

D. Kyriacou

Modern Electroorganic Chemistry



SPRINGER
LAB MANUAL



Digitized by the Internet Archive
in 2022 with funding from
Kahle/Austin Foundation

<https://archive.org/details/modernelectroorg0000kyri>

UNIVERSITY COLLEGE OF THE CARIBOO LIBRARY
BOX 3010, KAMLOOPS, B.C.
V2C 5N3

7364

SPRINGER LAB MANUAL



Demetrios Kyriacou

Modern Electroorganic Chemistry

UNIVERSITY COLLEGE OF THE CARIBOO LIBRARY
BOX 3010, KAMLOOPS, B.C.
V2C 5N3

With 16 Figures

Springer-Verlag
Berlin Heidelberg New York London Paris
Tokyo Hong Kong Barcelona Budapest

Professor DEMETRIOS KYRIACOU

University of Massachusetts
Department of Chemistry
One University Avenue
Lowell, MA 01854, USA

ISBN 3-540-57504-9 Springer-Verlag Berlin Heidelberg New York
ISBN 0-387-57504-9 Springer-Verlag New York Berlin Heidelberg

Library of Congress Cataloging-in-Publication Data. Kyriacou, Demetrios K. Modern electroorganic chemistry/Demetrios Kyriacou. p. cm. – (Springer laboratory) Includes bibliographical references. ISBN 0-387-57504-9 1. Organic electrochemistry. I. Title. II. Series. QD273.K98 1994 547.1'37 – dc20 94-13316

This work is subject to copyright. All rights are reserved, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting reuse of illustrations, recitation, broadcasting, reproduction on microfilm or in any other way, and storage in data banks. Duplication of this publication or parts thereof is permitted only under the provisions of the German Copyright Law of September 9, 1965, in its current version, and permissions for use must always be obtained from Springer-Verlag. Violations are liable for prosecution under the German Copyright Law.

© Springer-Verlag Berlin Heidelberg 1994
Printed in Germany

The use of general descriptive names, registered names, trademarks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

Typesetting: Best-set Typesetter Ltd., Hong Kong
51/3130-5 4 3 2 1 – Printed on acid-free paper

Preface

The last two decades (1970–1990) have probably seen more reviews and books about electroorganic chemistry than any other such short period in the history of this special branch of organic chemistry. The continuous progress in organic electrochemistry certainly requires frequent exposition and systematization of the new knowledge in the form of readily accessible up-to-date textbooks that could serve as guides and references for the expert and the neophyte alike.

In preparing this book as a retired industrial chemist, I had primarily in mind the widest possible community of industrial researchers and practitioners in the chemical and closely related biochemical, pharmaceutical and agrochemical fields. Organic electrochemical methodology can contribute very significantly to these fields, technologically and economically, and especially as regards the efforts toward a clean manufacturing technology. I would also hope that advanced students in the aforementioned fields would benefit from using the book in their studies as a textbook and a reference.

The book consists of five chapters. The first chapter is a synoptic introduction to organic electrochemistry. The second and third chapters deal separately with anodic and cathodic reactions of synthetic interest. The reactions are conveniently classified on the basis of functional groups in the organic molecules. Selected representative preparative examples are described in detail for illustrative purposes. The fourth and fifth chapters are concerned with indirect electrochemical reactions and some interesting special topics.

I would like to express my thanks to the Department of Chemistry of the University of Massachusetts Lowell for providing the necessary facilities for this work. Also, I thank Eleni, my wife, for her devoted efforts in the preparation of the manuscript. I thank professor E.G.E. Jahngen for valuable discussions.

Lowell, Massachusetts
May 1994

DEMETRIOS KYRIACOU

Contents

1	Introduction	1
1.1	Electroorganic Chemistry. Historical Perspective	1
1.2	Pertinent Fundamental Concepts and Principles in Organic Electrochemistry	2
1.2.1	The Overall Cell Reaction	2
1.2.2	The Generalized Electroorganic Reaction	3
1.2.2.1	Electrochemical Couplings and Cross Couplings	6
1.2.2.2	The Electron Transfer Step. Basic Qualitative Description	6
1.2.3	Thermodynamic and Kinetic Aspects	7
1.2.3.1	Nernstian Equation. Electrode Potential	7
1.2.3.1a	Free Energy of Cell Reaction and Cell Potential	9
1.2.3.2	Kinetic Aspects	10
1.2.4	Preparative Electrolysis under Activation (Kinetic) or Mass-Transfer Controlled Conditions	12
1.2.5	The Electrical Double Layer and its Significance in Electrosynthesis	14
	References	17
2	Anodic Reactions	18
2.1	Fundamental Nature	18
2.2	Hydrocarbons	19
2.2.1	Saturated Hydrocarbons	19
2.2.2	Unsaturated Hydrocarbons	22
2.2.3	Functionalizations of Hydrocarbons	25
2.3	Hydroxy Compounds	28
2.4	Oxidations at Oxide Covered Electrodes	30
2.5	Phenolic Compounds	36
2.6	Carbonyl Compounds	43
2.7	Carboxylic Acids	47
2.7.1	General Perspective	47
2.7.2	Oxidations in Fluorosulfuric Acid	52
2.7.3	Kolbe Synthesis in SPE Cells	52
2.7.4	Photokolbe Synthesis	54
2.8	Amines and Amides	54

2.8.1	Amines, in General	54
2.8.2	Amides	57
2.9	Ethers and Esters	60
2.10	Organic Halides	63
2.10.1	Alkyl Halides	63
2.10.2	Aromatic Halides	64
2.11	<i>N</i> -Heterocyclics	65
2.12	Organosulfur Compounds	74
2.12.1	Sulfides	74
2.12.2	Thiolates and Dithianes	75
2.12.3	Sulfonium Salts	77
2.13	Anodic Cyanations	79
2.14	Acetoxylation and Acetamidations	83
2.14.1	Acetoxylation	83
2.14.2	Acetamidations – Electrochemical Ritter-Type Reactions	86
2.15	Anodic Halogenations	88
2.16	Hydroxylations	91
2.17	Alkoxylation	92
2.18	Pyridinations	100
2.19	Nitrations	101
	References	102
3	Cathodic Organic Reactions	110
3.1	Phenomenological Nature	110
3.2	Carbon-Hydrogen Bond Formations, Unsaturated Systems	111
3.3	Carbonyl Compounds	113
3.3.1	General Reduction Mechanism	113
3.3.2	Reactions via the Carbonyl Electrophore	114
3.4	Carboxylic Acids and Esters	119
3.4.1	Preparation of Metal Carboxylates and Metal Alkoxides	120
3.4.2	Reduction of Esters	121
3.5	Organohalides	122
3.5.1	General Electroreduction Mechanism	122
3.5.2	Products from Aromatic and Aliphatic Halides	122
3.5.3	Various Reductive Dehalogenations	127
3.5.4	Electrohydrogenolysis of Polyhalogenated Compounds	128
3.5.5	Electrochemically Induced Nucleophilic $S_{RN}1$ Substitutions	131
3.5.6	Organic Fluorides	133

3.6	Nitrocompounds	133
3.6.1	<i>N</i> -Heterocyclizations	134
3.6.2	Reduction on Transition Metal Electrodes	138
3.7	<i>N</i> -Heterocyclics and Other Heteroatom Structures	138
3.7.1	Pyridines, Purines, and Similar Compounds	138
3.7.2	Pyridinium and Similar Salts	141
3.7.3	<i>N</i> -Heterocyclics with Carbonyl Groups	142
3.8	Organosulfur Compounds	145
3.9	Some Special Cleavages of C—O Bonds in Hydroxy Compounds	148
3.9.1	Cleavage of Ethers	150
3.10	Electrocarboxylations	150
3.10.1	Electroreduction of Carbon Dioxide	150
3.10.2	CO ₂ as Electrophile	151
3.10.3	Photoelectrochemical Reduction of Carbon Dioxide	153
3.11	Nitriles and Oximes	154
3.12	Various Cathodic Couplings	155
3.12.1	Acylation	155
3.12.2	Organophosphorus Compounds	156
3.12.3	Arene-Metal Complexes	157
3.12.4	Cathodic Reactions (Couplings) of Organometallics	158
	References	160
4	Indirect Electroorganic Reactions (Indirect Electrolysis)	166
4.1	Introduction	166
4.1.1	Basic Mechanisms	166
4.2	Oxidative Indirect Reactions	169
4.2.1	Metallic Ions and Oxyanions Mediators	169
4.2.2	Paired Oxidative Processes	172
4.2.3	Halide Ions as Mediators	174
4.2.4	Nitrate Ion as Mediator	178
4.2.5	Organic Mediators for Oxidations	178
4.3	Indirect Reductive Reactions	182
4.3.1	Metallic Ions as Catalysts	182
4.3.2	Reductions with Amalgams	185
4.3.3	Reductions with Diborane Formed in Situ	186
4.3.4	Organic Mediators	187
	References	188
5	Some Special Topics Relevant to Electrosynthesis	192
5.1	Electrolysis in Two-Phase Solvent Systems	192
5.2	Solid Polymer Electrolyte – Electrolysis	194
5.3	Reactions via Electrode Dissolution	196

5.4	Electropolymerizations. Conductive Polymers	198
5.4.1	General View	198
5.4.2	Conductive Polymers	201
5.5	Applications of Electrochemical Methodology to the Synthesis of Natural Products	203
5.6	Electroreductive Cyclizations for Natural Product Synthesis (Little-Baizer ERC Reaction)	206
5.7	Electrogenerative Systems	208
5.8	Electrogenerated Bases	212
5.9	Electroreduction of Enones (α,β -Unsaturated Ketones) ...	214
5.10	Oxygenations. The Superoxide Ion	215
	References	219
	Subject Index	225

1 Introduction

1.1 Electroorganic Chemistry. Historical Perspective

Electroorganic chemistry is a multidisciplinary science overlapping the vast fields of organic chemistry, biochemistry, physical chemistry and electrochemistry. As a branch of organic chemistry its principal practical aim is to enhance synthetic organic methodology in all its aspects.

Although as a pure science it has advanced to a very respectable status, as a technology, unfortunately, it has not, despite the fact that it is an old technology. Industrially, it is limited to the manufacture of some high-cost chemicals and pharmaceutical intermediates and perhaps a small number of specialty products.

Actually thousands of organic electrochemical transformations have been achieved in the laboratory but only relatively few of them advanced beyond the laboratory, apparently because of economic and technical barriers. The continuing progress in the fields of chemical engineering and materials science should provide the stimulus for the development of electroorganic technology on a much broader scale than has been possible heretofore.

The first electroorganic synthesis was performed by Michael Faraday (1834). It was the anodic decarboxylation of acetic acid in aqueous medium, and the formation of ethane via creation of a new carbon-carbon bond:



Henry Kolbe (1849) electrolyzed fatty acids and half-esters of dicarboxylic acids and established the practical basis of electroorganic synthesis. Near the end of the 19th century various electrolytic industrial processes emerged, mostly reductive, stimulated by the pioneering works of Kolbe, Haber, Fichter, Tafel and other notable contemporaries who expanded the foundation of organic electrochemical technology. Great progress in the understanding of fundamental mechanisms of electrochemical reactions has been achieved during the last few decades in parallel with the spectacular advances of electroanalytical and spectroanalytical methodologies [1] and the commercial availability of the relevant instruments.

1.2 Pertinent Fundamental Concepts and Principles in Organic Electrochemistry

1.2.1 The Overall Cell Reaction

Electrochemical reactions are performed in reactors known as electrolytic cells or electrolyzers, and are commonly referred to as cell reactions [2]. All overall cell reactions are *necessarily* the result of two *half-cell* reactions, the cathodic and the anodic. These reactions take place simultaneously and involve transfer of electrons at the electrode/solution interface, as is symbolically indicated by expressions 1.1, 1.2. The sum of the two half-reactions is the overall cell reaction:

Half-cell reactions



Overall cell reactions can proceed either spontaneously or by imposing on the cell a certain external electrical potential or a *driving* force [2]. Because of inhibiting thermodynamic or kinetic factors most organic cell reactions are not spontaneous. Therefore they must be *driven* by an imposed potential.

Electrodes

In organic electrosynthesis we are mainly interested in one of the half-cell reactions. This reaction occurs at the *working* electrode, which may be either the anode or the cathode. The other half-cell reaction takes place at the *auxiliary* or *counter* electrode and is usually of no *direct* synthetic interest. However, there are cases in which both the anodic and the cathodic reactions are synthetically useful (paired electrosynthesis).

Basic apparatus

In principle, the electrochemical method of synthesis, as practiced in the organic laboratory, is a relatively simple method. The basic laboratory apparatus is shown schematically in Fig. 1.1. It consists of an ordinary glass beaker, two electrodes, the anode and the cathode, a reference electrode (if needed) and a dc-power source. A voltmeter and an ammeter are inserted in the circuit for voltage and current measurements. Today's potentiostats incorporate the basic electrical components into one compact assembly. The electrochemical method of synthesis might be described very briefly as involving the following fundamental physical and chemical processes:

Physical and chemical processes

Motion of electrons in the external cell circuit (electronic current) and of ions in solution (ionic current) while electronations (reductions) and deelectronations (oxidations) of chemical species take place at the cathode

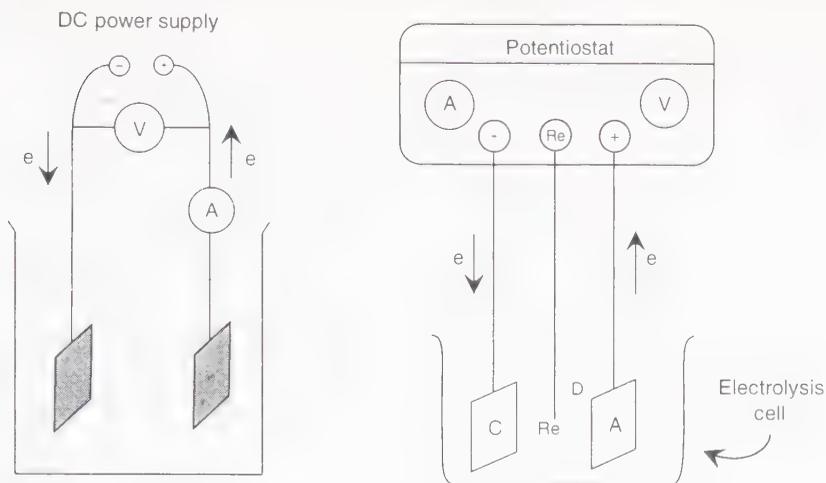


Fig. 1.1. Schematic of basic electrolysis apparatus, showing principle components (A), ammeter, (V), voltmeter, (Re), reference electrode, (−), cathode, (+), anode, D, diaphragm, if needed

and the anode, respectively. These primary electrodic redox reactions lead eventually to the isolated chemical products.

Preparative electrolyses are generally performed under either controlled potential or constant current conditions, in one-compartment or two-compartment cells depending on the particular electrosynthesis. Three types of solutions are commonly used: a. aqueous; b. aqueous-organic (homogeneous or heterogeneous mixtures) and c. Organic solutions made with protic or aprotic solvents. The organic substrates must be soluble or at least partially soluble in the solvent system. The solvents must be able to dissolve sufficient amounts of supporting electrolyte to become ionically conductive. The electrolyte may be a neutral salt, an acid or a base and must be ionized in the electrolysis medium. The ions of the electrolyte may or may not participate in the electrochemical reactions. It is now possible in some special electrosyntheses to avoid the need of a soluble electrolyte by employing cells with a solid polymer electrolyte (see Chapter 5).

Electrolysis conditions

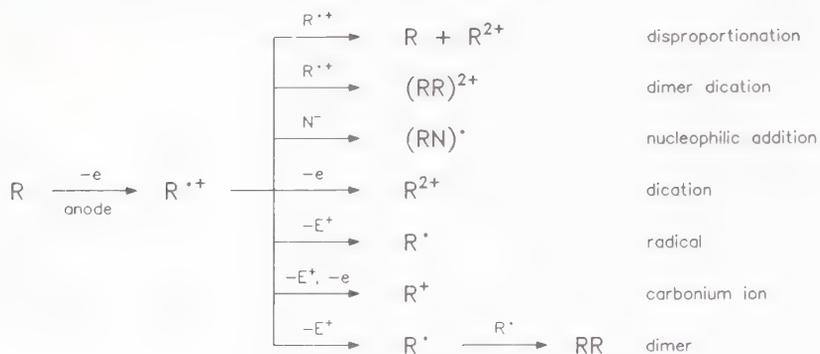
Solvents and electrolytes

1.2.2 The Generalized Electroorganic Reaction

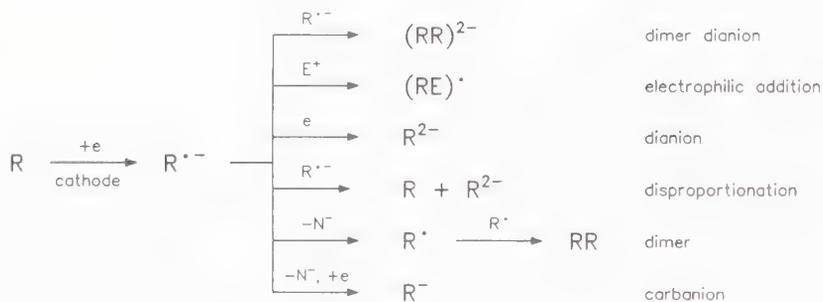
The fundamental events in electroorganic reactions are shown schematically in Fig. 1.2. The organic substrate, R, is considered to undergo an electron-transfer reaction (electroreaction) as a primary step in the overall electrochemical reaction. This primary electron transfer (ET) reaction is defined

Direct and Indirect ET reactions

Anodic reactions



Cathodic reactions



Indirect or mediated reactions



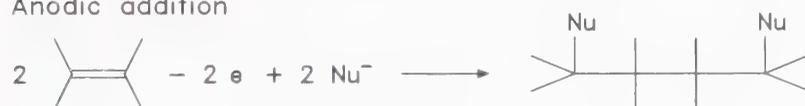
Fig. 1.2. Phenomenological classification of the generalized electroorganic reaction's fundamental events

as a *direct* reaction if the electron exchange takes place directly between the electrode and the organic substrate. If the organic substrate undergoes the primary electron exchange via a mediator the reaction is *indirect*. Direct ET reactions are typical heterogeneous reactions. Indirect reactions may be either homogeneous or heterogeneous, depending on whether the mediator is dissolved in the solution or immobilized physically or chemically on the electrode surface.

From a purely synthetic perspective organic electrode reactions are perceived as heterogeneous chemical processes involving transfer of electrons in the overall mechanistic reaction scheme.

Symmetrical Couplings

Anodic addition



Cathodic addition



Anodic elimination



Cathodic elimination



Unsymmetrical Couplings

Anodic



Cathodic



Scheme 1.1

1.2.2.1 Electrochemical Couplings and Cross Couplings

Electrochemical couplings and cross couplings constitute perhaps the broadest category of organic electrosynthetic reactions. Therefore, it appears that a formal synopsis of this type of reaction would be appropriate at this point. Most electrochemical couplings involve formations of C—C, C—O, C—N, C—S, N—N, and S—S bonds. These reactions are classified as *symmetrical* and *unsymmetrical*. They are accomplished either anodically (oxidatively) or cathodically (reductively) as is shown in Scheme 1.1. The symbols Nu⁻ and E⁺ stand for nucleophile and electrophile, respectively.

1.2.2.2 The Electron Transfer Step. Basic Qualitative Description

The experimentally observed high rates (currents) of electrodic reactions could not be adequately understood on the basis of the classical theory of rate processes. Modern views explain the high rates of electrodic reactions by considering the wave nature of the electron which enables *electron tunneling* through the energy barrier rather than passage of the electron over the barrier [2–4]. The applied potential or the electronic energy supplied to the electrode in contact with the solution brings about formation of equal electronic energy levels on both sides of the electrified interface, and thus the probability for radiationless electron transfer increases. This enhanced probability manifests itself in the observed high rates of electrodic reactions. Thermal reaction rates are expressed as functions of $e^{-E/RT}$ and electrodic reaction rates as functions of $e^{-\alpha\eta F/RT}$ where the symbols E and $\alpha\eta F$ denote thermal and electronic activation energies [6a]. Figure 1.3 is intended to represent a simple profile of possible energy barriers along the path of an electrodic reaction.

Molecular orbitals

When an organic molecule attains the transition complex state at the cathode the electron leaves the electrode and is accepted into the lowest in energy unoccupied molecular orbital (LUMO) of the molecule. The molecule is electronated. The opposite occurs when the molecule is de-electronated or oxidized at the anode. The electron leaves from the highest occupied molecular orbital (HOMO) and is accepted by the anode. In both cases available electronic energy levels must be present on both sides of the electrode-solution interface for the ET reaction to take place [2]. This availability of energy levels is determined by the prevailing electrode potential.

Electron transfers

The electroactivity of organic molecules depends heavily on their structure. For example, conjugated double bonds are, as a rule, more electroactive than nonconjugated double bonds. Conjugation lowers the LUMO and raises the HOMO energy levels, so that both cathodic and anodic ET reactions are facilitated. Functional group electroactivities are significantly

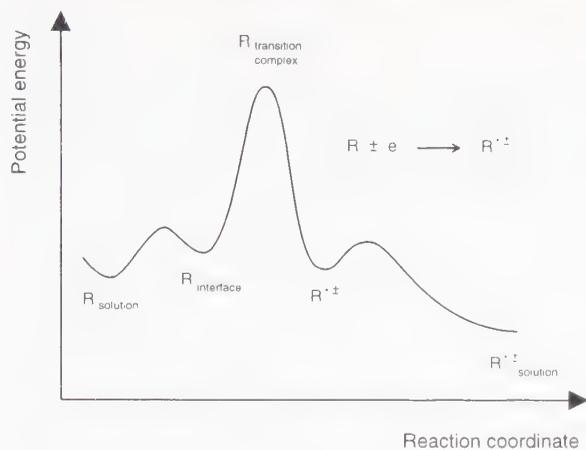


Fig. 1.3. Reaction path of an electrochemical reaction, showing possible energy barriers

influenced by the presence of activating groups (electron releasing or withdrawing groups) in the molecular structure. Steric barriers also have effects because such barriers may not allow the electroactive group to approach the electrode site at which the electroreaction occurs. Most organic electrode reactions involve more than one-electron step per molecule. The apparent two-electron step transfers, sometimes observed in practice, are actually two very rapid successive one-electron steps not distinguished by the ordinary experimental techniques in the organic laboratory. Molecular orbital theory [4] considering the repulsion of two electrons when added simultaneously to a certain molecular orbital predicts that addition of a second electron requires an energy of about 5 electron volts. However, solvation of a dianion lowers the separation energy between the first and second ET reaction to only about 0.5 electron volts. Sometimes the second ET occurs more readily than the first, and hence only one voltammetric two-electron wave or peak is experimentally observed in recording voltammetric current-potential curves. Analogously electron abstraction from a molecule is also facilitated by solvation effects [5].

1.2.3 Thermodynamic and Kinetic Aspects

1.2.3.1 Nernstian Equation. Electrode Potential

The fundamental thermodynamic equation in electrochemical reactions is the well-known Nernstian equation, given in simple form below:

$$E_e = E_e^\circ - \frac{RT}{nF} \ln Q \quad (1.4)$$

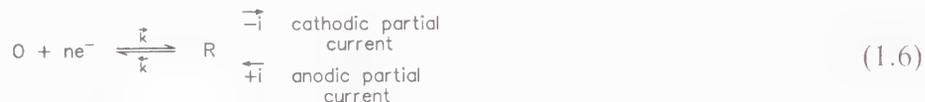
$$\text{or } E_e = E_e^\circ - \frac{0.059}{n} \log Q \text{ at } 25^\circ\text{C} \quad (1.5)$$

Meaning of electrode potential

In Eq. 1.5, Q represents the ratio of the activities of the products to the activities of the reactants of the electrodic reaction. The value E_e is the equilibrium potential of the electrode, and E_e° is the potential under standard state conditions, that is, when products and reactants are present at unit activities or when, in the general case, the numerical value of the quotient Q is unity, and therefore $E_e = E_e^\circ$. In common practice, concentrations are most often used instead of activities in Eq. 1.5 since activities are not available.

Reversible electrodic reaction

In a physical sense, the electrode potential expresses the energy of the electrons in the electrode in contact with the electrolysis medium [2,3]. When the electrode is negative it has an excess of electrons and when positive an excess of positive charges. Thus the electrode potential affects the energy required to add electrons to the electrode or remove electrons from it. It is important to understand the difference of the sign ($-$ or $+$) of electrode potential and the sign of the half-cell reaction. The sign in the former is a real physical property whereas the sign of the latter is a defined or conventional quantity and depends on how the reaction is written on paper. We now consider Nernst's equation in connection with a simple *reversible* electrodic organic reaction, as represented in Eq. 1.6



Equation 1.5 may be written in the usual practical form Eq. 1.7

$$E_e = E_e^\circ + \frac{RT}{nF} \ln \frac{C_O}{C_R} \quad (1.7)$$

Equilibrium potential

where C_O and C_R are concentrations of the oxidized and reduced forms of the redox couple O/R in Eq. 1.6. At the equilibrium state the electrode potential attains the steady value E_e . Any equilibrium, E_e , is the relative steady value of the electrode potential that is established in a cell in which the auxiliary electrode is a chosen standard reference electrode (e.g. the NHE) and under conditions that *no current* is allowed to flow in the external circuit. The established equilibrium is *dynamic* since electron transfers take place in both directions at equal rates, as implied by the partial currents $-i$ and $+i$ in Eq. 1.6. By defining the cathodic partial current as negative and the anodic as positive we can write the following expressions:

$$-i + i = 0$$

$$|-i| = |+i| = i_0$$

The symbol i_0 represents the *exchange current*. The exchange current is a fundamental characteristic of electrodic processes, in general. Exchange currents have been estimated to be in the range of $10^{-16} - 10^{-3} \text{ A/cm}^2$ at various electrodes at ordinary temperatures. Exchange currents vary with the concentration of the reacting species. For this reason a kinetic parameter, k , independent of concentration is defined [6], as given in Eq. 1.8

Exchange current

$$k = i_0 / nF C_0^{a_A} \cdot C_R^{a_C} \quad (1.8)$$

(a_A and a_C are the transfer coefficients for the anodic and cathodic partial reactions)

1.2.3.1a Free Energy of Cell Reaction and Cell Potential

Consider the hypothetical cell reaction



and assume that the free energy, ΔG , of this reaction is positive ($\Delta G > 0$). The reaction therefore must be driven by supplying to it electrical energy. This can be done by applying a voltage or potential across the cell. The minimum voltage, to be applied for the electrolysis to begin (that is, for the appearance of current in the external circuit) would correspond to the free energy of the reaction as given by the thermodynamic equation, Eq. 1.9

$$\Delta G = -nFE_{\text{cell}} \quad (1.9)$$

The value, E_{cell} , represents the theoretical *decomposition* potential, defined as $E_{\text{cell}} = E_a - E_c$. Since $\Delta G > 0$, E_{cell} is negative by definition. The values E_a and E_c represent the theoretical anodic and cathodic potentials, respectively. In practice the cell voltage will include the anodic and cathodic overpotentials and the (inevitable) potential drop, iR , across the cell. (Note: according to Bockris no electrodic reaction is ever possible without an overpotential) [6a]. The total cell voltage will be distributed across the cell according to Eq. 1.9a. The overpotentials are included in the terms E_a and E_c .

Overpotential

$$E_{\text{cell, total}} = E_a - E_c + iR \quad (1.9a)$$

The electrode potentials E_a and E_c are values (in volts) measured with reference to any suitable reference electrode, but the reference electrode must be the same for both the anode and the cathode in order for Eq. 1.9a to be applicable. We may note that absolute electrode potentials, although they exist, can not be measured experimentally [2]. All electrode potentials are relative values referred to a chosen standard electrode [1,2]. In electrochemical synthesis we are primarily interested in the potential of

the working electrode. Current-potential curves are usually obtained by plotting current (current densities) versus the potential applied to the working electrode. This potential is measured against a stable reference electrode (such as the SCE, Ag/Ag⁺ etc).

1.2.3.2 Kinetic Aspects

Tafel's equation Electrochemical reaction rates are generally expressed as current-potential (i-E) relationships. The most simple and practical current-potential relationship is Tafel's (1905) empirical equation,

$$\eta = a \pm b \log i \quad (1.10)$$

This equation relates the *activation* overpotential, η , to the current i or the rate of the electrochemical reaction, U , since the current is proportional to U , Eq. 1.11

$$i = nFU \quad (1.11)$$

The activation overpotential η is defined as the difference between the applied potential, E , and the theoretical equilibrium electrode potential, E_c , Eq. 1.12

$$\eta = E - E_c \quad (1.12)$$

The constants a and b in Eq. 1.10 are characteristic parameters of the particular electroodic reaction occurring at the anode or the cathode. It must be noted that the Tafel equation is applicable, in a strict sense, only when the slowest or rate determining step (rds) in the overall electrode process is the electron transfer step. Because overpotentials relative to true equilibria potentials, as defined in Eq. 1.12, are not available for most practical electrosynthesis work the Tafel equation is used in the more practical form given in Eq. 1.13

$$E = a \pm b \log i \quad (1.13)$$

In Eq. 1.13, E represents the relative electrode potential measured with reference to any suitable reference electrode. Plots of Eq. 1.13 are useful in selecting electrodes with regard to their electrocatalytic properties and for establishing optimum potentials for a given electrochemical reaction.

Equation 1.10 is a limiting form of the fundamental equation of electrode kinetics, Eq. 1.14, commonly known as the Butler-Volmer equation [2]:

$$i = i_0 \left[\exp\left(\frac{\alpha_A n F}{RT} \eta\right) - \exp\left(-\frac{\alpha_C n F}{RT} \eta\right) \right] \quad (1.14)$$

In this equation i is the observed current (or the *net* current), i_0 is the exchange current, and α_A and α_C are the anodic and cathodic *transfer*

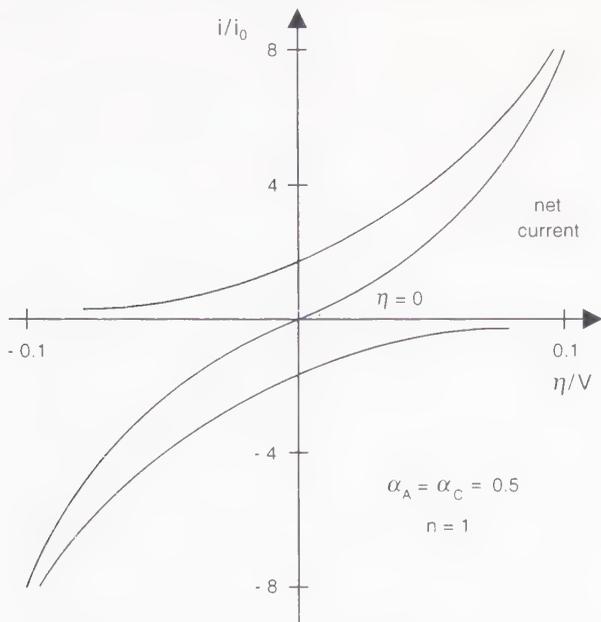


Fig. 1.4. The i - η relationship for a reversible electrochemical reaction, $R + e \rightleftharpoons R^-$.

coefficients, η is the overpotential and the other symbols have their usual meanings. Equation 1.14 is represented graphically in Fig. 1.4.

In most practical synthetic applications electrolysis is carried out at relatively high positive or negative electrode potentials, that is at potentials far from the equilibrium potential. Under such potentials, only one of the exponential terms in Eq. 1.14 is practically significant [1,2,7]. Thus at high anodic or cathodic potentials the limiting forms expressed in Eqs. 1.15 are derived from the general equation, Eq. 1.14. These limiting forms represent the detailed Tafel equation as derived from theoretical considerations, and indicate the meanings of the constants a and b in the original empirical Tafel equation.

$$\log i_{\text{anodic}} = \log i_0 + \frac{\alpha_A n F}{2.3RT} \eta \quad (1.15)$$

$$\log i_{\text{cathodic}} = \log i_0 - \frac{\alpha_C n F}{2.3RT} \eta$$

We further may note that on the basis of experience the sum of the transfer coefficients α_A and α_C is unity and hence only one of them is needed in Eq. 1.14. The α_A in the first exponential term of Eq. 1.14 can be replaced by $(1 - \alpha_C)$. At very low overpotentials another limiting form of Eq. 1.14 is derived by expanding the exponentials, Eq. 1.16,

$$i = i_0 \frac{nF}{RT} \eta \quad (1.16)$$

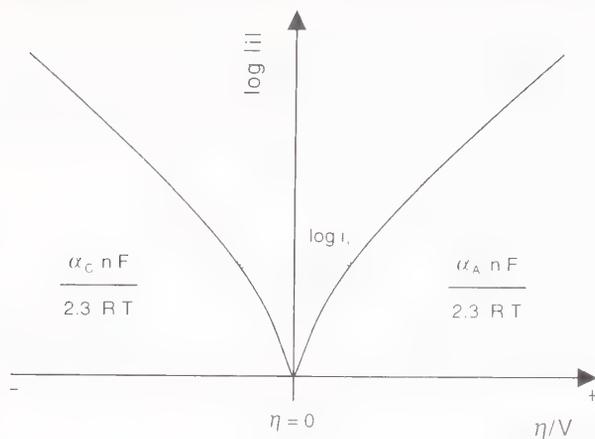


Fig. 1.5. Tafel plots for anodic and cathodic reactions ($\eta = E - E_c$)

It is thus possible to estimate exchange currents from experimental plots of Eqs. 1.15 and 1.16 as illustrated in Fig. 1.5, (provided η is known as $\eta = E - E_c$).

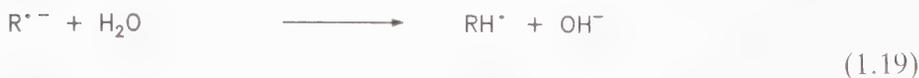
(**Note:** In the kinetic equations given above the symbol, n , refers to the number of electrons involved in the activation step. This number may be either equal to or less than the number of electrons in the particular half-cell reaction.)

1.2.4 Preparative Electrolysis Under Activation (Kinetic) or Mass-Transfer Controlled Conditions

Consider for example, the simple formal electroreduction, Eq. 1.17



performed electrolytically in aqueous solution using a mercury cathode. In most such electrochemical hydrogenations the reaction is irreversible, even though the first electron-transfer step may be reversible as is illustrated in the following overall reaction scheme:





A current-potential curve of this reaction (in unstirred solution) would resemble curve A in Figure 1.6.

In the rising portion of the curve A the current increases exponentially with the applied voltage E ($i = \text{constant} \cdot \exp(\alpha_c n F E / RT)$). In the potential region corresponding to the plateau (limiting current) region of the curve all the molecules of the substrate R reaching the electrode are reduced. A zone depleted in R is formed near the electrode surface (diffusion zone). The reaction rate (current) at this potential region is mass-transfer or diffusion controlled and independent of the electrode potential. Such limiting currents are common to both reversible (rapid) and irreversible (slow) electrochemical reactions but the shapes of the i - E curves are different as shown in Figure 1.6. A preparative electrolysis may be carried out under activation (kinetic) or mass-transfer control conditions, that is under potentials at the rising portion of the i - E curve or at limiting current or plateau region of the curve. The limiting current, i_l , under mass transfer conditions at a large electrode with an *active* area A is given by Eq. 1.22

$$i_l = n F D A C \delta \quad (1.22)$$

in which D is the diffusion coefficient (cm^2/s) of the electroactive species. C is the concentration of the species in the *bulk* of the solution, n is the number of electrons per molecule undergoing reaction, and δ the *thickness* of the Nernst diffusion layer, usually 0.1 mm.

For an electrolysis under limiting current conditions (plateau of the i - E curve) the current falls with electrolysis time, t , according to the following

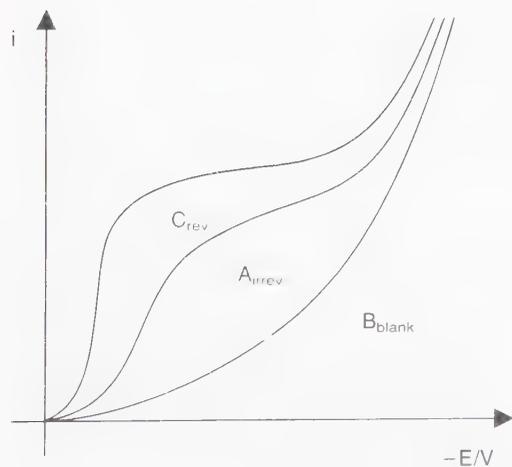


Fig. 1.6. Typical i - E voltammetric curves. Reversible reaction, curve C_{rev} ; Inreversible reaction, curve C_{ir} ; Curve B, blank, only solvent and electrolyte

i-t relation, Eq. 1.23 where i^0 is the starting current (amperes), V is the volume of the

$$\log i = \log i^0 - \frac{0.434 DA}{V\delta} t \quad (1.23)$$

solution (liters), and t is the time of electrolysis (seconds) and the other symbols have the same meanings as in Eq. 1.22. Some other practical equations derived from Faraday's laws are the following (assuming 100% current efficiency):

$$Q = \int_0^t i dt = nFN \quad (1.24)$$

$$m = \frac{M}{nF} it \quad \text{constant current} \quad (1.25)$$

$$m = \frac{M}{nF} \int_0^t i dt \quad \text{constant potential} \quad (1.26)$$

In the equations given above the symbols have the following meanings:

- Q = total charge consumed (coulombs) for N moles of substrate
- t = time (seconds)
- i = current (amperes)
- n = number of electrons involved in the reaction per molecule reduced or oxidized
- m = weight of substrate reduced or oxidized
- M = molecular weight of substrate

The following definitions pertain to synthetic electrolytic processes in general:

$$\text{current efficiency, CE,} = \frac{\text{theoretical ampere - hours}}{\text{actual ampere - hours}}$$

$$\text{voltage efficiency, VE,} = \frac{E_{\text{cell theoretical}}}{E_{\text{cell actual}}}$$

$$\text{Energy Efficiency, EE,} = (\text{CE}) \cdot (\text{VE})$$

$$(\text{faraday} = 96\,500 \text{ coulombs or } 26.806 \text{ ampere - hours})$$

1.2.5 The Electrical Double Layer and its Significance in Electrosynthesis

Adsorption It has been stated that the electrical double layer or the electrified interface between an electrode and a solution is the "innermost essence" of electrochemistry. Only a pictorial, simple representation of the electrical double layer, Fig. 1.7, can be made here in order to discuss most simply its

charge (pzc). However, adsorption of any species may occur by both chemical and physical forces (chemisorption, physisorption). In chemisorption chemical bonds are formed between electrode and adsorbate, whereas electrostatic adsorption occurs when adsorbent and adsorbate are oppositely charged. Chemisorption may occur even when the electrode and the chemical species adsorbed have similar charges. Such adsorption has been called *specific adsorption*. Situations, therefore, arise, as depicted in Fig. 1.7a,b,c, characterised by *inner* and *outer* Helmholtz planes (IHP, OHP).

**Location
of reacting
species**

The structure of the double layer is sometimes the most influential factor in the outcome of the reaction, as in the electrohydrodimerization of acrylonitrile, and in stereochemical reactions in which the electrode surface is covered with chiral compounds. The reacting species may be located at the OHP or at the IHP. It is to be noted that it is the potential that an organic molecule experiences that actually affects the electron transfer reaction, rather than the experimentally measured potential of the electrode. (The electric field intensities within the double layer are enormous, as high as 10^7 V/cm). Because the actual loci of the centers of the reacting molecules are usually not known – and it does not matter in most practical synthetic work, reproducible relative potentials are satisfactory. It is, however, important to be *consistent by precisely defining the physicochemical composition of the medium and the potential measurement techniques*. Best electric field uniformity is attainable with parallel plate electrodes of equal dimensions. In cases in which the electroactive organic species is specifically adsorbed it experiences the potential obtaining at the IHP. We should note that organic molecules vary in complexity. As a result they can assume unpredictable orientations when they are adsorbed on electrodes or immersed in the strong electric field near the electrode surface. Electrosyntheses therefore are often greatly influenced by special orientations of the reacting species. Aromatic molecules can be adsorbed in parallel or vertical positions with respect to the electrode surface. There would be no way to predict how a large biological molecule would fit within the electric double layer and hence how it will react stereospecifically or chemoselectively. A recent review about the electrical double layer has been presented by Parsons [7].

**Electric field
intensities**

From the aforesaid it would be obvious that the electrode potential, the electrical double layer, and the composition of the electrolysis medium are *very important parameters* in electrochemical reactions. Their relative importance varies, however, and many electrosyntheses, insofar as reproducibility is concerned, require only consistent operational conditions. Constant current electrolysis and indirect electrosyntheses do not require strict potential control in the sense that potentiostatic syntheses do. Furthermore, in practice it is impossible to achieve precise electrode potential control over the entire electrode surface. Also in practice “formal” elec-

trode potentials are used since thermodynamic activities are seldom known and are not necessary for practical synthetic work.

References

- 1a. Bard AJ (1966) *Electroanalytical chemistry*. Marcel-Dekker, New York
- 1b. Bard AJ, Faulkner LL (1980) *Electrochemical methods*. Wiley-Interscience, New York
- 1c. Southampton Electrochemistry Group (1985) *Instrumental methods in electrochemistry*. Ellis Horwood, Chichester
2. Bockris JOM, Reddy AKN (1970) *Modern electrochemistry*, vols 1 and 2, Plenum, New York
3. Ebersson L (1987) *Electron transfer reactions*. Springer, Berlin Heidelberg New York
4. Bard AJ (1971) *Pure App Chem* 25:379; Saveant JM (1980) *Accounts Chem Res* 13:323
5. Pysch ES, Yang NC (1983) *J Am Chem Soc* 85:2124; Fleischmann M, Pletcher D (1973) *Adv Phys Org Chem* 10:155
6. Ref. 1c, p 26
- 6a. Bockris JOM (1971) *J Chem Educ* 48:353
7. Parsons R (1990) *Chem Rev* 90:813

2 Anodic Reactions

2.1 Fundamental Nature

Anodic or electrooxidative organic reactions generally involve three fundamental intermediates [1,2,7,9,10,11]:

1. Cation radicals, $R^{\cdot+}$
2. Radicals, R^{\cdot}
3. Cations, R^+

These transient species are produced either by direct electron transfer from the organic substrate to the electrode, or indirectly by the action of a mediator [1–6]. It must be noted, with due emphasis, that a large number of anodic reactions proceed by oxidative steps involving continuously generated surface oxides or OH^{\cdot} species adsorbed on the electrode surface. Such oxidative steps are actually a special type of heterogeneous chemical oxidation occurring at the surface of an electronically conducting substrate in contact with an ionically conducting solution. In organic electrochemistry these oxidations are specifically viewed as heterogeneous electrocatalytic reactions [3,5,6]. We might also refer to the formation of cation radicals, by means of one-electron oxidants such as $SbCl_5$, PbO_2 and the organic tris(4-bromophenylaminium) ion. The first of these oxidants oxidizes aromatic hydrocarbons in dichloromethane solutions. The PbO_2 is a most effective one-electron oxidant in CF_3CO_2H/CH_2Cl_2 media. The organic ion is produced anodically (homogeneous electrocatalysis). The generation of cation radicals with PbO_2 and the anode as oxidants is formally shown below in order to provide, perhaps, a first notion of the potential inherent simplicity of an electrodic electron transfer process, as contrasted to a chemical one [7]:



The deelectronation of ArH by PbO_2 requires the breaking and formation of bonds and the use of at least stoichiometric amounts of reactants, as shown in the equation. By the direct anodic reaction cation radicals are

produced relatively more simply in solutions containing neutral organic molecules, and are especially easily produced if the molecules contain π -electron systems or heteroatoms with unshared π -electron pairs. Extended π -electron systems are most easily deelectronated at the anode. These transient species are best studied by electron spin resonance (ESR) spectroscopy and voltammetric techniques [2.7]. Well-known one-electron voltammetric standards are the compounds, ferrocene, 9,10-diphenylanthracene and dimethylstilbene [1,2].

2.2 Hydrocarbons

Hydrocarbons contain only the two elements carbon and hydrogen in their enormous diversity of molecular structures. Anodic transformations of hydrocarbons, therefore, take place by breaking of carbon-carbon or carbon-hydrogen bonds and making of new such bonds – if, and only if, no other chemical entities are present capable of reacting with the primary electrodic products of the hydrocarbons. Of the three structural types of hydrocarbons, alkanes, alkenes and aromatics, alkanes are distinctly the most resistant to direct anodic oxidation. Positive potentials as high as 3.0 V vs Pd/H₂ may be needed for electron release to the anode. At such potentials the solvent or the electrolyte may be, and usually is, more easily oxidized than the alkane molecule. In sharp contrast to alkanes, hydrocarbons with π -electron systems are generally readily oxidized at the anode because the π -electrons are much more available for release to the electrode than the electrons of single C—C or C—H bonds. Synthetically, the most important anodic reactions of hydrocarbons comprise two broad categories:

1. Inter- and intra-molecular bond formations (dehydrodimerizations, polymerizations) and
2. Various functionalizations (nucleophilic additions and substitutions).

2.2.1 Saturated Hydrocarbons

It would be quite difficult to conceptualize a plausible mechanism for the direct deelectronation of an alkane molecule at the anode. Yet, under certain, rather severe, conditions even alkanes can be prompted to donate electrons to the anode. In depth studies in this area have been carried out mainly by Pletcher and Fleischmann [1] (Southampton Electrochemistry Group). These studies confirmed that aliphatic hydrocarbons are susceptible to direct oxidation at platinum in FSO₃H solution containing electrochemically stable salts as electrolytes [2]. Such salts are those

General aspects

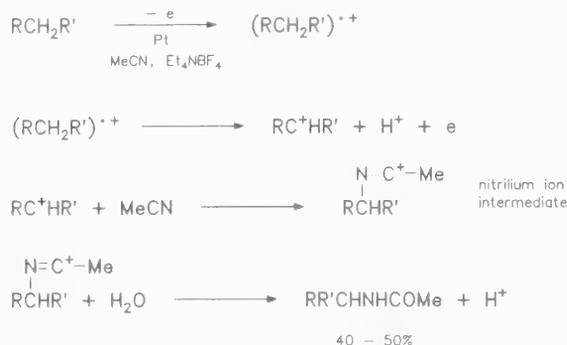
Oxidation in FSO₃H

whose anions are most difficult to oxidize at the anode (fluorosulfonates, tetrafluoroborates, hexafluorophosphates). In solutions of FSO₃H/0.1MKSO₃F alkanes are oxidized at potentials between 1 and 2.2 V vs Pd/H₂ electrode [1b]. For example, anodic peak potentials of typical alkanes are: isobutane (1.0), cyclohexane (1.1), *n*-hexane (1.5), *n*-octane (1.4), *n*-butane (1.85) and *n*-propane (2.2). The oxidation of alkanes in FSO₃H apparently proceeds via the protonated form of the alkane molecule. We mention in this connection that theoretical calculations by Kollmer and Smith [3] indicated that the CH₅⁺ cation contains a weak C—H bond (9.5 eV) which is much weaker than the average (16 eV) bond in the neutral CH₄ molecule. This possibility, by extension to alkanes, might explain the easier electron release to the anode from the protonated alkane molecule, RH₂⁺,



Oxidation in acetonitrile

Alkanes may also be oxidized in acetonitrile and some other solvents such as dichloromethane, nitromethane propylene carbonate and sulfolane. In these solvents the alkane is not protonated, but the solvents are resistant to anodic oxidation. For example, anodic oxidation of octane in acetonitrile affords mixtures of acetamides [1c], following hydrolysis of the intermediate nitrilium ion, Scheme 2.1. The reaction is accepted as proceeding as follows:



Scheme 2.1

Preparative examples

Preparative electrolyses are carried out in acetonitrile saturated with the alkane, using a platinum anode at a potential sufficient to oxidize the alkane (Fig. 2.1).

The anodic transformation of cyclohexane to a ketonic product [1b], as depicted in Scheme 2.2, occurs in FSO₃H/RCOOH medium at a platinum electrode (1.15 V vs Pd/H₂) in a divided cell. Both anolyte and catholyte are the same. The anolyte is saturated with the cyclohexane and is stirred during the electrolysis with dry nitrogen presaturated with cyclohexane.

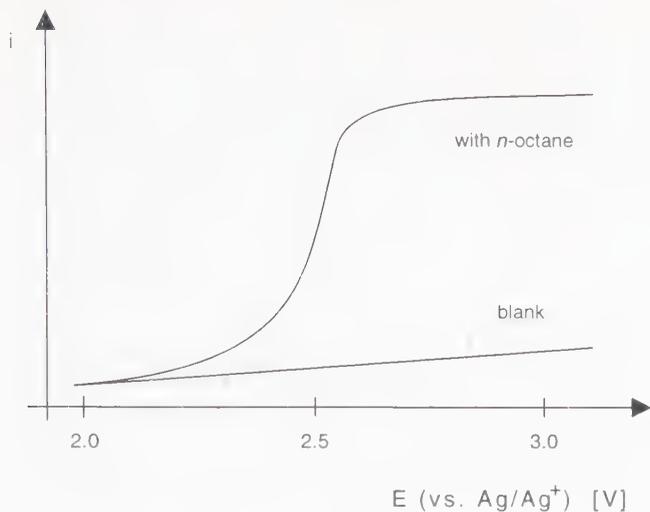
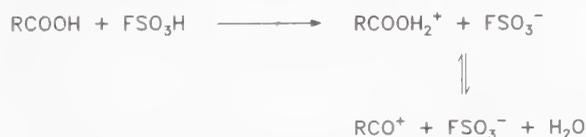
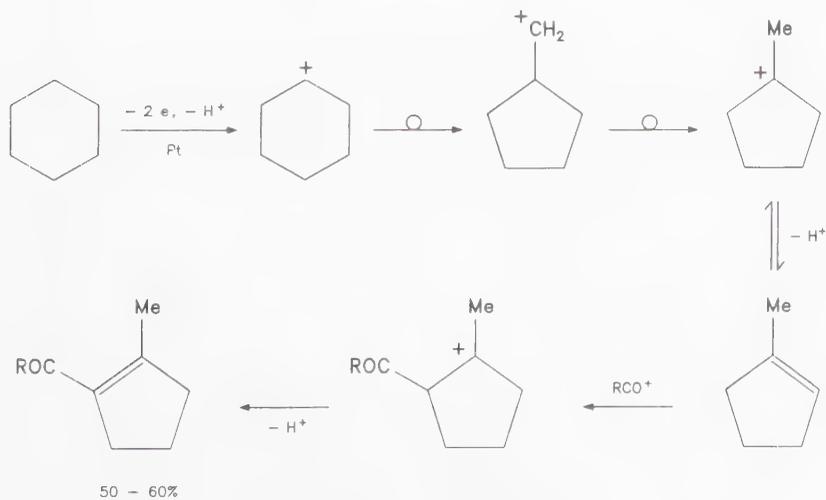


Fig. 2.1. Typical *i*-*E* voltammetric curve for the oxidation of an alkane (octane) at a platinum electrode in MeCN/ Et_4NBF_4 medium

Apparently the required acyl cation, RCO^+ , is generated in the solution by the reaction of FSO_3H with the carboxylic acid which acts as a base in the FSO_3H acid medium.

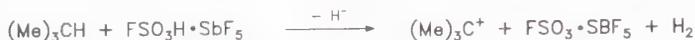


An excess of FSO_3H shifts the equilibrium as to favor RCO^+ formation, since the excess FSO_3H can bind the produced H_2O .



Scheme 2.2

The products can be recovered from the electrolysis medium by neutralization of the acids with Na_2CO_3 (cold solution) and extracting with ethyl ether. We may also consider that alkanes can afford similar ketonic products by chemical reactions in the so-called *superacid* $\text{FSO}_3\text{H}/\text{SbF}_5$ media containing carboxylic acids [4]. In such media alkanes give cations by loss of hydride ion, H^- .



The anodic method obviates the need of the expensive and difficult to handle SbF_5 .

**Oxidation
of alkanes
presence
 NO_3^- -ions**

Linear alkanes are partially transformed to ketonic products, by anodic electrolysis in *tert*-butanol/ H_2O media containing HNO_3 and saturated with oxygen. In this mediated oxidation the nitrate ions are presumably oxidized at the anode to give NO_3^\cdot radicals which abstract hydrogen atoms from the alkane. The resulting alkane radicals react with oxygen to form peroxides and are finally transformed to the ketonic products [5].

2.2.2 Unsaturated Hydrocarbons

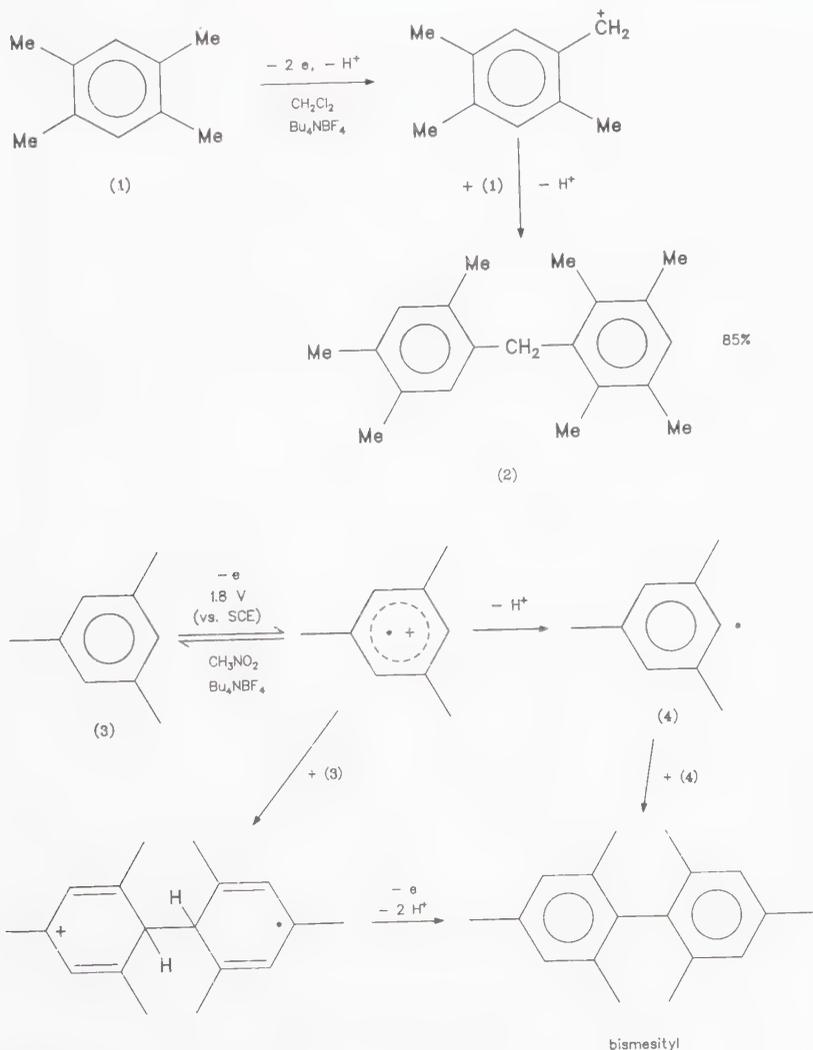
The presence of π -electrons in unsaturated hydrocarbons allows them to release electrons to the anode readily, and much more easily than the alkanes [6]. The electron release is further assisted by adsorption effects; π -electrons facilitate adsorption, and adsorption usually lowers the overpotential for an ET reaction. Most simple anodic oxidations of unsaturated hydrocarbons, in general, require potentials not higher than two volts vs the SCE, which are easily reached in the organic solvents commonly employed in organic electrosynthesis. The removal of an electron from a π -system in a hydrocarbon results in the formation of a very reactive cation radical which can react directly with a nucleophile or after releasing another electron to the anode. The nucleophile can be an anion species or a neutral species including the solvent (e.g. H_2O , MeOH , CH_3CN). In nonnucleophilic solvents (e.g. CH_2Cl_2 , CH_3NO_2 , sulfolane) and in the absence of any nucleophiles, dimerizations and polymerizations are very favorable reactions. A solvent ideally suitable for the generation of very active organic cations is liquid SO_2 (-50°C). This nonnucleophilic solvent can be purified prior to use by shaking it with anhydrous Al_2O_3 . Anthracene and 9,9'-bianthryl have been oxidized in $\text{SO}_2/\text{Bu}_4\text{NPF}_6$ medium and gave their very reactive dication [7]. We further note that alkyl substituted aromatics generally release electrons to the anode more readily as the number of alkyl groups increases: In acetonitrile the deelectro-nations of benzene, toluene, *p*-xylene and pentamethylbenzene occur at the respective potentials 2.0, 1.98, 1.56 and 1.28 vs Ag/Ag^+ electrode. The electron-releasing alkyl groups tend to increase the electron density

Nucleophiles

**Oxidation in
 SO_2**

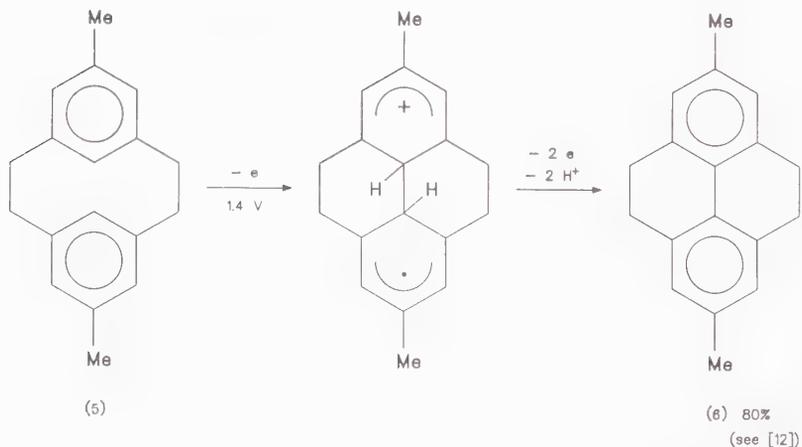
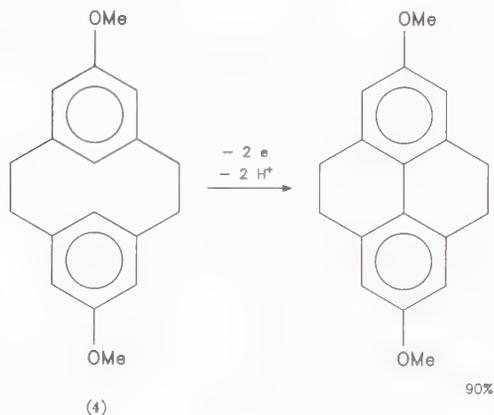
on the aromatic ring and thus assist the anodic removal of ring electrons. Fundamental research studies have confirmed that aromatics are generally easily oxidized at the anode in organic solvents to yield inter- and intra-molecular bond products in good to excellent yields. Following are selected typical examples with alkyl and methoxy substituents on the aromatic rings. Durene (**1**) gives the dimer (**2**) as major product upon oxidation at platinum in $\text{CH}_2\text{Cl}_2/0.1\text{M}\text{Bu}_4\text{NBF}_4$ medium by reaction of the generated cation with the durene molecule [9,10]. Two electrons are released from the starting molecule and H^+ is expelled from a methyl group to form the cation. Mesitylene (**3**) dimerizes by two routes [10] to give the bimesityl product:

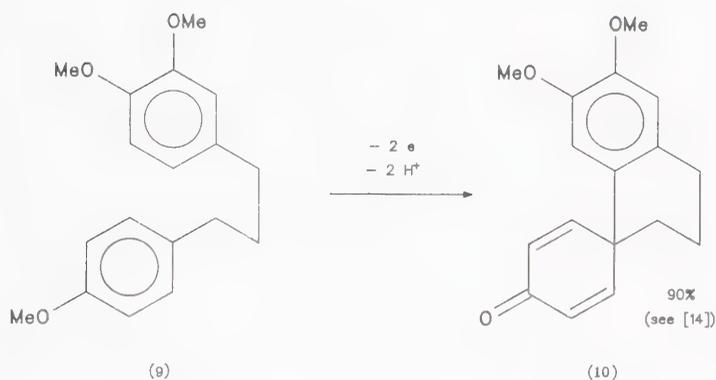
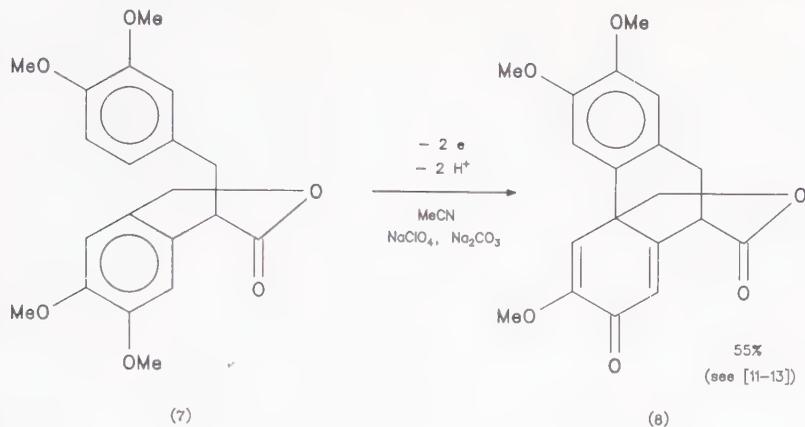
Oxidation of aromatics



Scheme 2.3

Although the following oxidation examples are not strictly referable to hydrocarbons they are very illustrative of the π -electron system anodic deelectronation, and will be included here parenthetically. The methoxy (4) and methyl substituted (5) [12] cyclophanes and the isochromanone compound (7) are transformed to the corresponding intra-cyclized products upon oxidation at platinum electrodes in MeCN/ Bu_4NClO_4 solution at 1.2 to 1.5 V vs Ag/Ag^+ electrode [11,12,13]. Anodic intramolecular cyclization of the aromatically substituted *n*-propane compound (9) in acetonitrile-fluoboric acid solution afforded the spirodienone compound (10) in high yield [14].





2.2.3 Functionalizations of Hydrocarbons

The initial step in the anodic functionalization of hydrocarbons usually is a one-electron transfer from the hydrocarbon to the electrode whereupon a cation radical is produced. This primary product is attacked by a nucleophile as is symbolically indicated below



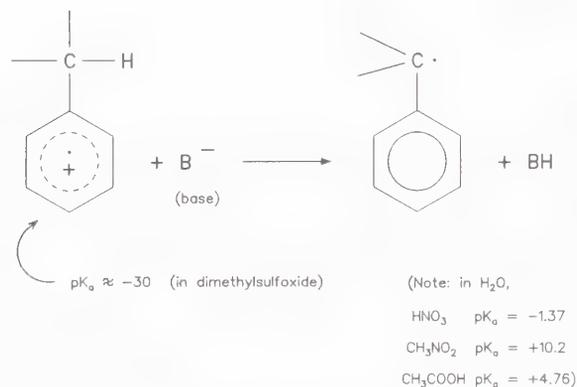
where Nu and E represent nucleophile and electrophile, respectively. In most cases E is a proton. The nucleophile may be a neutral or negatively charged species (e.g. H_2O , MeOH, MeCN, pyridine, RNH_2 , etc.), or

OH^- , RO^- , CN^- , RCOO^- , SCN^- , N_3^- , NO_3^- , I^- , Br^- , Cl^- , F^- (nucleophilicity in that order for halide ions).

We would note that a nucleophile bearing a negative charge, e.g. OH^- , would always be a stronger nucleophilic species than its conjugate acid H_2O , a neutral species. Further, we bear in mind that basicity is generally *thermodynamically controlled* but nucleophilicity is *kinetically controlled*, (solvent and other effects). Because most primary electrodic products are transitory, the nucleophilic addition takes place in the electrode's immediate vicinity. If the primary species survives long enough so as to diffuse into the bulk of the solution the chemical reactions can occur homogeneously in the absence of the strong electric field at the electrode vicinity. In cases in which the reactants RE and Nu are adsorbed on the electrode or if they are oriented in some special position at the electrode surface, stereochemical effects could be expected [17]. Most studies indicate that both aliphatic and aromatic hydrocarbons are adsorbed on the electrode surface [18] prior to the electron transfer to the electrode. Hydrocarbon cation radicals act both as very reactive electrophiles or proton donors, and avidly interact with nucleophiles or bases. Alkyl aromatic cation radicals are extremely strong carbon acids, as for example [19].

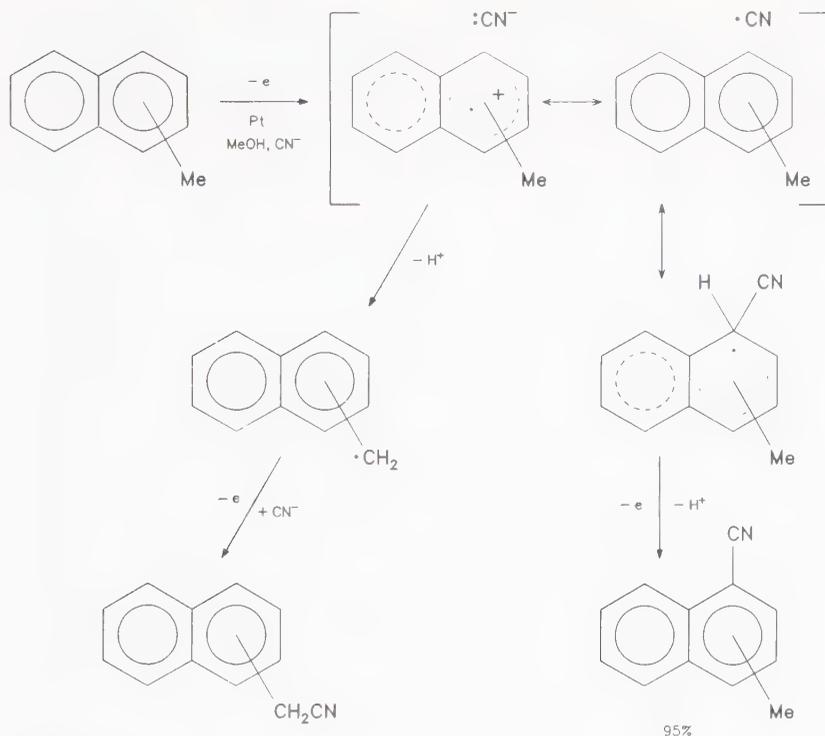
**Adsorption,
and
stereochemical
effects**

Carbon acids



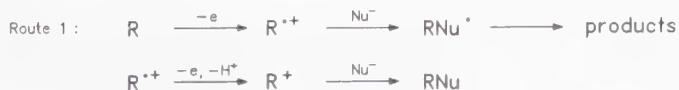
**Cyanation of
methylnaphthalenes**

Although cation radicals can dimerize, their tendency usually is to split a C—H bond and to undergo substitution of hydrogen by a nucleophile. A very typical example is the cyanation of methylnaphthalenes in methanol/ CN^- solution. According to Yoshida's studies [20] the cyanation occurs as shown in Scheme 2.4.



