Conference Attended and Paper Presented

1. Presented research paper “Ruthenium(III) mediated oxidation of thiamine hydrochloride by cerium(IV) in perchloric acid medium: a kinetic and mechanistic approach” at *International Conference on Current Trends in Chemistry and Biochemistry*, held at Central College Campus, Bangalore University, Bengaluru from 18\textsuperscript{th} - 19\textsuperscript{th} December, 2009.

2. Presented research paper “Kinetics and mechanism of permanganate oxidation of clopićogrel hydrogen sulfate sulfate – an antiplatelet drug in acid perchlorate solutions” at *29\textsuperscript{th} Annual Conference of Indian Council of Chemists* held at Department of Chemistry, Punjab University, Chandigarh from 19\textsuperscript{th}-21\textsuperscript{st} December, 2010.

3. Presented research paper “Catalytic activity of ruthenium(III) on the oxidation of an anticholinergic drug-atropine sulfate monohydrate by copper(III) periodate complex in aqueous alkaline medium – Decarboxylation and free radical mechanism” at *30\textsuperscript{th} Annual Conference of Indian Council of Chemists* held at Department of Chemistry, Osmania University, Hyderabad from 28\textsuperscript{th} - 30\textsuperscript{th} December, 2011.

4. Presented research paper “Spectral characterization of the binding and conformational changes of bovine serum albumin upon interaction with an antihistamine drug, ketotifen fumarate” at *31\textsuperscript{st} Annual Conference of Indian Council of Chemists* held at Department of Chemistry, Saurashtra University, Rajkot, Gujarat from 26\textsuperscript{th} – 28\textsuperscript{th} December, 2012.
Seminars Attended


Young Scientist Award

Received "Prof. S. C. Ameta Award" for the best oral presentation of paper entitled "Kinetics and mechanism of permanganate oxidation of clopidogrel hydrogen sulfate sulfate – an antiplatelet drug in acid perchlorate solutions’ at 29th Annual Conference of Indian Council of Chemists held at Department of Chemistry, Punjab University, Chandigarh from 19th-21st December, 2010.
Kinetics and Mechanism of Permanganate Oxidation of Clopidogrel Hydrogen Sulfate: An Antiplatelet Drug in Acid Perchlorate Solutions

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ABSTRACT: The oxidation of clopidogrel hydrogen sulfate, commercially known as Plavix, by permanganate ion in aqueous perchloric acid medium at a constant ionic strength (I = 0.06 mol dm \(^{-3}\)) has been investigated spectrophotometrically at 526 nm. The reaction between clopidogrel hydrogen sulfate and permanganate in acid medium exhibits a 5:4 stoichiometry. The identified oxidation products, 4,5,6,7-tetrahydrothieno[3,2-c]pyridine, (2-chlorophenyl)oxoacetic acid, and formaldehyde as a byproduct, are different from those obtained by biological metabolism. The reaction is first-order in MnO\(_4^-\) and less than first-order in both the clopidogrel hydrogen sulfate and H\(^+\) ion concentrations. The active species of permanganate was found to be HMnO\(_4\). The oxidation reaction in acid medium was found to proceed through a permanganate–clopidogrel complex that decomposes slowly in a rate-determining step followed by other fast steps to give the products. The main products were identified by spot test and IR and GC–MS spectral studies. The reaction constants involved in different steps of the mechanism were calculated at different temperatures. The activation parameters with respect to the slow step of the mechanism were computed, and thermodynamic quantities were also determined.

1. INTRODUCTION

Potassium permanganate is widely used as an oxidizing agent in both synthetic and analytical chemistry and also as a disinfectant. Among the six oxidation states of manganese from 2+ to 7+, permanganate, Mn(VII), is the most potent oxidation state in both acidic and alkaline media. Oxidation by permanganate ion finds extensive application in organic synthesis. In general, the reduction of permanganate in slightly basic or neutral solution and in acid media goes through Mn(IV) and Mn(II), with reduction potentials of 1.695 V for Mn(VII)/Mn(IV) and 1.51 V for Mn(VII)/Mn(II). In acid medium, permanganate exists in different forms, namely, HMnO\(_4\) and H\(_2\)MnO\(_4^+\), and depending on the nature of the reductant, the oxidant has been assigned both inner-sphere and outer-sphere mechanism pathways in their redox reactions.

Clopidogrel hydrogen sulfate (d-methyl[2-chlorophenyl]-5-(4,5,6,7-tetrahydrothieno)[3,2-c]pyridinyl acetate hydrogen sulfate) (C HS) is a thienopyridine prodrug used clinically to inhibit ADP-induced platelet aggregation. Clopidogrel is inactive in vitro and requires in vivo oxidation by hepatic/intestinal cytochrome P450 isoenzymes. The majority of clopidogrel is hydrolyzed by esterases to an inactive carboxylic acid derivative that accounts for 85% of the clopidogrel-related compounds circulating in plasma. P450 catalyzes the oxidation of the thiophene ring of clopidogrel to 2-oxo-clopidogrel. The 2-oxo intermediate is then oxidized further by P450. The second oxidation results in opening of the thiophene ring to form both a carboxyl group and a thiol group. The thiol group forms a disulfide bond with the P2Y\(_12\) ADP receptor on platelets. The biological metabolism of clopidogrel is depicted in Scheme 1.

