



(RESEARCH ARTICLE)



## On the formation of Oxydimorphine (pseudomorphine, 2.2'-bimorphine)

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### Abstract

In Beckurt's test for alkaloids the substance for assay, generally a salt, is treated with a 0.1 N solution of potassium permanganate. In his study he used the hydrochloride of the alkaloid. In this communication the reactivity of both reagent and substrate have been checked and commented. The electron donor property of the phenol in morphine is enhanced by reaction with a weak base such as water. A phenoxy ion and a hydronium ion are formed. Resonance produces a carbanion at C-2 which transfers an electron to permanganate ion. This reduction to manganate is concomitant to oxidation of the organic molecule. The free radical thus formed is stabilized by electron coupling and 2,2'-bimorphine is obtained.

**Keywords:** Carbanion; Electron coupling; Electron donor; Hydrochlorides; Manganate; Potassium permanganate

### 1. Introduction

Morphine is a well-known alkaloid used in Medicine as a potent analgesic, as well as a street drug (abuse drug). Due to the last use, it is very important depend on rapid and simple procedures for the detection of this substance. Thus, many field tests have been developed for morphine identification, in which a colour is produced in the test tube, avoiding the use of expensive and inconvenience apparatus.

In this communication, the Beckurt test for alkaloids has been inspected. He employed a 0.1 N solution of potassium permanganate, which is dripped to the hydrochloride of the assayed alkaloid. The result is variable, depending on the alkaloid employed. It can be separation of brown manganese dioxide, red or green colouration, or separation of white solid. With morphine there is separation of white oxydimorphine. This case is studied in the present article.

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

### 2. Study Method and Process

This is a Theoretical Study involving both Organic and Inorganic Chemistry. It is based on the chemical department 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 products are entirely commented, as well as the reaction mechanism.

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### 3. Antecedents

The test under study is due to Heinrich Beckurt (1885-1929), Professor of Pharmaceutical Chemistry at Braunschweig, Germany. His test for alkaloids was published in *Pharmacognosy, Pharmacy, and Toxicology Advances* [6], and was registered in a book of chemical tests, [7].

Some notes about the end product. Oxydimorphine is also known as pseudomorphine, and dehydromorphine. There is an interesting article on this compound [8], which was discovered by Pelletier, [9]. Experimental data on this product have been given, [10]. The structure of pseudomorphine was published in England, [11]. The determination of morphine has been done by means of potassium ferricyanide [12], via formation of pseudomorphine. A better name is 2,2'-bimorphine.

Remarks on the reagent. The electronic configuration of manganese K, L, M, N shells is: 2-8-13-2. The manganese subshells are: [Ar] 4s<sup>2</sup>3d<sup>5</sup>, [13].

Ground state electronic configuration of Mn<sup>7+</sup> ion: [Ar] 3d<sup>0</sup>4s<sup>0</sup>.

In manganate ion, Mn<sup>6+</sup>, there is a 3d<sup>1</sup> subshell. Due to the one unpaired electron, it is paramagnetic, attracted to a magnetic field [14, 15].

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### 4. Discussion

The semi-systematic name 2,2' bi-morphine is very important since it indicates the union sites in each morphine molecule, which is not the case with the three other names for this compound.