Scheme 2.4

In the above scheme it is seen that two competitive paths lead to two different products. Following the ET step the organic substrate assumes a positive charge which may not be uniformly distributed over the entire cation radical structure. If only electrostatic forces influence the reaction with the nucleophile CN^- the attack by CN^- would be on the carbon with the largest positive charge density. However, because of the influence of other factors substitution of hydrogen by CN^- may occur at carbons other than that with the largest positive charge density in the molecular structure [20]. In anodic substitutions there are usually two mechanistic possibilities to consider, Route 1 and Route 2.



R is a hydrocarbon molecule

Most recent opinions, based on experiment, point more to the first route if the organic substrate, R, is oxidized at a less positive potential than the nucleophile Nu⁻

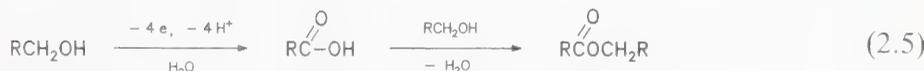
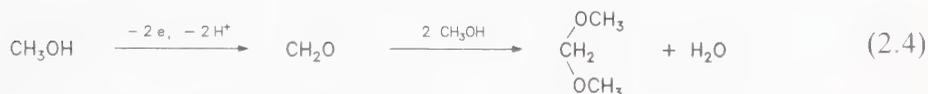
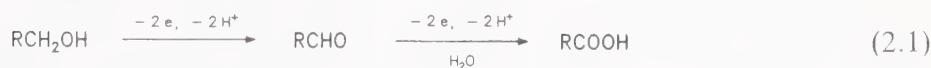
2.3 Hydroxy Compounds

General aspects The electrochemical oxidation of organic substances containing hydroxy groups is a wide and active research field because it attracts interest in both synthetic and energy conversion applications [1–8]. Low molecular weight alcohols and some hydroxy compounds of biomass origin have been studied intensely for energy conversion purposes (obtaining electricity from fuel cells) [9,11,16]. For synthetic applications only partial oxidation of the hydroxy molecule would be desired whereas for fuel cell-type uses complete oxidation to CO₂ would be the goal. For example, glucose when partially oxidized might afford gluconic acid as it does by indirect mediated oxidation (Chapter 4) whereas in a fuel cell the glucose molecule should preferably be oxidized all the way:



Oxidation of aliphatic alcohols Direct anodic oxidations of aliphatic alcohols at Pt, Au, and C electrodes are usually not so practical because they require high positive potentials for the alcohols to release electrons to these anodes. Indirect electrocatalytic (heterogeneous or homogeneous via mediators) methods are apparently much more practical [14,16,17]. Electrolysis can be performed in both aqueous and nonaqueous solutions and in mixed organic-aqueous media when the hydroxy compounds are not adequately soluble in water. Acidic, basic and neutral solutions can be used. The nature of the products, however, is influenced by the composition of the medium, the kind of electrode, and cell design. Recently, an interesting electrocatalysis has been reported [18] using a “composite-plated” electrode (Ni/PTFE) for the oxidation of alcohols in H₂O/KOH solutions. The effectiveness of this new type of electrode is attributed to its hydrophobic character (which apparently favors approach of the alcohol rather than water to the anode surface). It is prepared by *composite-plating* a piece of nickel plate in a nickel sulfonate polytetrafluoroethylene dispersion bath hence (Ni/PTFE). With this anode the oxidation of isopropyl alcohol to acetone was carried out with a current efficiency of about 70% and 84% yield. Formally, the anodic partial oxidation of monohydroxy alcohols and their possible oxidation products is conveniently summarized in Scheme 2.5. Oxidation to the aldehyde state requires removal of two electrons and a total of four electrons to the carboxylic acid state. It is usually difficult to stop at the

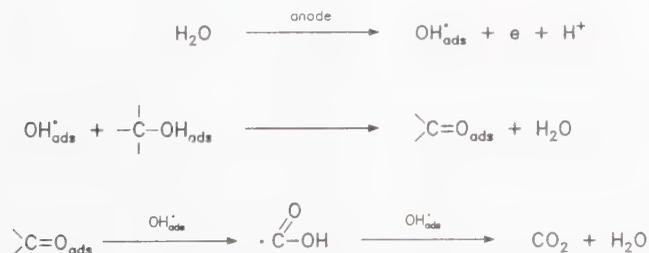
aldehyde state, but this state can be *trapped* in situ by formation of acetals, Eq. 2.4



Scheme 2.5

Note: High molecular weight alcohols tend to undergo C—C bond cleavage yielding a variety of products [19,20,21].

Because the direct oxidation of aliphatic alcohols at Pt, Au, or C requires high anodic potentials the anions of the supporting electrolyte must be more difficult to oxidize than the alcohols for the process to be synthetically efficient. Such anions are: BF_4^- , ClO_4^- , PF_6^- . At electrocatalytic electrodes the alcohols MeOH, EtOH and $\text{CH}\equiv\text{C}-\text{CH}_2\text{OH}$ can be oxidized all the way to CO_2 and H_2O via adsorbed fragments on the anode, the fragments being formed by dissociative adsorption. The oxidative path is probably as represented below:



In aprotic media with BF_4^- as anion of the electrolyte positive potentials may be reached at which alcohols can be directly oxidized at platinum

**Formation
of $\text{RCH}_2\text{O}^\cdot$
and $\cdot\text{CH}_2\text{OH}$
radicals**

electrodes. In alcoholic/NaOR solutions ($\text{R}=\text{alkyl}$) formation of radicals $\text{RCH}_2\text{O}^\cdot$ and $\cdot\text{CH}_2\text{OH}$ occurs via which alkoxyated and hydroalkoxyated products can be obtained. The electrolyzed solutions must not become too basic since this would lead to aldol-type condensations as the alcohols are oxidized to aldehydes.

2.4 Oxidations at Oxide Covered Electrodes

**General
aspects**

Oxide covered electrodes consist of metals whose surfaces are covered with a thin layer of metallic oxides [1]. These oxides are chemically active oxidizing agents, electrically conductive and insoluble in aqueous or aqueous-organic alkaline solutions. They are continuously electrogenerated during the electrolysis and remain firmly adhered to the electrode surface thus protecting the substrate metal from anodic dissolution. The metals commonly used as oxide covered electrodes are Ni, Ag, Co, Cu and Mn. Possible uses of nickel and silver oxide electrodes have been considered for synthetic [2], electrogenerative and biochemical sensor applications [2,3,4].

Concerning the PbO_2 electrode (used in sulfuric acid media) the generalized oxygen transfer reaction can be expressed as [8]



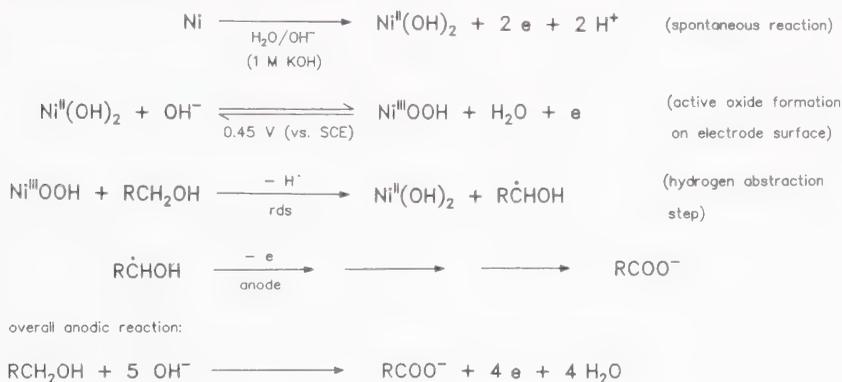
The PbO_2 electrode can act both as an electrocatalytic electrode by chemically oxidizing the organic species and as inert electrode for direct ET reactions as in the oxidation of phenolic compounds. Anodic oxidations of alcohols, aldehydes and amines at oxide covered electrodes of nickel or silver take place indirectly (electrocatalytically) by chemical reaction of the surface oxides with the organic substance. These oxidations occur usually at potentials 0.4 to 1.5 V vs SCE, in aqueous or aqueous-organic NaOH or KOH solutions. At these potential ranges the metal surface oxides are formed and are continuously regenerated during the electrolysis. If the organic substrate is not adequately soluble in the alkaline water solution a cosolvent, such as *tert*-butanol, may be used. Two primary oxidation paths are possible:

1. Direct electron transfer from the organic substrate to the electrode.
2. hydrogen atom abstraction from the organic substance by the surface oxide species [5–9].

Fleischmann and Pletcher [7] and Robertson [9] postulated a process of hydrogen atom abstraction by NiOOH formed in situ at a 0.45 V vs

SCE. The oxidation route of an alcohol to carboxylate at a nickel oxide electrode is depicted in Scheme 2.6. Both H⁺ abstraction and ET steps are involved in the overall scheme.

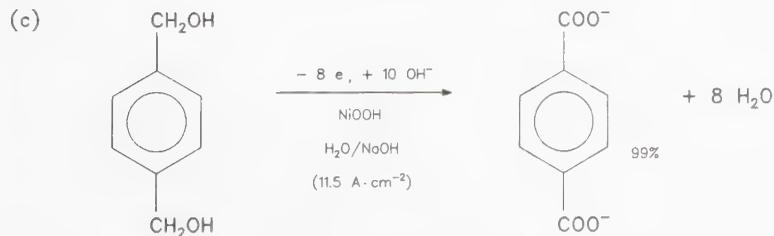
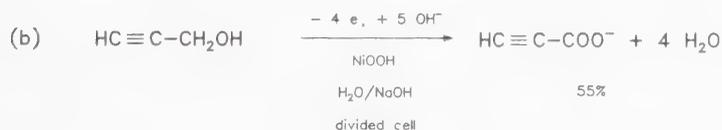
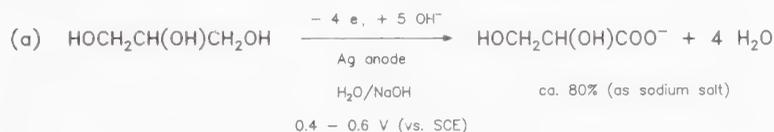
Nickel oxide
electrode



Scheme 2.6

The abstraction of hydrogen atom is the slowest step in the overall reaction leading to the RCO₂⁻ product. Electrocatalytic oxidations at these oxide electrodes consume four faradays and five moles of OH⁻ ion per mole of carboxylate in the product. This is exemplified by the oxidations of glycerol [10] and propargyl alcohol [11] to glyceric and propiolic acids, respectively, and the oxidation of *p*-xylene glycol to terephthalic acid [12], Scheme 2.6a,b,c.

Alcohol
oxidation
at NiOOH



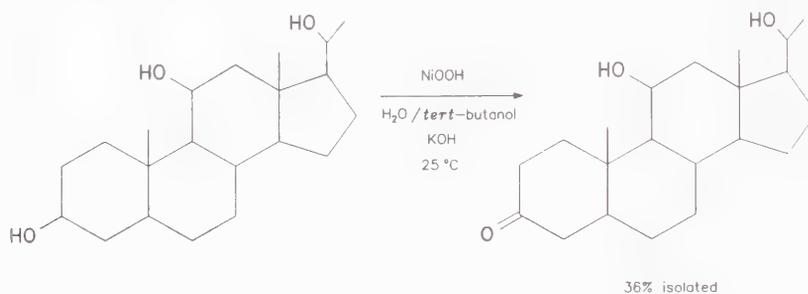
Scheme 2.6a,b,c

Steroid oxidation at NiOOH

Schäfer and Kaulen reported a very efficient oxidation of several alcohols and steroids at a NiOOH electrode in H₂O/NaOH solutions [5]. Typical yields of carboxylic acids obtained from the corresponding alcohols were as follows:

<i>n</i> -C ₇ H ₁₅ CH ₂ OH,	acid yield	65%
<i>n</i> -C ₃ H ₇ CH ₂ OH,	"	85%
<i>n</i> -C ₁₁ H ₂₃ CH ₂ OH,	"	80%
C ₂ H ₅ CH ₂ OH,	"	85%

The α,ω -diols afforded the corresponding dicarboxylates. We may note here that chemical oxidations by chromic acid or permanganate are less selective. Also direct anodic oxidation at platinum or carbon electrodes is not selective because of the very positive potentials needed for these oxidations, relative to the much *milder* oxidative conditions at the nickel oxide electrode in alkaline solutions at room temperature. The oxidation of steroids containing 3 α - and 3 β -hydroxy groups in the presence of 11 β - and 20 β -hydroxy positions was also found by Schäfer to be "surprisingly selective" at the NiOOH electrode [5]. The Openauer oxidation (a ketone with base as oxidizing agent) gives the 3-lactones, and chromic acid attacks preferentially the 11 β -hydroxy group, in contrast to the anodic oxidation at the NiOOH electrode which favors oxidation at the 3 β -hydroxy position, – probably because this position is closest to the electrode surface.

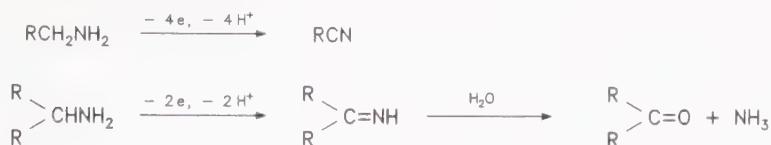


These oxidations can be conducted in one-compartment cells with a nickel net to function as anode and a stainless steel net as cathode. Electrolysis media are aqueous 0.1–0.3 M NaOH, or mixtures of water and *tert*-butanol with 0.1–0.3 M KOH, containing the organic substrate to be oxidized. The electrolysis is carried out at constant current at room temperature by applying an anode potential at least 0.45 vs SCE so as to cause the formation of the desired metallic oxide on the nickel electrode. The products are extracted with ether from the acidified (HCl) aqueous solution.

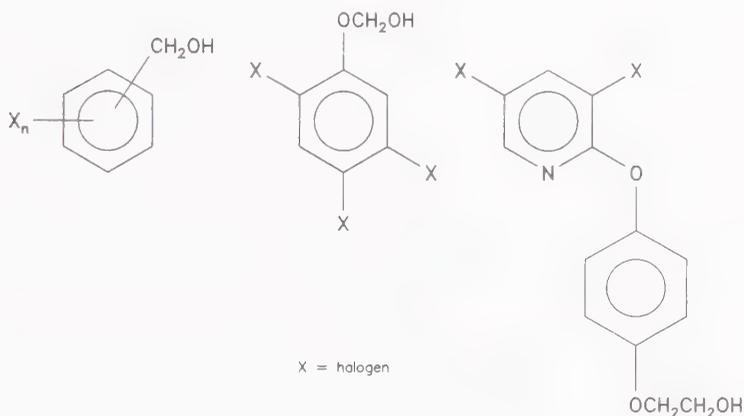
Oxidation of amines

Anodic oxidations of amines occur easily at Ni, Ag, and Cu electrodes covered with their respective oxides in aqueous or aqueous-organic basic solutions. These oxidations transform the amines to the corresponding

cyanides or ketones as indicated below. Ethylcyanide and propylcyanide are obtained from propylamine and *n*-butylamine, respectively, in 85% current yields [10].



Hydrophobic aromatic compounds, like the typical methylol compounds shown below, are very efficiently transformed into their carboxylic acid analogs by anodic electrolysis at NiO/NiOOH electrodes in H₂O/*tert*-butanol/KOH media [13].



The electrolysis is performed at 20–60°C at anode potentials between 0.5 and 1.0 V vs SCE. The cosolvent, *tert*-butanol enhances the solubility of the hydrophobic compounds. The products are recovered by acidifying with hydrochloric acid, extracting with CH₂Cl₂ and stripping off the solvent. Identification of products is made by comparing spectroscopic and chromatographic data with those of authentic samples. Yields of 70–90% are obtained.

Note: Usually – but not always necessary, the nickel electrode is activated before the preparative electrolysis by applying short polarity reversals on the electrode immersed in a solution containing some NiSO₄, NaOAc and NaOH. This is done until the nickel surface turns black, indicating that the electrode is covered with the active nickel oxides.

The anodic oxidation of propargyl alcohol to propiolic acid at a nickel electrode in aqueous NaOH solution will be described in detail – especially since this oxidative transformation can also be achieved in an electro-generative cell (Chapter 5). Because propargyl alcohol contains an acetylenic bond, a divided cell is necessary to avoid reduction of this bond

Oxidation of aromatics

Oxidation of propargyl alcohol

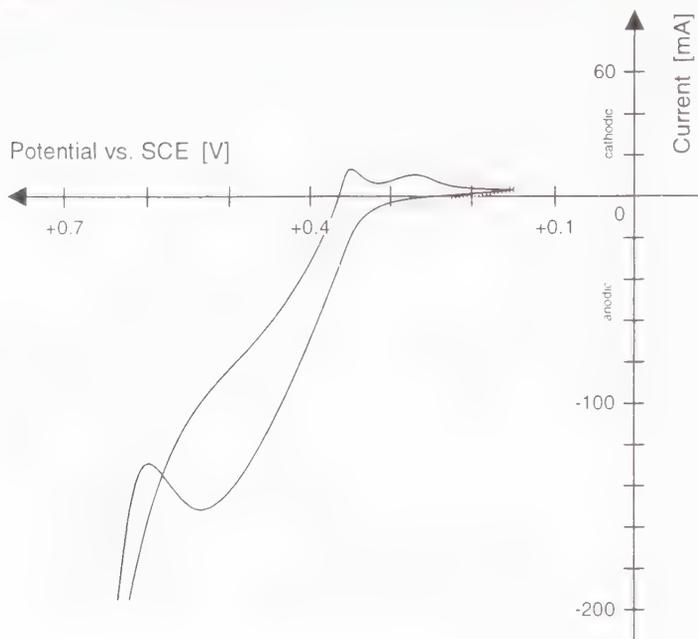


Fig. 2.2. Cyclic voltammogram of propargyl alcohol at a Ni wire electrode (2M NaOH). . . blank; — with propargyl alcohol, 0.01 M; scan rate 100 mV/s

and formation of acrylic acid instead of propiolic acid. In an undivided cell most of the propargyl alcohol is converted to acrylic acid. The anodic potential for this oxidation was chosen on the basis of the cyclic voltammogram, Figure 2.2, using a nickel wire as anode in $\text{H}_2\text{O}/\text{NaOH}$ solution in the presence and absence of propargyl alcohol. As is apparent from the *blank*, formation of the active nickel oxides occurs at 0.4–0.5 V vs SCE. The oxidation of the alcohol also occurs in that potential range.

Oxidation of Propargyl Alcohol to Propiolic Acid

The electrolysis was performed in an H-type cell with a Nafion cationic membrane as the divider, Figure 2.3. The potentiostat was an Electroynthesis Co. model 415 potentiostatic controller with a 36 V–5 A power supply. The anode was a nickel foil, 50 cm² exposed area and the cathode a nickel foil or a graphite rod. Typically, a solution of 2 g (0.03 mol) of propargyl alcohol was dissolved in 50 ml of 2 M aqueous NaOH solution. The catholyte was 50 ml of 2 M NaOH. Electrolysis was conducted at 5–8°C (optimum conditions) with the cell immersed in an ice bath, and at anodic potentials between 0.5 to 1.0 V vs SCE (sometimes it was necessary to raise the potential to 2.0 V for a few seconds in order to restore the activity of

the electrode). Currents of 1 to 0.3 A were passed until the total charge consumed was about 10–20% in excess of the theoretical. At the end of the electrolysis, the cold anolyte solution was slowly acidified to pH 1 with cold concentrated hydrochloric acid. The solution was saturated with sodium chloride and extracted with ether (2×50 ml). The combined ether extracts were treated with anhydrous magnesium sulfate or sodium sulfate and the ether was evaporated (vacuum). The liquid residue (1.2 g) was analyzed by chromatography and was identified as propionic acid by comparing IR and NMR spectra with spectra of an authentic sample. Yield 55%, 99% purity.

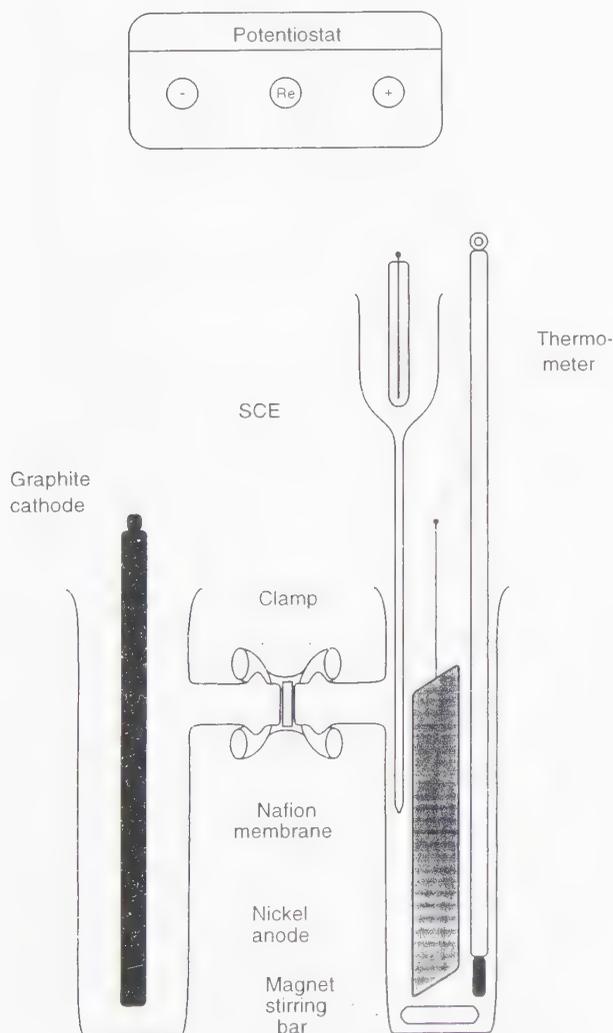
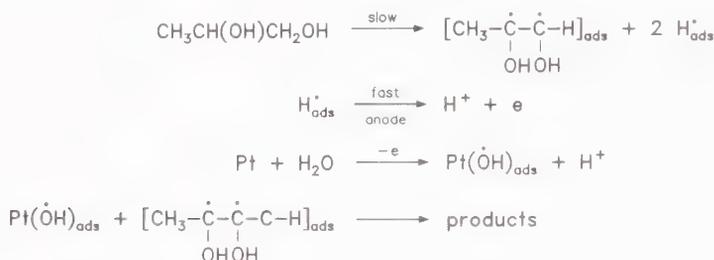


Fig. 2.3. Schematic of H-type cell for the anodic oxidation of propargyl alcohol to propionic acid

Note: Similar results were obtained by electrooxidation in 1M aqueous H_2SO_4 solution in a divided cell with a lead anode (PbO_2) and a graphite cathode. This method is used by BASF for the manufacture of propiolic acid.

Oxidation at adatoms

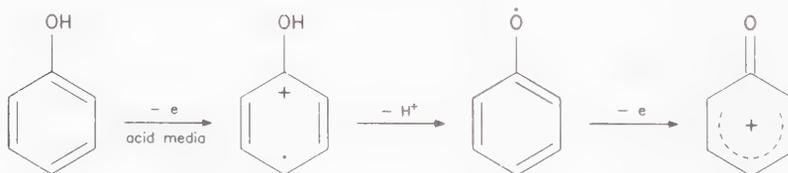
We may at this juncture digress to refer very briefly to the anodic oxidation of lower alcohols at *adatom* electrodes by the underpotential deposition method (UPD) [14]. Adatoms enhance the oxidation rate (of electrocatalysis, heterogeneous type) by preventing adsorption of *poisoning* species on the electrode surface, or perhaps by oxidation of the alcohol by oxygen containing species adsorbed on the foreign adatoms. The UPD adatoms are usually metals of Pb, Bi, Re, Ge, Cd deposited on precious metals, under potentials less negative than thermodynamic potentials. The oxidation of 1,2-propanediol [15], for example, was proposed to take place electrocatalytically at platinum electrodes modified by UPD adatoms of Re or Pb. The first step is a dissociative adsorption process. Oxidation of H_2O generates the active OH^* species, adsorbed on the electrode surface. These react with the adsorbed fragment of the alcohol, as shown in Scheme 2.7.



Scheme 2.7

2.5 Phenolic Compounds

The electrochemistry of phenolic substances is more versatile and also more complex than that of other hydroxy compounds [1]. In phenols the hydroxy group releases electrons to the ring and thus facilitates the release of ring electrons to the anode. The anodic deelectronation of phenol is indicated by Swenton as follows [2]:



In general, phenols are oxidized by strong oxidizing agents, dichromates, periodates, etc. in very acidic solutions. The anodic method would certainly be a good alternative for oxidation of phenols, especially for large scale production. Most phenols exhibit reversible anodic behavior in the time scale of cyclic voltammetry. As expected, phenols with more than one hydroxy groups are more easily oxidized than the monohydroxy analogs, as is apparent from their voltammetric peak potentials [3]: phenol, 0.53, catechol, 0.14, hydroquinone, 0.02V vs SCE. Alkoxy and Ar—O ring substituents also facilitate oxidation of phenols at the anode. The oxidation of phenols yields cations and neutral species as intermediates, Schemes 2.8 and 2.9, leading to various products in high yields [3]. In the presence of nucleophiles a wide variety of products can be obtained; for example, coumestan derivatives and related heterocyclic compounds [4], Scheme 2.9. Anodic electrolysis of phenols, in general, can be conducted in aqueous and aqueous-acetone solutions, which can be acidic, neutral or basic. Products like those of Scheme 2.9 are physiologically interesting and can be prepared in good yields by the electrochemical method.

Oxidation

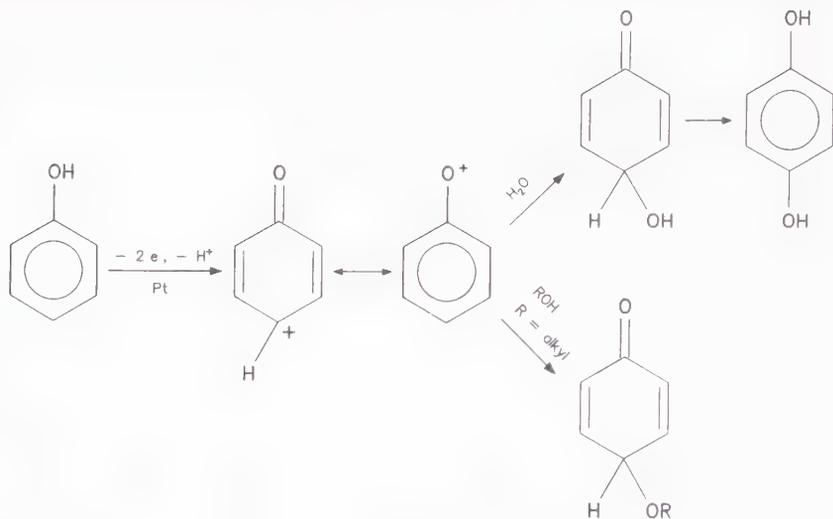
Preparation of Coumestan Compounds. General Electrolysis Procedure [4]

Electrolysis is performed in aqueous 0.1–1M sodium acetate solutions containing the starting materials, for example, catechol, A, and 4-hydroxy coumarin, B, Scheme 2.9, in an undivided cell with graphite or platinum electrodes at anodic potentials of 1.0–1.2V vs SCE. Because passivating films may sometimes cover the anode periodic removal of the films is required: Washing the anode with acetone restores the electrode active surface. The products are recovered from the electrolyzed solution after acidification with cold acetic acid whereupon the products precipitate and are then purified by recrystallization from methanol-acetone-ethanol mixed solvent or from acetone alone. Isolated yields are in the range of 90–95%.

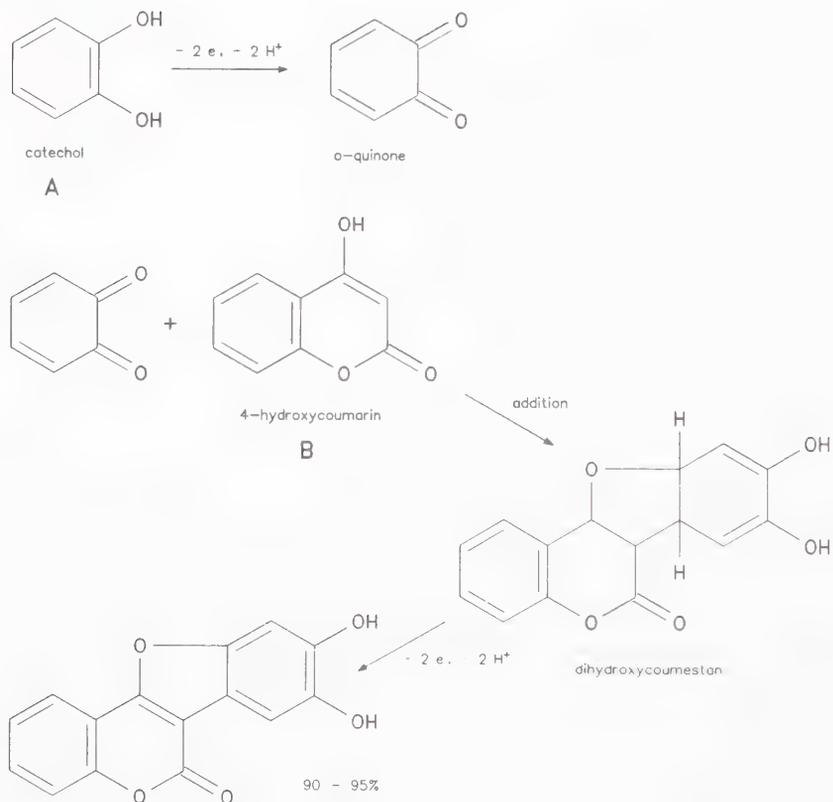
Parker and coworkers studied the anodic oxidation of natural phenolic compounds, the α -tocopherol family [4,5].

α -Tocopherol is oxidized reversibly with peak potentials at 0.74V and 0.80V vs SCE in $\text{CH}_2\text{Cl}_2/\text{TFA}/\text{Bu}_4\text{NF}_4$ medium. The primary oxidation product is the cation radical which is further transformed, as shown in Scheme 2.10.

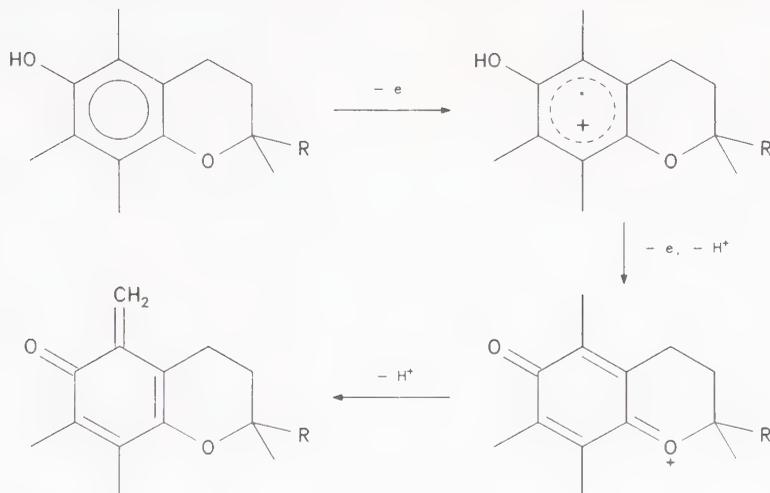
Oxidation of natural phenolic compounds



Scheme 2.8

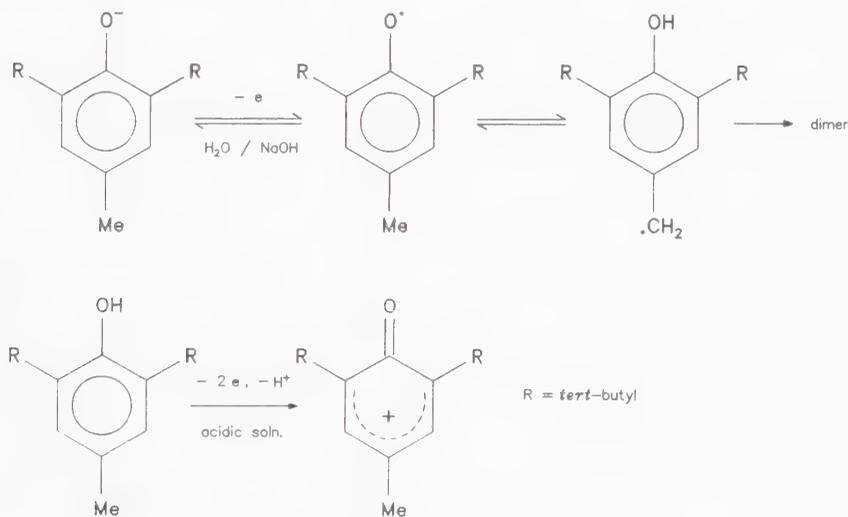


Scheme 2.9



Scheme 2.10

Sterically hindered cresols, when oxidized in basic aqueous solutions on graphite anodes, afford dimers [5]. In acidic solutions phenoxonium ions are formed, Scheme 2.11.

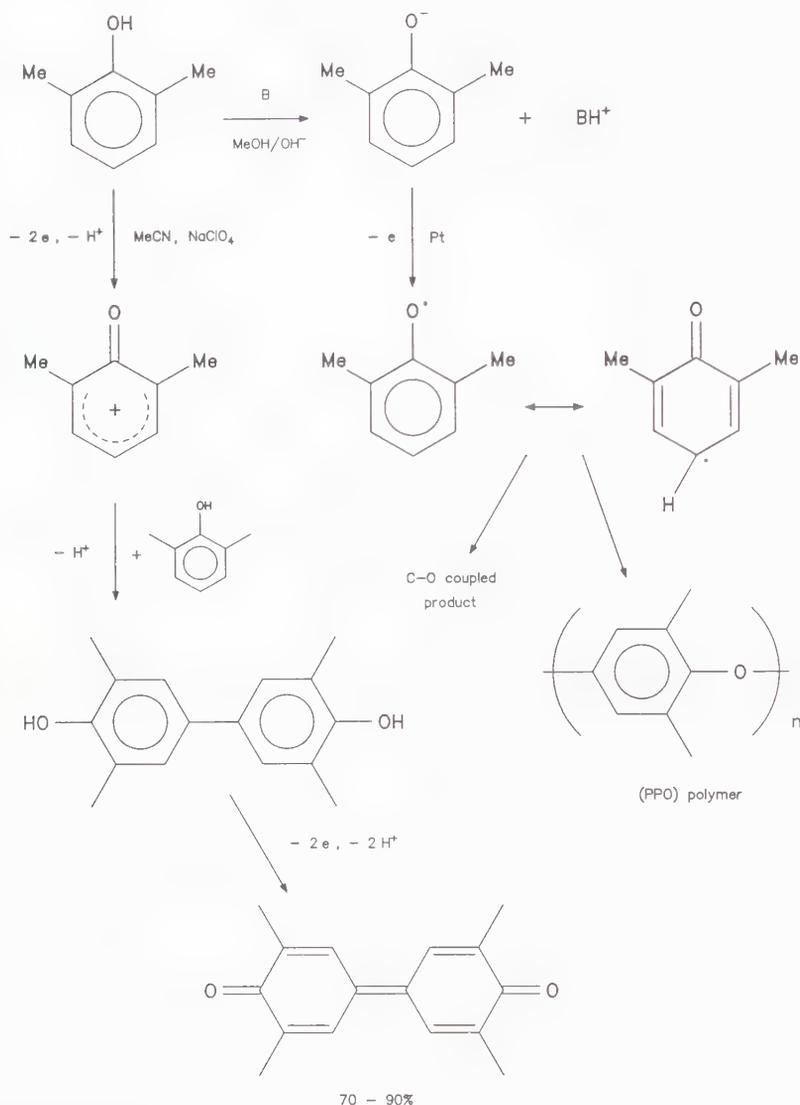


Scheme 2.11

Anodic couplings of methoxy-substituted phenols in methanolic-sodium hydroxide or in acetonitrile-sodium perchlorate solutions in divided cells afford quinones [6]. The oxidation of 2,6-dimethylphenol gave the C—O and the C—C coupled products, depending on the electrolysis medium in

Couplings of phenols

70–90% yields, and also poly(2,6-dimethyl-1,4-phenyleneoxide) (PPO), as indicated in Scheme 2.12.

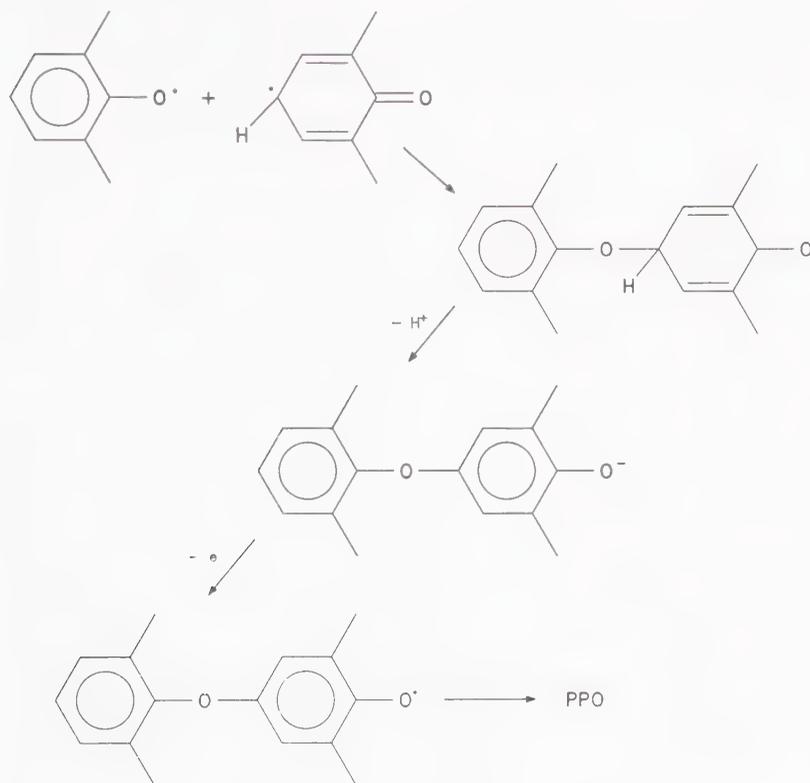


Scheme 2.12

Polymer formation

The polymer PPO (via C—C coupling) is most favorably formed in the MeOH/NaOH solution, but the dimer (via C—C coupling) forms in MeCN/NaClO₄ solution by electrophilic attack of the electrogenerated phenoxonium ion on the starting material. The C—O coupling of the

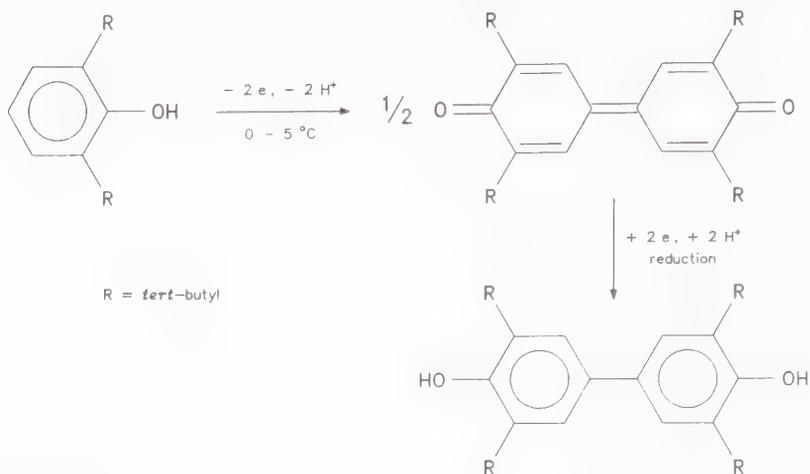
phenoxy radicals leading to the PPO polymer proceeds most likely according to the following path:



These electrolyses are conducted in divided cells with platinum electrodes under potentiostatic conditions [6]. Recently, Torii and coworkers reported an interesting anodic coupling of phenols [7]. The electrolysis was conducted in a divided cell as if it were a *paired* electrochemical process. The 2,6-*tert*-butylphenol was oxidized at a platinum anode in $CH_2Cl_2/MeOH/LiClO_4$ solution to give the diphenoquinone product which, by changing the current direction, was reduced at the platinum cathode to the biphenol product in high yield, Scheme 2.13.

In this connection we may consider the possibilities of applying electrochemical methods to the degradation of biomass materials such as the lignins, which are polymeric phenols. According to a recent study by Utley and coworkers [8], the electrochemical oxidation might be a better alternative than the chemical method. The latter requires quite severe reaction conditions, including the use of nitroaromatics as oxidants in concentrated alkali and temperatures of 150–200 °C. The anodic electrolysis achieves

**Electro-
chemical
degradation
of biomass
materials**

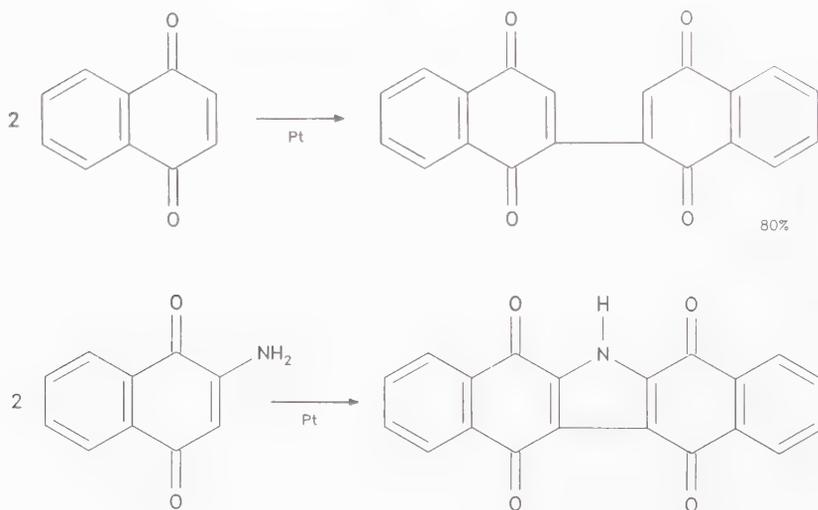


Scheme 2.13

similar results at ambient temperatures with nickel electrodes in aqueous alkaline solution. Thus an organo-sol spruce lignin with some nitrobenzene as additive to facilitate the oxidation afforded vanillin and syringaldehyde in 8–50% isolated yields. Recently, electrochemical oxidation of lignin in 1N NaOH solution was suggested for the electrolytic production of hydrogen, the lignin acting as anodic depolarizer [9].

Dimerization of Quinones

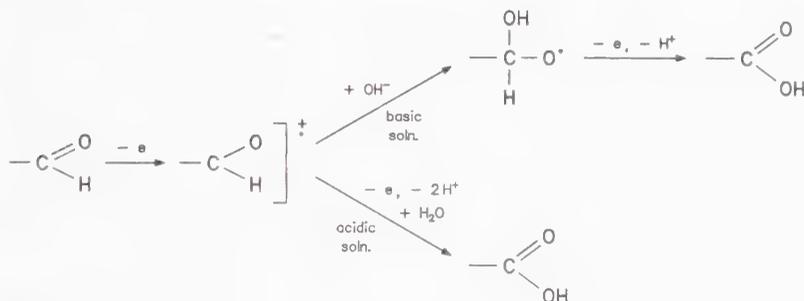
Quinones and derivatives thereof are easily dimerized by electrooxidation in 50% aqueous acetic acid containing $MgClO_4$ as electrolyte, in divided cells with platinum electrodes [10]. It is noted that chemical methods give dimer yields of less than 20%, as contrasted with 80% by the electrolytic oxidation method:



2.6 Carbonyl Compounds

Aldehydic carbonyls are good electroactive groups because they can undergo both reduction and oxidation at the cathode and anode, giving alcohols or carboxylic acids, respectively [1]. Ketonic carbonyls are also electroactive, although to a lesser degree than the aldehydic carbonyls. In principle, aldehydes can be oxidized to the carboxylic acid state by removal of two electrons from the aldehyde, in both acidic and basic aqueous or aqueous-organic solutions, Scheme 2.14. In acidic solutions platinum, graphite and PbO_2 are the usual anodes while in basic solutions oxide-covered electrodes of Ni, Ag, Cu, Co and Mn are the most effective electrodes, especially the first two. Direct anodic oxidation of potentially available aldehydic functions in carbohydrates have not yet been synthetically successful because of concurrent degradative reactions. Indirect (mediated) oxidations have been considerably more successful [2,3,4]. The direct oxidation of monosaccharides in aqueous alkaline solutions has been considered and studied in depth by Bockris and coworkers for fuel cell applications [3].

Direct and indirect oxidation

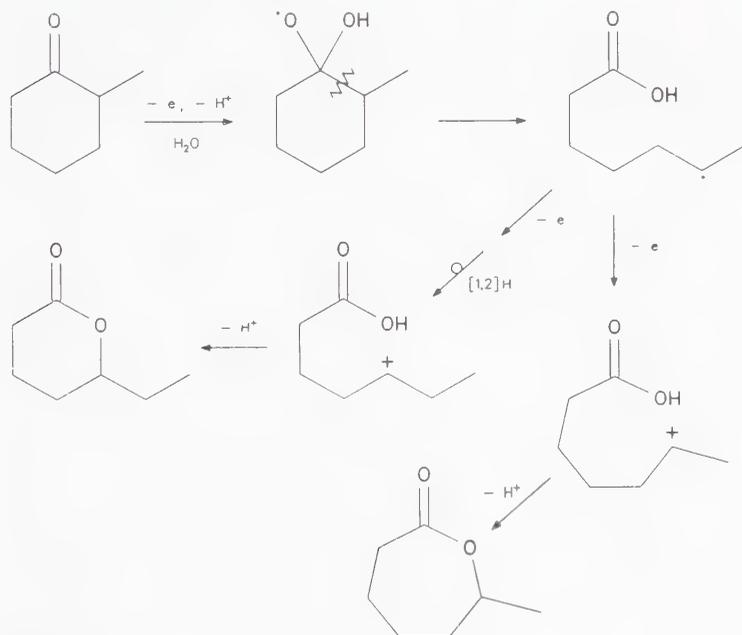


Scheme 2.14

Chiba [4] reported that the aldehydes $\text{C}_6\text{H}_5\text{CHO}$, $2\text{-CH}_3\text{-C}_6\text{H}_4\text{CHO}$, $2\text{Cl-C}_6\text{H}_4\text{CHO}$ and some others are anodically oxidized in MeOH/NaCN solutions at less positive potentials than in $\text{MeOH}/\text{LiClO}_4$ solutions. Apparently cyanohydrins, formed in situ, are involved in the initial chemical step. This is followed by oxidation of the cyanohydrin to the corresponding acyl cyanides, which then react with methanol to yield methyl esters (73–80%).

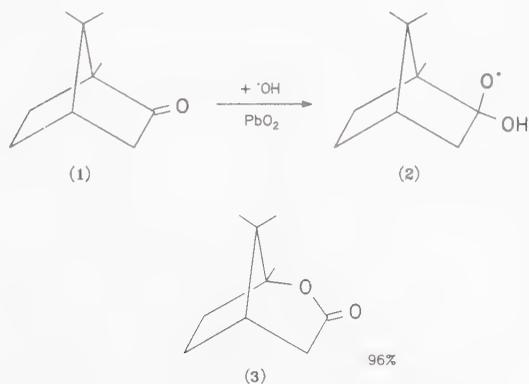
Ketones of the general formula RCOR [1] where R is benzyl, or alkyl secondary or tertiary group undergo α -cleavage of the cation radical generated at the anode, in $\text{MeCN}/\text{LiClO}_4$ solution containing small amounts of water [5,6]. Reactions, as depicted in Scheme 2.15, follow the first step of electron transfer to the anode.

Methylcyclohexanones undergo ring opening by electrolysis in EtOH/H₂O/NaClO₄ solutions at platinum electrodes [8]. Rearrangement of the opened ring gives lactones, Scheme 2.17.



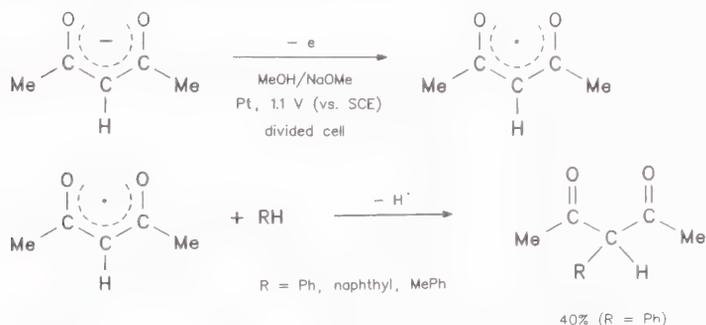
Scheme 2.17

Camphor (1) is transformed to lactone (3) via the intermediate (2) which apparently is produced at the PbO₂ anode by OH[•] addition to the carbonyl group, as a first step. [9] Further deelectronation and expulsion of a proton yields the lactone (3),



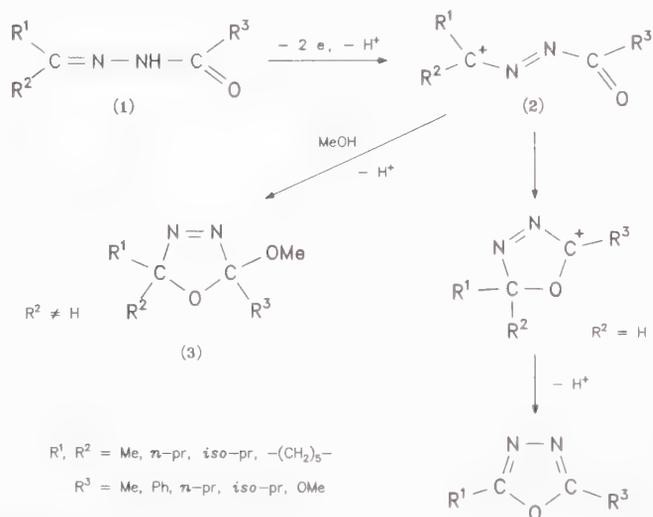
The electrolysis was performed in a mixed solvent consisting of aqueous 1M H₄SO₄ and acetonitrile in 1:1 volume ratio under a current of 10 mA/cm² at 20°C with PbO₂ or Pt anodes. This electrolysis was also

demonstrated with a plate and frame cell divided with a cation exchange membrane. Yields of 62–82% were obtained depending on electrolysis time. Certain carbonyls with structures possessing acidic hydrogens (carbon acids) yield anions by reaction in methanol solutions containing sodium methoxide (formed by adding sodium metal to the alcohol). These anions are readily oxidized at the anode so that substitutions are possible [9,10], as depicted in Scheme 2.18



Scheme 2.18

Anodic electrolysis of hydrazine derivatives of aldehydes and ketones in a divided cell, with carbon anode and platinum cathode, in MeOH/NaOAc solution, is an efficient method for the preparation of oxadiazolines. Chiba and Okimoto [11] proposed a reaction mechanism as depicted in Scheme 2.19 for the cyclization of *N*-acylhydrazones (1) to afford the Δ^3 -1,3,4-oxadiazoline (3). Yields of 30–77% are obtained depending on the type of R^1 , R^2 , R^3 substituents.



Scheme 2.19

Preparation of Oxadiazolines, (Scheme 2.19)

The electrolysis is conducted at room temperature in a 100-ml cell divided with a glass frit, and equipped with a carbon rod anode and a platinum foil cathode. Typically, 50 mmol of *N*-acylhydrazone is dissolved in 80 ml of methanol containing 15 mmol of sodium acetate. After 3.0 F/mol of charge is passed, at a constant current of 0.05 A, the methanol of the anolyte is evaporated in vacuo at room temperature. Water is added to the residue and the two phases are separated. The organic layer is extracted with ether (20 ml × 3) and the combined extracts are washed with water, dried with anhydrous sodium sulfate and concentrated in vacuo at room temperature. The residue is purified by silica-gel column chromatography with benzene as eluant (Adapted from (1992) *J Org Chem* 57:1375. Copyright American Chemical Society, 1992).

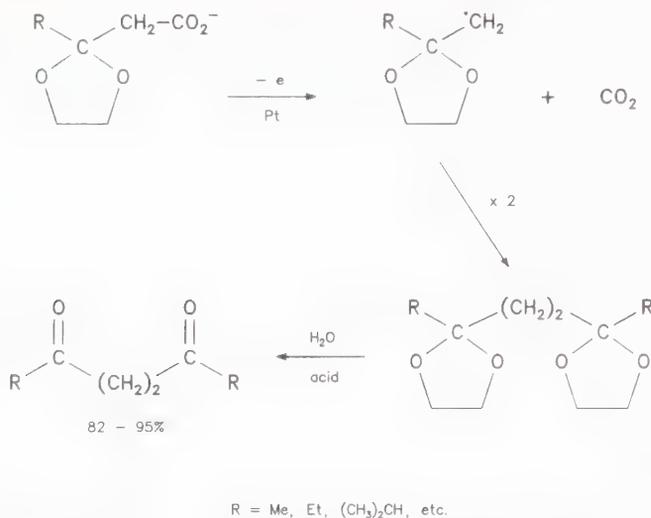
2.7 Carboxylic Acids

2.7.1 General Perspective

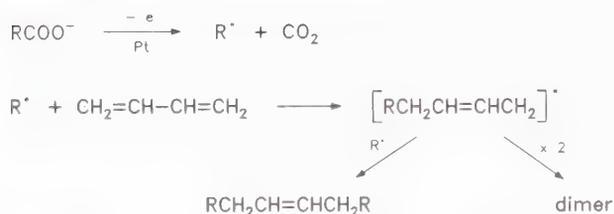
Electroorganic chemistry, it may be said, began with a typical C—C bond formation – which is the innermost essence of all organic chemistry. This first electrochemical reaction is now widely known as the *Kolbe Synthesis*[1]. In 1834 Faraday first observed the evolution of ethane during electrolysis of aqueous acetate solutions at smooth platinum electrodes. Kolbe later studied the practical possibilities of this electrolytic decarboxylation, although neither he nor Faraday had any idea of the oxidative reaction mechanism as it is accepted today. Kolbe had the plausible idea that it was the nascent oxygen, generated at the anode, that oxidized the acetic acid to give the products, ethane, carbon dioxide and water. The Kolbe reaction is now generally believed to occur directly, by an overall route initiated by an electron transfer from the carboxylate to the anode, as depicted below [2–6]:

Kolbe synthesis





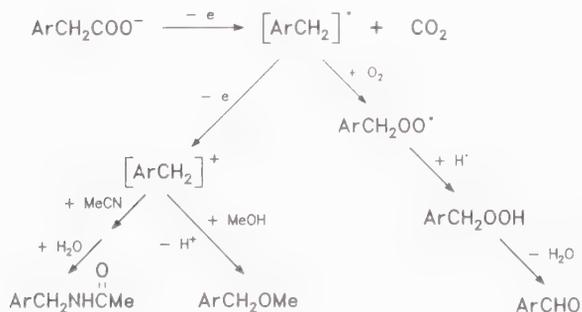
Scheme 2.21



Scheme 2.22



Anodic decarboxylations may lead to aldehydes via one-electron oxidation in the presence of molecular oxygen, and to acetals and acetamides by two-electron oxidation in methanol or acetonitrile solutions [9a]:



Trifluoromethoxylation of Methylacrylate (Scheme 2.23)

Using methylacrylate (MMA) as a substrate to be trifluoromethylated, the electrolysis was conducted in a one-compartment cell containing 23 ml of mixed solvent MeCN/H₂O, in the volume ratio of 20:3, platinum electrodes, 200 mg of MMA, 46 ml of TFA, and 24 mg of NaOH. A current of 24 mA (1 mA/cm²) was passed for 9 h (or 4 F/mol of MMA) while the cell temperature was kept at 0–5 °C. The electrolyzed solution was neutralized with sodium bicarbonate, the organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 × 4 ml). The combined extracts were washed with saturated sodium chloride solution, dried with sodium sulfate and concentrated in vacuo. The residue was separated by flash column chromatography, and gave 20% of product (1) and 5% of product (2) (Summarized from Ref. 10, copyright to American Chemical Society, 1988).

2.7.2 Oxidations in Fluorosulfuric Acid

Anodic oxidations of carboxylic acids occur at platinum electrodes in fluorosulfuric acid media containing potassium fluorosulfonate [11]. The oxidation of heptanoic, octanoic, 4-methylpentanoic and 5-methylhexanoic acids were thus oxidized and gave lactones and ketones as major products, Scheme 2.24. In this strongly acidic medium the carboxylic acids undergo C-H bond cleavage at carbons distant from the carboxyl group. NMR evidence suggests that the electroactive species is the protonated form of the carboxylic acid, as it happens with the oxidation of alkanes in FSO₃H. Apparently the molecule does not undergo decarboxylation under these electrolysis conditions.

This electrolysis is conducted in a divided cell at anode potentials of 1.8–2.0 V vs Pd/H₂. Short periodic cathodic pulses on the anode may be necessary to minimize possible electrode passivation. The products are extracted with ether, separated by chromatography and identified by comparing their IR spectra with spectra of authentic samples.

2.7.3 Kolbe Synthesis in SPE Cells

In the fifth chapter, we will consider potential applications of solid polymer electrolyte cells (SPE-Cells) as a new type of cells for electrochemical applications. Ogumi and coworkers [12] demonstrated the feasibility and

2.7.4 Photokolbe Synthesis

Some years ago Bard and Kraeutler [1] studied the oxidation of acetate ions in acetonitrile solution under illumination at a rutile TiO_2 crystal electrode (a semiconductor). They found that the decarboxylation could start to occur at potentials as low as -1.6 V vs $\text{Ag}/\text{Ag}^+\text{NO}_3^-$ reference electrode. The n-type TiO_2 electrode was in the form of either a single crystal or in vapor-deposited polycrystalline form. This photo-assisted oxidation on the semi-conductor electrode was explained as follows:



where the symbol P^+ denotes a photogenerated *hole* on the TiO_2 electrode. The electrolysis was conducted in acetonitrile containing tetrabutylammonium acetate and some acetic acid at 0.0 V vs a Ag/Ag^+ reference electrode. The cell was a vacuum type one-compartment pyrex glass vessel fitted with a flat window. The gases C_2H_6 and CO_2 that were produced at the anode were collected and analyzed by mass spectroscopy. (This interesting photoelectrochemical oxidation has the potential of utilizing solar energy for the production of hydrocarbons.)

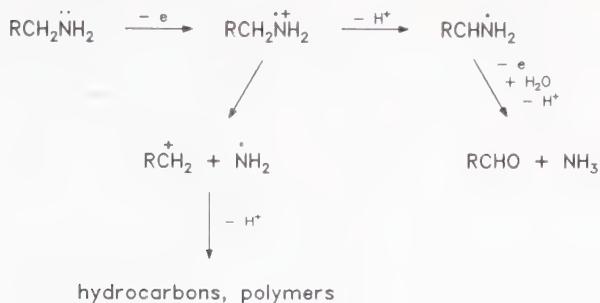
2.8 Amines and Amides

2.8.1 Amines, in General

Formation of the cation radical

Aliphatic and aromatic amines are readily oxidized at the anode in aqueous and organic solvents. Usually, anode potentials of $0.5\text{--}1.5\text{ V}$ vs SCE are adequate for the generation of the primary cation radicals of amino compounds [1–8]. The primary step is the transfer of an electron from the amino nitrogen to the anode, whereupon a cation radical is produced. Sometimes the first electron transfer step is followed by transfer of a second electron so that an apparent two-electron oxidation step is observed voltammetrically (one wave or peak). Because various difficult-to-control reactions usually follow the primary ET step, the anodic oxidation of aliphatic amines is synthetically less useful than that of aromatic amines which offers many possibilities [2,7,8]. Aliphatic amines give mixtures of unstable cation radicals, at platinum or carbon electrodes in various solutions, leading to mixtures of products:

Aliphatic amines

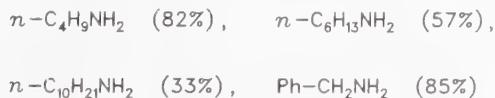


Aromatic amines yield cation radicals that are more stable than those of aliphatic amines. Often dimers are formed via C—C, C—N and N—N bonds, which are more easily oxidized than the starting aromatic monomers [9] (because of enhanced charge delocalization in the dimer intermediates).

Schäfer concluded that the method of anodic oxidation of primary amines at NiOOH electrodes (nickel oxide in alkaline solutions) is generally more effective synthetically than most ordinary chemical oxidation methods [10]. Such anodic oxidations can be performed with nickel electrodes that become covered with a layer of NiOOH continuously regenerated at 0.4–0.5 V vs SCE in MeCN/H₂O/KON solutions (see Sect. 2.4):



Typically, the following amines yielded their corresponding nitriles (% yields shown in parenthesis):

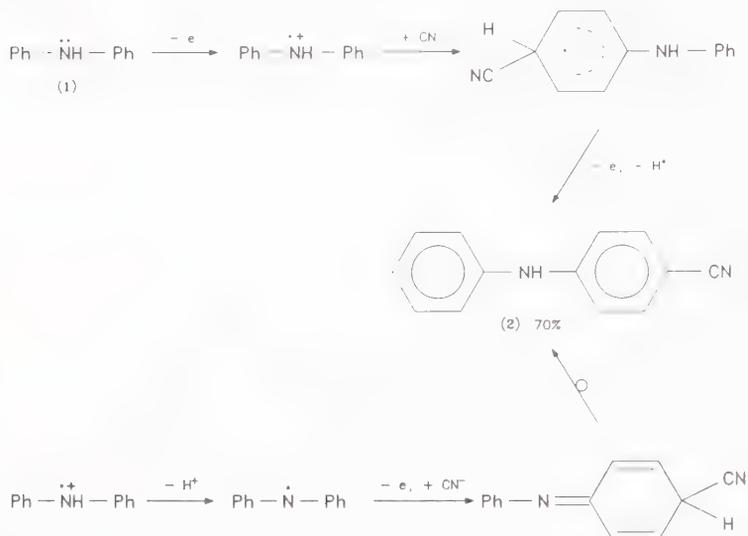


Chemical methods with lead tetraacetate, nickel peroxide or iodine pentafluoride achieve about equal conversion but require at least equivalent amounts of these oxidizing agents.

Aromatic amines

Production of nitriles

In this connection we mention the conversion of diphenylamine(1) to the nitrile compound(2) by anodic cyanation of the primary cation radical of (1) in MeCN/Et₄N⁺CN⁻ solution, as proposed by Serve [11], Scheme 2.25.

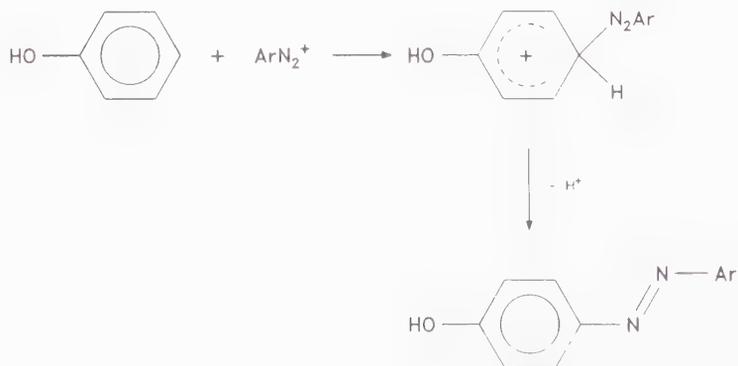


Scheme 2.25

Production of azobenzenes

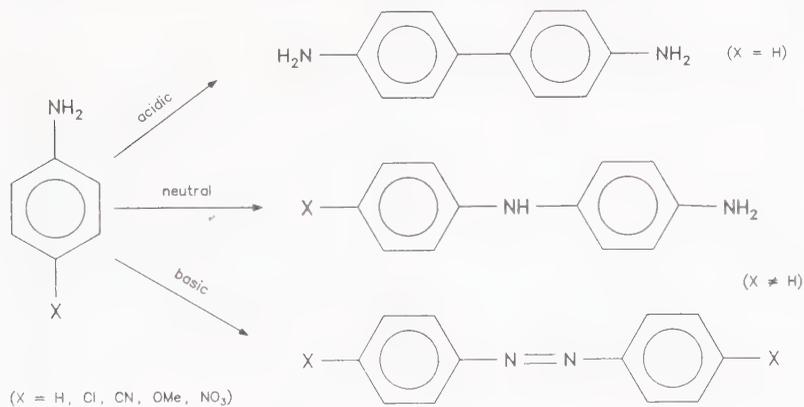
Anodic oxidations of anilines in MeCN/pyridine solutions afford azobenzenes [12]. The aniline monomer is polymerized in 0.5 M H₂SO₄, forming electrically conducting films [13].

Azobenzenes, it may be noted, can be produced via the chemical diazonium salt method if a strong electron-releasing group (e.g. OH) is on the ring to facilitate electrophilic attack by ArN₂⁺.



The anodic oxidation of aniline to the azobenzene can readily take place in water dispersions or in H₂O/DMF and also in H₂O/MeCN/pyridine solutions [14]. The type of dimers produced by anodic oxidation of anilines is influenced greatly by the pH of the solutions [12].

pH effect



Some aromatic amines when oxidized yield stable salts of their cation radicals with perchlorate or bromide as negative counterions (Wuster salts), both as solids and in solution [15]. Triarylamminium salts are best known as very effective one-electron oxidants. One such cation radical used in indirect electrolysis is the tri-*p*-bromophenylaminium ion Ar₃N⁺. Anodically produced stable organic salts are rare. They are usually sparingly soluble in the medium and tend to adhere to the electrode surface. They may require mechanical removal for the electrolysis to continue.

