
Chapter 1. Introduction

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Painting: "Vasco Da Gama Before The Zamoric Of Calicut" By Jose Maria Veloso Salgado, Showing Hysterical Moment In 1497, When Vasco Da Gama, A Portuguese Explorer Became 1st European Who Reached To India By Ocean Route, And Gifted Beautifully Decorated "SILVER MIRROR" To The King Of Calicut.

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1.1 Introduction of Tollens' reaction

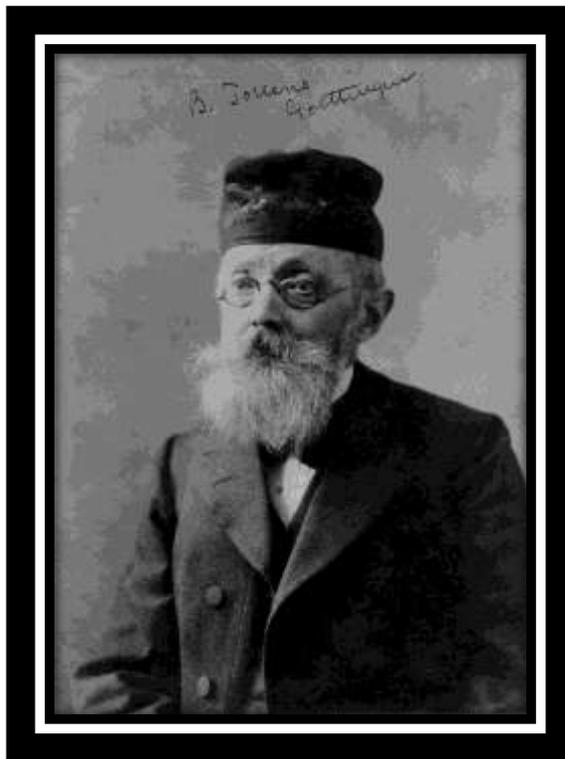


Figure F1.1.1: Photograph of Bernard Tollens¹

The Tollens' reagent is named after its inventor, "Bernard Christian Gottfried Tollens" (1841-1918), for his pioneering efforts. Bernard Tollens was a German Chemist, as shown in Figure F1.1.1, who worked on carbohydrates and investigated structures of several sugars.¹ Tollens' reagent is a silver(I) diammine complex, which is prepared by mixing silver nitrate (AgNO_3), sodium hydroxide (NaOH), and ammonia (NH_3).² On addition of sodium hydroxide to silver nitrate, unstable dihydroxyargentate(I) complex $[\text{Ag}(\text{OH})_2]^-$ forms, which immediately dehydrates to give silver(I) oxide (Ag_2O) water-insoluble brown solid. On addition to aqueous ammonia solution, these brown silver(I) oxide dissolves completely and forms diamminesilver(I) complex $[\text{Ag}(\text{NH}_3)_2]^+$, which is the active component of Tollens' reagent.² The oxidation reactions carried out using the silver ammine complex are known as Tollens' reactions.^{3,4} The traditional ionic equations for the overall reaction are shown below from equ.1-4.

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The Tollens' reagent acts as a mild oxidizing agent and selectively oxidizes aldehydes over ketones, thus used to confirm the presence of aldehydes.² As reaction proceeds, silver forms particles or clusters before aggregate or thin film formation. If the test is carried out in a clean glass test tube, it forms a beautiful shiny mirror on the inner walls of the test tube, therefore also known as the “**silver-mirror test**”, as shown in Figure F1.1.2. Thus, this reagent's overall simplicity and wide applicability made this redox-reaction a common test in undergraduate organic chemistry practical worldwide.⁵ The overall ionic equation for the reaction is shown in equ.5, where R refers to an alkyl or aryl group.⁶



Here, the addition of ammonia for the formation of a linear diamminesilver(I) complex decreases the reduction potential of silver(I), as presented in equ. 6-7.⁷