Clopidogrel hydrogen sulfate is freely soluble in water, but its solubility is strongly pH-dependent. The site of absorption of such drugs is restricted to the acidic environment of the stomach, and the bioavailability varies according to the actual pH of the gastrointestinal tract. The aqueous solution of clopidogrel hydrogen sulfate (100 mg/mL) is strongly acidic. Adjustment of the pH toward a physiologically acceptable value sharply decreases the solubility of the salt; above pH 5, the base form of the drug, which has a gummy consistency, is precipitated. The base form of the drug is practically insoluble in water, with a solubility of less than 0.02 mg/mL. A literature survey reveals that there are no reports on the oxidation of clopidogrel by any oxidant in either acidic or alkaline medium. In view of the potential pharmaceutical importance of clopidogrel and the lack of reported kinetic and mechanistic data on the oxidation of this drug by oxidants other than those involved in biological metabolism, a detailed oxidation study might elucidate the mechanism of conversion of such compounds. The present investigation is aimed at checking the reactivity of clopidogrel toward permanganate in acid medium, determining the redox chemistry of Mn(VII) in such media, and establishing a plausible mechanism.

2. EXPERIMENTAL SECTION

2.1. Materials and Reagents. All chemicals were of analytical reagent grade, and doubly distilled water was used throughout this work. An aqueous solution of clopidogrel hydrogen sulfate (C HS) (Viva Drugs Pvt. Ltd.) was prepared by maintaining the pH lower than 1.0. The purity of the drug was checked by comparing its IR spectrum and melting point with the literature data (mp 177 °C, lit 178 °C). Permanganate stock solution was obtained by dissolving potassium permanganate (Glaxo, Analar) in water and standardized by titrating with oxalic acid. Freshly prepared and standardized permanganate solutions were always used in the kinetics experiments. Manganese(II) solution was prepared and standardized permanganate solutions were always used in the kinetics experiments. Manganese(II) solution was prepared and standardized permanganate solutions were always used in the kinetics experiments. Manganese(II) solution was prepared and standardized permanganate solutions were always used in the kinetics experiments.

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Oxidation of a Anticholinergic Drug Atropine Sulfate Monohydrate by Alkaline Copper(III) Periodate Complex: A Kinetic and Mechanistic Study

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1. Introduction

Atropine, one of the solanaceous alkaloids, contains two cyclic structures, the alicyclic nitrogen-containing alcohol tropine and the aromatic tropic acid, joined by an ester linkage [1]. The most common atropine compound used in medicine is atropine sulfate monohydrate (ASM) (C17H23NO4, HSO4, H2O, the full chemical name is 10H,h2H-Tropan-3-a-ol(±)-tropate(estcr), sulfate monohydrate. The structure is shown below.

Atropine is found in many members of the Solanaceae family. The most commonly found sources are Atropa belladonna, Datura inoxia, D. metel, and D. stramonium. It is a secondary metabolite of these plants and serves as a drug with a wide variety of effects. It is a competitive antagonist for the muscarinic acetylcholine receptor. It is
Ruthenium(III) mediated oxidation of thiamine hydrochloride by cerium(IV) in perchloric acid medium: a kinetic and mechanistic approach

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Abstract Oxidation of thiamine hydrochloride (vitamin B₁) by cerium(IV) mediated by micro amounts (10⁻⁶ mol dm⁻³) of ruthenium(III) in aqueous perchloric acid medium has been studied spectrophotometrically at 25 °C and I = 1.10 mol dm⁻³. The reaction is first order in both cerium(IV) and ruthenium(III) concentrations. The order with respect to vitamin B₁ concentration varies from first order to zero order as the vitamin B₁ concentration increases. An increase in perchloric acid concentration decreases the reaction rate. The active species of oxidant and catalyst are [Ce(OH)³⁺] and [Ru(H₂O)₆]³⁺. A possible mechanism is proposed and reaction constants involved have been determined. The activation parameters for the slow step of the mechanism are determined.

Keywords Kinetics · Thiamine hydrochloride (vitamin B₁) · Cerium(IV) · Ruthenium(III) catalysis

Introduction

Thiamine hydrochloride is known as vitamin B₁. It was the first member of vitamin B family to be isolated and identified as a vitamin. Ruthenium(III) is an efficient catalyst in many redox reactions involving different complexities due to the formation of intermediate complexes, free radicals and multiple oxidation states of ruthenium [1]. Cerium (IV) is a well known oxidant in acidic media [2] having a reduction potential [3] of 1.70 V for the couple cerium(IV)/cerium(III) and is stable only at high acid concentration. In sulfuric acid and sulfate media, cerium(IV) forms several sulfato complexes [4, 5]. Similarly, in perchloric acid solutions [6], cerium(IV) exists as Ce⁴⁺, Ce(OH)³⁺, (Ce–O–Ce)⁶⁺ and Ce(OH₂)³⁺. A later potentiometric study [7] of the hydrolysis of cerium(IV) showed that Ce(OH)³⁺ was the predominant active species of cerium(IV) in the concentration range 0.30–2.0 mol dm⁻³ of perchloric acid, but its role has not received much attention so far. The oxidation of thiamine hydrochloride with alkaline potassium ferricyanide [8],

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