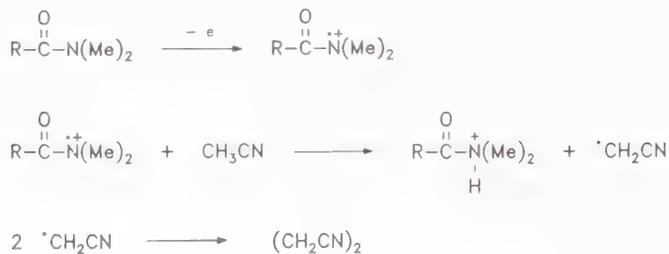
Production of organic salts

2.8.2 Amides

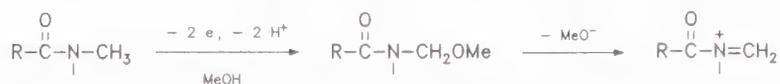
Amides are a special type of substituted amines. In general, they are oxidized at the anode, but at considerably more positive potentials than the amines. The carbonyl group delocalizes the lone electron pair of the nitrogen atom and thus makes these electrons less available for release to the anode:



An amide, upon surrendering an electron to the anode, is transformed into a cation radical which may abstract a hydrogen atom from the environment:

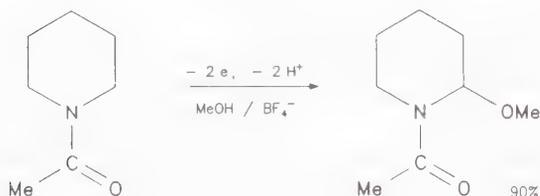


Dimethylformamide, if oxidized at a platinum anode in MeOH solution, yields polyalkoxylated products in 60–70% total yields, but much lower yields at graphite electrodes [16,17]. Tertiary amides are oxidized in MeOH in one-compartment cells under constant current electrolysis and give products from which α -acyliminium ions can be obtained [17]:



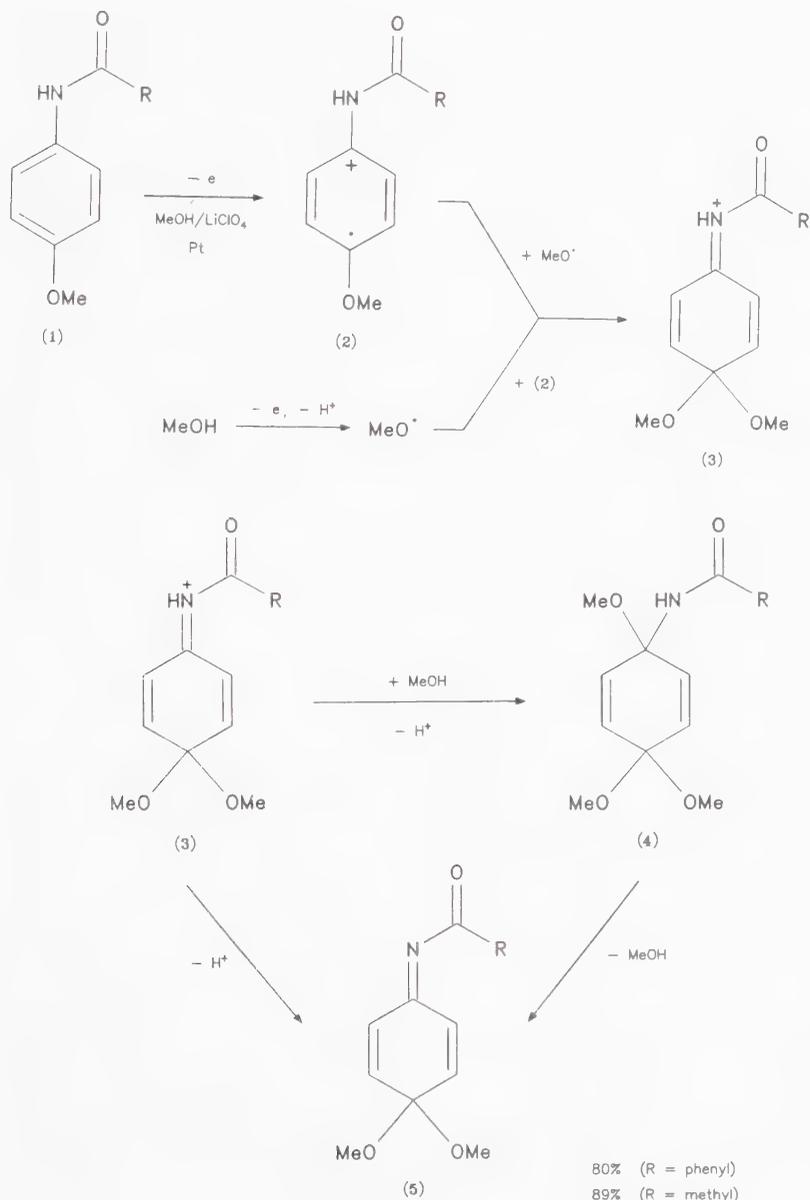
Tertiary amides have been studied as electrochemical models [18] for the oxidative *N*-dealkylations of amines by the cytochrome P-450 enzyme. The oxidation yields *N*-methamides in high yields via an ECE process involving ammonium intermediates.

N,N-dialkylamides and urethanes undergo anodic methoxylations affording synthetically useful intermediates [19]. For example, the methoxylation of the cyclic amide takes place very efficiently in MeOH/BF₄⁻ solution:



Urethanes thus methoxylated afforded intermediates that were chemically converted to the alkaloids, hydrogline, sedamine and others [17]. Urea is oxidized to the simplest oxidation products at platinum anodes [20]. Urethanes are produced in high yields by electrolyzing formamides in undivided cells with graphite anodes and halogenides as electrolytes [21]. Swenton and coworkers [22] recently studied the anodic oxidation of *p*-methoxyanilides (**1**) for the purpose of developing a method for the preparation of acylated quinone imine ketals (**5**). These compounds

are intermediates for the construction of a number of alkaloids. A very efficient and "reasonably general" method was developed and a plausible reaction mechanism (EEC_rC_p) was proposed for the anodic reaction, Scheme 2.26.



Scheme 2.26
(The EEC_rC_p mechanism)

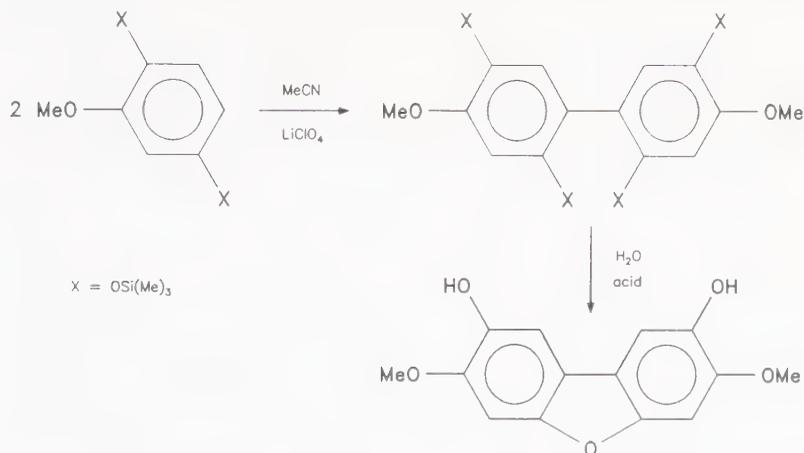
EEC_rC_p-type Electrolysis (Scheme 2.26)

This interesting anodic electrolysis is carried out at 0°C under constant current in MeOH/LiClO₄ solution containing the anilide in the presence of either sodium bicarbonate or 2,6-lutidine in a single-cell apparatus with platinum electrodes. The anodic potential is such that both the anilide and the methanol are oxidized by electron transfers to the anode while lithium ion is reduced at the cathode, and the metallic lithium reacts with methanol to liberate hydrogen. The electrolyzed solution is concentrated in vacuo at about 10°C, and the residue is extracted with methylene chloride (3 × 40 ml) after adding 40 ml of water. After work-up of the organic phase the acylated quinone ketals are recovered in yields of 80–89% (Adapted from Ref. 22, Copyright of the American Chemical Society, 1989).

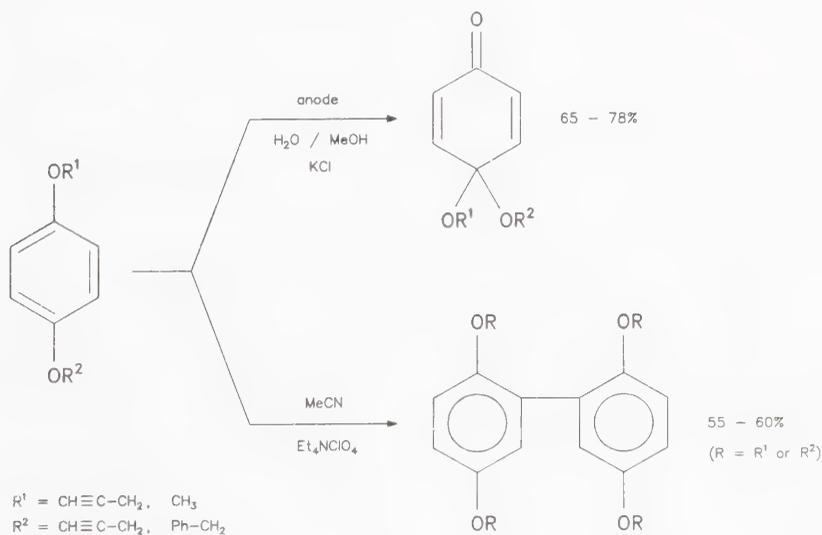
The notation EEC_rC_p, Scheme 2.26, implies two electron steps (EE), to generate the radical cation and the radical species; C_r refers to methoxy radical CH₃O· combining with cation radical (2), and C_p refers to the polar step, the proton removal from (3) to give (5) or addition of methanol to (3) to give (4) which loses methanol to give (5).

2.9 Ethers and Esters**Aromatic ethers**

Aromatic ethers are generally directly oxidized at the anode. In contrast, aliphatic ethers are extremely resistant to anodic oxidation, and this property allows them to be employed as electrolysis media, alone or as *cosolvents*, for certain electrosynthetic applications. Aromatic-alkoxy ethers are deelectronated quite easily because the alkoxy substituents tend to release electrons to the aromatic ring, from which the electrons are removed, and they also stabilize the produced cation radicals [1]. Aryl ethers, such as anisoles, couple readily upon oxidation in solvents containing trifluoroacetic acid (TFA). This type of anodic coupling can be followed by cathodic reduction of the *stable in the TFA medium cation radicals* of the coupled intermediates [2,3]. Miller reported an unexpected ring-ring coupling in the anodic oxidation of 2-methoxy-1,4-bis(trimethylsiloxy) benzene [4]:

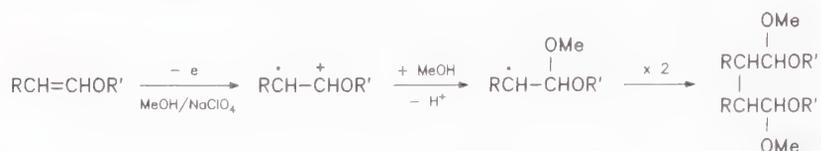


Apparently the presence of the methoxy group promotes anodic coupling rather than the expected cleavage at the OSiMe_3 , a reaction that would have led to the quinone product. Anodic oxidations of aryl ethers in aqueous methanol-potassium chloride solutions, afford quinone monoketals in 65–78% yields, and dimerized products by electrolysis in acetonitrile containing Et_4NClO_4 as electrolyte [5]:

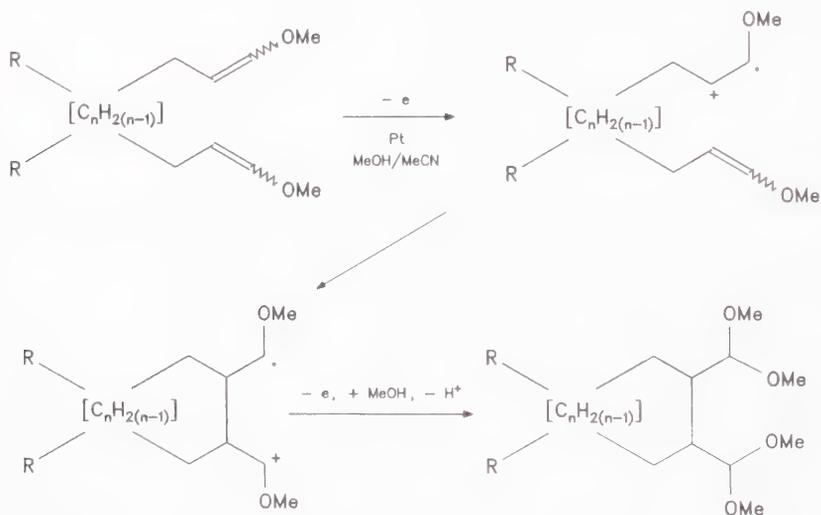


Saturated aliphatic ethers are indirectly methoxylated in MeOH/KOH solutions by reacting with $\text{CH}_3\text{O}^\cdot$ radicals generated from the oxidation of CH_3O^- ions [6]. Phenolic ethers are methoxylated directly, that is, via the generated cation radicals of the ethers, since these ethers are more easily deelectronated at the anode [2] than the CH_3OH or CH_3O^- ion. Enol

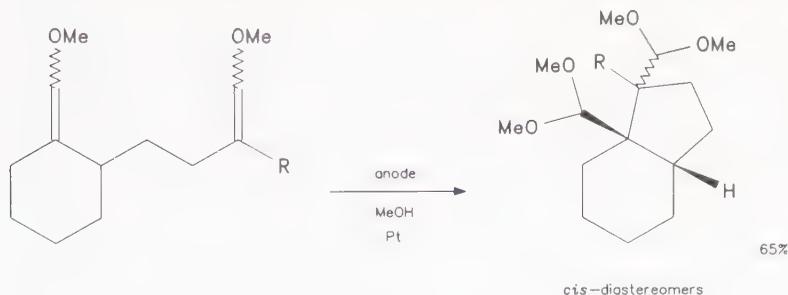
ethers are easily oxidized at the anode in methanolic solutions to give methoxylated dimer products [8]:



This reaction has been found useful for the synthesis of octaethylporphyrins.⁹ The coupled products from the oxidation of aldehyde enol ethers in methanol, gave by reaction with benzyl carbamate *N*-carboxybenzyloxy-pyrroles, which after deprotection and reaction with formaldehyde gave the porphyrins. Electrolysis of zinc-octaethylporphyrins in DMF/CN⁻ media gave the cyanoporphyrins [9]. Bis-enol ethers are synthetically interesting electron-rich olefinic compounds which can undergo efficient intramolecular coupling reactions by anodic oxidation [10]. Electrolysis can be carried out under constant current in an undivided cell with a platinum anode and 10% MeOH in MeCN in the presence of 2,6-lutidine as proton scavenger. Two typical examples are shown in the following:



50 - 70%
(n = 1, 2, 3; R = H, Me)

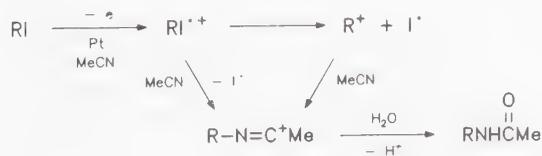


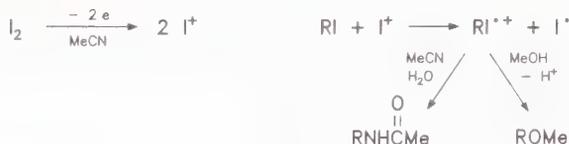
Construction of rings as represented above is of interest in the synthesis of natural products. The oxidation of dibenzyl ether [11] in acetonitrile yields *N*-benzylacetamide as one of the products via splitting of the intermediate carbonium ion $\text{Ph}\dot{\text{C}}\text{HOCH}_2\text{Ph}$. Esters undergo some anodic reactions depending on the kind of ester and the molecular structure. Straight chain esters undergo ω -1 substitutions [12]. Half esters, when oxidized in methanol at carbon electrodes and at low current densities, yield methoxylated products, and acetamidated products when oxidized in acetonitrile solvent [13].

2.10 Organic Halides

2.10.1 Alkyl Halides

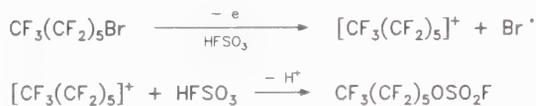
Anodic synthetic applications of organohalides are limited by comparison with the very wide range of their versatile cathodic applications. Oxidation of alkyl iodides can take place at platinum electrodes in $\text{MeCN}/\text{LiClO}_4$ solutions. An alkyl iodide yields, as primary anodic product, the organoiodo cation radical which by expelling an iodine atom is transformed to an organocation [1,2]. The cation radical may react directly with a nucleophile before expulsion of I^\cdot as depicted in Scheme 2.27. Alkyl iodides can also be oxidized indirectly by the iodonium ion, I^+ , which can be prepared externally by oxidizing iodine in acetonitrile solution:



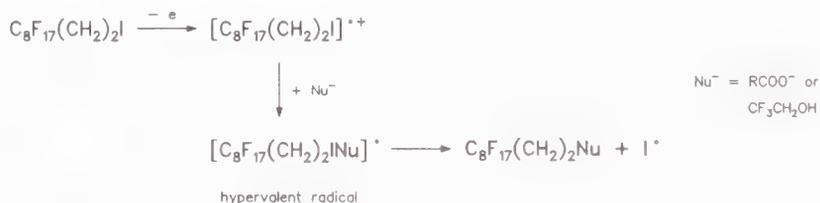


Scheme 2.27

Primary and tertiary bromoalkanes are directly oxidized at platinum electrodes in acetonitrile solutions containing LiClO_4 or Et_4NBF_4 electrolytes. Becker [5] proposed a reaction mechanism similar to that for the oxidation of iodoalkanes. An electron is released to the anode from the nonbonding orbital of bromine and a very unstable cation is generated, as would be expected from the quite high potential required for the electron release to occur (2.3–2.4 V vs Ag/Ag^+). We also note that anodic oxidation of bromofluoroalkanes in fluorosulfuric acid transforms them to the fluorosulfate analogs [6]. Bromine is released at the anode and is substituted in the starting molecule by the OSO_2F group. The process is mono-electronic and the released bromine acts as a catalyst (mediator) for the oxidation of the bromofluoroalkane.

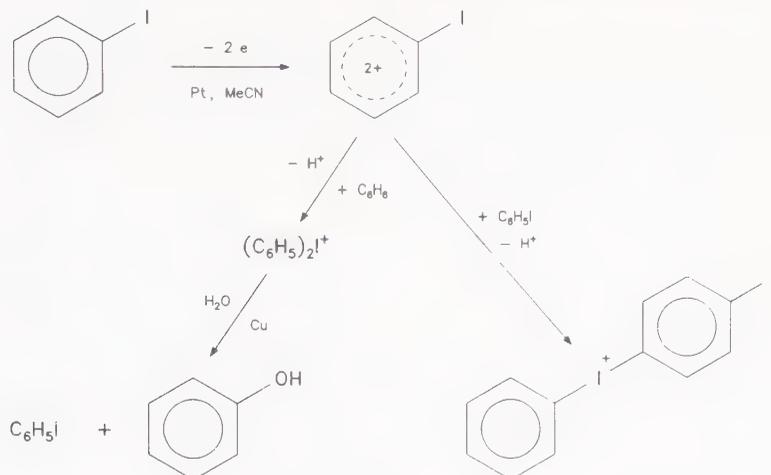


Polyfluoroalkyl iodides are oxidized to hypervalent iodanyl radicals which by releasing iodine result in the nucleophilically substituted product [7]:



2.10.2 Aromatic Halides

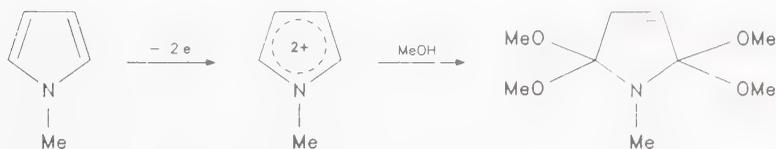
It has not yet been possible to achieve carbon-halogen bond cleavage of aromatic halides by direct anodic oxidation. Instead of carbon-halogen bond cleavage, the deelectronation is followed by hydrogen expulsion, which often leads to new C—C bond formations. A rather unique anodic oxidation is that of iodobenzene in the presence of benzene in acetonitrile [8].

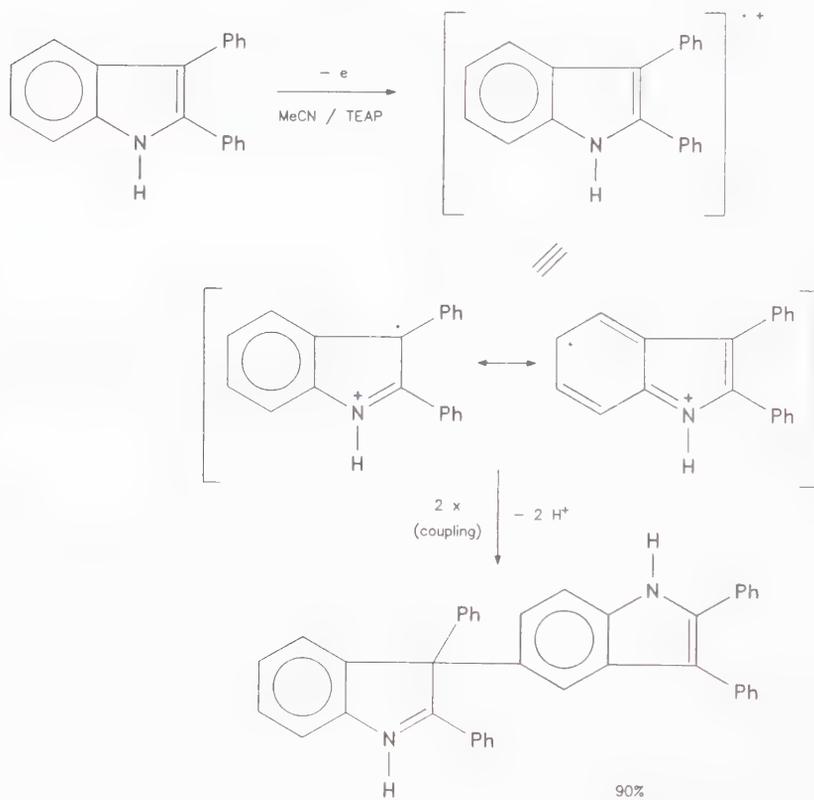
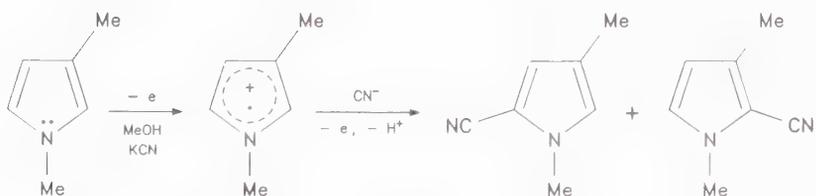
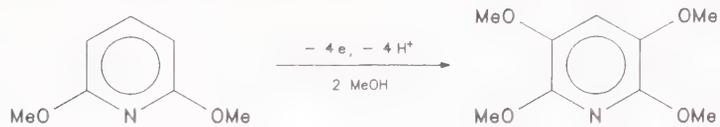


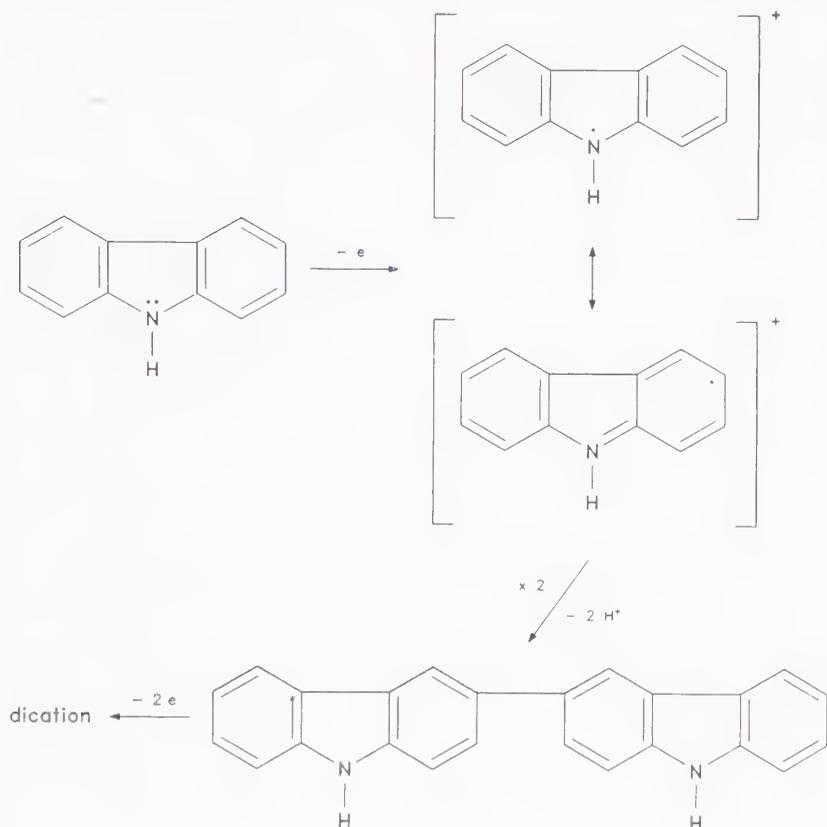
The iodobenzene may in effect be a recyclable mediator for the indirect oxidation of benzene to phenol. This is possible because benzene reacts easily with the $(\text{C}_6\text{H}_5\text{I})^{2+}$ species to give the dimer $(\text{C}_6\text{H}_5)_2\text{I}^+$ from which the phenol and the starting iodobenzene are obtained.

2.11 N-Heterocyclics

The electrochemistry of *N*-heterocyclic compounds is of very special interest because this class of organic substances has profound biological importance [1]. Here the discussion will be limited only to some highlights that are representative of the anodic electrochemistry of these materials, since an adequate presentation of this subject would require a separate monograph. Simple *N*-heterocyclics readily give their cation radicals or dicationic species which are rapidly attacked by a nucleophile, e.g. a CN^- ion, or enter into various coupling reactions, as in the following examples [1,2]:

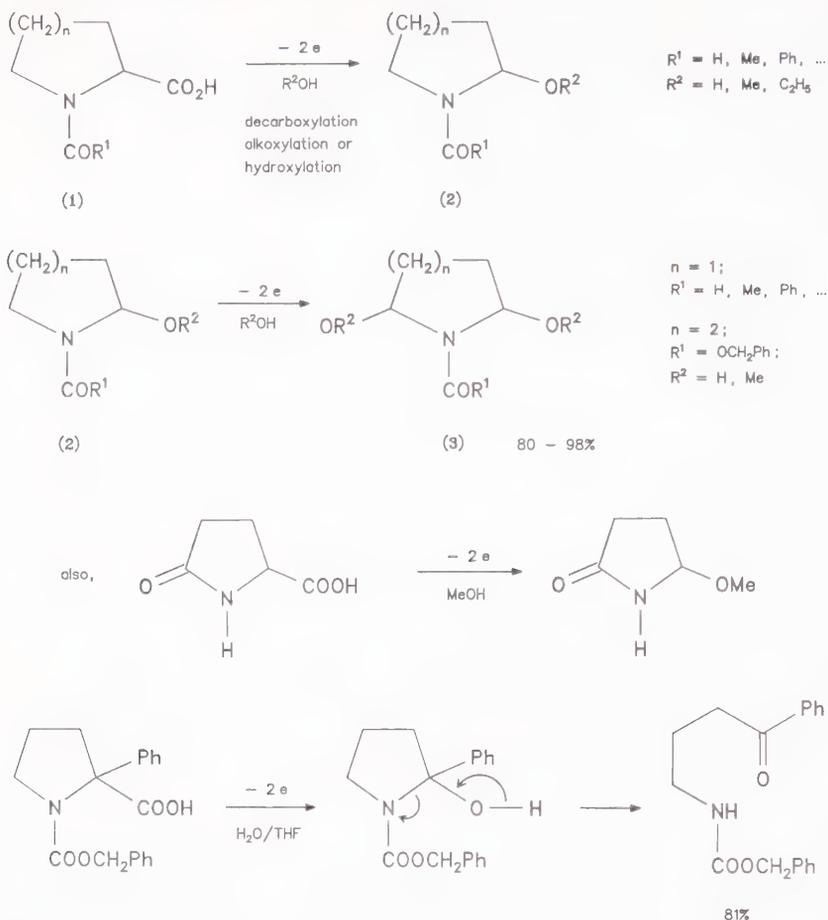






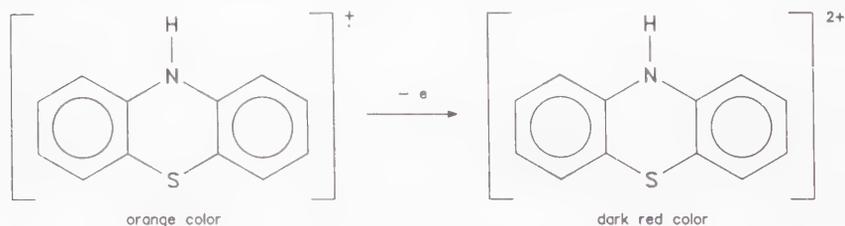
Callot and coworkers [3] studied the electrochemical oxidation of porphyrins and metalloporphyrins with relation to substituent effects. Cyanation at the meso (methine bridge) was achieved efficiently at the anode while chemical procedures failed practically. Zinc octaethylporphyrins are easily prepared, and are cyanated in a divided cell in DMF/ $\text{Et}_4\text{N}^+\text{CN}^-$ solution using platinum electrodes at the easily reached potentials of 0.4–0.9 V vs SCE. Meso-, mono-, di-, tri-, and tetra-cyanoporphyrins are thus produced in 35–95% yields. Cyanations of aromatic *N*-heterocyclics take place by mechanisms similar to those of aromatics, in general. Cyanations occur either by replacement of aromatic hydrogen or of hydrogen on the side chain [4].

Anodic oxidation of *N*-acylprolines and *N*-acylpipecolic acids is a very efficient method for the synthesis of *N*-acyl-*N*-*O*-acetals [5], Scheme 2.28. Methoxylation is carried out in MeOH/NaOMe solution, and hydroxylation in $\text{H}_2\text{O}/\text{THF}/\text{KOH}$ solution. Undivided cells with graphite electrodes are used and the electrolysis is performed under constant current of about 200 mA/cm². The dimethoxylated product is obtained by electrolysis in MeOH/ $\text{Et}_4\text{N}^+\text{OTf}^-$ solution.

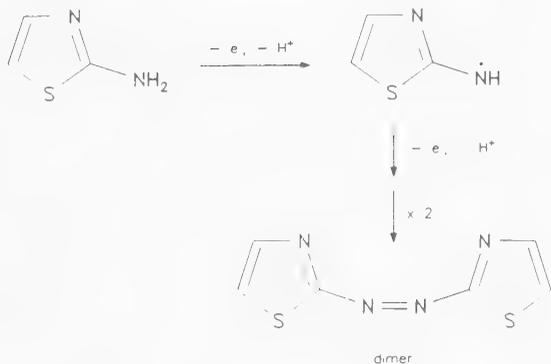
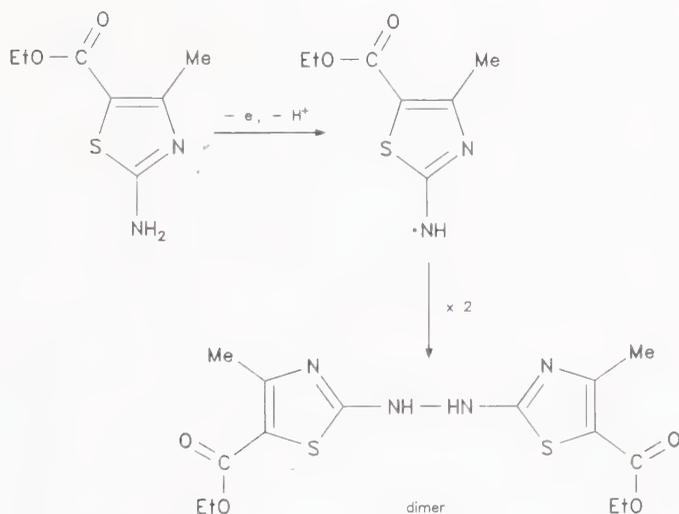


Scheme 2.28

Heteroaromatics in general, usually exhibit more than one voltammetric oxidation step forming first cation radicals. These, in many cases, are distinctly colored and stable enough to display reversible voltammetric behavior. For example, phenothiazine forms an orange-colored cation radical. This is further oxidized to a dark red dication which is stable for several days in the absence of air and moisture [6].

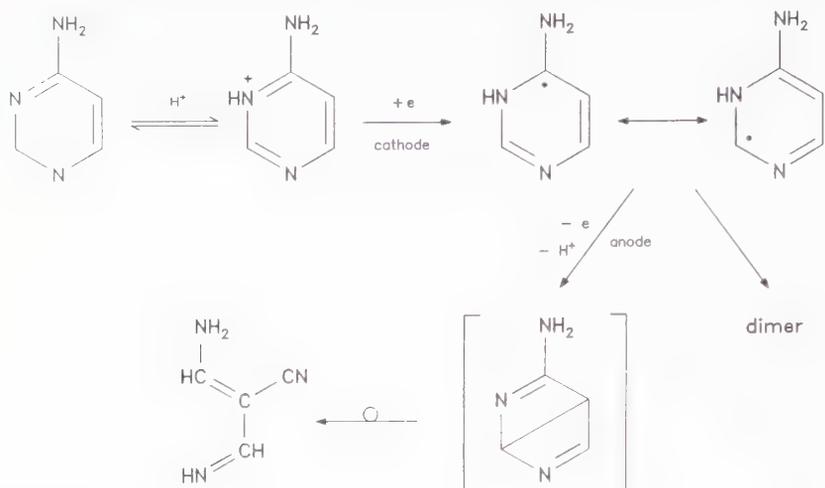


Cauquis studied the anodic oxidation of heterocyclic amidines which are precursors of biologically active materials [7]. Apparently the NH_2 group of these molecules is more easily deelectronated than the ring nitrogen. The anodic —HN—NH— and —N=N— couplings of aminothiazole compounds are explained by mechanisms as given in Scheme 2.29.



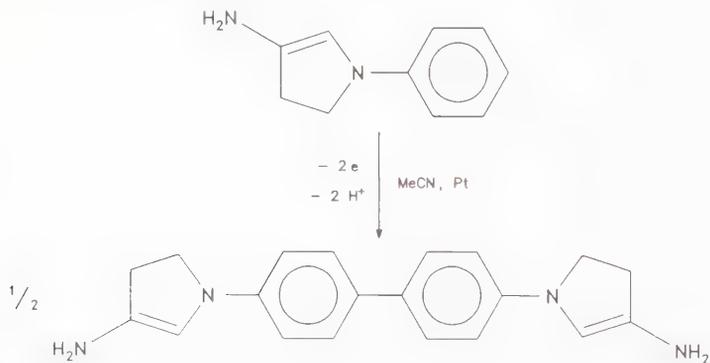
Scheme 2.29

Anodic oxidation of aminopyrimidines preceded by electroreduction in aqueous media affords open ring products [8] at the anode, as depicted in Scheme 2.30.

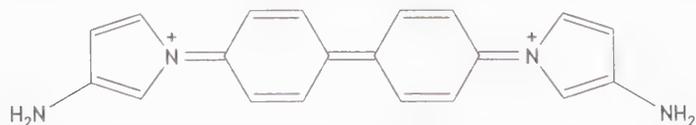


Scheme 2.30

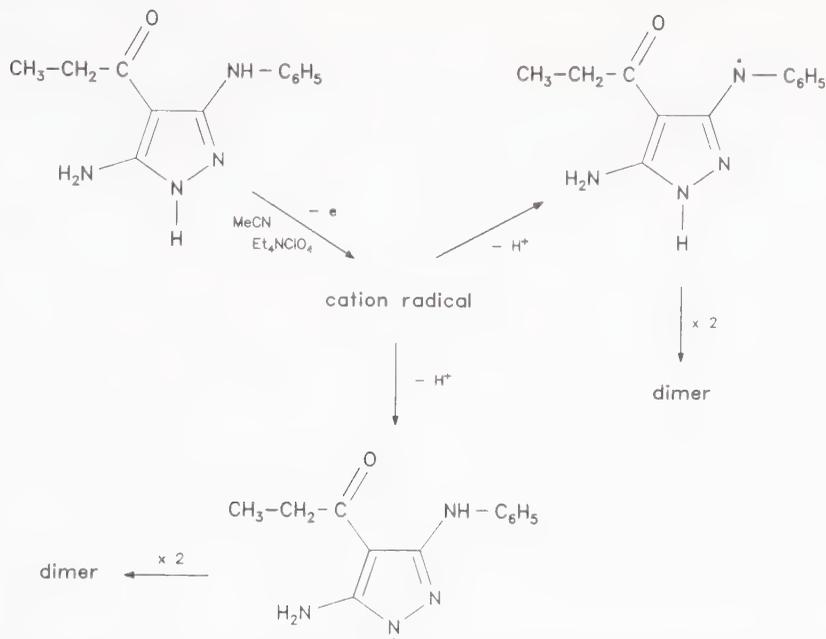
In the anodic oxidation of 1-phenyl-3-aminopyrazoline in acetonitrile the amino group remains intact while dimer formation takes place by joining the phenyl rings [9]:



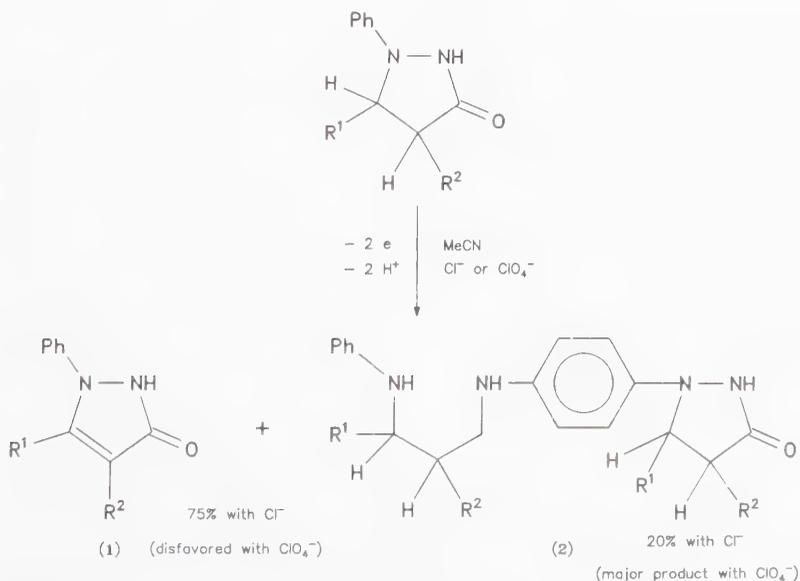
The dimer is further oxidized at more positive potentials by releasing a total of six electrons and four protons to give the dication,



Couplings of *N*-heterocyclics with nitrogens external to the ring may take place via *N*—*N* bonds by more than one path. Pyrazoles involve both ring and external to ring nitrogen, as indicated in the following example [10]:

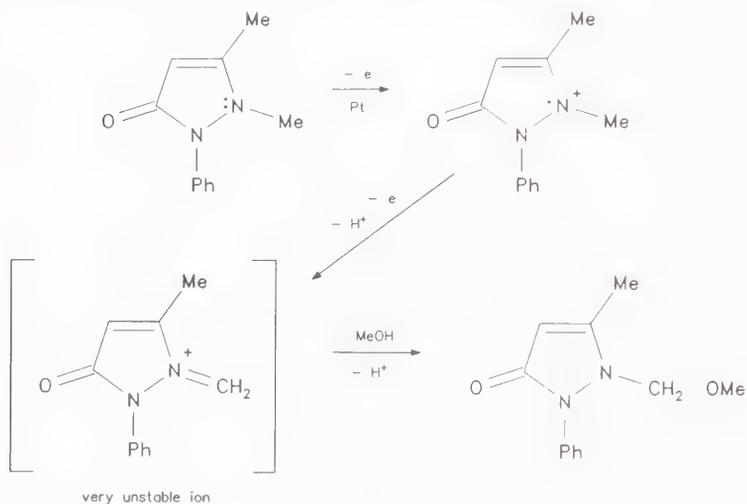


In the anodic oxidation of 1-phenylazolidin-3-ones under controlled potential, two products were formed the yield ratio of which was influenced by the kind of the anion of the electrolyte [10]. While perchlorate favored formation of the dimer (2) chloride ion suppressed formation of the dimer in favor of product (1), Scheme 2.31.



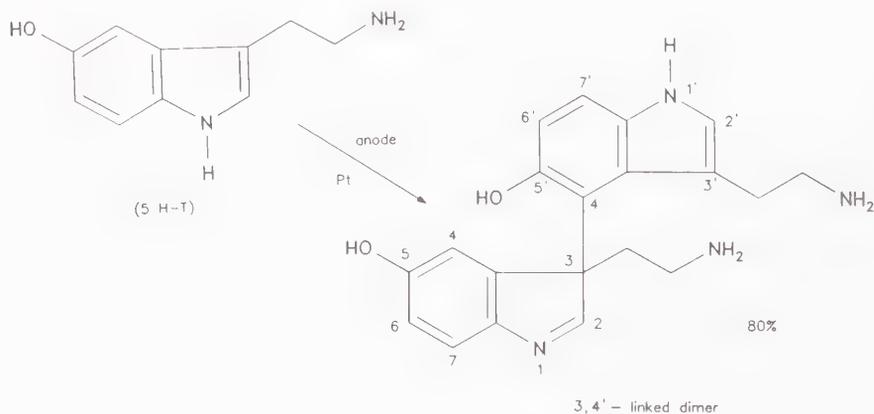
Scheme 2.31

The electrolyte effect was attributed to the fact that Cl^- ion behaves like a base in acetonitrile (HCl is 99% associated in this solvent), and this apparently affects the reaction course. Methoxylation of pyrrolidinols leads to the syntheses of *cis*-3-hydroxy-L-proline and *trans*-3-hydroxy-D-proline [11]. The methoxylation on the *N*-methyl group of antipyrine has been studied in connection with antipyrine metabolism [12]. The electrolysis was performed in MeOH/KOH solution. The methoxylation occurs on the methyl group attached to nitrogen, as shown in Scheme 2.32.

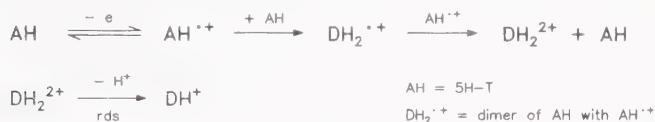


Scheme 2.32

Dryhurst [13] and Moiroux [14] independently studied the electrochemical oxidation of the biologically important *N*-heterocyclic substance 5-hydroxytryptamine (5H-T). The electrooxidation of 5H-T in acetonitrile containing perchloric acid at platinum electrode yields the 3,4'-linked indole-indolenine dimer in 80% yield [13]:



Moiroux also obtained 80% yield of the same dimer, and proposed the following reaction scheme:



Scheme 2.33

Oxidation of 5-Hydroxytryptamine [13,14] (5H-T) (Scheme 2.33)

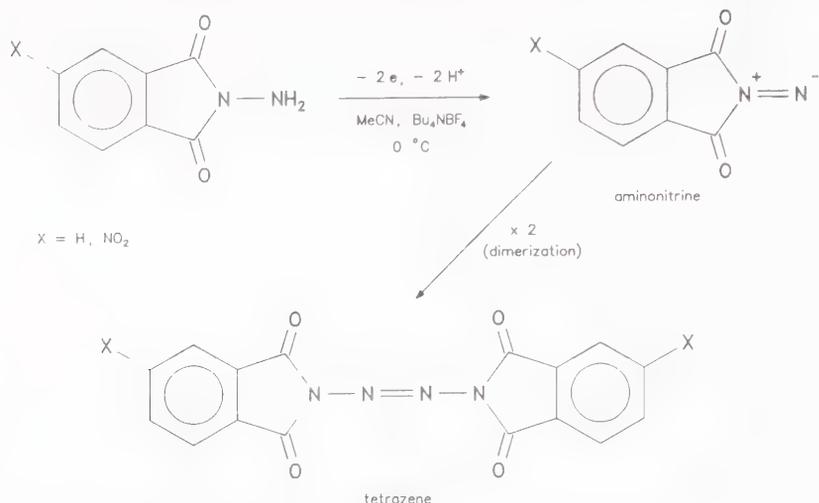
Electrolysis of 5H-T in aqueous solution (pH 2) gave predominantly the 4',4-linked dimer along with the 4',3, 4',2 and 4,6' dimeric products. It could not be concluded which of the two types of electrolytic oxidations best mimic the biological oxidation of 5H-T.

These microscale electrooxidations were performed in divided cells at 22–25 °C under anodic potentials near 0.5 V vs SCE, with 50 ml of anolyte solution into which a total of 30 mg of 5H-T was added incrementally as electrolysis progressed and the solution became deep purple. Electrolysis was ended when more than 95% of the starting compound was oxidized, as determined by periodic analysis of the solution by high performance liquid chromatography (HPLC). The eluted products were collected and identified by spectroscopic techniques.

The alkaloid-*N*-heterocyclics are readily oxidized at the anode, but because their molecular structures are very complex the oxidation mechanisms are not easily, if at all, elucidated. Picolines are clearly transformed to their carboxylic acids and may act also as nucleophiles [15,16].

The anodic oxidation of *N*-aminophthalimides affords tetrazane and tetrazene systems [17] apparently by a 2-electron deelectronation process and deprotonation of the NNH₂ group to give the intermediate aminonitrines which dimerize. Yields are less than 40%, and they seem to vary with the kind of electrolyte. Tetrazanes are converted to tetrazenes very readily.

Dihydropyrimidines are oxidized at a carbon anode in MeCN and are “self-protonated” in the process by the nascent protons from the starting molecule as it is deelectronated and deprotonated at the anode [18].



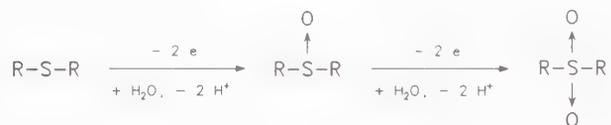
Scheme 2.34

2.12 Organosulfur Compounds

Sulfur containing organic substances are studied electrochemically with special interest because, apart from synthetic applications, the sulfur heteroatom is present in many biologically important substances.

2.12.1 Sulfides

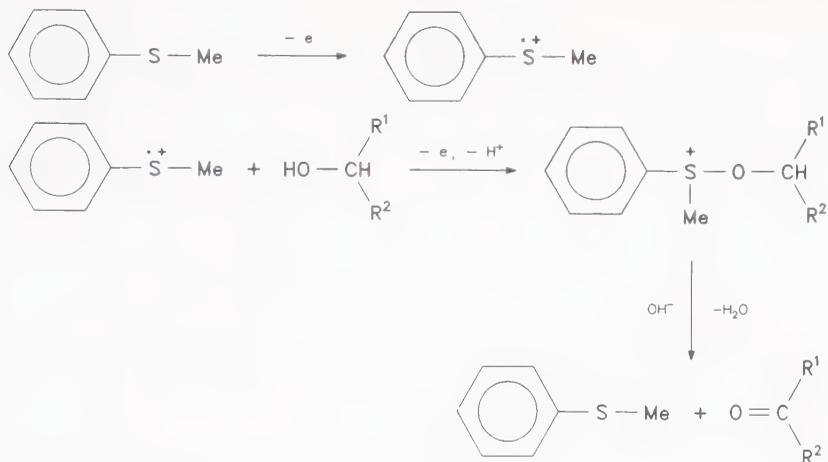
The anodic oxidation of organic sulfides in the presence of water proceeds clearly by two-electron successive steps to afford sulfoxides and sulfones [1] in good yields.



Anodic oxidation of sulfide salts, RSNa, afford disulfides by one-electron oxidation of the RS⁻ anion.



Thianthrene and thioanisole are readily oxidized and act as oxidative mediators, as in the following example in which the thioanisole is regenerated in the presence of base [2].



Sulfur compounds possessing the structure $R-N-C-S-$ are commercially interesting. Anodic oxidation leads to dimers, as in the industrial production of Thiourem M. Cuttler summarized the overall cell reaction for thiourem M as follows [4]:



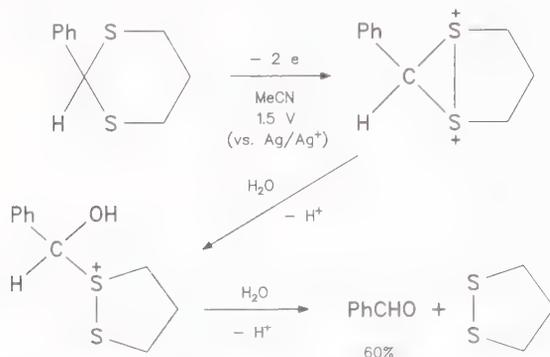
Scheme 2.35

This is an industrial example of *paired electrosynthesis*. Both half-cell reactions generate the required products for the desired overall cell reaction.

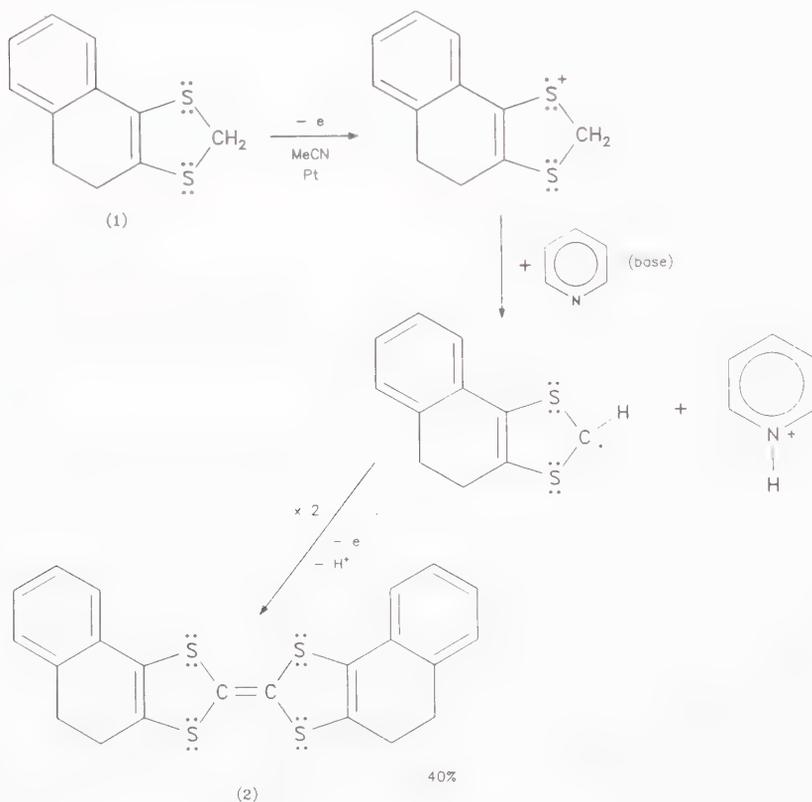
2.12.2 Thiolates and Dithianes

Thiolates and dithianes are electrochemically easily oxidized. This is of interest in some protective group-synthetic applications. Thiolates are prepared for carboxyl group protection. Deprotection of the carboxylic acid may be done by anodic indirect oxidation in aqueous acetonitrile in the presence of bromide ion as mediator [5]. Aldehydes and Ketones protected as 1,3-dithiane derivatives are deprotected by anodic electrolysis

in acetonitrile in divided cells. The partial regeneration of the protected benzaldehyde is depicted below [6]:

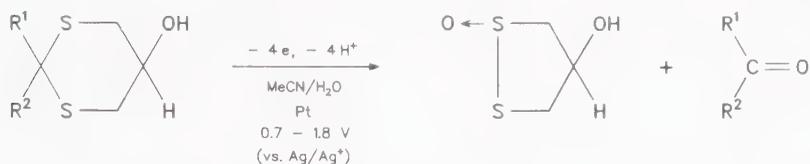


In the presence of pyridine, the 1,3-dithiane (**1**) was oxidized at a platinum anode and gave the tetrathiofulvalene (**2**) in 40% yield after 3 F/mole were passed [7]. The electrolysis was performed in MeCN with Bu_4NF as electrolyte. (Compound (**2**) is of interest as a one-dimensional electronic conductor.)



Scheme 2.36

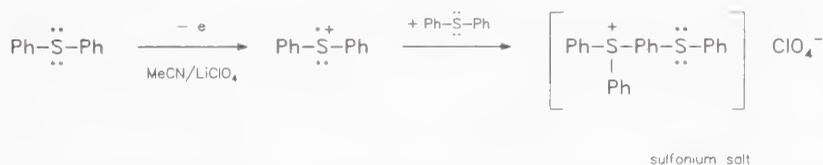
Dithianes are transformed to dithiolanes by an overall four-electron process in 20–70% yields [8]. Such oxidative transformations could probably be effected by indirect electrooxidation with ceric ion salts as mediators.



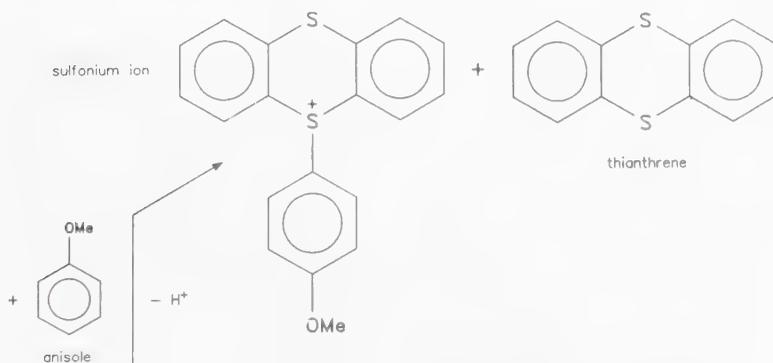
R¹ = H, Me, Ph ; R² = H, Me

2.12.3 Sulfonium Salts

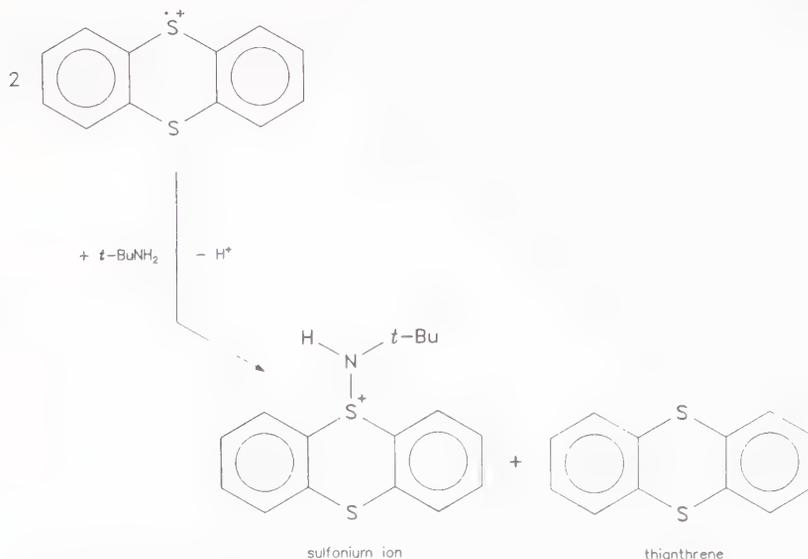
Oxidation of some sulfides in acetonitrile with small amounts of water and lithium perchlorate electrolyte affords both sulfoxides and sulfonium salts. Thus diphenyl sulfide is oxidized to diphenyl sulfoxide, 1,4-bisphenylthiobenzene and the sulfonium salt. The salt is formed by reaction of the anodically generated cation radical with the starting sulfide [9]:



Thianthrene is an interesting molecule. It acts as an oxidizing mediator and also forms sulfonium salts, as shown below, by anodic oxidation in acetonitrile in the presence of anisole or *tert*-butylamine [10]:

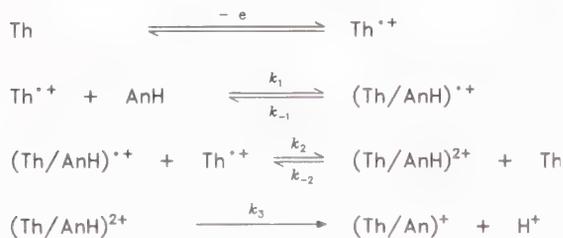


Thianthrene



Scheme 2.37

The thianthrene molecule releases an electron to the anode reversibly to give a cation radical which in the presence of anisole is further oxidized to a dication by the following mechanism, as proposed by Parker and Ebersson [12].



Th = thianthrene ; AnH = anisole ; (Th/An)⁺ = sulfonium ion

The (ThAnH)^{•+} is more easily deelectronated than the Th^{•+} thus by reaction with Th^{•+} gives the dication (Th/AnH)²⁺ and finally the sulfonium ion (Th-An⁺). The thianthrenium ion forms salts with aromatics containing electron donating groups, and also with amines and olefinic and acetylenic compounds [13]. In trifluoroacetic acid the thianthrenium cation radical survives for weeks, as is evident from cyclic voltammetry (ratio of anodic and cathodic peaks = 1.0). The trifluoroacetate salt can be obtained as a crystalline purple solid after evaporation of solvent at low temperatures [14].

2.13 Anodic Cyanations

Anodic cyanations are well established reactions by means of which carbon-carbon bonds are formed and the synthetically valuable nitrile intermediates are obtained. A wide literature has been developed since the detailed report of Andreades [4] (1969) on anodic cyanation of aromatic compounds [1–17]. It might be noted that aromatic rings are not easily cyanated by chemical procedures. Chemical methods are usually very laborious and require at least two major steps:

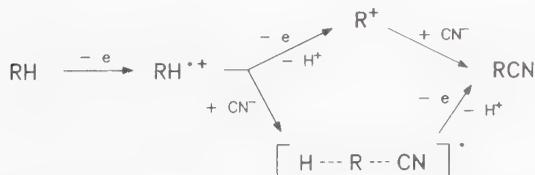
1. Introduction to the aromatic ring of a suitable leaving group, and
2. displacement of this group by the cyano group, chemically or photochemically.

Cyanation agents that have been used for the cyanation of aromatic hydrocarbons and phenols include organometallics in the presence of KCN, BrCN, and Cl₃CCN. The electrochemical method is much simpler. The electrocyanation can be carried out in acetonitrile or methanol solutions containing KCN or NaCN or Q₄N⁺CN⁻ salts which provide the CN⁻ ion and also function as electrolytes. Sometimes emulsions of CH₂Cl/H₂O are employed to overcome solubility difficulties. Usually, divided cells with platinum electrodes are used with the SCE or Ag/Ag⁺NO₃⁻ as reference electrodes.

Because the CN⁻ ion is easily oxidized at the anode, it is sometimes difficult to elucidate the cyanation mechanism. This may be further complicated by the ability of the CN⁻ ion to reduce the generated cation radical.



We note that in water the CN⁻ ion is oxidized at 0.6 V vs SCE but in methanol the anodic limit extends beyond 1.6 V. Most recent studies suggest that cyanations take place after the organic substrate is deelectronated to yield the cation radical RH^{•+} or the cation R⁺. These species are then attacked by the very powerful nucleophile CN⁻ as shown in Scheme 2.38.



Scheme 2.38

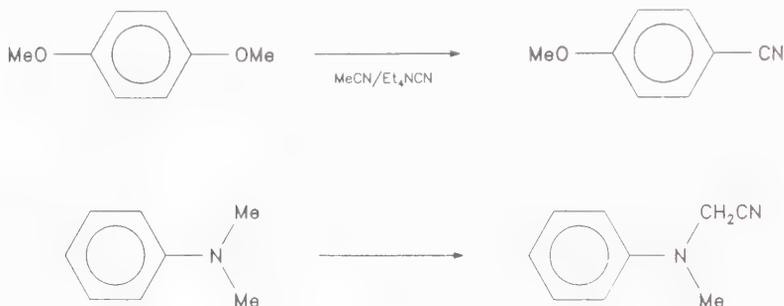
**Comparison
with chemical
methods**

**Cyanation
mechanism**

Initial electrochemical cyanations

In the initial electrochemical cyanations by Andreades and Zahnow [4] the electrolyses were carried out in anhydrous acetonitrile solutions with large concentrations of tetraethylammonium cyanide and selected aromatic substrates. Both divided and nondivided cells with smooth platinum electrodes were employed. In the undivided cells cylindrical electrodes concentrically arranged were employed, and a SCE reference electrode was placed with the tip near the anode. Potentials, for preparative synthesis, in the range of 0.9–2.0 V were applied. The anode was rotated during electrolysis so as to minimize concentration polarization effects at the anode. Typical reactants and product yields at 50% conversion of the aromatic reactants were: anisole, anisonitrile (5%), *p*-dimethoxybenzene, anisonitrile (95%), veratole, *o*-methoxybenzonitrile (94%), 1,2,3-trimethoxybenzene, 2,6-dimethoxybenzonitrile (86%). (Caution: Cyanations should always be carried out in well ventilated hoods.)

The cyanations of *p*-dimethoxybenzene and tertiary amines take place by displacement of a methoxy group in the former and cyanation of an alkyl group in the latter [4]:



Cyanation of naphthalines

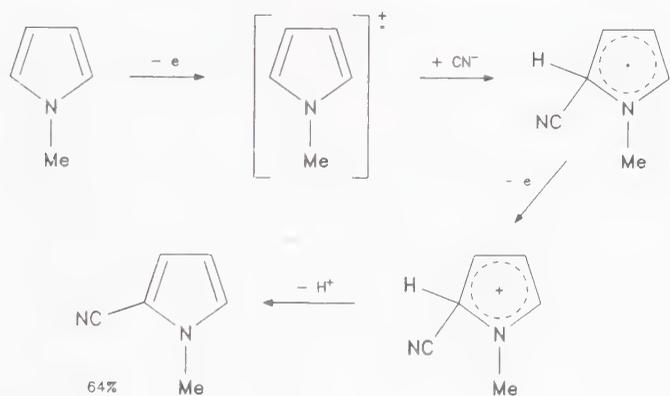
Yoshida [14] studied in depth the cyanation of various naphthalines. Naphthalenes with methyl or ethyl substituents form preferentially naphthonitriles instead of side-chain cyanation products. Chemically naphthonitriles are obtained by reaction of their corresponding halides with cuprous cyanide under quite severe conditions. According to Yoshida's observations (voltammetric *i*-*E* curves) the anodic cyanation occurs by an ET from the naphthalene molecule to the anode. This first step is followed by a rapid attack by CN⁻ ion on the cation radical (see Sect. 2.2, Scheme 2.4). Yoshida [18] also found that the anodic cyanations of pyrroles and indoles is a very efficient synthetic reaction and it seems to be a general reaction for cyanations of *N*-heterocyclic compounds. The chemical methods for the cyanation of pyrroles via Manish bases (RCO(CH₂)NH₂) or

Pyrroles and Indoles

aldoximes $\text{R}-\text{C}(\text{H})=\text{NOH} \xrightarrow{\text{Ac}_2\text{O}} \text{RCN}$ are complicated procedures, and give lower yields than the electrochemical procedures.

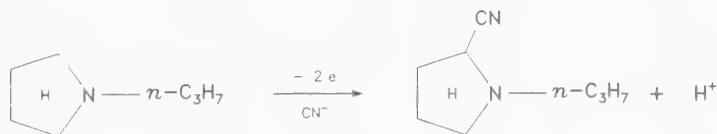
Cyanation of 1-Methylpyrrole

The anodic cyanation of 1-methylpyrrole yielding the 2-carbonitrile analog is carried out in MeOH/NaCN in a divided cell with a platinum anode set at 1.0 V vs SCE (the reaction mechanism is depicted in Scheme 2.39). The electrolyzed solution is subjected to distillation to remove the methanol and the residue is extracted with ether from a saturated NaCl aqueous solution. The ether extract is treated with MgSO_4 , and after filtration the ether is evaporated. The oily residue is distilled under vacuum to obtain the product (64%) (Adapted from Ref. 18, Copyright of the American Chemical Society, 1979).



Scheme 2.39

Cyanation of *N*-*n*-Propylpyrrolidine [19]

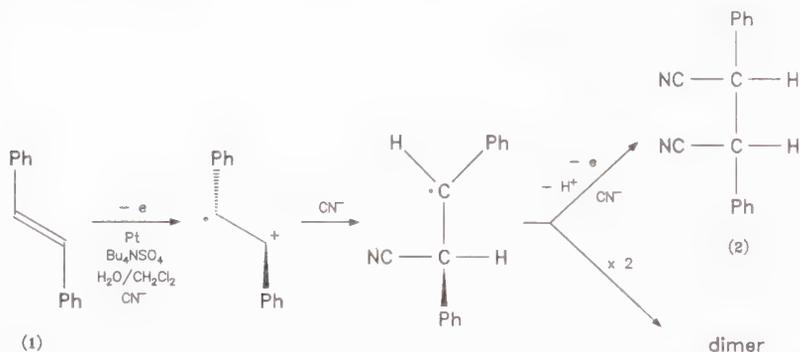


The electrolysis is performed in a 100-ml divided cell, using a porous cup for the catholyte. The anode is a cylindrical platinum net (4.5 cm in height, 11.0 cm in circumference, 55 mesh) and the cathode is a platinum coil. The reference electrode is the SCE. The electrolysis is carried out at 3°C with constant stirring by a magnetic bar. The anolyte contains 0.1 mol of the amine and 0.15 mol of sodium cyanide in 75 ml of 1:1 methanol-water solution. The catholyte is an aqueous methanol solution of sodium cyanide. Current is passed for 8 hours at

an anode potential in the range of 1.1 to 1.5 volts so as to maintain a constant current of 0.5 A during the entire electrolysis (0.15 F). At the conclusion of the electrolysis the anolyte is concentrated under reduced pressure at 35 °C on a rotary evaporator. The remaining liquid is saturated with anhydrous potassium carbonate. The organic layer is separated and the aqueous layer is extracted twice with 30 ml portions of ether. The combined extracts are dried with potassium carbonate and then analyzed by GLC. The distillation of the crude product at 114–119 °C (5.3 kPa) gives 8.2 g of colorless liquid, *N*-propyl-2-cyanopyrrolidine, as confirmed by IR, NMR, and elemental analysis of the picrate derivative. The yield and current efficiency are 59 and 79%, respectively (Adapted with permission from Ref. 19, Copyright American Chemical Society, 1977).

Methoxylation versus cyanation

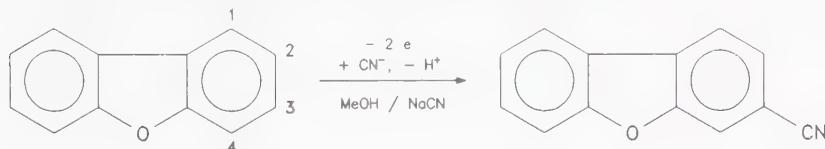
In methanol/cyanide solutions some substrates methoxylate rather than cyanate while others do the opposite. Yoshida [20] reported that benzene, toluene, *p*-xylene and tetralin prefer to methoxylate, and naphthalenes, anthracenes, biphenylacetylenes and bibenzyl undergo predominantly cyanation. The cyanation of *trans*-stilbene (**1**) and its dimethoxy derivative was carried out in H₂O/CH₂Cl emulsion [21]. Several products were obtained besides the desired product (**2**) which was favored at lower current densities.



Comparison of cyanation methods

The cyanation of dibenzofuran was recently carried out by electrochemical, chemical and photochemical methods [22]. Isomer distributions were different in these methods. The anodic method (MeOH/NaCN) gave mostly the 3-isomer of dibenzofurancarbonitrile in 71% of the total yield (40%). The chemical method (BrCN/AlCl₃/CS₂) and the photochemical (NaCN/MeOH/hv) method gave the 3-isomer in only 15% of the total yield (90%) and the photochemical method in 64% (total yield 85%). The electrochemical cyanation occurs via the ArH⁺ + CN⁻ paths, the chemical via the CN⁺ electrophilic path, and the photochemical via the ArH⁺ +

CN⁻ path. The anodic electrolysis was performed at constant current (0.5 A) in a nondivided cell with platinum electrodes.