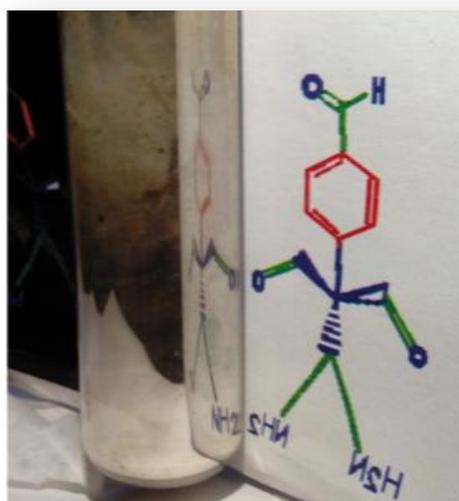
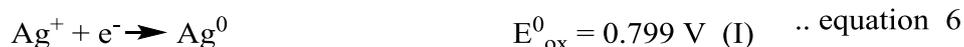


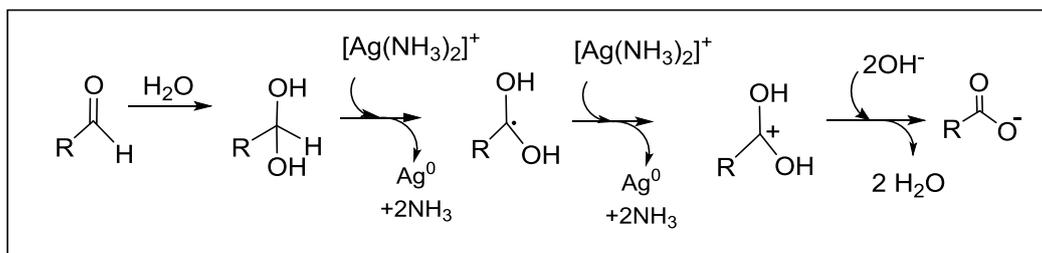
Figure F1.1.2: Photograph of Silver mirror

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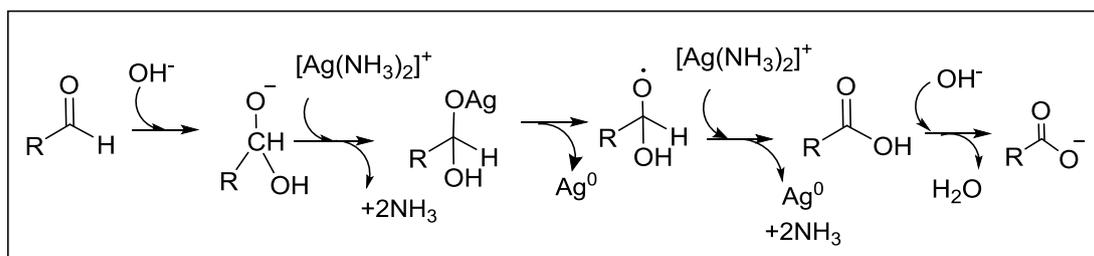
1.1.1 Proposed mechanisms for the Tollens' reaction of aldehyde

Different mechanisms were proposed for Tollens' reaction of aldehyde, which includes a single electron transfer reaction.⁶ The scheme S1.1.1 was proposed as a mechanism for the oxidation of aldehyde. In this mechanism, the *gem-diol* cation behaves as a very weak acid and undergoes radical pathway.

Scheme S1.1.1: Proposed mechanism for Tollens' Reaction



Scheme S1.1.2: Proposed mechanism for Tollens' Reaction

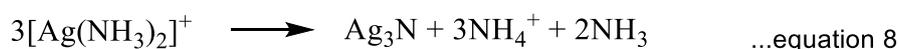


2nd mechanism was proposed as shown in scheme S1.1.2, and the fastened reaction was suggested by the *gem-diol* anion formation on the addition of the base.⁶ The addition of alkali makes the Tollens' test much more sensitive because the rate is much faster. The key feature seems to be the formation of the anion of the gem diol.⁶ The ease of formation of this anion varies with the aldehyde and correlates well with how rapidly it responds to Tollens' test.⁷

