with evolution of tellurated hydrogen. Noscapine gives a very brief rose colour, [10].

Tellurium is a Group 16, Period 5, element. It is classed as a chalcogen and a metalloid with silvery colour. Its electron shells are: 2, 8, 18, 18, 6. The electron configuration is:  $[\text{Kr}] 4d^{10}5s^25p^4$ . Oxidation states: -2, +2, +4, +6, [11]. Its electronegativity according to Pauling is 2.1. Tellurium gives a greenish blue flame when burnt in the air, dissolves in nitric acid, and is used in the manufacture of solar panels although it is a very rare element, [12]. If someone eats a tellurium compound, it gives them garlic breath, [13].

There are two forms of telluric acid.  $\text{Te}(\text{OH})_6$ , often written as  $\text{H}_6\text{TeO}_6$ , is ortho-telluric acid. It is a weak acid and dibasic. It is a crystalline solid. As oxidizer it is

reduced to  $\text{TeO}_2$ . Tellurous acid,  $\text{H}_2\text{TeO}_3$ , contains tellurium in its +4 oxidation state, [14].

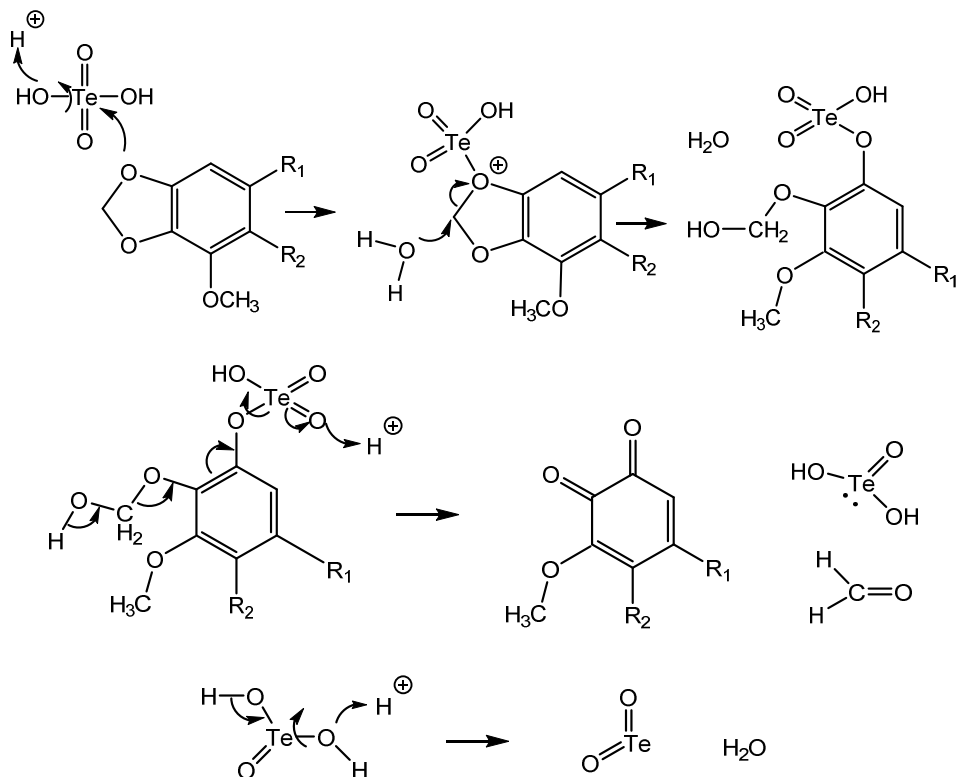
The other form of telluric acid is  $\text{H}_2\text{TeO}_4$ , meta-telluric acid, from which diammonium tellurate derives, [15, 16].

Tellurium dioxide is barely soluble in water and soluble in strong acids. The O-Te-O bond angle is  $140^\circ$ . Single crystals of tellurium oxide have a unique and ordered atomic structure which gives them high optical transparency, [17].

### 3. Discussion

The noscapine molecule has a tertiary amine, a lactam ring which is opened in basic medium, and three methoxy groups that are less reactive than the methylenedioxy group, that is, a benzodioxole, [18, 19].

Thus, the five-member cycle was elected for reaction. Figure 2.

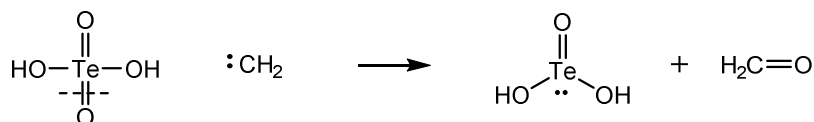


**Figure 2.** Oxidation of noscapine with ammonium tellurate in sulphuric acid.

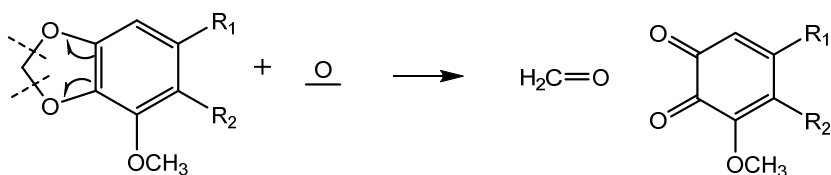
The anion present in ammonium tellurate reacts with sulfuric acid, giving meta-telluric acid whose protonation yields the reactive species that interacts with an oxygen atom of the methylenedioxy group. There is water loosening and formation of an oxonium salt which can explain the transient rose colouration observed in the test and due to halochromism, [20]. Reaction of water at the methylene group yields a hemiacetal and an organic tellurate. Protonation of the Te=O double bond gives rise to a concerted mechanism involving five electron-shifts. Tellurios acid, an ortho-benzoquinone, and formaldehyde are formed (redox reaction).

Dehydration of tellurios acid occurs via protonation of a hydroxy group and water loosening, giving tellurium dioxide. This compound is soluble in the reaction medium, sulphuric acid.

The reduction of telluric acid and formation of formaldehyde (redox reaction) can be visualized in a simple formulation:



The fragmentation yielding a methylene and the ortho-benzoquinone can be interpreted via a hypothetical free radical mechanism:



These two simple considerations are useful to explain rapidly the stoichiometry of this test.

#### 4. Conclusion

This Theoretical Organic Chemistry Study is based on the different reactivities shown by the functional groups present in the Noscaphine molecule. The methylenedioxy group was selected for reaction initiation due to its greater reactivity compared to that presented by the methoxy groups in other reactions.

Reaction of meta-telluric acid formed in situ produces a coloured oxonium salt when reacts with the alkaloid. Reaction of a water molecule at the methylene group gives rise

to a synchronic mechanism that yields a hemiacetal and an organic tellurate. Acidolysis of this reaction intermediate affords tellurous acid, an ortho-benzoquinone, and formaldehyde (redox step). Finally, tellurous acid can be dehydrated to tellurium dioxide.

## 5. Conflicts of Interest

There are no conflicts to declare.

## 6. Acknowledgement

Thanks are given to Martha Berros for support.

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