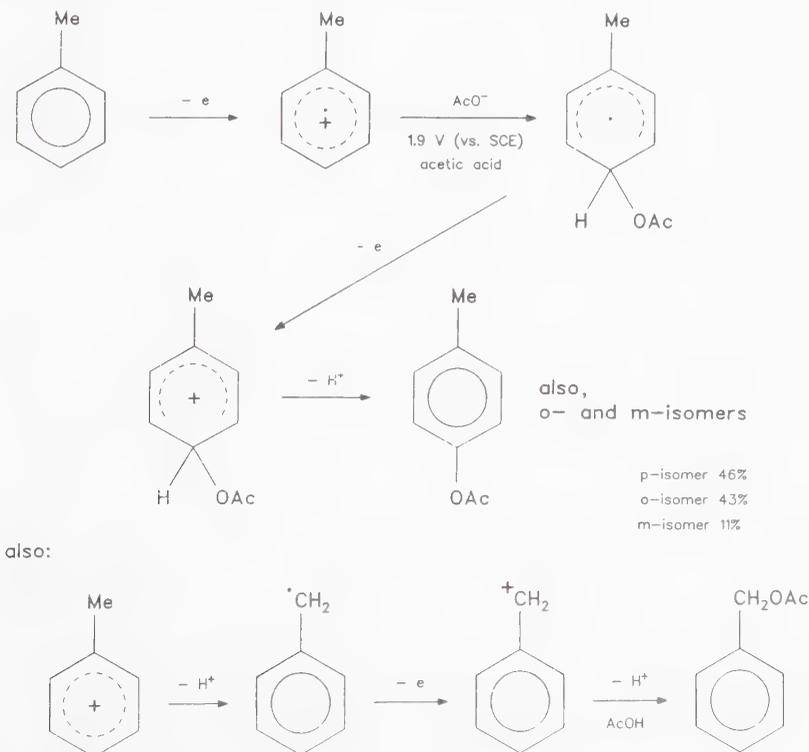


2.14 Acetoxylation and Acetamidations

2.14.1 Acetoxylation

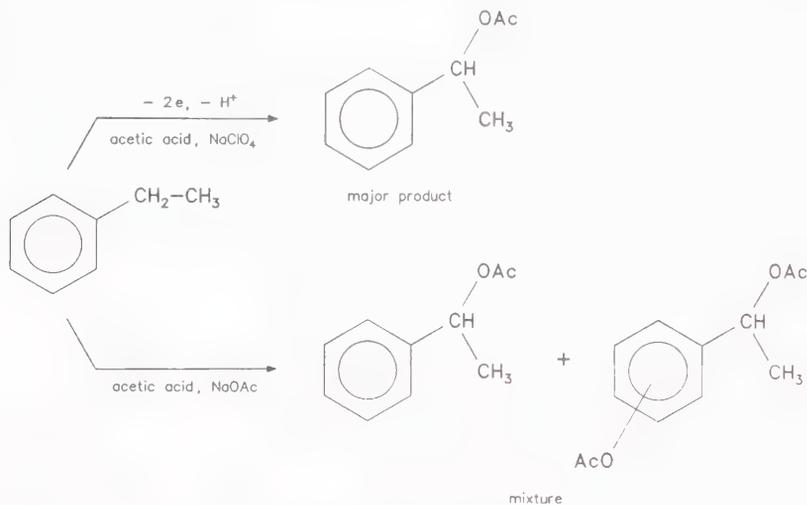
Acetoxylation, by the anodic method, represent a general type of electro-organic reactions for synthesis involving formation of C—O bonds. They have been extensively studied by Ebersson and coworkers [1–3] and several other electroorganic researchers [4–8].

The generally accepted acetoxylation mechanism is illustrated with toluene as a substrate, Scheme 2.40.



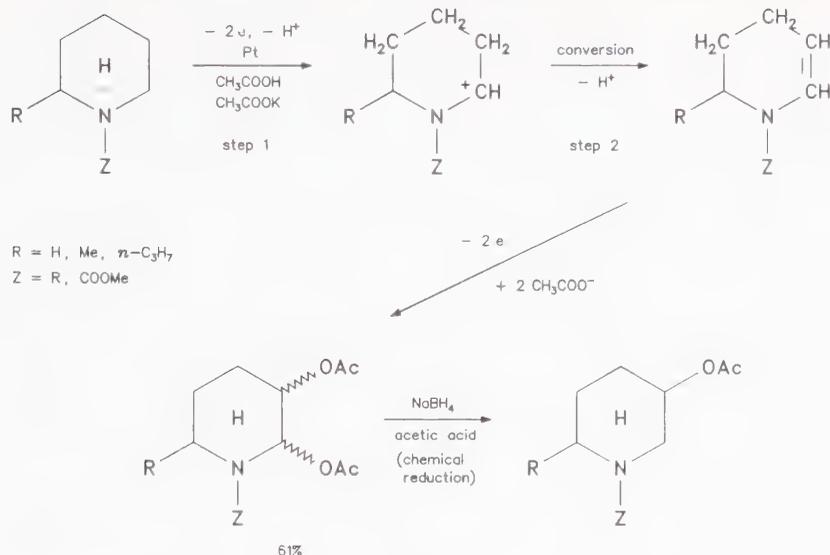
Scheme 2.40

The anodically generated cation radical is rapidly attacked by the AcO^- nucleophile or by the weaker neutral nucleophile CH_3COOH as indicated above for the acetoxylation via the benzyl radical of the toluene molecule. Electrochemical acetoxylation usually yield products similar to those obtained by chemical oxidations with metal oxidants, Pb(IV) , Ce(IV) , Co(III) , Mn(III) , Cu(II) , Cu(III) and Ag(II) in acetic acid solutions. The electrochemical method avoids the need to these oxidants and associated process problems, (product isolation, environmental problems). However, these oxidants may be considered as mediators for indirect electrosynthesis. It must be noted that the composition of the electrolysis medium influences the nature of the acetoxylation products [1,3,4], as is seen in Scheme 2.41.



Scheme 2.41

In performing an acetoxylation the most suitable anode potential is best selected from an *i*-E curve. It should be set at a value at which only the substrate is deelectronated, while the acetate or acetic acid remain free to react nucleophilically with the cation radical or cation produced at the anode. We consider here some interesting acetoxylation and trifluoroacetoxylation. The α,β -diacetoxylation of *N*-substituted piperidines was reported by Shono [9] as a functionalization method of a less reactive methylene group. Yields of acetoxylation products of 55–80% are obtained, Scheme 2.42



Scheme 2.42

Acetoxylation of Piperidines (Scheme 2.42)

The electrolysis was performed with 2 g substrate in 50 ml acetic acid/potassium acetate in a glass beaker with a platinum plate anode and a carbon rod cathode. A terminal cell voltage of 35 V was needed to pass a current of 0.4 A through the solution. The products were extracted with CH_2Cl_2 from a cold aqueous neutralized (NaHCO_3) solution. The extracts were dried with MgSO_4 , and the residue, after solvent removal (vacuo), was chromatographed on silica gel (ethyl acetate : hexane 1 : 1) to obtain the α,β -diacetoxy-*N*-(methoxycarbonyl) piperidine (61%). The chemical reduction step with NaBH_4 was done in acetic acid. From this mixture the β -acetoxy product was obtained by CH_2Cl_2 extraction and silica gel chromatography (Adapted from Ref. 9, Copyright of American Chemical Society, 1987).

Selective nuclear acetoxylation of alkylaromatics was achieved in an undivided cell utilizing a Pd-carbon catalyst [2]. This interesting system allows the hydrogen produced at the cathode to react with the benzylic acetate product and to cleave it. And thus, by continuously regenerating the starting substrate, it augments the yield of the nuclear-acetoxyated product. This product is apparently resistant to hydrogenolysis. Isodurene, *p*-xylene, mesitylene and durene were thus acetoxyated in acetic acid-potassium acetate media, giving yields of 75–98%. The anodes were

**Selective
nuclear
acetoxylation**

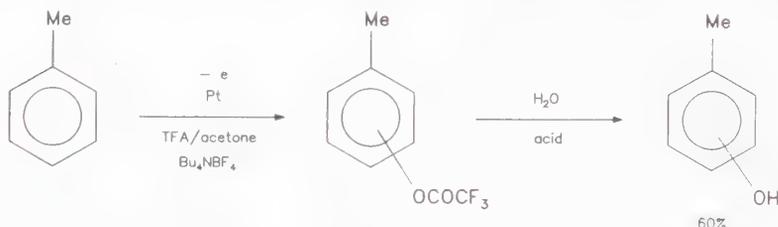
graphite cylinders and the cathodes stainless steel foils. Cell voltages of about 17 volts were needed for a current of 1.4 A to pass through the solution at 17–18 °C.

Trifluoroacetoxylation

Analogous to anodic acetoxylation are the trifluoroacetoxylation by means of which the trifluoroacetoxy group is introduced to organic molecules. Trifluoroacetoxylation are performed in organic media containing trifluoroacetic acid (TFA) or in net TAF. Such media are: TFA/CH₂Cl₂/Bu₄NPF₆, TFA/acetone/Bu₄NBF₄, TFA/Bu₄BF₄. *trans* Dichlorohexane and fatty acids were trifluoroacetoxylation [10], the first affording the 3,4-dichlorohexyl trifluoroacetate and the latter the ω-2 and ω-4 trifluoroacetoxylation products (~50%). In TFA solutions alkanes are oxidized to give cations which react with TFA to give trifluoroacetoxy products in 50–70% current yields [11].



Trifluoroacetates are very easily hydrolyzed to afford the hydroxy products. Trifluoroacetoxylation, therefore, provide a very convenient indirect route for the hydroxylation of aromatic hydrocarbons [8]:



2.14.2 Acetamidations – Electrochemical Ritter-Type Reactions

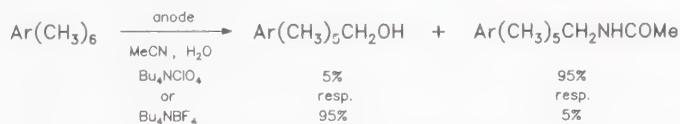
Anodic acetamidations are reactions of a general type taking place in acetonitrile solution, as depicted symbolically in Scheme 2.43



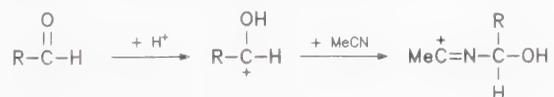
Scheme 2.43

For the acetamidation to be efficient the carbocation R⁺ should first be produced, and the solution should not contain nucleophiles that compete with acetonitrile. Eberson and Nyberg, and Baizer and Wagenknecht, independently established this useful version of the Ritter reaction [12,13]. The electrochemical Ritter reaction takes place with alkyl benzenes, alkyl halides, aliphatic ketones, olefins and even saturated hydrocarbons. In the

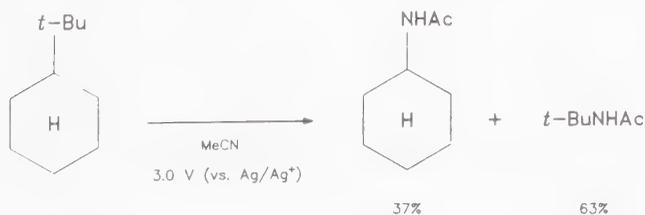
presence of H₂O competition with MeCN should be expected, that is, hydroxylation versus nitrilium ion formation. This would result in a mixture of hydroxylated and acetamidated products, in ratios that would be affected by the MeCN/H₂O ratio and also the reactivity of the carbocation R⁺. A striking example indicating the effect of the kind of electrolyte ions on the acetamidation in competition with hydroxylation is shown below [13a]:



It is seen that the product distribution is reversed by changing the electrolyte (these are probably double layer effects). Chemically, the Ritter reaction as represented below requires a strong acid to protonate the aldehydic carbonyl for the generation of the needed carbocation:



Acetamidations occur by substitution on the aromatic ring and also on side chains. Sometimes very dry acetonitrile may be required. In such cases trifluoroacetic anhydride (TFAA) is a most effective drying agent. Thus in acetonitrile/TFAA solution anthracene gave the 9-acetamido product in 80% yield [14]. Saturated and unsaturated hydrocarbons afford mixtures of acetamidated products by electrolysis in MeCN/0.1M Bu₄NBF₄ at smooth platinum electrodes [15], in 55–80% yields. *tert*-Butylcyclohexane undergoes cleavage to give the C—N coupled products [16]:

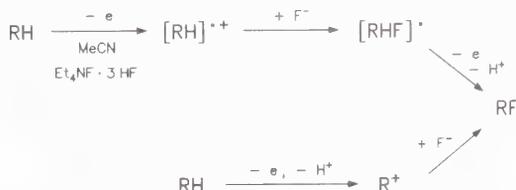


Anodic electrolysis of propylene in wet acetonitrile gives the *N*-allylacetamide [17,18]. Side chain acetamidations may sometimes lead to amines [19] through further hydrolysis:



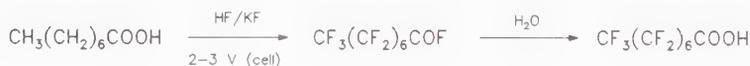
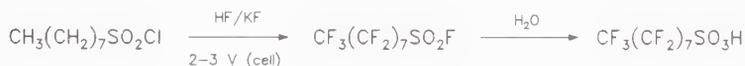
2.15 Anodic Halogenations

Halofunctionalizations take place mostly by indirect electrolysis in solutions containing a halide salt and the organic substrate. That is, the latter is halogenated by the anodically produced halogen species [1–4]. Fluorinations and some chlorinations are possible by direct oxidation of the organic substrate as a first step. This anodic step is followed by an attack on the oxidized substrate by the fluoride or chloride ion, as in the formal fluorination example:



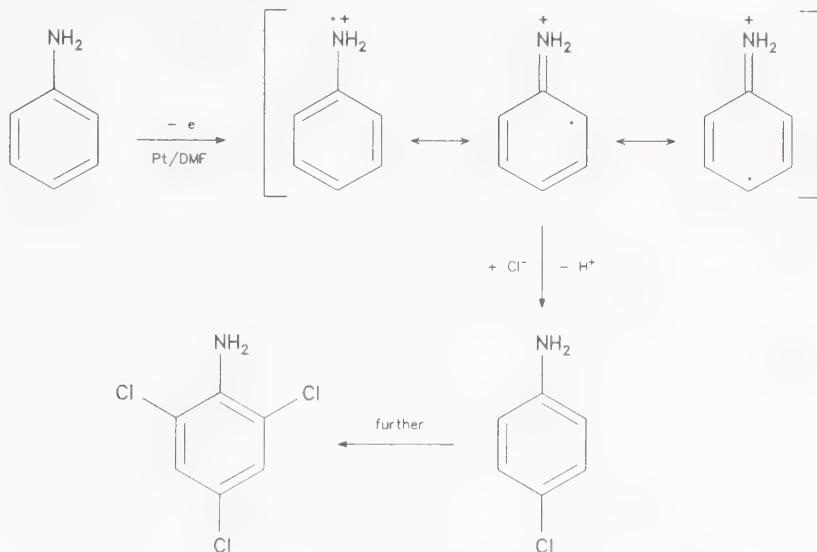
Large scale anodic fluorination

Anodic fluorination of hydrocarbons is performed on a large scale in liquid anhydrous hydrogen fluoride containing the organic material to be fluorinated (steel tanks). Cell voltages below that required for the oxidation of F^- ions are applied. Hydrogen gas is evolved at the cathode. The Simon's process [1] employs a divided cell (porous diaphragm) with an iron cathode and a nickel anode immersed in a liquid HF/KF mixture which dissolves a moderate amount of the starting hydrocarbon. At the nickel electrode a coating of K_2NiF_6 is produced which apparently donates fluorine to the organic substrate and is continuously regenerated to repeat the fluorination cycle (heterogeneous electrocatalysis). Following are a few examples indicating that all hydrogens are replaced by fluorine in the products, which are obtained in high yields [1].



Chlorination of aniline

Chlorination of aniline occurs directly in DMF or dimethylacetamide solvents. In these solvents the generated aniline cation radical is stable enough to be attacked by the chloride ion. Platinum, carbon and the DSA-type electrodes are suitable anodes for this reaction [5].

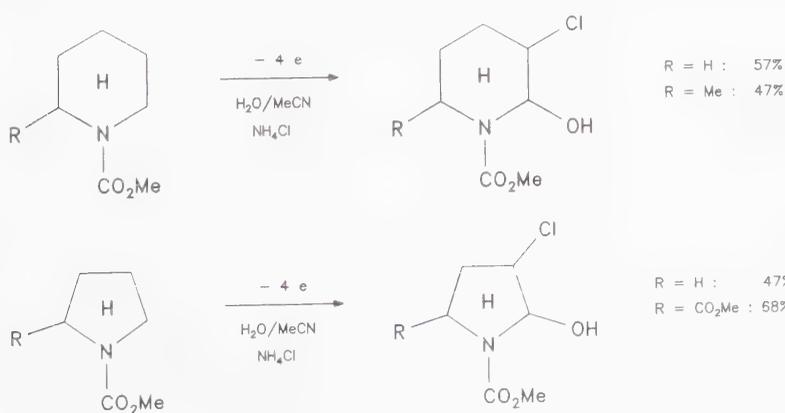


Anthracene can be brominated in MeCN/Et₄NBr at 1.2 V vs Ag/Ag. It must be noted that both the anthracene molecule and the bromide ion are oxidized at this anode potential. The product 9-bromoanthracene is obtained in 48% current yield. Similarly naphthalene gives the 1-bromo analog with 70% current efficiency [6].

Bromination of anthracene

Shono [7] reported a convenient method for chlorination of certain unreactive methylene groups in cyclic amines by electrolysis in aqueous acetonitrile containing ammonium chloride. *N*-methoxycarbonyl cyclic amines afforded the α -hydroxy- β -chloro analogs in good yields. We note that there are no general effective methods for such chlorination:

Chlorenation of methylene groups in cyclic amines



The α -OH group is easily removed by reduction with NaBH₄ and thus the β -chlorosubstituted products are obtained in 80% yields.

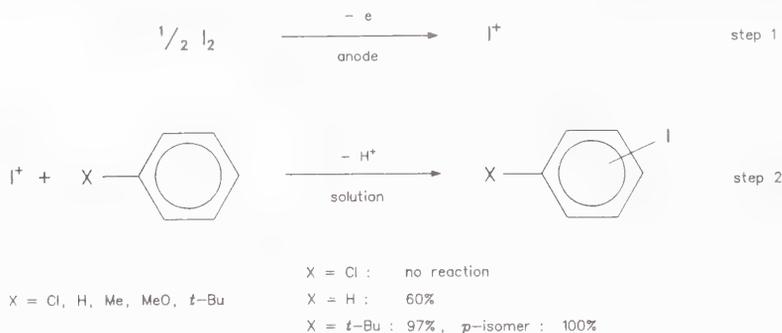
**Chlorination
of naphthalene
butadiene
and methoxy-
and ethoxy
benzenes**

Chlorination of naphthalene in $\text{H}_2\text{O}/\text{CH}_2\text{Cl}_2$ emulsion is facilitated by the presence of ZnCl_2 in the emulsion. It was proposed that a complex ZnCl_4 forms which is transferred into the organic phase where the chlorination of the naphthalene occurs [8]. Butadiene is easily chlorinated in $\text{MeCN}/\text{CoCl}_2$ solution by electrolysis in a divided cell at a graphite anode set at 1.7 V vs Ag/AgCl . The 1,4-dichlorobutane product (*trans*-isomer) is obtained in 90% yield [9]. Chemically this chlorination requires high temperatures and chlorine gas. Anodic chlorination of methoxy- and ethoxybenzenes [10] affords preferentially the *p*-chlorinated products.

The electrolysis is carried out in DMF or dimethylacetamide, DMA, containing LiCl in a divided cell with a platinum anode at a potential 1.0–1.5 V vs SCE. At this potentials both Cl^- and the organic substrate would be oxidized at the anode. Yields of about 90–95% are obtained. The *p*- to *o*-product ratio is 17:1 with DMF as solvent and 34:5 with DMA. (This difference may be attributed to different solvation effects.)

**Iodination
of aromatics**

Iodination of aromatics can be accomplished in a rather special way [11]. First, a solution of iodine in trimethylorthoformate $\text{CH}(\text{OCH}_3)_3$ (TMOF) is anodically electrolyzed to obtain an active positive species, I^+ , referred to as iodonium ion. The electrolytic oxidation is carried out in a divided cell in which the anolyte is a solution of iodine in TMOF/ $\text{LiClO}_4 \cdot 3\text{H}_2\text{O}$ and the catholyte the same solution without the iodine. Both electrodes are platinum. A current density of $0.1 \text{ A}/\text{cm}^2$ is sufficient to oxidize the iodine to I^+ . The anolyte solution containing the iodonium ion is then mixed with a solution of the aromatic in TMOF and the iodination occurs chemically. This iodination is selective with regard to the electron-donating substituent X on the aromatic ring, as summarized below:

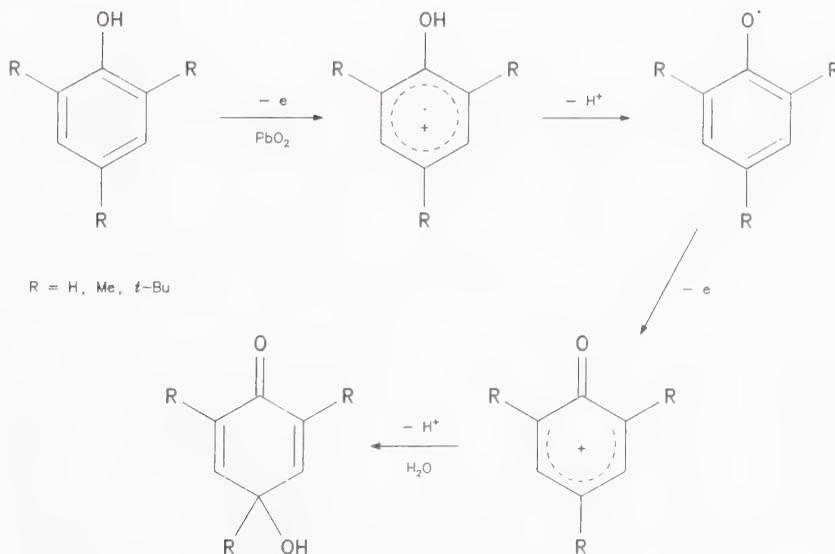
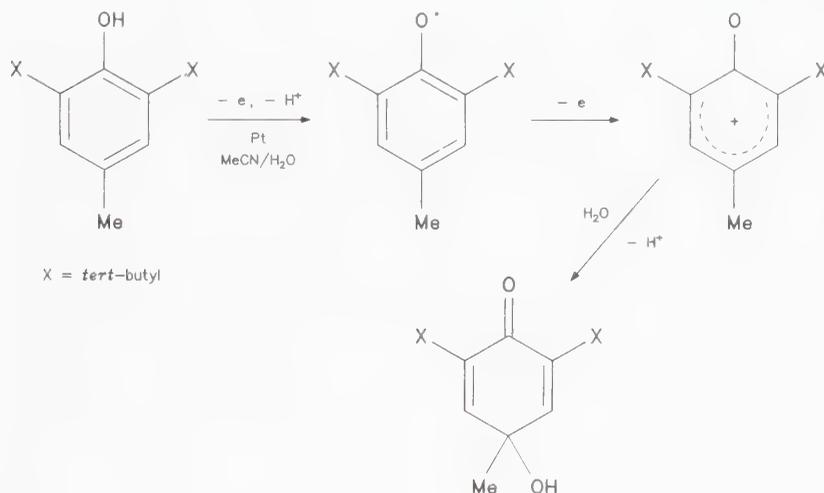


Iodinations via I^+ species are also possible by electrolysis in MeCN or $\text{CH}_2\text{Cl}_2/\text{TFA}$ media [12], but they are not as selective as they are in the TMOF medium.

2.16 Hydroxylations

Direct anodic hydroxylations in aqueous or organic-aqueous media are difficult because water is usually oxidized at the anode at less positive potentials than the organic substrate. However, if the organic substrate is oxidized before the water, direct hydroxylation is possible by reaction of water with the produced organic cations. Hydroxylation of phenols takes place at platinum, PbO_2 and other electrodes, as illustrated below [1,2]:

Phenols

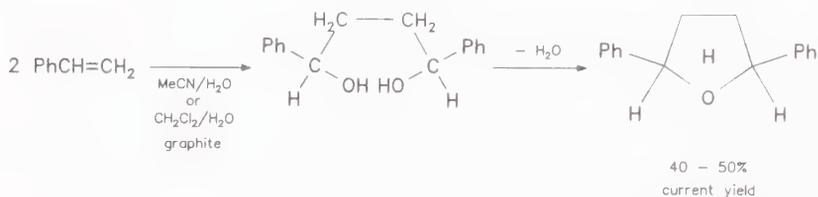


50 - 80%

Oxidations at the PbO_2 anode in acidic solutions may involve both electrocatalytic (via PbO_2) and direct electron transfer steps. The initial radical cation of the phenolic compound is most probably electrocatalytically formed while its further deelectronation leading to the oxonium ion may involve both indirect electrocatalytic and direct electron transfer steps. (Note: PbO_2 is not stable below 1.4 V vs SCE in 1 M H_2SO_4 .) In the anodic oxidation of phenols in general PbO_2 , C, Ni or Pt are suitable electrodes. Usually the PbO_2 is more effective. Benzene has been converted to *p*-benzoquinone at a PbO_2 electrode in sulfuric acid medium on a pilot-plant scale [3]. The reaction involves the hydroxylated intermediates. Anthracene is transformed into anthraquinone and bianthrone, via hydroxylated intermediates by electrolysis in MeCN/ H_2O media [4,5].

Side chains of aromatics

Hydroxylations on side chains of aromatics are possible by electrolysis in $\text{H}_2\text{O}/\text{MeCN}/\text{Et}_4\text{NBF}_4$ solutions or in organic/ H_2O emulsions [6,7]. Styrenes are thus dimerized upon hydroxylation, and by loss of water from the dihydroxy dimer afford the 2,5-diphenyltetrahydrofurans [8]:



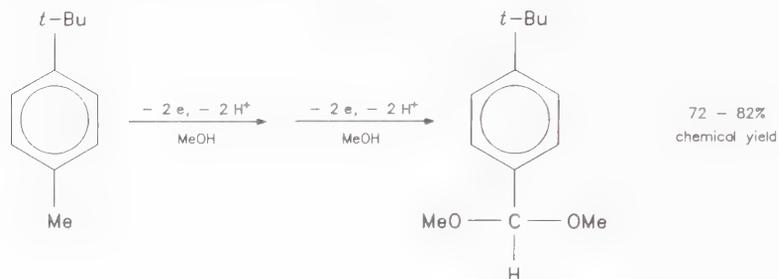
2.17 Alkoxylation

Methoxylation

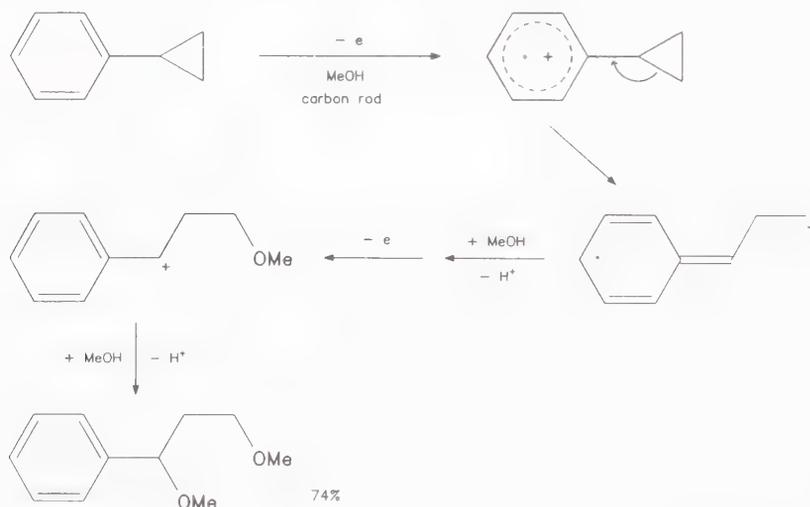
Anodic alkoxylation is a reaction of a general type by which intermolecular and intramolecular C—O bonds are formed leading to a wide variety of useful synthetic intermediates. Methoxylation is the most common type of alkoxylation. They are easily performed in methanol solutions containing the organic substrate and KOH, NaOH or the alkali methoxide salt. At the anode both methanol and methoxide ion are subject to oxidation by loss of an electron. For synthetic work the oxidation of MeOH or MeO^- ion must not advance beyond the one electron oxidation stage, or the alcohol must not undergo oxidation before the organic substrate so that it can act as a nucleophile for the desired methoxylation. Methoxylation can proceed along two paths, as illustrated in Scheme 244:



process in a bipolar cell with a packed bed electrode of graphite pellets. The side *p*-CH₃ chain was dimethoxylated in two steps in the chosen electrolysis medium MeOH/CH₃COOH/NaBF₄:

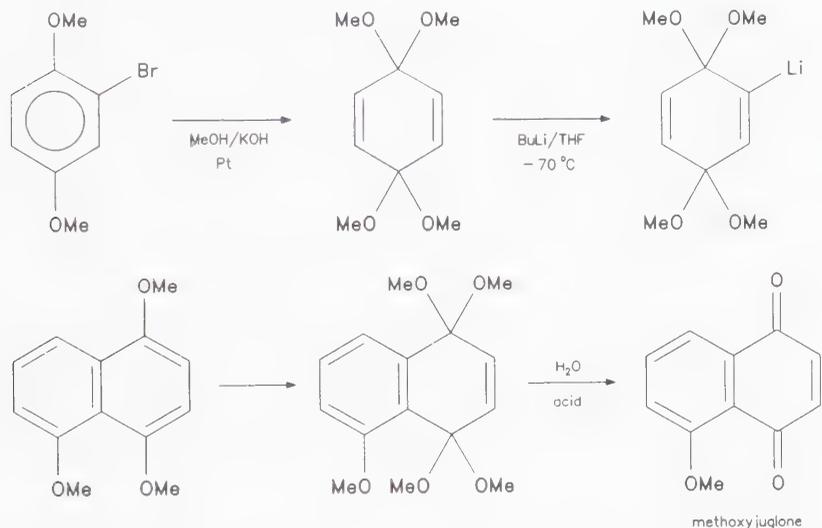


Some tar and oligomer formation were side products of this electrolysis. The electrolysis was carried out under constant current at 308 K. Cyclic voltammetry showed that the butyltoluene was oxidized at a less positive potential than the methanol, but under constant current conditions in the large scale process some methanol also was oxidized at the anode (because the anode potential had to be raised to keep the current constant). Arylcyclopropanes easily undergo dimethoxylation following opening of the cyclopropane ring, as illustrated in the following example [6,7]:

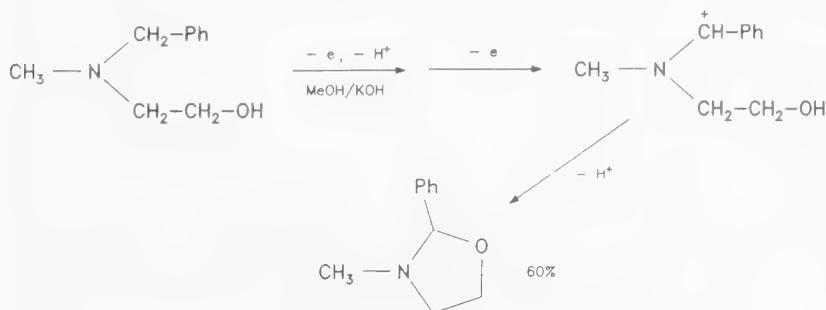


This electrolysis is performed in a three-neck flask equipped with carbon rod electrodes, anode and cathode, and a reflux condenser, with the substrate in methanol solution containing tetraethylammonium tosylate as electrolyte. The electrolyzed solution is diluted with water, and the products are extracted with ether and isolated by distillation in vacuo.

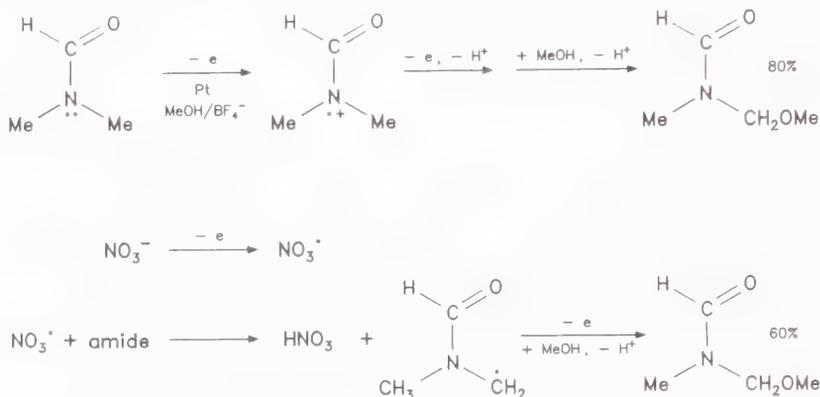
Swenton and coworkers [8] successfully employed electrochemical methoxylation in the synthesis of lithiated quinone ketals in connection with anthracycline antibiotic ring systems and the preparation of methoxyjuglone [9] (a natural product of biological importance), the latter from the starting compound 1,4,5-trimethoxynaphthalene. These reactions are synoptically depicted below:



Silyl-substituted 1,3-dienes are transformed to 1,1,4-trimethoxy derivatives [10] by anodic electrolysis on carbon anodes in MeOH/Et₄NOTs solutions in one-compartment cells [4]. The β -silyl group facilitates the deelectronation of the π bond and the C—Si bond splits easily. Methoxylation of piperidine and pyrrolidine-derived urethanes yield products that are intermediates for the synthesis of various alkaloids.^{11,12} The amino acids lysine and ornithine were prepared via the methoxylated *N*-acylpiperidine [13]. Anodic methoxylation of acetals in MeOH/KOH solutions affords orthoesters most likely via the anodically formed CH₃O[•] radicals [14,15]. Intramolecular alkoxylation of some ethanolamines leads to the formation of five-membered rings, like that of 1,3-oxazolidine [16]:



The methoxylation of *N,N*-dimethylformamide in MeOH/BF₄⁻ solution occurs directly via the cation radical of the amide and also indirectly in MeOH/NH₄NO₃ solution by the action of NO₃[•] radicals produced at the anode [17]. It is interesting to note that in the electrolysis of methanol/dimethylformamide mixtures the oxidation of methanol is inhibited by the amide. The amide is thus oxidized at the anode, before the BF₄⁻ ion, so that the direct methoxylation reaction becomes feasible. The reactions are summarized formally in Scheme 2.45:

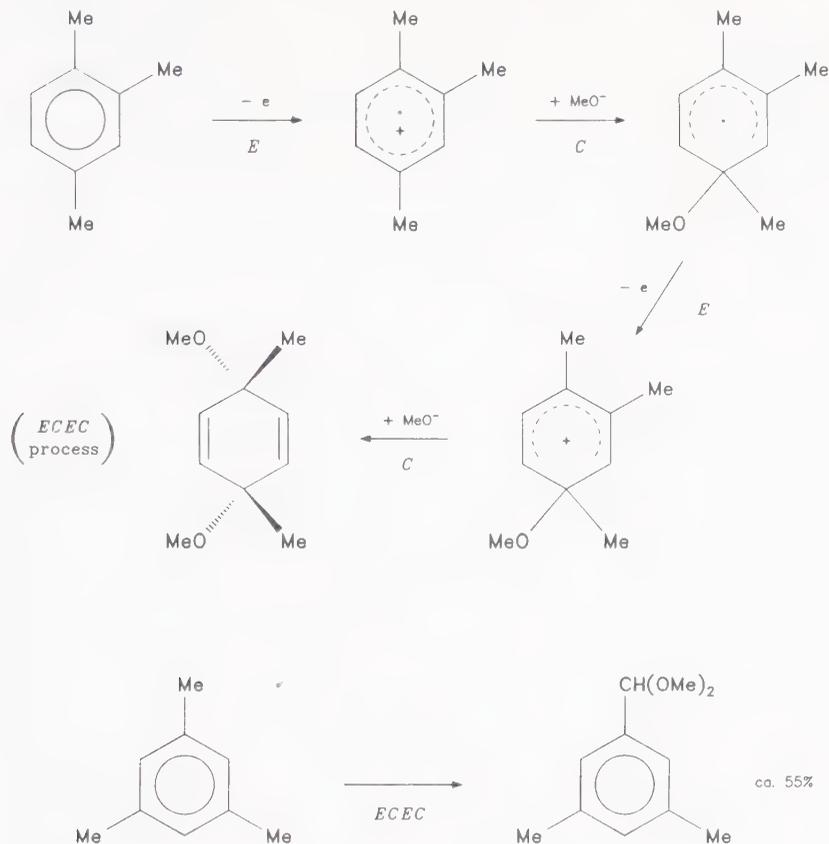


Scheme 2.45

Methoxylation of DMF (Scheme 2.45)

The methoxylation of the amide by direct electrolysis is conducted in a one-compartment cell (200 ml beaker) containing a solution of equal volumes of the amide and methanol (75 ml of each) and a few grams of Bu₄NBF₄ as electrolyte. Two platinum electrodes, placed two cm apart to minimize IR drop, serve as anode and cathode. A voltage is applied across the cell sufficient to allow a current of 2 A (1 A/cm²) to pass through the solution which is vigorously stirred by a magnet bar. When about one half of the amide has been oxidized, the electrolysis is stopped and the products are recovered by distillation, and are identified by vapor phase chromatography (VPC) using authentic samples as standards (Adapted from Ref. 17, Copyright of American Chemical Society, 1972).

The methoxylation of methylbenzenes provides a route for the preparation of cyclohexa-1,4-dienes. Barba and coworkers [18] confirmed that an ECEC reaction sequence, Scheme 2.46, leads to methoxylated products either by addition to the ring or by substitution on the methyl chain.

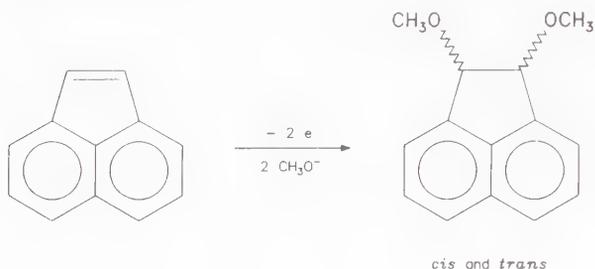


Methoxylation of Methylbenzenes, (Scheme 2.46)

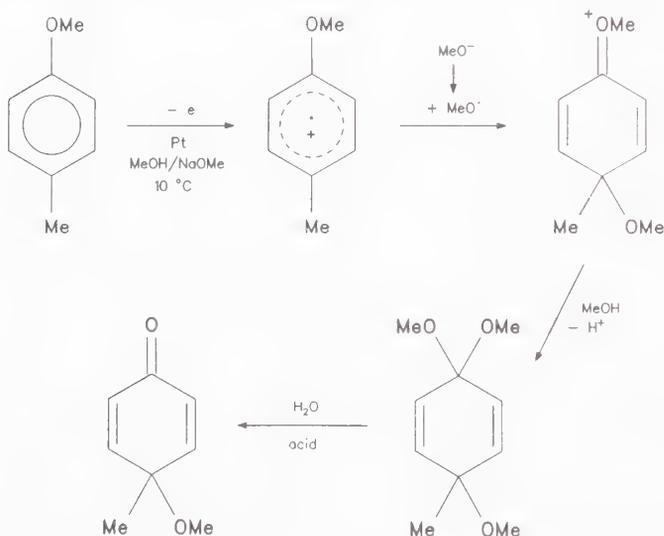
Typically, the methoxylation is performed in MeOH/NaOMe solution in an undivided cell under a current of 50–60 mA/cm² at 25–30 °C with carbon or platinum electrodes [21]. The sodium methoxide is prepared by addition of metallic sodium 0.2 g to 70 ml of methanol containing 1 g of the methylbenzene substrate. The products are isolated by flash chromatography on a carbon-Celite column with hexane/ethyl acetate eluant, and identified by spectroscopic techniques.

Stereospecific methoxylations affording *cis* and *trans* products have been demonstrated with molecules such as acenaphthene [19] and *p*-xylene [20]. The *cis* and *trans* forms of the acenaphthene products were formed in ratios of 67/31 *cis/trans* at platinum and 36/64 at graphite electrodes

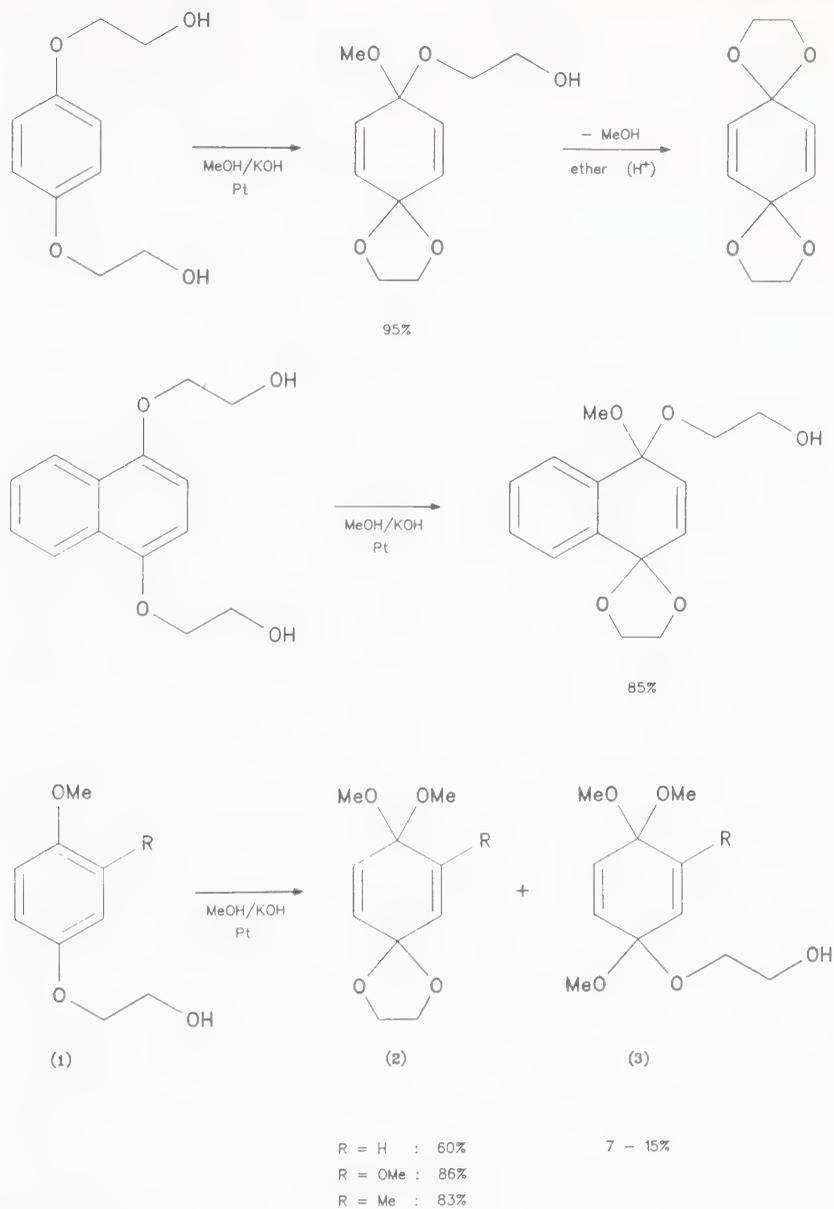
apparently because of different orientational adsorption effects on the electrodes [19].



The methoxylation of alkylanisoles in MeOH/NaOMe solutions proceeds readily by a direct one-electron transfer to the anode as a first step to give the cation radical. This may be attacked by any of the available nucleophilic species, methanol, methoxy radical or methoxide ion. Thus the nuclear methoxylation of *p*-methylanisole leads to the 2,5-dienone by controlled hydrolysis of the ketal intermediate, most likely according to the following path [21]:

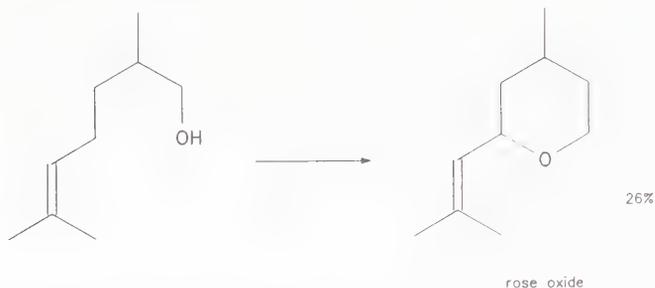


Intramolecular alkoxylation and cyclizations can be efficiently accomplished by anodic electrolysis in basic methanolic solution, as the following typical examples illustrate [22,23,24]:



Scheme 2.46

Citronellol is transformed to the cyclic ether by anodic electrolysis in MeCN/Et₄NOTs solution [22]:



Anodic Oxidation of Mixed Ethers of Hydroquinones

A typical experimental procedure concerning the aforementioned intramolecular alkoxylation is the procedure used by Swenton [23] for the oxidative transformation of compound (1) to (2) (see above formulas for 1 and 2 Scheme 2.46).

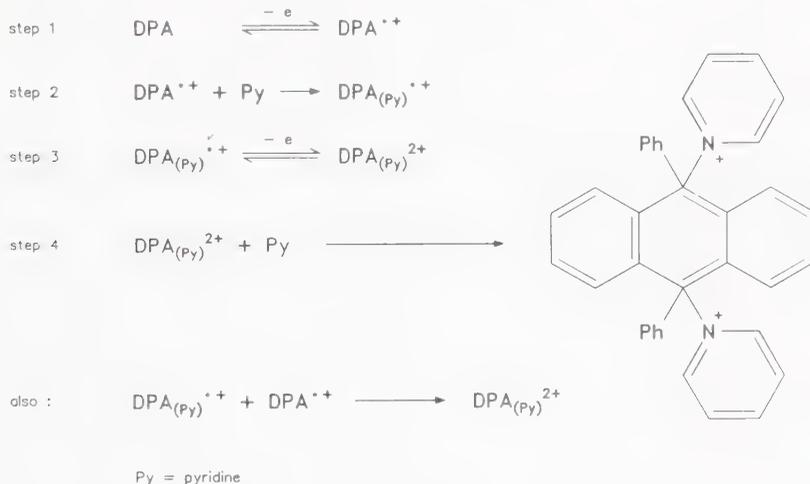
The electrolysis is carried out in an undivided cell equipped with platinum electrodes and a platinum wire to act as a reference electrode. A potentiostat is used as a dc power source. Three g of compound A is dissolved in 1% KOH methanolic solution (75% ml) and a current of 1 A is passed through the solution by properly adjusting the applied potential so as to keep the current constant as the electrolysis progresses. The potential region within which the desired oxidation occurs is determined from a *i*-*E* curve, as usual. The reaction is followed by periodic spectroscopic UV measurements at 288 nm, until the initial UV absorption falls to less than 5% of the initial value. The electrolyzed solution is then subjected to distillation in vacuo to remove the methanol, and to the residue is added 20 ml of water. From this aqueous solution the product is extracted with chloroform (3 × 20 ml) and the chloroform is evaporated. The colorless oily liquid that remains is chromatographed on a neutral alumina column to isolate the product B, which is a white crystalline solid. Identification of B is made by IR and NMR techniques (Adapted from Ref. 23, Copyright of the American Chemical Society, 1981).

2.18 Pyridinations

Pyridine is known to be a good nucleophile adding readily to various cation radicals and particularly to condensed aromatic compounds (anthracene, perylene, diphenylanthracene, and benzo(a)pyrene). The last

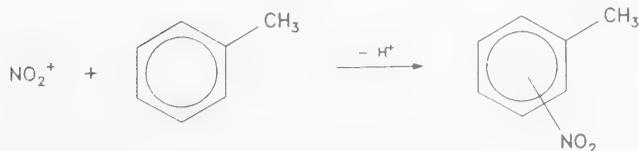
one is known as a potent carcinogen, and has been studied in connection with in vivo bonding of hydrocarbons to deoxyribonucleic acid (DNA) [1].

The pyridination of diphenylanthracene (DPA) has been proposed to occur with the pyridine adding successively to the cation radical and to the dication in the fourth step [2]. Spectroelectrochemical investigations indicated that these steps are fast [3].



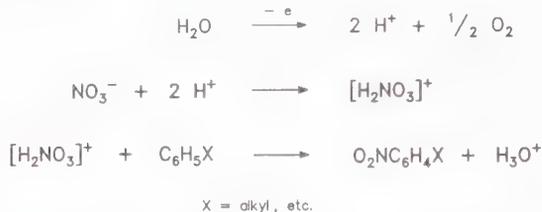
2.19 Nitrations

Aromatic nitrations are accomplished by anodic electrolysis in aqueous nitric acid and also in nitrite ion containing solutions [1–3]. The active nitronium ion, NO_2^+ , generated at the anode, as shown below, reacts with the aromatic compound to yield the substituted nitro derivative. Nitrogen dioxide, NO_2 , is in equilibrium with N_2O_4 .



The electrolysis system $\text{Bu}_4\text{N}^+\text{NO}_3^-/\text{MeCN}/\text{N}_2\text{O}_4$ can be used for nitrations. In such a medium the nitrogen dioxide is oxidized to NO_2^+ at 0.8 V

as Ag/Ag^+ . The possible existence and role of the positive ion N_2NO_3^+ near the anode might also be considered for certain nitrations as indicated below:



Nitrations of aromatics, alkenes, dienes, and others have been carried out in acetonitrile/ BF_4^- and $\text{CH}_2\text{Cl}_2/\text{BF}_4^-$ solutions at platinum electrodes using N_2O_4 , (NO_2^+), as the nitrating agent [4]. Also, nitrations have been conducted in MeCN solutions containing a quaternary ammonium nitrite salt and styrene derivatives as substrates [5] in which the vinylic hydrogen was substituted by NO_2 .

References

Section 2.1 Fundamental Nature

1. Yoshida K (1984) *Electrooxidation in organic chemistry*. Wiley-Interscience, New York
2. Bard AJ, Ledwith A, Shine H (1976) *Adv Phys Org Chem* 13:155
3. Baizer MM, Lund H (eds) (1983) *Organic electrochemistry*. Marcel-Dekker, New York
4. Kyriacou D (1981) *Basics of electroorganic synthesis*. Wiley-Interscience, New York
5. Kyriacou D, Jannakoudakis D (1986) *Electrocatalysis for organic synthesis*. Wiley-Interscience, New York
6. Fry AJ (1989) *Synthetic organic electrochemistry*. Wiley-Interscience, New York
7. Ebersson L (1982) *Adv Phys Org Chem* 18:79
8. Ebersson L (1987) *Electron transfer reactions*. Springer, Berlin Heidelberg New York
9. Ross SD, Finkelstein M, Rudd EJ (1975) *Anodic oxidations*. Academic press, New York
10. Uneama K, Steckhan E (eds) (1987) *Topics in current chemistry*, vol 142. Springer, Berlin Heidelberg New York
11. Weinberg NL, Weinberg HR (1968) *Chem Rev* 68:449

Section 2.2 Hydrocarbons

- 1a. Pletcher D, Fleischmann M, Korinek K (1971) *J Electroanal Chem* 33:478
- 1b. Clark DB, Fleischmann M, Pletcher D (1972) *J Electroanal Chem* 36:137
- 1c. Bertram J, Coleman JP, Fleischmann M, Pletcher D (1973) *J Chem Soc Perkin, Trans* 2:374
2. Coleman JP, and Pletcher D (1974) *Tetrahedron Lett* 147; Bertram J, Fleischmann M, Pletcher D (1978) *Tetrahedron Lett* 349

3. Kollmer H, Smith AO (1970) *Chem Physics Lett* 5:7
4. Olah GA (1967) *J Am Chem Soc* 89:2227
5. Tomat R, Rigo A (1986) *J Appl Electrochem* 16:8
6. Nyberg K (1971) *Acta Chem Scand* 25:534; Fleischmann M, Pletcher D (1969) *Tetrahedron Lett* 6225; Adams RN (1969) *Accounts Chem Res* 2:175; Brans K, Mann CK (1967) *J Org Chem* 32:1474
7. Dietrich M, Heinze J (1981) *Angew Chem* 24:508
8. Mann CK (1969) In: Bard AJ (ed) *Electroanalytical chemistry*, vol 3. Marcel-Dekker, New York
9. Steckhan E (1978) *J Am Chem Soc* 100:3526
10. Nyberg K (1970) *Acta Chem Scand* 24:1609
11. Becker JY, Miller LL, Boekelheide V, Morgan T (1976) *Tetrahedron Lett* 2939
12. Sato T, Kamada M (1977) *J Chem Soc Perkin Trans* 2:384
13. Sainsbury M, Schinazi RE (1972) *J Chem Soc Chem Commun* 718
14. Kotani E, Tekeuchi N, Tobinaga S (1975) *J Chem Soc Chem Commun* 550
15. Palmquist V, Nilsson A, Parker VD, Ronlan A (1976) *J Am Chem Soc* 98:2571
16. Sainsbury M, Wyatt J (1979) *J Chem Soc Perkin Trans* 1:108
17. Miller LL (1979) *Pure Appl Chem* 51:2125
18. Piersma BJ (1967) In: Gileadi E (ed) *Electrosorption*. Plenum Press, New York; Damhs H, Grear M (1963) *J Electrochem Soc* 110:1075; Bockris JOM (1966) *Modern aspects of electrochemistry*. Plenum Press, New York, chap 2
19. Bordaell FC, Cheng JP, Bausch MJ, Bases JE (1988) *J Phys Org Chem* 1:208
20. Yoshida K, Nagase S (1979) *J Am Chem Soc* 101:4268

Section 2.3 Hydroxy Compounds

1. Lund H (1971) In: Patai S (ed) *Chemistry of the hydroxy group*. Wiley-Interscience, London
2. Lund H (1957) *Acta Chem Scand* 11:491
3. Parker VD (1978) In: Bard AJ, Lund H (eds) *Encyclopedia of electrochemistry*. Marcel-Dekker, New York, vol VI, p 181
4. Fleischmann M, Korinek K, Pletcher D (1971) *Electroanal Chem* 31:39
5. Vertes G, Horanyi G, Nagg F (1972) *Tetrahedron* 28:377
6. Schäfer HJ, Kaulen J (1982) *Tetrahedron* 38:3299
7. Kaulen J, Schäfer HJ (1979) *Synthesis* 513
8. Lund T, Lund H (1984) In: *Extended abstracts*, vol 84. The Electrochemical Society Cincinnati, Ohio, Abst 330
9. Chum Li H, Ellis KJ, Islam N, Smith CZ, Sopher DW, Utley JHP (1984), *Extended abstracts*. The Electrochemical Society, Cincinnati, Ohio In: Abst 332
10. Chum Li H, Baizer MM (1985) *The electrochemistry of biomass and derived materials*. ACS Monograph
11. Bockris JOM, Piersma BJ, Gileadi E (1964) *Electrochim Acta* 9:1329
12. Pletcher D, Fleischmann M, Korinek K (1971) *J Electroanal Chem* 33:478
13. Hampton NA, Lee JB, MacDonald KI (1972) *Electrochim Acta* 19:921
14. Kyriacou D, Tougas TP (1987) *J Org Chem* 52:2318
15. McMillan JA (1962) *Chem Rev* 62:65
16. Kyriacou D, University of Massachusetts. Lowell (unpublished work)
17. Ref. 5, section 2.1
18. Kuguni Y, Nonaka T, Bochong Y, Watanaba N (1992) *Electrochim Acta* 37:353
19. Sundholm G (1971) *J Electrochem Soc* 31:265; (1971) *Acta Chem Scand* 25:3188
20. Belanger G (1976) *J Electrochem Soc* 123:818
21. Scholl PC, Lentsch SE, van de Mark MR (1976) *Tetrahedron* 32:303

Section 2.4 Oxide Covered Electrodes

1. Pohl JP, Pickett H (1988) In: Trassati S (ed) *Electrodes of conductive oxides*. Elsevier, New York, p 192
2. Kyriacou D, Janhgen EGE, Tougas TP, University of Massachusetts, Lowell. Silver oxide anodes as biosensors. a. DeBenedetto MJ (1991) PhD Thesis; b. DeMott J (1992) PhD Thesis
3. Stonehart P, Portandet EP (1968) *Electrochim Acta* 13:1805
4. Droog JMM, Huisman F (1980) *J Electroanal Chem* 15:211
5. Schäfer HJ, Kaulen J (1982) *Tetrahedron* 38:3299
6. Ref. 5, section 2.1
7. Fleischmann M, Korinek K, Pletcher D (1971) *J Electroanal Chem* 31:97; (1972) *J Chem Soc Perkin Trans* 2:1396
8. Fleischmann M, Pletcher D (1973) *Adv Phys Org Chem* 10:155; Pletcher D, Walsh F (1990) *Chem Rev* 90:837
9. Robertson PM (1980) *J Electroanal Chem* 111:97
10. Kyriacou D, Tougas TP (1987) *J Org Chem* 52:2318; Hampton NA, Lee JB, Morley JR, Scanton B (1969) *Can J Chem* 47:3789
11. Kyriacou D, University of Massachusetts, Lowell (unpublished work)
12. Bondarenko EG, Tomilov AP *Zh (1969) Prikl Khim* 42:2033
13. Campbell KD, Gulbankian AH, Edamura F, Kyriacou D (1985) US patent 4446440
14. Kolb DM (1978) *Adv Electrochem Engn* 11:125; Jütner K (1986) *Electrochim Acta* 31:8; Kokkinidis G, Theodoridou E, Jannakoudakis D, University of Thessaloniki, private communications; Adzic RR, Tripkovic AV, Markovic NM (1980) *J Electroanal Chem* 14:37; Kokkinidis G, Jannakoudakis D (1982) *J Electroanal Chem* 133:307
15. Ocon P, Beden B, Huser H, Lamy C (1987) *Electrochim Acta* 32:387

Section 2.5 Phenolic Compounds

1. Yoshida K (1984) *Electrooxidation in organic synthesis*. Wiley-Interscience, New York, p 229
2. Tablem A, Wang S, Swenton JS (1992) *J Org Chem* 57:2135
3. Nash RA, Skauen DM, Pardy WC (1958) *J Am Pharm Assoc* 47:443
4. Covitz FH (1980) French Patent 154350; Tabakovic I, Gruzic Z, Bejtovic Z (1983) *J Heterocyc Chem* 20:635
5. Svanholm V, Bechgaard K, Parker VD (1974) *J Am Chem Soc* 96:2409
6. Oyama N, Osaka T, Sazuki T (1987) *J Electrochem Soc* 134:3068
7. Torri S, Diminaka AL, Yoshikata A, Inokuchi T (1989) *Tetrahedron Lett* 30:2105
8. Smith C, Utley JHP, Petrescu M, Viertler H (1989) *J Appl Electrochem* 19:535
9. Lalvani SB, Rajagopal P (1992) *J Electrochem Soc* 139, No 1
10. Schutte JHP, du Plessis JAK, Lachman G, Vilgoen AM, Nelson AD (1989) *J Chem Soc Chem Commun* 1290

Section 2.6 Carbonyl Compounds

1. Weinberg NL, Weinberg HR (1968) *Chem Rev* 68:449
2. Fedorenko (1974) In: Tipson RS, Horton D (eds) *Advances in carbohydrate chemistry and biochemistry*. Academic Press, New York
3. Bockris JOM, Piersma BJ, Gileadi E (1964) *Electrochim Acta* 9:1329
4. Chiba T, Okimoto M, Nagai H, Takata Y (1982) *Bull Chem Soc (Japan)* 55:335
5. Koch VR, Miller LL (1982) *J Electroanal Chem* 43:318
6. Becker JY, Miller LL, Siegel TM (1975) *J Am Chem Soc* 97:849
7. Becker JY, Byrd RR, Miller LL, So YH (1975) *J Am Chem Soc* 97:853

8. Segura M, Barba F, Aldaz A (1986) *Electrochim Acta* 31:83
9. Ye S, Beck F (1991) *Tetrahedron* 47:5465
10. Ismail MT (1987) *Bull Soc Chim (France)* 438
11. Chiba T, Okimoto M (1992) *J Org Chem* 57:1375

Section 2.7 Carboxylic Acids

1. Kolbe H (1849) *Liebigs Ann* 69:257
2. Utley JHP (1974) In: Weinberg NL (ed) *Techniques of electroorganic synthesis part I*. Wiley-Interscience, New York, p 793
3. Weedon BCL (1960) *Adv Org Chem* 1:1
4. Finkelstein M, Petersen RC (1960) *J Org Chem* 25:136
5. Rand L, Mohar AF (1965) *J Org Chem* 30:388
6. Conway BE, Vigh AK (1967) *Electrochim Acta* 12:102
7. Vasiliev Yu B, Korsman ED, Freiden G (1982) *Electrochim Acta* 27:937
8. Einhorn J, Souler JL, Bucheet C (1983) *Can J Chem* 61:584
9. Vasiliev Yu B, Budetzky US, Korsman EP (1982) *Electrochim Acta* 27:929
- 9a. Wladislaw B, Ayers AMJ (1962) *J Org Chem* 27:281; Coleman JP, Utley JHP, Weedon BCL (1964) *J Chem Soc Chem Commun* 438
10. Uneama K, Namba H (1988) *J Org Chem* 53:4598
11. Pletcher D, Smith CZ (1975) *J Chem Soc Perkin Trans* 1:948
12. Ogumi Z, Yamashita H, Nishio K, Takehara Z, Yoshizawa S (1983) *Electrochim Acta* 28:1687
13. Kraeutler B, Bard AJ (1978) *J Am Chem Soc* 99:77; (1978) *J Am Chem Soc* 100:2239

Section 2.8 Amines and Amides

1. Lord SS, Rojers LB (1954) *Anal Chem* 26:284
2. Nelson RF, Adams RN (1968) *J Am Chem Soc* 90:3925
3. Portis LC, Klug TJ, Mann CK (1974) *J Org Chem* 39:3488
4. Cauquis G, Fauvelot G, Rigani J (1968) *Bull Soc Chim* 12:4928
5. Seo ET, Nelson RF, Fritsch JM, Marcoux LS, Leedy DW, Adams RN (1966) *J Am Chem Soc* 88:3498
6. Greason SC, Weeder J, Nelson RF (1972) *J Org Chem* 37:4440
7. Barns KK, Mann CK (1967) *J Org Chem* 32:1474
8. Smith PJ, Mann CK (1969) *J Org Chem* 34:1821
9. Serve D (1976) *Electrochim Acta* 21:1171
10. Feldhues V, Schäfer HJ (1982) *Synthesis* 82:145
11. Serve D (1975) *J Am Chem Soc* 97:432
12. Wawzonek S, McIntyre T (1967) *J Electrochem Soc* 114:1025
13. Esteban PC, Leger JM, Lamy C, Genies E (1989) *J Appl Electrochem* 19:462
14. Hand RL, Nelson RF (1978) *J Electrochem Soc* 125:1059
15. Lowert BA, Marcoux Y, Bard AJ (1972) *J Am Chem Soc* 94:5538
16. Finkelstein M, Nyberg K, Ross SD, Servin R (1978) *Acta Chem Scand* B32:182
17. Shono T, Matsumura Y, Tsubata K (1981) *J Am Chem Soc* 103:1172
18. Hall LR, Iowamoto RT, Haluznik RP (1989) *J Org Chem* 54:2446
19. Rudd EJ, Finkelstein M, Ross SD, Nyberg K, Servin R (1976) *Acta Chem Scand* B30:640
20. Bolzan AE, Iwasita T (1988) *Electrochim Acta* 33:109
21. Degner D (1989) *Dechema-Mon (Org Electrochem)* 375
22. Swenton JS, Brian RB, Cung-Pin C, Chun Tzer-C (1989) *J Org Chem* 54:51

Section 2.9 Ethers and Esters

1. Ronlan A, Behgaard K, Parker VD (1973) *Acta Chem Scand* 27:2375
2. Hammerich O, Moe NS, Parker VD (1972) *J Chem Soc Chem Commun* 156
3. Svanholm U, Parker VD (1972) *Tetrahedron Lett* 471
4. Stewart RF, Miller LL (1980) *J Am Chem Soc* 102:4999
5. Venkachadan CS et al. (1991) *Tetrahedron Lett* 51:7592
6. Shono T, Matsumura Y (1969) *J Am Chem Soc* 91:2003
7. Weinberg NL, Beleau B (1973) *Tetrahedron* 29:279
8. Koch D, Schafer HJ, Steckhan E (1974) *Chem Ber* 107:3640
9. Callot HJ, Louati A, Gross M (1983) *Bull Soc Chim* II:317
10. Moeller KD, Tinao LV (1992) *J Am Chem Soc* 114:1033
11. Boyd JW, Schmaltz PW, Miller LL (1980) *J Am Chem Soc* 162:3856
12. Miller LL, Ramachandra V (1974) *J Org Chem* 39:369
13. Yadav AK, Misra SC (1986) *Electrochim Acta* 31:507

Section 2.10 Organic Halides

1. Miller LL, Hoffman AK (1967) *J Am Chem Soc* 89:593
2. Laurent A, Laurent E, Tardivel R (1973) *Tetrahedron Lett* 4861
3. Laurent E, Tardivel R (1976) *Tetrahedron Lett* 1779
4. Miller LL, Kuzawa E, Campbell CP (1970) *J Am Chem Soc* 92:2821
5. Becker JY (1971) *J Org Chem* 42:3997; Coch VR, Miller LL (1973) *Tetrahedron Lett* 693
6. German A, Brunel D, Moreau P (1989) *J Fluorine Chem* 43:249
7. Becker JY, Smart E, Fukunga T (1988) *J Org Chem* 53:5714
8. Hoffender H, Lorch HW, Wendt H (1975) *J Electroanal Chem* 66:183

Section 2.11 N-Heterocyclics

1. a. Kwee S, Lund H (1969) *Acta Chem Scand* B23:2121; b. Weinberg NL, Weinberg HR (1968) *Chem Rev* 68:449; c. Babbit JM et al. (1966) *Chem Ind (London)* 2127; d. Eisner V, Kuthan J (1972) *Chem Rev* 72; e. Kuthan J, Kurfurst A (1982) *Ind Eng Chem Proc Res Div* 21:191; f. Ludvic J et al. (1987) *Electrochim Acta* 32:1063; g. Goyal RN et al. (1987) *Bull Soc Chim* 78
2. Yoshida K (1979) *J Am Chem Soc* 101:2116; Yoshida K (1978) *J Chem Soc Chem Commun* 1108
3. Ref. 9, section 2.9
4. Yoshida K, Kitabayshi H (1987) *Bull Chem Soc (Japan)* 60:3093
5. Iwasaki T, Horikawa H, Matsumoti K, Mioshi M (1979) *J Org Chem* 44:1552; Nyberg K (1976) *Synthesis*, 545
6. Billon JP, Cauquis G, Combrisson J, Li AM (1960) *Bull Soc Chim (France)* 2062
7. Cauquis G, Falmy HM, Pierre G, Elnagdi MH (1970) *J Heterocycl Chem* 16:413
8. Zzochralska B, Elving P (1981) *Electrochim Acta* 26:1755
9. Lacoutre F, Barbey G (1983) *Electrochim Acta* 28:1617
10. Bellamy AJ, Innes DI (1982) *J Chem Soc Perkin Trans* 2:1599
11. Thaning M, Wistrand G (1989) *Acta Chem Scand* B43:290
12. Laupp G, Koleli F, Grunden E (1985) *Auger Chem* 24:864
13. Wrona MA, Dryhurst G (1988) *J Org Chem* 54:2718
14. Anne A, Moiroux J (1988) *J Org Chem* 53:2816
15. Gupta PN, Rather GM (1988) *J Ind Chem Soc LXV* 633
16. Pragst E, Bock C (1975) *J Electrochem Soc* 61:47

