In the Name of God

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Faculty of Chemistry

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Electrochemical Study of Catechol Derivatives in Unbuffered, Borax Buffer and in the Presence of Various Nucleophiles

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Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of Doctor of Philosophy (Ph. D.) in Analytical Chemistry

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To my parents,

for their endless love

and patience

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List of Publications:

1) D. Nematollahi and M. Rafiee, *Catalytic Oxidation of Thiourea at Alumina Modified Pt Electrode*, ***Sensors***, 3 (2003) 534-543.

2) D. Nematollahi and M. Rafiee, *Electrochemical Oxidation of Catechols in the Presence of Acetylacetone*, ***J. Electroanal. Chem.***, 566 (2004) 31-37.

3) D. Nematollahi, D. Habibi, M. Rahmati and M. Rafiee, *A Facile Electrochemical Method for Synthesis of New Benzofuran Derivatives.* ***J. Org. Chem.***, 69 (2004) 2637-2640.

4) D. Nematollahi, M. Rafiee and A. Samadi-Maybodi, *Mechanistic Study of Electrochemical Oxidation of 4-tert-Butylcatechol. A Facile Electrochemical Method for the Synthesis of New Trimer of 4-tert-Butylcatechol*, **Electrochemica Acta**, 49 (2004) 2495-2502.

5) D. Nematollahi, A. Afkhami, F. Mosaed and M. Rafiee, *Investigation of the Electro-oxidation and Oxidation of Catechol in the Presence of Sulfanilic Acid*, ***Res. Chem. Intermed.***, 30 (2004) 299-309.

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7) *Diversity in electrochemical oxidation of dihydroxybenzoic acids in the presence of acetylacetone. A green method for synthesis of new benzofuran derivatives*, D. Nematollahi and M. Rafiee, ***Green Chemistry***, 7 (2005) 638–644.

8) M. Rafiee, *Electron: the simplest chemical reagent (Spotlight)*, ***Synlett*** 3 (2007) 503–504.

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10) D. Nematollahi, A. Alimoradi and M. Rafiee, *Kinetic study of electrochemically induced Michael reactions of o-quinones with 2-acetylcyclohexanone and 2-acetylcyclopentanone,* ***J. Phys. Org. Chem.***; 20 (2007) 49–54.

11) M. Rafiee, D. Nematollahi, *One-Pot Synthesis of Highly Conjugated Benzofuran Derivatives Based on Electrochemical Oxidation of Benzenediols in the Presence of Dibenzoylmethane,* ***Chem. Pharm. Bull.***, 55(2007), 915-917.

12) M. Rafiee, D. Nematollahi *Voltammetry of electro-inactive species using quinone/hydroquinone redox: A known redox system viewed in a new perspective,* ***Electroanalysis***, 19 (2007), 1382-1386.

13) M. Rafiee, D. Nematollahi, *Electrochemical Study of Boric acid Complex with Substituted Catechols,* ***Electrochim. Acta.*** In press.

14) D. Nematollahi, M. Rafiee and *H.R. Khavasi, Electrochemical Oxidation of 4-methylcatechols in the Presence of β-diketones,* ***Adv. Synth. Catal.,*** submitted.

Abstract

In this thesis, application of electrochemical methods, such as cyclic voltametry described to obtain some kinetic and thermodynamic information about chemical reactions. Also, the application of electrochemical methodes in organic synthesis are examined.

In chapter 2, electrochemical behavior of *p*-benzoquinone, hydroquinone and quinhydrone complex have been investigated in aqueous unbuffered solutions. The results revealed that in unbuffered solution the half wave potential of hydroquinone has a significant difference with quinone's half wave potential. It is shown that, added acid in an unbuffered solution of Q, give rise to a new reduction peak at a more positive potential than original reduction peak of Q. The half-peak potential of this new peak depends on acidity of added acid (pK_a) and its height is proportional to the acid concentration. Also, added base in an unbuffered solution of H_2Q, give rise to a new oxidation peak at a more negative potential than the original oxidation peak of H_2Q. The half-peak potential of this new peak is dependent on basicity of the added base (pK_b) and its height is proportional to the base concentration.