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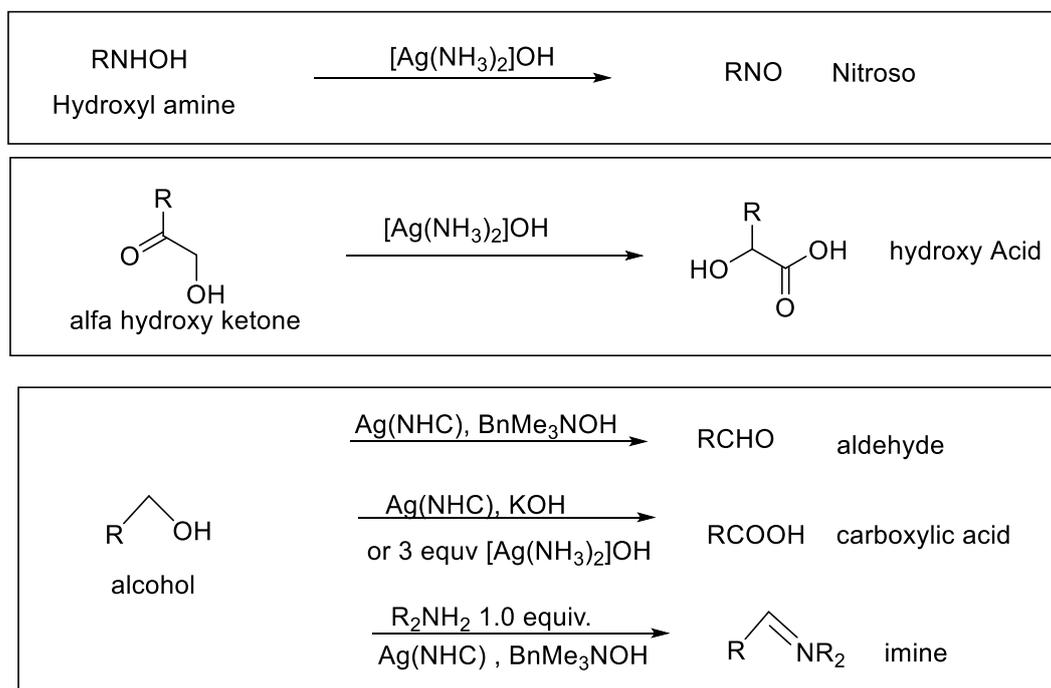
1.1.2 Precautions

Tollens' reagent is not commercially available as it has a short shelf life and can even be explosive. Therefore, it needs to be prepared *in-situ*. Freshly prepared Tollens' reagent is not explosive. But if it is stored longer, it can explode.⁸ Not only Tollens' reagent, but any system containing silver nitrate and liquor ammonia can turn out to be an explosive system if stored for a long time. The formation of silver imide, Ag_3N , and AgN_3 takes place in such systems; they decompose explosively into silver, nitrogen, and hydrogen, as shown in equ.8-9.⁹ Thus fresh reagents must be prepared, and an un-reacted silver ammonia complex should be discarded by treating with HCl.



1.1.3 Reported conversions using Silver ammine complex

Scheme S1.1.3: literature of silver ammine complex-mediated reactions



R, R' = aromatic or aliphatic

Tollens' reagent can oxidize hydroxylamine, α -hydroxyl ketone, and alcohols to nitroso, α -hydroxy acid, and aldehyde /acids compound, as shown in scheme S1.1.3.^{2,10,11} Apart from these, The silver ammine complexes were also reported for alcohol to aldehyde/ carboxylic acid/ imine conversions, by modifying reaction conditions.^{10,12} Interestingly, these tests

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remained unexplored for their exact product formation and detailed mechanism. Apart from this, Tollens' reagent is not explored for other organic transformations.¹¹⁻¹³