Section 2.12 Organosulfur Compounds

1. Cottrell PT, Mann CK (1969) *J Electrochem Soc* 116:1499
2. Shono T, Matsumara Y, Mizozuch M, Hayashi J (1979) *Tetrahedron Lett* 3861
3. Jansson R (1984) *Chem Eng News* 62:43
4. Cuttler LH (1979) *AIChE Symposium Ser* 185 75:103
5. Kimura M, Matsuhara S, Sawaki Y (1984) *J Chem Soc Chem Commun* 1619
6. Porter DN, Utley JHP (1978) *J Chem Soc Chem Commun* 255
7. Saeva FD, Morgan BP, Fisher MW, Haley NF (1984) *J Org Chem* 49:390
8. Glass RS, Petson A, Wilson G (1986) *J Org Chem* 51:4337
9. Uneama K, Torii S (1972) *J Org Chem* 37:367
10. Silber JJ, Shine HJ (1971) *J Org Chem* 36:2923
11. Kim K, Hull VJ, Shine HJ (1974) *J Org Chem* 39:2534
12. Parker VD, Eberson LJ (1970) *J Am Chem Soc* 92:7488
13. Ref. 1, section 2.1
14. Hammerich O, Moe NS, Parker VD (1972) *J Chem Soc Chem Commun* 156

Section 2.13 Anodic Cyanations

1. Nilsson S (1969) *Dis Faraday Soc* 45:242
2. Miller LL (1979) *Pure App Chem* 51:2125
3. Koyama K, Susuki T, Tsutsumi S (1967) *Tetrahedron* 23:2675
4. Andreades S, Zahnnow EW (1969) *J Am Chem Soc* 91:4181
5. Parker VD, Bargert BE (1965) *Tetrahedron Lett* 4065
6. Nilsson S (1973) *Acta Chem Scand* 27:329
7. Susuki T, Koyama K, Omori A, Tsutsumi S (1968) *Bull Chem Soc (Japan)* 41:2663
8. Yoshida K, Nagase S (1979) *J Am Chem Soc* 101:4268
9. Papouchado L, Adams RN, Felberg WS (1969) *J Electroanal Chem* 21:408
10. Cauquis G, Serve D (1979) *Bull Soc Chim (France)* 2:145
11. Shine JH, Ristagno CV (1972) *J Org Chem* 37:3424
12. Nyberg K (1976) *Acta Chem Scand* 30:2499
13. March J (1977) *Advanced organic chemistry*. McGraw-Hill International Student Edition Kagakusha, Ltd. p 503
14. Ref. 20, section 2.2
15. Eberson L, Parker VD (1969) *J Chem Soc Chem Commun* 340
16. Inoue T, Tsutsumi S (1965) *Bull Chem Soc (Japan)* 38:661
17. Nyberg K (1971) *Acta Chem Scand* 33:2499
18. Yoshida K (1979) *J Am Chem Soc* 99:6111
19. Chiba T, Takata Y (1977) *J Org Chem* 42:2973
20. Yoshida K, Fueno T (1970) *J Chem Soc Chem Commun* 711
21. Eberson L, Helgée B (1978) *Acta Chem Scand* B32:313
22. Eberson L, Radner F (1992) *Acta Chem Scand* 46:312

Section 2.14 Acetoxylation and Acetamidations

1. Eberson L (1967) *J Am Chem Soc* 89:4669
2. Eberson L, Oberrauch E (1981) *Acta Chem Scand* B35:193
3. Eberson L, Nyberg K (1966) *J Am Chem Soc* 88:1685
4. Nyberg K (1970) *Acta Chem Scand* B24:1609
5. Bum Z, Cedheim L, Eberson L (1977) *Acta Chem Scand* B31:662
6. Ross SD, Finkelstein M, Petersen RC (1970) *J Org Chem* 35:781
7. Ross SD, Finkelstein M, Petersen RC (1964) *J Am Chem Soc* 86:4139

8. So YH, Becker JY, Miller LL (1975) *J Chem Soc Chem Commun* 262
9. Shono T, Matsumura Y, Onomura O, Ozaki M, Kazanawa T (1987) *J Org Chem* 52:536
10. Hembrok A, Schäfer HJ (1985) *Angew Chem Int Ed Eng* 24:1655
11. Clark DB, Fleischmann M, Pletcher D (1973) *J Chem Soc Perkin Trans* 2:1578
12. Ebersson L, Nyberg K (1966) *Tetrahedron Lett* 2389
13. Baizer MM, Wagenknecht JH, Monsanto Chemical Co., USA
- 13a. Nyberg K (1969) *J Chem Soc Chem Commun* 774
14. Hammerich D, Parker VD (1974) *J Chem Soc Chem Commun* 245
15. Ref. 11, section 2.14
16. Laurent A, Laurent F, Locher P (1975) *Electrochim Acta* 20:857
17. Faïta G, Fleischmann M, Pletcher D (1970) *J Electroanal Chem* 25:455
18. Fleischmann M, Pletcher D (1972) *Chem Eng Techn* 44:187
19. Ebersson L, Olefsson B (1969) *Acta Chem Scand B*23:2355

Section 2.15 Anodic Halogenations

1. Meyers RA (ed) (1992) *Encyclopedia of physical science and technology*. Academic Press, New York, p 576
2. Childs WV (1982) In: Weinberg NL (ed) *Techniques of electroorganic synthesis*, vol 5. Wiley-Interscience, New York
3. O'Sullivan O, Klink EJP, Liu CC, Yeager EB (1985) *J Electrochem Soc* 132:2424
4. Drakesmith FG, Hughes DA (1986) *J Fluorine Chem* 32:103
5. Matsuda Y, Nishiki T, Sakota N, Nakagawa A (1984) *Electrochim Acta* 29:35
6. Casalbore G, Mastragostino M, Valchev S (1975) *J Electroanal Chem* 61:33
7. Shono T, Matsumura Y, Onomura O, Ozaki M, Kanazawa T (1987) *J Org Chem* 52:536
8. Ibvig Z, Pletcher D, Brooks WN, Healy KP (1985) *J Appl Electrochem* 15:719
9. Takasy Y, Matsuda Y, Shiniguchi A, Morita M, Saito M (1991) *Chemistry Lett. (Japan)* 1685
10. Matsuda Y, Hayashi H (1981) *Chemistry Lett (Japan)* 661
11. Shono T, Matsumura Y, Kalosh S, Ikeda K, Kamota T (1989) *Tetrahedron Lett* 30:1649
12. Miller LL, Watkins BF (1976) *J Am Chem Soc* 98:1515; Lines R, Parker VD (1980) *Acta Chem Scand B*34:47

Section 2.16 Hydroxylations

1. Ronlan A (1971) *J Chem Soc Chem Commun* 1643
2. Nilsson A, Ronlan A, Parker VD (1973) *J Chem Soc Perkin Trans* 1:2337
3. Fremery M, Höver H, Schwartzlose G (1974) *Chem Ing Tech* 46:635
4. Majeski EJ, Stuart JD, Obnesoge WE (1968) *J Am Chem Soc* 90:633
5. Parker VD (1970) *Acta Chem Scand B*24:2757
6. Sternerup H (1974) *Acta Chem Scand B*28:579
7. Ponsold K, Kash H (1979) *Tetrahedron Lett* 4463
8. Steckhan E, Schäfer HJ (1974) *Angew Chem* 13:472

Section 2.17 Alkoxylation

1. Inoue T et al. (1963) *Tetrahedron Lett* 1409
2. Couture R, Belew B (1972) *Can J Chem* 50:3424
3. Brettell R, Sutton JR (1975) *J Chem Soc Perkin Trans* 1:1947
4. Engles R, Schäfer HJ, Steckhan E (1977) *Justus Liebigs Ann Chem* 204

5. Kim HJ, Kusabak K, Hokazono S, Morooka S, Kato S (1987) *J Appl Electrochem* 17:1213
6. Shono T, Matsumura Y (1970) *J Org Chem* 35:4157
7. Brettle R, Sutton JR (1975) *J Chem Soc Perkin Trans* 1:1955
8. Manning MJ, Reynolds PW, Swenton JS (1976) *J Am Chem Soc* 98:5008
9. Jackson DK, Swenton JS (1977) *Synth Commun* 7:333
10. Yoshida J, Murata T, Isoe S (1987) *Tetrahedron Lett* 28:211
11. Shono T, Matsumura Y, Tsubaka K (1981) *J Am Chem Soc* 103:1172
12. Palmquist V, Nilsson A, Ronian A, Parker VD (1979) *J Org Chem* 44:196
13. Warning K, Mitzlaff M, Jensen H (1978) *Justus Liebigs Ann Chem Ann Chem* 1707
14. Shono T, Matsumura Y (1969) *J Am Chem Soc* 91:2803
15. Goosens HJM, Top AWH (1978) *Synthesis* 283
16. Weinberg NL, Brown EA (1966) *J Org Chem* 31:4054
17. Rudd EJ, Finkelstein M, Ross DS (1972) *J Org Chem* 37:1763
18. Barba I, Chincilla R, Gomez C (1991) *J Org Chem* 56, 3673
19. Weinberg NL, Weinberg HR (1968) *Chem Rev* 471
20. Barba I, Alonso F (1989) *J Org Chem* 54:4365
21. Nilsson A, Palmquist V, Peterson T, Ronlan A (1978) *J Chem Soc Perkin Trans* 1:708
22. Shono T, Ikeda A, Kimura T (1971) *Tetrahedron Lett* 3599; Margaretha P, Tissol P (1975) *Helv Chim Acta* 58:933
23. Dolson MG, Swenton JS (1981) *J Org Chem* 46:177
24. Dolson MG, Swenton JS (1981) *J Am Chem Soc* 103:2361

Section 2.18 Pyridinations

1. Parker VD, Ebersson L (1970) *Acta Chim Scand* B24:3542; Blackman GM, Will JP (1974) *J Chem Soc Chem Commun* 67; Yoshida K, Nagasi S (1979) *J Am Chem Soc* 101:4268
2. Manning G, Parker VD, Adams RN (1969) *J Am Chem Soc* 91:7584
3. Blount HN, Kuwana T (1973) *J Electroanal Chem* 27:271

Section 2.19 Nitrations

1. Achord JM, Hussey C (1981) *J Electrochem Soc* 128:2556
2. Kargin Yu M (1987) *J Gen Chem (USSR)* 56:1863
3. Bloom AJ, Fleischmann M, Mellor JM (1987) *Electrochim Acta* 32:785
4. Ebersson L, Radner F (1986) *Acta Chem Scand* B40:71
5. Laurent A, Laurent E, Locher P (1975) *Electrochim Acta* 20:857

3 Cathodic Organic Reactions

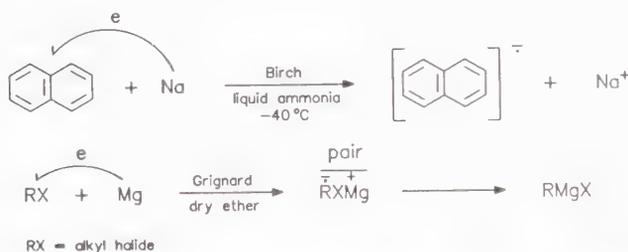
3.1 Phenomenological Nature

Anion radical formation

Cathodic or electroreductive organic reactions proceed by means of the electrolytically generated primary intermediate products, anion radicals, $R^{\cdot-}$, radicals, R^{\cdot} , and anions, R^- . Anion radicals result from either direct electron transfer of an electron from the electrode to an organic neutral molecule or indirectly by the action of a mediator. Organic anion radicals may act as bases and as reducing agents, depending on the environment in which they are generated. Because of the presence (or potential presence) of the extremely electrophilic proton in most of the commonly used electrolysis media the study of anion radicals per se is much more difficult than the study of the anodically produced cation radicals.

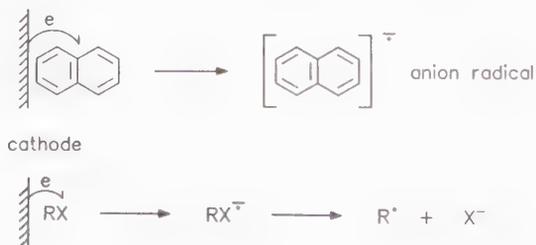
Birch reduction. Grignard reaction

Two typical examples of one-electron transfer reactions in conventional chemical organic synthesis are the *Birch reduction* and the *Grignard reaction*, as indicated by the examples below:



Direct Electron transfer reactions

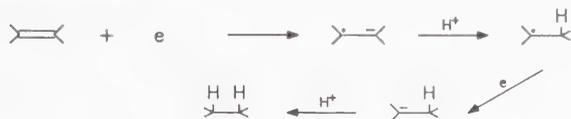
In electrolytic cells the ET reactions would be effected by direct ET from the cathode to the organic molecule, as depicted below:



3.2 Carbon-Hydrogen Bond Formations. Unsaturated Systems

Hydrogenation of unsaturated carbon-carbon bonds can be electrochemically effected directly or indirectly, as is symbolically indicated below:

direct
electroreduction



indirect,

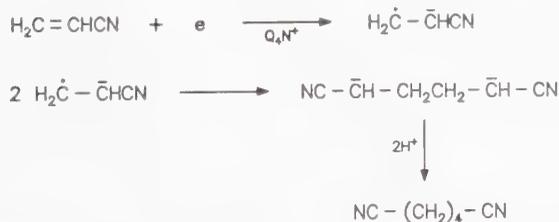
electrocatalytic reduction
(black Pt, Raney Nickel surfaces)



Conjugated and polycyclic aromatic systems are generally much more easily reduced than are nonconjugated or monocyclic systems. Ethylene has not yet been directly electroreduced, whereas butadiene is reduced (-2.5 V vs SCE). Benzene requires severe Birch-type reduction conditions but naphthalene and anthracene are readily reduced at the cathode [1].

Activated olefins are easily electroreduced, and under controlled conditions yield the corresponding hydrodimers in high yields. For example, acrylonitrile, upon direct one-electron per molecule reduction, gives the useful material adiponitrile in high yield [2,3], Scheme 3.1.

**Activated
olefins**



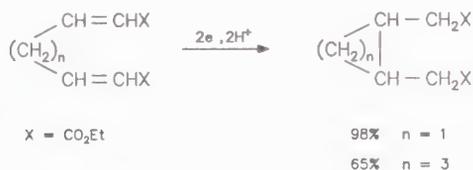
Scheme 3.1

This electrohydrodimerization reaction forms the basis of the largest known electroorganic industrial process in the world today [3] (Baizer process, Monsanto Co., USA).

Baizer process

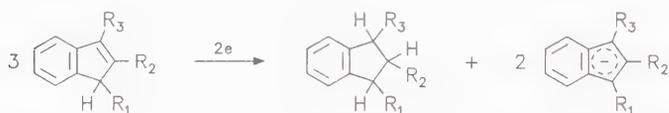
Cathodic reductions of unsaturated systems in protonic media tend to produce hydrogenated products. Hydrodimers would be produced if proton availability is limited near the electrode surface where the primary radical anions are generated. In the case of the electrohydrodimerization of acrylonitrile, the presence of the quaternary ammonium ion, Scheme 3.1, apparently modifies the structure of the electrical double layer so that the availability of protons from H_2O within this double layer region is considerably limited. This double layer structure effect allows the monoanions to couple rather than hydrogenate, thus affording predominantly adiponitrile instead of propionitrile. Such synthetically very important *double layer effects* on the course of electrochemical reactions have been referred to as "electrocatalysis of the second kind" [4]. Intramolecular reductive cyclization of activated olefins is exemplified below [5]:

Double layer effects



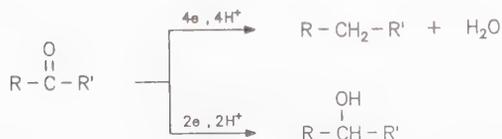
Good proton donors

Carbon-hydrogen bond formations, or protonations, proceed readily in media that are good proton donors. In the absence of water, good proton sources may be acidic substances such as benzoic acid, phenol, and the so-called carbon acids (e.g. diethyl malonate). Some compounds may act as self-protonating sources as it happens in the cathodic reduction of indenes to indans [6]:



It would be interesting to note that electrolysis in DMF and in H_2O gave different isomers as major products: the *cis* isomer in the former and the *trans* isomer in the latter medium.

Ketones can be electrocatalytically converted to hydrocarbons and alcohols at platinized platinum electrodes:



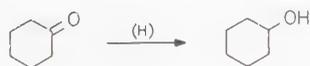
Catalytic hydrogenation

Pletcher studied this type of reduction in relation to medium composition and observed that the hydrocarbon yield of acetophenones increased as

the ethanol content in the ethanol-water medium increased [7]. Catalytic hydrogenations are favored at low overpotential electrodes (Pt, Ni, Cu, Fe) whereas direct electroreductions and dimerization would be most efficient at high-overpotential electrodes (Hg, Pb, Cd). Hydrogen overpotential values vary from 0.0 V for platinized platinum to 1.2 V for Cd relative to the normal hydrogen electrode [8]. High- and low-hydrogen overvoltage electrodes have been used on an industrial scale [9]. Aqueous media are preferred if the organic substrate is soluble in water. Pyridine and tetrahydrocarbazole are hydrogenated at lead cathodes in aqueous sulfuric acid solution (Hoechst, BASF, Germany) and adiponitrile is reduced to 1,6-hexadamine at nickel-copper electrode in aqueous hydrochloric acid solution. In protogenic media such as methanol-sodium hydroxide, hydrogenations are possible at electrocatalytic electrodes, such as electrodes having surfaces of black platinum, Raney nickel, or graphite modified with platinum. Pletcher and coworkers studied the use of high surface electrocatalytic electrodes (Ni, Pt, Pd, Re, Rh) for the hydrogenation of various functional groups [10]. Excellent efficiencies were obtained at these electrodes with substrates, such as the following:

Direct electro-reductions and dimerization

Electrocatalytic electrodes



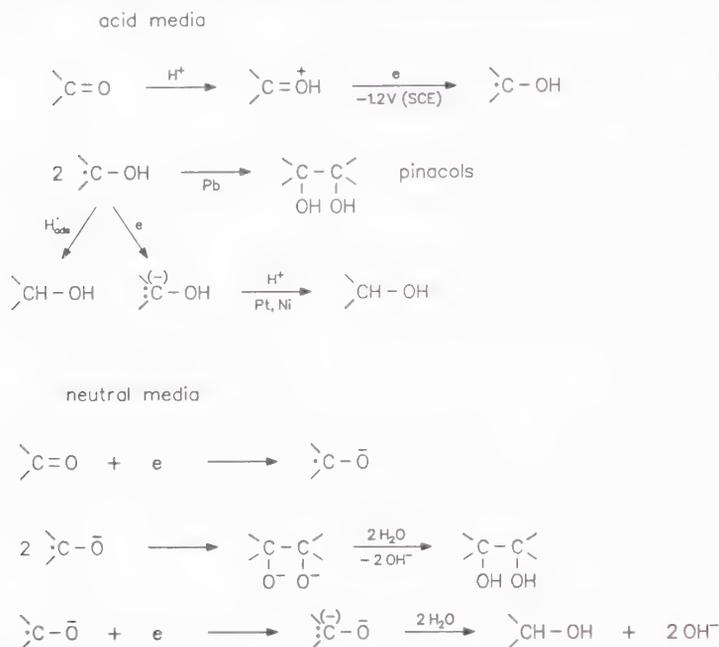
These hydrogenations were performed in MeOH/NaOH media under constant current of about 50 mA/cm². Electrocatalytic electrode surfaces can be prepared in situ by electrodeposition of the catalytic metal ion [10].

3.3 Carbonyl Compounds

3.3.1 General Reduction Mechanism

The carbonyl function is a good and versatile electrophore. In principle, a carbonyl group can be reduced by one- two- and four-electron processes giving respectively a diol, a monohydroxy alcohol and even a hydrocarbon.

Zuman proposed [1] general overall reduction mechanisms, in acidic and neutral solutions. They are summarized in Scheme 3.2



Scheme 3.2

Acetone is reduced to alcohol, pinacol, and propane (at Cd) depending on the cathode material; pinacol formation is favored at lead cathodes [2].

Electrohydrogenations have been studied using nickel, copper and tin cathodes. Copper cathodes modified with electrodeposited nickel were found to be most effective [3]. Electrocatalytic hydrogenations were performed using slurry-type electrodes [4].

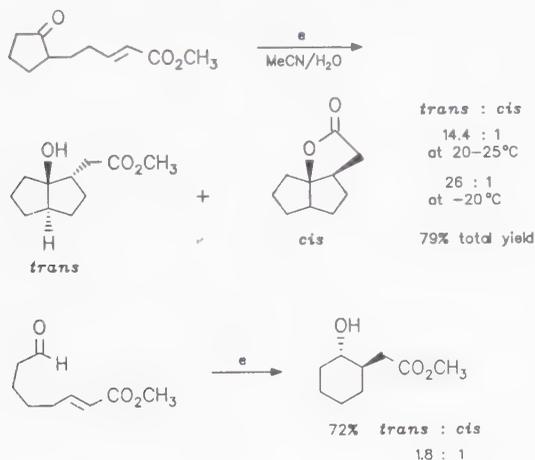
3.3.2 Reactions via the Carbonyl Electrophore

The carbonyl group is both a good electrophore and an activating group. It can therefore participate in a great variety of intermolecular and intramolecular electrochemical bond formations. Hydrogens on α -carbons to carbonyl are easily abstracted by electrogenerated bases; and hydroxyl groups on such carbons are cathodically replaced by hydrogen.

Little and coworkers [5] reported an electroreductive intramolecular cyclization involving ketonic or aldehydic groups and α,β -unsaturated ester subunits in the molecular structure. The electrolysis is carried out in a

divided cell in acetonitrile-water solution using a mercury cathode. Thus the construction of ring systems was effected, as shown in Scheme 3.3. It was proposed that the unsaturated ester subunit was the electrophile.

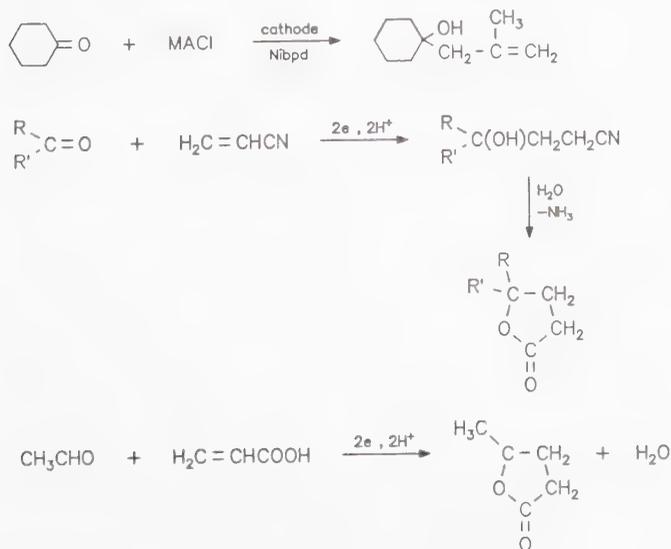
Construction of ring systems



Scheme 3.3

Electroreductive couplings of carbonyls with methylalkyl chloride (MACl) are facilitated by the presence of Ni(II) bipyridine (Nibpd) complexes [6]. Mixed couplings of ketones with activated olefins afford lactones via cyclization of the intermediate hydroxy products [7]. Also couplings of aldehydes with acrylic acid yield lactones [8]. These couplings are shown in Scheme 3.4

Electroreductive couplings



Scheme 3.4

Electrohydrodimerizations

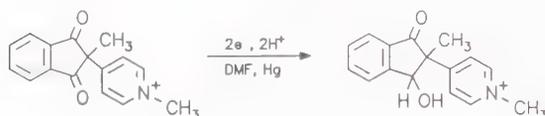
Electrohydrodimerizations of cyclohexanones give the glycol and the hydroxy ketone products, the glycol product being predominant as the water content in the mixed MeCN/H₂O solvent increases [9].

Electrocatalytic reductions

Pletcher and Lain [10] demonstrated that electrocatalytic reductions of carbonyl compounds are possible at graphite cathodes modified by electrodeposited Ni²⁺ ions. Thus benzaldehyde and acetophenone were reduced to their corresponding alcohols and hydrocarbons (mixed products) by electrolysis in acidic ethanol-water solutions containing 10⁻² M Ni²⁺ ion. Some hydrogen also is evolved in these electrolyses.

Synthesis of biochemically interesting compounds

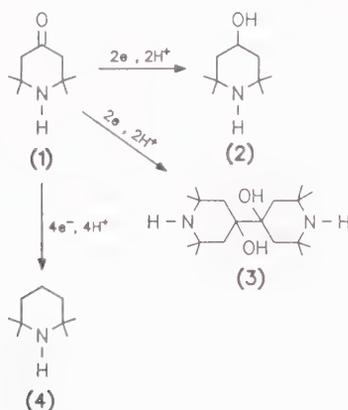
Electrochemical studies of carbonyls has been pursued in connection with the synthesis of biochemically interesting compounds. For example, the synthesis of 2-pyridyl substituted 1,3-indandiones was studied in basic, acidic and aprotic media [11]. In all these media the indandione moiety is reduced at less negative potentials than the pyridinium part of the molecule, Scheme 3.5. This is an example of the difficulty in predicting the actual electrophore in a complex molecular structure.



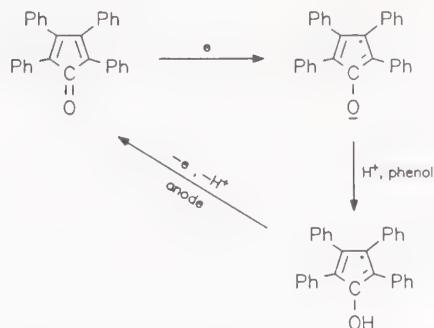
Scheme 3.5

Reduction of triacetoneamine

The electroreduction of triacetoneamine (**1**) was studied by Smirnov et al. [12] at a zinc electrode. The products were the monoalcohol (**2**), the dimer (**3**) and the tetramethylpiperidine (**4**).



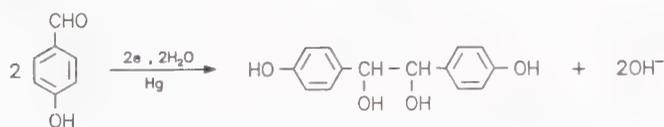
Some ketonic compounds may be reduced at the cathode in organic solvents that contain phenol as a proton donor. The following example is interesting. The primary radical anion is protonated and can be reoxidized at the anode to give the starting compound [13].



Steroidal carbonyls are electroreduced to give their methylene analogs in fairly good yields. If the electrolysis is performed in deuteriosulfuric acid at lead cathodes the oxygen of the carbonyl is replaced by deuterium [14].

Electrolytic reduction of aldehydes affords hydrodimerization products by a one-electron reduction process. Formaldehyde is thus dimerized to glycol [15]. A pilot-plant process was developed for the production of 4,4'-dihydrobenzoin from *p*-hydroxybenzaldehyde [16]. The electrolysis was performed in an aqueous 2 M NaOH solution at a mercury cathode (mercury gave more reproducible yields than a cadmium electrode in this case).

Reduction of aldehydes



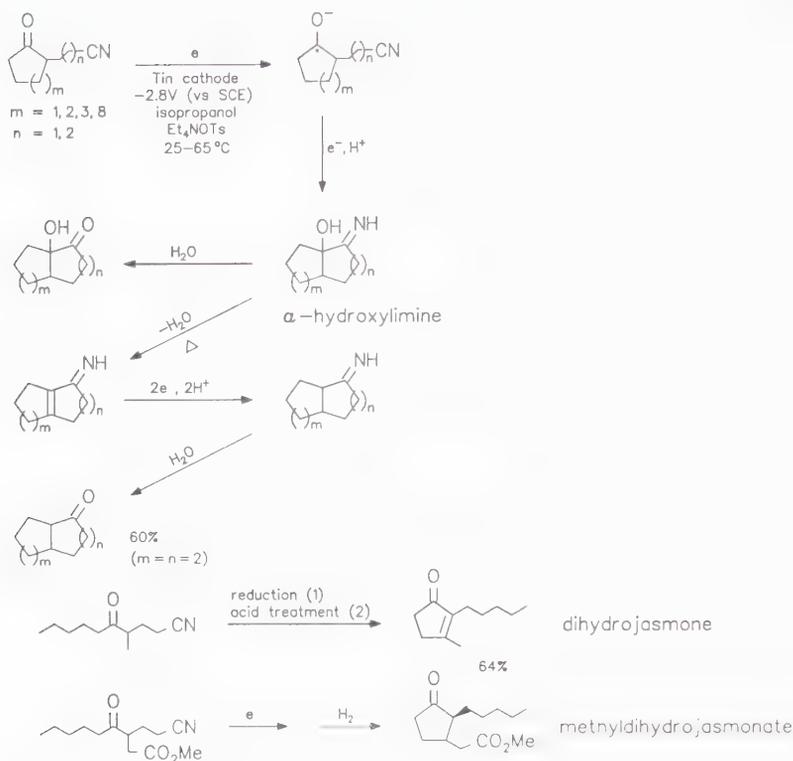
In principle, aldehydic carbonyls may be hydrogenated all the way to give hydrocarbons and water:



Acrolein and crotonaldehyde have been reduced to mixtures of saturated and unsaturated hydrocarbons [17]. In the presence of primary amines aldehydes undergo amination. Ketones also react similarly [18].

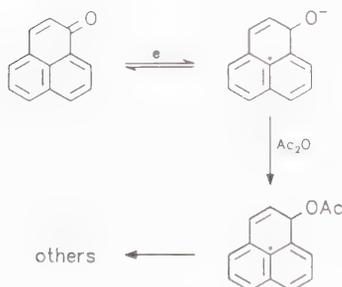
Recently, Shono reported an electroreductive cyclization method using γ and δ cyanoketones [19]. By this method five-membered rings can be constructed such as those of the natural products dihydrojasmonone and methylidihydrojasmonate. The reaction is initiated by direct electronation of the carbonyl group. This step is followed by intramolecular bond formation with the cyano group and further reduction to the α -hydroximine, and then to the final cyclized products. The reaction is summarized in Scheme 3.6

Cyclization of cyanoketones



Scheme 3.6

Some ketonic structures such as that of phenalin-1-one react with acetic anhydride following electroreduction in DMF/ Bu_4NClO_4 medium [20]. Mono- and diacetoxy derivatives are obtained.



Electroreductive splitting of C—H bonds in ketones

It was mentioned earlier that hydrogens on α -carbons relative to a carbonyl group are acidic. In this connection we note that Bukhtiarov and coworkers [21] reported that aliphatic ketones undergo electro-reductive splitting of C—H bonds at transition metals as cathodes (Pt, Ni, Fe, Co)

in aprotic solvents containing quaternary ammonium salts as electrolytes. Hydrogen is produced at the cathode, while the anions may react in various ways depending on the composition of the electrolysis medium:



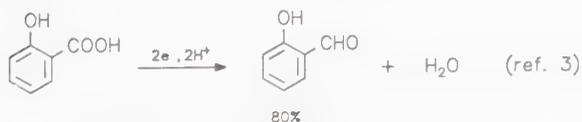
An interesting electroreduction of α -hydroxyaldehydes was recently reported [22]. This reduction is selective at carbon electrodes coated with films of dimethyldioctadecyl ammonium salts. The films apparently provide a hydrophobic surface on the electrode, and this surface allows reductive selective replacement of the hydroxyl group by hydrogen. The electrolysis is carried out in buffered (pH 7) aqueous solution at 20°C, in a divided cell and at a cathode potential of -1.5 V versus the SCE. This is also an example of the activating influence of the carbonyl group on the C—OH bond α to the carbonyl.

Electro-reduction of α -hydroxy-aldehydes



3.4 Carboxylic Acids and Esters

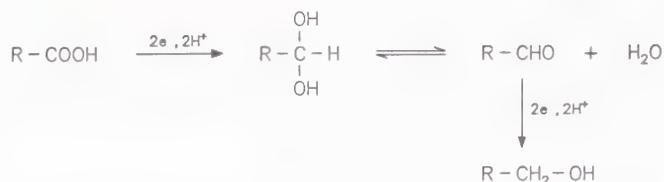
Direct reduction of the COOH group has not generally been feasible at the cathode thus far. Only in salicylic [1] acid and some other hydroxybenzoic acids has the carboxyl group been reduced [2].



The reduction can advance to the alcohol stage at lead cathodes in sulfuric acid solutions. Alkire [3] observed that imposition of an alternating current component on the direct current component facilitated these reductions as regards both yields and reaction rates. In the case of salicylic acid the apparent rest potential shifted to a less negative value and the yield increased from 30 to 80% when the ac component was applied to dc component during the electrolysis [3].

Effect of an alternating current component

The electroreduction of a carboxylic acid to the corresponding alcohol is formally expressed as a two-step process [4]:



Because the aldehyde is more easily reduced than the acid, the reduction most often advances past the aldehyde stage. It is possible sometimes to arrest the reduction at the aldehyde stage. Heterocyclic and α,β -unsaturated carboxylic acids may be reduced to their aldehydes [5,6]. It has been claimed (patent) that the benzyl alcohol was obtained from benzoic acid in 83% yield and 85% current efficiency when 2-ethyl-1-hexanol was added to the electrolysis medium [7].

3.4.1 Preparation of Metal Carboxylates and Metal Alkoxides

Aliphatic acids are not reduced to alcohols by the cathodic method but they yield carboxylate ions as a result of their proton reduction. When transition metals are used as anodes a *paired electrosynthesis* is achieved whereby transition metal carboxylates are produced, the electrochemical cell processes occurring according to the general Scheme 3.7

**Paired
electrosyn-
thesis**



M = transition metal anode

Scheme 3.7

Carboxylates of Cr, Mn, Ni, Co, Cu and Fe were prepared by electrolysis in organic solvents containing various carboxylic acids including long chain fatty acids [9]. Small amounts of Et_4NClO_4 may be added to enhance the conductivity of the medium.

**Consumable
anode
methodology**

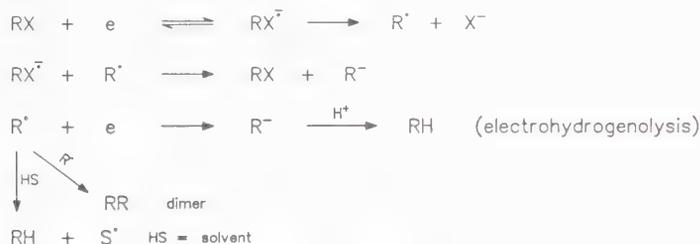
Alkoxides also can be prepared by this methodology. Tungsten alkoxides were prepared using a tungsten plate as anode in absolute methanol or ethanol [10]. The *consumable anode* methodology has been considered for various applications [11,12].

Direct electrochemical synthesis of metal alkoxides by anode dissolution of the appropriate metals can be effected in absolute alcohols mixed with polar solvents so as to enhance the conductivity of the medium. Undivided cells are used. The alkoxides of Sc, Ti, Zn, Nb, Ta and Ge have thus been prepared. Suitable electrolytes are the salts Bu_4NBr , Bu_4NBF_4 , Et_4NBr ,

3.5 Organohalides

3.5.1 General Electroreduction Mechanism

The electrochemical reduction of organohalides has been very widely investigated since the first studies of Stackelberg and Stracke [1] in 1949. It is now generally accepted [2] that the reduction of a carbon-halogen (C—X) bond takes place according to the general mechanism shown in Scheme 3.8.

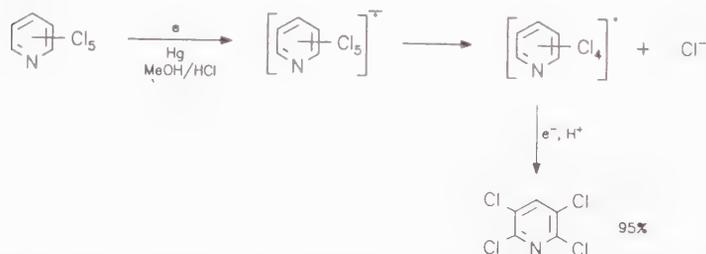


Scheme 3.8

Conceivably, a C—X bond may be cleaved by a concerted mechanism without the intermediate generation of the anion radical $\text{RX}^{\cdot-}$.

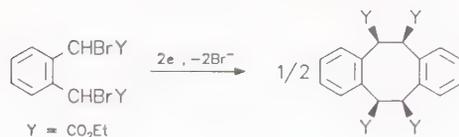
3.5.2 Products from Aromatic and Aliphatic Halides

The cathodic reduction of aromatic halides in general yields anion radicals as primary products which are rapidly decomposed into radicals and halide ions [3]. The aromatic fragments, Ar^{\cdot} , are very often more electrophilic than the anion radical $\text{ArX}^{\cdot-}$ and are immediately electronated to yield the anion Ar^- which reacts with an electrophile to produce the substituted product, as for example [3a], in the very selective electrohydrogenolysis of pentachloropyridine:



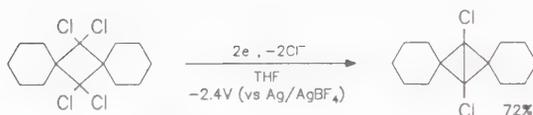
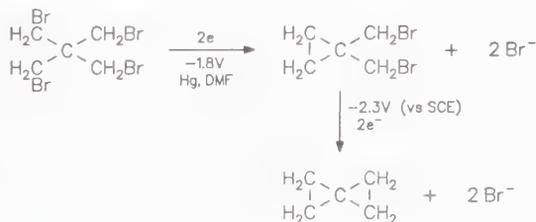
Relative ease of reduction

Aliphatic short chain halides are reduced at lower potentials than do aromatic and vinyl halides. With vinyl halides stereoisomers are formed [4].



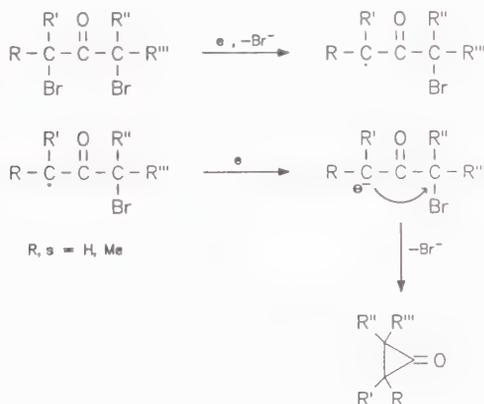
Cathodic dehalogenation, strained structures

Highly strained hydrocarbons can be prepared by cathodic dehalogenation of certain polyhalogenides [13–16]. Examples of strained structures are shown below:



Cyclopropanations

Dehalogenation of certain dihalides may easily lead to cyclopropanations. An example is the dehalogenation of α,α' dihaloketones [17] at mercury cathode in DMF solution. The cyclization process is considered occurring as follows:



3.5.2.1 Sacrificial Anode Methodology Using Organohalides

In this section we consider the potential usefulness of *sacrificial* metallic anodes for organic synthesis with organic halides as cathodic reactants. Sacrificial anodes are usually electrodes of the metals zinc, magnesium and

aluminum. These electrodes dissolve upon anodic polarization to give the corresponding metal ions. To be useful for synthetic application they must dissolve before any other species surrounding the electrode is oxidized – either because of thermodynamic or kinetic reasons, so that the main anodic half-reaction is the dissolution of the electrode, e.g.



The practical merit of this type of electrolysis is that it makes possible the use of undivided cells – a significant advantage as regards cell construction and minimum potential drop in the solution (especially when the solvent is organic). Also, the metal ions generated in situ are sometimes essential for the occurrence of the desired reaction.

Sacrificial zinc anodes were employed by Sibille and coworkers in electrochemical cyclopropanations [18]. Alkenes and *gem*-dihaloalkanes are the starting materials, which in the presence of zinc ions generated in situ react as shown in Scheme 3.9. It was proposed that an organozinc carbenoid forms as an intermediate for this cyclopropanation as it happens in the chemical cyclopropanation methods.



Scheme 3.9

General Cyclopropanation Procedure. Scheme 3.9 Alkenes and *gem*-dibromoalkanes or the diiodo analogs are electrolyzed in a one-compartment cell fitted with a carbon fiber cathode and a sacrificial zinc anode. A 90/10 $\text{CH}_2\text{Cl}_2/\text{DMF}$ solvent mixture with Bu_4NBr as electrolyte containing the alkene and an excess of the dihalo compound is electrolyzed at 40°C under constant current (200 mA) and an argon atmosphere. The products are recovered by extraction with ether or pentane and are purified by column chromatography (silica gel-pentane, ether). Some typical alkenes and dihalides and respective cyclopropane product yields are the following:

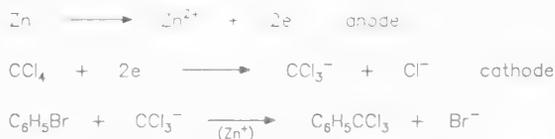


Undivided
cells

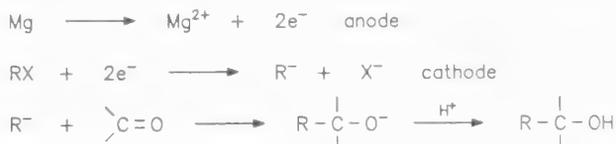
Zinc anodes

Organo metallic chemistry

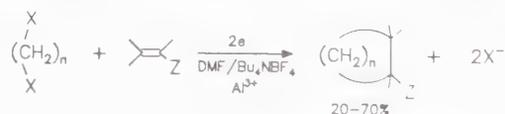
Electrosynthetic methods using sacrificial anodes should be of interest in organo metallic chemistry. The following coupling reaction is especially interesting since the CCl_3^- anion produced under other conditions decomposes rapidly to yield the carbene CCl_2 . The in situ generated zinc ions are shown in the reaction scheme to point out that they are necessary for this coupling reaction [19].

 $\text{CCl}_3^-/\text{Zn}^{2+}$ **Aluminum or magnesium anodes**

Organic halides electroreduced in the presence of carbonyls and with aluminum or magnesium sacrificial anodes afford alcohols [20]. The cell reaction is shown symbolically below with magnesium as anode.

**Couplings, carboxylations**

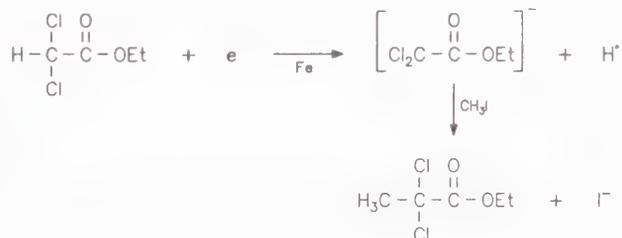
A sacrificial aluminum anode was used for the electroreductive coupling of α -halogenoesters with aryl or vinyl halides. Moderate to good yields of β,γ -unsaturated esters were obtained [21]. A good review on the use of sacrificial anodes in synthetic electrochemistry specifically for processes involving carbon dioxide has been recently presented by Silvestri and coworkers [22]. Reductive electrocarboxylations and the reduction of CO_2 alone are discussed. Alicyclic three-, five- and six-membered ring products were formed by electroreductive coupling of dimethyl maleate with alkyl dihalides in undivided cells fitted with sacrificial aluminum anodes to provide the apparently needed Al^{3+} ions [22].

Alicyclic rings

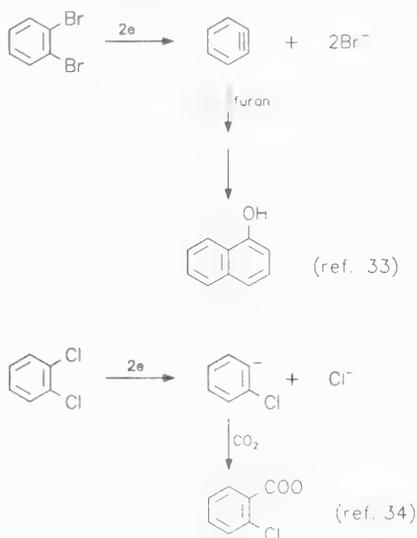
Electrolysis of bromotrifluoromethane in DMF solution in a one-compartment cell fitted with a sacrificial zinc anode converts the bromo compound to trifluoromethyl alcohol and some organozinc compounds (CF_3ZnBr , $(\text{CF}_3)_2\text{Zn}$). Addition of tetramethylene diamine to the electrolysis medium seem to promote alcohol formation [22,23].

**Splitting
C—H bonds**

In certain halogen containing molecular structures it is possible to split a C—H bond instead of a carbon-halogen bond if the electrolysis is performed in aprotic media and the cathode is a transition metal (Fe, Ni, Pt). This is possible because the C—H bonds in these molecules (carbon acids) are relatively weak and the transition metal surfaces are good catalysts for hydrogen formation [30–32]. An example is the following [30]:

**Benzyne**

Reductive dehalogenations of aromatic dihalides in aprotic solutions may generate intermediates like the benzyne or anions which enter into reactions as exemplified in Scheme 3.10 [33,34].



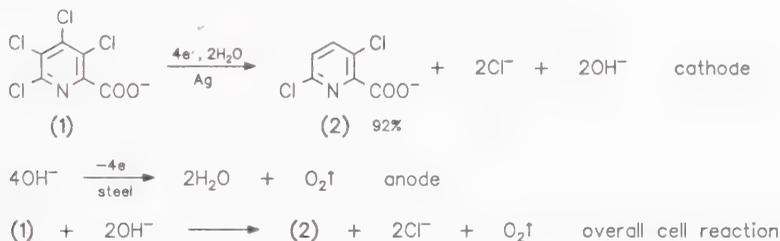
Scheme 3.10

3.5.4 Electrohydrogenolysis of Polyhalogenated Compounds

Electrohydrogenolysis of polyhalogenated pyridines (agricultural chemicals) was investigated from an industrial perspective [35]. Pentachloropyridine and tetrachloropicolinic acid were electroreduced selectively

to symmetrical tetrachloropyridine and 3,6-dichloropicolinic acid, respectively. The latter was produced on a commercial scale (under the trade name Lontrel, Dow Chemical Co., California). Lontrel is one of the most valuable (biodegradable) plant growth regulators and was until recently manufactured in an unpartitioned "frame and plate" cell with a *spongy* silver cathode and stainless steel anode in 10% aqueous NaOH solutions. The overall cell reaction is shown in Scheme 3.11. This electrochemical process has been viewed as a typical large scale heterogeneous organic electrocatalysis process [36].

**3,6-Dichloro-
picolinic acid –
"Lontrel"**



Scheme 3.11

Preparation of 3,6-Dichloropicolinic Acid by Electrohydrogenolysis of Tetrachloropicolinic Acid (Scheme 3.11)

This very selective electrohydrogenolysis (that is, hydrogenolysis of C—Cl bonds by electrolysis) is achieved in a simple undivided cell in aqueous alkaline solution. The electrolysis cell is a 400-ml glass beaker fitted with a 20-mesh silver screen cathode and a stainless steel rod anode positioned concentrically by means of a neoprene rubber disc as shown in the cell schematic, Fig. 3.1. The solution to be electrolyzed consists of 150 ml distilled water, 12 g reagent grade sodium hydroxide and 10 g of tetrachloropicolinic acid (added in steps). The cell is placed in a water bath thermostated at 25–35 °C. The solution (suspension) is vigorously stirred during electrolysis.

a. *Activation of the silver cathode:* Before adding the organic acid to the solution in the cell the silver electrode is *anodized* by applying to it a positive potential starting from zero and gradually raising it to +0.6 V (vs SCE). The potential is held at 0.6 V for about 3 minutes until practically all the electrode surface becomes covered with silver oxides and the current begins falling towards a minimum value. The polarity is then reversed and the silver electrode potential is set at –1.3 V, which is the optimum potential for the desired reaction. The surface silver oxides are reduced and the current falls to a steady value (ca 0.3 A) when all the oxides are apparently reduced and the

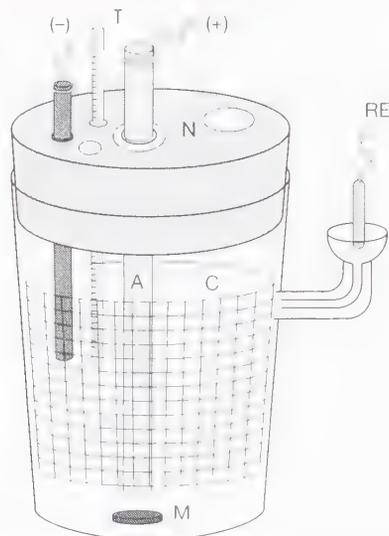


Fig. 3.1. Schematic of electrolysis cell, for the electrohydrogenolysis of tetrachloropicolinic acid

A, stainless steel rod anode

C, cathode, silver screen

N, neoprene rubber stopper with holes for gas exit

RE, reference electrode, SCE

M, magnet bar

T, thermometer

silver surface assumes a “spongy” structure (believed to be the active form).

b. *Electrolysis:* The electrolysis is now carried out at -1.3 V potentiostatically, the organic acid being added to the solution in the cell in several steps: About 2 g of the organic acid is macerated with a small portion of the alkaline solution from the cell and the mixture is added to the solution in the cell. The current rapidly rises from 0.3 to 3 A as a result of the electroreduction of the organic acid (the sodium salt in solution). The whole amount (10 g) of the organic acid is thus added to the cell in steps over a period of about 8 hours. When all the acid is reacted the current falls to 0.3 A and the electrolysis is ended. The electrolyzed solution is acidified with 25 ml of conc. hydrochloric acid, whereupon copious precipitation (white crystals) of the product, 3,6-dichloropicolinic acid, occurs. The product is recovered by filtration, and after washing with dilute hydrochloric acid and some distilled water, it is dried (100°C oven) (7 g, 98% purity, 90% yield). Identification is made by comparing IR, NMR and chromatographic data with those of an authentic sample. The impurities (2%) were trichloropicolinic acid and a trace of monochloropicolinic acid.

In situ reactivation of cathode

It was found that periodic activation in situ of the cathode by anodization (every 3 hours) was very beneficial. Also, best reproducibility was obtained by cleaning the used silver cathode after every run with 1:1 conc. HCl/H₂O. This procedure was found to remove traces of electrodeposited metals, Fe, Cu, Ni, Pb which were present in the materials used, and which adversely affected the electrode's activity. The anodization procedures (as was determined by X-ray fluorescence analysis) removed most metallic impurities except copper, which apparently had the worst effect on the effectiveness of the silver cathode.

It would be reasonable to postulate that two forces are largely responsible for this very selective electrohydrogenolysis: a) *specific adsorption* forces on the spongy silver and b) orientational electrostatic forces favoring electron transfer to 4 and 5 positions of the ring.

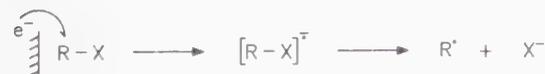
It should be noted that practically no reduction was possible on a shiny silver surface; and the reduction was not selective at other electrodes (Hg, Cu, C).

3.5.5 Electrochemically Induced Nucleophilic S_{RN}1 Substitutions

Aryl and Heteroaryl halides have been used as substrates for some electrochemically induced nucleophilic substitutions [37]. In conventional organic reactions movement of electrons in general occurs as a movement of an electron pair or a movement of the bond by an S_N² process (polar process):



For radical producing chemical or electrodic processes one-electron transfers take place from the nucleophile, N⁻, or from the electrode to the organic substrate R—X as depicted below:



cathode

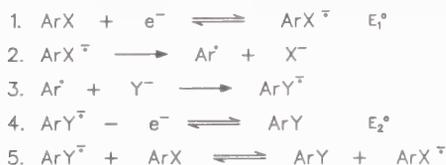
Cathodic reductions of aromatic halides, Ar X generally afford as primary products anion radicals:



The anion radical is usually an unstable species and decomposes rapidly to an organic radical and the halide ion,

**Electron transfer****Aromatic halides → anion radicals****Anion radicals → organic radical**

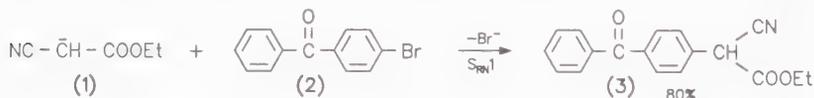
The fragment Ar^\cdot is more electrophilic than the ArX^\ominus species and the carbon which was bound with the halide X tends to combine with a nucleophile and also to abstract a hydrogen atom from the environment. Thus competitive chemical reactions would occur. For our present purposes consider the reaction sequence below:



If $E_2^\circ < E_1^\circ$, reaction 5 will be thermodynamically favored, and X will be substituted by Y, thus yielding the new product ArY and also the anion radical ArX^\ominus to repeat the catalytic cycle (chain reaction). The electron "shuttles" between the electrode and the solution so that in principle there should be no *net* charge passed through the cell. The electron itself is the electrocatalyst. The process is designated as an $\text{S}_{\text{RN}}1$ process (or radical nucleophilic unimolecular). By analogy to proton transfer catalysis $\text{H}^+\text{C} \text{H}^+$ it is also designated as an E C E process. In Alder's view [38] "there is no logical reason why electron transfer catalysis should not be as general as acid base (proton transfer) catalysis." A typical example of $\text{S}_{\text{RN}}1$ -type synthesis is the aromatic substitution reported by Saveant [39], Scheme 3.11a. The monoanion (1) derived from a β -cyanocarbonyl compound reacts with the benzoyl substituted aromatic bromohalide (2) to give the substituted products (3). The electrolysis is carried out in DMF at the potential of the first voltammetric wave, the height of which decreases upon addition of the nucleophile (1), as expected.

**Substitution
and catalytic
cycle**

**The electron
electrocatalyst**



Scheme 3.11a

A rather unique $\text{S}_{\text{RN}}1$ -type electrosynthesis was recently reported by Degrand concerning the direct preparation of diaryl diselenides and ditellurides [40]. The overall reaction is shown below:

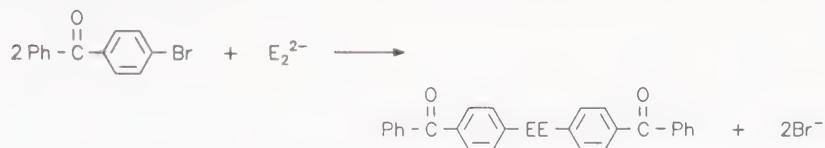


ArX = arylhalide
E = Se or Te

Cathodic polarization of Se or Te electrodes generates the E_2^{2-} dianions so that the reactions (1) and (2) become possible;



Thus the dichalcogenides of the 4-bromobenzophenone are obtained:



This electrolysis is performed in an H-type cell in acetonitrile or dimethylsulfoxide containing a quaternary ammonium salt as electrolyte, and at a cathode potential of -1.6 to -1.7 V versus SCE. Simultaneous generation of E_2^{2-} anions and reduction of 4-bromobenzophenone take place. The Se and Te were contained in the form of pellets in a tea-bag type electrode.

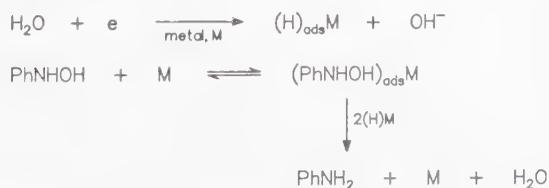
3.5.6 Organic Fluorides

Perfluorocyclopentene and perfluorocyclobutene afford polymers by electrolysis in aprotic solvents containing Et_4NBF_4 as electrolyte [41]. The polymers form as lustrous blue-black needles attached to the electrode (platinum) surface. They are electronic conductors. No polymers are formed if the electrolyte is lithium perchlorate.

3.6 Nitrocompounds

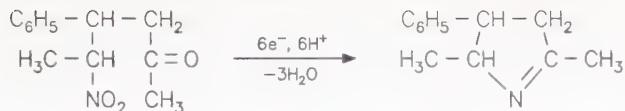
The nitro group is one of the most versatile electrophores in organic electrosynthesis [1,2]. Nitroalkanes are reduced in both hydrous and anhydrous media, giving hydroxylamines and amines. In basic solutions the reduction is difficult because the *aci* anion form of the nitroalkane is resistant to electroreduction.

Electroreduction of nitrobenzene occurs at copper and nickel electrodes in neutral and basic hydrous methanolic solutions [3]. Phenylhydroxylamine and aniline are produced depending on the potential of the electrode. Electrocatalytic hydrogenations at Devarda copper and Raney nickel electrodes takes place by reaction of adsorbed species as depicted in Scheme 3.12

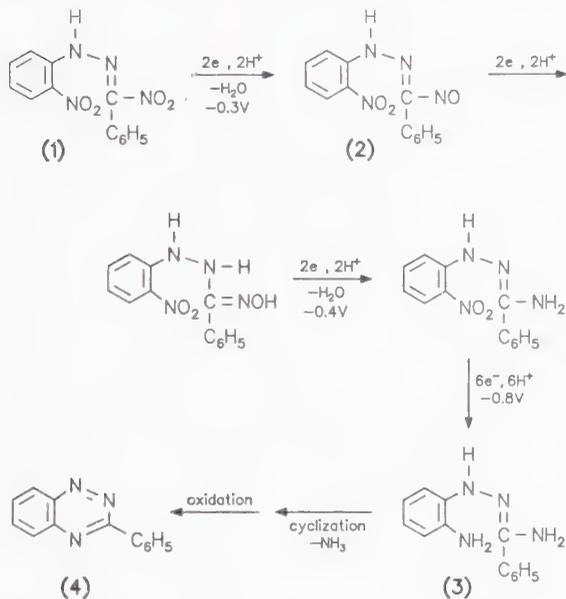


Scheme 3.12

**Copper
and nickel
electrodes**

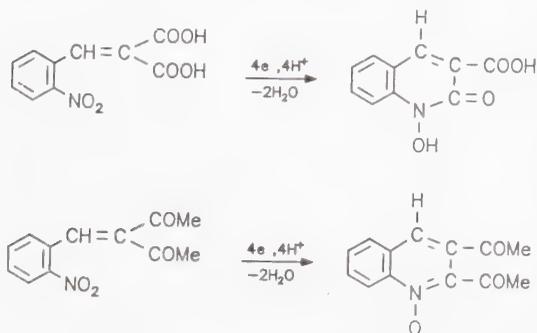


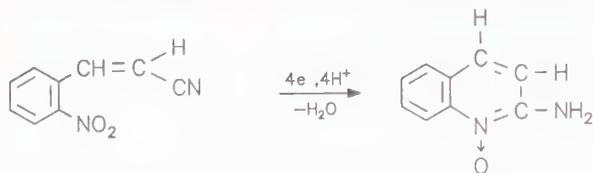
Controlled potential electrolysis of *o*-nitrophenylazophenylnitromethane (**1**) led to the 1,2,4-triazine compound (**4**) in high yield despite the very complex reduction process [13], Scheme 3.13.



Scheme 3.13

Quinoline-*N*-oxides and *N*-hydroxyquinoliones can be prepared in good yields by controlled potential electrolysis [14], Scheme 3.14.



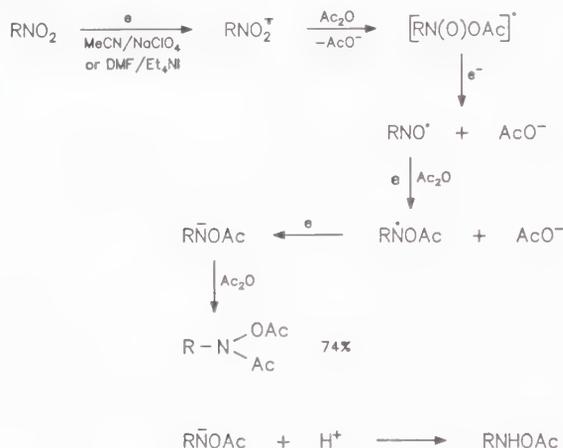


Scheme 3.14

Wagenknecht and Johnson [15], synthesized more than eighty new products according to the overall reaction scheme below:



In aprotic solvents in the presence of acetic anhydride reductive acylations of aliphatic and aromatic nitro compounds take place [16]. (Nitroso compounds also afford similar products.) The reactions are shown in Scheme 3.15.



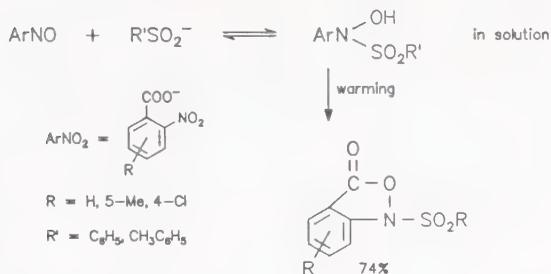
Scheme 3.15

These electrolyses are carried out in divided cells using mercury cathodes at -0.3 to -0.6 V (vs Ag/AgBr) and platinum anodes. Generally, isolated product yields are in the range of 40–70%.

Paired electrosynthesis

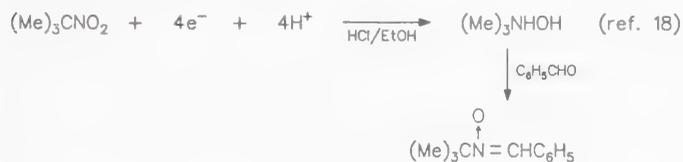
An efficient paired electrosynthesis was recently developed by Cault and Moinet [17] for the preparation of *N*-sulfonylbenzisoxazolones from 2-nitrobenzoic and sulfinic acids. The electrolysis is carried out in aqueous phosphate buffered solutions in a cell fitted with porous electrodes. The cell reaction is represented in Scheme 3.16.





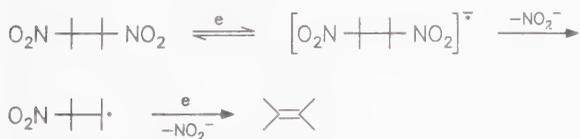
Scheme 3.16

Reduction of *tert*-nitroalkanes [18] and aliphatic or aromatic nitroolefins [19] in acidic alcoholic solutions are interesting since they give products useful in organic synthesis:



3.6.1 Dinitro Compounds

Vicinal nitro compounds are converted to olefinic derivatives by electroreductive elimination of NO_2^- ions [20]. Evans and Bower [21] studied a series of vicinal dinitro compounds and proposed a mechanism including expulsion of nitrite anion, as is formally depicted in Scheme 3.16a.



typical compounds



Scheme 3.16a

3.6.2 Reduction on Transition Metal Electrodes

Aliphatic nitro compounds exhibit properties of carbon acids. They are readily reduced on transition metal electrodes by splitting C—H bonds and producing hydrogen and nitroanions at the cathode [22].



R, R' = H, Me, Et

Organometallic complexes can be produced if the anode is a metal that is anodically dissolved and its cation able to complex with the organic nitroanion formed at the cathode in an undivided cell.

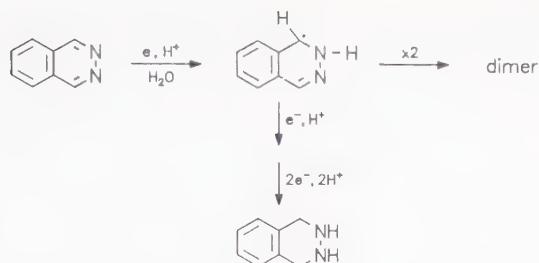
The Nitro group can be reduced by metal powders generated in situ by electrolysis of sulfate salts of metals (Sn, Zn, Fe, Cu). Tin and zinc were found to be most effective powders for these reductions. The electrolysis was performed in benzene-water emulsions (two-phase solvent system) with a carbon tube anode and a rotating carbon or aluminum cylinder as cathode [23].

3.7 N-Heterocyclics and Other Heteroatom Structures

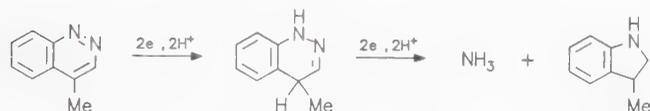
The cathodic electrochemistry of *N*-heterocyclics has been intensely studied and continues to be of great interest because of the biological significance of these compounds [1].

3.7.1 Pyridines, Purines, and Similar Compounds

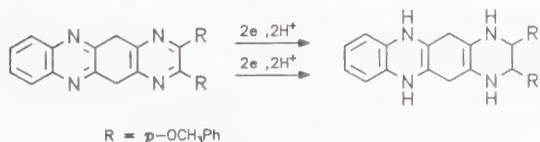
Pyridine and quinoline have been electroreduced to piperidine and tetrahydroquinoline, respectively, on an industrial scale. At mercury and lead cathodes purines [2], pyrimidines and pyridopyrazines [3] have been reduced to give hydroderivatives and other products. Pyridine is reduced at -3.1 V (vs Ag/Ag^+) in aprotic solutions at a mercury cathode. In the presence of $\text{EtOC}(\text{O})\text{Cl}$ the product *N*-(ethoxycarbonyl)pyridine is formed [4]. Reduction of pyridine at lead cathode in aqueous sulfuric acid and in the presence of zinc salts gives α,α' -bipiperidyl [5]. Phthalazine reduction in alkaline medium gives the hydro dimer and the hydrogenated product [6].



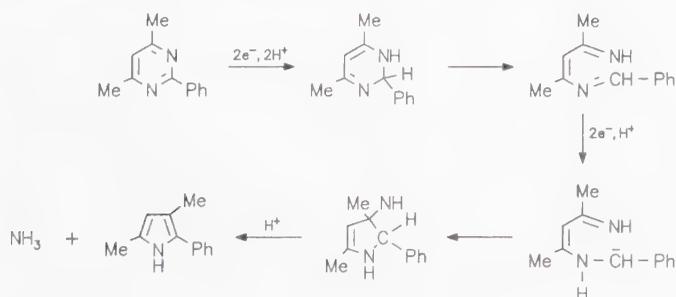
Purine, upon reduction and hydrolysis of the product undergoes opening of the six-membered ring. Cinnolines undergo ring contraction with expulsion of ammonia [6].