In chapter 3, the electrochemical behavior of catechols-boric acid complex in aqueous solutions has been studied using cyclic voltammetry and steady-state voltammetry at the rotating disk electrode. Different pattern of reactivity and various kinetic pathways has been examined. According to a CE mechanism, the dissociation constant and homogeneous rate constants of complex formation and dissociation were estimated for each pathway by comparing the experimental cyclic voltammograms with the digitally simulated results. Also the effects of pH and substituted groups on dissociation constants and reaction kinetic were studied.

In chapter 4, the reaction of electrochemically generated *o*-benzoquinones, as Michael acceptors, with 2-acetylcyclohexanone and 2-acetylcyclopentanone, as nucleuphiles, has been studied in various pHs using cyclic voltammetry. The results indicate that the participation of *o*-benzoquinones in the Michael reaction with acetylcyclohexanone to form the corresponding catechol derivatives. Based on an EC mechanism, the homogeneous rate constants were estimated by comparing the experimental cyclic voltammetric responses with the digital simulated results.

In chapter 5, electrochemical oxidation of dihydroxybenzoic acid derivatives of benzoic acid have been studied in the presence of acetylacetone as nucleophile in aqueous solutions, using cyclic voltammetry and controlled-potential coulometry. The results indicate that the quinones derived from dihydroxybenzoic acids participate in Michael addition reactions with acetylacetone and via various mechanisms convert to the corresponding benzofurans. In this work, we derived various products with good yields based on electrochemical oxidation in the controlled potential condition in aqueous solutions, without toxic reagents and solvents using environmentally friendly method.

In chapter 6, electrochemical oxidation of benzenediols has been studied in the presence of dibenzoylmethane as a nucleophile using cyclic voltammetry and controlled-potential coulometry. The results indicate that the electrochemically generated quinones participate in Michael addition reaction with dibenzoylmethane via various mechanisms to produce new benzofuran derivatives.

In chapter 7 Electrochemical oxidation of 4-methylcatechol in the presence of, benzoylacetone, dibenzoylmethane, 3-hydroxy-1*H*-phenalen-1-on, acetylacetone, dimedone and 2-acetylcyclohexanone as nucleophiles has been studied in detail by cyclic voltammetry and controlled-potential coulometry. The results indicate that the electrochemically generated quinones participate in Michael addition reaction with these nucleophiles via various mechanisms to produce new organic compounds. The results show that structure of intermediates and their interactions are very effective on formation of final product in controlled potential conditions. We obtained various products based on selective oxidation in the controlled potential condition, at carbon electrode in an undivided cell.

In chapter 8, electrochemical oxidation of catechols has been studied in the presence of cyanoacetone and methyl cyanoacetate as nucleophile in aqueous solution, by means of cyclic voltammetry and controlled-potential coulometry and digital simulation. Overall reaction is ECEC mechanisms and final products are nitrile containing benzofuranes. The rate constants of first intermolecular and second intramolecular Michael addition were obtained by digital simulation, also the ability of desierd rection to production of some functionalize benzofurans were examined.

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Chapter 1

Introduction

1.1. Electrosynthesis

Organic electrochemistry is concerned with the reduction or oxidation of organic molecules at electrodes. Although the electrochemical community has just celebrated the 200th anniversary of the discovery of the Volta pile, it wasn't until 1830-1850 that the investigation of organic electrochemical processes, pioneered by Faraday and Kolbe.