1.1.4 Use of Silver ammine complex

Tollens' reagent and its modification received an application in thin silver mirror film formation for the generation of silver nanoparticles synthesis, in the last 3 decades.^{3,7,11,14,15} The literature cites only a few reducing agents for reducing silver ammine complex into metallic silver but explored a range of surfactants and polymer assemblies to control nanoparticles' shape, size, and overall growth.¹⁶⁻¹⁸ This originality in the laboratory for the formation of thin silver film/ metal has opened up several niche applications. Silver has precious properties such as high reflective power, **highest thermal conductivity** 429 W/(m·K) (at 27 °C), **lowest electric** resistivity 15.87 nΩ·m (at 20 °C) of any metals. Silver shows anti-microbial activity.¹⁹⁻²¹ The interdisciplinary nature of this reagent makes it interesting to organic, inorganic, and physical chemistry. In anatomic pathology, ammonical silver nitrate is used in the **fontana-Masson stain**, which is a silver stain technique used in the detection of melamine, argentaftin, and lipo-fucin in tissue section and cancerous cells.²²⁻²⁴

Apart from this, the Tollens' reactions are also used for coating of large objects such as telescopes²⁵, smoothening of micro- or nanostructured surfaces, microcontact printing²⁶, lithography²⁷, Water purification^{28,29}, wound dressings³⁰, flexible electrically conductive fabrics synthesis³¹, solar panels³², wearable electronics³³, photocatalytic applications³, e-textile technologies³⁴, electromagnetic interference shielding³⁵, and other medical instruments³⁶.

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1.2 Thesis outline

The thesis uncovers Tollens' reagent's ability for various transformations, and in general multiple dimensions in chemistry. The present work revolves around an in-depth understanding of Tollens' reaction. The thesis has been arranged into five chapters, in which 1st chapter is an introduction and summary. The specific aims for each chapter have been heightened below:

Chapter-2 deals with exploring Tollens' reagent or silver ammine complex for efficient C-C oxidative coupling of phenol and 2-Naphthol derivatives.³⁷ The optimization of the reaction was carried out and discussed briefly for 2-naphthol. The gram-scale reactions were attempted. After standardizing experimental conditions, the reaction was performed on a total of eight derivatives of naphthol and phenols. The addition of a quantitative amount of NaOH in the *para-para* coupling reaction leads to substantial quinone formation. Total ten C-C oxidative homo-coupled products were isolated with good yields (75-95%), purified, and characterized using mass-spectrometry, FT-NMR (¹H and ¹³C), and FT-IR spectroscopic analysis. The novel catalytic behavior of reagent was realized, where reaction proceeds homogeneously for ensuing complete conversion of reactants and then transforms to heterogeneous condition for easy recovery of the products. The recycling and reuse of reagent have been explored and the silver was quantified using the *conductometric* titration method. The mechanism for the C-C oxidative coupling reaction of 2-naphthol has been proposed.

In chapter-3, Tollens' reagent has been explored for C-C oxidative cross-coupling reactions of phenol and 2-naphthol derivatives. Total six C-C cross-coupled products were obtained quantitatively out of 28 cross-coupling reactions using silver amine complex reagent. These products were characterized using mass-spectrometry, FT-NMR (¹H and ¹³C), and FT-IR spectroscopic analysis. The effect of temperature, dilution, and amount of reagent on product formation has been studied. Based on product formation radical-radical coupling reaction mechanism has been proposed. Then a study was converted into a curious experiment, where coupling reactions carried out in an eppendorf tube (polypropylene surface) resulted in the silver particle formation over the typical formation of a silver mirrored film. This prompted us to carry out the reaction, on different surfaces, such as borosilicate glass, Teflon, eppendorf tube, etc., and observe possible selectivity in the organic product formation. The reactions of selected phenols were attempted over different surfaces, to observe selectivity for

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oxidative C-C homo-coupling and/or C-C cross-coupling of phenol derivatives using the surface as a non-conventional method. By using a plastic or Teflon vessel instead of a typical borosilicate glass vessel (test tube or round bottom flask), the reaction between 2,6-dimethoxyphenol and 2,6-di-*tert*-butyl-phenol yielded 70% to 10% cross-coupled product, respectively. This chemo-selectivity in the cross-coupling is correlated with the growth of silver formation.³⁸ Therefore, deposited/precipitated silver was analyzed through optical microscopy, FE-SEM, and P-XRD analysis. Therefore, to confirm findings, reactions were repeated several times to check reproducibility. A detailed study of surface effect on cross-coupling has been shown, and macroscopic interactions assisted chemo-selective reaction mechanisms has been proposed. Thus present study highlights, the importance of the growth of metallic silver aggregation and its role during concurrent chemo-selective oxidative coupling product formation. To confirm the proposed mechanism, a new synthetic scheme was designed and discussed in chapter 4.