Compounds containing the pyrazine ring undergo hydrogenation of the pyrazine nitrogens [7] in a stepwise reduction process:

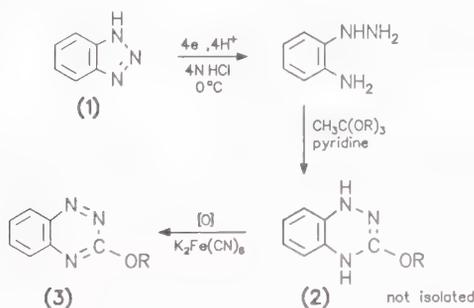


Pyrimidines are reduced by a complex four-electron process to give contracted ring products [8] as shown in Scheme 3.17



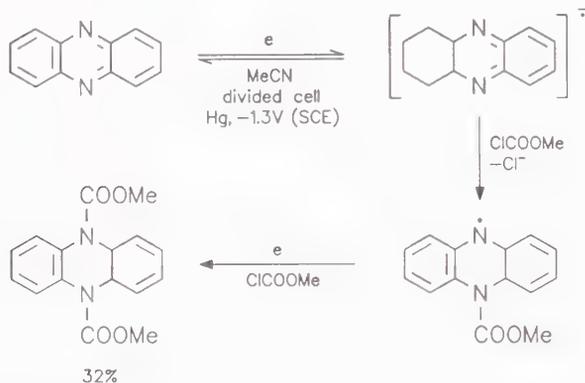
Scheme 3.17

Triazoles are converted to 1,2,4-triazines in two steps [9]: first, electroreduction of (1) to obtain the expanded ring product (2), and second, chemical oxidation of (2) to obtain the triazino product (3), as shown in Scheme 3.18.



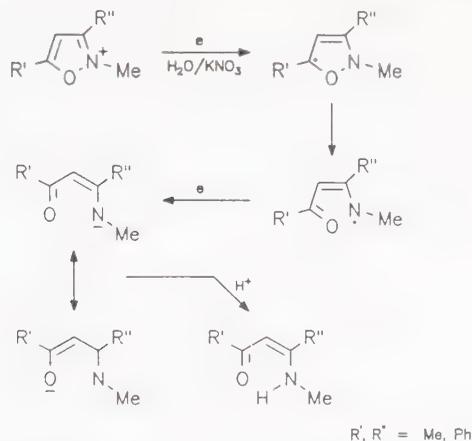
Scheme 3.18

The incorporation of the COOMe group to phenazine has been effected by cathodic reduction of phenazine in acetonitrile containing chloroformate and tetraethylammonium perchlorate as supporting electrolyte [10], Scheme 3.19.



Scheme 3.19

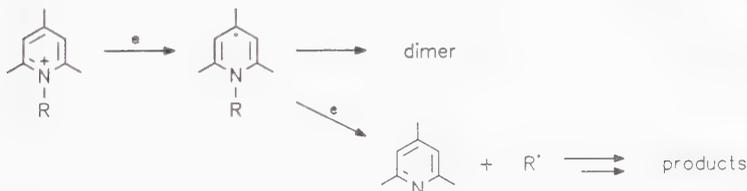
Preparation of β -enaminoketones is accomplished by cathodic electrolysis of *N*-alkylisoxazolium tetrafluoroboranes in aqueous solutions at mercury electrodes [11]. Yields of 90–95% are obtained. The following plausible reaction mechanism was proposed, Scheme 3.20.



Scheme 3.20

3.7.2 Pyridinium and Similar Salts

Simple pyridinium salts are cathodically reduced by one- or two-electron processes, giving dimers or products from the cleavage of $\text{N}-\text{R}$ bonds:

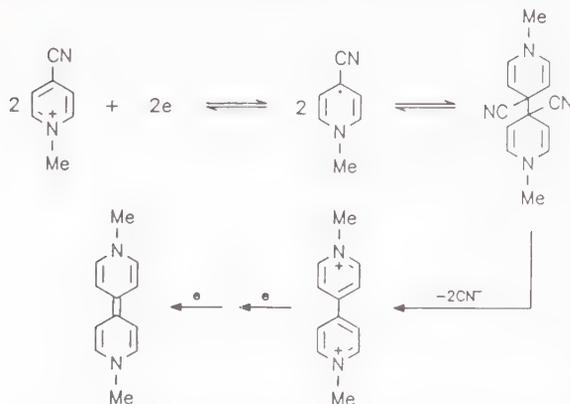


**Dimers
and cleavage
products**

Pragst and coworkers reduced a series of 1-substituted 2,4,6-trimethylpyridinium ions and obtained the 3,10-diaza-tricyclo 5.3.1.1 dodeca-4,8-dienes [12].

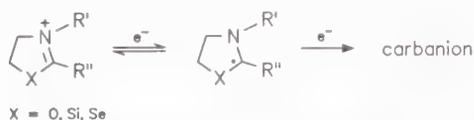
Weber and Osteryoung [13] studied the reduction of 4-cyano-1-methylpyridinium ion in acetonitrile. Two reduction waves were observed. Dimerization products were obtained when controlled potential electrolysis was performed at potentials corresponding to either of the two polarographic waves. Thus the conclusion was drawn that reduction products were dependent on the time scale of the experimental techniques used. The process was explained as follows:

**Polarography
of pyridinium**



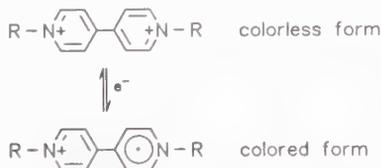
Stable radicals and carbanions

Heteroazolium salts with ring heteroatoms of O, Si and Se are reduced at mercury in dimethylformamide reversibly, affording stable radicals which at more negative potentials give their carbanions [14].



Electrochromic applications

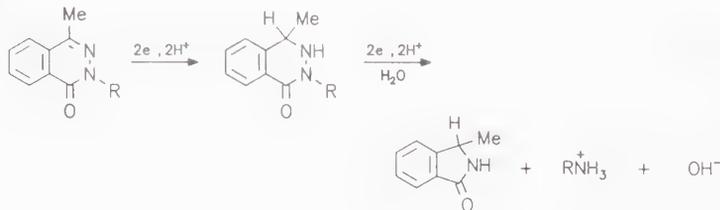
The electroreduction of *n*-heptyl viologen (heptyl V) was studied with regard to electrochromic applications [15]. The one-electron transfer is rapid and reversible between the colorless and colored forms:



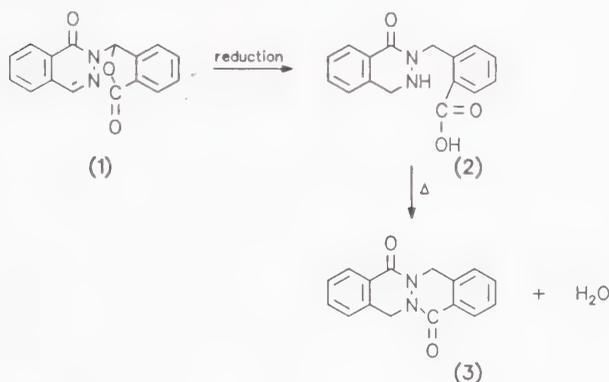
3.7.3 N-Heterocyclics with Carbonyl Groups

Phthalazinones

Phthalazinones, pyridazinones, pyridones and pyrimidones undergo complex electroreductive transformations and reactions with various substances present in the electrolysis media. Phthalazinones can be reduced without reducing the carbonyl group under potentiostatic electrolysis conditions [16].



An efficient intramolecular C—N bond formation is the cathodic conversion of 1(2*H*)-phthalazinone, (**1**), to the phthalazino(2,3-*b*) pathalazine-5, 12(7*H*,14*H*)-dione [**3**]. This reduction could not be effected satisfactorily by chemical methods for the intended large scale production process. The electrochemical method was found to be very effective. It will be discussed in detail as a typical electroorganic synthesis example (for possible laboratory practice). The desired overall cyclization reaction is shown in Scheme 3.21.



Scheme 3.21

a. *Working hypothesis*: It was assumed that if compound (**1**) could be reduced to give the intermediate compound (**2**) the desired dione compound (**3**) would be produced by elimination of water from the intermediate (**2**). It is reasonable to expect, therefore, that electrolytic reduction of (**1**) to (**2**) at 90–95°C would give directly, in one step, the desired product (**3**). A voltammetric wave with a tin wire electrode showed that reduction took place at about -1.3 to -1.5 V versus the SCE, very close to the potential for hydrogen evolution. Because compound (**1**) is only slightly soluble in water a suitable aqueous-organic solvent system would be required for preparative electrolysis. After several trials a 1/1 mixture of water/sulfolane was found to be most suitable. Maximum yields were obtained by electrolysis in a divided cell at pH 5.8 to 6.2 and at temperatures of 90–95°C.

b. *Electrolysis Cell. Procedure*: The cell is a 250-ml glass beaker at the center of which is positioned a porous ceramic cup to contain the anolyte, 20 ml of dilute hydrochloric acid, and the anode, a graphite rod, placed at the center of the cup. The catholyte is 50 ml of a 1/1 water/sulfolane mixture containing 5 g of the substrate (**1**), 4 g of sodium chloride and 4 g of sodium acetate trihydrate. A few drops of conc. hydrochloric acid is added to the catholyte to adjust the pH to 5.8–6.0. This pH value is periodically adjusted during the electrolysis by addition of a few drops

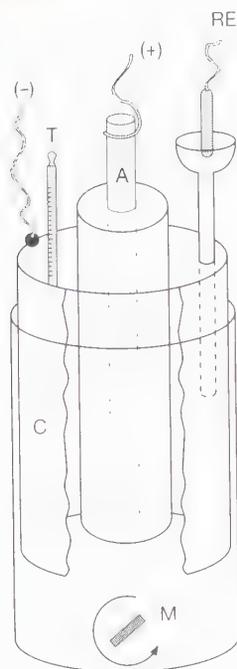
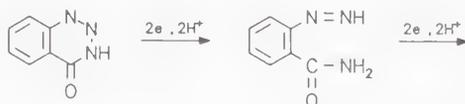


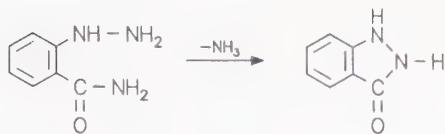
Fig. 3.2. Schematic of electrolysis cell
 C, cylindrical tin foil cathode
 A, graphite rod anode into ceramic cup anode compartment
 RE, reference electrode with Luggin capillary
 T, thermometer
 M, magnet stirring bar

of hydrochloric acid. The reference electrode is an ordinary saturated calomel electrode (SCE). The cell is placed in a mineral oil bath thermostated at 90–95°C, and the electrodes are connected to the potentiostat. The cell assembly is schematically shown in Fig. 3.2. The cathode potential is set at -1.35 V and a current of 1.5 A is passed for about 5 h, while the catholyte is magnetically stirred. The catholyte is then withdrawn and diluted with 500 ml of warm water (60°C) whereupon copious crystallization of the product occurs. The solids are filtered, washed and dried in vacuo at 60°C, giving 3.9 g of product (**3**) of 98% purity (82% yield). Identification of the product is made by spectroscopic and chromatographic analysis and comparison of data with those of an authentic sample.

Contracted rings

Electroreductive ring contractions of *N*-heterocyclics with more than one nitrogen in the ring are useful reactions for the formation of five-membered rings. Hydrogenation of ring nitrogens and elimination of ammonia affords contracted ring products. Thus the indalozinones [18] are obtained from benzo-1,2,3-triazine-4(3*H*)-ones as shown in Scheme 3.22.

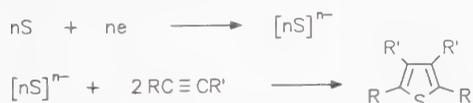




Scheme 3.22

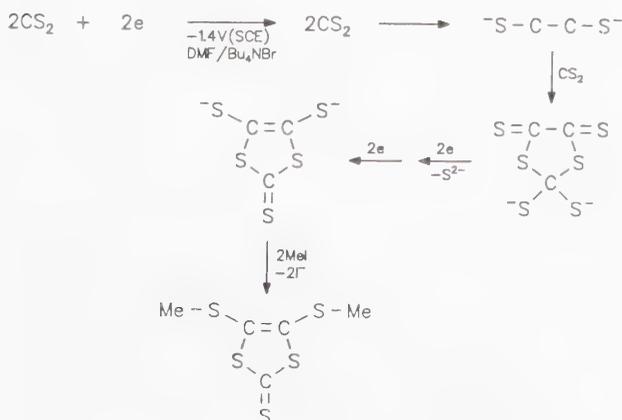
3.8 Organosulfur Compounds

The reductive electrochemistry of organosulfur compounds has been, and continues to be, widely investigated [1]. Elemental sulfur itself is electro-reduced and may be used as such for certain synthetic applications [2]. Simonet prepared thiophenes by an interesting procedure using an intimate mixture of sulfur and carbon powder as cathode, and suggested that electrochemically formed sulfur anion radicals attacked the acetylenic substrate $RC\equiv CR'$ so that the thiophene product was formed as indicated in the following scheme:



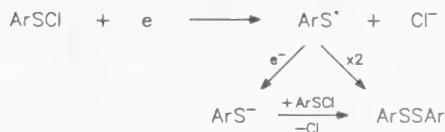
In general, reduction of single C—S bonds is very difficult, while double bonds are reduced relatively easily, as may be seen from polarographic observations [3]. (With mercury electrodes certain sulfur compounds readily form organomercury compounds.)

Carbon disulfide is readily reduced at the cathode in aprotic solvents. The reduction product can enter into reactions with alkyl halides as indicated below [4]:

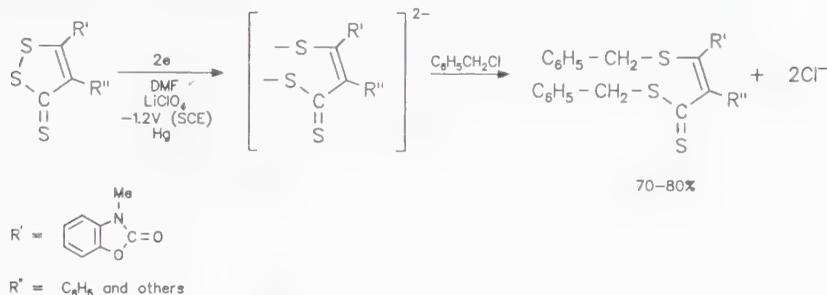


Thiophenes

Organo-mercury compounds



Sulfonyl halogen bonds are more easily reduced (cleaved) than sulfonyl or S—S bonds. Electrochemical alkylation of dithioethiones is easier than the chemical alkylation. The following is an example [13]:



Alkylation

These alkylations may be effected in situ or ex situ depending on the relative reduction potentials of the alkylating agent and the sulfur compound [14]. Thiols undergo cleavage of the SH bond to give thiolate anions, RS^- , and mixed coupled products [15]:

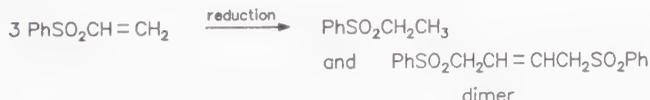


Thiolate anions

Splittings of S—H bonds occur on transition metal electrodes. Activated thiols such as $\text{EtOCOCH}_2\text{SH}$ (pK 7.8) yield hydrogen at the cathode most likely by direct reduction of dissociated protons and can do so on other than transition metalelectrodes [15].

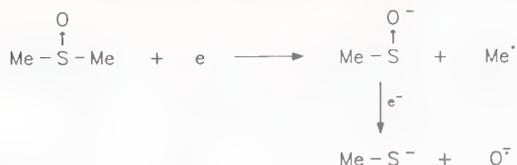
Splitting of S—H bonds

Sulfoxides and sulfones are reduced to sulfides. Sulfones may be reduced to sulfinic acids and mercaptans [5,16]. Simonet reported an “unexpected” dimerization of phenyl vinyl sulfone in slightly protic media [16]:



Sulfides, sulfinic acids, and mercaptans

Dimethyl sulfoxide is reduced at the cathode by cleavage of the C—S bond, indicating the semipolar nature of the S—O bond [17]:



Composite C—S electrode

Recently an interesting composite carbon-sulfur electrode was invented by Simonet and coworkers [18]. This electrode acts as a source of polysulfides with nucleophilic properties. Upon cathodic polarization the sulfur dissolves and chemical reactions can take place in the catholyte compartment in an electrolysis cell, as illustrated below:

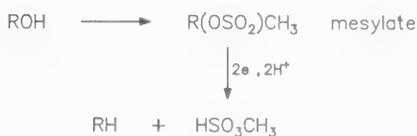


3.9 Some Special Cleavages of C—O Bonds in Hydroxy Compounds

There is a distinct interest in the cleavage of hydroxy groups in organic substances [1]. Only a few C—OH bonds can be transformed to C—H bonds by direct electrohydrogenolysis. Alcohol derivatives provide an indirect way for converting C—OH bonds to C—H bonds, if the hydroxy group can be replaced by a good leaving group prior to electrolysis, such as a bromo or iodo group:



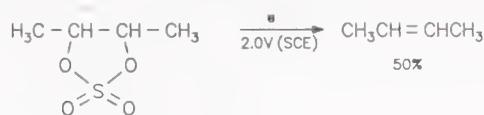
In the reduction of phenols the intermediate diethylphosphates, and in certain cases the mesylates, may be used as leaving groups [1b,d]:



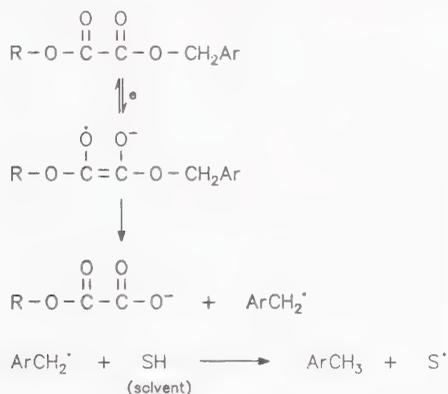
Tosylates mesylates

In this connection we note that tosylates are electroreduced by cleavage of their O—S bonds (hence they are used to protect hydroxy groups). In contrast, mesylates split their C—O bonds preferentially, giving the hydrocarbon products [1c]. Propylene carbonate and other diol carbonate derivatives are reduced at the dcathode only with great difficulty [2] (very negative potentials are required). Cyclic sulfate derivatives of diols yield

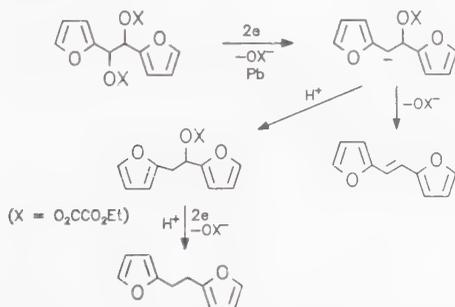
the corresponding alkenes along with other products, the alkenes being produced by a one-electron process as indicated below [3,4]:



The electrochemical reduction (deoxygenations) of hydroxy compounds via esterification as indicated above is effective but it requires very negative potentials. The reduction of esters of oxalic, squaric and oxamic acids is an easier operation for practical purposes. Utley and coworkers [5] studied such cathodic cleavages. For benzylic esters a one-electron reduction process was indicated as follows:



An example of the electroreduction of oxalate esters is given in Scheme 3.24. The oxalate esters are formed in situ by transesterification with diethyl oxalate.



Scheme 3.24

Furfuryl alcohols and hydroxyfuroin are reduced as expected. Butane-2,3-diol must be converted to the sulfonate analog in order to deoxygenate. Such deoxygenations could possibly be applied to lignocellulosics

Alkenes

Benzylic esters

Oxalate esters

Organic feedstocks

to provide organic feedstocks [5]. We might note that electroreductive cleavages of substituted 9,10-anthraquinone esters have been of interest in biochemical research studies [6,7].

3.9.1 Cleavage of Ethers

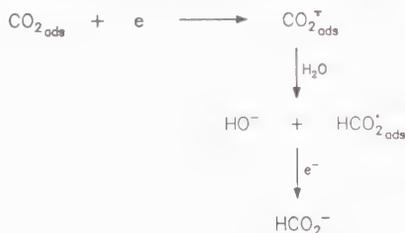
Diphenyl ethers, phenoxynaphthalenes and dinaphthyl ethers can be cleaved at very negative potentials in a one-electron process [8].



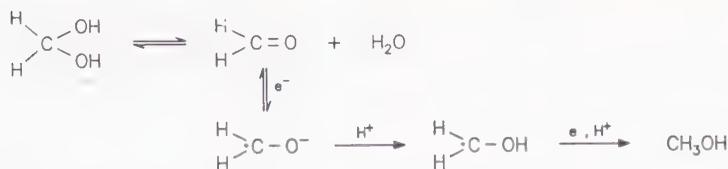
Radical anions of 1- and 2-phenoxynaphthalenes survive longer than one minute in very dry dimethylformamide. A rare type of cathodically cleaved ether bond is one with the picolyl group [9]. The picolyl group is a protective group for alcohols:

Picolyl group**3.10 Electrocarboxylations****3.10.1 Electroreduction of Carbon Dioxide****Formic acid, formaldehyde and methanol**

Carbon dioxide can be electrochemically reduced to give hydrogen containing products. The electrochemical conversion of CO_2 to formic acid, formaldehyde, and methanol is a very active research field [1]. As a biomass derived material it is receiving very special attention [1c]. Electroreduction of CO_2 to formate ion takes place via adsorbed species [2]

Formate ion

Reduction to formic acid can be almost complete, but formic acid cannot be practically reduced to methanol. The reduction of formaldehyde to methanol proceeds via the dehydrated molecule [3]:



It has been reported that at ruthenium electrodes the reduction of CO_2 may go all the way to methane [4]



Bard [5] and Sammels [6] studied the reduction of carbon dioxide at copper electrodes and obtained high faradaic efficiencies. Gas diffusion electrodes were recommended for high reduction rates. Metal impregnated polytetrafluoroethylene-bonded gas diffusion electrodes were used in aqueous solutions [7] (pH 1–5). The catalytic activity of these electrodes for the reduction of carbon dioxide to formic acid was in the order $\text{Pb} > \text{In} > \text{Sn}$. A complete process to produce oxalic acid on a large scale was developed using a consumable zinc anode [8]. Zinc oxalate was formed and this was treated with sulfuric acid to yield oxalic acid and zinc sulfate.

At low temperatures CO_2 has been converted to methane and ethane at Al, Co, Mn and In electrodes [9]. The gas phase reduction of CO_2 to hydrocarbons was studied at metal/SPE interfaces using Nafion 117 and 417 membranes as the SPE, the polymer cells possessing the configuration,



The metal, Cu, was deposited onto the SPE by electroless deposition using as reductants $\text{NaBH}_4/\text{NaOH}$ or $\text{N}_2\text{H}_4/\text{NaOH}$. Many metals were thus tested as electrocatalysts for the conversion of CO_2 to hydrocarbons [10]. It appears that large scale applications need more research and development studies. SPE methodology may enable gas-phase electrolysis to overcome the inherent mass-transfer limitations imposed by low solubilities of gaseous reactants.

3.10.2 CO_2 as Electrophile

As an electrophile CO_2 combines with organic anion radicals and anions. Numerous such carboxylations have been reported [11]. Acetylenes, olefins, ketones, alkyl halides and *N*-heterocyclics are good substrates for electrocarboxylations. These substrates are usually reduced at the cathode before carbon dioxide. The generated organic anion radical is attacked by the electrophilic CO_2 as is indicated in the following example [11a]:

Methane

Oxalic acid

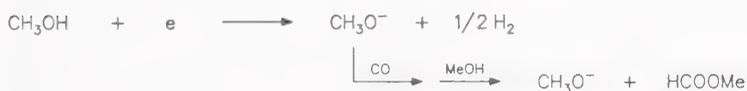
**Methane
and ethane**

Electrocarboxylations

It is possible sometimes to effect carboxylations by electrogenerated CO_2^- radical anions if the organic substrate is reduced at more negative potential than the CO_2 . Butadiene and ethylene are thus carboxylated [19]:



We also refer here to the possibilities of electrosynthesis utilizing CO , inasmuch as CO is a reduced product of CO_2 . Electroreduction of CO in DMF solution affords the interesting structurally squaric acid and in MeOH solution the formate [20]:



Electroreduction using CO and alcohols afford dialkyl carbonates if NH_4Br or LiBr are the electrolytes, while with Bu_4NBr as electrolyte formates are produced as major products [21].

3.10.3 Photoelectrochemical Reduction of Carbon Dioxide

The process of photosynthesis, on which all life on earth depends, is formally expressed in textbooks most simply as:

Photosynthesis



This expression denotes that water reduces carbon dioxide under the assistance of light-energy; and via the mediation of chlorophyll and enzymes the carbohydrates are produced in the cells of the leaves of plants [22]. In this very complex natural process the first fundamental event is now believed to be in effect a light-assisted indirect, chlorophyll-mediated electron transfer from water to carbon dioxide. A very complex sequence of enzyme-catalyzed chemical reactions leads to the formation of the carbohydrates (despite the fact that the photosynthesis as a reaction is thermodynamically not possible (not spontaneous)).

Electrochemically viewed, the reduction of CO_2 by H_2O cannot be spontaneous, as is apparent by considering the relevant potentials for the half-cell reactions and the overall cell reaction:

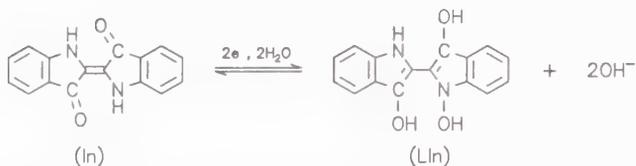


$$E^\circ_{\text{cell}} = -1.43\text{V}$$

$$\Delta G^\circ = 5.72\text{eV}, \quad \Delta G^\circ > 0$$

The electrocatalytic or variously mediated reduction of CO_2 provides a stimulus for interesting electrochemical research. One area of such research is concerned with solar cells. In a recent solar cell, CO_2 is reduced to methanol by oxidizing leucoindigo (LIn) to indigo (In) in a six-electron overall cell reaction [23]:

Solar cells

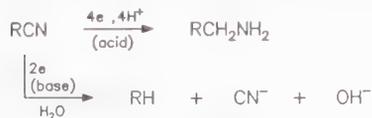


Artificial photosynthesis

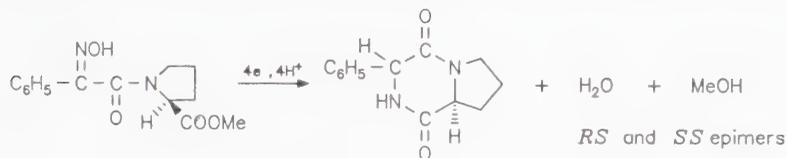
Artificial photosynthetic processes are actively studied for the purpose of converting solar energy to chemical energy. The light-assisted electron transfer in such processes would occur across a membrane in a manner similar to natural photosynthesis. Recently Khaled and coworkers studied the electrooxidation of carotenoids in CH_2Cl_2 medium. Carotenoids may play an active role in photosynthesis via the carotenoid radical cation. The oxidation was found to involve two electrons with β -carotene as the substrate [24].

3.11 Nitriles and Oximes

In acidic solutions nitriles and oximes are reduced to their corresponding amines. In basic solutions cleavage of the $\text{C}-\text{CN}$ bond occurs [1]:



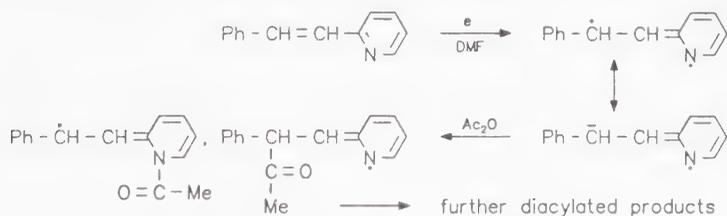
Udupa studied the reduction of lawronitrile and stearonitrile on a catalytic nickel black cathode [2]. The reduction to amines was most efficient, probably as a result of the high surface area provided by the deposited nickel on the graphite substrate plate. Tallec and coworkers [3] studied the electroreductive cyclization of methyl benzhydroxyiminoformyl(S) proline and obtained the two epimers RS and SS of pyrrolo [1,2a] 3-phenyl 1,4-diketopierazine with the SS epimer predominating (optical yield 34%)



3.12 Various Cathodic Couplings

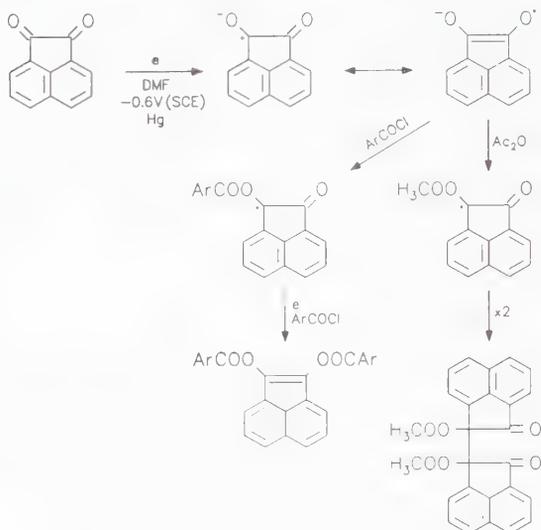
3.12.1 Acylations

Electrochemical acylations take place in aprotic media containing organic substrate and acetic anhydride as acylating agent. First, the organic substrate is reduced at the cathode to produce an anion radical which is attacked by acetic anhydride as exemplified below [1]:



Benzophenone is thus acylated by reduction at a mercury cathode in MeCN/Et₄NBr/Ac₂O solution to give the ketoacetate analog in 66% yield [2]. Aryl olefins have been acylated in aprotic solutions via their anion radicals or the dianions in the presence of an acid anhydride or an acylating electrophilic solvent [3]. Methyl methacrylate [4] and the carotenoid canthaxantin [5] were thus acylated. The acylation of 1,2-acenaphthenedione gave two products, depending on the acylating agent [6], Scheme 3.25

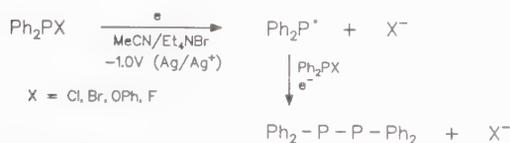
**Aryl olefins
acylation**



Scheme 3.25

3.12.2 Organophosphorus Compounds

Phosplines Cathodic couplings with trivalent organophosphorus compounds are efficient reactions [7]. Halodiphenylphosphines may be cleaved by reduction at platinum or monel electrodes in dry acetonitrile (treated with P_2O_5 in a divided cell to give exclusively the tetraphenylphosphine compound, as shown in Scheme 3.26:

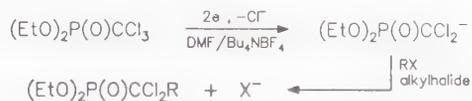


Scheme 3.26

Bicycloalkanes Trichloro- phosphonates

Electroreduction of certain olefinic enol phosphates in DMF at a mercury cathode gives, by double cyclization, bicycloalkanes [8] in 50–60% yields.

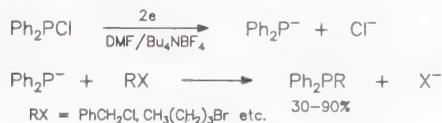
Cathodic reduction of trichlorophosphonates leads to the synthesis of their dichloro alkylated analogs [9], Scheme 3.27:



Scheme 3.27

For this synthesis the alkyl halide, RX, should have a cathodic potential greater than -1.2 V vs Ag/AgI so that only the phosphonate compound is reduced.

Alkylations of halodiphenylphosphines are effected in undivided cells fitted with magnesium (sacrificial) anodes and stainless steel cathodes, in aprotic solvents. Perichon and coworkers developed such methods for the synthesis of many phosphines from organic halides and chlorophosphines:

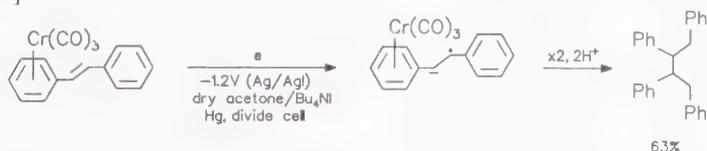


Electroreductive couplings via formation of P—C and S—C bonds have been studied in CH₂Cl₂ media. They have been synoptically shown as follows:¹¹

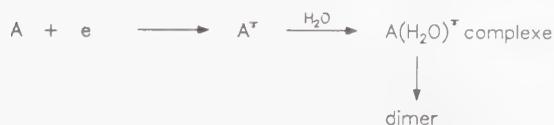


3.12.3 Arene-Metal Complexes

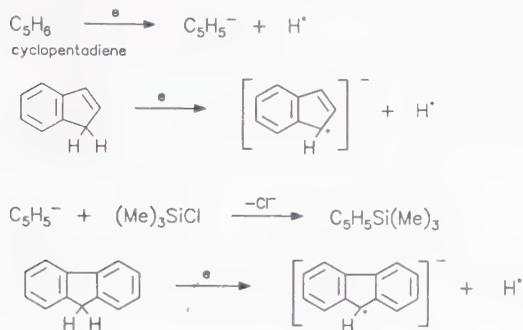
Arenes are activated towards hydrodimerization by forming chromium tricarbonyl complexes [12]. Stilbene forms such a complex and hydrodimerizes at less negative potential than it does in the uncomplexed form [12]:



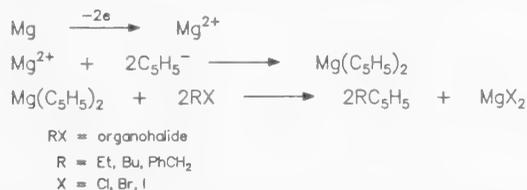
In contrast to stilbene, phenanthrene prefers to hydrogenate. Probably, complexation with the ring electrons stabilizes the anion radical and this tends to favor hydrodimer formation. In this connection Saveant's observation that traces of water may speed the dimerization of certain olefins comes to mind. The effect of water was ascribed to a possible complex intermediate, as is formally shown below, which by stabilizing the radical anion speeds up the dimerization reaction [13]:



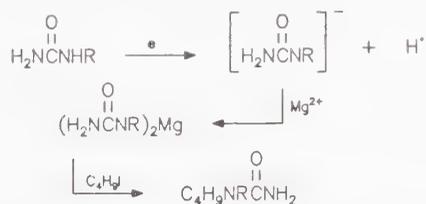
chlorotrimethylsilane, and the trimethylsilyl derivatives were produced in good yields:



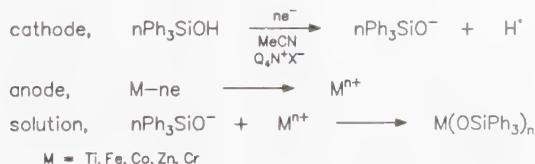
If the electrolyzer is equipped with a magnesium anode organometallic compounds are formed which upon treatment with alkyl halides or chlorosilanes are converted to the corresponding derivatives:



Such cathodic reactions are also possible with compounds containing N—H bonds, such as ureas, thioureas and *N*-acetylurea. If a magnesium anode is used in the electrolysis the produced organomagnesium compound upon treatment with butyl iodide affords the butyl derivative [18b]:



In this connection we consider the possibilities of *paired* organometallic synthesis. Bukhtiarov and coworkers [19] studied this type of electrosynthesis using transition metal electrodes for the formation of triphenylsiloxy derivatives. Current efficiencies of 50–100% were realized. This electro-synthesis is formally indicated below:



Organo-magnesium compounds

Organo-metallic compounds (transition metals)

References

Section 3.2 Carbon-Hydrogen Bond Formations

1. Coleman JA, Wagenknecht JH (1981) *J Electrochem Soc* 128:322
2. Baizer MM (1969) US Patent 3193408
3. Jansson R (1984) *Chem Eng News*, Special Report, November 19, p 43
4. Kyriacou D, Jannakoudakis D (1986) *Electrocatalysis for organic synthesis*. Wiley-Interscience, New York
5. Petrovich J, Anderson JR, Baizer MM (1966) *J Org Chem* 31:3897
6. Farnia G, Sandova C (1988) *J Chem Soc Perkin Trans 2*:247; Tezovek JR, Mark HB (1970) *J Phys Chem* 74:1627
7. Pletcher D, Razak M (1981) *Electrochim Acta* 26:819
8. Popp FD, Schultz HP (1962) *Chem Rev* 62:22
9. Horanyi G (1986) *Electrochim Acta* 31:1095
10. Cassadei MA, Pletcher D (1988) *Electrochim Acta* 33:117; Lain MJ, Pletcher D (1987) *Electrochim Acta* 32:99

Section 3.3 Carbonyl Compounds

1. Zuman P, Barus D, Ravalova KA (1968) *Discuss Faraday Soc* 45:202
2. Leary KJ, Babiowski AD (1976) *Abstracts of Papers, Meeting of the Electrochemical Society*. Washington, August, p 694
3. Filardo G, LaRosa F, Alfeo C, Cambino S, Silvestri G (1983) *J Appl Electrochem* 13:403
4. van Der Plase JF, Barendrech E, Zeilmaker H (1980) *Electrochim Acta* 25:1471
5. Little RD et al. (1988) *J Org Chem* 53:2287
6. Sibillo S, d'Inkan E, DePort L (1987) *Tetrahedron Lett* 28:55
7. Sugino K, Nonaka T (1968) *Electrochim Acta* 13:613
8. Ferles M (1975) *Coll Czech Chem Commun* 40:2183
9. Tissot P, Surbek JP, Gülarar FO (1981) *Helv Chim Acta* 64:1570
10. Lain MJ, Pletcher D (1987) *Electrochim Acta* 32:109
11. Stradius J, Benders J, Kadysh V (1986) *Electrochim Acta* 31:637
12. Smirnov VA et al. (1986) *Doklady Akad Nauk, Eng Ed* 288:203
13. Oryoruk H, Pekmez K, Yildiz A (1987) *Electrochim Acta* 32:574
14. Troup L, Tokec L (1967) *J Am Chem Soc* 89:4789
15. Barber JJ (1985) US Patent 4517062
16. King JH (1979) *J Chem Techn, Biotechn* 29:741
17. Horanyi G, Torkos K (1982) *J Electroanal Chem* 136:301
18. Pienemann T, Schäfer HJ (1989) *Dechema Monog Electroorg* 112:367
19. Shono T and Kise N (1990) *Tetrahedron Lett* 31:1303
20. Khnenitskaya E, Razgonyava ID, Solodar SL (1985) *Zh Obs Khim* 54:1495
21. Bukhtiarov AV et al. (1990) *J Gen Chem USSR* 59:1505
22. Kunugi Y, Nonaka T, Tien-H (1990) *Electrochim Acta* 35:1167

Section 3.4 Carboxylic Acids and Esters

1. Vilambi NRK, Chin D-T (1987) *J Electrochem Soc* 134:3074
2. Oi R, Shimakawa C, Shimakawa Y, Takenaka S (1987) *Bull Chem Soc (Japan)* 60:4193
3. Alkire RC, Tsai JE (1982) *J Electrochem Soc* 129:1158; Chin E-T, Cheng CY (1985) *J Electrochem Soc* 132:2605

- Iversen PE, Lund H (1967) *Acta Chem Scand* 21:389
- Dillon CS (1948) *British Patent* 611674; (1949) *Chem Abst* 43:4589; Wagenknecht J (1972) *J Org Chem* 37:1513
- Lund H (1963) *Acta Chem Scand* 17:972; Horner L, Holn H (1977) *Liebigs Ann* 2036; Deprez D, Margraff R, Bizot J, Pulicani JP (1987) *Tetrahedron Lett* 28:4679
- Tan Z et al. (1989) *Chem Abst* 111:30216z
- Oi T, Takenaka S (1989) *Chem Abst* 110:221484c
- Kumar N, Tuck DG, Watson KD (1987) *Can J Chem* 65:740; Kyriacou D (unpublished work)
- Kucheico SI, Turova N Ya, Shreider VA (1986) *J Gen Chem USSR* 55:3130
- Said FF, Tuck DG (1982) *Ing Chim Acta* 59:1
- Kumar R, Tuck DG (1985) *J Organomet Chem* 281:47
- Baizer MM, Anderson JM (1964) *J Electrochem Soc* 111:233
- Nishiguchi I, Hirashima T (1983) *Angew Chem, Int Ed Eng* 22:52
- Aray K, Shaw C, Nozawa K, Kawai K, Nakagima S (1987) *Tetrahedron Lett* 28:441
- Fox DP, Little RD, Baizer MM (1985) *J Org Chem* 50:2202

Section 3.5 Organohalides

- Stackelberg M, Stracke W (1941) *Z Electrochem* 53:118
- Eiving PJ, Pullman B (1961) *Adv Chem Phys* 3:1; Casanova BS, Ebersson L (1974) In: Patai S (ed) *Chemistry of the carbon-halogen bond*. Interscience, New York
- Ulery HE (1969) *J Electrochem Soc* 116:1201; Bard AJ, Merz A (1979) *J Am Chem Soc* 101:2939; Andrieux CP, Gallardo I, Saveant JM, Su KB (1986) *Ibid.* 108:638; Koch A, Henne BJ, Bartak RE (1987) *J Electrochem Soc* 134:3062; Benefice-Malouef S, Blanoce H, Calas P, Comeyaras A (1988) *J Fluorine Chem* 39:125
- Kyriacou D (unpublished work)
- Fry AJ, Mitnick MA (1969) *J Am Chem Soc* 91:6207
- Miller LL, Riekema E (1969) *J Org Chem* 34:3359
- Wawzonek S, Duty RD (1961) *J Electrochem Soc* 108:1135
- Wawzonek S, Wagenknecht JH (1963) *J Electrochem Soc* 110:420
- Covitz FH (1967) *J Am Chem Soc* 89:540
- Gilch H (1966) *J Polymer Sci* 4:1351
- Fritz HP, Kornrumpf W (1978) *Liebigs Ann Chem* 1416
- Ref. 3, section 3.5
- de Lua C, Inesi A, Rampazzo L (1983) *J Chem Soc, Perkin Trans* 2:1821
- Rifi MR (1971) *J Org Chem* 36:1018
- Covitz FH (1967) *J Am Chem Soc* 89:4442
- Fry AJ, Chang LL (1976) *Tetrahedron Lett* 17:645
- Fry AJ, Britton WE (1973) *J Org Chem* 38:2620
- va Tilborg WJM, Plomb R, de Ruiter R, Smit CJ (1980) *Recl Trav Chim* 99:206
- Durandetti S, Sibille S, Perichon J (1991) *J Org Chem* 56:3255
- Chaussard J, Folest J-C, Nedelek JY, Perichon J, Sibille S, Troupel M (1990) *Synthesis* 369; Nedelec JY, Mouloud HAH, Folest J-C, Perichon J (1988) *J Org Chem* 53:4721
- Sibille S, d'Inkan E, Leport L, Perichon J (1986) *Tetrahedron Lett* 27:3132
- Conan A, Sibille S, d'Inkan E, Perichon J (1990) *J Chem Soc Chem Commun* 48
- Silvestri G, Gambino S, Filardo G (1991) *Acta Chem Scand* 45:987-992; Lu YW, Nedelec JT, Folest JC, Perichon J (1990) *J Org Chem* 55:2503; Sibille S, Meharek S, Perichon J (1989) *Tetrahedron* 45:1448
- Folest JC, Nedelec JY, Perichon J (1988) *Synth Commun* 18:1491
- Gishbrech JP, Lund H (1985) *Acta Chem Scand* B39:823

25. Bèrubè D, Renaud RN (1983) *Electrochim Acta* 28:1367
26. Lund H, Haboth E (1976) *Acta Chem Scand* B30:895
27. Cipris D (1987) *J Appl Electrochem* 8:537
28. Casadei MA, Inesi A, Morocci FM, Occhialini D (1989) *Tetrahedron* 45:6885
29. Voigtlander R, Matschriner H, Krzreminski C, Biering H (1985) *J Prakt Chem* 327:649
30. Bukhtiarov AV, Colyshin VH, Tomilov AP, Kuz'min OV (1988) *J Gen Chem (USSR)* 58:1296
31. Hansen PE, Berg A, Lund H (1976) *Acta Chem Scand* B30:267
32. Kristensen LH, Lund H (1979) *Acta Chem Scand* B33:735
33. Wawzonek S, Wagenknecht JH (1963) *J Electrochem Soc* 110:420
34. Barba F, Guidaro A, Zapata A (1982) *Electrochim Acta* 27:1335
35. Kyriacou D (unpublished work); Jansson R (1984) *Chem Eng News*, Nov. 19, p 43
36. Kyriacou D, Edamura F, Love J (1980) US Patent 4217185
37. Saveant JM (1980) *Acc Chem Rev* 18:223 and 13:323; Saveant JM (1988) *Bull Soc Chim*, No 2, 225; Bunnet JF (1985) *Acc Chem Res* 18:212
38. Alder RW (1980) *J Chem Soc, Chem Commun* 1184
39. Oturan MA, Pinson J, Saveant JM, Thiebault A (1989) *Tetrahedron Lett* 30:1373
40. Thobie-Coutier, Degrand C (1991) *J Org Chem* 56:5703; Degrand C, Prest R (1990) *J Electroanal Chem* 282:218
41. Brisoe MW, Chamber RD, Silvester MJ (1988) *Tetrahedron Lett* 29:12995

Section 3.6 Nitrocompounds

1. Fry AJ (1982) In: Patai S (ed) *The chemistry of the nitro and azo compounds*. Wiley, London, p 139, etc.
2. Lund H (1983) In: Baizer MM, Lund H (eds) *Organic electrochemistry*. Dekker, New York, p 285
3. Cyr A, Huot P, Belot G, Lessard J (1990) *Electrochim Acta* 35:147
4. Gunawardena NE, Pletcher RD (1983) *Acta Chem Scand* B37:549
5. Sayo H, Tsukitani Y, Masui M (1968) *Tetrahedron* 24:1717
6. Ogumi Z, Inaba M, Quashi S, Uchida M, Takehara Z (1988) *Electrochim Acta* 33:365
7. Haber F (1898) *Z Electrochem* 4:506
8. Beck F, Gabriel W (1985) *Angew Chem* 24:77
9. Ravichandran C et al. (1989) *J Appl Electrochem* 19:49
10. Stutts KJ, Scortichini CL, Repucci CM (1989) *J Org Chem* 54:3744
11. Marquez J, Pletcher D (1981) *Electrochim Acta* 26:1751
12. Hazard R, Jubault M, Tallec A (1983) *Can J Chem* 61:2359
13. Kuee S, Lund H (1969) *Acta Chem Scand* 23:2711
14. Chibani A, Hazard R, Jubault M, Tallec A (1987) *Bull Soc Chim* 795
15. Wagenknecht JH, Johnson GV (1987) *J Electrochem Soc* 134:2754
16. Christensen L, Iverson PE (1979) *Acta Chem Scand* B33:352
17. Cault C, Moinet C (1989) *Tetrahedron* 45:3429
18. Iversen PE, Christensen TB (1977) *Acta Chem Scand* B31:733
19. Shono T et al. (1983) *J Org Chem* 48:2103
20. Petsom A, Lund H (1980) *Acta Chem Scand* B34:614
21. Bawer WJ, Evans H (1988) *J Org Chem* 53:5234
22. Bukhtiarov AV et al. (1989) *Dokladi Chemistry Proceedings of the Academy of Sciences* 304:35
23. Ref. 4, section 3.6

Section 3.7 *N*-Heterocyclics and other Heteroatom Structures

1. Lund H (1968) *Discus Faraday Soc* 45:193; Lund H (1970) *Adv Heterocycl Chem* 12:213; Lund H, Tabacovic I (1984) *Adv Heterocycl Chem* 36:173

- O'Reiley JE, Elving PJ (1971) *J Am Chem Soc* 93:1871
- Armand J, Chekir K, Pinson J (1978) *Can J Chem* 56:1894
- (1983) *Chem Abst* 98:34503e
- Navda J, Givadinovitch H, Devaud M (1983) *J Chem Res Synop* 1992
- Janic B, Elving PJ (1968) *Chem Rev* 68:295
- Boullares L, Bellec C, Pinson J (1987) *Can J Chem* 65:1619
- Martigny P, Lund H (1979) *Acta Chem Scand* B33:575
- Falsig M, Iversen PE (1977) *Acta Chem Scand* B31:15
- Armand J, Bellec C, Boullares L, Pinson J (1983) *J Org Chem* 48:2847
- Barrado E, Pardo R, Batanero RS, Alberola A, Laguna MA, Pulido FJ (1988) *Electrochim Acta* 33:171
- Pragst F, Henrion A, Abraham W, Michael G (1987) *J Prakt Chem* 329:1071
- Webber A, Osteryoung J (1982) *J Electrochem Soc* 129:273
- Tsveniashvili VS et al. (1984) *J Gen Chem (USSR)* 54:546
- Mangi A, Oloman CW (1987) *J Appl Electrochem* 17:532
- Kyriacou D (1981) *Basics of electroorganic synthesis*. Wiley-Interscience, New York, p 107
- Kyriacou D (unpublished work); also ref. 16, section 3.7
- Holst HH, Lund H (1979) *Acta Chem Scand* B33:233; Hazard R, Tallec A (1976) *Bull Soc Chim* 433

Section 3.8 Organosulfur Compounds

- Saveant JM (1969) *CR Acad Sci* 258:585; Mairanovsky VG (1976) *Angew Chem, Int Ed Eng* 15:218; Degrand C, Lund H (1979) *Acta Chem Scand* 33B:512; Iversen PE, Lund H (1974) *Acta Chem Scand* 28B:827; Montenegro MI (1986) *Electrochim Acta* 31:607
- LeGuillanton G, Do QT, Simonet J (1986) *Tetrahedron Lett* 27:2261; (1989) *Bull Soc Chim, No 3*, 433
- Donahue J, Oliver JW (1969) *Anal Chem* 41:753
- Falsig M, Lund H (1980) *Acta Chem Scand* B34:591; Chambers JQ (1974) *J Org Chem* 39:51
- Barnard D, Evans M, Higgins G, Smith J (1961) *Chem Ind* 20
- Fleizer B, Sanecki P (1982) *Electrochim Acta* 27:429
- Pragst F, Kaltofen B (1982) *Electrochim Acta* 27:1181
- Langer LK, Schmidtke ST, Volz J (1987) *Chem Ber* 120:67
- Falsig M, Lund H, Nadjo L, Saveant JM (1980) *Acta Chem Scand* B34:685
- Degrand C, Lund H (1979) *Acta Chem Scand* B33:512
- Lund H, Kristense LH (1979) *Acta Chem Scand* B33:495
- Johansson BL, Persson B (1978) *Acta Chem Scand* B32:431
- Darchen A et al. (1986) *J Heterocyc Chem* 23:1603
- Voss J, Wiegand G, Huelmeyer K (1985) *Chem Ber* 118:4806
- Bukhtiarov AV, Mikheev VV, Lebedev AV, Tomilov AP, Kuz'min OV (1988) *J Gen Chem. (USSR)* 58:605
- Simonet J et al. (1989) *Electrochimica Acta* 34:1615
- Bukhtiarov AV, Lebedev AV, Tonilov AP (1989) *J Gen Chem. (USSR)* 58:2420
- Le Guillanton G, Do QT, Simonet J (1989) *Bull Soc Chim, No 3*, 433

Section 3.9 Some Specific Cleavages of C—O Bonds in Hydroxy Compounds

- a. Lund H, Doupeux H, Mickel MA, Mousset G, Simonet J (1974) *Electrochim Acta* 19:629; b. Shono T, Matsumura Y, Tsubata K, Sugihara Y (1979) *J Org Chem* 44:4508; c. Sopher, WW, Utley JHP (1981) *J Chem Soc Chem Commun* 134; d. Islam N (1987) *Tetrahedron* 43:2741

2. Nonaka T, Baizer MM (1983) *Electrochim Acta* 28:661
3. Eggert G, Heilbaum J (1986) *Electrochim Acta* 31:1448
4. Chum HL, Baizer MM (1985) *The electrochemistry of biomass and derived materials*, ACS Monograph 183, p 161
5. Ellis KG, Islam N, Sopher DW, Utley JHP, Chum HC (1987) *J Electrochem Soc* 134:3058
6. Blankespoor RL, Hsung R, Schutt P (1988) *J Org Chem* 53:3232
7. Kempt DS, Reizek J (1977) *Tetrahedron Lett* 1031; Pan SS, Peterson L, Bochor NR (1981) *Mol Pharmacology* 19:184
8. Thonton TA et al. (1989) *J Am Chem Soc* 111:2434
9. Widitz S, Schäfer HJ (1983) *Acta Chem Scand B* 37:475

Section 3.10 Electrocarboxylations

1. a. Lapidus AL, Ping YY (1981) *Russian Chem Rev* 50:63; b. Russel PG, Srinivasan N, Steinberg M (1977) *J Electrochem Soc* 124:1329; c. Ref. 4, section 3.9; d. Kyriacou G, Anagnostopoulos A (1992) *J Electroanal Chem* 322:233; (1992) *Ibid.* 328:233
2. Paik W, Anderson T, Eyring H (1969) *Electrochim Acta* 14:1217
3. Schiffrin DI (1974) *Discuss Faraday Soc* 56:75
4. Frese KW, Leach S (1985) *J Electrochem Soc* 132:259
5. DeWulf DW, Jim T, Bard JA (1989) *J Electrochem Soc* 136:1688
6. Cook RL, MacDuff RC, Sammels AF (1989) *J Electrochem Soc* 136:1982
7. Mahmood MN, Mashender D, Hartly CJ (1987) *J Appl Electrochem* 17:1159
8. Fisher J, Lehmann T, Heitz E (1981) *J Appl Electrochem* 11:743
9. Azuna M, Watanaba M (1989) *J Electroanal Chem* 260:441
10. Cook RL, MacDuff RD, Sammels AF (1990) *J Electrochem Soc* 137:187
11. a. Wawzonek S, Wearing D (1959) *J Am Chem Soc* 81:2067; b. Berkey R, Runner ME (1955) *J Electrochem Soc* 102:235; c. Tyssee DA, Baizer MM (1974) *J Org Chem* 39:2823; d. Lamy E, Nadjo L, Saveant JM (1979) *Nouv J Chim* 3:21
12. Fuchs P, Hess V, Holst HH, Lund H (1981) *Acta Chem Scand B* 35:185
13. Chaussard J, Troupel M, Robin Y, Jacob G, Juhasz JP (1989) *J Appl Electrochem* 19:345
14. Matue T et al. (1982) *Denk Kagaku Oyobi Kogyo* 50:732
15. Weinberg NL, Hoffmann AK, Reddy TR (1971) *Tetrahedron Lett* 277
16. Sock O, Troupel M, Perichon J (1985) *Tetrahedron Lett* 26:1509; McHarek S, Heintz M, Troupel M, Perichon J (1989) *Bull Soc Chim*, No 1, 95
17. Janietz S, Rüttinger HH, Matschiner H (1988) *J Prakt Chem* 330:147
18. (1985) Japanese Patent 6024386; (1985) CA. 103:13560c
19. van Tilborg WJM, Smit OJ (1981) *Recl Trav Chim* 100:437; Neikam WC (1967) US Patent 3344045
20. Baizer MM (1984) *Tetrahedron* 40:935
21. Cipris D (1980) *J Electrochem Soc* 127:1045
22. Meyers TJ (1989) *Acc Chem Res* 22:163
23. Ogura K, Yoshida I (1987) *Electrochim Acta* 32:1191
24. Khaled M et al. (1990) *J Phys Chem* 94:5164

Section 3.11 Nitriles and Oximes

1. Lund H (1959) *Acta Chem Scand* 13:249; Nonaka H (1967) *J Electrochem Soc* 114:1255; Lund H (1968) *Tetrahedron Lett* 3651
2. Krishnan V, Mahalingam H, Udupa HVK (1979) *J Chem Tech Biotechn* 29:703
3. Boulmedais A, Jubault M, Tallec A (1989) *Tetrahedron* 45:5497

Section 3.12 Various Cathodic Couplings

1. Lund H, Degrand C (1979) *Acta Chem Scand* B33:57
2. Layoff T (1979) *J Org Chem* 26:383
3. Engels R, Schäfer HJ (1978) *Angew Chem, Int Ed Eng* 17:460
4. Lund H, Degrand C (1977) *Tetrahedron Lett* 3593
5. Hall EAH, Moss CP, Utley JHP, Weedon BCL (1976) *J Chem Soc Chem Commun* 586
6. Guirado A, Barba F, Hurshouse M, Arcas A (1989) *J Org Chem* 54:3205
7. Hall TJ, Hargis JH (1986) *J Org Chem* 51:4185
8. Gassman PG, Lee C (1989) *J Am Chem Soc* 111:739
9. Cristophe LeMenn J, Sarrazin J (1989) *J Chem Research* 26
10. Folest JC, Nedelec JY, Perichon J (1987) *Tetrahedron Lett* 28:1885
11. Petrosyan VA et al. (1989) *Doklady Chemistry* 302:283
12. Lin Chiu Y, San'ana AEG, Utley JHP (1987) *Tetrahedron Lett* 28:1349
13. Saveant JM (1983) *Acta Chem Scand* B37:365
14. Tuck DG (1979) *Pure Appl Chem* 51:2005
- 14a. Feasson C, Devaud M (1982) *J Chem Research* 152
15. Coriu R, Dabosi G, Martineau M (1980) *J Organometal Chem* 188:63; Benkeser R, Tinker C (1988) *J Organometal Chem* 196:139; Yoshida J, Murata T, Isoe S (1987) *Tetrahedron Lett* 27:373
16. Tomilov AP et al. (1985) *J Gen Chem (USSR)* 54:2145
17. Yoshida J, Muraki K, Funahash H, Kawabata N (1986) *J Org Chem* 51:3996
18. a. Bukhtiarov AV, Golyshin VN, Tomilov AV, Lebedev AV (1989) *J Gen Chem (USSR)* 59:366; b. (1989) *Ibid.* 59:372
19. Bukhtiarov AV, Golyshin VN, Rodnikov IA, Melekhin PG, Makarov YV (1989) *J Gen Chem USSR* 59:953

4 Indirect Electroorganic Reactions (Indirect Electrolysis)

4.1 Introduction

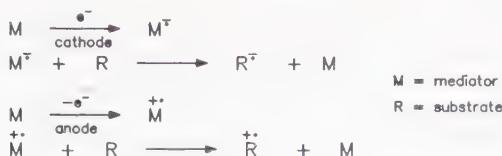
A formal definition of direct and indirect electroorganic reactions was given in Chapter 1. The purpose of the present chapter is to provide a fundamental understanding of indirect electrolysis for organic synthesis. In Steckhan's view [1] indirect electroorganic synthesis is a "modern chapter in organic electrochemistry." Conceptually, almost any electrosynthesis may be considered feasible by either direct or indirect electrolysis. However, in practice there are some distinct differences between these two general types of electrochemical processes. The practical significance of the difference would depend on the specific goal of the project undertaken and the scale of the process in the laboratory or in the plant. Both direct and indirect electrochemical processes have come into existence since the birth of electrochemical technology. Indirect electrolysis processes have been recently considered from both theoretical and practical perspectives by Steckhan [1] (1986), Alkire [2] (1986) and Pitchaichanarong [3] (1990). We may note that many apparently chemical processes in which redox reagents are used are actually electrochemical processes if we consider that the redox reagents were prepared in some electrochemical cells, although in places remote from the actual place of use. (The scholarly M. Baizer used to call these processes "cryptoelectrochemical".)

Redox electrocatalysis per se and electron transfer reactions in general have been theoretically dealt with by Saveant [4] and by Eberson [5]. (Springer-Verlag plans to begin a series of volumes in electrochemistry including indirect electrolysis under the editorship of Professor E. Steckhan.)

4.1.1 Basic Mechanisms

**Homogeneous
and
heterogeneous
reactions**

Indirect electroorganic reactions are viewed as electrocatalytic homogeneous reactions if the mediator reacts catalytically with the organic substrate in solution [1,6,7]. If the mediator is immobilized in some way at the electrode surface, the reaction occurs in effect as a heterogeneous indirect process. In either case the basic mechanisms are simply depicted as follows:



The overall reaction rate and the catalytic efficiency would depend on the chemical reaction rate of the mediator with the organic substrate and the number of cycles of mediator regeneration (turnovers). Another type of indirect reactions is one in which very reactive inorganic or organic species are generated in situ such as Cl^\cdot , H^\cdot , $\text{O}_2\cdot^-$, OH^\cdot , $:\text{CCl}_2$, $\cdot\text{CH}_2\text{NO}$ and $\cdot\text{CH}_2\text{OH}$. These species react with organic substrates which may or may not be electroactive under the electrolysis conditions. A very special feature of indirect electrolysis is that *exotic* reagents may be generated in situ as and when needed for a particular organic synthesis. Table 4.1 lists a number of redox couples that are potential mediators for indirect electro-organic synthesis.

Special feature

Table 4.1 Common Redox Mediators

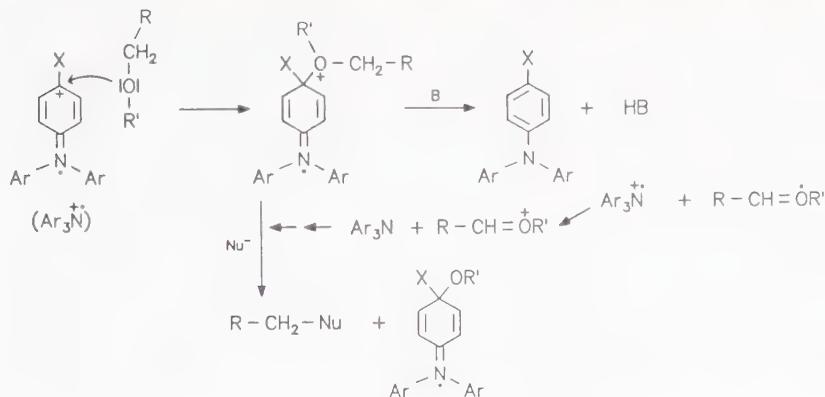
Ce(IV)/Ce(III)	I^+/I^- , I_2/I^-
Ti(III)/Ti(II)	Br^+/Br^- , Br_2/Br^-
Ti(IV)/Ti(III)	$\text{Ag(II)}/\text{Ag(I)}$
Sn(IV)/Sn(II)	$\text{Mn(III)}/\text{Mn(II)}$
Cr(III)/Cr(II)	$\text{Hg(II)}/\text{Hg(I)}$
Os(VIII)/Os(VI)	$\text{Pd(II)}/\text{Pd(0)}$
Cr(VI)/Cr(III)	$\text{V(V)}/\text{V(IV)}$
Cl^+/Cl^- , Cl_2/Cl^-	$\text{Cu(II)}/\text{Cu(I)}$

Some of the mediators in Table 4.1 have been used on an industrial scale (with in situ or ex situ regeneration of the mediator). Alkali and alkaline earth amalgams and active metallic oxides on oxide covered electrodes may also be included in this list of mediators (heterogeneous electrocatalysis). Several organic mediators are also known [8,9]. The most important properties of a mediator redox catalyst are:

1. chemical stability and
2. rapid chemical reversibility.

In general, inorganic redox systems of metallic ions and oxyanions in simple or complexed forms are more stable and more reversible than organic redox mediators. It must be noted that the thermodynamic potential by itself may not qualify a redox system as a mediator. For example, both redox couples $\text{Ag}^{2+}/\text{Ag}^+$ and $\text{Co}^{3+}/\text{Co}^{2+}$ are powerful oxidizing agents. However, Co^{3+} ions are unstable in aqueous media and therefore

Mediator properties



It is sometimes observed in practice that a given redox couple is an effective mediator for a given indirect oxidation or reduction; while an electrode set at the same potential which is characteristic of the redox couple cannot achieve the same oxidation or reduction. This *apparent paradox* is *not* a thermodynamic violation. It is only a kinetic consequence, common to many electrochemical reactions, organic and inorganic. For example, the electrolytic production of chlorine by electrolysis of brines is possible because kinetic factors suppress the thermodynamically favored oxygen evolution from the oxidation of water at the anode as they also do in the Kolbe reaction (Chapter 2).

Kinetic factors

4.2 Oxidative Indirect Reactions

High-valent transition metal ions, simple or complexed are common mediators for indirect oxidations. Also organic radical cations of aromatic and heteroaromatic substances and some trialkyl amines may be very effective oxidative mediators in certain cases. Positive halide ions, (haloniums), I⁺, Br⁺, have been shown to be good mediators for the oxidation of alcohols. With halonium ion mediators a bonded-type mechanism apparently operates, since a transitory chemical bond is formed between the halogen mediator and the organic substrate during the oxidation course.

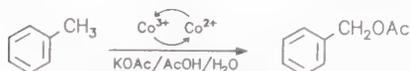
Oxidative mediators

4.2.1 Metallic Ions and Oxyanions Mediators

The oxidation of side chains in aromatics has been demonstrated with transition metal mediators, on a laboratory and industrial scale of synthesis. Thus toluene has been oxidized to benzaldehyde on a plant scale

Oxidation of toluene

(Zurich) using the redox couple mediator $\text{Ce}^{4+}/\text{Ce}^{3+}$. Regeneration of the redox catalyst is done in situ or ex situ (internally or externally) for industrial processes [1–5]. Acetoxylation of toluene on the methyl group is effected in the presence of cobaltic acetate as a mediator [1]. The cobaltic acetate complex is generated in situ, as is formally depicted below:

**Oxidation of alkenes**

Indirect oxidations of alkylbenzenes by recycled (ex situ) $\text{NH}_4\text{Ce}(\text{NO}_3)_6$ in aqueous or methanolic acetic acid media was studied by Torii [2]. Anisaldehyde was thus obtained from *p*-methoxytoluene in 94% yield. The electrogeneration of the Ce(IV) salt was easily effected by electrolysis in methanol solution containing the Ce(III) complex, yellow crystals, which were recovered from the reaction mixture after solvent evaporation and extraction of anisaldehyde with benzene.

Ce(IV)/Ce(III) mediator**Oxidation of alkylbenzenes**

Ruthenates are studied as potential oxidation mediators. The oxidant species Ru(VI) is fixed at the electrode surface (heterogeneous electrocatalyst) and is continuously regenerated thereon by deelectronation of the reduced species Ru(V). Thus alkenes have been oxidized using lead and bismuth ruthenates [3]. It is assumed that the nonstoichiometric lead ruthenates are the active catalysts. Organic ruthenium(IV) complexes were found to be very effective mediators for the oxidation of alcohols, cyclic ketones and C—H bonds adjacent to aromatic or olefinic group, such as *p*-xylene or toluene which are oxidized to terephthalic acid and benzoic acid respectively [4,5]. The Ru(IV) oxidant was used in the complex form $[\text{Ru}(\text{trpy})(\text{bpy})(\text{O})]^{2+}$, (trpy is 2,2',2''-terpyridine, and bpy is 2,2'-bipyridine). For example, the electrocatalytic oxidation of the isopropyl alcohol to acetone is expressed as follows:



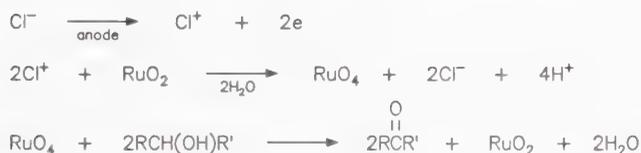
Electrocatalytic oxidation of isopropyl alcohol to acetone

Electrocatalytic Oxidation of Isopropyl Alcohol to Acetone

This electrolysis was conducted in a divided cell equipped with platinum electrodes and a SCE as reference for the anode. The oxidation of isopropanol was carried out in aqueous solution (pH 6.8, $\text{HPO}_4^-/\text{H}_2\text{PO}_4^-$) at 25 °C under nitrogen. The anolyte contained the

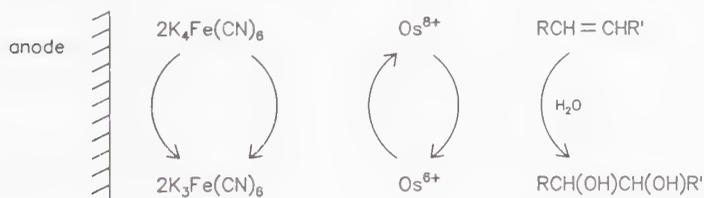
alcohol and the Ru(IV) complex in the millimolar ratio of 1000/1 and the anode potential was set to 0.8 V vs SCE which was sufficient for the regeneration of the catalyst. Hydrogen was evolved at the cathode. Product yields were determined by gas chromatography and were in the range of 90–100%.