The study of organic electrode processes has nevertheless received considerable attention up to end of the 19th century and general laboratory practice of organic chemistry made very little use of electrochemical methods. Maybe this is one important reason that mechanistic organic electrochemistry was only in its infancy and that the problem of formulating mechanisms in this field is of enormous complexity due to the heterogeneity of the electrode process.[1]

Toward the end of the 19th century, investigators such as Tafel and Haber made significant contributions to the knowledge of organic electrode processes. Haber, for instance, in his now famous paper on the reduction of nitrobenzene (Z Elektrochem 4: 506, 1898), recognized the significance of the electrode potential. The application of electrolysis as a means of preparing organic compounds continued in the first half of the 20th century. This development took place along with the invention of new electroanalytical techniques for the study of electrode processes, for instance, polarography at the dropping mercury electrode introduced by Heyrovsky in the early 1920s. Other important contributions were made by Lingane, Kolthoff, Laitinen, and Delahay. The theoretical foundations, for the analysis of kinetics and mechanisms by, for instance, cyclic voltammetry and related techniques were mostly published in the 1960s and 1970s. Follow were a period of intense activity in the calculation of the electrode response for many different mechanisms. Most notable of the large volume of papers published are those of Nicholson and coworkers [2-4] and of the Saveant group [5,6].

The application of such techniques has resulted in a steadily increasing understanding of the kinetics and mechanisms of organic electrochemical processes. Parallel to the development of electrochemical techniques for investigation of reaction mechanisms, advantage and adaptability of electrosyntheses were shown by many scientists. Then electrosynthesis convert to noteworthy method for organic synthesis.

Figure. 1.1 Manuel M. Baizer (1914-1988) was the foremost internationally recognized authority on electrosynthesis.

Among the electrochemists that work on development of electrochemical synthesis professor Manuel M. Baizer, well known for his contributions to preparative organic electrochemistry, his foremost achievement being the development of the electrohydrodimerization of acrylonitrile into a highly successful industrial process for the manufacture of adiponitrile.

Now electrochemistry is an esteemed method in organic synthesis. Sometimes, when common synthetic methods fail, electrochemistry is chosen as a last possibility, which often leads to success but also to disappointment due to the high expectancy. Additionally, there are features of organic electrochemistry that cannot be compared with organic chemistry because they are unique to this field and have no counterpart elsewhere in common chemistry. The reactive intermediates can be generated, which in another way are not or only in a limited extent accessible, such as radical ions. Mechanisms can be studied in otherwise not accessible depth from time-resolved electrical signals of starting materials, products, or intermediates. [7]

Electro-organic reactions may be conveniently classified on the basis of chemical reaction into the following categories:

1. Conversion reactions (one functional group into another one),
2. Substitution reactions,
3. Addition reactions,
4. Elimination reactions,
5. Coupling reactions,
6. Cleavage reactions,

All of these reactions types can be affected at the cathode or the anode. However, since organic electrode processes often occur via a blend of radical and ionic mechanisms, it should be stressed that the simplicity of the classification scheme above does not imply that the electrochemical oxidation or reduction of a given substrate results in only one type of reaction.[1]

Electrosynthetic techniques such as electrogeneration of base, anodic oxidation, and ac (alternating current) synthesis provide simple and inexpensive alternative routes to the synthesis of many inorganic materials such as thin films, coatings, nanoparticulate, metastable phases and metallic complexes. [8] But in this thesis (section), we survey illustrative examples to highlight the potential application of these techniques in organic synthesis.

1.2. Study of Electrochemical Reactions

1.2.1. Cyclic voltammetry

Electrochemical methods are widely used to gain information about the kinetics and mechanisms of chemical reactions associated with the electron transfer at an electrode. A unique feature of these methods is that the electrode serves both as the means of generating an intermediate, for instance a radical ion, and as the means to monitor its reactions to products. Many electrochemical techniques presented for study of chemical reactions but cyclic voltammetry has become a very popular technique for initial electrochemical studies of new systems and has proven very useful in obtaining information about fairly complicated electrode reactions. Organic and inorganic chemists often use cyclic voltammetry to determine redox properties, electronic states, and reactivities of electroactive species, including unstable intermediates.

Voltammetry in unstirred solution where the predominant mode of mass transport is limited to diffusion is one of the most useful techniques for the study of electrochemical reactions. Most often, a triangular potential-time waveform with equal positive and negative slopes is used, and usually also the initial potential ($E_{initial}$) and final potential (E_{finail}) are the same as illustrated in Figure 1.2.