The reaction of Tollens' reagent and 2-Naphthol forms BINOL in the racemic mixture, in normal conditions. Chapter 4 discusses 3 different approaches to obtain optically active/stereo-selective BINOL by modifying Tollens' reaction. In the 1st approach, based on literature, on aiming co-crystallization/diastereomer formation of optically pure BINOL, Reactions (between Tollens' reagent and 2-naphthol) have been attempted (i) by replacing ammonia with chiral amines and amino acids (total 16), and (ii) by adding chiral amines and amino acids (total 16) in the reaction mixture. A brief study shows the formation of optically active BINOL is elusive. In the 2nd and 3rd approaches, based on a previous study (chapter-3) and proposed mechanism, the Tollens' reaction on inorganic chiral surfaces has been studied to obtain stereo-selectivity. The quartz surface and freshly generated **silver-coated surface** (obtained from traditional Tollens' reaction of *D/L*-glucose in a borosilicate glass tube) have been used for the enantioselective synthesis of BINOL. In the former case, the BINOL was obtained with 90-92% yield and up to 57% enantiomeric excess of (*S*)-enantiomer.³⁹ These experiments were repeated several times, and the observed optical purity was calculated based on *polarimetry* analysis. The resultant silver coating and silver particles were analyzed using optical microscopy, electronic microscopy (SEM and FE-SEM), and P-XRD analysis. Aggregate formation of Silver during Tollens' test were correlated as a driving force for enantio-selective BINOL formation, and the mechanism is discussed. Thus, the novel

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efficient methods for the asymmetric synthesis of BINOL without using any extra organic reagents and/or complexes, have been discovered.

Chapter 5 discusses studies of Tollens' reactions, on different aspects of chemistry, as an extensional activity not limited to educational experiments. This chapter is divided into 3 sections: 5.1) Selective oxidation, 5.2) Interesting ways to mix reducing agents with $[\text{Ag}(\text{NH}_3)_2]^+$, and 5.3) synthesis of silver nanoparticles.

- Section-5.1 discusses the chemo-selectivity of Tollens' reagent, which is further divided into two sections. In the 1st study 5.1.1, chemo-selective oxidations of aldehydes versus C-C oxidative coupling of phenol were studied by attempting Tollens' reaction of aldehyde and phenol functionally in (I) two different molecules and (II) same molecule. In 2nd study 5.1.2, the oxidation of aldehyde and alcohol derivatives of hetero-aromatic have been studied. The Tollens' reaction of HMF resulted in chemo-selective FFCA formation, with possible to two ways of mechanism. To confirm it, Tollens' reaction of mono functionalized aldehyde and methanol derivatives (total eight) of other hetero-aromatic compounds was carried out. The products were isolated and analyzed using spectroscopic analysis.
- The part-5.2 presents an experimental demonstration of modified methods to mix Tollens' reagent with reducing agents in interesting ways. The Tollens' reactions were performed by (I) co-spotting Tollens' reagent and phenols on TLC plate, (II) carrying C-C oxidative coupling during sublimation, (III) silver film formation by keeping capillary tubes in the reaction mixture, and (IV) silver film formation on tissue paper: by connecting vial containing Tollens' reagent and reducing agent solution using a paper strip. These methods can find applications in modern-day technologies and are not limited to educational activity
- In part-5.3, the silver nanoparticles have been synthesized using modified Tollens' reagent and studied with various reducing agents due to challenging and fascinating fields. The silver nanoparticles were analyzed using DLS and UV-Spectroscopic analysis. Different sizes of nanoparticles were also synthesized by changing reaction conditions, aldehyde used, and its concentrations.

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