Torii [6] reported an interesting double mediator system for the oxidation of alcohols and aldehydes. For example, the oxidation of secondary alcohols to the corresponding ketonic products occurs as depicted formally in Scheme 4.2



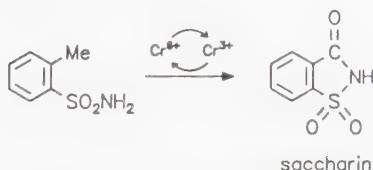
Scheme 4.2

This electrolysis medium is an aqueous-organic two-phase system. Another double mediator system is the $\text{OsO}_4/\text{OsO}_3\text{-K}_4\text{Fe}(\text{CN})_6/\text{K}_3\text{Fe}(\text{CN})_6$ combination. This system was used for the hydroxylation of olefinic compounds [7], as depicted in Scheme 4.3



Scheme 4.3

Interesting examples of external regeneration of the redox catalyst are the systems $\text{Cr}^{6+}/\text{Cr}^{3+}$, $\text{Ce}^{4+}/\text{Ce}^{3+}$ and $\text{Co}^{3+}/\text{Co}^{2+}$ in acidic solutions. Saccharin was produced by oxidative conversion of *o*-toluenesulfonamide by electrolysis using the $\text{Cr}^{6+}/\text{Cr}^{3+}$ couple in aqueous sulfuric acid [8], and a lead dioxide anode.



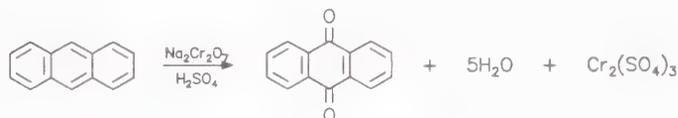
Double mediator systems

Hydroxylation of olefinic compounds

Saccharin

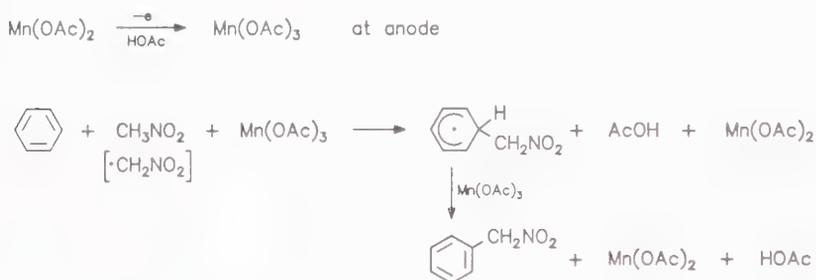
Oxidation of toluene and anthracene

The oxidation of toluene to benzaldehyde by ex situ regenerated ceric ion is very efficient (99% yield) [9]. The process is used commercially (Zurich). Anthracene is industrially oxidized to anthraquinone by electro-generated chromic acid (Holiday, U.K.). A paste consisting of small anthracene particles is oxidized in sulfuric acid by the dichromate and the resulting chromic sulfate is reoxidized in an electrolysis cell and is used again [10].



Carboxymethyl and nitromethyl radicals

Electrochemically generated Mn(III) ions in acetic acid are oxidative mediators producing reactive carboxymethyl and nitromethyl radicals capable of reacting with olefins and aromatics [11–13]. The Mn(III) species is directly generated at the anode and reacts in solution with acetic acid or nitromethane to yield the corresponding radicals $[\text{CH}_2\text{COOH}]^\cdot$ and $[\text{CH}_2\text{NO}_2]^\cdot$ which enter into reaction as shown in Scheme 4.4.

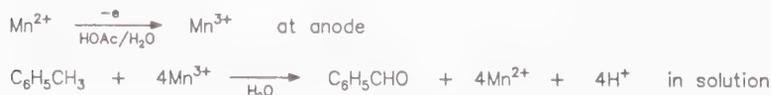


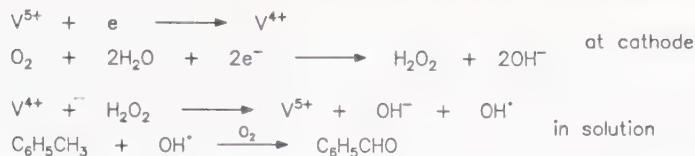
Scheme 4.4

4.2.2 Paired Oxidative Processes

Oxidation of toluene

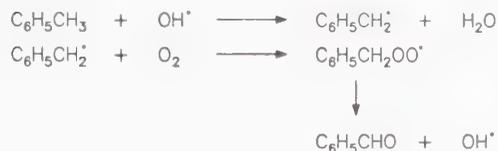
It may be sometimes possible to develop efficient *indirect paired* electro-synthetic processes. An example is the oxidation of toluene to benzaldehyde [14], as shown in Scheme 4.5. The anodic mediator for the oxidation of toluene is the $\text{Mn}^{3+}/\text{Mn}^{2+}$ couple while at the cathode the couple $\text{V}^{5+}/\text{V}^{4+}$ is generating OH^\cdot radicals which also oxidize toluene so that both half-cell reactions lead to the mediated production of the desired aldehyde, Scheme 4.5





Scheme 4.5

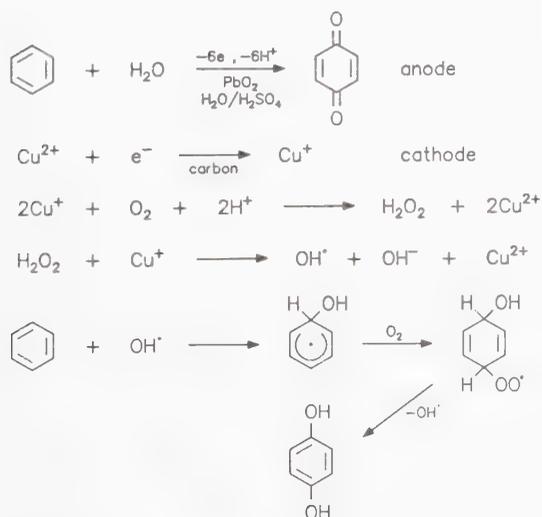
The reaction via OH^\cdot radicals most probably involves chemical steps as indicated below:



Thus in theory the efficiency of this cell reaction should be 200% in terms of product yield. Another paired electrosynthesis example was recently reported [15]. Benzene is oxidized to hydroquinone at the cathode compartment indirectly, while at the anode, (PbO_2/H_2SO_4), benzene is oxidized to benzoquinone. The pertinent reactions are shown in Scheme 4.6. The electrolysis is performed in a divided cell. The anolyte is aqueous sulfuric acid containing 10 ml of benzene per 100 ml of solution and the catholyte aqueous 0.1 M acetate solutions with some acetonitrile and 10 ml of benzene. Oxygen is bubbled through the catholyte during electrolysis in order to generate the desired OH^\cdot radicals for the oxidation of benzene. The current efficiency is above 90%.

**Paired
oxidations
of benzene**

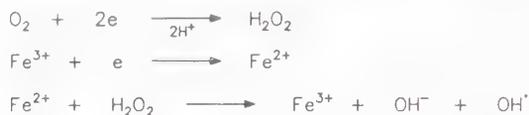
**OH^\cdot radicals
from O_2**



Scheme 4.6

Hydroxylations of certain organic compounds
Fenton's reagent

Electroreduction of molecular oxygen in the presence of Fe^{3+} ions in aqueous solutions generates Fenton's reagent for in situ hydroxylations of certain organic compounds [16–18]. Recently, a study was made concerning the oxidation of aromatics by Fenton's reagent. It was concluded that the reaction is actually very complex for both batch and continuous processes [19]. The oxidizing agent is the OH^\cdot radical resulting from the reduction of dioxygen to H_2O_2 and reduction of H_2O_2 by Fe^{2+} ,



Graft copolymerization

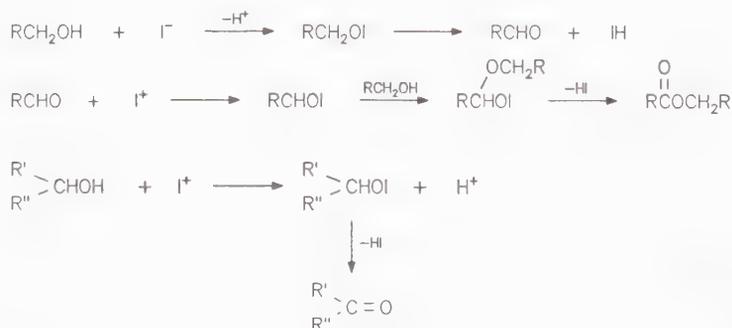
The couples $\text{Cu}^{2+}/\text{Cu}^+$ and $\text{V}^{4+}/\text{V}^{3+}$ may also be used for the generation of OH^\cdot radicals [20,21]. The $\text{Fe}^{3+}/\text{Fe}^{2+}$ couple may be most conveniently generated by the in situ dissolution of a consumable iron anode. This technique has been successfully used in a recent electroinitiated graft copolymerization of cellulose with acrylonitrile [22]. Cellulose radicals were generated and reacted with acrylonitrile to form the copolymer product.

4.2.3 Halide Ions as Mediators

Halonium ions

Molecular halogens and hypohalites or positive halonium ions, I^+ , Br^+ may be very easily generated to act as mediators in situ for a variety of oxidative reactions. Small amounts of NaOCl generated in aqueous solutions are sufficient to oxidize hydroxy compounds such as menthol, isoborneol 2-octanol and other secondary alcohols to their corresponding ketones in high yields [1]. Iodonium ion, I^+ , is especially able to oxidize primary alcohols and aldehydes to esters [2], and secondary alcohols to ketones [3], as illustrated in Scheme 4.7.

Ketones and esters



Scheme 4.7

Anodic electrolysis of methanolic solutions of aldehydes in the presence of KI or KBr in undivided cells transforms the aldehyde hemiacetals to esters by oxidation of the hemiacetal by the electrogenerated iodonium ion,

Esters

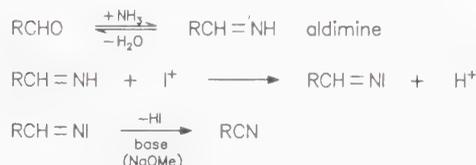


Benzyl benzoate (a pharmaceutical) has thus been prepared by electrolysis in aqueous solution containing benzyl alcohol and potassium iodide [4]. Aromatic aldehydes are oxidized by catalytic amounts of KI in methanol-NaOMe medium to give the corresponding methyl carboxylates using only theoretical amounts of electricity [5]. Aliphatic aldehydes with α -hydrogens are not suitable substrates because they undergo aldol condensations.

Methyl carboxylates

In the presence of NH_3 nitriles can be obtained via the aldimine intermediates which are in equilibrium with the aldehyde, Scheme 4.8

Nitriles



Scheme 4.8

The NaOMe facilitates removal of HI from the iodo intermediates. (Caution: formation of the explosive $\text{NI}_3(\text{I}_2 + \text{NH}_3)$ is possible.)

Warning, NI_3

Indirect epoxidations using the couples Cl_2/Cl^- and Br_2/Br^- were recently studied from an electrochemical engineering aspect by Alkire and Köhler [6]. Aqueous dispersions of 1-hexene were electrolyzed in undivided cells with parallel-plate electrodes in the presence of the halide catalysts. Epoxide current efficiencies of 65% were attained. Steckhan and coworkers [7] demonstrated that it is possible to methoxylate N-protected aminoacid esters in the α -position relative to nitrogen by indirect electrolysis in methanol solution using chloride ion as primary mediator. For example, the methoxylation of N-benzoyl glycine methyl ester occurs by an overall process involving the in situ generated MeOCl reagent as indicated in Scheme 4.9. The process is analogous to the chemical process in which *tert*-butyl hypochlorite would be employed in at least stoichiometric amounts.

Aminoacid esters

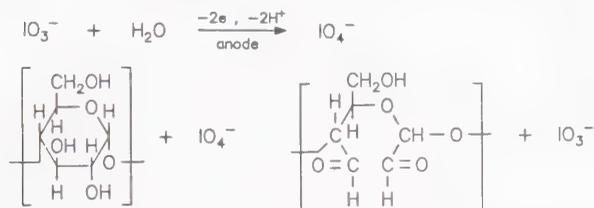


Scheme 4.10

This technique takes advantage of two opposite indirect reactions, an anodic oxidation and a cathodic reduction, and may therefore be viewed as a paired *doubly indirect* electrosynthesis process.

Polysaccharides have been indirectly oxidized using the $\text{IO}_4^-/\text{IO}_3^-$ or the Cr(IV)/Cr(III) redox couples as mediators. The mediated oxidation of starch to dialdehyde starch was practiced for some time on an industrial scale [12]. The IO_4^- was regenerated either in situ or ex situ. The process was discontinued apparently because the product demand was limited.

**Oxidation
of poly-
saccharides**



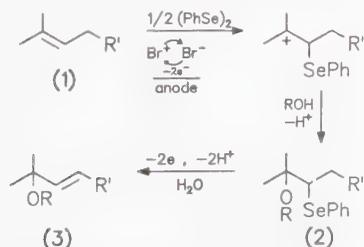
The periodate-iodate redox mediatory system has been considered for the oxidation of a number of biomass-derived materials. An optimization study was conducted for the “in-cell” indirect conversion of 2,3-butanediol to acetaldehyde in a divided cell and with lead dioxide as anode [13]. The needed periodate is formed at the anode while the diol is oxidized in solution to give 80% yields of acetaldehyde. Direct anodic oxidation gave low aldehyde yields. In order to minimize catalyst losses and improve product recovery Yoshida and coworkers developed a technique using hydrobromides of polymeric amines such as poly(4-vinylpyridine) in the form of beads which are stirred between anode and cathode. The immobilized oxidant is most probably the Br^- groups on the surface of the beads [14].

**Oxidation
of biomass-
derived
materials**

Indirect oxyselenylation and deselenylation for the one-step transformation of olefins into allylic alcohols and ethers has been accomplished with the Br^+/Br^- redox couple as mediator. By such a process a reaction with the olefin in the presence of an alcohol takes place [15]:

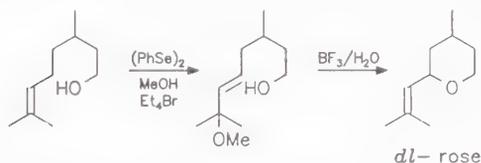
**Immobilized
oxidant**

**Oxyseleny-
lation and
deselenylation**

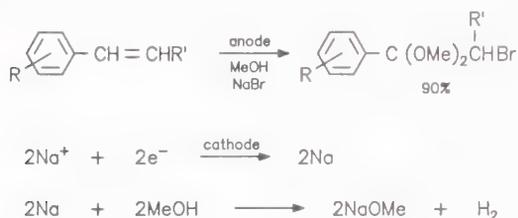


Scheme 4.11

The essential step in this reaction, Scheme 4.11, is the formation of the intermediate (2) which by further oxidation leads to compound (3). Torii et al. reported the conversion of citronellol to the cyclic ether, *dl*-rose [15] by electrolysis in methanolic solution containing $(\text{PhSe})_2$ and Et_4Br , and hydrolysis of the intermediate methoxylated product,



Conjugated aryl olefins are transformed to α -bromoketals by indirect oxidation in methanol/bromide solutions in undivided cells. The electrode reactions are shown in Scheme 4.12 [16].

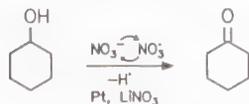


Scheme 4.12

4.2.4 Nitrate Ion as Mediator

Oxidation of alcohols

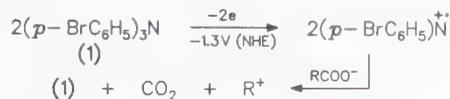
The nitrate ion may act as an effective mediator in the oxidation of some alcohols that are difficult to oxidize directly at the anode. For example, 2-butanol requires a potential about 2.4 V versus the Ag/Ag^+ to deelectronate at a platinum anode. In the presence of nitrate ion high yields of the ketonic product are obtained. A potential of 1.6 V at which the NO_3 radical is generated is sufficient for the oxidation of the alcohol [1]. Hexanol is oxidized by NO_3 radicals to the ketonic product in 80% current yield whereas the yield in the absence of NO_3^- is only 5%.



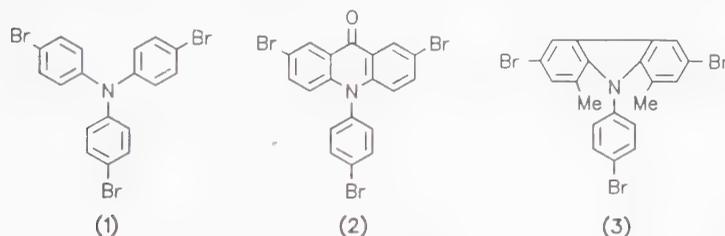
4.2.5 Organic Mediators for Oxidations

Electrogenerated organic cation radicals may act as electron transfer oxidants in a catalytic manner provided the redox couple is stable and

reversible in the particular electrolysis system. The couple tri-*p*-bromophenylamine and its cation radical is an effective electrocatalytic couple for indirect oxidations of organic compounds [1]. An example is the homogeneous electrocatalytic decarboxylation of *n*-alkylcarboxylates ($n = 6, 7, 12$) in the presence of tris-(4-bromophenyl)amine in acetonitrile solution. Esters and nitriles are thus produced:

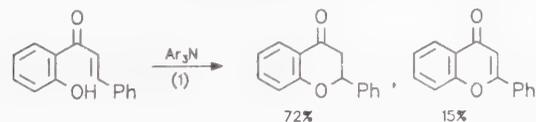


Steckhan and Schmidt prepared several triarylamines and tested them as redox catalysts [2]. Typical of such amines are the following:



Standard potentials of these materials are in the range 0.75 to 1.96 V, depending on the structure and ring substituents.

Anodic cyclization by indirect electrolysis of 2-hydroxychalcones to obtain flavonoids has been accomplished by electrolysis in methanol-dichloromethane solvent in divided cells in the presence of tris-(4-bromophenyl)amine as catalyst [3].



Another effective organic mediator for the oxidation of alcohols to aldehydes and ketones is the compound *N*-hydroxyphthalimide. Electrolysis is conducted in acetonitrile containing pyridine and sodium perchlorate. Thus 2-butanol gave 88% yield of ethylmethyl ketone [4].

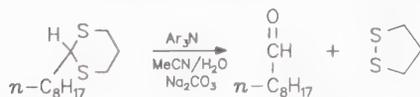
It is to be noted that oxidations catalyzed by the aforementioned organic mediators can be carried out under very mild conditions which allow successful selective oxidations of sensitive substrates and facile cleavages of protective groups as for example in the deprotection of the aldehyde shown below [5,6]:

Production of esters and nitriles

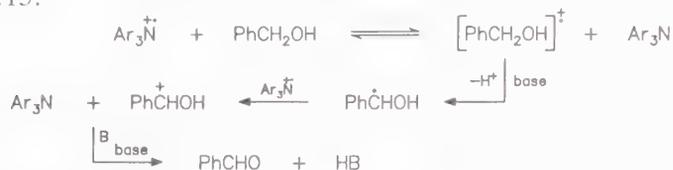
Triarylamines

Flavonoids

Aldehydes and ketones

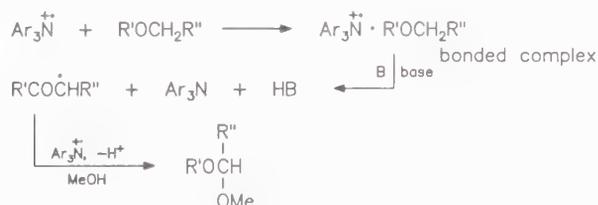


Benzaldehydes Benzylic alcohols are oxidized to their corresponding benzaldehydes in good yields in the presence of catalytic amounts of a triarylamine mediator and a weak base, such as Na_2CO_3 or 2,6-lutidine, to facilitate proton abstraction from the intermediate products [6], as is indicated in Scheme 4.13:



Scheme 4.13

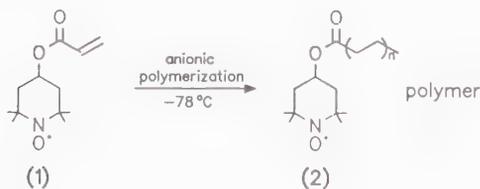
Bonded-type mechanism It is of interest to note that esters and acetals, which are very difficult to oxidize directly at the anode, are easily oxidized by the action of triarylamine cation radicals. These reactions occur most likely by a *bonded-type* (inner sphere mechanism), as proposed by Steckhan [7] in the α -methoxylation of aliphatic ethers, Scheme 4.14:



Scheme 4.14

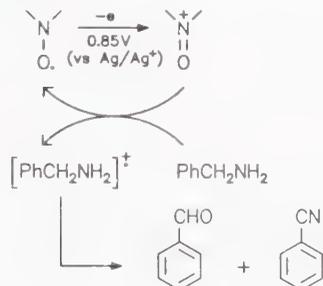
According to Ebersson, such *bonded* or *inner-sphere* mechanisms would operate most effectively when there is a large potential difference between the substrate and the mediator [8].

Electroactive organic films as oxidative mediators Some attention has been given to potential applications of electroactive organic films as oxidative mediators [9,10]. Such films are functionalized polypyrroles, polyanilines and polymeric nitroxides. The last are good one-electron transfer catalysts [10]. The polymer (2) made from the nitroxide monomer (1) is an efficient mediator for the oxidation of amines [10].



The catalytic activity of the polymer(2) is depicted below for the oxidation of benzylamine. The electrolysis is carried out in acetonitrile-lithium perchlorate medium with a graphite fiber cloth electrode coated with a monolayer of polymer(2). This heterogeneous electrocatalytic oxidation gave benzaldehyde and benzonitrile with 78% and 22% current efficiencies, respectively.

Polymer coated electrode



A polyaniline modified stainless steel electrode was found to be an effective electrode for the oxidation of hydroquinone to benzoquinone [9]. Electroactive organic films with electrocatalytic properties are easily tested for their effectiveness by cyclic voltammetry. The electrode is coated with a thin layer of the polymeric organic film and cyclic voltammograms are recorded with the film-modified electrode using a suitable electrolysis medium. If the film is reversibly electroactive two peaks of equal height appear as shown in Figure 4.1. The peaks will change in some way when an organic substrate that is oxidized or reduced by the mediator film added to the solution. The effective film-life may also be tested by periodic voltammetric scans during prolonged electrolysis conditions.

Benzoquinone

Polyaniline modified electrode

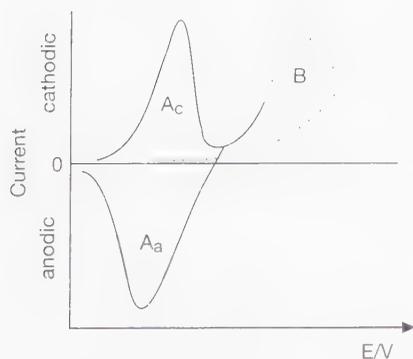


Fig. 4.1. Cyclic voltammogram of a hypothetical electroactive film *A*: in the absence of organic substrate *B*: in the presence of organic substrate (oxidizable in this case)

4.3 Indirect Reductive Reactions

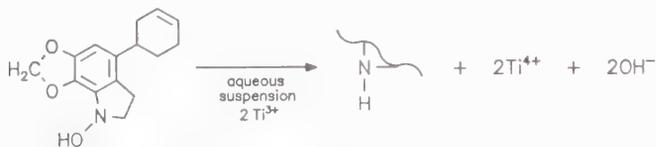
Homogeneous electrocatalysts

In indirect reductive methodology low-valent metallic ions and oxyanions are the usual mediators or homogeneous electrocatalysts. In aqueous or aqueous-organic media the electroreduction of high-valent ions to the lower valency states occurs preferably before hydrogen evolution at the cathode.

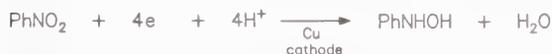
4.3.1 Metallic Ions as Catalysts

Reductive Mediators Ti^{4+}/Ti^{3+} couple

Ordinary metallic ions in their lower oxidation states, such as the ions Fe^{2+} , Cr^{2+} , Sn^{2+} and Ti^{3+} are effective reductive mediators. Even in cases of direct heterogeneous electrolysis the overall electrochemical process may be improved by the addition of appropriate amounts of the mediators. Mediated electrochemical reductions may sometimes eliminate the need of the reducing agents lithiumaluminum hydride or tributyltin that are necessary for certain difficult chemical reductions of organic compounds. Thus an N—OH function can be selectively reduced to the N—H function by electrolysis in aqueous media in the presence of the Ti^{4+}/Ti^{3+} couple [1].

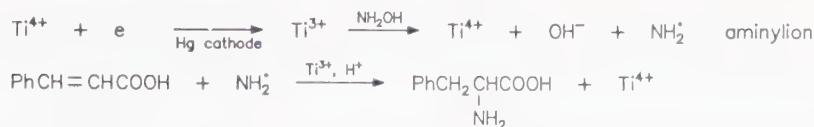


The compounds *p*-nitrosophenol and *m*-nitrotoluene are indirectly reduced to *p*-aminophenol and *m*-toluidine, respectively in the presence of the Ti^{3+}/Ti^{4+} redox couple [2]. The titanium couple enhances the yield of aniline from the direct reduction of nitrobenzene in acidic solution [3]:

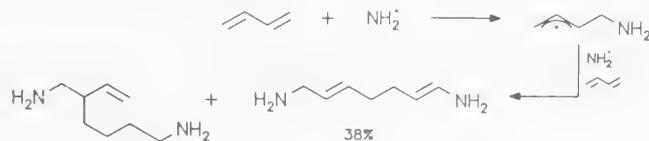


Aniline Amino acid synthesis

The Ti^{3+}/Ti^{4+} couple was employed successfully in electroaminations for the synthesis of amino acids. Aspartic acid was obtained by electrolysis of hydroxylamine in the presence of Ti^{3+} and maleic acid [4]. This couple was used to prepare dl-phenylalanine by electrolyzing cinnamic or 3,4-dihydrocinnamic acid in $2MH_2SO_4$ solution via generation of aminyl radicals according to the method used by Sammels [5], as shown below:

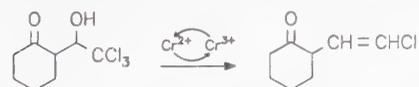


Aminyl ions thus generated add to certain unsaturated systems to give diamino compounds [6]:



Yeager and coworkers [7] recently reported on the catalytic effects of heat-treated mixtures of polyacrylonitrile with Co(II) or Fe(II) salts for the electrolytic reduction of oxygen in both alkaline and acidic solutions. An extension of this catalysis system to organic electrosynthesis might be contemplated. Titanous salts can be used as mediators in micellar electrolysis systems [9,10]. In such media the electrolysis is facilitated by the enhanced miscibility of the organic substrate with the aqueous phase, although sometimes the micelles formed are of a type that inhibit rather than enhance the desired effect, depending on whether they are anionic, cationic or monionic. It was reported that the cyanation of methoxybenzenes was favored by cationic micelles but inhibited by the other types [11].

Wolf and Steckhan studied the mediated reduction of trichloromethyl carbinols and their corresponding ethers in $\text{H}_2\text{O}/\text{DMF}$ media containing chromous chloride as a mediator. It was thus possible to obtain Z-monochlorovinyl compounds in good yields in one step.



The chromous ion was generated in situ and ex situ. These reductions are greatly facilitated by the trichloromethyl group in the α -position with respect to OH or the ether oxygen position in the starting molecules. Pinacolizations (reductions of ketones) are assisted by chromous ion – which, although is not able to reduce the ketonic carbonyl, forms a CrIII-carbonyl complex which is easily reduced at the cathode [13]

A natural reductive mediator is the biologically important cobalt-containing vitamin B₁₂. This cobalt complex and some much simpler models thereof have been found to be reductive catalysts for dehalogenations and couplings of organic compounds [15]. Under appropriate irradiation conditions they also catalyze additions and alkylations [15].

Reductive reactions using cobalt complexes as mediators may be useful for the synthesis of some natural, biologically interesting compounds. Thus cleavage of C—Br bonds in certain olefins or acetylenes by elec-

Aminyl ions

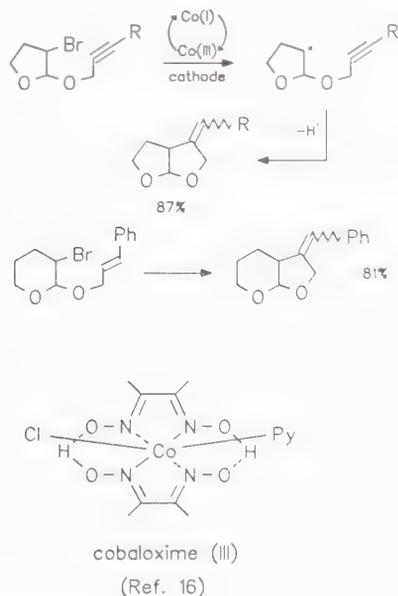
Z-mono-chlorovinyl compounds

Vitamin B₁₂

Cobalt complexes mediators

Cyclopentanoid products

tolysis with the Cobalt(I)/Cobalt(III) complex redox couple as mediator leads to the formation of cyclopentanoid products [16], as indicated in Scheme 4.15. The cobaloxime(I) is generated at the cathode from cobaloxime(III) at -1.45 V (vs Ag^+/Ag).



Scheme 4.15

These electrolyses are performed in divided cells equipped with platinum electrodes in methanol solution containing tetraethylammonium tosylate as electrolyte. The catholyte contains the bromo compound and cobaloxime(III) in about 3:1 ratio. A constant current of 15 mA cm^{-2} is passed through the solution under an inert gas atmosphere. The products are extracted with hexane-ether solvent from the diluted with cold water catholyte solution. They are purified chromatographically and characterized spectroscopically by the usual techniques and elemental analysis. It is noted that these cyclizations can be effected chemically in aprotic solvents with trialkyltin hydride as reductant.

Symmetrical ketones

Symmetrical ketones were obtained by electrocarboxylation catalyzed by nickel bipyridyl complexes, Ni^0bpyCO , by electrolysis in DMF or *N*-methylpyrrolidone containing an organic halide [17,18] in one-compartment cells with a consummable magnesium anode:

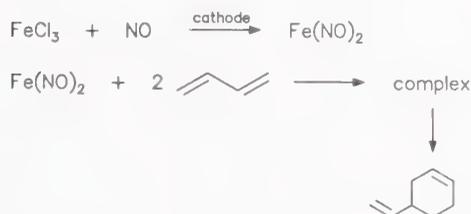


Aliphatic, allyl and benzyl halides afford mainly ketonic products while aryl and vinyl halides are transformed to their acyl analogs.

Substituted olefins have been prepared via catalytic couplings of aromatic halides and alkenes with in situ generated organonickel-phosphine complexes [19] as catalysts:



Dinitrosyliron complexes have been used as catalysts for cyclodimerizations of conjugated dienes [20]. The iron complexes are generated in situ by reduction of FeCl_3 in the presence of NO in a propylene carbonate solution:



4.3.2 Reductions with Amalgams

Reductions with amalgams of the alkali and alkaline earth metals and the more powerful reductants, the tetraalkylammonium ($\text{Q}_4\text{N}(\text{Hg}_5)$) amalgams are a special type of indirect electrochemical reductions [21–23]. These amalgams are produced by electrolysis at very negative potentials, using mercury pool cathodes. The produced amalgams are believed to be formed stoichiometrically as indicated with the organic Q_4N^+ cation:



Also tin, bismuth and lead form similar amalgams. Graphite forms *intercalation* compounds between its layers which may act like amalgams in certain reductions [24]. Amalgams are able to transfer electrons to organic compounds that are difficult to electronate, such as aryl fluorides, aliphatic ketones, benzene, benzofurans, aryl esters and aryl amides. The amalgam can be continuously regenerated by applying the required potential to the mercury cathode. Therefore, the reduction can be viewed as an electrocatalytic mediated heterogeneous reductive process. These reductions fall in the general category of *dissolving metal* reductions or *Birch-type* reductions in which direct electron transfer takes place from the metal or the Q_4N^+ radical species to the organic substrate in contact with the amalgam or with the metal in liquid ammonia:

Acyl analogs

Substituted olefins

Iron complexes



Electrolysis of olefins is performed similarly in diglyme-NaI-NaBH₄ medium, giving the following typical yields of the corresponding alcohols:

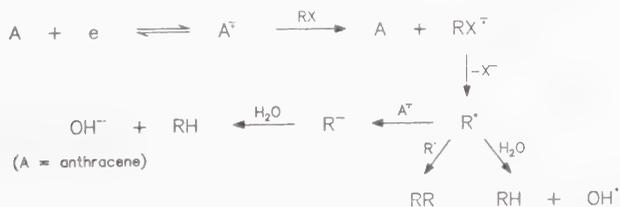


(Conventionally such reductions are effected by reactions with metallic hydrides and catalytic hydrogenation.)

4.3.4 Organic Mediators

Organic mediators for electrochemical reductions are substances that can be reversibly reduced at the cathode to yield anion radicals that are stable in the electrolysis medium and also able to transfer an electron to the organic substrate. Typical such mediators are: azobenzenes, anthracenes, benzonitriles, phenanthridines, some organometallic complexes and metalloporphyrins. For example, anthracene is a mediator for the hydrogenolysis of halobenzenes and halopyridines [1]:

Anthracene



Anthracene effectively mediates the reduction of benzyl and aryl halides by transferring electron in steps to produce radicals B[·] and anions B⁻, from the benzyl or aryl halides [3]. The anions act both as bases and as nucleophiles. Couplings of B[·] with B⁻ are insignificant:

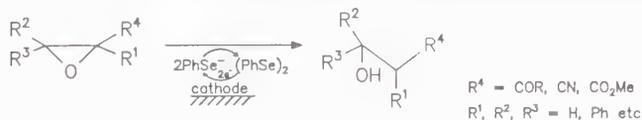


Azobenzene

Azobenzene is a good redox catalyst in acetonitrile solution for organic halides such as bromobenzophenone.

**Diphenyl-
diselenides and
ditellurides**

Diphenyldiselenides and ditellurides are good reductive mediators for the transformation of α,β -epoxy compounds to β -hydroxy carbonyl compounds [4]. Also, α,β -epoxyketones and α,β -epoxy esters and nitriles are easily converted to aldols and β -hydroxy analogs in the presence of these mediators. A formal typical example is depicted below:

**DMP⁺**

Dimethylpyrrolidinium ion (DMP⁺) is a mediator for reductions at lead electrodes [5]. This electrocatalysis is heterogeneous in the sense that the reduction of DMP⁺ forms an amalgam-type (DMPPb₅) monolayer at the surface of the lead electrode. This monolayer amalgam acts catalytically for the reduction of alkyl halides – but not for other substrates. Organorhodium complexes are effective reductive mediators [6]. Bis(bipyridine) rhodium is an efficient two-electron transfer agent for the electrochemical generation of NADH from NAD⁺. Direct reduction of NAD⁺ gave mainly dimers of NAD.

**Organor-
hodium
complexes****Biological
redox catalysts**

In concluding this section we refer to the biological redox catalysts such as the various metalloporphyrins, chlorophylls, hemoglobin and vitamin B₁₂ which are indispensable catalysts for life processes in plants and animals [7,8]. The catalytic activity of these organometallic substances is attributed to the reversible electron transfer process of the transition metal (Mg, Fe, Co) in the *N*-macrocyclic complex.

References

Section 4.1 Introduction

1. Steckhan E (1986) *Angew Chem, Int Ed Eng* 25:683; Gross-Brinkhaus KH, Steckhan E, Schmidt W (1983) *Acta Chem Scand* B37:499
2. Alkire R, LaRoche R, Cera G, Stadtherr M (1986) *J Electrochem Soc* 133:290
3. Pichaichanarong P, Spotnitz RM, Kreh RP, Goldfarb SM, Lundquist JT (1990) *Chem Eng Commun* 94:119
4. Andrieux CP, Celis L, Saveant JM (1990) *J Am Chem Soc* 112:786
5. Ebersson L (1980) *Acta Chem Scand* B34:481; (1984) *Acta Chem Scand* B38:439
6. Kyriacou D, Jannakoudakis D (1986) *Electrocatalysis for organic synthesis*. Wiley-Interscience, New York
7. Wendt H (1984) *Electrochim Acta* 29:1513
8. Schmidt W, Steckhan E (1978) *J Electroanal Chem* 89:221
9. Shono T, Matsumura Y, Hayashi J, Mizoguchi M (1979) *Tetrahedron Lett* 165

- 9a. Ghaladi EA, Belccadi S (1988) *J Appl Electrochem* 18:27
- 9b. Taube H, Myers H, Rich RT (1983) *J Am Chem Soc* 75:4118
10. Ebersson L, Saik SS (1990) *J Am Chem Soc* 112:4484; Andrieux CP, Celis L, Medielle M, Pinon J, Saveant JM (1990) *J Am Chem Soc* 112:3509; Kochi JK (1990) *Acta Chem Scand* 44:409
11. Steckhan E, Dapperhed S, Grose Brinkhaus H, Sech T (1991) *Chem Ber* 124:255

Section 4.2 Oxidative Indirect Reactions (4.2.1 and 4.2.2)

1. Koel WJ (1969) US Patent 3448021
2. Torii S et al. (1982) *J Org Chem* 47:1647
3. Van Veen JAR, Van Der Eijk, DeRuter R, Huizinga S (1988) *Electrochim Acta* 33:1
4. Moyer BA, Thompson MS, Meyer TJ (1980) *J Am Chem Soc* 102:2310
5. Thompson MS, De Giovanni WF, Moyer BA (1984) *J Org Chem* 49:4972
6. Torii S, Inokutchi T, Sugiera T (1986) *J Org Chem* 51:55
7. Mayell JS (1968) *Ind Eng Chem, Proc Res Dev* 7:129
8. Kuhn AT, Birkett M (1979) *J Appl Electrochem* 9:777
9. Ibl N, Kramer K, Pinto L, Robertsen R, (1974) *AIChE Symposium Series* 18575:45
10. Chung RH (1978) In: *Kirk-Othmer Encyclopedia of Chemistry and Technology*, vol 2, 3rd edn, Wiley, New York, p 702
11. Heiba EI, Desau RM, Rodewald PG (1974) *J Am Chem Soc* 96:7977
12. Kurz ME, Chen TYR (1978) *J Org Chem* 43:239
13. Bellamy AJ (1971) *Acta Chem Scand* B33:208
14. Jow JJ, Lee TC (1987) *J Appl Electrochem* 17:753
15. Ito S, Katayama R, Kunai A, Sasaki K (1989) *Tetrahedron Lett* 30:205
16. Steckhan E, Wellman J (1976) *Angew Chem Int Ed Eng* 15:294
17. Tomat F, Rigo A (1976) *J Appl Electrochem* 6:257
18. Wellman J, Steckhan E (1977) *Chem Ber* 110:3561
19. Tzedakis T, Savall A, Clifton MJ (1989) *J Appl Electrochem* 19:911
20. Feszar B, Sobkoviak A (1983) *Electrochim Acta* 28:1351
21. Kinoshita T, Harada J, Ito S, Sasaki K (1983) *Angew Chem Int Ed Eng* 22:502
22. Bhadani SN, Ansari Q (1988) *Makromol Chem Rapid Commun* 9:171

Section 4.2.3 Halide Ions as Mediators

1. Stevens RV, Chapman KT, Weller HN (1980) *J Org Chem* 45:2030
2. Shono T, Matsumura Y, Hayski J, Mitsoguchi M (1979) *Tetrahedron Lett* 165
3. Shono T et al. (1985) *J Org Chem* 50:4917
4. Dixit G, Rastogi R, Zutshi K (1982) *Electrochim Acta* 27:561
5. Okimoto M, Chiba T (1988) *J Org Chem* 53:218
6. Alkire R, Köhler J (1988) *J Appl Electrochem* 18:405
7. Ginzel KD, Brungs P, Steckhan E (1989) *Tetrahedron* 45:1691
8. Barba F, Garsia PA, Guirado A, Zapata A (1982) *Carbohydr Res* 105:158
9. Iwasaki T, Nishitani T, Horikawa H, Inoue I (1982) *J Org Chem* 47:3799
10. Jackson C, Kuhn AT (1973) In: Kuhn AT (ed) *Industrial electrochemical processes*. Elsevier, Amsterdam, p 153
11. Thomas HG, Lux E (1972) *Tetrahedron Lett* 10:965
12. Mehlretter CL, Rankin JC, Watson PR (1957) *Ind Eng Chem* 49:350
13. Yoshizawa TC, Nonaka T, Baizer MM, Chou TC (1985) *Bull Chem Soc (Japan)* 58:201
14. Yoshida J, Hashimoto J, Kawaba N (1982) *J Org Chem* 47:3575
15. Torii S, Uneama K, Ono M, Barnou T (1981) *J Am Chem Soc* 103:4606
16. Nikishin GI, Elinson MH, Makhova IV (1988) *Tetrahedron Lett* 29:1603

Section 4.2.4 Nitrate Ion as Mediator

1. Leonard JE, Scholl PC, Steckel TP (1980) *Tetrahedron Lett* 21:4695

Section 4.2.5 Organic Mediators for Oxidations

1. Schmidt W, Steckhan E (1978) *J Electroanal Chem* 89:215; Gunic J, Tabakovic I (1990) *Electrochim Acta* 35:225; Lund H, Tabakovic I (1984) *Adv Heterocycl Chem* 36:235
2. Schmidt W, Steckhan E (1980) *Chem Ber* 113:577
3. Sanicarin Z, Tabakovic I (1986) *Tetrahedron Lett* 27:407
4. Masui M, Ushima T, Ozaki S (1983) *J Chem Soc Chem Commun* 479
5. Platen M, Steckhan E (1978) *Angew Chem, Int Ed Eng* 17:673
6. Platen M, Steckhan E (1980) *Tetrahedron Lett* 21:511; Platen M, Steckhan E (1984) *Liebigs Ann Chem* 1563
7. Cinzel KD, Steckhan E (1987) *Tetrahedron* 43:5597
8. Eberson L (1982) *Adv Phys Org Chem* 18:79
9. Derongier A, Moutet JC (1989) *Acc Chem Res* 22:249
10. MacCorquodale F, Crayston JA, Walton JC, Worsfold DJ (1990) *Tetrahedron Lett* 31:771

Section 4.3 Indirect Reductive Reactions

Section 4.3.1–4.3.3 Metallic Ions as Catalysts

1. Fegori G, Lund H (1976) *Acta Chem Scand B*30:651
2. Unatharaman PN, Udupa HVK (1983) *J Electrochem Soc (India)* 32:51
3. Kargin YM, Kamalova GA (1989) *J Cen Chem (USSR)* 58:2063
4. Farnia G, Sandova G, Viamello E (1978) *J Electroanal Chem* 88:147
5. Cook RI, Sammels AF (1989) *J Electrochem Soc* 136:1845
6. Chiba T, Takata Y (1978) *Bull Chem Soc (Japan)* 51:1481
7. Gupta S, Tryk D, Bae I, Aldred W, Yeager E (1989) *J Appl Electrochem* 19:19
8. Ref. 4, section 4.3.1
9. Udupa HVK (1980) *Electrochim Acta* 25:1083
10. Eberson L, Helgee B (1975) *Acta Chem Scand B*29:451
11. Laurent E, Rauniar G, Tomala M (1982) *Nouv J Chim* 6:515
12. Wolf R, Steckhan E (1986) *J Chem Soc Perkin Trans* 1:733
13. Sopher DW, Uteley JHP (1979) *J Chem Soc Chem Commun* 1087
14. Fournier F, Bertbelot J, Paskal YL (1984) *Tetrahedron* 40:339
15. Lexa RSD, Saveant JM, Sauplet JP (1979) *J Electroanal Chem* 100:159; Margel S, Anson FC (1978) *J Electrochem Soc* 125:1232
16. Torii S, Inokuchi T, Yukawa T (1985) *J Org Chem* 50:5875
17. Troupel M, Rollin V, Perichon J, Fauvarque JF (1981) *Nouv J Chim* 5:621
18. Fauvarque JF, Jutand D, Francois M (1988) *J Appl Electrochem* 18:109
19. Rollin Y, Meyer G, Troupel M, Fauvarque JF, Perichon J (1983) *J Chem Soc Chem Commun* 793
20. Le Roy E, Huchette D, Mortreaux A, Petit F (1980) *Nouv J Chim* 4:173
21. Settineri WJ, McKeever D (1975) In: Weinberg NL (ed) *Technique of electroorganic synthesis* Wiley-Interscience, New York, p 397
22. Kariv-Miller E, Lawin PB, Vajtner Z (1985) *J Electroanal Chem* 195:435
23. Simonet J, Lund H (1977) *J Electroanal Chem* 75:719
24. Birch AJ, Nasipari D (1959) *Tetrahedron* 6:148; Horner L, Newman H (1965) *Chem Ber* 98:3462
25. Shumdo R, Matsubara Y, Nishiguchi I (1992) *Bull Chem Soc (Japan)* 65:530

Section 4.3.4 Organic Mediators

1. Simonet J, Michel NA, Lund H (1974) *Acta Chem Scand* B29:900
2. Avaca LA, Gonzales ER, Ticianelli EA (1983) *Electrochim Acta* 28:1473
3. Degrand C, Prest R (1987) *J Org Chem* 52:5224
4. Inokucuchi T, Kusomoto M, Torii S (1990) *J Org Chem* 55:1548
5. Lawin PB, Hutson AC, Kariv-Miller E (1989) *J Org Chem* 54:526
6. Wienkamp R, Steckhan E (1982) *Angew Chem, Int Ed Eng* 21:782
7. Dolphin D, Felton RH (1974) *Acc Chem Res* 7:26
8. Lexa D, Saveant JM (1983) *Acc Chem Res* 16:235

5 Some Special Topics Relevant to Electrosynthesis

In this chapter we overview some special topics of importance to organic electrosynthesis. Only a very brief general discussion of each topic is possible within the space of this book.

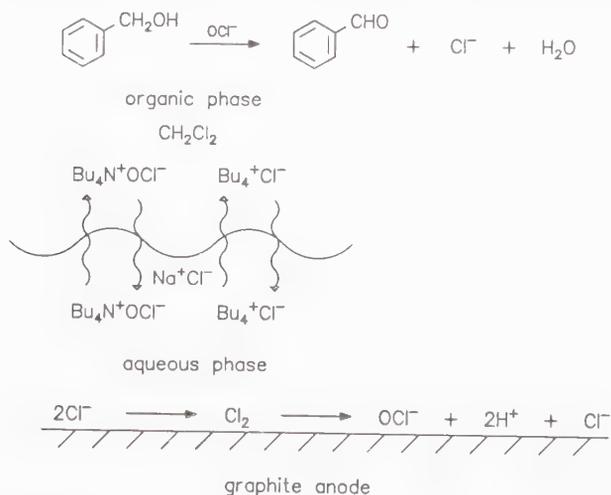
5.1 Electrolysis in Two-Phase Solvent Systems

Immiscible solvents, emulsions, dispersions, and micelles

Phase-transfer catalyst (PTC)

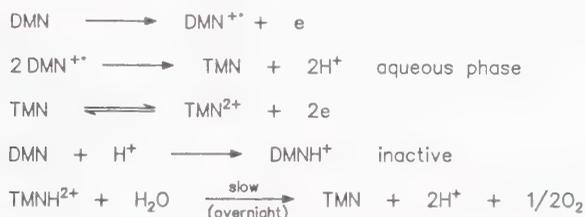
Benzaldehyde

Some electrochemical syntheses may be advantageously conducted in two-phase electrolysis media that are composed of two immiscible solvents, usually water and an organic solvent, such as dichloromethane or nitrobenzene. Emulsions, dispersions and micellar electrolysis media have been used as two-phase media for various synthetic applications. The recent reviews by Feess and Wendt [1] and reports by Pletcher [2] and Ebersson [3] and others [4–11] contain valuable information regarding this methodology. Two-phase electrolyses usually require the presence of a phase-transfer catalyst (PTC) such as a quaternary ammonium salt. A typical example is the indirect oxidation of benzyl alcohol to benzaldehyde, in $\text{CH}_2\text{Cl}_2/\text{H}_2\text{O}$ emulsion. The process is depicted in Scheme 5.1



Scheme 5.1

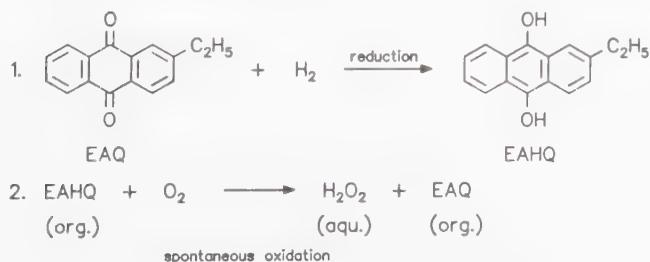
The benzyl alcohol is oxidized by the ClO^- ion which *shuttles* between the organic and the aqueous phase by associating with PTC. In a typical experiment [5] the two-phase system consisted of dichloromethane and 0.1 M NaCl aqueous solution, 70 ml of each. The concentration of benzyl alcohol in the CH_2Cl_2 solvent was 0.5 M, and the PTC was Bu_4NSO_4 . The anode potential was set at 1.3 V versus SCE, which is sufficient to oxidize Cl^- to Cl_2 . Current was passed under vigorous stirring of the emulsion (mechanical stirring 500 rpm). Benzaldehyde is produced with higher than 80% current efficiency. Naphthalenes are chlorinated in $\text{CH}_2\text{Cl}_2/\text{H}_2\text{O}/\text{NaCl}$ emulsions and afford their monochlorinated analogs in 40–90% yields [10]. It is possible in certain cases to achieve higher yields by two-phase electrolysis [12]. Thus optimum yields of *N,N,N',N'*-tetramethyl-1,1'-naphthadine (TMN) were obtained by electrolysis of *N,N*-dimethyl-1-naphthalamine (DMN) in water/nitrobenzene/ NaClO_4 emulsion. The optimization was ascribed to preferential removal of the generated protons into the aqueous phase thus minimizing formation of the inactive DMNH^+ . Scheme 5.2



Scheme 5.2

Styrene was polymerized in a two-phase medium consisting of styrene and formamide with zinc salts as electrolytes [13].

The electrochemical reduction of 2-ethylanthraquinone (EAQ) to 2-ethylanthrahydroquinone (EAHQ) in a two-phase system consisting of a mixture of 2-ethylbenzene and tributyl phosphate, and aqueous 2 M sodium hydroxide was recently studied under well-defined conditions by Tobias and coworkers [14]. It was found that the direct electrochemical reduction of EAQ was a feasible process as an alternate step in the industrial production of hydrogen peroxide. The manufacture of hydrogen peroxide involves two chemical steps:



Chlorination of naphthalenes

Polymerization of styrene

EAQ to EAHQ

Hydrogen peroxide manufacture

Direct electroreduction of EAQ took place at a lead cathode at the boundary of the organic/aqueous/electrode system. The electrolysis was carried out in a cell divided with a Nafion cation exchange membrane under controlled potential and an inert atmosphere. The catholyte was magnetically stirred so as to disperse the organic phase in the aqueous 2M NaOH phase. The anolyte was aqueous NaOH solution and the anode a nickel foil. Current efficiencies of about 100% and current densities of 30 mA/cm² were attained with cylindrical electrodes under vigorous turbulence electrolysis conditions. A cell voltage of 1.8 V was sufficient to start the electrolysis as shown by immediate red coloration of the catholyte solution. The overall reaction at the cathode was a two-electron process, expressed as follows:



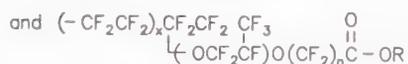
5.2 Solid Polymer Electrolyte – Electrolysis

Organic membranes

A solid polymer electrolyte, SPE, is an organic membrane, a polyelectrolyte, which while acting as a cell divided allows the passage of either anions or cations through it so that the electric current can be carried across the cell without the presence of a soluble electrolyte (supporting electrolyte).

Metal particles

It is possible to prepare SPE membranes with selective electrocatalytic properties by incorporating metallic particles on one or both sides of the membrane [5,6]. Thus far the Nafions 415, 417 and 315 have been given most consideration. A combination of cathode and anode is fabricated with the SPE membrane *sandwiched* between anode and cathode so that the cell is in effect divided by the SPE membrane. The metal particles can be deposited on the membrane either by electroplating or by chemical reduction of chloroplatinic acid with hydrazine [7]. Nafion-SPE are polyfluorinated ion exchange membranes based on perfluoroethylene-perfluoropropane oxide copolymers [4,8] with chemical structures represented as



SPE composite electrode

Poly(ethyleneoxide) and other materials are also investigated for uses as SPE [9]. A Nafion-415 cation exchange membrane modified with Cu-Pt was successfully used as a SPE *composite* electrode for the reduction of

nitrobenzene to aniline [7]. Current efficiencies of 95% were attained. Two sheets of expanded titanium mesh covered with platinum gauze were firmly pressed onto both sides of the SPE composite electrode to function as *current feeders*. The catholyte was a 30% nitrobenzene in methanol and the anolyte pure water. Thus no supporting electrolyte was needed in this system. The water was the proton source for the formation of aniline as the nitrobenzene was electronated at the cathode side of the SPE.

Metal-SPE-type electrodes have much larger active areas than ordinary metal electrodes of the same apparent geometric area. It was observed that the oxidation of CO on a Au-SPE composite electrode was about 100 times faster than at a gold electrode of similar geometric area [10]. The oxidations of isopropanol, *n*-octanol and propargyl alcohol were studied using SPE-cells. High yields of oxidized products were obtained [11]. Electrocatalytic oxidations of alkyl alcohol vapors at Au-Nafion 117 composite electrodes were recently reported [12]. Poly(aniline)-Nafion and poly(3-methylthiophene)-Nafion composite films were prepared by a one-step electrolysis in propylene carbonate using Li^+ -Nafion and H^+ -Nafion and the monomer precursors of the electronically conducting polymers poly(aniline) or poly(3-methylthiophene) [13]. Such materials may find uses as SPE for some special synthetic applications. Figure 5.1 represents typical SPE cells.

Reduction of nitrobenzene

Current feeders

Oxidations of isopropanol, *n*-octanol, and propargyl alcohol

Oxidation of alkyl alcohol vapor

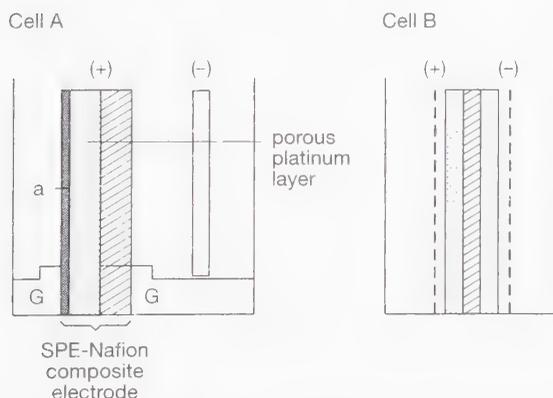


Fig. 5.1. Schematics of SPE-Composite electrode Cells

Cell A: With one side Pt-SPE composite electrode as anode. a: current collector, a platinum screen firmly pressed against the porous platinum layer deposited on the SPE membrane (nafion). G: teflon gaskets

Cell B: With Pt-SPE composite electrodes on both sides of the SPE membrane. One side acting as anode and the other as cathode

5.3 Reactions via Electrode Dissolution

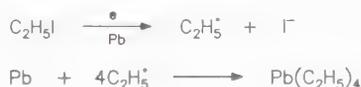
Organometallics

Under certain electrolysis conditions the electrode itself may become one of the reactants or a special catalyst in the overall synthetic reaction [1]. Electrogenerated radicals may attack the metal electrode thus causing formation of organometallics containing carbon-metal bonds. Such possibilities are more common at cathodes than at anodes. Tetraalkyl lead compounds are produced by attack of alkyl radicals on the lead electrode (Nalco process [2]):



Tetraethyl lead

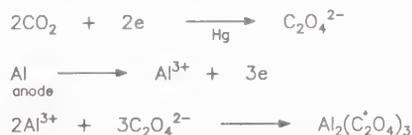
Ethyl iodide produces radicals at a lead cathode which attack the electrode to form tetraethyl lead:



Alkylation of aromatic rings

Aluminum anodes in the presence of alkyl halides afford upon anodic dissolution Friedel-Crafts catalysts for in situ chemical alkylation of aromatic rings [3]. Electroreduction of CO_2 in DMF/0.1 M Bu_4NBr and dissolution of an aluminum anode result in the formation of aluminum oxalate [4] with 38% current yield.

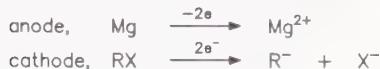
Aluminum oxalate



Carboxylations of alkenes, ketones, organohalides, aldehydes and imines

The dissolvable anode methodology makes possible the use of undivided cells and the application of high pressures needed for certain electrosynthetic processes [1]. Cathodic carboxylations of a wide variety of organic substrates have been reported in recent years using metallic anodes which thermodynamic and kinetic factors allow to dissolve upon anodic polarization in organic solvents. Carboxylations of alkenes, ketones, organohalides, aldehydes and imines are conveniently performed in cells with dissolvable metallic anodes. The dissolved metals may be recovered by electrolytic reduction or by precipitation with OH^- and subsequent isolation as metallic oxides. Activated methylene compounds are very easily monoalkylated in undivided cells fitted with consumable magnesium anodes, in DMF/ Bu_4NBF_4 media [5]. Constant current electrolysis in an undivided cell with a magnesium rod anode and a cylindrical stainless steel cathode gave high yields (80–85%) of alkylated products according to the following reaction scheme:

Monoalkylation



overall cathodic reaction

RX = EtBr, PhCH₂Cl

RCH₂A = active methylene substrate eg. PhCH₂CO₂Et, PhCH₂CN

Alkoxides of metals and metalloids have been prepared electrolytically using metals or metalloids as anodes [6]. Tetraethyl silicate is produced by electrolysis in ethanol solution and a ferrosilicon anode. Tetramethylsilane and dimethyldichlorosilane were obtained by electrolysis in LiCl-CH₃Cl-cellosolve with Si-Cu or Si-Ca anodes by dissolution of the silicon-containing electrode [7].

Cationic polymerizations are initiated by anodic dissolution of certain sacrificial anodes [8]. The polymerization of styrene lactones and other monomers was effected by electrolysis in CH₂Cl₂ or CH₃NO₂ solvents with Bu₄NClO₄ as electrolyte using mercury or aluminum sacrificial anodes. (Cu, Ag, Sn, Pb were not effective for polymer initiation.) Benzoaniline was electrocarboxylated to give the corresponding α-amino acid in a filter-press type cell with semicontinuous renewal of sacrificial electrodes [9].

We have already referred to the electrochemical preparation of metallic salts of aliphatic carboxylic acids and the preparation of metallic alkoxides by anodic dissolution of metal electrodes. The preparation of metal thiolates of Zn, Cd, Hg, Pb and Sn by anodic dissolution of these metals has been recently reported [10].

Dissolution of elemental sulfur and silicon may result in the formation of organoelemental bonds as shown below [10]:



Electrochemical preparation of tetradentate Schiff-base complexes of Zn(II), Cd(II) and Ni(II) have been effected using the appropriate metal as the consumable anode in acetonitrile containing the ligand (H₂L) and tetrabutylammonium perchlorate as electrolyte [11], as indicated below:

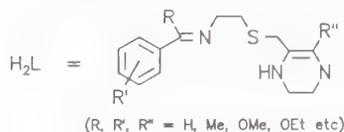
**Alkoxides,
silicates,
and silanes**

**Cationic
polymerization**

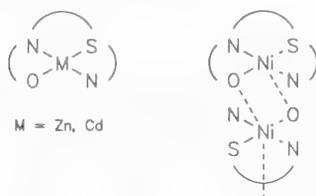
α-amino acids

Metal thiolates

**Tetradentate
Schiff-base
complexes**



The complexes were isolated as powders, monomeric with zinc and cadmium and at least dimeric with nickel, as implied in the abbreviated structures below:



A review concerning consumable anode methodology has been published recently [12].

5.4 Electropolymerizations. Conductive Polymers

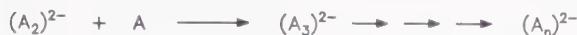
5.4.1 General View

Although it has been known for quite a long time that organic monomers can polymerize by electrolytic methods there is no reference in the open literature to any industrial electropolymerization process. Electropolymerizations differ from the usual polymerization in that the former processes occur at the electrode surface and the electrode may become coated with the polymer. The process may thus stop unless the coating polymer is electrically conductive. Therefore conditions must be used that allow rapid diffusion of the initially generated low molecular weight polymer species to diffuse away from the electrode surface so that further polymerization may continue in solution.

Acrylonitrile monomer

Electropolymerizations have been carried out by both anodic and cathodic initiation [1,2,3]. An anionic-initiated polymerization such as one with the acrylonitrile monomer, A, may be described as follows:



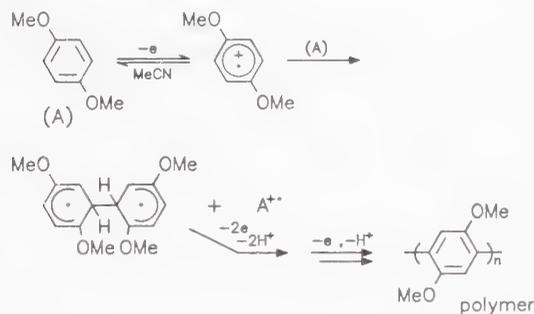


A free radical polymerization of styrene, S, can be initiated by a free radical species as one derived from the anodic oxidation of a carboxylate ion:



In electrolytic polymerization it is relatively easy to control the molecular weight distribution and possibly the polymer structure by manipulating the current-time parameter as in the "living polymer" process in which the reaction can be terminated by a single polarity reversal [1].

Anodic polymerizations of aromatics are well-known reactions. Benzene and *p*-methoxy derivatives are polymerized by an one-electron initiated process [3]:



Anodic polymerization of benzene in liquid sulfur dioxide yields poly-*para*-phenylene films which are electroactive if the electrolyte is Bu_4NBF_4 but non-electroactive if the electrolyte is Bu_4NClO_4 . Electropolymerization of *ortho*- and *meta*-toluidine in aqueous sulfuric acid yields polymer films which have electrochromic properties [5].

Anodic polymerization of dithienylbenzenes in CH_2Cl_2/Bu_4NBF_4 solution gave polymeric films that could be cycled between yellow (reduced) and blue (oxidized) forms [5a]:



Electrooxidation of naphthalene in dry acetonitrile or in 1,2-dichloroethane with Q_4BF_4 salts as electrolytes gives the 1,4-polynaphthalene [6]. Hydro-

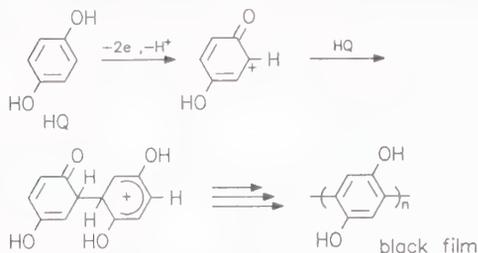
Styrene monomer

Control of molecular weight distribution and polymer structure

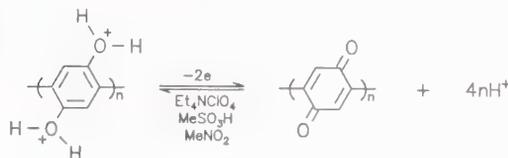
Electroactive and non-electroactive films

Films with electrochromic properties

quinone is polymerized by oxidation in $\text{CH}_3/\text{NO}_2/\text{Q}_4/\text{NClO}_4$ solution [7]. The polymerization proceeds cationically:

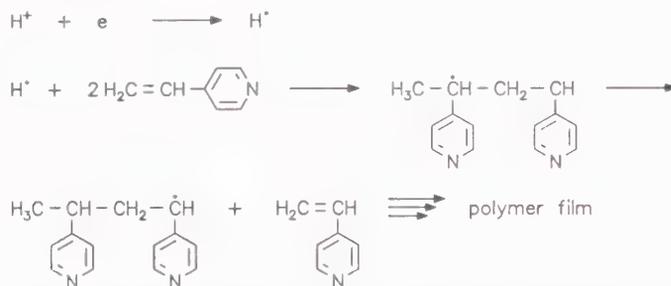


In acidic media the electroactivity involves the protonated polymer:



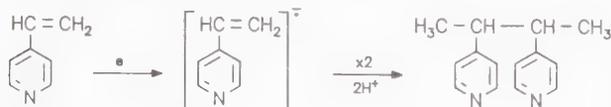
Vinylpyridine polymer

At a silver electrode in aqueous solution electrochemically initiated polymerization of 4-vinylpyridine was proposed to take place as depicted below [8]:



Vinylpyridine dimer

This electropolymerization occurs at the potential region of -0.1 to -1.0 V (vs Ag/AgCl). If the applied potential is more negative than -1.5 V the vinylpyridine molecules are directly electronated to give the anion radicals which dimerize to give dianions and are then protonated to afford the neutral dimer product:

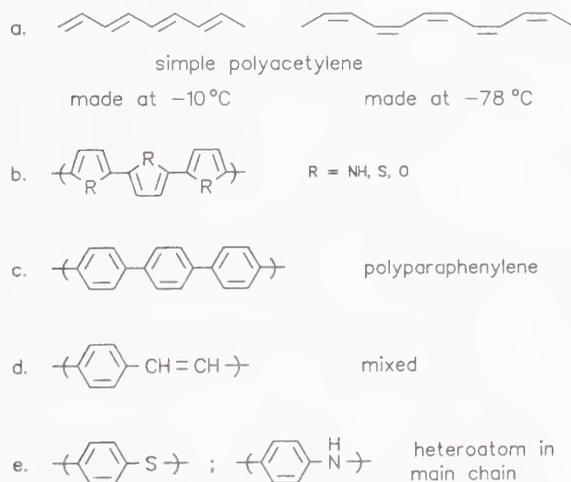


5.4.2 Conductive Polymers

In recent years – and particularly as a result of the developing semiconductor technology, the search for organic materials exhibiting electronic conductivity has become an active subject of study by both chemists and physicists. Following Little's article [9] (1964) the interest in *organic metals* grew exponentially. Polyacetylene was the first polymeric synthetic metal [10,12]. Following this work various polymers were synthesized exhibiting electronic conductivities in their oxidized or reduced states [11].