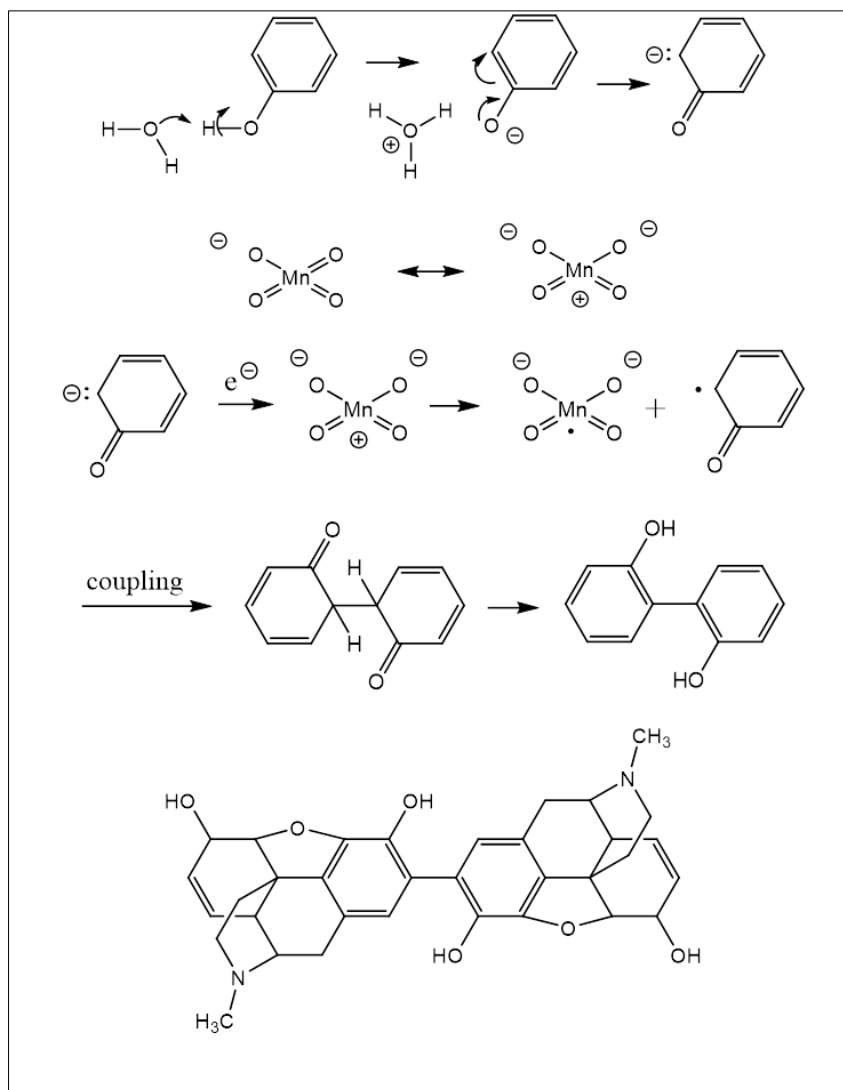
The electrodotic effect [16] of the phenol group at C-3 is responsible of carbanion formation at C-2, preferably in alkaline medium. However, in water solution, the hydrogen in the OH of phenol can break away in the presence of this weak base. A phenoxide ion and a hydronium ion are formed, [17]. Figure 1.

The reactivity of phenol group in acidic medium is interesting since protonation of the electron donor phenolate would diminish its reactivity. Notwithstanding, phenol can be nitrated in dilute nitric acid to o- and p-phenol, and in strong nitric acid to 2,4,6-trinitro-phenol [18]. This is explained as follows: the phenoxide ion formed by reaction with water is rapidly stabilized by resonance to carbanion, less stable and thus more reactive. Interaction with a nitronium ion (nitration step) occurs previously to protonation of the phenolate.

Protonation of phenols is difficult because the lone pair of electrons on the oxygen are delocalized due to resonance. This facilitates electrophilic substitution or other reactions.

The phenolic group at C-3 in morphine forms a carbanion at C-2 in similar ways as just described. Beckurt employed a KMnO<sub>4</sub> solution as reagent and this is reduced to manganate by one-electron transfer from the secondary carbanion (oxidation of the organic molecule). The electron configuration of manganate ion is given in 'Antecedents'. The remaining free-radical at C-2 is stabilized by coupling, yielding the dimerization product (2,2'-bimorphine) after enolization of the two intermediate ketones. The dimer is transoid in order to eliminate repulsion between the ketones. Sigma radicals are very reactive because there is no stabilization by resonance.

The solubility of morphine in water is very low (1g/5L) and it is considered insoluble, [19]. The morphine salts such as hydrochloride and sulphate are around 300 times more water soluble than the parent molecule [20], 10.2 mg/mL, [21]. That's why Beckurt used morphine hydrochloride.



**Figure 1** Reaction route of 2,2'-bimorphine formation

## 5. Conclusion

The reactivity of both substrate (morphine) and reagent (potassium permanganate) were checked carefully, as well as, the electron configuration of one of the end products (potassium manganate).

A morphine salt (morphine hydrochloride) was chosen by Beckurt because of the great solubility of this compound compared to the parent substance.

The reaction occurs via carbanion formation at C-2 and redox reaction of this reactive intermediate with permanganate ion. Potassium manganate and a free radical in the organic molecule are formed. The last species is stabilized by electron coupling. Carbanion formation is independent of acidic medium and reacts with an electrophile present.

## Compliance with ethical standards

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*Disclosure of conflict of interest*

There is no conflict of interest to declare.

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