Organic metals

Polymeric organic conductors



It is apparent that all the polymers in these systems possess conjugated π -electron systems – otherwise they could not be conductive. In their pure state they are usually not conductive, but some of them may have semi-conductive properties. They become conductive upon “doping” by suitable chemical or electrochemical oxidations. By the process of doping they undergo injection of electrical charges into their main chains. These charges may be either positive or negative or only charges of one kind. Polypyrrole, polythiophene, polyaniline and derivatives are easily prepared by anodic oxidation methods [11,14,15]. Doping may be accomplished by intercalation and by controlled potential electrochemical procedures. Conductive organic polymers may be useful for a number of practical applications, e.g. light weight energy storage devices (solar batteries) and in electronic circuitry applications [16].

“Doping”

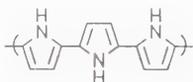
Electrochemical synthesis of conductive polymers allows preparation of layers of polymers of the desired thicknesses and shapes and dimensions generally not possible by chemical methods [17].

Solar batteries and electronic circuitry applications

Thus far most promising conductive polymers have been those made from the monomers of pyrrole, thiophene, aniline and benzene. These

polymers can be easily prepared electrolytically in organic or aqueous solutions. Conductivities are usually in the semiconductor range [10^{-9} to $(100 \Omega \text{ cm})^{-1}$]. The conductivities of today's polyacetylenes approach that of metallic copper. In general, the method of electrolysis affects to a great degree the electrical and physical properties of the polymer [18]. Polypyrrole is the best known of the conductive polymers. It does not require added dopants to be conductive [19]. Its chemical structure is written as

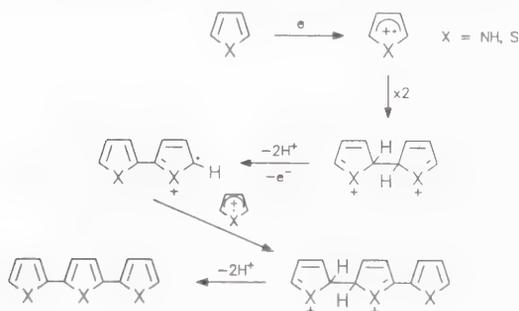
**Polypyrrole
the best known
conductive
polymer**



**Conductive-
nonconductive
switching**

This polymer "switches" between a black conductive form and a yellow nonconductive form by changing the applied potential on the underlying electrode so as to reduce or oxidize the π -electron network of the polymer. This switching may occur once per second. Polypyrrole films can be very easily obtained electrooxidatively in acetonitrile or water at platinum electrodes and can be peeled off from the electrode as free-standing films for various studies [20]. An account of various applications of polypyrrole films was recently given by Moutet [21].

The general mechanism of anodic electropolymerization of five-membered rings such as those of pyrrole or thiophene is analogous to that of the couplings of aromatic compounds [22]:



**Polyaniline
films**

Polymers of pyrrole, aniline, phenols, thiophene, furan and selenophene have been studied and continue to be studied very actively, especially since these polymers can be very conveniently prepared by simple electrochemical methods [23]. Polyaniline films are prepared by anodic oxidation of the monomer in aqueous hydrochloric acid solution [24].

**Photo-
sensitivity**

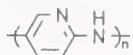
Electrochemical and photoelectrochemical synthesis of polypyrrole films containing TiO_2 particles exhibit photosensitivity. The electrosynthesis was carried out in ethanol under illumination of TiO_2 and in aqueous TiO_2 suspensions containing small amounts of electrolytes [25].

**Methylthio-
phene polymer**

Electropolymerization can often be easily accomplished in undivided cells. Electropolymerization of 3-methylthiophene monomer in nitroben-

zene/tetrabutylammonium hexafluorophosphate medium affords highly conducting films [26]. The films were 2000–4000 Å thick and had conductivities^a of 895–1975 S cm⁻¹. Electrooxidative polymerization of aminopyridine was carried out in an undivided cell fitted with platinum electrodes, in MECN/TetNBF₄ solution [27]. The structure of the polymer was given as,

**Aminopyridine
polymer**



Electronically conducting polymers were obtained by electrolysis of a mixture of 3-dodecylthiophene and 3-methylthiophene in nitrobenzene/Et₄NPF₆ medium [28]. An undivided cell fitted with an indium/tin oxide anode and a platinum cathode was used. The electrolysis was carried out at 5 °C and with a current of 2 mA/cm². Some electropolymerizations may be carried out in undivided cells using only the monomers without any solvent. Murray and coworkers [29] polymerized aniline and pyrrole by electrolyzing the monomers under nitrogen without any dilution of the monomer, except addition of the electrolyte, Bu₄NClO₄ or Et₄NOTS.

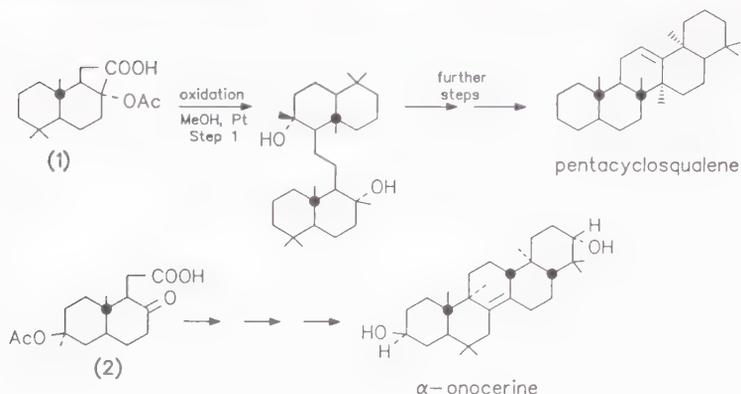
Organic polymers formed on electrode surfaces as films or in solution are expected to find applications as “composite” electrode materials or as polymers per se [30].

5.5 Applications of Electrochemical Methodology to the Synthesis of Natural Products

The synthesis of natural products is one of the most challenging tasks in synthetic organic chemistry. An important common characteristic of biosynthesis and electroorganic synthesis is that they involve reactions occurring under *mild conditions*. Various bond formations and particularly synthesis of cyclic intermediates for total synthesis of natural products may often be best achieved by electrochemical methods [1–4].

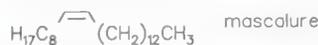
It is interesting to note that the oldest and first electroorganic method, that is, the Kolbe synthesis, has also been one from among the first methods to be applied to the electrochemical synthesis of natural products. The total syntheses of pentacyclosqualene [5] and α-onocerine [6] were accomplished some years ago starting with the carboxylic acids (1) and (2). The desired products were synthesized by well-planned combinations of Kolbe dimerization and chemical steps – admittedly, steps that only experts may hope to carry out successfully!

**Kolbe
synthesis**

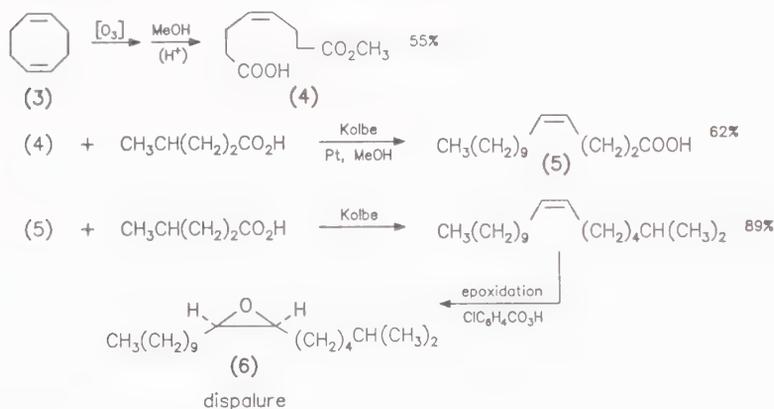


Pheromone synthesis

The Kolbe oxidation has been applied to the synthesis of some pheromones. Mascalure, the pheromone of the housefly, has been made by coelectrolysis of oleic and heptanoic acids [2,7] in 80% yield.



Klunenburg and Schäfer synthesized dispalure (6), the pheromone of the gypsy moth by double Kolbe electrolysis of *Z*-4-octanediacid half-ester (4) which was made from the cyclooctadiene (3). The synthesis is summarized in Scheme 5.3

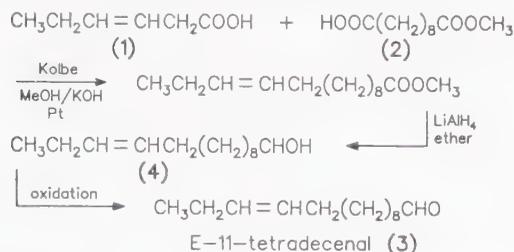


Scheme 5.3

The Kolbe electrolysis was conducted in methanol containing the mixed acids and some KOH to neutralize about 1% of the acids, in a cell fitted with platinum electrodes and under a current density of 240 mA/cm². Distillation of solvent followed by epoxidation of the electrolysis product gave the dispalure product. The pheromone of the eastern spruce budworm *E*-11-tetradecenal (3) and also the tetradecenol intermediate (4) shown

below were prepared by combining Kolbe-cross couplings with known chemical methods [9], Scheme 5.4

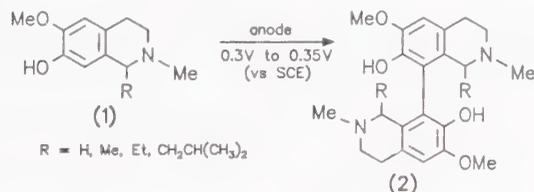
Kolbe cross couplings



Scheme 5.4

The Kolbe reaction was carried out in an undivided cell with two platinum (7cm^2) electrodes closely positioned to minimize the IR drop of the methanolic solution containing the substrates 1.4 g of (1) and 0.5 g of (2) and 0.8 g of KOH. The cell voltage was adjusted so as to allow a current of 0.2A/cm^2 to pass through the solution. The electrolyzed solution was diluted with water neutralized and extracted with ether (57% yield). After purification by elution chromatography the product was chemically transformed by reduction and oxidation to the desired pheromone *E*-11-tetradecenal. The electrochemical oxidation of a series of isoquinoline alkaloids was studied in depth by Bobbitt et al. in relation to biosynthetic oxidations involving C—C and C—O—C dimer formations [9a]. It was concluded that the anodic oxidation was more successful in regard to specificity than the catalytic oxidation method over platinum catalyst. The oxidation of corypalline (1) was studied in 0.1 M HCl and 0.1 M $\text{Na}_2\text{B}_4\text{O}_7$ solutions under controlled potential at $5\text{--}10^\circ\text{C}$ and under a nitrogen atmosphere. Anodes of Pt, Hg, and graphite felt were used. The reaction and product yields are shown in Scheme 5.5

Isoquinoline alkaloids Biosynthetic oxidations



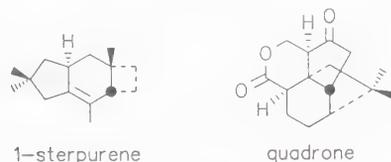
Medium	Electrode, %yield of (2)		
$\text{H}_2\text{O}_2/\text{Na}_2\text{B}_4\text{O}_7$	Pt, 50%	Hg, 70%	Graphite, 85%
$\text{H}_2\text{O}/\text{HCl}$	10–20%	—	35–40%

Scheme 5.5

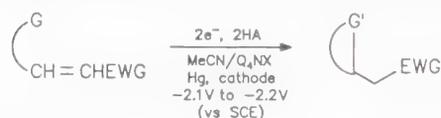
5.6 Electroreductive Cyclizations for Natural Product Synthesis (Little-Baizer ERC Reaction)

Construction of ring systems

A potentially most useful electroreductive cyclization reaction (ERC) has emerged from the recent studies of professors R. D. Little and the late M. M. Baizer at the University of California [10]. This novel electrochemical reaction can be of great synthetic value for the synthesis of natural products. It provides a new and efficient route [11] "for the construction of ring systems such as the five-membered ring subunit of sterpurene and the five- and six-membered rings found in the bicyclo 3,2,1 subunit of quadrone."



The general ERC reaction is synoptically expressed as follows:



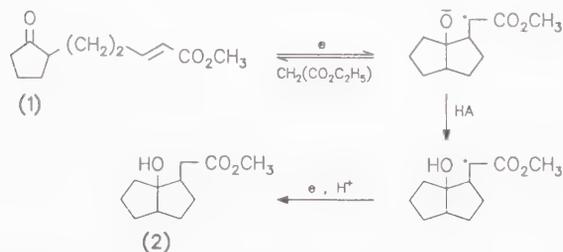
G = CH₂OMe, COR, C(=NR)R'

G' = CH₃, CH₂OH, CHOHR, CH(NHR)R'

EWG = electron withdrawing group, eg. CO₂CH₃

HA = proton source

The electroreduction proceeds by an one-electron transfer from the mercury cathode to the unsaturated unit, CH=CHEWG, of the substrate molecule, producing the anion radical. The anion radical undergoes closure onto G and protonates to give a neutral intermediate radical which electronates and protonates to afford finally the cyclized product. Suitable proton sources were found to be the carbon acids dimethyl and diethyl malonates. Thus reduction of the keto ester (1) to the cyclized product (2) occurs by an ECE process, Scheme 5.6

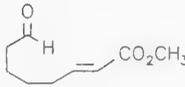
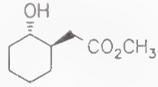
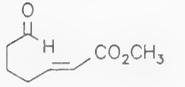
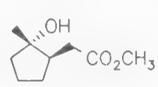
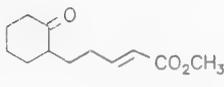
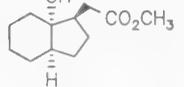
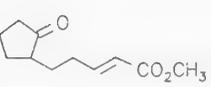
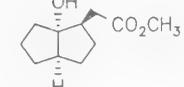


Scheme 5.6

The ERC reaction is carried out in an H-type cell with mercury pool as cathode at -2.2V (vs SCE) and a platinum foil as anode. The solvent for both anolyte and catholyte is dry degassed acetonitrile containing Et_4NOTs as electrolyte. The catholyte contains the substrate and the proton source in the molar ratio 4:1, respectively. The electrolyzed solution (the catholyte) is treated with acetic acid and the products after workup with water are isolated by chromatography (silica gel, 15–40% ether in skellysolve F). Table 5.1 includes typical substrates and products obtained by the ERC method. It is seen that the ERC method gives products with varying stereoselectivities with the OH and the ester group, *trans* to each other about the new σ -bond. The *trans* forms predominate when lower temperatures are used in the electrolysis. The results in Table 5.1 refer to electrolysis in 10% aqueous acetonitrile with Et_4NOTs as electrolyte. The electrolysis can be conducted in $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ media with careful addition (dropwise of acetic acid to prevent pH changes higher than the starting pH value, to prevent saponification).

Table 5.1 Typical substrates and products concerning the ERC method. (Only *trans* isomers are shown)

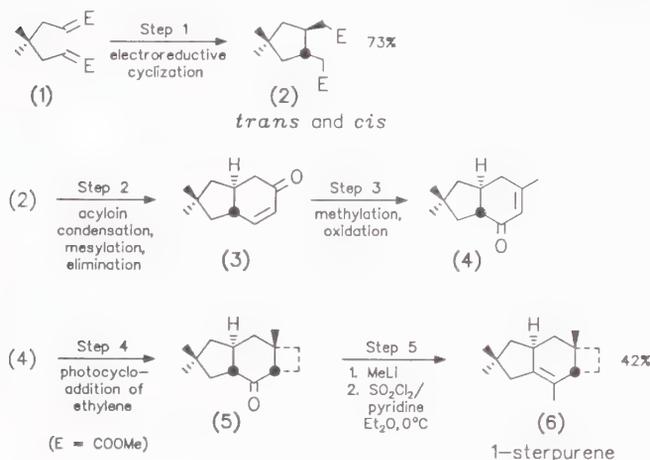
J. Org. Chem. 53:2287, 1988. Copyright of the American Chemical Society, 1988

substrate	product	<i>trans</i> : <i>cis</i>	%yield
		1.8 : 1	72
		1.4 : 1	70
		12.5 : 1	74
		11.4 : 1	79

In the total synthesis of 1-sterpurene (**6**), Scheme 5.7, (which is a fungus metabolite agent of the silver leaf disease) the ERC method was used [12] for the stereoselective cyclization via conversion of the bisenoate (**1**) to the *trans* diester (**2**). The electrolysis was performed in $\text{MeCN}/0.2\text{M Bu}_4\text{NBr}$ solution containing CeCl_3 (1.3 equivalents), 2 equivalents of $\text{CH}_2(\text{CO}_2\text{Et})_2$ and 0.033M of the bisenoate. The cathode was a mercury pool at a

Synthesis of 1-sterpurene

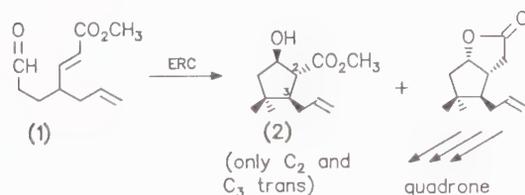
potential of -2.3 V (vs SCE). It was assumed that a complex of CeCl_3 with the substrate was formed which favored the desired stereoselectivity (14.8:1 *trans*:*cis*) for the desired diester intermediate products (2).



Scheme 5.7

Quadrone

The ERC method was used for the total synthesis of quadrone [13]. This synthesis is very complex to be described here. The reaction starts with an electroreductive, stereoselective cyclization step with the unsaturated ester (1) via which the first of the four rings of quadrone are produced. By a sequence of several, very sophisticated, chemical steps the required structure was achieved which led to the quadrone product, Scheme 5.8



Scheme 5.8

5.7 Electrogenerative Systems

According to Langer [1] “electrogenerative processes are those in which favorable thermodynamics are exploited together with requisite kinetic and mechanistic factors to produce a desired chemical while generating by-product electricity.” This very interesting electrochemically methodology

has not been fully appreciated, although it has considerable practical potential [2].

The most fundamental requirement for the establishment of an electrogenerative system is that the cell reaction be exothermic ($\Delta G^\circ \ll 0$). The thermodynamic cell efficiency defined as $\Delta G^\circ/\Delta H^\circ$ increases as the entropy term $T\Delta S^\circ$ decreases, since $\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$.

The generated cell voltage, E_g , theoretically would be given as

$$E_g = E_{\text{cell}} - IR$$

where I and R denote current and resistance and E° is the standard thermodynamic potential. The theoretical voltage output of an electrogenerative cell can be estimated from the thermodynamic relation of the energy ΔG° of the cell reaction with the cell potential E°

$$\Delta G^\circ = -nFE^\circ$$

For example, in the air/ethanol electrogenerative cell in which ethanol is oxidized to acetaldehyde the thermodynamic parameters are [1]:

$$\Delta H^\circ = -52 \text{ kcal/mol}$$

$$\Delta G^\circ = -48 \text{ kcal/mol}$$

$$E^\circ = 1.05 \text{ V}$$

The measured cell potential exhibited by this cell was found to be 0.64 V. Sometimes values of experimental cell potentials happen to be quite close to theoretical values even when the processes are irreversible. The electrogenerative hydrogenations of benzene and ethylene are two such examples [1]:



A simple, typical schematic construction of an electrogenerative cell is given below with an olefin, S, and Cl_2 as reactants, Figure 5.2.

Electrogenerative cells are fitted with porous catalytic electrodes in order to minimize voltage losses caused by increasing overpotentials at higher current densities (overpotentials increase with current density). Catalytic electrodes can be made by bonding metal powders (e.g. platinum black) with teflon or polyethylene [3]. Recently, Stafford [4] reported the electrogenerative oxidation of propylene on a pilot-plant scale in a cell with a gas-diffusion palladium electrode. The major products were acrolein, acrylic acid and CO_2 . Langer [5] et al. developed an electrogenerative process whereby selective oxidation of alcohols to esters or carboxylic acids takes place. The electrocatalysts were transition metal surfaces modified by treatment with SO_2 . Chemisorbed sulfur species covered the

Electrodes for electrogenerative cells

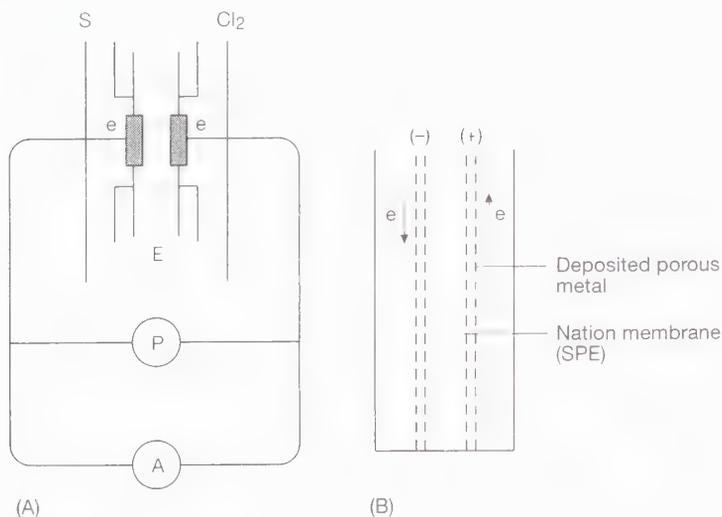
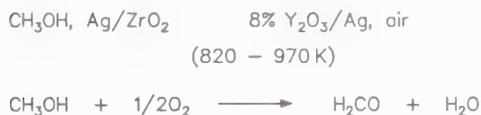


Fig. 5.2A,B. Schematic representation of electrogenerative cells. (A) Type A. e, electrodes E, electrolyte flowing between electrodes. P and A, potentiometer and ammeter. B Type B. SPE-type electrogenerative cell

electrocatalyst particle. Ethanol was thus oxidized to ethyl acetate with 43% conversion and 3.4 A/cm² byproduct electricity.

Zirconia electrochemical reactor

Michaels and Vayenas [6] developed an electrogenerative process for the oxidative dehydrogenation of ethylbenzene to produce styrene, using a zirconia electrochemical reactor. The process was proposed as an alternative to the endothermic dehydrogenation of ethylbenzene (580°C) and its equilibrium limited conversion (55–60%). The electrogenerative process allows quantitative conversion in a single pass with cogeneration of electricity. Also, using this type of zirconia solid electrolyte reactor, methanol was converted to formaldehyde with 85–92% selectivity [7]. The electrogenerative cell was described as follows:



Pietsch and Langer studied the electrogenerative preparation of halo-hydrins and halogenated alkenes and indicated the possible integration of an ethylene-chlorine cell with a chlor-alkali facility [8]. The overall electrogenerative reaction was given as follows:



Recently Otsuka and coworkers [9] reported an electrogenerative system for the selective synthesis of acetaldehyde. The cell is described as:



In this fuel-type cell C_2H_4 is oxidized to acetaldehyde with greater than 97% selectivity. The pertinent electrode reactions are:



This system avoids the use of corrosive aqueous solutions (PdCl_2 , CuCl_2 , HCl) needed in the chemical method, and facilitates greatly the separation of reactants and products.

Electrogenerative systems using biomass-derived materials are studied for the purpose of exploiting biomass wastes and perhaps producing useful products and coproduct electricity [10]. Oxidation of carbohydrates and alcohols of biomass origin take place spontaneously in aqueous NaOH solution at metal oxide electrodes (Ni , Ag). The electrogenerative cell is acidobasic. The anolyte is alkaline and the catholyte is aqueous sulfuric or hydrochloric acid in which a platinum or graphite is used as cathode. The catholyte contains oxidizing ions such as Fe^{3+} , NO_3^+ , Ce^{4+} , etc. With glucose as the biomass material in the basic anolyte compartment cell voltages as high as 1.3 V and currents of about 50 mA/cm^2 are attained at 40°C . Gluconates and saccharates appear to be among the oxidation products. In the absence of oxidizing ions in the catholyte hydrogen is copiously evolved at the platinum cathode at $40\text{--}60^\circ\text{C}$. The electrogenerative cell is shown schematically in Figure 5.3

Electrogenerative systems using biomass-derived materials

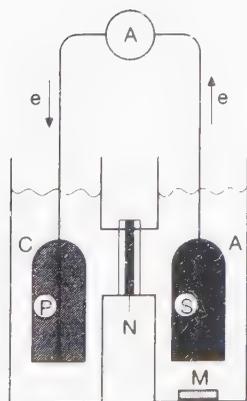


Fig. 5.3. Acidobasic electrogenerative cell utilizing biomass. *P*, Platinum cathode *S*, Silver anode, *N* Nafion cation exchange membrane *A*, anolyte $\text{NaOH}/\text{H}_2\text{O}/\text{glucose}$ *C*, catholyte $\text{HCl}/\text{H}_2\text{O}$, for molecular hydrogen evolution

In this type of cell (silver electrode) propargyl alcohol is spontaneously oxidized to propiolic acid (50% yield) with byproduct electricity.

5.8 Electrogenerated Bases

Proton transfer reagents

Certain organic compounds may be converted electrochemically into strong bases in suitable organic solutions. These electrogenerated bases, EGB, can be used in situ as proton transfer reagents analogous to electron transfer mediators in indirect electrochemical reactions [1]. An EGB abstracts protons from carbon acids and thus may initiate a sequence of reactions. If an EGB is regenerated in situ it can act electrocatalytically. Substances capable of affording EGBs are called probases, PB. Radical anions and anions may act as EGBs and also as nucleophiles and as reducing agents depending on their structure. Steric hindrance at the basic center makes an EGB more effective as a base than as a nucleophile. In the presence of suitable electrophiles chemical reactions occur, as in the case with CO_2 whereby carboxylations are effected according to an overall scheme,

Probases

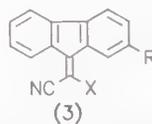
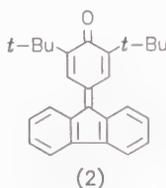
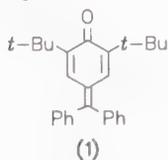


Upon reduction of a PB the produced EGB may be in the form of an anion radical, an anion, or a dianion. Phenols, amides, and carboxylic acids afford EGBs by one-electron reduction:



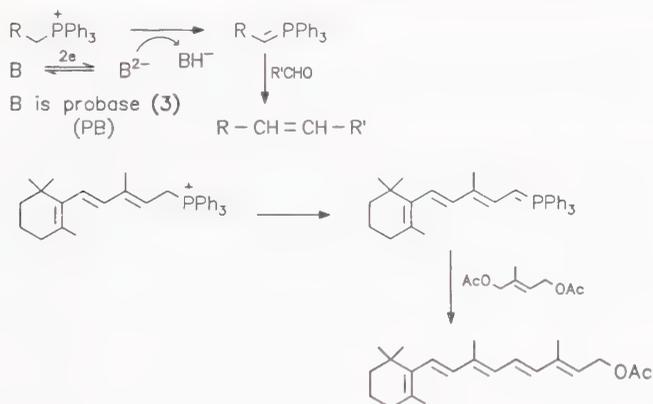
Efficient probases

Some typical efficient probases are pyrrolidones, *N*-methylacetamide, L-tryptophan, methionine, azobenzenes, Ph_3CH and CCl_4 (giving CCl_3^-) and oxygen giving the superoxide ion. Utley et al. recently prepared organic bases from the PBs quinomethides (1) (2) and derivatives of fluoren-9-ylidenemethane (3) and demonstrated their use in Wittig-type reactions [2,3].



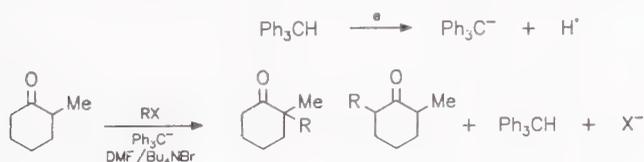
Cyclic voltammetry at a mercury electrode indicates that these substances are reversibly reduced in DMF solutions at the low potentials of -0.1 to -0.2 and -0.7 to -0.9 (vs Ag/AgI) giving anion radicals and dianions which are able to abstract protons from phosphonium salts added in the electrolysis medium. These salts are reduced at -1.4 to -1.45 V. Preparative electrolyses (Wittig-reaction route) were carried out in divided cells with a mercury pool cathode in DMF solvent containing the PB, the phosphonium salt and the carbonyl compound. Suitable electrolytes are Bu_4NBF_4 , LiClO_4 or MgClO_4 . The preparation of vitamin A acetate [3], Scheme 5.9, was effected (30–40% yields with LiClO_4 as electrolyte; no yield was possible with $\text{Bu}_4\text{N}^+\text{BF}_4$ in this case).

Wittig reaction route

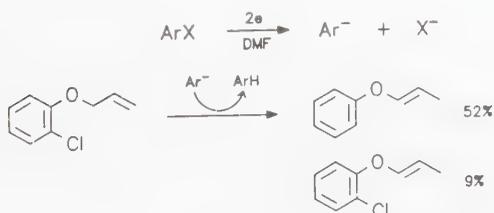


Scheme 5.9

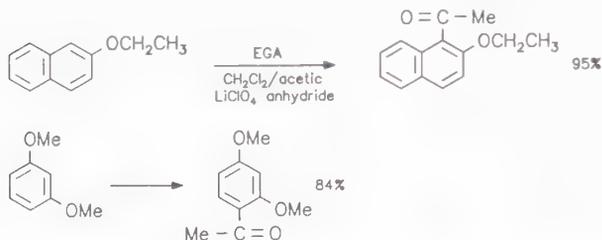
Regioselective alkylation of the cyclic ketone shown below was effected [4] by electrolysis in the presence of the PB, Ph_3CH :



An interesting isomerization was reported by Kimura et al. involving an aromatic enol ether and an EGB as shown below [5]:



An efficient acylation reaction most probably promoted by an electro-generated acid (EGA) catalyst was recently reported by Gatti [6]. Electro-generated acids, like EGBs, may act as catalysts [7], in reactions involving electron-rich substrates as in the following examples [6]:

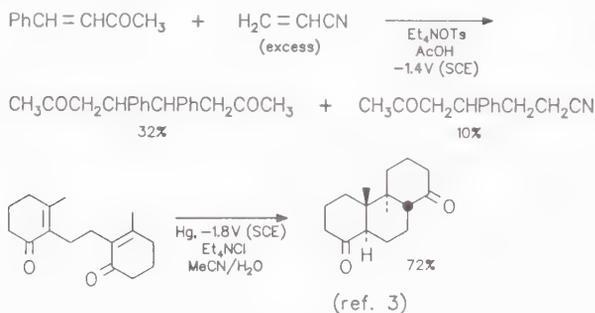


5.9 Electroreduction of Enones (α,β -Unsaturated Ketones)

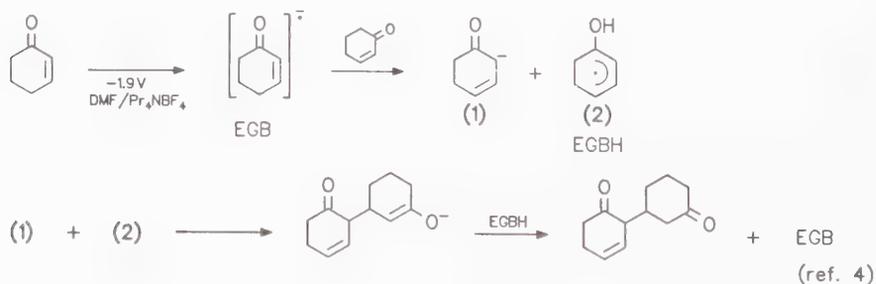
The enone is a very useful functional group in organic synthesis, in general. Its electrochemistry has been widely studied and was reviewed by Little and Baizer [1]. Only a few typical reactions will be included here.

Hyrodimeri- zations

Reductive hydrodimerizations of enones take place at mercury electrodes in aqueous and in organic solutions. Intermolecular and intramolecular hydrodimerizations are possible [2,3]:

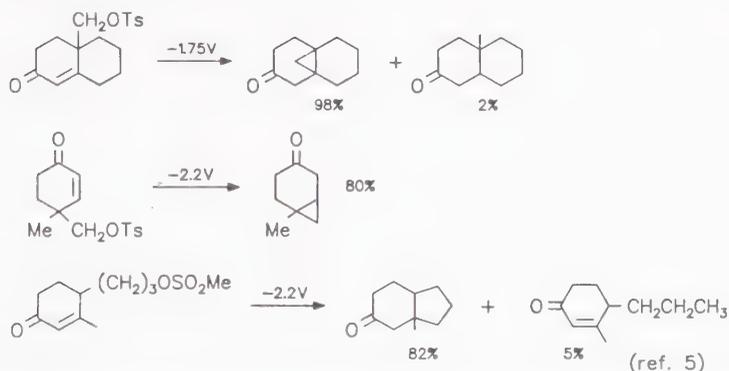


The anion radical of an enone can act as an EGB as in the following example [4]:



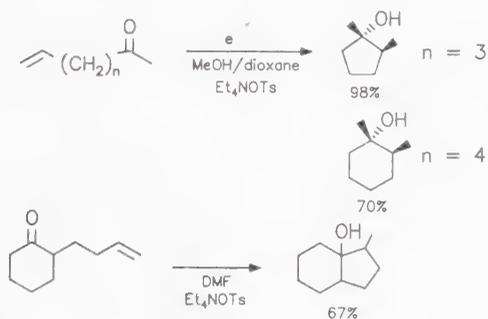
Pinacolizations and saturation of C=C bonds are also possible reductive reactions of enones. Electroreductive cyclizations of certain enone esters occur readily in dry DMF/ Bu_4NBF_4 in divided cells with mercury cathodes [5]. With tosylate as a leaving group the following cyclization occurs:

Pinacolizations and saturation of C=C bonds Cyclizations



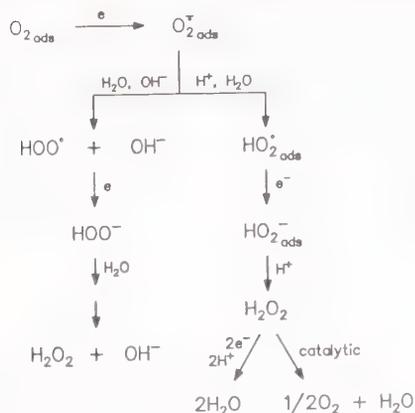
Electroreduction of nonconjugated enones makes possible the construction of five- and six-membered rings [6].

Ring construction



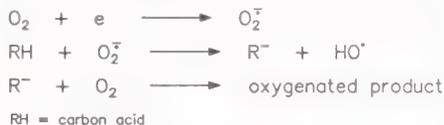
5.10 Oxygenations. The Superoxide Ion

Molecular oxygen is easily electroreduced in both aqueous and organic media. In aqueous acidic media oxygen is reduced to H_2O and in basic media to OH^- ion. The oxygen molecule is assumed to accept an electron from the cathode to become a superoxide ion usually written as O_2^- . In aqueous media this ion is rapidly decomposed as indicated below:

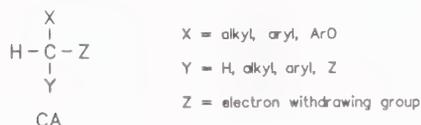


Various functions of the superoxide ion

In dry organic solvents molecular oxygen is reduced at the cathode at -0.8 V vs SCE to give the $\text{O}_2^{\cdot -}$ ion. In these media the superoxide ion is fairly soluble and quite stable and can function in several useful ways for synthetic purposes [1–5]: as an electron transfer agent, a radical, a nucleophile and an efficient electrogenerated base (EGB). As an EGB superoxide ion is able to abstract protons from carbon acids of low pKa. As a result sequential reactions are possible as indicated below in the presence of both $\text{O}_2^{\cdot -}$ and O_2 :



Carbon acids suitable for such reactions are represented by the general formula, CA, below [5]:

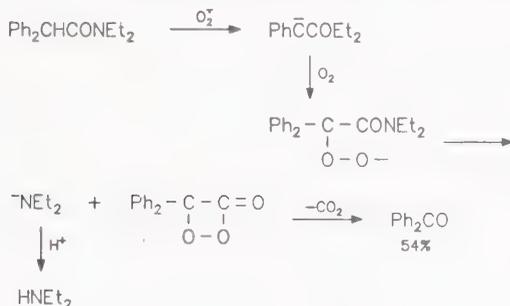


Oxygenation of *N,N*-diethylamide

Thus electrolysis in the presence of both $\text{O}_2^{\cdot -}$ and O_2 brings about the oxygenation of esters, nitriles, *N,N*-dialkylamides, sulfones and nitro compounds. The esters $\text{MeCH}_2\text{COOEt}$, in $\text{Ph}_2\text{CHCOOMe}$ for example were transformed to the corresponding hydroxy analogs MeCH(OH)COOEt (15%) $\text{Ph}_2\text{C(OH)COOMe}$ (40%). Similarly oxidative decyanations of nitriles such as Ph_2CHCN and $\text{Ph}_2\text{CH}(\text{CH}_3)\text{CN}$ gave the ketonic products Ph_2CO (95%) and PhCOCH_3 (72%). Typically, such electrolytic oxygenations are performed in divided, H-type cells, with mercury pool cathodes (-1.0 V vs SCE) and platinum anodes in dry DMF/ Bu_4NBr media containing 5–10 mmol of substrate per 100 ml solvent. A stream of dry oxygen is passed through the catholyte so that both $\text{O}_2^{\cdot -}$ and

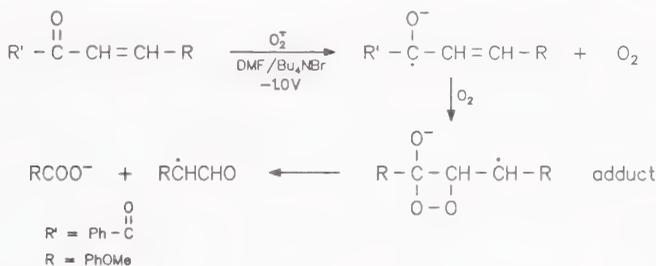
O₂ are present for the oxygenation reaction. The products are isolated by distilling off the solvent in vacuo, repeated extractions with ether and washing with minimum amounts of water [5]. The following possible reaction sequence was suggested for the oxygenation of *N,N*-diethylamide:

Ph₂CH(CH₃)-CN



Cleavages via in situ generated superoxide ion occur as exemplified in the oxygenation of chalcones in the presence of oxygen [6], Scheme 5.10:

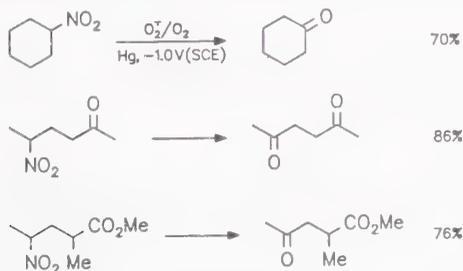
Oxygenation of chalcones



Scheme 5.10

Nitroalkanes are converted to ketones by electrolysis in an H-type cell in MeCN under a stream of oxygen [6a]:

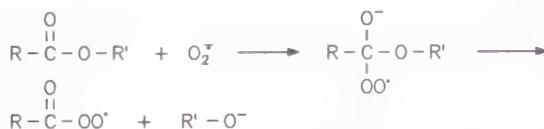
Ketone conversion



In these reactions electrogenerated superoxide ion abstracts a proton from the nitroalkane to give the nitronate ion which is then oxidized by molecular oxygen to give the ketone. The superoxide ion reacts with organohalides by an S_N2 process [6b]:

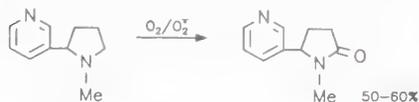


Also with esters,

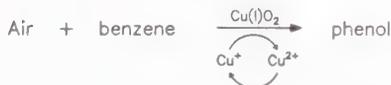


(**Note:** Some organic carbanions or dicarbanions may absorb oxygen. Reactions carried out in the presence of oxygen may yield oxygenated side products.)

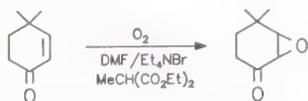
Tosylhydrazones are fragmented by superoxide ion to give alkenes. Secondary alcohols react with superoxide to give ketones [7]. Nicotine is converted to cotinine [8],



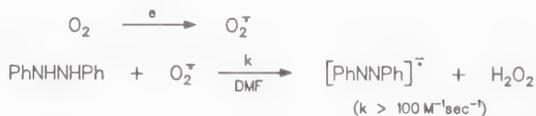
Diphenylmethane, cyclohexane and *ortho*- and *para*-cresols give benzophenone, cyclohexanone and benzylic acids, respectively, in 55–68% yields [9]. Catalytically induced oxygenations are effected in the presence of cuprous ions and air (oxygen) with benzene as substrate, apparently via the Cu(I)O_2 adduct [9a]:



Epoxidation of enones In situ epoxidation of enones in the presence of oxygen and a carbon acid gave high yields of products [10]:

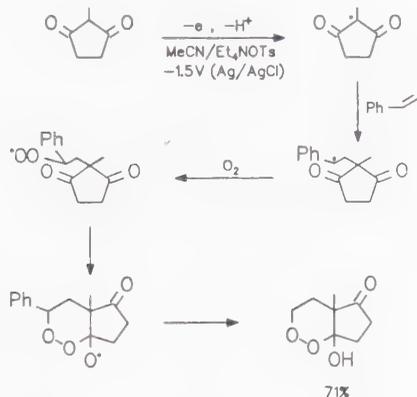


Dehydrogenation of dihydrophenazine Rapid dehydrogenation of dihydrophenazine occurs by a concerted transfer of an N-H proton and a N-H hydrogen atom [11]:



An interesting oxygenation process was reported by Yoshida et al. [12], in which oxygen, olefins and 1,3-diketones react to give [2+2+2] cycloaddition products by anodic electroinitiation. The organic substrate is deelectronated and the resulting radicals react with molecular oxygen by a radical chain mechanism as is depicted below with cyclopentadione and styrene as substrates:

Cycloaddition products by anodic electroinitiation

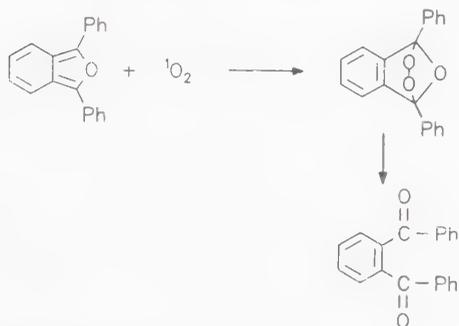


Bard and Mayeda [13] obtained singlet oxygen by electrolytic oxidation of ferrocene and reduction of oxygen and the subsequent or parallel homogeneous electron transfer reaction,

Singlet oxygen



Singlet Oxygen enters in chemical reactions such as,



References

Section 5.1 Electrolysis in Two-phase Systems

1. Feess H, Wendt H (1980) *J Chem Techn Biotechn* 30:297
2. Pletcher D, Camlen PH, Healy KP (1982) *J Appl Electrochem* 12:693
3. Ebersson L, Helg e B (1978) *Acta Chem Scand* B32:313
4. Georges J, Desmettre S (1986) *Electrochim Acta* 31:1519

5. Do JS, Chou T-C (1989) *J Appl Electrochem* 19:922
6. McIntire GL, Blount NH (1979) *J Am Chem Soc* 101:7720
7. McIntire GL (1981) *J Electrochem Soc* 128:427
8. Laurent E, Raunier G, Tomalla M (1982) *Nouv J Chim* 6:515
9. Girault HH (1987) *Electrochim Acta* 32:383
10. Forsyth SR, Pletcher D, Healy KP (1987) *J Appl Electrochem* 17:905
11. Fleischmann M, Tennakoun CLK, Baufield HA, William RJ (1983) *J Appl Electrochem* 13:593
12. Vettorazzi N, Fernandez H, Silber JJ, Sereno L (1990) *Electrochim Acta* 35:1081
13. Bhakte RC (1987) *J Macrom Sci-Chem A24*:993
14. Knarr RT, Velasco M, Lynn S, Tobias CW (1992) *J Electrochem Soc* 139:948

Section 5.2 Solid Polymer Electrolyte-Electrolysis

1. Nakgima H et al. (1987) *Electrochimica Acta* 32:791
2. Rubinstein I, Bard AJ (1981) *J Am Chem Soc* 103:5007
3. Srinivasann S, Lu WP (1979) *J Appl Electrochem* 9:269
4. Verbrugge MW, Hills RE (1990) *J Electrochem Soc* 137:893
5. Yeo RS (1979) *J Electrochem Soc* 103:533
6. Ogumi Z et al. (1983) *Electrochim Acta* 28:1687
7. Ogumi Z, Inaba M, Ohashi S, Ushida M, Takehara ZI (1987) *Electrochim Acta* 33:365
8. Ukihashi H et al. (1986) *Synthesis* 513
9. Tada H, Kawahara H (1988) *J Electrochem Soc* 135:1728
10. Kita H, Nagagima H (1986) *Electrochim Acta* 31:193
11. Fabiunke R et al. (1989) *Dechema-monog* 112:299-315
12. Enea O (1988) *J Electrochem Soc* 135:1601
13. Bidan G, Ehui B (1989) *J Chem Soc Chem Commun* 1568

Section 5.3 Reactions via Electrode Dissolution

1. Silvestri G, Gambino S, Filardo C (1991) *Acta Chem Scand* 45:487, review
2. Danley DE (1979) *Kirk-Othmer encyclopedia of chemistry and technology*, vol 8, 3rd edn. Wiley, p 762
3. Silvestri G, Gambino S, Filardo G (1987) *Electrochim Acta* 32:965
4. Gambino S, Silvestri G (1973) *Tetrahedron Lett* 32:3125
5. Folest JC, Guibe S, Nedelec JY, Perichon J (1990) *J Chem Res* 258
6. Lehmkul H, et al. (1975) *Justus Liebigs Ann* 672
7. Urabe N, Hory F, Kenkyu Hokoko (1973) 2381
8. Pierre G, Limosin D (1988) *Makromol Chem* 189:1484
9. Silvestri G, Gambino S, Filardo G (1989) *J Appl Electrochem* 19:946
10. Said FF, Tuck DG (1982) *Inorg Chem Acta* 59 1; Chada RK, Kumar R, Tuck DG (1987) *Can J Chem* 65:1336
11. Sausa A et al. (1990) *J Chem Soc Dalton Trans* 2101
12. Chaussard J, Folest JC, Nedelec JY, Perichon J, Sibille S, Troupel M (1990) *Synthesis* 5 369

Section 5.4 Electropolymerizations. Conductive Polymers

1. Roberts R et al. (1982) *Industrial applications of electroorganic synthesis*. Ann Arbor Science Publishers, Ann Arbor
2. Kanazawa KK, Diaz AF, Street GB (1980) *J Electrochem Soc* 127:83C
3. Rubinstein I (1983) *J Polymer Sci* 21 3035; Yamamoto K et al. (1988) *Polymer Bull* 19:533

4. Soubiran P, Aeiych S, Aaron JJ, Delamar M, Lacaze PC (1988) *J Electrochem Soc* 251:89
5. Leclerc M, Gway J, DaoLe H (1988) *J Electroanal Chem* 251:21
- 5a. Pelter A, Maud JM, Jenkins I, Sadeka C, Coles G (1989) *Tetrahedron Lett* 30:3461
6. Zecchin S, Tomat R, Sciavon G, Cotti G (1988) *Synth Metals* 25:393
7. Yamamoto K, Asada T, Nishide H, Tsuchida E (1990) *Bull Chem Soc (Japan)* 63:1216
8. Tashiro K, Matsumura K, Kobayashi M (1990) *J Phys Chem* 94 3197
9. Little WA (1964) *Phys Rev A*134:1416
10. Chiang CK et al. (1978) *J Chem Phys* 69:5098
11. Seymour RB (ed) (1981) *Conductive polymers*, Plenum, New York; (1987) *Polymer* 28:533
12. Metzger RM et al. (1987) *Synthetic Metals* 18:797
13. Reynolds JR (1988) *Chemtech* (July) 440
14. Makaruk L, Pron A (1990) *Intern Polym Sci Techn* 17 T81
15. Genies EM, Tsintavis C (1988) *J Electroanal Chem* 200 127
16. Frommer JF, Chance RR (1990) In: Grayson M, Kroschwitz J (eds) *Encyclopedia of polymer science and engineering*, vol 5, 2nd edn. Wiley, New York, p 461
17. Ferraris JP, Skiles GD (1987) *Polymer* 28:582
18. Marcos ML et al. (1987) *Electrochim Acta* 32:1453
19. Andrieux CP et al. (1990) *J Am Chem Soc* 112:2439
20. Kyriacou D, unpublished work
21. Deronjier A, Moutet J-C (1989) *Acc Chem Res* 22:249
22. Ponkali J (1992) *Chem Rev* 92:711-738
23. Diaz AF, Kanazawa KK, Gardini GP (1979) *J Chem Soc Chem Commun* 635
24. Gottsfield S, Redondo A (1987) *J Electrochem Soc* 134:271
25. Kawan K, Mihara N, Kawabata S, Yoneyama H (1990) *J Electrochem Soc* 137:1793
26. Poncali J, Yassar A, Garnier F (1988) *J Chem Soc Chem Commun* 581
27. Hayat V et al. (1986) *Polymer Commun* 27:362
28. Sato M, Shimitzu T, Yamauchi A (1990) *Makromol Chem* 191:313
29. McCarley RL, Morita M, Wilbourn KO, Murray RW (1988) *J Electroanal Chem* 245:321
30. Marks J (1985) *Science* 227:881

Section 5.5 and 5.6 Applications of Electrochemical Methodology to the Synthesis of Natural Products

1. Nelson RF (1975) In: Weinberg NL (ed) *Techniques of electroorganic synthesis*. Wiley-Interscience, New York, p 269
2. Scheafer HJ (1978) *Electrosynthesis of natural products*. IUPAC Int Symposium, British Library London
3. Weedon BCL (1963) *Adv Org Chem* 1:1
4. Little RD, Fox DP, Moens L, Wolin R, Baizer MM (1987) In: Torii S (ed) *Recent advances in electroorganic synthesis*. Kadansha, Tokyo, Japan
5. Corey EJ, Sauers RR (1959) *J Am Chem Soc* 81:1739
6. Storc G, Meisels A, Davis JE (1963) *J Am Chem Soc* 85:3419
7. Gribble JW, Sanstead JK (1973) *J Chem Soc Chem Commun* 735; Seidel W, Schäfer HJ, ref. 2
8. Klünenburg H, Schäfer HJ (1978) *Angew Chem, Int Ed Eng* 17:47
9. Singh KN, Singh M, Misra RA (1991) *Ind J Chem* 30B:867
- 9a. Bobbitt JM, Yagi H, Shibuay S, Stork JT (1971) *J Org Chem* 36:3006
10. Little RD, Fox DP, van Hijfte L, Denneker R, Sowell G, Wolin RL, Moens L, Baizer MM (1988) *J Org Chem* 53:2287

11. Fox DP, Little RD, Baizer MM (1985) *J Org Chem* 50:2202; Nujent ST, Baizer MM, Little RD (1982) *Tetrahedron Lett* 23:1339; Amptch MA, Little RD, private communication; Bode HE, Sowell CG, Little RD (1990) *Tetrahedron Lett* 31:2225
12. Moens L, Baizer MM, Little RD (1986) *J Org Chem* 51:4497
13. Sowell CG, Wolin RL, Little RD (1990) *Tetrahedron Lett* 31:485

Section 5.7 Electrogenenerative Systems

- 1a. Langer SH, Card JC, Forel MJ (1986) *Pure Appl Chem* 58:895
- 1b. Sakellaropoulos GP, Langer SH (1976) *J Catalysis* 44:25; Langer SH (1975) *J Electrochem Soc* 122:242
2. Langer SH, Sakellaropoulos GP (1979) *Ind Eng Chem Res Dev* 18:507
3. Langer SH, Collec-Rios JA (1985) *Chemtech* April, p 226; also ref. 1b
4. Stafford GP (1987) *Electrochim Acta* 32:1137
5. Langer SH, Foral MG, Card JC (1988) U.S. Patent, 4793905
6. Michael J, Vayenas C (1984) International Society of Electrochemistry Meeting, extended abstracts, Berkeley, California, p 763
7. Neophytides S, Vayenas CG (1990) *J Electrochem Soc* 137:839
8. Pietsch SJ, Langer SH (1979) *AIChE Symposium Series*, 1857551
9. Otsuka K, Shimitzu Y, Yamanaka I (1990) *J Electrochem Soc* 137:2076
10. Kyriacou D (unpublished work)

Section 5.8 Electrogenerated Bases

1. Baizer MM (1984) *Tetrahedron*, 40:935; Hallcher RD, White DA, Baizer MM (1979) *J Electrochem Soc* 126:404; Saveant JM, Bin SK (1977) *J Org Chem* 42:1249; Komori T, et al. (1987) *Bull Chem Soc, Japan* 60:3365
2. Goulard MDF, Ling-Chung SK, Utley JHP (1987) *Tetrahedron Lett* 6083
3. Mheta RR, Pardini VL, Utley JHP (1982) *J Chem Soc Perkin Trans* 1:2921
4. Fuchigani T, Suzuki K, Nonaka T (1990) *Electrochim Acta* 35:239
5. Kimura M, Mihahara H, Moritani H, Sawaki Y (1990) *J Org Chem* 55:3897
6. Gatti N (1990) *Tetrahedron Lett* 31:3933
7. Uneama K (1987) *Topics in Curr Chem* 142:167

Section 5.9 Electroreduction of Enones (α,β -unsaturated ketones)

1. Little RD, Baizer MM (1989) In: Patai S (ed) *The chemistry of enones*, Wiley, New York, chap. 14
2. Baizer MM, Andersen JD (1965) *J Org Chem* 30:3138
3. Mandell L, Daley RF, Day J (1976) *J Org Chem* 41:4087
4. Baizer MM (1984) *Tetrahedron* 40:1935
5. Gassman PG, Rasmy OM, Burdock TO, Saito K (1981) *J Org Chem* 40:5455
6. Shono T, Nishiguchi I, Ohmitzu H, Mitani M (1978) *J Am Chem Soc* 100:545

Section 5.10 Oxygenations, Superoxide Ion

1. Allen PM, Hess U, Foote GS, Baizer MM (1982) *Synthet Commun* 12:1236
2. Lee-Ruff E (1979) *Chem Soc Rev* 12:105
3. Wilkshire J, Sawyer DT (1979) *Acc Chem Res* 12:105
4. Nanni EJ, Sawyer DT (1980) *J Am Chem Soc* 102, 7591
5. Little RD et al. (1983) *Acta Chem Scand* B37:509
6. Singh M, Singh KN, Mistra RA (1991) *Bull Chem Soc Japan* 64:2599
- 6a. Monte WT, Baizer MM, Little RD (1983) *J Org Chem* 48:803
- 6b. Bere AL, Berger Y (1966) *Bull Soc Chim* 2263

7. Singh M, Mishra RA (1989) *Synthesis* 5:403
8. (1983) *Chem Abst* 99, p 657 (710556)
9. Zutshi K, Rastogi R, Dixit G (1984) International Society of Electrochemistry, extended abstracts Berkeley, California, p 760
- 9a. Kinoshita T, Horada J, Ito S, Sasaki K (1983) *Angew Chem* 22:502
10. Mitchio S, Baizer MM (1983) *J Org Chem* 48:9931
11. Ruez OA, Vuldez CM, Fector J, Sawyer DT (1988) *J Org Chem* 53:2166
12. Yoshida J, Sakaguchi K, Ise S, Hirotsu K (1987) *Tetrahedron Lett* 28:667
13. Bard AJ, Mayeda EA (1973) *J Am Chem Soc* 95:6223

Subject Index

- Active Electrode Area 13
- adipic acid 49
- adiponitrile 111
- adsorption at electrode surfaces 15, 16, 26
- acetals 29, 50, 95
- acetamidations 86
- acetamido compounds 44, 50, 51
- acenaphthene 97
- acetoxylation
 - mechanism 83
 - intramolecular 95
 - of alkyl aromatics 85
 - of piperidines 84, 85
 - trifluoroacetoxylation 86
- acetone 114
- acetophenones 112, 113
- acetylenes 151, 183, 201
- acidobasic cell 211
- acylation 136, 155, 214
- acylprolines, acylpipercolic acids 67
- acylated quinone imine ketals 58, 59
- acrylic acid 115, 209
- acrolein 209
- alcohols
 - oxidation products 28, 29
 - at oxide covered electrodes 30, 31, 32
 - at adatom electrodes 36
 - aliphatic acids 120
- alkaloids 73, 205
- alkanes, oxidation 20, 21
- alkanoates 49
 - coupling 49
- alkenes
 - cyclopropanations 125
- alkoxylation 92, 93
- alkyl halides, iodides 63
- amides 57, 58
- amines, oxidation 32, 33, 55–57
- amino acids 182
- amidines 64
- aminopyrimidines 69
- aminotriazines 69
- aminopyrazolines 70
- aminophthalimides 73, 131, 132
- aniline 134
- anion radicals 110, 111, 150, 214
- anodic reaction
 - fundamental nature 18
 - direct, indirect 4
 - intramolecular cyclizations 24, 25
- anthracene 100, 172, 187
- aspartic acid 182
- azobenzene, redox catalyst 188
- Baizer process 111
- basicity 26
- benzene 128, 173
- benzophenone 155
- benzoquinone 173, 181
- benzyl alcohol 120, 192
- benzyl benzoate 175
- benzylic esters 149
- benzyne 128
- biomass, anodic degradation 41
- bismesityl 23
- Birch reductions 110
- butadiene 90
- Butler-Volmer rate equation 10
- camphor 45
- carbenes
 - dichloro compounds 123
 - cyclopropanations with 124, 125
 - couplings 126
- carbon acids 26
- carbon disulfide 75
- carbon-silicon bonds 158
- carbonyls, couplings 113
- carboxylic acids
 - Kolbe synthesis 47–49, 53
 - mixed couplings 49
- cathodic reactions 2, 3, 5
 - couplings 6, 115
- cation radicals 26, 55, 57, 60
- catechol 38
- cell potential 9
 - and free energy 9
- cells with consumable anodes 125

- cinnolines 134
citronellol 99, 178
composite electrodes 134
consumable anodes 120
coumestan compounds 37, 38
couplings, in general 5
cresols 39
current
 types of 2, 8
 exchange 8, 9, 11
 limiting 13
 efficiency 14
cyanation
 mechanism 79
 typical reactions 27,80–82
cyanide ion 79
cyanoporphyrins 67
cyclohexane, oxidation 21
cyclopropanes 94

deelectronations 18
decarboxylations 50
dehalogenations 127
 couplings 128
 of dimethyl maleate with alkyl dihalides 126
dehydrodimerizations of hydrocarbons 19
deoxygenations 149
N,N-dialkylamides 58
dibenzyl ether 64
diglyme as solvent 186
diffusion coefficient 133
dihydrobenzoin 117
dihydroxycoumestan 38
dihydropyrimidines 73
diketones 49
dimethylformamide 58, 96
dimethylphenol 39
dimethylpyrrolidinium ion 188
diphenoquinone mediator 41
dissolvable anode methodology 196
 organometallics
doping of electronically conductive polymers 201
double layer, electrical 14, 212
double mediator systems 171
1,3-dithiane 76
dithiolanes 77
durene 23

electroactivity 6
Electrodes
 (anode, cathode, working, counter) 2
electrode potential 8, 9
 physical meaning of 9

Electrolysis
 basic apparatus 2
 solvents 3
 in two-phase solvent systems 192
 conditions 3, 12, 13
 basic physical-chemical processes 3
electrocarboxylations 151
electrocatalysis 31, 113, 114, 132, 133, 170, 188, 195
electron transfers
 possible reaction barriers 6, 7
 inner, outer, spheres 168
electrohydrogenation 114
electrophydrolysis 122, 128, 129
electrogenerative systems
 Langer's definition 208
 cell construction, schematic 210, 211
 using biomass 211
electrogenerated bases (EGB) 212
electroorganic reaction, generalized 4
electropolymerizations 198
electrophiles 25, 151
electrophore 113, 114
electroreduction, direct, C–H bond formations 111
equilibrium potential 8
ethylcyanide 33
ethers, aromatic, alkoxy 60, 61
 bis-enol 62
 mixed 100
esters 63, 121, 175
enamino ketones, preparation 140

Faraday's Laws 14
Fenton's reagent 174
flavonoids 179
five-member ring, polymerizations 202
Friedel-Crafts catalyst, with aluminum anodes 196
films, electrochromic 199
fluorine 158
fluorosulfuric acid, carboxylic acid oxidations in 52

gas diffusion electrodes 151
glucose, oxidation 28, 176
glycerol, oxidation 31
graft-copolymerization 174
graphite intercalation compounds as amalgams 185
Grignard pair 110

half-cell, anodic, cathodic reactions 3
halide ions, mediators 174
halides, general cathodic reduction mechanism 122
halodiphenylphosphines 156
halofunctionalizations 88
heteroaromatics 68
heteroazolium salts 142

- heterocyclics 65, 68, 145
heterocyclizations 195
hydrocarbons
 highly strained 124
 main anodic oxidations 10
 in FSO₃H 19, 20
 in SO₂ 22
 in organic solvents 22, 23
hydrazine derivatives 46
hydrogenations, catalytic 112, 113
hydrodimers, formations 112, 116, 117
hydrogen peroxide 193
hydroxy groups
 direct anodic oxidation 28, 29
 in aprotic media 29
 at oxide covered electrodes 30, 31, 33
 oxidation mechanism at NiOOH electrodes 30, 31
hydroquinones 100
hydroxy radicals, adsorbed 36
p-hydroxybenzaldehyde 117
hydroxycoumarin 38
hydroxylation of styrenes 91
α-hydroxylimine 118
5-hydroxytryptamine (5H-T) 72
hypervalent iodanyl radicals 64

indirect processes 172
 electron transfer mechanisms 168
 paired 172
 epoxidations 175
indandiones 116
indigo 154
indoles 80
immobilized oxidant 177
intramolecular cyclizations 24, 25, 114
iodides, mediators 176
iodinations 90
iodobenzene, oxidation 65
iodonium ion 63, 90
isopropyl alcohol 170

Kolbe synthesis, in SPE cells 47
 decarboxylative possible routes 48
 aldehydes from 50
 Kolbe radicals 49

Ketones
 reduction 112, 113
 cyanoketones, cyclizations 108
 splitting of C-H bonds 118, 158
 α-cleavages 43
 α,α'-dihaloketones, cyclization 124

lactones 45, 115
lawronitrile 155

leucoindigo 154
lithiated ketals 95
Little-Baizer ERC reaction 206
lignin-organosol, anodic oxidation 42
living polymer 194
locations of reacting species in double layer 16
Lontrel 129

magnesium anode 124
maleic acid 182
mesitylene 23
mesylates 148
metal complexes, novel 121, 159, 184
metallic ions, mediators 182
metal/SPE interfaces, electrocatalysts 151
metal carboxylates and alkoxides 120
methane from CO₂ 151
methoxylations
 N-methylamides 58
 methylacrylate 52
 methylcyclohexanones 45
 1-methylpyrrole 81
 methoxylation vs cyanation 82
methylene groups, chlorination 89
monosaccharides, direct oxidation 43
Mn³⁺/Mn⁺ couple, mediator 172

natural product synthesis 203
 Kolbe oxidative steps in 204, 205
 pheromones 204
 1-sterpurene 208
 quadrone 208
 corypalline 205
Nerst's equation 7
nitrate ion, mediator 178
nitration of aromatics 178
nitrite anion 137
nitroalkanes 217
nitroanions 138
nitriles 55, 56, 154, 175
nitronium ion 101
nitrosophenol 182
m-nitrotoluene 182
nucleophiles 25
nucleophilicity 26

octaethylporphyrins 62
n-octanol 195
n-octane, oxidations in MeCN/NO₃ 22
olefins activated, reduction 111
 from dinitro's 137
organic metals 201
organohalides, iodides 63
organoelemental bonds 197

- organic cation radicals 178
oxadiazolines 46, 47
oxalate esters 149
oxidations, paired 173
oxide covered electrodes 30, 31, 54, 55
 for carboxylic acids 32, 33
 oxidation of amines, aromatics and steroids 32, 33
oxolanes 49
1,3-oxazolidines 95
oximes 154
oxygen
 reduction 215, 216
 superoxide ion 216
 electrolysis in oxygen-superoxide solutions 217,
 218
 singlet oxygen 219
oxyselenylation 177

palladium-carbon catalyst 85
paired processes 172
periodate-iodate catalyst 177
perfluorocyclopentene-butene polymers 133
phase transfer catalysts 192
phenols 36, 38, 148
 anodic couplings 39, 41
 hydroxylation 91
phenothiazene 68
phenoxonium ion 39
phenylazolidine-3-ones 71
phenylvinylsulfone 147
phosphines 157
 complexes 185
phosphorus compounds 166
photosynthesis 153, 154
potassium iodide catalyst 176
polymer cells 151, 209
polymer films on electrodes 181
 electronic conductors 201, 203
polymerizations 199, 200
polypyrrole 202
pyrazines 139
pyrazoles 70
pyridinations 100
pyrimidines 137
pyrrolidines 72

quinoline 138
quinomethides 212
quinones 38, 42
quinone imineketals 54, 58
 monoketals 65

Raney nickel electrodes 133

redox mediators 167, 171
reversible electrodic reactions 8, 11, 13
Ritter-type electrochemical reactions 86
rose-oxide 100
ruthenates 170
ruthenium electrode 151
rhodium complexes 188

saccharin 171
sacrificial anodes 124, 126
sebacic acid 49
selenium electrode 132
selenophene 202
silanes 197
silylating agents 197
silver cathode 202
solar cells 159
solid polymer electrolyte (SPE) 194, 195
steroids 32, 117
Steckhan's organic mediators 179
styrene polymer 193
sulfide salts 74
sulfenyl, sulfonyl compounds 147
sulfones 147
sulfoxides 147
sulfonium salts 77, 78
sulfur, elemental 145
Swenton's EEC_{r,C_p} mechanism 59, 60

underpotential deposition (UPD) 36
Urethanes 58, 95
unsaturated carboxylic acids 120
unsaturated ketones (enones) 214, 215

vicinal nitro compounds 137
vitamin B₁₂ 183, 188
4-vinylpyridine 200
vitamin A acetate 213
voltage distribution in cells 9
voltammetric curves 13
 reaction reversibility 181
 alkane oxidation 21
 propargyl alcohol 34

Wittig-type reactions with EBG 213

Yoshida beads-oxidants 177

zinc electrode 126
zinc chloride 90
 octaethylporphyrins 67
 oxalate 151
p-zylene 82, 85

Springer-Verlag and the Environment

We at Springer-Verlag firmly believe that an international science publisher has a special obligation to the environment, and our corporate policies consistently reflect this conviction.

We also expect our business partners – paper mills, printers, packaging manufacturers, etc. – to commit themselves to using environmentally friendly materials and production processes.

The paper in this book is made from low- or no-chlorine pulp and is acid free, in conformance with international standards for paper permanency.



Modern Electroorganic Chemistry

In preparing this book, the author as a retired chemist, had primarily in mind the widest possible community of industrial researchers and practitioners in the chemical and closely related biochemical, pharmaceutical and agrochemical fields, technologically and economically, and specially as regards the efforts toward a clean manufacturing technology. The book consists of five chapters. The first chapter is a synoptic introduction to organic electrochemistry. The second and third chapters deal separately with anodic and cathodic reactions of synthetic interest. The reactions are conveniently classified on the basis of functional groups in the organic molecules. The fourth and fifth chapters are concerned with indirect electrochemical reactions and some interesting special topics.